Systematic review report for question PRP2-5,7

Clinical Question: Can peri operative management be optimised?

PICO: *In patients diagnosed with colorectal cancer and undergoing surgical tumour resection, does mechanical bowel preparation with or without antibiotic prophylaxis, when compared to usual care, achieve better outcomes in terms of anastomotic leakage, surgical site infection, length of hospital stay and ileus?*

Population	Intervention	Comparator	Outcomes
Patients diagnosed with colorectal cancer and undergoing surgical tumour resection of curative intent	Either: 1) Mechanical bowel preparation with oral and intravenous antibiotic prophylaxis or 2) Mechanical bowel preparation and intravenous antibiotic prophylaxis or 3) Mechanical bowel preparation and oral antibiotic prophylaxis	No mechanical bowel preparation	- Anastomotic leakage/dehiscence rates - Rate of surgical site/wound infection - Length of hospital stay - Ileus

1. Identification of existing relevant guidelines

1. 1 Methods

Relevant recent (from 2005 onwards) guidelines were identified by scanning the citations identified by the literature search and searching the National Guideline Clearinghouse (http://guideline.gov/) and the Guidelines Resource Centre (www.cancerview.ca).

To be considered for adoption guidelines had to meet the pre-specified criteria of scores of greater or equal to 70% for the domains rigour of development, clarity of presentation and editorial independence of the AGREE II instrument (http://www.agreetrust.org/resource-centre/agree-ii/).

2. Methods

2.1 Search for relevant guidelines

In March 2016 the search for relevant guidelines identified potentially relevant guidelines, however, these were not included as they did not meet the pre-specified criteria. These guidelines are detailed in Appendix C.

2.2 Literature Search

PubMed (01/01/2004 to 31/08/2016), Embase (01/01/2004 to 31/08/2016), CINAHL (01/01/2004 to 31/08/2016), PsycINFO (01/01/2004 to 31/08/2016), Cochrane Database of Systematic Reviews (01/01/2004 to 31/08/2016), Database of Abstracts of Reviews of Effects and Health Technology Assessment databases (01/01/2004 to 31/08/2016) were searched using text terms and, where available, database specific subject headings.

Each database was searched for articles dealing with colorectal cancer. In PubMed, Embase, CINAHL and PsycINFO databases the colorectal cancer search was coupled with a search for mechanical bowel preparation as well as surgical resection and database specific filters for identifying randomised controlled trials, systematic reviews and meta-analyses.

To identify studies which considered Aboriginal and Torres Strait Islanders (ATSI) these searches were then coupled with search terms for ATSI. A complete list of the terms used for all search strategies are included as Appendix A. Reference lists of all relevant articles were checked for potential additional articles.

Monthly alerts were established for both PubMed and Embase searches to identify relevant articles published before 31st August 2016 which were either published after the initial search was completed and/or added to the relevant database after the search was completed. Alerts were checked until December 2016. Cochrane Database of Systematic Reviews, CINAHL, PsycINFO, Database of Abstracts of Reviews of Effect and Health Technology Assessments databases were searched regularly up until December 2016 for relevant reviews published after the initial search.

1.3 Inclusion and exclusion Criteria

Selection criteria	**Inclusion criteria**	**Exclusion criteria**
Study type	Intervention studies	
Study design	Systematic reviews of Level II evidence, randomised controlled trials	
Population	Patients diagnosed with colorectal cancer and undergoing surgical tumour resection of curative intent	Palliative patients, emergent surgery, >33% non-colorectal cancer patients
Intervention	1) Mechanical bowel preparation with oral and intravenous antibiotic prophylaxis or 2) Mechanical bowel preparation and intravenous antibiotic prophylaxis or 3) Mechanical bowel preparation and oral antibiotic prophylaxis or 4) No mechanical bowel preparation and intravenous antibiotic prophylaxis	
Comparator	No mechanical bowel preparation	
Outcomes	- Anastomotic leakage/dehiscence rates - Rate of surgical site/wound infection - Length of hospital stay - Ileus	Outcomes related to colonoscopy
Language	English	
Publication period	From 1/01/2004 to 31/08/2016	

3. Results

3.1 Results of Literature Search

Figure 1 outlines the process of identifying relevant articles for the systematic review. The PubMed search identified 491 citations, the Embase search an additional 695 citations, the search of the Cochrane Database of Systematic Reviews 658 citations, the PsycINFO search identified 788 citations, the CINAHL search 19 citations, the search of Database of Abstracts of Reviews of Effects 1053 citations and Health Technology Assessment database identified an additional 256 citations, resulting in a total of 3960 citations. Titles and abstracts were examined and 85 articles were retrieved for a more detailed evaluation. No additional citations were identified from the reference list of retrieved articles.

14 trials reported in 16 articles (one trial reported in 2 articles and the data from another trial reported in full in one article with subgroup data in the second article) met the inclusion criteria and were included in the review. There were no studies of ATSI that met the inclusion criteria.

The retrieved articles that were not included and the reason for their exclusion are documented in Appendix C. In summary, most articles were excluded because they contained inappropriate studies (n=17), were reviews (n=12) or contained inappropriate comparators/populations (n=9/n=8)

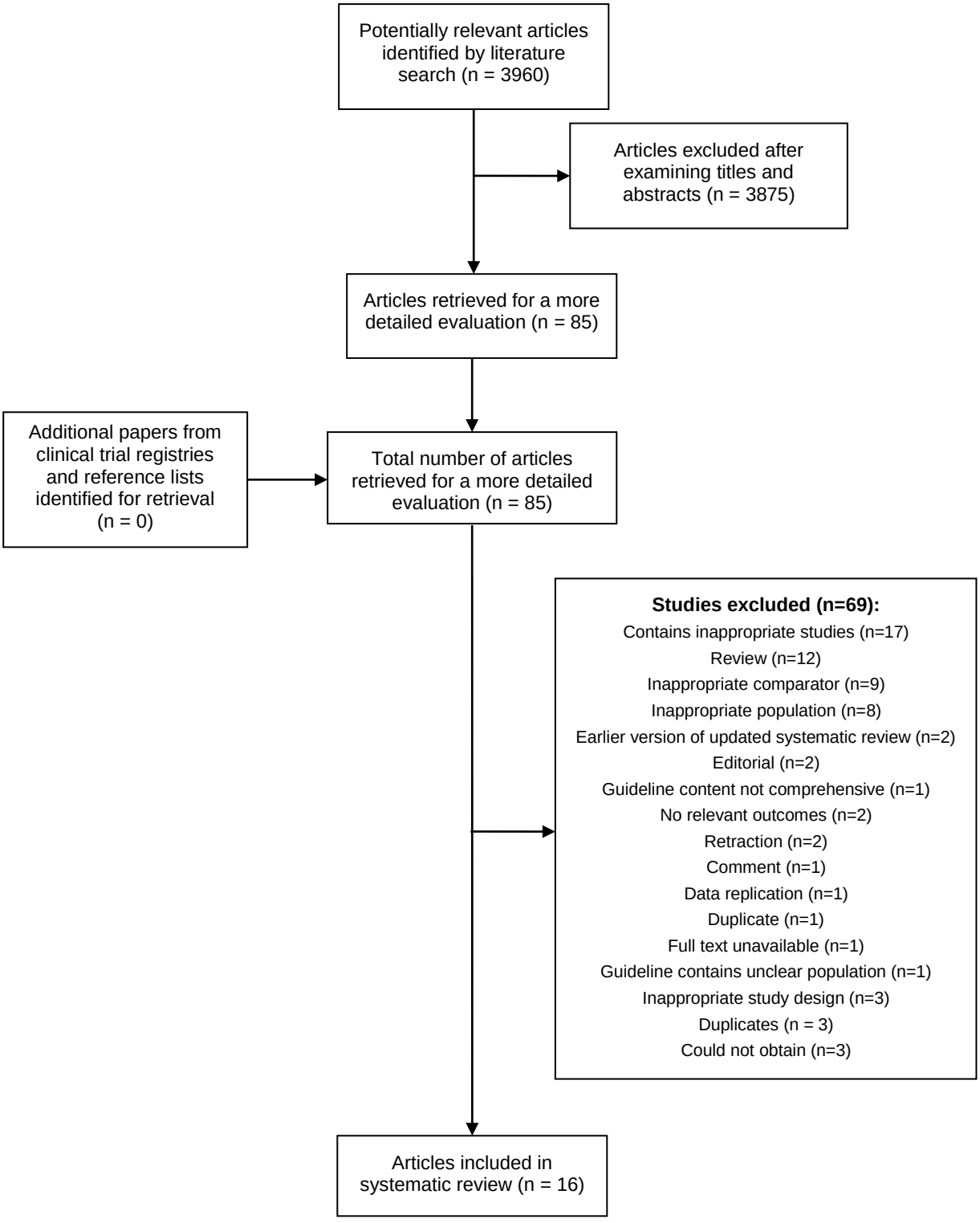

Figure 1. Process of inclusion and exclusion of studies

3.2. Study Characteristics

Characteristics of included studies are described in Tables 1 - 15.

Table 1: Randomised controlled trials comparing mechanical bowel preparation (with antibiotic prophylaxis) vs no mechanical bowel preparation (with or without antibiotic prophylaxis) in colorectal cancer patients: study characteristics

Study	Participants	Design	Intervention	Comparison	Outcomes	Comments
Bhattacharjee 2015 (India)	Single centre trial with patients randomised from 05/2010 to 04/2013. Inclusion criteria was age ≥15 years admitted for elective colorectal resection, giving wilful informed consent to participate in this trial **Mean age (SD)**: MBP: 47.45 (±10.34) years No MBP: 46.64 (±10.06) years **Gender F/M (%)** MBP: 45/55 No MBP: 61/39 **N = 71**	RCT (single centre)	MBP + IV antibiotic prophylaxis MBP: commercial preparation of PEG (118 g), sodium chloride (2.93 g), potassium chloride (1.484 g), sodium bicarbonate (3.37 g), and anhydrous sodium sulfate (11.36 g) with choice of flavours (PEGWASH®) Patients were asked to dissolve one pack with the flavoring agent in 2 L of water and start drinking from the afternoon prior to surgery, at the rate of 200 ml every 10–15 min so that 1 L is consumed in 1 h. They were told to drink the remaining solution till stool becomes watery. IV antibiotic prophylaxis: single-dose prophylactic antibiotic injections (1.5 g cefuroxime and 500 mg metronidazole) 1 h before surgery Other: IV fluid on morning of surgery Type of surgery: Open (100%) Type of resection: left hemicolectomy, right hemicolectomy, sigmoid colectomy, low anterior resection, abdominoperineal resection, total proctocolectomy, extended right hemicolectomy. **N = 38**	IV antibiotic prophylaxis Dietary preconditions: Clear fluids and avoid solid foods for 2 days prior to surgery and nothing per oral since the morning of surgery IV antibiotic prophylaxis: single-dose prophylactic antibiotic injections (1.5 g cefuroxime and 500 mg metronidazole) 1 h before surgery Other: IV fluid on morning of surgery Type of surgery: Open (100%) Type of resection: left hemicolectomy, right hemicolectomy, sigmoid colectomy, low anterior resection, abdominoperineal resection, total proctocolectomy, extended right hemicolectomy. **N = 33**	**Primary:** *Anastomotic leak* **Secondary:** *Wound infection, intraabdominal abscess, necessity for reexploration, and mortality* **Follow up:** *30 days*	Patients were excluded if they were unwilling to take part in the trial or those with gross comorbidities (which may otherwise adversely affect the outcome of surgery) were excluded from the trial. Patients undergoing emergency colorectal surgeries were not included either. Eighty percent (n=57) of the patients had malignant disease. Fourteen patients had benign conditions like polyposis coli, ulcerative colitis, and ileocaecal tuberculosis, including two patients with half turn volvulus who were initially treated conservatively. Majority of the patients had hand sewn anastomosis, and only low anterior resections (without proximal diverting ileostomy) were done with circular staplers. Fifty-three percent (n=38) of patients had ileo-colic anastomosis, and side to side or end to side anastomoses were preferred wherever feasible.

N = number of participants; RCT= randomised controlled trial; M= male; F= female; SD = standard deviation; MBP = mechanical bowel preparation; IV = intravenous; mg = milligram; g = gram; mL = millilitre; L = litre; h = hour; min = minutes; PEG = polyethylene glycol

Table 2: Randomised controlled trials comparing mechanical bowel preparation (with antibiotic prophylaxis) vs no mechanical bowel preparation (with or without antibiotic prophylaxis) in colorectal cancer patients: study characteristics

Study	Participants	Design	Intervention	Comparison	Outcomes	Comments
Brentagnol 2010 (France)	Multicentre trial with patients randomised from 10/2007 to 01/2009. Inclusion criteria was ≥18 years with rectal cancer, (ie, within 15 cm from the anal verge) who underwent laparoscopic or open elective rectal resection with mesorectal excision and sphincter preservation **Median age (range)**: MBP: 65 (57-73) years No MBP: 62 (54-71) years **Gender F/M (%)** MBP: 37/63 No MBP: 48/52 **N = 178 analysed**	RCT (multicentre, 8 centres)	MBP + enema + IV antibiotic prophylaxis Dietary preconditions: After MBP, diet was confined to clear fluids all the day. Fasting from midnight (ie, no clear fluids or carbohydrate). MBP: senna solution (X-PREP sarget) (1 or 2 120-mg package of flavored powder diluted in a glass of water according to the colon cleanliness) 24 hours pre-surgery Enema: Retrograde enema 1 L of povidone-iodine enema on the evening before, and early in the morning, (at least 2 hours) pre-surgery IV antibiotic prophylaxis: 500 mg of metronidazole and 1 g of ceftriaxone diluted in 125 mg of saline solution infused for 15 minutes by IV at anesthetic induction and were continued every 2 hours during the surgical procedure. Indication for operation: Rectal cancer (100%) Pre-operative radiotherapy: 71% Type of surgery: Open (18%); laparoscopy (82%) Type of resection: NR Technique of anastomosis: Stapled colorectal anastomosis (54%); hand-sewn coloanal anastomosis (46%); colonic pouch or side-to-end anastomosis (49%); temporary ileostomy (80%); pelvic drainage (96%) **N = 89 analysed**	IV antibiotic prophylaxis Dietary preconditions: No preoperative dietary restrictions up to midnight the day before operation. From midnight patients were required to fast (ie, no clear fluids or carbohydrate) IV antibiotic prophylaxis: 500 mg of metronidazole and 1 g of ceftriaxone diluted in 125 mg of saline solution infused for 15 minutes by IV at anesthetic induction and were continued every 2 hours during the surgical procedure. Indication for operation: Rectal cancer (100%) Pre-operative radiotherapy: 72% Type of surgery: Open (17%); laparoscopy (83%) Type of resection: NR Technique of anastomosis: Stapled colorectal anastomosis (53%); hand-sewn coloanal anastomosis (47%); colonic pouch or side-to-end anastomosis (39%); temporary ileostomy (83%); pelvic drainage (99%) **N = 89 analysed**	**Primary:** *Overall 30 day postoperative morbidity rate* **Secondary:** *Anastomotic leakage rate (asymptomatic or clinical), infectious morbidity rate including abdominal (pelvic abscess, peritonitis, wound abscess, etc) and extra-abdominal (urinary tract infection, pneumophathy etc) complications, noninfectious complications rate, major morbidity rate, hospital stay, discomfort of preparation for patient, and assessment of the colon cleansing by the operating surgeon.* **Follow-up:** 30 days	ITT analysis performed Patients excluded if had very low rectal tumors requiring abdominoperineal excision, liver or lung metastases, T4 rectal cancer requiring extra-anatomical dissection, synchronous adenocarcinomas, and/or gastrointestinal disease (IBD, familial polyposis) requiring extensive colonic surgery Randomisation: 1:1 ratio Patients with advanced local disease (T3 and/or N1) received long-course preoperative radiotherapy or radiochemotherapy. Operations were performed 6-8 weeks post-irraadiation Patient numbers reflect those analysed. Original total number of patients were 186 randomised with exclusion reasons due to missing consent form (n=5), refusal of surgery (n=1) and loss to follow up (n=1). Anastomotic leakage was defined as asymptomatic if demonstrated by routine contrast enema before ileostomy closure and as clinical if symptoms related to leakage were noted (ie, gas, pus, or faecal discharge from the drain, peritonitis, discharge of pus per rectum). Treatment stratified according to primary tumour site (upper part of rectum vs mid and low parts) and type of surgical procedure (open versus laparoscopic)

N = number of participants; RCT= randomised controlled trial; M= male; F= female; NR = not reported; MBP = mechanical bowel preparation; IV = intravenous; ITT = Intention to treat; cm = centimetres; mg = milligram; g = gram; L = litre; IBD = inflammatory bowel disease; PEG = polyethylene glycol

Table 3: Randomised controlled trials comparing mechanical bowel preparation (with antibiotic prophylaxis) vs no mechanical bowel preparation (with or without antibiotic prophylaxis) in colorectal cancer patients: study characteristics

Study	Participants	Design	Intervention	Comparison	Outcomes	Comments
Contant 2007 (Netherlands)	Multicentre trial with patients randomised from 04/1998 to 02/2004. Inclusion criteria was age ≥18 years with indication for elective colorectal surgery with primary anastomosis **Mean age (SD)**: MBP: 67 (±13) years No MBP: 67 (±12) years **Gender F/M (%)** MBP: 50/50 No MBP: 50/50 **Patients with ASA-score ≥3 (%):** No MBP: 12.3% No MBP: 12.4% **N = 1354 analysed**	RCT (multicentre, 13 centres)	MBP + IV antibiotic prophylaxis Dietary preconditions: Fluid diet (of beverages, yoghurt, and soup) on the day before their operations. MBP: 2–4 L of PEG bowel lavage solution in combination with bisacodyl (at 11 hospitals; 88%) or sodium phosphate solution (at two hospitals; 12%) IV antibiotic prophylaxis: Cefuroxim+metronidazole (48%) Cefazolin+metronidazole (12%) Cefamandole+metronidazole (10%) Gentamycine+metronidazole (8%) Amoxicillin-clavulanate (19%) Others (3%) Indication for operation: Colorectal cancer (73%); IBD (18%); Other (9%) Pre-operative radiotherapy: 5% Type of surgery: NR Type of resection: NR Technique of anastomosis: Stapled (30%); Handsewn (66%); End-to-end (43%); Side-to-end (37%); Side-to-side (15%); End-to-side (3%); Pouch (1%) Type of anastomosis: Ileocolic (28%); Colonic (31%); Colorectal (34%); Coloanal anastomosis or ilorectal anastomosis (4%) **N = 670 analysed**	IV antibiotic prophylaxis Dietary preconditions: Normal meals allowed IV antibiotic prophylaxis: Cefuroxim+metronidazole (48%) Cefazolin+metronidazole (12%) Cefamandole+metronidazole (12%) Gentamycine+metronidazole (8%) Amoxicillin-clavulanate (19%) Others (1%) Indication for operation: Colorectal cancer (79%); IBD (15%); Other (6%) Pre-operative radiotherapy: 3% Type of surgery: NR Type of resection: NR Technique of anastomosis: Stapled (30%); Handsewn (68%); End-to-end (46%); Side-to-end (34%); Side-to-side (17%); End-to-side (2%); Pouch (1%) Type of anastomosis: Ileocolic (31%); Colonic (35%); Colorectal (31%); Coloanal anastomosis or ilorectal anastomosis (4%) **N = 684 analysed**	**Primary:** *Anastomotic leak* **Secondary:** *Septic complications (wound infection, urinary infection, pneumonia, and intra-abdominal abscesses); fascia dehiscence; and death.* **Follow up (median, IQR):** *24 (17-34) days*	Per protocol patients analysed only Patients were excluded if they had acute laparotomy; had laparoscopic colorectal surgery; had a contraindication for the use of mechanical bowel preparation; had an a priori deviating ileal stoma Randomisation: 1:1 ratio Stratification occurred by centre Asymptomatic leakage was not screened Patient numbers reflect those analysed. Original total number of patients were 1431 with 707 randomised to intervention arm and 724 to comparison arm. Patients in the "other" indication for operation category had radiation induced stenosis, endometriosis, and correction of Hartmann's procedure

N = number of participants; RCT= randomised controlled trial; M= male; F= female; SD = standard deviation; NR = not reported; ASA = American society of anaesthesiologists; MBP = mechanical bowel preparation; IV = intravenous; L = litre; IBD = irritable bowel disease; PEG = polyethylene glycol; IQR = interquartile range

Table 4: Randomised controlled trials comparing mechanical bowel preparation (with antibiotic prophylaxis) vs no mechanical bowel preparation (with or without antibiotic prophylaxis) in colorectal cancer patients: study characteristics

Study	Participants	Design	Intervention	Comparison	Outcomes	Comments
van't Sant 2010 (Netherlands)	See Contant 2007 for original inclusion criteria. Inclusion criteria for subgroup analysis: Elective low anterior resection with primary anastomosis	RCT (multicentre, 13 centres)	MBP + IV antibiotic prophylaxis Dietary preconditions: Fluid diet (of beverages, yoghurt, and soup) on the day before their operations. MBP: 2–4 L of PEG bowel lavage solution in combination with bisacodyl (at 11 hospitals) or sodium phosphate solution (at two hospitals) IV antibiotic prophylaxis: Cefuroxim+metronidazole or Cefazolin+metronidazole or Cefamandole+metronidazole or Gentamycine+metronidazole or Amoxicillin-clavulanate or Others Indication for operation: Colorectal cancer, IBD or other Type of surgery: Open surgery (100%) Type of resection: Low anterior resection (100%) Technique of anastomosis: Stapled or Handsewn Type of anastomosis: Colorectal, End-to-end, Side-to-end	IV antibiotic prophylaxis Dietary preconditions: Normal meals allowed IV antibiotic prophylaxis: Cefuroxim+metronidazole or Cefazolin+metronidazole or Cefamandole+metronidazole or Gentamycine+metronidazole or Amoxicillin-clavulanate or Others Indication for operation: Colorectal cancer, IBD or other Type of surgery: Open surgery (100%) Type of resection: Low anterior resection (100%) Technique of anastomosis: Stapled or Handsewn Type of anastomosis: Colorectal, End-to-end, Side-to-end or Other	**Primary:** *Anastomotic leakage* **Secondary:** *Septic complications and mortality* **Follow up (median, IQR):** 24 (17-34) days	This paper is a retrospective subgroup analysis of Contant 2007 See Contant 2007 for original exclusion criteria 449 patients undergoing a low anterior resection Randomisation: 1:1 ratio Stratification occurred by centre Asymptomatic leakage was not screened Low anterior resections were defined as anastomosis performed below the level of the peritoneal verge. The peritoneal verge divides the intraperitoneal colon and cranial part of the rectum from the extraperitoneal part of the rectum. The peritoneal verge may also be called peritoneal reflection, pelvic diaphragm, or visceral pelvic fascia. Wound infection was defined as mild in case of erythema or discharge of seroma and as severe in case of discharge of pus, wound necrosis, or wound dehiscence. The follow-up period was defined as the time from operation until first outpatient visit after discharge from the hospital, which usually occurred after 2 weeks. No exact criteria for the appliance of a diverting ileostomy were stated and a diverting ileostomy was applied when assumed necessary by the surgeon. Common reasons for applying a diverting ileostomy were difficult operation, fecal contamination, tension on the anastomosis, very low anastomosis, high comorbidity, and incomplete donuts when a circular stapler was used
	N = 449 analysed		**N = 236 analysed**	**N = 213 analysed**		

N = number of participants; RCT= randomised controlled trial; M= male; F= female; NR = not reported; MBP = mechanical bowel preparation; IV = intravenous; L = litre; PEG = polyethylene glycol

Table 5: Randomised controlled trials comparing mechanical bowel preparation (with antibiotic prophylaxis) vs no mechanical bowel preparation (with or without antibiotic prophylaxis) in colorectal cancer patients: study characteristics

Study	Participants	Design	Intervention	Comparison	Outcomes	Comments
Fa Si Oen 2005 (Netherlands)	Multicentre trial with patients randomised from 10/1998 to 10/2002. Inclusion criteria was those who underwent elective colon surgery. Included surgical procedures varied from right hemicolectomies to sigmoid resections **Median age (range)**: MBP: 68.3 (27.7-86.5) years No MBP: 70.7 (28.8-89.0) years **Gender F/M (%)** MBP: 67/58 No MBP: 69/56 **N = 250**	RCT (multicentre, 5 centres)	MBP + IV antibiotic prophylaxis Dietary preconditions: NR MBP: 4 L of PEG preoperatively IV antibiotic prophylaxis: systemic antibiotic prophylaxis by way of cefazoline 2 g and metronidazole 1.5 g or gentamicin 240 mg and metronidazole 1.5 g within 30 minutes before surgery Indication for operation: Colorectal cancer (72%); Recurrent diverticular disease (15.2%); Other (12.8%) Type of surgery: Open (100%) Type of resection: Right colectomy (52.4%), transverse colectomy (2.4%), left colectomy (8.1%), sigmoid resection (33.1%), additional procedures (4.8%) Technique of anastomosis: Stapled (7.2%); Handsewn (92.8%) **N = 125**	IV antibiotic prophylaxis Dietary preconditions: normal meal up to 10 hours before surgery without additional bowel cleaning procedures IV antibiotic prophylaxis: systemic antibiotic prophylaxis by way of cefazoline 2 g and metronidazole 1.5 g or gentamicin 240 mg and metronidazole 1.5 g within 30 minutes before surgery Indication for operation: Colorectal cancer (73.6%); Recurrent diverticular disease (18.4%); Other (8.0%) Type of surgery: Open (100%) Type of resection: Right colectomy (42.1%), transverse colectomy (2.4%), left colectomy (7.9%), sigmoid resection (42.9%), additional procedures (4.0%) Technique of anastomosis: Stapled (8.0%); Handsewn (92.0%) **N = 125**	**Primary:** *Wound infection, bacteriologic results of intraoperative swabs and anastomotic leakage.* **Secondary:** *Duration of ileus, total hospital stay, and number of relaparatomies* **Follow-up:** 3 months	ITT analysis performed Patients were excluded if they underwent previous radiotherapy and/or chemotherapy, patients with idiopathic inflammatory bowel disease, patients with obstructive tumors, patients undergoing an emergency laparotomy, and those receiving MBP for diagnostic reasons up to one week before surgery. Patients undergoing ileocecal resections and resections below the peritoneal reflection were also excluded Randomisation: permuted blocks of eight with stratification according to centre Patients in the "other" indication for operation category had restoration of a Hartmann procedure or colectomy for a benign lesion or stricture. Anastomotic leakage was defined as major when leakage was clinically significant leading to a relaparotomy and minor when leakage was subclinical, verified by radiographic examination, and treated conservatively. Wound infection was defined as a clinically significant infection of the skin for which the wound had to be evacuated. Duration of ileus was defined as the number of days before signs of restoration of the bowel function appeared (bowel movement, flatus, and stool) after which oral intake was restarted. Total hospital stay was defined as the number of days from date of surgery until hospital discharge.

N = number of participants; RCT= randomised controlled trial; M= male; F= female; NR = not reported; MBP = mechanical bowel preparation; IV = intravenous; ITT = Intention to treat; mg = milligram; g = gram; mL = millilitre; L = litre; h = hour; PEG = polyethylene glycol

Table 6: Randomised controlled trials comparing mechanical bowel preparation (with antibiotic prophylaxis) vs no mechanical bowel preparation (with or without antibiotic prophylaxis) in colorectal cancer patients: study characteristics

Study	Participants	Design	Intervention	Comparison	Outcomes	Comments
Horvat 2010 (Slovenia)	Single centre trial, randomisation dates not reported. Inclusion criteria was ≥18 years admitted for abdominal and general surgery with a histologically confrmed diagnosis of adenocarcinoma of the colon **Median age (range)**: MBP: 65 (52-78) years No MBP C1: 62 (42-86) years No MBP C2: 62 (29-80) years **Gender F/M (%)** MBP: 45/55 No MBP C1: 55/45 No MBP C2: 64/36 **N = 68**	RCT (single centre)	MBP + antibiotic prophylaxis (administration undefined) Dietary preconditions: Breakfast day before procedure MBP: 75 mL of X-Prep® oral solution (Mundipharma, Vienna, Austria), containing 1.95 g senna plant extract standardized on hydroxyanthracene glycoside calculated as Sennoside B 150 mg, 142.5 mg potassium sorbate and 49.5 g saccharose. Followed by 4 L hyperosmolar Golitely solution (product of hospital pharmacist laboratory) taken orally and prepared from a 9.4 g sachet composed of dried sodium sulfate 5.6 g, sodium chloride 1.4 g, potassium chloride 0.7 g and sodium hydrogen carbonate 1.7 g to which 59.0 g of PEG 4000 (macrogol 4000) is added and mixed with 2 L water. Patients took 75 mL X-Prep® after breakfast and 4 L Golitely solution after mid-day the day before the procedure Indication for operation: Colon cancer (100%) Type of resection: Right hemicolectomy (45%), left hemicolectomy (10%), rectosigmoid resection (40%), low anterior resection (5%) **N = 20**	**Comparison 1:** Synbiotics + antibiotic prophylaxis (administration undefined) Dietary preconditions: 24 h pre-surgery only oral fluids were permitted Synbiotics: multi-strain/multi-fiber Synbiotic 2000™ (Medipharm, Kågeröd Sweden and Des Moines, Iowa, USA), containing four lactobacilli, one from each of four main genera: Lactobacillus, paracasei, paracasei 19, Active, 10^10 cfu/sachet; Lactobacillus, plantarum, 2362, Active, 10^10 cfu/sachet; Pediococcus, pentosaceus, 5–33:3, Active, 10^10 cfu/sachet; Leuconostoc, mesenteroides, 32–77:1, Active, 10^10 cfu/sachet. Each dose contains 40 billion lactobacilli plus 10 g of bioactive plant fibers (2.5 g betaglucan, 2.5 g inulin, 2.5 g pectin, 2.5 g resistant starch) in sachets. Patients mixed the contents with 100 mL of sterile water and drank it twice daily for three days before operation Indication for operation: Colon cancer (100%) Type of resection: Right hemicolectomy (35%), resection of transverse colon (5%), rectosigmoid resection (35%), low anterior resection (25%) **N=20** **Comparison 2:** Prebiotics + heat deactivated probiotics + IV antibiotic prophylaxis (antibiotic administration undefined) Dietary preconditions: 24 h before surgery only oral fluids were permitted Prebiotics + heat deactivated probiotics: Lactobacillus, paracasei paracasei, 19, Heat-inactivated; Lactobacillus, plantarum, 2362, Heat-inactivated; Pediococcus, pentosaceus, 5–33:3, Heat-inactivated; Leuconostoc, mesenteroides, 32–77:1, Heat-inactivated. Patients mixed the contents with 100 mL of sterile water and drank it twice daily for three days before operation Indication for operation: Colon cancer (100%) Type of resection: Right hemicolectomy (35.7%), left hemicolectomy (3.6%), rectosigmoid resection (50%), low anterior resection (10.7%) **N=28**	**Primary:** *Systemic inflammatory response* **Secondary:** *First day of bowel movement, passing flatus and stool, diarrhoea, constipation, vomiting, abdominal cramps, or distention, major and minor complications and hospital stay.* **Follow up:** NR	Per protocol analysis performed Exclusion factors were age <18 years, multiple colon malignancy, any clinical, laboratory or imaging signs of advanced malignant disease (invasion of adjacent organs, distant metastases), signs of gastrointestinal obstruction, history of IBD, ASA group > 3, and those not willing to participate Randomisation: 1:1 ratio All patients in the study received concomitant preventive antibiotics, analgesics, parenteral and enteral nutrition, as needed. Type of surgery, technique of anastomosis and type of anastomosis was not reported for each arm

N = number of participants; RCT= randomised controlled trial; M= male; F= female; C1 = comparison 1; C2 = comparison 2; ASA = American society of anaesthesiologists; IBD = Inflammatory bowel disease; MBP = mechanical bowel preparation; IV = intravenous; cfu = colony forming units; mg = milligram; g = gram; mL = millilitre; L = litre; PEG = polyethylene glycol

Table 7: Randomised controlled trials comparing mechanical bowel preparation (with antibiotic prophylaxis) vs no mechanical bowel preparation (with or without antibiotic prophylaxis) in colorectal cancer patients: study characteristics

Study	Participants	Design	Intervention	Comparison	Outcomes	Comments
Jung 2007 (Sweden)	Multicentre trial with patients randomised from 01/1999 to 03/2005. Inclusion criteria was Patients undergoing elective open surgery for cancer, adenoma or diverticular disease of the colon involving an anastomosis, aged 18- 85 years with an ASA grade of I, II or III **Mean age (range)**: MBP: 69 (35-85) years No MBP: 69 (28-86) years **Gender F/M (%)** MBP: 55.4/44.6 No MBP: 51.8/48.2 **N = 1343 analysed**	RCT (multicentre, 21 centres)	MBP + IV or oral antibiotic prophylaxis Dietary preconditions: NR MBP: MBP was performed according to local standards in each unit. Oral agents used for bowel preparation were PEG (Laxabon®; AstraZeneca, Oslo, Norway) (47.2% of patients) and sodium phosphate (Phosphoral®; Ferring Pharmaceuticals, Limhamn, Sweden) (48.5% of patients). 4.3% of patients in this arm underwent enemas only IV or oral antibiotic prophylaxis: Oral sulfamethoxazole–trimethoprim + metronidazole or IV cephalosporin + metronidazole or IV Doxycycline + metronidazole Indication for operation: Colorectal cancer (81.6%); Adenoma (15.2%); Diverticular disease (14.7%) Type of surgery: Open (100%) Type of resection: NR Technique of anastomosis: Stapled (33.3%); Handsewn (66.7%) Type of anastomosis: Ileocolic or ilorectal (54.5%); Colonic or colorectal (45.5%) **N = 686 analysed**	IV or oral antibiotic prophylaxis Dietary preconditions: No restrictions IV or oral antibiotic prophylaxis: Oral sulfamethoxazole–trimethoprim + metronidazole or IV cephalosporin + metronidazole or IV Doxycycline + metronidazole Indication for operation: Colorectal cancer (78.8%); Adenoma (16.4%); Diverticular disease (14.2%) Type of surgery: Open (100%) Type of resection: NR Technique of anastomosis: Stapled (36.2%); Handsewn (64.2%) Type of anastomosis: Ileocolic or ilorectal (56.9%); Colonic or colorectal (43.1%) **N = 657 analysed**	**Primary:** *Cardiovascular complications, general infectious complications and surgical-site complications* **Secondary:** *Postoperative death and reoperation* **Follow-up:** 30 days	ITT analysis performed Trial acronym: Boniec Patients were excluded if they had laparoscopic surgery, procedures involving a stoma, ASA score IV and life expectancy of less than 6 months. 20 Swedish colorectal units and one German unit participated in the trial Stratification occurred by centre and patients were randomized in blocks of permutations of four Patient numbers reflect those analysed. Original total number of patients randomised were 1484 with 753 randomised to intervention arm and 731 to comparison arm. Primary and secondary endpoints differs between protocol and paper. Paper endpoints are reported here. In total 46% of participants were administered Oral sulfamethoxazole–trimethoprim + metronidazole, 33% IV cephalosporin + metronidazole and 14% IV Doxycycline + metronidazole Mean number of inclusions per centre was 72 (range 2–246) patients No patient with a stoma was included in the analysis. Some 1243 patients had one dose of prophylactic antibiotics before surgery whereas 102 had more than one dose (47 in MBP and 55 in no MBP group)

N = number of participants; RCT= randomised controlled trial; M= male; F= female; NR = not reported; ASA = American society of anaesthesiologists; MBP = mechanical bowel preparation; IV = intravenous; ITT = Intention to treat; PEG = polyethylene glycol

Table 8: Randomised controlled trials comparing mechanical bowel preparation (with antibiotic prophylaxis) vs no mechanical bowel preparation (with or without antibiotic prophylaxis) in colorectal cancer patients: study characteristics

Study	Participants	Design	Intervention	Comparison	Outcomes	Comments
Krebs 2016 (Slovenia)	Single centre trial, randomisation dates not reported. Inclusion criteria was patients with preceding large bowel elective operation for colorectal cancer **Median age (range)**: MBP: 67 (52-78) years No MBP C1: 62 (43-87) years No MBP C2: 64 (46-81) years **Gender F/M (%)** MBP: 43.75/56.25 No MBP C1: 38.9/61.1 No MBP C2: 35/65 **N = 54**	RCT (Single centre)	MBP + IV antibiotic prophylaxis Dietary preconditions: Liquid diet two days before surgery. Light breakfast allowed the day before surgery MBP: Day before surgery patients drank 75 mL of Coloclens® (Senna glykosides). After few hours, afternoon patients consumed 4 L of hyperosmolar liquid Golitely (PEG), provided by the hospital pharmacy IV antibiotic prophylaxis: one dose of antibiotic cefuroksim and metronidasole Indication for operation: Colorectal cancer (100%) Type of surgery: NR **N = 16**	**Comparison 1:** Synbiotics + IV antibiotic prophylaxis Dietary preconditions: Liquid diet two days before surgery Synbiotics: Synbiotic 2000 FORTE. It consists 1011 of each of four LAB: *Pediacoccus pentosaceus* 5–33:3, *Leuconostoc mesenteroides* 32–77:1, *Lactobacillus paracasei* subsp paracasei 19, and *Lactobacillus plantarum* 2362. This makes 400 billion LAB per dose or if supplemented twice daily 800 billion LAB per day. Also included in the sachet is 2.5 g of each of the four fermentable fibres – probiotics: betaglucan, inulin, pectin and resistant starch. Synbiotic 2000 FORTE was produced and marketed by Medipharm, Kageröd Sweden and Des Moines, Iowa, USA. Taken twice a day three days before operation IV antibiotic prophylaxis: one dose of antibiotic cefuroksim and metronidasole Indication for operation: Colorectal cancer (100%) Type of surgery: NR **N=18** **Comparison 2:** Prebiotics + IV antibiotic prophylaxis Dietary preconditions: Liquid diet two days before surgery Prebiotics: 2.5 g of each of the four fermentable fibres (prebiotics): betaglucan, inulin, pectin and resistant starch. Taken twice a day three days before operation IV antibiotic prophylaxis: one dose of antibiotic cefuroksim and metronidasole Indication for operation: Colorectal cancer (100%) Type of surgery: NR **N=20**	**Primary:** *Concentrations of LAB on the colonic mucosa* **Secondary:** *Systemic inflammatory response after surgery, postoperative complications, postoperative course.* **Follow-up:** 25 days	Per protocol patients analysed only Patients were excluded if they had any chronic disease or health condition which in opinion of investigators may interfere with the patient's ability to comply with protocol, place the subject at unnecessary risk, or interfere with the evaluation of the study drugs, signs or symptoms of bowel obstruction, patients who could not take the mechanic preoperative bowel preparation, and chronic IBD. Some patients were removed from the study if one or more of the following had occurred: significant protocol violation or non-compliance on the part of the patient, refusal of the patient to continue treatment or decision of the investigator that termination is in the patient's best medical interest. 26 sigma resections, 16 right hemicolectomies, 8 anterior rectal resection, 3 left hemicolectomies and one resection of transversal colon were performed in total

N = number of participants; RCT= randomised controlled trial; M= male; F= female; NR = not reported; ASA = American society of anaesthesiologists; MBP = mechanical bowel preparation; IV = intravenous; LAB = lactic acid bacteria; BMI= body mass index; g = gram; mL = millilitre; IBD = irritable bowel disease; PEG = polyethylene glycol

Table 9: Randomised controlled trials comparing mechanical bowel preparation (with antibiotic prophylaxis) vs no mechanical bowel preparation (with or without antibiotic prophylaxis) in colorectal cancer patients: study characteristics

Study	Participants	Design	Intervention	Comparison	Outcomes	Comments
Pena-Soria 2008 **Pena-Soria 2007** (Spain)	Single centre trial with patients randomised from 10/2001 to 01/2007. Inclusion criteria was age ≥18 years scheduled to undergo an elective colorectal procedure with a primary intraperitoneal anastomosis without intraoperative colonoscopy, had not had an endoscopic exploration in the prior week and had given informed consent **Mean age (SD)**: MBP: 67.2 (±13) years No MBP: 67.4 (±16) years **Gender F/M (%)** MBP: 44.6/55.4 No MBP: 50/50 **N = 129 analysed**	RCT (Single centre)	MBP + enema + IV antibiotic prophylaxis + anti-thrombotic prophylaxis Dietary preconditions: Liquid diet for 24 h prior to the procedure MBP: 3 L of PEG and conventional enema over 24 h IV antibiotic prophylaxis: Gentamicin and metronidazole (80 mg and 500 mg, respectively), 30 min before incising the skin and every 8 h postoperatively (three doses) Anti-thrombotic prophylaxis was based on preoperative and postoperative administration of subcutaneous low molecular weight heparin (enoxaparin 40 mg or 60 mg depending on individual risk factors). Indication for operation: Colorectal cancer (78.3%); IBD (6.2%); Other (15.5%) Type of surgery: NR Type of resection: NR Technique of anastomosis: Stapled (23.3%); Handsewn (27.1%) Type of anastomosis: Ileocolostomy (40%); ileorectostomy (4.6%); colocolostomy (12.3%); colorectostomy (43.1%) **N = 65 analysed**	IV antibiotic prophylaxis + anti-thrombotic prophylaxis Dietary preconditions: Regular diet until the night before surgery where oral intake cessation was ordered 9–12 h before the operation IV antibiotic prophylaxis: Gentamicin and metronidazole (80 mg and 500 mg, respectively), 30 min before incising the skin and every 8 h postoperatively (three doses) Anti-thrombotic prophylaxis was based on preoperative and postoperative administration of subcutaneous low molecular weight heparin (enoxaparin 40 mg or 60 mg depending on individual risk factors). Indication for operation: Colorectal cancer (77%); IBD (4.6%); Other (18.5%) Type of surgery: NR Type of resection: NR Technique of anastomosis: Stapled (17.8%); Handsewn (31.8%) Type of anastomosis: Ileocolostomy (51.6%); ileorectostomy (1.6%); colocolostomy (9.4%); colorectostomy (37.5%) **N = 64 analysed**	**Primary:** *Surgical site infection* **Secondary:** *Anastomotic leakage* **Follow-up:** 30 days	Per protocol patients analysed only Patients were excluded after randomisation if they underwent active immunosuppression (including poorly controlled conditions that could increase the infection risk, such as diabetes mellitus, HIV infection, etc.), preoperative chemoradiation, diverting stoma, and perforated or obstructed tumour Randomisation: 1:1 ratio No IV fluids were administered as a part of the preoperative protocol. Patient numbers reflect those analysed. Original number of patients randomised was 142 with 71 randomised to intervention arm and 71 to comparison arm. Six patients in the intervention arm and 7 patients in the comparison arm met exclusion criteria and were not analysed.

N = number of participants; RCT= randomised controlled trial; M= male; F= female; SD = standard deviation; NR = not reported; MBP = mechanical bowel preparation; IV = intravenous; HIV= human immunodeficiency virus; mg = milligram; min = minute; h = hour; PEG = polyethylene glycol

Table 10: Randomised controlled trials comparing mechanical bowel preparation (with antibiotic prophylaxis) vs no mechanical bowel preparation (with or without antibiotic prophylaxis) in colorectal cancer patients: study characteristics

Study	Participants	Design	Intervention	Comparison	Outcomes	Comments
Platell 2006 (Australia)	Single centre trial with patients randomised from 01/2000 to 02/2005. Inclusion criteria was age ≥18 years undergoing elective resection of the colon and/or rectum, with an anastomosis, and with or without a defunctioning stoma **Mean age (SD)**: MBP: 65 (±14) years No MBP: 66 (±14) years **Gender F/M (%)** MBP: 87.8/12.2 No MBP: 83.7/16.3 **N = 294**	RCT (single centre)	MBP + IV antibiotic prophylaxis Dietary preconditions: Clear liquids for 24 h before surgery MBP: 3 L of Glycoprep (PEG 159 g; Pharmatel, Hornsby, New South Wales, Australia) on the day before surgery IV antibiotic prophylaxis: Timentin® (ticarcillin disodium and clavulanate potassium) (GlaxoSmithKline, Melbourne, Victoria, Australia) 3·1 g, intravenously with induction of anaesthesia, or gentamicin 2 mg/kg and metronidazole 500 mg intravenously Indication for operation: Colorectal cancer (82.3%); Colorectal adenoma (8.2%); IBD (3.4%); Diverticular disease (3.4%); Rectal pathology (56.5%) Pre-operative radiotherapy: 12.9% Type of surgery: Right hemicolectomy (27.9%); High anterior resection (28.6%); Low anterior resection (3.4%); Ultralow anterior resection (32.0%); Reconstructive proctolectomy (0.7%); Other (7.5%) Type of resection: Open (100%) Anastomosis: 148 in 147 patients Technique of anastomosis: Stapled (66.9%); Handsewn (33.1%) Covering stoma: 38.8% **N = 147**	Enema + IV antibiotic prophylaxis Dietary preconditions: Clear liquids for 24 h before surgery Enema: single sodium phosphate enema (133 mL; CB Fleet, Braeside, Victoria, Australia) 2–4 h before surgery IV antibiotic prophylaxis: Timentin® (ticarcillin disodium and clavulanate potassium) (GlaxoSmithKline, Melbourne, Victoria, Australia) 3·1 g, intravenously with induction of anaesthesia, or gentamicin 2 mg/kg and metronidazole 500 mg intravenously Indication for operation: Colorectal cancer (77.6%); Colorectal adenoma (9.5%); IBD (4.1%); Diverticular disease (6.8%); Rectal pathology (49.7%) Pre-operative radiotherapy: 12.9% Type of surgery: Right hemicolectomy (35.4%); High anterior resection (28.6%); Low anterior resection (2.0%); Ultralow anterior resection (24.5%); Reconstructive proctolectomy (2.7%); Other (6.8%) Type of resection: Open (100%) Anastomosis: 148 in 147 patients Technique of anastomosis: Stapled (59.2%); Handsewn (40.8%) Covering stoma: 32.0% **N = 147**	**Primary:** *Anastomotic leakage* **Secondary:** *30 day or within timeframe of hospital admission mortality, infection* **Follow-up:** 30 days	Per protocol analysis performed for outcomes of interest. Patients whose treatment violated the therapeutic protocol were also included in the analysis. Patients were excluded if they had undergone mechanical bowel preparation within 2 days of the operation date as well as those undergoing laparoscopic surgery Patients were not excluded on the basis of the underlying disease process, old age or sex Randomisation: 1:1 ratio A clinically significant anastomotic leak was defined as a leak that required active intervention. Patient numbers reflect per protocol population. ITT analysis was performed on outcomes not of interest and consisted of 170 in intervention group and 165 in comparison group Other surgery type comprises transverse or subtotal colectomy Wound infection was defined as the discharge of pus or the presence of a serous discharge that contained pathogens. Intra-abdominal abscess was defined as either visual evidence of a localized collection of pus at relaparotomy, or the demonstration on imaging of a localized collection that on aspiration contained pathogens.

N = number of participants; RCT= randomised controlled trial; M= male; F= female; SD = standard deviation; MBP = mechanical bowel preparation; IV = intravenous; ITT = intention to treat; kg = kilogram; mg = milligram; g = gram; mL = millilitre; L = litre; h = hour; IBD = irritable bowel disease; PEG = polyethylene glycol

Table 11: Randomised controlled trials comparing mechanical bowel preparation (with antibiotic prophylaxis) vs no mechanical bowel preparation (with or without antibiotic prophylaxis) in colorectal cancer patients: study characteristics

Study	Participants	Design	Intervention	Comparison	Outcomes	Comments
Ram 2005 (Israel)	Single centre trial with patients randomised from 04/1999 to 03/2002. Inclusion criteria was adult patients admitted for elective large bowel colorectal surgery **Mean age (SD)**: MBP: 68.17 (±11.5) years No MBP: 68.11 (±9.5) years **Gender F/M (%)** MBP: 39.6/60.4 No MBP: 38.2/61.8 **N = 329**	RCT (single centre)	MBP + IV antibiotic prophylaxis Dietary preconditions: Low residue diet 1 day before surgery. Parenteral hydration was given on the morning of surgery. MBP: Soffodex (2.4 g of monobasic sodium phosphate and 0.9 g of dibasic sodium phosphate) IV antibiotic prophylaxis: 1 hour before induction we used 500 mg of metronidazole IV and 1 g of ceftriaxone Indication for operation: Colorectal cancer (75%); benign disease (25%) Type of surgery: Open (100%) Type of resection: Right hemicolectomy (11.0%); Left hemicolectomy (23.2%); Sigmoidectomy (24.4%); Subtotal colectomy (4.3%); Abdominoperineal resection (11.0%); Transverse colectomy (0.6%); Anterior resection (18.3%); Low anterior resection (7.3%) Technique of anastomosis: Stapled (93.9%); Handsewn (6.1%); **N = 164**	IV antibiotic prophylaxis Dietary preconditions: Low residue diet 1 day before surgery. Parenteral hydration was given on the morning of surgery. IV antibiotic prophylaxis: 1 hour before induction we used 500 mg of metronidazole IV and 1 g of ceftriaxone Indication for operation: Colorectal cancer (87.9%); benign disease (12.1%) Type of surgery: Open (100%) Type of resection: Right hemicolectomy (14.5%); Left hemicolectomy (21.8%); Sigmoidectomy (27.9%); Subtotal colectomy (2.4%); Abdominoperineal resection (9.7%); Transverse colectomy (1.2%); Anterior resection (12.1%); Low anterior resection (10.3%) Technique of anastomosis: Stapled (97.6%); Handsewn (2.4%); **N = 165**	*Mortality and morbidity* **Follow-up:** 1, 3 and 6 weeks	Per protocol patient analysis Patients were excluded if they had taken antibiotics for the last 10 days before surgery or if there was evidence of infection. Patients undergoing emergency operations were not included. Patients randomized to group 2 were excluded if they had bowel preparation for colonoscopy within 6 days prior to surgery. Patients undergoing proctectomy with low rectal anastomosis or surgery for polypoid lesion were also excluded. Randomisation: 1:1 ratio Patients in both arms continued to receive the same IV antibiotic prophylaxis for 48 hours following the operation Benign disease included IBD or diverticulosis The majority of anastomoses were colocolonic, colorectal, or coloanal; in only 42 patients (12.8%) was the anastomosis ileocolic. Wound infection was indicated by the presence of pus or discharge resulting in a culture positive for bacteria. Abdominal or pelvic infection comprised discharge or abscess, which was defined as a typical finding in ultrasonography or computed tomography, and a culture positive for bacteria from the puncture or drain.

N = number of participants; RCT= randomised controlled trial; M= male; F= female; SD = standard deviation; MBP = mechanical bowel preparation; IV = intravenous; mg = milligram; g = gram; IBD = irritable bowel disease

Table 12: Randomised controlled trials comparing mechanical bowel preparation (with antibiotic prophylaxis) vs no mechanical bowel preparation (with or without antibiotic prophylaxis) in colorectal cancer patients: study characteristics

Study	Participants	Design	Intervention	Comparison	Outcomes	Comments
Reddy 2007 (United Kingdom)	Single centre trial, randomisation dates not reported. Inclusion criteria was elective surgical patients requiring colectomy **Median age (range)**: MBP I1: 68.5 (61-75) years MBP I2: 72.5 (53-81) years MBP I3: 68.5 (62.5-74) years No MBP: 65 (56-75) **Gender F/M (%)** MBP: 54.2/45.8 MBP I2: 40.9/59.1 MBP I3: 55/45 No MBP: 50:50 **Patients with ASA-score ≥3 (%):** MBP: 54.2% MBP I2: 50% MBP I3: 3% No MBP: 31.8 **N = 88**	RCT (Single centre)	**Intervention 1:** MBP only MBP: two sachets of Picolax® (sodium picosulphate and magnesium citrate; Ferring Pharmaceuticals, Langley, UK) administered the day before surgery. Indication for operation: Colorectal cancer (83.3%); non cancer patients (6.7%) Type of resection: Right hemicolectomy (33.3%); Left hemicolectomy (16.7%); Anterior resection (37.5%); Subtotal colectomy (83.3%); Panproctocolectomy (4.2%) **N=24** **Intervention 2:** MBP (same as intervention 1) + oral antibiotic prophylaxis Oral antibiotic prophylaxis: 3 g oral neomycin in three divided doses Indication for operation: Colorectal cancer (95.6%); non cancer patients (4.4%) Type of resection: Right hemicolectomy (36.4%); Left hemicolectomy (9.1%); Anterior resection (40.9%); Abdominoperineal resection (13.6%) **N=22** **Intervention 3:** MBP (same as intervention 1) + synbiotics + oral antibiotic prophylaxis Synbiotics: Prebiotic was 15 g oligofructose powder twice daily and the probiotic preparation was Trevis® capsules (Chr. Hansen, Hørsholm, Denmark) three times daily. Each capsule contained 4 × 109 colony forming units of *Lactobacillus acidophilus* La5, *Lactobacillus bulgaricus, Bifidobacterium lactis* BB-12 and *Streptococcus thermophilus.* Oral antibiotic prophylaxis: 3 g oral neomycin in three divided doses Indication for operation: Colorectal cancer (85%); non cancer patients (15%) Type of resection: Right hemicolectomy (20.0%); Left hemicolectomy (10.0%); Anterior resection (45.0%); Abdominoperineal resection (5.0%); Hartmann's procedure (10.0%); Subtotal colectomy (5.0%); Panproctocolectomy (5.0%) **N=20**	Synbiotics + oral antibiotic prophylaxis Synbiotics: The prebiotic used was 15 g oligofructose powder twice daily and the probiotic preparation was Trevis® capsules (Chr. Hansen, Hørsholm, Denmark) three times daily. Each capsule contained 4 × 109 colony forming units of *Lactobacillus acidophilus* La5, *Lactobacillus bulgaricus, Bifidobacterium lactis* BB-12 and *Streptococcus thermophilus.* Oral antibiotic prophylaxis: 3 g oral neomycin in three divided doses Indication for operation: Colorectal cancer (72.7%); non cancer patients (27.3%) Type of resection: Right hemicolectomy (18.2%); Left hemicolectomy (27.3%); Anterior resection (40.9%); Abdominoperineal resection (9.1%); Hartmann's procedure (9.1%); Panproctocolectomy (4.5%) **N=22**	**Primary:** *Prevalence of Entero-bacteriaceae in gut microflora* **Secondary:** *Inflammatory response and postoperative septic morbidity* **Follow-up:** NR	Per protocol patients analysed Patients excluded if evidence of intraperitoneal sepsis pre-surgery Patient numbers reflect those analysed. Original number at randomisation was 92. Reasons for exclusion involved two patients with rectal cancer who were sent for neoadjuvant chemoradio-therapy after recruitment, one with an inoperable cancer and one who did not consume the probiotic capsules as requested. All patients underwent open surgery and fasted for a minimum of 6 h before surgery Septic morbidity was the summation of wound infection and intra-abdominal collection

N = number of participants; RCT= randomised controlled trial; M= male; F= female; NR = not reported; ASA = American society of anaesthesiologists; I1 = Intervention 1 (MBP only); I2 = Intervention 2 (MBP + oral antibiotic prophylaxis); I3 = Intervention 3 (MBP + synbiotics + oral antibiotic prophylaxis); MBP = mechanical bowel preparation; IV = intravenous; g = gram

Table 13: Randomised controlled trials comparing mechanical bowel preparation (with antibiotic prophylaxis) vs no mechanical bowel preparation (with or without antibiotic prophylaxis) in colorectal cancer patients: study characteristics

Study	Participants	Design	Intervention	Comparison	Outcomes	Comments
Sasaki 2012 (Japan)	Single centre trial with patients randomised from 01/2009 to 12/2009. Inclusion criteria was patients who underwent elective open or laparascopic colonic resection for cancer with a primary tumor located between the cecum and the sigmoid colon, an ASA grade of I or II and. **Mean age (SD)**: MBP: 69.3 (52-92) years No MBP: 66.2 (44-84) years **Gender F/M (%)** MBP: 55.3/44.7 No MBP: 41.5/58.5 **TNM stage: I-IV** **N = 79**	RCT (single centre)	MBP + IV antibiotic prophylaxis Dietary preconditions: low-residue diet upon arrival at the hospital. Patients in the MBP group were prohibited from eating, starting on the morning of the day before surgery MBP: 10 mL of sodium picosulfate hydrate (Laxoberon®) in the evening 2 days before surgery, followed by 2,000 mL of an oral agent consisting of PEG (Niflec®) in the morning of the day before surgery. IV antibiotic prophylaxis: Flomoxef (1 g) at the induction of anesthesia and every 3 h during surgery Indication for operation: Colon cancer (100%) Type of surgery: Open (50%); Laparoscopic (50%) Type of resection: NR Technique of anastomosis: Stapled (55.3%); Handsewn (44.7%) Type of anastomosis: NR **N = 38**	IV antibiotic prophylaxis Dietary preconditions: low-residue diet upon arrival at the hospital. Patients ate in the evening of the day before surgery and did not receive any special pretreatment IV antibiotic prophylaxis: Flomoxef (1 g) at the induction of anesthesia and every 3 h during surgery Indication for operation: Colon cancer (100%) Type of surgery: Open (29.3%); Laparoscopic (70.7%) Type of resection: NR Technique of anastomosis: Stapled (30%); Handsewn (70%) Type of anastomosis: NR **N = 41**	**Primary:** *Postoperative gastrointestinal motility and mobility* **Secondary:** *Operative outcomes and postoperative complications* **Follow-up:** 105 days	Per protocol analysis Patients were excluded if they had a stoma, a complete intestinal obstruction that needed decompression or a past history of another colonic resection. Randomisation: 1:1 ratio

N = number of participants; RCT= randomised controlled trial; M= male; F= female; SD = standard deviation; NR = not reported; TNM = Tumour Node Metastasis Classification of Malignant Tumours; MBP = mechanical bowel preparation; IV = intravenous; mL = millilitre; g = gram; h = hour; PEG = polyethylene glycol

Table 14: Randomised controlled trials comparing mechanical bowel preparation (with antibiotic prophylaxis) vs no mechanical bowel preparation (with or without antibiotic prophylaxis) in colorectal cancer patients: study characteristics

Study	Participants	Design	Intervention	Comparison	Outcomes	Comments
Watanabe 2010 (Japan)	Single centre trial, randomisaion dates not reported. Inclusion criteria was patients with colonic cancer who underwent elective primary surgery **Median age (range)**: MBP: 72 (55-85) years No MBP: 74 (49-89) years **Gender F/M (%)** MBP: 57.1/42.9 No MBP: 52.4/47.6 **Patients with ASA-score ≥3 (%):** No MBP: 0.0% No MBP: 0.0% **N = 42 analysed**	RCT (single centre)	MBP + enema + IV antibiotic prophylaxis Dietary preconditions: Regular diet until noon on the day before surgery and water consumption until midnight. MBP: 1·8 L of magnesium citrate pharmaceutical isocratic liquid (Magcorol P® ; Horii Pharmaceutical, Osaka, Japan) 16–19 h before surgery. The MBP was usually taken 3–5 h after the last solid meal. Enema: 120 ml of glycerine enema (GLYCERINE ENEMA OHTA®; Nichi-iko, Toyama, Japan) on the day of surgery. IV antibiotic prophylaxis: No patient received preoperative oral antibiotics. All patients received intraoperative broadspectrum intravenous antibiotics (Cefmetazon®; DaiichiSankyo, Tokyo, Japan) every 3 h, and continued to receive prophylactic intravenous antibiotics until the day after surgery. Indication for operation: Colon cancer (100%) Tumour location: Left (52.4%); Right (47.6%) Type of surgery: Open (23.8%); laparoscopic (76.2%) Type of resection: NR Technique of anastomosis: NR Type of anastomosis: NR **N = 21 analysed**	IV antibiotic prophylaxis Dietary preconditions: Regular diet until 2 days before surgery and asked to ingest a liquid diet on the day before operation IV antibiotic prophylaxis: No patient received preoperative oral antibiotics. All patients received intraoperative broadspectrum intravenous antibiotics (Cefmetazon®; DaiichiSankyo, Tokyo, Japan) every 3 h, and continued to receive prophylactic intravenous antibiotics until the day after surgery. Indication for operation: Colon cancer (100%) Tumour location: Left (52.4%); Right (47.6%) Type of surgery: Open (23.8%); Laparoscopic (76.2%) Type of resection: NR Technique of anastomosis: NR Type of anastomosis: NR **N = 21 analysed**	**Primary:** *Perioperative bacterial microflora and faecal organic acid content of faecal material* **Secondary:** *Infectious complications* **Follow-up:** 30 days	Per protocol patient analysis Patients were excluded if they had intestinal obstruction or perforation, a physical status of ASA IV or V, and a history of colonic resection. In addition, patients who required a diverting stoma proximal to the anastomosis and those found to have an abdominal abscess at the time of surgery Patients were first stratified according to tumour location and then randomly assigned to one of two groups using the permuted block method. Patient analysis numbers reflects the same number of patients at randomisation.

N = number of participants; RCT= randomised controlled trial; M= male; F= female; NR = not reported; ASA = American society of anaesthesiologists; MBP = mechanical bowel preparation; IV = intravenous; L = litre; h = hour; PEG = polyethylene glycol

Table 15: Randomised controlled trials comparing mechanical bowel preparation (with antibiotic prophylaxis) vs no mechanical bowel preparation (with or without antibiotic prophylaxis) in colorectal cancer patients: study characteristics

Study	Participants	Design	Intervention	Comparison	Outcomes	Comments
Zmora 2006 (Israel)	Single centre trial with patients randomised from 1997 to 2001. Inclusion criteria was patients undergoing elective colon and rectal surgery. **Mean age (range)**: MBP: 68 (22-82) years No MBP: 70 (30-92) years **Gender F/M (%)** MBP: 44/56 No MBP: 50/50 **N = 249 analysed**	RCT (single centre)	MBP ± enema + IV antibiotic prophylaxis Dietary preconditions: Regular diet until midnight before surgery, and were not required to have a low residue or liquid diet as part of their preparation MBP: One gallon of PEG one day prior to surgery. MBP was routinely given to patients after dinner the evening prior to the procedure. Enema: Patients who were planned for rectal surgery were given one phosphate enema on the day of surgery, to avoid extrusion of stool when using a transanal stapler. IV antibiotic prophylaxis: Preoperatively, all patients received 3 oral doses of non-absorbable antibiotics (1 g neomycin and 1 g erythromycin) the day prior to surgery and one IV dose of broad-spectrum antibiotics (500 mg metronidazole, 240 mg gentamicin, and 1 g ampicillin) on call to the operating room. Indication for operation: CRC (68%); Diverticular disease (18%); IBD (4%); Benign polyp (3%); Other (7%) Type of surgery: NR Type of resection: Left colectomy (10%); sigmoidectomy (32%); anterior resection (36%); low anterior resection (5%); closure of Hartmann's (17%) Technique of anastomosis: Stapled (89%); Handsewn (11%) Type of anastomosis: Colocolonic anastomosis (21%); colorectal anastomosis (74%); coloanal anastomosis (5%) **N = 120 analysed**	IV antibiotic prophylaxis ± enema Dietary preconditions: Regular diet until midnight before surgery, and were not required to have a low residue or liquid diet as part of their preparation Enema: Patients who were planned for rectal surgery were given one phosphate enema on the day of surgery, to avoid extrusion of stool when using a transanal stapler. IV antibiotic prophylaxis: Preoperatively, all patients received 3 oral doses of non-absorbable antibiotics (1 g neomycin and 1 g erythromycin) the day prior to surgery and one IV dose of broad-spectrum antibiotics (500 mg metronidazole, 240 mg gentamicin, and 1 g ampicillin) on call to the operating room. Indication for operation: CRC (76%); Diverticular disease (14%); IBD (2%); Benign polyp (4%); Other (4%) Type of surgery: NR Type of resection: Left colectomy (16%); sigmoidectomy (43%); anterior resection (31%); low anterior resection (2%); closure of Hartmann's (8%) Technique of anastomosis: Stapled (91%); Handsewn (9%) Type of anastomosis: Colocolonic anastomosis (25%); colorectal anastomosis (73%); coloanal anastomosis (2%) **N = 129 analysed**	**Primary:** *Postoperative complications* **Follow-up:** 30 days	Per protocol patients analysed Exclusion criteria was patients with tumours preoperatively assessed to be <2 cm in diameter (since intraoperative endoscopy may be required for tumour localization.) Patients who had a diverting stoma proximal to the left-sided anastomosis were excluded from the data analysis. Consequently, 4 MBP and 3 no MBP were excluded from analysis. Patient numbers reflect those analysed. In order to specifically assess the safety of left-sided anastomosis, only patients in whom a primary colocolonic, colorectal or colo-anal anastomosis was performed were included in data analysis Wound infection defined as a wound erythema requiring initiation of antibiotic treatment, or drainage of purulent collection. Anastomotic leak was called if demonstrated by imaging or documented in surgery, or if fecal drainage was evident through a peri-anastomotic drain. Abdominal abscess was defined as fluid collection demonstrated by CT, in conjunction with elevated temperature or WBC count.

N = number of participants; RCT= randomised controlled trial; M= male; F= female; NR = not reported; MBP = mechanical bowel preparation; IV = intravenous; CRC = colorectal cancer; cm = centimetres; mg = milligram; g = gram; IBD = irritable bowel disease; PEG = polyethylene glycol; CT = computer tomography; WBC = white blood cell

3.3. Study risk of bias

Methodological risk of bias of included randomised controlled trials is described in Table 16 and 17

Table 16: Methodological risk of bias of included randomised controlled trials (n = 15)

Risk of bias categories	N (%)
1. What was the risk of bias from the random sequence generation?	
Low: a random component in the sequence generation process	6 (40%)
High: a non-random component in the sequence generation process	1 (6.7%)
Unclear: Insufficient information about the sequence generation process	8 (53.3%)
2. What was the risk of bias from the allocation concealment?	
Low: Participants and investigators could not foresee assignment	6 (40%)
High: Participants and investigators could possibly foresee assignments	3 (20%)
Unclear: Insufficient information to permit judgement	6 (40%)
3. What was the risk of bias from the blinding of participants and personnel and outcome assessors?	-
Low: Blinding of participants and key study personnel ensured	6 (40%)
High: No blinding or incomplete blinding	9 (60%)
Unclear: Insufficient information to permit judgement	
4. What was the risk of bias from incomplete outcome data?	
Low:No missing outcome data	10 (66.7%)
High: Reason for missing outcome data likely to be related to true outcome	3 (20%)
Unclear: Insufficient information to permit judgement	2 (13.3%)
5. What was the risk of bias from selective outcome reporting?	
Low: study protocol is available and all of the study's pre-specified outcome	2 (13.3%)
High: Not all of the study's pre-specified primary outcomes have been reported	12 (80%)
Unclear: Insufficient information to permit judgement	1 (6.7%)
6. What was the risk of bias from other sources?	
Low: study appears to be free of other sources of bias	3 (20%)
High: There is at least one important risk of bias	12 (80%)
Unclear: Insufficient information to permit judgement	-

Table 17: Risk of bias summary assessment of included RCTs (n = 15)

Trial	Random sequence generation	Allocation concealment	Blinding	Incomplete outcome data	Selective outcome reporting	Other sources of bias	**Overall risk of bias**
Bhattacharjee 2015	Low	Unclear	Unclear	Low	Low	High	**At risk**
Brentagnol 2010	Unclear	Low	High	Low	Unclear	High	**At risk**
Contant 2007	Low	Low	High	Low	High	High	**At risk**
van't Sant 2010	Low	Low	High	High	High	High	**At risk**
Fa Si Oen 2005	High	Low	Unclear	Low	Low	High	**At risk**
Horvat 2010	Low	High	High	Low	High	Low	**At risk**
Jung 2007	Low	Low	Unclear	High	High	High	**At risk**
Krebs 2016	Unclear	High	Unclear	Unclear	High	Low	**At risk**
Pena-Soria 2008	Low	Unclear	High	Unclear	Low	High	**At risk**
Platell 2006	Unclear	Unclear	Unclear	High	High	High	**At risk**
Ram 2005	Unclear	Unclear	Unclear	Low	High	High	**At risk**
Reddy 2007	Unclear	High	High	Low	High	Low	**At risk**
Sasaki 2012	Unclear	Low	Unclear	Low	High	High	**At risk**
Watanabe 2010	Unclear	Unclear	Unclear	Low	High	High	**At risk**
Zmora 2006	Unclear	Unclear	Unclear	Low	High	High	**At risk**

Key to overall risk of bias rating
Low risk of bias: A study rated at low risk of bias for all domains
At risk of bias: A study rated at high or unclear risk of bias for one or more domains

3.4. Study Results

Study results described in Tables 18-25

Table 18. Results of RCTs comparing mechanical bowel preparation (with antibiotic prophylaxis) vs no mechanical bowel preparation (with or without antibiotic prophylaxis) for colorectal cancer patients

Study	Outcome	N actual	MBP	No MBP	Effect size	CI (95%)	p-value[a]	Follow up
Bhattacharjee 2015 (India)	**Anastomotic leak** *Rate of postoperative anastomotic leak within 30 days after surgery*	71	10.5% (4) N=38	6.1% (2) N=33	NR	NR	0.68	30 days
	Wound infection *Rate of postoperative wound infection within 30 days after surgery*	71	29.0% (11) N=38	18.8% (6) N=33	NR	NR	0.40	
	Intraabdominal abscess *Rate of postoperative intraabdominal abscess within 30 days after surgery*	71	7.9% (3) N=38	3.0% (1) N=33	NR	NR	0.62	
Bretagnol 2010[b] (France)	**Overall anastomotic leak** *Rate of postoperative overall anastomotic leak within 3 months after surgery*	187	11.0% (8) N=89	19.0% (17) N=89	NR	NR	0.09	3 months
	Clinical anastomotic leak[c] *Rate of postoperative clinical anastomotic leak within 3 months after surgery*	187	7.0% (6) N=89	16.0% (14) N=89	NR	NR	0.06	
	Asymptomatic anastomotic leak[c] *Rate of postoperative asymptomatic anastomotic leak within 3 months after surgery*	187	2.0% (2) N=89	3.0% (3) N=89	NR	NR	NR	
	Clinical anastomotic leak[c] *Rate of postoperative clinical anastomotic leak within 30 days after surgery*	187	7.0% (6) N=89	16.0% (14) N=89	NR	NR	NR	30 days
	Infectious abdominal complications[d] *Rate of postoperative infectious abdominal complications within 30 days after surgery*	187	17.0% (15) N=89	38.0% (34) N=89	NR	NR	NR	
	Wound abscess *Rate of postoperative wound abscess within 30 days after surgery*	187	3.0% (3) N=89	1.0% (1) N=89	NR	NR	NR	
	Peristomial abscess *Rate of postoperative peristomial abscess within 30 days after surgery*	187	1.0% (1) N=89	1.0% (1) N=89	NR	NR	NR	
	Length of hospital stay[e] *Median (range) length of hospital stay, days*	187	11 (9-15) N=89	12 (10-17) N=89	NA	NA	0.15	

N= number of participants; MBP = mechanical bowel preparation; NR = not reported; NA = not applicable; CI = confidence interval; OR = odds ratio; [a]P-values derived from two-sided tests, p-value <0.05 was considered to be statistically significant; [b]Outcome data is presented for intention to treat population only; [c] Anastomotic leakage was defined as being asymptomatic if demonstrated by routine contrast enema before ileostomy closure and as clinical if symptoms related to leakage were noted (ie, gas, pus, or faecal discharge from the drain, peritonitis, discharge of pus per rectum); [d]Includes abscess and wound infection; [e]Comparison by log-rank test

Table 19. Results of RCTs comparing mechanical bowel preparation (with antibiotic prophylaxis) vs no mechanical bowel preparation (with or without antibiotic prophylaxis) for colorectal cancer patients

Study	Outcome		N actual	MBP	No MBP	Effect size[b]	CI (95%)	p-value[c]	Follow up
Contant 2007[a] (Netherlands)	**Anastomotic leak** *Rate of postoperative overall, major or minor anastomotic leak within 24 days after surgery*	**Overall**	1354	4.8% (32) N=670	5.4% (37) N=684	Difference =0.6	-1.7, 2.9	0.69	24 days
		Major	1354	3.9% (26) N=670	4.5% (31) N=684	Difference =0.6	-1.6, 2.8	0.64	
		Minor	1354	0.9% (6) N=670	0.9% (6) N=684	Difference =0.0	-1.0, 1.0	1.0	
	Wound infection *Rate of postoperative overall, mild and severe wound infection within 24 days after surgery*	**Overall**	1354	13.4% (90) N=670	14.0% (96) N=684	Difference =0.6	-3.2, 4.4	0.82	
		Severe	1354	6.1% (41) N=670	6.6% (45) N=684	Difference =0.4	-2.2, 3.0	0.83	
		Mild	1354	7.3% (49) N=670	7.4% (51) N=684	Difference =0.1	-2.7, 2.9	1.0	
	Intra-abdominal abscess[e] *Rate of intra-abdominal abscess overall, with anastomotic leakage and without anastomotic leakage within 24 days after surgery*	**Overall**	1354	2.2% (15) N=670	4.7% (32) N=684	Difference =2.4	0.5, 4.4	0.02	
		With AL	1354	0.3% (2) N=670	2.5% (17) N=684	Difference =2.2	0.9, 3.4	0.001	
		Without AL	1354	1.9% (13) N=670	2.2% (15) N=684	Difference =0.3	-1.3, 1.8	0.85	
	Length of hospital stay[d] *Median (IQR) length of hospital stay, days*		1325	10 (8-14) N=CD	10 (8-13) N=CD	Difference =0.0	-1.0 1.0	0.40	

N= number of participants; MBP = mechanical bowel preparation; NR = not reported; NA = not applicable; CI = confidence interval; IQR = interquartile range; AL = Anastomotic leakage; [a]Per protocol patients analysed only, number of participants for whom data were missing was <1% for all variables except hospital stay (n=29); [b]The study was designed to test the hypothesis that patients given no mechanical bowel preparation before colorectal surgery do not have a higher risk of anastomotic leakage than those given mechanical bowel preparation. The study specified that for non-inferiority to apply, the upper limit of the two-sided 95% CI for the difference in anastomotic leakage rates (no MBP group minus bowel preparation group) had to be less than 3% [c]P-values derived from two-sided tests, p-value <0.05 was considered to be statistically significant; complication rates between groups were compared using χ^2 test or Fisher's exact and length of hospital stay was compared using the Mann- Whitney test; [d]Excluding postoperative deaths; [e] When 1400 patients were analysed due to inclusion of those who did not undergo bowel resection, intra-abdominal abscess was the only secondary outcome that changed and did not differ between groups

Table 20. Results of RCTs comparing mechanical bowel preparation (with antibiotic prophylaxis) vs no mechanical bowel preparation (with or without antibiotic prophylaxis) for colorectal cancer patients

Study	Outcome			N actual	MBP	No MBP	Effect size	CI (95%)	p-value[b]	Follow up
van't Sant 2010[a] (Netherlands)	**Anastomotic leakage** *Rate of postoperative anastomotic leakage within 24 days after surgery*	**Overall**	**LAR with lower colorectal anastomosis**	449	7.6% (18) N=236	6.6% (14) N=213	Difference =1.0	-3.7, 5.7	0.80	24 days
			With diverting ileostomy	48	3.7% (1) N=27	9.5% (2) N=21	NR	NR	NS	
		Major	**LAR with lower colorectal anastomosis**	449	6.0% (14) N=236	5.0% (11) N=213	NR	NR	NS	
			With diverting ileostomy	48	0.0% (0) N=27	4.8% (1) N=21	NR	NR	NS	
		Minor	**LAR with lower colorectal anastomosis**	449	2.0% (4) N=236	1.0% (3) N=213	NR	NR	NS	
			With diverting ileostomy	48	3.7% (1) N=27	4.8% (1) N=21	NR	NR	NS	
	Wound infection *Rate of postoperative wound infection within 24 days after surgery*	**Overall**	**LAR with lower colorectal anastomosis**	449	NR (NR) N=236	NR (NR) N=213	NR	NR	0.43	
			With diverting ileostomy	48	18.5% (5) N=27	23.8% (5) N=21	NR	NR	NS	
		Severe	**LAR with lower colorectal anastomosis**	449	9.0% (21) N=236	7.0% (14) N=213	NR	NR	NS	
			With diverting ileostomy	48	11.1% (3) N=27	14.3% (3) N=21	NR	NR	NS	
		Mild	**LAR with lower colorectal anastomosis**	449	8.0% (18) N=236	10.0% (22) N=213	NR	NR	NS	
			With diverting ileostomy	48	7.4% (2) N=27	9.5% (2) N=21	NR	NR	NS	
	Intraabdominal abscess *Rate of postoperative intraabdominal abscess within 24 days after surgery*		**LAR with lower colorectal anastomosis**	449	3.0% (6) N=236	4.0% (9) N=213	NR	NR	0.43	
			With diverting ileostomy	48	3.7% (1) N=27	4.8% (1) N=21	NR	NR	NS	
	Fascia dehiscence *Rate of postoperative fascia dehiscence within 24 days after surgery*		**LAR with lower colorectal anastomosis**	449	3.0% (7) N=236	4.0% (9) N=213	NR	NR	0.61	
			With diverting ileostomy	48	7.4% (2) N=27	0.0% (0) N=21	NR	NR	NS	

N= number of participants; MBP = mechanical bowel preparation; NR = not reported; NA = not applicable; CI = confidence interval; AL = Anastomotic leakage; LAR= low anterior resection;
[a]Subgroup analysis of Contant 2007; Per protocol patients analysed only; [b]χ2 test or Fisher exact test

Table 21. Results of RCTs comparing mechanical bowel preparation (with antibiotic prophylaxis) vs no mechanical bowel preparation (with or without antibiotic prophylaxis) for colorectal cancer patients

Study	Outcome		N actual	MBP	No MBP	Effect size	CI (95%)	p-value[a]	Follow up
Fa Si Oen 2005[b] (Netherlands)	**Anastomotic leak** *Rate of postoperative anastomotic leak within 3 months after surgery*	**Total**	250	6.4% (8) N=125	4.8% (6) N=125	NR	NR	NR	3 months
		Major	250	5.6% (7) N=125	4.8% (6) N=125	RR=0.86	0.30-2.48	0.78	
		Minor	250	0.8% (1) N=125	0.0% (0) N=125	NR	NR	NR	
	Clinically significant wound infection *Rate of postoperative clinically significant wound infection within 3 months after surgery*		250	7.2% (9) N=125	5.6% (7) N=125	RR=0.78	0.30-2.02	0.61	
	Anastomotic leak and wound infection *Rate of concurrent postoperative anastomotic leak and wound infection within 3 months after surgery*		250	2.4% (3) N=125	1.6% (2) N=125	RR=0.67	0.11-3.92	0.65	
	Ileus *Mean (SD) duration of postoperative ileus, days*		250	5.0 (2.7) N=125	4.7 (1.7) N=125	NA	NA	0.25	
	Length of hospital stay *Median (range) length of hospital stay, days*		250	10 (2-221) N=125	9 (4-55) N=125	NA	NA	0.97	
Horvat 2010[c] (Slovenia)	**Wound infection** *Rate of postoperative mild wound infection*		68	5.0% (1) N=20	**C1** 5.0%(1) N=20 **C2** 0.0% (0) N=28	NR	NR	NR	NR
	Length of hospital stay *Mean (SD) length of hospital stay, days*		68	9.5 (NR) N=20	**C1** 10.95 (NR) N=20 **C2** 9.21 (NR) N=28	NA	NA	0.225	

N= number of participants; MBP = mechanical bowel preparation; NR = not reported; NA = not applicable; SD = standard deviation; RR = relative risk; CI = confidence interval; C1 = comparison 1 (synbiotics and antibiotic prophylaxis); C2 = comparison 2 (prebiotics, heat deactivated probiotics and antibiotic prophylaxis); [a]*P-values derived from two-sided tests, p-value <0.05 was considered to be statistically significant;* [b]***Pearson's χ^2** test was used to compare frequencies while **Student's t**-test was used for continuous outcome measures where normal distribution occurred and the Mann–Whitney test was used for nonparametric outcomes; Outcome data is presented for intention to treat population only* [c]*Per protocol analysis performed*

Table 22. Results of RCTs comparing mechanical bowel preparation (with antibiotic prophylaxis) vs no mechanical bowel preparation (with or without antibiotic prophylaxis) for colorectal cancer patients

Study	Outcome	N actual	MBP	No MBP	Effect size	CI (95%)	p-value[a]	Follow up
Jung 2007[b] (Sweden)	**Superficial wound infection** *Rate of postoperative superficial wound infection within 30 days*	1343	7.8% (54) N=686	6.4% (42) N=657	NR	NR	NS	30 days
	Deep abscess *Rate of postoperative deep abscess within 30 days*	1343	0.7% (5) N=686	1.7% (11) N=657	NR	NR	NS	
	Anastomotic dehiscence *Rate of postoperative anastomotic dehiscence within 30 days*	1343	1.9% (13) N=686	2.6% (17) N=657	NR	NR	NS	
	Subcutaneous wound disruption *Rate of postoperative subcutaneous wound disruption within 30 days*	1343	1.5% (10) N=686	2.0% (13) N=657	NR	NR	NS	
	Ileus/bowel paralysis *Rate of postoperative ileus/bowel paralysis within 30 days*	1343	0.7% (5) N=686	0.8% (5) N=657	NR	NR	NS	
	Length of hospital stay *Mean (SD) length of hospital stay, days*	1343	8.6 (7.0) N=686	8.8 (6.9) N=657	NA	NA	NR	
Krebs 2016 (Slovenia)	**Length of hospital stay** *Median (range) length of hospital stay, days*	54	11.30 (NR) N=16	**C1** 10.16 (NR) N=18 **C2** 11.30 (NR) N=20	NA	NA	0.51	NA

N= number of participants; MBP = mechanical bowel preparation; NR = not reported; NA = not applicable; SD = standard deviation; CI = confidence interval; C1 = comparison 1 (synbiotics and IV antibiotic prophylaxis); C2 = comparison 2 (prebiotics and IV antibiotic prophylaxis); [a]*P-values derived from two-sided tests, p-value <0.05 was considered to be statistically significant;* [b]*Outcome data is presented for intention to treat population only; Pearson's χ^2 test was used to compare frequencies while Student's t-test was used for continuous outcome measures where normal distribution occurred and the Mann–Whitney test was used for nonparametric outcomes*

Table 23. Results of RCTs comparing mechanical bowel preparation (with antibiotic prophylaxis) vs no mechanical bowel preparation (with or without antibiotic prophylaxis) for colorectal cancer patients

Study	Outcome		N actual	MBP	No MBP	Effect size	CI (95%)	p-value[a]	Follow up
Pena-Soria 2008[b] (Spain)	**Anastomotic dehiscence** *Rate of postoperative surgical site infection within 30 days*	**Total**	129	6.2% (4) N=65	4.7% (3) N=64	NR	NR	NS	30 days
		Ileocolostomy	59	3.8% (1) N=26	0.0% (0) N=33	NR	NR	NR	
		Ileorectostomy	4	33.3% (1) N=3	0.0% (0) N=1	NR	NR	NR	
		Colocolostomy	14	12.5% (1) N=8	16.7% (1) N=6	NR	NR	NR	
		Colorectostomy	52	3.6% (1) N=28	8.3% (2) N=24	NR	NR	NR	
	Surgical site infection *Rate of postoperative surgical site infection within 30 days*	**Total**	129	29.2% (19) N=65	17.2% (11) N=64	NR	NR	NS	
		Organ/space	129	4.6% (3) N=65	0.0% (0) N=64	NR	NR	NS	
		Superficial incisional	129	24.6% (16) N=65	17.2% (11) N=64	NR	NR	NS	
Platell 2006[c] (Australia)	**Anastomotic leakage**[d] *Rate of postoperative anastomotic leakage within 30 days*	**Total**	294	2.0% (3) N=147	4.8% (7) N=147	OR=1.42	0.1, 1.64	0.20	30 days
		Clinically significant	294	0.7% (1) N=147	4.1% (6) N=147	OR=1.75	0.02, 1.35	0.06	
	Wound infection *Rate of postoperative wound infection within 30 days*		294	12.9% (19) N=147	14.3% (21) N=147	NR	NR	NS	
	Intra-abdominal abscess *Rate of postoperative intra-abdominal abscess formation within 30 days*		294	0.7% (1) N=147	0.7% (1) N=147	NR	NR	NS	
	Length of hospital stay *Mean (SD) length of hospital stay, days*		294	9.0 (3.1) N=147	9.4 (4.3) N=147	NA	NA	NS	

N= number of participants; MBP = mechanical bowel preparation; NR = not reported; NA = not applicable; SD = standard deviation; CI = confidence interval; [a]P-values derived from two-sided tests, p-value <0.05 was considered to be statistically significant; [b]Per protocol analysis performed; Student's t, Pearson's Chi square, and Fisher exact tests were used for analyses; [c]Intention to treat analysis performed; [d] Pearson's Chi square test used for analysis performed; A clinically significant anastomotic leak was defined as a leak that required active intervention.

Table 24. Results of RCTs comparing mechanical bowel preparation (with antibiotic prophylaxis) vs no mechanical bowel preparation (with or without antibiotic prophylaxis) for colorectal cancer patients

Study	Outcome	N actual	MBP			No MBP	Effect size	CI (95%)	p-value[a]	Follow up
Ram 2005[b] (Israel)	**Wound infection** *Rate of postoperative wound infection within 6 weeks*	329	9.8% (16) N=164			6.1% (10) N=165	NR	NR	NS	6 weeks
	Wound dehiscence *Rate of postoperative wound dehiscence within 6 weeks*	329	1.8% (3) N=164			1.2% (11) N=165	NR	NR	NS	
	Anastomotic dehiscence *Rate of postoperative anastomotic dehiscence within 6 weeks*	329	0.6% (1) N=164			1.2% (2) N=165	NR	NR	NS	
	Ileus *Rate of postoperative ileus within 6 weeks*	329	8.5% (14) N=164			6.7% (11) N=165	NR	NR	NS	
	Length of hospital stay *Mean (SD) length of hospital stay, days*	329	8.2 (5.1) N=164			8.0 (2.7) N=165	NA	NA	NS	
Reddy 2007[c] (United Kingdom)	**Total septic morbidity**[d] *Rate of postoperative total septic morbidity*	88	**I1** 20.8% (5) N=24	**I2** 18.2% (4) N=22	**I3** 15.0% (3) N=20	13.6% (3) N=22	NR	NR	0.93	NR
	Wound infection *Rate of postoperative wound infection*	88	**I1** 12.5% (3) N=24	**I2** 13.6% (3) N=22	**I3** 0.0% (0) N=20	13.6% (3) N=22	NR	NR	0.99	
Sasaki 2012[e] (Japan)	**Anastomotic leakage** *Rate of postoperative anastomotic leakage within 105 days*	79	2.6% (1) N=38			7.3% (3) N=41	NR	NR	0.35	105 days
	Wound infection *Rate of postoperative wound infection within 105 days*	79	0.0% (0) N=38			0.0% (0) N=41	NR	NR	NS	
	Intra-abdominal infection *Rate of postoperative intra-abdominal infection within 105 days*	79	2.6% (1) N=38			2.4% (1) N=41	NR	NR	0.96	
	Ileus *Rate of postoperative ileus within 105 days*	79	2.6% (1) N=38			4.9% (2) N=41	NR	NR	0.35	
	Length of hospital stay *Median (range) length of hospital stay, days*	79	19.9 (8-105) N=38			15.5 (8-81) N=41	NA	NA	0.28	

N= number of participants; MBP = mechanical bowel preparation; NR = not reported; NA = not applicable; SD = standard deviation; CI = confidence interval; I1 = Intervention 1 (MBP only); I2 = Intervention 2 (MBP + oral antibiotic prophylaxis); I3 = Intervention 3 (MBP + synbiotics + oral antibiotic prophylaxis) [a]*P-values derived from two-sided tests, p-value <0.05 was considered to be statistically significant;* [b]*Per protocol analysis performed; unpaired t tests were used for hospital stay and χ^2 test or Fisher exact test was used to calculate complication differences.* [c]*Per protocol analysis performed; ANOVA or Kruskal–Wallis test used for categorical data comparison.* [d]*Consisting of intra-abdominal collection and wound infection* [e] *Per protocol analysis performed; Comparisons performed by Mann-Whitney U-test and Student's t-test*

Table 25. Results of RCTs comparing mechanical bowel preparation (with antibiotic prophylaxis) vs no mechanical bowel preparation (with or without antibiotic prophylaxis) for colorectal cancer patients

Study	Outcome		N actual	MBP	No MBP	Effect size	CI (95%)	p-value[a]	Follow up
Watanabe 2010[b] (Japan)	**Surgical site infection** *Rate of postoperative surgical site infection within 30 days*	**Superficial**	42	4.8% (1) N=21	0.0% (0) N=21	NR	NR	NS	30 days
		Organ/space	42	4.8% (1) N=21	4.8% (1) N=21	NR	NR	NS	
	Paralytic ileus *Rate of postoperative paralytic ileus within 30 days*		42	9.5% (2) N=21	0.0% (0) N=21	NR	NR	NS	
	Length of hospital stay *Mean (SD) length of hospital stay, days*		42	8 (6-53) N=21	6 (5-100) N=21	NA	NA	0.17	
Zmora 2006[c] (Israel)	**Infectious complications**[d] *Rate of postoperative infectious complications within 30 days*		249	12.4% (15) N=120	13.0% (17) N=129	NR	NR	NS	30 days
	Anastomotic leak *Rate of postoperative anastomotic leak within 30 days*	**Total**	249	4.2% (5) N=120	2.3% (3) N=129	NR	NR	NS	
		Hand-sewn	20	NR (NR) N=11	NR (NR) N=9	NR	NR	NS	
		Stapled	180	NR (NR) N=89	NR (NR) N=91	NR	NR	NS	
	Abdominal abscess *Rate of postoperative abdominal abscess within 30 days*		249	1.6% (2) N=120	0.7% (1) N=129	NR	NR	NS	
	Wound infection *Rate of postoperative wound infection within 30 days*		249	6.6% (8) N=120	10.0% (13) N=129	NR	NR	NS	
	Length of hospital stay *Mean (SD) length of hospital stay, days*		249	4.0 (NR) N=120	4.2 (NR) N=129	NA	NA	0.73	

N= number of participants; MBP = mechanical bowel preparation; NR = not reported; NA = not applicable; SD = standard deviation; CI = confidence interval; [a]P-values derived from two-sided tests, p-value <0.05 was considered to be statistically significant; [b]Per protocol analysis performed; comparisons performed by χ2 test for qualitative data and the Mann–Whitney U test; [c] Per protocol analysis performed; Comparisons performed by Fischer's exact test, or Student's unpaired t test; patients underwent left sided large bowel anastomosis only; [d]Consisting of wound infection, anastomotic leak and abdominal abscess

3.5. Body of evidence

Effects of interventions on relevant outcomes are described in Tables 26-33.

I Anastomotic leakage

Table 26. Body of evidence examining the effect of mechanical bowel preparation (with antibiotic prophylaxis) compared to no mechanical bowel preparation (with or without antibiotic prophylaxis) in colorectal cancer patients on anastomotic leakage/dehiscence

Name of study	Study type	Level of evidence[a]	Risk of bias	N	Results summary	Size of effect rating	95% CI	p value	Relevance of evidence[a]
Bhattacharjee 2015	RCT	II	At risk	71	**Anastomotic leak within 30 days** MBP:10.5% No MBP: 6.1%	NR	NR	0.68	I
Bretagnol 2010	RCT	II	At risk	187	**Overall anastomotic leak within 3 months** MBP:11.0% No MBP: 19.0%	NR	NR	0.09	I
				187	**Clinical anastomotic leak within 3 months** MBP:7.0% No MBP: 16.0%	NR	NR	0.06	
				187	**Asymptomatic anastomotic leak within 3 months** MBP:2.0% No MBP: 3.0%	NR	NR	NR	
				187	**Clinical anastomotic leak within 30 days** MBP:7.0% No MBP: 16.0%	NR	NR	NR	
Contant 2007	RCT	II	At risk	1354	**Overall anastomotic leak within 24 days** MBP:4.8% No MBP: 5.4%	Difference =0.6	-1.7, 2.9	0.69	I
				1354	**Major anastomotic leak within 24 days** MBP:3.9% No MBP: 4.5%	Difference =0.6	-1.6, 2.8	0.64	
				1354	**Minor anastomotic leak within 24 days** MBP:0.9% No MBP: 0.9%	Difference =0.0	-1.0, 1.0	1.0	

N = number of participants; RCT = randomised control trial; CI = confidence interval; MBP = mechanical bowel preparation; NR = not reported; OR = odds ratio; [a] Definitions located in Appendix B

Table 27. Body of evidence examining the effect of mechanical bowel preparation (with antibiotic prophylaxis) compared to no mechanical bowel preparation (with or without antibiotic prophylaxis) in colorectal cancer patients on anastomotic leakage/dehiscence

Study	Outcome		N actual	MBP	No MBP	Effect size	CI (95%)	p-value[b]	Follow up
van't Sant 2010	RCT	II	At risk	449	**Anastomotic leakage within 24 days, LAR with lower colorectal anastomosis, overall** MBP:7.6% No MBP: 6.6%	Difference =1.0	-3.7, 5.7	0.80	
				48	**Anastomotic leakage within 24 days, with diverting ileostomy, overall** MBP:3.7% No MBP: 9.5%	NR	NR	NS	
				449	**Anastomotic leakage within 24 days, LAR with lower colorectal anastomosis, major** MBP:6.0% No MBP: 5.0%	NR	NR	NS	I
				48	**Anastomotic leakage within 24 days, with diverting ileostomy, major** MBP:0.0% No MBP: 4.8%	NR	NR	NS	
				449	**Anastomotic leakage within 24 days, LAR with lower colorectal anastomosis, minor** MBP:2.0% No MBP: 1.0%	NR	NR	NS	
				48	**Anastomotic leakage within 24 days, with diverting ileostomy, minor** MBP:3.7% No MBP: 4.8%	NR	NR	NS	
Fa Si Oen 2005	RCT	II	At risk	250	**Total anastomotic leak within 3 months** MBP: 6.4% No MBP: 4.8%	NR	NR	NR	
				250	**Major anastomotic leak within 3 months** MBP: 5.6% No MBP: 4.8%	RR=0.86	0.30-2.48	0.78	I
				250	**Minor anastomotic leak within 3 months** MBP: 0.8% No MBP: 0.0%	NR	NR	NR	
Fa Si Oen 2005	RCT	II	At risk	250	**Anastomotic leak and wound infection within 3 months** MBP:2.4% No MBP: 1.6%	RR=0.67	0.11-3.92	0.65	I
Jung 2007	RCT	II	At risk	1343	**Anastomotic dehiscence within 30 days** MBP:1.9% No MBP: 2.6%	NR	NR	NS	I

N = number of participants; RCT = randomised control trial; CI = confidence interval; MBP = mechanical bowel preparation; NR = not reported; NS = not significant; RR = relative risk; LAR = low anterior resection; [a] *Definitions located in Appendix B*

Table 28. Body of evidence examining the effect of mechanical bowel preparation (with antibiotic prophylaxis) compared to no mechanical bowel preparation (with or without antibiotic prophylaxis) in colorectal cancer patients on anastomotic leakage/dehiscence

Name of study	Study type	Level of evidence[a]	Risk of bias	N	Results summary	Size of effect rating	95% CI	p value	Relevance of evidence[a]
Pena-Soria 2008	RCT	II	At risk	129	**Anastomotic dehiscence within 30 days, total** MBP:6.2% No MBP: 4.7%	NR	NR	NS	I
				59	**Anastomotic dehiscence within 30 days, ileocolostomy** MBP:3.8% No MBP: 0.0%	NR	NR	NR	
				4	**Anastomotic dehiscence within 30 days, ileorectostomy** MBP:33.3% No MBP: 0.0%	NR	NR	NR	
				14	**Anastomotic dehiscence within 30 days, colocolostomy** MBP:12.5% No MBP: 16.7%	NR	NR	NR	
				52	**Anastomotic dehiscence within 30 days, colorectostomy** MBP:3.6% No MBP: 8.3%	NR	NR	NR	
Platell 2006	RCT	II	At risk	294	**Anastomotic leakage within 30 days, total** MBP:2.0% No MBP: 4.8%	OR=1.42	0.1, 1.64	0.20	I
				294	**Anastomotic leakage within 30 days, clinically significant** MBP:0.7% No MBP: 4.1%	OR=1.75	0.02, 1.35	0.06	
Ram 2005	RCT	II	At risk	329	**Total anastomotic dehiscence within 6 weeks** MBP: 0.6% No MBP: 1.2%	NR	NR	NS	I
Sasaki 2012	RCT	II	At risk	79	**Anastomotic leakage within 105 days** MBP:2.6% No MBP: 7.3%	NR	NR	0.35	I
Zmora 2006	RCT	II	At risk	249	**Anastomotic leakage within 30 days, total** MBP:4.2% No MBP: 2.3%	NR	NR	NS	I
				20	**Anastomotic dehiscence within 30 days, hand-sewn** MBP:NR No MBP: NR	NR	NR	NS	
				180	**Anastomotic dehiscence within 30 days, stapled** MBP:NR No MBP: NR	NR	NR	NS	

N = number of participants; RCT = randomised control trial; MBP = mechanical bowel preparation; NR = not reported; NS = not significant; OR = odds ratio; [a] Definitions located in Appendix B

II Surgical site/wound infection

Table 29. Body of evidence examining the effect of mechanical bowel preparation (with antibiotic prophylaxis) compared to no mechanical bowel preparation (with or without antibiotic prophylaxis) in colorectal cancer patients on surgical site/wound infection

Name of study	Study type	Level of evidence[a]	Risk of bias	N	Results summary	Size of effect rating	95% CI	p value	Relevance of evidence[a]
Bhattacharjee 2015	RCT	II	At risk	71	**Wound infection within 30 days** MBP: 29.0% No MBP: 18.8%	NR	NR	0.40	I
				71	**Intraabdominal abscess within 30 days** MBP: 7.9% No MBP: 3.0%	NR	NR	0.62	
Bretagnol 2010	RCT	II	At risk	187	**Infectious abdominal complications within 30 days** MBP: 17.0% No MBP: 38.0%	NR	NR	NR	I
				187	**Wound abscess within 30 days** MBP: 3.0% No MBP: 1.0%	NR	NR	NR	
				187	**Peristomial abscess within 30 days** MBP: 1.0% No MBP: 1.0%	NR	NR	NR	
Contant 2007	RCT	II	At risk	187	**Overall wound infection within 24 days** MBP: 13.4% No MBP: 14.0%	Difference =0.6	-3.2, 4.4	0.82	I
				187	**Severe wound infection within 24 days** MBP: 6.1% No MBP: 6.6%	Difference =0.4	-2.2, 3.0	0.83	
				187	**Mild wound infection within 24 days** MBP: 7.3% No MBP: 7.4%	Difference =0.1	-2.7, 2.9	1.0	
				187	**Overall intra-abdominal abscess within 24 days** MBP: 2.2% No MBP: 4.7%	Difference =2.4	0.5, 4.4	0.02	
				187	**Abdominal abscess with AL within 24 days** MBP: 0.3% No MBP: 2.5%	Difference =2.2	0.9, 3.4	0.001	
				187	**Abdominal abscess without AL within 24 days** MBP: 1.9% No MBP: 2.2%	Difference =0.3	-1.3, 1.8	0.85	
van't Sant 2010	RCT	II	At risk	449	**Wound infection within 24 days, LAR with lower colorectal anastomosis, overall** MBP:NR No MBP: NR	NR	NR	0.43	I
				48	**Wound infection within 24 days, with diverting ileostomy, overall** MBP:18.5% No MBP: 23.8%	NR	NR	NS	
				449	**Wound infection within 24 days, LAR with lower colorectal anastomosis, severe** MBP:9.0% No MBP: 7.0%	NR	NR	NS	

N = number of participants; RCT = randomised control trial; CI = confidence interval; MBP = mechanical bowel preparation; NR = not reported; NS = Not significant; LAR = low anterior resection; [a] *Definitions located in Appendix B*

Table 30. Body of evidence examining the effect of mechanical bowel preparation (with antibiotic prophylaxis) compared to no mechanical bowel preparation (with or without antibiotic prophylaxis) in colorectal cancer patients on surgical site/wound infection

Name of study	Study type	Level of evidence[a]	Risk of bias	N	Results summary	Size of effect rating	95% CI	p value	Relevance of evidence[a]
van't Sant 2010	RCT	II	At risk	48	**Wound infection within 24 days, with diverting ileostomy, severe** MBP:11.1% No MBP: 14.3%	NR	NR	NS	I
				449	**Wound infection within 24 days, LAR with lower colorectal anastomosis, mild** MBP:8.0% No MBP: 10.0%	NR	NR	NS	
				48	**Wound infection within 24 days, with diverting ileostomy, mild** MBP:7.4% No MBP: 9.5%	NR	NR	NS	
				449	**Intraabdominal abscess within 24 days, LAR with lower colorectal anastomosis** MBP:3.0% No MBP: 4.0%	NR	NR	0.43	
				48	**Intraabdominal abscess within 24 days, with diverting ileostomy** MBP:3.7% No MBP: 4.8%	NR	NR	NS	
				449	**Fascia dehiscence within 24 days, LAR with lower colorectal anastomosis** MBP:3.0% No MBP: 4.0%	NR	NR	0.61	
				48	**Fascia dehiscence within 24 days, with diverting ileostomy** MBP:7.4% No MBP: 0.0%	NR	NR	NS	
Fa Si Oen 2005	RCT	II	At risk	250	**Wound infection within 3 months, clinically significant** MBP: 7.2% No MBP: 5.6%	RR=0.78	0.30-2.02	0.61	I
Horvat 2010	RCT	II	At risk	68	**Wound infection, mild** MBP: 5.0% No MBP C1: 5.0% C2: 0.0%	NR	NR	NR	I
Jung 2007	RCT	II	At risk	1343	**Wound infection within 30 days, superficial** MBP: 7.8% No MBP: 6.4%	NR	NR	NS	I
				1343	**Deep abscess within 30 days** MBP: 0.7% No MBP: 1.7%	NR	NR	NS	
				1343	**Wound disruption within 30 days, subcutaneous** MBP: 1.5% No MBP: 2.0%	NR	NR	NS	

N = number of participants; RCT = randomised control trial; CI = confidence interval; MBP = mechanical bowel preparation; NR = not reported; NS = not significant; RR = relative risk; LAR = low anterior resection; [a] *Definitions located in Appendix B*

Table 31. Body of evidence examining the effect of mechanical bowel preparation (with antibiotic prophylaxis) compared to no mechanical bowel preparation (with or without antibiotic prophylaxis) in colorectal cancer patients on surgical site/wound infection

Name of study	Study type	Level of evidence[a]	Risk of bias	N	Results summary	Size of effect rating	95% CI	p value	Relevance of evidence[a]
Pena-Soria 2008	RCT	II	At risk	129	**Surgical site infection within 30 days, total** MBP: 29.2% No MBP: 17.2%	NR	NR	NS	I
				129	**Surgical site infection within 30 days, organ/space** MBP: 4.6% No MBP: 0.0%	NR	NR	NS	
				129	**Surgical site infection within 30 days, superficial incisional** MBP: 24.6% No MBP: 17.2%	NR	NR	NS	
Platell 2006	RCT	II	At risk	294	**Wound infection within 30 days** MBP: 12.9% No MBP: 14.3%	NR	NR	NS	I
				294	**Intra-abdominal abscess within 30 days** MBP: 0.7% No MBP: 0.7%	NR	NR	NS	
Ram 2005	RCT	II	At risk	329	**Wound infection within 6 weeks** MBP: 9.8% No MBP: 6.1%	NR	NR	NS	I
				329	**Wound dehiscence within 6 weeks** MBP: 1.8% No MBP: 1.2%	NR	NR	NS	
Reddy 2007	RCT	II	At risk	88	**Septic morbidity, total** MBP I1: 20.8% MBP I2: 18.2% MBP I3: 15.0% No MBP: 13.6%	NR	NR	0.93	I
				88	**Wound infection** MBP I1: 12.5% MBP I2: 13.6% MBP I3: 0.0% No MBP: 13.6%	NR	NR	0.99	
Sasaki 2012	RCT	II	At risk	79	**Wound infection within 105 days** MBP: 0.0% No MBP: 0.0%	NR	NR	NS	I
				79	**Intra-abdominal infection within 105 days** MBP: 2.6% No MBP: 2.4%	NR	NR	0.96	
Watanabe 2010	RCT	II	At risk	42	**Surgical site infection within 30 days, superficial** MBP: 4.8% No MBP: 0.0%	NR	NR	NS	I
				42	**Surgical site infection within 30 days, organ/space** MBP: 4.8% No MBP: 4.8%	NR	NR	NS	
Zmora 2006	RCT	II	At risk	249	**Infectious complications within 30 days** MBP: 12.4% No MBP: 13.0%	NR	NR	NS	I
				249	**Abdominal abscess within 30 days** MBP: 1.6% No MBP: 0.7%	NR	NR	NS	
				249	**Wound infection within 30 days** MBP: 6.6% No MBP: 10.0%	NR	NR	NS	

N = number of participants; RCT = randomised control trial; CI = confidence interval; MBP = mechanical bowel preparation; NR = not reported; NS = not significant; MBP = mechanical bowel preparation; I1 = Intervention 1 (MBP only); I2 = Intervention 2 (MBP + oral antibiotic prophylaxis); I3 = Intervention 3 (MBP + synbiotics + oral antibiotic prophylaxis); [a] *Definitions located in Appendix B*

III Length of hospital stay

Table 32. Body of evidence examining the effect of mechanical bowel preparation (with antibiotic prophylaxis) compared to no mechanical bowel preparation (with or without antibiotic prophylaxis) in colorectal cancer patients on length of hospital stay

Name of study	Study type	Level of evidence[a]	Risk of bias	N	Results summary	Size of effect rating	95% CI	p value	Relevance of evidence[a]
Bretagnol 2010	RCT	II	At risk	187	**Length of hospital stay, median, days** MBP: 11 No MBP: 12	NA	NA	0.15	I
Contant 2007	RCT	II	At risk	1325	**Length of hospital stay, median, days** MBP: 10 No MBP: 10	Difference =0.0	-1.0 1.0	0.40	I
Fa Si Oen 2005	RCT	II	At risk	250	**Length of hospital stay, median, days** MBP: 10 No MBP: 9	NA	NA	0.97	I
Horvat 2010	RCT	II	At risk	68	**Length of hospital stay, mean, days** MBP: 9.5 No MBP C1: 10.95 C2: 9.21	NA	NA	0.225	I
Jung 2007	RCT	II	At risk	1343	**Length of hospital stay, mean, days** MBP: 8.6 No MBP: 8.8	NA	NA	NR	I
Krebs 2016	RCT	II	At risk	54	**Length of hospital stay, median, days** MBP: 11.3 No MBP C1: 10.16 C2: 11.3	NA	NA	0.51	I
Platell 2006	RCT	II	At risk	294	**Length of hospital stay, mean, days** MBP: 9.0 No MBP: 9.4	NA	NA	NS	I
Ram 2005	RCT	II	At risk	329	**Length of hospital stay, mean, days** MBP: 8.2 No MBP: 8.0	NA	NA	NS	I
Sasaki 2012	RCT	II	At risk	79	**Length of hospital stay, median, days** MBP: 19.9 No MBP: 15.5	NA	NA	0.28	I
Watanabe 2010	RCT	II	At risk	42	**Length of hospital stay, mean, days** MBP: 8 No MBP: 6	NA	NA	0.17	I
Zmora 2006	RCT	II	At risk	249	**Length of hospital stay, mean, days** MBP: 4.0 No MBP: 4.2	NA	NA	0.73	I

N = number of participants; RCT = randomised control trial; CI = confidence interval; MBP = mechanical bowel preparation; NS = not significant; NA = not applicable; C1 = comparison 1; C2 = comparison 2; [a] *Definitions located in Appendix B*

IV Ileus

Table 33. Body of evidence examining the effect of mechanical bowel preparation (with antibiotic prophylaxis) compared to no mechanical bowel preparation (with or without antibiotic prophylaxis) in colorectal cancer patients on ileus

Name of study	Study type	Level of evidence[a]	Risk of bias	N	Results summary	Size of effect rating	95% CI	p value	Relevance of evidence[a]
Fa Si Oen 2005	RCT	II	At risk	250	**Duration of ileus, mean, days** MBP: 5.0 No MBP: 4.7	NA	NA	0.25	I
Jung 2007	RCT	II	At risk	1343	**Ileus/bowel paralysis within 30 days** MBP: 0.7% No MBP: 0.8%	NR	NR	NS	I
Ram 2005	RCT	II	At risk	329	**Ileus within 6 weeks** MBP: 8.5% No MBP: 6.7%	NR	NR	NS	I
Sasaki 2012	RCT	II	At risk	79	**Ileus within 105 days** MBP: 2.6% No MBP: 4.9%	NR	NR	0.35	I
Watanabe 2010	RCT	II	At risk	42	**Paralytic ileus within 30 days** MBP: 9.5% No MBP: 0.0%	NR	NR	NS	I

N = number of participants; RCT = randomised control trial; CI = confidence interval; MBP = mechanical bowel preparation; NR = not reported; NS = not significant; NA = not applicable; OR = odds ratio; [a] Definitions located in Appendix

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APPENDICES

Appendix A: Search strategies used

For PubMed database:

#	Searches
1	Colorect* [title/abstract] or colon [title/abstract] or colonic [title/abstract] or rectal* [title/abstract] or rectum* [title/abstract] or anus [title/abstract] or bowel* [title/abstract]
2	Cathartics [MeSH terms] or preoperative care [MeSH terms]
3	Mechanical bowel prepara* [title/abstract] or mechanical bowel cleans* [title/abstract] or mechanical prepara* [title/abstract] or mechanical cleans* [title/abstract] or bowel prepara* [title/abstract] or bowel cleans* [title/abstract]
4	2 OR 3
5	Elective Surgical Procedures [MeSH terms] or Colorectal surgery [MeSH terms] or (colonic diseases [mh] and surgery [sh]) or (colon [mh] and surgery [sh]) or (rectal diseases [mh] and surgery [sh]) or colectomy [MeSH terms] or (colonic neoplasms[mh] and surgery[sh]) or (sigmoid neoplasms[mh] and surgery[sh]) or (colon,sigmoid[mh] and surgery[sh]) or Colon Resect*[tiab] or Colorectal Resect*[tiab] or Colorectal Excision*[tiab] or Colon Surg*[tiab] or Colorectal Surg*[tiab] or Colon Remov*[tiab] or colectom*[tiab] or Rectal Resect*[tiab] or Rectal Excision*[tiab] or Rectal Surg*[tiab] or Rectal Surg*[tiab] or Bowel Resect*[tiab] or Bowel Excision*[tiab] or Bowel Surg*[tiab] or Bowel Surg*[tiab] or Bowel Remov*[tiab]
6	1 AND 4 AND 5
7	English[la] AND 2004:3000[dp]
8	meta-analysis[mesh:noexp] OR metaanalysis[tiab] OR metaanalyses[tiab] OR meta analysis[tiab] OR meta analyses[tiab] OR meta analysis[pt] OR systematic review[tiab] OR systematic reviews[tiab] OR systematic overview[tiab] OR systematic overviews[tiab] OR literature review[tiab] OR randomized controlled trial[pt] OR controlled clinical trial[pt] OR placebo[tiab] OR randomi?ed[tiab] OR randomly[tiab] OR trial[tiab] OR group[tiab]
9	6 AND 7 AND 8
10	"clinical conference"[Publication Type] OR "comment"[Publication Type] OR "editorial"[Publication Type] OR "historical article"[Publication Type] OR "letter"[Publication Type] OR "news"[Publication Type] OR "newspaper article"[Publication Type]
11	9 NOT 10
12	animals[mh] NOT humans[mh]
13	11 NOT 12

Used the Cochrane sensitivity maximizing filters for identifying randomized controlled trials (http://handbook.cochrane.org, accessed 20/02/2013/ Centre for Reviews and Dissemination systematic review/ meta-analyses strategy 2.(Lee et al, (2012) An optimal search filter for retrieving systematic reviews and meta-analyses. ***BMC Medical Research Methodology*** *12:51)*

ATSI search terms used for Pubmed

#	Searches
1	australia[mh] OR Australia*[tiab]
2	ancestry group, oceanic[mh] OR ancestry groups, oceanic[mh] OR aborigine, australian[mh] OR aborigines, australian[mh] OR australian aborigine[mh] OR australian aborigines[mh] OR aborigin*[tiab] OR indigenous[tiab]
3	1 AND 2
4	torres strait islander*[tiab]
5	3 OR 4
6	colorect*[tiab] OR colon*[tiab] OR bowel*[tiab]
7	(cancer*[tiab] OR neoplas*[tiab] OR oncolog*[tiab] OR malignan*[tiab] OR tumor*[tiab] OR tumour*[tiab] OR carcinoma*[tiab] OR adenocarcinoma*[tiab] OR colorectal neoplasms[mh] OR colonic neoplasms[mh])
8	6 AND 7
9	5 AND 8
10	english[la] AND 2004:3000[dp]
11	9 AND 10

From the Lowitja Institute at http://www.lowitja.org.au/litsearch-background-information accessed 30/09/2013)

For Embase database:

#	Search
1	(colo$ or intestin$ or bowel or rectal or rectum or anus or anal).tw.
2	Intestine preparation/ or preoperative care/ or mechanical bowel preparation/
3	Mechanical adj4 (bowel prepara$ or bowel cleans$).tw OR (bowel adj1 (prepara$ or cleans$)).tw
4	2 OR 3
5	rectum surgery/ or colorectal surgery/ or elective surgery/ or colon resection/
6	(Colorectal or colon* or rect* or bowel) adj3 (resect$ or excis$ or surg$ or remov$).tw
7	5 OR 6
8	1 AND 4 AND 7
9	Meta analysis/
10	metaanaly$.tw.
11	meta analy$.tw.
12	(systematic adj (review$ or overview$)).tw.
13	(review adj5 literature).mp.
14	systematic review/
15	randomized controlled trial/
16	controlled clinical trial/ or clinical trial/
17	placebo.ab.
18	randomi?ed.ab.
19	randomly.ab.
20	trial.ab.
21	groups.ab.
22	9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21
23	8 AND 22
24	limit 23 to english language
25	limit 24 to yr="2004-Current"
26	exp animal/ not human/
27	25 NOT 26
28	(journal conference abstract or journal conference paper or journal letter or journal note or letter or note).pt.
29	27 NOT 28

*Used the SIGN filter for identifying randomized controlled trials (*www.sign.ac.uk/methodology/filters.html#systematic *accessed 20/02/2013)*

ATSI search terms used for Embase (via Ovid):

#	Searches
1	exp Australia/ OR Australia$.ti,ab
2	Oceanic ancestry group/ OR aborigin$.ti,ab. OR indigenous.mp.
3	1 AND 2
4	torres strait$ islander$.ti,ab
5	3 OR 4
6	(colorect$ or colon$ or rectal$ or rectum$ or anus$ or bowel$).ti,ab.
7	(cancer$ or neoplas$ or oncolog$ or malignan$ or tumo?r$ or carcinoma$ or adeno).ti,ab.
8	6 AND 7
9	hereditary nonpolyposis colorectal cancer/ or colorectal polyp/ or colorectal tumor/ or colorectal cancer/ or colorectal anastomosis/ or colorectal carcinoma/ or colorectal adenoma/ or colorectal.mp. or hereditary colorectal cancer/
10	colon anastomosis/ or colon carcinoma/ or colon polyposis/ or colon adenocarcinoma/ or colon tumor/ or colon.mp. or colon cancer/ or colon adenoma/ or colon carcinogenesis/ or colon polyp/ or familial colon polyposis/
11	rectum cancer/ or rectum tumor/ or rectum anastomosis/ or rectum carcinoma/ or rectum adenoma/ or rectum/ or rectum polyp/ or rectum.mp.
12	9 OR 10 OR 11
13	8 OR 12
14	5 AND 13
15	limit 14 to english language
16	limit 15 to yr="2004-Current"

For Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects and Health Technology Assessment database:

#	Searches
1	(colorect$ or colon$ or rectal$ or rectum$ or anus$ or bowel$).ti,ab.
2	(cancer$ or neoplas$ or oncolog$ or malignan$ or tumo?r$ or carcinoma$ or adeno).ti,ab.
3	1 AND 2
4	hereditary nonpolyposis colorectal cancer/ or colorectal polyp/ or colorectal tumor/ or colorectal cancer/ or colorectal anastomosis/ or colorectal carcinoma/ or colorectal adenoma/ or colorectal.mp. or hereditary colorectal cancer/
5	colon anastomosis/ or colon carcinoma/ or colon polyposis/ or colon adenocarcinoma/ or colon tumor/ or colon.mp. or colon cancer/ or colon adenoma/ or colon carcinogenesis/ or colon polyp/ or familial colon polyposis/
6	rectum cancer/ or rectum tumor/ or rectum anastomosis/ or rectum carcinoma/ or rectum adenoma/ or rectum/ or rectum polyp/ or rectum.mp.
7	4 OR 5 OR 6
8	3 OR 7
9	7 AND 8
10	limit 9 to english language
11	limit 10 to yr="2014-Current"

For PsycINFO (via Ovid) database:

#	Searches
1	(colorect$ or colon$ or rectal$ or rectum$ or anus$ or bowel$).ti,ab.
2	(cancer$ or neoplas$ or oncolog$ or malignan$ or tumo?r$ or carcinoma$ or adeno).ti,ab.
3	1 AND 2
4	hereditary nonpolyposis colorectal cancer/ or colorectal polyp/ or colorectal tumor/ or colorectal cancer/ or colorectal anastomosis/ or colorectal carcinoma/ or colorectal adenoma/ or colorectal.mp. or hereditary colorectal cancer/
5	colon anastomosis/ or colon carcinoma/ or colon polyposis/ or colon adenocarcinoma/ or colon tumor/ or colon.mp. or colon cancer/ or colon adenoma/ or colon carcinogenesis/ or colon polyp/ or familial colon polyposis/
6	rectum cancer/ or rectum tumor/ or rectum anastomosis/ or rectum carcinoma/ or rectum adenoma/ or rectum/ or rectum polyp/ or rectum.mp.
7	4 OR 5 OR 6
8	3 OR 7
9	7 AND 8
10	limit 9 to english language
11	limit 10 to yr="2014-Current"

For CINAHL database:

#	**Searches**
1	colorectal (TX All Text)
2	cancer (TX All Text)
3	(mechanical bowel preparation or mechanical bowel cleanse or mechanical bowel cleansing or bowel preparation or bowel cleanse or bowel cleansing) (TX All Text)
4	1 AND 2 AND 3
5	2004-2016 (DT Publication Date)
6	4 AND 5

Appendix B:

Level of Evidence rating criteria – Intervention studies

Level	Study type
I	Meta-analysis or a systematic review of level II studies
II	Randomised controlled trial or a phase III/IV clinical trial
III-1	Pseudo-randomised controlled trial or a meta-analysis/systematic review of level III-1 studies
III-2	Comparative study with concurrent controls: - Phase II clinical trial - Non-randomised, experimental trial9 - Controlled pre test/post test study - Adjusted indirect comparisons - Interrupted time series with a control group - Cohort study - Case-control study or a meta-analysis/systematic review of level III-2 studies
III-3	A comparative study without concurrent controls: - Phase I clinical trial - Historical control study - Two or more single arm study10 - Unadjusted indirect comparisons - Interrupted time series without a parallel control group or a meta-analysis/systematic review of level III-3 studies
IV	Case series with either post-test or pre-test/post-test outcomes or a meta-analysis/systematic review of level IV studies

According to the standards of the National Health and Medical Research Council

Appendix B continued.

Relevance of the evidence

Rating	Relevance
1	Evidence of an effect on patient-relevant clinical outcomes including benefits and harms, quality of life and survival.
2	Evidence of an effect on a surrogate outcome* that has been shown to be predictive of patient-relevant outcomes for the same intervention.
3	Evidence of an effect on proven surrogate outcomes but for a different intervention.
4	Evidence of an effect on proven surrogate outcomes but for a different intervention and population.
5	Evidence confined to unproven surrogate outcomes.

**'surrogate outcome' refers to reasonable indicators of whether there has been some effect (e.g. blood pressure measurements or levels of serum cholesterol)*

Points for considering patient-relevant outcomes:
i) The goal of decision making in health care is to choose the intervention(s) (which may include doing nothing) that is (are) most likely to deliver the outcomes that patients find desirable.
ii) Surrogate outcomes (such as blood pressure measurements or levels of serum cholesterol) may be reasonable indicators of whether there has been some effect. However, they should not be the basis for clinical decisions unless they reliably predict an effect on the way the patient feels, otherwise they will not be of interest to the patient or their carers.
iii) All possible outcomes that are of most interest to patients (particularly harms) should be identified and evaluated.

Adapted from table 1.10 of: National Health and Medical Research Council. How to use the evidence: assessment and application of scientific evidence. Canberra: NHMRC; 2000. http://www.nhmrc.gov.au/_files_nhmrc/file/publications/synopses/cp69.pdf

Appendix C:
Potentially relevant guidelines identified and reason why not adopted

Year	Organisation	Title of Guideline	Reason why not adopted
2016	Hellenic society of medical oncology (HeSMO)	Clinical practice guidelines for the surgical management of colon cancer: a consensus statement of the Hellenic and Cypriot Colorectal Cancer Study Group by the HeSMO	Outdated content
2014	Working group of the Société francaise d'anesthésie et réanimation (SFAR), the Société francaise de chirurgie digestive (SFCD)	French guidelines for enhanced recovery after elective colorectal surgery	Content not comprehensive, no systematic search performed, no inclusion/exclusion criteria
2013	Enhanced Recovery After Surgery (ERAS) Society	Guidelines for Perioperative Care in Elective Colonic Surgery: Enhanced Recovery After Surgery (ERAS) Society Recommendations	Content too simplistic and outdated, search strategy not relevant.
2013	SAGES		Outdated content
2010	Canadian Society of Colon and Rectal Surgeons	Preoperative bowel preparation for patients undergoing elective colorectal surgery: a clinical practice guideline endorsed by the Canadian Society of Colon and Rectal Surgeons	Guideline does not specify population as cancer patients and contains outdated content
2011	Scottish Intercollegiate Guidelines Network (SIGN)	Diagnosis and Management of Colorectal Cancer	Content too brief
2007	Italian Society of Colo-Rectal Surgery (ISCS)	Laparoscopic surgery for colorectal cancer: clinical practice guidelines of the Italian Society of Colo-Rectal Surgery	Outdated content

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Excluded studies

Study	Reason for Exclusion
Aldrink 2015	Inappropriate population
Alfonsi 2014	Guideline not comprehensive
Al-Mulhim 2007	Inappropriate population
Badawi 2015	Review
Basu 2008	Editorial
Beerdawood 2014	Unable to retrieve
Bertani 2011	Inappropriate study design
Bhat 2016	Full text unavailable
Bretagnol 2007	Inappropriate study design
Bucher 2006	Inappropriate population
Bucher 2005	Inappropriate population
Bucher 2004	Contains inappropriate studies
Bucher 2004	Duplicate
Bucher 2004	Contains inappropriate studies
Cao 2012	Contains inappropriate studies
Chattopadhyay 2004	Inappropriate population
Collin 2014	No relevant outcomes
Courtney 2015	Contains inappropriate studies
Dahabreh 2014	Contains inappropriate studies
Dahabreh 2015	Contains inappropriate studies
Ellis 2010	Review
Eskicioglu 2010	Guideline contains unclear population
Espin-Basany 2005	Inappropriate comparator
Ezri 2006	Inappropriate comparator
Fa-Si-Oen 2005	Data replication
Fry 2011	Review
Gravante 2009	Editorial
Gravante 2008	Contains inappropriate studies
Gray 2005	Contains inappropriate studies
Guenaga 2005	Earlier version of updated systematic review
Guenaga 2011	Contains inappropriate studies
Guenaga 2009	Earlier version of updated systematic review
Gustafsson 2012	Guideline content not comprehensive
Horie 2007	Inappropriate comparator
Itani 2008	Review
Itani 2007	Inappropriate comparator
Kaska 2010	Inappropriate comparators
Khan 2011	Could not obtain
Kolovrat 2012	Inappropriate study design
Kumar 2013	Inappropriate population
Matsou 2011	Contains inappropriate studies
McCoubrey 2007	Contains inappropriate study
Muller-Stich 2006	Contains inappropriate studies
Murray 2016	Review
Murray 2010	Review
O'Neal 2016	Review
Pearson 2004	Unable to retrieve
Peppas 2008	Review
Phatak 2012	Inappropriate comparators
Pineda 2008	Contains inappropriate studies
Platell 2007	Comment
Rovera 2006	Review
Scabini 2012	Retraction
Scabini 2010	Retraction

Shapira 2010	Inappropriate comparator
Shawki 2008	Review
Slim 2009	Contains inappropriate studies
Slim 2004	Contains inappropriate studies
Suzuki 2011	Inappropriate comparator
Valantas 2004	Review
Valverde 2006	Inappropriate comparator
van't Sant 2015	No relevant outcomes
van't Sant 2011	Inappropriate population
Wille-Jorgensen 2005	Contains inappropriate studies
Zhu 2010	Contains inappropriate studies
Zingg 2008	Inappropriate population
Zmora 2008	Review

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