Comparing the Real-World Effectiveness of Competing Colonoscopy Preparations: Results of a Prospective Trial

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OBJECTIVES: **National societies provide little guidance regarding which colonoscopy bowel preps are best tolerated and most effective; this reflects a lack of comparative effectiveness studies that directly evaluate the available preps in a "real-world" setting. To address this gap, we conducted a prospective, commercially unfunded comparative effectiveness study of currently available bowel preps and measured their impact on bowel cleansing.**

METHODS: **We included patients aged ≥18 years, who presented for an outpatient colonoscopy at a large medical center serving more than 70 academic and community-based endoscopists who are free to prescribe the bowel prep of their choice. The primary outcome was bowel cleansing quality as measured by the Boston Bowel Preparation Scale. We performed regression models with random effects on the outcomes to adjust for confounding.**

RESULTS: **Approximately 4,339 colonoscopies were performed by 75 endoscopists. Magnesium citrate, MiraLAX with Gatorade, MoviPrep, OsmoPrep, Prepopik/Clenpiq, and Suprep all had significantly higher prep tolerability compared with GoLYTELY (all $P < 0.05$). For bowel cleansing, Suprep (7.28 ± 1.66; $P < 0.001$), MoviPrep (7.11 ± 1.62; $P = 0.004$), and MiraLAX with Gatorade (7.09 ± 1.64; $P < 0.001$) had higher total Boston Bowel Preparation Scale scores compared with GoLYTELY (6.67 ± 1.87); there were no significant differences among the remaining preps. Split-prep dosing was associated with better cleansing; however, men, opioid and tricyclic antidepressent users, and patients with diabetes and cirrhosis had worse cleansing (all $P < 0.05$).**

CONCLUSIONS: **In this prospective, real-world comparative effectiveness study of available bowel preps, we found that MiraLAX with Gatorade, MoviPrep, and Suprep were prospectively associated with superior tolerability and bowel cleansing.**

SUPPLEMENTARY MATERIAL accompanies this paper at http://links.lww.com/AJG/A16 and http://links.lww.com/AJG/A17.

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INTRODUCTION

Although colorectal cancer (CRC) is largely preventable, it remains a major public health issue and is the third most common malignancy in the United States in both men and women (1). The US Preventive Services Task Force recommends that all Americans undergo screening starting at age 50 with one of several supported approaches, including fecal-based tests, computed tomographic colonography, and flexible sigmoidoscopy (2). However, colonoscopy remains the gold standard; it is the only test that is both cancer detecting and cancer preventing through the removal of adenomatous polyps—the CRC precursor (3–5).

More than 14 million colonoscopies are performed annually in the United States (6). Selecting the optimal bowel prep has a major impact on the effectiveness of colonoscopic CRC screening and is a critical process measure along the path toward improved screening outcomes (7). Although adequate bowel cleansing is essential for a successful colonoscopy, inadequate preparation occurs in up to 25% of procedures (8,9), leading to impaired visualization, missed polyps, and lower adenoma detection rates (ADRs), thereby increasing the risk of interval CRC (10).

As of September 2018, there are more than 10 commercially available bowel preps, with each varying in volume, tolerability,

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and formulation. Despite the importance of bowel cleansing, national societies provide minimal guidance regarding which preps are best tolerated and most effective or how best to navigate among the available options (11,12). Current guidelines only recommend selection of a prep that accounts for a patient's medical history, medications, and cleansing adequacy from previous examinations (11,12). This nonspecific recommendation reflects a lack of comparative effectiveness studies that directly evaluate the available preps in a "real world" setting. Most of the available data are from randomized controlled trials (RCTs) comparing 2 or 3 preps at a time in the context of tightly controlled research protocols that may not accurately reflect real-world conditions (11).

Although the efficacy of the various bowel preps has been well studied in RCTs, clinical effectiveness of these preps in daily clinical practice is largely unstudied. The lack of comparative evidence data creates uncertainty among patients, clinicians, and other stakeholders regarding which bowel preps to use in CRC screening programs. Moreover, without prospective comparative effectiveness data, the clinicians may be using preps that appear efficacious in RCTs but are not equally effective in everyday clinical practice where issues around tolerability intersect with patients' knowledge, attitudes, and beliefs about CRC screening (13,14), leading to complexities in administering and achieving effective bowel preps (8,9). To address this gap in knowledge, we aimed to conduct a prospective, naturalistic, commercially unfunded comparative effectiveness study to assess the impact of currently available preps on bowel cleansing quality and tolerability in real-world conditions.

METHODS

Study design, patients, and setting

We performed a prospective, naturalistic comparative effectiveness study at Cedars-Sinai Medical Center, a quaternary care hospital and multispecialty health science center that provides healthcare for the diverse population of Los Angeles, California. Cedars-Sinai is affiliated with more than 70 academic and community-based endoscopists who perform more than 4,000 inpatient and outpatient colonoscopies annually at the medical center. These clinicians have individual choice to use any available bowel prep and are not bound by a restrictive formulary.

We enrolled patients aged ≥18 years, who presented for an outpatient colonoscopy for any indication between August 4, 2016, and July 31, 2018. All patients were assessed prospectively at the time of colonoscopy using the Boston Bowel Preparation Scale (BBPS), a validated and widely used measure of bowel cleansing. The BBPS score is documented as part of routine clinical care by the procedure nurse rather than any members of the research team (see Primary outcome—bowel cleansing section for more details) (15,16). Individuals with surgically absent colon segments or in whom the procedure was aborted for reasons unrelated to bowel prep (e.g., technical difficulties, patient instability or intolerance) were excluded from the study because these scenarios cannot be completely scored using the BBPS. We also excluded those who received a 2-day "double" bowel prep. The study was approved by the Cedars-Sinai Medical Center's Institutional Review Board (IRB# Pro41005).

Primary outcome—bowel cleansing

The primary outcome was bowel cleansing measured using the BBPS (15,16). We assessed bowel cleansing in 2 ways: (i) total BBPS score and (ii) adequate bowel cleansing, which was defined as a total BBPS score of ≥6, with each segment BBPS score of ≥2 (right, transverse, and left colon).

For every colonoscopy performed at Cedars-Sinai, the BBPS score for each segment of the colon is assessed and documented in the electronic health record (EHR) by the procedure nurse. The evaluation is performed independently by the nurse, and a survey of the nursing staff revealed that the proceduralists rarely provide input on the BBPS score. Although this process is already part of routine clinical care, research investigators (P.G. and C.V.A.) conducted in-services with the endoscopy nurses about 1 month before (July 14, 2016) and 6 months (February 23, 2017) after initiation of the study to reinforce correct application of the BBPS during the withdrawal phase and once all cleansing has been completed. During both sessions, the instructors guided the nursing staff through the BBPS Educational Program (vimeo.com/31111826) developed by the Boston University School of Medicine Clinical Outcomes Research Initiative (15,16). Moreover, to support continued appropriate use of the BBPS throughout the study and to account for staff turnover, the EHR BBPS module was updated before initiation of the study to include hover text explaining each BBPS score (15,16): (i) N/A—surgically absent colon segment or segment not seen for reasons unrelated to bowel prep, such as technical difficulties or patient instability or intolerance; (ii) 0—unprepared colon segment, mucosa not seen because of solid stool; (iii) 1—portion of mucosa of the colon seen, residual stool; (iv) 2—minor amount of residual staining, mucosa seen; and (v) 3—entire mucosa of colon segment seen well, no residual staining.

Secondary outcome—bowel prep tolerability

We assessed bowel prep tolerability by determining whether the patient completed the bowel prep as prescribed. Before each colonoscopy, the pre-procedure nurse asked all patients "How much of the bowel prep did you ingest?"; the answer options in the EHR included the following: (i) all (100%) of the prep, (ii) 75%–99% of the prep, (iii) <75% of the prep, and (iv) unsure. For the purposes of the study, we dichotomized responses to (i) fully completed the prep and (ii) did not fully complete the prep.

Covariates—prescribed bowel preps and dosing

All endoscopists were free to prescribe the prep and dosing of their choice. To determine the prescribed prep, pre-procedure nurses asked all patients "What bowel prep did you take?" The answer options included the following: (i) GoLYTELY, (ii) Colyte, (iii) NuLYTELY, (iv) Trilyte, (v) MoviPrep, (vi) MiraLAX with Gatorade, (vii) Suprep, (viii) Suclear, (ix) Prepopik, (x) OsmoPrep, (xi) magnesium citrate, (xii) other, and (xiii) unknown. Bowel prep "face sheets" that included pictures of the packaging of the commonly used preps were located at all pre-procedure bays to assist patients who had difficulty remembering their prescribed prep. We also validated the accuracy of the patients' self-reported prep by manually examining 100 random charts and found that in 95% of cases the prep reported by patients matched the prep documented in their clinic notes. Dosing information was also collected in the pre-procedure setting, where the nurses asked all patients "Did you ingest all of the bowel prep yesterday OR did you split the bowel prep by ingesting half of it yesterday and finishing the rest of it today?"

Colyte, NuLYTELY, and Trilyte were not commonly prescribed, so they were consolidated into the GoLYTELY category

because they have similar formulation and volume. Suclear was similarly grouped with Suprep. Clenpiq was approved by the US Food and Drug Administration (FDA) after initiation of the study and was combined with the Prepopik group. As part of this study, the use of adjunctive measures, such as bisacodyl, was not systematically collected to reduce the documentation burden on the preprocedure nurses and to minimize the impact on laboratory efficiency. Moreover, the use of adjunctive agents has not been definitively shown to improve outcomes; a study by Gerard and colleagues comparing MiraLAX with Gatorade with or without bisacodyl found no difference in bowel cleansing between the groups (17). Of note, interviews with providers at our institution revealed that bisacodyl was often given along with MiraLAX with Gatorade.

Covariates—patients, procedure, and endoscopist characteristics

We collected data on patient-, procedure-, and provider-level variables with potential to affect bowel prep effectiveness and tolerability. Patient-related factors included demographics (age, gender, race/ethnicity, primary language), body mass index (BMI), medication use (opioids, tricyclic antidepressants), and relevant comorbidities (diabetes, cirrhosis). Procedure- and provider-level factors included the primary performing endoscopists, whether another procedure (e.g., upper endoscopy, endoscopic ultrasound) was performed in addition to colonoscopy, fellow trainee involvement, and withdrawal time (defined as time cecum reached—time scope was removed).

Statistical analysis

All statistical analyses were performed in Stata 13.1 (StataCorp LP, College Station, TX). A 2-tailed P value of <0.05 was considered statistically significant. In bivariate analyses, continuous and categorical variables were compared using Student t test and chi-squared test, respectively.

To evaluate the independent impact of the different bowel preps on tolerability and cleansing effectiveness, we performed multivariable regression models with random effects to adjust for confounding. For our primary outcomes of total BBPS score and adequate bowel cleansing, we used linear and logistic regressions, respectively, to calculate adjusted P values and odds ratios (ORs) with 95% confidence intervals (CIs). Both models adjusted for prep-level characteristics (type of prep, completion, dosing), procedure-level characteristics (procedure in addition to colonoscopy, fellow involvement, withdrawal time), and patient-level characteristics (demographics, BMI, medication use, relevant comorbidities), as well as accounted for individual endoscopist-level factors via random effects. For the secondary outcome of prep tolerability, the logistic regression model with random effects adjusted for prep-, individual provider-, and patient-level covariates. In all analyses, GoLYTELY served as the baseline comparator prep because it is the criterion standard according to the American Society for Gastrointestinal Endoscopy (ASGE) (12). We also performed subgroup analyses stratified by prep dosing; the above regression analyses were conducted among those who were prescribed day-before prep dosing and in those given a split prep.

RESULTS

Study population

Overall, 5,253 outpatient colonoscopies were performed between August 4, 2016, and July 31, 2018. We excluded 914 cases that met exclusion criteria or had missing data: patients aged <18 years (n = 257), use of 2-day bowel prep or unknown prep dosing (n = 184), the BBPS could not be completely scored because of either surgically absent colon segments or early procedural termination for reasons unrelated to bowel prep (n = 90), and missing bowel prep or bowel cleansing score data (n = 383). Thus, our analytic sample included 4,339 colonoscopies performed in 3,908 patients. We describe the study cohort's demographics in Table 1.

Performing endoscopists

The colonoscopies were performed by 75 providers who have been independently practicing for a median of 11 years (interquartile range [IQR], 5–23; range, 1–40). The cohort included 34 (45.3%) community general gastroenterologists, 13 (17.3%) colorectal surgeons, 6 (8.0%) academic general gastroenterologists, 6 (8.0%) academic inflammatory bowel disease specialists, 5 (6.7%) academic interventional endoscopists, 4 (5.3%) academic hepatologists, 3 (4.0%) academic gastrointestinal motility

Table 1. Demographics of the study population (N = 4,339)

Variable	n	%
Age (yr)		
18–49	1,087	25.1
50–64	1,763	40.6
≥65	1,489	34.3
Gender		
Female	2,222	51.2
Male	2,117	48.8
Race/ethnicity		
Non-Hispanic white	2,952	68.0
Non-Hispanic black	499	11.5
Latino	425	9.8
Asian	278	6.4
Other/unknown	185	4.3
Primarily English speaker	3,983	91.8
BMI (kg/m^2)		
<25	1,899	43.8
25–29.9	1,312	30.2
≥30	1,073	24.7
Unknown	55	1.3
Opioid use	677	15.6
Tricyclic antidepressant use	73	1.7
Type I or II diabetes	700	16.1
Liver cirrhosis	75	1.7
Procedure in addition to colonoscopy	1,449	33.4
Fellow trainee involvement	614	14.2
Withdrawal time (min)		
≥6	3,557	82.0
<6	265	6.1
Unknown	517	11.9

BMI, body mass index.

specialists, 3 (4.0%) academic pediatric gastroenterologists, and 1 (1.3%) community interventional endoscopist. The median number of colonoscopies performed per physician was 25 (IQR, 9–62; range, 1–435).

Bowel prep regimens

Table 2 lists the bowel preps prescribed during the study period. The most commonly prescribed prep was MiraLAX with Gatorade, followed by GoLYTELY, Suprep, MoviPrep, and Prepopik/Clenpiq. OsmoPrep and magnesium citrate were used less often. With respect to dosing, 61.7% were single dosed the day before and 38.3% were split dosed.

Among the 75 endoscopists, the median number of prep types ordered was 4 (IQR, 2–5; range, 1–7). The proportion of providers who had prescribed each prep was as follows: MiraLAX with Gatorade 88.0% (n = 66); GoLYTELY 72.0% (n = 54); Suprep 60.0% (n = 45); MoviPrep 49.3% (n = 37); Prepopik/Clenpiq 48.0% (n = 36); magnesium citrate 34.7% (n = 26); and OsmoPrep 17.3% (n = 13).

Bowel prep tolerability

Among the 4,339 colonoscopies, data on bowel prep completion were available for 4,299 cases. Patients reported fully completing the prep in 92.0% cases (n = 3,955). Completion rates varied among the preps, which were as follows: Prepopik/Clenpiq 99.1% (n = 221); magnesium citrate 98.1% (n = 51); Suprep 94.4% (n = 439); OsmoPrep 92.7% (n = 76); MiraLAX with Gatorade 92.6% (n = 2,487); MoviPrep 91.4% (n = 264); and GoLYTELY 82.9% (n = 417). After adjusting for prep-, provider-, and patient-related factors in multivariable logistic regression analysis with random effects, we found that patients receiving Prepopik/Clenpiq ($P < 0.001$), magnesium citrate ($P = 0.014$), Suprep ($P < 0.001$), OsmoPrep ($P = 0.003$), MiraLAX with Gatorade ($P < 0.001$), and MoviPrep ($P = 0.001$) were all significantly more likely to complete the prep compared with those prescribed GoLYTELY.

Compared with single dose, day-before preps (91.4%, n = 2,423), no difference in compliance was observed for split preps (92.9%, n = 1,532; $P = 0.73$). Conversely, men (94.3%, n = 1,977) were more likely to fully ingest the prep than women (89.8%, n = 1,978; $P < 0.001$). The remaining patient demographic factors were not significantly associated with bowel prep tolerability.

Table 2. Bowel prep and procedure-related characteristics (N = 4,339)

Variable	n	%
Prescribed bowel prep		
GoLYTELY[a]	512	11.8
MoviPrep	293	6.8
MiraLAX with Gatorade	2,703	62.3
Prepopik/Clenpiq	226	5.2
Suprep[b]	470	10.8
Magnesium citrate	53	1.2
OsmoPrep	82	1.9
Completely finished the bowel prep	3,955	91.2
Bowel prep dosing		
Day-before dosing	2,676	61.7
Split dosing	1,663	38.3

[a]Also includes Colyte, NuLYTELY, and Trilyte.
[b]Also includes Suclear.

Subgroup analysis—stratification by prep dosing

We performed subgroup analyses among those prescribed day-before prep dosing (n = 2,650) and in those given a split prep (n = 1,649). For day-before dosing, we found differential completion rates among the different preps compared with GoLYTELY (83.1%, n = 304) after adjusting for prep, provider, and patient factors: Prepopik/Clenpiq 98.5% (n = 128; $P < 0.001$); magnesium citrate 97.0% (n = 32; $P = 0.05$); OsmoPrep 96.8% (n = 61; $P = 0.002$); Suprep 94.0% (n = 233; $P < 0.001$); MiraLAX with Gatorade 92.1% (n = 1,509; $P < 0.001$); and MoviPrep 91.2% (n = 156; $P = 0.03$).

Even among those prescribed a split prep, we still found significant differences in tolerability compared with GoLYTELY 82.5% (n = 113); Prepopik/Clenpiq 100% (n = 93; $P < 0.001$); magnesium citrate 100% (n = 19; $P < 0.001$); Suprep 94.9% (n = 206; $P < 0.001$); MiraLAX with Gatorade 93.5% (n = 978; $P < 0.001$); and MoviPrep 91.5% (n = 108; $P = 0.02$). However, no difference was seen for OsmoPrep 79.0% (n = 15; $P = 0.97$).

Bowel cleansing outcomes—overall

Overall, the average BBPS score was 7.05 ± 1.68 and 3,942 (90.9%) had adequate bowel cleansing (i.e., total BBPS score of ≥6, with each segment BBPS score of ≥2). Scores had the following distribution: 0 (0.2%, n = 10), 1 (0.2%, n = 9), 2 (0.1%, n = 6), 3 (3.3%, n = 145), 4 (1.3%, n = 56), 5 (3.5%, n = 152), 6 (41.9%, n = 1,819), 7 (6.1%, n = 265), 8 (11.3%, n = 491), and 9 (31.9%, n = 1,386). The average withdrawal time associated with each prep was as follows: GoLYTELY (19.7 ± 13.8 minutes), MiraLAX with Gatorade (19.3 ± 15.8 minutes), OsmoPrep (17.6 ± 9.8 minutes), magnesium citrate (17.0 ± 14.1 minutes), MoviPrep (17.0 ± 11.3 minutes), Prepopik/Clenpiq (14.9 ± 9.8 minutes), and Suprep (14.6 ± 9.3 minutes).

Table 3 presents findings from the multivariable regressions on BBPS total score and adequate bowel cleansing. With respect to BBPS total score, MoviPrep ($P = 0.004$), MiraLAX with Gatorade ($P < 0.001$), and Suprep ($P < 0.001$) had significantly higher scores compared with GoLYTELY, even after adjusting for confounders. No differences were seen among the remaining preps. Those prescribed split-prep dosing ($P = 0.001$) also had higher BBPS total scores. Conversely, men ($P < 0.001$), opioid ($P < 0.001$) and tricyclic antidepressant users ($P = 0.005$), and patients with diabetes ($P = 0.001$) and liver cirrhosis ($P = 0.005$) had lower bowel cleansing scores.

We noted the following adequate bowel cleansing rates for each prep: MiraLAX with Gatorade 92.5% (n = 2,499); MoviPrep 91.1% (n = 267); Prepopik/Clenpiq 90.7% (n = 205); Suprep 90.6% (n = 426); magnesium citrate 90.6% (n = 48); GoLYTELY 84.0% (n = 430); and OsmoPrep 81.7% (n = 67). Even after adjusting for prep-, procedure-, endoscopist-, and patient-level factors, we found that MiraLAX with Gatorade (OR, 1.76; 95% CI, 1.24–2.49) had higher odds for adequate cleansing compared with GoLYTELY. Although MoviPrep and Suprep had numerically higher BBPS scores compared with GoLYTELY, the difference in adequate bowel cleansing rates was not significant. We also found no differences among the remaining preps.

Table 3. Multivariable regressions on BBPS total score and adequate bowel cleansing (N = 4,339)

Variable	BBPS total score, mean ± s.d.	Adjusted *P* value[a]	Adequate bowel cleansing,[b] n (%)	OR (95% CI)[a]
Prescribed bowel prep				
GoLYTELY	6.67 ± 1.87	Reference	430 (84.0)	Reference
MoviPrep	7.11 ± 1.62	0.004	267 (91.1)	1.44 (0.85–2.44)
MiraLAX with Gatorade	7.09 ± 1.64	<0.001	2,499 (92.5)	1.76 (1.24–2.49)
Prepopik/Clenpiq	7.01 ± 1.59	0.18	205 (90.7)	1.24 (0.70–2.21)
Suprep	7.28 ± 1.66	<0.001	426 (90.6)	1.37 (0.86–2.16)
Magnesium citrate	6.89 ± 1.56	0.39	48 (90.6)	1.54 (0.57–4.17)
OsmoPrep	7.04 ± 1.86	0.27	67 (81.7)	0.70 (0.36–1.37)
Bowel prep completion				
Did not complete prep	6.89 ± 1.88	Reference	298 (86.6)	Reference
Fully completed the prep	7.07 ± 1.66	0.23	3,606 (91.2)	1.36 (0.96–1.93)
Unknown	7.43 ± 1.52	0.07	38 (95.0)	2.82 (0.64–12.37)
Bowel prep dosing				
Day-before dosing	6.97 ± 1.70	Reference	2,392 (89.4)	Reference
Split dosing	7.18 ± 1.63	0.001	1,550 (93.2)	1.35 (1.05–1.74)
Procedure in addition to colonoscopy				
No	7.09 ± 1.65	Reference	2,647 (91.6)	Reference
Yes	6.99 ± 1.74	0.19	1,295 (89.4)	0.82 (0.65–1.04)
Fellow involvement				
No	7.07 ± 1.68	Reference	3,390 (91.0)	Reference
Yes	6.98 ± 1.66	0.59	552 (89.9)	0.96 (0.70–1.31)
Withdrawal time (min)				
≥6	7.12 ± 1.62	Reference	3,253 (91.5)	Reference
<6	7.31 ± 1.68	0.08	250 (94.3)	1.42 (0.80–2.50)
Unknown	6.48 ± 1.97	<0.001	439 (84.9)	0.55 (0.42–0.74)
Age (yr)				
18–49	7.11 ± 1.73	Reference	976 (89.8)	Reference
50–64	7.08 ± 1.71	0.74	1,600 (90.8)	1.06 (0.79–1.42)
≥65	6.98 ± 1.61	0.15	1,366 (91.7)	1.09 (0.79–1.50)
Gender				
Female	7.16 ± 1.66	Reference	2,034 (91.5)	Reference
Male	6.95 ± 1.69	<0.001	1,908 (90.1)	0.82 (0.65–1.02)
Race/ethnicity				
Non-Hispanic white	7.05 ± 1.66	Reference	2,687 (91.0)	Reference
Non-Hispanic black	6.87 ± 1.78	0.07	450 (90.2)	0.87 (0.61–1.24)
Latino	7.05 ± 1.74	0.51	373 (87.8)	0.71 (0.49–1.02)
Asian	7.35 ± 1.57	0.002	259 (93.2)	1.42 (0.85–2.37)
Other/unknown	7.15 ± 1.65	0.35	173 (93.5)	1.44 (0.78–2.69)
Primarily language				
English speaker	7.07 ± 1.68	Reference	3,623 (91.0)	Reference
Non-English speaker	6.92 ± 1.69	0.51	319 (89.6)	1.08 (0.71–1.66)
BMI (kg/m^2)				
<25	7.04 ± 1.68	Reference	1,712 (90.2)	Reference

Table 3. (*continued*)

Variable	BBPS total score, mean ± s.d.	Adjusted *P* value[a]	Adequate bowel cleansing,[b] n (%)	OR (95% CI)[a]
25–29.9	7.13 ± 1.66	0.005	1,202 (91.6)	1.25 (0.96–1.62)
≥30	6.97 ± 1.69	0.60	976 (91.0)	1.23 (0.93–1.64)
Unknown	7.29 ± 1.67	0.51	52 (94.6)	1.72 (0.52–5.70)
Opioid use				
No	7.12 ± 1.62	Reference	3,371 (92.1)	Reference
Yes	6.69 ± 1.91	<0.001	571 (84.3)	0.51 (0.39–0.65)
Tricyclic antidepressant use				
No	7.06 ± 1.67	Reference	3,884 (91.1)	Reference
Yes	6.47 ± 1.99	0.005	58 (79.5)	0.36 (0.20–0.67)
Type I or II diabetes				
No	7.11 ± 1.67	Reference	3,322 (91.3)	Reference
Yes	6.79 ± 1.72	0.001	620 (88.6)	0.76 (0.56–1.03)
Liver cirrhosis				
No	7.07 ± 1.67	Reference	3,886 (91.1)	Reference
Yes	6.29 ± 1.79	0.005	56 (74.7)	0.45 (0.24–0.83)

BBPS, Boston Bowel Preparation Scale; BMI, body mass index; CI, confidence interval; OR, odds ratio.
[a]The multivariable linear and logistic regression models with random effects included all variables in the table.
[b]Adequate bowel cleansing was defined as total BBPS score of ≥6, with each segment BBPS score of ≥2.

The odds for adequate bowel cleansing was higher in patients receiving split dosing (OR, 1.35; 95% CI, 1.05–1.74). By contrast, adequate bowel cleansing was lower in those taking opioids (OR, 0.51; 95% CI, 0.39–0.65) and tricyclic antidepressants (OR, 0.36; 95% CI, 0.20–0.67) and in those with liver cirrhosis (OR, 0.45; 95% CI, 0.24–0.83).

Subgroup analysis—stratification by prep dosing

We performed subgroup analyses among those prescribed day-before prep dosing (n = 2,676) (see Table, Supplementary Digital Content 1, http://links.lww.com/AJG/A16) and in those given a split prep (n = 1,663) (see Table, Supplementary Digital Content 2, http://links.lww.com/AJG/A17). Of those who had day-before dosing, we found that MoviPrep ($P = 0.007$), MiraLAX with Gatorade ($P < 0.001$), and Suprep ($P < 0.001$) had significantly higher BBPS total scores compared with GoLYTELY. However, only MiraLAX with Gatorade was associated with increased odds for adequate bowel cleansing (OR, 1.99; 95% CI, 1.36–2.92) compared with GoLYTELY. Among those with split-prep dosing, we found that OsmoPrep was associated with lower odds for adequate bowel cleansing (OR, 0.14; 95% CI, 0.04–0.51) compared with GoLYTELY. No significant differences were seen among the remaining preps with respect to BBPS total scores or rates of adequate bowel cleansing.

Table 4. Multivariable regression on adequate bowel cleansing rates by colon segment (i.e., Boston Bowel Preparation Scale ≥2) (N = 4,339)

Prescribed bowel prep	Right colon		Transverse colon		Left colon	
	Adequate bowel cleansing, n (%)	OR (95% CI)[a]	Adequate bowel cleansing, n (%)	OR (95% CI)[a]	Adequate bowel cleansing, n (%)	OR (95% CI)[a]
GoLYTELY	444 (86.7)	Reference	464 (90.6)	Reference	461 (90.0)	Reference
MoviPrep	270 (92.2)	1.30 (0.75–2.28)	281 (95.9)	2.06 (1.04–4.07)	279 (95.2)	1.74 (0.92–3.28)
MiraLAX with Gatorade	2,526 (93.5)	1.61 (1.11–2.35)	2,584 (95.6)	1.97 (1.33–2.92)	2,575 (95.3)	1.80 (1.23–2.62)
Prepopik/Clenpiq	207 (91.6)	1.08 (0.59–1.98)	218 (96.5)	2.05 (0.92–4.59)	218 (96.5)	2.05 (0.92–4.55)
Suprep	433 (92.1)	1.40 (0.85–2.29)	452 (96.2)	2.19 (1.21–3.99)	451 (96.0)	2.02 (1.13–3.61)
Magnesium citrate	48 (90.6)	1.23 (0.45–3.38)	50 (94.3)	1.71 (0.49–5.94)	52 (98.1)	5.22 (0.69–39.36)
OsmoPrep	67 (81.7)	0.55 (0.28–1.10)	77 (93.9)	1.33 (0.48–3.64)	76 (92.7)	1.02 (0.40–2.61)

CI, confidence interval; OR, odds ratio.
[a]The multivariable logistic regression model with random effects adjusted for all prep-, procedure-, and patient-level factors seen in Table 3.

Bowel cleansing outcomes—by colon segment

Table 4 includes findings from the multivariable logistic regression analysis among the overall cohort, predicting adequate bowel cleansing rates for each colon segment, stratified by the individual preps. MiraLAX with Gatorade had significantly higher satisfactory bowel cleansing rates for all segments of the colon compared with GoLYTELY. Suprep had higher rates for the transverse and left colon, whereas MoviPrep had improved cleansing for the transverse colon. No significant differences were seen for the remaining preps.

Compared with day-before dosing, split-prep dosing was associated with improved cleansing rates in the right colon (OR, 1.33; 95% CI, 1.02–1.74), transverse colon (OR, 1.56; 95% CI, 1.11–2.17), and left colon (OR, 1.46; 95% CI, 1.07–2.01). Men (right colon: OR, 0.73; 95% CI, 0.58–0.93; transverse colon: OR, 0.69; 95% CI, 0.51–0.93; and left colon: OR, 0.74; 95% CI, 0.56–0.99) and those on opioids (right colon: OR, 0.48; 95% CI, 0.36–0.62; transverse colon: OR, 0.47; 95% CI, 0.34–0.65; and left colon: OR, 0.48; 95% CI, 0.35–0.66) had lower adequate cleansing rates throughout the colon. Patients on tricyclic antidepressants also had worse cleansing in the right colon (OR, 0.38; 95% CI, 0.20–0.72), transverse colon (OR, 0.26; 95% CI, 0.13–0.51), and left colon segments (OR, 0.36; 95% CI, 0.17–0.74). Patients with diabetes had inferior cleansing only in the right colon (OR, 0.71; 95% CI, 0.52–0.98), whereas those with cirrhosis had lower odds for adequate cleansing only in the transverse colon (OR, 0.45; 95% CI, 0.22–0.95) and left colon (OR, 0.38; 95% CI, 0.19–0.76).

DISCUSSION

In this large, prospective comparative effectiveness study comparing the real-world effectiveness of 7 commonly used bowel preps, we found that MiraLAX with Gatorade, MoviPrep, and Suprep were better tolerated and associated with superior bowel cleansing compared with GoLYTELY. Consistent with previous research (18–23), we also found that split dosing improves the odds for adequate cleansing, whereas use of opioids and tricyclic antidepressants and presence of diabetes and cirrhosis are associated with worse cleansing.

The current study has several strengths. First, to our knowledge, this is the largest, prospective comparative effectiveness study evaluating the real-world tolerability and effectiveness of the available bowel preps. Our study included data from more than 4,300 outpatient colonoscopies performed by a diverse set of providers. Second, by leveraging Cedars-Sinai's pluralistic structure where both academic and community-based clinicians are free to prescribe the bowel prep of their choice, we were able to compare outcomes among commonly used preps. This is in contrast to traditional RCTs, which usually compare a small number of bowel regimens in carefully controlled protocols, often with patient remuneration (12). Third, our study cohort included all-comers undergoing an outpatient colonoscopy and reflected the population referred for endoscopy in everyday clinical practice. Previous RCTs typically excluded patients with chronic opioid use, inflammatory bowel disease, chronic kidney disease, congestive heart failure, and cirrhosis, among others (24–28). Fourth, and perhaps most importantly, the naturalistic and observational study design allowed us to determine how the available preps perform in clinical practice, free from the Hawthorne effect (i.e., observer bias). Previous bowel prep RCTs focused on efficacy and were performed in tightly controlled settings that do not closely mirror real-world conditions. For example, multiple RCTs have found that GoLYTELY, a high-volume 4-L prep, has similar efficacy to comparator low-volume preps (12). However, in these trials, the Hawthorne effect and remuneration may have influenced patients in the GoLYTELY arms to be more willing to fully ingest the prep, even despite its higher volume and unpalatable taste compared with other available formulations. In the absence of observer bias and protocolized monitoring, patients in everyday practice may be less likely to tolerate large-volume and unsavory preps, leading to differential bowel cleansing as observed in this comparative effectiveness study.

We found that MiraLAX with Gatorade was prospectively associated with superior cleansing compared with GoLYTELY; this may result from an improved flavor profile and enhanced tolerability of the former regimen. Yet, previous studies have provided mixed results, because MiraLAX with Gatorade has been found to have either similar (24,25,29), better (30), and even worse (26,31,32) outcomes compared with GoLYTELY. A meta-analysis using a fixed-effects model by Siddique et al. (33) on 1,418 patients concluded that MiraLAX with Gatorade is associated with lower bowel prep quality compared with GoLYTELY ($P = 0.04$). However, when Zhang used random effects using the same data, there was no significant difference between the groups ($P = 0.19$) (34). Our results contrast with previous findings, because we found that MiraLAX with Gatorade is associated with higher total BBPS scores compared with the GoLYTELY reference standard. Again, this discrepancy may result from differences between comparative efficacy and effectiveness studies. In the absence of careful oversight and study protocols, patients in our study revealed lower tolerability of GoLYTELY, which likely influenced its suboptimal bowel cleansing results. However, we should mention that whereas MiraLAX with Gatorade (7.09 ± 1.64) has a statistically higher average total BBPS score compared with GoLYTELY (6.67 ± 1.87), the impact of this difference on clinical outcomes is unclear. To our knowledge, the minimal clinically important difference for total BBPS score with respect to outcomes such as ADR and interval CRC has not been defined. Because of this issue, we also opted to assess adequate bowel cleansing rates as an outcome (MiraLAX with Gatorade 92.5% vs GoLYTELY 84.0%). Though a process measure, it is nonetheless important as those with inadequate bowel cleansing (i.e., BBPS score of <6) should undergo a repeat colonoscopy within 1 year (12), thereby leading to increased healthcare utilization and costs and failure to detect prevalent lesions (35).

It is important to note that although MiraLAX with Gatorade is commonly used in clinical practice and is recognized by the ASGE (12), it is not approved by the US FDA as a colonoscopy purgative. There are also concerns that it is hyposmotic and can result in hyponatremia (17). When formally studied, though, MiraLAX with Gatorade does not lead to clinically significant electrolyte changes from baseline compared with GoLYTELY (24,25,29). Moreover, when collectively studied in a meta-analysis, no differences are seen between the preps for side effects including nausea, cramping, and bloating (33).

We also found that Suprep—a low-volume, sodium sulfate-based bowel prep approved by the US FDA—is associated with superior tolerability and cleansing compared with GoLYTELY. Our results are consistent with an RCT by Rex

et al. (36) which found that patients taking Suprep have improved bowel prep quality than patients taking NuLYTELY. We also noted that MoviPrep similarly is associated with better tolerability and cleansing. However, for the remaining preps (i.e., magnesium citrate, OsmoPrep, and Prepopik/Clenpiq), we found that patients are more likely to fully ingest these formulations in comparison with GoLYTELY, but we found no significant differences in bowel cleansing. Our findings are similar to previous RCTs and meta-analyses that also found OsmoPrep (37) and Prepopik (38) to be noninferior but better tolerated than GoLYTELY. It is also worth mentioning that nearly 100% of patients fully completed magnesium citrate, which is likely a function of its very low volume. Although we could not assess for significant differences in bowel cleansing outcomes because of its small sample size, magnesium citrate appears to at least lead to comparable bowel cleansing compared with 4 L of GoLYTELY. Of note, the prep's low use at our institution may reflect recommendations by the ASGE to avoid its use in those with renal insufficiency and in the elderly, as well as the fact that it is not a US FDA-approved bowel prep (12).

Our study also confirmed several factors known to affect bowel cleansing. We found that split dosing increases the odds for adequate cleansing compared with day-before dosing, which is consistent with a meta-analysis of 47 RCTs with 13,487 patients by Martel et al. (18). Although split-prep dosing has definitively been shown to improve bowel cleanliness, only 38% of cases in our study used this regimen, suggesting persistent under-use of a dosing schedule that improves bowel cleansing (18) and ADR (39). Further research is needed to assess the use of and barriers to split-prep dosing at other institutions, particularly those with a pluralistic structure, and to develop strategies for improving implementation and uptake. It is also worth noting that in our subgroup analysis among those with split-prep dosing, the differences in BBPS total scores and adequate bowel cleansing rates among the various bowel preps largely were no longer statistically significant. Although this may be a function of reduced power because of smaller sample sizes, this remains an area worthy of continued research as use of split-prep dosing becomes more prevalent. We also found that male gender, opioid use, tricyclic antidepressant use, diabetes, and cirrhosis are all associated with worse cleansing, as observed in previous studies (19–23,40,41). Other factors noted to lead to higher odds for inadequate bowel prep but not adjusted for in our analysis include lower educational attainment, constipation, hypertension, Parkinson's disease, and stroke/dementia (40,41). However, in contradistinction to these 2 previous studies (40,41), we did not find significant associations between bowel cleansing and age and BMI.

Our study has limitations. First, this was a single-site study and may not be generalizable to other medical centers and healthcare systems. However, the large sample size and diverse provider and patient cohorts lend generalizability. Second, blinded reviewers could not confirm the accuracy of the nurses' BBPS scores or assess for interobserver differences for each case, because labeling of endoscopic images and bowel cleansing documentation was not systematically performed by the 75 endoscopists. However, this pragmatic study reflects everyday clinical practice and was designed to avoid risk of observer bias that might arise by stationing study staff in the procedure rooms. Relying on nurses' BBPS assessments also may be a strength because they use the scale on a regular basis; some physicians in our study either may not know how to properly apply the BBPS or use a different scoring system (e.g., Ottawa Bowel Preparation Scale, Aronchick Scale). We also would expect any inaccurate BBPS scoring to have been evenly distributed among the various prep groups, so it thereby should not have affected the regression analyses. Regardless, we sought to address this limitation by holding in-service training with the endoscopy laboratory staff to ensure consistent and appropriate scoring among the evaluators. The nurses' BBPS module in the EHR also included hover text for each score, further supporting continued appropriate scoring after the in-services and for new staff. Moreover, our results identified many of the same predictors of bowel prep quality as seen in previous studies (e.g., split dosing, opioids, tricyclic antidepressants, diabetes, cirrhosis), offering further evidence of generalizability and accuracy of nurse-based BBPS recordings. Third, procedure nurses were not blinded to the prescribed preps documented by the pre-procedure nurses. However, documentation of preps and BBPS scoring is standard of care in our center, and it is unlikely that the nurses had intrinsic preferences for one prep formulation over another. There were also more than 40 nurses who rotated through the multiple procedure rooms in the endoscopy unit during the study period; we would not expect systematic and significant scoring bias to have occurred among the staff. Fourth, there may have been confounding related to variable bowel cleanliness thresholds among the 75 endoscopists. In other words, the findings could have been biased if certain preps were only used by a limited number of proceduralists who were aggressive at washing and cleansing the colon on withdrawal. Along the same lines, some endoscopists may have provided input on the BBPS scores entered in the nurses' EHR BBPS module, although the nurses stated that these occurrences were rare. We addressed these potential limitations by using multivariable regression with random effects to account for clustering and unmeasurable factors as it related to the individual proceduralists (e.g., endoscopic skills and experience, personal bowel cleanliness thresholds, patient population). The impact of this bias is also limited because of the wide distribution of preps used among the 75 endoscopists; the 4 preps with differential bowel cleansing (i.e., GoLYTELY, MiraLAX with Gatorade, MoviPrep, and Suprep) were used by 49%–88% of physicians. Finally, we were unable to identify the preps taken by patients who either did not present to or canceled their procedure at the last minute. Those prescribed large-volume and unpalatable purgatives may not have tolerated them while at home, leading to early termination and missing their appointment. Thus, we may have underestimated the differences in tolerability and bowel cleansing between GoLYTELY and other preps.

In summary, our study reveals that MiraLAX with Gatorade, MoviPrep, and Suprep are better tolerated and associated with superior bowel cleansing compared with GoLYTELY. Future large, pragmatic, multicenter comparative effectiveness studies are needed to confirm these findings and to extend them to evaluate the impact on other outcomes, including ADR and cancer detection and prevention.

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Study Highlights

WHAT IS KNOWN

- ✓ There is a wide variety of commercially available colonoscopy bowel prep regimens, each varying in volume, tolerability, and formulation.
- ✓ National societies provide minimal guidance regarding which preps are best tolerated and most effective; current guidelines only recommend accounting for a patient's medical history, medications, and previous procedure history when selecting a prep.
- ✓ Nonspecific guidance reflects a lack of comparative effectiveness studies that directly evaluate preps in a "real-world" setting; most data are from randomized trials of a limited number of preps in the context of tightly controlled research protocols that may not accurately reflect real-world conditions.

WHAT IS NEW HERE

- ✓ In a large-scale, prospective, commercially unfunded comparative effectiveness study of 4,339 colonoscopies, there was differential tolerability and bowel cleansing effectiveness among 7 commonly available bowel preps.
- ✓ MiraLAX with Gatorade, MoviPrep, and Suprep were better tolerated and prospectively associated with superior bowel cleansing compared with GoLYTELY in everyday clinical practice.

CONFLICTS OF INTEREST

Guarantor of the article: Christopher V. Almario, MD, MSHPM.

Specific author contributions: P.G.: planning and conducting the study, collecting and interpreting data, drafting the manuscript, and approval of final draft submitted. D.L., S.J.O., A.V., J.K., K.H., E.M., and V.P.: conducting the study, collecting and interpreting data, drafting the manuscript, and approval of final draft submitted. T.B. and G.F.: conducting the study, interpreting data, drafting the manuscript, and approval of final draft submitted. B.M.R.S.: planning and conducting the study, interpreting data, drafting the manuscript, and approval of final draft submitted. C.V.A.: planning and conducting the study, collecting and interpreting data, drafting the manuscript, and approval of final draft submitted.

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