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Editorial Board Member of *World Journal of Gastroenterology*, Oscar Teramoto-Matsubara, MD, AGAF, FACG, FACP, Associate Specialist, Department of Gastroenterology, ABC Medical Center, Mexico City 11000, Mexico. teramotomd@prodigy.net.mx

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Novel frontiers of agents for bowel cleansing for colonoscopy

Milena Di Leo, Andrea Iannone, Monica Arena, Giuseppe Losurdo, Maria Angela Palamara, Giuseppe Iabichino, Pierluigi Consolo, Maria Rendina, Carmelo Luigiano, Alfredo Di Leo

ORCID number: Milena Di Leo 0000-0002-5933-8474; Andrea Iannone 0000-0002-5468-9515; Monica Arena 0000-0002-2958-3655; Giuseppe Losurdo 0000-0001-7038-3287; Maria Angela Palamara 0000-0002-2544-5685; Giuseppe Iabichino 0000-0003-3786-7292; Pierluigi Consolo 0000-0002-4850-8191; Maria Rendina 0000-0003-0077-6629; Carmelo Luigiano 0000-0001-5719-3948; Alfredo Di Leo 0000-0003-2026-1200.

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Milena Di Leo, Monica Arena, Maria Angela Palamara, Giuseppe Iabichino, Carmelo Luigiano, Unit of Digestive Endoscopy, San Paolo Hospital, Milan 20090, Italy

Andrea Iannone, Giuseppe Losurdo, Maria Rendina, Alfredo Di Leo, Section of Gastroenterology, Department of Emergency and Organ Transplantation, University of Bari, Bari 70124, Italy

Pierluigi Consolo, Unit of Digestive Endoscopy, University of Messina, Hospital "G. Martino", Messina 98121, Italy

Corresponding author: Alfredo Di Leo, MD, PhD, Doctor, Full Professor, Section of Gastroenterology, Department of Emergency and Organ Transplantation, University of Bari, Piazza Giulio Cesare, Bari 70124, Italy. alfredo.dileo@uniba.it

Abstract

The incidence of colorectal cancer (CRC) is characterized by rapid declines in the wake of widespread screening. Colonoscopy is the gold standard for CRC screening, but its accuracy is related to high quality of bowel preparation (BP). In this review, we aimed to summarize the current strategy to increase bowel cleansing before colonoscopy. Newly bowel cleansing agents were developed with the same efficacy of previous agent but requiring less amount of liquid to improve patients' acceptability. The role of the diet before colonoscopy was also changed, as well the contribution of educational intervention and the use of adjunctive drugs to improve patients' tolerance and/or quality of BP. The review also described BP in special situations, as lower gastrointestinal bleeding, elderly people, patients with chronic kidney disease, patients with inflammatory bowel disease, patients with congestive heart failure, inpatient, patient with previous bowel resection, pregnant/lactating patients. The review underlined the quality of BP should be described using a validate scale in colonoscopy report and it explored the available scales. Finally, the review explored the possible contribution of bowel cleansing in post-colonoscopy syndrome that can be related by a transient alteration of gut microbiota. Moreover, the study underlined several points needed to further investigations.

Key Words: Colonoscopy; Bowel preparation; Cleansing agents; Polyethylene glycol; Adequate cleansing; Constipation

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Core Tip: Colonoscopy is the best modality for colorectal cancer (CRC) screening, preventing death from CRC through removal of adenomatous polyps and early detection of CRC. The accuracy of colonoscopy is related to quality of bowel preparation (BP). International guidelines underlined the methods to improve BP. In this review, we aimed to summarize the current strategy to increase bowel cleansing before colonoscopy.

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INTRODUCTION

Colorectal cancer (CRC) is the third most common cancer in both genders[1] with an incidence characterized by rapid declines in the wake of widespread screening. Colonoscopy is considered the gold standard for CRC screening. Colonoscopy with removal of adenomatous polyps prevents death from CRC[2].

To perform screening colonoscopy, the high quality of endoscopic procedure is mandatory. An adequate bowel preparation (BP) is one of the most important factors, ensuring a high accuracy of procedure, thought an optimal visualization of colonic mucosa increasing adenoma detection rate (ADR)[3-5]. ADR is defined as the percentage of screening colonoscopies in which one or more conventional adenomas are detected[6]. ADR is inversely associated with the risks of interval and lower long-term CRC incidence and mortality[7,8].

Moreover, an inadequate BP is associate to prolonged procedures, higher cost leaded to repeat colonoscopy (longer hospital stay and no cost/efficacy of screening program), lower cecal intubation rates, higher risk of electrocautery and unsatisfactory patient experience with an increased likelihood of repeat procedure.

Despite European Society of Gastrointestinal Endoscopy (ESGE) Guidelines recommended a minimum of 90% procedure with adequate BP, with a target of > 95% [9], suboptimal BP is still encountered in clinical practice[10].

Other review papers regarding bowel cleansing were published[11,12]. However, new evidences change same feature of bowel cleansing process.

The aim of the present review is to describe the current literature regarding BP options, in order to explore factors that can be improved.

BP QUALITY SCALE

ESGE guidelines recommend recording the BP quality using a validated scale[9]. Validity refers to how well the scale measures what it is aimed to assess. For BP, validity could be assessed by comparison of different scales or with another parameter of colonoscopy quality. Another essential attribute of a scale is the reliability that indicates the reproducibility of the results in the same operator (intrarater reliability) or between different endoscopist (interrater reliability).

Several scales were proposed in the last decades to describe the quality of BP of colonoscopy.

The first one was the Aronchick Scale[13] and it is still one of the most commonly used validated BP quality scales in clinical trials and clinical practice.

The quality of the preparation is described as the percentage of entire colonic mucosa covered by stool, before washing or suctioning, ranging from 1 (excellent) to 5 (inadequate). No study has evaluated a threshold to define adequate the BP described by Aronchick Scale.

Validity was not evaluated in clinical studies, while inter-observer reliability was assessed in one study (coefficient was 0.77 in the total colon)[14].

The second developed scale was the Ottawa Bowel Preparation Quality Scale (OBPQS)[14]. This scale is composed by two separate scores. One score is assigned

according to global fluid quantity in the entire colon, from 0 (small amount of fluid) to 2 (large amount of fluid). The second score quantifies the visibility of three separate colon segments (right colon, mid colon and rectosigmoid colon) and also the amount of washing or suctioning required achieving optimal visualization and it ranges from 0 to 4. The total score is obtained by adding the score of each segment and total colon fluid score, ranging from 0 (excellent) to 14 (poor), before washing or suctioning. In one study, the value of at least 8 was proven to be an optimal cut-off value to define inadequate BP because of the inability to detect a 5 mm polyp[15].

The validity was also demonstrated in two study comparing OBPQS with visual analogue scale[16] and with Boston Bowel Preparation Scale (BBPS)[17].

The study of Martinato *et al*[16] detected also a good agreement between nurses and physicians, [$r = 0.6010$ (95%CI for r 0.4877 to 0.6944)]. One prospective study demonstrated the high interobserver agreement and reliability of OBPQS compared to Aronchick Scale[14] with no statistically significant differences between segment evaluations. Intra-observer reliability and clinical relevance were not evaluated.

BBPS described the colonic mucosa that can be evaluated. The advantages of this scale are multiple. First of all, it is a numeric score ranging from 0 (unprepared colon mucosa) to 9 (entire mucosa well seen) for the entire colon, avoiding the use of qualitative and subjective terms. Second vantage is that a score is assigned for each colonic segment (right colon, transverse, left colon-each one from 0 to 3), allowing a detailed description of BP. Third, the score is assigned after washing and suctioning as recommended by United States Multi-Society Task Force on Colorectal Cancer[18]. Finally, the validity and the reliability of this score has been evaluated in several studies.

The validity of the score was proven in several studies, demonstrating the association with polyp detection rate, insertion and withdrawn times, needed to repeat colonoscopy for inadequate BP. Lai *et al*[19], including 633 screening colonoscopies (22 clinicians), found an association with BBPS ≥ 5 , higher polyp-detection rate, an inversely correlation with BBPS and insertion and withdrawal times, and an inverse relation between BBPS and the need to repeat colonoscopy for an inadequate preparation. The latest inverse correlation was confirmed in the study of Calderwood *et al*[20] and in the study of Kim *et al*[21] that also confirmed a correlation with polyp detection rate (PDR). Calderwood conducted a second study with a very large sample size (74 endoscopists performed 2516 colonoscopies) finding that a total score of ≥ 6 and score of ≥ 2 for each segment is the definition of adequate BP[22]. The best cut-off of 2 in each segment as definition of adequate BP is proven also by Clark *et al*[23].

The reliability was determinate in different studies demonstrating a good interobserver agreement, quantified as intraclass correlation coefficient or weighted kappa (ranging between 0.67-0.93)[19-21,24,25]. Indeed, a good intraobserver agreement were found in three different studies (weighted kappa = 0.77; 95%CI: 0.66-0.87[19]; weighted kappa = 0.78; 95%CI: 0.73-0.84)[20] and weighted kappa = 0.67; 95%CI: 0.51-0.84)[24].

The results of these large and very well conducted studies corroborating the validity and the reliability of BBPS, allowed to suggest the routine use of BBPS in the clinical practice as proposed by Parmar *et al*[26].

Promising data come from artificial intelligence, as recently described by Zhou *et al* [27]. They developed a deep convolution neural network called ENDOANGEL to assign BBPS, with a 91.9% of accuracy. In the unique study on this topic, so further data are needed to support the routinely use of this system.

Bubbles scale

None of the previous scales provided an adequate evaluation of presence of bubbles that can impact on mucosa evaluation. This inadequacy affects also the strength of the conclusions of two recent meta-analyses reporting a benefit of added oral simethicone to increase BP[28,29].

The amount of foam/bubble interfering with colonic visualization was also measured in different studies regarding BP[30-42].

Parente *et al*[30] evaluated the presence of bubble in terms of the overall impact on mucosal visualization, as excellent (clear imaging, no or minimal amount of bubbles or foam that can be easily removed), fair (modest amount of bubbles and foam that can be cleared, with some waste of time) and insufficient (a large amount of foam and bubbles that reduces significantly the clear visualization of the mucosa) in each bowel segment.

A Bowel Bubble Scale, a four-point scoring system (0, no bubbles; 1, minimal or occasional bubbles; 2, moderate or obviously present; and 3, severe or many bubbles that vision is obscured) was developed by McNally *et al*[32] and used by Guo *et al*[31] and Yuanchao *et al*[33].

Another intraluminal Bubbles Scale was used in studies performed by Matro *et al* [34] graded 4 segments of the colon (cecum, right colon and hepatic flexure, transverse colon and splenic flexure, and colon distal to the splenic flexure) and each colon segment was graded using a 3-point scale (A = no/minimal bubbles, B = moderate bubbles/interfere with detecting a 5 mm polyp, and C = severe bubbles/interfere with detecting a 10 mm polyp).

Repici *et al* [35] measured the bubble score according the overall mucosal visibility using a 3-grading scale from grade 0 (optimal) to grade 2 (insufficient), the same scale was used by Spada *et al* [38] to assess mucosal visibility.

Yoo *et al* [36,37] used a scale assigned the bubble score in accordance with the degree of obscuration by bubbles, bile, or debris from 0 (severe obscuration) to 3 (no obscuration), applied also by Zhang *et al* [40].

A revised version of this scale was adopted by Rishi *et al* [39], who assigned the score (from 1 to 4) according the percent circumference of colonic mucosa clear of all bubbles/foam, not divided between segments of the colon.

Movareji *et al* [41] used a bubble scale used adapted from the one previously described by Sudduth *et al* [42], evaluating the entire colon by adding each individual segment score (from 0, no or minimal bubbles, to 3, bubbles filling the entire lumen).

In the two latest studies, the authors failed to validate and establish the reliability of the colon bubble scales. In particular, the interobserver agreement for bubble scale score was moderate ($\kappa = 0.537$ [41], $\kappa = 0.4024$ [39]).

Recently a new scale, named Colon Endoscopic Bubble Scale (CEBuS) was developed and its reliability was determined in a multicentre prospective observational study [43]. The scale CEBuS ranged from 0 (no or minimal bubbles, covering < 5% of the surface) to 2 (bubbles covering > 50%). A high intraobserver reliability [$\kappa = 0.82$ (95% CI: 0.75-0.88) *vs* 0.86 (95% CI: 0.85-0.88)] and high interobserver agreement [ICC 0.83 (0.73-0.89) *vs* 0.90 (0.86-0.94)] were reported in both experts group and mix expert/non-expert group. These encouraging preliminary results needed to be confirmed with a larger study.

CLEANSING AGENTS FOR BP

Four-liter high-volume polyethylene glycol (PEG)-based preparations were the first formulations introduced for bowel cleansing prior to colonoscopy. These isosmotic solutions provide rates of adequate BP > 90% [44-47], without producing relevant fluid shifts or electrolyte imbalances [11]. Despite high efficacy and safety, the large volume of liquids and poor solution taste may decrease patients' compliance to the assumption of these preparations [12].

PEG-based and non-PEG-based low-volume solutions have been developed in order to reduce the total volume of preparation and improve patients' acceptability. The hyperosmotic 2 L PEG-based agents (containing PEG plus ascorbate, citrate, or bisacodyl) showed similar efficacy in bowel cleansing with higher patients' tolerability and willingness to repeat the preparation compared to high-volume PEG-based solutions in meta-analyses [44,45] and randomized trials [38,48-51]. Additionally, comparable adenoma detection rates were found between 2 L PEG plus ascorbate and 4 L PEG solutions [49,50]. A recently developed low-volume solution of 1 L PEG plus ascorbate had similar quality of BP, adenoma detection rate, and safety profile compared to 2 L PEG plus ascorbate in a randomized trial [52]. This preparation showed higher rate of adequate colon cleansing compared to 4 L high-volume PEG (84.3% *vs* 77.4%, $P = 0.039$) in hospitalized patients, with no differences in electrolyte imbalances, creatinine and haematocrit [53]. However, these results are based on a post-hoc analysis of an observational study. The non-PEG-based hyperosmotic low-volume preparations include magnesium citrate with sodium picosulfate, oral sulfate solution (*i.e.* trisulfate), and oral sodium phosphate. As the PEG-based low-volume solutions, these formulations showed non-inferiority in terms of efficacy and better safety profile as well as patients' tolerability compared to 4 LPEG [54-58].

On these bases, current ESGE guidelines recommend low-volume PEG-based and non-PEG-based solutions as alternatives of equal efficacy to high-volume PEG-based formulation for routine BP, with the exception of oral sodium phosphate for the relevant risk of kidney injury [59]. However, safety concerns have been raised on hyperosmotic low-volume agents in patients at risk for hydroelectrolyte imbalances, such as those suffering from severe renal insufficiency or congestive heart failure. Moreover, ascorbate-containing solutions are contraindicated in people with phenylketonuria or glucose-6-phosphate dehydrogenase deficiency [60]. Thus, the

choice of the adequate preparation for bowel cleansing prior to colonoscopy should be individualized, especially in specific categories of patients at high risk of adverse events.

TIMING OF BP

Timing of consuming BP is highly important. The last dose of BP should be started in the 5 h before colonoscopy and ended 2 h before the scheduled time of the procedure [59]. This recommendation is translated in clinical practice in two different timing for colonoscopy of the morning and colonoscopy of the afternoon.

For morning colonoscopy, both American and European Guidelines strongly recommend split-dose regimens [59,61,62].

Split-dose regimen is defined as assuming half of the BP the day before the colonoscopy and half on the day of the colonoscopy. Several evidences provided the superiority of split dose regimens over a day-before preparation to achieve a better colon cleaning, regardless the cleansing agent [48,63-69]. Moreover, the split-dose preparation showed better patient tolerability and higher proportion of patients willing to repeat the regimen [47,70].

Effectiveness of colonoscopy is highly dependent on the quality of BP. Different observational studies and also a recent meta-analysis found that split dose preparations increase adenoma detection rate [69,71-75]. The meta-analysis demonstrated also an increase rate of advance adenomas and sessile serrated polyps in split-dose regimen, including seven trials comparing split-dose *vs* day-before BP regimens. No differences in the same variables were found comparing split-dose and same-day BPs [75]. Another meta-analysis did not confirm the increase of ADR with split dose regimen, but it included only 4 randomized controlled trials (RCTs) [70] with moderate overall quality of evidence.

For afternoon colonoscopy, the same-day BP is recommended [59].

Considering studies including higher number of colonoscopies scheduled in the afternoon, same-day BP showed similar rate of adequate bowel cleaning, with no difference in tolerability and patient willingness to repeat it, comparing to split-dose regimens. The ADR was similar for the two regimens as showed by two different meta-analysis [75,76]. Moreover, patients in same-day regimens reported better sleep quality (OR 0.44, 95% CI: 0.24-0.82) [77].

Instead, the same-day regimen showed a significantly lower quality of BP considering studies including only morning colonoscopies [78], or lower patient tolerability and compliance [79,80], with lower willingness to repeat the same preparation in the future [79].

DIET BEFORE COLONOSCOPY

Diet restriction has traditionally been recommended before colonoscopy because it can reduce the amount of stools in the intestines, but adherence is low. The European and American Societies of Gastrointestinal Endoscopy actually recommended the use of a low residue diet (LRD) for colonoscopy defined as a diet with a total fiber intake inferior of 10 g/day [59,81].

Two meta-analysis [82,83] including studies comparing LRD with clear liquid diet (CLD) on the day before colonoscopy examination, found a significantly higher odds of tolerability and willingness to repeat preparation with no differences in adequate BPs or adverse effects.

In the last year two new meta-analysis comparing LRD *vs* CLD for BP before colonoscopy were published [84,85].

Zhang *et al* [84] performed a systematic literature search until September 2019 and they included twenty RCTs. Adequacy of bowel cleansing and polyps detection rate were similar in both groups ($P = 0.79$ and $P = 0.68$ respectively). There were significantly fewer adverse events in individuals in LRD group: nausea ($P = 0.02$) vomiting ($P = 0.04$), hunger ($P < 0.001$), and headache ($P = 0.02$). In addition, significantly more individuals in the LRD group found it easy to complete the diet ($P = 0.01$) and showed willingness to repeat it ($P = 0.005$).

Chen *et al* [85] included 16 studies and found a significantly better tolerability and willingness to repeat intestinal preparation in patients with LRD compared with CLD (both $P < 0.05$), but no differences with adequate intestinal preparations, detected polyp or overall adverse reactions.

These latest evidences showed that LRD is a promising approach for BP before colonoscopy with comparable adequacy of BP with that of CLD.

A recent study of Gimeno-Garcia *et al*[86] aimed to assess if a 3 d LRD is better regarding bowel cleansing than a single day LRD regimen, concluded that there is not a concrete advantage.

Recently, Avalos *et al*[87] performed a meta-analysis of randomized trials comparing BP outcomes between a LRD or regular diet (RD) compared with a CLD. Twelve RCTs, grouped patients taking a LRD (8 RCTs) or a RD (4 RCTs) and compared them to patients taking a CLD. In the 7 high-quality studies included, they no found differences in BP quality among the LRD/RD and CLD groups (RR 0.98; 95%CI: 0.93-1.04). Tolerability and willingness to repeat were better in the liberalized diet arm. There was no significant difference in the adenoma detection rate, whereas hunger was more common in the CLD group (RR 1.93, 95%CI: 1.13-3.3)[87]. Further studies are needed to confirm other findings, [Table 1](#).

ADJUNCTIVE DRUGS

Various adjuvant drugs have been added to standard BP regimens to increase quality of BP by direct action (as simethicone) or by the improving of patient experience.

Simethicone

Simethicone is an antifoaming agent using to reduce excessive gas, abdominal discomfort, and bubble formation in the gastrointestinal tract.

Several RCTs have investigated the effect of oral simethicone on bowel cleansing.

Since 2011, four meta-analyses were conducted. The first one[88] included 7 RCTs (714 patients) comparing purgative plus Simethicone with purgative alone for colonoscopy. The air bubbles were significantly decreased, while no difference in adequate colon preparation was found.

The role of added oral simethicone on ADR was investigated in meta-analysis of Pan *et al*[89]. Such meta-analysis included 6 RCTs (1855 patients) and found an increase of ADR in simethicone group. Different result was found by another meta-analysis[28], including 12 randomized controlled studies (6003 participants) that found no difference in ADR between the groups with or without simethicone.

The last meta-analysis by Moolla *et al*[29] aimed to determine the effect that simethicone has on bowel cleanliness, ADR and tolerability, and included 16 RCTs (5630 patients) using PEG for bowel agent cleaning. Authors found an increase rate of adequate BP in PEG cohort with simethicone compared with PEG alone (OR 1.48), considering all 16 RCTs.

This finding was confirmed in three subgroup analysis: (1) Excluding RCT with bisacodyl or with different volume preparation; (2) Including only preparation with PEG 2 L; and (3) PEG single dosing the day before. On the other hand, considering patients with split dose regimen, no difference was found in adequate bowel colonoscopy rate between PEG group and PEG + simethicone group.

Regarding ADR, no difference was found considering all studies evaluating ADR (7 studies). However, ADR was significantly higher increase in simethicone group and in the subgroup analysis considering single-dosing preparations (3 RCTs). Moreover, the authors found an increase of bloating in PEG alone group, while no differences were found in the incidence of nausea, vomiting and abdominal pain.

Currently, ESGE guidelines suggest the use of oral simethicone for BP[59].

Instead, the routine use of simethicone through the working channel is advised against by ESGE guidelines[90], due to evidence that simethicone may contribute to biofilm formation in the endoscope working channel, reducing reprocessing effectiveness[91].

Recently, multi-society guideline[92] underlined factors associated to simethicone persistence in the endoscope channel. The first is the concentration, the second is the modality of delivering. So, when simethicone is needed, the guideline suggested the use of lowest concentration (less the 5%) and the smallest volume needed avoiding the simethicone delivering *via* water bottle/irrigation jet channel.

Similar recommendations were reported by Gastroenterological Society of Australia [93], despite allowing the administration of simethicone the endoscope irrigation channel.

Both guidelines recommended a strict adherence to manufactures' instruction for each passage of simethicone use (way for simethicone administration, cleaning and disinfection of the scope).

Table 1 Low fiber diet on the day preceding colonoscopy

Type of food	Allow	Avoid
Milk and milk products	Skim or low-fat milk; Buttermilk; Low-fat cheeses; Low-fat ice cream; Sherbet; Yogurt without seeds, berries, rinds or nuts	Yogurt with seeds, berries, rinds or nuts
Vegetables	Any well-cooked vegetables without seeds (<i>e.g.</i> , carrots, pumpkin); Lettuce; Potatoes without skin; Strained vegetable juice	All raw vegetables, except lettuce; Broccoli; Brussels sprouts; Cabbage and sauerkraut; Cauliflower; Corn; Fried vegetables; Greens (mustard, turnip, collards); Mushrooms; Okra; Onions; Peppers; Potato skins
Meats and other protein foods	Eggs; Smooth nut butters; Tofu; Tender, well-cooked meat, poultry and fish	Chunky nut butters; Legumes; Nuts or seeds; Tough or chewy cuts of meat
Grains	Bread, bagels, rolls, crackers, pasta and cereals made from white or refined flour (<i>e.g.</i> , crispy rice cereal and cornflakes); Cooked cereals (farina and creamy rice); White rice	Brown rice and wild rice; Cereals made from whole grains; Grain products made with seeds or nuts; Whole-wheat or whole-grain breads, rolls, crackers or pasta
Fruits	Fruit juice without pulp (except prune juice); Most canned, soft and pureed fruit without skin (except pineapple); Peeled apple; Ripe banana or melons	All raw fruits except peeled apple, ripe bananas and melon; Canned berries, canned cherries; Dried fruits, including raisins; Prunes and prune juice
Beverages	Coffee, tea, chamomile; Sports drinks; Water	
Condiments	Ketchup and mustard; Margarine, butter, oils, mayonnaise, sour cream and salad dressing; Plain gravies; Spices, cooked herbs, bouillon, broth, and soups made with allowed vegetables; Sugar, clear jelly, honey and syrup	

Agents improving patient experience

To increase the quality of BPs, several adjuncts were evaluated. All of them act through the increasing of tolerability and palatability of bowel cleaning agents.

Four studies evaluated the role of drinks different from water. One study evaluated the BP, the palatability and the adverse effects of Coca-Cola (Coke) Zero as solvent for PEG comparing with water. The authors found a better quality of BP and palatability in Coke group, with no difference in rate of adverse events neither in PDR[94]. The palatability is also increased with orange juice intake before drinking 2 L of PEG plus ascorbic acid[95], while no differences were found in quality of BP. Also, pineapple juice was tested to increase palatability of BP. In one single randomized study[96], patients were assigned to one of the following regimens: 4 L PEG or 2 L PEG or 2 L PEG plus 1 L of pineapple juice. The third group had better quality of bowel cleansing in the right side and in transverse colon, but no difference in tolerability.

A prospective, randomized controlled recent study of Hao *et al*[97] aimed to evaluate the effectiveness and safety of concomitant use of green tea (GT) with 2 L PEG in BP for colonoscopy. Adding GT increased the compliance, reduced adverse events with comparable bowel cleanliness in BP.

Five studies evaluated the role of tablets and gum chewing in the BP. The study of Lan *et al*[98] compared two groups of patients received 2 L PEG alone or plus citrus reticulata peel in form of "buccal tablet" eaten between drinks. The second group had higher acceptable taste, lower rate of swallowing difficulty and adverse events with no differences in quality of colonic cleansing. Three randomized studies evaluation the contribution of gum chewing[99-101] and in all of them, patients' tolerability was better in gum chewing group than the other group. In one study[99], better quality was reached in gum chewing group, no difference was found in the other two studies.

The menthol candy drops[102] were used in one randomized study demonstrating the better grade preparation in candy drops-added group, with no difference in side effects.

A recent systematic review and meta-analysis was performed including 6 single-blind RCTs (1187 patients)[103]. The included adjuncts were citrus reticulata peel, orange juice, menthol candy drops, simethicone, Coke Zero and sugar-free chewing gum. The study concluded that the adjunct improved palatability and willingness to repeat BP, with fewer side effects as bloating, vomiting, but no difference in nausea or abdominal pain. Moreover, the rate of adequate BP was higher in the adjunct group.

EDUCATIONAL INTERVENTION

In the effort to improve BP, several methods emphasizing the importance of BP quality and the instructions for BP were evaluated. Different methods were tested, including

pictures, cartoon visual aids, booklets, video, instructions by the nurse, short message service, smartphone applications were evaluated separately with conflicting results.

Seven meta-analyses[104-110] were conducted to compare the adequacy of BP in patients who received enhanced instructions and patients who received standard ones. All of them demonstrated that enhanced instructions are useful to improve the quality of BP, and in the same time to increased ADR.

So, both European and United States guidelines suggested the enhanced instruction before colonoscopy[18,59].

SPECIFIC CATEGORIES OF PATIENTS

Lower gastrointestinal bleeding

Colonoscopy has an important role for optimal management of acute lower gastrointestinal bleeding (LGIB), with diagnostic and therapeutic potential[111].

Colonoscopy should be performed after hemodynamic stabilization. Moreover, adequate colon cleansing is crucial to achieve before performing colonoscopy for LGIB, because of the increasing risk of perforation, and major risk of missed bleeding mucosal lesions in poorly prepped colon and properly evaluation of the entire mucosa [112].

However, cleansing the colon from stool, clots and blood is difficult to accomplish [111].

According to the latest European guidelines, preparation for colonoscopy should include 4-6 L of a polyethylene glycol solution or the equivalent, administered over 3-4 h until the rectal effluent is clear. A nasogastric tube can be placed to facilitate colon preparation in intolerant to oral intake patients. Prokinetic/anti-emetic agent immediately prior to initiating the colon preparation may reduce nausea and facilitate gastric emptying[59].

Although colonoscopy has several advantages in the management of LGIB (identification of bleeding sources, multiple therapeutic options, definitive diagnosis, reduction of hospital length of stay and safety), it also has several disadvantages (need for colon preparation and sedation, experienced staff and endoscopy facilities, low prevalence of stigmata of hemorrhage, invasive nature, and rare but serious complications)[111].

A higher risk of urgent colonoscopy adverse events may occur in elderly patients with comorbidities or on antithrombotic therapy[113,114]. BP may increase the risk of vomiting, aspiration pneumonia a volume overload[111].

Niikura *et al*[115] in a retrospective review investigated adverse events and hemodynamic instability during BP and colonoscopy in hospitalized patients with acute LGIB. They showed that during BP, the 9% of LGIB patients experienced an adverse event. None of them experienced volume overload, aspiration pneumonia or loss of consciousness; however, 7% had hypotension and 2% vomited. There were no significant differences in the five BP-related adverse events between LGIB and non-LGIB patients.

The use of lower volume or alternative colon preparation solutions in LGIB patients is not well defined, only preliminary data are available and seems encouraging[116].

The American College of Gastroenterology, ESGE and British Society of Gastroenterology recommends against un-prepped colonoscopy in the setting of acute LGIB[59, 117,118].

A prospective pilot study of Repaka *et al*[119] in severe LGIB subjects reported the feasibility and safety of unprepared hydroflush colonoscopy that combined three 1-L tap water enemas, a water-jet pump irrigation system, and a mechanical suction device to cleanse the colon. Cecal intubation was performed in 69.2% of patients and definitive bleeding sources of 38.5% of patients were detected. However, localization of diverticular bleeding, can be difficult in the setting of residual blood and stool and poor visualization may also increase the risk of perforation.

A recent single-center study performed on elderly patients with severe LGIB investigated the efficacy, safety and outcomes of unprepared polyethylene glycol-flush retrograde colon cleansing colonoscopy[120]. In this study cecal intubation was 100%, the rate of definitive bleeding sources was 90.9%. They concluded that this approach was safe, effective and reduced the time of hospital stay, therefore further data are necessary.

Although, the international guidelines recommend BP of this cohort of patients, the best modality to achieve the cleaning of the colon is still an open problem.

Chronic kidney disease and hemodialysis

The assessment of renal function is a key point in the choice of the most adequate and safe bowel cleansing agent prior to colonoscopy, since the assumption of hyperosmotic solutions may lead to dehydration and electrolyte imbalances in people with pre-existing chronic renal disease[59]. Although the relevance of the issue, high quality evidence on different preparations for this high-risk population is lacking, with available data deriving from observational studies. Lee *et al*[121] found no difference in electrolytes or estimated glomerular filtration rate (eGFR) between 4 L PEG and 2 L PEG plus ascorbate in patients with an eGFR < 60 mL/min before colonoscopy. A transient > 30% rise in creatinine levels was recorded in 7.5% and 11.5% of high-volume and low-volume group, respectively ($P > 0.05$). In a similar population, Russman *et al*[122] showed that oral sodium phosphate was associated with a 12.6 (95% CI: 1.5-106.5) times increased risk of renal function worsening compared to 4 L PEG. Frazzoni *et al*[53] compared 1 L PEG plus ascorbate with 4 L PEG, including 52 patients with chronic kidney disease, showing no different shift in serum electrolytes levels and creatinine. Considering these results, PEG-based preparations may be a safe choice in people with pre-existing mild to moderate chronic kidney disease (eGFR ranging from 89 to 30 mL/min), whereas current international guidelines do not recommend hyperosmotic low-volume PEG-based agents in people with severe renal insufficiency (eGFR < 30 mL/min) for the high risk of electrolyte imbalances. However, high quality randomized trials are needed to better clarify the safety profile of PEG-based solutions in the setting of chronic kidney disease. On opposite, the use of non-PEG-based low volume preparations should be avoided in this population due to possible magnesium toxicity or acute phosphate nephropathy[53,123].

Some warnings have been raised on the safety of bowel cleansing agent administration in people on haemodialysis[124]. Indeed, potential intravascular depletion following bowel cleansing agent intake may lead to hypotension and thrombosis of the arteriovenous fistula. Moreover, the association of BP assumption and hemodialysis treatment may cause severe hypovolaemia. Additionally, high-volume PEG-based solutions may produce fluid overload in these anuric patients. Despite these relevant concerns, there is currently no high quality evidence on the safety of the different formulations of bowel cleansing agents in this population, which has been systematically excluded from randomized trials. Only two studies explored the efficacy and safety of PEG-based preparations prior to colonoscopy in patients with pre-existing chronic kidney disease, including a cohort of people receiving hemodialysis[121,125]. The authors found no significant variation in serum electrolyte levels after the assumption of PEG-based formulations. However, these studies have a retrospective observational design and enrolled a total of 37 patients on hemodialysis. On these bases, specific recommendations on the use of bowel cleansing agents in this at-risk population are not provided. The first randomized trial comparing the efficacy and safety of 4 L PEG *vs* 2 L PEG plus citrate prior to colonoscopy in people receiving hemodialysis is currently ongoing (NCT04709770).

Inflammatory bowel disease

Adequate BP is crucial to assess disease activity in patients with inflammatory bowel disease (IBD). Moreover, the widespread promotion of dye-based and virtual chromoendoscopy as appropriate diagnostic techniques for neoplasia surveillance in this population at high risk of CRC further emphasizes the relevance of achieving high quality BP[126-128].

Evidence from randomized trials showed comparable efficacy between high-volume and low-volume PEG-based solutions in people with IBD. Manes *et al*[129] found no significant difference in adequate bowel cleansing between 4 L PEG and 2 L PEG plus bisacodyl in 216 patients with ulcerative colitis (75.0% *vs* 81.5%, respectively). Kim *et al* [130] demonstrated comparable rates of satisfactory BP between 4-liter PEG and 2-liter PEG plus ascorbate (96.2% *vs* 92.9%; $P = 0.68$) in a cohort of 109 participants with ulcerative colitis. Similarly, Kato *et al*[131] showed the non-inferiority of 2 L PEG plus ascorbate in terms of bowel cleansing compared to 4 L PEG in 70 patients with ulcerative colitis or Crohn's disease. In these trials low-volume formulations had higher patients' tolerability and willingness to repeat the preparation than 4 L PEG. Based on these results, both high-volume and low-volume PEG-based BPs are recommended in patients with IBD before colonoscopy[59], although low-volume agents may be a more advisable choice in people undergoing a considerable number of colonoscopies during their lifetime[132]. Conversely, low-volume non-PEG-based preparations should be avoided in this population, since they may cause mucosal alterations mimicking IBD[18,59]. Lawrance *et al*[133] showed a 10-fold higher rate of

preparation-induced mucosal inflammation with magnesium citrate plus sodium picosulfate and sodium phosphate compared to 4 L PEG in a randomized trial enrolling 634 participants without pre-existing or suspected IBD. Sodium phosphate-related inflammatory abnormalities were detected in 3.3% of patients in a prospective observational study including 730 participants without previous diagnosis of IBD and not using non-steroidal anti-inflammatory drugs[134].

Inpatient

Previous evidence underlined that inpatient status is one of the associated factors with inadequate BP[135-138]. In this cohort of patients, the percentage of colonoscopy with adequate preparation is between 50% and 75%[135,139,140], thus increasing the hospital length and costs[138].

It is crucial to identify predictive factors associated with inadequate BP in this cohort of patients, and in the same time, to found the best bowel cleansing agent.

The explanation could be the worse American Society of Anesthesiologists status in inpatient setting[141] prolonged immobility and the use of concomitant drugs that can impair bowel motility[142], as opiate drug[139].

The multicenter observational study of Fuccio *et al*[143] identified the factors associated with a more proper colon cleansing (physicians' meetings to optimize BP, written and oral instructions to patients, admission to gastroenterology unit, split-dose regimens, a 1 L polyethylene glycol-based purge, and 75% or more intake of BP). The authors, also, found factors associated to an increased risk of inadequate colon cleansing (bedridden status, constipation, diabetes mellitus, use of anti-psychotic drugs, and 7 or more days of hospitalization).

Considering the modifiable factors, Gkolfakis *et al*[140] evaluated the role of education interventions to increase adequate BP in a recent meta-analysis. In the six included studies, the adequacy was achieved in 77% (62%-91%) of patients with education interventions *vs* 50% (32%-68%) of patients with no intervention. However, this strategy is not enough to reach to 90% of adequate colonoscopy as required by ESGE guidelines.

Regarding the choice of BP, only one study was aimed to assess the role of low volume PEG solution in inpatient cohort. In a retrospective post-hoc propensity matching score analysis of a previously prospective observational study, Frazzoni *et al* [53] found a higher rate of adequate bowel cleansing in group prepared with 1 L-PEG plus ascorbate hyperosmolar preparation than patients with the 4 L-PEG preparation. A specifically designed study is needed to better investigate the efficacy and the safety of low volume bowel agent in this setting of patients.

Elderly people

Patients with more than 65 years require special attention during the BP before colonoscopy, due to fragile equilibrium and/or increase incidence of concomitant diseases. Large volume of BP has a better risk profile, causing less electrolyte abnormalities and low risk of dehydration, but requires a high patient's compliance. Low volume cleaning agents with magnesium citrate or bisacodyl or sodium phosphate should be avoided in this fragile category of patients, due to an increased risk of electrolyte unbalance, ischemic colitis and renal function impairment, respectively [144-146].

Only two RCTs were specifically designed to evaluate BP in elderly people. Jung *et al*[48] enrolled 230 patients aged > 65 years with normal renal function and electrolytes, randomly assigned to one of 3 arms (single-dose 4 L-PEG on the day before colonoscopy; split-dose 4 L-PEG; or split-dose 2 L-PEGA). The rate of adverse events did not differ among the 3 groups, however, patients in 2 L-PEGA group had higher willingness to repeat the same preparation than other groups. The second study[57] evaluated the efficacy safety and efficacy, safety, and acceptability of the oral sulfate solution (OSS) preparation, comparing to 4 L-PEG, in elderly patients. This RCT, enrolling 193 patients, concluded that OSS with a split-dose regimen has greater acceptability and comparable efficacy in bowel cleansing compared to 4 L PEG.

So, despite low evidence, ESGE guidelines[59] suggested the use of PEG solution in elderly patients, and ASGE guidelines[147] recommended to avoid sodium phosphate preparations in these patients.

Congestive heart failure

People with congestive heart failure are at high risk of electrolyte imbalances following the intake of BPs. Indeed, this clinical condition is associated with a decrease in renal blood flow and eGFR. This may lead to acute phosphate nephropathy, due to the reduction in phosphate excretion, or hyponatraemia, linked to hypovolaemia and

high-volume water assumption[124]. Despite the substantial lack of evidence on the efficacy and safety of BPs in this population, high-volume isotonic PEG-based solutions may represent the most adequate option for their reduced risk of causing electrolyte imbalances and fluid shifts[59,124]. Low-volume PEG-based solutions may be an alternative approach due to the reduction in the total volume of liquid intake, although they are currently not recommended in patients with significant congestive cardiac failure (New York Heart Association class III or IV) for the potential harms linked to the osmotically active components included in the formulations[59]. Regardless of the preparation used, strict monitoring is advocated when PEG-based bowel cleansing agents are administered in people with congestive heart failure. On the other hand, low-volume non-PEG based solutions should be avoided in patients with congestive cardiac failure, especially oral sodium phosphate for the risk of causing acute phosphate nephropathy[59,124].

Randomized trials comparing high-volume *vs* low-volume PEG-based preparations in people with congestive heart failure are needed to assess the efficacy and safety of these agents and inform clinical decisions.

Patients with constipation

Constipation is a common gastrointestinal disorder in the community with a global prevalence of 12%–17%[148]. It has been found that constipation exists in 11.9%–17.5% of patients undergoing colonoscopy[137,149] and it is considered one of the risk factors for inadequate BP[137,149–151].

Chen *et al*[152] investigated the efficacy, tolerance, and safety of oral sodium phosphate compared with PEG in patients with chronic constipation and demonstrated that oral sodium phosphate provides better quality BP, despite a smaller amount of intestinal air bubbles than standard 4-L PEG.

Another study of Pereyra *et al*[153] compared the efficacy of different doses of sodium phosphate (NaP) and PEG alone or with bisacodyl for colonic cleansing in constipated and non-constipated patients. In constipated patients the combination of NaP plus bisacodyl presented higher rates of satisfactory colonic cleansing than PEG (95% *vs* 66%; $P = 0.03$).

Although NaP has been shown to be effective in BP of patients with constipation, its use may be causally related to serious organ toxicity (*i.e.* renal damage and permanent renal failure). Therefore, its routine use is not recommended[59].

Despite the low quality of the evidence, additional bowel purgatives are often considered in patients with chronic constipation[59].

An Italian RCT[30] compared bowel cleansing efficacy, tolerability and acceptability of 2 L polyethylene-glycolcitrate-simethicone (PEG-CS) plus 2 d bisacodyl (reinforced regimen) *vs* 4 L PEG in patients with chronic constipation undergoing colonoscopy. There was no statistically significant difference in bowel-cleansing efficacy between the enhanced regimen 2 L PEG-CS plus 2-d bisacodyl and split-dose 4 L PEG in patients with chronic constipation. However, the low-volume PEG preparation containing simethicone showed greater patient acceptability and compliance and was associated with a reduced amount of foam and bubbles over the colonic mucosa.

In a study of Lu *et al*[154] 90 patients with constipation were enrolled and randomly divided into study group (lactulose oral solution and polyethylene glycol electrolyte powder), and control group (polyethylene glycol electrolyte powder only) with 45 patients in each group. Cleansing was significantly better in the study group than in the control group ($P < 0.05$).

One nonrandomized study of Kunz *et al*[155], including 372 patients, compared the effectiveness of high-volume (4 L) PEG solution with low-volume (2 L) PEG solution with ascorbate in constipated and non-constipated adults: no statistically significant difference between the two group was found.

A prospective, randomized, investigator-blinded trial[156] randomized 227 patients with constipation into three groups; enema before purgative use, enema after purgative use, and no enema. The authors found a statistically significant better colon cleansing in the female patients in the enema before purgative group and they concluded that use of enemas before purgatives in patients with constipation significantly improves adequacy of right colon cleansing.

In a multicenter, retrospective cohort study of Yoshida *et al*[157], the efficacy of short duration of polyethylene glycol plus electrolytes (PEG + E Movicol) in improving BP with highly concentrated PEG for colonoscopy in patients with chronic constipation was analyzed. Two or four sachets of PEG + E were prescribed for 1 wk before colonoscopy. They found an improvement rate of BP of 72.6%, regardless of gender, age, and underlying diseases. Also, insertion time and pain score were improved.

Recently, Dang *et al*[158] performed a systematic review of the literature aimed to determine the ideal BP regimen for patients with chronic constipation. Patients receiving NaP had a higher chance of a successful BP than patients receiving PEG ($P = 0.003$). So, they concluded that, in chronically constipated patients undergoing colonoscopy, the use of NaP may result in superior colonic cleanliness when compared to PEG, however quality of evidence was low. In summary, evidence that would allow recommendation of a special regimen or supplemental treatment for BP in patients with chronic constipation is still lacking. Further studies are needed to establish patient-specific colonoscopy preparation protocols, indeed ESGE does not suggest any specific BP in patients with constipation[59].

Patient with previous bowel resection

Patients with previous bowel resection for neoplasia need to undergo a strictly follow up with colonoscopy to detect anastomotic recurrence and prevent metachronous lesion[159]. A good BP is extremely important in these cohorts of patients. Unfortunately, the history of colorectal surgery is a risk factor for inadequate colon preparation. In fact, the study performed by Lim *et al*[160] is the first one demonstrating that the percentage of inadequate BP is higher in the resection group (gastric or colonic resection) than in the control group. This data was confirmed by Pontone *et al*[161] using the same cleaning agent (4 L PEG).

However, other evidence did not support this data. Indeed, In Yoo *et al*[162] did not found a statistically significant difference in adequate cleansing between patients with colonic resection and control group. So, if the patients with colonic resection are a category of patients “hard to prepare” is still debated.

Moreover, the right bowel cleaning agent is still an open problem for this cohort. In a study by Yoo *et al*[162], the BP was performed using two types of agents (2 L and 4 L). In the resection group, the univariate analysis showed a better bowel cleansing in patients who received 2 L of PEG-Asc (1 L at 8:00 PM the day before the colonoscopy, the second 1 L 5 h before the procedure).

A specifically designed study to assess the better cleaning agent in this cohort of patients was performed by Mussetto *et al*[163]. The authors did not find any difference in adequate BP between patients with prior colorectal resection using low volume *vs* high volume preparation; however, the first preparation was better tolerated. The authors demonstrated as well a greater efficacy of low volume preparation in the right colon. However, this finding needs to be taken with caution because the study was not adequately sized and powered to specifically assess this issue. So, a larger study is needed to investigate the better cleaning agent for these patients.

Recently, a prospective, single-center, randomized controlled, endoscopist-blinded study was performed aiming to compare morning-only 2 L PEG group or a split-dose 4 L PEG in patients with previous colorectal surgery for CRC[164]. Adequate BP rate and patients’ satisfaction were higher in the 4 L PEG group than in the other one.

No significant differences were found in PDR, ADR, patient compliance, tolerance, willingness to repeat the preparation or difficulty of the BP process.

Pregnant/lactating patients

Colonoscopy should be performed only if is strongly indicated in pregnant/breast-feeding women. According to ESGE guidelines there are insufficient evidence to determine for or against the use of specific regimens. PEG regimens may be preferred and tap water enemas may be considered for sigmoidoscopy[59].

Limited information is available about the safety of bowel cleansing agents during pregnancy. The systemic absorption of PEG is minimal and abdominal bloating and gas symptoms are infrequent. However, polyethylene glycol solutions have not been studied during pregnancy. Sodium phosphate solutions should be avoided during pregnancy because of it may cause fluid and electrolyte disturbance and may be associated with the risk of phosphate nephropathy. In addition, newborns may have bone demineralization and bone growth failure because of maternal phosphate overload. BP with phosphate enemas before flexible sigmoidoscopy may be safe, but has not been studied in pregnancy; instead, sigmoidoscopy with tap water enemas may be sufficient.

Therefore, flexible sigmoidoscopy with tap water enemas is preferred instead of colonoscopy[165,166]. To our knowledge, no study in the publicly available literature has yet reported the safety profiles of the various BP agents/regimens in lactating women. Interrupting breastfeeding during and after BP with cathartic agents or application of a tap water enema for sigmoidoscopy it would seem the more careful choice[167].

BP AND POST-COLONOSCOPY SYNDROME

Post-colonoscopy syndrome is a condition characterized by persistent abdominal pain, discomfort and bloating after the procedure. In more than 30% of patients, the symptoms affected the normal activity and became persistent for at least 48 h after the procedure[168].

It is more common in females and when the procedural time is long, and may be predicted by conscious sedation and irritable bowel syndrome diagnosis[169].

In this regard, it has been speculated that a transient alteration of gut microbiota, induced by bowel cleansing, could partially concur to its pathogenesis.

It is easily hypothesizable that a profound cleansing induced by ingestion of a purgative solution rich in minerals and PEG may induce a change in microbiota composition. Several studies have tried to address this issue.

In a study on ten adult patients receiving a 4 L-PEG solution, after one month a reduction in *Firmicutes* and an increase in *Proteobacteria* was observed; in particular gamma-proteobacteria were 2.5 times more abundant. At family level, an increase of *Enterobacteriaceae* and a suppression of *Lactobacillaceae* was recorded; overall, authors concluded that this profile change was hallmarked by a reduction of beneficial species [170]. In another study conducted on a pediatric population of 31 children receiving sodium picosulphate, magnesium citrate and senna, a lower diversity in microbial communities was observed after preparation, with increased *Faecalibacterium* and decreased *Ruminococcus*, *Escherichia*, *Pseudobutyrvibrio* and *Subdoligranum*[171]. Chen *et al*[172] enrolled twenty male overweight adults undergoing bowel cleansing with water and sodium phosphate and checked microbiota composition 28 d after the procedure. They identified two different microbiota phenotypes at baseline: *Bacteroides*-dominant and *Prevotella*-dominant. In the first group, preparation induced *Bulleida* appearance, while in the second one an increase in *Akkermansia* was noted. Interesting, authors underlined that both *Bulleida* and *Akkermansia* are associated with type 2 diabetes and obesity.

It is a debated topic whether the change in microbiota composition is transient. Mai *et al*[173] have demonstrated that these alterations may persist for several weeks.

On the other hand, a study[174] conducted on 23 healthy adults receiving 2 L-PEG and ascorbate showed a 31-fold reduction of microbiota load. However, within 14 d, normalization of such imbalance was observed. Interestingly, a single dose (instead of split preparation) implied more profound changes with increase of *Proteobacteria* and *Fusobacteria*. Additionally, it was demonstrated that the preparation increased pH, thus lowering species producing short chain fatty acids and reducing mucous layer. Someone has speculated that in this study the reversion to microbiota normality could have been justified by the fact that only young patients have been enrolled, thus prompting the need of studies on a more variegated population[175].

However, some studies did not find radical difference in taxonomic abundance after BP[176]. For example, in a Japanese study[177] on eight young adults receiving sodium picosulphate and sennosides, it was observed only a transient modification with increase of *Streptococcus* that reverted after 14 d. However, in this study, a more evident change in microbiota-derived metabolites was found, with increase in alanine, carnitine, choline and others. Similarly, O'Brien *et al*[178] recruited 15 adults who were given 2 L-PEG plus bisacodyl, and, after 3 mo, only four patients did not return to pre-colonoscopy microbiota state.

Only one study was specifically aimed to evaluate the microbiota composition in post-colonoscopy syndrome. In a South Korean study[179], 24 patients underwent colonoscopy after 2 L-PEG plus ascorbate bowel cleansing with evaluation of microbiota composition. Five out of 24 experienced abdominal pain, discomfort, distension, constipation or diarrhea after the endoscopy. It was found that these patients had a high ratio *Firmicutes*/*Bacteroidetes* compared to those without post-colonoscopy syndrome. Moreover, they exhibited a higher alpha diversity, which progressively improved after the colonoscopy, paralleling the regression of symptoms.

Two RCT studies evaluated the role of probiotic administration after colonoscopy in the resolution of bloating, abdominal pain and altered bowel function post colonoscopy. In the first one probiotic group had a lower number of pain day after colonoscopy performed with air insufflation[180]. The same group did not found significant difference in post-procedural discomfort, bloating nor time to return of normal bowel function between probiotic and placebo groups, after colonoscopies performed with CO₂ insufflation[181].

Therefore, despite the evidences are scarce and worth of investigation in the future, these researches could represent a hint about the involvement of microbiota, BP and insufflation in pathogenesis of minor complications after colonoscopy.

REFERENCES

- 1 Siegel RL, Miller KD, Jemal A. Cancer statistics, 2020. *CA Cancer J Clin* 2020; **70**: 7-30 [PMID: 31912902 DOI: 10.3322/caac.21590]
- 2 Zauber AG, Winawer SJ, O'Brien MJ, Lansdorp-Vogelaar I, van Ballegooijen M, Hankey BF, Shi W, Bond JH, Schapiro M, Panish JF, Stewart ET, Waye JD. Colonoscopic polypectomy and long-term prevention of colorectal-cancer deaths. *N Engl J Med* 2012; **366**: 687-696 [PMID: 22356322 DOI: 10.1056/NEJMoal100370]
- 3 Sulz MC, Kröger A, Prakash M, Manser CN, Heinrich H, Misselwitz B. Meta-Analysis of the Effect of Bowel Preparation on Adenoma Detection: Early Adenomas Affected Stronger than Advanced Adenomas. *PLoS One* 2016; **11**: e0154149 [PMID: 27257916 DOI: 10.1371/journal.pone.0154149]
- 4 Clark BT, Rustagi T, Laine L. What level of bowel prep quality requires early repeat colonoscopy: systematic review and meta-analysis of the impact of preparation quality on adenoma detection rate. *Am J Gastroenterol* 2014; **109**: 1714-1723; quiz 1724 [PMID: 25135006 DOI: 10.1038/ajg.2014.232]
- 5 Pontone S, Hassan C, Maselli R, Pontone P, Angelini R, Brighi M, Patrizi G, Pironi D, Magliocca FM, Filippini A. Multiple, zonal and multi-zone adenoma detection rates according to quality of cleansing during colonoscopy. *United European Gastroenterol J* 2016; **4**: 778-783 [PMID: 28408995 DOI: 10.1177/2050640615617356]
- 6 Rex DK, Bond JH, Winawer S, Levin TR, Burt RW, Johnson DA, Kirk LM, Litlin S, Lieberman DA, Waye JD, Church J, Marshall JB, Riddell RH; U. S. Multi-Society Task Force on Colorectal Cancer. Quality in the technical performance of colonoscopy and the continuous quality improvement process for colonoscopy: recommendations of the U.S. Multi-Society Task Force on Colorectal Cancer. *Am J Gastroenterol* 2002; **97**: 1296-1308 [PMID: 12094842 DOI: 10.1111/j.1572-0241.2002.05812.x]
- 7 Corley DA, Jensen CD, Marks AR, Zhao WK, Lee JK, Doubeni CA, Zauber AG, de Boer J, Fireman BH, Schottinger JE, Quinn VP, Ghai NR, Levin TR, Quesenberry CP. Adenoma detection rate and risk of colorectal cancer and death. *N Engl J Med* 2014; **370**: 1298-1306 [PMID: 24693890 DOI: 10.1056/NEJMoal1309086]
- 8 Cross AJ, Robbins EC, Saunders BP, Duffy SW, Wooldrage K. Higher Adenoma Detection Rates at Screening Associated With Lower Long-Term Colorectal Cancer Incidence and Mortality. *Clin Gastroenterol Hepatol* 2020 [PMID: 32931959 DOI: 10.1016/j.cgh.2020.09.020]
- 9 Kaminski MF, Thomas-Gibson S, Bugajski M, Bretthauer M, Rees CJ, Dekker E, Hoff G, Jover R, Suchanek S, Ferlitsch M, Anderson J, Roesch T, Hultcranz R, Racz I, Kuipers EJ, Garborg K, East JE, Rupinski M, Seip B, Bennett C, Senore C, Minozzi S, Bisschops R, Domagk D, Valori R, Spada C, Hassan C, Dinis-Ribeiro M, Rutter MD. Performance measures for lower gastrointestinal endoscopy: a European Society of Gastrointestinal Endoscopy (ESGE) quality improvement initiative. *United European Gastroenterol J* 2017; **5**: 309-334 [PMID: 28507745 DOI: 10.1177/2050640617700014]
- 10 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 [PMID: 22381531 DOI: 10.1016/j.gie.2012.01.005]
- 11 Rutherford CC, Calderwood AH. Update on Bowel Preparation for Colonoscopy. *Curr Treat Options Gastroenterol* 2018; **16**: 165-181 [PMID: 29404921 DOI: 10.1007/s11938-018-0165-3]
- 12 Millien VO, Mansour NM. Bowel Preparation for Colonoscopy in 2020: A Look at the Past, Present, and Future. *Curr Gastroenterol Rep* 2020; **22**: 28 [PMID: 32377915 DOI: 10.1007/s11894-020-00764-4]
- 13 Aronchick CA, Lipshutz WH, Wright SH, Dufrayne F, Bergman G. A novel tableted purgative for colonoscopic preparation: efficacy and safety comparisons with Colyte and Fleet Phospho-Soda. *Gastrointest Endosc* 2000; **52**: 346-352 [PMID: 10968848 DOI: 10.1067/mge.2000.108480]
- 14 Rostom A, Jolicoeur E. Validation of a new scale for the assessment of bowel preparation quality. *Gastrointest Endosc* 2004; **59**: 482-486 [PMID: 15044882 DOI: 10.1016/s0016-5107(03)02875-x]
- 15 Chan M, Birnstein E, Patel N, Chan L, Laine L, Kline M. Ottawa score of 8 or greater is an optimal cut-off point for inadequate bowel preparation. *Am J Gastroenterol* 2011; **106**: S431-S432 [DOI: 10.14309/00000434-201110002-01156]
- 16 Martinato M, Frankovic I, Caccaro R, Scacchi M, Cesaro R, Marzari F, Colombara F, Compagno D, Judet S, Sturniolo GC. Assessment of bowel preparation for colonoscopy: comparison between different tools and different healthcare professionals. *Dig Liver Dis* 2013; **45S**: S195-S196 [DOI: 10.1016/S1590-8658(13)60558-7]
- 17 Lee YJ, Kim ES, Cho KB, Park KS, Lee Jy, Lee YS, Choi WY, Kwon TH. Comparison of Ottawa and Boston bowel preparation scales for adenoma detection rate. *Gastrointest Endosc* 2016; **85**: AB413 [DOI: 10.1016/j.gie.2016.03.1043]
- 18 Johnson DA, Barkun AN, Cohen LB, Dominitz JA, Kaltenbach T, Martel M, Robertson DJ, Boland CR, Giardello FM, Lieberman DA, Levin TR, Rex DK; 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 [PMID: 25239068 DOI: 10.1053/j.gastro.2014.07.002]
- 19 Lai EJ, Calderwood AH, Doros G, Fix OK, Jacobson BC. The Boston bowel preparation scale: a valid and reliable instrument for colonoscopy-oriented research. *Gastrointest Endosc* 2009; **69**: 620-

- 625 [PMID: [19136102](#) DOI: [10.1016/j.gie.2008.05.057](#)]
- 20 **Calderwood AH**, Jacobson BC. Comprehensive validation of the Boston Bowel Preparation Scale. *Gastrointest Endosc* 2010; **72**: 686-692 [PMID: [20883845](#) DOI: [10.1016/j.gie.2010.06.068](#)]
- 21 **Kim EJ**, Park YI, Kim YS, Park WW, Kwon SO, Park KS, Kwak CH, Kim JN, Moon JS. A Korean experience of the use of Boston bowel preparation scale: a valid and reliable instrument for colonoscopy-oriented research. *Saudi J Gastroenterol* 2014; **20**: 219-224 [PMID: [25038207](#) DOI: [10.4103/1319-3767.136950](#)]
- 22 **Calderwood AH**, Schroy PC 3rd, Lieberman DA, Logan JR, Zurfluh M, Jacobson BC. Boston Bowel Preparation Scale scores provide a standardized definition of adequate for describing bowel cleanliness. *Gastrointest Endosc* 2014; **80**: 269-276 [PMID: [24629422](#) DOI: [10.1016/j.gie.2014.01.031](#)]
- 23 **Clark BT**, Protiva P, Nagar A, Imaeda A, Ciarleglio MM, Deng Y, Laine L. Quantification of Adequate Bowel Preparation for Screening or Surveillance Colonoscopy in Men. *Gastroenterology* 2016; **150**: 396-405; quiz e14-e15 [PMID: [26439436](#) DOI: [10.1053/j.gastro.2015.09.041](#)]
- 24 **Gao Y**, Lin JS, Zhang HD, Lin MX, Cheng CS, Wu SZ. Pilot validation of the Boston Bowel Preparation Scale in China. *Dig Endosc* 2013; **25**: 167-173 [PMID: [23368700](#) DOI: [10.1111/j.1443-1661.2012.01356.x](#)]
- 25 **Schindler AE**, Chan WW, Laborde CJ, Obstein KL. Reliability of the Boston Bowel Preparation Scale in the Endoscopy Nurse Population. *Clin Gastroenterol Hepatol* 2016; **14**: 775-776 [PMID: [25460559](#) DOI: [10.1016/j.cgh.2014.11.011](#)]
- 26 **Parmar R**, Martel M, Rostom A, Barkun AN. Validated Scales for Colon Cleansing: A Systematic Review. *Am J Gastroenterol* 2016; **111**: 197-204; quiz 205 [PMID: [26782820](#) DOI: [10.1038/ajg.2015.417](#)]
- 27 **Zhou J**, Wu L, Wan X, Shen L, Liu J, Zhang J, Jiang X, Wang Z, Yu S, Kang J, Li M, Hu S, Hu X, Gong D, Chen D, Yao L, Zhu Y, Yu H. A novel artificial intelligence system for the assessment of bowel preparation (with video). *Gastrointest Endosc* 2020; **91**: 428-435.e2 [PMID: [31783029](#) DOI: [10.1016/j.gie.2019.11.026](#)]
- 28 **Yeh JH**, Hsu MH, Tseng CM, Chen TH, Huang RY, Lee CT, Lin CW, Wang WL. The benefit of adding oral simethicone in bowel preparation regimen for the detection of colon adenoma: A systematic review and meta-analysis. *J Gastroenterol Hepatol* 2019; **34**: 830-836 [PMID: [30311262](#) DOI: [10.1111/jgh.14508](#)]
- 29 **Moolla M**, Dang JT, Shaw A, Dang TNT, Tian C, Karmali S, Sultanian R. Simethicone decreases bloating and improves bowel preparation effectiveness: a systematic review and meta-analysis. *Surg Endosc* 2019; **33**: 3899-3909 [PMID: [31451919](#) DOI: [10.1007/s00464-019-07066-5](#)]
- 30 **Parente F**, Vailati C, Bargiggia S, Manes G, Fontana P, Masci E, Arena M, Spinzi G, Baccarin A, Mazzoleni G, Testoni PA. 2-Litre polyethylene glycol-citrate-simethicone plus bisacodyl vs 4-litre polyethylene glycol as preparation for colonoscopy in chronic constipation. *Dig Liver Dis* 2015; **47**: 857-863 [PMID: [26232311](#) DOI: [10.1016/j.dld.2015.06.008](#)]
- 31 **Guo R**, Wang YJ, Liu M, Ge J, Zhang LY, Ma L, Huang WY, Zhai HH. The effect of quality of segmental bowel preparation on adenoma detection rate. *BMC Gastroenterol* 2019; **19**: 119 [PMID: [31286888](#) DOI: [10.1186/s12876-019-1019-8](#)]
- 32 **McNally PR**, Maydonovitch CL, Wong RK. The effect of simethicone on colonic visibility after night-prior colonic lavage. A double-blind randomized study. *J Clin Gastroenterol* 1989; **11**: 650-652 [PMID: [2584664](#) DOI: [10.1097/00004836-198912000-00010](#)]
- 33 **Yuanchao H**, Xueping L, Tao L, Jianping N, Man M. The advantage of polyethylene glycol electrolyte solution combined with lactulose in patients with long interval preparation-to-colonoscopy. *Turk J Gastroenterol* 2020; **31**: 23-29 [PMID: [32009610](#) DOI: [10.5152/tjg.2020.18888](#)]
- 34 **Matro R**, Tupchong K, Daskalakis C, Gordon V, Katz L, Kastenber D. The effect on colon visualization during colonoscopy of the addition of simethicone to polyethylene glycol-electrolyte solution: a randomized single-blind study. *Clin Transl Gastroenterol* 2012; **3**: e26 [PMID: [23238113](#) DOI: [10.1038/ctg.2012.16](#)]
- 35 **Repici A**, Cestari R, Annese V, Biscaglia G, Vitetta E, Minelli L, Trallori G, Orselli S, Andriulli A, Hassan C. Randomised clinical trial: low-volume bowel preparation for colonoscopy - a comparison between two different PEG-based formulations. *Aliment Pharmacol Ther* 2012; **36**: 717-724 [PMID: [22924336](#) DOI: [10.1111/apt.12026](#)]
- 36 **Yoo IK**, Lee JS, Chun HJ, Jeon YT, Keum B, Kim ES, Choi HS, Lee JM, Kim SH, Nam SJ, Kang HS, Lee HS, Kim CD, Um SH, Seo YS, Ryu HS. A randomized, prospective trial on efficacy and tolerability of low-volume bowel preparation methods for colonoscopy. *Dig Liver Dis* 2015; **47**: 131-137 [PMID: [25464897](#) DOI: [10.1016/j.dld.2014.10.019](#)]
- 37 **Yoo IK**, Jeon YT, Kang SH, Lee JH, Kim SH, Lee JM, Choi HS, Kim ES, Keum B, Chun HJ, Lee HS, Kim CD. Improving of bowel cleansing effect for polyethylene glycol with ascorbic acid using simethicone: A randomized controlled trial. *Medicine (Baltimore)* 2016; **95**: e4163 [PMID: [27428209](#) DOI: [10.1097/MD.0000000000004163](#)]
- 38 **Spada C**, Cesaro P, Bazzoli F, Saracco GM, Cipolletta L, Buri L, Crosta C, Petruzzello L, Ceroni L, Fuccio L, Giordano C, Elia C, Rotondano G, Bianco MA, Simeth C, Consalvo D, De Roberto G, Fiori G, Campanale M, Costamagna G. Evaluation of Clensia®, a new low-volume PEG bowel preparation in colonoscopy: Multicentre randomized controlled trial vs 4L PEG. *Dig Liver Dis* 2017; **49**: 651-656 [PMID: [28233684](#) DOI: [10.1016/j.dld.2017.01.167](#)]

- 39 **Rishi M**, Kaur J, Ulanja M, Manasewitsch N, Svendsen M, Abdalla A, Vemala S, Kewanyama J, Singh K, Singh N, Gullapalli N, Osgard E. Randomized, double-blinded, placebo-controlled trial evaluating simethicone pretreatment with bowel preparation during colonoscopy. *World J Gastrointest Endosc* 2019; **11**: 413-423 [PMID: [31236194](#) DOI: [10.4253/wjge.v11.i6.413](#)]
- 40 **Zhang S**, Zheng D, Wang J, Wu J, Lei P, Luo Q, Wang L, Zhang B, Wang H, Cui Y, Chen M. Simethicone improves bowel cleansing with low-volume polyethylene glycol: a multicenter randomized trial. *Endoscopy* 2018; **50**: 412-422 [PMID: [29132175](#) DOI: [10.1055/s-0043-121337](#)]
- 41 **Moraveji S**, Casner N, Bashashati M, Garcia C, Dwivedi A, Zuckerman MJ, Carrion A, Ladd AM. The role of oral simethicone on the adenoma detection rate and other quality indicators of screening colonoscopy: a randomized, controlled, observer-blinded clinical trial. *Gastrointest Endosc* 2019; **90**: 141-149 [PMID: [30926430](#) DOI: [10.1016/j.gie.2019.03.018](#)]
- 42 **Sudduth RH**, DeAngelis S, Sherman KE, McNally PR. The effectiveness of simethicone in improving visibility during colonoscopy when given with a sodium phosphate solution: a double-blind randomized study. *Gastrointest Endosc* 1995; **42**: 413-415 [PMID: [8566629](#) DOI: [10.1016/s0016-5107\(95\)70041-2](#)]
- 43 **Taveira F**, Hassan C, Kaminski MF, Ponchon T, Benamouzig R, Bugajski M, de Castelbajac F, Cesaro P, Chergui H, Goran L, Minelli Grazioli L, Janičko M, Januszewicz W, Lamonaca L, Lenz J, Negreanu L, Repici A, Spada C, Spadaccini M, State M, Szlak J, Veseliny E, Dinis-Ribeiro M, Areia M. The Colon Endoscopic Bubble Scale (CEBuS): a two-phase evaluation study. *Endoscopy* 2020 [PMID: [33285583](#) DOI: [10.1055/a-1331-4325](#)]
- 44 **Xie Q**, Chen L, Zhao F, Zhou X, Huang P, Zhang L, Zhou D, Wei J, Wang W, Zheng S. A meta-analysis of randomized controlled trials of low-volume polyethylene glycol plus ascorbic acid vs standard-volume polyethylene glycol solution as bowel preparations for colonoscopy. *PLoS One* 2014; **9**: e99092 [PMID: [24902028](#) DOI: [10.1371/journal.pone.0099092](#)]
- 45 **Clark RE**, Godfrey JD, Choudhary A, Ashraf I, Matteson ML, Bechtold ML. Low-volume polyethylene glycol and bisacodyl for bowel preparation prior to colonoscopy: a meta-analysis. *Ann Gastroenterol* 2013; **26**: 319-324 [PMID: [24714413](#)]
- 46 **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 4L of Polyethylene Glycol: A Prospective Randomized Study. *Dis Colon Rectum* 2019; **62**: 1518-1527 [PMID: [31567921](#) DOI: [10.1097/DCR.0000000000001499](#)]
- 47 **Barkun AN**, Martel M, Epstein IL, Hallé P, Hilsden RJ, James PD, Rostom A, Sey M, Singh H, Sultanian R, Telford JJ, von Renteln D. The Bowel CLEANsing National Initiative: A Low-Volume Same-Day Polyethylene Glycol (PEG) Preparation vs Low-Volume Split-Dose PEG With Bisacodyl or High-Volume Split-Dose PEG Preparations-A Randomized Controlled Trial. *Am J Gastroenterol* 2020; **115**: 2068-2076 [PMID: [32740079](#) DOI: [10.14309/ajg.0000000000000760](#)]
- 48 **Jung YS**, Lee CK, Eun CS, Park DI, Han DS, Kim HJ. Low-Volume Polyethylene Glycol with Ascorbic Acid for Colonoscopy Preparation in Elderly Patients: A Randomized Multicenter Study. *Digestion* 2016; **94**: 82-91 [PMID: [27553205](#) DOI: [10.1159/000448887](#)]
- 49 **Moon CM**, Park DI, Choe YG, Yang DH, Yu YH, Eun CS, Han DS. Randomized trial of 2-L polyethylene glycol + ascorbic acid vs 4-L polyethylene glycol as bowel cleansing for colonoscopy in an optimal setting. *J Gastroenterol Hepatol* 2014; **29**: 1223-1228 [PMID: [24955451](#) DOI: [10.1111/jgh.12521](#)]
- 50 **Zorzi M**, Valiante F, Germanà B, Baldassarre G, Coria B, Rinaldi M, Heras Salvat H, Carta A, Bortoluzzi F, Cervellin E, Polo ML, Bulighin G, Azzurro M, Di Piramo D, Turrin A, Monica F; TriVeP Working Group. Comparison between different colon cleansing products for screening colonoscopy. A noninferiority trial in population-based screening programs in Italy. *Endoscopy* 2016; **48**: 223-231 [PMID: [26760605](#) DOI: [10.1055/s-0035-1569574](#)]
- 51 **Kojecky V**, Matous J, Keil R, Dastyh M, Kroupa R, Zadorova Z, Varga M, Dolina J, Kment M, Hep A. A head-to-head comparison of 4-L polyethylene glycol and low-volume solutions before colonoscopy: which is the best? *Int J Colorectal Dis* 2017; **32**: 1763-1766 [PMID: [28944412](#) DOI: [10.1007/s00384-017-2901-x](#)]
- 52 **Bisschops R**, Manning J, Clayton LB, Ng Kwet Shing R, Álvarez-González M; MORA Study Group. Colon cleansing efficacy and safety with 1 L NER1006 vs 2 L polyethylene glycol + ascorbate: a randomized phase 3 trial. *Endoscopy* 2019; **51**: 60-72 [PMID: [30025414](#) DOI: [10.1055/a-0638-8125](#)]
- 53 **Frazzoni L**, Spada C, Radaelli F, Mussetto A, Laterza L, La Marca M, Piccirelli S, Cortellini F, Rondonotti E, Paci V, Bazzoli F, Fabbri C, Manno M, Aragona G, Manes G, Occhipinti P, Cadoni S, Zagari RM, Hassan C, Fuccio L. 1L- vs. 4L-Polyethylene glycol for bowel preparation before colonoscopy among inpatients: A propensity score-matching analysis. *Dig Liver Dis* 2020; **52**: 1486-1493 [PMID: [33250131](#) DOI: [10.1016/j.dld.2020.10.006](#)]
- 54 **Jin Z**, Lu Y, Zhou Y, Gong B. Systematic review and meta-analysis: sodium picosulfate/magnesium citrate vs. polyethylene glycol for colonoscopy preparation. *Eur J Clin Pharmacol* 2016; **72**: 523-532 [PMID: [26818765](#) DOI: [10.1007/s00228-016-2013-5](#)]
- 55 **Rex DK**, Di Palma JA, Rodriguez R, McGowan J, Cleveland M. A randomized clinical study comparing reduced-volume oral sulfate solution with standard 4-liter sulfate-free electrolyte lavage solution as preparation for colonoscopy. *Gastrointest Endosc* 2010; **72**: 328-336 [PMID: [20646695](#) DOI: [10.1016/j.gie.2010.03.1054](#)]
- 56 **Yang HJ**, Park SK, Kim JH, Im JP, Yeom DH, Seo GS, Park DI. Randomized trial comparing oral

- sulfate solution with 4-L polyethylene glycol administered in a split dose as preparation for colonoscopy. *J Gastroenterol Hepatol* 2017; **32**: 12-18 [PMID: [27349220](#) DOI: [10.1111/jgh.13477](#)]
- 57 **Kwak MS**, Cha JM, Yang HJ, Park DI, Kim KO, Lee J, Shin JE, Joo YE, Park J, Byeon JS, Kim HG. Safety and Efficacy of Low-Volume Preparation in the Elderly: Oral Sulfate Solution on the Day before and Split-Dose Regimens (SEE SAFE) Study. *Gut Liver* 2019; **13**: 176-182 [PMID: [30400725](#) DOI: [10.5009/gnl18214](#)]
 - 58 **Cheng J**, Tao K, Shuai X, Gao J. Sodium phosphate vs polyethylene glycol for colonoscopy bowel preparation: an updated meta-analysis of randomized controlled trials. *Surg Endosc* 2016; **30**: 4033-4041 [PMID: [26679172](#) DOI: [10.1007/s00464-015-4716-6](#)]
 - 59 **Hassan C**, East J, Radaelli F, Spada C, Benamouzig R, Bisschops R, Bretthauer M, Dekker E, Dinis-Ribeiro M, Ferlitsch M, Fuccio L, Awadie H, Gralnek I, Jover R, Kaminski MF, Pellisé M, Triantafyllou K, Vanella G, Mangas-Sanjuan C, Frazzoni L, Van Hooft JE, Dumonceau JM. Bowel preparation for colonoscopy: European Society of Gastrointestinal Endoscopy (ESGE) Guideline - Update 2019. *Endoscopy* 2019; **51**: 775-794 [PMID: [31295746](#) DOI: [10.1055/a-0959-0505](#)]
 - 60 **Mehta JB**, Singhal SB, Mehta BC. Ascorbic-acid-induced haemolysis in G-6-PD deficiency. *Lancet* 1990; **336**: 944 [PMID: [1976956](#) DOI: [10.1016/0140-6736\(90\)92317-b](#)]
 - 61 **Johnson DA**, Barkun AN, Cohen LB, Dominitz JA, Kaltenbach T, Martel M, Robertson DJ, Richard Boland C, Giardello FM, Lieberman DA, Levin TR, Rex DK; 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. *Am J Gastroenterol* 2014; **109**: 1528-1545 [PMID: [25223578](#) DOI: [10.1038/ajg.2014.272](#)]
 - 62 **Hassan C**, Bretthauer M, Kaminski MF, Polkowski M, Rembacken B, Saunders B, Benamouzig R, Holme O, Green S, Kuiper T, Marmo R, Omar M, Petruzzello L, Spada C, Zullo A, Dumonceau JM; European Society of Gastrointestinal Endoscopy. Bowel preparation for colonoscopy: European Society of Gastrointestinal Endoscopy (ESGE) guideline. *Endoscopy* 2013; **45**: 142-150 [PMID: [23335011](#) DOI: [10.1055/s-0032-1326186](#)]
 - 63 **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 [PMID: [25863216](#) DOI: [10.1053/j.gastro.2015.04.004](#)]
 - 64 **Manes G**, Repici A, Hassan C; MAGIC-P study group. Randomized controlled trial comparing efficacy and acceptability of split- and standard-dose sodium picosulfate plus magnesium citrate for bowel cleansing prior to colonoscopy. *Endoscopy* 2014; **46**: 662-669 [PMID: [25019969](#) DOI: [10.1055/s-0034-1365800](#)]
 - 65 **Schulz C**, Müller J, Sauter J, Miehke S, Schmöcker C, Hartmann D, Malfertheiner P, Badiola C. Superiority of a Split-dose Regimen of Sodium Picosulfate/Magnesium Citrate (SPMC) in Comparison to a Prior-day Schedule (AM/PM) for Colonoscopy Preparation. A Randomized Single-blinded Study. *J Gastrointest Liver Dis* 2016; **25**: 295-302 [PMID: [27689192](#) DOI: [10.15403/jgld.2014.1121.253.mag](#)]
 - 66 **Kiesslich R**, Schubert S, Mross M, Klugmann T, Klemm-Kropp M, Behnken I, Bonnaud G, Keulen E, Groenen M, Blaker M, Ponchon T, Landry W, Stoltenberg M. Efficacy and safety of PICOPREP tailored dosing compared with PICOPREP day-before dosing for colon cleansing: a multi-centric randomised study. *Endosc Int Open* 2017; **5**: E282-E290 [PMID: [28393103](#) DOI: [10.1055/s-0043-102433](#)]
 - 67 **Mohamed R**, Hilsden RJ, Dube C, Rostom A. Split-Dose Polyethylene Glycol Is Superior to Single Dose for Colonoscopy Preparation: Results of a Randomized Controlled Trial. *Can J Gastroenterol Hepatol* 2016; **2016**: 3181459 [PMID: [27446836](#) DOI: [10.1155/2016/3181459](#)]
 - 68 **Horton N**, Garber A, Hasson H, Lopez R, Burke CA. Impact of Single- vs. Split-Dose Low-Volume Bowel Preparations on Bowel Movement Kinetics, Patient Inconvenience, and Polyp Detection: A Prospective Trial. *Am J Gastroenterol* 2016; **111**: 1330-1337 [PMID: [27377521](#) DOI: [10.1038/ajg.2016.273](#)]
 - 69 **Radaelli F**, Paggi S, Hassan C, Senore C, Fasoli R, Anderloni A, Buffoli F, Savarese MF, Spinzi G, Rex DK, Repici A. Split-dose preparation for colonoscopy increases adenoma detection rate: a randomised controlled trial in an organised screening programme. *Gut* 2017; **66**: 270-277 [PMID: [26657900](#) DOI: [10.1136/gutjnl-2015-310685](#)]
 - 70 **Spadaccini M**, Frazzoni L, Vanella G, East J, Radaelli F, Spada C, Fuccio L, Benamouzig R, Bisschops R, Bretthauer M, Dekker E, Dinis-Ribeiro M, Ferlitsch M, Gralnek I, Jover R, Kaminski MF, Pellisé M, Triantafyllou K, Van Hooft JE, Dumonceau JM, Marmo C, Alfieri S, Chandrasekar VT, Sharma P, Rex DK, Repici A, Hassan C. Efficacy and Tolerability of High- vs Low-Volume Split-Dose Bowel Cleansing Regimens for Colonoscopy: A Systematic Review and Meta-analysis. *Clin Gastroenterol Hepatol* 2020; **18**: 1454-1465.e14 [PMID: [31683057](#) DOI: [10.1016/j.cgh.2019.10.044](#)]
 - 71 **Pohl J**, Halphen M, Kloess HR, Fischbach W. Impact of the quality of bowel cleansing on the efficacy of colonic cancer screening: a prospective, randomized, blinded study. *PLoS One* 2015; **10**: e0126067 [PMID: [25950434](#) DOI: [10.1371/journal.pone.0126067](#)]
 - 72 **Gurudu SR**, Ramirez FC, Harrison ME, Leighton JA, Crowell MD. Increased adenoma detection rate with system-wide implementation of a split-dose preparation for colonoscopy. *Gastrointest Endosc* 2012; **76**: 603-8.e1 [PMID: [22732876](#) DOI: [10.1016/j.gie.2012.04.456](#)]
 - 73 **Jover R**, Zapater P, Polania E, Bujanda L, Lanás A, Hermo JA, Cubiella J, Ono A, González-Méndez Y, Peris A, Pellisé M, Seoane A, Herreros-de-Tejada A, Ponce M, Marín-Gabriel JC,

- Chaparro M, Cacho G, Fernández-Díez S, Arenas J, Sopeña F, de-Castro L, Vega-Villaamil P, Rodríguez-Soler M, Carballo F, Salas D, Morillas JD, Andreu M, Quintero E, Castells A; COLONPREV study investigators. Modifiable endoscopic factors that influence the adenoma detection rate in colorectal cancer screening colonoscopies. *Gastrointest Endosc* 2013; **77**: 381-389.e1 [PMID: [23218945](#) DOI: [10.1016/j.gie.2012.09.027](#)]
- 74 **Radaelli F**, Paggi S, Repici A, Gullotti G, Cesaro P, Rotondano G, Cugia L, Trovato C, Spada C, Fuccio L, Occhipinti P, Pace F, Fabbri C, Buda A, Manes G, Feliciangeli G, Manno M, Barresi L, Anderloni A, Dulbecco P, Rogai F, Amato A, Senore C, Hassan C. Barriers against split-dose bowel preparation for colonoscopy. *Gut* 2017; **66**: 1428-1433 [PMID: [27196589](#) DOI: [10.1136/gutjnl-2015-311049](#)]
- 75 **Zawaly K**, Rumbolt C, Abou-Setta AM, Neilson C, Rabbani R, Zarychanski R, Singh H. The Efficacy of Split-Dose Bowel Preparations for Polyp Detection: A Systematic Review and Meta-Analysis. *Am J Gastroenterol* 2019; **114**: 884-892 [PMID: [30865011](#) DOI: [10.14309/ajg.000000000000155](#)]
- 76 **Avalos DJ**, Castro FJ, Zuckerman MJ, Keihanian T, Berry AC, Nutter B, Sussman DA. Bowel Preparations Administered the Morning of Colonoscopy Provide Similar Efficacy to a Split Dose Regimen: A Meta Analysis. *J Clin Gastroenterol* 2018; **52**: 859-868 [PMID: [28885304](#) DOI: [10.1097/MCG.0000000000000866](#)]
- 77 **Cheng YL**, Huang KW, Liao WC, Luo JC, Lan KH, Su CW, Wang YJ, Hou MC. Same-day Versus Split-dose Bowel Preparation Before Colonoscopy: A Meta-analysis. *J Clin Gastroenterol* 2018; **52**: 392-400 [PMID: [28727630](#) DOI: [10.1097/MCG.0000000000000860](#)]
- 78 **Shah H**, Desai D, Samant H, Davavala S, Joshi A, Gupta T, Abraham P. Comparison of split-dosing vs non-split (morning) dosing regimen for assessment of quality of bowel preparation for colonoscopy. *World J Gastrointest Endosc* 2014; **6**: 606-611 [PMID: [25512770](#) DOI: [10.4253/wjge.v6.i12.606](#)]
- 79 **Kotwal VS**, Attar BM, Carballo MD, Lee SS, Kaura T, Go B, Zhang H, Trick WE. Morning-only polyethylene glycol is noninferior but less preferred by hospitalized patients as compared with split-dose bowel preparation. *J Clin Gastroenterol* 2014; **48**: 414-418 [PMID: [24406474](#) DOI: [10.1097/MCG.0b013e31829f30e9](#)]
- 80 **Chan WK**, Azmi N, Mahadeva S, Goh KL. Split-dose vs same-day reduced-volume polyethylene glycol electrolyte lavage solution for morning colonoscopy. *World J Gastroenterol* 2014; **20**: 14488-14494 [PMID: [25339836](#) DOI: [10.3748/wjg.v20.i39.14488](#)]
- 81 **ASGE Standards of Practice Committee**, Saltzman JR, Cash BD, Pasha SF, Early DS, Muthusamy VR, Khashab MA, Chathadi KV, Fanelli RD, Chandrasekhara V, Lightdale JR, Fonkalsrud L, Shergill AK, Hwang JH, Decker GA, Jue TL, Sharaf R, Fisher DA, Evans JA, Foley K, Shaukat A, Eloubeidi MA, Faulx AL, Wang A, Acosta RD. Bowel preparation before colonoscopy. *Gastrointest Endosc* 2015; **81**: 781-794 [PMID: [25595062](#) DOI: [10.1016/j.gie.2014.09.048](#)]
- 82 **Nguyen DL**, Jamal MM, Nguyen ET, Puli SR, Bechtold ML. Low-residue vs clear liquid diet before colonoscopy: a meta-analysis of randomized, controlled trials. *Gastrointest Endosc* 2016; **83**: 499-507.e1 [PMID: [26460222](#) DOI: [10.1016/j.gie.2015.09.045](#)]
- 83 **Song GM**, Tian X, Ma L, Yi LJ, Shuai T, Zeng Z, Zeng XT. Regime for Bowel Preparation in Patients Scheduled to Colonoscopy: Low-Residue Diet or Clear Liquid Diet? *Medicine (Baltimore)* 2016; **95**: e2432 [PMID: [26735547](#) DOI: [10.1097/MD.0000000000002432](#)]
- 84 **Zhang X**, Wu Q, Wei M, Ding Y, Gu C, Liu S, Wang Z. Low-residual diet vs clear-liquid diet for bowel preparation before colonoscopy: meta-analysis and trial sequential analysis of randomized controlled trials. *Gastrointest Endosc* 2020; **92**: 508-518.e3 [PMID: [32376331](#) DOI: [10.1016/j.gie.2020.04.069](#)]
- 85 **Chen E**, Chen L, Wang F, Zhang W, Cai X, Cao G. Low-residue vs clear liquid diet before colonoscopy: An updated meta-analysis of randomized, controlled trials. *Medicine (Baltimore)* 2020; **99**: e23541 [PMID: [33285772](#) DOI: [10.1097/MD.00000000000023541](#)]
- 86 **Gimeno-García AZ**, de la Barreda Heuser R, Reygosa C, Hernandez A, Mascareño I, Nicolás-Pérez D, Jiménez A, Lara AJ, Alarcon-Fernández O, Hernandez-Guerra M, Romero R, Alonso I, González Y, Adrian Z, Hernandez G, Hernandez D, Delgado R, Quintero E. Impact of a 1-day vs 3-day low-residue diet on bowel cleansing quality before colonoscopy: a randomized controlled trial. *Endoscopy* 2019; **51**: 628-636 [PMID: [30943553](#) DOI: [10.1055/a-0864-1942](#)]
- 87 **Avalos DJ**, Sussman DA, Lara LF, Sarkis FS, Castro FJ. Effect of Diet Liberalization on Bowel Preparation. *South Med J* 2017; **110**: 399-407 [PMID: [28575897](#) DOI: [10.14423/SMJ.0000000000000662](#)]
- 88 **Wu L**, Cao Y, Liao C, Huang J, Gao F. Systematic review and meta-analysis of randomized controlled trials of Simethicone for gastrointestinal endoscopic visibility. *Scand J Gastroenterol* 2011; **46**: 227-235 [PMID: [20977386](#) DOI: [10.3109/00365521.2010.525714](#)]
- 89 **Pan P**, Zhao SB, Li BH, Meng QQ, Yao J, Wang D, Li ZS, Bai Y. Effect of supplemental simethicone for bowel preparation on adenoma detection during colonoscopy: A meta-analysis of randomized controlled trials. *J Gastroenterol Hepatol* 2019; **34**: 314-320 [PMID: [30069899](#) DOI: [10.1111/jgh.14401](#)]
- 90 **Beilenhoff U**, Biering H, Blum R, Brljak J, Cimbri M, Dumonceau JM, Hassan C, Jung M, Kampf B, Neumann C, Pietsch M, Pineau L, Ponchon T, Rejchrt S, Rey JF, Schmidt V, Tillett J, van Hooft JE. Reprocessing of flexible endoscopes and endoscopic accessories used in gastrointestinal endoscopy: Position Statement of the European Society of Gastrointestinal Endoscopy (ESGE) and

- European Society of Gastroenterology Nurses and Associates (ESGENA) - Update 2018. *Endoscopy* 2018; **50**: 1205-1234 [PMID: [30458567](#) DOI: [10.1055/a-0759-1629](#)]
- 91 **Ofstead CL**, Wetzler HP, Johnson EA, Heymann OL, Maust TJ, Shaw MJ. Simethicone residue remains inside gastrointestinal endoscopes despite reprocessing. *Am J Infect Control* 2016; **44**: 1237-1240 [PMID: [27497824](#) DOI: [10.1016/j.ajic.2016.05.016](#)]
 - 92 **Day LW**, Muthusamy VR, Collins J, Kushnir VM, Sawhney MS, Thosani NC, Wani S. Multisociety guideline on reprocessing flexible GI endoscopes and accessories. *Gastrointest Endosc* 2021; **93**: 11-33.e6 [PMID: [33353611](#) DOI: [10.1016/j.gie.2020.09.048](#)]
 - 93 **Devereaux BM**, Taylor ACF, Athan E, Wallis DJ, Brown RR, Greig SM, Bailey FK, Vickery K, Wardle E, Jones DM. Simethicone use during gastrointestinal endoscopy: Position statement of the Gastroenterological Society of Australia. *J Gastroenterol Hepatol* 2019; **34**: 2086-2089 [PMID: [31242327](#) DOI: [10.1111/jgh.14757](#)]
 - 94 **Seow-En I**, Seow-Choen F. A prospective randomized trial on the use of Coca-Cola Zero® vs water for polyethylene glycol bowel preparation before colonoscopy. *Colorectal Dis* 2016; **18**: 717-723 [PMID: [26682533](#) DOI: [10.1111/codi.13243](#)]
 - 95 **Choi HS**, Shim CS, Kim GW, Kim JS, Lee SY, Sung IK, Park HS, Kim JH. Orange juice intake reduces patient discomfort and is effective for bowel cleansing with polyethylene glycol during bowel preparation. *Dis Colon Rectum* 2014; **57**: 1220-1227 [PMID: [25203380](#) DOI: [10.1097/DCR.0000000000000195](#)]
 - 96 **Altinbas A**, Hamamci M, Karakose M, Delibasi T, Yuksel O. Pineapple juice ingestion for gastric discomfort in diabetic gastroparesis. *Acta Gastroenterol Belg* 2013; **76**: 72-73 [PMID: [23650790](#)]
 - 97 **Hao Z**, Gong L, Shen Q, Wang H, Feng S, Wang X, Cai Y, Chen J. Effectiveness of concomitant use of green tea and polyethylene glycol in bowel preparation for colonoscopy: a randomized controlled study. *BMC Gastroenterol* 2020; **20**: 150 [PMID: [32404056](#) DOI: [10.1186/s12876-020-01220-3](#)]
 - 98 **Lan HC**, Liang Y, Hsu HC, Shu JH, Su CW, Hung HH, Hou MC, Lin HC, Lee SD, Wang YJ. Citrus reticulata peel improves patient tolerance of low-volume polyethylene glycol for colonoscopy preparation. *J Chin Med Assoc* 2012; **75**: 442-448 [PMID: [22989539](#) DOI: [10.1016/j.jcma.2012.06.022](#)]
 - 99 **Ergül B**, Filik L, Koçak E, Doğan Z, Sarıkaya M. Efficacy and safety of gum chewing in adjunct to high-dose senna for bowel cleansing before colonoscopy: a single-blind randomized controlled trial. *Saudi J Gastroenterol* 2014; **20**: 356-359 [PMID: [25434316](#) DOI: [10.4103/1319-3767.145325](#)]
 - 100 **Fang J**, Wang SL, Fu HY, Li ZS, Bai Y. Impact of gum chewing on the quality of bowel preparation for colonoscopy: an endoscopist-blinded, randomized controlled trial. *Gastrointest Endosc* 2017; **86**: 187-191 [PMID: [27327849](#) DOI: [10.1016/j.gie.2016.05.051](#)]
 - 101 **Lee J**, Lee E, Kim Y, Kim E, Lee Y. Effects of gum chewing on abdominal discomfort, nausea, vomiting and intake adherence to polyethylene glycol solution of patients in colonoscopy preparation. *J Clin Nurs* 2016; **25**: 518-525 [PMID: [26818376](#) DOI: [10.1111/jocn.13086](#)]
 - 102 **Sharara AI**, El-Halabi MM, Abou Fadel CG, Sarkis FS. Sugar-free menthol candy drops improve the palatability and bowel cleansing effect of polyethylene glycol electrolyte solution. *Gastrointest Endosc* 2013; **78**: 886-891 [PMID: [23769143](#) DOI: [10.1016/j.gie.2013.05.015](#)]
 - 103 **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? *United European Gastroenterol J* 2020; **8**: 1217-1227 [PMID: [32838693](#) DOI: [10.1177/2050640620953224](#)]
 - 104 **Chang CW**, Shih SC, Wang HY, Chu CH, Wang TE, Hung CY, Shieh TY, Lin YS, Chen MJ. Meta-analysis: The effect of patient education on bowel preparation for colonoscopy. *Endosc Int Open* 2015; **3**: E646-E652 [PMID: [26716129](#) DOI: [10.1055/s-0034-1392365](#)]
 - 105 **Kurlander JE**, Sondhi AR, Waljee AK, Menees SB, Connell CM, Schoenfeld PS, Saini SD. How Efficacious Are Patient Education Interventions to Improve Bowel Preparation for Colonoscopy? *PLoS One* 2016; **11**: e0164442 [PMID: [27741260](#) DOI: [10.1371/journal.pone.0164442](#)]
 - 106 **Guo X**, Yang Z, Zhao L, Leung F, Luo H, Kang X, Li X, Jia H, Yang S, Tao Q, Pan Y, Guo X. Enhanced instructions improve the quality of bowel preparation for colonoscopy: a meta-analysis of randomized controlled trials. *Gastrointest Endosc* 2017; **85**: 90-97.e6 [PMID: [27189659](#) DOI: [10.1016/j.gie.2016.05.012](#)]
 - 107 **Desai M**, Notalapati V, Bansal A, Buckles D, Bonino J, Olyae M, Rastogi A. Use of smartphone applications to improve quality of bowel preparation for colonoscopy: a systematic review and meta-analysis. *Endosc Int Open* 2019; **7**: E216-E224 [PMID: [30705956](#) DOI: [10.1055/a-0796-6423](#)]
 - 108 **Guo X**, Li X, Wang Z, Zhai J, Liu Q, Ding K, Pan Y. Reinforced education improves the quality of bowel preparation for colonoscopy: An updated meta-analysis of randomized controlled trials. *PLoS One* 2020; **15**: e0231888 [PMID: [32343708](#) DOI: [10.1371/journal.pone.0231888](#)]
 - 109 **Chandan S**, Arora S, Mohan BP, Khan SR, Chandan OC, Kassab LL, Murali AR. Multimedia based education on bowel preparation improves adenoma detection rate: Systematic review & meta-analysis of randomized controlled trials. *Dig Endosc* 2020 [PMID: [32794240](#) DOI: [10.1111/den.13809](#)]
 - 110 **Tian X**, Xu LL, Liu XL, Chen WQ. Enhanced Patient Education for Colonic Polyp and Adenoma Detection: Meta-Analysis of Randomized Controlled Trials. *JMIR Mhealth Uhealth* 2020; **8**: e17372 [PMID: [32347798](#) DOI: [10.2196/17372](#)]
 - 111 **Lhewa DY**, Strate LL. Pros and cons of colonoscopy in management of acute lower gastrointestinal bleeding. *World J Gastroenterol* 2012; **18**: 1185-1190 [PMID: [22468081](#) DOI: [10.3748/wjg.v18.i11.1185](#)]

- 10.3748/wjg.v18.i11.1185]
- 112 **Laine L**, Shah A. Randomized trial of urgent vs. elective colonoscopy in patients hospitalized with lower GI bleeding. *Am J Gastroenterol* 2010; **105**: 2636-2641; quiz 2642 [PMID: [20648004](#) DOI: [10.1038/ajg.2010.277](#)]
 - 113 **ASGE Standards of Practice Committee**, Anderson MA, Ben-Menachem T, Gan SI, Appalaneni V, Banerjee S, Cash BD, Fisher L, Harrison ME, Fanelli RD, Fukami N, Ikenberry SO, Jain R, Khan K, Krinsky ML, Lichtenstein DR, Maple JT, Shen B, Strohmeyer L, Baron T, Dominitz JA. Management of antithrombotic agents for endoscopic procedures. *Gastrointest Endosc* 2009; **70**: 1060-1070 [PMID: [19889407](#) DOI: [10.1016/j.gie.2009.09.040](#)]
 - 114 **ASGE Standards of Practice Committee**, Pasha SF, Shergill A, Acosta RD, Chandrasekhara V, Chathadi KV, Early D, Evans JA, Fisher D, Fonkalsrud L, Hwang JH, Khashab MA, Lightdale JR, Muthusamy VR, Saltzman JR, Cash BD. The role of endoscopy in the patient with lower GI bleeding. *Gastrointest Endosc* 2014; **79**: 875-885 [PMID: [24703084](#) DOI: [10.1016/j.gie.2013.10.039](#)]
 - 115 **Niikura R**, Nagata N, Shimbo T, Sakurai T, Aoki T, Moriyasu S, Sekine K, Okubo H, Watanabe K, Yokoi C, Yamada A, Hirata Y, Koike K, Akiyama J, Uemura N. Adverse Events during Bowel Preparation and Colonoscopy in Patients with Acute Lower Gastrointestinal Bleeding Compared with Elective Non-Gastrointestinal Bleeding. *PLoS One* 2015; **10**: e0138000 [PMID: [26368562](#) DOI: [10.1371/journal.pone.0138000](#)]
 - 116 **Pontone S**, Palma R, Panetta C, Eberspacher C, Angelini R, Pironi D, Filippini A, Pontone P. Polyethylene glycol-based bowel preparation before colonoscopy for selected inpatients: A pilot study. *J Dig Dis* 2018; **19**: 40-47 [PMID: [29266839](#) DOI: [10.1111/1751-2980.12571](#)]
 - 117 **Strate LL**, Gralnek IM. ACG Clinical Guideline: Management of Patients With Acute Lower Gastrointestinal Bleeding. *Am J Gastroenterol* 2016; **111**: 755 [PMID: [27151132](#) DOI: [10.1038/ajg.2016.155](#)]
 - 118 **Oakland K**, Chadwick G, East JE, Guy R, Humphries A, Jairath V, McPherson S, Metzner M, Morris AJ, Murphy MF, Tham T, Uberoi R, Veitch AM, Wheeler J, Regan C, Hoare J. Diagnosis and management of acute lower gastrointestinal bleeding: guidelines from the British Society of Gastroenterology. *Gut* 2019; **68**: 776-789 [PMID: [30792244](#) DOI: [10.1136/gutjnl-2018-317807](#)]
 - 119 **Repaka A**, Atkinson MR, Faulx AL, Isenberg GA, Cooper GS, Chak A, Wong RC. Immediate unprepared hydroflush colonoscopy for severe lower GI bleeding: a feasibility study. *Gastrointest Endosc* 2012; **76**: 367-373 [PMID: [22658390](#) DOI: [10.1016/j.gie.2012.03.1391](#)]
 - 120 **Gül Utku Ö**, Karatay E. Immediate unprepared polyethylene glycol-flush colonoscopy in elderly patients with severe lower gastrointestinal bleeding. *Geriatr Gerontol Int* 2020; **20**: 559-563 [PMID: [32207216](#) DOI: [10.1111/ggi.13903](#)]
 - 121 **Lee JM**, Keum B, Yoo IK, Kim SH, Choi HS, Kim ES, Seo YS, Jeon YT, Chun HJ, Lee HS, Um SH, Kim CD, Kim MG, Jo SK. Polyethylene glycol plus ascorbic acid for bowel preparation in chronic kidney disease. *Medicine (Baltimore)* 2016; **95**: e4755 [PMID: [27603372](#) DOI: [10.1097/MD.0000000000004755](#)]
 - 122 **Russmann S**, Lamerato L, Motsko SP, Pezzullo JC, Faber MD, Jones JK. Risk of further decline in renal function after the use of oral sodium phosphate or polyethylene glycol in patients with a preexisting glomerular filtration rate below 60 mL/min. *Am J Gastroenterol* 2008; **103**: 2707-2716 [PMID: [18945285](#) DOI: [10.1111/j.1572-0241.2008.02201.x](#)]
 - 123 **Mandolesi D**, Frazzoni L, Bazzoli F, Fuccio L. The management of 'hard-to-prepare' colonoscopy patients. *Expert Rev Gastroenterol Hepatol* 2017; **11**: 731-740 [PMID: [28594580](#) DOI: [10.1080/17474124.2017.1338947](#)]
 - 124 **Connor A**, Tolan D, Hughes S, Carr N, Tomson C. Consensus guidelines for the safe prescription and administration of oral bowel-cleansing agents. *Gut* 2012; **61**: 1525-1532 [PMID: [22842619](#) DOI: [10.1136/gutjnl-2011-300861](#)]
 - 125 **Yoshida N**, Naito Y, Murakami T, Hirose R, Ogiso K, Inada Y, Dohi O, Okayama T, Kamada K, Uchiyama K, Ishikawa T, Handa O, Konishi H, Siah KT, Yagi N, Itoh Y. Safety and Efficacy of a Same-Day Low-Volume 1 L PEG Bowel Preparation in Colonoscopy for the Elderly People and People with Renal Dysfunction. *Dig Dis Sci* 2016; **61**: 3229-3235 [PMID: [27487795](#) DOI: [10.1007/s10620-016-4262-7](#)]
 - 126 **Bisschops R**, East JE, Hassan C, Hazewinkel Y, Kamiński MF, Neumann H, Pellisé M, Antonelli G, Bustamante Balen M, Coron E, Cortas G, Iacucci M, Yuichi M, Longcroft-Wheaton G, Mouzyka S, Pilonis N, Puig I, van Hooft JE, Dekker E. Advanced imaging for detection and differentiation of colorectal neoplasia: European Society of Gastrointestinal Endoscopy (ESGE) Guideline - Update 2019. *Endoscopy* 2019; **51**: 1155-1179 [PMID: [31711241](#) DOI: [10.1055/a-1031-7657](#)]
 - 127 **Iannone A**, Ruospo M, Wong G, Principi M, Barone M, Strippoli GFM, Di Leo A. Chromoendoscopy for Surveillance in Ulcerative Colitis and Crohn's Disease: A Systematic Review of Randomized Trials. *Clin Gastroenterol Hepatol* 2017; **15**: 1684-1697.e11 [PMID: [27890853](#) DOI: [10.1016/j.cgh.2016.11.021](#)]
 - 128 **Iannone A**, Ruospo M, Palmer SC, Principi M, Barone M, Di Leo A, Strippoli GFM. Systematic review with network meta-analysis: endoscopic techniques for dysplasia surveillance in inflammatory bowel disease. *Aliment Pharmacol Ther* 2019; **50**: 858-871 [PMID: [31502284](#) DOI: [10.1111/apt.15493](#)]
 - 129 **Manes G**, Fontana P, de Nucci G, Radaelli F, Hassan C, Ardizzone S. Colon Cleansing for Colonoscopy in Patients with Ulcerative Colitis: Efficacy and Acceptability of a 2-L PEG Plus

- Bisacodyl Versus 4-L PEG. *Inflamm Bowel Dis* 2015; **21**: 2137-2144 [PMID: 26164666 DOI: 10.1097/MIB.0000000000000463]
- 130 **Kim ES**, Kim KO, Jang BI, Kim EY, Lee YJ, Lee HS, Jeon SW, Kim HJ, Kim SK; Crohn's and Colitis Association in Daegu-Gyeongbuk (CCAiD). Comparison of 4-L Polyethylene Glycol and 2-L Polyethylene Glycol Plus Ascorbic Acid in Patients with Inactive Ulcerative Colitis. *Dig Dis Sci* 2017; **62**: 2489-2497 [PMID: 28639128 DOI: 10.1007/s10620-017-4634-7]
 - 131 **Shingo Kato**, Kani K, Taisuke Kobayashi, Ryuichi Yamamoto, Sumiko Nagoshi, Koji Yakabi. The Safety and Feasibility Study of Bowel Cleaning Agents MoviPrep® Versus Niflec® for the Patients With Inflammatory Bowel Diseases Undergoing Colonoscopy and Balloon Enteroscopy: a Single Center Randomized Controlled Trial. *Gastrointest Endosc* 2015; **81**: AB320 [DOI: 10.1016/j.gie.2015.03.1435]
 - 132 **Iacucci M**, Cannatelli R, Tontini GE, Panaccione R, Danese S, Fiorino G, Matsumoto T, Kochhar GS, Shen B, Kiesslich R, Ghosh S. Improving the quality of surveillance colonoscopy in inflammatory bowel disease. *Lancet Gastroenterol Hepatol* 2019; **4**: 971-983 [PMID: 31696831 DOI: 10.1016/S2468-1253(19)30194-3]
 - 133 **Lawrance IC**, Willert RP, Murray K. Bowel cleansing for colonoscopy: prospective randomized assessment of efficacy and of induced mucosal abnormality with three preparation agents. *Endoscopy* 2011; **43**: 412-418 [PMID: 21547879 DOI: 10.1055/s-0030-1256193]
 - 134 **Rejchrt S**, Bures J, Siroký M, Kopáková M, Slezák L, Langr F. A prospective, observational study of colonic mucosal abnormalities associated with orally administered sodium phosphate for colon cleansing before colonoscopy. *Gastrointest Endosc* 2004; **59**: 651-654 [PMID: 15114307 DOI: 10.1016/s0016-5107(04)00158-0]
 - 135 **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**: 819-826 [PMID: 29847488 DOI: 10.1097/MEG.0000000000001175]
 - 136 **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 [PMID: 15758907 DOI: 10.1016/s0016-5107(04)02776-2]
 - 137 **Dik VK**, Moons LM, Hüyük M, van der Schaar P, de Vos Tot Nederveen Cappel WH, Ter Borg PC, Meijssen MA, Ouwendijk RJ, Le Fèvre DM, Stouten M, van der Galiën O, Hiemstra TJ, Monkelbaan JF, van Oijen MG, Siersema PD; Colonoscopy Quality Initiative. Predicting inadequate bowel preparation for colonoscopy in participants receiving split-dose bowel preparation: development and validation of a prediction score. *Gastrointest Endosc* 2015; **81**: 665-672 [PMID: 25600879 DOI: 10.1016/j.gie.2014.09.066]
 - 138 **Yadlapati R**, Johnston ER, Gregory DL, Ciolino JD, Cooper A, Keswani RN. Predictors of Inadequate Inpatient Colonoscopy Preparation and Its Association with Hospital Length of Stay and Costs. *Dig Dis Sci* 2015; **60**: 3482-3490 [PMID: 26093612 DOI: 10.1007/s10620-015-3761-2]
 - 139 **Garber A**, Sarvepalli S, Burke CA, Bhatt A, Ibrahim M, McMichael J, Morris-Stiff G, Rizk MK, Vargo JJ, Rothberg MB. Modifiable Factors Associated with Quality of Bowel Preparation Among Hospitalized Patients Undergoing Colonoscopy. *J Hosp Med* 2019; **14**: 278-283 [PMID: 30986186 DOI: 10.12788/jhm.3173]
 - 140 **Gkolfakis P**, Tziatzios G, Papanikolaou 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 [PMID: 31191646 DOI: 10.1155/2019/5147208]
 - 141 **Qureshi A**, Ismail S, Azmi A, Murugan P, Husin M. Poor bowel preparation in patients undergoing colonoscopy. *Med J Malaysia* 2000; **55**: 246-248 [PMID: 19839154]
 - 142 **Asher RA**. The dangers of going to bed. *Br Med J* 1947; **2**: 967 [PMID: 18897489 DOI: 10.1136/bmj.2.4536.967]
 - 143 **Fuccio L**, Frazzoni L, Spada C, Mussetto A, Fabbri C, Manno M, Aragona G, Zagari RM, Rondonotti E, Manes G, Occhipinti P, Cadoni S, Bazzoli F, Hassan C, Radaelli F; QIPS study group. Factors That Affect Adequacy of Colon Cleansing for Colonoscopy in Hospitalized Patients. *Clin Gastroenterol Hepatol* 2021; **19**: 339-348.e7 [PMID: 32200083 DOI: 10.1016/j.cgh.2020.02.055]
 - 144 **Adamcewicz M**, Bearely D, Porat G, Friedenberg FK. Mechanism of action and toxicities of purgatives used for colonoscopy preparation. *Expert Opin Drug Metab Toxicol* 2011; **7**: 89-101 [PMID: 21162694 DOI: 10.1517/17425255.2011.542411]
 - 145 **Ryan F**, Anobile T, Scutt D, Hopwood M, Murphy G. Effects of oral sodium picosulphate Picolax on urea and electrolytes. *Nurs Stand* 2005; **19**: 41-45 [PMID: 16050231 DOI: 10.7748/ns2005.07.19.45.41.c3912]
 - 146 **Ajani S**, Hurt RT, Teeters DA, Bellmore LR. Ischaemic colitis associated with oral contraceptive and bisacodyl use. *BMJ Case Rep* 2012; **2012** [PMID: 22843752 DOI: 10.1136/bcr-12-2011-5451]
 - 147 **Johnson DA**, Barkun AN, Cohen LB, Dominitz JA, Kaltenbach T, Martel M, Robertson DJ, Bolland CR, Giardello FM, Lieberman DA, Levin TR, Rex DK. Optimizing adequacy of bowel cleansing for colonoscopy: recommendations from the U.S. multi-society task force on colorectal cancer. *Gastrointest Endosc* 2014; **80**: 543-562 [PMID: 25220509 DOI: 10.1016/j.gie.2014.08.002]
 - 148 **Suares NC**, Ford AC. Prevalence of, and risk factors for, chronic idiopathic constipation in the community: systematic review and meta-analysis. *Am J Gastroenterol* 2011; **106**: 1582-1591; quiz 1581, 1592 [PMID: 21606976 DOI: 10.1038/ajg.2011.164]
 - 149 **Gimeno-García AZ**, Baute JL, Hernandez G, Morales D, Gonzalez-Pérez CD, Nicolás-Pérez D,

- Alarcon-Fernández O, Jiménez A, Hernandez-Guerra M, Romero R, Alonso I, Gonzalez Y, Adrian Z, Carrillo M, Ramos L, Quintero E. Risk factors for inadequate bowel preparation: a validated predictive score. *Endoscopy* 2017; **49**: 536-543 [PMID: 28282690 DOI: 10.1055/s-0043-101683]
- 150 **Lewis SJ**, Heaton KW. Stool form scale as a useful guide to intestinal transit time. *Scand J Gastroenterol* 1997; **32**: 920-924 [PMID: 9299672 DOI: 10.3109/00365529709011203]
- 151 **Guo X**, Shi X, Kang X, Luo H, Wang X, Jia H, Tao Q, Wang J, Zhang M, Lu X, Ma S, Lin T, Jing Y, Pan Y, Guo X, Fan D. Risk Factors Associated with Inadequate Bowel Preparation in Patients with Functional Constipation. *Dig Dis Sci* 2020; **65**: 1082-1091 [PMID: 31605278 DOI: 10.1007/s10620-019-05847-5]
- 152 **Chen H**, Li X, Ge Z. Comparative study on two colonic bowel preparations for patients with chronic constipation. *Scand J Gastroenterol* 2009; **44**: 375-379 [PMID: 19005996 DOI: 10.1080/00365520802538211]
- 153 **Pereyra L**, Cimmino D, González Malla C, Laporte M, Rotholtz N, Peczan C, Lencinas S, Pedreira S, Catalano H, Boerr L. Colonic preparation before colonoscopy in constipated and non-constipated patients: a randomized study. *World J Gastroenterol* 2013; **19**: 5103-5110 [PMID: 23964144 DOI: 10.3748/wjg.v19.i31.5103]
- 154 **Lu J**, Cao Q, Wang X, Pu J, Peng X. Application of Oral Lactulose in Combination With Polyethylene Glycol Electrolyte Powder for Colonoscopy Bowel Preparation in Patients With Constipation. *Am J Ther* 2016; **23**: e1020-e1024 [PMID: 26658804 DOI: 10.1097/MJT.0000000000000351]
- 155 **Kunz L**, Gillespie D. A Comparison of Bowel Preparations for Colonoscopy in Constipated Adults. *Gastroenterol Nurs* 2017; **40**: 364-372 [PMID: 28957968 DOI: 10.1097/SGA.0000000000000257]
- 156 **Yıldar M**, Yaman İ, Başbuğ M, Çavdar F, Topfedaisi H, Derici H. A new approach in bowel preparation before colonoscopy in patients with constipation: A prospective, randomized, investigator-blinded trial. *Turk J Surg* 2017; **33**: 29-32 [PMID: 28589184 DOI: 10.5152/UCD.2015.3189]
- 157 **Yoshida N**, Inagaki Y, Fukumoto K, Yoriki H, Inada Y, Murakami T, Tomita Y, Hashimoto H, Sugino S, Hirose R, Dohi O, Inoue K, Itoh Y. 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 [PMID: 33299407 DOI: 10.1155/2020/8886073]
- 158 **Dang JT**, Moolla M, Dang TT, Shaw A, Tian C, Karmali S, Sultanian R. Sodium phosphate is superior to polyethylene glycol in constipated patients undergoing colonoscopy: a systematic review and meta-analysis. *Surg Endosc* 2021; **35**: 900-909 [PMID: 32124060 DOI: 10.1007/s00464-020-07464-0]
- 159 **Kahi CJ**, Boland CR, Dominitz JA, Giardiello FM, Johnson DA, Kaltenbach T, Lieberman D, Levin TR, Robertson DJ, Rex DK; United States Multi-Society Task Force on Colorectal Cancer. Colonoscopy Surveillance After Colorectal Cancer Resection: Recommendations of the US Multi-Society Task Force on Colorectal Cancer. *Gastroenterology* 2016; **150**: 758-768.e11 [PMID: 26892199 DOI: 10.1053/j.gastro.2016.01.001]
- 160 **Lim SW**, Seo YW, Sinn DH, Kim JY, Chang DK, Kim JJ, Rhee JC, Shim SG, Kim YH. Impact of previous gastric or colonic resection on polyethylene glycol bowel preparation for colonoscopy. *Surg Endosc* 2012; **26**: 1554-1559 [PMID: 22170320 DOI: 10.1007/s00464-011-2068-4]
- 161 **Pontone S**, Leonetti G, Lamazza A, Fiocca F, Filippini A, Fanello G, Cereatti F, Fiori E, Angelini R, Patrizi G, Brighi M, Vetere S, Antoniozzi A, Pironi D, Manfredelli S, Pontone P. A Retrospective Case-Control Study Evaluating the Bowel Preparation Quality during Surveillance Colonoscopy after Colonic Resection. *ISRN Gastroenterol* 2014; **2014**: 681978 [PMID: 24729880 DOI: 10.1155/2014/681978]
- 162 **Yoo IK**, Jeon YT, Choi SJ, Choi HS, Keum B, Kim ES, Chun HJ, Lee HS, Kim CD. Evaluation of bowel preparation quality in patients with a history of colorectal resection. *Turk J Gastroenterol* 2019; **30**: 278-283 [PMID: 30666966 DOI: 10.5152/tjg.2018.17517]
- 163 **Mussetto A**, Frazzoni L, Paggi S, Dari S, Laterza L, Radaelli F, Hassan C, Triossi O, Fuccio L. Split dosing with a low-volume preparation is not inferior to split dosing with a high-volume preparation for bowel cleansing in patients with a history of colorectal resection: a randomized trial. *Endoscopy* 2015; **47**: 917-924 [PMID: 25910064 DOI: 10.1055/s-0034-1391987]
- 164 **Liu Z**, Li YY, Luo XT, Guo CG, Zhang MM, Li Z, Li LX, Zhang Y, Li YQ. Split-dose 4-L polyethylene glycol regimen for patients with previous colorectal surgery in bowel preparation before colonoscopy: A randomized, controlled, single-blind study. *J Dig Dis* 2018; **19**: 359-368 [PMID: 29790278 DOI: 10.1111/1751-2980.12608]
- 165 **Savas N**. Gastrointestinal endoscopy in pregnancy. *World J Gastroenterol* 2014; **20**: 15241-15252 [PMID: 25386072 DOI: 10.3748/wjg.v20.i41.15241]
- 166 **Friedel D**, Stavropoulos S, Iqbal S, Cappell MS. Gastrointestinal endoscopy in the pregnant woman. *World J Gastrointest Endosc* 2014; **6**: 156-167 [PMID: 24891928 DOI: 10.4253/wjge.v6.i5.156]
- 167 **Lim YJ**, Hong SJ. What is the best strategy for successful bowel preparation under special conditions? *World J Gastroenterol* 2014; **20**: 2741-2745 [PMID: 24659865 DOI: 10.3748/wjg.v20.i11.2741]
- 168 **Ko CW**, Riffle S, Shapiro JA, Saunders MD, Lee SD, Tung BY, Kuver R, Larson AM, Kowdley KV, Kimmey MB. Incidence of minor complications and time lost from normal activities after screening or surveillance colonoscopy. *Gastrointest Endosc* 2007; **65**: 648-656 [PMID: 17173914]

DOI: [10.1016/j.gie.2006.06.020](https://doi.org/10.1016/j.gie.2006.06.020)

- 169 **Lee YC**, Wang HP, Chiu HM, Lin CP, Huang SP, Lai YP, Wu MS, Chen MF, Lin JT. Factors determining post-colonoscopy abdominal pain: prospective study of screening colonoscopy in 1000 subjects. *J Gastroenterol Hepatol* 2006; **21**: 1575-1580 [PMID: [16928219](https://pubmed.ncbi.nlm.nih.gov/16928219/) DOI: [10.1111/j.1440-1746.2006.04145.x](https://doi.org/10.1111/j.1440-1746.2006.04145.x)]
- 170 **Drago L**, Toscano M, De Grandi R, Casini V, Pace F. Persisting changes of intestinal microbiota after bowel lavage and colonoscopy. *Eur J Gastroenterol Hepatol* 2016; **28**: 532-537 [PMID: [27015015](https://pubmed.ncbi.nlm.nih.gov/27015015/) DOI: [10.1097/MEG.0000000000000581](https://doi.org/10.1097/MEG.0000000000000581)]
- 171 **Shaw AG**, Black N, Rushd A, Sim K, Randell P, Kroll JS, Epstein J. Assessing the Colonic Microbiota in Children: Effects of Sample Site and Bowel Preparation. *J Pediatr Gastroenterol Nutr* 2017; **64**: 230-237 [PMID: [27070657](https://pubmed.ncbi.nlm.nih.gov/27070657/) DOI: [10.1097/MPG.0000000000001233](https://doi.org/10.1097/MPG.0000000000001233)]
- 172 **Chen HM**, Chen CC, Wang SC, Wang CL, Huang CH, Liou JS, Liu TW, Peng HL, Lin FM, Liu CY, Weng SL, Cheng CJ, Hung YF, Liao CC, Huang HD. Gut microbiome changes in overweight male adults following bowel preparation. *BMC Genomics* 2018; **19**: 904 [PMID: [30598081](https://pubmed.ncbi.nlm.nih.gov/30598081/) DOI: [10.1186/s12864-018-5285-6](https://doi.org/10.1186/s12864-018-5285-6)]
- 173 **Mai V**, Greenwald B, Morris JG Jr, Raufman JP, Stine OC. Effect of bowel preparation and colonoscopy on post-procedure intestinal microbiota composition. *Gut* 2006; **55**: 1822-1823 [PMID: [17124165](https://pubmed.ncbi.nlm.nih.gov/17124165/) DOI: [10.1136/gut.2006.108266](https://doi.org/10.1136/gut.2006.108266)]
- 174 **Jalanka J**, Salonen A, Salojärvi J, Ritari J, Immonen O, Marciani L, Gowland P, Hoad C, Garsed K, Lam C, Palva A, Spiller RC, de Vos WM. Effects of bowel cleansing on the intestinal microbiota. *Gut* 2015; **64**: 1562-1568 [PMID: [25527456](https://pubmed.ncbi.nlm.nih.gov/25527456/) DOI: [10.1136/gutjnl-2014-307240](https://doi.org/10.1136/gutjnl-2014-307240)]
- 175 **Mai V**, Stine OC. Bowel preparation for colonoscopy: relevant for the gut's microbiota? *Gut* 2015; **64**: 1504-1505 [PMID: [25681401](https://pubmed.ncbi.nlm.nih.gov/25681401/) DOI: [10.1136/gutjnl-2014-308937](https://doi.org/10.1136/gutjnl-2014-308937)]
- 176 **Nishimoto Y**, Mizutani S, Nakajima T, Hosoda F, Watanabe H, Saito Y, Shibata T, Yachida S, Yamada T. High stability of faecal microbiome composition in guanidine thiocyanate solution at room temperature and robustness during colonoscopy. *Gut* 2016; **65**: 1574-1575 [PMID: [27340192](https://pubmed.ncbi.nlm.nih.gov/27340192/) DOI: [10.1136/gutjnl-2016-311937](https://doi.org/10.1136/gutjnl-2016-311937)]
- 177 **Nagata N**, Tohya M, Fukuda S, Suda W, Nishijima S, Takeuchi F, Ohsugi M, Tsujimoto T, Nakamura T, Shimomura A, Yanagisawa N, Hisada Y, Watanabe K, Imbe K, Akiyama J, Mizokami M, Miyoshi-Akiyama T, Uemura N, Hattori M. Effects of bowel preparation on the human gut microbiome and metabolome. *Sci Rep* 2019; **9**: 4042 [PMID: [30858400](https://pubmed.ncbi.nlm.nih.gov/30858400/) DOI: [10.1038/s41598-019-40182-9](https://doi.org/10.1038/s41598-019-40182-9)]
- 178 **O'Brien CL**, Allison GE, Grimpén F, Pavli P. Impact of colonoscopy bowel preparation on intestinal microbiota. *PLoS One* 2013; **8**: e62815 [PMID: [23650530](https://pubmed.ncbi.nlm.nih.gov/23650530/) DOI: [10.1371/journal.pone.0062815](https://doi.org/10.1371/journal.pone.0062815)]
- 179 **Kim JH**, Choi YJ, Kwon HJ, Jung K, Kim SE, Moon W, Park MI, Park SJ. Effect of gut microbiome on minor complications after a colonoscopy. *Intest Res* 2021; **19**: 341-348 [PMID: [33166441](https://pubmed.ncbi.nlm.nih.gov/33166441/) DOI: [10.5217/ir.2020.00057](https://doi.org/10.5217/ir.2020.00057)]
- 180 **D'Souza B**, Slack T, Wong SW, Lam F, Muhlmann M, Koestenbauer J, Dark J, Newstead G. Randomized controlled trial of probiotics after colonoscopy. *ANZ J Surg* 2017; **87**: E65-E69 [PMID: [26183594](https://pubmed.ncbi.nlm.nih.gov/26183594/) DOI: [10.1111/ans.13225](https://doi.org/10.1111/ans.13225)]
- 181 **Mullaney TG**, Lam D, Kluger R, D'Souza B. Randomized controlled trial of probiotic use for post-colonoscopy symptoms. *ANZ J Surg* 2019; **89**: 234-238 [PMID: [30414225](https://pubmed.ncbi.nlm.nih.gov/30414225/) DOI: [10.1111/ans.14883](https://doi.org/10.1111/ans.14883)]



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