

Health economic analysis of laparoscopic lavage *versus* Hartmann's procedure for diverticulitis in the randomized DILALA trial

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Background: Open surgery with resection and colostomy (Hartmann's procedure) has been the standard treatment for perforated diverticulitis with purulent peritonitis. In recent years laparoscopic lavage has emerged as an alternative, with potential benefits for patients with purulent peritonitis, Hinchey grade III. The aim of this study was to compare laparoscopic lavage and Hartmann's procedure with health economic evaluation within the framework of the DILALA (DIverticulitis – LAparoscopic LAVage *versus* resection (Hartmann's procedure) for acute diverticulitis with peritonitis) trial.

Methods: Clinical effectiveness and resource use were derived from the DILALA trial and unit costs from Swedish sources. Costs were analysed from the perspective of the healthcare sector. The study period was divided into short-term analysis (base-case A), within 12 months, and long-term analysis (base-case B), from inclusion in the trial throughout the patient's expected life.

Results: The study included 43 patients who underwent laparoscopic lavage and 40 who had Hartmann's procedure in Denmark and Sweden during 2010–2014. In base-case A, the difference in mean cost per patient between laparoscopic lavage and Hartmann's procedure was €–8983 (95 per cent c.i. –16 232 to –1735). The mean(s.d.) costs per patient in base-case B were €25 703(27 544) and €45 498(38 928) for laparoscopic lavage and Hartmann's procedure respectively, resulting in a difference of €–19 794 (95 per cent c.i. –34 657 to –4931). The results were robust as demonstrated in sensitivity analyses.

Conclusion: The significant cost reduction in this study, together with results of safety and efficacy from RCTs, support the routine use of laparoscopic lavage as treatment for complicated diverticulitis with purulent peritonitis.

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Introduction

Diverticulosis is a common condition in the Western world and increases with age. Some 15–25 per cent of patients with diverticulosis also develop an inflammatory condition, diverticulitis¹. Diverticulitis can be divided into uncomplicated and complicated disease. In the 1970s, Hinchey and colleagues² suggested that the more complicated condition should be classified using intraoperative findings. Hinchey grade III indicates perforated colon with purulent peritonitis and grade IV represents perforated colon with faecal leakage into the abdomen.

For Hinchey grade III and IV diverticulitis the standard treatment has been emergency surgery, commonly open surgery with resection of the diseased bowel segment³. An end colostomy is constructed and the rectal stump is oversewn or stapled (Hartmann's procedure)^{3,4}. The stoma can be reversed in a future operation, although with associated risk of morbidity and mortality⁵. Another less common option is colonic resection with primary anastomosis with or without a diverting ileostomy⁴. Recent reports^{6,7} have shown that an alternative, comprising laparoscopy, lavage and drainage without colonic resection or stoma, exists for Hinchey grade III.

Four RCTs have been initiated comparing open resection with laparoscopic lavage, and three have reported results^{8–11}: DILALA, SCANDIV (Scandinavian Diverticulitis trial) and LOLA (treatment arm in Laparoscopic Peritoneal Lavage or Resection for General Peritonitis for Perforated Diverticulitis (LADIES) trial). The primary composite endpoint of LOLA, major morbidity and mortality within 1 year after index surgery, was reached in 67 per cent in the laparoscopic lavage group and 60 per cent in the sigmoid resection group¹⁰. The primary outcome in the SCANDIV trial was severe post-operative complications at 90 days, which affected 31 per cent of patients in the lavage group and 26 per cent in the colonic resection group⁹. Neither of these trials reported statistically significant differences in primary endpoints. The primary endpoint of DILALA was percentage of patients undergoing one or more reoperation within 12 months: 28 per cent in the laparoscopic lavage group and 63 per cent in the Hartmann's procedure group, a significant difference ($P=0.004$)¹¹. Furthermore, duration of surgery, length of hospital stay, time in the recovery room and number of transfusions differed significantly between the groups in favour of laparoscopic lavage. There were no significant differences in secondary outcomes such as complications, mortality, or health-related quality of life measured with EQ-5D™ (EuroQol Group, Rotterdam, The Netherlands) and Short Form 36 (SF-36®; QualityMetric, Lincoln, Rhode Island, USA)^{8,11}.

However, economic evaluations comparing laparoscopic lavage and colonic resection for complicated diverticulitis are still lacking. One RCT¹² reported the costs associated with Hartmann's procedure and resection with primary anastomosis in patients with complicated diverticulitis, and found no significant difference with regard to in-hospital costs for these procedures. The aim of the present study was to assess the costs of laparoscopic lavage *versus* Hartmann's procedure and to relate them to clinical effectiveness in the DILALA trial.

Methods

DILALA trial

DILALA is an RCT comparing the outcomes of laparoscopic lavage *versus* Hartmann's procedure for perforated diverticulitis with purulent peritonitis (Hinchey grade III)¹³. The study was conducted at nine centres in Sweden and Denmark from February 2010 to February 2014. Inclusion criteria comprised radiological examination showing intra-abdominal fluid or gas, and the decision to perform surgery. Each patient gave informed consent before surgery. The procedure started with a diagnostic

laparoscopy; if diverticulitis Hinchey grade III was found, the patient was randomized to laparoscopic lavage or Hartmann's procedure. Clinical information was collected for the operative and postoperative phases, as well as for follow-up at 6–12 weeks, 6 months and 1 year¹³. Elective colonic resection at a later stage was not recommended as routine in the trial protocol. It was recommended only if considered necessary as an emergency procedure in the event of recurrent complicated diverticulitis or to treat complications after the initial diverticulitis (for example fistulas or colonic strictures).

The present economic analysis of the DILALA trial is reported according to the CHEERS guideline, as recommended by the EQUATOR network¹⁴.

Health economic methodology

As laparoscopic lavage resulted in significantly fewer reoperations than Hartmann's procedure, superiority in terms of effectiveness was demonstrated. For the cost analysis, resource use was recorded in the DILALA trial, from all centres in Denmark and Sweden. Unit costs were derived from Swedish sources and subsequently applied to all patients in the study. All randomized patients were included and analysis was by intention to treat. The analysis included two time intervals; one included all costs accumulated during 12 months in the trial (base-case A) and the other included all costs from inclusion in the trial throughout the patient's expected lifetime (base-case B). The costs were analysed from the perspective of the healthcare sector.

Data collection

Resource use was collected at patient level in the DILALA trial. For the present analysis some resource use items were aggregated into meaningful measures. The principle of 'gross-costing' was applied for predictable combinations of specific resource use items, expected to be driven in some predetermined way by, for example, hospital procurement decisions rather than differences associated with the surgical interventions studied¹⁵.

Resource use

Basic laparoscopic equipment was the same regardless of hospital; therefore, a set of equipment was identified at Sahlgrenska University Hospital, Sweden. The number of laparoscopic procedures from 2013 and 2014 was extracted from an administrative database at the same hospital. None of the procedures was robot-assisted. The total cost of equipment was divided by number of laparoscopic procedures to obtain a cost per laparoscopic operation. This cost was used for all procedures in the laparoscopic lavage group.

Surgical instruments needed per surgical technique were: vessel-sealing instruments, stapling instrument to divide the colon and close the rectal remnant, suture materials and laparoscopic ports. The use of disposable instruments was collected individually and applied in the analysis. Saline for rinsing of the abdomen was included in this category of resource use. The decision on available instrument brand was made at departmental level, and was therefore unrelated to type of surgical technique¹⁵.

Duration of anaesthesia, time in the recovery room, number of transfusions, length of hospital stay, frequency of reoperations and length of hospital stay during readmission without reoperation were collected at the patient level. It was assumed that the exact items of resource use for the two treatments were the same for duration of anaesthesia (except basic laparoscopic equipment and surgical instruments), time in recovery room, number of transfusions, length of hospital stay, colonoscopies and reoperations. The same assumption was made for stoma reversal and sigmoidectomy in the base-case B analysis. Therefore, gross-costing was used for all variables in this section.

In both base-case analyses, a colonoscopy was included for all patients in the laparoscopic lavage group during the first year after primary surgery to diagnose cancer if present. All patients in the Hartmann's procedure group who had stoma reversal surgery were also assumed to undergo preoperative diagnostic colonoscopy. In base-case B, the cost of colonoscopy was added for all patients who underwent stoma reversal surgery.

A standard antibiotic treatment per type of infectious adverse event was assumed to be 3 days of intravenous piperacillin and tazobactam, and an additional 7 days of oral metronidazole and cephalosporin. Only infectious adverse events occurring within 90 days of the index operation were assumed to relate to the index surgical procedure.

Relatively few patients (5 of 43 in the laparoscopic lavage group and 5 of 37 in the Hartmann's procedure group) were admitted to the ICU. Time in the ICU was excluded from the cost analysis because it was deemed unrelated to the underlying surgical technique.

Presence of a stoma is expected to lead to a difference in resource use between the treatments. All patients undergoing Hartmann's procedure have a colostomy from the index operation onwards and the stoma was reversed either during the trial, after the trial, or not at all. Days with a stoma were calculated. The resource items needed per day for stoma care were estimated for a typical patient with a stoma in collaboration with a specialized stoma nurse. After the 1-year follow-up in the trial, there are patients who may still have a stoma. Although it is possible to reverse the colostomy, many studies have concluded that

the colostomy may not be reversed¹⁶. This is important when considering the comparative costs of the procedures because a stoma will incur costs each year for the duration of the patient's expected lifetime. To model the expected cost for a patient with a stoma after 12 months, a decision tree with corresponding probabilities and unit costs was set up¹⁷. The events included were stoma reversal later than 12 months (25 per cent) and non-reversal (75 per cent), and concurrent events included success (86 per cent), creation of another stoma owing to failure to reverse (13 per cent) and death (1 per cent) (*Fig. S1*, supporting information). These probabilities were derived from a population-based study by Salem and colleagues¹⁸ on Hartmann's procedure and reversal in diverticulitis. The study included 5420 colostomies performed between 1987 and 2000, and used a Washington State administrative database. The cost per branch in the decision model was multiplied by the probability of the event occurring during a patient's lifetime, resulting in a total expected cost per patient added to the base-case B analysis. The mean life expectancy was calculated for patients with a stoma at 12 months, and was 20 years.

For laparoscopic lavage, the inflamed part of the bowel was not resected during the index operation. After 12 months some patients may undergo a secondary operation to resect the affected bowel segment owing to recurrence (although this is debated) or further complications^{19,20}. As the last follow-up was at 12 months, it was assumed that 25 per cent of the patients who underwent laparoscopic lavage would later require a resection with primary anastomosis and the creation of a loop ileostomy (25 per cent) or not (75 per cent) (*Fig. S2*, supporting information). The ileostomy was assumed to be reversed after 3 months. These events were modelled using a decision tree model with cost weighted by the probability of their occurrence, and the expected costs were included in the base-case B analysis¹⁷.

Probabilities and costs for the decision tree models can be found in *Tables S1* and *S2* (supporting information).

Unit costs

The unit costs for basic laparoscopic equipment and surgical instruments were derived from region Västera Götaland in Sweden, which procures healthcare goods and services centrally for a region of approximately 1.6 million inhabitants. A full list of instruments and other disposable materials used in this study and their unit costs can be found *Tables S3* and *S4* (supporting information).

The unit costs for duration of anaesthesia, time in the recovery room, transfusions, length of hospital stay,

Table 1 Baseline characteristics

	Laparoscopic lavage (n = 43)	Hartmann's procedure (n = 40)
Age (years)*	64 (50–76)	68 (56–79)
Sex ratio (M : F)	21 : 22	16 : 24
BMI (kg/m ²)*†	25.6 (24.9–27.8)	24.9 (22.5–28.2)
ASA fitness grade‡		
I: healthy	7	9
II: mild systemic disease	24	13
III: severe systemic disease	9	13
IV: severe life-threatening systemic disease	0	2

*Values are median (i.q.r.). †Data missing for ten patients in lavage group and 12 in Hartmann's group; ‡data missing for three patients in each group.

colonoscopy and readmissions were collected after interviews with an economist at Sahlgrenska University Hospital, Sweden. It was ascertained that the unit cost represented the actual cost per unit and did not entail the cost of composite variables in the present study. The cost per day for stoma material (in both base-case analyses) and the cost per dose of the antibiotic treatment were obtained from pharmacy retail prices in Sweden. The unit cost per type of reoperation (classified using the Nordic Medico-Statistical Committee (NOMESCO) Classification of Surgical Procedures version 1.16) was collected from the national cost per patient database (Swedish Association of Local Authorities and Regions). Unit costs for elective readmission and sigmoidectomy (with and without ileostomy) and stoma reversal used in the two models were also collected from this source. The unit costs for reoperations per NOMESCO code can be found in *Table S5* (supporting information).

All costs are expressed in euros (1 Swedish krona = 0.11 euros; exchange rate 22 March 2016).

Table 2 Clinical resource use

	Laparoscopic lavage (n = 43)	Hartmann's procedure (n = 40)	Source
Basic laparoscopic equipment	43	–	Estimated by personnel from operating ward
Surgical instruments†	Actual use	Actual use	DILALA
Duration of anaesthesia (min)*	129(8)	222(10)	DILALA
Transfusions (units)*	0.3(0.1)	0.4(0.2)	DILALA
Time in recovery room (min)*	383(74)	470(79)	DILALA
Length of hospital stay, index surgery (days)*	9(1)	11(1)	DILALA
Patients requiring antibiotics (infectious adverse events)	27	18	DILALA
Colonoscopy	40	21	DILALA
Reoperation	15	32	DILALA
Time with stoma (days)*	16(10)	206(21)	DILALA
Length of hospital stay, readmission (days)*	5(2)	1(1)	DILALA

*Value are mean(s.d.). †Surgical instrument use was determined at the patient level; for exact resource utilization see *Table S4* (supporting information).

Statistical analysis

Data on cost and resource use collected alongside clinical trials often exhibit a right-skewed distribution²¹. Arithmetic mean costs and 95 per cent percentile confidence intervals (c.i.) in the laparoscopic lavage group and the Hartmann procedure group were calculated using a non-parametric bootstrap method²².

Two methods have been recommended as a minimum requirement to account for censoring, referred to as Lin, and Bang and Tsiatis²³. In the Lin method²⁴, the mean cost per patient at each time point is weighted by the corresponding probability of survival. In the present cost analysis, the time points consist of follow-up times (6–12 weeks, 6 months and 12 months after surgery). The Bang and Tsiatis²⁵ method involves weighting the patient-specific cost by the inverse probability of the patient being observed (not censored) at the beginning of each follow-up. Results of both methods are presented as sensitivity analyses. One-way sensitivity analysis was employed to assess the impact of variables with considerable influence on the base-case results. The costs were changed by 30 per cent for one variable at a time for either laparoscopic lavage or Hartmann's procedure.

All analyses were performed in Stata[®] release 14 (Stata-Corp, College Station, Texas, USA).

Results

Of 139 enrolled patients undergoing diagnostic laparoscopy, 83 were randomized to laparoscopic lavage (43 patients) or Hartmann's procedure (40). Baseline clinical characteristics are presented in *Table 1*. During the course of the trial six patients died and three were lost to follow-up in the laparoscopic lavage group, and six and four respectively in the Hartmann's procedure group; these patients

Table 3 Unit cost per resource use variable

	Unit cost (€)	Unit	Source
Basic laparoscopic equipment	197	Per laparoscopic lavage	Region Västra Götaland, Sweden
Surgical instruments*	Cost per item	Per laparoscopic lavage and Hartmann's procedure	Region Västra Götaland, Sweden
Duration of anaesthesia	25	Per minute	Sahlgrenska University Hospital, Gothenburg, Sweden
Transfusion	137	Per unit	Sahlgrenska University Hospital, Gothenburg, Sweden
Time in recovery room	64	Per hour	Sahlgrenska University Hospital, Gothenburg, Sweden
Length of hospital stay, index operation	720	Per day	Sahlgrenska University Hospital, Gothenburg, Sweden
Antibiotics (infectious adverse events)	99–131	Per antibiotic treatment	Pharmacy retail price
Colonoscopy	468	Per examination	Sahlgrenska University Hospital, Gothenburg, Sweden
Reoperation*	See Methods	Per type of reoperation	Swedish Association of Local Authorities and Regions
Stoma material	8	Per day with ileostomy	Pharmacy retail price
	13	Per day with colostomy	
Length of hospital stay, readmission	720	Per day	Sahlgrenska University Hospital, Gothenburg, Sweden
Expected cost, stoma†	67 236	Per stoma	
Expected cost, sigmoid resection‡	4282	Per sigmoid resection	

*Unit costs of surgical instruments and reoperations are available in *Tables S3* and *S4* (supporting information). †The expected costs for stoma and sigmoid resection after cessation of the clinical trial are included in the base-case B analysis. These costs are added only for eligible patients. For detailed calculations see *Tables S1–S3* (supporting information).

were censored. The resource use and corresponding unit costs are shown in *Tables 2* and *3* respectively.

The mean cost per laparoscopic lavage and Hartmann's procedure per resource use variable is shown in *Table 4*. The cost-driving variables for both base-case analyses were duration of anaesthesia (mean(s.d.) difference €–2344(2541), the cost of stoma material in the 12 months after index surgery (difference €–2385(2656)), reoperations (difference €–6253(29 178) and length of hospital stay for readmissions (difference €1707(9538)).

For base-case B analysis, the difference in mean costs per treatment group for the sigmoid resection and stoma reversal models were €3670(–) and €18 889(55 045) respectively. Details of the expected costs for both models are available in *Table S6* (supporting information).

Total mean cost and difference in mean cost per treatment are shown in *Table 5*. In the base-case A analysis, mean(s.d.) costs were €18 025(14 646) for laparoscopic lavage and €27 009(18 445) for Hartmann's procedure; the difference was €–8983 (95 per cent c.i. –16 232 to

Table 4 Mean cost per patient per surgical technique and difference in mean cost per resource use variable and surgical technique

	Laparoscopic lavage (€)	Hartmann's procedure (€)	Difference (lavage – Hartmann's) (€)
Basic laparoscopic equipment	197	–	197(–)
Surgical instruments	236(20)	231(48)	5(74)
Duration of anaesthesia	3189(1190)	5534(1350)	–2344(2541)
Transfusion	39(97)	56(139)	–16(243)
Time in recovery room	372(483)	436(478)	–64(963)
Length of hospital stay, index operation	5542(3926)	6252(4007)	–710(7944)
Antibiotics (infectious adverse events)	65(64)	47(82)	18(146)
Reoperation	5624(10 013)	11 877(17 805)	–6253(29 178)
Colonoscopy	435(121)	298(229)	138(354)
Stoma material	199(804)	2584(1672)	–2385(2656)
Length of hospital stay, readmission	2571(6196)	864(2797)	1707(9538)
Sigmoid resection model, > 12 months*†	3670(1520)	–	3670(–)
Stoma reversal model, > 12 months‡	5763(19 096)	24 652(32 953)	–18 889(55 045)

Values are mean(s.d.). *Undiscounted. †No patient in the Hartmann's group was eligible for sigmoid resection model. ‡Three patients in the laparoscopic lavage group had a stoma at 12 months and were therefore eligible for the stoma reversal model. For detailed calculations see *Tables S1–S3* (supporting information).

Table 5 Mean total cost and difference in mean total cost per surgical technique in different models

	Laparoscopic lavage (€)*	Hartmann's procedure (€)*	Difference (lavage – Hartmann's) (€)	s.d.	95% c.i.	P
Base-case A	18 025(14 646)	27 009(18 445)	–8983	33 190	–16 232, –1735	0.016
Non-parametric bootstrap				32 553	–16 218, –2191	0.012
Base-case B	25 703(27 544)	45 498(38 928)	–19 794	67 889	–34 657, –4931	0.010
Non-parametric bootstrap				66 938	–34 200, –5488	0.007
Lin	18 480(14 696)	30 133(17 156)	–11 653	31 876	–18 614, –4691	0.001
Non-parametric bootstrap				31 100	–18 531, –5488	0.001
Bang and Tsiatis	18 952(16 681)	29 874(21 166)	–10 922	37 972	–19 215, –2629	0.011
Non-parametric bootstrap				38 007	–19 707, –3256	0.009

*Values are mean(s.d.). Non-parametric bootstrap based on 2000 iterations; corresponding confidence intervals are calculated using the value of the 2.5 and 97.5 per cent percentiles as confidence limits.

–1735; $P=0.016$). In the base-case B analysis, the costs were €25 703(27 544) and €45 498(38 928) for laparoscopic lavage and Hartmann's procedure respectively, with a difference in mean total cost of €–19 794 (95 per cent c.i. –34 657 to –4931). The bootstrap method did not change the results significantly. Adjusting for censoring in

the base-case A analysis augmented the cost difference in favour of laparoscopic lavage.

One-way sensitivity analysis was conducted including the variables that influenced results the most (*Table 6*). Robustness was demonstrated for 30 per cent changes in total costs for duration of anaesthesia, stoma material and

Table 6 Sensitivity analyses

	Difference in mean total cost (lavage – Hartmann's) (€)	
	Base-case A	Base-case B
Sigmoid resection model		
Laparoscopic lavage –30%	–	–20 690 (–35 582, –5799)
Laparoscopic lavage +30%	–	–18 898 (–33 735, –4061)
Stoma reversal model		
Laparoscopic lavage –30%	–	–21 201 (–35 354, –7049)
Laparoscopic lavage +30%	–	–18 387 (–33 972, –2802)
Hartmann's procedure –30%	–	–14 247 (–27 064, –1431)
Hartmann's procedure +30%	–	–25 341 (–42 462, –8219)
Duration of anaesthesia		
Laparoscopic lavage –30%	–9829 (–17 030, –2628)	–20 640 (–35 456, –5824)
Laparoscopic lavage +30%	–8138 (–15 436, –839)	–18 949 (–33 860, –4037)
Hartmann's procedure –30%	–7531 (–14 746, –315)	–18 341 (–33 161, –3522)
Hartmann's procedure +30%	–10 436 (–17 723, –3149)	–21 247 (–36 156, –6337)
Length of hospital stay, index operation		
Laparoscopic lavage –30%	–10 646 (–17 794, –3498)	–21 457 (–36 246, –6667)
Laparoscopic lavage +30%	–7321 (–14 687, 46)	–18 131 (–33 076, –3187)
Hartmann's procedure –30%	–7201 (–14 426, 23)	–18 012 (–32 839, –3185)
Hartmann's procedure +30%	–10 765 (–18 057, –3474)	–21 576 (–36 486, –6666)
Stoma material		
Laparoscopic lavage –30%	–9029 (–16 244, –1814)	–19 840 (–34 669, –5010)
Laparoscopic lavage +30%	–8912 (–16 163, –1661)	–19 723 (–34 594, –4852)
Hartmann's procedure –30%	–8218 (–15 428, –1009)	–19 029 (–33 789, –4269)
Hartmann's procedure +30%	–9722 (–16 982, –2463)	–20 533 (–35 475, –5591)
Length of hospital stay, readmission		
Laparoscopic lavage –30%	–10 061 (–17 096, –3025)	–20 872 (–35 608, –6135)
Laparoscopic lavage +30%	–8554 (–15 997, –1111)	–19 365 (–34 259, –4471)
Hartmann's procedure –30%	–8951 (–16 168, –1734)	–19 762 (–34 584, –4939)
Hartmann's procedure +30%	–9664 (–16 894, –2433)	–20 474 (–35 268, –5681)
Reoperation		
Laparoscopic lavage –30%	–10 670 (–17 591, –3750)	–21 481 (–35 974, –6988)
Laparoscopic lavage +30%	–7296 (–15 080, 488)	–18 107 (–33 220, –2994)
Hartmann's procedure –30%	–5420 (–11 594, 753)	–16 231 (–30 239, –2223)
Hartmann's procedure +30%	–12 546 (–21 217, –3876)	–23 357 (–39 068, –7646)

Values in parentheses are 95 per cent confidence intervals. Confidence intervals are not based on non-parametric bootstrap.

length of hospital stay for readmission. Changes in the total cost for length of hospital stay after the index operation and reoperations affected the results the most. In base-case B, the results were even more robust and therefore less sensitive to changes in costs of each variable, as the cost difference became larger because of the addition of costs for stoma material and reversal surgery.

In DILALA, laparoscopic lavage was demonstrated to be more effective and in the present study also less costly. No cost-effectiveness analysis was warranted to complete the health economic assessment of the DILALA study.

Discussion

In this health economic evaluation, laparoscopic lavage as treatment for perforated diverticulitis with purulent peritonitis resulted in significantly lower costs than Hartmann's procedure. These results add an economic perspective to the demonstrated efficacy and safety of laparoscopic lavage as treatment for this condition.

There are three other recently published or ongoing randomized trials comparing laparoscopic lavage with resection for perforated diverticulitis with purulent peritonitis. None has so far reported economic evaluations. Two of the other trials^{9,10} have reported primary endpoints with no significant differences between laparoscopic lavage and resection. In the DILALA trial, there was a lower risk of reoperation for patients undergoing laparoscopic lavage, with no significant difference in rate of adverse events¹¹. The fourth RCT²⁶ has not yet reported results.

In DILALA, infectious adverse events were observed more frequently in the laparoscopic lavage group, whereas serious cardiovascular adverse events were more common in the Hartmann's procedure group. The effects of these adverse events have been included in the costing in the present study. Similar findings were made within 90 days in SCANDIV⁹.

In the DILALA trial, stoma reversal was considered a reoperation. This is because stoma reversal is associated with severe morbidity and even death. Thus, from the patient's and as well as a health economic point of view, it is a burdensome procedure. Moreover, successful stoma reversal could improve health-related quality of life. In fact, the cost of an uncomplicated stoma reversal corresponds to a few years of cost for stoma material, so it seems reasonable to strive for stoma reversal whenever possible.

Many studies of the clinical course after Hartmann's procedure for diverticulitis have reported stoma reversal rates

of about 50 per cent within 12 months¹⁵. In the DILALA trial the corresponding figure was 72 per cent¹¹. This was probably attributed to the trial setting focusing on stoma reversal more than is usually the case in routine clinical practice. This makes for a conservative cost estimation for the Hartmann group in the present cost analysis and therefore strengthens the results.

Costs related to long-term stoma care and possible sigmoid resection beyond the time period of the DILALA trial were included in the base-case B analysis. The models addressing these extrapolations include assumptions based on published data, and the results of the model analyses are therefore uncertain. Broderick-Villa and co-authors²⁰ analysed treatment for recurrent diverticulitis in a retrospective cohort study including 3165 patients with acute diverticulitis. They found that approximately 13 per cent of patients had recurrence once or twice after initial non-operative treatment. Another study²⁷ of 743 patients, who presented with acute diverticulitis, reported that 242 patients underwent surgery at baseline. During follow-up, the recurrence rate for these patients was 5.8 per cent and the rate of emergency surgery 1.3 per cent. The 25 per cent rate of sigmoid resection beyond 12 months used in the base-case B analysis here can be regarded as in favour of the Hartmann's procedure group. Furthermore, the cost difference in base-case B remained robust even when allowing for 30 per cent changes in expected future costs for stoma reversal or sigmoid resection.

Stoma use makes the cost of Hartmann's procedure increase over time and the difference in costs compared with laparoscopic lavage is thus expected to grow. This highlights the importance of including both short- and long-term costs and consequences in economic evaluations. This study incorporated potential uncertainties regarding laparoscopic lavage. Some patients may need sigmoidectomy, as the bowel is not resected in the emergency operation, and also colonoscopies to make certain that a cancer is not present. Even with the assumption of a relatively high probability of resection after the trial, the expected costs of sigmoidectomy are not comparable to the future expected costs of a stoma in the Hartmann's procedure group.

As the cost difference increases after cessation of the clinical trial, the authors have chosen not to discount future costs. Results without discounting probably overestimate the cost to the advantage of laparoscopic lavage. As it is not known when the events in the model would occur, discounting would be uncertain. However, the sensitivity analyses provide a general impression of how discounting would have affected the results.

In the cost analysis, most variables relating to resource use were collected prospectively in the setting of a

randomized trial with long follow-up and few missing data. Significant differences were found in the majority of resource use variables^{8,11}. From the sensitivity analyses, it is concluded that the results are robust to significant changes in costs.

The study could be criticized for its small cohort size. However, as the efficacy results, the majority of clinical resource use variables, and all the calculated costs were statistically significantly in favour of laparoscopic lavage, the sample size appears to be sufficient.

Data on productivity loss from paid or unpaid work were not collected and time in the ICU was not included in the analysis. Both of these resource use variables may give rise to rare but extreme costs, which can influence the entire result of the study and single-handedly tip the result in one direction, especially if the study contains few patients as is the case here¹⁵. It was reported recently that patients who underwent open colectomy were absent from work on average 2.75 days more than those who had laparoscopic surgery²⁸. Based on these results, if sick leave costs were included, it is likely that Hartmann's procedure would be even more costly than laparoscopic lavage. Any future analysis of a larger cohort should include productivity losses as well as time in the ICU.

The authors chose to not model incisional hernia in the base-case B analysis. According to the 5-year results from the CLASICC (Conventional *versus* Laparoscopic-Assisted Surgery in Colorectal Cancer) trial²⁹, 9.2 per cent of patients in the open group experienced hernia compared with 8.6 per cent in the laparoscopic group. In the same study, 23 of 39 hernias were managed by surgery. However, as the CLASICC trial included mainly laparoscopic resections and thus a single incision for removal of the specimen, it is difficult to translate frequencies directly.

In conclusion, we have shown significant cost reduction when using laparoscopic lavage compared with Hartmann's resection as a treatment for perforated diverticulitis with purulent peritonitis. This and available data on the efficacy and safety from other randomized trials argue for routine use of laparoscopic lavage as a treatment in this patient group.

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Supporting information

Additional supporting information may be found in the online version of this article:

Fig. S1 Decision tree for stoma reversal model (Word document)

Fig. S2 Decision tree for sigmoid resection model (Word document)

Table S1 Unit costs of stoma and sigmoid resection models (Word document)

Table S2 Probabilities and costs of stoma and sigmoid resection models (Word document)

Table S3 Resource use of surgical instruments and antibiotics (Word document)

Table S4 Unit costs for surgical instruments and antibiotics (Word document)

Table S5 Unit cost per type of reoperation (Word document)

Table S6 Results and expected costs of stoma and sigmoid resection models (Word document)