Comparative Effectiveness Review
Number 128

Effective Health Care Program

Oral Mechanical Bowel Preparation for Colorectal Surgery

Executive Summary

Background

In the United States, oral mechanical bowel preparation (OMBP), defined as the use of an oral preparation given prior to surgery to clear fecal material from the bowel lumen, is often prescribed preoperatively for patients undergoing elective colorectal surgery.[1] OMBP is sometimes used as a precaution in anticipation of possible iatrogenic bowel injury during abdominal and pelvic surgeries that do not entail resection of the colon or rectum (e.g., urologic or gynecologic procedures). OMBP is also routinely prescribed prior to colonoscopy to allow maximal visualization of the intraluminal bowel during the procedure, although that use is not within the scope of this report.[2]

In 2009, more than 250,000 colorectal surgeries were recorded,[3] most commonly for cancer or diverticulitis,[4] and, in the majority of cases, in adults. In the context of colorectal surgery many have considered OMBP necessary for decreasing infectious complications, in particular by lowering anastomosis leakage rates associated with surgery.[5] Gross spillage of fecal material in the operative field increases the need for a stoma, which can impact patients' quality of life. Moreover, a stoma requires additional surgery to reverse it, and possibly other surgeries if complications such as bowel obstructions or incisional hernia arise.[6,7] Complication rates for elective colorectal surgery range between

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4 and 36 percent.[8,9] A surgical site infection can substantially lengthen hospital stay from approximately 4 days to 21 days and increase costs from approximately $11,000 to $43,000.[8] Therefore, reducing complication rates of elective colorectal surgery is an important goal.

However OMBP is not risk free. Most patients start the OMBP at home the day before surgery. Elderly and frail patients may undergo OMBP in the hospital. OMBP is at the least a hassle for patients. (Some preparations are unpleasant tasting; ingesting large quantities of fluids and spending long periods on the toilet are also unpleasant.) OMBP can also lead to complications. Some patients experience vomiting and dehydration severe enough to require medical attention, or even to delay the surgery. Additionally, liquid bowel contents from OMBP use may be less safely handled during surgery than solid contents and may result in infections. Individuals who may be at greater risk of adverse effects of OMBP are the elderly (≥65 years of age) and those with comorbidities such as cardiovascular and pulmonary disease, diabetes, kidney disease, and compromised immune conditions.

OMBP for colon or rectal surgery appears to be a widespread practice in the United States. A 2003 survey found that more than 99 percent of colorectal surgeons routinely employed OMBP,[10] and a recent study (2007–09) of 24 Michigan hospitals reported use of OMBP in 86 percent of all colorectal surgeries.[11] The initial adoption of OMBP prior to colorectal surgery was based on expert opinion and observational data.[12,13] However, several recent trials (mostly conducted in Europe) failed to identify a statistically significant benefit for use of OMBP prior to colon surgery.[14,15] 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,[16] 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.

In addition to uncertainty over the net benefit of OMBP, both bowel preparation strategies and adjunctive therapies have changed over time. The U.S. Food and Drug Administration (FDA) has approved several OMBP regimens that are available over the counter. Most commonly used are large-volume (approximately 4 liters) osmotically balanced polyethylene glycol (PEG) solutions (e.g., MiraLAX®, GoLYTELY®, NuLYTELY®) or reduced-volume PEG (approximately 2 liters) plus bisacodyl (HalfLytely®). PEG solutions evacuate the bowel by washout, with no substantial fluid or electrolyte shifts.[8] Bisacodyl, a poorly absorbed diphenylmethane, stimulates colonic peristalsis. Hyperosmotic preparations (e.g., Fleet®) that draw water into the bowel to achieve washout are less used because of concern about electrolyte imbalances.[2] Older, more aggressive OMBP strategies, such as whole-gut irrigation through nasogastric tubes or multiday strategies, are no longer used.

OMBP is often administered together with several cointerventions. An enema is sometimes given the night before or the morning of surgery. Antibiotics, parenteral or oral, are also often administered preoperatively for systemic coverage and for reducing the concentration of anaerobic bacteria in the gut.[17,18] Because any of these may act synergistically or competitively with OMBP, it is important to consider potential interactions when assessing the impact of various OMBP strategies on surgical outcomes.

A recent Cochrane systematic review (covering studies up to December 1, 2010) found no benefit for OMBP in terms of anastomotic leakage, other surgical complications, or mortality for mixed populations of patients undergoing colon or rectal resection.[1] However, several studies have been published since the last search of the Cochrane Review, suggesting that an updated synthesis is needed. Furthermore, there is reason to believe that OMBP could have a different impact depending on the—

- Anatomic location of surgery. For example, colon and rectal surgeries often use different operative techniques and have different complication rates.
- Type of surgery (open vs. laparoscopic). For example, it has been suggested that preparation makes manipulation of the bowel more difficult during laparoscopic surgery.
- Whether OMBP is combined with an enema (because the latter may be adequate for preparation in some cases).

Finally, large variation in practice persists in different parts of the world, perhaps suggesting that existing syntheses of the evidence do not adequately address all major decisionmaking uncertainties.

The purpose of this review was to systematically evaluate experimental and observational evidence on the 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.

Key Questions

On the basis of the original topic nomination and an extensive stakeholder-driven process of topic development and refinement, we formulated the following Key Questions to guide the review:

Key Question 1: How do various preoperative OMBP strategies compare with either no OMBP or with each other with respect to their effectiveness for preventing surgical or postsurgical complications? Does the effect vary by elective (a) right colon, (b) left colon, and (c) rectal surgery?

Key Question 2: How do various preoperative OMBP strategies compare with either no OMBP or with each other with respect to presurgical and postsurgical adverse events? How do comparative adverse events vary (a) by OMBP strategy and (b) in subgroups of especially susceptible patients?

Methods

We performed a systematic review of the published literature using established methodologies, as outlined in the Agency for Healthcare Research and Quality (AHRQ) "Methods Guide for Effectiveness and Comparative Effectiveness Reviews" (Methods Guide[a]). We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement in the reporting of this review.[19] A full description of all review steps is included in the full report and the study protocol. The PROSPERO registration number of the protocol is CRD42013004381. PROSPERO is an international database of prospectively registered systematic reviews in health and social care.

External Stakeholder Input

A Technical Expert Panel (TEP) provided input to help refine the Key Questions, identify important issues, and define parameters for the review of evidence. The nine TEP members included representatives of professional societies, experts in colorectal surgery, experts on the preoperative preparation of patients undergoing elective surgery, and an infectious disease specialist.

Literature Search and Abstract Screening

We searched MEDLINE®, the Cochrane Central Trials Registry, EMBASE™, and CINAHL® without any language or publication date restrictions (last search on September 6, 2013). See Appendix A of the full report for the exact search queries. We also did a targeted search of the FDA 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 OMBP preparation manufacturers. Finally, we searched the ClinicalTrials.gov Web site (last searched May 16, 2013) to identify ongoing comparative trials of alternative OMBP strategies. We did not consider unpublished data other than data included in FDA documents or ClinicalTrials.gov. Titles and abstracts were manually screened in duplicate following a standardization exercise.

Study Selection and Eligibility Criteria

Two investigators reviewed full-text articles independently for eligibility. Disagreements were resolved by consensus including at least one additional investigator.

We included English-language full-text reports of randomized controlled trials (RCTs) with at least 10 patients per arm and nonrandomized comparative studies (NRCSs) with 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 at least 80 percent of surgeries involved the large bowel. For harms we also included cohort studies of at least 200 participants.

We defined as OMBP the use of any preparation for surgery that was administered orally or through a nasogastric tube but without need for other (e.g., endoscopic) intervention. Cointerventions could include oral or parenteral antibiotics, dietary modification, or enema. Eligible studies compared alternative OMBP strategies or OMBP versus no preparation.

We included studies reporting on a predetermined set of clinical outcomes, including overall and cause-specific survival, infectious outcomes, anastomotic leakage, planned and unplanned stomas, failed attempts to restore bowel continuity, and venous thromboembolism; health system and resource utilization outcomes, such as readmissions after surgery, reoperation, additional interventional procedures, length of stay, and admission to intensive care unit/nursing care; and patient-centered outcomes, such as patient satisfaction and quality of

[a]Available at www.effectivehealthcare.ahrq.gov/methodsguide.cfm; accessed May 11, 2013.

life. For Key Question 2 we considered the following prespecified adverse events (harms): nausea; vomiting; dehydration; electrolyte imbalance; kidney damage; emergency admissions prior to surgery; canceled, delayed, or rescheduled surgeries; allergic reactions; and seizures. Studies reporting harms were included regardless of causal attribution to OMBP.

Data Extraction

A single investigator extracted data from each study; quantitative results were verified by a second reviewer. Disagreements were resolved by consensus involving a third investigator. Following pilot testing, data were extracted into electronic forms stored in the Systematic Review Data Repository using separate forms for each Key Question.[20] We took particular care to avoid double counting (both in qualitative and quantitative analyses) when published papers reported on potentially (fully or partially) 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 papers.

Risk of Bias and Completeness of Reporting of Individual Studies

We assessed the risk of bias for each outcome following the processes described in the Methods Guide. For RCTs, we based our assessment on items derived from the Cochrane risk-of-bias tool.[21] For NRCSs and single-group studies, we used items from the Newcastle-Ottawa tool, with the addition of items relevant to statistical analysis.[22] We provide qualitative assessments regarding publication bias based on the number of available studies, the number of studies contributing information for each outcome, sample size, and the statistical significance of reported comparisons.

Synthesis

For each Key Question, we synthesized results qualitatively and assessed whether studies were sufficiently similar to be combined in a meta-analysis.

We used both pairwise and network meta-analysis. We did pairwise meta-analyses for outcome comparisons with more than three nonoverlapping studies. For outcomes with at least six studies, we used network meta-analysis to jointly analyze evidence for "OMBP with or without enema," "enema alone," and "no OMBP or enema." Studies comparing "enema alone" and "no OMBP or enema" were not in the scope of this report, and such studies (if any exist) are not included the analyses. In structural sensitivity analyses we split the "OMBP with or without enema" strategy into "OMBP alone" and "OMBP plus enema" interventions. We did not construct or analyze networks that include comparisons between alternative "active" OMBP interventions because of substantial concerns that head-to-head studies between "active" OMBP strategies are not similar to studies included in the above network. We assessed inconsistency qualitatively, by comparing results from pairwise and network meta-analyses, because formal tests for inconsistency are known to be underpowered.

Estimation was done in the generalized linear mixed-modeling framework, with binomial families and a logit link function.[23] 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 frequentist methods. Prior distributions for all model parameters were noninformative and were subjected to extensive sensitivity analyses, including the use of informative priors and the use of frequentist methods (which do not require prior specification). In network meta-analyses we assumed homogeneity of the random-effects variances at the between-study level because few studies provided information for each comparison in the network. Heterogeneity was assessed based on the posterior distribution of the between-study heterogeneity parameter.

Subgroup, Metaregression, and Sensitivity Analyses

We explored between-study heterogeneity using subgroup and metaregression analyses (e.g., year of publication or items related to study risk of bias). We also performed sensitivity analyses, such as leave-one-out analyses, analyses assuming a fixed-effects model, analyses including a retracted study, and analyses evaluating alternative network topologies.

Software

All analyses were performed using Stata IC (version 12.1/SE Stata Corp., College Station, TX). We did not perform any adjustments for multiple comparisons. Markov-chain Monte Carlo estimation for Bayesian analysis was done in WinBUGS (version 1.4.3; MRC Biostatistics Unit, Cambridge, UK) through calls from Stata.

Grading the Body of Evidence and Assessing Applicability

We followed the Methods Guide to evaluate the strength of the body of evidence (high, moderate, low, or insufficient) for each Key Question with respect to the following domains: risk of bias, consistency, directness, precision, and reporting bias. We followed the Methods Guide[24] to evaluate the applicability of included studies to patient populations of interest, as guided by the Key Questions.

Results

Our literature search yielded 11,869 citations, of which 901 were reviewed in full text. Sixty unique studies (in 65 publications) were included: 44 RCTs, 10 NRCSs; and 6 single-group cohorts. Fifty-eight studies were included in main analyses. One retracted publication and one possible duplicate were excluded. (See the full report for details on the literature flow.) The most common reasons for exclusion of articles were related to study design (e.g., we excluded uncontrolled case series) and language of publication. Up to 2010 only four relevant non–English-language studies were available. These studies reported on few patients and very low numbers of events, so their inclusion would not appreciably affect our results. See Appendix B of the full report for a list of the excluded studies and reasons for exclusion. Data extraction forms and summary tables for all included studies are available online in the Systematic Review Data Repository (http://srdr.ahrq.gov/).

Effectiveness: OMBP Versus No OMBP or Enema; Alternative OMBP Strategies (Key Question 1)

Forty-four RCTs and 10 NRCSs met criteria for Key Question 1. Forty-two of the 44 RCTs were included in main analyses. The published report of one RCT was retracted and was not included in the main analyses, and one RCT was considered to report on a subset of patients of a larger trial (possible duplicate). Two RCTs enrolled exclusively children, and one RCT compared inpatient versus outpatient preparation in adults. The remaining 39 RCTs were classified into two mutually exclusive groups: trials comparing OMBP versus no OMBP, each with or without enema (active versus inactive comparison) and trials comparing alternative active OMBP strategies (active versus active comparison).

Compared with studies of OMBP versus no OMBP, studies of active OMBP regimens were conducted in earlier years (median year of enrollment start, 1986 vs. 2001) and more often, or even exclusively, employed preparations that have fallen out of use (e.g., several-day-long preparations, multiple enemas, and whole-gut irrigation with large volumes administered through nasogastric tubes). Most importantly, perioperative parenteral antibiotics were used in almost all arms of studies of OMBP versus no OMBP (1 study reported unclear information), compared with only 26 of the 46 OMBP-treated arms. Because of these differences, we considered comparisons of OMBP versus no OMBP separately from comparisons among alternative active OMBP strategies. The former appear to be applicable to contemporary decisionmaking regarding preoperative preparation, whereas the latter are less so.

OMBP Versus No OMBP

Eighteen RCTs and seven NRCSs contributed information to the main analysis. Common indications for surgery were colorectal cancer and diverticular disease. Details on the surgical approach (e.g., operation types, anastomosis methods, open vs. surgical surgery) were generally poorly reported. With respect to stratification by surgical site, one study enrolled exclusively patients undergoing rectal surgery and two studies enrolled only patients undergoing left-sided colorectal surgeries. In total, through author contact and previous reviews, we could obtain results stratified by anatomic location or restricted to a single location from 11 trials for the outcome of anastomotic leakage.

All but two studies enrolled adult patients (or did not provide relevant information). Two RCTs explicitly reported that the study population consisted of both adults and children but did not report results stratified by age group. Because children are probably the minority of the study sample and for consistency with previous work, we included these studies together with studies enrolling exclusively adults. In sensitivity analyses, we assessed the robustness of our results to their removal from the dataset.

RCTs

Eighteen RCTs compared OMBP versus no OMBP. Studies used a variety of OMBP regimens: seven used PEG, five used other laxatives or cathartics, and six used other methods (including combinations of the aforementioned regimens). Almost all studies reported using intravenous antibiotics in the perioperative period (one study provided unclear information) and three studies reported also using oral antibiotics.

The majority of RCTs were considered to be at moderate risk of bias. Overall, based on the number of items

considered indicative of "low" risk, eight studies were considered to be at high risk of bias, nine to be at moderate risk of bias, and one to be at low risk of bias.

In order to extract the maximum amount of information from the available RCTs, we used two meta-analytic approaches: (1) a pairwise meta-analysis of trials directly comparing OMBP with either enema or no preparation and (2) a network meta-analysis of the same trials as the basis for calculating the probability that each intervention was best/second best/worst. Both approaches were subjected to extensive sensitivity analyses. We based our assessment of the evidence on the results of all these analyses.

Table A shows pairwise Bayesian random-effects meta-analyses of all RCTs for six clinical outcomes and analyses stratified by whether enema was administered in the comparator group. For all outcomes the 95% credible intervals (CrIs) included an odds ratio (OR) of 1 (i.e., 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. There was some indication of between-study heterogeneity, particularly for the comparison of OMBP with or without enema versus enema, but the CrIs around the between-study variance estimates were very broad.

For outcomes reported by 10 or more studies (all-cause mortality, anastomotic leakage, and wound infection), we also investigated whether the effect of OMBP varied by anatomic location (colon vs. rectum), year of publication, or items related to study risk of bias (specifically, randomized sequence generation and allocation concealment).

Separate analyses by anatomic location 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 10 studies (11 publications) that used heterogeneous subgroup definitions. The OR for anastomotic leakage comparing OMBP versus enema or no preparation was 1.01 (95% CrI, 0.57 to 1.96) for colon surgery (9 studies) and 0.91 (95% CrI, 0.42 to 2.45) for rectal surgery (7 studies, 6 of which provided information for both subgroups).

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

Outcome	Comparison	N Studies (N Events/N Patients Per Group)	OR (95% CrI)	Between-Study Variance (95% CrI)
All-cause mortality	OMBP ± enema vs. enema/no prep	14 (45/2,550 vs. 44/2,544)	1.17 (0.67 to 2.67)	0.12 (0.00 to 1.99)
	OMBP ± enema vs. no prep	10 (38/2,024 vs. 40/2,014)	1.09 (0.57 to 2.99)	0.17 (0.00 to 2.61)
	OMBP ± enema vs. enema	4 (7/526 vs. 4/530)	1.99 (0.27 to 18.45)	0.82 (0.00 to 3.76)
Anastomotic leakage	OMBP ± enema vs. enema/no prep	16 (126/2,702 vs. 124/2,680)	1.08 (0.79 to 1.63)	0.08 (0.00 to 0.72)
	OMBP ± enema vs. no prep	12 (102/2,176 vs. 103/2,150)	1.06 (0.73 to 1.73)	0.09 (0.00 to 0.95)
	OMBP ± enema vs. enema	4 (24/526 vs. 21/530)	1.24 (0.38 to 4.72)	0.61 (0.00 to 3.59)
Wound infection	OMBP ± enema vs. enema/no prep	16 (266/2,612 vs. 239/2,603)	1.19 (0.93 to 1.63)	0.04 (0.00 to 0.41)
	OMBP ± enema vs. no prep	12 (218/2,086 vs. 190/2,073)	1.27 (0.95 to 1.88)	0.05 (0.00 to 0.50)
	OMBP ± enema vs. enema	4 (48/526 vs. 49/530)	1.04 (0.37 to 3.34)	0.52 (0.00 to 3.46)
Peritonitis/ intra-abdominal abscess	OMBP ± enema vs. enema/no prep	14 (51/2,381 vs. 70/2,362)	0.84 (0.50 to 1.66)	0.25 (0.00 to 1.77)
	OMBP ± enema vs. no prep	10 (45/1,855 vs. 64/1,832)	0.84 (0.45 to 2.00)	0.38 (0.00 to 2.74)
	OMBP ± enema vs. enema	4 (6/526 vs. 6/530)	0.99 (0.21 to 4.68)	0.42 (0.00 to 3.51)
Reoperation	OMBP ± enema vs. enema/no prep	8 (124/1,967 vs. 119/1,945)	1.14 (0.57 to 2.65)	0.38 (0.00 to 3.23)
	OMBP ± enema vs. no prep	6 (117/1,742 vs. 111/1,723)	1.15 (0.73 to 2.50)	0.09 (0.00 to 1.82)
	OMBP ± enema vs. enema	2 (7/225 vs. 8/222)	0.50 (0.03 to 6.12)	2.49 (0.27 to 3.93)
SSI	OMBP ± enema vs. enema/no prep	7 (206/1,279 vs. 197/1,230)	1.19 (0.56 to 2.63)	0.64 (0.11 to 2.91)
	OMBP ± enema vs. no prep	5 (173/1,087 vs. 171/1,040)	1.10 (0.41 to 3.05)	0.76 (0.10 to 3.39)
	OMBP ± enema vs. enema	2 (33/192 vs. 26/190)	1.50 (0.24 to 10.42)	1.20 (0.02 to 3.79)

CrI = credible interval; no prep = no OMBP and no enema; OMBP = oral mechanical bowel preparation; OR = odds ratio; SSI = surgical site infection

Note: OR values lower than 1 indicate that events are less common among OMBP-treated groups (i.e., that OMBP is beneficial).

Regression analyses did not reveal any time trends and suggested that randomized sequence generation methods did not have a major impact on the effect size for all outcomes considered. Similarly, allocation concealment method was not associated with the effect sizes for all-cause mortality or wound infection. CrIs were wide, indicating substantial uncertainty regarding effect modification by these factors. However, trials with adequate and clearly reported allocation concealment methods suggested that OMBP has a protective effect (i.e., OR <1) for anastomotic leakage, whereas trials with inadequate or unclearly reported allocation concealment methods had a summary effect in the opposite direction (i.e., OR >1); the relative OR comparing these results was 0.45 (95% CrI, 0.23 to 0.85). We caution against interpreting this result as "proof" for the presence of bias because—

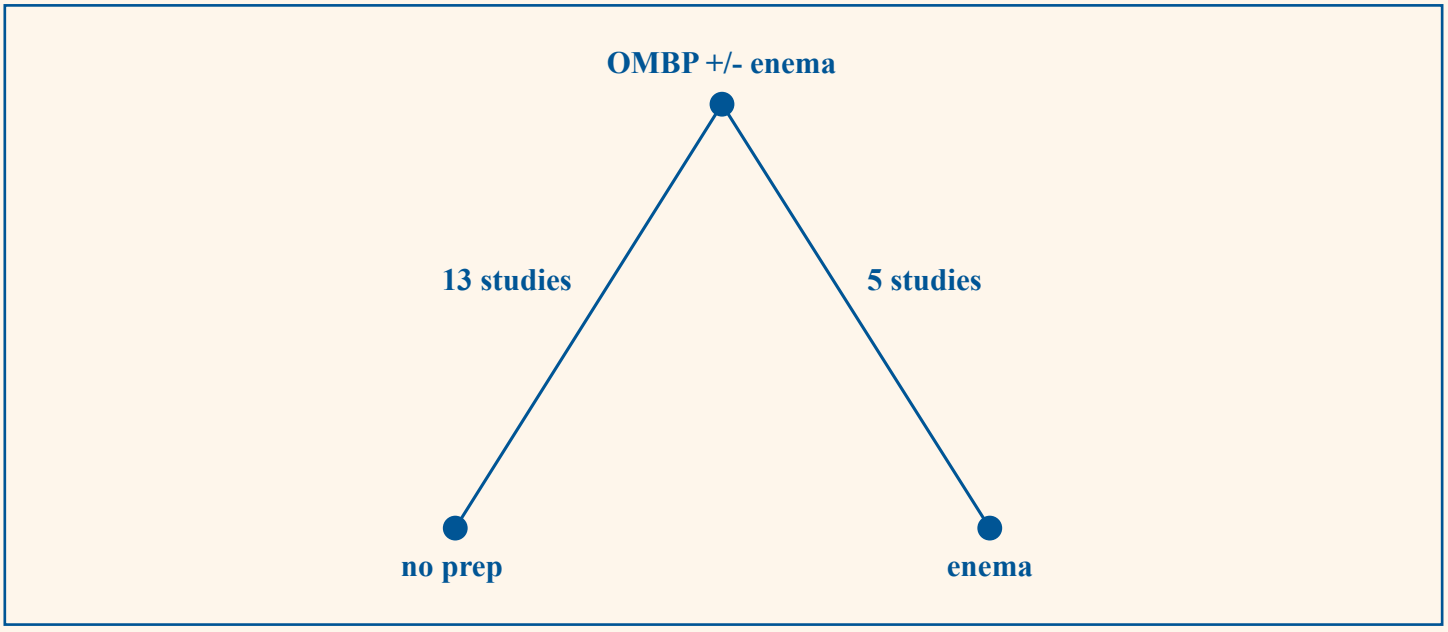
- The reporting of allocation concealment was incomplete in the reviewed studies. (The adequacy of allocation concealment could not be determined in 10 studies.)
- Other study characteristics that may be associated with allocation concealment methods (and reporting) could not be accounted for in the analysis.
- The association was observed for only one of the outcomes of interest and in one of several regression analyses.
- The relative OR was extreme and fairly imprecise.

Of note, in the subgroup of studies with adequate allocation concealment, the CrI of the OR for anastomotic leakage comparing OMBP versus enema or no preparation included the null value; OR = 0.81 (95% CrI, 0.56 to 1.19). These findings, in conjunction with the wide CrIs observed in the overall meta-analysis, support the need for more research.

Using network meta-analysis we compared "OMBP with or without enema," "enema," and "no preparation" (Figure A). This analysis "respects" the randomization procedure within each study and allows us to "borrow strength" from all studies in estimating between-study heterogeneity. The point estimates in Table B are similar to those from pairwise meta-analyses (Table A).

Results were robust in all sensitivity analyses: use of informative priors, leave-one-out analyses, analyses assuming a fixed-effects model, and reanalyses after excluding a group of studies. Finally, we separated the "OMBP with or without enema" strategy into "OMBP

Figure A. Three-node network structure



No prep = no OMBP and no enema; OMBP = oral mechanical bowel preparation

Note: Network structure for the 3-node network meta-analysis comparing OMBP +/- enema vs. enema alone vs. no preparation. Nodes indicate the treatments compared. Connecting lines depict direct comparisons and are labeled with the total number of available studies. (Not all studies contributed data for all outcomes.) A total of 18 studies reported information on at least 1 of the outcomes of interest. Some studies did not report information on some outcomes. (This is why the number of studies for each outcome in Table A is not 18.)

Table B. Summary estimates from the three-node network meta-analysis

Outcome	Comparison	OR (95% CrI)
All-cause mortality	OMBP ± enema vs. no prep	1.08 (0.56 to 3.02)
	OMBP ± enema vs. enema	1.88 (0.40 to 10.56)
Anastomotic leakage	OMBP ± enema vs. no prep	1.07 (0.73 to 1.73)
	OMBP ± enema vs. enema	1.20 (0.57 to 2.61)
Wound infection	OMBP ± enema vs. no prep	1.27 (0.94 to 1.91)
	OMBP ± enema vs. enema	1.00 (0.59 to 1.76)
Peritonitis/intra-abdominal abscess	OMBP ± enema vs. no prep	0.82 (0.46 to 1.82)
	OMBP ± enema vs. enema	0.99 (0.24 to 4.07)

CrI = credible interval; no prep = no OMBP and no enema; OMBP = oral mechanical bowel preparation; OR = odds ratio
Note: OR values lower than 1 indicate that events are less common among treatment groups receiving the first-listed treatment for each comparison. Results based on indirect comparisons were very imprecise and are not shown. Outcomes with fewer than 6 studies were not analyzed with network meta-analysis; analyses for reoperation and surgical site infections produced very wide CrIs and are not shown.

with enema" and "OMBP without enema" in a second network meta-analysis (a four-node network), but the data were not adequate to draw definitive conclusions due to imprecision.

NRCSs

Seven NRCSs reported information on the comparison of OMBP versus no preparation. Because of heterogeneity in patient selection and outcomes reported, differences in study design, and concerns regarding risk for residual confounding, we did not perform meta-analysis. In sum, 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, CrIs were generally broad (e.g., could not exclude a 50% change in odds in either direction). Studies were at substantial risk of bias, mostly due to confounding factors that had not been adequately controlled in the design or analysis of these investigations.

Alternative Active OMBP Strategies

Twenty-three RCTs and two NRCSs provided information on comparisons among active OMBP strategies for patients undergoing elective colorectal surgery. We first examine the findings of RCTs, followed by the findings of NRCSs.

RCTS in Adults

Twenty-one of the 23 RCTs enrolled primarily adult patients and 2 enrolled exclusively children. The most common indications for surgery were colorectal cancer and diverticular disease. Information on the surgical approach (e.g., operation types, anastomosis methods, open versus laparoscopic surgery) and on the breakdown of surgical sites into right colon, left colon, and rectum was generally not reported.

The majority of RCTs (19 out of 23) had 2 treatment groups, 3 had 3 groups, and 1 had 4 groups, for a total of 51 active OMBP groups and 34 possible pairwise contrasts. Studies compared diverse OMBP strategies. We grouped OMBP strategies into seven grand categories to facilitate synthesis and presentation: PEG, PEG combined with laxatives or cathartics, hyperosmotic sodium solutions, other laxatives or cathartics, whole-gut irrigation with electrolyte solutions (other than PEG), mixed/other (e.g., combinations of OMBP drugs), and dietary interventions. The most common comparisons were PEG versus whole-gut irrigation (examined in 5 RCTs) and PEG-based versus laxative/cathartic-based OMBP (5 RCTs).

Many items necessary for detailed assessment of risk of bias were not reported in most studies. Overall, based on the number of items considered indicative of "low" risk, 10 studies were considered to be at high risk of bias, 12 to be at intermediate risk of bias, and 1 to be at low risk of bias.

We did not perform a meta-analysis because of the extensive diversity of the OMBP strategies employed, the heterogeneity in the assessed outcomes, and concerns regarding selective outcome reporting (and other risk-of-bias dimensions). Instead, we summarize the information extracted from studies qualitatively. Briefly, we observed that—

- **Only 13 out of the 28 possible comparisons had some empirical information** (i.e., at least 1 study provided evidence about them). The "density" of

observed versus possible comparisons is somewhat optimistic: we were quite lenient in categorizing the individual active OMBP comparisons into the seven broad categories represented by the rows and columns in each panel.

- **Outcomes were assessed or reported in sufficient detail in a minority of the conducted studies,** perhaps with the exception of wound infection. When two or more studies provided information for the same outcome, no conclusions could be reached regarding the comparative effectiveness of interventions.
- **Some of the outcomes of interest to this review, such as surgical site infections, pulmonary embolism, and venous thrombosis, were not reported in any study.** The empirical evidence that is available to a literature-based review is but a small fraction of what could have been available. This represents a lost opportunity.
- **The majority of available studies were small and probably underpowered to detect modest or small effect sizes, let alone relatively rare harms.** Across all 106 analyzable results (outcome/comparison combinations), 1 was statistically significant.[b] This proportion (2%) is less than the 5 percent that would be expected by chance if the null hypothesis of no association were true. Because the true distribution of effects in this body of literature is unknown and because these analyses are not independent (when results are derived from the same study, analyses are performed in the same patient population), one cannot simply infer that all identified statistically significant findings are false. Nevertheless, this observation is congruent with the notion that very few, if any, genuine differences exist among active OMBP strategies in the included studies.

RCTS in Children

Two studies, both conducted in India, compared alternative active OMBP strategies in children undergoing colorectal surgery. The first study compared whole-gut irrigation with normal saline with added potassium versus PEG. The second study compared whole-gut irrigation with normal saline, PEG, or Ringer's lactate. Both studies were considered to be at high risk of bias and did not provide conclusive evidence on the comparative effectiveness of the OMBP strategies they evaluated.

NRCSs

Only two NRCSs reported information on the comparison of alternative active OMBP strategies, including preparations that are no longer in clinical use (e.g., mannitol). The same observations that apply to the RCTs of alternative active interventions apply here as well.

Inpatient Versus Outpatient OMBP

One RCT and one retrospective NRCS compared inpatient versus outpatient use of OMBP using PEG. Both studies were considered to be at high risk of bias. No statistically significant differences among arms were reported. However, results were inconclusive due to the very small number of events for all reported outcomes.

Harms: OMBP Versus No OMBP or Enema; Different OMBP Strategies (Key Question 2)

To address Key Question 2 we summarize the evidence on the following predefined potential adverse events of OMBP: nausea; vomiting; dehydration; electrolyte imbalance; kidney damage; emergency admissions prior to surgery; canceled, delayed, or rescheduled surgeries; allergic reactions; and seizures. The organization of the subsequent sections follows that of Key Question 1. We first discuss comparative studies of OMBP versus enema or no preparation, followed by comparative and noncomparative (single-group) studies of alternative active OMBP strategies. We did not attempt a meta-analysis because of the substantial diversity in outcome definitions, and variation in the reporting of adverse events.

OMBP Versus No OMBP

Of the 18 RCTs included in our main analyses comparing OMBP with or without enema versus enema alone or no preparation, only two provided information on harms (1 for nausea and 1 for renal failure). In the study reporting data on nausea, 9 out of 95 OMBP-treated patients and 8 of 90 controls reported experiencing nausea ($p = 0.77$). In the other study, 3 of 89 patients receiving OMBP versus 1 of 89 patients receiving no preparation experienced acute renal failure ($p = 0.62$). None of the seven NRCSs comparing OMBP versus no preparation reported information on the prespecified adverse events.

[b]These results pertain to the following outcomes: all-cause mortality, cause-specific mortality, anastomotic leakage, wound infection, wound dihiscence, peritonitis/intra-abdominal abscess, surgical site infections, infectious complications (not otherwise specified), extra-abdominal infections, reoperation, pulmonary embolism, and venous thrombosis.

Alternative Active OMBP Strategies

RCTs in Adults

As discussed in the corresponding section of Key Question 1, studies of alternative active OMBP strategies used diverse OMBP strategies, assessed heterogeneous outcomes, and, raised concerns of selective outcome reporting (and other risk-of-bias dimensions). Regarding the assessment of adverse events, studies utilized a diverse set of symptom scales to measure severity of patient-reported adverse events (nausea, vomiting, fatigue, bloating, cramping, etc.). In most studies adverse event definitions were not clearly described, making it impossible to consistently compare outcomes across studies. For these reasons, we have used the same approach as in Key Question 1 and summarize findings qualitatively.

We make observations similar to those for Key Question 1: empirical information is available only for some out of many possible contrasts, and when provided, it is poorly reported. For example, most reported data fall into the outcome category "other patient-reported adverse events," which is indicative of nonstandardized reporting. Renal failure, an outcome considered important given that many OMBP strategies involve ingestion of large volumes of electrolyte solutions, was not reported in any study. Further, the majority of the available studies were small and probably underpowered to detect modest or small effect sizes, let alone relatively rare harms. Across all 88 analyzable results (outcome/comparison combinations), 27 were statistically significant. However, there is no readily discernible pattern. Because the true distribution of effects in this body of literature is unknown and because many of these analyses are not independent (e.g., nausea often accompanies vomiting), one cannot make statements on whether the identified statistically significant findings are more than what would be expected by chance.

RCTs in Children

The studies comparing alternative active OMBP strategies in children undergoing colorectal surgery did not provide conclusive evidence on the adverse events of the OMBP strategies they evaluated.

NRCSs

The two NRCSs comparing alternative active OMBP strategies versus no preparation did not report information on the prespecified adverse events.

Single-Group Cohorts

Six studies met our inclusion criteria for single-group cohorts and reported results on at least one of the prespecified adverse events. Overall, reporting of adverse events was partial and was limited to vomiting, nausea, vomiting and nausea, and allergic reactions. Almost universally, the rates of reported adverse events were below 4 percent. The exception was a cohort of patients receiving OMBP with sodium phosphate with or without oral antibiotics, for whom the rate of vomiting was approximately 17 percent (51 of 300 patients). No study made causal attributions of the adverse events to the OMBP drugs or to the cointerventions. No studies reported adverse events by any of the prespecified subgroups of interest.

Inpatient Versus Outpatient OMBP

The two studies (1 RCT and 1 NRCS) comparing inpatient versus outpatient administration of OMBP did not report information on the prespecified adverse events of interest.

Discussion

Key Findings

We reviewed 60 studies spanning 40 years of empirical research on the benefits and harms of alternative OMBP strategies for elective colorectal surgery and noted a striking shift in the design and focus of research over time. In the early 1970s OMBP was widely considered highly desirable on the basis of pathophysiological arguments, and the majority of research focused on determining which OMBP strategy was best.[5] It appears that those earlier assumptions are being questioned by an increasing number of studies comparing OMBP with no OMBP, while few recent studies compare alternative active OMBP strategies. It is probably fair to state that the most relevant question is whether or not to use OMBP with any of the relatively short-duration preparation regimens that are used in current practice.

After examining the literature for a wide range of clinical outcomes, we found no evidence that OMBP with or without enema differs from enema or no preparation. However, the uncertainty accompanying the estimated treatment effects was considerable. Based on the boundaries of the credible intervals, one cannot exclude a modest (e.g., 30–50%) change in odds in either direction for all-cause mortality, anastomotic leakage, wound infection, and peritonitis. This uncertainty is explained by the relatively small sample size of included studies and the relative rarity of key clinical events such as death, anastomotic leakage, reoperation, and severe infection. Of more concern, information on important subgroups, such as by anatomic location (colon vs. rectum) and

type of surgery (laparoscopic vs. open), was sparsely reported in the published literature, as was information on important potential effect modifiers (e.g., oral or parenteral antibiotics). We also attempted to assess the comparative effectiveness of different OMBP strategies, but the studies were too small and heterogeneous for firm conclusions, and in any case most of the strategies compared are no longer in use, rendering the results nonapplicable. Similarly, we attempted to assess harms, but too few studies collected harms consistently.

Assessment of the Strength of Evidence

Table C presents a summary of the report's key findings for each Key Question. When appropriate, results are presented separately for each of the populations and outcomes of interest. Please see the Methods section of the full report for a detailed discussion of our approach to rating the strength of evidence. Overall, we found weak evidence that OMBP and no preparation had similar effectiveness with respect to the outcomes of all-cause mortality, anastomotic leakage, wound infection, and peritonitis. The ORs for these outcomes were all close to 1 and the CrIs from pairwise meta-analyses excluded large differences (e.g., increasing the odds of an outcome by 2-3 times). For all other outcomes for this comparison, results were too imprecise to exclude even larger treatment effects and thus insufficient to draw conclusions. Similarly, we found that evidence on the comparison of OMBP versus enema was insufficient for all outcomes of interest.

Compared with the most recent Cochrane Review of OMBP,[1] we included a broader spectrum of study designs (including NRCSs and single-group cohorts) and performed more extensive data analyses using Bayesian network meta-analysis. Furthermore, we identified several studies published after the last search of the Cochrane Review and 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.[1,25-28] While, like those reviews, we did not find evidence of clear benefit from OMBP, the wider CrIs 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 (e.g., coadministration of oral antibiotics, type of surgery, location of surgery), which existing studies do not adequately address. 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 papers. Second, we excluded studies not published in English, although this is unlikely to cause major bias, since previous work identified only four relevant non–English-language publications including a total of 269 patients. Third, we relied mainly on electronic database searches and perusal of reference lists to identify relevant studies. Unpublished relevant studies may have been missed. Fourth, indexing of nonrandomized studies, and single-group cohort studies in particular, is less complete than indexing of randomized trials and we may have failed to identify relevant studies. However, in order to increase the sensitivity of our searches, we did not use search filters that limit results to specific study designs.

Applicability

The existing evidence base comparing OMBP, with or without enema, versus enema or no preparation appears to be applicable to U.S. 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 U.S. clinical practice. However, none of these studies was conducted in the United States, raising the possibility that system-level differences (e.g., differences in policies on oral antibiotics, preoperative fluid use, or fasting) may render findings less applicable to U.S. 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. Similarly, the applicability of our findings to patients undergoing laparoscopic colorectal surgery is unclear because few studies reported relevant information. Regarding studies comparing alternative active OMBP strategies, applicability appears to be severely limited because they examined OMBP regimens that have fallen out of use in modern practice, such as whole-gut irrigation with non-PEG electrolyte solutions and mannitol.

Table C. Summary assessment of the strength of evidence				
Population	**Outcome**	**Comparison**	**Assessment of Strength of Evidence**	**Key Findings and Comments***
KQ1: Adult patients undergoing colorectal surgery	All-cause mortality	OMBP vs. no prep	Low (for lack of difference)	The OR in meta-analysis of 10 studies was 1.09 (95% CrI, 0.57 to 2.99), indicating moderate to substantial uncertainty in the summary estimate. Studies were at moderate ROB. There was no indication of selective outcome reporting. There was no statistical evidence of inconsistency; however, because there are only a few studies and most of them are small, statistical heterogeneity cannot be reliably detected.
		OMBP vs. enema	Insufficient	The OR in meta-analysis of 4 studies was 1.99 (95% CrI, 0.27 to 18.45), indicating substantial uncertainty in the summary estimate. Studies were at moderate ROB. There was no indication of selective outcome reporting. There was no statistical evidence of inconsistency; however, because there are only a few studies and most of them are small, statistical heterogeneity cannot be reliably detected.
	Anastomotic leakage	OMBP vs. no prep	Low (for lack of difference)	The OR in meta-analysis of 12 studies was 1.06 (95% CrI, 0.73 to 1.73), indicating moderate uncertainty in the summary estimate. Pairwise analysis concurred. Studies were at moderate ROB. There was no indication of selective outcome reporting. There was no statistical evidence of inconsistency; however, because there are only a few studies and most of them are small, statistical heterogeneity cannot be reliably detected.
		OMBP vs. enema	Insufficient	The OR in meta-analysis of 4 studies was 1.24 (95% CrI, 0.38 to 4.72), indicating substantial uncertainty in the summary estimate. Studies were at moderate ROB. There was no indication of selective outcome reporting. There was no statistical evidence of inconsistency; however, because there are only a few studies and most of them are small, statistical heterogeneity cannot be reliably detected.

Table C. Summary assessment of the strength of evidence (continued)				
Population	**Outcome**	**Comparison**	**Assessment of Strength of Evidence**	**Key Findings and Comments***
KQ1: Adult patients undergoing colorectal surgery (continued)	Wound infection	OMBP vs. no prep	Low (for lack of difference)	The OR in meta-analysis of 12 studies was 1.27 (95% CrI, 0.95 to 1.88), indicating moderate uncertainty in the summary estimate. Studies were at moderate ROB. There was no indication of selective outcome reporting. There was no statistical evidence of inconsistency; however, because there are only a few studies and most of them are small, statistical heterogeneity cannot be reliably detected.
		OMBP vs. enema	Insufficient	The OR in meta-analysis of 4 studies was 1.04 (95% CrI, 0.37 to 3.34), indicating substantial uncertainty in the summary estimate. Studies were at moderate ROB. There was no indication of selective outcome reporting. There was no statistical evidence of inconsistency; however, because there are only a few studies and most of them are small, statistical heterogeneity cannot be reliably detected.
	Peritonitis/ intra-abdominal infection	OMBP vs. no prep	Low (for lack of difference)	The OR in meta-analysis of 10 studies was 0.84 (95% CrI, 0.45 to 2.00), indicating moderate uncertainty in the summary estimate. Studies were at moderate ROB. There was no indication of selective outcome reporting. There was no statistical evidence of inconsistency; however, because there are only a few studies and most of them are small, statistical heterogeneity cannot be reliably detected.
		OMBP vs. enema	Insufficient	The OR in meta-analysis of 4 studies was 0.99 (95% CrI, 0.21 to 4.68), indicating substantial uncertainty in the summary estimate. Studies were at moderate ROB. There was no indication of selective outcome reporting. There was no statistical evidence of inconsistency; however, because there are only a few studies and most of them are small, statistical heterogeneity cannot be reliably detected.

Table C. Summary assessment of the strength of evidence (continued)				
Population	**Outcome**	**Comparison**	**Assessment of Strength of Evidence**	**Key Findings and Comments***
KQ1: Adult patients undergoing colorectal surgery (continued)	Reoperation	OMBP vs. no prep	Insufficient	The OR in meta-analysis of 6 studies was 1.15 (95% CrI, 0.73 to 2.50), indicating substantial uncertainty in the summary estimate. Studies were at moderate ROB. There was some concern regarding selective outcome reporting. There was statistical evidence of inconsistency. However, because there are only a few studies and most of them are small, statistical heterogeneity cannot be reliably detected; the 2.5th percentile of the posterior distribution of the between-study variance of the log-OR was 0.27.
		OMBP vs. enema	Insufficient	The OR in meta-analysis of 2 studies was 0.50 (95% CrI, 0.03 to 6.12), indicating substantial uncertainty in the summary estimate. Studies were at moderate ROB. There was some concern regarding selective outcome reporting. There was statistical evidence of inconsistency; however, estimates were imprecise.
	All other effectiveness outcomes	OMBP vs. no prep	Insufficient	Few if any studies reported information; study-specific results were imprecise. There was concern about selective outcome reporting.
		OMBP vs. enema	Insufficient	Few if any studies reported information; study-specific results were imprecise. There was concern about selective outcome reporting.
	All outcomes	Alternative active OMBP strategies vs. each other	Insufficient	Individual studies compared diverse interventions and reported outcomes heterogeneously, precluding synthesis. Study-specific results were imprecise. Studies were at moderate to high ROB. There was no indication of selective outcome reporting. There was no statistical evidence of inconsistency; however, because there are only a few studies and most of them are small, statistical heterogeneity cannot be reliably detected.
		Inpatient vs. outpatient OMBP	Insufficient	Only 2 studies were available (1 RCT at moderate ROB and 1 NRCS at high ROB). Study-specific estimates were imprecise.

Table C. Summary assessment of the strength of evidence (continued)				
Population	**Outcome**	**Comparison**	**Assessment of Strength of Evidence**	**Key Findings and Comments***
KQ1: Children undergoing elective colorectal surgery	All outcomes	All comparisons	Insufficient	Only 2 studies provided evidence on children undergoing elective colorectal surgery. Studies reported information only for wound infection (no other effectiveness outcomes were assessed) and produced imprecise results.
KQ1: Patients undergoing elective surgery for right-sided or left-sided colon, or rectal surgery	All outcomes	All comparisons	Insufficient	Only a minority of studies provided anatomic-location–specific results (and only for anastomotic leakage). Subgroup analyses did not reveal a difference in the effect of OMBP compared with enema or no preparation between colon and rectal surgery population with respect to the outcome of anastomotic leakage. Results were very imprecise for both subgroups and anatomic location was heterogeneously defined across studies. There is concern regarding selective analysis reporting.
KQ2: Patients undergoing elective colorectal surgery (general surgical population)	Adverse events	All comparisons	Insufficient	When interpreting the data available for this review, results are insufficient. Most prespecified adverse events of interest were evaluated by a small minority of studies or not examined at all. When reported, study-specific results did not lead to definitive conclusions due to imprecise results and lack of validation of the measurement scales used (for patient symptom scores). However, the evolution of the preparation strategies used in trials (with most recent studies using PEG-based strategies, possibly in combination with laxatives) indicates that these preparations may be considered the safest or more palatable for patients.
KQ2: Patients undergoing elective surgery who may be at particular risk for adverse events	Adverse events	All comparisons	Insufficient	No relevant studies were identified.

CrI = credible interval; KQ = Key Question; no prep = no OMBP and no enema; NRCS = nonrandomized comparative study; OMBP = oral mechanical bowel preparation; OR = odds ratio; PEG = polyethylene glycol; RCT = randomized controlled trial; ROB = risk of bias

*Summary estimates reported in this table are from the pairwise Bayesian meta-analysis. Results from extensive sensitivity analyses and network meta-analyses were consistent with those presented in the table.

Limitations of the Evidence

On the basis of the reviewed studies, we believe that the evidence regarding OMBP for colorectal surgery is limited in the following ways:

- Most studies enrolled small numbers of patients and reported low event rates for major clinical events during followup.
- Studies did not report results for important clinical subgroups, particularly those defined by anatomic location of surgery (colon vs. rectal surgery) and type of surgical procedure performed (e.g., open vs. laparoscopic surgery).
- Studies did not consistently report information on potential effect modifiers (particularly the coadministration of oral antibiotics).
- The literature comparing alternative active OMBP strategies for colorectal surgery was fragmented because studies used a large number of diverse preparation regimens and reported results for heterogeneous, often poorly defined, outcomes.
- Nonrandomized trials, and particularly observational studies, could not effectively supplement the results of randomized trials because of shortcomings in their analysis.

Evidence Gaps

Given the uncertainty of the evidence base, evidence gaps exist for all the Key Questions addressed in this review. In addition, there is particularly limited and incomplete information on those undergoing elective rectal surgery or laparoscopic surgery. The examined literature provided only limited information for key adverse events of interest, and none on whether the adverse events associated with OMBP use are more common in frail patients and patients with very compromised function of major systems (e.g., cardiac, pulmonary, renal, immune).

Ongoing Research

A search on May 15, 2013, in the ClinicalTrials.gov registry identified five records of studies that are expected to provide information relevant to the Key Questions of this report. They may provide more data on OMBP for laparoscopic surgery and rectal surgery, OMBP versus enema, and comparisons among alternative OMBP strategies. Additional trials will be needed to answer all the questions that remain.

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. 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 prior to colorectal surgery. Such a study should be feasible in the U.S. 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 followup is needed. A noninferiority design could be used to explore whether omission of OMBP does not worsen outcomes. Given the increasing interest in reevaluating the role of oral antibiotics in colorectal surgery preparation (especially when OMBP is omitted), factorial designs could efficiently evaluate both main effects (i.e., OMBP vs. no OMBP, oral antibiotics vs. no antibiotics) and treatment-by-treatment interactions. It is important to collect data according to anatomic location and type of surgery (open vs. laparoscopic).

An individual patient data meta-analysis of existing trials of OMBP (specifically, recent trials of OMBP vs. enema or no preparation) 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. Finally, observational studies can inform the comparative effectiveness of alternative OMBP strategies, particularly for susceptible groups that have not been represented in the RCTs thus far. Such studies should have large sample sizes (to account for the low incidence of most outcome events) 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 (e.g., propensity score or instrumental variable methods). Further, exposure assessment should include the collection of details regarding the preparation strategy (i.e., the OMBP regimen and any cointerventions), and outcome ascertainment should be done using standardized definitions for all outcomes of interest. Although the use of observational data always requires additional assumptions for valid inference on treatment effects (compared

with randomized designs), well-designed observational studies can offer valuable information regarding both the effectiveness and adverse effects of OMBP.

Conclusions

We found weak evidence suggesting that OMBP has similar effectiveness as 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 decisionmaking 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.

References

1. Guenaga KF, Matos D, Wille-Jorgensen P. Mechanical bowel preparation for elective colorectal surgery. Cochrane Database Syst Rev. 2011;(9):CD001544. PMID: 21901677.
2. Nelson DB, Barkun AN, Block KP, et al. Technology Status Evaluation report. Colonoscopy preparations. May 2001. Gastrointest Endosc. 2001 Dec;54(6):829-32. PMID: 11726878.
3. Centers for Disease Control and Prevention. National Hospital Discharge Survey. 2009. www.cdc.gov/nchs/nhds.htm.
4. Wick EC, Shore AD, Hirose K, et al. Readmission rates and cost following colorectal surgery. Dis Colon Rectum. 2011 Dec;54(12):1475-9. PMID: 22067174.
5. Nichols RL, Condon RE. Preoperative preparation of the colon. Surg Gynecol Obstet. 1971 Feb;132(2):323-37. PMID: 4929735.
6. Aydin HN, Remzi FH, Tekkis PP, et al. Hartmann's reversal is associated with high postoperative adverse events. Dis Colon Rectum. 2005 Nov;48(11):2117-26. PMID: 16228835.
7. Vermeulen J, Coene PP, Van Hout NM, et al. Restoration of bowel continuity after surgery for acute perforated diverticulitis: should Hartmann's procedure be considered a one-stage procedure? Colorectal Dis. 2009 Jul;11(6):619-24. PMID: 18727727.
8. Eagye KJ, Nicolau DP. Deep and organ/space infections in patients undergoing elective colorectal surgery: incidence and impact on hospital length of stay and costs. Am J Surg. 2009 Sep;198(3):359-67. PMID: 19306972.
9. Pena-Soria MJ, Mayol JM, Anula R, et al. Single-blinded randomized trial of mechanical bowel preparation for colon surgery with primary intraperitoneal anastomosis. J Gastrointest Surg. 2008 Dec;12(12):2103-8; discussion 2108-9. PMID: 18820977.
10. Zmora O, Wexner SD, Hajjar L, et al. Trends in preparation for colorectal surgery: survey of the members of the American Society of Colon and Rectal Surgeons. Am Surg. 2003 Feb;69(2):150-4. PMID: 12641357.
11. Englesbe MJ, Brooks L, Kubus J, et al. A statewide assessment of surgical site infection following colectomy: the role of oral antibiotics. Ann Surg. 2010 Sep;252(3):514-9; discussion 519-20. PMID: 20739852.
12. Beck DE, Fazio VW, Jagelman DG. Comparison of oral lavage methods for preoperative colonic cleansing. Dis Colon Rectum. 1986 Nov;29(11):699-703. PMID: 3095080.
13. Duthie GS, Foster ME, Price-Thomas JM, et al. Bowel preparation or not for elective colorectal surgery. J R Coll Surg Edinb. 1990 Jun;35(3):169-71. PMID: 2395132.
14. Jung B, Pahlman L, Nystrom PO, et al. Multicentre randomized clinical trial of mechanical bowel preparation in elective colonic resection. Br J Surg. 2007 Jun;94(6):689-95. PMID: 17514668.
15. Contant CM, Hop WC, van't Sant HP, et al. Mechanical bowel preparation for elective colorectal surgery: a multicentre randomised trial. Lancet. 2007 Dec 22;370(9605):2112-7. PMID: 18156032.
16. Eskicioglu C, Forbes SS, Fenech DS, et al. Preoperative bowel preparation for patients undergoing elective colorectal surgery: a clinical practice guideline endorsed by the Canadian Society of Colon and Rectal Surgeons. Can J Surg. 2010 Dec;53(6):385-95. PMID: 21092431.
17. Morotomi M, Guillem JG, Pocsidio J, et al. Effect of polyethylene glycol-electrolyte lavage solution on intestinal microflora. Appl Environ Microbiol. 1989 Apr;55(4):1026-8. PMID: 2729976.
18. Nichols RL, Broido P, Condon RE, et al. Effect of preoperative neomycin-erythromycin intestinal preparation on the incidence of infectious complications following colon surgery. Ann Surg. 1973 Oct;178(4):453-62. PMID: 4743867.
19. Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Ann Intern Med. 2009 Aug 18;151(4):264-9, W64. PMID: 19622511.
20. Ip S, Hadar N, Keefe S, et al. A Web-based archive of systematic review data. Syst Rev. 2012;1:15. PMID: 22588052.
21. Higgins JP, Altman DG, Gotzsche PC, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ. 2011;343:d5928. PMID: 22008217.
22. Deeks JJ, Dinnes J, D'Amico R, et al. Evaluating non-randomised intervention studies. Health Technol Assess. 2003;7(27):iii-x, 1-173. PMID: 14499048.

23. Dias S, Sutton AJ, Ades AE, et al. Evidence synthesis for decision making 2: a generalized linear modeling framework for pairwise and network meta-analysis of randomized controlled trials. Med Decis Making. 2013 Jul;33(5):607-17. PMID: 23104435.

24. Methods Guide for Effectiveness and Comparative Effectiveness Reviews. AHRQ Publication No. 10(11)-EHC063-EF. Rockville (MD): Agency for Healthcare Research and Quality; March 2011. Chapters available at www.effectivehealthcare.ahrq.gov.

25. Cao F, Li J, Li F. Mechanical bowel preparation for elective colorectal surgery: updated systematic review and meta-analysis. Int J Colorectal Dis. 2012 Jun;27(6):803-10. PMID: 22108902.

26. Pineda CE, Shelton AA, Hernandez-Boussard T, et al. Mechanical bowel preparation in intestinal surgery: a meta-analysis and review of the literature. J Gastrointest Surg. 2008 Nov;12(11):2037-44. PMID: 18622653.

27. Slim K, Vicaut E, Launay-Savary MV, et al. Updated systematic review and meta-analysis of randomized clinical trials on the role of mechanical bowel preparation before colorectal surgery. Ann Surg. 2009 Feb;249(2):203-9. PMID: 19212171.

28. Phatak UR, Pedroza C, Millas SG, et al. Revisiting the effectiveness of interventions to decrease surgical site infections in colorectal surgery: a Bayesian perspective. Surgery. 2012 Aug;152(2):202-11. PMID: 22828141.

Full Report

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