Bowel Preparation: Always, Sometimes, Never?

12

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Introduction

The administration of bowel preparation prior to elective colorectal resection is contentious. There is dogma and strongly held opinion both for and against. At present there is a cultural divide between the USA and many countries in Europe, particularly regarding guidelines and recommendations in this area advocated by the Enhanced Recovery After Surgery (ERAS®) Society and the American Society for Enhanced Recovery (ASER) [1–3]. This chapter tries to address the evidence that exists with regard to benefits or otherwise of mechanical bowel preparation (MBP) alone or MBP combined with oral antibiotics in different circumstances and in the context of ERAS.

The original work on what has come to be known as "enhanced recovery after surgery" (ERAS) was in the field of colorectal surgery [4], and this remains the area in which the most research evidence exists. One of the dogmas of colorectal surgery has been the necessity to administer mechanical bowel preparation for patients undergoing colorectal resection, and this is an element of treatment that has been challenged in the context of ERAS. Its avoidance has been a central tenet of colorectal ERAS since its inception.

Bowel preparation was first established during an era of open surgery, limited antibiotics, and sutured anastomoses, which necessitated opening the bowel within the abdominal cavity. Modern colorectal surgery with its emphasis on laparoscopy and the use of stapling technologies avoids this in most circumstances, and so it is possible that the rationale for bowel preparation is no longer valid. Indeed it has been shown in numerous studies that surgical site infection (SSI) rates are significantly lower in patients who have undergone laparoscopic surgery [5].

The questions are firstly whether mechanical bowel preparation prior to surgery is effective in reducing infective complications (that includes superficial and deep surgical site infections and including anastomotic leaks) and secondly whether bowel preparation has a negative impact on fluid and electrolyte balance of patients prior to surgery that might have an adverse outcome in terms of complications and recovery. It is possible that both are correct and then we must consider the balance of risk and benefit.

There are a number of variables that need to be considered with regard to mechanical bowel preparation. The variable that is attracting the most attention and is mostly responsible for the schism in bowel preparation guidelines is the synchronous use of oral nonabsorbable antibiotics. This chapter will go on to analyze the data that exists in this area.

Arguments in Favor of Mechanical Bowel Preparation

Effective mechanical bowel preparation results in a macroscopically cleaner bowel with potentially easier bowel handling and a theoretical lower risk of gross peritoneal or wound contamination. It also results in a reduction in the quantity of bowel content at the site of anastomosis for a period of time postoperatively, or longer where the anastomosis is defunctioned with a proximal stoma.

It has been assumed that the bacterial load in the colon is reduced but this is incorrect [6]. Additionally, there is no need for a preoperative enema or distal washout of the rectum prior to inserting mechanical staplers into the rectum, and the operation itself might be seen to be aesthetically less unpleasant.

From an outcome perspective, it is believed by many surgeons that it results in a lower risk of surgical site infection and anastomotic leak. It is also believed that if patients receive bowel preparation and are defunctioned with a proximal stoma, then any leak that does occur will be easier to

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manage and have less disastrous consequences. This chapter will go on to address the evidence that exists in this area. The findings of recent meta-analyses and systematic reviews are summarized in Table 12.1 [6–15].

Lastly, while there is evidence that bowel preparation can cause significant electrolyte disturbance, there is evidence to the contrary that with modern preparations and appropriate use the risk of this can be negated [16].

Table 12.1 Summary of meta-analyses and systematic reviews regarding mechanical bowel preparation and antibiotics

Authors	Origin of study	Population/ studies included	Comparison	Outcome measures	Important findings	Limitations of study/ comments
Rollins et al. [7]	United Kingdom, *Annals of Surgery* 2018	28 RCTs, 12 cohort studies	1. Combined antibiotics + MBP vs MBP 2. Combined antibiotics + MBP vs combined antibiotics 3. Combined antibiotics + MBP vs no NMBP 4. Combined antibiotics vs NMBP 5. Combined antibiotics vs MBP	SSI, anastomotic leak, 30-day mortality, morbidity, development of ileus, *C. difficile* infection rates	Combined antibiotics with MBP showed significant reduction of all outcome measures, no increase in *C-diff* rates No difference between combined antibiotics and MBP vs combined antibiotics alone in terms of SSI and leak. Reduction in 30-day mortality and ileus Combined antibiotics with MBP associated with lowest risk of SSI	Limited data regarding comparison between combined antibiotics + MBP vs combined antibiotics alone
Toh et al. [8]	Australia, *Journal of the American Medical Association* 2018	38 RCTs	1. MBP vs NMBP 2. Combined antibiotics with MBP vs combined antibiotics 3. Combined antibiotics with MBP versus MBP	SSI, superficial and deep, anastomotic leak, mortality, readmission, urinary infections, pulmonary complications	Combined antibiotics with MBP associated with lowest risk of SSI No significant difference found in comparison between combined antibiotics with MBP versus combined antibiotics alone MBP alone conferred no benefit	Limited data regarding comparison between combined antibiotics + MBP vs combined antibiotics alone Most studies assessed open surgery
Rollins et al. [6]	United Kingdom, *World Journal of Gastroenterology*, 2018	23 RCTs, 12 observational studies	MBP vs NMBP vs rectal enema	Anastomotic leak, SSI, deep SSI, length of hospital stay, mortality	Overall analysis showed no difference Analysis of RCTs alone showed no difference Observational studies found in favor of MBP in nearly all outcome measures, although not when compared with rectal enema	Did not take into account MIS Did not take into account use of antibiotics
Dahabreh et al. [9]	United States, *Diseases of the Colon and Rectum*, 2015	18 RCTs, 7 nonrandomized trials, 6 single group cohorts	MBP vs NMBP	Length of hospital stay, quality of life and adverse events, postoperative complications	Overall analysis showed no difference	States data reporting with regard to surgical access and antibiotics poor
Güenaga et al. [10]	Brazil, *Cochrane Review*, 2011	18 RCTs	MBP vs NMBP vs rectal enema	Anastomotic leak, SSI	No statistically significant differences between MBP, NMBP, and rectal enema alone Rectal and colonic surgery analyzed separately—no significant difference	Only a small proportion of patients had minimally invasive surgery

Table 12.1 (continued)

Authors	Origin of study	Population/ studies included	Comparison	Outcome measures	Important findings	Limitations of study/ comments
McSorley et al. [11]	United Kingdom, *British Journal of Surgery*, 2018	14 RCTs, 8 observational studies	Combined antibiotics + MBP vs MBP	SSI, anastomotic leak, postoperative ileus, readmission, mortality	IOMBP significantly reduced SSI in both RCTs and observational studies Sub-analysis assessing deep space SSI, anastomotic leak rates, postoperative ileus, readmission rates, and mortality found significantly in favor of IOMBP, but only when cohort studies considered. RCTs either showed no difference or did not assess	Variations in type of MBP and antibiotic regimen used Limitations of cohort studies
Koullouros et al. [12]	United Kingdom, *International Journal of Colorectal Diseases*, 2017	23 RCTs, 8 cohort studies	1. Oral antibiotics vs intravenous antibiotics 2. Combined antibiotics + MBP vs MBP 3. Combined antibiotics vs combined antibiotics + MBP	SSI (superficial and deep)	Both RCTs and cohorts found significantly in favor of combined antibiotics versus one modality Found no difference between combined antibiotics alone vs IOMBP, both in RCTs and cohort studies	Majority of RCTs published in the 1980s Heterogeneity in antibiotics and MBP regimens
Chen et al. [13]	China, *Diseases of the Colon and Rectum*, 2016	7 RCTs	MBP vs combined antibiotics + MBP	SSI (superficial and deep)	IOMBP had statistically significant lower incisional SSI rates Equivocal result with regard to deep SSI	States studies were not blinded Reporting of antibiotic regimens poor
Allegranzi et al. [14]	World Health Organization, *Lancet*, 2016	11 RCTs comparing (1), 13 RCTs comparing (2)	1. Combined antibiotics + MBP vs MBP 2. MBP vs NMBP	SSI, anastomotic leak	IOMBP reduces SSI rate, no difference in rates of anastomotic leak Equivocal result regarding MBP vs NMBP	Heterogeneity regarding antibiotic and bowel preparation protocols
Nelson et al. [15]	United Kingdom, *Cochrane Review*, 2014	96 RCTs	1. Antibiotics vs no antibiotics 2. Oral antibiotics vs intravenous antibiotics 3. Combined antibiotics vs intravenous antibiotics 4. Timing of antibiotic doses 5. Pathogenic coverage	SSI (abdominal wound infection)	Antibiotic prophylaxis should cover anaerobic and aerobic pathogens Both OAB and IAB significantly reduce SSI, with combined regimens having the greatest effect	Did not take into account MBP

RCTs randomized controlled studies, *MBP* mechanical bowel preparation, *NMBP* no mechanical bowel preparation, *SSI* surgical site infection, *MIS* minimally invasive surgery, *IO* combined antibiotics, *OAB* oral antibiotics, *IAB* intravenous antibiotics, *IOMBP* intravenous and oral antibiotics with mechanical bowel preparation

Arguments Against the Routine Use of Mechanical Bowel Preparation

There are many mechanical bowel preparation regimes, but they all require the ingestion of large volumes of fluid. However, there are some new lower volume (1 L) bowel preparations now on the market [17].

They are undoubtedly unpleasant for the patient and can be very challenging, particularly in the elderly and frail, and are known to cause hypovolemia and electrolyte imbalance including hyponatremia, hypernatremia, hypokalemia, hypocalcemia, hypomagnesemia, and phosphate nephropathy. MBP may therefore be particularly dangerous in patients with cardiac and renal comorbidity [18, 19].

They are also variably effective, and there is a recognized failure or partial failure rate that can result in a situation that is worse for the surgeon than having no bowel preparation at all [20]. A dilated fluid-filled colon and rectum is probably more hazardous than an unprepared large bowel [21]. Furthermore, it is possible to precipitate acute bowel obstruction (albeit relatively rarely) by giving bowel preparation to patients with impending obstruction, which in itself may necessitate a change of surgical approach—usually to the detriment of the patient. There is also evidence to suggest exacerbation of postoperative ileus and impaired anastomotic healing [22].

By comparison, rectal enemas are usually well tolerated, are safe in almost all circumstances, and are generally effective in emptying the rectum and the left colon—although they may not empty the colon proximal to a stenosing lesion.

Patient Effects and Considerations

One of the principles of effective ERAS is to bring the patient to surgery in an optimized state, which includes a status of normovolemia and normal electrolyte balance. This is achieved by maintaining oral hydration and supplementation in the 24 hours prior to surgery. Mechanical bowel preparation has a capacity to disrupt this and indeed may be hazardous in patients with cardiac and renal dysfunction in particular [18, 19]. The need to purge may also cause significant sleep disturbance.

This may then impact on fluid requirement during the operative and postoperative period that may increase complications and hospital stay. Mechanical bowel preparation is often self-administered in an unsupervised environment, which may result in poor recognition of these problems and may also result in non-compliance and failed preparation. Frail patients may receive bowel preparation in hospital under supervision and be administered in conjunction with intravenous rehydration, but the overall fluid and electrolyte impact of these two interventions is difficult to gauge. Inpatient preparation also does not safeguard against significant complications [23]. Simple estimations of serum urea and electrolytes following these interventions may not accurately reflect significant disruptions in homeostasis. Patient factors that must be taken into account when considering MBP are outlined in Table 12.2.

Most colonoscopy studies report a failure rate of between 20% and 40%, with only about 1:5 patients with failed preparation reporting not following instructions adequately. This failure rate relates to inadequacy for colonoscopic purposes with reduced adenoma detection rates in particular but nevertheless gives an idea of the limitations [18, 19, 23]. Risk factors for failed or inadequate preparation are outlined in Table 12.3 [24–26]. In addition to bowel preparation not necessarily clearing the bowel adequately of stool, it is unlikely to have much impact upon bacteriology in the lumen.

Table 12.2 Patient factors when considering mechanical bowel preparation

The patient	Is the patient at high risk of dehydration and electrolyte imbalance? Is the patient immunocompromised? Is the patient at increased risk of infection? Diabetic/obese? What is the risk of failure of mechanical bowel preparation if it is administered?
The pathology	Does the patient have impending bowel obstruction? Does the patient have malignancy or inflammatory bowel disease? Is there pre-existing infection? Has the patient had preoperative radiotherapy?
The operation	Does the operation involve an anastomosis? If so, where is the anastomosis: ileocolic, colocolic, colorectal, ileo-rectal? Is the anastomosis to be defunctioned? Is the operation being performed laparoscopically or via a laparotomy?
The trials	Which bowel preparation regime is being tested? What is it being compared to—enema or none? What synchronous antibiotic regime is used? Are oral nonabsorbable antibiotics used?

Table 12.3 Risk factors for failed mechanical bowel preparation

Risk factors for inadequate bowel preparation	Instructions not followed properly Previously failed bowel preparation Procedural indication as constipation Use of tricyclic antidepressants Male patient Hospitalized patient Medical history of stroke, cirrhosis, dementia

Surgical Site Infection and Anastomotic Leak Rates

It should be noted that the question of whether any antibiotics should be used prior to colorectal surgery has been answered. The evidence is categorical that they should be administered, and controversy regarding this was laid to rest many years ago [27, 28]. There have, however, been more recent meta-analyses, the findings of which have been concordant with earlier work. In a 2014 Cochrane review, Nelson et al. found a risk ratio (RR) of 0.34 when comparing antibiotics to no antibiotics or placebo with regard to surgical wound infections (Fig. 12.1) [15].

Indeed, many recent papers that cite the use of "mechanical bowel preparation alone" in fact refer to the use of MBP with systemic antibiotics prior to surgery, but without additional oral antibiotics. Furthermore, papers that cite "no bowel preparation or antibiotics" do in fact mean that perioperative systemic antibiotics had been given, but no oral antibiotics. Therefore, for the remainder of the chapter, "MBP" refers to the administration of mechanical bowel preparation and systemic intravenous antibiotics at the time of anesthetic induction.

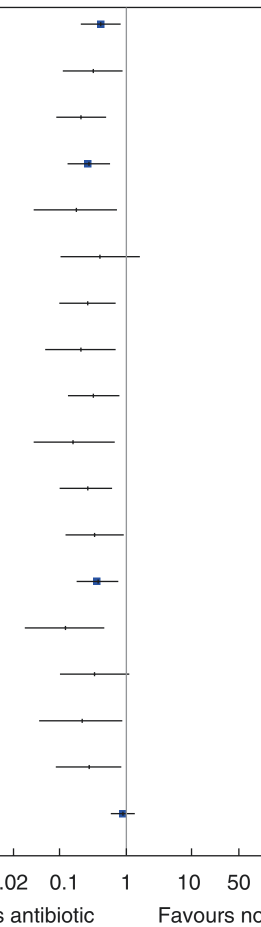
a **Analysis 1.1. Comparison I antibiotic versus no antibiotic/placebo, outcome I surgical wound infection (SWI).**

Review: Antimicrobial prophylaxis for colorectal surgery

Comparison: I antibiotic versus no antibiotic/placebo

Outcome: I surgical wound infection (SWI)

Study or subgroup	Antibiotic n/N	No antibiotic n/N	Risk ratio MH, random, 95% CI	Weight	Risk ratio MH, random, 95% CI
Matheson 1978	9/51	25/59		6.1 %	0.42 [0.21, 0.81]
Keighley 1976	4/33	11/29		2.9 %	0.32 [0.11, 0.90]
Wenzel 1982	5/52	22/48		3.8 %	0.21 [0.09, 0.51]
Wetterfors 1980	7/58	27/60		5.0 %	0.27 [0.13, 0.57]
Goldring 1975	2/25	11/25		1.6 %	0.18 [0.04, 0.74]
Nichols 1973	2/10	5/10		1.7 %	0.40 [0.10, 1.60]
Gillespie 1978	4/34	17/37		3.1 %	0.26 [0.10, 0.69]
Hunt 1979	3/40	11/31		2.2 %	0.21 [0.06, 0.69 l
Durig 1980	5/49	16/50		3.5 %	0.32 [0.13, 0.80 l
Winker 1983	2/30	11/27		1.6 %	0.16 [0.04, 0.67]
Clarke 1977	5/56	21/60		3.7 %	0.26 [0.10, 0.63]
Schneiders 1976	4/50	14/58		2.8 %	0.33 [0.12, 0.94]
Gottrup 1985	11/94	13/41		5.5 %	0.37 [0.18, 0.75]
Ulrich 1981	2/25	16/24		1.7 %	0.12 [0.03, 0.47]
Mendes 1977	3/24	8/22		2.2 %	0.34 [0.10, 1.13]
Cunha 1986	2/20	9/20		1.6 %	0.22 [0.05, 0.90]
Proud 1979	3/24	11/24		2.4 %	0.27 [0.09, 0.86]
Sato 2009	20/46	23/47		11.0 %	0.89 [0.57, 1.38]



(*Continued...*)

Fig. 12.1 (**a, b**) Antibiotic versus antibiotic/placebo, Outcome 1 surgical wound infection (SWI). (Reprinted with permission from Nelson et al. [15])

b (*Continued...*)

Study or subgroup	Antibiotic n/N	No antibiotic n/N	Risk ratio MH, random, 95% CI	Weight	Risk ratio MH, random, 95% CI
Nygaard 1980	7/108	8/49		3.3 %	0.40 [0.15, 1.03]
Utley 1984	3/13	11/19		2.7 %	0.40 [0.14, 1.16]
Olsen 1983	5/65	16/64		3.4 %	0.31 [0.12, 0.79]
Montariol 1979	1/46	5/41		0.8 %	0.18 [0.02, 1.46]
Eykyn 1979	6/33	15/23		4.7 %	0.28 [0.13, 0.61]
Schiessel 1984	2/29	12/31		1.6 %	0.18 [0.04, 0.73]
Hagen 1980	2/17	8/21		1.6 %	0.31 [0.08, 1.27]
Höjer 1978	6/58	26/60		4.4 %	0.24 [0.11, 0.54]
Bjerkeset 1980	1/25	8/31		0.8 %	0.16 [0.02, 1.16]
Hughes 1979	12/78	31/81		7.4 %	0.40 [0.22, 0.72]
Rosenberg 1971	9/40	17/43		5.9 %	0.57 [0.29, 1.13]
Andersen 1979	1/45	5/42		0.8 %	0.19 [0.02, 1.53]
Total (95% CI)	**1278**	**1177**		**100.0 %**	**0.34 [0.28, 0.41]**

Total events: 148 (Antibiotic), 433 (No antibiotic)
Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 32.94$, df = 29 ($P = 0.28$); $I^2 = 12\%$
Test for overall effect: $Z = 11.39$ ($P < 0.00001$)
Test for subgroup differences: not applicable

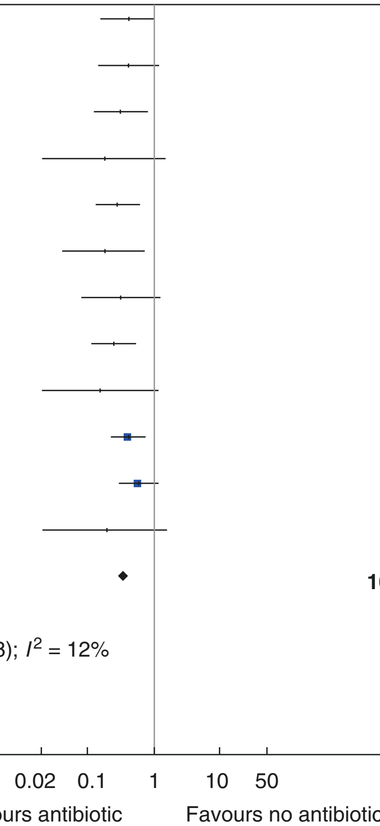


Fig. 12.1 (continued)

There are, however, three further questions regarding the outcomes of bowel preparation in relation to surgical site infection that can be addressed in the literature:

- What is the evidence that mechanical bowel preparation on its own reduces surgical site infection or anastomotic leak in colorectal resection when compared to no preparation at all or compared to rectal enemas alone?
- What is the evidence that mechanical bowel preparation when combined with the administration of oral nonabsorbable antibiotics reduces surgical site infection or anastomotic leak?
- What is the evidence that systemic and oral antibiotics without mechanical bowel preparation reduce surgical site infection or anastomotic leak when compared to mechanical bowel preparation in combination with antibiotics?

Analysis of the data is problematic for all questions because of the heterogeneity of the studies. Colonic resections with different pathologies and different anatomical anastomoses are often pooled together. Rectal anastomoses that are defunctioned are sometimes excluded. Different mechanical bowel preparation regimes are used and sometimes combined with enemas. The surgical approach (open or laparoscopic) varies and is not always quantified. There are also many retrospective database studies, analysis of which carries inherent risks of significant bias. There are, however, many recent meta-analyses that have largely assessed randomized controlled trials (RCTs). These are summarized in Table 12.1 [6–15].

Mechanical Bowel Preparation Versus No Preparation

There is extensive data available for analysis that answers the question of whether bowel preparation, with or without additional oral antibiotics, is effective or not. This includes many randomized controlled trials and observational studies.

These have all recently been subjected to a good quality meta-analysis [6]. This can be seen in the context of a previous Cochrane review [10] and meta-analyses that all have the same conclusion [9, 14, 29]. This is that there is no evidence of reduced surgical site infection rate or anastomotic leak rate with mechanical bowel preparation when compared to no bowel preparation or rectal enema alone. These conclusions are similar whether the meta-analysis includes RCTs only or if the observational studies are included. If, however, the observational studies are looked at in isolation, there is an apparent benefit that is difficult to explain.

Whether bowel preparation should be administered prior to low rectal resection with a defunctioned anastomosis is uncertain, and it remains most surgeons' practice to do so. Leaving a colon full of feces proximal to a low rectal anastomosis with a defunctioning ileostomy proximal to this seems illogical. There is some evidence that an ileostomy in itself inhibits colonic peristalsis [30]. It is therefore feasible that the combination of a rectal enema to empty the left colon and a proximal ileostomy may be as effective as full bowel prep in preventing the passage of fecal material past a newly formed rectal anastomosis, and the purported surgical complications.

There is evidence to support this theory. As discussed previously, Rollins et al. found that although RCTs showed no benefit to MBP in terms of reducing SSI, analysis of observational studies alone did show a statistically significant reduction. This, however, was negated when compared to studies that utilized a rectal enema in place of full MBP [6]. In their Cochrane review of 18 RCTs, Güenaga et al. found no difference in SSI rates or complications between MBP and rectal enema [10].

It should be noted that the overwhelming majority of patients included in these meta-analyses had at least systemic antibiotics perioperatively. A smaller proportion had additional oral antibiotics, and a smaller proportion still had oral antibiotics in isolation.

Mechanical Bowel Preparation with Combined Versus Unimodal Antibiotics

The question of whether combined antibiotics—systemic and oral—in conjunction with bowel preparation are effective at reducing SSI has also been assessed by meta-analysis in recent years. The meta-analyses have compared SSI rates with patients receiving solely systemic antibiotics and mechanical bowel preparation.

The intention of systemic antibiotics is to achieve an adequate concentration in tissues at the time of operation and opening of the colon. There is a belief, however, that intraluminal organisms are unaffected by this, therefore necessitating the use of oral antibiotics. A logical inference from this is that emptying of the colon reduces bacterial load and the three interventions combined would result in the lowest rate of SSI, and potentially other complications.

In a 2018 meta-analysis, Rollins et al. found that combined antibiotics with MBP were associated with a significant reduction in SSI risk when compared with MBP (RR: 0.51) (Fig. 12.2) [7]. This remained the case when assessing solely RCTs or cohort studies. In terms of overall analysis and when considering cohort studies, combined antibiotics were also associated with a reduced risk of anastomotic leak, 30-day mortality, and morbidity. When considering RCTs alone, there was no significant difference. Overall analysis revealed a lower risk of ileus with combined antibiotics, but not when cohort studies or RCTs were analyzed in isolation [7].

In their analysis of RCTs only, Chen et al. found that combined antibiotics with mechanical bowel prep significantly reduced SSI (7.2% vs 16%), but had no effect on organ space SSI [13]. This was in accordance with the findings of Koullouros et al., who arrived at a risk reduction (RR) of 0.48 in favor of a combined rather than unimodal regimen [12].

McSorley et al. found the same when analyzing RCTs for SSI (OR: 0.45) [11]. In addition, when analyzing observational studies, they found significantly reduced rates of anastomotic leak, postoperative ileus, readmission, and mortality. This was not replicated when RCTs were considered (Fig. 12.3) [11]. The World Health Organization (WHO) arrived at similar conclusions with regard to all SSIs, but no difference when assessing anastomotic leak rates (OR: 0.56) (Fig. 12.4) [14].

In their assessment of 19 RCTs, Toh et al. found a significant reduction in SSI rate with combined antibiotics and MBP versus MBP alone, but no difference in terms of other outcome measures (OR: 0.7) [29].

A recent Europe-wide audit by the European Society of Coloproctology (ESCP) looking primarily at anastomotic leak was found in favor of combined antibiotics in addition to MBP. Of note, it also found that less than 20% of participating centers in the study utilized this regimen [31].

This question has also been tackled by a large number of observational studies in the United States. These studies utilize data from large, regional databases concerning colorectal surgery [32–34]. They have all found in favor of combined antibiotics in addition to mechanical bowel preparation. This is the case whether their comparator is unimodal antibiotics with bowel preparation or unimodal antibiotics without bowel preparation.

As mentioned before, analysis of these studies is problematic. A large number of the cases were performed via the open approach. It is also difficult to extract data such as exact site of resection, various relevant patient factors such as comorbidity and fitness, and method of preparation used. Missing data excludes significant numbers from analysis and there is a large potential for selection and reporting bias. While not necessarily negating findings from such studies, it should qualify their interpretation.

Study or subgroup	MBP+OAB Events	MBP+OAB Total	MBP Events	MBP Total	Weight	Risk ratio M–H, random, 95% CI
RCT						
Anjum 2017	8	91	26	93	1.8%	0.31 [0.15, 0.66]
Coppa 1988	9	169	15	141	1.6%	0.50 [0.23, 1.11]
Espin-Basany 2005	15	200	6	100	1.2%	1.25 [0.50, 3.12]
Hanel 1980	0	33	0	34		Not estimable
Hata 2016	21	289	37	290	3.6%	0.57 [0.34, 0.95]
Ikeda 2016	20	255	20	256	2.7%	1.00 [0.55, 1.82]
Ishida 2001	8	72	17	71	1.7%	0.46 [0.21, 1.01]
Kaiser 1983	2	63	7	56	0.4%	0.25 [0.06, 1.17]
Khubchandani 1989	4	55	14	47	0.9%	0.24 [0.09, 0.69]
Kobayashi 2007	17	242	26	242	2.8%	0.65 [0.36, 1.17]
Lau 1988	6	65	7	67	1.0%	0.88 [0.31, 2.49]
Lazorthes 1982	1	30	4	30	0.2%	0.25 [0.03, 2.11]
Lewis 2002	5	104	17	104	1.1%	0.29 [0.11, 0.77]
McArdle 1995	8	82	20	87	1.7%	0.42 [0.20, 0.91]
Monrozies 1983	2	30	5	30	0.4%	0.40 [0.08, 1.90]
Nohr 1990	6	77	7	72	0.9%	0.80 [0.28, 2.27]
Oshima 2013	6	97	22	98	1.4%	0.28 [0.12, 0.65]
Peruzzo 1987	4	39	0	41	0.1%	9.45 [0.53, 169.95]
Playforth 1988	9	61	16	58	1.9%	0.53 [0.26, 1.11]
Reddy 2007	3	22	3	24	0.5%	1.09 [0.25, 4.85]
Reynolds 1989	9	107	26	223	1.9%	0.72 [0.35, 1.49]
Sadahiro 2014	10	99	22	95	2.1%	0.44 [0.22, 0.87]
Stellato 1990	3	51	2	51	0.3%	1.50 [0.26, 8.60]
Takesue 2000	2	38	4	45	0.4%	0.59 [0.11, 3.06]
Taylor 1994	17	159	30	168	3.1%	0.60 [0.34, 1.04]
Uchino 2017	26	163	37	162	4.4%	0.70 [0.44, 1.10]
Subtotal (95% CI)		**2693**		**2685**	**38.3%**	**0.57 [0.48, 0.68]**
Total events	221		390			
Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 27.39$, df = 24 ($P = 0.29$); $I^2 = 12\%$						
Test for overall effect: $Z = 6.28$ ($P < 0.00001$)						
Cohort						
Cannon 2012	311	3400	768	3839	21.6%	0.46 [0.40, 0.52]
Englesbe 2010	17	370	46	370	3.3%	0.37 [0.22, 0.63]
Ichimanda 2017	13	166	25	178	2.4%	0.56 [0.30, 1.05]
Konishi 2006	19	195	52	361	3.8%	0.68 [0.41, 1.11]
Midura 2018	489	16860	895	15175	23.2%	0.49 [0.44, 0. 55]
Ozdemir 2016	16	45	32	45	4.7%	0.50 [0.32 , 0.77]
Rohwedder 1993	3	100	96	718	0.8%	0.22 [0.07, 0.69]
Sun 2017	6	199	10	122	1.1%	0.37 [0.14, 0.99]
Vo 2018	3	40	13	49	0.7%	0.28 [0.09, 0.92]
Subtotal (95% CI)		**21375**		**20857**	**61.7%**	**0.48 [0.44, 0.51]**
Total events	877		1937			
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 6.55$, df = 8 ($P = 0.59$); $I^2 = 0\%$						
Test for overall effect: $Z = 18.91$ ($P < 0.00001$)						
Subtotal (95% CI)		**24068**		**23542**	**100.0%**	**0.51 [0.46, 0.56]**
Total events	1098		2327			
Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 38.14$, df = 33 ($P = 0.25$); $I^2 = 13\%$						
Test for overall effect: $Z = 12.85$ ($P < 0.00001$)						
Test for subgroup differences: $Chi^2 = 3.22$, df = 1 ($P = 0.07$), $I^2 = 69.0\%$						

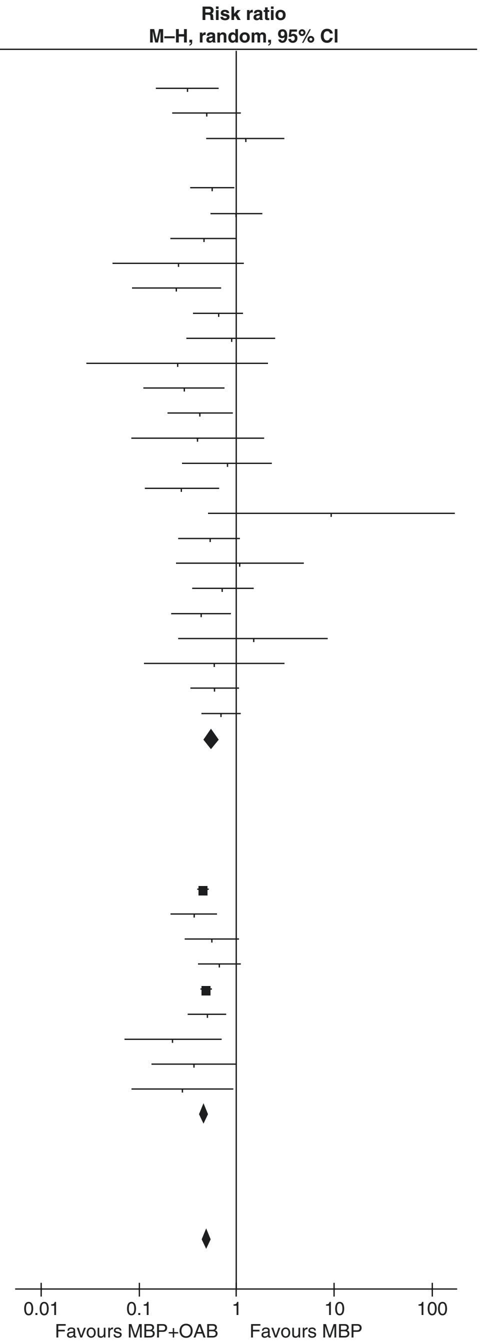


Fig. 12.2 Forest plot comparing surgical site infection rate for patients receiving MBP + OAB versus MBP alone, divided by evidence from RCTs and cohort studies. A Mantel–Haenszel random effects model was used to perform the meta-analysis, and risk ratios are quoted including 95% confidence intervals. (Reprinted with permission from Rollins et al. [7])

Systemic and Oral Antibiotics Without Mechanical Bowel Preparation

Evidence regarding this question is limited. One large retrospective database study from the United States found no benefit to MBP combined with oral and systemic antibiotics when compared with oral and systemic antibiotics alone [35]. Another study of similar methodology found that combined antibiotics in conjunction with MBP was superior [36]. Further papers addressing this issue are scarce. Although small subsets of patients fall into this group in other observational or retrospective studies, the inherent limitations remain.

In their 2018 meta-analysis—assessing four studies that looked at the issue (two RCTs and two cohort studies)—

Reference	SSI rate: Oral antibiotics	SSI rate: Control	Weight (%)	Odds ratio
RCTs				
Barber *et al.*[14]	2 of 31	3 of 28	1·7	0·57 (0·09, 3·72)
Hanel *et al.*[15]	0 of 33	0 of 34		Not estimable
Kaiser *et al.*[16]	2 of 63	7 of 56	4·2	0·23 (0·05, 1.15)
Lau *et al.*[17]	3 of 65	5 of 67	2·8	0·60 (0·14, 2·62)
Reynolds *et al.*[19]	9 of 107	26 of 223	9·1	0·70 (0·31, 1·54)
Khubchandani *et al.*[18]	5 of 55	14 of 47	8·1	0·24 (0·08, 0·72)
Stellato *et al.*[20]	3 of 51	2 of 51	1·1	1·53 (0·24, 9·57)
Ishida *et al.*[21]	8 of 72	17 of 71	9·0	0·40 (0·16, 0·99)
Lewis[22]	5 of 104	17 of 104	9·6	0·26 (0·09, 0·73)
Espin-Basany *et al.*[23]	15 of 200	6 of 100	4·4	1·27 (0·48, 3·38)
Kobayashi *et al.*[24]	6 of 242	14 of 242	8·1	0·41 (0·16, 1·10)
Oshima *et al.*[25]	6 of 97	22 of 98	12·1	0·23 (0·09, 0·59)
Sadahiro *et al.*[26]	6 of 99	17 of 95	9·6	0·30 (0·11, 0·79)
Hata *et al.*[27]	21 of 289	37 of 290	20·2	0·54 (0·31, 0·94)
Subtotal	91 of 1508	187 of 1506	100·0	0·45 (0·34, 0·59)
Heterogeneity: $\chi^2 = 13{\cdot}60$, 12 d.f., $P = 0{\cdot}33$; $I^2 = 12\%$				
Test for overall effect: $Z = 5{\cdot}88$, $P < 0{\cdot}001$				
Cohort studies				
Konishi *et al.*[28]	19 of 195	52 of 361	1·2	0·64 (0·37, 1·12)
Cannon *et al.*[29]	311 of 3400	768 of 3839	22·9	0·40 (0·35, 0·46)
Hendren *et al.*[30]	71 of 1357	281 of 2701	6·2	0·48 (0·36, 0·62)
Scarborough *et al.*[4]	48 of 1494	174 of 2322	4·6	0·41 (0·30, 0·57)
Morris *et al.*[31]	162 of 2486	452 of 3779	11·7	0·51 (0·43, 0·62)
Kiran *et al.*[33]	145 of 2324	462 of 3822	11·5	0·48 (0·40, 0·59)
Moghadamyeghaneh *et al.*[32]	31 of 1386	150 of 2248	3·9	0·32 (0·22, 0·47)
Koller *et al.*[2]	583 of 10643	1210 of 11836	37·9	0·51 (0·46, 0·56)
Subtotal	1370 of 23285	3549 of 30908	100·0	0·47 (0·44, 0·50)
Heterogeneity: $\chi^2 = 13{\cdot}45$, 7 d.f., $P = 0{\cdot}06$; $I^2 = 48\%$				
Test for overall effect: $Z = 22{\cdot}65$, $P < 0{\cdot}001$				
Test for subgroup differences: $\chi^2 = 0{\cdot}10$, 1 d.f., $P = 0{\cdot}75$; $I^2 = 0\%$				

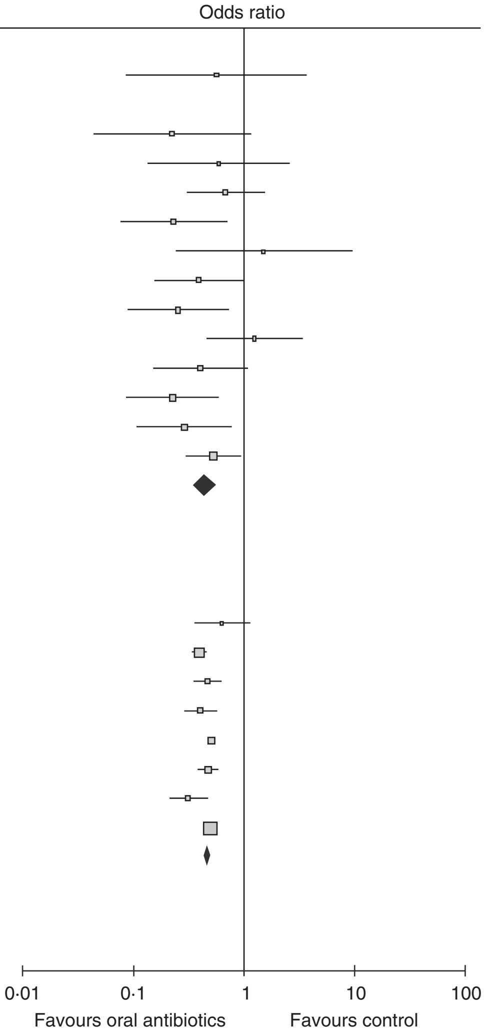


Fig. 12.3 Forest plot of studies that used preoperative oral antibiotics the day before colorectal surgery to prevent surgical-site infection (SSI). A Mantel–Haenszel fixed-effect model was used for meta-analysis. Odds ratios are shown with 95% confidence intervals. (Reprinted with permission from McSorley et al. [11])

Study or subgroup	Oral antibiotics Events	Oral antibiotics Total	No oral antibiotics Events	No oral antibiotics Total	Weight	Odds ratio M-H, random, 95% CI
Espin-Basany 2005	15	200	6	100	9.0%	1.27 [0.48, 3.38]
Horie 2007	10	46	5	45	7.3%	2.22 [0.69, 7.12]
Ishida 2001	8	72	17	71	9.6%	0.40 [0.16, 0.99]
Kobayashi 2007	17	242	26	242	12.9%	0.63 [0.33, 1.19]
Lewis 2002	5	104	17	104	8.4%	0.26 [0.09, 0.73]
Oshima 2013	6	97	22	98	9.2%	0.23 [0.09, 0.59]
Roos 2011	10	143	19	146	10.8%	0.50 [0.23, 1.12]
Sadahiro 2014	10	99	22	95	10.8%	0.37 [0.17, 0.84]
Stellato 1990	6	51	2	51	4.5%	3.27 [0.63, 17.02]
Takesue 2000	2	38	4	45	4.1%	0.57 [0.10, 3.29]
Taylor 1994	18	159	39	168	13.3%	0.42 [0.23, 0.78]
Total (95% CI)		**1251**		**1165**	**100.0%**	**0.56 [0.37, 0.83]**
Total events	107		179			
Heterogeneity: $Tau^2 = 0.22$; $Chi^2 = 20.35$, df = 10 ($P = 0.03$); $I^2 = 51\%$						
Test for overall effect: $Z = 2.85$ ($P = 0.004$)						

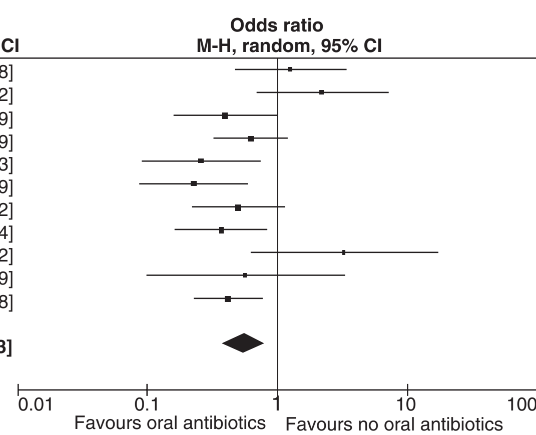


Fig. 12.4 Mechanical bowel preparation (MBP) and oral antibiotics versus MBP and no oral antibiotics, outcome surgical site infection (SSI). M-H Mantel–Haenszel (test), CI confidence interval. (Reproduced with permission from the World Health Organization [42])

Rollins et al. found no difference between combined antibiotics with MBP and combined antibiotics without MBP in terms of SSI and anastomotic leak [6]. The researchers did find a significantly lower 30-day mortality in patients who had MBP and combined antibiotics, and a lower risk of ileus. The researchers did cite concerns regarding limited data to answer this question, however [6]. Toh et al. found no significant difference between combined antibiotics with MBP versus combined antibiotics alone, but, again, the meta-analysis was subject to a limited number of studies—three RCTs [29].

As discussed by Nelson et al. in their Cochrane review, "it is not known whether oral antibiotics would still be effective when the colon is not empty" [15]. Given that evidence exists to highlight the negative aspects of bowel preparation, notwithstanding its unpleasantness, this would appear to be an area of study that should be probed with some urgency [22].

The need for this endeavor highlights another problem however. SSI rates, and indeed other commonly reported complication rates, are relatively low, and by many accounts, reducing [37]. This means that RCTs would require unfeasible numbers of patients to avoid being underpowered. The issues afflicting retrospective database analysis have previously been discussed. This therefore raises the question of how this issue could most appropriately be answered.

With regard to clinical considerations, there are legitimate concerns that routinely giving combined antibiotics to all elective colorectal patients may also increase the rate of *Clostridium difficile* infection, for example. Evidence regarding this is conflicting, and interpretation, as before, should depend on methodological quality [38–40]. There are currently few RCTs or systematic reviews directly assessing this, however, Rollins et al. found no significant difference in rates of infection when comparing patients receiving MBP and combined antibiotics versus those receiving MBP [7].

Regarding antibiotics, an exciting recent area of study concerns the idea that anastomotic dehiscence is less affected by, for example, ischemia, but rather by microbial pathogenesis. In a murine model, Shogan et al. found that topical application of antibiotics that acted on *Enterococcus faecalis*, or indeed direct deactivation of the intestinal metalloproteinase MMP 9, inhibited anastomotic leak [41]. Work in this field may have future implications for type of antibiotics used and may answer whether bowel preparation is a variable in the development of postoperative complications at all.

Site of Resection

Many of the papers discussed show that postoperative complications are more common in patients undergoing rectal surgery versus colonic resections. The use of MBP tends to be lower in colonic surgery [6, 9, 10, 34].

What is scarcely reported on, and subjected to statistical analysis, however, is whether the site of resection has a bearing on whether MBP in addition to various antibiotic regimens may be of benefit. This could be considered as something of a missed opportunity, as many of the papers report the site of resection in their demographic data.

Three review articles sub-categorized groups according to anatomical site of resection. Lobo et al. separately analyzed rectal surgery, but not colonic resections. As stated before, they found no benefit to the use of MBP [6]. Güenaga et al. separately analyzed colonic and rectal resections, finding no benefit to MBP in any site of operation [10]. Dahabreh et al. produced a similar analysis, with concordant results [9].

One of the large database studies [34] was limited to colonic surgery. As discussed before, they were found in favor of bowel preparation with concurrent antibiotic administration [33].

Though more limited in terms of numbers, the findings with regard to the utility of MBP according to anatomical site of location closely mirror those when all colorectal resections are grouped together.

Conclusion

Contemporary thinking regarding mechanical bowel preparation has altered substantially over the past 50 years. This chapter has aimed to delineate current data regarding the overall utility of MBP, in what context and with which simultaneous therapy it may be of benefit. It also highlights where gaps in the scientific literature exist.

There is substantial data that suggests MBP is potentially dangerous, particularly in the comorbid patient. This argument is compounded by the fact that there is a substantial failure rate to bowel preparation and that a poorly prepared bowel can make the operation more technically difficult for the surgeon. There are now several high-quality meta-analyses that concur that there is no benefit to MBP in isolation, both in terms of SSI and anastomotic leak.

Some papers, though few in number, have shown that any benefit to MBP versus no MBP is negated when compared to the use of a rectal enema. A rectal enema carries few, if any, of the risks of MBP and may achieve the same aim of clearing the site of anastomosis. The use of a rectal enema in the context of rectal surgery is therefore an interesting area of future study.

It seems, therefore, that mechanical bowel preparation in isolation should not be recommended. In recent years, however, the question of whether combined oral and systemic antibiotics in addition to MBP may be of benefit in reducing SSI and other complications has been raised. While not as clear-cut an answer, recent meta-analyses are starting to converge on the idea that combined antibiotics combined with MBP confer a benefit when compared with MBP in isolation. This is more apparent in terms of SSI but less so with regard to other complications.

The comparison that has not been answered in the literature is whether combined antibiotics in the absence of MBP are as effective as MBP in addition to combined antibiotics. Given the potentially negative effects of MBP, and at best debatable benefit, it is an area that needs to be explored. This work should be done in the context of the theoretical potential for an increased risk of *Clostridium difficile* infection and other antibiotic-related complications.

While a falling SSI rate is certainly a cause for celebration, it makes answering the last question more difficult. Conducting a modern, adequately randomized RCT is rendered difficult owing to the prohibitively large number of participants that would be required in order to reach statistical significance. The alternative of large prospective database studies can provide useful information, but is limited in its interpretation.

Summary

The question of whether bowel preparation, with or without antibiotics, should be administered "always, sometimes, or never" cannot currently be answered definitively. However, mechanical bowel preparation on its own, in most circumstances, is almost certainly unnecessary and can be detrimental. Whether mechanical bowel preparation should be administered in order to enable or increase the efficacy of orally administered antibiotics awaits further investigation. Surgical site infection, and anastomotic leak in particular, is multifactorial, and it is possible that packages of care and surgical technique that do not include mechanical bowel preparation or oral antibiotics can produce equally good or indeed better outcomes. This is evidenced by studies from single institutions or individual series with much better outcomes than is evident in the large retrospective databases on which much of current guidance is being developed.

References

1. Nygren J, Thacker J, Carli F, Fearon K, Norderval S, Lobo D, Ljungqvist O, Soop M, Ramirez J. Guidelines for peroperative care in elective rectal/pelvic surgery: Enhanced Recovery After Surgery. ERAS. Clin Nutr. 2012;31(6):801–16.
2. Gustafsson UO, Scott MJ, Schwenk W, Demartines N, Roulin D, Francis N, et al. Enhanced Recovery After Surgery (ERAS) society, for perioperative care; European Society for Clinical Nutrition and Metabolism (ESPEN); International Association for Surgical Metabolism and Nutrition (IASMEN). Guidelines for perioperative care in elective colonic surgery: Enhanced Recovery After Surgery (ERAS®) society recommendations. World J Surg. 2013;37(2):259–84.
3. McEvoy MD, Scott MJ, Gordon DB, Grant SA, Thacker JKM, Wu CL, et al. American Society for Enhanced Recovery (ASER) and Perioperative Quality Initiative (POQI) joint consensus statement on optimal analgesia within an enhanced recovery pathway for colorectal surgery: part 1—from the preoperative period to PACU. Perioper Med (Lond). 2017;6:8.
4. Kehlet H. Multimodal approach to control postoperative pathophysiology and rehabilitation. Br J Anaesth. 1997;78(5):606–17.
5. Kulkarni N, Arulampalam T. PTH-310 does laparoscopic surgery reduce the incidence of surgical site infections compared to open surgery for colorectal procedures: systematic review and meta analysis. Gut. 2015;64:A545–6.
6. Rollins KE, Javanmard-Emamghissi H, Lobo DN. Impact of mechanical bowel preparation in elective colorectal surgery: a meta-analysis. World J Gastroenterol. 2018;24(4):519–36.
7. Rollins KE, Javanmard-Emamghissi H, Acheson AG, Lobo DN. The role of oral antibiotic preparation in elective colorectal surgery: a meta-analysis. Ann Surg. 2019;270(1):43–58.
8. Toh JWT, Phan K, Hitos K, Pathma-Nathan N, El-Khoury T, Richardson AJ, et al. Association of mechanical bowel preparation and oral antibiotics before elective colorectal surgery with surgical site infection: a network meta-analysis. JAMA Netw Open. 2018;1(6):e183226.
9. Dahabreh IJ, Steele DW, Shah N, Trikalinos TA. Oral mechanical bowel preparation for colorectal surgery: systematic review and meta-analysis. Dis Colon Rectum. 2015;58(7):698–707.
10. Güenaga KF, Matos D, Wille-Jørgensen P. Mechanical bowel preparation for elective colorectal surgery. Cochrane Database Syst Rev. 2011;9:CD001544.
11. McSorley ST, Steele CW, McMahon AJ. Meta-analysis of oral antibiotics, in combination with preoperative intravenous antibiotics and mechanical bowel preparation the day before surgery, compared with intravenous antibiotics and mechanical bowel preparation alone to reduce surgical-site infections in elective colorectal surgery. BJS Open. 2018;2(4):185–94.
12. Koullouros M, Khan N, Aly EH. The role of oral antibiotics prophylaxis in prevention of surgical site infection in colorectal surgery. Int J Color Dis. 2017;32:1–18.
13. Chen M, Song X, Chen LZ, Lin ZD, Zhang XL. Comparing mechanical bowel preparation with both oral and systemic antibiotics versus mechanical bowel preparation and systemic antibiotics alone for the prevention of surgical site infection after elective colorectal surgery: a meta-analysis of randomized controlled clinical trials. Dis Colon Rectum. 2016;59(1):70–8.
14. Allegranzi B, Bischoff P, De JS, Kubilay NZ, Zayed B, Gomes SM, et al. New WHO recommendations on preoperative measures for surgical site infection prevention: an evidence-based global perspective. Lancet Infect Dis. 2016;16(12):e276–87.
15. Nelson R, Gladman E, Barbateskovic M. Antimicrobial prophylaxis for colorectal surgery. Cochrane Database Syst Rev. 2014;5:CD001181.
16. Lee KJ. Electrolyte changes after bowel preparation for colonoscopy: a randomized controlled multicenter trial. World J Gastroenterol. 2015;21(10):3041–8.
17. Schreiber S. Colon cleansing efficacy and safety with 1 L NER1006 versus sodium picosulfate with magnesium citrate: a randomized phase 3 trial. Endoscopy. 2019;51(1):73–84.
18. Shapira Z, Feldman L, Lavy R, Weissgarten J, Haitov Z, Halevy A. Bowel preparation: comparing metabolic and electrolyte changes when using sodium phosphate/polyethylene glycol. Int J Surg. 2010;8(5):356–8.
19. Belsey J, Epstein O, Heresbach D. Systematic review: Oral bowel preparation for colonoscopy. Aliment Pharmacol Ther. 2007;25(4):373–84.

20. Kazarian ES, Carreira FS, Toribara NW, Denberg TD. Colonoscopy completion in a large safety net health care system. Clin Gastroenterol Hepatol. 2008;6(4):438–42.
21. Mahajna A, Krausz M, Rosin D, Shabtai M, Hershko D, Ayalon A, et al. Bowel preparation is associated with spillage of bowel contents in colorectal surgery. Dis Colon Rectum. 2005;48(8):1626–31.
22. Yamada T, Yokoyama Y, Takeda K, Takahashi G. Negative effects of mechanical bowel preparation on the postoperative intestinal motility of patients with colorectal cancer. In: Fukushima R, Kaibori M, editors. Enhanced recovery after surgery. Singapore: Springer; 2018. p. 101–7.
23. Padmanabhan H, Brooks M, McKaig B, Murugunathan A, Mangalika M, Widak M, et al. Outcomes from the first UK bowel cancer screening programme (BCSP) site: screening and surveillance experience since 2006. Gut. 2015;64(Suppl 1):A211–2.
24. Borg BB, Gupta NK, Zuckerman GR, Banerjee B, Gyawali CP. Impact of obesity on bowel preparation for colonoscopy. Clin Gastroenterol Hepatol. 2009;7(6):670–5.
25. Fayad NF, Kahi CJ, Abd El-Jawad KH, Shin AS, Shah S, Lane KA, et al. Association between body mass index and quality of split bowel preparation. Clin Gastroenterol Hepatol. 2013;11(11):1478–85.
26. Levenstein S, Li Z, Almer S, Barbosa A, Marquis P, Moser G, et al. Predictors of inadequate bowel preparation for colonoscopy. Am J Gastroenterol. 2001;96(6):1797–802.
27. Itani KM, Wilson SE, Awad SS, Jensen EH, Finn TS, Abramson MA. Ertapenem versus cefotetan prophylaxis in elective colorectal surgery. N Engl J Med. 2006;355(25):2640–51.
28. Nichols RL, Broido P, Condon RE, Gorbach SL, Nyhus LM. Effect of preoperative neomycin-erythromycin intestinal preparation on the incidence of infectious complications following colon surgery. Ann Surg. 1973;178(4):453–62.
29. Toh JWT, Phan K, Ctercteko G, Pathma-Nathan N, El-Khoury T, Richardson A, et al. The role of mechanical bowel preparation and oral antibiotics for left-sided laparoscopic and open elective restorative colorectal surgery with and without faecal diversion. Int J Color Dis. 2018;33(12):1781–91.
30. Ali JM, Rajaratnam SG, Upponi S, Hall NR, Fearnhead NS. Colonic transit in the empty colon after defunctioning ileostomy: do we really know what happens? Tech Coloproctol. 2015;19(3):165–72.
31. 2017 European Society of Coloproctology (ESCP) Collaborating Group. Association of mechanical bowel preparation with oral antibiotics and anastomotic leak following left sided colorectal resection: an international, multi-Centre, prospective audit. Color Dis. 2018;20(Suppl 6):15–32.
32. Morris MS, Graham LA, Chu DI, Cannon JA. Oral antibiotic bowel preparation significantly reduces surgical site infection rates and readmission rates in elective colorectal surgery. Ann Surg. 2015;261(6):1034–40.
33. Kiran RP, Murray AC, Chiuzan C, Estrada D, Forde K. Combined preoperative mechanical bowel preparation with oral antibiotics significantly reduces surgical site infection, anastomotic leak, and ileus after colorectal surgery. Ann Surg. 2015;262(3):416–25.
34. Midura EF, Jung AD, Hanseman DJ, Dhar V, Shah SA, Rafferty JF, et al. Combination oral and mechanical bowel preparations decreases complications in both right and left colectomy. Surgery. 2018;163(3):528–34.
35. Garfinkle R, Abou-Khalil J, Morin N, Ghitulescu G, Vasilevsky CA, Gordon P, et al. Is there a role for oral antibiotic preparation alone before colorectal surgery? ACS-NSQIP analysis by coarsened exact matching. Dis Colon Rectum. 2017;60(7):729–37.
36. Kaslow SR, Gani F, Alshaikh HN, Canner JK. Clinical outcomes following mechanical plus oral antibiotic bowel preparation versus oral antibiotics alone in patients undergoing colorectal surgery. BJS Open. 2018;2(4):238–45.
37. European Centre for Disease Prevention and Control. Surgical site infections – annual epidemiological report 2016 (2014 data). October 24, 2016. Available from: https://ecdc.europa.eu/en/publications-data/surgical-site-infections-annual-epidemiological-report-2016-2014-data.
38. Wren SM, Ahmed N, Jamal A, Safadi BY. Preoperative oral antibiotics in colorectal surgery increase the rate of Clostridium difficile colitis. Arch Surg. 2005;140(8):752–6.
39. Krapohl GL, Phillips LR, Campbell DA, Hendren S, Banerjee M, Metzger B, et al. Bowel preparation for colectomy and risk of Clostridium difficile infection. Dis Colon Rectum. 2011;54(7):810–7.
40. Kim EK, Sheetz KH, Bonn J, DeRoo S, Lee C, Stein I, et al. A statewide colectomy experience: the role of full bowel preparation in preventing surgical site infection. Ann Surg. 2014;259(2):310–4.
41. Shogan BD, Belogortseva N, Luong PM, Zaborin A, Lax S, Bethel C, et al. Collagen degradation and MMP9 activation by Enterococcus faecalis contribute to intestinal anastomotic leak. Sci Transl Med. 2015;7(286):286ra68.
42. World Health Organization. WHO surgical site infection prevention guidelines web appendix 6 summary of a systematic review on mechanical bowel preparation and the use of oral antibiotics appendix 4: comparisons. Comparison 1a, page 18. https://www.who.int/gpsc/appendix6.pdf?ua=1. Accessed 29 June 2019.