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Research Article

Post-Operative Outcomes with Combination Bowel Preparation Compared to Oral Non-Absorbable Antibiotics or no Preparation: An Update of Systematic Review and Meta-Analysis

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Abstract

Purpose: This is an update of a recent review on the role of combination bowel preparation (mechanical bowel preparation with oral non-absorbable antibiotics) in reducing postoperative complications in colorectal surgery for adults and pediatrics.

Methods: We searched the literature in Medline, Embase and Cochrane databases for studies published after Oct 2015, comparing combination bowel preparation to oral antibiotics alone or no preparation for adults and pediatrics undergoing elective bowel surgery (small bowel or large bowel). The search strategy from the original review was used.

Results: We identified five cohort studies, one of which was a retrospective study in pediatric population. Two studies were excluded from the meta-analysis due to overlapping patients. In comparing MBP/OA vs no prep, pooled results showed significant reduction in overall SSI (OR 0.50 [95%CI 0.31-0.79]), readmissions (OR of 0.82 [95%CI 0.76, 0.89]), and reoperation rate (OR 0.70 [95%CI 0.62-0.79]). There was no difference in occurrence of superficial SSI, or anastomotic leaks. One study assessed outcomes for MBP/OA vs OA and suggested improved overall SSI, post-op ileus and reoperation rate with MBP/OA.. Another study assessed of C. Difficile occurrence and found no difference for any of the prep modalities.

Conclusion: The update review showed moderate quality evidence of reduced overall SSI with OA, consistent with the previous review, and no clear risk of C. diff. There is some evidence to suggest superiority of MBP/OA over OA alone in reducing post-operative complications. Further randomized studies will be required to verify the findings.

Keywords: Bowel surgery; Colorectal surgery; SSI; Oral antibiotics; Pediatric surgery

Introduction

Colorectal surgery is associated with high rates of Surgical site infection (SSI) in both children and adults, reported in excess of 25%, attracting great interest for patient care quality improvement [1]. In a recent NSQIP-Pediatric database review, colorectal procedures accounted for 2.5% of the caseload and contributed 7.1% of the SSI burden, making this group of procedures an important target for SSI reduction [2]. Nichols and Condon popularized bowel preparation in 1972 and 1973, after showing reduction of post-operative infectious complications with the use of MBP and OA [3,4]. The regimen extended over three-days, requiring hospital admission, diet alteration (low residue / clear diet), and oral and rectal mechanical bowel preparation (MBP and oral antibiotics (OA). This has since changed to a shorter prep, yet the regimen of OA (neomycin and erythromycin or metronidazole PO, 4 doses starting afternoon before surgery) is still cited as most commonly used in adult studies [3]. The possibility of increase in colonic bacterial resistance moved surgeons away from OA, but recent adult studies have showed the contrary, renewing interest in their use [4].

The use of mechanical bowel preparation alone has fallen out of favor due to lack of evidence for benefit and potential increase risk of post-operative complications [5-7]. Oral antibiotics (with or without MBP) were shown to reduce SSI in the adult literature [8,9]. One systematic review and meta-analysis of 16 randomized controlled trials with 2669 participants showed significant reduction in wound infection rate when OA and intravenous (IV) antibiotics on induction were used compared to IV antibiotics alone (RR: 0.57 [95% CI: 0.43-0.76], p=0.0002) [9]. A retrospective study of pediatric patients with anorectal malformation undergoing colostomy closure found no difference in SSI rates between groups (MBP/OA: 13% *vs.* MBP alone: 17%) [10]. The authors found that MBP use was associated with a greater risk for wound infection (14% vs. 6%, p=0.04) and a longer hospital length of stay.

Koullouros et al. published a review and meta-analysis that included twenty-three Randomized-Controlled Trails (RCTs) with 5325 participants and eight cohort studies with 58,107 participants of all age groups [11]. There was a statistically significant reduction in SSIs with the use of OA and systemic IV antibiotic prophylaxis when compared to systemic antibiotics alone (OR: 0.44 (95%; CI: 0.33-

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0.58)). The addition of MBP to OA and IV antibiotics was assessed in 2 cohort studies with pooled result showing no difference between the two preparations (RR: 0.94 (95 %; CI: 0.73-1.20), p=0.62) [11].

The literature shows strong evidence on the benefit of using OA for bowel surgery. However, there is lack of evidence to inform use OA alone versus in combination with MBP in both adult and pediatric literature. The aim of this review is to provide an update on the literature after October 2015 to compare combination bowel preparation (MBP with OA) to OA alone or no bowel preparation in reduction of post-operative complications.

Materials and Methods

Inclusion criteria

Patients: We limited our search to comparative studies that were published after Oct 2015. The targeted population was adults and pediatrics undergoing elective small bowel or colorectal surgery.

Intervention: We were interested in studies addressing these three comparisons: combination bowel preparation (MBP/OA) *vs.* OA; MBP/OA *vs.* no bowel preparation (none); and OA *vs.* no prep. Standard care includes intravenous antibiotics with adequate coverage to gut flora (usually second or third generation cephalosporin and metronidazole, depending on the institution policy and patients' allergies). This is widely practiced and expected for each of the study groups. There was no restriction on the type or route of MBP (oral or rectal), and all formulations of oral antibiotics were allowed.

Outcomes: The outcomes of interest included post-operative complication, specifically occurrence of surgical site infection (either skin site infection, intra-abdominal abscess, and/or anastomotic leak). We were also interested in length of hospital stay, need for re-operation, need for readmission, development of C. difficile colitis, and electrolyte imbalance. We excluded studies that compared two different interventions of same group (e.g. one form of oral antibiotics with another). We also excluded studies with no comparison, and studies not reporting on any of the outcomes of interest.

Search methods

Electronic searches: We searched MEDLINE (ahead-of-print and MEDLINE daily, 1946 to present), EMBASE (1974 to present), and the Cochrane Central Register of Controlled Trials (CENTRAL), limiting to studies published from Nov 2015 to Aug 2019. The search strategy used by Koullouros et al. (the review to be updated) was used and modified to include small bowel surgery [11]. Searches were conducted using terms related to bowel surgery (colorectal and small bowel), mechanical bowel preparation and oral antibiotic prophylaxis and any synonyms as text words and Mesh terms as appropriate. We further checked the references of the included studies.

Risk of bias assessment: Two independent reviewers reviewed the included studies for risk of bias. We planned to use Cochrane Risk of Bias Tool for randomized-controlled trials, along with Risk of Bias tool RoB 2.0 [12,13]. Risk of bias was assessed in the following areas: bias arising from randomization process, risk of bias due to deviations from the intended interventions, missing outcome data, bias in measurement of the outcome, and bias is selection of the reported results.

ROBINs-I tool was used to assess risk of bias for non-randomized studies. Each paper was assessed for the following: bias due to confounding; bias in selection of participants for the study; bias in classification of intervention; bias due to deviations from intended interventions; bias due to missing data; bias in measurement of outcomes; and bias in selection of the reported result. Each study received a final assessment as low, moderate, serious, critical or no information. Differences in opinion were resolved by discussion involving a third reviewer for final opinion when needed.

Measures of treatment effect: For all dichotomous outcomes, we used the actual event rate to calculate Odds-Ratio (OR) and 95% confidence interval for the presentation of results. For the continuous outcome (length of hospital stay), we intended to use mean and standard deviation when possible. Data were combined using the Mantel-Hanzel method in RevMan5 [14]. We used the random-effect model because we anticipated significant heterogeneity from the wide age group and the different interventions included.

For the continuous outcome, length of stay, two of the studies reported median and interquartile range (as range or Q1 and Q3 values). Further calculations to convert median/range to mean/standard deviation were found to be non-feasible since length of stay due to its nature is most likely positively skewed. Instead a narrative synthesis for this outcome was generated.

Dealing with missing data: For published studies, missing patient information led to exclusion of these patients from the final analysis.

Assessment of heterogeneity: Heterogeneity between pooled trials was defined visually by inspecting the forest plots and assessing the degree of overlap in confidence intervals, and objectively using the Chi-squared test value (with statistical significance set at $P<0.05$) and the I^2 statistic. The latter was assessed as 'might not be important' (0% to 40%), 'moderate' (30% to 60%), 'substantial' (50% to 90%) or 'considerable' (75% to 100%) as recommended [15].

Subgroup analysis and investigation of heterogeneity: An a-priori decision was made to analyze data in subgroups according to population age group (adults and pediatric), study design (randomized and non-randomized studies) and site of anastosis (small bowel , large bowel, both) for all outcomes when applicable.

Assessment of certainty of evidence: For each comparison (MBP/OA *vs.* OA, MBP/OA *vs.* none, OA *vs.* none), the quality of evidence per outcome was assessed using the GRADE approach related to each of the key outcomes being investigated [16].

Subgroup analysis and investigation of hetrogeneity: Subgroup and sensitivity analyses were decided a priori. A sensitivity analysis was carried out to explore the impact of removing studies at overall serious risk of bias from the analyses on the pooled results.

Results

Description: results of the search

The search for studies published from Nov 2015 resulted in five studies matching the criteria. Two studies were excluded from the meta-analysis due to the use of overlapping patient datasets. Shown PRISMA chart with the process of inclusion (Figure 1).

Included studies

The 5 included studies included adults (>18 years) and pediatrics (<10 years of age); the latter were about 1100 patients (see Table 1 for further details). All studies were cohort studies obtained from prospectively collected databases.

The identified studies were not consistent in their populations. Ares 2018 looked at pediatric patients (<10years) through PHIS

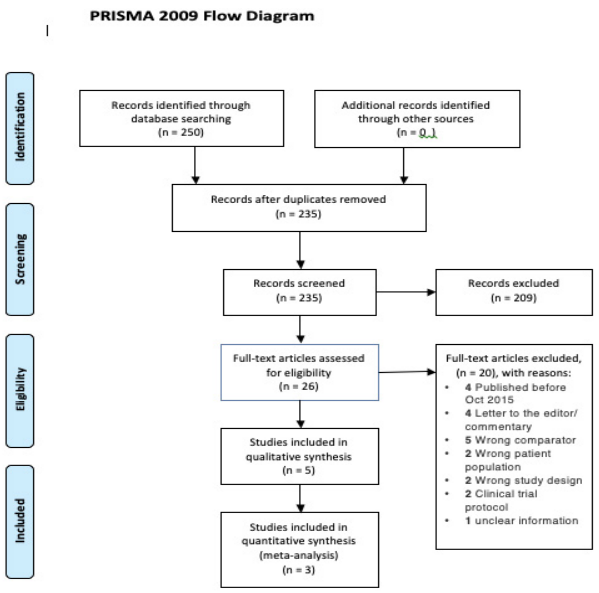

Figure 1: Inflammatory changes and bowel wall thickening centred.

database and identified patients who underwent elective colon surgery 2011-2014 through billing findings [17]. The choice of age for inclusion was to capture patients who were more likely to be admitted for bowel preparation as opposed to the older children who may have received their bowel preparation at home. The other four studies used data from ACS-NSQIP database [18-21]. Midura et al. [20] was the largest cohort study including about 29,000 adult patients identified from ACS-NSQIP database, and contributed to the majority of the patient population in the meta-analysis. The included cases were reflective of the study population, covering elective colon or rectal cases.

Agents for bowel preparation (mechanical prep and/or oral antibiotics) were not specified in any of the studies. Also, preoperative intravenous antibiotic type and timing (standard care) was not specified in any of the studies. The outcomes of interest were captured in most studies, with overall SSI being most reported factor. C. difficile infection was captured by one study [21], length of hospital stay was report by 3 of the 5 studies in median and interquartile range. The data for this outcome wasn't pooled since that would require estimation of mean and standard deviation, which may introduce further source of error. Instead, descriptive analysis of the data was provided. None of the studies reported on electrolyte imbalance.

Risk of bias assessment

Our assessment of the risk of bias in the individual included studies was shown in Figure 2. The most consistent aspect was moderate to serious risk of confounding in all 5 published studies, with overall risk of bias being moderate to serious. This was determined to be the most significant domain due to the nature of studies (non-randomized).

Effect of interventions

See summary of finding tables for the three comparisons MBP/OA *vs.* none (Table 2), MBP/OA *vs.* OA (Table 3), and OA *vs.* none (Table 4).

Comparison A: MBP/OA *vs.* none (refer to Table 2)

Overall SSI

Overall SSI was assessed in 2 studies [17,20], with pooled results for 29,910 participants showing reduction in overall SSI rate with MBP/OA compared to no prep, OR: 0.50 [95%; CI: 0.31-0.79] (Figure 3). This translates to a Relative Risk Reduction (RRR) of 50% (29% to 69%). There is an absolute effect reduction of 35 SSI per 1000. The heterogeneity observed could be partially explained by the difference in population age (pediatrics *vs.* adults). The quality of evidence is moderate due to the overall serious risk of bias, mainly due to confounding. Bias due to inconsistency, imprecision or indirectness was unlikely.

Superficial SSI (S-SSI)

This was assessed by one study [17], which showed reduction in S-SSI rate with combination bowel prep compared to no prep, OR: 1.45 [95%; CI: 0.66-3.17]. There is an absolute effect reduction of 16

Table 1: Characteristics of included trials.

No.	Study ID	Study design	Patient population	Total N	Comparison groups	Age (yrs mean ± SD)	Primary outcome
1	Ares 2018	Multicenter retrospective cohort, PHIS database	Children <10 years undergoing elective colon surgery with no diversion ostomy.	1581	No preparation (n=1,007)	2.1 ± 2.3	SSI within 30 d from surgery
					*MBP alone (n=429)**	*2.8 ± 1.7*	
					MBP + OA (n=145)	2.6 ± 2.3	
2	Garfinkle 2017	Multicenter retrospective cohort, using NSQIP database 2012-2014	Adults undergoing elective colorectal procedures.	40446	No prep (n=13,219)	61.4 ± 16.5	SSI (as above)
					*MBP alone (n=13,935)**	*62.3 ± 14.81*	
					OA alone (n=1,572)	57.9 ± 17.02	
					MBP + OA (n=11,720)	60.6 ± 14.50	
3	Koller 2018	Multicenter retrospective cohort, using NSQIP database 2012-2014	Adults undergoing elective colorectal procedures	32359	No prep (n=8,640)	61.1 ± 15.6	SSI (as above)
					*MBP alone (n=11,836)**	*61.7 ± 14.2*	
					OA alone (n=1,240)	58.0 ± 16.4	
					MBP + OA (n=10,643)	60.3 ± 14.2	
4	Midura 2018	Multicenter retrospective cohort, using NSQIP database 2012-2015	Adults undergoing elective colorectal procedures.	45724	No prep (n=11,898)	63	SSI (as above), post-op ileus
					*MBP alone (n=15,175)**	*62*	
					OA alone (n=1,791)	61	
					MBP + OA (n=16,860)	61	
5	Toh 2018	Multicenter retrospective cohort, using NSQIP database 2015	Adults undergoing elective colorectal procedures.	5729	No prep (n=1,096)	MEDIAN (IQR): 60.5 (51.0-69.0)	SSI (as above), post-op ileus
					*MBP alone (n=1,713)**	*60 (51-69)*	
					OA alone (n=199)	61	
					MBP + OA (n=2,721)	59 (51-68)	

*MBP alone group wasn't included in analysis

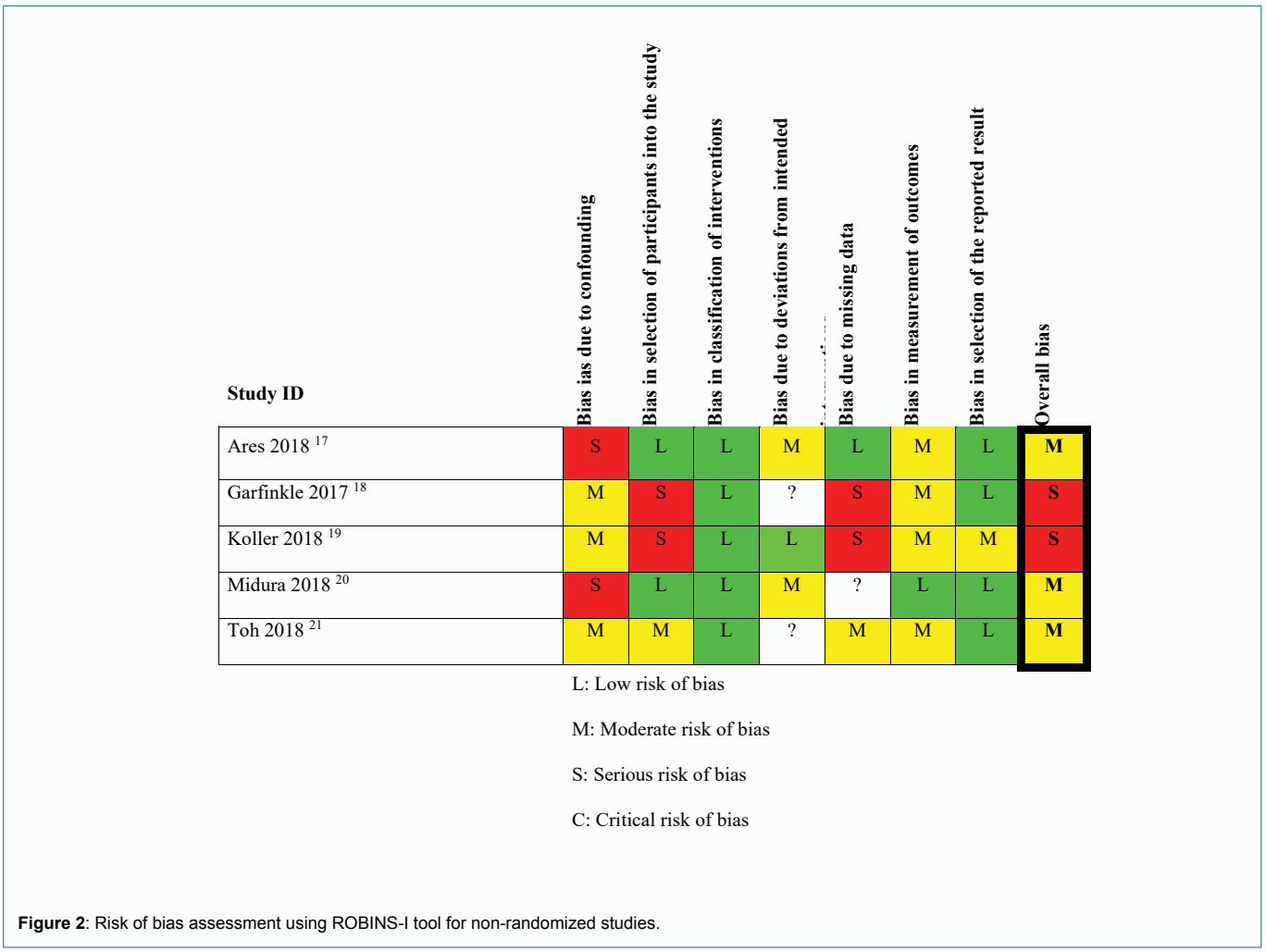

Figure 2: Risk of bias assessment using ROBINS-I tool for non-randomized studies.

S-SSI per 1000. The study was found to have a moderate overall risk of bias, with serious risk of bias due to confounding. The overall quality of evidence is low due to serious risk of bias and imprecision.

Post-op ileus

This outcome was assessed in one study [20], with OR: 0.70 [95%; CI: 0.65-0.75], In favor of combination bowel prep. This study has a moderate overall risk of bias mainly due to confounding. The overall quality of evidence is moderate due to the study design.

Anastomotic leak

The pooled data from 2 studies (29910 participants) [17,20], suggested a trend towards decreased anastomotic leaks with MBP/OA compared to no bowel preparation OR: 0.61 [95%; CI: 0.35-1.05] (Figure 4). This was not statistically significant. The effect observed was influenced by Midura et al. [20], which accounted for 71.8% of the weight. Individually, Midura et al. [20] study showed OR: 0.51 [0.45-0.59], while Ares 2018 showed OR: 0.95 [0.42-2.14]. There was poor overlap in 95% CI of the two studies, with moderate heterogeneity. One reason would be age group difference (adults *vs.* pediatrics). The quality of evidence is moderate, and was downgraded for serious risk of bias and imprecision.

Length of Hospitalization (LOH)

This outcome was reported in 2 studies [17,20], and was reported as median and IQR. For Midura et al. [20], the no prep group had slightly longer length of stay with median (IQR) of 5 (3-7) compared to MBP/OA group 4 (3-6), but the two overlapped. For Ares et al. [17], similar pattern was seen with median (IQR) of 4 (2-6) for no prep group and 6 (4.5-7.5) for MBP/OA, respectively. In the latter study, pre-op admission for bowel preparation was done for the MBP/OA group, yet that didn't reflect significantly on the LOH. Although deemed overall statistically significantly different in both studies, one could argue that the difference isn't clinically meaningful. The data from the two studies wasn't pooled, since that would require estimation of mean (SD) and introduce chances of error.

Readmission

The pooled effect from two studies (29910 patients) [17,20], showed an OR: 0.82 [95%; CI: 0.76-0.89] in favor of MBP/OA (Figure 5). This translates to a RRR of 18% (range 11% to 24%). There is no established minimally important difference for readmission, but this arguably is clinically significant. The overall quality of evidence is moderate, with serious risk of bias mainly due to confounding.

Reoperation

This outcome was assessed by only one study [20], with an OR: 0.70 [95%; CI: 0.62-0.79], in favor of combination bowel preparation. This is both statistically significant and clinically important, with a RRR of 30% (range 21% to 38%). The overall quality of evidence is moderate, with a serious risk of bias.

Table 2: Comparisons MBP/OA *vs.* none.

Summary of findings:					
MBP/OA compared to none for elective intestinal surgery in adults and pediatrics					
Patient or population: elective intestinal surgery in adults and pediatrics					
Setting: Tertiary centers - database studies					
Intervention: MBP/OA					
Comparison: none					
Outcomes	**Anticipated absolute effects* (95% CI)**		**Relative effect (95% CI)**	**№ of participants (studies)**	**Certainty of the evidence (GRADE)**
	Risk with none	Risk with MBP/OA			
Any SSI	74 per 1,000	38 per 1,000 (24 to 59)	OR 0.50 (0.31 to 0.79)	29910 (2 observational studies)	⨁⨁⨁◯ MODERATE[a]
Superficial-SSI	39 per 1,000	55 per 1,000 (26 to 113)	OR 1.45 (0.66 to 3.17)	1152 (1 observational study)	⨁⨁◯◯ LOW[a,b]
Anatomotic leak	43 per 1,000	26 per 1,000 (15 to 45)	OR 0.61 (0.35 to 1.05)	29910 (2 observational studies)	⨁⨁⨁⨁ HIGH[a]
Post-op ileus	127 per 1,000	92 per 1,000 (86 to 98)	OR 0.70 (0.65 to 0.75)	28758 (1 observational study)	⨁⨁⨁◯ MODERATE[c]
Readmission	102 per 1,000	86 per 1,000 (80 to 92)	OR 0.82 (0.76 to 0.89)	29910 (2 observational studies)	⨁⨁⨁◯ MODERATE[a]
Reoperation	45 per 1,000	32 per 1,000 (28 to 36)	OR 0.70 (0.62 to 0.79)	28758 (1 observational study)	⨁⨁⨁◯ MODERATE[c]
Length of hospitalization (LOH)	For Midura 2018, the no prep group had slightly longer length of stay with median of 5 days (IQR 3-7) compared to MBP/OA group 4 (3-6).			29910	⨁◯◯◯
	For Ares 2018, a similar pattern was seen with a median 4 days (IQR 2-6) for no prep group and 6 (4.5-7.5) for MBP/OA.			(2 observational studies)	VERY LOW[a,d,e,f]
C.difficile infection (C. diff)	13 per 1,000	12 per 1,000 (5 to 28)	OR 0.87 (0.36 to 2.12)	1992 (1 observational study)	⨁⨁⨁◯ MODERATE[g]

Table 3: Comparisons MBP/OA *vs.* OA.

Summary of findings:					
Bowel preparation (oral antibiotics + mechanical bowel preparation) compared to none for elective intestinal surgery for pediatric patients					
Patient or population: elective intestinal surgery for pediatric patients					
Setting: Outpatient (clinic), or inpatient					
Intervention: bowel preparation (oral antibiotics + mechanical bowel preparation)					
Comparison: oral antibiotics alone					
Outcomes	**Anticipated absolute effects* (95% CI)**		**Relative effect (95% CI)**	**№ of participants (studies)**	**Certainty of the evidence (GRADE)**
	Risk with oral antibiotics alone	Risk with bowel preparation (oral antibiotics + mechanical bowel preparation)			
Any SSI	460 per 1,000	346 per 1,000 (295 to 402)	OR 0.62 (0.49 to 0.79)	18651 (1 observational study)	⨁⨁⨁◯ MODERATE[a]
Post-op ileus	113 per 1,000	92 per 1,000 (80 to 106)	OR 0.80 (0.68 to 0.93)	18651 (1 observational study)	⨁⨁⨁◯ MODERATE[a]
Anastomotic leak	29 per 1,000	22 per 1,000 (16 to 29)	OR 0.75 (0.56 to 1.01)	18651 (1 observational study)	⨁⨁⨁◯ MODERATE[a]
Reoperation	47 per 1,000	32 per 1,000 (25 to 40)	OR 0.67 (0.53 to 0.85)	18651 (1 observational study)	⨁⨁⨁◯ MODERATE[a]
Readmission	80 per 1,000	81 per 1,000 (69 to 96)	OR 1.02 (0.85 to 1.22)	18651 (1 observational study)	⨁⨁⨁◯ MODERATE[a]
Length of hospitalization (LOH)	Median LOH for both MBP/OA and OA only groups was 4 days, with IQR 3-6.			(1 observational study)	⨁⨁⨁◯ MODERATE[a]
C. difficile infection (C. Diff)	10 per 1,000	8 per 1,000 (4 to 20)	OR 0.87 (0.36 to 2.12)	1567 (1 observational study)	⨁⨁⨁◯ MODERATE[b]

Comparison B: MBP/OA *vs.* OA: Refer to Table 3.

Two studies compared combination bowel prep to OA alone. Rate of C.difficile infection was assessed by Toh et al. [21], and is reviewed separately below. Midura et al. [20] (18,651 patients) found a reduction in overall SSI (0.62 [0.49, 0.79]), post-op ileus (0.80 [0.68, 0.93]), and reoperation rate (OR: 0.67 [0.53, 0.85]), in favor of combination prep. There was no statistically significant difference in anastomotic leak (OR: 0.75 [0.56, 1.01]) and readmission OR: 1.02 [0.85, 1.22]. LOH was the same from the two groups with median of 4d (IQR 3-6). The study has a moderate overall risk of bias, with high risk of bias due to confounding. The level of evidence was moderate for all outcomes.

Comparison C: OA vs. none: Refer to Table 4.

Two studies compared OA vs. no prep. Rate of C.difficile infection was assessed by Toh et al. [21] and is reviewed separately. The outcomes assessed by Midura et al. [20] were in favor of combination bowel prep in terms of lower overall SSI with (OR: 0.67 [0.53, 0.84]), and anastomotic leak (OR: 0.68 [0.51, 0.91]). Values for readmission were statistically significant but potentially not clinically significant (OR: 0.81 [0.67, 0.97]. There was no difference in effect observed in post-op ileus between OA alone and no prep (0.87 [0.75, 1.02] and readmission (OR: 1.05 [0.83, 1.32]). The LOH was slightly shorter for

Table 4: Comparisons OA *vs.* none.

Summary of findings:					
OA compared to none for elective intestinal surgery in adults and pediatrics					
Patient or population: elective intestinal surgery in adults and pediatrics					
Setting: as above					
Intervention: OA					
Comparison: none					
Outcomes	**Anticipated absolute effects*(95% CI)**		**Relative effect (95% CI)**	**№ of participants (studies)**	**Certainty of the evidence (GRADE)**
	Risk with none	Risk with OA			
Any SSI	67 per 1,000	46 per 1,000 (37 to 57)	OR 0.67 (0.53 to 0.84)	13689 (1 observational study)	⨁⨁⨁◯ MODERATE[a]
Anatomotic leak	42 per 1,000	26 per 1,000 (15 to 44)	OR 0.61 (0.35 to 1.05)	13689 (1 observational study)	⨁⨁⨁◯ MODERATE[a]
Post-op ileus	127 per 1,000	112 per 1,000 (98 to 129)	OR 0.87 (0.75 to 1.02)	13689 (1 observational study)	⨁⨁⨁◯ MODERATE[b]
Readmission	9 per 1,000	8 per 1,000 (6 to 8)	OR 0.81 (0.67 to 0.87)	13689 (2 observational studies)	⨁⨁⨁◯ MODERATE[a]
Reoperation	45 per 1,000	32 per 1,000 (28 to 36)	OR 0.70 (0.62 to 0.79)	28758 (1 observational study)	⨁⨁⨁◯ MODERATE[b]
Length of hospitalization (LOH)	Assessed by Midura 2018: LOH was slightly shorter for OA alone vs no prep: 4 (3-6) and 5 (3-7) respectively			29910 (1 observational study)	⨁⨁◯◯ LOW[a,c]
C. difficile infection (C. diff)	13 per 1,000	10 per 1,000 (1 to 74)	OR 0.73 (0.09 to 5.99)	631 (1 observational study)	⨁⨁◯◯ LOW[d,e]
*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).					
CI: Confidence interval; **OR:** Odds ratio					
GRADE Working Group grades of evidence					
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect					
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different					
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect					
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect					

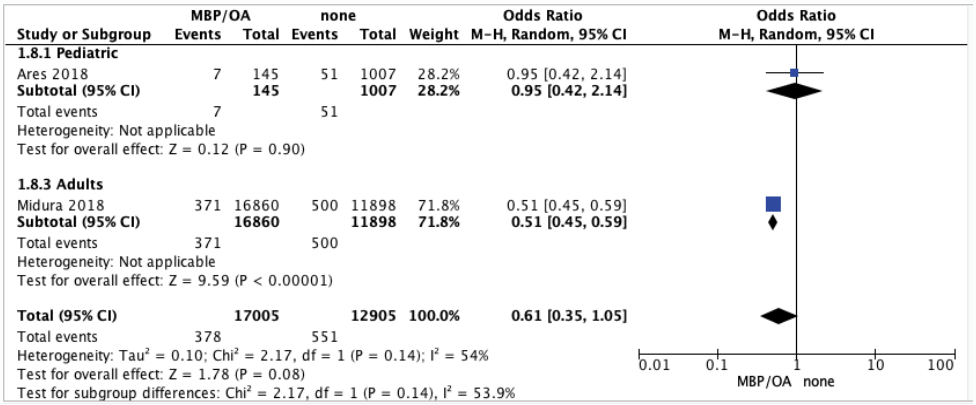

Figure 3: Forest plot of pooled results on overall SSI in combination bowel prep (MBP/OA) vs. none.

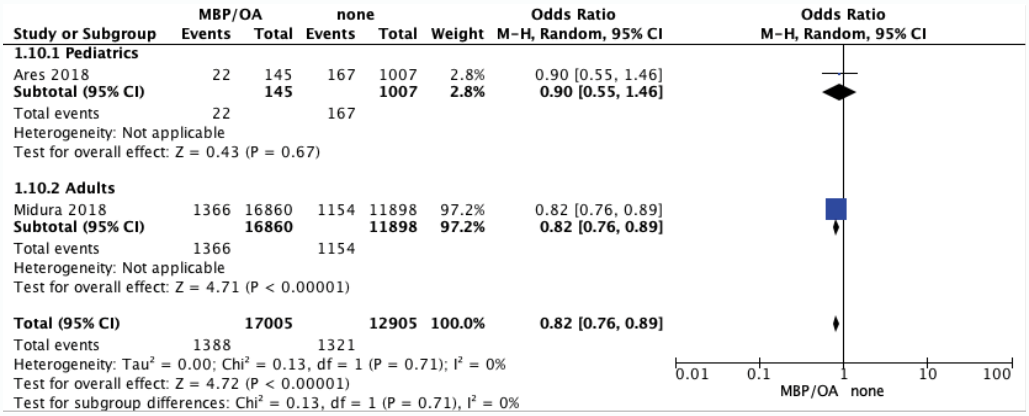

Figure 4: Forest plot of pooled results on anastomotic leak in combination bowel prep (MBP/OA) *vs.* none.

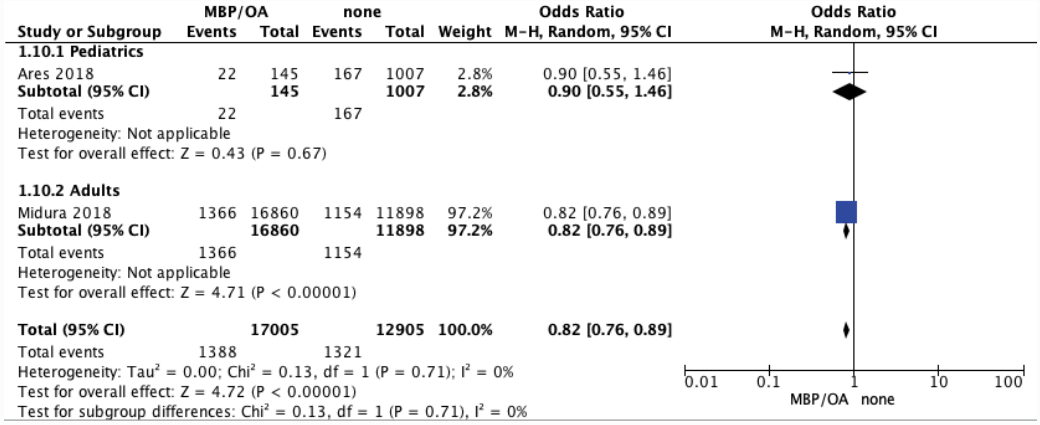

Figure 5: Forest plot of pooled results on readmission in combination bowel prep (MBP/OA) *vs.* none.

OA alone vs. no prep: 4 (3-6) and 5 (3-7) respectively. The overall risk of bias of this study is moderate, with high risk due to confounding. The overall quality of evidence is moderate.

Rate of C. difficile infection for all comparisons

Toh et al. [21] was the only study that assessed this outcome, and found no difference for all three comparison groups: MBP/OA *vs.* none (OR: 0.87 [0.36, 2.12]), combination prep *vs.* OA (OR: 1.20 [0.16, 9.09]), and OA *vs.* none (0.73 [0.09, 5.99]). The wider range reflects the fewer number of events. This study has a moderate overall risk of bias. The overall quality of evidence is very low for serious risk of bias, and inconsistency.

Discussion

Summary of main results and certainty of evidence

Bowel preparation has been a subject of interest for decades, with literature shifting from sole mechanical bowel preparation, to IV antibiotics with mechanical bowel alone, and we now see a trend going back to the use of oral antibiotics with mechanical bowel preparation. The use of oral non-absorbable antibiotics is well supported in the adult literature, and a few studies in the pediatric literature that suggest a similar trend [8-10]. In their review and meta-analysis, Koullouros et al. identified 8 cohort studies, 3 of which compared MBP/OA to OA alone in the presence of standard IV antibiotics with no effect on SSI prevention (RR: 0.94 (95%; CI: 0.73-1.20; p=0.62)) [11]. They concluded that there is no benefit gained by adding MBP with the need for RCT to verify observed findings.

In the current review, we identified 5 cohort studies, 3 of which were part of the meta-analysis. Combination bowel prep (MBP/OA) was compared to OA in one large cohort study with moderate quality of evidence, and showed reduction in overall SSI, anastomotic leak, post-op ileus and re-operation with MBP/OA compared to OA. There was also no evidence of increase of C. diff rate with bowel preparation. This additional finding wasn't seen in the previous review, and will require higher quality evidence to confirm it and inform practice guidelines. We also had set off to review use of bowel preparation in small bowel surgery, but were unable to identify any studies that included this subset of patients. The equipoise still exists in these matters, and requires a large multi-center randomized-controlled trial to address it and to overcome the shortages of the current existing literature.

This review was limited by the nature of the studies recovered. The evidence was of moderate level, with moderate to serious risk of bias. There was also significant heterogeneity in the study, partially explained by the different populations (pediatrics and adults) as well as varying MBP and OA protocols, making it difficult to draw any meaningful conclusions.

Conclusion

The results seen in our review support the notion suggested by the literature that there is benefit gained by using oral antibiotics, for preoperative bowel preparation for colorectal surgery. There is new evidence suggesting a decrease in overall post-operative complications appreciated with MBP/OA bowel preparation when compared to no preparation or OA alone. The quality of evidence, however, is moderate at best with heterogeneity in population and types of intervention. This calls for higher quality evidence in the form of RCT to address the biases observed and shortcomings of the available studies.

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