

## Review Article

# Comparison of two litre polyethylene glycol plus bisacodyl versus four litre polyethylene glycol as preparation for colonoscopy in colon disease: a systemic review and meta-analysis

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**Abstract:** Aim: The aim of this study is to gauge the efficacy and outcomes of Polyethylene glycol split 2-L PEG plus bisacodyl versus standard 4-L PEG solution in colonoscopic procedures. Methods: All appropriate articles were scrutinized and assessed. Articles not relevant to this study had been omitted simply because it hadn't satisfied the inclusion standards. The literature search was carried out by subsequent phrases such as low-volume polyethylene glycol as well as Bisacodyl and 4 L or standard-volume polyethylene glycol and colonoscopy procedure. Results: Forest's plot showed equal bowel preparation efficacy (measured by Ottawa score) of the 2 L PEG + bisacodyl and 4 L PEG. Forest plot showed quality of bowel preparation of 2 L PEG + bisacodyl and 4 L PEG for (A) excellent, (B) successful, (C) poor. 2 L PEG + bisacodyl groups had excellent bowel preparation outcome but the same successful and poorer bowel preparation outcome with 4 L PEG groups. Results of Forest's plot revealed more people in 4 L PEG groups rather try another regimen next time than in 2 L PEG + bisacodyl. Forest's plot justified there were no differences in adenoma detection rate with 2 L PEG + bisacodyl and 4 L PEG. Conclusion: Patient consciousness and medico's guidance could seriously help to decide on the variety of bowel preparation modality and positively participate in the research to get more detailed legitimate outcomes.

**Keywords:** Colonoscopy, PEG, polyethylene glycol, bisacodyl

## Introduction

Colonoscopy is a frequently conducted diagnostic and remedial procedure necessitating satisfactory bowel preparation to visualize the colonic mucosa and also to identify polyps. Symptomatic reliability together with therapeutic basic safety of colonoscopy count on the caliber bowel preparation [1-3]. Presently, colonoscopy comprises the most efficient screening process device for colorectal cancer as well as the technique permitting the synchronized recognition and elimination of colon polyps [4].

Particularly, the grade of bowel preparation ahead to the colonoscopy incorporates an immediate effect on the standard of colonoscopy. Insufficient bowel groundwork, which could appear in approximately one-third of colo-

noscopies in medical practice, is related to the maximum skipped adenoma, higher distress to the patient and reduced monitoring time intervals, in accordance with referrals given by qualified specialist institutions [3, 5-7]. The potency of colonoscopy in the screening process of colorectal cancer is predicated on acceptable rates of adenoma recognition. It is fundamentally influenced by both endoscopist's skill and the caliber of the bowel preparation [8, 9].

Polyethylene glycol (PEG) solutions are commonly used because they're effective and safe. Nevertheless, the significant quantity (4 L) to generally be used might be a substantial load to the patient. In medical practice the subordinate tolerability on account of large volume and salty flavor of PEG solutions may bring about minimal compliance towards the guidance by

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sufferers. They consume lower than the right amount with the consequence of suboptimal efficaciousness [10].

Lately, incorporating ascorbic acid, a laxative, with PEG revealed possibility to lessen the volume required in efficient colonic cleaning, whilst potentially strengthening threshold. The absorption of ascorbic acid actually reaches vividness at substantial dosages [11, 12]. Researchers have demonstrated that the dose of 2-day bisacodyl plus split 2-L PEG-CS isn't preferable over divided 4-L PEG when it comes to cleaning effectiveness, but is superior contrary to typical regimen regarding colonic mucosa visual images, patient endorsement and conformity [13, 14]. Additionally, randomized controlled trials have established that low-volume PEG plus bisacodyl preparation was competitive with the conventional volume level PEG preparation and much better patient total satisfaction and concurrence [14-16].

With the current study, we carried out an organized overview and meta-analysis to summarize the results of high-quality RCT, which is published up to 2015 that compared low-volume PEG plus bisacodyl with standard-volume PEG preparation in terms of bowel preparation for colonoscopy. Additionally, we looked for excellence of bowel preparation compliance and tolerability. Excellence of bowel preparation differed among randomized trails analyzing low volume PEG and bisacodyl. Consequently, we carried out a meta-analysis to examine the low volume (2 L) PEG with bisacodyl versus full-dose (4 L) PEG for bowel preparation in advance of colonoscopy.

### Material and methods

#### *Search strategy*

An electronic search was carried out by two unbiased researchers (WXW. & CGY.) in PubMed/Medline, EMBASE, the Cochrane Library, and Yahoo and goggle scholar to recognize pertinent articles publicized up to 2015. All appropriate articles were scrutinized and assessed. Letters to editor and responses were being omitted simply because it hadn't satisfied the inclusion standards.

The abstracts were extracted for reliability and completeness of data assortment. The litera-

ture search was carried out by sing subsequent phrases such as low-volume polyethylene glycol as well as Bisacodyl and 4 L or standard-volume polyethylene glycol and colonoscopy procedure.

#### *Selection criteria*

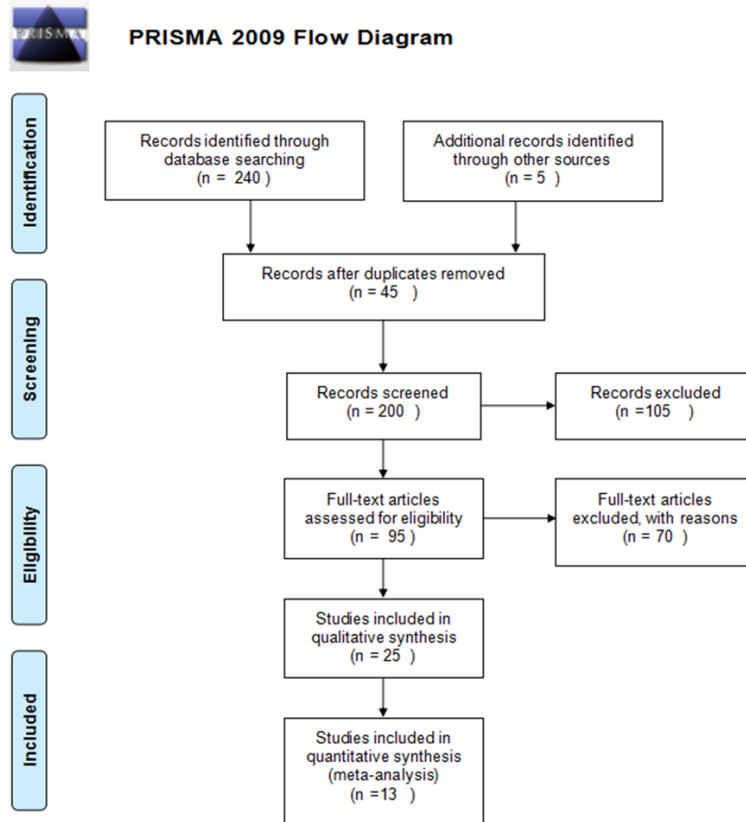
Two evaluators (WXW. and CGY.) look at the titles and abstracts of authentic reports that contrast the results of effectiveness to be low-volume PEG plus bisacodyl with standard volume PEG. Most of the chosen articles were obtained and evaluated to ascertain their qualifications for comprehensive evaluation. The inclusion criteria were: (i) Randomized controlled trials (RCTs), (ii) Adult patients undergoing elective colonoscopy, and (iii) Using 2 L PEG plus bisacodyl and 4 L PEG preparations. Exclusion criteria were considered as duplicate publication's deficiencies in specific information on preparation quality or compliance. Overview, editorials, correspondence to the editor, and articles enlisting individuals less than 18 years of age were being also omitted. Study selection disputes were reconciled by general opinion following mutual conversation.

#### *Outcomes*

The outcomes were evaluated as follows: bowel preparation efficacy. This was prespecified as an Ottawa score less than 5, or an excellent or good bowel preparation designation on the Aronchik scale or other non-validated 3-, 4-, or 5-point scales (excellent, good, fair, poor, very poor). Qualities of bowel preparation, more excellent bowel preparation outcome were also assessed.

As an assessment of bowel preparation tolerability and side effects, a patient's subjective evaluation of their level of satisfaction and acceptability of the bowel preparation was recorded by studies that administered before the procedure non-standardized questionnaire to the patient. The additional secondary outcomes of willingness to repeat the same bowel preparation and side effects, including abdominal cramping/pain, abdominal bloating, vomiting, and nausea, rather try another regimen; adenoma detection; represented affirmative responses to the relevant question from the questionnaires.

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**Figure 1.** Prisma Flowchart of study is illustrated.

### Statistical analysis

A meta-analysis was performed comparing low-volume PEG plus Bisacodyl with standard-volume PEG solution as bowel preparation for colonoscopy by calculating pooled estimates of the quality of the bowel preparation, compliance with the preparation, willingness to repeat the same preparation, and side effects using the odds ratio (OR) with fixed- or random-effects models. Publication bias was assessed using funnel plots. Heterogeneity among studies was assessed by calculating the  $I^2$  measure of inconsistency, which was considered significant if  $I^2$  is 50%. The Stata 12.0 was used for the statistical analysis.

### Results

Prisma Flowchart of study is illustrated in **Figure 1** [17]. 245 studies were identified using electronic searches. Excluding duplicates, 96 abstracts were assessed, of which 24 appeared relevant, and the full studies were assessed. Ultimately, 13 studies were identified for inclu-

sion and data extraction. In this study, we included all the randomized control trial in order to find the facts and outcomes to two different regime of bowel preparation. Summary of studies comparing treatment of 2 L PEG plus bisacodyl versus Standard 4 L PEG as bowel preparation for colonoscopy in 13 studies is illustrated in **Table 1**. Seven study compared the bowel preparation efficacy [13-15, 18-21] (**Figure 2**). Forest plot showed equal bowel preparation efficacy (measured by Ottawa score) of the 2 L PEG + bisacodyl and 4 L PEG.

All included study compared the quality of bowel preparation efficacy [6, 13-15, 18-26] (**Figure 3**). Forest plot showed quality of bowel preparation of 2 L PEG + bisacodyl and 4 L PEG for (A) excellent, (B) successful, (C) poor. 2 L PEG + bisacodyl groups had more excellent bowel preparation outcome but the same successful and poor bowel preparation outcome with 4 L PEG groups.

Seven studies compared the events of nausea [16, 19-22, 24, 26]. Forest plot showed fewer nausea events with 2 L PEG + bisacodyl than 4 L PEG (**Figure 4**). Five studies contrasted the vomiting events [19, 21, 22, 24, 26]. Forest plot showed fewer vomiting events with 2 L PEG + bisacodyl than 4 L PEG (**Figure 5**). Bloating events has been documented in six studies [16, 19-22, 24]. Forest plot showing fewer bloating events with 2 L PEG + bisacodyl than 4 L PEG (**Figure 6**).

Five studies have compared the abdominal cramps following the both regime [16, 19, 21, 22, 24]. Forest plot showed no difference between 2 L PEG + bisacodyl and 4 L PEG in Cramps or abdominal pain events (**Figure 7**). Five studies have reported the patient preferences and choices of enema [13, 16, 18, 20, 26]. Forest plot showed more people in 2 L PEG + bisacodyl groups intake of all solution than in 4 L PEG (**Figure 8**).

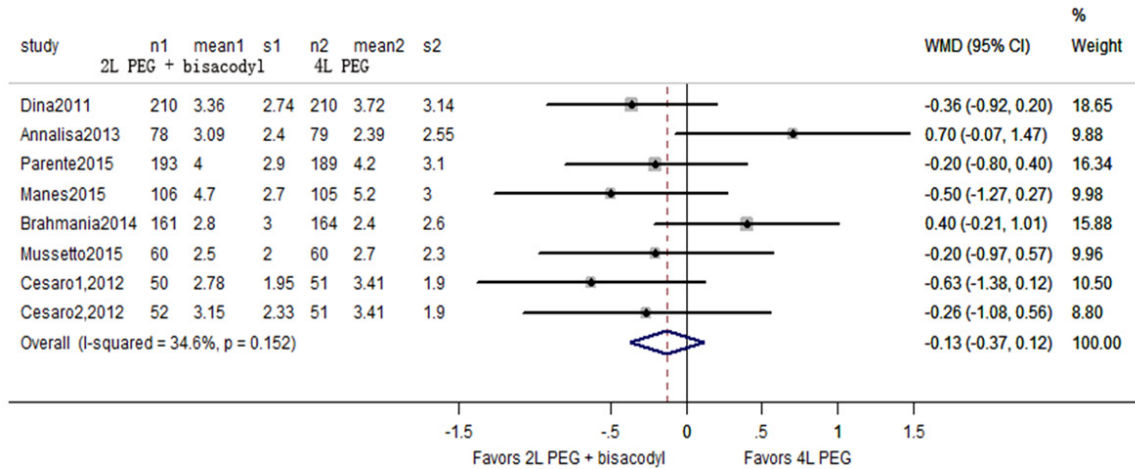
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**Table 1.** Summary of studies comparing treatment of 2 L PEG plus bisacodyl as bowel preparation for colonoscopy

Study	Year	Type of study	Blinding	Country	N		Age		Male,%		Bowel preparation	Dosing	Prep scale	Jadad score
					2 L	4 L	2 L	4 L	2 L	4 L				
Dina	2011	RCT	Single	Canada	210	210	50.8§	49.8§	35.2	41.7	2 L PEG + 20 mg B vs 4 L PEG	Full-dose (morning procedures), split-dose (afternoon procedures)	Ottawa	3
Annalisa	2013	RCT	Single	Italy	78	79	61.8 (10.8)&	60.9 (12)&	38.5	34.7	2 L PEG-CS + 15 or 20 mg (for constipation) B vs 4 L PEG	Full-dose (2 L)/split-dose (4 L)	Ottawa	3
ParenteΦ	2015	RCT	Single	Italy	193	189	60 (13)	59 (14)	46	40	2 L PEG-CS + 15 mg B vs 4 L PEG	Split-dose	Ottawa	3
DiPalma	2003	RCT	Single	US	93	93	NR	NR	NR	NR	2 L PEG-CS + 15 mg B vs 4 L PEG	Split-dose	Aronchick (4')	3
Valiante	2013	RCT	Single	Italy	138	126	62.5 (7.4)		61.7		2 L PEG-CS + 15 mg B vs 4 L PEG	Split-dose	mAronchick (5')	3
Huppertz-Hauss	2005	RCT	Single	Norway	71	76	57.9 (27-78)‡	57.4 (25-83)‡	47.9	38.2	2 L PEG + 10 mg B vs 4 L PEG	Full-dose (morning procedures), split-dose (afternoon procedures)	mAronchick (6')	3
Manesζ	2015	RCT	Single	Italy	106	105	52.4 (15.3)	48.7 (13.6)	59.4	60	2 L PEG + 10 mg B vs 4 L PEG	Full-dose/split-dose	Ottawa	3
Brahmania	2014	RCT	Single	Canada	161	164	55.6 (10.5)	56.5 (11.9)	49.7	52.4	2 L PEG + 15 mg B vs 4 L PEG	Split-dose	Boston/Ottawa	3
Mussettoψ	2015	RCT	Single	Italy	60	60	65 (9.7)	68.3 (9.9)	48.3	56.7	2 L PEG-CS + 15 mg B vs 4 L PEG	Split-dose	mOttawa/Aronchick (5')	3
Cesaro1	2012	RCT	Single	Italy	50	51	56 (26-78)	56 (32-79)	42	51	2 L PEG-CS+ 10~20 mg B vs 4 L PEG	Full-dose (same day, 2 L)/split-dose (4 L)	Ottawa	3
Cesaro2	2012	RCT	Single	Italy	52	51	61 (21-82)	56 (32-79)	42	51	2 L PEG-CS + 10~20 mg B vs 4 L PEG	Full-dose (day before, 2 L)/split-dose (4 L)	Ottawa	3
Sharma	1998	RCT	Single	US	46	59	60.3	63	98.7		2 L PEG-S + 20 mg B vs 4 L PEG	Full-dose night before	Aronchick (4')	2
Ker	2006	RCT	Single	US	150	150	61.8 (17-86)	59.3 (19-79)	50	62	2 L PEG + 20 mg B vs 4 L PEG	Full-dose night before	mAronchick (5')	2
Adams	1994	RCT	Single	Australia	191	191	59.3 (14.4)	61.1 (14.5)	37.2	44	2 L PEG + 15 mg B vs 4 L PEG	Full-dose night before	mAronchick (5')	3

Cesaro1, 2 L PEG was taken the same day with procedures; Cesaro1, 2 L PEG was taken the s day before procedures. Φpatients with chronic constipation; ζpatients with ulcerative colitis; ψpatients with history of colorectal resection. §values represent mean age; &values represent mean (standard difference); ‡values. NR, not report; 2 L, 2 L polyethylene glycol plus bisacodyl; 4 L, polyethylene glycol. PEG, polyethylene glycol; B, bisacodyl; CS, citrate simeticone.

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**Figure 2.** Forest plot showing equal bowel preparation efficacy (measured by Ottawa score) of the 2 L PEG + bisacodyl and 4 L PEG.

Four studies compared the patient preferences to another regime [13, 15, 16, 19]. Results of Forest plot revealed more people in 4 L PEG groups rather try another regimen next time than in 2 L PEG + bisacodyl (**Figure 9**). Three studies have reported the detection of adenoma by comparing both regime [14-16]. Forest plot justified there were no difference in adenoma detection rate with 2 L PEG + bisacodyl and 4 L PEG (**Figure 10**).

### Discussion

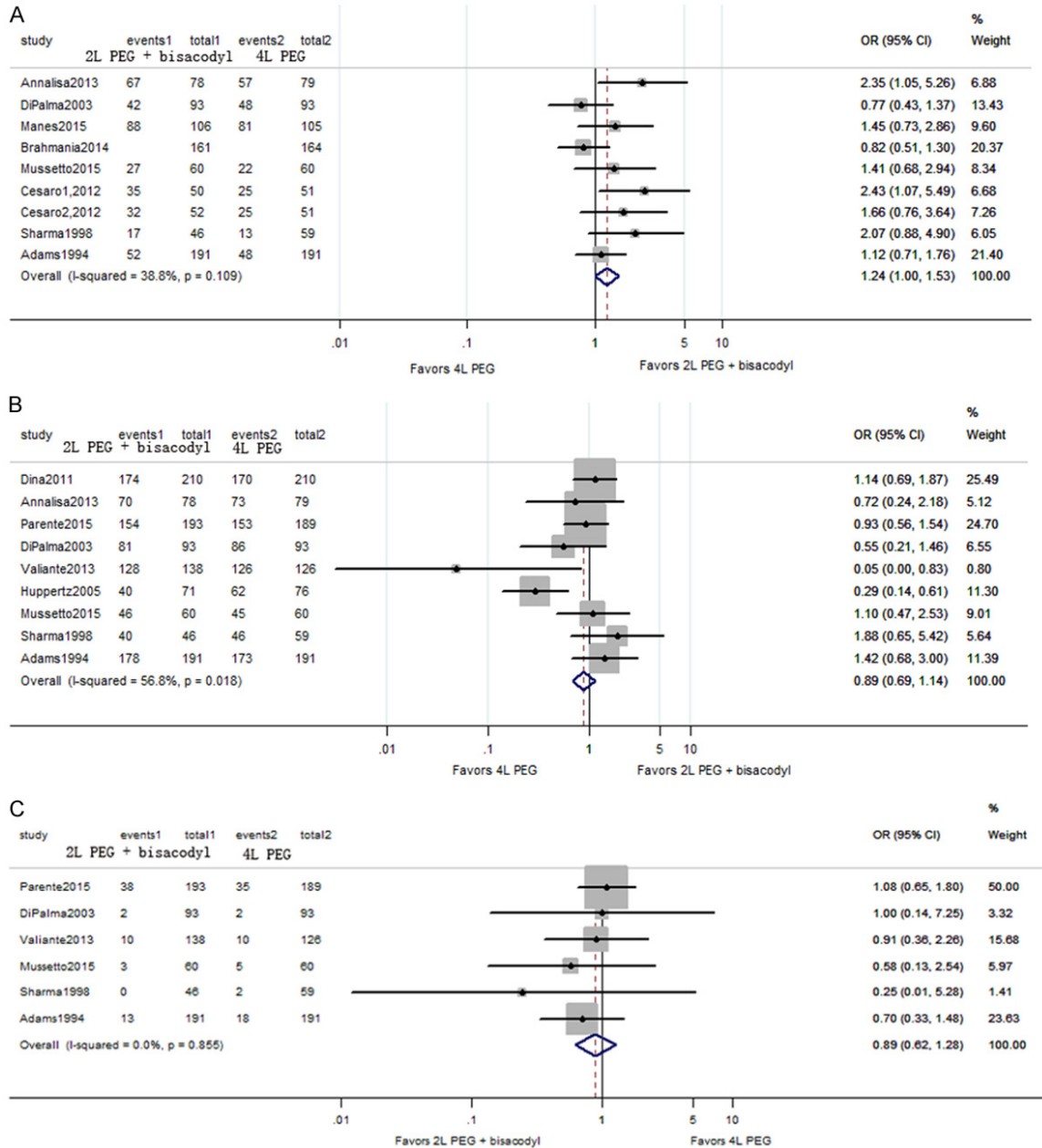
Complete bowel preparation is a vital aspect to make certain of high-quality in colonoscopy and prevents missing polyps and lesions [27, 28]. The optimal preparation for patients entails an affordable solution which will thoroughly clean the colon easily without any gross or histologic alteration in the mucosa, is endurable, as well as doesn't trigger any damage, for instance, electrolytes shifting. For the physician, optimum cleansing works well for cecal intubation and adenoma detection rates and prevents to do it again [3, 29, 30]. A recent survey among a considerable nationwide sample of gastroenterologists in the United States established that patients' aspects are the most typical factors of sub-optimal bowel preparation. Specifically, probably often documented health issue was chronic bowel irregularity and diabetes mellitus [31].

Research discovered that there's no statistically significant difference in bowel cleansing efficiency involving the improved regimen of PEG-CS plus 2-day bisacodyl and split-dose 4-L

PEG in patients with chronic constipation [13, 18, 19]. Split 2-L PEG-CS plus bisacodyl wasn't more than split 4-L PEG for colonoscopy bowel cleansing in patients with chronic constipation. On the other hand, it carried out much better than the conventional regimen concerning colonic mucosa visualization, patient acknowledgement and satisfying [13]. Moreover, problems of standard-volume PEG with lots of patients are not able or hesitant to consume a 4-L preparation [32, 33]. It has revealed that the low-volume 2-L PEG preparation may signify a legitimate substitute for conventional 4-L PEG using an at the least comparable efficacy and also a much better compliance, tolerance, and acceptability [13, 18]. In addition to efficiency, basic safety and acceptability, it really is extremely important concerns that need consideration when recommending a preparation for colonoscopy in ulcerative colitis [18]. They added that patients with IBD are occasionally extremely fragile due to cleansing procedure and vulnerable to acquire additional complications possibly from colonoscopy. Additionally, his analysis is interested because the achievable aftereffect of colonic inflammation on the quality preparation just isn't recognized and has been never ever evaluated formerly [18].

Brahmania et al [19] Preferred 4 hours as being the cutoff from planning for colonoscopy since prior reports revealed the suitable time period between the last doses of bowel preparation as well as the procedure for being three to five hours [34-36]. The time interval from solution intake and colonoscopy is an essential factor

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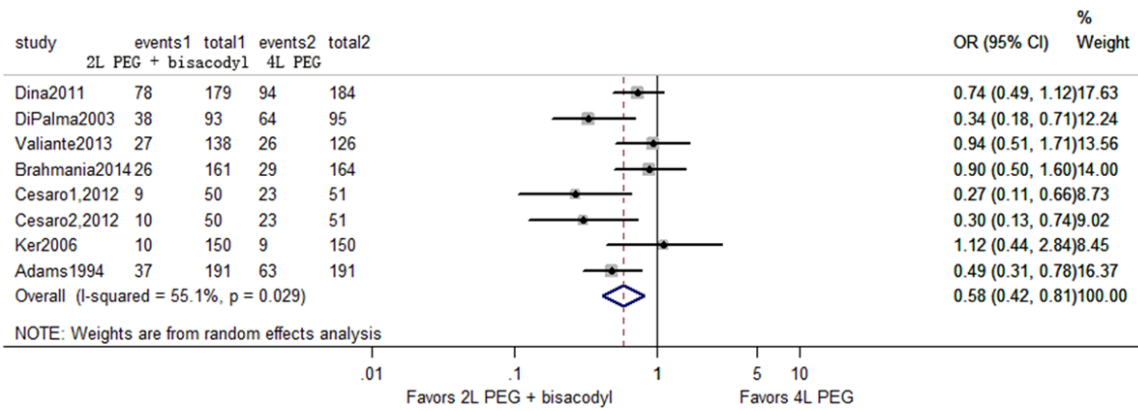
**Figure 3.** Forest plot showing quality of bowel preparation of 2 L PEG + bisacodyl and 4 L PEG for (A) excellent, (B) successful, (C) poor. 2 L PEG + bisacodyl groups had more excellent bowel preparation outcome but the same successful and poor bowel preparation outcome with 4 L PEG groups.

impacting quality of bowel cleansing and really should be reduced to lower than Six hours within the sufferer with ulcerative colitis [18]. This concurs with research expressing that when informed to the patients about the benefits of split dosing, most patients (80%) might be prepared to get up very early and have subsequent dosage prior to an early-morning colonoscopy [34]. We assume that various people have different opinion regarding their health and health

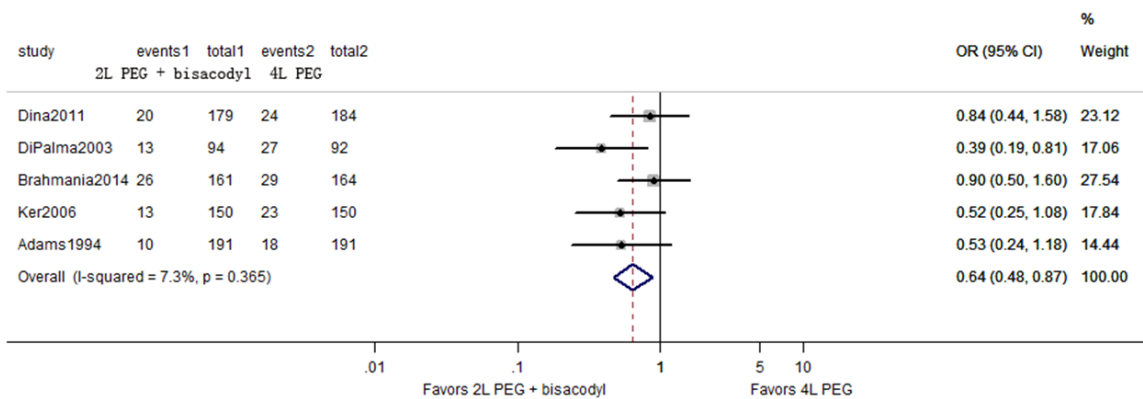
checkup timing. Most people want to see the doctors at morning schedule, and some prefer at afternoon.

We perform our colonoscopic procedure at noon and few need sedatives and short-acting anesthesia and accompanied by their relative's make them comfortable to adjust the time and care the patient after the procedure until take home. In this way patient, relative could take

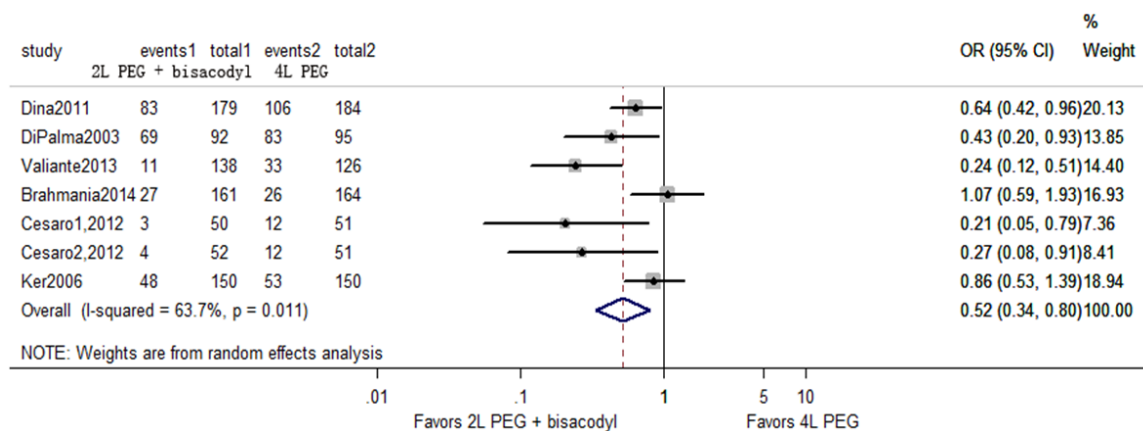
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**Figure 4.** Forest plot showing fewer nausea events with 2 L PEG + bisacodyl than 4 L PEG.



**Figure 5.** Forest plot showing fewer vomiting events with 2 L PEG + bisacodyl than 4 L PEG.

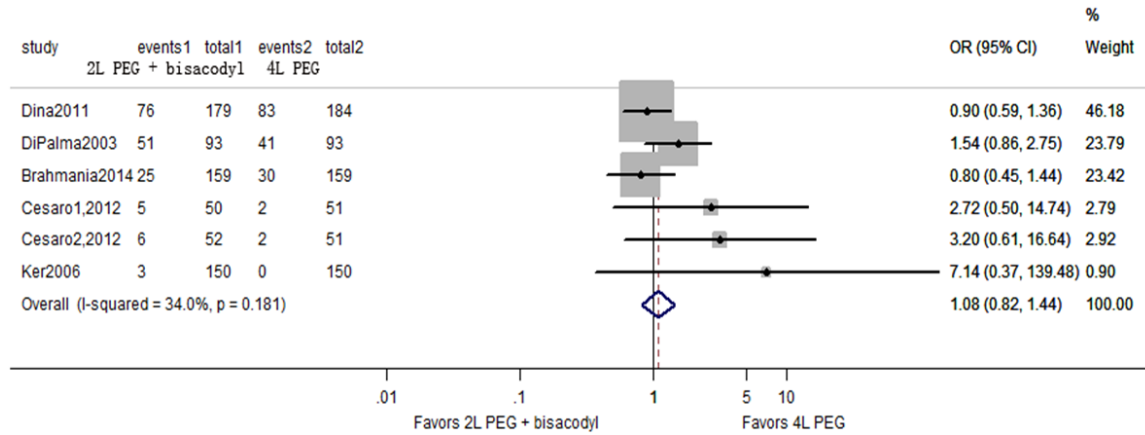


**Figure 6.** Forest plot showing fewer bloating events with 2 L PEG + bisacodyl than 4 L PEG.

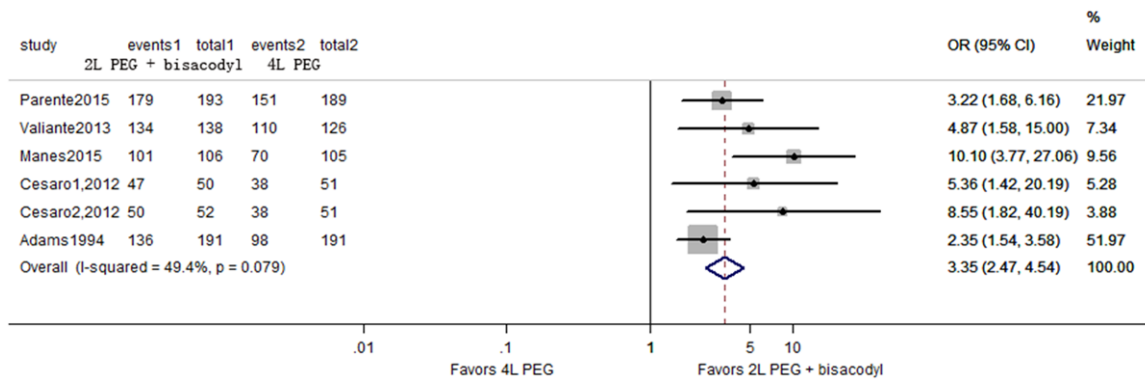
care of daily important events in the morning session. It would be interesting to have an extended study on the timing of colonoscopy comparing the efficacy of in every disease group such as adenoma, colonic polyp, Chronic constipation. We believe this study could provide us an innovative result.

While, Brahmania et al also addressed a selected group of patients, excluding those with constipation, taking narcotics, or with previous colon resection [19]. They didn't strength the study to identify any variations in adenoma detection rate and irrespective of whether an impact was witnessed in afternoon versus mo-

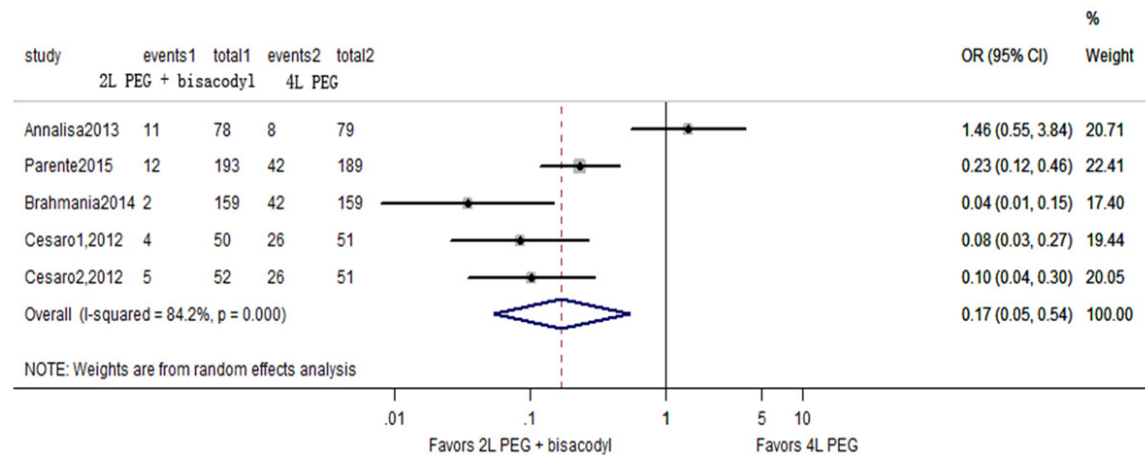
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**Figure 7.** Forest plot showing no difference between 2 L PEG + bisacodyl and 4 L PEG in Cramps or abdominal pain events.



**Figure 8.** Forest plot showing more people in 2 L PEG + bisacodyl groups intake of all solution than in 4 L PEG.



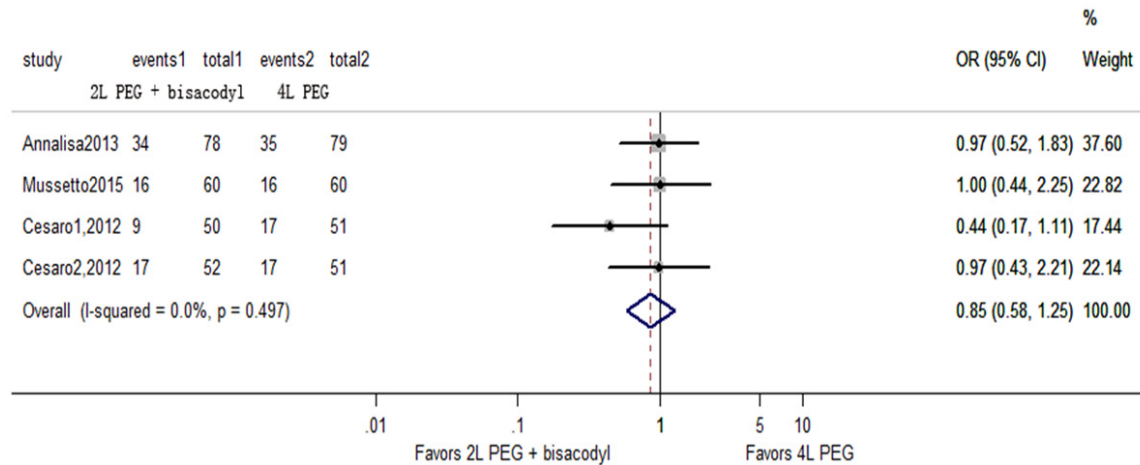
**Figure 9.** Forest plot showing more people in 4 L PEG groups rather try another regimen next time than in 2 L PEG + bisacodyl.

ring colonoscopies simply because equally formulations had been consumed four hours prior to the procedure [19].

Quite a few aspects may play a role in heterogeneity among the studies. For instance, time variance in bowel preparation may affect prep-



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**Figure 10.** Forest plot showing no difference in adenoma detection rate with 2 L PEG + bisacodyl and 4 L PEG.

ration excellence. The amount of time in which the bowel preparation was started off had not been consistent in included studies. Subsequent, deviation within the quantity of PEG solution may additionally influence bowel preparation effectiveness. The schedule dosages incorporated to non-split, which required ingesting the complete dosage, for instance, evening hours ahead of the day of the planned colonoscopy, along with a split-dosage formulation which required consuming 50 percent of the dose in the afternoon preceding another 50 percent in the morning on the procedure day. Among the list of studies incorporated, the dietary guidelines just weren't consistent, which range from a normal diet plan to some very pure fluid diet for lunch plus a clear liquid diet at nighttime. Finally, the varied utilization of bowel preparation scales perhaps resulted in heterogeneity.

Few authors used 2-L solution of PEG added with simethicone as a study drug [13, 18]. Simethicone is usually an ingredient which assists to reduce bubble's formation also it might enhance the cleansing aftereffect of this product and therefore, brings out a potential confounding aspect in the analysis of the determining factors of the caliber of preparation [37].

The safety profile of the PEG-CS plus 2-day bisacodyl as a result of the collection of adverse effects and tolerability questionnaire was free of concerns [13]. The low-volume formulation was associated too much better tolerability, acceptableness and compliance for bowel

preparation [14, 18, 20]. Complete bowel preparation is an important component to ensure high quality in colonoscopy and minimize the risk of missing polyps and lesions [27, 38]. Specifically, no event severe abdominal pain and suspected ischemic colitis was witnessed in the bisacodyl group. This was detailed in certain publicized case reports [39, 40]. However, in a recent study, there were no serious adverse events reported [14].

Study demonstrates that low-volume PEG solution plus bisacodyl may represent a valid alternative to standard 4-L PEG solution [13, 14, 18]. Few studies affirm better patient compliance [13, 14, 18, 20], tolerance [14, 18, 20], and acceptability [13, 14, 18, 20] with low dose of PEG. These factors may have a positive impact on the quality of colonoscopy and may play an important role on patients' adherence to surveillance programs [18, 20].

### Conclusion

Our study demonstrates that a low-volume bowel preparation can be viewed as a risk-free, efficient, and well-tolerated alternative to popular the high-volume regimen, predominantly considering the patient compliance, acceptability and tolerance. On the other hand, advancements are required to lessen the unwanted effects within both sorts of preparation and additional research ought to be performed making it possible for the patient to choose the cleansing procedure. Patient consciousness and medico's guidance could seriously help to decide on the variety of bowel preparation mo-

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dality and positively participate in the research to get more detailed legitimate outcomes. Expected additional researches are warranted to ensure this result more robust, specifically for the sufferer of IBD and co-morbid conditions in correlation with timing of cleansing procedure.

### Disclosure of conflict of interest

None.

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