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Oral Mechanical Bowel Preparation for Colorectal Surgery: Systematic Review and Meta-Analysis

Issa J. Dahabreh, M.D., M.S.[1,2] • Dale W. Steele, M.D., M.S.[1,3] • Nishit Shah, M.D.[4]
Thomas A. Trikalinos, M.D., Ph.D.[1,2]

1 Center for Evidence-Based Medicine, School of Public Health, Brown University, Providence, Rhode Island
2 Department of Health Services, Policy, and Practice, School of Public Health, Brown University, Providence, Rhode Island
3 Departments of Emergency Medicine and Pediatrics, Alpert Medical School, Brown University, Providence, Rhode Island
4 Department of Surgery, Alpert Medical School, Brown University, Providence, Rhode Island

BACKGROUND: Oral mechanical bowel preparation is often used before elective colorectal surgery to reduce postoperative complications.

OBJECTIVE: The purpose of this study was to synthesize the evidence on the comparative effectiveness and safety of oral mechanical bowel preparation versus no preparation or enema.

DATA SOURCES: We searched MEDLINE, the Cochrane Central Register of Controlled Trials, Embase, and CINAHL without any language restrictions (last search on September 6, 2013). We also searched the US Food and Drug Administration Web site and ClinicalTrials.gov and supplemented our searches by asking technical experts and perusing reference lists.

STUDY SELECTION: We included English-language, full-text reports of randomized clinical trials and nonrandomized comparative studies of patients undergoing elective colon or rectal surgery. For adverse events we also included single-group cohort studies of at least 200 participants.

INTERVENTIONS: Interventions included oral mechanical bowel preparation, oral mechanical bowel preparation plus enema, enema only, and no oral mechanical bowel preparation or enema.

MAIN OUTCOME MEASURES: Anastomotic leakage, all-cause mortality, wound infection, peritonitis/intra-abdominal abscess, reoperation, surgical site infection, quality of life, length of stay, and adverse events were measured. We synthesized results across studies qualitatively and with Bayesian random-effects meta-analyses.

RESULTS: A total of 18 randomized clinical trials, 7 nonrandomized comparative studies, and 6 single-group cohorts were included. In meta-analyses of randomized clinical trials, the credibility intervals of the summary OR included the null value of 1.0 for comparisons of oral mechanical bowel preparation and either no oral preparation or enema for overall mortality, anastomotic leakage, wound infection, peritonitis, surgical site infection, and reoperation. These results were robust to extensive sensitivity analyses. Evidence on adverse events was sparse.

LIMITATIONS: The study was limited by weaknesses in the underlying evidence, such as incomplete reporting of relevant information, exclusion of non-English and relevant unpublished studies, and possible missed indexing of nonrandomized studies.

CONCLUSIONS: Our results could not exclude modest beneficial or harmful effects of oral mechanical bowel preparation compared with no preparation or enema.

KEY WORDS: Colorectal surgery; Meta-analysis; Oral mechanical bowel preparation; Systematic review.

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Correspondence: Issa J. Dahabreh, M.D., M.S., Department of Health Services, Policy, and Practice and Center for Evidence-Based Medicine, School of Public Health, Brown University, 121 South Main St, Providence, RI 02903. E-mail: issa_dahabreh@brown.edu

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Each year, more than 250,000 colorectal surgeries are performed in the United States.[1,2] Complication rates for elective colorectal surgery range between 4% and 36%; thus, identifying interventions that can reduce these rates is an important goal.[3,4] Development of a surgical site infection (SSI) is the most frequent complication, is a major source of morbidity, and can substantially lengthen hospital stay from ≈4 days to 21 days, along with an increase in costs from approximately $11,000 to $43,000.[3] In addition, infectious complications may require reoperation, including the possible need for a stoma.[5,6] Traditionally, oral mechanical bowel preparation (OMBP) has been used preoperatively for patients undergoing elective colorectal surgery.[7,8] The rationale for the use of OMBP is that it decreases the bacterial load in the colon, thereby decreasing infectious complications. OMBP is a common practice in the United States. For example, a 2003 survey found that >99% of colorectal surgeons routinely used OMBP,[9] and a recent (2007–2009) study of 24 Michigan hospitals reported the use of OMBP in 86% of all colorectal surgeries.[10]

However, in recent years, OMBP has come under increasing scrutiny. Patients frequently report that OMBP solutions have an unpleasant taste, and some experience dehydration and electrolyte derangements. Furthermore, several recent trials have failed to identify a statistically significant benefit to the use of OMBP before colon surgery.[11,12] Citing some of these trials, the 2010 guidelines of the Canadian Society of Colon and Rectal Surgeons favored omitting OMBP in the preoperative management of patients undergoing elective open right-sided and left-sided colorectal surgical resections[13] but deemed the evidence insufficient to support or refute omitting OMBP for patients undergoing low anterior resection (with or without diverting stomas) and those undergoing laparoscopic colorectal surgery.

A recent Cochrane systematic review (covering studies up to December 1, 2010) found no benefit for OMBP in terms of decreasing anastomotic leaks, other surgical complications, or mortality for mixed populations of patients undergoing colon or rectal resection.[7] Several studies have been published since the last search of the Cochrane review, suggesting that an updated synthesis is needed. Systematic reviews on the effectiveness of OMBP have used methods that do not properly represent uncertainty in the available evidence and have often reached sweeping conclusions, typically suggesting that OMBP should be omitted in all cases.[14,15] In addition, large variation in OMBP use exists among different parts of the world, further suggesting that existing syntheses of the evidence do not adequately address major decision-making uncertainties. To address these uncertainties, we systematically evaluated experimental and observational evidence on the potential benefits and adverse events associated with the use of OMBP in patients undergoing elective colorectal surgery. We also aimed to identify patient and procedural characteristics that modify the effect of OMBP on outcomes.

MATERIALS AND METHODS

This article is based on an evidence report prepared by the Brown University Evidence-Based Practice Center under contract with the Agency for Healthcare Research and Quality. Based on an extensive stakeholder-driven process of topic development and refinement, we formulated the following key questions to guide the review: First, how do various preoperative OMBP strategies compare with either no OMBP or with each other with respect to their effectiveness for preventing operative or postoperative complications? Second, how do various preoperative OMBP strategies compare with either no OMBP or with each other with respect to operative or postoperative adverse events? Stakeholders were involved either as members of a key informant group (including a patient, frontline clinicians, and representatives of professional societies) or members of a technical expert panel (including academic surgeons, infectious disease specialists, and health services researchers).

The evidence report addressed the comparison of OMBP versus no OMBP, as well as direct comparisons among alternative active OMBP strategies. We found that studies comparing active OMBP preparations had generally limited applicability (clinical relevance) to current surgical practice; for this reason, this article focuses on the comparison of OMBP versus no OMBP. The complete evidence report is available on the Effective Health Care Program Web site (http://www.effectivehealthcare.ahrq.gov). We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement in the reporting of our methods and results.[16] The PROSPERO registration number of the review protocol is CRD42013004381.

Literature Search and Abstract Screening

We searched MEDLINE, the Cochrane Central Register of Controlled Trials, Embase, and CINAHL without any language or publication date restriction (last search on September 6, 2013). The full evidence report provides the complete search queries. We also performed a targeted search of the US Food and Drug Administration Web site (last search performed on May 17, 2013). We supplemented searches by asking technical experts to provide additional relevant citations and by perusing reference lists of eligible studies, clinical practice guidelines, and narrative and systematic reviews. We requested supplementary information from manufacturers of OMBP solutions. Finally, we searched the ClinicalTrials.gov Web site (with the last search performed on May 16, 2013) to identify ongoing comparative trials of alternative OMBP strategies.

We did not consider unpublished data other than that included in US Food and Drug Administration documents or at ClinicalTrials.gov. Titles and abstracts were manually screened in duplicate, following a standardization exercise.

Study Selection and Eligibility Criteria

2 investigators (I.J.D. and D.W.S.) independently reviewed full-text articles for eligibility. Disagreements were resolved by consensus including at least 1 additional investigator. For this article, eligible studies compared OMBP versus no preparation or adverse events from OMBP. We defined OMBP as any preparation for surgery that was administered orally or through a nasogastric tube without the need for other (eg, endoscopic) intervention. Cointerventions could include oral or parenteral antibiotics, dietary modification, or enema.

We included English-language, full-text reports of randomized clinical trials (RCTs; at least 10 patients per arm) and nonrandomized comparative studies (NRCSs; at least 100 patients per arm) in adults or children undergoing elective colon or rectal surgery. Studies reporting on both colorectal and noncolorectal surgery were included if results were presented by anatomic site or if ≥80% of surgeries involved the large bowel. For adverse events we also included single-group cohort studies of ≥200 participants.[17]

For our first key question, we included studies reporting on a predetermined set of clinical outcomes (overall and cause-specific survival, infectious outcomes, anastomotic leakage, planned and unplanned ostomies; failed attempts to restore bowel continuity, and venous thromboembolism), health system and resource use outcomes (readmissions after surgery, reoperation, additional interventional procedures, length of stay, and admission to intensive care unit/nursing care), and patient-centered outcomes (patient satisfaction and quality of life). Improvements in these outcomes represent the intended effects of OMBP. For the second key question, we considered the following prespecified adverse events: nausea, vomiting, dehydration, electrolyte imbalance, kidney damage, and emergency admissions before surgery; cancelled, delayed, or rescheduled surgeries; and allergic reactions and seizures. When possible (ie, when studies reported their outcome definitions), we used the SSI definition proposed by the Centers for Disease Control and Prevention.[18] However, most studies did not provide such information, and we had to accept the terminology used at face value.

Data Extraction

A single investigator extracted data from each study; a second reviewer verified quantitative results. Disagreements were resolved by consensus involving a third investigator. After pilot testing, data were extracted into electronic forms stored in the Systematic Review Data Repository using separate forms per the key question.[19] We took particular care to avoid double counting when published articles reported on potentially overlapping patient populations. Potential overlap was assessed on the basis of the sampling population of each study, the enrollment period for each publication, the patient selection criteria, and information on overlap provided by the authors in the published articles.

Risk of Bias and Completeness of Reporting of Individual Studies

For RCTs, we based our assessment on items from the Cochrane risk-of-bias tool.[20] For NRCSs and single-group studies, we used items from the Newcastle-Ottawa tool, with the addition of items relevant to statistical analysis.[21] We assessed publication and reporting bias qualitatively on the basis of the number of available studies, number of studies contributing information for each outcome, sample size, and statistical significance of reported comparisons.

Evidence Synthesis

For each key question, we synthesized results qualitatively and assessed whether studies were sufficiently similar to be combined in a meta-analysis. For RCTs, we performed pairwise meta-analyses for outcome comparisons with more than 3 nonoverlapping studies. NRCS and single-group cohorts were not included in meta-analyses. Estimation was done in the generalized linear mixed modeling framework, using the binomial distribution to represent within-study variability and the logit link function.[22] Models accounted for between-study heterogeneity. Primary analyses used Bayesian-Markov chain Monte Carlo methods. These methods incorporate uncertainty in the summary estimates of treatment effects more fully than traditional meta-analysis methods. Heterogeneity was assessed based on the posterior distribution of the between-study variance parameter. We explored between-study heterogeneity using subgroup and meta-regression analyses. We also performed sensitivity analyses, such as leave-one-out analyses, analyses assuming a fixed-effects model, and analyses including a retracted study. Previous distributions for all of the model parameters were noninformative and were subjected to extensive sensitivity analyses, including the use of informative priors, use of the DerSimonian-Laird meta-analysis method (which does not require previous specification), and use of network meta-analysis methods. These analyses produced results qualitatively similar to our main analyses and are omitted from the article for parsimony; they are presented in detail in the full evidence report.

All of the analyses were performed using Stata IC (version 12.1; Stata Corp, College Station, TX). We did not perform any adjustments for multiple comparisons. Mar-

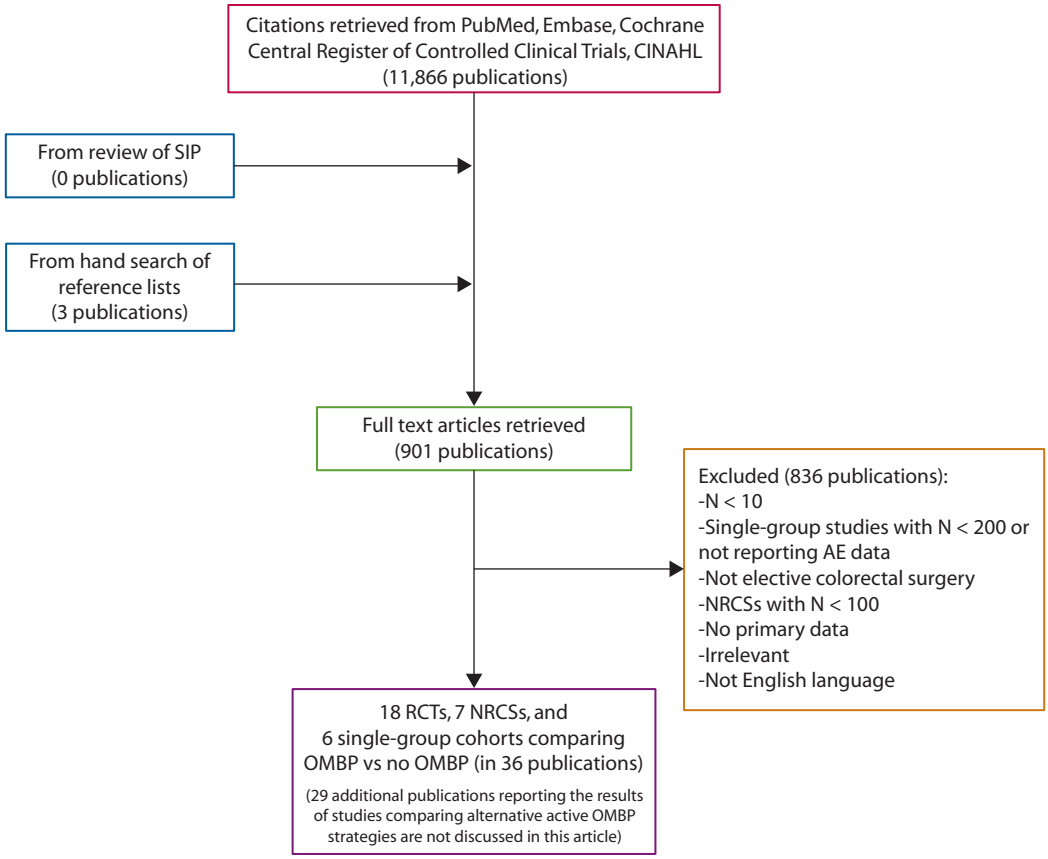

Figure 1. Literature flow diagram. KQ = key question; SIP = submission information package; OMBP = oral mechanical bowel preparation; AE = ; RCT = randomized clinical trial; NRCS = nonrandomized comparative study. Some publications reported data from the same study.

kov-Chain Monte Carlo estimation for Bayesian analysis was done in WinBUGS (version 1.4.3; MRC Biostatistics Unit, Cambridge, United Kingdom) through calls from Stata. We report medians and 95% central credibility intervals (CrIs) for quantities of interest.

RESULTS

Search Results and Included Studies

Our search yielded 11,869 citations, of which 901 were reviewed in full text. Eighteen RCTs, 7 NRCSs, and 6 single-group cohorts contributed information to main analyses (Fig. 1). Common indications for surgery were colorectal cancer and diverticular disease. Details on the surgical approach (eg, operation types, anastomosis methods, and open versus surgical surgery) were generally poorly reported. The complete extracted data and summary tables for all of the included studies are available online on the Systematic Review Data Repository (http://srdr.ahrq.gov).

Randomized Comparisons of OMBP Versus No OMBP: Postoperative Complications

Eighteen RCTs (reported in 23 publications) compared OMBP versus no OMBP and were included in main analyses (see Supplemental Table 1, http://links.lww.com/DCR/A181).[4,11,12,23–42] One additional study had been retracted and was only considered in sensitivity analysis,[43,44] while another study[45] reported results on a patient population that overlapped with a larger trial,[24] and thus was excluded. Studies used a variety of OMBP regimens: 7 used polyethylene glycol, 5 used other laxatives or cathartics, and 6 used other methods (including combinations of the aforementioned regimens). Almost all of the studies reported using intravenous antibiotics in the perioperative period (1 study provided unclear information), and 3 studies reported also using oral antibiotics.

Table 1 summarizes the results of pairwise Bayesian random effects meta-analyses of all of the RCTs for 6 clinical outcomes and analyses stratified by whether enema was administered in the comparator group. For all of the outcomes, the 95% CrIs did not exclude an OR of 1 (ie, no effect); however, these intervals were wide and did not exclude clinically important differences in either direction. These results were robust to extensive sensitivity analyses using alternative specifications for the previous between-study variance. Similarly, there was some indication for between-study heterogeneity, particularly for the comparison of OMBP with or without enema versus enema, but the CrIs around the between-study variance

Table 1. Pairwise meta-analysis results for the comparison of OMBP versus enema or no preparation

Outcome	*Comparison*	*N studies (N events/N patients, per group)*	*OR (95% CI)*	*Between-study variance (95% CrI)*
All-cause mortality	OMBP ± enema vs enema/no prep	14 (45/2550 vs 44/2544)	1.17 (0.67–2.67)	0.12 (0.00–1.99)
	OMBP ± enema vs no prep	10 (38/2024 vs 40/2014)	1.09 (0.57–2.99)	0.17 (0.00–2.61)
	OMBP ± enema vs enema	4 (7/526 vs 4/530)	1.99 (0.27–18.45)	0.82 (0.00–3.76)
Anastomotic leakage	OMBP ± enema vs enema/no prep	16 (126/2702 vs 124/2680)	1.08 (0.79–1.63)	0.08 (0.00–0.72)
	OMBP ± enema vs no prep	12 (102/2176 vs 103/2150)	1.06 (0.73–1.73)	0.09 (0.00–0.95)
	OMBP ± enema vs enema	4 (24/526 vs 21/530)	1.24 (0.38–4.72)	0.61 (0.00–3.59)
Wound infection	OMBP ± enema vs enema/no prep	16 (266/2612 vs 239/2603)	1.19 (0.93–1.63)	0.04 (0.00–0.41)
	OMBP ± enema vs no prep	12 (218/2086 vs 190/2073)	1.27 (0.95–1.88)	0.05 (0.00–0.50)
	OMBP ± enema vs enema	4 (48/526 vs 49/530)	1.04 (0.37–3.34)	0.52 (0.00–3.46)
Peritonitis/ intra-abdominal abscess	OMBP ± enema vs enema/no prep	14 (51/2381 vs 70/2362)	0.84 (0.50–1.66)	0.25 (0.00–1.77)
	OMBP ± enema vs no prep	10 (45/1855 vs 64/1832)	0.84 (0.45–2.00)	0.38 (0.00–2.74)
	OMBP ± enema vs enema	4 (6/526 vs 6/530)	0.99 (0.21–4.68)	0.42 (0.00–3.51)
Reoperation	OMBP ± enema vs enema/no prep	8 (124/1967 vs 119/1945)	1.14 (0.57–2.65)	0.38 (0.00–3.23)
	OMBP ± enema vs no prep	6 (117/1742 vs 111/1723)	1.15 (0.73–2.50)	0.09 (0.00–1.82)
	OMBP ± enema vs enema	2 (7/225 vs 8/222)	0.50 (0.03–6.12)	2.49 (0.27–3.93)
SSI	OMBP ± enema vs enema/no prep	7 (206/1279 vs 197/1230)	1.19 (0.56–2.63)	0.64 (0.11–2.91)
	OMBP ± enema vs no prep	5 (173/1087 vs 171/1040)	1.10 (0.41–3.05)	0.76 (0.10–3.39)
	OMBP ± enema vs enema	2 (33/192 vs 26/190)	1.50 (0.24–10.42)	1.20 (0.02–3.79)

OR values <1 indicate that events are less common among OMBP-treated groups (ie, that OMBP is beneficial). CrI = credibility interval; no prep = no OMBP and no enema; OMBP = oral mechanical bowel preparation; SSI = surgical site infection.

estimates were very broad. Figure 2 presents study level results and meta-analytic summaries for anastomotic leakage; Supplemental Figs. 1–5, http://links.lww.com/DCR/A182 present the same information for additional clinical outcomes.

With respect to stratification by surgical site, 1 study exclusively enrolled patients undergoing rectal surgery, and 2 studies enrolled only patients undergoing left-sided colorectal surgeries. In total, through author contact and previous reviews, we obtained results stratified by anatomic location or restricted to a single location from 10 trials (for anastomotic leakage). Separate analyses by anatomic location (colon versus rectum) were possible only for the outcome of anastomotic leakage; there was no evidence of effect modification by anatomic location; however, summary estimates were imprecise, and evidence was available from a small number of studies using heterogeneous subgroup definitions. The OR for anastomotic leakage comparing OMBP versus enema or no preparation was 0.82 (95% CrI, 0.45–1.81) for colon surgery (9 studies) and 0.91 (95% CrI, 0.43–2.54) for rectal surgery (7 studies).

Randomized Comparisons of OMBP Versus No OMBP: Length of Stay

Nine studies comparing OMBP versus no preparation reported information on mean or median length of hospital stay (6 studies on total and 3 studies on postoperative length of stay) but did not report information to enable statistical testing. The difference in mean or median length of stay between groups ranged from –5.0 days to 4.4 days and was positive in 4 studies, negative in 2 studies, and (reported as) exactly 0 in 2 studies (positive values indicate longer average length of stay for patients in the OMBP-treated group). Statistical comparisons of the duration of stay were possible only in 5 of the studies (3 reporting on total length of stay and 2 reporting on postoperative stay); differences were statistically nonsignificant in 1 study (longer total duration in the OMBP-treated group). Three studies comparing OMBP versus enema reported information on mean or median total length of hospital stay (no studies reported information separately for the preoperative and postoperative periods) but did not report information to enable statistical testing. The difference in mean or median length of stay ranged from 0.1 days to 0.9 days.

Randomized Comparisons of OMBP Versus No OMBP: Patient Satisfaction, Quality of Life, and Adverse Events

No studies reported information on patient satisfaction and quality of life using appropriate measurement scales. In addition, no studies provided information on unplanned ostomies, failed attempts to restore bowel continuity, readmissions after surgery, additional interventional procedures, admission to intensive care unit, or admission to nursing care.

Of the 18 RCTs included in our main analyses comparing OMBP with or without enema versus enema alone or no preparation, only 2 provided information on adverse events (1 for nausea and 1 for renal failure). In the study reporting data on nausea, 9 of 95 OMBP-treated patients and 8 of 90 control subjects reported experiencing nausea. In the other study, 3 of 89 patients receiving OMBP versus 1 of 89 patients receiving no preparation experienced acute renal failure. No trials reported information on other prespecified adverse events of interest (ie, vomiting; dehydration; electrolyte imbalance; emergency

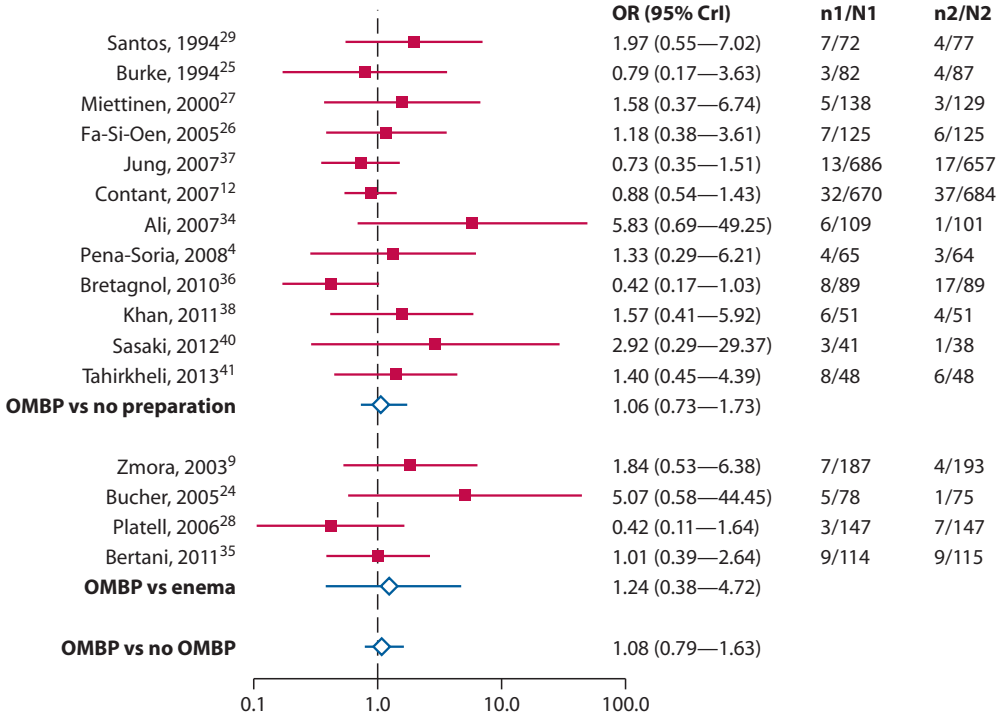

Figure 2. Anastomotic leakage meta-analysis results for studies comparing OMBP (with or without enema) versus enema or no preparation. CrI = credibility interval; NA = not applicable; OMBP = oral mechanical bowel preparation. The solid squares (and horizontal lines) indicate the point estimate of the OR (and the corresponding 95% CI) for individual studies; the diamonds (and horizontal lines) indicate the summary estimate of the OR (and corresponding 95% central CrI). The number of events and the sample size of each treatment group are shown to the right of the plot. The dashed line indicates an OR of 1.

admissions before surgery; cancelled, delayed, or rescheduled surgeries; allergic reactions; or seizures).

Risk of Bias Assessment for RCTs

Information on trial design needed to assess the risk of bias of individual studies was not fully reported. Among the 18 RCTs comparing OMBP versus no OMBP, information on the randomized sequence generation and allocation concealment was deemed unclear in 8 and 10 studies. In addition, blinding of patients, care providers, and outcome assessors was unclear in 14, 10, and 12 of the studies. In contrast, information on withdrawals and dropouts was better reported. Of the studies reporting relevant information, only 2 reported a dropout rate of >10% (both only in their no-OMBP trial groups), and no study had evidence of differential dropout (defined as a >10% difference in the dropout rate between treatment groups). Overall, 8 studies were considered to be at high risk of bias, 9 to be at intermediate risk of bias, and 1 to be at low risk of bias. As always, aggregated risk of bias assessments needs to be interpreted with caution, given our inability to fully distinguish inappropriate study design and conduct from poor reporting.

In meta-regression analyses (comparing OMBP versus enema or no preparation) on randomized sequence generation and year of publication, the 95% CrI of the relative OR included the null value for all of the key outcomes with 10 or more available studies (Table 2). However, CrIs were wide, indicating substantial uncertainty regarding effect modification. For allocation concealment, the OR comparing OMBP versus enema or no preparation was lower in trials considered at low risk of bias compared with trials at higher or unclear risk (ie, in low risk of bias studies, OMBP was less likely to increase the odds of leakage versus enema or no preparation, as compared with trials of higher or unclear risk of bias). Of note, in the low risk of bias subgroup of studies, the CrI of the OR comparing OMBP versus enema or preparation included the null value.

Evidence From NRCSs and Single-Group Cohorts

Seven NRCSs (1 of which was a nonrandomized experimental study) reported information on the comparison of OMBP versus omission of preparation.[46–52] Because of heterogeneity in patient selection and outcomes reported, differences in study design, and concerns regarding risk for residual confounding, we did not perform a meta-analysis of these studies. The NRCSs reported results consistent with those of RCTs and did not demonstrate significant differences between OMBP and no-OMBP strategies. At the same time, CIs were generally wide (eg, could not exclude a 50% change in odds in either direction). Studies

Table 2. Meta-regression results for studies comparing OMBP (with or without enema) versus enema or no preparation

Outcome	*Potential modifier*	*rOR (95% CrI)*
All-cause mortality	ROB for randomized sequence generation (low vs moderate/high/unclear)	0.33 (0.07–1.40)
	ROB for allocation concealment (low vs moderate/high/unclear)	0.88 (0.23–4.39)
	Year of publication	0.98 (0.90–1.04)
Anastomotic leakage	ROB for randomized sequence generation (low vs moderate/high/unclear)	0.72 (0.35–1.56)
	ROB for allocation concealment (low vs moderate/high/unclear)	0.45 (0.23–0.86)[a]
	Year of publication	0.98 (0.91–1.05)
Wound infection	ROB for randomized sequence generation (low vs moderate/high/unclear)	0.90 (0.51–1.72)
	ROB for allocation concealment (low vs moderate/high/unclear)	0.64 (0.38–1.08)
	Year of publication	1.00 (0.97–1.03)

CrI = credibility interval; ROB = risk of bias; rOR = relative OR; SSI = surgical site infection.
[a]Results are suggestive of an association.

were at substantial risk of bias, mostly because of confounding factors that had not been adequately controlled in the design or analysis of these investigations. None of the 7 NRCSs comparing OMBP with no preparation reported information on the prespecified adverse events.

Six studies met our inclusion criteria for single-group cohorts and reported results on at least 1 of the prespecified adverse events of interest.[53–58] Of note, all 6 of the studies were large comparative studies of antibiotic treatments (5 studies) or enema use (1 study) for patients with colorectal cancer. Reporting of adverse events was incomplete and was limited to vomiting, nausea, vomiting and nausea, and allergic reactions. Almost universally, the rates of reported adverse events were <4%. The exception was a cohort of patients receiving OMBP with sodium phosphate with or without oral antibiotics, for whom the rate of vomiting was ≈17% (51 of 300 patients). No study made causal attributions of the adverse events to the OMBP drugs or cointerventions.

DISCUSSION

Summary of Key Findings

We found no evidence that OMBP with or without enema differs from enema or no oral preparation. However, the uncertainty accompanying the estimated treatment effects was considerable. Based on the boundaries of the credible intervals, one cannot exclude a modest (eg, 30%–50%) change in odds in either direction for all-cause mortality, anastomotic leakage, wound infection, and peritonitis. This uncertainty is explained by the small sample size of most included studies and the relative rarity of clinical events, such as death, anastomotic leakage, reoperation, and severe infection. Of more concern is that important subgroups, such as anatomic location and type of surgery (eg, laparoscopic versus open) were sparsely reported in the published literature, as was information on important potential effect modifiers (eg, oral or parenteral antibiotics). Similarly, too few studies consistently collected adverse events.

Compared with the most recent Cochrane review of OMBP,[7] we have included a broader spectrum of study designs and have performed more extensive data analyses using Bayesian random effects meta-analysis methods. Furthermore, we identified several studies published after the last search of the Cochrane review and have excluded from main analyses (and subjected to sensitivity analyses) a recently retracted study that had been included in the Cochrane review. As a result of using analyses that more fully account for the uncertainties in the synthesis of evidence, our interpretation of the evidence base is more conservative than that of the Cochrane review and other recent meta-analyses.[7,14,15,59,60] Although, similar to those reviews, we did not find evidence of clear benefit from OMBP, the wider credible intervals around our results lead us to conclude that modest benefit or harm cannot be excluded. Given the very large number of colorectal surgeries performed annually, modest effects can be clinically significant, and, therefore, further research is urgently needed to provide a definitive answer. Furthermore, there are a number of potentially important factors that could modify the effect of OMBP that existing studies do not adequately address. For example, there has been a revival of interest in the potential value of nonabsorbable oral antibiotics in combination with OMBP.[49] Existing studies do not adequately address the effect of OMBP in patients undergoing laparoscopic operations or fast-track recovery programs[61–63] and do not provide information on whether the location of surgery modifies the effect of OMBP. Therefore, we believe that additional studies are needed to assess the comparative effectiveness of alternative OMBP strategies.

Limitations of This Review

Several limitations need to be considered when interpreting our results. First, our conclusions, to a large extent, reflect weaknesses of the underlying evidence base. For example, our ability to perform important subgroup analyses to explore the impact of patient-, disease-, or system-level characteristics on the effectiveness of OMBP is limited by the incomplete reporting of relevant information in the published articles. Included studies were deemed to be at moderate risk of bias because of issues related to the generation

of the randomized sequence, allocation concealment, and blinding. Second, we excluded studies not published in English, although this is unlikely to cause major bias since previous work identified only 4 relevant non–English-language publications, including a total of 269 patients. Third, we have relied mainly on electronic database searches and perusal of reference lists to identify relevant studies. Unpublished relevant studies may have been missed, and, if unpublished studies have results that differ systematically from the results of published studies, our results may be biased. However, we believe that our comprehensive literature searches and attempts to contact the manufacturers of OMBP solutions limit the extent to which publication bias may have affected our results. Fourth, indexing of nonrandomized studies is less complete than that of randomized trials, and we may have failed to identify relevant studies. However, we did not use search filters that limit results to specific study designs, to increase the sensitivity of our searches.

Applicability of Review Findings

The existing evidence base comparing OMBP with or without enema versus enema or no preparation appears to be applicable to US settings. Studies enrolled patients with an age distribution similar to that of patients undergoing colorectal surgery in the United States and for indications that represent the most prevalent indications in US clinical practice. However, none of these studies have been conducted in the United States, raising the possibility that system-level differences (eg, differences in policies on oral antibiotics, preoperative fluid use, or fasting) may render findings less applicable to US surgical practice. Findings may be most applicable to patients undergoing colon surgery; data on patients undergoing rectal surgery were sparse, and thus the applicability of findings to this population is at best unclear; the wide credible intervals around subgroup-specific estimates do not support definitive conclusions. Similarly, the applicability of our findings to patients undergoing laparoscopic colorectal surgery is unclear, because few studies reported relevant information.

Implications for Future Research

Although we found no evidence that using OMBP improves outcomes, the evidence base was too weak to confidently exclude either modest benefit or modest harm. Because elective colorectal surgery is a common procedure, even a modest treatment effect would affect a significant number of patients, and therefore further research is important to verify or rule out any such effect. We believe that there is need for a large, pragmatic, and definitive RCT examining all combinations of using versus not using OMBP, oral antibiotics, and enema before colorectal surgery. Such a study should be very feasible in the US setting, given that a large volume of procedures are performed annually, the interventions to be tested are low cost (or already part of standard care), and only short follow-up is needed. A noninferiority design could be used to explore whether omission of OMBP does not worsen outcomes. Given the increasing interest in re-evaluating the role of oral antibiotics in colorectal surgery preparation, a factorial design could efficiently evaluate both main effects and treatment-by-treatment interactions between OMBP and oral antibiotics. It would be important to collect data according to anatomic location and type of surgery (open versus laparoscopic) and to estimate treatment effects for all of the important clinical outcomes using appropriate ascertainment methods (eg, leakage and SSI rates, mortality, and specific infectious complications). An individual patient data meta-analysis of existing trials of OMBP is a lower cost alternative for obtaining information on important subgroups, but it would likely not succeed in reducing the uncertainty around the effectiveness of OMBP. Its results could be used to inform the design of future primary trials. Observational studies can also be used to gather information on the comparative effectiveness of alternative OMBP strategies, particularly for susceptible groups that have not been represented in the RCTs. Such studies should have large sample sizes chosen on the basis of prospective power analyses, include patients representative of those seen in clinical practice, and use strong methods to address confounding bias. Exposure assessment should include the collection of details regarding the preparation strategy, and outcome ascertainment should be done using standardized definitions for all outcomes of interest.

CONCLUSION

We found weak evidence suggesting that OMBP has similar effectiveness compared with no preparation with respect to all-cause mortality, anastomotic leakage, wound infection, and peritonitis for patients undergoing elective surgery for colorectal cancer. However, the evidence base was too weak to confidently exclude either modest (30%–50%) benefit or modest harm. Evidence on the comparative effectiveness of OMBP versus no preparation was insufficient for all other outcomes, as was evidence on the comparative effectiveness of OMBP versus enema for all outcomes. The body of literature on alternative active OMBP strategies was largely irrelevant to current surgical decision making because the trials were underpowered, reported poorly defined outcomes, and compared preparations no longer in use. Future studies, including pooled reanalyses of existing data and new comparative studies (both randomized and nonrandomized), hold promise for informing clinical decisions.

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