

Split dose and MiraLAX-based purgatives to enhance bowel preparation quality becoming common recommendations in the US

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Abstract:

Objectives: Rates of suboptimal bowel preparation up to 30% have been reported. Liberalized precolonoscopy diet, split dose purgative, and the use of MiraLAX-based bowel preparation (MBBP) prior to colonoscopy are recently developed measures to improve bowel preparation quality but little is known about the utilization prevalence of these measures. We examined the patterns of utilization of these newer approaches to improve precolonoscopy bowel preparation quality among American gastroenterologists.

Methods: Surveys were distributed to a random sample of members of the American College of Gastroenterologists. Participants were queried regarding demographics, practice characteristics, and bowel preparation recommendations including recommendations for liberal dietary restrictions, split dose purgative, and the use of MBBP. Approaches were evaluated individually and in combination.

Results: Of the 999 eligible participants, 288 responded; 15.2% recommended a liberal diet, 60.0% split dose purgative, and 37.4% MBBP. Diet recommendations varied geographically with gastroenterologists in the West more likely to recommend a restrictive diet (odds ratio [OR] 2.98, 95% confidence interval [CI] 1.16–7.67) and physicians in the Northeast more likely to recommend a liberal diet more likely. Older physicians more often recommended split dosing (OR 1.04, 95% CI 1.04–2.97). Use of MBBP was more common in suburban settings (OR 2.14, 95% CI 1.23–3.73). Evidence suggests that physicians in private practice were more likely to prescribe split dosing ($p = 0.03$) and less often recommended MBBP ($p = 0.02$). Likelihood of prescribing MBBP increased as weekly volume of colonoscopy increased ($p = 0.03$).

Conclusions: To enhance bowel preparation quality American gastroenterologists commonly use purgative split dosing. The use of MBBP is becoming more prevalent while a liberalized diet is infrequently recommended. Utilization of these newer approaches to improve bowel preparation quality varies by physician and practice characteristics. Further evaluation of the patterns of usage of these measures is indicated.

Keywords: bowel preparation, colonoscopy, liberal diet, MiraLAX, split dose purgative

Introduction

Declining rates in the incidence of colorectal cancer (CRC) in the past decade have been attributed to the upsurge in CRC screening, particularly with the use of colonoscopy [Edwards *et al.* 2010]. Nationally, 64.7% of Americans in 2010 reported

having ever had an endoscopic exam as screening for CRC [Centers for Disease Control and Prevention, 2011]. Reports indicate, however, that as many as 30% of precolonoscopy bowel preparations are not optimal [Kazarian *et al.* 2008]. As progressively more Americans screen

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for CRC with colonoscopy, bowel preparation quality becomes increasingly important. Poor bowel preparation not only impacts the quality and completeness of the endoscopic examination, but can inflate the cost of screening, require longer inspection time, and result in repeat procedure [Ben-Horin *et al.* 2007; Froehlich *et al.* 2005; Rex *et al.* 2002]. Most importantly, poorly prepared bowels that limit the endoscopist's ability to visualize the colonic mucosa are associated with lower adenoma detection rates and missed neoplasia [Lebwohl *et al.* 2011; Rex *et al.* 2002].

The combined use of cathartics and dietary restrictions is safe and effective for bowel preparation prior to colonoscopy but there exists no consensus regarding which preparation results in optimal bowel cleansing [Parra-Blanco, 2006], thus regimens vary widely [DiPalma *et al.* 1984]. The predominant method of bowel preparation in use today is oral gastrointestinal (GI) lavage using balanced electrolyte solutions with polyethylene glycol (PEG) [A-Rahim and Falchuk, 2011]. Evidence suggests that a clear liquid diet prior to the purgative and colonoscopy is a beneficial adjunct to bowel cleansing methods [Wexner *et al.* 2006]; however, patients complain about the large volume of purgative that needs to be ingested with many regimens and the requirement for a clear liquid diet [Hookey *et al.* 2004]. In addition, ingestion of the purgative has been often cited as the most unpleasant part of the colonoscopy experience for many patients [Ko *et al.* 2007].

In order to increase patient tolerability, minimize side effects, and improve cleansing efficacy of preparations, newer methods of bowel preparation have been developed and include the use of laxative supplements, flavoring additives, timing of purgative in relation to procedure time, medical management of side effects, and modified PEG purgative preparations [A-Rahim and Falchuk, 2011]. While not approved by the Food and Drug Administration (FDA), MiraLAX-based bowel preparations (MBBP) have emerged as a popular bowel preparation choice due to their low volume and palatability [Enestvedt *et al.* 2011a]. MiraLAX is an osmotic laxative composed of PEG (average molecular weight 3350) without electrolytes that is FDA-approved for the treatment of constipation. This agent is available without prescription and has been prescribed 'off label' as a bowel preparation agent. Split dosing of the purgative, that is, the administration of a portion of the purgative on the day of colonoscopy, has been

consistently shown to improve bowel preparation quality [Abdul-Baki *et al.* 2008; Kilgore *et al.* 2011; Marmo *et al.* 2010; Park *et al.* 2007, 2010]. With regard to precolonoscopy diet, several studies have examined the impact of alternative dietary recommendations (low-residue [Delegge and Kaplan, 2005; Rapier and Houston, 2006; Wu *et al.* 2011] or fiber-free diet [Soweid *et al.* 2010], light breakfast followed by clear liquids [Scott *et al.* 2005], and regular diet followed by clear liquids or low-residue meals [Aoun *et al.* 2005]) with a variety of purgative agents and found that bowel cleansing and patient tolerability were at least as good as with a clear liquid diet, if not better. The relative use of some of these newer methods among US physicians in clinical practice is unknown.

As part of a larger study to assess barriers to optimal bowel preparations [Clarke Hillyer *et al.* 2012], we sought to examine the prevalence and patterns of utilization of three newer approaches to bowel preparation for colonoscopy among gastroenterologists in the US. Specifically, we examined use of liberalized diet, purgative split dosing, and MBBP to gain insight to the uptake of these newer methods.

Methods

A full description of the study methods can be found elsewhere [Clarke Hillyer *et al.* 2012]. Briefly, a complete American College of Gastroenterology membership list was obtained ($n = 10,228$). Those with nonclinical affiliations (e.g. pharmaceutical companies) and credentials were excluded. As it was not feasible to survey all members, we chose to randomly select a 20% sample of physicians (MD or DO). The advantage of randomization was that it created a study group with a balanced and representative distribution of the factors under consideration while accounting, quantitatively, for potential confounders associated with alternative sample selection techniques [Rothman and Greenland, 2008]. Screening telephone calls were placed to each practice and an additional 354 were excluded (deceased, $n = 4$; unable to locate, $n = 33$; retired, $n = 27$; and not a practicing gastroenterologist, only pediatric patients or other specialist that did not routinely perform screening colonoscopies, $n = 290$). To the 999 eligible physicians, a Web-based or postal survey and an introductory letter of invitation was sent between September 2010 and March 2011. A small incentive was offered upon completion of

the survey. Approval of the Columbia University Institutional Review Board was granted.

Participants were queried about age, gender, race, country of medical school training, specialty, and board certification. Practice characteristics included geographic location, practice setting (urban, suburban, or rural) and type (private or hospital/university), teaching hospital affiliation, and number of colonoscopies performed per week (<10, 11–20, 21–30 and >30). Additional questions determined the use of liberal *versus* restrictive liquid diet, purgative split dosing, and MBBP and concomitant use of Gatorade®. Liberal diet was considered to be a recommendation that included any solid food in the 24-hour period prior to colonoscopy.

Univariate and bivariate analyses were conducted. Pearson's Chi-square test was used to test associations between those participants who did and did not recommend liberal diet, split dosing, MBBP, and demographic and practice characteristics. Multivariate analysis was conducted using covariates with *p* value < 0.1. We performed analyses using SAS version 9.2 (SAS Institute, Cary, NC).

Results

A total of 1355 physicians were invited to participate among whom 999 were eligible and sent a survey; 288 (28.8%) responded to the survey. Overall, the majority of respondents were male, white, US medical school graduates, and GI specialist/board certified. The median age was 48 years.

Of the 269 physicians who responded to the dietary restriction questions, 15% (*n* = 41) indicated that they prescribe a liberalized diet that included any food in the 24-hour period preceding colonoscopy (Table 1). Compared with those who prefer to recommend a restrictive liquid diet, these physicians tended to be >48 years of age (17.3% *versus* 13.2%), white (17.5% *versus* 9.0%), and have a board certification other than GI (20.5% *versus* 14.2%). Diet recommendations varied by geographic location with physicians in the Northeast section of the US twice as often and more than three times as often prescribing a liberalized diet compared with those in the South and West including Hawaii (25% *versus* 12.8% and 7.6%, respectively) and significantly more likely to recommend liberal diet compared with a

more restrictive diet (*p* = 0.004). Physicians in the West were nearly three times as likely to recommend restrictive diets (odds ratio [OR] 2.98, 95% confidence interval [CI] 1.16–7.67).

A total of 60% (170/283) of respondents stated that they recommend split dosing of the purgative to their patients (Table 1). These physicians more often graduated from US medical schools, were certified in gastroenterology, and performed more than 30 colonoscopies per week. In comparison with those who did not recommend split dose purgatives, those that did were more likely to be older (>48 years; 67.2% *versus* 53.2% for younger age, *p* = 0.018), in private *versus* hospital/university practice types (63.8% *versus* 50.5%, *p* = 0.03), and affiliated with nonteaching hospitals (68.0% *versus* 55.1%, *p* = 0.034). After controlling for country where the physician attended medical school, type of practice (private *versus* university/hospital), and teaching hospital affiliation, older age (>48 years) remained a strong predictor of use of split dosing (OR 1.76, 95% CI 1.04–2.97).

More than one-third of respondents indicated that they prescribe MBBP (106/283) and of these, half practice in suburban settings (50.0% *versus* 38.9% in rural settings and 29.1% in urban settings, *p* = 0.003) (Table 1). Recommendation of MBBP was significantly more common among physicians in private practice than those in a hospital or university-based setting (43.5% *versus* 29.0%, *p* = 0.02). Furthermore, a positive linear association was observed with regard to the number of reported colonoscopies performed per week and the proportion of physicians using MBBP (*p* = 0.04) with physicians performing >30 colonoscopies per week more than twice as often recommending MBBP than those performing ≤10 per week. Only suburban practice (OR 2.14, 95% CI 1.23–3.73), however, was significant after controlling for other covariates. Of those who prescribed MBBP, 82.1% also recommended Gatorade® (*p* < 0.0001) (data not shown).

Of the 267 respondents who answered all three questions, we examined concurrent recommendation of these newer approaches; 17.6% use none of these methods and 3.7% used all three (Table 2). Split dosing alone (36.0%) and with MBBP (15.7%) and MBBP alone (15.7%) were most commonly reported whereas liberal diet alone or in combination with split dose purgative

Table 1. Physician and practice characteristics associated with recommendation of liberal versus restrictive diet, split dose purgative regimen, and MiraLAX-based bowel preparations (MBBP) in preparation for screening colonoscopy among average risk adults.

	Diet				Split dose purgative regimen				MiraLAX-based purgative									
	Liberal (n = 41, 15.2%)	Restrictive (n = 228, 84.8%)	p value	OR	95%CI	Split dose (n = 170, 60.0%)	No split dose (n = 113, 40.0%)	p value	OR	95%CI	MiraLAX (n = 106, 37.4%)	No MiraLAX (n = 177, 62.6%)	p value	OR	95%CI			
Age	N	%				N	N	%			N	N	%					
≤48	18	13.2	118	86.8	0.35	75	53.2	66	57	40.4	1.00	-	141	50.5	84	59.6	0.33	
>48	23	17.3	110	82.7		92	67.2	45	48	34.8	1.76	1.04-2.97	138	49.5	90	65.2	0.93	
Gender					0.64													
Male	36	15.4	198	84.6		146	60.6	95	90	37.3			241	85.1	151	62.7		
Female	5	12.5	35	87.5	0.07	24	57.1	18	16	38.1			42	14.9	26	61.9	0.75	
Race																		
White	34	17.5	160	82.5	1.00	126	62.1	77	37.9				77	37.9	126	62.1		
Other	7	9.0	71	91.0	0.46	42	53.9	36	46.1	0.066			28	35.9	50	64.1	0.63	
Medical school					0.63													
US	30	15.1	169	84.9		129	62.6	77	37.4				76	36.9	130	63.1		
Non-US	7	12.5	49	87.5	0.31	28	49.1	29	50.9	0.16			23	40.4	34	59.6	0.96	
Specialty/ Board Cert																		
GI	33	14.2	200	85.8		148	61.7	92	38.3				89	37.1	151	62.9		
Non-GI	8	20.5	31	79.5	0.004	20	50.0	20	50.0	0.17			15	37.5	25	62.5	0.67	
Region																		
Northeast	22	25.0	66	75.0	1.00	50	53.8	43	46.2				37	40.2	55	59.8		
South	12	12.8	82	87.2	1.45	65	67.0	32	33.0	0.63-3.33			37	38.1	60	61.9		
West*	7	7.6	85	92.4	2.98	55	59.1	38	40.9	1.16-7.67			32	34.0	62	66.0		
Setting					0.62					0.90								
Urban	21	13.7	132	86.3		95	59.7	64	40.3				46	29.1	112	70.9	1.00	
Suburban	18	17.8	83	82.2		63	61.2	40	38.8				52	50.0	52	50.0	2.14	
Rural	2	11.8	15	88.2	0.86	10	55.6	8	44.4	1.16-7.67			7	38.9	11	61.1	1.29	
Type of practice										0.03								0.02
Private	26	15.1	146	84.9		113	63.8	64	36.2				77	43.5	100	56.5	1.00	
Hospital/ University	12	14.3	72	85.7	0.71	47	50.5	46	49.5	0.79	0.42-1.48		27	29.0	66	71.0	0.94	
Hospital affiliation										0.034								0.70
Teaching	27	15.7	145	84.3		98	55.1	80	44.9				65	36.5	113	63.5		
Nonteaching	14	14.0	86	86.0	0.71	70	68.0	33	32.0	0.69	0.37-1.31		40	38.8	63	61.2		

Table 1. (Continued)

Diet	Restrictive (n = 228, 84.8%)				Split dose purgative regimen				MiraLAX-based purgative					
	Liberal (n = 41, 15.2%)	OR	95%CI	p value	Split dose (n = 170, 60.0%)	No split dose (n = 113, 40.0%)	p value	OR	95%CI	MiraLAX (n = 106, 37.4%)	No MiraLAX (n = 177, 62.6%)	p value	OR	95%CI
Number of colonoscopies per week				0.24			0.21					0.04		
≤10	5	17.9	3	82.1	17	56.7	13	43.3	6	20.7	23	79.3	0.42	0.14–1.27
11–20	8	8.8	83	91.2	51	54.3	43	45.7	29	30.8	65	69.2	0.59	0.29–1.20
21–30	17	17.9	78	82.1	57	59.4	39	40.6	42	43.7	54	56.3	0.94	0.48–1.82
>30	11	18.6	48	81.4	44	71.0	18	29.0	28	44.4	35	55.6	1.00	-

†Including Hawaii.

CI, confidence interval; GI, gastroenterology; OR, odds ratio.

Table 2. Self-reported use of combined approaches of liberal diet, split dosing, and MiraLAX-based bowel preparations (MBBP) (n = 267).

Regimen	N	%
None	47	17.6
Liberal diet only	10	3.7
Split dose only	96	36.0
MBBP only	42	15.7
Liberal diet and split dose	14	5.2
Liberal diet and MBBP	6	2.2
Split dose and MBBP	42	15.7
Liberal diet, split dose, and MBBP	10	3.7

or MBBP (3.7%, 5.2%, and 2.2%) were the least frequently utilized methods.

Table 3 displays comparisons between the three approaches demonstrating that those who recommended split dose purgative were less likely to use MBBP (32.5% versus 67.5%, $p = 0.03$). No significant association between the recommendation of a liberal diet and use of split dosing or MBBP was found.

Discussion

Of the three newer approaches to bowel preparation examined (liberalized diet, split dose purgative and MBBP) among a random sample of members of the American College of Gastroenterologists, purgative split dosing is most commonly reported (60%), followed by MBBP (37%), and liberalized diet (15%). In our study, a surprisingly large number of physicians, particularly those in suburban locations and private practice, indicated that they recommend MBBP for their adult patients and over 80% combine MBBP use with Gatorade®. We also found that physicians in higher colonoscopy volume practices and those who were less likely to use split dosing were more likely to adopt this newer approach to bowel preparation.

Good quality preparation for colonoscopy is critical to an accurate and thorough examination of the bowel. Multiple variations to bowel preparation regimens have been explored with the purpose of increasing patient compliance, improving quality, and addressing issues of safety, effective administration, and tolerability. The current study examined the self-reported utilization of

Table 3. Comparison of diet versus split dose, diet versus MiraLAX-based bowel preparation MBBP, and split dose versus MBBP.

	Diet		<i>p</i> value	Split dose		<i>p</i> value
	Liberal	Restricted		Yes	No	
Split dose			0.91			–
Yes	24 (60.0)	139 (61.0)		–	–	
No	16 (40.0)	89 (39.0)		–	–	
MBBP			0.81			0.03
Yes	16 (39.0)	84 (37.0)		55 (32.5)	51 (45.1)	
No	25 (61.0)	143 (63.0)		114 (67.5)	62 (54.9)	

Note: Diet versus split dose, *n* = 268; diet versus MBBP, *n* = 268; and split dose versus MBBP, *n* = 282.

three newer approaches to bowel quality improvement and demonstrated that recommendations for each vary by and are associated with physician and practice characteristics.

Although MBBP is not FDA-approved for precolonoscopy bowel preparation, its efficacy and tolerability as a bowel cleansing agent in pediatric populations is well known [Adamiak *et al.* 2010; Pashankar *et al.* 2004; Safder *et al.* 2008], but reports among adults are mixed. Stratton and colleagues, in a letter to the editor of the *American Journal of Gastroenterology*, reported the efficacy, tolerability, safety, and compliance with PEG 3350 (MBBP) among adults in their community clinic [Stratton *et al.* 2008]. Beyond this, the researchers stated that PEG 3350 has several advantages over other single-agent preparations that included easy accessibility to patients, as it is an over-the-counter formulation, lower cost, and a less-complicated regimen for patients to follow. Conversely, two randomized controlled studies of the bowel cleansing efficacy of MBBP found that, compared with 4 liters of PEG (GoLytely), MBBP was not as effective in bowel cleansing but that patients found the preparation experience to be at least as tolerable/satisfactory as PEG [Enestvedt *et al.* 2011a; Hjelkrem *et al.* 2011]. Another study, a *post hoc* analysis of the adenoma detection rate of MBBP versus GoLytely, showed that MBBP produced fewer high-quality bowel preparations and a lower adenoma detection rate than GoLytely [Enestvedt *et al.* 2011b]. Our finding that use of MBBP increases with colonoscopy volume may indicate that in high-throughput practices and among those less likely to use split dosing, in spite of its failings, MBBP is gaining popularity which may be due to patient preference and tolerability over more traditional single-dose preparations.

That the majority of gastroenterologists recommend splitting the purgative dose is not surprising since this method has been more intensively studied, has demonstrated efficacy [Abdul-Baki *et al.* 2008; Aoun *et al.* 2005; El Sayed *et al.* 2003; Kilgore *et al.* 2011; Marmo *et al.* 2010; Park *et al.* 2007, 2010], and is advocated in published guidelines [Rex *et al.* 2009; Wexner *et al.* 2006]. Our findings suggest that among those who split the purgative dose, strict adherence to liquid diet is a lesser issue, most likely because of the effectiveness of split dosing in cleansing the bowel. We surmise that, for similar reasons, those who prescribe split dosing were also less likely to recommend MBBP. In our sample population, the majority of physicians who routinely recommend split dosing were the older physicians in private practice suggesting the adoption of bowel cleansing strategies that are more amenable to their private patients.

Interestingly, most research conducted on the use of split dosing has been conducted outside of the United States [Abdul-Baki *et al.* 2008; Aoun *et al.* 2005; El Sayed *et al.* 2003; Frommer, 1997; Marmo *et al.* 2010; Park *et al.* 2007, 2010; Parra-Blanco, 2006; Rostom *et al.* 2006]. A single US study by Matro and colleagues explored the efficacy of split dose versus morning-only use of PEG finding that these two methods are equivalent with regard to quality of cleansing and polyp detection [Matro *et al.* 2010]. Another study of 300 colonoscopy patients and their drivers demonstrated that 85% of those surveyed would be willing to rise in the middle of the night to consume a second dose of purgative, and of 107 patients, 78% actually did comply with this protocol [Unger *et al.* 2010]. No others, however, have demonstrated that splitting the purgative

dose (AM/PM) compared with ingestion on the day prior to the procedure can be successfully implemented among American hospital outpatients. Our findings support the existence of barriers to the more complete implementation of this procedure among younger US physicians in hospital/university and teaching settings where rates of suboptimal bowel preparation is more commonly encountered.

Despite the lack of rigorous evidence for the superiority of a clear liquid diet, many gastroenterologists continue to recommend this stringent diet during the 24-hour period preceding a colonoscopy, but this recommendation is by no means uniform. Clear liquid-only diet is recommended in review articles on this subject and in the consensus statement on bowel preparation prior to colonoscopy offered by the task force including the American Society of Gastrointestinal Endoscopy and the American Society of Colon and Rectal Surgeons [A-Rahim and Falchuk, 2011; Wexner *et al.* 2006]. Studies of precolonoscopy diet, however, show that the efficacy of cleansing is comparable for clear liquid diet and other diets that include any food, whether low residue [Delegge and Kaplan, 2005; Rapier and Houston, 2006; Wu *et al.* 2011], fiber-free [Soweid *et al.* 2010], or regular [Aoun *et al.* 2005; Scott *et al.* 2005]. Of the physicians in this study that do recommend a liberal diet, respondents in the Northeastern US were twice as likely as physicians in the South and more than three times as likely as physicians in the West, including Hawaii, to use this approach.

Choice of diet has been shown to enhance tolerability of the purgative [Rapier and Houston 2006; Soweid *et al.* 2010] and may influence compliance with the prescribed purgative. While data regarding the impact of diet on the quality of experience from the patient's perspective are sparse, bowel preparation remains the most unpleasant aspect of colonoscopy [Ko *et al.* 2007] and a diet that is more lenient than that of clear liquids only is rated more favorably [Delegge and Kaplan, 2005]. In the context of a procedure that is performed on more than 14 million individuals annually in the United States [Seeff *et al.* 2004], seemingly minor changes in dietary recommendations may have a substantial public health impact on purgative compliance. A more palatable precolonoscopy experience may increase screening rates and discourage 'cheating' on the preprocedure bowel preparation, resulting in higher-quality colonoscopic examinations and a

greater aggregate impact on cancer incidence and mortality.

This study has its limitations. The response rate was 28.8% and is comparable to, if not better than, other studies of the membership of the American College of Gastroenterologists [Cattau, 2010; Cohen *et al.* 2006; Sorbi *et al.* 2003; Spergel *et al.* 2011; Trindade *et al.* 2011; Wasan *et al.* 2011]. Response rates in these studies ranged from 5.8% to 32.7% and covered topics such as medication adherence among patients with inflammatory bowel disease [Trindade *et al.* 2011], management of variceal bleeding [Sorbi *et al.* 2003], and current practices in endoscopy and sedation [Cohen *et al.* 2006]. For whatever reason, whether continual bombardment with requests for survey participation, lack of interest in the topic, lack of time, or lack of proper incentives, response rate among this group has been repeatedly demonstrated to be low. By comparison, our rate of response is consistent with that of others. In addition, our study relied on self-report of behaviors and may not reflect the complex judgment process involved in individual recommendations for bowel preparation regimens.

Conclusions

While the literature on MBBP is limited and suggests that these regimens are not as effective as FDA-approved bowel preparation regimens [Enestvedt *et al.* 2011a, 2011b; Hjelkrem *et al.* 2011], our results indicate that a large proportion of gastroenterologists throughout the US prescribe MBBP. With this practice becoming more popular among high-volume gastroenterologists, an even higher proportion of patients in the US are being offered MBBP. Further studies regarding safety, efficacy, and optimal dosing data of MBBP are needed given the apparent popularity of these regimens. As split dosing is considered to be a key measure to improve the quality and cost-effectiveness of colonoscopy, that so many routinely use this method is encouraging. Because patient populations in hospital/university and teaching settings most likely differ dramatically from private practice in terms of demographic and socioeconomic characteristics, further investigation of the acceptability and desirability of this procedure among certain American populations is warranted. Continuing medical education to increase uptake of the split dose purgative method is indicated as well as evaluation of barriers to use in nonprivate practice settings. Lastly, although

the use of a more liberalized diet is becoming more popular in the Northeast, it is far from becoming an accepted practice. Additional research on the importance of dietary restriction in the context of better purgative compliance may lead to less stringent dietary requirements in the future and more widespread acceptance of this approach.

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Conflict of interest statement

The authors no conflicts of interest in preparing this article.

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