National Institute for Health and Care Excellence

Final

Diverticular disease: diagnosis and management

[J] Evidence review for timing of surgery for complicated acute diverticulitis

NICE guideline NG147

Intervention evidence review

November 2019

Final

This evidence review was developed by the National Guideline Centre

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1 Management of acute diverticulitis

1.1 Review question: What is the most appropriate time for surgery in people with complicated acute diverticulitis?

1.2 Introduction

Over the last decade there have been marked changes in the surgical management of patients with complications of acute complicated diverticular disease. Resections are now frequently undertaken laparoscopically with the use of laparoscopic lavage in the emergency setting. The thresholds for elective resection after recurrent episodes of acute diverticulitis have changed with a greater focus on tailored decision making with the patient. There have been alterations to the threshold for primary anastomosis especially in the emergency setting. This review of the evidence aimed to provide information for both clinicians and patient on what were the clinically and cost effective surgical approaches to the management of acute complicated diverticular disease.

1.3 PICO table

For full details see the review protocol in appendix A.

Table 1: PICO characteristics of review question

Population	Adults 18 years and over with complicated acute diverticulitis
Interventions	Elective surgery Emergency surgery
Comparisons	Compared to each other No surgical intervention

Outcomes	Critical outcomes:
	• Quality of life
	• Mortality
	• Morbidity
	• Progression of disease
	• Complications:
	  ○ infections
	  ○ abscesses
	  ○ perforation
	  ○ fistula
	  ○ stricture
	• Recurrence rates of acute diverticulitis
	• Hospitalisation
	• Need for further surgery
	
	Important outcomes:
	• Symptom control/recurrence, for example pain relief, bowel habit

Study design	Randomised controlled trials (RCTs), systematic reviews of RCTs. If no RCT evidence is available, search for observational studies

1.4 Clinical evidence

1.4.1 Included studies

Eight studies were included in the review; [18, 29, 47, 131, 165, 174, 177, 183] these are summarised in Table 2 below. Evidence from these studies is summarised in the clinical evidence summary below (Tables 3-8).

The review was stratified by diverticular complication. There were three studies included in the abscess strata[18, 29, 47, 165], one in fistula[131], one in stricture[165] and three in the overall strata.[174, 177, 183]

See also the study selection flow chart in appendix C, study evidence tables in appendix D, forest plots in appendix E and GRADE tables in appendix F.

1.4.2 Excluded studies

See the excluded studies list in appendix I.

1.4.3 Summary of clinical studies included in the evidence review

Table 2: Summary of studies included in the evidence review

Study	Intervention and comparison	Population	Outcomes	Concomitant treatments/ Comments	Patient selection for intervention
Bachmann 2011[18] Non-randomised study n= 421	**Emergency surgery**: defined as early elective surgery in this study. Performed at median of 2 days post-admission. **Elective surgery:** defined as delayed elective surgery in this study. Performed at 6-8 weeks post admission.	Patients aged 18 years and over with diverticulitis complicated by abscess (Hinchey stages I and II). Confirmed by CT scan.	Mortality Morbidity Complications (infections) Need for further surgery	Emergency: Antibiotics received at admission until surgery performed. Elective: Received 5-7 days antibiotic course on admission.	Emergency: • Mean age, 63.5±13.1 years. • Elective: Mean age, 64.2±12.6 years. Similar disease severity (proportion of Hinchey I and II cases) and comorbidity (ASA grades 1-4) between groups. Assigned to groups based on clinical data, surgeon preference and medical condition of patient.
Buchwald 2017[29] Non-randomised study n=107	**Elective surgery:** does not specify timeframe within which elective surgery was performed relative to admission. **No surgical intervention:** Study included two groups that it considered to represent conservative	Patients aged 18 years and over with diverticulitis complicated by abscess (Hinchey stages I and II). Diverticulitis diagnosed in all patients by CT scan. Clinical findings, blood tests,	Recurrence rates of acute diverticulitis	Some patients in the cohort were being treated with NSAIDs or steroids, or receiving treatment for diabetes. Does not specify the total number in each treatment arm.	Elective surgery: • Mean age, 65.5±13.4 years. No surgery: • Mean age, 64.2±17.2 years. Treatment at discretion of surgeon – possible more

Study	Intervention and comparison	Population	Outcomes	Concomitant treatments/ Comments	Patient selection for intervention
	treatment: antibiotics alone and percutaneous drainage + antibiotics. These two groups were combined. No details given for the timing/type/dose of antibiotics used.	endoscopic and/or surgical finding and radiology also used for diagnosis.			severe cases selected for surgery. 'No differences in immunosuppression'. No details for other comorbidities between groups.
Elagili 2015[47] Non-randomised study N=146	**Emergency surgery:** Sigmoidectomy done within 24-28 hrs after admission due to clinical deterioration in spite of initial diverticular abscess treatment **Elective surgery:** Planned operation typically carried out 4-6 wks after symptomatic relief following initial abscess treatment	Strata: Abscess Patients with an abscess of at least 3 cm diameter undergoing surgery for pathology-proven sigmoid diverticulitis admitted 1994-2012 Exclusion: Requirement for urgent or emergent surgery decided immediately following admission	Mortality Morbidity	Antibiotics: Wide-spectrum intravenous antibiotics progressively switched to oral preparations for a total treatment course of 1-3 weeks Percutaneous drainage: Plus antibiotics as above	No demographics reported for emergency vs elective surgery Retrospective review – surgeons decided which intervention.
Radwan 2013[131] Non-randomised study n=53	**Elective surgery:** does not specify timeframe within which elective surgery was performed relative to admission. **No surgical intervention:** defined as conservative treatment. 5 patients in the conservative group were	Strata: Fistula Patients aged 18 years and over with fistula secondary to diverticular disease. Fistula confirmed by contrast enema CT scan in 92% of cases in the total cohort of the study, which	Mortality	Study cohort consisted of patients with fistula secondary to various conditions, but outcomes were given separately for those secondary to diverticular disease and these were extracted.	Elective surgery: • Mean age (range): 69 (42-90) years. No surgery: • Mean age (range): 76 (39-87) years. ASA grading proportions differed between the two

Study	Intervention and comparison	Population	Outcomes	Concomitant treatments/ Comments	Patient selection for intervention
	prescribed long-term low-dose antibiotics for management of fistulas. No details of treatment for the remaining patients in this group.	consisted of fistula secondary to various conditions, but does not specify this specifically for patients with fistula secondary to diverticular disease. No details for the method of diverticular disease diagnosis.			groups: • ASA 1 and 2: 78% in elective and 38% in no surgery. • ASA 3 and 4: 22% in elective and 62% in no surgery. Retrospective review – surgeons decided which intervention.
Tudor 1994[165] Non-randomised study n=300	**Emergency surgery:** does not specify timeframe within which emergency surgery was performed relative to admission. **No surgical intervention:** defined as 'no operation' in this study. No other details.	Strata: Abscess and Stricture Patients aged 18 years and over with complicated diverticular disease. Complications extracted included acute phlegmon, pericolic abscess and bowel obstruction. Diagnosed clinically on emergency admission.	Mortality	Procedures this study considered to be surgical were: laparotomy alone, drainage alone, loop stoma, Hartmann's procedure, and resection and primary anastomosis with or without a stoma. Two different strata in the study: abscess and stricture. Abscess strata included abscess and phlegmon groups. Stricture strata included the bowel obstruction group.	Age only given for whole cohort, not specific complications or interventions: • Median age (range), 68 (31-94) years. No details of co-morbidities in the two intervention groups (for specific complications or for the whole cohort). No details regarding how patients were assigned to each group – likely to have been surgeon/specialist preference/based on overall health?
Vinas-salas 2001[174] Non-	**Emergency surgery** **Elective surgery** Does not specify	Strata: overall Patients aged 18 years and over with	Morbidity		Average age (unclear if mean or median): • Men, 53 (34-84) years

Study	Intervention and comparison	Population	Outcomes	Concomitant treatments/ Comments	Patient selection for intervention
randomised study n=353	timeframe within which emergency/elective surgery was performed relative to admission.	complicated diverticular disease. Method of diagnosis not reported.			• Women, 62 (36-92) years. Note that this age includes those in the cohort with recurrent cases, and we extracted outcomes only for those without previous episodes. Age was not given for each intervention or for those that had not experienced previous episodes. No details of comorbidities or the way in which patients were assigned to emergency/elective surgery.
Warwas 2018[177] Non-randomised study N=378	**Early elective surgery:** People who had been hospitalised for the treatment of an acute attack of diverticular disease by the hospital's outpatient department. All surgery took place within this hospitalisation. Mean time to surgery not reported. **Elective surgery:**	Strata: Overall People who underwent elective laparoscopic sigmoid resection due to diverticulitis during 2008 and 2012	Mortality Bleeding	Early elective surgery: Received pre-operative antibiotic for a median of 8 days (IQR 3).	Emergency surgery: Mean age 63.6 yrs, comorbidities ASA median 2 (IQR2), CCI median 0 (IQR 0) Elective surgery: Mean age 61.9 yrs, comorbidities ASA median 2 (IQR2), CCI median 0 (IQR 0) Patient selection based on symptoms

Study	Intervention and comparison	Population	Outcomes	Concomitant treatments/ Comments	Patient selection for intervention
	Referred to hospital by a GP to evaluate whether operative treatment for diverticular disease or not. At the time of admission, these patients did not suffer from any symptoms of an acute attack. Time to surgery at least 4 to six weeks after their diverticulitis episode had abated				
Zingg 2007[183] Non-randomised study n=178	**Emergency surgery:** defined as early elective surgery performed during the same hospitalisation as the acute episode. Mean time to surgery was 7 days (range 1-16 days). **Elective surgery:** defined as delayed elective surgery after a minimum of 6 weeks in a second hospitalisation. Mean time to surgery was 13 weeks (range 6-87 weeks).	Strata: overall Patients aged 18 years and over with complicated acute diverticulitis. Acute diverticulitis diagnosed by clinical examination, laboratory tests such as C-reactive protein and leucocytes, and abdominal triple contrast CT scan in all patients.	Mortality Morbidity	Study reports data for uncomplicated and complicated diverticulitis, but outcomes were given separately for the complicated cases and these were extracted All patients received initial antibiotic therapy, antibiotic type depended on renal function.	Mean age: • Emergency: 60.7±12.5 years • Elective: 60.8±11.9 years. Mean ASA score similar between groups: 1.73 in emergency and 1.77 in elective (range for both was 1-3). Age and ASA score for complicated and uncomplicated cases combined. Mean age not given separately for complicated subpopulation.

Study	Intervention and comparison	Population	Outcomes	Concomitant treatments/ Comments	Patient selection for intervention
					Timing of surgery based on surgeon/patient preference. Surgeon generally offered both alternatives so patient made definitive decision.

See appendix D for full evidence tables.

1.4.4 Quality assessment of clinical studies included in the evidence review

1.4.4.1 Overall stratum

Table 3: Clinical evidence summary: emergency surgery compared to elective surgery

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Elective surgery	Risk difference with Overall Strata: emergency (95% CI)
Mortality at 30 days	347 (2 studies) 30 days	⨁⊖⊖⊖ VERY LOW[b,c] due to risk of bias, imprecision	Not estimable	Moderate	
				0 per 1000	0 fewer per 1000 (from 2 fewer to 2 more)[a]
Morbidity	104 (2 studies)	⨁⊖⊖⊖ VERY LOW[b] due to risk of bias	OR 4.64 (1.58 to 13.68)	Moderate	
				39 per 1000	119 more per 1000 (from 21 more to 318 more)
Bleeding	378 (1 study)	⨁⊖⊖⊖ VERY LOW[b,d] due to risk of bias, imprecision	RR 1.67 (0.62 to 4.47)	Moderate	
				36 per 1000	24 more per 1000 (from 14 fewer to 125 more)

[a]Risk difference (95% CI) calculated as 0 events in both arms

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Elective surgery	Risk difference with Overall Strata: emergency (95% CI)

[b]Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[c]Risk difference (95% CI) analysis method was used as there were zero events in both arms, and sample size was <70.
[d]Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

1.4.4.2 Fistula stratum

Table 4: Clinical evidence summary: elective surgery compared to no surgical intervention

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with No intervention	Risk difference with Elective surgery (95% CI)
Mortality at 3 years	53 (1 study) 3 years	⨁⊖⊖⊖ VERY LOW[a,b] due to risk of bias, imprecision	RR 1.28 (0.76 to 2.16)	Moderate	
				462 per 1000	129 more per 1000 (from 111 fewer to 536 more)

[a]Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[b]Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

1.4.4.3 Abscess stratum

Table 5: Clinical evidence summary: emergency surgery compared to elective surgery

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Elective surgery	Risk difference with Abscess strata: emergency (95% CI)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Elective surgery	Risk difference with Abscess strata: emergency (95% CI)
Mortality (in-hospital)	413 (1 study) 5 years[a]	⨁⊖⊖⊖ VERY LOW[b,c] due to risk of bias, imprecision	OR 0.49 (0.03 to 9.2)	Moderate	
				7 per 1000	4 fewer per 1000 (from 7 fewer to 54 more)
Morbidity	413 (1 study) 5 years[a]	⨁⊖⊖⊖ VERY LOW[b,c] due to risk of bias, imprecision	RR 1.33 (0.77 to 2.28)	Moderate	
				114 per 1000	38 more per 1000 (from 26 fewer to 146 more)
Complications: infections	413 (1 study) 5 years[a]	⨁⊖⊖⊖ VERY LOW[b,c] due to risk of bias, imprecision	RR 1.56 (0.78 to 3.09)	Moderate	
				71 per 1000	40 more per 1000 (from 16 fewer to 148 more)
Need for further surgery	413 (1 study) 5 years[a]	⨁⊖⊖⊖ VERY LOW[b,c] due to risk of bias, imprecision	RR 1.43 (0.65 to 3.12)	Moderate	
				57 per 1000	25 more per 1000 (from 20 fewer to 121 more)
Mortality (antibiotics)	32 (1 study)	See comment	Not estimable	Moderate	
					0 fewer per 1000 (from 16 fewer to 16 more)[d]
Morbidity (antibiotics)	32 (1 study)	⨁⊖⊖⊖ VERY LOW[b] due to risk of bias	RR 3.60 (1.5 to 8.65)	Moderate	
				208 per 1000	541 more per 1000 (from 104 more to 1000 more)
Mortality (drainage)	114 (1 study)	⨁⊖⊖⊖ VERY LOW[b] due to risk of bias	RR 29.91 (1.6 to 558.23)	Moderate	
					140 more per 1000 (from 10 fewer to 300 more)[e]
Morbidity (drainage)	114 (1 study)	⨁⊖⊖⊖ VERY LOW[b] due to risk of bias	RR 2.46 (1.62 to 3.73)	Moderate	
				290 per 1000	423 more per 1000 (from 180 more to 792 more)

[a]Retrospective study assessing patient records over a 5 year period
[b]Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Elective surgery	Risk difference with Abscess strata: emergency (95% CI)
at very high risk of bias [c]Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs [d]Risk difference (95% CI) calculated as there were zero events in both arms [e]Risk difference was used as low event rate					

Table 6: Clinical evidence summary: elective surgery compared to no surgical intervention

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with No intervention	Risk difference with Elective surgery (95% CI)
Recurrence rates of acute diverticulitis	107 (1 study) 110 months	⨁⊖⊖⊖ VERY LOW[a] due to risk of bias	RR 0.16 (0.04 to 0.66)	Moderate	
				292 per 1000	245 fewer per 1000 (from 99 fewer to 280 fewer)
[a]Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias					

Table 7: Clinical evidence summary: emergency surgery compared to no surgical intervention

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with No intervention	Risk difference with Emergency surgery (95% CI)
30-day mortality (post-admission)	138 (1 study) 30 days	⨁⊖⊖⊖ VERY LOW[a,b] due to risk of bias, imprecision	RR 2.23 (0.56 to 8.97)	Moderate	
				38 per 1000	47 more per 1000 (from 17 fewer to 303 more)
[a]Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was					

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with No intervention	Risk difference with Emergency surgery (95% CI)
at very high risk of bias [b]Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs					

1.4.4.4 Stricture stratum

Table 8: Clinical evidence summary: emergency surgery compared to no surgical intervention

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with No intervention	Risk difference with emergency surgery (95% CI)
30-day mortality (post-admission)	31 (1 study) 30 days	⨁⊖⊖⊖ VERY LOW[a,b] due to risk of bias, imprecision	OR 3.28 (0.05 to 219.76)	Moderate	
				0 per 1000	70 more per 1000 (from 210 fewer to 360 more)[c]
[a]Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias [b]Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs [c]Risk difference (95% CIs) reported as there are zero events in control arm.					

See appendix F for full GRADE tables.

1.5 Economic evidence

1.5.1 Included studies

Two health economic studies were identified with the relevant comparison and have been included in this review.[18] [183] These are summarised in the health economic evidence profile below (Table 9) and the health economic evidence tables in appendix H.

1.5.2 Excluded studies

No health economic studies that were relevant to this question were excluded due to assessment of limited applicability or methodological limitations.

See also the health economic study selection flow chart in appendix G.

1.5.3 Summary of studies included in the economic evidence review

Table 9: Health economic evidence profile: Early versus delayed elective resection for complicated acute diverticulitis

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost effectiveness	Uncertainty
Bachmann 2011[18] (Germany)	Partially applicable[(a)]	Potentially serious limitations [(b)]	Cost consequences analysis within a non-randomised controlled trial. Clinical follow-up data obtained by review of hospital records and through direct communication with patients and physicians.	Early elective resection saves £1,329 per patient	**Mortality (in-hospital):** -4/1000 **Morbidity:** +38/1000 **Wound infection:** +40/1000 **Reoperation:**+25/1000	n/a	n/a
Zingg 2007 [183] (Switzerland)	Partially applicable[(c)]	Potentially serious limitations[(d)]	Retrospective analysis of individual level data for outcomes and invoice system of Zurich for data on costs. Cost components included all medical treatment, outpatient colonoscopy and intensive care days.	Early elective laparoscopically-assisted resection saves £204 per patient	**Mortality (30 days):** +0/1000 **Morbidity:** -137/1000	n/a	n/a

Abbreviations: ARD: absolute risk difference; n/a: not applicable; OR: odds ratio

(a) German health insurance company perspective

(b) Non-randomised allocation to treatment arms by surgeon, which could produce selection bias. Some clinical follow up data was obtained directly from patients and physicians and may be subject to recall bias. No cost year was reported, though the trial period was 2004-2009. Follow-up not reported for outcomes other than costs; no follow-up for costs, which were noted to include only the costs of the interventions. Costs did not include any visits to general practitioners either after the hospitalisations or between the two hospitalisations for the delayed resection group. No detailed analysis of direct cost to hospital undertaken. No quality of life outcome was assessed, deviating from the NICE reference case

(c) Switzerland hospital perspective

(d) Treatment effects from retrospective Zingg study only. No randomisation; the decision to undergo early or delayed surgery was made through shared decision making between the surgeon and person with acute diverticulitis, which could lead to selection bias. Follow-up not reported. Cost components not clearly defined. Outcome data based on those presenting 1997-2005; cost data derived from a subgroup presenting 2004-2005. Subgroup for cost analysis restricted to those who exclusively received all medical treatment at the institution, could lead to bias. People in the delayed group may have received initial conservative treatment of unknown type and duration outside of the institution. Percentage male not reported. No regression to account for baseline differences, though statistically significant difference in American Society of Anaesthesiologists score (no statistically significant differences in other baseline characteristics). More complicated cases in the early group (73% (n=56) in the early group compared with 13% (n=13) in the delayed group). No quality of life outcome was assessed, deviating from the NICE reference case.

1.5.4 Unit costs

The unit costs below were presented to the Committee, to aid consideration of cost effectiveness.

Table 10: NHS cost of non-elective sigmoid resection

Procedure (OPCS4)	Healthcare Resource Group (HRG) code and description	Unit Cost	Average Length of Stay	Source
Sigmoid colectomy and anastomosis	FF33 Distal Colon Procedures, 19 years and over, inclusive of non-elective short stay and non-elective long stay with excess bed days, weighted for complications and co morbidities for HRG codes: FF33A and FF33B; as recorded for Non-Elective Inpatients	£7,091	9.0 days	NHS Reference Costs 2016-2017
Sigmoid colectomy and ileostomy HFQ Or Sigmoid colectomy and exteriorisation of bowel NEC	FF31 Complex Large Intestine Procedures, 19 years and over, inclusive of non-elective short stay and non-elective long stay with excess bed days, weighted for complications and co morbidities for HRG codes: FF31A, FF31B, FF31C and FF31D; as recorded for Non-Elective Inpatients	£8,312	11.0 days	NHS Reference Costs 2016-2017

Table 11: NHS cost of elective sigmoid resection

	Currency Description	Unit Cost	Average Length of Stay	Source
Sigmoid colectomy and anastomosis	FF33 Distal Colon Procedures, 19 years and over, inclusive of excess bed days, weighted for complications and co morbidities for HRG codes: FF33A and FF33B; as recorded for Elective Inpatients	£6,487	5.2 days	NHS Reference Costs 2016-2017
Sigmoid colectomy and ileostomy HFQ Or Sigmoid colectomy and exteriorisation of bowel NEC	FF31 Complex Large Intestine Procedures, 19 years and over, inclusive of excess bed days, weighted for complications and co morbidities for HRG codes: FF31A, FF31B, FF31C and FF31D; as recorded for Elective Inpatients	£8,140	7.6 days	NHS Reference Costs 2016-2017
Closure of ileostomy	FF22 Major Small Intestine Procedures, 19 years and over, inclusive of excess bed days, weighted for complications and co morbidities for HRG codes: FF22A, FF22B, FF22C and FF22C; as recorded for Elective Inpatients	£5,151	5.97 days	NHS Reference Costs 2016-2017

1.6 Evidence statements

1.6.1 Clinical evidence statements

Overall strata

- Clinically important benefit for elective over emergency surgery was found in two small studies for morbidity (very low quality, n=104) and in a single study for bleeding (very low quality, n=378). No clinically important difference was seen in mortality when looking at 2 studies (very low quality, n=347).

Fistula stratum

- The only evidence included for this stratum was from a small single study looking at mortality at 3 years follow-up, which found a possible clinically important harm for elective surgery (very low quality, n=53).

Abscess stratum

- When comparing elective surgery with emergency surgery, clinically important benefit for elective surgery was seen in morbidity outcomes; one looking at surgery post-antibiotics treatment and the other post-percutaneous drainage (n=32 and 124 respectively, very low quality). No clinically important difference was seen for the other outcomes extracted for this comparison.
- Clinically important benefit of elective surgery was seen in the recurrent rates of acute diverticulitis when compared to no surgery for a single study (n=110, very low quality).
- Clinically important harm from emergency surgery was seen in the 30 day post-admission mortality rate when compared to no surgery in a single study (n=138, very low quality).

Stricture stratum

- Clinically important harm from emergency surgery was seen in the 30 day post-admission mortality rate when compared to no surgery in a single small study (n=31, very low quality).

1.6.2 Health economics evidence statements

Two cost-consequences analyses found that early surgery was cost saving compared with later surgery. The studies were inconsistent with regard to the impact on health outcomes. The studies were rated as partially applicable with potentially serious limitations.

1.7 The committee's discussion of the evidence

1.7.1 Interpreting the evidence

1.7.1.1 The outcomes that matter most

The guideline committee agreed that for this review quality of life, mortality, morbidity, progression of disease, recurrence rates of acute diverticulitis, hospitalisation, need for further surgery and complications (infection, abscess, perforation, fistula and stricture) were considered critical outcomes. The results from these would be given more weight when forming recommendations. Outcomes considered important were symptom control (for example pain relief and bowel habit) and recurrence.

In this review, no clinical evidence was identified for the following critical outcomes; progression of disease, abscess, perforation, fistula and stricture. There was no evidence identified for the important outcome symptom control.

1.7.1.2 The quality of the evidence

The evidence included in this review was of very low quality due to selection bias, performance bias and imprecision. The extent of selection bias was a big concern for the committee as it was likely people in the emergency surgery arm of the studies were more severely affected than those in the elective surgery arm. All the evidence was obtained from non-randomised studies, as there were no randomised controlled trials that matched the review protocol criteria.

1.7.1.3 Benefits and harms

While discussing the evidence presented in this evidence review, the committee expressed their concerns over the significant selection bias present across all of the outcomes. The assignment of interventions; emergency surgery, elective surgery or no intervention, was determined by surgeons based on the clinical presentation of the individuals for all of the studies included. Therefore, the groups of people compared within each trial may not have been comparable at baseline for severity of disease. Thus, the committee were unable to make a confident assessment of the clinical benefit or harm of the outcomes presented as they were unsure as to whether the observed effects were a result of the method used for patient assignment. For example, the committee were concerned that those selected for surgery, as opposed to conservative management, may have been those that the surgeons considered to be the most severe cases. Similarly, it was more likely that patients needing emergency surgery would have worse clinical outcomes as a result of their more negative health status compared with those able to wait for an elective (delayed) surgical procedure.

1.7.2 Cost effectiveness and resource use

The committee were informed by the current unit costs of elective inpatient and non-elective inpatient surgeries. The costs of non-elective operations were higher than the equivalent elective operations, which were associated with a shorter average length of stay.

Two published health economic studies addressing the timing of surgery were included and assessed as partially applicable with potentially serious limitations. The cost consequences analyses had German health insurance company and Swiss hospital perspectives. The committee noted that allocation of the people with acute diverticulitis to the arms of studies was by the operating surgeon or by shared decision making between the surgeon and patient, respectively. The committee felt that this method of allocation was likely to lead to more severe cases of acute diverticulitis being allocated to the early surgery arm, while more stable cases undergo delayed surgery. No statistically significant differences in baseline characteristics were reported in the study from the German health insurance company perspective, however, the study from the Swiss hospital perspective included people in the early surgery arm with lower BMIs than in the delayed surgery arm and did not undertake a regression analysis.

The study from the German health insurance company perspective concluded that early elective surgery saved £1,329 per patient compared with delayed elective surgery, while the study from the Swiss hospital perspective found early surgery to save £204. These costs included only the costs of the interventions, with no follow up. Neither study offered a detailed breakdown of costs, though the study from the German health insurance company perspective noted that the difference in costs arose mainly as a result of the initial intravenous antibiotic treatment in the delayed surgery arm. The studies both reported longer overall length of stay, including both the initial and the subsequent hospital spells, in the early than in the delayed surgery arms.

The committee noted that the studies included only people who underwent surgery, however, there is likely to be a subgroup of people in whom delayed surgery is planned and then do not subsequently require surgery. The inclusion of this group of people, who benefit from the

delaying of their surgery and contribute fewer costs to the delayed surgery arm, might influence the conclusions of the studies.

The cost of colostomy was higher than that of colectomy with anastomosis and the committee mentioned that colectomy with anastomosis would likely be preferable to the person with acute diverticulitis, if deemed feasible. The committee considered that the decision to operate early might sometimes affect the surgical procedure chosen.

As the studies did not include follow up costs, the committee discussed the likely downstream costs which have been omitted. Notably, the committee highlighted that stoma reversal may be warranted where the type of surgery was colectomy without anastomosis. In addition, further ongoing costs may arise from stoma maintenance in those people who do not undergo stoma reversal. If the rates of the different surgery types differ between early and delayed arms, these downstream costs could impact the conclusions of cost effectiveness analyses.

Given that both clinical and cost effectiveness evidence was inconclusive, the committee decided to make a research recommendation.

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Appendices

Appendix A: Review protocols

Table 12: Review protocol: Timing of surgery

Field	Content
Review question	What is the most appropriate time for surgery in people with complicated acute diverticulitis?
Type of review question	intervention review A review of health economic evidence related to the same review question was conducted in parallel with this review. For details see the health economic review protocol for this NICE guideline.
Objective of the review	To determine the most appropriate timing for surgery in people with acute diverticulitis
Eligibility criteria – population / disease / condition / issue / domain	Adults 18 years and over with complicated acute diverticulitis
Eligibility criteria – intervention(s) / exposure(s) / prognostic factor(s)	Elective surgery Emergency surgery
Eligibility criteria – comparator(s) / control or reference (gold) standard	Compared to each other No surgical intervention

Outcomes and prioritisation	Critical outcomes:
	• Quality of life
	• Mortality
	• Morbidity
	• Progression of disease
	• Complications:
	  ○ infections
	  ○ abscesses
	  ○ perforation
	  ○ fistula
	  ○ stricture
	Recurrence rates of acute diverticulitis
	• Hospitalisation
	• Need for further surgery
	
	Important outcomes:
	Symptom control/recurrence, for example pain relief, bowel habit

Eligibility criteria – study design	Randomised controlled trials (RCTs), systematic reviews of RCTs. If no RCT evidence is available, search for observational studies
Other inclusion exclusion criteria	Exclusions: Children and young people aged 17 years and younger Prevention
Proposed sensitivity /	Strata:

Field	Content
subgroup analysis, or meta-regression	• fistula • stricture • perforation • abscess Subgroups: Age: <50 vs >50 years people of Asian family origin as they are known to develop right-sided diverticula
Selection process – duplicate screening / selection / analysis	Studies are sifted by title and abstract. Potentially significant publications obtained in full text are then assessed against the inclusion criteria specified in this protocol.
Data management (software)	Pairwise meta-analyses performed using Cochrane Review Manager (RevMan5). GRADEpro used to assess the quality of evidence for each outcome Bibliographies, citations and study sifting managed using EndNote Data extractions performed using EviBase, a platform designed and maintained by the National Guideline Centre (NGC)
Information sources – databases and dates	Medline, Embase, The Cochrane Library
Identify if an update	Not applicable
Author contacts	https://www.nice.org.uk/guidance/conditions-and-diseases/digestive-tract-conditions/diverticular-disease
Highlight if amendment to previous protocol	For details please see section 4.5 of Developing NICE guidelines: the manual.
Search strategy – for one database	For details please see appendix B
Data collection process – forms / duplicate	A standardised evidence table format will be used, and published as appendix D of the evidence report.
Data items – define all variables to be collected	For details please see evidence tables in Appendix D (clinical evidence tables) or H (health economic evidence tables).
Methods for assessing bias at outcome / study level	Standard study checklists were used to critically appraise individual studies. For details please see section 6.2 of Developing NICE guidelines: the manual The risk of bias across all available evidence was evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group http://www.gradeworkinggroup.org/
Criteria for quantitative synthesis	For details please see section 6.4 of Developing NICE guidelines: the manual.
Methods for quantitative analysis – combining studies and exploring (in)consistency	For details please see the separate Methods report (chapter R) for this guideline.
Meta-bias assessment – publication bias, selective reporting bias	For details please see section 6.2 of Developing NICE guidelines: the manual.
Confidence in cumulative evidence	For details please see sections 6.4 and 9.1 of Developing NICE guidelines: the manual.
Rationale / context – what is known	For details please see the introduction to the evidence review.

Field	Content
Describe contributions of authors and guarantor	A multidisciplinary committee developed the evidence review. The committee was convened by the National Guideline Centre (NGC) and chaired by James Dalrymple in line with section 3 of Developing NICE guidelines: the manual. Staff from NGC undertook systematic literature searches, appraised the evidence, conducted meta-analysis and cost-effectiveness analysis where appropriate, and drafted the evidence review in collaboration with the committee. For details please see Developing NICE guidelines: the manual.
Sources of funding / support	NGC is funded by NICE and hosted by the Royal College of Physicians.
Name of sponsor	NGC is funded by NICE and hosted by the Royal College of Physicians.
Roles of sponsor	NICE funds NGC to develop guidelines for those working in the NHS, public health and social care in England.
PROSPERO registration number	Not registered

Table 13: Health economic review protocol

Review question	All questions – health economic evidence
Objectives	To identify health economic studies relevant to any of the review questions.
Search criteria	• Populations, interventions and comparators must be as specified in the clinical review protocol above. • Studies must be of a relevant health economic study design (cost–utility analysis, cost-effectiveness analysis, cost–benefit analysis, cost–consequences analysis, comparative cost analysis). • Studies must not be a letter, editorial or commentary, or a review of health economic evaluations. (Recent reviews will be ordered although not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered.) • Unpublished reports will not be considered unless submitted as part of a call for evidence. • Studies must be in English.
Search strategy	A health economic study search will be undertaken using population-specific terms and a health economic study filter – see appendix B below.
Review strategy	Studies not meeting any of the search criteria above will be excluded. Studies published before 2002, abstract-only studies and studies from non-OECD countries or the USA will also be excluded. Each remaining study will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist which can be found in appendix H of Developing NICE guidelines: the manual (2014).[110] **Inclusion and exclusion criteria** • If a study is rated as both 'Directly applicable' and with 'Minor limitations' then it will be included in the guideline. A health economic evidence table will be completed and it will be included in the health economic evidence profile. • If a study is rated as either 'Not applicable' or with 'Very serious limitations' then it will usually be excluded from the guideline. If it is excluded then a health economic evidence table will not be completed and it will not be included in the health

economic evidence profile.

- If a study is rated as 'Partially applicable', with 'Potentially serious limitations' or both then there is discretion over whether it should be included.

Where there is discretion

The health economist will make a decision based on the relative applicability and quality of the available evidence for that question, in discussion with the guideline committee if required. The ultimate aim is to include health economic studies that are helpful for decision-making in the context of the guideline and the current NHS setting. If several studies are considered of sufficiently high applicability and methodological quality that they could all be included, then the health economist, in discussion with the committee if required, may decide to include only the most applicable studies and to selectively exclude the remaining studies. All studies excluded on the basis of applicability or methodological limitations will be listed with explanation in the excluded health economic studies appendix below.

The health economist will be guided by the following hierarchies.

Setting:

- UK NHS (most applicable).
- OECD countries with predominantly public health insurance systems (for example, France, Germany, Sweden).
- OECD countries with predominantly private health insurance systems (for example, Switzerland).
- Studies set in non-OECD countries or in the USA will be excluded before being assessed for applicability and methodological limitations.

Health economic study type:

- Cost–utility analysis (most applicable).
- Other type of full economic evaluation (cost–benefit analysis, cost-effectiveness analysis, cost–consequences analysis).
- Comparative cost analysis.
- Non-comparative cost analyses including cost-of-illness studies will be excluded before being assessed for applicability and methodological limitations.

Year of analysis:

- The more recent the study, the more applicable it will be.
- Studies published in 2002 or later but that depend on unit costs and resource data entirely or predominantly from before 2002 will be rated as 'Not applicable'.
- Studies published before 2002 will be excluded before being assessed for applicability and methodological limitations.

Quality and relevance of effectiveness data used in the health economic analysis:

- The more closely the clinical effectiveness data used in the health economic analysis match with the outcomes of the studies included in the clinical review the more useful the analysis will be for decision-making in the guideline.

Appendix B: Literature search strategies

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual 2014, updated 2017

For more detailed information, please see the Methodology Review.

B.1 Clinical search literature search strategy

Searches were constructed using a PICO framework where population (P) terms were combined with Intervention (I) and in some cases Comparison (C) terms. Outcomes (O) are rarely used in search strategies for interventions as these concepts may not be well described in title, abstract or indexes and therefore difficult to retrieve. Search filters were applied to the search where appropriate.

Table 14: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 13 November 2018	Exclusions Randomised controlled trials Systematic review studies Observational studies
Embase (OVID)	1974 – 13 November 2018	Exclusions Randomised controlled trials Systematic review studies Observational studies
The Cochrane Library (Wiley)	Cochrane Reviews to 2018 Issue 11 of 12 CENTRAL to 2018 Issue 11 of 12 DARE, and NHSEED to 2015 Issue 2 of 4 HTA to 2016 Issue 2 of 4	None

Table 15: Medline (Ovid) search terms

1.	diverticul*.mp.
2.	limit 1 to English language
3.	letter/
4.	editorial/
5.	news/
6.	exp historical article/
7.	Anecdotes as Topic/
8.	comment/
9.	case report/
10.	(letter or comment*).ti.
11.	or/3-10
12.	randomized controlled trial/ or random*.ti,ab.
13.	11 not 12
14.	animals/ not humans/
15.	exp Animals, Laboratory/
16.	exp Animal Experimentation/
17.	exp Models, Animal/
18.	exp Rodentia/
19.	(rat or rats or mouse or mice).ti.
20.	or/13-19
21.	2 not 20

22.	randomized controlled trial.pt.
23.	controlled clinical trial.pt.
24.	randomi#ed.ti,ab.
25.	placebo.ab.
26.	randomly.ti,ab.
27.	Clinical Trials as topic.sh.
28.	trial.ti.
29.	or/22-28
30.	Meta-Analysis/
31.	exp Meta-Analysis as Topic/
32.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
33.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
34.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
35.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
36.	(search* adj4 literature).ab.
37.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
38.	cochrane.jw.
39.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
40.	or/50-59
41.	Epidemiologic studies/
42.	Observational study/
43.	exp Cohort studies/
44.	(cohort adj (study or studies or analys* or data)).ti,ab.
45.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
46.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
47.	Controlled Before-After Studies/
48.	Historically Controlled Study/
49.	Interrupted Time Series Analysis/
50.	(before adj2 after adj2 (study or studies or data)).ti,ab.
51.	or/30-39
52.	exp case control study/
53.	case control*.ti,ab.
54.	or/41-42
55.	40 or 43
56.	Cross-sectional studies/
57.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
58.	or/45-46
59.	40 or 47
60.	40 or 43 or 47
61.	21 and (29 or 40 or 60)

Table 16: Embase (Ovid) search terms

1.	diverticul*.mp.

2.	limit 1 to English language
3.	letter.pt. or letter/
4.	note.pt.
5.	editorial.pt.
6.	case report/ or case study/
7.	(letter or comment*).ti.
8.	or/3-7
9.	randomized controlled trial/ or random*.ti,ab.
10.	8 not 9
11.	animal/ not human/
12.	nonhuman/
13.	exp Animal Experiment/
14.	exp Experimental Animal/
15.	animal model/
16.	exp Rodent/
17.	(rat or rats or mouse or mice).ti.
18.	or/10-17
19.	2 not 18
20.	random*.ti,ab.
21.	factorial*.ti,ab.
22.	(crossover* or cross over*).ti,ab.
23.	((doubl* or singl*) adj blind*).ti,ab.
24.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
25.	crossover procedure/
26.	single blind procedure/
27.	randomized controlled trial/
28.	double blind procedure/
29.	or/20-28
30.	systematic review/
31.	meta-analysis/
32.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
33.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
34.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
35.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
36.	(search* adj4 literature).ab.
37.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
38.	cochrane.jw.
39.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
40.	or/30-39
41.	Clinical study/
42.	Observational study/
43.	family study/
44.	longitudinal study/

45.	retrospective study/
46.	prospective study/
47.	cohort analysis/
48.	follow-up/
49.	cohort*.ti,ab.
50.	48 and 49
51.	(cohort adj (study or studies or analys* or data)).ti,ab.
52.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
53.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
54.	(before adj2 after adj2 (study or studies or data)).ti,ab.
55.	or/41-47,50-54
56.	exp case control study/
57.	case control*.ti,ab.
58.	or/56-57
59.	55 or 58
60.	cross-sectional study/
61.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
62.	or/60-61
63.	55 or 62
64.	55 or 58 or 62
65.	19 and (29 or 40 or 64)

Table 17: Cochrane Library (Wiley) search terms

#1.	diverticul*.mp.

B.2 Health Economics literature search strategy

Health economic evidence was identified by conducting a broad search relating to Diverticular Disease population in NHS Economic Evaluation Database (NHS EED – this ceased to be updated after March 2015) and the Health Technology Assessment database (HTA) with no date restrictions. NHS EED and HTA databases are hosted by the Centre for Research and Dissemination (CRD). Additional searches were run on Medline and Embase for health economics, economic modelling and quality of life studies.

Table 18: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	1946 – 13 November 2018	Exclusions Health economics studies Health economics modelling studies Quality of life studies
Embase	1974 – 13 November 2018	Exclusions Health economics studies Health economics modelling studies Quality of life studies

Database	Dates searched	Search filter used
Centre for Research and Dissemination (CRD)	HTA - Inception – 13 November 2018 NHSEED - Inception to March 2015	None

Table 19: Medline (Ovid) search terms

1.	diverticul*.mp.
2.	limit 1 to English language
3.	letter/
4.	editorial/
5.	news/
6.	exp historical article/
7.	Anecdotes as Topic/
8.	comment/
9.	case report/
10.	(letter or comment*).ti.
11.	or/3-10
12.	randomized controlled trial/ or random*.ti,ab.
13.	11 not 12
14.	animals/ not humans/
15.	exp Animals, Laboratory/
16.	exp Animal Experimentation/
17.	exp Models, Animal/
18.	exp Rodentia/
19.	(rat or rats or mouse or mice).ti.
20.	or/13-19
21.	2 not 20
22.	Economics/
23.	Value of life/
24.	exp "Costs and Cost Analysis"/
25.	exp Economics, Hospital/
26.	exp Economics, Medical/
27.	Economics, Nursing/
28.	Economics, Pharmaceutical/
29.	exp "Fees and Charges"/
30.	exp Budgets/
31.	budget*.ti,ab.
32.	cost*.ti.
33.	(economic* or pharmaco?economic*).ti.
34.	(price* or pricing*).ti,ab.
35.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
36.	(financ* or fee or fees).ti,ab.

37.	(value adj2 (money or monetary)).ti,ab.
38.	or/22-37
39.	exp models, economic/
40.	*Models, Theoretical/
41.	markov chains/
42.	monte carlo method/
43.	exp Decision Theory/
44.	(markov* or monte carlo).ti,ab.
45.	econom* model*.ti,ab.
46.	(decision* adj2 (tree* or analy* or model*)).ti,ab.
47.	Models, Organizational/
48.	*models, statistical/
49.	*logistic models/
50.	models, nursing/
51.	((organi?ation* or operation* or service* or concept*) adj3 (model* or map* or program* or simulation* or system* or analys*)).ti,ab.
52.	(econom* adj2 (theor* or system* or map* or evaluat*)).ti,ab.
53.	(SSM or SODA).ti,ab.
54.	(strateg* adj3 (option* or choice*) adj3 (analys* or decision*)).ti,ab.
55.	soft systems method*.ti,ab.
56.	(Meta-heuristic* or Metaheuristic*).ti,ab.
57.	(dynamic* adj2 (model* or system*)).ti,ab.
58.	(simulation adj3 (model* or discrete event* or agent)).ti,ab.
59.	(microsimulation* or "micro* simulation*").ti,ab.
60.	((flow or core) adj2 model*).ti,ab.
61.	(data adj2 envelopment*).ti,ab.
62.	system* model*.ti,ab.
63.	or/41-64
64.	quality-adjusted life years/
65.	sickness impact profile/
66.	(quality adj2 (wellbeing or well being)).ti,ab.
67.	sickness impact profile.ti,ab.
68.	disability adjusted life.ti,ab.
69.	(qal* or qtime* or qwb* or daly*).ti,ab.
70.	(euroqol* or eq5d* or eq 5*).ti,ab.
71.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
72.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
73.	(hui or hui1 or hui2 or hui3).ti,ab.
74.	(health* year* equivalent* or hye or hyes).ti,ab.
75.	discrete choice*.ti,ab.
76.	rosser.ti,ab.
77.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
78.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
79.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
80.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.

81.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
82.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
83.	or/22-40
84.	21 and (38 or 63 or 83)

Table 20: Embase (Ovid) search terms

1.	diverticul*.mp.
2.	limit 1 to English language
3.	letter.pt. or letter/
4.	note.pt.
5.	editorial.pt.
6.	case report/ or case study/
7.	(letter or comment*).ti.
8.	or/3-7
9.	randomized controlled trial/ or random*.ti,ab.
10.	8 not 9
11.	animal/ not human/
12.	nonhuman/
13.	exp Animal Experiment/
14.	exp Experimental Animal/
15.	animal model/
16.	exp Rodent/
17.	(rat or rats or mouse or mice).ti.
18.	or/10-17
19.	2 not 18
20.	Economics/
21.	Value of life/
22.	exp "Costs and Cost Analysis"/
23.	exp Economics, Hospital/
24.	exp Economics, Medical/
25.	Economics, Nursing/
26.	Economics, Pharmaceutical/
27.	exp "Fees and Charges"/
28.	exp Budgets/
29.	budget*.ti,ab.
30.	cost*.ti.
31.	(economic* or pharmaco?economic*).ti.
32.	(price* or pricing*).ti,ab.
33.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
34.	(financ* or fee or fees).ti,ab.
35.	(value adj2 (money or monetary)).ti,ab.

36.	or/20-35
37.	statistical model/
38.	*theoretical model/
39.	nonbiological model/
40.	stochastic model/
41.	decision theory/
42.	decision tree/
43.	exp nursing theory/
44.	monte carlo method/
45.	(markov* or monte carlo).ti,ab.
46.	econom* model*.ti,ab.
47.	(decision* adj2 (tree* or analy* or model*)).ti,ab.
48.	((organi?ation* or operation* or service* or concept*) adj3 (model* or map* or program* or simulation* or system* or analys*)).ti,ab.
49.	(econom* adj2 (theor* or system* or map* or evaluat*)).ti,ab.
50.	(SSM or SODA).ti,ab.
51.	(strateg* adj3 (option* or choice*) adj3 (analys* or decision*)).ti,ab.
52.	soft systems method*.ti,ab.
53.	(Meta-heuristic* or Metaheuristic*).ti,ab.
54.	(dynamic* adj2 (model* or system*)).ti,ab.
55.	(simulation adj3 (model* or discrete event* or agent)).ti,ab.
56.	(microsimulation* or "micro* simulation*").ti,ab.
57.	((flow or core) adj2 model*).ti,ab.
58.	(data adj2 envelopment*).ti,ab.
59.	system* model*.ti,ab.
60.	or/39-61
61.	quality adjusted life year/
62.	"quality of life index"/
63.	short form 12/ or short form 20/ or short form 36/ or short form 8/
64.	sickness impact profile/
65.	(quality adj2 (wellbeing or well being)).ti,ab.
66.	sickness impact profile.ti,ab.
67.	disability adjusted life.ti,ab.
68.	(qal* or qtime* or qwb* or daly*).ti,ab.
69.	(euroqol* or eq5d* or eq 5*).ti,ab.
70.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
71.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
72.	(hui or hui1 or hui2 or hui3).ti,ab.
73.	(health* year* equivalent* or hye or hyes).ti,ab.
74.	discrete choice*.ti,ab.
75.	rosser.ti,ab.

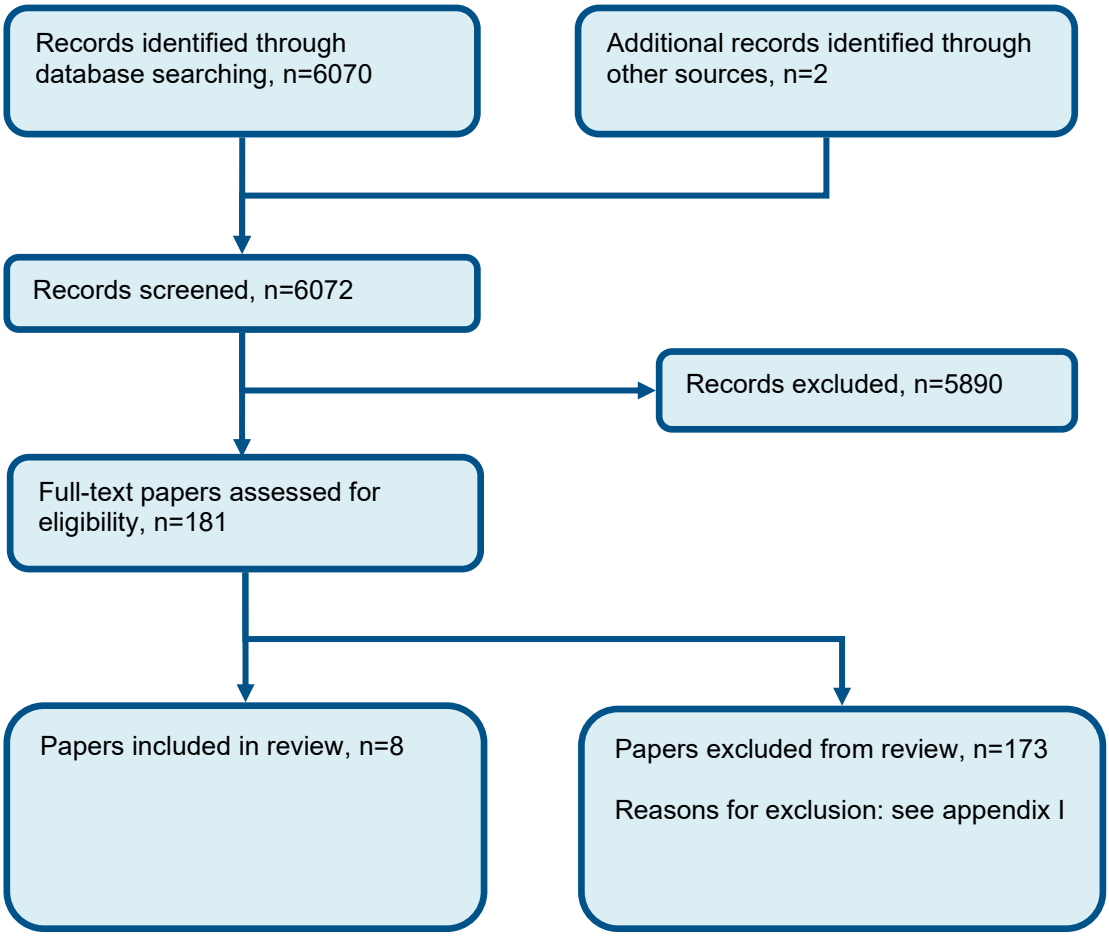
76.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
77.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
78.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
79.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
80.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
81.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
82.	or/20-40
83.	19 and (36 or 60 or 82)

Table 21: NHS EED and HTA (CRD) search terms

#1.	diverticul*

Appendix C: Clinical evidence selection

Figure 1: Flow chart of clinical study selection for the review of timing of surgery



Appendix D: Clinical evidence tables

Table 22: Clinical evidence tables

Study	**Bachmann 2011[18]**
Study type	Non-randomised comparative study
Number of studies (number of participants)	1 (n=421)
Countries and setting	Conducted in Germany; Setting: Hospital
Line of therapy	1st line
Duration of study	Other: 5 years prospective follow-up
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: CT scan
Stratum	Abscess: Complications are localised abscess and
Subgroup analysis within study	Not applicable
Inclusion criteria	Individuals with clear indication for surgery with complicated diverticulitis, Hinchey stage 1 and 2.
Exclusion criteria	Individuals with perforation.
Recruitment/selection of patients	Individuals planned to have resectional surgery.
Age, gender and ethnicity	Age - Mean (SD): 64 (13) years. Gender (M:F): 0.44/0.56. Ethnicity:

Further population details	
Extra comments	All individuals with planned elective surgical resection for complicated sigmoidal diverticulitis between the years 2004 and 2009 were analysed. .
Indirectness of population	No indirectness
Interventions	(n=272) Intervention 1: Emergency surgery. Early elective surgery performed at a median of 2 days post-admission. . Duration 2 days. Concurrent medication/care: Antibiotics at admission until surgery ; 2-4 days. . Indirectness: No indirectness (n=149) Intervention 2: Elective surgery. delayed elective surgery . Duration 6-8weeks post admission. Concurrent medication/care: 5-7 days antibiotic course. . Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: EMERGENCY SURGERY (EARLY ELECTIVE) versus ELECTIVE SURGERY

Protocol outcome 1: Mortality
- Actual outcome for Abscess: Mortality at 5 year period; Group 1: 1/272, Group 2: 1/141
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 8

Protocol outcome 2: Morbidity
- Actual outcome for Abscess: Overall morbidity at 5 year period; Group 1: 41/272, Group 2: 16/141
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 8

Protocol outcome 3: Complications (infections)
- Actual outcome for Abscess: Wound infection at 5 year period; Group 1: 30/272, Group 2: 10/141
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low,

Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 8 Protocol outcome 4: Need for further surgery - Actual outcome for Abscess: Reoperation at 5 year period; Group 1: 22/272, Group 2: 8/141 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 8	
Protocol outcomes not reported by the study	Quality of life; Progression of disease; Complications (abscesses); Complications (perforation); Complications (fistula); Complications (stricture); Recurrence rates of acute diverticulitis ; Hospitalisation; Symptom control/recurrence (e.g. pain relief, bowel habit)

Study	Buchwald 2017[29]
Study type	Retrospective cohort study
Number of studies (number of participants)	(n=107)
Countries and setting	Conducted in New Zealand; Setting: Secondary care - hospital.
Line of therapy	1st line
Duration of study	Intervention time: Prospective collection in database between 1998 and 2009. Patients followed up until 1st January 2014.
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Diverticulitis diagnosed based on clinical findings, blood tests, endoscopic and/or surgical finding and radiology. Sigmoid diverticulitis diagnosed in all patients by computed tomography.
Stratum	Abscess: Diagnosed with Hinchey I or II abscess due to complicated diverticulitis.
Subgroup analysis within study	Not applicable
Inclusion criteria	Diverticulitis complicated by abscess (Hinchey stages I or II).
Exclusion criteria	Patients with previous diverticular attacks, post-operative abscesses or right-sided diverticulitis. Those whose patient charts were not available for validation.
Recruitment/selection of patients	Those with diverticulitis complicated by abscess in database that was prospectively obtained between 1998 and 2009.
Age, gender and ethnicity	Age - Mean (SD): Total cohort, 66 (15.6) years - conservative (antibiotics and antibiotics + percutaneous drainage groups), 64.2 (17.2) years; elective surgery, 65.5 (13.4) years.. Gender (M:F): Total cohort, 60/47 - conservative (antibiotics and antibiotics + percutaneous drainage groups), 38/26; elective surgery, 22/21. .

	Ethnicity: Not reported.
Further population details	
Extra comments	32/107 patients with abscess in this cohort were taking NSAIDs, 6/107 were taking steroids and 3/107 were being treated for diabetes. Does not specify the numbers for the conservative and surgery groups separately.
Indirectness of population	No indirectness
Interventions	(n=42) Intervention 1: Elective surgery. Does not provide a definition of elective surgery in this study. Mean abscess size, 4.6±1.6 cm. Mean follow-up time, 114±39 months.. Duration Not reported. . Concurrent medication/care: In the total cohort of this study, 32/107 were being treated with NSAIDs, 6/107 were being treated with steroids and 3/107 were being treated for diabetes. The number of patients receiving these treatments in the elective surgery group was not specified.. Indirectness: No indirectness Comments: Does not explicitly state is elective surgery, but wording throughout the paper suggests that it is elective surgery they are referring to, rather than emergency surgery or a mixture of the two. (n=65) Intervention 2: No surgical intervention - No intervention. Study separates conservative treatment into two separate groups: antibiotics and antibiotics + percutaneous drainage. Outcome data have been combined for these two groups under conservative treatment to compare with surgical intervention. No details of the treatments reported, eg. types/doses of antibiotics or timing of percutaneous drainage after antibiotics initiated. Combined mean abscess size, 3.9±2.3 cm (3.1±1.8 cm in antibiotics group and 5.6±2.4 cm in antibiotics +percutaneous drainage group). Combined mean follow-up time, 102±34 months (96±35 months in antibiotics group and 114±30 months in antibiotics + percutaneous drainage group).. Duration Not reported.. Concurrent medication/care: In the total cohort of this study, 32/107 were being treated with NSAIDs, 6/107 were being treated with steroids and 3/107 were being treated for diabetes. The number of patients in the conservative group (antibiotics and antibiotics + percutaneous groups combined) receiving these treatments was not specified.. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ELECTIVE SURGERY versus NO INTERVENTION (CONSERVATIVE TREATMENT) Protocol outcome 1: Recurrence rates of acute diverticulitis - Actual outcome for Abscess: Recurrence - readmission due to diverticulitis at 110 months; Group 1: 2/42, Group 2: 19/65 Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Comments - Outcome reporting: follow-up slightly shorter in the conservative group compared with surgery group. ; Indirectness of outcome: No indirectness ; Baseline details: Authors made error for male/female ratio in each group – do not add to correct totals for antibiotics and surgery groups. Cannot assess difference between gender in groups. Some patients receiving treatment with NSAIDs or steroids, or have diabetes - does not specify breakdown in each group.; Key confounders: Age, gender; Group 1 Number missing: 0; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Quality of life; Mortality; Morbidity; Progression of disease; Complications (infections); Complications (abscesses); Complications (perforation); Complications (fistula); Complications (stricture); Hospitalisation; Need for further surgery; Symptom control/recurrence (e.g. pain relief, bowel habit)

Study	Radwan 2013[131]
Study type	Retrospective cohort study
Number of studies (number of participants)	(n=53)
Countries and setting	Conducted in United Kingdom, Unknown; Setting: Secondary care - hospital.
Line of therapy	1st line
Duration of study	Follow up (post intervention): Reviewed notes of those diagnosed over a 7-year period.
Method of assessment of guideline condition	Unclear method of assessment/diagnosis: Fistula (as a result of diverticular disease or other indications) was confirmed by contrast enema CT scan in 57 (92%) of cases. Does not specify the method used for those cases that were secondary to diverticular disease. No method specified for diagnosis of diverticular disease.
Stratum	Fistula: Data available for 53 patients with colovesical fistula secondary to diverticular disease.
Subgroup analysis within study	Not applicable
Inclusion criteria	Colovesical fistula diagnosis secondary to diverticular disease.
Exclusion criteria	Not reported.
Recruitment/selection of patients	Reviewed notes of all patients diagnosed with colovesical fistula secondary to diverticular disease in single district general hospital.
Age, gender and ethnicity	Age - Mean (range): Elective surgery, 69 (42-90); conservative, 76 (39-87).. Gender (M:F): Elective surgery, 16/11; conservative, 9/17.. Ethnicity: Not reported.
Further population details	

Indirectness of population	No indirectness
Interventions	(n=27) Intervention 1: Elective surgery. Does not provide definition of elective surgery in this study. Surgical methods included 25 patients with an open procedure and 2 with laparoscopic resection. . Duration Not reported.. Concurrent medication/care: Not reported. . Indirectness: No indirectness (n=26) Intervention 2: No surgical intervention - No intervention. Conservative treatment. 5 patients in conservative group prescribed long-term low-dose antibiotics as definitive management on diagnosis of their fistula. No details for the treatment of the remaining patients in this group.. Duration Not reported.. Concurrent medication/care: Not reported.. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ELECTIVE SURGERY versus NO INTERVENTION (CONSERVATIVE)

Protocol outcome 1: Mortality
- Actual outcome for Fistula: 30-day mortality at 30 days; Group 1: 4/27, Group 2: 2/26
Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Very high, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Proportion of patients with ASA grade III or IV substantially different between two groups: elective surgery, 22%; conservative, 62%. Therefore patients in conservative group in poorer overall health than the surgery group.; Key confounders: Age, gender; Group 1 Number missing: 0; Group 2 Number missing: 0
- Actual outcome for Fistula: 1-year mortality at 1 year; Group 1: 10/27, Group 2: 6/26
Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Very high, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Proportion of patients with ASA grade III or IV substantially different between two groups: elective surgery, 22%; conservative, 62%. Therefore patients in conservative group in poorer overall health than the surgery group.; Key confounders: Age, gender; Group 1 Number missing: 0; Group 2 Number missing: 0
- Actual outcome for Fistula: 3-year mortality at 3 years; Group 1: 16/27, Group 2: 12/26
Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Very high, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Comments - ; Indirectness of outcome: No indirectness ; Baseline details: Proportion of patients with ASA grade III or IV substantially different between two groups: elective surgery, 22%; conservative, 62%. Therefore patients in conservative group in poorer overall health than the surgery group.; Key confounders: Age, gender; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcomes not reported by the study	Quality of life; Morbidity; Progression of disease; Complications (infections); Complications (abscesses); Complications (perforation); Complications (fistula); Complications (stricture); Recurrence rates of acute diverticulitis; Hospitalisation; Need for further surgery; Symptom control/recurrence (e.g. pain relief, bowel habit)

Study	Tudor 1994 (stricture)[165]
Study type	Prospective cohort study
Number of studies (number of participants)	(n=300)
Countries and setting	Conducted in United Kingdom; Setting: Secondary care - hospitals
Line of therapy	1st line
Duration of study	Intervention + follow up: 3 year prospective audit, 1985-1988
Method of assessment of guideline condition	Unclear method of assessment/diagnosis: Considered on clinical grounds to have complicated diverticular disease. Bowel obstruction was indicated by left-sided abdominal pain with radiographic evidence of small or large bowel obstruction.
Stratum	Stricture: Reported as bowel obstruction in the study.
Subgroup analysis within study	Not applicable:
Inclusion criteria	Complicated diverticular disease with left-sided abdominal pain and radiographic evidence of a small or large bowel obstruction.
Exclusion criteria	Not reported.
Recruitment/selection of patients	Consecutive patients admitted to 30 hospitals with complicated diverticular disease between 1985 and 1988.
Age, gender and ethnicity	Age - Median (range): Whole cohort (data not given separately for those with obstruction), 68 (31-94) years. Gender (M:F): Whole cohort (data not given separately for those with obstruction), 115/185. Ethnicity: Not reported.

Further population details	
Indirectness of population	No indirectness
Interventions	(n=27) Intervention 1: Emergency surgery. No time frame within which emergency surgery was performed specified. Procedures that were considered to be surgical in this study and were used to treat bowel obstruction were as follows: Laparotomy alone, loop stoma, Hartmann's procedure, and resection and primary anastomosis with or without a stoma.. Duration Not reported.. Concurrent medication/care: Not reported. Bowel obstruction group in study was included under the 'stricture' stratum.. Indirectness: No indirectness (n=4) Intervention 2: No surgical intervention - No intervention. Defined as 'no operation' in the study. Details of treatments received instead of operation not reported.. Duration Not reported.. Concurrent medication/care: Not reported. Bowel obstruction group in study was included under the 'stricture' stratum.. Indirectness: No indirectness
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: EMERGENCY SURGERY versus NO INTERVENTION (NO OPERATION) Protocol outcome 1: Mortality - Actual outcome for Stricture: Mortality at within 30 days of admission; Group 1: 2/27, Group 2: 0/4 Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported for the total cohort, but not individually for those within the bowel obstruction subgroup.; Key confounders: Age, gender; Group 1 Number missing: 0; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Quality of life; Morbidity; Progression of disease; Complications (infections); Complications (abscesses); Complications (perforation); Complications (fistula); Complications (stricture); Recurrence rates of acute diverticulitis; Hospitalisation; Need for further surgery; Symptom control/recurrence (e.g. pain relief, bowel habit)

Study	Tudor 1994 (abscess)[165]
Study type	Prospective cohort study
Number of studies (number of participants)	(n=300)
Countries and setting	Conducted in United Kingdom; Setting: Secondary care - hospitals
Line of therapy	1st line
Duration of study	Intervention + follow up: 3 year prospective audit, 1985-1988.
Method of assessment of guideline condition	Unclear method of assessment/diagnosis: Considered on clinical grounds to have complicated diverticular disease. Acute phlegmon, localised left iliac fossa mass without fever; pericolic abscess, left iliac fossa mass, swinging pyrexia and leucocytosis often with a mass confirmed by ultrasonography.
Stratum	Abscess: Included those in the study with 'acute phlegmon' and 'pericolic abscess' in the abscess stratum.
Subgroup analysis within study	Not applicable
Inclusion criteria	Not reported.
Exclusion criteria	Not reported.
Recruitment/selection of patients	Consecutive patients admitted to 30 hospitals with complicated diverticular disease between 1985 and 1988.
Age, gender and ethnicity	Age - Median (range): Whole cohort (data not given separately for those with abscess and pericolic abscess), 68 (31-94) years. . Gender (M:F): Whole cohort (data not given separately for those with acute phlegmon and pericolic abscess), 115/185.. Ethnicity: Not reported.
Further population details	

Extra comments	Note that we have combined data reported for acute phlegmon and pericolic abscess under the abscess stratum for this study.
Indirectness of population	No indirectness
Interventions	(n=59) Intervention 1: Emergency surgery. No time frame within which emergency surgery was performed specified. Procedures that were considered to be surgical in this study and were used to treat acute phlegmon or pericolic abscess were as follows: Laparotomy alone, drainage alone, loop stoma, Hartmann's procedure, and resection and primary anastomosis with or without resection.. Duration Not reported.. Concurrent medication/care: Not reported. Note that we have combined data reported for acute phlegmon and pericolic abscess under the abscess stratum for this study.. Indirectness: No indirectness (n=79) Intervention 2: No surgical intervention - No intervention. Defined as 'no operation' in the study. Details of treatments received instead of operation not reported.. Duration Not reported.. Concurrent medication/care: Not reported. Note that we have combined data reported for acute phlegmon and pericolic abscess under the abscess stratum for this study.. Indirectness: No indirectness
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: EMERGENCY SURGERY versus NO INTERVENTION (NO OPERATION) Protocol outcome 1: Mortality - Actual outcome for Abscess: Mortality at within 30 days of admission; Group 1: 5/59, Group 2: 3/79 Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported for the total cohort, but not individually for those groups with phlegmon or abscess.; Key confounders: Age, gender; Group 1 Number missing: 0; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Quality of life; Morbidity; Progression of disease; Complications (infections); Complications (abscesses); Complications (perforation); Complications (fistula); Complications (stricture); Recurrence rates of acute diverticulitis; Hospitalisation; Need for further surgery; Symptom control/recurrence (e.g. pain relief, bowel habit)

Study	**Vinas-salas 2001[174]**
Study type	Retrospective cohort study
Number of studies (number of participants)	(n=353)
Countries and setting	Conducted in Paraguay, Spain; Setting: Secondary care - hospitals
Line of therapy	Unclear
Duration of study	Intervention + follow up: Retrospective review of those admitted between July 1989 and June 1999 (Asuncion, Paraguay) or 1992 and 1999 (Lledia, Spain).
Method of assessment of guideline condition	Unclear method of assessment/diagnosis: Not specified.
Stratum	Overall:
Subgroup analysis within study	Not applicable
Inclusion criteria	Not reported.
Exclusion criteria	Not reported.
Recruitment/selection of patients	Consecutive patients treated for complications of diverticular disease.
Age, gender and ethnicity	Age - Mean (range): Have only specified average age, not whether is mean or median. Asuncion: Men, 53 (34-84); women, 62 (36-92). Note this includes those with recurrent cases.. Gender (M:F): Asuncion, 110/93. Note this includes those with recurrent cases.. Ethnicity: Not reported.
Further population details	

Extra comments	The study included data for two populations (at locations in Asuncion, Paraguay and Lleida, Spain), but only data for Asuncion were extracted due to insufficient information for the Lleida cases. Haemorrhage (low digestive), inflammatory disease and diffuse peritonitis were considered to indicate complicated diverticular disease in this study. .
Indirectness of population	No indirectness: Population of study as a whole was indirect due to some cases being recurrent cases, but outcomes were extracted for the non-recurrent cases only, so does not need to be downgraded.
Interventions	(n=9) Intervention 1: Elective surgery. Does not provide a definition for elective surgery in this study.. Duration Not reported.. Concurrent medication/care: Not reported.. Indirectness: No indirectness Comments: Number of participants here refers to the non-recurrent cases only. (n=26) Intervention 2: Emergency surgery. Does not provide a definition for emergency surgery in this study.. Duration Not reported.. Concurrent medication/care: Not reported.. Indirectness: No indirectness Comments: Number of participants here refers to the non-recurrent cases only.
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ELECTIVE SURGERY versus EMERGENCY SURGERY

Protocol outcome 1: Morbidity
- Actual outcome: Complications of surgery at Not reported.; Group 1: 0/9, Group 2: 14/26
Risk of bias: All domain - Very high, Selection - high, Blinding - High, Incomplete outcome data - Low, Outcome reporting - high, Measurement - High, Crossover - Low, Subgroups - Low, Other 1 - Low, Comments - ; Indirectness of outcome: No indirectness ; Baseline details: Baseline details for only the non-recurrent cases not given separately. Cannot evaluate.; Key confounders: Age, Gender; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcomes not reported by the study	Quality of life; Mortality; Progression of disease; Complications (infections); Complications (abscesses); Complications (perforation); Complications (fistula); Complications (stricture); Recurrence rates of acute diverticulitis; Hospitalisation; Need for further surgery; Symptom control/recurrence (e.g. pain relief, bowel habit)

Study (subsidiary papers)	Zingg 2007[183]
Study type	Retrospective cohort study
Number of studies (number of participants)	(n=178)
Countries and setting	Conducted in Switzerland; Setting: Secondary care.
Line of therapy	1st line
Duration of study	Follow up (post intervention): Between January 1997 and December 2005.
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Acute diverticulitis diagnosed by clinical examination, laboratory tests such as C-reactive protein and leucocytes, and abdominal triple contrast CT scan in all patients.
Stratum	Overall:
Subgroup analysis within study	Unclear: Acute diverticulitis cases were split into uncomplicated and complicated cases.
Inclusion criteria	Elective laparoscopic-assisted sigmoid resection for diverticular disease between January 1997 and December 2005.
Exclusion criteria	Patients undergoing emergency surgery for free perforation with peritonitis. Those that had emergency open surgery as initial antibiotic therapy was not successful within 48 hours, as evidenced by persisting pain, increasing inflammatory parameters or clinical evidence of peritonitis was present.
Recruitment/selection of patients	All cases undergoing elective laparoscopic-assisted sigmoid resection for diverticular disease between January 1997 and December 2005 at Triemli Hospital, Zurich, Switzerland.
Age, gender and ethnicity	Age - Mean (SD): Early elective, 60.7 (12.5) years; Delayed elective, 60.8 (11.9) years.. Gender (M:F): Not reported.. Ethnicity: Not reported.

Further population details	
Extra comments	Complicated diverticulitis defined as covered perforation with phlegmon or abscess. Data not given separately for the different complications.
Indirectness of population	No indirectness
Interventions	(n=56) Intervention 1: Emergency surgery. Defined as early elective surgery in the study. Early elective surgery defined as surgery performed during the same hospitalisation as the acute episode and after initial antibiotic therapy. Mean interval between hospital admission and surgery for uncomplicated and complicated cases combined was 7 days (range, 1-16 days).. Duration Mean operating time, 193 +/- 99 min.. Concurrent medication/care: All patients received initial antibiotic therapy consisting of amoxicillin-clavulanic acid and netilmicinum or ceftriaxone and metronidazole, according to renal function. Full clinical and laboratory response was required before surgery was performed.. Indirectness: No indirectness Comments: Number of participants with complicated diverticulitis is given. Data for uncomplicated cases not extracted. (n=13) Intervention 2: Elective surgery. Defined as delayed elective surgery in the study. Delayed elective surgery defined as surgery after a minimum or 6 weeks in a second hospitalisation. Mean interval between initial hospitalisation and surgery for uncomplicated and complicated cases combined was 13 weeks (range, 6-87 weeks).. Duration Mean operating time, 182 +/- 49 min.. Concurrent medication/care: All patients received initial antibiotic therapy consisting of amoxicillin-clavulanic acid and netilmicinum or ceftriaxone and metronidazole, according to renal function. Duration not specified. Some patients in the delayed elective group received initial conservative treatment outside of the institution this study was performed in, meaning duration and type of antibiotics not always known.. Indirectness: No indirectness Comments: Number of patients with complicated diverticulitis given. Data for uncomplicated cases not extracted.
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ELECTIVE SURGERY (DELAYED ELECTIVE) versus EMERGENCY SURGERY (EARLY	

ELECTIVE) Protocol outcome 1: Mortality - Actual outcome: 30-day mortality at In-hospital and 30 day follow-up.; Group 1: 0/13, Group 2: 0/56 Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Comments - Outcome reporting bias: no mention of 30-day mortality in methods section. Not clear whether post-surgery or post-admission.; Indirectness of outcome: No indirectness ; Baseline details: Age and gender distribution in the two groups not specified for complicated cases separately. Age well-matched in early and delayed elective groups for the whole cohort (uncomplicated and complicated cases combined).; Key confounders: Age and gender; Group 1 Number missing: 0, Reason: Does not specify that any participants were lost to follow-up/excluded for this comparison.; Group 2 Number missing: 0, Reason: Does not specify that any participants were lost to follow-up/excluded for this comparison. Protocol outcome 2: Morbidity - Actual outcome: Surgical morbidity at Not reported.; Group 1: 1/13, Group 2: 12/56; Comments: Surgical morbidity defined as the following: anastomotic leak, intra-abdominal abscess, wound infection, postoperative bleeding, ureteral injury and prolonged paralysis. Given as % but calculated event rates from this. Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Comments - Outcome reporting bias: does not specify time-point for which surgical morbidity was measured up until.; Indirectness of outcome: No indirectness ; Baseline details: Age and gender distribution in the two groups not specified for complicated cases separately. Age well-matched in early and delayed elective groups for the whole cohort (uncomplicated and complicated cases combined).; Key confounders: Age and gender; Group 1 Number missing: 0; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Quality of life; Progression of disease; Complications (infections); Complications (abscesses); Complications (perforation); Complications (fistula); Complications (stricture); Recurrence rates of acute diverticulitis; Hospitalisation; Need for further surgery; Symptom control/recurrence (e.g. pain relief, bowel habit)

Appendix E: Forest plots

E.1 Overall stratum

E.1.1 Emergency surgery compared to elective surgery

Figure 2: Mortality at 30 days: complicated acute diverticulitis

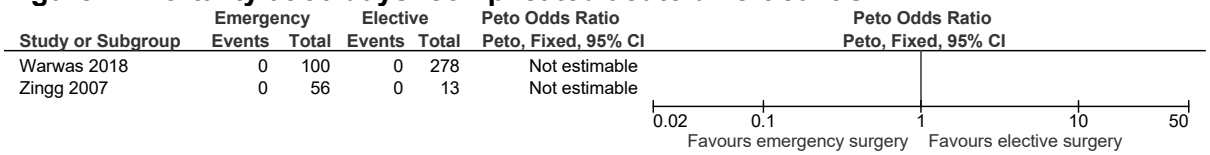


Figure 3: Morbidity: complicated acute diverticulitis

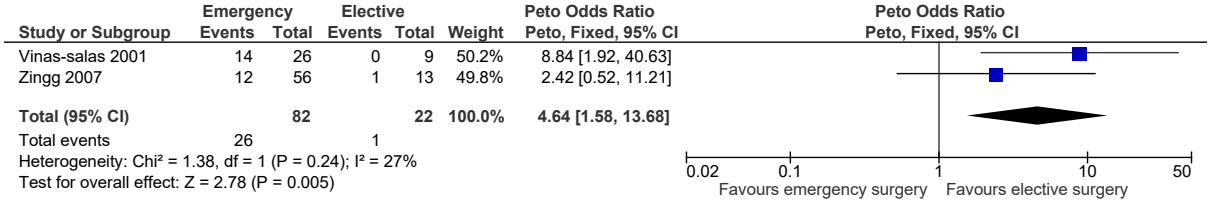
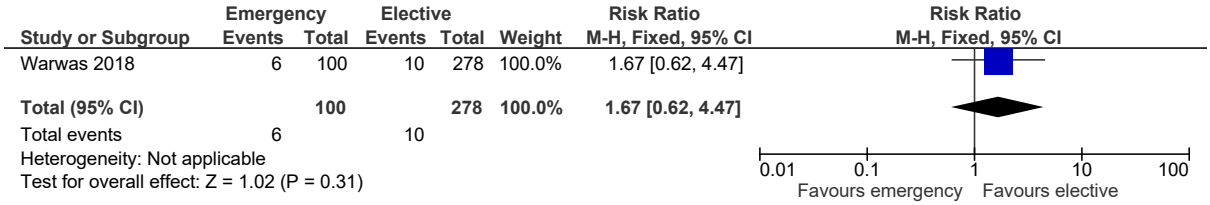


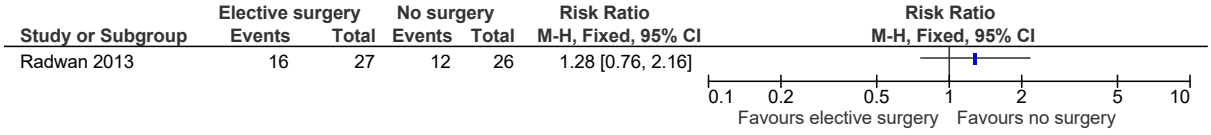
Figure 4: Bleeding



E.2 Fistula stratum

E.2.1 Elective surgery compared to no surgical intervention

Figure 5: Mortality at 3 years: complicated acute diverticulitis



E.3 Abscess stratum

E.3.1 Emergency surgery compared to elective surgery

Figure 6: Mortality (in-hospital): complicated acute diverticulitis

Study or Subgroup	Emergency surgery Events	Total	Elective surgery Events	Total	Peto Odds Ratio Peto, Fixed, 95% CI
Bachmann 2011	1	272	1	141	0.49 [0.03, 9.20]

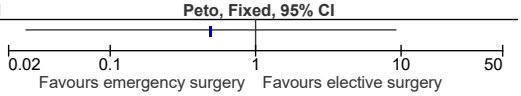


Figure 7: Morbidity: complicated acute diverticulitis

Study or Subgroup	Emergency surgery Events	Total	Elective surgery Events	Total	Risk Ratio M-H, Fixed, 95% CI
Bachmann 2011	41	272	16	141	1.33 [0.77, 2.28]

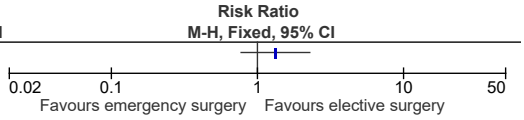


Figure 8: Complications (infections): complicated acute diverticulitis

Study or Subgroup	Emergency surgery Events	Total	Elective surgery Events	Total	Risk Ratio M-H, Fixed, 95% CI
Bachmann 2011	30	272	10	141	1.56 [0.78, 3.09]

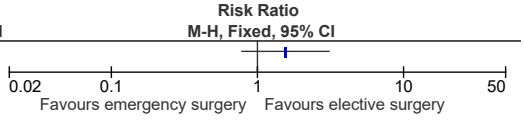


Figure 9: Need for further surgery: complicated acute diverticulitis

Study or Subgroup	Emergency surgery Events	Total	Elective surgery Events	Total	Risk Ratio M-H, Fixed, 95% CI
Bachmann 2011	22	272	8	141	1.43 [0.65, 3.12]

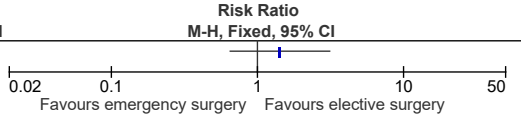


Figure 10: Mortality: antibiotics first line treatment: complicated acute diverticulitis

Study or Subgroup	Emergency surgery Events	Total	Elective surgery Events	Total	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
Elagii 2014	0	8	0	24		Not estimable
Total (95% CI)		**8**		**24**		**Not estimable**
Total events	0		0			

Heterogeneity: Not applicable
Test for overall effect: Not applicable

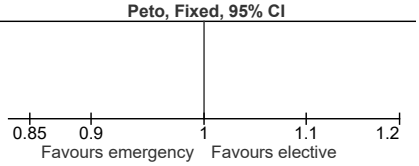


Figure 11: Morbidity: antibiotics first line treatment: complicated acute diverticulitis

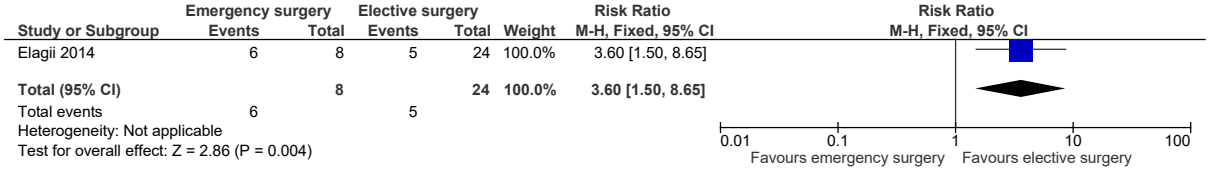


Figure 12: Mortality: percutaneous drainage first line treatment: complicated acute diverticulitis

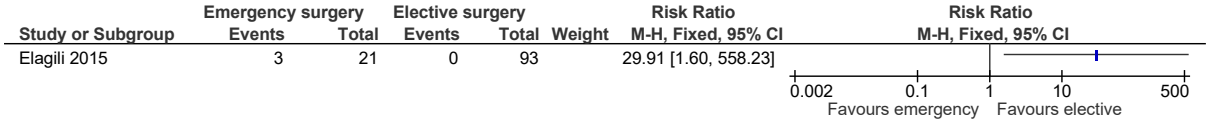
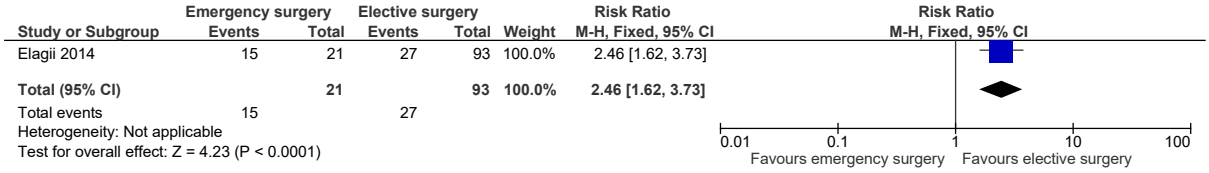
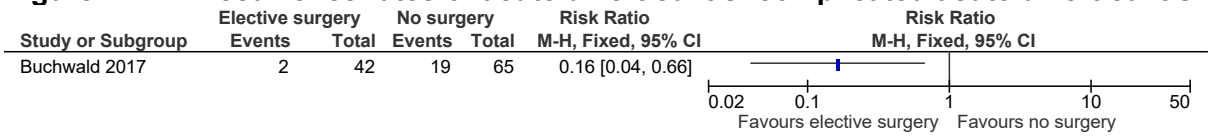


Figure 13: Morbidity: antibiotics first line treatment: complicated acute diverticulitis



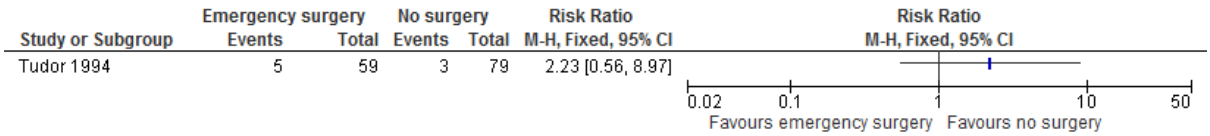
E.3.2 Elective surgery compared to no surgical intervention

Figure 14: Recurrence rates of acute diverticulitis: complicated acute diverticulitis



E.3.3 Emergency surgery compared to no surgical intervention

Figure 15: Mortality at 30 days (post-admission): complicated acute diverticulitis

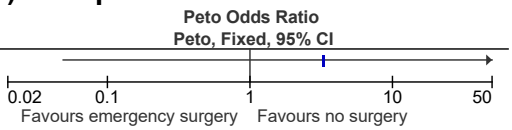


E.4 Stricture stratum

E.4.1 Emergency surgery compared to no surgical intervention

Figure 16: Mortality at 30 days (post-admission): complicated acute diverticulitis

Study or Subgroup	Emergency surgery Events	Total	No surgery Events	Total	Peto Odds Ratio Peto, Fixed, 95% CI
Tudor 1994	2	27	0	4	3.28 [0.05, 219.76]



Appendix F: GRADE tables

1.7.2.1 Overall stratum

Table 23: Clinical evidence profile: emergency surgery compared to elective surgery

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Overall Strata: emergency	Elective surgery	Relative (95% CI)	Absolute		
Mortality at 30 days (follow-up 30 days)												
2	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	0/156 (0%)	0%	-	0 fewer per 1000 (from 2 fewer to 2 more)[3]	⊕OOO VERY LOW	CRITICAL
Morbidity												
2	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	26/82 (31.7%)	3.9%	OR 4.64 (1.58 to 13.68)	119 more per 1000 (from 21 more to 318 more)	⊕OOO VERY LOW	CRITICAL
Bleeding												
1	observational	very	no serious	no serious	very serious[4]	none	6/100	3.6%	RR 1.67	24 more per 1000	⊕OOO	CRITICAL

	studies	serious[1]	inconsistency	indirectness			(6%)		(0.62 to 4.47)	(from 14 fewer to 125 more)	VERY LOW	

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Risk difference (95% CI) analysis method was used as there were zero events in both arms, and sample size was <70.
[3] Risk difference (95% CI) calculated as 0 events in both arms
[4] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

1.7.2.2 Fistula stratum

Table 24: Clinical evidence profile: elective surgery compared to no surgical intervention

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Elective surgery	No intervention	Relative (95% CI)	Absolute		
Mortality at 3 years (follow-up 3 years)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	16/27 (59.3%)	46.2%	RR 1.28 (0.76 to 2.16)	129 more per 1000 (from 111 fewer to 536 more)	⊕OOO VERY LOW	CRITICAL

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

1.7.2.3 Abscess stratum

Table 25: Clinical evidence profile: emergency surgery compared to elective surgery

Quality assessment	No of patients	Effect	Quality	Importance

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Abscess strata: emergency	Elective surgery	Relative (95% CI)	Absolute		
Mortality (in-hospital) (follow-up 5 years[1])												
1	observational studies	very serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	1/272 (0.37%)	0.7%	OR 0.49 (0.03 to 9.2)	4 fewer per 1000 (from 7 fewer to 54 more)	⊕OOO VERY LOW	CRITICAL
Morbidity (follow-up 5 years[1])												
1	observational studies	very serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	41/272 (15.1%)	11.4%	RR 1.33 (0.77 to 2.28)	38 more per 1000 (from 26 fewer to 146 more)	⊕OOO VERY LOW	CRITICAL
Complications: infections (follow-up 5 years[1])												
1	observational studies	very serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	30/272 (11%)	7.1%	RR 1.56 (0.78 to 3.09)	40 more per 1000 (from 16 fewer to 148 more)	⊕OOO VERY LOW	CRITICAL
Need for further surgery (follow-up 5 years[1])												
1	observational studies	very serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	22/272 (8.1%)	5.7%	RR 1.43 (0.65 to 3.12)	25 more per 1000 (from 20 fewer to 121 more)	⊕OOO VERY LOW	CRITICAL
Mortality (antibiotics)												

1	observational studies	very serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	0/8 (0%)	0%	-	0 fewer per 1000 (from 16 fewer to 16 more)[4]	⊕OOO VERY LOW	CRITICAL
Morbidity (antibiotics)												
1	observational studies	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	6/8 (75%)	20.8%	RR 3.60 (1.5 to 8.65)	541 more per 1000 (from 104 more to 1000 more)	⊕OOO VERY LOW	CRITICAL
Mortality (drainage)												
1	observational studies	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	3/21 (14.3%)	0%	RR 29.91 (1.6 to 558.23)	140 more per 1000 (from 10 fewer to 300 more)[5]	⊕OOO VERY LOW	CRITICAL
Morbidity (drainage)												
1	observational studies	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	15/21 (71.4%)	29%	RR 2.46 (1.62 to 3.73)	423 more per 1000 (from 180 more to 792 more)	⊕OOO VERY LOW	CRITICAL

[1] Retrospective study assessing patient records over a 5 year period
[2] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[3] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
[4] Risk difference (95% CI) calculated as there were zero events in both arms
[5] Risk difference was used as low event rate

Table 26: Clinical evidence profile: elective surgery compared to no surgical intervention

Quality assessment	No of patients	Effect	Quality	Importance

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Elective surgery	No intervention	Relative (95% CI)	Absolute		
Recurrence rates of acute diverticulitis (follow-up mean 110 months)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	2/42 (4.8%)	29.2%	RR 0.16 (0.04 to 0.66)	245 fewer per 1000 (from 99 fewer to 280 fewer)	⊕OOO VERY LOW	CRITICAL

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

Table 27: Clinical evidence profile: emergency surgery compared to no surgical intervention

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Emergency surgery	No intervention	Relative (95% CI)	Absolute		
30-day mortality (post-admission) (follow-up 30 days)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	5/59 (8.5%)	3.8%	RR 2.23 (0.56 to 8.97)	47 more per 1000 (from 17 fewer to 303 more)	⊕OOO VERY LOW	CRITICAL

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

1.7.2.4 Stricture stratum

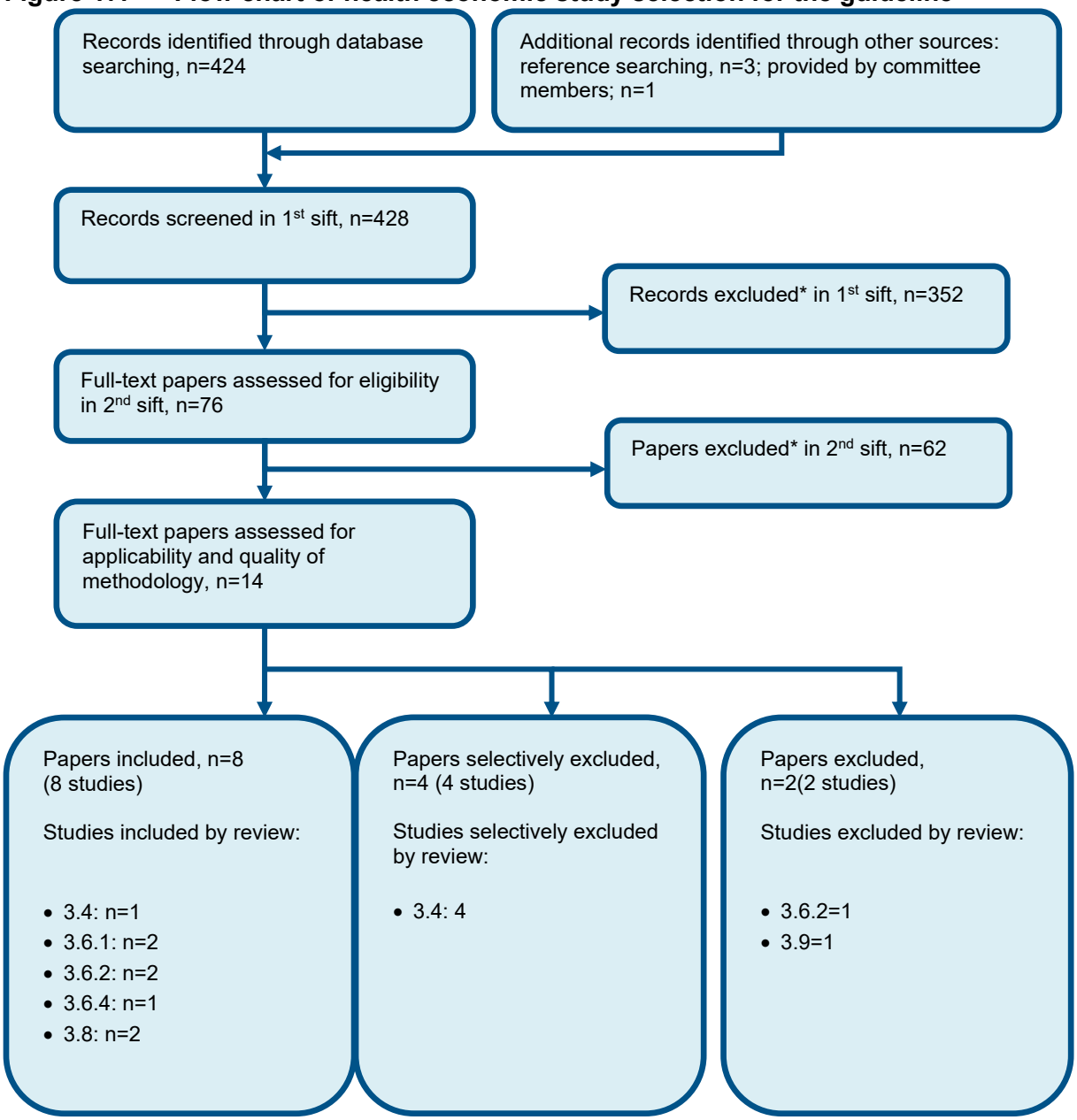
Table 28: Clinical evidence profile: emergency surgery compared to no surgical intervention

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Emergency surgery	No intervention	Relative (95% CI)	Absolute		
30-day mortality (post-admission) (follow-up 30 days)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	2/27 (7.4%)	0%	OR 3.28 (0.05 to 219.76)	70 more per 1000 (from 210 fewer to 360 more)[3]	⊕OOO VERY LOW	CRITICAL

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
[3] Risk difference (95% CIs) reported as there are zero events in control arm.

Appendix G: Health economic evidence selection

Figure 17: Flow chart of health economic study selection for the guideline



* Non-relevant population, intervention, comparison, design or setting; non-English language

3.4 Non-surgical treatment of acute diverticulitis (Evidence review H)

3.6.1 Timing of surgery (Evidence review J)

3.6.2 Laparoscopic versus open resection (Evidence review K)

3.6.4 Primary versus secondary anastomosis (Evidence review M)

3.8 Laparoscopic lavage versus resection for perforated diverticulitis (Evidence review O)

3.9 Management of recurrent diverticulitis (Evidence review P)

Appendix H: Health economic evidence tables

Table 29: Health economic evidence tables

Study	Bachmann 2011 [18]			
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost effectiveness**
Economic analysis: CCA (health outcomes: mortality, morbidity, wound infection, reoperation) **Study design:** Within-trial analysis (non-randomised controlled trial) **Approach to analysis:** Analysis of individual level data for mortality, morbidity, wound infection, reoperation and costs. **Perspective:** Germany Health insurance company perspective **Follow-up:** Costs: None; Outcomes: NR **Discounting:** Costs: n/a; Outcomes: n/a	**Population:** People with complicated acute diverticulitis without perforation (Hinchey Grade I-II), in whom elective surgical resection was planned **Patient characteristics:** n= 421 Mean age: 63 ±13 years Male: 44% Hinchey Grade I: 86% Hinchey Grade II: 14% **Intervention 1:** Delayed elective resection: Treatment with intravenous antibiotics for 5-7 days, then discharged and readmitted for elective resection after 6-8 weeks **Intervention 2:** Early elective resection: Treatment with antibiotics for 2-4 days (median of 2 days) before resection	**Total costs (mean per patient):** Intervention 1: £8,703 Intervention 2: £7,374 Incremental (2−1): Saves £1,329 (95% CI: NR; p≤0.001) **Currency & cost year:** 2004-2009 euros (cost year not specified), presented here as 2009 UK pounds[(b)] **Cost components incorporated:** Costs of hospital spell, including costs of interventions and length of stay (including second admission in delayed resection arm).	**Mortality (in-hospital):** Peto OR: 0.49 (95% CI: 0.03-9.20); ARD: -4 per 1000 **Morbidity:** RR: 1.33 (95% CI: 0.77- 2.28); ARD: +38 per 1000 **Wound infection:** RR: 1.56 (95% CI: 0.78- 3.09); ARD: +40 per 1000 **Reoperation:** RR: 1.43 (95% CI: 0.65- 3.12); ARD: +25 per 1000	**ICER (Intervention 2 versus Intervention 1):** n/a **Analysis of uncertainty:** n/a

Data sources

Health outcomes: Treatment effects from Bachmann study only. Baseline event rate from control arm of single non-randomised controlled trial, with comparable baseline characteristics (age, sex, Hinchey grade, American Society of Anaesthesiologists score) between patients in both arms of trial. Clinical follow-up data obtained by review of hospital records and through direct communication with patients and physicians. **Quality-of-life weights:** n/a **Cost sources:** Costs were obtained by review of invoices to health insurance companies and were based on diagnosis related groups in Germany between 2004-2009. Costs were calculated based on intention-to-treat analysis.

Comments

Source of funding: NR **Limitations:** People were allocated to either the early or delayed arms by the operating surgeon, without randomisation, which could produce selection bias. Some clinical follow up data was obtained directly from patients and physicians and may be subject to recall bias. No regression to account for any baseline differences, though no statistically significant differences reported. No cost year was reported, though the trial period was 2004-2009. Follow-up not reported for outcomes other than costs; no follow-up for costs, which were noted to include only the costs of the interventions. Costs did not include any visits to general practitioners either after the hospitalisations or between the two hospitalisations for the delayed resection group. No detailed analysis of direct cost to hospital undertaken. No quality of life outcome was assessed, deviating from the NICE reference case. **Other:** Primary anastomosis without a diverting stoma was possible in 92% of people in the study (n=387). 77% of people in the study (n=323) underwent laparoscopic resection. 5% (n=8) of those allocated to delayed resection required urgent surgery. Operating time (p<0.001) and hospital stay (p=0.043) were significantly shorter in the delayed resection group based on intention-to-treat analysis. Discussion section states that cost difference is mainly due to costs incurred during the initial intravenous antibiotic treatment.

Overall applicability: Partially applicable[(c)] **Overall quality:** Potentially Serious Limitations[(d)]

Abbreviations: ARD: absolute risk difference; CCA: cost–consequences analysis; 95% CI: 95% confidence interval; ICER: incremental cost-effectiveness ratio; n/a: not applicable; NR: not reported; OR: odds ratio; RR: risk ratio

(a) Converted using 2009 purchasing power parities[117]

(b) Directly applicable / Partially applicable / Not applicable

(c) Minor limitations / Potentially serious limitations / Very serious limitations

Study	Zingg 2007 [183]			
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost effectiveness**
Economic analysis: CCA (health outcomes: mortality at 30 days, morbidity) **Study design:** Retrospective cohort analysis without multivariate regression **Approach to analysis:** Retrospective analysis of individual level data for outcomes and invoice system of Zurich for data on costs. Outcome data was from all eligible people with acute diverticulitis undergoing laparoscopic-assisted sigmoid resection at Triemli Hospital, Zurich 1997-2005.Cost data was from a subgroup of people with acute diverticulitis who underwent either early or delayed resection and received all medical treatment exclusively at Triemli Hospital, Zurich 2004-2005. **Perspective:** Switzerland hospital perspective **Follow-up**: Costs: NR; Mortality: 30 days; Morbidity: NR	**Population:** People with acute diverticulitis without free perforation and peritonitis, undergoing elective laparoscopic-assisted sigmoid resection **Patient characteristics:** Age: Intervention 1: 60.8±11.9 years Intervention 2: 60.7±12.5 years BMI (kg/m^2), mean (standard deviation): Intervention 1: 26.6 ±4.1 Intervention 2: 25.5 ±3.4 p=0.035 Male: NR **Intervention 1:** Delayed elective laparoscopic-assisted sigmoid resection delivered in a second hospitalisation, 6 weeks after the acute episode **Intervention 2:** Early elective laparoscopic-assisted sigmoid resection performed during the same hospitalisation as the acute	**Total costs (mean per patient):** Intervention 1: £7,226 Intervention 2: £7,022 Incremental (2−1): Saves £204 (95% CI: NR; p=0.788) **Currency & cost year:** 2004-2005 euros (presented here as 2005 UK pounds[(b)]) **Cost components incorporated:** All medical treatment including outpatient colonoscopy, intensive care days. Earnings of hospital calculated using daily and flat case rates.	**Mortality (30 days):** Peto OR: Not estimable (95% CI: Not estimable) ARD: 0 per 1000 **Morbidity:** Peto OR: 2.42 (95% CI: 0.52- 11.21) ARD: -137 per 1000	**ICER (Intervention 2 versus Intervention 1):** n/a **Analysis of uncertainty:** n/a

Discounting: Costs: n/a; Outcomes: n/a	episode and following initial antibiotic therapy			

Data sources

Health outcomes: Treatment effects from Zingg study only. Baseline event rate from those who underwent delayed elective laparoscopic-assisted sigmoid resection, without regression to control for differences in baseline characteristics. Data obtained from analysis of medical reports, anaesthetic protocols and surgery reports. **Quality-of-life weights:** n/a **Cost sources:** Costs were calculated by the Administration and Financial department of Triemli Hospital, Zurich, Switzerland, using the invoice system of the state of Zurich 2004-2005.

Comments

Source of funding: NR **Limitations:** Treatment effects from retrospective Zingg study only. No randomisation; the decision to undergo early or delayed surgery was made through shared decision making between the surgeon and person with acute diverticulitis, which could lead to selection bias. Follow-up not reported for costs and morbidity. Cost components not clearly defined. Outcome data based on those presenting 1997-2005; cost data derived from a subgroup presenting 2004-2005. Subgroup for cost analysis restricted to those who exclusively received all medical treatment at the institution, could lead to bias. People in the delayed group may have received initial conservative treatment of unknown type and duration outside of the institution. Percentage male not reported. No regression to account for baseline differences, though statistically significant difference in BMI (no statistically significant differences in other baseline characteristics). More complicated cases in the early group (73% (n=56) in the early group compared with 13% (n=13) in the delayed group). No quality of life outcome was assessed, deviating from the NICE reference case. **Other:** While no statistically significant difference found in total treatment costs between early and delayed elective laparoscopically-assisted resection, the total earnings of the hospital were found to be higher in the delayed group (taken from discussion; actual figure not reported).

Overall applicability: Partially applicable[(c)] **Overall quality:** Potentially serious limitations[(d)]

Abbreviations: ARD: absolute risk difference; BMI: body mass index; CCA: cost–consequences analysis; 95% CI: 95% confidence interval; ICER: incremental cost-effectiveness ratio; n/a: not applicable; NR: not reported; OR: odds ratio

(a) Converted using 2005 purchasing power parities[117]

(b) Directly applicable / Partially applicable / Not applicable

(c) Minor limitations / Potentially serious limitations / Very serious limitations

Appendix I: Excluded studies

I.1 Excluded clinical studies

Table 30: Studies excluded from the clinical review

Study	Exclusion reason
Agnifili 2004[1]	Not in English
Alecha 2014[3]	>10% recurrent in elective group
Alexander 1983[4]	Incorrect study design. Inappropriate comparison
Al-khamis 2016[2]	Not review population
Alvarez 2007[5]	>10% recurrent cases
Alvarez 2009[6]	Not review population. Inappropriate comparison. >10% recurrent diverticulitis. No suitable data to extract
Ambrosetti 1992[9]	Incorrect study design. No relevant outcomes
Ambrosetti 1993[11]	Inappropriate comparison. Incorrect interventions
Ambrosetti 1994[10]	Not review population. Incorrect study design
Ambrosetti 1996[8]	Not review population
Ambrosetti 2005[7]	No relevant outcomes to extract
Ames 2009[12]	Incorrect study design. Not review population
Amin 1984[13]	Incorrect study design. Inappropriate comparison. Incorrect interventions
Anania 2014[14]	Not review population. Incorrect study design. Inappropriate comparison. Incorrect interventions
Anaya 2005[15]	Not review population. No relevant outcome data
Anderson 1997[16]	Not review population. Inappropriate comparison. Incorrect interventions
Antolovic 2009[17]	Not review population. Inappropriate comparison. >10% recurrent diverticulitis
Bacon 1967[19]	Not review population. Incorrect study design. Incorrect interventions
Bargellini 2013[20]	Indications for treatment not comparable among different treatment arms
Belmonte 1996[21]	Incorrect study design. Inappropriate comparison
Binda 2012[22]	>10% recurrent diverticulitis
Bolt 1966[23]	Not review population. Incorrect study design. Inappropriate comparison. Incorrect interventions
Boselli 2017[24]	Inappropriate comparison
Boudart 2008[25]	Not review population. >10% recurrent diverticulitis. >10% uncomplicated diverticulitis
Brandl 2016[26]	Not review population
Bridoux 2014[27]	No relevant outcomes
Broderick-villa 2005[28]	Not review population. No relevant outcomes
Caputo 2015[30]	Not review population. Incorrect study design. Inappropriate comparison. Incorrect interventions
Carpenter 1972[31]	Incorrect study design. Inappropriate comparison. Incorrect interventions
Castro 1969[32]	Incorrect study design. Not review population. Inappropriate comparison. Incorrect interventions

Study	Exclusion reason
Chen 1993[33]	Not in English - full text not ordered
Chung 2016[34]	Not review population. No relevant outcomes
Cirocchi 2013[37]	Systematic review is not relevant to review question or unclear PICO. Incorrect interventions
Cirocchi 2014[35]	Inappropriate comparison. Incorrect interventions. Systematic review is not relevant to review question or unclear PICO
Cirocchi 2015[36]	Not review population. Systematic review is not relevant to review question or unclear PICO. Inappropriate comparison. Incorrect interventions
Colorectal writing group for the 2015[38]	Not review population. Inappropriate comparison. Incorrect interventions
Cunningham 1997[39]	Not review population
Dalmia 2015[40]	Not review population. Incorrect study design. Inappropriate comparison. Incorrect interventions
Devaraj 2016[41]	Not review population. >10% recurrent cases. Inappropriate comparison
Dharmarajan 2011[42]	Inappropriate comparison. Incorrect interventions
Edna 2014[43]	Inappropriate comparison. Incorrect interventions
Egger 2008[44]	Not review population. No relevant outcomes for complicated cases only
Eisenstat 1983[45]	Not review population. Incorrect study design. Inappropriate comparison. Incorrect interventions
El-sayed 2018[46]	Not review population
Farmakis 1994[48]	Incorrect interventions
Felder 2013[49]	No relevant outcomes
Finlay 1987[50]	Not review population. Incorrect interventions
Floyd 1971[51]	Incorrect study design. Not review population. Inappropriate comparison. Incorrect interventions
Frileux 2010[52]	Not review population
Gala 2014[53]	>10% recurrent diverticular disease. No relevant outcomes
Garfinkle 2016[54]	Incorrect study design. Inappropriate comparison. Incorrect interventions
Gillett 1970[55]	Incorrect study design. Inappropriate comparison. Incorrect interventions
Greenberg 2005[56]	Not review population
Gregersen 2016[58]	Not review population
Gregersen 2016[57]	>10% recurrent diverticulitis
Gregg 1987[59]	Not review population. >10% recurrent diverticulitis. Incorrect study design
Guzzo 2004[60]	Not review population. Incorrect study design. Inappropriate comparison. Incorrect interventions
Haas 2016[61]	Systematic review: quality assessment is inadequate. Not review population. Systematic review: methods are not adequate/unclear
Haglund 1979[62]	Not review population
Hoffmann 2012[63]	Not review population
Holmer 2011[64]	Not review population
Holmer 2011[65]	Full text not in English
Horesh 2015[66]	Incorrect study design. Inappropriate comparison. Incorrect interventions

Study	Exclusion reason
Hsiao 2013[67]	Not review population
Humes 2007[68]	Clinical guideline - no data to extract
Humes 2011[69]	Clinical guideline - no data to extract
Humes 2012[70]	Inappropriate comparison. Incorrect interventions
Hussain 2008[71]	>10% recurrent diverticular disease
Jalouta 2017[72]	Incorrect study design. Inappropriate comparison. Incorrect interventions
Janes 2005[73]	Incorrect study design. Literature review
Jeyarajah 2009[74]	Not review population
Kaiser 2005[75]	Not review population. Inappropriate comparison. >10% recurrent diverticulitis
Katz 2013[76]	Systematic review is not relevant to review question or unclear PICO. Inappropriate comparison. Incorrect interventions
Khan 2017[77]	Incorrect interventions. Recurrent diverticulitis - incorrect population
Kim 2007[78]	Not guideline condition. Not review population
Kirchhoff 2011[79]	Not review population. Recurrent diverticulitis
Klarenbeek 2010[80]	>10% recurrent diverticulitis
Klima 2012[81]	Not guideline condition. Not review population
Koo 2007[82]	>10% recurrent cases
Kronborg 1986[83]	Incorrect interventions
Kurumboor 2017[84]	Not review population. Inappropriate comparison. Incorrect interventions. >10% recurrent diverticulitis
Lamb 2014[85]	Systematic review is not relevant to review question or unclear PICO. Lack of data to extract. Systematic review: study designs inappropriate
Lambert 1986[86]	Incorrect interventions
Larson 1976[87]	Not review population
Levy 1967[88]	Not review population. Incorrect interventions. >10% recurrent diverticulitis
Li 2014[90]	Inappropriate comparison. Incorrect interventions
Li 2016[89]	Not review population. Incorrect interventions
Lidor 2011[91]	Not review population
Lim 1999[92]	Incorrect study design
Lubbers 1976[93]	Not review population
Maconi 2011[94]	Not review population. Systematic review is not relevant to review question or unclear PICO. Inappropriate comparison. Incorrect interventions
Maggard 1999[96]	>10% recurrent diverticulitis
Maggard 2001[95]	Not review population. >10% recurrent diverticulitis
Manabe 2015[97]	Not review population. Inappropriate comparison. Incorrect interventions
Martel 2010[98]	Not review population. Inappropriate comparison. Incorrect interventions
Mcleod 2006[99]	No data to extract
Menenakos 2003[100]	Not review population. Inappropriate comparison. Incorrect interventions
Miyaso 2012[101]	Surgical indications in treatment arms not comparable
Mizrahi 2018[102]	Not review population

Study	Exclusion reason
Moon 2007[103]	No relevant outcomes
Moran-atkin 2014[104]	Not review population. Inappropriate comparison. Incorrect interventions
Morse 1974[105]	Not guideline condition. Not review population. Inappropriate comparison
Mueller 2005[106]	Inappropriate comparison. Incorrect interventions
Munson 1996[107]	Incorrect interventions
Murphy 2016[108]	Incorrect study design. No relevant outcome data
Natarajan 2004[109]	Not review population. Inappropriate comparison. Incorrect interventions
Nelson 2008[111]	>10% recurrent diverticulitis in non-operative group
Neumann 1991[112]	Not in English
Niebling 2013[113]	Incorrect study design. Inappropriate comparison. Incorrect interventions
Nigri 2015[114]	Not review population. Systematic review is not relevant to review question or unclear PICO. Incorrect interventions
Nylamo 1990[115]	>10% recurrent cases for one or more arms
Occhionorelli 2016[116]	Inappropriate comparison
Ouriel 1983[118]	Incorrect study design. Inappropriate comparison. Incorrect interventions
Pappalardo 2013[119]	Incorrect interventions. Inappropriate comparison
Parker 2017[120]	Not review population. Inappropriate comparison. Incorrect interventions
Parks 1970[121]	Not review population
Partsch 2005[122]	Not review population. Incorrect study design. Inappropriate comparison. Incorrect interventions
Paton 2008[123]	Not guideline condition. Not review population
Pattyn 1996[124]	Not review population. Incorrect study design. Inappropriate comparison. Incorrect interventions
Peery 2013[125]	Literature review
Peppas 2007[126]	Not review population
Pheils 1982[127]	Not review population. Incorrect study design. Inappropriate comparison. Incorrect interventions
Pisanu 2012[128]	Inappropriate comparison. Incorrect interventions
Pisanu 2013[129]	Incorrect interventions. Inappropriate comparison
Raats 2015[130]	Not guideline condition. Not review population
Reissfelder 2006[132]	Not review population. >10% recurrent diverticulitis. Incorrect interventions
Reyes-espejel 2015[133]	Not in English - full text not ordered
Rodkey 1984[134]	Inappropriate comparison. Incorrect interventions
Roig 2016[135]	Incorrect study design
Roscoe 2017[136]	Abstract only
Rose 2015[137]	Not review population
Rosen 2017[138]	Incorrect study design. Inappropriate comparison. Incorrect interventions
Rotholtz 2009[139]	Not review population. Recurrent diverticulitis
Royds 2012[140]	No comparator group. Inappropriate comparison. Incorrect interventions

Study	Exclusion reason
Ryan 1974[141]	Incorrect study design
Salem 2004[142]	Not review population
Sallinen 2014[143]	Inappropriate comparison. Incorrect interventions
Sarin 1991[144]	Inappropriate comparison. Incorrect interventions
Sarin 1994[145]	Different treatment groups made up of different types of complication
Schneider 2015[146]	Not review population. No relevant outcomes. Incorrect interventions. Inappropriate comparison
Schwandner 2005[147]	Not review population. Inappropriate comparison. Incorrect interventions
Sengupta 2017[148]	Not guideline condition. Not review population. Incorrect interventions
Sher 1997[149]	Incorrect interventions
Simianu 2014[150]	No relevant outcomes
Simianu 2016[151]	Not review population. Inappropriate comparison. Incorrect interventions
Slim 2006[152]	No extractable data
Slim 2008[153]	No extractable data
Smirniotis 1992[154]	Incorrect interventions
Solkar 2005[155]	Incorrect population
Spanjersberg 2011[156]	Not guideline condition. Not review population. Incorrect interventions
Spivak 1997[157]	Incorrect study design. Not review population
Sutherland 2013[158]	Not guideline condition. Not review population. Systematic review is not relevant to review question or unclear PICO. Inappropriate comparison. Incorrect interventions
Takano 2013[159]	Not review population. Incorrect interventions. Inappropriate comparison. >10% recurrent diverticulitis
Tam 2014[160]	Not guideline condition. Not review population. Incorrect study design. Inappropriate comparison. Incorrect interventions
Tan 2013[161]	No relevant outcomes
Thiede 1992[162]	Not in English - full text not ordered
Titos-garcia 2017[163]	Inappropriate comparison. Incorrect interventions
Trenti 2015[164]	Not review population. Inappropriate comparison. Incorrect interventions
Van de wall 2010[166]	Not review population
Van de wall 2013[169]	Not review population. Systematic review is not relevant to review question or unclear PICO. Inappropriate comparison. Incorrect interventions
Van de wall 2013[167]	Inappropriate comparison. Incorrect interventions
Van de wall 2013[168]	Inappropriate comparison. Incorrect interventions
Van de wall 2017[170]	Not review population
Vasilevsky 1998[171]	Incorrect study design. Inappropriate comparison
Venara 2015[172]	Incorrect study design. Inappropriate comparison. Incorrect interventions
Vetter 2016[173]	Inappropriate comparison. Incorrect interventions
Violi 2000[175]	Incorrect study design. Inappropriate comparison. Incorrect interventions
Walker 2002[176]	Not guideline condition. Not review population. Inappropriate

Study	Exclusion reason
	comparison. Incorrect interventions
Woods 1988[178]	Inappropriate comparison. Incorrect interventions
Yucel 2012[179]	Full text not in English
Zapletal 2007[180]	Inappropriate comparison. Incorrect interventions
Zdichavsky 2013[181]	Inappropriate comparison
Zeitoun 2000[182]	Incorrect interventions

Appendix J: Research recommendations

J.1 Surgical management of complicated acute diverticulitis

Research question: What are the clinically and cost effective surgical approaches to managing complicated acute diverticulitis, including timing of surgery (elective or emergency)?

Why this is important:

The management of diverticular abscess and perforation have been dealt with by the clinical review in terms of initial management and treatment by antibiotics, percutaneous drainage or surgery (lavage and resectional). A number of patient groups however need to be considered in particular those who undergo treatment for diverticular abscess or perforation who are treated conservatively without initial surgery. No studies were found to guide the management of these patients and it is not clear as to whether they should be offered resectional surgery either during the initial admission or following discharge.

Table 31: Criteria for selecting high-priority research recommendations:

PICO question	**Population:** Patients treated conservatively without initial surgery for diverticular abscess or perforation. **Intervention/comparison:** Planned surgery versus no surgery **Outcomes:** Mortality Morbidity (anastomotic leak, stoma, readmission with further complicated acute diverticulitis)
Importance to patients or the population	There are no clear evidence based guidelines on the treatment of ths patient group. Patient could be given information on the need for resection of the affected segment of bowel following development of complicated acute diverticulitis.
Relevance to NICE guidance	Research in this area would inform NICE guidelines on the most appropriate management for this group of patients.
Relevance to the NHS	This group of patients place a large burden on health care services and the development of further complications and readmissions are unknown leading to uncertainty as to the best way to manage these patients.
Current evidence base	There is no randomised or observational evidence currently to support decision making in this area.
Equality	Not applicable
Study design	Cohort studies of patients identified through routinely collected data or RCT.
Feasibility	It may be difficult to recruit patients into an RCT without prior observational studies demonstrating the potential outcomes.
Importance	The committee consider this an important area for further research although they are aware of current research ongoing in the area