



Simethicone decreases bloating and improves bowel preparation effectiveness: a systematic review and meta-analysis

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Abstract

Background Simethicone is an adjunct frequently used during bowel preparation before colonoscopy and currently there is no consensus on whether it should be recommended in standard bowel preparation. We performed a systematic review and meta-analysis to determine the effect simethicone has on bowel cleanliness, adenoma detection rate (ADR), and tolerability.

Methods We searched the literature for studies that compared colon cleansing of patients that received standard bowel preparation alone and in combination with simethicone prior to colonoscopy. The primary outcomes were colon cleanliness, ADR, and tolerability.

Results Sixteen randomized controlled trials with 5630 patients were included in meta-analysis. Overall, polyethylene glycol (PEG) with simethicone improves colon cleansing compared with PEG alone (odds ratio [OR] 1.48, CI 1.11 to 1.97, $P=0.008$). This improvement was seen for single dosing (OR 1.83, CI 1.20 to 2.79, $P=0.005$) but not for split dosing (OR 1.32, CI 0.72 to 2.43, $P=0.38$). Overall, simethicone had no effect on ADR (OR 1.22, CI 0.81 to 1.83, $P=0.33$), but in patients receiving single dosing, simethicone significantly increased ADR (OR 1.96, CI 1.22 to 3.16, $P=0.005$). The rates of nausea (OR 0.96, CI 0.75 to 1.24, $P=0.75$), vomiting (OR 1.00, CI 0.69 to 1.44, $P=0.99$), and abdominal pain (OR 0.69, CI 0.40 to 1.18, $P=0.17$) were not significantly different between PEG and PEG + simethicone cohorts. For abdominal bloating, the PEG cohort had greater odds of experiencing bloating than the PEG + simethicone cohort (OR 2.33, CI 1.70 to 3.20, $P<0.00001$).

Conclusions Simethicone improves colon cleanliness and ADR; however, this improvement is not seen in patients receiving split-dose PEG. Furthermore, simethicone decreases abdominal bloating but has no effect on nausea, vomiting, and abdominal pain. Simethicone may be a useful bowel preparation adjunct in patients unable to receive split-dose PEG.

Keywords Sodium phosphate · Biofilm · Endoscope · Simethicone · Colonoscopy

Colonoscopy is the procedure of choice in the evaluation of several conditions affecting the colon such as unexplained gastrointestinal bleeding and inflammatory bowel disease, and is considered to be the gold standard for examining the colonic mucosa and detecting pre-malignant and malignant colorectal lesions [1–3]. Adequate visualization of the

mucosa is essential in order to diagnose and treat diseases of the colon. Poor quality of bowel preparation results in impaired visualization of the mucosa, prolonged cecal intubation time, reduced detection of polyps, and substantial increases in economic costs [3]. To optimize the quality of bowel preparations, various adjuncts have been added to standard bowel preparation regimens. One of these additives is simethicone, an antifoaming agent shown to reduce excessive gas, abdominal discomfort, and bubble formation in the colon [1, 4]. Simethicone is a non-toxic agent composed of a mixture of polydimethylsiloxane and silica gel [5]. Several randomized controlled trials have investigated the effect of simethicone on bowel cleansing but there is currently no consensus as to whether or not simethicone should be routinely added to standard bowel preparations [6]. A

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previous meta-analysis conducted in 2011 analyzed three randomized controlled trials and found that simethicone did not improve bowel preparation [7]. The American Society of Gastrointestinal Endoscopy offers no recommendation on simethicone use while the European Society of Gastrointestinal Endoscopy currently recommends simethicone as an adjunct for bowel preparation prior to colonoscopy [6].

One of the concerns associated with the routine use of simethicone is the growing body of evidence demonstrating that simethicone adhered to the lining of the working channel of some of the endoscopes despite reprocessing [8]. Simethicone residues get cultured, and non-pathogenic strains of *Bacillus subtilis*, *Micrococcus* spp., and *Staphylococcus* spp. are found on the endoscopes after cleaning [8]. Given the conflicting evidence regarding the effectiveness of simethicone as an adjunct to bowel preparation combined with the recent data suggesting simethicone may contribute to biofilm formation in the endoscope working channel, it is important to reassess the potential benefits of simethicone when added to bowel preparation regimes prior to colonoscopy.

The aim of this review was to systematically review the literature to examine the effect that the addition of simethicone to standard bowel preparation regimens has on bowel cleanliness, adenoma detection rate (ADR), and patient tolerability.

Materials and methods

Search criteria

A comprehensive search of electronic databases (MEDLINE, EMBASE, SCOPUS, and Web of Science) using search terms “Simethicone AND Colonoscopy AND Random” AND (Bowel preparation OR Polyethylene OR Macrogol OR PEG OR Klean-Prep OR Golytely OR Nulytely OR Isocolan OR Colo prep OR Colopog OR Colyte OR Sodium phosphate OR Sodium phosphate OR Fleet OR Phospho-soda OR Visicol OR Senna OR X-prep OR Citrate OR Magnesium OR Citramag OR Picosulphate OR Picolax OR Mannitol OR lactulose OR sulfate) was completed from January 1946 to July 2018. An additional manual search of a reference list obtained from a previous literature search on colonoscopy was performed to identify potentially missed articles.

Selection criteria

Only randomized controlled trials were included. Abstracts and titles were screened for inclusion by two independent reviewers (A.S. and M.M.) and selected based on the following inclusion criteria: adult patients (age ≥ 18 years),

studies comparing a bowel preparation with simethicone to a bowel preparation without simethicone, and studies that assessed the effectiveness of the bowel preparation. Exclusion criteria included non-English studies, non-human studies, studies only published as abstracts, and studies with less than 10 patients. Full-text articles of all selected abstracts were reviewed more thoroughly by two reviewers (A.S. and M.M.) using the same criteria and disputes were resolved with a third reviewer (J.D.). Studies were then assessed for methodological quality and bias using the Cochrane risk of bias tool for randomized controlled trials [9].

Data extraction

Pertinent data were collected from full-text articles by two independent reviewers (A.S. and M.M.) and discrepancies were resolved by consensus. The primary outcomes of interest included tolerability, ADR, and the bowel preparation quality. Secondary outcomes of interest included type of dosing (single or split), serious adverse events, and the scale the authors chose to assess bowel cleansing. Single dosing was defined as when the patient ingested the entire bowel preparation being taken the evening before colonoscopy, whereas split dosing was defined as the ingestion of divided doses bowel preparation being taken the night before and the morning of the colonoscopy. Adenoma detection rate (ADR) is defined as the percentage of patients who have one or more histologically confirmed adenomas removed [10].

Studies varied in the way tolerability was assessed; however, most reported symptoms and tolerability data were obtained by recording the number of patients who experienced nausea, vomiting, abdominal pain, and abdominal bloating in each trial arm.

Studies scored the quality of bowel preparations using either the Boston Bowel Preparation Scale (BBPS), Ottawa Bowel Preparation Quality Scale (OBPS), Aronchick Scale, or their own non-validated scales. Bowel preparations were considered adequate or inadequate depending on the numerical score given by the endoscopist performing the colonoscopy. For studies using the BBPS, a total score of 6 or higher was deemed adequate. For studies using the OBPS, a total score of 6 or lower was deemed adequate. An exception to this exists, however, as one study using the OBPS did not use total scores and instead required the score to be 2 or less in each of the three colon segments for the bowel preparation to be considered adequate [11]. The study did not provide the OBPS scores but only the percentage of adequate preparations. However, since the total score would still have been 6 or less to be deemed adequate by the authors, the results were included. For studies using the Aronchick scale, a score between 1 and 3 was deemed adequate. For studies not using a validated scale, their scale's judgement of adequate and inadequate was used.

Statistical analysis

Descriptive categorical data were expressed as frequencies and percentages while continuous data were expressed as weighted mean \pm standard deviation (SD). Meta-analysis was used to compare the number of successful bowel preparations among patients receiving PEG versus patients receiving PEG + simethicone. In studies that reported ADR, meta-analysis was used to compare ADR between patients receiving PEG versus patients receiving PEG + simethicone. For studies that recorded patient symptoms, meta-analysis was used to compare the rates of nausea, vomiting, abdominal pain, and abdominal bloating among patients receiving PEG versus patients receiving PEG + simethicone. The estimated effects were calculated using RevMan 5.3 software provided by the Cochrane website [12]. A random-effects method was used in our analysis, with the assumption that the true effect estimates varied among studies. Statistical significance was set at $P=0.05$. Included studies were also tested for heterogeneity using the Chi² test with significance set at $P=0.10$ and the amount of heterogeneity quantified by the I^2 statistic.

Results

Study selection

Preliminary database search of the literature yielded 63 studies after duplicates were removed (Fig. 1). One of these studies was obtained from the reference list of a previous literature search. After initial screening of titles and abstracts, 36 studies underwent full-text assessment for eligibility. Of these, 18 studies met the inclusion criteria with 16 assessing the addition of simethicone to polyethylene glycol (PEG) and 2 assessing the addition of simethicone to sodium phosphate (NaP). All 18 studies meeting the inclusion criteria were included in the review; however, only the 16 PEG studies were meta-analyzed due to inadequate number of NaP studies for quantitative synthesis.

Study characteristics

Among PEG studies there were 6686 patients and 5630 patients were included for meta-analysis (Table 1). Of those, 2789 (49.5%) patients received simethicone and 2841 (50.5%) patients did not receive simethicone. The weighted mean age was 56.5 years and weighted sex was 46.0% female.

All studies had at least one treatment arm containing simethicone and at least one treatment arm without simethicone, allowing for the effect of simethicone on bowel cleanliness to be assessed. Four studies scored the quality

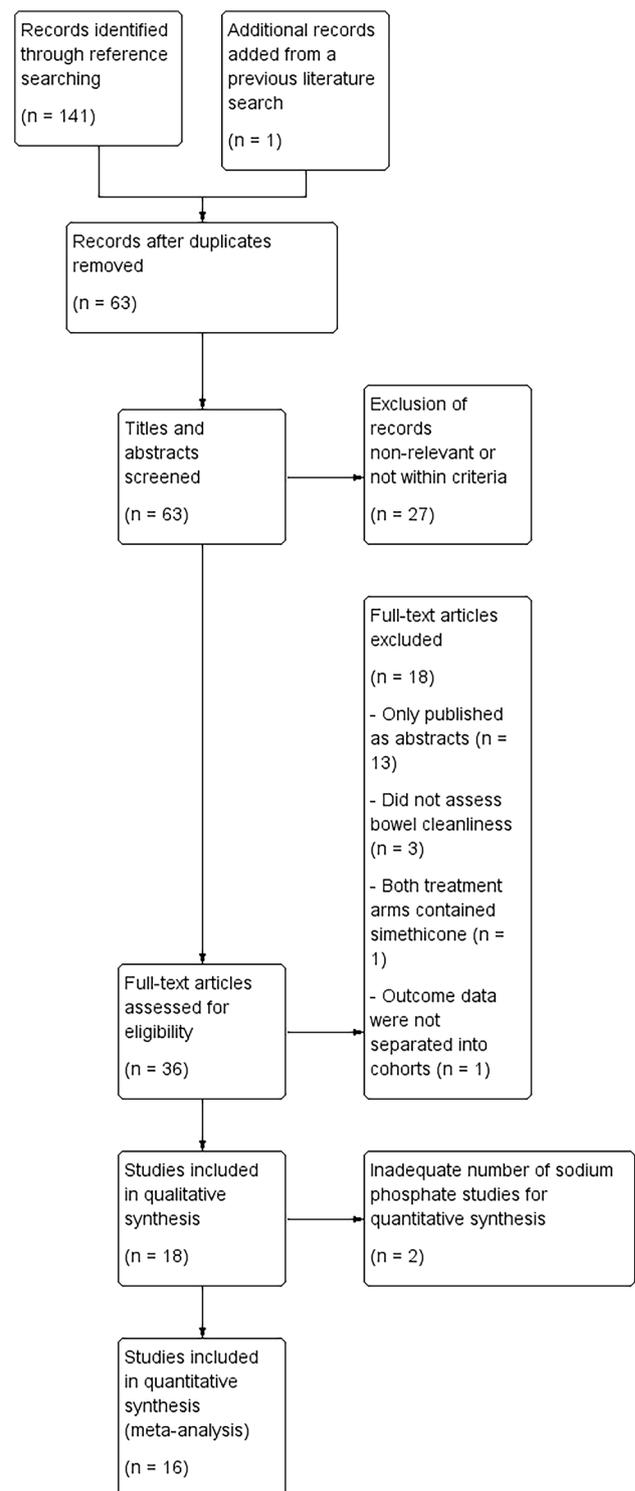


Fig. 1 Flow diagram of study selection

of bowel preparation using the BBPS, four studies used the OBPS, two studies used the Aronchick scale, and five studies used their own non-validated scales (Table 1). Data on the adenoma detection rate were reported in seven studies

Table 1 Basic study demographics [11, 13–27, 34, 35]

Study	Indication for colonoscopy	Data collection	Arm	Dosing	Age (year)	Patients (n)	Female (%)	Bowel assessment
Altintas (2008)	GI symptoms, screening, polyp history, and others	Single center	NaP	Split	51.7	83	49.4	Non-validated scale
			NaP + Alverine Citrate + Sime- thicone	Split	51.9	82	48.8	
Bai (2017)	GI symptoms, screening, polyp history, and others	Multicenter	PEG	Single	50.7	300	47.0	BBPS
			PEG + Simethi- cone	Single	50.1	300	46.0	
Cesaro (2013)	Not specified	Single center	PEG	Split	56.0	51	49.0	OBPS
			PEG + Biso- codyl (day before) + Cit- rates + Sime- thicone	Single	61.0	52	58.0	
			PEG + Bisacodyl (day of) + Cit- rates + Sime- thicone	Single	56.0	50	58.0	
Gentile (2013)	GI symptoms, screening, and others	Single center	2L	Single	55.0	60	43.4	Aronchick
			PEG + Ascor- bic acid	Single	53.0	60	51.7	
			4L PEG + Sime- thicone					
Lazzaroni (1993)	IBD follow-up	Single center	4L PEG + Pla- cebo	Split	35.0	48	45.8	Non-validated scale
			4L PEG + Sime- thicone	Single	36.0	57	35.1	
Manes (2015)	Ulcerative colitis follow-up	Multicenter	2L PEG + Cit- rates + Sime- thicone + Biso- codyl	Single or Split	52.4 48.7	106 105	40.6 40.0	OBPS
			4L PEG	Single or Split				
Matro (2012)	Symptoms and screening	Single center	PEG	Split	–	61	48.0	Non-validated scale
			PEG + Simethi- cone	Split	–	62	48.0	
Mcnally (1989)	Not specified	Single center	PEG + Placebo	Single	61.0	12	50.0	Non-validated scale
			PEG + Simethi- cone	Single	61.0	14	42.9	
Parente (2015)	Chronic constipation patients for GI symptoms, screening, and polyp history	Multicenter	4L PEG	Split	59.0	189	60.0	OBPS
			2L PEG + Sime- thicone + Cit- rates + Biso- codyl	Split	60.0	193	54.0	
Pontone (2011)	Not specified	Single center	2L	Single	60.1 (median)	72	45.0	Aronchick
			PEG + Ascor- bic acid	Single	57.6 (median)	72	50.0	
			4L PEG + Sime- thicone					
Repici (2012)	Not specified	Multicenter	2L	Single	59.4	204	48.5	BBPS
			PEG + Ascor- bic acid	Single	59.1	204	52.0	
			2L PEG + Cit- rates + Sime- thicone + Biso- codyl					

Table 1 (continued)

Study	Indication for colonoscopy	Data collection	Arm	Dosing	Age (year)	Patients (n)	Female (%)	Bowel assessment
Shaver (1988)	Not specified	Single center	PEG	Single	63.1	59	0.0	Non-validated scale
			PEG + Simethicone	Single	62.3	28	0.0	
Spada (2017)	Routine colonoscopy for symptoms, screening, and surveillance	Multicenter	PEG	Single	58.4	209	46.0	OBPS
			PEG + Citrates + Simethicone	or Split	56.4	213	51.0	
				Single or Split				
Tongprasert (2009)	GI symptoms or screening	–	NaP + Placebo	Split	56.5	60	61.7	Non-validated scale
			NaP + Simethicone	Split	57.5	62	56.5	
Valiante (2013)	Fecal occult blood test positive patients	Single center	4L PEG	Split	61.3	126	35.7	Non-validated scale
			2L PEG + Bisacodyl + Citrates + Simethicone	Split	63.6	138	40.6	
Yoo (2016)	Screening, symptoms, constipation, prior abdominal surgery	Single center	PEG-Asc	Split	53.3	130	65.0	BBPS
			PEG-Asc + Simethicone	Split	57.0	130	59.0	
Zhang (2017)	Symptoms, screening, and polyp history	Multicenter	2L PEG	Single	45.5	290	40.0	BBPS
			2L PEG + Simethicone	Single	44.7	289	43.4	
Zorzi (2016)	Screening fecal occult blood test positive patients	Multicenter	4L PEG	Split	59.9	938	42.8	Aronchick
			2L PEG + Ascorbate	Split	59.8	924	44.5	
			2L PEG + Citrates + Simethicone + Bisacodyl	Split	59.8	940	45.2	

GI gastrointestinal, L liters, NaP sodium phosphate, PEG polyethylene glycol, BBPS Boston Bowel Preparation Scale, OBPS Ottawa Bowel Preparation Quality Scale, IBD inflammatory bowel disease, PEG-Asc polyethylene glycol-ascorbic acid

[13–19]. For tolerability assessment, eleven studies reported nausea and abdominal pain rates [13–18, 20–24], seven studies reported vomiting rates [13, 15–18, 21, 25], and nine reported abdominal bloating rates [13–15, 17, 18, 20, 22–24].

A total of 37 serious adverse events were reported and 22 occurred in patients receiving PEG while 15 occurred in patients receiving PEG + simethicone [19, 23]. Parente et al. reported 1 intestinal occlusion and Zorzi et al. reported nine major bleeding events, 25 vasovagal reactions, and 1 perforation [19, 23].

The indications for colonoscopy were similar between studies with most patients receiving colonoscopy for colorectal cancer screening (Table 1). All studies were assessed for methodological quality using the Cochrane Risk of Bias Tool [9]. All studies had methodological flaws. 14/16 studies suffered from inadequate blinding of research participants.

For many studies, the risk was unclear due to insufficient information regarding the allocation concealment.

Quality of bowel preparation

The PEG + Simethicone cohort had a 1.48 greater odds of having a successful bowel preparation than the PEG cohort (16 trials [11, 13–27], $n = 5630$, OR 1.48, CI 1.11 to 1.97, $P = 0.008$) (Fig. 2). Heterogeneity was moderate and statistically significant across studies ($P = 0.0004$, $I^2 = 63\%$).

Eight studies that incorporated bisacodyl or used different volume preparations between the cohorts were removed and a subgroup analysis of the remaining studies was performed. The PEG + Simethicone cohort had a 2.38 greater odds of having an adequate bowel preparation than the PEG cohort (8 trials [13–15, 17, 18, 22, 26, 27], $n = 1546$, OR 2.38, CI 1.53 to 3.70, $P = 0.0001$) (Fig. 3). Heterogeneity

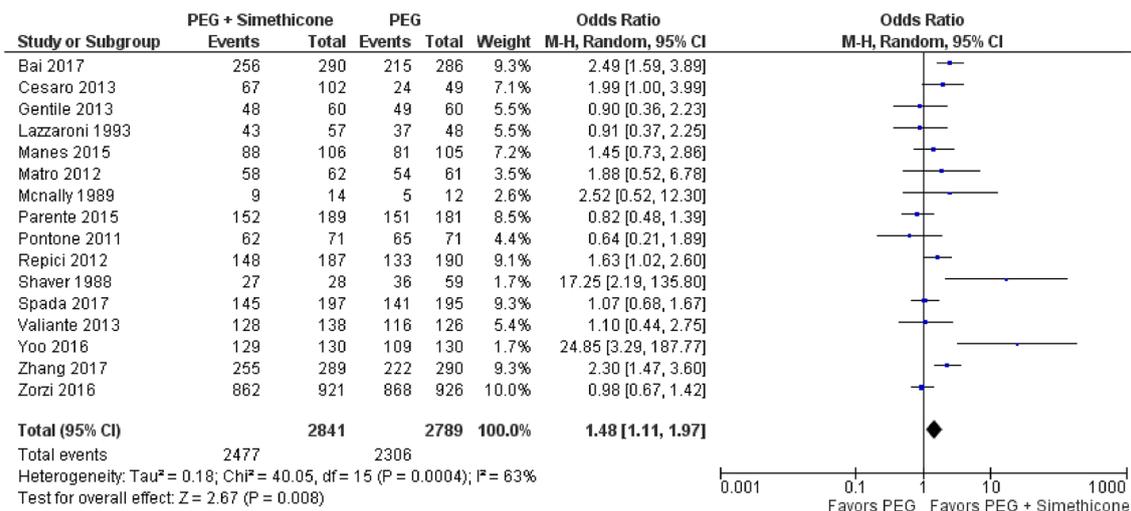


Fig. 2 Successful bowel preparation rates comparing PEG versus PEG + Simethicone

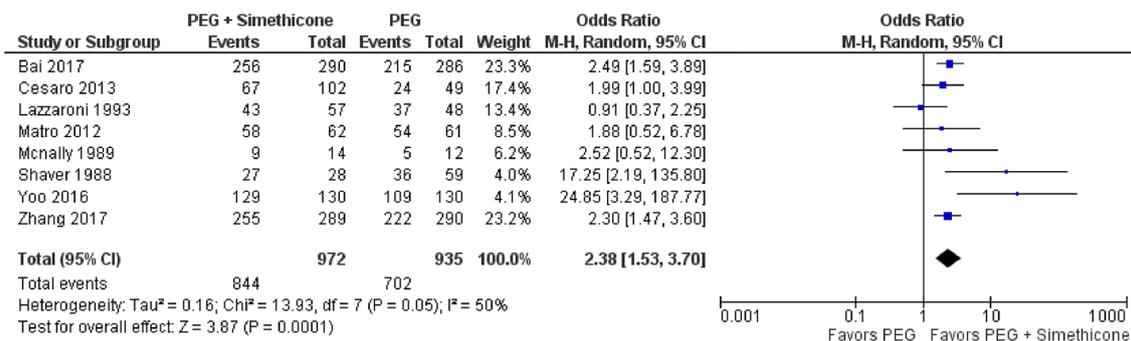


Fig. 3 Successful bowel preparation rates comparing PEG versus PEG + Simethicone with the removal of studies that included bisacodyl or different volume preparations between cohorts

was moderate and statistically significant across studies ($P=0.05$, $I^2=50\%$).

A subgroup analysis of successful bowel preparation rates comparing PEG versus PEG + Simethicone for 2L preparations only was performed. The PEG + Simethicone cohort had a 2.29 greater odds of having a successful bowel preparation than the PEG cohort (5 trials [13, 15, 17, 18, 24], $n=1915$, OR 2.29, CI 1.53 to 3.43, $P<0.0001$). Heterogeneity was moderate and statistically significant across studies ($P=0.10$, $I^2=48\%$).

A subgroup analysis of successful bowel preparations comparing the use of simethicone in single-dosing and split-dosing regimens was performed. In the single-dosing analysis, the PEG + Simethicone cohort had a 1.83 greater odds of having a successful bowel preparation than the PEG cohort (7 trials [13, 16, 18, 21, 24, 26, 27], $n=1907$, CI 1.20 to 2.79, $P=0.005$) (Fig. 4). Heterogeneity was moderate and statistically significant across studies ($P=0.04$, $I^2=56\%$). However, in the split-dose subgroup, the difference between

PEG and PEG + Simethicone was not statistically significant (5 trials [15, 17, 19, 20, 23], $n=2864$, CI 0.72 to 2.43, $P=0.38$) (Fig. 4). Heterogeneity was high and statistically significant across studies ($P=0.02$, $I^2=67\%$).

Adenoma detection rate

Overall, there was no significant difference in ADR between the PEG and PEG + Simethicone cohort (7 trials [13–19], $n=3711$, OR 1.22, CI 0.81 to 1.83, $P=0.33$) (Fig. 5). Heterogeneity was high and statistically significant across studies ($P<0.0001$, $I^2=82\%$).

A subgroup analysis comparing PEG versus PEG + Simethicone for single-dosing preparations was performed. The PEG + Simethicone cohort had a 1.96 greater odds of having a successful bowel preparation than the PEG cohort (3 trials [13, 16, 18], $n=331$, CI 1.22 to 3.16, $P=0.005$) (Fig. 6). Heterogeneity was moderate but not statistically significant ($P=0.07$, $I^2=62\%$).

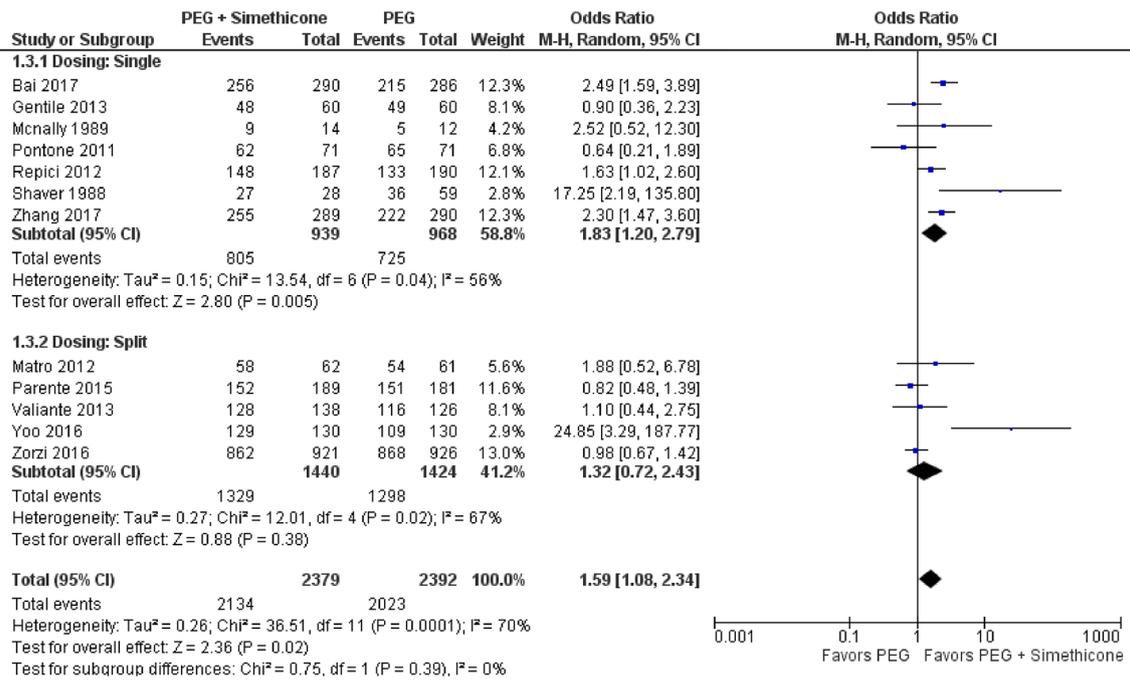


Fig. 4 Subgroup analysis of successful bowel preparations comparing the use of Simethicone in single-dosing and split-dosing regimens

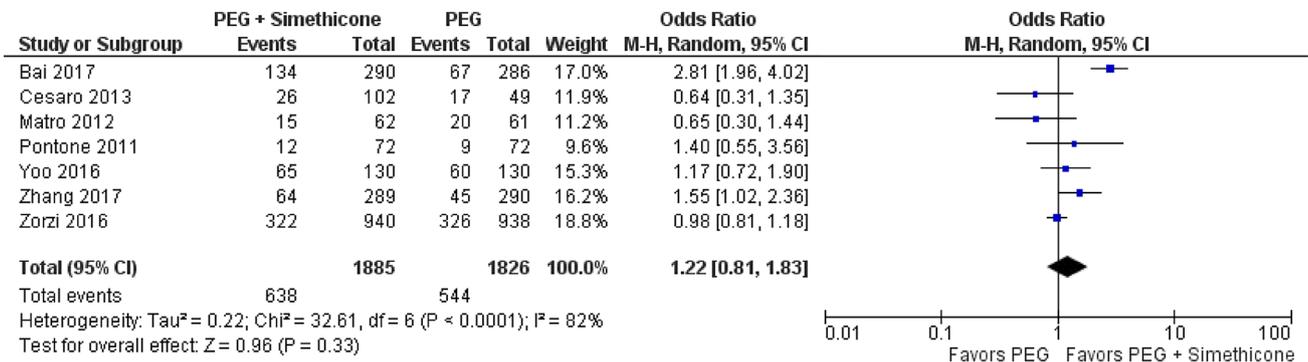


Fig. 5 Adenoma detection rate comparing PEG versus PEG + Simethicone

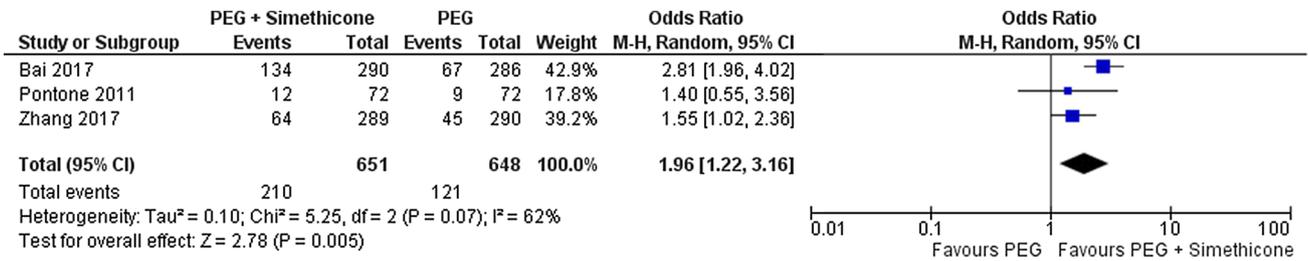


Fig. 6 Subgroup analysis of adenoma detection rate comparing PEG versus PEG + Simethicone in patients receiving single-dosing bowel preparation

Tolerability

Studies that incorporated bisacodyl or used different volume preparations between cohorts were removed and the rates of nausea, vomiting, abdominal pain, and abdominal bloating were analyzed. The rates of nausea (6 trials [13–15, 17, 18, 22], $n = 1803$, OR 0.96, CI 0.75 to 1.24, $P = 0.75$), vomiting (4 trials [13, 15, 17, 18], $n = 1545$, OR 1.00, CI 0.69 to 1.44, $P = 0.99$), and abdominal pain (6 trials [13–15, 17, 18, 22], $n = 1803$, OR 0.69, CI 0.40 to 1.18, $P = 0.17$) were not statistically significant between groups. For the abdominal bloating analysis, the PEG group cohort had a 2.33 greater odds of experiencing bloating than the PEG + simethicone cohort (6 trials [13–15, 17, 18, 22], $n = 1803$, CI 1.70 to 3.20, $P < 0.00001$) (Fig. 7). Studies were homogenous for nausea ($P = 0.33$), vomiting ($P = 0.42$), and abdominal bloating ($P = 0.19$). For abdominal pain, heterogeneity was moderate and statistically significant across studies ($P = 0.03$, $I^2 = 60\%$).

Discussion

To date, there has been very little consensus in literature in regard to the recommendation of simethicone as an adjunct for bowel preparation prior to colonoscopy [6]. Results of our meta-analysis reveal that adding simethicone to PEG is associated with significantly increased odds of an adequate bowel preparation. This association became stronger after the removal of studies that incorporated bisacodyl or used different volume preparations between the cohorts. With respect to single and split dosing, the subgroup analysis showed simethicone was associated with significantly increased odds of adequate bowel preparation for single dosing but not split dosing. With regard to patient tolerability, adding simethicone to PEG was associated with significantly lower odds of experiencing abdominal bloating but had no effect on nausea, vomiting, and abdominal pain. In terms

of ADR, although simethicone failed to demonstrate a significant effect, when subgroup analysis assessed ADR in patients undergoing single-dosing bowel preparations, simethicone significantly improved the ADR.

The quality of bowel preparation is integral to the success of colonoscopy as both a diagnostic and therapeutic procedure. Poor bowel preparation is linked to increased adverse events and a decreased adenoma detection rate [1]. Simethicone’s utility as an adjunct to bowel preparation lies in its ability to function like a detergent and reduce the formation of bubbles that obscure visualization of the mucosa [1]. Its addition to oral bowel preparation dates as early as 1978, with the consensus until now being that it is effective at reducing adherent bubbles but not at improving bowel preparation quality [1, 28]. This was the conclusion of a previous meta-analysis conducted in 2011 [7]. However, since then, several randomized controlled trials have been conducted, all of which, to our knowledge, have been captured by this meta-analysis. As an antifoaming agent it is easy to understand simethicone’s ability to reduce bubble formation; however, the mechanism by which it increases the quality of the bowel preparation is less clear. One plausible mechanism that has been suggested is that foam in the colon acts as an adhesive agent for fecal residue and simethicone interrupts foam formation thus decreasing the residual stool seen on colonoscopy [13]. An alternative explanation may be that simethicone’s ability to reduce bloating allows for a more tolerable bowel preparation, with this increased tolerability promoting greater completion rates of the bowel preparation [1]. This explanation is supported by our finding that simethicone significantly decreases the odds of experiencing bloating. Similarly, other researchers have found single dosing to be associated with lower tolerability and therefore an increase in tolerability would likely produce a larger effect in patients receiving single dosing [1].

Although simethicone was found to improve bowel preparation of single dosing, this was not seen in split dosing. This can be explained by recent findings in a meta-analysis

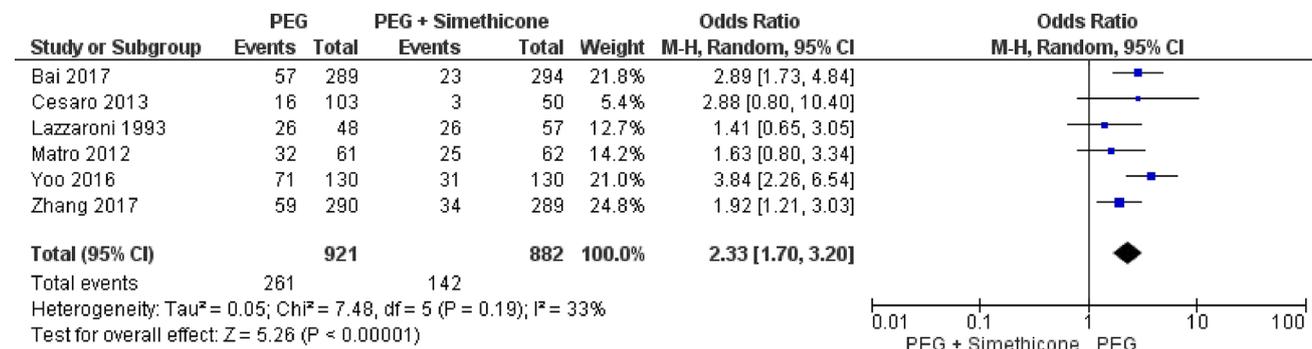


Fig. 7 Tolerability analysis on abdominal bloating rates comparing PEG versus PEG+Simethicone groups with the removal of studies that included bisacodyl or different volume preparations between cohorts

involving 1232 patients showing that split-dosing PEG increased the number of satisfactory bowel preparations by almost fourfold compared to single-dosing PEG. Additionally, split dosing was also found to decrease nausea and a patient's discontinuation of the preparation by almost half, thereby increasing a patient's willingness to repeat the split-dose prep [29]. Although the decrease in nausea and increase in patient's compliance and tolerance likely relates to volume [30], the mechanism by which increased bowel cleanliness is achieved by split dosing compared to single dosing can be explained by the decrease in the time between the last drink of laxative and the beginning of colonoscopy, or "runway time." Runway time is important as it decreases the amount of time that the colon can secrete mucous immediately prior to the colonoscopy and increases clearance of fecal residue just shortly prior to colonoscopy. This was shown in a meta-analysis that found the quality of bowel preparation between split and single dosing became less significant as "runway time" increased, and disappeared altogether when the runway time exceeded 5 h [31]. Thus, although simethicone improved quality of bowel preparation in single dosing by increasing patient tolerance and compliance decreasing residual fecal matter, split dosing was able to achieve improved bowel preparation by many of these similar mechanisms. Given these competing findings, a more thorough evaluation of simethicone's mechanism of action and role is warranted.

Despite the clear benefit of simethicone on bowel cleanliness in certain situations, whether or not simethicone should be recommended is complicated by the recent evidence regarding endoscope contamination [6]. In a study conducted on endoscope reprocessing effectiveness, researchers found simethicone-containing fluid on endoscopes despite following reprocessing guidelines [8]. The researchers were unable to identify whether the simethicone found on the endoscopes were introduced via bowel preparation or from application during colonoscopy [8]. Furthermore, microbial cultures of the fluid were positive for non-pathogenic strains of *Bacillus subtilis*, *Micrococcus* spp, and *Staphylococcus* spp [8]. This is concerning because liquid simethicone products contain carbohydrates—a key ingredient for the growth of microorganisms and the production of biofilms [8]. Should a simethicone-related biofilm in the inner channel of an endoscope be colonized with pathogenic bacteria, it would be untreatable by current decontamination protocols and could potentially result in an infectious outbreak in patients receiving colonoscopy with a contaminated endoscope [32]. It is important to note that while non-pathogenic bacteria and residue were found in the endoscopes, Ofstead et al. [8] did not find any evidence of biofilms present.

Further doubt as to whether simethicone should be recommended as a bowel preparation adjunct comes from the finding of our meta-analysis which showed that the addition

of simethicone does not offer a significant improvement in ADR. The finding that simethicone was only able to improve ADR for patients undergoing single dosing may be explained by a previous meta-analysis which assessed the impact of bowel preparation quality on ADR [33]. In their analysis, the authors found that there was no significant difference in ADR between high-quality and intermediate-quality bowel preparation and only low-quality bowel preparations suffered from a reduced ADR [33]. The superiority of split dosing over single dosing at improving bowel preparation quality has been demonstrated by numerous studies [29]. As a result, while simethicone is able to improve bowel preparation, in patients receiving the standard split-dose PEG, the majority of bowel preparations are likely of sufficient quality, such that any improvement in colonic cleanliness produced by simethicone will be unable to increase the ADR. Whereas in patients receiving single-dose PEG, where the bowel preparation is of a lower quality, an improvement in colonic cleanliness produced by simethicone is more likely to translate into an increase in ADR. This is consistent with our finding that simethicone did not improve bowel preparation quality or ADR in patients receiving split dosing but improved both bowel preparation and ADR in patients receiving single dosing.

The current standard of care for colonoscopy involves a split-dose preparation of PEG [1]. Our results demonstrated that simethicone offers no significant improvement in bowel cleanliness in patients receiving split-dose PEG. As a result, using simethicone in this population may only offer the benefit of reduced abdominal bloating. However, in circumstances where patients cannot receive a split-dose preparation, using simethicone should enhance the quality of bowel preparation and increase ADR, therefore increasing the effectiveness of screening colonoscopy. Regardless, in centers using simethicone, we recommend increased surveillance on endoscope reprocessing effectiveness due to potentially increased risk of biofilm formation.

One of the limitations of our study is that there was considerable variability in scales used to assess bowel preparation. While most studies used one of the commonly used validated bowel preparation assessment tools, for 5 of the 16 PEG studies we had to rely on the author's definition of adequate and inadequate during data extraction. Another limitation is that the studies were found to have significant heterogeneity that did not disappear after different subgroup analyses. This may have been due to the extensive variability in the primary bowel preparation used across studies. Moreover, several studies exhibited a high risk of bias, largely due to insufficient blinding of research participants.

In conclusion, simethicone was a useful adjunct in patients receiving single-dose PEG bowel preparations, but not in those receiving split-dose PEG. This improved visualization was seen in higher rates of bowel cleanliness and

higher ADRs. More research is warranted to elucidate other potential areas where simethicone may improve visualization during colonoscopy.

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Compliance with ethical standards

Disclosure Dr. Sultanian serves as a consultant for Boston Scientific. Muhammad Moolla and Drs. Dang, Shaw, Dang, Tian, and Karmali have no conflicts of interest or financial ties to disclose.

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