Randomized clinical trial

Randomized clinical trial of selective decontamination of the digestive tract in elective colorectal cancer surgery (SELECT trial)

G. S. A. Abis[1], H. B. A. C. Stockmann[4], H. J. Bonjer[1], N. van Veenendaal[1], M. L. M. van Doorn-Schepens[2], A. E. Budding[2], J. A. Wilschut[3], M. van Egmond[1] and S. J. Oosterling[4], on behalf of the SELECT trial study group[†]

Departments of [1]Surgery, [2]Medical Microbiology and Infection Control, and [3]Epidemiology and Biostatistics, VU University Medical Centre, Amsterdam, and [4]Department of Surgery, Spaarne Gasthuis, Haarlem/Hoofddorp, the Netherlands

Correspondence to: Dr G. S. A. Abis, VU University Medical Centre, Boelelaan 1117, 1081 HV Amsterdam, the Netherlands (e-mail: g.abis@vumc.nl; @VUmcAmsterdam, @spaarnegasthuis)

Background: **Infectious complications and anastomotic leakage affect approximately 30 per cent of patients after colorectal cancer surgery. The aim of this multicentre randomized trial was to investigate whether selective decontamination of the digestive tract (SDD) reduces these complications of elective colorectal cancer surgery.**

Methods: **The effectiveness of SDD was evaluated in a multicentre, open-label RCT in six centres in the Netherlands. Patients with colorectal cancer scheduled for elective curative surgery with a primary anastomosis were eligible. Oral colistin, tobramycin and amphotericin B were administered to patients in the SDD group to decontaminate the digestive tract. Both treatment and control group received intravenous cefazolin and metronidazole for perioperative prophylaxis. Mechanical bowel preparation was given for left-sided colectomies, sigmoid and anterior resections. Anastomotic leakage was the primary outcome; infectious complications and mortality were secondary outcomes.**

Results: **The outcomes for 228 patients randomized to the SDD group and 227 randomized to the control group were analysed. The trial was stopped after interim analysis demonstrated that superiority was no longer attainable. Effective SDD was confirmed by interspace DNA profiling analysis of rectal swabs. Anastomotic leakage was observed in 14 patients (6·1 per cent) in the SDD group and in 22 patients (9·7 per cent) in the control group (odds ratio (OR) 0·61, 95 per cent c.i. 0·30 to 1·22). Fewer patients in the SDD group had one or more infectious complications than patients in the control group (14·9 *versus* 26·9 per cent respectively; OR 0·48, 0·30 to 0·76). Multivariable analysis indicated that SDD reduced the rate of infectious complications (OR 0·47, 0·29 to 0·76).**

Conclusion: **SDD reduces infectious complications after colorectal cancer resection but did not significantly reduce anastomotic leakage in this trial. Registration number: NCT01740947 (https://www.clinicaltrials.gov).**

[†]Members of the SELECT trial study group can be found under the heading Collaborators

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Introduction

Colorectal cancer is a common cancer worldwide, affecting more than one million patients annually[1]. Surgical resection remains the mainstay for curative treatment, but infectious complications affect 20–40 per cent of patients[2,3]. Anastomotic leakage is the most severe complication of colorectal surgery, with an incidence ranging from 5 to 15 per cent[3,4] and a mortality rate of 6–30 per cent[3,5]. Management of surgical-site infection (SSI) in colorectal cancer surgery requires specialized care and can increase costs by 40 per cent, up to €17 500 per case[6]. Although several possible risk factors for anastomotic leakage have been proposed, the patient's microbiome may play a role in the pathophysiology[7]. Postoperative abdominal, pulmonary or other infectious complications implicate digestive tract microorganisms in other organ spaces or the blood

circulation. Furthermore, blood-borne Gram-negative bacteria and their endotoxins contribute to the pathogenesis of sepsis, shock and multiple organ failure[8].

Selective decontamination of the digestive tract (SDD) is based on the administration of oral non-absorbable antibiotics to minimize the impact of endogenous infections from gut microorganisms including aerobic Gram-negative bacteria, *Staphylococcus aureus* and fungi[9]. SDD was introduced in the ICU setting, where it reduced mortality in ventilated patients[10]. In oesophagogastric and digestive surgery there are data[11,12] showing that infectious complications and anastomotic leakage are reduced by SDD. The aim of this multicentre RCT was to investigate the effects of SDD on anastomotic leakage and infectious complications in patients undergoing elective colorectal cancer resection with a primary anastomosis.

Methods

Study design

The SELECT trial was a superiority, open-label, multicentre, randomized trial conducted at one university medical centre and five teaching hospitals in the Netherlands. The study was designed by members of the protocol committee. The local investigators and the coordinating investigator collected the data. The authors analysed and vouch for the accuracy of the data and fidelity of the study to the protocol. The trial was registered with ClinicalTrials.gov (number NCT01740947).

Patients

Patients were eligible for inclusion if they had a biopsy-proven colorectal carcinoma (or a high index of suspicion of carcinoma on biopsy) with no imaging signs of distant metastasis, and were candidates for elective surgery with a primary anastomosis via laparoscopic or open surgery. Exclusion criteria included other malignancy, inflammatory bowel disease, previous surgery for diverticular disease, ASA grade IV, polyposis/familial cancer syndromes, or inability to give informed consent[13]. The ethics board at the VU University Medical Centre and the institutional review board at each participating centre approved the study. All patients provided written informed consent.

Randomization and masking

After inclusion and exclusion criteria had been verified and informed consent obtained, randomization was performed via an internet-based program. Allocation of patients was stratified for participating centre and tumour localization (colonic or rectal) and type of resection (laparoscopic or open). A unique patient identification code was generated and corresponded with the allocated intervention or standard treatment regimen. A standardized online case record form was used via a secured internet module.

Procedures and quality control

All patients were presented at multidisciplinary team meetings to determine individual management (in accordance with the Dutch guidelines on colorectal cancer).

Study drug

Patients in the SDD arm received orally a 10-ml suspension containing 5 ml amphotericin B (500 mg) and 5 ml colistin sulphate (100 mg) and tobramycin (80 mg).

Intervention group

The intervention group received the study drug orally four times daily, starting 3 days before surgery. Medication was continued until either normal bowel motion occurred or for a minimum of 3 days after surgery. In patients who had a nasogastric tube after surgery, the tube was clamped for 30 min after administration of SDD. Normal bowel passage was defined as toleration of a normal diet and oral intake of more than 1 litre of fluid per 24 h. In addition, a single preoperative parenteral dose of 1000 mg cefazolin and 500 mg metronidazole was given; this was repeated if the operation took more than 4 h. A preoperative rectal swab was taken from all patients. All perioperative care fulfilled the Enhanced Recovery After Surgery (ERAS) criteria[14]. Oral mechanical bowel preparation was given for left-sided colonic, sigmoid and low anterior resections.

Control group

The control group routinely received a single preoperative parenteral dose of 1000 mg cefazolin and 500 mg metronidazole; this was repeated if the operation took more than 4 h. A preoperative rectal swab was taken from all patients. All perioperative care fulfilled the ERAS criteria[14]. Oral mechanical bowel preparation was given for left-sided colonic, sigmoid and low anterior resections.

Study endpoints

The primary endpoint was anastomotic leakage rate at 30 days after surgery. Anastomotic leakage was diagnosed either clinically or radiologically and considered

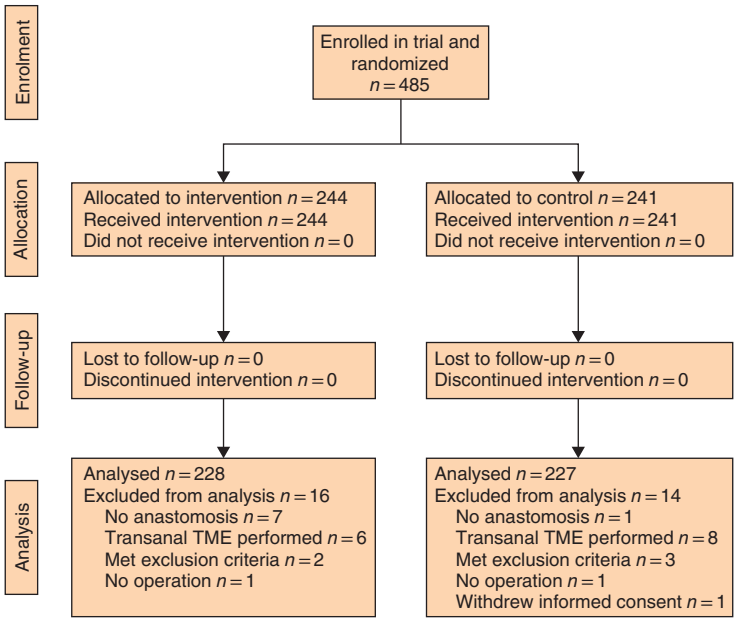

Fig. 1 CONSORT diagram for the study. SDD, selective decontamination of digestive tract; TME, total mesorectal excision

as such if surgical or radiological intervention was required. Abscesses in the proximity of the anastomosis were also considered as anastomotic leakage.

Secondary short-term endpoints were infectious complications, mortality, ICU admission, reoperation/reintervention within 30 days of surgery, readmission and hospital stay.

Follow-up

Follow-up was done at least twice a year in the first 2 years after surgery and then yearly according the Dutch guidelines on colorectal cancer.

Verification of decontamination

To verify the decontaminating effect of SDD on the presence of potential pathogenic microorganisms in the gut, microbial analysis was performed by the interspace (IS) profiling technique (IS-pro™; IS-Diagnostics, Amsterdam, the Netherlands) on rectal swabs of a subset of patients.

Rectal swabs

Rectal swabs (FLOQSwabs™ 552C; Copan, California, USA) were taken before surgery. Swab tips were transported in a sterile container containing 500 µl reduced transport fluid (RTF) buffer. Within half an hour of transportation, containers were stored at a temperature of −20 °C before sample handling.

Interspace profiling of intestinal microbiota

Analysis on the intestinal microbiota was performed with the IS-pro™ technique, which discriminates bacterial species based on the length of the 16–23S rDNA IS region, as described previously[15].

Bacterial DNA was isolated with the *in vitro* diagnostic (IVD)-labelled, automated NucliSENS® easyMag® extraction system (bioMérieux, Marcy-l'Étoile, France) according to the instructions for use in the IS-pro™ Research kit 14000 (IS Diagnostics). The DNA was eluted in 110 µl buffer and stored at 4 °C before PCR amplification.

IS fragments were amplified in two separate PCR reactions with phylum-specific fluorescent labels. In the first PCR reaction, IS fragments of bacteria belonging to the phyla Firmicutes, Bacteroidetes, Actinobacteria, Fusobacteria and Verrucomicrobia were amplified. In the second PCR reaction, IS fragments of bacteria belonging to the phylum Proteobacteria were amplified. Amplifications were performed on a GeneAmp® PCR system 9700 (Applied Biosystems, Foster City, California, USA).

Subsequently, DNA fragment analysis was performed on an ABI Prism® 3500 Genetic Analyzer (Applied Biosystems). All data were preprocessed with the proprietary software suite (IS-Diagnostics) and analysed further with the Spotfire® software package (TIBCO, Palo Alto, California, USA).

Table 1 Baseline characteristics

	SDD ($n = 228$)	Control ($n = 227$)
Age (years)*	67·5(8·4)	68·1(9·0)
Sex ratio (M : F)	131 : 97	134 : 93
ASA fitness grade		
I (healthy)	60 (26·3)	64 (28·2)
II (mild systemic disease)	137 (60·1)	129 (56·8)
III (severe systemic disease)	31 (13·6)	33 (14·5)
Missing	0 (0)	1 (0·4)
BMI (kg/m^2)*	26·7(4·3)	25·9(4·3)
Diabetes	36 (15·9)	24 (10·7)
Missing	1	2
Preoperative haemoglobin level (mmol/l)*	8·2(1·2)	8·2(1·2)
Active smoker	29 (14·1)	32 (15·4)
Missing	23	19
Neoadjuvant therapy	6 (2·6)	13 (5·7)
Surgical intervention		
Right hemicolectomy	84 (36·8)	78 (34·4)
Transverse colectomy	11 (4·8)	6 (2·6)
Left hemicolectomy (extended)	21 (9·2)	20 (8·8)
Sigmoid resection	60 (26·3)	64 (28·2)
Low anterior resection	47 (20·6)	56 (24·7)
Other	5 (2·2)	3 (1·3)
Type of surgery		
Laparoscopic	224 (98·2)	223 (98·2)
Open	4 (1·8)	4 (1·8)
Bowel preparation	155 (68·0)	161 (70·9)
Diverting ileostomy	12 (5·3)	11 (4·8)
Conversion	24 of 224 (10·7)	30 (13·2)
Time in theatre (min)*	193(58)	185(45)
Missing	56	55
Blood loss (ml)†	50	50
Missing	93	81
Pathological stage		
I (T1–2 N0 M0)	73 (32·0)	63 (27·8)
II (T3–4 N0 M0)	76 (33·3)	68 (30·0)
III (Tx N+ M0)	70 (30·7)	85 (37·4)
ypT0 N0	1 (0·4)	3 (1·3)
pT0 (dysplasia)	8 (3·5)	8 (3·5)

Values in parentheses are percentages unless indicated otherwise; values are *mean(s.d.) and †median. SDD, selective decontamination of the digestive tract.

To determine phylum, family and species abundance, a box plot was made for the abundance of Proteobacteria, Enterobacteriaceae and *Escherichia coli*. The *x*-axis depicted treatment, and the *y*-axis showed $\log_2$ intensity, measured in relative fluorescence units. *P* values for difference in abundance in the SDD *versus* control group were calculated for these taxonomic groups, by performing a two-sample *t* test.

Statistical analysis

With anastomotic leakage as a primary endpoint, a power of 80 per cent at a confidence level of 95 per cent was used. Considering a 9 per cent anastomotic leakage rate in the control group, based on numbers of the Dutch Surgical Colorectal Audit at onset of the trial[3], and an estimated 4 per cent in the intervention group, 381 patients needed to be included per treatment arm (total of 762 patients). All data were collected in an online OpenClinica® database (https://www.openclinica.com), and statistical analyses were performed using SPSS® 21.0 (IBM, Armonk, New York, USA).

An interim analysis was performed approximately halfway through the trial after a decrease in anastomotic leakage rate from 9 per cent in 2010 to 6 per cent in 2015 was reported by the Dutch Surgical Colorectal Audit[3]. The interim analysis, carried out by an independent statistician and reviewed by the statistician involved in the trial, was performed to evaluate whether the power was still sufficient to continue the trial. The final decision was made by the principal investigator of the trial.

The main analyses were performed on a modified intention-to-treat basis, without exclusion of patients after randomization. Odds ratios (ORs) were determined for the binary outcome measures, and difference in means for the continuous outcome measure. Potential confounders for complication rates were identified based on the literature: age, sex, BMI, ASA classification, smoking history, diabetes, bowel preparation, surgical procedure performed, diverting ileostomy and conversion. Adjusted ORs were determined by logistic regression. To limit the number of co-variables, confounders were selected based on their prognostic value, using a threshold *P* value of 0·150 in univariable analysis. Given the low percentage of patients with missing observations in the confounders (less than 1 per cent), these patients were omitted from the logistic regression analysis.

Results

A total of 485 patients were enrolled from May 2013 until March 2017 (*Fig. 1*). The trial was stopped after interim analysis demonstrated that superiority could not be reached for the primary outcome at the parameters set *a priori*; the power to detect a difference of 55 per cent was too low.

Baseline characteristics

Baseline characteristics are shown in *Table 1*. Missing data were equally distributed over the two arms of the trial.

Clinical outcomes

Anastomotic leakage was recorded in 14 patients (6·1 per cent) in the SDD group and 22 (9·7 per cent) in the control

Table 2 Results of primary and secondary outcomes

	SDD ($n = 228$)	Control ($n = 227$)	Odds ratio*
Anastomotic leakage†	14 (6·1)	22 (9·7)	0·61 (0·30, 1·22)
Required intervention for anastomotic leakage			
Reoperation	12 (86)	18 (82)	
Transrectal drainage	1 (7)	3 (14)	
Percutaneous drainage	1 (7)	1 (5)	
≥ 1 infectious complication (including anastomotic leakage)	34 (14·9)	61 (26·9)	0·48 (0·30, 0·76)
Surgical-site infection	5 (2·2)	24 (10·6)	
Pneumonia	11 (4·8)	19 (8·4)	
Urinary tract	4 (1·8)	6 (2·6)	
Other	0 (0)	3 (1·3)	
≥ 1 non-infectious complication	33 (14·5)	37 (16·3)	0·87 (0·52, 1·45)
Ileus	11 (4·8)	12 (5·3)	
Cardiac	5 (2·2)	11(4·8)	
Pulmonary embolism	4 (1·8)	3 (1·3)	
Fascial dehiscence	1 (0·4)	5 (2·2)	
Other	13 (5·7)	14 (6·2)	
30-day mortality	3 (1·3)	4 (1·8)	0·74 (0·16, 3·36)

Values in parentheses are percentages unless indicated otherwise; *values in parentheses are 95 per cent confidence intervals (univariable analysis). †Anastomotic leakage and/or abscess defined as clinical and/or radiological evidence of anastomotic dehiscence requiring surgical or radiological (re)intervention. SDD, selective decontamination of the digestive tract.

Table 3 Logistic regression analysis for one or more infectious complications

	Univariable analysis		Multivariable analysis	
	Odds ratio	*P*	Odds ratio	*P*
Treatment effect (SDD *versus* control)	0·48 (0·30, 0·76)	0·002	0·47 (0·29, 0·76)	0·002
Age (> 70 years)	1·29 (0·67, 2·16)	0·283		
Male sex	1·30 (0·81, 2·07)	0·275		
BMI (> 30 kg/m^2)	1·20 (0·97, 1·08)	0·543		
Smoker	0·91 (0·48, 1·74)	0·773		
Diabetes	1·32 (0·70, 2·49)	0·390		
Bowel preparation	0·74 (0·46, 1·19)	0·214		
ASA fitness grade				
II *versus* I	1·18 (0·68, 2·05)	0·553	1·21 (0·70, 2·11)	0·495
III *versus* I	1·96 (0·97, 3·97)	0·063	1·99 (0·97, 4·07)	0·060
Low anterior *versus* other resection	1·04 (0·61, 1·78)	0·892		
Neoadjuvant therapy	1·80 (0·67, 4·87)	0·247		
Diverting ileostomy	1·06 (0·38, 2·92)	0·917		
Conversion	1·54 (0·81, 2·94)	0·187		

Values in parentheses are 95 per cent confidence intervals. SDD, selective decontamination of the digestive tract.

group (OR 0·61, 95 per cent c.i. 0·30 to 1·22). Twelve of the patients in the SDD group with anastomotic leak required reoperation, and the remaining two underwent drainage either percutaneously or via the rectum. In the control group, 18 of the 22 patients required reoperation and four were drained percutaneously or via the rectum (*Table 2*).

Thirty-four patients (14·9 per cent) in the SDD group had one or more infectious complications compared with 61 (26·9 per cent) in the control group (OR 0·48, 95 per cent c.i. 0·30 to 0·76) (*Table 2*). The total number of infectious complications was 34 (14·9 per cent) in the SDD group and 74 (32·6 per cent) in the control group (OR 0·36, 0·23 to 0·57). There was a statistically significant difference for SSI between the groups (OR 0·19, 0·07 to 0·51), but not for pneumonia, urinary tract infection or other infections (1 intravascular catheter-related infection and 2 oral infections with *Candida*). No infections with multidrug-resistant bacteria or *Clostridium difficile* occurred.

Thirty-three non-infectious complications (14·5 per cent) were recorded in the SDD group and 37 (16·3 per cent) in the control group, with no significant difference. Ileus, cardiac complications, pulmonary embolism, fascial dehiscence and other non-infectious complications also showed no significant difference between groups (*Table 2*). The 30-day mortality rate did not differ between study arms, with three deaths (1·3 per cent) in the SDD arm and four (1·8 per cent) in the control arm. No differences were found in median time to first intake, first defecation,

Table 4 Logistic regression analysis for anastomotic leakage

	Univariable analysis		Multivariable analysis	
	Odds ratio	*P*	Odds ratio	*P*
Treatment effect (SDD *versus* control)	0·61 (0·30, 1·22)	0·164	0·63 (0·31, 1·29)	0·208
Age (> 70 years)	1·29 (0·64, 2·63)	0·475		
Male sex	1·02 (0,98, 1·06)	0·439		
BMI (> 30 kg/m^2)	1·00 (0·92, 1·08)	0·901		
Smoker	0·33 (0·08, 1·40)	0·133	0·37 (0·09, 1·62)	0·196
Diabetes	2·00 (0·87, 4·63)	0·105	2·63 (1·09, 6·37)	0·032
Bowel preparation	2·92 (1·11, 7·69)	0·030	1·95 (0·69, 5·49)	0·205
ASA fitness grade				
II *versus* I	1·24 (0·54, 2·89)	0·614		
III *versus* I	1·78 (0·62, 5·15)	0·287		
Low anterior *versus* other resection	3·05 (1·52, 6·14)	0·002	2·08 (0·91, 4·75)	0·083
Neoadjuvant therapy	4·67 (1·58, 13·80)	0·005	2·59 (0·75, 9·01)	0·134
Diverting ileostomy	0·55 (0·16, 1·95)	0·356		
Conversion	1·55 (0·61, 3·91)	0·357		

Values in parentheses are 95 per cent confidence intervals. SDD, selective decontamination of the digestive tract.

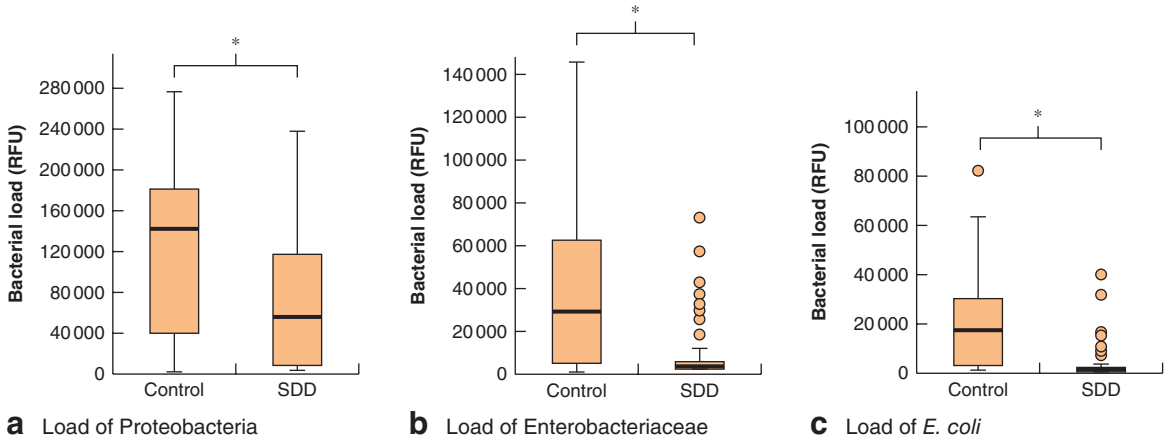

Fig. 2 Abundance analysis of bacterial loads in patients with colorectal cancer who had selective decontamination of the digestive tract *versus* controls. Load of **a** Proteobacteria, **b** Enterobacteriaceae and **c** *Escherichia coli*. Median values, interquartile ranges and ranges (excluding outliers, shown as circles) are denoted by horizontal bars, boxes and error bars respectively. RFU, relative fluorescence units; SDD, selective decontamination of the digestive tract. *$P < 0·001$ (two-sample *t* test)

median hospital stay, readmission within 30 days and ICU admissions.

Administration of SDD was according to protocol in 224 (98·2 per cent) of the patients. In the four non-compliant patients, at least six doses were taken before intake was discontinued. The reason for discontinuing the study medication was related to taste in all four patients.

Univariable and multivariable analysis

Infectious complications

Treatment with SDD and higher ASA fitness grade had an effect on the occurrence of at least one infectious complication in univariable analysis (*Table 3*). In multivariable analysis, SDD had a strong protective effect against infectious complications (OR 0·47, 95 per cent c.i. 0·29 to 0·76). ASA grade showed no significant relation with any infectious complication.

Anastomotic leakage

SDD, smoking, diabetes, bowel preparation, neoadjuvant therapy and low anterior resection had an effect on anastomotic leakage in univariable analysis (*Table 4*). In multivariable analysis only diabetes was associated with anastomotic leakage (OR 2·63, 95 per cent c.i. 1·09 to 6·37).

Non-infectious complications

Conversion to open surgery was the only factor associated with the occurrence of a non-infectious complication (OR 2·48, 95 per cent c.i. 1·05 to 4·22).

Any complication

No significant associations were found for the occurrence of any complication, either infectious or non-infectious (data not shown).

Effectiveness of decontamination

The loads of both Proteobacteria and Enterobacteriaceae were significantly reduced in the SDD group compared with the control group (both $P < 0{\cdot}001$). In the SDD group, the total *E. coli* load was significantly lower than that in the control group ($P < 0{\cdot}001$), and adequate decontamination was achieved in patients who had SDD (*Fig. 2*).

Discussion

SDD reduced the rate of SSI but did not significantly affect anastomotic leakage in this RCT. The microbiome is the microbial ecosystem of the body and resides largely in the digestive tract. In recent years, DNA and RNA sequencing studies have revealed that the diversity and metabolic interactions of this microbial community greatly influence the development of infection and disease[16]. When balance in the microbiome is lost and potentially pathogenic microorganisms predominate the bowel environment, a 'disease-promoting microbiome' occurs that facilitates the occurrence of disease and infectious complications[17]. The vast majority of SSIs following colorectal surgery are caused by endogenous bacteria from the digestive tract[18,19]. The integrity of this mucosal barrier is disrupted by opening the gut during surgery. In addition, the composition of the microbiome changes profoundly following colorectal surgery owing to delayed or impaired gut peristalsis in the postoperative phase[20].

Experimental studies linking the microbiome and specific pathogens to anastomotic leakage have been published[21]. Recently, in an experimental study in rats, Olivas and colleagues[22] showed that the addition of *Pseudomonas aeruginosa* in the bowel increased the anastomotic leakage rate after colonic resection combined with radiotherapy (common in rectal cancer) to 60 per cent, compared with 0 per cent in a control group that had resection and radiotherapy alone. This was attributed to transformation of *P. aeruginosa* to a tissue-destroying phenotype at the anastomotic site. Leakage was virtually prevented when expression of this phenotype was inhibited in *P. aeruginosa*, implying that microorganisms can have a direct effect on anastomotic healing[22]. Comparable results were found for *Enterococcus faecalis*, *P. aeruginosa* and *Serratia marcescens* strains that showed increased virulence factors contributing to anastomotic leakage[16,23,24].

SDD is based on the administration of oral non-absorbable antibiotics and fungicides to eliminate potentially pathogenic microorganisms in the bowel[9]. Infectious complications after colorectal surgery remain a major source of postoperative morbidity, even in this era of minimally invasive surgery. In the present trial, the infectious complication rate was in accordance with that found in other studies[25], and was significantly reduced by SDD.

In smaller single-centre studies, it was shown previously that SDD decreases infectious complications in oesophagogastric cancer surgery[11,26]. Roos and co-workers[12,27] published a retrospective case–control study and a smaller single-centre RCT of SDD in patients undergoing gastrointestinal surgery. Their RCT demonstrated a significant decrease in infectious complications and anastomotic leak rates as a combined endpoint in patients undergoing various gastointestinal operations, including colorectal, oesophageal and gastric resections for both benign and malignant disease[12].

Recently, two trials, one large retrospective US-based study of the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP®) database[28] and a Chinese randomized trial[25], indicated a preventive role for SSI and anastomotic leakage with the use of both mechanical bowel preparation (MBP) and oral antibiotic. In the present study, MBP did not have this effect on infections or anastomotic leakage in a multivariable logistic regression analysis. In the ACS-NSQIP® study[28], the use of oral antibiotics was at the preference of the surgeon, and selection bias cannot be excluded. Oral antibiotics used in the Chinese study[25] were not selective, but seemed to have an impact; however, the sample size was small and thus the study was possibly underpowered.

The present study has some limitations. Originally, it was designed to show superiority of the addition of SDD to standard antibiotic prophylaxis compared with standard prophylaxis alone for the prevention of anastomotic leakage. The power analysis was based on published Dutch data on the incidence of this complication. However, during the trial recruitment period, the Dutch Surgical Colorectal Audit reported that rates of anastomotic leakage were lower than those reported when the trial was designed[3]. A subsequent interim analysis showed that it would not be possible to demonstrate superiority of SDD *versus* standard care in the prevention of anastomotic leakage. Hence, the SELECT trial steering group decided to discontinue the study. No placebo was included in the study design.

The primary endpoint of anastomotic leakage and the most important secondary endpoint of infectious complications are, however, not susceptible to a placebo effect because they are hard endpoints.

A strength of this study is the effect of SDD on the intestinal microbiota by IS profiling, a technique that was shown recently[29] to provide excellent and reproducible microbiota profiles. This PCR-based profiling technique for high-throughput analysis of the human intestinal microbiota provides insight on a much more detailed level than that provided by conventional culture-based techniques[15]. IS profiling showed that SDD was effective in reducing the load of Proteobacteria, Enterobacteriaceae and *E. coli*, compared with those in the control group.

No adverse effects attributable to the study medication were reported in this trial, and no infections with multidrug-resistant microorganisms or *C. difficile* were observed. The safety of SDD with respect to resistance development has been shown in studies performed in ICU populations[30,31]. Cost-effectiveness was not considered in the present study, but de Smet *et al.*[10] showed SDD to be cost-effective in an ICU population; costs for SDD per patient are around €40. In conclusion, SDD reduced infectious complications after colorectal cancer resection but did not significantly affect the rate of anastomotic leakage in this trial.

Collaborators

Members of the SELECT trial study group: G. S. A. Abis, H. J. Bonjer, N. van Veenendaal, M. L. M. van Doorn-Schepens, A. E. Budding, E. S. M. de Lange, J. B. Tuynman, C. M. J. E. Vandenbroucke-Grauls, J. A. Wilschut, M. van Egmond (VU University Medical Centre Amsterdam); H. B. A. C. Stockmann, G. J. van der Bij, N. de Korte, S. J. Oosterling (Spaarne Gasthuis, Haarlem/Hoofddorp); Y. I. Z. Acherman (MC Slotervaart, Amsterdam); F. C. den Boer (Zaans Medisch Centrum, Zaandam), D. J. A. Sonneveld (Westfries Gasthuis, Hoorn); L. Poort (IS-Diagnostics, Amsterdam).

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European Colorectal Congress

28 November – 1 December 2022, St.Gallen, Switzerland

Monday, 28 November 2022

09.50
Opening and welcome
Jochen Lange, St.Gallen, CH

10.00
It is leaking! Approaches to salvaging an anastomosis
Willem Bemelman, Amsterdam, NL

10.30
Predictive and diagnostic markers of anastomotic leak
Andre D'Hoore, Leuven, BE

11.00
SATELLITE SYMPOSIUM
ETHICON

11.45
Of microbes and men – the unspoken story of anastomotic leakage
James Kinross, London, UK

12.15
LUNCH

13.45
Operative techniques to reduce anastomotic recurrence in Crohn's disease
Laura Hancock, Manchester, UK

14.15
Innovative approaches in the treatment of complex Crohn Diseases perianal fistula
Christianne Buskens, Amsterdam, NL

14.45
To divert or not to divert in Crohn surgery – technical aspects and patient factors
Pär Myrelid, Linköping, SE

15.15
COFFEE BREAK

15.45
Appendiceal neoplasia – when to opt for a minimal approach, when and how to go for a maximal treatment
Tom Cecil, Basingstoke, Hampshire, UK

16.15
SATELLITE SYMPOSIUM
Medtronic
Further,Together

17.00
Outcomes of modern induction therapies and Wait and Watch strategies, Hope or Hype
Antonino Spinelli, Milano, IT

17.30
EAES Presidential Lecture - Use of ICG in colorectal surgery: beyond bowel perfusion
Salvador Morales-Conde, Sevilla, ES

18.00
Get-Together with your colleagues
Industrial Exhibition

Tuesday, 29 November 2022

9.00
CONSULTANT'S CORNER
Michel Adamina, Winterthur, CH

10.30
COFFEE BREAK

11.00
SATELLITE SYMPOSIUM
INTUITIVE

11.45
Trends in colorectal oncology and clinical insights for the near future
Rob Glynne-Jones, London, UK

12.15
LUNCH

13.45
VIDEO SESSION

14.15
SATELLITE SYMPOSIUM
BD

15.00
COFFEE BREAK

15.30
The unsolved issue of TME: open, robotic, transanal, or laparoscopic – shining light on evidence and practice
Des Winter, Dublin, IE
Jim Khan, London, UK
Brendan Moran, Basingstoke, UK

16.30
SATELLITE SYMPOSIUM
Takeda

17.15
Lars Pahlman lecture
Søren Laurberg, Aarhus, DK

Thursday, 1 December 2022
Masterclass in Colorectal Surgery
Proctology Day

Wednesday, 30 November 2022

9.00
Advanced risk stratification in colorectal cancer – choosing wisely surgery and adjuvant therapy
Philip Quirke, Leeds, UK

09.30
Predictors for Postoperative Complications and Mortality
Ronan O'Connell, Dublin, IE

10.00
Segmental colectomy versus extended colectomy for complex cancer
Quentin Denost, Bordeaux, FR

10.30
COFFEE BREAK

11.00
Incidental cancer in polyp - completion surgery or endoscopy treatment alone?
Laura Beyer-Berjot, Marseille, FR

11.30
SATELLITE SYMPOSIUM

12.00
Less is more – pushing the boundaries of full-thickness rectal resection
Xavier Serra-Aracil, Barcelona, ES

12.30
LUNCH

14.00
Management of intestinal neuroendocrine neoplasia
Frédéric Ris, Geneva, CH

14.30
Poster Presentation & Best Poster Award
Michel Adamina, Winterthur, CH

15.00
SATELLITE SYMPOSIUM
OLYMPUS

15.45
COFFEE BREAK

16.15
Reoperative pelvic floor surgery – dealing with perineal hernia, reoperations, and complex reconstructions
Guillaume Meurette, Nantes, FR

16.45
Salvage strategies for rectal neoplasia
Roel Hompes, Amsterdam, NL

17.15
Beyond TME – technique and results of pelvic exenteration and sacrectomy
Paris Tekkis, London, UK

19.30
FESTIVE EVENING

Information & Registration **www.colorectalsurgery.eu**