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OREGON HEALTH AND SCIENCE UNIVERSITY
OFFICE OF CLINICAL INTEGRATION AND EVIDENCE-BASED PRACTICE

Evidence-Based Practice Summary
Bowel Prep Regimens for Colonoscopy

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BACKGROUND

Bowel preparation evaluation is a crucial quality indicator of colonoscopy by professional societies. An adequate bowel cleansing is essential for colon mucosa assessment during the examination procedure, while an incomplete preparation prolongs the procedure time and increases the likelihood of missing lesions with cancerous potential. Nevertheless, the gold standard agent and regimen for bowel preparation is still debated. One of the most widely used agents is polyethylene glycol due to proven safety and efficacy; however, patients can be intolerant of the taste and large amount of ingested fluid (Cheng 2016).

This review seeks to determine the evidence for the best bowel-cleansing regimen for colonoscopy, analyzing quality indicators as well as patient-important outcomes such as taste and compliance.

ASK THE QUESTION

Question 1: In patients prepping for colonoscopy, what bowel preparation regimen achieves improved clinical (e.g. adenoma detection rate) and patient (e.g. patient satisfaction, patient compliance, decreased rescheduling) outcomes?

SEARCH FOR EVIDENCE

Databases included Ovid MEDLINE, Cochrane Database of Systematic Reviews, and National Guideline Clearinghouse.
Search strategy included:

1 exp Colonoscopy/ (28696)
2 exp Cathartics/ (21455)
3 exp Polyethylene Glycols/ (64721)
4 2 or 3 (84710)
5 1 and 4 (1247)

6 ((bowel* or colon*) adj5 (prep or prepar* or evac* or clean*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (6144)
7 1 and 6 (1907)
8 ((bowel* or colon*) adj5 (prep or prepar* or evac* or clean*) adj10 (colonoscop* or sigmoidoscop*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (1512)
9 7 or 8 (2101)
10 ((bowel* or colon*) adj5 (prep or prepar* or evac* or clean*) adj10 (success* or accura* or qualit* or effectiv* or complet* or total* or discover* or detect* or diagnos* or find* or found or identif* or locat*)).mp. (1718)
11 5 or 9 or 10 (3047)
12 exp Prognosis/ (1478376)
13 exp "Outcome and Process Assessment (Health Care)"/ (997809)
14 exp "Sensitivity and Specificity"/ (544466)
15 exp Health Behavior/ (159094)
16 exp Attitude to Health/ (381603)
17 exp "Attitude of Health Personnel"/ (147516)
18 exp early diagnosis/ (41936)
19 exp "costs and cost analysis"/ (221342)
20 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 (2691051)
21 11 and 20 (1068)
22 limit 21 to (english language and humans) (968)
23 limit 22 to (comparative study or controlled clinical trial or evaluation studies or guideline or meta analysis or randomized controlled trial or systematic reviews) (539)
24 exp Epidemiologic Studies/ (2242856)
25 22 and 24 (403)
26 23 or 25 (704)

Filters/limits included systematic reviews published in English in the last 5 years.

CRITICALLY ANALYZE THE EVIDENCE

The literature search resulted in more than 700 articles that analyzed bowel prep regimens prior to colonoscopy. We narrowed the search to include twenty-two systematic reviews and relevant RCTs conducted in the United States and Europe from 2013-2017. In order to simplify the review process, we grouped the evidence into modalities: (1) Miralax with Gatorade; (2) Diet; (3) Polyethylene glycol (PEG) with Lubiprostone; (4) 2L vs 4L PEG; (5) Split Dose Regimens; (6) Sodium Picosulfate; and (7) Sodium Phosphate:

1. Miralax with Gatorade: One systematic review assessed the use of Miralax-Gatorade(M-G) versus PEG for bowel preparation before colonoscopy (Siddique 2014). The review included five RCTS with over 1,400 participants. When pooled and weighted via meta-analysis, statistically significantly fewer satisfactory bowel preparations were noted for patients receiving the M – G preparation as compared with those receiving PEG (OR 0.65; 95 % confidence interval (CI): 0.43 – 0.98; P = 0.04). There was no statistically significant difference between the regimens in detecting polyps (OR 0.94; 95 % CI: 0.71 – 1.24; P = 0.65), nausea (OR 0.88; 95 % CI: 0.46 – 1.72; P = 0.71), cramping (OR 1.09; 95 % CI: 0.47 – 2.52; P = 0.84), or bloating (OR 0.81; 95 % CI: 0.43 – 1.51; P = 0.50). The M – G group demonstrated statistically significantly higher willingness to repeat the bowel preparation as compared with the PEG group (OR 7.32; 95 % CI: 4.88 – 10.98; P < 0.01).

Overall Level of Evidence: High to support PEG vs. M-G for satisfactory preparations and no statistical difference in patient- important or safety outcomes.

2. Diet: One systematic review (Avalos 2017) compared bowel preparation outcomes between a low-residue diet (LRD) or regular diet (RD) compared with a clear liquid diet (CLD). Twelve RCTs with over three thousand patients were included in the review. The authors found no difference in quality of bowel preparation outcomes between dietary groups (RR 1.00, 95% CI 0.97–1.04, P = 0.83). Patients in the LRD/ RD arm were the most likely participants to consume a targeted amount of the bowel laxative (RR 1.04, 95% CI 1.01–1.08, P =0.02) and repeat the colonoscopy process (RR 1.08, 95% CI 1.01–1.16, P = 0.03). Adverse events were reported in 10 of the 12 trials. Among the adverse events, hunger reached statistical significance, with more events in the CLD group (RR 1.93, 95% CI 1.13–3.3, P = 0.017).

Overall Level of Evidence: High to support LRD/RD versus CLD for patient-important and safety outcomes with no statistical difference in the quality of bowel preparation.

3. Polyethylene glycol (PEG) with Lubiprostone: Two RCTs assessed PEG with a single dose of Lubiprotone. The first RCT (Banerjee 2026) assessed the adequacy of PEG preparation with the addition of single dose of Lubiprotone (LB [24mcg]) vs placebo and efficacy of reduced dose PEG+LB compared with full dose PEG+LB. The study was divided into two parts. In part one; patients were randomized to receive placebo (GrA) or single dose of LB (GrB) prior to PEG preparation. In part two, patients were randomized to receive LB + 1.5 L PEG (GrC) or LB + 1 L PEG (GrD) and compared to placebo. The results for part one indicated that the use of LB resulted in significant improvement in total scores (p < 0.0001). The results in part two indicated no difference in scores with lower doses (Gr C&D) compared to standard (GrB). The second RCT (Sofi 2015)

assessed the efficacy of lubiprostone (versus placebo) plus PEG as a bowel cleansing preparation for colonoscopy. Patients scheduled for screening colonoscopy were randomized 1:1 to lubiprostone (group 1) or placebo (group 2) plus 1 gallon of PEG. For the outcome of quality of bowel prep and patient tolerability, there were no significant differences between the control and placebo group.

Overall Level of Evidence: Low to support the addition of Lubiprostone to a PEG regimen.

4. 2L vs 4L PEG: Eight RCTs investigated the difference between 2 liter versus 4 liter PEG regimens. The first RCT (Gentile 2013) compared low-volume PEG-based solution combined with ascorbic acid with high-volume PEG-based solution combined with simethicone in terms of efficacy and patient tolerability. In terms of efficacy as measured by adequate bowel prep, patient tolerability, and adverse events, there was no statistical difference between the two groups. The second RCT (Mathus –Vliegen 2013) compared the safety, acceptance, and efficacy of 2-L PEG solution enriched in vitamin C (PEG-Asc) with 4-L PEG solution. An adequate score was obtained by 97.4% of the 2L PEG group and by 98.4% of the 4L PEG group with a nonsignificant difference of 1.0% in favor of 4L PEG, but, because the lower level of the 95% CI was above −14, the no inferiority assumption of 2L PEG was proven. Adverse events associated with the intake of the bowel preparations were not different and mainly consisted of abdominal distension, irritated anus, cold feelings, and abdominal cramps. The patient tolerability and willingness to repeat the same preparation was twice as high in the 2L PEG group. The third RCT (Parente 2015) compared bowel cleansing efficacy, tolerability and acceptability of 2-L polyethylene-glycol-citrate-simethicone (PEG-CS) plus 2-day bisacodyl (reinforced regimen) vs. 4-L PEG in patients with chronic constipation undergoing colonoscopy. The investigators found no significant difference between the two preparations with regard to the primary endpoint of bowel cleansing score. No significant difference was observed between the two treatment groups with regard to sleep loss and interference with daily activities. The 2-L PEG-CS + bisacodyl regimen was significantly better accepted in terms of ease of administration (67% vs 47%, P<0.001) and willingness to repeat (94% vs 78%, P< 0.001). In terms of adverse events, there was no significant difference between the regimens. The fourth RCT (Ponchon 2013) compared the efficacy, safety and acceptability of a 2L PEG+ascorbate solution with a standard 4-L PEG solution. In terms of bowel preparation superiority, this study failed to show superiority of the 2-L solution over the standard 4-L preparation. However, in terms of patient tolerability, more subjects were willing to take the 2L PEG+ascorbate solution again (87% versus 51%, P<0.001), found it easier to drink (80% versus 70%, P=0.025) and with a better taste (P=0.01). In terms of adverse events, fewer treatment-related adverse events were reported with the 2-L solution (80.2% versus 89.9%, P=0.011). The fifth RCT (Rivas 2014) compared the bowel-cleansing efficacy of same-day ingestion of 4-L sulfa-free polyethylene glycol (4-L SF-PEG) vs 2-L polyethylene glycol solution with ascorbic acid (2-L PEG + Asc) in patients undergoing afternoon colonoscopy. The 4-L SF-PEG resulted in lower overall scores compared to 2-L PEG + Asc (4.2 vs 4.9), (P = 0.0186). However, there was no statistical difference with regards to total polyp detection, adenoma detection or advanced adenoma detection rates between the two arms. Concerning patient tolerability and satisfaction, there was no statistical difference between the two arms. With regards to adverse events, the 4-L

group experienced less bloating than those who received the 2-L PEG + Asc solution (11.5% vs 23.1%, P = 0.0235). The sixth RCT (Valiante 2012) also compared the efficacy, safety and acceptability of 2-L PEG+ascorbic acid (PEG + Asc) vs 4-L PEG for colonoscopy. There was no statistically significant difference in adequate bowel preparations between the groups (P=0.2). In terms of patient tolerability and acceptability, a good to excellent acceptability score was rated more frequently in the 2-L PEG + Asc arm as compared with the 4-L PEG group (83% vs 76%; p = 0.02). There were no significant differences in reported side effects between the PEG + Asc and the 4-L PEG groups. The most common reported side effects were nausea and vomiting. The seventh RCT (Gimeno-Garcia 2017) compared 4-L split-dose polyethylene-glycol (PEG) regimen vs. 2-L split-dose PEG plus ascorbic acid (PEG+Asc) in patients with previous colonoscopy with inadequate bowel preparation. Overall, patients allocated to PEG 4-L had a more effective colon cleansing than those in the PEG+Asc 2-L group (81.1 vs. 67.4%, OR: 2.07, 95% CI: 1.163–3.689, P =0.012). Both preparation regimens were similar regarding taste, problems encountered during the bowel preparation intake or willingness to take the same bowel preparation in the future and the most frequent side effect was the nausea in 24.9% followed by vomiting in 5% (no statistical difference between the groups). The eighth RCT (Musetto 2015) compared the efficacy of bowel cleansing using a low-volume mixed preparation (15 mg bisacodyl plus 2 L polyethylene glycol [PEG] solution) versus a standard high-volume preparation (4 L PEG) in patients with previous colorectal resection. No significant difference was observed between the low-volume and high-volume preparations in achievement of adequate bowel cleansing. The low volume preparation had better tolerability in terms of intake of the whole amount of the preparation (P < 0.001). No statistical difference was observed in terms of adverse events between the low volume and high volume groups.

Overall Level of Evidence: Moderate to support no statistical difference between 2L and 4L PEG in terms of bowel cleansing and adverse events and High to support 2L over 4L PEG in terms of patient acceptability.

5. Split-Dose Regimens: Four studies, one systematic review and three RCTs evaluated split-dose regimens. The systematic review (Martel 2015) examined the efficacy of split-dose vs other colon preparation regimens, the optimal products for use, and the most effective preparation volumes analyzing 47 trials with over 13,000 patients. In terms of bowel preparations their analysis found that split-dose preparations provided significantly better colon cleansing than day-before preparations (OR 2.51; 95% CI, 1.86-3.39; P<0.01). In terms of patient tolerability, a higher proportion of patients were willing to repeat split-dose vs day-before cleansing (OR, 1.90; 95% CI, 1.05-3.46; P<0.01), and low-volume split-dose preparations vs high-volume split-dose preparation (OR, 4.95; 95% CI, 2.21-11.10; P<0.01). The first RCT (Mohamed 2016) compared the efficacy, safety, and tolerability of PEG lavage and split-dose PEG lavage with specific emphasis on the cleanliness of the right colon. The authors found that, in total, the bowel preparation was superior in the split-dose group compared with the single dose group (P<0.05). There was no statistical difference in patient tolerability and the mean number of adverse events experienced during the lavage was higher in the single-dose group compared with the split-dose group (2.60 versus 2.01; P= 0.05). The second RCT (Radelli 2017) evaluated whether a split regimen (SDG) was superior to the traditional 'full-dose, day-before' (DBG) regimen in terms of adenoma detection rates (ADR). At a per-patient analysis, the proportion of subjects with at least one ADR was significantly

higher in the SDG than in the DBG (53.0% vs 40.9%, RR 1.22, 95% CI 1.03 to 1.46; P=0.002). The proportion of patients with successful colon cleansing was significantly higher in the SDG than in the DBG (95.4% vs 89.0%, P=0.001). Significantly better compliance and tolerability endpoints were observed in the SDG (P values ranged from 0.005 to 0.048) and no differences in adverse events. The third RCT (Schulz 2016) compared the efficacy and safety of a split-dose regimen of sodium picosulfate/magnesium citrate (SPMC) with a prior-day schedule (AM/PM). The authors found a significantly higher proportion of patients in the split-dose regimen demonstrated an adequate bowel preparation (AM/PM: 30.8% vs split-dose: 79.9%; p<0.0001). There was no statistically significant difference in terms of patient acceptability or adverse events other than patients in the AM/PM group were more hungry (P=0.009).

Overall Level of Evidence: High to support split-dose regimens over single-dose regimens in terms of bowel cleansing and Moderate to support split dose-regimens over single dose regimens in terms of patient acceptability and no statistical differences in adverse events.

6. <u>Sodium Picosulfate vs PEG:</u> Four RCTs compared the efficacy, tolerability and safety of sodium picosulfate versus PEG. The first RCT (Katz 2013) investigated the efficacy, safety, and tolerability of day-before administration of sodium picosulfate and magnesium citrate P/MC vs. 2L polyethylene glycol solution and two 5-mg bisacodyl tablets in adult patients preparing for colonoscopy. In terms of efficacy, the authors found the lower bound of the one-sided 97.5 % confidence interval for treatment difference in overall colon cleansing between the bowel preparations was greater than − 9.0 % ; therefore, the efficacy of P / MC was determined to be non-inferior to 2L PEG-3350 and bisacodyl tablets. Overall, the distribution of patient rating of acceptability and tolerability for P / MC was significantly superior to 2L PEG-3350 and bisacodyl tablets (P < 0.0001). There were no statistically significant differences in adverse events between the regimens. The second RCT (Kojecky 2014) compared the efficacy and tolerance of sodium picosulphate/magnesium citrate (PMC) (PEG) in a single or split dose regimen for colonoscopy bowel preparation. There was no statistically significant difference in satisfactory bowel cleansing scores. The PMC prepared subjects reported the best tolerance (score 1) more frequently than the PEG prepared ones (p < 0.001). Nausea occurred most frequently in the PEG and less frequently with PMC (P< 0.001). Abdominal pain was reported less frequently after PMC when compared to PEG (p =0.021). The third RCT (Munoz-Navas 2015) compared the efficacy and acceptability of an evening-before regimens of sodium picosulfate/magnesium citrate (SPMC) and PEG as bowel cleansers. No significant differences were found between the two regimens for the cleansing scores of the five segments of the colon evaluated. Treatment success was significantly higher in subjects assigned to the regimen of SPMC vs. subjects assigned to PEG (P<0.001). There were no serious adverse events that were considered treatment-related in either group. The fourth RCT (Munsterman 2015) examined the effectiveness of Kleanprep (PEG) and Picoprep (SPMC) using a split-dose regimen and an objective bowel cleansing score system. There was no significant difference in cleansing scores between the regimens. Patients using SPMC scored significantly better on the aspects of convenience and flavor of the preparation agent compared with

patients using PEG (P<0.001). Side effects such as nausea (P=0.011), vomiting (P=0.001), headache (P=0.003) and bloating (P<0.001) were experienced less significantly by patients using SPMC.

Overall Level of Evidence: Moderate to support no significant difference in terms of bowel cleansing and adverse events and to support Picosulfate over PEG in terms of patient acceptability.

7. Sodium Phosphate vs PEG: Two studies, one systematic review and one RCT compared the efficacy, safety, and tolerability between sodium phosphate (NaP) and PEG bowel prep regimens. The systematic review (Cheng 2016) sought to determine which of the two regimens should be considered the gold standard in terms of bowel prep regimens. A total of seven trials included in the review reported on the rate of adequate preparation comparing both regimens. There was no significant difference between NaP and PEG bowel cleansing regimen (OR 1.05; 95 % CI 0.40–2.74; P = 0.92). Six randomized controlled trials described the quality scores in both regimens. The summarized result suggested that patients undergoing NaP cleansing was graded with lower scores than that of PEG management (WMD: -0.78; 95 % CI -1.32 to -0.23; P = 0.005). In terms of patient tolerability, five trials contained comparative data of patient compliance in terms of NaP or PEG cleansing. A better patient compliance was explored within NaP cleansing group than PEG regimen (OR 4.31; 95 % CI 1.61–11.50; P = 0.004). Five included trials mentioned comparison of patient acceptability between both cleansing regimens. NaP displayed higher level of acceptability compared to PEG cleansing (OR 2.80; 95 % CI 1.24–6.32; P = 0.01). In terms of adverse events, the incidence of nausea and vomiting was statistically significantly less in the NaP group (P<0.05). The included RCT (Ell 2014) compares the efficacy, safety and acceptability of bowel preparation with polyethylene glycol, sodium sulfate and electrolytes (PEG+Asc) or sodium phosphate (NaP). In terms of efficacy, The total difference in the mean segmental cleansing scores between the two treatment groups was statistically significant in favor of PEGþAsc (P<0.001). Participants rated the overall taste significantly better for PEGþAsc than for NaP (P=0.04). A significantly greater percentage of participants who received PEGþAsc (88.4%) indicated that they would be willing to take it again in the case of another colonoscopy compared to those who received NaP (78.1%) (P=0.0001). There was no statistically significant difference in adverse events between the regimens.

Overall Level of Evidence: Moderate to support no significant difference in terms of adequate bowel cleansing and adverse events, to support Sodium Phosphate in terms of patient acceptability, and to support PEG in terms of cleansing scores.

PICO Question: In patients prepping for colonoscopy, what bowel preparation regimen achieves improved clinical (e.g. adenoma detection rate) and patient (e.g. patient satisfaction, patient compliance, decreases rescheduling) outcomes?						Lower Quality Rating if: ☐ Studies inconsistent (*wide variation of treatment effect across studies, populations, interventions, or outcomes varied)* ☐ Studies are indirect *(PICO question is quite different from the available evidence in regard to population, intervention, comparison, or outcome)* ☐ Studies are imprecise (*When studies include few patients and few events and thus have wide confidence intervals and the results are uncertain)* ☐ Publication Bias *(e.g. pharmaceutical company sponsors study on effectiveness of drug, only small, positive studies found)* Increase Quality Rating if: ☐ Large Effect ☐ Dose-response gradient ☐ Plausible confounders or other
Modality: Miralax with Gatorade **Outcome:** Improved Outcomes						
Author/Date	*Purpose of Study*	*Study Design & Methods*	*Sample*	*Outcomes*	*Design Limitations*	
Total # of Studies: 1 # of Systematic Reviews: 1						
Siddique, S., et al. (2014). *American Journal of Gastroenterology*	To assess the use of Miralax-Gatorade (M-G) vs. PEG for bowel preparation before colonoscopy.	Systematic Review with meta-analysis	5 studies with 1,418 participants	**Quality of Preparation:** When pooled and weighted via meta-analysis, **statistically significantly fewer satisfactory bowel preparations were noted for patients receiving the M – G preparation as compared with those receiving PEG** (OR 0.65; 95 % confidence interval (CI): 0.43 – 0.98; P = 0.04) **Polyp Detection:** Despite the preparation quality, two studies (N = 902) examined polyp detection and **found no statistically significant difference between those receiving the M – G preparation** (292 / 601, 48.6 %) **and those receiving PEG** (151 / 301, 50.2 %) (OR 0.94; 95 % CI: 0.71 – 1.24; P = 0.65). **Side Effects:** No serious adverse events were reported in the studies**. No statistically significant difference was noted between the M – G group and the PEG group for nausea** (24 / 251, 9.6 % vs. 17 / 155, 11 % ; OR 0.88; 95 % CI: 0.46 – 1.72; P = 0.71), **cramping** (16 / 251, 6.4 % vs. 9 / 155, 5.8 % ; OR 1.09; 95 % CI: 0.47 – 2.52; P = 0.84), or **bloating** (26 / 251, 10.4 % vs. 24 / 155,15.5 % ; OR 0.81; 95 % CI: 0.43 – 1.51; P = 0.50) **Willingness to repeat prep**: The **M – G** group (unweighted 497 / 537, 92.6 %)	Study Limitations = ☒ None ***Systematic Review*** ☐ Review did not address focused clinical question ☐ Search was not detailed or exhaustive ☐ Quality of the studies was not appraised or studies were of low quality ☐ Methods and/or results were inconsistent across studies	

				demonstrated statistically significantly higher willingness to repeat the bowel preparation as compared with the PEG group (unweighted 238 / 357, 66.7 %) (OR 7.32; 95 % CI: 4.88 – 10.98; P < 0.01)		biases increase certainty of effect Quality (certainty) of evidence for studies as a whole: ☒ High ☐ Moderate ☐ Low ☐ Very Low

The GRADE criteria were used to evaluate the quality of evidence presented in research articles reviewed during the development of this guideline. For more detailed information, see Appendix A.

PICO Question: In patients prepping for colonoscopy, what bowel preparation regimen achieves improved clinical (e.g. adenoma detection rate) and patient (e.g. patient satisfaction, patient compliance, decreases rescheduling) outcomes?						Lower Quality Rating if:
Modality: Diet **Outcome:** Improved Outcomes						☐ Studies inconsistent (*wide variation of treatment effect across studies, populations, interventions, or outcomes varied)* ☐ Studies are indirect *(PICO question is quite different from the available evidence in regard to population, intervention, comparison, or outcome)* ☐ Studies are imprecise (*When studies include few patients and few events and thus have wide confidence intervals and the results are uncertain)* ☐ Publication Bias *(e.g. pharmaceutical company sponsors study on effectiveness of drug,*
Author/Date	*Purpose of Study*	*Study Design & Methods*	*Sample*	*Outcomes*	*Design Limitations*	
Total # of Studies: 1 # of Systematic Reviews: 1 # of RCTs: Click here to enter text. **# of Non-Randomized Studies:** Click here to enter text. **# of Diagnostic Studies:** Click here to enter text.						
Avalos , D. J., et al. (2017). *Southern Medical Journal*	To compare bowel preparation outcomes between a low-residue diet (LRD) or regular diet (RD) compared with a clear liquid diet (CLD).	Systematic Review with meta-analysis	12 studies, 3163 patients (1583 subjects in the CLD arm and 1580 in the LRD/RD arm)	**Bowel Preparation:** No difference in quality of bowel preparation outcomes was noted between dietary groups (RR 1.00, 95% CI 0.97–1.04, P = 0.83) **Tolerability/compliance:** Tolerability and compliance were combined as one endpoint. The pooled RR for tolerability/compliance was 1.04 (95% CI 1.01–1.08, P =0.02). Patients in the LRD/ RD arm were the most likely participants to consume a targeted amount of the bowel laxative. **Willingness to repeat prep:** Patients consuming an LRD/RD diet were more likely to repeat the colonoscopy process (RR 1.08, 95% CI 1.01–1.16, P = 0.03) **Adverse events:** Adverse events were reported in 10 of the 12 trials. Among the	Study Limitations = ☒ None ***Systematic Review*** ☐ Review did not address focused clinical question ☐ Search was not detailed or exhaustive ☐ Quality of the studies was not appraised or studies were of low quality ☐ Methods and/or results were inconsistent across studies	

				adverse events, hunger reached statistical significance, with more events in the CLD group (RR 1.93, 95% CI 1.13–3.3, P = 0.017).		*only small, positive studies found)* Increase Quality Rating if: ☐ Large Effect ☐ Dose-response gradient ☐ Plausible confounders or other biases increase certainty of effect Quality (certainty) of evidence for studies as a whole: ☒ High ☐ Moderate ☐ Low ☐ Very Low

The GRADE criteria were used to evaluate the quality of evidence presented in research articles reviewed during the development of this guideline. For more detailed information, see Appendix A.

PICO Question: In patients prepping for colonoscopy, what bowel preparation regimen achieves improved clinical (e.g. adenoma detection rate) and patient (e.g. patient satisfaction, patient compliance, decreases rescheduling) outcomes?						
Modality: Polyethylene glycol (PEG) with Lubiprostone **Outcome:** Improved Outcomes						
Author/Date	*Purpose of Study*	*Study Design & Methods*	*Sample*	*Outcomes*	*Design Limitations*	Lower Quality Rating if: ☒ Studies inconsistent (*wide variation of treatment effect across studies, populations, interventions, or outcomes varied)* ☐ Studies are indirect *(PICO question is quite different from the available evidence in regard to population, intervention, comparison, or outcome)* ☐ Studies are imprecise (*When studies include few patients and few events and thus have wide confidence intervals and the*
Total # of Studies: 2 # of Systematic Reviews: Click here to enter text. **# of RCTs: 2 # of Non-Randomized Studies:** Click here to enter text. **# of Diagnostic Studies:** Click here to enter text.						
Banerjee, R., et al. (2016). *BMC*	To assess adequacy of PEG preparation with addition of single dose LB (24mcg) vs placebo and efficacy of reduced dose	RCT. Part 1: Patients for colonoscopy randomized to receive placebo (GrA) or single dose of LB (GrB) prior to PEG preparation Part 2: patients randomized to receive LB + 1.5 L PEG (GrC; 75) or LB + 1 L PEG (GrD; 71) and compared to placebo	588 patients	**Part 1 Quality of bowel prep per Boston Bowel Prep Scale:** LB resulted in significant improvement in total BBPS (7.44 + 0.14 vs. 6.36 + 0.16, p < 0.0001). **66.5 % Gr B vs 38 % Gr A had excellent prep; 42.5% GrB vs 24 % GrA had adequate prep. Repeat procedure needed 9.5 % Gr B vs 16.7 % Gr A (P < 0.01).** **Part 2 Quality of bowel prep per Boston**	Study Limitations = ☒ None ***RCTS*** ☐ Lack of blinding ☐ Lack of allocation concealment ☐ Stopped early for benefit ☐ Incorrect analysis of ITT ☐ Selective reporting of	

	PEG+LB compared with full dose PEG+LB.			**Bowel Prep Scale:** No difference in BBPS scores with lower doses (Gr C&D) compared to standard (GrB)	measures (e.g., no effect outcome) ☐ Large losses to F/U ☐ Difference in important prognostic factors at baseline	*results are uncertain)* ☐ Publication Bias *(e.g. pharmaceutical company sponsors study on effectiveness of drug, only small, positive studies found)*
Sofi, A. A., et al. (2015). *American Journal of Therapeutics*	To assess the efficacy of lubiprostone (versus placebo) plus PEG as a bowel cleansing preparation for colonoscopy	RCT. Patients scheduled for screening colonoscopy were randomized 1:1 to lubiprostone (group 1) or placebo (group 2) plus 1 gallon of PEG.	123 patients	**Quality of Prep:** There was no significant difference in overall colon cleansing scores between the drug and placebo groups **Table 2.** Comparison of overall cleansing scores* between the drug groups. N / Mean ± SD / P Group 1 (lubiprostone) 57 1.24 ± 0.59 0.163 Group 2 (placebo) 66 1.38 ± 0.49 **Patient Tolerability:** There was no significant difference in response between the 2 groups (P=0.553) **Table 4.** Comparison of lubiprostone tolerance between the drug groups. Group / N / Easy, N (%) / Tolerable, N (%) / Slightly difficult, N (%) / P Lubiprostone 52 0 (0) 50 (96.2) 2 (3.9) 0.553 Placebo 64 1 (1.6) 61 (95.3) 2 (3.1)	Study Limitations = ☐ None ***RCTS*** ☐ Lack of blinding ☒ Lack of allocation concealment ☐ Stopped early for benefit ☐ Incorrect analysis of ITT ☐ Selective reporting of measures (e.g., no effect outcome) ☐ Large losses to F/U ☐ Difference in important prognostic factors at baseline	Increase Quality Rating if: ☐ Large Effect ☐ Dose-response gradient ☐ Plausible confounders or other biases increase certainty of effect Quality (certainty) of evidence for studies as a whole: ☐ High ☐ Moderate ☒ Low ☐ Very Low

The GRADE criteria were used to evaluate the quality of evidence presented in research articles reviewed during the development of this guideline. For more detailed information, see Appendix A.

PICO Question: In patients prepping for colonoscopy, what bowel preparation regimen achieves improved clinical (e.g. adenoma detection rate) and patient (e.g. patient satisfaction, patient compliance, decreases rescheduling) outcomes?						Lower Quality Rating if: ☒ Studies inconsistent (*wide variation of treatment effect across studies, populations, interventions, or outcomes varied)* ☐ Studies are indirect
Modality: 2L vs 4L PEG **Outcome:** Improved Outcomes						
Author/Date	*Purpose of Study*	*Study Design & Methods*	*Sample*	*Outcomes*	*Design Limitations*	
Total # of Studies: 8 # of Systematic Reviews: Click here to enter text. **# of RCTs: 8 # of Non-Randomized Studies:** Click here to enter text. **# of Diagnostic Studies:** Click here to enter text.						
Gentile, M., et al. (2013). *Surgical*	To compare low-volume	RCT. Patients were randomized to receive either 2 L PEG plus ascorbic	120 patients, 60 in each	**Bowel Preparation:** adequate examinations were achieved in 81.67% of	Study Limitations = ☒ None	

Laparoscopy, Endoscopy & Percutaneous Techniques	PEG-based solution combined with ascorbic acid with high-volume PEG-based solution combined with simethicon in terms of efficacy and patient tolerability.	acid (PEG+Asc) or 4 L PEG plus simethicon (PEG+Sim).	group	the 2LPEG+Asc group versus 80% in the 4LPEG+Sim group. This difference was not statistically significant (P=1.000) **Compliance/Tolerability:** Considering only the patients expressing a good disposition, 63.3% of the patients taking PEG+Asc and 73.3% of the patients taking PEG+Sim (P=0.3265) reported that they would rather try another preparation for a future colonoscopy. **Adverse events:** The most common reported side effect was nausea that occurred in 10% of the PEG+Asc patients and 20% of the PEG+Sim patients. Vomiting was observed in 5% and 6.6%, respectively (P=1.0000).	***RCTS*** ☐ Lack of blinding ☐ Lack of allocation concealment ☐ Stopped early for benefit ☐ Incorrect analysis of ITT ☐ Selective reporting of measures (e.g., no effect outcome) ☐ Large losses to F/U ☐ Difference in important prognostic factors at baseline	*(PICO question is quite different from the available evidence in regard to population, intervention, comparison, or outcome)* ☐ Studies are imprecise (*When studies include few patients and few events and thus have wide confidence intervals and the results are uncertain)* ☐ Publication Bias *(e.g. pharmaceutical company sponsors study on effectiveness of drug, only small, positive studies found)*
Mathus -Vliegen, E. M. and K. van der Vliet (2013). *Diseases of the Colon & Rectum*	To compare the safety, acceptance, and efficacy of 2-L polyethylene glycol electrolyte solution enriched in vitamin C with 4-L polyethylene glycol electrolyte solution	RCT. Consecutive outpatients were randomly assigned to receive 4-L polyethylene glycol electrolyte solution or 2-L polyethylene glycol electrolyte solution enriched in vitamin C with 2 L of clear fluids in a single-dose or a split-dose regime	188 patients, 98 in the 2L PEG and 90 in the 4L PEG	**Bowel Preparation:** An adequate Aronchick score was obtained by 97.4% of the PEG-ELS-Asc group and by 98.4% of the PEG-ELS group with a nonsignificant difference of 1.0% in favor of PEG-ELS, but, because the lower level of the 95% CI was above −14, the noninferiority assumption of PEG-ELS-Asc was proven. An adequate Ottawa score was obtained by 87.0% of the PEG-ELS-Asc and by 92.3% of the PEG-ELS group with a nonsignificant difference of 5.3% in favor of PEG-ELS **Adverse events:** Gastrointestinal complaints associated with the intake of the bowel preparation were not different and mainly consisted of abdominal distension, irritated anus, cold feelings, and abdominal cramps.	Study Limitations = ☒ None ***RCTS*** ☐ Lack of blinding ☐ Lack of allocation concealment ☐ Stopped early for benefit ☐ Incorrect analysis of ITT ☐ Selective reporting of measures (e.g., no effect outcome) ☐ Large losses to F/U ☐ Difference in important prognostic factors at baseline	Increase Quality Rating if: ☐ Large Effect ☐ Dose-response gradient ☐ Plausible confounders or other biases increase certainty of effect Quality (certainty) of evidence for studies as a whole: ☐ High ☒ Moderate ☐ Low ☐ Very Low

				Compliance/Tolerability: The willingness to repeat the same preparation was almost twice as high in the PEG-ELS-Asc group.		
Parente, F., et al. (2015). *Digestive & Liver Disease*	To compare bowel cleansing efficacy, tolerability and acceptability of 2-L polyethylene-glycol-citrate-simethicone (PEG-CS) plus 2-day bisacodyl (reinforced regimen) vs. 4-L PEG in patients with chronic constipation undergoing colonoscopy.	RCT. Adult outpatients undergoing colonoscopy were randomly allocated to 2-L PEG-CS/bisacodyl or 4-L PEG, taken as split regimens before colonoscopy	400 patients	**Bowel Preparation: There was no significant difference between the two preparations with regard to the primary endpoint of bowel cleansing score**. 2-L PEG plus bisacodyl was not found to be superior to 4-L PEG as the confidence interval of the difference between the mean scores exceeds zero **Compliance/Tolerability: No significant difference was observed between the two treatment groups with regard to sleep loss** (>2 h, 23% vs 19%) **and interference with daily activity** (moderate and severe interference, 10% vs 14%). \ There was **a statistically significant difference in the proportion of patients regarding the amount of oral solution taken for bowel preparation** (p = 0.002). **Adverse events:** In the PEG-CS group the most frequent adverse events were headache (1%) and chills (1%), and in the 4-L PEG group they were headache (1.6%), vomiting (1%) and dizziness (1%). No significant differences were seen in the rate and severity of gastrointestinal symptoms, which are determinants for tolerability, i.e. nausea (no or mild 2-L PEG-CS 89% vs 4-L PEG 85%), bloating (no or mild 93% vs 92%), abdominal pain/cramping (no or mild 92% vs 94%).	Study Limitations = ☒ None ***RCTS*** ☐ Lack of blinding ☐ Lack of allocation concealment ☐ Stopped early for benefit ☐ Incorrect analysis of ITT ☐ Selective reporting of measures (e.g., no effect outcome) ☐ Large losses to F/U ☐ Difference in important prognostic factors at baseline	
Ponchon , T., et al. (2013). *Digestive & Liver Disease*	To compare the efficacy, safety and acceptability of a 2L polyethylene	RCT. Adults referred for colonoscopy were randomised to 2-L polyethylene glycol+ascorbate or 4-L polyethylene glycol solution.	400 patients	**Bowel Preparation:** Successful colon cleansing (HCS grade A or B) allowing 100% of mucosal visualization was observed in 94.1% of patients in the low volume 2-L PEG + ascorbate group, versus 90.9% in the standard 4-L PEG group in	Study Limitations = ☐ None ***RCTS*** ☐ Lack of blinding ☒ Lack of allocation concealment	

	glycol+ascorbate solution with a standard 4-L polyethylene glycol solution.			the ITT population **(NS, p = 0.232)** as judged by the independent experts. Similar results were obtained in the PP population; therefore, **the study failed to show superiority of the 2-L solution over the standard 4-L preparation**. **There were no differences between the two treatment groups with regard to the number of colonoscopies stopped, or repeated, owing to the poor quality of the preparation (p > 0.05).** **For all other examination results there were no significant differences between treatment groups** (duration of the colonoscopy, time to reach the caecum, number of biopsies and polypectomies performed, time spent on mucosal examination during withdrawal of the colonoscope) **(p > 0.05).** **Compliance/Tolerability:** More subjects were willing to take the 2L PEG+ascorbate solution again (87% versus 51%, p<0.001), found it easier to drink (80% versus 70%, p=0.025), with a better taste (p=0.01). **Adverse events:** Fewer treatment-related adverse events were reported with the 2-L solution (80.2% versus 89.9%, p=0.011).	☐ Stopped early for benefit ☐ Incorrect analysis of ITT ☐ Selective reporting of measures (e.g., no effect outcome) ☐ Large losses to F/U ☐ Difference in important prognostic factors at baseline	
Rivas , J. M., et al. (2014). *World Journal of Gastroenterology*	To compare the bowel cleansing efficacy of same day ingestion of 4-L sulfa-free polyethylene glycol (4-L SF-PEG) vs 2-L polyethylene glycol solution with ascorbic acid (2-L PEG + Asc) in patients	RCT. Patients undergoing outpatient screening or surveillance colonoscopies were prospectively randomized to receive either 4-L SF-PEG or 2-L PEG + Asc solution	206 patients	**Bowel Preparation:** Eight patients required shortening of future screening interval due to unsatisfactory preparation quality (5 assigned to 4-L SF-PEG and 3 to 2-L PEG + Asc). **4-L SF-PEG resulted in lower overall Ottawa scores compared to 2-L PEG + Asc** (4.2 vs 4.9), (P = 0.0186). **There was no difference with regards to total polyp detection, adenoma detection or advanced adenoma detection rates**	Study Limitations = ☐ None ***RCTS*** ☐ Lack of blinding ☒ Lack of allocation concealment ☐ Stopped early for benefit ☐ Incorrect analysis of ITT ☐ Selective reporting of measures (e.g., no effect outcome) ☐ Large losses to F/U ☐ Difference in important prognostic factors at baseline	

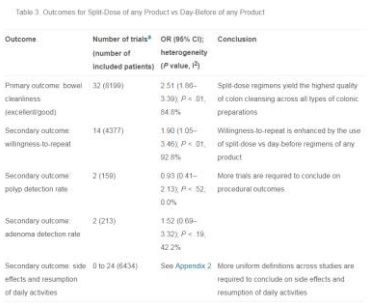
	undergoing afternoon colonoscopy			**between the two arms.** The 4-L solution was also more likely to result in optimal preparation for total scores lower than 5 (64% vs 46%); P = 0.019. At Ottawa scores of less than seven, there was still a trend favoring 4-L SF-PEG (P = 0.072) **Compliance/Tolerability:** There was no difference in patient satisfaction among the study groups as measured by multiple questions assessing this. **Adverse events:** those randomized to 4-L experienced less bloating than those who received the 2-L PEG + Asc solution (11.5% vs 23.1%), (P = 0.0235)		
Valiante, F., et al. (2012). *Digestive & Liver Disease*	To compare the efficacy, safety and acceptability of 2-L PEG+ascorbic acid vs 4-L PEG for colonoscopy	RCT. Patients undergoing colonoscopies were prospectively randomized to receive either 4-L PEG or 2-L PEG + Asc solution		**Bowel Preparation:** According to Aronchick scale, bowel preparation was considered to be adequate in 143 (ITT: 84.6%; PP: 86.2%) patients in the 2-L PEG ± Asc arm and 128 (ITT: 75.3%; PP: 77%) in the 4-L PEG, respectively (ITT, p = 0.04; PP, p = 0.2NS) **Compliance/Tolerability** Patient questionnaire findings by preparation group tolerability were recorded. A good-excellent acceptability was rated more frequently in the 2-L PEG + Asc arm as compared with the 4-L PEG group (83% vs 76%; p = 0.02). **Adverse events:** There were no significant differences in reported side effects between the PEG + Asc and the 4-L PEG groups. The most common reported side effects were nausea and vomiting.	Study Limitations = ☒ None ***RCTS*** ☐ Lack of blinding ☐ Lack of allocation concealment ☐ Stopped early for benefit ☐ Incorrect analysis of ITT ☐ Selective reporting of measures (e.g., no effect outcome) ☐ Large losses to F/U ☐ Difference in important prognostic factors at baseline	
Gimeno-Garcia, A. Z., et al. (2017).	To compare two intensive bowel cleansing	RCT. Patients with inadequate cleansing at index colonoscopy were randomized to 4-L split-dose	256 patients	**Bowel Preparation: Overall, patients allocated to Group 1 (PEG 4-L) had a more effective colon cleansing than those**	Study Limitations = ☐ None ***RCTS***	

American Journal of Gastroenterology	regimens in patients with previous colonoscopy with inadequate bowel preparation.	polyethylene-glycol (PEG) regimen vs. 2-L split-dose PEG plus ascorbic acid (PEG+Asc) regimen.		**in Group 2** (PEG+Asc 2-L) (81.1 vs. 67.4%, OR: 2.07, 95% CI: (1.163–3.689), P =0.012). **Patients allocated to Group 1 had a more effective bowel cleansing than those in Group 2** (86.6 vs. 71.7%, OR: 2.55, 95% CI: [1.316–4.922], P =0.005). **ADR, PDR, diminute ADR, diminute PDR, and number of polyps or adenoma per patient did not defer between groups either.** **Tolerability/compliance:** In the same way, both preparation regimens were similar regarding taste, problems encountered during the bowel preparation intake or willingness to take the same bowel preparation in the future Table 4. Tolerance, acceptance and willingness to take the same preparation Group 1[a] (n=127) | Group 2[b] (n=129) | OR (95% CI) | P value Adverse effects, n (%)[c] | 45 (35.4) | 47 (36.4) | 0.96 (0.575–1.596) | 0.88 Taste, n (%)[d] | 28 (22.0) | 27 (20.9) | 0.83 (0.515–1.700) | 0.83 Problems to take the prepa-ration, n (%)[e] | 28 (22.0) | 25 (19.4) | 1.18 (0.642–2.156) | 0.60 Willigness, n (%)[f] | 106 (83.5) | 106 (82.8) | 1.05 (0.544–2.018) | 0.89 **Adverse events:** The most frequent side effect was the nausea in 24.9% followed by vomits in 5%.	☐ Lack of blinding ☒ Lack of allocation concealment ☐ Stopped early for benefit ☐ Incorrect analysis of ITT ☐ Selective reporting of measures (e.g., no effect outcome) ☐ Large losses to F/U ☐ Difference in important prognostic factors at baseline	
Mussetto ,A., et al. (2015). *Endoscopy*	To compare the efficacy of bowel cleansing using a low-volume mixed preparation (15 mg bisacodyl	RCT. Patients with prior colorectal resection for cancer undergoing surveillance colonoscopy were randomized to receive either a split-dose low-volume or high-volume preparation for bowel cleansing	120 patients	**Bowel Preparation:** No significant difference was observed between the low-volume and high-volume preparations in achievement of adequate cleansing (i. e. mOBPS <= 4; low-volume vs. high-volume group, 85.0 % vs. 81.7 %, P = 0.624). **Compliance/Tolerability:** Low volume	Study Limitations = ☒ None ***RCTS*** ☐ Lack of blinding ☐ Lack of allocation concealment ☐ Stopped early for benefit ☐ Incorrect analysis of ITT	

	plus 2 L polyethylene glycol [PEG] solution) versus a standard high-volume preparation (4 L PEG) in patients with previous colorectal resection.			had better tolerability in terms of intake of the whole amount of the preparation (P < 0.001) **Adverse events:** No adverse events related to bowel preparation were reported in the high-volume group. One patient in the low-volume group reported an allergic rash that developed the evening before the procedure, 2 hours after taking the bisacodyl, and resolved after 3 days of oral steroids. The patient successfully completed intake of the whole preparation and the procedure was performed without any problem.	☐ Selective reporting of measures (e.g., no effect outcome) ☐ Large losses to F/U ☐ Difference in important prognostic factors at baseline	

The GRADE criteria were used to evaluate the quality of evidence presented in research articles reviewed during the development of this guideline. For more detailed information, see Appendix A.

PICO Question: In patients prepping for colonoscopy, what bowel preparation regimen achieves improved clinical (e.g. adenoma detection rate) and patient (e.g. patient satisfaction, patient compliance, decreases rescheduling) outcomes?						Lower Quality Rating if:
Modality: Split Dose **Outcome:** Improved Outcomes						☐ Studies inconsistent (*wide variation of treatment effect across studies, populations, interventions, or outcomes varied)* ☐ Studies are indirect *(PICO question is quite different from the available evidence in regard to population, intervention, comparison, or outcome)* ☐ Studies are imprecise (*When studies include few patients and few events and thus have wide confidence intervals and the results are uncertain)*
Author/Date	*Purpose of Study*	*Study Design & Methods*	*Sample*	*Outcomes*	*Design Limitations*	
Total # of Studies: 3 # of Systematic Reviews: 1 # of RCTs: 3 # of Non-Randomized Studies: Click here to enter text. **# of Diagnostic Studies:** Click here to enter text.						
Martel , M., et al. (2015). *Gastroenterology*	To determine the efficacy of split-dose vs other colon preparation regimens, the optimal products for use, and the most effective preparation volumes.	Systematic Review with meta-analysis.	47 trials,13,487 patients	**Bowel Preparation: Split-dose preparations provided significantly better colon cleansing than day-before preparations** (odds ratio [OR], 2.51; 95% confidence interval, 1.86-3.39), **as well as day-before preparations with PEG** (OR, 2.60; 95% confidence interval, 1.46-4.63), **sodium phosphate** (OR, 9.34; 95% confidence interval, 2.12-41.11), or **picosulfate** (OR, 3.54; 95% confidence interval, 1.95-6.45). **PEG split-dose preparations of 3 L or more yielded greater bowel cleanliness than lower-volume split-dose regimens** (OR, 1.89; 95% confidence interval, 1.01-3.46). **ADR,**	Study Limitations = ☒ None ***Systematic Review*** ☐ Review did not address focused clinical question ☐ Search was not detailed or exhaustive ☐ Quality of the studies was not appraised or studies were of low quality ☐ Methods and/or results were inconsistent across studies	

				PDR, diminute ADR, diminute PDR, and number of polyps or adenoma per patient did not defer between groups either. **<u>Tolerability/compliance:</u> A higher proportion of patients were willing to repeat split-dose vs day-before cleansing** (OR, 1.90; 95% confidence interval, 1.05-3.46), **and low-volume split-dose preparations vs high-volume split-dose preparation** (OR, 4.95; 95% confidence interval, 2.21-11.10). 		☐ Publication Bias *(e.g. pharmaceutical company sponsors study on effectiveness of drug, only small, positive studies found)* <u>Increase Quality Rating if:</u> ☐ Large Effect ☐ Dose-response gradient ☐ Plausible confounders or other biases increase certainty of effect Quality (certainty) of evidence for studies as a whole: ☒ High ☐ Moderate ☐ Low ☐ Very Low
Mohamed , R., et al. (2016). *Canadian Journal of Gastroenterology & Hepatology*	To compare the efficacy, safety, and tolerability of PEG lavage and split-dose PEG lavage with specific emphasis on the cleanliness of the right colon.	RCT. Patients were allocated to receive either a single 4L PEG lavage or a split-dose PEG lavage.	249 patients	**<u>Bowel Preparation:</u>** In total, the bowel preparation was superior in the split-dose group compared with the single dose group (mean Ottawa score: 3.50± 2.89 versus 5.96± 3.53; $P < 0.05$). Split-dose PEG resulted in a lower, and therefore better, mean Ottawa score across all segments of the colon **<u>Compliance/Tolerability:</u>** Both preparations were generally well tolerated and completed as directed by the majority of participants (90% in split-dose group versus 85% in single-dose group; *P*= NS) **<u>Adverse events:</u>** The mean number of	Study Limitations = ☒ None ***RCTS*** ☐ Lack of blinding ☐ Lack of allocation concealment ☐ Stopped early for benefit ☐ Incorrect analysis of ITT ☐ Selective reporting of measures (e.g., no effect outcome) ☐ Large losses to F/U ☐ Difference in important prognostic factors at baseline	

				adverse events experienced during the lavage was higher in the single-dose group compared with the split-dose group (2.60 versus 2.01; *P* = 0.05) No adverse events causing discontinuations were reported.		
Radaelli , F., et al. (2017). *Gut*	To evaluate whether a split regimen was superior to the traditional 'full-dose, day-before' regimen in terms of ADR.	RCT. subjects undergoing first colonoscopy after positive-fecal immunochemical test within an organized colorectal cancer organized screening programs were 1:1 randomized to receive low-volume 2-L polyethylene glycol (PEG)-ascorbate solution in a 'split-dose' (Split-Dose Group, SDG) or 'day-before' regimen (Day-Before Group, DBG).	690 subjects	**Adenoma Detection Rate:** At a per-patient analysis, the proportion of subjects with at least one adenoma (ADR) was significantly higher in the SDG than in the DBG (53.0% vs 40.9%, RR 1.22, 95% CI 1.03 to 1.46); corresponding figures for advanced adenomas were 26.4% versus 20.0% (RR 1.35, 95% CI 1.06 to 1.73) **Bowel Preparation:** The proportion of patients with successful colon cleansing (HCS grade A or B) was significantly higher in the SDG than in the DBG, either when considering the whole (95.4% vs 89.0%, p=0.001) or the right colon (94.5% vs 88.1%, p=0.002). **Compliance/Tolerability:** Significantly better compliance and tolerability endpoints were observed in the SDG. Overall, 19 (2.8%) and 5 (0.7%) patients reported the need of travel interruption and the occurrence of fecal incontinence during the transfer to the endoscopy service; 603 (87.4%) reported they would be willing to repeat the same preparation regimen in future. No difference was observed in the SDG and DBG for these figures.	Study Limitations = ☒ None ***RCTS*** ☐ Lack of blinding ☐ Lack of allocation concealment ☐ Stopped early for benefit ☐ Incorrect analysis of ITT ☐ Selective reporting of measures (e.g., no effect outcome) ☐ Large losses to F/U ☐ Difference in important prognostic factors at baseline	
Schulz, C., et al. (2016). *Journal of Gastrointestinal & Liver Diseases*	To compare the efficacy and safety of a split-dose regimen of sodium picosulfate/magnesium citrate (SPMC) with a	RCT. Subjects who met the selection criteria were randomly allocated to receive one of two regimens of SPMC in a ratio 1:1.	326 subjects	**Bowel Preparation:** A significantly higher proportion of patients in the split-dose regimen demonstrated an adequate bowel preparation (AM/PM: 30.8% vs split-dose: 79.9%; p<0.0001) When the rating of bowel cleansing was assessed in	Study Limitations = ☐ None ***RCTS*** ☐ Lack of blinding ☒ Lack of allocation concealment ☐ Stopped early for benefit ☐ Incorrect analysis of ITT	

	prior-day schedule (AM/PM).			four categories, there was also a significant difference between both treatment regimens favoring the split-dose schedule (p<0.0001) **Compliance/Tolerability:** The majority of subjects considered treatment with SPMC as easy or very easy to take, regardless of the regimen (AM/PM:96.2% vs split-dose: 93.7%). The majority of subjects also found the taste very or somewhat pleasant (AM/PM: 76.9% vs split-dose: 78.0%). An overall good or very good tolerance was observed in 87.2% of subjects in the AM/PM group and in 84.9% of subjects in the split-dose group. Most subjects in both groups were willing to retake the treatment in the future (AM/PM: 96.8% vs split-dose: 96.2%). **Adverse events:** physical discomfort (p=0.10) and nausea (p=0.34) were significantly more frequent in subjects receiving the split-dose regimen, while hunger(p=0.009) was significantly more frequent in subjects receiving AM/PM regimen	☐ Selective reporting of measures (e.g., no effect outcome) ☐ Large losses to F/U ☐ Difference in important prognostic factors at baseline	

The GRADE criteria were used to evaluate the quality of evidence presented in research articles reviewed during the development of this guideline. For more detailed information, see Appendix A

PICO Question: In patients prepping for colonoscopy, what bowel preparation regimen achieves improved clinical (e.g. adenoma detection rate) and patient (e.g. patient satisfaction, patient compliance, decreases rescheduling) outcomes?						Lower Quality Rating if: ☒ Studies inconsistent (*wide variation of treatment effect across studies, populations, interventions, or outcomes varied)* ☐ Studies are indirect *(PICO question is quite different from the available evidence in*
Modality: Sodium Picosulfate **Outcome:** Improved Outcomes						
Author/Date	*Purpose of Study*	*Study Design & Methods*	*Sample*	*Outcomes*	*Design Limitations*	
Total # of Studies: 4 # of Systematic Reviews: 0 # of Non-Randomized Studies: 4 **# of Diagnostic Studies:** Click here to enter text.						
Katz , P. O., et al. (2013). *American Journal of*	To investigate the efficacy, safety, and tolerability of	RCT. Patients were randomized to either sodium picosulfate and magnesium citrate P/MC or 2L polyethylene glycol solution and two	603 patients	**Bowel Preparation:** Using the Aronchick scale, overall colon cleansing in preparation for colonoscopy was similar in those patients who received P / MC compared	Study Limitations = ☐ None ***RCTS*** ☐ Lack of blinding ☒ Lack of allocation	

Gastroenterology	day-before administration of sodium picosulfate and magnesium citrate P/MC vs. 2L polyethylene glycol solution and two 5-mg bisacodyl tablets in adult patients preparing for colonoscopy	5-mg bisacodyl tablets		with those who received 2L PEG-3350 and bisacodyl tablets. The lower bound of the one-sided 97.5 % confidence interval for treatment difference in overall colon cleansing between the bowel preparations was greater than − 9.0 % ; therefore, the efficacy of P / MC was determined to be non-inferior to 2L PEG-3350 and bisacodyl tablets **Compliance/Tolerability:** Overall, the distribution of patient rating of acceptability and tolerability for P / MC was significantly superior to 2L PEG-3350 and bisacodyl tablets (P < 0.0001) **Adverse events:** The overall incidence of treatment-emergent AEs (TEAEs) was similar in patients receiving P / MC (73.6 %) and 2L PEG-3350 and bisacodyl tablets (79.8 %). Nausea, headache, and vomiting were the most common TEAEs.	concealment ☐ Stopped early for benefit ☐ Incorrect analysis of ITT ☐ Selective reporting of measures (e.g., no effect outcome) ☐ Large losses to F/U ☐ Difference in important prognostic factors at baseline	*regard to population, intervention, comparison, or outcome)* ☐ Studies are imprecise (*When studies include few patients and few events and thus have wide confidence intervals and the results are uncertain)* ☐ Publication Bias *(e.g. pharmaceutical company sponsors study on effectiveness of drug, only small, positive studies found)* Increase Quality Rating if: ☐ Large Effect ☐ Dose-response gradient ☐ Plausible confounders or other biases increase certainty of effect Quality (certainty) of evidence for studies as a whole: ☐ High ☒ Moderate ☐ Low ☐ Very Low
Kojecky , V., et al. (2014). *Journal of Gastrointestinal & Liver Diseases*	To compare the efficacy and tolerance of sodium picosulphate/magnesium citrate (PMC) and polyethylene glycol (PEG) in a single or split dose regimen for colonoscopy bowel preparation.	RCT. The patients were randomly assigned to receive PMC (PMC4/0) or PEG (PEG4/0) in a single dose 4L day before colonoscopy or a split dose 2+2L PMC (PMC2/2) or 3+1L PEG (PEG3/1) one day before and in the morning before the colonoscopy.	600 patients	**Bowel Preparation:** Satisfactory preparation (defined as Aronchick score 1 or 2) was present in 82.6% PMC4/0, 81.6% PMC2/2, 87.3% PEG3/1 and 73.0% PEG4/0. these rates were similar in all groups with the exception of PEG4/0 subjects (p = 0.024). The split dose of PEG or any of the PMC based regimens were superior to the PEG 4/0 (42.5% PEG3/1, 37.9% PMC4/0, 38.4% PMC2/2 vs. 22.6% PEG4/0, p = 0.003). Splitting the PMC preparation had no benefit (37.9% vs. 38.4%). When comparing single dose regimens, PMC performed better than PEG (37.9% vs. 22.6%) **Compliance/Tolerability**: The PMC prepared subjects reported the best tolerance (score 1) more frequently than the PEG prepared ones (PMC4/0 vs. PEG4/0 or PEG3/1, PMC2/2 vs. PEG4/0 orPEG3/1, p	Study Limitations = ☒ None ***RCTS*** ☐ Lack of blinding ☐ Lack of allocation concealment ☐ Stopped early for benefit ☐ Incorrect analysis of ITT ☐ Selective reporting of measures (e.g., no effect outcome) ☐ Large losses to F/U ☐ Difference in important prognostic factors at baseline	

				< 0.001), without a difference in the PMC group (60.6% vs. 56.0%). The split dose of PEG was not tolerated better than the conventional 4 L of PEG (23.1% vs.24.1%) **Adverse events:** Nausea occurred most frequently in the PEG4/0 group (32.8%) and less frequently after a single dose of PMC (6.1%,p < 0.001). Abdominal pain was reported less frequently after PMC4/0 (6.1%) when compared to other preparations (p =0.021).		
Munoz -Navas, M., et al. (2015). *International Journal of Colorectal Disease*	is to compare the efficacy and acceptability of an evening-before regimens of sodium picosulfate/magnesium citrate (SPMC) and polyethylene glycol (PEG) as bowel cleansers and to explore the results of a same-day regimen of SPMC.	RCT. Subjects who met the selection criteria were randomly allocated to receive an evening-before regimen of PEG or SPMCsolutions or a same-day schedule of SPMC in a ratio 4:4:1.The later group was included for exploratory purposes	499 subjects	**Bowel Preparation:** More subjects in the same-day SPMC group (86 %) were considered to exhibit an excellent or good bowel preparation compared with the other two regimens (67 % in each group). No significant differences were found between the two evening-before regimens for the Residual Stool Score or for the cleansing of the five segments of the colon evaluated. **Compliance/Tolerability**: Treatment success was significantly higher in subjects assigned to the evening-before regimen of SPMC vs. subjects assigned to the evening-before PEG (68 vs. 46 %, p<0.001). When evaluating the two individual components for treatment success, there were significant differences in the ease of completion, (easy to take or tolerable in 99 % of subjects receiving the SPMC evening-before regimen compared with 69 % in PEG group) but not in the quality of preparation. **Adverse events:** Forty-one (19 %) PEG-treated subjects exhibited adverse events, compared with 14 (6 %) and 6 (11 %) of those receiving the evening-before regimen or the same-day regimen of SPMC, respectively. There were no serious adverse events that were considered treatment-	Study Limitations = ☒ None ***RCTS*** ☐ Lack of blinding ☐ Lack of allocation concealment ☐ Stopped early for benefit ☐ Incorrect analysis of ITT ☐ Selective reporting of measures (e.g., no effect outcome) ☐ Large losses to F/U ☐ Difference in important prognostic factors at baseline	

				related in either group.		
Munsterman , I. D., et al. (2015). *European Journal of Gastroenterology & Hepatology*	To examine the effectiveness of Kleanprep and Picoprep was using a split-dose regimen and an objective bowel cleansing score system.	RCT. Subjects were randomized to receive Kleanprep or Picoprep split-dose regimen.	173 patients	**Bowel Preparation:** The overall Boston Bowel Preparation Score between Kleanprep and Picoprep was not significantly different (P=0.182). **Compliance/Tolerability**: Patients using Picoprep scored significantly better on the aspects of convenience and flavor of the preparation agent compared with patients using Kleanprep (P<0.001). **Adverse events:** Side effects such as nausea (P=0.011), vomiting (P=0.001), headache (P=0.003) and bloating (P<0.001) were experienced less significantly by patients using Picoprep.	Study Limitations = ☒ None ***RCTS*** ☐ Lack of blinding ☐ Lack of allocation concealment ☐ Stopped early for benefit ☐ Incorrect analysis of ITT ☐ Selective reporting of measures (e.g., no effect outcome) ☐ Large losses to F/U ☐ Difference in important prognostic factors at baseline	

The GRADE criteria were used to evaluate the quality of evidence presented in research articles reviewed during the development of this guideline. For more detailed information, see Appendix A

PICO Question: In patients prepping for colonoscopy, what bowel preparation regimen achieves improved clinical (e.g. adenoma detection rate) and patient (e.g. patient satisfaction, patient compliance, decreases rescheduling) outcomes?						Lower Quality Rating if:
Modality: Sodium Phosphate **Outcome:** Improved Outcomes						☒ Studies inconsistent (*wide variation of treatment effect across studies, populations, interventions, or outcomes varied)*
Author/Date	*Purpose of Study*	*Study Design & Methods*	*Sample*	*Outcomes*	*Design Limitations*	
Total # of Studies: 2 # of Systematic Reviews: 1 # of RCTs: 1 # of Non-Randomized Studies: Click here to enter text. **# of Diagnostic Studies:** Click here to enter text.						
Cheng , J., et al. (2016). *Surgical Endoscopy*	To compare sodium phosphate or polyethylene glycol as the gold standard agent for bowel preparation.	Systematic Review with meta-analysis	15 studies	**Bowel Preparation:** A total of seven trials reported on the rate of adequate preparation comparing both regimens. there was no significant difference between NaP and PEG bowel cleansing regimen (OR 1.05; 95 % CI 0.40–2.74; P = 0.92). Six randomized controlled trials described the Ottawa bowel preparation quality scale of total colon in both regimens. The summarized result suggested that patients	Study Limitations = ☒ None ***Systematic Review*** ☐ Review did not address focused clinical question ☐ Search was not detailed or exhaustive ☐ Quality of the studies was not appraised or studies were of low quality ☐ Methods and/or results were inconsistent across studies	☐ Studies are indirect *(PICO question is quite different from the available evidence in regard to population, intervention, comparison, or outcome)* ☐ Studies are

				undergoing NaP cleansing was graded with lower scores than that of PEG management (WMD: -0.78; 95 % CI -1.32 to -0.23; P = 0.005). **Tolerability/compliance:** Five original trials contained comparative data of patient compliance in terms of NaP or PEG cleansing. A better patient compliance was explored within NaP cleansing group than PEG regimen (OR 4.31; 95 % CI 1.61–11.50; P = 0.004). Five included trials mentioned comparison of patient acceptability between both cleansing regimens. NaP displayed higher level of acceptability compared to PEG cleansing (OR 2.80; 95 % CI 1.24–6.32; P = 0.01). **Adverse events:** Incidence of nausea and vomiting was statistically significantly less in the NaP group(P<0.05)		imprecise (*When studies include few patients and few events and thus have wide confidence intervals and the results are uncertain)* ☐ Publication Bias *(e.g. pharmaceutical company sponsors study on effectiveness of drug, only small, positive studies found)* Increase Quality Rating if: ☐ Large Effect ☐ Dose-response gradient ☐ Plausible confounders or other biases increase certainty of effect Quality (certainty) of evidence for studies as a whole: ☐ High ☒ Moderate ☐ Low ☐ Very Low
Ell , C., et al. (2014).	To compare the efficacy, safety and acceptability of bowel preparation with polyethylene glycol (PEG), ascorbic acid, sodium ascorbate (ascorbate components), sodium sulfate and electrolytes	RCT. Consenting adults undergoing elective out-patient colonoscopy for CRC were randomized to take 2 L PEG+Asc or 90 mL NaP (control) following manufacturer's instructions.	356 patients	**Bowel Preparation** The total difference in the mean segmental cleansing scores between the two treatment groups was statistically significant in favor of PEGþAsc (p<0.001). **Tolerability/compliance** Participants rated the overall taste on a verbal rating scale; the scores were significantly better for PEGþAsc than for NaP (p=0.04). A significantly greater percentage of participants who received PEGþAsc (88.4%) indicated that they would be willing to take it again in the case of another colonoscopy compared to those	Study Limitations = ☒ None ***RCTS*** ☐ Lack of blinding ☐ Lack of allocation concealment ☐ Stopped early for benefit ☐ Incorrect analysis of ITT ☐ Selective reporting of measures (e.g., no effect outcome) ☐ Large losses to F/U ☐ Difference in important prognostic factors at baseline	

	(PEG+Asc) or sodium phosphate (NaP).			who received NaP (78.1%) (p=0.0001) **Adverse events:** Similar proportions of participants in each group reported at least one adverse event (AE) (44.2% for PEGþAsc and 49.1% for NaP). Most AEs were classed as mild (83.1% for PEGþAsc, 82.2% for NaP)		

The GRADE criteria were used to evaluate the quality of evidence presented in research articles reviewed during the development of this guideline. For more detailed information, see Appendix A

Guideline Issuer	American Society of Gastrointestinal Endoscopy 2015	US Multi-Society Taskforce 2014
1. Transparency	A	A
2. Conflict of interest	A	A
3. Development group	NR	A
4. Systematic Review	A	A
5. Supporting evidence	A	A
6. Recommendations	A	A
7. External Review	NR	A
8. Currency and updates	B	A

See appendix B for full description of the Trustworthy Guideline grading system

Guideline Recommendations:

The 2015 American Society of Gastrointestinal Endoscopy recommends the following:

1. That bowel preparations be individualized by the prescribing provider for each patient based on efficacy, cost, safety, and tolerability considerations balanced with the patient's overall health, comorbid conditions, and preferences. *High Quality Evidence*
2. That a low-residue diet be used in conjunction with FDA-approved purgatives for bowel preparation before colonoscopy. *Moderate Quality Evidence*
3. Split-dose regimens for all patients and/or same day preparations for afternoon colonoscopy with a portion of the preparation taken within 3 to 8 hours of the procedure to enhance colonic cleansing and patient tolerance. *Moderate Quality Evidence*

The 2014 US Multi-Society Taskforce recommends:

1. Use of a split-dose bowel cleansing regimen is strongly recommended for elective colonoscopy. *Strong recommendation, high-quality evidenc*e
2. A same-day regimen is an acceptable alternative to split dosing, especially for patients undergoing an afternoon examination. *Strong recommendation, high-quality evidence*
3. The second dose of split preparation ideally should begin 4–6 h before the time of colonoscopy with completion of the last dose at least 2 h before the procedure time. *Strong recommendation, moderate-quality evidence*
4. By using a split-dose bowel cleansing regimen, diet recommendations can include either low-residue or full liquids until the evening on the day before colonoscopy. *Weak recommendation, moderate-quality evidence*
5. Selection of a bowel-cleansing regimen should take into consideration the patient's medical history, medications, and, when available, the adequacy of bowel preparation reported from prior colonoscopies. *Strong recommendation, moderate-quality evidence*
6. A split-dose regimen of 4 l PEG-ELS provides high-quality bowel cleansing. *Strong recommendation, high-quality evidence*
7. In healthy non-constipated individuals, a 4-L PEG-ELS formulation produces a bowel-cleansing quality that is not superior to a lower-volume PEG formulation. *Strong recommendation high-quality evidence*
8. Split-dose bowel cleansing is associated with greater willingness to repeat regimen compared with the day before regimen. *Strong recommendation, high-quality evidence*
9. The use of low-volume bowel cleansing agents is associated with greater willingness to undergo a repeat colonoscopy. *Strong recommendation, high-quality evidence*

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Appendix A. GRADE criteria for rating a body of evidence on an intervention

Developed by the GRADE Working Group

Grades and interpretations:

High: Further research is very unlikely to change our confidence in the estimate of effect. Moderate: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. Low: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. Very low: Any estimate of effect is very uncertain.

Type of evidence and starting level

Randomized trial–high Observational study–low Any other evidence–very low

Criteria for increasing or decreasing level

Reductions Study quality has serious (–1) or very serious (–2) problems Important inconsistency in evidence (–1) Directness is somewhat (–1) or seriously (–2) uncertain Sparse or imprecise data (–1) Reporting bias highly probable (–1) **Increases** Evidence of association† strong (+1) or very strong (+2) †Strong association defined as significant relative risk (factor of 2) based on consistent evidence from two or more studies with no plausible confounders Very strong association defined as significant relative risk (factor of 5) based on direct evidence with no threats to validity.

Appendix B. Trustworthy Guideline rating scale

The University of Pennsylvania's Center for Evidence-Based Practice Trustworthy Guideline rating scale is based on the Institute of Medicine's "Standards for Developing Trustworthy Clinical Practice Guidelines" (IOM), as well as a review of the AGREE Enterprise and Guidelines International Network domains.

The purpose of this scale is to focus on the weaknesses of a guideline that may reduce the trust a clinical user can have in the guideline, and distinguish weaknesses in documentation (e.g. guide-line does not have a documented updating process) from weaknesses in the guidance itself (e.g. recommendations are outdated). Current quality scales like AGREE emphasize documentation. They are important checklists for developers of new guidelines, but are less useful for grading existing guidelines. These scales also are harder for clinicians and other persons who are not methodology experts to apply, and their length discourages their use outside formal technology assessment reports. This new scale is brief, balanced, and easy and consistent to apply.

We do not attempt to convert the results of this assessment into a numeric score. Instead we present a table listing the guidelines and how they are rated on each standard. This facilitates qualitative understanding by the reader, who can see for what areas the guideline base as a whole is weak or strong as well as which guidelines are weaker or stronger.

1. Transparency

A	Guideline development methods are fully disclosed.
B	Guideline development methods are partially disclosed.
C	Guideline development methods are not disclosed.

The grader must refer to any cited methods supplements or other supporting material when evaluating the guideline. Methods should include:
Who wrote the initial draft
How the committee voted on or otherwise approved recommendations
Evidence review, external review and methods used for updating are not addressed in this standard.

2. Conflict of interest

A	Funding of the guideline project is disclosed, disclosures are made for each individual panelist, and financial or other conflicts do not apply to key authors of the guideline or to more than 1 in 10 panel members).
B	Guideline states that there were no conflicts (or fewer than 1 in 10 panel members), but does not disclose funding source.
C	Lead author, senior author, or guideline panel members (at least 1 in 10) have conflict of interest, or guideline project was funded by industry sponsor with no assurance of independence.
NR	Guideline does not report on potential conflict of interests.

For purposes of this checklist, conflicts of interest include employment by, consulting for, or holding stock in companies doing business in fields affected by the guideline, as well as related financial conflicts. This definition should not be considered exclusive. As much as anything,

this is a surrogate marker for thorough reporting, since it may be assumed that guideline projects are funded by the sponsoring organization and many authors think it unnecessary to report a non-conflict.

3. Guideline development group

A	Guideline development group includes 1) methodological experts and clinicians and 2) representatives of multiple specialties.
B	Guideline development group includes one of the above, but not both.
C	Guideline developers all from one specialty or organization, and no methodologists.
NR	Affiliations of guideline developers not reported

The purpose of this standard is to ensure that supporters of competing procedures, or clinicians with no vested interest in utilization of one procedure or another, are involved in development of the guideline. Both AGREE II and IOM call for patient or public involvement: very few guideline panels have done so to date, so this is not necessary for guidelines to be rated A. Involvement of methodologists or HTA specialists in the systematic review is sufficient involvement in the guideline development group for our purposes. In the absence of any description of the guideline group, assume the named authors are the guideline group.

4. Systematic review

A	Guideline includes a systematic review of the evidence or links to a current review.
B	Guideline is based on a review which may or may not meet systematic review criteria.
C	Guideline is not based on a review of the evidence.

In order to qualify as a systematic review, the review must do all of the following:
Describe itself as systematic or report search strategies using multiple databases
Define the scope of the review (including key questions and the applicable population)
Either include quantitative or qualitative synthesis of the data or explain why it is not indicated

Note: this element does not address the quality of the systematic review: simply whether or not it exists. Concerns about quality or bias of the review will be discussed in text, where the analyst will explain whether the weaknesses of the review weaken the validity or reliability of the guideline.
Note: a guideline may be rated B on this domain even if the review on which it is based is not available to us. This potential weakness of the guideline should be discussed in text of the report.

5. Grading the supporting evidence

A	Specific supporting evidence (or lack thereof) for each recommendation is cited and graded
B	Specific supporting evidence (or lack thereof) for each recommendation is cited but the recommendation is not graded.
C	Recommendations are not supported by specific evidence.

To score a B on this domain there should be specific citations to evidence tables or individual references for each relevant recommendation in the guideline, or an indication that no evidence was available. Any standardized grading system is acceptable for purposes of this rating. If a guideline reports that there is no evidence available despite a thorough literature search, it may be scored B on this domain, or even A if evidence for other recommendations is cited and graded.

6. Recommendations

A	Considerations for each recommendation are documented (i.e. benefits and harms of a particular action, and/or strength of the evidence); and recommendations are presented in an actionable form.
B	Either one or the other of the above criteria is met.
C	Neither of the above criteria are met

In order to be actionable, the guideline should specify the specific population to which the guideline applies, the specific intervention in question, and the circumstances under which it should be carried out (or not carried out). The language used in the recommendations should also be consistent with the strength of the recommendation (e.g. directive and active language like “should” or “should not” for strong recommendations, and passive language like “consider” for weak recommendations). A figure or algorithm is considered actionable as long as it is complete enough to incorporate all the applicable patients and interventions. Please see the forthcoming NICE manual (24) for a good discussion of actionability in guidelines.

7. External review

A	Guideline was made available to external groups for review.
B	Guideline was reviewed by members of the sponsoring body only.
C	Guideline was not externally reviewed.
NR	No external review process is described.

8. Updating and currency of guideline

A	Guideline is current and an expiration date or update process is specified.
B	Guideline is current but no expiration date or update process is specified.
C	Guideline is outdated.

A guideline is considered current if it is within the developers’ stated validity period, or if no period or expiration data is stated, the guideline was published in the past three years (NOTE: the specific period may be changed at the analyst’s discretion, based on whether the technology is mature and whether there is a significant amount of recent evidence). A guideline must address new evidence when it is updated. A guideline which is simply re-endorsed by the panel without searching for new evidence must be considered outdated.