



Comparative Effectiveness Review
Number 233

Management of Colonic Diverticulitis



Comparative Effectiveness Review

Number 233

Management of Colonic Diverticulitis

Prepared for:

Agency for Healthcare Research and Quality
U.S. Department of Health and Human Services
5600 Fishers Lane
Rockville, MD 20857
www.ahrq.gov

Contract No. 290-2015-00002-I

Prepared by:

Brown Evidence-based Practice Center
Providence, RI

Investigators:

Ethan M. Balk, M.D., M.P.H.
Gaelen P. Adam, M.L.I.S., M.P.H.
Wangnan Cao, Ph.D.
Kristin Danko, Ph.D.
Monika Reddy Bhuma, B.D.S, M.P.H.
Shivani Mehta, B.A.
Ian J. Saldanha, M.B.B.S., M.P.H., Ph.D.
Michael D. Beland, M.D.
Nishit Shah, M.D.

AHRQ Publication No. 20(21)-EHC025

October 2020

Addendum March 2022

This report is based on research conducted by the Brown Evidence-based Practice Center (EPC) under contract to the Agency for Healthcare Research and Quality (AHRQ), Rockville, MD (Contract No. 290-2015-00002-I). The findings and conclusions in this document are those of the authors, who are responsible for its contents; the findings and conclusions do not necessarily represent the views of AHRQ. Therefore, no statement in this report should be construed as an official position of AHRQ or of the U.S. Department of Health and Human Services.

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

The information in this report is intended to help healthcare decision makers—patients and clinicians, health system leaders, and policymakers, among others—make well-informed decisions and thereby improve the quality of healthcare services. This report is not intended to be a substitute for the application of clinical judgment. Anyone who makes decisions concerning the provision of clinical care should consider this report in the same way as any medical reference and in conjunction with all other pertinent information, i.e., in the context of available resources and circumstances presented by individual patients.

This report is made available to the public under the terms of a licensing agreement between the author and the Agency for Healthcare Research and Quality. This report may be used and reprinted without permission except those copyrighted materials that are clearly noted in the report. Further reproduction of those copyrighted materials is prohibited without the express permission of copyright holders.

AHRQ or U.S. Department of Health and Human Services endorsement of any derivative products that may be developed from this report, such as clinical practice guidelines, other quality enhancement tools, or reimbursement or coverage policies, may not be stated or implied.

AHRQ appreciates appropriate acknowledgment and citation of its work. Suggested language for acknowledgment: This work was based on an evidence report, Management of Colonic Diverticulitis, by the Evidence-based Practice Center Program at the Agency for Healthcare Research and Quality (AHRQ).

Suggested citation: Balk EM, Adam GP, Cao W, Danko K, Bhuma MR, Mehta S, Saldanha IJ, Beland MD, Shah N. Management of Colonic Diverticulitis. Comparative Effectiveness Review No. 233. (Prepared by the Brown Evidence-based Practice Center under Contract No. 290-2015-00002-I.) AHRQ Publication No. 20(21)-EHC025. Rockville, MD: Agency for Healthcare Research and Quality; October 2020. Addendum March 2022. DOI: <https://doi.org/10.23970/AHRQEPCCER233>. Posted final reports are located on the Effective Health Care Program [search page](#).

Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-based Practice Centers (EPCs), sponsors the development of systematic reviews to assist public- and private-sector organizations in their efforts to improve the quality of healthcare in the United States. These reviews provide comprehensive, science-based information on common, costly medical conditions, and new healthcare technologies and strategies.

Systematic reviews are the building blocks underlying evidence-based practice; they focus attention on the strength and limits of evidence from research studies about the effectiveness and safety of a clinical intervention. In the context of developing recommendations for practice, systematic reviews can help clarify whether assertions about the value of the intervention are based on strong evidence from clinical studies. For more information about AHRQ EPC systematic reviews, see <https://effectivehealthcare.ahrq.gov/about/epc/evidence-synthesis>.

AHRQ expects that these systematic reviews will be helpful to health plans, providers, purchasers, government programs, and the healthcare system as a whole. Transparency and stakeholder input are essential to the Effective Health Care Program. Please visit the website (www.effectivehealthcare.ahrq.gov) to see draft research questions and reports or to join an email list to learn about new program products and opportunities for input.

If you have comments on this systematic review, they may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 5600 Fishers Lane, Rockville, MD 20857, or by email to epc@ahrq.hhs.gov.

Gopal Khanna, M.B.A.
Director
Agency for Healthcare Research and Quality

Arlene S. Bierman, M.D., M.S.
Director
Center for Evidence and Practice
Improvement
Agency for Healthcare Research and Quality

Stephanie Chang, M.D., M.P.H.
Director
Evidence-based Practice Center Program
Center for Evidence and Practice
Improvement
Agency for Healthcare Research and Quality

Lionel L. Bañez, M.D.
Task Order Officer
Center for Evidence and Practice
Improvement
Agency for Healthcare Research and Quality

Acknowledgments

The authors gratefully acknowledge the following individuals for their contributions to this project: Task Order Officer Lionel Bañez, M.D., from AHRQ; EPC Program Director Stephanie Chang, M.D., M.P.H., from AHRQ; Associate Editor Timothy Wilt, M.D., M.P.H., from the Minnesota Evidence-based Practice Center; and Colleen Kelly, M.D., FACG, at the Alpert Medical School, Brown University.

Key Informants

In designing the study questions, the EPC consulted several Key Informants who represent the end-users of research. The EPC sought the Key Informant input on the priority areas for research and synthesis. Key Informants are not involved in the analysis of the evidence or the writing of the report. Therefore, in the end, study questions, design, methodological approaches, and/or conclusions do not necessarily represent the views of individual Key Informants.

Key Informants must disclose any financial conflicts of interest greater than \$5,000 and any other relevant business or professional conflicts of interest. Because of their role as end-users, individuals with potential conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any conflicts of interest.

The list of Key Informants who provided input to this report follows. (One Key Informant declined to be acknowledged in our report.)

Sharon Dudley-Brown, Ph.D.
Division of Gastroenterology and
Hepatology
Johns Hopkins Medicine
Baltimore, MD

James E. Duncan, M.D., FACS, FASCRS
Department of Colon and Rectal Surgery
VA Medical Center
Washington, DC

Nick Fitterman, M.D., MACP., SFHM*
ACP Clinical Guidelines Committee
Donald and Barbara Zucker School of
Medicine at Hofstra/Northwell
Huntington Hospital, Northwell Health
Huntington, NY

Samuel J. Galgano, M.D.*
Department of Radiology
University of Alabama at Birmingham
Birmingham, AL

Debra A. Gervais, M.D.
Department of Radiology
Massachusetts General Hospital
Boston, MA

Jennifer S. Lin, M.D., M.C.R., FACP*
ACP Clinical Guidelines Committee
Kaiser Permanente EPC
Portland, OR

Karlene Souto (Patient Representative)
Seekonk, RI

Neil Stollman M.D., FACP, AGAF, FACG.*
Division of Gastroenterology
University of California San Francisco
Alta Bates Summit Medical Center
San Francisco, CA

Marion F. Winkler, Ph.D., R.D., L.D.N.,
C.N.S.C.*
Department of Surgery
Alpert Medical School of Brown University
Department of Surgery/Nutrition Support
Service
Rhode Island Hospital
Providence, RI

* Provided input on Draft Report

Technical Expert Panel

In designing the study questions and methodology at the outset of this report, the EPC consulted several technical and content experts. Broad expertise and perspectives were sought. Divergent and conflicted opinions are common and perceived as healthy scientific discourse that results in a thoughtful, relevant systematic review. Therefore, in the end, study questions, design, methodologic approaches, and/or conclusions do not necessarily represent the views of individual technical and content experts.

Technical Experts must disclose any financial conflicts of interest greater than \$5,000 and any other relevant business or professional conflicts of interest. Because of their unique clinical or content expertise, individuals with potential conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any potential conflicts of interest identified.

The list of Technical Experts who provided input to this report follows. Note that in this instance, the Key Informants also served as Technical Experts; thus, the panels were composed of the same members.

Sharon Dudley-Brown, Ph.D.
Division of Gastroenterology and
Hepatology
Johns Hopkins Medicine
Baltimore, MD

James E. Duncan, M.D., FACS, FASCRS
Department of Colon and Rectal Surgery
VA Medical Center
Washington, DC

Nick Fitterman, M.D., MACP., SFHM*
ACP Clinical Guidelines Committee
Donald and Barbara Zucker School of
Medicine at Hofstra/Northwell
Huntington Hospital, Northwell Health
Huntington, NY

Samuel J. Galgano, M.D.*
Department of Radiology
University of Alabama at Birmingham
Birmingham, AL

Debra A. Gervais, M.D.
Department of Radiology
Massachusetts General Hospital
Boston, MA

Jennifer S. Lin, M.D., M.C.R., FACP*
ACP Clinical Guidelines Committee
Kaiser Permanente EPC
Portland, OR

Karlene Souto (Patient Representative)
Seekonk, RI

Neil Stollman M.D., FACP, AGAF, FACG*
Division of Gastroenterology
University of California San Francisco
Alta Bates Summit Medical Center
San Francisco, CA

Marion F. Winkler, Ph.D., R.D., L.D.N.,
C.N.S.C.*
Department of Surgery
Alpert Medical School of Brown University
Department of Surgery/Nutrition Support
Service
Rhode Island Hospital
Providence, RI

* Provided input on Draft Report

Peer Reviewers

Prior to publication of the final evidence report, EPCs sought input from independent Peer Reviewers without financial conflicts of interest. However, the conclusions and synthesis of the scientific literature presented in this report do not necessarily represent the views of individual reviewers.

Peer Reviewers must disclose any financial conflicts of interest greater than \$5,000 and any other relevant business or professional conflicts of interest. Because of their unique clinical or content expertise, individuals with potential nonfinancial conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any potential nonfinancial conflicts of interest identified.

The list of Peer Reviewers follows:

Anne Peery, M.D., M.C.S.R
Division of Gastroenterology and
Hepatology
University of North Carolina
Chapel Hill, NC

Victor F. Sai, M.D.
Department of Radiological Sciences
David Geffen School of Medicine at UCLA
Los Angeles, CA

Management of Colonic Diverticulitis

Structured Abstract

Background. There remain uncertainties about the effectiveness and harms of various nonsurgical treatment options for acute diverticulitis, clinical consequences of diagnostic imaging, detection strategies for colorectal cancer (CRC) in patients with recent diverticulitis, and preventive options for long-term recurrence.

Methods. We searched Medline[®], the Cochrane databases, Embase[®], CINAHL[®], and ClinicalTrials.gov from 1990 through June 1, 2020. We included existing systematic reviews (SRs) of computed tomography (CT) test accuracy, randomized controlled trials, adequately adjusted nonrandomized comparative studies for all topics, and larger single-group studies that addressed specific questions.

Results. We included 77 primary studies and 2 SRs. With moderate strength of evidence (SoE), CT has high sensitivity (94%) and specificity (99%) to diagnose acute diverticulitis. There is low SoE that CT imaging leads to appropriate management decisions and that misdiagnoses on CT do not result in poor clinical outcomes. Incidental findings on CT may be common (low SoE), but their clinical significance is unclear. There is insufficient evidence about CT test accuracy to stage acute diverticulitis. For patients with uncomplicated acute diverticulitis, there is low SoE that initial outpatient or inpatient management have similar risks of recurrence or elective surgery, but insufficient evidence regarding risk of treatment failure and other outcomes. For patients with uncomplicated acute diverticulitis, there is low SoE that antibiotic treatment does not affect clinically important outcomes. There is insufficient evidence regarding percutaneous drainage to manage complicated acute diverticulitis. There is low SoE that patients with recent acute diverticulitis may be at increased risk of CRC compared with the general population, but that those who undergo colonoscopy soon after acute diverticulitis may ultimately have similar rates of CRC as those who do not. Patients 50 years and older may be at increased risk of CRC (moderate SoE) or premalignant lesions (low to high SoE) compared with younger patients. Colonoscopy after acute diverticulitis rarely results in complications or incomplete procedures (high SoE). The risk of recurrence is not reduced by 5-aminosalicylic acid (5-ASA) (high SoE). The evidence regarding other nonsurgical interventions to prevent recurrence is insufficient. In patients with prior complicated or smoldering/frequently recurrent (after uncomplicated) diverticulitis, elective surgery reduces the risk of diverticulitis recurrence (high SoE), but there is no evidence regarding which patients may benefit most from surgery.

Conclusion. Important questions about which interventions should be used for which patients remain either unanswered or answered with only low SoE. New high-quality research is needed.

March 2022 update: An addendum is located at the end of the main report, before the appendixes.

Contents

Evidence Summary	ES-1
Introduction.....	1
Background	1
Purpose of the Review	3
Methods.....	4
Review Approach.....	4
Key Questions.....	4
Analytic Framework	6
Study Selection	6
Risk of Bias Assessment.....	8
Data Synthesis and Analysis	8
Grading the Strength of the Body of Evidence.....	8
Results	9
Overview of the Evidence Base Addressing All Key Questions.....	9
Key Question 1. Computed Tomography	9
Key Points	9
Findings Pertaining to CT Imaging.....	9
Summary of Evidence Pertaining to CT Imaging.....	17
Key Question 2. Medical Management of Acute Diverticulitis.....	19
Key Question 2a. Outpatient Versus Inpatient Management of Acute Diverticulitis	19
Key Question 2b. Antibiotic Treatment for Acute Diverticulitis	24
Key Question 2c. Interventional Radiology for Acute Diverticulitis	33
Key Question 3. Colonoscopy After Acute Diverticulitis	38
Key Points	38
Findings Pertaining to Colonoscopy	38
Summary of Evidence Pertaining to Colonoscopy	50
Key Question 4. Interventions To Prevent Recurrence	53
Key Questions 4a and 4b. Nonsurgical Interventions.....	53
Key Question 4c. Elective Surgery	64
Discussion.....	74
Findings in Relation to the Decisional Dilemma(s).....	74
Computed Tomography Imaging.....	74
Nonsurgical Treatment of Acute Diverticulitis.....	74
Colonoscopy After an Episode of Acute Diverticulitis	75
Prevention of Recurrence.....	75
Strengths and Limitations	75
Applicability	77
Implications for Clinical Practice, Education, Research, or Health Policy	77
CT Imaging	78
Nonsurgical Treatment of Acute Diverticulitis.....	78
Colonoscopy After an Episode of Acute Diverticulitis	79
Prevention of Recurrence.....	80
Future Research	80
Conclusions	81
References.....	82
Addendum.....	93

Tables

Table 1. Study eligibility criteria by Key Question	6
Table 2. Test accuracy of initial staging, per Jurowich 2011	13
Table 3. CT imaging sequelae and incidental findings.....	14
Table 4. Evidence profile for CT imaging for acute diverticulitis.....	18
Table 5. Outpatient versus inpatient management: Treatment failure.....	20
Table 6. Outpatient versus inpatient management: Quality of life	22
Table 7. Evidence profile for outpatient versus inpatient management of uncomplicated acute diverticulitis	23
Table 8. Evidence profile for antibiotic treatment for acute left-sided diverticulitis.....	32
Table 9. Interventional radiology: All outcomes	34
Table 10. Evidence profile for interventional radiology.....	37
Table 11. Evidence profile for colonoscopy after acute diverticulitis	52
Table 12. Nonsurgical treatments to prevent recurrence: Continuous outcomes	56
Table 13. Nonsurgical treatments to prevent recurrence: Categorical outcomes not meta-analyzed	57
Table 14. Adverse events of 5-ASA	61
Table 15. Evidence profile for nonsurgical interventions to prevent recurrence.....	63
Table 16. Elective surgery versus no surgery: Categorical outcomes	65
Table 17. Elective surgery versus no surgery: Continuous outcomes	66
Table 18. Adverse events of elective surgery	69
Table 19. Evidence profile for elective surgery.....	73

Figures

Figure 1. Summary ROC curve of CT test accuracy to diagnose acute diverticulitis	11
Figure 2. Meta-analysis of outpatient versus inpatient management: Recurrence of diverticulitis	21
Figure 3. Meta-analysis of outpatient versus inpatient management: Elective surgery for diverticulitis	22
Figure 4. Meta-analysis of antibiotics versus no antibiotics/placebo: Long-term recurrence of left-sided diverticulitis	27
Figure 5. Meta-analysis of colonoscopy versus no colonoscopy: Colorectal cancer	40
Figure 6. Meta-analysis of colonoscopy after diverticulitis versus in healthy controls: Colorectal cancer	42
Figure 7. Summary meta-analysis estimates of colonic lesions found on colonoscopy	44
Figure 8. Summary meta-analysis estimates of subgroup analyses	47
Figure 9. Meta-analysis of colonoscopy after acute diverticulitis: Percent with failed or incomplete colonoscopy.....	50
Figure 10. Meta-analysis of 5-ASA versus placebo: Recurrence of diverticulitis	54
Figure 11. Meta-analysis of elective surgery for diverticulitis versus no surgery: Recurrence of diverticulitis	66

Appendixes

Appendix A. Methods

Appendix B. Excluded Articles

Appendix C. Search Results; Study Design, Arm Details, Baselines, and Quality
Appendix D. Full Results

Evidence Summary

Main Points

- **Computed tomography (CT) diagnosis and clinical sequelae**
 - CT accurately diagnoses acute diverticulitis (moderate strength of evidence [SoE]) and may increase appropriate management versus clinical diagnosis (low SoE). Due to sparse data, there is insufficient evidence about CT accuracy to stage acute diverticulitis. Misdiagnoses on CT may not increase the risk of poor clinical outcomes (low SoE). The significance of incidental findings is unclear (low SoE).
- **Treatment of patients with acute diverticulitis**
 - Outpatient management: For patients with uncomplicated acute diverticulitis, outpatient management may be as effective as inpatient care (low SoE), but there is insufficient evidence regarding important clinical outcomes, including treatment failure, mortality, or emergency surgery.
 - Antibiotic treatment: For patients with uncomplicated diverticulitis, antibiotic treatment may not affect pain symptoms, length of hospital stay, recurrence risk, quality of life, or need for surgery compared to no antibiotic treatment (low SoE). For patients who do receive antibiotics, the evidence is insufficient to guide choice of antibiotic regimen.
 - Interventional radiology: The evidence is insufficient regarding the benefits or harms of percutaneous drainage for patients with complicated acute diverticulitis.
- **Colonoscopy following an episode of acute diverticulitis**
 - There is low SoE that patients with recent diverticulitis (within 6-12 months) may be more likely to have colorectal cancer (CRC) than the general population.
 - With low SoE, among patients with recent diverticulitis, those who undergo colonoscopy may, ultimately, have similar rates of CRC diagnoses as those who did not; however, no studies evaluated comparative risks of CRC death.
 - Patients who are 50 or older or who had complicated diverticulitis (with abscess, peritonitis, etc.) are at increased risk of having CRC (moderate SoE), advanced colonic neoplasia (high SoE), or advanced adenoma (low SoE) on colonoscopy.
 - Colonoscopies conducted within 1.5 to 12 months after acute diverticulitis rarely have complications or incomplete tests (high SoE).
- **Nonsurgical interventions to prevent recurrent diverticulitis**
 - 5-aminosalicylic acid (5-ASA) offers no benefit to patients to reduce the risk of recurrence of diverticulitis (high SoE). Evidence for other interventions is insufficient.
- **Elective surgery to prevent recurrent diverticulitis**
 - For patients with prior complicated or smoldering/frequently recurrent (after uncomplicated) diverticulitis, elective surgery reduces the risk of recurrent diverticulitis (high SoE). However, there is no evidence regarding which patients would benefit most from elective surgery. With low to moderate SoE, serious surgical complications included 30-day mortality (0.7%), 30-day readmission (7.3%), and reoperation (5.5%).

Background and Purpose

Colonic diverticulitis is caused by inflammation of abnormal outpouchings (diverticula) in the wall of the large intestine. Acute episodes of diverticulitis may be uncomplicated or accompanied by complications, such as perforations, peritonitis, abscesses, fistulas, and

strictures. Traditional management for patients with uncomplicated diverticulitis includes hospitalization, bowel rest, antibiotics, and intravenous fluids. Complicated diverticulitis may require more invasive interventions, such as surgery or interventional radiology procedures. There remain uncertainties about the effectiveness and harms of various treatment options, preventive options for long-term recurrence, and detection strategies for CRC.

This systematic review evaluates: (1) the accuracy of CT and harms related to false positive, false negative, and incidental findings on CT imaging; (2) the effectiveness and harms of hospitalization for acute uncomplicated diverticulitis, antibiotics for acute diverticulitis, and interventional radiology for acute complicated diverticulitis; (3) the need for colonoscopy in people with a history of diverticulitis; and (4) the effectiveness and harms of pharmacologic, nonpharmacologic, and elective surgery to prevent recurrent diverticulitis. The findings of the review are expected to inform healthcare providers, policymakers, and patients, and support new guidance on diagnosis, staging, and nonsurgical treatment of acute diverticulitis, and interventions to prevent recurrence, and CRC screening in people with a history of diverticulitis.

Methods

We employed methods consistent with those outlined in the Agency for Healthcare Research and Quality Evidence-based Practice Center Program Methods Guidance (<https://effectivehealthcare.ahrq.gov/topics/ceer-methods-guide/overview>). Our searches covered studies published from 1990 to June 1, 2020.

Results

CT: Existing reviews found high sensitivity (94%) and specificity (99%) of CT to diagnose acute diverticulitis (moderate SoE). There is insufficient evidence to evaluate diverticulitis staging criteria. There is low SoE that: (1) CT imaging leads to appropriate management decisions for patients with acute diverticulitis, (2) misdiagnoses on CT do not result in poor clinical outcomes, and (3) incidental findings, although common, have unclear clinical significance. There is insufficient evidence about staging diverticulitis by CT imaging.

Outpatient management of acute diverticulitis: The evidence is insufficient to make conclusions about whether or not outpatient management of patients with uncomplicated diverticulitis leads to higher rates of treatment failure, mortality, and emergency surgery than inpatient management. Adverse outcomes, such as mortality and emergency surgery are uncommon (3% of patients or fewer), regardless of setting. Studies found no evidence of differences in rates of long-term diverticulitis recurrence or elective surgery based on management setting (low SoE).

Antibiotic treatment of acute diverticulitis: With low SoE, studies did not find that antibiotic treatment for patients with uncomplicated diverticulitis resulted in differences in pain symptoms, length of hospital stay, recurrence risk, quality of life, but may reduce need for surgery compared to no antibiotic treatment. Evidence regarding death, treatment failure, diverticulitis-related morbidities, rehospitalization, and adverse events are mostly rare and evidence is insufficient to make conclusions. These events are mostly rare. Studies that compared antibiotic regimens each evaluated different regimens. Thus, there is insufficient evidence about their relative effectiveness.

Interventional radiology: The evidence is insufficient to make conclusions regarding the potential benefits or harms of percutaneous drainage.

Colonoscopy: There is low SoE that patients with recent acute diverticulitis may be at about 3 times the risk of finding CRC on colonoscopy than healthy controls, but the finding is not statistically significant. With low SoE, studies comparing patients who underwent colonoscopy soon after an episode of acute diverticulitis (within about 2-12 months) with those who did not undergo colonoscopy, found no evidence of differences, ultimately, in rates of CRC; however, no studies evaluated comparative risks of CRC death. Among these patients, about 2 percent have CRC, 7 percent have advanced colonic neoplasia (CRC or advanced adenoma), and between 1 and 3 percent have specific premalignant lesions (moderate to high SoE). There is also variable (low to high) SoE that older patients (≥ 50 years) and patients with recent complicated diverticulitis are at particularly high risk of CRC and various premalignant lesions. There is high SoE that procedural complications are rare (fewer than 1% of patients) and that colonoscopy failure rates are also uncommon (3.5%) soon after acute diverticulitis.

Nonsurgical interventions to prevent recurrent diverticulitis: There is high SoE that 5-ASA does not reduce the risk of recurrence and is not more harmful than placebo. Evidence for other interventions (rifaximin, combination 5-ASA and rifaximin, combination 5-ASA and probiotics, probiotics, and burdock tea) is too sparse to make conclusions (insufficient). No studies evaluated medical nutrition therapy.

Elective surgery to prevent recurrent diverticulitis: There is high SoE that elective surgery reduces the risk of recurrence of diverticulitis among patients with prior complicated or frequently recurrent diverticulitis, but no evidence regarding which patients may benefit most from surgery. There was low to moderate SoE that serious adverse events are uncommon with elective surgery, including that fewer than 1 percent of patients die postoperatively.

Limitations

With few exceptions, the evidence base examined in this review for each specific question is based on very few studies or of low SoE. Evidence is particularly sparse for questions related to the benefits and harms of CT scanning for acute diverticulitis, the appropriateness of outpatient management of uncomplicated or mildly complicated diverticulitis, interventional radiology for nonsurgical complicated diverticulitis, and various interventions for prevention of recurrent diverticulitis. In addition, there is limited evidence regarding which patients might benefit most from (or be most harmed by) the various interventions. Regarding colonoscopy, the studies have not adequately addressed whether patients who undergo colonoscopy after diverticulitis are at decreased risk of dying from CRC compared to patients who forgo colonoscopy.

Implications and Conclusions

Many of the important questions about which interventions should be used for which patients remain either unanswered or answered with only low SoE.

Prior reviews have demonstrated that CT imaging accurately diagnoses acute diverticulitis. While the clinical implications of false positive, false negative, and incidental findings remain unclear, there is a low SoE that misdiagnoses on CT did not result in poor clinical outcomes. Of note, there is insufficient evidence regarding the test accuracy of clinical staging classifications based on CT imaging.

For selected patients with uncomplicated acute diverticulitis, outpatient management may be as effective as inpatient care. In addition, for patients with uncomplicated diverticulitis, antibiotic treatment may not affect pain symptoms, length of hospital stay, risk of recurrence, or quality of life but may reduce the need for surgery. For patients who do receive antibiotics, the evidence is

insufficient to guide choice of antibiotic regimen. The evidence is insufficient to assess the clinical value of percutaneous drainage.

Patients with recent episodes of diverticulitis are at increased risk of having undiagnosed CRC or advanced colonic neoplasia, particularly if they are at least 50 years of age or have had complicated diverticulitis. However, there is no evidence regarding whether colonoscopy soon after an episode of acute diverticulitis affects CRC mortality.

5-ASA offers no benefit to patients to reduce the risk of recurrence of diverticulitis. There is insufficient evidence regarding other potential prophylactic treatments. In particular, despite clinical and patient interest, there is no comparative evidence regarding medical nutrition therapies.

Patients with a history of prior complicated or frequently recurrent diverticulitis who undergo elective surgery are at greatly reduced risk of recurrent diverticulitis; however, there is no evidence regarding which patients would most benefit from elective surgery. Postoperative mortality is uncommon, but patients not uncommonly require readmission or reoperation.

The evidence base, particularly for comparisons of interventions is mostly of low strength of evidence (or insufficient or completely lacking). To enable better guidance about best options for patient management, there is a clear need for high-quality research to address the unanswered questions. Ideally, large-scale, multicenter trials should be conducted in unrestricted populations (i.e., without eligibility restrictions that may reduce applicability of findings) with appropriate subgroup analyses and, as needed, analytic methods to account for the inherent differences between people who receive different treatments.

Introduction

Background

Colonic diverticulitis is caused by inflammation of abnormal outpouchings (diverticula) in the wall of the large intestine. The precursor to diverticulitis is diverticulosis, in which the diverticula are not inflamed. They typically are asymptomatic.^{1, 2} Overall, about 5 to 10 percent of patients with diverticulosis develop acute diverticulitis,³ and the number of emergency department admissions for diverticulitis has been increasing over time.⁴ Diverticulosis has generally regarded to be a disease affecting the elderly; about 60 percent of people over the age of 60 have diverticulosis.^{5, 6} However, recent data have revealed a marked increase in younger patients, with about 30 percent or more of Americans younger than 40 years having diverticulosis and thus being at increased risk for developing acute diverticulitis.^{7, 8} Nevertheless, the risk of developing acute diverticulitis rises rapidly with age from 7.1 per 100,000 for those in the 18 to 29 age group, through 113.9 per 100,000 for 50 to 59 year old adults, to 263.7 per 100,000 for those over age 80 (per the Nationwide Inpatient Sample from 2000 to 2010).⁹ Overall, the incidence rate is higher among women (103.1 per 100,000 in 2010) than men (79.5 per 100,000). Younger men (<50 years) have higher incidence than younger women, while older women have higher incidence than older men.⁹ White Americans have about double the incidence (61.8 per 100,000 from 2000 to 2010) than Blacks (29.1), Hispanics (32.4), and Native Americans (25.8); Asian/Pacific Islanders have relatively low incidence (10.4 per 100,000).⁹ Due to high hospitalization rates and related costs, in the setting of potentially feasible outpatient management, diverticulitis has been prioritized as a measure to compare and reduce variability across national emergency department admission rates.¹⁰

Symptoms of diverticulitis typically involve acute or subacute lower abdominal pain, often associated with nausea, diarrhea, or constipation. While early studies suggested that diverticulitis is a recurrent disease of a progressive nature, more recent studies in the era of improved medical treatment and more reliable diagnostic imaging suggest the course of diverticulitis is less severe than it was in the past, with fewer episodes of complicated diverticulitis.^{11, 12} Nevertheless, about one-quarter of patients have recurrence after a first episode of acute diverticulitis, and even if not complicated, these unpredictable recurrences can be a great source of distress to patients.

Computed tomography (CT) scanning is currently the mainstay for diagnosis of suspected diverticulitis. There are about 200,000 hospital discharges for acute diverticulitis in the U.S. annually,¹³ suggesting that several hundred thousand adults are undergoing CT scanning each year to diagnose or rule out acute diverticulitis. The ubiquitous use of abdominal CT has raised concerns about diagnostic errors (whether false positive or false negative) and the potential impact of incidental findings on CTs conducted to rule out or assess diverticulitis (e.g., incidental liver masses that may need invasive or costly workups).

Acute episodes of diverticulitis may be complicated or uncomplicated. Complications are mostly caused by small or large diverticular perforations, which may introduce gut bacteria into the peritoneal space. Complications, including abscesses, peritonitis, fistulas, and strictures, occur in about 12 percent of cases of acute diverticulitis.¹⁴ Several schema to classify diverticulitis severity have been published,¹⁵ from the earliest one by Hughes in 1963,¹⁶ to one recently proposed by the European Association for Endoscopic Surgery.¹⁷ Most widely used is the Hinchey Classification,¹⁸ which has been modified to include mild clinical disease,¹⁹ and further updated to reflect CT findings to help not just with diagnosis but also with prognosis.^{20, 21}

Multiple other classification schemes exist that mostly stage severity, complications, and relapses,^{17, 22, 23} or CT findings.^{21, 24}

Traditional management for patients with uncomplicated diverticulitis includes bowel rest, antibiotics, and hydration, and may involve hospitalization for intravenous (IV) antibiotics and fluids, and monitoring. In recent years emerging concepts in the pathogenesis from alteration in the gut microbiome, gut dysmotility, and inflammatory rather than infectious etiology has questioned this established approach.²⁵⁻²⁷ Management of complicated diverticulitis may require more intensive and invasive interventions, including open or laparoscopic surgeries with or without interventional radiology procedures to remove the affected portion of bowel or to drain or cleanse the peritoneal space. Several controversies have emerged with regards to the optimal management of acute diverticulitis.²⁸ Recent narrative reviews highlighted where current common practices in the management of acute diverticulitis, including medical, surgical, and interventional radiological, may not be supported by the evidence for all patients. These include universal hospitalization, use of IV antibiotics, and colectomy and other aggressive surgical procedures for complicated episodes.^{28, 29} For example, a recent randomized controlled trial suggested there was no difference in treatment failure between hospital admission and outpatient management with considerable cost savings in the latter group.³⁰ The duration of antibiotic treatment³¹ and the need for antibiotic treatment^{32, 33} have been questioned. A recent systematic review (SR) of current strategies for uncomplicated diverticulitis revealed unproven differences in outcomes between observational management and antibiotic therapy and between oral and IV antibiotics.³⁴

Due to the increased morbidity and mortality associated with emergent surgery for acute complicated diverticulitis, in the absence of peritonitis, physicians have opted to delay definitive surgical management by employing antibiotic treatment and interventional radiology procedures, such as percutaneous drainage of abscess, in appropriate patients; but the supporting evidence for this approach is unclear. There has been an increase in interventional radiology approaches to manage acute complicated diverticulitis, such as percutaneous abscess drainage via ultrasound or CT image-guided catheter placements. Initially reserved for the sickest, highest-risk surgical patients, drainage and antibiotic treatment is now used as definitive treatment to avoid surgery and allow shorter hospital stay and faster recovery.^{35, 36}

Patients with a diverticulitis complicated by an abscess have traditionally been offered an interval (non-emergency, elective) colectomy after treatment with antibiotics and possible percutaneous drainage. The rationale for subsequent surgery was to prevent future complications, but recent studies have found that nonsurgical, continued medical treatment of diverticulitis is safe, with low rates of subsequent surgery.³⁷ More recent literature has increasingly revealed that diverticulitis is not a progressive disease as once thought, and that increasing number of episodes do not lead to more complications or the need for urgent operative management. Indeed, studies have found that the greatest risk of free perforation and peritonitis is during the first episode of the disease.³⁸ Moreover, the risk of recurrence is likely much lower than previously thought.³⁹ Nevertheless, the rate of elective colectomies in the U.S. following an episode of acute diverticulitis continues to rise (through 2016), particularly among those between 65 and 79 years old (while the rate of urgent/emergent colectomies has been stable or declined).⁴⁰

The natural course of diverticulitis was once thought to be more severe in younger patients (<50 years) than it is currently believed to be;^{41, 42} thus age is no longer used as a criterion to electively operate on younger patients with a history of diverticulitis. In contrast, a lower threshold for both elective and emergency surgical intervention continues to be recommended for

immunocompromised patients, such as people with organ transplants, receiving chemotherapy, or with chronic kidney disease.^{43, 44}

Strategies to reduce (or eliminate) diverticulitis recurrence have evolved. Despite very low quality of evidence,^{45, 46} guidelines recommend high-fiber diets, but no longer recommend avoiding seeds, nuts, and popcorn. Various pharmacologic treatments are used in clinical practice, although uncertainty remains. For example, the 2015 American Gastroenterological Association guideline recommended against using mesalamine (5-aminosalicylic acid or 5-ASA), an anti-inflammatory agent that is effective for ulcerative colitis.⁴⁶

There remain unanswered questions regarding the potential adverse consequences of CT imaging (related to false positive tests or incidental findings that may lead to further invasive testing and surgery) to diagnose uncomplicated and complicated diverticulitis. The evidence regarding this potential harm has not been summarized to date.

Another area of controversy includes the appropriateness of performing colonoscopy following a resolved episode of diverticulitis to detect occult colonic malignancy.⁴⁷ CT features of acute diverticulitis may mimic colon cancer;⁴⁸ thus professional societies have recommended followup colonoscopy to exclude colon cancer after an episode of acute diverticulitis.⁴⁹ However, the prevalence of colorectal cancer in this setting has been found to be low for patients with uncomplicated diverticulitis,⁵⁰ leading some authors to question the need for routine colon evaluation for these patients. The value of CT (or virtual) colonography, noninvasive imaging of the interior lumen of the colon, for colon evaluation in this setting requires more study. Although it may be associated with less pain, fewer complications, and improved patient tolerance, its diagnostic accuracy is uncertain.⁵¹

Purpose of the Review

The American College of Physicians (ACP) nominated the topic of management of acute diverticulitis to the Agency for Healthcare Research and Quality for a systematic review (SR).^{52, 53} The ACP develops guidelines based on the needs of its members and the internal medicine community.⁵⁴ The scope of the current SR was developed to support the ACP in its effort to create a new clinical practice guideline that will address diagnosis and staging of acute diverticulitis, nonsurgical treatment of acute diverticulitis, colorectal cancer screening in people with a history of diverticulitis, and interventions to prevent recurrence of acute diverticulitis.

Specifically, (1) the SR summarizes existing SRs on the test accuracy of CT imaging for diagnosis of acute diverticulitis and conducts a *de novo* review test accuracy for CT staging and of harms related to false positive, false negative, and incidental findings on CT imaging for suspected acute diverticulitis; (2) it addresses effectiveness, comparative effectiveness, and harms of hospitalization for acute uncomplicated diverticulitis, antibiotics use for acute complicated or uncomplicated diverticulitis, and interventional radiology techniques for acute complicated diverticulitis; (3) it reviews the benefits and harms of colonoscopy in people with a history of diverticulitis; and (4) it evaluates pharmacologic, nonpharmacologic, and elective surgical interventions to prevent recurrent diverticulitis. Of note, this review does not evaluate the need for, or the choice of, surgery for the patient with acute diverticulitis.

The intended audience includes guideline developers, clinicians and other providers of care for patients with diverticulitis, healthcare policy makers, and patients.

Methods

Review Approach

The Brown Evidence-based Practice Center conducted this systematic review (SR) based on the Agency for Healthcare Research and Quality (AHRQ) Methods Guide for Effectiveness and Comparative Effectiveness Reviews (available at <https://effectivehealthcare.ahrq.gov/topics/cer-methods-guide/overview>). This SR also reports in accordance with the Preferred Items for Reporting in Systematic Reviews and Meta-Analyses (PRISMA),⁵⁵ A Measurement Tool to Assess Systematic Reviews (AMSTAR 2),⁵⁶ and any relevant extension statements.

A more detailed version of the SR methodology used can be found in Appendix A. Excluded studies are listed in Appendix B. Search results and descriptive data for all included studies are included in Appendix C. Extracted study results are in Appendix D.

The topic of this report and preliminary Key Questions (KQs) arose through a process involving the nominators (the American College of Physicians), a panel of Key Informants (KI), a Technical Expert Panel (TEP), the public, and AHRQ. Initially, the KI panel gave input on the KQs, including the outcomes, to be examined. AHRQ then posted these KQs and solicited public comment through its Effective Health Care (EHC) Program website and on the Federal Register. No comments were received. The TEP provided high-level content and methodological expertise throughout development of the review protocol. The final protocol was posted on the EHC website at <https://effectivehealthcare.ahrq.gov/products/diverticulitis/protocol> on September 12, 2019. We submitted the protocol for registration in PROSPERO in November 2019. On April 29, 2020, PROSPERO published the protocol with registration number CRD42020151246.

Key Questions

KQ 1: In CT imaging for the diagnosis or staging of acute diverticulitis,

KQ 1a. What is the test accuracy of CT imaging for the diagnosis or staging of acute diverticulitis?

KQ 1b. What are the effects of CT imaging on clinical outcomes and changes in clinical management?

KQ 1c. What are the downstream outcomes related to false positive or false negative CT readings of acute uncomplicated or complicated diverticulitis?

KQ 1d. For patients presenting with acute abdominal pain, with the possibility of acute diverticulitis, what are the downstream outcomes related to incidental findings?

- Does the accuracy or do the effects vary by patient characteristics, presentation of illness, or other factors?

KQ 2: What are the benefits and harms of various treatment options for the treatment of acute diverticulitis?

KQ 2a. For patients with acute uncomplicated diverticulitis, what are the effectiveness and harms of hospitalization versus outpatient management of the acute episode?

- Do the effects and harms vary by patient characteristics, presentation or course of illness, or other factors?

KQ 2b. For patients with acute uncomplicated or complicated diverticulitis, what are the effects, comparative effects, and harms of antibiotic treatment?

- Do the effects and harms vary between patients with complicated or uncomplicated diverticulitis?
- Do the (comparative) effects and harms vary by route of administration of antibiotics, type of antibiotic, and duration of course of antibiotics?
- Do the (comparative) effects and harms vary by patient characteristics, presentation or course of illness, or other factors?

KQ 2c. For patients with acute complicated diverticulitis, what are the effects and harms of interventional radiology procedures compared with conservative management?

- Do the effects and harms vary by patient characteristics, presentation or course of illness, or other factors?

KQ 3: What are the benefits and harms of colonoscopy (or other colon imaging tests) following an episode of acute diverticulitis?

KQ 3a. What is the incidence of malignant and premalignant colon tumors found by colonoscopy, and what is the incidence of colon cancer mortality among patients undergoing screening?

KQ 3b. What are the procedure-related and other harms of colonoscopy or CT colonography?

KQ 3c. What is the frequency of inadequate imaging due to intolerance or technical feasibility?

- Do the benefits and harms vary by patient characteristics, course of illness, or other factors?

KQ 4: What are the effects, comparative effects, and harms of pharmacological interventions (e.g., mesalamine), non-pharmacological interventions (e.g., medical nutrition therapy), and elective surgery to prevent recurrent diverticulitis?

- Do the (comparative) effects and harms vary by patient characteristics, course of illness, or other factors?

Analytic Framework

Based on discussions with KIs and TEP, we developed analytic frameworks (Appendix A Figures A-1 to A-4). These graphically lay out the populations, interventions, outcomes, and modifiers that pertain to each KQ.

Study Selection

Literature searches were conducted in Medline[®] (via PubMed[®]), the Cochrane Register of Clinical Trials, the Cochrane Database of Systematic Reviews, Embase[®], CINAHL[®], and ClinicalTrials.gov, restricted to 1990 through June 1, 2020. The search was restricted to recent studies (since 1990) based on important changes in diagnosis and clinical management of diverticulitis based on increased use of CT imaging since the 1990s.

Table 1 presents the major eligibility criteria for each KQ. More detailed criteria are presented in Appendix A. We included randomized controlled trials (RCTs), nonrandomized comparative studies (NRCSSs), single group studies (noncomparative between interventions), and existing SRs.

Table 1. Study eligibility criteria by Key Question

Eligibility Categories	Criteria
KQ 1 (CT imaging): Population	Adults with suspected or known acute colonic diverticulitis or with acute abdominal pain
KQ 1: Intervention/Comparator	Abdominopelvic CT scan Comparison with other diagnostic imaging test. No comparator necessary.
KQ 1: Outcomes	KQ 1a (diagnostic accuracy) Test accuracy for diagnosis Test accuracy for staging KQ 1b (clinical outcomes) Short, medium, and long-term clinical outcomes (e.g., time to resolution) Resources (e.g., length of hospital stay) KQ 1c (harms) Harms related to overtreatment (due to false positive CT) Harms related to undertreatment (due to false negative CT) KQ 1d (incidental findings) Sequelae related to incidental findings (e.g., unnecessary liver biopsy)
KQ 1: Design	KQ 1a: Existing systematic reviews KQ 1b-d: Unbiased sampling (eligibility based only on pre-imaging criteria) N≥100
KQ 2 (acute treatments): Population	Adults with <i>acute</i> colonic diverticulitis, either complicated or uncomplicated
KQ 2: Intervention/Comparator	KQ 2a (hospitalization) Hospitalization vs. outpatient management (no hospitalization) KQ 2b (antibiotics) Antibiotics (any) vs. No antibiotics Other antibiotics Other antibiotic regimens (e.g., 4 vs. 7 days, oral vs. intravenous) KQ 2c (interventional radiology) Interventional radiology procedure (any) vs. No interventional radiology procedure Other interventional radiology procedure or technique <i>Exclude laparoscopic and other surgical procedures</i>

Eligibility Categories	Criteria
KQ 2: Outcomes	<p>Clinical diverticulitis outcomes E.g., Death, resolution, time to resolution, diverticulitis-related morbidities ("complications"), (avoided) procedures/surgery, recurrent diverticulitis</p> <p>Other patient-centered outcomes E.g., Quality of life; functional outcomes; missed work</p> <p>Resources E.g., Length of hospital stay, return to hospital (or ED), clinic visits</p> <p>Harms KQ 2a: hospital-based infections, other major harms KQ 2b: Adverse events attributable to antibiotics (major), including C diff infection KQ 2c: Adverse events related to procedures. E.g., major bleeds and infections</p>
KQ 2: Design	<p>RCT: N≥10 NRCS: Mostly restrict to studies that use analytic methods to minimize selection bias ^a N≥30 Single group studies: N≥100 (for harms only)</p>
KQ 3 (colonoscopy): Population	Adults with history of resolved acute diverticulitis
KQ 3: Intervention/Comparator	<p>Elective colonoscopy No comparator necessary No colonoscopy (or other colon imaging) Other colon imaging (complete or partial)</p>
KQ 3: Outcomes	<p>Colorectal cancer Colorectal cancer death High-risk colonic premalignant lesions: adenoma with high-grade dysplasia; adenoma ≥10 mm, villous adenoma, serrated polyp, ≥3 adenomas/patient Tolerance, feasibility, procedure completion, technical adequacy Harms/adverse events attributable to procedure</p>
KQ 3: Design	<p>RCT: N≥10 NRCS: N≥100 per group (200 total) Single group studies (for harms only): N≥200</p>
KQ 4 (recurrence prevention): Population	Adults with history of resolved acute diverticulitis
KQ 4: Intervention/Comparator	<p>KQ 4a: Nonsurgical interventions, including pharmacologic treatments and nonpharmacologic interventions (e.g., medical nutrition therapy) Vs. no intervention or vs. other nonsurgical intervention KQ 4b: Elective surgery (<i>exclude delayed surgery for acute diverticulitis</i>) Vs. no surgery <i>Not comparisons of surgery types or approaches</i> <i>Exclude natural history studies or undefined/unspecified interventions or comparators</i></p>
KQ 4: Outcomes	<p>Clinical diverticulitis outcomes E.g., Death, recurrent diverticulitis Surgery-related clinical outcomes E.g., Stoma placement (avoidance) Other patient-centered outcomes E.g., Quality of life; functional outcomes; missed work</p> <p>Resources E.g., Length of hospital stay, return to hospital (or ED), clinic visits</p> <p>Harms Major surgical adverse events: Clavien-Dindo Grade II (require medical intervention), Grade III (require surgical intervention), Grade IV (organ dysfunction, Grade V (death)</p>
KQ 4: Design	<p>RCT: N≥10 NRCS: Mostly restrict to studies that use analytic methods to minimize selection bias ^a N≥30 Single group studies (for harms only): Nonsurgical N≥100; Surgical N≥500</p>

Abbreviations: C diff = Clostridioides difficile, CT = computed tomography, ED = emergency department, KQ = Key Question, NRCS = nonrandomized comparative study, RCT = randomized controlled trial.

^a Restricted to studies that use modeling or other analytic methods to minimize selection bias (due to inherent differences between people who receive one or the other intervention) or that restrict study eligibility criteria such that comparisons being made are between patients with similar presentations. However, allow crude (unadjusted) comparisons of long-term outcomes

under the assumption that characteristics during acute diverticulitis that were associated with treatment choice would not have a major impact on long-term outcomes. (NRCS that do not meet these criteria were assessed as possibly eligible single group studies.)

Risk of Bias Assessment

We evaluated each study for risk of bias and methodological quality. Because we included a variety of study designs, we incorporated items from three different commonly-used tools and tailored the set of items for each study design.

For RCTs, we used all the items from the Cochrane Risk of Bias tool,⁵⁷ including randomization and allocation concealment methodology; blinding; completeness of data reporting; and selective reporting.

For NRCSs, we used specific elements from the Risk Of Bias In Non-randomised Studies - of Interventions (ROBINS-I) tool related to confounding and selection bias.⁵⁸ We also used items from the Cochrane Risk of Bias tool that were not specific to randomized trials.

For single-group studies, we used the items from the above-mentioned tools that related to participant loss to followup, incomplete outcome data, selective reporting, and adequacy of descriptions of study eligibility criteria, interventions, and outcomes.

Data Synthesis and Analysis

Within the main report, data are summarized either in succinct tables that focus on outcome, interventions, and comparative (when applicable) results or in forest plots or succinct summary tables (for most topics). Appendix D contains the succinct summary tables for the antibiotics Key Question because of their large number and length. The rest of Appendix D includes the more detailed, study-level results for each topic. Appendix C contains detailed tables that describe study and participant characteristics, intervention (and comparator) details, outcomes (and definitions), and arm- and comparison-level results. Appendix C also includes tables providing study-level risk of bias assessments.

When feasible and appropriate, we conducted random effects model pairwise meta-analyses. Details are in Appendix A. Of note, for harms data related to KQ 4 (elective surgery), we meta-analyzed adverse event rates (proportions) when two or more studies reported sufficiently similar adverse events. The goal of these meta-analyses was to allow concise presentation of the adverse event results data; thus, we did not restrict these meta-analyses based on the similarities of the investigated surgeries or on the statistical heterogeneity among included studies (the differences in adverse event rates). To indicate the heterogeneity across studies, we also report the range of adverse event rates across studies.

Grading the Strength of the Body of Evidence

We evaluated the strength of evidence (SoE) addressing each major analysis for each KQ. We graded the SoE as per the AHRQ Methods Guide.^{59, 60} For each SoE assessment, we considered the number of studies, the study limitations, the directness of the evidence to the KQs, the consistency of study results, the precision of any estimates of effect, and other limitations (particularly sparseness of evidence). Based on these assessments, we assigned a SoE rating as being either high, moderate, low, or insufficient to estimate an effect. Outcomes with highly imprecise estimates (95% confidence interval extends beyond both 0.50 and 2.0), highly inconsistent findings across studies, or with data from only one study were deemed to have insufficient evidence to allow a conclusion.

Results

The Results Chapter is organized by Key Question (KQ) and, as pertinent, by subquestion. High-level summary tables and forest plots describing overall findings across studies are included in the main report. More detailed summary tables describing each study and other detailed information are in Appendixes C and D. Each section (either by KQ or by subsection) has a list of Key Points that includes the strength of evidence (SoE) for the conclusions. This is followed by the findings and a summary of findings with a SoE table.

Overview of the Evidence Base Addressing All Key Questions

The literature database searches yielded 15,199 citations. We found 722 citations to retrieve for further screening. Ultimately 77 primary studies (reported in 88 articles) and 2 systematic reviews (SRs) were eligible and included. The most frequent reasons for exclusion of articles were: existing SR (n=93), single-group study of elective surgery with N<500 (KQ 4, n=59), no specific intervention (n=54; e.g., natural history study), secondary publication with no unique data of interest (n=50), computed tomography (CT) study without clinical or management outcomes (n=45), not intervention of interest (n=44), surgery for acute diverticulitis (n=36), article not available (n=34; most are likely conference abstracts), and single-group study of interventions with N<100 (n=31). See literature flow figure in Appendix C (Figure C-1) and the list of rejected studies in Appendix B for more details.

Key Question 1. Computed Tomography

Key Points

- Existing SRs have demonstrated very high sensitivity (94%) and specificity (99%) of CT to diagnose acute diverticulitis (moderate SoE)
- There is insufficient evidence to evaluate diverticulitis staging criteria due to sparse data.
- Based on 2 studies, CT imaging led to appropriate surgical or medical management of acute diverticulitis (low SoE); however, no studies have compared CT imaging to no imaging.
- Based on 3 studies, misdiagnoses on CT (i.e., false positive or negative CT scans) did not clearly result in poor clinical outcomes (low SoE)
- Based on 2 studies of CT imaging performed in the emergency department for acute abdomen, incidental findings (unrelated to the abdominal pain) were common, but it remains unclear what the clinical significance (either beneficial or harmful) of these findings are (low SoE)

Findings Pertaining to CT Imaging

Key Question 1a. Test Accuracy of CT Imaging

Diagnosis of Acute Diverticulitis

Two existing systematic reviews have summarized the evidence for diagnostic test accuracy of CT for patients with suspected diverticulitis.^{61, 62} Despite the span of time between the two

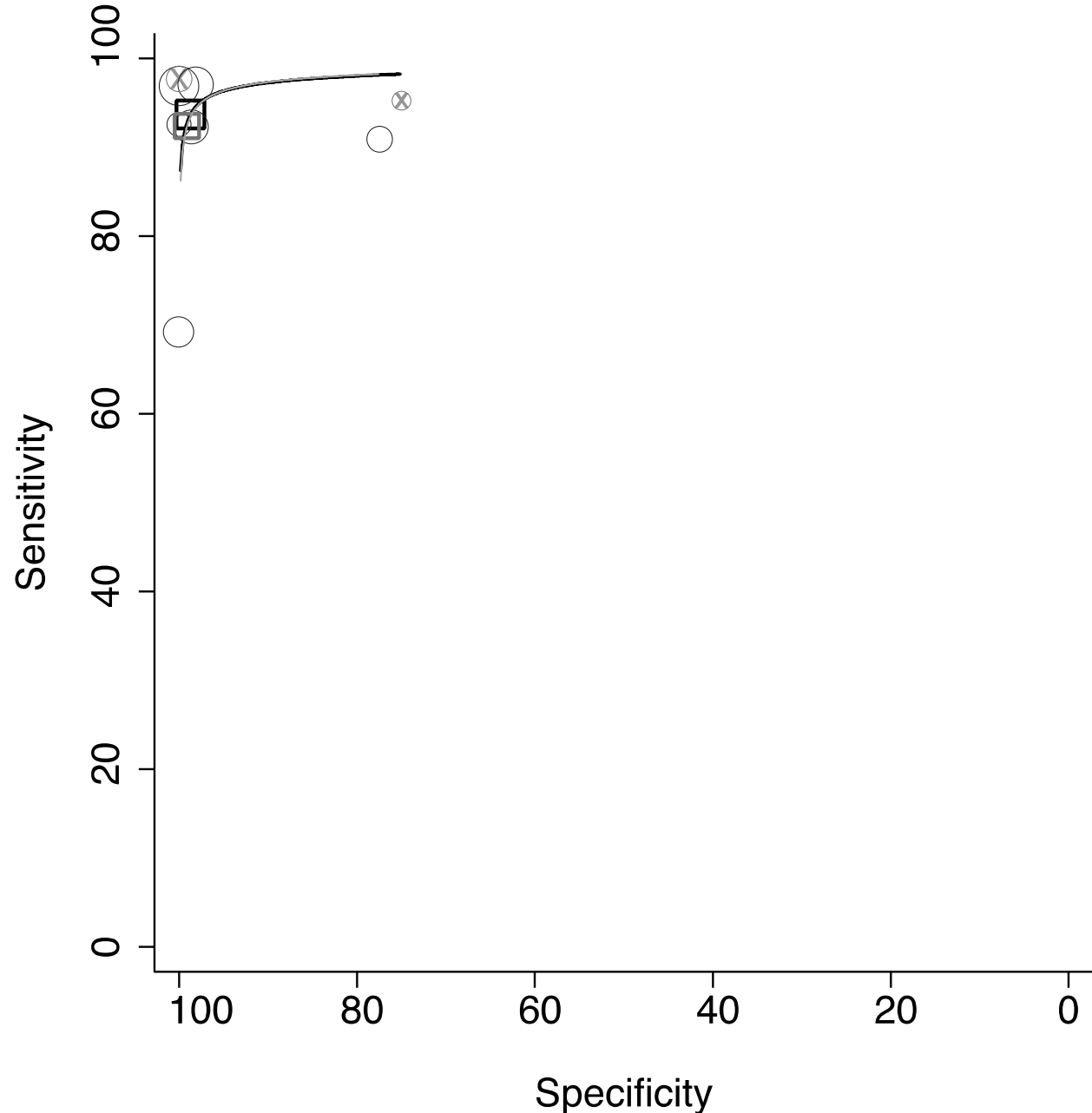
publications (2008 to 2014), both reviews included the same eight primary studies, which had been published between 1990 and 2005.⁶³⁻⁷⁰ The later review (Andeweg 2014) conducted its literature search in PubMed, Embase, and the Cochrane Library of Systematic Reviews through December 2013.⁶² This SR did not report its funding source. The earlier review (Laméris 2008) also searched CINAHL.⁶¹ This SR was funded by a Dutch nonprofit organization. Both reviews included studies that evaluated the diagnostic performance of CT (and other imaging tests) in patients with suspected acute colonic diverticulitis. None of the primary studies reported their funding source. Andeweg 2014 excluded two German language studies because they “did not report a consecutive series of patients”,^{63, 68} although, they graded them as being of moderate quality. However, while the two articles do not provide much detail regarding their selection of participants, in our determination the included patients were likely enrolled consecutively. In addition, Andeweg 2014 used a substandard meta-analytic method that treated sensitivity and specificity as independent measures. Therefore, we recalculated their analyses with bivariate random effects model meta-analysis, which appropriately jointly meta-analyzes sensitivity and specificity. Laméris 2008 used this method.

The original primary studies each included between 33 and 150 patients (684 total) whose mean ages ranged from 51 to 71 years (the studies included 19 to 98 year olds). Women accounted for 54 to 72 percent of the samples. Prevalence rates of final diagnosis of acute diverticulitis and of complicated diverticulitis varied, ranging from 36 to 68 percent with acute diverticulitis and 10 to 60 percent of those with diverticulitis having complicated disease.

Laméris 2008⁶¹ judged the overall quality of the evidence to be “moderate” based on the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) tool,⁷¹ primarily due to issues with the reference standard. Notably, the reference standard was not independent of the index test (final diagnosis was based, in part, on CT findings) and a lack of uniform verification (only a subset of individuals had surgical or colonoscopic verification of diagnosis).

With or without the two German studies, pooled sensitivity and specificity were high and similar. With all studies included, summary sensitivity was 94 percent (95% confidence interval [CI] 87 to 97) and specificity was 98.9 percent (95% CI 90 to 99.9). Excluding the two German studies yielded a summary sensitivity of 92 percent (95% CI 84 to 97) and specificity of 99.2 percent (91 to 99.9). The summary receiver operator characteristics (ROC) graph is depicted in Figure 1.

Figure 1. Summary ROC curve of computed tomography test accuracy to diagnose acute diverticulitis



Each circle represents an included study, with the size of the circles corresponding to the relative sample sizes of each study. The squares indicate the summary sensitivities and specificities. The curve represents the summary receiver operating characteristics (ROC) curve. The black box and ROC curve represent the meta-analysis of all eight studies. The grey box and ROC curve exclude the two studies excluded by Andeweg 2014,⁶² which are indicated by grey circles with X's in them.

Staging of Acute Diverticulitis

Only one study evaluated the test accuracy of a clinical classification system to stage acute diverticulitis and reported sufficient data to estimate all test accuracy statistics (e.g., both sensitivity and specificity). However, the study evaluated a staging system that is not commonly used in clinical practice in the United States.

Jurowich 2011 evaluated the Hansen and Stock (H&S) classification system,⁷² which was initially published in 1999 in German only.⁷³ The H&S system does not appear to have been published in English. According to the Jurowich 2011 article,⁷³ it is commonly used in Germany.

The H&S system includes the following categories:

- Type 0 Asymptomatic diverticulosis (not further discussed here)
- Type I Uncomplicated diverticulitis, first episode
 - Potential intestinal wall thickening and/or enhancement of pericolic fatty tissue; sometimes no morphologic features visible on CT
- Type IIA Complicated “phlegmonous diverticulitis”
 - Type I criteria and edema/phlegmonous inflammation, but no free air
- Type IIB Complicated “covered perforation”
 - Type IIA criteria and air inclusions, corresponding with abscesses
- Type IIC Complicated “free perforation”
 - Free air, free intra-abdominal contrast media escape, and/or free fluid
- Type III *Uncomplicated* diverticulitis, recurrent
 - Apparently, the same CT criteria as Type I, but with knowledge of two or more episodes of recurrence (presumably including the current episode)

As suggested by these criteria, the H&S staging system is a “CT-based predictive system,” not a CT-only staging system; it also includes clinical assessment. Furthermore, an unreported number of patients staged as Type IIC (perforated diverticulitis with diffuse peritonitis) did not receive CT imaging, but instead went for immediate emergency surgery. In addition, an unreported number of patients with uncomplicated diverticulitis (Type I) were imaged with ultrasound, not CT.

The final diagnosis (reference standard) was based on operative findings or recovery with conservative therapy (initially diagnosed as Type I or IIA). Patients initially classified as Type IIA who had recovery within 24 hours of conservative therapy were given a final classification of Type I (uncomplicated) diverticulitis. For patients who were reclassified postoperatively as uncomplicated diverticulitis, no distinction was made between Type I (who did not require surgery, per protocol) and Type III (who did require surgery, per protocol).

Given the incomplete assessment by CT, the inclusion of non-CT information in the staging, and the imprecise reference standard, the study was deemed to be of poor methodological quality (to assess CT for staging the severity of acute diverticulitis).

The study evaluated 318 consecutive patients (including 11 patients with acute diverticulitis who had preoperative misdiagnoses of acute appendicitis, incarcerated hernia, or ileus) with acute sigmoid diverticulitis. The patients’ median age was 64 years (range 26 to 97) and 57 percent were men.

Among these patients, 242 underwent surgery; only these patients are included in the test accuracy analyses. Details about the initial and final staging of the evaluated patients and our approach to analyzing the reported data are presented in Appendix D.

As summarized in Table 2, test sensitivity and specificity of the H&S categories varied widely depending on stage and whether one considers each stage as an individual classification or as a maximum or minimum threshold. The largest discrepancy between initial and postoperative staging was among the 83 evaluated patients with Type IIA (“phlegmonous diverticulitis”), 64 percent of whom were misclassified (53% were reclassified to Type IIB, 11% were reclassified to Type I or Type III [the article did not distinguish the two categories]).

The article did not adequately report whether patients who underwent surgery based on initial staging all required the surgery (based on postoperative findings). The study also did not report on the clinical sequelae of patients with Types IIA or IIB diverticulitis who did not undergo recommended surgery.

Table 2. Test accuracy of initial staging, per Jurowich 2011⁷³

Comparison	Stages	Final +	Final -	Sn	Sp	PPV	NPV
Stage vs. all others	III	46	8	78.0	95.6	85.2	93.1
	Not III	13	175	(65.3, 87.7)	(91.6, 98.1)	(74.2, 92.0)	(89.3, 95.6)
	2A	30	53	93.8	74.8	36.1	98.7
	Not 2A	2	157	(79.2, 99.2)	(68.3, 80.5)	(30.6, 42.1)	(95.3, 99.7)
	2B	71	7	58.2	94.2	91.0	68.9
	Not 2B	51	113	(48.9, 67.1)	(88.4, 97.6)	(83.0, 95.5)	(64.1, 73.3)
	2C	27	0	93.1	100	100	99.1
	Not 2C	2	213	(77.2, 99.2)	(98.3, 100)	(NA)	(96.6, 99.8)
Stage max vs. higher stages	III^a	46	8	78.0	95.6	85.2	93.1
	2A or 2B or 2C	13	175	(65.3, 87.7)	(91.6, 98.1)	(74.2, 92.0)	(89.3, 95.6)
	2A or III	86	51	94.5	66.2	62.8	95.2
	2B or 2C	5	100	(87.6, 98.2)	(58.1, 73.7)	(57.3, 68.0)	(89.4, 97.9)
	2B or 2A or III	213	2	100	93.1	99.1	100
	2C	0	27	(98.3, 100)	(77.2, 99.2)	(96.6, 99.8)	(NA)
Stage min vs. lower stages	2A or 2B or 2C^b	175	13	95.6	78.0	93.1	85.2
	III	8	46	(91.6, 98.1)	(65.3, 87.7)	(89.3, 95.6)	(74.2, 92.0)
	2B or 2C^c	100	5	66.2	94.5	95.2	62.8
	III or 2A	51	86	(58.1, 73.7)	(87.6, 98.2)	(89.4, 97.9)	(57.3, 68.0)
	2C^d	27	0	93.1	100	100	99.1
	III or 2A or 2B	2	213	(77.2, 99.2)	(98.3, 100)	(NA)	(96.6, 99.8)

Estimates for test accuracy of different evaluated stages.

The section *Stage vs. all others* compares each individual stage with not that stage (both more and less severe stages).

The section *Stage max vs. higher stages* evaluates each stage and lesser severity stages compared with more severe stages.

The section *Stage min vs. lower stages* evaluates each stage and greater severity stages compared with less severe stages.

Abbreviations: max = maximum, min = minimum, NPV = negative predictive value, PPV = positive predictive value, Sn = sensitivity, Sp = specificity.

^a Note that this is identical to III vs. Not III.

^b Note that this is the inverse of III vs. Not III (or III vs. 2A or 2B or 2C). I.e., Sn and Sp, and PPV and NPV, are flipped.

^c Note that this is the inverse of 2A or III vs. 2B or 2C. I.e., Sn and Sp, and PPV and NPV, are flipped.

^d Note that this is identical to 2C vs. Not 2C.

Key Questions 1b to 1d. Sequelae of CT Imaging

We found only five studies that reported either clinical sequelae related to CT imaging for patients suspected of acute diverticulitis or incidental findings on abdominal CTs performed in the emergency department for acute abdomen. Overall, the studies did not report or analyze clear, clinically relevant results data pertinent to the Key Questions and were deemed to be of poor methodological quality as pertains to reporting of sequelae of CT imaging. In particular, none of the studies compared CT-guided care versus care without CT guidance. Andeweg 2011 reported no funding for their study,⁷⁴ and Shuaib 2014 reported no commercial funding for their study.⁷⁵ The other three studies did not report funding source.⁷⁶⁻⁷⁸ All studies are summarized in Table 3 and Appendix C.

Table 3. CT imaging sequelae and incidental findings

Study, PMID	N	CT Errors	Good Clinical Sequelae	Poor Clinical Sequelae	Incidental Findings
Martín Arévalo 2007, ⁷⁷ 17883294	102	CRC: 2/86 (2.3%) ^a	14/26 spared surgery (that was presumptively indicated by clinical diagnosis) (17% of all) 2/58 received (presumably appropriate) surgery (that was presumptively <i>not</i> indicated by clinical diagnosis) (2.4%)	2/86 missed CRC diagnosis, but unclear that this resulted in actual poor clinical sequelae.	None reported
Salem 2005, ⁷⁶ 16108882	81	1 FN	6 with (incorrect) clinical diagnosis of diverticulitis were correctly diagnosed with other conditions by CT ^b 2 with missed clinical diagnosis of diverticulitis managed correctly after CT ^c 2 mis-staged clinically managed correctly after CT ^d	1 FN (on CT) died prior to surgery ^e	None reported
Andeweg 2011, ⁷⁴ 21346548	287	None reported	NR	No unnecessary surgeries (poor clinical sequelae) were reported	None reported
Kelly 2015, ⁷⁸ 25576049	1155	NR	NR	NR	74 (6.4%) "indeterminate" requiring further workup ^f
Shuaib 2014, ⁷⁵ 24475484	290	NR	NR	NR	9 new g "worrisome" ^h 73 new "indeterminate" ⁱ

Abbreviations: CRC = colorectal cancer, CT = computed tomography, FN = false negative (finding), NR = not reported (no data), PMID = PubMed identifier.

^a 2 erroneous diagnoses of diverticulitis that intraoperatively proved to be sigmoid colorectal cancer complicated by an abscess.

^b Dissecting aortic aneurysm, left adrenal tumor, left pyonephrosis, metastatic colorectal cancer, acute appendicitis, and inflammatory bowel disease.

^c 1 clinically diagnosed with acute abdomen had perforated diverticulitis on CT (managed surgically). 1 clinically diagnosed with intra-abdominal bleeding had (uncomplicated, implicitly) diverticulitis on CT (managed medically).

^d 1 with a small bowel obstruction missed on clinical examination, 1 who did not have a clinically diagnosed perforation.

^e Diagnosis made post-mortem.

^f 24: clinically silent occult neoplasms (pancreas, colorectal, kidney, liver, sarcoma, lung, gallbladder, gastric, gynecologic), 5: <50 years old, 6: deemed early local disease with good potential for curative resection, 7: adrenal adenoma, 5: colorectal polyps, 2: perforated diverticulitis/mass, 1: complex renal cyst, 1: thickening/lesion of lower esophagus, 34: benign clinically insignificant findings.

^g Not previously known per clinical notes or previous imaging studies.

^h Only 3/9 new worrisome incidental findings received a recommendation by radiologist for further workup; all 3 had a change in clinical management based on the CT findings. Of the remaining 6 with no recommendation for further workup, only 2 had a change in clinical management.

ⁱ 23/73 new indeterminate incidental findings received a recommendation by radiologist for further workup; of these 16 had a change in clinical management based on the CT finding. Of the 50 with new indeterminate incidental findings with no recommendation for a further workup, 1 had a change in clinical management.

Key Question 1b. Effects of CT Imaging on Clinical Outcomes and Clinical Management (Good Clinical Sequelae)

Two studies reported specific good clinical sequelae related to abdominal CT imaging of people presenting with clinical diagnoses of acute diverticulitis or acute abdomen, not including implied good clinical sequelae based on accurate diagnosis of diverticulitis (or other cause of acute abdomen).

Martín Arévalo 2007 evaluated 102 adults with clinical diagnoses of acute diverticulitis;⁷⁷ despite vague eligibility criteria. All received abdominal CT, although contrast was used only if an abscess was clinically suspected. Among these 102 patients, 84 were diagnosed with acute diverticulitis by CT imaging, of whom 71 percent had uncomplicated diverticulitis, 10 percent each had small abscesses, large abscesses, or diffuse peritonitis. The authors reported that 14 people were spared surgery among 26 people for whom surgery for complicated diverticulitis was indicated based on clinical criteria (17% of all with diverticulitis). Another 2 patients received surgery that was not indicated based on clinical criteria alone (2.4% of all with diverticulitis); it was implied that the surgeries were appropriate.

Salem 2005 evaluated 211 adults with acute abdomen, 48 of whom had acute diverticulitis (although the diagnostic criteria were not reported).⁷⁶ Among these patients, 81 had abdominal CTs (with contrast)—16 of whom had a final diagnosis of diverticulitis—and 130 did not have CT imaging—32 of whom had a final clinical diagnosis of diverticulitis. The authors report that among those who received CT imaging, 6 had incorrect clinical diagnoses of diverticulitis that were, implicitly, managed correctly due to the CT diagnoses. These patients had, by CT imaging, a dissecting aortic aneurysm, an adrenal tumor, pyonephrosis, metastatic colorectal cancer, acute appendicitis, and inflammatory bowel disease. In addition, two patients were correctly diagnosed with diverticulitis on CT, which had been missed on clinical examination. One of these patients was clinically diagnosed with intra-abdominal bleeding but had diverticulitis that was successfully managed medically. The other patient was clinically diagnosed with “acute abdomen” and was found to have perforated diverticulitis on CT. This patient was managed surgically; it is unclear whether clinical sequelae were altered for this patient. A further two patients had their diverticulitis clinically mis-staged; one had a small bowel obstruction that had been missed on clinical examination and one did not have a perforation that had been diagnosed on clinical examination. The first patient received surgical treatment (although it was not reported what the pre-CT surgical plan was); the second patient was treated medically.

Key Question 1c. Outcomes Related to False Positive or False Negative CT Readings (Poor Clinical Sequelae)

Three studies reported on poor clinical sequelae related to erroneous readings of abdominal CTs. These included the two studies described above (for good clinical sequelae) and a third study of patients hospitalized for acute abdomen.

As noted, Martín Arévalo 2007 evaluated 102 adults with clinical diagnoses of acute diverticulitis;⁷⁷ 84 had final diagnoses of acute diverticulitis, mostly (81%) uncomplicated. The authors reported that two patients had false positive abdominal CTs (for diverticulitis) and were found to have colorectal cancer at surgery. Both had sigmoid colon cancers complicated by an abscess. However, the article does not report whether there were any actual poor clinical sequelae based on the missed CT diagnoses.

Also as noted above, Salem 2005 evaluated 211 adults with acute abdomen, 48 of whom had acute diverticulitis.⁷⁶ The study compared 81 patients who had abdominal CTs (16 with a final

diagnosis of diverticulitis) and 130 who did not have CT imaging (32 with a final diagnosis of diverticulitis). Among the 81 who had a CT, the authors report that one patient had a false negative CT reading (for diverticulitis) who subsequently died. The diagnosis was made on post-mortem examination; although the article did not report on an investigation into the role of the misdiagnosis in the patient's death. Among the 130 people who did not have a CT, no (poor) clinical sequelae or misdiagnoses were noted related to the lack of CT imaging.

Andeweg 2011 evaluated 287 people who were hospitalized with acute abdominal pain who did not require immediate surgery;⁷⁴ although the eligibility criteria were vague. The study was designed to create a predictive algorithm for diagnosis of diverticulitis, not to report on clinical sequelae related to CT imaging. All patients had an abdominal CT for "suspected diverticulitis" or "left lower quadrant pain". In their sample, 124 had acute left-sided diverticulitis, 31 of whom had surgical management. The authors reported that there were no unnecessary surgeries (i.e., no poor clinical sequelae based on CT diagnoses).

Key Question 1d. Clinically Important Incidental Findings

Our search yielded two studies that reported on incidental findings on abdominal CT imaging performed for acute abdomen in the emergency department. None of the three studies discussed for KQ 1c or 1d that reported on clinical sequelae related to CT imaging reported on incidental findings.

Kelly 2015 reported on 1155 patients who received an emergency abdominal CT in the Emergency Department of a tertiary referral hospital.⁷⁸ The study did not report on CT or final diagnoses (including diverticulitis). The authors reported that 74 patients (6.4%) had "indeterminate" findings on CT that required further workup, 34 of which were determined to be "benign, clinically insignificant findings." Of the remaining 40 patients (3.5%), 24 (2.1%) had "clinically silent occult neoplasms": pancreas, colorectal, kidney, liver, sarcoma, lung, gallbladder, gastric, and gynecologic. Five of these patients were younger than 50 years of age and six of the cancers were deemed to be "early local disease with good potential for curative resection". Among the remaining patients, seven had adrenal adenomas, five colorectal polyps, two perforated diverticulitis, one complex renal cyst, and one a thickening/lesion of the lower esophagus. It is unclear why the two patients found to have complicated diverticulitis were classified as having incidental findings on their emergency abdominal CT. The study did not report on downstream clinical sequelae of the incidental findings on CT imaging.

Shuaib 2014 reported on 290 patients who had abdominopelvic CTs for nontraumatic acute abdominal pain in the Emergency Department.⁷⁵ The study did not report on CT or final diagnoses (including diverticulitis). The study described the numbers of patients who had "indeterminate" and "worrisome" findings on CT, how many of these resulted in suggestions by the radiologist for further workup, and how many patients had changes in clinical management. The study reported that 139 patients (48%) had incidental findings, but most were previously known per clinical notes or previous imaging studies. The study reported 9 (3.1%) patients with new worrisome incidental findings. It was not reported what these findings were. For only three of the patients did the radiologist recommend further workup; all three had a change in clinical management due to the worrisome incidental finding. Of the six patients with worrisome CT findings but without a recommendation for further workup, only two had a subsequent change in clinical management. The study further reported that 73 patients (25%) had new worrisome CT findings, for whom 23 received a recommendation for further workup. Of these, 16 had a change in clinical management based on the CT finding. Of the 50 people with a worrisome CT finding

without a recommendation for further workup, only one had a change in clinical management. The study did not report on downstream clinical sequelae of the incidental findings on CT imaging (beyond receiving a workup).

Summary of Evidence Pertaining to CT Imaging

Based on meta-analysis of multiple, consistent studies, there is moderate SoE that CT imaging of patients with suspected acute colonic diverticulitis has very high sensitivity (94%; 95% CI 87% to 97%) and specificity (99.2%; 95% CI 81% to 99.9%). The primary deficiency of studies was that the reference standard was not definitive for most patients (since surgical or colonoscopic diagnoses were not available).

Based on two studies, there is low SoE that abdominal CT imaging may lead to appropriate surgical or medical management and that for some patients, at least, appropriate management might not have occurred without CT imaging. However, neither study compared CT imaging to no imaging.

Based on three studies, there is low SoE regarding poor clinical sequelae related to diverticulitis-related misdiagnoses on CT. The studies did not clearly identify that the poor clinical outcomes were direct consequences of the misdiagnoses (i.e., that better outcomes would have been likely with correct diagnoses).

Based on two studies, there is low SoE that among patients receiving emergency abdominal CTs for nontraumatic acute abdomen in the emergency department incidental findings may not be uncommon. The larger study found that important incidental clinical diagnoses are made on CT. The smaller study found that radiologists do not suggest further workup for most new indeterminate or worrisome incidental findings on CT. Neither study reported on clinical outcomes or sequelae related to the incidental findings. Full evidence profiles are in Table 4.

Table 4. Evidence profile for CT imaging for acute diverticulitis

Topic	No. Studies (Subjects)	Risk of Bias	Consistency	Precision	Directness	Other	Overall SoE	Conclusion statements
CT accuracy to diagnose acute diverticulitis	8 (684)	Moderate ^a	Consistent	Precise	Direct	None	Moderate	Sn 94%, Sp 99%
CT accuracy to stage acute diverticulitis	1 (318)	High	N/A	Precise	Indirect ^b	Sparse	Insufficient	No conclusion
Good clinical sequelae	2 (183)	High	Consistent	Precise	Indirect ^c	Sparse	Low	CT resulted in appropriate management of diverticulitis
Poor clinical sequelae	3 (470)	High	Consistent	Imprecise	Indirect ^d	None	Low	Misdiagnoses on CT that result in poor clinical outcomes may be rare
Incidental findings	2 (1445)	High	Consistent	Precise	Indirect ^e	None	Low	Incidental findings are common, although their clinical significance is unclear

Abbreviations: CT = computed tomography, N/A = not applicable, Sn = sensitivity, Sp = specificity, SoE = strength of evidence.

^a Per Laméris 2008,⁶¹ based on QUADAS tool.⁷¹

^b Evaluated uncommonly applied staging system that incorporates non-CT criteria.

^c Unclear that good sequelae would not have occurred without CT. No clear concept of good clinical sequelae in articles.

^d Unclear that poor sequelae would not have occurred without CT. No clear concept of poor clinical sequelae in articles.

^e The clinical course of sequelae of the incidental findings was poorly reported and analyzed.

Key Question 2. Medical Management of Acute Diverticulitis

Key Question 2a. Outpatient Versus Inpatient Management of Acute Diverticulitis

Key Points

- Adverse outcomes were rare, regardless of outpatient or inpatient management: death 0.2%, emergency surgery 1.3%. The evidence is insufficient regarding comparison of management settings due to sparse and imprecise data.
- Outpatient treatment led to inconsistent findings on treatment failure in two studies, with no statistically significant difference observed in one randomized controlled trial (RCT) and a benefit in favor of *outpatient* care (despite adjustment for patient morbidity) in one nonrandomized comparative study (NRCS) (insufficient SoE).
- With low SoE, studies found no evidence of differences in rates of long-term diverticulitis recurrence or elective surgery based on management setting.

Findings Pertaining to Outpatient Versus Inpatient Management

One small RCT³⁰ and five NRCSs⁷⁹⁻⁸³ evaluated outpatient treatment protocols compared to inpatient care for the management of an acute uncomplicated diverticulitis episode. With the exception of Moya 2012, all the NRCSs were retrospective. The average age was similar across studies, with participants in their mid to late 50s and between 37 and 64 percent being male. Although we sought to include only NRCS with adjusted analyses, we made some exceptions, providing justifications. The RCT reported nonindustry funding; funding for all five NRCSs was not reported. Appendix C Table C-2a-1 provides detailed descriptions of the six studies.

The RCT (Biondo 2014) enrolled 132 participants with uncomplicated diverticulitis who were responsive to initial treatment in the ED (i.e., improvement of pain and fever), were able to tolerate oral intake, and were willing to continue treatment at home under supervision. Initial treatment in the emergency department (ED) included a first dose of antibiotics (IV amoxicillin/clavulanate or ciprofloxacin).

The prospective NRCS (Moya 2012) studied adults with uncomplicated diverticulitis who could tolerate oral intake and had adequate family and social support to be discharged to outpatient care. The study used a pre-post interrupted time series design around a hospital policy change regarding discharging patients. Although not formally adjusted, we included this study since it is unlikely that patients in each time period systematically differed from each other and no differences were observed for baseline predictors.

The remaining four NRCSs (Bolkenstein 2018, Lorente 2013, Ünlü 2013, and Joliat 2017) used a retrospective design to compare outpatient to inpatient treatment protocols. Bolkenstein 2018 studied adults with a first episode of uncomplicated diverticulitis who did not receive antibiotics (2 weeks prior to, or 24 hours after presentation to the hospital). For a single outcome, the study adjusted for the fact that patients in the inpatient group tended to be sicker than those discharged to outpatient care at baseline (i.e., higher levels of C-reactive protein [CRP], white blood cell counts, and symptoms of fever and nausea).

We derived long-term outcomes (average 17- to 60-month followup) from three NRCSs that were unadjusted despite baseline imbalances. Patients treated as inpatients were generally sicker.

We determined that the baseline imbalances are relatively unlikely to confound outcomes more than a year later. The first of these studies, Lorente 2013, studied adults with uncomplicated diverticulitis who met the hospitals' criteria to be treated at home (i.e., tolerated oral intake, adequate family and social support, absence of comorbidities). Ünlü 2013 studied adults treated for their first episode of uncomplicated diverticulitis and compared outcomes of those discharged to outpatient care within 24 hours of presenting to the hospital to those admitted to inpatient care. Joliat 2017 studied adults with uncomplicated or mild complicated diverticulitis and assessed long-term outcomes via a patient survey.

The RCT was low risk of bias for randomization, blinding of outcome assessors (due to objective nature of the outcomes), and incomplete outcome data but high risk of bias for blinding of participants and personnel, and unclear risk of bias for selective outcome reporting (Appendix C Table C-2a-2). The NRCSs had high risk of bias for confounding, as all but one study reported crude event proportions rather than an effect estimate adjusted for important confounders (full risk of bias in Appendix C Table C-2a-3). The NRCSs had low risk of bias for participant selection with the exception of one study (Joliat 2017) that recruited patients and assessed their outcomes by means of a survey. Full study results and risk of bias assessment are in Appendixes C and D.

Mortality

Death was rare. Only two of 1009 (0.2%) died due to acute diverticulitis across three studies (Biondo 2014, Bolkenstein 2018, and Ünlü 2013).

Treatment Failure

The RCT (Biondo 2014) and the adjusted NRCS (Bolkenstein 2018) reported treatment failure (Table 5).^{30, 83}

The RCT (Biondo 2014) found that treatment failure occurred at similar rates between inpatient- and outpatient-treated groups and was uncommon (~5%). Their findings yielded an imprecise comparison (odds ratio [OR] 0.74, 95% CI 0.16 to 3.43). Treatment failure was defined as persistence, increase, or recurrence of abdominal pain and/or fever, inflammatory bowel obstruction, need for radiological abscess drainage or immediate surgery due to complicated diverticulitis, need for hospital admission, and mortality during the first 60 days after discharge.

In contrast, the adjusted NRCS (Bolkenstein 2018) found that patients treated as outpatients had significantly fewer treatment failures compared to inpatients (adjusted OR 0.41, 0.20 to 0.83). Treatment failure was defined as (re)admittance, mortality, complications (perforation, abscess, colonic obstruction, urinary tract infection, pneumonia) or need for antibiotic treatment, operative intervention, or percutaneous abscess drainage within 30 days after initial presentation.

Table 5. Outpatient versus inpatient management: Treatment failure

Outcome	Study Year PMID	Intervention	Followup, mo	n/N (%)	OR (95% CI)	Reported P-value
Treatment failure	Biondo 2014, ³⁰ 23732265	Outpatient	2	3/66 (4.5)	0.74 (0.16, 3.43) ^a	0.62
		Inpatient		4/66 (6.1)		
	Bolkenstein 2018, ⁸³ 29679152	Outpatient	≤24	12/264 (4.5)	0.41 (0.20, 0.83) ^b (adjusted ^c)	0.01
		Inpatient		34/301 (11.3)		

Abbreviations: CI = confidence interval, NR = not reported, OR = odds ratio, PMID = Pubmed identifier.

- ^a Defined as persistence, increase, or recurrence of abdominal pain and/or fever, inflammatory bowel obstruction, need for radiological abscess drainage or immediate surgery due to complicated diverticulitis, need for hospital admission, and mortality during the first 60 days after discharge.
- ^b Defined as (re)admittance, mortality, complications (perforation, abscess, colonic obstruction, urinary tract infection, pneumonia) or need for antibiotic treatment, operative intervention, or percutaneous abscess drainage within 30 days after initial presentation.
- ^c Adjusted for sex, age, American Society of Anesthesiologists score > 2, no rebound tenderness, C-reactive protein (mg/L).

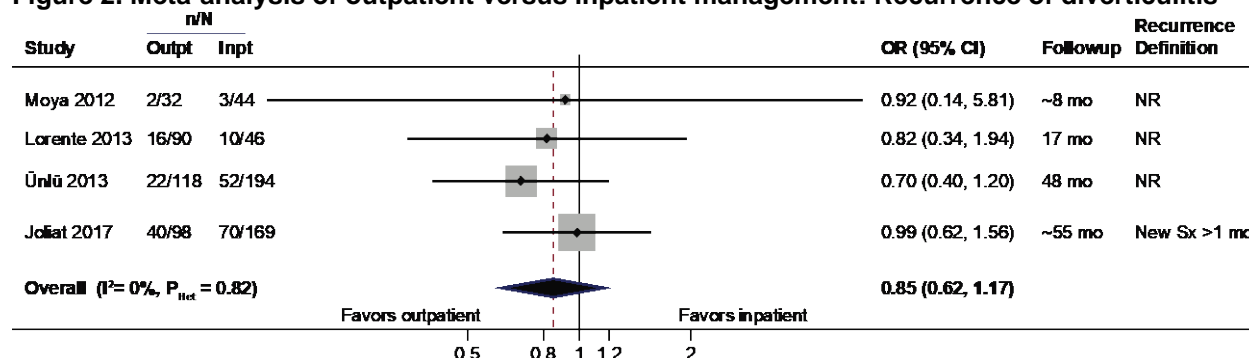
Emergency Surgery

The RCT (Biondo 2014) and the pre-post study (Moya 2012) both reported that no patients (of 208 total) required emergency surgery, regardless of treatment assignment.^{30, 79} Given the small numbers of patients reported on, however, this suggests a relatively wide 95 percent confidence interval (0% to 3.7%).

Recurrence

The four NRCSSs that reported unadjusted analyses of recurrence had average followup ranging from approximately 8 to 55 months.⁷⁹⁻⁸² Recurrence rates across the studies, mostly undefined, tracked with average followup time (6.6% at about 8 months,⁷⁹ 19% at 17 months,⁸⁰ 24% at 48 months,⁸² and 41% at about 55 months⁸¹). By meta-analysis (Figure 2), the summary OR showed no evidence of a difference in recurrence rates between outpatient and inpatient management (summary OR 0.85, 95% CI 0.62 to 1.17). Although, in these unadjusted analyses, it was likely that patients treated as inpatients had more severe episodes of acute diverticulitis, there was no suggestion that these patients were more likely to have recurrence in the long-term.

Figure 2. Meta-analysis of outpatient versus inpatient management: Recurrence of diverticulitis

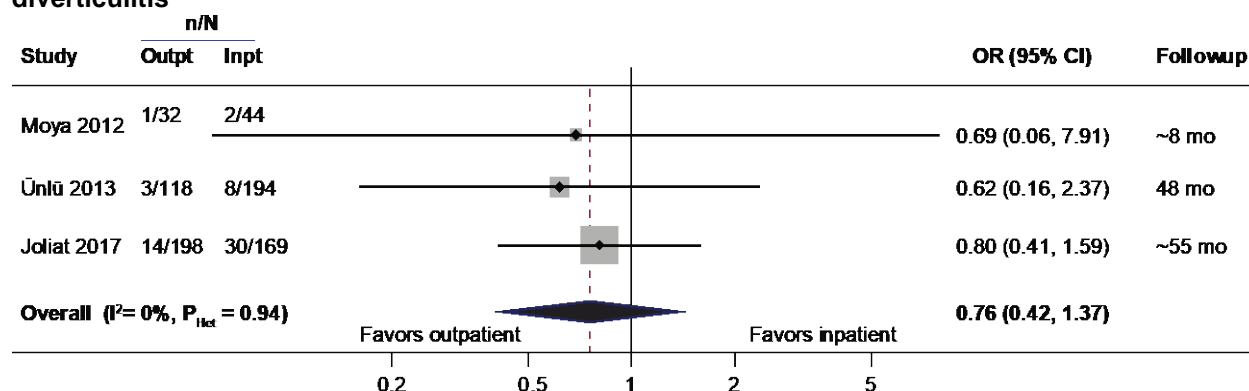


Abbreviations: CI = confidence interval, I² = measure of statistical heterogeneity (% of heterogeneity not due to random chance), Inpt = inpatient management, mo = months, NR = not reported, OR = odds ratio, Outpt = outpatient management, P_{Het} = statistical heterogeneity P value, Sx = symptoms (of acute diverticulitis).

Elective Surgical Treatment

In three NRCSSs, with an average followup ranging from approximately 8 to 55 months, there was no statistically significant difference in elective surgical treatment between outpatient and inpatient management across studies.^{79, 81, 82} Two studies had elective surgery rates of 4 percent at about 8 months (Moya 2012) and 48 months (Ünlü 2013); in the third study, 16 percent had elective surgery during about 55 months of followup. By meta-analysis (Figure 3), the summary OR showed no evidence of a difference in rates of elective surgery between outpatient and inpatient management (summary OR 0.76, 95% CI 0.42 to 1.37).

Figure 3. Meta-analysis of outpatient versus inpatient management: Elective surgery for diverticulitis



Abbreviations: CI = confidence interval, I² = measure of statistical heterogeneity (% of heterogeneity not due to random chance), Inpt = inpatient management, mo = months, NR = not reported, OR = odds ratio, Outpt = outpatient management, P_{Het} = statistical heterogeneity P value.

Quality of Life

The RCT (Biondo 2014) reported on quality of life and found no difference in physical (P=0.59) and mental health (P=0.99) scales of the Short Form-12 (SF-12) between the outpatient and inpatient arms at 2 months (Table 6).³⁰

Table 6. Outpatient versus inpatient management: Quality of life

Study Year PMID	Outcome	Time	Arm	N	Mean (SD)	Difference	Reported P value
Biondo 2014, ³⁰ 23732265	SF-12 physical	2 mo	Outpatient	66	50.3 (7.2)	0.7 (-2.0, 3.4)	0.59
			Inpatient	66	49.6 (8.7)		
	SF-12 mental	2 mo	Outpatient	66	53.0 (8.6)	0.4 (-2.7, 3.5)	0.99
			Inpatient	66	52.6 (9.5)		

Abx = antibiotic, CI = confidence interval, ED = emergency department, IV = intravenously, mo = month, NR = not reported, PMID = Pubmed identifier, RCT = randomized controlled trial, SD = standard deviation, wk = week.

Summary of Evidence Pertaining to Outpatient Versus Inpatient Management

For patients with uncomplicated diverticulitis, the evidence comparing outpatient versus inpatient management is inconclusive (insufficient) about the difference among in risk of death, treatment failure, need for emergency surgery, and quality of life (Table 7), but it does not suggest increased risk of adverse outcomes with outpatient management. With low SoE, the studies suggest there may be no differences in rates of long-term recurrence or elective surgery regardless of outpatient versus inpatient management.

Table 7. Evidence profile for outpatient versus inpatient management of uncomplicated acute diverticulitis

Outcome	No. Studies (Subjects)	Risk of Bias	Consistency	Precision	Directness	Other	Overall SoE	Conclusion statements
Death	3 (1009)	Moderate	Consistent	Imprecise	Direct	Sparse	Insufficient	No conclusion regarding outpatient vs. inpatient. Rare event
Treatment failure	2 (697)	Moderate	Inconsistent	Unclear	Direct	None	Insufficient	No conclusion regarding outpatient vs. inpatient
Emergency surgery	2 (208)	Moderate	Consistent	Imprecise	Direct	Sparse	Insufficient	No conclusion regarding outpatient vs. inpatient. Rare event
Recurrence (~8-55 mo)	4 (791)	High	Consistent	Precise	Direct	Unadjusted	Low	No difference found unadj OR 0.85 (0.62, 1.17)
Elective surgery (~8-55 mo)	3 (655)	High	Consistent	Precise	Direct	Unadjusted	Low	No difference found unadj OR 0.76 (0.42, 1.37)
Quality of life	1 (132)	Moderate	N/A	Precise	Direct	Sparse	Insufficient	No conclusion regarding outpatient vs. inpatient

Abbreviations: N/A = not applicable, OR = odds ratio (with 95% confidence interval), SoE = strength of evidence, unadj = unadjusted.

Key Question 2b. Antibiotic Treatment for Acute Diverticulitis

Key Points

- Overall, for patients with uncomplicated or mild diverticulitis, the evidence does not support that there are differences in most clinically important outcomes between either use of antibiotics or not or in choice of antibiotic regimens
 - Specifically, studies found no evidence of differences in pain symptoms, length of hospital stay, risk of recurrence, and quality of life (low SoE). The risk of surgery at 6 to 12 months after the episode of acute diverticulitis may be lower among patients who received antibiotics, but the finding was highly nonsignificant.
 - Evidence for comparative rates of death, treatment failure, diverticulitis-related morbidities, rehospitalization, and adverse events is insufficient to make conclusions, largely due to sparse events.
- Although seven studies have compared antibiotic regimens, each evaluated a different comparison (of antibiotics, durations, or routes); therefore, the data are overall insufficient. However, in general, no evidence of differences in clinical outcomes were found for different regimens.

Findings Pertaining to Antibiotic Treatment

Overall, 13 studies addressed the use of antibiotics in patients with acute diverticulitis. These included nine RCTs and four NRCSs. All NRCSs reported multivariable-adjusted comparisons. From the NRCSs, we include only those short-term outcomes that were analyzed by multivariable regression. To be consistent with other reviewed topics, we allowed unadjusted analyses of long-term outcomes under the assumption that inherent differences between those patients who received different regimens (in NRCSs) would not be confounded with long-term outcomes.

Across the studies, there were comparisons of antibiotics and no antibiotics (including placebo) and of different antibiotic regimens (including either different antibiotics or different durations of treatment).

One RCT (Schug-Pass 2010) was industry-funded. Four RCTs and one NRCS were funded by nonindustry sources, including the AVOD (Antibiotika Vid Okomplicerad Divertikulit), DIABOLO (Diverticulitis: Antibiotics or Close Observation), and STAND (Selective Treatment with Antibiotics for Non-complicated Diverticulitis) trials, the RCT by Ribas 2010, and the NRCS by Hjern 2007. The other studies did not report industry funding.

In contrast with other sections, because of the large number of comparisons and outcomes evaluated regarding antibiotic treatment, the summary tables (with basic results) are located at the start of Appendix D.

Antibiotics Versus No Antibiotics

Four RCTs in eight reports^{32, 33, 84-89} and two NRCSs^{90, 91} compared antibiotic treatment with either no antibiotics or placebo in patients with acute, uncomplicated diverticulitis. Appendix C Tables C-2b-1 to C-2b-5 describe the characteristics of the six studies. The numbers of enrolled participants across the studies comparing antibiotics with antibiotics or placebo ranged from 125 to 623. The average ages of participants ranged from 37 to 62 years.

STAND was the only one of the four trials that was blinded with a placebo comparator;⁸⁸ the other three were open-label with comparisons to no antibiotics. In the STAND trial (which to date is reported in a prepublication manuscript), patients assigned to the antibiotic treatment group received 5 days of oral amoxicillin/clavulanate; at the discretion of the surgical team an unreported number of these patients were treated initially with up to 2 days of IV cefuroxime and oral metronidazole (for a total of 5 to 7 days of treatment, most of which was received outpatient). All patients, at enrollment, had CT-diagnosed Hinchey stage 1a uncomplicated diverticulitis. The study reported short-term outcomes (up to 30 days after discharge).

The other three RCTs comparing antibiotic treatment with no antibiotics were AVOD, DIABOLO, and Kim 2019. In AVOD, the treating clinicians were allowed to choose the antibiotics to be administered. All patients had left-sided diverticulitis; about 40 percent had recurrent diverticulitis. Broad-spectrum antibiotics were commonly used, and treatment was initiated with IV followed by oral antibiotics. All patients had acute lower-abdominal pain with tenderness, fever, and increased white blood cell (WBC) counts or CRP.

Kim 2019 compared a combination of IV cephalosporin and metronidazole with placebo in patients with modified Hinchey stage 1a (per Wasvary,¹⁹ uncomplicated) *right-sided diverticulitis* (the study was conducted in South Korea, where right sided diverticulitis is predominant). Because of the demographic, clinical, and prognostic differences between left- and right-sided diverticulitis,^{92, 93} further descriptions of the Kim 2019 study are separated out and findings are not combined with findings of studies of left-sided diverticulitis.

The DIABOLO trial compared IV amoxicillin/clavulanate with no antibiotics in patients with modified Hinchey stage 1a or 1b (per Wasvary,¹⁹ uncomplicated or complicated with pericolic or mesenteric abscess <5 cm) or “mild” left-sided acute diverticulitis (per Ambrosetti criteria²⁰). For all participants, this was their first episode of diverticulitis.

In addition, an individual-patient data meta-analysis (IPD MA) of the AVOD and DIABOLO trials was also recently conducted.⁹⁴ The results of this analysis are also reported here.

The two NRCSs (Hjern 2007 and de Korte 2012) compared antibiotic treatment with no antibiotics for a minimum of 7 days. Hjern 2007 evaluated a combination of IV cephalosporin and metronidazole, followed by oral quinolone and metronidazole. de Korte 2012 was a multicenter NRCS, in which antibiotic regimens differed across centers. All patients in both NRCSs had acute mild sigmoid (left-sided) diverticulitis that had been treated conservatively. In Hjern 2007 about 30 percent had a previous episode of diverticulitis. Such patients were included in the de Korte 2012 study, but the numbers were not reported.

Details of the risk of bias assessment for all studies are in Appendix C. All four RCTs had adequate sequence generation and allocation concealment. STAND blinded participants, providers, and outcome assessors, but AVOD, DIABOLO, and Kim 2019 did not. All four RCTs had low levels of loss to followup. Both the NRCSs adjusted for possible confounding and had low risk of bias in selection of participants into the study, but the outcome assessors were not masked. Both NRCSs had low levels of loss to followup.

Mortality

Three trials (STAND, AVOD, and DIABOLO) reported on mortality (Appendix D Table D-2b-1). All estimates were imprecise or near imprecise. In DIABOLO, diverticulitis-mortality at 24 months was uncommon (0.8%, total), thus the comparison between groups was imprecise (OR 0.33, 95% CI 0.03 to 3.15). In AVOD, only one of 623 patients (total) died at 30 days, but in very long-term followup (11 years), about 10 percent of patients died in both groups (OR 1.06,

95% 0.60 to 1.86). STAND reported mortality at only 30 days. One patient in the antibiotics arm died of a non-diverticulitis related event (stroke with aspiration pneumonia).

Treatment Failure

Two RCTs reported on treatment failure, but one was conducted in patients with left-sided and one in patients with right-sided diverticulitis, and each defined the outcome differently (Appendix D Table D-2b-1). DIABOLO reported recovery as return to normal bowel function at 6 months, which we inverted for treatment failure. Patients with first episode of left-sided diverticulitis treated with amoxicillin/clavulanate had nonsignificantly lower rates of treatment failure than patients not treated with antibiotics (OR 0.61, 95% CI 0.33 to 1.13). Median times to recovery in the two groups were 12 days (interquartile range [IQR] 7 to 30) and 14 days (IQR 6 to 35), respectively, which were not significantly different.

The IPD MA of DIABOLO and AVOD redefined outcomes in the AVOD trial to analyze “ongoing diverticulitis” within 3 months of treatment.⁹⁴ The combined rate of ongoing diverticulitis was nonsignificantly lower with antibiotics (5.0%) than no antibiotics (7.2%, $P=0.062$, where the threshold for statistical significance was set at 0.025 to account for multiple testing).

Kim 2019 defined treatment failure as nonrecovery and/or readmission after 10 days of treatment. In patients with right-sided diverticulitis, the comparison of treatment failure between combination cephalosporin and metronidazole and placebo was imprecise (OR 0.34, 95% CI 0.03 to 3.35).

The STAND trial also reported on unplanned procedural interventions; however, neither intervention was related to a failure of antibiotics, per se, for uncomplicated diverticulitis. One patient (assigned to antibiotics) was initially misdiagnosed on CT and subsequently received surgery for complicated diverticulitis. A second patient (also assigned to antibiotics) developed pneumonia with effusion, which required drainage.

Length of Hospital Stay

All four RCTs reported on length of hospital stay (Appendix D Table D-2b-2). The three RCTs of patients with left-sided diverticulitis (STAND, AVOD, and DIABOLO) had somewhat conflicting findings. AVOD found a mean difference (MD) of 0 days. STAND found a statistically nonsignificant shorter median stay with antibiotics than placebo (−5.9 hours, IQR −15.5 to 3.7). DIABOLO found a statistically significantly shorter length of stay in the antibiotics group compared with the no antibiotics group (2 vs. 3 days, $P=0.006$). Across studies, the summary difference between groups was nonsignificant, but nominally favored antibiotics (−7.7 hours, 95% CI −20.2 to 4.8; $I^2=52\%$). The conclusion of the IPD MA also nominally favored the no antibiotics group: median 3 days (antibiotics) versus 2 days (no antibiotics), $P=0.037$ (which was considered to be statistically nonsignificant to account for multiple testing).⁹⁴

The RCT of right-sided diverticulitis (Kim 2019) found a mean difference (MD) of 0 days between antibiotics versus placebo.

Rehospitalization

STAND and DIABOLO reported on the outcome of rehospitalization (Appendix D Table D-2b-1). STAND reported *more* rehospitalizations at 1 week in those treated with antibiotics (6.0% vs. 1.1%, $P=0.07$), but no significant difference at 1 month (6.0% vs. 10.6%; OR 0.53, 95% CI 0.17 to 1.62). DIABOLO reported both rehospitalization for diverticulitis and, separately,

rehospitalization for diverticulitis-related complications, at various time-points. No statistically significant differences in rate of rehospitalization were found at 6 and 24 months, although both estimates tended to favor amoxicillin/clavulanate versus placebo (OR 0.64, 95% CI 0.39 to 1.05 at 6 months; OR 0.71, 95% CI 0.44 to 1.15 at 24 months).

Surgery for Diverticulitis

Two RCTs reported on the outcome of having elective surgery for diverticulitis (6 to 12 months later) (Appendix D Table D-2b-1 to D-2b-3). DIABOLO focused on elective surgery at 6 months and reported an OR of 0.36 (95% CI 0.10 to 1.38) comparing amoxicillin/clavulanate with no antibiotics. AVOD focused on sigmoidectomy at 12 months and reported an OR of 0.33 (95% CI 0.07 to 1.63) comparing antibiotic treatment with no antibiotics. The IPD MA of the two trials,⁹⁴ found no statistically significant difference in sigmoid resection rates at 1 month (P=0.82) or approximately 1 year (P=0.21).

Recurrence

All five studies reported on recurrence of diverticulitis; two within 12 months (short-term recurrence) and four beyond 12 months (long-term recurrence) (Appendix D Table D-2b-1).

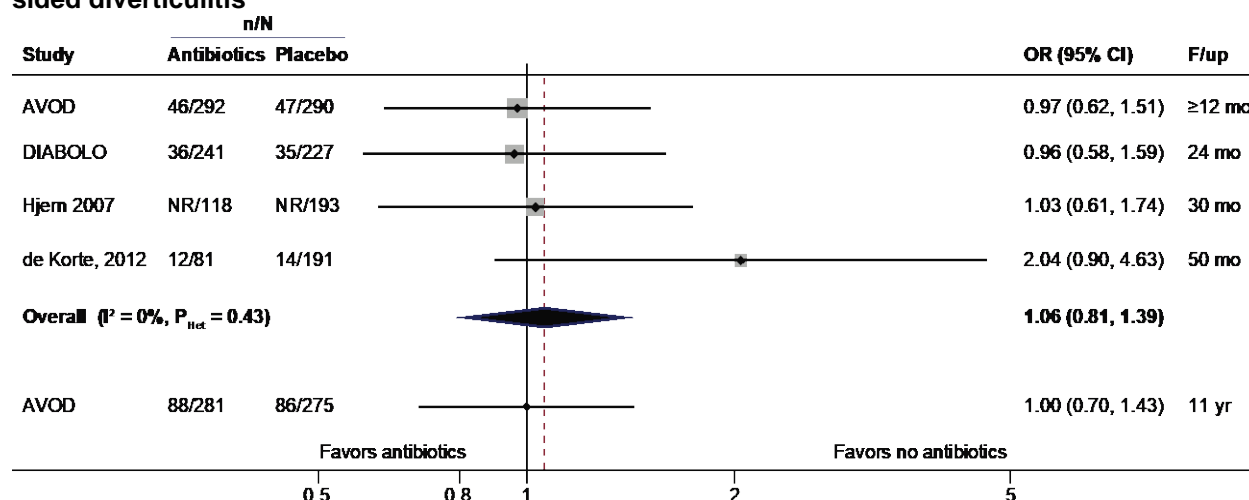
One RCT (DIABOLO) reported recurrence at 6 months. The between-group effect size was imprecise and near the null. In this trial, all participants had no prior episodes of diverticulitis.

Two RCTs (AVOD and DIABOLO) and two NRCSs (Hjern 2007 and de Korte 2012) reported on long-term (≥ 12 months) recurrence in patients with left-sided diverticulitis (Figure 4). Each study had an imprecise comparison, but across studies, the summary OR for recurrence was 1.06 (95% CI 0.70 to 1.43; $I^2=0\%$), suggesting no evidence of a difference in the rate of long-term recurrence with or without antibiotics. Each of these trials included participants with and without prior episodes of diverticulitis. The IPD MA of AVOD and DIABOLO also concluded no significant difference in recurrence rates (9.6% [antibiotics] vs. 8.6%, P=0.61).⁹⁴

AVOD also reported that long-term recurrence at 11 years was similar between patients with or without antibiotics (OR 1.00, 95% CI 0.70 to 1.43).

The RCT of right-sided diverticulitis (Kim 2019) reported diverticulitis at 6 or more weeks and found a between-group effect size was imprecise and near the null.

Figure 4. Meta-analysis of antibiotics versus no antibiotics/placebo: Long-term recurrence of left-sided diverticulitis



Abbreviations: CI = confidence interval, F/up = Follow up, OR = odds ratio, P_{het} = P value of test for statistical heterogeneity.

Diverticulitis-Related Morbidities

Two RCTs (AVOD and DIABOLO) described diverticulitis-related morbidities, such as abscess, fistula, stenosis, and obstruction (Appendix D Table D-2b-1). Both studies reported that these morbidities occurred in 3 percent of patients or fewer, regardless of intervention. No evidence of differences with or without antibiotic treatment was evident, although in AVOD, 0.9 percent of patients receiving placebo developed abscesses as opposed to none of those on antibiotics ($P=0.08$). The IPD MA found no statistically significant differences in episodes of complicated diverticulitis within 1 month ($P=0.20$) or approximately 1 year ($P=0.079$).⁹⁴ However, at end of followup (~1 year), the rate of complications were about double in the no antibiotics groups (4.0%) than the antibiotic treatment groups (2.1%).

Pain or Tenderness

Three RCTs reported on pain or tenderness outcomes (Appendix D Table D-2b-2).

Regarding short-term pain, STAND (24 hours) and AVOD (1 to 5 days) both reported no significant differences in acute pain by visual analogue scale (VAS). However, AVOD reported a small, statistically significant *worse* tenderness score with antibiotic treatment (MD 0.2, 95% CI 0.01 to 0.39; on a 4-point scale). DIABOLO also found no difference in pain, assessed as experiencing pain of at least 4 on VAS within 10 days (OR 0.99, 95% CI 0.60 to 1.46).

In the long term, AVOD reported on three types of pain. All effect sizes were imprecise, including likelihood of severe periodic pain at 12 months, and chronic pain at both 12 months and 11 years.

Quality of Life

Two RCTs reported on quality of life at various time points (Appendix D Table D-2b-2).

DIABOLO reported mean quality of life scores over 3, 6, 12, and 24 months, with adjustment for baseline scores, using three health-related quality of life instruments: the EuroQoL-5D, the Short Form-36 (SF-36), and the Gastrointestinal Quality of Life Index (GIQLI). For each instrument and at each time point, quality of life was similar when comparing combination amoxicillin/clavulanate with no antibiotic use.

AVOD reported quality of life at 11 years of followup using the EuroQoL-5D. However, the items in the tool were rare events among the patients, so evaluations each of the five domains were imprecise (anxiety/depression, mobility, pain/discomfort, self-care, and usual activities).

Adverse Events

Only AVOD reported on adverse events (Appendix D Table D-2b-10). They reported an imprecise estimate of differences in “any adverse event,” which actually occurred *more* frequently among those on placebo.

Heterogeneity of Treatment Effects (Subgroup Differences)

Only the IPD MA evaluated potential differences in effectiveness of antibiotic treatment (vs. no antibiotics) across subgroups.⁹⁴ To increase power, the analysis evaluated the composite outcome “ongoing or complicated diverticulitis or sigmoid resection.” However, analyses of interactions between antibiotic treatment and pain scores at presentation, white blood cell count at presentation, and primary (vs. recurrent) diverticulitis were all highly imprecise, with no indication about whether antibiotics or more (or less) effective in any subgroup.

Comparisons Between Various Antibiotic Regimens

Appendix D Tables D-2b-1 to D-2b-3 describes the characteristics of the seven studies that compared various antibiotic regimens. These included five RCTs (Kellum 1992,⁹⁵ Ridgway 2009,⁹⁶ Ribas 2010,⁹⁷ Schug-Pass 2010,³¹ and Park 2019⁹⁸) and two NRCSs (Scarpa 2015⁹⁹ and Etzioni 2010¹⁰⁰). Comparisons were either between antibiotics (or combinations of antibiotics), between different routes of administration of the same antibiotic(s), or between different doses of the same antibiotic(s). As for the comparison of antibiotics versus placebo, results from the Park 2019 RCT are separated out and not combined with evidence pertaining to left-sided diverticulitis.

Each study evaluated a different comparison of antibiotic regimens. They compared:

- Kellum 1992 (RCT): combination gentamicin and clindamycin vs. cefoxitin
- Ridgway 2009 (RCT): combination ciprofloxacin and metronidazole, IV vs. oral
- Ribas 2010 (RCT): amoxicillin/clavulanate, IV then oral vs. IV only
- Schug-Pass 2010 (RCT): ertapenem, 4 days vs. 7 days
- Scarpa 2015 (NRCS): IV antibiotics (various), ≤ 5 days vs. 6-14 days
- Etzioni 2010 (NRCS): two comparisons
 - combination fluoroquinolone and metronidazole vs. other antibiotics
 - any antibiotic: <10 days, 10-13 days, and ≥ 14 days
- Park 2019 (RCT of right-sided diverticulitis): combination cephalosporin and metronidazole, 1 day vs. 4 days

All RCTs and NRCSs enrolled patients with image-proven acute diverticulitis. Kellum 1992, Ribas 2010, Schug-Pass 2010, and Etzioni 2010 included all patients with diverticulitis. Ridgway 2008 and Scarpa were restricted to patients with uncomplicated (Hinchey I¹⁸ or modified Hinchey 0 [clinically mild] or Ia [confined inflammation]²¹) diverticulitis. Park 2019 included patients with right-sided diverticulitis exclusively (in South Korea).

Appendix C includes the findings of our assessment of risk of bias in all the RCTs and NRCSs. Four RCTs (Kellum 1992, Ridgway 2009, Ribas 2010, and Park 2019) used appropriate methods for random sequence generation and allocation concealment, while one RCT (Schug-Pass 2010) was unclear on these details. Among the RCTs, only Park 2019 blinded patients. All five RCTs had low levels of loss to followup. Among the NRCSs, Etzioni 2010 conducted appropriate adjustment for potential confounding, but Scarpa 2015 reported only unadjusted analyses. Thus, we included only long-term outcomes from Scarpa 2015 (>12 month recurrence). Both NRCSs had low risk of bias in selection of participants into the study and had low levels of loss to followup.

The numbers of participants enrolled in the RCTs and NRCSs ranged from 50 to 176. The average ages of the patients ranged from 41 to 68 years. Ribas 2010, an RCT, reported that 32 percent of participants had experienced previous episodes of diverticulosis. Other studies either did not report on prior episodes or excluded patients with prior episodes.

Treatment Failure

Two RCTs (Ribas 2010 and Ridgway 2008) and one NRCS (Etzioni 2010) reported on treatment failure in patients with left-sided diverticulitis, but definitions of the outcome differed. In all studies, comparisons between antibiotic regimens were imprecise with OR estimates close to 1.00 (Appendix D Tables D-2b-1 to D-2b-3). Ribas 2010 defined treatment failure as persistent pain (within 8 days) or not getting discharged on the expected day. Ridgway 2008 defined treatment failure as readmission within 30 days of completing antibiotic treatment. The

Etzioni 2010 NRCS defined treatment failure as either nonelective hospitalization or evaluation in an emergency department within 60 days.

The RCT of right-sided diverticulitis (Park 2019) defined treatment failure as readmission within 30 days of completing antibiotic treatment. The comparison between 1- and 4-day combination cephalosporin and metronidazole provided an imprecise estimate of differences in treatment failure, with the OR estimate close to 1.00.

Surgery for Diverticulitis

Two RCTs (Kellum 1992 and Schug-Pass 2010) reported on the outcome of surgery for diverticulitis (Appendix D Table D-2b-1). In Kellum 1992, 6 of 30 patients on cefoxitin had surgery after 6 weeks, while none of 21 patients on combination gentamicin and clindamycin did, but due to the overall small number of patients the estimate of OR was nonsignificant and near imprecise (OR 11.4, 95% CI 0.61 to 215). The comparison between 7- and 4-day courses of ertapenem for up to 12 months elective surgery by Schug-Pass 2010 was also near-imprecise, but nominally favoring the shorter, 4-day, course (OR 1.31, 95% CI 0.57 to 3.04).

Length of Hospital Stay

One RCT (Schug-Pass 2010) reported that patients on a 7-day course of ertapenem had a longer mean hospital or intensive care unit stay than patients on a 4-day course (9.7 vs. 7.8 days; MD 1.9 days, 95% CI 0.70 to 3.10) (Appendix D Table D-2b-2).

Recurrence of Diverticulitis

One RCT (Schug-Pass 2010) and one NRCS (Scarpa 2015) reported on the outcome of recurrence of diverticulitis, both at 1 year and later (Appendix D Table D-2b-1). All comparisons, though, were imprecise.

Diverticulitis-Related Morbidities

Schug-Pass 2010 reported on rates of abscesses, interenteric fistulas, and postinflammatory stenoses at 1 year comparing patients who had received 7-day versus 4-day courses of ertapenem (Appendix D Tables D-2b-1 to D-2b-3). Rates of each morbidity were less than 3 percent and were similar between the groups.

Pain or Tenderness

Ridgway 2008 reported that Wexford tenderness scores at 3 days were similar between patients who had received IV and oral combinations of ciprofloxacin and metronidazole (MD -0.06, 95% CI -0.50 to 0.38; on a 0 to 4 scale) (Appendix D Tables D-2b-1 to D-2b-3).

Adverse Events

Schug-Pass 2010 reported on the outcomes of any adverse event, serious adverse events, major allergic reactions, and headaches within 12 months, comparing patients who had received 7-day and 4-day courses of ertapenem (Appendix D Table D-2b-3). Rates of each outcome were 5 percent or fewer between groups.

Summary of Evidence Pertaining to Antibiotic Treatment

Despite there being 13 comparative studies overall, and six studies specifically comparing use of antibiotics to no antibiotics (or placebo), the evidence base is generally too sparse or inconsistent to make strong conclusions about the value of antibiotics for patients with

uncomplicated or mild diverticulitis. Two of these studies were conducted in patients with right-sided acute diverticulitis (in South Korea).

As summarized in the evidence profile (Table 8), there is insufficient evidence regarding the relative value of antibiotic treatment to affect the most pertinent clinical outcomes of death, treatment failure, diverticulitis-related morbidities, tenderness, rehospitalization, or adverse events. Largely, this was due to sparse events or only a single study with evidence, making estimates highly imprecise or inconclusive. There is, however, low SoE that pain, length of hospital stay, recurrence rates, and quality of life may be similar regardless of use of antibiotics. Similarly, with low SoE, there is no evidence of a difference in risk of surgery at 6 to 12 months, but the two studies that evaluated this outcome both found that about 3-times as many patient who were not given antibiotics had surgery than those given placebo, but with wide confidence intervals. It is unclear whether risk of recurrence or future surgery (or effect on quality of life) may differ between patients being treated for a first-time or recurrent episode of acute diverticulitis

Seven studies compared different antibiotic regimens in patients with acute diverticulitis. However, each compared different sets of regimens, either different antibiotics (3 studies); different, largely nonoverlapping comparisons of durations of treatment (4 studies); and different routes (1 study). In addition to the problem of only a single study evaluating any given comparison, clinical outcomes were generally sparse within studies, resulting in highly imprecise comparisons of regimens. Thus, the only difference found was that a 7-day course of ertapenem resulted in a shorter length of hospital stay (by about 2 days) than a 4-day course.³¹ The full evidence profile is in Table 8.

Table 8. Evidence profile for antibiotic treatment for acute left-sided diverticulitis^a

Topic	Outcome	No. Studies (Subjects)	Risk of Bias	Consistency	Precision	Directness	Other	Overall SoE	Conclusion Statements
Abx vs. no Abx	Death	3 (1329)	Moderate	Consistent	Imprecise	Direct	Sparse events	Insufficient	No conclusion regarding antibiotic vs. placebo. Rare event.
	Treatment failure ^b	2 (706)	Low	Consistent	Imprecise	Indirect ^c	Sparse	Insufficient	No conclusion regarding antibiotic vs. placebo
	Length of hospital stay ^b	3 (1329)	Moderate	Inconsistent	Precise	Direct	None	Low	No evidence of a difference Difference -7.7 hr (-20.2, 4.8)
	Rehospitalization	2 (706)	Moderate	Consistent	Precise	Direct	Sparse ^d	Insufficient	No conclusion regarding antibiotic vs. placebo
	Surgery at 6-12 months	2 (1110)	Moderate	Consistent	Imprecise	Direct	None	Low	No evidence of a difference, but possible trend toward lower risk with antibiotics OR 0.33 (0.07, 1.63) ^e
	Recurrence ^f	4 (1624)	Moderate	Consistent	Precise	Indirect ^g	None	Low	No evidence of a difference Summary OR 1.06 (0.81, 1.39)
	Diverticulitis-related morbidities	2 (1151)	Moderate	Consistent	Imprecise	Direct	Sparse events	Insufficient	No conclusion regarding antibiotic vs. placebo. Rare event.
	Pain/tenderness	3 (1230)	Moderate	Inconsistent	Imprecise	Direct	None	Low	No evidence of clinically significant difference
	Quality of life	2 (732)	Moderate	Consistent	Precise	Direct	Sparse, per analysis	Low	No evidence of a difference
Various Abx regimens	Adverse events	1 (1197)	Moderate	N/A	Precise	Direct	Sparse	Insufficient	No conclusion regarding antibiotic vs. placebo
	All	7 (1405)	Moderate	N/A	Imprecise	Direct	Sparse, per analysis ^h	Insufficient	No conclusion comparing antibiotic regimens

Abbreviations: Abx = antibiotics, LOS = length of stay, MD = mean difference, N/A = not applicable, OR = odds ratio (with 95% confidence interval), SoE = strength of evidence.

^a The two trials of right-sided diverticulitis (Kim 2019 and Park 2019) are omitted. Evidence pertaining to right-sided diverticulitis is insufficient due to sparseness of studies.

Footnotes indicate which outcomes were reported by the studies of right-sided diverticulitis.

^b One study provided insufficient evidence about antibiotics vs. placebo in right sided diverticulitis.

^c The study described treatment failure at 6 months followup.

^d Across 2 trials, only a single estimate at each time point (1 week, 1 month, 6 months, 24 months).

^e AVOD finding at 12 months. DIABOLO had similar finding at 6 months (OR 0.36, 95% CI 0.10, 1.38).

^f One study provided insufficient evidence about antibiotics vs. placebo in right sided diverticulitis.

^g Time points ranged from 12 to 50 months. AVOD also found similar results at 11 years.

^h Each study evaluated a different comparison of antibiotic regimens.

Key Question 2c. Interventional Radiology for Acute Diverticulitis

Key Points

- The evidence is insufficient to make conclusions regarding the potentially beneficial effects of percutaneous drainage for treatment of acute complicated diverticulitis due to sparse and imprecise data.
- No comparative studies have reported on procedural adverse events.

Findings Pertaining to Interventional Radiology

Only two studies, both retrospective NRCSs, reported the effects and harms of interventional radiology (specifically, percutaneous drainage) compared with conservative management (no percutaneous drainage) in patients with acute complicated diverticulitis.^{101, 102} The two NRCSs, with a total of 483 participants, are summarized in Appendix C Tables C-2c-1 to C-2c-3; results are in Appendix D Table D-2c-1.

Lambrichts 2019, for which the funding source was not reported, studied 447 adults with modified Hinchey category Ib or II acute complicated diverticulitis (with confined or distant abscesses, per Wasvary¹⁹). Three-quarters of the patients received percutaneous drainage. Patients were on average in their early 60s. Approximately two-thirds of patients (62% of patients receiving drainage and 72% not receiving it) were undergoing their first episode of diverticulitis. Of note, at baseline, patients receiving percutaneous drainage had higher levels of inflammatory parameters, such as CRP and WBCs, were more likely to have modified Hinchey II (distant abscesses) diverticulitis, and had larger abscesses than patients not receiving percutaneous drainage (median 6.4 vs. 3.6 cm). Given these clinically important differences in baseline characteristics, we evaluated only short-term outcomes that had multivariable analyses which adjusted for these and other factors. For long-term outcomes from Lambrichts 2019, we calculated unadjusted between-arm effect sizes under the assumption that long-term outcomes would not be confounded by differences in severity of the index episode of acute diverticulitis.

Mali 2019, which was funded by non-industry sources, studied 36 adults with acute diverticular abscesses of at least 4 cm. Eighteen patients who had received percutaneous drainage were compared with 18 matched patients with similar abscess size (± 0.5 cm) who had not received percutaneous drainage. Patients were on average in their 60s. Approximately two-thirds of patients (56% of patients receiving drainage and 67% not receiving it) were undergoing their first episode of diverticulitis. Demographic, inflammatory, and radiologic factors were similar between the two arms. Because the patients were matched, we considered patients to be adequately similar at baseline and calculated unadjusted effect sizes for all reported outcomes from this NRCS.

We assessed both NRCSs to be at low risk of confounding bias because they used adequate methods to account for potential confounding (see Appendix C). Neither study blinded participants, providers, or outcome assessors; however, the impact of this is likely to be minimal because all outcomes were objective outcomes. We did not detect any issues with other potential biases.

Table 9 summarizes the included results.

Table 9. Interventional radiology: All outcomes

Outcome	Study Year, PMID	Time	Intervention	n/N (%)	Effect Size (95% CI)	Reported P-value
Diverticulitis-related mortality, short-term	Mali 2019, ¹⁰² 31320921	30 d	Percutaneous drainage	1/18 (5.6)	OR 1.00 (0.06, 17.3)	1.00
			Antibiotics	1/18 (5.6)		
All-cause mortality, long-term	Lambrichts 2019, ¹⁰¹ 30811050	6 yr	Percutaneous drainage	12/115 (10.4)	Unadj OR 2.30 (1.05, 5.02)	NR
			No drainage	16/332 (4.8)		
Sigmoid resection, short-term	Lambrichts 2019, ¹⁰¹ 30811050	30 d	Percutaneous drainage	16/115 (13.9)	Adj OR 1.29 (0.56, 2.99)	0.55
			No drainage	24/332 (7.2)		
	Mali 2019, ¹⁰² 31320921	During initial admission	Percutaneous drainage	5/18 (27.8)	OR 1.00 (0.23, 4.30)	1.00
			Antibiotics	5/18 (27.8)		
Sigmoid resection, long-term	Lambrichts 2019, ¹⁰¹ 30811050	6 yr	Percutaneous drainage	37/115 (32.2)	Adj OR 1.08 (0.69, 1.69)	0.74
			No drainage	87/332 (26.2)		
	Mali 2019, ¹⁰² 31320921	71 mo	Percutaneous drainage	9/12 (75.0)	OR 1.50 (0.25, 8.84)	1.00
			Antibiotics	8/12 (66.7)		
Stoma	Mali 2019, ¹⁰² 31320921	30 d	Percutaneous drainage	2/12 (16.7)	OR 0.60 (0.08, 4.45)	NR
			Antibiotics	3/12 (25.0)		
Treatment failure (Death or need for surgery)	Lambrichts 2019, ¹⁰¹ 30811050	30 d	Percutaneous drainage	41/115 (35.7)	Adj OR 1.47 (0.81, 2.68)	0.19
			No drainage	79/332 (23.8)		
	Mali 2019, ¹⁰² 31320921	30 d	Percutaneous drainage	6/18 (33.3)	OR 0.63 (0.16, 2.41)	0.49
			Antibiotics	8/18 (44.4)		
Readmission, short-term	Mali 2019, ¹⁰² 31320921	30 d	Percutaneous drainage	2/18 (11.1)	OR 0.63 (0.09, 4.28)	1.00
			Antibiotics	3/18 (16.7)		
Length of hospital stay	Mali 2019, ¹⁰² 31320921	30 d	Percutaneous drainage	6 d [3, 12] ^a	Median Difference = 0	0.73
			Antibiotics	6 d [3, 10] ^a		
Recurrence of diverticulitis, Any, long-term	Lambrichts 2019, ¹⁰¹ 30811050	6 yr	Percutaneous drainage	29/115 (25.2)	Unadj OR 0.87 (0.53, 1.41)	NR
			No drainage	93/332 (28.0)		
	Mali 2019, ¹⁰² 31320921	71 mo	Percutaneous drainage	1/12 (8.3)	OR 0.45 (0.04, 5.81)	1.00
			Antibiotics	2/12 (16.7)		
Recurrence of diverticulitis, Complicated, long-term	Mali 2019, ¹⁰² 31320921	71 mo	Percutaneous drainage	1/12 (8.3)	OR 1.00 (0.06, 18.1)	1.00
			Antibiotics	1/12 (8.3)		

Abbreviations: Adj = adjusted, CI = confidence interval, d = days, IQR = interquartile range, mo = months, NR = not reported, OR = odds ratio, PMID = PubMed identifier, Unadj = unadjusted (analysis of unmatched nonrandomized comparative study), yr = years.

^a Median [interquartile range].

Mortality

Mali 2019 reported that an equal number of patients in each arm (1 of 18) had diverticulitis-related mortality at 30 days (OR 1.00, 95% CI 0.06 to 17.3).

Lambrichts 2019 reported that patients receiving percutaneous drainage had higher all-cause mortality at 6 years (unadjusted OR 2.30, 95% CI 1.05 to 5.02).

Surgery for Diverticulitis

Both studies reported on the need for surgery for diverticulitis, specifically sigmoid resection. But both analyses were imprecise or near-imprecise for this outcome, due to insufficient power.

Lambrichts 2019 found no evidence that percutaneous drainage was associated with a reduction in need for sigmoid resection at 30 days, at which point the comparison was imprecise (adjusted OR 1.29, 95% CI 0.56 to 2.99) or at 6 years (adjusted OR 1.08, 95% CI 0.69 to 1.69).

Mali 2019 reported that an equal number of patients in each arm (5 of 18) needed sigmoid resection during initial admission, although the comparison was imprecise (OR 1.00, 95% CI 0.23 to 4.30). The comparison of sigmoid resection rates at 71 months was imprecise (OR 1.50, 95% CI 0.25 to 8.84).

Stoma

Mali 2019 reported on stoma rates, but the comparison was imprecise (OR 0.60, 95% CI 0.08 to 4.45).

Treatment Failure

Both NRCSSs reported on failure of percutaneous drainage, however each defined failure differently.

Lambrichts 2019 defined treatment failure as complications related to acute complicated diverticulitis, such as perforation, obstruction, and fistula. The estimate of relative failure rates between the percutaneous drainage and no percutaneous drainage arms at 30 days was imprecise (adjusted OR 1.47, 95% CI 0.81 to 2.68).

Mali 2019 defined treatment failure as death or need for surgery. The comparison of failure rates between the percutaneous drainage and no percutaneous drainage arms at 30 days was imprecise (OR 0.63, 95% CI 0.16 to 2.41).

Hospitalization for Diverticulitis

Mali 2019 found an imprecise association between percutaneous drainage and need for rehospitalization at 30 days (OR 0.63, 95% CI 0.09 to 4.28). The median length of hospital stay was the same (6 days) in patients who had received percutaneous drainage and those who had not.

Recurrence of Diverticulitis

Both NRCSSs reported on the outcome of recurrence of diverticulitis.

Lambrichts reported that recurrence rates were similar between the percutaneous drainage and no percutaneous drainage arms at 6 years of follow-up (unadjusted OR 0.87, 95% CI 0.53 to 1.41).

In Mali 2019, the between-group comparisons of recurrence of diverticulitis were imprecise, both for recurrence of any diverticulitis (OR 0.45, 95% CI 0.04 to 5.81) and specifically of complicated diverticulitis (OR 1.00, 95% CI 0.06 to 18.1).

Adverse Events

Neither NRCS reported on any adverse events that were attributable to percutaneous drainage. Mali 2019, though, reported on stoma rates, between-group comparisons of which were imprecise. Comparing percutaneous drainage with no drainage, the OR was 0.60 (95% CI 0.08 to 4.45).

Summary of Evidence Pertaining to Interventional Radiology

The evidence profile (Table 10) summarizes the findings. Overall evidence was insufficient to make conclusions.

Two NRCSs, one small with matching (36 participants) and one large with some adjusted and some unadjusted estimates (447 participants), compared patients who underwent percutaneous drainage with those who did not. Estimates were imprecise and generally sparse for comparisons of diverticulitis-related mortality, acute sigmoid resection, stoma rates, and short-term rehospitalization for diverticulitis or complications. Based primarily on a single study, no differences in outcomes were found with use of percutaneous drainage for treatment failure at 30 days, length of hospital stay, or long-term recurrence of diverticulitis. Neither study reported on procedure-specific adverse events.

Table 10. Evidence profile for interventional radiology

Outcome	N Studies (Subjects)	Risk of Bias	Consistency	Precision	Directness	Other	Strength of Evidence	Conclusions
Diverticulitis-related mortality, within 30 days	1 (36)	Low	Not applicable	Imprecise	Direct	Sparse	Insufficient	No conclusion regarding interventional radiology vs. no procedure
Sigmoid resection at 30 days	2 (483)	Low	Consistent	Imprecise	Direct	None	Insufficient	No conclusion regarding interventional radiology vs. no procedure. Rare event.
Stoma	1 (24)	Low	Not applicable	Imprecise	Direct	Sparse	Insufficient	No conclusion regarding interventional radiology vs. no procedure
Treatment failure at 30 days	2 (483)	Low	Consistent	Precise	Direct	Sparse ^a	Insufficient	No conclusion regarding interventional radiology vs. no procedure. Rare event
Rehospitalization for diverticulitis or complications	1 (36)	Low	Not applicable	Imprecise	Direct	Sparse	Insufficient	No conclusion regarding interventional radiology vs. no procedure
Length of hospital stay	1 (36)	Low	Not applicable	Imprecise	Direct	Sparse	Insufficient	No conclusion regarding interventional radiology vs. no procedure
Recurrence of diverticulitis	2 (483)	Low	Consistent	Imprecise	Direct	Sparse ^a	Insufficient	No conclusion regarding interventional radiology vs. no procedure
Adverse event	0							No evidence

^a One study highly imprecise. Therefore, the conclusion is based on only one study.

Key Question 3. Colonoscopy After Acute Diverticulitis

Key Points

- With low SoE, studies comparing patients who underwent colonoscopy soon after an episode of acute diverticulitis (within ~2-12 months) with those who did not undergo colonoscopy, found no evidence of differences, ultimately, in rates of colorectal cancer (CRC); however, no studies evaluated comparative risks of CRC death.
- Among people undergoing colonoscopy, those with a recent diagnosis of acute diverticulitis (within 6-12 months) may be more likely to have CRC than healthy controls (low SoE). It remains unclear whether or not people with recent acute diverticulitis are more likely to be found to have colonic premalignant lesions (insufficient due to imprecise estimates).
- After an episode of acute diverticulitis, about 0.5% to 0.8% die of CRC within approximately 4 years (low SoE).
- Colonoscopy after acute diverticulitis (within 6 weeks to 12 months) finds that about 2% of people have CRC (moderate SoE), 7% have advanced colonic neoplasia (CRC or advanced adenoma; moderate SoE), 3% have advanced adenoma (large, villous, or high-grade; high SoE), 1.5% have adenomas with high-grade dysplasia (moderate SoE), and 2.4% have large adenomas (≥ 10 mm; high SoE).
- Among patients with recent acute diverticulitis, those who are age 50 years or older are at about 3-times increased risk of CRC than younger patients (moderate SoE), about 8-times increased risk of advanced colonic neoplasia (high SoE), and possibly at increased risk of advanced adenoma (low SoE).
- Patients with recent complicated acute diverticulitis are at almost 6-times increased risk of CRC than those with recent uncomplicated diverticulitis (high SoE), about 3-times increased risk of advanced colonic neoplasia (high SoE), and probably 2-times increased risk of advanced adenoma (moderate SoE).
- Colonoscopies performed from approximately 6 weeks up to 1 year after acute diverticulitis are incomplete (or fail) in approximately 3.5% of patients (high SoE). No complications associated with colonoscopy were reported among 878 patients, implying a risk of complications of $\leq 0.9\%$ (high SoE).

Findings Pertaining to Colonoscopy

Overall, 20 studies addressed use of colonoscopy after episodes of acute diverticulitis for the purpose of assessing risk of CRC. Three of these compared colonoscopy to no colonoscopy in patients with recent diverticulitis,¹⁰³⁻¹⁰⁵ three compared colonoscopy in patients with recent diverticulitis to healthy controls,¹⁰⁶⁻¹⁰⁸ one compared early (in-hospital) colonoscopy to later colonoscopy,¹⁰⁹ and 13 were single-group studies of patients who underwent colonoscopy.¹¹⁰⁻¹²² Appendix C Tables C-3-1 to C-3-4 give descriptions of the studies; results are in Appendix D Tables D-3-1 to D-3-7. An additional study of interest that did not meet eligibility criteria is also discussed together with the comparative studies.¹²³

Colonoscopy Versus No Colonoscopy

Three NRCS, all retrospective,¹⁰³⁻¹⁰⁵ evaluated colonoscopy compared to no colonoscopy in patients with recent acute diverticulitis. All study participants had recent acute colonic

diverticulitis confirmed by CT. None of the studies reported on family history of CRC. Across studies, participants who underwent colonoscopy were on average in their 50s and about half were men. The studies are at high risk of bias since they did not adjust for differences between groups. None of the studies reported funding sources.

Lau 2011 included 1088 patients with acute left-sided diverticulitis or complicated diverticulitis.¹⁰³ The total number of participants with complicated diverticulitis was not reported, but 7.5 percent had abscesses, 6.9 percent had local perforations, and 2.0 percent had fistulas. No data were reported on prior history of diverticulitis. The study also did not have access to, and thus did not report, participants' treatment or surgical histories.

Sallinen 2014 included 536 patients with clinically and CT-diagnosed acute colonic diverticulitis that was treated conservatively, either first attack (75%) or recurrent (25%).¹⁰⁴ The percentage of participants with complicated diverticulitis was not reported, but 24 percent had an abscess, and 0.3 percent had a fistula.

In contrast to the other two studies, Soh 2018 included 227 patients presenting with their first episode of CT-proven acute diverticulitis without complications who were managed conservatively.¹⁰⁵

The three studies used different comparators as the no colonoscopy arm. Lau 2011 used data from the Western Australian Cancer Registry (within 1 year of CT scan) for whom colonoscopy reports were not available after an episode of acute diverticulitis. It is unclear whether all these patients indeed did not have colonoscopy. Sallinen 2014 included patients followed after treatment of acute diverticulitis who did not undergo colonoscopy for various reasons (e.g., prior colonoscopy within 2 years, patients declined, patients too old). CRC data were obtained from hospital medical records and the Finnish Cancer Registry at least 2 years after the episode of diverticulitis. Soh 2018 included patients who were recommended to have colonoscopy after their diverticulitis who did not undergo followup colonic evaluation. Diagnoses of CRC were sought in national electronic health records at an unreported time point.

In Lau 2011, colonoscopy was conducted within 1 year of diagnostic CT scan. In Sallinen 2014, colonoscopy was performed on average 4 months after hospital discharge. In Soh 2018, colonoscopy was recommended for 6 to 8 weeks after hospital discharge; median interval period was 9 weeks.

The sample sizes varied from 135 to 394 for patients who underwent colonoscopy and 92 to 769 for patients who did not undergo colonoscopy.

Colorectal Cancer Death

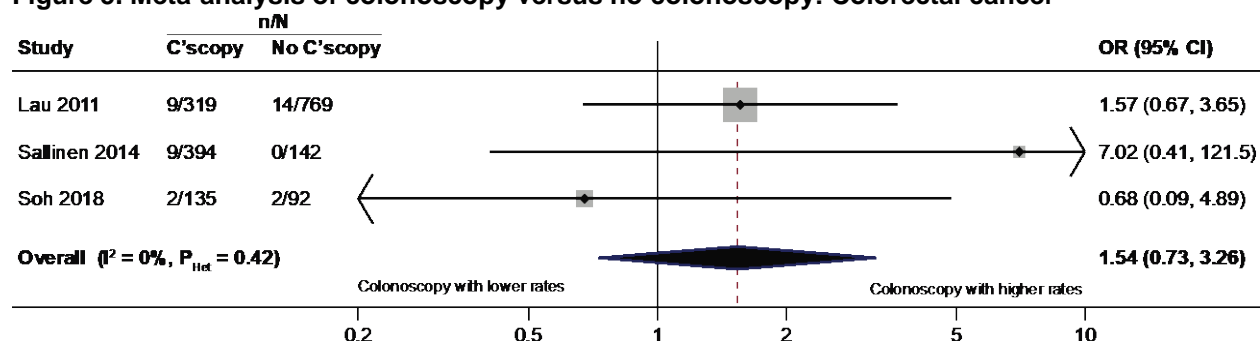
None of the comparative studies reported on rates of CRC death.

Colorectal Cancer

All three studies reported on CRC findings (Figure 5). Under the assumption that the three studies were sufficiently similar to each other, the summary unadjusted OR for CRC was 1.54 (95% CI 0.73 to 3.27; $I^2 = 0\%$), suggesting no evidence of a difference in rates of CRC ultimately diagnosed among those who did or did not have interval colonoscopy. All of the studies were imprecise (or nearly imprecise) regarding the difference in CRC rates between those who underwent colonoscopy after an episode of acute diverticulitis and comparator groups of people with a history of diverticulitis who did not undergo colonoscopy. ORs ranged from 0.68 to 7.02 across studies. Any suggestion that those who underwent colonoscopy may be at increased risk for having CRC may be due to underlying biases regarding who completed their colonoscopy

(e.g., possibly people with a family history of CRC or more complicated diverticulitis are more likely to have colonoscopy).

Figure 5. Meta-analysis of colonoscopy versus no colonoscopy: Colorectal cancer



Abbreviations: CI = confidence interval, C'scopy = colonoscopy, I² = measure of statistical heterogeneity (% of heterogeneity not due to random chance), OR = odds ratio, P_{Het} = statistical heterogeneity P value.

An additional study evaluated the broader question of the association between colonoscopy and CRC in patients with a history of acute diverticulitis. Mortensen 2017 queried the Danish national registry for all long-term residents who had been hospitalized with a primary diagnosis of symptomatic diverticulitis (as adults) over an 18-year period (N=40,496).¹²³ The primary purpose of this study was to compare rates of CRC (up to 18 years after diverticulitis or colonoscopy) among people with and without a history of diverticulitis (and with and without a colonoscopy). The study did not restrict its analysis to colonoscopies done soon after an episode of diverticulitis nor did they report the relative timeframes of episodes of diverticulitis and colonoscopy (thus, *the study did not meet eligibility criteria*). This study also did not evaluate lesions found at colonoscopy. Furthermore, the primary analyses included people whose CRC diagnoses occurred before or simultaneous to their diverticulitis-related hospitalization; although, we focus on subgroup analyses excluding these patients. In this subgroup, there were 39,911 adults with a history of hospitalization for diverticulitis. The study did not exclude people who had a colectomy.

In Mortensen 2017, among the 22,646 with a history of diverticulitis who had a colonoscopy (at any time before or after diverticulitis) 2.4 percent (542) were diagnosed with CRC (at any time up to 18 years after their diverticulitis episode). Among the 17,265 who never had a colonoscopy, 3.5 percent (596) were at some point diagnosed with CRC. The unadjusted risk ratio (RR) was 0.69 (95% CI 0.62 to 0.78); an adjusted RR was not reported.

Colonoscopy After Diverticulitis Versus Healthy Controls

Three NRCS, all retrospective,¹⁰⁶⁻¹⁰⁸ evaluated colonoscopy among patients with diverticulitis and compared findings with matched healthy controls who also underwent colonoscopy. Across studies, the majority of patients had uncomplicated diverticulitis (86% to 92%). Age and sex were generally comparable between two arms within each study. The mean ages of participants ranged from 47 to 61 years old, and males accounted for 41 to 60 percent of the participants. Choi 2014 and Daniels 2015 adjusted only their analysis of advanced adenomas. Lecleire 2014 reported only unadjusted analyses. Choi 2014 did not report funding source; the other two studies were explicitly not funded by industry.

Daniels 2015 compared cohort of patients from two trials who underwent colonoscopy,¹⁰⁷ patients with uncomplicated acute diverticulitis (from the DIABOLO trial) with colonoscopies

within 6 months and a primary colonoscopy screening population (from the Colonoscopy or Colonography for Screening [COCOS] trial).¹²⁴ The DIABOLO trial included adults with first episode of CT-proven left-sided acute diverticulitis. The majority of the participants (93%) had modified Hinchey 1a (pericolic inflammation or phlegmon, per Wasvary¹⁹) and 7.5 percent had modified Hinchey 1b (pericolic abscess) diverticulitis; 9.5 percent had a family history of CRC. Participants from the COCOS trial includes individuals from the general population (aged 50 to 75 years) invited for primary colonoscopy screening. No data on their diverticulitis status/history were reported, but 15.3 percent had a family history of CRC. All patients had left-sided diverticulitis.

Choi 2014 compared patients who underwent colonoscopy within 1 year of acute diverticulitis to age- and sex-matched controls identified from healthy individuals who underwent screening colonoscopy. About 14 percent of the diverticulitis patients had complicated disease and 2.6 percent had a family history of CRC. Of note, the patients with diverticulitis who did not undergo colonoscopy were less likely to have had complicated disease (8.2%, $P=0.051$) than patients who did; a similar percentage of them had a family history of CRC (3.1%). No CRC-related data are reported for the group who did not undergo colonoscopy.

Lecleire 2014 matched patients who underwent colonoscopy within 6 months following an episode of acute diverticulitis with sex- and age-matched healthy controls with a family history of CRC or colorectal adenoma (after age 50 years) who also had undergone colonoscopy. The majority (90%) of diverticulitis patients had uncomplicated disease.

Colorectal Cancer Death

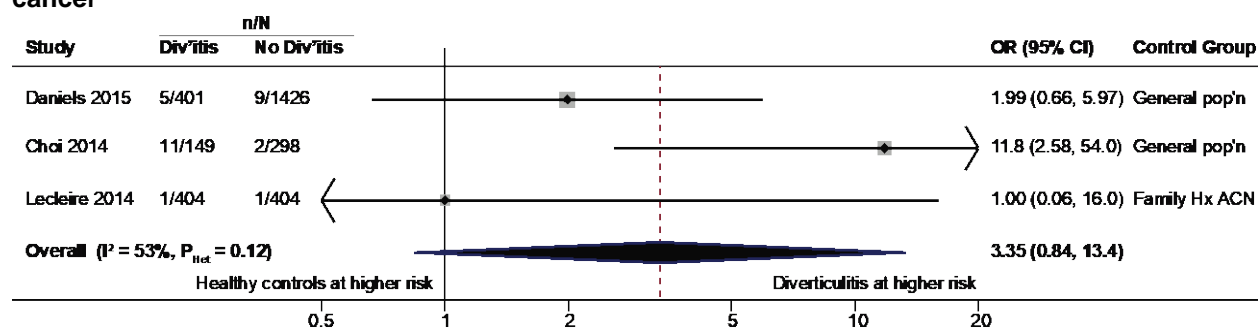
None of the comparative studies reported on rates of CRC death.

Colorectal Cancer

All three studies reported on CRC findings (Figure 6) but reported only unadjusted results for CRC. Under the assumption that the three studies were sufficiently similar to each other, the summary unadjusted OR for CRC was 3.35 (95% CI 0.84 to 13.4), with some heterogeneity among studies ($I^2=53\%$), overall suggesting possible evidence of a difference in CRC rates among adults with a recent history of diverticulitis and the general population. However, a large difference in CRC rates cannot be excluded. Only Choi 2014 reported a statistically significant higher rate of CRC among patients with diverticulitis than the general population matched controls (7.4% vs. 0.7%).

Daniels found no significant difference in left-sided (vs. right-sided) CRC lesions compared with study participants without diverticulitis (5/5 vs. 7/9; $P=0.51$). All patients had left-sided diverticulitis.

Figure 6. Meta-analysis of colonoscopy after diverticulitis versus in healthy controls: Colorectal cancer



Abbreviations: CI = confidence interval, Div'titis = diverticulitis, Family Hx ACN = family history of advanced colonic neoplasia (colorectal cancer or advanced adenoma), I^2 = measure of statistical heterogeneity (% of heterogeneity not due to random chance), OR = odds ratio, P_{Het} = statistical heterogeneity P value, pop'n = population.

Mortensen 2017, the Danish national registry study described above, also compared people with a history of diverticulitis-related hospitalizations to matched controls without a history of diverticular disease (including diverticulosis).¹²³ The primary study matched each adult with diverticulitis to 10 controls. However, in their subgroup analysis excluding those with a history of CRC prior to or simultaneous with the diverticulitis episode, it is unclear who they included among general population controls (although the discrepancy was only 1.4% “too many” control patients). Of note, adults in the general population who had a colonoscopy were at markedly increased risk of CRC compared with those who did not have a colonoscopy (RR = 4.57, 95% CI 4.38 to 4.76; 7.6% [3087/40,777] vs. 1.7% [6040/364,183]). Based on reported numbers, we calculated that the OR comparing those people with a history of diverticulitis (without prior or simultaneous CRC) who had a colonoscopy at any timepoint with (an apparently high-risk population of) adults without a history of diverticulitis who also had a colonoscopy was 0.30 (95% CI 0.27 to 0.33).

High-Risk Colonic Premalignant Lesions

All three NRCSs reported high-risk colonic premalignant lesions, but findings were inconsistent.

Daniels 2015 found lower rates of various high-risk lesions than in the general population, opposite in direction to their (statistically nonsignificant) findings about relative of CRC. The crude (unadjusted) ORs for serrated polyps, large adenomas (≥ 10 mm), adenomas with high-grade dysplasia, advanced adenomas, and advanced colonic neoplasias (CRC or advanced adenoma) were between 0.14 and 0.34, all highly statistically significant. However, the authors note that the statistically significant difference in rates of advanced adenomas ($P=0.036$) became just nonsignificant after adjustment for age, family history of CRC, smoking, body mass index (BMI), and cecal intubation ($P=0.052$); although, no adjusted effect size was reported. Daniels found no significant difference in left-sided (vs. right-sided) advanced colonic neoplasia lesions compared with study participants without diverticulitis (77.4% [24/31] vs. 71.5% [123/172]; $P=0.50$).

Similarly, Lecleire 2014 found lower risks of premalignant lesions among those with recent diverticulitis. The unadjusted ORs for large adenomas (≥ 10 mm) and advanced adenomas were similar (advanced adenoma 0.39, 95% CI 0.19 to 0.80; large adenoma 0.38, 95% CI 0.17 to 0.83). The OR for adenomas with high-grade dysplasias was similar, but near imprecise (OR 0.33, 95% CI 0.07 to 164).

In contrast, Choi 2014 reported higher rates of advanced adenoma in the diverticulitis group than the general population (OR 5.14, 95% CI 0.99 to 26.8) and of advanced colonic neoplasia (OR 8.84, 2.90 to 27.0). These findings were consistent with the higher rates of CRC also found.

Rates of Colorectal Cancer and Abnormal Lesions on Colonoscopy

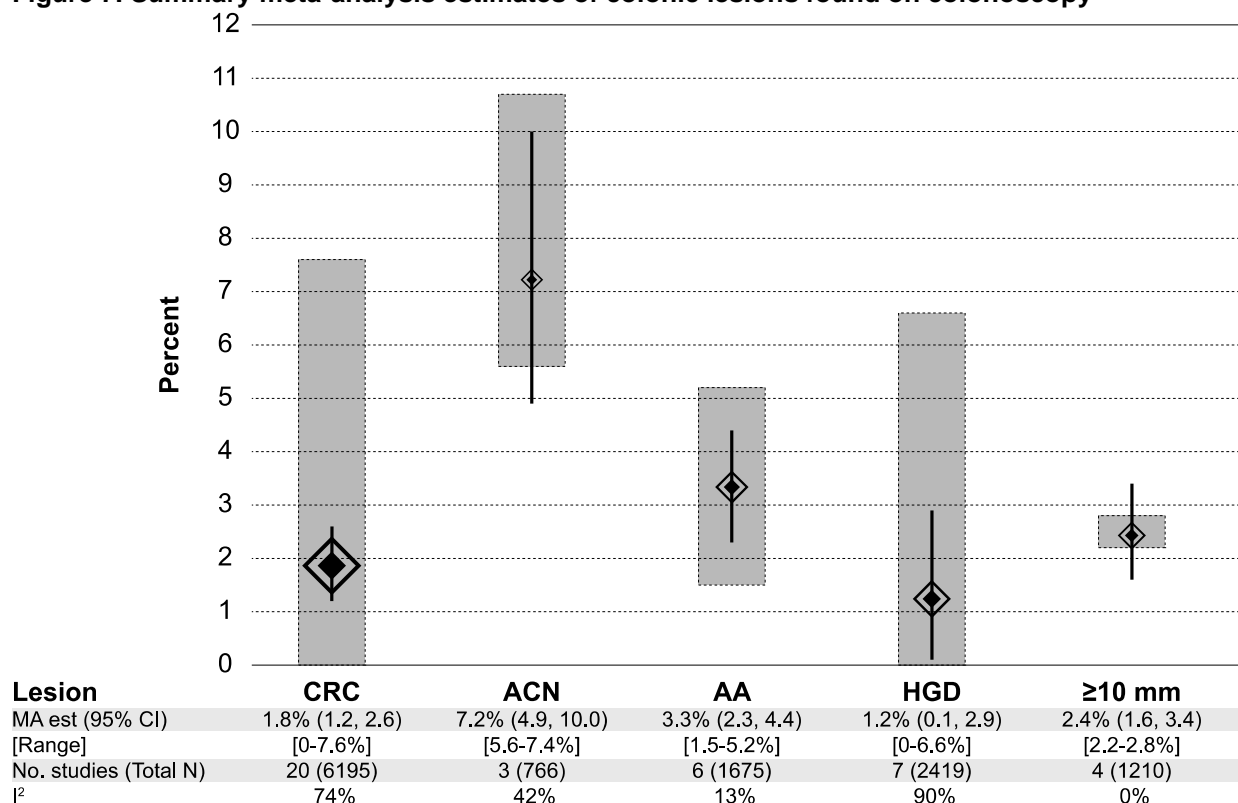
We identified 13 single group studies, all retrospective, that evaluated colonoscopy outcomes.¹¹⁰⁻¹²² The 13 studies were each conducted at a single center and all patients received followup colonoscopy after treatment of acute diverticulitis treatment. The mean age of participants across studies ranged from 41 to 64 years old. The sample size varied from 216 to 645 across studies. Among the eight studies that reported relevant data, the majority of the participants had uncomplicated diverticulitis (ranging from 70% to 100%). Although these studies were conducted in eight different countries, they were similar in terms of participants' age, sex, and the course of diverticulitis.

For the evaluation of rates of CRC and abnormal lesions, we combined the 13 single-group studies with the similar groups in the six comparative studies described above. In addition, a study that compared early (in-hospital) versus "late" (at 6 weeks) colonoscopy was also included here. This latter study is described further in the section on feasibility, below. Therefore, a total of 20 studies were included in the meta-analysis to determine an overall level of CRC and high-risk colonic premalignant lesions following colonoscopy.

The studies were at generally low risk of bias with regards to reporting rates of colonoscopy findings, with clear descriptions of eligibility criteria and outcomes, and no evidence of selection bias (except in regard to which patients were willing to undergo colonoscopy). Two studies were explicitly not funded by industry (Lecleire 2014 and Daniels 2015); the rest did not report funding source.

Figure 7 summarizes the lesions for which meta-analysis was conducted (i.e., all outcomes except CRC death and serrated polyps). The lesion-specific figures are included in Appendix D.

Figure 7. Summary meta-analysis estimates of colonic lesions found on colonoscopy



Summary estimates (by meta-analysis) and range of estimates across studies for each lesion. The diamond and vertical line indicate the summary estimate and 95% CI across studies. The size of the diamond is scaled to the total number of individuals across studies. The grey boxes indicate the range of estimates across studies.

Abbreviations: ≥10 mm = large adenomas (≥10 mm), AA = advanced adenoma, ACN = advanced colonic neoplasia, CI = confidence interval, CRC = colorectal cancer, HGD = (adenoma with) high-grade dysplasia, I² = estimate of the statistical heterogeneity across studies (which ranges from 0-100%, where higher values indicate greater heterogeneity across studies), MA est = meta-analysis (summary) estimate.

Colorectal Cancer Death

Two studies reported on CRC death.^{112, 116} Among 402 patients who underwent colonoscopy, Elmi 2013 reported two CRC deaths among 402 people undergoing colonoscopy (0.5%, 95% CI 0.1 to 2.0) at 2 to 4 years of followup. Among 645 patients who underwent colonoscopy, Ramphal 2018 reported five CRC deaths (0.8%, 95% CI 0.3 to 1.8) with the median 39 month followup.

Colorectal Cancer

A total of 20 studies reported on rates of CRC following colonoscopy (Figure 7 and Appendix Figure D-3-1). The 20 studies were conducted in 12 countries, including Australia, Canada, Finland, France, Israel, the Netherlands, Portugal, Singapore, South Korea, Spain, the United States, and the United Kingdom (these are noted in Appendix Figure D-3-1). Each of these countries has different underlying rates of CRC. Only four eligible studies were conducted in North America.^{111, 112} Of note, studies generally excluded participants with recent (pre-diverticulitis) colonoscopies).

Across studies, the summary estimate was that 1.8 percent (95% CI 1.2 to 2.6) of people had CRC found on colonoscopy after an episode of acute diverticulitis. The estimates ranged from 0 to 7.6 percent across studies with no clear explanation for the heterogeneity ($I^2 = 74\%$) (e.g., based on participant age, sex, family history of CRC, or severity of diverticulitis). There was no clear pattern by country (or continent); for example, the two studies with the lowest and highest rates of CRC were both conducted in Israel. The three studies conducted in the U.S. (Elmi 2013, Alcantar 2019, and Studniarek 2019) had estimates of CRC ranging from 0 to 2.2 percent.

Although Choi 2014 (7.4%) and Khoury 2019 (7.6%) did not clearly include different participants than the other studies, excluding these two “outliers,” as expected, reduced the summary estimate somewhat to 1.5 percent (95% CI 1.0 to 2.1), but still with unexplained heterogeneity ($I^2 = 60\%$).

Of note, Mortensen 2017,¹²³ the Danish national registry study described above, reported that of the 1051 people who were diagnosed with CRC after their episode of diverticulitis hospitalization, 626 (59.6%) were diagnosed within 500 days.^a This translates to 1.6 percent of the people hospitalized for diverticulitis who did not have a prior or simultaneous diagnosis of CRC. There was no indication of when (or if) colonoscopies were conducted for those diagnosed with CRC.

Advanced Colonic Neoplasia

Three studies reported on rates of advanced colonic neoplasia, defined as either CRC or advanced adenoma (Figure 7 and Appendix Figure D-3-2).^{106, 107, 118} Across studies, the summary estimate was that 7.2 percent (95% CI 4.9 to 10.0) of people had advanced colonic neoplasia found on colonoscopy after an episode of acute diverticulitis. However, the studies were somewhat heterogeneous ($I^2 = 42\%$) with estimates ranging from 5.6 to 10.7 percent. We found no clear explanation for the heterogeneity.

High-Risk Colonic Premalignant Lesions

Here we describe each high-risk colonic lesion individually, although it is important to note that these lesions are not mutually exclusive. An individual may have separate lesions of different types and individual lesions may be classified as one of several, or perhaps as multiple, lesion types. Furthermore, most studies reported only specific lesions (either due to varying definitions of the lesions or due to omissions). Thus, the summary estimates of frequencies of lesions cannot be simply summed across lesions.

Advanced Adenoma

Eight studies reported on rates of advanced adenoma (Figure 7 and Appendix Figure D-3-3).^{105, 106, 108, 110, 111, 118, 119, 122} Most studies defined advanced adenomas as either large (≥ 10 mm), villous, or of high grade. Lecleire 2014 also included invasive cancer, but for our analysis, we have excluded the one patient with CRC. Brar 2013 and Studniarek 2019 also included serrated adenomas and are thus excluded from the meta-analysis. Suhardja 2017 did not define advanced adenoma.

Across the six studies (excluding Brar 2013 and Studniarek 2019), the summary estimate was that 3.3 percent (95% CI 2.3 to 4.4) of people had advanced adenomas found on colonoscopy after an episode of acute diverticulitis. The study-level estimates ranged from 1.5 to 5.2 percent, with minor statistical heterogeneity across studies.

^a Based on Figure 2 in the article, subtracting out the 87 simultaneous diagnoses of diverticulitis and CRC.

Brar 2013 and Studniarek 2019 found correspondingly higher estimates of advanced adenoma that included serrated polyps: 9.2 percent (95% CI 5.9 to 13.5) and 5.5 percent (95% CI 3.9 to 7.6), respectively.^{111, 122}

Adenomas With High-Grade Dysplasia

Seven studies reported on rates of adenomas with “high-grade dysplasia” (Figure 7 and Appendix Figure D-3-4). This term may be variably defined and implicitly or explicitly included various other lesions.

Across studies, the summary estimate was that 1.2 percent (95% CI 0.1 to 2.9) of people had adenomas with high-grade dysplasia found on colonoscopy after an episode of acute diverticulitis, with high heterogeneity ($I^2 = 90\%$). Five of the seven studies had estimates that ranged from 0 to 1.0 percent, but two studies had much higher estimates, at 3.0 and 6.6 percent. The heterogeneity may in part be due to differing definitions of high-grade dysplasia, although the studies generally did not define the outcome. Excluding the two “high estimate” studies yields a summary estimate of 0.4 percent (95% CI 0.1 to 1.0; $I^2 = 45\%$). Excluding just the highest estimate (Meireles 2015) yields a summary estimate of 0.6 percent (95% CI 0.1 to 1.5; $I^2 = 70\%$). Although, these alternative scenarios are presented, it should be noted that there is no intrinsic reason to think that the excluded studies are “less correct” than the remaining.

Adenoma ≥ 10 mm

Four studies reported on rates of adenomas ≥ 10 mm (Figure 7 and Appendix Figure D-3-5).^{103, 107-109} Across studies, the summary estimate was that 2.4 percent (95% CI 1.6 to 3.4) of people had large adenomas found on colonoscopy after an episode of acute diverticulitis. The estimates were all very similar, with no heterogeneity.

Serrated Polyp

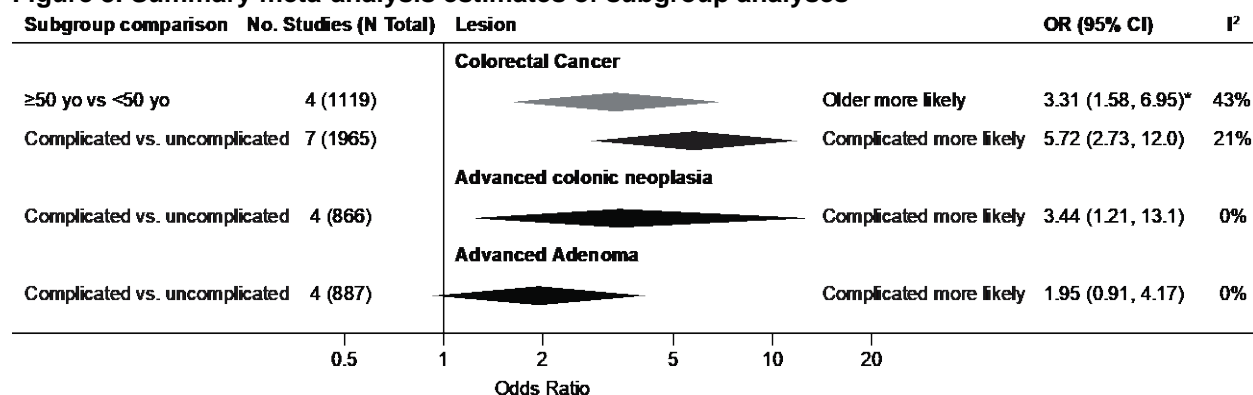
Two studies reported on rates of serrated polyps.^{107, 118} The two reported very different rates of serrated polyps, possibly due to differing definitions. Daniels 2015 reported a high rate (54/401; 13.2%, 95% CI 10.1 to 16.9) from the Dutch DIABOLO study. Seoane Urgorri 2018 reported a low rate (2/216; 0.9%, 95% CI 0.1 to 3.3) in a Spanish sample of patients.

Subgroup Analyses

Ten studies compared rates of CRC and other dysplasias among subgroups of participants.^{105, 106, 110-113, 115, 116, 118, 119} Of primary interest were comparisons by age and recent complicated (vs. uncomplicated) diverticulitis. Other comparisons included sex, right versus left sided diverticulitis, and others. As described below, only three studies conducted multivariable analyses.^{106, 110, 111} The other studies are at high risk of bias due to potentially unadjusted differences between compared subgroups. None of the studies reported funding source.

Figure 8 summarizes the comparisons between subgroups for which meta-analysis was conducted. The comparison-specific figures are included in Appendix D.

Figure 8. Summary meta-analysis estimates of subgroup analyses



Summary estimates (by meta-analysis) for each subgroup analysis. Each diamond indicates the summary estimate and 95% CI across studies.

Abbreviations: CI = confidence interval, I² = estimate of the statistical heterogeneity across studies (which ranges from 0-100%, where higher values indicate greater heterogeneity across studies), OR = odds ratio, yo = years old.

* Peto odds ratio

Age (≥50 Versus <50 Years)

Five studies compared patients older than versus at least 50 years of age.^{106, 110, 111, 113, 115} Notably, this is the age threshold that the U.S. Preventive Services Task Force (USPSTF),¹²⁵ American College of Physicians (ACP),¹²⁶ and the U.S. Multi-Society Task Force of Colorectal Cancer (which includes the American Gastroenterological Association [AGA]¹²⁷) recommend screening for CRC in all adults (although the USPSTF recommendations are being updated). As will be described, Brar 2013 also evaluated age as a continuous variable.¹¹¹

Colorectal Cancer

Four studies compared the rate of CRC following colonoscopy among patients older and younger than 50 years of age (Figure 8 and Appendix Figure D-3-6).^{106, 111, 113, 115} Under the assumption that the four studies were sufficiently similar to each other, the summary Peto OR for CRC among older (vs. younger) adults was 3.31 (95% CI 1.58 to 6.95), with moderate heterogeneity. Three of the studies found no CRC among patients under age 50. There was no obvious difference between the fourth study, Meireles 2015, which found 4 percent of people age 50 or younger to have CRC and the other three studies.

We found, and included, one study restricted to younger adults (≤50 years, mean 40.7). Consistent with most of the studies that compared age subgroups, Alcantar 2019 found no instances of CRC among the 111 participants (0%, 95% CI 0 to 6.8).¹²⁰

Advanced Colonic Neoplasia

Four studies conducted multivariable analyses and reported statistically significant higher rates of advanced colonic neoplasia (CRC or advanced adenoma) in older patients.^{106, 110, 111, 118} Andrade 2016 and Choi 2014 had similar findings with adjusted OR = 8.12 (95% CI 2.46 to 45.1) and 9.13 (95% CI 1.97 to 42.3), respectively that patients of ages 50 years and older were more likely to have advanced colonic neoplasia. Seoane Urgorri 2018 reported that 7.8 percent of patients >50 years old had advanced colonic neoplasias compared with none (0%) for younger people (P = 0.02), but they did not report the numbers of study participants in each age subgroup.

Brar 2013 also evaluated age, but as a continuous variable, and found an adjusted OR of 1.04 (95% CI 1.01 to 1.08) for advanced colonic neoplasia per year of age.

Advanced Adenoma

Brar 2013 and Choi 2014 each found no significant difference in rates of advanced adenoma by age group,^{106, 111} although both trended toward more frequent advanced adenomas in those over age 50 years. Brar 2013 yielded an OR of 3.27 (95% CI 0.93 to 11.5). Choi 2014 yielded an OR of 1.68 (95% CI 0.27 to 10.3).

Complicated Versus Uncomplicated Diverticulitis

Seven studies compared patients with and without complicated diverticulitis (or with or without abscess).^{106, 110-112, 115, 118, 119}

Colorectal Cancer

All seven studies compared the rate of CRC following colonoscopy between patients with complicated diverticulitis and patients with uncomplicated diverticulitis (Figure 8 and Appendix Figure D-3-7).^{106, 110-112, 115, 118, 119} In contrast with the other studies, Elmi 2013 compared those who had had abscesses to those who did not. Combining all studies (assuming for the purpose of this analysis that in Elmi 2013 everyone with complicated diverticulitis had an abscess), the summary unadjusted OR for CRC was 5.72 (95% CI 2.73 to 12.0), with little heterogeneity across studies ($I^2 = 21\%$). Across studies, ORs ranged from 2.5 to 40.4. Excluding Elmi 2013 resulted in a similar summary estimate (OR = 6.89, 95% CI 2.57 to 18.5, $I^2 = 41\%$).

Advanced Colonic Neoplasia

Four studies that compared complicated versus uncomplicated diverticulitis evaluated advanced colonic neoplasia (Figure 8 and Figure D-3-8).^{106, 110, 111, 118} As indicated in the figure, three reported multivariable analyses and one of those evaluated abscess versus no abscess. All studies provided similar ORs for relative rate of advanced colonic neoplasia between those with and without complicated diverticulitis. The overall summary OR was 3.44 (95% CI 1.99 to 13.1) suggesting complicated diverticulitis being associated with increased risk of advanced colonic neoplasia on colonoscopy.

Advanced Adenoma

Four studies evaluated advanced adenomas (Figure 8 and Figure D-3-9).^{106, 110, 118, 119} Each study's estimate of the association between complicated diverticulitis and risk of advanced adenoma was not statistically significant. Across studies, the summary OR of complicated versus uncomplicated diverticulitis for risk of advanced adenoma was near significant at 1.95 (95% CI 0.91 to 4.17), suggesting possible increased risk among people with complicated diverticulitis.

Adenomas With High-Grade Dysplasias

Meireles 2015 reported that 9 of 80 (11%) patients with complicated diverticulitis had adenomas with high-grade dysplasia found on colonoscopy compared with 19 of 347 (5.5%) with uncomplicated diverticulitis. This translated into a near-significant OR of 2.19 (95% CI 0.95 to 5.03).

Other Subgroup Analyses

Appendix D Tables D-3-1 to D-3-7 present more results on colonoscopy subgroup analyses.

Left Versus Right Sided Diverticulitis

Two studies from East Asia compared people with right or left sided diverticulitis.^{105, 106} Of note, right-sided diverticulitis is more common in East Asia.

Both reported risks of CRC but provided imprecise estimates. Choi 2014 reported 2 CRC among 23 (8.7%) patients with left-sided diverticulitis and 9 of 126 (7.1%) with right-sided (OR = 1.24, 95% CI 0.25 to 6.13). Soh 2018 reported 2 of 54 (3.7%) left sided versus 2 of 178 (1.1%) right sided (OR = 3.38, 95% CI 0.47 to 24.6).

Choi 2014 also reported comparative rates of advanced colonic neoplasia (OR 1.30, 95% CI 0.34 to 4.99) and advanced adenoma (OR 1.39, 95% CI 0.15 to 12.99).

Male Versus Female

Two studies provided imprecise estimates of the relative rates of CRC or advanced colonic neoplasia by sex.^{106, 112} Elmi 2013 found that 1.2 percent (2/167) of men and 3.0 percent (7/235) of women had CRC (OR 0.39, 95% CI 0.08 to 1.92). Choi 2014 reported a multivariable analysis that found an adjusted OR of 1.08 (95% CI 0.35 to 3.34); they did not report event counts by sex.

Alarm Symptoms

Ramphal 2018 reported that 9 of 205 (4.4%) patients with alarm symptoms, but only 1 of 440 (0.2%) patients without alarm symptoms had CRC.¹¹⁶ This translated into an OR of 20.2, 95% CI 2.54 to 160). Alarm symptoms included unintentional weight loss, a change in bowel habits, bloody stool and/or persistent abdominal pain.

Anemia

In their multivariable analysis, Brar 2013 found no significant association between anemia and risk of advanced colonic neoplasia (adjusted OR 0.78, 95% CI 0.24 to 2.57).

Previous Attack of Diverticulitis

Brar 2013 also found no significant association between history of prior diverticulitis and risk of advanced colonic neoplasia (OR 2.28, 95% CI 0.76 to 7.46). The definition of previous attack, however, was not completely clear.

Colonoscopy: Complications, Tolerance, Feasibility, and Completion of Procedure

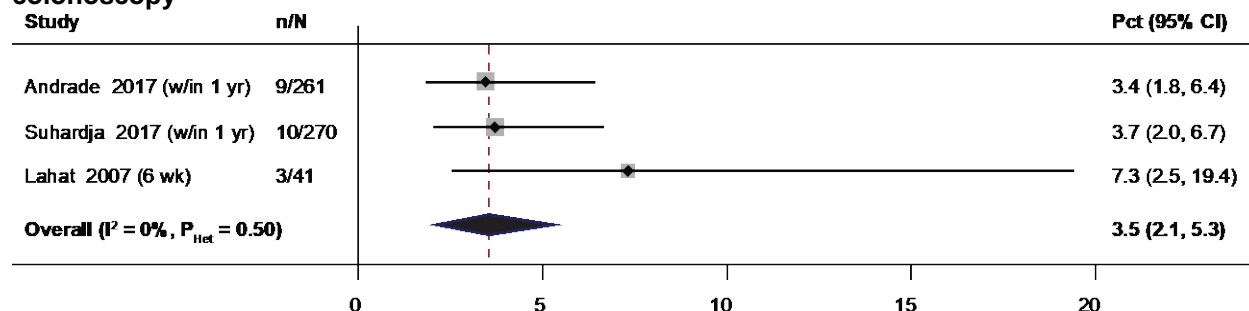
Four studies explicitly reported no major complications (Meireles 2015 and Seoane Urgorri 2018)^{115, 118} or (overall) no complications (Choi 2014 and Lahat 2007)^{106, 109} related to colonoscopy across 878 patients overall, implying a confidence interval of 0 to 0.9 percent. Colonoscopies were conducted within 6 to 7 weeks,^{109, 118} 4 months,¹¹⁵ or 1 year¹⁰⁶ after the episode of acute diverticulitis. The other 13 studies did not report on complications associated with colonoscopy.

Three studies reported on rates of failed/incomplete colonoscopy procedure (Figure 9).^{109, 110, 119} Combination of the three cohorts that performed colonoscopy after hospital discharge (within 1 year or at approximately 6 weeks) yielded a summary estimate that 3.5 percent (95% CI 2.1 to 5.3) of patients had a failed or incomplete procedure.

Lahat 2007 was designed to compare in-hospital colonoscopy with later colonoscopy (at only 6 weeks after discharge).¹⁰⁹ The study found a nonsignificantly higher rate of incomplete colonoscopies among those with in-hospital rather than later colonoscopy (17.8% vs. 7.3%; P = 0.16). However, the study also found that only 3/45 (6.7%) of those with inpatient colonoscopy

failed to show (or refused) colonoscopy, as opposed to 10/41 (24.4%) who did not show for their 6 week colonoscopy ($P=0.03$). In total 34/45 (75.6%) of in-hospital colonoscopy patients had a completed colonoscopy.

Figure 9. Meta-analysis of colonoscopy after acute diverticulitis: Percent with failed or incomplete colonoscopy



Abbreviations: CI = confidence interval, I^2 = measure of statistical heterogeneity (% of heterogeneity not due to random chance), Pct = percent, P_{het} = chi-squared P value of statistical heterogeneity (not the P value of the estimate), wk = weeks (after hospitalization).

Summary of Evidence Pertaining to Colonoscopy

The evidence profile summarizing results and providing SoE is in Table 11.

Three studies compared groups of patients who had recent episodes of acute diverticulitis who did or did not undergo post-recovery colonoscopy. None addressed the clinically most important outcome of CRC death. Likely because of lack of power (due to the relatively low percentage of people with CRC discovered after acute diverticulitis), overall, with low SoE, the studies do not support that CRC is uncovered more frequently among those receiving colonoscopy soon after diverticulitis (summary OR 1.54, 95% CI 0.73 to 3.26). Any suggestion that those who underwent colonoscopy may be at increased risk for having CRC may be due to underlying biases regarding who completed their colonoscopy (e.g., possibly people with a family history of CRC or more complicated diverticulitis are more likely to have colonoscopy).

Three studies compared people undergoing colonoscopy with and without recent episodes of acute diverticulitis. Again, none evaluated CRC death. Based on only unadjusted analyses, there is low SoE that those with recent acute diverticulitis may be more likely to have CRC than the general population (OR 3.35, 95% CI 0.84 to 13.4).

Twenty studies provided variable SoE regarding likelihood of CRC and high-risk colonic lesions among people with recent episodes of acute diverticulitis. In summary, CRC death occurred in about 0.5 to 0.8 percent of patients (2 studies), and colonoscopy revealed CRC in 2.1 percent (95% CI 1.4 to 3.0; 20 studies), advanced colonic neoplasia in 7.2 percent (95% CI 4.9 to 10.0; 3 studies), advanced adenoma in 3.3 percent (95% CI 2.3 to 4.4; 6 studies), adenomas with high-grade dysplasia (which likely includes other specific lesions) in 1.2 percent (95% CI 0.1 to 2.9; 7 studies), large adenomas in 2.4 percent (95% CI 1.6 to 3.4; 4 studies).

Ten studies evaluated various risk factors for different abnormal colonoscopy findings; most of the analyses were conducted by only single studies. Among the more commonly reported analyses, patients 50 years or older were probably about 3-times as likely to have CRC than younger patients (OR 3.31, 95% CI 1.58 to 6.95; 4 studies; moderate SoE), 8- to 9-times more likely to have advanced colonic neoplasias (3 studies; high SoE), and maybe 1.7- to 3.3-times higher risk of advanced adenomas (2 studies; low SoE). Patients with recent complicated diverticulitis (compared with those with uncomplicated diverticulitis) were about 6-times more

likely to have CRC (OR 5.72, 95% CI 2.73 to 12.0; 7 studies; high SoE), 3-times more likely to have advanced colonic neoplasia (OR 3.44, 95% CI 1.99 to 5.94, 4 studies; high SoE), and probably about twice as likely to have advanced adenomas (OR 1.95, 95% CI 0.91 to 4.17; 4 studies; moderate SoE).

Complications due to colonoscopy after acute diverticulitis are rare. Based on six studies that explicitly reported on complications, none (of 878) patients experienced a procedure-related complication (95% CI 0 to 0.9%; high SoE). Failed or incomplete colonoscopies were reported to be uncommon (3.5%, 95% CI 2.1 to 5.3; 3 studies; high SoE). One RCT compared in-hospital colonoscopy to colonoscopy about 6 weeks after discharge finding similar rates of completed colonoscopies between the groups.

Table 11. Evidence profile for colonoscopy after acute diverticulitis

Comparison	Outcome	No. Studies (Subjects ^a)	Risk of Bias	Consistency	Precision	Directness	Other	Overall SoE	Findings and Conclusions
Colonoscopy vs. no colonoscopy	CRC death	0							No evidence
	CRC	3 (1851)	Moderate	Consistent	Imprecise	Direct	None	Low	No evidence of a difference OR 1.54 (0.73, 3.26)
Diverticulitis vs. general population	CRC death	0							No evidence
	CRC	3 (954)	Moderate	Inconsistent	Precise	Direct	None	Low	Possible increased risk after diverticulitis OR 3.35 (0.84, 13.4)
	Premalignant lesions	3 (954)	Moderate	Inconsistent	Imprecise	Direct	None	Insufficient	No conclusion regarding colonoscopy in diverticulitis vs. general population
Rates of abnormal findings (no comparison)	CRC death	2 (1047)	Low	Consistent	Imprecise	Direct	Sparse	Low	0.5% or 0.8%
	CRC	20 (6195)	Low	Inconsistent	Precise	Direct	None	Moderate	1.8% (1.2, 2.6)
	ACN	3 (766)	Low	Inconsistent	Precise	Direct	None	Moderate	7.2% (4.9, 10.0)
	Advanced adenoma	6 (1675)	Low	Consistent	Precise	Direct	None	High	3.3% (2.3, 4.4)
	High-grade dysplasia	7 (2419)	Low	Inconsistent	Precise	Direct	None	Moderate	1.2% (0.1, 2.9)
	Adenoma ≥10 mm	4 (1210)	Low	Consistent	Precise	Direct	None	High	2.4% (1.6, 3.4)
	Serrated polyp	2 (617)	Low	Inconsistent	Imprecise	Direct	Sparse	Insufficient	Estimate unclear
Age ≥50 vs. <50 y	CRC	4 (1158)	Low	Inconsistent	Precise	Direct	None	Moderate	Older at increased risk OR 3.31 (1.58, 6.95)
	ACN	3 (650)	Low	Consistent	Precise	Direct	None	High	Older at increased risk OR ~8 to 9
	Advanced adenoma	2 (398)	Low	Consistent	Imprecise	Direct	Sparse	Low	Possibly older at increased risk OR 1.7 or 3.3, but imprecise or NS
Complicated vs. uncomplicated	CRC	7 (1965)	Low	Consistent	Precise	Direct	None	High	Hx of complicated at increased risk OR 5.72 (2.73, 12.0)
	ACN	4 (866)	Low	Consistent	Precise	Direct	None	High	Hx of complicated at increased risk OR 3.44 (1.99, 5.94)
	Advanced adenoma	3 (671)	Low	Consistent	Imprecise	Direct	None	Moderate	Hx of complicated maybe at increased risk OR 1.95 (0.91, 4.17)
	High-grade dysplasia	1 (427)	Low	N/A	Precise	Direct	Sparse	Insufficient	No conclusion regarding complicated vs. uncomplicated
Complications (no comparison)	Complications	4 (878)	Low	Consistent	Precise	Direct	None	High	0% (0 to 0.9)
Feasibility (no comparison)	Incomplete colonoscopy	3 (572)	Low	Consistent	Precise	Direct	None	High	3.5% (2.1, 5.3)

Abbreviations: ACN = advanced colonic neoplasia, CRC = colorectal cancer, Hx of = history of (recent), NS = not statistically significant, OR = odds ratio (with 95% confidence interval), SoE = strength of evidence.

^a With recent acute diverticulitis

Key Question 4. Interventions To Prevent Recurrence

Key Questions 4a and 4b. Nonsurgical Interventions

Key Points

- In patients with a history of acute diverticulitis, 5-aminosalicylic acid (5-ASA) probably does not reduce the risk of recurrence of diverticulitis (high SoE) and may increase the risk by a small amount.
- The evidence does not suggest that 5-ASA increases the risk of adverse events compared with placebo treatments (high SoE).
- There was insufficient evidence to make conclusions for other outcomes or other interventions due to sparse evidence and underpowered studies. These included rifaximin, combination 5-ASA and rifaximin, probiotics, and burdock tea.
- Notably, no comparative study evaluated medical nutrition therapy.

Findings Pertaining to Nonsurgical Interventions

Twelve studies (10 RCTs, one NRCS, and one single-group study) evaluated nonsurgical (pharmacologic and nonpharmacologic) interventions to prevent recurrent diverticulitis (Appendix C Tables C-4ab-1 to C-4ab-3). The results of the studies are summarized in Appendix D Tables D-4ab-1 to D-4ab-2.

The average age of participants ranged from 48 years to 67 years across studies. Between 31 and 66 percent of study participants were male. All studies included patients who had a documented prior episode of acute diverticulitis; however, two RCTs (the PREVENT-1 and PREVENT-2 trials [undefined acronyms], published in the same article¹²⁸) included 0.3 and 0.5 percent of patients without prior diverticulitis, respectively. Five RCTs were funded by industry,¹²⁸⁻¹³¹ and one was explicitly not funded by industry¹³²; the remaining six studies did not report their funding sources.

Six RCTs compared 5-ASA (mesalamine) to placebo. Other comparisons between interventions were evaluated by single studies only. These included comparisons of probiotics versus placebo, rifaximin versus placebo, combination 5-ASA and probiotics versus placebo, combination 5-ASA and probiotics versus probiotics alone, combination 5-ASA and probiotics versus 5-ASA alone, combination rifaximin and 5-ASA versus rifaximin alone, and 5-ASA versus rifaximin. The only comparative study of nonpharmacologic interventions was one RCT that compared burdock tea to control. Finally, one single-group study reported on harms of 5-ASA. Of note, none of the studies evaluated medical nutrition therapy.

We did not detect any major methodological concerns in six RCTs (the PREVENT-1 and PREVENT-2 trials, the SAG-37 and SAG-51 trials [undefined acronyms], Lanas 2013, and Mizuki 2019) (Appendix C Table C-4ab-2). The RCT that compared combination rifaximin and 5-ASA with rifaximin alone (Tursi 2002) did not report the random sequence generation method or whether allocation was concealed. Three RCTs (Tursi 2002, Tursi 2007, and Kvasnovsky 2007) did not conduct blinding of participants, care providers, or outcome assessors. One RCT (Stollman 2013) followed only participants who were compliant with 12 weeks of therapy, and thus had a high withdrawal rate. We assessed the NRCS (Festa 2017) at low risk of confounding bias because it reported conducting multivariate Cox regression to account for potential confounding. We assessed Festa 2017 at low risk of bias in selection of participants into the

study. We could not adequately assess the risk of bias in the single-group study (Silva Sanchez 2014) because it has been reported only as a conference abstract.

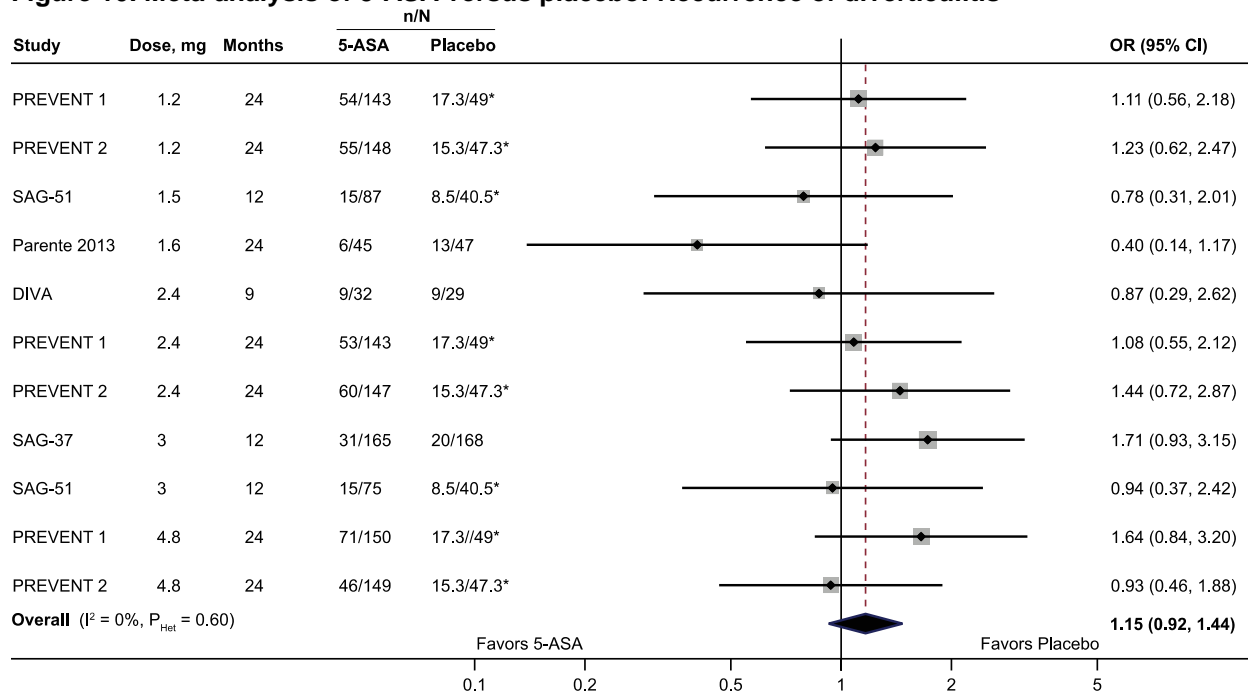
5-ASA Versus Placebo

5-ASA is an anti-inflammatory drug typically used for inflammatory bowel disease (ulcerative colitis and Crohn's disease). Six RCTs (the PREVENT-1 and PREVENT-2 [both in Raskin 2014], SAG-37 and SAG-31 trials [both in Kruis 2017], Parente 2013, and Stollman 2013) compared 5-ASA (a variety of doses) with placebo in a total of 1836 participants, almost all of whom had prior histories of acute diverticulitis.^{128, 130, 132, 133} In addition, one single-group study reported harms in 45 patients receiving 4.8 g/day of 5-ASA.¹³⁴

Recurrence of Diverticulitis

All six RCTs reported on the outcome of recurrence of diverticulitis. Both the PREVENT-1 and PREVENT-2 trials compared three doses of 5-ASA (1.2, 2.4, and 4.8 g/day) with placebo. SAG-51 compared two doses of 5-ASA (1.5 and 3 g/day) with placebo. Parente 2013, Stollman 2013 (DIVA [undefined acronym]), and SAG-37 each compared a single dose (1.6, 2.4, and 3 g/day, respectively) with placebo. To allow meta-analysis, we split the number of people in the placebo groups of the multidose studies to avoid double-counting the placebo groups. By meta-analysis, the summary OR for diverticulitis recurrence with 5-ASA was 1.15 (95% CI 0.92 to 1.44), suggesting 5-ASA may *increase* the risk of recurrence by a small amount (Figure 10). There was no statistical evidence of heterogeneity across studies. Other than different doses of 5-ASA, we did not identify important clinical differences across studies. However, consistent with the lack of statistical heterogeneity across studies, we did not see evidence that effects differ by dose (note that the forest plot is arranged by 5-ASA dose), which may also suggest a lack of effect.

Figure 10. Meta-analysis of 5-ASA versus placebo: Recurrence of diverticulitis



Abbreviations: 5-ASA = 5-aminosalicylic acid, CI = confidence interval, I^2 = measure of statistical heterogeneity (% of heterogeneity not due to random chance), mg = milligrams, OR = odds ratio, P_{Het} = statistical heterogeneity P value.

* The numbers of participants in placebo groups were divided by the number of nonplacebo groups to avoid double counting.

Three RCTs (Parente 2013, SAG-51, and DIVA [Stollman 2013]) reported on time to recurrence (in days) (Table 12) but had conflicting results. Parente 2013 reported *worse* outcomes with 5-ASA: patients receiving 1.6 g/day of 5-ASA (10 d/mo) had a *shorter* mean time to recurrence than patients receiving placebo (mean difference [MD] –151 days, 95% CI –366 to –66). The other two trials found no statistically significant differences between 5-ASA and placebo (Parente 2013: hazard ratio [HR] 1.02 for 3 g/d and 0.74 for 1.5 g/d; Stollman 2013: 209 days *longer* before recurrence with 5-ASA, but reported as statistically nonsignificant, implying a very wide confidence interval).

Stollman 2013 reported the numbers of patients who withdrew from the study because of surgery for diverticulitis (Table 13). These included two patients in the 5-ASA group and one in the placebo group, implying an OR = 2.11 (95% CI 0.18 to 24.2).

Symptom Scores

Parente 2013 reported on the impact of therapy on physical condition at 24 months using the Therapy Impact Questionnaire (TIQ) (Table 12). Scores on the TIQ range from 0 to 40, with lower scores suggesting a better outcome. At 24 months, patients in the 5-ASA arm had lower mean TIQ scores than patients in the placebo arm (MD –2.9, 95% CI –4.8 to –1.0), suggesting a beneficial effect of 5-ASA. However, we found no information regarding what a minimal clinically important difference would be. Also of note, the study gathered data on the quality of life component of the TIQ but did not report followup data or analyses for this component.

Stollman 2013 reported changes in a Global Symptom Score (GSS), which was developed for the study (see Table 12 footnote). Data were incompletely reported but found that GSS scores were lower (better) with 5-ASA than placebo at all followup timepoints, but mostly nonsignificantly so. The study does not claim any differences were clinically significant. The study also reported numbers of patients who achieved a “GSS response” (score of 0-1 of 6 on all 10 subscales) and a “complete GSS response” (score of 0 on all subscales). At 12 months, the study found no significant difference (implicitly) in GSS response between 5-ASA (67%) and placebo (50%), but a just-significant difference in complete GSS response (41% vs. 18%, $P=0.45$).

Table 12. Nonsurgical treatments to prevent recurrence: Continuous outcomes ^a

Comparison	Outcome	Study, PMID	Time (Mo)	Arm	N	Mean (SD or 95% CI)	Effect Size (95% CI)	Reported P Value
5-ASA vs. placebo	Time to recurrence of diverticulitis (days)	SAG-51 2017, ¹³³ 28543263	12	5-ASA (3.0 g/d)	NR	191 (125)	HR 1.02 (0.53, 1.94)	0.96
				5-ASA (1.5 g/d)	NR	116 (134)	HR 0.74 (0.38, 1.43)	0.37
				Placebo	NR	147 (162)	Reference	
		Parente 2013, ¹³⁰ 23754545	24	5-ASA (1.6 g/d), 10 d/mo	45	219 (180)	MD -151 (-236, -66)	NR
				Placebo	47	370 (227)		
		Stollman 2013, ¹³² 23426454	12	5-ASA (2.4 g/d)	25	308.7 (NR)	MD 208.6 (NR)	NS
				Placebo	28	100.1 (NR)		
	Therapy Impact Questionnaire (TIQ score) ^b	Parente 2013, ¹³⁰ 23754545	24†	5-ASA (1.6 g/d), 10 d/mo	45	0: 8.1 (3.8) 24: 5.4 (2.7)	24: MD -2.9 (-4.8, -1.0) ^c	MD 0.022†
				Placebo	47	0: 8.7 (4.4) 24: 8.3 (5.7)	0-24: NMD -2.3 (-4.1, -0.5) ^c	
	Global Symptom Score (GSS)†	Stollman 2013, ¹³² 23426454	12	5-ASA (2.4 g/d)	27	0: 22.0 (8.6) 9: 1.0 [median]	12: MD ~-4.0	NS
				Placebo	29	0: 23.5 (9.1) 9: 5.0 [median]	0-12: NMD ~-2.5	
(5-ASA + probiotics) vs. placebo	Time to recurrence of diverticulitis (days)	Stollman 2013, ¹³² 23426454	12	5-ASA (2.4 g/d) + probiotics	27	280.7 (NR)	MD: 180.6 (NR)	NS
				Placebo	29	100.1 (NR)		
	Global Symptom Score (GSS) ^d	Stollman 2013, ¹³² 23426454	12	5-ASA (2.4 g/d) + probiotics	27	0: 19.4 (NR) 12: 4.4 [median]	12: MD ~-0.6	NS
				Placebo	29	0: 23.5 (9.1) 12: 5.0 [median]	0-12: NMD ~-3.5	
Burdock tea vs. no treatment	Acute colonic diverticulitis-free time (mo)	Mizuki 2019, ¹³⁵ 31043657	30	Burdock tea (4.5 g/d)	44	59.3 (54.0, 64.7)	MD 14.2 (4.5, 23.9)	0.012
				No intervention	44	45.1 (37.1, 53.0)		

Abbreviations: 5-ASA = 5-aminosalicylic acid, CI = confidence interval, d = days, HR = hazard ratio, mo = month, MD = mean difference (between groups), NMD = net mean difference (difference-in-difference), NR = not reported, NS = not statistically significant, OR = odds ratio, PMID = PubMed identifier, SD = standard deviation, TIQ = Therapy Impact Questionnaire (0 to 40, lower better), y = years.

^a For comparisons between active therapies (e.g., combination 5-ASA plus rifaximin vs. rifaximin), see Appendix Table D-4ab-2.

^b Score to measure physical condition. Maximum (worst) score: 40. No information is available regarding minimal clinical important difference. Quality of life component was also measured but followup data were not reported.

^c However, based on figure displaying TIQ physical condition scores every 3 months, the difference between 5-ASA and placebo appears to be widest at 24 months, while it was narrowest at 21 months.

^d Score developed for this study. Ten domains, each ranging from 0-6 (most severe): 1) abdominal pain, 2) abdominal tenderness, 3) bloating, 4) urgency without bowel movement, 5) diarrhea, 6) constipation, 7) painful straining with bowel movement, 8) nausea/vomiting, 9) mucus in stool, 10) dysuria. The study based its power calculation on a 30% difference in change in GSS scores between groups (or 2 points).

Table 13. Nonsurgical treatments to prevent recurrence: Categorical outcomes not meta-analyzed^a

Comparison	Outcome	Study, PMID	Time (mo)	Arm	n/N (%)	Effect Size (95% CI)	Reported P-value
5-ASA vs. placebo	Surgery for recurrent diverticulitis	Stollman 2013, ¹³² 23426454	12	5-ASA (2.4 g/d)	2/40 (5.0)	OR 2.11 (0.18, 24.2)	NR
				Placebo	1/41 (2.4)		
Probiotics vs. placebo	Diverticulitis recurrence	Kvasnovsky 2017, ¹²⁹ 28528364	3	Probiotics (Symprove 1 mL/kg/d)	3/71 (4.2)	OR 0.09 (0.03, 0.33)	NR
				Placebo	23/72 (31.9)		
(5-ASA + probiotics) vs. placebo	Diverticulitis recurrence	Stollman 2013, ¹³² 23426454	12	5-ASA (2.4 g/d) + probiotics	10/27 (37.0)	OR 1.31 (0.43, 3.96)	NR
				Placebo	9/29 (31.0)		
	Surgery for recurrent diverticulitis	Stollman 2013, ¹³² 23426454	12	5-ASA (2.4 g/d) + probiotics	0/36 (0)	NA	NR
				Placebo	1/41 (2.4)		
Rifaximin vs. placebo	Diverticulitis recurrence	Lanas 2013, ¹³¹ 23092785	NR	Rifaximin (800 mg/d) 1 wk/mo + fiber 7 g/d	8/77 (10.4)	Adj OR 0.31 (0.11, 0.86)	0.025
				Placebo + fiber 7 g/d	17/88 (19.3)		
	Hospitalization for diverticulitis	Lanas 2013, ¹³¹ 23092785	NR	Rifaximin (800 mg/d) 1 wk/mo + fiber 7 g/d	2/77 (2.6)	OR 0.36 (0.07, 1.86)	NR
				Placebo + fiber 7 g/d	6/88 (6.8)		
Burdock tea vs. no treatment	Diverticulitis recurrence	Mizuki 2019, ¹³⁵ 31043657	30	Burdock tea (4.5 g/d)	5/47 (10.6)	OR 0.26 (0.08, 0.78)	0.013
				No intervention	14/44 (31.8)		

Abbreviations: 5-ASA = 5-aminosalicylic acid, Adj = adjusted, CI = confidence interval, d = days, HR = hazard ratio, mo = months, NA = not applicable, NR = not reported, OR = odds ratio, PMID = PubMed identifier, RR = risk ratio.

^a For comparisons between active therapies (e.g., combination 5-ASA plus rifaximin vs. rifaximin), see Appendix Table D-4ab-1.

Probiotics Versus Placebo

Probiotics are live microorganisms that are used to “restore” or “improve” the gut flora. One RCT (Kvasnovsky 2017) compared the probiotic Symprove (1 mL/kg/day) with placebo in 143 participants.¹²⁹

The trial reported substantially lower diverticulitis recurrence rates at 3 months among patients in the probiotics arm than in the placebo arm (OR 0.09, 95% CI 0.03 to 0.33) (Table 13).

Rifaximin Versus Placebo

Rifaximin is an antibiotic that is used for its anti-inflammatory properties for the treatment of irritable bowel syndrome and other gastrointestinal conditions. One RCT (Lanas 2013) compared rifaximin (800 mg/day, 1 week per month) with placebo in 165 participants.¹³¹ All participants also ingested daily fiber.

The trial reported substantially lower diverticulitis recurrence rates at 12 months among patients in the rifaximin arm than in the placebo arm after adjusting for age, sex, duration and localization of illness, time from last episode, and center recruitment rate (adjusted OR 0.31, 95% CI 0.11 to 0.86) (Table 13). The study was underpowered for hospitalization for diverticulitis, providing an imprecise comparison (OR 0.36, 95% CI 0.07 to 1.86).

5-ASA Plus Probiotics Versus Placebo

One RCT (Stollman 2013), a three-arm study, compared combination 5-ASA (2.4 g/d) plus probiotics (*Bifidobacterium infantis* 35624) for 12 weeks with placebo.

At 12-month followup, similar numbers of patients had episodes of diverticulitis recurrence, yielding an imprecise OR = 1.31 (95% CI 0.43 to 3.96) (Table 13). Patients on combination therapy went 181 days longer in time to diverticulitis recurrence than with placebo (Table 12), but the difference between treatments was implicitly nonsignificant, further implying a very wide confidence interval.

No patients (of 36) on combination therapy had surgery for recurrent diverticulitis, compared with 1 of 41 on placebo. Lower percentages of patients on combination therapy had GSS response or complete GSS response (see *5-ASA Versus Placebo/Symptom Scores* section, above, for descriptions) than with placebo, but none of the differences was described as statistically significant (see Appendix Table D-4ab-1). The changes in GSS score were nonsignificantly different between interventions (Table 12).

Burdock Tea Versus No Treatment

One RCT (Mizuki 2019) compared the use of burdock tea (1.5 g 3 times a day) with no intervention in 91 patients.¹³⁵ Burdock tea is a diuretic and antipyretic tea commonly used in Asian medicine.

The trial reported substantially lower rates of diverticulitis recurrence over a median observation period of 30 months among patients in the burdock tea arm than in the no intervention arm (OR 0.26, 95% CI 0.08 to 0.78) (Table 13). In addition, patients in the burdock tea arm were free of diverticulitis symptoms for a mean of 14.2 (95% CI 4.53 to 23.9) more months than those in the no intervention arm (Table 12).

Combination 5-ASA + Rifaximin Versus Rifaximin Alone

One RCT (Tursi 2002) compared use of a combination of balsalazide (1.6 g/day) and rifaximin (800 mg/day) with use of rifaximin alone (800 mg/day, all for 7 d/mo) in 218 participants.¹³⁶ Balsalazide is metabolized to 5-ASA in the colon.

The comparison between intervention treatments of 12-month mortality was imprecise, with one death in each study group (Appendix Table D-4ab-1). Combination 5-ASA and rifaximin resulted in lower rates of recurrence of diverticulitis at 12 months compared with rifaximin alone (OR 0.13, 95% CI 0.04 to 0.44) (Appendix Table D-4ab-1).

About twice as many patients taking combination 5-ASA and rifaximin were symptom-free at 12 months compared with rifaximin alone (RR 2.02, 95% CI 1.58 to 2.58) (Appendix Table D-4ab-1), with similar findings at 3, 6, and 9 months.

5-ASA Versus Rifaximin

One NRCS (Festa 2017) compared the use of rifaximin (800 mg/day) with use of 5-ASA (2.4 g/day), each for 10 days/month in 124 participants.¹³⁷

Festa 2017 reported that patients in the rifaximin arm had lower rates of recurrence of diverticulitis compared with patients in the 5-ASA arm (adjusted HR 0.27, 95% CI 0.10 to 0.72) (Table Appendix Table D-4ab-1).

5-ASA Plus Probiotics Versus 5-ASA Alone

One RCT (Stollman 2013) compared combination mesalamine (2.4 g/d) and probiotics (*Bifidobacterium infantis* 35624) with mesalamine alone, each daily for 12 weeks, with 12-month followup.¹³²

The trial was underpowered for recurrence of diverticulitis, resulting in an imprecise comparison (OR 1.50, 95% CI 0.50 to 4.50) (Table Appendix Table D-4ab-1). Time to recurrence of diverticulitis was similar between arms (280.7 vs. 308.7 days, combination vs. 5-ASA) (Appendix Table D-4ab-2). There was no significant difference in numbers of patients who had surgery for recurrent diverticulitis (0/36 vs. 2/40).

As described under *5-ASA Versus Placebo/Symptom Scores*, the study reported changes in a GSS. Data were incompletely reported but found that GSS scores were lower (better) with 5-ASA than combination 5-ASA plus probiotics at all followup timepoints, but nonsignificantly so (Appendix Table D-4ab-2). Rates of GSS response (29.2% vs. 50%) and complete GSS response (8.3% vs. 40.7%) were considerably higher with 5-ASA alone than combination therapy, but the study does not report that the difference was statistically significant (Appendix Table D-4ab-1).

5-ASA Plus Probiotics Versus Probiotics Alone

One RCT (Tursi 2007) compared combination balsalazide (2.25 g/d) and probiotics (VSL #3) with use of probiotics alone, each for 15 days/month.¹³⁸

The trial was underpowered for recurrence of diverticulitis, resulting in an imprecise comparison (OR 0.38, 95% CI 0.07 to 1.92) (Appendix Table D-4ab-1).

Adverse Events

Serious Adverse Events

Five RCTs (the PREVENT-1, PREVENT-2, SAG-37, Parente 2013, Stollman 2013) evaluating a variety of doses of 5-ASA (ranging from 0.8 to 4.8 g/day) reported adverse events

that the authors named as serious. However, they did not define the outcome (Table 14). Serious adverse event rates ranged between 8 and 14 percent across 5-ASA arms. But in all trials, similar serious adverse event rates were seen in the placebo groups.

Other Adverse Events

Three RCTs (PREVENT-1, PREVENT-2, Stollman 2013), which compared 1.2 to 4.8 g/day doses of 5-ASA with placebo, reported on specific adverse events, namely sepsis, acute myocardial infarction, and urinary tract infections. Sepsis and acute myocardial infarction were rare (Table 14). No differences were found in rates of urinary tract infections between each of the 5-ASA groups and placebo. The single group study (Silva Sanchez 2014) also found a similar rate of urinary tract infections as in the two trials). Stollman 2013 reported no headaches in either the 5-ASA or placebo arm; Silva Sanchez 2014 reported that 9.0 percent of patients taking 5-ASA complained of headache (without a comparator group).

Adverse Events Leading to Discontinuation

Three RCTs (SAG-37, Parente 2013, Stollman 2013) reported on adverse events that led to discontinuation (Table 14). All RCTs reported that, compared with placebo, 5-ASA use was associated with a higher likelihood of discontinuation due to adverse events, but while the SAG-37 trial found a statistically significant difference, the other two trials were (near) imprecise.

Table 14. Adverse events of 5-ASA

Outcome	Study, PMID	Arm	n/N (%)	OR (95% CI)
Serious AEs	PREVENT-1 2014, ¹²⁸ 25038431	5-ASA (4.8 g/d)	18/150 (12.0)	1.12 (0.55, 2.28)
		5-ASA (2.4 g/d)	15/143 (10.5)	0.96 (0.46, 2.02)
		5-ASA (1.2 g/d)	16/143 (11.2)	1.03 (0.49, 2.15)
		Placebo	16/147 (10.9)	Reference
	PREVENT-2 2014, ¹²⁸ 25038431	5-ASA (All doses)	36/444 (8.1)	0.75 (0.40, 1.41)
		Placebo	15/142 (10.6)	
	SAG-37 2017, ¹³³ 28543263	5-ASA (3.0 g/d)	55/387 (14.2)	1.46 (0.91, 2.36)
		Placebo	29/285 (10.2)	
	Parente 2013, ¹³⁰ 23754545	5-ASA (800 mg/d)	4/45 (8.9)	2.20 (0.38, 12.6)
		Placebo	2/47 (4.3)	
Sepsis	PREVENT-1 2014, ¹²⁸ 25038431	5-ASA (4.8 g/d)	1/150 (0.7)	NA
		5-ASA (2.4 g/d)	0/143 (0)	
		5-ASA (1.2 g/d)	1/143 (0.7)	
		Placebo	0/147 (0)	
Acute myocardial infarction	PREVENT-1 2014, ¹²⁸ 25038431	5-ASA (4.8 g/d)	0/150 (0)	NA
		5-ASA (2.4 g/d)	0/143 (0)	
		5-ASA (1.2 g/d)	1/143 (0.7)	
		Placebo	2/147 (1.4)	
Urinary tract infection requiring antibiotics	PREVENT-1 2014, ¹²⁸ 25038431	5-ASA (4.8 g/d)	8/150 (5.3)	0.43 (0.18, 1.03)
		5-ASA (2.4 g/d)	12/143 (8.4)	0.70 (0.32, 1.52)
		5-ASA (1.2 g/d)	14/143 (9.8)	0.83 (0.39, 1.75)
		Placebo	17/147 (11.6)	Reference
	PREVENT-2 2014, ¹²⁸ 25038431	5-ASA (4.8 g/d)	10/149 (6.7)	1.39 (0.51, 3.75)
		5-ASA (2.4 g/d)	14/147 (9.5)	2.03 (0.79, 5.19)
		5-ASA (1.2 g/d)	11/148 (7.4)	1.55 (0.58, 4.11)
		Placebo	7/142 (4.9)	Reference
	Stollman 2013, ¹³² 23426454	5-ASA (2.4 g/d)	1/40 (2.5)	NA
		Placebo	0/41 (0)	
Headache	Stollman 2013, ¹³² 23426454	5-ASA (2.4 g/d)	0/40 (0)	NA
		Placebo	0/41 (0)	
	Silva Sanchez 2014, No PMID	5-ASA (4.8 g/d)	27/299 (9.0)	NA
AEs leading to discontinuation	SAG-37 2017, ¹³³ 28543263	5-ASA (3.0 g/d)	97/387 (25.1)	OR 1.53 (1.05, 2.24)
		Placebo	51/285 (17.9)	
	Parente 2013, ¹³⁰ 23754545	5-ASA (800 mg/d)	8/45 (17.8)	OR 2.32 (0.65, 8.34)
		Placebo	4/47 (8.5)	
	Stollman 2013, ¹³² 23426454	5-ASA (2.4 g/d)	5/40 (12.5)	OR 1.81 (0.40, 8.14)
		Placebo	3/41 (7.3)	

Abbreviations: 5-ASA = 5-aminosalicylic acid, AE = adverse event, CI = confidence interval, NA = not applicable, OR = odds ratio, PMID = PubMed identifier.

Summary of Evidence Pertaining to Nonsurgical Interventions

The evidence profile (Table 15) summarizes the findings for which there is sufficient evidence, which were only risk of diverticulitis recurrence and adverse events from 5-ASA treatment.

Eleven studies evaluated various nonsurgical interventions to prevent recurrent diverticulitis. However, except for the comparison between 5-ASA and placebo, only a single study evaluated each intervention or comparison. Notably, no comparative study evaluated medical nutrition therapy.

The most extensively evaluated treatment is 5-ASA. All six RCTs that compared 5-ASA to placebo found no statistically significant difference in diverticulitis recurrence between groups. Across studies, there is high SoE that 5-ASA does not reduce risk of recurrence. The summary

OR actually nominally favored placebo with an OR of 1.15 (95% CI 0.92 to 1.44) suggesting a higher risk of recurrence with 5-ASA treatment. No differences in effect were seen based on the different doses of 5-ASA tested (ranging from 1.2 to 4.8 g/day). Evidence about time to recurrence was conflicting among three studies (insufficient evidence). Evidence about undergoing surgery for recurrent diverticulitis, and symptoms scores are sparse (insufficient evidence). There is high SoE (6 studies) that reports of adverse events are similar among patients taking 5-ASA or placebo.

Other interventions were evaluated by only a single study each; thus, all with insufficient evidence.

Table 15. Evidence profile for nonsurgical interventions to prevent recurrence

Topic	No. Studies (Subjects)	Risk of Bias	Consistency	Precision	Directness	Other	Overall SoE	Conclusion Statements
5-ASA to prevent recurrence (vs. placebo)	6 (1898)	Low	Consistent	Precise	Direct	None	High	5-ASA does not reduce the risk of recurrence OR 1.15 (0.92, 1.44), nominally favoring placebo
5-ASA adverse events	6 (1898)	Low	Consistent	Precise	Direct	None	High	Adverse events are no more common with 5-ASA than placebo
Other treatments to prevent recurrence ^a	7 (30-218)	Moderate	N/A	Mixed	Direct	Sparse ^b	Insufficient	No conclusions

Abbreviations: N/A = not applicable, OR = odds ratio (with 95% confidence interval), SoE = strength of evidence.

^a Rifaximin, probiotics, combination 5-ASA and rifaximin, combination 5-ASA and probiotics, and burdock tea

^b Each study made a unique comparison.

Key Question 4c. Elective Surgery

Key Points

- Recurrence of diverticulitis in patients with either complicated or smoldering/frequently recurring (after uncomplicated) diverticulitis was about 5- to 7-times lower among those who underwent elective surgery than those treated medically (high SoE). No eligible studies evaluated the relative effect of elective surgery for patients with nonrecurrent uncomplicated diverticulitis.
- The 30-day mortality rate was 0.7 percent across studies (moderate SoE). Specific serious adverse events were uncommon with elective surgery (low to moderate SoE). The most common adverse events were reoperation (5.5%) and anastomotic leakage (4.3%) (both low SoE). Other adverse events occurred in less than 2 percent of patients (low to moderate SoE).
- There was insufficient evidence to allow conclusions for other outcomes due to sparse or imprecise data.

Findings Pertaining to Elective Surgery

Elective Surgery Compared to Nonoperative Management

Two small RCTs in four reports¹³⁹⁻¹⁴² and one large NRCS¹⁴³ with adjusted analyses evaluated elective surgery (laparoscopic sigmoid colectomy,¹³⁹ laparoscopic sigmoidectomy,¹⁴⁰⁻¹⁴² and colectomy¹⁴³) compared to nonoperative management. Nonoperative management was described as conservative management,¹⁴⁰⁻¹⁴² observation,¹³⁹ or simply nonoperative management.¹⁴³ The NRCS conducted propensity score adjusted analyses on some of their reported outcomes.

Full baseline data are in Appendix C Tables C-4c-1 to C-4c-5; Appendix D, Tables D-4c-1 to D-4c-3 provide study-level results. The RCTs each enrolled just over 100 participants with a previous episode of acute diverticulitis. However, the two RCTs included different patients. The DIRECT trial (van de Wall 2017, undefined acronym) included patients with uncomplicated disease who had either smoldering symptoms (persisting >3 months) or frequent recurring symptoms (≥ 3 within 2 years) while You 2018 evaluated patients with a history of complicated diverticulitis manifested as extraluminal air with or without abscess (although not statistically different, 58% of patients in the surgery arm had a history of an abscess while only 42% did in the observation group). The NRCS (Aquino 2019) included 7072 patients with a history of an acute diverticular abscess (complicated diverticulitis).

Participant ages were similar across studies, with participants in their mid 50s, and between 28 and 54 percent male. One RCT was industry funded (You 2018), the other was non-industry funded; the NRCS did not report funding source. Both RCTs were of low risk of bias for randomization, incomplete outcome data, and selective reporting, but high risk of bias for blinding.¹³⁹⁻¹⁴² The NRCS had a low risk of bias for confounding and selection bias.¹⁴³ Full risk of bias in Appendix C; full results are in Appendix D.

Mortality

The You 2018 and DIRECT RCTs reported mortality at 3 and 5 years, respectively (Table 16). In both studies, there were no deaths in the elective surgery arms and one death (total) in the

nonoperative treatment arm. The studies were underpowered to evaluate mortality within 3 to 5 years.

The NRCS (Aquina 2019) reported an unadjusted analysis of diverticulitis-related death but found a large difference. The death rate was substantially lower in the elective surgery group (0.2%) at 5 years than the nonsurgical treatment group (1.9%), implying an unadjusted OR of 0.13 (95% CI 0.03 to 0.29), suggesting the number needed to treat (NNT) to prevent one death was 57 (95% CI 46 to 76). Note that strictly speaking, this analysis does not meet criteria for being included in the review because the analysis was unadjusted for underlying differences between people who do and do not undergo elective surgery. However, we include it because it is the largest study, by far, that directly compares elective surgery to no surgery.

Table 16. Elective surgery versus no surgery: Categorical outcomes

Outcome	Study Year PMID	Followup Time	Arm	n/N (%)	OR (95% CI)
Mortality	You 2018, ¹³⁹ 29683483	3 y	Elective surgery	0/26 (0)	0 events
			No surgery	0/81 (0)	
	DIRECT 2017, ¹⁴⁰ 28404008	5 y	Elective surgery	0/53 (0)	0.51 (0.02, 15.6)
			No surgery	1/56 (1.8)	
	Aquina 2019, ¹⁴³ 30335195	5 y	Elective surgery	3/1660 (0.2)	0.09 (0.03, 0.29) ^a
			No intervention	104/5412 (1.9)	
Diverticulitis recurrence	You 2018, ¹³⁹ 29683483	3 y	Elective surgery	2/26 (7.7)	0.18 (0.04, 0.80)
			No surgery	26/81 (32.1)	
	DIRECT 2017, ¹⁴⁰ 28404008	5 y	Elective surgery	6/53 (11.3)	0.29 (0.11, 0.81)
			No surgery	17/56 (30.4)	
	Aquina 2019, ¹⁴³ 30335195	5 y	Elective surgery	70/1660 (4.2)	0.13 (0.10, 0.17) ^a
			No surgery	1340/5412 (24.8)	
Stoma	Aquina 2019, ¹⁴³ 30335195	5 y	Elective surgery	166/1660 (10.0)	1.88 (1.50, 2.36) ^a
			No surgery	309/5412 (5.7)	

Abbreviations: CI = confidence interval, PMID = PubMed identifier, OR = odds ratio, PMID = PubMed identifier, RCT = randomized controlled trial, y = year.

^a Unadjusted odds ratio from a nonrandomized comparative study.

Recurrence

The two RCTs found that at 3 and 5 years, elective surgery had substantially lower rates of recurrence than nonoperative treatment (Table 16). One RCT (You 2018) of 107 people with a first episode of acute diverticulitis complicated by extraluminal air and with or without abscess, which had initially been treated with successful nonoperative management, reported an OR of 0.18 (95% CI 0.04 to 0.80) favoring surgery (7.7% vs. 32.1%), suggesting a number-needed-to-treat (NNT) to prevent one recurrence of 4.1 (95% CI 2.6 to 10.0). The second RCT (DIRECT 2017 [van de Wall 2017]) of 109 people with either ongoing abdominal complaints or frequently recurring left-sided diverticulitis (mean number of recurrences 3.61 [SD 1.67]) reported an OR of 0.29 (95% CI 0.11 to 0.81) favoring surgery (11.3% vs. 30.4%), suggesting a NNT of 5.3 (95% CI 3.0 to 23.4). The You 2018 RCT also reported that time to recurrence (Table 17) was significantly longer in the elective surgery arm (median 11 months) than the nonoperative treatment arm (median 7 months; $P=0.015$).

Of note, in the DIRECT trial 26 of 56 (46%) of patients randomized to conservative therapy ultimately had surgery during the 5-year followup period “due to severe ongoing abdominal complaints”.¹⁴² Although not clearly reported, in the You 2018 RCT, all patients assigned to observation were managed nonoperatively for 3 years.¹³⁹

The NRCS (Aquina 2019) reported an unadjusted analysis of recurrence rates (Table 16) but found a large difference. The recurrence rate was substantially lower in the elective surgery group (4.2%) than the nonsurgical treatment group (24.8%), implying an unadjusted OR of 0.13 (95% CI 0.10 to 0.17), suggesting an NNT of 4.9 (95% CI 4.5 to 5.3). Similar to the mortality analysis, this analysis does not meet criteria for being included in the review (since it was unadjusted), but we include it because it is the largest study, by far, that directly compares elective surgery to no surgery.

Although the NRCS did not report an adjusted analysis, we decided, *post hoc*, to meta-analyze the three studies based on their similar results. As shown in Figure 11, the summary OR was 0.16 (95% CI 0.09 to 0.27). The implied summary NNT to prevent one recurrence is 4.6 (95% CI 2.7 to 7.9).

Table 17. Elective surgery versus no surgery: Continuous outcomes ^a

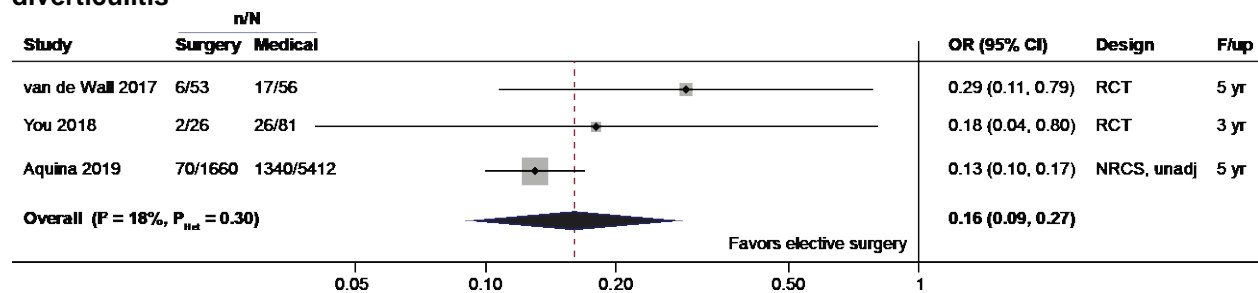
Outcome	Study Year PMID	Arm	N	Results	Difference (95% CI)	Reported P Value
Time to recurrence	You 2018, ¹³⁹ 29683483	Elective surgery	26	Median 11 mo (IQR 8, 14)	4 mo ^b	0.015
		No surgery	81	Median 7 mo (IQR 3.25, 15)		
Hospital length of stay	You 2018, ¹³⁹ 29683483	Elective surgery	26	Median 5.5 d (IQR 4, 8.5)	0.5 d ^b	0.90
		No surgery	81	Median 5 d (IQR 4, 8)		
	Aquina 2019, ¹⁴³ 30335195	Elective surgery	1660	Mean 8.0 d (SD 7.8)	Adj IRR = 2.16 (1.89, 2.47)	NR
		No surgery	5412	Mean 4.6 d (SD 18.5)		

Abbreviations: Adj = adjusted, IRR = “incidence rate ratio” (ratio of means), CI = confidence interval, d = days, IQR = interquartile range, mo = months, NR = not reported, PMID = PubMed identifier, SD = standard deviation.

^a Quality of life and pain (visual analog scale) results are reported in Appendix D Table D-4c-2.

^b Difference of median values. Confidence interval not estimated.

Figure 11. Meta-analysis of elective surgery for diverticulitis versus no surgery: Recurrence of diverticulitis



Abbreviations: CI = confidence interval, F/up = followup, I² = measure of statistical heterogeneity (% of heterogeneity not due to random chance), NRCS, unadj = unadjusted nonrandomized comparative study, OR = odds ratio, P_{Het} = statistical heterogeneity P value.

Stoma

The NRCS (Aquina 2019) reported a propensity score-adjusted comparison of stoma rates among patients who underwent elective surgery versus those who received nonoperative management. In the operative group, stomas were created during their elective surgery. In the nonoperative group, stomas were created during diverticulitis-related admissions during the 5-year followup period. As predicted by the researchers, those receiving elective surgery were more likely to have a stoma created, with an adjusted OR of 1.88 (95% CI 1.50 to 2.36).

Length of Hospital Stay

Two studies reported on length of hospital stay (Table 17). In the You 2018 RCT there was no difference in length of stay between elective surgery (median 5.5 days) and nonoperative management (median 5 days). In the Aquina 2019 NRCS, the elective surgery arm had a longer mean length of stay at 8 days compared to the nonoperative treatment arm (4.6 days). The propensity-score adjusted ratio of the length of stay (operative/nonoperative) was 2.16 (95% CI 1.89 to 2.47). An unadjusted estimate of the difference in days is 3.4 days (95% CI 2.8 to 4.0) longer for operative management.

Quality of Life and Pain

The DIRECT 2017 RCT reported on quality of life and pain in 109 participants (Appendix D Table D-4c-2). Across four scales (GIQLI, SF-36 mental and physical, and EuroQol-5D), people in the elective surgery group had greater improvements in quality of life and pain measures at both 6 months and 5 years, compared with baseline.

On the GIQLI scale at 6 months, the net difference (difference-in-difference) between arms from baseline was 13.6 units (95% CI 5.2 to 22.0; $P=0.0001$) on a scale from 0 to 144 where higher scores are desirable. At 5 years, the net difference between arms from baseline was 9.3 (95% CI 1.3, to 17.3; $P=0.018$). Note that the study was powered to detect a minimal clinical important difference of 10 points on the GIQLI scale.

On the SF-36 mental health scale at 6 months, the net difference between arms from baseline was 4.1 units (95% CI -0.4 to 8.6; $P=0.26$) on a scale of 0 to 100, with higher scores indicating better quality of life. At 5 years, there was a statistically significant net difference between arms from baseline of 6.4 (95% CI 2.2, to 10.6; $P=0.010$). On the SF-36 physical health scale at 6 months, the net difference between arms from baseline was 3.9 units (95% CI 1.1 to 6.7; $P=0.016$) and at 5 years 4.9 units (95% CI 1.5, to 8.3; $P=0.030$).

On the EuroQol-5D scale (0 to 1, with 1 reflecting best possible health) at both 6 months and 5 years, the net differences between arms from baseline were 0.16 units (95% CI 0.08 to 0.24; $P=0.001$).

On the VAS scale for pain (0-100, with 0 = no pain), the net difference at 6 months was -18.4 units (95% CI -26.4 to -10.4); $P<0.0001$) and at 5 years -11.0 (95% CI -20.1 to -1.9 ; $P=0.011$) favoring elective surgery.

The authors report these differences to be “clinically measurable,” and the GIQLI differences are above the published minimal clinically important differences (MCID) in a GIQLI validation study in cholecystectomy patients.¹⁴⁴ A systematic review suggests that for a category that includes gastroenterology, the differences reported in this paper are above the high range of the MCID for the GIQLI, SF-36, and EuroQol-5D.¹⁴⁵ Finally, the net difference on the VAS scale was above that determined to indicate a clinically important difference in patients recovering from surgery.¹⁴⁶

Notably, none of the studies evaluated psychosocial outcomes such as anxiety, stress, or fear related to the risk of recurrent episodes of acute diverticulitis.

Adverse Events Associated With Elective Surgery

Serious adverse events associated with elective surgery were reported in 17 studies (2 RCTs,¹³⁹⁻¹⁴² 1 NRCS,¹⁴³ and 14 eligible single-group studies in 15 reports¹⁴⁷⁻¹⁶¹). We did not review nonserious adverse events. Of note, for the purpose of this review, single group studies are studies of elective surgery *without* a comparison to nonsurgical management. Thus, studies that compared two or more specific surgeries, but no nonsurgical group, were considered to be

single group studies of surgery. As relevant, we note differences between surgeries, but this was not a question of interest, *per se*.

The characteristics of the comparative studies are described above. The single-group studies were all either non-industry funded or did not report funding source. The inclusion criteria were either having undergone elective surgery for diverticulitis (15 studies) or having a diagnosis of diverticulitis (2 studies). Very few studies reported on time between acute diverticulitis incident and surgery or number of prior episodes of diverticulitis. The median percentage of men across studies was 47 percent (range 29 to 52), and the mean age ranged from 55 to over 76. Surgeries included sigmoidectomy or left colectomy (with or without stoma). Most surgeries were reported to be laparoscopic or not reported, but in one study all surgeries were open^{150, 161} and in another study 28 percent were open.¹⁵² Full baseline data are in Appendix C Tables C-4c-1 to C-4c-5.

Risk of bias was low in all studies for incomplete outcome data, prespecification of eligibility criteria, and prespecification and clear measurement of outcomes. One study had a high risk of bias for selective outcome reporting,^{150, 161} and in another it was unclear.¹⁵⁶ Two studies had a high risk of bias unclear reporting of the intervention.^{148, 149}

Overall Adverse Event Rates

In general, composite adverse events (of multiple events) were common, but individual adverse event rates were low. Each specific adverse event was reported by only a small subset of the 18 included studies. The most commonly reported adverse event was 30-day mortality, which was reported by nine studies. Five adverse events were reported by five to seven studies (sepsis, unplanned reoperation, anastomotic leakage, myocardial infarction, and pulmonary embolism). Ten listed adverse events were reported by only one or two studies. Given the frequently large range of adverse event rates across studies, it is likely that the estimates derived from small numbers of studies are likely to change with future evidence.

We summarize the adverse events in Table 18, where adverse events are sorted by their frequency (full results are in Appendix D Table D-4c-3). For the purpose of providing a single, if rough, estimate of specific adverse event rates, we meta-analyzed outcomes when at least two studies (or cohorts) reported the same adverse event, regardless of the possible lack of commonality of populations, surgeries, or specific adverse event definitions. To demonstrate heterogeneity (differences across studies), we also provide the range of specific adverse event rates reported across studies. When articles reported adverse event rates for different cohorts (e.g., different specific surgeries) separately, we treated each cohort as a separate study for the purpose of meta-analysis.

Across a subset of four of the 18 studies, 25 percent of patients undergoing elective surgery had some serious adverse event; although, the definitions of serious adverse events were generally unclear and likely varied widely (and likely included nonserious adverse events). The range of event rates was 4 to 70 percent.

Of the individual adverse events, 30-day mortality was 0.7 percent across nine studies; 30-day readmission was 7.3 percent across three studies. Other common adverse events included major pulmonary events (7.8% in one study) and reoperation (5.5% across 6 studies). All outcomes are listed in Table 18.

Although, likely not strictly an adverse event, we note that in one study, 12.6 percent of patients had unplanned or planned ostomies.

Table 18. Adverse events of elective surgery

Adverse Event (Clavien-Dindo Classification, As Applicable)	n/N (Total)	Summary Percentage (95% CI)	Range Across Studies	Evidence Base
Serious AE (composite or not otherwise specified)	544/2928	25.1 (3.7, 57.0)	4.0 – 69.8	4 studies ^{139-142, 156, 157}
Ostomy (either planned or unplanned, implied)	3006/23,752	12.6 (12.2, 13.1)	12.6	1 study ^{150, 161}
Major pulmonary event, composite (CD IV) (Respiratory tract complications, acute bacterial pneumonia, acute respiratory failure)	1782/22,752	7.8 (7.5, 8.2)	7.8	1 study ^{150, 161}
30-day readmission (CD IV)	983/14,380	7.3 (3.8, 11.8)	4.2 – 11.0	3 studies ^{152, 156, 160}
Reoperation, unplanned (CD III)	4256/49,004	5.5 (3.1, 8.5)	0 – 12.7	6 studies ^{139, 149, 150, 152, 157, 159, 161}
Anastomotic leakage requiring procedure (CD III)	1077/15,367	4.3 (2.2, 6.9)	1.5 – 13.2	6 studies ^{140-142, 147, 149, 154, 156, 158}
Urinary tract infections requiring antibiotics (CD II)	84/3079	3.9 (1.6, 7.2)	2.1 – 7.5	3 studies ^{140-142, 154, 159}
Small bowel obstruction requiring procedure (CD III)	1/26	3.8 (0.5, 22.8)	3.8	1 study ¹³⁹
C diff infection	17/576	3.0 (1.8, 4.7)	3.0	1 study ¹⁴⁷
Acute renal failure	879/34,526	2.0 (0.7, 3.9)	0.7 – 3.4	3 studies ^{149, 150, 154, 161}
Pulmonary edema (CD IV)	10/582	1.7 (0.9, 3.2)	1.7	1 study ¹⁵⁴
Incisional hernia requiring procedure (CD III)	10/576	1.7 (0.9, 3.2)	1.7	1 study ¹⁴⁷
Sepsis (CD IV)	1719/82,597	1.6 (1.0, 2.3)	0.6 – 2.9	7 studies ^{149, 150, 152-155, 159, 161}
Surgical site infections requiring antibiotics (CD II)	40/3272	1.4 (0.8, 1.9)	0.9 – 4.0	4 studies ^{139, 147, 148, 154}
Pneumonia (CD IV)	48/14,218	1.3 (0, 4.4)	0.8 – 4.5	3 studies ^{149, 154, 159}
Ileus	30/2294	1.3 (0.1, 3.8)	0.2 – 4.0	3 studies ^{139, 147, 158}
Intra-abdominal abscess (CD IV)	138/11,192	1.2 (1.0, 1.5)	1.2	1 study ¹⁴⁹
Bleed requiring transfusion (CD II)	515/27,946	1.1 (0.6, 1.8)	0.7 – 2.0	3 studies ^{150, 155, 158, 161}
Acute respiratory distress syndrome (CD IV)	114/11,192	1.0 (0.8, 1.2)	1.0	1 study ¹⁴⁹
30-day mortality (CD V)	4957/199,915	0.7 (0.3, 1.4)	0.18 – 3.5	9 studies ^{143, 149, 150, 152-156, 158, 161}
Myocardial infarction (CD IV)	702/65,459	0.7 (0.1, 1.6)	0.2 – 2.5	5 studies ^{150, 152-154, 159, 161}
Cardiac arrest (CD IV)	160/25,205	0.6 (0, 1.7)	0.1 – 1.9	3 studies ^{140-142, 151, 153}
DVT	293/36,970	0.6 (0.2, 1.1)	0.2 – 1.1	4 studies ^{149, 150, 154, 159, 161}
Reintubation (CD IV)	282/39,681	0.6 (0.4, 0.9)	0.5 – 0.8	2 studies ^{152, 153}
Stroke (CD IV)	3/582	0.5 (0.2, 1.6)	0.5	1 study ¹⁵⁴
Pulmonary embolism (CD IV)	167/43,818	0.3 (0.1, 0.6)	0.2 – 3.8	5 studies ^{140-142, 152-155}

Adverse events reported by at least four studies are emphasized in bold font.

Abbreviations: AE=adverse event; C diff = Clostridioides difficile; CD=Clavien-Dindo Classification; CPR = cardiopulmonary resuscitation; DVT=deep vein thrombosis; OR=operating room; SAE= serious adverse event.

Predictors of Adverse Events

Four of the single-arm studies reported on adverse events in various subgroups, including age, simple/complicated diverticulitis, BMI, and comorbidities (Appendix D Table D-4c-3).^{147, 156, 158, 161}

Age as a Predictor

Two studies evaluated age as a predictor of various adverse events (Sheer 2011¹⁶¹ and Tsilimparis 2010¹⁵⁸).

Risk of 30-Day Mortality

Both studies evaluated age as a predictor of 30-day mortality after elective surgery. Sheer 2011, in a study of Medicare beneficiaries with an overall death rate of 1.22 percent, found that the OR for the oldest (85 and older) compared to the youngest age group (65 to 69) was 10.2 (95% CI 6.49, 16.0), and the odds increased with every age in between. Tsilimparis 2010 was underpowered for death, with only a single death, which occurred in the 70 and older subgroup.¹⁵⁸

Risk of Bleed

Both studies also reported on risk of bleed requiring transfusion. Sheer 2011, found inconsistent results across age groups. The overall hemorrhage rate was 2.0 percent. Compared with the youngest age group (65-69), only the 75- to 79-year-old subgroup had a statistically significant adjusted OR of hemorrhage (OR 1.4, 95% CI 1.09 to 1.80). The other age subgroups had adjusted ORs of 1 or 1.1 (nonsignificant). Tsilimparis 2010 reported that the event rate was 0.6 percent in the youngest age group (<60), 0 in the middle age group (60-69), and 1.9 percent in the oldest age group (>69) (P value across age groups 0.06). However, they also reported that hemorrhage requiring surgery was most common in the youngest age group (1.7%) compared with the middle group (0.4%) and no one in the oldest group.

Risk of Other Adverse Events

Other adverse events were reported by only one study each. Among evaluated adverse events, From a multivariable analysis, Sheer 2011 found evidence supportive of older age increasing risks for shock or sepsis (OR 3.5, 95% CI 2.47 to 4.98; 1.9% overall), pulmonary complications (OR 2.8, 95% CI 2.26 to 3.40; 7.2% overall), acute kidney insufficiency (OR 2.4, 95% CI 1.72 to 3.41; 2.4% overall), colostomy (OR 2.2, 95% CI 1.92 to 2.58; 9.1%), and cardiac complications (OR 2.2, 95% CI 1.59 to 3.09; 2.4% overall). Mixed findings (variable association and significance across age groups) for wound complications (4.4% overall) and ileostomy (2.2% overall). No associations were found for thromboembolic events (1.0% overall).

Tsilimparis 2010 also reported that age was not associated with risk of ileus (which occurred among 0.8% overall) or 30-day hospital readmission (3.9% overall).

Simple Versus Complicated Diverticulitis as Predictors of Adverse Events

Two studies (Bhakta 2016 and Silva-Velazco 2016) reported information on type of diverticulitis as a predictor of adverse events with elective laparoscopic surgery, but each adverse event was reported only in a single study (Appendix D Table D-4c-3).^{147, 156}

Bhakta 2016 reported that a history of complicated diverticulitis increased the risks of ileus (8.6% vs. 3.2%; unadjusted OR 2.85, 95% CI 1.29, 6.33). No associations were found for surgical site infection, anastomotic leak, incisional hernia, or C. diff infection.

In a multivariable analysis, Silva-Velazco, 2016 found that a history of complicated diverticulitis increased the risk of anastomotic leak and/or pelvic abscess (10.7% vs. 4.3%; OR

2.37, 95% CI 1.36 to 4.11) and may have somewhat increased the risk for overall postoperative morbidity (36% vs. 25%; OR 1.32, 95% CI 0.96 to 1.82). Postoperative morbidity included clinical anastomotic leak, abdominal and/or pelvic abscess, postoperative bleeding, deep vein thrombosis, dehydration, ileus, mechanical small bowel obstruction, small bowel leak, stoma complications, C. diff infection, sepsis, wound infection, wound dehiscence, urinary, renal, cardiovascular and other respiratory morbidities.

Other Predictors of Adverse Events

One study (Silva-Velazco 2016) reported information on body weight as a predictor of adverse events of laparoscopic surgery (Appendix D Table D-4c-3).¹⁵⁶ In multivariable analyses, morbid obesity (BMI ≥ 35 kg/m²), but not obesity (BMI 30-35 kg/m²), was associated with a higher rate of postoperative anastomotic leak and/or abdominopelvic abscess (OR 2.30, 95% CI 1.16 to 4.55). BMI was not associated with risk of any postoperative morbidity.

One study (Sheer 2011) reported on the comorbidities chronic obstructive pulmonary disease (COPD) and congestive heart failure (CHF) as predictors of a range of adverse events in multivariable analyses of patients undergoing elective laparoscopic surgery (Appendix D Table D-4c-3).¹⁶¹ COPD was associated with increased risks of pulmonary complications (OR 2.2, 95% CI 1.94 to 2.50) and wound complications (OR 1.4, 95% CI 1.19 to 1.67), but not other complications (in-hospital death, colostomy, ileostomy, hemorrhage, acute kidney insufficiency, cardiac complications, shock/sepsis, or thromboembolic events). CHF, on the other hand, was statistically significantly and strongly associated with in-hospital death (OR 3.5, 95% CI 2.59 to 4.63), cardiac complications (OR 4.6), pulmonary complications (OR 4.2), acute kidney injury (OR 4.1), shock or sepsis (OR 3.2); weakly but significantly, associated with colostomy (OR 1.9), wound infection (OR 1.9), thromboembolic event (OR 1.6), and hemorrhage (OR 1.5); but not ileostomy.

Summary of Evidence Pertaining to Elective Surgery

The evidence profile (Table 19) summarizes the findings for which there is sufficient evidence (and selected outcomes with insufficient evidence).

Two relatively small RCTs and one large NRCS (with propensity score adjustment) compared people with a history of acute diverticulitis who underwent elective surgery versus those who continued medical management. The two RCTs were in different populations (prior uncomplicated or complicated diverticulitis [extraluminal air, half with an abscess]); the NRCS was also conducted in patients with a history of complicated diverticulitis (all with an abscess). The NRCS reported some propensity-score adjusted analyses. The RCTs were too small to evaluate death, but the NRCS found a large (unadjusted) difference favoring surgery (0.2% vs. 1.9% at 5 years). With high SoE, all three studies found that about 6-times as many recurrences of diverticulitis occurred among those who were treated nonsurgically. However, from the NRCS, almost twice as many people who underwent elective surgery ended up with a stoma after about 5 years of followup. The one RCT and the NRCS that evaluated (total) length of hospital stay (regardless of reason for hospitalization) found conflicting results either of no difference (in the RCT) or favoring nonoperative management (in the adjusted NRCS). One RCT found that people in the elective surgery group had better quality of life and less pain at 6 months and 5 years. No studies evaluated psychosocial outcomes.

Elective surgery for diverticulitis may be associated with frequent total serious adverse events, but the frequency across studies was highly variable (4% to 70%) and likely related to definitions of adverse events (thus, there was insufficient evidence to estimate the frequency of

total serious adverse events). The most commonly reported adverse event, which was reported by 9 of 17 studies, was 30-day mortality which occurred, on average, in 0.7% of patients undergoing elective surgery (moderate SoE). The more common adverse events (that were reported by at least 4 studies) were unplanned reoperations (5.5%; low SoE) and anastomotic leakage requiring a procedure (4.3%; low SoE). Less common adverse events (reported by at least 4 studies) included sepsis (1.6%; moderate SoE), surgical site infection requiring antibiotics (1.4%; moderate SoE), myocardial infarction (0.7%; moderate SoE), deep vein thrombosis (0.6%; Moderate SoE), and pulmonary embolism (0.3%; moderate SoE).

Four studies evaluated subgroups of patients as predictors of various adverse events related to elective surgery for diverticulitis. However, each finding was based on only a single study. Strong associations (OR >2) were found for older patients and increased likelihood of death and risk for shock or sepsis, pulmonary complications, acute kidney insufficiency, colostomy, and cardiac complications. A history of complicated diverticulitis was strongly associated with ileus and, separately, anastomotic leak and/or pelvic abscess. Other strong predictors of adverse events (based on one study each) were morbid obesity and anastomotic leak and/or pelvic abscess, COPD and pulmonary complications, and CHF and in-hospital death, cardiac complications, pulmonary complications, acute kidney injury, and shock or sepsis.

Table 19. Evidence profile for elective surgery

Topic	Outcome	No. Studies (Subjects)	Risk of Bias	Consistency	Precision	Directness	Other	Overall SoE	Conclusion Statements
Elective surgery vs. nonoperative management	Death	3 (7288)	Moderate	Unclear ^a	Imprecise	Direct	None	Insufficient ^b	No conclusion regarding surgery vs. no surgery. Rare event
	Recurrence	3 (7288)	Moderate	Consistent	Precise	Direct	None	High ^c	Elective surgery has lower recurrence OR 0.16 (0.09, 0.27) ^d
	Length of hospital stay	2 (7179)	High	Inconsistent	Imprecise	Direct	Sparse	Insufficient	No conclusion regarding surgery vs. no surgery.
Adverse events	Total serious AE	4 (2928)	Low	Inconsistent	Imprecise	Indirect ^e	None	Insufficient	Estimate unclear
	30-day mortality	9 (199,915)	Low	Inconsistent	Precise	Direct	None	Moderate	0.7% (0.3, 1.4)
	Reoperation	6 (49,004)	Low	Inconsistent	Imprecise	Direct	None	Low	5.5% (3.1, 8.5)
	Anastomotic leakage	6 (15,367)	Low	Inconsistent	Imprecise	Direct	None	Low	4.3% (2.2, 6.9)
	Sepsis	7 (82,597)	Low	Inconsistent	Precise	Direct	None	Moderate	1.6% (1.0, 2.3)
	Site infection	4 (3272)	Low	Inconsistent	Precise	Direct	None	Moderate	1.4% (0.8, 1.9)
	MI	5 (65,459)	Low	Inconsistent	Precise	Direct	None	Moderate	0.7% (0.1, 1.6)
	DVT	4 (36,970)	Low	Inconsistent	Precise	Direct	None	Moderate	0.6% (0.2, 1.1)
Predictors of AE	Pulmonary embolism	5 (43,818)	Low	Inconsistent	Precise	Direct	None	Moderate	0.3% (0.1, 0.6)
	Various AE	4 (25,233)	Low	Inconsistent	Imprecise	Direct	Sparse	Insufficient	Estimate unclear

Abbreviations: AE = adverse events, DVT = deep vein thrombosis, MI = myocardial infarction, OR = odds ratio (with 95% confidence interval), SoE = strength of evidence.

^a The two randomized controlled trials (RCTs) were underpowered, but the nonrandomized comparative study (NRCS) found a very large association.

^b Only one unadjusted NRCS provided adequate data. The two RCTs were underpowered, with one death between them. Thus the conclusions are based on a single study only.

^c Although, the studies had some risk of bias, it was unlikely to be severe enough to change the conclusions of the very strong effect size

^d For patients with a history of complicated diverticulitis (2 studies) or smoldering or frequently recurrent diverticulitis after an episode of uncomplicated diverticulitis (1 study). No study evaluated patients with single episode of uncomplicated diverticulitis.

^e It was unclear what was meant by total serious adverse events for several studies.

Discussion

Findings in Relation to the Decisional Dilemma(s)

Most of the clinical questions posed by this systematic review (SR) about nonsurgical management of patients with acute colonic diverticulitis and medical and surgical interventions to prevent recurrence remain unanswered. Much of the evidence base is sparse and many of the studies, though of at least fair methodological quality, did not address the most pertinent clinical questions or were underpowered to effectively do so.

Computed Tomography Imaging

As was understood prior to our review, there is moderate strength of evidence (SoE) that computed tomography (CT) imaging has high sensitivity and specificity to diagnose acute diverticulitis among patients presenting to the ED with clinical suspicion of diverticulitis. Since studies had to rely primarily on clinical diagnoses of diverticulitis (which included CT imaging results), the studies' reference standard was imperfect. However, clinical examination (based on history, physical examination, and laboratory test) is poor at differentiating acute diverticulitis from other causes of abdominal pain and cannot accurately differentiate complicated from uncomplicated disease.

Nonsurgical Treatment of Acute Diverticulitis

Outpatient Management

Regarding management decisions for patients with acute diverticulitis, very few adequately conducted studies have addressed the question of the need for hospitalization of those patients with relatively mild disease or the value of interventional radiology procedures for those patients with abscesses. Although the evidence is relatively sparse and of insufficient to low SoE, the evidence suggests that patients with uncomplicated disease are likely to do as well with outpatient management as hospitalization.

Antibiotic Treatment

Low SoE found no statistical or clinically important differences for most outcomes between use of antibiotic treatment or not for patients with uncomplicated diverticulitis, specifically related to pain symptoms, length of hospital stay, recurrence risk, and quality of life. The risk of surgery at 6 to 12 months after the episode of acute diverticulitis may be lower among patients who received antibiotics, but the finding was highly nonsignificant. Evidence regarding other outcomes and comparing different antibiotic regimens is insufficient.

Interventional Radiology

Very few adequate studies have compared interventional radiology procedures (specifically percutaneous drainage) to usual medical care alone. Most studies that compared these approaches failed to control for the inherent differences between patients selected (and willing) to undergo abscess drainage and those who are treated medically or surgically. Ultimately, the evidence is insufficient to assess the clinical value of percutaneous drainage compared to avoiding the procedure.

Colonoscopy After an Episode of Acute Diverticulitis

There is low SoE that patients who undergo colonoscopy soon after an episode of acute diverticulitis (~2-12 months) may, ultimately, have similar rates of colorectal cancer (CRC) than those who do not undergo colonoscopy; however, no studies evaluated comparative risks of CRC death. However, there is also low SoE that patients with recent diverticulitis (within 6-12 months) may have an increased likelihood of having undiagnosed CRC. There was no eligible evidence regarding CT colonography or other cancer screening tests post-diverticulitis.

The evidence suggests that among people with recent acute diverticulitis, those 50 or older or who had complicated diverticulitis are at increased risk of having CRC or premalignant lesions on colonoscopy. Colonoscopies conducted within 1.5 to 12 months after acute diverticulitis rarely have complications or incomplete tests.

Prevention of Recurrence

Nonsurgical Interventions

Among nonsurgical interventions to prevent recurrence of diverticulitis, only 5-aminosalicylic acid (5-ASA, mesalamine) has been evaluated by more than one or two comparative studies. There is high SoE that 5-ASA does not reduce the risk of diverticulitis, and there is even a suggestion that people using 5-ASA may be at a small *increased* risk of recurrence. There is, though, also high SoE that 5-ASA does not cause important adverse events. Evidence pertaining to other pharmacologic interventions, including rifaximin, probiotics, and combinations of these three interventions, are sparse, each having been evaluated by only a single comparative study. Burdock tea, a diuretic and antipyretic tea commonly used in Asian medicine, has also been evaluated by a single study. Of note, no eligible studies have evaluated any medical nutrition therapies.

Elective Surgery

Among patients with either a history of complicated diverticulitis or smoldering or frequently recurring diverticulitis, there is a high SoE indicated that elective surgery resulted in much lower rates of diverticulitis recurrence than nonsurgical interventions. However, no eligible studies evaluated the relative effect of elective surgery for patients with nonrecurrent uncomplicated diverticulitis. Serious adverse events, including 30-day mortality (at 0.7%), need for reoperation (5.5%), and anastomotic leakage (4.3%) were not uncommon. The evidence is sparse to evaluate risk of long-term death, but there is some indication that at 5 years of followup, patients who underwent elective surgery were at reduced risk of death. In addition, none of the studies evaluated psychosocial outcomes such as anxiety, stress, or fear related to the risk of recurrent episodes of acute diverticulitis.

Strengths and Limitations

With few exceptions, the evidence base examined in this SR is sparse or of low SoE. As noted, many important clinical questions have not been addressed by sufficient numbers of studies that meet basic criteria (for most questions, comparative studies with appropriate adjustment for inherent differences between compared groups). Evidence is particularly sparse for questions related to the benefits and harms of CT scanning for acute diverticulitis, the appropriateness of outpatient management of uncomplicated or mildly complicated diverticulitis, interventional radiology for nonsurgical complicated diverticulitis, and various interventions for

prevention of recurrent diverticulitis. In addition, there is very limited evidence regarding which patients might benefit most from (or be most harmed by) the various interventions. The lack of evidence about heterogeneity of treatment effects (which patients would most benefit), arguably, is most important for elective surgery because, despite the strong evidence of an important clinical benefit to surgery, clearly elective surgery cannot, and probably should not, be recommended for all patients with a history of acute diverticulitis. It is of paramount importance to determine criteria to establish who would most benefit.

Only for patients undergoing colonoscopy have studies systematically addressed which patients are at highest risk of outcomes. However, while the studies have found that older patients and those with recent complicated diverticulitis are at particularly high risk of CRC and advance colonic neoplasia, the studies comparing patients with diverticulitis to the general population have not evaluated whether younger patients or those with recent uncomplicated diverticulitis, specifically, are at higher risk of CRC than patients in the general population. Also, importantly, the studies have not adequately addressed whether patients who undergo colonoscopy after diverticulitis are at decreased risk of dying from CRC compared to patients who forgo colonoscopy. Ultimately, this is the primary unanswered clinical question pertaining to colonoscopy.

From a methodological perspective, it was common that studies were underpowered (too small) to address the most important clinical outcomes, failed to address the clinically important outcomes, or were inadequately analyzed. For many of the questions pertaining to treatment dilemmas, the randomized controlled trials (RCTs) tended to be too small (thus, underpowered) to detect differences between treatments in important, but relatively rare, clinical outcomes (such as treatment failure, unplanned emergency surgery, and death). The RCTs mostly evaluated less clinically important outcomes. Many of the nonrandomized comparative studies (NRCSs) were designed to be large enough to address at least some of the clinically important outcomes, but did not, or did not adequately, control for the inherent differences between groups. Thus, the findings of these NRCSs may have been biased toward findings that more intensive interventions are associated with worse outcomes (because the more intensive interventions were mostly used in the sicker patients who, by definition, are at highest risk of poor outcomes). Several of the colonoscopy and elective surgery studies were based on registries or administrative databases. However, these data sources are unlikely to be accurate or sufficiently granular about differences in disease severity across patients and other clinical factors such as patient comorbidities, not to mention patient preferences and life goals, which can influence the threshold for intervention (e.g., whether to undergo colonoscopy or to have elective sigmoidectomy).

We believe that our literature search was complete and did not systematically miss studies. We did not reject any study due to language restrictions or study setting (including country). It appears that the large majority of studies that were unavailable to us were conference abstracts, so we might have missed some cutting-edge studies. We restricted the evidence base to the past 30 years, based on changing diagnostic criteria for acute diverticulitis in the 1990s. We might have, thus, missed some important older studies that might still be pertinent. However, none of the stakeholders we collaborated with knew of such studies or were concerned by the choice of dates. While we restricted some study designs based on sample sizes, we do not think the smaller studies would have altered conclusions. Additional studies of the harms of elective surgery might have made our estimates more precise but are unlikely to have changed our overall conclusions that surgical complications are uncommon. Smaller comparative studies are highly unlikely to have been adequately analyzed. Our protocol did not cover all management decisions for the care

of patients with acute diverticulitis or history of diverticulitis; for example, we did not address questions related to dietary restrictions during episodes of acute diverticulitis.

We were fairly liberal about decisions to perform meta-analyses. However, where one might have reasonably chosen not to meta-analyze studies (because of clinical heterogeneity of included studies or *post hoc* decision making), we explicitly point this out. We chose to use meta-analysis mostly as an indicator of possible effect (or of likelihood of an outcome or finding) rather than to provide precise estimates. In particular, for meta-analyses of colonoscopy findings (rates of findings) and elective surgical harms, we conducted meta-analyses to provide an indication of how common (or rare) outcomes are. For evaluations of elective surgery complications, we acknowledge that we did not adequately account for the differences across studies of surgery or patient characteristics. However, no clear patterns were seen across studies to explain the statistically large differences in surgical complication rates.

Applicability

The evidence base, even where insufficient to make conclusions about intervention effect, appeared to be generally applicable to patients with either suspicion of acute diverticulitis, diagnosed acute diverticulitis, or history of diverticulitis (depending on the evaluated intervention). Most studies (at least for nonsurgical interventions) described their eligibility criteria sufficiently to determine that the included participants are those for whom the intervention is potentially appropriate. However, many studies did not provide sufficient detail to understand the detailed level of severity of disease or of potential risk factors for poor outcomes. Arguably, more importantly, as described above, studies rarely evaluated subgroups (except for studies of colonoscopy) and failed to address heterogeneity of treatment effect. Such analyses could allow a better understanding of whom the findings are most applicable to. Many of the single group studies of elective surgery (often from registries or other large databases) did not clearly describe their included patients.

The one caveat about applicability in regard to patient or disease characteristics is that the large majority of studies were conducted in “western” countries, where left-sided diverticulitis is predominant. Only four studies were from East Asia (specifically South Korea and Japan), where right-sided diverticulitis is predominant.

Implications for Clinical Practice, Education, Research, or Health Policy

This review was nominated by the American College of Physicians to summarize the evidence base for a planned new clinical practice guideline on management of patients with diverticulitis. This goal informed the scope of the review to primarily address the needs of nonsurgical decision makers and patients. Unfortunately, many of the important questions about which interventions should be used for which patients remain either unanswered or answered with only low SoE. It is likely that many specific recommendations for management will be weak suggestions based largely on expert opinion. These include important questions related to benefits and harms of CT imaging, appropriateness of outpatient management of mild acute diverticulitis, interventional radiology for complicated diverticulitis, who needs antibiotic treatment and choice of antibiotics, whether colonoscopy is needed for patients under age 50 (particularly those with uncomplicated diverticulitis), what nonsurgical interventions are

effective to reduce the risk of recurrence (and who would most benefit), and which patients should be referred for possible elective surgery to prevent recurrent diverticulitis.

CT Imaging

Despite the lack of a definitive reference standard to diagnose acute diverticulitis (since only a minority of patients have surgical, pathological, or colonoscopy confirmation of disease), the evidence supports the common understanding that CT imaging is accurate to diagnose acute diverticulitis. However, there is a lack of evidence to support the accuracy of CT imaging for staging severity of disease. In particular, no studies evaluated test accuracy of staging systems commonly used in the U.S.

The clinical implications of false positive, false negative, and incidental findings remain unclear. While the studies suggest a low SoE that misdiagnoses on CT did not result in poor clinical outcomes, the studies were relatively few and small and did not adequately address what good outcomes were clearly a result of findings on CT or what bad outcomes (including unnecessary interventions and their harms) occurred as a result of errors on CT.

While a small number of studies of patients undergoing CT for possible diverticulitis found that incidental findings were common among patients undergoing CT for acute abdomen, the clinical significance of the findings (either beneficial or harmful) was not adequately evaluated.

Nonsurgical Treatment of Acute Diverticulitis

Outpatient Management

For selected patients with uncomplicated diverticulitis (or mild complicated diverticulitis) whose pain and other symptoms can be controlled in the emergency department, outpatient treatment leads to clinical outcomes that are no worse than inpatient treatment. Poor clinical outcomes, including the need for emergency surgery, were uncommon in this group of patients, suggesting that most patients do relatively well, regardless of whether they recover in-hospital or at home. Even long-term outcomes appear to be similar in those treated for their acute diverticulitis either inpatient or outpatient.

Antibiotic Treatment

It appears that *avoidance* of antibiotics for patients with uncomplicated acute diverticulitis may be safe (as effective, without increased harms) for the large majority of patients. However, this conclusion is largely based on the fact that complications, including death, emergency surgery, diverticulitis-related complications, and treatment failure are rare events for these patients. Because of the low rate of these adverse outcomes, estimates of effects are highly imprecise. There is, though, low SoE that pain, length of hospital stay, recurrence rates, quality of life are similar regardless of use of antibiotics; although, based on nonstatistically significant findings, the risk of medium-term surgery (6-12 months) may be lower among patients who received antibiotics. For patients who do receive antibiotics, the evidence is insufficient to guide choice of antibiotic regimen. Each study evaluated a unique pair of antibiotic regimens that differed in choice of antibiotics, route, and duration of treatment.

Interventional Radiology

The evidence base provides sparse evidence to guide the decision whether to use percutaneous drainage or other interventional radiology procedures for patients with acute complicated diverticulitis.

Colonoscopy After an Episode of Acute Diverticulitis

For patients treated for acute diverticulitis who do not undergo emergency surgery (such as sigmoidectomy), an important clinical consideration is whether they should have a colonoscopy to rule out CRC or high-risk lesions that might have played a role in the development of the acute diverticulitis. There is concern that these patients might be at increased risk for having colon neoplasias (whether related to their having diverticulitis or to possible misdiagnosis of inflamed CRC as acute diverticulitis). While three studies provide low SoE that rates of ultimate diagnoses of CRC are similar among those who undergo colonoscopy as part of their post-diverticulitis care and those who do not, none of the studies address the most important clinical question of whether having a colonoscopy affects the risk of death from CRC. Overall, patients with a recent episode of acute diverticulitis (who undergo colonoscopy) are likely at increased risk of having CRC compared with the general population of individuals undergoing routine colonoscopy screening. However, it is unclear to what extent this difference is related to differences among those who choose to undergo colonoscopy (e.g., because of a family history of CRC or gastrointestinal symptoms, such as rectal bleeding) and those who decline colonoscopy. One large registry study from Denmark evaluated the association between a history of diverticulitis and a history of CRC, finding a strong association; but the study did not assess the relative clinical value of colonoscopy soon after an episode of diverticulitis. Nevertheless, the study did find that most new diagnoses of CRC (after diverticulitis) occurred within 500 days of the diverticulitis hospitalization.¹²³ The study also suggested that those patients who undergo colonoscopy (with or without a history of diverticulitis) are more likely to have CRC, strongly suggesting that people are undergoing colonoscopy based on risk factors for CRC beyond diverticulitis alone.

CRC and high-risk lesions are relatively common among patients with recent acute diverticulitis. About 2 percent have been found to have CRC (moderate SoE), 7 percent advanced colonic neoplasia (CRC or advanced adenoma; moderate SoE), and up to 3 percent have each of advanced adenoma, adenomas with high-grade dysplasia, or large adenomas. Incomplete (or failed) colonoscopies are uncommon in this population and procedure-related complications are rare. The evidence base is internationally very diverse, with only one study each from the U.S. or Canada; however, there were no clear patterns in CRC rates across countries (or continents). While there may be concerns about risks of complications or failed colonoscopies soon after bouts of acute diverticulitis, the evidence does not support that these are common events. Notably, none of 878 patients who underwent colonoscopy had a complication (e.g., major bleeding or perforation). As a point of reference, a 2017 systematic review found that across 39 studies (mostly from the U.S. or Europe), the pooled overall risk of major bleeding after colonoscopy (for any reason) was 0.08 percent (95% confidence interval [CI] 0.018 to 0.163) and the overall risk of perforation was 0.007 percent (95% CI 0.0006 to 0.017).¹⁶²

However, most patients with diverticulitis are over age 50. The current guidance from multiple societies is for (essentially) all people in this age group to undergo colonoscopy.¹²⁵⁻¹²⁷ Consistent with this recommendation, there is moderate SoE that older (≥ 50 years) patients with diverticulitis are at about 3-times increased risk of CRC than younger patients and high SoE that

they are at about 8-times increased risk of advanced colonic neoplasia. Although across all studies, we do not have a clear indication of the risk of CRC among younger (<50 years) patients, in three of the four studies that compared age subgroups, no one under age 50 was found to have CRC. In addition to older age, recent complicated (versus uncomplicated) diverticulitis has been shown to be a strong risk factor for abnormal colorectal findings on colonoscopy. There is high SoE that patients with complicated diverticulitis have almost 6-times increased risk of CRC and 3-times increased risk of advanced colonic neoplasia.

Prevention of Recurrence

Nonsurgical Interventions

Despite its apparent safety, the evidence strongly supports (with high SoE) that 5-ASA is not effective to reduce the risk of recurrent diverticulitis. There is even a suggestion that people using 5-ASA may be at a small *increased* risk of recurrence. Although several other nonsurgical interventions have been evaluated in comparative studies, each has been evaluated by only a single study; thus, the evidence base does not support any conclusions regarding their effectiveness. Although of particular interest to patients and clinicians, medical nutrition therapies have not been evaluated by comparative studies.

Elective Surgery

An important consideration for patients with a history of acute diverticulitis is whether to undergo elective sigmoidectomy or colectomy with the goal of preventing recurrent episodes and the possible need for emergency surgery and a colostomy. Surgery studies have evaluated patients with either a history of complicated diverticulitis or multiple recurrent diverticulitis, those patients most likely to be offered elective surgery. Among these patients, studies consistently found a large benefit for elective surgery in terms of prevention of recurrent diverticulitis. However, none of the studies addressed which patients may benefit more (or less) from elective surgery, in particular based on factors such as severity or frequency of diverticulitis, comorbidities, or age. Notably, serious adverse events, were not uncommon.

Future Research

There is a clear need for high-quality research to address all these issues. Ideally, large-scale, multicenter RCTs should be conducted in unrestricted populations (i.e., without eligibility restrictions that may reduce applicability) with appropriate subgroup analyses. RCTs should be large enough to evaluate potential clinically important differences in rates of the most important outcomes to patients (e.g., death, treatment failure, emergency surgery, and time to recurrence) and important harms, adverse events, and complications (e.g., risk of *C. difficile* infection from antibiotics, which can be devastating for patients who already have diverticulitis; postoperative death; and permanent stomas).

Alternatively, large databases should be adequately analyzed to compare interventions. It is our strong belief that no (or rare) future studies should be considered that compare groups of patients who are inherently different without adequate adjustment for these differences. Unadjusted comparisons of, for example, hospitalized versus discharged patients or those who undergo or do not undergo percutaneous drainage of abscesses, can generally only conclude that sicker patients (who are, for example, more likely to be hospitalized or to undergo percutaneous drainage) fare worse. Ideally, propensity score analysis (or similar techniques) should be used.

These analyses estimate the likelihood that each patient had one or the other intervention and control for this likelihood. They generally require relatively large numbers of patients for whom there is granular data about their risk factors for outcomes.

Furthermore, future studies should emphasize evaluations of heterogeneity of treatment effect to better understand which patients may most benefit from (or may be most harmed by) a given intervention. This can be done relatively simply with subgroup analyses, but more sophisticated evaluations may be appropriate. As for the NRCSs, it is important that the subgroup comparisons be adequately adjusted. For example, in a given set of patients, those with complicated diverticulitis may be fundamentally different from those with uncomplicated disease (beyond the presence or absence of abscesses).

Conclusions

Many questions remain inadequately answered regarding the best management of patients with acute diverticulitis or to prevent future recurrences. Prior reviews have demonstrated that CT imaging accurately diagnoses acute diverticulitis. For selected patients, outpatient management may be as effective as inpatient care. For patients with acute uncomplicated diverticulitis, it may be safe and appropriate to forgo antibiotics. The evidence base is inconclusive, though, about choice of antibiotic regimen for patients with complicated diverticulitis. The evidence is insufficient to assess the clinical value of percutaneous drainage. Patients with recent episodes of diverticulitis are at risk of having undiagnosed CRC or advanced colonic neoplasia, particularly if they are at least 50 years of age or have had complicated diverticulitis. The use of 5-ASA does not reduce (and may increase) the risk of recurrence of diverticulitis but is not more harmful than placebo. Patients with a history of complicated diverticulitis or who have smoldering or frequently recurring diverticulitis who undergo elective surgery are at greatly reduced risk of recurrent diverticulitis; serious surgery-related adverse events are uncommon. However, for elective surgery in particular, and for all other evaluated interventions, the evidence does not adequately address which patients would benefit most from a given intervention. There is a compelling need for future, well-conducted studies that address both effectiveness (and harms) of interventions and heterogeneity of treatment effect.

References

1. Jarbrink-Sehgal ME, Rassam L, Jasim A, et al. Diverticulosis, Symptoms and Colonic Inflammation: A Population-Based Colonoscopy Study. *The American journal of gastroenterology*. 2019 Mar;114(3):500-10. doi: 10.14309/ajg.000000000000113. PMID: 30839393.
2. Peery AF, Keku TO, Addamo C, et al. Colonic Diverticula Are Not Associated With Mucosal Inflammation or Chronic Gastrointestinal Symptoms. *Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association*. 2018 Jun;16(6):884-91.e1. doi: 10.1016/j.cgh.2017.05.051. PMID: 28603053.
3. Shahedi K, Fuller G, Bolus R, et al. Long-term risk of acute diverticulitis among patients with incidental diverticulosis found during colonoscopy. *Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association*. 2013 Dec;11(12):1609-13. doi: 10.1016/j.cgh.2013.06.020. PMID: 23856358.
4. Greenwood-Ericksen MB, Havens JM, Ma J, et al. Trends in Hospital Admission and Surgical Procedures Following ED visits for Diverticulitis. *The western journal of emergency medicine*. 2016 Jul;17(4):409-17. doi: 10.5811/westjem.2016.4.29757. PMID: 27429691.
5. Bollom A, Austrie J, Hirsch W, et al. Emergency Department Burden of Diverticulitis in the USA, 2006-2013. *Digestive diseases and sciences*. 2017 Oct;62(10):2694-703. doi: 10.1007/s10620-017-4525-y. PMID: 28332105.
6. Shah SD, Cifu AS. Management of Acute Diverticulitis. *Jama*. 2017 Jul 18;318(3):291-2. doi: 10.1001/jama.2017.6373. PMID: 28719679.
7. Everhart JE, Ruhl CE. Burden of digestive diseases in the United States part II: lower gastrointestinal diseases. *Gastroenterology*. 2009 Mar;136(3):741-54. doi: 10.1053/j.gastro.2009.01.015. PMID: 19166855.
8. Peery AF, Keku TO, Martin CF, et al. Distribution and Characteristics of Colonic Diverticula in a United States Screening Population. *Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association*. 2016 Jul;14(7):980-5.e1. doi: 10.1016/j.cgh.2016.01.020. PMID: 26872402.
9. Wheat CL, Strate LL. Trends in Hospitalization for Diverticulitis and Diverticular Bleeding in the United States From 2000 to 2010. *Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association*. 2016 Jan;14(1):96-103.e1. doi: 10.1016/j.cgh.2015.03.030. PMID: 25862988.
10. Lin MP, Weissman J, Sinnette C, et al. 87 Prioritizing Conditions for Which to Compare Emergency Department Admission Rates. *Annals of Emergency Medicine*. 2014 2014/10/01;64(4, Supplement):S31-S2. doi: 10.1016/j.annemergmed.2014.07.112.
11. Buchs NC, Konrad-Mugnier B, Jannot AS, et al. Assessment of recurrence and complications following uncomplicated diverticulitis. *The British journal of surgery*. 2013 Jun;100(7):976-9; discussion 9. doi: 10.1002/bjs.9119. PMID: 23592303.
12. Lahat A, Avidan B, Sakhnini E, et al. Acute diverticulitis: a decade of prospective follow-up. *Journal of clinical gastroenterology*. 2013 May-Jun;47(5):415-9. doi: 10.1097/MCG.0b013e3182694dbb. PMID: 23328302.
13. Tsoukas S, Khiew YC, Dumitra T-C, et al. National Demographic and Economic Trends of Acute Diverticulitis in the United States From 2000-2015. *American Journal of Gastroenterology*. 2018;113:S103-4.
14. Bharucha AE, Parthasarathy G, Ditah I, et al. Temporal Trends in the Incidence and Natural History of Diverticulitis: A Population-Based Study. *The American journal of gastroenterology*. 2015 Nov;110(11):1589-96. doi: 10.1038/ajg.2015.302. PMID: 26416187.

15. Klarenbeek BR, de Korte N, van der Peet DL, et al. Review of current classifications for diverticular disease and a translation into clinical practice. *International journal of colorectal disease*. 2012 Feb;27(2):207-14. doi: 10.1007/s00384-011-1314-5. PMID: 21928041.
16. Hughes ES, Cuthbertson AM, Carden AB. The surgical management of acute diverticulitis. *The Medical journal of Australia*. 1963 May 25;50(1):780-2. PMID: 13955553.
17. Kohler L, Sauerland S, Neugebauer E. Diagnosis and treatment of diverticular disease: results of a consensus development conference. The Scientific Committee of the European Association for Endoscopic Surgery. *Surgical endoscopy*. 1999 Apr;13(4):430-6. PMID: 10094765.
18. Hinchey EJ, Schaaf PG, Richards GK. Treatment of perforated diverticular disease of the colon. *Advances in surgery*. 1978;12:85-109. PMID: 735943.
19. Wasvary H, Turfah F, Kadro O, et al. Same hospitalization resection for acute diverticulitis. *The American surgeon*. 1999 Jul;65(7):632-5; discussion 6. PMID: 10399971.
20. Ambrosetti P, Grossholz M, Becker C, et al. Computed tomography in acute left colonic diverticulitis. *J Surg*. 1997;84:532-4.
21. Kaiser AM, Jiang JK, Lake JP, et al. The management of complicated diverticulitis and the role of computed tomography. *The American journal of gastroenterology*. 2005 Apr;100(4):910-7. doi: 10.1111/j.1572-0241.2005.41154.x. PMID: 15784040.
22. Hansen O, Graupe F, Stock W. [Diagnosis of diverticulitis in routine practice: progress due to pelvic CT?]. *Langenbecks Arch Chir Suppl Kongressbd*. 1998;115:170-3. PMID: 9931605.
23. Kruse E, Leifeld L. Prevention and Conservative Therapy of Diverticular Disease. *Viszeralmedizin*. 2015 Apr;31(2):103-6. doi: 10.1159/000377651. PMID: 26989379.
24. Sartelli M, Moore FA, Ansaloni L, et al. A proposal for a CT driven classification of left colon acute diverticulitis. *World journal of emergency surgery : WJES*. 2015;10:3. doi: 10.1186/1749-7922-10-3. PMID: 25972914.
25. Bassotti G, Battaglia E, De Roberto G, et al. Alterations in colonic motility and relationship to pain in colonic diverticulosis. *Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association*. 2005 Mar;3(3):248-53. doi: 10.1016/s1542-3565(04)00614-7. PMID: 15765444.
26. Kvasnovsky CL, Leong LEX, Choo JM, et al. Clinical and symptom scores are significantly correlated with fecal microbiota features in patients with symptomatic uncomplicated diverticular disease: a pilot study. *Eur J Gastroenterol Hepatol*. 2018 Jan;30(1):107-12. doi: 10.1097/meg.0000000000000995. PMID: 29084074.
27. Barbara G, Scaiola E, Barbaro MR, et al. Gut microbiota, metabolome and immune signatures in patients with uncomplicated diverticular disease. *Gut*. 2017 Jul;66(7):1252-61. doi: 10.1136/gutjnl-2016-312377. PMID: 27618836.
28. Nally DM, Kavanagh DO. Current Controversies in the Management of Diverticulitis: A Review. *Digestive surgery*. 2018 Apr 19. doi: 10.1159/000488216. PMID: 29672283.
29. Isacson D, Andreasson K, Nikberg M, et al. No antibiotics in acute uncomplicated diverticulitis: does it work? *Scandinavian journal of gastroenterology*. 2014 Dec;49(12):1441-6. doi: 10.3109/00365521.2014.968861. PMID: 25369865.
30. Biondo S, Golda T, Kreisler E, et al. Outpatient versus hospitalization management for uncomplicated diverticulitis: a prospective, multicenter randomized clinical trial (DIVER Trial). *Annals of surgery*. 2014 Jan;259(1):38-44. doi: 10.1097/SLA.0b013e3182965a11. PMID: 23732265.
31. Schug-Pass C, Geers P, Hugel O, et al. Prospective randomized trial comparing short-term antibiotic therapy versus standard therapy for acute uncomplicated sigmoid diverticulitis. *International journal of colorectal disease*. 2010 Jun;25(6):751-9. doi: 10.1007/s00384-010-0899-4. PMID: 20140619.

32. Chabok A, Pahlman L, Hjern F, et al. Randomized clinical trial of antibiotics in acute uncomplicated diverticulitis. *The British journal of surgery*. 2012 Apr;99(4):532-9. doi: 10.1002/bjs.8688. PMID: 22290281.
33. Daniels L, Unlu C, de Korte N, et al. Randomized clinical trial of observational versus antibiotic treatment for a first episode of CT-proven uncomplicated acute diverticulitis. *The British journal of surgery*. 2017 Jan;104(1):52-61. doi: 10.1002/bjs.10309. PMID: 27686365.
34. Mege D, Yeo H. Meta-analyses of Current Strategies to Treat Uncomplicated Diverticulitis. *Diseases of the colon and rectum*. 2019 Mar;62(3):371-8. doi: 10.1097/dcr.0000000000001295. PMID: 30570549.
35. Elagili F, Stocchi L, Ozuner G, et al. Outcomes of percutaneous drainage without surgery for patients with diverticular abscess. *Diseases of the colon and rectum*. 2014 Mar;57(3):331-6. doi: 10.1097/DCR.0b013e3182a84dd2. PMID: 24509455.
36. Harisinghani MG, Gervais DA, Hahn PF, et al. CT-guided transgluteal drainage of deep pelvic abscesses: indications, technique, procedure-related complications, and clinical outcome. *Radiographics : a review publication of the Radiological Society of North America, Inc*. 2002 Nov-Dec;22(6):1353-67. doi: 10.1148/rg.226025039. PMID: 12432107.
37. Garfinkle R, Kugler A, Pelsser V, et al. Diverticular Abscess Managed With Long-term Definitive Nonoperative Intent Is Safe. *Diseases of the colon and rectum*. 2016 Jul;59(7):648-55. doi: 10.1097/dcr.0000000000000624. PMID: 27270517.
38. Ritz JP, Lehmann KS, Frericks B, et al. Outcome of patients with acute sigmoid diverticulitis: multivariate analysis of risk factors for free perforation. *Surgery*. 2011 May;149(5):606-13. doi: 10.1016/j.surg.2010.10.005. PMID: 21145569.
39. Hall JF, Roberts PL, Ricciardi R, et al. Long-term follow-up after an initial episode of diverticulitis: what are the predictors of recurrence? *Diseases of the colon and rectum*. 2011 Mar;54(3):283-8. doi: 10.1007/DCR.0b013e3182028576. PMID: 21304297.
40. Strassle PD, Kinlaw AC, Chaumont N, et al. Rates of Elective Colectomy for Diverticulitis Continued to Increase After 2006 Guideline Change. *Gastroenterology*. 2019 Dec;157(6):1679-81.e11. doi: 10.1053/j.gastro.2019.08.045. PMID: 31499038.
41. Lopez-Borao J, Kreisler E, Millan M, et al. Impact of age on recurrence and severity of left colonic diverticulitis. *Colorectal disease : the official journal of the Association of Coloproctology of Great Britain and Ireland*. 2012 Jul;14(7):e407-12. doi: 10.1111/j.1463-1318.2012.02976.x. PMID: 22321968.
42. Ritz JP, Lehmann KS, Stroux A, et al. Sigmoid diverticulitis in young patients--a more aggressive disease than in older patients? *Journal of gastrointestinal surgery : official journal of the Society for Surgery of the Alimentary Tract*. 2011 Apr;15(4):667-74. doi: 10.1007/s11605-011-1457-2. PMID: 21318443.
43. Brandl A, Kratzer T, Kafka-Ritsch R, et al. Diverticulitis in immunosuppressed patients: A fatal outcome requiring a new approach? *Canadian journal of surgery Journal canadien de chirurgie*. 2016 Aug;59(4):254-61. doi: 10.1503/cjs.012915. PMID: 27240131.
44. Yoo PS, Garg R, Salamone LF, et al. Medical comorbidities predict the need for colectomy for complicated and recurrent diverticulitis. *American journal of surgery*. 2008 Nov;196(5):710-4. doi: 10.1016/j.amjsurg.2008.07.017. PMID: 18954602.
45. Carabotti M, Annibale B, Severi C, et al. Role of Fiber in Symptomatic Uncomplicated Diverticular Disease: A Systematic Review. *Nutrients*. 2017 Feb 20;9(2). doi: 10.3390/nu9020161. PMID: 28230737.

46. Stollman N, Smalley W, Hirano I. American Gastroenterological Association Institute Guideline on the Management of Acute Diverticulitis. *Gastroenterology*. 2015 Dec;149(7):1944-9. doi: 10.1053/j.gastro.2015.10.003. PMID: 26453777.
47. Agarwal AK, Karanjawala BE, Maykel JA, et al. Routine colonic endoscopic evaluation following resolution of acute diverticulitis: is it necessary? *World journal of gastroenterology*. 2014 Sep 21;20(35):12509-16. doi: 10.3748/wjg.v20.i35.12509. PMID: 25253951.
48. Balthazar EJ, Megibow A, Schinella RA, et al. Limitations in the CT diagnosis of acute diverticulitis: comparison of CT, contrast enema, and pathologic findings in 16 patients. *AJR American journal of roentgenology*. 1990 Feb;154(2):281-5. doi: 10.2214/ajr.154.2.2105015. PMID: 2105015.
49. Stollman NH, Raskin JB. Diagnosis and management of diverticular disease of the colon in adults. Ad Hoc Practice Parameters Committee of the American College of Gastroenterology. *The American journal of gastroenterology*. 1999 Nov;94(11):3110-21. doi: 10.1111/j.1572-0241.1999.01501.x. PMID: 10566700.
50. Sharma PV, Eglinton T, Hider P, et al. Systematic review and meta-analysis of the role of routine colonic evaluation after radiologically confirmed acute diverticulitis. *Annals of surgery*. 2014 Feb;259(2):263-72. doi: 10.1097/sla.0000000000000294. PMID: 24169174.
51. Chabok A, Smedh K, Nilsson S, et al. CT-colonography in the follow-up of acute diverticulitis: patient acceptance and diagnostic accuracy. *Scandinavian journal of gastroenterology*. 2013 Aug;48(8):979-86. doi: 10.3109/00365521.2013.809597. PMID: 23834748.
52. Effective Health Care Program. Management of Acute Diverticulitis. <https://effectivehealthcare.ahrq.gov/get-involved/nominated-topics/management-acute-diverticulitis>. 2018.
53. Effective Health Care Program. Management of Acute Diverticulitis Topic Nomination. <https://effectivehealthcare.ahrq.gov/system/files/docs/acute-diverticulitis-topic-nomination.pdf>. 2018.
54. American College of Physicians. Guideline Process: How Does ACP Develop Clinical Recommendations? <https://www.acponline.org/clinical-information/guidelines/guideline-process>. 2019.
55. Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *J Clin Epidemiol*. 2009 Oct;62(10):1006-12. doi: 10.1016/j.jclinepi.2009.06.005. PMID: 19631508.
56. Shea BJ, Reeves BC, Wells G, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. *BMJ (Clinical research ed)*. 2017 Sep 21;358:j4008. doi: 10.1136/bmj.j4008. PMID: 28935701.
57. Higgins JP, Altman DG, Gotzsche PC, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ (Clinical research ed)*. 2011 Oct 18;343:d5928. doi: 10.1136/bmj.d5928. PMID: 22008217.
58. Sterne JA, Hernán MA, Reeves BC, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ (Clinical research ed)*. 2016;355:i4919.
59. Berkman ND, Lohr KN, Ansari M, et al. AHRQ Methods for Effective Health Care Grading the Strength of a Body of Evidence When Assessing Health Care Interventions for the Effective Health Care Program of the Agency for Healthcare Research and Quality: An Update. *Methods Guide for Effectiveness and Comparative Effectiveness Reviews*. Rockville (MD): Agency for Healthcare Research and Quality (US); 2008.
60. Berkman ND, Lohr KN, Ansari MT, et al. Grading the strength of a body of evidence when assessing health care interventions: an EPC update. *J Clin Epidemiol*. 2015 Nov;68(11):1312-24. doi: 10.1016/j.jclinepi.2014.11.023. PMID: 25721570.

61. Lameris W, van Randen A, Bipat S, et al. Graded compression ultrasonography and computed tomography in acute colonic diverticulitis: meta-analysis of test accuracy. *European radiology*. 2008 Nov;18(11):2498-511. doi: 10.1007/s00330-008-1018-6. PMID: 18523784.
62. Andeweg CS, Wegdam JA, Groenewoud J, et al. Toward an evidence-based step-up approach in diagnosing diverticulitis. *Scandinavian journal of gastroenterology*. 2014 Jul;49(7):775-84. doi: 10.3109/00365521.2014.908475. PMID: 24874087.
63. Doringe E, Ferner R. [Computed tomography of colonic diverticulitis]. *Rofo*. 1990 Jan;152(1):76-9. doi: 10.1055/s-2008-1046821. PMID: 2154015.
64. Cho KC, Morehouse HT, Alterman DD, et al. Sigmoid diverticulitis: diagnostic role of CT--comparison with barium enema studies. *Radiology*. 1990 Jul;176(1):111-5. doi: 10.1148/radiology.176.1.2191360. PMID: 2191360.
65. Stefansson T, Nyman R, Nilsson S, et al. Diverticulitis of the sigmoid colon. A comparison of CT, colonic enema and laparoscopy. *Acta Radiol*. 1997 Mar;38(2):313-9. doi: 10.1080/02841859709172071. PMID: 9093173.
66. Rao PM, Rhea JT, Novelline RA, et al. Helical CT with only colonic contrast material for diagnosing diverticulitis: prospective evaluation of 150 patients. *AJR American journal of roentgenology*. 1998 Jun;170(6):1445-9. doi: 10.2214/ajr.170.6.9609151. PMID: 9609151.
67. Werner A, Diehl SJ, Farag-Soliman M, et al. Multi-slice spiral CT in routine diagnosis of suspected acute left-sided colonic diverticulitis: a prospective study of 120 patients. *European radiology*. 2003 Dec;13(12):2596-603. doi: 10.1007/s00330-003-1887-7. PMID: 12740709.
68. Farag Soliman M, Wustner M, Sturm J, et al. [Primary diagnostics of acute diverticulitis of the sigmoid]. *Ultraschall Med*. 2004 Sep;25(5):342-7. doi: 10.1055/s-2004-813381. PMID: 15368137.
69. Tack D, Bohy P, Perlot I, et al. Suspected acute colon diverticulitis: imaging with low-dose unenhanced multi-detector row CT. *Radiology*. 2005 Oct;237(1):189-96. doi: 10.1148/radiol.2371041432. PMID: 16126929.
70. Pradel JA, Adell JF, Taourel P, et al. Acute colonic diverticulitis: prospective comparative evaluation with US and CT. *Radiology*. 1997 Nov;205(2):503-12. doi: 10.1148/radiology.205.2.9356636. PMID: 9356636.
71. Whiting P, Rutjes AW, Reitsma JB, et al. The development of QUADAS: a tool for the quality assessment of studies of diagnostic accuracy included in systematic reviews. *BMC Med Res Methodol*. 2003 Nov 10;3:25. doi: 10.1186/1471-2288-3-25. PMID: 14606960.
72. Hansen O, Stock W. [Prophylactic resection in diverticular disease--treatment by precise staging]. *Langenbecks Arch Chir Kongressbd*. 1999;116 (Suppl II):1257-60.
73. Jurowich CF, Jellouschek S, Adamus R, et al. How complicated is complicated diverticulitis?--phlegmonous diverticulitis revisited. *International journal of colorectal disease*. 2011 Dec;26(12):1609-17. doi: 10.1007/s00384-011-1280-y. PMID: 21830036.
74. Andeweg CS, Knobben L, Hendriks JC, et al. How to diagnose acute left-sided colonic diverticulitis: proposal for a clinical scoring system. *Annals of surgery*. 2011 May;253(5):940-6. doi: 10.1097/SLA.0b013e3182113614. PMID: 21346548.
75. Shuaib W, Johnson JO, Salastekar N, et al. Incidental findings detected on abdomino-pelvic multidetector computed tomography performed in the acute setting. *Am J Emerg Med*. 2014 Jan;32(1):36-9. doi: 10.1016/j.ajem.2013.09.019. PMID: 24475484.
76. Salem TA, Molloy RG, O'Dwyer PJ. Prospective study on the role of the CT scan in patients with an acute abdomen. *Colorectal disease : the official journal of the Association of Coloproctology of Great Britain and Ireland*. 2005 Sep;7(5):460-6. doi: 10.1111/j.1463-1318.2005.00822.x. PMID: 16108882.

77. Martin Arevalo J, Garcia-Granero E, Garcia Botello S, et al. [Early use of CT in the management of acute diverticulitis of the colon]. *Rev Esp Enferm Dig.* 2007 Jun;99(6):320-4. doi: 10.4321/s1130-01082007000600003. PMID: 17883294.
78. Kelly ME, Heeney A, Redmond CE, et al. Incidental findings detected on emergency abdominal CT scans: a 1-year review. *Abdom Imaging.* 2015 Aug;40(6):1853-7. doi: 10.1007/s00261-015-0349-4. PMID: 25576049.
79. Moya P, Arroyo A, Perez-Legaz J, et al. Applicability, safety and efficiency of outpatient treatment in uncomplicated diverticulitis. *Tech Coloproctol.* 2012 Aug;16(4):301-7. doi: 10.1007/s10151-012-0847-0. PMID: 22706731.
80. Lorente L, Cots F, Alonso S, et al. [Outpatient treatment of uncomplicated acute diverticulitis: Impact on healthcare costs]. *Cir Esp.* 2013 Oct;91(8):504-9. doi: 10.1016/j.ciresp.2013.01.016. PMID: 23764519.
81. Joliat GR, Emery J, Demartines N, et al. Antibiotic treatment for uncomplicated and mild complicated diverticulitis: outpatient treatment for everyone. *International journal of colorectal disease.* 2017 Sep;32(9):1313-9. doi: 10.1007/s00384-017-2847-z. PMID: 28664347.
82. Unlu C, Gunadi PM, Gerhards MF, et al. Outpatient treatment for acute uncomplicated diverticulitis. *Eur J Gastroenterol Hepatol.* 2013 Sep;25(9):1038-43. doi: 10.1097/MEG.0b013e328361dd5b. PMID: 23636075.
83. Bolkenstein HE, Draaisma WA, van de Wall B, et al. Treatment of acute uncomplicated diverticulitis without antibiotics: risk factors for treatment failure. *International journal of colorectal disease.* 2018 Jul;33(7):863-9. doi: 10.1007/s00384-018-3055-1. PMID: 29679152.
84. Juncadella AC, Feuerstein JD. In uncomplicated, left-sided acute diverticulitis, observation did not differ from antibiotics for recovery. *Ann Intern Med.* 2017 Feb 21;166(4):Jc18. doi: 10.7326/acpjc-2017-166-4-018. PMID: 28241291.
85. van Dijk ST, Daniels L, de Korte N, et al. Quality of Life and Persistent Symptoms After Uncomplicated Acute Diverticulitis. *Diseases of the colon and rectum.* 2019 May;62(5):608-14. doi: 10.1097/dcr.0000000000001361. PMID: 30807455.
86. van Dijk ST, Daniels L, Unlu C, et al. Long-Term Effects of Omitting Antibiotics in Uncomplicated Acute Diverticulitis. *The American journal of gastroenterology.* 2018 Jul;113(7):1045-52. doi: 10.1038/s41395-018-0030-y. PMID: 29700480.
87. Isacson D, Smedh K, Nikberg M, et al. Long-term follow-up of the AVOD randomized trial of antibiotic avoidance in uncomplicated diverticulitis. *The British journal of surgery.* 2019 Oct;106(11):1542-8. doi: 10.1002/bjs.11239. PMID: 31386199.
88. Jaung R, Nisbet S, Gosselink MP, et al. Antibiotics Do Not Reduce Length of Hospital Stay for Uncomplicated Diverticulitis in a Pragmatic Double-Blind Randomized Trial. *Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association.* 2020 Mar 30. doi: 10.1016/j.cgh.2020.03.049. PMID: 32240832.
89. Kim JY, Park SG, Kang HJ, et al. Prospective randomized clinical trial of uncomplicated right-sided colonic diverticulitis: antibiotics versus no antibiotics. *International journal of colorectal disease.* 2019 Aug;34(8):1413-20. doi: 10.1007/s00384-019-03343-w. PMID: 31267222.
90. de Korte N, Kuyvenhoven JP, van der Peet DL, et al. Mild colonic diverticulitis can be treated without antibiotics. A case-control study. *Colorectal disease : the official journal of the Association of Coloproctology of Great Britain and Ireland.* 2012 Mar;14(3):325-30. doi: 10.1111/j.1463-1318.2011.02609.x. PMID: 21689302.
91. Hjern F, Josephson T, Altman D, et al. Conservative treatment of acute colonic diverticulitis: are antibiotics always mandatory? *Scandinavian journal of gastroenterology.* 2007 Jan;42(1):41-7. doi: 10.1080/00365520600780650. PMID: 17190761.

92. Chung BH, Ha GW, Lee MR, et al. Management of Colonic Diverticulitis Tailored to Location and Severity: Comparison of the Right and the Left Colon. *Ann Coloproctol*. 2016 Dec;32(6):228-33. doi: 10.3393/ac.2016.32.6.228. PMID: 28119866.
93. Kim CN. What is the Difference Between Right- and Left-Sided Colonic Diverticulitis? *Ann Coloproctol*. 2016 Dec;32(6):206-7. doi: 10.3393/ac.2016.32.6.206. PMID: 28119862.
94. van Dijk ST, Chabok A, Dijkgraaf MG, et al. Observational versus antibiotic treatment for uncomplicated diverticulitis: an individual-patient data meta-analysis. *The British journal of surgery*. 2020 Feb 19. doi: 10.1002/bjs.11465. PMID: 32073652.
95. Kellum JM, Sugerman HJ, Coppa GF, et al. Randomized, prospective comparison of cefoxitin and gentamicin-clindamycin in the treatment of acute colonic diverticulitis. *Clin Ther*. 1992 May-Jun;14(3):376-84. PMID: 1638578.
96. Ridgway PF, Latif A, Shabbir J, et al. Randomized controlled trial of oral vs intravenous therapy for the clinically diagnosed acute uncomplicated diverticulitis. *Colorectal disease : the official journal of the Association of Coloproctology of Great Britain and Ireland*. 2009 Nov;11(9):941-6. doi: 10.1111/j.1463-1318.2008.01737.x. PMID: 19016815.
97. Ribas Y, Bombardo J, Aguilar F, et al. Prospective randomized clinical trial assessing the efficacy of a short course of intravenously administered amoxicillin plus clavulanic acid followed by oral antibiotic in patients with uncomplicated acute diverticulitis. *International journal of colorectal disease*. 2010 Nov;25(11):1363-70. doi: 10.1007/s00384-010-0967-9. PMID: 20526718.
98. Park JH, Park HC, Lee BH. One-day versus four-day antibiotic treatment for acute right colonic uncomplicated diverticulitis: A randomized clinical trial. *Turk J Gastroenterol*. 2019 Jul;30(7):605-10. doi: 10.5152/tjg.2019.17775. PMID: 31290747.
99. Scarpa CR, Buchs NC, Poncet A, et al. Short-term Intravenous Antibiotic Treatment in Uncomplicated Diverticulitis Does Not Increase the Risk of Recurrence Compared to Long-term Treatment. *Ann Coloproctol*. 2015 Apr;31(2):52-6. doi: 10.3393/ac.2015.31.2.52. PMID: 25960972.
100. Etzioni DA, Chiu VY, Cannom RR, et al. Outpatient treatment of acute diverticulitis: rates and predictors of failure. *Diseases of the colon and rectum*. 2010 Jun;53(6):861-5. doi: 10.1007/DCR.0b013e3181cdb243. PMID: 20484998.
101. Lambrichts DPV, Bolkenstein HE, van der Does D, et al. Multicentre study of non-surgical management of diverticulitis with abscess formation. *The British journal of surgery*. 2019 Mar;106(4):458-66. doi: 10.1002/bjs.11129. PMID: 30811050.
102. Mali J, Mentula P, Leppaniemi A, et al. Determinants of treatment and outcomes of diverticular abscesses. *World journal of emergency surgery : WJES*. 2019;14:31. doi: 10.1186/s13017-019-0250-5. PMID: 31320921.
103. Lau KC, Spilsbury K, Farooque Y, et al. Is colonoscopy still mandatory after a CT diagnosis of left-sided diverticulitis: can colorectal cancer be confidently excluded? *Diseases of the colon and rectum*. 2011 Oct;54(10):1265-70. doi: 10.1097/DCR.0b013e31822899a2. PMID: 21904141.
104. Sallinen V, Mentula P, Leppaniemi A. Risk of colon cancer after computed tomography-diagnosed acute diverticulitis: is routine colonoscopy necessary? *Surgical endoscopy*. 2014 Mar;28(3):961-6. doi: 10.1007/s00464-013-3257-0. PMID: 24178863.
105. Soh NYT, Chia DKA, Teo NZ, et al. Prevalence of colorectal cancer in acute uncomplicated diverticulitis and the role of the interval colonoscopy. *International journal of colorectal disease*. 2018 Jul;33(7):991-4. doi: 10.1007/s00384-018-3039-1. PMID: 29663068.

106. Choi YH, Koh SJ, Kim JW, et al. Do we need colonoscopy following acute diverticulitis detected on computed tomography to exclude colorectal malignancy? *Digestive diseases and sciences*. 2014 Sep;59(9):2236-42. doi: 10.1007/s10620-014-3151-1. PMID: 24723071.
107. Daniels L, Unlu C, de Wijkerslooth TR, et al. Yield of colonoscopy after recent CT-proven uncomplicated acute diverticulitis: a comparative cohort study. *Surgical endoscopy*. 2015 Sep;29(9):2605-13. doi: 10.1007/s00464-014-3977-9. PMID: 25472747.
108. Lecleire S, Nahon S, Alatawi A, et al. Diagnostic impact of routine colonoscopy following acute diverticulitis: A multicenter study in 808 patients and controls. *United European Gastroenterol J*. 2014 Aug;2(4):301-6. doi: 10.1177/2050640614541765. PMID: 25083288.
109. Lahat A, Yanai H, Menachem Y, et al. The feasibility and risk of early colonoscopy in acute diverticulitis: a prospective controlled study. *Endoscopy*. 2007 Jun;39(6):521-4. doi: 10.1055/s-2007-966399. PMID: 17554647.
110. Andrade P, Ribeiro A, Ramalho R, et al. Routine Colonoscopy after Acute Uncomplicated Diverticulitis - Challenging a Putative Indication. *Digestive surgery*. 2017;34(3):197-202. doi: 10.1159/000449259. PMID: 27941344.
111. Brar MS, Roxin G, Yaffe PB, et al. Colonoscopy following nonoperative management of uncomplicated diverticulitis may not be warranted. *Diseases of the colon and rectum*. 2013 Nov;56(11):1259-64. doi: 10.1097/DCR.0b013e3182a26bfd. PMID: 24105001.
112. Elmi A, Hedgire SS, Pargaonkar V, et al. Is early colonoscopy beneficial in patients with CT-diagnosed diverticulitis? *AJR American journal of roentgenology*. 2013 Jun;200(6):1269-74. doi: 10.2214/ajr.12.9539. PMID: 23701063.
113. Horesh N, Saeed Y, Horesh H, et al. Colonoscopy after the first episode of acute diverticulitis: challenging management paradigms. *Tech Coloproctol*. 2016 Jun;20(6):383-7. doi: 10.1007/s10151-016-1478-7. PMID: 27170283.
114. Khoury T, Mahamid M, Lubany A, et al. Underlying Colorectal Cancer Was Rarely Detected After an Episode of Acute Diverticulitis: a Retrospective Analysis of 225 Patients. *J Gastrointest Cancer*. 2019 Jan 10. doi: 10.1007/s12029-019-00202-3. PMID: 30632029.
115. Meireles LC, Fernandes SR, Ribeiro LC, et al. Role of endoscopy after an acute episode of diverticulitis: analysis of a cohort of Portuguese patients from a tertiary referral center. *Eur J Gastroenterol Hepatol*. 2015 Dec;27(12):1429-32. doi: 10.1097/meg.0000000000000474. PMID: 26378691.
116. Ramphal W, Schreinemakers MJ, Seerden TCJ, et al. Tumour Characteristics of Patients with Colorectal Cancer after Acute Uncomplicated Diverticulitis. *Dig Dis*. 2018;36(5):362-8. doi: 10.1159/000489926. PMID: 29945147.
117. Schout PJ, Spillenaar Bilgen EJ, Groenen MJ. Routine screening for colon cancer after conservative treatment of diverticulitis. *Digestive surgery*. 2012;29(5):408-11. doi: 10.1159/000345332. PMID: 23171930.
118. Seoane Urgorri A, Zaffalon D, Pera Roman M, et al. Routine lower gastrointestinal endoscopy for radiographically confirmed acute diverticulitis. In whom and when is it indicated? *Rev Esp Enferm Dig*. 2018 Sep;110(9):571-6. doi: 10.17235/reed.2018.5524/2018. PMID: 29900742.
119. Suhardja TS, Norhadi S, Seah EZ, et al. Is early colonoscopy after CT-diagnosed diverticulitis still necessary? *International journal of colorectal disease*. 2017 Apr;32(4):485-9. doi: 10.1007/s00384-016-2749-5. PMID: 28035461.
120. Alcantar DC, Rodriguez C, Fernandez R, et al. The Necessity of a Colonoscopy after an Acute Diverticulitis Event in Adults Less Than 50 Years Old. *Cureus*. 2019 Sep 16;11(9):e5666. doi: 10.7759/cureus.5666. PMID: 31720142.

121. O'Donohoe N, Chandak P, Likos-Corbett M, et al. Follow up colonoscopy may be omissible in uncomplicated left-sided acute diverticulitis diagnosed with CT- a retrospective cohort study. *Sci Rep*. 2019 Dec 27;9(1):20127. doi: 10.1038/s41598-019-56641-2. PMID: 31882879.
122. Studniarek A, Kochar K, Warner C, et al. Findings on Colonoscopy after Diverticulitis: A Multicenter Review. *The American surgeon*. 2019 Dec 1;85(12):1381-5. PMID: 31908222.
123. Mortensen LQ, Burcharth J, Andresen K, et al. An 18-Year Nationwide Cohort Study on The Association Between Diverticulitis and Colon Cancer. *Annals of surgery*. 2017 May;265(5):954-9. doi: 10.1097/sla.0000000000001794. PMID: 27192351.
124. Stoop EM, de Haan MC, de Wijkerslooth TR, et al. Participation and yield of colonoscopy versus non-cathartic CT colonography in population-based screening for colorectal cancer: a randomised controlled trial. *Lancet Oncol*. 2012 Jan;13(1):55-64. doi: 10.1016/s1470-2045(11)70283-2. PMID: 22088831.
125. USPSTF. Screening for colorectal cancer: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med*. 2008 Nov 4;149(9):627-37. doi: 10.7326/0003-4819-149-9-200811040-00243. PMID: 18838716.
126. Qaseem A, Crandall CJ, Mustafa RA, et al. Screening for Colorectal Cancer in Asymptomatic Average-Risk Adults: A Guidance Statement From the American College of Physicians. *Ann Intern Med*. 2019 Nov 5;171(9):643-54. doi: 10.7326/m19-0642. PMID: 31683290.
127. Rex DK, Boland CR, Dominitz JA, et al. Colorectal Cancer Screening: Recommendations for Physicians and Patients From the U.S. Multi-Society Task Force on Colorectal Cancer. *Gastroenterology*. 2017 Jul;153(1):307-23. doi: 10.1053/j.gastro.2017.05.013. PMID: 28600072.
128. Raskin JB, Kamm MA, Jamal MM, et al. Mesalamine did not prevent recurrent diverticulitis in phase 3 controlled trials. *Gastroenterology*. 2014 Oct;147(4):793-802. doi: 10.1053/j.gastro.2014.07.004. PMID: 25038431.
129. Kvasnovsky CL, Bjarnason I, Donaldson AN, et al. A randomized double-blind placebo-controlled trial of a multi-strain probiotic in treatment of symptomatic uncomplicated diverticular disease. *Inflammopharmacology*. 2017 May 20. doi: 10.1007/s10787-017-0363-y. PMID: 28528364.
130. Parente F, Bargiggia S, Prada A, et al. Intermittent treatment with mesalazine in the prevention of diverticulitis recurrence: a randomised multicentre pilot double-blind placebo-controlled study of 24-month duration. *International journal of colorectal disease*. 2013 Oct;28(10):1423-31. doi: 10.1007/s00384-013-1722-9. PMID: 23754545.
131. Lanas A, Ponce J, Bignamini A, et al. One year intermittent rifaximin plus fibre supplementation vs. fibre supplementation alone to prevent diverticulitis recurrence: a proof-of-concept study. *Dig Liver Dis*. 2013 Feb;45(2):104-9. doi: 10.1016/j.dld.2012.09.006. PMID: 23092785.
132. Stollman N, Magowan S, Shanahan F, et al. A randomized controlled study of mesalamine after acute diverticulitis: results of the DIVA trial. *Journal of clinical gastroenterology*. 2013 Aug;47(7):621-9. doi: 10.1097/MCG.0b013e31828003f6. PMID: 23426454.
133. Kruis W, Kardalinos V, Eisenbach T, et al. Randomised clinical trial: mesalazine versus placebo in the prevention of diverticulitis recurrence. *Aliment Pharmacol Ther*. 2017 Aug;46(3):282-91. doi: 10.1111/apt.14152. PMID: 28543263.
134. Silva Sanchez SD, Wan H, Streck P, et al. Long-term safety of once-daily multimatrix mesalazine: a pooled clinical trials analysis. *Journal of gastroenterology and hepatology (australia)*. 2014;29:106-7. doi: 10.1111/jgh.12736-6. PMID: CN-01056300.

135. Mizuki A, Tatemichi M, Nakazawa A, et al. Effects of Burdock tea on recurrence of colonic diverticulitis and diverticular bleeding: An open-labelled randomized clinical trial. *Sci Rep*. 2019 May 1;9(1):6793. doi: 10.1038/s41598-019-43236-0. PMID: 31043657.
136. Tursi A, Brandimarte G, Daffina R. Long-term treatment with mesalazine and rifaximin versus rifaximin alone for patients with recurrent attacks of acute diverticulitis of colon. *Dig Liver Dis*. 2002 Jul;34(7):510-5. doi: 10.1016/s1590-8658(02)80110-4. PMID: 12236485.
137. Festa V, Spila Alegiani S, Chiesara F, et al. Retrospective comparison of long-term ten-day/month rifaximin or mesalazine in prevention of relapse in acute diverticulitis. *Eur Rev Med Pharmacol Sci*. 2017 Mar;21(6):1397-404. PMID: 28387885.
138. Tursi A, Brandimarte G, Giorgetti GM, et al. Balsalazide and/or high-potency probiotic mixture (VSL#3) in maintaining remission after attack of acute, uncomplicated diverticulitis of the colon. *International journal of colorectal disease*. 2007 Sep;22(9):1103-8. doi: 10.1007/s00384-007-0299-6. PMID: 17390144.
139. You K, Bendl R, Taut C, et al. Randomized clinical trial of elective resection versus observation in diverticulitis with extraluminal air or abscess initially managed conservatively. *The British journal of surgery*. 2018 Jul;105(8):971-9. doi: 10.1002/bjs.10868. PMID: 29683483.
140. van de Wall BJM, Stam MAW, Draaisma WA, et al. Surgery versus conservative management for recurrent and ongoing left-sided diverticulitis (DIRECT trial): an open-label, multicentre, randomised controlled trial. *Lancet Gastroenterol Hepatol*. 2017 Jan;2(1):13-22. doi: 10.1016/s2468-1253(16)30109-1. PMID: 28404008.
141. Bolkenstein HE, de Wit GA, Consten ECJ, et al. Cost-effectiveness analysis of a multicentre randomized clinical trial comparing surgery with conservative management for recurrent and ongoing diverticulitis (DIRECT trial). *The British journal of surgery*. 2019;106(1365-2168 (Electronic)):448-57. PMID: 30566245.
142. Bolkenstein HE, Consten ECJ, van der Palen J, et al. Long-term Outcome of Surgery Versus Conservative Management for Recurrent and Ongoing Complaints After an Episode of Diverticulitis: 5-year Follow-up Results of a Multicenter Randomized Controlled Trial (DIRECT-Trial). *Annals of surgery*. 2019;269(4):612-20. PMID: 30247329.
143. Aquina CT, Becerra AZ, Xu Z, et al. Population-based study of outcomes following an initial acute diverticular abscess. *The British journal of surgery*. 2019 Mar;106(4):467-76. doi: 10.1002/bjs.10982. PMID: 30335195.
144. Shi HY, Lee KT, Lee HH, et al. The minimal clinically important difference in the Gastrointestinal Quality-of-Life Index after cholecystectomy. *Surgical endoscopy*. 2009 Dec;23(12):2708-12. doi: 10.1007/s00464-009-0475-6. PMID: 19430834.
145. Jayadevappa R, Cook R, Chhatre S. Minimal important difference to infer changes in health-related quality of life-a systematic review. *J Clin Epidemiol*. 2017 Sep;89:188-98. doi: 10.1016/j.jclinepi.2017.06.009. PMID: 28676426.
146. Myles PS, Myles DB, Gallagher W, et al. Measuring acute postoperative pain using the visual analog scale: the minimal clinically important difference and patient acceptable symptom state. *Br J Anaesth*. 2017 Mar 1;118(3):424-9. doi: 10.1093/bja/aew466. PMID: 28186223.
147. Bhakta A, Tafen M, Glotzer O, et al. Laparoscopic sigmoid colectomy for complicated diverticulitis is safe: review of 576 consecutive colectomies. *Surgical endoscopy*. 2016 Apr;30(4):1629-34. doi: 10.1007/s00464-015-4393-5. PMID: 26275534.
148. Bordeianou L, Cauley CE, Patel R, et al. Prospective Creation and Validation of the PREVENTT (Prediction and Enaction of Prevention Treatments Trigger) Scale for Surgical Site Infections (SSIs) in Patients With Diverticulitis. *Annals of surgery*. 2019 Dec;270(6):1124-30. doi: 10.1097/sla.0000000000002859. PMID: 29916880.

149. Ilyas MI, Zangbar B, Nfonsam VN, et al. Are there differences in outcome after elective sigmoidectomy for diverticular disease and for cancer? A national inpatient study. *Colorectal disease : the official journal of the Association of Coloproctology of Great Britain and Ireland*. 2017 Mar;19(3):260-5. doi: 10.1111/codi.13461. PMID: 27422847.
150. Lidor AO, Schneider E, Segal J, et al. Elective surgery for diverticulitis is associated with high risk of intestinal diversion and hospital readmission in older adults. *Journal of gastrointestinal surgery : official journal of the Society for Surgery of the Alimentary Tract*. 2010 Dec;14(12):1867-73; discussion 73-4. doi: 10.1007/s11605-010-1344-2. PMID: 20878256.
151. Masoomi H, Buchberg B, Nguyen B, et al. Outcomes of laparoscopic versus open colectomy in elective surgery for diverticulitis. *World J Surg*. 2011 Sep;35(9):2143-8. doi: 10.1007/s00268-011-1117-4. PMID: 21732208.
152. Moghadamyeghaneh Z, Carmichael JC, Smith BR, et al. A comparison of outcomes of emergent, urgent, and elective surgical treatment of diverticulitis. *American journal of surgery*. 2015 Nov;210(5):838-45. doi: 10.1016/j.amjsurg.2015.04.010. PMID: 26116319.
153. Papageorge CM, Kennedy GD, Carchman EH. National Trends in Short-term Outcomes Following Non-emergent Surgery for Diverticular Disease. *Journal of gastrointestinal surgery : official journal of the Society for Surgery of the Alimentary Tract*. 2016 Jul;20(7):1376-87. doi: 10.1007/s11605-016-3150-y. PMID: 27120447.
154. Pessaux P, Muscari F, Ouellet JF, et al. Risk factors for mortality and morbidity after elective sigmoid resection for diverticulitis: prospective multicenter multivariate analysis of 582 patients. *World J Surg*. 2004 Jan;28(1):92-6. doi: 10.1007/s00268-003-7146-x. PMID: 14639493.
155. Russ AJ, Obma KL, Rajamanickam V, et al. Laparoscopy improves short-term outcomes after surgery for diverticular disease. *Gastroenterology*. 2010 Jun;138(7):2267-74. doi: 10.1053/j.gastro.2010.02.048. PMID: 20193685.
156. Silva-Velazco J, Stocchi L, Costedio M, et al. Is there anything we can modify among factors associated with morbidity following elective laparoscopic sigmoidectomy for diverticulitis? *Surgical endoscopy*. 2016 Aug;30(8):3541-51. doi: 10.1007/s00464-015-4651-6. PMID: 26541732.
157. Simianu VV, Sinanan MN, Bastawrous AL, et al. The impact of delaying elective resection of diverticulitis on laparoscopic conversion rate. *American journal of surgery*. 2015;209(5):913-9. doi: 10.1016/j.amjsurg.2014.12.027. PMID: 25773308.
158. Tsilimparis N, Haase O, Wendling P, et al. [Laparoscopic "fast-track" sigmoidectomy for diverticulitis disease in Germany. Results of a prospective quality assurance program]. *Dtsch Med Wochenschr*. 2010 Sep;135(36):1743-8. doi: 10.1055/s-0030-1263305. PMID: 20812161.
159. Valizadeh N, Suradkar K, Kiran RP. Specific Factors Predict the Risk for Urgent and Emergent Colectomy in Patients Undergoing Surgery for Diverticulitis. *The American surgeon*. 2018 Nov 1;84(11):1781-6. PMID: 30747633.
160. Varma S, Mehta A, Canner JK, et al. Surgery After an Initial Episode of Uncomplicated Diverticulitis: Does Time to Resection Matter? *J Surg Res*. 2019 Feb;234:224-30. doi: 10.1016/j.jss.2018.09.043. PMID: 30527478.
161. Sheer AJ, Heckman Je Fau - Schneider EB, Schneider Eb Fau - Wu AW, et al. Congestive heart failure and chronic obstructive pulmonary disease predict poor surgical outcomes in older adults undergoing elective diverticulitis surgery. *Diseases of the colon and rectum*. 2011;54(11):1430-7. PMID: 21979190.
162. Vermeer NC, Snijders HS, Holman FA, et al. Colorectal cancer screening: Systematic review of screen-related morbidity and mortality. *Cancer Treat Rev*. 2017 Mar;54:87-98. doi: 10.1016/j.ctrv.2017.02.002. PMID: 28236723.

Management of Colonic Diverticulitis: Addendum

This addendum details updated results for Key Question 2b (Antibiotic Treatment for Acute Diverticulitis), Key Question 3 (Colonoscopy), and Key Question 4b (Adverse Events Associated With Elective Surgery).

An updated search using the same search strategy from the original report was conducted on November 16, 2020. The search update yielded 1,934 citations, of which 22 were retrieved for full-text screening. Ultimately, 4 additional studies (2 of which were reported in one article) were added.¹⁶³⁻¹⁶⁶

The methods used for this update were the same as in the original report except that the update excluded right-sided colonic diverticulitis.

Revised text pertaining to the main report is underlined (compared with original text). Explanations for the changes are in italic text. All table rows presented for Appendixes C and D are new entries.

Key Question 2b (Antibiotics)

Comparisons Between Various Antibiotic Regimens

One new article, which reported two studies, was found (reference 163).

Gaber 2021 reported two retrospective nonrandomized comparative studies (NRCSs) that compared oral combination metronidazole and a fluoroquinolone (either ciprofloxacin or levofloxacin) with oral amoxicillin/clavulanate.¹⁶³ The drugs were compared in two outpatient databases: MarketScan (2001 to 2018; N=119,592; median age 52 years) and Medicare (2007 to 2015; N=20,348; median age 73 years) among patients with first-time acute diverticulitis. The NRCSs were deemed to be at low risk of bias, having conducted propensity-score analyses. The studies reported on 1-year hospitalization, urgent surgery, elective surgery, and *Clostridium difficile* infection.

Hospitalization

No differences in risk of 1-year hospitalization were found between fluoroquinolone + metronidazole and amoxicillin/clavulanate: MarketScan RR 1.04 (95% CI 0.93 to 1.18), Medicare RR 1.04 (95% CI 0.83 to 1.38).

Urgent Surgery

No differences in risk of 1-year urgent surgery were found between fluoroquinolone + metronidazole and amoxicillin/clavulanate: MarketScan RR 1.04 (95% CI 0.75 to 1.55), Medicare RR 0.63 (95% CI 0.34 to 1.66).

Elective Surgery

No differences in risk of 1-year elective surgery were found between fluoroquinolone + metronidazole and amoxicillin/clavulanate: MarketScan RR 1.05 (95% CI 0.93 to 1.19), Medicare RR 0.87 (95% CI 0.66 to 1.21).

Clostridium difficile

The two studies reported by Gaber 2021 found different RRs of *C. difficile* infection in the two populations. In the analysis of younger patients (MarketScan), there were no differences in

risk of *C. difficile* (RR 1.16, 95% CI 0.76 to 1.96). However, in the Medicare population study, patients prescribed fluoroquinolone + metronidazole were about twice as likely to have a *C. difficile* infection than amoxicillin/clavulanate (RR 2.13, 95% CI 1.25 to 4.33).

Summary of Evidence Pertaining to Antibiotic Treatment

Despite there being 15 comparative studies overall, and six studies specifically comparing use of antibiotics to no antibiotics (or placebo), the evidence base is generally too sparse or inconsistent to make strong conclusions about the value of antibiotics for patients with uncomplicated or mild diverticulitis.

Nine studies compared different antibiotic regimens in patients with acute diverticulitis. However, each compared different sets of regimens, either different antibiotics (5 studies); different, largely nonoverlapping comparisons of durations of treatment (4 studies); and different routes (1 study). Except for the pair of studies analyzed and reported together by Gaber 2021, only a single study evaluated any given comparison and clinical outcomes were generally sparse within studies, resulting in highly imprecise comparisons of regimens. (For the purpose of counting studies, we chose to evaluate each cohort within Gaber 2021 as a separate study. However, for the purpose of assessing SoE, since the two studies were analyzed together, we treated them as one study providing sparse evidence.) The only differences found were that a 7-day course of ertapenem resulted in a shorter length of hospital stay (by about 2 days) than a 4-day course³¹ and in a Medicare population, but not a younger cohort, *C. difficile* infection was twice as likely with fluoroquinolone + metronidazole than amoxicillin/clavulanate.¹⁶³ The full evidence profile is in Table 8.

Table 8. Evidence profile for antibiotic treatment for acute left-sided diverticulitis

Topic	Outcome	No. Studies (Subjects)	Risk of Bias	Consistency	Precision	Directness	Other	Overall SoE	Conclusion Statements
Various Abx regimens	All	9 (141,274) ¹	Moderate	N/A	Imprecise	Direct	Sparse per analysis	Insufficient	No conclusions comparing antibiotic regimens

Abbreviations: Abx = antibiotics, LOS = length of stay, MD = mean difference, N/A = not applicable, OR = odds ratio (with 95% confidence interval), SoE = strength of evidence.

¹ One article, which reported on 2 studies (Gaber 2021), included a total of 139 869 participants; the remaining 7 studies included 1405 participants.

Key Question 3. Colonoscopy After Acute Diverticulitis

Colonoscopy After Diverticulitis Versus Healthy Controls

High-Risk Colonic Premalignant Lesions

Correction of typographical error on page 42:

The OR for adenomas with high-grade dysplasias was similar, but near imprecise (OR 0.33, 95% CI 0.07 to 1.64).

Rates of Colorectal Cancer and Abnormal Lesions on Colonoscopy

One new study found (reference 164)

We identified 13 single group studies,¹¹⁰⁻¹²² all retrospective that evaluated colonoscopy outcomes, and one retrospective NRCS that compared colonoscopy with flexible sigmoidoscopy.¹⁶⁴

Colorectal Cancer

The text and Figure 7 are unchanged except for the addition of 1 study (N=120). The estimates and ranges for CRC are unchanged.

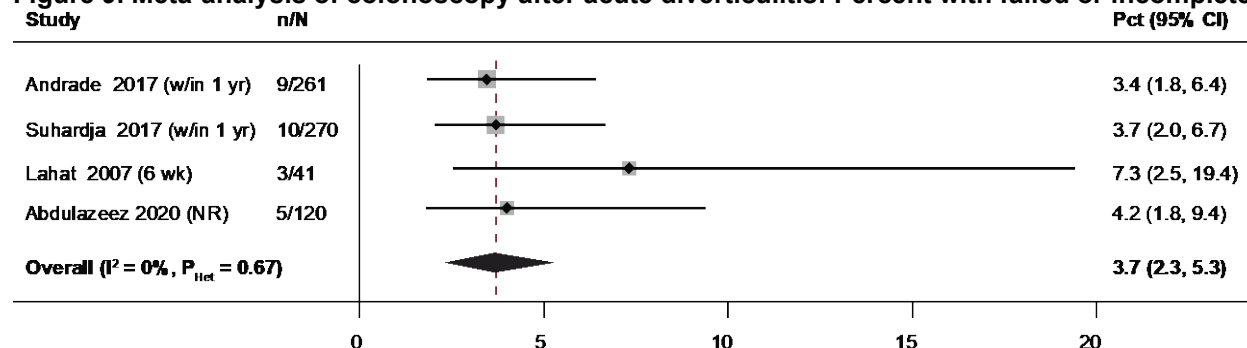
Colonoscopy: Complications, Tolerance, Feasibility, and Completion of Procedure

Five studies explicitly reported no major complications (Meireles 2015 and Seoane Ugorri 2018)^{115, 118} or (overall) no complications (Abdulazeez, 2020, Choi 2014 and Lahat 2007)^{106, 109, 164} related to colonoscopy across 998 patients overall, implying a confidence interval of 0 to 0.8 percent. Colonoscopies were conducted within 6 to 7 weeks,^{109, 118} 4 months,¹¹⁵ or 1 year¹⁰⁶ after the episode of acute diverticulitis (or not reported¹⁶⁴).

Four studies reported on rates of failed/incomplete colonoscopy procedure (Figure 9).^{109, 110, 119, 164} Combination of the four cohorts that performed colonoscopy after hospital discharge (within 1 year or at approximately 6 weeks or not reported) yielded a summary estimate that 3.7 percent (95% CI 2.3 to 5.3) of patients had a failed or incomplete procedure.

Abdulazeez 2020 compared patients who received colonoscopy with those who received flexible sigmoidoscopy.¹⁶⁴ Failed or incomplete procedure was more common with colonoscopy (4.2%) than flexible sigmoidoscopy (2.5%), but the difference was imprecise (OR 1.70, 95% CI 0.40 to 7.26).

Figure 9. Meta-analysis of colonoscopy after acute diverticulitis: Percent with failed or incomplete colonoscopy



Summary of Evidence Pertaining to Colonoscopy

Complications due to colonoscopy after acute diverticulitis are rare. Based on five studies that explicitly reported on complications, none (of 998) patients experienced a procedure-related complication (95% CI 0 to 0.8%; high SoE). Failed or incomplete colonoscopies were reported to be uncommon (3.7%, 95% CI 2.3 to 5.3; 4 studies; high SoE). One RCT compared in-hospital colonoscopy to colonoscopy about 6 weeks after discharge finding similar rates of completed colonoscopies between the groups. One NRCS compared colonoscopy and flexible sigmoidoscopy and found no significant difference in rates of incomplete procedures.

Table 11. Evidence profile for colonoscopy after acute diverticulitis

Comparison	Outcome	No. Studies (Subjects)	Risk of Bias	Consistency	Precision	Directness	Other	Overall SoE	Findings and Conclusions
Rates of abnormal findings (no comparison)	CRC	<u>21 (6,335)</u>	Low	Inconsistent	Precise	Direct	None	Moderate	1.8% (1.2, 2.6)
Complications (no comparison)	Complications	<u>5 (998)</u>	Low	Consistent	Precise	Direct	None	High	0% (0 to <u>0.8</u>)
Feasibility (no comparison)	Incomplete colonoscopy	<u>4 (692)</u>	Low	Consistent	Precise	Direct	None	High	<u>3.7%</u> (<u>2.3</u> , 5.3)

Abbreviations: ACN = advanced colonic neoplasia, CRC = colorectal cancer, Hx of = history of (recent), NS = not statistically significant, OR = odds ratio (with 95% confidence interval), SoE = strength of evidence.

Key Question 4c. Elective Surgery

Adverse Events Associated With Elective Surgery

Two new studies found (references 165 and 166)

Serious adverse events associated with elective surgery were reported in 19 studies (2 RCTs,¹³⁹⁻¹⁴² 1 NRCS,¹⁴³ and 16 eligible single-group studies in 17 reports^{147-161, 165, 166}).

The characteristics of the comparative studies are described above. The single-group studies were all either non-industry funded or did not report funding source. The inclusion criteria were either having undergone elective surgery for diverticulitis (17 studies) or having a diagnosis of diverticulitis (2 studies).

Overall Adverse Event Rates

Of the individual adverse events, 30-day mortality was 0.7 percent across 10 studies; 30-day readmission was 7.3 percent across three studies. Other common adverse events included major pulmonary events (7.8% in one study) and reoperation (4.3% across 8 studies). All outcomes are listed in Table 18.

Table 18. Adverse events of elective surgery

Adverse Event (Clavien-Dindo Classification, As Applicable)	n/N (Total)	Summary Percentage (95% CI)	Range Across Studies	Evidence Base
Reoperation, unplanned (CD III)	1236/15,367	4.3 (2.2, 6.9)	0 – 13.2	8 studies 139, 149, 150, 152, 157, 159, 161, <u>165</u> , <u>166</u>
Incisional hernia requiring procedure (CD III)	139/7387	1.9 (1.6, 2.2)	1.7 – 1.9	2 studies 147, <u>165</u>
30-day mortality (CD V)	4957/199,915	0.7 (0.3, 1.4)	0.18 – 3.5	10 studies 143, 149, 150, 152-156, 158, 161, <u>166</u>

Adverse events reported by at least four studies are emphasized in bold font.

Abbreviations: AE=adverse event; C diff = Clostridioides difficile; CD=Clavien-Dindo Classification; CPR = cardiopulmonary resuscitation; DVT=deep vein thrombosis; OR=operating room; SAE= serious adverse event.

Summary of Evidence Pertaining to Elective Surgery

Elective surgery for diverticulitis may be associated with frequent total serious adverse events, but the frequency across studies was highly variable (4% to 70%) and likely related to definitions of adverse events (thus, there was insufficient evidence to estimate the frequency of total serious adverse events). The most commonly reported adverse event, which was reported by 10 of 19 studies, was 30-day mortality which occurred, on average, in 0.7% of patients undergoing elective surgery (moderate SoE). The more common adverse events (that were reported by at least 4 studies) were unplanned reoperations (4.3%; low SoE) and anastomotic leakage requiring a procedure (4.3%; low SoE). Less common adverse events (reported by at least 4 studies) included sepsis (1.6%; moderate SoE), surgical site infection requiring antibiotics

(1.4%; moderate SoE), myocardial infarction (0.7%; moderate SoE), deep vein thrombosis (0.6%; Moderate SoE), and pulmonary embolism (0.3%; moderate SoE).

Table 19. Evidence profile for elective surgery

Topic	Outcome	No. Studies (Subjects)	Risk of Bias	Consistency	Precision	Directness	Other	Overall SoE	Findings and Conclusions
Adverse events	30-day mortality	<u>10</u> (203,426)	Low	Inconsistent	Precise	Direct	None	Moderate	0.7% (0.3, 1.4)
	Reoperation	<u>8</u> (53,196)	Low	Inconsistent	Imprecise	Direct	None	Low	<u>4.3%</u> (<u>2.2</u> , <u>6.9</u>)

Abbreviations: AE = adverse events, DVT = deep vein thrombosis, MI = myocardial infarction, OR = odds ratio (with 95% confidence interval), SoE = strength of evidence.

References

163. Gaber CE, Kinlaw AC, Edwards JK, et al. Comparative effectiveness and harms of antibiotics for outpatient diverticulitis: two nationwide cohort studies. *Ann Intern Med.* 2021;174:737-746. doi:10.7326/M20-6315. PMID: 33617725.
164. Abdulazeez Z, Kukreja N, Qureshi N, et al. Colonoscopy and flexible sigmoidoscopy for follow-up of patients with left-sided diverticulitis. *Ann R Coll Surg Engl.* 2020;102:744-7. doi:10.1308/rcsann.2020.0181. PMID: 32820657.
165. Perez NP, Chang DC, Goldstone RN, et al. Relationship between diverticular disease and incisional hernia after elective colectomy: a population-based study. *J Gastrointest Surg.* 2021;25:1297-1306. doi:10.1007/s11605-020-04762-9. PMID: 32748338.
166. von Strauss Und Torney M, Moffa G, Kaeck M, et al.. Risk of emergency surgery or death after initial nonoperative management of complicated diverticulitis in Scotland and Switzerland. *JAMA Surg.* 2020;155:600-6. doi:10.1001/jamasurg.2020.0757. PMID: 32401298.

Appendix C

Study Design Details and Arms, Risk of Bias

Key Question 2b (Antibiotics)

Table C-2b-1. KQ 2b. Design details

Author, Year, PMID, Study Name, Country, Funder	Study Design	Study Dates, Setting	Inclusion criteria	Exclusion criteria	How was diverticulitis diagnosed?
Gaber, 2021 33617725 US Nonindustry	NRCS (Retrospective)	2001-18 2007-15 Outpatient	First episode diverticulitis	Prior diverticulitis-related diagnostic code, percutaneous drain, or colectomy (for any indication), immunocompromised or immunosuppressed	Outpatient diagnostic code

Table C-2b-2. KQ 2b. Arm details

Author, Year, PMID, Study Name, Country	Arm	Arm Description	Dose	Frequency	Route	Duration of Intervention
Gaber, 2021 33617725 US Nonindustry	Fluoroquinolone + metronidazole	Prescription fill for metronidazole with oral ciprofloxacin or levofloxacin	NR	NR	Oral	NR
	Amoxicillin-clavulanate	Prescription fill for oral amoxicillin-clavulanate	NR	NR	Oral	NR

Table C-2b-3. KQ 2b. Baselines

Author, Year, PMID, Study Name	Arm	Male, %	Race/Ethnicity	Age, Mean (SD) or %	Participants with Un/Complicated Diverticulitis, %	Number of Prior Episodes of Diverticulitis, %	History of (Prior) Complicated Diverticulitis, %	Time Since Last Episode of Diverticulitis, Mean (SD)
Gaber, 2021 33617725 MarketScan	Fluoroquinolone + metronidazole	53%	NR	Median (IQR) 52 (45-58)	NR	0	0	N/A
	Amoxicillin-clavulanate	52%	White 91%, Black 4.3%	53 (46-59)	NR	0	0	N/A
Medicare	Fluoroquinolone + metronidazole	32%	NR	73 (69-79)	NR	0	0	N/A
	Amoxicillin-clavulanate	32%	White 92%, Black 3.5%	74 (69-80)	NR	0	0	N/A

Table C-2b-5. KQ 2b. Risk of bias, nonrandomized comparative studies

Author, Year, PMID, Study Name, Country	Bias due to confounding	Bias in selection of participants into the study	Blinding of outcome assessors/statisticians	Incomplete outcome data (attrition bias)	Selective Reporting (reporting bias)	Were eligibility/selection criteria for the study population prespecified and clearly described?	Was the test /service / intervention clearly described and delivered consistently across the study population?	Were the outcome measures prespecified, clearly defined, valid, reliable, and assessed consistently across all study participants?
Gaber, 2021 3361772 5 US	Low (propensity score adjustment/weighting : age at diagnosis; sex; race (Medicare data only); geographic region; concomitant medications; comorbidities; CT imaging; outpatient visits in the prior year; days spent as an inpatient in the prior year; recent prior inpatient admission; and product terms for age-by-sex, age-by-region, age-by-CT imaging, and year-by-CT imaging.)	No	No	No	No	Yes	No	Yes

Key Question 3 (Colonoscopy)

Table C-3-1. KQ3. Design details

Author, Year, PMID, Country	Study Design	Funder	Years	Inclusion criteria	Exclusion criteria
Abdulazeez, 2020, 32820657, UK	NRCS, Retrospective	Not reported (or unclear)	2016, 2019	Left-sided acute diverticulitis, ≥18 years, follow-up colonoscopy or flexible sigmoidoscopy	Extensive or right-sided diverticulitis

Table C-3-2. KQ 3. Arm details

Author, Year, PMID, Country	Arm	Colon imaging type	Time since bout of diverticulitis, Mean (SD)
Abdulazeez, 2020, 32820657, UK	Colonoscopy	Full colonoscopy 100%	NR
	Flexible sigmoidoscopy	Flexible sigmoidoscopy, 100%	NR

Key Question 4c (Elective Surgery)

Table C-4c-1. KQ 4c. Design details

Author, year, PMID, Study Name, Country	Study Design	Funder	Study Dates	Inclusion Criteria	Exclusion Criteria	How Was Diverticulitis Diagnosed?
Perez, 2020, 32748338, New York Statewide Planning and Research Cooperative System (SPARCS), US	Single group (Retrospective)	Non-industry (fully)	2010, 2016	18 years old and older, undergoing elective open or laparoscopic sigmoid or left hemicolectomy (by ICD-9 code) for diverticulitis (by ICD-9 code)	index colectomy were excluded, as well as patients with colon cancer who had been noted to have diverticular disease at any point prior to their colectomy. prior abdominal surgeries, concurrent stoma creations, hernia repairs, or surgeries of the liver, spleen, pancreas, kidneys, or uterus during their index colectomy, abdominal operations during their index admission after their index colectomy, organ space abscess, anastomotic leak, or wound disruption/infection within 30 days after index colectomy; inflammatory bowel disease; chemotherapy within 6 months prior to or after index colectomy; radiation therapy any time prior to or within 6 months after index colectomy; history of rectal, anal, or prostate cancer; and history of congenital abdominal wall defect.	NR

Author, year, PMID, Study Name, Country	Study Design	Funder	Study Dates	Inclusion Criteria	Exclusion Criteria	How Was Diverticulitis Diagnosed?
von Strauss und Torney, 2020, 32401298, Switzerland & UK Nonindustry	Single group (Retrospective)	Non-industry (fully)	2005, 2015	(ICD-10) diagnosis of primary colonic diverticulitis or diverticulosis in combination with a complication of acute diverticulitis as the primary diagnosis (eg, peritonitis or sepsis), who underwent elective interval resection.	NR	NR

Table C-4c-2. KQ 4c. Arm details

Author, Year, PMID, Study Name, Country	Arm	Surgery Type	Time Frame of Elective Surgery in Relation to Last Acute Diverticulitis
Perez, 2020, 32748338, New York Statewide Planning and Research Cooperative System (SPARCS), US	Elective surgery	Open or laparoscopic sigmoid or left hemicolectomy	NR
von Strauss und Torney, 2020, 32401298, Switzerland & UK Nonindustry	Elective surgery	Any	NR

Supplement Table B-4c-3. KQ 4c Baselines

Author, year, PMID, Study Name, Country	Arm	Male %	Race/ ethnicity	Age, mean (SD) or %	Participants With Un/Complicated Diverticulitis, %	Specific Complications of Diverticulitis %	Number of Prior Episodes of Diverticulitis, %	Time Since Last Episode of Diverticulitis, Mean (SD)
Perez, 2020, 32748338, New York Statewide Planning and Research Cooperative System (SPARCS), US	Elective surgery	50.1	White 81.7%, Black 3.9%, Hispanic/ Latino 7.1%, Asian 0.4%	55.9 (95% CI 55.6, 56.2)	NR	NR	NR	NR
von Strauss und Torney, 2020, 32401298, Switzerland & UK Non-industry	Elective surgery	NR	NR	NR	0/100	NR	NR	NR

Table C-4c-5. KQ 4c. Risk of bias, single-group studies

Author, year, PMID, Study Name, Country	Incomplete Outcome Data (Attrition Bias)	Selective Reporting (Reporting Bias)	Were Eligibility/ Selection Criteria for the Study Population Prespecified and Clearly Described?	Was the Test/Service/ Intervention Clearly Described and Delivered Consistently Across the Study Population?	Were the Outcome Measures Prespecified, Clearly Defined, Valid, Reliable, and Assessed Consistently Across All Study Participants?
Perez, 2020, 32748338, New York Statewide Planning and Research Cooperative System (SPARCS), US	Low	Low	Yes	Yes	Yes
von Strauss und Torney, 2020, 32401298, Switzerland & UK Non-industry	Low	Low	Yes	No	Yes

Table C-3-3. KQ3. Baselines

Author, Year, PMID, Study Name, Country	Arm	Male %	Participant age, mean (SD)	Age ≥50, %	Complicated/ Uncomplicated diverticulitis %
Abdulazeez, 2020, 32820657, UK	Colonoscopy	35	70 (10.2) [range 46, 90]	NR	NR
	Flexible sigmoidoscopy	37	72 (13.9) [range 28, 91]	NR	NR

Table C-3-4. KQ 3. Risk of bias

Author, Year, PMID, Country	Adjusted results in arm (subgroup) differences reported	Eligibility/selection criteria prespecified	Clear outcome definition
Abdulazeez, 2020, 32820657, UK	No	Yes	Yes

Appendix D

Full Results

Key Question 2b (Antibiotics)

Table D-2B. Antibiotics

Outcome	Study	Time	Arm	n/N (%)	OR (95% CI)	Reported P value
Hospitalization	Gaber, 2021 33617725 MarketScan	1 yr	Fluoroquinolone + metronidazole	NR/106,361	RR 1.04 (0.93, 1.18)	
			Amoxicillin/clavulanate	NR/13,160		
	Medicare	1 yr	Fluoroquinolone + metronidazole	NR/17,639	RR 1.04 (0.83, 1.38)	
			Amoxicillin/clavulanate	NR/2709		
Surgery, urgent	Gaber, 2021 33617725 MarketScan	1 yr	Fluoroquinolone + metronidazole	NR/106,361	RR 1.04 (0.75, 1.55)	
			Amoxicillin/clavulanate	NR/13,160		
	Medicare	1 yr	Fluoroquinolone + metronidazole	NR/17,639	RR 0.63 (0.34, 1.66)	
			Amoxicillin/clavulanate	NR/2709		
Surgery, elective	Gaber, 2021 33617725 MarketScan	1 yr	Fluoroquinolone + metronidazole	NR/106,361	RR 1.05 (0.93, 1.19)	
			Amoxicillin/clavulanate	NR/13,160		
	Medicare	1 yr	Fluoroquinolone + metronidazole	NR/17,639	RR 0.87* (0.66, 1.21)	
			Amoxicillin/clavulanate	NR/2709		
C. difficile infection	Gaber, 2021 33617725 MarketScan	1 yr	Fluoroquinolone + metronidazole	NR/106,361	RR 1.16 (0.76, 1.96)	
			Amoxicillin/clavulanate	NR/13,160		
	Medicare	1 yr	Fluoroquinolone + metronidazole	NR/17,639	RR 2.13 (1.25, 4.33)	
			Amoxicillin/clavulanate	NR/2709		

* Reported as RR 1.87 (0.66, 1.21).

Key Question 3 (Colonoscopy)

Table D-3-3. KQ 3. Categorical outcomes, single group studies

Author, Year, PMID, Country, Funding	Design	Population, Diverticulitis Details, Family Hx CRC, Setting	Outcome	Arm	Age, Sex	Age ≥50, %, Complicated/ Uncomplicated diverticulitis %	n/N (%)
Colorectal cancer							
Abdulazeed, 2020, 32820657, UK	NRCS	Left sided acute diverticulitis, ≥18 years, Family history of CRC: not reported. Single center.	Colorectal cancer	Colonoscopy	70 (10.2) [range 46, 90] NR	NR NR	0/120 (0%)
				Flex sig	72 (13.9) [range 28, 91] NR	NR NR	0/120 (0%)

Table D-3-7. KQ 3. Colonoscopy tolerance, feasibility, and completion of procedure; technical adequacy

Procedure Type	Author, Year, PMID, Country, Funding	Design	Outcome	Arm/Subgroup	n/N (%)	Effect Size	Reported P value
Procedural complication	Abdulazeez, 2020, 32820657, UK	NRCS	Procedural complication	Colonoscopy	0/120 (0%)	N/A	
Failed/ incomplete procedure	Abdulazeez, 2020, 32820657, UK	NRCS	Failed/incomplete procedure	Colonoscopy	5/120 (4.2%)	OR 1.70 (0.40, 7.26)*	NR
				Flexible sigmoidoscopy	3/120 (2.5%)		

Key Question 4c (Elective Surgery)

Table D-4c-3. KQ 4c. Adverse events

Study Year, PMID, Country, Funding	Design	Outcome	Arm/Subgroup	Arm/Subgroup Details	Age, Sex	n/N (%)	Effect Size	Reported P Value
Perez, 2020, 32748338, New York Statewide Planning and Research Cooperative System (SPARCS), US Not reported	Single group (Retrospective)	AE - Return to OR or unplanned procedure: Incisional hernia repair	Elective surgery	Open or laparoscopic sigmoid or left hemicolectomy	55.9 years 50.1% male	1 year: 129/6811 (1.9%) 3 year: 272/6811 (4.0%) 5 year: 334/6811 (4.9%)		
von Strauss und Torney, 2020, 32401298, Switzerland & UK Non-industry	Single group (Retrospective)	AE - 30 day mortality (post-surgical, CD V)	Elective surgery		NR	30/3511 (0.85)		
	Single group (Retrospective)	AE - Return to OR or unplanned procedure (CD III)	Elective surgery		NR	159/3511 (4.5)		

Appendix Table of Contents

Appendix A. Methods	A-1
Analytic Frameworks	A-1
Study Selection (Details)	A-3
Database Search Strategies	A-4
Inclusion/Exclusion Criteria Details	A-6
Data Extraction (Details)	A-12
Risk of Bias Assessment (Details)	A-12
Data Synthesis and Analysis (Details)	A-13
Overall Synthesis	A-13
Metrics	A-13
Meta-Analysis	A-14
Interpretation of Estimates	A-14
Grading the Strength of the Body of Evidence (Details)	A-14
Peer Review and Public Commentary	A-15
Glossary of Terms and Abbreviations	A-15
Terms	A-15
Abbreviations	A-16
References for Appendix A	A-17
Appendix B. Excluded Articles	B-1
Appendix C. Search Results; Study Design, Arm Details, Baselines, and Quality	C-1
Search Results	C-1
Included Studies	C-2
Key Question 1 (CT Imaging)	C-2
Key Question 2a (Outpatient)	C-2
Key Question 2b (Antibiotics)	C-2
Key Question 2c (Interventional Radiology)	C-4
Key Question 3 (Colonoscopy)	C-4
Key Questions 4a-b (Prevention, Nonsurgical)	C-5
Key Question 4c (Elective Surgery)	C-6
Study Design Details and Arms, Risk of Bias	C-8
Key Question 1 (CT Imaging)	C-8
Key Question 2a (Outpatient)	C-11
Key Question 2b (Antibiotics)	C-14
Key Question 2c (Interventional Radiology)	C-27
Key Question 3 (Colonoscopy)	C-29
Key Questions 4a-b (Prevention, Nonsurgical)	C-36
Key Question 4c (Elective Surgery)	C-40
Appendix D. Full Results Tables	D-1
Key Question 1a (CT Grading)	D-1
Key Questions 1b-d (CT Clinical Sequelae)	D-3

Key Question 2a (Outpatient)	D-5
Key Question 2b (Antibiotics)	D-8
Key Question 2c (Interventional Radiology)	D-16
Key Question 3 (Colonoscopy)	D-18
Meta-Analysis Figures	D-18
Data Tables	D-22
Key Questions 4a-b (Prevention, Nonsurgical)	D-44
Key Question 4c (Elective Surgery)	D-54

Figures and Tables

Table C-1-1. KQ 1. Description.....	C-8
Table C-1-2. KQ 1. Population and diagnostic descriptives.....	C-9
Table C-1-3. KQ 1. Quality	C-10
Table C-2a-1. KQ 2a Design Details and Arms	C-11
Table C-2a-2. KQ 2a Risk of Bias Assessment for Primary Studies – Randomized Controlled Trials (RCTs)	C-12
Table C-2a-3. KQ 2a Risk of Bias Assessment for Primary Studies – Nonrandomized Comparative Studies (NRCSSs) – Assessment of Confounding and Selection Bias	C-13
Table C-2b-1. KQ 2b Design Details.....	C-14
Table C-2b-2. KQ 2b Arm Details.....	C-18
Table C-2b-3. KQ 2b Baselines	C-22
Table C-2b-4. KQ 2b Risk of Bias Randomized Comparative Studies	C-25
Table C-2b-5. KQ 2b Risk of Bias Nonrandomized Comparative Studies	C-26
Table C-2c-1. KQ 2c Design and Arm Details	C-27
Table C-2c-2. KQ 2c Risk of Bias Assessment NRCSSs, Assessment of Confounding and Selection Bias.....	C-27
Table C-2c-3. KQ 2c Risk of Bias Assessment NRCSSs, Assessment of Remaining Biases and Quality	C-28
Table C-3-1. KQ3 Design Details.....	C-29
Table C-3-2. KQ 3 Arm Details.....	C-32
Table C-3-3. KQ3 Baselines	C-33
Table C-3-4. KQ 3 Risk of Bias.....	C-35
Table C-4ab-1. KQ 4ab Design Details and Arms	C-36
Table C-4ab-2. KQ 4ab Risk of Bias RCTs.....	C-39
Table C-4ab-3. KQ 4ab Risk of bias NRCSSs.....	C-39
Table C-4c-1. KQ 4c Design Details	C-40
Table C-4c-2. KQ 4c Arm Details	C-43
Table C-4c-3. KQ 4c Baselines	C-44
Table C-4c-4. KQ 4c Risk of Bias RCTs and NRCS	C-48
Table C-4c-5. KQ 4c Risk of Bias Single-Group Studies	C-49
Table D-1-1. Hansen and Stock Classification system*	D-2
Table D-1-2. Initial and final classification of patients in Jurowich 2011.....	D-2
Table D-1-3: KQ1 Results	D-3
Table D-2a-1: KQ2a Categorical Outcomes	D-5

Table D-2a-2: KQ 2a Continuous Outcomes.....	D-7
Table D-2b-1. Antibiotics: Mortality.....	D-8
Table D-2b-2. Antibiotics: Treatment Failure	D-8
Table D-2b-3. Antibiotics: Surgery for diverticulitis	D-9
Table D-2b-4. Antibiotics: Hospitalization or rehospitalization.....	D-10
Table D-2b-5 Antibiotics: Length of hospital stay	D-10
Table D-2b-6. Recurrence of diverticulitis	D-11
Table D-2b-7. Antibiotics: Diverticulitis-related morbidities	D-12
Table D-2b-8. Antibiotics: Pain or tenderness.....	D-13
Table D-2b-9. Antibiotics: Quality of life	D-14
Table D-2b-10 Antibiotics: Adverse events	D-15
Table D-2c-1. KQ 2c All Results.....	D-16
Table D-3-1 KQ 3 Categorical outcomes, colonoscopy versus no colonoscopy after acute diverticulitis	D-22
Table D-3-2 KQ 3 Categorical outcomes, colonoscopy after acute diverticulitis versus general screening (no diverticulitis)	D-23
Table D-3-3 KQ 3 Categorical outcomes, single group studies	D-30
Table D-3-4 KQ 3 Categorical outcomes, Subgroup Analysis: Age ≥ 50 vs. Age < 50	D-38
Table D-3-5 KQ 3 Subgroup Analysis: Complicated vs. Uncomplicated Diverticulitis.....	D-39
Table D-3-6 KQ 3 Categorical outcomes, Subgroup Analysis: Others	D-42
Table D-3-7 KQ 3, Colonoscopy Tolerance, Feasibility, and Completion of Procedure; Technical Adequacy.....	D-43
Table D-4ab-1: KQ 4ab Categorical Outcomes.....	D-44
Table D-4ab-2: KQ 4ab Continuous Outcomes.....	D-49
Table D-4ab-3: KQ 4ab Adverse Events	D-50
Table D-4c-1. KQ 4c Treatment Comparisons, Categorical Outcomes	D-54
Table D-4c-2. KQ 4c Treatment Comparisons, Continuous Outcomes	D-56
Table D-4c-3. KQ 4c Adverse Events	D-60

Figure A-1. Analytic Framework for Key Question 1: Computed tomography for acute diverticulitis.	A-1
Figure A-2. Analytic Framework for Key Question 2: Treatment options for acute diverticulitis.	A-1
Figure A-3. Analytic Framework for Key Question 3: Screening for colorectal cancer.....	A-2
Figure A-4. Analytic Framework for Key Question 4: Treatments to prevent recurrent diverticulitis.	A-2

Figure C-1. Literature flow diagram.....	C-1
--	-----

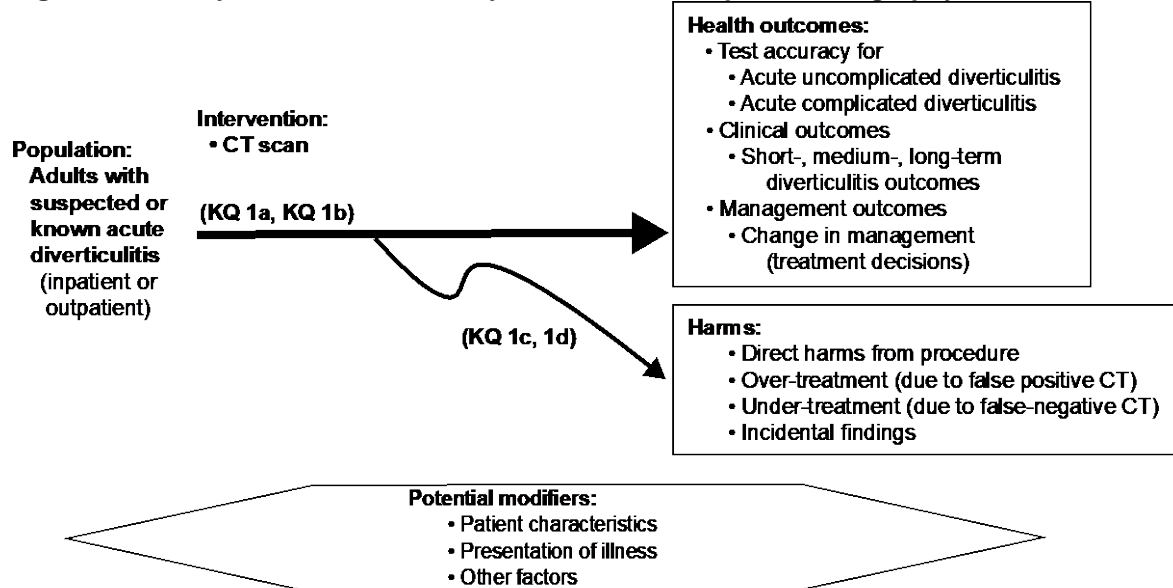
Figure D-KQ3-1. Meta-analysis of colonoscopy after diverticulitis: Percent with colorectal cancer	D-18
Figure D-KQ3-2. Meta-analysis of colonoscopy after diverticulitis: Percent with advanced colonic neoplasia.....	D-18
Figure D-KQ3-3. Meta-analysis of colonoscopy after diverticulitis: Percent with advanced adenoma	D-19

Figure D-KQ3-4. Meta-analysis of colonoscopy after diverticulitis: Percent with adenomas with high-grade dysplasia	D-19
Figure D-KQ3-5. Meta-analysis of colonoscopy after diverticulitis: Percent with adenoma ≥ 10 mm	D-20
Figure D-KQ3-6. Meta-analysis of older (≥ 50 years) versus younger adults with acute diverticulitis: Colorectal cancer	D-20
Figure D-KQ3-7. Meta-analysis of complicated versus uncomplicated acute diverticulitis: Colorectal cancer	D-20
Figure D-KQ3-8. Meta-analysis of complicated versus uncomplicated acute diverticulitis: Advanced colonic neoplasia	D-21
Figure D-KQ3-9. Meta-analysis of complicated versus uncomplicated acute diverticulitis: Advanced adenoma	D-21

Appendix A. Methods

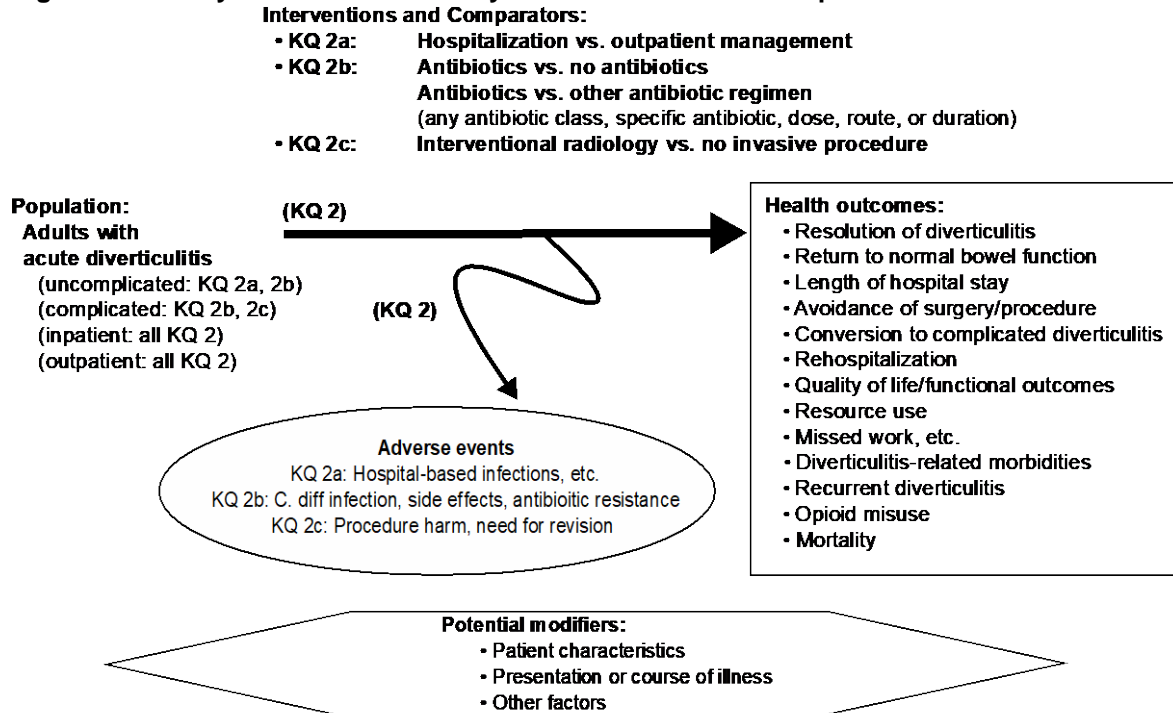
Analytic Frameworks

Figure A-1. Analytic framework for Key Question 1: Computed tomography for acute diverticulitis



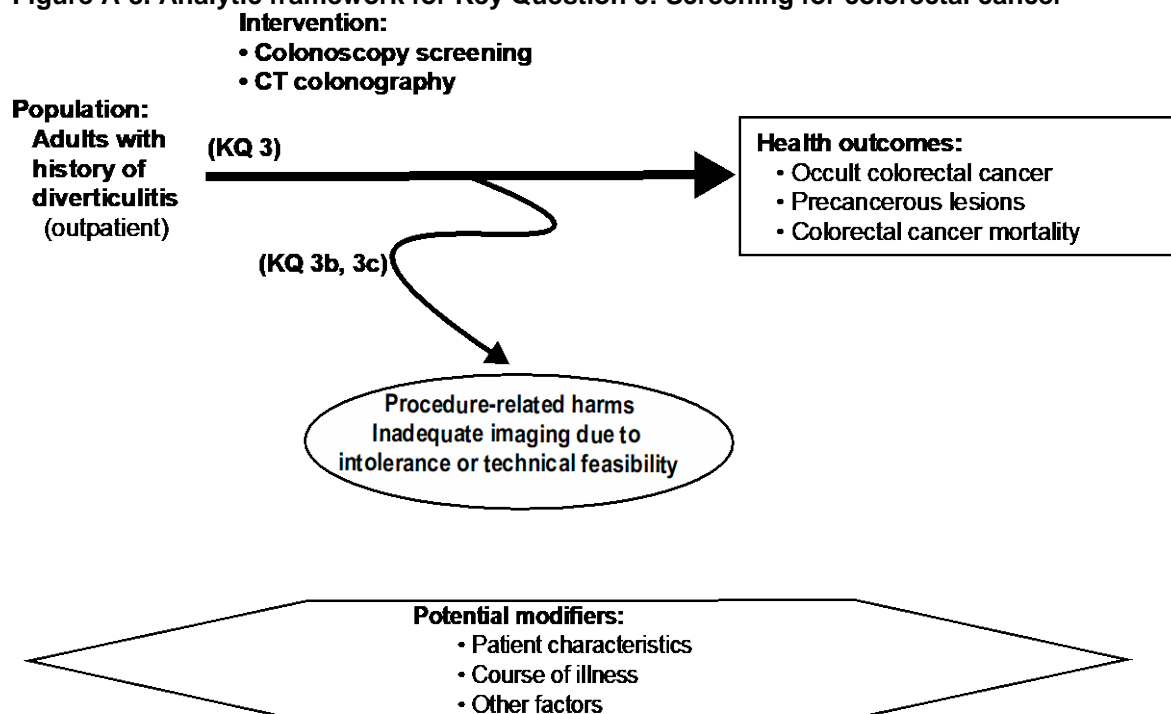
Abbreviations: CT = computed tomography, KQ = Key Question, MRI = magnetic resonance imaging.

Figure A-2. Analytic framework for Key Question 2: Treatment options for acute diverticulitis



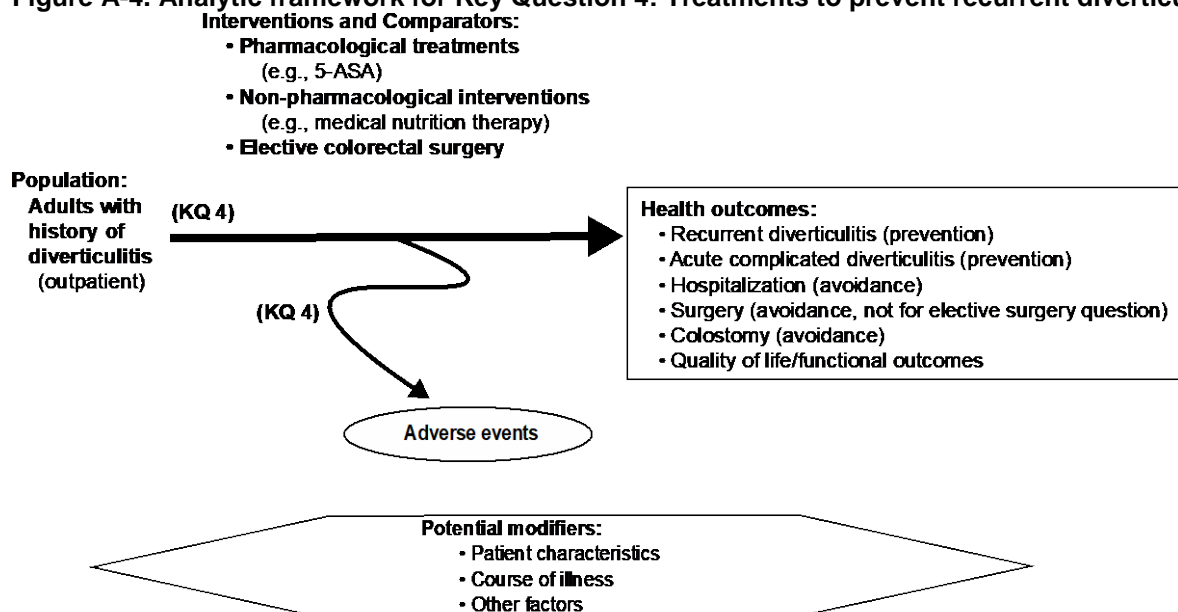
Abbreviations: C. diff = Clostridioides difficile, KQ = Key Question.

Figure A-3. Analytic framework for Key Question 3: Screening for colorectal cancer



Abbreviations: CT = computed tomography, KQ = Key Question.

Figure A-4. Analytic framework for Key Question 4: Treatments to prevent recurrent diverticulitis



Abbreviations: 5-ASA = 5-aminosalicylic acid (also known as mesalamine or mesalazine), KQ = Key Question.

Study Selection (Details)

We searched for studies and existing systematic reviews in MEDLINE (via PubMed), the Cochrane Register of Clinical Trials, the Cochrane Database of Systematic Reviews, Embase, and CINAHL. Separate, overlapping searches were conducted for each Key Question, then combined. As part of methods project, an independent search was undertaken, which used text-mining software to identify additional relevant keywords and MeSH search terms. This search was also independently peer reviewed. Duplicate citations were removed prior to screening. Searches were restricted to 1990 or later, with no language restriction. (The date restriction was included after discussion with the Key Informants based on important changes in diagnosis and clinical management of diverticulitis based on increased use of computed tomography [CT] imaging.) Search strategies included filters to remove nonhuman studies and articles that were not primary studies, systematic reviews, or clinical practice guidelines.

The searches included MeSH or Emtree terms, along with free-text words, related to diverticulitis, diverticulosis, and diverticular disease (since we have found that numerous articles misname or misclassify diverticulitis as diverticulosis); CT imaging; hospitalization, antibiotics, and interventional radiology for acute diverticulitis; colonoscopy and colonography; treatments to prevent recurrence and elective surgery. We also searched for CT imaging and acute abdomen (regardless of diverticular disease). Searches were independently peer reviewed.

Searches were also conducted in the ClinicalTrials.gov registry for unpublished study protocols, unpublished study results, and ongoing studies. The reference lists of relevant existing systematic reviews were screened for additional eligible studies. A Supplemental Evidence And Data for Systematic review (SEADS) portal was available for this review. Additional articles suggested to us from any source, including peer and public review, were screened applying identical eligibility criteria. Non-English language articles were screened and data extracted either by readers of the relevant languages or after translation via Google Translate (<https://translate.google.com/>).

Citations from all electronic databases were entered into Abstrackr software (<http://abstrackr.cebm.brown.edu/>) to enable abstract screening. We compared the search results with the results of our screening from the topic refinement phase (during protocol development). We then prepopulated the software with 753 citations with appropriate labels (accept or reject). The team conducted three rounds of pilot screening, during which each member of the team screen the same 100 abstracts, after which we discussed conflicts, with the goals of training the team in the nuances of the eligibility criteria and refining them as needed. Thereafter, we screened remaining abstracts in duplicate. The Abstrackr software has machine learning capabilities that predict the likelihood of relevance of each citation. Nightly, the list of unscreened abstracts were sorted so that most potentially-relevant articles are presented first the next day. After the software suggested that no remaining unscreened abstracts were likely to be relevant (when the predictor value was <0.40), we single screened an additional 2000 abstracts, none of which were accepted. We then single screened all remaining abstracts. In total 2816 citations were double screened and the remaining 11,233 were single screened (without any accepts). Of note, the number of citations that required double screening was relatively small compared to most projects. This was due to our ability to prepopulate the corpus with the 753 known accepts and rejects.

Potentially relevant citations were retrieved in full text. These articles were entered into an evidence map which captured study design, sample size, start year of study, and which Key

Question the study is relevant to. Rejection reasons were captured at this stage. All decisions to include or reject an article were confirmed by at least one additional senior researcher.

Database Search Strategies

PubMed 1946 to June 1, 2020

Key question 1: CT diagnosis

("Diverticulitis"[Mesh] OR "Diverticulosis, Colonic"[Mesh] OR diverticulitis [tiab] OR diverticulosis [tiab] OR diverticular [tiab] OR "Abdomen, Acute"[Mesh] OR "acute abdomen" OR ((acute or nonspecific OR non-specific OR emergen*) AND (abdome* OR abdomi*) AND pain) OR peritonitis)

AND

("Tomography, X-Ray Computed"[Mesh] OR CT scan OR "cat scan" OR tomography OR "low dose CT" OR LDCT OR "Spiral CT")

Key question 2: Treatment of acute diverticulitis

("Diverticulitis"[Mesh] OR "Diverticulosis, Colonic"[Mesh] OR diverticulitis [tiab] OR diverticulosis [tiab] OR diverticular [tiab])

AND

(Hospital OR hospitals OR hospitalization OR "Hospitalization"[Mesh] OR Inpatient* OR discharge* OR outpatient OR "Ambulatory Care"[Mesh] OR antibiotic* OR "Anti-Bacterial Agents"[Mesh] OR medication* OR medical OR "Radiology, Interventional"[Mesh] OR interventional radiology)

Key question 3: Interval colonoscopy

("Diverticulitis"[Mesh] OR "Diverticulosis, Colonic"[Mesh] OR diverticulitis [tiab] OR diverticulosis [tiab] OR diverticular [tiab])

AND

(Colonoscopy OR Colonography OR "Colonography, Computed Tomographic"[Mesh] OR "Colonoscopy"[Mesh] OR ((colon OR colorectal) AND (cancer or carcinoma or neoplasm*) AND screen*) OR ((colon OR colorectal) AND "Early Detection of Cancer"[Mesh]) OR ("Colonic Neoplasms"[Mesh] AND screen*))

Key question 4: Prevention of recurrence

("Diverticulitis"[Mesh] OR "Diverticulosis, Colonic"[Mesh] OR "Diverticulosis, Small Intestinal" [Supplementary Concept] OR diverticulitis[tiab] OR diverticulosis[tiab] OR diverticular[tiab])

AND

(Recur* OR repet* OR repeat OR attacks OR "Elective Surgical Procedures"[Mesh] OR Mesalazine OR Mesalamine OR "Mesalamine"[Mesh] OR 5-ASA OR "5 ASA" OR Aminosalicic Acid OR Pentacol OR "Diet Therapy"[Mesh] OR diet OR fiber OR fibre OR rifaximin OR "Probiotics"[Mesh] OR probiotic* OR balsalazide OR VSL#3 OR Lactobacillus casei OR ((surger* OR surgic* OR resect* OR operation OR operate) and elective))

Searches combined with OR

NOT

("addresses"[pt] or "autobiography"[pt] or "bibliography"[pt] or "biography"[pt] or "case reports"[pt] or "comment"[pt] or "congresses"[pt] or "dictionary"[pt] or "directory"[pt] or "festschrift"[pt] or "government publications"[pt] or "historical article"[pt] or "interview"[pt] or "lectures"[pt] or "legal cases"[pt] or "legislation"[pt] or "news"[pt] or "newspaper article"[pt] or "patient education handout"[pt] or "periodical index"[pt] or "comment on" or ("Animals"[Mesh] NOT "Humans"[Mesh]) OR rats[tw] or cow[tw] or cows[tw] or chicken*[tw] or horse[tw] or horses[tw] or mice[tw] or mouse[tw] or bovine[tw] or sheep or ovine or murinae)

Embase 1947 to June 1, 2020

#30 (#6 OR #28) AND ([article]/lim OR [article in press]/lim)

#29 #6 OR #28

#28 #8 AND #27

#27 #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26

#26 'elective surgery'/de

#25 'lactobacillus casei'/de

#24 'balsalazide'/de

#23 'probiotic agent'/de

#22 'rifaximin'/de

#21 'fiber'/de

#20 'diet therapy'/de

#19 'aminosalicylic acid'/de

#18 'mesalazine'/de

#17 'colonography'/de

#16 'colonoscopy'/de

#15 'interventional radiology'/de

#14 'drug therapy'/de

#13 'antibiotic agent'/de

#12 'ambulatory care'/de

#11 'outpatient'/de

#10 'hospital patient'/de

#9 'hospitalization'/de

#8 #1 OR #2 Diverticulitis

#7 #4 AND #5 AND ([article]/lim OR [article in press]/lim)

#6 #4 AND #5

#5 #1 OR #2 OR #3

#4 'computer assisted tomography'/de

#3 'acute abdomen'/de

#2 'diverticulosis'/de

#1 'diverticulitis'/de

Cochrane to June 1, 2020

((Diverticulitis OR diverticulosis OR diverticular OR “acute abdomen” OR ((acute or nonspecific OR non-specific OR emergen*) AND (abdome* OR abdomi*) AND pain) OR peritonitis)

AND

(“CT scan” OR “cat scan” OR tomography)) OR (Diverticulitis OR diverticulosis OR diverticular)

CINAHL 1961 to June 1, 2020

((Diverticulitis OR diverticulosis OR diverticular OR “acute abdomen” OR ((acute or nonspecific OR non-specific OR emergen*) AND (abdome* OR abdomi*) AND pain) OR peritonitis) AND (“CT scan” OR “cat scan” OR tomography))

OR

(Diverticulitis OR diverticulosis OR diverticular)

Inclusion/Exclusion Criteria Details

Study Eligibility Criteria for KQ 1 (CT Imaging)

Population(s):

- KQ 1 (all): Adults with suspected or known diagnosis of acute colonic diverticulitis
 - Suspected diagnosis for diagnosis of acute diverticulitis
 - Known diagnosis for staging of disease
 - Exclude: Non-colonic diverticulitis (except for KQ 1d)
- KQ 1d: Adults with acute abdominal pain who receive an abdominal CT

Intervention:

- CT (computed tomography) scan
 - With or without IV (intravenous), oral, or rectal contrast

Comparators:

- No CT scanning (as an explicit comparator)
- MRI (magnetic resonance imaging)
- Ultrasonography
- Other diagnostic interventions
- No comparator (single group studies)

Outcomes:

- KQ 1a: Diagnostic accuracy (from existing systematic reviews only)
 - Acute diverticulitis vs. other condition
 - Complicated vs. uncomplicated diverticulitis
 - For staging of severity
- KQ 1b: Clinical outcomes
 - Short-term (≤ 1 month)
 - Time to resolution of acute diverticulitis
 - Length of hospital stay
 - Conversion to complicated diverticulitis
 - Diverticulitis-related morbidities (e.g., abscess formation) and mortality
 - Change in management (treatment decisions)

- Medium- (>1 to <12 mo) to long-term (≥ 1 year)
 - Recurrent diverticulitis
 - Future episode of complicated diverticulitis
 - Diverticulitis-related morbidities (e.g., strictures) and mortality
- KQ 1c: Harms
 - Harms of over-treatment (due to false positive findings; e.g., surgery, stress)
 - Harms of under-treatment (due to false negative findings; e.g., peritonitis, unnecessary surgery for other condition)
- KQ 1d: Incidental findings
 - Sequelae related to incidental findings (e.g., unnecessary liver biopsy)

Modifiers/Subgroups of interest

- Patient characteristics (e.g., prior history of diverticulitis, age)
- Presentation of illness (e.g., specific signs or symptoms, such as large volume ascites)
- Other factors (e.g., complicated or uncomplicated diverticulitis, hospital setting)

Timing

- Any

Setting

- Inpatient, emergency department (or equivalent), outpatient

Design

- KQ 1a: For test accuracy:
 - Existing systematic reviews
- KQ 1b, 1c, 1d: For clinical outcomes and harms:
 - Prospective
 - Retrospective only if unbiased sampling (inclusion criteria based on pre-imaging criteria only)
 - $N \geq 100$ receiving CT
 - Publication since 1990

Study Eligibility Criteria for KQ 2 (Treatment of Acute Diverticulitis)

Population(s):

- Adults with acute complicated or uncomplicated diverticulitis, whether first or recurrent episode
 - KQ 2a: Intervention = hospitalization: uncomplicated diverticulitis
 - KQ 2b: Intervention = antibiotics: uncomplicated or complicated diverticulitis
 - KQ 2c: Intervention = interventional radiology: complicated diverticulitis (e.g., abscess)
- Exclude: Complicated diverticulosis, without diverticulitis (e.g., hemorrhagic diverticulosis)
- Exclude: Symptomatic uncomplicated diverticular disease (SUDD)
- Exclude: Meckel's diverticula (unless concurrent acute diverticulitis)
- Exclude: Non-colonic diverticulitis

Interventions versus Comparators:

- Hospitalization versus No hospitalization (for patients not requiring surgery)

- Antibiotics versus No antibiotics or versus Alternative antibiotic regimen (for any patient)
 - Any class, route, treatment duration, or initiation time, and comparisons among these
 - Use of any antibiotics (e.g., at clinician's discretion) or specific antibiotics
- Interventional radiology procedure versus No procedure (conservative management; for patients with complicated diverticulitis for whom no procedure is an option)
 - Any interventional radiology procedure appropriate for the severity and type of complication
 - Exclude: Comparison of intervention radiology procedures or techniques

Outcomes:

- Short-term (≤ 30 days)
 - Resolution of diverticulitis
 - Return to normal bowel function
 - Length of hospital (or intensive care unit) stay
- Short- and medium-term (< 1 year)
 - Interventional radiology procedure for diverticulitis (avoidance) (exclude for comparisons of interventional radiology procedure with conservative management)
- Medium- to long term (> 1 month)
 - Recurrent diverticulitis
 - Opioid misuse
- Any duration (short-, medium-, or long-term)
 - Conversion to complicated diverticulitis
 - Surgery for diverticulitis (avoidance)
 - Including colostomy (avoidance)
 - Rehospitalization for diverticulitis or complications
 - Quality of life/Functional outcomes
 - Resource use
 - Missed work, employment, school outcomes, etc.
 - Diverticulitis-related morbidities
 - Mortality, both diverticulitis-related and all-cause
- All categorical "effectiveness" outcomes include time to outcome
- Harms, adverse events, side effects of interventions (any time frame)
 - Hospitalization comparison:
 - Hospital-based infections and other harms
 - Antibiotics comparisons:
 - Side effects/adverse events attributable to antibiotics
 - Clostridioides difficile (C diff) infection
 - Antibiotic resistance
 - Interventional radiology comparisons:
 - Adverse events related to procedures, including bleeding and catheter infections
 - Need for second procedures or revisions

Modifiers/Subgroups of interest:

- Patient characteristics (e.g., prior history of diverticulitis, age)
- Presentation or course of illness (e.g., specific symptoms)
- Other factors (e.g., complicated or uncomplicated diverticulitis, hospital setting)

Timing:

- Minimum duration of follow-up = treatment duration (hospitalization, antibiotic use)

Setting:

- Inpatient, emergency department (or equivalent), outpatient

Design:

- Randomized controlled trials (all subquestions)
 - $N \geq 10$ /arm
- Nonrandomized comparative studies
 - Antibiotics (all outcomes) or hospitalization and IR comparisons (short- to medium-term outcomes; < 1 year)
 - Restrict to studies that use modeling or other analytic methods to minimize selection bias (due to inherent differences between people who receive one or the other intervention), or that restrict study eligibility criteria such that comparisons being made are between patients with similar presentations.
 - Long-term outcomes, hospitalization and IR comparisons (long-term outcomes; ≥ 1 year)
 - Allow crude comparisons of long-term outcomes under the assumption that characteristics during acute diverticulitis that were associated with treatment decision (e.g., older patients being more likely to be hospitalized) would not have a major impact on long-term outcomes.
 - Hospitalization and antibiotics: $N \geq 30$ /arm; Interventional radiology $N \geq 10$ /arm
- Single group studies
 - Only for adverse events
 - $N > 100$
- Longitudinal (Exclude: cross-sectional)
- Prospective or retrospective
- Publication since 1990
- Exclude: Case reports (and series of case reports)

Study Eligibility Criteria for KQ 3 (Colonoscopy)**Population(s)**

- Adults with history of (resolved) acute diverticulitis
- Exclude: Active diverticulitis
- Exclude: History of related condition (only), e.g., complicated diverticulosis, SUDD
- Exclude: Meckel's diverticula (unless concurrent acute diverticulitis)
- Exclude: Non-colonic diverticulitis

Interventions:

- Elective colonoscopy (full colon)
- Elective CT colonography

Comparators:

- No colon cancer screening
- Flexible sigmoidoscopy and barium enema
- Limited colonoscopy (e.g., left-sided)
- Virtual colonoscopy
- Stool guaiac testing (etc.)
- Other colon cancer screens (e.g., DNA tests)
- Different intervals, Different initial colonoscopy timing after acute episode
- No comparator

Outcomes:

- Colorectal cancer death
- Colorectal cancer
- High-risk colonic premalignant lesions
 - Adenoma, high grade dysplasia
 - Adenoma ≥ 10 mm
 - Adenoma, villous
 - Serrated polyp
- Tolerance, feasibility, and completion of procedure; technical adequacy
- Harms, adverse events, and side effects of colonoscopy (e.g. perforation, bleeding)

Modifiers/Subgroups of interest:

- Patient characteristics (e.g., age, family history)
- Course of illness (e.g., prior complicated vs. uncomplicated diverticulitis)
- Alarm symptoms
- Other factors (e.g., timing since last episode of acute diverticulitis)

Timing:

- Start of colorectal cancer screening after resolution of acute disease

Setting:

- Outpatient

Design:

- Randomized controlled trials
 - $N \geq 10$ /arm
- Nonrandomized comparative studies
 - No restriction based on analytic methods
 - Including comparisons with healthy (non-diverticulitis) people
 - $N \geq 200$ (total)
- Single group studies
 - $N \geq 200$ (receiving colonoscopy or CT colonography)
- Case-control studies
 - Including comparisons with healthy (non-diverticulitis) people
 - $N \geq 100$ /arm
- Prospective or retrospective
- Publication since 1990
- Exclude: Case reports (and series of case reports)

Study Eligibility Criteria for KQ 4 (Prevention of Recurrence)

Population(s):

- Adults with history of (resolved) acute diverticulitis
- Exclude: Ongoing acute diverticulitis
- Exclude: History of related condition (only), e.g., complicated diverticulosis, SUDD
- Exclude: Meckel's diverticula (unless concurrent acute diverticulitis)
- Exclude: Non-colonic diverticulitis

Interventions:

- Pharmacological treatments
 - Any class, route, regimen, treatment duration, or initiation time
- Non-pharmacological interventions
 - Any class/type, route/method, regimen, treatment duration, or initiation time
- Elective surgery
 - Laparoscopic, open, robot-assisted, or any other type of colon surgery conducted as an elective (non-emergent) procedure
- Exclude: Natural history or undefined/unspecified intervention or undefined/unspecified comparator

Comparators:

- Pharmacological and non-pharmacological intervention comparisons:
 - Alternative pharmacologic or non-pharmacologic intervention (or regimen)
 - Pharmacologic vs. non-pharmacologic intervention
 - Other class/type
 - Other intervention within class/type
 - Same intervention different treatment duration
 - Same intervention, different initiation time
 - No intervention
 - Placebo
 - "Usual care" (needs to be defined)
- Elective surgery comparisons:
 - No or deferred elective surgery
 - Exclude: Comparisons with other surgical approaches or techniques
- All:
 - Exclude: Natural history or undefined/unspecified intervention or comparator

Outcomes:

- Recurrent diverticulitis
- Acute complicated diverticulitis
- Surgery for diverticulitis (avoidance; except for elective surgery comparisons)
 - Including colostomy (avoidance)
- Hospitalization for diverticulitis or diverticulitis-related complications (e.g., fistula, stricture)
- Quality of life/Functional outcomes
- All categorical "effectiveness" outcomes include time to outcome
- Harms, adverse events, or side effects of interventions (e.g., surgical complications)
 - From single-group studies of elective surgery, only serious, major, or clinically important adverse events/complications

Modifiers/Subgroups of interest:

- Patient characteristics (e.g., age)
- Course of illness (e.g., prior complicated vs. uncomplicated diverticulitis)
- Other factors (e.g., time since last episode of diverticulitis)

Timing:

- No minimum duration of follow-up
- Hospitalization, unit stay, post-hospitalization

Setting:

- Inpatient, emergency department (or equivalent), outpatient

Design:

- Randomized controlled trials
 - $N \geq 10/\text{arm}$
- Nonrandomized comparative studies
 - Restrict to studies that use modeling or other analytic methods to minimize selection bias (due to inherent differences between people who receive one or the other intervention)
 - $N \geq 30/\text{arm}$
- Single group studies
 - Only for adverse events
 - Elective surgery
 - $N \geq 500$
 - Other interventions
 - $N \geq 100$
- Longitudinal (Exclude: cross-sectional)
- Prospective or retrospective
- Publication since 1990
- Exclude: Case reports (and series of case reports)

Data Extraction (Details)

For KQ 2 to 4, data were extracted directly into the Systematic Review Data Repository (SRDR) at <https://srdhr.ahrq.gov/>. For KQ 1, data were extracted directly into summary tables, which will be uploaded into SRDR. We created a combined data extraction form for KQ 2 and 4 (on treatments) and, separately a form for KQ 3 (on colonoscopy). We extracted information on study characteristics, eligibility criteria, participant characteristics, intervention and comparator details, outcome definitions, and results (including event numbers, effect sizes, and P values). Study- and outcome-level risk of bias assessment was conducted during data extraction within SRDR.

Risk of Bias Assessment (Details)

We evaluated each study for risk of bias and methodological quality. Because we included a variety of study designs, we incorporated items from three different existing commonly-used tools and tailored the set of items for each study design. The three tools were the Cochrane Risk of Bias Tool,¹ the Risk of Bias in Nonrandomized Studies (ROBINS-I) Tool,² and the National Heart, Lung, and Blood Institute (NHLBI) Quality Assessment Tool.³

For RCTs, we used all the items from the Cochrane Risk of Bias Tool,¹ focusing on issues related to randomization and allocation concealment methodology; blinding of patients, study personnel/care providers, objective outcome assessors, and subjective outcome assessors; incomplete outcome data; selective outcome reporting; and other issues that could be related to bias. We also used items from the NHLBI Tool focusing on the adequacy of descriptions of study eligibility criteria, interventions, and outcomes.³

For NRCSs, we used specific sections of the ROBINS-I Tool² that pertain to confounding and selection bias. ROBINS-I requires the identification of specific confounders of interest for the SR. For the purpose of assessing for the presence of potential confounding in studies, we considered age, severity of headache (or history of headache), and frequency of headache (or history of headache). Because NRCSs, like RCTs, can be impacted by the lack of blinding and by participant loss to followup, we also used the items from the Cochrane Risk of Bias Tool¹ that focus on issues related to blinding of patients, study personnel/care providers, objective outcome assessors, and subjective outcome assessors; incomplete outcome data; selective outcome reporting; and other issues that could be related to bias. We also used items from the NHLBI Tool that pertain to the adequacy of descriptions of study eligibility criteria, interventions, and outcomes.³

For single-group studies, we used the items from the Cochrane Risk of Bias Tool¹ that pertain to issues of participant loss to followup, specifically, incomplete outcome data, selective outcome reporting, and other issues that could be related bias. We also used items from the NHLBI Tool focusing on the adequacy of descriptions of study eligibility criteria, interventions, and outcomes.³

Data Synthesis and Analysis (Details)

Overall Synthesis

We summarized the evidence both qualitatively and quantitatively. For each set of studies, we provide summary descriptions of their design, characteristics, and included participants. We focus, as pertinent, on demographics and descriptions of participants' course of diverticulitis such as complications. We also summarize the risk of bias or methodological concerns for each set of studies. With rare exceptions, we do not narratively describe each study.

Within the main report we summarize findings either in high-level summary tables that focus on the intervention, sample size, outcome, and results. Further details are included in Appendixes C and D.

Metrics

As pertinent, we calculated event (or findings) rates (i.e., the percentage of participants with the outcome), the odds ratio (OR), or differences between groups. For continuous outcomes other than quality of life (QoL) or related functional outcomes, we estimated mean differences between groups or net mean differences (difference-in-differences) between groups based on reported data. When multivariable metrics (e.g., OR) were reported, we preferentially used those over the unadjusted (crude) metrics.

Notably, with few exceptions (that are called out), from nonrandomized comparative studies (NRCS) we summarized (included) only outcomes for which there were multivariable analyses (or equivalent, such as from matched studies). Since we excluded NRCSs that reported only

unadjusted comparisons between inherently different groups, we similarly excluded unadjusted comparisons from articles that reported other multivariable adjusted analyses.

Meta-Analysis

Per protocol, we considered the possibility of conducting network meta-analysis but determined that the evidence base does not contain sufficient data to allow meaningful network meta-analyses for any KQ.

Except as noted below, we conducted meta-analyses when at least three studies (or study groups) were sufficiently similar and reported the same outcome.

For KQ 1 (CT imaging), we drew a summary receiver operating characteristics (ROC) curve for the studies included in the eligible existing systematic reviews. We used the *metandi* program in Stata 15.1, which conducts a bivariate normal model.

For KQ 2b (antibiotics) and KQ 4a (pharmacologic) we conducted restricted maximum likelihood (REML) model meta-analyses of the OR for outcomes. We used the *metaan* program in Stata 15.1.

For KQ 3 (colonoscopy), we conducted REML meta-analyses of ORs for comparisons between groups (either study groups or subgroups). In one instance, with very rare events across studies, we estimated the summary Peto OR, also in *metaan*. To combine estimates of proportions, we used the Freeman-Tukey double arcsine transformation to overcome the nonnormal distribution of proportion estimates (because values are truncated at 0). Proportions were converted to percentages. For this, we used the *metaprop* program in Stata 15.1.

For KQ 4c (elective surgery), we meta-analyzed all included adverse events, regardless of the clinical heterogeneity between studies (or groups). As an example, we meta-analyzed adverse events from studies that evaluated different types of elective surgery. In addition, we ran meta-analyses of only two studies. The proportions (adverse event rates) were again meta-analyzed with the Freeman-Tukey double arcsine transformation.

Interpretation of Estimates

In determining conclusions based on the estimates, both for individual studies and from meta-analyses, we interpreted estimates based on their precision. While we do not universally highlight statistical significance, we note when conclusions (e.g., evidence of an association) are based on estimates that are not statistically significant. We labeled OR estimates with 95 percent confidence intervals that extend beyond both 0.5 and 2.0 (or close to that) as imprecise. Regardless of the magnitude of the estimate, we do not suggest directionality or effect when the confidence is imprecise.

Grading the Strength of the Body of Evidence (Details)

We evaluated the strength of evidence (SoE) addressing each major conclusion for each KQ (and subquestion). We graded the SoE as per the Agency for Healthcare Research and Quality (AHRQ) Methods Guide.^{4,5}

For each SoE assessment, we considered the number of studies, the study limitations (i.e., risk of bias and overall methodological quality), the directness of the evidence to the KQs, the consistency of study results, the precision of any estimates of effect, the likelihood of reporting bias, other limitations, and the overall findings across studies. Based on these assessments, we assigned a SoE rating as being either high, moderate, low, or insufficient to estimate an effect.

For conclusions that are based on ORs, we deemed the evidence to be imprecise if the nonsignificant lower confidence interval is <0.8 (for estimates >1) or upper confidence interval is >1.25 (for estimates <1).

Outcomes with highly imprecise estimates, highly inconsistent findings across studies, or with data from only one study were deemed to have insufficient evidence to allow a conclusion. In this instance, we defined highly imprecise as above, for individual studies, when the OR's 95 percent confidence intervals extends beyond both 0.5 and 2.0. This overall approach is consistent with the concept that for imprecise evidence "any estimate of effect is very uncertain," the definition of Very Low quality evidence per GRADE.⁶

Peer Review and Public Commentary

A preliminary draft version of this report was reviewed from March 17 to April 14, 2020 by invited reviewers, an AHRQ Associate Editor, and AHRQ personnel. A revised version was provided for a public review process from June 2 to 30, 2020. Revisions to the drafts were made to address reviewer comments. The findings and conclusions are those of the authors, who are responsible for the contents of the report.

Glossary of Terms and Abbreviations

Terms

Acute colonic diverticulitis	An acute bout of inflammation of diverticula in the colon. Usually associated with lower abdominal pain, fever, and gastrointestinal symptoms.
Clavien Dindo classification	Rating system of the severity of postoperative harms or complications. Briefly, <ul style="list-style-type: none"> I No treatment required (e.g., small wound infection) II Pharmacologic treatment required, including blood transfusion III Procedure required (e.g., return to operating room) IV Life-threatening, involving one or more organs V Death
Complicated diverticulitis	Acute diverticulitis with complications. Complications are mostly caused by perforations to the diverticula. Complications include abscesses, peritonitis, fistulas, and strictures.
Hinchey classification	A schema that has been modified several times to classify the severity of diverticulitis and complications. Briefly, <ul style="list-style-type: none"> 0 mild clinical diverticulitis 1a confined inflammation without obvious abscess 1b small confined abscess II distant or large abscesses III generalized purulent peritonitis IV fecal peritonitis (free fecal material in the peritoneum)
Meta-analysis	Statistical method to quantitative combine study results

Strength of evidence

Structured, qualitative method to assess the body of evidence pertaining to each specific conclusion. Rated as high, moderate, and low, or insufficient.

Abbreviations

5-ASA	5-aminosalicylic acid, mesalamine
ACP	American College of Physicians
AGA	American Gastroenterology Association
AHRQ	Agency for Healthcare Research and Quality
CD	Clavien Dindo classification
CHF	congestive heart failure
CI	confidence interval (about an estimate)
COPD	chronic obstructive pulmonary disease
CRC	colorectal cancer
CRP	C-reactive protein
CT	computed tomography imaging test
ED-5D	EuroQoL 5 dimensions scale of quality of life and function
EHC	Effective Health Care (program)
GIQLI	Gastrointestinal Quality of Life Index
H&S	Hansen & Stock classification system (to grade severity)
I ²	a measure of statistical heterogeneity; the percentage of the differences in study results across studies <i>not</i> attributable to random chance
IPD MA	individual-patient data meta-analysis
IV	intravenous
KQ	Key Question
NRCS	nonrandomized comparative study
OR	odds ratio
Peto OR	an approximation of the summary OR estimated when events are rare in one or both study groups
RCT	randomized controlled trial
ROBINS-I	Risk of Bias in Nonrandomized Studies of Interventions
ROC	receiver operator characteristics (curve)
SF-12/36	Short Form 12/36 question quality of life scale
SoE	strength of evidence
SR	systematic review
TEP	Technical Expert Panel
TIQ	Therapy Impact Questionnaire, a measure of physical function
USPSTF	US Preventive Services Task Force
VAS	visual analog scale (pain severity scale)
WBC	white blood cell

References for Appendix A

1. Higgins JP, Altman DG, Gotzsche PC, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ* (Clinical research ed). 2011 Oct 18;343:d5928. doi: 10.1136/bmj.d5928. PMID: 22008217.
2. Sterne JA, Hernan MA, Reeves BC, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ* (Clinical research ed). 2016 Oct 12;355:i4919. doi: 10.1136/bmj.i4919. PMID: 27733354.
3. National Heart, Lung, and Blood Institute. Study Quality Assessment Tools.; 2019. <https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools>. Accessed on January 23, 2020.
4. Berkman ND, Lohr KN, Ansari M, et al. AHRQ Methods for Effective Health Care Grading the Strength of a Body of Evidence When Assessing Health Care Interventions for the Effective Health Care Program of the Agency for Healthcare Research and Quality: An Update. *Methods Guide for Effectiveness and Comparative Effectiveness Reviews*. Rockville (MD): Agency for Healthcare Research and Quality (US); 2008.
5. Berkman ND, Lohr KN, Ansari MT, et al. Grading the strength of a body of evidence when assessing health care interventions: an EPC update. *Journal of clinical epidemiology*. 2015 Nov;68(11):1312-24. doi: 10.1016/j.jclinepi.2014.11.023. PMID: 25721570.
6. Guyatt GH, Oxman AD, Kunz R, et al. Going from evidence to recommendations. *BMJ* (Clinical research ed). 2008 May 10;336(7652):1049-51. doi: 10.1136/bmj.39493.646875.AE. PMID: 18467413.

Appendix B. Excluded Articles

[Anonymous]. Laparoscopic washout versus radiological drainage in patients with Hinchey grade III acute diverticulitis: pragmatic data from a national prospective cohort study. Colorectal disease. *Not available*

Abbas, M. A.; Cannom, R. R.; Chiu, V. Y.; Burchette, R. J.; Radner, G. W.; Haigh, P. I.; Etzioni, D. A. Triage of patients with acute diverticulitis: are some inpatients candidates for outpatient treatment?. Colorectal Dis. PMID 23061533.

I: No specific intervention

Abbas, S. Resection and primary anastomosis in acute complicated diverticulitis, a systematic review of the literature. Int J Colorectal Dis. PMID 16437211.
SR

Abraha, I.; Binda, G. A.; Montedori, A.; Arezzo, A.; Cirocchi, R. Laparoscopic versus open resection for sigmoid diverticulitis. Cochrane Database Syst Rev. PMID 29178125.
SR

Abujudeh H. H.; Kaewlai R.; McMahon P. M.; Binder W.; Novelline R. A.; Gazelle G. S.; Thrall J. H. Abdominopelvic CT increases diagnostic certainty and guides management decisions: a prospective investigation of 584 patients in a large academic medical center. AJR Am J Roentgenol. PMID 21257870.

P: Not colonic diverticulitis

Achkasov S. I.; Shelygin Y. A.; Moskalev A. I.; Trubacheva Y. L.; Senashenko S. A. Short-term outcomes of laparoscopic-assisted procedures for chronic complications of diverticular disease. Khirurgiia (Mosk). PMID 29560954.
Duplicate (no unique data)

Achkasov, S. I.; Shelygin, Y. A.; Moskalev, A. I.; Trubacheva, Y. L.; Senashenko, S. A. [Short-term outcomes of laparoscopic-assisted procedures for chronic complications of diverticular disease]. Khirurgiia (Mosk). PMID 29560954.
D: Single group, Surgery, N<500 analyzed

Actrn. Antibiotics in acute diverticulitis. [Http://www.who.int/trialsearch/trial2.aspx?Trialid=actrn12615000249550](http://www.who.int/trialsearch/trial2.aspx?Trialid=actrn12615000249550).
NCT: No results posted

Acuna, S. A.; Wood, T.; Chesney, T. R.; Dossa, F.; Wexner, S. D.; Quereshey, F. A.; Chadi, S. A.; Baxter, N. N. Operative Strategies for Perforated Diverticulitis: A Systematic Review and Meta-

analysis. Dis Colon Rectum. PMID 30371549.
SR

Acuna SA, Dossa F. Comment on "Long-term Outcome of Surgery Versus Conservative Management for Recurrent and Ongoing Complaints After an Episode of Diverticulitis": Statistically Significant Results Are Not Necessarily Clinically Important. Annals of surgery. 2020 Apr 8. doi: 10.1097/sla.0000000000003809. PMID: 32282376.
D: Not primary study or SR

Adamova Z.; Slovacek R.; Sankot J. Recurrent diverticulitis - risk factors. Rozhl Chir. PMID 24295478.
Duplicate (no unique data)

Adamova, Z.; Slovacek, R.; Sankot, J. [Recurrent diverticulitis - risk factors]. Rozhl Chir. PMID 24295478.
Not available

Afshar, S.; Kurer, M. A. Laparoscopic peritoneal lavage for perforated sigmoid diverticulitis. Colorectal Dis. PMID 21689299.
SR

Ahmadi; N.; Howden; W. B.; Byrne; C. M.; Young; C. J. Increasing primary anastomosis rate over time for the operative management of acute diverticulitis. ANZ J Surg. PMID .
D: Single group, Tx, N<100 analyzed

Ahmed, A. M.; Moahammed, A. T.; Mattar, O. M.; Mohamed, E. M.; Faraag, E. A.; AlSafadi, A. M.; Hirayama, K.; Huy, N. T. Surgical treatment of diverticulitis and its complications: A systematic review and meta-analysis of randomized control trials. Surgeon. PMID 30033140.
SR

Al-Mansouri; S.; Salama; E.; Lachance; S.; Faris-Sabboobeh; S.; Savard; J.; Morin; N.; Vasilevsky; C. A.; Ghitulescu; G.; Faria; J.; Boutros; M. A north american single-blinded pilot randomized controlled trial for outpatient non-antibiotic management of acute uncomplicated diverticulitis (mud trial): feasibility and lessons learned. Surgical endoscopy. PMID .
D: RCT N<10/arm

Al-Sahaf; O.; Al-Azawi; D.; Fauzi; M. Z.; El-Masry; S.; Gillen; P. Early discharge policy of patients with acute colonic diverticulitis following initial CT scan. Int J Colorectal Dis. PMID .
D: NRCS, Tx, N<30/arm analyzed

Alamili, M.; Gogenur, I.; Rosenberg, J. Acute complicated diverticulitis managed by laparoscopic lavage. *Dis Colon Rectum*. PMID 19571714.
SR

Alecha; J. S.; Pais; S. A.; Marin; X. B.; Martinez; B. O.; Ribera; E. B.; Irazabal; C. Y. Safety of nonoperative management after acute diverticulitis. *Annals of Coloproctology*. PMID 25360428.
D: NRCS, Tx, Crude analyses only

Alexandersson, B. T.; Hreinsson, J. P.; Stefansson, T.; Jonasson, J. G.; Bjornsson, E. S. The risk of colorectal cancer after an attack of uncomplicated diverticulitis. *Scand J Gastroenterol*. PMID 24621325.
Colonoscopy single gp, N<200

Alonso, S.; Pera, M.; Pares, D.; Pascual, M.; Gil, M. J.; Courtier, R.; Grande, L. Outpatient treatment of patients with uncomplicated acute diverticulitis. *Colorectal Dis*. PMID 19906059.
D: Single group, Tx, N<100 analyzed

Alshamari, M.; Norrman, E.; Geijer, M.; Jansson, K.; Geijer, H. Diagnostic accuracy of low-dose CT compared with abdominal radiography in non-traumatic acute abdominal pain: prospective study and systematic review. *Eur Radiol*. PMID 26385800.
O: CT, No clinical or management outcomes

Altinel Y, Cavallaro PM, Ricciardi R, et al. Can We Predict Surgically Complex Diverticulitis in Elective Cases? *Diseases of the colon and rectum*. 2020 May;63(5):646-54. doi: 10.1097/dcr.0000000000001600. PMID: 32032203.
I: Surgery for acute diverticulitis

Alvarez, J. A.; Baldonado, R. F.; Bear, I. G.; Otero, J.; Pire, G.; Alvarez, P.; Jorge, J. I. Presentation, management and outcome of acute sigmoid diverticulitis requiring hospitalization. *Dig Surg*. PMID 18057894.
I: Not intervention of interest (not KQ 1-4)

Alvarez, J. A.; Baldonado, R. F.; Bear, I. G.; Otero, J.; Pire, G.; Alvarez, P.; Jorge, J. I. Outcome and prognostic factors of morbidity and mortality in perforated sigmoid diverticulitis. *Int Surg*. PMID 20187519.
Not available

Alves, A.; Panis, Y.; Slim, K.; Heyd, B.; Kwiatkowski, F.; Manton, G. French multicentre prospective observational study of laparoscopic versus open colectomy for sigmoid diverticular disease. *Br J Surg*. PMID 16231279.
D: Single group, Surgery, N<500 analyzed

Ambrosetti P.; Morel P. Acute left-sided colonic diverticulitis: diagnosis and surgical indications after successful conservative therapy of first time acute diverticulitis. *Zentralbl Chir*. PMID 10063549.
O: CT, No clinical or management outcomes

Ambrosetti, P. Value of CT for acute left-colonic diverticulitis: the surgeon's view. *Dig Dis*. PMID 22572685.
I: Not intervention of interest (not KQ 1-4)

Ambrosetti, P.; Becker, C.; Terrier, F. Colonic diverticulitis: impact of imaging on surgical management -- a prospective study of 542 patients. *Eur Radiol*. PMID 11976860.
O: No outcome (or harm) of interest

Ambrosetti, P.; Gervaz, P.; Fossung-Wiblishauser, A. Sigmoid diverticulitis in 2011: many questions; few answers. *Colorectal Dis*. PMID 22404743.
D: Not primary study or SR

Ambrosetti, P.; Grossholz, M.; Becker, C.; Terrier, F.; Morel, P. Computed tomography in acute left colonic diverticulitis. *Br J Surg*. PMID 9112910.
O: No outcome (or harm) of interest

Ambrosetti, P.; Jenny, A.; Becker, C.; Terrier, T. F.; Morel, P. Acute left colonic diverticulitis--compared performance of computed tomography and water-soluble contrast enema: prospective evaluation of 420 patients. *Dis Colon Rectum*. PMID 11052512.
O: No outcome (or harm) of interest

Ambrosetti, P.; Morel, P. [Acute left-sided colonic diverticulitis: diagnosis and surgical indications after successful conservative therapy of first time acute diverticulitis]. *Zentralbl Chir*. PMID 10063549.
O: CT, No clinical or management outcomes

Ambrosetti, P.; Robert, J. H.; Witzig, J. A.; Mirescu, D.; Mathey, P.; Borst, F.; Rohner, A. Acute left colonic diverticulitis: a prospective analysis of 226 consecutive cases. *Surgery*. PMID 8178252.
O: CT, No clinical or management outcomes

Ambrosetti, P.; Robert, J.; Witzig, J. A.; Mathey, P.; Mirescu, D.; Rohner, A. [Value of computerized tomography in acute diverticulitis of the left colon]. *Schweiz Med Wochenschr*. PMID 8511546.
D: Intervention <1990

Ambrosetti, P.; Robert, J.; Witzig, J. A.; Mirescu, D.; de Gautard, R.; Borst, F.; Meyer, P.; Rohner, A. Prognostic factors from computed tomography in acute left colonic diverticulitis. *Br J Surg*. PMID 1555056.
D: Intervention <1990

Anaya, D. A.; Flum, D. R. Risk of emergency colectomy and colostomy in patients with diverticular

disease. Arch Surg. PMID 16027334.

I: Surgery for acute diverticulitis

Andersen, J. C.; Bundgaard, L.; Elbrond, H.; Laurberg, S.; Walker, L. R.; Stovring, J. Danish national guidelines for treatment of diverticular disease. Dan Med J. PMID 22549495.

SR

Anderson, S. W.; Soto, J. A.; Lucey, B. C.; Ozonoff, A.; Jordan, J. D.; Ratevosian, J.; Ulrich, A. S.; Rathlev, N. K.; Mitchell, P. M.; Rebholz, C.; Feldman, J. A.; Rhea, J. T. Abdominal 64-MDCT for suspected appendicitis: the use of oral and IV contrast material versus IV contrast material only. AJR Am J Roentgenol. PMID 19843742.

P: Not colonic diverticulitis

Andeweg, C. S.; Berg, R.; Staal, J. B.; ten Broek, R. P.; van Goor, H. Patient-reported Outcomes After Conservative or Surgical Management of Recurrent and Chronic Complaints of Diverticulitis: Systematic Review and Meta-analysis. Clin Gastroenterol Hepatol. PMID 26305068.

SR

Andeweg, C. S.; Mulder, I. M.; Felt-Bersma, R. J.; Verbon, A.; van der Wilt, G. J.; van Goor, H.; Lange, J. F.; Stoker, J.; Boermeester, M. A.; Bleichrodt, R. P. Guidelines of diagnostics and treatment of acute left-sided colonic diverticulitis. Dig Surg. PMID 23969324.

SR

Andeweg, C. S.; Wegdam, J. A.; Groenewoud, J.; van der Wilt, G. J.; van Goor, H.; Bleichrodt, R. P. Toward an evidence-based step-up approach in diagnosing diverticulitis. Scand J Gastroenterol. PMID 24874087.

SR

Andeweg, C.; Peters, J.; Bleichrodt, R.; van Goor, H. Incidence and risk factors of recurrence after surgery for pathology-proven diverticular disease. World J Surg. PMID 18330623.

D: Single group, Surgery, N<500 analyzed

Angenete, E.; Bock, D.; Rosenberg, J.; Haglind, E. Laparoscopic lavage is superior to colon resection for perforated purulent diverticulitis-a meta-analysis. Int J Colorectal Dis. PMID 27567926.

SR

Antolovic, D.; Reissfelder, C.; Koch, M.; Mertens, B.; Schmidt, J.; Buchler, M. W.; Weitz, J. Surgical treatment of sigmoid diverticulitis--analysis of predictive risk factors for postoperative infections, surgical complications, and mortality. Int J Colorectal Dis. PMID 19190921.

D: Single group, Surgery, N<500 analyzed

Arnold MH. The management of diverticulitis: a review of the guidelines. The Medical journal of Australia. 2020 May;212(9):434-.e1. doi: 10.5694/mja2.50526. PMID: 32115703.

D: Not primary study or SR

Asaad P, Hajibandeh S, Rahm M, et al. Should a colonoscopy be offered routinely to patients with CT proven acute diverticulitis? A retrospective cohort study and meta-analysis of best available evidence. World J Gastrointest Endosc. 2019 Jul 16;11(7):427-37. doi: 10.4253/wjge.v11.i7.427. PMID: 31367268. *D: CT or colonoscopy, N<100 (had CT/colonoscopy) analyzed*

Au, S.; Aly, E. H. Treatment of Uncomplicated Acute Diverticulitis Without Antibiotics: A Systematic Review and Meta-Analysis. Dis Colon Rectum. PMID 30663999.

SR

Azhar N, Buchwald P, Ansari HZ, et al. Risk of colorectal cancer following CT-verified acute diverticulitis: a nationwide population-based cohort study. Colorectal disease : the official journal of the Association of Coloproctology of Great Britain and Ireland. 2020 Apr 16. doi: 10.1111/codi.15073. PMID: 32301257.

I: Not intervention of interest (not KQ 1-4)

Azhar, N.; Kulstad, H.; Palsson, B.; Kurt Schultz, J.; Lydrup, M. L.; Buchwald, P. Acute uncomplicated diverticulitis managed without antibiotics - difficult to introduce a new treatment protocol but few complications. Scand J Gastroenterol. PMID 30650309.

D: NRCS, Tx, N<30/arm analyzed

Bachmann, K.; Krause, G.; Rawnaq, T.; Tomkotter, L.; Vashist, Y.; Shahmiri, S.; Izbicki, J. R.; Bockhorn, M. Impact of early or delayed elective resection in complicated diverticulitis. World J Gastroenterol. PMID 22219596.

D: Single group, Surgery, N<500 analyzed

Balasubramanian, I.; Fleming, C.; Mohan, H. M.; Schmidt, K.; Haglind, E.; Winter, D. C. Out-Patient Management of Mild or Uncomplicated Diverticulitis: A Systematic Review. Dig Surg. PMID 27701164.

SR

Baldock; T. E.; Brown; L. R.; McLean; R. C. Perforated diverticulitis in the North of England: trends in patient outcomes, management approach and the influence of subspecialisation. Ann R Coll Surg Engl. PMID 31155922.

D: NRCS, Tx, Crude analyses only

Baldoli, D.; Musco, F.; Scalambra, M.; Balsamo, F.; Galli, A.; Rebuffat, C. [Laparoscopy in patients with colonic diverticulitis. Results of a prospective data base]. Ann Ital Chir. PMID 17345988.

Not available

Baldoli, D.; Musco, F.; Scalambra, M.; Balsamo, F.; Galli, A.; Rebuffat, C. Laparoscopy in patients with colonic diverticulitis. Results of a prospective data base. Ann Ital Chir. PMID duplicate.

Duplicate (no unique data)

Ballian, N.; Rajamanickam, V.; Harms, B. A.; Foley, E. F.; Heise, C. P.; Greenberg, C. C.; Kennedy, G. D. Predictors of mortality after emergent surgery for acute colonic diverticulitis: Analysis of National Surgical Quality Improvement Project data. Journal of Trauma & Acute Care Surgery. PMID .

I: Surgery for acute diverticulitis

Balthazar, E. J.; Megibow, A.; Schinella, R. A.; Gordon, R. Limitations in the CT diagnosis of acute diverticulitis: comparison of CT, contrast enema, and pathologic findings in 16 patients. AJR Am J Roentgenol. PMID 2105015.

D: Intervention <1990

Banasiewicz, T.; Francuzik, W.; Bobkiewicz, A.; Krokowicz, L.; Borejsza-Wysocki, M.; Paszkowski, J.; Studniarek, A.; Krokowicz, P.; Grochowalski, M.; Szczepkowski, M.; Lorenc, Z. The influence of rifaximin on diverticulitis rate and quality of life in patients with diverticulosis. Pol Przegl Chir. PMID 28522790.

D: NRCS, Tx, Crude analyses only

Bargellini, T.; Martellucci, J.; Tonelli, P.; Valeri, A. Long-term results of treatment of acute diverticulitis: still lessons to be learned?. Updates Surg. PMID 23271440.

I: Not intervention of interest (not KQ 1-4)

Barry, B. D.; Leroy, J.; Mutter, D.; Wu, H. S.; Marescaux, J. Minimally invasive surgical treatment of sigmoid diverticulitis. Langenbecks Arch Surg. PMID 22644602.

SR

Bassi R. Preventing recurrence of symptomatic diverticular disease of the colon: mesalazine with or without Lactobacillus casei: a prospective randomized, open label study. Colorectal disease.

Not available

Bates, D. D. B.; Fernandez, M. B.; Ponchiardi, C.; von Plato, M.; Teich, J. P.; Narsule, C.; Anderson, S. W.; Gupta, A.; LeBedis, C. A. Surgical management in acute diverticulitis and its association with multi-detector CT, modified Hinchey classification, and clinical parameters. Abdom Radiol (NY). PMID

29204676.

I: Not intervention of interest (not KQ 1-4)

Belmonte, C.; Klas, J. V.; Perez, J. J.; Wong, W. D.; Rothenberger, D. A.; Goldberg, S. M.; Madoff, R. D. The Hartmann procedure. First choice or last resort in diverticular disease?. Arch Surg. PMID 8645067.

D: Single group, Surgery, N<500 analyzed

Bergamaschi, R.; Tuetch, J. J.; Pessaux, P.; Arnaud, J. P. Intracorporeal vs laparoscopic-assisted resection for uncomplicated diverticulitis of the sigmoid. Surg Endosc. PMID 10890956.

D: Single group, Surgery, N<500 analyzed

Berger A.; Zinzindohoue F.; Pardies P.; Wind P.; Cellier C.; Barbier J. P.; Cugnenc P. H. Selective segmental colectomy in diverticular sigmoiditis. The surgical risk is not increased after 70 years of age. Ann Chir. PMID 10520494.

D: Single group, Surgery, N<500 analyzed

Berger, A.; Zinzindohoue, F.; Pardies, P.; Wind, P.; Cellier, C.; Barbier, J. P.; Cugnenc, P. H. [Selective segmental colectomy in diverticular sigmoiditis. The surgical risk is not increased after 70 years of age]. Ann Chir. PMID 10520494.

D: Single group, Surgery, N<500 analyzed

Berthou, J. C.; Charbonneau, P. Elective laparoscopic management of sigmoid diverticulitis. Results in a series of 110 patients. Surg Endosc. PMID 10227941.

D: Single group, Surgery, N<500 analyzed

Beyer-Berjot, L.; Maggiori, L.; Loiseau, D.; De Korwin, J. D.; Bongiovanni, J. P.; Lesprit, P.; Salles, N.; Rousset, P.; Lescot, T.; Henriot, A.; Lefrancois, M.; Cotte, E.; Parc, Y. Emergency Surgery in Acute Diverticulitis: A Systematic Review. Dis Colon Rectum. PMID 30694823.

I: Not intervention of interest (not KQ 1-4)

Bianchi M.; Festa V.; Ciaco A.; Luchetti R.; Dezi A.; Papi C.; Capurso L.; Koch M. Rifaximin reduces symptoms and complications in patients with symptomatic diverticular disease. A systematic review of the literature and a metaanalysis. Digestive and liver disease.

Not available

Binda, G. A.; Amato, A.; Serventi, A.; Arezzo, A. Clinical presentation and risks. Dig Dis. PMID 22572695.

I: Not intervention of interest (not KQ 1-4)

Biondo S.; Golda T.; Moreno E. K.; Valls F. V.; Espin E.; Oteiza F.; Cazador A. C.; Pujadas M.; Flor B. Ambulatory treatment versus hospitalisation for uncomplicated diverticulitis. Colorectal disease.

Not available

Biondo, S.; Borao, J. L.; Kreisler, E.; Golda, T.; Millan, M.; Frago, R.; Fracalvieri, D.; Guardiola, J.; Jaurrieta, E. Recurrence and virulence of colonic diverticulitis in immunocompromised patients. *Am J Surg*. PMID 22444713.

I: No specific intervention

Biondo, S.; Lopez Borao, J.; Millan, M.; Kreisler, E.; Jaurrieta, E. Current status of the treatment of acute colonic diverticulitis: a systematic review. *Colorectal Dis*. PMID 21848896.

SR

Blake, M. F.; Dwivedi, A.; Tootla, A.; Tootla, F.; Silva, Y. J. Laparoscopic sigmoid colectomy for chronic diverticular disease. *Jsls*. PMID .

D: Single group, Tx, N<100 analyzed

Blasco. Trial Assessing the Efficacy of a Short Course of Intravenous Antibiotic Followed by Oral Antibiotic in Uncomplicated Acute Diverticulitis. <https://clinicaltrials.gov/show/nct00917592>. PMID Nct.

NCT: No results posted

Boermeester, M. A.; Humes, D. J.; Velmahos, G. C.; Soreide, K. Contemporary Review of Risk-Stratified Management in Acute Uncomplicated and Complicated Diverticulitis. *World J Surg*. PMID 27206400.

SR

Bolkenstein, H. E.; van Dijk, S. T.; Consten, E. C. J.; Heggelman, B. G. F.; Hoeks, C. M. A.; Broeders, Iamj; Boermeester, M. A.; Draaisma, W. A. Conservative Treatment in Diverticulitis Patients with Pericolic Extraluminal Air and the Role of Antibiotic Treatment. *J Gastrointest Surg*. PMID 30859428.

O: No outcome (or harm) of interest

Bolkenstein; H. E.; Consten; E. C. J.; Broeder; Iamj; Boermeester; M. A.; Bemelman; W. A.; Lange; J. F.; Draaisma; W. A. Elective sigmoidectomy leads to higher quality of life in patients with recurrent and ongoing diverticulitis; 5 year results of the direct-trial. *Surgical endoscopy*. PMID conference abstract. *Not available*

Bolkenstein; H. E.; De Wit; G. D. A.; Consten; E. C. J.; Van De Wall; B. J. M.; Broeder; Iamj; Draaisma; W. A. Long term cost-effectiveness of surgery versus conservative management for recurrent and ongoing diverticulitis: the direct trial. *Surgical endoscopy*. PMID .

Duplicate (no unique data)

Boostrom, S. Y.; Wolff, B. G.; Cima, R. R.; Merchea, A.; Dozois, E. J.; Larson, D. W. Uncomplicated diverticulitis, more complicated than we thought. *J*

Gastrointest Surg. PMID 22696233.

I: Surgery for acute diverticulitis

Boselli, C.; Gemini, A.; Cirocchi, R.; Grassi, V.; Avenia, S.; Polistena, A.; Sanguinetti, A.; Pironi, D.; Santoro, A.; Tabola, R.; Burattini, M. F.; Avenia, N. Is it safe and useful, laparoscopic peritoneal lavage in the treatment of acute diverticulitis of octogenarian patients? A multicenter retrospective observational study. *Aging Clin Exp Res*. PMID 27830520.

D: Single group, Tx, N<100 analyzed

Bosker, R.; Hoogenboom, F.; Groen, H.; Hoff, C.; Ploeg, R.; Pierie, J. P. Elective laparoscopic recto-sigmoid resection for diverticular disease is suitable as a training operation. *Int J Colorectal Dis*. PMID 20145937.

D: Single group, Surgery, N<500 analyzed

Boudart, C.; Simoons, Ch; Thill, V.; Debergh, N.; Smets, D.; Mendes da Costa, P. Management of sigmoid diverticulitis: a retrospective study of 268 patients. *Hepatogastroenterology*. PMID 19260478. *Not available*

Boutros. Outpatient Treatment of Uncomplicated Diverticulitis With Either Antibiotic or Nonantibiotic Treatment.

<https://clinicaltrials.gov/show/nct03146091>. PMID Nct.

NCT: No results posted

Brandlhuber, M.; Genzinger, C.; Brandlhuber, B.; Sommer, W. H.; Muller, M. H.; Kreis, M. E. Long-term quality of life after conservative treatment versus surgery for different stages of acute sigmoid diverticulitis. *Int J Colorectal Dis*. PMID 29397430.

I: No specific intervention

Brandt, D.; Gervaz, P.; Durmishi, Y.; Platon, A.; Morel, P.; Poletti, P. A. Percutaneous CT scan-guided drainage vs. antibiotherapy alone for Hinchey II diverticulitis: a case-control study. *Dis Colon Rectum*. PMID 16988856.

D: NRCS, Tx, Crude analyses only

Brengman, M. L.; Otchy, D. P. Timing of computed tomography in acute diverticulitis. *Dis Colon Rectum*. PMID 9715160.

I: Not intervention of interest (not KQ 1-4)

Bridoux, V.; Antor, M.; Schwarz, L.; Cahais, J.; Khalil, H.; Michot, F.; Tuech, J. J. Elective operation after acute complicated diverticulitis: is it still mandatory?. *World J Gastroenterol*. PMID 25009389.

O: Single arm study without harms data

Brochmann, N. D.; Schultz, J. K.; Jakobsen, G. S.; Oresland, T. Management of acute uncomplicated diverticulitis without antibiotics: a single-centre cohort study. *Colorectal Dis.* PMID 27089051.
D: NRCS, Tx, Crude analyses only

Broderick-Villa, G.; Burchette, R. J.; Collins, J. C.; Abbas, M. A.; Haigh, P. I. Hospitalization for acute diverticulitis does not mandate routine elective colectomy. *Arch Surg.* PMID 15967905.
I: No specific intervention

Broderick, R. C.; Fuchs, H. F.; Harnsberger, C. R.; Chang, D. C.; McLemore, E.; Ramamoorthy, S.; Horgan, S. The price of decreased mortality in the operative management of diverticulitis. *Surg Endosc.* PMID 25159639.
I: Surgery for acute diverticulitis

Bruzzi, J. F.; Moss, A. C.; Brennan, D. D.; MacMathuna, P.; Fenlon, H. M. Efficacy of IV Buscopan as a muscle relaxant in CT colonography. *Eur Radiol.* PMID .
O: CT, No clinical or management outcomes

Buchs, N. C.; Konrad-Mugnier, B.; Jannot, A. S.; Poletti, P. A.; Ambrosetti, P.; Gervaz, P. Assessment of recurrence and complications following uncomplicated diverticulitis. *Br J Surg.* PMID 23592303.
I: No specific intervention

Buchwald, P.; Dixon, L.; Wakeman, C. J.; Eglinton, T. W.; Frizelle, F. A. Hinchey I and II diverticular abscesses: long-term outcome of conservative treatment. *ANZ J Surg.* PMID 27062439.
D: NRCS, Tx, Crude analyses only

Bulje. Randomized Multicentric Trial to Evaluate a Free Diet With a Progressive Diet in the Treatment of Acute Diverticulitis.
<https://clinicaltrials.gov/show/nct03496090>. PMID Nct.
I: Not intervention of interest (not KQ 1-4)

Caputo, P.; Rovagnati, M.; Carzaniga, P. L. Is it possible to limit the use of CT scanning in acute diverticular disease without compromising outcomes? A preliminary experience. *Ann Ital Chir.* PMID 25816854.
Not available

Carter, F.; Alsayb, M.; Marshall, J. K.; Yuan, Y. Mesalamine (5-ASA) for the prevention of recurrent diverticulitis. *Cochrane Database Syst Rev.* PMID 28973845.
SR

Cassini, D.; Depalma, N.; Grieco, M.; Cirocchi, R.; Manoochchri, F.; Baldazzi, G. Robotic pelvic

dissection as surgical treatment of complicated diverticulitis in elective settings: a comparative study with fully laparoscopic procedure. *Surg Endosc.* PMID 30406387.
D: Single group, Surgery, N<500 analyzed

Catalano O. Computerized tomography in the study of acute sigmoid diverticulosis. *Radiol Med.* PMID 9036450.
Duplicate (no unique data)

Catalano, O. [Computerized tomography in the study of acute sigmoid diverticulosis]. *Radiol Med.* PMID 9036450.
O: CT, No clinical or management outcomes

Cavallaro A.; Loschiavo V.; Potenza A. E.; Modugno P.; Fabbri M. C.; Revelli L.; Colli R. Diverticular disease: complications and treatment. *Chir Ital.* PMID 12469467.
Duplicate (no unique data)

Cavallaro, A.; Loschiavo, V.; Potenza, A. E.; Modugno, P.; Fabbri, M. C.; Revelli, L.; Colli, R. [Diverticular disease: complications and treatment]. *Chir Ital.* PMID 12469467.
I: No specific intervention

Cerdan Santacruz, C.; Merichal Resina, M.; Sierra Granon, J. E.; Olsina Kissler, J. J. Comment on "Long Term Outcome of Surgery Versus Conservative Management for Recurrent and Ongoing Complaints After an Episode of Diverticulitis. 5-year Follow-up Results of a Multicenter Randomized Control Trial (DIRECT-Trial)". *Ann Surg.* PMID 31205063.
D: Not primary study or SR

Ceresoli, M.; Coccolini, F.; Montori, G.; Catena, F.; Sartelli, M.; Ansaloni, L. Laparoscopic lavage versus resection in perforated diverticulitis with purulent peritonitis: a meta-analysis of randomized controlled trials. *World J Emerg Surg.* PMID 27582782.
SR

Chabok, A.; Andreasson, K.; Nikberg, M. Low risk of complications in patients with first-time acute uncomplicated diverticulitis. *Int J Colorectal Dis.* PMID 29038965.
D: Single group, Tx, N<100 analyzed

Chabok, A.; Smedh, K.; Nilsson, S.; Stenson, M.; Pahlman, L. CT-colonography in the follow-up of acute diverticulitis: patient acceptance and diagnostic accuracy. *Scand J Gastroenterol.* PMID 23834748.
Colonoscopy single gp, N<200

Chabok, A.; Pahlman, L.; Hjern, F.; Haapaniemi, S.; Smedh, K. No value of antibiotics for acute uncomplicated diverticulitis: a randomised study.

Colorectal disease. PMID .

Duplicate (no unique data)

Chambers A.; Halligan S.; Goh V.; Dhillon S.; Hassan A. Therapeutic impact of abdominopelvic computed tomography in patients with acute abdominal symptoms. *Acta Radiol.* PMID 15239417.
D: CT or colonoscopy, N<100 (had CT/colonoscopy) analyzed

Chan D. K. H.; Tan K. K. There Is No Role for Colonoscopy after Diverticulitis among Asian Patients Less than 50 Years of Age. *Gastrointest Tumors.* PMID 28611980.
Duplicate (no unique data)

Chan, D. K. H.; Tan, K. K. There Is No Role for Colonoscopy after Diverticulitis among Asian Patients Less than 50 Years of Age. *Gastrointest Tumors.* PMID 28611980.
D: Single group, Tx, N<100 analyzed

Chan, D. K. H.; Tan, K. K. Asian patients with Hinchey Ia acute diverticulitis: a condition for the ambulatory setting?. *Int J Colorectal Dis.* PMID 29090326.
O: Single arm study without harms data

Chapman, J.; Davies, M.; Wolff, B.; Dozois, E.; Tessier, D.; Harrington, J.; Larson, D. Complicated diverticulitis: is it time to rethink the rules?. *Ann Surg.* PMID 16192818.
I: Surgery for acute diverticulitis

Chautems, R. C.; Ambrosetti, P.; Ludwig, A.; Mermillod, B.; Morel, P.; Soravia, C. Long-term follow-up after first acute episode of sigmoid diverticulitis: is surgery mandatory?: a prospective study of 118 patients. *Dis Colon Rectum.* PMID 12130887.
I: Not intervention of interest (not KQ 1-4)

Chin J. Y.; Goldstraw E.; Lunniss P.; Patel K. Evaluation of the utility of abdominal CT scans in the diagnosis, management, outcome and information given at discharge of patients with non-traumatic acute abdominal pain. *Br J Radiol.* PMID 22919012.
D: CT or colonoscopy, N<100 (had CT/colonoscopy) analyzed

Cho, K. C.; Morehouse, H. T.; Alterman, D. D.; Thornhill, B. A. Sigmoid diverticulitis: diagnostic role of CT--comparison with barium enema studies. *Radiology.* PMID 2191360.
D: Intervention <1990

Choi, K. K.; Martinolich, J.; Canete, J. J.; Valerian, B. T.; Chismark, D. A.; Ata, A.; Lee, E. C. Elective Laparoscopic Sigmoid Colectomy for Diverticulitis--an Updated Look at Recurrence After Surgery. *J*

Gastrointest Surg. PMID 30671801.

D: Single group, Surgery, N<500 analyzed

Chouillard E.; Benhaim L.; Ata T.; Etienne J. C.; Ghiles E.; Fingerhut A. Elective laparoscopic colectomy in uncomplicated diverticulitis: when should surgery be performed. *Cir Esp.* PMID 17403357.
D: Single group, Tx, N<100 analyzed

Chouillard, E.; Benhaim, L.; Ata, T.; Etienne, J. C.; Ghiles, E.; Fingerhut, A. [Elective laparoscopic colectomy in uncomplicated diverticulitis: when should surgery be performed]. *Cir Esp.* PMID 17403357.
D: Single group, Surgery, N<500 analyzed

Chung, B. H.; Ha, G. W.; Lee, M. R.; Kim, J. H. Management of Colonic Diverticulitis Tailored to Location and Severity: Comparison of the Right and the Left Colon. *Ann Coloproctol.* PMID 28119866.
I: No specific intervention

Cirocchi, R.; Afshar, S.; Shaban, F.; Nascimbeni, R.; Vettoretto, N.; Di Saverio, S.; Randolph, J.; Zago, M.; Chiarugi, M.; Binda, G. A. Perforated sigmoid diverticulitis: Hartmann's procedure or resection with primary anastomosis--a systematic review and meta-analysis of randomised control trials. *Tech Coloproctol.* PMID 29995173.
SR

Cirocchi, R.; Arezzo, A.; Renzi, C.; Cochetti, G.; D'Andrea, V.; Fingerhut, A.; Mearini, E.; Binda, G. A. Is laparoscopic surgery the best treatment in fistulas complicating diverticular disease of the sigmoid colon? A systematic review. *Int J Surg.* PMID 26584958.
SR

Cirocchi, R.; Arezzo, A.; Vettoretto, N.; Cavaliere, D.; Farinella, E.; Renzi, C.; Cannata, G.; Desiderio, J.; Farinacci, F.; Barberini, F.; Trastulli, S.; Parisi, A.; Fingerhut, A. Role of damage control surgery in the treatment of Hinchey III and IV sigmoid diverticulitis: a tailored strategy. *Medicine (Baltimore).* PMID 25437034.
SR

Cirocchi, R.; Cochetti, G.; Randolph, J.; Listorti, C.; Castellani, E.; Renzi, C.; Mearini, E.; Fingerhut, A. Laparoscopic treatment of colovesical fistulas due to complicated colonic diverticular disease: a systematic review. *Tech Coloproctol.* PMID 24848529.
SR

Cirocchi, R.; Di Saverio, S.; Weber, D. G.; Tabola, R.; Abraha, I.; Randolph, J.; Arezzo, A.; Binda, G. A. Laparoscopic lavage versus surgical resection for acute diverticulitis with generalised peritonitis: a

systematic review and meta-analysis. Tech Coloproctol. PMID 28197792.
SR

Cirotchi, R.; Farinella, E.; Trastulli, S.; Sciannameo, F.; Audisio, R. A. Elective sigmoid colectomy for diverticular disease. Laparoscopic vs open surgery: a systematic review. Colorectal Dis. PMID 21689339.
SR

Cirotchi, R.; Randolph, J. J.; Binda, G. A.; Gioia, S.; Henry, B. M.; Tomaszewski, K. A.; Allegritti, M.; Arezzo, A.; Marzaioli, R.; Ruscelli, P. Is the outpatient management of acute diverticulitis safe and effective? A systematic review and meta-analysis. Tech Coloproctol. PMID 30684110.
SR

Cirotchi, R.; Trastulli, S.; Desiderio, J.; Listorti, C.; Boselli, C.; Parisi, A.; Noya, G.; Liu, L. Treatment of Hinchey stage III-IV diverticulitis: a systematic review and meta-analysis. Int J Colorectal Dis. PMID 23242271.
SR

Cirotchi, R.; Trastulli, S.; Farinella, E.; Desiderio, J.; Listorti, C.; Parisi, A.; Noya, G.; Boselli, C. Is inferior mesenteric artery ligation during sigmoid colectomy for diverticular disease associated with increased anastomotic leakage? A meta-analysis of randomized and non-randomized clinical trials. Colorectal Dis. PMID 22632654.
SR

Cirotchi, R.; Trastulli, S.; Vettoretto, N.; Milani, D.; Cavaliere, D.; Renzi, C.; Adamenko, O.; Desiderio, J.; Burattini, M. F.; Parisi, A.; Arezzo, A.; Fingerhut, A. Laparoscopic peritoneal lavage: a definitive treatment for diverticular peritonitis or a 'bridge' to elective laparoscopic sigmoidectomy?: a systematic review. Medicine (Baltimore). PMID 25569649.
SR

Coccolini, Federico; Trevisan; Mattia; Montori; Giulia; Sartelli; Massimo; Catena; Fausto; Ceresoli; Marco; Costanzo; Antonio; Heyer; Arianna; Ansaloni; Luca; on behalf of the Complicated Intra-Abdominal Infection Observational; Study; the Complicated Intra-Abdominal Infection Observational World; Group. Mortality Rate and Antibiotic Resistance in Complicated Diverticulitis: Report of 272 Consecutive Patients Worldwide: A Prospective Cohort Study. Surgical Infections. PMID .

I: Not intervention of interest (not KQ 1-4)

Cole, K.; Fassler, S.; Suryadevara, S.; Zebley, D. M. Increasing the number of attacks increases the conversion rate in laparoscopic diverticulitis surgery.

Surg Endosc. PMID 18528617.

O: Single arm study without harms data

Comparato, G.; Fanigliulo, L.; Cavallaro, L. G.; Aragona, G.; Cavestro, G. M.; Iori, V.; Maino, M.; Mazzocchi, G.; Muzzetto, P.; Colla, G.; Sianesi, M.; Franze, A.; Mario, F. D. Prevention of complications and symptomatic recurrences in diverticular disease with mesalazine: a 12-month follow-up. Dig Dis Sci. PMID 17410435.

P: Not colonic diverticulitis

Constantinides, V. A.; Tekkis, P. P.; Athanasiou, T.; Aziz, O.; Purkayastha, S.; Remzi, F. H.; Fazio, V. W.; Aydin, N.; Darzi, A.; Senapati, A. Primary resection with anastomosis vs. Hartmann's procedure in nonelective surgery for acute colonic diverticulitis: a systematic review. Dis Colon Rectum. PMID 16752192.
SR

Costi, R.; Cauchy, F.; Le Bian, A.; Honart, J. F.; Creuze, N.; Smadja, C. Challenging a classic myth: pneumoperitoneum associated with acute diverticulitis is not an indication for open or laparoscopic emergency surgery in hemodynamically stable patients. A 10-year experience with a nonoperative treatment. Surg Endosc. PMID 22274929.

O: No outcome (or harm) of interest

Courtot, L.; Bridoux, V.; Lakkis, Z.; Piessen, G.; Manceau, G.; Mulliri, A.; Meurette, G.; Bouayed, A.; Venara, A.; Blanc, B.; Tabchouri, N.; Salame, E.; Ouaisi, M. Long-term outcome and management of right colonic diverticulitis in western countries: Multicentric Retrospective Study. J Visc Surg. PMID 30685223.

I: Not intervention of interest (not KQ 1-4)

CTRI. A clinical trial to study the safety and efficacy of mesalazine (5-ASA) in patients with a history of diverticulitis over 104 weeks.

[Http://www.who.int/trialsearch/trial2.aspx?Trialid=ctri/2009/091/000450](http://www.who.int/trialsearch/trial2.aspx?Trialid=ctri/2009/091/000450).

NCT: No results posted

Cunningham MA, Davis JW, Kaups KL. Medical versus surgical management of diverticulitis in patients under age 40. American journal of surgery. 1997;174(6):733-5. PMID: 9409607.

D: NRCS, Tx, N<30/arm analyzed

Dahl, C.; Crichton, M.; Jenkins, J.; Nucera, R.; Mahoney, S.; Marx, W.; Marshall, S. Evidence for Dietary Fibre Modification in the Recovery and Prevention of Reoccurrence of Acute, Uncomplicated Diverticulitis: A Systematic Literature Review.

Nutrients. PMID 29382074.
SR

Daniels; L.; Unlu; C.; de Wijkerslooth; T. R.; Dekker; E.; Boermeester; M. A. Routine colonoscopy after left-sided acute uncomplicated diverticulitis: a systematic review. *Gastrointest Endosc.* PMID 24434085.
SR

De Chaisemartin C.; Panis Y.; Mognol P.; Valleur P. Laparoscopic sigmoid resection for diverticulitis: is learning phase associated with increased morbidity?. *Ann Chir.* PMID 12657543.
Duplicate (no unique data)

De Chaisemartin, C.; Panis, Y.; Mognol, P.; Valleur, P. [Laparoscopic sigmoid resection for diverticulitis: is learning phase associated with increased morbidity?]. *Ann Chir.* PMID 12657543.
D: Single group, Tx, N<100 analyzed

de Korte, N.; Unlu, C.; Boermeester, M. A.; Cuesta, M. A.; Vrouenreats, B. C.; Stockmann, H. B. Use of antibiotics in uncomplicated diverticulitis. *Br J Surg.* PMID 21523694.
SR

De Magistris, L.; Arru, L.; De Blasi, V.; Poulain, V.; Lens, V.; Mertens, L.; Goergen, M.; Azagra, J. S. Management of acute diverticulitis in a tertiary care institution. *Bull Soc Sci Med Grand Duche Luxemb.* PMID 24437073.
D: Single group, Surgery, N<500 analyzed

De Magistris, L.; Azagra, J. S.; Goergen, M.; De Blasi, V.; Arru, L.; Facy, O. Laparoscopic sigmoidectomy in moderate and severe diverticulitis: analysis of short-term outcomes in a continuous series of 121 patients. *Surg Endosc.* PMID 23436080.
D: Single group, Tx, N<100 analyzed

de Vries, H. S.; Boerma, D.; Timmer, R.; van Ramshorst, B.; Dieleman, L. A.; van Westreenen, H. L. Routine colonoscopy is not required in uncomplicated diverticulitis: a systematic review. *Surg Endosc.* PMID 24488358.
SR

Desai, M.; Fathallah, J.; Nutalapati, V.; Saligram, S. Antibiotics Versus No Antibiotics for Acute Uncomplicated Diverticulitis: A Systematic Review and Meta-Analysis. *Dis Colon Rectum.* PMID 30664553.
SR

Devaraj, B.; Liu, W.; Tatum, J.; Cologne, K.; Kaiser, A. M. Medically Treated Diverticular Abscess Associated With High Risk of Recurrence and Disease Complications. *Dis Colon Rectum.* PMID

26855395.
D: Single group, Tx, N<100 analyzed

Dharmarajan, S.; Hunt, S. R.; Birnbaum, E. H.; Fleshman, J. W.; Mutch, M. G. The efficacy of nonoperative management of acute complicated diverticulitis. *Dis Colon Rectum.* PMID 21552049.
I: No specific intervention

Di Mario, F.; Aragona, G.; Leandro, G.; Comparato, G.; Fanigliulo, L.; Cavallaro, L. G.; Cavestro, G. M.; Iori, V.; Maino, M.; Moussa, A. M.; Gnocchi, A.; Mazzocchi, G.; Franze, A. Efficacy of mesalazine in the treatment of symptomatic diverticular disease. *Dig Dis Sci.* PMID 15810646.
P: Not colonic diverticulitis

Díaz JJT, Asenjo BA, Soriano MR, et al. Efficacy of colonoscopy after an episode of acute diverticulitis and risk of colorectal cancer. *Ann Gastroenterol.* 2020 Jan-Feb;33(1):68-72. doi: 10.20524/aog.2019.0437. PMID: 31892800.
Colonoscopy single gp, N<200

Doringe E.; Ferner R. Computed tomography of colonic diverticulitis. *Rofo.*
O: CT, No clinical or management outcomes

Doringe, E.; Ferner, R. [Computed tomography of colonic diverticulitis]. *Rofo.* PMID 2154015.
D: Intervention <1990

Dreifuss; N. H.; Schlottmann; F.; Piatti; J. M.; Bun; M. E.; Rotholtz; N. A. Safety and feasibility of laparoscopic sigmoid resection without diversion in perforated diverticulitis. *Surg Endosc.* PMID .
D: Single group, Surgery, N<500 analyzed

Dughera, L.; Serra, A. M.; Battaglia, E.; Tibaudi, D.; Navino, M.; Emanuelli, G. Acute recurrent diverticulitis is prevented by oral administration of a polybacterial lysate suspension. *Minerva Gastroenterol Dietol.* PMID 15722985.
Not available

Durmishi; Y.; Gervaz; P.; Brandt; D.; Bucher; P.; Platon; A.; Morel; P.; Poletti; P. A. Results from percutaneous drainage of Hinchey stage II diverticulitis guided by computed tomography scan. *Surg Endosc.* PMID .
D: Single group, Tx, N<100 analyzed

Ebersole J, Medvecz AJ, Connolly C, et al. Comparison of American Association for the Surgery of Trauma grading scale with modified Hinchey classification in acute colonic diverticulitis: A pilot study. *J Trauma Acute Care Surg.* 2020 Jun;88(6):770-5. doi: 10.1097/ta.0000000000002650. PMID: 32118825.
I: Not intervention of interest (not KQ 1-4)

Egger, B.; Peter, M. K.; Candinas, D. Persistent symptoms after elective sigmoid resection for diverticulitis. *Dis Colon Rectum*. PMID 18449609.
D: Single group, Surgery, N<500 analyzed

Eggesbo, H. B.; Jacobsen, T.; Kolmannskog, F.; Bay, D.; Nygaard, K. Diagnosis of acute left-sided colonic diverticulitis by three radiological modalities. *Acta Radiol*. PMID 9571951.
D: NRCS, Tx, N<30/arm analyzed

Eglinton, T. W. Randomized clinical trial of antibiotics in acute uncomplicated diverticulitis (Br J Surg 2012; 99: 532-539). *Br J Surg*. PMID 22396052.
D: Not primary study or SR

Eijssbouts, Q. A.; de Haan, J.; Berends, F.; Sietses, C.; Cuesta, M. A. Laparoscopic elective treatment of diverticular disease. A comparison between laparoscopic-assisted and resection-facilitated techniques. *Surg Endosc*. PMID 10954818.
I: Surgery for acute diverticulitis

El-Sayed C, Radley S, Mytton J, et al. Risk of Recurrent Disease and Surgery Following an Admission for Acute Diverticulitis. *Diseases of the colon and rectum*. 2018 Mar;61(3):382-9. doi: 10.1097/dcr.0000000000000939. PMID: 29420430.
I: No specific intervention

El Zarrok Elgazwi, K.; Baca, I.; Grzybowski, L.; Jaacks, A. Laparoscopic sigmoidectomy for diverticulitis: a prospective study. *Jsls*. PMID 21605507.
D: Single group, Surgery, N<500 analyzed

Elagili Faisal; Stocchi Luca; Ozuner Gokhan; Mody Rekha; Baker Mark E.; Kiran Ravi P. Predictors of postoperative outcomes for patients with diverticular abscess initially treated with percutaneous drainage. *American Journal of Surgery*. PMID 25172167.
O: Single arm study without harms data

Elagili, F.; Stocchi, L.; Ozuner, G.; Kiran, R. P. Antibiotics alone instead of percutaneous drainage as initial treatment of large diverticular abscess. *Tech Coloproctol*. PMID 25417122.
O: Single arm study without harms data

Emile, S. H.; Elfeki, H.; Sakr, A.; Shalaby, M. Management of acute uncomplicated diverticulitis without antibiotics: a systematic review, meta-analysis, and meta-regression of predictors of treatment failure. *Tech Coloproctol*. PMID 29980885.
SR

Ernst S.; Wypior H. J.; Stark V.; Rath M. The computed tomography of acute sigmoid diverticulitis.

Rofo. PMID 8679970.

O: CT, No clinical or management outcomes

Ernst, S.; Wypior, H. J.; Stark, V.; Rath, M. [The computed tomography of acute sigmoid diverticulitis]. *Rofo*. PMID 8679970.
O: CT, No clinical or management outcomes

Esses, D.; Birnbaum, A.; Bijur, P.; Shah, S.; Gleyzer, A.; Gallagher, E. J. Ability of CT to alter decision making in elderly patients with acute abdominal pain. *Am J Emerg Med*. PMID 15258866.
O: CT, No clinical or management outcomes

Esteban Hernandez J. M.; Maldonado Blanco L.; Leon Guijarro J. L.; Pascual Moreno I.; Nogues Pelayo E. Value of ultrasonography as the initial diagnostic method in acute sigmoid diverticulitis. *Gastroenterol Hepatol*. PMID 9882930.
Duplicate (no unique data)

Esteban Hernandez, J. M.; Maldonado Blanco, L.; Leon Guijarro, J. L.; Pascual Moreno, I.; Nogues Pelayo, E. [Value of ultrasonography as the initial diagnostic method in acute sigmoid diverticulitis]. *Gastroenterol Hepatol*. PMID 9882930.
Not available

Estrada Ferrer; O.; Ruiz Edo; N.; Hidalgo Grau; L. A.; Abadal Prades; M.; Del Bas Rubia; M.; Garcia Torralbo; E. M.; Heredia Budo; A.; Sunol Sala; X. Selective non-antibiotic treatment in sigmoid diverticulitis: is it time to change the traditional approach?. *Tech Coloproctol*. PMID .
D: NRCS, Tx, Crude analyses only

Eucetr D. E. Rifaximin tablets in the prevention of recurrent acute diverticulitis and diverticular complications.
[Http://www.who.int/trialsearch/trial2.aspx?Trialid=eucetr2017-002708-28-de](http://www.who.int/trialsearch/trial2.aspx?Trialid=eucetr2017-002708-28-de).
NCT: No results posted

Eucetr E. S. Randomized clinical trial to compare the treatment of mild acute diverticulitis with or without antibiotics.
[Http://www.who.int/trialsearch/trial2.aspx?Trialid=eucetr2016-001596-75-es](http://www.who.int/trialsearch/trial2.aspx?Trialid=eucetr2016-001596-75-es).
D: NRCS, Tx, Crude analyses only

Eucetr E. S. Double-blind, dose-response, randomised, placebo-controlled, parallel group, multicentre phase III clinical study on the efficacy and tolerability of mesalazine granules vs. placebo for the prevention of recurrence of diverticulitis - Mesalazine granules vs. placebo for the prevention of recurrence of diverticulitis.
[Http://www.who.int/trialsearch/trial2.aspx?Trialid=eucetr2009-015158-39-es](http://www.who.int/trialsearch/trial2.aspx?Trialid=eucetr2009-015158-39-es).
Duplicate (no unique data)

Eutr G. B. A Phase III, Randomised, Double-Blind, Dose-Response, Stratified, Placebo-Controlled Study Evaluating the Safety and Efficacy of SPD476 versus Placebo over 104 weeks in the Prevention of Recurrence of Diverticulitis.

[Http://www.who.int/trialsearch/trial2.aspx?](http://www.who.int/trialsearch/trial2.aspx?Trialid=eutr2007-004895-37-gb)

Trialid=eutr2007-004895-37-gb.

Duplicate (no unique data)

Eutr G. B. Mechanistic randomised controlled trial of Mesalazine in symptomatic diverticular disease.

[Http://www.who.int/trialsearch/trial2.aspx?](http://www.who.int/trialsearch/trial2.aspx?Trialid=eutr2006-006198-26-gb)

Trialid=eutr2006-006198-26-gb.

I: Not intervention of interest (not KQ 1-4)

Eutr H. U. Rifaximin tablets in the prevention of recurrent acute diverticulitis and diverticular complications.

[Http://www.who.int/trialsearch/trial2.aspx?](http://www.who.int/trialsearch/trial2.aspx?Trialid=eutr2017-002708-28-hu)

Trialid=eutr2017-002708-28-hu.

NCT: No results posted

Eutr I. T. Efficacy of mesalazine in the long term prevention of diverticulitis relapses. Randomised study, double blind, controlled vs placebo.

[Http://www.who.int/trialsearch/trial2.aspx?](http://www.who.int/trialsearch/trial2.aspx?Trialid=eutr2005-001459-39-it)

Trialid=eutr2005-001459-39-it.

NCT: No results posted

Eutr L. T. A comparative study on the efficacy of oral Rifamycin SV-MMX® 400 mg two times daily vs. Rifamycin SV-MMX® 600 mg three times daily vs. placebo (no active medication) in the treatment of acute uncomplicated diverticulitis

(inflammation of protuberances of the bowel mucosa). [Http://www.who.int/trialsearch/trial2.aspx?](http://www.who.int/trialsearch/trial2.aspx?Trialid=eutr2012-003300-13-lt)

Trialid=eutr2012-003300-13-lt.

NCT: No results posted

Eurboonyanun K, Rungwiriyanich P, Chamadol N, et al. Accuracy of Nonenhanced CT vs Contrast-Enhanced CT for Diagnosis of Acute Appendicitis in Adults. *Curr Probl Diagn Radiol*. 2020 Jan 9. doi: 10.1067/j.cpradiol.2020.01.010. PMID: 32037023.

O: CT, No clinical or management outcomes

Farag Soliman; M.; Wustner; M.; Sturm; J.; Werner; A.; Diehl; S. J.; Duber; C.; Post; S. Primary diagnostics of acute diverticulitis of the sigmoid. *Ultraschall Med*. PMID 15368137.

O: CT, No clinical or management outcomes

Ferulano, G. P.; Dilillo, S.; D'Ambra, M.; Saviano, C.; Brunaccino, R.; Lionetti, R.; Fico, D. [Timing and results of the surgical treatment of the diverticular disease of the colon]. *Ann Ital Chir*. PMID 17343233.

Not available

Ferulano; G. P.; Dilillo; S.; D'Ambra; M.; Saviano; C.; Brunaccino; R.; Lionetti; R.; Fico; D. Timing and

results of the surgical treatment of the diverticular disease of the colon. *Ann Ital Chir*. PMID 17343233.

Duplicate (no unique data)

Flament J. B.; Avisse C.; Greffier D.; Palot J. P.; Delattre J. F. Thoughts on the treatment of diverticular sigmoiditis. Apropos of 191 cases. *Chirurgie*. PMID 8665814.

Duplicate (no unique data)

Flament, J. B.; Avisse, C.; Greffier, D.; Palot, J. P.; Delattre, J. F. [Thoughts on the treatment of diverticular sigmoiditis. Apropos of 191 cases]. *Chirurgie*. PMID 8665814.

D: Intervention <1990

Flor, N.; Maconi, G.; Sardanelli, F.; Lombardi, M. A.; Colombo, B.; Di Leo, G.; Falleni, M.; Cornalba, G.; Pickhardt, P. J. Prognostic Value of the Diverticular Disease Severity Score Based on CT Colonography: Follow-up in Patients Recovering from Acute Diverticulitis. *Acad Radiol*. PMID 26482263.

Colonoscopy single gp, N<200

Forgione, A.; Guraya, S. Y. Elective colonic resection after acute diverticulitis improves quality of life, intestinal symptoms and functional outcome: experts' perspectives and review of literature. *Updates Surg*. PMID 27015932.

SR

Francis, N. K.; Sylla, P.; Abou-Khalil, M.; Arolfo, S.; Berler, D.; Curtis, N. J.; Dolejs, S. C.; Garfinkle, R.; Gorter-Stam, M.; Hashimoto, D. A.; Hassinger, T. E.; Molenaar, C. J. L.; Pucher, P. H.; Schuermans, V.; Arezzo, A.; Agresta, F.; Antoniou, S. A.; Arulampalam, T.; Boutros, M.; Bouvy, N.; Campbell, K.; Francone, T.; Haggerty, S. P.; Hedrick, T. L.; Stefanidis, D.; Truitt, M. S.; Kelly, J.; Ket, H.; Dunkin, B. J.; Pietrabissa, A. EAES and SAGES 2018 consensus conference on acute diverticulitis management: evidence-based recommendations for clinical practice. *Surg Endosc*. PMID 31250244.

SR

Friend K.; Mills A. M. Is outpatient oral antibiotic therapy safe and effective for the treatment of acute uncomplicated diverticulitis?. *Ann Emerg Med*. PMID 21770056.

SR

Frileux; P.; Dubrez; J.; Burdy; G.; Rouillet-Audy; J. C.; Dalban-Sillas; B.; Bonnaventure; F.; Frileux; M. A. Sigmoid diverticulitis. Longitudinal analysis of 222 patients with a minimal follow up of 5 years. *Colorectal Dis*. PMID .

I: No specific intervention

Fuchs, H. F.; Broderick, R. C.; Harnsberger, C. R.; Chang, D. C.; McLemore, E. C.; Ramamoorthy, S.; Horgan, S. Variation of outcome and charges in operative management for diverticulitis. Surg Endosc. PMID 25539698.

I: Not intervention of interest (not KQ 1-4)

Fung, A. K.; Ahmeidat, H.; McAteer, D.; Aly, E. H. Validation of a grading system for complicated diverticulitis in the prediction of need for operative or percutaneous intervention. Ann R Coll Surg Engl. PMID 26263806.

I: Not intervention of interest (not KQ 1-4)

Gaertner, W. B.; Kwaan, M. R.; Madoff, R. D.; Willis, D.; Belzer, G. E.; Rothenberger, D. A.; Melton, G. B. The evolving role of laparoscopy in colonic diverticular disease: a systematic review. World J Surg. PMID 23192170.

SR

Gaertner, W. B.; Willis, D. J.; Madoff, R. D.; Rothenberger, D. A.; Kwaan, M. R.; Belzer, G. E.; Melton, G. B. Percutaneous drainage of colonic diverticular abscess: is colon resection necessary?. Dis Colon Rectum. PMID 23575402.

D: Single group, Tx, N<100 analyzed

Galbraith, N.; Carter, J. V.; Netz, U.; Yang, D.; Fry, D. E.; McCafferty, M.; Galandiuk, S. Laparoscopic Lavage in the Management of Perforated Diverticulitis: a Contemporary Meta-analysis. J Gastrointest Surg. PMID 28608041.

SR

Galetin, T.; Galetin, A.; Vestweber, K. H.; Rink, A. D. Systematic review and comparison of national and international guidelines on diverticular disease. Int J Colorectal Dis. PMID 29349481.

D: Not primary study or SR

Garcia-Gomez M. A.; Belmonte-Montes C.; Cosme-Reyes C.; Aguirre Garcia M. P. Prognostic value of the presence of pericolic air bubbles detected by computed tomography in acute diverticulitis. Cir Cir. PMID 27955857.

Duplicate (no unique data)

Garcia-Gomez, M. A.; Belmonte-Montes, C.; Cosme-Reyes, C.; Aguirre Garcia, M. P. [Prognostic value of the presence of pericolic air bubbles detected by computed tomography in acute diverticulitis]. Cir Cir. PMID 27955857.

I: No specific intervention

Garcia-Marin, A.; Rodriguez-Cazalla, L.; Bernabeu-Herraiz, C.; Madrid-Banos, B.; Morales-Calderon, M.; Compan-Rosique, A. [Tratamiento ambulatorio de la diverticulitis aguda no complicada. Analisis de

nuestra experiencia]. Cir Cir. PMID 30600803.

D: Single group, Tx, N<100 analyzed

Garcia-Martin, A.; Rodriguez-Cazalla, L.; Bernabeu-Herriz, C.; Madrid-Baos, B.; Morales-Calderon, M.; Compan-Rosique, A. Outpatient treatment of uncomplicated acute diverticulitis. Analysis of our experience. Cirugia y Cirujanos (English Edition). PMID .

Duplicate (no unique data)

Gardner C. S.; Jaffe T. A.; Nelson R. C. Impact of CT in elderly patients presenting to the emergency department with acute abdominal pain. Abdom Imaging. PMID 25862547.

O: CT, No clinical or management outcomes

Garrett, K. A.; Champagne, B. J.; Valerian, B. T.; Peterson, D.; Lee, E. C. A single training center's experience with 200 consecutive cases of diverticulitis: can all patients be approached laparoscopically?. Surg Endosc. PMID 18347863.

D: Single group, Surgery, N<500 analyzed

Gatta, L.; Vakil, N.; Vaira, D.; Pilotto, A.; Curlo, M.; Comparato, G.; Leandro, G.; Ferro, U.; Lera, M.; Milletti, S.; Di Mario, F. Efficacy of 5-ASA in the treatment of colonic diverticular disease. J Clin Gastroenterol. PMID 19561530.

SR

Germer, C. T.; Reibetanz, J. High risk of recurrence after conservative management of complicated diverticulitis. Chirurg. PMID .

I: No specific intervention

Gervaz, P.; Inan, I.; Perneger, T.; Schiffer, E.; Morel, P. A prospective, randomized, single-blind comparison of laparoscopic versus open sigmoid colectomy for diverticulitis. Ann Surg. PMID 20505508.

I: Surgery for acute diverticulitis

Gervaz, P.; Mugnier-Konrad, B.; Morel, P.; Huber, O.; Inan, I. Laparoscopic versus open sigmoid resection for diverticulitis: long-term results of a prospective, randomized trial. Surg Endosc. PMID 21556992.

I: Surgery for acute diverticulitis

Gielens, M. P.; Mulder, I. M.; van der Harst, E.; Gosselink, M. P.; Kraal, K. J.; Teng, H. T.; Lange, J. F.; Vermeulen, J. Preoperative staging of perforated diverticulitis by computed tomography scanning. Tech Coloproctol. PMID 22752330.

I: Surgery for acute diverticulitis

Goh, V.; Halligan, S.; Taylor, S. A.; Burling, D.; Bassett, P.; Bartram, C. I. Differentiation between diverticulitis and colorectal cancer: quantitative CT

perfusion measurements versus morphologic criteria-initial experience. Radiology. PMID 17255417.

O: CT, No clinical or management outcomes

Goldwag J. L.; Lyn R. V.; Wilson L. R.; Wilson M. Z.; Ivatury S. J. Effect of Elective Sigmoidectomy for Diverticulitis on Bowel Function Patient-Reported Outcomes. J Surg Res. PMID 31022679.

D: Single group, Tx, N<100 analyzed

Gonzalez, R.; Smith, C. D.; Mattar, S. G.; Venkatesh, K. R.; Mason, E.; Duncan, T.; Wilson, R.; Miller, J.; Ramshaw, B. J. Laparoscopic vs open resection for the treatment of diverticular disease. Surg Endosc. PMID 14691707.

I: Surgery for acute diverticulitis

González Plo D, Plá Sánchez P, León Gámez CL, et al. Update on the management of uncomplicated acute diverticulitis at our centre. Equally effective, more efficient. Gastroenterol Hepatol. 2020 May 17. doi: 10.1016/j.gastrohep.2020.01.006. PMID: 32434733.

Not available

Gottlieb M.; Shah N.; Yu B. Can Acute Uncomplicated Diverticulitis Be Safely Treated Without Antibiotics?. Ann Emerg Med. PMID 30318374.
SR

Grahnat, C. J.; Herard, S.; Ackzell, A.; Andersson, R. E. High Probability of an Underlying Colorectal Cancer Among Patients Treated for Acute Diverticulitis. A Population-Based Cohort Follow-Up Study. World J Surg. PMID 26956904.

D: CT or colonoscopy, N<100 (had CT/colonoscopy) analyzed

Gralista, P.; Moris, D.; Vailas, M.; Angelou, A.; Petrou, A.; Felekouras, E.; Papalampros, A. Laparoscopic Approach in Colonic Diverticulitis: Dispelling Myths and Misperceptions. Surg Laparosc Endosc Percutan Tech. PMID 28212260.

SR

Grass, F.; Crippa, J.; Mathis, K. L.; Kelley, S. R.; Larson, D. W. Feasibility and safety of robotic resection of complicated diverticular disease. Surg Endosc. PMID 30868321.

I: Not intervention of interest (not KQ 1-4)

Greenberg; A. S.; Gal; R.; Coben; R. M.; Cohen; S.; Dimarino; A. J.; Jr. A retrospective analysis of medical or surgical therapy in young patients with diverticulitis. Aliment Pharmacol Ther. PMID .

D: NRCS, Tx, N<30/arm analyzed

Gregersen, R.; Andresen, K.; Burcharth, J.; Pommergaard, H. C.; Rosenberg, J. Long-term

mortality and recurrence in patients treated for colonic diverticulitis with abscess formation: a nationwide register-based cohort study. Int J Colorectal Dis. PMID 29511842.

D: NRCS, Tx, Crude analyses only

Gregersen, R.; Mortensen, L. Q.; Burcharth, J.; Pommergaard, H. C.; Rosenberg, J. Treatment of patients with acute colonic diverticulitis complicated by abscess formation: A systematic review. Int J Surg. PMID 27741423.

SR

Gregersen; R.; Andresen; K.; Burcharth; J.; Pommergaard; H. C.; Rosenberg; J. Short-term mortality, readmission, and recurrence in treatment of acute diverticulitis with abscess formation: a nationwide register-based cohort study. Int J Colorectal Dis. PMID .

D: NRCS, Tx, Crude analyses only

Grevfors, N.; Torkzad, M. R.; Bergman, A.; Pahlman, L. Can acute abdominal CT prioritize patients with suspected diverticulitis for a subsequent clean colonic examination?. Colorectal Dis. PMID 21899711.

I: Not intervention of interest (not KQ 1-4)

Guzzo, J.; Hyman, N. Diverticulitis in young patients: is resection after a single attack always warranted?. Dis Colon Rectum. PMID 15148645.

I: No specific intervention

Ha, G. W.; Lee, M. R.; Kim, J. H. Efficacy of conservative management in patients with right colonic diverticulitis. ANZ J Surg. PMID 25786747.

O: Single arm study without harms data

Haas, J. M.; Singh, M.; Vakil, N. Mortality and complications following surgery for diverticulitis: Systematic review and meta-analysis. United European Gastroenterol J. PMID 27733913.

SR

Hachigian, M. P.; Honickman, S.; Eisenstat, T. E.; Rubin, R. J.; Salvati, E. P. Computed tomography in the initial management of acute left-sided diverticulitis. Dis Colon Rectum. PMID 1473412.

D: Intervention <1990

Hajibandeh S, Loutfi M, Hajibandeh S, et al. Routine versus selective computed tomography in non-traumatic acute abdominal pain: meta-analysis of randomised trials. Langenbecks Arch Surg. 2020 May;405(3):283-91. doi: 10.1007/s00423-020-01884-1. PMID: 32388716.

O: No outcome (or harm) of interest

Hall J, Hardiman K, Lee S, et al. The American Society of Colon and Rectal Surgeons Clinical

Practice Guidelines for the Treatment of Left-Sided Colonic Diverticulitis. Diseases of the colon and rectum. 2020 Jun;63(6):728-47. doi: 10.1097/dcr.0000000000001679. PMID: 32384404. SR

Hall, J. F.; Roberts, P. L.; Ricciardi, R.; Marcello, P. W.; Scheirey, C.; Wald, C.; Scholz, F. J.; Schoetz, D. Colonic diverticulitis: does age predict severity of disease on CT imaging?. Dis Colon Rectum. PMID 20087085.

I: Not intervention of interest (not KQ 1-4)

Hall, J. F.; Roberts, P. L.; Ricciardi, R.; Read, T.; Scheirey, C.; Wald, C.; Marcello, P. W.; Schoetz, D. J. Long-term follow-up after an initial episode of diverticulitis: what are the predictors of recurrence?. Dis Colon Rectum. PMID .

D: NRCS, Tx, Crude analyses only

Haller O.; Karlsson L.; Nyman R. Can low-dose abdominal CT replace abdominal plain film in evaluation of acute abdominal pain?. Ups J Med Sci. PMID 19878040.

D: CT or colonoscopy, N<100 (had CT/colonoscopy) analyzed

Hansen O.; Graupe F.; Stock W. Diagnosis of diverticulitis in routine practice: progress due to pelvic CT?. Langenbecks Arch Chir Suppl Kongressbd. PMID 9931605.

O: CT, No clinical or management outcomes

Hansen O.; Zarras K.; Graupe F.; Dellana M.; Stock W. Surgical treatment of diverticulitis of the large intestine--a plea for early elective resection. Zentralbl Chir. PMID 8867345.

Duplicate (no unique data)

Hansen O.; Zarras K.; Graupe F.; Stock W. Surgical therapy of sigmoid diverticulitis in elderly patients.--What decides against early elective resection. Langenbecks Arch Chir Suppl Kongressbd. PMID 9101902.

Duplicate (no unique data)

Hansen, O.; Graupe, F.; Stock, W. [Diagnosis of diverticulitis in routine practice: progress due to pelvic CT?]. Langenbecks Arch Chir Suppl Kongressbd. PMID 9931605.

O: CT, No clinical or management outcomes

Hansen, O.; Zarras, K.; Graupe, F.; Dellana, M.; Stock, W. [Surgical treatment of diverticulitis of the large intestine--a plea for early elective resection]. Zentralbl Chir. PMID 8867345.

D: Single group, Surgery, N<500 analyzed

Hansen, O.; Zarras, K.; Graupe, F.; Stock, W. [Surgical therapy of sigmoid diverticulitis in elderly

patients.--What decides against early elective resection]. Langenbecks Arch Chir Suppl Kongressbd. PMID 9101902.

Not available

Hashimoto, R.; Matsuda, T.; Chonan, A. Colonoscopy After Computed Tomography-diagnosed Acute Right-sided Diverticulitis May Be Unnecessary. J Clin Gastroenterol. PMID 26974757. *Colonoscopy single gp, N<200*

Hassan, I.; Cima, R. R.; Larson, D. W.; Dozois, E. J.; O'Byrne, M. M.; Larson, D. R.; Pemberton, J. H. The impact of uncomplicated and complicated diverticulitis on laparoscopic surgery conversion rates and patient outcomes. Surg Endosc. PMID 17593455.

D: No analysis of interest

Herzog, T.; Janot, M.; Belyaev, O.; Sulberg, D.; Chromik, A. M.; Bergmann, U.; Mueller, C. A.; Uhl, W. Complicated sigmoid diverticulitis--Hartmann's procedure or primary anastomosis?. Acta Chir Belg. PMID 22299325.

D: NRCS, Tx, N<30/arm analyzed

Heverhagen, J. T.; Sitter, H.; Zielke, A.; Klose, K. J. Prospective evaluation of the value of magnetic resonance imaging in suspected acute sigmoid diverticulitis. Dis Colon Rectum. PMID 18443876.

O: CT, No clinical or management outcomes

Hildebrand, P.; Kropp, M.; Stellmacher, F.; Roblick, U. J.; Bruch, H. P.; Schwandner, O. Surgery for right-sided colonic diverticulitis: results of a 10-year-observation period. Langenbecks Arch Surg. PMID 17072664.

D: Single group, Tx, N<100 analyzed

Hill, B. C.; Johnson, S. C.; Owens, E. K.; Gerber, J. L.; Senagore, A. J. CT scan for suspected acute abdominal process: impact of combinations of IV, oral, and rectal contrast. World J Surg. PMID 20054539.

P: Not colonic diverticulitis

Hjern, F.; Jonas, E.; Holmstrom, B.; Josephson, T.; Mellgren, A.; Johansson, C. CT colonography versus colonoscopy in the follow-up of patients after diverticulitis - a prospective, comparative study. Clin Radiol. PMID 17556033.

D: CT or colonoscopy, N<100 (had CT/colonoscopy) analyzed

Hjern, F.; Josephson, T.; Altman, D.; Holmstrom, B.; Johansson, C. Outcome of younger patients with acute diverticulitis. Br J Surg. PMID .

I: Not intervention of interest (not KQ 1-4)

Ho VP, Nash GM, Milsom JW, et al. Identification of diverticulitis patients at high risk for recurrence and poor outcomes. *J Trauma Acute Care Surg*. 2015 Jan;78(1):112-9. doi: 10.1097/ta.0000000000000466. PMID: 25539211.

I: No specific intervention

Hoffmann, H.; Dell-Kuster, S.; Genstorfer, J.; Heizmann, O.; Kettelhack, C.; Langer, I.; Oertli, D.; Rosenthal, R. Impact of tutorial assistance in laparoscopic sigmoidectomy for acute recurrent diverticulitis. *Surg Today*. PMID 24281782.

D: Single group, Surgery, N<500 analyzed

Hoffmann, H.; Dell-Kuster, S.; Genstorfer, J.; Kettelhack, C.; Langer, I.; Rosenthal, R.; Oertli, D.; Heizmann, O. Surgical treatment of acute recurrent diverticulitis: early elective or late elective surgery. An analysis of 237 patients. *World J Surg*. PMID 22311143.

D: No analysis of interest

Holmer, C.; Lehmann, K. S.; Engelmann, S.; Frericks, B.; Loddenkemper, C.; Buhr, H. J.; Ritz, J. P. Microscopic findings in sigmoid diverticulitis--changes after conservative therapy. *J Gastrointest Surg*. PMID 20186500.

I: Not intervention of interest (not KQ 1-4)

Holmer, C.; Lehmann, K. S.; Engelmann, S.; Grone, J.; Buhr, H. J.; Ritz, J. P. Long-term outcome after conservative and surgical treatment of acute sigmoid diverticulitis. *Langenbecks Arch Surg*. PMID 21688045.

I: Surgery for acute diverticulitis

Holzer B.; Ausch C.; Feil W. The surgical point of view of the geriatric patient - Sigmoid diverticulitis. *Acta Chirurgica Austriaca*.

D: Not primary study or SR

Hong, M. K.; Skandarajah, A. R.; Joy, M. P.; Hayes, I. P. Elective colectomy after acute diverticulitis: an international comparison. *Colorectal Dis*. PMID 30980588.

I: No specific intervention

Horesh, N.; Zbar, A. P.; Nevler, A.; Haim, N.; Gutman, M.; Zmora, O. Early experience with laparoscopic lavage in acute complicated diverticulitis. *Dig Surg*. PMID 25765997.

D: Single group, Tx, N<100 analyzed

Hsiao, K. C.; Wann, J. G.; Lin, C. S.; Wu, C. C.; Jao, S. W.; Yang, M. H. Colonic diverticulitis with comorbid diseases may require elective colectomy. *World J Gastroenterol*. PMID 24151389.

I: No specific intervention

Humes, D.; Simpson, J.; Spiller, R. C. Colonic diverticular disease. *BMJ Clin Evid*. PMID 19454119.

SR

Humes, D.; Spiller, R. C. Colonic diverticular disease: medical treatments for acute diverticulitis. *BMJ Clin Evid*. PMID 26854496.

SR

Hupfeld; L.; Burcharth; J.; Pommergaard; H. C.; Rosenberg; J. Risk factors for recurrence after acute colonic diverticulitis: a systematic review. *Int J Colorectal Dis*. PMID .

I: No specific intervention

Huston; J. M.; Zuckerbraun; B. S.; Moore; L. J.; Sanders; J. M.; Duane; T. M. Antibiotics versus No Antibiotics for the Treatment of Acute Uncomplicated Diverticulitis: Review of the Evidence and Future Directions. *Surg Infect (Larchmt)*. PMID .

D: Not primary study or SR

Hwang, S. S.; Cannom, R. R.; Abbas, M. A.; Etzioni, D. Diverticulitis in transplant patients and patients on chronic corticosteroid therapy: a systematic review. *Dis Colon Rectum*. PMID 21178867.

SR

Iannone, A.; Ruospo, M.; Wong, G.; Barone, M.; Principi, M.; Di Leo, A.; Strippoli, G. F. M. Mesalazine for People with Diverticular Disease: A Systematic Review of Randomized Controlled Trials. *Can J Gastroenterol Hepatol*. PMID 30320044.

SR

Ide C.; Van Beers B.; Pauls C.; Pringot J. Diagnosis of acute colonic diverticulitis: comparison with echography and tomodesitometry. *J Belge Radiol*. PMID 7829459.

Duplicate (no unique data)

Ide, C.; Van Beers, B.; Pauls, C.; Pringot, J. [Diagnosis of acute colonic diverticulitis: comparison with echography and tomodesitometry]. *J Belge Radiol*. PMID 7829459.

Not available

Ignjatovic, D.; Zivanovic, V.; Vasic, G.; Ilic, I. [Meta-analysis on minimally invasive surgical therapy of sigmoid diverticulitis]. *Acta Chir Iugosl*. PMID 16018362.

SR

Ince, A. T.; Baysal, B.; Kayar, Y.; Arabaci, E.; Bilgin, M.; Hamdard, J.; Yay, A.; Senturk, H. Comparison of tomographic and colonoscopic diagnoses in the presence of colonic wall thickening.

Int J Clin Exp Med. PMID 25550962.

O: CT, No clinical or management outcomes

Isacson, D.; Andreasson, K.; Nikberg, M.; Smedh, K.; Chabok, A. No antibiotics in acute uncomplicated diverticulitis: does it work?. Scand J Gastroenterol. PMID 25369865.

D: NRCS, Tx, Crude analyses only

Isacson, D.; Andreasson, K.; Nikberg, M.; Smedh, K.; Chabok, A. Outpatient management of acute uncomplicated diverticulitis results in health-care cost savings. Scand J Gastroenterol. PMID 29543100.

I: No specific intervention

Isacson, D.; Thorisson, A.; Andreasson, K.; Nikberg, M.; Smedh, K.; Chabok, A. Outpatient, non-antibiotic management in acute uncomplicated diverticulitis: a prospective study. Int J Colorectal Dis. PMID 25989930.

O: Single arm study without harms data

Isacson, D.; Thorisson, A.; Andreasson, K.; Nikberg, M.; Smedh, K.; Chabok, A. Erratum to: Outpatient, non-antibiotic management in acute uncomplicated diverticulitis: a prospective study. Int J Colorectal Dis. PMID 26084881.

O: Single arm study without harms data

Isrctn. Laparoscopic-assisted or -facilitated sigmoidectomy for diverticulitis? A prospective randomised trial.

[http://www.who.int/trialsearch/trial2.aspx?](http://www.who.int/trialsearch/trial2.aspx?Trialid=isrctn23817011)

Trialid=isrctn23817011.

NCT: No results posted

Isrctn. Randomised controlled trial of oral versus intravenous therapy for clinically diagnosed acute uncomplicated diverticulitis.

[http://www.who.int/trialsearch/trial2.aspx?](http://www.who.int/trialsearch/trial2.aspx?Trialid=isrctn42685776)

Trialid=isrctn42685776.

NCT: No results posted

Jackson, J. D.; Hammond, T. Systematic review: outpatient management of acute uncomplicated diverticulitis. Int J Colorectal Dis. PMID 24859874. *SR*

Jacobsen T.; Nygaard K. Diverticulitis of the colon. Diagnosis and treatment illustrated by a patient material. Tidsskr Nor Laegeforen. PMID 8658452.

Duplicate (no unique data)

Jacobsen, T.; Nygaard, K. [Diverticulitis of the colon. Diagnosis and treatment illustrated by a patient material]. Tidsskr Nor Laegeforen. PMID 8658452.

I: Not intervention of interest (not KQ 1-4)

Jalouta, T.; Jrebi, N.; Luchtefeld, M.; Ogilvie, J. W., Jr. Diverticulitis recurrence after percutaneous

abscess drainage. Int J Colorectal Dis. PMID 28555444.

O: Single arm study without harms data

Janes, S.; Meagher, A.; Frizelle, F. A. Elective surgery after acute diverticulitis. Br J Surg. PMID 15685694.

D: Not primary study or SR

Jang, H. J.; Lim, H. K.; Lee, S. J.; Lee, W. J.; Kim, E. Y.; Kim, S. H. Acute diverticulitis of the cecum and ascending colon: the value of thin-section helical CT findings in excluding colonic carcinoma. AJR Am J Roentgenol. PMID 10789802.

O: CT, No clinical or management outcomes

Jeger, V.; Pop, R.; Forudastan, F.; Barras, J. P.; Zuber, M.; Piso, R. J. Is there a role for procalcitonin in differentiating uncomplicated and complicated diverticulitis in order to reduce antibiotic therapy? A prospective diagnostic cohort study. Swiss Med Wkly. PMID 29185246.

I: Not intervention of interest (not KQ 1-4)

Jones, O. M.; Stevenson, A. R.; Clark, D.; Stitz, R. W.; Lumley, J. W. Laparoscopic resection for diverticular disease: follow-up of 500 consecutive patients. Ann Surg. PMID 19092355.

I: Surgery for acute diverticulitis

Jones R, Olatunbode D, Dean J, et al. A feasibility randomised controlled trial to evaluate the role of computed tomography in adults with atypical right iliac fossa pain. Ann R Coll Surg Engl. 2019 Nov;101(8):546-51. doi: 10.1308/rcsann.2019.0077. PMID: 31219315.

P: Not colonic diverticulitis

Jprn Umin. Is it effective Burdock tea to prevent of reattack of colonoc diverticulitis, diverticuler bleeding. [http://www.who.int/trialsearch/trial2.aspx?](http://www.who.int/trialsearch/trial2.aspx?Trialid=jprn-umin000022990)

Trialid=jprn-umin000022990.

NCT: No results posted

Juszczyk K, Ireland K, Thomas B, et al. Safety and efficacy of outpatient management for elderly patients with uncomplicated acute diverticulitis. Eur J Intern Med. 2020 Jun;76:123-4. doi: 10.1016/j.ejim.2020.02.032. PMID: 32199730.

I: Not intervention of interest (not KQ 1-4)

Juszczyk, K.; Ireland, K.; Thomas, B.; Kroon, H. M.; Hollington, P. Reduction in hospital admissions with an early computed tomography scan: results of an outpatient management protocol for uncomplicated acute diverticulitis. ANZ J Surg. PMID 31206250.

I: No specific intervention

Kaewlai, R.; Nazinitsky, K. J. Acute colonic diverticulitis in a community-based hospital: CT

evaluation in 138 patients. Emerg Radiol. PMID 17136376.

I: No specific intervention

Kaiser, A. M.; Jiang, J. K.; Lake, J. P.; Ault, G.; Artinyan, A.; Gonzalez-Ruiz, C.; Essani, R.; Beart, R. W., Jr. The management of complicated diverticulitis and the role of computed tomography. Am J Gastroenterol. PMID 15784040.

I: No specific intervention

Kaser, S. A.; Glauser, P. M.; Basilicata, G.; Muller, D. A.; Maurer, C. A. Timing of rectosigmoid resection for diverticular disease: the patient's view. Colorectal Dis. PMID 22093049.

O: Single arm study without harms data

Katz L. H.; Guy D. D.; Lahat A.; Gaftor-Gvili A.; Bar-Meir S. Diverticulitis in the young is not more aggressive than in the elderly, but it tends to recur more often: systematic review and meta-analysis. J Gastroenterol Hepatol. PMID 23701446.

I: No specific intervention

Kaushik, M.; Bhullar, J. S.; Bindroo, S.; Singh, H.; Mittal, V. K. Minimally Invasive Management of Complicated Diverticular Disease: Current Status and Review of Literature. Dig Dis Sci. PMID 26547753. SR

Kechagias A, Rautio T, Kechagias G, et al. The role of C-reactive protein in the prediction of the clinical severity of acute diverticulitis. The American surgeon. 2014 Apr;80(4):391-5. PMID: 24887672.

I: Diagnostic test, not CT or colonoscopy

Keller, D. S.; Flores-Gonzalez, J. R.; Sandhu, J.; Ibarra, S.; Madhoun, N.; Haas, E. M. SILS v SILS+1: a Case-Matched Comparison for Colorectal Surgery. J Gastrointest Surg. PMID 26282851.

D: Single group, Surgery, N<500 analyzed

Khan, M. A.; Ali, B.; Lee, W. M.; Howden, C. W. Mesalamine Does Not Help Prevent Recurrent Acute Colonic Diverticulitis: Meta-Analysis of Randomized, Placebo-Controlled Trials. Am J Gastroenterol. PMID 27125717.

SR

Khan; R. M. A.; Hajibandeh; S. Early elective versus delayed elective surgery in acute recurrent diverticulitis: A systematic review and meta-analysis. Int J Surg. PMID 28882772.

SR

Killingback, M.; Barron, P. E.; Dent, O. F. Elective surgery for diverticular disease: an audit of surgical pathology and treatment. ANZ J Surg. PMID 15230784.

D: Single group, Surgery, N<500 analyzed

Kim. Randomized Clinical Trial for the Uncomplicated Diverticulitis in Right Colon.

<https://clinicaltrials.gov/show/nct02314013>. PMID Nct.

NCT: No results posted

Kim, D. H.; Kim, H. J.; Jang, S. K.; Yeon, J. W.; Shin, K. S. CT Predictors of Unfavorable Clinical Outcomes of Acute Right Colonic Diverticulitis. AJR Am J Roentgenol. PMID 28981351.

I: No specific intervention

Kim, M. J.; Woo, Y. S.; Kim, E. R.; Hong, S. N.; Chang, D. K.; Rhee, P. L.; Kim, J. J.; Lee, S. J.; Kim, Y. H. Is colonoscopy necessary after computed tomography diagnosis of acute diverticulitis?. Intest Res. PMID 25349596.

D: Single group, Tx, N<100 analyzed

Kim, M. R.; Kye, B. H.; Kim, H. J.; Cho, H. M.; Oh, S. T.; Kim, J. G. Treatment of right colonic diverticulitis: the role of nonoperative treatment. J Korean Soc Coloproctol. PMID 21221240.

I: Surgery for acute diverticulitis

Kim, Y. C.; Chung, J. W.; Baek, J. H.; Lee, W. S.; Kim, D.; Park, Y. H.; Yang, J. Y.; Lee, W. K. Risk Factors for Recurrence of Right Colonic Diverticulitis. Dig Surg. PMID 30408791.

I: No specific intervention

King; W. C.; Shuaib; W.; Vijayasarathi; A.; Fajardo; C. G.; Cabrera; W. E.; Costa; J. L. Benefits of sonography in diagnosing suspected uncomplicated acute diverticulitis. J Ultrasound Med. PMID .

I: Diagnostic test, not CT or colonoscopy

Kircher, M. F.; Rhea, J. T.; Kihiczak, D.; Novelline, R. A. Frequency, sensitivity, and specificity of individual signs of diverticulitis on thin-section helical CT with colonic contrast material: experience with 312 cases. AJR Am J Roentgenol. PMID 12034590.

O: CT, No clinical or management outcomes

Kirchhoff, P.; Matz, D.; Dincler, S.; Buchmann, P. Predictive risk factors for intra- and postoperative complications in 526 laparoscopic sigmoid resections due to recurrent diverticulitis: a multivariate analysis. World J Surg. PMID 21184078.

D: Single group, Surgery, N<500 analyzed

Klarenbeek, B. R.; Bergamaschi, R.; Veenhof, A. A.; van der Peet, D. L.; van den Broek, W. T.; de Lange, E. S.; Bemelman, W. A.; Heres, P.; Lacy, A. M.; Cuesta, M. A. Laparoscopic versus open sigmoid resection for diverticular disease: follow-up assessment of the randomized control Sigma trial. Surg Endosc. PMID 20872022.

I: Surgery for acute diverticulitis

Klarenbeek, B. R.; Coupe, V. M.; van der Peet, D. L.; Cuesta, M. A. The cost effectiveness of elective laparoscopic sigmoid resection for symptomatic diverticular disease: financial outcome of the randomized control Sigma trial. Surg Endosc. PMID 20661750.

D: Single group, Surgery, N<500 analyzed

Klarenbeek, B. R.; Samuels, M.; van der Wal, M. A.; van der Peet, D. L.; Meijerink, W. J.; Cuesta, M. A. Indications for elective sigmoid resection in diverticular disease. Ann Surg. PMID 20224374.

D: No analysis of interest

Klarenbeek, B. R.; Veenhof, A. A.; Bergamaschi, R.; van der Peet, D. L.; van den Broek, W. T.; de Lange, E. S.; Bemelman, W. A.; Heres, P.; Lacy, A. M.; Engel, A. F.; Cuesta, M. A. Laparoscopic sigmoid resection for diverticulitis decreases major morbidity rates: a randomized control trial: short-term results of the Sigma Trial. Ann Surg. PMID 19106674.

I: Surgery for acute diverticulitis

Koo CH, Chang JHE, Syn NL, et al. Systematic Review and Meta-analysis on Colorectal Cancer Findings on Colonic Evaluation After CT-Confirmed Acute Diverticulitis. Diseases of the colon and rectum. 2020 May;63(5):701-9. doi: 10.1097/dcr.0000000000001664. PMID: 32271220. SR

Koo, V.; Strange, J.; Lam, C. Y.; Epanomeritakis, M. Young patients with diverticular disease: a preliminary quality of life study. Int J Surg. PMID 17660131.

D: NRCS, Tx, N<30/arm analyzed

Kotzampassakis, N.; Pittet, O.; Schmidt, S.; Denys, A.; Demartines, N.; Calmes, J. M. Presentation and treatment outcome of diverticulitis in younger adults: a different disease than in older patients?. Dis Colon Rectum. PMID 20173482.

O: No outcome (or harm) of interest

Krajicek EJ, Imperiale TF. Colonoscopy after acute diverticulitis: from clinical epidemiology to clinical management. Are we there yet? Gastrointest Endosc. 2020 Mar;91(3):641-2. doi: 10.1016/j.gie.2019.10.030. PMID: 32087901.

D: Not primary study or SR

Krokowicz, L.; Stojcev, Z.; Kaczmarek, B. F.; Kociemba, W.; Kaczmarek, E.; Walkowiak, J.; Krokowicz, P.; Drews, M.; Banasiewicz, T. Microencapsulated sodium butyrate administered to patients with diverticulosis decreases incidence of diverticulitis - A prospective randomized study. International Journal of Colorectal Disease. PMID .
P: Not colonic diverticulitis

Kruis. Two Doses Mesalazine Granules Versus Placebo for the Prevention of Recurrence of Diverticulitis.

<https://clinicaltrials.gov/show/nct01038739>. PMID Nct.

NCT: No results posted

Kruis. Mesalazine Granules vs. Placebo for the Prevention of Recurrence of Diverticulitis.

<https://clinicaltrials.gov/show/nct00695643>. PMID Nct.

NCT: No results posted

Kruis W.; Kardalinos V.; Curtin A.; Dorofeyev A. E.; Zakko S. F.; Wolkner J.; Diez Alonso M. M.; Peeters H.; Koutroubakis I. E.; Talley N. J.; et al. Daily mesalamine fails to prevent recurrent diverticulitis in a large placebo controlled multicenter trial. Gastroenterology. PMID AGA abstract.

Duplicate (no unique data)

Kruis W1, Meier E, Schumacher M, Mickisch O, Greinwald R, Mueller R; German SAG-20 Study Group. Randomised clinical trial: mesalazine (Salofalk granules) for uncomplicated diverticular disease of the colon--a placebo-controlled study. Aliment Pharmacol Ther. PMID 23414061.

I: Not intervention of interest (not KQ 1-4)

La Torre M, Mingoli A, Brachini G, et al. Differences between computed tomography and surgical findings in acute complicated diverticulitis. Asian J Surg. 2020 Mar;43(3):476-81. doi: 10.1016/j.asjsur.2019.07.016. PMID: 31439460.

O: CT, No clinical or management outcomes

Lahat, A.; Avidan, B.; Sakhnini, E.; Katz, L.; Fiddler, H. H.; Meir, S. B. Acute diverticulitis: a decade of prospective follow-up. J Clin Gastroenterol. PMID 23328302.

I: No specific intervention

Lahat, A.; Yanai, H.; Sakhnini, E.; Menachem, Y.; Bar-Meir, S. Role of colonoscopy in patients with persistent acute diverticulitis. World J Gastroenterol. PMID 18461662.

Colonoscopy single gp, N<200

Lahner, E.; Bellisario, C.; Hassan, C.; Zullo, A.; Esposito, G.; Annibale, B. Probiotics in the Treatment of Diverticular Disease. A Systematic Review. J Gastrointest Liver Dis. PMID 27014757.
O: No outcome (or harm) of interest

Lam T. J.; Meurs-Szojda M. M.; Gundlach L.; Belien J. A.; Meijer G. A.; Mulder C. J.; Felt-Bersma R. J. There is no increased risk for colorectal cancer and adenomas in patients with diverticulitis: a retrospective longitudinal study. Colorectal Dis.

PMID 19575738.

I: No specific intervention

Lamb, M. N.; Kaiser, A. M. Elective resection versus observation after nonoperative management of complicated diverticulitis with abscess: a systematic review and meta-analysis. *Dis Colon Rectum*. PMID 25380010.

SR

Lambrichts D. P. V.; Vennix S.; Musters G. D.; Mulder I. M.; Swank H. A.; Vermeulen J.; Van Dieren S.; Bemelman W. A.; Lange J. F. Hartmann's procedure or primary anastomosis for perforated diverticulitis with purulent or faecal peritonitis: results of the randomised ladies trial. *Surgical endoscopy*.

Not available

Lambrichts DPV, Vennix S, Musters GD, et al. Hartmann's procedure versus sigmoidectomy with primary anastomosis for perforated diverticulitis with purulent or faecal peritonitis (LADIES): a multicentre, parallel-group, randomised, open-label, superiority trial. *Lancet Gastroenterol Hepatol*. 2019 Aug;4(8):599-610. doi: 10.1016/s2468-1253(19)30174-8. PMID: 31178342.

I: Not intervention of interest (not KQ 1-4)

Lameris, W.; van Randen, A.; Bipat, S.; Bossuyt, P. M.; Boermeester, M. A.; Stoker, J. Graded compression ultrasonography and computed tomography in acute colonic diverticulitis: meta-analysis of test accuracy. *Eur Radiol*. PMID 18523784.

SR

Laqmani, A.; Veldhoen, S.; Dulz, S.; Derlin, T.; Behzadi, C.; Schmidt-Holtz, J.; Wassenberg, F.; Sehner, S.; Nagel, H. D.; Adam, G.; Regier, M. Reduced-dose abdominopelvic CT using hybrid iterative reconstruction in suspected left-sided colonic diverticulitis. *Eur Radiol*. PMID 26070499.

O: CT, No clinical or management outcomes

Larson, D. W.; Batdorf, N. J.; Touzios, J. G.; Cima, R. R.; Chua, H. K.; Pemberton, J. H.; Dozois, E. J. A fast-track recovery protocol improves outcomes in elective laparoscopic colectomy for diverticulitis. *J Am Coll Surg*. PMID 20822739.

D: Single group, Surgery, N<500 analyzed

Le Moine, M. C.; Fabre, J. M.; Vacher, C.; Navarro, F.; Picot, M. C.; Domergue, J. Factors and consequences of conversion in laparoscopic sigmoidectomy for diverticular disease. *Br J Surg*. PMID 12555302.

D: Single group, Surgery, N<500 analyzed

Le Neel J. C.; Denimal F.; Letessier E.; Bernard P.; Jurczak F.; Armstrong O. Complicated colonic diverticulosis. Results of surgical treatment between 1981 and 1998 in 370 patients. *Ann Chir*. PMID 10900734.

Duplicate (no unique data)

Le Neel, J. C.; Denimal, F.; Letessier, E.; Bernard, P.; Jurczak, F.; Armstrong, O. [Complicated colonic diverticulosis. Results of surgical treatment between 1981 and 1998 in 370 patients]. *Ann Chir*. PMID 10900734.

D: Single group, Surgery, N<500 analyzed

Lee, I. K.; Jung, S. E.; Gorden, D. L.; Lee, Y. S.; Jung, D. Y.; Oh, S. T.; Kim, J. G.; Jeon, H. M.; Chang, S. K. The diagnostic criteria for right colonic diverticulitis: prospective evaluation of 100 patients. *Int J Colorectal Dis*. PMID 18704462.

O: CT, No clinical or management outcomes

Leicht W.; Thomas C.; Thüroff J.; Roos F. Colovesical fistula caused by diverticulitis of the sigmoid colon: diagnosis and treatment. *Urologe A*. PMID 22772496.

Duplicate (no unique data)

Leicht, W.; Thomas, C.; Thüroff, J.; Roos, F. [Colovesical fistula caused by diverticulitis of the sigmoid colon: diagnosis and treatment]. *Urologe A*. PMID 22772496.

D: Single group, Tx, N<100 analyzed

Leicht, W.; Thomas, C.; Thüroff, J.; Roos, F. Kolovesikaler Fisteln auf dem Boden einer Sigmadivertikulitis : Diagnose und Therapie. *Der Urologe A*. PMID .

Duplicate (no unique data)

Levack, M. M.; Savitt, L. R.; Berger, D. L.; Shellito, P. C.; Hodin, R. A.; Rattner, D. W.; Goldberg, S. M.; Bordeianou, L. Sigmoidectomy syndrome? Patients' perspectives on the functional outcomes following surgery for diverticulitis. *Dis Colon Rectum*. PMID 22156862.

I: Surgery for acute diverticulitis

Levack, M.; Berger, D.; Sylla, P.; Rattner, D.; Bordeianou, L. Laparoscopy decreases anastomotic leak rate in sigmoid colectomy for diverticulitis. *Arch Surg*. PMID 21339434.

D: Single group, Surgery, N<500 analyzed

Li, D.; Baxter, N. N.; McLeod, R. S.; Moineddin, R.; Nathens, A. B. The Decline of Elective Colectomy Following Diverticulitis: A Population-Based Analysis. *Dis Colon Rectum*. PMID 26953992.

O: Single arm study without harms data

Li, D.; de Mestral, C.; Baxter, N. N.; McLeod, R. S.; Moineddin, R.; Wilton, A. S.; Nathens, A. B. Risk of readmission and emergency surgery following nonoperative management of colonic diverticulitis: a population-based analysis. *Ann Surg*. PMID 25115418.

I: No specific intervention

Lidor, A. O.; Segal, J. B.; Wu, A. W.; Yu, Q.; Feinberg, R.; Schneider, E. B. Older patients with diverticulitis have low recurrence rates and rarely need surgery. *Surgery*. PMID 21801956.

I: Not intervention of interest (not KQ 1-4)

Liljegren, G.; Chabok, A.; Wickbom, M.; Smedh, K.; Nilsson, K. Acute colonic diverticulitis: a systematic review of diagnostic accuracy. *Colorectal Dis*. PMID 17573739.

SR

Lips, L. M.; Cremers, P. T.; Pickhardt, P. J.; Cremers, S. E.; Janssen-Heijnen, M. L.; de Witte, M. T.; Simons, P. C. Sigmoid cancer versus chronic diverticular disease: differentiating features at CT colonography. *Radiology*. PMID 25426771.

P: Not colonic diverticulitis

Lipscomb, G.; Loughrey, G.; Thakker, M.; Rees, W.; Nicholson, D. A prospective study of abdominal computerized tomography and colonoscopy in the diagnosis of colonic disease in an elderly population. *Eur J Gastroenterol Hepatol*. PMID 8889456.

Not available

Lohrmann, C.; Ghanem, N.; Pache, G.; Makowiec, F.; Kotter, E.; Langer, M. CT in acute perforated sigmoid diverticulitis. *Eur J Radiol*. PMID 16168267.

I: No specific intervention

Longstreth, G. F.; Iyer, R. L.; Chu, L. H.; Chen, W.; Yen, L. S.; Hodgkins, P.; Kawatkar, A. A. Acute diverticulitis: demographic, clinical and laboratory features associated with computed tomography findings in 741 patients. *Aliment Pharmacol Ther*. PMID 22967027.

I: Not intervention of interest (not KQ 1-4)

Lopez-Borao, J.; Kreisler, E.; Millan, M.; Trenti, L.; Jaurrieta, E.; Rodriguez-Moranta, F.; Miguel, B.; Biondo, S. Impact of age on recurrence and severity of left colonic diverticulitis. *Colorectal Dis*. PMID 22321968.

I: No specific intervention

Lu, C. T.; Ho, Y. H. Elective laparoscopic surgical management of recurrent and complicated sigmoid diverticulitis. *Tech Coloproctol*. PMID .

D: Single group, Tx, N<100 analyzed

Lutkov I. V. Evaluation of alpha-normiks (rifaximin) efficacy in the treatment of patients with diverticular disease associated with medium and severe intestinal dysbacteriosis. *Eksp Klin Gastroenterol*. PMID 19552027.

Not available

Luu, L. H.; Vuong, N. L.; Yen, V. T. H.; Phuong, D. T. T.; Vu, B. K.; Thanh, N. V.; Khanh, N. T.; Van Hai, N. Laparoscopic diverticulectomy versus non-operative treatment for uncomplicated right colonic diverticulitis. *Surg Endosc*. PMID 31309310.

I: Surgery for acute diverticulitis

MacKersie A. B.; Lane M. J.; Gerhardt R. T.; Claypool H. A.; Keenan S.; Katz D. S.; Tucker J. E. Nontraumatic acute abdominal pain: unenhanced helical CT compared with three-view acute abdominal series. *Radiology*. PMID 16183928.

D: CT or colonoscopy, N<100 (had CT/colonoscopy) analyzed

Magdeburg, J.; Glatz, N.; Post, S.; Kienle, P.; Rickert, A. Long-term functional outcome of colonic resections: how much does faecal impairment influence quality of life?. *Colorectal Dis*. PMID 27647736.

I: Surgery for acute diverticulitis

Maggard, M. A.; Chandler, C. F.; Schmit, P. J.; Bennion, R. S.; Hines, O. J.; Thompson, J. E. Surgical diverticulitis: treatment options. *Am Surg*. PMID 11768827.

I: Surgery for acute diverticulitis

Makela, J. T.; Kiviniemi, H. O.; Laitinen, S. T. Elective surgery for recurrent diverticulitis. *Hepatogastroenterology*. PMID 17708266.

Not available

Mäkelä JT, Klintrup K, Rautio T. The role of low CRP values in the prediction of the development of acute diverticulitis. *International journal of colorectal disease*. 2016 Jan;31(1):23-7. doi: 10.1007/s00384-015-2410-8. PMID: 26519151.

O: CT, No clinical or management outcomes

Mäkelä JT, Klintrup K, Takala H, et al. The role of C-reactive protein in prediction of the severity of acute diverticulitis in an emergency unit.

Scandinavian journal of gastroenterology. 2015

May;50(5):536-41. doi:

10.3109/00365521.2014.999350. PMID: 25665622.

O: CT, No clinical or management outcomes

Mali, J. P.; Mentula, P. J.; Leppaniemi, A. K.; Sallinen, V. J. Symptomatic Treatment for Uncomplicated Acute Diverticulitis: A Prospective Cohort Study. *Dis Colon Rectum*. PMID 27145310.

I: No specific intervention

Mantovani, G.; Volpe, E.; Soardi, G. A.; Merizzi, R.; Laveneziana, M. S.; Imperio, S.; Rossetti, G. [Ultrasonography in acute diverticulitis of the colon: semiologic features]. *Radiol Med*. PMID 9045242.
Not available

Marasco G, Verardi FM, Eusebi LH, et al. Diagnostic imaging for acute abdominal pain in an Emergency Department in Italy. *Intern Emerg Med*. 2019 Oct;14(7):1147-53. doi: 10.1007/s11739-019-02189-y. PMID: 31493199.

O: CT, No clinical or management outcomes

Marshall, J. R.; Buchwald, P. L.; Gandhi, J.; Schultz, J. K.; Hider, P. N.; Frizelle, F. A.; Eglinton, T. W. Laparoscopic Lavage in the Management of Hinchey Grade III Diverticulitis: A Systematic Review. *Ann Surg*. PMID 27631772.

SR

Martel, G.; Bouchard, A.; Soto, C. M.; Poulin, E. C.; Mamazza, J.; Boushey, R. P. Laparoscopic colectomy for complex diverticular disease: a justifiable choice?. *Surg Endosc*. PMID 20186433.

D: Single group, Surgery, N<500 analyzed

Martin Arevalo J.; Garcia-Granero E.; Garcia Botello S.; Munoz E.; Cervera V.; Flor Lorente B.; Lledo S. Early use of CT in the management of acute diverticulitis of the colon. *Rev Esp Enferm Dig*. PMID 17883294.

Duplicate (no unique data)

Mathews SN, Lamm R, Yang J, et al. Factors Associated with Repeated Health Resource Utilization in Patients with Diverticulitis. *Journal of gastrointestinal surgery : official journal of the Society for Surgery of the Alimentary Tract*. 2017 Jan;21(1):112-20. doi: 10.1007/s11605-016-3245-5. PMID: 27613732.

I: No specific intervention

Matsushima, K. Management of right-sided diverticulitis: A retrospective review from a hospital in Japan. *Surg Today*. PMID 20339986.

O: Single arm study without harms data

McCarthy C, Cavallaro P, Mueller P, et al. Percutaneous management of acute diverticulitis: multi-institutional study of 401 patients. *Journal of Vascular and Interventional Radiology*. 2019;30(3):S234.

O: No outcome (or harm) of interest

McDermott, F. D.; Collins, D.; Heeney, A.; Winter, D. C. Minimally invasive and surgical management strategies tailored to the severity of acute diverticulitis. *Br J Surg*. PMID 24258427.

SR

Medina-Fernandez, F. J.; Rodriguez-Ortiz, L.; Garcilazo-Arismendi, D. J.; Navarro-Rodriguez, E.; Torres-Tordera, E. M.; Diaz-Lopez, C. A.; Briceno, J. Impact of barium enema on acute diverticulitis recurrence: A retrospective cohort study of 349 patients. *J Dig Dis*. PMID 28548239.

I: Not intervention of interest (not KQ 1-4)

Mege, D.; Yeo, H. Meta-analyses of Current Strategies to Treat Uncomplicated Diverticulitis. *Dis Colon Rectum*. PMID 30570549.

SR

Melchior, S.; Cudovic, D.; Jones, J.; Thomas, C.; Gillitzer, R.; Thuroff, J. Diagnosis and surgical management of colovesical fistulas due to sigmoid diverticulitis. *J Urol*. PMID 19616793.

O: CT, No clinical or management outcomes

Meyer, J.; Orci, L. A.; Combescure, C.; Balaphas, A.; Morel, P.; Buchs, N. C.; Ris, F. Risk of Colorectal Cancer in Patients With Acute Diverticulitis: A Systematic Review and Meta-Analysis of Observational Studies. *Clin Gastroenterol Hepatol*. PMID 30056181.

SR

Milone, M.; Campana, G.; Bianco, P.; Musella, M.; Milone, F. Laparoscopic sigmoidectomy for complicated diverticulitis: a modified caudal-to-cranial approach and preliminary results in a single-center experience. *Int J Colorectal Dis*. PMID 26519148.

I: Surgery for acute diverticulitis

Min Ju; Kim Hyun; Kim Sang; Yang Dal; Rhee Sun; Oh Jiyoung; Ahn Sung; Min Ju Hwa; Kim Hyun Cheol; Kim Sang Won; Yang Dal Mo; Rhee Sun Jung; Ahn Sung Eun. The value of initial sonography compared to supplementary CT for diagnosing right-sided colonic diverticulitis. *Japanese Journal of Radiology*. PMID 28488205.

O: CT, No clinical or management outcomes

Minardi, A. J., Jr.; Johnson, L. W.; Sehon, J. K.; Zibari, G. B.; McDonald, J. C. Diverticulitis in the young patient. *Am Surg*. PMID 11379649.

I: No specific intervention

Mirza A.; Arumugam D.; Pannu A.; Hajibandeh S. Laparoscopic peritoneal lavage versus sigmoidectomy for management of perforated diverticulitis: meta-analysis of randomized controlled trials. *Surgical endoscopy and other interventional techniques*.

Not available

Miyagaki, H.; Rhee, R.; Shantha Kumara, H. M.; Yan, X.; Njoh, L.; Cekic, V.; Whelan, R. L. Surgical Treatment of Diverticulitis: Hand-Assisted

Laparoscopic Resection Is Predominantly Used for Complex Cases and Is Associated With Increased Postoperative Complications and Prolonged Hospitalization. *Surg Innov*. PMID 26611789.

I: Surgery for acute diverticulitis

Mizrahi, I.; Al-Kurd, A.; Chapchay, K.; Ag-Rejuan, Y.; Simanovsky, N.; Eid, A.; Mazeh, H. Long-term outcomes of sigmoid diverticulitis: a single-center experience. *J Surg Res*. PMID 29229157.

D: Single group, Surgery, N<500 analyzed

Mizuki A.; Nagata H.; Tatemichi M.; Kaneda S.; Tsukada N.; Ishii H.; Hibi T. The out-patient management of patients with acute mild-to-moderate colonic diverticulitis. *Aliment Pharmacol Ther*. PMID 15801924.

D: Single group, Tx, N<100 analyzed

Mocanu, V.; Dang, J. T.; Switzer, N.; Tavakoli, I.; Tian, C.; de Gara, C.; Birch, D. W.; Karmali, S. The role of antibiotics in acute uncomplicated diverticulitis: A systematic review and meta-analysis. *Am J Surg*. PMID 29454479.

SR

Moll R.; Mittelkotter U.; Reith H. B.; Schindler G.; Thiede A. Which imaging in case of sigmoid diverticulitis? The value of ultrasound (Conventional B-mode in combination with hydrocolonosonography and colour flow Doppler) in comparison to the well-established modalities like contrast enema and helical computertomography. *Zentralbl Chir*. PMID 12085279.

O: CT, No clinical or management outcomes

Moll, R.; Mittelkotter, U.; Reith, H. B.; Schindler, G.; Thiede, A. [Which imaging in case of sigmoid diverticulitis? The value of ultrasound (Conventional B-mode in combination with hydrocolonosonography and colour flow Doppler) in comparison to the well-established modalities like contrast enema and helical computertomography]. *Zentralbl Chir*. PMID 12085279.

Duplicate (no unique data)

Moloney, F.; James, K.; Twomey, M.; Ryan, D.; Grey, T. M.; Downes, A.; Kavanagh, R. G.; Moore, N.; Murphy, M. J.; Bye, J.; Carey, B. W.; McSweeney, S. E.; Deasy, C.; Andrews, E.; Shanahan, F.; Maher, M. M.; O'Connor, O. J. Low-dose CT imaging of the acute abdomen using model-based iterative reconstruction: a prospective study. *Emerg Radiol*. PMID 30448900.

D: CT or colonoscopy, N<100 (had CT/colonoscopy) analyzed

Moniuszko A, Rydzewska G. The effect of cyclic rifaximin therapy on symptoms of diverticular

disease from the perspective of the gastroenterology outpatient clinic: a "real-life" study. *Prz Gastroenterol*. 2017;12(2):145-51. doi:

10.5114/pg.2017.68167. PMID: 28702105.

P: Not colonic diverticulitis

Moon, H. J.; Park, J. K.; Lee, J. I.; Lee, J. H.; Shin, H. J.; Kim, W. S.; Kim, M. S.; Jeong, J. H.

Conservative treatment for patients with acute right colonic diverticulitis. *Am Surg*. PMID 18186379.

I: No specific intervention

Mora Lopez L.; Serra Pla S.; Serra-Aracil X.; Ballesteros E.; Navarro S. Application of a modified Neff classification to patients with uncomplicated diverticulitis. *Colorectal Dis*. PMID 24192258.

O: CT, No clinical or management outcomes

Mora Lopez, L.; Flores Clotet, R.; Serra Aracil, X.; Montes Ortega, N.; Navarro Soto, S. The use of the modified Neff classification in the management of acute diverticulitis. *Rev Esp Enferm Dig*. PMID 28376628.

I: Diagnostic test, not CT or colonoscopy

Mora Lopez, L.; Ruiz-Edo, N.; Serra Pla, S.; Pallisera Llovera, A.; Navarro Soto, S.; Serra-Aracil, X. Multicentre, controlled, randomized clinical trial to compare the efficacy and safety of ambulatory treatment of mild acute diverticulitis without antibiotics with the standard treatment with antibiotics. *Int J Colorectal Dis*. PMID .

D: NRCS, Tx, Crude analyses only

Mortensen LQ, Burcharth J, Andresen K, et al. An 18-Year Nationwide Cohort Study on The Association Between Diverticulitis and Colon Cancer. *Annals of surgery*. 2017 May;265(5):954-9. doi: 10.1097/sla.0000000000001794. PMID: 27192351.

I: Not intervention of interest (not KQ 1-4)

Moya, P.; Bellon, M.; Arroyo, A.; Galindo, I.; Candela, F.; Lacueva, J.; Calpena, R. Outpatient treatment in uncomplicated acute diverticulitis: 5-year experience. *Turk J Gastroenterol*. PMID .

O: Single arm study without harms data

Mueller, M. H.; Glatzle, J.; Kasperek, M. S.; Becker, H. D.; Jehle, E. C.; Zittel, T. T.; Kreis, M. E. Long-term outcome of conservative treatment in patients with diverticulitis of the sigmoid colon. *Eur J Gastroenterol Hepatol*. PMID 15879727.

D: Intervention <1990

Munson, K. D.; Hensien, M. A.; Jacob, L. N.; Robinson, A. M.; Liston, W. A. Diverticulitis. A comprehensive follow-up. *Dis Colon Rectum*. PMID 8603555.

I: No specific intervention

Muscari; F.; Suc; B.; Msika; S.; Hay; J. M.; Flamant; Y.; Fourtanier; G.; Guller; U.; Lorimier; G.; Dziri; C.; Fingerhut; A. Surgeon-dependent predictive factors for mortality after elective colorectal resection and immediate anastomosis for cancer or nonacute diverticular disease: multivariable analysis of 2,605 patients. *J Am Coll Surg*. PMID 19183536.

P: Not colonic diverticulitis

Musters Gijsbert D.; Swank Hilko A.; Boermeester Marja A.; Bemelman Willem A.; Vennix Sandra; Kruij Philip M.; Nienhuijs Simon W.; Vermeulen Jeffrey; van Dieren Susan; Mulder Irene M.; Lange Johan F.; Consten Esther C.; Belgers Eric H.; van Geloven Anna A.; Gerhards Michael F.; Govaert Marc J.; van Grevenstein Wilhelmina M.; Hoofwijk Anton G. Laparoscopic peritoneal lavage or sigmoidectomy for perforated diverticulitis with purulent peritonitis: a multicentre, parallel-group, randomised, open-label trial. *Lancet*. PMID 26209030.

I: Not intervention of interest (not KQ 1-4)

Nct. Mesalamine for Uncomplicated Diverticular Disease: a Randomized, Double-blind, Placebo-controlled Study.

<https://clinicaltrials.gov/show/nct01627262>.

I: Not intervention of interest (not KQ 1-4)

Nct. A Multicentre, Randomized as a Double Blind Study, Triple Placebo, Comparative of the Efficacy and Safety of an Association Secnidazol-Ciprofloxacin Compared With Amoxicillin-Clavulanic Acid for the Treatment of Uncomplicated Episode of Diverticular Sigmoiditis Among Adults. <https://clinicaltrials.gov/show/nct01733966>.

NCT: No results posted

Nct. Hospitalization or Ambulatory Treatment of Acute Diverticulitis.

<https://clinicaltrials.gov/show/nct01081054>.

NCT: No results posted

Nct. Mechanistic Randomized Controlled Trial (RCT) of Mesalazine in Symptomatic Diverticular Disease. <https://clinicaltrials.gov/show/nct00663247>.

NCT: No results posted

Nct. Rifamycin SV-MMX® 400 mg b.i.d. vs. Rifamycin SV-MMX® 600 mg t.i.d. vs. Placebo in Acute Uncomplicated Diverticulitis.

<https://clinicaltrials.gov/show/nct01847664>.

NCT: No results posted

Nct. Rifaximin Delayed Release for the Prevention of Recurrent Acute Diverticulitis and Diverticular Complications.

<https://clinicaltrials.gov/show/nct03469050>.

NCT: No results posted

Nct. Study to Evaluate the Duration of Treatment With Ertapenem in Acute Attacks of Sigmoid Diverticulitis.

<https://clinicaltrials.gov/show/nct00097734>.

NCT: No results posted

Nelson, R. S.; Ewing, B. M.; Wengert, T. J.; Thorson, A. G. Clinical outcomes of complicated diverticulitis managed nonoperatively. *Am J Surg*. PMID 19095117.

I: Surgery for acute diverticulitis

Nelson, R. S.; Velasco, A.; Mukesh, B. N. Management of diverticulitis in younger patients. *Dis Colon Rectum*. PMID 16897326.

I: Surgery for acute diverticulitis

Ng C. S.; Watson C. J.; Palmer C. R.; See T. C.; Beharry N. A.; Housden B. A.; Bradley J. A.; Dixon A. K. Evaluation of early abdominopelvic computed tomography in patients with acute abdominal pain of unknown cause: prospective randomised study. *Bmj*. PMID 12480851.

P: Not colonic diverticulitis

Ng; Z. Q.; Moe; K. S.; Wijesuriya; R. Routine Colonoscopy After Acute Diverticulitis: is it Warranted?. *Surg Laparosc Endosc Percutan Tech*. PMID 31107852.

Colonoscopy single gp, N<200

Ng ZQ, Wijesuriya R, Misur P, et al. The role of quantitative radiological measures of visceral adiposity in diverticulitis. *Surgical endoscopy*. 2020 Feb 18. doi: 10.1007/s00464-020-07427-5. PMID: 32072285.

I: Not intervention of interest (not KQ 1-4)

Nguyen, L. K.; Wong, D. D.; Fatovich, D. M.; Yeung, J. M.; Persaud, J.; Wood, C. J.; de Vos, D.; Mendelson, R. M. Low-dose computed tomography versus plain abdominal radiography in the investigation of an acute abdomen. *ANZ J Surg*. PMID 22507493.

D: CT or colonoscopy, N<100 (had CT/colonoscopy) analyzed

Nicholson, B. D.; Hyland, R.; Rembacken, B. J.; Denyer, M.; Hull, M. A.; Tolan, D. J. Colonoscopy for colonic wall thickening at computed tomography: a worthwhile pursuit?. *Surg Endosc*. PMID 21359889.

D: Single group, Tx, N<100 analyzed

Niebling, M.; van Nunspeet, L.; Zwaving, H.; Eddes, E. H.; Bosker, R.; Eeftinck Schattenkerk, M. Management of colovesical fistulae caused by diverticulitis: 12 years of experience in one medical centre. *Acta Chir Belg*. PMID 23550466.

D: Single group, Tx, N<100 analyzed

Nielsen, K.; Richir, M. C.; Stolk, T. T.; van der Ploeg, T.; Moormann, G. R.; Wiarda, B. M.; Schreurs, W. H. The limited role of ultrasound in the diagnostic process of colonic diverticulitis. *World J Surg*. PMID 24366280.

I: Diagnostic test, not CT or colonoscopy

Occhionorelli, S.; Zese, M.; Tartarini, D.; Lacavalla, D.; Maccatrozzo, S.; Groppo, G.; Sibilla, M. G.; Stano, R.; Cappellari, L.; Vasquez, G. An approach to complicated diverticular disease. A retrospective study in an Acute Care Surgery service recently established. *Ann Ital Chir*. PMID 27830672.

I: No specific intervention

Oomen, J. L.; Engel, A. F.; Cuesta, M. A. Outcome of elective primary surgery for diverticular disease of the sigmoid colon: a risk analysis based on the POSSUM scoring system. *Colorectal Dis*. PMID 16412067.

D: Single group, Surgery, N<500 analyzed

Ou, G.; Rosenfeld, G.; Brown, J.; Chan, N.; Hong, T.; Lim, H.; Bressler, B. Colonoscopy after CT-diagnosed acute diverticulitis: Is it really necessary?. *Can J Surg*. PMID 26022155.

Colonoscopy single gp, N<200

Özdemir O.; Metin Y.; Taşçi F.; Metin N.O.; Bilir Ö, Yavaş, Küpeli A. Added value of diffusion-weighted MR imaging to non-enhanced CT in the evaluation of acute abdominopelvic pain. *Biomedical Research (India)*.

I: Diagnostic test, not CT or colonoscopy

Padidar, A. M.; Jeffrey, R. B., Jr.; Mindelzun, R. E.; Dolph, J. F. Differentiating sigmoid diverticulitis from carcinoma on CT scans: mesenteric inflammation suggests diverticulitis. *AJR Am J Roentgenol*. PMID 8010253.

D: CT of prediagnosed groups

Panghaal, V. S.; Chernyak, V.; Patlas, M.; Rozenblit, A. M. CT features of adnexal involvement in patients with diverticulitis. *AJR Am J Roentgenol*. PMID 19304701.

D: NRCS, Tx, N<30/arm analyzed

Pappalardo, G.; Frattaroli, F. M.; Coiro, S.; Spolentini, D.; Nunziale, A.; Favella, L.; Vestri, A. R.; Gualdi, G. F.; Casciani, E.; Mobarhan, S. Effectiveness of clinical guidelines in the management of acute sigmoid diverticulitis. Results of a prospective diagnostic and therapeutic clinical trial. *Ann Ital Chir*. PMID 23697994.

O: No outcome (or harm) of interest

Parisi, A.; Gemini, A.; Desiderio, J.; Petrino, A.; Trastulli, S.; Grassi, V.; Sani, M.; Pironi, D.; Santoro, A. Laparoscopic peritoneal lavage: our experience

and review of the literature. *Wideochir Inne Tech Maloinwazyjne*. PMID 27458487.

I: Surgery for acute diverticulitis

Park, H. C.; Chang, M. Y.; Lee, B. H. Nonoperative management of right colonic diverticulitis using radiologic evaluation. *Colorectal Dis*. PMID 19016818.

O: Single arm study without harms data

Park, H. C.; Kim, B. S.; Lee, B. H. Management of right colonic uncomplicated diverticulitis: outpatient versus inpatient management. *World J Surg*. PMID 21409607.

D: NRCS, Tx, Crude analyses only

Park, H. C.; Lee, B. H. Suspected uncomplicated cecal diverticulitis diagnosed by imaging: initial antibiotics vs laparoscopic treatment. *World J Gastroenterol*. PMID 20939115.

D: NRCS, Tx, Crude analyses only

Park, S. J.; Choi, S. I.; Lee, S. H.; Lee, K. Y. Image-guided conservative management of right colonic diverticulitis. *World J Gastroenterol*. PMID 19998506.

O: Single arm study without harms data

Park, S. M.; Kwon, T. S.; Kim, D. J.; Lee, Y. S.; Cheung, D. Y.; Oh, S. T.; Kim, J. G.; Lee, I. K. Prediction and management of recurrent right colon diverticulitis. *Int J Colorectal Dis*. PMID 24997717.

O: Single arm study without harms data

Park, H. C.; Kim, B. S.; Lee, K.; Kim, M. J.; Lee, B. H. Risk factors for recurrence of right colonic uncomplicated diverticulitis after first attack. *Int J Colorectal Dis*. PMID .

I: No specific intervention

Pasternak, I.; Wiedemann, N.; Basilicata, G.; Melcher, G. A. Gastrointestinal quality of life after laparoscopic-assisted sigmoidectomy for diverticular disease. *Int J Colorectal Dis*. PMID 22200793.

O: Single arm study without harms data

Patel R, Zagadailov P, Merchant AM. Laparoscopic colectomy for diverticulitis in patients with pre-operative respiratory comorbidity: analysis of post-operative outcomes in the United States from 2005 to 2017. *Surgical endoscopy*. 2020 Apr;34(4):1665-77. doi: 10.1007/s00464-019-06943-3. PMID: 31286256.

I: Not intervention of interest (not KQ 1-4)

Pautrat, K.; Bretagnol, F.; Hutten, N.; de Calan, L. Acute diverticulitis in very young patients: a frequent surgical management. *Dis Colon Rectum*. PMID 17164966.

I: No specific intervention

Pecere S, Gibiino G, La Milia DI, et al. Acute uncomplicated diverticulitis: key points for early management. A single-centre retrospective study. *Eur Rev Med Pharmacol Sci*. 2020 Mar;24(5):2710-8. doi: 10.26355/eurrev_202003_20543. PMID: 32196622.

D: NRCS, Tx, Crude analyses only

Pendlimari, R.; Touzios, J. G.; Azodo, I. A.; Chua, H. K.; Dozois, E. J.; Cima, R. R.; Larson, D. W. Short-term outcomes after elective minimally invasive colectomy for diverticulitis. *Br J Surg*. PMID 21254022.

I: Surgery for acute diverticulitis

Penna, M.; Markar, S. R.; Mackenzie, H.; Hompes, R.; Cunningham, C. Laparoscopic Lavage Versus Primary Resection for Acute Perforated Diverticulitis: Review and Meta-analysis. *Ann Surg*. PMID 28338510.

SR

Peppas, G.; Bliziotis, I. A.; Oikonomaki, D.; Falagas, M. E. Outcomes after medical and surgical treatment of diverticulitis: a systematic review of the available evidence. *J Gastroenterol Hepatol*. PMID 17716342.

SR

Pereira F, Linhares M, Tristan J, et al. A selective approach for colonoscopy after acute diverticulitis. *Ann Gastroenterol*. 2020 Mar-Apr;33(2):222. doi: 10.20524/aog.2020.0461. PMID: 32127747.

Colonoscopy single gp, N<200

Petruzzello, C.; Migneco, A.; Cardone, S.; Covino, M.; Saviano, A.; Franceschi, F.; Ojetti, V. Supplementation with *Lactobacillus reuteri* ATCC PTA 4659 in patients affected by acute uncomplicated diverticulitis: a randomized double-blind placebo controlled trial. *Int J Colorectal Dis*. PMID 31011868.

D: Single group, Tx, N<100 analyzed

Pistoia, M. A.; Lombardi, L.; Rossi, M.; Vittorini, C.; Cavaliere, G. F.; Pistoia, F. Does rifaximin prevent complications of diverticular disease? A retrospective study. *Eur Rev Med Pharmacol Sci*. PMID 15745388.

P: Not colonic diverticulitis

Pittet, O.; Kotzampassakis, N.; Schmidt, S.; Denys, A.; Demartines, N.; Calmes, J. M. Recurrent left colonic diverticulitis episodes: more severe than the initial diverticulitis?. *World J Surg*. PMID 19148697.

O: Single arm study without harms data

Polese, L.; Bressan, A.; Savarino, E.; Vecchiato, M.; Turollo, A.; Frigo, A.; Sturniolo, G. C.; De Manzini, N.; Petri, R.; Merigliano, S. Quality of life after laparoscopic sigmoid resection for uncomplicated

diverticular disease. *Int J Colorectal Dis*. PMID 29525902.

O: Single arm study without harms data

Poletti, P. A.; Platon, A.; Rutschmann, O.; Kinkel, K.; Nyikus, V.; Ghiorghiu, S.; Morel, P.; Terrier, F.; Becker, C. D. Acute left colonic diverticulitis: can CT findings be used to predict recurrence?. *AJR Am J Roentgenol*. PMID 15100111.

I: Not intervention of interest (not KQ 1-4)

Pomazkin, V. I.; Khodakov, V. V. Long-term results of surgical treatment of diverticular disease of colon. *Vestn Khir Im I I Grek*. PMID 30427159.

D: No analysis of interest

Porta, E.; Germano, A.; Ferrieri, A.; Koch, M. The natural history of diverticular disease of the colon: a role for antibiotics in preventing complications? A retrospective study. *Riv Eur Sci Med Farmacol*. PMID 7761680.

Not available

Pradel, J. A.; Adell, J. F.; Taourel, P.; Djafari, M.; Monnin-Delhom, E.; Bruel, J. M. Acute colonic diverticulitis: prospective comparative evaluation with US and CT. *Radiology*. PMID 9356636.

O: CT, No clinical or management outcomes

Priola, A. M.; Priola, S. M.; Volpicelli, G.; Giraudo, M. T.; Martino, V.; Fava, C.; Veltri, A. Accuracy of 64-row multidetector CT in the diagnosis of surgically treated acute abdomen. *Clin Imaging*. PMID 23764231.

O: CT, No clinical or management outcomes

Proposito D.; Hidalgo M.; Rubio de Molina J.; Ibanez Cabeza E.; Negro P.; Carboni M. Diverticular disease. Our experience. *Rev Esp Enferm Dig*. PMID 9004782.

Duplicate (no unique data)

Proposito, D.; Hidalgo, M.; Rubio de Molina, J.; Ibanez Cabeza, E.; Negro, P.; Carboni, M. [Diverticular disease. Our experience]. *Rev Esp Enferm Dig*. PMID 9004782.

D: Intervention <1990

Purkayastha, S.; Constantinides, V. A.; Tekkis, P. P.; Athanasiou, T.; Aziz, O.; Tilney, H.; Darzi, A. W.; Heriot, A. G. Laparoscopic vs. open surgery for diverticular disease: a meta-analysis of nonrandomized studies. *Dis Colon Rectum*. PMID 16534656.

SR

Ramesh J.; Bang J. Y.; Trevino J.; Varadarajulu S. Comparison of outcomes between endoscopic ultrasound-guided transcolonic and transrectal drainage of abdominopelvic abscesses. *J*

Gastroenterol Hepatol. PMID 23215873.

D: Single group, Tx, N<100 analyzed

Rao, P. M.; Rhea, J. T. Colonic diverticulitis: evaluation of the arrowhead sign and the inflamed diverticulum for CT diagnosis. Radiology. PMID 9844673.

O: CT, No clinical or management outcomes

Rao, P. M.; Rhea, J. T.; Novelline, R. A.; Dobbins, J. M.; Lawrason, J. N.; Sacknoff, R.; Stuk, J. L. Helical CT with only colonic contrast material for diagnosing diverticulitis: prospective evaluation of 150 patients. AJR Am J Roentgenol. PMID 9609151.

O: CT, No clinical or management outcomes

Raue, W.; Paolucci, V.; Asperger, W.; Albrecht, R.; Buchler, M. W.; Schwenk, W. Laparoscopic sigmoid resection for diverticular disease has no advantages over open approach: midterm results of a randomized controlled trial. Langenbecks Arch Surg. PMID 21779829.

D: Single group, Surgery, N<500 analyzed

Regenbogen, S. E.; Hardiman, K. M.; Hendren, S.; Morris, A. M. Surgery for diverticulitis in the 21st century: a systematic review. JAMA Surg. PMID 24430164.

SR

Reginelli A.; Russo A.; Pinto A.; Stanzione F.; Martiniello C.; Cappabianca S.; Brunese L.; Squillaci E. The role of computed tomography in the preoperative assessment of gastrointestinal causes of acute abdomen in elderly patients. Int J Surg. PMID 25157993.

D: Not primary study or SR

Reibetanz, J.; Germer, C. T. [Does the routine colonoscopy after acute sigmoid colon diverticulitis make sense? : Results of a meta-analysis]. Chirurg. PMID 24696318.

D: Not primary study or SR

Reissfelder, C.; Buhr, H. J.; Ritz, J. P. What is the optimal time of surgical intervention after an acute attack of sigmoid diverticulitis: early or late elective laparoscopic resection?. Dis Colon Rectum. PMID 17036202.

D: No analysis of interest

Reissfelder, C.; Buhr, H. J.; Ritz, J. P. Can laparoscopically assisted sigmoid resection provide uncomplicated management even in cases of complicated diverticulitis?. Surg Endosc. PMID 16736310.

D: Single group, Surgery, N<500 analyzed

Reznitsky P. A.; Yartsev P. A.; Shavrina N. V. Treatment of inflammatory complications of colic

diverticular disease at the emergency surgical care hospital. Khirurgiia (Mosk). PMID 28805779.

Duplicate (no unique data)

Reznitsky, P. A.; Yartsev, P. A.; Shavrina, N. V. [Treatment of inflammatory complications of colic diverticular disease at the emergency surgical care hospital]. Khirurgiia (Mosk). PMID 28805779.

I: No specific intervention

Rink, A. D.; Vestweber, B.; Hahn, J.; Alfes, A.; Paul, C.; Vestweber, K. H. Single-incision laparoscopic surgery for diverticulitis in overweight patients. Langenbecks Arch Surg. PMID 26283162.

D: Single group, Surgery, N<500 analyzed

Ritz J. P.; Grone J.; Engelmann S.; Lehmann K. S.; Buhr H. J.; Holmer C. What is the actual benefit of sigmoid resection for acute diverticulitis? : Functional outcome after surgical and conservative treatment. Chirurg. PMID 23519381.

Duplicate (no unique data)

Ritz J. P.; Reissfelder C.; Holmer C.; Buhr H. J. Results of sigma resection in acute complicated diverticulitis : method and time of surgical intervention. Chirurg. PMID 18335181.

Duplicate (no unique data)

Ritz, J. P.; Grone, J.; Engelmann, S.; Lehmann, K. S.; Buhr, H. J.; Holmer, C. [What is the actual benefit of sigmoid resection for acute diverticulitis? : Functional outcome after surgical and conservative treatment]. Chirurg. PMID 23519381.

D: Single group, Surgery, N<500 analyzed

Ritz, J. P.; Lehmann, K. S.; Frericks, B.; Stroux, A.; Buhr, H. J.; Holmer, C. Outcome of patients with acute sigmoid diverticulitis: multivariate analysis of risk factors for free perforation. Surgery. PMID 21145569.

I: No specific intervention

Ritz, J. P.; Lehmann, K. S.; Loddenkemper, C.; Frericks, B.; Buhr, H. J.; Holmer, C. Preoperative CT staging in sigmoid diverticulitis--does it correlate with intraoperative and histological findings?. Langenbecks Arch Surg. PMID 20574812.

I: Not intervention of interest (not KQ 1-4)

Ritz, J. P.; Reissfelder, C.; Holmer, C.; Buhr, H. J. [Results of sigma resection in acute complicated diverticulitis : method and time of surgical intervention]. Chirurg. PMID 18335181.

D: Single group, Surgery, N<500 analyzed

Rizzuto, A.; Lacamera, U.; Zittel, F. U.; Sacco, R. Single incision laparoscopic resection for diverticulitis. Int J Surg. PMID 25986059.

D: Single group, Surgery, N<500 analyzed

Robinson, K. A.; O'Donnell, M. E.; Pearson, D.; Kriegshauser, J. S.; Odeleye, M.; Kalkbrenner, K.; Bodnar, Z.; Young-Fadok, T. M. Portomesenteric venous thrombosis following major colon and rectal surgery: incidence and risk factors. *Surg Endosc*. PMID 25159636.

D: Single group, Surgery, N<500 analyzed

Rodriguez-Cerrillo, M.; Poza-Montoro, A.; Fernandez-Diaz, E.; Matesanz-David, M.; Inurrieta Romero, A. Treatment of elderly patients with uncomplicated diverticulitis, even with comorbidity, at home. *Eur J Intern Med*. PMID 23623263.

D: NRCS, Tx, N<30/arm analyzed

Rose, J.; Parina, R. P.; Faiz, O.; Chang, D. C.; Talamini, M. A. Long-term Outcomes After Initial Presentation of Diverticulitis. *Ann Surg*. PMID 25654646.

I: Surgery for acute diverticulitis

Rosen DR, Pott EG, Cologne KG, et al. Percutaneous drainage for hinchey Ib and II acute diverticulitis with abscess improves outcomes. *Turk J Gastroenterol*. 2019 Nov;30(11):976-83. doi: 10.5152/tjg.2019.18602. PMID: 31767552.

I: Not intervention of interest (not KQ 1-4)

Rosen M. P.; Siewert B.; Sands D. Z.; Bromberg R.; Edlow J.; Raptopoulos V. Value of abdominal CT in the emergency department for patients with abdominal pain. *Eur Radiol*. PMID 12599010.

P: Not colonic diverticulitis

Rotholtz, N. A.; Montero, M.; Laporte, M.; Bun, M.; Lencinas, S.; Mezzadri, N. Patients with less than three episodes of diverticulitis may benefit from elective laparoscopic sigmoidectomy. *World J Surg*. PMID 19641950.

D: Single group, Surgery, N<500 analyzed

Rottier SJ, van Dijk ST, Boermeester MA. Author response to Comment on: Meta-analysis of the role of colonoscopy after an episode of left-sided acute diverticulitis. *The British journal of surgery*. 2020 Jan;107(1):154. doi: 10.1002/bjs.11449. PMID: 31869466.

D: Not primary study or SR

Rottier, S. J.; van Dijk, S. T.; van Geloven, A. A. W.; Schreurs, W. H.; Draaisma, W. A.; van Enst, W. A.; Puylaert, Jbcm; de Boer, M. G. J.; Klarenbeek, B. R.; Otte, J. A.; Felt, R. J. F.; Boermeester, M. A. Meta-analysis of the role of colonoscopy after an episode of left-sided acute diverticulitis. *Br J Surg*. PMID 31260589.

SR

Royds, J.; O'Riordan, J. M.; Eguare, E.; O'Riordan, D.; Neary, P. C. Laparoscopic surgery for

complicated diverticular disease: a single-centre experience. *Colorectal Dis*. PMID 22182066.

D: Single group, Surgery, N<500 analyzed

Rueda, J. C.; Jimenez, A.; Caro, A.; Feliu, F.; Escuder, J.; Gris, F.; Spuch, J.; Vicente, V. Home treatment of uncomplicated acute diverticulitis. *Int Surg*. PMID 23113847.

D: Single group, Tx, N<100 analyzed

Sai, V. F.; Velayos, F.; Neuhaus, J.; Westphalen, A. C. Colonoscopy after CT diagnosis of diverticulitis to exclude colon cancer: a systematic literature review. *Radiology*. PMID 22517956.

SR

Sakai T.; Yagihashi N.; Osawa T.; Harada O.; Ito H. Evaluation of the usefulness of computed tomography on diagnosis and management of acute abdomen. *Japanese Journal of Gastroenterological Surgery*.

P: Not colonic diverticulitis

Sakhnini, E.; Lahat, A.; Melzer, E.; Apter, S.; Simon, C.; Natour, M.; Bardan, E.; Bar-Meir, S. Early colonoscopy in patients with acute diverticulitis: results of a prospective pilot study. *Endoscopy*. PMID 15202046.

D: Single group, Tx, N<100 analyzed

Sala E.; Beadsmoore C.; Gibbons D.; Shaw A.; Gaskarth M.; Groot-Wassink T.; Watson C.; Dixon A. K. Unexpected changes in clinical diagnosis: early abdomino-pelvic computed tomography compared with clinical evaluation. *Abdom Imaging*. PMID 17901913.

D: CT or colonoscopy, N<100 (had CT/colonoscopy) analyzed

Sala, E.; Watson, C. J.; Beadsmoore, C.; Groot-Wassink, T.; Fanshawe, T. R.; Smith, J. C.; Bradley, A.; Palmer, C. R.; Shaw, A.; Dixon, A. K. A randomized, controlled trial of routine early abdominal computed tomography in patients presenting with non-specific acute abdominal pain. *Clin Radiol*. PMID 17765461.

O: CT, No clinical or management outcomes

Salem, L.; Flum, D. R. Primary anastomosis or Hartmann's procedure for patients with diverticular peritonitis? A systematic review. *Dis Colon Rectum*. PMID 15622591.

SR

Sallinen. LASER Trial. LAParoscopic Elective Sigmoid Resection Following divERTiculitis - a Multicenter, Prospective, Randomized Clinical Trial. <https://clinicaltrials.gov/show/nct02174926>. PMID Nct.

NCT: No results posted

Sallinen, V. J.; Mentula, P. J.; Leppaniemi, A. K. Nonoperative management of perforated diverticulitis with extraluminal air is safe and effective in selected patients. *Dis Colon Rectum*. PMID 24901689.

I: Not intervention of interest (not KQ 1-4)

Samdani, T.; Pieracci, F. M.; Eachempati, S. R.; Benarroch-Gampel, J.; Weiss, A.; Pietanza, M. C.; Barie, P. S.; Nash, G. M. Colonic diverticulitis in chemotherapy patients: should operative indications change? A retrospective cohort study. *Int J Surg*. PMID 25448673.

I: Surgery for acute diverticulitis

Sanchez-Velazquez, P.; Grande, L.; Pera, M. Outpatient treatment of uncomplicated diverticulitis: a systematic review. *Eur J Gastroenterol Hepatol*. PMID 26891198.

SR

Sarin, S.; Boulos, P. B. Long-term outcome of patients presenting with acute complications of diverticular disease. *Ann R Coll Surg Engl*. PMID 8154804.

D: Intervention <1990

Sartelli, M.; Binda, G. A.; Brandara, F.; Borasi, A.; Feroci, F.; Vadala, S.; Labricciosa, F. M.; Birindelli, A.; Luridiana, G.; Coccolini, F.; Di Saverio, S.; Catena, F.; Ansaloni, L.; Campanile, F. C.; Agresta, F.; Piazza, D. IPOD Study: Management of Acute Left Colonic Diverticulitis in Italian Surgical Departments. *World J Surg*. PMID 27834014.

I: No specific intervention

Sartelli, M.; Catena, F.; Ansaloni, L.; Coccolini, F.; Griffiths, E. A.; Abu-Zidan, F. M.; Di Saverio, S.; Ulrych, J.; Kluger, Y.; Ben-Ishay, O.; Moore, F. A.; Ivatury, R. R.; Coimbra, R.; Peitzman, A. B.; Leppaniemi, A.; Fraga, G. P.; Maier, R. V.; Chiara, O.; Kashuk, J.; Sakakushev, B.; Weber, D. G.; Latifi, R.; Biffl, W.; Bala, M.; Karamarkovic, A.; Inaba, K.; Ordonez, C. A.; Hecker, A.; Augustin, G.; Demetrashvili, Z.; Melo, R. B.; Marwah, S.; Zachariah, S. K.; Shelat, V. G.; McFarlane, M.; Rems, M.; Gomes, C. A.; Faro, M. P.; Junior, G. A.; Negroi, I.; Cui, Y.; Sato, N.; Vereczkei, A.; Bellanova, G.; Birindelli, A.; Di Carlo, I.; Kok, K. Y.; Gachabayov, M.; Gkiokas, G.; Bouliaris, K.; Colak, E.; Isik, A.; Rios-Cruz, D.; Soto, R.; Moore, E. E. WSES Guidelines for the management of acute left sided colonic diverticulitis in the emergency setting. *World J Emerg Surg*. PMID 27478494.

SR

Sartelli M, Weber DG, Kluger Y, et al. 2020 update of the WSES guidelines for the management of acute colonic diverticulitis in the emergency setting. *World journal of emergency surgery* : WJES. 2020 May

7;15(1):32. doi: 10.1186/s13017-020-00313-4.

PMID: 32381121.

SR

Scaglione M.; Romano L.; Pinto A.; Forner A. L.; De Lutio di Castelguidone E.; Giovine S.; Pinto F.; Grassi R. The role of spiral computed tomography in sigmoid diverticulitis and the diagnostic-therapeutic implications. *Radiol Med*. PMID 10879164.

Duplicate (no unique data)

Scaglione, M.; Romano, L.; Pinto, A.; Forner, A. L.; De Lutio di Castelguidone, E.; Giovine, S.; Pinto, F.; Grassi, R. [The role of spiral computed tomography in sigmoid diverticulitis and the diagnostic-therapeutic implications]. *Radiol Med*. PMID 10879164.

I: No specific intervention

Scarpa, M.; Griggio, L.; Rampado, S.; Ruffolo, C.; Citton, M.; Pozza, A.; Borsetto, L.; Dall'olmo, L.; Angriman, I. Long-term health-related quality of life after minimally invasive surgery for diverticular disease. *Langenbecks Arch Surg*. PMID 21336815.

D: NRCS, Tx, N<30/arm analyzed

Schechter, S.; Eisenstat, T. E.; Oliver, G. C.; Rubin, R. J.; Salvati, E. P. Computerized tomographic scan-guided drainage of intra-abdominal abscesses. Preoperative and postoperative modalities in colon and rectal surgery. *Dis Colon Rectum*. PMID 7924719.

D: Intervention <1990

Schluskel, A. T.; Lustik, M. B.; Chong, N. B.; Maykel, J. A.; Hatch, Q. M.; Steele, S. R. Right-Sided Diverticulitis Requiring Colectomy: an Evolving Demographic? A Review of Surgical Outcomes from the National Inpatient Sample Database. *J Gastrointest Surg*. PMID 27619806.

I: Surgery for acute diverticulitis

Schmedt C. G.; Bittner R.; Schroter M.; Ulrich M.; Leibl B. Surgical therapy of colonic diverticulitis--how reliable is primary anastomosis?. *Chirurg*. PMID 10734590.

Duplicate (no unique data)

Schmedt, C. G.; Bittner, R.; Schroter, M.; Ulrich, M.; Leibl, B. [Surgical therapy of colonic diverticulitis--how reliable is primary anastomosis?]. *Chirurg*. PMID 10734590.

D: Single group, Surgery, N<500 analyzed

Schmidt, S.; Ismail, T.; Puhon, M. A.; Soll, C.; Breitenstein, S. Meta-analysis of surgical strategies in perforated left colonic diverticulitis with generalized peritonitis. *Langenbecks Arch Surg*. PMID 29931505.

SR

Schmilovitz-Weiss, H.; Yalunin, E.; Boaz, M.; Sehayek-Shabbat, V.; Levin, I.; Chervinski, A.; Atar, E.; Niv, Y.; Shirin, H. Does a colonoscopy after acute diverticulitis affect its management?: a single center experience. *J Clin Gastroenterol*. PMID 22186742.
Colonoscopy single gp, N<200

Schreyer A. G.; Furst A.; Agha A.; Kikinis R.; Scheibl K.; Scholmerich J.; Feuerbach S.; Herfarth H.; Seitz J. Magnetic resonance imaging based colonography for diagnosis and assessment of diverticulosis and diverticulitis. *Int J Colorectal Dis*. PMID 15088109.

D: CT or colonoscopy, N<100 (had CT/colonoscopy) analyzed

Schwandner O.; Farke S.; Bruch H.-P. Laparoscopic surgery for acute and recurrent sigmoid diverticular disease: Prospective results of 536 patients. *Viszeralchirurgie*. PMID .
Not available

Schwandner, O.; Farke, S.; Bruch, H. P. Laparoscopic colectomy for diverticulitis is not associated with increased morbidity when compared with non-diverticular disease. *Int J Colorectal Dis*. PMID 15459774.

D: Single group, Surgery, N<500 analyzed

Schwandner, O.; Farke, S.; Fischer, F.; Eckmann, C.; Schiedeck, T. H.; Bruch, H. P. Laparoscopic colectomy for recurrent and complicated diverticulitis: a prospective study of 396 patients. *Langenbecks Arch Surg*. PMID 14985985.

D: Single group, Surgery, N<500 analyzed

Schwenk W.; Hücke H. P.; Stock W. Postoperative complications of elective resection of the colon in diverticulitis. *Dtsch Med Wochenschr*. PMID 1730200.

D: Intervention <1990

Schwenk, W. [The LAPDIV-CAMIC Study. Multicenter prospective randomized study of short-term and intermediate-term outcome of laparoscopic and conventional sigmoid resection in diverticular disease]. *Chirurg*. PMID 15098095.

D: Not primary study or SR

Schwenk, W.; Hücke, H. P.; Stock, W. [Postoperative complications of elective resection of the colon in diverticulitis]. *Dtsch Med Wochenschr*. PMID 1730200.

Duplicate (no unique data)

Shaban, F.; Carney, K.; McGarry, K.; Holtham, S. Perforated diverticulitis: To anastomose or not to anastomose? A systematic review and meta-analysis. *Int J Surg*. PMID 30165109.

SR

Shabanzadeh, D. M.; Wille-Jorgensen, P. Antibiotics for uncomplicated diverticulitis. *Cochrane Database Syst Rev*. PMID 23152268.
SR

Shaikh, F. M.; Stewart, P. M.; Walsh, S. R.; Davies, R. J. Laparoscopic peritoneal lavage or surgical resection for acute perforated sigmoid diverticulitis: A systematic review and meta-analysis. *Int J Surg*. PMID 28089941.

SR

Shaikh, S.; Krukowski, Z. H. Outcome of a conservative policy for managing acute sigmoid diverticulitis. *Br J Surg*. PMID 17380481.

I: No specific intervention

Shapiro, S. B.; Lambert, P. J.; Mathiason, M. A. A comparison of open and laparoscopic techniques in elective resection for diverticular disease. *Wmj*. PMID 18935898.

D: Single group, Surgery, N<500 analyzed

Sharma, P. V.; Eglinton, T.; Hider, P.; Frizelle, F. Systematic review and meta-analysis of the role of routine colonic evaluation after radiologically confirmed acute diverticulitis. *Ann Surg*. PMID 24169174.

SR

Shen, S. H.; Chen, J. D.; Tiu, C. M.; Chou, Y. H.; Chang, C. Y.; Yu, C. Colonic diverticulitis diagnosed by computed tomography in the ED. *Am J Emerg Med*. PMID 12369031.

D: Single group, Tx, N<100 analyzed

Shen; S. H.; Chen; J. D.; Tiu; C. M.; Chou; Y. H.; Chiang; J. H.; Chang; C. Y.; Lee; C. H.

Differentiating colonic diverticulitis from colon cancer: the value of computed tomography in the emergency setting. *J Chin Med Assoc*. PMID .

I: Diagnostic test, not CT or colonoscopy

Shin, S.; Kim, D.; Kang, U. R.; Yang, C. S. Impact of CT imaging on predicting the surgical management of acute diverticulitis. *Ann Surg Treat Res*. PMID 29854710.

I: Not intervention of interest (not KQ 1-4)

Shrier, D.; Skucas, J.; Weiss, S. Diverticulitis: an evaluation by computed tomography and contrast enema. *Am J Gastroenterol*. PMID 1928038.

Not available

Shyung, L. R.; Lin, S. C.; Shih, S. C.; Kao, C. R.; Chou, S. Y. Decision making in right-sided diverticulitis. *World J Gastroenterol*. PMID 12632528.

D: NRCS, Tx, N<30/arm analyzed

Siddiqui, M. R.; Sajid, M. S.; Khatri, K.; Cheek, E.; Baig, M. K. Elective open versus laparoscopic sigmoid colectomy for diverticular disease: a meta-analysis with the Sigma trial. *World J Surg.* PMID 20714895.
SR

Siddiqui, M. R.; Sajid, M. S.; Qureshi, S.; Cheek, E.; Baig, M. K. Elective laparoscopic sigmoid resection for diverticular disease has fewer complications than conventional surgery: a meta-analysis. *Am J Surg.* PMID 20637347.
SR

Sielezneff, I.; Malouf, A. J.; Pirro, N.; Cesari, J.; Brunet, C.; Sastre, B. Short-term functional outcome following elective surgery for complicated sigmoid diverticular disease: sutured or stapled end-to-end anastomosis to the proximal rectum?. *Colorectal Dis.* PMID 12791016.

D: Single group, Surgery, N<500 analyzed

Siewert, B.; Raptopoulos, V.; Mueller, M. F.; Rosen, M. P.; Steer, M. Impact of CT diagnosis and management of acute abdomen in patients initially treated without surgery. *American Journal of Roentgenology.* PMID .

P: Not colonic diverticulitis

Simianu, V. V.; Fichera, A.; Bastawrous, A. L.; Davidson, G. H.; Florence, M. G.; Thirlby, R. C.; Flum, D. R. Number of Diverticulitis Episodes Before Resection and Factors Associated With Earlier Interventions. *JAMA Surg.* PMID 26864286.

O: No outcome (or harm) of interest

Simianu VV, Strate LL, Billingham RP, et al. The Impact of Elective Colon Resection on Rates of Emergency Surgery for Diverticulitis. *Annals of surgery.* 2016 Jan;263(1):123-9. doi: 10.1097/sla.0000000000001053. PMID: 26111203.

O: No outcome (or harm) of interest

Simon, T.; Orango, G. R.; Ambroze, W. L.; Armstrong, D. N.; Schertzer, M. E.; Choat, D.; Pennington, E. E. Factors associated with complications of open versus laparoscopic sigmoid resection for diverticulitis. *Jsls.* PMID 15791973.

D: Single group, Surgery, N<500 analyzed

Singh S.; Singh P. P.; Murad M. H.; Singh H.; Samadder N. J. Prevalence, risk factors, and outcomes of interval colorectal cancers: a systematic review and meta-analysis. *Am J Gastroenterol.* PMID 24957158.

P: Not colonic diverticulitis

Sirany, A. E.; Gaertner, W. B.; Madoff, R. D.; Kwaan, M. R. Diverticulitis Diagnosed in the Emergency Room: Is It Safe to Discharge Home?. *J*

Am Coll Surg. PMID 28450063.

D: NRCS, Tx, Crude analyses only

Sirinthornpunya, S. Characteristics and Treatment Outcomes of Colonic Diverticulitis in Hospitalized Patients in Thailand. *J Med Assoc Thai.* PMID 27266228.

Not available

Slim, K.; Raspado, O.; Brugere, C.; Lanay-Savary, M. V.; Chipponi, J. Failure of a meta-analysis on the role of elective surgery for left colonic diverticulitis in young patients. *Int J Colorectal Dis.* PMID 18379793.

SR

Smith J.; Humes D.; Garsed K.; Lam C.; Zaitoun A.; Bennett A.; Scholefield J.; Spiller R. Mechanistic randomised control trial of mesalazine in symptomatic diverticular disease. *Gut.* PMID abstract.

P: Not colonic diverticulitis

Smith, T. R.; Cho, K. C.; Morehouse, H. T.; Kratka, P. S. Comparison of computed tomography and contrast enema evaluation of diverticulitis. *Dis Colon Rectum.* PMID 2295271.

O: CT, No clinical or management outcomes

Solomkin JS, Gardovskis J, Lawrence K, et al. IGNITE4: Results of a Phase 3, Randomized, Multicenter, Prospective Trial of Eravacycline vs Meropenem in the Treatment of Complicated Intraabdominal Infections. *Clin Infect Dis.* 2019 Aug 30;69(6):921-9. doi: 10.1093/cid/ciy1029. PMID: 30561562.

P: Not colonic diverticulitis

Song; M. E.; Jung; S. A.; Shim; K. N.; Song; E. M.; Kwon; K. J.; Kim; H. I.; Yoon; S. Y.; Cho; W. Y.; Kim; S. E.; Jung; H. K.; Moon; I. H. Clinical characteristics and treatment outcome of colonic diverticulitis in young patients. *Korean J Gastroenterol.* PMID 23458984.

I: No specific intervention

Spasojevic, M.; Naesgaard, J. M.; Ignjatovic, D. Perforated midgut diverticulitis: revisited. *World J Gastroenterol.* PMID 23002340.

I: No specific intervention

Stam, M.; Draaisma, W. A.; Pasker, P.; Consten, E.; Broeders, I. Sigmoid resection for diverticulitis is more difficult than for malignancies. *Int J Colorectal Dis.* PMID 28084549.

D: Single group, Surgery, N<500 analyzed

Stam; M.; Wall Vd; B.; Draaisma; W. A.; Bemelman; W. A.; Boermeester; M. A.; Broeders; Iamj; Belgers; E.; Toorenvliet; B.; Prins; H. A.; Consten; E. C. J.

Surgery versus conservative treatment for recurrent and ongoing diverticulitis; results of a multicenter randomized controlled trial (directtrial). United European Gastroenterology Journal. PMID .
Duplicate (no unique data)

Stam; M.; Wall; B.; Draaisma; W.; Bemelman; W. A.; Boermeester; M. A.; Broeders; J. M. J.; Consten; E. Surgery versus conservative treatment for recurrent and ongoing diverticulitis; results of a multicenter randomized controlled trial (DIRECT).
 Gastroenterology. PMID .
Duplicate (no unique data)

Stefansson, T.; Nyman, R.; Nilsson, S.; Ekbom, A.; Pahlman, L. Diverticulitis of the sigmoid colon. A comparison of CT, colonic enema and laparoscopy. Acta Radiol. PMID 9093173.
P: Not colonic diverticulitis

Steurer J. Unkomplizierte Divertikulitis: mit oder ohne Antibiotika-Therapie? [Uncomplicated diverticulitis: with or without antibiotic therapy?]. Praxis (Bern 1994).
D: Not primary study or SR

Stollman N.; Magowan S.; Shanahan F.; Quigley E. Efficacy of delayed-release mesalamine in the prevention of GI symptoms following acute diverticulitis: results of the diva trial. American Journal of Gastroenterology. PMID abstract.
Duplicate (no unique data)

Stollman, N.; Smalley, W.; Hirano, I. American Gastroenterological Association Institute Guideline on the Management of Acute Diverticulitis. Gastroenterology. PMID 26453777.
SR

Suarez Alecha, J.; Amoza Pais, S.; Batlle Marin, X.; Oronoz Martinez, B.; Balen Ribera, E.; Yarnoz Irazabal, C. Safety of nonoperative management after acute diverticulitis. Ann Coloproctol. PMID 25360428.
I: No specific intervention

Subhas, G.; Rana, G.; Bhullar, J.; Essad, K.; Mohey, L.; Mittal, V. K. Percutaneous drainage of a diverticular abscess should be limited to two attempts for a resilient diverticular abscess. Am Surg. PMID 24987892.
D: NRCS, Tx, Crude analyses only

Sugrue J, Lee J, Warner C, et al. Acute diverticulitis in renal transplant patients: should we treat them differently? Surgery. 2018 Apr;163(4):857-65. doi: 10.1016/j.surg.2017.11.013. PMID: 29289391.
I: No specific intervention

Syed U.; Companioni R. A. C.; Bansal R.; Alkhawam H.; Walfish A. Diverticulitis in the young population: Reconsidering conventional recommendations. Acta Gastro-Enterologica Belgica. PMID 28209102.
D: Single group, Tx, N<100 analyzed

Tack, D.; Bohy, P.; Perlot, I.; De Maertelaer, V.; Alkeilani, O.; Sourtzis, S.; Gevenois, P. A. Suspected acute colon diverticulitis: imaging with low-dose unenhanced multi-detector row CT. Radiology. PMID 16126929.
O: CT, No clinical or management outcomes

Tadlock; Mathew D.; Karamanos; Efstathios; Skiada; Dimitra; Inaba; Kenji; Talving; Peep; Senagore; Anthony; Demetriades; Demetrios. Emergency surgery for acute diverticulitis: Which operation? A National Surgical Quality Improvement Program study. Journal of Trauma & Acute Care Surgery. PMID .
I: Not intervention of interest (not KQ 1-4)

Takano, S.; Reategui, C.; da Silva, G.; Maron, D. J.; Wexner, S. D.; Weiss, E. G. Surgical outcomes and their relation to the number of prior episodes of diverticulitis. Gastroenterol Rep (Oxf). PMID 24759669.
I: Surgery for acute diverticulitis

Tan; J. P.; Barazanchi; A. W.; Singh; P. P.; Hill; A. G.; McCormick; A. D. Predictors of acute diverticulitis severity: A systematic review. Int J Surg. PMID .
I: No specific intervention

Tandon; A.; Fretwell; V. L.; Nunes; Q. M.; Rooney; P. S. Antibiotics versus no antibiotics in the treatment of acute uncomplicated diverticulitis - a systematic review and meta-analysis. Colorectal Dis. PMID 29323778.
SR

Taourel P.; Baron M. P.; Pradel J.; Fabre J. M.; Senterre E.; Bruel J. M. Acute abdomen of unknown origin: impact of CT on diagnosis and management. Gastrointest Radiol. PMID 1426841.
O: CT, No clinical or management outcomes

Tappouni, R.; Mathew, P.; Connelly, T. M.; Luke, F.; Messaris, E. Measurement of visceral fat on preoperative computed tomography predicts complications after sigmoid colectomy for diverticular disease. Am J Surg. PMID 25840842.
I: Not intervention of interest (not KQ 1-4)

Teeuwen, P. H.; Chouten, M. G.; Bremers, A. J.; Bleichrodt, R. P. Laparoscopic sigmoid resection for diverticulitis decreases major morbidity rates: a randomized controlled trial. Ann Surg. PMID

19743532.

D: Not primary study or SR

Tehrani S, Klinge M, Saul M, et al. Prevalence of colorectal cancer and advanced adenoma in patients with acute diverticulitis: implications for follow-up colonoscopy. *Gastrointest Endosc.* 2020 Mar;91(3):634-40. doi: 10.1016/j.gie.2019.08.044. PMID: 31521778.

I: No specific intervention

Thaler, K.; Baig, M. K.; Berho, M.; Weiss, E. G.; Nogueras, J. J.; Arnaud, J. P.; Wexner, S. D.; Bergamaschi, R. Determinants of recurrence after sigmoid resection for uncomplicated diverticulitis. *Dis Colon Rectum.* PMID 12626916.

D: Single group, Surgery, N<500 analyzed

Thaler, K.; Weiss, E. G.; Nogueras, J. J.; Arnaud, J. P.; Wexner, S. D.; Bergamaschi, R. Recurrence rates at minimum 5-year follow-up: laparoscopic versus open sigmoid resection for uncomplicated diverticulitis. *Surg Laparosc Endosc Percutan Tech.* PMID 14571169.

D: Single group, Surgery, N<500 analyzed

Thaler, K.; Weiss, E. G.; Nogueras, J. J.; Arnaud, J. P.; Wexner, S. D.; Bergamaschi, R. Recurrence rates at minimum five-year follow-up: laparoscopic versus open sigmoid resection for uncomplicated diverticulitis. *Acta Chir Iugosl.* PMID 15771287.

D: Single group, Surgery, N<500 analyzed

Thalheimer, A.; Germer, C. T. [Antibiotic therapy of acute uncomplicated diverticulitis : Results of a prospective randomized multicenter study]. *Chirurg.* PMID 22407463.

D: Not primary study or SR

Thorisson, A.; Nikberg, M.; Andreasson, K.; Smedh, K.; Chabok, A. Non-operative management of perforated diverticulitis with extraluminal or free air - a retrospective single center cohort study. *Scand J Gastroenterol.* PMID 30353758.

O: Single arm study without harms data

Thorisson A, Nikberg M, Torkzad MR, et al. Diagnostic accuracy of acute diverticulitis with unenhanced low-dose CT. *BJS Open.* 2020 May 20. doi: 10.1002/bjs.5.50290. PMID: 32431087.

O: CT, No clinical or management outcomes

Thorisson, A.; Smedh, K.; Torkzad, M. R.; Pahlman, L.; Chabok, A. CT imaging for prediction of complications and recurrence in acute uncomplicated diverticulitis. *Int J Colorectal Dis.* PMID 26490053.

O: CT, No clinical or management outcomes

Thornblade LW, Simianu VV, Davidson GH, et al. Elective Surgery for Diverticulitis and the Risk of

Recurrence and Ostomy. *Annals of surgery.* 2019 Oct 22. doi: 10.1097/sla.0000000000003639. PMID: 31651534.

I: Surgery for acute diverticulitis

Timerbulatov, V. M.; Mekhdiyev, D. I.; Men'shikov, A. M.; Verzakova, I. V.; Mikheeva, E. A.; Koval'skaia, S. F.; Galliamov, A.Kh. [Treatment strategy in diverticulosis of the colon]. *Khirurgiia (Mosk).* PMID 11026203.

Not available

Titos-Garcia, A.; Aranda-Narvaez, J. M.; Romacho-Lopez, L.; Gonzalez-Sanchez, A. J.; Cabrera-Serna, I.; Santoyo-Santoyo, J. Nonoperative management of perforated acute diverticulitis with extraluminal air: results and risk factors of failure. *Int J Colorectal Dis.* PMID 28717840.

D: Single group, Tx, N<100 analyzed

Tocchi, A.; Mazzoni, G.; Fornasari, V.; Miccini, M.; Daddi, G.; Tagliacozzo, S. Preservation of the inferior mesenteric artery in colorectal resection for complicated diverticular disease. *Am J Surg.* PMID 11574089.

D: Single group, Surgery, N<500 analyzed

Toorenvliet, B. R.; Bakker, R. F.; Breslau, P. J.; Merkus, J. W.; Hamming, J. F. Colonic diverticulitis: a prospective analysis of diagnostic accuracy and clinical decision-making. *Colorectal Dis.* PMID 19183330.

I: Diagnostic test, not CT or colonoscopy

Toorenvliet, B. R.; Swank, H.; Schoones, J. W.; Hamming, J. F.; Bemelman, W. A. Laparoscopic peritoneal lavage for perforated colonic diverticulitis: a systematic review. *Colorectal Dis.* PMID 19788490.

SR

Toro, A.; Mannino, M.; Reale, G.; Cappello, G.; Di Carlo, I. Primary anastomosis vs Hartmann procedure in acute complicated diverticulitis. Evolution over the last twenty years. *Chirurgia (Bucur).* PMID 23116833.

SR

Tou S.; You K.; Giuratrabocchetta S.; Sullivan R.; Denoya P.; Bergamaschi R. Should elective resection follow nonoperative management of first episode of acute sigmoid diverticulitis with abscess/extraluminal air? A randomised controlled trial. *Colorectal disease.*

Not available

Trebuchet, G.; Lechaux, D.; Lecalve, J. L. Laparoscopic left colon resection for diverticular disease. *Surg Endosc.* PMID 11961597.

D: Single group, Surgery, N<500 analyzed

Trenti, L.; Kreisler, E.; Galvez, A.; Golda, T.; Frago, R.; Biondo, S. Long-term evolution of acute colonic diverticulitis after successful medical treatment. *World J Surg*. PMID 25189456.

I: No specific intervention

Trepsi E.; Colla C.; Panizza P.; Polino M. G.; Venturini A.; Bottani G.; De Vecchi P.; Matti C. Therapeutic and prophylactic role of mesalazine (5-ASA) in symptomatic diverticular disease of the large intestine. 4 year follow-up results. *Minerva Gastroenterol Dietol*. PMID 16498335.

Duplicate (no unique data)

Trepsi, E.; Colla, C.; Panizza, P.; Polino, M. G.; Venturini, A.; Bottani, G.; De Vecchi, P.; Matti, C. [Therapeutic and prophylactic role of mesalazine (5-ASA) in symptomatic diverticular disease of the large intestine. 4 year follow-up results]. *Minerva Gastroenterol Dietol*. PMID 16498335.

Not available

Trepsi E.; Panizza P.; Colla C.; Bottani G.; De Vecchi P.; Matti C. Efficacy of low dose mesalazine (5-ASA) in the treatment of acute inflammation and prevention of complications in patients with symptomatic diverticular disease. Preliminary results. *Minerva Gastroenterol Dietol*. PMID 16501486.

Duplicate (no unique data)

Trepsi, E.; Panizza, P.; Colla, C.; Bottani, G.; De Vecchi, P.; Matti, C. [Efficacy of low dose mesalazine (5-ASA) in the treatment of acute inflammation and prevention of complications in patients with symptomatic diverticular disease. Preliminary results]. *Minerva Gastroenterol Dietol*. PMID 16501486.

Not available

Tsilimparis; N.; Haase; O.; Wendling; P.; Kipfmüller; K.; Schmid; M.; Engemann; R.; Schwenk; W. Laparoscopic 'fast-track' sigmoidectomy for diverticulitis disease in Germany. Results of a prospective quality assurance program. *Dtsch Med Wochenschr*. PMID same as 20812161.

Duplicate (no unique data)

Tsushima, Y.; Yamada, S.; Aoki, J.; Motojima, T.; Endo, K. Effect of contrast-enhanced computed tomography on diagnosis and management of acute abdomen in adults. *Clin Radiol*. PMID 12069469.

O: CT, No clinical or management outcomes

Tucci, G.; Torquati, A.; Grande, M.; Stroppa, I.; Sianesi, M.; Farinon, A. M. Major acute inflammatory complications of diverticular disease of the colon: planning of surgical management. *Hepatogastroenterology*. PMID 8884300.

I: Surgery for acute diverticulitis

Tursi A.; Brandimarte G.; Elisei W.; Picchio M.; Forti G.; Pianese G.; Rodino S.; D'Amico T.; Sacca N.; Portincasa P.; Capezzuto E.; Lattanzio R.; Spadaccini A.; Fiorella S.; Polimeni F.; Polimeni N.; Stoppino V.; Stoppino G.; Giorgetti G. M.; Aiello F.; Danese S. Randomised clinical trial: mesalazine and/or probiotics in maintaining remission of symptomatic uncomplicated diverticular disease--a double-blind, randomised, placebo-controlled study. *Aliment Pharmacol Ther*. PMID 23957734.

P: Not colonic diverticulitis

Tursi A.; Papa A.; Danese S. Review article: the pathophysiology and medical management of diverticulosis and diverticular disease of the colon. *Aliment Pharmacol Ther*. PMID 26202723.

D: Not primary study or SR

Tursi, A.; Brandimarte, G.; Giorgetti, G. M.; Elisei, W. Continuous versus cyclic mesalazine therapy for patients affected by recurrent symptomatic uncomplicated diverticular disease of the colon. *Dig Dis Sci*. PMID 17253134.

P: Not colonic diverticulitis

Tursi, A.; Brandimarte, G.; Giorgetti, G. M.; Elisei, W. Mesalazine and/or *Lactobacillus casei* in preventing recurrence of symptomatic uncomplicated diverticular disease of the colon: a prospective, randomized, open-label study. *J Clin Gastroenterol*. PMID 16633103.

P: Not colonic diverticulitis

Tursi, A.; Brandimarte, G.; Giorgetti, G.; Elisei, W.; Maiorano, M.; Aiello, F. The clinical picture of uncomplicated versus complicated diverticulitis of the colon. *Dig Dis Sci*. PMID 18231855.

I: Not intervention of interest (not KQ 1-4)

Tursi, A.; Di Mario, F.; Brandimarte, G.; Elisei, W.; Picchio, M.; Loperfido, S.; Dal Bo, N.; Ferrara, F.; Marcello, R.; Heras Salvat, H.; Scarpignato, C. Intermittent versus every-day mesalazine therapy in preventing complications of diverticular disease: a long-term follow-up study. *Eur Rev Med Pharmacol Sci*. PMID 24338468.

D: NRCS, Tx, Crude analyses only

Tursi, A.; Elisei, W.; Giorgetti, G. M.; Inchingolo, C. D.; Nenna, R.; Picchio, M.; Maiorano, M.; Penna, A.; Lecca, P. G.; Brandimarte, G. Effectiveness of different therapeutic strategies in preventing diverticulitis recurrence. *Eur Rev Med Pharmacol Sci*. PMID 23426537.

D: NRCS, Tx, Crude analyses only

Tursi, A.; Picchio, M. Mesalazine in preventing acute diverticulitis occurrence: a meta-analysis of randomized controlled trials. *J Gastrointest Liver*

Dis. PMID 27689212.

SR

Udayasankar, U. K.; Li, J.; Baumgarten, D. A.; Small, W. C.; Kalra, M. K. Acute abdominal pain: value of non-contrast enhanced ultra-low-dose multi-detector row CT as a substitute for abdominal radiographs. *Emerg Radiol*. PMID 18597128.

D: CT or colonoscopy, N<100 (had CT/colonoscopy) analyzed

Unlu, C.; Beenen, L. F.; Fauquenot, J. M.; Jensch, S.; Bemelman, W. A.; Dijkgraaf, M. G.; Vrouenraets, B. C.; Boermeester, M. A.; Stoker, J. Inter-observer reliability of computed tomographic classifications of diverticulitis. *Colorectal Dis*. PMID 24344689.

O: CT, No clinical or management outcomes

Unlu, C.; Daniels, L.; Vrouenraets, B. C.; Boermeester, M. A. A systematic review of high-fibre dietary therapy in diverticular disease. *Int J Colorectal Dis*. PMID 21922199.

SR

Unlu, C.; Daniels, L.; Vrouenraets, B. C.; Boermeester, M. A. Systematic review of medical therapy to prevent recurrent diverticulitis. *Int J Colorectal Dis*. PMID 22576905.

SR

Unlu, C.; de Korte, N.; Daniels, L.; Consten, E. C.; Cuesta, M. A.; Gerhards, M. F.; van Geloven, A. A.; van der Zaag, E. S.; van der Hoeven, J. A.; Klicks, R.; Cense, H. A.; Roumen, R. M.; Eijssbouts, Q. A.; Lange, J. F.; Fockens, P.; de Borgie, C. A.; Bemelman, W. A.; Reitsma, J. B.; Stockmann, H. B.; Vrouenraets, B. C.; Boermeester, M. A. A multicenter randomized clinical trial investigating the cost-effectiveness of treatment strategies with or without antibiotics for uncomplicated acute diverticulitis (DIABOLO trial). *BMC Surg*. PMID .

O: No outcome (or harm) of interest

Urushidani, S.; Kuriyama, A.; Matsumura, M. 5-aminosalicylic acid agents for prevention of recurrent diverticulitis: A systematic review and meta-analysis. *J Gastroenterol Hepatol*. PMID 28623877.

SR

Uyeda J. W.; Yu H.; Ramalingam V.; Devalapalli A. P.; Soto J. A.; Anderson S. W. Evaluation of Acute Abdominal Pain in the Emergency Setting Using Computed Tomography Without Oral Contrast in Patients With Body Mass Index Greater Than 25. *J Comput Assist Tomogr*. PMID 26248155.

P: Not colonic diverticulitis

Van Arendonk, K. J.; Tymitz, K. M.; Gearhart, S. L.; Stem, M.; Lidor, A. O. Outcomes and costs of elective surgery for diverticular disease: a

comparison with other diseases requiring colectomy. *JAMA Surg*. PMID 23715829.

I: Surgery for acute diverticulitis

van de Wall B. J.; Poerink J. A.; Draaisma W. A.; Reitsma J. B.; Consten E. C.; Broeders I. A. Diverticulitis in young versus elderly patients: a meta-analysis. *Scand J Gastroenterol*. PMID 23330633.

I: No specific intervention

van de Wall B. J.; Reuling E. M.; Consten E. C.; van Grinsven J. H.; Schwartz M. P.; Broeders I. A.; Draaisma W. A. Endoscopic evaluation of the colon after an episode of diverticulitis: a call for a more selective approach. *Int J Colorectal Dis*. PMID 22407442.

I: Not intervention of interest (not KQ 1-4)

van de Wall, B. J.; Draaisma, W. A.; Consten, E. C.; van der Graaf, Y.; Otten, M. H.; de Wit, G. A.; van Stel, H. F.; Gerhards, M. F.; Wiezer, M. J.; Cense, H. A.; Stockmann, H. B.; Leijten, J. W.; Zimmerman, D. D.; Belgers, E.; van Wagenveld, B. A.; Sonneveld, E. D.; Prins, H. A.; Coene, P. P.; Karsten, T. M.; Klaase, J. M.; Statius Muller, M. G.; Crolla, R. M.; Broeders, I. A. DIRECT trial. Diverticulitis recurrences or continuing symptoms: Operative versus conservative treatment. A multicenter randomised clinical trial. *BMC Surg*. PMID 20691040.

Duplicate (no unique data)

van de Wall, B. J.; Draaisma, W. A.; Consten, E. C.; van der Kaaij, R. T.; Wiezer, M. J.; Broeders, I. A. Does the presence of abscesses in diverticular disease prelude surgery?. *J Gastrointest Surg*. PMID 23242845.

P: Mix complicated & uncomplicated in antibiotics analysis

van de Wall, B. J.; Draaisma, W. A.; van Iersel, J. J.; Consten, E. C.; Wiezer, M. J.; Broeders, I. A. Elective resection for ongoing diverticular disease significantly improves quality of life. *Dig Surg*. PMID 23838742.

D: Single group, Surgery, N<500 analyzed

van Dijk, S. T.; Bos, K.; de Boer, M. G. J.; Draaisma, W. A.; van Enst, W. A.; Felt, R. J. F.; Klarenbeek, B. R.; Otte, J. A.; Puylaert, Jbcm; van Geloven, A. A. W.; Boermeester, M. A. A systematic review and meta-analysis of outpatient treatment for acute diverticulitis. *Int J Colorectal Dis*. PMID 29532202.

SR

van Dijk, S. T.; Daniels, L.; Nio, C. Y.; Somers, I.; van Geloven, A. A. W.; Boermeester, M. A. Predictive factors on CT imaging for progression of

uncomplicated into complicated acute diverticulitis. Int J Colorectal Dis. PMID 29075917.

I: Not intervention of interest (not KQ 1-4)

van Dijk, S. T.; Doelare, S. A. N.; van Geloven, A. A. W.; Boermeester, M. A. A Systematic Review of Pericolic Extraluminal Air in Left-Sided Acute Colonic Diverticulitis. Surg Infect (Larchmt). PMID 29608422.

SR

Varga, J. Surgical treatment of diverticulitis of the sigmoid. Acta Chir Hung. PMID 9408407.

Not available

Vasilevsky, C. A.; Belliveau, P.; Trudel, J. L.; Stein, B. L.; Gordon, P. H. Fistulas complicating diverticulitis. Int J Colorectal Dis. PMID 9638488.
D: NRCs, Tx, N<30/arm analyzed

Vennix S.; Musters G. D.; Swank H. A.; Mulder I. M.; Consten E. C. J.; Boermeester M. A.; Van Dieren S.; Lange J. F.; Bemelman W. A. Laparoscopic peritoneal lavage or sigmoidectomy for generalized peritonitis due to perforated diverticulitis; results of a multicenter randomised trial (the ladies trial). Surgical endoscopy and other interventional techniques.

Not available

Vennix, S.; Boersema, G. S.; Buskens, C. J.; Menon, A. G.; Tanis, P. J.; Lange, J. F.; Bemelman, W. A. Emergency Laparoscopic Sigmoidectomy for Perforated Diverticulitis with Generalised Peritonitis: A Systematic Review. Dig Surg. PMID 26551040.
SR

Vennix, S.; Morton, D. G.; Hahnloser, D.; Lange, J. F.; Bemelman, W. A. Systematic review of evidence and consensus on diverticulitis: an analysis of national and international guidelines. Colorectal Dis. PMID 24801825.
SR

Vestweber, B.; Galetin, T.; Lammerting, K.; Paul, C.; Giehl, J.; Straub, E.; Kaldowski, B.; Alfes, A.; Vestweber, K. H. Single-incision laparoscopic surgery: outcomes from 224 colonic resections performed at a single center using SILS. Surg Endosc. PMID 22806519.

D: Single group, Surgery, N<500 analyzed

Vestweber, B.; Vestweber, K. H.; Paul, C.; Rink, A. D. Single-port laparoscopic resection for diverticular disease: experiences with more than 300 consecutive patients. Surg Endosc. PMID 25829061.

D: Single group, Surgery, N<500 analyzed

Victor J.; Roxana P.; Farschad F.; Pierre B. J.; Markus Z.; Jan P. R. Is there a role for procalcitonin

in differentiating uncomplicated and complicated diverticulitis in order to reduce antibiotic therapy? A prospective diagnostic cohort study. Swiss Medical Weekly. PMID 29185246.

Duplicate (no unique data)

Victor; J.; Roxana; P.; Farschad; F.; Pierre; B. J.; Markus; Z.; Jan; P. R. Is there a role for procalcitonin in differentiating uncomplicated and complicated diverticulitis in order to reduce antibiotic therapy? A prospective diagnostic cohort study. Swiss Medical Weekly. PMID .

I: No specific intervention

Violi, V.; Roncoroni, L.; Boselli, A. S.; Trivelli, M.; Peracchia, A. Diverticulitis of the caecum and ascending colon: an unavoidable diagnostic pitfall?. Int Surg. PMID 10817430.

I: Surgery for acute diverticulitis

Wahl, W.; Wern, T.; Kirsch, D.; Junginger, T. [Status of discontinuity resection in septic diverticular complications. History or a still current procedure?]. Zentralbl Chir. PMID 11396243.

I: Surgery for acute diverticulitis

Wahl; W.; Wern; T.; Kirsch; D.; Junginger; T. Status of discontinuity resection in septic diverticular complications. History or a still current procedure?. Zentralbl Chir. PMID .

Duplicate (no unique data)

Walker, A. S.; Bingham, J. R.; Janssen, K. M.; Johnson, E. K.; Maykel, J. A.; Ocampo, O.; Gonzalez, J. P.; Steele, S. R. Colonoscopy after Hinchey I and II left-sided diverticulitis: utility or futility?. Am J Surg. PMID 27287835.

Colonoscopy single gp, N<200

Walter, S. S.; Maurer, M.; Storz, C.; Weiss, J.; Archid, R.; Bamberg, F.; Kim, J. H.; Nikolaou, K.; Othman, A. E. Effects of Radiation Dose Reduction on Diagnostic Accuracy of Abdominal CT in Young Adults with Suspected Acute Diverticulitis: A Retrospective Intraindividual Analysis. Acad Radiol. PMID 30268717.

D: Single group, Tx, N<100 analyzed

Warwas, F. B.; Schneider, B. Elective vs. early elective surgery in diverticular disease: a retrospective study on the optimal timing of non-emergency treatment. Int J Colorectal Dis. PMID 29536239.

D: No analysis of interest

Wehrli H.; Akovbiantz A. Surgical therapy of diverticular disease at the Waid City Hospital, Zurich, 1980-1990. Helv Chir Acta. PMID 1592647.
Duplicate (no unique data)

Wehrli, H. [Diverticular disease: When to operate?]. Ther Umsch. PMID 1926008.
D: Intervention <1990

Wehrli, H.; Akovbiantz, A. [Surgical therapy of diverticular disease at the Waid City Hospital, Zurich, 1980-1990]. Helv Chir Acta. PMID 1592647.
Not available

Wehrli, H. Diverticular disease: When to operate?. Ther Umsch. PMID .
D: Single group, Surgery, N<500 analyzed

Weinrich JM, Bannas P, Avanesov M, et al. MDCT in the Setting of Suspected Colonic Diverticulitis: Prevalence and Diagnostic Yield for Diverticulitis and Alternative Diagnoses. AJR American journal of roentgenology. 2020 Apr 22;1-10. doi: 10.2214/ajr.19.21852. PMID: 32319796.
O: CT, No clinical or management outcomes

Werner, A.; Diehl, S. J.; Farag-Soliman, M.; Duber, C. Multi-slice spiral CT in routine diagnosis of suspected acute left-sided colonic diverticulitis: a prospective study of 120 patients. Eur Radiol. PMID 12740709.
O: CT, No clinical or management outcomes

Westwood David A.; Eglinton Tim W. Antibiotics may not improve short-term or long-term outcomes in acute uncomplicated diverticulitis. Evidence Based Medicine. PMID 22723593.
D: Not primary study or SR

Westwood, D. A.; Eglinton, T. W.; Frizelle, F. A. Routine colonoscopy following acute uncomplicated diverticulitis. Br J Surg. PMID 21713756.
I: Diagnostic test, not CT or colonoscopy

Wiedswang G.; Carlsen E. Patients with diagnosed colonic diverticulitis admitted to a department of surgery. Tidsskr Nor Laegeforen. PMID 10613089.
Duplicate (no unique data)

Wiedswang, G.; Carlsen, E. [Patients with diagnosed colonic diverticulitis admitted to a department of surgery]. Tidsskr Nor Laegeforen. PMID 10613089.
I: No specific intervention

Wildman-Tobriner B, Ehieli WL, Dixon AX, et al. Computed tomography of the acute abdomen. Applied Radiology. 2019;48(6):32-9.
D: Not primary study or SR

Wilson, S. R.; Toi, A. The value of sonography in the diagnosis of acute diverticulitis of the colon. AJR Am J Roentgenol. PMID 2110728.
D: Intervention <1990

Winde, G.; Schaudig, F.; Herwig, R.; Schmid, K. W.; Senninger, N. [Standardization in sigmoid

diverticulitis surgery planning: indications based on evaluation with the Hughes classification]. Langenbecks Arch Chir Suppl Kongressbd. PMID 9574354.
Not available

Winde, G.; Schaudig, F.; Herwig, R.; Schmid, K. W.; Senninger, N. Standardization in sigmoid diverticulitis surgery planning: indications based on evaluation with the Hughes classification. Langenbecks Arch Chir Suppl Kongressbd. PMID .
Duplicate (no unique data)

Wise, K. B.; Merchea, A.; Cima, R. R.; Colibaseanu, D. T.; Thomsen, K. M.; Habermann, E. B. Proximal intestinal diversion is associated with increased morbidity in patients undergoing elective colectomy for diverticular disease: an ACS-NSQIP study. J Gastrointest Surg. PMID 25416544.
P: Not colonic diverticulitis

Wu, K. L.; Lee, K. C.; Liu, C. C.; Chen, H. H.; Lu, C. C. Laparoscopic versus Open Surgery for Diverticulitis: A Systematic Review and Meta-Analysis. Dig Surg. PMID 27941315.
SR

Xia, J.; Paul Olson, T. J.; Rosen, S. A. Robotic-assisted surgery for complicated and non-complicated diverticulitis: a single-surgeon case series. J Robot Surg. PMID 30673981.
I: Surgery for acute diverticulitis

Yang, H. R.; Huang, H. H.; Wang, Y. C.; Hsieh, C. H.; Chung, P. K.; Jeng, L. B.; Chen, R. J. Management of right colon diverticulitis: a 10-year experience. World J Surg. PMID 16983473.
I: No specific intervention

Yesilagac H, Arer IM, Gulalp B, et al. Generalist versus Abdominal Subspecialist Radiologist Interpretations of Abdominopelvic Computed Tomography Performed on Patients with Abdominal Pain and its Impact on the Therapeutic Approach. Adv J Emerg Med. 2020 Spring;4(2):e21. doi: 10.22114/ajem.v0i0.288. PMID: 32322789.
O: CT, No clinical or management outcomes

Youatou P.; Ngatchou W.; Yondou G.; Nde F.; Mols P.; Ramadan A. S.; Ngassa M. Acute colonic diverticulitis : outcome according to general practice management prior to referral and criteria predictive of complications. A 10-year experience in a University Hospital. Rev Med Brux. PMID 28525195.
Duplicate (no unique data)

Youatou, P.; Ngatchou, W.; Yondou, G.; Nde, F.; Mols, P.; Ramadan, A. S.; Ngassa, M. [Acute colonic diverticulitis : outcome according to general practice

management prior to referral and criteria predictive of complications. A 10-year experience in a University Hospital]. Rev Med Brux. PMID 28525195.

I: No specific intervention

Zaman; S.; Chapman; W.; Mohammed; I.; Gill; K.; Ward; S. T. Patients with computed tomography-proven acute diverticulitis require follow-up to exclude colorectal cancer. Intest Res. PMID 28522949.

Colonoscopy single gp, N<200

Zangos, S.; Steenburg, S. D.; Phillips, K. D.; Kerl, J. M.; Nguyen, S. A.; Herzog, C.; Schoepf, U. J.; Vogl, T. J.; Costello, P. Acute abdomen: Added diagnostic value of coronal reformations with 64-slice multidetector row computed tomography. Acad Radiol. PMID 17178362.

P: Not colonic diverticulitis

Zehetner, J.; Szabo, K.; Wayand, W.; Shamiyeh, A. Lessons learned from the analysis of 200 laparoscopic sigmoid resections for diverticulitis. Surg Laparosc Endosc Percutan Tech. PMID 19390278.

D: Single group, Surgery, N<500 analyzed

Zimmermann, M.; Hoffmann, M.; Laubert, T.; Meyer, K. F.; Jungbluth, T.; Roblick, U. J.; Bruch, H. P.; Schloricke, E. Laparoscopic versus open reversal of a Hartmann procedure: a single-center study. World J Surg. PMID 24668452.

D: Single group, Tx, N<100 analyzed

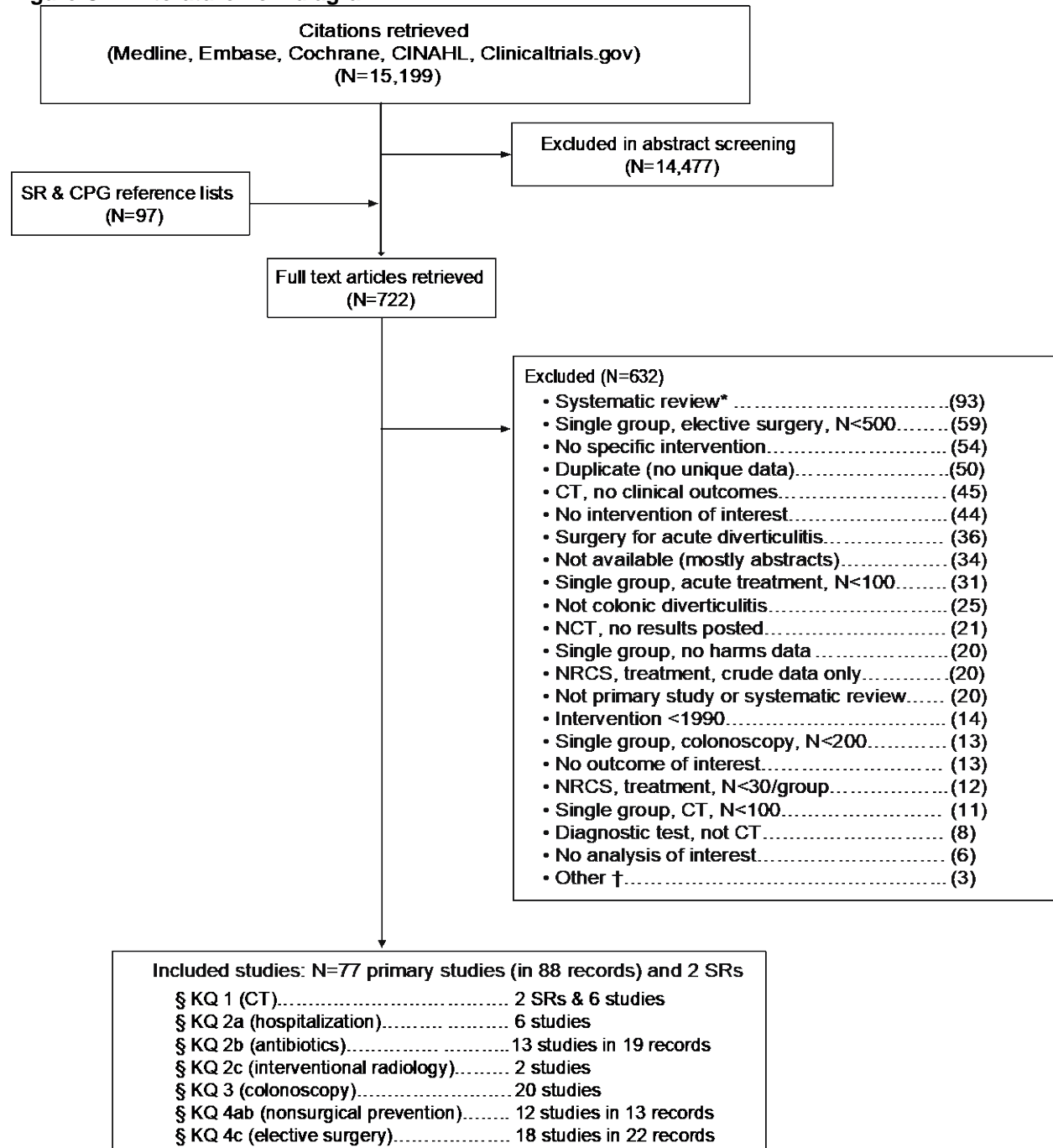
Zingg, U.; Pasternak, I.; Guertler, L.; Dietrich, M.; Wohlwend, K. A.; Metzger, U. Early vs. delayed elective laparoscopic-assisted colectomy in sigmoid diverticulitis: timing of surgery in relation to the acute attack. Dis Colon Rectum. PMID 17851720.

D: Single group, Surgery, N<500 analyzed

Appendix C. Search Results; Study Design, Arm Details, Baselines, and Quality

Search Results

Figure C-1. Literature flow diagram



Abbreviations: CPG = clinical practice guideline, CT = computed tomography (imaging), KQ = Key Question, NCT = ClinicalTrials.gov record, NRCS = nonrandomized comparative study, SR = systematic review.

* These systematic reviews do not include the two included for Key Question 1.

† CT of prediagnosed groups, not for diagnosis or staging (N=1), randomized controlled trial, N<10/arm (N=1), antibiotics used for both complicated and uncomplicated diverticulitis, not separated (N=1)

Included Studies

Key Question 1 (CT Imaging)

Andeweg, C. S.; Knobben, L.; Hendriks, J. C.; Bleichrodt, R. P.; van Goor, H. How to diagnose acute left-sided colonic diverticulitis: proposal for a clinical scoring system. *Ann Surg*. PMID 21346548

Jurowich, C. F.; Jellouschek, S.; Adamus, R.; Loose, R.; Kaiser, A.; Isbert, C.; Germer, C. T.; von Rahden, B. H. How complicated is complicated diverticulitis?--phlegmonous diverticulitis revisited. *Int J Colorectal Dis*. PMID 21830036.

Kelly ME, Heeney A, Redmond CE, Costelloe J, Nason GJ, Ryan J, Brophy D, Winter DC. Incidental findings detected on emergency abdominal CT scans: a 1-year review. *Abdom Imaging*. 2015 Aug;40(6):1853-7. doi: 10.1007/s00261-015-0349-4. PMID 25576049

Martin Arevalo, J.; Garcia-Granero, E.; Garcia Botello, S.; Munoz, E.; Cervera, V.; Flor Lorente, B.; Lledo, S. [Early use of CT in the management of acute diverticulitis of the colon]. *Rev Esp Enferm Dig*. PMID 17883294

Salem, T. A.; Molloy, R. G.; O'Dwyer, P. J. Prospective study on the role of the CT scan in patients with an acute abdomen. *Colorectal Dis*. PMID 16108882

Shuaib W, Johnson JO, Salastekar N, Maddu KK, Khosa F. Incidental findings detected on abdomino-pelvic multidetector computed tomography performed in the acute setting. *Am J Emerg Med*. 2014 Jan;32(1):36-9. PMID 24475484

Key Question 2a (Outpatient)

Biondo, S.; Golda, T.; Kreisler, E.; Espin, E.; Vallribera, F.; Oteiza, F.; Codina-Cazador, A.; Pujadas, M.; Flor, B. Outpatient versus hospitalization management for uncomplicated diverticulitis: a prospective, multicenter randomized clinical trial (DIVER Trial). *Ann Surg*. PMID 23732265

Bolkenstein, H. E.; Draaisma, W. A.; van de Wall, B.; Consten, E.; Broeders, I. Treatment of acute uncomplicated diverticulitis without antibiotics: risk factors for treatment failure. *Int J Colorectal Dis*. PMID 29679152

Joliat, G. R.; Emery, J.; Demartines, N.; Hubner, M.; Yersin, B.; Hahnloser, D. Antibiotic treatment for uncomplicated and mild complicated diverticulitis: outpatient treatment for everyone. *Int J Colorectal Dis*. PMID 28664347

Lorente, L.; Cots, F.; Alonso, S.; Pascual, M.; Salvans, S.; Courtier, R.; Gil, M. J.; Grande, L.; Pera, M. Outpatient treatment of uncomplicated acute diverticulitis: Impact on healthcare costs. *Cir Esp*. PMID 23764519

Moya, P.; Arroyo, A.; Perez-Legaz, J.; Serrano, P.; Candela, F.; Soriano-Irigaray, L.; Calpena, R. Applicability, safety and efficiency of outpatient treatment in uncomplicated diverticulitis. *Tech Coloproctol*. PMID 22706731

Unlu, C.; Gunadi, P. M.; Gerhards, M. F.; Boermeester, M. A.; Vrouenraets, B. C. Outpatient treatment for acute uncomplicated diverticulitis. *Eur J Gastroenterol Hepatol*. PMID 23636075

Key Question 2b (Antibiotics)

AVOD. Chabok, A.; Pahlman, L.; Hjern, F.; Haapaniemi, S.; Smedh, K. Randomized clinical trial of antibiotics in acute uncomplicated diverticulitis. *Br J Surg*. PMID 22290281

AVOD. Isacson. Long-term follow-up of the AVOD randomized trial of antibiotic avoidance in uncomplicated diverticulitis. *Br J Surg*. PMID 31386199

- DIABOLO.** Daniels, L.; Unlu, C.; de Korte, N.; van Dieren, S.; Stockmann, H. B.; Vrouenraets, B. C.; Consten, E. C.; van der Hoeven, J. A.; Eijsbouts, Q. A.; Faneyte, I. F.; Bemelman, W. A.; Dijkgraaf, M. G.; Boermeester, M. A. Randomized clinical trial of observational versus antibiotic treatment for a first episode of CT-proven uncomplicated acute diverticulitis. *Br J Surg*. PMID 27686365
- DIABOLO.** Juncadella and Anna C.; Feuerstein and Joseph D. In uncomplicated, left-sided acute diverticulitis, observation did not differ from antibiotics for recovery. *Annals of Internal Medicine*. PMID 28241291
- DIABOLO.** van Dijk, S. T.; Daniels, L.; de Korte, N.; Stockmann, H. B.; Vrouenraets, B. C.; EC, J. Consten; JA, B. van der Hoeven; Faneyte, I. F.; MG, W. Dijkgraaf; Boermeester, M. A. Quality of Life and Persistent Symptoms After Uncomplicated Acute Diverticulitis. *Dis Colon Rectum*. PMID 30807455
- DIABOLO.** van Dijk, S. T.; Daniels, L.; Unlu, C.; de Korte, N.; van Dieren, S.; Stockmann, H. B.; Vrouenraets, B. C.; Consten, E. C.; van der Hoeven, J. A.; Eijsbouts, Q. A.; Faneyte, I. F.; Bemelman, W. A.; Dijkgraaf, M. G.; Boermeester, M. A. Long-Term Effects of Omitting Antibiotics in Uncomplicated Acute Diverticulitis. *Am J Gastroenterol*. PMID 29700480
- AVOD and DIABOLO (individual-patient data meta-analysis).** van Dijk ST, Chabok A, Dijkgraaf MG, et al. Observational versus antibiotic treatment for uncomplicated diverticulitis: an individual-patient data meta-analysis. *The British journal of surgery*. PMID: 32073652.
- Schug-Pass trial.** Schug-Pass, C.; Geers, P.; Hugel, O.; Lippert, H.; Kockerling, F. Prospective randomized trial comparing short-term antibiotic therapy versus standard therapy for acute uncomplicated sigmoid diverticulitis. *Int J Colorectal Dis*. PMID 20140619
- Schug-Pass trial.** Schug-Pass C.; Geers P.; Hugel O.; Lippert H.; Kockerling F. Erratum: prospective randomized trial comparing short-term antibiotic therapy versus standard therapy for acute uncomplicated sigmoid diverticulitis (*International Journal of Colorectal Disease* DOI: 10.1007/s00384-010-0899-4). *Int J Colorectal Dis*. 2010 Jun;25(6):785. No PMID
- STAND.** Jaung R, Nisbet S, Gosselink MP, et al. Antibiotics Do Not Reduce Length of Hospital Stay for Uncomplicated Diverticulitis in a Pragmatic Double-Blind Randomized Trial. *Clinical Gastroenterology and Hepatology*. PMID: 32240832.
- de Korte, N.; Kuyvenhoven, J. P.; van der Peet, D. L.; Felt-Bersma, R. J.; Cuesta, M. A.; Stockmann, H. B. Mild colonic diverticulitis can be treated without antibiotics. A case-control study. *Colorectal Dis*. PMID 21689302
- Etzioni; D. A.; Chiu; V. Y.; Cannom; R. R.; Burchette; R. J.; Haigh; P. I.; Abbas; M. A. Outpatient treatment of acute diverticulitis: rates and predictors of failure. *Dis Colon Rectum*. PMID 20484998
- Hjern, F.; Josephson, T.; Altman, D.; Holmstrom, B.; Mellgren, A.; Pollack, J.; Johansson, C. Conservative treatment of acute colonic diverticulitis: are antibiotics always mandatory?. *Scand J Gastroenterol*. PMID 17190761
- Kellum, J. M.; Sugerman, H. J.; Coppa, G. F.; Way, L. R.; Fine, R.; Herz, B.; Speck, E. L.; Jackson, D.; Duma, R. J. Randomized, prospective comparison of cefoxitin and gentamicin-clindamycin in the treatment of acute colonic diverticulitis. *Clin Ther*. PMID 1638578
- Kim; J. Y.; Park; S. G.; Kang; H. J.; Lim; Y. A.; Pak; K. H.; Yoo; T.; Cho; W. T.; Shin; D. W.; Kim; J. W. Prospective randomized clinical trial of uncomplicated right-sided colonic diverticulitis: antibiotics versus no antibiotics. *Int J Colorectal Dis*. PMID 31267222
- Park; J. H.; Park; H. C.; Lee; B. H. One-day versus four-day antibiotic treatment for acute right colonic uncomplicated diverticulitis: A randomized clinical trial. *Turk J Gastroenterol*. PMID 31290747
- Ribas; Y.; Bombardo; J.; Aguilar; F.; Jovell; E.; Alcantara-Moral; M.; Campillo; F.; Lleonart; X.; Serra-Aracil; X. Prospective randomized clinical trial assessing the efficacy of a short course of intravenously administered amoxicillin plus clavulanic acid followed by oral antibiotic in patients with uncomplicated acute diverticulitis. *Int J Colorectal Dis*. PMID 20526718

- Ridgway, P. F.; Latif, A.; Shabbir, J.; Ofriokuma, F.; Hurley, M. J.; Evoy, D.; O'Mahony, J. B.; Mealy, K. Randomized controlled trial of oral vs intravenous therapy for the clinically diagnosed acute uncomplicated diverticulitis. *Colorectal Dis*. PMID 19016815
- Scarpa, C. R.; Buchs, N. C.; Poncet, A.; Konrad-Mugnier, B.; Gervaz, P.; Morel, P.; Ris, F. Short-term Intravenous Antibiotic Treatment in Uncomplicated Diverticulitis Does Not Increase the Risk of Recurrence Compared to Long-term Treatment. *Ann Coloproctol*. PMID 25960972

Key Question 2c (Interventional Radiology)

- Lambrichts; D. P. V.; Bolkenstein; H. E.; van der Does; Dche; Dieleman; D.; Crolla; Rmiph; Dekker; J. W. T.; van Duijvendijk; P.; Gerhards; M. F.; Nienhuijs; S. W.; Menon; A. G.; de Graaf; E. J. R.; Consten; E. C. J.; Draaisma; W. A.; Broeders; Iamj; Bemelman; W. A.; Lange; J. F. Multicentre study of non-surgical management of diverticulitis with abscess formation. *Br J Surg*. PMID 30811050
- Mali, J.; Mentula, P.; Leppaniemi, A.; Sallinen, V. Determinants of treatment and outcomes of diverticular abscesses. *World J Emerg Surg*. PMID 31320921

Key Question 3 (Colonoscopy)

- Alcantar, D.; Rodriguez, C.; Fernandez, R.; Kumar, S.; Junia, C. The necessity of a colonoscopy after an acute diverticulitis event in adults less than 50 years old. *Cureus*. PMID 31720142
- Andrade, P.; Ribeiro, A.; Ramalho, R.; Lopes, S.; Macedo, G. Routine Colonoscopy after Acute Uncomplicated Diverticulitis - Challenging a Putative Indication. *Dig Surg*. PMID 27941344
- Brar, M. S.; Roxin, G.; Yaffe, P. B.; Stanger, J.; MacLean, A. R.; Buie, W. D. Colonoscopy following nonoperative management of uncomplicated diverticulitis may not be warranted. *Dis Colon Rectum*. PMID 24105001
- Choi, Y. H.; Koh, S. J.; Kim, J. W.; Kim, B. G.; Lee, K. L.; Im, J. P.; Kim, J. S.; Jung, H. C. Do we need colonoscopy following acute diverticulitis detected on computed tomography to exclude colorectal malignancy?. *Dig Dis Sci*. PMID 24723071
- Daniels, L.; Unlu, C.; de Wijkerslooth, T. R.; Stockmann, H. B.; Kuipers, E. J.; Boermeester, M. A.; Dekker, E. Yield of colonoscopy after recent CT-proven uncomplicated acute diverticulitis: a comparative cohort study. *Surg Endosc*. PMID 25472747
- Elmi, A.; Hedgire, S. S.; Pargaonkar, V.; Cao, K.; McDermott, S.; Harisinghani, M. Is early colonoscopy beneficial in patients with CT-diagnosed diverticulitis?. *AJR Am J Roentgenol*. PMID 23701063
- Horesh, N.; Saeed, Y.; Horesh, H.; Berger, Y.; Speter, C.; Pery, R.; Rosin, D.; Gutman, M.; Zmora, O. Colonoscopy after the first episode of acute diverticulitis: challenging management paradigms. *Tech Coloproctol*. PMID 27170283
- Khoury, T.; Mahamid, M.; Lubany, A.; Safadi, M.; Farah, A.; Sbeit, W.; Mari, A. Underlying Colorectal Cancer Was Rarely Detected After an Episode of Acute Diverticulitis: a Retrospective Analysis of 225 Patients. *J Gastrointest Cancer*. PMID 30632029
- Lahat, A.; Yanai, H.; Menachem, Y.; Avidan, B.; Bar-Meir, S. The feasibility and risk of early colonoscopy in acute diverticulitis: a prospective controlled study. *Endoscopy*. PMID 17554647
- Lau, K. C.; Spilsbury, K.; Farooque, Y.; Kariyawasam, S. B.; Owen, R. G.; Wallace, M. H.; Makin, G. B. Is colonoscopy still mandatory after a CT diagnosis of left-sided diverticulitis: can colorectal cancer be confidently excluded?. *Dis Colon Rectum*. PMID 21904141
- Lecleire, S.; Nahon, S.; Alatawi, A.; Antonietti, M.; Chaput, U.; Di-Fiore, A.; Alhameedi, R.; Marteau, P.; Ducrotte, P.; Dray, X. Diagnostic impact of routine colonoscopy following acute diverticulitis: A multicenter study in 808 patients and controls. *United European Gastroenterol J*. PMID 25083288
- Meireles, L. C.; Fernandes, S. R.; Ribeiro, L. C.; Velosa, J. Role of endoscopy after an acute episode of diverticulitis: analysis of a cohort of Portuguese patients from a tertiary referral center. *Eur J Gastroenterol Hepatol*. PMID 26378691

- O'Donohoe, N.; Chandak, P.; Likos-Corbett, M.; Yee, J.; Hurndall, K.; Rao, C.; Engledow, A. Follow up colonoscopy may be omissible in uncomplicated left-sided acute diverticulitis diagnosed with CT- a retrospective cohort study. *Scientific Reports*. PMID 31882879
- Ramphal, W.; Schreinemakers, J. M.; Seerden, T. C.; Crolla, R. M.; Rijken, A. M.; Gobardhan, P. D. What is the Risk of Colorectal Cancer After an Episode of Acute Diverticulitis in Conservatively Treated Patients?. *J Clin Gastroenterol*. PMID 26125459
- Ramphal, W.; Schreinemakers, J. M. J.; Seerden, T. C. J.; Gobardhan, P. D. Tumour Characteristics of Patients with Colorectal Cancer after Acute Uncomplicated Diverticulitis. *Dig Dis*. PMID 29945147
- Sallinen, V.; Mentula, P.; Leppaniemi, A. Risk of colon cancer after computed tomography-diagnosed acute diverticulitis: is routine colonoscopy necessary?. *Surg Endosc*. PMID 24178863
- Schout, P. J.; Spillenaar Bilgen, E. J.; Groenen, M. J. Routine screening for colon cancer after conservative treatment of diverticulitis. *Dig Surg*. PMID 23171930
- Seoane Urgorri, A.; Zaffalon, D.; Pera Roman, M.; Batlle Garcia, M.; Riu Pons, F.; Dedeu Cusco, J. M.; Pantaleon Sanchez, M.; Bessa Caserras, X.; Barranco Priego, L.; Alvarez-Gonzalez, M. A. Routine lower gastrointestinal endoscopy for radiographically confirmed acute diverticulitis. In whom and when is it indicated?. *Rev Esp Enferm Dig*. PMID 29900742
- Studniarek, A.; Kochar, K.; Warner, C.; Eftaiha, S.; Naffouj, S.; Borsuk, D.; Mellgren, A.; Park, J.; Cintron, J.; Harrison, J. Findings on colonoscopy after diverticulitis: A multicenter review. *The American Surgeon*. PMID 31908222.
- Suhardja, T. S.; Norhadi, S.; Seah, E. Z.; Rodgers-Wilson, S. Is early colonoscopy after CT-diagnosed diverticulitis still necessary?. *Int J Colorectal Dis*. PMID 28035461

Key Questions 4a-b (Prevention, Nonsurgical)

- DIVA.** Stollman, N.; Magowan, S.; Shanahan, F.; Quigley, E. M. A randomized controlled study of mesalamine after acute diverticulitis: results of the DIVA trial. *J Clin Gastroenterol*. PMID 23426454
- PREVENT-1.** Kamm. Prevention of Recurrence of Diverticulitis. <https://clinicaltrials.gov/show/nct00545740>. NCT00545740
- PREVENT-2.** Eucr and N. L. The purpose of this study is to determine whether SPD476 is effective in reducing recurrence of diverticulitis. <http://www.who.int/trialsearch/trial2.aspx?Trialid=eucr2007-004896-20-nl>. NCT00545103
- PREVENT-1 & PREVENT-2.** Raskin, J. B.; Kamm, M. A.; Jamal, M. M.; Marquez, J.; Melzer, E.; Schoen, R. E.; Szaloki, T.; Barrett, K.; Streck, P. Mesalamine did not prevent recurrent diverticulitis in phase 3 controlled trials. *Gastroenterology*. PMID 25038431
- PREVENT-1 & PREVENT-2.** Silva Sanchez S. D.; Wan H.; Streck P.; Willshire D.; Raskin J. B. Long-term safety of once-daily multimatrix mesalazine: a pooled clinical trials analysis. *Journal of gastroenterology and hepatology (Australia)*. No PMID
- SAG-37 and SAG-51.** Kruis, W.; Kardalinos, V.; Eisenbach, T.; Lukas, M.; Vich, T.; Bunganic, I.; Pokrotnieks, J.; Derova, J.; Kondrackiene, J.; Safadi, R.; Tuculanu, D.; Tulassay, Z.; Banai, J.; Curtin, A.; Dorofeyev, A. E.; Zakko, S. F.; Ferreira, N.; Bjorck, S.; Diez Alonso, M. M.; Makela, J.; Talley, N. J.; Dilger, K.; Greinwald, R.; Mohrbacher, R.; Spiller, R. Randomised clinical trial: mesalazine versus placebo in the prevention of diverticulitis recurrence. *Aliment Pharmacol Ther*. PMID 28543263
- Festa, V.; Spila Alegiani, S.; Chiesara, F.; Moretti, A.; Bianchi, M.; Dezi, A.; Traversa, G.; Koch, M. Retrospective comparison of long-term ten-day/month rifaximin or mesalazine in prevention of relapse in acute diverticulitis. *Eur Rev Med Pharmacol Sci*. PMID 28387885
- Kvasnovsky, C. L.; Bjarnason, I.; Donaldson, A. N.; Sherwood, R. A.; Papagrigoriadis, S. A randomized double-blind placebo-controlled trial of a multi-strain probiotic in treatment of symptomatic uncomplicated diverticular disease. *Inflammopharmacology*. PMID 28528364

- Lanas, A.; Ponce, J.; Bignamini, A.; Mearin, F. One year intermittent rifaximin plus fibre supplementation vs. fibre supplementation alone to prevent diverticulitis recurrence: a proof-of-concept study. *Dig Liver Dis*. PMID 23092785
- Mizuki, A.; Tatemichi, M.; Nakazawa, A.; Tsukada, N.; Nagata, H.; Kinoshita, Y. Effects of Burdock tea on recurrence of colonic diverticulitis and diverticular bleeding: An open-labelled randomized clinical trial. *Sci Rep*. PMID 31043657
- Parente, F.; Bargiggia, S.; Prada, A.; Bortoli, A.; Giacosa, A.; Germana, B.; Ferrari, A.; Casella, G.; De Pretis, G.; Miori, G. Intermittent treatment with mesalazine in the prevention of diverticulitis recurrence: a randomised multicentre pilot double-blind placebo-controlled study of 24-month duration. *Int J Colorectal Dis*. PMID 23754545
- Tursi, A.; Brandimarte, G.; Daffina, R. Long-term treatment with mesalazine and rifaximin versus rifaximin alone for patients with recurrent attacks of acute diverticulitis of colon. *Dig Liver Dis*. PMID 12236485
- Tursi, A.; Brandimarte, G.; Giorgetti, G. M.; Elisei, W.; Aiello, F. Balsalazide and/or high-potency probiotic mixture (VSL#3) in maintaining remission after attack of acute, uncomplicated diverticulitis of the colon. *Int J Colorectal Dis*. PMID 17390144

Key Question 4c (Elective Surgery)

- Aquina, C. T.; Becerra, A. Z.; Xu, Z.; Justiniano, C. F.; Noyes, K.; Monson, J. R. T.; Fleming, F. J. Population-based study of outcomes following an initial acute diverticular abscess. *Br J Surg*. PMID 30335195
- Bhakta, A.; Tafen, M.; Glotzer, O.; Canete, J.; Chismark, A. D.; Valerian, B. T.; Stain, S. C.; Lee, E. C. Laparoscopic sigmoid colectomy for complicated diverticulitis is safe: review of 576 consecutive colectomies. *Surg Endosc*. PMID 26275534
- Bolkenstein; H. E.; Consten; E. C. J.; van der Palen; J.; van de Wall; B. J. M.; Broeders; Iamj; Bemelman; W. A.; Lange; J. F.; Boermeester; M. A.; Draaisma; W. A. Long-term Outcome of Surgery Versus Conservative Management for Recurrent and Ongoing Complaints After an Episode of Diverticulitis: 5-year Follow-up Results of a Multicenter Randomized Controlled Trial (DIRECT-Trial). *Ann Surg*. PMID 30247329
- Bolkenstein; H. E.; de Wit; G. A.; Consten; E. C. J.; Van de Wall; B. J. M.; Broeders; Iamj; Draaisma; W. A. Cost-effectiveness analysis of a multicentre randomized clinical trial comparing surgery with conservative management for recurrent and ongoing diverticulitis (DIRECT trial). *Br J Surg*. PMID 30566245
- Bordeianou, L.; Cauley, C. E.; Patel, R.; Bleday, R.; Mahmood, S.; Kennedy, K.; Ahmed, K. F.; Yokoe, D.; Hooper, D.; Rubin, M. Prospective Creation and Validation of the PREVENTT (Prediction and Enaction of Prevention Treatments Trigger) Scale for Surgical Site Infections (SSIs) in Patients With Diverticulitis. *Ann Surg*. PMID 29916880
- Ilyas, M. I.; Zangbar, B.; Nfonsam, V. N.; Maegawa, F. A.; Joseph, B. A.; Patel, J. A.; Wexner, S. D. Are there differences in outcome after elective sigmoidectomy for diverticular disease and for cancer? A national inpatient study. *Colorectal Dis*. PMID 27422847
- Lemini and R.; Spaulding and A. C.; Osagiede and O.; Cochuyt and J. J.; Naessens and J. M.; Crandall and M.; Cima and R. R.; Colibaseanu and D. T. Disparities in elective surgery for diverticulitis: Identifying the gap in care. *Am J Surg*. PMID 30878216
- Lidor, A. O.; Schneider, E.; Segal, J.; Yu, Q.; Feinberg, R.; Wu, A. W. Elective surgery for diverticulitis is associated with high risk of intestinal diversion and hospital readmission in older adults. *J Gastrointest Surg*. PMID 20878256
- Masoomi, H.; Buchberg, B.; Nguyen, B.; Tung, V.; Stamos, M. J.; Mills, S. Outcomes of laparoscopic versus open colectomy in elective surgery for diverticulitis. *World J Surg*. PMID 21732208
- Moghadamyeghaneh, Z.; Carmichael, J. C.; Smith, B. R.; Mills, S.; Pigazzi, A.; Nguyen, N. T.; Stamos, M. J. A comparison of outcomes of emergent, urgent, and elective surgical treatment of diverticulitis. *Am J Surg*. PMID 26116319

- Novitsky, Y. W.; Sechrist, C.; Payton, B. L.; Kercher, K. W.; Heniford, B. T. Do the risks of emergent colectomy justify nonoperative management strategies for recurrent diverticulitis?. *Am J Surg*. PMID 18639223
- Papageorge, C. M.; Kennedy, G. D.; Carchman, E. H. National Trends in Short-term Outcomes Following Non-emergent Surgery for Diverticular Disease. *J Gastrointest Surg*. PMID 27120447
- Pessaux, P.; Muscari, F.; Ouellet, J. F.; Msika, S.; Hay, J. M.; Millat, B.; Fingerhut, A.; Flamant, Y. Risk factors for mortality and morbidity after elective sigmoid resection for diverticulitis: prospective multicenter multivariate analysis of 582 patients. *World J Surg*. PMID 14639493
- Russ, A. J.; Obma, K. L.; Rajamanickam, V.; Wan, Y.; Heise, C. P.; Foley, E. F.; Harms, B.; Kennedy, G. D. Laparoscopy improves short-term outcomes after surgery for diverticular disease. *Gastroenterology*. PMID 20193685
- Sheer, A. J.; Heckman, J. E.; Schneider, E. B.; Wu, A. W.; Segal, J. B.; Feinberg, R.; Lidor, A. O. Congestive heart failure and chronic obstructive pulmonary disease predict poor surgical outcomes in older adults undergoing elective diverticulitis surgery. *Dis Colon Rectum*. PMID 21979190
- Silva-Velazco, J.; Stocchi, L.; Costedio, M.; Gorgun, E.; Kessler, H.; Remzi, F. H. Is there anything we can modify among factors associated with morbidity following elective laparoscopic sigmoidectomy for diverticulitis?. *Surg Endosc*. PMID 26541732
- Simianu, V. V.; Sinanan, M. N.; Bastawrous, A. L.; Billingham, R. P.; Fichera, A.; Florence, M. G.; Herzig, D. O.; Johnson, E. K.; Steele, S. R.; Thirlby, R. C.; Flum, D. R. The impact of delaying elective resection of diverticulitis on laparoscopic conversion rate. *Am J Surg*. PMID 25773308
- Tsilimparis, N.; Haase, O.; Wendling, P.; Kipfmuller, K.; Schmid, M.; Engemann, R.; Schwenk, W. [Laparoscopic 'fast-track' sigmoidectomy for diverticulitis disease in Germany. Results of a prospective quality assurance program]. *Dtsch Med Wochenschr*. PMID 20812161
- Valizadeh, N.; Suradkar, K.; Kiran, R. P. Specific Factors Predict the Risk for Urgent and Emergent Colectomy in Patients Undergoing Surgery for Diverticulitis. *Am Surg*. PMID 30747633
- van de Wall, B. J. M.; Stam, M. A. W.; Draaisma, W. A.; Stellato, R.; Bemelman, W. A.; Boermeester, M. A.; Broeders, J. A. M.; Belgers, E. J.; Toorenvliet, B. R.; Prins, H. A.; Consten, E. C. J. Surgery versus conservative management for recurrent and ongoing left-sided diverticulitis (DIRECT trial): an open-label, multicentre, randomised controlled trial. *Lancet Gastroenterol Hepatol*. PMID 28404008
- Varma, S.; Mehta, A.; Canner, J. K.; Azar, F.; Efron, D. T.; Efron, J.; Safar, B.; Sakran, J. V. Surgery After an Initial Episode of Uncomplicated Diverticulitis: Does Time to Resection Matter?. *J Surg Res*. PMID 30527478
- You, K.; Bendl, R.; Taut, C.; Sullivan, R.; Gachabayov, M.; Bergamaschi, R. Randomized clinical trial of elective resection versus observation in diverticulitis with extraluminal air or abscess initially managed conservatively. *Br J Surg*. PMID 29683483

Study Design Details and Arms, Risk of Bias

Key Question 1 (CT Imaging)

Table C-1-1. KQ 1. Description

Study, PMID	Country, Years	Eligibility Criteria	Signs/Symptoms	Imaging	Diagnostic Criteria
Andeweg 2011 21346548	Netherlands 2002-06	Hospitalized with acute abdominal pain, not requiring immediate surgery. CT for “suspected diverticulitis” or “left LLQ pain”.	NR	Abdominal CT	Signs of thickening of the colonic wall of ≥ 4 mm, with signs of inflammation of the pericolic fat with or without abscess formation or contained or free perforation.
Jurowich 2011 21830036	Germany 2004-06	Undergoing treatment for diverticulitis of the sigmoid colon	NR	CT, with enema and IV contrast Not all had CT, including some requiring emergency surgery (no imaging) and some with uncomplicated (ultrasound)	Hansen & Stock*
Kelly 2015 25576049	Ireland 2012	Emergency abdominal CT at a tertiary referral hospital	NR	Abdominal CT, oral contrast	N/A
Martín Arévalo 2007 17883294	Spain NR	Clinical diagnosis of acute diverticulitis	NR	CT, with IV contrast dye if suspected abscess	Hulnick (1984) †
Salem 2005 16108882	UK 2003-04	Acute abdominal pain, ≥ 25 yo. Exclude trauma or clear need for laparotomy or selected medical conditions	Acute abdominal pain	CT, with oral and IV contrast	NR
Shuaib 2014 24475484	US 2012	Nontraumatic acute abdominal pain who underwent CT	Acute abdominal pain (not pregnant)	Abdominopelvic CT, oral and/or IV contrast	N/A

Abbreviations: CT = computed tomography, ESR = erythrocyte sedimentation rate, IV = intravenous, LLQ = (abdominal) left lower quadrant pain, N/A = not applicable (study not restricted to diverticulitis), NR = not reported, PMID = Pubmed identifier, yo = years old.

* Hansen O, Stock W. [Prophylactic resection in diverticular disease—treatment by precise staging.] *Langenbecks Arch Chir Kongressbd.* 1999; 116 (Suppl II):1257-60. (No PMID; German)

† Hulnick DH, Megibow AJ, Balthazar EJ, et al. Computed tomography in the evaluation of diverticulitis. *Radiology.* 1984;152(2):491-5. doi: 10.1148/radiology.152.2.6739821. PMID: 6739821.

Table C-1-2. KQ 1. Population and diagnostic descriptives

Study, PMID	N Analyzed	Female, % Age Race	Diagnoses, N	CT Findings*
Andeweg 2011 21346548	287	62% ≤50 yo: 81% NR	Diverticulitis, acute left-sided: 124 Other: 163	Surgically managed diverticulitis: TP 31/31 Medically managed diverticulitis: NR FN 0/163
Jurowich 2011 21830036	318 (total) 242 (fully)	43% Median 64 (range 26-97) NR	Diverticulitis 100%	I (uncomplicated, 1 st episode): 30 (9.4%; not further analyzed) IIA ("phlegmonous"): 112 (35.2%); 83 (34.3%) analyzed IIB (covered perforation): 84 (26.4%); 78 (32.2%) analyzed IIC (open perforation): 27 (8.5%); 11.2% of analyzed III (uncomplicated, recurrent): 54 (17.0%); 22.3% of analyzed
Kelly 2015 25576049	1155	54% Median 57 (range 16-96) NR	Diverticulitis: NR Other: NR	NR
Martín Arévalo 2007 17883294	102	51% 59.4 (15) NR	Diverticulitis: 84 Other: 18	I (uncomplicated): 60 (59%) IIa (abscess <3 cm): 8 (7.8%) IIb (abscess >3 cm): 8 (7.8%) III (diffuse peritonitis): 8 (7.8%)
Salem 2005 16108882	211 81 w/CT	61% 62.4 (range 27-92) NR	Diverticulitis: 16 Other: 65	Diverticulitis with abscess: 15/16 Colitis/IBD: 1/16
	130 no CT		Diverticulitis: 32 Other: 98	N/A
Shuaib 2014 24475484	290	NR NR NR	Diverticulitis: NR Other: NR	NR

Abbreviations: CAD = complicated acute diverticulitis, CT = computed tomography, FN = false negative (missed diagnosis of diverticulitis on CT), NR = not reported, PMID = Pubmed identifier, TP = true positive (correct diagnosis of diverticulitis on CT), UAD = uncomplicated acute diverticulitis.

* Among those with final diagnosis of diverticulitis.

Table C-1-3. KQ 1. Quality

Study, PMID	Clear Eligibility Criteria	Adequate Intervention Description	Clear Outcome Definition	Clear Relevant Results
Andeweg 2011 21346548	No (vague)	Yes	No (vague ^A)	No (vague ^A)
Jurowich 2011 21830036	Yes (but excluded nonsurgical patients from analyses)	No (not all received CT scan)	No (unclear final diagnosis of nonsurgical patients; unclear distinction between Type I (who did not require surgery, per protocol) and Type III (who did require surgery, per protocol))	Yes (for test accuracy); No (to evaluate need for surgery)
Kelly 2015 25576049	Yes (but not restricted to diverticulitis)	Yes	No (vague ^B)	No (not clinically oriented ^C)
Martín Arévalo 2007 17883294	No (vague)	Yes	Mostly ^D	Yes
Salem 2005 16108882	Yes	No (no diagnostic criteria)	Yes	Yes
Shuaib 2014 24475484	Yes (but not restricted to diverticulitis)	Yes	Yes	No (vague ^E)

^A Study primarily designed to create a predictive algorithm for diverticulitis diagnosis.

^B Definition of “incidental finding” unclear. E.g., finding of complicated diverticulitis on an emergency abdominal CT was considered incidental.

^C No explanation of the clinical significance of most of the incidental findings.

^D Unclear whether the missed CT diagnoses of colorectal cancer impacted treatment (e.g., type or need for surgery).

^E Focus more on whether radiologists recommended further workup based on incidental findings and whether changes in clinical management occurred. No reporting of specific new incidental findings.

Key Question 2a (Outpatient)

Table C-2a-1. KQ 2a. Design details and arms

Study Year PMID Country Funding	Design	N	Population, Diverticulitis Details, Setting	Arm	Arm Details	Age Sex	Prior Episodes Eiverticulitis
Biondo, 2014, 23732265, DIVER Trial, Spain, Non- industry	RCT	132	Uncomplicated diverticulitis, tolerate oral intake with good response to first treatment measures in emergency, willing to continue treatment at home under supervision. Tertiary care, academic	Outpatient management	Discharged after 1st dose of IV Abx in the ED	Mean=55.9 (13.4) 52% male	Mean=0.47 (SD=10.9)
				Inpatient management	Admitted	Mean=56.8 (12.8) 58% male	Mean=0.39 (SD=1.0)
Bolkenstein, 2018, 29679152, Netherlands, NR	NRCS (Retrospective)	565	First episode uncomplicated diverticulitis, no Abx treatment 2wks prior or 24hr after presentation to hospital Single center	Outpatient management	Not hospitalized within 24hr of presentation	Mean=57 (SD=12) 39% male	None (by design)
				Inpatient management	Hospitalized within 24hr of presentation	Mean=59 (SD=13) 42% male	None (by design)
Joliat, 2017, 28664347, Switzerland, NR	NRCS (Retrospective)	267	Uncomplicated or mild complicated diverticulitis. Single hospital	Outpatient management	Single dose Abx (IV) in ED followed by Abx (oral) for 10 days	Median=53 (Range=44–64) 64% male	None (72%)
				Inpatient management	Abx and fluids (IV), switched to Abx (oral) when pain was managed by non-opioid analgesics and able to tolerate oral medication (also discharged). No alimentary restrictions in hospital	Median=61 (Range=50–72) 50% male	None (71%)
Lorente, 2013, 23764519, Spain, NR	NRCS (Retrospective)	136	Uncomplicated diverticulitis, tolerate oral intake, absence of comorbidities, adequate family or social support. Single hospital	Outpatient management	Abx for 7 days (oral) and analgesia (oral), liquid diet for 2 days. Follow up assessment between 4-7 days after diagnosis to confirm clinical course	Mean=58.75 (SD=15) 44% male	≥1: 19%
				Inpatient management	Abx (IV) until improvement in symptoms then discharged to continue Abx (oral) at home	Mean=60.52 (SD=19) 43% male	Previous episodes (30%)

Study Year PMID Country Funding	Design	N	Population, Diverticulitis Details, Setting	Arm	Arm Details	Age Sex	Prior Episodes Eiverticulitis
Moya, 2012, 22706731, Spain, NR	NRCS (Prospective)	76	Uncomplicated diverticulitis, tolerate oral intake, adequate family and social support network. Academic	Outpatient management	10 d oral Abx, oral analgesics, and dietary restrictions	Median=56.1 (Range=32–83) 50% male	≥1: 16%
				Inpatient management	5 d IV Abx, IV analgesic, and dietary restrictions	Median=59.7 (Range=36–84) 45% male	≥1: 18%
Ünlü, 2013, 23636075, Netherlands, NR	NRCS (Retrospective)	312	First episode uncomplicated diverticulitis Two hospitals	Outpatient management	IV Abx in ED, 7-10 d oral Abx	Mean=54.5 (SD=11.1) 42% male	None (by design)
				Inpatient management	IV Abx while inpatient, then 7-10 d oral Abx	Mean=59.3 (SD=14.6) 37% male	None (by design)

Abx = antibiotic, ED = emergency department, mos = month, NR = not reported, NRCS = non-randomized controlled study, OR = odds ratio, PMID = Pubmed identifier, RCT = randomized controlled trial, SD = standard deviation, wk = week.

Table C-2a-2. KQ 2a. Risk of bias assessment for primary studies – randomized controlled trials (RCTs)

Study, Year, PMID	Random Sequence Generation	Allocation Conceal- ment	Blinding of Participants	Blinding of Personnel/ Care Providers	Blinding of Outcome Assessor (Objective Outcomes)	Blinding of Outcome Assessor (Subjective Outcomes)	Incomplete Outcome Data	Selective Outcome Reporting	Other Bias	Eligibility Criteria Prespecified and Clearly Described	Intervention Clearly Described and Delivered Consistentl y	Outcomes Prespecified, Clearly Defined, Valid, Reliable, and Assessed Consistently
Biondo, 2014, 23732265	Low	Low	High	High	Low	Low	Low	Unclear	Low	Yes	Yes	Yes

KQ = Key Question, PMID = PubMed Identifier. Ratings are color coded for emphasis only.

From the Cochrane Risk of Bias Tool (each item rated as **Low**, **High**, **Unclear**, or N/A)

- Random sequence generation (selection bias): Selection bias (biased allocation to interventions) due to inadequate generation of a randomized sequence;
- Allocation concealment (selection bias): Selection bias (biased allocation to interventions) due to inadequate concealment of allocations prior to assignment;
- Blinding of participants (performance bias): Performance bias due to knowledge of the allocated interventions by participants during the study;
- Blinding of personnel/care providers (performance bias): Performance bias due to knowledge of the allocated interventions by personnel/care providers during the study;
- Blinding of outcome assessor (detection bias): Detection bias due to knowledge of the allocated interventions by outcome assessors;
- Incomplete outcome data (attrition bias): Attrition bias due to amount, nature or handling of incomplete outcome data;
- Selective outcome reporting (outcome reporting bias): Bias arising from outcomes being selectively reported based on the direction and/or strength of the results;
- Other Bias: Bias due to problems not covered elsewhere in the table.

From the National Heart, Lung, and Blood Institute (NHLBI) Quality Assessment Tool (each item rated as **Yes**, **No**, or **Unclear**)

- Eligibility criteria prespecified and clearly described: potentially related to selection bias;
- Intervention clearly described and delivered consistently: potentially related to performance bias;

- Outcomes prespecified, clearly defined, valid, reliable, and assessed consistently: potentially related to detection bias.

Table C-2a-3. KQ 2a. Risk of bias assessment for primary studies – nonrandomized comparative studies (NRCSSs) – assessment of confounding and selection bias

Study, Year, PMID	1.1 Potential for Any Confounding	1.2 Potential for Time-Varying Confounding?	1.4 Appropriate Analysis Method For Confounding?	1.5 Appropriate Confounding Variables Used?	1.6 Inappropriate Control of Post-Intervention Variables?	Judgement – Risk of Bias Related to Confounding	2.1 Participant Selection Based on Post-Intervention Variables?	2.2 Post-intervention Variables Associated With Intervention?	2.3 Post-intervention Variables associated with Outcome?	2.4 Start and Followup (Duration) Coincide	Start and Followup Calendar Years Coincide	2.5 Appropriate Adjustment for Selection Bias	Judgement – Risk of Bias Related to Selection Bias
Bolkenstein, 2018, 29679152	Yes	No	Yes	Unsure	No	Serious	No	N/A	N/A	Yes	No	N/A	Low
Joliat, 2017, 28664347	Yes	No	No	N/A	N/A	Critical	PY	PY	PY	Yes	No	No	Critical
Lorente, 2013, 23764519	Yes	No	No	N/A	N/A	Critical	No	N/A	N/A	Yes	No	N/A	Low
Moya, 2012, 22706731	Yes	Yes	No	N/A	N/A	Critical	No	N/A	N/A	Yes	No	N/A	Low
Ünlü, 2013, 23636075	Yes	No	No	N/A	N/A	Critical	No	N/A	N/A	Yes	No	N/A	Low

KQ = Key Question, PMID = PubMed Identifier, Responses to Risk of Bias in Nonrandomized Studies of Interventions (ROBINS-I) signaling questions 1.1 to 1.6 and 2.1 to 2.5 are in regular font. Each item rated as Yes, PY (probably yes), NI (no information), PN (probably no), No, or N/A (not applicable).

Judgements about confounding and selection bias are in **bold font**. (each item rated as **Low**, **Moderate**, **Serious**, or **Critical**).

Key Question 2b (Antibiotics)

Table C-2b-1. KQ 2b. Design details

Author, Year, PMID, Study Name, Country, Funder	Study Design	Study Dates	Inclusion Criteria	Exclusion Criteria	How Was Diverticulitis Diagnosed?
AVOD Trial, Sweden, Non-Industry	RCT	2003, 2009	Age 18-75 years, Has at least 2 of following symptoms: fever, abdominal resistance, leukocyte >10,000/ μ l, CRP (\geq 20 and \geq 2 mg/dl), detection of sigmoid diverticulitis using contrast medium. CT evidence, multicenter	CT or other evidence of complicated diverticulitis or other disease, immunosuppressive Tx, pregnancy, ongoing antibiotics	
de Korte, 2012, 21689302, Netherlands Not Reported	NRCS (Retrospective)	2001, 2007	Image-confirmed acute mild diverticulitis of the sigmoid colon in which the decision (implied based on review of charts) was made to treat conservatively	NR	image confirmed acute mild based on Ambrosetti or Hinchey 1a criteria
DIABOLO Trial, Sweden, Nonindustry	RCT	2010, 2012	Left-sided uncomplicated acute diverticulitis, clinical and diagnostic (ultrasound or CT) proven, modified Hinchey stages 1a-b (abscess size up to 5 cm) and Ambrosetti's 'mild' diverticulitis stage included.	Previous radiologically proven diverticulitis, higher modified Hinchey stages or Ambrosetti's 'severe' diverticulitis stage, sepsis, antibiotic use in the previous 4 weeks.	Patients were eligible if they had a first episode of left-sided, uncomplicated, acute diverticulitis, confirmed within 24 h by CT.
Etzioni, 2010, 20484998, USA Not Reported	NRCS (Retrospective)	2006, 2007	evaluated in Kaiser Permanente ED for a primary assigned diagnosis of acute diverticulitis, continuously enrolled as a member in Kaiser Permanente system before the index treatment episode	admitted for inpatient treatment, prior diagnosis of diverticulitis, colorectal cancer, inflammatory bowel disease, did not have CT within 1 year of ED evaluation	ICD codes
Hjern, 2007, 17190761, Sweden, Nonindustry	NRCS (Prospective)	2000, 2002	Clinical diagnosis of Acute Diverticulitis confirmed by CT	Diagnoses only based on clinical findings, operated immediately following admission because of clinical signs of peritonitis, perforated AD confirmed by CT	Clinical diagnosis of Acute Diverticulitis confirmed by CT

Author, Year, PMID, Study Name, Country, Funder	Study Design	Study Dates	Inclusion Criteria	Exclusion Criteria	How Was Diverticulitis Diagnosed?
Jaung, 2019, 32240832, STAND, New Zealand and Australia	RCT	2015-2019	CT-proven Hinchey 1a uncomplicated acute diverticulitis	≥2 criteria for Systemic Inflammatory Response Syndrome (SIRS), temperature <36° or >38° C, heart rate >90 beats per minute, respiratory rate >20 breaths per minute or PaCO ₃ <32mmHg, white cell count <4 or >12 x 10 ⁹ /L; were unable to give consent, language barrier or cognitive impairment; previous drug reactions; prior usage of steroids; had been administered regular immunomodulators or biologics within the six months prior to presentation; used regular NSAIDs for greater than a week prior to presentation; had been administered >1 dose of intravenous or >2 doses of oral antibiotics during this illness but prior to enrolment in the study; were pregnant; had an American Society of Anesthesiologists physical status classification (ASA) ≥4; or had CT evidence of complicated acute diverticulitis.	CT
Kellum, 1992, 1638578, USA Not reported	RCT	NR	Acute diverticulitis considered present if there was abdominal tenderness, signs of infection (fever or leukocytosis), and radiological, surgical or pathological evidence.	Creatinine ≥/ 3mg/dl	Acute diverticulitis considered present if there was abdominal tenderness, signs of infection (fever or leukocytosis), radiological, surgical or pathological evidence.

Author, Year, PMID, Study Name, Country, Funder	Study Design	Study Dates	Inclusion Criteria	Exclusion Criteria	How Was Diverticulitis Diagnosed?
Kim, 2019, 31267222, S Korea Not reported	RCT	2014, 2018	(1) age 18–80 years; (2) <i>right-sided colonic diverticulitis (cecum, ascending colon, or proximal transverse colon)</i> ; and (3) uncomplicated diverticulitis (grade Ia)	(1) age < 18 or > 80 years; (2) distal transverse, left-sided, or sigmoid colonic diverticulitis; (3) complicated colonic diverticulitis (grades Ib, II, III, or IV); (4) sepsis; (5) systemic inflammatory response syndrome (SIRS); (6) immunocompromised patients (taking corticosteroid or immunosuppressive drugs, transplantation, or chronic renal failure with hemodialysis); (7) allergy to quinolone antibiotics; (8) pregnant or lactating patients; (9) American Society of Anesthesiologists (ASA) score > 3; (10) social, psychiatric, or cognitive impairment	Intravenous (IV) contrast-enhanced computed tomography (CT) was performed to confirm the diagnosis. Uncomplicated diverticulitis is defined as grade Ia and complicated diverticulitis includes grades Ib, II, III, and IV.
Park, 2019, 31290747, S Korea, Not Reported	RCT	2011, 2014	<i>Right colonic diverticulitis</i> in emergency or hospital setting, CT proven,	Abscess >3 cm in diameter, Hinchey II diseases or worse, ongoing antibiotic therapy from other hospital, pregnancy, or cephalosporin allergy	Inflamed diverticulum, phlegmon formation (Hinchey Ia), and small (≤ 3 cm) pericolic abscess formation (partial Hinchey Ib) were considered to be consistent with the diagnosis of CT-based uncomplicated diverticulitis
Ribas, 2010, 20526718, Spain, Non-industry	RCT	NR	Clinical diagnosis of uncomplicated acute diverticulitis, CT confirmed within 28-48 h	(1) immunocompromised patients, (2) patients under 18 years of age, (3) pregnant women, (4) clinical suspicion or CT confirmation of complicated acute diverticulitis, (5) Karnofsky performance score less than 50%, or (6) allergy to penicillin	The clinical diagnosis of sigmoid diverticulitis was suggested in patients with abdominal pain localized to the left lower quadrant and tenderness upon physical examination. The presence of fever, change in bowel habits, dysuria, urinary frequency and urgency, as well as leukocytosis was also taken into account to reach the diagnosis of diverticulitis.
Ridgway, 2008, 19016815, Ireland, Not Reported	RCT	2002, 2004	Acute uncomplicated diverticulitis. Hinchey type 1, multicenter	Hinchey types III or IV	Plain radiology and relevant blood investigation
Scarpa, 2015, 25960972, Switzerland Not Reported	NRCS (Prospective)	2007, 2012	1st episode CT-confirmed uncomplicated diverticulitis requiring hospitalization	complicated diverticulitis (Hinchey-Ib class and above), <18 yrs of age, chronic IBD or a tumor	physical examination and laboratory tests revealing an inflammatory syndrome and was confirmed by using an abdominal CT scan

Author, Year, PMID, Study Name, Country, Funder	Study Design	Study Dates	Inclusion Criteria	Exclusion Criteria	How Was Diverticulitis Diagnosed?
Schug-Pass, 2010, 20140619, Germany, Industry	RCT	2004, 2008	Sigmoid diverticulitis using contrast medium, CT proven, multi-center	Study Tx or other betalactam. Hypersensitivity to betalactam. Immunosuppressant use. Antibiotic Tx within 2 weeks before enrollment. Incurable hematological/oncological diseases. Pregnancy. Existing sigmoid diverticulitis requiring surgery.	

Table C-2b-2. KQ 2b. Arm details

Author, Year, PMID, Study Name, Country	Arm	Arm Description	Dose	Frequency	Route	Duration of Intervention
AVOD Trial, Sweden, Non-Industry	Antibiotics: Multiple (discretionary or undefined)	IV combination of a second- or third-generation cephalosporin (cefuroxime or cefotaxime) and metronidazole, or with carbapenem antibiotics (ertapenem, meropenem or imipenem) or piperacillin – tazobactam. Orally administered antibiotics such as ciprofloxacin or cefadroxil combined with metronidazole were initiated subsequently on the ward or at discharge.	NR	NR	IV	≥ 7 days
	Placebo	IV fluids only	NR	NR	IV	N/A
de Korte, 2012, 21689302, Netherlands	Antibiotics: Multiple (discretionary or undefined)	Two hospitals, different antibiotic protocols. No formal protocol at H1; antibiotics not routinely given. H2 had protocol for antibiotic treatment of diverticulitis: combination of piperacillin and metronidazole (IV; no doses given) when admitted to surgical ward; amoxicillin–clavulanic acid (IV; no doses given) when admitted to the internal medicine or gastroenterology wards. Continued for 7-10 days depending on clinical status	NR	NR	IV	7-10 days
	No intervention (non-placebo)	Restriction of oral intake, intravenous fluid rehydration and observation. When symptoms resided, a normal diet was started. No specific foods were avoided. Analgesics were given as appropriate, starting with acetaminophen and nonsteroid anti-inflammatory drugs (NSAIDs) as needed.	NR	NR	NR	NR
DIABOLO Trial, Sweden, Nonindustry	No intervention (non-placebo)	No antibiotic	NR	NR	NR	NR
	Antibiotics: Amoxicillin + Clavulanate	IV amoxicillin–clavulanic acid was chosen as broad-spectrum antibiotic treatment of choice. Was switched to oral administration after 10 days if tolerated. In the event of allergy, a switch was made to the combination of ciprofloxacin and metronidazole.	1200 mg	4/day	IV for 10 days, switched to oral after if tolerated	10 days

Author, Year, PMID, Study Name, Country	Arm	Arm Description	Dose	Frequency	Route	Duration of Intervention
Etzioni, 2010, 20484998, USA	Fluoroquinolone + metronidazole	Most commonly used	NR	NR	Oral	N/A
	Antibiotic duration: 14+ days	N/A	N/A	N/A	N/A	N/A
	Antibiotic duration: 10-13 days	N/A	N/A	N/A	N/A	N/A
	Antibiotic duration: <10 days	N/A	N/A	N/A	N/A	N/A
	Multiple (discretionary or undefined)	trimethoprim/sulfamethoxazole, amoxicillin, extended-spectrum beta-lactamases, clindamycin, doxycycline, and cephalosporins	NR	NR	Oral	N/A
Hjern, 2007, 17190761, Sweden	No intervention (non-placebo)	Careful observation, iv fluids, restriction of oral intake, no antibiotics				
	Antibiotics: Cephalosporin + Metronidazole	Careful observation, iv fluids, restriction of oral intake, antibiotics			Oral cephalosporine and metronidazole given iv, followed by oral administration of quinolone with metronidazole	10-14 days
Jaung, 2019, 32240832, STAND, New Zealand and Australia	Antibiotics: po amoxicillin/clavulanic +- IV cefuroxime & po metronidazole	Initial regimen (IV cefuroxime 750 mg every 6 hours and oral metronidazole 400 mg three times a day), and oral antibiotics (amoxicillin/clavulanic acid 625 mg three times a day). Use of "IV regimen" at the discretion of the surgical team.	cefuroxime 750 mg; metronidazole 400 mg; amoxicillin/clavulanic acid 625 mg	cefuroxime every 6 hours; oral metronidazole 3 t.i.d; amoxicillin/clavulanic acid t.i.d	first iv and oral, then oral	5-7 days (outpatient after first approximately 2 days)
	Placebo	N/A	N/A	N/A	N/A	5-7 days (outpatient after first approximately 2 days)
Kellum, 1992, 1638578, USA	Antibiotics: Gentamicin-Clindamycin		1 to 1.4 gm	Every 8 hours	IV	NR
	Antibiotics: Cefoxitin		1 to 2 gm	Every 6 hours	IV	NR

Author, Year, PMID, Study Name, Country	Arm	Arm Description	Dose	Frequency	Route	Duration of Intervention
Kim, 2019, 31267222, S Korea	Placebo	Admitted, administered IV fluids, and given bowel rest for at least 3 days (and up to 5 days)				
	Antibiotics: Cephalosporin + Metronidazole	Antibiotics	Ceftriaxone, 2 g and metronidazole, 500 mg	Ceftriaxone, once daily and metronidazole, three times daily	IV was first used, then changed to oral when oral intake was toleratedIV	10 days
Park, 2019, 31290747, S Korea	Antibiotics: Cephalosporin + Metronidazole	1-day group	Cefmetazole (2000mg/day) and metronidazole (1500 mg/day)		IV	1 day
	Antibiotics: Cephalosporin + Metronidazole	4-day group	Cefmetazole (2000mg/day) and metronidazole (1500 mg/day)		57 received 4 days of IV; 32 received 3 days of IV and 1 day oralIV	4 day
Ribas, 2010, 20526718, Spain	Antibiotics: Amoxicillin + Clavulanate	antibiotics intravenously administered at first and then orally administered when symptoms improved (pain decrease, less tenderness, and absence of fever)	amoxicillin plus clavulanic acid 1g every 8h	3/day	inpatients (IV+oral) then outpatient (oral)IV	inpatients (IV (1-2 days) + oral (2-3 days)) then outpatient (oral) (10 days)
	Antibiotics: Amoxicillin + Clavulanate	antibiotics intravenously administered	amoxicillin plus clavulanic acid 1g every 8h	3/day	inpatients (IV only) then outpatient (oral)IV	inpatients (IV) (8-9 days) then outpatient (oral) (5 days)
Ridgway, 2009, 19016815, Ireland	Antibiotics: Ciprofloxacin + Metronidazole	Oral	500 mg, 400 mg	NR	Conversion to IV as per attending physicianIV	
	Antibiotics: Ciprofloxacin + Metronidazole	IV	400 mg, 500 mg	NR	Conversion to IV as per attending physicianIV	

Author, Year, PMID, Study Name, Country	Arm	Arm Description	Dose	Frequency	Route	Duration of Intervention
Scarpa, 2015, 25960972, Switzerland	Antibiotics: short course IV	All patients received an IV antibiotic treatment of ceftriaxone (2,000 mg/day) and metronidazole (1,500 mg/day) except when contraindicated. Antibiotic treatment for 5 days or less.	IV: ceftriaxone (2,000 mg/day); metronidazole (1,500 mg/day); oral: ciprofloxacin (1,000-mg/day); metronidazole (1,500-mg/day)	IV: ceftriaxone (2,000 mg/day); metronidazole (1,500 mg/day); oral: ciprofloxacin (1,000-mg/day); metronidazole (1,500-mg/day)	Oral/IV	up to 5 days for IV (followed by 5 days oral antibiotics) (NB. results report mean length of treatment 4.7 days)
	Antibiotics: long course IV	All patients received an IV antibiotic treatment of ceftriaxone (2,000 mg/day) and metronidazole (1,500 mg/day) except when contraindicated. Antibiotic treatment for 6 days, possibly up to 14 days.	ceftriaxone (2,000 mg/day); metronidazole (1,500 mg/day)	ceftriaxone (2,000 mg/day); metronidazole (1,500 mg/day)	IV	6-14 days for IV (NB. results report mean length of treatment 8.7 days)
Schug-Pass, 2010, 20140619, Germany	Antibiotic: Ertapenem	4 days	1 g	1/day	IV	4 days
	Antibiotic: Ertapenem	7 days	1 g	1/day	IV	7 days

Table C-2b-3. KQ 2b. Baselines

Author, Year, PMID, Study Name, Country	Arm	Male %	Race/Ethnicity	Age, Mean (SD) or %	Participants with Un/Complicated Diverticulitis, %	Number of Prior Episodes of Diverticulitis, %	History of (Prior) Complicated Diverticulitis %	Time Since Last Episode of Diverticulitis, Mean (SD)
AVOD Trial, Sweden	Antibiotics: Multiple (discretionary or undefined)	35	NR	57.4 (12.8)	100/0	at least one episode 35.6	NR	NR
	Placebo (IV fluids only)	36	NR	57.1 (13.2)	100/0	at least one episode 44.8	NR	NR
de Korte, 2012, 21689302, Netherlands	Antibiotics: Multiple (discretionary or undefined)	29	NR	61 [Range 27–92]	0/100	NR	NR	NR
	No intervention (non-placebo)	46.4	White 94%, Black 3.8%, Hispanic/Latino 16.6%, Asian 0.3%, Other 1.9%	56.1 (11.04)	NR	none 0.5, one 59.7, two 22.7, four to five 5.8, six to ten 1.9	NR	16.5 weeks [range 0, 122 weeks]
DIABOLO Trial, Sweden,	No intervention (non-placebo)	50.6	NR	57.4	NR	NR	NR	NR
	Antibiotics: Amoxicillin + Clavulanate	54.7	NR	59.4 (12.1)	NR	NR	NR	NR
Etzioni, 2010, 20484998, USA	Total	46	NR	58.5	NR	NR	NR	NR
Hjern, 2007, 17190761, Sweden	No intervention (non-placebo)	35	NR	59	NR	NR	30	NR
	Antibiotics: Cephalosporin + Metronidazole	37	NR	60	NR	NR	25	NR
Jaung, 2019, 32240832, STAND, New Zealand and Australia	Antibiotics: po amoxicillin/clavulanic +- IV cefuroxime & oral metronidazole	40	NR	Probably Median 56 (probably IQR 53-59)	0	71	NR	NR
	Placebo	44	NR	Probably Median 59 (probably IQR 57-62)	0	68	NR	NR

Author, Year, PMID, Study Name, Country	Arm	Male %	Race/Ethnicity	Age, Mean (SD) or %	Participants with Un/Complicated Diverticulitis, %	Number of Prior Episodes of Diverticulitis, %	History of (Prior) Complicated Diverticulitis %	Time Since Last Episode of Diverticulitis, Mean (SD)
Kellum, 1992, 1638578, USA	Antibiotics: Cefoxitin	NR	NR	64.5 (SE 2)	NR	NR	12	NR
	Antibiotics: Gentamicin-Clindamycin	NR	NR	60.8 (SE 3)	NR	NR	NR	NR
Kim, 2019, 31267222, S Korea	Placebo (admitted, administered IV fluids, and given bowel rest for at least 3 days (and up to 5 days))	57.8	NR	38.9 (9.5)	100/0	NR	NR	NR
	Antibiotics: Cephalosporin + Metronidazole	65.6	NR	37.9 (8.4)	100/0	NR	NR	NR
Park, 2019, 31290747, S Korea	Antibiotics: Cephalosporin + Metronidazole (1-day group)	54.0	NR	42.0 (11.1)	100/0	none 100	0	NR
	Antibiotics: Cephalosporin + Metronidazole (4-day group)	55.1	NR	40.2 (11.2)	100/0	none 100	0	NR
Ribas, 2010, 20526718, Spain	Antibiotics: Amoxicillin + Clavulanate (IV then Oral)	52	NR	56 (95%CI 50, 62)	100/0	Mean 1.2 (95%CI 0.9, 1.5)	NR	NR
	Antibiotics: Amoxicillin + Clavulanate (IV)	52	NR	56 (95%CI 45, 57)	100/0	Mean 1.5 (95%CI 0.9, 2.1)	NR	NR
Ridgway, 2009, 19016815, Ireland	Antibiotics: Ciprofloxacin + Metronidazole (Oral)	39.02	NR	Median 68 [Range 31-84]	NR	NR	NR	NR
	Antibiotics: Ciprofloxacin + Metronidazole (IV)	44.74	NR	Median 66 [Range 41-86]	NR	NR	NR	NR

Author, Year, PMID, Study Name, Country	Arm	Male %	Race/Ethnicity	Age, Mean (SD) or %	Participants with Un/Complicated Diverticulitis, %	Number of Prior Episodes of Diverticulitis, %	History of (Prior) Complicated Diverticulitis %	Time Since Last Episode of Diverticulitis, Mean (SD)
Scarpa, 2015, 25960972, Switzerland	Antibiotics: short course IV	47.8	NR	Median 55.5 [Range 24–81]	100/0	none 100	0	NR
	Antibiotics: long course IV	51.0	NR	Median 60 [Range 30–86]	100/0	none 100	0	NR
Schug-Pass, 2010, 20140619, Germany	Antibiotic: Ertapenem (4 days)	54	NR	60.6 (12.2)	NR	NR	NR	NR
	Antibiotic: Ertapenem (7 days)	55.4	NR	58.5 (11.9)	NR	NR	NR	NR

Table C-2b-4. KQ 2b. Risk of bias, randomized comparative studies

Author, Year, PMID, Study Name, Country	Random Sequence Generation	Allocation Concealment	Blinding of Participants	Blinding of Personnel/ Care Providers	Incomplete Outcome Data	Selective Outcome Reporting	Were Eligibility/Selection Criteria for the Study Population Prespecified and Clearly Described?	Was the Test/Service/Intervention Clearly Described and Delivered Consistently Across the Study Population?	Were the Outcome Measures Prespecified, Clearly Defined, Valid, Reliable, and Assessed Consistently Across All Study Participants?
AVOD Trial, Sweden	Low	Low	High	High	Low	Low	Yes	Yes	Yes
DIABOLO Trial, Sweden,	Low	Low	High	High	Low	Low	Yes	Yes	Yes
Jaung, 2019, 32240832, STAND, New Zealand and Australia	Low	Low	Low	Low	Low	Low	Yes	Yes	Yes
Kellum, 1992, 1638578, USA	Low	Low	High	High	Low	Low	Yes	Yes	Yes
Kim, 2019, 31267222, S Korea	Low	Low	High	High	Low	Low	Yes	Yes	Yes
Park, 2019, 31290747, S Korea	Low	Low	Low	Low	Low	Low	Yes	Yes	Yes
Ribas, 2010, 20526718, Spain	Low	Low	High	High	Low	Low	Yes	Yes	Yes
Ridgway, 2009, 19016815, Ireland	Low	Unclear	Unclear	High	Low	Low	Yes	Yes	Yes
Schug-Pass, 2010, 20140619, Germany	Unclear	Unclear	High	High	Low	Unclear	Yes	Yes	Yes

KQ = Key Question, PMID = PubMed Identifier. Ratings are color coded for emphasis only. See Table C-2a-2 for full legend.

Table C-2b-5. KQ 2b. Risk of bias, nonrandomized comparative studies

Author, Year, PMID, Study Name, Country	Bias Due to Confounding	Bias in Selection of Participants Into the Study	Random Sequence Generation (Selection Bias)	Allocation Concealment (Selection Bias)	Blinding of Personnel/ Care Providers (Performance Bias)	Incomplete Outcome Data (Attrition Bias)	Selective Reporting (Reporting Bias)	Were Eligibility/Selection Criteria for the Study Population Prespecified and Clearly Described?	Was the Test/Service/Intervention Clearly Described and Delivered Consistently Across the Study Population?	Were the Outcome Measures Prespecified, Clearly Defined, Valid, Reliable, and Assessed Consistently Across All Study Participants?
de Korte, 2012, 21689302, Netherlands	Yes	No	N/A	N/A	No	No	Unsure	Yes	No	No
Etzioni, 2010, 20484998, USA	Low	No			No	No	No	Yes	No	Yes
Hjern, 2007, 17190761, Sweden	Yes	No								
Scarpa, 2015, 25960972, Switzerland	Yes	No	N/A	N/A	No	No	Yes	Yes	Yes	Yes

KQ = Key Question, PMID = PubMed Identifier.

Key Question 2c (Interventional Radiology)

Table C-2c-1. KQ 2c. Design and arm details

Study, Year, PMID, Country, Funding	Design	Population Description	Arm	Arm Details	Age, Sex	Number of Prior Episodes of Diverticulitis
Lambrichts, 2019, 30811050, Netherlands, NR	NRCS (Retrospective)	CT-diagnosed abscess (Hinchey 1b/II); (Hinchey III/IV), sepsis, or fistula excluded	Interventional radiology	Percutaneous drainage	Mean 63 (SD 13), 62.6% male	None: 61.7% ≥1: 38.3%
			No intervention	No percutaneous drainage	Mean 60 (SD 13), 58.1% male	None: 72.0% ≥1: 28.0%
Mali, 2019, 31320921, Finland, Non-industry	NRCS (Retrospective)	CT-diagnosed abscess ≥4 cm; colon cancer excluded	Interventional radiology	Percutaneous drainage	Median 60 (IQR 50, 69), 61% male	None: 56% ≥1: 44%
			Antibiotics: Multiple	Discretionary, undefined antibiotics oral or IV	Median 67, (IQR 55, 78), 39% male	None: 67% ≥1: 33%

Abbreviations: CT = computed tomography, IQR = interquartile range, IV = intravenous, NR = not reported, NRCS = nonrandomized comparative study, PMID = PubMed identifier, SD = standard deviation.

Table C-2c-2. KQ 2c. Risk of bias assessment, NRCSSs, assessment of confounding and selection bias

Study, Year, PMID	1.1 Potential for Any Confounding?	1.2 Potential for Time-Varying Confounding?	1.3 Intervention Switches Related to Prognostic Factors?	1.4 Appropriate Analysis Method for Confounding?	1.5 Appropriate cConfounding Variables Used?	1.6 Inappropriate Control of Post-Intervention Variables?	Judgement – Risk of Bias Related to Confounding		2.1 Participant Selection Based on Post-Intervention Variables?	2.2 Post-Intervention Variables Associated with Intervention?	2.3 Post-Intervention Variables Associated with Outcome?	2.4 Start and Follow-Up (Duration) Coincide	2.5 Appropriate Adjustment for Selection Bias	Judgement – Risk of Bias Related to Selection Bias
Lambrichts, 2019, 30811050	Yes	No	N/A	Yes	Yes	No	Low		No	N/A	N/A	Yes	N/A	Low
Mali, 2019, 31320921	Yes	No	N/A	Yes	Yes	No	Low		No	N/A	N/A	Yes	N/A	Low

KQ = Key Question, NRCS = nonrandomized comparative studies, PMID = PubMed Identifier, Responses to Risk of Bias in Nonrandomized Studies of Interventions (ROBINS-I) signaling questions 1.1 to 1.6 and 2.1 to 2.5 are in regular font. Each item rated as Yes, PY (probably yes), NI (no information), PN (probably no), No, or N/A (not applicable). Judgements about confounding and selection bias are in **bold font**. (each item rated as **Low**, **Moderate**, **Serious**, or **Critical**).

Table C-2c-3. KQ 2c. Risk of bias assessment, NRCSSs, assessment of remaining biases and quality

Study, Year, PMID	Blinding of Participants	Blinding of Personnel/ Care Providers	Blinding of Outcome Assessors (Objective Outcomes)	Blinding of Outcome Assessors (Subjective Outcomes)	Incomplete Outcome Data	Selective Outcome Reporting	Other Bias	Eligibility Criteria Prespecified and Clearly Described	Intervention Clearly Described and Consistently Delivered	Outcomes Prespecified, Clearly Defined, Valid, Reliable, and Consistently Assessed
Lambrichts, 2019, 30811050	High	High	Unclear	Unclear	Low	Unclear	Low	Yes	Yes	Yes
Mali, 2019, 31320921	High	High	High	High	Low	Low	Low	Yes	Yes	Yes

KQ = Key Question, NRCS = nonrandomized comparative study, PMID = PubMed Identifier. Ratings are color coded for emphasis only. See Table C-2a-2 for full legend.

Key Question 3 (Colonoscopy)

Table C-3-1. KQ3. Design details

Author, Year, PMID, Country	Study Design	Funder	Years	Inclusion Criteria	Exclusion Criteria
Alcantar, 2019, 31720142, USA	Single group, Retrospective	Not reported (or unclear)	2007, 2017	Patients between the ages of 18 and 49 years with acute diverticulitis	Patients without CT verification of diverticulitis, and patients greater than 50 years old were excluded
Andrade, 2017, 27941344, Portugal	Single group,	Not reported (or unclear)	2008, 2013	patients who underwent a colonoscopy within 1 year after the conservative management of CT-proven acute diverticulitis	emergency surgery, incomplete colonoscopy
Brar, 2013, 24105001, Canada	Single group, Retrospective	Not reported (or unclear)	2007, 2010	patients successfully treated nonoperatively for acute left-sided diverticulitis, and all endoscopy reports before index admission and within 1 year after admission	patients underwent endoscopies more than 1 year after admission, patients underwent complete colonoscopy within the 2 years before admission
Choi, 2014, 24723071, S Korea	NRCS, Retrospective	Not reported (or unclear)	2001, 2013	underwent CT, followed by colonoscopy within a year and diagnosed with acute diverticulitis. For each diverticulitis case, two age- (± 5 years) and sex matched control individuals were identified from among healthy individuals who underwent screening colonoscopy.	colorectal cancer, colorectal surgery, underwent colonoscopy 1 year prior to the diagnosis of diverticulitis.
Daniels, 2015, 25472747, Netherlands	NRCS, Retrospective	Non-industry (fully)	2009, 2013	Primary colonoscopy screening population: Only those participants who were randomly invited for primary colonoscopy screening and decided to participate were included in the current study, 50-75 years. Uncomplicated Diverticulitis Population: adult patients, CT proven uncomplicated left sided acute diverticulitis, participating in DIABOLO trial. Patients who had undergone follow up colonoscopy within 6 months were included in his study.	Primary colonoscopy screening population: not willing to participate Uncomplicated Diverticulitis Population: excluded based on DIABOLO trial exclusion criteria
Elmi, 2013, 23701063, USA	Single group, Retrospective	Not reported (or unclear)	2000, 2004	>49 years, acute diverticulitis, evaluation of the colon using colonoscopy	history of colorectal cancer

Author, Year, PMID, Country	Study Design	Funder	Years	Inclusion Criteria	Exclusion Criteria
Horesh, 2016, 27170283, Israel	Single group, Retrospective	Not reported (or unclear)	2008, 2012	patients admitted for a first episode of acute diverticulitis diagnosed based on clinical signs and CT findings and were successfully treated conservatively	patients who underwent colonoscopy during the year prior to presentation
Khoury, 2019, 30632029, Israel	Single group, Retrospective	Not reported (or unclear)	2014, 2018	>16 years, acute diverticulitis, patients who underwent colonoscopy in the period of 6 months following the diagnosis with acute diverticulitis, or patients who performed virtual CT colonography in the case of contraindication to colonoscopy.	Exclusion criteria included patients with undetermined diagnosis of acute diverticulitis; patient who did not complete colonoscopy in the scheduled time; history of inflammatory bowel conditions such as inflammatory bowel disease, collagenous colitis, microscopic colitis, and eosinophilic colitis; patients with oncological diseases; and patients with immunosuppressive therapy.
Lahat, 2007, 17554647, Israel	RCT	Not reported (or unclear)	2004, 2006	All patients underwent abdominal CT, and only those with characteristic findings on CT compatible with the diagnosis of acute diverticulitis	Patients with CT findings of pericolic air or fluid adjacent to a diverticulum and, obviously, patients with free perforation; patients with a lesion seen on CT scan that was suspicious of colonic cancer; patients who had undergone a colonoscopy within the year prior to the current episode of acute diverticulitis
Lau, 2011, 21904141, Australia	NRCS, Retrospective	Not reported (or unclear)	2003, 2009	diverticulitis confirmed by CT, colonoscopy patients only included who had a follow up colonoscopy within 1 year from the date of CT scan	colonoscopy >1 year from the date of CT scan
Lecleire, 2014, 25083288, France	NRCS, Retrospective	Non-industry (fully)	2005, 2011	Group 1: acute diverticulitis, underwent colonoscopy within 6 months following the acute episode Group 2: sex and age matched with a familial history of colorectal adenoma or neoplasia	patients with haematochezia, recent change in bowel habits, personal history of colorectal neoplasia, undergone colonoscopy within the 2 years before the episode of diverticulitis
Meireles, 2015, 26378691, Portugal	Single group, Retrospective	Not reported (or unclear)	2004, 2013	patients subjected to endoscopy following the primary episode of diverticulitis	patients with a history of colorectal cancer, diverticular bleeding, or who underwent emergency surgery
O'Donohoe, 2019, 31882879, United Kingdom	Single group, Retrospective	Not reported (or unclear)	2014, 2017	Patients over the age of 18 with CT-diagnosed uncomplicated left-sided diverticulitis (with a modified Hinchey classification of 0 or 1a), admitted 2014–2017, with a follow-up colonoscopy 4–6 weeks after admission	Patients with right sided diverticulitis or complicated diverticulitis

Author, Year, PMID, Country	Study Design	Funder	Years	Inclusion Criteria	Exclusion Criteria
Ramphal, 2018, 29945147, Netherlands	Single group, Retrospective	Not reported (or unclear)	2008, 2013	Hinchey 0 and 1	Hinchey II-IV, previous colorectal cancer, previous episodes of diverticulitis
Sallinen, 2014, 24178863, Finland	NRCS, Retrospective	Not reported (or unclear)	2006, 2010	Clinically and CT diagnosed acute diverticulitis	NR
Schout, 2012, 23171930, Netherlands	Single group, Retrospective	Not reported (or unclear)	2000, 2010	Patients who underwent radiological or surgical abscess drainage only without colon resection	patients who underwent surgical treatment, had a history of colon cancer, had another underlying disease which caused an intra-abdominal abscess, or underwent colonoscopy in the diagnostic process of the episode of diverticulitis
Seoane Urgorri, 2018, 29900742, Spain	Single group, Retrospective	Not reported (or unclear)	2005, 2013	Colonoscopy performed after CT-confirmed diagnosis of acute diverticulitis.	Endoscopy within 2 years prior to episode of acute diverticulitis
Soh, 2018, 29663068, Singapore	NRCS, Retrospective	Not reported (or unclear)	2007, 2011	first episode of CT-proven acute diverticulitis with no complications	NR
Studniarek, 2019, 31908222, USA	Single group, Retrospective	Not reported (or unclear)	2005, 2017	A history of acute diverticulitis as the indication for the colonoscopy, and colonoscopy performed within one year from the initial diagnosis of diverticulitis	NR
Suhardja, 2017, 28035461, Australia	Single group, Retrospective	Not reported (or unclear)	2011, 2013	Patients diagnosed with acute colonic diverticulitis on CT scan and received follow-up colonoscopy	NR

NR: Not reported

Table C-3-2. KQ 3. Arm details

Author, Year, PMID, Country	Arm	Colon Imaging Type	Time Since Bout of Diverticulitis, Mean (SD)
Alcantar, 2019, 31720142, USA	Colonoscopy	Full colonoscopy 100%	
Andrade, 2017, 27941344, Portugal	Colonoscopy	Full colonoscopy 100%	16 weeks (11.4 weeks)
Brar, 2013, 24105001, Canada	Colonoscopy	Full colonoscopy 98.4%; Flexible sigmoidoscopy 1.6%;	Median 90 days
Choi, 2014, 24723071, S Korea	Diverticulitis with colonoscopy	Full colonoscopy 100%	
Choi, 2014, 24723071, S Korea	Healthy sex matched controls	Full colonoscopy 100%	
Daniels, 2015, 25472747, Netherlands	Diverticulitis patients (DIABOLO trial)	Full colonoscopy 100%	Median 55 days
Daniels, 2015, 25472747, Netherlands	Screening individuals (COCOS trial)	Full colonoscopy 100%	
Elmi, 2013, 23701063, USA	Colonoscopy	Full colonoscopy 100%	5.3 years; 34.8% in first 6 months
Horesh, 2016, 27170283, Israel	Colonoscopy	Full colonoscopy	Median 3.25 months (range 0.5, 24 months)
Khoury, 2019, 30632029, Israel	Colonoscopy	Full colonoscopy; CT colonography (if there is a contraindication to colonoscopy)	6 months after the diagnosis of acute diverticulitis
Lahat, 2007, 17554647, Israel	Colonoscopy (early; in-hospital)	Full colonoscopy 100%	Median 5.2 days (range 3, 11)
Lahat, 2007, 17554647, Israel	Colonoscopy (late, 6 weeks later)	Full colonoscopy 100%	Median 7.8 days (range 6, 19)
Lau, 2011, 21904141, Australia	Colonoscopy	Full colonoscopy 95%; Flexible sigmoidoscopy 5%; incomplete colonoscopy 6.6%	
Lecleire, 2014, 25083288, France	Acute diverticulitis	Full colonoscopy	
Lecleire, 2014, 25083288, France	Sex and age matched controls	Full colonoscopy	
Meireles, 2015, 26378691, Portugal	Colonoscopy	Full colonoscopy	Median 4.0 months (IQR 1.2, 7.1)
O'Donohoe, 2019, 31882879, United Kingdom	Colonoscopy	Full colonoscopy 100%	Median 37 days (range 27, 68)
Ramphal, 2018, 29945147, Netherlands	Colonoscopy		The patients who underwent colonoscopy between 6 weeks and 3 months after their acute episode of diverticulitis were eligible for analysis.
Sallinen, 2014, 24178863, Finland	Colonoscopy	Full colonoscopy 100%	122 days (180 days)
Schout, 2012, 23171930, Netherlands	Colonoscopy	Full colonoscopy; Flexible sigmoidoscopy; Barium enema; CT colonography	6-10 weeks after discharge

Author, Year, PMID, Country	Arm	Colon Imaging Type	Time Since Bout of Diverticulitis, Mean (SD)
Seoane Urgorri, 2018, 29900742, Spain	Colonoscopy	Full colonoscopy 100%	Median 6-7 weeks
Soh, 2018, 29663068, Singapore	Colonoscopy	Full colonoscopy 98.5%; Barium enema 0.7%; CT colonography 0.7%	Range 6, 8 weeks
Studniarek, 2019, 31908222, USA	Colonoscopy	Full colonoscopy 100%	
Suhardja, 2017, 28035461, Australia	Colonoscopy	Full colonoscopy 100%	100% in first year

Table C-3-3. KQ3. Baselines

Author, Year, PMID, Study Name, Country	Arm	Male %	Participant Age, Mean (SD)	Age ≥50, %	Complicated/ Uncomplicated Diverticulitis %
Alcantar, 2019, 31720142, USA	Colonoscopy	60.3	40.7	NR	22.5/77.5
Andrade, 2017, 27941344, Portugal	Colonoscopy	49.2	Median 55 [IQR 11.1]	NR	NR
Brar, 2013, 24105001, Canada	Colonoscopy	49	55 [range 27, 90]; 63.5% >55	63.5	29.7/70.3
Choi, 2014, 24723071, S Korea	Diverticulitis with colonoscopy	59.7	48.6 (16.5)	NR	14.1/85.9
Choi, 2014, 24723071, S Korea	Healthy sex matched controls	59.9	46.6 (16.6)	NR	8.2/91.8
Daniels, 2015, 25472747, Netherlands	Diverticulitis patients (DIABOLO trial)	47.6	Median 57 [range 49, 65]	NR	NR
Daniels, 2015, 25472747, Netherlands	Screening individuals (COCOS trial)	50.9	Median 60 [range 55, 65]	NR	NR
Elmi, 2013, 23701063, USA	Colonoscopy	42	100% >55	100	NR
Horesh, 2016, 27170283, Israel	Colonoscopy	45.4	62.6 [range 21, 98]; 30.6% >55	30.6	18.5/81.5
Khoury, 2019, 30632029, Israel	Colonoscopy	62	55.73 (13.81) [range 24, 93]	NR	NR
Lahat, 2007, 17554647, Israel	Colonoscopy (early)	31.1	60.5 (11.4)	NR	NR
Lahat, 2007, 17554647, Israel	Colonoscopy (late)	34.1	60.3 (14.7)	NR	NR
Lau, 2011, 21904141, Australia	Colonoscopy	53	15-39y: 7.2%, 40-64y: 55.5%, 65+: 37.3%	NR	NR
Lau, 2011, 21904141, Australia	No Colonoscopy	47.6	15-39y: 8.5%, 40-64y: 54.2%, 65+: 37.3%	NR	NR
Lecleire, 2014, 25083288, France	Acute diverticulitis	41	60.9 (12.6)	NR	10.0/90.0
Lecleire, 2014, 25083288, France	Sex and age matched controls	41	60.7 (13.4)	NR	NR
Meireles, 2015, 26378691, Portugal	Colonoscopy	49.6	64.4 (13.5) [range 23, 103]	NR	28.8/81.2
O'Donohoe, 2019, 31882879, UK	Colonoscopy	28	Median 63 (range 29, 90)	NR	0/100
Ramphal, 2018, 29945147, Netherlands	Colonoscopy	NR	59	NR	NR
Schout, 2012, 23171930, Netherlands	Colonoscopy	NR	NR	NR	NR

Author, Year, PMID, Study Name, Country	Arm	Male %	Participant Age, Mean (SD)	Age ≥50, %	Complicated/ Uncomplicated Diverticulitis %
Seoane Urgorri, 2018, 29900742, Spain	Colonoscopy	48	59 (15)	NR	27/73
Studniarek, 2019, 31908222, USA	Colonoscopy	51	Median 53 (range 22, 88)	NR	NR
Suhardja, 2017, 28035461, Australia	Colonoscopy	46.1	59.3	NR	27.4/72.6

NR = Not reported

Table C-3-4. KQ 3. Risk of bias

Author, Year, PMID, Country	Adjusted Results in Arm (Subgroup) Differences Reported	Eligibility/Selection Criteria Prespecified	Clear Outcome Definition
Alcantar, 2019, 31720142, USA	No	Yes	Yes
Andrade, 2017, 27941344, Portugal	Yes*	Yes	Yes
Brar, 2013, 24105001, Canada	Yes*	Yes	Yes
Choi, 2014, 24723071, S Korea	Yes*	Yes	Yes
Daniels, 2015, 25472747, Netherlands	Yes †	Yes	Yes ‡
Elmi, 2013, 23701063, USA	No	Yes	Yes
Horeish, 2016, 27170283, Israel	No	Yes	Yes
Khoury, 2019, 30632029, Israel	No	Yes	Yes
Lahat, 2007, 17554647, Israel	No	Yes	Yes
Lau, 2011, 21904141, Australia	No	Yes	Yes ‡
Lecleire, 2014, 25083288, France	No	Yes	Yes ‡
Meireles, 2015, 26378691, Portugal	No	Yes	Yes ‡
O'Donohoe, 2019, 31882879, United Kingdom	No	Yes	Yes
Ramphal, 2018, 29945147, Netherlands	No	Yes	Yes
Sallinen, 2014, 24178863, Finland	No	Yes	Yes ‡
Schout, 2012, 23171930, Netherlands	No	Yes	Yes
Seoane Urgorri, 2018, 29900742, Spain	No	Yes	Yes
Soh, 2018, 29663068, Singapore	No	Yes	Yes
Studniarek, 2019, 31908222, USA	No	Yes	Yes
Suhardja, 2017, 28035461, Australia	No	Yes	Yes ‡

Abbreviations: KQ = Key Question, PMID = PubMed Identifier.

Ratings are color coded for emphasis only. Each item rated as Yes (lower risk of bias) or No (higher risk of bias).

* Conducted multivariable analyses for the outcome of advanced colonic neoplasia.

† Adjusted (e.g., age, family history of CRC) for the outcome of advanced adenomas.

‡ Did not define the outcome of high-grade dysplasia.

Key Questions 4a-b (Prevention, Nonsurgical)

Table C-4ab-1. KQ 4ab. Design details and arms

Study, Year, PMID, Country, Funding	Design	Population Description	Arm	Arm Details	Age Sex	Number of Prior Episodes
Festa, 2017, 28387885, Italy, NR	NRCS (Retrospective)	≥18 yr, with ≥1 documented episode of acute diverticulitis in the previous 24 mo that resolved w/o surgery. History of IBD and prior abdominal surgery excluded.	Rifaximin	800 mg/d, 10 d/mo	≤65 years 45.8, >65 years 54.2, 47.2% male	One 86.1% Two or more 13.9%
			5-ASA	2.4 g/d, 10 d/mo	≤65 years 51.9, >65 years 48.1, 42.3% male	One 90.4% Two or more 9.6%
Kruis, 2017, 28543263, SAG-37, Germany, NR	RCT	40-80 yr old w/left-sided uncomplicated acute diverticulitis confirmed by CT or ultrasonography w/≥1 diverticulum in left colon	5-ASA (3.0 g/d)	3.0 g/d	Mean 58.8 SD 9.1 38.2% male	One 55.8% Two 30.9% Three or more 6.7%
			Placebo		Mean 58.3 SD 9.5 44% male	One 54.2% Two 30.4% Three or more 5.4%
Kruis, 2017, 28543263, SAG-51, USA/Germany, NR	RCT	30-80 yr old w/left-sided uncomplicated acute diverticulitis confirmed by CT or ultrasonography w/≥1 diverticulum in left colon	5-ASA (1.5 g/d)	1.5 g/d	Mean 55.6 SD 10.4 30.9% male	One 53.7% Two 29.3% Three or more 5.7%
			5-ASA (3.0 g/d)	3.0 g/d	Mean 55.2 SD 11.3 43.3% male	One 53.3% Two 26.7% Three or more 7.7%
			Placebo		Mean 55.4 SD 10.3 44.1% male	One 46.8% Two 36.9% Three or more 9.0%
Kvasnovsky, 2017, 28528364, International, Industry	RCT	Abdominal symptoms ≥3 mo w/uncomplicated diverticulitis	Probiotics Symprove	1 mL/kg/d	Median 60 (IQR 52, 72) 55.6% male	NR
			Placebo		Median 63.5 (IQR 54, 72.5) 44.4% male	NR

Study, Year, PMID, Country, Funding	Design	Population Description	Arm	Arm Details	Age Sex	Number of Prior Episodes
Lanas, 2013, 23092785, Spain, Industry	RCT	≥18 years w/≥1 acute diverticulitis in remission at enrollment. Acute ep at recruitment excluded.	Rifaximin	Rifaximin (800 mg/d) + fiber 3.5 g/d	53.6 (12.0) 66.2% male	At least one: 100%
			Placebo	Placebo + fiber 3.5 g/d	54.7 (13.2) 62.5% male	At least one: 100%
Mizuki, 2019, 31043657, Japan, NR	RCT	Diagnosed with CDB or uncomplicated ACD and aged between 20-85 years	Burdock tea	NR	Mean 48 (Range 24, 82) 55.3% male	At least one: 18%
			No intervention (non-placebo)		Mean 53 (Range 27, 79) 47.7% male	At least one 8%
Parente, 2013, 23754545, Italy, Industry	RCT	18-85 yo w/diverticular disease of left colon and/or ep. Of uncomplicated diverticulitis. Complicated diverticulitis excluded.	5-ASA	800 mg 2/d for 10 d/mo	Mean 61.9 (Range 35, 80) SD 10 44.4% male	None 100%
			Placebo		Mean 61.1 (Range 23, 84) SD 12.2 53.2% male	None 100%
Raskin, 2014, 25038431, PREVENT-1, International, Industry	RCT	1 documented episodes of acute diverticulitis in the previous 24 mo that resolved w/o colonic resection, and w/o signs/symptoms of diverticulitis within 6 wks of enrollment. Confirmation of diverticulosis via endoscopic evaluation of the sigmoid colon w/at ≥3 diverticula noted	5-ASA (1.2 g/d)	1.2 g/d	55.3 (11.39) 52.8% male	None 0.3% One 58.1% Two 25.4% Four or five 5.5% Six to ten 2.1
			5-ASA (2.4 g/d)	2.4 g/d		
			5-ASA (4.8 g/d)	4.8 g/d		
			Placebo	Daily		
Raskin, 2014, 25038431, PREVENT-2, International, Industry	RCT	1 documented episodes of acute diverticulitis in the previous 24 mo that resolved w/o colonic resection, and w/o signs/symptoms of diverticulitis within 6 wks of enrollment. Confirmation of diverticulosis via endoscopic evaluation of the sigmoid colon w/at ≥3 diverticula noted	5-ASA (1.2 g/d)	1.2 g/d	Mean 56.1 SD 11.04 46.4% male	None 0.5% One 59.7% Two 22.7% Four to Five 5.8% Six to Ten 1.9%
			5-ASA (2.4 g/d)	2.4 g/d		
			5-ASA (4.8g/d)	4.8 g/d		
			Placebo	Daily		

Study, Year, PMID, Country, Funding	Design	Population Description	Arm	Arm Details	Age Sex	Number of Prior Episodes
Silva Sanchez, 2014, International, NR	Single-group (Unclear)	NR (abstract)	5-ASA (4.8 g/d)	4.8 g/d	NR	NR
Stollman, 2013, 23426454, DIVA, USA, Industry	RCT	35-85 yr old, acute diverticulitis (first, second, or third attack) confirmed by CT scan, a GSS score ≥ 12 at baseline, an abdominal pain assessment score > 2 . Patients initially enrolled with acute diverticulitis, but randomization occurred after resolution, up to 14 days later	5-ASA + Probiotic (<i>Bifidobacterium infantis</i> 35624)	5-ASA 2.4 g/day + Probiotic: 1/day, 12 wk	Mean 59.1 SD 10.1 47.2% male	None 52.8% One 22.2% Two 25.0%
			5-ASA	2.4 g/day, 12 wk	Mean 57.7 SD 12.8 42.5% male	None 45.0% One 35.0% Two 20.0%
			Placebo	Placebos for 5-ASA and for probiotic, 12 wk	Mean 56.1 SD 11.1 53.7% male	None 51.2% One 34.1% Two 14.6%
Tursi, 2002, 12236485, Italy, NR	RCT	Diverticulitis w/ ≥ 2 attacks of acute diverticulitis in previous yr	5-ASA + Rifaximin	5-ASA (1.6 g/d) + rifaximin (800 mg/d), 7 d/mo†	Mean 66.5 59% male	Two: 82.6% Three or more: 17.4%
			Rifaximin	Rifaximin (800 mg/d), 7 d/mo	Mean 62.1 61.4% male	Two: 84.4% Three or more: 15.6%
Tursi, 2007, 17390144, Italy, NR	RCT	Uncomplicated acute diverticulitis	5-ASA + Probiotic	Balsalazide (2.25 mg/d), 10 d/mo + VSL#3 (1 bag/d), 15 d/mo*	Mean 60.1 (Range 47, 75)	Two: 83.5% Three or more: 16.5%
			Probiotics	VSL#3 (1 bag/d), 15 d/mo*		

d = day, wk = weeks, mo = month, NR = not reported, PMID = PubMed identifier, y = years, g/d = grams/per day, * = During the first 10 days of treatment, patients in both groups also took rifaximin 800 g/d., † During the first 7 days of treatment, 5-ASA 2.4 g/d + rifaximin 800 mg/d vs. rifaximin 800 mg/d.

Table C-4ab-2. KQ 4ab. Risk of bias, RCTs

Author, Year, PMID, Study Name, Country	Random Sequence Generation (Selection Bias)	Allocation Concealment (Selection Bias)	Blinding of Participants, Personnel, Care Providers, Outcome Assessor	Incomplete Outcome Data (Attrition Bias)	Selective Reporting (Reporting Bias)	Other Bias
Kruis, 2017, 28543263, SAG-37, Germany	Low	Low	Low	Low	Low	Low
Kruis, 2017, 28543263, SAG-57, USA/Germany	Low	Low	Low	Low	Low	Low
Kvasnovsky, 2017, 28528364, International	High	High	High	Low	High	Low
Lanas, 2013, 23092785, Spain	Low	Low	High	Low	Low	High
Mizuki, 2019, 31043657, Japan	Low	Low	Low	Low	Low	Low
Parente, 2013, 23754545, Italy	Unclear	Unclear	Low	Low	High	Low
Raskin, 2014, 25038431, PREVENT1, International	Low	Low	Low	Low	Low	Low
Raskin, 2014, 25038431, PREVENT2, International	Low	Low	Low	Low	Low	Low
Stollman, 2013, 23426454, DIVA, USA	Low	Low	Low	High	Low	Low
Tursi, 2002, 12236485, Italy	High	High	High	Low	Low	Low
Tursi, 2007, 17390144, Italy	Unclear	High	High	Low	Low	Low

KQ = Key Question, PMID = PubMed Identifier. Ratings are color coded for emphasis only. See Table C-2a-2 for full legend.

Table C-4ab-3. KQ 4ab. Risk of bias, NRCSSs

Author, year, PMID, Study Name, Country	Random Sequence Generation (Selection Bias)	Allocation Concealment (Selection Bias)	Blinding of Participants, Personnel, Care Providers, Outcome Assessor	Incomplete Outcome Data (Attrition Bias)	Selective Reporting (Reporting Bias)	Were Eligibility/Selection Criteria for the Study Population Prespecified And Clearly Described?	Was the Test/Service/Intervention Clearly Described and Delivered Consistently Across the Study Population?	Were the Outcome Measures Prespecified, Clearly Defined, Valid,	No Bias Due to Confounding	No Bias in Selection of Participants Into The Study
Festa, 2017, 28387885, Italy	N/A	N/A	Low	High	High	Yes	Yes	Yes	No	Yes

KQ = Key Question, PMID = PubMed Identifier. Ratings are color coded for emphasis only. See Table C-2a-2 for full legend.

Key Question 4c (Elective Surgery)

Table C-4c-1. KQ 4c. Design details

Author, year, PMID, Study Name, Country	Study Design	Funder	Study Dates	Inclusion Criteria	Exclusion Criteria	How Was Diverticulitis Diagnosed?
Aquina, 2019, 30335195, USA	NRCS (Retrospective)	Not reported (or unclear)	2002, 2010	at least 18 years, acute diverticular abscess	laparotomy, laparoscopy, colectomy or stoma creation within 2 days of admission; concurrent diagnosis of colorectal cancer, cirrhosis, or ascites	NR
Bhakta, 2016, 26275534, Albany Medical Center 2001-13, USA	Single group (Prospective)	Non-industry (fully)	2001, 2013	diverticulitis requiring elective surgery	none	diverticulitis was defined as either a physician-documented or self-reported episode of left lower quadrant abdominal pain and tenderness, with or without fever and leukocytosis.
Boostrom, 2012, 22696233, Mayo Clinic, Rochester, USA	Single group (Retrospective)	Not reported (or unclear)	2005, 2009	patients who underwent sigmoid resection for a diagnosis of diverticulitis	emergent resection	<p>Acute resolving uncomplicated diverticulitis is defined as discrete episodes of left lower quadrant abdominal pain, fever, leukocytosis, and evidence of inflammation on imaging that resolve with conservative management.</p> <p>Chronic/ smoldering uncomplicated diverticulitis is defined as symptoms of left lower quadrant abdominal pain and evidence of inflammation (elevated white blood cell count, fever, CT evidence of inflammation) that does not improve with the traditional antibiotic regimen, or re-exacerbation with cessation of antibiotics, for at least 3 months' duration.</p> <p>Atypical uncomplicated diverticulitis is defined as symptoms of left lower quadrant pain and possible alterations in bowel habits for a period of at least 3 months; however, other clinical and radiographic evidence of diverticulitis is not present.</p>
Bordeianou, 2019, 29916880, PREVENTT, USA	Single group (Prospective)	Not reported (or unclear)	2010, 2016	underwent surgery for diverticulitis	< 18 years of age, underwent a colectomy with a diagnosis of colon or rectal cancer or IBD.	NR
Ilyas, 2017, 27422847, Nationwide Inpatient Sample (2004-2001), USA	Single group (Retrospective)	Non-industry (fully)	2004, 2011	Procedure codes were used from ICD-9 to identify patients who underwent elective sigmoid resection.	Patients with acute diverticulitis, perforated diverticulitis, preoperative weight loss and metastatic disease were excluded.	Patients with an ICD-9 diagnosis code of diverticulitis were identified. (ICD-9 codes 562.11 and 562.13)

Author, year, PMID, Study Name, Country	Study Design	Funder	Study Dates	Inclusion Criteria	Exclusion Criteria	How Was Diverticulitis Diagnosed?
Lidor, 2010, 20878256, USA	Single group (Retrospective)	Non-industry (fully)	2004, 2007	≥65 years old; primary admission diagnosis of diverticulitis by ICD-9	concurrent diagnosis of colorectal cancer	NR
Masoomi, 2011, 21732208, Nationwide Inpatient Sample (2002-2007), USA	Single group (Retrospective)	Non-industry (fully)	2002, 2007	Hospitalizations resulting from elective colon resection were identified with ICD procedure code and then divided into open surgery and laparoscopy groups.	Urgent colon resection	All discharges with International Classification of Disease (ICD) procedure codes [sigmoidectomy (45.76) or anterior resection (48.62, 48.63)] with a primary diagnosis of diverticulitis (codes 562.11 and 562.13) were selected from 2002 to 2007; those patients with the admission code for an elective operation were identified and utilized in the study.
Moghadamyeghaneh, 2015, 26116319, ACS-NSQIP 2012-13, USA	Single group (Retrospective)	Not reported (or unclear)	2012, 2013	Diverticulitis who underwent colon resections using procedural and diagnosis codes as specified by the ICD 9th Revision.	Underwent colon surgery without colon resection and patients < 18 yo	Colonic diverticulitis based on ICD 9 code 562.11. Colon resection based on Current Procedural Terminology codes: 44140 to 44147, 44204 to 44208, 45110, and 45113.
Novitsky, 2009, 18639223, Nationwide Inpatient Sample (2001-2002), USA	Single group (Retrospective)	Non-industry (fully)	2001, 2002	Patients with ICD codes who underwent elective surgery for diverticulitis.	Patients ≥18 years and those with a diagnosis of colon cancer were excluded from the analysis.	Patients with ICD codes for diverticulitis diagnostic codes were identified. Patients with colectomy procedure codes were then cross referenced to obtain patients who underwent elective surgery for diverticulitis.
Papageorge, 2016, 27120447, ACS-NSQIP 2005-13, USA	Single group (Retrospective)	Not reported (or unclear)	2005, 2013	Primary procedure CPT code or one of the secondary CPT codes (from the "other procedure" variables) was for partial colectomy or colostomy.	Cases performed emergently, patients of ASA class 5 or unknown ASA class, cases performed by a surgical specialist in a field other than general surgery, presence of preoperative SIRS, sepsis or septic shock, and preoperative ventilator dependence.	Acute diverticulitis w/o hemorrhage or diverticulosis w/o hemorrhage by ICD-9 codes 562.11 and 562.1.
Pessaix, 2004, 14639493, French Association for Surgical Research, France	Single group (Retrospective)	Not reported (or unclear)	1985, 1998	elective sigmoid resection by laparotomy at least 1.5 month after an acute episode of diverticulitis, followed by primary anastomosis with or without protective stoma.	prior colon resection, emergency resection, surgery without resection, resection without primary anastomosis, and patients undergoing laparoscopic resection	NR
Russ, 2010, 20193685, ACS-NSQIP 2005-08, USA	Single group (Retrospective)	Not reported (or unclear)	2005, 2008	Emergency and nonemergency cardiac and noncardiac surgery. Diverticular disease were identified by ICD-9 codes and then categorized based on procedure type using CPT codes.	Defined by the NSQIP to have undergone emergency surgery. Definition includes patients who had surgery within 12 hours of admission.	Diverticular disease were identified by ICD-9 codes
Silva-Velazco, 2016, 26541732, USA	Single group (Prospective)	Non-industry (fully)	1992, 2013	elective, restorative procedures for sigmoid diverticulitis performed using a minimally invasive approach	disease presentations requiring urgent surgery	diverticulitis was radiologically confirmed in 1032 patients (97.5 %), while outside preoperative imaging was not available in our institutional records in the remaining 27 patients

Author, year, PMID, Study Name, Country	Study Design	Funder	Study Dates	Inclusion Criteria	Exclusion Criteria	How Was Diverticulitis Diagnosed?
Simianu, 2015, 25773308, Surgical Care and Outcomes Assessment Program (SCOAP), USA	Single group (Prospective)	Non-industry (fully)	2010, 2013	underwent laparoscopic colon resection for diverticulitis	none	NR
Tsilimparis, 2010, 20812161, Fast-track Kolon II, Germany	Single group (Prospective)	Not reported (or unclear)	2005, 2008	all patients with elective laparoscopic sigma resection for diverticulitis	emergency surgery within 24 hours of admission, ileus, perforation, <18 years old, pregnant	NR
Valizadeh, 2018, 30747633, ACS-NSQIP 2012-13, USA	Single group (Retrospective)	Not reported (or unclear)	2012, 2013	Chronic diverticular disease or acute diverticulitis	NR	NR
van de Wall, 2017, 28404008, DIRECT trial, Netherlands	RCT	Non-industry (fully)	2010, 2014	patients aged 18–75 years who presented to trial centres with either ongoing abdominal complaints or frequently recurring left-sided diverticulitis after a confirmed (ie, seen with CT scan, ultrasonography, or endoscopy) episode of diverticulitis.	1) previous elective or emergency surgery for acute sigmoid diverticulitis, OR 2) an absolute operation indication, OR 3) suspicion of a colorectal malignancy, OR 4) patients classified with a preoperative or postoperative risk of greater than III on the American Society of Anesthesiologists (ASA) classification	The Hinchey classification was used to classify the primary episode of diverticulitis and was based on findings of either CT scan or ultrasonography
Varma, 2019, 30527478, California State Inpatient Database 2005-13, USA	Single group (Retrospective)	Non-industry (fully)	2005, 2011	experienced an initial episode of uncomplicated diverticulitis (562.10, 562.11), were medically managed during their initial presentation, and underwent a bowel resection afterward	diagnoses for malignancy (153, 196, 197, 198), undergoing spinal cord (3.9), thorax (33.2, 34.9), ventral hernia (53.4, 53.5), and salpingo-oophorectomies (65.4, 65.6) procedures; or missing clinical factors	NR
You, 2018, 29683483, USA	RCT	Industry (fully or in part)	2011, 2016	≥18 with a first episode of acute diverticulitis of the sigmoid colon complicated by extraluminal air with or without abscess, first treated with successful non-operative management and colonoscopy negative for malignancy.	history of previous diverticulitis of the sigmoid colon; history of diverticulitis of the sigmoid colon, colonic cancer at colonoscopy, immunosuppression, acute diverticulitis of the sigmoid colon complicated by peritonitis and/or distant free air, pregnancy, or inability to sign informed consent.	Not explicitly described

Table C-4c-2. KQ 4c. Arm details

Author, Year, PMID, Study Name, Country	Arm	Surgery Type	Time Frame of Elective Surgery in Relation to Last Acute Diverticulitis
Aquina, 2019, 30335195, USA	Elective surgery	Colectomy	< 6 months
	No intervention (Nonoperative management)	N/A	NR
Bhakta, 2016, 26275534, Albany Medical Center 2001-13, USA	Elective surgery	Laparoscopic	NR
Boostrom, 2012, 22696233, Mayo Clinic, Rochester, USA	Elective surgery (Arm 1: Acute resolving uncomplicated diverticulitis)	Sigmoidectomy (any 24%, laparoscopic 25%, hand-assisted 50%, robot-assisted 0.3%)	NR
	Elective surgery (Arm2: Chronic/ smoldering uncomplicated diverticulitis)	Sigmoidectomy (any 12%, laparoscopic 30%, hand-assisted 56%, robot-assisted 2%)	NR
	Elective surgery (Arm3: Atypical uncomplicated diverticulitis)	Sigmoidectomy (any 15%, laparoscopic 30%, hand-assisted 55%)	NR
Bordeianou, 2019, 29916880, PREVENTT, USA	Elective surgery	Any	NR
Ilyas, 2017, 27422847, Nationwide Inpatient Sample (2004-2001), USA	Elective surgery	Sigmoidectomy	NR
Lidor, 2010, 20878256, USA	Elective surgery	Left colectomyLeft colectomy with ileostomy	NR
Masoomi, 2011, 21732208, Nationwide Inpatient Sample (2002-2007), USA	Elective surgery (Open surgery)	Open	NR
	Elective surgery (Laparoscopy)	Laparoscopic	NR
Moghadamyeghaneh, 2015, 26116319, ACS-NSQIP 2012-13, USA	Elective surgery (2012-2013)	Open 28%Laparoscopic (72%)	NR
Novitsky, 2009, 18639223, Nationwide Inpatient Sample (2001-2002), USA	Elective surgery	Left colectomyLeft colectomy with ostomyLeft colectomy with ileostomy1	NR
Papageorge, 2016, 27120447, ACS-NSQIP 2005-13, USA	Elective surgery (2005/06)	Laparoscopic approach and ostomy creation, as defined by the CPT code.	NR
	Elective surgery (2007)		NR
	Elective surgery (2008)		NR
	Elective surgery (2009)		NR
	Elective surgery (2010)		NR
	Elective surgery (2011)		NR
	Elective surgery (2012)		NR
Pessaux, 2004, 14639493, French Association for Surgical Research, France	Elective surgery (2013)		NR
	Elective surgery (elective laparotomy for colon or rectal resection for diverticulitis)	Sigmoidectomy	> 1.5 months
Russ, 2010, 20193685, ACS-NSQIP 2005-08, USA	Elective surgery (Open procedure)	Open	NR
	Elective surgery (Laparoscopic procedure)	Laparoscopic	NR
Silva-Velazco, 2016, 26541732, USA	Elective surgery	Laparoscopic	range 6, 8 weeks
Simianu, 2015, 25773308, Surgical Care and Outcomes Assessment Program (SCOAP), USA	Elective surgery	Laparoscopic	NR
Tsilimparis, 2010, 20812161, Fast-track Kolon II, Germany	Elective surgery	Laparoscopic	>1 day
Valizadeh, 2018, 30747633, ACS-NSQIP 2012-13, USA	Elective surgery	NR	NR

Author, Year, PMID, Study Name, Country	Arm	Surgery Type	Time Frame of Elective Surgery in Relation to Last Acute Diverticulitis
van de Wall, 2017, 28404008, DIRECT trial, Netherlands	Elective surgery (Laparoscopic surgery)	Sigmoidectomy, laparoscopic	NR
	No intervention (Conservative management treatment: current daily practice)	n/a	NR
Varma, 2019, 30527478, California State Inpatient Database 2005-13, USA	Elective surgery	Any	median 3.8 months (IQR 2.3, 8.1 months; range 30 days, 2 years)
You, 2018, 29683483, USA	No intervention (Observation)	none	NR
	Elective surgery (underwent elective resection of the sigmoid colon with colorectal anastomosis via a minimally invasive access.)	Laparoscopic	NR

Table C-4c-3. KQ 4c. Baselines

Author, year, PMID, Study Name, Country	Arm	Male %	Race/Ethnicity	Age, Mean (SD) or %	Participants With Un/Complicated Diverticulitis, %	Specific Complications of Diverticulitis %	Number of Prior Episodes of Diverticulitis, %	Time Since Last Episode of Diverticulitis, Mean (SD)
Aquina, 2019, 30335195, USA	Elective surgery	51.8	White 87.1%, Black 4.8%, Other 5.6%, Unknown 2.5%	Median 56 (IQR 47, 66); <=50 years 35.3, 51-65 years 39.2, >65 years 25.5	.		at least one 16.3	
	No intervention (non-placebo) (Nonoperative management)	46.3	White 74.2%, Black 11.9%, Other 11.1%, Unknown 2.7%	Median 58 (IQR 47, 72); <=50 years 33.8, 51-65 years 30.7, >65 years 35.6	.		at least one 10.0	
Bhakta, 2016, 26275534, Albany Medical Center 2001-13, USA	Elective surgery	47		55.7	75.9/24.1	abscess 8.3, perforated diverticulitis 0.7, stricture 3.6, immunocompromised 0.5	Mean 3.1 [range 1, 12]	
Boostrom, 2012, 22696233, Mayo Clinic, Rochester, USA	Elective surgery (Arm 1: Acute resolving uncomplicated diverticulitis)	45		Median 63			Median 3 [range 1, 15]	
	Elective surgery (Arm2: Chronic/smoldering uncomplicated diverticulitis)	38		Median 66				
	Elective surgery (Arm3: Atypical uncomplicated diverticulitis)	37		Median 64				

Author, year, PMID, Study Name, Country	Arm	Male %	Race/Ethnicity	Age, Mean (SD) or %	Participants With Un/Complicated Diverticulitis, %	Specific Complications of Diverticulitis %	Number of Prior Episodes of Diverticulitis, %	Time Since Last Episode of Diverticulitis, Mean (SD)
Bordeianou, 2019, 29916880, PREVENTT, USA	Total	43.6	White 93.4%, Hispanic/Latino 3.2%	59.9 (12.7)			at least one 50	
Ilyas, 2017, 27422847, Nationwide Inpatient Sample (2004-2001), USA	Elective surgery	45.7	White 82.3%	65.7 (13.1)				
Lidor, 2010, 20878256, USA	Elective surgery	28.9	White 95.35%, Black 3.1%, Other 1.55%	73.9 (5.9); 65-69 years 28.8, 70-74 years 29.7, 75-79 years 23.5, 80-85 years 12.6, 85+ years 5.5				
Masoomi, 2011, 21732208, Nationwide Inpatient Sample (2002-2007), USA	Elective surgery (Open surgery)	47.1	White 89%, Black 3.4%, Hispanic/Latino 4.9%, Asian 0.3%	57				
	Elective surgery (Laparoscopy)	47.4	White 84.9%, Black 3.7%, Hispanic/Latino 8.8%, Asian 0.1%	55				
Moghadamyeghan eh, 2015, 26116319, ACS-NSQIP 2012-13, USA	Elective surgery (2012-2013)	45.9	White 91.8%, Black 6.4%, Asian 1%, Other 0.7%	58 (12)				
Novitsky, 2009, 18639223, Nationwide Inpatient Sample (2001-2002), USA	Elective surgery	41.8		67.1 (13.8)				

Author, year, PMID, Study Name, Country	Arm	Male %	Race/Ethnicity	Age, Mean (SD) or %	Participants With Un/Complicated Diverticulitis, %	Specific Complications of Diverticulitis %	Number of Prior Episodes of Diverticulitis, %	Time Since Last Episode of Diverticulitis, Mean (SD)
Papageorge, 2016, 27120447, ACS-NSQIP 2005-13, USA	Elective surgery (2005/06)	48		<50 years 29.7, 65+ years 29.6				
	Elective surgery (2007)	47.6		<50 years 28.5, 65+ years 28.8				
	Elective surgery (2008)	46.8		<50 years 27.9, 65+ years 29				
	Elective surgery (2009)	45		<50 years 27.3, 65+ years 30				
	Elective surgery (2010)	44.6		<50 years 25.9, 65+ years 29.7				
	Elective surgery (2011)	45.2		<50 years 25.9, 65+ years 29.7				
	Elective surgery (2012)	46.2		<50 years 24.5, 65+ years 31.8				
	Elective surgery (2013)	44.5		<50 years 24.2, 65+ years 32.3				
Pessaux, 2004, 14639493, French Association for Surgical Research, France	Elective surgery (elective laparotomy for colon or rectal resection for diverticulitis)	46.6		<58 years 37.5, 59-75 years 45.8, >76 years 16.7				[range >1.5 months]
Russ, 2010, 20193685, ACS-NSQIP 2005-08, USA	Elective surgery (Open procedure)	46.9	White 79.2%, Black 6.9%, Other 14%	59.2				
	Elective surgery (Laparoscopic procedure)	49.1	White 83.5%, Black 3.4%, Other 13.2%	55.6				
Silva-Velazco, 2016, 26541732, USA	Elective surgery	52		55 (12)		Preoperative percutaneous abscess drainage 6	.	[range 6, 8 weeks]
Simianu, 2015, 25773308, Surgical Care and Outcomes Assessment Program (SCOAP), USA	Elective surgery	47	White 87.2%	57.8 (12.7)		Colovesicular fistula 8.7, current GI bleed 2.3, stricture 4.4	none 13.9, one 15.2, two 14.5, at least three 52.5	
Tsilimparis, 2010, 20812161, Fast-track Kolon II, Germany	Elective surgery	42		63 [Range 23, 91]; <60 years 42, 60-69 years 33, >69 years 25	100/0			

Author, year, PMID, Study Name, Country	Arm	Male %	Race/Ethnicity	Age, Mean (SD) or %	Participants With Un/Complicated Diverticulitis, %	Specific Complications of Diverticulitis %	Number of Prior Episodes of Diverticulitis, %	Time Since Last Episode of Diverticulitis, Mean (SD)
Valizadeh, 2018, 30747633, ACS-NSQIP 2012-13, USA	Elective surgery	nr		>65 years 31.5				
van de Wall, 2017, 28404008, DIRECT trial, Netherlands	Elective surgery (Laparoscopic surgery)	28		Median 54.1 (IQR 44.6-62.1)			Mean 3.1 (SD 1.0)	
	No intervention (non-placebo) (Conservative management treatment: current daily practice)	43		Median 56.5 (IQR 48.3-63.2)			Mean 4.1 (SD 2.0)	
Varma, 2019, 30527478, California State Inpatient Database 2005-13, USA	Elective surgery	48.4	White 69.0%, Black 3.5%, Hispanic/Latino 18.9%, Other/missing 8.6%	55.3 (13.8)	89/11		one 70.8, two 21.8, at least three 7.4	[range 30d, 2y]
You, 2018, 29683483, USA	Placebo (Observation)	63		55.2 (13.1)		Abscess 42, extraluminal air 100	none 100	
	Elective surgery	54		53.3 (13.5)		Abscess 58, extraluminal air 100	none 100	

Table C-4c-4. KQ 4c. Risk of bias, RCTs and NRCS

Author, Year, PMID, Study Name, Country	Random Sequence Generation (Selection Bias)	Allocation Concealment (Selection Bias)	Blinding OF Participants, Personnel, Care Providers, Outcome Assessor	Incomplete Outcome Data (Attrition Bias)	Selective Reporting (Reporting Bias)	Were Eligibility/Selection Criteria for the Study Population Prespecified and Clearly Described?	Was the Test/Service/Intervention Clearly Described and Delivered Consistently Across the Study Population?	Were the Outcome Measures Prespecified, Clearly Defined, Valid, Reliable, and Assessed	Bias Due to Confounding	Bias in Selection of Participants Into the Study
Aquina, 2019, 30335195, USA	High	High	High	Low	Low	Yes	Yes	Yes	Low	Low
van de Wall, 2017, 28404008, DIRECT trial, Netherlands	Low	Low	High	Low	Low	Yes	Yes	Yes	Low	Low
You, 2018, 29683483, USA	Low	Unclear	High	Low	Low	Yes	No	Yes	Low	Low

KQ = Key Question, PMID = PubMed Identifier. Ratings are color coded for emphasis only. See Table C-2a-2 for full legend.

Table C-4c-5. KQ 4c. Risk of bias, single-group studies

Author, year, PMID, Study Name, Country	Incomplete Outcome Data (Attrition Bias)	Selective Reporting (Reporting Bias)	Were Eligibility/ Selection Criteria for the Study Population Prespecified and Clearly Described?	Was the Test/Service/ Intervention Clearly Described and Delivered Consistently Across the Study Population?	Were the Outcome Measures Prespecified, Clearly Defined, Valid, Reliable, and Assessed Consistently Across All Study Participants?
Bhakta, 2016, 26275534, Albany Medical Center 2001-13, USA	Low	Low	Yes	Yes	Yes
Boostrom, 2012, 22696233, Mayo Clinic, Rochester, USA	Low	Low	Yes	Yes	Yes
Bordeianou, 2019, 29916880, PREVENTT, USA	Low	Low	Yes	No	Yes
Ilyas, 2017, 27422847, Nationwide Inpatient Sample (2004-2001), USA	Low	Low	Yes	No	Yes
Lidor, 2010, 20878256, USA	Low	High	Yes	Yes	Yes
Masoomi, 2011, 21732208, Nationwide Inpatient Sample (2002-2007), USA	Low	Low	Yes	Yes	Yes
Moghadamyeghaneh, 2015, 26116319, ACS-NSQIP 2012-13, USA	Low	Low	Yes	Yes	Yes
Novitsky, 2009, 18639223, Nationwide Inpatient Sample (2001-2002), USA	Low	Low	Yes	Yes	Yes
Papageorge, 2016, 27120447, ACS-NSQIP 2005-13, USA	Low	Low	Yes	Yes	Yes
Pessaux, 2004, 14639493, French Association for Surgical Research, France	Low	Low	Yes	Yes	Yes
Russ, 2010, 20193685, ACS-NSQIP 2005-08, USA	Low	Low	Yes	Yes	Yes
Silva-Velazco, 2016, 26541732, USA	Low	Unclear	Yes	Yes	Yes
Simianu, 2015, 25773308, Surgical Care and Outcomes Assessment Program (SCOAP), USA	Low	Low	Yes	Yes	Yes
Tsilimparis, 2010, 20812161, Fast-track Kolon II, Germany	Low	Low	Yes	Yes	Yes
Valizadeh, 2018, 30747633, ACS-NSQIP 2012-13, USA	Low	Low	Yes	Yes	Yes
Varma, 2019, 30527478, California State Inpatient Database 2005-13, USA	Low	Low	Yes	Yes	Yes

KQ = Key Question, PMID = PubMed Identifier. Ratings are color coded for emphasis only: Low/Yes, High/No, or Unclear.

Appendix D. Full Results

Key Question 1a (CT Grading)

Among the included patients 84 had initial (CT and clinical) diagnoses of uncomplicated diverticulitis, 30 (9.4%) Type I and 54 (17%) recurrent Type III; 112 (35%) Type IIA diverticulitis, 84 (26%) Type IIB, and 27 (8.5%) Type IIC.

All 30 Type I patients were successfully treated conservatively; all 54 Type III patients had surgery, at which 8 (15%) were found to have complicated diverticulitis. Among patients initially diagnosed with complicated diverticulitis 29 of 112 (26%) with Type IIA declined surgery, as did 6 of 84 (7.1%) with Type IIB. All patients diagnosed with Type IIC diverticulitis underwent surgery. The article does not describe the clinical course (or final staging) of the 35 people treated conservatively for complicated diverticulitis.

Among the 83 people who underwent surgery for Type IIA diverticulitis, 9 (11%) were found to have uncomplicated diverticulitis (i.e., they were “overstaged”) and 44 (53%) were found to have Type IIB (i.e., they were “understaged”).

Among the 78 people who underwent surgery for Type IIB diverticulitis, 5 (6.4%) were overstaged (4 had uncomplicated diverticulitis; 1 had Type IIA) and 2 (2.6%) were understaged.

All 27 people diagnosed with Type IIC diagnosis were found to have correct staging at surgery.

We took four approaches to analyze these data.

1. As the study authors did, we first calculated test accuracy for each stage separately (e.g., the sensitivity of a Type IIB classification versus all others: IIA or IIC or III).
2. We calculated the test accuracy of each stage as a maximum category (e.g., IIB or IIA or III vs. IIC)
3. We calculated the test accuracy of each stage as a minimum category (e.g., IIB or IIC vs. IIA or III)
4. We attempted to evaluate whether the initial staging resulted in an appropriate decision regarding surgery

For the test accuracy of staging, *per se*, we included only those patients who underwent surgery (thus excluding all Type I and the Type IIA and IIB patients who refused surgery). This is consistent with the approach taken by the study authors. Thus, our calculated specificities (and negative predictive values) are likely low estimates of true values (under the assumption that all 30 Type I patients were correctly classified; although, it is unclear how possible misclassification among the 35 people who refused surgery might affect test accuracy estimates).

Table D-1-1. Hansen and Stock Classification system*

The H&S system includes the following categories:

- Type 0 Asymptomatic diverticulosis (not further discussed here)
- Type I Uncomplicated diverticulitis, first episode
 - Potential intestinal wall thickening and/or enhancement of pericolic fatty tissue; sometimes no morphologic features visible on CT
- Type IIA Complicated “phlegmonous diverticulitis”
 - Type I criteria and edema/phlegmonous inflammation, but no free air
- Type IIB Complicated “covered perforation”
 - Type IIA criteria and air inclusions, corresponding with abscesses
- Type IIC Complicated “free perforation”
 - Free air, free intra-abdominal contrast media escape, and/or free fluid
- Type III *Uncomplicated* diverticulitis, recurrent
 - Apparently the same CT criteria as Type I, but with knowledge of two or more episodes of recurrence (presumably including the current episode)

* Jurowich CF, Jellouschek S, Adamus R, Loose R, Kaiser A, Isbert C, Germer CT, von Rahden BH. How complicated is complicated diverticulitis?--phlegmonous diverticulitis revisited. *Int J Colorectal Dis.* 2011 Dec;26(12):1609-17. PMID 21830036.

Table D-1-2. Initial and final classification of patients in Jurowich 2011

Initial Stage	Total N	Conserv Tx*	Surgery	Postop I	Postop I/II	Postop II A	Postop II B	Postop II C
I	30	30	0
III	54	0	54	0	46	1	7	0
Ila	112	29	83	0	9	30	44	0
Ilb	84	6	78	0	4	1	71	2
Ilc	27	0	27	0	0	0	0	27
FN †	11	0	11
Total	318	65	242 ‡	.	59	32	122	29

Numbers represent the number of people in each category. Dots represent unanalyzed or unreported categories. The numbers within the thick-lined box were the data used to estimate test accuracy.

* Omitted from test accuracy analysis of classification system.

† Incidental findings intraoperative. Initial diagnoses were suspected appendicitis (N=8), incarcerated hernia (N=2), ileus (N=1).

‡ Excluding false negatives

Abbreviations: Conserv Tx = conservative (nonsurgical) treatment, Postop = postoperative (staging).

Key Questions 1b-d (CT Clinical Sequelae)

Table D-1-3. KQ 1 results

Study, PMID	Study Group	CT Errors	Good Clinical Sequelae	Poor Clinical Sequelae	Incidental Findings
Andeweg 2011 21346548	CT	None reported	NR	No unnecessary surgeries were reported	None reported
Kelly 2015 25576049	CT	NR	NR	NR	74 (6.4%) "indeterminate" requiring further workup ^A
Martín Arévalo 2007 17883294	CT	CRC: 2/86 (2.3%) ^B	14/26 spared surgery (that was presumptively indicated by clinical diagnosis) (17% of all) 2/58 received (presumably appropriate) surgery (that was presumptively <i>not</i> indicated by clinical diagnosis) (2.4%)	2/86 missed CRC diagnosis, but unclear that this resulted in actual poor clinical sequelae.	None reported
Salem 2005 16108882	CT	1 FN	6 with (incorrect) clinical diagnosis of diverticulitis were correctly diagnosed with other conditions by CT ^C 2 with missed clinical diagnosis of diverticulitis managed correctly after CT ^D 2 mis-staged clinically managed correctly after CT ^E	1 FN (on CT) died prior to surgery ^F	None reported
	No CT	N/A	N/A	No sequelae or misdiagnoses noted for those with diverticulitis with no CT	N/A
Shuaib 2014 24475484	CT	NR	NR	NR	9 new ^G "worrisome" ^H 73 new "indeterminate" ^I

Abbreviations: CAD = complicated acute diverticulitis, CT = computed tomography, FN = false negative (missed diagnosis of diverticulitis on CT), IBD = inflammatory bowel disease, IBD = inflammatory bowel disease, N/A = not applicable (no CT done), N/A = not applicable (no CT done), NR = not reported, PMID = Pubmed identifier, TP = true positive (correct diagnosis of diverticulitis on CT), UAD = uncomplicated acute diverticulitis.

^A 24 clinically silent occult neoplasms (pancreas, colorectal, kidney, liver, sarcoma, lung, gallbladder, gastric, gynecologic)
5 <50 yo
6 deemed early local disease with good potential for curative resection

- 7 adrenal adenoma
- 5 colorectal polyps
- 2 perforated diverticulitis/mass
- 1 complex renal cyst
- 1 thickening/lesion of lower esophagus
- 34 benign clinically insignificant findings

^B 2 erroneous diagnoses of diverticulitis that intraoperatively proved to be sigmoid colorectal cancer complicated by an abscess.

^C Dissecting aortic aneurysm, left adrenal tumor, left pyonephrosis, metastatic colorectal cancer, acute appendicitis and inflammatory bowel disease.

- ^D 1 clinically diagnosed with acute abdomen had perforated diverticulitis on CT (managed surgically). 1 clinically diagnosed with intra-abdominal bleeding had (uncomplicated, implicitly) diverticulitis on CT (managed medically).
- ^E 4 required surgery as a result of CT findings or failure to improve with medical treatment; no further data reported.
- ^F Diagnosis made post-mortem.
- ^G Not previously known per clinical notes or previous imaging studies.
- ^H Only 3/9 new worrisome incidental findings received a recommendation by radiologist for further workup; all 3 had a change in clinical management based on the CT findings. Of the remaining 6 with no recommendation for further workup, only 2 had a change in clinical management.
- ^I 23/73 new indeterminate incidental findings received a recommendation by radiologist for further workup; of these 16 had a change in clinical management based on the CT finding. Of the 50 with new indeterminate incidental findings with no recommendation for a further workup, 1 had a change in clinical management.

Key Question 2a (Outpatient)

Table D-2a-1. KQ2a categorical outcomes

Study Year PMID, Design	Outcome	Time	Arm	Arm Details	n/N (%)	Effect Size (95% CI), Adjusted	Reported P Value
Biondo, 2014, 23732265, RCT	Treatment failure ^A	2 mo	Outpatient management	Discharged after 1st dose of IV Abx in the ED	3/66 (4.5)	0.74 (0.16, 3.43)	0.62
			Inpatient management	Admitted	4/66 (6.1)		
Bolkenstein, 2018, 29679152, NRCS (Retrospective)	Treatment failure ^B	<24 mo	Outpatient management	Not hospitalized within 24hr of presentation	12/264 (5)	0.41 (0.20, 0.83) ^C	0.01
			Inpatient management	Hospitalized within 24hr of presentation	34/301 (11)		
Joliat, 2017, 28664347, NRCS (Retrospective)	Elective surgery	Median=47 mo (29-74)	Outpatient management	Single dose Abx (IV) in ED followed by Abx (oral) for 10 days	14/98 (14)	NR	0.50 ^D
		Median=60 mo (Range=34- 82)	Inpatient management	Abx and fluids (IV), switched to Abx (oral) when pain was managed by non-opioid analgesics and able to tolerate oral medication (also discharged). No alimentary restrictions in hospital	30/169 (18)		
	Recurrence ^E	Median=47 mo (Range=29- 74)	Outpatient management	Single dose Abx (IV) in ED followed by Abx (oral) for 10 days	40/98 (41)	NR	NR ^D
		Median=60 mo (Range=34- 82)	Inpatient management	Abx and fluids (IV), switched to Abx (oral) when pain was managed by non-opioid analgesics and able to tolerate oral medication (also discharged). No alimentary restrictions in hospital	70/169 (41)		
Lorente, 2013, 23764519, NRCS (Retrospective)	Recurrence ^F	Mean=17 mo (SD=5)	Outpatient management	Abx for 7 days (oral) and analgesia (oral), liquid diet for 2 days. Follow up assessment between 4-7 days after diagnosis to confirm clinical course	16/90 (17.8)	NR	0.6 ^G
		Mean=17 mo (SD=5)	Inpatient management	Abx (IV) until improvement in symptoms then discharged to continue Abx (oral) at home	10/46 (21.7)		
Moya, 2012, 22706731, NRCS (Prospective)	Elective surgical treatment	Mean=7 mo (SD=9)	Outpatient management	10 d oral Abx,, oral analgesics, and dietary restrictions	1/32 (3.12)	NR	0.76 ^H
		Mean=9 mo (SD=18)	Inpatient management	5 d IV Abx, IV analgesic, and dietary restrictions	2/44 (4.5)		

Study Year PMID, Design	Outcome	Time	Arm	Arm Details	n/N (%)	Effect Size (95% CI), Adjusted	Reported P Value
	Recurrence ^F	Mean=7 mo (SD=9)	Outpatient management	Abx for 10 days (oral), analgesics (oral), and liquid diet. Assessed days 4 and 7; if satisfactory, prescribed low-fiber and fiber-rich diet, respectively	2/32 (6.25)	NR	0.86 ^H
		Mean=9 mo (SD=18)	Inpatient management	Abx for 5 days (IV), analgesics (IV), and liquid diet. Assessed day 3, if satisfactory, started liquid diet. Discharged day 5 and prescribed a fiber-rich diet and Abx for 7 days (oral)	3/44 (6.81)		
Ünlü, 2013, 23636075, NRCS (Retrospective)	Elective surgery	Mean=48 mo (SD=26)	Outpatient management	Hospital admission <24 hr, all managed in the ED; Ab (IV) in hospital and continued Ab (oral) at discharge 7-10 days depending on clinical status	3/118 (3)	NR	NR ^I
		Mean=48 mo (SD=26)	Inpatient management	Treated as inpatients, Abx (IV) in hospital and continued Abx (oral) at discharge 7-10 days depending on clinical status	8/194 (4)	NR	
	Recurrence ^F	Mean=48 mo (SD=26)	Outpatient management	Hospital admission <24 hr, all managed in the ED; Ab (IV) in hospital and continued Ab (oral) at discharge 7-10 days depending on clinical status	22/118 (19)	NR	NR ^I
		Mean=48 mo (SD=26)	Inpatient management	Treated as inpatients, Abx (IV) in hospital and continued Abx (oral) at discharge 7-10 days depending on clinical status	52/194 (27)	NR	

Abx = antibiotic, CI = confidence interval, hr = hour, IV = intravenously, mo = month, NR = not reported, NRCS = non-randomized controlled study, OR = odds ratio, PMID = Pubmed identifier, RCT = randomized controlled trial, SD = standard deviation, wk = week

- ^A Defined as persistence, increase, or recurrence of abdominal pain and/or fever, inflammatory bowel obstruction, need for radiological abscess drainage or immediate surgery due to complicated diverticulitis, need for hospital admission, and mortality during the first 60 days after discharge.
- ^B Defined as (re)admittance, mortality, complications (perforation, abscess, colonic obstruction, urinary tract infection, pneumonia) or need for antibiotics, operative intervention, or percutaneous abscess drainage within 30 days after initial presentation.
- ^C Adjusted for female gender, age, ASA score > 2, no rebound tenderness, C-reactive protein (mg/L).
- ^D Unadjusted analysis; during their acute attack, patients in the inpatient group had statistically significant higher levels of C-reactive protein and comorbidities (as assessed by the Charlson index), and were more likely to have more severe diverticulitis (according to the Ambrosetti score). Outcomes from this study should be interpreted with caution to the extent these baseline differences may affect long-term outcomes
- ^E Defined as new symptoms appearing >1 month after initial treatment.

^F Not defined.

^G Unadjusted analyses; during their acute attack, patients in the inpatient group had statistically significant higher rates of fever and pericolic free fluid. Outcomes in this study should be interpreted with caution to the extent that these baseline may affect long-term outcomes.

^H Unadjusted analyses; however no observed differences in baseline predictors.

^I Unadjusted analyses; during their acute attack, patients in the inpatient group had higher levels of inflammatory parameters such as C-reactive protein (CRP) and white blood cells and were more likely to have symptoms of fever, nausea, and vomiting. Outcomes in this study should be interpreted with caution to the extent that these baseline may affect long-term outcomes.

Table D-2a-2. KQ 2a continuous outcomes

Study, Year, PMID, Design	Outcome	Time	Arm	Arm Details	N	Mean (SD)	Difference	Reported P Value
Biondo, 2014, 23732265, RCT	SF-12 physical	2 mo	Outpatient management	Discharged after 1st dose of Abx (IV) in the ED	66	50.3 (7.2)	NR	0.59
			Inpatient management	Admitted after 1st dose of Abx (IV) in the ED	66	49.6 (8.7)		
	SF-12 mental	2 mo	Outpatient management	Discharged after 1st dose of Abx (IV) in the ED	66	53.0 (8.6)	NR	0.99
			Inpatient management	Admitted after 1st dose of Abx (IV) in the ED	66	52.6 (9.5)		

Abx = antibiotic, CI = confidence interval, ED = emergency department, IV = intravenously, mo = month, NR = not reported, PMID = Pubmed identifier, RCT = randomized controlled trial, SD = standard deviation, wk = week.

Key Question 2b (Antibiotics)

Table D-2b-1. Antibiotics: Mortality

Outcome	Study	Time	Arm	n/N (%)	OR (95% CI)	Reported P Value
Antibiotics vs. none: All-cause mortality	AVOD	30 d	Multiple antibiotics*	1/314 (0.3)	2.96 (0.12, 73.0)	
			Placebo	0/309 (0)		
		11 y	Multiple antibiotics*	28/275 (10.0)	1.06 (0.60, 1.86)	
			Placebo	26/275 (9.5)		
	STAND	30 d	Oral amoxicillin / clavulanate +- IV cefuroxime & oral metronidazole	1/84	3.40 (0.14, 84.48)	0.3
			Placebo	0/84		
Antibiotics vs. none: Diverticulitis-related mortality	DIABOLO	24 mo	Amoxicillin/clavulanate	1/266 (0.4)	0.33 (0.03, 3.15)	0.43
			No antibiotics	3/262 (1.1)		

Abbreviations: CI = confidence interval, d=days, mo = months, OR = odds ratio, PMID = PubMed identifier, RCT = randomized controlled trial.

* Discretionary.

Table D-2b-2. Antibiotics: Treatment failure

Outcome	Study	Time	Arm	n/N (%)	OR (95% CI)	Reported P Value
Antibiotics vs. none: Nonrecovery and/or readmission	Kim, 2019, 31267222	10 d	Cephalosporin + metronidazole	1/61 (1.6)	0.34 (0.03, 3.35)	0.62
			Placebo	3/64 (4.7)		
Antibiotics vs. none: Need for procedural intervention	STAND	30 d	Po Amoxicillin/clavulanate +- IV cefuroxime & po metronidazole	2/84	5.73 (0.27, 121.02)	0.1
			Placebo	0/94 (0)		
Antibiotics vs. none: No return to normal bowel function	DIABOLO	6 mo	Amoxicillin/clavulanate	18/266 (6.7)	0.61 (0.33, 1.13)	0.18
			No antibiotics	28/262 (10.7)		
Antibiotics vs. none: Time to recovery	DIABOLO	6 mo	Amoxicillin/clavulanate	Median 12 (IQR 7, 30)		
			No antibiotics	Median 14 (IQR 6, 35)		
Different regimens: Treatment failure	Ribas, 2010, 20526718	4-8 d	Amoxicillin/clavulanate (IV and oral)	2/22 (9.1)	2.10 (0.18, 25.0)	
			Amoxicillin/clavulanate (oral)	1/22 (4.5)		
Different regimens: Treatment failure	Ridgway, 2008, 19016815	30 d	Ciprofloxacin + metronidazole (IV)	1/38 (2.6)	1.08 (0.07, 17.9)	
			Ciprofloxacin + metronidazole (oral)	1/41 (2.4)		
Different regimens: Treatment failure	Park, 2019, 31290747	30 d	Cephalosporin + metronidazole (4 days)	19/89 (21.3)	1.30 (0.61, 2.77)	0.49
			Cephalosporin + metronidazole (1 day)	15/87 (17.2)		

Outcome	Study	Time	Arm	n/N (%)	OR (95% CI)	Reported P Value
Different regimens: Treatment failure	Etzioni, 2010, 20484998	60 d	Fluoroquinolone + metronidazole	34/589 (5.8)	1.05 (0.38, 2.92) Adjusted	
			Multiple (undefined)	5/104 (4.8)		
Different regimens: Treatment failure	Etzioni, 2010, 20484998	60 d	≥14 d antibiotics	5/101 (5.0)	0.68 (0.20, 2.35) Adjusted	
			10-13 d antibiotics	27/485 (5.6)	0.72 (0.29, 1.78) Adjusted	
			<10 d antibiotics	7/107 (6.5)	Reference	

Abbreviations: Adj = adjusted, CI = confidence interval, d=days, IQR=interquartile range, IV = intravenous, mo = months, OR = odds ratio, PMID = PubMed identifier, RCT = randomized controlled trial.

Table D-2b-3. Antibiotics: Surgery for diverticulitis

Outcome	Time	Study	Arm	n/N (%)	OR (95% CI)	Reported P Value
Antibiotics vs. none: Elective surgery	6 mo	DIABOLO	Amoxicillin/clavulanate	3/266 (1.1)	0.36 (0.10, 1.38)	0.25
			No antibiotics	8/262 (3.1)		
Antibiotics vs. none: Sigmoid resection	12 mo	AVOD	Multiple antibiotics*	2/292 (0.6)	0.33 (0.07, 1.63)	0.15
			Placebo	6/290 (1.9)		
Different regimens: Elective Surgery	>6 wk	Kellum, 1992, 1638578	Cefoxitin	6/30 (20.0)	11.4 (0.61, 215)	
			Gentamicin and clindamycin	0/21 (0)		
Different regimens: Elective Surgery	<12 mo	Schug-Pass, 2010, 20140619	Ertapenem (7 days)	21/48 (42.9)	1.31 (0.57, 3.04)	NS
			Ertapenem (4 days)	16/43 (37.2)		

Abbreviations: CI = confidence interval, mo = months, NS = not statistically significant, OR = odds ratio, PMID = PubMed identifier, RCT = randomized controlled trial, wk = weeks.

* Discretionary

Table D-2b-4. Antibiotics: Hospitalization or rehospitalization

Outcome	Time	Study	Arm	n/N (%)	OR (95% CI)	Reported P Value
Antibiotics vs. none: Readmission	1 wk	STAND	Po Amoxicillin/clavulanate +- IV cefuroxime & po metronidazole	5/84 (6.0)	OR 5.89 (0.67, 51.44)	0.07
			Placebo	1/94 (1.1)		
Antibiotics vs. none: Readmission	30 d	STAND	Po Amoxicillin/clavulanate +- IV cefuroxime & po metronidazole	5/84 (6.0)	OR 0.53 (0.17, 1.62)	0.3
			Placebo	10/94 (10.6)		
Antibiotics vs. none: Rehospitalization for diverticulitis	6 mo	DIABOLO	Amoxicillin/clavulanate	32/266 (12.0)	0.64 (0.39, 1.05)	0.15
			No antibiotics	46/262 (17.6)		
Antibiotics vs. none: Rehospitalization for diverticulitis	24 mo	DIABOLO	Amoxicillin/clavulanate	35/266 (13.2)	OR 0.71 (0.44, 1.15)	0.15
			No antibiotics	66/262 (25.2)		

Abbreviations: CI = confidence interval, d= days, wk= weeks, m = months, OR = odds ratio, PMID = PubMed identifier, RCT = randomized controlled trial, y = years.

Table D-2b-5 Antibiotics: Length of hospital stay

Outcome	Study	Arm	Mean or Median	Reported P Value
Antibiotics vs. none: Length of hospital (or intensive care unit) stay (days)	AVOD	Multiple *	Mean 2.9 (SE 1.9) Median 3 (Range 0, 25)	0.72
		Placebo	Mean 2.9 (SE 1.6) Median 3 (Range 0, 25)	
Antibiotics vs. none: Length of hospital stay (days)	Kim, 2019, 31267222	Cephalosporin + metronidazole	Mean 5.3 (SD 0.8)	0.96
		Placebo	Mean 5.3 (SD 0.8)	
Antibiotics vs. none: Length of hospital (or intensive care unit) stay (days)	DIABOLO	Amoxicillin/clavulanate	Median 3 (IQR 2, 3)	0.006
		No antibiotics	Median 2 (IQR 1, 3)	
Antibiotics vs. none: Length of hospital stay	STAND	Po Amoxicillin/clavulanate +- IV cefuroxime & po metronidazole	Median 40 (IQR 24.4, 57.6)	
		Placebo	Median 45.8 (IQR 26.5, 60.2)	
Different regimens: Length of hospital (or intensive care unit) stay (days)	Schug-Pass, 2010, 20140619	Ertapenem (7 days)	Mean 9.7 (SD 3.2)	0.002
		Ertapenem (4 days)	Mean 7.8 (SD 2.8)	

Abbreviations: CI = confidence interval, IQR = interquartile range, OR = odds ratio, PMID = PubMed identifier, RCT = randomized controlled trial, SD = standard deviation, SE = standard error.

* Discretionary

Table D-2b-6. Recurrence of diverticulitis

Outcome	Time	Study	Arm	n/N (%)	OR (95% CI)	Reported P Value
Antibiotics vs. none: Recurrence	≥6 wk	Kim, 2019, 31267222	Cephalosporin + metronidazole	5/64 (7.8)	1.00 (0.27, 3.64)	0.69
			Placebo	5/64 (7.8)		
Antibiotics vs. none: Recurrence	6 mo	DIABOLO	Amoxicillin/clavulanate	8/266 (3.0)	0.87 (0.33, 2.29)	0.49
			No antibiotics	9/262 (3.4)		
Antibiotics vs. none: Recurrence	≥12 mo	AVOD	Multiple antibiotics*	46/292 (15.8)	0.97 (0.62, 1.51)	0.88
			Placebo	47/290 (16.2)		
Antibiotics vs. none: Recurrence	24 mo	DIABOLO	Amoxicillin/clavulanate	36/241 (14.9)	0.96 (0.58, 1.60)	0.89
			No antibiotics	35/227 (15.4)		
Antibiotics vs. none: Recurrence	11 y	AVOD	Multiple antibiotics*	88/281 (31.3)	1.00 (0.70, 1.43)	0.49
			Placebo	86/275 (31.3)		
Antibiotics vs. none: Recurrence and/or subsequent surgery	Mean 30 m	Hjern, 2007, 17190761	Cephalosporin + metronidazole	NR	Adj 1.03 (0.61, 1.74)	
			No antibiotics	NR		
Antibiotics vs. none: Recurrence	Mean 50 m	de Korte, 2012, 21689302	Multiple antibiotics*	12/81 (15.0)	Adj 2.04 (0.83, 4.75)	
			No antibiotics	14/191 (7.0)		
Different regimens: Recurrence	1 y	Schug-Pass, 2010, 20140619	Ertapenem (7 days)	5/48 (10.4)	1.43 (0.32, 5.46)	NS
			Ertapenem (4 days)	3/40 (7.5)		
Different regimens: Failure of treatment	1 y	Schug-Pass, 2010, 20140619	Ertapenem (7 days)	2/56 (3.6)	0.58 (0.09, 3.62)	NS
			Ertapenem (4 days)	3/50 (6.0)		
Different regimens: Recurrence	>12 mo	Scarpa, 2015, 25960972	Long course IV (6 to 14 days)	52/210 (25.0)	1.05 (0.59, 2.21) Unadjusted (NRCS)	0.90
			Short course IV (<=5 days)	11/46 (24.0)		

Abbreviations: Adj = adjusted, CI = confidence interval, d=days, IV = intravenous, m = months, NR = not reported, NRCS = nonrandomized comparative study, NS = not statistically significant, OR = odds ratio, PMID = PubMed identifier, RCT = randomized controlled trial, y = years.

* Discretionary # Unadjusted

Table D-2b-7. Antibiotics: Diverticulitis-related morbidities

Outcome	Time	Study	Arm	n/N (%)	Reported P Value
Antibiotics vs. none: Abscess	30 d	AVOD	Multiple antibiotics *	0/314 (0)	0.08
			Placebo	3/309 (0.9)	
Antibiotics vs. none: Abscess >5 cm	6 mo	DIABOLO	Amoxicillin/clavulanate	2/266 (0.7)	0.68
			No antibiotics	2/262 (0.8)	
Antibiotics vs. none: Abscess >5 cm	24 m	DIABOLO	Amoxicillin/clavulanate	3/241 (1.2)	
			No antibiotics	2/227 (0.9)	
Antibiotics vs. none: Fistula	6 mo	DIABOLO	Amoxicillin/clavulanate	0/266 (0)	0.55
			No antibiotics	1/262 (0.4)	
Antibiotics vs. none: Fistula	24 mo	DIABOLO	Amoxicillin/clavulanate	1/241 (0.4)	
			No antibiotics	1/227 (0.4)	
Antibiotics vs. none: Obstruction	6 mo	DIABOLO	Amoxicillin/clavulanate	2/266 (0.7)	0.44
			No antibiotics	4/262 (1.5)	
Antibiotics vs. none: Obstruction	24 mo	DIABOLO	Amoxicillin/clavulanate	2/241 (0.8)	
			No antibiotics	4/227 (1.8)	
Different regimens: Abscess	1 y	Schug-Pass, 2010, 20140619	Ertapenem (7 days)	0/48 (0)	NS
			Ertapenem (4 days)	1/43 (2.3)	
Different regimens: Fistula, interenteric	1 y	Schug-Pass, 2010, 20140619	Ertapenem (7 days)	1/43 (2.3)	NS
			Ertapenem (4 days)	0/48 (0)	
Different regimens: Post-inflammatory stenosis	1 y	Schug-Pass, 2010, 20140619	Ertapenem (7 days)	1/48 (2.1)	NS
			Ertapenem (4 days)	1/40 (2.5)	

Abbreviations: CI = confidence interval, m = months, NS = not statistically significant, PMID = PubMed identifier, RCT = randomized controlled trial, y = years.

* Discretionary

Table D-2b-8. Antibiotics: Pain or tenderness

Outcome Measurement	Time	Study	Arm	n/N (%)	OR (95% CI)	Reported P Value
Antibiotics vs. none: Pain, Visual Analog Scale (0 to 10)	1-5 d	AVOD	Multiple antibiotics*		NR	All NS
			Placebo			
Antibiotics vs. none: Tenderness (0 to 4)	1-5 d	AVOD	Multiple antibiotics*	Mean 1.0 (SD NR)	MD 0.2 (0.008, 0.39)	0.041
			Placebo	Mean 0.8 (SD NR)		
Antibiotics vs. none: Abdominal pain, Visual Analog Scale (0 to 10)	<10 d	DIABOLO	Amoxicillin/clavulanate	79/219 (36.1)	OR 0.99 (0.60, 1.46)	0.37
			No antibiotic	75/210 (35.7)		
Antibiotics vs. none: Pain Visual Analog Scale (0 to 10)	30 d	STAND	Po Amoxicillin/clavulanate +- IV cefuroxime & po metronidazole	Median 2 (1,3)		0.9
			Placebo	Median 3 (2,3)		
Antibiotics vs. none: Severe periodic pain	12 mo	AVOD	Multiple antibiotics*	12/292 (4.2)	OR 0.99 (0.44, 2.25)	NS
			Placebo	12/290 (4.1)		
Antibiotics vs. none: Chronic abdominal pain	12 mo	AVOD	Multiple antibiotics*	5/292 (1.7)	OR 1.25 (0.33, 4.69)	NS
			Placebo	4/290 (1.4)		
Antibiotics vs. none: Chronic abdominal pain	11 y	AVOD	Multiple antibiotics*	3/281 (0.9)	OR 6.92 (0.36, 135)	NS
			Placebo	0/275 (0)		
Different regimens: Tenderness, Wexford score	3 d	Ridgway, 2008, 19016815	Ciprofloxacin + metronidazole (IV)	Mean 1.20 (SD NR)	MD -0.06 (-0.50, 0.38)	0.79
			Ciprofloxacin + metronidazole (oral)	Mean 1.26 (SD NR)		

Abbreviations: CI = confidence interval, d = days, m = months, MD = mean difference, NR = not reported, NS = not statistically significant, OR = odds ratio, PMID = PubMed identifier, RCT = randomized controlled trial, y = years.

*Discretionary

Table D-2b-9. Antibiotics: Quality of life

Outcome	Measurement Instrument	Time	Study	Arm	n/N (%) or Mean (SD)	OR (95% CI)	Reported P Value
Antibiotics vs. none: Quality of life	EQ-5D	MES	DIABOLO	Amoxicillin/clavulanate	Mean 76.4 (SD NR)	MD 0.8	0.32
				No antibiotics	Mean 77.2 (SD NR)		
Antibiotics vs. none: Quality of life, Emotional	GIQLI	MES	DIABOLO	Amoxicillin/clavulanate	Mean 16.5 (SD NR)	MD 0	0.89
				No antibiotics	Mean 16.5 (SD NR)		
Antibiotics vs. none: Quality of life, Gastrointestinal symptoms	GIQLI	MES	DIABOLO	Amoxicillin/clavulanate	Mean 62.9 (SD NR)	MD 0.3	0.56
				No antibiotics	Mean 62.6 (SD NR)		
Antibiotics vs. none: Quality of life, Physical	GIQLI	MES	DIABOLO	Amoxicillin/clavulanate	Mean 20.7 (SD NR)	MD 0	0.91
				No antibiotics	Mean 20.7 (SD NR)		
Antibiotics vs. none: Quality of life, Social	GIQLI	MES	DIABOLO	Amoxicillin/clavulanate	Mean 16.5 (SD NR)	MD -0.1	0.69
				No antibiotics	Mean 16.6 (SD NR)		
Antibiotics vs. none: Quality of life	SF-36	MES	DIABOLO	Amoxicillin/clavulanate	Mean 49.9 (SD NR)	MD -0.5	0.48
				No antibiotics	Mean 50.4 (SD NR)		
Antibiotics vs. none: Quality of life, Physical	SF-36	MES	DIABOLO	Amoxicillin/clavulanate	Mean 46.5 (SD NR)	MD -0.7	0.32
				No antibiotics	Mean 47.2 (SD NR)		
Antibiotics vs. none: Quality of life, Cumulative Index score	EQ-5D	11 y	AVOD	Multiple antibiotics*	Mean 0.834 (SD NR)	MD 0.015	0.46
				Placebo	Mean 0.819 (SD NR)		
Antibiotics vs. none: Quality of life, Anxiety/depression Level 3 (major problems)	EQ-5D	11 y	AVOD	Multiple antibiotics*	1/142 (0.7)	OR 0.05 (0.01, 0.41)	0.35
				Placebo	2/163 (1.3)		
Antibiotics vs. none: Quality of life, Mobility Level 3 (major problems)	EQ-5D	11 y	AVOD	Multiple antibiotics*	0/142 (0)	OR 0.28 (0.01, 6.35)	0.34
				Placebo	0/163 (0)		
Antibiotics vs. none: Quality of life, Pain/discomfort Level 3 (major problems)	EQ-5D	11 y	AVOD	Multiple antibiotics*	3/142 (2.1)	OR 7.01 (0.35, 141.2)	0.77
				Placebo	5/163 (3.1)		
Antibiotics vs. none: Quality of life, Self-care Level 3 (major problems)	EQ-5D	11 y	AVOD	Multiple antibiotics*	2/281 (0.7)	OR 0.39 (0.07, 2.01)	0.83
				Placebo	16/275 (5.7)		
Antibiotics vs. none: Quality of life, Usual activities Level 3 (major problems)	EQ-5D	11 y	AVOD	Multiple antibiotics*	3/142 (2.1)	OR 0.20 (0.06, 0.70)	0.72
				Placebo	3/163 (1.9)		

Abbreviations: CI = confidence interval, d = days, EQ-5D= EuroQoL General Health-related Quality of Life Scale measured in 5 dimensions, GIQLI = Gastrointestinal Quality of Life Index, MD = mean difference, MES=Mean estimated scores over 3, 6, 12, and 24 months, with adjustments for baseline scores, NR = not reported, OR = odds ratio, PMID = PubMed identifier, RCT = randomized controlled trial, SD = standard deviation, SF-36=short form 36, y = years.

* Discretionary

Table D-2b-10 Antibiotics: Adverse events

Outcome	Time	Study	Arm	n/N (%)	OR (95% CI)	Reported P Value
Antibiotics vs. none: Any	30 d	AVOD	Multiple antibiotics*	3/314 (0.9)	0.49 (0.12, 1.97)	0.30
			Placebo	6/309 (1.9)		
Antibiotics vs. none: Complications after treatment	6 mo	DIABOLO	Amoxicillin/clavulanate	8/241 (3.3)	0.67 (0.27, 1.71)	0.40
			No antibiotics	11/227 (4.8)		
Different regimens: Serious	<12 mo	Schug-Pass, 2010, 20140619,	Ertapenem (7 days)	0/56 (0)		
			Ertapenem (4 days)	0/50 (0)		
Different regimens: Allergic reaction	<12 mo	Schug-Pass, 2010, 20140619,	Ertapenem (7 days)	0/56 (0)		
			Ertapenem (4 days)	1/50 (2.0)		
Different regimens: Headache	<12 mo	Schug-Pass, 2010, 20140619,	Ertapenem (7 days)	0/56 (0)		
			Ertapenem (4 days)	2/50 (4.0)		
Different regimens: Any	<12 mo	Schug-Pass, 2010, 20140619,	Ertapenem (7 days)	0/56 (0)		
			Ertapenem (4 days)	3/50 (5.1)		

Abbreviations: CI = confidence interval, d = days, m = months, NR = not reported, OR = odds ratio, PMID = PubMed identifier, RCT = randomized controlled trial.

* Discretionary

Key Question 2c (Interventional Radiology)

Table D-2c-1. KQ 2c. All results

Study, Year, PMID	Outcome	Time	Arm	Arm Details	Subgroup	n/N (%) or Median (IQR)	Effect Size (95% CI)	P Value
Lambrichts, 2019, 30811050	All-cause mortality	6 y	Interventional radiology	Percutaneous drainage	All participants	12/115 (10.4)	Unadj OR 2.30 (1.05, 5.02)*	0.048
					Hinchey Ib	2/18 (11.1)		
					Hinchey II	8/197 (4.1)		
			No intervention	No percutaneous drainage	All participants	16/332 (4.8)		
					Hinchey Ib	10/97 (10.3)		
					Hinchey II	8/135 (5.9)		
Lambrichts, 2019, 30811050	Sigmoid resection	30 d	Interventional radiology	Percutaneous drainage	All participants	16/115 (13.9)	Adj. OR 1.29 (0.56, 2.99)	0.554
					Hinchey Ib	1/18 (6)		
					Hinchey II	15/97 (15)		
			No intervention	No percutaneous drainage	All participants	24/332 (7.2)		
					Hinchey Ib	10/197 (5.1)		
					Hinchey II	14/135 (10.4)		
Lambrichts, 2019, 30811050	Sigmoid resection	6 y	Interventional radiology	Percutaneous drainage	All participants	37/115 (32.2)	Adj. OR 1.08 (0.69, 1.69)	0.736
					Hinchey Ib	6/18 (33.3)		
					Hinchey II	31/97 (32)		
			No intervention	No percutaneous drainage	All participants	87/332 (26.2)		
					Hinchey Ib	57/197 (28.9)		
					Hinchey II	30/135 (22.2)		
Lambrichts, 2019, 30811050	Treatment failure	30 d	Interventional radiology	Percutaneous drainage	All participants	41/115 (35.7)	Adj OR 1.47 (0.81, 2.68)	0.185
					Hinchey Ib	6/18 (33.3)		
					Hinchey II	35/97 (36)		
			No interventional radiology	No percutaneous drainage	All participants	79/332 (23.8)		
					Hinchey Ib	44/197 (22.3)		
					Hinchey II	35/135 (25.9)		
Lambrichts, 2019, 30811050	Recurrence of diverticulitis (Any)	6 y	Interventional radiology	Percutaneous drainage	All participants	29/115 (25.2)	Unadj OR 0.87 (0.53, 1.41)*	NR
					Hinchey Ib	7/18 (38.9)		
					Hinchey II	54/197 (27.4)		
			No interventional radiology	No percutaneous drainage	All participants	93/332 (28.0)		
					Hinchey Ib	22/97 (22.7)		
					Hinchey II	39/135 (28.9)		
Mali, 2019, 31320921	Diverticulitis-related mortality	30 d	Interventional radiology	Percutaneous drainage	All participants	1/18 (6)	OR 1.00 (0.06, 17.33)*	1.00
			Antibiotics: Multiple	Discretionary, undefined antibiotics oral or IV	All participants	1/18 (6)		

Study, Year, PMID	Outcome	Time	Arm	Arm Details	Subgroup	n/N (%) or Median (IQR)	Effect Size (95% CI)	P Value
Mali, 2019, 31320921	Sigmoid resection	During initial admission	Interventional radiology	Percutaneous drainage	All participants	5/18 (28)	OR 1.00 (0.23, 4.30)*	1.00
			Antibiotics: Multiple	Discretionary, undefined antibiotics oral or IV	All participants	5/18 (28)		
Mali, 2019, 31320921	Sigmoid resection	71 mo	Interventional radiology	Percutaneous drainage	All participants	9/12 (75.0)	OR 1.50 (0.25, 8.84)	0.74
			Antibiotics: Multiple	Discretionary, undefined antibiotics oral or IV	All participants	8/12 (66.7)		
Mali, 2019, 31320921	Readmission	30 d	Interventional radiology	Percutaneous drainage	All participants	2/18 (11)	OR 0.63 (0.09, 4.28)	1.00
			Antibiotics: Multiple	Discretionary, undefined antibiotics oral or IV	All participants	3/18 (17)		
Mali, 2019, 31320921, Finland	Length of hospital stay	30 d	Interventional radiology	Percutaneous drainage	All participants	Median 6 d [IQR 3, 12]	Median Difference = 0 d	0.73
			Antibiotics: Multiple	Discretionary, undefined antibiotics oral or IV	All participants	Median 6 d [IQR 3, 10]		
Mali, 2019, 31320921	Treatment failure	30 d	Interventional radiology	Percutaneous drainage	All participants	6/18 (33)	OR 0.63 (0.16, 2.41)*	0.49
			Antibiotics: Multiple	Discretionary, undefined antibiotics oral or IV	All participants	8/18 (44)		
Mali, 2019, 31320921	Recurrence of diverticulitis (Any)	71 mo	Interventional radiology	Percutaneous drainage	All participants	1/12 (8)	OR 0.45 (0.04, 5.81)*	0.54
			Antibiotics: Multiple	Discretionary, undefined antibiotics oral or IV	All participants	2/12 (17)		
Mali, 2019, 31320921	Recurrence of diverticulitis (Complicated)	71 mo	Interventional radiology	Percutaneous drainage	All participants	1/12 (8)	OR 1.00 (0.06, 18.09)*	1.00
			Antibiotics: Multiple	Discretionary, undefined antibiotics oral or IV	All participants	1/12 (8)		
Mali, 2019, 31320921	Stoma	30 d	Interventional radiology	Percutaneous drainage	All participants	2/12 (16.7)	OR 0.60 (0.08, 4.45)*	NR
			Antibiotics: Multiple	Antibiotics	All participants	3/12 (25.0)		

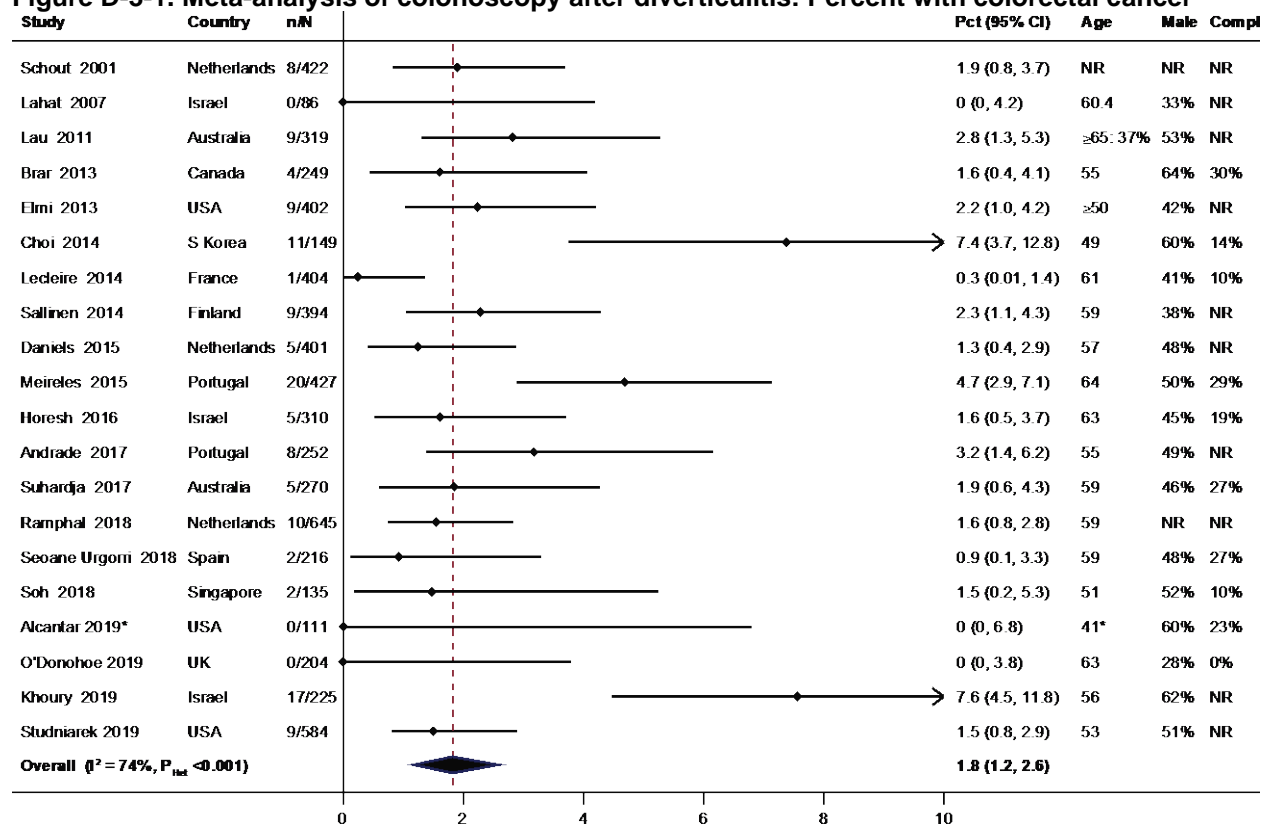
Abbreviations: Adj = adjusted, CI = confidence interval, d = days, IV = intravenous, mo = months, NR = not reported, NRCS = nonrandomized comparative study, OR = odds ratio, PMID = PubMed identifier, w = weeks, y = years.

* Calculated by us based on reported arm-specific data. This was done only for studies with arms with baseline characteristics considered by us to be similar.

Key Question 3 (Colonoscopy)

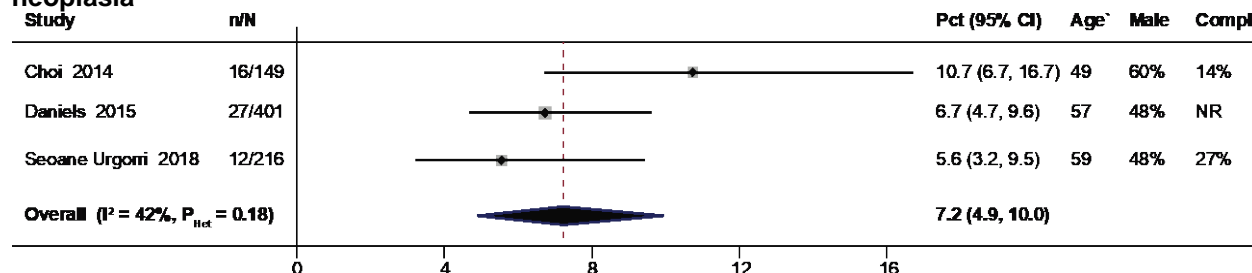
Meta-Analysis Figures

Figure D-3-1. Meta-analysis of colonoscopy after diverticulitis: Percent with colorectal cancer



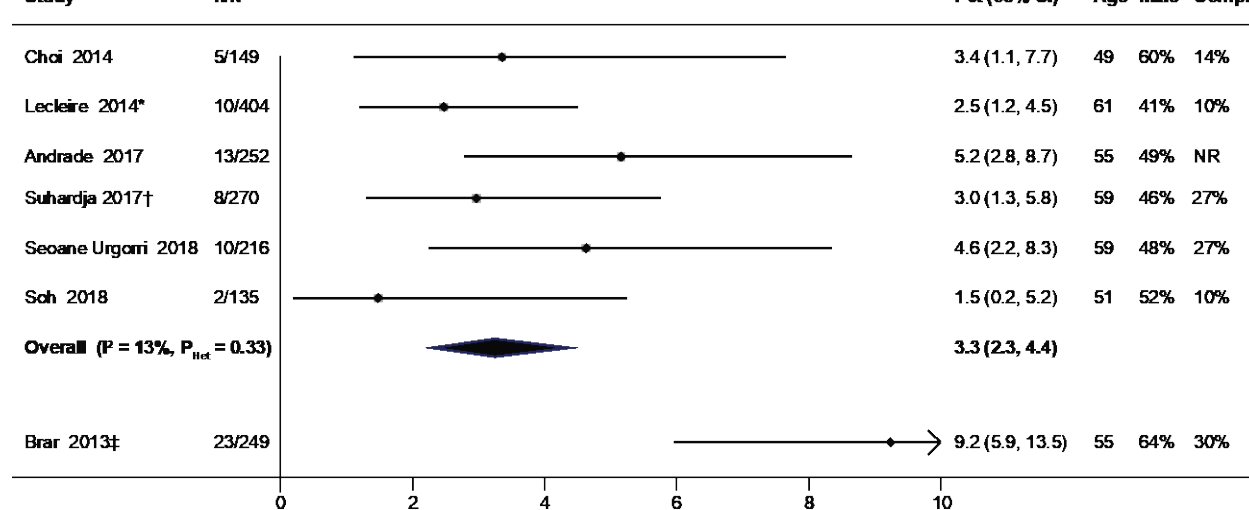
Abbreviations: CI = confidence interval, Compl = complicated diverticulitis (%), I^2 = measure of statistical heterogeneity (% of heterogeneity not due to random chance), NR = not reported, Pct = percent, P_{het} = chi-squared P value of statistical heterogeneity (not the P value of the estimate).

Figure D-3-2. Meta-analysis of colonoscopy after diverticulitis: Percent with advanced colonic neoplasia



Abbreviations: CI = confidence interval, Compl = complicated diverticulitis (%), I^2 = measure of statistical heterogeneity (% of heterogeneity not due to random chance), NR = not reported, Pct = percent, P_{het} = chi-squared P value of statistical heterogeneity (not the P value of the estimate).

Figure D-3-3. Meta-analysis of colonoscopy after diverticulitis: Percent with advanced adenoma

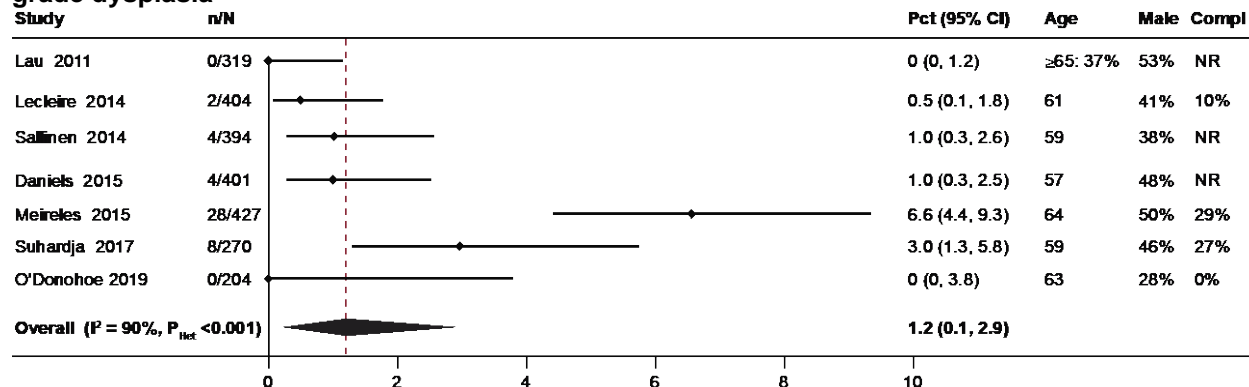


Abbreviations: CI = confidence interval, Compl = complicated diverticulitis (%), I² = measure of statistical heterogeneity (% of heterogeneity not due to random chance), NR = not reported, Pct = percent, P_{Het} = chi-squared P value of statistical heterogeneity (not the P value of the estimate).

* This estimate excludes the one patient with CRC who was included by Lecleire 2014 as also having advanced adenoma.

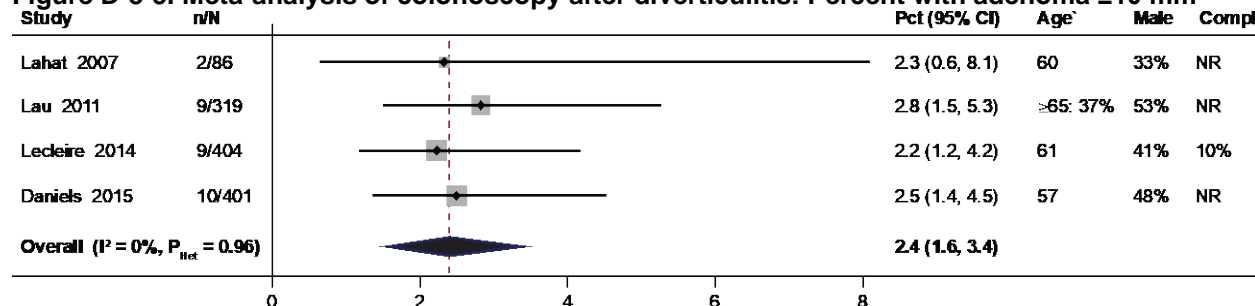
† Suhardja 2017 did not define advanced adenoma.

Figure D-3-4. Meta-analysis of colonoscopy after diverticulitis: Percent with adenomas with high-grade dysplasia



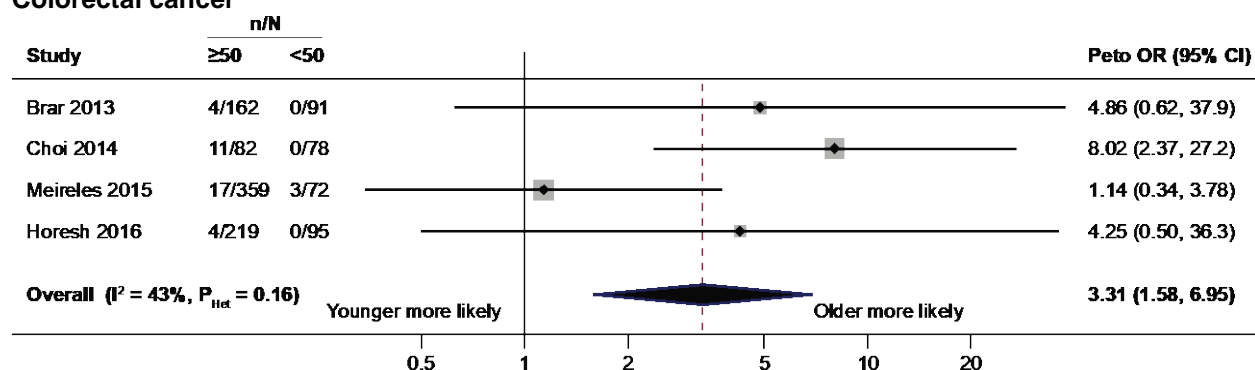
Abbreviations: CI = confidence interval, Compl = complicated diverticulitis (%), I² = measure of statistical heterogeneity (% of heterogeneity not due to random chance), NR = not reported, Pct = percent, P_{Het} = chi-squared P value of statistical heterogeneity (not the P value of the estimate).

Figure D-3-5. Meta-analysis of colonoscopy after diverticulitis: Percent with adenoma ≥ 10 mm



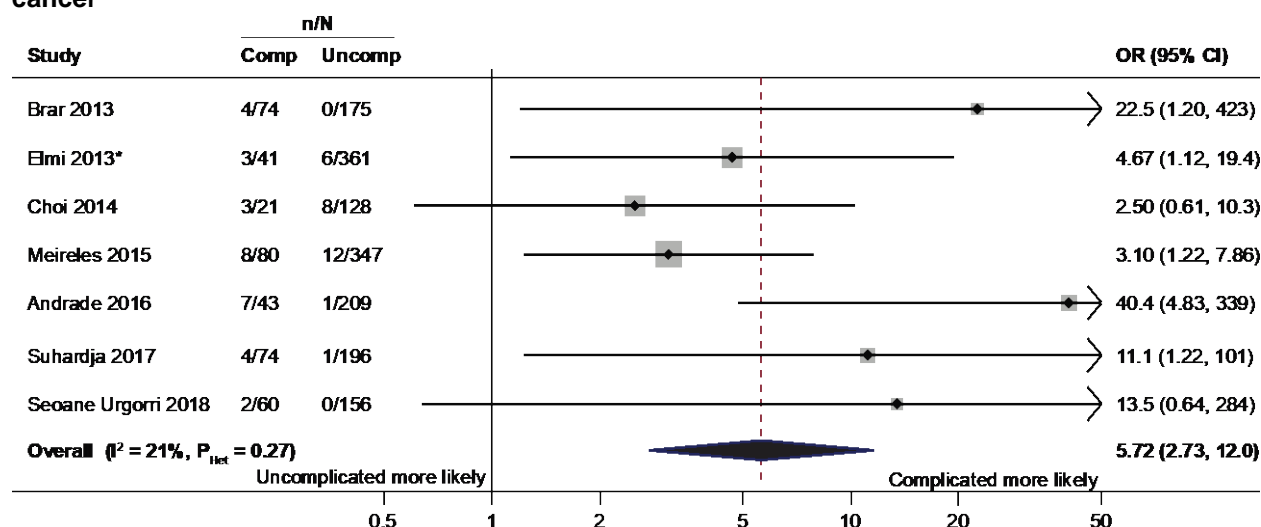
Abbreviations: CI = confidence interval, Compl = complicated diverticulitis (%), I^2 = measure of statistical heterogeneity (% of heterogeneity not due to random chance), NR = not reported, Pct = percent, P_{Het} = chi-squared P value of statistical heterogeneity (not the P value of the estimate).

Figure D-3-6. Meta-analysis of older (≥ 50 years) versus younger adults with acute diverticulitis: Colorectal cancer



Abbreviations: CI = confidence interval, I^2 = measure of statistical heterogeneity (% of heterogeneity not due to random chance), OR = odds ratio, P_{Het} = chi-squared P value of statistical heterogeneity (not the P value of the estimate).

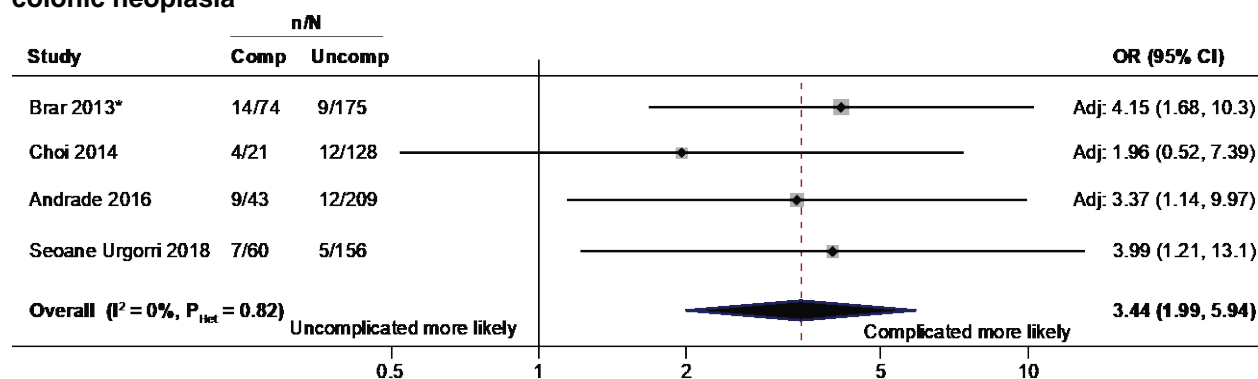
Figure D-3-7. Meta-analysis of complicated versus uncomplicated acute diverticulitis: Colorectal cancer



Abbreviations: CI = confidence interval, Compl = complicated diverticulitis, I^2 = measure of statistical heterogeneity (% of heterogeneity not due to random chance), OR = odds ratio, P_{Het} = chi-squared P value of statistical heterogeneity (not the P value of the estimate), Uncomp = uncomplicated diverticulitis.

* Comparison of abscess versus no abscess.

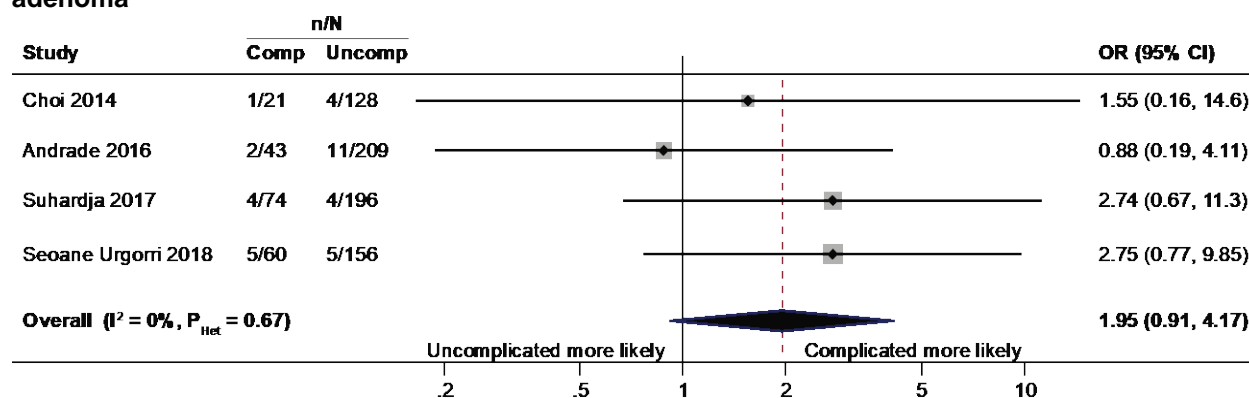
Figure D-3-8. Meta-analysis of complicated versus uncomplicated acute diverticulitis: Advanced colonic neoplasia



Abbreviations: CI = confidence interval, Compl = complicated diverticulitis, I^2 = measure of statistical heterogeneity (% of heterogeneity not due to random chance), OR = odds ratio, P_{Het} = chi-squared P value of statistical heterogeneity (not the P value of the estimate), Uncompl = uncomplicated diverticulitis.

* Comparison of abscess versus no abscess.

Figure D-3-9. Meta-analysis of complicated versus uncomplicated acute diverticulitis: Advanced adenoma



Abbreviations: CI = confidence interval, Compl = complicated diverticulitis, I^2 = measure of statistical heterogeneity (% of heterogeneity not due to random chance), OR = odds ratio, P_{Het} = chi-squared P value of statistical heterogeneity (not the P value of the estimate), Uncompl = uncomplicated diverticulitis.

Data Tables

Table D-3-1. KQ 3. Categorical outcomes, colonoscopy versus no colonoscopy after acute diverticulitis

Author, Year, PMID, Country, Funding	Design	Population Diverticulitis Details Family Hx CRC Setting	Outcome	Arm	Age Sex	Age ≥50, % Complicated/ Uncomplicated Diverticulitis %	n/N (%)	Effect Size	Report ed P Value
Lau, 2011, 21904141, Australia, NR	NRCS (Retros pective)	Diverticulitis confirmed by CT and had a follow up colonoscopy within 1 year from the date of CT scan. Family history of CRC: not available (claimed by the author). Multicenter.	Colorectal cancer	Colonoscopy	15-39y: 7.2%, 40-64y: 55.5%, 65+: 37.3% 53% male	NR NR	9/319 (2.8%)	OR 1.57 (0.67, 3.65)*	
				No Colonoscopy	15-39y: 8.5%, 40-64y: 54.2%, 65+: 37.3% 48% male	NR NR	14/769 (1.8%)		
Sallinen, 2014, 24178863, Finland, NR	NRCS (Retros pective)	Clinically and CT diagnosed acute diverticulitis. Family history of CRC: not reported. Single center.	Colorectal cancer	Colonoscopy	58.5 (13.9) 38% male	NR NR	9/394 (2.3%)	OR 7.02 (0.41, 121)*	
				No Colonoscopy	NR NR	NR NR	0/142 (0)		
Soh, 2018, 29663068, Singapore, NR	NRCS (Retros pective)	First episode of CT-proven acute diverticulitis with no complications. Family history of CRC: not reported. Single center.	Colorectal cancer	Colonoscopy	50.9 [range 18, 96] 52% male	NR 10.0%/90.0%	2/135 (1.5%)	OR 0.68 (0.09, 4.89)*	
				No Colonoscopy	NR NR	NR NR	2/92 (2.2%)		

Abbreviations: CRC = colorectal cancer, CT = computed tomography, Hx = history, NR = not reported, NRCS = nonrandomized controlled study, OR = odds ratio.

* Calculated by review team.

Table D-3-2. KQ 3. Categorical outcomes, colonoscopy after acute diverticulitis versus general screening (no diverticulitis)

Author, Year, PMID, Country, Funding	Design	Population Diverticulitis Details Family Hx CRC Setting	Outcome	Arm	Age Sex	Age ≥50, % Complicated/ Uncomplicated Diverticulitis %	n/N (%)	Effect Size	Report ed P Value
Choi, 2014, 24723071, S Korea, NR	NRCS (Retrospective)	Underwent CT, followed by colonoscopy within a year and diagnosed with acute diverticulitis. For each diverticulitis case, two age-(±5 years) and sex matched control individuals were identified from healthy individuals who underwent screening colonoscopy. Family history of CRC: 2.6% among diverticulitis patients and 3.1% among controls. Multicenter.	Colorectal cancer	Diverticulitis with colonoscopy	48.6 (16.5) 60% male	NR 14.1%/85.9%	11/149 (7.4%)	OR 11.80 (2.58, 54.0)	0.001
				Sex matched controls	46.6 (16.6) 60% male	NR 8.2%/91.8%	2/298 (0.7%)		
Daniels, 2015, 25472747, Netherlands, Non-industry	NRCS (Retrospective)	Primary colonoscopy screening population: randomly invited for primary colonoscopy screening and 50-75 years. Uncomplicated Diverticulitis Population: adult, CT proven uncomplicated left sided acute diverticulitis, participating in DIABOLO trial, having follow up colonoscopy within 6 months. Family history of CRC: 9.5% among diverticulitis patients and 15.3% among screening individuals. Multicenter.	Colorectal cancer	Diverticulitis patients (DIABOLO trial)	Median 57 [range 49, 65] 48% male	NR NR	5/401 (1.2%)	OR 1.99 (0.66, 5.97)*	0.673
				Screening individuals (COCOS trial)	Median 60 [range 55, 65] 51% male	NR NR	9/1426 (0.6%)		

Author, Year, PMID, Country, Funding	Design	Population Diverticulitis Details Family Hx CRC Setting	Outcome	Arm	Age Sex	Age ≥50, % Complicated/ Uncomplicated Diverticulitis %	n/N (%)	Effect Size	Report ed P Value
Lecleire, 2014, 25083288, France, Non-industry	NRCS (Retrospective)	Group 1 patients: acute diverticulitis, underwent colonoscopy within 6 months following the acute episode. Group 2 patients: sex and age matched with a familial history of colorectal adenoma or neoplasia. Group 2 patients had a family history of colorectal adenoma or neoplasia. Multicenter.	Colorectal cancer	Acute diverticulitis	60.9 (12.6) 41% male	NR 10.0%/90.0%	1/404 (0.3%)	OR 1.00 (0.06, 16.0)*	
				Sex and age matched controls	60.7 (13.4) 41% male	NR NR	1/404 (0.3%)		
Daniels, 2015, 25472747, Netherlands, Non-industry	NRCS (Retrospective)	Primary colonoscopy screening population: randomly invited for primary colonoscopy screening and 50-75 years. Uncomplicated Diverticulitis Population: adult, CT proven uncomplicated left sided acute diverticulitis, participating in DIABOLO trial, having follow up colonoscopy within 6 months. Family history of CRC: 9.5% among diverticulitis patients and 15.3% among screening individuals. Multicenter.	Adenoma ≥10 mm	Diverticulitis patients (p DIABOLO trial)	Median 57 [range 49, 65] 48% male	NR NR	10/401 (2.5%)	OR_0.36 (0.18, 0.69)*	0.002
				Screening individuals (COCOS trial)	Median 60 [range 55, 65] 51% male	NR NR	95/1426 (6.7%)		

Author, Year, PMID, Country, Funding	Design	Population Diverticulitis Details Family Hx CRC Setting	Outcome	Arm	Age Sex	Age ≥50, % Complicated/ Uncomplicated Diverticulitis %	n/N (%)	Effect Size	Report ed P Value
Lecleire, 2014, 25083288, France, Non-industry	NRCS (Retrospective)	Group 1 patients: acute diverticulitis, underwent colonoscopy within 6 months following the acute episode. Group 2 patients: sex and age matched with a familial history of colorectal adenoma or neoplasia. Group 2 patients had a family history of colorectal adenoma or neoplasia. Multicenter.	Adenoma ≥10 mm	Acute diverticulitis	60.9 (12.6) 41% male	NR 10.0%/90.0%	9/404 (2.2%)	OR 0.38 (0.17, 0.83)*	
				Sex and age matched controls	60.7 (13.4) 41% male	NR NR	23/404 (5.7%)		
Choi, 2014, 24723071, S Korea, NR	NRCS (Retrospective)	Underwent CT, followed by colonoscopy within a year and diagnosed with acute diverticulitis. For each diverticulitis case, two age- (±5 years) and sex matched control individuals were identified from healthy individuals who underwent screening colonoscopy. Family history of CRC: 2.6% among diverticulitis patients and 3.1% among controls. Multicenter.	Advanced adenoma	Diverticulitis with colonoscopy	48.6 (16.5) 60% male	NR 14.1%/85.9%	5/149 (3.4%)	OR 5.14 (0.99, 26.8)	0.052
				Sex matched controls	46.6 (16.6) 60% male	NR 8.2%/91.8%	2/298 (0.7%)		

Author, Year, PMID, Country, Funding	Design	Population Diverticulitis Details Family Hx CRC Setting	Outcome	Arm	Age Sex	Age ≥50, % Complicated/ Uncomplicated Diverticulitis %	n/N (%)	Effect Size	Report ed P Value
Lecleire, 2014, 25083288, France, Non-industry	NRCS (Retrospective)	Group 1 patients: acute diverticulitis, underwent colonoscopy within 6 months following the acute episode. Group 2 patients: sex and age matched with a familial history of colorectal adenoma or neoplasia. Group 2 patients had a family history of colorectal adenoma or neoplasia. Multicenter.	Advanced adenoma	Acute diverticulitis	60.9 (12.6) 41% male	NR 10.0%/90.0%	11/404 (2.7%)	OR_0.39 (0.19, 0.80)*	0.01
				Sex and age matched controls	60.7 (13.4) 41% male	NR NR	27/404 (6.7%)		
Daniels, 2015, 25472747, Netherlands, Non-industry	NRCS (Retrospective)	Primary colonoscopy screening population: randomly invited for primary colonoscopy screening and 50-75 years. Uncomplicated Diverticulitis Population: adult, CT proven uncomplicated left sided acute diverticulitis, participating in DIABOLO trial, having follow up colonoscopy within 6 months. Family history of CRC: 9.5% among diverticulitis patients and 15.3% among screening individuals. Multicenter.	Advanced adenomas	Diverticulitis patients (DIABOLO trial)	Median 57 [range 49, 65] 48% male	NR NR	22/401 (5.5%)	OR_0.61 (0.38, 0.97)*	0.053 †
				Screening individuals (COCOS trial)	Median 60 [range 55, 65] 51% male	NR NR	124/1426 (8.7%)		

Author, Year, PMID, Country, Funding	Design	Population Diverticulitis Details Family Hx CRC Setting	Outcome	Arm	Age Sex	Age ≥50, % Complicated/ Uncomplicated Diverticulitis %	n/N (%)	Effect Size	Report ed P Value
Choi, 2014, 24723071, S Korea, NR	NRCS (Retrospective)	Underwent CT, followed by colonoscopy within a year and diagnosed with acute diverticulitis. For each diverticulitis case, two age- (±5 years) and sex matched control individuals were identified from healthy individuals who underwent screening colonoscopy. Family history of CRC: 2.6% among diverticulitis patients and 3.1% among controls. Multicenter.	Advanced colonic neoplasia	Diverticulitis with colonoscopy	48.6 (16.5) 60% male	NR 14.1%/85.9%	16/149 (10.7%)	OR 8.84 (2.90, 27.0)	<0.001
				Sex matched controls	46.6 (16.6) 60% male	NR 8.2%/91.8%	4/298 (1.3%)		
Daniels, 2015, 25472747, Netherlands, Non-industry	NRCS (Retrospective)	Primary colonoscopy screening population: randomly invited for primary colonoscopy screening and 50-75 years. Uncomplicated Diverticulitis Population: adult, CT proven uncomplicated left sided acute diverticulitis, participating in DIABOLO trial, having follow up colonoscopy within 6 months. Family history of CRC: 9.5% among diverticulitis patients and 15.3% among screening individuals. Multicenter.	Advanced colonic neoplasia	Diverticulitis patients (DIABOLO trial)	Median 57 [range 49, 65] 48% male	NR NR	27/401 (6.7%)	OR 0.72 (0.47, 1.11)*	0.132
				Screening individuals (COCOS trial)	Median 60 [range 55, 65] 51% male	NR NR	130/1426 (9.1%)		

Author, Year, PMID, Country, Funding	Design	Population Diverticulitis Details Family Hx CRC Setting	Outcome	Arm	Age Sex	Age ≥50, % Complicated/ Uncomplicated Diverticulitis %	n/N (%)	Effect Size	Report ed P Value
Daniels, 2015, 25472747, Netherlands, Non-industry	NRCS (Retrospective)	Primary colonoscopy screening population: randomly invited for primary colonoscopy screening and 50-75 years. Uncomplicated Diverticulitis Population: adult, CT proven uncomplicated left sided acute diverticulitis, participating in DIABOLO trial, having follow up colonoscopy within 6 months. Family history of CRC: 9.5% among diverticulitis patients and 15.3% among screening individuals. Multicenter.	Adenoma, high grade dysplasia	Diverticulitis patients (DIABOLO trial)	Median 57 [range 49, 65] 48% male	NR NR	4/401 (1.0%)	OR_0.41 (0.15, 1.17)*	0.111
				Screening individuals (COCOS trial)	Median 60 [range 55, 65] 51% male	NR NR	34/1426 (2.4%)		
Lecleire, 2014, 25083288, France, Non-industry	NRCS (Retrospective)	Group 1 patients: acute diverticulitis, underwent colonoscopy within 6 months following the acute episode. Group 2 patients: sex and age matched with a familial history of colorectal adenoma or neoplasia. Group 2 patients had a family history of colorectal adenoma or neoplasia. Multicenter.	Adenoma, high grade dysplasia	Acute diverticulitis	60.9 (12.6) 41% male	NR 10.0%/90.0%	2/404 (0.5%)	OR_0.33 (0.07, 1.64)*	
				Sex and age matched controls	60.7 (13.4) 41% male	NR NR	6/404 (1.5%)		

Author, Year, PMID, Country, Funding	Design	Population Diverticulitis Details Family Hx CRC Setting	Outcome	Arm	Age Sex	Age ≥50, % Complicated/ Uncomplicated Diverticulitis %	n/N (%)	Effect Size	Report ed P Value
Lecleire, 2014, 25083288, France, Non-industry	NRCS (Retrospective)	Group 1 patients: acute diverticulitis, underwent colonoscopy within 6 months following the acute episode. Group 2 patients: sex and age matched with a familial history of colorectal adenoma or neoplasia. Group 2 patients had a family history of colorectal adenoma or neoplasia. Multicenter.	Adenoma, villous	Acute diverticulitis	60.9 (12.6) 41% male	NR 10.0%/90.0%	3/404 (0.7%)	OR_1.00 (0.20, 4.98)*	
				Sex and age matched controls	60.7 (13.4) 41% male	NR NR	3/404 (0.7%)		
Daniels, 2015, 25472747, Netherlands, Non-industry	NRCS (Retrospective)	Primary colonoscopy screening population: randomly invited for primary colonoscopy screening and 50-75 years. Uncomplicated Diverticulitis Population: adult, CT proven uncomplicated left sided acute diverticulitis, participating in DIABOLO trial, having follow up colonoscopy within 6 months. Family history of CRC: 9.5% among diverticulitis patients and 15.3% among screening individuals. Multicenter.	Serrated polyp	Diverticulitis patients (DIABOLO trial)	Median 57 [range 49, 65] 48% male	NR NR	53/401 (13.2%)	OR_0.41 (0.30, 0.56)*	<0.001
				Screening individuals (COCOS trial)	Median 60 [range 55, 65] 51% male	NR NR	388/1426 (27.2%)		

Abbreviations: CRC = colorectal cancer, CT = computed tomography, Hx = history, NR = not reported, NRCS = nonrandomized controlled study, OR = odds ratio.

* Calculated by review team.

† The statistically significant difference in rates of advanced adenomas (P=0.036) became just nonsignificant after adjustment for age, family history of CRC, smoking, BMI, and cecal intubation (P=0.053); although, no adjusted effect size was reported.

Table D-3-3. KQ 3. Categorical outcomes, single group studies

Author, Year, PMID, Country, Funding	Design	Population Diverticulitis Details Family Hx CRC Setting	Outcome	Arm	Age Sex	Age ≥50, % Complicated/ Uncomplicated Diverticulitis %	n/N (%)
Alcantar, 2019, 31720142, USA, NR	Single group (Retrospective)	Patients between the ages of 18 and 49 years with acute diverticulitis. Family history of CRC: not reported. Single center.	Colorectal cancer	Colonoscopy	Mean 40.7 60.3% male	NR 22.5%/77.5%	0/111 (0%)
Andrade, 2017, 27941344, Portugal, NR	Single group (Retrospective)	Underwent a colonoscopy within 1 year after the conservative management of CT-proven acute diverticulitis. Family history of CRC: not reported. Single center.	Colorectal cancer	Colonoscopy	Median 55 [IQR 11.1] 49% male	NR NR	8/252 (3.2%)
Brar, 2013, 24105001, Canada, NR	Single group (Retrospective)	Successfully treated nonoperatively for acute left-sided diverticulitis, and all endoscopy reports before index admission and within 1 year after admission. Family history of CRC: not reported. Single center.	Colorectal cancer found within a year of admission	Colonoscopy	55 [range 27, 90]; 63.5% >55 49% male	63.5% 29.7%/70.3%	4/249 (1.6%) ^A
Choi, 2014, 24723071, S Korea, NR	NRCS (Retrospective)	Underwent CT, followed by colonoscopy within a year and diagnosed with acute diverticulitis. For each diverticulitis case, two age- (±5 years) and sex matched control individuals were identified from healthy individuals who underwent screening colonoscopy. Family history of CRC: 2.6% among diverticulitis patients and 3.1% among controls. Multicenter.	Colorectal cancer	Colonoscopy	48.6 (16.5) 60% male	NR 14.1%/85.9%	11/149 (7.4%)
Elmi, 2013, 23701063, USA, NR	Single group (Retrospective)	Acute diverticulitis, evaluation of the colon using colonoscopy. Family history of CRC: not reported. Single center.	Colorectal cancer	Colonoscopy	100% >49 42%	100% NR	9/402 (2.2%)
Daniels, 2015, 25472747, Netherlands, Non-industry	NRCS (Retrospective)	Primary colonoscopy screening population: randomly invited for primary colonoscopy screening and 50-75 years. Uncomplicated Diverticulitis Population: adult, CT proven uncomplicated left sided acute diverticulitis, participating in DIABOLO trial, having follow up colonoscopy within 6 months. Family history of CRC: 9.5% among diverticulitis patients and 15.3% among screening individuals. Multicenter.	Colorectal cancer	Colonoscopy	Median 57 [range 49, 65] 48% male	NR NR	5/401 (1.2%)

Author, Year, PMID, Country, Funding	Design	Population Diverticulitis Details Family Hx CRC Setting	Outcome	Arm	Age Sex	Age ≥50, % Complicated/ Uncomplicated Diverticulitis %	n/N (%)
Horesh, 2016, 27170283, Israel, NR	Single group (Retrospective)	Admitted for a first episode of acute diverticulitis diagnosed based on clinical signs and CT findings and were successfully treated conservatively. Family history of CRC: not reported. Single center.	Colorectal cancer	Colonoscopy	62.6 [range 21, 98]; 30.6% >55 45% male	30.6% 18.5%/81.5%	5/310 (1.6%)
Khoury, 2019, 30632029, Israel, NR	Single group (Retrospective)	Acute diverticulitis, patients who underwent colonoscopy in the period of 6 months following the diagnosis with acute diverticulitis, or patients who performed virtual CT colonography in the case of contraindication to colonoscopy. Family history of CRC: not reported. Single center.	Colorectal cancer	Colonoscopy	55.7 (13.8) [range 24, 93] 62% male	NR NR	17/225 (7.6%)
Lahat, 2007, 17554647, Israel, NR	RCT	Findings on CT compatible with the diagnosis of acute diverticulitis Family history of CRC: not reported. Not sure.	Colorectal cancer	Colonoscopy	60.4 33% male	NR NR	0/86 (0)
Lau, 2011, 21904141, Australia, NR	NRCS (Retrospective)	Diverticulitis confirmed by CT and had a follow up colonoscopy within 1 year from the date of CT scan. Family history of CRC: not available (claimed by the author). Multicenter.	Colorectal cancer	Colonoscopy	15-39y: 7.2%, 40-64y: 55.5%, 65+: 37.3% 53% male	NR NR	9/319 (2.8%)
Lecleire, 2014, 25083288, France, Non-industry	NRCS (Retrospective)	Group 1 patients: acute diverticulitis, underwent colonoscopy within 6 months following the acute episode. Group 2 patients: sex and age matched with a familial history of colorectal adenoma or neoplasia. Group 2 patients had a family history of colorectal adenoma or neoplasia. Multicenter.	Colorectal cancer	Colonoscopy	60.9 (12.6) 41% male	NR 10.0%/90.0%	1/404 (0.3%)
Meireles, 2015, 26378691, Portugal, NR	Single group (Retrospective)	Subjected to endoscopy following the primary episode of diverticulitis. Family history of CRC: not reported. Single center.	Colorectal cancer	Colonoscopy	64.4 (13.5) [range 23, 103] 50% male	NR 28.8%/81.2%	20/427 (4.7%)

Author, Year, PMID, Country, Funding	Design	Population Diverticulitis Details Family Hx CRC Setting	Outcome	Arm	Age Sex	Age ≥50, % Complicated/ Uncomplicated Diverticulitis %	n/N (%)
O'Donohoe, 2019, 31882879, United Kingdom, NR	Single group (Retrospective)	Patients over the age of 18 with CT-diagnosed uncomplicated left-sided diverticulitis (with a modified Hinchey classification of 0 or 1a), admitted 2014–2017, with a follow-up colonoscopy 4–6 weeks after admission. Family history of CRC: not reported. Single center.	Colorectal cancer	Colonoscopy	Median 63 (range 29, 90) 28% male	NR 0/100%	0/204 (0)
Ramphal, 2018, 29945147, Netherlands, NR	Single group (Retrospective)	Diagnosed with acute colonic diverticulitis (Hinchey 0 and 1) and offered colonoscopy to rule out CRC. Family history of CRC: among 10 identified colorectal cancer cases, 2 had a family history of CRC and 1 had a positive family history for Crohn's disease. Single center.	Colorectal cancer	Colonoscopy	59 NR	NR ^B NR	10/645 (1.6%)
Sallinen, 2014, 24178863, Finland, NR	NRCS (Retrospective)	Clinically and CT diagnosed acute diverticulitis. Family history of CRC: not reported. Single center.	Colorectal cancer	Colonoscopy	58.5 (13.9) 38% male	NR NR	9/394 (2.3%)
Schout, 2012, 23171930, Netherlands, NR	Single group (Retrospective)	Underwent radiological or surgical abscess drainage only without colon resection. Family history of CRC: not reported. Single center.	Colorectal cancer	Colonoscopy	NR NR	NR NR	8/422 (1.9%)
Seoane Urgorri, 2018, 29900742, Spain, NR	Single group (Retrospective)	Colonoscopy performed after CT-confirmed diagnosis of acute diverticulitis. Family history of CRC: not reported. Single center.	Colorectal cancer	Colonoscopy	59 (15) 48% male	NR 27.0%/73.0%	2/216 (0.9%)
Soh, 2018, 29663068, Singapore, NR	NRCS (Retrospective)	First episode of CT-proven acute diverticulitis with no complications. Family history of CRC: not reported. Single center.	Colorectal cancer	Colonoscopy	50.9 [range 18, 96] 52% male	NR 10.0%/90.0%	2/135 (1.5%)
Studniarek, 2019, 31908222, USA, NR	Single group (Retrospective)	A history of acute diverticulitis as the indication for the colonoscopy, and colonoscopy performed within one year from the initial diagnosis of diverticulitis. Family history of CRC: not reported. Multicenter.	Colorectal cancer	Colonoscopy	Median 53 (range 22, 88) 51% male	NR NR	9/584 (1.5%)

Author, Year, PMID, Country, Funding	Design	Population Diverticulitis Details Family Hx CRC Setting	Outcome	Arm	Age Sex	Age ≥50, % Complicated/ Uncomplicated Diverticulitis %	n/N (%)
Suhardja, 2017, 28035461, Australia, NR	Single group (Retrospective)	Diagnosed with acute colonic diverticulitis on CT scan and received follow-up colonoscopy. Family history of CRC: not reported. Single center.	Colorectal cancer	Colonoscopy	59.3 46% male	NR 27.4%/72.6%	5/270 (1.9%)
Daniels, 2015, 25472747, Netherlands, Non-industry	NRCS (Retrospective)	Primary colonoscopy screening population: randomly invited for primary colonoscopy screening and 50-75 years. Uncomplicated Diverticulitis Population: adult, CT proven uncomplicated left sided acute diverticulitis, participating in DIABOLO trial, having follow up colonoscopy within 6 months. Family history of CRC: 9.5% among diverticulitis patients and 15.3% among screening individuals. Multicenter.	Adenoma ≥10 mm	Colonoscopy	Median 57 [range 49, 65] 48% male	NR NR	10/401 (2.5%)
Lahat, 2007, 17554647, Israel, NR	RCT	Findings on CT compatible with the diagnosis of acute diverticulitis. Family history of CRC: not reported. Not sure.	Adenoma ≥10 mm	Colonoscopy	60.4 33% male	NR NR	2/86 (2.3%)
Lau, 2011, 21904141, Australia, NR	NRCS (Retrospective)	Diverticulitis confirmed by CT and had a follow up colonoscopy within 1 year from the date of CT scan. Family history of CRC: not available (claimed by the author). Multicenter.	Adenoma ≥10 mm	Colonoscopy	15-39 y: 7.2%, 40-64 y: 55.5%, 65+: 37.3% 53% male	NR NR	9/319 (2.6%)
Lecleire, 2014, 25083288, France, Non-industry	NRCS (Retrospective)	Group 1 patients: acute diverticulitis, underwent colonoscopy within 6 months following the acute episode. Group 2 patients: sex and age matched with a familial history of colorectal adenoma or neoplasia. Group 2 patients had a family history of colorectal adenoma or neoplasia. Multicenter.	Adenoma ≥10 mm	Colonoscopy	60.9 (12.6) 41% male	NR 10.0%/90.0%	9/404 (2.2%)
Andrade, 2017, 27941344, Portugal, NR	Single group (Retrospective)	Underwent a colonoscopy within 1 year after the conservative management of CT-proven acute diverticulitis. Family history of CRC: not reported. Single center.	Advanced adenomas	Colonoscopy	Median 55 [IQR 11.1] 49% male	NR NR	13/252 (5.1%)

Author, Year, PMID, Country, Funding	Design	Population Diverticulitis Details Family Hx CRC Setting	Outcome	Arm	Age Sex	Age ≥50, % Complicated/ Uncomplicated Diverticulitis %	n/N (%)
Brar, 2013, 24105001, Canada, NR	Single group (Retrospective)	Successfully treated nonoperatively for acute left-sided diverticulitis, and all endoscopy reports before index admission and within 1 year after admission. Family history of CRC: not reported. Single center.	Advanced adenomas ^c	Colonoscopy	55 [range 27, 90]; 63.5% >55 49% male	63.5% 29.7%/70.3%	19/249 (7.6%)
Choi, 2014, 24723071, S Korea, NR	NRCS (Retrospective)	Underwent CT, followed by colonoscopy within a year and diagnosed with acute diverticulitis. For each diverticulitis case, two age- (±5 years) and sex matched control individuals were identified from healthy individuals who underwent screening colonoscopy. Family history of CRC: 2.6% among diverticulitis patients and 3.1% among controls. Multicenter.	Advanced adenoma	Colonoscopy	48.6 (16.5) 60% male	NR 14.1%/85.9%	5/149 (3.4%)
Lecleire, 2014, 25083288, France, Non-industry	NRCS (Retrospective)	Group 1 patients: acute diverticulitis, underwent colonoscopy within 6 months following the acute episode. Group 2 patients: sex and age matched with a familial history of colorectal adenoma or neoplasia. Group 2 patients had a family history of colorectal adenoma or neoplasia. Multicenter.	Advanced adenoma	Colonoscopy	60.9 (12.6) 41% male	NR 10.0%/90.0%	11/404 (2.7%)
Seoane Urgorri, 2018, 29900742, Spain, NR	Single group (Retrospective)	Colonoscopy performed after CT-confirmed diagnosis of acute diverticulitis. Family history of CRC: not reported. Single center.	Advanced adenoma	Colonoscopy	59 (15) 48% male	NR 27.0%/73.0%	10/216 (4.6%)
Soh, 2018, 29663068, Singapore, NR	NRCS (Retrospective)	First episode of CT-proven acute diverticulitis with no complications. Family history of CRC: not reported. Single center.	Advanced adenoma	Colonoscopy	50.9 [range 18, 96] 52% male	NR 0%/100%	2/135 (1.5%)
Studniarek, 2019, 31908222, USA, NR	Single group (Retrospective)	A history of acute diverticulitis as the indication for the colonoscopy, and colonoscopy performed within one year from the initial diagnosis of diverticulitis. Family history of CRC: not reported. Multicenter.	Advanced adenoma ^c	Colonoscopy	Median 53 (range 22, 88) 51% male	NR NR	32/584 (5.4%)

Author, Year, PMID, Country, Funding	Design	Population Diverticulitis Details Family Hx CRC Setting	Outcome	Arm	Age Sex	Age ≥50, % Complicated/ Uncomplicated Diverticulitis %	n/N (%)
Suhardja, 2017, 28035461, Australia, NR	Single group (Retrospective)	Diagnosed with acute colonic diverticulitis on CT scan and received follow-up colonoscopy. Family history of CRC: not reported. Single center.	Advanced adenoma	Colonoscopy	59.3 46% male	NR 27.4%/72.6%	8/270 (3.0%)
Choi, 2014, 24723071, S Korea, NR	NRCS (Retrospective)	Underwent CT, followed by colonoscopy within a year and diagnosed with acute diverticulitis. For each diverticulitis case, two age- (±5 years) and sex matched control individuals were identified from healthy individuals who underwent screening colonoscopy. Family history of CRC: 2.6% among diverticulitis patients and 3.1% among controls. Multicenter.	Advanced colonic neoplasia	Colonoscopy	48.6 (16.5) 60% male	NR 14.1%/85.9%	16/149 (10.7%)
Daniels, 2015, 25472747, Netherlands, Non-industry	NRCS (Retrospective)	Primary colonoscopy screening population: randomly invited for primary colonoscopy screening and 50-75 years. Uncomplicated Diverticulitis Population: adult, CT proven uncomplicated left sided acute diverticulitis, participating in DIABOLO trial, having follow up colonoscopy within 6 months. Family history of CRC: 9.5% among diverticulitis patients and 15.3% among screening individuals. Multicenter.	Advanced colonic neoplasia	Colonoscopy	Median 57 [range 49, 65] 48% male	NR NR	27/401 (6.7%)
Seoane Urgorri, 2018, 29900742, Spain, NR	Single group (Retrospective)	Colonoscopy performed after CT-confirmed diagnosis of acute diverticulitis. Family history of CRC: not reported. Single center.	Advanced colonic neoplasia	Colonoscopy	59 (15) 48% male	NR 27.0%/73.0%	12/216 (5.5%)
Daniels, 2015, 25472747, Netherlands, Non-industry	NRCS (Retrospective)	Primary colonoscopy screening population: randomly invited for primary colonoscopy screening and 50-75 years. Uncomplicated Diverticulitis Population: adult, CT proven uncomplicated left sided acute diverticulitis, participating in DIABOLO trial, having follow up colonoscopy within 6 months. Family history of CRC: 9.5% among diverticulitis patients and 15.3% among screening individuals. Multicenter.	Adenoma, high grade dysplasia	Colonoscopy	Median 57 [range 49, 65] 48% male	NR NR	4/401 (1.0%)

Author, Year, PMID, Country, Funding	Design	Population Diverticulitis Details Family Hx CRC Setting	Outcome	Arm	Age Sex	Age ≥50, % Complicated/ Uncomplicated Diverticulitis %	n/N (%)
Lau, 2011, 21904141, Australia, NR	NRCS (Retrospective)	Diverticulitis confirmed by CT and had a follow up colonoscopy within 1 year from the date of CT scan. Family history of CRC: not available (claimed by the author). Multicenter.	Adenoma, high grade dysplasia	Colonoscopy	15-39y: 7.2%, 40-64y: 55.5%, 65+: 37.3% 53% male	NR NR	0/319 (0)
Lecleire, 2014, 25083288, France, Non-industry	NRCS (Retrospective)	Group 1 patients: acute diverticulitis, underwent colonoscopy within 6 months following the acute episode. Group 2 patients: sex and age matched with a familial history of colorectal adenoma or neoplasia. Group 2 patients had a family history of colorectal adenoma or neoplasia. Multicenter.	Adenoma, high grade dysplasia	Colonoscopy	60.9 (12.6) 41% male	NR 10.0%/90.0%	2/404 (0.5%)
Meireles, 2015, 26378691, Portugal, NR	Single group (Retrospective)	Subjected to endoscopy following the primary episode of diverticulitis. Family history of CRC: not reported. Single center.	Adenoma, high grade dysplasia	Colonoscopy	64.4 (13.5) [range 23, 103] 50% male	NR 28.8%/81.2%	28/427 (6.6%)
Sallinen, 2014, 24178863, Finland, NR	NRCS (Retrospective)	Clinically and CT diagnosed acute diverticulitis. Family history of CRC: not reported. Single center.	Adenoma, high grade dysplasia	Colonoscopy	58.5 (13.9) 38% male	NR NR	4/394 (1.0%)
Suhardja, 2017, 28035461, Australia, NR	Single group (Retrospective)	Diagnosed with acute colonic diverticulitis on CT scan and received follow-up colonoscopy. Family history of CRC: not reported. Single center.	Adenoma, moderate-/high-grade dysplasia	Colonoscopy	59.3 46% male	NR 27.4%/72.6%	8/270 (3.0%)
Lau, 2011, 21904141, Australia, NR	NRCS (Retrospective)	Diverticulitis confirmed by CT and had a follow up colonoscopy within 1 year from the date of CT scan. Family history of CRC: not available (claimed by the author). Multicenter.	Moderately differentiated adenocarcinoma	Colonoscopy	15-39y: 7.2%, 40-64y: 55.5%, 65+: 37.3% 53% male	NR NR	1/319 (0.3%)

Author, Year, PMID, Country, Funding	Design	Population Diverticulitis Details Family Hx CRC Setting	Outcome	Arm	Age Sex	Age ≥50, % Complicated/ Uncomplicated Diverticulitis %	n/N (%)
Daniels, 2015, 25472747, Netherlands, Non-industry	NRCS (Retrospective)	Primary colonoscopy screening population: randomly invited for primary colonoscopy screening and 50-75 years. Uncomplicated Diverticulitis Population: adult, CT proven uncomplicated left sided acute diverticulitis, participating in DIABOLO trial, having follow up colonoscopy within 6 months. Family history of CRC: 9.5% among diverticulitis patients and 15.3% among screening individuals. Multicenter.	Serrated polyp	Colonoscopy	Median 57 [range 49, 65] 48% male	NR NR	53/401 (13.2%)
Seoane Urgorri, 2018, 29900742, Spain, NR	Single group (Retrospective)	Colonoscopy performed after CT-confirmed diagnosis of acute diverticulitis. Family history of CRC: not reported. Single center.	Serrated polyp	Colonoscopy	59 (15) 48% male	NR 27.0%/73.0%	2/216 (0.9%)

Abbreviations: CRC = colorectal cancer, CT = computed tomography, Hx = history, NR = not reported, NRCS = nonrandomized controlled study, OR = odds ratio, RCT = randomized controlled trial..

- ^A No colorectal cancer was found beyond 1 year of admission.
^B Mean age of patients who had colon cancer 68 years (range, 42 to 94).
^C Included patients with serrated polyps among those with advanced adenoma.

Table D-3-4. KQ 3. Categorical outcomes, subgroup analysis: Age ≥50 vs. age <50

Author, Year, PMID, Country, Funding	Outcome	Subgroup	n/N (%)	Effect Size Between Subgroups	Reported P Value
Brar, 2013, 24105001, Canada, NR	Colorectal cancer found within a year of admission	Colonoscopy among patients age ≥50	4/158 (2.5%)	OR 5.32 (0.28, 99.9)*	
		Colonoscopy among patients age <50	0/91 (0)		
Choi, 2014, 24723071, S Korea, NR	Colorectal cancer	Colonoscopy among patients age ≥50	11/82 (13.4%)	OR 25.27 (1.46, 437)*	
		Colonoscopy among patients age <50	0/78 (0)		
Horesh, 2016, 27170283, Israel, NR	Colorectal cancer	Colonoscopy among patients age ≥50	4/215 (1.9%)	OR 1.78 (0.20, 16.2)*	
		Colonoscopy among patients age <50	1/95 (1.1%)		
Meireles, 2015, 26378691, Portugal, NR	Colorectal cancer	Colonoscopy among patients age >50	17/342 (5.0%)	OR 1.15 (0.33, 4.04)*	
		Colonoscopy among patients age <50	3/69 (4.3%)		
Andrade, 2017, 27941344, Portugal, NR	Advanced colonic neoplasia	Colonoscopy among patients age ≥50	NR	OR 8.12 (2.46, 45.1)	0.017
		Colonoscopy among patients age <50	NR		
Seoane Urgorri, 2018, 29900742, Spain, NR	Advanced colonic neoplasia	Colonoscopy among patients age >50	7.8%		0.02
		Colonoscopy among patients age ≤50	0		
Choi, 2014, 24723071, S Korea, NR	Advanced colonic neoplasia	Colonoscopy among patients age ≥50	14/71 (19.7%)	OR 9.13 (1.97, 42.3)	0.005
		Colonoscopy among patients age <50	2/78 (2.6%)		
Brar, 2013, 24105001, Canada, NR	Advanced adenomas †	Colonoscopy among patients age ≥50	16/158 (10.1%)	OR 3.31 (0.94, 11.7)*	
		Colonoscopy among patients age <50	3/91 (3.3%)		
Choi, 2014, 24723071, S Korea, NR	Advanced adenomas	Colonoscopy among patients age ≥50	3/71 (4.2%)	OR 1.68 (0.27, 10.3)	
		Colonoscopy among patients age <50	2/78 (2.6%)		

* Calculated by review team.

† Included serrated adenomas.

Table D-3-5. KQ 3. Subgroup analysis: Complicated vs. uncomplicated diverticulitis

Author, Year, PMID, Country, Funding	Outcome	Subgroup	n/N (%)	Effect Size Between Subgroups	Report ed P Value
Andrade, 2017, 27941344, Portugal, NR	Colorectal cancer	Colonoscopy among patients with Hinchey \geq Ib	7/43 (16.3%)	OR 40.44 (4.83, 339)*	<0.001
		Colonoscopy among patients with Hinchey Ia	1/209 (0.5%)		
Brar, 2013, 24105001, Canada, NR	Colorectal cancer found within a year of admission	Colonoscopy among patients with complicated diverticulitis	4/74 (5.4%)	OR 22.50 (1.20, 424)*	
		Colonoscopy among patients with uncomplicated diverticulitis	0/175 (0)		
Choi, 2014, 24723071, S Korea, NR	Colorectal cancer	Colonoscopy among patients with complicated diverticulitis	3/21 (14.3%)	OR 2.50 (0.61, 10.3)	0.188
		Colonoscopy among patients with uncomplicated diverticulitis	8/128 (6.3%)		
Elmi, 2013, 23701063, USA, NR	Colorectal cancer	Colonoscopy among patients with abscess	NR	OR 4.67 (1.12, 19.4)	
		Colonoscopy among patients with no abscess	NR		
Meireles, 2015, 26378691, Portugal, NR	Colorectal cancer	Colonoscopy among patients with complicated diverticulitis	8/80 (10.0%)	OR 3.10 (1.22, 7.86)*	
		Colonoscopy among patients with uncomplicated diverticulitis	12/347 (3.5%)		
Suhardja, 2017, 28035461, Australia, NR	Colorectal cancer	Colonoscopy among patients with complicated diverticulitis	4/74 (5.4%)	OR 11.14 (1.22, 101)*	
		Colonoscopy among patients with uncomplicated diverticulitis	1/196 (0.5%)		
Seoane Urgorri, 2018, 29900742, Spain, NR	Colorectal cancer	Colonoscopy among patients with complicated diverticulitis	2/60 (3.3)	OR 13.45 (0.64, 284)*	0.07
		Colonoscopy among patients with uncomplicated diverticulitis	0/156 (0)		
Alcantar, 2019, 31720142, USA, NR	Colorectal cancer	Colonoscopy among patients with complicated diverticulitis	0/25 (0)		
		Colonoscopy among patients with uncomplicated diverticulitis	0/86 (0)		

Author, Year, PMID, Country, Funding	Outcome	Subgroup	n/N (%)	Effect Size Between Subgroups	Report ed P Value
Andrade, 2017, 27941344, Portugal, NR	Advanced adenoma	Colonoscopy among patients with Hinchey ≥Ib	2/43 (4.7%)	OR 0.88 (0.19, 4.11)*	0.74
		Colonoscopy among patients with Hinchey Ia	11/209 (5.3%)		
Choi, 2014, 24723071, S Korea, NR	Advanced adenoma	Colonoscopy among patients with complicated diverticulitis	1/21 (4.8%)	OR 1.55 (0.16, 14.6)*	0.537
		Colonoscopy among patients with uncomplicated diverticulitis	4/128 (3.1%)		
Seoane Urgorri, 2018, 29900742, Spain, NR	Advanced adenoma	Colonoscopy among patients with complicated diverticulitis	5/60 (8.6%)	OR 2.75 (0.77, 9.85)*	0.1
		Colonoscopy among patients with uncomplicated diverticulitis	5/156 (3.2%)		
Suhardja, 2017, 28035461, Australia, NR	Advanced adenoma	Colonoscopy among patients with complicated diverticulitis	4/74 (5.4%)	OR 2.74 (0.67, 11.3)*	
		Colonoscopy among patients with uncomplicated diverticulitis	4/196 (2.0%)		
Andrade, 2017, 27941344, Portugal, NR	Advanced colonic neoplasia	Colonoscopy among patients with Hinchey ≥Ib	9/43 (20.9%)	OR 3.37 (1.55, 13.5)	0.035
		Colonoscopy among patients with Hinchey Ia	12/209 (5.7%)		
Brar, 2013, 24105001, Canada, NR	Advanced colonic neoplasia	Abscess	14/74 (18.9%)	OR 4.15 (1.68, 10.3)*	0.002
		No abscess	9/175 (5.1%)		
Choi, 2014, 24723071, S Korea, NR	Advanced colonic neoplasia	Colonoscopy among patients with complicated diverticulitis	4/21 (19.0%)	OR 3.53 (0.96, 13.0)*	0.245
		Colonoscopy among patients with uncomplicated diverticulitis	12/128 (9.4%)		
Seoane Urgorri, 2018, 29900742, Spain, NR	Advanced colonic neoplasia	Colonoscopy among patients with complicated diverticulitis	7/60 (11.7%)	OR 3.99 (1.21, 13.1)*	0.02
		Colonoscopy among patients with uncomplicated diverticulitis	5/156 (3.2%)		

Author, Year, PMID, Country, Funding	Outcome	Subgroup	n/N (%)	Effect Size Between Subgroups	Report ed P Value
Meireles, 2015, 26378691, Portugal, NR	Adenoma, high grade dysplasia	Colonoscopy among patients with complicated diverticulitis	9/80 (11.3%)	OR 2.19 (0.95, 5.04)*	
		Colonoscopy among patients with uncomplicated diverticulitis	19/347 (5.5%)		
Suhardja, 2017, 28035461, Australia, NR	Adenoma, moderate-/high-grade dysplasia	Colonoscopy among patients with complicated diverticulitis	4/74 (5.4%)	OR 2.74 (0.67, 11.3)*	
		Colonoscopy among patients with uncomplicated diverticulitis	4/196 (2.0%)		
Suhardja, 2017, 28035461, Australia, NR	Higher risk adenomas	Colonoscopy among patients with complicated diverticulitis	8/74 (10.8%)	OR 4.63 (1.46, 14.7)*	
		Colonoscopy among patients with uncomplicated diverticulitis	5/196 (2.6%)		

* Calculated by review team

Table D-3-6. KQ 3. Categorical outcomes, subgroup analysis: Others

Author, Year, PMID, Country, Funding	Outcome	Subgroup	n/N (%)	Effect Size Between Subgroups	Report ed P Value
Choi, 2014, 24723071, S Korea, NR	Colorectal cancer	Diverticulitis on the left side of colon	2/23 (8.7%)	OR 1.24 (0.25, 6.13)*	0.679
		Diverticulitis on the right side of colon	9/126 (7.1%)		
Soh, 2018, 29663068, Singapore, NR	Colorectal cancer	Diverticulitis on the left side of colon	2/54 (3.7%)	OR 3.38 (0.47, 24.6)*	
		Diverticulitis on the right side of colon	2/278 (1.1)		
Elmi, 2013, 23701063, USA, NR	Colorectal cancer	Colonoscopy among female patients	7/235 (3.0%)	OR 2.53 (0.52, 12.5)*	0.041
		Colonoscopy among male patients	2/167 (1.2%)		
Choi, 2014, 24723071, S Korea, NR	Colorectal cancer	Colonoscopy among female patients	NR	OR 1.08 (0.35, 3.34)*	
		Colonoscopy among male patients	NR		
Ramphal, 2018, 29945147, Netherlands, NR	Colorectal cancer	Patients with alarm symptoms	9/205 (4.4%)	OR 20.2 (2.54, 160)*	0.0002
		Patients with no alarm symptoms	1/440 (0.2%)		
Choi, 2014, 24723071, S Korea, NR	Advanced adenoma	Diverticulitis on the left side of colon	1/23 (4.3%)	OR 1.39 (0.15, 13.0)*	0.052
		Diverticulitis on the right side of colon	4/126 (3.2%)		
Choi, 2014, 24723071, S Korea, NR	Advanced colonic neoplasia	Diverticulitis on the left side of colon	3/23 (13.0%)	OR 1.30 (0.34, 4.99)*	0.715
		Diverticulitis on the right side of colon	13/126 (10.3%)		
Brar, 2013, 24105001, Canada, NR	Advanced colonic neoplasia	Anemia	NR	OR 0.78 (0.24, 2.57)	0.69
		No anemia	NR		
Brar, 2013, 24105001, Canada, NR	Advanced colonic neoplasia	Previous attack of diverticulitis	NR	OR 2.28, (0.76, 7.46)	0.14
		No previous attack of diverticulitis	NR		

* Calculated by review team.

Table D-3-7. KQ 3. Colonoscopy tolerance, feasibility, and completion of procedure; technical adequacy

Author, Year, PMID, Country, Funding	Design	Outcome	Arm/Subgroup	n/N (%)	Effect Size	Reported P Value
Lau, 2011, 21904141, Australia, NR	NRCS (Retrospective)	Perforation	Colonoscopy	0/319 (0)		
Lahat, 2007, 17554647, Israel, NR	RCT	Procedural complication	Colonoscopy (late, 6 weeks later)	0/41 (0)		
			Colonoscopy (early; in-hospital colonoscopy)	0/45 (0)		
O'Donohoe, 2019, 31882879, United Kingdom, NR	Single group (Retrospective)	Procedural complication	Colonoscopy	0/204 (0)		
Lahat, 2007, 17554647, Israel, NR	RCT	Failed/incomplete procedure	Colonoscopy (late, 6 weeks later)	3/41 (7.3%)	OR 0.37 (0.09, 1.48)*	NS
			Colonoscopy (early; in-hospital colonoscopy)	8/45 (17.8%)		
Andrade, 2017, 27941344, Portugal, NR	Single group (Retrospective)	Failed/incomplete procedure	Colonoscopy	9/261 (3.4%)		
Suhardja, 2017, 28035461, Australia, NR	Single group (Retrospective)	Failed/incomplete procedure	Colonoscopy (all)	10/270 (3.7%)		
			Colonoscopy among patients with complicated diverticulitis	2/74 (2.7%)	OR 9.65 (0.14, 3.15)*	
			Colonoscopy among patients with uncomplicated diverticulitis	8/196 (4.1%)		
Lahat, 2007, 17554647, Israel, NR	RCT	No show for the colonoscopy	Colonoscopy (late, 6 weeks later)	10/41 (24.4%)	OR 4.52 (1.15, 17.8)*	0.033
			Colonoscopy (early; in-hospital colonoscopy)	3/45 (6.7%)		
Lahat, 2007, 17554647, Israel, NR	RCT	No show or incomplete exam	Colonoscopy (late, 6 weeks later)	13/41 (31.7%)	OR 1.44 (0.56, 3.70)*	
			Colonoscopy (early; in-hospital colonoscopy)	11/45 (24.4%)		

* Calculated by review team.

Key Questions 4a-b (Prevention, Nonsurgical)

Table D-4ab-1: KQ 4ab Categorical Outcomes

Study, Year, PMID	Outcome	Time	Arm	Subgroup	n/N (%)	Effect Size (95% CI), Adjusted	P Value, Adjusted	Effect Size (95% CI), Unadjusted	P Value, Unadjusted
Kvasnovsky, 2017, 28528364	No recurrence		Probiotics Symprove	All	NR (4)			HR 0.12 (0.01, 0.97)	
			Placebo	All	NR (32)				
Parente, 2013, 23754545	Recurrence of diverticulitis	2 yr	5-ASA	All	6/45 (13.3)			OR 0.40 (0.14, 1.17)	>0.05
			Placebo	All	13/47 (27.7)				
Lanas, 2013, 23092785	Recurrence of diverticulitis		Pharm Rifaximin	All	8/77 (10.4)	OR 0.31* (0.11, 0.86)	0.025		
			Placebo	All	17/88 (19.3)				
Lanas, 2013, 23092785	Hospitalization (or re-hospitalization) for diverticulitis		Pharm Rifaximin	All	2/77 (3)			OR 0.36 (0.07, 1.86)	
			Placebo	All	6/88 (7)				
Tursi, 2002, 12236485	Mortality - All-cause	12 mo	Rifaximin	All	1/109 (0.9)			OR 1.00 (0.06, 16.19)	
			5-ASA + Rifaximin	All	1/109 (0.9)				
Tursi, 2002, 12236485	Recurrence of diverticulitis	12 mo	5-ASA + Rifaximin	All	3/109 (2.75)			OR 0.13 (0.04, 0.44)	<0.01
			Rifaximin	All	20/109 (17.98)				
Tursi, 2002, 12236485	Resolution of diverticulitis symptoms	3 mo	5-ASA + Rifaximin	All	44/109 (40.36)			OR 3.21 (1.72, 5.99)	<0.005
			Rifaximin	All	19/109 (17.43)				
Tursi, 2002, 12236485	Resolution of diverticulitis symptoms	6 mo	5-ASA + Rifaximin	All	68/109 (62.96)			OR 4.17 (2.36, 7.37)	<0.001
			Rifaximin	All	31/109 (29.80)				

Study, Year, PMID	Outcome	Time	Arm	Subgroup	n/N (%)	Effect Size (95% CI), Adjusted	P Value, Adjusted	Effect Size (95% CI), Unadjusted	P Value, Unadjusted
Tursi, 2002, 12236485	Resolution of diverticulitis symptoms	9 mo	5-ASA + Rifaximin	All	79/109 (73.83)			OR 4.92 (2.77, 8.75)	<0.0001
			Rifaximin	All	38/109 (39.27)				
Tursi, 2002, 12236485	Resolution of diverticulitis symptoms	12 mo	5-ASA + Rifaximin	All	89/109 (85.57)			OR 6.57 (3.54, 12.2)	<0.0005
			Rifaximin	All	44/109 (49.43)				
Tursi, 2002, 12236485	Return to normal bowel function	3 mo	5-ASA + Rifaximin	All	42/109 (38.53)			OR 2.97 (1.59, 5.56)	<0.005
			Rifaximin	All	19/109 (17.43)				
Tursi, 2002, 12236485	Return to normal bowel function	6 mo	5-ASA + Rifaximin	All	57/109 (52.77)			OR 2.52 (1.45, 4.40)	<0.001
			Rifaximin	All	33/109 (31.73)				
Tursi, 2002, 12236485	Return to normal bowel function	9 mo	5-ASA + Rifaximin	All	71/109 (66.35)			OR 2.56 (1.48, 4.42)	<0.001
			Rifaximin	All	46/109 (47.42)				
Tursi, 2002, 12236485	Return to normal bowel function	12 mo	5-ASA + Rifaximin	All	82/109 (78.85)			OR 3.21 (1.81, 5.70)	<0.001
			Rifaximin	All	53/109 (59.55)				
Tursi, 2007, 17390144	Recurrence of diverticulitis	12 mo	5-ASA + Probiotic	All	3/15 (20.0)			OR 0.38 (0.07, 1.92)	
			Probiotics	All	6/15 (46.7)				
Raskin, 2014, 25038431, PREVENT1	No recurrence	104 wk	5-ASA (1.2 g/d)	All	89/143 (62.2)		0.780 (vs. placebo)	OR 0.90 (0.56, 1.46)	
			5-ASA (2.4 g/d)	All	90/143 (62.9)		0.741 (vs. placebo)	OR 0.93 (0.58, 1.50)	
			5-ASA (4.8 g/d)	All	79/150 (52.7)		0.047 (vs. placebo)	OR 0.61 (0.38, 0.97)	
			Placebo	All	95/147 (64.6)				

Study, Year, PMID	Outcome	Time	Arm	Subgroup	n/N (%)	Effect Size (95% CI), Adjusted	P Value, Adjusted	Effect Size (95% CI), Unadjusted	P Value, Unadjusted
Raskin, 2014, 25038431, PREVENT2	Without recurrence	104 wk	5-ASA (1.2 g/d)	All	93/148 (62.8)		0.368 (vs. placebo)	OR 0.81 (0.50, 1.32)	
			5-ASA (2.4 g/d)	All	87/147 (59.2)		0.159 (vs. placebo)	OR 0.69 (0.43, 1.12)	
			5-ASA (4.8 g/d)	All	103/149 (69.1)		0.778 (vs. placebo)	OR 1.07 (0.65, 1.76)	
			Placebo	All	96/142 (67.7)				
Mizuki, 2019, 31043657	Recurrence of diverticulitis		Burdock tea	All	5/47 (10.6)			OR 0.26 (0.08, 0.78)	0.013
			No intervention (non-placebo)	All	14/44 (31.8)				
Kruis, 2017, 28543263, SAG-37	Without recurrence	48 wk	5-ASA (3.0 g/d)	All	112/165 (67.9)			OR 0.73 (0.45, 1.17)	0.226
			Placebo	All	125/168 (74.4)				
Kruis, 2017, 28543263, SAG-37	Without recurrence	48 wk	5-ASA (3.0 g/d)	1 episode	61/92 (66.3)			OR 0.55 (0.29, 1.07)	
			Placebo	1 episode	71/91 (78)				
Kruis, 2017, 28543263, SAG-37	Without recurrence	48 wk	5-ASA (3.0 g/d)	>1 episode	51/73 (69.9)			OR 0.94 (0.47, 1.91)	
			Placebo	>1 episode	54/76 (71.1)				
Kruis, 2017, 28543263, SAG-37	Recurrence of diverticulitis	48 wk	5-ASA (3.0 g/d)	All	31/165 (18.8)			HR 0.60 (0.34, 1.05)	
			Placebo	All	20/168 (11.9)				
Kruis, 2017, 28543263, SAG-51	Without recurrence	48 wk	Pharm 5-ASA (1.5 g/d)	All	40/87 (46)			OR 0.62 (0.33, 1.13) vs. placebo	
			Pharm 5-ASA (3.0 g/d)	All	39/75 (52)			OR 0.78 (0.42, 1.48) vs. placebo	
			Placebo	All	47/81 (58)				

Study, Year, PMID	Outcome	Time	Arm	Subgroup	n/N (%)	Effect Size (95% CI), Adjusted	P Value, Adjusted	Effect Size (95% CI), Unadjusted	P Value, Unadjusted
Kruis, 2017, 28543263, SAG-51	Without recurrence	96 wk	Pharm 5-ASA (1.5 g/d)	All	4/58 (6.9)			OR 0.25 (0.07, 0.82) vs. placebo	
			Pharm 5-ASA (3.0 g/d)	All	5/51 (9.8)			OR 0.36 (0.12, 1.12) vs. placebo	
			Placebo	All	12/52 (23.1)				
Kruis, 2017, 28543263, SAG-51	Without recurrence	48 wk	Pharm 5-ASA (1.5 g/d)	1 episode	26/47 (55.3)			OR 0.80 (0.33, 1.99) vs. placebo	
			Pharm 5-ASA (3.0 g/d)	1 episode	21/38 (55.3)			OR 0.80 (0.31, 2.07) vs. placebo	
			Placebo	1 episode	20/33 (60.6)				
Kruis, 2017, 28543263, SAG-51	Without recurrence	48 wk	Pharm 5-ASA (1.5 g/d)	>1 episode	14/40 (35)			OR 0.42 (0.18, 0.99) vs. placebo	
			Pharm 5-ASA (3.0 g/d)	>1 episode	18/37 (48.6)			OR 0.74 (0.31, 1.74) vs. placebo	
			Placebo	>1 episode	27/48 (56.3)				
Kruis, 2017, 28543263, SAG-51	Recurrence of diverticulitis	48 wk	Pharm 5-ASA (1.5 g/d)	All	15/87 (17.2)			OR 0.78 (0.36, 1.70) vs. placebo	
			Pharm 5-ASA (3.0 g/d)	All	15/75 (20)			OR 0.94 (0.43, 2.05) vs. placebo	
			Placebo	All	17/81 (21)				
Stollman, 2013, 23426454, DIVA	Recurrence of diverticulitis	52 wk	5-ASA (2.4 g/d) + probiotics (1/day)	All	10/27 (37)			OR 1.31 (0.43, 3.96) vs. placebo	
			5-ASA (2.4 g/d)	All	9/32 (28.1)			OR 0.87 (0.29, 2.62) vs. placebo	
			Placebo	All	9/29 (31)				

Study, Year, PMID	Outcome	Time	Arm	Subgroup	n/N (%)	Effect Size (95% CI), Adjusted	P Value, Adjusted	Effect Size (95% CI), Unadjusted	P Value, Unadjusted
Stollman, 2013, 23426454, DIVA	Surgery for diverticulitis	52 wk	5-ASA (2.4 g/d) + probiotics (1/day)	All	0/36 (0)				
			5-ASA (2.4 g/d)	All	2/40 (5)				
			Placebo	All	1/41 (2.4)				
Stollman, 2013, 23426454, DIVA	GSS response (0-1 on all 10 components of GSS)	52 wk	5-ASA (2.4 g/d) + probiotics (1/day)	All	29.2% (N<27)				
			5-ASA (2.4 g/d)	All	66.7% (N<32)				
			Placebo	All	50% (N<29)				
Stollman, 2013, 23426454, DIVA	Complete GSS response (0 on all components)	52 wk	5-ASA (2.4 g/d) + probiotics (1/day)	All	8.3% (N<27)				0.0452 (all)
			5-ASA (2.4 g/d)	All	40.7% (N<32)				
			Placebo	All	18.2% (N<29)				
Festa, 2017, 28387885	Recurrence of diverticulitis	15 mo	5-ASA	All	14/52 (26.9)	HR 0.27 (0.10, 0.72)			
			Rifaximin	All	7/72 (9.7)				
Festa, 2017, 28387885	Surgery for diverticulitis, including colostomy	15 mo	5-ASA	All	2/52 (4)				
			Rifaximin	All	2/72 (3)				

* Adjusted for age, sex, duration and localization of illness, time from last episode, and center recruitment rate.

Table D-4ab-2. KQ 4ab. Continuous outcomes

Study, Year, PMID	Outcome	Time	Arm	Subgroup	N	Result	Effect Size (95% CI), Adjusted	P Value, Adjusted	Effect Size (95% CI), Unadjusted	P Value, Unadjusted
Parente, 2013, 23754545	Physical condition*	2 yr	5-ASA	All	45	Mean 5.4 SD 2.7			-2.9 (-5.4, -0.4)	0.022
			Placebo	All	47	Mean 8.3 SD 5.7				
Parente, 2013, 23754545	Time to recurrence (days)	2 yr	5-ASA	All	45	Mean 219 SD 180			-151 (-366, 65)	0.17
			Placebo	All	47	Mean 369.8 SD 226.9				
Mizuki, 2019, 31043657	Acute colonic diverticulitis-free time (months)		Burdock tea	All	44	Mean 59.3			14.2 (3.1, 25.3)	0.012
			No intervention (non-placebo)	All	44	Mean 45.1				
Kruis, 2017, 28543263, SAG-51	Time to recurrence (days)	48 wk	Pharm 5-ASA (1.5 g/d)	All	NR	Mean 116 SD 134			HR 0.74 (0.38, 1.43) vs. placebo	0.369
			Pharm 5-ASA (3.0 g/d)	All	NR	Mean 191 SD 125			HR 1.02 (0.53, 1.94) vs. placebo	0.957
			Placebo	All	NR	Mean 147 SD 162				
Stollman, 2013, 23426454, DIVA	Time to recurrence (days)	52 wk	5-ASA (2.4 g/d) + probiotics (1/day)	All	27	Mean 280.7				
			5-ASA (2.4 g/d)	All	32	Mean 308.7				
			Placebo	All	29	Mean 100.1				
Stollman, 2013, 23426454, DIVA	Global symptom score (GSS), median or mean (SD)	Baseline 52 wk	5-ASA (2.4 g/d) + probiotics (1/day)	All	≤27	0: 19.4 52: 4.4				NS (vs. placebo)
			5-ASA (2.4 g/d)	All	≤32	0: 22.0 (8.6) 52: 1.0				NS (vs. placebo)
			Placebo	All	≤29	0: 23.5 (9.1) 52: 5.0				

CI = confidence interval, NR = not reported, OR = odds ratio, PMID = PubMed identifier

Table D-4ab-3. KQ 4ab. Adverse events

Study, Year, PMID	Outcome	Time	Arm	Subgroup	n/N (%)	Effect Size (95% CI), Adjusted	P Value, Adjusted	Effect Size (95% CI), Unadjusted	P Value, Unadjusted
Parente, 2013, 23754545	Adverse event – any	2 yr	5-ASA	All	6/45 (13.3)			OR 2.26 (0.53, 9.63)	
			Placebo	All	3/47 (6.4)				
Lanas, 2013, 23092785	Adverse event – any		Pharm Rifaximin	All	17/77 (22.1)			OR 1.63 (0.74, 3.63)	0.225
			Placebo	All	13/88 (14.8)				
Raskin, 2014, 25038431, PREVENT1	Adverse event – any ≥1 TEAE	104 wk	5-ASA (1.2 g/d)	All	109/143 (76.2)			OR 1.00 (0.58, 1.72) vs. placebo	
			5-ASA (2.4 g/d)	All	106/143 (74.1)			OR 0.90 (0.53, 1.53) vs. placebo	
			5-ASA (4.8 g/d)	All	101/150 (67.3)			OR 0.64 (0.39, 1.07) vs. placebo	
			Placebo	All	112/147 (76.2)				
Raskin, 2014, 25038431, PREVENT2	Adverse event – any ≥1 TEAE	104 wk	5-ASA (1.2 g/d)	All	108/148 (73)			OR 0.95 (0.56, 1.60) vs. placebo	
			5-ASA (2.4 g/d)	All	111/147 (75.5)			OR 1.09 (0.64, 1.85) vs. placebo	
			5-ASA (4.8 g/d)	All	110/149 (73.8)			OR 0.99 (0.59, 1.68) vs. placebo	
			Placebo	All	105/142 (73.9)				
Kruis, 2017, 28543263, SAG-37	Adverse event – Any	48 wk	5-ASA (3.0 g/d)	All	327/387 (85)			OR 1.45 (0.98, 2.16)	
			Placebo	All	225/285 (79)				
Festa, 2017, 28387885	Adverse event - any	15 mo	5-ASA	All	1/52 (2)				
			Rifaximin	All	0/72 (0)				
Silva Sanchez, 2014	Adverse event – any (TEAE)		5-ASA (4.8 g/d)	All	211/299 (71)				
Parente, 2013, 23754545	AE - Serious	2 yr	5-ASA	All	4/45 (8.9)			OR 2.20 (0.38, 12.62)	
			Placebo	All	2/47 (4.3)				

Study, Year, PMID	Outcome	Time	Arm	Subgroup	n/N (%)	Effect Size (95% CI), Adjusted	P Value, Adjusted	Effect Size (95% CI), Unadjusted	P Value, Unadjusted
Raskin, 2014, 25038431, PREVENT1	AE – Serious	104 wk	5-ASA (1.2 g/d)	All	16/143 (11.19)			OR 1.03 (0.49, 2.15) vs. placebo	
			5-ASA (2.4 g/d)	All	15/143 (10.49)			OR 0.96 (0.46, 2.02) vs. placebo	
			5-ASA (4.8 g/d)	All	18/150 (12)			OR 1.12 (0.55, 2.28) vs. placebo	
			Placebo	All	16/147 (10.9)				
Raskin, 2014, 25038431, PREVENT2	AE – Serious	104 wk	5-ASA (1.2 g/d)	All	(8.1)				
			5-ASA (2.4 g/d)	All					
			5-ASA (4.8 g/d)	All					
			Placebo	All	15/142 (10.56)				
Kruis, 2017, 28543263, SAG-37	AE – Serious	48 wk	5-ASA (3.0 g/d)	All	55/387 (14)			OR 1.46 (0.91, 2.36)	
			Placebo	All	29/285 (10)				
Parente, 2013, 23754545	AE - Severe	2 yr	5-ASA	All	8/45 (17.8)			OR 0.91 (0.32, 2.62)	
			Placebo	All	9/47 (19.2)				
Parente, 2013, 23754545	AE – Leading to discontinuation	2 yr	5-ASA	All	8/45 (17.8)			OR 2.32 (0.65, 8.34)	
			Placebo	All	4/47 (8.5)				
Kruis, 2017, 28543263, SAG-37	AE – Leading to discontinuation	48 wk	5-ASA (3.0 g/d)	All	97/387 (25)			OR 1.53 (1.05, 2.24)	
			Placebo	All	51/285 (18)				

Study, Year, PMID	Outcome	Time	Arm	Subgroup	n/N (%)	Effect Size (95% CI), Adjusted	P Value, Adjusted	Effect Size (95% CI), Unadjusted	P Value, Unadjusted
Raskin, 2014, 25038431, PREVENT1	AE – Sepsis (CD IV)	104 wk	5-ASA (1.2 g/d)	All	1/143 (0.7)				
			5-ASA (2.4 g/d)	All	0/143 (0)				
			5-ASA (4.8 g/d)	All	1/150 (0.67)				
			Placebo	All	0/147 (0)				
Raskin, 2014, 25038431, PREVENT1	AE – Major cardiac event (CD IV) Acute MI	104 wk	5-ASA (1.2 g/d)	All	1/143 (0.70)				
			5-ASA (2.4 g/d)	All	0/143 (0)				
			5-ASA (4.8 g/d)	All	0/150 (0)				
			Placebo	All	2/147 (1.36)				
Raskin, 2014, 25038431, PREVENT1	AE – Infection requiring Abx (CD II) UTI	104 wk	5-ASA (1.2 g/d)	All	14/143 (9.8)			OR 0.83 (0.39, 1.75) vs. placebo	
			5-ASA (2.4 g/d)	All	12/143 (8.4)			OR 0.70 (0.32, 1.52) vs. placebo	
			5-ASA (4.8 g/d)	All	8/150 (5.3)			OR 0.43 (0.18, 1.03) vs. placebo	
			Placebo	All	17/147 (11.6)				
Raskin, 2014, 25038431, PREVENT2	AE – Infection requiring Abx (CD II) UTI	104 wk	5-ASA (1.2 g/d)	All	11/148 (7.4)			OR 1.55 (0.58, 4.11) vs. placebo	
			5-ASA (2.4 g/d)	All	14/147 (9.5)			OR 2.03 (0.79, 5.19) vs. placebo	
			5-ASA (4.8 g/d)	All	10/149 (6.7)			OR 1.39 (0.51, 3.75) vs. placebo	
			Placebo	All	7/142 (4.9)				

Study, Year, PMID	Outcome	Time	Arm	Subgroup	n/N (%)	Effect Size (95% CI), Adjusted	P Value, Adjusted	Effect Size (95% CI), Unadjusted	P Value, Unadjusted
Stollman, 2013, 23426454, DIVA	AE – Serious	12 wk	5-ASA (2.4 g/d) + probiotics (1/day)	All	0/36 (0)			OR 0.67 (0.11, 4.22) combined vs. placebo	
			5-ASA (2.4 g/d)	All	2/40 (5)				
			Placebo	All	3/41 (7.3)				
Stollman, 2013, 23426454, DIVA	AE – Infection requiring Abx (CD II) UTI	12 wk	5-ASA (2.4 g/d) + probiotics (1/day)	All	1/36 (2.8)				
			5-ASA (2.4 g/d)	All	1/40 (2.5)				
			Placebo	All	0/41 (0)				
Stollman, 2013, 23426454, DIVA	Adverse event - headache	12 wk	5-ASA (2.4 g/d) + probiotics (1/day)	All	1/36 (2.8)				
			5-ASA (2.4 g/d)	All	0/40 (0)				
			Placebo	All	0/41 (0)				
Stollman, 2013, 23426454, DIVA	AE – Leading to discontinuation	12 wk	5-ASA (2.4 g/d) + probiotics (1/day)	All	1/36 (2.8)			OR 0.36 (0.04, 3.64) vs. placebo	
			5-ASA (2.4 g/d)	All	5/40 (12.5)				
			Placebo	All	3/41 (7.3)				
Silva Sanchez, 2014	AE - Infection requiring Abx (CD II) UTI		5-ASA (4.8 g/d)	All	18/299 (6)				
Silva Sanchez, 2014	Adverse event - headache		5-ASA (4.8 g/d)	All	27/299 (9)				

CI = confidence interval, NR = not reported, OR = odds ratio, PMID = PubMed identifier.

Key Question 4c (Elective Surgery)

Table D-4c-1. KQ 4c. Treatment comparisons, categorical outcomes

Study Year PMID Country Funding	Design	Population Diverticulitis Details Setting	Outcome	Followup Time	Arm	Arm Details	Age Sex	Severity Prior Episodes*	n/N (%)	Effect Size	Reported P Value
You, 2018, 29683483, USA Industry	RCT	1 prior episode complicated diverticulitis with successful medical management Single center	Diverticulitis recurrence	3 y	Elective surgery	Laparoscopic sigmoid colectomy	53.3 (13.5) 54% male	Abscess 58% Median size 3.7 cm (IQR 2.4, 5.75) Extraluminal air 100%	2/26 (8%)	OR 0.18 (0.04, 0.80)	0.009 (Bonferroni adjustment)
					No treatmen t	Medical observation	55.2 (13.1) 63% male	Abscess 42% Median size 3.8 cm (IQR (2.15, 6.1) Extraluminal air 100%	26/81 (32%)		
van de Wall, 2017, 28404008, DIRECT trial, Netherland s Non- industry	RCT	Ongoing abdominal complaints or frequently recurring left- sided diverticulitis after a confirmed episode of diverticulitis. Multicenter	Diverticulitis recurrence	5 y	Elective surgery	Laparoscopic sigmoidecto my,	Median 54.1 (IQR 44.6-62.1) 28% male	Mean number previous episodes 3.1 (SD 1.0)	6/53 (11)	0.3 (0.1, 0.8)	
					No interventi on	Conservative management	Median 56.5 (IQR 48.3-63.2) 43% male	Mean number previous episodes 4.1 (SD 2.0)	17/56 (30)		

Study Year PMID Country Funding	Design	Population Diverticulitis Details Setting	Outcome	Followup Time	Arm	Arm Details	Age Sex	Severity Prior Episodes*	n/N (%)	Effect Size	Reported P Value
Aquina, 2019, 30335195, USA	NRCS (retrospective)	With acute diverticular abscess	Diverticulitis recurrence	5 y	Elective surgery	Colectomy	Median 56 (IQR 47, 66) 51.8% male	At least 1 prior episode, 16.3	70/1660 (4.2)	0.1 (0.1, 0.2)	<0.001
					No intervention	Nonoperative management	Median 58 (IQR 47, 72) 46.3% male	At least 1 prior episode, 10.1	1340/5412 (24.8)		
You, 2018, 29683483, USA Industry	RCT	1 prior episode complicated diverticulitis with successful medical management. Single center	Mortality	3 y	Elective surgery	Laparoscopic sigmoid colectomy	53.3 (13.5) 54% male	Abscess 58% Median size 3.7 cm (IQR 2.4, 5.75) Extraluminal air 100%	0/26 (0%)		
					No treatment	Medical observation	55.2 (13.1) 63% male	Abscess 42% Median size 3.8 cm (IQR (2.15, 6.1) Extraluminal air 100%	0/81 (0%)		
van de Wall, 2017, 28404008, DIRECT trial, Netherlands Non-industry	RCT	Ongoing abdominal complaints or frequently recurring left-sided diverticulitis after a confirmed episode of diverticulitis. Multicenter	Mortality	5 y	Elective surgery	Laparoscopic sigmoidectomy,	Median 54.1 (IQR 44.6-62.1) 28% male	Mean number previous episodes 3.1 (SD 1.0)	0/53 (0)	0.5 (0, 15.6)	
					No intervention	Conservative management	Median 56.5 (IQR 48.3-63.2) 43% male	Mean number previous episodes 4.1 (SD 2.0)	1/56 (1.8)		

Study Year PMID Country Funding	Design	Population Diverticulitis Details Setting	Outcome	Followup Time	Arm	Arm Details	Age Sex	Severity Prior Episodes*	n/N (%)	Effect Size	Reported P Value
Aquina, 2019, 30335195, USA NR	NRCS (retrospective)	With acute diverticular abscess	Mortality – diverticulitis related	30 d	Elective surgery	Colectomy	Median 56 (IQR 47, 66) 51.8% male	At least 1 prior episode, 16.3	3/166 0 (0.2)	0.1 (0, 0.3)	
					No interventi on	Nonoperative management	Median 58 (IQR 47, 72) 46.3% male	At least 1 prior episode, 10.1	104/5 412 (1.9)		

LCUD = left colon uncomplicated diverticulitis, OR = odds ratio, PMID = PubMed identifier, RCT = randomized controlled trial.

* Median (range) data in square brackets; otherwise mean (SD)

Table D-4c-2. KQ 4c. Treatment comparisons, continuous outcomes

Study Year PMID Country	Design	Population Diverticulitis Details Setting	Arm	Age Sex	Severity Prior Episodes	Outcome	Followup Time	N, Intervention (Control)	Results intervention (control)	Difference (95%CI)	Reported Difference (95%CI)	Reported P Value
You, 2018, 29683483, USA Industry	RCT	1 prior episode complicated diverticulitis with successful medical management. Single center	Elective surgery	53.3 (13.5) 54% male	Abscess median 3.8 (range 3.8- 7.7); extraluminal air 100	Length of hospital stay	30 d	26	Median 5.5 d, IQR 4, 8.5			0.903
			No treatment	55.2 (13.1) 63% male	Abscess median 1 (range 1- 1.5); extraluminal air 100			81	Median 5 d, IQR 4, 8			
Aquina, 2019, 30335195, USA Not reported	NRCS (retrospective)	Mortality – diverticulitis related	Elective surgery	Median 56 (IQR 47, 66) 51.8% male	At least 1 prior episode, 16.3	Length of hospital stay	30 d	1660	8.0 (7.8)	3.4 (2.95, 3.85)		<0.001

Study Year PMID Country	Design	Population Diverticulitis Details Setting	Arm	Age Sex	Severity Prior Episodes	Outcome	Followup Time	N, Intervention (Control)	Results intervention (control)	Difference (95%CI)	Reported Difference (95%CI)	Report P Value
			No intervention	Median 58 (IQR 47, 72) 46.3% male	At least 1 prior episode, 10.1			5412	4.6 (18.5)			
You, 2018, 29683483, USA Industry	RCT	1 prior episode complicated diverticulitis with successful medical management. Single center	Elective surgery	53.3 (13.5) 54% male	Abscess median 3.8 (range 3.8- 7.7); extraluminal air 100	Time to recurrence	3 y	26	Median 11 m, IQR 8, 14			0.015
			No treatment	55.2 (13.1) 63% male	Abscess median 1 (range 1- 1.5); extraluminal air 100			81	Median 7 m, IQR 3.25, 15			
van de Wall, 2017, 28404008, DIRECT trial, Netherlands Non- industry	RCT	Ongoing abdominal complaints or frequently recurring left- sided diverticulitis after a confirmed episode of diverticulitis. Multicenter	Elective surgery	Median 54.1 (IQR 44.6- 62.1) 28% male	Mean number previous episodes 3.1 (SD 1.0)	Quality of life GIQLI	Baseline 6 m 5 y	53	92.6 (22.8) 114.4 (22.3) 118.2 (21.0)	6m 13.6 (5.2, 22) 5y 9.3 (1.3, 17.3)		6 m 0.0001 favors elective surger 5 y 0.018 favors elective surger
			No intervention	Median 56.5 (IQR 48.3- 63.2) 43% male	Mean number previous episodes 4.1 (SD 2.0)			56	92.2 (21.3) 100.4 (22.7) 108.5 (20.0)			

Study Year PMID Country	Design	Population Diverticulitis Details Setting	Arm	Age Sex	Severity Prior Episodes	Outcome	Followup Time	N, Intervention (Control)	Results intervention (control)	Difference (95%CI)	Reported Difference (95%CI)	Report P Value
van de Wall, 2017, 28404008, DIRECT trial, Netherlands Non- industry	RCT	Ongoing abdominal complaints or frequently recurring left- sided diverticulitis after a confirmed episode of diverticulitis. Multicenter	Elective surgery	Median 54.1 (IQR 44.6- 62.1) 28% male	Mean number previous episodes 3.1 (SD 1.0)	Quality of life SF-36 mental	Baseline 6 m 5 y	53	41.6 (14.5) 47.7 (12.4) 50.7 (9.4)	6m 4.1 (-0.4, 8.6) 5y 6.4 (2.2, 10.6)		6 m 0.263 favors elective surger 5 y 0.010 favors elective surger
			No intervention	Median 56.5 (IQR 48.3- 63.2) 43% male	Mean number previous episodes 4.1 (SD 2.0)			56	43.3 (9.5) 45.3 (10.3) 46.0 (9.2)			
van de Wall, 2017, 28404008, DIRECT trial, Netherlands Non- industry	RCT	Ongoing abdominal complaints or frequently recurring left- sided diverticulitis after a confirmed episode of diverticulitis. Multicenter	Elective surgery	Median 54.1 (IQR 44.6- 62.1) 28% male	Mean number previous episodes 3.1 (SD 1.0)	Quality of life SF-36 physical	Baseline 6 m 5 y	53	37.0 (7.1) 43.5 (8.8) 47.6 (9.9)	6m 3.9 (1.1, 6.7) 5y 4.9 (1.5, 8.3)		6 m 0.016 favors elective surger 5 y 0.030 favors elective surger
			No intervention	Median 56.5 (IQR 48.3- 63.2) 43% male	Mean number previous episodes 4.1 (SD 2.0)			56	36.9 (6.7) 39.5 (7.0) 42.6 (10.5)			

Study Year PMID Country	Design	Population Diverticulitis Details Setting	Arm	Age Sex	Severity Prior Episodes	Outcome	Followup Time	N, Intervention (Control)	Results intervention (control)	Difference (95%CI)	Reported Difference (95%CI)	Report P Value
van de Wall, 2017, 28404008, DIRECT trial, Netherlands Non- industry	RCT	Ongoing abdominal complaints or frequently recurring left- sided diverticulitis after a confirmed episode of diverticulitis. Multicenter	Elective surgery	Median 54.1 (IQR 44.6- 62.1) 28% male	Mean number previous episodes 3.1 (SD 1.0)	Quality of life EQ-5D	Baseline	53	0.69 (0.21)	6m 0.2 (0.1, 0.2) 5y 0.2 (0.1, 0.2)		6 m 0.001 favors elective surger 5 y 0.016 favors elective surger
			No intervention	Median 56.5 (IQR 48.3- 63.2) 43% male	Mean number previous episodes 4.1 (SD 2.0)		6 m 5 y	56	0.74 (0.20) 0.73 (0.19) 0.74 (0.21)			
van de Wall, 2017, 28404008, DIRECT trial, Netherlands Non- industry	RCT	Ongoing abdominal complaints or frequently recurring left- sided diverticulitis after a confirmed episode of diverticulitis. Multicenter	Elective surgery	Median 54.1 (IQR 44.6- 62.1) 28% male	Mean number previous episodes 3.1 (SD 1.0)	Pain (VAS, 0- 10)	Baseline	53	63.3 (21.7)	6m -18.4 (- 26.4, - 10.4) 5y -11 (-20.1, -1.9)		6 m <0.000 favors elective surger 5 y 0.011 favors elective surger
			No intervention	Median 56.5 (IQR 48.3- 63.2) 43% male	Mean number previous episodes 4.1 (SD 2.0)		6 m 5 y	56	69.3 (13.6) 48.3 (22.9) 47.5 (25.1)			

CI = confidence interval, HR = hazard ratio, LCUD = left colon uncomplicated diverticulitis, NR = not reported, PMID = PubMed identifier, RCT = randomized controlled trial, SD = standard deviation.

Table D-4c-3. KQ 4c. Adverse events

Study Year PMID Country Funding	Design	Outcome	Arm/Subgroup	Arm/Subgroup Details	Age Sex	n/N (%)	Effect Size	Reported P Value
You, 2018, 29683483, USA Industry	RCT	AE - Infection requiring Abx (CD II): Deep incisional Surgical Site Infection	Elective surgery	Laparoscopic sigmoid colectomy	53.3 (13.5) 54% male	1/26 (4%)		
			No treatment	Medical observation	55.2 (13.1) 63% male	0/81 (0%)		
You, 2018, 29683483, USA Industry	RCT	AE - Return to OR or unplanned procedure (CD III): Small bowel obstruction	Elective surgery	Laparoscopic sigmoid colectomy	53.3 (13.5) 54% male	1/26 (4%)		
			No treatment	Medical observation	55.2 (13.1) 63% male	0/81 (0%)		
You, 2018, 29683483, USA Industry	RCT	AE - Return to OR or unplanned procedure (CD III): Reoperation	Elective surgery	Laparoscopic sigmoid colectomy	53.3 (13.5) 54% male	0/26 (0%)		
			No treatment	Medical observation	55.2 (13.1) 63% male	0/81 (0%)		
You, 2018, 29683483, USA Industry	RCT	AE - Serious	Elective surgery	Laparoscopic sigmoid colectomy	53.3 (13.5) 54% male	1/26 (4%)		
			No treatment	Medical observation	55.2 (13.1) 63% male	0/81 (0%)		
You, 2018, 29683483, USA Industry	RCT	AE - Ileus	Elective surgery	Laparoscopic sigmoid colectomy	53.3 (13.5) 54% male	1/26 (4%)		

Study Year PMID Country Funding	Design	Outcome	Arm/Subgroup	Arm/Subgroup Details	Age Sex	n/N (%)	Effect Size	Reported P Value
			No treatment	Medical observation	55.2 (13.1) 63% male	0/81 (0%)		
van de Wall, 2017, 28404008, DIRECT trial, Netherlands Non-industry	RCT	AE - Serious (SAE) Any	Elective surgery	Laparoscopic sigmoidectomy,	Median 54.1 (IQR 44.6- 62.1) 28% male	6m: 18/53 (34.0) 5 y: 37/53 (69.8)		
			No intervention	Conservative management	Median 56.5 (IQR 48.3- 63.2) 43% male	6m: 23/56 (41.1) 5y: 45/56 (80.4)		
van de Wall, 2017, 28404008, DIRECT trial, Netherlands Non-industry	RCT	AE - Infection requiring Abx (CD II) urinary tract infection	Elective surgery	Laparoscopic sigmoidectomy,	Median 54.1 (IQR 44.6- 62.1) 28% male	6m: 4/53 (7.5) 5y: 0/53 (0)		
			No intervention	Conservative management	Median 56.5 (IQR 48.3- 63.2) 43% male	6m: 2/56 (3.6) 5y: 1/56 (1.8)		
van de Wall, 2017, 28404008, DIRECT trial, Netherlands Non-industry	RCT	AE - Major pulmonary event (CD IV) Pulmonary embolism	Elective surgery	Laparoscopic sigmoidectomy,	Median 54.1 (IQR 44.6- 62.1) 28% male	6m: 0/53 (0) 5y: 2/53 (3.8)		

Study Year PMID Country Funding	Design	Outcome	Arm/Subgroup	Arm/Subgroup Details	Age Sex	n/N (%)	Effect Size	Reported P Value
			No intervention	Conservative management	Median 56.5 (IQR 48.3- 63.2) 43% male	6m: 1/56 (1.8) 5y: 1/56 (1.8)		
van de Wall, 2017, 28404008, DIRECT trial, Netherlands Non-industry	RCT	AE - Return to OR or unplanned procedure (CD III) CPR in OR	Elective surgery	Laparoscopic sigmoidectomy,	Median 54.1 (IQR 44.6- 62.1) 28% male	1/53 (1.9)		
			No intervention	Conservative management	Median 56.5 (IQR 48.3- 63.2) 43% male	0/56 (0)		
van de Wall, 2017, 28404008, DIRECT trial, Netherlands Non-industry	RCT	AE - Return to OR or unplanned procedure (CD III) anastomotic leakage	Elective surgery	Laparoscopic sigmoidectomy,	Median 54.1 (IQR 44.6- 62.1) 28% male	7/53 (13.2)		
			No intervention	Conservative management	Median 56.5 (IQR 48.3- 63.2) 43% male	0/56 (0)		
Aquina, 2019, 30335195, USA Not reported	NRCS (retrospective)	AE - Stoma	Elective surgery	Colectomy	Median 56 (IQR 47, 66) 51.8% male	166/1660 (10.0)		<0.001

Study Year PMID Country Funding	Design	Outcome	Arm/Subgroup	Arm/Subgroup Details	Age Sex	n/N (%)	Effect Size	Reported P Value
			No intervention	Nonoperative management	Median 58 (IQR 47, 72 46.3% male	309/5412 (5.7)		
Bhakta, 2016, 26275534, Albany Medical Center 2001- 13, USA Non-industry	Single group (Prospective)	AE - Infection requiring Abx (CD II) organ or space surgical site infection	Elective surgery (all)	Laparoscopic	55.7 47% male	13/576 (2.3)		
			Elective surgery (simple diverticulitis)	Laparoscopic		9/437 (2.1)		
			Elective surgery (complicated diverticulitis)	Laparoscopic		5/139 (3.6)		
Bhakta, 2016, 26275534, Albany Medical Center 2001- 13, USA Non-industry	Single group (Prospective)	AE - Ileus	Elective surgery (all)	Laparoscopic	55.7 47% male	22/576 (3.8)		
			Elective surgery (simple diverticulitis)	Laparoscopic		14/437 (3.2)		
			Elective surgery (complicated diverticulitis)	Laparoscopic		12/139 (8.6)		

Study Year PMID Country Funding	Design	Outcome	Arm/Subgroup	Arm/Subgroup Details	Age Sex	n/N (%)	Effect Size	Reported P Value
Bhakta, 2016, 26275534, Albany Medical Center 2001- 13, USA Non-industry	Single group (Prospective)	AE - Return to OR or unplanned procedure (CD III) Anastomatic leak	Elective surgery (all)	Laparoscopic	55.7 47% male	12/576 (2.1)		
			Elective surgery (simple diverticulitis)	Laparoscopic		10/437 (2.3)		
			Elective surgery (complicated diverticulitis)	Laparoscopic		2/139 (1.4)		
Bhakta, 2016, 26275534, Albany Medical Center 2001- 13, USA Non-industry	Single group (Prospective)	AE - Return to OR or unplanned procedure (CD III) Incisional hernia	Elective surgery (all)	Laparoscopic	55.7 47% male	10/576 (1.8)		
			Elective surgery (simple diverticulitis)	Laparoscopic		7/437 (1.6)		
			Elective surgery (complicated diverticulitis)	Laparoscopic		4/139 (2.9)		
Bhakta, 2016, 26275534, Albany Medical Center 2001- 13, USA Non-industry	Single group (Prospective)	AE - Clostridioides difficile (C diff) infection	Elective surgery (all)	Laparoscopic	55.7 47% male	17/576 (3.0)		
			Elective surgery (simple diverticulitis)	Laparoscopic		13/437 (2.9)		
			Elective surgery (complicated diverticulitis)	Laparoscopic		4/139 (2.9)		
Bordeianou, 2019, 29916880, PREVENTT, USA Not reported	Single group (Prospective)	AE - Infection requiring Abx (CD II) Total Surgical Site Infection	Elective surgery (all)	Any	59.9 (12.7) 43.6% male	284/1506 (18.9)		

Study Year PMID Country Funding	Design	Outcome	Arm/Subgroup	Arm/Subgroup Details	Age Sex	n/N (%)	Effect Size	Reported P Value
Bordeianou, 2019, 29916880, PREVENTT, USA Not reported	Single group (Prospective)	AE - Infection requiring Abx (CD II) Organ space Surgical Site Infection	Elective surgery (all)	Any	59.9 (12.7) 43.6% male	73/1506 (4.8)		
Bordeianou, 2019, 29916880, PREVENTT, USA Not reported	Single group (Prospective)	AE - Infection requiring Abx (CD II) Deep Surgical Site Infection	Elective surgery (all)	Any	59.9 (12.7) 43.6% male	13/1506 (0.9)		
Bordeianou, 2019, 29916880, PREVENTT, USA Not reported	Single group (Prospective)	AE - Infection requiring Abx (CD II) Superficial Surgical Site Infection	Elective surgery (all)	Any	59.9 (12.7) 43.6% male	224/1506 (14.9)		
Silva-Velazco, 2016, 26541732, USA Non-industry	Single group (Prospective)	AE - 30-day mortality	Elective surgery (all)	Laparoscopic	55 (12) 52% male	2/1059 (0.19)		
Silva-Velazco, 2016, 26541732, USA Non-industry	Single group (Prospective)	AE - Unplanned (re)hospitalization 30 d rehospitalization	Elective surgery (all)	Laparoscopic	55 (12) 52% male	120/1059 (11)		

Study Year PMID Country Funding	Design	Outcome	Arm/Subgroup	Arm/Subgroup Details	Age Sex	n/N (%)	Effect Size	Reported P Value
Silva-Velazco, 2016, 26541732, USA Non-industry	Single group (Prospective)	AE - Return to OR or unplanned procedure postoperative anastomotic leak and/or abdomino- pelvic abscess	Elective surgery (all)	Laparoscopic	55 (12) 52% male	39/1059 (3.7)		
			Elective surgery (BMI <30)	Laparoscopic	55 (12) 52% male		Ref	
			Elective surgery (BMI 30-35)	Laparoscopic	55 (12) 52% male		OR 1.33 (95%CI 0.69, 2.55)	P=0.39
			Elective surgery (BMI ≥ 35)	Laparoscopic	55 (12) 52% male		OR 2.30 (95%CI 1.16, 4.55)	P=0.017
			Elective surgery (Uncomplicated diverticulitis)	Laparoscopic	55 (12) 52% male		Ref	
			Elective surgery (Complicated diverticulitis)	Laparoscopic	55 (12) 52% male		OR 2.37 (95%CI 1.36, 4.11)	P=0.002

Study Year PMID Country Funding	Design	Outcome	Arm/Subgroup	Arm/Subgroup Details	Age Sex	n/N (%)	Effect Size	Reported P Value
Silva-Velazco, 2016, 26541732, USA Non-industry	Single group (Prospective)	AE - Serious (SAE) clinical anastomotic leak, abdominal and/or pelvic abscess, postoperative bleeding, DVT, dehydration, ileus, mechanical small bowel obstruction, small bowel leak, stoma complications, Clostridium difficile, sepsis, wound infection, wound dehiscence, urinary, renal, cardiovascular and other respiratory morbidity.	Elective surgery (all)	Laparoscopic	55 (12) 52% male	296/1059 (28)		
			Elective surgery (BMI <30)	Laparoscopic	55 (12) 52% male		Ref	
			Elective surgery (BMI 30-35)	Laparoscopic	55 (12) 52% male		OR 1.31 (95%CI 0.93, 1.84)	P=0.12
			Elective surgery (BMI ≥ 35)	Laparoscopic	55 (12) 52% male		1.05 (95%CI 0.68, 1.60)	P=0.84
			Elective surgery (Uncomplicated diverticulitis)	Laparoscopic	55 (12) 52% male		Ref	
			Elective surgery (Complicated diverticulitis)	Laparoscopic	55 (12) 52% male		OR 1.32 (95%CI 0.96, 1.82)	P=0.08

Study Year PMID Country Funding	Design	Outcome	Arm/Subgroup	Arm/Subgroup Details	Age Sex	n/N (%)	Effect Size	Reported P Value
Simianu, 2015, 25773308, Surgical Care and Outcomes Assessment Program (SCOAP), USA Non-industry	Single group (Prospective)	AE - Serious (SAE) In-hospital complications, including cardiac, pulmonary, renal, infectious, or other, requiring nonoperative intervention	Elective surgery	Laparoscopic	57.8 (12.7) 47% male	139/1790 (7.8)		
Simianu, 2015, 25773308, Surgical Care and Outcomes Assessment Program (SCOAP), USA Non-industry	Single group (Prospective)	AE - Return to OR or unplanned procedure (CD III) composite adverse events (CAE), including cardiac, pulmonary, renal, infectious, or other complications requiring nonoperative intervention + reoperative interventions and in- hospital deaths	Elective surgery	Laparoscopic	57.8 (12.7) 47% male	210/1790 (11.7)		
Tsilimparis, 2010, 20812161, Fast-track Kolon II, Germany Not reported	Single group (Prospective)	AE – 30-day mortality	Elective surgery (all)	Laparoscopic	63 [Range 23, 91] 42% male	2/846 (0.2)		
			Elective surgery (age <60)	Laparoscopic		0/358 (0)		
			Elective surgery (age 60-69)	Laparoscopic		0/277 (0)		
			Elective surgery (age >69)	Laparoscopic		2/211 (1)		

Study Year PMID Country Funding	Design	Outcome	Arm/Subgroup	Arm/Subgroup Details	Age Sex	n/N (%)	Effect Size	Reported P Value
Tsilimparis, 2010, 20812161, Fast-track Kolon II, Germany Not reported	Single group (Prospective)	AE - Return to OR or unplanned procedure Anastomosis	Elective surgery (all)	Laparoscopic	63 [Range 23, 91 42% male	17/846 (2)		P-value across age groups 0.605
			Elective surgery (age <60)	Laparoscopic		6/358 (1.7)		
			Elective surgery (age 60-69)	Laparoscopic		5/277 (1.8)		
			Elective surgery (age >69)	Laparoscopic		6/211 (2.8)		
Tsilimparis, 2010, 20812161, Fast-track Kolon II, Germany Not reported	Single group (Prospective)	AE - Return to OR or unplanned procedure hemorrhage requiring revision	Elective surgery (all)	Laparoscopic	63 [Range 23, 91] 42% male	7/846 (0.8)		P-value across age groups 0.042
			Elective surgery (age <60)	Laparoscopic		6/358 (1.7)		
			Elective surgery (age 60-69)	Laparoscopic		1/277 (0.4)		
			Elective surgery (age >69)	Laparoscopic		0/211 (0)		

Study Year PMID Country Funding	Design	Outcome	Arm/Subgroup	Arm/Subgroup Details	Age Sex	n/N (%)	Effect Size	Reported P Value
Tsilimparis, 2010, 20812161, Fast-track Kolon II, Germany Not reported	Single group (Prospective)	AE – Ileus Paralytic Ileus	Elective surgery (all)	Laparoscopic	63 [Range 23, 91] 42% male	5/846 (0.6)		P-value across age groups 0.155
			Elective surgery (age <60)	Laparoscopic		0/358 (0)		
			Elective surgery (age 60-69)	Laparoscopic		3/277 (1.1)		
			Elective surgery (age >69)	Laparoscopic		2/211 (1)		
Tsilimparis, 2010, 20812161, Fast-track Kolon II, Germany Not reported	Single group (Prospective)	AE - Ileus	Elective surgery (all)	Laparoscopic	63 [Range 23, 91] 42% male	2/846 (0.2)		P-value across age groups 0.05
			Elective surgery (age <60)	Laparoscopic		0/358 (0)		
			Elective surgery (age 60-69)			0/277 (0)		
			Elective surgery (age >69)	Laparoscopic		2/211 (1)		

Study Year PMID Country Funding	Design	Outcome	Arm/Subgroup	Arm/Subgroup Details	Age Sex	n/N (%)	Effect Size	Reported P Value
Tsilimparis, 2010, 20812161, Fast-track Kolon II, Germany Not reported	Single group (Prospective)	Hospitalization for diverticulitis 30-day readmission	Elective surgery (all)	Laparoscopic	63 [Range 23, 91] 42% male	33/846 (3.9)		P-value across age groups 0.81
			Elective surgery (age <60)	Laparoscopic		15/358 (4.2)		
			Elective surgery (age 60-69)	Laparoscopic		9/277 (3.3)		
			Elective surgery (age >69)	Laparoscopic		9/211 (4.3)		
Tsilimparis, 2010, 20812161, Fast-track Kolon II, Germany Not reported	Single group (Prospective)	AE - Bleed requiring transfusion (CD II)	Elective surgery (all)	Laparoscopic	63 [Range 23, 91] 42% male	6/846 (0.7)		P-value across age groups 0.06
			Elective surgery (age <60)	Laparoscopic		2/358 (0.6)		
			Elective surgery (age 60-69)	Laparoscopic		0/277 (0)		
			Elective surgery (age >69)	Laparoscopic		4/211 (1.9)		

Study Year PMID Country Funding	Design	Outcome	Arm/Subgroup	Arm/Subgroup Details	Age Sex	n/N (%)	Effect Size	Reported P Value
Boostrom, 2012, 22696233, Mayo Clinic, Rochester, USA Not reported	Single group (Retrospective)	AE – 30-day mortality	Elective surgery (Acute resolving uncomplicated diverticulitis)	Sigmoidectomy	Median 63 45% male	2/564 (0.4)		
			Elective surgery (Chronic/ smoldering uncomplicated diverticulitis)	Sigmoidectomy	Median 66 38% male	0/66 (0)		
			Elective surgery (Atypical uncomplicated diverticulitis)	Sigmoidectomy	Median 64 37% male	0/54 (0)		
Boostrom, 2012, 22696233, Mayo Clinic, Rochester, USA Not reported	Single group (Retrospective)	AE - Acute Renal Failure	Elective surgery (Acute resolving uncomplicated diverticulitis)	Sigmoidectomy	Median 63 45% male	5/564 (0.9)		
			Elective surgery (Chronic/ smoldering uncomplicated diverticulitis)	Sigmoidectomy	Median 66 38% male	0/66 (0)		
			Elective surgery (Atypical uncomplicated diverticulitis)	Sigmoidectomy	Median 64 37% male	0/54 (0)		

Study Year PMID Country Funding	Design	Outcome	Arm/Subgroup	Arm/Subgroup Details	Age Sex	n/N (%)	Effect Size	Reported P Value
Boostrom, 2012, 22696233, Mayo Clinic, Rochester, USA Not reported	Single group (Retrospective)	AE - Bleed requiring transfusion	Elective surgery (Acute resolving uncomplicated diverticulitis)	Sigmoidectomy	Median 63 45% male	28/564 (5)		
			Elective surgery (Chronic/ smoldering uncomplicated diverticulitis)	Sigmoidectomy	Median 66 38% male	1/66 (1.5)		
			Elective surgery (Atypical uncomplicated diverticulitis)	Sigmoidectomy	Median 64 37% male	0/54 (0)		
Boostrom, 2012, 22696233, Mayo Clinic, Rochester, USA Not reported	Single group (Retrospective)	AE - Infection requiring Abx Urinary tract infection	Elective surgery (Acute resolving uncomplicated diverticulitis)	Sigmoidectomy	Median 63 45% male	12/564 (2)		
			Elective surgery (Chronic/ smoldering uncomplicated diverticulitis)	Sigmoidectomy	Median 66 38% male	1/66 (1.5)		
			Elective surgery (Atypical uncomplicated diverticulitis)	Sigmoidectomy	Median 64 37% male	1/54 (2)		

Study Year PMID Country Funding	Design	Outcome	Arm/Subgroup	Arm/Subgroup Details	Age Sex	n/N (%)	Effect Size	Reported P Value
Boostrom, 2012, 22696233, Mayo Clinic, Rochester, USA Not reported	Single group (Retrospective)	AE - Major cardiac event atrial fibrillation or myocardial infarction	Elective surgery (Acute resolving uncomplicated diverticulitis)	Sigmoidectomy	Median 63 45% male	9/564 (1.6)		
			Elective surgery (Chronic/ smoldering uncomplicated diverticulitis)	Sigmoidectomy	Median 66 38% male	2/66 (3)		
			Elective surgery (Atypical uncomplicated diverticulitis)	Sigmoidectomy	Median 64 37% male	2/54 (3.7)		
Boostrom, 2012, 22696233, Mayo Clinic, Rochester, USA Not reported	Single group (Retrospective)	AE - Major pulmonary event respiratory failure or pulmonary embolus or deep venous thrombosis	Elective surgery (Acute resolving uncomplicated diverticulitis)	Sigmoidectomy	Median 63 45% male	8/564 (1.4)		
			Elective surgery (Chronic/ smoldering uncomplicated diverticulitis)	Sigmoidectomy	Median 66 38% male	0/66 (0)		
			Elective surgery (Atypical uncomplicated diverticulitis)	Sigmoidectomy	Median 64 37% male	0/54 (0)		

Study Year PMID Country Funding	Design	Outcome	Arm/Subgroup	Arm/Subgroup Details	Age Sex	n/N (%)	Effect Size	Reported P Value
Boostrom, 2012, 22696233, Mayo Clinic, Rochester, USA Not reported	Single group (Retrospective)	AE - Return to OR or unplanned procedure anastomotic leakage	Elective surgery (Acute resolving uncomplicated diverticulitis)	Sigmoidectomy	Median 63 45% male	8/564 (1.4)		
			Elective surgery (Chronic/ smoldering uncomplicated diverticulitis)	Sigmoidectomy	Median 66 38% male	0/66 (0)		
			Elective surgery (Atypical uncomplicated diverticulitis)	Sigmoidectomy	Median 64 37% male	1/54 (2)		
Boostrom, 2012, 22696233, Mayo Clinic, Rochester, USA Not reported	Single group (Retrospective)	AE – Stroke Ischemic stroke	Elective surgery (Acute resolving uncomplicated diverticulitis)	Sigmoidectomy	Median 63 45% male	2/564 (0.4)		
			Elective surgery (Chronic/ smoldering uncomplicated diverticulitis)	Sigmoidectomy	Median 66 38% male	0/66 (0)		
			Elective surgery (Atypical uncomplicated diverticulitis)	Sigmoidectomy	Median 64 37% male	0/54 (0)		
Ilyas, 2017, 27422847, Nationwide Inpatient Sample (2004-2001), USA Non-industry	Single group (Retrospective)	AE – 30-day mortality	Elective surgery	Sigmoidectomy	65.7 (13.1) 45.7% male	4,413/124,421 (3.5)		

Study Year PMID Country Funding	Design	Outcome	Arm/Subgroup	Arm/Subgroup Details	Age Sex	n/N (%)	Effect Size	Reported P Value
Ilyas, 2017, 27422847, Nationwide Inpatient Sample (2004-2001), USA Non-industry	Single group (Retrospective)	AE - Acute Renal Failure	Elective surgery	Sigmoidectomy	65.7 (13.1)	385/11192 (3.4)		
Ilyas, 2017, 27422847, Nationwide Inpatient Sample (2004-2001), USA Non-industry	Single group (Retrospective)	AE - DVT	Elective surgery	Sigmoidectomy	45.7% male	18/11192 (0.2)		
Ilyas, 2017, 27422847, Nationwide Inpatient Sample (2004-2001), USA Non-industry	Single group (Retrospective)	AE - Infection requiring Abx Intra-abdominal abscess	Elective surgery	Sigmoidectomy	65.7 (13.1)	138/11192 (1.2)		
Ilyas, 2017, 27422847, Nationwide Inpatient Sample (2004-2001), USA Non-industry	Single group (Retrospective)	AE - Major pulmonary event Acute respiratory distress syndrome	Elective surgery	Sigmoidectomy	45.7% male	114/11192 (1.0)		
Ilyas, 2017, 27422847, Nationwide Inpatient Sample (2004-2001), USA Non-industry	Single group (Retrospective)	AE - Major pulmonary event Pneumonia	Elective surgery	Sigmoidectomy	65.7 (13.1)	1.5/11192 (166)		
Ilyas, 2017, 27422847, Nationwide Inpatient Sample (2004-2001), USA Non-industry	Single group (Retrospective)	AE - Return to OR or unplanned procedure Reoperation	Elective surgery	Sigmoidectomy	45.7% male	679/11192 (6.1)		

Study Year PMID Country Funding	Design	Outcome	Arm/Subgroup	Arm/Subgroup Details	Age Sex	n/N (%)	Effect Size	Reported P Value
Ilyas, 2017, 27422847, Nationwide Inpatient Sample (2004-2001), USA Non-industry	Single group (Retrospective)	AE - Sepsis	Elective surgery	Sigmoidectomy	65.7 (13.1)	120/11192 (1.1)		
Ilyas, 2017, 27422847, Nationwide Inpatient Sample (2004-2001), USA Non-industry	Single group (Retrospective)	AE - Return to OR or unplanned procedure Anastomotic leakage	Elective surgery	Sigmoidectomy	45.7% male	929/11192 (8.3)		

Study Year PMID Country Funding	Design	Outcome	Arm/Subgroup	Arm/Subgroup Details	Age Sex	n/N (%)	Effect Size	Reported P Value
Lidor, 2010, 20878256, USA Non- industry	Single group (Retrospective)	AE – 30-day mortality	Elective surgery (all)	Left colectomy with ileostomy	73.9 (5.9) 28.9% male	277/22752 (1.22)		
			Elective surgery (Age 65-69)	Left colectomy with ileostomy		N = 6622	reference category	
			Elective surgery (Age 70-74)	Left colectomy with ileostomy		N = 6817	OR 1.6 (95%CI 1.05, 2.61)	
			Elective surgery (Age 75-79)	Left colectomy with ileostomy		N = 5336	OR 2.8 (95%CI 2.46, 6.05)	
			Elective surgery (Age 80-84)	Left colectomy with ileostomy		N = 2816	OR 3.8 (95%CI 2.46, 6.05)	
			Elective surgery (Age 85+)	Left colectomy with ileostomy		N = 1161	OR 10.2 (95%CI 6.49, 15.98)	
			Elective surgery (CHF)	Left colectomy with ileostomy		N = 1486	OR 3.5 (95%CI 2.59, 4.63) compared to no CHF	
			Elective surgery (COPD)	Left colectomy with ileostomy		N = 4116	OR 1.2 (95%CI 0.91, 1.63) compared to no COPD	

Study Year PMID Country Funding	Design	Outcome	Arm/Subgroup	Arm/Subgroup Details	Age Sex	n/N (%)	Effect Size	Reported P Value
Lidor, 2010, 20878256, USA Non- industry	Single group (Retrospective)	AE - Infection requiring Abx Infection, Seroma, Dehiscence, Nonhealing wound, or Emphysema (subcutaneous)	Elective surgery (all)	Left colectomy with ileostomy	73.9 (5.9) 28.9% male	1052/22752 (4.6)		
			Elective surgery (Age 65-69)	Left colectomy with ileostomy		N = 6622	reference category	
			Elective surgery (Age 70-74)	Left colectomy with ileostomy		N = 6817	OR 0.9 (95%CI 0.80, 1.10)	
			Elective surgery (Age 75-79)	Left colectomy with ileostomy		N = 5336	OR 0.9 (95%CI 0.79, 1.12)	
			Elective surgery (Age 80-84)	Left colectomy with ileostomy		N = 2816	OR 0.7 (95%CI 0.56, 0.89)	
			Elective surgery (CHF)	Left colectomy with ileostomy		N = 1486	OR 1.9 (95%CI 1.50, 2.39) compared to no CHF	
			Elective surgery (COPD)	Left colectomy with ileostomy		N = 4116	OR 1.4 (95%CI 1.19, 1.67) Compared to no COPD	

Study Year PMID Country Funding	Design	Outcome	Arm/Subgroup	Arm/Subgroup Details	Age Sex	n/N (%)	Effect Size	Reported P Value
Lidor, 2010, 20878256, USA Non- industry	Single group (Retrospective)	AE - Acute renal failure	Elective surgery (all)	Left colectomy with ileostomy	73.9 (5.9) 28.9% male	490/22752 (2.49)		
			Elective surgery (Age 65-69)	Left colectomy with ileostomy		N = 6622	reference category	
			Elective surgery (Age 70-74)	Left colectomy with ileostomy		N = 6817	OR 1.3 (95%CI 0.98, 1.63)	
			Elective surgery (Age 75-79)	Left colectomy with ileostomy		N = 5336	OR 1.7 (95%CI 1.34, 2.22)	
			Elective surgery (Age 80-84)	Left colectomy with ileostomy		N = 2816	OR 1.7 (95%CI 1.26, 2.25)	
			Elective surgery (CHF)	Left colectomy with ileostomy		N = 1486	OR 4.1 (95%CI 3.22, 5.12) compared to no CHF	
			Elective surgery (COPD)	Left colectomy with ileostomy		N = 4116	OR 0.9 (95%CI 0.74, 1.17) compared to no COPD	

Study Year PMID Country Funding	Design	Outcome	Arm/Subgroup	Arm/Subgroup Details	Age Sex	n/N (%)	Effect Size	Reported P Value
Lidor, 2010, 20878256, USA Non- industry	Single group (Retrospective)	AE - Major cardiac event Complications, Acute myocardial infarction	Elective surgery (all)	Left colectomy with ileostomy	73.9 (5.9) 28.9% male	594/22752 (2.5)		
			Elective surgery (Age 65-69)	Left colectomy with ileostomy		N = 6622	reference	
			Elective surgery (Age 70-74)	Left colectomy with ileostomy		N = 6817	OR 1.1 (95%CI 0.87, 1.45)	
			Elective surgery (Age 75-79)	Left colectomy with ileostomy		N = 5336	OR 1.4 (95%CI 1.12, 1.85)	
			Elective surgery (Age 80-84)	Left colectomy with ileostomy		N = 2816	OR 2.2 (95%CI 1.59, 3.09)	
			Elective surgery (Age 85+)	Left colectomy with ileostomy		N = 1161	OR 1.7 (95%CI 1.28, 2.24)	
			Elective surgery (CHF)	Left colectomy with ileostomy		N = 1486	OR 4.6 (95%CI 3.68, 5.74) compared to no CHF	
			Elective surgery (COPD)	Left colectomy with ileostomy		N = 4116	OR 0.9 (95%CI 0.76, 1.20) compared to no COPD	

Study Year PMID Country Funding	Design	Outcome	Arm/Subgroup	Arm/Subgroup Details	Age Sex	n/N (%)	Effect Size	Reported P Value
Lidor, 2010, 20878256, USA Non- industry	Single group (Retrospective)	AE - Infection requiring Abx Respiratory tract complications, Acute bacterial pneumonia, Acute respiratory failure	Elective surgery (all)	Left colectomy with ileostomy	73.9 (5.9) 28.9% male	1782/22752 (7.5)		
			Elective surgery (Age 65-69)	Left colectomy with ileostomy		N = 6622	reference	
			Elective surgery (Age 70-74)	Left colectomy with ileostomy		N = 6817	OR 1.1 (95%CI 0.98, 1.33)	
			Elective surgery (Age 75-79)	Left colectomy with ileostomy		N = 5336	OR 1.5 (95%CI 1.32, 1.80)	
			Elective surgery (Age 80-84)	Left colectomy with ileostomy		N = 2816	OR 1.9 (95%CI 1.60, 2.22)	
			Elective surgery (Age 85+)	Left colectomy with ileostomy		N = 1161	OR 2.8 (95%CI 2.26, 3.40)	
			Elective surgery (CHF)	Left colectomy with ileostomy		N = 1486	OR 4.2 (95%CI 3.59, 4.85) compared to no CHF	
			Elective surgery (COPD)	Left colectomy with ileostomy		N = 4116	OR 2.2 (95%CI 1.94, 2.50) compared to no COPD	

Study Year PMID Country Funding	Design	Outcome	Arm/Subgroup	Arm/Subgroup Details	Age Sex	n/N (%)	Effect Size	Reported P Value
Lidor, 2010, 20878256, USA Non- industry	Single group (Retrospective)	AE – Sepsis Postoperative SIRS, sepsis, or Septicemia	Elective surgery (all)	Left colectomy with ileostomy	73.9 (5.9) 28.9% male	495/22752 (2.08)		
			Elective surgery (Age 65-69)	Left colectomy with ileostomy		N = 6622	reference	
			Elective surgery (Age 70-74)	Left colectomy with ileostomy		N = 6817	OR 1.1 (95%CI 0.81, 1.48)	
			Elective surgery (Age 75-79)	Left colectomy with ileostomy		N = 5336	OR 1.6 (95%CI 1.23, 2.19)	
			Elective surgery (Age 80-84)	Left colectomy with ileostomy		N = 2816	OR 2.3 (95%CI 1.69, 3.14)	
			Elective surgery (Age 85+)	Left colectomy with ileostomy		N = 1161	OR 3.5 (95%CI 2.47, 4.98)	
			Elective surgery (CHF)	Left colectomy with ileostomy		N = 1486	OR 3.2 (95%CI 2.53, 4.35) compared to no CHF	
			Elective surgery (COPD)	Left colectomy with ileostomy		N = 4116	OR 1.1 (95%CI 0.82, 1.38) compared to no COPD	
Lidor, 2010, 20878256, USA Non- industry	Single group (Retrospective)	AE – DVT Acute pulmonary embolism or Acute deep vein thrombosis	Elective surgery (all)	Left colectomy with ileostomy	73.9 (5.9) 28.9% male	259/22752 (1.09)		
			Elective surgery (Age 65-69)	Left colectomy with ileostomy		N = 6622	reference	
			Elective surgery (Age 70-74)	Left colectomy with ileostomy		N = 6817	OR 1.0 (95%CI 0.72, 1.46)	

Study Year PMID Country Funding	Design	Outcome	Arm/Subgroup	Arm/Subgroup Details	Age Sex	n/N (%)	Effect Size	Reported P Value
			Elective surgery (Age 75-79)	Left colectomy with ileostomy		N = 5336	OR 1.3 (95%CI 0.90, 1.83)	
			Elective surgery (Age 80-84)	Left colectomy with ileostomy		N = 2816	OR 2.3 (95%CI 1.69, 3.14)	
			Elective surgery (Age 85+)	Left colectomy with ileostomy		N = 1161	OR 1.3 (95%CI 0.72, 2.30)	
			Elective surgery (CHF)	Left colectomy with ileostomy		N = 1486	OR 1.6 (95%CI 1.00, 2.43) compared to no CHF	
			Elective surgery (COPD)	Left colectomy with ileostomy		N = 4116	OR 1.0 (95%CI 0.71, 1.42) compared to no COPD	
Lidor, 2010, 20878256, USA Non- industry	Single group (Retrospective)	AE - Return to OR or unplanned procedure Colostomy	Elective surgery (all)	Left colectomy with ileostomy	73.9 (5.9) 28.9% male	2071/22752 (9.1)		
			Elective surgery (Age 65-69)	Left colectomy with ileostomy		N = 6622	reference category	
			Elective surgery (Age 70-74)	Left colectomy with ileostomy		N = 6817	OR 1.1 (95%CI 0.98, 1.29)	
			Elective surgery (Age 75-79)	Left colectomy with ileostomy		N = 5336	OR 1.1 (95%CI 1.28, 1.68)	
			Elective surgery (Age 80-84)	Left colectomy with ileostomy		N = 2816	OR 2.2 (95%CI 1.92, 2.58)	
			Elective surgery (Age 85+)	Left colectomy with ileostomy		N = 1161	OR 4.3 (95%CI 3.69, 5.29)	

Study Year PMID Country Funding	Design	Outcome	Arm/Subgroup	Arm/Subgroup Details	Age Sex	n/N (%)	Effect Size	Reported P Value
			Elective surgery (CHF)	Left colectomy with ileostomy		N = 1486	OR 1.1 (95%CI 0.98, 1.25) compared to no CHF	
			Elective surgery (COPD)	Left colectomy with ileostomy		N = 4116	OR 1.9 (95%CI 1.68, 2.27) compared to no COPD	
Lidor, 2010, 20878256, USA Non- industry	Single group (Retrospective)	AE - Return to OR or unplanned procedure Ileostomy	Elective surgery (all)	Left colectomy with ileostomy	73.9 (5.9) 28.9% male	3006/23764 (12.7)		
			Elective surgery (Age 65-69)	Left colectomy with ileostomy		N = 6622	reference category	
			Elective surgery (Age 70-74)	Left colectomy with ileostomy		N = 6817	OR 1.3 (95%CI 1.05, 1.74)	
			Elective surgery (Age 75-79)	Left colectomy with ileostomy		N = 5336	OR 1.9 (95%CI 1.42, 2.52)	
			Elective surgery (Age 80-84)	Left colectomy with ileostomy		N = 2816	OR 1.4 (95%CI 1.11, 1.90)	
			Elective surgery (Age 85+)	Left colectomy with ileostomy		N = 1161	OR 1.0 (95%CI 0.59, 1.61)	
			Elective surgery (CHF)	Left colectomy with ileostomy		N = 1486	OR 1.2 (95%CI 0.88, 1.77) compared to no CHF	
			Elective surgery (COPD)	Left colectomy with ileostomy		N = 4116	OR 1.1 (95%CI 0.87, 1.41) compared to no COPD	

Study Year PMID Country Funding	Design	Outcome	Arm/Subgroup	Arm/Subgroup Details	Age Sex	n/N (%)	Effect Size	Reported P Value
Lidor, 2010, 20878256, USA Non- industry	Single group (Retrospective)	AE - Return to OR or unplanned procedure Ileostomy	Elective surgery (all)	Left colectomy with ileostomy	73.9 (5.9) 28.9% male	470/22752 (1.98)		
			Elective surgery (Age 65-69)	Left colectomy with ileostomy		N = 6622	reference	
			Elective surgery (Age 70-74)	Left colectomy with ileostomy		N = 6817	OR 1.0 (95%CI 0.75, 1.32)	
			Elective surgery (Age 75-79)	Left colectomy with ileostomy		N = 5336	OR 1.4 (95%CI 1.09, 1.80)	
			Elective surgery (Age 80-84)	Left colectomy with ileostomy		N = 2816	OR 1.1 (95%CI 0.82, 1.60)	
			Elective surgery (Age 85+)	Left colectomy with ileostomy		N = 1161	OR 1.1 (95%CI 0.74, 1.72)	
			Elective surgery (CHF)	Left colectomy with ileostomy		N = 1486	OR 1.5 (95%CI 1.01, 2.11) compared to no CHF	
			Elective surgery (COPD)	Left colectomy with ileostomy		N = 4116	OR 0.8 (95%CI 0.63, 1.11) compared to no COPD	
Moghadamyeghaneh, 2015, 26116319, ACS-NSQIP 2012- 13, USA Not reported	Single group (Retrospective)	AE – 30-day mortality	Elective surgery	Open (28%) Laparoscopic (72%)	58 (12) 45.9% male	20/9788 (0.2)		
Moghadamyeghaneh, 2015, 26116319, ACS-NSQIP 2012- 13, USA Not reported	Single group (Retrospective)	AE - Major cardiac event Myocardial infarction	Elective surgery	Open (28%) Laparoscopic (72%)	58 (12) 45.9% male	20/9788 (0.2)		

Study Year PMID Country Funding	Design	Outcome	Arm/Subgroup	Arm/Subgroup Details	Age Sex	n/N (%)	Effect Size	Reported P Value
Moghadamyeghaneh, 2015, 26116319, ACS-NSQIP 2012-13, USA Not reported	Single group (Retrospective)	AE - Major cardiac event Cardiac arrest	Elective surgery	Open (28%) Laparoscopic (72%)	58 (12) 45.9% male	10/9788 (0.1)		
Moghadamyeghaneh, 2015, 26116319, ACS-NSQIP 2012-13, USA Not reported	Single group (Retrospective)	AE - Major pulmonary event Pulmonary embolism	Elective surgery	Open (28%) Laparoscopic (72%)	58 (12) 45.9% male	29/9788 (0.3)		
Moghadamyeghaneh, 2015, 26116319, ACS-NSQIP 2012-13, USA Not reported	Single group (Retrospective)	AE - Reintubation Unplanned intubation	Elective surgery	Open (28%) Laparoscopic (72%)	58 (12) 45.9% male	49/9788 (0.5)		
Moghadamyeghaneh, 2015, 26116319, ACS-NSQIP 2012-13, USA Not reported	Single group (Retrospective)	AE - Return to OR or unplanned procedure	Elective surgery	Open (28%) Laparoscopic (72%)	58 (12) 45.9% male	401/9788 (4.1)		
Moghadamyeghaneh, 2015, 26116319, ACS-NSQIP 2012-13, USA Not reported	Single group (Retrospective)	AE - Sepsis Septic shock	Elective surgery	Open (28%) Laparoscopic (72%)	58 (12) 45.9% male	59/9788 (0.6)		
Moghadamyeghaneh, 2015, 26116319, ACS-NSQIP 2012-13, USA Not reported	Single group (Retrospective)	AE - Unplanned (re)hospitalization (CD IV)	Elective surgery	Open (28%) Laparoscopic (72%)	58 (12) 45.9% male	715/9788 (7.3)		
Novitsky, 2009, 18639223, Nationwide Inpatient Sample (2001-2002), USA Non-industry	Single group (Retrospective)	Surgery for diverticulitis colostomy	Elective surgery	Left colectomy/Left colectomy with ostomy/Left colectomy with ileostomy	67.1 (13.8) 41.8% male	213/3716 (6)		

Study Year PMID Country Funding	Design	Outcome	Arm/Subgroup	Arm/Subgroup Details	Age Sex	n/N (%)	Effect Size	Reported P Value
Novitsky, 2009, 18639223, Nationwide Inpatient Sample (2001-2002), USA Non-industry	Single group (Retrospective)	Morbidity	Elective surgery	Left colectomy/Left colectomy with ostomy/Left colectomy with ileostomy	67.1 (13.8) 41.8% male	557/3716 (15)		
Papageorge, 2016, 27120447, ACS- NSQIP 2005-13, USA Not reported	Single group (Retrospective)	AE - 30-day mortality	Elective surgery	Laparoscopic approach and ostomy creation	<50 years 24.2% to 29.7%, 65+ years 2	115/29893 (0.4)		
Papageorge, 2016, 27120447, ACS- NSQIP 2005-13, USA Not reported	Single group (Retrospective)	AE - Sepsis	Elective surgery	Laparoscopic approach and ostomy creation	<50 years 24.2% to 29.7%, 65+ years 2	878/29893 (2.9)		
Papageorge, 2016, 27120447, ACS- NSQIP 2005-13, USA Not reported	Single group (Retrospective)	AE - Major cardiac event Myocardial Infarction	Elective surgery	Laparoscopic approach and ostomy creation	<50 years 24.2% to 29.7%, 65+ years 2	76/29893 (0.3)		
Papageorge, 2016, 27120447, ACS- NSQIP 2005-13, USA Not reported	Single group (Retrospective)	AE - Major pulmonary event Pulmonary embolism	Elective surgery	Laparoscopic approach and ostomy creation	<50 years 24.2% to 29.7%, 65+ years 2	124/29893 (0.4)		
Papageorge, 2016, 27120447, ACS- NSQIP 2005-13, USA Not reported	Single group (Retrospective)	AE - Reintubation	Elective surgery	Laparoscopic approach and ostomy creation	<50 years 24.2% to 29.7%, 65+ years 2	233/29893 (0.8)		

Study Year PMID Country Funding	Design	Outcome	Arm/Subgroup	Arm/Subgroup Details	Age Sex	n/N (%)	Effect Size	Reported P Value
Papageorge, 2016, 27120447, ACS- NSQIP 2005-13, USA Not reported	Single group (Retrospective)	AE - Major cardiac event Cardiac arrest	Elective surgery	Laparoscopic approach and ostomy creation	<50 years 24.2% to 29.7%, 65+ years 2	43/29893 (0.1)		
Pessaux, 2004, 14639493, French Association for Surgical Research, France Not reported	Single group (Retrospective)	AE - 30-day mortality	Elective surgery	Laparotomy for colon or rectal resection for diverticulitis	<58 years 37.5%, 59-75 years 45.8%, >76 years 16.7% 46.6% male	7/582 (1.2)		
Pessaux, 2004, 14639493, French Association for Surgical Research, France Not reported	Single group (Retrospective)	AE - Return to OR or unplanned procedure anastomotic leakage	Elective surgery	Laparotomy for colon or rectal resection for diverticulitis	<58 years 37.5%, 59-75 years 45.8%, >76 years 16.7% 46.6% male	9/582 (1.5)		
Pessaux, 2004, 14639493, French Association for Surgical Research, France Not reported	Single group (Retrospective)	AE - Major pulmonary event pulmonary edema	Elective surgery	Laparotomy for colon or rectal resection for diverticulitis	<58 years 37.5%, 59-75 years 45.8%, >76 years 16.7% 46.6% male	10/582 (1.7)		

Study Year PMID Country Funding	Design	Outcome	Arm/Subgroup	Arm/Subgroup Details	Age Sex	n/N (%)	Effect Size	Reported P Value
Pessaux, 2004, 14639493, French Association for Surgical Research, France Not reported	Single group (Retrospective)	AE - Stroke	Elective surgery	Laparotomy for colon or rectal resection for diverticulitis	<58 years 37.5%, 59-75 years 45.8%, >76 years 16.7% 46.6% male	3/582 (0.5)		
Pessaux, 2004, 14639493, French Association for Surgical Research, France Not reported	Single group (Retrospective)	AE - Major cardiac event myocardial infarction	Elective surgery	Laparotomy for colon or rectal resection for diverticulitis	<58 years 37.5%, 59-75 years 45.8%, >76 years 16.7% 46.6% male	5/582 (0.9)		
Pessaux, 2004, 14639493, French Association for Surgical Research, France Not reported	Single group (Retrospective)	AE - DVT	Elective surgery	Laparotomy for colon or rectal resection for diverticulitis	<58 years 37.5%, 59-75 years 45.8%, >76 years 16.7% 46.6% male	4/582 (0.7)		

Study Year PMID Country Funding	Design	Outcome	Arm/Subgroup	Arm/Subgroup Details	Age Sex	n/N (%)	Effect Size	Reported P Value
Pessaux, 2004, 14639493, French Association for Surgical Research, France Not reported	Single group (Retrospective)	AE - Major pulmonary event Pulmonary embolism	Elective surgery	Laparotomy for colon or rectal resection for diverticulitis	<58 years 37.5%, 59-75 years 45.8%, >76 years 16.7% 46.6% male	1/582 (0.2)		
Pessaux, 2004, 14639493, French Association for Surgical Research, France Not reported	Single group (Retrospective)	AE - Major pulmonary event pneumonia	Elective surgery	Laparotomy for colon or rectal resection for diverticulitis	<58 years 37.5%, 59-75 years 45.8%, >76 years 16.7% 46.6% male	26/582 (4.5)		
Pessaux, 2004, 14639493, French Association for Surgical Research, France Not reported	Single group (Retrospective)	AE - Infection requiring Abx Urinary tract infection	Elective surgery	Laparotomy for colon or rectal resection for diverticulitis	<58 years 37.5%, 59-75 years 45.8%, >76 years 16.7% 46.6% male	29/582 (5.0)		

Study Year PMID Country Funding	Design	Outcome	Arm/Subgroup	Arm/Subgroup Details	Age Sex	n/N (%)	Effect Size	Reported P Value
Pessaux, 2004, 14639493, French Association for Surgical Research, France Not reported	Single group (Retrospective)	AE - Infection requiring Abx Urinary tract infection	Elective surgery	Laparotomy for colon or rectal resection for diverticulitis	<58 years 37.5%, 59-75 years 45.8%, >76 years 16.7% 46.6% male	5/582 (1.8)		
Pessaux, 2004, 14639493, French Association for Surgical Research, France Not reported	Single group (Retrospective)	AE - Acute Renal Failure	Elective surgery	Laparotomy for colon or rectal resection for diverticulitis	<58 years 37.5%, 59-75 years 45.8%, >76 years 16.7% 46.6% male	4/582 (0.7)		
Pessaux, 2004, 14639493, French Association for Surgical Research, France Not reported	Single group (Retrospective)	AE - Sepsis (CD IV)	Elective surgery	Laparotomy for colon or rectal resection for diverticulitis	<58 years 37.5%, 59-75 years 45.8%, >76 years 16.7% 46.6% male	9/582 (1.5)		

Study Year PMID Country Funding	Design	Outcome	Arm/Subgroup	Arm/Subgroup Details	Age Sex	n/N (%)	Effect Size	Reported P Value
Pessaux, 2004, 14639493, French Association for Surgical Research, France Not reported	Single group (Retrospective)	AE- Morbidity	Elective surgery	Laparotomy for colon or rectal resection for diverticulitis	<58 years 37.5%, 59-75 years 45.8%, >76 years 16.7% 46.6% male	145/582 (24.9)		
Pessaux, 2004, 14639493, French Association for Surgical Research, France Not reported	Single group (Retrospective)	AE - Infection requiring Abx Deep infection	Elective surgery	Laparotomy for colon or rectal resection for diverticulitis	<58 years 37.5%, 59-75 years 45.8%, >76 years 16.7% 46.6% male	13/582 (1.4)		
Russ, 2010, 20193685, ACS- NSQIP 2005-08, USA Not reported	Single group (Retrospective)	AE - 30-day mortality	Elective surgery	Open	59.2 46.9% male	14/3502 (0.4)		0.0004
			Elective surgery	Laparoscopic	55.6 49.1% male	38/3468 (1.1)		
Russ, 2010, 20193685, ACS- NSQIP 2005-08, USA Not reported	Single group (Retrospective)	AE - Bleed requiring transfusion	Elective surgery	Open	59.2 46.9% male	32/3502 (0.9)		<0.0001
				Laparoscopic	55.6 49.1% male	232/3468 (6.7)		

Study Year PMID Country Funding	Design	Outcome	Arm/Subgroup	Arm/Subgroup Details	Age Sex	n/N (%)	Effect Size	Reported P Value
Russ, 2010, 20193685, ACS- NSQIP 2005-08, USA Not reported	Single group (Retrospective)	AE - Sepsis	Elective surgery	Open	59.2 46.9% male	77/3502 (2.2)	OR 0.659 (95%CI 0.48, 0.90) favors laparoscopic	<0.0001
				Laparoscopic	55.6 49.1% male	156/3468 (4.5)		
Russ, 2010, 20193685, ACS- NSQIP 2005-08, USA Not reported	Single group (Retrospective)	AE - Sepsis Septic shock	Elective surgery	Open	59.2 46.9% male	77/3502 (2.2)	OR 0.44 (95%CI 0.26, 0.76) favors laparoscopic	<0.0001
				Laparoscopic	55.6 49.1% male	156/3468 (4.5)		
Russ, 2010, 20193685, ACS- NSQIP 2005-08, USA Not reported	Single group (Retrospective)	AE - Major pulmonary event Pulmonary embolism	Elective surgery	Open	59.2 46.9% male	11/3502 (0.3)	0.49 (95%CI 0.23, 1.05) favors laparoscopic	0.039
				Laparoscopic	55.6 49.1% male	28/3468 (0.8)		
Valizadeh, 2018, 30747633, ACS- NSQIP 2012-13, USA Not reported	Single group (Retrospective)	AE - Sepsis	Elective surgery		>65 years 31.5%	64/2444 (2.6)		
Valizadeh, 2018, 30747633, ACS- NSQIP 2012-13, USA Not reported	Single group (Retrospective)	AE - Sepsis Septic shock	Elective surgery		>65 years 31.5%	17/2444 (0.7)		
Valizadeh, 2018, 30747633, ACS- NSQIP 2012-13, USA Not reported	Single group (Retrospective)	AE - Return to OR or unplanned procedure	Elective surgery		>65 years 31.5%	108/2444 (4.4)		

Study Year PMID Country Funding	Design	Outcome	Arm/Subgroup	Arm/Subgroup Details	Age Sex	n/N (%)	Effect Size	Reported P Value
Valizadeh, 2018, 30747633, ACS- NSQIP 2012-13, USA Not reported	Single group (Retrospective)	AE - DVT	Elective surgery		>65 years 31.5%	12/2444 (0.5)		
Valizadeh, 2018, 30747633, ACS- NSQIP 2012-13, USA Not reported	Single group (Retrospective)	AE - Major cardiac event Myocardial infarction	Elective surgery		>65 years 31.5%	7/2444 (0.3)		
Valizadeh, 2018, 30747633, ACS- NSQIP 2012-13, USA Not reported	Single group (Retrospective)	AE - Infection requiring Abx Urinary tract infection	Elective surgery		>65 years 31.5%	51/2444 (2.1)		
Valizadeh, 2018, 30747633, ACS- NSQIP 2012-13, USA Not reported	Single group (Retrospective)	AE - Infection requiring Abx Pneumonia	Elective surgery		>65 years 31.5%	20/2444 (0.8)		
Varma, 2019, 30527478, California State Inpatient Database 2005-13, USA Non-industry	Single group (Retrospective)							