The Role of Oral Antibiotic Preparation in Elective Colorectal Surgery

A Meta-analysis

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Objectives: To compare the impact of the use of oral antibiotics (OAB) with or without mechanical bowel preparation (MBP) on outcome in elective colorectal surgery.

Summary Background Data: Meta-analyses have demonstrated that MBP does not impact upon postoperative morbidity or mortality, and as such it should not be prescribed routinely. However, recent evidence from large retrospective cohort and database studies has suggested that there may be a role for combined OAB and MBP, or OAB alone in the prevention of surgical site infection (SSI).

Methods: A meta-analysis of randomized controlled trials and cohort studies including adult patients undergoing elective colorectal surgery, receiving OAB with or without MBP was performed. The outcome measures examined were SSI, anastomotic leak, 30-day mortality, overall morbidity, development of ileus, reoperation and *Clostridium difficile* infection.

Results: A total of 40 studies with 69,517 patients (28 randomized controlled trials, n = 6437 and 12 cohort studies, n = 63,080) were included. The combination of MBP+OAB versus MBP alone was associated with a significant reduction in SSI [risk ratio (RR) 0.51, 95% confidence interval (CI) 0.46–0.56, P < 0.00001, I² = 36%], anastomotic leak (RR 0.62, 95% CI 0.55–0.70, P < 0.00001, I² = 0%), 30-day mortality (RR 0.58, 95% CI 0.44–0.76, P < 0.00001, I² = 0%), overall morbidity (RR 0.67, 95% CI 0.63–0.71, P < 0.00001, I² = 0%), and development of ileus (RR 0.72, 95% CI 0.52–0.98, P = 0.04, I² = 36%), with no difference in *Clostridium difficile* infection rates. When a combination of MBP+OAB was compared with OAB alone, no significant difference was seen in SSI or anastomotic leak rates, but there was a significant reduction in 30-day mortality, and incidence of postoperative ileus with the combination. There is minimal literature available on the comparison between combined MBP+OAB versus no preparation, OAB alone versus no preparation, and OAB versus MBP.

Conclusions: Current evidence suggests a potentially significant role for OAB preparation, either in combination with MBP or alone, in the prevention of postoperative complications in elective colorectal surgery. Further high-quality evidence is required to differentiate between the benefits of combined MBP+OAB or OAB alone.

Keywords: anastomotic leak, colorectal, mechanical bowel preparation, oral antibiotics, surgery, surgical site infection

*Surgical site infection (SSI) is a major burden for patients undergoing elective colorectal surgery. It adds significantly to the cost of health care, and administration of preoperative bowel preparation has been proposed to reduce the incidence of SSI. The role of mechanical bowel preparation (MBP) with polyethylene glycol or sodium phosphate has been studied in randomized controlled trials (RCTs), with perceived benefits including ease of manipulation of the bowel, reduced spillage and resultant contamination, reduced luminal pressure, and lesser bacterial load. However, a recent meta-analysis of 36 RCTs and cohort studies, and an earlier one of 14 RCTs found that the administration of MBP did not impact upon postoperative morbidity or mortality. This, in combination with high rates of patient dissatisfaction and fluid and electrolyte disturbances, has led to the conclusion that MBP should not be prescribed routinely. This is reflected in Guidelines from the Enhanced Recovery After Surgery Society, the National Institute of Health and Care Excellence, and the American Society for Enhanced Recovery, all of which suggest that MBP should not be administered routinely. However, although the American Society for Enhanced Recovery guidelines suggest that MBP should not be given in isolation, they recommend routine use of an isosmotic bowel preparation and combined oral antibiotic prior to elective colorectal surgery.

The use of oral antibiotic (OAB) prophylaxis, in the form of nonabsorbable luminal antibiotics, was first proposed in 1971 by Rosengerg et al in a RCT of 150 patients undergoing large bowel surgery receiving MBP alone, or MBP in combination with phthalyl-sulphathiazole or phthalysulphathiazole and neomycin. The combination of MBP+OAB was associated with a significant reduction in SSI (23% vs. 40%), anastomotic leak rates (24% vs. 52%), and sepsis rates (33% vs. 64%). Although several studies provided evidence for the role of oral antibiotics in elective colorectal surgery, the regimens included large volume preparations, prolonged preoperative hospital admission, and in the setting of prolonged preoperative starvation protocols, dehydration, and electrolyte disturbances were commonplace. Decreased compliance and inconsistent bowel...
cleansing resulted in a reduced intervention effect and, this, combined with reduced preoperative admission times, resulted in the practice of combined MBP+OAB dwindling in favor of more restrictive MBP regimens alone. However, recently there has been resurgent interest in the use of OAB in colorectal surgery, particularly in light of a large number of retrospective cohort and database studies, many of which originated from the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) targeted colectomy database. Evidence for the role of OAB has been summarized in several narrative reviews as well as meta-analyses, which have supported a reduction in SSI associated with combined MBP, OAB, and parenteral antibiotics over MBP and parenteral antibiotics alone. However, the most recent of these studies have been flawed in their inclusion of multiple studies based on the NSQIP database which have large degrees of cross-over of the same study population and have mostly focused upon SSI alone rather than other postoperative outcomes. In addition, recent studies have suggested that OAB alone may provide equivalent prophylaxis in terms of SSI and anastomotic leak rates when compared with a combined regimen of MBP+OAB.

The aims of this meta-analysis of RCTs and observational cohort studies in patients undergoing elective colorectal surgery were to:

- Compare the impact of OAB with or without MBP in elective colorectal surgery in terms of SSI, anastomotic leak, 30-day mortality, overall morbidity, development of ileus, reoperations, and Clostridium difficile infection.
- Compare evidence derived from RCTs and cohort studies.
- Compare the role of administration of OAB with and without MBP in the setting of laparoscopic versus open surgery.

METHODS

Search Strategy

The PubMed, Google Scholar, MEDLINE, and the Cochrane Library databases were searched to identify studies evaluating the effect of OAB in adults undergoing elective colorectal surgery published between January 1, 1981 and May 30, 2018. This date restriction was imposed as recommendations that parenteral antibiotics should be administered routinely for prophylaxis against SSI in colorectal surgery were made in 1981 and it was felt that all studies considering the role of oral prophylaxis should include parenteral antibiotic prophylaxis to reflect current perioperative care. The search terms used were: (oral antibiotic OR oral antibacterial) AND (colon OR rectal OR colorectal) AND surgery.

Data were entered into RevMan 5.3 software. Dichotomous variables were calculated as risk ratios (RR) with a 95% confidence interval using the Mantel–Haenszel random effects model. From this, forest plots were derived, with a P value of less than 0.05 on 2-tailed testing representing a statistically significant difference. Data from RCTs and cohort studies were included separately within each forest plot, with a summative analysis of all the evidence performed in addition. Inconsistency and heterogeneity between studies were estimated using the I² statistic; ≤25% represented low heterogeneity, 25% to 50% represented moderate, and >50% high heterogeneity.

Protocol Registration

The protocol for this meta-analysis was registered with the PROSPERO database (www.crd.york.ac.uk/prospero)—registration number CRD42018098950.

RESULTS

From the 520 studies identified in the initial search, 40 studies on 69,517 participants were included (Supplementary Figure 1, http://links.lww.com/SLA/B542). Of these
28 were RCTs with 6437 participants\textsuperscript{49–53,55–67,69–73,75,76,78–80,83} and 12 were cohort (case control) studies with 63,080 participants.\textsuperscript{31,41,43,45,46,54,60,68,74,77,81,82} The risk of bias in the RCTs included was variable, with poor levels of documentation particularly surrounding randomization methods, allocation concealment, and blinding in the earlier studies (Table 1). Six studies\textsuperscript{57,58,62,64–66} administered different parenteral antibiotic regimens depending upon whether the patient was receiving MBP + OAB or MBP alone, which may provide significant source of bias in terms of SSI prevention. In addition, 1 study\textsuperscript{73} included 2 differing parenteral antibiotic regimens, both in combination with MBP, versus OAB, MBP and parenteral antibiotics. As both of the parenteral antibiotic regimens were considered eligible for inclusion, these were grouped together to form the MBP alone group. In terms of oral antibiotics, 2 studies administered OAB preparation only on the day of surgery; one\textsuperscript{64} gave ciprofloxacin 1 g 1 hour preoperatively and the other\textsuperscript{54} ciprofloxacin 750 mg 1 to 3 hour preoperatively. A subgroup of another study\textsuperscript{31} received only 1 dose of OAB the day before surgery, with the remainder receiving 3 doses. These 3 studies may, therefore, have an attenuated the intervention effect from the OAB administered.

### Patient Demographics

Two studies\textsuperscript{53,55} focused on surgery using laparoscopic techniques, 21 on open surgery alone,\textsuperscript{46,50,52,58,61,68,74,76,78,80} with 9 studies\textsuperscript{31,41,43,45,51,54,60,75,77,81,82} mixing both open and laparoscopic techniques and the remaining 8 studies not providing this information.\textsuperscript{31,43,51,53,59,61,78,83} The most recent publication\textsuperscript{31} included patients undergoing robotic surgery. The indication for surgery was colorectal cancer in 8 studies,\textsuperscript{46,54,55,59,61,75,78,81} inflammatory bowel disease in 2\textsuperscript{80} with the remaining including a mixture of benign and malignant pathologies. Patient demographics and

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**Table 1. Risk of Bias Within Randomized Controlled Trials Included Within the Meta-analysis**

| Reference               | Random Sequence Generation | Allocation Concealment | Blinding of Participants and Personnel | Blinding of Outcome Assessment | Incomplete Outcome Data | Selective Reporting | Other Bias                                                                 |
|-------------------------|----------------------------|------------------------|----------------------------------------|-------------------------------|------------------------|----------------------|-----------------------------------------------------------------------------|
| Anjum et al 2017\textsuperscript{49} | +                         | +                      | ?                                      | +                             | +                      | +                    | 36 patients in the MBP+OAB group received reduced doses of kanamycin due to prescription error |
| Coppa et al 1998\textsuperscript{50} | ?                         | ?                      | –                                      | –                             | +                      | +                    |                                                                                           |
| Espin-Basany et al 2005\textsuperscript{51} | ?                         | ?                      | –                                      | –                             | –                      | –                    |                                                                                           |
| Hanel et al 1980\textsuperscript{52} | –                         | ?                      | –                                      | +                             | –                      | –                    |                                                                                           |
| Hata et al 2016\textsuperscript{53} | +                         | +                      | –                                      | –                             | +                      | +                    |                                                                                           |
| Ikeda et al 2016\textsuperscript{54} | +                         | –                      | –                                      | +                             | +                      | –                    | Different IV antibiotic regimens given to the 2 groups                           |
| Ishida et al 2001\textsuperscript{55} | –                         | –                      | –                                      | –                             | –                      | –                    | Different IV antibiotic regimens given to the 2 groups                           |
| Kaiser et al 1983\textsuperscript{56} | ?                         | +                      | +                                      | +                             | +                      | –                    |                                                                                           |
| Khubchandani et al 1989\textsuperscript{57} | ?                         | ?                      | +                                      | +                             | –                      | –                    |                                                                                           |
| Kobayashi et al 2007\textsuperscript{58} | +                         | ?                      | –                                      | –                             | –                      | –                    |                                                                                           |
| Lau et al 1988\textsuperscript{59} | –                         | ?                      | –                                      | –                             | –                      | –                    |                                                                                           |
| Lazorthes et al 1982\textsuperscript{60} | ?                         | ?                      | ?                                      | ?                             | ?                      | ?                    | Different IV antibiotic regimens given to the 2 groups                           |
| Lewis 2002\textsuperscript{61} | –                         | –                      | +                                      | +                             | +                      | +                    | Different IV antibiotic regimens given to the 2 groups                           |
| McArle et al 1995\textsuperscript{62} | ?                         | ?                      | ?                                      | ?                             | +                      | ?                    | Different IV antibiotic regimens given to the 2 groups                           |
| Monroeies et al 1983\textsuperscript{63} | ?                         | ?                      | ?                                      | ?                             | +                      | ?                    | Different IV antibiotic regimens given to the 2 groups                           |
| Nohr et al 1990\textsuperscript{64} | ?                         | ?                      | +                                      | +                             | –                      | –                    | Different IV antibiotic regimens given to the 2 groups                           |
| Oshima et al 2013\textsuperscript{65} | ?                         | ?                      | –                                      | –                             | +                      | +                    |                                                                                           |
| Peruzzo et al 1987\textsuperscript{66} | ?                         | ?                      | ?                                      | ?                             | +                      | +                    | Group also randomized to probiotics—not included within meta-analysis            |
| Playforth et al 1988\textsuperscript{67} | ?                         | ?                      | ?                                      | ?                             | +                      | +                    | Two different IV antibiotic regimens in the MBP group                           |
| Ram et al 2005\textsuperscript{68} | –                         | –                      | ?                                      | ?                             | +                      | +                    | Group also randomized to probiotics—not included within meta-analysis            |
| Reddy et al 2007\textsuperscript{69} | +                         | +                      | –                                      | –                             | +                      | +                    |                                                                                           |
| Reynolds et al 1989\textsuperscript{70} | +                         | –                      | ?                                      | ?                             | –                      | –                    |                                                                                           |
| Sadahiro et al 2014\textsuperscript{71} | +                         | –                      | +                                      | +                             | ?                      | ?                    |                                                                                           |
| Stellato et al 1990\textsuperscript{72} | +                         | ?                      | +                                      | +                             | –                      | –                    |                                                                                           |
| Takesue et al 2000\textsuperscript{73} | ?                         | ?                      | ?                                      | ?                             | –                      | –                    |                                                                                           |
| Taylor et al 1994\textsuperscript{74} | –                         | +                      | –                                      | –                             | +                      | +                    |                                                                                           |
| Uchino et al 2017\textsuperscript{75} | +                         | +                      | –                                      | –                             | –                      | –                    | C difficile toxin and faecal cultures only preop                                   |
| Zmora et al 2003\textsuperscript{76} | +                         | +                      | ?                                      | ?                             | –                      | –                    |                                                                                           |

$+$ indicates low risk of bias; $–$, high risk of bias; $?$, unclear risk of bias.
### TABLE 2. Summary of Studies Included

| Reference          | Study Methodology                  | Number of Patients | Indication for Surgery                      | Type of Resection | Laparoscopic or Open | OAB Agent                  | MBP Agent             | Parenteral Antibiotics                              | Comparison Included                                       |
|--------------------|-----------------------------------|--------------------|---------------------------------------------|-------------------|----------------------|---------------------------|------------------------|-----------------------------------------------------|---------------------------------------------------------|
| Anjum et al 2017<sup>29</sup> | RCT                              | 190                | Gastrourinary tract fistula                  | Right colicetomy—47 | Laparoscopic—40        | Metronidazole 400 mg and levofloxacin 200 mg TDS on the day before surgery | Sodium phosphate 133 mL, twice a day on the day before surgery | Second generation cephalosporin + metrotetracycline 30–40 min preincision, every 3 h intrap, then 24 h postop | MBP vs. OAB vs. MBP                                    |
| Cooney et al 2012<sup>27</sup> | Retrospective database study—Veterans Affairs Surgical Quality Improvement Program | 9440               | Malignancy Neoplasm—7617                  | Right colicetomy—844 | Partial colicetomy—6847 | Polyethylene glycol, phospho-soda or magnesium citrate | Not stated | Not stated | MBP vs. OAB vs. MBP                                  |
| Coppa et al 1988<sup>11</sup> | RCT                              | 350                | Cancer—255 Inflammatory—46                 | Not stated—1248    | Not stated            | Neomycin 8 g and erythromycin 4 g, then 5 g divided doses for 24 h preop | Flecithophos-soda 20% 9% Phospho-soda 5% Flecithenemycin 38.5% | Neomycin 1 g given preoperatively, then 3 g every 6 h for the first 24 h | MBP vs. OAB vs. MBP                                    |
| Englesbe et al 2005<sup>15</sup> | RCT                              | 740                | Retrospective propensity-matched database study—Michigan Surgical Quality Collaborative—Colostomy Best Practices Project | Not stated—2031 | Neomycin and erythromycin 76.3% | Neomycin alone 7.9% | MBP vs. OAB vs. MBP                                  |
| Espin-Brassey et al 2006<sup>31</sup> | RCT                              | 300                | Cancer—269 BDI—21                          | Segmental resection—120 | Not stated—60          | Neomycin 1 g and metronidazole 1 g EFTER TDS the day before surgery | Sodium phosphate 0.5 mL diluted in 90 mL water, HD the day before surgery | Ceftriaxin 1 g preincision and two doses at 8 and 16 h postop | MBP vs. OAB vs. MBP                                    |
| Hata et al 1980<sup>7</sup> | RCT                              | 77                 | Adenoma—2 Carcinoma—48                    | Right colicetomy—15 | Not stated—60          | Neomycin 1 g and metronidazole 1 g EFTER TDS the day before surgery | Four day standard mechanical preparation including a low residue diet, and alternating enemas or washouts. | Clindamycin 7 mg/kg and neomycin 1 g, given at the start of the anesthetic | MBP vs. OAB vs. MBP                                    |
| Ishida et al 2003<sup>16</sup> | RCT                              | 143                | Colorectal malignancy Adenoma               | Colitis—376       | All laparoscopic       | Kanamycin 1 g and metronidazole 750 mg BD at 13 h and 9 h preop | Sodium psoresulfate 75 mg and magnesium citrate 34 g with 800 mL water, HD the day before surgery | Cefmetazole 1 g 30 min preincision then every 3 h intraop | MBP vs. OAB vs. MBP                                    |
| Ichimanda et al 2017<sup>33</sup> | Retrospective controlled series | 344                | All colorectal cancer                      | Not stated—181     | Laparoscopic—293       | Kanamycin 1 g TDS and metronidazole 1 g TDS for 24 h prior to surgery | Polyethylene glycol 2 L and mannitol (Paluverd) 24 mg | Second generation cephalosporin on the day of surgery until the second postop day | MBP vs. OAB vs. MBP                                    |
| Ikeda et al 2016<sup>6</sup> | RCT                              | 511                | Colorectal malignancy                      | Colonic surgery—309 | All laparoscopic       | Kanamycin 1 g and metronidazole 750 mg BD at 13 h and 9 h preop | Magnesium citrate and sodium phosphate the day before surgery | Ceftriaxin 1 g at least 30 min preincision, every 3 h intraop and for 24 h postop | MBP vs. OAB vs. MBP                                    |
| Ishida et al 2003<sup>16</sup> | RCT                              | 143                | Cancer—135 BDI—4                          | Colicetomy—76      | Not stated—3          | Kanamycin 2 g and erythromycin 1.6 g divided doses from 2.4 prior to surgery | Polyethylene glycol 2 L given the day before surgery | Ceftriaxin 1 g after radiation, 1 g at one hour after completion of surgery and 4 additional doses given HD for 2 consecutive days | MBP vs. OAB vs. MBP                                    |
TABLE 2. (Continued)

| Reference | Study Methodology | Number of Patients | Indication for Surgery | Type of Resection | Laparoscopic or Open | OAB Agent | MBP Agent | Parenteral Antibiotics | Comparison Included |
|-----------|-------------------|--------------------|------------------------|-------------------|----------------------|-----------|-----------|-----------------------|---------------------|
| Kaiser et al 1983 | RCT | 119 | Local malignancy—50 Metastatic malignancy—30 Diverticulitis—17 Polyps—9 HBD—9 | Right colectomy—34 Left colectomy—25 Sigmoid resection—25 APR—11 Anterior resection—7 Subtotal colectomy—6 Operative colostomy—6 Total colectomy—3 Colostomy closure—2 | All open | Neomycin 1 g TDS and erythromycin 1 g TDS the day prior to surgery | Magnesium citrate and cleansing enemas for 2 days prior to surgery | Cefazolin 2 g with the 'on call' medications, 1 g intraoperatively and 1 g every 6 h following surgery for four doses in the MBP alone group | MBP+ OAB vs. MBP |
| Khoshsandani et al 1989 | RCT | 155 | Colonic surgery | Not stated | Broccoli reaction with anastomosis Segmental colectomy with anastomosis | Laparoscopic—465 | Not stated | Not stated | Neomycin 1 g and erythromycin 1 g at 12 h the day before surgery | MBP+ OAB vs. MBP |
| Kim et al 2014 | Retrospective propensity-matched database study— Michigan Surgical Quality Collaborative— Colectomy Best Practices Project | 1914 | Not stated | Colon—248 Rectum—243 | Open—1049 Laparoscopic—465 | Neomycin 1 g and erythromycin 1 g at 12 h the day before surgery | Cefazolin 1 g given 1 h before surgery, then 500 mg at 6 and 12 h postop in MBP alone group | MBP+ OAB vs. MBP |
| Kobayashi et al 2007 | RCT | 484 | Colorectal malignancy Surgical procedure: Colon—248 Rectum—243 | Not stated | Kanamycin 1 g and erythromycin 400 mg TDS the day before surgery | Polyethylene glycol 2 L the morning of the day before surgery | Cefotaxime 1 g at induction, an additional dose if operation exceeded 3 h, then BD for 3 days postop. | MBP+ OAB vs. MBP |
| Kim et al 2006 | Retrospective case controlled series— National Nosocomial Infection Surveillance program | 556 | Not stated | Right colectomy—94 Left colectomy—155 Other colectomy—90 LAR—126 APR—51 Total colectomy or proctocolectomy—34 Hartmann’s procedure—6 Additional concomitant procedures: Osmotic closure—47 Osmotic formation—106 Multiple organ reaction—93 | Laparoscopic—465 | Neomycin 1 g and erythromycin 1 g at 12 h the day prior to surgery | Metronidazole 500 mg and gentamycin 2 mg/kg body weight given 30 min prior to incision repeated every 3 h intraop and stopped within 24 h after the operation | MBP+ OAB vs. MBP |
| Lai et al 1984 | RCT | 194 | All cancer | Right colectomy—39 Left colectomy—7 Sigmoid resection—9 | All open | Neomycin 1 g and erythromycin 1 g at 12 h the day prior to surgery | Metronidazole 500 mg and gentamycin 2 mg/kg body weight given 30 min prior to surgery, then repeated at 8 h intervals for two further doses | MBP+ OAB vs. MBP |
| Lau et al 1982 | RCT | 90 | Cancer—51 Colostomy closure—23 Benign disease—46 | All open | Kanamycin 1 g QDS and metronidazole 1 g QDS for 3 days prior to surgery | Three days of low residue diet, enemas and magnesium sulphate enemas | MBP+ OAB vs. MBP |

References:
1. RCT = Randomized Controlled Trial
2. Retrospective = Retrospective study
3. Prospective = Prospective study
4. Propensity-matched = Propensity-matched study
5. Case-controlled = Case-controlled study
6. Retrospective Case-Controlled = Retrospective Case-Controlled study

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| Reference            | Study Methodology | Number of Patients | Indication for Surgery | Type of Resection | Laparoscopic or Open | OAB Agent | MBP Agent | Parenteral Antibiotics | Comparison Included |
|----------------------|-------------------|--------------------|------------------------|-------------------|----------------------|------------|-----------|-----------------------|---------------------|
| Lessons et al 2002   | RCT               | 208                | Cancer — 150, IBD — 55, Diverticular disease — 15 | Colon resection — 55, Rectal resection — 15, Right colectomy — 15 | All open | Neomycin 3 g and metronidazole 2 g | Sodium phosphate the day before surgery, with saline enema if this did not result in a clear effluent | MBP vs. OAB vs. MBP |
| McArdle et al 1995   | RCT               | 169                | Cancer (cancer related) — 151, Diverticular disease — 15 | Colon resection — 15, Right colectomy — 15, Transverse colectomy — 15 | All open | Ciprofloxacin 1 g 1 h prior to surgery | Gentamycin 120 mg + metronidazole 900 mg at induction, one group received gentamycin 90 mg + metronidazole 300 mg at 8 and 16 h postop and one group received gentamycin 90 mg + metronidazole 300 mg TDS for 3 days. | MBP vs. OAB vs. MBP |
| Midura et al 2018     | Database study — ACS NSQIP | 45,724             | Cancer, Diverticulitis, Others | Colon resection — 43, Right colectomy — 17, Small bowel resection — 14 | All open | Magnesium sulphate and enemas | Ceftriaxone 1 g, and metronidazole 1 g | MBP vs. MBP |
| Mik et al 2016       | Retrospective cohort study | 2240               | Colorectal malignancy | Colon resection — 43, Right colectomy — 17, Small bowel resection — 14 | All open | Ceftriaxone 1 g, and metronidazole 1 g | Ceftriaxone 1 g, and metronidazole 1 g directly before incision, and broadened to 3 doses if surgery lasted longer than 3 h | MBP vs. MBP |
| Montesinos et al 1983 | RCT               | 60                 | Cancer — 34, Closure of colostomy — 35, Benign — 18 | Colon resection — 35, Right colectomy — 15, Others — 10 | All open | Magnesium sulphate and enemas | Ceftriaxone 1 g, and metronidazole 1 g | MBP vs. MBP |
| Nohe et al 1990      | RCT               | 149                | Cancer — 116, Complicated diverticulitis — 9, Crohn’s disease — 8 | Colon resection — 29, Right colectomy — 19, Others — 27 | All open | Flucloxacillin 2 tablets 2 days preop and magnesium sulphate (75 mg) daily for 2 d postop | Ampicillin 1 g within 1 h preop in MBP/OAB group | MBP vs. OAB vs. MBP |
| Oshita et al 2013     | RCT               | 200                | Ulcerative colitis | Restorative proctocolectomy with ileal pouch-anal anastomosis (IPAA) | All open | Magnesium citrate 1.8 L the day before surgery | Flomoxef 30 min before surgery, repeated every 3 h intraop and then 24 h postop | MBP vs. OAB vs. MBP |
| Oudekerk et al 2016   | Retrospective cohort study | 90                 | Colonic malignancy | Colon resection — 17, Right colectomy — 10, Transverse colectomy — 9 | All open | Sodium bicarbonate 45 mL, BD at 12 and 10 h postop, first enema 8 and 3–4 h postop | Ceftriaxone 1 g and metronidazole 1 g during anesthetic induction, continued BD for 5 d postop. | MBP vs. MBP |
### TABLE 2. (Continued)

| Reference                  | Study Methodology | Number of Patients | Indication for Surgery | Type of Resection | Laparoscopic or Open | OAB Agent | MBP Agent | Parenteral Antibiotics | Comparison Included |
|---------------------------|------------------|--------------------|------------------------|-------------------|----------------------|-----------|-----------|----------------------|---------------------|
| Penato et al 1987         | RCT              | 80                 | Cancer—61              | Right colectomy—17| All open             | Neomycin 1 g at 19, 18 and 9 h preop and 2 g oral tinidazole | According to standard practice. | MBP vs. OAB         |
| Playforth et al 1988      | RCT              | 119 + 83 men randomized cohort (not included) | Cancer (curative)—66 | Right colon—38 | All open             | Neomycin 1 g every 6 h and metronidazole 300 mg every 8 h for 24 h prior to surgery | Metronidazole 500 mg at the time of premedication | MBP vs. OAB         |
| Ram et al 2003            | RCT              | 329                | Cancer—268             | Right colectomy—42| All open             | Neomycin 1 g in 1 L water the day before surgery | Metronidazole 500 mg and ceftiraxone 1 g given 1 h preinduction and continued for 48 h postop. | MBP vs. OAB         |
| Reddy et al 2007          | RCT              | 92 (46 pertinent to Cancer and benign this meta-analysis) | Cancer—247 Benign—61 | Left colectomy—16 | All open             | Sodium piosulfate and magnesium citrate given the day before surgery | Not stated | MBP vs. OAB         |
| Reynolds et al 1989       | RCT              | 330                | Cancer—247 Benign—5    | Right colectomy—65| All open             | Metronidazole 400 mg given 1 h prior to surgery | Magnesium sulphate up to 8 h + 4 g doses for 48 h starting 2 h preop. Followed by two doses of sodium piosulfate the day before surgery | MBP vs. OAB         |
| Rohleder et al 1993       | Retrospective historical case controlled (100 MBP vs. OAB, 718 MBP) | 818                 | Of those with MBP: OAB | Right colectomy—14 | All open             | Ciprofloxacin 750 mg taken between 1 and 3 h preop | Gentamycin 80 mg and metronidazole 300 mg at the beginning of induction, then gentamycin 80 mg every 8 h for 3 d | MBP vs. OAB         |
| Sadahiro et al 2014       | RCT              | 294                | Colorectal malignancy 89 | Right colectomy—23 | Open—214             | Kanamycin sulphate 500 mg + metronidazole 500 mg preop and 2 L polyethylene glycol the day before surgery | Sodium piosulfate 10 mL 2 days preop and 2 L polyethylene glycol the day before surgery | MBP vs. OAB         |
| Stellato et al 1990       | RCT              | 146                | Cancer—123 Polyp—11    | Right colectomy—44| All open             | Neomycin 1 g and oxytetracycline 1g TDS on the day before surgery | Magnesium citrate 1.745 g in 296 mL in the morning and an enema 19 g sodium biphosphate and 7 g sodium phosphate in 118 mL in the evening 2 days prior to surgery | MBP vs. OAB         |
|                           |                  |                    | Diverticular disease—2 | Left colectomy—17 |                    | Magnesium citrate 1.745 g in 296 mL in the morning and an enema (19 g sodium biphosphate and 7 g sodium phosphate in 118 mL in the evening 2 days prior to surgery) | Magnesium citrate 1.745 g in 296 mL in the morning and an enema until clear in the evening of the day before surgery | MBP vs. OAB         |
### TABLE 2. (Continued)

| Reference | Study Methodology | Number of Patients | Indication for Surgery | Type of Resection | Laparoscopic or Open | OAB Agent | MBP Agent | Parenteral Antibiotics | Comparison Included |
|-----------|-------------------|--------------------|------------------------|-------------------|----------------------|------------|----------|------------------------|---------------------|
| Sun et al 2018<sup>14</sup> | Retrospective case controlled series | 321 | Malignancy—306  Benign—12 | Right colectomy—46  Left colectomy—24  Sigmoid colectomy—65 | Laparoscopic or Open | Neomycin 1 g and erythromycin 1 g at 20 and 10 h prior to surgery | Fleet phospho-soda 45 mL  Cefazolin 1 g at induction | MBP vs OAB vs MBP |
| Takesue et al 2000<sup>15</sup> | RCT | 83 | Dukes A—16  Dukes B—43  Dukes C—24 | Right colectomy—5  Left colectomy—3  Transverse colectomy—6 | All open | Kanamycin 500 mg and metronidazole 500 mg at 2 h, 3 h, 11 h the day before surgery | Polymethylglycol commence at 10 am the day before surgery | MBP vs OAB vs MBP |
| Taylor et al 1994<sup>16</sup> | RCT | 327 | Benign—53  Cancer—259  IBD—15 | Anastomosis right colon—93  Anastomosis left colon/rectum—168  Hartmann’s resection—6 | Ciprofloxacin 500 mg BD the day before surgery | Sodium picosulfate one sachet BD the day before surgery | Penicillin 4 g at induction of anesthesia | MBP vs OAB vs MBP |
| Uchino et al 2017<sup>17</sup> | RCT | 325 | Crohn’s disease | Small bowel resection | All open | Kanamycin 500 mg and metronidazole 500 mg TDS the day before surgery | Sodium picosulfate hydrate (20 mL of 0.75%) preoperatively  Flomoxef sodium 30 min before surgery, every 3 h intraperitoneally then 24 h postoperatively | MBP vs OAB vs MBP |
| Vo et al 2018<sup>18</sup> | Retrospective case controlled series | 89 | Colorectal cancer | Left colectomy—14  Sigmoid colectomy—16  LAR—35  APR—14  Subtotal colectomy or other—10 | Open—21  Minimally invasive—68  Commenced one day prior to surgery | Neomycin sulphate 1 g and metronidazole hydrochloride 1 g TDS 246 mL twice daily  Commenced 1 d prior to surgery | Flupred-nomethasone—42  Non-steroid—7 | MBP vs OAB vs MBP |
| Wren et al 2005<sup>19</sup> | Retrospective case controlled study | 304 | Not stated | Colon and/or rectal resection—258  Colostomy creation or take down—46 | Open and laparoscopic | Neomycin 1 g and erythromycin 1 g  Gel, TYLEIY, magnesium citrate or Fleet phospho-soda | Cefazolin and metronidazole 39.2%  Second generation cephalosporin 21.0%  Piocillin and metronidazole or clindamycin 9.5%  First-generation cephalosporin alone 3.9%  Extended-spectrum penicillin 16% | MBP vs OAB vs MBP |
| Zmora et al 2003<sup>20</sup> | RCT | 380 | Cancer—266  Diverticulitis disease—16  Hartmann’s procedure (for closure)—29  Benign polyp—14  IBD—12  Not stated—12 | Right colectomy—113  Left colectomy—33  Sigmoidectomy—89  Anterior resection—83  Closure of Hartmann’s—29  Subtotal/total abdominal colectomy—24  Total proctectomy and ileal pouch—9 | Not stated | Neomycin and erythromycin | Polymethylglycol 1 gallon 12 to 16 h prep  Oral surgery—given Fleet enema | MBP vs OAB vs OAB |

APR indicates abdominopereanal resection; IBD, inflammatory bowel disease; LAR, low anterior resection; MBP, mechanical bowel preparation; OAB, oral antibiotics; RCT, randomized controlled trial.
surgical variables as well as the details of MBP, OAB, and parenteral antibiotics administered are detailed in Table 2.

Surgical Site Infection (SSI)

**MBP+OAB Versus MBP**

The comparison between MBP+OAB versus MBP alone was performed in 35 studies; 26 RCTs and 9 cohort studies with a total of 47,610 patients. When all studies were considered (Fig. 1), the combination of MBP+OAB was associated with a significant reduction in SSI versus MBP alone (RR 0.51, 95% CI 0.46–0.56, P < 0.00001, I² = 13%). The results remained consistent when just RCT studies were examined (5378 patients; RR 0.57, 95% CI 0.48–0.68, P < 0.00001, I² = 12%), as well as cohort studies (42,232 patients; RR 0.48, 95% CI 0.44–0.51, P < 0.00001, I² = 0%).

**FIGURE 1.** 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.

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MBP + OAB Versus OAB

The analysis of MBP + OAB versus OAB alone was considered by 4 studies; 2 RCTs71,83 and 2 cohort studies31,45 including 23,483 patients (Fig. 2). Overall, the combination of MBP + OAB was not associated with any difference in the incidence of SSI versus OAB alone (RR 0.98, 95% CI 0.64–1.50, P = 0.92), with high heterogeneity (I² = 77%). When RCTs alone were considered, again no difference was seen (RR 1.36, 95% CI 0.78–2.35, P = 0.28, I² = 0%), as with cohort studies (RR 0.83, 95% CI 0.48–1.43, P = 0.51, I² = 90%).

MBP + OAB Versus No Preparation

No RCTs considered the comparison between combined MBP + OAB and no preparation, with evidence arising from just 4 cohort studies (36,642 patients).31,41,45,66 The combination of MBP + OAB was associated with a significant reduction in SSI (RR 0.54, 95% CI 0.43–0.68, P < 0.00001, I² = 82%) when compared with no preparation.

OAB Alone Versus No Preparation

No RCTs focused upon the comparison between OAB alone versus no preparation, with evidence arising from 16,390 patients included in 2 cohort studies.31,45 OAB alone reduced the incidence of SSI versus no preparation (RR 0.56, 95% CI 0.38–0.83, P = 0.004, I² = 81%).

OAB Versus MBP

Two studies31,45 considered the incidence of SSI with OAB alone versus MBP alone, with OAB associated with a reduction in SSI rates. However, this did not reach statistical significance (RR 0.57, 95% CI 0.31–1.05, P = 0.07, I² = 93%).

Anastomotic Leak

MBP + OAB Versus MBP

Rates of anastomotic leak in those receiving combined MBP + OAB versus MBP alone were compared in 22 studies (Fig. 3); 17 RCTs49–53,55,56,58,61,63,64,66,69,70,75,76,78 and 5 cohort studies.31,68,74,77,81 Only 2 RCTs49,52 included data regarding the management of the anastomotic leak, with none of the 124 patients receiving combined MBP + OAB requiring return to theater for anastomotic leakage compared with 2 of 127 patients receiving MBP alone. Overall, the combination of MBP + OAB was associated with a significant reduction in anastomotic leak rates (RR 0.62, 95% CI 0.55–0.70, P < 0.00001, I² = 0%), and when evidence from cohort studies alone was considered (RR 0.45, 95% CI 0.25–0.80, P = 0.007, I² = 22%), but no significant difference was seen when RCTs were analyzed (RR 0.69, 95% CI 0.43–1.11, P = 0.13, I² = 0%). Six studies51,53,55,68,77,81 included data on the use of a diverting stoma, with 133 patients of 1028 in the combined MBP + OAB group and 99 patients of 862 in the MBP alone group undergoing a protective stoma formation.

MBP + OAB Versus OAB

The combination of MBP + OAB versus OAB alone was considered by 3 studies; 2 RCTs71,83 and 1 cohort study.31 with no difference observed in anastomotic leakage compared with 2 of 127 patients receiving MBP alone. Overall, the combination of MBP + OAB was associated with a significant reduction in anastomotic leak rates compared with 2 of 127 patients receiving MBP alone. However, the combination of MBP + OAB was associated with a significant reduction in anastomotic leak rates (RR 0.54, 95% CI 0.43–0.68, P < 0.00001, I² = 82%), and when evidence from cohort studies alone was considered (RR 0.45, 95% CI 0.25–0.80, P = 0.007, I² = 22%), but no significant difference was seen when RCTs were analyzed (RR 0.69, 95% CI 0.43–1.11, P = 0.13, I² = 0%). Six studies51,53,55,68,77,81 included data on the use of a diverting stoma, with 133 patients of 1028 in the combined MBP + OAB group and 99 patients of 862 in the MBP alone group undergoing a protective stoma formation.

Other Comparisons

The comparison of anastomotic leak rates between OAB alone versus no preparation and OAB versus MBP was each only considered by 1 cohort study,31 and as such meta-analysis was not feasible.
30-day Mortality

**MBP+OAB Versus MBP**

Seventeen studies (35,633 patients) examined 30-day mortality rates between those receiving MBP+OAB versus MBP alone; 14 RCTs and 3 cohort studies (Fig. 4). Overall, the combination of MBP+OAB was associated with a significant reduction in 30-day mortality versus MBP alone (RR 0.58, 95% CI 0.44–0.76, *P* < 0.0001, I² = 0%). This was also the case when evidence arising from cohort studies alone was considered (RR 0.56, 95% CI 0.42–0.76, *P* = 0.0002, I² = 0%), but not when RCTs alone were examined (RR 0.66, 95% CI 0.35–1.25, *P* = 0.20, I² = 0%).

**MBP+OAB Versus No Preparation**

Just 2 cohort studies including 29,350 patients considered the impact of MBP+OAB versus no preparation on 30-day mortality. The combination of MBP+OAB was associated with a significant reduction in 30-day mortality (RR 0.36, 95% CI 0.17–0.76, *P* = 0.008, I² = 46%).

**Other Comparisons**

Comparison of 30-day mortality between those receiving OAB versus no preparation and OAB versus MBP included just a single cohort study, thus meta-analysis was not conducted.

**Overall Morbidity**

Only studies comparing MBP+OAB versus MBP alone were considered in terms of overall morbidity rates due to a paucity of data available for all other comparisons. When all 6 studies, including 1 RCT, were considered, MBP+OAB was associated with a significant reduction in overall morbidity (RR 0.55, 95% CI 0.34–0.97, *P* = 0.04, I² = 0%). However, no difference was observed in RCTs (RR 1.02, 95% CI 0.30–3.50, *P* = 0.97, I² = 0%).
were compared, the combination of MBP + OAB was associated with a significant reduction in overall morbidity (RR 0.67, 95% CI 0.63–0.71, \(P < 0.00001, I^2 = 0%\)), as well as when evidence from cohort studies alone\(^31,68\) was considered (RR 0.67, 95% CI 0.63–0.71, \(P < 0.00001, I^2 = 0%\)). However, with RCTs alone\(^61,62,66,76\), there was no difference in overall morbidity between preparation methods (RR 0.71, 95% CI 0.41–1.24, \(P = 0.23, I^2 = 9%\)).

### Development of Ileus

#### MBP+OAB Versus MBP

Five studies\(^31,43,51,53,54\) were included in the comparison of MBP+OAB versus MBP; 2 RCTs\(^31,53\) (879 patients) and 3 cohort studies (33,119 patients).\(^31,43,54\) Only 1 study\(^43\) provided a definition of ileus. Overall, the combination of MBP+OAB was associated with a significant reduction in the incidence of postoperative ileus (RR 0.71, 95% CI 0.41–1.24, \(P = 0.23, I^2 = 9%\)).

#### MBP+OAB Versus OAB

Three studies\(^31,71,83\) were included in the comparison between MBP+OAB versus OAB; 2 RCTs\(^71,83\) and 1 cohort study.\(^31\) None of these studies provided a definition for ileus. Overall, the combination of MBP+OAB was associated with a significant reduction in ileus (RR 0.83, 95% CI 0.73–0.95, \(P = 0.008, I^2 = 0%\)), mostly determined by the large single cohort study.\(^31\) However, no difference was seen when RCTs were considered (RR 1.25, 95% CI 0.68–2.33, \(P = 0.47, I^2 = 0%\)).

#### MBP+OAB Versus No Preparation

No RCTs considered the comparison between MBP+OAB versus no preparation, with evidence arising from 2 cohort studies only.\(^31,41\) Only 1 study\(^41\) provided a definition of ileus. This demonstrated that the combination of MBP+OAB was associated with a significant reduction in ileus (RR 0.72, 95% CI 0.68–0.77, \(P < 0.00001, I^2 = 0%\)).

### Other Comparisons

The comparison in reoperation rates between OAB alone versus no preparation and OAB versus MBP were each only considered by 1 cohort study,\(^31\) thus meta-analysis was not performed.

### Reoperation

Insufficient data were available for any of the planned analyses on reoperation rates, with 2 studies including data comparing MBP+OAB versus MBP (1 RCT\(^49\) and 1 cohort study\(^31\)), and just 2
studies comparing MBP+OAB versus OAB alone (again 1 RCT) and 1 cohort study. Thus, no meta-analysis was performed. The comparisons of reoperation rates between MBP+OAB versus no preparation, OAB alone versus no preparation and OAB versus MBP were each only considered by 1 cohort study, and as such meta-analysis was not performed. However, the largest cohort study showed a significant reduction (P = 0.001) in reoperation rates with combined MBP+OAB (3.2%) compared with OAB alone (4.7%), MBP alone (4.2%), and no preparation (4.5%).

**Clostridium difficile Infection**

**MBP+OAB Versus MBP**

Data on *Clostridium difficile* infection were sufficient only for the comparison between MBP+OAB versus MBP alone, with data from 14 studies, including 10 RCTs, 3,5,51,61,62,65,67,69,75,78,80 and 4 cohort studies. 

No difference in *C difficile* infection rates were seen when all evidence was considered (RR 0.94, 95% CI 0.55–1.61, P = 0.81, I² = 37%), nor when just RCT studies or cohort studies alone were analyzed (RR 0.79, 95% CI 0.21–2.96, P = 0.72, I² = 10% and RR 0.97, 95% CI 0.54–1.75, P = 0.92, I² = 64%, respectively).

**Laparoscopic Versus Open Procedures**

Nineteen RCTs provided data on SSI rates in patients undergoing open elective colorectal procedures between patients receiving combined MBP+OAB versus MBP alone, and 2 RCTs provided data on laparoscopic procedures alone. The remaining studies included either both open and laparoscopic procedures which could not be separated for analysis or did not state the surgical approach. No other comparison between preparations was considered due to a paucity of data. The combination of MBP+OAB versus MBP alone was associated with a significant reduction in SSI rates in patients undergoing an open resection (RR 0.55, 95% CI 0.44–0.69, P < 0.00001, I² = 5%); however, no significant difference was seen in patients undergoing a laparoscopic procedure (RR 0.74, 95% CI 0.43–1.29, P = 0.29, I² = 50%), although it should be borne in mind that this evidence was based upon 2 studies (1090 patients).

When anastomotic leak rates were compared between MBP+OAB versus MBP alone, divided by open and laparoscopic procedures, data could be analyzed from 9 RCTs in the open group and 2 RCTs in the laparoscopic group. There was no significant difference in anastomotic leak rates in either the open or laparoscopic groups (RR 0.69, 95% CI 0.30–1.60, P = 0.39, I² = 13% and RR 0.68, 95% CI 0.28–1.65, P = 0.39, I² = 0%, respectively).

**Main Findings**

This meta-analysis has provided evidence to suggest that MBP+OAB should be given serious consideration in patients undergoing elective colorectal surgery to reduce the risk of SSI. In addition, it has shown that the combination of MBP+OAB is associated with significant reductions in anastomotic leak rates, 30-day mortality, overall morbidity, and the incidence of postoperative ileus, without increasing the risk of developing *C difficile* infection (Table 3). Its findings are in contradiction with previous meta-analyses that did not account for the role of luminal antibiotics and showed that MBP on its own was of no benefit when compared with no bowel preparation or rectal enemas alone.

However, as only 9.3% (6437 patients) of the 69,517 patients included were studied in the context of RCTs, the results must be interpreted with some caution. Hence, when evidence arising from RCTs alone was considered, the combination of MBP+OAB was associated with a significant reduction in SSI alone. The evidence for the combination of MBP+OAB to reduce SSI rates is, thus, strong. European data reporting the results of colorectal surgery in the context of Enhanced Recovery After Surgery protocols where mechanical bowel preparation is not used routinely, have shown SSI rates of >10%, whereas the US NSQIP studies have shown that SSI rates are approximately 3% with a combination of MBP+OAB, 6% with MBP alone and 7% with no preparation.

When the combination of MBP+OAB was compared with OAB alone, a significant reduction in 30-day mortality and incidence of postoperative ileus was seen, but no difference was seen between the 2 preparations in RCTs alone. There are no RCTs focusing on the combinations of MBP+OAB versus no preparation, OAB alone versus no preparation or OAB alone versus MBP alone. However, evidence from cohort studies suggests that the combination of MBP+OAB versus no preparation is associated with a significant reduction in SSI, anastomotic leak, 30-day mortality, and postoperative ileus. For OAB versus no preparation, the only significant reduction was in SSI rates, and for OAB versus MBP there was no significant difference in any of the clinical outcome measures. When a planned subgroup analysis of patients undergoing open versus laparoscopic surgery was undertaken, the combination of MBP+OAB versus MBP alone was associated with a significant reduction in SSI rates in patients undergoing open procedures, but not in those undergoing laparoscopic procedures.

**Strengths and Weaknesses**

The main weakness of this meta-analysis is the inclusion of both RCTs and cohort studies. While this lowers the overall quality of evidence, the decision to include cohort studies and large database studies was made as a large proportion of the recent evidence supporting the potential role of OAB or combined MBP+OAB has arisen from such studies. However, every analysis was conducted separately using evidence from RCT and cohort studies alone, as well as a summative analysis, to provide a more robust interpretation of the data.

The role of parenteral antibiotic prophylaxis is considered a standard of care in current practice, with evidence published in 1981 providing evidence for its benefit in terms of infection prevention and overall mortality and dictating that no further placebo or no intervention trials should be conducted. Definitive support was provided in a Cochrane Review demonstrating a significant reduction in SSI in patients receiving parenteral antibiotic prophylaxis versus those receiving no antibiotics or placebo (RR 0.34, 95% CI 0.28–0.41, P < 0.0001).

The practice of mechanical bowel preparation has changed significantly since the early 1980s. The regimen of Lazorthes et al included admission 3 days prior to surgery and administration of a low-residue diet and standard mechanical procedures such as enemas and magnesium sulphate purges. In contrast, more modern regimens are typically administered the day before surgery and are less invasive. This is particularly important in the setting of prolonged starvation protocols in vogue prior to the more modern ones, as they resulted in increased preoperative dehydration and electrolyte disturbances which are known to have adverse effects on postoperative complications. It should, however, be considered that each study level comparison between preparation types should have been exposed to the same level of bias, thus making the results more comparable. The OAB agent, dosing, and timing as well as the parenteral antibiotic details were also inconsistent between studies, with insufficient data from each differing combination to perform a meaningful analysis. Several included just 1 preparative dose of OAB, or differing parenteral antibiotic regimens depending upon
which preparation regimen the patient received which exerts a potential significant bias. In addition, because of limited data, we have been unable to discern conclusively whether the reduction in morbidity is a result of OAB on their own or in combination with MBP.

The definition of anastomotic leak was not stipulated for inclusion within this meta-analysis, with the data from each individual study included, irrespective of whether this was based upon clinical or radiological diagnosis of anastomotic leak. However, the definition of leak was consistent within individual studies, thus the data from each study were comparable, attenuating this potential weakness.

Interpretation of the Data in Context of Other Recent Studies
A recent meta-analysis²⁵ included 23 RCTs and 8 cohort studies published between 1980 and 2015. However, multiple cohort studies arising from the NSQIP database were included within this study,²⁵ and this probably represents multiple reporting of the same patient datasets. This study²⁵ reported a significant reduction in SSI rates in patients included within cohort studies receiving MBP, OAB, and IV antibiotics versus those receiving MBP and IV antibiotics alone (RR 0.48, 95% CI 0.44–0.52, P = 0.00001, I² = 45%). However, 4 of the 5 studies included within this analysis arose from the ACS NSQIP database. Bellows et al²² previously performed a meta-analysis on the role of oral nonabsorbable and intravenous antibiotics versus intravenous antibiotics alone in colorectal surgery, focusing on SSI. This study included 16 RCTs encompassing 2669 patients published between 1980 and 2011, with all studies including MBP within the protocol. This meta-analysis found that the combination of oral and IV antibiotics versus IV antibiotics alone was associated with a significant reduction in wound infection rates (RR 1.36, 95% CI 0.54–2.35, P = 0.04, I² = 64%). No difference

| Preparation Considered | Outcome Measure | All Studies | RCTs Only | Cohort Studies Only |
|------------------------|----------------|------------|-----------|---------------------|
| MBP+OAB vs. MBP        | Surgical site infection | Significant | (RR 0.57, 95% CI 0.48–0.68, P < 0.00001, I² = 13%) | No difference | (RR 0.48, 95% CI 0.44–0.51, P < 0.00001, I² = 0%) |
|                        | Anastomotic leak | Significant | (RR 0.69, 95% CI 0.43–1.11, P = 0.13, I² = 0%) | No difference | (RR 0.45, 95% CI 0.25–0.80, P = 0.007, I² = 22%) |
|                        | 30-day mortality | Significant | (RR 0.66, 95% CI 0.35–1.25, P = 0.20, I² = 0%) | No difference | (RR 0.56, 95% CI 0.42–0.76, P = 0.0002, I² = 0%) |
|                        | Overall morbidity | Significant | (RR 0.71, 95% CI 0.41–1.24, P = 0.23, I² = 9%) | No difference | (RR 0.67, 95% CI 0.63–0.71, P < 0.00001, I² = 0%) |
|                        | Development of ileus | Significant | (RR 0.72, 95% CI 0.52–0.98, P = 0.04, I² = 36%) | No difference | (RR 0.62, 95% CI 0.14–2.67, P = 0.52, I² = 50%) |
|                        | C difficile infection | No difference | (RR 0.87, 95% CI 0.55–1.61, P = 0.81, I² = 37%) | No difference | (RR 0.79, 95% CI 0.21–2.96, P = 0.72, I² = 10%) |
| MBP+OAB vs. OAB        | Surgical site infection | No difference | (RR 0.98, 95% CI 0.64–1.50, P = 0.92, I² = 77%) | No difference | (RR 1.36, 95% CI 0.78–2.35, P = 0.28, I² = 0%) |
|                        | Anastomotic leak | No difference | (RR 1.39, 95% CI 0.47–4.10, P = 0.55, I² = 0%) | No difference | (RR 0.97, 95% CI 0.54–1.75, P = 0.92, I² = 64%) |
|                        | 30-day mortality | Significant | (RR 1.02, 95% CI 0.30–3.50, P = 0.97, I² = 0%) | No difference | (RR 0.83, 95% CI 0.48–1.43, P = 0.51, I² = 90%) |
|                        | Overall morbidity | No difference | (RR 0.79, 95% CI 0.19–3.72, P = 0.67, I² = 45%) | No difference | — |
|                        | Development of ileus | Significant | (RR 1.25, 95% CI 0.68–2.33, P = 0.47, I² = 0%) | No difference | — |
|                        | C difficile infection | — | — | — |
| MBP+OAB vs. no preparation | Surgical site infection | — | — | — |
|                        | Anostomatic Leak | — | — | — |
|                        | 30-day mortality | — | — | — |
|                        | Overall morbidity | — | — | — |
|                        | Development of ileus | — | — | — |
|                        | C difficile infection | — | — | — |

— indicates insufficient data for conduct of meta-analysis; OAB versus no preparation: only outcome was surgical site infection in cohort studies alone which demonstrated a significant | with OAB; OAB versus MBP: only outcome was surgical site infection in cohort studies alone which demonstrated no difference.
CONCLUSION
The present meta-analysis is the largest and most comprehensive study to date examining the role of bowel preparation prior to colorectal surgery, and supports a potentially significant benefit for OAB preparation, either in combination with MBP or alone, in the prevention of postoperative complications. While evidence arising from large retrospective cohort and database studies suggests a strong positive benefit, these are tempered when evidence arising from RCTs alone is considered. However, the evidence presented would suggest a benefit from OAB preparation in terms of SSI, which represents a major source of morbidity and increased healthcare costs. Further high-quality evidence is required to differentiate between the benefits of combined MBP+OAB or OAB alone in this setting before more definitive recommendations can be made.

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