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#### **ABOUT COVER**

Editorial Board Member of World Journal of Meta-Analysis, Dr. Fabio Coppedè is an Associate Professor of Medical Genetics at the "Department of Translational Research and of New Surgical and Medical Technologies" of University of Pisa. Professor Coppedè received a Master's Degree in Biological Sciences (November 2000) and a PhD in Microbiology and Genetics (February 2005), both from the Faculty of Science of University of Pisa. He has worked as an Academic Visitor at King's College London, Visiting Researcher at the University of California at Berkeley, and Postdoctoral Researcher at the Karolinska Institutet of Stockholm. He was awarded tenure for the rank of Associate Professor of Medical Genetics at the University of Pisa in 2015, and has held the position since. His ongoing research interests involve genetic association studies, meta-analysis of such, and epigenetic investigations in human diseases, focusing on the one-carbon metabolic pathway. (L-Editor: Filipodia)

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META-ANALYSIS

# Split-dose vs same-day bowel preparation for afternoon colonoscopies: A meta-analysis of randomized controlled trials

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# Abstract

#### BACKGROUND

Quality of bowel preparation in afternoon colonoscopies has been a struggle. Currently, a choice of same-day preparation (SaD) or split-dose preparation (SpD) exists; however, randomized controlled trials' results have varied.

## AIM

To examine the outcomes of SaD and SpD for afternoon colonoscopies.

#### **METHODS**

An extensive literature search was conducted using multiple databases. Only randomized controlled trials (RCTs) in adults that compared SaD to SpD with Ottawa bowel preparation score (OBPS) were included. Odds ratio (OR) or mean difference was used to analyze outcomes.

#### RESULTS

Eleven RCTs were included (n = 1846). No difference was observed for satisfactory bowel preparation based on OBPS among participants receiving SaD *vs* SpD (OR 0.77; 95%CI: -0.57-1.03; *P* = 0.07; *I*<sup>2</sup> = 5%). Subgroup analysis showed no difference in terms of satisfactory bowel preparation based on OBPS between the two groups when receiving same preparation formula (polyethylene glycol) (OR 0.83; 95%CI: 0.51-1.35; P = 0.46;  $I^2 = 39\%$ ) as well as receiving same formula



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and volume (4 L polyethylene glycol) (OR 1.14; 95%CI: 0.65-2.01; P = 0.64;  $l^2 = 0$ %).

#### CONCLUSION

In patients undergoing afternoon colonoscopies, SaD is comparable with SpD in terms of satisfactory bowel preparation. Further studies are needed to validate these results and determine the optimal formula and dosages.

Key Words: Afternoon; Colonoscopy; Preparation; Split-dose; Same-day; Meta-analysis

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**Core Tip:** Afternoon colonoscopies have considerably more inadequate bowel preparations than morning colonoscopies. Different bowel preparation regimens have been tried to help improve preparation quality in afternoon colonoscopies, including split-dose and same-day bowel preparations. Studies have shown conflicting results on which preparation regimen is optimal. Therefore, we conducted a meta-analysis on this subject and found that split-dose bowel preparation shows no difference in satisfactory bowel preparations vs same-day bowel preparation for afternoon colonoscopies. Therefore, either preparation may be utilized.

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# INTRODUCTION

Colorectal cancer (CRC) is a common and devastating disease resulting in significant cancer deaths around the world<sup>[1,2]</sup>. Colonoscopy remains the screening test of choice for CRC and the only method which encompasses both diagnostic and therapeutic potential<sup>[3]</sup>. Afternoon colonoscopies have higher rates of suboptimal bowel preparation<sup>[4]</sup>. Suboptimal bowel preparations are associated with prolonged procedure time, low adenoma detection rate, and increased patient discomfort, complications, and healthcare costs<sup>[5-7]</sup>.

Several studies have suggested that the quality of bowel cleansing for afternoon colonoscopies depends on timing and quantity of the bowel preparation<sup>[8,9]</sup>. Some studies have shown that split-dosing bowel preparations (SpD) is superior to sameday preparation (SaD, the morning of the procedure) with regard to both cleansing efficacy and tolerability, while other studies report that SaD has a better cleansing and tolerability compared with SpD. Currently, the U.S. Multi-Society Task Force on Colorectal Cancer (USMSTF) recommends SaD regimen as an alternative for SpD for colonoscopies in the afternoon<sup>[10]</sup> This recommendation was made based on the results of one prospective study comparing the SaD regimen with the SpD regimen and two randomized controlled trials (RCTs) using controls with day-prior regimens<sup>[6,11,22]</sup>.

Recently published RCTs on this topic report mixed results. Moreover, data pooling from the RCTs is challenging given varied bowel preparation regimens and bowel preparation scales. Therefore, a meta-analysis of the RCTs to compare the SaD with the SpD regimens for afternoon colonoscopies was performed.

## MATERIALS AND METHODS

#### Literature search and study selection

Literature search was conducted with a three-fold system. First, multiple databases, including EMBASE, Cochrane databases, MEDLINE/PubMed, Google Scholar, CINAHL, and Scopus were searched in November 2019 for afternoon and colonoscopy. Second, major conference proceeding abstracts (Digestive Disease Week,



American College of Gastroenterology, United European Gastroenterology meetings) were searched through November 2019. Third, references from identified studies were searched for any potentially omissions. If data required clarification, we communicated with the authors.

#### Data extraction

All RCTs on adults comparing the SaD with SpD regimen for afternoon colonoscopies, using the Ottawa bowel preparation score (OBPS) were included. Exclusion criteria were patients < 18 years old or non-RCTs. To reduce confounding, subgroup analyses were performed for the same formulation and volume of bowel preparation using polyethylene glycol with electrolytes (PEG). Two authors (Parsa NP and Grisham EA) independently reviewed all the studies for inclusion and extracted data using standard forms. Any disagreements on inclusion or data extraction were settled by the senior author (Bechtold ML).

#### Quality assessment of studies

The Cochrane's Collaboration Risk of Bias Tool was used to assess the quality of studies<sup>[13-15]</sup>. For each study, a grade, as described as low, moderate, or high, was based on the assessment of limitations, effect magnitude, precision, publication and other forms of bias, and consistency of results<sup>[13-15]</sup>.

#### Statistical analysis

A meta-analysis was conducted comparing SaD and SpD for afternoon colonoscopies by calculating pooled estimates of quality of bowel preparation. Outcomes were analyzed using mean difference (MD) or odds ratio (OR) by the DerSimonian and Laird method (the random-effects model). The  $l^2$  measure of inconsistency was used to assess heterogeneity (P < 0.10 or  $I^2 > 50\%$  was deemed significant). If heterogeneity was discovered, researchers used performed a sensitivity analysis to remove the least amount of studies necessary to reach non-significant heterogeneity by comparing results to the original pooled data. RevMan 5.3 (Review Manager, Version 5.3, Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2012) was used for statistical analysis. Funnel plots assessed for publication bias.

#### RESULTS

#### Article search and quality assessment

Evaluation of titles and abstracts resulted in 663 articles being identified. After review, 21 articles remaining in which 11 satisfied the inclusion criteria (n = 1846) with mean age range of 51.6-61.8 years<sup>[16-26]</sup> (Figure 1). Studies were global, including many countries (United States, Spain, Italy, China, Korea, India) (Table 1). Most of the studies were deemed high-quality studies based on quality assessment (Table 2).

#### **Overall results**

Eight RCTs reported the mean OBPS (n = 1328)<sup>[17-21,23-25]</sup>. Eight studies reported the number of satisfactory bowel preparations (n = 1483)<sup>[16,19,21-26]</sup>. Of these, 1202 had satisfactory bowel preparations with 578 in the SaD group and 624 in the SpD group. There was no difference between SaD and SpD for the mean OBPS (MD 0.33; 95%CI: -0.09-0.75; P = 0.13;  $I^2 = 74\%$ ) (Figure 2A) or the number satisfactory bowel preparations (79.1% *vs* 83%; OR 0.77; 95%CI: 0.57-1.03; *P* = 0.07; *I*<sup>2</sup> = 5%) (Figure 2B) despite a trend favoring SpD. Given significant heterogeneity in the mean OBPS analysis, a sensitivity analysis was performed which showed similar results without significant heterogeneity when one study<sup>[23]</sup> was eliminated (OR 0.18; 95%CI: -0.11-0.46; P = 0.22;  $I^2 =$ 36%).

#### Same formulation bowel preparation (PEG)

Five studies reported the mean OBPS (n = 877)<sup>[17,20,21,23,25]</sup>. There was no difference between SaD and SpD for mean OBPS (MD 0.45; 95%CI: -0.13-1.02; P = 0.13; l<sup>2</sup> = 78%) (Figure 3A). Five studies reported the number of satisfactory bowel preparations (n =1045)<sup>[21-23,25,26]</sup>. Of these, 862 had satisfactory bowel preparations (82.5%) with 415 in the SaD group and 447 in the SpD group. There was no difference between SaD and SpD for number satisfactory bowel preparations (81% vs 84%; OR 0.83; 95% CI: 0.51-1.35; P = 0.46;  $l^2$  = 39%) (Figure 3B). Given significant heterogeneity in the mean OBPS analysis, a sensitivity analysis was performed which showed similar results without



Table 1 Descr	iption of st	udies included	in the meta-analysis				
Ref.	Country	Number of patients ( <i>n</i> )	Bowel preparation times (dose 1)	Patients per group ( <i>n</i> )	Bowel preparation scale	Satisfactory bowel preparations ( <i>n</i> )	OBPS (mean score ± SD)
Parra-Blanco et al <sup>[16]</sup> , 2006	Spain	88	Same day PEG 3 L	43	Ottawa	34	ND
<i>et al</i> <sup>100</sup> , 2006			Split-dose NaP 45 mL/45 mL	45	Ottawa	36	ND
Kang <i>et al</i> <sup>[24]</sup> ,	South	196	Same day NaP 1/1	97	Ottawa	59	$4.05\pm1.56$
2014	Korea		Split-dose PEG 2 L/2 L	99	Ottawa	71	$3.8 \pm 1.55$
Shah <i>et al</i> <sup>[17]</sup> ,	India	159	Same day PEG 2 L	80	Ottawa	ND	$6.02 \pm 1.34$
2014			Split-dose PEG 1 L/1 L	79	Ottawa	ND	$5.52 \pm 1.23$
Cesaro <i>et al</i> <sup>[18]</sup> , 2013	Italy	101	Same day Halflytely 2 L/10-20 mg Bisacodyl	50	Ottawa	ND	$2.78 \pm 1.95$
			Split-dose PEG 3 L/1 L	51	Ottawa	ND	$3.41 \pm 1.90$
de Leone <i>et al</i> <sup>[19]</sup> , 2013	Italy	154	Same day Halflytely 2 L/10-20 mg Bisacodyl	78	Ottawa	70	$3.09 \pm 2.4$
			Split-dose PEG 2 L/2 L	76	Ottawa	70	$2.39 \pm 2.55$
Kim <i>et al</i> <sup>[25]</sup> ,	South	100	Same day PEG 4 L	50	Ottawa	41	$4.98 \pm 1.78$
2014	Korea		Split-dose PEG 2 L/2 L	50	Ottawa	42	$4.98 \pm 1.57$
Kotwal <i>et al</i> <sup>[20]</sup> , 2014	United	103	Same day PEG 3 L	51	Ottawa	ND	$7.15\pm3.58$
<i>et al</i> <sup>1</sup> , 2014	States		Split-dose PEG 2 L/2 L	52	Ottawa	ND	$7.38 \pm 3.65$
Seo <i>et al</i> <sup>[21]</sup> , 2013	South Korea	197	Same day PEG 2 L	97	Ottawa	72	$3.76 \pm 2.07$
2013	Korea		Split-dose PEG 2 L/2 L	100	Ottawa	75	$3.67 \pm 1.57$
Zhang <i>et al</i> <sup>[23]</sup> ,	China	318	Same day PEG 2 L	159	Ottawa	126	$4.4 \pm 2.7$
2014			Split-dose PEG 1 L/2 L	159	Ottawa	143	$2.9 \pm 2.4$
Alkhairi at $al^{[26]}$ 2017	United	300	Same day PEG 4 L	142	Ottawa	142	ND
et al <sup>[26]</sup> , 2017	States		Split-dose PEG 2 L/2 L	158	Ottawa	156	ND
Castro <i>et al</i> <sup>[22]</sup> ,	United	130	Same day PEG 4 L	65	Ottawa	34	ND
2019	States		Split-dose PEG 2 L/2 L	65	Ottawa	31	ND

#### OBPS: Ottawa bowel preparation score; PEG: Polyethylene glycol; ND: Not detected.

significant heterogeneity when one study<sup>[23]</sup> was eliminated (OR 0.26; 95%CI: -0.02-0.54; P = 0.07;  $I^2 = 0\%$ ).

#### Same formulation and volume bowel preparation (4 L PEG)

Three studies reported the mean OBPS  $(n = 362)^{[17,20,25]}$ . There was no difference between SaD and SpD for mean OBPS (MD 0.30; 95% CI: -0.08-0.68; *P* = 0.12; *I*<sup>2</sup> = 12%) (Figure 4A). Three studies reported the number of satisfactory bowel preparations (n =530)<sup>[22,25,26]</sup>. Of these, 446 had satisfactory bowel preparations with 217 in the SaD group and 229 in the SpD group. There was no difference between SaD and SpD for number satisfactory bowel preparations (84.4% vs 83.9%; OR 1.14; 95%CI: 0.65-2.01; P = 0.64; I<sup>2</sup> = 0%) (Figure 4B).

#### **Publication bias**

For any outcome, no significant publication bias was identified (Figure 5).

#### DISCUSSION

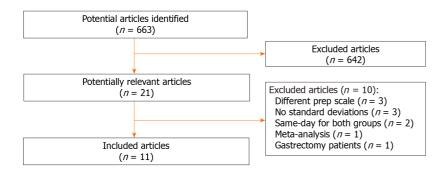
The USMSTF currently recommends the SaD bowel preparation as an alternative to SpD for afternoon colonoscopies<sup>[10]</sup>. This recommendation, which is based on "high-



#### Table 2 Quality assessment of studies included in meta-analysis based upon Cochrane's Collaboration Risk of Bias tool

Ref.	Study design	Random sequence generation	Allocation concealment	Blinding	Blinding outcome assessment	Incomplete outcome data	Selective reporting	Other bias	Quality assessment
Parra- Blanco <i>et al</i> <sup>[16]</sup> , 2006	RCT	Adequate	Adequate	Single- blinded	Adequate	None	None	None	High
Kang et al <sup>[24]</sup> , 2014	RCT	Adequate	Adequate	Single- blinded	Adequate	None	None	None	High
Shah <i>et al</i> <sup>[17]</sup> , 2014	RCT	Adequate	Adequate	Single- blinded	Adequate	None	None	None	High
Cesaro <i>et al</i> <sup>[18]</sup> , 2013	RCT	Adequate	Adequate	Single- blinded	Adequate	None	None	None	High
de Leone <i>et al</i> <sup>[19]</sup> , 2013	RCT	Adequate	Adequate	Single- blinded	Adequate	None	None	None	High
Kim <i>et al</i> <sup>[25]</sup> , 2014	RCT	Not described	Adequate	Single- blinded	Adequate	None	None	None	Moderate
Kotwal <i>et al</i> <sup>[20]</sup> , 2014	RCT	Adequate	Adequate	Single- blinded	Adequate	None	None	None	High
Seo <i>et al</i> <sup>[21]</sup> , 2013	RCT	Adequate	Adequate	Single- blinded	Adequate	None	None	None	High
Zhang <i>et al</i> <sup>[23]</sup> , 2014	RCT	Adequate	Adequate	Single- blinded	Adequate	None	None	None	High
Castro <i>et al</i> <sup>[22]</sup> , 2019	RCT	Adequate	Adequate	Single- blinded	Adequate	None	None	None	High
Alkhairi <i>et al</i> <sup>[26]</sup> , 2017	RCT	Not described	Not described	Single- blinded	Adequate	None	None	None	Moderate

RCT: Randomized controlled trial



#### Figure 1 Details of search algorithm.

quality evidence", is based on one prospective study and two RCTs that their control groups received a day-prior bowel preparation regimen<sup>[6,11,12]</sup>. Since this recommendation, several high-quality trials have evaluated and compared the efficacy of SaD vs SpD for afternoon colonoscopies, supporting the value of this study.

The practice of SaD bowel preparation was supported by two meta-analyses published in 2017. Both studies concluded the noninferiority of the SaD compared with the SpD regimen with regards to bowel preparation for afternoon colonoscopies, consistent with the findings of our study<sup>[27,28]</sup>. Avalos et al<sup>[27]</sup> conducted a meta-analysis on 11 RTCs comparing the efficacy of bowel preparation quality between the SaD and SpD regimens and reported a similar results for the bowel preparation quality, patient willingness to repeat the procedure and adenoma detection rate, although SaD patients reported less bloating and improved quality of sleep. Cheng et al<sup>[28]</sup> pooled the results of 14 RTCs and reported comparable results between the SaD and SpD regimens for bowel preparation with substantial heterogeneity ( $I^2 = 60\%$ ), so subgroup



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	Sai	ne Da	У	Spl	it-Dos	е		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl
Cesaro 2013	2.78	1.95	50	3.41	1.9	51	11.5%	-0.63 [-1.38, 0.12]	
de Leone 2013	3.09	2.4	78	2.39	2.55	76	11.1%	0.70 [-0.08, 1.48]	
Kang 2014	4.05	1.56	97	3.8	1.55	99	15.2%	0.25 [-0.19, 0.69]	-+ <b>-</b>
Kim 2014	4.98	1.78	50	4.98	1.57	50	12.6%	0.00 [-0.66, 0.66]	<b>_</b>
Kotwal 2014	7.15	3.58	51	7.38	3.65	52	6.0%	-0.23 [-1.63, 1.17]	
Seo 2013	3.76	2.07	97	3.67	1.57	100	14.3%	0.09 [-0.42, 0.60]	
Shah 2014	6.02	1.34	80	5.52	1.23	79	15.6%	0.50 [0.10, 0.90]	
Zhang 2014	4.4	2.7	159	2.9	2.4	159	13.7%	1.50 [0.94, 2.06]	
Total (95% CI)			662			666	100.0%	0.33 [-0.09, 0.75]	•
Heterogeneity: Tau <sup>2</sup> = Test for overall effect:				f=7(P:	= 0.00	04); I² =	74%		-4 -2 0 2
restion overall ellect.	2-1.00	(	5.13)						Favors Same Day Favors Split-Dose

D		Same	Day	Split-D	ose		Odds Ratio	Odds Ratio
	Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
	Alkhairi 2017	34	65	31	65	16.8%	1.20 [0.60, 2.39]	
	Castro 2019	142	142	156	158	0.9%	4.55 [0.22, 95.64]	
	de Leone 2013	70	78	70	76	6.8%	0.75 [0.25, 2.27]	
	Kang 2014	59	97	71	99	21.8%	0.61 [0.34, 1.11]	
	Kim 2014	41	50	42	50	7.6%	0.87 [0.31, 2.47]	
	Parra-Blanco 2006	34	43	36	45	7.7%	0.94 [0.34, 2.66]	
	Seo 2013	72	97	75	100	19.2%	0.96 [0.51, 1.82]	
	Zhang 2014	126	159	143	159	19.1%	0.43 [0.22, 0.81]	
	Total (95% CI)		731		752	100.0%	0.77 [0.57, 1.03]	•
	Total events	578		624				
	Heterogeneity: Tau <sup>2</sup> =	0.01; Ch	i² = 7.3	6, df = 7 (	P = 0.3	9); l² = 59	6	0.01 0.1 1 10 100
	Test for overall effect:	Z=1.79	(P = 0.0	17)				Favors Split-Dose Favors Same Day

Figure 2 Forest plot showing overall bowel preparation results between same-day preparation vs split-dose preparation for afternoon colonoscopies. A: Mean Ottawa bowel preparation score; B: Number of satisfactory bowel preparations.

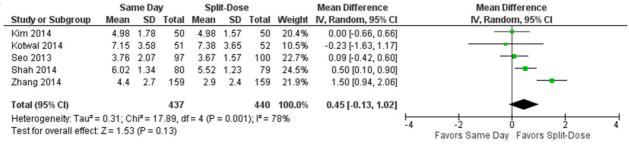
> analysis was performed to evaluate the influence of bisacodyl on bowel preparation. Comparing SaDs with bisacodyl to SpDs without it the previous evening showed the results favored SaDs ( $I^2 = 0\%$ ). If both arms eliminated adjuvants, the analysis revealed that patients in the SpD arm had better bowel preparation with no heterogeneity (OR 0.66; 95%CI: 0.49-0.88). Heterogeneity was a significant limitation of these metaanalyses as many studies used varied bowel preparation scales in the study arms. Furthermore, neither compared the SaD and SpD regimens among patients who received same formula and volume bowel preparation.

> This meta-analysis is the first comparing SaD vs SpD bowel preparation for afternoon colonoscopies that used identical validated scales to evaluate the bowel preparation quality. No significant differences were identified between the SaD and SpD regimens for quality of bowel preparation by total OBPS. Moreover, we performed a comprehensive subgroup analysis in order to minimize potential confounding factors. Further subgroup analyses showed no differences in terms of satisfactory bowel preparation based on OBPS between the two groups when receiving the same preparation formula (PEG) as well as receiving same preparation formula and volume (4 L PEG). Only RCTs in adult patients were evaluated and used in this meta-analysis. Moreover, by using the OBPS, which evaluates the bowel preparation quality before the application of any cleansing maneuvers, the amount of time and adequacy of cleaning was not an issue, thereby limiting confounding variables. Results of our study can help guide clinicians and patients to select the optimal method for bowel preparation. The current guidelines indicate that providers are responsible for maintaining optimal bowel preparations at greater than 85%, which is often affected by inadequate bowel preparation ingestion by patients<sup>[10]</sup>. Given a lack of clinical differences, both SaD and SpD regimens should be offered to patients and their preference should be considered in order to maximize their adherence. This may potentially minimize procedure cancellations and increase the success rates of afternoon colonoscopies.

> The strengths of this meta-analysis are abundant. Inclusion of worldwide RCTs in varying populations, including China, Korea, Spain, Italy, India, and United States, allows for generalization to many populations. Second, the quality of RCTs included were moderate-to-high. Given the lack of ability to blind the patient to the bowel



Α



В										
		Same	Day	Split-D	ose		Odds Ratio		Odds Ratio	
	Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl		M-H, Random, 95% Cl	
-	Alkhairi 2017	34	65	31	65	26.1%	1.20 [0.60, 2.39]			
	Castro 2019	142	142	156	158	2.5%	4.55 [0.22, 95.64]			
	Kim 2014	41	50	42	50	15.6%	0.87 [0.31, 2.47]			
	Seo 2013	72	97	75	100	28.0%	0.96 [0.51, 1.82]			
	Zhang 2014	126	159	143	159	27.9%	0.43 [0.22, 0.81]			
	Total (95% CI)		513		532	100.0%	0.83 [0.51, 1.35]		•	
	Total events	415		447						
	Heterogeneity: Tau <sup>2</sup> =	0.12; Chi	<sup>2</sup> = 6.5	9, df = 4 (	P = 0.1	6); I <sup>2</sup> = 39	%	0.01		100
	Test for overall effect:	Z= 0.74 (	(P = 0.4	16)				0.01	Favors Split-Dose Favors Same Day	100

Figure 3 Forest plot showing same bowel preparation results between same-day preparation vs split-dose preparation for afternoon colonoscopies. A: Mean Ottawa bowel preparation score; B: Number of satisfactory bowel preparations.

Α		Sar	ne Day	1	Spl	it-Dose	е		Mean Difference	Mean Difference
	Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% C	CI IV, Random, 95% CI
	Kim 2014	4.98	1.78	50	4.98	1.57	50	29.0%	0.00 [-0.66, 0.66	6]
	Kotwal 2014	7.15	3.58	51	7.38	3.65	52	7.2%	-0.23 [-1.63, 1.17	7]
	Shah 2014	6.02	1.34	80	5.52	1.23	79	63.8%	0.50 [0.10, 0.90	oj - <b></b> -
	Total (95% CI)			181			181	100.0%	0.30 [-0.08, 0.68	a] 🔶
	Heterogeneity: Tau <sup>2</sup> = Test for overall effect:				= 2 (P =	0.32);	I <sup>2</sup> = 12%	<b>b</b>		-4 -2 0 2 4 Favors Same Day Favors Split-Dose
B		Sam	ne Day		Split-Do	se			Odds Ratio	Odds Ratio
В	Study or Subgroup	San Even				se Total	Weigh		Odds Ratio Random, 95% Cl	Odds Ratio M-H, Random, 95% Cl
В	Study or Subgroup Alkhairi 2017	Even	ts To				Weigh 67.39	nt M-H,		
В	, , ,	Even	ts To 34	tal E	vents	Total		nt M₋H, %	Random, 95% Cl	
B	Alkhairi 2017	Even 3	ts To 34 42 1	tal E 65	vents 31	Total 65	67.39	nt M-H, % %	Random, 95% Cl 1.20 [0.60, 2.39]	
В	Alkhairi 2017 Castro 2019	Even 3	ts To 34 42 1 41	tal E 65 42	vents 31 156	Total 65 158	67.39 3.49 29.29	nt <u>M-H,</u> % %	Random, 95% Cl 1.20 [0.60, 2.39] 4.55 [0.22, 95.64]	
В	Alkhairi 2017 Castro 2019 Kim 2014	Even 14 2	ts To 34 42 1 41	tal E 65 42 50	vents 31 156	Total 65 158 50	67.39 3.49 29.29	nt <u>M-H,</u> % %	Random, 95% Cl 1.20 [0.60, 2.39] 4.55 [0.22, 95.64] 0.87 [0.31, 2.47]	

Figure 4 Forest plot showing same bowel preparation (type and volume) results between same-day preparation vs split-dose preparation for afternoon colonoscopies. A: Mean Ottawa bowel preparation score; B: Number of satisfactory bowel preparations.

> preparation, the included studies were the highest exceptional quality possible. Third, to minimize confounding factors, extensive subgroup analyses were performed and only studies with the same bowel preparation and the same bowel preparation with same volume were evaluated. This effort limits significant confounding factors. Finally, the OBPS was used which limits confounding variables of cleaning effort and cleaning time since evaluated prior to cleaning. Limitations of this meta-analysis were observed. First, significant heterogeneity was observed in two outcomes. Besides a diversity of bowel preparation across studies, there were slightly varied preparations within study arms. Furthermore, some using SaD or SpD preparations with or without

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Test for overall effect: Z = 0.47 (P = 0.64)

Favors Split-Dose Favors Same Day

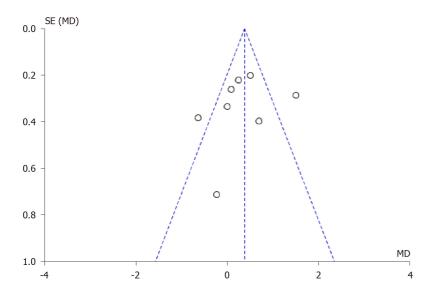


Figure 5 Funnel plot showing no publication bias.

bisacodyl. For those two outcomes with significant heterogeneity, sensitivity analyses were performed with similar results without significant heterogeneity when Zhang et al<sup>[23]</sup> was removed. Second, the type of diet as well as the length of diet restriction during preparation varied among studies and therefore, the influence of diet on bowel preparation could not be further analyzed.

### CONCLUSION

In conclusion, our meta-analysis showed that no difference exists between SaD and SpD bowel preparation for the number of satisfactory bowel preparations in the afternoon colonoscopies. Both options should be offered to patients in order to maximize adherence and increase afternoon colonoscopy success rates.

## ARTICLE HIGHLIGHTS

#### Research background

Bowel preparation for afternoon colonoscopies is important for screening for colorectal cancer.

#### Research motivation

Bowel preparation for afternoon colonoscopies is controversial. Examining the best approach would be beneficial for patients and those performing colonoscopies.

#### Research objectives

This meta-analysis examines the use of same-day preparation (SaD) or split-dose preparation (SpD) for afternoon colonoscopies.

#### Research methods

An extensive literature search was conducted using multiple databases. Only randomized controlled trials in adults that compared SaD to SpD with Ottawa bowel preparation score (OBPS) were included. Odds ratio or mean difference was used to analyze outcomes.

#### Research results

No differences were observed for satisfactory bowel preparation based on OBPS among participants receiving SaD vs SpD overall (P = 0.07), when the two groups received the same preparation formula (polyethylene glycol, PEG) (P = 0.46), and when the two groups received the same formula and volume (4 L PEG) (P = 0.64).



#### Research conclusions

In patients undergoing afternoon colonoscopies, SpD is comparable with SaD in terms of satisfactory bowel preparations.

#### Research perspectives

Patients and proceduralists may be confident in using either SaD or SpD for afternoon colonoscopies.

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