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Does Mechanical Bowel Preparation Reduce the Risk of Developing Infectious Complications in Pediatric Colorectal Surgery? A Systematic Review and Meta-Analysis

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Objectives To evaluate whether the application of mechanical bowel preparation (MBP) before colorectal surgery reduces the risk of developing infectious complications in children.

Study design In this systematic review and meta-analysis, PubMed, Embase, and the Cochrane Library were systematically searched to identify all articles comparing pediatric patients receiving MBP with pediatric patients not receiving MBP before colorectal surgery. Results are presented with weighted risk differences based on the number of events and sample size per study.

Results Six original studies were included comparing MBP (n = 810) and no MBP (n = 1167). The overall risk of developing infectious complications was 10.1% in patients with MBP, compared with 9.1% in patients without MBP, resulting in a nonsignificant risk difference of –0.03% (95% CI, –0.09% to 0.03%). Concerning the number of wound infections and anastomotic leaks, we found nonsignificant risk differences of –0.03% (95% CI, –0.08% to 0.02%) and 0.01% (95% CI, –0.01% to 0.02%), respectively.

Conclusion Based on the current literature, there is insufficient evidence to indicate that the use of MBP leads to a significant difference in the risk of developing infectious complications in pediatric colorectal surgery. *(J Pediatr 2018;■■:■■-■■).*

Infectious complications are an important cause of postoperative morbidity and a healthcare cost burden in pediatric colorectal surgery.[1-3] Generally, there are 4 main strategies for reducing the incidence of these complications: systemic antibiotic prophylaxis, oral antibiotic prophylaxis, mechanical bowel preparation (MBP), and dietary modifications.[4,5] Various strategies and combinations of strategies are in use, based on the perspective of the individual pediatric surgeon or hospital protocol.[5-8] There is general agreement on the benefit of systemic antibiotic prophylaxis; however, the benefit of the other 3 strategies has been a subject of discussion for years.

MBP has been applied since the 1930s.[9] Polyethylene glycol (PEG)-based solutions are most commonly used and are known from their use in bowel preparation before colonoscopy.[5,10] In the pediatric population, MBP is often performed in the hospital and frequently requires insertion of a nasogastric tube. This results in additional costs and patient discomfort.[11] The aim of MBP is to reduce infectious complications caused by fecal bacterial contamination by cleansing the bowel with a large amount of osmotic solution.[4,9,12] This theoretical effect has never been supported by clinical evidence, however.[4,7] In addition, recent meta-analyses in adult literature have provided no significant evidence that patients benefit from MBP.[13,14] Nonetheless, a recent national survey of US pediatric surgeons showed that a large proportion of them are still performing MBP in daily clinical practice.[6] An evidence-based answer to the question of whether the use of MBP is associated with a significant difference in the risk of infectious complications in pediatric surgery is needed. Several retrospective studies[12,15-18] have addressed this question in pediatric colorectal surgery, and 2 randomized clinical trials comparing MBP and no MBP were recently reported.[11,19] The aim of the present systematic review and meta-analysis was to determine whether the use of MBP before pediatric colorectal surgery leads to a reduction in infectious and other complications.

IBD	Inflammatory bowel disease
LOS	Length of stay
MBP	Mechanical bowel preparation
NBM	Nothing by mouth
OAP	Oral antibiotic prophylaxis
PEG	Polyethylene glycol
RCT	Randomized controlled trial

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Methods

This systematic review and meta-analysis was conducted in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement.[20] PubMed, Embase, and the Cochrane Library were systematically searched using predefined search terms up to February 15, 2018, to identify all articles comparing MBP and no MBP in the pediatric population before elective colorectal surgery. The following search string was used for PubMed: "((bowel[Title/Abstract] OR gut*[Title/Abstract] OR intestin*[Title/Abstract]) AND (prep[Title/Abstract] OR preparation*[Title/Abstract] OR clean*[Title/Abstract])) OR "Cathartics"[Mesh] OR "Cathartics"[Pharmacological Action] AND Infant*[Title/Abstract] OR child*[Title/Abstract] OR pediatric*[Title/Abstract] OR pediatric*[Title/Abstract] OR adolescent*[Title/Abstract] OR "Child"[Mesh] OR "Infant"[Mesh] OR "Adolescent"[Mesh] AND surger*[Title/Abstract] OR operation*[Title/Abstract] OR procedure*[Title/Abstract] OR "Digestive System Surgical Procedures"[Mesh]". In Embase and the Cochrane Library, the same search string was used with equivalent search commands. No language restrictions or time horizons were applied. No review protocol exists for this systematic review and meta-analysis.

Study Selection Criteria

All articles were assessed for eligibility using a set of predefined criteria as follows:

- Population: children and adolescents (age 0-21 years) undergoing any form of elective colorectal surgical procedure
- Intervention: the application of MBP documented as a PEG-, mannitol-, or magnesium citrate-based solution
- Comparator: no application of MBP
- Outcomes: minimally one of the outcome measures mentioned below
- Study design: all original articles describing prospective randomized controlled trials (RCTs) and retrospective comparative studies.

All studies meeting the study selection criteria were included in the meta-analysis; no specific exclusion criteria were used.

Outcomes of Interest

The outcome measures of primary interest were the overall rate of infectious complications (defined as the reported overall rate of infectious complications in the assessed article or the sum of the individually described rates of wound infection), anastomotic leakage, intra-abdominal infection or abscess, *Clostidium difficile* infection, and sepsis. The separate rates of wound infection and anastomotic leakage were outcome measures of primary interest as well. Taking into account the possible interference of additional bowel preparation strategies, we treated non-MBP strategies applied in the assessed studies as outcomes of secondary interest. The administration of MBP often requires that patients be admitted to the hospital 1 day earlier. To evaluate whether this also leads to a longer hospital stay, the length of stay (LOS) was another outcome of secondary interest.

Data Extraction

After filtering duplicates from the different databases, 2 of the authors examined titles and abstracts from all retrieved records independently. Subsequently, full-text articles from potentially relevant papers were screened. A cross-reference check of the included articles was performed, but this did not add any relevant articles. No authors were contacted regarding unavailable studies. From all included articles, the following data were extracted by the same 2 authors: year of publication, period of study, number of participants, study population characteristics, study design, study protocol details, primary endpoints, and type of surgical procedure. The methodological quality and risk of bias were assessed for all included articles by 2 authors. The Cochrane Collaboration's tool for risk of bias assessment was used for the RCTs. In addition, a risk estimation was established for the baseline comparability and concurrency of interventions for all studies, including the retrospective comparative studies.[21]

Statistical Analyses

Studies with corresponding outcome measures of interest were pooled in a meta-analysis. Trials with zero events in both arms were excluded from the meta-analysis. Risk differences and 95% CIs were calculated to establish forest plots. Considering the small number of events in the studies evaluated in this meta-analysis, risk differences were calculated instead of risk ratios. The Mantel-Haenszel random-effects model was applied to reduce the influence of heterogeneity between the studies, caused by different sample sizes and study design. Weight was assigned to studies based on the number of events and the sample size. The Higgins χ^2 test was applied, and I^2 values were calculated to analyze heterogeneity and inconsistency among studies, respectively. The number of studies was too small to allow the detection of possible systematic heterogeneity or other forms of bias on the basis of funnel plots. Instead, the Cochrane Collaboration tool was used to analyze the risk of bias assessment. All analyses were performed using RevMan version 5.3.5 (Cochrane Community).

Results

A total of 1236 potentially relevant publications were identified. Title-abstract and full-text screening resulted in 6 relevant studies for this systematic review and meta-analysis. **Figure 1** present a flowchart showing our study selection process. The included studies investigated MBP versus no MBP in the pediatric population between 1990 and 2014 and enrolled a total of 1977 patients. Primary endpoints were comparable in all the studies; however, there was significant variation in the number and age of the patients included, the use of oral antibiotic prophylaxis, and the type of surgery performed. Details are summarized in **Table I**.

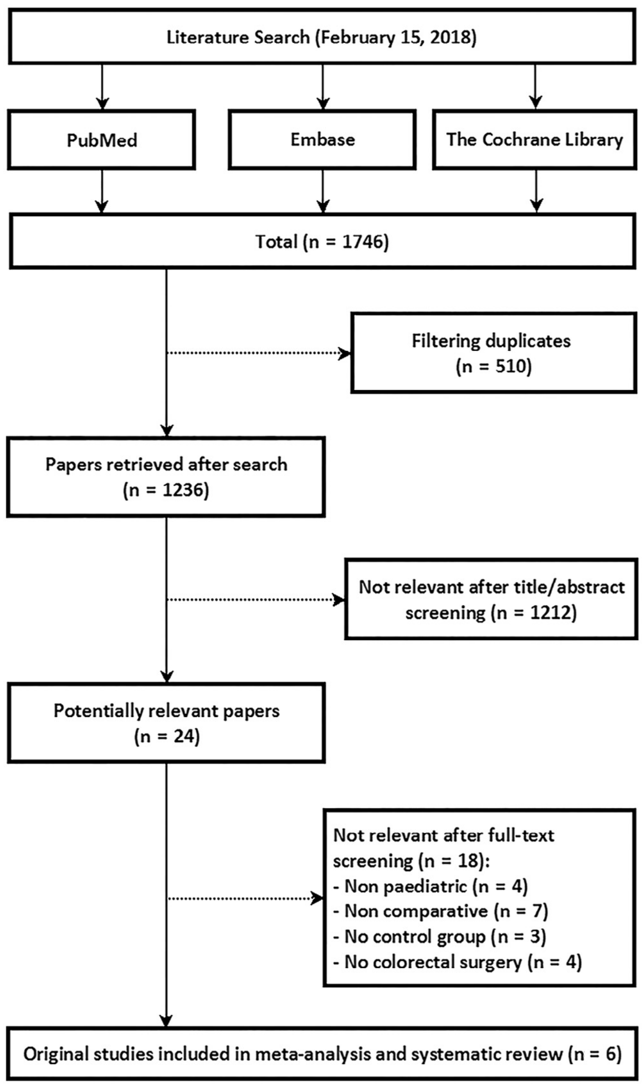

Figure 1. Flowchart of the study selection process.

Risk of Bias Assessment

The methodological quality of the studies included in our meta-analysis was generally poor. Four of the 6 studies were retrospective,[12,15-18] and only 2 were RCTs.[11,19] One RCT showed a high risk of selection bias.[11] Three studies showed baseline incomparability in their study populations,[11,16,18] and 3 studies did not achieve concurrency of the intervention.[12,15,16] The risk of bias assessment of the included studies is shown in **Table II**.

Primary Outcomes of Interest

The overall rate of infectious complications was 10.1% (82 of 810) in patients receiving MBP versus 9.1% (106 of 1167) in patients not receiving MBP, with a nonsignificant risk difference of –0.03% (95% CI, –0.09% to 0.03%) (**Figure 2**). Comparison between the subcategorization of RCTs and retrospective comparative studies showed corresponding results; the risk differences for the overall infectious complication rates were –0.04% (95% CI, –0.32 to 0.25) vs –0.03% (95% CI, –0.09 to 0.04), respectively (**Figure 2**).

The risk of developing postoperative wound infections was 6.7% (54 of 810) in patients who received MBP vs 4.9% (49 of 1167) in patients who did not, with a nonsignificant risk difference of –0.03% (95% CI, –0.08% to 0.02%) (**Figure 3**; available at www.jpeds.com). The risk of developing an anastomotic leak was 3.0% (23 of 768) in patients who received MBP vs 4.7% (54 of 1159) in those who did not, with a nonsignificant risk difference of 0.01% (95% CI, –0.01% to 0.02%) (**Figure 4**; available at www.jpeds.com).

Additional Bowel Preparation Strategies

Along with MBP, additional strategies were used to reduce the incidence of infectious complications in the included studies. Regarding dietary modifications, in the studies by Shah et al and Aldrink et al, a clear liquid diet for 1 day preoperatively was used in both the MBP and no MBP groups.[11,19] In the study by Aldrink et al, this covered the entire day and also involved a nothing by mouth (NBM) policy starting at midnight before surgery.[19] In the study by Shah et al, the clear liquid diet was started at noon on preoperative day 1 and NBM was maintained for 2-6 hours before surgery.[11] In the study by Leys et al, a clear liquid diet for 1 day preoperatively was applied in the no MBP group, and no diet restrictions were mentioned for the MBP group.[15] In the study by Serrurier et al, all patients in the MBP group received a free diet on preoperative day 1 until MBP was administered. In the no MBP group, 26 of the 85 patients received a clear liquid diet for 1 day preoperatively and the remainder received a free diet until midnight.[12] In the studies by Breckler et al and Ares et al, dietary modifications were not described.[16,18]

With respect to oral antibiotic prophylaxis (OAP), in the study by Breckler et al this was used equally in both the MBP and no MBP groups.[16] In the study by Serrurier et al, OAP was provided to 52% of the patients in the MBP group but to none of the patients in the no MBP group.[12] In the study by Leys et al, OAP was provided to a limited and not otherwise specified number of patients in the MBP group but to no patients in the no MBP group.[15] In the studies by Shah et al, Ares et al, and Aldrink et al, no OAP was used.[11,18,19]

In the studies by Shah et al, Serrurier et al, Breckler et al, and Aldrink et al, systemic antibiotics were used equally in both the MBP and no MBP groups.[11,12,16,19] However, in the study by Leys et al, systemic antibiotics were administered for a markedly longer period in the MBP group compared with the no MBP group.[15] Ares et al did not mention the use of systemic antibiotics.[18]

Hospital LOS

Two studies did not describe any differences in hospital LOS between the MBP and non-MBP groups.[11,16] Two other studies reported a significantly shorter LOS, of approximately 1 day, in the non-MBP group.[12,18] Another study described a trend of shorter LOS in the non-MBP group, which was not significant.[15] Aldrink et al did not find a significant difference between the non-MBP and MBP groups, despite the fact that patients in the MBP group had to arrive at the hospital a day earlier to receive the MBP.[19]

Table I. Studies comparing MBP vs no MBP before colorectal surgery in pediatric patients

Authors	Year	Period	n	Age, y	Design	SP	Groups	Primary endpoints	Indication for surgery
Leys et al[15]	2005	1990-2003	143	<20	Retrospective comparative (mainly)	–	MBP and no MBP	Wound infection, anastomotic leak, intra-abdominal abscess	Hirschsprung disease, anorectal malformation, IBD, NEC, colon atresia, trauma
Breckler et al[16]	2009	1996-2007	118	<18	Retrospective comparative	–	MBP, MBP + OAP, OAP only	Wound infection	Imperforate anus
Serrurier et al[12]	2011	1998-2010	272	<15	Retrospective comparative	–	MBP and no MBP	Wound infection, abdominal abscess, anastomotic leak	Hirschsprung disease, anorectal malformation, NEC, trauma
Aldrink et al[19]	2015	2010-2013	44	<22	Prospective randomized	–	MBP and no MBP	Anastomotic leak, intra-abdominal abscess, wound infection	Hirschsprung disease, imperforate anus, IBD
Shah et al[11]	2016	2009-2013	32	<19	Prospective randomized	+	MBP and no MBP	Difference in morbidity and mortality (overall complication rate)	Hirschsprung disease, anorectal malformation, IBD, FAP, trauma
Ares et al[18]	2017	2011-2014	1581	<10	Retrospective comparative	–	MBP, MBP + OAP, no MBP	Infectious complications, wound infection, anastomotic leak, wound dehiscence	Hirschsprung disease, anorectal malformation, IBD

FAP, familial adenomatous polyposis; *NEC*, necrotizing enterocolitis; *SP*, Study conducted according to protocol.

Variability in Surgical Procedures

Most of the assessed studies[11,12,15,18,19] included patients with the following underlying diseases: Hirschprung disease, anorectal malformations, and inflammatory bowel disease (IBD). Leys et al reported rates of the aforementioned disorders of 84.8% in the non-MBP group and 87.3% in the MBP group, with the highest incidence of Hirschsprung disease (46.1%) in both groups.[15] Serrurier et al did not include patients with IBD; most of their patients were diagnosed with an anorectal malformation: 87% in the MBP group and 81% in the non-MBP group.[12] The percentages of Hirschsprung disease in the 2 groups were 4.8% and 5.9%, respectively.[12] Aldrink et al reported that 81.1% of their patients, in both the MBP and the non-MBP groups, had the aforementioned underlying diseases.[19] According to Shah et al, these diseases were present in 72.2% of the patients in the MBP group and 85.7% of those in the non-MBP group, with anorectal malformation the most frequent underlying disease.[11] In the study by Ares et al, 24.8% of the patients had an anorectal malformation, 10.8% had Hirschsprung disease, and 3.0% had IBD.[18] Less commonly reported diseases in the assessed studies were rectal trauma or perforation, necrotizing enterocolitis, familial adenomatous polyposis, duplication cysts, colon atresia, and meconium ileus. In contrast to the other studies, Breckler et al included only children with a diagnosis of imperforate anus.[16] The surgical procedures used in the studies included colostomy closure, colostomy takedown, elective bowel resections, colonic anastomoses, ileostomy, and other procedures involving the colon and/or rectum (not further specified).

In a subgroup analysis, Aldrink et al found potentially different outcomes of the effect of MBP among patients with various underlying diseases.[19] This subgroup analysis showed no difference in primary endpoints between the various diagnoses.[19] None of the other studies included such subgroup analyses and did not describe differences in the effect of MBP in patients with varying underlying diseases.

Discussion

In the reviewed literature, the application of MBP compared with no MBP did not lead to a significant difference in the risk

Table II. Risk of bias assessment of the RCTs and retrospective studies comparing MBP and no MBP

Studies	Baseline incomparability	No concurrency of the intervention	Selection bias	Performance bias	Attrition bias	Detection bias	Reporting bias	Potential other bias
RCTs								
Aldrink et al[19]	–	–	–	+	+	+	–	*
Shah et al[11]	+	–	+	+	+	+	–	
Retrospective studies								
Ares et al[18]	+	–						†, ‡
Breckler et al[16]	+	+						§
Serrurier et al[12]	–	+						¶
Leys et al[15]	–	+						§,**

+, high-risk; –, low-risk.
*A substantial number of patients received more perioperative antibiotics than outlined by the protocol.
†Only patients younger than 10 years were included.
‡Infectious complications were captured on reported billing codes and not based on clinical chart review.
§Different kinds of MBP have been administered, based on the preference of the operating surgeon.
¶The use of MBP was at the discretion of the surgeon's preference.
**All patients not receiving MBP were managed by a single surgeon.

Study or Subgroup	Favors No MBP Events	Favors No MBP Total	MBP Events	MBP Total	Weight	Risk Difference M-H, Random, 95% CI	Year
1.1.1 RCTs							
Aldrink et al 2015	4	20	9	24	4.6%	−0.17 [−0.44, 0.09]	2015
Shah et al 2016	4	14	3	18	3.8%	0.12 [−0.17, 0.41]	2016
Subtotal (95% CI)		**34**		**42**	**8.4%**	**−0.04 [−0.32, 0.25]**	
Total events	8		12				
Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 2.16$, df = 1 ($P = .14$); $I^2 = 54\%$							
Test for overall effect: Z = 0.24 ($P = .81$)							
1.1.2 Retrospective comparative studies							
Leys et al 2005	1	33	3	110	26.0%	0.00 [−0.06, 0.07]	2005
Breckler et al 2009	0	8	7	42	8.0%	−0.17 [−0.35, 0.02]	2009
Serrurier et al 2011	7	85	31	187	22.8%	−0.08 [−0.16, −0.00]	2011
Ares et al 2017	90	1007	29	429	34.7%	0.02 [−0.01, 0.05]	2017
Subtotal (95% CI)		**1133**		**768**	**91.6%**	**−0.03 [−0.09, 0.04]**	
Total events	98		70				
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 9.31$, df = 3 ($P = .03$); $I^2 = 68\%$							
Test for overall effect: Z = 0.82 ($P = .41$)							
Total (95% CI)		**1167**		**810**	**100.0%**	**−0.03 [−0.09, 0.03]**	
Total events	106		82				
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 11.79$, df = 5 ($P = .04$); $I^2 = 58\%$							
Test for overall effect: Z = 0.91 ($P = .37$)							
Test for subgroup differences: $Chi^2 = 0.00$, df = 1 ($P = .95$), $I^2 = 0\%$							

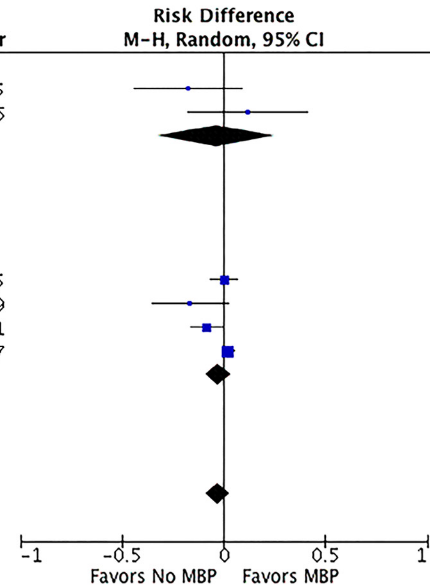

Figure 2. Meta-analysis of the overall infectious complication rate in patients receiving MBP vs no MBP, with subcategorization of RCTs and retrospective comparative studies. Risk differences are shown with 95% CIs.

of developing infectious and other complications in pediatric colorectal surgery. Regarding separate complications, this meta-analysis reveals a nonsignificant risk difference for developing wound infections and anastomotic leakage in pediatric patients with MBP vs those without MBP. This is in line with recent meta-analyses in adult patients suggesting that MBP is not associated with a lower rate of complications and can be safely omitted.[13,14] These results also correspond to the overall conclusions of all individual studies assessed in this meta-analysis.[11,12,15-19] However, not all of the studies on the application of MBP report similar results. Recently published robust evidence in the adult population indicates that the use of MBP and OAP together results in significantly lower rates of infectious complications compared with no preparation at all or either MBP or OAP alone.[22,23] Klinger et al demonstrated that MBP alone does not offer a significant benefit compared with no MBP, whereas OAP does need to be combined with MBP to achieve a significant reduction in infectious complications.[22]

There are drawbacks to the use of MBP. Pediatric patients often require a nasogastric tube for MBP administration, which results in additional costs and increased patient discomfort.[11] In addition, MBP is associated with an increased risk of electrolyte imbalance and dehydration.[24] Together with a nonsignificant difference in reducing overall infectious complications, this possibly could tip the balance toward favoring no MBP in pediatric colorectal surgery.

The main strength of our systematic review and meta-analysis is the comprehensive literature search and overview. We provide the first summary of all available data regarding the risk difference in developing infectious complications in patients receiving MBP compared with those without MBP before pediatric colorectal surgery. This study also has several limitations that must be considered. Four of the 6 studies had a retrospective study design, which could have introduced various forms of bias. The 2 RCTs included were likely underpowered, having enrolled only 32 and 44 patients, respectively. In addition, there were high-risk forms of bias in all 6 studies, as shown in Table II. However, because it is not possible to blind the practice of MBP, not all forms of bias could be prevented, making performance bias and detection bias inevitable. The analyzed data were significantly heterogeneous with regard to age, because 1 study included patients up to age 21 years, with a mean age of 7.3 years.[19] Despite this, a subgroup analysis by age in that study did not reveal any significant differences in primary and secondary outcomes (data not shown). The other studies included patients up to age 20 years,[15] 18 years,[11,16] 15 years,[12] and 10 years.[18] None of these studies included a subgroup analysis by age. In addition, differences in diet, OAP, and systemic antibiotics might have contributed to dissimilarities among the assessed studies. Another important limitation is the variability in surgical indications and operations undertaken. Only 1 study included a subgroup analysis showing no difference in primary endpoints across the various diagnoses. The other studies did not perform such analyses and did not report any differences in outcomes among patients with various underlying diseases. Ideally, we would have performed stratified analyses by age group and for specific surgical indications; however, the assessed studies did not provide sufficient detail on these topics, making this impossible.

Owing to the aforementioned limitations of this review, the possibility of a type II error inevitably arises. Consequently, the hypothesis that MBP before pediatric colorectal surgery does not lead to a reduction in infectious complications could be falsely negatively accepted; therefore, we must be careful in drawing definitive conclusions.

Based on the current literature, there is insufficient evidence that the application of MBP compared with no MBP leads to a significant difference in the risk of developing infectious and other complications in pediatric colorectal surgery. However, to finally establish a well-substantiated opinion on the role of MBP in the pediatric population, a large multicenter RCT is warranted. Taking into the account the comparable discussion that exists in the application of OAP and the possible synergistic effect in reducing the incidence of infectious complications in the pediatric population, a trial including OAP as an additional intervention arm is recommended. ■

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Study or Subgroup	No MBP Events	No MBP Total	MBP Events	MBP Total	Weight	Risk Difference M-H, Random, 95% CI	Year
1.2.1 RCTs							
Aldrink et al 2015	2	20	5	24	4.7%	-0.11 [-0.32, 0.10]	2015
Shah et al 2016	3	14	2	18	3.2%	0.10 [-0.16, 0.36]	2016
Subtotal (95% CI)		**34**		**42**	**7.9%**	**-0.02 [-0.22, 0.19]**	
Total events	5		7				
Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 1.55$, df = 1 ($P = .21$); $I^2 = 36\%$							
Test for overall effect: Z = 0.16 ($P = .87$)							
1.2.2 Retrospective comparative studies							
Leys et al 2005	0	33	1	110	28.8%	-0.01 [-0.05, 0.04]	2005
Breckler et al 2009	0	8	7	42	5.7%	-0.17 [-0.35, 0.02]	2009
Serrurier et al 2011	5	85	27	187	21.2%	-0.09 [-0.16, -0.01]	2011
Ares et al 2017	39	1007	12	429	36.4%	0.01 [-0.01, 0.03]	2017
Subtotal (95% CI)		**1133**		**768**	**92.1%**	**-0.03 [-0.08, 0.02]**	
Total events	44		47				
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 10.83$, df = 3 ($P = .01$); $I^2 = 72\%$							
Test for overall effect: Z = 1.11 ($P = .27$)							
Total (95% CI)		**1167**		**810**	**100.0%**	**-0.03 [-0.08, 0.02]**	
Total events	49		54				
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 12.54$, df = 5 ($P = .03$); $I^2 = 60\%$							
Test for overall effect: Z = 1.14 ($P = .26$)							
Test for subgroup differences: $Chi^2 = 0.01$, df = 1 ($P = .91$), $I^2 = 0\%$							

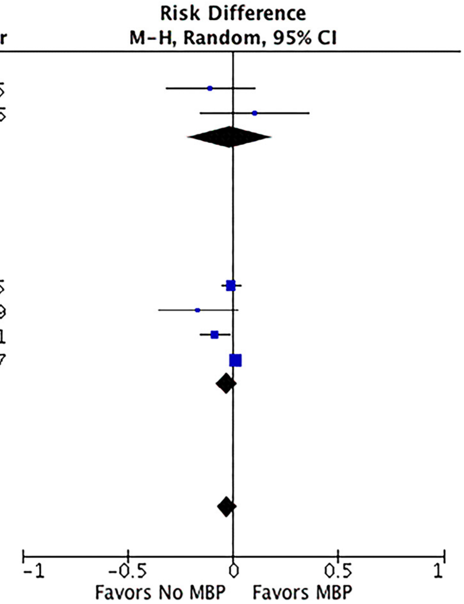

Figure 3. Meta-analysis of the presence of wound infections in patients receiving MBP vs no MBP with categorization of RCTs and retrospective comparative studies. Risk differences are shown with 95% CIs.

Study or Subgroup	No MBP Events	No MBP Total	MBP Events	MBP Total	Weight	Risk Difference M-H, Random, 95% CI	Year
1.3.1 RCTs							
Aldrink et al 2015	1	20	1	24	1.8%	0.01 [-0.12, 0.13]	2015
Shah et al 2016	0	14	1	18	1.2%	-0.06 [-0.21, 0.10]	2016
Subtotal (95% CI)		**34**		**42**	**3.0%**	**-0.02 [-0.11, 0.08]**	
Total events	1		2				
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.41$, df = 1 ($P = .52$); $I^2 = 0\%$							
Test for overall effect: Z = 0.36 ($P = .72$)							
1.3.2 Retrospective comperative studies							
Leys et al 2005	1	33	2	110	6.9%	0.01 [-0.05, 0.08]	2005
Serrurier et al 2011	1	85	2	187	37.3%	0.00 [-0.03, 0.03]	2011
Ares et al 2017	51	1007	17	429	52.9%	0.01 [-0.01, 0.03]	2017
Subtotal (95% CI)		**1125**		**726**	**97.0%**	**0.01 [-0.01, 0.02]**	
Total events	53		21				
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.40$, df = 2 ($P = .82$); $I^2 = 0\%$							
Test for overall effect: Z = 0.84 ($P = .40$)							
Total (95% CI)		**1159**		**768**	**100.0%**	**0.01 [-0.01, 0.02]**	
Total events	54		23				
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.02$, df = 4 ($P = .91$); $I^2 = 0\%$							
Test for overall effect: Z = 0.77 ($P = .44$)							
Test for subgroup differences: $Chi^2 = 0.25$, df = 1 ($P = .62$), $I^2 = 0\%$							

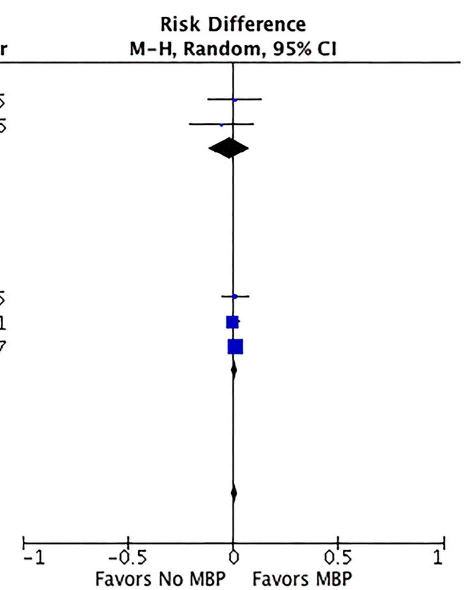

Figure 4. Meta-analysis of the presence of an anastomotic leak in patients receiving MBP vs no MBP with categorization of RCTs and retrospective comparative studies. Risk differences are shown with 95% CIs.