

# Split- versus single-dose preparation tolerability in a multiethnic population: decreased side effects but greater social barriers

Gabriel Perreault<sup>a</sup>, Adam Goodman<sup>b</sup>, Sebastian Larion<sup>c</sup>, Ahana Sen<sup>d</sup>, Kirsten Quiles<sup>b</sup>, Michael Poles<sup>e</sup>, Renee Williams<sup>b</sup>

New York University Langone Medical Center, NY; New York University School of Medicine, NY; Augusta University, GA; University of Texas Southwestern Medical Center, Dallas, TX; Veteran Affairs New York Harbor Healthcare System, Manhattan Campus, NY, USA

## Abstract

**Background** This study was performed to compare patient-reported tolerability and its barriers in single- vs. split-dose 4-L polyethylene glycol (PEG) bowel preparation for colonoscopy in a large multiethnic, safety-net patient population.

**Methods** A cross-sectional, dual-center study using a multi-language survey was used to collect patient-reported demographic, medical, socioeconomic, and tolerability data from patients undergoing outpatient colonoscopy. Univariate and multivariate analyses were used to identify demographic and clinical factors significantly associated with patient-reported bowel preparation tolerability.

**Results** A total of 1023 complete surveys were included, of which 342 (33.4%) completed single-dose and 681 (66.6%) split-dose bowel preparation. Thirty-nine percent of the patients were Hispanic, 50% had Medicaid or no insurance, and 34% had limited English proficiency. Patients who underwent split-dose preparation were significantly more likely to report a tolerable preparation, with less severe symptoms, than were patients who underwent single-dose preparation. Multiple logistic regression revealed that male sex and instructions in the preferred language were associated with tolerability of the single-dose preparation, while male sex and concerns about medications were associated with tolerability of the split-dose preparation.

**Conclusions** In a large multiethnic safety-net population, split-dose bowel preparation was significantly more tolerable and associated with less severe gastrointestinal symptoms than single-dose preparation. The tolerability of split-dose bowel preparation was associated with social barriers, including concerns about interfering with other medications.

**Keywords** Colonoscopy, bowel preparation, single-dose, split-dose, tolerability, safety-net

*Ann Gastroenterol* 2018; 31 (3): 356-364

<sup>a</sup>Department of Medicine, New York University Langone Medical Center, New York (Gabriel Perreault); <sup>b</sup>Division of Gastroenterology, New York University School of Medicine, New York (Adam Goodman, Kirsten Quiles, Renee Williams); <sup>c</sup>Augusta University, Augusta, GA (Sebastian Larion); <sup>d</sup>University of Texas Southwestern Medical Center, Dallas, TX (Ahana Sen); <sup>e</sup>Veteran Affairs New York Harbor Healthcare System, Manhattan Campus, New York (Michael Poles), USA

Conflict of Interest: None

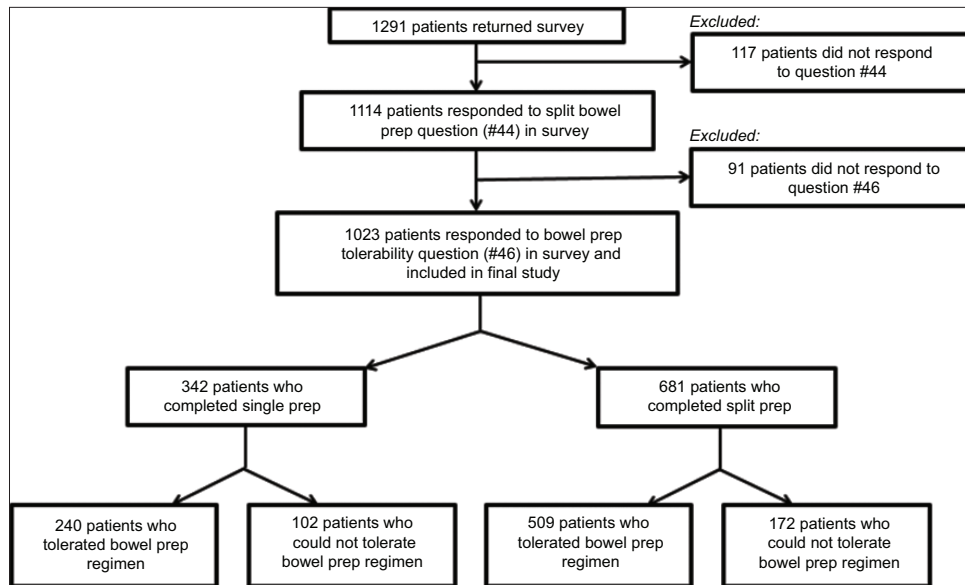
Correspondence to: Gabriel Perreault, M.D., New York University School of Medicine, 462 1<sup>st</sup> Avenue, NBV 16 North 30, New York, NY 10016, USA, e-mail: Gabriel.Perreault@nyumc.org

Received 7 November 2017; accepted 22 February 2018; published online 28 March 2018

DOI: <https://doi.org/10.20524/aog.2018.0254>

## Introduction

Colorectal cancer (CRC) is the third leading cause of cancer death in both men and women in the United States, with an estimated 140,250 new cases and 50,630 deaths expected in 2018 [1]. Screening colonoscopy is known to decrease mortality from CRC [2,3] and the quality of the bowel preparation is critical to the success of the procedure [4]. However, concerns regarding bowel preparation have been one of the most commonly cited reasons for patients refusing to undergo screening colonoscopy. Bowel preparation has been consistently reported as one of the most unpleasant and burdensome parts of the procedure [5-8]. Poor quality bowel preparation has been shown to decrease the adenoma detection rate, slow the time to



**Figure 1** Inclusion and cohort design

cecal intubation, prolong withdrawal time, and increase costs because of the need for repeat procedures [9-13]. Inadequate bowel preparation exposes patients to longer, less effective procedures and increases the financial burden on the patient and the hospital.

Efficacy and tolerability have been identified as the two essential “ingredients” of adequate bowel preparation [4]. To date, the majority of studies have focused primarily on efficacy rather than tolerability. Furthermore, most studies of bowel preparation have drawn on a patient population that tends to be racially and ethnically homogenous, native English-speaking, health literate, and privately insured. It is important to investigate potential barriers to colonoscopy in high-risk patient populations, including the uninsured, underinsured, those with limited English proficiency and patients with low health literacy served by safety-net hospitals. Thus, support for bowel preparation as a quality measure for colonoscopy is growing, suggesting it may soon play a role in reimbursement schemes in the emerging pay-for-performance climate and value-based care [14,15].

Safety-net hospitals, defined as those that predominantly treat the poor and underserved, have been shown to benefit less from quality performance measures than non-safety-net hospitals [16-18]. Bellevue Hospital Center (BHC) is a one of the largest safety-net public hospitals in the United States, as well as being the central referral center for the public hospital network of New York City. BHC is known for serving a racially and ethnically diverse high-risk immigrant population. Likewise, the Manhattan campus of the Veterans Affairs New York Harbor Healthcare system is a regional referral center serving a multiethnic veteran population. The issues recruiting underrepresented groups for research studies are well documented in the literature [17-19]. Studies of colonoscopy preparation quality measures including tolerability are similarly limited by a lack of inclusion of underrepresented groups.

Split-dose preparation has been shown to increase the quality of cleansing and has been associated with greater patient

compliance in two recent meta-analyses, explaining why split-dosing has become an attractive quality measure [20,21]. The implementation of a split-dose preparation regimen and associated educational materials has even been shown to increase preparation quality in this safety-net hospital population [22]. However, there are only limited data concerning the impact of split-dose preparation on patient tolerability. The purpose of this study was to evaluate the determinants of tolerability between single- vs. split-dose bowel preparation in a socially diverse safety-net patient population.

## Patients and methods

A prospective, dual-center study was conducted at BHC and the New York Harbor Healthcare Veterans Administration (VA) Manhattan Campus. All outpatients were asked to complete surveys upon presentation for colonoscopy. Surveys were available in English, Chinese and Spanish. Certified medical interpreter services were available to assist in administering the survey in other languages. Patients who declined to complete the survey were excluded from the study. The standard bowel preparation instruction was 4 L polyethylene glycol (PEG) administered as a split dose for patients at Bellevue and a single dose for patients at the VA, along with 20 mg of bisacodyl. At the time of study, the single-dose regimen was the standard practice at the VA. Per survey responses, a subset of the BHC population opted for a single-dose preparation. The study was classified as exempt after review by the Institutional Review Board across institutions.

## Questionnaire design

A multi-language survey was constructed using select elements extracted from the Mayo Bowel Prep Tolerability

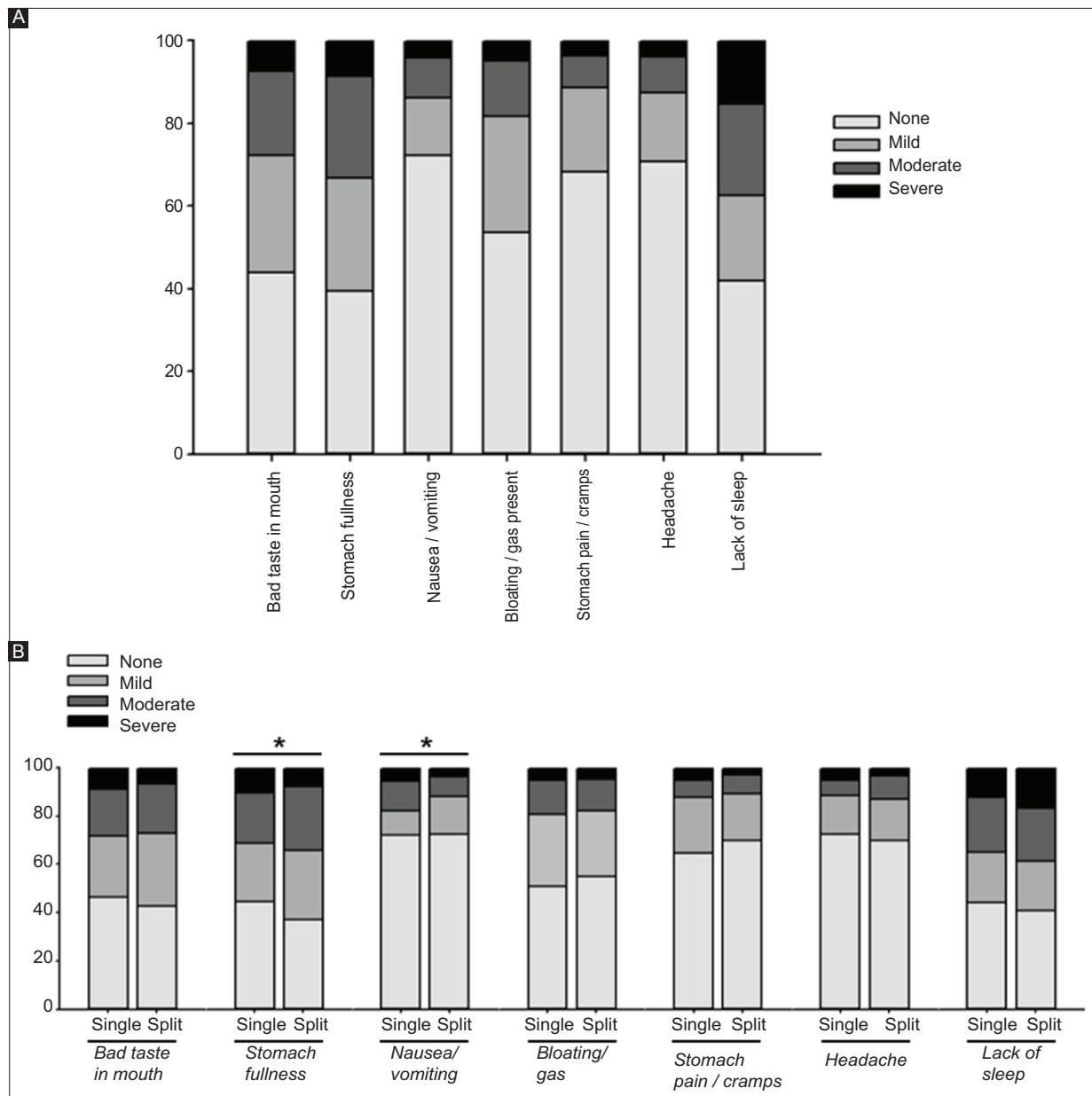
**Table 1** Patient demographics (%) compared between single- vs. split-dose colon preparation groups (N=1023)

Characteristic	Single-dose preparation (N=342)	Split-dose preparation (N=681)	P-value
Male <sup>1</sup>	60.3	53.7	0.060
Age <sup>2</sup>			0.026
<40	6.1	5.5	
40-49	8.5	5.9	
50-59	35.7	43.0	
60-69	29.9	32.6	
70-79	17.7	11.1	
80+	2.1	1.9	
Race <sup>3</sup>			0.397
White	13.5	16.3	
Black	24.9	22.5	
Hispanic	41.8	37.7	
Asian	11.1	13.2	
Other	8.8	10.3	
Education <sup>4</sup>			0.557
Grade school	14.6	14.2	
High school	42.7	40.1	
Graduate	13.9	12.4	
College	28.8	33.3	
Income <sup>5</sup>			0.305
<\$10,000	34.3	35.3	
\$10,000-24,999	28.6	32.7	
\$25,000-49,999	24.9	24.9	
\$50,000-74,999	7.0	5.0	
\$75,000-99,999	1.9	0.7	
>\$100,000	3.3	1.4	
Marital status <sup>6</sup>			0.193
Single, never married	29.5	35.4	
Married	43.7	40.0	
Divorced	18.5	18.8	
Widowed	8.3	5.8	
Insurance <sup>7</sup>			0.163
Private	9.4	6.3	
Other	10.2	9.8	
Medicare	23.7	19.8	
Medicaid	20.5	23.6	
None	36.3	40.4	
English fluency <sup>8</sup>	67.2	64.0	0.356

<sup>1</sup>Available in 95% of respondents, <sup>2</sup>Available in 95% of respondents, <sup>3</sup>Available in 95% of respondents, <sup>4</sup>Available in 94% of respondents, <sup>5</sup>Available in 78% of respondents, <sup>6</sup>Available in 89% of respondents, <sup>7</sup>Available in 89% of respondents. Insurance status was categorized by highest level of coverage, <sup>8</sup>Available in 96% of respondents. English fluency was determined by patient self-report

Questionnaire, a validated investigational tool used to assess patient tolerability between various types of colon

preparations [23]. Additional information was included following a literature search using PubMed, Google Scholar



**Figure 2** Adverse effects. (A) Adverse effects for entire study cohort. (B) Gastrointestinal symptoms compared between single- vs. split-dose colon prep group

\*Significantly different at  $P < 0.05$

and Web of Science using the terms “bowel preparation”, “tolerability”, “questionnaire” and “survey.” The questionnaire captured detailed medical and social history, as well as novel elements specific to our safety-net patient population. These included English fluency, time off of work, home responsibilities, embarrassment, family or friends’ lack of understanding of bowel preparation, availability of food, concerns about interfering with other medications, and side effects such as bad taste, fullness, nausea, vomiting, bloating, stomach pain and headaches (See supplementary Table). The primary outcome was patient-reported bowel preparation tolerability. The survey was then translated into Spanish and Chinese and distributed

to outpatients in the endoscopy suite prior to their undergoing routine colonoscopy for. Survey data were entered using Research Electronic Data Capture (REDCap), a secure online data storage and management tool [24].

### Statistical analysis

The primary outcome was patient-reported bowel preparation tolerability. Patients reporting that preparation was “somewhat tolerable” or “very tolerable” were included in the “tolerated bowel preparation” group, while patients

**Table 2** Tolerability of single- vs. split-dose preparation

Level of tolerability	Single-dose (%)	Split-dose (%)	P-value
			0.005
Very tolerable	34.5	32	
Somewhat tolerable	35.7	42.7	
Somewhat intolerable	17.3	18.6	
Very intolerable	12.6	6.6	

reporting “somewhat intolerable” or “very intolerable” were included in the “could not tolerate bowel preparation” group. Data are shown for the entire study cohort and were assessed for tolerability within individual cohorts. Tabulated results are presented as frequencies and percentages and the chi-square test was used to assess differences in proportions between groups. Factors significant ( $P < 0.05$ ) on univariate analysis were then inputted into a multiple logistic regression in order to identify patient demographic and clinical factors independently associated with preparation tolerability. Hosmer-Lemeshow analysis was used to assess model goodness-of-fit. Results are presented as odds ratios (OR) with 95% confidence intervals (CI). Cells missing data were omitted from calculations. Values may not add up to 100% because of rounding. All statistical tests were performed using SigmaPlot v10.2 (Systat Software, San Jose, CA).

## Results

A total of 1291 patients returned the survey, of whom 1023 (79.2%) successfully specified whether the bowel preparation regimen was split or not and answered tolerability questions; these patients were included in the final analysis (Fig. 1). Patients were predominantly non-white, male, had Medicaid or were uninsured, reported a high-school education or less, and earned less than \$25,000 per year (Table 1). More than one third of patients were not fluent in English, with 30.4% of respondents requiring the services of an interpreter to complete the survey.

Of the entire study population, the most commonly reported social barriers to bowel preparation tolerability were concerns about medications (18.8%), availability of appropriate foods/drinks (18.6%), and patient responsibilities at home (18.6%). The most frequently reported moderate and severe gastrointestinal symptoms relating to colon preparation completion were stomach fullness, a bad taste in the mouth, and lack of sleep (Fig. 2A). Of the entire study population, 18.2% and 8.6% of patients reported that the colon preparation was “somewhat” or “very” intolerable, while 40.4% and 32.8% of patients reported that the preparation was “somewhat” or “very” tolerable, respectively.

The study population was stratified into two cohorts, single-dose ( $N=342$ , 33.4%) and split-dose ( $N=681$ , 66.6%) preparation, individually assessed for tolerability. The two cohorts were demographically similar, except for a slight predominance of older patients in the single-dose cohort (Table 1). Comparing tolerability between cohorts, patients reported single-dose preparation as “very intolerable” approximately twice as often as patients who completed split-dose preparation (12.6% vs. 6.6%;  $P=0.005$ , Table 2), with a significantly greater proportion of “severe” nausea/vomiting and stomach fullness in the single- vs. split-dose group (Fig. 2B).

Univariate analysis of the single-dose preparation cohort identified that tolerability was significantly associated with male sex ( $P < 0.001$ ), English fluency ( $P=0.005$ ), instructions in the patient’s preferred language ( $P=0.016$ ), and having an interpreter present for preparation instructions ( $P=0.007$ , Table 3). Medical comorbidities and social barriers did not correlate with tolerability in the single-dose preparation cohort. The four factors significant on univariate analysis (male sex, English fluency, nursing instructions in preferred language, and interpreter present) were included in a multiple logistic regression, of which male sex (OR 3.056, 95%CI 1.77-5.27;  $P < 0.05$ ) and nursing instructions in preferred language (OR 2.2, 95%CI 1.03-4.82;  $P < 0.05$ ) were independently associated with tolerability in patients who completed single-dose colon preparation (Table 3). The Hosmer-Lemeshow statistic was not significant (5.736;  $P=0.68$ ), indicating that the model fit the data. In a sensitivity analysis, including race ( $P=0.28$ ) as an additional factor in the regression equation did not change factor significance ( $P < 0.05$ ). Q. Please mention the exact P values; if P is less than 0.001, then quote  $P < 0.001$

Male sex ( $P < 0.001$ ) and race ( $P < 0.001$ ) were significantly associated with patient-reported tolerability in the split-dose preparation cohort, with a greater proportion of white (19.7% vs. 10.0%) and black (25.5% vs. 18.8%) patients tolerating a split dose than Hispanic patients (35.1% vs. 55.0%; Table 3). Older age ( $P=0.051$ ) and English fluency ( $P=0.077$ ) also showed a trend toward tolerability, with more patients in the 60-69 year-old age group (35.4% vs. 24.2%) than in the 50-59 year-old age group (40.4% vs. 50.9%) tolerating split-dose preparation. Medical comorbidities, interpreter services ( $P=0.106$ ) or respondents reporting nursing instructions in preferred language ( $P=0.878$ ) did not differ between patients who could or could not tolerate split-dose colon preparation. However, patient-reported responsibilities at home ( $P=0.007$ ) and concerns about medications ( $P < 0.001$ ) were significantly more common in patients who could not tolerate split-dose colon preparation (Table 4). Factors significant on univariate analysis (male sex, race, responsibilities at home, concerns about medications) were included in a multiple logistic regression, which revealed that male sex (OR 2.40, 95%CI 1.64-3.52;  $P < 0.05$ ) and concerns about medications (OR 0.55, 95%CI 0.35-0.86;  $P < 0.05$ ) were independently associated with tolerability in patients who completed split-dose colon preparation (Table 5). The Hosmer-Lemeshow statistic was not significant (8.25;  $P=0.41$ ), indicating that the model fit the data. In a sensitivity analysis, including either race ( $P=0.33$ ) or race

**Table 3** Univariate analyses of patient demographics in single- and split-dose preparation cohorts, comparing patients who tolerated bowel preparation vs. those who could not

Variable	Single-dose preparation (%)			Split-dose preparation (%)		
	Tolerated bowel prep (N=240)	Could not tolerate bowel prep (N=102)	P-value	Tolerated bowel prep (N=509)	Could not tolerate bowel prep (N=172)	P-value
Male	65.8	37.3	<0.001	59.2	37.3	<0.001
Age			0.756			0.051
<40	5.2	8.1		4.6	8.1	
40-49	8.7	8.1		6.1	5.6	
50-59	34.1	39.4		40.4	50.9	
60-69	30.6	28.3		35.4	24.2	
70-79	19.2	14.1		11.7	9.3	
80+	2.1	2.0		1.9	1.9	
Race			0.094			<0.001
White	13.3	13.7		19.7	10.0	
Black	27.5	18.6		25.5	18.8	
Hispanic	38.8	49.0		35.1	55.0	
Asian	12.9	6.9		14.5	12.5	
Other	7.5	11.8		5.2	3.8	
Education			0.825			0.884
Grade school	13.7	16.7		13.6	15.7	
High school	43.4	41.1		40.7	38.4	
Graduate	13.3	15.6		12.2	13.2	
College	29.6	26.7		33.5	32.7	
Income			0.157			0.853
<\$10,000	32.7	38.6		34.0	39.8	
\$10,000-24,999	26.9	33.3		34.0	28.0	
\$25,000-49,999	25.0	24.6		24.6	25.8	
\$50,000-74,999	9.6	0.0		1.5	4.3	
\$75,000-99,999	2.6	0.0		5.2	1.1	
>\$100,000	3.2	3.5		0.6	1.1	
Marital status			0.471			0.329
Single, never married	31.7	24.5		34.0	39.6	
Married	40.9	50.0		39.7	40.9	
Divorced	18.8	18.1		19.9	15.6	
Widowed	8.7	7.4		6.4	3.9	
Insurance			0.653			0.595
Private	10.4	6.9		6.1	7.0	
Other	10.8	8.8		10.0	9.3	
Medicare	24.6	21.6		21.2	15.7	
Medicaid	19.6	22.5		23.2	25.0	
None	34.6	40.2		39.5	43.0	
English fluency	72.1	55.2	0.005	66.0	57.9	0.077
Preferred language	92.1	83.2	0.016	92.9	92.2	0.878
Interpreter present	25.0	40.2	0.007	29.1	36.0	0.106

**Table 4** Social barriers in single-dose vs. split-dose preparation by tolerability

Social barrier	Single-dose			Split-dose		
	Tolerated bowel prep (N=240)	Could not tolerate bowel prep (N=102)	P-value	Tolerated bowel prep (N=509)	Could not tolerate bowel prep (N=172)	P-value
Time off of work	13.8	11.8	0.75	15.7	19.8	0.27
Responsibilities at home	16.7	17.6	0.95	16.9	26.7	0.01
Embarrassment about bathroom trips	13.8	16.7	0.60	17.3	21.5	0.26
Family/friends lack of understanding	12.5	16.7	0.39	13.6	12.8	0.90
Availability of appropriate food/drinks	17.9	20.6	0.67	17.1	22.7	0.13
Concerns about medications	16.7	23.5	0.18	15.7	27.9	<0.001

( $P=0.422$ ) and English fluency ( $P=0.423$ ) as additional factors into the regression equation did not change factor significance ( $P<0.05$ ).

## Discussion

In a large safety-net patient population, split-dose preparation was associated with significantly greater tolerability with fewer side effects than single-dose preparation. Males were more likely to tolerate either bowel preparation regimen. Language-related instructional factors more commonly affected patient tolerability of single-dose preparation, while social barriers, such as medication concerns, more commonly affected the tolerability of split-dose preparation.

Split-dose preparation has been previously associated with greater tolerability in relatively homogenous populations [20,21,25], and this study extends those findings to a multiethnic and socio-economically diverse cohort. In contrast to the current data, previous studies primarily focusing on efficacy endpoints did not report an association between split-dose preparation and tolerability [26,27]. Tellez-Avila *et al* reported that in-patients undergoing split-dose preparation tended to report fewer symptoms than those undergoing single-dose [28]. This study further found that split-dose preparation was associated with less severe symptoms (Fig. 2B).

Male patients were more likely to report a tolerable bowel preparation experience than female patients, consistently with previously published literature [29,30]. These earlier studies are unlikely to represent the diverse patient population included in this study, further suggesting that sex is an independent risk factor for bowel preparation tolerability. Earlier studies have speculated that men may simply have a higher tolerance threshold than women. However, we argue that men may simply be more likely to endorse tolerability and may in fact underreport the challenges of bowel preparation, presenting a complicated challenge for providers.

To date, there has been little investigation into the impact of language and race on bowel preparation tolerability; thus, our findings associating single-dose preparation with language barriers and split-dose preparation with race are novel. It is somewhat surprising that language barriers were significantly associated with single-dose and not the more complicated split-dose preparation. This highlights one limitation of our study, that patients facing language barriers may have been more likely to self-select the simpler single-dose preparation, introducing a potential patient selection bias that would have been best addressed by a randomized intention-to-treat analysis. Further studies of multilingual patient populations would help further elucidate these connections.

This study also sheds light on social barriers to tolerability that appear to be unique to split-dose bowel preparation. Taking into account the increased time and required morning of commitment, our study suggests that split-dose preparation would be more likely to interfere with domestic responsibilities and existing morning medication regimens. Another recent study assessing split-dose regimen uptake also found that social factors, including morning appointments, travel time to endoscopy, and low education level, were associated with limited uptake of the split-dose regimen [31]. It may be important for health systems and providers to specifically address these social barriers to ensure bowel preparation tolerability, given that split-dose is currently the standard of care. Furthermore, it will be critical to consider the variable impact of quality measures, as they may impact safety-net hospital populations differently compared to the homogenous and insured populations, more represented in the literature. Our study focused on patient-reported outcomes, intending to amplify the needs and concerns of this underrepresented and understudied population.

Major strengths of our study are the large sample size, the significant diversity of the population, and results based solely on patient-reported outcomes. In addition, our results are generalizable to the real-world setting, as our study population



**Table 5** Multiple regression analysis

Single-dose preparation multiple regression analysis			
Variable	Odds ratio	95%CI	P-value
Male	3.06	1.77-5.27	<0.001
English fluency	1.24	0.56-2.749	0.6
Interpreter at office	0.93	0.410-2.11	0.86
Split-dose preparation multiple regression analysis			
Variable	Odds ratio	95%CI	P-value
Male	2.40	1.64-3.52	<0.001
Race	0.91	0.76-1.09	0.32
Responsibilities at home	0.64	0.41-1.01	0.06
Concerns about medications	0.55	0.35-0.86	0.01

### Summary Box

#### What is already known:

- Patient-reported tolerability is critical to achieve adequate bowel preparation
- Split-dose bowel preparation is associated with greater efficacy and tolerability in homogenous, well-insured patient populations
- Male sex is significantly associated with patient-reported bowel preparation tolerability

#### What the new findings are:

- Split-dose bowel preparation is associated with greater tolerability in a diverse, safety-net hospital population
- Split-dose bowel preparation is associated with less severe symptoms
- The tolerability of split-dose bowel preparation is associated with concerns about interference with other medications

encompassed two of the largest healthcare organizations in America today: the VA and the public hospital system. The focus of this study on patient-reported determinants of tolerability is an additional strength that diversifies the existing knowledge on bowel preparation. However, while our questionnaire was constructed using a previously validated survey, the study format excluded patients without proficient reading and writing abilities in one of the few languages in which our survey was available. Furthermore, the design of our recruitment strategy did not allow for the number of

patients who decline to participate to be counted, which may have introduced a response bias. Lastly, the discrepancy in regimen instructions between the VA and public hospitals, as well as issues relating to patients' self-selection of a preparation regimen that could be age-related, may limit the generalizability of our findings. The split- and single-dose cohorts were well-matched (Table 1), but the possibility of sampling bias cannot be excluded. Despite these limitations, this study represents a critical early step towards a growing understanding of the barriers to tolerable bowel preparation in a broader and more diverse population than previously considered.

In conclusion, there are multiple factors affecting split-dose preparation tolerability in a racially diverse, safety-net population. Given its poor health literacy, there is concern that this population may be unable or unwilling to perform split-dose preparation. We have previously shown that a split-dose regimen increases the adequacy of bowel preparation [22]. A recent randomized controlled trial also found that a split-dose regimen increases the adenoma detection rate, making uptake of this regimen essential [32]. In this study, we demonstrated that split-dose preparation was more tolerable than single-dose preparation and reduced symptom severity. However, this more complicated regimen also introduces additional social barriers of which providers need to be aware. Our findings are in agreement with the current recommendations for the use of split-dose preparation from the United States Multi-Society Task Force on optimizing bowel cleansing for CRC screening [33]. Further studies of emerging quality measures in colonoscopy preparation, including this patient population, are warranted.

### References

1. Siegel RL, Miller KD, Jemal A. Cancer Statistics, 2017. *CA Cancer J Clin* 2018;**68**:7-30.
2. Baxter NN, Goldwasser MA, Paszat LF, Saskin R, Urbach DR, Rabeneck L. Association of colonoscopy and death from colorectal cancer. *Ann Intern Med* 2009;**150**:1-8.
3. Nishihara R, Wu K, Lochhead P, et al. Long-term colorectal-cancer incidence and mortality after lower endoscopy. *N Engl J Med* 2013;**369**:1095-1105.
4. Rex DK. Bowel preparation for colonoscopy: entering an era of increased expectations for efficacy. *Clin Gastroenterol Hepatol* 2014;**12**:458-462.
5. Harewood GC, Wiersema MJ, Melton LJ 3<sup>rd</sup>. A prospective, controlled assessment of factors influencing acceptance of screening colonoscopy. *Am J Gastroenterol* 2002;**97**:3186-3194.
6. Nicholson FB, Korman MG. Acceptance of flexible sigmoidoscopy and colonoscopy for screening and surveillance in colorectal cancer prevention. *J Med Screen* 2005;**12**:89-95.
7. Ristvedt SL, McFarland EG, Weinstock LB, Thyssen EP. Patient preferences for CT colonography, conventional colonoscopy, and bowel preparation. *Am J Gastroenterol* 2003;**98**:578-585.
8. van Gelder RE, Birnie E, Florie J, et al. CT colonography and colonoscopy: assessment of patient preference in a 5-week follow-up study. *Radiology* 2004;**233**:328-337.



9. Lebowhl B, Kastrinos F, Glick M, Rosenbaum AJ, Wang T, Neugut AI. The impact of suboptimal bowel preparation on adenoma miss rates and the factors associated with early repeat colonoscopy. *Gastrointest Endosc* 2011;**73**:1207-1214.
10. Harewood GC, Sharma VK, de Garmo P. Impact of colonoscopy preparation quality on detection of suspected colonic neoplasia. *Gastrointest Endosc* 2003;**58**:76-79.
11. Chokshi RV, Hovis CE, Hollander T, Early DS, Wang JS. Prevalence of missed adenomas in patients with inadequate bowel preparation on screening colonoscopy. *Gastrointest Endosc* 2012;**75**:1197-1203.
12. Froehlich F, Wietlisbach V, Gonvers JJ, Burnand B, Vader JP. Impact of colonic cleansing on quality and diagnostic yield of colonoscopy: the European Panel of Appropriateness of Gastrointestinal Endoscopy European multicenter study. *Gastrointest Endosc* 2005;**61**:378-384.
13. Rex DK, Imperiale TF, Latinovich DR, Bratcher LL. Impact of bowel preparation on efficiency and cost of colonoscopy. *Am J Gastroenterol* 2002;**97**:1696-1700.
14. Ketwaroo GA, Sawhney MS. Quality measures and quality improvements in colonoscopy. *Curr Opin Gastroenterol* 2015;**31**:56-61.
15. Jang JY, Chun HJ. Bowel preparations as quality indicators for colonoscopy. *World J Gastroenterol* 2014;**20**:2746-2750.
16. Werner RM, Goldman LE, Dudley RA. Comparison of change in quality of care between safety-net and non-safety-net hospitals. *JAMA* 2008;**299**:2180-2187.
17. Vesey GA. Recruitment and retention of minority elders in health-related research: A community-based approach. In: Curry L, Jackson JS, eds. *The science of inclusion: recruitment and retaining racial and ethnic elders in health research*. Washington, DC: Gerontological Society of America; 2003.
18. King TE Jr. Racial disparities in clinical trials. *N Engl J Med* 2002;**346**:1400-1402.
19. UyBico SJ, Pavel S, Gross CP. Recruiting vulnerable populations into research: a systematic review of recruitment interventions. *J Gen Intern Med* 2007;**22**:852-863.
20. Martel M, Barkun AN, Menard C, Restellini S, Kherad O, Vanasse A. Split-dose preparations are superior to day-before bowel cleansing regimens: a meta-analysis. *Gastroenterology* 2015;**149**:79-88.
21. Buccic C, Rotondano G, Hassan C, et al. Optimal bowel cleansing for colonoscopy: split the dose! A series of meta-analyses of controlled studies. *Gastrointest Endosc* 2014;**80**:566-576.
22. Srisarajivakul N, Chua D, Williams R, et al. How we cleaned it up: a simple method that improved our practice's bowel prep. *Am J Gastroenterol* 2016;**111**:1079-1081.
23. Patel M, Staggs E, Thomas CS, Lukens F, Wallace M, Almansa C. Development and validation of the Mayo Clinic Bowel Prep Tolerability Questionnaire. *Dig Liver Dis* 2014;**46**:808-812.
24. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research Electronic Data Capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform* 2009;**42**:377-381.
25. Parente FR, Repici A, Crosta C, et al. Overall acceptability and efficacy of commonly used bowel preparations for colonoscopy in Italian clinical practice. A multicentre prospective study. *Dig Liv Dis* 2014;**46**:795-802.
26. Rostom A, Jolicoeur E, Dubé C, et al. A randomized prospective trial comparing different regimens of oral sodium phosphate and polyethylene glycol-based lavage solution in the preparation of patients for colonoscopy. *Gastrointest Endosc* 2006;**64**:544-552.
27. El Sayed AM, Kanafani ZA, Mourad FH, et al. A randomized single-blind trial of whole versus split-dose polyethylene glycol-electrolyte solution for colonoscopy preparation. *Gastrointest Endosc* 2003;**58**:36-40.
28. Téllez-Ávila FI, Murcio-Pérez E, Saúl A, et al. Efficacy and tolerability of low-volume (2L) versus single- (4L) versus split-dose (2L+2L) polyethylene glycol bowel preparation for colonoscopy: randomized clinical trial. *Dig Endosc* 2014;**26**:731-736.
29. Holt EW, Yimam KK, Ma H, Shaw RE, Sundberg RA, Verhille MS. Patient tolerability of bowel preparation is associated with polyp detection rate during colonoscopy. *J Gastrointest Liver Dis* 2014;**23**:135-140.
30. Lawrance IC, Willert RP, Murray K. A validated bowel-preparation tolerability questionnaire and assessment of three commonly used bowel-cleansing agents. *Dig Dis Sci* 2013;**58**:926-935.
31. Radaelli F, Paggi S, Repici A, et al. Barriers against split-dose bowel preparation for colonoscopy. *Gut* 2017;**66**:1428-1433.
32. Radaelli F, Paggi S, Hassan C, et al. Split-dose preparation for colonoscopy increases adenoma detection rate: a randomised controlled trial in an organised screening programme. *Gut* 2017;**66**:270-277.
33. Johnson DA, Barkun AN, Cohen LB, et al; US Multi-Society Task Force on Colorectal Cancer. Optimizing adequacy of bowel cleansing for colonoscopy: recommendations from the US multi-society task force on colorectal cancer. *Gastroenterology* 2014;**147**:903-924.