Original article

Cost-effectiveness analysis of a multicentre randomized clinical trial comparing surgery with conservative management for recurrent and ongoing diverticulitis (DIRECT trial)

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Background: **The results of the DIRECT trial, an RCT comparing conservative management with elective sigmoid resection in patients with recurrent diverticulitis or persistent complaints, showed that elective sigmoid resection leads to higher quality of life. The aim of this study is to determine the cost-effectiveness of surgical treatment at 1- and 5-year follow-up from a societal perspective.**

Methods: **Clinical effectiveness and resource use were derived from the DIRECT trial. The actual resource use and quality of life (EQ-5D-3L™ score) were documented prospectively per individual patient and analysed according to the intention-to-treat principle for up to 5 years after randomization. The main outcome was the incremental cost-effectiveness ratio (ICER), expressed as costs per quality-adjusted life-year (QALY).**

Results: **The study included 106 patients, of whom 50 were randomized to surgery and 56 to conservative treatment. At 1- and 5-year follow-up an incremental effect (QALY difference between groups) of 0·06 and 0·43 respectively was found, and an incremental cost (cost difference between groups) of €6957 and €2674 respectively, where surgery was more expensive than conservative treatment. This resulted in an ICER of €123 365 per additional QALY at 1-year follow-up, and €6275 at 5 years. At a threshold of €20 000 per QALY, operative treatment has 0 per cent probability of being cost-effective at 1-year follow-up, but a 95 per cent probability at 5 years.**

Conclusion: **At 5-year follow-up, elective sigmoid resection in patients with recurring diverticulitis or persistent complaints was found to be cost-effective. Registration number: NTR1478 (www.trialregistrer.nl).**

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Introduction

Diverticulosis is a common disease that poses a great financial burden on healthcare. It is one of the costliest gastrointestinal diseases worldwide. In the USA the costs are estimated at $2·2 billion per year[1]. Approximately 20 per cent of patients develop recurrence after an initial episode of diverticulitis, and up to 33 per cent continue to experience ongoing complaints such as pain and discomfort[2,3]. Patients with recurrent diverticulitis or persistent complaints after an episode of diverticulitis can be treated conservatively or surgically, but high-level evidence supporting either of these treatment strategies has been lacking.

Traditionally, elective resection was advised after a second episode of diverticulitis, as it was thought that patients with recurrent attacks were more likely to develop complications[4]. Recent studies have proven that complications arise primarily in the first episode of diverticulitis, and therefore resection for recurrent diverticulitis does not seem warranted to prevent complications[5]. Quality of life (QoL) is therefore becoming the most important factor in the decision whether or not to perform elective sigmoid resection[3,6].

The DIRECT trial was a multicentre RCT comparing conservative management with elective sigmoid resection in patients with recurring diverticulitis and/or ongoing complaints after an episode of left-sided diverticulitis[7]. The primary aim was to determine which treatment strategy led to greater QoL. At 6 months of follow-up, the study demonstrated a significant higher disease-specific and generic QoL following elective sigmoid resection compared with conservative management[8], and this persisted throughout the 5-year follow-up[9]. The aim of the present study was to assess the cost-effectiveness of surgical *versus* conservative treatment alongside the DIRECT trial[7] from a societal perspective at 1- and 5-year follow-up.

Methods

Study design and participants

The DIRECT trial was designed as an open-label multicentre RCT. The trial is registered with trialregistrer.nl (number NTR1478). The study design has been described in detail elsewhere[7]. Briefly, patients aged 18–75 years presenting with either recurrent or persistent abdominal complaints after a proven (by ultrasonography, CT or endoscopy) episode of left-sided diverticulitis were included. Ongoing complaints were defined as ongoing left lower abdominal pain and/or persistent changes in bowel habit for a period of more than 3 months after an episode of diverticulitis. Frequently recurring diverticulitis was defined as a total of three or more presentations with clinical signs of acute diverticulitis within a period of 2 years. A minimum symptom-free interval of 3 months between presentations was mandatory for the complaint to be counted as a recurrence.

Patients were assigned randomly to either conservative management or elective (laparoscopic) sigmoid resection. All patients signed informed consent before inclusion. When patients in the conservative group presented themselves repeatedly to the hospital with severe abdominal complaints, elective resection could be offered. It was at the patients' and physicians' discretion whether the complaints were deemed too unbearable to pursue a conservative strategy during the follow-up period[7].

Economic evaluation

The present cost-effectiveness analysis of the DIRECT trial was performed according to guidelines for health economic analysis issued by the Dutch Healthcare Institute[10]. The primary outcome is the incremental cost-effectiveness ratio (ICER), expressed as costs per quality-adjusted life-year (QALY), converted from the EQ-5D-3L™ score (EuroQol Group, Rotterdam, the Netherlands)[11]. The incremental effect is the difference in QALY between the two groups, and the incremental costs are the difference in costs between the two groups. The ICER is then calculated by dividing the incremental costs by the incremental effect. The ICER was calculated from a societal perspective, thus including all direct and indirect costs (inside as well as outside the healthcare sector).

Quality-adjusted life-years

The EQ-5D-3L™ score was used to measure QoL at 3, 6, 9 and 12 months, and 3 and 5 years after inclusion or surgery (if randomized for surgery). The results of the EQ-5D-3L™ questionnaires were converted into utility values using the Dutch EQ-5D™ tariff. These utility values range from 0 to 1, where 1 represents optimal QoL[11]. QALYs were calculated by multiplying these utility values by the time spent in this health state, using interpolation between two observations. As QALYs were calculated over a 5-year interval, the maximum obtainable QALY was 5 (5×1, optimal EQ-5D-3L™ score). Missing QoL data were handled using multiple imputation, taking into account all other cost information, as well as age, sex, randomization group and treatment (for instance, whether the patient had actually received operative intervention or conservative management)[12].

Resource use

Resource use was documented prospectively at patient level in the DIRECT trial according to the predefined protocol[7]. It was documented within the clinical registration form or retrieved from the regular patient-reported questionnaires completed at inclusion, 3, 6, 9 and 12 months, and 3 and 5 years after inclusion or surgery (if randomized for surgery).

Direct medical costs included the primary surgery, primary hospital admission (ward and ICU stay), all additional procedures such as surgical reinterventions and percutaneous interventions, diagnostic imaging, outpatient consultation visits (with surgeon, gastroenterologist, occupational physician, general practitioner, physiotherapist), emergency department visits, readmissions, stoma care, stoma reversal surgery, medication, dietary costs and formal home care (nursing, personal care). Data on out-of-pocket costs (travel, dietary and other costs) and hours of informal home care were also collected from the regular patient-reported questionnaires at the above time points. Indirect non-medical costs resulting from absence from paid work or lowered productivity while at work were determined using the Health and Labour Questionnaire (HLQ)[13], which was administered together with the cost questionnaire. The friction costs method was used to estimate the duration of lost productivity[14]. Costs were estimated based on the age-adjusted mean daily wages, as described in the Dutch guideline for health economic analysis[10]. Missing cost data were handled using a multiple imputation model, as described above[12].

Unit costs

Table 1 shows the unit costs for different types of resource use. All values reflect cost levels in 2014. Different sources were used to derive estimates of unit costs. The Dutch guideline on costing research in healthcare and the recommendations of the Dutch Healthcare Authority (NZa) were used to estimate direct medical costs[10,15]. The unit costs for the index operation were obtained from the hospital administration, based on bottom-up cost calculations. These bottom-up calculations were performed for each procedure (laparoscopic and open sigmoid resection, with or without protective stoma and (re)operations for adverse events). Procedure costs included costs for all reusable instruments and disposables, personnel costs per time unit, and overhead costs. All healthcare consumption was valued at the level of units of consumption, not at the level of diagnosis-related groups.

Statistical analysis

All patients were analysed according to the intention-to-treat principle. Continuous variables and outcomes are presented as mean(s.d.) or median (i.q.r.), according to their distribution. For categorical variables and outcomes,

Table 1 Unit cost per resource use variable

	Unit cost (€)	Unit	Source
Surgery*			
Surgical instruments + disposables	110·85	Per operation	Meander Medical Centre
Operating time†	22	Per min	Meander Medical Centre
Specialist fee	116	Per hour	Dutch guideline[12]
Duration of hospital stay			
Ward	443	Per day	Dutch guideline[12]
ICU	2015	Per day	Dutch guideline[12]
Stoma material			
Ileostomy	8	Per day	Pharmacy retail price
Colostomy	13	Per day	Pharmacy retail price
Adverse events			
Percutaneous drainage	220·81	Per procedure	NZa[16]
Dilatation	94·42	Per procedure	NZa[16]
Diagnostic imaging/procedures			
Laboratory tests	28·80	Per test	Dutch guideline[12]
Ultrasonography	84·85	Per ultrasound	Dutch guideline[12]
CT	145	Per scan	Dutch guideline[12]
MRI	229	Per scan	Dutch guideline[12]
Chest X-ray	55·81	Per radiograph	www.diagnostiekvooru.nl
Abdominal X-ray	84·85	Per radiograph	www.diagnostiekvooru.nl
Colonic X-ray	161·26	Per radiograph	www.diagnostiekvooru.nl
Colonoscopy	352·48	Per colonoscopy	NZa[16]
Sigmoidoscopy	232·77	Per sigmoidoscopy	NZa[16]
Other costs			
Emergency room	259	Per visit	Dutch guideline[12]
General practitioner	33	Per visit	Dutch guideline[12]
Outpatient clinic	73	Per visit	Dutch guideline[12]
Occupational physician	136	Per visit	ArboNed tariff 2015
Medication	Variable	Per ATC code	Pharmacy retail price
Productivity loss	34·75	Per hour	Dutch guideline[12]
Formal home care			
Nursing	73	Per hour	Dutch guideline[12]
Caretaking	50	Per hour	Dutch guideline[12]
Domestic help	23	Per hour	Dutch guideline[12]
Informal domestic help	14	Per hour	Dutch guideline[12]

*Includes primary operation and (re)operation for adverse events. †Mean costs, including personnel costs and overhead costs. NZa, Nederlandse Zorg Autoriteit (Dutch Healthcare Authority); ATC, Anatomical Therapeutic Chemical.

counts and percentages are presented. The difference in EQ-5D™ score between the groups was analysed using a mixed model with repeated measures over time, and included all available data from patients for the first 5 years after randomization. The variance–co-variance matrix was modelled as unstructured. The fixed effects were time (categorical), treatment group, a group–time interaction, and the baseline EQ-5D™ score. For the cost-effectiveness analysis, differences in total costs were compared with the differences in QALYs, derived from the EQ-5D™ score. Differences in total costs were analysed with an independent-samples *t* test. The bias-corrected and accelerated bootstrapping method (5000 replications) was used to estimate uncertainty around the cost-effectiveness ratios[16,17]. Cost-effectiveness acceptability curves (CEACs) are presented to illustrate decision uncertainty[18]. The CEAC shows the probability that elective sigmoid resection is cost-effective compared with conservative treatment for a range of threshold values for willingness-to-pay per additional QALY. A threshold value of €20 000 is commonly used in the Netherlands for relatively mild, non-fatal diseases[19]. All analyses were performed using the statistical software package SPSS® 24.0 (IBM, Armonk, New York, USA).

Sensitivity analysis

As well as the societal perspective, cost-effectiveness was also calculated from a healthcare perspective, thus excluding all non-medical costs such as productivity losses, travel costs and informal home care.

Results

The CONSORT[20] flow diagram is shown in *Fig. 1*. Between 1 July 2010 and 1 April 2014, a total of 109 patients were enrolled in the DIRECT trial. Fifty-three patients were randomized to elective resection. In this group five patients (9 per cent) declined surgery and were treated conservatively. Three of these patients contributed

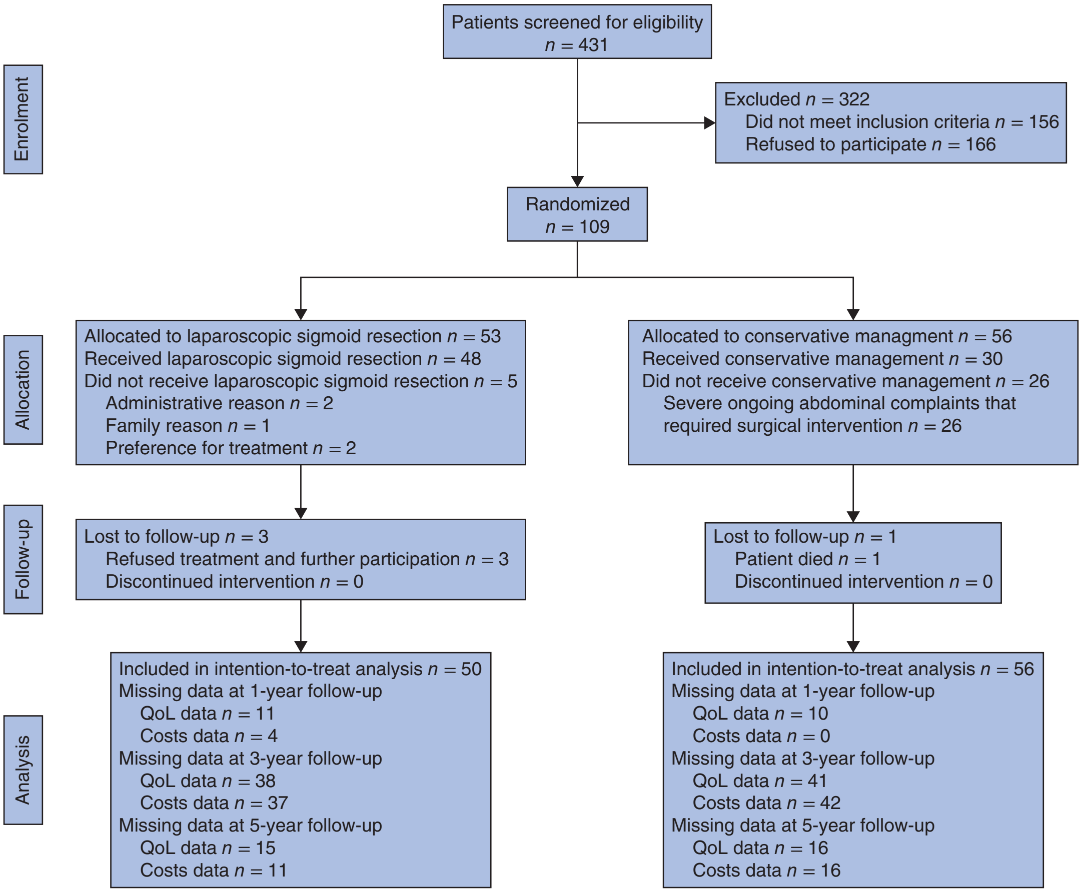

Fig. 1 CONSORT diagram for the trial. QoL, quality of life

no data because they were lost to follow-up directly after they declined surgery and were therefore excluded from the analysis, leaving 50 patients. Fifty-six patients were randomized to conservative management. Twenty-six (46 per cent) of these patients underwent surgery due to severe ongoing abdominal complaints during the 5-year follow-up. One patient in the conservative group died from non-diverticulitis-related disease. Baseline characteristics were comparable for the two groups (*Table 2*).

Response rate to questionnaires

At 12 months of follow-up, complete data on resource use and productivity losses were available for 102 patients (96 per cent) and 85 patients (80 per cent) had completed QoL questionnaires (*Fig. 1*). At 3-year follow-up this was the case for 27 (25 per cent) and 27 patients (25 per cent) respectively, and at 5-year follow-up for 79 (75 per cent) and 75 patients (71 per cent) respectively. Baseline characteristics of responders did not differ from those of non-responders (data not shown).

Table 2 Baseline characteristics

	Operative group ($n = 50$)	Conservative group ($n = 56$)
General characteristics		
Age (years)*	53·0 (43·8–61·3)	56·0 (47·3–63·0)
No. of men	14 (28)	24 (43)
BMI (kg/m^2)†	28·9(4·7)	27·8(4·9)
No. in paid work	27 (54)	31 (55)
ASA grade		
I	24 (48)	26 (46)
II	26 (52)	29 (52)
III	0 (0)	1 (2)
Stratification		
Recurring diverticulitis	17 (34)	23 (41)
Ongoing complaints	33 (66)	33 (59)
No. of episodes before inclusion†	2·6(1·5)	3·1(1·9)
Duration of symptoms (weeks)*‡	27·0 (13·8–53·8)	30·0 (16·3–63·0)
Hinchey grade for primary episode		
H1	34 (68)	51 (91)
H1B	9 (18)	4 (7)
H2	1 (2)	0 (0)
H3	1 (2)	0 (0)
H4	0 (0)	0 (0)
Undefined§	5 (10)	1 (2)
Medication		
Pain medication	12 (24)	14 (25)
Laxatives	22 (44)	28 (50)
Quality of life†¶		
VAS for pain	60·8(23·5)	67·8(15·8)
GIQLI	92·6(22·8)	92·2(21·3)
EQ-5D™	0·69(0·21)	0·74(0·20)

Values in parentheses are percentages unless indicate otherwise; values are *median (i.q.r.) and †mean(s.d.). ‡Applies only to patients with ongoing complaints. §Could not be classified because endoscopy was performed or Hinchey classification was not described in the radiological report. ¶Visual Analogue Scale (VAS) score ranged from 0 to 100; Gastrointestinal Quality of Life Index (GIQLI) score ranged from 0 to 144; EQ-5D™ score ranged from 0 to 1.

Resource use

Table 3 lists the most commonly used healthcare resource items and productivity losses. Infrequently used healthcare resource items have been included in the total costs. At 1-year follow-up, surgery was associated with longer duration of hospital stay and more diagnostic tests (laboratory tests and chest X-ray). At 5-year follow-up the difference in hospital stay was less pronounced. Operative intervention was still associated with more diagnostic tests (chest X-ray). Conservative treatment was associated with more general practitioner visits at 5 years.

Costs

The mean costs (including mean differences) per patient group per resource use variable are shown in *Table 4*. At 1-year follow-up, total mean(s.d.) societal costs were €15 174(12 788) for the operative group and €8217(10 398) for the conservatively treated group. The mean cost difference between groups was €6957 (95 per cent c.i. 2487 to 11 428; $P = 0·003$). At 5-year follow-up, total mean(s.d.) societal costs were €22 045(14 454) for the operative group and €19 371(17 721) for the conservative group. The mean cost difference between groups was €2674 (−3601 to 8949; $P = 0·400$). The cost-driving variables for both groups were duration of surgery, length of hospital stay and productivity losses.

Productivity losses throughout the study follow-up period are illustrated in *Fig. 2*. In the operative group, productivity losses were especially high in the first 3 months of follow-up, directly after elective sigmoid resection. After the first 3 months, productivity losses declined greatly in the operative group and continued to be lower compared with losses in the conservative group (except at 1-year follow-up, due to high productivity losses in one patient in the operative group who had not yet undergone surgery owing to family circumstances). Differences in productivity losses were, however, not statistically significant ($P = 0·095$ at 1 year and $P = 0·215$ at 5 years).

A high rate of anastomotic leakage substantially increased the costs in the operative group. Seven patients (14 per cent) in the surgery group had anastomotic leakage, compared with one patient (2 per cent) in the conservative group. Costs in the operative group were also raised because of stoma care and stoma reversal surgery. In 14

Table 3 Resource use per treatment group

	1-year follow-up			5-year follow-up		
	Operative (*n* = 50)	Conservative (*n* = 56)	*P*‡	Operative (*n* = 50)	Conservative (*n* = 56)	*P*‡
Duration of hospital stay (days)	9(9)	4(7)	0·002	12(10)	8(11)	0·055
Duration of surgery (min)*	120(28)	103(32)	0·110	121(29)	121(56)	0·996
Diagnostic imaging						
Abdominal ultrasonography	0·4(0·7)	0·2(0·4)	0·072	0·6(1·1)	0·5(1·1)	0·354
CT abdomen	0·6(0·9)	0·7(1·0)	0·545	1·1(1·9)	1·7(2·5)	0·188
MRI abdomen	0·0(0·0)	0·0(0·1)	0·347	0·1(0·3)	0·2(0·5)	0·092
Chest X-ray	0·4(0·1)	0·1(0·3)	0·018	0·6(1·7)	0·1(0·5)	0·035
Abdominal X-ray	0·0(0·2)	0·0(0·1)	0·497	0·1(0·2)	0·1(0·4)	0·631
Colonic X-ray	0·0(0·2)	0·0(0·1)	0·497	0·0(0·2)	0·0(0·1)	0·530
Diagnostic procedure						
Colonoscopy	0·4(0·7)	0·3(0·6)	0·173	0·7(1·2)	0·6(0·8)	0·404
Laboratory tests	4·8(3·7)	1·7(2·9)	< 0·001	6·8(10·2)	3·9(11·7)	0·179
Visits						
Emergency department	1·0(1·1)	1·1(1·1)	0·517	1·7(1·6)	2·0(1·8)	0·420
General practitioner	3·3(3·7)	4·1(4·6)	0·304	6·8(6·1)	11·2(10·9)	0·012
Occupational physician†	0·9(2·0)	0·6(2·0)	0·374	1·6(2·2)	2·2(5·2)	0·438
Specialist	6·6(5·0)	5·7(3·8)	0·322	8·0(7·4)	10·1(11·0)	0·268
Productivity losses						
Absence from work (h)†	228(223)	187(242)	0·519	236(218)	229(291)	0·919
Lost productivity while at work (h)†	23(44)	21(38)	0·879	66(107)	60(98)	0·824

Values are mean (s.d.). *Applies only to patients who had surgery; †applies only to patients in paid work. ‡Independent-samples *t* test.

Table 4 Costs per treatment group

	1-year follow-up			5-year follow-up		
	Operative (*n* = 50)*	Conservative (*n* = 56)*	Difference†	Operative (*n* = 50)*	Conservative (*n* = 56)*	Difference†
Hospital stay	4683(5184)	1867(3280)	2816 (1163, 4469)	5779(5611)	3778(6819)	2001 (−430, 1981)
Operation	2703(1105)	785(1253)	1919 (1461, 2376)	2772(1038)	1314(1588)	1485 (934, 2025)
Stoma care	246(518)	65(333)	181 (−44, 405)	443(1660)	106(386)	337 (−323, 997)
Imaging	150(224)	133(191)	17 (−64, 97)	271(444)	345(452)	−73 (−246, 100)
Diagnostic procedures	322(335)	189(305)	133 (9, 256)	632(746)	466(1144)	166 (−210, 543)
ED, GP, OP and outpatient visits	992(848)	924(608)	68 (−214, 350)	1490(1071)	1914(1603)	−424 (−966, 108)
Productivity losses	5150(7772)	3973(7371)	1177 (−1741, 4094)	5670(7939)	5119(9104)	550 (−2758, 3859)
Total healthcare costs	9914(7838)	4139(4844)	5775 (3220, 8329)	16 111(10 701)	13 502(12 442)	2608 (−1888, 7105)
Total societal costs	15 174(12 788)	8217(10 398)	6957 (2487, 11 428)	22 045(14 454)	19 371(17 721)	2674 (−3601, 8949)

*Values are mean(s.d.); †values in parentheses are 95 per cent confidence intervals. ED, emergency department; GP, general practitioner; OP, occupational physician.

patients a protective stoma was created (12 in the operative group and 2 in the conservative group). Most protective stomas (8 of 14) were created during reoperation for anastomotic leakage. Thirteen of these patients had stoma reversal surgery within 1 year (11 in the operative group and 2 in the conservative group). The median time between stoma creation and reversal surgery was 118 (i.q.r. 59–188) days. Nine patients (18 per cent) in the operative group and two (4 per cent) in the conservative group required operative repair of an incisional or trocar-site hernia.

Quality of life

At 1-year follow-up, mean(s.d.) EQ-5D™ scores in the operative and conservative groups were 0·84(0·14) and 0·74(0·22) respectively ($P = 0·003$) (*Fig. 3*). At 5-year follow-up, EQ-5D™ scores were significantly higher for operative treatment (mean(s.d.) 0·82(0·18) *versus* 0·72(0·22) in the conservative group; $P = 0·011$). The mean EQ-5D™ score over the entire study follow-up interval was 0·80 (95 per cent c.i. 0·76 to 0·84) in the operative group compared with 0·71 (0·67 to 0·74) in the conservative group ($P = 0·001$).

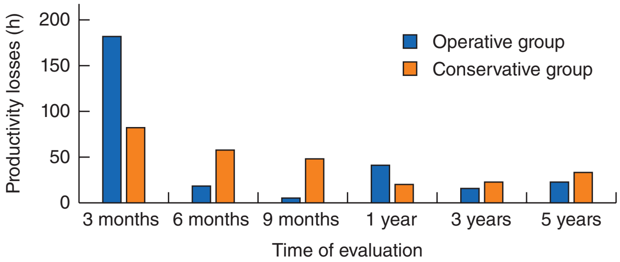

Fig. 2 Productivity losses in patients with paid work during 5-year follow-up

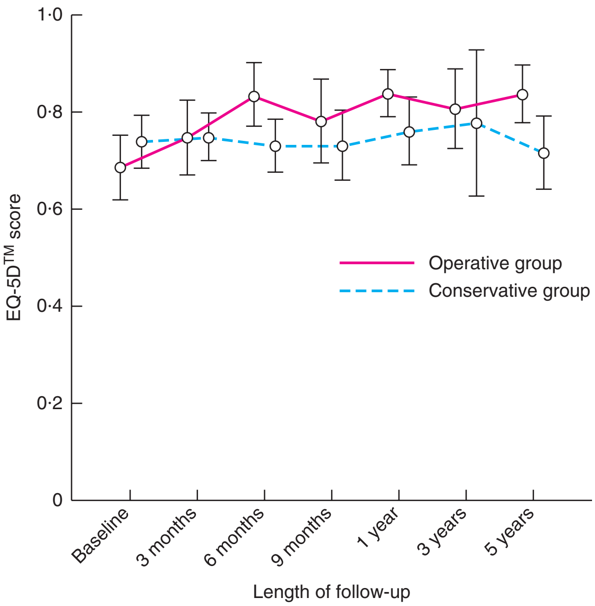

Fig. 3 EQ-5D™ score for operative and conservative groups during 5-year follow-up. $P = 0{\cdot}001$ for entire study period (mixed model with repeated measures over time)

Cost-effectiveness

At 1-year follow-up, the bootstrapping method revealed an incremental effect (QALY difference between groups) of 0·06 and an incremental cost (cost difference between groups) of €6957. This resulted in an ICER of €123 365 per additional QALY. The corresponding CEAC is shown in *Fig. 4*; at the threshold of €20 000 per QALY, operative treatment had 0 per cent probability of being cost-effective at 1 year.

At 5-year follow-up, the bootstrapping method revealed an incremental effect of 0·43 QALYs and an incremental cost of €2674. This resulted in an ICER of €6275 per additional QALY. The corresponding CEAC is shown in *Fig. 5*; at the threshold value of €20 000 per QALY, operative treatment had 95 per cent probability of being cost-effective after 5 years.

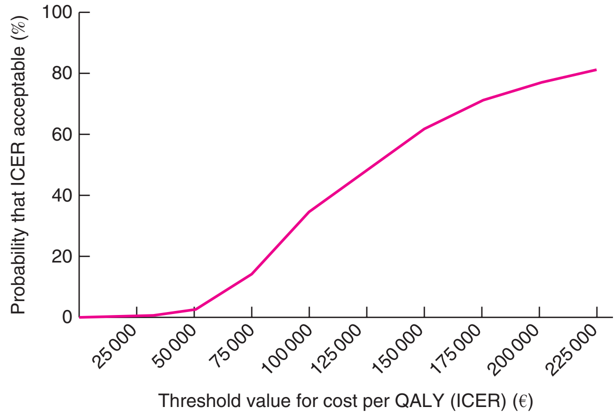

Fig. 4 Cost-effectiveness acceptability curve at 1-year follow-up. QALY, quality-adjusted life-year; ICER, incremental cost-effectiveness ratio

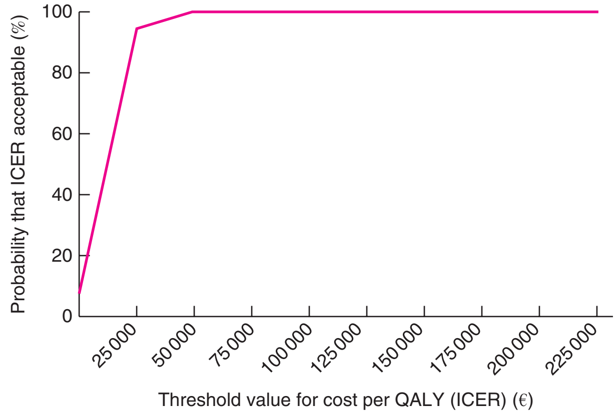

Fig. 5 Cost-effectiveness acceptability curve at 5-year follow-up. QALY, quality-adjusted life-year; ICER, incremental cost-effectiveness ratio

Sensitivity analyses

Costs and cost-effectiveness at 5-year follow-up were also calculated from a healthcare perspective. This showed an incremental effect of 0·43 and incremental cost of €2608, resulting in an ICER of €6110 per additional QALY. In this analysis, operative treatment has a 96 per cent probability of being cost-effective at the threshold of €20 000 per QALY. In the conservative group, one patient had a very complicated course after endoscopic retrograde cholangiopancreatography for a pancreatic divisum, which was accompanied by high costs. This patient eventually died after a prolonged hospital stay.

An extra sensitivity analysis was performed to evaluate the effect of this outlier. When this patient was excluded from the analysis, the mean cost difference between the operative and conservative groups increased to €3595 (95 per cent c.i. −2430 to 9620; $P = 0{\cdot}239$). QALYs remained higher in the operative group, with a difference of 0·40 (0·10 to 0·70) ($P = 0{\cdot}010$). Bootstrapping revealed an ICER of €9072 per additional QALY. At a threshold of €20 000 per QALY, operative treatment still had 89 per cent probability of being cost-effective.

Discussion

This study assessed the cost-effectiveness of elective sigmoid resection *versus* conservative management in patients with recurring diverticulitis and/or ongoing complaints after an episode of left-sided diverticulitis. The results add an economic perspective to the demonstrated efficacy of elective sigmoid resection in the DIRECT trial[8,9].

At 1-year follow-up the overall costs for elective sigmoid resection were, as anticipated, significantly higher than those for conservative management. However, at 5 years the cost difference between the two groups was much less pronounced, due to rising costs in the conservative group. The effect difference between the two treatment groups was in favour of elective sigmoid resection with an increase in QoL (EQ-5D™ score) at 1 year, and persisted over the following years.

After 5 years of follow-up, the costs per QALY gained were €6275. This is far below the threshold value of €20 000 per QALY that is commonly deemed acceptable for relatively mild diseases, whereas for more severe diseases a threshold value of €80 000 per additional QALY is maintained. Although (uncomplicated) diverticulitis is deemed a relatively mild disease, the results of the QoL questionnaires indicate that the disease burden for this patient group is high, with on average a 17–24 per cent loss of QoL compared with that for age-matched peers[3,8,9]. In the cost-effectiveness analysis, the probability of operative intervention being cost-effective was 95 per cent at a threshold of €20 000 per additional QALY, and even 100 per cent at the higher threshold of €80 000 per QALY. The authors therefore claim that operative treatment is cost-effective and should be offered more routinely to this patient group.

The cost differences between randomization groups were as expected. At 1-year follow-up, increased costs were found in the operative group as a result of surgical intervention and concomitant hospitalization. However, 26 patients (46 per cent) in the conservative group ultimately required elective sigmoid resection due to severe ongoing complaints, thereby increasing the long-term costs. Productivity losses contributed strongly to increased costs in both groups. However, in the operative group most productivity losses were reported directly after surgery and, although not statistically significant, were lower than in the conservative group throughout the study.

A high rate of anastomotic leakage strongly increased the costs in the intervention group. A total of eight patients (11 per cent of 74 surgically treated patients) had anastomotic leakage (7 in the operative group and 1 in the conservative group). This number is rather high compared with current literature demonstrating rates of 6 per cent for anastomotic leakage[21–24]. The present authors cannot provide a satisfying explanation for this high figure, nor could a formal regression analysis be performed to identify factors associated with anastomotic leakage, because the absolute numbers were too small. It can be explained only by the fact that the DIRECT trial has been a pragmatic trial with no specific selection of surgeons or centres, thus reflecting real complication rates and accompanying costs. It may also indicate that elective sigmoid resection for recurrent diverticulitis or persistent complaints is accompanied by a higher chance of complications than anticipated by the literature, owing to procedural challenges during surgery. Remarkably, despite these high rates of anastomotic leakage and resultant reinterventions, QoL was still higher in the operative group, strengthening the conclusion that elective surgery has an important impact on improvement of QoL.

A major strength of this study is its randomized multicentre design. Furthermore, the study was performed from a societal perspective and used a precise and comprehensive cost registration method. All resources use was documented prospectively and all healthcare consumption was valued at the level of units of consumption, not at the level of diagnosis-related groups. Therefore, the results represent an accurate estimation of the actual cost per patient. Another strength of the study is the fact that the authors were able to collect cost data and QoL data during a 5-year follow-up, providing a unique opportunity to analyse cost-effectiveness at two different time points during follow-up. The fact that cost-effectiveness strongly improved over prolonged follow-up emphasizes the importance of long-term follow-up in cost-effectiveness studies.

The study also has some limitations. At 3-year follow-up, the response rate to QoL, HLQ and health consumption questionnaires was low (25 per cent). This could have led to attrition bias. To avoid this, multiple imputation techniques were used to handle missing data[12]. At 5-year follow-up, the response rate was much higher (71–75 per cent), strengthening the validity of the present results. Some 46 per cent of patients in the conservative group had severe, ongoing abdominal complaints and were eventually operated on, which may have led to an underestimation of the incremental effect on QoL of elective sigmoid resection, making the results of the intention-to-treat analysis somewhat uncertain. Despite this, elective sigmoid resection was still found to be cost-effective. There are several issues regarding the generalizability of the results. First, inclusion criteria for the DIRECT trial were quite strict as only patients who had experienced more than two episodes of diverticulitis within 2 years or who had persistent complaints for more than 3 months were eligible for the study. Moreover, included patients came from a selected population already in the secondary care circuit. Results are therefore not directly applicable to all patients with frequently recurring diverticulitis or persistent complaints after an episode in general. Second, a pragmatic approach adhering to the Dutch situation was used to define conservative management and establish the primary episode of diverticulitis by using both CT, ultrasonography and endoscopy. There are differences across countries with regard to these topics, and therefore costs for conservative management could vary between countries. Moreover, resource use and costs of laparoscopic sigmoid resection vary between countries, thereby hampering translation of the present results to international contexts[25,26].

Elective sigmoid resection resulted in a significantly increased QoL at 5-year follow-up compared with conservative management. Costs were only slightly higher in the operative group, and at a willingness-to-pay of €20 000 per additional QALY, operative treatment has a 95 per cent probability of being cost-effective. These results add a favourable economic perspective to the efficacy of elective sigmoid resection demonstrated in the DIRECT trial.

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