

REVIEW ARTICLE

The unmet needs for identifying the ideal bowel preparation

Gian E Tontini,* Alberto Prada,† Sandro Sferrazza,‡ Giorgio Ciprandi§ and Maurizio Vecchi*

*Department of Internal Medicine, Gastroenterology and Endoscopy Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, †Digestive Endoscopy, Istituto Auxologico Italiano, Milan, ‡Gastroenterology and Endoscopy Unit, Area Chirurgia Specialistica, Santa Chiara Hospital, Trento and §Outpatient Department, Casa di Cura Villa Montallegro, Genoa, Italy

Key words

bowel preparation, colonoscopy, patient satisfaction.

Accepted for publication 21 August 2021.

Correspondence

Giorgio Ciprandi, Via P. Boselli 5,
16146 Genoa, Italy.
Email: giocip@me.com

Declaration of conflict of interest: GET, AP, SS, and MV have no conflict of interests, and GC is a consultant of NTC Pharma.

Abstract

Colonoscopy, since it was first employed over 60 years ago, is now the gold standard method for visualizing the mucosa of the colon, but should be of good quality. Many factors affect quality, including the type of health service organization, type of facility, staff, equipment, patient characteristics, and bowel preparation (BP). The adequacy of bowel cleansing is critical, but, unfortunately, may be inadequate in up to one-third of procedures. The current article will present and discuss the main BPs and their drawbacks, which include patient-dependent and procedure-dependent factors. Cleansing quality depends on the ease/complexity of solution preparation, volume, taste, and timing of consumption. Consequently, important positive factors include simple instructions, easy preparation of the solution, low volume, pleasant taste, short drinking time (e.g. <30 min), and splitting the dose between the evening before and the morning of the colonoscopy (or even better, only one dose in the early morning to avoid night-time problems), and short onset of action. The BP solution must also be safe with negligible side effects. Furthermore, a positive experience supports patient willingness to repeat the procedure.

Introduction

Colonoscopy, since it was first employed over 60 years ago, has become the gold standard method for visualizing the mucosa of the colon. Some 20 million such procedures are performed in Europe and the United States annually.¹ The main indications for colonoscopy are screening, diagnosis confirmation, and surveillance, as summarized in Table 1.² The demand for colonoscopy has doubled in the last few years because of the aging of the general population and the implementation of bowel cancer screening programs.³ Good quality colonoscopy is essential,⁴ but unfortunately, up to one-third of procedures may be of inadequate quality and so of little use.^{5,6}

Many factors affect colonoscopy quality, including the type of health service organization, type of facility, staff, equipment, patient characteristics, and the bowel preparation (BP) process (Table 2). High-quality colonoscopy is essential for successful screening programs and effective diagnosis.^{7,8} The BP process is especially important.^{9–11} Inadequate BP results in a lengthy procedure, incomplete colonoscopy, incorrect diagnosis or diagnostic delay, increased costs due to the need to repeat the procedure, adverse events, and patient unwillingness to repeat the examination.^{12–15} BP is inadequate in 18–35% of colonoscopies.¹⁶ The main factors affecting the BP procedure are the patient's characteristics and the BP reconstitution/consumption process, as reported in Table 3.

Various guidelines and recommendations have been published.^{12–21} Over 90% of procedures should meet a minimum standard (measured by validated scales), as recently recommended by the

European Society of Gastrointestinal Endoscopy (ESGE).¹⁵ The American Society for Gastroenterology Endoscopy (ASGE) has stated that BP should effectively clear the colon of stool and provide maximal visualization of mucosa, preserve the gross and microscopic integrity of the colon, and be easily administered, well tolerated, inexpensive, and safe, avoiding shifts in fluids and electrolytes.¹⁸ Remarkably, none of the currently available BP products meet all of these requirements. This article will analyze and discuss the various aspects of BP in clinical practice. Currently available BP formulations will be described, and unmet needs will be discussed in order to identify the ideal preparation as envisaged in the literature.^{22–26}

BP quality assessment

A good quality colonoscopy is required to identify colonic lesions and, if possible, treat them, as in screening programs for colorectal cancer.^{27,28} Rex *et al.* described in detail the requirements for good quality colonoscopy.¹ Therefore, it is clinically important to assess BP quality²⁹ and several scales are used, including the Aronchick Scale, Boston Bowel Preparation Scale (BBPS), Chicago Bowel Preparation Scale, Harefield Cleansing Scale, Marden Bowel Preparation Classification, and Ottawa Bowel Preparation Scale (OBPS), as reported in Table 4.^{30,31} Each of these scales has different advantages, so the endoscopist picks one based on personal experience, local protocols, and guidelines. However, the OBPS and the BBPS are the most commonly used in clinical practice. The OBPS is preferred for evaluating the efficacy of preparation before intervention,

Table 1 Indications for colonoscopy

| | |
|--------------|---|
| Screening | Colorectal cancer screening programs Subjects with a family history of colorectal cancer |
| Diagnosis | Gastrointestinal bleeding Unexplained weight loss Sideropenic anemia Persistent and relevant change in bowel movements Unexplained abdominal pain |
| Confirmation | Colorectal alterations previously detected by barium enema, computed tomography, or magnetic resonance After virtual colonoscopy |
| Surveillance | Patients with intestinal adenoma and/or polyps Patients with chronic inflammatory intestinal disease Follow-up after bowel cancer surgery |

Table 2 Factors affecting the quality of colonoscopy

| | |
|-----------------------------|--|
| Health service organization | Public hospital Private insurance Open access |
| Facility | Inpatient Outpatient |
| Staff | Operator (ability, attitude) Nursing (communication) |
| Equipment | Endoscope reliability |
| Bowel preparation | Purgatives Medications Diet Timing Instructions Arrangement |
| Patient | Age Sex Education Cognitive status Health literacy Fear Humiliation Embarrassment Modesty Depression Adherence Tolerability Palatability Adverse event experience |

while the BBPS is used to evaluate the efficacy of preparation after aspiration and lavage, hereby measuring the ability to visualize the mucosa and the real diagnostic reliability of each colonoscopy.

BP products

BP products can be mainly classified into two broad categories: polyethylene glycol (PEG)-based products and hyperosmotic products (Table 5). Both types can produce adequate bowel cleansing, but with variable tolerance, preparation-induced mucosal changes, and adverse events.

Table 3 Factors associated with quality of bowel preparation

| | |
|---------------------------|--|
| Patient-dependent factors | Motivation Instruction Health literacy Education Socioeconomic status Adherence Comorbidities and hospitalization Discomfort |
| Product-dependent factors | Volume Mechanism of action Osmolarity Taste Dosing Complexity of the split schedule Timing Runway time Safety (adverse events, including intestinal gas) Tolerability |

PEG is a polymer prepared by the polymerization of ethylene oxide and is widely used in medicine and vaccine preparation. Standard PEG-based BP involves the consumption of 2–4 L of solution in 2 h. PEG usually causes significant fluid and/or electrolyte shifts that offset each other to minimize their effect.

A variety of PEG-based formulations are available, which differ regarding solution volume, electrolyte content, requirement for an adjuvant laxative, the addition of oral simethicone, and the presence of artificial sweeteners. They are usually safe but can have uncommon, but potentially serious, adverse effects, including electrolyte disturbance, allergic reaction, and renal failure.³²

Hyperosmotic preparations contain poorly absorbed multi-valent cations or anions with osmotic effects and increase intraluminal water, causing bowel distension and evacuation. These agents include sodium phosphate (NaP), sodium picosulfate, and magnesium citrate (MC).

NaP preparations are effective and better tolerated than PEG-based preparations because of their low volume.³³ However, NaP can have adverse effects including fluid shifts, hyperphosphatemia, electrolyte abnormalities, tonic-clonic seizure, mucosal damage, and acute renal failure, such as acute phosphate nephropathy.³⁴ Indeed, the Food and Drug Administration (FDA) has issued a black box warning because of the nephropathy, and NaP as a BP has been removed from the US market.

MC is a hyperosmotic laxative but is not approved by the FDA for BP.

A new dual-action hyperosmotic preparation contains sodium picosulfate (stimulant laxative) and magnesium (osmotic agent). It is better tolerated than PEG-based formulations with a similar degree of bowel cleansing, but can precipitate severe hyponatremia in older adults.

BP volume

An obstacle to successful BP is the large volume of reconstituted solution. Patients drinking 4 L of PEG-based formulation frequently experience cramps, fullness, nausea, and/or vomiting due

Table 4 Bowel preparation scales available in clinical practice

| Scale | Scale range | Excellent score | Inadequate score |
|---|-------------|-----------------|------------------|
| Aronchick Score | | | |
| Ottawa Bowel Preparation Scale | 0–14 | 0 | 14 |
| Boston Bowel Preparation Scale | 0–9 | 9 | 0 |
| Harefield Cleansing Scale | 0–20 | 20 | 0 |
| Chicago Bowel Preparation Scale | 0–36 | 36 | 0 |
| Marden Bowel Preparation Classification | 1–4 | 4 | 1 |

to the unpleasant sulfate taste; consequently, about 15% of patients do not complete BP.³⁵ However, low-volume PEG and sulfate-free solutions (2 L) have now been developed. A further option is to split the preparation volume into two doses so that half of the dose (1 L only) is taken the night before and the other half (1 L) on the day of the procedure. There is overwhelming evidence that a split-dose regimen is better than a single dose given the day before, as demonstrated by three meta-analyses.^{36–38} A recent meta-analysis, including 17 randomized controlled trials, also showed that a low-volume (≤ 2 L) split-dose regimen is as effective as a high-volume split-dose regimen for cleansing but is better tolerated and has superior compliance.²³

Same-day preparation (early in the morning) is used for afternoon colonoscopy. Several studies have showed no substantial differences between split-dose and same-day schedules.^{39–42} However, the schedule chosen should be based on the patient's clinical characteristics, including comorbidities, concomitant medications, and hospitalization, and socioeconomic status.^{41,43}

Recently, a 1-L PEG-based BP (with ascorbic acid, sodium aspartate, and sulfate) was found to be as effective for colon cleansing as a regular PEG split-dose regimen.⁴⁴ This combined product has been approved by the FDA for BP for colonoscopy.⁴⁵ A small meta-analysis confirmed efficacy and safety.⁴⁶

BP timing

Another critical issue is the interval between consumption of the last dose of preparation solution and the beginning of colonoscopy (“runway time”), as outlined by a recent study conducted in 3205 patients.⁴⁷ An inverse correlation was consistently found between mucosal cleanliness and runway time; the optimal time for the last dose is 3 h before colonoscopy as recommended by the ESGE guidelines.¹⁵ The same considerations apply to the consumption of a clear liquid diet. Thus, according to the American Society of Anesthesiologists, 2 h is the minimum interval between any ingestion and the procedure.⁴⁸

Adjuvant drugs

Bisacodyl, a diphenylmethane derivative and stimulant laxative, has been available as a laxative since 1952. It has dual activity in the colon, an anti-absorptive-secretory effect and a direct prokinetic effect, through stimulation of parasympathetic nerve endings in the colonic mucosa.⁴⁹ It acts locally in the large bowel by stimulating myoelectrical and motor activity and intestinal secretion, thus enhancing colon motility, reducing overall colonic transit time, and increasing the water content of stool. For these

reasons, it has been successfully combined with 2-L PEG with improved tolerability.^{15,50}

Prokinetics are also used to reduce the laxative dose. Mosapride citrate, a selective 5-hydroxytryptamine-4 receptor agonist, when used with a split dose of PEG plus ascorbic acid, increased BP efficacy in elderly patients and reduced adverse events, mainly abdominal fullness.⁵¹

A meta-analysis showed that prucalopride, a 5-hydroxytryptamine-4 receptor agonist that stimulates gastrointestinal peristalsis, when combined with low-volume BP was as effective as standard low-volume BP solutions but had fewer adverse events.⁵² However, conclusive evidence is lacking, so the ESGE guidelines do not recommend the routine use of prokinetic medications for BP.¹⁵

Simethicone

Simethicone is a silicon dioxide derivative used as an anti-foaming agent to reduce bloating, discomfort, or pain caused by excessive gas. The presence of foam is a disturbing element during colonoscopy as it reduces endoscopic visibility and makes additive washing maneuvers necessary. There is evidence that oral simethicone reduces gas volume, as documented by four randomized controlled trials, and improves bowel cleanliness, as demonstrated by randomized controlled trials.⁵³ Consequently, its use is recommended by the ESGE guidelines,¹⁵ and several simethicone-added PEG formulations are available worldwide.

Diet

A low-residue diet, for instance containing <10 g fiber per day, or a clear liquid diet are recommended for BP. According to a recent meta-analysis, the low residue/regular diet is associated with higher willingness to repeat the colonoscopy (relative risk [RR] 1.08, 95% confidence interval [CI] 1.01–1.16), better tolerability (RR 1.04, 95% CI 1.01–1.08), and adherence (RR 1.04, 95% CI 1.01–1.08) when compared with a clear liquid diet.⁵⁴ Traditionally, dietary restriction was recommended for 3 days before colonoscopy, but the acceptance rate was very low. A recent study confirmed a previous meta-analysis, showing that a 3-day low-residue diet did not result in better BP quality than a 1-day diet.⁵⁵ As a result, the ESGE guidelines recommend a low-fiber diet on the day preceding colonoscopy.¹⁵

Instructions

BP education is essential for achieving quality colonoscopy. Nursing staff should provide oral and written instructions, but they are often supplied by other staff or even sent by email.

Table 5 Bowel preparation products: main characteristics

| BP products | Total volume ingested | Regimen | BP efficacy (adequate colonoscopies) | | ADR | PDR | Indication | Limitations | Adverse events (most common) |
|-------------------------|-----------------------|---------|--------------------------------------|--------|--------|-----|---|---|---|
| | | | 71–92% | 27–34% | | | | | |
| PEG-ELS | 4 L | Split | 71–92% | 27–34% | | | Preferred in patients with IBD, renal failure. Liver disease Consider in elderly and inpatients Consider in otherwise healthy outpatients Consider in young people | High volume and side effects | Abdominal pain, bloating, nausea, vomiting, incontinence |
| PEG-ELS + ascorbic acid | 2.95 L | Split | 74–93% | 18–25% | | | | Avoid in patients with G6PD deficiency | Nausea, gastralgia, vomiting, dizziness, dehydration |
| PEG 3350 without ELS | 1.9 L | Split | 67–81% | 47% | | | Avoid in patients with severe constipation and in patients with hemorrhage as the onset of action is slow | Avoid in patients with severe constipation and in patients with hemorrhage as the onset of action is slow | Nausea, abdominal fullness, bloating |
| Magnesium citrate | 2.3 L | Split | 75–90% | | | | Constipation | Elderly patients and patients with nephropathy, congestive heart failure, hypermagnesemia. Additional water drinking could be advised in some patients with the evening dose | Nausea, vomiting, abdominal pain. Electrolyte imbalance. Dehydration. Headache |
| Sodium phosphate | 1.6 L | Split | 84–90% | 27–36% | 54% | | Effective in patients with constipation | Avoid in elderly patients, concomitant use of NSAID and ACEi for nephrotoxicity, and patients with suspected IBD | Abdominal bloating, nausea, abdominal pain, vomiting. Phosphate nephropathy (rare) |
| Sodium sulfate | 2.84 L | Split | 93–98% | 26% | 50% | | Alternative to sodium phosphate | Avoid in gout (possible increase of serum uric acid) | Overall discomfort, abdominal distension, abdominal pain, nausea, vomiting, headache |
| Sodium picosulfate | 2.2 L | Split | 81–88% | 23–31% | 38–42% | | Consider in patients with gastric resection (low volume) | Avoid in elderly patients because of the risk of hyponatremia. | Nausea, vomiting, headache |

ADR, adenoma detection rate; BP, bowel preparation; ELS, electrolyte lavage solution; IBD, inflammatory bowel disease; PDR, polyp detection rate.

Table 6 Advantages and disadvantages of current bowel preparation formulations

| | | |
|---------------------------------------|---|---|
| Current disadvantages | Instructions difficult to understand | |
| | Complex preparation | |
| | Large volume | |
| | Unpleasant taste | |
| | Long duration of drinking | |
| | Split-dose-dependent factors (sleep disturbance, incontinence, long procedure) | |
| | Cleansing quality | |
| | Dissatisfaction with bowel preparation | |
| | Unwillingness to repeat the colonoscopy | |
| | Adverse events (nausea, vomiting, abdominal pain, hypovolemia, electrolyte shift) | |
| | Required advantages | Simple instruction for a simple procedure |
| | | Easy solution preparation |
| | | Low volume |
| Pleasant taste | | |
| Short drinking time (<30 min) | | |
| Only one dose | | |
| Early morning ingestion | | |
| Short onset of action | | |
| Negligible side effects | | |
| Willingness to repeat the colonoscopy | | |

Inadequate instruction can result in misunderstanding that, in turn, discourages colonoscopy uptake.⁵⁶ Thus, the use of enhanced instructions for BP is recommended.¹⁵ Indeed, a meta-analysis of 18 randomized controlled trials (with 6536 patients) confirmed that better education improves BP quality. Reminder systems based on automated time-released text message and/or telephone call to patients who are due for colonoscopy examinations can also significantly improve adherence, BP quality, and adenoma detection^{57–59} (X).

Patient factors

Many patient-associated factors can affect BP quality. The most important predictor of inadequate preparation is previous inadequate preparation.¹⁴ Age, sex, physical activity, socioeconomic status, educational level, and comorbidity may significantly affect colonoscopy quality.^{1,60,61} Predictors of poor BP include age (odds ratio [OR] = 1.14), tobacco use (OR = 1.28), narcotic use (OR = 1.28), hypertension (OR = 1.25), diabetes mellitus (OR = 1.38), obesity (OR = 1.46), low education (OR = 1.49), dementia (OR = 2.09), and calcium-channel blockers (OR = 3.2), as reported in different reviews and meta-analyses.^{61–64} Hospitalization is another independent predictor of poor BP.⁶⁵ A recent Italian multicenter study developed and validated a model to identify hospitalized patients with inadequate bowel cleansing.⁶⁶

Patient acceptance

Different dosing regimens, timing, and preparations have been investigated for improving patient acceptance of BP.^{46,67–74} Low volume PEG (*vs* high volume PEG) and split-dose or same-day regimens (*vs* day-before regimens) have been usually shown to achieve higher acceptance rate and willing to repeat the

endoscopic procedure.¹⁵ However, the ideal regimen has not yet been defined. Coskun and Yuksel proposed a split high-dose (1 g) sennoside solution as an alternative to 4 L of PEG as patients taking senna experienced less vomiting and nausea, but they did have more abdominal pain.⁷⁵

Conclusions

BP quality is influenced by patient and procedural factors. As a rule, low adherence and/or poor tolerance of BP significantly affect outcome, even though one study found that less than 20% of patients with inadequate colon preparation reported failure to adequately follow preparation instructions.⁷⁶ The lack of efficacy of a BP protocol also depends on patient diet and the cleansing products used. Timing, including runway time, seems to be crucial. The type of administration (full or split-dose) is likewise important. In particular, the split-dose regimen has shown several advantages in terms of colon cleansing and patient tolerability, but it also involves patient inconvenience, sleep disruption, and incontinence.

Personalized medicine is being increasingly implemented in clinical practice. The characteristics of the patient, including their comorbidities, emotional status, education, and socioeconomic level, can affect BP acceptance and efficacy. The most important issue is adherence to the BP process, so detailed discussion with the patient regarding BP is crucial. Patient engagement is also essential for successful BP⁷⁷ and so should be multidisciplinary, involving all staff. Shared responsibility between the clinician and the patient is similarly important for achieving optimal BP and involves selecting the type of preparation for each patient and the provision of clear instructions to optimize patient understanding and compliance.

BP procedures also have some shortcomings.⁷⁸ These include the complexity of solution preparation, large volume, unpleasant taste, long duration of drinking (possibly >1 h), cleansing quality, and splitting schedule. Moreover, adverse events can occur, with a very few being serious.

Consequently, the BP procedure needs to be improved (Table 6). This includes the provision of simple instructions for a simple procedure, easy solution preparation, low volume, pleasant taste, short drinking time (e.g. <30 min), only one dose in the early morning, so avoiding night-time problems, and short onset of action. From an organizational perspective, if the patient could consume the solution in the early morning, the procedure could be performed in the late morning. Products with negligible side effects are also important as a positive experience will make the patient more willing to repeat the procedure.

In conclusion, the ideal BP for colonoscopy should be effective, safe, easily self-administered; have good patient acceptance; and be of low cost. Although currently available preparations are reasonably effective and safe, patient acceptance can still be improved, so further studies are necessary.

References

- 1 Rex DK, Schoenfeld PS, Cohen J *et al.* Quality indicators for colonoscopy. *Gastrointest. Endosc.* 2015; **81**: 31–53.

- 2 Fassil H, Adams KF, Weinmann S *et al.* Approaches for classifying the indications for colonoscopy using detailed clinical data. *BMC Cancer*. 2014; **14**: 95.
- 3 Joseph DA, Meester RGS, Zauber AG *et al.* Colorectal cancer screening: estimated future colonoscopy need and current volume and capacity. *Cancer*. 2016; **122**: 2479–86.
- 4 Shenbagaraj L, Thomas-Gibson S, Stebbing J *et al.* Endoscopy in 2017: a national survey of practice in the UK. *Frontline Gastroenterol*. 2019; **10**: 7–15.
- 5 Chapman W. The importance of adequate bowel cleansing for effective colonoscopy. *Br. J. Nurs.* 2020; **29**: S3–8.
- 6 Gkolfakis P, Tziatzios G, Papanicolaou IS, Triantafyllou K. Strategies to improve inpatients' quality of bowel preparation for colonoscopy: a systematic review and meta-analysis. *Gastroenterol. Res. Pract.* 2019; **2019**: 5147208.
- 7 John J, Al-Douri A, Candelaria B *et al.* Colonoscopy quality and adherence to postpolypectomy surveillance guidelines in an underinsured clinic system. *Gastroenterol. Res. Pract.* 2020; **2020**: 6240687.
- 8 Siegel RL, Miller KD, Jemal AL. Cancer statistics, 2019. *CA Cancer J. Clin.* 2018; **69**: 7–34.
- 9 Doubeni CA, Laiyemo AO, Major JM *et al.* Socioeconomic status and the risk of colorectal cancer. *Cancer*. 2012; **118**: 3636–44.
- 10 Millien VO, Mansour NM. Bowel preparation for colonoscopy in 2020: a look at the past, present, and future. *Curr. Gastroenterol. Rep.* 2020; **22**: 28.
- 11 Bechtold ML, Mir F, Puli SR, Nguyen DL. Optimizing bowel preparation for colonoscopy. A guide to enhance quality of visualization. *Ann. Gastroenterol.* 2016; **29**: 137–46.
- 12 Sharma P, Burke CA, Johnson DA, Cash BD. The importance of colonoscopy bowel preparation for the detection of colorectal lesions and colorectal cancer prevention. *Endosc. Int Open*. 2020; **8**: E673–83.
- 13 KastenberG D, Bertiger G, Brogadir S. Bowel preparation quality scales for colonoscopy. *World J. Gastroenterol.* 2018; **24**: 2833–43.
- 14 Saltzman JR, Cash BD, Pasha SF *et al.* Bowel preparation before colonoscopy. *Gastrointest. Endosc.* 2015; **81**: 781–94.
- 15 Hassan C, East J, Radaelli F *et al.* Bowel preparation for colonoscopy: European Society of Gastrointestinal Endoscopy (ESGE) Guideline - Update 2019. *Endoscopy*. 2019; **51**: 775–94.
- 16 Park JH, Kim SJ, Hyun JH *et al.* Correlation between bowel preparation and the adenoma detection rate in screening colonoscopy. *Ann. Coloproctol.* 2017; **33**: 93–8.
- 17 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**: 1197–203.
- 18 ASGE Technology Committee. Colonoscopy preparation. *Gastrointest. Endosc.* 2009; **69**: 1201–9.
- 19 Matus-Vliegen E, Pellisé M, Heresbach D *et al.* Consensus guidelines for the use of bowel preparation prior to colonic diagnostic procedures: colonoscopy and small bowel video capsule endoscopy. *Curr. Med. Res. Opin.* 2013; **29**: 931–45.
- 20 Johnson DA, Barkun AN, Cohen LB *et al.* Optimizing adequacy of bowel cleansing for colonoscopy: recommendations from the U.S. Multi-Society Task Force on colorectal cancer. *Gastrointest. Endosc.* 2014; **80**: 543–62.
- 21 Spada C, Cannizzaro R, Bianco MA *et al.* Preparation for colonoscopy: recommendations by an expert panel in Italy. *Dig. Liver Dis.* 2018; **50**: 1124–32.
- 22 Sarvepalli S, Garber A, Burke CA *et al.* Comparative effectiveness of commercial bowel preparations in ambulatory patients presenting for screening or surveillance colonoscopy. *Dig. Dis. Sci.* 2021; **66**: 2059–68.
- 23 Kamran U, Abbasi A, Tahir I, Hodson J, Siau K. Can adjuncts to bowel preparation for colonoscopy improve patient experience and result in superior bowel cleanliness? A systematic review and meta-analysis. *UEG J.* 2020; **8**: 1217–27.
- 24 Barsky M, Meserve J, Le H *et al.* Understanding determinants of patient preferences between stool tests and colonoscopy for the assessment of disease activity in inflammatory bowel disease. *Dig. Dis. Sci.* 2020; **66**: 2564–69.
- 25 Rogers BD, Shy C, Rampgopal R *et al.* Patient engagement with interactive text message system improves successful colonoscopy rates in an outpatient endoscopy center. *Dig. Dis.* 2021; **39**: 399–406.
- 26 Kaminski M, Marlicz W, Koulaouzidis A. Googling on colonoscopy. A retrospective analysis of search engine statistics. *Clin. Exp. Gastroenterol.* 2020; **13**: 397–405.
- 27 American Cancer Society. *Colorectal Cancer Facts & Figures 2017–2019*. Atlanta, GA: American Cancer Society, 2017. Available from URL: <https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/colorectal-cancer-facts-and-figures/colorectal-cancer-facts-and-figures-2017-2019.pdf>.
- 28 Zauber AG, Winawer SJ, O'Brien MJ *et al.* Colonoscopic polypectomy and long-term prevention of colorectal-cancer deaths. *N. Engl. J. Med.* 2012; **366**: 687–96.
- 29 Parekh PJ, Oldfield EC, Johnson DA. Bowel preparation for colonoscopy: what is best and necessary for quality? *Curr. Opin. Gastroenterol.* 2019; **35**: 51–7.
- 30 Rostom A, Jolicoeur E. Validation of a new scale for the assessment of bowel preparation quality. *Gastrointest. Endosc.* 2004; **59**: 482–6.
- 31 Gerard DP, Foster DB, Raiser M, Holden J, Holden JL, Karrison TG. Validation of a new bowel preparation scale for measuring colon cleansing for colonoscopy: the Chicago bowel preparation scale. *Clin. Transl. Gastroenterol.* 2013; **4**: 1–11.
- 32 Belsey J, Epstein O, Heresbach D. Systematic review: adverse event reports for oral sodium phosphate and polyethylene glycol. *Aliment. Pharmacol. Ther.* 2009; **29**: 15–28.
- 33 Sodium sulfate-based tablets (Sutab) for colonoscopy preparation. *Med. Lett. Drugs Ther.* 2021; **63**: 33–6.
- 34 Anastassopoulos K, Farraye FA, Knight T, Colman S, Cleveland MV, Pelham RW. A comparative study of treatment-emergent adverse events following use of common bowel preparations among a colonoscopy screening population: results from a post-marketing observational study. *Dig. Dis. Sci.* 2016; **61**: 2993–3006.
- 35 Pockros PJ, Foroozan P. Golytel lavage versus a standard colonoscopy preparation. Effect on normal colonic mucosal histology. *Gastroenterology*. 1985; **88**: 545–8.
- 36 Hoy SM, Scott LJ, Wagstaff AJ. Sodium picosulfate/magnesium citrate: a review of its use as a colorectal cleanser. *Drugs*. 2009; **69**: 123–36.
- 37 Kilgore TW, Abdinoor AA, Szary NM *et al.* Bowel preparation with split-dose polyethylene glycol before colonoscopy: a meta-analysis of randomized controlled trials. *Gastrointest. Endosc.* 2011; **73**: 1240–5.
- 38 Bucci 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**: 566–76.e2.
- 39 Menees SB, Kim HM, Schoenfeld P. Split-dose bowel preparation improves adequacy of bowel preparation and gastroenterologists' adherence to national colorectal cancer screening and surveillance guidelines. *World J. Gastroenterol.* 2018; **24**: 716–24.
- 40 Seo M, Gweon TG, Huh CW, Ji JS, Choi H. Comparison of bowel cleansing efficacy, safety, bowel movement kinetics, and patient tolerability of same-day and split-dose bowel preparation using 4 L of polyethylene glycol: a prospective randomized study. *Dis. Colon Rectum.* 2019; **62**: 1518–27.
- 41 Castro FJ, Al-Khairi B, Singh H, Mohameden M, Tandon K, Lopez R. Randomized controlled trial: split-dose and same-day large volume bowel preparation for afternoon colonoscopy have similar quality of preparation. *J. Clin. Gastroenterol.* 2019; **53**: 724–30.
- 42 Kang X, Zhao L, Zhu Z *et al.* Same-day single dose of 2 liter polyethylene glycol is not inferior to the standard bowel preparation

- regimen in low-risk patients: a randomized, controlled trial. *Am. J. Gastroenterol.* 2018; **113**: 601–10.
- 43 Mahmood S, Farooqui SM, Madhoun MF. Predictors of inadequate bowel preparation for colonoscopy: a systematic review and meta-analysis. *Eur. J. Gastroenterol. Hepatol.* 2018; **30**: 819–26.
- 44 DeMicco MP, Clayton LB, Pilot J, Epstein MS, NOCT Study Group. Novel 1 L PEG based bowel preparation NER 1006 for overall and right-sided colon cleansing: a randomized controlled phase 3 trial versus trisulfate. *Gastrointest. Endosc.* 2018; **87**: 677–87.e3.
- 45 Frellick M. FDA approves smaller, 1 liter bowel prep for colonoscopies. *Medscape.* 2018.
- 46 Maida M, Macaluso FS, Sferrazza S, Ventimiglia M, Sinagra E. Effectiveness and safety of NER1006 versus standard bowel preparations: a meta-analysis of randomized phase-3 clinical trials. *Dig. Liver Dis.* 2020; **52**: 833–9.
- 47 Zad M, Do CN, Hefferman A, Johnston L, Al-Ansan M. Factors affecting bowel preparation adequacy and procedural time. *JGH Open.* 2020; **4**: 206–14.
- 48 American Society of Anesthesiologists Committee. Practice guidelines for preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration: application to healthy patients undergoing elective procedures. *Anesthesiology.* 2017; **126**: 376–93.
- 49 Manabe N, Cremonini F, Camilleri M, Sandborn WJ, Burton DD. Effects of bisacodyl on ascending colon emptying and overall colonic transit in healthy volunteers. *Aliment. Pharmacol. Ther.* 2009; **30**: 930–6.
- 50 Kallestrup K, Møller Jensen T, Grode LB, Behrmdtz Brandsborg S, Dige AK, Brix LD. Split-dose regimen with bisacodyl increases the quality of bowel preparation for colonoscopy. *Gastroenterol. Nurs.* 2021; **44**: 14–20.
- 51 Lee J, Jeong J, Kim TH *et al.* Efficacy of mosapride citrate with a split dose of polyethylene glycol plus ascorbic acid for bowel preparation in elderly. *Medicine.* 2020; **99**: e18702.
- 52 Park S-W, Shin S-P, Hong JT. Efficacy and tolerability of prucalopride in bowel preparation for colonoscopy: a systematic review and meta-analysis. *Adv. Ther.* 2020; **37**: 2507–19.
- 53 Moolla M, Dang JT, Shaw A *et al.* Simethicone decreases bloating and improves bowel preparation effectiveness: a systematic review and meta-analysis. *Surg. Endosc.* 2019; **33**: 3899–909.
- 54 Avalos DJ, Sussman DA, Lara LF, Sarkis FS, Castro FJ. Effect of diet liberalization on bowel preparation. *South. Med. J.* 2017; **110**: 399–407.
- 55 Friedemann-Sanchez G, Griffin JM, Partin MR. Gender differences in colorectal cancer screening barriers and information needs. *Health Expect.* 2007; **10**: 148–60.
- 56 Decruz GM, Ng CH, Lim KT *et al.* Afterthoughts on colonoscopy. Was it that bad? *J. Med. Screen.* 2021; **28**: 63–9.
- 57 Nayor J, Feng A, Qazi T, Hurwitz S, Saltzman JR. Impact of automated time-released reminders on patient preparedness for colonoscopy. *J. Clin. Gastroenterol.* 2019; **53**: e456–62.
- 58 Walter B, Klare P, Strehle K *et al.* Improving the quality and acceptance of colonoscopy preparation by reinforced patient education with short message service: results from a randomized, multicenter study (PERICLES-II). *Gastrointest. Endosc.* 2019; **89**: 506–513.e4.
- 59 Lee YJ, Kim ES, Choi JH *et al.* Impact of reinforced education by telephone and short message service on the quality of bowel preparation: a randomized controlled study. *Endoscopy.* 2015; **47**: 1018–27.
- 60 Kutyla MJ, Gray MA, von Hippel C *et al.* Improving the quality of bowel preparation: rewarding patients for success or intensive patient education? *Dig. Dis.* 2021; **39**: 113–18.
- 61 Serper M, Gawron AJ, Smith SG *et al.* Patient factors that affect quality of colonoscopy preparation. *Clin. Gastroenterol. Hepatol.* 2014; **12**: 451–7.
- 62 Hwang Y-J, Shin D-W, Kim N *et al.* Sex difference in bowel preparation quality and colonoscopy time. *Korean J. Intern. Med.* 2021; **36**: 322–31.
- 63 Froehlich F, Wietlisbach V, Gonvers JJ, Burnand B, Vader J-P. 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**: 378–84.
- 64 Ben-horin S, Bar-meir S, Avidan B. The outcome of a second preparation for colonoscopy after preparation failure in the first procedure. *Gastrointest. Endosc.* 2009; **69**(3 Pt 2): 626–30.
- 65 Argyropoulos SK, Mahmood SK, Campbell EJ, Richter JM. Improving the quality of inpatient bowel preparation for colonoscopies. *Dig. Dis. Sci.* 2018; **63**: 338–44.
- 66 Fuccio L, Frazzoni L, Spada C *et al.* Factors that affect adequacy of colon cleansing for colonoscopy in hospitalized patients. *Clin. Gastroenterol. Hepatol.* 2021; **19**: 339–48.e7.
- 67 Hernandez PV, Horsley-Silva JL, Snyder DL *et al.* Effect of bowel preparation volume in inpatient colonoscopy. Results of a prospective, randomized, comparative pilot study. *BMC Gastroenterol.* 2020; **20**: 227.
- 68 Yi L-J, Tian X, Shi B *et al.* Low-volume polyethylene glycol improved patient attendance in bowel preparation before colonoscopy: a meta-analysis with trial sequential analysis. *Front. Med.* 2019; **6**: 92.
- 69 Sey MSL, von Renteln D, Sultanian R, McDonald C, Martel M, Barkun A. Multicentre endoscopist-blinded randomized clinical trial to compare two bowel preparations after a colonoscopy with inadequate cleansing: a study protocol. *BMJ Open.* 2019; **9**: e029573.
- 70 Yoshida N, Inagaki Y, Fukumoto K *et al.* The efficacy of short-duration polyethylene glycol plus electrolytes for improving bowel preparation of colonoscopy in patients with chronic constipation. *Gastroenterol. Res. Pract.* 2020; **2020**: 8886073.
- 71 Cuffari C, Ciciora SL, Ando M, Boules M, Croffie JM. Pediatric bowel preparation: sodium picosulfate, magnesium oxide, citric acid vs polyethylene glycol, a randomized trial. *World J. Gastroenterol.* 2020; **26**: 6260–9.
- 72 Jaiswal AK, Chaudhary S. Effectiveness in bowel cleansing and patient tolerability of polyethylene glycol versus sodium picosulphate in patients undergoing colonoscopy. *Adv. Med.* 2020; **2020**: 1234341.
- 73 Rostom A, Dube C, Bishay K, Antonova L, Heitman SJ, Hilsden R. A randomized clinical prospective trial comparing split-dose picosulfate/magnesium citrate and polyethylene glycol for colonoscopy preparation. *PLoS One.* 2019; **14**: e021136.
- 74 Szaflarska-Poplawska A, Tunowska D, Sobieska-Poszwa O, Gorecka A, Krogulska A. The effectiveness, tolerability, and safety of different 1-day bowel preparation regimens for pediatric colonoscopy. *Gastroenterol. Res. Pract.* 2019; **2019**: 3230654.
- 75 Coskun Y, Yuksel I. Polyethylene glycol versus divided high dose senna for bowel preparation: a comparative prospective randomized study. *J. Gastroenterol. Hepatol.* 2020; **35**: 1923–9.
- 76 Ness RM, Manam R, Hoen H, Chalasani N. Predictors of inadequate preparation for colonoscopy. *Am. J. Gastroenterol.* 2001; **96**: 1797–802.
- 77 Dubois H, Creutzfeldt J, Törnqvist M, Bergenmar M. Patient participation in gastrointestinal endoscopy - From patients' perspectives. *Health Expect.* 2020; **23**: 893–903.
- 78 Sinagra E, Sferrazza S, Vitello A *et al.* Effectiveness and tolerability of very-low volume preparation for colonoscopy: a narrative review. *Curr. Drug Metab.* 2021; **22**: 85–8.