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Colonoscopy Outcomes by Duration of NPO Status Prior to Colonoscopy with Moderate or Deep Sedation

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PREFACE

Quality Enhancement Research Initiative's (QUERI) Evidence-based Synthesis Program (ESP) was established to provide timely and accurate syntheses of targeted healthcare topics of particular importance to Veterans Affairs (VA) clinicians, managers and policymakers as they work to improve the health and healthcare of Veterans. The ESP disseminates these reports throughout the VA, and some evidence syntheses inform the clinical guidelines of large professional organizations.

QUERI provides funding for four ESP Centers and each Center has an active university affiliation. The ESP Centers generate evidence syntheses on important clinical practice topics, and these reports help:

- develop clinical policies informed by evidence;
- guide the implementation of effective services to improve patient outcomes and to support VA clinical practice guidelines and performance measures; and
- set the direction for future research to address gaps in clinical knowledge.

In 2009, the ESP Coordinating Center was created to expand the capacity of HSR&D Central Office and the four ESP sites by developing and maintaining program processes. In addition, the Center established a Steering Committee comprised of QUERI field-based investigators, VA Patient Care Services, Office of Quality and Performance, and Veterans Integrated Service Networks (VISN) Clinical Management Officers. The Steering Committee provides program oversight, guides strategic planning, coordinates dissemination activities, and develops collaborations with VA leadership to identify new ESP topics of importance to Veterans and the VA healthcare system.

Comments on this evidence report are welcome and can be sent to Nicole Floyd, ESP Coordinating Center Program Manager, at Nicole.Floyd@va.gov.

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EXECUTIVE SUMMARY

INTRODUCTION

Fourteen million colonoscopies are performed annually in the United States for screening, diagnosis, surveillance, and treatment of numerous colonic conditions. Colonoscopies require bowel preparation for cleansing to sufficiently visualize the colon lining, identify and treat suspected lesions, and maximize quality and safety. To optimize colon lining visualization, patients are advised to divide the bowel preparation regimen over two sessions (known as "split-dose preparation"): 1) the evening prior to the colonoscopy (PM dose) and 2) the morning of the colonoscopy (AM dose), the latter taken ideally within 2-6 hours of the planned procedure. In addition, some level of sedation (typically moderate or deep) is used in almost all colonoscopies to facilitate patient comfort and procedure quality.

There is significant variation among anesthesia providers as to the acceptable timing of NPO ("nothing by mouth"), including how many hours prior to the planned procedure the last bowel preparation dose can be taken, in order to minimize anesthesia risk (primarily pulmonary aspiration requiring hospitalization). Practice guidelines from the American Society of Anesthesiologists suggest a minimum fasting period of 2 hours for clear liquids and 6 hours for a light meal (*ie*, toast and clear liquids). The guideline authors note that published clinical evidence is insufficient to clearly define a relationship between NPO status and risk of emesis/reflux or aspiration.

There is a need to balance optimal colonic preparation, patient convenience, and scheduling efficiency (typically a shorter NPO window status) with anesthesia safety concerns for an elective procedure (typically a longer NPO status). In addition, performing procedures with moderate or deep sedation requires development of and adherence to local and/or national policy measures that cross multiple procedures and physician specialties. These policies include recommendations regarding NPO status.

The purpose of this report was to review the evidence on the relationship between timing of NPO and 1) the incidence of aspiration and other anesthesia-related harms during elective colonoscopy and 2) colonoscopy rescheduling. We also reviewed the evidence on the benefits and harms of variable timing of NPO status on colonoscopy outcomes including colonoscopy quality measures, resource use, and patient satisfaction. The review may be used to guide policy within the VA. We addressed the following key questions:

Key Question 1. Does the incidence of aspiration and other anesthesia-related harms for colonoscopy vary by NPO status or bowel prep timing (*eg*, > 6 hours, 2-6 hours, < 4 hours, and < 2 hours)? Does the incidence of anesthesia-related harms by NPO status vary by: a) patient characteristics (age, race, sex, obesity, comorbidities) or b) sedation (moderate, deep)?

Key Question 2. What is the effect of variable timing of bowel prep and NPO status on the quality of the bowel preparation, diagnostic yield, and colonoscopy procedural quality indicators (*eg*, completion rates, adenoma detection rate, total procedure time, cecal intubation time and withdrawal time)?

Key Question 3. What is the effect of NPO status prior to colonoscopy on resource use (*eg*, costs, unused procedure slots, delays in rescheduling, delays in diagnosis, increased volume of procedures, scheduler and nursing time associated with cancelled or delayed procedures)?

Key Question 4. What is the effect of bowel preparation and NPO status prior to colonoscopy on patient adherence to bowel preparation, colonoscopy, and/or rescheduled colonoscopy, and satisfaction with bowel preparation and/or colonoscopy?

METHODS

Data Sources and Searches

We searched MEDLINE (OVID) for articles published from 1990 through October 2014. Our search was designed to identify studies of any design. We limited the search to studies involving human subjects published in the English language. Search terms included the following Medical Subject Headings (MeSH): Colonoscopy, Cathartics, Polyethylene Glycols, Phosphates, and Respiratory Aspiration of Gastric Contents. We also searched reference lists of guidelines, existing reviews, and included studies and we received reference suggestions from stakeholders, Technical Expert Panel (TEP) members, and peer reviewers.

Study Selection

Abstracts of citations identified from the literature search were assessed for relevance by an investigator. Full text reports of studies identified as potentially eligible (or indeterminate, *eg*, title only) were obtained for further review by 2 independent investigators. We included studies of any design that reported outcomes following bowel preparation if at least one preparation was completed within 8 hours of the colonoscopy procedure. Only studies of adults, undergoing colonoscopy with moderate or deep sedation, and reporting outcome during colonoscopy or recovery from colonoscopy were included. We also included population-based studies of adverse events during colonoscopy.

Data Abstraction and Risk of Bias Assessment

From studies of different preparation-to-procedure or NPO intervals, study characteristics (inclusion/exclusion criteria and details about the preparation interventions or NPO status), patient characteristics, and outcomes data were abstracted onto tables by one investigator and verified by a second. Risk of bias (low, moderate, or high) was determined for each included study.

Data Synthesis and Analysis

We described and qualitatively compared the patient characteristics, study characteristics, intervention timing, and findings of included studies. Due to variation in the preparation-to-procedure interval and/or NPO status across studies and different systems used to report outcomes, we summarized most outcomes narratively. Strength of evidence was assessed for primary and secondary outcomes.

RESULTS

Results of Literature Search

Our literature search yielded 1177 abstracts or titles. We excluded 1069 and performed a full text review of 108 articles, excluding 74 articles and including 34. A hand-search of reference lists of guidelines, existing reviews, and included studies yielded another 6 articles for a total of 40 included studies of different bowel preparation or NPO status intervals (28 randomized controlled trials [RCTs], 2 controlled clinical trials [CCTs], and 10 observational studies). Of the 28 RCTs, 10 were low risk of bias, 16 were moderate risk of bias, and 2 were high risk of bias. Of the 10 observational studies, 3 were low risk of bias, 6 were moderate risk of bias, and one was high risk of bias. Both CCTs were high risk of bias.

Overview

An overview of outcomes reported is presented in Executive Summary Table 1. Our predefined primary and secondary outcomes were rarely reported. All but one study reported quality of the bowel preparation. Few or no studies reported other secondary or intermediate outcomes.

Executive Summary Table 1. Summary of Outcomes Reported in Included Studies

Category	Outcome (Number of Studies Reporting)[a]
Primary Outcomes	Aspiration (k=6)
	Rescheduled Colonoscopies (k=1)
Secondary Outcomes	Bowel Perforation (k=1)
	Other Adverse Events (k=7)
	Diagnostic Yield (k=3)
	Completion Rate (k=11)
	Adenoma Detection Rate (k=7)
	False Negative Colonoscopy
Intermediate Outcomes	Hospitalizations
	Costs
	Quality of Bowel Preparation (k=39)
	Total Procedure Time (k=3)
	Cecal Intubation Time (k=4)
	Withdrawal Time (k=5)
	Patient Adherence (k=11)[b]
	Patient Satisfaction (k=11)[b]
	Unused Procedure Slots
	Delays, Rescheduling
	Delays, Diagnosis
	Increased Volume, Procedures
	Scheduler/Nurse Time
	Volume of Gastric Contents (k=2)
	pH of Gastric Contents

[a] Total of 40 studies included in review

[b] Data on patient adherence and patient satisfaction extracted only from studies using same bowel preparation substance in the study groups (k=21)

Summary of Results for Key Questions

Key Question 1. *Does the incidence of aspiration and other anesthesia-related harms for colonoscopy vary by NPO status or bowel prep timing (eg, > 6 hours, 2-6 hours, < 4 hours, and < 2 hours)? Does the incidence of anesthesia-related harms by NPO status vary by: a) patient characteristics (age, race, sex, obesity, comorbidities) or b) sedation (moderate, deep)?*

Five studies (3 RCTs and 2 observational studies, total n=2,318) of split-dose bowel preparation regimens (completed at least 2 hours before colonoscopy) compared to evening-before regimens reported either no aspiration events during colonoscopy or in the 30 days following colonoscopy, or no complications related to sedation. Two of the 5 studies also specified that liquids were allowed up to 3 hours prior to the procedure. One of the observational studies reported no difference in gastric volume.

An additional RCT compared morning-only preparation to a split-dose regimen with both groups completing bowel preparation 4 hours before colonoscopy but allowed clear liquids up to 2.5 hours before. This study reported one aspiration event requiring 24 hour hospital observation in the morning-only group.

Although hospital- or population-based studies have reported on aspiration requiring hospitalization during colonoscopy, none documented NPO status of the patients at the time of the colonoscopy. One study reported a slightly higher incidence of aspiration requiring hospitalization (0.14% vs 0.10%) for Medicare patients having diagnostic colonoscopy with deep sedation versus moderate sedation. An Australian study of 23,508 outpatient colonoscopies reported one patient (0.004%) who had colonoscopy following general anesthesia had an aspiration event requiring hospitalization.

In an Italian study of 3,155 colonoscopies, there were 5 aspiration events requiring “some intervention by an anesthesiologist” (0.16%) but it was unclear what type of sedation the 5 patients received. Patients followed fasting guidelines of the study time period which allowed clear liquids at least 2 hours before the procedure and a light meal at least 6 hours before.

Key Question 2. *What is the effect of variable timing of bowel prep and NPO status on the quality of the bowel preparation, diagnostic yield, and colonoscopy procedural quality indicators (eg, completion rates, adenoma detection rate, total procedure time, cecal intubation time and withdrawal time)?*

Thirty-nine studies (28 RCTs, 2 CCTs, and 9 observational studies) reported on the effect of variable timing of bowel preparation on quality of the bowel preparation. Eleven of these studies (6 RCTs, 1 CCT, 4 observational) also reported the time prior to colonoscopy when water or other clear liquids were allowed, ranging from 4 hours until the time of the procedure. Although different rating scales were used to rate the quality of the bowel preparation, quality was consistently rated higher for NPO intervals of 6 hours or less compared to intervals of more than 8 hours. The difference was observed whether the minimum time was based on the completion of bowel preparation to procedure time (1 to 6 hours) or the time that liquids were allowed prior to the procedure (0 to 4 hours).

Pooled results from 5 RCTs (total n=1,795) found no difference in completion rate between shorter and longer NPO status (based on bowel preparation) groups. A retrospective observational study (n=5,175) reported a significantly higher completion rate (96% vs 94%, P = .008) in the shorter NPO group. One RCT reported no difference in adenoma detection rate based on NPO status while pooled results from 3 observational studies showed an improved detection rate with shorter NPO time. Diagnostic yield was reported in 3 RCTs with mixed findings for all polyps or lesions. One RCT reported no documented complications of bowel perforation on discharge from the endoscopy unit. No studies reported on false negative colonoscopies or hospitalizations.

Key Question 3. *What is the effect of NPO status prior to colonoscopy on resource use (eg, costs, unused procedure slots, delays in rescheduling, delays in diagnosis, increased volume of procedures, scheduler and nursing time associated with cancelled or delayed procedures)?*

One moderate risk of bias RCT (n=113) reported a significantly lower percentage of rescheduled colonoscopies (3%) in the split-dose group compared to 2 groups that completed preparation the evening before the colonoscopy (8% and 24%). However, preparation agents differed in the 3 study groups. No other resource use outcomes were reported.

Key Question 4. *What is the effect of bowel preparation and NPO status prior to colonoscopy on patient adherence to bowel preparation, colonoscopy, and/or rescheduled colonoscopy, and satisfaction with bowel preparation and/or colonoscopy?*

We extracted data on adherence and satisfaction from studies where the same bowel preparation substance (*eg*, polyethylene glycol) was used for all patients. Adherence to the bowel preparation regimen was typically higher with a split-dose regimen but several studies reported no difference between split-dose and same day (day before colonoscopy) regimens.

We extracted elements of satisfaction that would be impacted by different schedules for bowel preparation. Results were inconsistent for time lost from work or school and sleep disruption.

DISCUSSION

Key Findings and Strength of Evidence

- Hospital- or population-based studies have reported that the risk of aspiration serious enough to require hospitalization during colonoscopy is very low (1 in 1000 or less). However, these studies have not documented NPO status and it is possible that the low rates are driven by more individuals having longer rather than shorter NPO status.

- In 3 RCTs and 2 observational studies (total n=2,318) comparing shorter NPO status to NPO status of at least 8 hours, no aspiration events were reported. Bowel preparation was completed at least 2 hours prior to colonoscopy in 2 studies and at least 3 hours prior to colonoscopy in one study. Another study allowed clear liquids up to 3 hours prior to colonoscopy and the remaining study only reported that bowel preparation was completed in the morning for an afternoon colonoscopy.

- One small RCT (n=113) reported a significantly lower percentage of rescheduled colonoscopies in the split-dose group compared to 2 groups that completed preparation the evening before the colonoscopy, although different preparation agents were used in the 3 groups. No studies reported on other resource use outcomes including unused procedure slots or increased volume of procedures by NPO status.

- Few studies assessing NPO status specified adverse events associated with colonoscopy as an outcome of interest and therefore adverse events may be underreported.

- Time from completion of colonic preparation to colonoscopy of 1 to 6 hours is associated with greater bowel preparation quality than time intervals of greater than 8 hours. Of 24 studies comparing split-dose versus non-split-dose preparation, 20 reported higher quality of bowel preparation with split-dose.

- Completion rate was not significantly different between NPO status groups in 5 RCTs; one large observational study reported a greater completion rate with shorter NPO status. Results were mixed for diagnostic yield and adenoma detection rate with no consistent findings based on NPO status. One study reported no documented complications of bowel perforation; no study reported on false negative colonoscopy.

- Among studies reporting adherence to the bowel preparation regimen, time lost from work, or sleep disruption, results were mixed with no clear benefit of split-dose regimens over same day regimens.

- Studies of NPO status typically excluded patients with serious comorbidities.

- For our co-primary outcomes, strength of evidence was low for aspiration and insufficient for rescheduled colonoscopies. For secondary outcomes, strength of evidence was moderate for completion rate based on pooled results from 5 RCTs, low for adenoma detection rate based on pooled results from 3 observational studies, and insufficient for diagnostic yield, bowel perforation, and false-negative colonoscopy.

Applicability

Populations enrolled in eligible studies were broadly applicable to many individuals undergoing elective colonoscopy in the United States. Eligible studies typically included patients 45 to 65 years with approximately 50% of patients enrolled in studies done in the US. Nearly one-half patients were male and two-thirds of colonoscopies were performed for cancer screening. The largest study reporting on aspirations requiring hospitalization was completed in a US Medicare population. However, aspiration by NPO status was not provided in this study and few other studies were adequately designed to directly assess the role of NPO status on aspirations requiring hospitalizations or colonoscopy rescheduling.

Research Gaps/Future Research

Future studies are needed that systematically assess duration of NPO status in relation to timing of colonoscopy and record serious adverse events, including aspiration requiring hospitalization. Such studies could include prospective registries or pooling currently collected adverse event outcomes across the Veterans Health Administration (VHA). Future studies are also needed to determine and understand variability in NPO duration policies and practices across VA (especially practices that appear not to adhere to national society guidance statement) and to implement interventions to reduce variation. There is also a need for larger studies comparing shorter durations of NPO prior to colonoscopy (such as 2 to 4 hours) to longer intervals of NPO prior to colonoscopy (such as $\geq$ 6 hours) that directly assess for colonoscopy effectiveness (such as detection rate of adenoma and neoplasia, completion rate) and safety outcomes. We also need studies evaluating the effect of variable duration of NPO status prior to colonoscopy on patient satisfaction, adherence to colonoscopy, and impact on endoscopy scheduling processes, including delays in timely receipt of colonoscopy. Finally, evidence-based multi-society consensus conference guidelines are needed that bring together patient representatives and members from anesthesia, gastroenterology, and general medicine. Important items include determining the “clinically important” balance between important outcomes to anesthesiologists, gastroenterologists and patients including aspiration rates due to NPO status, colonoscopy quality measures, resource use, and patient satisfaction and adherence.

Conclusions

Aspiration incidence requiring hospitalization during colonoscopy with moderate or deep sedation is very low and on the order of magnitude commonly accepted for adverse effects of similar clinical importance due to other elective procedures. Participants in hospital- and population-based studies likely had wide ranges of timing from NPO to colonoscopy and many were likely longer than 2 to 4 hours. No study documenting NPO status found that shorter NPO status prior to colonoscopy increased aspiration risk. We did not find direct evidence of the effect of NPO status on colonoscopy rescheduling. Shorter time from completion of colonic preparation to colonoscopy is associated with greater bowel preparation quality than longer time intervals.

ABBREVIATIONS TABLE

ASA	American Society of Anesthesiologists
CCT	Controlled clinical trial
NPO	Nil per os (nothing by mouth)
RCT	Randomized, controlled trial
VA	Department of Veterans Affairs
VHA	Veterans Health Administration

EVIDENCE REPORT

INTRODUCTION

Fourteen million colonoscopies are performed annually in the United States for screening, diagnosis, surveillance, and treatment of numerous colonic conditions. Colonoscopies require bowel preparation for cleansing to sufficiently visualize the colon lining and maximize quality and safety. However, inadequate preparation occurs in approximately 25% of colonoscopies, leading to cancellations, rescheduling, difficulty in detecting colonic polyps or other pathology,[1,2] poor patient adherence, as well as longer procedure time. Increased financial and opportunity costs and patient dissatisfaction result.[3]

To optimize colon lining visualization, patients are advised to divide the bowel preparation regimen over two sessions (known as "split-dose preparation"): 1) the evening prior to the colonoscopy (PM dose) and 2) the morning of the colonoscopy (AM dose); the latter taken ideally within 2-6 hours of the planned procedure.[4-7] In addition, some level of sedation (typically moderate or deep) is used in almost all colonoscopies to facilitate patient comfort and procedure quality.[8,9]

For both moderate and deep sedation there is significant variation among anesthesia providers as to the acceptable timing of NPO ("nothing by mouth") including how many hours prior to the planned procedure the last bowel preparation dose can be taken in order to minimize anesthesia risk (primarily aspiration). Practice guidelines from the American Society of Anesthesiologists Committee on Standards and Practice Parameters for preoperative fasting for healthy patients undergoing elective procedures suggest the following minimum fasting periods with the goal of minimizing anesthesia-related risks (primarily aspiration): 2 hours for clear liquids (*eg*, water, fruit juice without pulp, carbonated beverages, clear tea, and black coffee), 6 hours for non-human milk, and 6 hours for a light meal (*ie*, toast and clear liquids).[10] The guideline authors note that published clinical evidence is insufficient to clearly define a relationship between NPO status and risk of emesis/reflux or pulmonary aspiration. Furthermore, it is unclear how different bowel preparation agents would be classified (clear liquids or not), how the potential toxicity of bowel preparation agents might impact anesthesia-related risks, and how the volume of bowel preparation agent consumed might differ from the volume of liquids considered acceptable in the guidelines.

An optimal bowel preparation and NPO status seeks to balance the need for optimal colonic preparation, patient convenience, and scheduling efficiency (typically a shorter NPO window status) with anesthesia safety concerns for an elective procedure (typically a longer NPO status). Furthermore, performing procedures with moderate or deep sedation requires development of and adherence to local and/or national policy measures that cross multiple procedures and physician specialties. These policies include recommendations regarding NPO status. Failure to adhere to NPO status can result in cancellation or rescheduling of procedures or poor procedure preparation. This can lead to reduced procedure quality, resource efficiency, patient satisfaction, and adherence.

The purpose of this report was to review the evidence on the relationship between timing of NPO and the incidence of aspiration and other anesthesia-related harms during elective colonoscopy as

well as colonoscopy rescheduling. In addition, we also reviewed the evidence on the benefits and harms of variable timing of NPO status on colonoscopy outcomes including colonoscopy quality measures, rescheduling, resource use, and patient satisfaction. The review may be used to guide policy within the VA. With input from stakeholders and TEP members, we developed the following Key Questions:

Key Question 1. Does the incidence of aspiration and other anesthesia-related harms for colonoscopy vary by NPO status or bowel prep timing (*eg*, > 6 hours, 2-6 hours, < 4 hours, and < 2 hours)? Does the incidence of anesthesia-related harms by NPO status vary by: a) patient characteristics (age, race, sex, obesity, comorbidities) or b) sedation (moderate, deep)?

Key Question 2. What is the effect of variable timing of bowel prep and NPO status on the quality of the bowel preparation, diagnostic yield, and colonoscopy procedural quality indicators (*eg*, completion rates, adenoma detection rate, total procedure time, cecal intubation time and withdrawal time)?

Key Question 3. What is the effect of NPO status prior to colonoscopy on resource use (*eg*, costs, unused procedure slots, delays in rescheduling, delays in diagnosis, increased volume of procedures, scheduler and nursing time associated with cancelled or delayed procedures)?

Key Question 4. What is the effect of bowel preparation and NPO status prior to colonoscopy on patient adherence to bowel preparation, colonoscopy, and/or rescheduled colonoscopy, and satisfaction with bowel preparation and/or colonoscopy?

We defined the following Population, Intervention, Comparator, Outcomes, Timing, and Setting (PICOTS) for the review:

Population: Adults undergoing bowel preparation and elective colonoscopy with moderate or deep sedation
Intervention(s): NPO status 2-4 hours (liquids and bowel preparation allowed up to 2 hours prior to procedure)
Comparator(s): Alternative timing of NPO
Outcome(s): (NOTE: limited to findings according to NPO status prior to colonoscopy)

Co-primary outcomes: aspiration, rescheduled colonoscopies
Secondary outcomes: adverse events (including bowel perforation and other anesthesia-related harms), diagnostic yield, completion rate, adenoma detection rate, false negative colonoscopies
Intermediate outcomes: quality of bowel preparation, hospitalizations, costs, total procedure time, cecal intubation time, withdrawal time, unused procedure slots, delays in rescheduling, delays in diagnosis, increased volume of procedures, scheduler and nursing time, patient adherence, patient satisfaction, volume of gastric contents, pH of gastric contents

Timing: Start of sedation for colonoscopy to completion of sedation for colonoscopy
Setting: Inpatient or outpatient clinics

METHODS

TOPIC DEVELOPMENT

This topic was nominated by Jason Dominitz, MD, MHS, National Program Director for Gastroenterology, Office of Patient Care Services. Additional stakeholders were identified to include both gastroenterology and anesthesiology: John Sum-Ping, MD, Chair, National Director, Anesthesia Service; Art Wallace, MD, PhD, Chief, Anesthesia Service, San Francisco VA Medical Center; and Deborah Fisher, MD, MHS, Chair, National VA Gastroenterology Field Advisory Committee. The key questions were formulated with input from a Technical Expert Panel (TEP) consisting of gastroenterologists and anesthesiologists.

SEARCH STRATEGY

We searched MEDLINE (OVID) for articles published from 1990 through October 2014. Our search was designed to identify studies of any design. We limited the search to studies involving human subjects published in the English language. Search terms included the following Medical Subject Headings (MeSH): Colonoscopy, Cathartics, Polyethylene Glycols, Phosphates, and Respiratory Aspiration of Gastric Contents. The full search strategy is presented in Appendix A. We also searched reference lists of guidelines, existing reviews, and included studies and we received reference suggestions from stakeholders and TEP members.

STUDY SELECTION

Abstracts of citations identified from the literature search were assessed for relevance by an investigator. We included studies of any design that reported outcomes following bowel preparation if at least one preparation was completed within 8 hours of the colonoscopy procedure. We also include population-based studies of adverse events during colonoscopy. Additional inclusion criteria were as follows:

- Study of adults
- Study of colonoscopy with moderate or deep sedation (studies related to colorectal surgery or involving general anesthesia were excluded)
- Reports outcomes of interest during colonoscopy or recovery from colonoscopy (*ie,* studies of aspiration during bowel preparation were excluded)

Full text reports of studies identified as potentially eligible (or indeterminate, *eg,* title only) were obtained for further review using the inclusion and exclusion criteria described above. Each article was independently reviewed by 2 investigators. Reasons for excluding a study at full text review were noted.

DATA ABSTRACTION

Eligible studies were reviewed for outcomes of interest by investigators. From studies of different preparation-to-procedure or NPO intervals, study characteristics (inclusion/exclusion criteria and details about the preparation interventions or NPO status), patient characteristics, and outcomes data were abstracted onto tables by one investigator and verified by a second. Our

focus was on outcomes from different preparation-to-procedure intervals and not different preparation substances.

RISK OF BIAS ASSESSMENT

We assessed the risk of bias of randomized controlled trials (RCTs) and controlled clinical trials (CCTs) based the following criteria: allocation sequence generation, allocation concealment, blinding, completeness of outcome reporting, and selectiveness of outcome reporting – a modification of the Cochrane approach to determining risk of bias.[11] For observational studies we identified the following criteria and evaluated risk of bias for each study:

1) Study design (prospective vs retrospective)
2) Population (consecutive or not)
3) Analysis of findings
   a. Was the method for handling missing data reported and appropriate?
   b. Were the characteristics the different NPO groups similar?

Individual studies were rated as low, moderate, or high risk of bias. Low risk of bias RCTs had adequate allocation sequence generation and allocation concealment, blinding, and few patients with incomplete data. Low risk of bias observational studies were prospective, enrolled consecutive patients, had appropriate methods for handling missing data (or no missing data), and characteristics of the NPO groups were similar.

DATA SYNTHESIS

We described and qualitatively compared the patient characteristics, study characteristics, intervention timing, and findings of included studies. Due to variation in the preparation-to-procedure interval and/or NPO status across studies and different systems used to report outcomes, we summarized most outcomes narratively.

RATING THE BODY OF EVIDENCE

We rated the overall strength of the body of evidence for our primary and secondary outcomes using the method reported by Owens et al.[12] Separate ratings were generated for RCTs/CCTs and observational studies.

PEER REVIEW

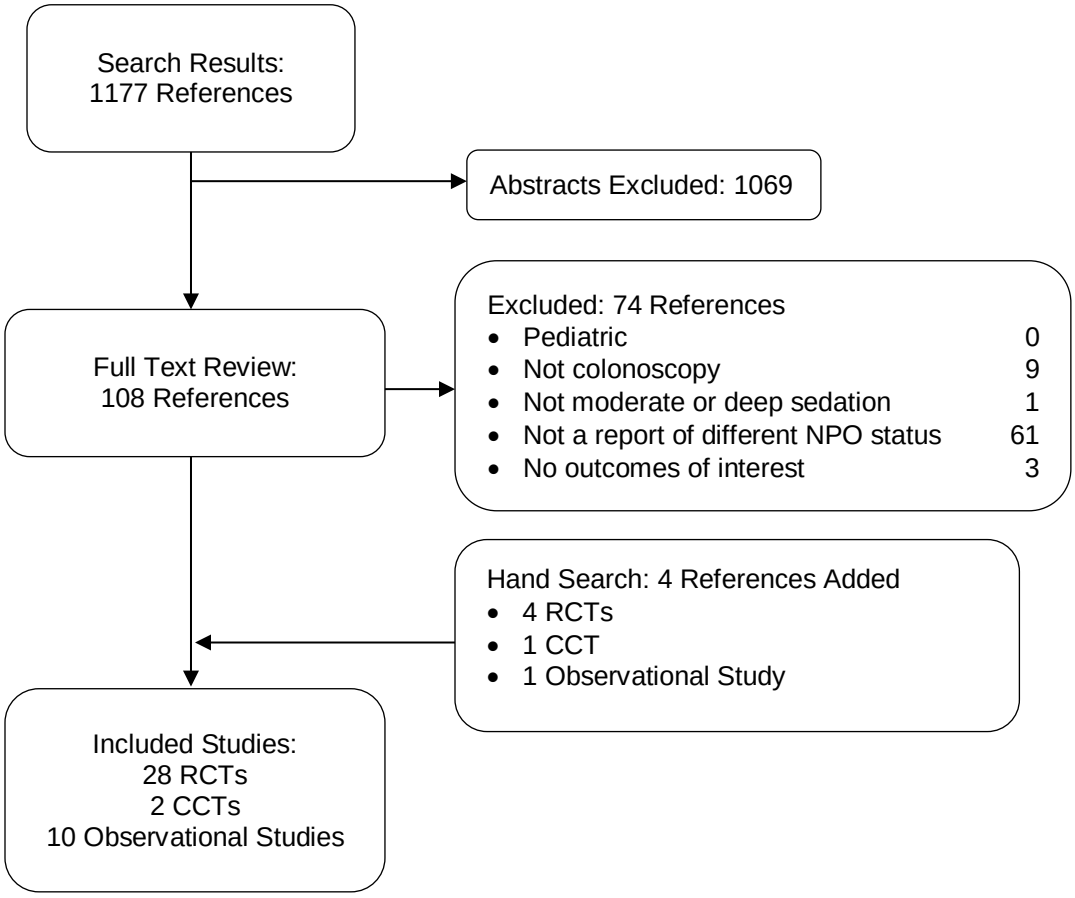
A draft version of this report was reviewed by clinical content experts and clinical leadership. Their comments and our responses are presented in Appendix B and the report has been modified as needed.

RESULTS

LITERATURE FLOW

Our literature search yielded 1177 abstracts or titles (Figure 1). After reviewing the abstracts we excluded 1069 and performed full text review of 108 articles. We excluded 74 articles and included 34. A hand-search of reference lists of guidelines, existing reviews, and included studies yielded another 6 articles for a total of 40 included studies of different bowel preparation or NPO status intervals (28 RCTs, 2 controlled CCTs, and 10 observational studies).

Figure 1: Literature Flow Chart



OVERVIEW

Baseline characteristics for the 40 RCTs, CCTs, and observational studies[13-53] reporting outcomes of interest are presented in Table 1. A total of 22,936 patients were evaluated; approximately one-half of the patients were from the United States or Canada. Mean age was 57 years in the 34 studies reporting. Sixty-one percent of colonoscopies were screening colonoscopies. Detailed study characteristics and risk of bias criteria are presented in Appendix C, Table 1.

From each included study, we identified a minimum time from the end of preparation until the procedure. Three studies[36,38,43] did not provide enough information to determine a minimum time. We also extracted information about timing of liquids allowed prior to the procedure from the 11 studies that reported that information. Figure 2 displays the minimum times based on bowel preparation time and the time before the procedure that clear liquids were allowed.

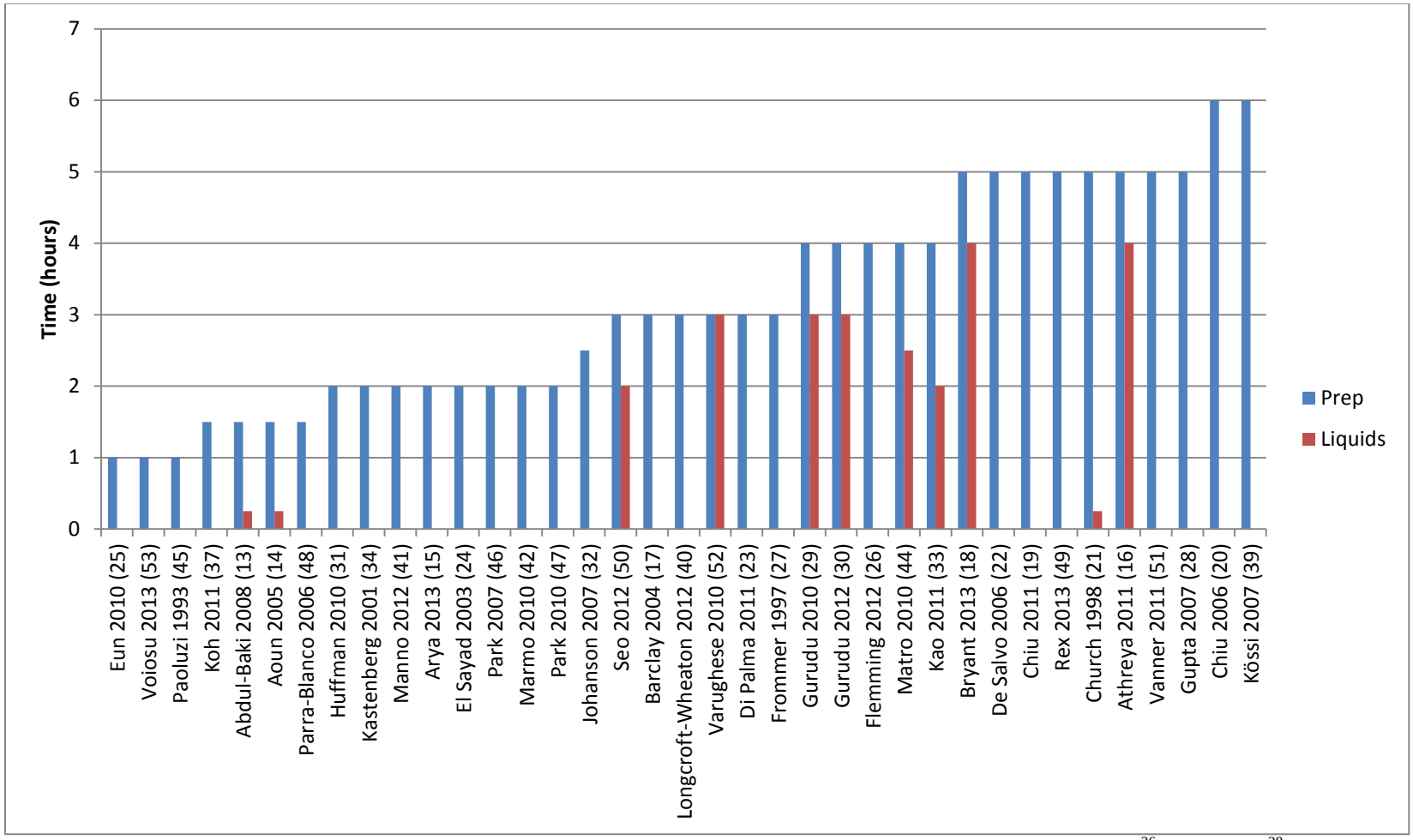
An overview of outcomes reported in each study is presented in Table 2. An NPO status of > 8 hours indicates that the bowel preparation was completed the night before colonoscopy but the exact time of completion and time of colonoscopy were not reported. Our predefined primary and secondary outcomes were rarely reported. Six studies reported our co-primary outcome of aspiration[29,31,41,43,44,52]; one reported rescheduled colonoscopies.[38] Of our secondary and intermediate outcomes, all but one study reported quality of the bowel preparation. Few studies reported other adverse events, diagnostic yield, completion rates, adenoma detection rate, total procedure time, cecal intubation time, withdrawal time, patient adherence, patient satisfaction, or volume of gastric contents. No studies reported false negative colonoscopies, hospitalizations, costs, unused procedure slots, delays in rescheduling, delays in diagnosis, increased volume of procedures, scheduler and nursing time, or acidity of the gastric contents. Detailed outcome data are presented in Appendix C, Tables 2 through 6.

Table 1. Summary of Baseline Characteristics

Characteristic	Mean (range) *Unless Otherwise Noted*	Number of Studies Reporting
Total number of patients evaluated	22,936 (80 to 5175)	40
Randomized controlled trials, number of patients	9304 (80 to 895)	28
Controlled clinical trials, number of patients	740 (328 to 412)	2
Observational studies, number patients	12,892 (100 to 5175)	10
Age of subjects, years (range of means)	57 (44 to 63)	34
Age of subjects, range of median years	55 to 65	3
Gender, male, % of patients	46 (28 to 81)	38
Indication for colonoscopy-screening, % of patients	61 (0[a] to 100)	20
Location - USA/Canada, number of patients	12,208 (100 to 5175)	17
Location - Asia/Australia, number of patients	8045 (80 to 3079)	14
Location - Europe, number of patients	2683 (160 to 895)	9

[a] Two studies reported that screening was not an indication for colonoscopy. Chiu 2006[20] included participants who had colorectal neoplasms detected at a screening colonoscopy and were scheduled for a second colonoscopic examination for either elective polypectomy or endoscopic mucosectomy. Manno 2012[40] included participants with a positive fecal occult test or those in surveillance post-polypectomy.

Figure 2. Minimum Time from End of Bowel Preparation to Procedure (Blue Lines) or Time Before Procedure when Liquids were Stopped (Red Lines)[a,b,c]



[a] 3 studies did not provide sufficient information to determine a minimum time from end of preparation to procedure (Khan 2010,[36] Kolts 1993,[38] Mathus-Vliegen 2013[43])

[b] Studies where patients were allowed liquids until time of procedure are indicated by a time of 0.25 hours

[c] Citations are author, year (reference number)

Table 2. Overview of Outcomes Reported

Author, Year NPO Status Groups[a]	Primary Outcomes		Secondary Outcomes						Intermediate Outcomes														
	Aspiration (k=6)	Rescheduled Colonoscopies (k=1)	Bowel Perforation (k=1)	Other Adverse Events (k=7)	Diagnostic Yield (k=3)	Completion Rate (k=11)	Adenoma Detection Rate (k=7)	False Negative Colonoscopy	Hospitalizations	Costs	Quality of Bowel Preparation (k=39)	Total Procedure Time (k=3)	Cecal Intubation Time (k=4)	Withdrawal Time (k=5)	Patient Adherence (k=11)[b]	Patient Satisfaction (k=11)[b]	Unused Procedure Slots	Delays, Rescheduling	Delays, Diagnosis	Increased Volume, Procedures	Scheduler/Nurse Time	Volume of Gastric Contents (k=2)	pH of Gastric Contents
Abdul-Baki 2008[13] Group 1: ≥ 1.5 hours Group 2: > 8 hours											✓				✓	✓							
Aoun 2005[14] Group 1: ≥ 1.5 hours Group 2: > 8 hours											✓				✓	✓						✓	
Arya 2013[15] Group 1: ≥ 2 hours Group 2: > 8 hours											✓												
Athreya 2011[16] Group 1: 5-9 hours Group 2: > 8 hours											✓	✓	✓	✓									
Barclay 2004[17] Group 1: < 3 hours Group 2: ≥ 5 hours				✓							✓				✓	✓							
Bryant 2013[18] Group 1: 5-7.5 hours Group 2: > 8 hours											✓												
Chiu 2011[19] Group 1: 5-9 hours Group 2: >8 hours							✓				✓												
Chiu 2006[20] Group 1: 6-8 hours Group 2: > 8 hours					✓	✓					✓												
Church 1998[21] Group 1: 5-8 hours Group 2: > 8 hours				✓		✓					✓		✓	✓									

Author, Year NPO Status Groups[a]	Primary Outcomes		Secondary Outcomes						Intermediate Outcomes															
	Aspiration (k=6)	Rescheduled Colonoscopies (k=1)	Bowel Perforation (k=1)	Other Adverse Events (k=7)	Diagnostic Yield (k=3)	Completion Rate (k=11)	Adenoma Detection Rate (k=7)	False Negative Colonoscopy	Hospitalizations	Costs	Quality of Bowel Preparation (k=39)	Total Procedure Time (k=3)	Cecal Intubation Time (k=4)	Withdrawal Time (k=5)	Patient Adherence (k=11)[b]	Patient Satisfaction (k=11)[b]	Unused Procedure Slots	Delays, Rescheduling	Delays, Diagnosis	Increased Volume, Procedures	Scheduler/Nurse Time	Volume of Gastric Contents (k=2)	pH of Gastric Contents
De Salvo 2006[22] Group 1: 5-8 hours Group 2: >8 hours						✓					✓													
Di Palma 2011[23] Group 1: 3-9 hours Group 2: > 8 hours											✓													
El Sayed 2003[24] Group 1: ≥ 2 hours Group 2: > 8 hours											✓													
Eun 2011[25] Group 1: ≥ 1 hour Group 2: > 7 hours											✓				✓									
Flemming 2012[26] Group 1: ≥ 4 hours Group 2: > 8 hours			✓	✓		✓					✓													
Frommer 1997[27] Group 1: 3-9 hours Group 2: > 8 hours											✓													
Gupta 2007[28] Group 1: ≥5 hours Group 2: > 8 hours											✓					✓								
Gurudu 2010[29] Group 1: ≥ 4 hours Group 2: > 8 hours	✓						✓				✓													
Gurudu 2012[30] Group 1: ≥ 4 hours Group 2: > 8 hours						✓	✓				✓			✓										
Huffman 2010[31] Group 1: ≥ 2 hours Group 2: > 8 hours	✓																					✓		

Author, Year NPO Status Groups[a]	Primary Outcomes		Secondary Outcomes						Intermediate Outcomes															
	Aspiration (k=6)	Rescheduled Colonoscopies (k=1)	Bowel Perforation (k=1)	Other Adverse Events (k=7)	Diagnostic Yield (k=3)	Completion Rate (k=11)	Adenoma Detection Rate (k=7)	False Negative Colonoscopy	Hospitalizations	Costs	Quality of Bowel Preparation (k=39)	Total Procedure Time (k=3)	Cecal Intubation Time (k=4)	Withdrawal Time (k=5)	Patient Adherence (k=11)[b]	Patient Satisfaction (k=11)[b]	Unused Procedure Slots	Delays, Rescheduling	Delays, Diagnosis	Increased Volume, Procedures	Scheduler/Nurse Time	Volume of Gastric Contents (k=2)	pH of Gastric Contents
Johanson 2007[32] Group 1: 2.5-4.5 hours Group 2: > 8 hours				✓							✓													
Kao 2011[33] Group 1: 4-8 hours Group 2: > 8 hours											✓													
Kastenberg 2001, 2007[34,35] Group 1: 2-4 hours Group 2: > 8 hours						✓					✓													
Khan 2010[36] Group 1: Split-dose[c] Group 2: > 8 hours											✓													
Koh 2011[37] Group 1: 1.5-3.5 hours Group 2: 6-8 hours											✓													
Kolts 1993[38] Group 1: Split-dose[c] Group 2: > 8 hours Group 3: > 8 hours		✓									✓													
Kössi, 2007[39] Group 1: ≤ 6 hours Group 2: 6-12 hours Group 3: ≥ 12 hours						✓					✓					✓								
Longcroft-Wheaton 2012[40] Group 1: > 3 hours Group 2: > 5 hours							✓				✓				✓	✓								
Manno 2012[41] Group 1: 2 hours Group 2: >8 hours	✓										✓				✓	✓								

Author, Year NPO Status Groups[a]	Primary Outcomes		Secondary Outcomes						Intermediate Outcomes															
	Aspiration (k=6)	Rescheduled Colonoscopies (k=1)	Bowel Perforation (k=1)	Other Adverse Events (k=7)	Diagnostic Yield (k=3)	Completion Rate (k=11)	Adenoma Detection Rate (k=7)	False Negative Colonoscopy	Hospitalizations	Costs	Quality of Bowel Preparation (k=39)	Total Procedure Time (k=3)	Cecal Intubation Time (k=4)	Withdrawal Time (k=5)	Patient Adherence (k=11)[b]	Patient Satisfaction (k=11)[b]	Unused Procedure Slots	Delays, Rescheduling	Delays, Diagnosis	Increased Volume, Procedures	Scheduler/Nurse Time	Volume of Gastric Contents (k=2)	pH of Gastric Contents
Marmo 2010[42] Group 1: ≤ 2 hours Group 2: >8 hours						✓					✓													
Mathus-Vliegen 2013[43] Group 1: Split-dose[c] Group 2: > 8 hours	✓			✓							✓													
Matro 2010[44] Group 1: 4 hours Group 2: 4 hours (split-dose)	✓				✓	✓	✓				✓	✓		✓	✓	✓								
Paoluzi 1993[45] Group 1: 1-2.5 hours Group 2: > 8 hours											✓													
Park 2007[46] Group 1: ≥ 2 hours Group 2: > 8 hours											✓		✓		✓	✓								
Park 2010[47] Group 1: 2-5 hours Group 2: > 8 hours											✓				✓	✓								
Parra-Blanco 2006[48] Group 1: 1.7-7 hours Group 2: > 8 hours					✓		✓				✓													
Rex 2013[49] Group 1: 5-9 hours Group 2: > 8 hours				✓		✓					✓				✓									
Seo 2012[50] Group 1: ≤ 3 hours Group 2: > 8 hours											✓													

Author, Year NPO Status Groups[a]	Primary Outcomes		Secondary Outcomes						Intermediate Outcomes														
	Aspiration (k=6)	Rescheduled Colonoscopies (k=1)	Bowel Perforation (k=1)	Other Adverse Events (k=7)	Diagnostic Yield (k=3)	Completion Rate (k=11)	Adenoma Detection Rate (k=7)	False Negative Colonoscopy	Hospitalizations	Costs	Quality of Bowel Preparation (k=39)	Total Procedure Time (k=3)	Cecal Intubation Time (k=4)	Withdrawal Time (k=5)	Patient Adherence (k=11)[b]	Patient Satisfaction (k=11)[b]	Unused Procedure Slots	Delays, Rescheduling	Delays, Diagnosis	Increased Volume, Procedures	Scheduler/Nurse Time	Volume of Gastric Contents (k=2)	pH of Gastric Contents
Vanner 2011[51] Group 1: > 5 hours Group 2: > 8 hours						✓					✓												
Varughese 2010[52] Group 1: ≥ 3 hours Group 2: > 8 hours	✓						✓				✓	✓	✓	✓	✓	✓							
Voiosu 2013[53] Group 1: 1-7 hours Group 2: > 8 hours				✓							✓												

[a] NPO status > 8 hours indicates bowel preparation completed the night before colonoscopy but exact time of completion and time of colonoscopy not reported
[b] Data on patient adherence and patient satisfaction extracted only from studies using same bowel preparation substance in the study groups (k=21)
[c] Time of morning dose or time of colonoscopy not reported

KEY QUESTION 1. Does the incidence of aspiration and other anesthesia-related harms for colonoscopy vary by NPO status or bowel prep timing (*eg*, > 6 hours, 2-6 hours, < 4 hours, and < 2 hours)?

Does the incidence of anesthesia-related harms by NPO status vary by:

A) Patient characteristics (age, race, sex, obesity, comorbidities)

B) Sedation (moderate, deep)?

Findings from Trials of Different Bowel Preparation Protocols

Aspiration Risk (Appendix C, Table 2)

Six studies reported on aspiration (sample sizes ranged from 136 to 1,345).[29,31,41,43,44,52] In 5 of these studies no aspirations occurred during colonoscopy[29,31] or during colonoscopy or within the 30 days post-colonoscopy,[43] or there were no complications related to sedation.[41,52]

One observational study (moderate risk of bias) reported no aspiration events in 1,345 patients.[29] Bowel preparation regimens were completed either the morning of the procedure (at least 4 hours prior to colonoscopy) or the evening before the colonoscopy. All patients were allowed to drink clear liquids up to 3 hours before the procedure.

The second study, also observational and moderate risk of bias, enrolled 301 patients.[31] One group completed bowel preparation at least 2 hours before the procedure (mean NPO time of 5.1 hours). The second group completed bowel preparation the evening before (mean NPO time of 13.5 hours). No patient had “clinical evidence” of aspiration. The volume of the gastric contents did not differ significantly.

One RCT used medical charts and a complications database to identify aspiration events during colonoscopy or in the 30 days following colonoscopy for 200 patients.[43] No events were reported.

The 2 studies reporting no complications related to sedation were both RCTs with enrollments of 136[52] and 336[41] respectively. In the first study, with moderate risk of bias, patients in one group completed preparation by 10 am for an afternoon colonoscopy (1 pm or later); the other group completed preparation the night before the procedure.[52] Both groups were allowed clear liquids until 10 am. In the second study, with low risk of bias, one group completed preparation 2 hours before the procedure and the other group completed preparation the day before.[41]

One small (n=125 randomized), low risk of bias RCT reported one aspiration event requiring hospitalization during colonoscopy under moderate sedation.[44] The patient was described as severely obese (BMI = 40 kg/m^2) but with no other obvious risk factors for aspiration. The patient was assigned to consume 1 L of a bowel preparation agent 7 hours before colonoscopy and an additional 1 L 4 hours before. Patients in this trial were allowed clear liquids until 2.5 hours before the procedure. The patient was hospitalized for 24 hours and treated with oral antibiotics for one week.

Other Harms (Appendix C, Table 5)

Seven studies (6 moderate risk of bias, 1 low risk of bias) reported on other harms. In 4 studies, there were no adverse events, specifically no complications of bowel perforation or bleeding up to the time of leaving the endoscopy office[26] or no serious adverse events.[17,21,53] One of these studies interviewed patients 2 days post-colonoscopy,[17] one recorded adverse events through approximately 2 hours post-colonoscopy,[53] and one did not provide a timeframe.[17]

Three studies reported adverse events with harms occurring in less than or equal to 1% of procedures. In 2 studies, there was one event in the longer NPO status group and no events in the shorter NPO status group.[32,43] One RCT with 402 patients reported lower gastrointestinal bleeding post-colonoscopy in one patient (0.5%) who completed bowel preparation more than 8 hours before colonoscopy.[32] Another RCT, with 200 patients, reported severe retrosternal pain in one patient (1%) 3 hours after the colonoscopy. Anteroseptal infarction was diagnosed. The patient was in the group that had morning colonoscopies following bowel preparation completed the evening before.[43] A third RCT, with 603 patients, reported acute pancreatitis in one patient (0.3%) who completed bowel preparation between 5-9 hours before colonoscopy and non-cardiac chest pain in one patient (0.3%) who completed bowel preparation more than 8 hours before colonoscopy.[49] It was unclear if these events occurred during bowel preparation, during colonoscopy, or post-colonoscopy. The study included follow-up visits at 24 to 48 hours, one week, and 4 weeks.

Gastric Volume and Acidity (Appendix C, Table 6)

Two studies reported no difference in volume of gastric contents. In one low risk of bias RCT,[14] 141 patients were assigned to complete bowel preparation the morning of and at least 1.5 hours prior to the procedure or the evening before the procedure. Both groups were allowed water until the time of the procedure. Approximately 25% of patients in each group underwent tandem esophagogastroduodenoscopy (EGD) and gastric volume was assessed. The second study was a moderate risk of bias observational study.[31] The split-dose preparation group completed preparation by 2 hours prior to the procedure. Findings were compared to a group that completed bowel preparation the day before the colonoscopy; additional clear fluids were allowed "as desired." EGD was performed immediately before colonoscopy for both groups. No study reported the acidity of the gastric contents.

Additional Studies of Aspiration during Colonoscopy

Several hospital- or population-based studies have also reported on aspiration during colonoscopy. However, none documented duration of NPO status prior to the colonoscopy. In a large database study, the incidence of aspiration requiring hospitalization during 165,527 outpatient diagnostic colonoscopies in 100,359 Medicare patients age 66 years and older (mean age = 76 years) was 0.14% for patients having colonoscopy under deep sedation requiring anesthesia assistance (as identified by a *CPT-4* code) and 0.10% for patients under moderate sedation without anesthesia assistance.[54] A study of 23,508 outpatient colonoscopies at 3 hospitals in Australia reported one case (0.004%) of aspiration requiring hospitalization in a patient undergoing colonoscopy with general anesthesia.[55] A study of 3,155 colonoscopies performed with sedation managed by an anesthesiologist in adults at a single hospital in Italy reported that 0.16% of patients undergoing colonoscopy had an aspiration requiring "some intervention by an anesthesiologist."[56] Aspirations requiring hospitalizations were not reported.

Patients were instructed to fast according to guidelines in place at the time – clear liquids up to 2 hours before the procedure and a light meal (toast and clear liquid) up to 6 hours before the procedure.

KEY QUESTION 2. What is the effect of variable timing of bowel prep and NPO status on the quality of the bowel preparation, diagnostic yield, and colonoscopy procedural quality indicators (*eg*, completion rates, adenoma detection rate, total procedure time, cecal intubation time and withdrawal time)?

Quality of the Bowel Preparation

Thirty-nine studies (28 RCTs, 2 CCTs, and 9 observational studies) reported on the effect of variable timing of bowel preparation on quality of the bowel preparation (Appendix C, Table 3).[13-30,32-53] Eleven of these studies (6 RCTs, 1 CCT, 4 observational) also reported the time prior to colonoscopy when water or other clear liquids were allowed, ranging from 4 hours until the time of the procedure.[13,14,16,18,21,29,30,33,44,50,52] Although different rating scales were used to rate the quality of the bowel preparation, quality of the bowel preparation was consistently rated higher for NPO intervals of 6 hours or less compared to intervals of more than 8 hours.

Of the 28 studies (n=11,698) that only reported timing of bowel preparation and compared shorter (1-6 hours) versus longer intervals (8-12 hours) between bowel preparation administration and colonoscopy, 21 reported significantly higher quality of bowel preparation with a shorter interval between preparation and colonoscopy and 7 reported no significant difference.

Limited data suggest that consumption of water or clear liquids, including preparation solutions, from 0 to 4 hours prior to colonoscopy does not affect quality of the bowel preparation. Of the 11 studies (n=10,931) reporting timing of liquid consumption, 3 allowed water or other clear liquids up to the time of the procedure and 2, 1, 3, and 2 studies allowed water intake up to 2 hours, 2.5 hours, 3 hours, and 4 hours prior to colonoscopy, respectively. Nine studies reported significantly higher quality rating of the preparation in the group completing bowel preparation less than 8 hours prior to colonoscopy (minimum NPO status based on bowel preparation of 1.5 to 6 hours) compared to the group completing bowel preparation more than 8 hours prior to colonoscopy. One study reported no significant difference in quality of preparation between groups completing bowel preparation the morning of the colonoscopy or in a split-dose (evening before/morning of colonoscopy). Both groups completed bowel preparation 4 hours prior to colonoscopy. The remaining study reported higher quality in the shorter NPO duration group but no statistical analysis was possible.

Other Secondary or Intermediate Outcomes

Few studies reported other secondary or intermediate outcomes.

Diagnostic yield (k=3) (Appendix C, Table 3; Figure 3)

One moderate risk of bias RCT (n=121) reported a significantly higher total number of lesions detected in patients with who completed bowel preparation 6 to 8 hours before colonoscopy compared to more than 8 hours (2.8 vs 1.9, P = .03).[20] No differences were noted for either

proximal lesions or advanced lesions. All patients in this study had colon neoplasms detected during a previous colonoscopy.

A second moderate risk of bias RCT (n=197) reported a significantly greater yield of flat lesions in patients who completed bowel preparation 1 to 7 hours before colonoscopy compared to those who completed preparation more than 8 hours before (22% vs 9%, P < .05); no difference were reported for "any polyp" (52% vs 45%) or "protruding polyps" (40% vs 42%).[48]

A low risk of bias RCT (n=125) reported significantly more "findings" (adenoma or cancer) per patient (0.70 vs 0.46, P = .047) in the group that completed bowel preparation in the morning compared to a group that used a split-dose protocol.[44] Both groups completed the preparation 4 hours prior to colonoscopy and were allowed clear liquids up to 2.5 hours before the procedure.

Completion rates (k=11) (Appendix C, Table 3; Figure 3; Figure 4)

Results from 5 RCTs providing sufficient information to permit pooling found no difference in completion rates between shorter and longer NPO status (RR 1.00 [95%CI 0.98, 1.01).[20-22,26,34]

One additional low risk of bias RCT (n=895) reported an overall completion rate of 95% but significantly fewer aborted procedures due to inadequate bowel preparation when the preparation was completed 2 hours or less before colonoscopy (93%) compared to more than 8 hours before colonoscopy (79%).[42]

A high risk of bias observational study (n=5,175) reported a significantly higher colonoscopy completion rate in patients completing bowel preparation 4 hours or more before colonoscopy (96%) compared to 8 hours or more (94%). Patients in both groups were allowed liquids until 3 hours before the procedure.[30]

Another study, a low risk of bias RCT not included in the figure because both groups completed bowel preparation 4 hours before colonoscopy, reported no significant difference in completion rate between the single dose (98%) or split-dose (100%) groups.[44]

Three studies provided completion rates but did not report separate results for the NPO status groups: a moderate sized RCT,[49] a moderate sized observational study,[39] and a small observational study.[51] The completion rates were 96%,[39] 99%,[49] and 95%.[51]

Adenoma detection rate (k=7) (Appendix C, Table 3; Figure 3; Figure 4)

One high risk of bias observational study (n=5,175) reported a significantly higher adenoma detection rate of in patients who completed bowel preparation 4 hours or more before colonoscopy compared to those completing preparation more than 8 hours before (32% vs 27%, P < .001).[30] All patients in this study were allowed liquids until 3 hours prior to the procedure. Another observational study (n=3,079, moderate risk of bias) found significantly higher detection of proximal adenomas in patients who completed bowel preparation 5 to 9 hours before colonoscopy compared to more than 8 hours (11% vs 9%, P = .04) although overall detection did not differ (17% vs 15%, P = .11).[19] Four studies (3 moderate risk of bias, 1 low risk of bias) reported no difference in detection rate between groups with shorter versus longer times between completion of bowel preparation and the procedure.[29,40,48,52] One of the studies allowed liquids until 3 hours prior to the procedure.[29]

In the study comparing single dose to split-dose preparation, both completing preparation 4 hours before colonoscopy with liquids allowed until 2.5 hours before, the overall detection rate was higher in the morning-only preparation group (37% vs 25%, P = .04).[44] For high-risk adenoma or cancer, the difference was not significantly different (13% vs 11%, P = .28).

Total procedural time (k=3) (Appendix C, Table 4)

Total procedure time, reported in 3 studies, did not differ between groups. In one high risk of bias CCT (n=325) completion of bowel preparation 5 to 9 hours before the procedure was compared to preparation the night before.[16] In the second study, a moderate risk of bias RCT (n=136), bowel preparation was completed 3 hours or more before the procedure compared to more than 8 hours.[52] The third study, a low risk of bias RCT (n=125), compared morning-only preparation to split-dose preparation.[44] One of these studies allowed patients to consume clear fluids up to 4 hours before the procedure[16] and another up to 2.5 hours before the procedure.[44] The other study required all patients to be NPO after 10 am for an afternoon colonoscopy.[52]

Cecal intubation time (k=4) (Appendix C, Table 4)

One low risk of bias RCT (n=303) reported shorter cecal intubation time (a measure of higher bowel preparation and colonoscopy quality) in patients who completed bowel preparation at least 2 hours before colonoscopy compared to more than 8 hours.[46] Times did not differ in the 2 other, moderate risk of bias, RCTs (n=453)[21,52] or the CCT (n=325)[16] reporting this outcome. In one of the RCTs finding no difference, patients were allowed water until the time of the procedure.[21] The other 2 studies (1 moderate risk of bias RCT, 1 high risk of bias CCT) allowed clear fluids until 4 hours before the procedure[16] or required patients to be NPO after 10 am prior to an afternoon colonoscopy.[52]

Withdrawal time (k=5) (Appendix C, Table 4)

One high risk of bias observational study (n=5,175) reported a shorter withdrawal time (a measure of higher bowel preparation and colonoscopy quality) in patients with a time from completion of bowel preparation of 4 hours or greater compared to more than 8 hours (12 minutes vs 15 minutes, P < .001).[30] Patients were allowed clear liquids until 3 hours before colonoscopy. Three other studies (1 low risk of bias RCT, 2 moderate risk of bias RCTs, and one high risk of bias CCT) reporting withdrawal time found no difference between shorter and longer NPO intervals[16,21,52] or between morning-only and split-dose preparation.[44] One RCT allowed water until the time of the procedure, one RCT allowed clear liquids up to 2.5 hours before the procedure, one RCT required patients to be NPO after 10 am for an afternoon procedure, and the CCT allowed clear fluids until 4 hours before colonoscopy.

Figure 3. Completion Rate, Adenoma Detection Rate, and Diagnostic Yield: Outcomes from Randomized Controlled Trials

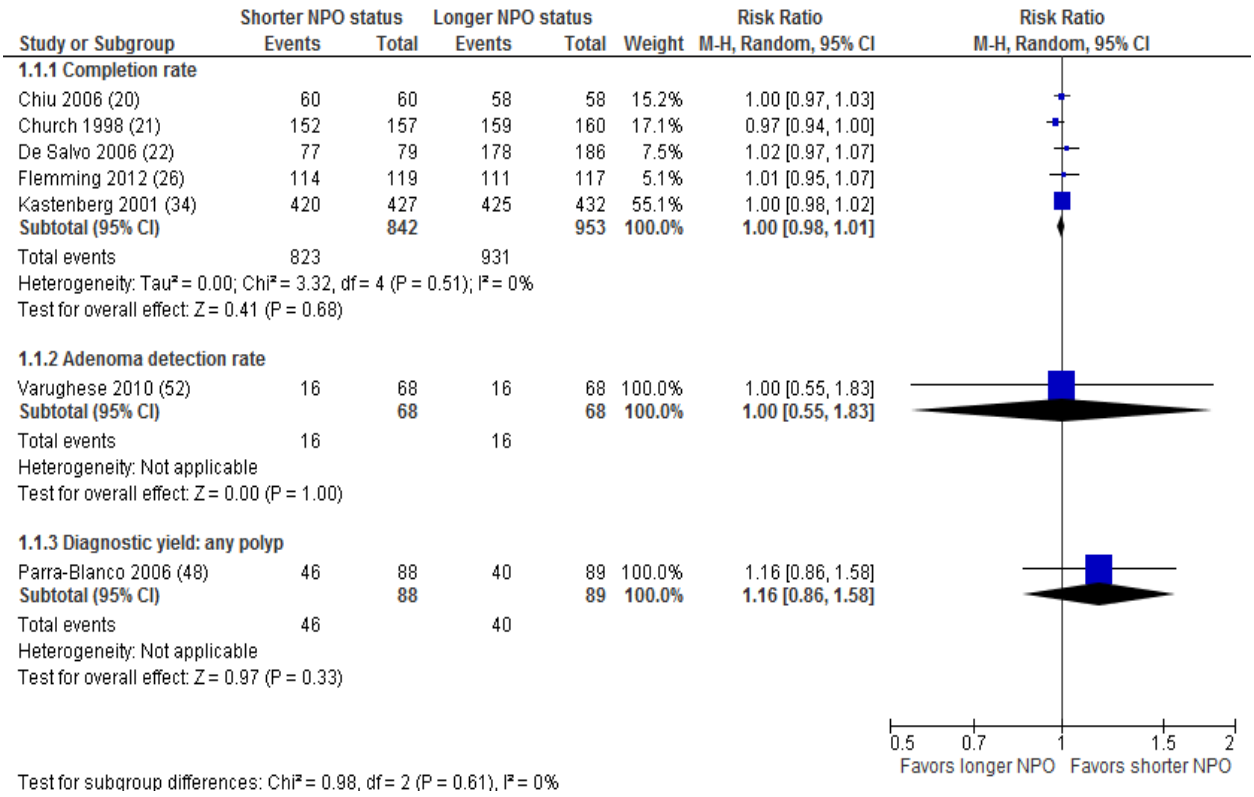
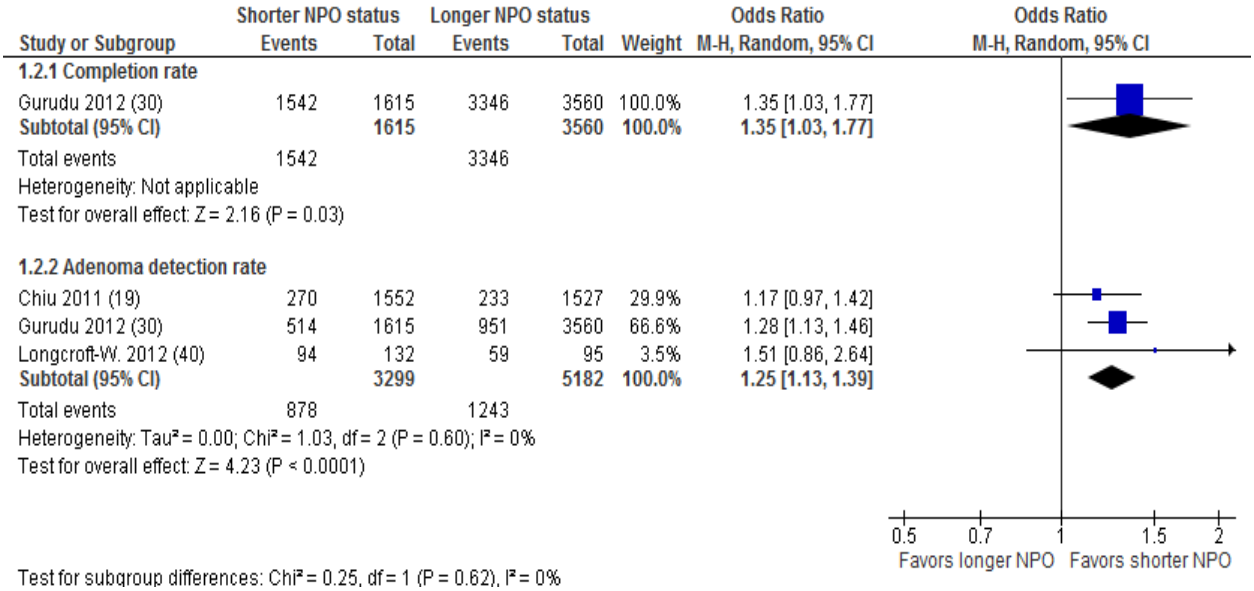


Figure 4. Completion Rate and Adenoma Detection Rate: Outcomes from Observational Studies



KEY QUESTION 3. What is the effect of NPO status prior to colonoscopy on resource use (*eg*, costs, unused procedure slots, delays in rescheduling, delays in diagnosis, increased volume of procedures, scheduler and nursing time associated with cancelled or delayed procedures)?

One moderate risk of bias RCT reported rescheduled colonoscopies.[38] The percentage of rescheduled colonoscopies was significantly lower (P = .011) in the group that completed bowel preparation on the morning of the procedure (3%) taking a split-dose of a sodium phosphate regimen than in groups consuming a polyethylene glycol solution (8%) or a castor oil solution (24%) the evening before the procedure. Differences in the bowel preparation solutions between groups limit our ability to draw firm conclusions about the role of NPO status on rescheduling.

No other study reported resource use. Although some studies reported inadequate bowel preparation quality, they did not report whether the colonoscopy was repeated.

KEY QUESTION 4. What is the effect of bowel preparation and NPO status prior to colonoscopy on patient adherence to bowel preparation, colonoscopy, and/or rescheduled colonoscopy and satisfaction with bowel preparation and/or colonoscopy?

Data are limited on the effect of bowel preparation and NPO status on patient adherence, colonoscopy rescheduling, and satisfaction. We extracted data on adherence and satisfaction from studies where the same bowel preparation substance (*eg*, polyethylene glycol) was used for all patients (Appendix C, Table 4). Compared to a same-day regimen (completed the day before colonoscopy), a split-dose regimen was associated with greater adherence to bowel preparation in 4 studies[13,14,41,46] with a significantly greater adherence in 2 of those studies, both low risk of bias RCTs.[13,14] Two studies, one low risk of bias observational study and one moderate risk of bias RCT, that included a dose on the day of the procedure for all patients reported better completion of the preparation in patients who finished the preparation closer to the time of the procedure (approximately 3 hours vs 5 hours or more in both studies).[17,40] A third study, a low risk of bias observational study, reported no difference between groups completing bowel preparation less than 4 versus more than 4 hours prior to colonoscopy.[25] Three studies, high, moderate, and low risk of bias RCTs, reported no difference in compliance with a split-dose regimen compared to a same day regimen.[44,47,52] One low risk of bias RCT reported treatment-emergent adverse events leading to discontinuation of the preparation in 2 of 603 patients (0.3%) with no difference between the split-dose or same-day groups.[49]

We extracted elements of satisfaction that would be impacted by different schedules for bowel preparation (Appendix C, Table 4). Five studies reported on work or school time lost. Two low risk of bias RCTs found no difference in the percentage of patients reporting work or school time missed between split-dose and same-day groups.[13,14] Another low risk of bias RCT reported that 85% of the morning-only preparation group compared to 55% of the split-dose group (P = .019) reported no interference with work on the day before the procedure. One moderate risk of bias RCT reported significantly fewer hours lost form work with a split-dose regimen.[28] The fourth study, a low risk of bias observational study, reported that completion of the bowel preparation

regimen closer to the time of the procedure (3 hours or more compared to 5 hours or more) caused less interruption of sleep.[40]

Eight studies reported on sleep disturbance. Two moderate risk of bias RCTs found less sleep disruption in patients on a split-dose protocol[28,52] and a third low risk of bias observational study found less sleep disruption with a protocol that required completion of the preparation regimen closer to the procedure time (3 hours or more compared to 5 hours or more).[40] Five RCTs, 3 low and 1 high risk of bias, found no difference in sleep disruption between split-dose and same-day regimens.[13,14,44,45,47] One low risk of bias observational study reported no differences in difficulty traveling to the colonoscopy among patients who completed the preparation fewer than 6 hours (3.8%), 6 to 12 hours (5.6%), or more than 12 hours (4.9%) before the procedure.[39]

SUMMARY AND DISCUSSION

KEY FINDINGS AND STRENGTH OF EVIDENCE

Key Findings and Strength of Evidence

- Hospital- or population-based studies have reported that the risk of aspiration serious enough to require hospitalization during colonoscopy is very low (1 in 1000 or less). However, these studies have not documented NPO status and it is possible that the low rates are driven by more individuals having longer rather than shorter NPO status.

- In 3 RCTs and 2 observational studies (total n=2,318) comparing shorter NPO status to NPO status of at least 8 hours, no aspiration events were reported. Bowel preparation was completed at least 2 hours prior to colonoscopy in 2 studies and at least 3 hours prior to colonoscopy in one study. Another study allowed clear liquids up to 3 hours prior to colonoscopy and the remaining study only reported that bowel preparation was completed in the morning for an afternoon colonoscopy.

- One small RCT (n=113) reported a significantly lower percentage of rescheduled colonoscopies in the split-dose group compared to 2 groups that completed preparation the evening before the colonoscopy, although different preparation agents were used in the 3 groups. No studies reported on other resource use outcomes including unused procedure slots or increased volume of procedures by NPO status.

- Few studies assessing NPO status specified adverse events associated with colonoscopy as an outcome of interest and therefore adverse events may be underreported.

- Time from completion of colonic preparation to colonoscopy of 1 to 6 hours is associated with greater bowel preparation quality than time intervals of greater than 8 hours. Of 24 studies comparing split-dose versus non-split-dose preparation, 20 reported higher quality of bowel preparation with split-dose.

- Completion rate was not significantly different between NPO status groups in 5 RCTs; one large observational study reported a greater completion rate with shorter NPO status. Results were mixed for diagnostic yield and adenoma detection rate with no consistent findings based on NPO status. One study reported no documented complications of bowel perforation; no study reported on false negative colonoscopy.

- Among studies reporting adherence to the bowel preparation regimen, time lost from work, or sleep disruption, results were mixed with no clear benefit of split-dose regimens over same day regimens.

- Studies of NPO status typically excluded patients with serious comorbidities.

- For our co-primary outcomes, strength of evidence was low for aspiration and insufficient for rescheduled colonoscopies. For secondary outcomes, strength of evidence was moderate for completion rate based on pooled results from 5 RCTs, low for adenoma

detection rate based on pooled results from 3 observational studies, and insufficient for diagnostic yield, bowel perforation, and false-negative colonoscopy (Appendix D).

DISCUSSION

Colonoscopy is now the most frequently performed procedure in the US.[57] The indications for colonoscopy include diagnostic evaluation of symptoms, screening, and surveillance. The goals of a successful colonoscopy program are safe and high-quality colonoscopic exams. Challenges to these goals include limited colonoscopy capacity, complexity of patient scheduling, and adequate bowel cleansing to ensure a high-quality exam. Quality of bowel preparation may be improved by administering the purgative agent closer to the time of colonoscopy, a practice widely adopted by the gastroenterology community in the form of split-dose preparation. However, optimizing bowel preparation quality needs to be balanced against potential increased risk of adverse events related to shorter duration of NPO status prior to colonoscopy.

This systematic review was conducted to review the evidence on the relationship between timing of NPO and the incidence of aspiration and colonoscopy rescheduling. Other outcomes included other anesthesia-related harms, bowel preparation quality, colonoscopy quality measures, resource use, and patient satisfaction.

NPO Status and Aspiration Requiring Hospitalization

The most important potential risk of a shorter NPO duration is aspiration requiring hospitalization. The overall reported risk of aspiration events serious enough to require hospitalization during colonoscopy is extremely low. A population-based study in the US reported that between 0.1% and 0.14% of adults age 66 and older (mean = 75 years) had an aspiration requiring hospitalization during colonoscopy. Aspiration requiring hospitalization reported in adults of younger age was much lower. Although aspiration risk appears to be related to deep sedation, it is unknown if other factors, such as patient comorbidities, may be confounding that relationship. We found 5 studies (n=2,318) reporting no episodes of aspiration or sedation-related complications with NPO durations as low as 2 to 4 hours. One additional RCT (n=125) reported a single aspiration event but NPO status was 4 hours or less in both study groups. The “tolerable” rate of aspiration threshold for individuals undergoing an elective procedure that could potentially be modified by NPO status is not known. However, as with all procedures, adverse events will not be zero and the reported percents of aspirations requiring hospitalization events are of similar magnitude to other commonly accepted adverse effects of similar severity encountered in other procedures. Although the studies enrolled a total of 2,443 patients, the numbers may be still too small to assess for a rare outcome such as aspiration. We found 7 studies assessing other harms related to colonoscopy but none of the harms were related to timing of NPO prior to colonoscopy.

Gastric volume and acidity are regarded as markers of potential aspiration risk and severity. We found 2 studies that showed no difference in gastric volume with shorter (less than 2 hours before colonoscopy) versus overnight duration of NPO status prior to colonoscopy.[14,31] Other studies of NPO status and gastric volume/pH before endoscopy or surgery also reported no differences. A 1996 study measured volume and pH of gastric aspirate in 88 patients undergoing endoscopy.[58] Patients were randomly assigned to an overnight fast (both food and fluids) or consumption of 330 ml water at 7:30 am on the day of the procedure (with no food after

midnight). The mean time from the fluid intake until endoscopy was 117 minutes. There was no significant difference between the 2 study groups in gastric volume (12.5 ml in the fluid intake group, 10.0 ml in the fasting group) or pH (2.0 in both groups). A subsequent study found no difference in gastric volume or pH between groups of patients assigned to drink 200 ml of water or full fat milk 90 minutes before endoscopy.[59] Similarly, a study of 126 patients scheduled for elective surgery with general anesthesia found no difference in gastric fluid volume or pH between groups of patients who drank 300 mL of clear liquid of their choice 2 hours before the procedure and those who continued to fast after midnight.[60] These results suggest that gastric volume and acidity do not differ whether water or other liquids are consumed 2 hours prior to a procedure compared to longer NPO durations.

It is important to note that not all aspirations are clinically significant pulmonary aspirations and many authors may include passive regurgitation. Warner et al[61] outlined the diagnostic criteria for pulmonary aspirations as follows: 1) the presence of bilious secretions or particulate matter within the tracheo-bronchial tree by direct suctioning or by fiberoptic bronchoscopy, or 2) after the episode of passive regurgitation, postoperative chest radiograph demonstrated a new infiltrate that did not exist in the preoperative chest radiograph or on physical examination and that developed postoperatively within 24 hours. Using these criteria, a large population-based study reported a 4 year retrospective analysis (2001-2004) of perioperative pulmonary aspiration events.[62] Of 99,441 surgical cases in adults performed with anesthesia, 14 had aspiration events for a rate of 1 in 7,103 or 0.014%. Ten of the 14 cases (70%) were the result of improper anesthesia technique. This suggests that the true risk of pulmonary aspiration may be lower than 1 in 1000. Studies of a US Medicare population,[54] outpatients from 3 hospitals in Australia,[55]and a single hospital in Italy[56] provide supporting evidence. For aspiration events serious enough to require hospitalization, the risk may be as low as 0.01%. These risks need to be weighed against the benefit of shorter NPO.

The concern shared by anesthesia providers is the risk of aspiration due to short duration between administration of purgative and the procedure. This concern is addressed by the American Society of Anesthesiology (ASA) guideline that recommends 2 hours of NPO prior to moderate sedation.[10] Adherence to this guideline would permit use of split-dose regimens and reduce procedure cancellations due to patient oral ingestion at intervals greater than 2 hours prior to a procedure. However, based on responses from 55 VA chiefs of anesthesiology in March 2014, anesthesiologists across VHA appear to have differing policies and practices regarding NPO for elective procedures. For example 38% stated they require NPO after midnight, 15% require NPO for 6 hours, 11% require NPO for 6 hours for food and 4 hours for clear liquids (including 1 liter of bowel preparation solution), 32% require NPO for 6 hours for food and 2 hours for clear liquids (including 1 liter of bowel preparation solution), 2% require NPO for 6 hours for food and one hour for clear liquids (including 1 liter of bowel preparation solution), and 4% don't have a rule for NPO status for gastrointestinal procedures.(Personal Communication, Art Wallace, March 2014)

Possible reasons for not adhering to the ASA guidelines are concerns that laxatives may not be treated similar to ingestion of clear liquids and that the volume of laxative may be larger than that of other clear liquids. Studies that evaluated ingestion of clear liquids up to 2 hours prior to anesthesia administration suggest that this ingestion does not affect stomach volume or pH compared to earlier ingestion.[14,31,58-60] Other reasons for non-adherence of anesthesia providers to the ASA guidelines need to be explored.

NPO Status and Adequacy of Bowel Cleansing

For an effective and safe colonoscopy program, the adequacy of bowel cleansing is paramount. We found 39 studies (n=22,629) that reported the association of duration of NPO and quality of preparation comparing shorter (1 to 6 hours) versus longer duration (8 to 12 hours) between bowel preparation and colonoscopy. Thirty-one reported higher quality of bowel preparation with a shorter interval between preparation and colonoscopy and 8 reported no significant difference.

We were most interested in studies that reported NPO of < 4 hours compared to longer durations of NPO, as this is likely the most commonly used duration of NPO with the newer split-dose bowel preparations. We found 23 studies (RCTs or observational) that compared or included duration of NPO of < 4 hours to longer durations (usually > 8 hours). Nineteen reported a higher quality preparation with shorter duration (< 4) of NPO, 3 showed no difference, and 1 did not report on prep quality.

Multiple gastroenterology societies in the US and Europe have established guidelines in response to the recognized importance of adequate bowel preparation quality. The US Multi-Society Task Force on Colorectal Cancer, the European Society of Gastrointestinal Endoscopy and others[5,7,63] now recommend using split-dose regimens for bowel preparation, such that the second dose of laxative is administered 4 to 6 hours before the colonoscopy with completion at least 2 hours before the exam.

Inadequate bowel preparation has multiple adverse consequences, both direct and downstream, that can broadly be categorized as the following:

1) Efficacy: Inadequate bowel preparation is associated with lower adenoma detection rates and lower cecal intubation rates which are risk factors for missed lesions, thus reducing the effectiveness of colonoscopy.[64,65]

2) Safety: Inadequate bowel preparation is associated with increased risk of electrocautery, longer procedure time, and reduced patient comfort, which can reduce the safety of colonoscopy.[66]

3) Capacity: Demand for colonoscopy is high given both screening and diagnostic indications, and the current capacity is inadequate to meet this demand. The VHA devotes a large amount of resources to improve the colonoscopic capacity and many VA facilities rely heavily on fee-basis and non-VA care to meet the colonoscopic capacity. Hence, maximizing capacity is of key importance in the VHA. Inadequate bowel preparation may reduce the colonoscopic capacity through cancelled procedures and resources required for rescheduling. Additionally, this may lead to poor patient satisfaction and delays in care. One study reported that for every 1% increase in inadequate bowel preparation, the cost of colonoscopy delivery increased by 1%.[3]

4) Effectiveness: Inadequate bowel preparation impairs a thorough inspection of the colonic mucosa and results in incomplete exams. Patients with incomplete exams may never reschedule, or at the very least, have delayed diagnostic evaluation due to rescheduling. Delays in diagnostic or screening exams may reduce the effectiveness of a colonoscopy

> program. The current VHA directive requires a colonoscopy within 60 days of a positive FOBT. Inadequate bowel preparation resulting in rescheduling colonoscopy may contribute to delays in colonoscopy. Unsatisfactory quality of cleansing also results in physicians recommending a repeat colonoscopy exam at a shorter interval compared to intervals recommended by multi-society guidelines. In one study, bowel preparations of fair quality were associated with more aggressive follow-up intervals in 60% of average risk asymptomatic individuals undergoing screening colonoscopy.[67]

Furthermore, quality of bowel preparation, adenoma detection rate, and cecal intubation rate are proposed quality measures for colonoscopy programs, at the facility and individual level. These have been adopted by the Centers for Medicare & Medicaid Services (CMS) as metrics in the physician quality reporting system (PQRS), associated with financial incentives, and starting in 2015, financial penalties to eligible practices.[68]

There are multiple bowel preparation agents available in the US, all with a single goal of achieving high quality of colon cleansing. Recent studies have focused on the different regimens of administration of the purgative and clearly demonstrate that, for better cleansing, splitting the dose, in which the laxative is split into two doses taken the day before and the day of colonoscopy, is superior to administering the entire laxative the night before the colonoscopy.[4] A recent meta-analysis of 29 studies comparing split-dose regimens to night-before regimens reported a rate difference of 22% (95%CI 16%, 27%) in achieving better cleansing with split-dose prep.[69] The study also found that the time interval between last administration of laxative and colonoscopy was the main factor driving the effect. The risk difference between split and non-split preparation was maintained when colonoscopy was performed within 3 hours from the end of laxative intake, but decreased after 4 to 5 hours (risk difference 18%), and was not statistically significant when the time interval was >5 hours. The authors also found higher compliance with the split-dose regimen (risk difference 9.4%; 95%CI 0.06, 0.13) regardless of type of laxative.

NPO Status and Other Outcomes

We also examined the effect of variable timing of NPO on resource use, such as no-shows, cancellation, rescheduling, and other missed opportunities. Hypothetically, a shorter duration of NPO could improve capacity, if it reduced cancellations or aborted procedures due to poor preparation. On the contrary, a shorter duration of prep could be more difficult to adhere to, or to tolerate, resulting in missed appointments that would need to be rescheduled. We found one study (insufficient evidence) that reported fewer rescheduled colonoscopies in the shorter NPO status group and no studies reporting on other resource use outcomes.

Eleven studies reported on adherence to preparation or colonoscopy. Of these, 2 reported significantly higher adherence to preparation regimens with NPO of $\geq$ 1.5 hours versus > 8 hours and NPO of < 3 hours versus > 8 hours respectively.[13,21] The other 9 studies reported no difference in adherence to colonoscopy or to the preparation with variable duration of NPO. Patient satisfaction and willingness to repeat the preparation was higher with shorter duration of NPO, while less sleep loss was reported in 2 studies with NPO durations of $\geq$ 5 hours versus > 8 hours and $\geq$ 3 hours versus > 8 hours respectively. Of note, most studies had broad time ranges for duration of NPO status, and we were unable to derive a mean or median estimate.

Summary of Evidence

In summary, we found low-strength evidence that procedure-related harms, such as risk of aspiration or other anesthesia-related harms from colonoscopy are not related to duration of NPO status prior to colonoscopy (Appendix D). Aspiration requiring hospitalizations among individuals undergoing colonoscopy is very low (1 in 1000 or less) and consistent in magnitude with complications of similar severity occurring during elective procedures. It is important to acknowledge that in the US there are no systematic tracking methods to track complications from colonoscopy, especially related to NPO status, and there is the possibility of under- or mis-reporting. We found evidence that shorter duration of NPO status prior to colonoscopy (< 4 hours) is associated with higher-quality bowel cleansing compared to longer duration of NPO prior to colonoscopy (> 8 hours). We found moderate strength evidence that shorter duration of NPO is not associated with higher rates of completion, and insufficient or low-strength evidence that shorter duration of NPO affects adenoma detection rates, diagnostic yield, or false negative colonoscopy (Appendix D). While there are many studies evaluating the association of bowel preparation quality and colonoscopy yield and quality indicators, there is limited evidence showing the direct relationship between duration of NPO and these outcomes. Only one study reported the effect of NPO status prior to colonoscopy on resource use. Results were mixed for patient adherence and patient satisfaction.

LIMITATIONS AND APPLICABILITY

Our findings are limited by the relative paucity of information directly addressing the key questions. None of the studies were directly designed to address the key questions. Instead we used studies that primarily evaluated the effect of different regimens on bowel preparation to assess the effect of varying NPO status on the outcomes of interest for this report. Except for bowel preparation quality, few studies reported our outcomes of interest. In fact, only 5 studies reported on aspiration according to NPO status and one reported on rescheduling (our co-primary outcomes). Most studies examining different bowel preparation and NPO status were not adequately powered to detect aspirations requiring hospitalizations or designed to assess rescheduling due to NPO status.

Hospital- or population-based studies that reported on aspiration for individuals undergoing colonoscopy with sedation did not report NPO status. The largest study, and the only one conducted in the US, reported on patients age 66 and older (mean age 75 years). The applicability of results to younger individuals is uncertain, though the reported percentage may overestimate aspiration risk. Participants likely had wide ranges of NPO status timing, especially time from NPO to colonoscopy longer than 2 to 4 hours. Thus it is difficult to determine from these studies if and by how much aspiration risk may be effected by varying NPO status.

Definitions of aspiration methods for diagnosing aspiration varied. We were limited to reporting what was provided in published articles.

Many studies excluded patients with serious comorbidities. Few studies recorded mean or range of NPO status timing (including time of last ingestion of water, clear liquids, or bowel preparation substance). Furthermore, only 26 of 40 included studies reported on use of sedation during colonoscopy.

Populations enrolled in eligible studies were broadly applicable to many individuals undergoing elective colonoscopy in the United States. Eligible studies typically included patients 45 to 65 years with approximately 50% of patients enrolled in studies done in the US. Nearly one-half of patients were male and two-thirds of colonoscopies were performed for cancer screening. The largest study reporting on aspirations requiring hospitalization was completed in a US Medicare population. However, aspiration by NPO status was not provided in this study and few other studies were adequately designed to directly assess the role of NPO status on aspirations requiring hospitalizations or colonoscopy rescheduling.

RESEARCH GAPS/FUTURE RESEARCH

Our findings indicate important gaps including: 1) accurate assessment of aspiration requiring hospitalization and other serious anesthesia-related adverse events according to NPO status, 2) extent of and reasons for variation in anesthesia NPO status practice and policy, 3) effect of NPO status on procedure rescheduling and patient adherence and satisfaction, and 4) reasons for reduced patient adherence to recommendations for NPO status and bowel preparation.

Future studies to close these knowledge gaps could improve care quality. Studies are needed that systematically assess duration of NPO status in relation to timing of colonoscopy and record serious adverse events, such as aspiration requiring hospitalization, with standardized diagnostic criteria. This can be done through setting up prospective registries of Veterans undergoing colonoscopy to record timing of preparation, duration of NPO, and sedation procedures, and then tracking adverse events over the next 48 to 72 hours. Reporting of anesthesia-related complications is required per VHA and Joint Commission policy, and most VA medical centers have electronic reporting systems in place. Future efforts could be directed towards developing standard methods to collate this information and initiate analyses to assess the association of duration of NPO and colonoscopy outcome. In this regard, special populations at higher risk of aspiration and other anesthesia-related outcomes would be of particular interest, such as elderly patients, patients with high comorbidities, and those with disabilities that limit ability to follow and complete the bowel preparation instructions.

Future studies are also needed to determine and understand variability in NPO duration policies and practices across VA (especially practices that may not adhere to national society guidance statements) and to implement interventions to reduce variation. There is also a need to evaluate the effect of variable durations of NPO status prior to colonoscopy on patient satisfaction, adherence to colonoscopy, and impact on endoscopy scheduling processes, including delays in timely receipt of colonoscopy. A better understanding of why some patients do not adhere to NPO status recommendations and methods to improve communication and adherence are needed. Alternative scheduling methods, including later but same day colonoscopy, could also be evaluated to reduce “cancellations” due to NPO non-adherence. Colonoscopy without moderate or deep sedation, commonly used in other developed countries, could be offered to some patients, though concerns exist regarding patient comfort and colonoscopy quality.

National and international multi-society (gastroenterology, gastrointestinal endoscopy, colon and rectal surgery, and gastrointestinal and endoscopic surgery) guidelines[5,7,63] now recommend using split-dose regimens for bowel preparation, such that the second dose of laxative is administered 4 to 6 hours before the colonoscopy, with completion at least 2 hours before the exam. Additionally, the ASA guidelines support NPO of 2 hours after clear liquids.[10] However,

there is a need for larger studies comparing shorter durations of NPO prior to colonoscopy (such as 2 to 4 hours) to longer intervals of NPO prior to colonoscopy (such as ≥ 6 hours) that directly assess for colonoscopy effectiveness (such as detection rate of adenoma and neoplasia, completion rate) and safety outcomes (including aspiration). We also need studies evaluating the effect of variable duration of NPO status prior to colonoscopy on patient satisfaction, adherence to colonoscopy, and impact on endoscopy scheduling processes, including delays in timely receipt of colonoscopy.

Finally, evidence-based multi-society consensus guidelines are needed that bring together patient representatives and members from anesthesia, gastroenterology, and general medicine. Recommendations for NPO status also affect other gastroenterology procedures as well as procedures performed by other specialties (*eg,* pulmonary and cardiology). Therefore, including representatives across a wide range of disciplines and procedures would be helpful in developing evidence-based recommendations targeted to specific procedures and likely benefits and harms. Important items in guideline development include determining the "clinically important" balance between critical outcomes to anesthesiologists, gastroenterologists (and other specialty groups performing procedures), and patients, including aspiration rates due to NPO status, colonoscopy quality measures, resource use, and patient satisfaction and adherence.

CONCLUSIONS

Aspiration incidence requiring hospitalization during colonoscopy with moderate or deep sedation is very low and on the order of magnitude commonly accepted for adverse effects of similar clinical importance due to other elective procedures. Participants in hospital- and population-based studies likely had wide ranges of timing from NPO to colonoscopy and many were likely longer than 2 to 4 hours. No study documenting NPO status found that shorter NPO status prior to colonoscopy increased aspiration risk. We did not find direct evidence of the effect of NPO status on colonoscopy rescheduling. Shorter time from completion of colonic preparation to colonoscopy is associated with greater bowel preparation quality than longer time intervals.

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APPENDIX A. SEARCH STRATEGY

Database: Ovid MEDLINE(R)

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1 colonoscopy/
2 colonic.ti,ab.
3 (endoscop$ and (colon$ or rect$)).ti,ab.
4 or/1-3

5 cathartics/ or polyethylene glycols/ or phosphates/ or laxatives/ or senna extract/ or bisacodyl/ or cascara/ or enema/ or administration, oral/
6 (prepara$ or enema$ or cathart$ or (polyethylene adj glycol$) or phosphat$ or laxativ$ or (senna adj extract$) or bisacodyl or cascara or PEG or miralax or golytely or nulytely or halflytely or fleet or dulcolax or pico selax or bowel prep$ or bowel purgative or oral or liquid).mp.
7 5 or 6

8 respiratory aspiration of gastric contents/ or respiratory aspiration/ or pneumonia, aspiration/ or dyspnea/ or vomiting/
9 (emesis or vomit$ or reflux or bronchoaspirat$ or aspirat$ or quality or detection).ti,ab.
10 8 or 9

11 4 and 7 and 10

12 limit 11 to yr="1990 -Current"
13 limit 12 to English language
14 limit 13 to humans
15 limit 14 to ("all infant (birth to 23 months)" or "all child (0 to 18 years)" or "newborn infant (birth to 1 month)" or "infant (1 to 23 months)" or "preschool child (2 to 5 years)" or "child (6 to 12 years)" or "adolescent (13 to 18 years)")
16 limit 14 to ("all adult (19 plus years)" or "young adult (19 to 24 years)" or "adult (19 to 44 years)" or "young adult and adult (19-24 and 19-44)" or "middle age (45 to 64 years)" or "middle aged (45 plus years)" or "all aged (65 and over)" or "aged (80 and over)")

17 14 not 15
18 16 or 17

APPENDIX B. PEER REVIEW COMMENTS/AUTHOR RESPONSES

Are the objectives, scope, and methods for this review clearly described?	
Yes	Thank you
Yes	
Yes	
Yes	
Yes	
Yes	
Yes	
Yes	
Is there any indication of bias in our synthesis of the evidence?	
No	Thank you
No	
No	
No	
No	
No	
No	
No	
Are there any published or unpublished studies that we may have overlooked?	
Yes - Diagnostic and Therapeutic Endoscopy published online July 14, 2008 (see comments below, and also attachment) Complications Following Colonoscopy With Anesthesia Assistance: A Population-Based Analysis FREE Gregory S. Cooper, MD; Tzuyung D. Kou, PhD; Douglas K. Rex, MD	Thank you for the suggestions. The first article is Schanz 2008. We have reviewed this article and would not include it because all three groups completed the prep regimen by 7 am for an afternoon colonoscopy. The article does not report aspiration or other adverse events associated with the colonoscopy procedure. The article is a comparison of prep agents, not timing. The second article suggested is Cooper 2013 which we have already included.
No	
No	
No	
No	
No	
No	
Yes - Though it seems reasonable on the face of it to restrict the review only to papers that compare different durations of NPO status, one could make an argument for inclusion of papers that examine the impact of an inadequate bowel preparation on colonoscopic findings. Though this could be considered indirect evidence, there is direct evidence that longer NPO status is associated with lower quality bowel preparation. Therefore, I believe that many key references may have been missed, especially concerning the impact of a poor bowel preparation on neoplasia miss rates. For example: 1) Froehlich	As noted, the suggested references do not directly assess the effect of NPO status, the focus of the review. Froehlich 2005 and Harewood 2003 provide no information about NPO status. Siddiqui 2009 compared prep completed < 14 hours before colonoscopy to > 14 hours.

F, Wietlisbach V, Gonvers JJ, et al. 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. 2) Harewood GC1, Sharma VK, de Garmo P. Impact of colonoscopy preparation quality on detection of suspected colonic neoplasia. Gastrointest Endosc. 2003 Jul;58(1):76-9. Also, 3) Siddiqui AA1, Yang K, Spechler SJ, Cryer B, Davila R, Cipher D, Harford WV. Duration of the interval between the completion of bowel preparation and the start of colonoscopy predicts bowel-preparation quality. Gastrointest Endosc. 2009 Mar;69(3 Pt 2):700-6. doi: 10.1016/j.gie.2008.09.047.	We have modified the discussion to address the reviewer's point about indirect evidence.
Additional suggestions or comments can be provided below. If applicable, please indicate the page and line numbers from the draft report.	
1. There was not any discussion regarding the risk of aspiration of the actual prep solution which was used for the bowel preps. In private practice, there is some amount of variability with the choice of preps used (sodium phosphate vs PEG) and the fact that PEG is hygroscopic, and may incite an ongoing inflammatory resp reaction once aspirated, whereas sodium phosphate may be more benign, although there does not seem to be much evidence in animal literature to support that. 2. Diagnostic and Therapeutic Endoscopy July 14, 2008 (published online) compared sodium phosphate to PEG and found greater patient tolerability and at least equivocal conditions for colonoscopy with 2PEG prep volume deliveries. For difficult, non-compliant patients, this may be a good option for the VA population, since this is a much lower volume fluid, and provided at least as good scoping conditions for most endoscopists (it was a double-blinded study). 3. In reading the actual JAMA article on complications from colonoscopy (JAMA Intern Med. 2013;173(7):551-556. doi:10.1001/jamainternmed.2013.2908.), the authors did identify some possible origins of the 173 occurrences of aspiration, including a deeper plane of anesthesia with anesthesia providers, and higher patient morbidity, which may also affect prep potential, going along with patient compliance with prep instructions and ability to complete the volume load prior to the scope.	1. Discussion of individual prep agents and aspiration during bowel preparation were outside the scope of our review. 2. Schanz 2008. As noted above, this is a comparison of prep agents and not timing. The focus of our review is a comparison of NPO status prior to colonoscopy. 3. We would refrain from suggesting certain populations may be better candidates for shorter NPO based on anesthesia risk, since we find such little evidence to support risk overall with shorter NPO.
My answer to the last boiler-plate Q should be "I don't know". Additionally: 1. Only moderate and deep sedation are mentioned as far as anesthesia methods are concerned. In fact - most of anesthestics delivered by anesthesia teams for colonoscopies are TIVA (total intravenous anesthesia), i.e. general anesthesia (GA) (be it - without airway instrumentation). Per ASA document from 2011, the definition of GA is: "General Anesthesia is a drug-induced loss of consciousness during which patients are not arousable, even by painful stimulation. The ability to independently maintain ventilatory function is often impaired. Patients often require assistance in maintaining a patent airway, and positive pressure ventilation may be required because of depressed spontaneous ventilation or drug-induced depression of neuromuscular function. Cardiovascular function may be impaired." Since the goal of our intervention is to have an insensate/ amnestic and IMMOBILE patient (i.e. not responding with movement to painful stimulation) - what we do easily satisfies the definition of GA (and we code it locally as such). 2. Page 4, lines 26-29: what is the meaning of the statement "... two (studies) reported aspiration with no episodes"?	1. The key questions, developed with input from stakeholders and technical expert panel members, focused on moderate or deep sedation. We could only comment on the level of sedation as reported (or often not reported) in the individual studies. 2. Two studies reported that they were specifically monitoring patients for aspiration events but did not observe any events. We have attempted to clarify this statement. 3. That is correct – the stakeholders nominated the topic and may use the findings of the review to guide VA policy. As with a journal, peer reviewers do not have an ongoing connection to the topic. 4. Thank you.

3. Page 8, lines 13-19: I did not see my name among the stakeholders. As such I understand that my input into this project is completed. 4. I read very carefully the "executive summary" and speed-read the detailed report. It is exhaustive and well executed.	
1. Please note that the four studies that addressed aspiration and sedation related complications did not include those with significant comorbidities. This is a key theme that needs to be emphasized. Subjects that may be at a theoretical risk for aspiration are not necessarily included in the studies addressing the efficacy of split dose preps. 2. Another important issue is the definition of aspiration and how it would be diagnosed. Clearly one could theorize that a transient episode of hypoxemia during the colonoscopy may in and of itself the related to an aspiration episode. However without radiographic evidence or clinical suspicion this would be undetected. 3. In the studies addressing gastric volume and acidity, please ensure that potential confounders such as the concomitant use of anti-secretary agents, antispasmodics or narcotic analgesics have been included in the methodology. 4. We still do not know whether deeper levels of sedation do indeed impart an increased risk for aspiration. According to the ASA Continuum of Sedation, we would expect this to be the case. 5. Additionally, all cases that are performed under anesthesia assistance, please comment as to whether elective endotracheal intubation was performed. This would perhaps, lead to confounding by protecting the airway as opposed to MAC without ET intubation. All of this needs to be discussed in the Research Gaps/Future Research section	1. This was noted in the Limitations section of the full report. We have also added a statement to the key findings in the Executive Summary. 2. Thank you – we have added a statement addressing this limitation in the Limitations section. We also updated the discussion on aspiration definitions and implications. Most clinicians would agree that aspiration needs to be a clinically significant event. Having said that, we were limited by the definition used by individual studies. 3. One of the studies reporting gastric volume did not report on the potential confounders listed. The other reported only that patients taking metoclopramide without proven gastroparesis were not excluded. 4. Risk of aspiration appears greater with deeper sedation, but we did not find enough studies to distinguish the harms of moderate versus deeper sedation prior to colonoscopy in relation to NPO. We have added this concern to the Research Gaps/Future Research section. 5. We provided information about sedation as reported in the published studies. Unfortunately, few details were provided. Furthermore, if the overall risk of aspiration is low, it would not be helpful to split it between anesthesia with or without endotracheal intubation. We have modified the Research Gaps/Future Research to address these concerns.
It would been better if moderate sedation, deep sedation and general anesthesia are reviewed separately. There is mention that aspiration rate is higher with deep sedation compare to moderate sedation. Would the rate be even higher with general anesthesia and how would the rate change if the patient was intubated versus no intubation. The other comment is that there is not enough research to answer the questions asked.	As noted in the review, only 26 of 40 included studies reported on use of sedation during colonoscopy and few details were provided. We agree that more research is needed.

The review is well written and comes to well formulated and reasonable conclusions based on the evidence. I would make a few minor changes. The most fundamental is the concept of low risk. To an anesthesiologist 0.1% risk of aspiration is not low risk. That is a significant risk. Page 4 Line 24: I would not say "the risk of aspiration during colonoscopy is very low (1 in 1000 or less). If the risk is 0.1%, that is a high risk to an anesthesiologist. The risk of aspiration during general anesthesia for C-Section without intubation is listed as 1:200. That risk is considered, extremely high. The risk for general anesthesia is quoted as 1:20,000. So, 1:1000 is high. Page 5 Line26 I would not say "Aspiration incidence during colonoscopy with moderate or deep sedation is very low. 0.1% is a high risk to an anesthesiologist. Page 6 Line 39. You need to include a statement about the contents and volume of colon prep solutions. Colon prep solutions contain ethylene glycol which is toxic to the lung. Colon prep solutions may be transparent but would not be considered "clear liquids". Moreover, the volume, 1 liter, is more than what is standard in NPO guidelines. Page 6 Line 16 If colon preps are inadequate 25% of the time, the efforts of GI docs to understand and correct that causes of failure: compliance, volume, diet may be more fruitful than merely having the prep closer to the time of anesthesia. Page 19 Paragraph 30-38. This paragraph isn't clear enough. There are two very separate issues. What is the time for NPO for clear liquids (water, clear juice) and what is the time for completing bowel preparations? The liquids in bowel prep solutions are very different from water. They have ethylene glycol. This paragraph needs to be in two parts. Time for NPO for clear liquids (water, clear juice). Then there needs to be a separate paragraph for Time for NPO for bowel preparation solutions. The issues are fundamentally separate to an anesthesiologist. Aspirating water is different from aspirating a liter of ethylene glycol containing salt water. Page 20 line 9: 8 hours versus 1-7 isn't very helpful. The range of 1-7 is too wide. Page25 Line 13 1:1000 is not "very low". To an anesthesiologist, 1:1000 is a serious problem. Page 25 Line 24 The granularity of your time scale is too coarse. 1-6 hours versus 8 is not very helpful. How about 0-2, 2-4, 4-6? Is there a difference in 0-2, 2-4, 4-6? Page 25 Line 19 An absence of reported complications does not imply an absence of complications. I am suspicious when there are no events reported. No hospitalizations after a procedure is suspicious. Page 28 Line 34 "Many studies excluded patients with serous comorbidities. " This sentence is critical to applicability. The VA patients have a high risk population with higher ages and many, many comorbidities. Page 29 Paragraph 11-31 Yes. Very well stated. Page 29 Line 35 An aspiration risk of 0.1% is NOT very low. 1:1000 is a big deal to an anesthesiologist.	Thank you. In general a 0.1% risk of an event, where the clinical consequences are not clear, would be regarded as low. Page 4. See above Page 5. See above Page 6. We have added information about contents and volume. Page 6. We have included the need to better understand patient compliance in our Research Gaps/Future Research section. Page 19. This section has been rearranged for clarity. No study reported on differences in quality of preparation between water up to the time of procedure vs no water. The studies that allowed liquids up to the time of procedure did so for all patients. Page 20. Few studies provided exact times between completion of preparation and procedure. We are only able to be as precise as the reported information. Page 25. See above Page 25. There were few comparisons between 0-2, 2-4, etc. so we are comfortable with this statement as written. Page 25. We have modified this statement to clarify that few studies specified adverse events as an outcome of interest. Page 28. As noted above, we have added this statement to the key findings. Page 29. Thank you. Page 29. See above

This was a very high quality review. I have few comments on the methodology. Unfortunately, the evidence base itself was insufficient to enable a meaningful conclusion regarding the key questions posed. My comments are mostly minor: Page 4 "Of 16 studies with NPO duration prior to colonoscopy (either bowel preparation or liquids) as low as 0 to 2 hours, 2 reported aspiration with no episodes." – No episodes of what? Reported no episodes or did aspiration events not occur? Page 4 "Strength of evidence was insufficient for our primary outcomes of aspiration" – Does this mean the strength of evidence was insufficient for the entire meta-analysis or only for this one key question? " and rescheduled colonoscopy." – Was the primary outcome rescheduling? Were there multiple primary outcomes? There is some confusion here between key questions (of which there can be many) and primary outcomes (of which there should only be one) Page 5 – Conclusion- This is very well written and very clear Page 6 Lines 35-37 – these are important since they define what current standards of practice are for NPO. Later this will factor in when reviewing the literature since few of the studies examined NPO status outside of these standard windows. Thus, few studies contributed to any new knowledge on this topic. Page 9 Line 26 – What scale or system was used to assess risk of bias? Please also specify at this point in the report what constitutes low, moderate or high risk of bias. Also, I applaud the investigators for not using the GRADE system. There is an increasing trend for evidence-synthesizing bodies to use GRADE –However, GRADE is very subjective and not an optimal system	Thank you. Page 4. We have clarified this statement. Page 4. Strength of evidence is evaluated for key outcomes. For aspiration and for rescheduled colonoscopies, our primary outcomes of interest, we found insufficient evidence. We have separated this into 2 bullet points to clarify. Although "primary" implies only one, we chose to designate a harm (aspiration) and a resource use (rescheduled colonoscopy) outcome as the key outcomes for the review based on input from stakeholders and Technical Expert Panel members. Page 5. Thank you Page 6. As noted, the guideline authors acknowledge that there is insufficient clinical evidence. Page 9. For RCTs we used a modification of the Cochrane approach. For observational studies, we used a 3 criteria system that we developed. We have added information about what we considered low, moderate, or high risk of bias.
1) Page 11, Table 1: There appear to be errors in the row labels. Specifically, the age values appear to be the "range of means" not the actual range of ages. Also, the Location percentages seem to be incorrectly labeled. 2) There seems to be an important gap in the analysis of the evidence with respect to the impact of an inadequate bowel preparation on patient outcomes. The authors do a very nice job reviewing the direct evidence linking NPO status with bowel preparation quality. However, while there may be limited direct evidence on the impact of NPO status on downstream patient outcomes, such as adenoma detection rate (ADR) or interval cancers, there is considerable evidence on the impact of an inadequate bowel preparation on these important outcomes. Recent evidence has linked the ADR to interval colorectal cancer incidence and mortality (Corley NEJM 2014). Since longer NPO status results in lower quality bowel preparation, and other studies have documented that lower quality bowel preparation is associated with lower rates of adenoma or polyp detection, then it would seem that this would be indirect evidence of lower adenoma detection with longer NPO status. This would then raise concern that longer NPO status will result in increased risk of interval cancer incidence and mortality. The risk of cancer in a VA screening colonoscopy population is between 0.5% and 1%. Among FOBT/FIT positive patients, it is as high as 5%. The lifetime risk of colorectal cancer is around 7% and it is estimated that around 5% of all cancers are now interval cancers. Most of these interval cancers are believe to be due	1. The row labels have been corrected 2. The Discussion section has been modified to address the indirect evidence. 3. We have modified this statement. 4. We have modified this paragraph. 5. See above – we have modified this paragraph. 6. We have modified the reporting of the survey results. 7. The Research Gaps/Future Research section has been modified. 8. We have modified this paragraph.

to missed lesions during colonoscopy. Therefore, the impact of poor bowel preparation on true patient outcomes is more than a hypothetical concern. 3) Page 26, line 14: The study showing higher aspiration incidence associated with deep sedation may be due to confounding by indication (i.e. patients at higher risk for aspiration may have anesthesia assistance brought in to reduce the risk). Endoscopists chose to have anesthesia assistance for any of a number of reasons, including significant comorbidity. 4) Page 27, line 39: The Discussion on resource implications seems incomplete. Clearly if a longer NPO status leads to lower quality bowel preparation, there will be important resource implications. Current guidelines call for repeating the exam within 1 year (Johnson et al. USMSTF Guidelines. Gastro 2014). In many cases, the patient is asked to ingest additional bowel preparation and return the following day. The paper by Rex et al. discusses the cost of inadequate bowel preparation. Within the VA, there are many facilities that lack adequate capacity for providing colonoscopy to the Veterans who need it and, therefore, they send the Veterans to the community at considerable expense. Besides the direct financial implications, there are also direct and indirect patient costs. Moreover, some Veterans decline to return for a follow-up examination, increasing the risk of missed pathology (and subsequent increased risk of morbidity and mortality). Another key related issue is that the variable policies of individual anesthesiologists with respect to NPO status leads to canceled procedures. It is common practice at my facility for anesthesiologists to cancel a colonoscopy on the day of the procedure because the patient ingested bowel preparation <6 hours before the procedure even when some of their colleagues have a 2 hour NPO rule. This variability has resulted in our nurses advising all patients to ingest their preparation the night before and to be NPO for 6 hours. Therefore, our anesthesia cases frequently have a poor quality preparation and need to return for a repeat procedure. This exposes the Veteran to increased risk from repeat procedures and repeat sedation, in addition to the inconvenience and cost. Despite the lack of studies on this issue, these issues are commonplace in the VA and merit discussion. 5) Page 27, line 42: It seems strange to hypothesize that a shorter NPO status might be more difficult to tolerate or adhere to when there are published meta-analyses that demonstrate that patients generally prefer a split-dose prep which generally requires a shorter NPO status. Which is even stated by the authors at line 52. 6) Page 28: Applicability Section: It is interesting that this informal survey was included in the report. There is no doubt that some patients will have an aspiration event during sedation. But there are two major issues with presenting this information. First, related to risk: what evidence is there that a 2 hour NPO status would increase the risk of aspiration compared to 4 or 6 hours? The data presented from the EGD studies shows that there is no difference in gastric contents between shorter and longer NPO status. Since liquids empty very rapidly, it is unlikely that there is a clinically significant difference. Second, there is no consideration of the benefits of a shorter NPO status. Clearly, anesthesiologists focus on trying to reduce the risk of sedation-related complications. However, it is the responsibility of the care team (including the endoscopy AND the anesthesiologist) to consider both the risks and benefits of the procedure. If the colonoscopy has an inadequate bowel preparation, then there is risk of missed neoplasia AND risk of sedation for an inadequate examination. The authors should take a step back and discuss the overall risks and benefits. I suspect a survey of gastroenterologists will yield anecdotal reports of poor bowel preparation, interval cancers and patients who have cases canceled by	

anesthesiologists and then never show for their repeat exam. What value is added by including this section other than to document that anesthesiologists don't follow their own professional society guidelines? This variability leads to endoscopy units being held hostage by the anesthesia providers. 7) Page 29: Research Gaps: While it would be nice to have high quality evidence to answer all questions in clinical practice, the reality is that this is unlikely to happen. Given that the current standard of care is to use split-dose bowel preparation for all colonoscopy, one might question the ethics of a randomized study of 2 hour vs. 6 hour NPO status. The current European guidelines state that the bowel preparation should be finished no more than 4 hours before the procedure begins. The USMSTF guidelines state that the last dose of preparation (typically 1-2 liters) should begin no more than 4-6 hours prior to the procedure (essentially finished 2-4 hours before the procedure start time). Therefore, any study that requires completing the preparation more than 6 hours before the procedure is intentionally asking patients to expose themselves to a greater risk of a poor bowel preparation. As noted by the authors, there is no evidence of harm from a shorter NPO status. Therefore, it is questionable whether an IRB would actually approve such a study. Even if it was ethical to do such a study, the low risk of aspiration would suggest that a study would need tens of thousands of subjects in each treatment arm. Perhaps the authors should include an estimated sample size for a randomized study (e.g. to show a 30% increase in aspiration risk, a study would require X subjects in each arm). There are some patients who decline a split-dose bowel preparation and have a >6 hour NPO status. However, they are not randomly selected. This raises concern about bias in observational studies in an era of split-dose preparation. 8) As noted by the anesthesiologist survey results, there is variable practice within the VA. As noted by the authors, there is no evidence that longer NPO status increases safety for colonoscopy. Can the authors shed any light on why the anesthesiologists believe that more than 2 hours is required despite the ASA recommendation for 2 hours for clear liquids?	

APPENDIX C. EVIDENCE TABLES

Table 1. Study Characteristics

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	NPO status groups	Risk of Bias
Abdul-Baki 2008[13] **Location: Lebanon** **Study design: RCT (4-way)** **Funding source: Industry**	Inclusion Criteria: ambulatory outpatient adults undergoing elective colonoscopies Exclusion Criteria: patients <18 years of age, presence of severe renal impairment, moderate or severe hepatic impairment, a history of bowel obstruction, known allergies to PEG or tegaserod	N=382 Age (yr): 55 Gender (Male %): ~61 Race (%): NR BMI: NR Co-existing conditions (%) Inflammatory bowel disease: 4 Indications for colonoscopy (%) Screening: 25 Abdominal pain: 24 Changes in bowel habits: 15 Rectal bleeding: 21 Anemia: 4 Surveillance of colon cancer/polyps: 7	NPO status group 1a: Split-dose PEG-E with 2L consumed evening before and 2L day of colonoscopy (to be completed 2 hours before the procedure) + tegaserod 6 mg pills (1 tablet night before and one 2.5 hours before procedure); (n=92) NPO status group 1b: matched placebo (n=107) Patients allowed regular diet until 6 pm day before colonoscopy and water until procedure time NPO status group 2a: PEG-E consumed evening before colonoscopy + tegaserod 6 mg pills (1 tablet night before and one 1.5 hours before procedure) (n=94) NPO status group 2b: matched placebo (n=89) Patients allowed liquid diet until 6 pm day before colonoscopy and water until procedure time Sedation: conscious Study withdrawals: none	*For RCTs* Sequence generation: adequate Allocation concealment: adequate Blinding: yes, endoscopist, participant (tegaserod) Incomplete outcome data: no Selective outcome reporting: no **Risk of bias**: Low

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	NPO status groups	Risk of Bias
Aoun 2005[14] **Location: Lebanon** **Study design: RCT** **Funding source: None reported**	Inclusion Criteria: ambulatory outpatient adults undergoing elective colonoscopies Exclusion Criteria: patients <18 years of age, presence of a severe illness (cardiac, renal, or metabolic), active alcoholism, drug addiction, major psychiatric illness, known allergies to PEG	N=141 Age (yr): 57 (range 20-84) Gender (Male %): 57 Race (%): NR BMI: NR Co-existing conditions (%) Inflammatory bowel disease: 4 Indications for colonoscopy (%) Abdominal pain: 28 Screening: 25 Changes in bowel habits: 15 Rectal bleeding: 14 Anemia: 4 Family history of colorectal cancer: <1	NPO status group 1: PEG-E split-dose - 2L night prior and 2L morning; finish morning dose at least 1.5 hours before procedure, regular diet until 6:30 pm day before colonoscopy; water allowed up to colonoscopy (n=68) NPO status group 2: 4L PEG-E - 6:00 to 10:00 pm day before procedure; liquid diet only day before colonoscopy; only water after midnight (n=73) Sedation: conscious Study withdrawals: none	*For RCTs* Sequence generation: adequate Allocation concealment: adequate Blinding: yes, endoscopists Incomplete outcome data: no Selective outcome reporting: no **Risk of bias**: :Low
Arya 2013[15] **Location: USA** **Study design: RCT** **Funding source: None reported**	Inclusion Criteria: patients 21–70 years of age referred for colonoscopy with good general physical status (American Society of Anesthesiologists [ASA] class 1 or 2) Exclusion Criteria: history of chronic heart, liver, or kidney disease; hypertension, diabetes mellitus, arthritis (spine, shoulder, hip and knee joints) severe constipation, or concurrent severe diarrhea, ileus, suspected intestinal obstruction, bowel perforation, previous gastrointestinal tract surgery, gastro-paresis, toxic colitis, ulcerative colitis, pregnancy, and lactation	N=147, 14 excluded. 133 completed study (demographics based on 133) Age (yr): 44 Gender (Male %): 38 Race (%): white 88; black 8 BMI: NR Co-existing conditions (%): NR Indications for colonoscopy (%) Screening: 42 Rectal bleeding: 20 Mild constipation: 19 Abdominal pain: 11 Anemia: 3 Mild diarrhea: 3	NPO status group 1: Rapid-prep Shudh™ colon cleanse (SCC) - patients start SCC around 6 am on morning of colonoscopy drinking 240-480 ml every 5 minutes (total 1-2 L); last glass ≥2 hours prior to procedure (n=74) Day prior to colonoscopy, patients instructed to eat light breakfast up to 12 pm and then stay on clear liquids NPO status group 2: Half-Lytely® colon prep (HCP) - 2 bisacodyl delayed-release tablets taken at 1 pm; patients start drinking 2L solution after a bowel movement or around 7 pm if no bowel activity occurred (n=73) Patients stay on clear liquids entire day prior to colonoscopy Sedation: NR Study withdrawals: 10% (n=14) excluded prior to procedure (no-shows)	*For RCTs* Sequence generation: adequate Allocation concealment: unclear Blinding: yes, endoscopists Incomplete outcome data: yes Selective outcome reporting: no **Risk of bias**: Moderate

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	NPO status groups	Risk of Bias
Athreya 2011[16] **Location: Australia** **Study design: CCT** **Funding source: None reported**	Inclusion Criteria: elective colonoscopy patients Exclusion Criteria: prior surgical resection, patients who had taken GlycoPrep™ (polyethylene glycol electrolyte) as the bowel preparation or those administered a Fleet™ enema on arrival, and failure to achieve caecal intubation	N=325 Age (yr): 57 (24-92) Gender (Male %): 50 Race (%): NR BMI: NR Co-existing conditions (%): NR Indications for colonoscopy (%) Symptoms (not specified): 36 Screening: 35 Family history: 21 Family history & symptoms: 8	NPO status group 1: PM group- 2 sachets PicoPrep-3™ day prior and 3rd sachet 6 to 7 am on day of procedure; solids ceased after 8 am day prior; clear fluids continued until 4 hrs prior to procedure (n=150) NPO status group 2: AM group- 3 sachets PicoPrep-3™ day prior to procedure; solids ceased after 8 am day prior; clear fluids continued until midnight prior to procedure (n=175) Sedation: conscious Study withdrawals: none	*For RCTs* Sequence generation: not applicable Allocation concealment: inadequate (alteration) Blinding: Investigator Incomplete outcome data: no Selective outcome reporting: no **Risk of bias**: High
Barclay 2004[17] **Location: USA** **Study design: RCT** **Funding source: Industry**	Inclusion Criteria: ambulatory outpatient adults undergoing elective colonoscopies Exclusion Criteria: patients <18 years of age, congestive heart failure, renal insufficiency (creatinine > 120 lmol/L), ascites	N=303 randomized, 47 excluded. 256 completed study (demographics based on 256) Age (yr): medians 57-59 Gender (Male %): 45 Race (%): NR BMI: NR Co-existing conditions (%) Diabetes: 9 On diuretics: 11 Indications for colonoscopy (%) Rectal bleeding/+ FOBT: 29 Abdominal pain: 25 Screening: 23 Changes in bowel habits: 20	NPO status group 1: 3-dose regimen; aqueous NaP day before procedure; 2nd dose 5 hours later; 3rd dose 3 hours before scheduled time of procedure (n=131) NPO status group 2: 2-dose regimen (n=125) a) morning colonoscopy; aqueous NaP day before procedure; 2nd dose 5 hours later (same day) b) afternoon colonoscopy; aqueous NaP day before procedure; 2nd dose 5 hours before scheduled time of procedure All patients: clear fluid diet for 24 hours before colonoscopy; instructed to drink 3.8L of commercially available carbohydrate-electrolyte solution during preparation period Sedation: NR Study withdrawals: 18% (n=47) excluded prior to procedure	*For RCTs* Sequence generation: adequate Allocation concealment: not reported Blinding: yes, endoscopists Incomplete outcome data: yes Selective outcome reporting: no **Risk of bias**: Moderate

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	NPO status groups	Risk of Bias
Bryant 2013[18] **Location: Australia** **Study design: Retrospective observational** **Funding source: None reported**	Inclusion Criteria: mostly outpatients (89%) undergoing colonoscopy Exclusion Criteria: patients with a prior history of large bowel resection, colonoscopies where cecal intubation could not be achieved due to an obstructing lesion, and colonoscopy reports which did not report on bowel preparation	N=1,785 Age (yr): <55 34%; ≥55 66% Gender (Male %): 53 Race (%): NR BMI: NR Co-existing conditions (%): NR Indications for colonoscopy (%) Anemia/Rectal bleeding: 37 Screening: 34 Altered bowel habit: 12 Colitis: 6 Other: 11	NPO status group 1: Afternoon colonoscopies; prep to procedure interval 5-7.5 hrs (n=768) a) 2L PEG at 5-7 pm day before + 2L PEG before 8 am day of colonoscopy b) 2 sachets sodium picosulphate at 1 pm and 5 pm day before + 1L PEG before 8 am day of colonoscopy NPO status group 2: Morning colonoscopies; prep to procedure interval 8.5-17 h; (n=1,017) a) 4L PEG between 2 pm and 7 pm day before colonoscopy b) 2 sachets sodium picosulphate at 9 am and 1 pm day before + 1L PEG at 4 pm All patients: low-residue diet 2 days before and only clear fluids 1 day before colonoscopy; fast for 4-6 hours before procedure Sedation: by proceduralist using fentanyl and midazolam, or with propofol sedation by anesthetist Study withdrawals (%): NA	1) Study design: retrospective 2) Population: consecutive 3) Analysis of findings a. Was the method for handling missing data reported and appropriate? appears to be no missing data b. Were the characteristics of the different NPO groups similar? unclear **Risk of bias**: Moderate
Chiu 2006[20] **Location: Taiwan** **Study design: RCT** **Funding source: None** **Note: *Secondary colonoscopy***	Inclusion Criteria: patients who had colon neoplasms detected during the first screening colonoscopy Exclusion Criteria: inability to discontinue the use of antiplatelet agents or anticoagulants, presence of minute polyps that had been removed during the screening colonoscopy using biopsy forceps, invasive cancer that required surgical intervention, failure to complete total colonoscopy for any reason at the health checkup	N=121 Age (yr): 57 Gender (Male %): 68 Race (%): NR, presumed all Asian BMI: 25 Co-existing conditions (%): NR Indications for colonoscopy (%) Colorectal neoplasms 100	NPO status group 1: PEG-ELS; 2L between 5 and 6 am day of colonoscopy (6-8 hr NPO interval) (n=61) NPO status group 2: PEG-ELS 2L at 8 pm evening before colonoscopy (13-16 hr NPO interval) (n=60) Low-fiber diet advised for two days before the procedure Sedation: conscious Study withdrawals: 3 (2%) did not ingest prep and were excluded	*For RCTs* Sequence generation: not described Allocation concealment: unclear (“sealed envelopes”) Blinding: colonoscopist Incomplete outcome data: yes Selective outcome reporting: no **Risk of bias**: Moderate

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	NPO status groups	Risk of Bias
Chiu 2011[19] **Location: Taiwan** **Study design: Retrospective observational** **Funding source: In part by research grant from Department of Health of Taiwan**	Inclusion Criteria: Chinese patients age 40 to 80 years; received total colonoscopy; considered average-risk (a) no history CRC, adenoma, or IBD; b) no criteria for hereditary non-polyposis CRC, familial adenomatous polyposis, or other polyposis syndrome; c) no 1st degree relative with CRC; d) no symptoms of colorectal malignancy [bloody stool, abdominal pain, change in body weight, or documented iron deficiency anemia]; e) no history of CRC screening tests within 5 yrs; and f) no long-term use of aspirin, non-steroidal anti-inflammatory drug, or a cyclooxygenase 2 inhibitor) Exclusion Criteria: NR	N=3,079 Age (yr): 51 Gender (Male %): 53 Race (%): Asian 100 BMI: NR (abdominal girth reported) Co-existing conditions (%): NR Indications for colonoscopy (%): NR	NPO status group 1: PEG-ELS 2L between 3 and 4 am morning of colonoscopy (5-9 hr NPO interval) (n=1,552) NPO status group 2: PEG-ELS 2L between 8 and 9 pm evening before colonoscopy (>8 hr NPO interval) (n=1,527) 2 days before procedure, patients advised to start low-fiber diet; 1 day before procedure, patients advised to drink only clear liquids and avoid solid foods Sedation: NR Study withdrawals: None	1) Study design: retrospective 2) Population: consecutive 3) Analysis of findings a. Was the method for handling missing data reported and appropriate? appears to be no missing data b. Were the characteristics of the different NPO groups similar? no, differences in abdominal girth between groups **Risk of bias**: Moderate
Church 1998[21] **Location: USA** **Study design: RCT** **Funding source: None reported**	Inclusion Criteria: ambulatory outpatient adults undergoing elective colonoscopies in the afternoon Exclusion Criteria: NR	N=317 Age (yr): 60 Gender (Male %): 57 Race (%): NR BMI: NR Co-existing conditions (%): NR Indications for colonoscopy (%) Neoplasm follow-up: 48 Family history of CRC: 14 Symptoms (not specified): 14 Polyp on prior exam: 11 Other: 13	NPO status group 1: 4L PEG starting at 8 am day of procedure (n=157) NPO status group 2: 4L PEG starting at 6 pm evening before procedure (n=160) All patients; liquid diet day before; after prep allowed water by mouth only until examination Sedation: NR Study withdrawals: none	*For RCTs* Sequence generation: not described Allocation concealment: not described Blinding: yes, endoscopists Incomplete outcome data: no Selective outcome reporting: no **Risk of bias**: Moderate

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	NPO status groups	Risk of Bias
De Salvo 2006[22] **Location: Italy** **Study design: RCT** **Funding source: None reported**	Inclusion Criteria: patients scheduled for colonoscopy who were able to follow cleansing regimen Exclusion Criteria: pregnancy, age >75 years, previous operation on small/large bowel, renal failure, known electrolyte disorders, heart failure, liver disease with ascities	N=273 (demographic information for 265 who followed the cleansing regimen) Age (yr): 61 Gender (Male %): 53 Race (%): NR BMI: NR Co-existing conditions (%): NR Indications for colonoscopy (%): NR	NPO status group 1: Sodium phosphate 40 mL at 6 pm day prior to colonoscopy and 6 am day of colonoscopy (≥5 hours) (n=83) NPO status group 2: Magnesium sulfate 15mg and senna 12mg in 200 mL water 5 pm day prior to colonoscopy (>8 hours) (n=92) NPO status group 3: PEG 2 L at 6 pm day prior to colonoscopy plus Biscodyl 4 tablets at 10 pm day prior to colonoscopy (>8 hours) (n=98) On day before colonoscopy, patients to avoid solid food after 12 pm; colonoscopy performed after 11 am Study withdrawals: 8/273 (3%)	*For RCTs* Sequence generation: adequate Allocation concealment: NR Blinding: colonoscopists that scored bowel preparation Incomplete outcome data: yes Selective outcome reporting: **Risk of bias**: Moderate

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	NPO status groups	Risk of Bias
Di Palma 2011[23] **Location: USA** **Study design: RCT** **Funding source: Industry**	Inclusion Criteria: adult outpatients undergoing colonoscopy for routine clinical indications Exclusion Criteria: ileus or suspected bowel obstruction, bowel perforation, previous alimentary tract surgery, significant gastroparesis or gastric outlet obstruction, toxic colitis or megacolon, severe ulcerative colitis or those pregnant or lactating	Study 1 (ITT population) N=364 Age (yr): 56 Gender (Male %): 46 Race (%): white 86, black 9 BMI: NR Indications for colonoscopy (%): NR Study 2 (ITT population) N=387 Age (yr): 57 Gender (Male %): 45 Race (%): white 87, black 11 BMI: NR Indications for colonoscopy (%): NR Co-existing conditions (%): Overall 356/787 subjects (45%) had a history of heart disease, renal failure, hypertension, and diabetes	Study 1 (split dose) NPO status group 1a: oral sulfate solution (16 oz + additional water) evening before colonoscopy; 2nd dose at approximately 6 am day of colonoscopy (hours unclear) (n=190) NPO status group 1b: 1L PEG-EA evening before colonoscopy and 1L approximately 6 am day of colonoscopy (hours unclear) (n=189) Study withdrawals: 16/379 (4%) Study 2 (same day) NPO status group 2a: oral sulfate solution (total of 32oz + additional water) evening before colonoscopy (hours unclear) (n=204) NPO status group 2b: 2L PEG-EA evening before colonoscopy (hours unclear) (n=204) Study withdrawals: 26/408 (6%) Sulfate preparation subjects had light breakfast and clear liquids for lunch and dinner; PEG-EA subjects had normal breakfast, light lunch, and clear soup or yogurt for dinner Sedation: NR	*For RCTs* Sequence generation: adequate Allocation concealment: adequate Blinding: colonoscopists Incomplete outcome data: yes Selective outcome reporting: no **Risk of bias**: Moderate

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	NPO status groups	Risk of Bias
El Sayed 2003[24] **Location: Lebanon** **Study design: RCT** **Funding source: None Reported**	Inclusion Criteria: ambulatory outpatients scheduled for elective morning colonoscopy Exclusion Criteria: age < 18, presence of serious conditions such as severe cardiac, renal or metabolic diseases, active alcoholism, drug addiction, major psychiatric illness; known allergy to PEG or bisacodyl, and refusal to consent to the study	N=187 Age (yr): 56 Gender (Male %): 56 Race (%): NR BMI: NR Co-existing conditions (%) History of surgery: None: 95 Abdominoperineal resection: 1 Left colectomy: 2 Right colectomy: 1 Segmental colectomy: 1 Indications for colonoscopy (%) Anemia: 6 Abdominal pain: 23 Rectal bleeding: 24 Follow-up after colonic resection: 5 Family history of CRC: 7 Change in bowel habits: 24 Follow-up after polypectomy: 4 Positive FOBT: 3 Screening: 18 Follow-up of IBD: 5	NPO status group 1: 2L PEG at 6 pm day before colonoscopy; no dietary restrictions except for light liquid dinner before 7 pm; 5mg of bisacodyl at 8 pm; 1L PEG at least 2 hrs before colonoscopy (n=91) NPO status group 2: 3 Sachets of PEG in 3L of water beginning 6 pm (finish within 4 hrs); start clear liquid diet on morning of day before colonoscopy; fast after midnight (n=96) Sedation: Moderate sedation (Midazolam and Mepiridine) Study withdrawals: NR	*For RCTs* Sequence generation: adequate Allocation concealment: adequate Blinding: single-blinded (endoscopist) Incomplete outcome data: no Selective outcome reporting: no **Risk of bias**: Low

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	NPO status groups	Risk of Bias
Eun 2011[25] **Location: Korea** **Study design: Prospective observational** **Funding source: Research Fund of Hanyang University**	Inclusion Criteria: Outpatients aged between 18 and 80 years scheduled for elective colonoscopy Exclusion Criteria: Age<18, presence of serious illness such as severe cardiac, renal or metabolic disease, drug addiction or major psychiatric illness; known allergy to PEG, prior history of bowel resection and refusal of consent to study	N=300 Age (yr): 52 Gender (Male %): 51 Race (%): NR BMI: 23 Co-existing conditions (%) Chronic diseases: 32 Constipation: 11 Prior Hysterectomy: 11 Indications for colonoscopy (%) Screening: 25 Family history of CRC: 2 Surveillance: 6 Hematochezia: 12 Anemia: 3 Abdominal pain: 30 Bowel habit changes: 17 Suspicion of polyp on imaging: 6	NPO status group 1: 4L PEG consumed over 3 hours starting at 5 am for morning colonoscopy (mean time from end of prep to procedure = 3.7 hrs) (n=149) NPO status group 2: Same but starting at 8 am for afternoon colonoscopy (mean time from end of prep to procedure = 4.9 hrs; P < .001 vs group 1) (n=151) Sedation: NR Study withdrawals: 7 failed to reach cecum	1) Study design: prospective 2) Population consecutive 3) Analysis of findings a. Was the method for handling missing data reported and appropriate? none reported b. Were the characteristics of the different NPO groups similar? yes **Risk of bias**: Low

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	NPO status groups	Risk of Bias
Flemming 2012[26] **Location: Canada** **Study design: RCT** **Funding source: University research unit**	Inclusion Criteria: age 18 and older, elective colonoscopy at 1 hospital Exclusion Criteria: ileus or bowel obstruction, significant constipation (<3 bowel movements/week with or without regular laxatives), previous colorectal surgery, ascites, previously recognized renal impairment, active IBD, pregnancy, recent (<6 mos) MI or unstable angina	N=250 enrolled; demographic data for 236 (14 randomized but never participated because target numbers reached) Age (yr): 56 Gender (Male %): 46 Race (%): NR BMI: NR Co-existing conditions (%) Hypertension: 28% Diabetes: 7% Indications (%) Family history CRC: 44% Screening: 12% History of adenoma: 18% Positive FOBT: 6.8% Bleeding: 6.9% Altered bowel habits: 6.0% Diarrhea: 3.4% Other: 3.0%	NPO status group 1: Picosulfate, magnesium oxide, & citric acid (Pico-Salax); 1st dose at 7 pm, 2nd dose 4 hrs before colonoscopy (n=119) NPO status group 2: Pico-Salax; 2 doses evening before colonoscopy (5 pm, 11 pm) (n=117) Both groups: 2 5-mg tablets bisacodyl for 2 consecutive nights before colonoscopy; only clear fluids on day before colonoscopy; encouraged to drink 3-4 L Gatorade or similar evening before colonoscopy Sedation: NR Study withdrawals: 14 (6%); 6 split dose, 8 evening before dose	*For RCTs* Sequence generation: adequate Allocation concealment: adequate Blinding: endoscopists blinded to dosing regimen Incomplete outcome data: 6% withdrawals Selective outcome reporting: **Risk of bias**: Moderate

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	NPO status groups	Risk of Bias
Frommer 1997[27] **Location: Australia** **Study design: RCT** **Funding source: In part by CB Fleet Company Inc.**	Inclusion Criteria: NR Exclusion Criteria: inability to understand instructions, heart failure, pregnancy, age above 90, raised creatinine, right hemicolectomy, use of additional agents (enemas or defoaming agents), a significant error in having performed cleansing instructions, and failure to reach cecum or IC valve	N=487 Age (yr): 63 Gender (Male %): 55 Race (%): NR BMI: NR Co-existing conditions (%): Diverticulosis:3.3 Indications for colonoscopy (%): NR	NPO status group 1: 45 ml NaP solution at 6 pm day before colonoscopy and 6 am on morning of colonoscopy (n=166) NPO status group 2: 3L PEG at 2 pm day before colonoscopy (N=160) NPO status group 3: 45ml NaP at 7 am and 7 pm on day before colonoscopy; instructed to drink minimum of 800 ml water or clear fluid within 1 hr (n=161) All patients: avoid foods with small seeds and nuts for 5 days; take 3 tablets of bisacodyl in afternoon two days before colonoscopy; day before colonoscopy no solid food/clear liquids throughout the day Sedation: NR Study withdrawals: NR	*For RCTs* Sequence generation: unclear Allocation concealment: unclear Blinding: single blinded Incomplete outcome data: no Selective outcome reporting: no **Risk of bias**: Moderate
Gupta 2007[28] **Location: India** **Study design: RCT** **Funding source: Not reported**	Inclusion Criteria: age between 18 and 80 Exclusion Criteria: prior bowel surgery, suspected bowel obstruction, contraindication to phosphate preparation (cardiovascular or renal insufficiency); inconvenienced by the timing of bowel preparation	N=201 Age (yr): NR Gender (Male %): NR Race (%): NR BMI: NR Co-existing conditions (%): NR Indications for colonoscopy (%): NR NOTE: reported groups were comparable in terms of demographic data and indications for colonoscopy	NPO status group 1: NaP-based fluid (90 mL with 300 mL lemonade) at 6 am on day of colonoscopy ("colonoscopy preferably scheduled" after11 am) (n=102) NPO status group 2: NaP-based fluid (same) at 5 pm day before ("timing of colonoscopy for the evening group was adjusted as indicated by the scheduled appointment list") (n=99) Both groups: allowed to consume clear liquids (as desired) in the preceding 12 hours (UNCLEAR WHAT THIS MEANS) Sedation: combination of pethidine hydrochloride (50mg) and midazolam (2mg) as an intravenous bolus unless contraindicated (1/2 dose for pts over 65 yrs) Study withdrawals: None	*For RCTs* Sequence generation: unclear Allocation concealment: adequate Blinding: investigators blinded to timing of prep Incomplete outcome data: no Selective outcome reporting: no **Risk of bias**: Moderate

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	NPO status groups	Risk of Bias
Gurudu 2010[29] **Location: USA** **Study design: Retrospective observational** **Funding source: None**	Inclusion Criteria: consecutive afternoon colonoscopies (after 1 pm) from July 2008 to April 2009 Exclusion Criteria: None	N=1,345 Age (yr): 61 Gender (Male %): 52 Race (%): NR BMI: Overall NR, reported for poor, good prep etc. Co-existing conditions (%): NR Indications for colonoscopy (%): Screening/surveillance: 61% Anemia/bleeding: 11% Diarrhea: 8% Abdominal pain; 4% Colitis: 3% Constipation: 2% Other: 11%	NPO status group 1: Split-dose prep 1) 4L PEG am (n=226): start 4L PEG at 5 am day of procedure 2) 2L PEG am (n=39): start 2L PEG + 4 tablets bisacodyl at 5 am day of procedure 3) Split Dose: 2L PEG evening before procedure and starting at 5 am day of (n=48) NPO status group 2: 1 day prep 1) 2L PEG pm (n=656): 2L PEG + 4 tablets bisacodyl day prior to procedure 2) 4L PEG pm (n=376): 4L PEG day prior All patients allowed drink clear liquids up to 3 hrs before procedure Sedation: Conscious sedation Study withdrawals: None	1) Study design: retrospective 2) Population: consecutive 3) Analysis of findings a. Was the method for handling missing data reported and appropriate? appears to be no missing data b. Were the characteristics of the different NPO groups similar? bowel preparations were not distributed equally (difference adjusted statistically) **Risk of bias**: Moderate
Gurudu 2012[30] **Location: USA** **Study design: Retrospective observational** **Funding source: None**	Inclusion Criteria: patients undergoing screening/ surveillance colonoscopy Exclusion Criteria: incomplete data, prior colon resection, and colonoscopy for indications of bleeding, anemia, IBD, repeated colonoscopy in same patient during the study after an initial colonoscopy detected adenomas was also excluded	N=5,175 Age (yr): 61 Gender (Male %): 50 Race (%): NR BMI: 28 Co-existing conditions (%): NR Indications for colonoscopy (%): Screening and surveillance included only	NPO status group 1: POST-SDP - Split prep (PEG or MoviPrep), 3L night before starting at 6 pm and 1 L at least 4 hours before scheduled procedure; NPO for at least 3 hours prior to procedure (n=1,615) NPO status group 2: Pre-SDP - All prep (PEG or MoviPrep) the night before (n=3,560) All patients instructed to be NPO for at least 3 hrs before procedure Sedation: mainly moderate, few got MAC also Study withdrawals: NR	1) Study design: retrospective 2) Population: consecutive 3) Analysis of findings a. Was the method for handling missing data reported and appropriate? yes, all included b. Were the characteristics of the different NPO groups similar? yes **Risk of bias**: High

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	NPO status groups	Risk of Bias
Huffman 2010[31] **Location: USA** **Study design: Prospective observational** **Funding source: None**	Inclusion Criteria: scheduled for EGD and colonoscopy on same day after split-dose bowel prep Exclusion Criteria: gastric resection, known gastroparesis, or slow GE	N=301 Age (yr): 55 Gender (Male %): 41 Race (%): NR BMI: NR Co-existing conditions (%): DM: 18 Opioid use:15 Metocloporamide Use: 3 Indications for colonoscopy (%): NR	NPO status group 1: Various split-dose bowel preps (PEG, NaP); complete prep by at least 2 hrs before procedure (mean NPO = 5.1 hrs) (n=254) NPO status group 2: Various bowel preps (PEG, NaP) evening before (mean NPO = 13.5 hrs) (n=47) Sedation: NR Study withdrawals: NR	1) Study design: prospective 2) Population: not consecutive 3) Analysis of findings a. Was the method for handling missing data reported and appropriate? NR b. Were the characteristics of the different NPO groups similar? yes, group sizes and outpatient to inpatient ratios differed between groups **Risk of bias**: Moderate

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	NPO status groups	Risk of Bias
Johanson 2007[32] **Location: 10 sites, USA** **Study design: RCT** **Funding source: Pharmaceutical industry**	Inclusion Criteria: males and non-pregnant, non-lactating females ≥18 years; scheduled for colonoscopy Exclusion Criteria: renal insufficiency; serum electrolyte abnormalities at screening; uncontrolled CHF, unstable angina, untreated dysrhythmia, current use of digitalis preparations or medications known to prolong QT interval; MI, PTCA or CABG within previous 3 months; ascites; current acute exacerbation of IBD; toxic colitis or toxic mega-colon; severe chronic constipation; ileus; perforation; ileostomy; colostomy, hypomotility syndrome; gastric bypass or stapling; history of gastric retention; impaired gag reflex; history of aspiration; dysphagia; treatment with investigational drug or product; participation in drug study within past 30 days; treatment within 21 days with another NaP preparation; known allergy to NaP; or any other clinically significant disease that would expose the patient to increased risk of an adverse event	N=402 Age (yr): 56 Gender (Male %): 44 Race (%): white 86; black 10; other 3 BMI: NR Co-existing conditions (%): NR Indications for colonoscopy (%): NR	NPO status group 1: 20 NaP tablets at 6 pm evening before colonoscopy and 12 tablets next day 3-5 hrs before colonoscopy (n=200); this group was allowed light breakfast day before colonoscopy (up to 12 noon) with no solid food after noon (clear liquids only) NPO status group 2: 4 bisacodyl tablets with water at 12 noon day prior colonoscopy followed by 2L PEG taken after a bowel movement or a maximum of 6 hrs after ingestion of bisacodyl tablets (n=202); this group allowed only clear liquids entire day before colonoscpy Sedation: Patients were sedated but type of sedation not reported Study withdrawals: 1 patient withdrew; 16% excluded from final analysis	*For RCTs* Sequence generation: not described Allocation concealment: adequate Blinding: single blinded Incomplete outcome data: 16% excluded from final analysis Selective outcome reporting: no **Risk of bias**: Moderate

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	NPO status groups	Risk of Bias
Kao 2011[33] **Location: Canada** **Study design: RCT** **Funding source: None**	Inclusion Criteria: ambulatory GI clinic patients between 18-75 years who underwent elective outpatient colonoscopy Exclusion Criteria: renal insufficiency, CHF, acute coronary syndrome recent or unstable angina, liver cirrhosis or ascites, chronic furosemide therapy, previous colon resection, and known or suspected bowel obstruction, megacolon or ileus	N= 834 Age (yr): 50 Gender (Male %): 39 Race (%): NR BMI: NR Co-existing conditions (%): NR Indications for colonoscopy (%): NR	NPO status group 1: PM colonoscopy; 4 different regimens 8-10 H before colonoscopy (n=287); included PEG, NaP, Pico-Salax+magnesium citrate NPO status group 2: AM colonoscopy; 4 different prep regimens 10-14 h before colonoscopy (n=491) All patients; clear liquid diet the day before colonoscopy; hydrate liberally with water or clear electrolyte replacement solution until 2 hrs before procedure Sedation: NR Study withdrawals: None	*For RCTs* Sequence generation: adequate Allocation concealment: adequate Blinding: single blinded Incomplete outcome data: no Selective outcome reporting: no **Risk of bias**: Low

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	NPO status groups	Risk of Bias
Kastenberg 2001, 2007[34,35] **Location: Multiple sites, USA** **Study design: RCT** **Funding source: Pharmaceutical Industry**	Inclusion Criteria: either gender, at least 18 years old, scheduled for colonoscopy, able to swallow tablets without difficulty, and gave written informed consent Exclusion Criteria: evidence of acute or chronic renal insufficiency; cardiovascular disease (uncontrolled congestive heart failure, unstable angina pectoris, or, within past 3 months, PTCA, MI, or CABG); ascites; electrolyte imbalance (hyponatremia, hyperphosphatemia, or hypocalcemia); colon disease (acute exacerbation of chronic IBD, chronic constipation [<2 bowel movements per week for >1 year], ileus and/or acute obstruction, ileostomy, right or transverse colostomy, subtotal colectomy [≥50% of colon removed] with ileosigmoidostomy [patients with right or left hemicolectomy alone were eligible], hypomotility syndrome, megacolon, or idiopathic pseudoobstruction	N=886 randomized (859 received study product) Age (yr): 56 Gender (Male %): 48 Race (%): white 87, African-American 8, Hispanic 5 BMI: NR Co-existing conditions (%): NR Indications for colonoscopy (%): NR	NPO status group 1: 20 tablets NaP at 6 pm evening before and repeat 3-5 hrs before colonoscopy (n=420) NPO status group 2: 4L PEG evening before colonoscopy (n=425) Sedation: NR Study withdrawals: 1.6% (14 patients)	*For RCTs* Sequence generation: adequate Allocation concealment: adequate Blinding: single blinded Incomplete outcome data: no Selective outcome reporting: no **Risk of bias**: Low

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	NPO status groups	Risk of Bias
Khan 2010[36] **Location: USA** **Study design: CCT** **Funding source: Not reported**	Inclusion Criteria: adults, scheduled for outpatient colonoscopy Exclusion Criteria: NR	N=412 Age (yr): NR Gender (Male %): NR Race (%): NR BMI: NR Co-existing conditions (%): NR Indications for colonoscopy (%): NR	NPO status group 1: NaP tablets (n=93) or 2L PEG + ascorbic acid (n=64) administered by split-dose (exact timing unknown) (total n=157) NPO status group 2: 4L PEG the evening before (exact timing unknown) (n=255) Sedation: NR Study withdrawals (%): bowel preparation scoring incomplete for 49/412 (12%)	*For RCTs and CCTs* Sequence generation: not applicable Allocation concealment: not described Blinding: unclear Incomplete outcome data: yes Selective outcome reporting: no **Risk of bias**: High
Koh 2011[37] **Location: Korea** **Study design: RCT** **Funding source: University research fund**	Inclusion Criteria: NR Exclusion Criteria: diabetes mellitus, hyperthyroidism or hypothyroidism, taking prokinetic or antispasmotic medication, history of bowel resection	N=80 Age (yr): 53 Gender (Male %): 66 Race (%): NR BMI: NR Co-existing conditions (%): chronic disease 23; previous abdominal surgery 11 Indications for colonoscopy (%) Screening: 48 Altered bowel habit: 28 Bowel symptoms: 18 Anemia: 8	NPO status group 1: 4L PEG between 6 and 8 am; ate lunch between 12 and 12:30 pm (n=40) NPO status group 2: 4L PEG between 6 and 8 am; no lunch (n=40) All colonoscopies between 2 and 4 pm Sedation: conscious sedation/analgesia with IV midazolam and pethidine titrated as required	*For RCTs and CCTs* Sequence generation: inadequate (odd and even days) Allocation concealment: inadequate Blinding: endoscopists were blinded Incomplete outcome data: no Selective outcome reporting: no **Risk of bias**: High

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	NPO status groups	Risk of Bias
Kolts 1993[38] **Location: USA** **Study design: RCT** **Funding source: University research fund**	Inclusion Criteria: consecutive outpatients requiring an elective colonoscopy Exclusion Criteria: acute diverticulitis, active IBD, unstable cardiovascular or respiratory status, allergies to all available conscious sedation medications, MI or cerebrovascular accident in last 2 months, serum creatinine > 2.0 mg/dl, massive ascites, delayed gastric emptying	N=113 Age (yr): 54 Gender (Male %): 39 (lower % male in NPO group 1) Race (%): NR BMI: NR Co-existing conditions (%): NR Indications for colonoscopy (%) GI bleed: 36 Polyps: 39 Anemia: 4 Diarrhea: 9 Constipation: 3	NPO status group 1: NaP (90ml fluid) at 6 pm and 6 am plus at least 36oz water 1 hour after 6 pm dose (n=34) NPO status group 2: 4L GoLYTELY (PEG) at 6 pm day before (n=38) NPO status group 3: Castor oil (60ml fluid) at 6 pm plus at least 36oz water 1 hour after (n=41) All patients: liquid diet day before with NPO after midnight Sedation: IV sedation	*For RCTs and CCTs* Sequence generation: unclear Allocation concealment: pharmacist distributed preparations Blinding: endoscopists were blinded Incomplete outcome data: no Selective outcome reporting: no **Risk of bias**: Moderate
Kössi 2007[39] **Location: USA** **Study design: Prospective observational** **Funding source: Not reported**	Inclusion Criteria: consecutive outpatients Exclusion Criteria: None reported	N=214 enrolled; demographic data for 204 analyzed Age (yr): 54 Gender (Male %): 45 Race (%): NR BMI: NR Co-existing conditions (%) Diverticulosis (moderate to severe): 11 Indications for colonoscopy (%): NR	*Morning colonoscopies*: 45 ml NaP at 7 am and 7 pm day before colonoscopy *Afternoon colonoscopies*: 45 ml NaP at 6 pm day before and 6 am on day of colonoscopy *Created 3 groups:* NPO status group 1: 6 hours or less between 2nd dose of prep and colonoscopy (n=53) NPO status group 2: 6 to 12 hours between 2nd dose of prep and colonoscopy (n=90) NPO status group 3: 12 hours or more between 2nd dose of prep and colonoscopy (n=61) All patients: instructed to not eat vegetables, berries, fruits, or bread containing seeds for 1 wk before colonoscopy; encouraged to drink 2-3 liters of clear liquids during bowel prep Sedation: NR Study withdrawals: 5% (10/214)	1) Study design: prospective 2) Population: consecutive 3) Analysis of findings a. Was the method for handling missing data reported and appropriate? yes b. Were the characteristics of the different NPO groups similar? yes **Risk of bias**: Low

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	NPO status groups	Risk of Bias
Longcroft-Wheaton 2012[40] **Location: UK** **Study design: Obsersvational (Prospective Cohort)** **Funding source: None reported**	Inclusion Criteria: receiving colonoscopy under National Bowel Cancer Screening Programme; age 59 to 70 years Exclusion Criteria: known renal impairment (CKD grade 3, Creatinine>150; eGFR<40); congestive cardiac failure; sodium <130	N=227 Age (yr): median 65 (range: 60-71) Gender (Male %): 75 Race (%): NR BMI: NR Co-existing conditions (%): NR Indications for colonoscopy (%): NR	NPO status group 1: same-day regimen, 2 sachets of sodium picosulphate at 7 and 10 am on morning of afternoon procedure; NPO <3 hours (n=132) NPO status group 2: 2-day regimen, pts used 3 sachets of sodium picosulphate at noon and 5 pm on day before and 1 at 8am on day of afternoon procedure; NPO 4-8 hours (n=95) All patients: light diet day before procedure (no vegetables/fruit); increase fluid intake for 24 hrs leading up to procedure Sedation: NPO Status 1: 1.27, NPO Status 2: 1.20 (Mean sedation level where 1=awake, 2=drowsy, 3=asleep) Study withdrawals: NR	1) Study design: prospective 2) Population: consecutive 3) Analysis of findings a. Was the method for handling missing data reported and appropriate? appears all were included b. Were the characteristics of the different NPO groups similar? yes Note: endoscopist and screening nurse were blinded to the preparation regimen. **Risk of bias**: Low
Manno 2012[41] **Location: Italy** **Study design: RCT** **Funding source: None reported**	Inclusion Criteria: 18 years of age or older, either a positive FOBT or in surveillance post-polypectomy with elective colonoscopy scheduled between 9:00 am and 1:00 pm Exclusion Criteria: presence of severe cardiac, renal or hepatic impairment; known allergy or hypersensitivity to any constituent of preparation	N=336 Age (yr): 61 Gender (Male %): 71 Race (%): NR BMI: NR Co-existing conditions (%) Prior abdominal surgery: 21 Constipation: 10 Diabetes: 4 Indications for colonoscopy (%) Positive FOBT: 70 Polypectomy follow-up: 30	NPO status group 1: 3L PEG starting at 3 pm day before and 1L PEG over 1 hr starting 3 hrs before procedure (n=168) NPO status group 2: 4L PEG over 4 hrs starting at 3 pm day before colonoscopy (n=168) All patients: low fiber diet for 3 days before procedure Sedation: conscious sedation Study withdrawals: None	*For RCTs* Sequence generation: adequate Allocation concealment: adequate Blinding: investigator Incomplete outcome data: no Selective outcome reporting: no **Risk of bias**: Low

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	NPO status groups	Risk of Bias
Marmo 2010[42] **Location: Italy** **Study design: RCT** **Funding source: None reported**	Inclusion Criteria: "appropriate indication" to colonoscopy Exclusion Criteria: pregnant or lactating women; age <18 years; significant gastroparesis or gastric outlet obstruction or ileus; known or suspected bowel obstruction or perforation; phenylketonuria or glucose-6-phosphate dehydrogenase deficiency; severe chronic renal failure (creatinine clearance <30 mL/minute); severe congestive heart failure (New York Heart Association class III or IV); dehydration; severe acute inflammatory disease; compromised swallowing reflex or mental status; uncontrolled hypertension (SBP ≥170 mm Hg, DBP ≥100 mm Hg); toxic colitis; or megacolon	N=randomized 895 (ITT includes 868) Age (yr): 58 Gender (Male %): 58 Race (%): NR BMI: NR Co-existing conditions (%): Diabetes: 5 Indications for colonoscopy (%): Symptoms: 41 Screening: 13 Surveillance: 16 Polypectomy/resection: 8	NPO status group 1: High volume (4L PEG-ES) or low volume (2L PEG-ES + ascorbic acid); half taken afternoon before, half early morning on day of colonoscopy (n=435) NPO status group 2: Same as above with doses taken 2 hours apart starting around 6:30 pm evening before colonoscopy (n=433) All patients: low fiber diet for 3 days before procedure; light breakfast and lunch plus semiliquid dinner day before taking bowel prep; NPO after midnight before procedure Sedation: NR Study withdrawals (%): Type of prep unknown:18 (2) Incorrect prep 9 (1)	*For RCTs* Sequence generation: adequate Allocation concealment: adequate Blinding: single-blind Incomplete outcome data: yes (3%) Selective outcome reporting: no **Risk of bias**: Low

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	NPO status groups	Risk of Bias
Mathus-Vliegen 2013[43] **Location: Netherlands** **Study design: RCT** **Funding source: NR**	Inclusion Criteria: consecutive ambulant patients referred for colonoscopy; age ≥ 18; physically able to take bowel preparation at home Exclusion Criteria: pregnant or lactating, inpatient, heart failure, severe dehydration, GI ulcers, hypersensitivity to PEG< ileus, (partial) colectomy, colostomy, phenylketonuria, glucose-6-phosphate deficiency, enrolled in population-screening program	N=200 randomized (12 did not receive allocated intervention); patients were randomized to PEG or PEG+ascorbate solution and then completed split-dose or single-dose prep based colonoscopy time Age (yr): 60 Gender (Male %): 48 Race (%): NR BMI: NR Co-existing conditions (%): NR Indications for colonoscopy (%): Polyp surveillance: 37 GI bleeding: 21 Changed stool pattern: 21 Familiar screening/surveillance: 12 Anemia: 5 IBD: 4	NPO status group 1 (afternoon colonoscopies): 2L PEG or PEG+ascorbate solution starting at 6 pm day before and 2L morning of procedure (exact time not reported) (n=89) NPO status group 2 (morning colonoscopies): 4L PEG or PEG+ascorbate solution starting at 6 pm evening before (n=99) All patients: 2-day low-fiber diet recommended Sedation: NR Study withdrawals (%): Did not receive allocated intervention: 6% For efficacy outcome: a. Failed examination: 6% of those receiving intervention b. Missing data: 9% of those receiving intervention	*For RCTs* Sequence generation: adequate Allocation concealment: adequate Blinding: endoscopists were blinded Incomplete outcome data: yes (efficacy data missing for 20%, safety data missing for 6%) Selective outcome reporting: no **Risk of bias**: Moderate

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	NPO status groups	Risk of Bias
Matro 2010[44] **Location: USA** **Study design: RCT** **Funding source: Industry**	Inclusion Criteria: age ≥ 18; scheduled for elective, outpatient afternoon (12 pm or later) colonoscopy Exclusion Criteria: pregnancy, breast feeding, known or suspected gastroparesis, chronic nausea or vomiting, bowel obstruction, hypomotility syndrome, severe constipation, >50% colon resection, known glucose-6-phosphate dehydrogenase deficiency, PEG allergy, significant psychiatric illness	N=125 randomized (9 withdrew prior to taking prep; 1 additional patient in AM group did not undergo colonoscopy) Age (yr): 52 Gender (Male %): 46 Race (%): NR BMI: NR Co-existing conditions (%): Diabetes: 8 Thyroid disease: 7 Hypertension: 30 GERD: 9 IBD: 4 Pulmonary disease: 4 Cardiovascular disease: 24 Indications for colonoscopy (%): Screening: 51 Surveillance: 17 Symptoms: 32	NPO status group 1 (AM prep): 1L PEG 7 hours before procedure and 1L 4 hours before procedure (n=65) NPO status group 2 (PM/AM prep): 1L PEG + 250 ml clear liquid at 6 pm and 1L 4 hours before procedure (n=60) All patients: low-residue breakfast before 10 am day before then clear liquids until 2.5 hours before colonoscopy (medications with sips of water allowed within 2.5 hours of procedure) Sedation: monitored anesthesia with propofol-based sedation Study withdrawals (%): 7% did not take prep	*For RCTs* Sequence generation: adequate Allocation concealment: adequate Blinding: endoscopists were blinded Incomplete outcome data: 7% Selective outcome reporting: no **Risk of bias**: Low
Paoluzi 1993[45] **Location: Italy** **Study design: RCT** **Funding source: NR**	Inclusion Criteria: NR Exclusion Criteria: presence of stenosis, suspected perforation of the gut, colonic resection, pregnancy	N=160 randomized; data for 132 Age (yr): 51 Gender (Male %): 60 Race (%): NR BMI: NR Co-existing conditions (%): NR Indications for colonoscopy (%): IBD: 46 Cancer: 4 Polyps: 17 Haematochezia: 19	NPO status group 1: 2L PEG at 6 to 8 pm evening before; 1L PEG at 6 to 7 am; fast or clear liquids after starting prep (n=80) NPO status group 2: 35g castor oil at 4 pm day before; cleansing enema evening before and morning of procedure; low residual semi-liquid diet for 2 days before exam with fast from eve of exam (n=80) Colonoscopies performed 8-9:30 am Sedation: NR Study withdrawals: 24/160 (15%) did not present on day of examination; additional 4 patients in PEG group did not complete solution because of side effects and did not complete adequacy of prep outcomes	*For RCTs* Sequence generation: unclear Allocation concealment: unclear Blinding: endoscopists were blinded Incomplete outcome data: 17.5% Selective outcome reporting: no **Risk of bias**: Moderate

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	NPO status groups	Risk of Bias
Park 2007[46] **Location: Korea** **Study design: RCT** **Funding source: None reported**	Inclusion Criteria: consecutive individuals undergoing medical check−up colonoscopy at university−affiliated medical center Exclusion Criteria: age < 18 years; serious medical conditions such as severe cardiac, renal, or metabolic disease; active alcoholism, drug addiction, or major psychiatric illness; known allergy to PEG; previous surgical bowel resection or gynecologic surgery; refusal of consent to participate in study	N=303 Age (yr): 49 Gender (Male %): 81 Race (%): NR BMI: NR Co-existing conditions (%): NR Indications for colonoscopy (%): NR	NPO status group 1: 3L PEG between 8 and 11 pm evening before procedure; 1L PEG early morning (at least 2 hours prior to procedure) (n=152) NPO status group 2: 4L PEG between 8 and 11 pm evening before procedure (n=151) Colonoscopies performed 8-9:30 am Sedation: NR Study withdrawals: None	*For RCTs* Sequence generation: not described Allocation concealment: not described Blinding: Colonoscopists blinded, groups evenly allocated Incomplete outcome data: no Selective outcome reporting: no **Risk of bias**: Low
Park 2010[47] **Location: Korea** **Study design: RCT** **Funding source: No funding**	Inclusion Criteria: men and women >18 years of age scheduled for colonoscopy in the morning Exclusion Criteria: serious medical conditions such as severe cardiac, renal, hepatic, or metabolic diseases; active alcoholism, drug addiction, or major psychiatric illness; known allergy to PEG; history of prior colon or rectal surgery	N=285randomized (analyzed 232) Age (yr): 52 Gender (Male %): 63 Race (%): NR BMI: 24 Co-existing conditions (%): NR Indications for colonoscopy (%): NR	NPO status group 1: 2L PEG 8 pm evening before procedure, 2L PEG 5 am day of procedure (n=80) NPO status group 2: 250 ml magnesium citrate 8 pm evening before procedure, 2L PEG 5 am day of procedure (n=73) NPO status group 3: 4L PEG 10 pm evening before procedure (n=79) All patients: thick liquid diet at dinner evening before procedure; NPO after 6 pm Sedation: NR Study withdrawals: 19% (postponed or canceled procedure or changed to pm)	*For RCTs* Sequence generation: adequate Allocation concealment: inadequate (an investigator managed the printed allocation schedule) Blinding: investigator Incomplete outcome data: yes Selective outcome reporting: no **Risk of bias**: High

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	NPO status groups	Risk of Bias
Parra-Blanco 2006[48] **Location: Spain** **Study design: RCT** **Funding source: Government, Education**	Inclusion Criteria: consecutive outpatients, scheduled for elective colonoscopy (morning or afternoon), age 18-85 Exclusion Criteria: Pregnancy, partial or total colectomy, IBD (known or suspected)	N=197 randomized, 177 included in analysis Age (yr): 54 Gender (Male %): 48 Race (%): NR BMI: NR Co-existing conditions (%): NR Indications for colonoscopy (%) Chronic constipation: 24 Polyp surveillance: 13	NPO status group 1: 3L PEG-ELS starting at 6 am day of colonoscopy (n=43) (NOTE: 39.5% had morning colonoscopy) NPO status group 2: 45 mL NaP 8 pm evening before and 45 mL 6 am day of colonoscopy (n=45)[a] (NOTE: 53.3% had morning colonoscopy) NPO status group 3: 3L PEG-ELS starting at 8 pm evening before colonoscopy (n=45) (NOTE: 68.9% had morning colonoscopy) NPO status group 4: 45mL NaP at 3 pm and 8 pm day before colonoscopy (n=44)[a] (NOTE: 77.3% had morning colonoscopy) Colonoscopies: 9 am to 3 pm Patients NaP groups encouraged to drink fluids liberally (at least 2L) during cleansing period All patients: received Bysacodyl (15 mg) day before colonoscopy and low-fiber diet recommended; allowed clear fluids after completing bowel preparation Sedation: NR Study withdrawals: 10 (20/197 consecutive outpatients initially included in the study)	*For RCTs* Sequence generation: adequate Allocation concealment: unclear Blinding: endoscopists and attending nurse blinded to prep regimen Incomplete outcome data: yes Selective outcome reporting: no **Risk of bias**: Moderate

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	NPO status groups	Risk of Bias
Rex 2013[49] **(SEE CLEAR I study)** **Location: USA** **Study design: RCT** **Funding source: Industry**	Inclusion Criteria: men and women, 18 to 80 years, at least 3 spontaneous bowel movements/week for 1 month before colonoscopy Exclusion Criteria: acute abdominal conditions; active IBD; colon disease (including toxic megacolon, toxic colitis, idiopathic pseudo-obstruction, hypomotility syndrome); ascites; GI disorders (such as active ulcers, gastric outlet obstruction, retention, gastroparesis, and ileus); uncontrolled angina and/or MI within past 3 months; CHF or uncontrolled hypertension; known renal insufficiency with abnormal creatinine or serum potassium levels at screening; history of colorectal surgery or upper GI surgery Use of lithium, laxatives, constipating drugs, antidiarrheal agents, or oral iron preparations not allowed during the study	N=608 randomized; demographic data for 603 Age (yr): 55 (median) Gender (Male %): 41 Race (%): white 88; black/African American 11 BMI: 29.5 Co-existing conditions (%): NR Indications for colonoscopy (%): NR	NPO status group 1: P/MC; first dose in 5 oz water between 5 and 9 pm evening before followed by 40 oz clear liquid over next several hours; second dose in 5 oz water 5 to 9 hours before procedure followed by 24 oz clear liquid (n=305) NPO status group 2: 2 5-mg bisacodyl tablets taken in afternoon before colonoscopy; after first bowel movement or 6 hours 2L PEG-3550 (n=298) All patients limited to clear liquid diet 24 hours before procedure Sedation: NR Study withdrawals: 0.8% not treated and excluded; 0.7% did not complete study	*For RCTs* Sequence generation: unclear Allocation concealment: adequate Blinding: gastroenterologists and assistants were blinded Incomplete outcome data: yes (1%) Selective outcome reporting: no **Risk of bias**: Low

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	NPO status groups	Risk of Bias
Seo 2012[50] **Location: Korea** **Study design: Prospective observational** **Funding source: NR**	Inclusion Criteria: 18 to 85 years, outpatients Exclusion Criteria: pregnancy, breastfeeding, history of surgical large-bowel resection, severe renal failure, drug addiction or major psychiatric illness, allergy to PEG, refusal to participate in study	N=366 Age (yr): 55 Gender (Male %): 48 Race (%): NR BMI: 23 Co-existing conditions (%) Hypertension: 14 Diabetes: 7 Stroke: 1 Liver cirrhosis: 2 Constipation: 20 Indications for colonoscopy (%) Screening: 40 Surveillance: 17 Symptoms: 43	NPO status group 1: 2L PEG at 6 pm on day before, 2L PEG at least 2 hours before procedure (n=366) NPO status group 2: N/A All patients instructed to start low fiber diet 3 days before colonoscopy; regular diet for breakfast and lunch and soft diet for dinner the day before colonoscopy; allowed only clear liquids until 2 hours before colonoscopy Sedation: NR Study withdrawals: None	1) Study design: prospective 2) Population: consecutive 3) Analysis of findings a. Was the method for handling missing data reported and appropriate? appears all were included b. Were the characteristics the different NPO groups similar? unclear **Risk of bias**: Moderate
Vanner 2011[51] **Location: Canada** **Study design: Prospective observational** **Funding source: Internal funding only**	Inclusion Criteria: colonoscopy for routine clinical indication Exclusion Criteria: congestive heart failure, renal insufficiency, ileus or bowel obstruction, previous colorectal surgery, ascites, active IBD, recent (<6 mo) MI or unstable angina	N=100 Age (yr): 60 Gender (Male %): 42 Race (%): NR BMI: NR Co-existing conditions (%): NR Indications for colonoscopy (%): NR	NPO status group 1: PSLX, 1st dose at 7 pm, 2nd dose at 6 am before colonoscopy scheduled after 11 am (interval >5 hrs) (n=32) NPO status group 2: PSLX 1st dose at 5 pm, 2nd dose at 10 pm evening before colonoscopy scheduled before 11 am (interval >9 hrs) (n=68) All patients: 10 mg bisacodyl tablet at 6 pm days 3 and 2 before colonoscopy; low fiber diet 5 days before colonoscopy; clear fluid diet day before colonoscopy; encouraged to drink 4L of carbohydrate electrolye sports drink on day of clear fluids and until leaving home for procedure Sedation: NR Study withdrawals: unclear; 5 incomplete colonoscopies (4 abdominal discomfort, 1 poor preparation and sigmoid stricture)	1) Study design: prospective 2) Population: unclear if consecutive 3) Analysis of findings a. Was the method for handling missing data reported and appropriate? appears all were included b. Were the characteristics the different NPO groups similar? unclear **Risk of bias**: Moderate

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	NPO status groups	Risk of Bias
Varughese 2010[52] **Location: USA** **Study design: RCT** **Funding source: No funding**	Inclusion Criteria: age > 19 years, elective colonoscopy scheduled from 1 pm onward Exclusion Criteria: history of colon resection, suspicion of bowel obstruction	N=136 randomized Age (yr): 52 Gender (Male %): 52 Race (%): white 45; Hispanic 49; other 6 BMI: 28.5 Co-existing conditions (%): NR Indications for colonoscopy (%): CRC screening: 54 Diagnostic/therapeutic: 46 NOTE: study terminated early - interim analysis showed larger effect size than anticipated	NPO status group 1: 1 gallon PEG between 6 am and 10 am day of colonoscopy (interval >3 hrs) (n=68) NPO status group 2: 1 gallon PEG between 5 pm and 9 pm day before colonoscopy (interval >16 hrs) (n=68) Group 1 was allowed breakfast on day before colonoscopy followed by clear liquids for lunch and dinner; Group 2 advised to take only clear liquid on day before colonoscopy *Both groups allowed clear liquids the morning of the procedure with NPO after 10 am* Sedation: Meperidine+midazolam (32%); monitored anesthesia care (68%) Study withdrawals: None	*For RCTs* Sequence generation: adequate Allocation concealment: unclear Blinding: yes, endoscopists were blinded Incomplete outcome data: no Selective outcome reporting: no **Risk of bias**: Moderate
Voiosu 2013[53] **Location: Romania** **Study design: RCT** **Funding source: NR**	Inclusion Criteria: clear indication for colonoscopy, age >18 years Exclusion Criteria: refusal to sign consent or preference for a specific bowel prep product, stenosing colorectal cancer or intestinal obstruction, previous colonic resection, severe concomitant disease (heart, renal or liver failure; pulmonary disease; electrolyte imbalance; neuropsychiatric conditions)	N=181 randomized (patient characteristics for n=165) Age (yr): 60 Gender (Male %): 54 Race (%): NR BMI: NR Co-existing conditions (%): NR Indications for colonoscopy (%): Rectal bleeding: 24 CRC screening: 18 Diarrhea: 14 Anemia: 10 Constipation: 7 Abdominal pain: 7 Referral for polypectomy: 6 Other: 16	NPO status group 1: 2L PEG at 5 to 7 pm day before and 2L PEG at 5 to 7 am day of colonoscopy (n=94 randomized, 95 analyzed) NPO status group 2: P/MC 1st dose at 1 pm, 2nd dose at 7 pm day before colonoscopy (plus 250 ml fluid/hour between1 and 11 pm) (n=87 randomized, 80 analyzed) Colonoscopies: 8 am to 2 pm Sedation: propofol at 1 center, midazolam at 1 center Study withdrawals: 9.6% of group 1, 8.0% of group 2	*For RCTs* Sequence generation: unclear Allocation concealment: adequate Blinding: endoscopists were blinded Incomplete outcome data: yes Selective outcome reporting: no **Risk of bias**: Moderate

AE = adverse event; CRC = colorectal cancer; DBP = diastolic blood pressure; FOBT = fecal occult blood test; hrs = hours; IBD = inflammatory bowel disease; L = liter(s); MI = myocardial infarction; CHF = congestive heart failure; NaP = sodium phosphate; PEG = polyethylene glycol; PEG-E or PEG-ELS = polyethylene glycol electrolyte solution; P/MC or PSLX = sodium picosulfate and magnesium citrate; SBP = systolic blood pressure

[a] Patients with co-morbid conditions (chronic renal failure, symptomatic ischemic heart disease, congestive heart failure, hypertension with poor pharmacological control) allocated to NaP groups were given PEG-ELS instead (Group 2 followed Group 1 protocol, Group 4 followed Group 3 protocol) and evaluated on an intention-to-treat analysis

Table 2. Primary Outcomes

Study NPO Status (Intervention/ Control)	Aspiration, n/N (%)		Rescheduled colonoscopies, n/N (%)	
	NPO group 1	NPO group 2	NPO group 1	NPO group 2
Gurudu 2010[29] NPO status 1: ≥ 4 hours NPO status 2: > 8 hours	No episodes of bronchoaspiration were recorded, including in the procedures performed in patients taking same-day bowel preparation		NR	NR
Huffman 2010[31] NPO status 1: ≥ 2 hours NPO status 2: > 8 hours	None of the patients in any group had clinical evidence of aspiration during their procedures		NR	NR
Kolts 1993[38] NPO status 1: Hours unclear (last dose 6 am) NPO status 2: > 8 hours NPO status 3: > 8 hours	NR		1/34 (3%)	Group 2: 3/38 (8%) Group 3: 10/41 (24%) (P = .011)
Manno 2012[41] NPO status 1: 2 hours NPO status 2: > 8 hours	No major complications related to sedation		NR	NR
Mathus-Vliegen 2013[43] NPO status 1: Hours unclear (Split-dose, PM exam) NPO status 2: > 8 hours	No events during 30-day period (from charts of patients and a complication database)		NR	NR
Matro 2010[44] NPO status 1: 4 hours (am prep only) NPO status 2: 4 hours (pm/am prep)	1.6 (1/62) Aspirated during procedure	0/54	NR	NR
Varughese 2010[52] NPO status 1: ≥ 3 hours NPO status 2: > 8 hours	No sedation complications		NN	NR

NPO = nil per os; NR = not reported

Bowel preparation completed the day before colonoscopy designated as NPO status > 8 hours

Table 3. Procedural Outcomes

Study NPO Status (Intervention/ Control)	Quality of bowel preparation[a] % (n/N) or Mean (±SD)		Diagnostic yield % (n/N) or Mean (±SD)		Completion rate % (n/N)		Adenoma detection rate % (n/N)		False negative colonoscopies % (n/N)	
	NPO group 1	NPO group 2	NPO group 1	NPO group 2	NPO group 1	NPO group 2	NPO group 1	NPO group 2	NPO group 1	NPO group 2
Abdul-Baki 2008[13] NPO status 1: ≥ 1.5 hours NPO status 2: > 8 hours	Excellent 45 (90/199) Excellent/Good 89 (177/199) (Sharma et al.)	Excellent 9 (16/183) Excellent/Good 43 (78/183); P < .001	NR	NR	NR	NR	NR	NR	NR	NR
Aoun 2005[14] NPO status 1: ≥ 1.5 hours NPO status 2: > 8 hours	Excellent 44 (30/68) Excellent/Good 76 (52/68) (Sharma et al.)	Excellent 6 (4/73) P < .001 Excellent/Good 56 (41/73) P = .01	NR	NR	NR	NR	NR	NR	NR	NR
Arya 2013[15] NPO status 1: ≥ 2 hours NPO status 2: > 8 hours	Success (Grade A+B) 91 (59/65) Grade A 57 (37/65) (Author scale)	Success (Grade A+B) 97 (66/68) P = NS Grade A 72 (49/68)	NR	NR	NR	NR	NR	NR	NR	NR
Athreya 2011[16] NPO status 1: 5-9 hours NPO status 2: > 8 hours	Satisfactory Rectum 91 (136/150) Sigmoid 87 (130/150) Descending 68 (102/150) Transverse 57 (86/150) Ascending 47 (70/150) (Author scale)	Satisfactory Rectum 92 (161/175) P = .52 Sigmoid 92 (161/175) P = .15 Descending 82 (143/175) P = .005 Transverse 73 (128/175) P = .002 Ascending 62 (108/175) P = .007	NR	NR	NR	NR	NR	NR	NR	NR

Study NPO Status (Intervention/ Control)	Quality of bowel preparation[a] % (n/N) or Mean (±SD)		Diagnostic yield % (n/N) or Mean (±SD)		Completion rate % (n/N)		Adenoma detection rate % (n/N)		False negative colonoscopies % (n/N)	
	NPO group 1	**NPO group 2**	**NPO group 1**	**NPO group 2**	**NPO group 1**	**NPO group 2**	**NPO group 1**	**NPO group 2**	**NPO group 1**	**NPO group 2**
Barclay 2004[17] NPO status 1: < 3 hours NPO status 2: ≥ 5 hours	Excellent/Good 89 (116/130) (Author scale)	Excellent/Good *morning* 60 (n NR) P < .0001 vs NPO status 1 Excellent/Good *afternoon (split)* 76 (n NR) P = .03 vs.NPO status 1	NR	NR	NR	NR	NR	NR	NR	NR
Bryant 2013[18] NPO status 1: 5-7.5 hours NPO status 2: > 8 hours	Satisfactory/ good preparation 89 (684/768) (Author scale)	Satisfactory/ good preparation 86 (873/1017) P = .04	NR	NR	NR	NR	NR	NR	NR	NR

Study NPO Status (Intervention/ Control)	Quality of bowel preparation[a] % (n/N) or Mean (±SD)		Diagnostic yield % (n/N) or Mean (±SD)		Completion rate % (n/N)		Adenoma detection rate % (n/N)		False negative colonoscopies % (n/N)	
	NPO group 1	NPO group 2	NPO group 1	NPO group 2	NPO group 1	NPO group 2	NPO group 1	NPO group 2	NPO group 1	NPO group 2
Chiu 2011[19] NPO status 1: 5-9 hours NPO status 2: > 8 hours	Excellent 13 (197/1552) Good 60 (930/1552) (Aronchick et al.)	Excellent 3 (38/1527) P < .001 Good 32 (481/1527) P < .001	NR	NR	NR	NR	Overall 17 (270/1552) proximal 11 (175/1552) Advanced overall 4 (68/1552) proximal 2 (34/1552) Nonpoly- poid overall 6 (98/1552) Proximal 5 (71/1552) Advanced 2 (25/1552)	Overall 15 (233/1527) P = .11 proximal 9 (138/1527) P = .04 Advanced overall 3 (46/1527) P = .04 proximal 2 (25/1527) Nonpoly- poid overall 4 (67/1527) P = .02 Proximal 3 (40/1527) P = .004 Advanced 1 (12/1527	NR	NR
Chiu 2006[20] NPO status 1: 6-8 hours NPO status 2: > 8 hours Note: lesions detected in first and second colonoscopies	Adequate 93 (56/60) (Sharma et al.)	Adequate 72 (42/58) P < .0001	Total lesions 2.78 (0.29) Proximal 1.52 (0.22) Advanced 0.87 (0.13)	Total lesions 1.90 (0.27) P = .028 Proximal 0.97 (0.24) P = .094 Advanced 0.55 (0.10) P = .056	100 (60/60)	100 (58/58)	NR	NR	NR	NR

Study NPO Status (Intervention/ Control)	Quality of bowel preparation[a] % (n/N) or Mean (±SD)		Diagnostic yield % (n/N) or Mean (±SD)		Completion rate % (n/N)		Adenoma detection rate % (n/N)		False negative colonoscopies % (n/N)	
	NPO group 1	NPO group 2	NPO group 1	NPO group 2	NPO group 1	NPO group 2	NPO group 1	NPO group 2	NPO group 1	NPO group 2
Church 1998[21] NPO status 1: 5-8 hours NPO status 2: > 8 hours	Excellent Cecum 62 (97/157) Ascending 66 (103/157) Transverse 65 (102/157) Left colon 59 (93/157) Excellent/Good Cecum 90 (142/157) Ascending 93 (148/157) Transverse 97 (152/157) Left colon 93 (148/157) (Author scale)	Excellent Cecum 9 (14/160) Ascending 9 (14/160) Transverse 9 (15/160) Left colon 11 (18/160) Excellent/Good Cecum 73 (117/160) Ascending 76 (121/160) Transverse 82 (131/160) Left colon 83 (132/160) P < .01 for all groups	NR	NR	97 (152/157)	99 (159/160) P = NS	NR	NR	NR	NR
De Salvo 2006[22] NPO status 1: 5-8 hours (NaP) NPO status 2a: > 8 hours ($MgSO_4$) NPO status 2b: > 8 hours (PEG)	Good 67 (53/79) (Author scale)	Good $MgSO_4$ 39 (35/90) P < .001 PEG 50 (48/96) P = .02	NR	NR	98 (77/79)	$MgSO_4$ 97 (86/90) PEG 96 (92/96) P = NS	NR	NR	NR	NR
Di Palma 2011[23] NPO status 1: 3-9 hours; 2 arms, sulfate and PEG-EA NPO status 2: > 8 hours; 2 arms, sulfate and PEG-EA)	Success Sulfate 97 (175/181) PEG-EA 97 (175/183) Excellent Sulfate 63 (114/181) PEG-EA 53 (96/53) (Author scale)	Success Sulfate 82 (159/194) PEG-EA 80 (155/193) P < .001 for both arms Excellent Sulfate 45 (86/194) PEG-EA 37 (72/193)	NR	NR	NR	NR	NR	NR	NR	NR

Study NPO Status (Intervention/ Control)	Quality of bowel preparation[a] % (n/N) or Mean (±SD)		Diagnostic yield % (n/N) or Mean (±SD)		Completion rate % (n/N)		Adenoma detection rate % (n/N)		False negative colonoscopies % (n/N)	
	NPO group 1	NPO group 2	NPO group 1	NPO group 2	NPO group 1	NPO group 2	NPO group 1	NPO group 2	NPO group 1	NPO group 2
El Sayed 2003[24] NPO status 1: ≥ 2 hours NPO status 2: > 8 hours	Excellent 39 (35/91) Satisfactory 83 (75/91) (Church)	Excellent 19 (18/96) P = .005 Satisfactory 69 (66/96) P < .05	NR	NR	NR	NR	NR	NR	NR	NR
Eun 2011[25] NPO status 1: ≤ 4 hours NPO status 2: > 4 hours (Analysis by PC time with hourly intervals from ≤2 hours to >7 hours)	Ottawa 3.49 (2.11) (Rostom et al.)	Ottawa 4.10 (2.45) P = .02	NR	NR	NR	NR	NR	NR	NR	NR
Flemming 2012[26] NPO status 1: ≥ 4 hours NPO status 2: > 8 hours	Ottawa 4.05 (2.37) (Rostom et al.) Excellent/good 94 (107/114) (Aronchick et al.)	Ottawa 5.51 (2.74) P < .001 Excellent/good 67 (74/110) P < .001	NR	NR	96 (114/119)	95 (111/117) P = NS	NR	NR	NR	NR
Frommer 1997[27] NPO status 1: 3-9 hours NPO status 2: > 8 hours, 2 arms	Cleanliness/ Visibility Score 4.11 (0.67) (Author scale)	Arm 1: 3.34 (0.97) Arm 2: 3.22 (0.85) Both P < .0005 vs NPO 1	NR	NR	NR	NR	NR	NR	NR	NR
Gupta 2007[28] NPO status 1: ≥ 5 hours (morning) NPO status 2: > 8 hours (evening before)	Ottawa 4.7 (2.8) (Rostom et al.) Excellent/good 36 (37/102) (Aronchick et al.)	Ottawa 4.7 (2.9) P = .87 Excellent/good 35 (35/99)	NR	NR	NR	NR	NR	NR	NR	NR
Gurudu 2010[29] NPO status 1: ≥ 4 hours NPO status 2: > 8 hours	Good or excellent cleansing for same day preps (NPO status 1) compared to previous day (NPO status 2): OR 3.42 (1.81, 6.47); P < .001 (Aronchick et al., modified)		NR	NR	NR	NR	OR 1.17 [95%CI 0.94, 1.45] for same day vs prior day prep dosing		NR	NR

Study NPO Status (Intervention/ Control)	Quality of bowel preparation[a] % (n/N) or Mean (±SD)		Diagnostic yield % (n/N) or Mean (±SD)		Completion rate % (n/N)		Adenoma detection rate % (n/N)		False negative colonoscopies % (n/N)	
	NPO group 1	NPO group 2	NPO group 1	NPO group 2	NPO group 1	NPO group 2	NPO group 1	NPO group 2	NPO group 1	NPO group 2
Gurudu 2012[30] NPO status 1: ≥ 4 hours NPO status 2: > 8 hours	Excellent/good 54 (871/1615) (Aronchick et al., modified)	Excellent/good 35 (1241/3560) P < .001	NR	NR	96 (1542/ 1615)	94 (3346/ 3560) P = .008	32 (514/ 1615)	27 (951/ 3560) P < .001	NR	NR
Huffman 2010[31] NPO status 1: ≥ 2 hours NPO status 2: > 8 hours	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Johanson 2007[32] NPO status 1: 2.5-4.5 hours NPO status 2: > 8 hours	Excellent 64 (132/205) Excellent/good 90 (184/205) Overall score 1.5 (0.74) (Aronchick et al.)	Excellent 39 (80/206) Excellent/good 82 (169/206) Overall score 1.8 (0.76) P < .0001	NR	NR	NR	NR	NR	NR	NR	NR
Kao 2011[33] NPO status 1: 4-8 hours NPO status 2: > 8 hours	Total Score: PEG 4L 2.59 PEG+B 3.08; NaP 3.51 PSMC+M 2.82 (Rostom et al.)	Total score- PEG 4.14 PEG+B 3.51 NaP 5.37 PSMC+M 3.84	NR	NR	NR	NR	NR	NR	NR	NR
Kastenberg 2001, 2007[34,35] NPO status 1: 2-4 hours NPO status 2: > 8 hours	Mean score 1.75 (0.75) Excellent/Good 84 (354/420) (Aronchick et al.)	Mean score 1.81 (0.82) P = .1175 Excellent/Good 77 (326/425) P = .006	NR	NR	98 (420/427)	98 (425/432)	NR	NR	NR	NR
Khan 2010[36] NPO status 1: Hours unclear (Split-dose) NPO status 2: > 8 hours	No bowel content seen or clear lavage and >50% visualization 89% (Lai et al.)	70% P < .0001	NR	NR	NR	NR	NR	NR	NR	NR

Study NPO Status (Intervention/ Control)	Quality of bowel preparation[a] % (n/N) or Mean (±SD)		Diagnostic yield % (n/N) or Mean (±SD)		Completion rate % (n/N)		Adenoma detection rate % (n/N)		False negative colonoscopies % (n/N)	
	NPO group 1	NPO group 2	NPO group 1	NPO group 2	NPO group 1	NPO group 2	NPO group 1	NPO group 2	NPO group 1	NPO group 2
Koh 2011[37] NPO status 1: 1.5-3.5 hours NPO status 2: 6-8 hours	Ottawa Scale (mean) 5.61 (2.54) Ottawa Fluid 0.72 (0.58)	Ottawa Scale (mean) 5.08 (2.31) P = .58 Ottawa Fluid 0.58 (0.67) P = .55	NR	NR	NR	NR	NR	NR	NR	NR
Kolts 1993[38] NPO status 1: Hours unclear (last dose 6 am) NPO status 2: > 8 hours NPO status 3: > 8 hours	Excellent or Good: 80% (Author scale)	Group 2 Excellent or Good: 64% P < .05 Group 3 Excellent or Good: 32% P < .05	NR	NR	NR	NR	NR	NR	NR	NR
Kössi 2007[39] NPO status 1: ≤ 6 hours NPO status 2: 6-12 hours NPO status 3: ≥ 12 hours	Group 1 4.00 (0.12) (Frommer)	Group 2 3.56 (0.12) P= .023 vs Gr 1 Group 3 2.64 (0.14) P = .0001 vs Gr 1 and Gr 2	NR	NR	95.8% completion; no failure was related to bowel cleansing		NR	NR	NR	NR
Longcroft-Wheaton 2012[40] NPO status 1: > 3 hours NPO status 2: > 5 hours	Excellent 46.9 (38.7-55.5) Overall better cleansing in NPO group 1 (P = .0046) (Chilton et al.)	Excellent 49.5 (39.6-59.4)	NR	NR	NR	NR	71 (94/132)	62(59/95) P = .2	NR	NR
Manno 2012[41] NPO status 1: 2 hours NPO status 2: > 8 hours	Excellent 68 (115/168) Excellent/good (Adequate) 95 (160/168) (Di Palma et al.)	Excellent 38 (63/168) P < .001 Excellent/good (Adequate) 98 (156/168)	NR	NR	NR	NR	NR	NR	NR	NR

Study NPO Status (Intervention/ Control)	Quality of bowel preparation[a] % (n/N) or Mean (±SD)		Diagnostic yield % (n/N) or Mean (±SD)		Completion rate % (n/N)		Adenoma detection rate % (n/N)		False negative colonoscopies % (n/N)	
	NPO group 1	NPO group 2	NPO group 1	NPO group 2	NPO group 1	NPO group 2	NPO group 1	NPO group 2	NPO group 1	NPO group 2
Marmo 2010[42] NPO status 1: ≤ 2 hours NPO status 2: > 8 hours	Excellent/ Good 75 (327/435) (Rostom et al.)	Excellent/ Good 43 (186/433) P < .001	NR	NR	Overall completion: 95% Aborted procedures 93 (402/432)	Aborted procedures 79 (339/430) P < .0001	NR	NR	NR	NR
Mathus-Vliegen 2013[43] NPO status 1: Hours unclear (Split-dose, PM exam) NPO status 2: > 8 hours	Adequate 98% (Aronchick ≤2) 93% (Ottawa ≤7)	Adequate 99%; P = NS (Aronchick ≤2) 87%; P = NS (Ottawa ≤7)	NR	NR	NR	NR	NR	NR	NR	NR
Matro 2010[44] NPO status 1: 4 hours (am prep only) NPO status 2: 4 hours (pm/am prep)	Excellent/good 92% Fair/poor 8% (Author scale)	Excellent/good 94% Fair/poor 6% P = .01 for non-inferiority	"Findings" per patient 0.70 (1.3)	"Findings" per patient 0.46 (1.0) P = .047	98 (60/61)	100 (54/54)	Low risk adenoma 23 (14/60) High risk adenoma 12 (7/60) Cancer 2 (1/60)	Low risk 15 (8/54) High risk 9 (5/54) Cancer 2 (1/54) P = .038 overall	NR	NR
Paoluzi 1993[45] NPO status 1: 1-2.5 hours NPO status 2: > 8 hours	Excellent/ adequate 84 (51/61) (Author scale)	Excellent/ adequate 63 (45/71) P < .05	NR	NR	NR	NR	NR	NR	NR	NR
Park 2007[46] NPO status 1: ≥ 2 hours NPO status 2: > 8 hours	Ottawa Scale Good 5.9 (2.6) 79 (119/151) (Rostom et al.)	Ottawa Scale Good 8.5 (2.5) 76 (116/152) P = .60	NR	NR	NR	NR	NR	NR	NR	NR

Study NPO Status (Intervention/ Control)	Quality of bowel preparation[a] % (n/N) or Mean (±SD)		Diagnostic yield % (n/N) or Mean (±SD)		Completion rate % (n/N)		Adenoma detection rate % (n/N)		False negative colonoscopies % (n/N)	
	NPO group 1	NPO group 2	NPO group 1	NPO group 2	NPO group 1	NPO group 2	NPO group 1	NPO group 2	NPO group 1	NPO group 2
Park 2010[47] NPO status 1: 2-5 hours (PEG) NPO status 2: 2-5 hours (Mg citrate NPO status 3: > 8 hours	Excellent PEG 25 (20/80) Mg citrate 34 (25/73) Excellent/good PEG 76 (61/80) Mg citrate 75 (55/73) (Aronchick et al.)	Excellent 18 (14/79) Excellent/good 51 (40/79 P < .01 versus both groups	NR	NR	NR	NR	NR	NR	NR	NR
Parra-Blanco 2006[48] NPO status 1: 1.5-7 hours (PEG) NPO status 2: 1.5-7 hours (NaP) NPO status 3: > 8 hours (PEG) NPO status 4: > 8 hours (NaP)	Excellent/Good PEG 79 (33/43) NaP 80 (36/45) (Author scale)	Excellent/Good PEG 27 (12/45) P < .001 NaP 7 (3/44) P < .001	Groups 1 & 2 Any polyp 52 (46/88) Flat lesions 22 (19/88) Protruding polyps 40 (35/88)	Groups 3 & 4 Any polyp 45 (40/89) Flat lesions 9 (8/89) P = .02 Protruding polyps 42 (37/89)	NR	NR	Histological confirmation for 83 (152/183) polyps 70 (107/152) were adenomas		NR	NR
Rex 2013[49] NPO status 1: 5-9 hours NPO status 2: > 8 hours	Successful 84 (256/304) (Aronchick et al., modified) Ottawa scale 87 (264/304) (Rostom et al.)	Successful 74 (221/297) P = .003 Ottawa scale 75 (224/297) P < .01	NR	NR	Overall completion rate was 98.7%		NR	NR	NR	NR

Study NPO Status (Intervention/ Control)	Quality of bowel preparation[a] % (n/N) or Mean (±SD)		Diagnostic yield % (n/N) or Mean (±SD)		Completion rate % (n/N)		Adenoma detection rate % (n/N)		False negative colonoscopies % (n/N)	
	NPO group 1	NPO group 2	NPO group 1	NPO group 2	NPO group 1	NPO group 2	NPO group 1	NPO group 2	NPO group 1	NPO group 2
Seo 2012[50] NPO status 1: ≤ 3 hours / NPO status 2: > 3 hours Analysis by PC time with hourly intervals from ≤3 hours to >8 hours	Ottawa Scale 5.08 (2.17) (0 = perfect, 14 = solid stool and fluid) (Rostom et al.)	Ottawa Scale NPO status 3-4 hrs: 4.25 (1.85) 4-5 hrs: 4.70 (2.12) 5-6 hrs: 5.11 (2.34) 6-7 hrs: 4.86 (1.85) 7-8 hrs 5.20* (1.79) >8 hrs 5.92 (2.01) P < .05 vs 3-4 hour mean	NR	NR	NR	NR	NR	NR	NR	NR
Vanner 2011[51] NPO status 1: > 5 hours NPO status 2: > 8 hours	Ottawa Scale 5.03 (2.8) (Rostom et al.) Aronchick no significant differences between groups (Aronchick et al.)	Ottawa Scale 5.22 (3.1) P = .77	NR	NR	Overall completion rate 95% (95/100)		NR	NR	NR	NR
Varughese 2010[52] NPO status 1: ≥ 3 hours NPO status 2: > 8 hours	Ottawa Scale 4.7 (2.4) (Rostom et al.)	Ottawa Scale 7.1 (2.7) P < .01	NR	NR	NR	NR	24 (16/68)	24(15/68) P = NS	NR	NR
Voiosu 2013[53] NPO status 1: 1-7 hours NPO status 2: > 8 hours	Excellent (4) 30 (25/85) (Rex et al.)	Excellent (4) 21 (17/80) P = .23	NR	NR	NR	NR	NR	NR	NR	NR

NaP = sodium phosphate; NPO = nil per os; NR = not reported; NS = not statistically significant; PC = preparation-to-colonoscopy; PEG = polyethylene glycol; P/MC = sodium picosulfate and magnesium citrate; SD = standard deviation

Bowel preparation completed the day before colonoscopy designated as NPO status > 8 hours

[a] Rating system references ("Author scale" indicates scale was developed by study authors and is described in the study reference)
Sharma VK et al. *Gastrointest Endosc*. 1998;47:167-71.
Arya V et al. *Dig Dis Sci*. 2013;58:2156-66.
Aronchick CA et al. *Gastrointest Endosc*. 2000;52:346-52.
Church JM. *Dis Colon Rectum*. 1998;41:1223-5.
Rostom A et al. (Ottawa). *Gastrointest Endosc*. 2004;59:482-6.
Lai EJ et al. (Boston). *Gastrointest Endosc*. 2009;69(Suppl 3);620-5.
Frommer D. *Dis Colon Rectum*. 1997;40:100-4.
Chilton A et al. Quality assurance guidelines for colonoscopy. Sheffield: NHS Cancer Screening Programmes; 2010.
Di Palma JA et al. *Gastrointest Endosc*. 1990;36:285-9.
Rex DK et al. *Am J Gastroenterol*. 2006;101:873-85.

Table 4. Time and Patient Outcomes

Study NPO Status (Intervention/ Control)	Total procedure time, mean (SD)		Cecal intubation time, mean (SD)		Withdrawal time, mean (SD) [a]		Patient adherence to preparation or colonoscopy, % (n/N)		Patient satisfaction, preparation or colonoscopy, % (n/N)	
	NPO group 1	NPO group 2	NPO group 1	NPO group 2	NPO group 1	NPO group 2	NPO group 1	NPO group 2	NPO group 1	NPO group 2
Abdul-Baki 2008[13] NPO status 1: ≥ 1.5 hours NPO status 2: > 8 hours)	NR	NR	NR	NR	NR	NR	Adherence 91%	Adherence 69% P < .001	Work/school missed 10 (20/199) Sleep disturbed 15 (30/199)	Work/school missed 13 (23/183) P = NS Sleep disturbed 21 (38/183) P = NS
Aoun 2005[14] NPO status 1: ≥ 1.5 hours NPO status 2: > 8 hours)	NR	NR	NR	NR	NR	NR	Drank as instructed 90 (61/68)	Drank as instructed 78 (57/73) P = .06	Work/school missed 12 (8/68) Sleep disturbed 20 (29/68) Willingness to take again 84 (57/68)	Work/school missed 21 (15/73) P = NS Sleep disturbed 24 (33/73) P = NS Willingness to take again 75 (55/73) P = .21
Athreya 2011[16] NPO status 1: 5-9 hours NPO status 2: > 8 hours	*n=150* 11.40 min (SD NR)	*n=175* 11.16 min (SD NR) P=0.40	*n=150* 6.58 min (SD NR)	*n=175* 7.05 min (SD NR) P=0.78	*n=150* 4.42 min (SD NR)	*n=175* 4.11 min (SD NR) P=0.10	NR	NR	NR	NR
Barclay 2004[17] NPO status 1: < 3 hours NPO status 2: ≥ 5 hours	NR	NR	NR	NR	NR	NR	Completed 95 (117/123)[a]	Completed 88 (114/130)[a] P = .04	Prefer alternative in future 34 (44/130)[a]	Prefer alternative in future 15 (19/123)[a] P < .001
Church 1998[21] NPO status 1: 5-8 hours NPO status 2: >8 hours	NR	NR	*n=157* 19.5 min (2.2)	*n=160* 20.0 min (1.6)	*n=157* 11.9 min (0.8)	*n=160* 13.1 min (0.7)	NR	NR	NR	NR

Study NPO Status (Intervention/ Control)	Total procedure time, mean (SD)		Cecal intubation time, mean (SD)		Withdrawal time, mean (SD) [a]		Patient adherence to preparation or colonoscopy, % (n/N)		Patient satisfaction, preparation or colonoscopy, % (n/N)	
	NPO group 1	NPO group 2	NPO group 1	NPO group 2	NPO group 1	NPO group 2	NPO group 1	NPO group 2	NPO group 1	NPO group 2
Eun 2011[25] NPO status 1: ≤ 4 hours NPO status 2: > 4 hours (Analysis by PC time; hourly intervals from ≤ 2 hours to > 7 hours)	NR	NR	NR	NR	NR	NR	Completed 81 (120/149)	Completed 85 (129/151) P = .51	NR	NR
Gupta, 2007[28] NPO status 1: ≥ 5 hours NPO status 2: > 8 hours	NR	NR	NR	NR	NR	NR	NR	NR	Work hrs lost 8.0 (2.1) hrs Sleep disturbed 15 (15/102)	Work hrs lost 10.2 (3.9) hrs P < .001 Sleep disturbed 42 (42/99) P < .001
Gurudu 2012[30] NPO status 1: ≥ 4 hours NPO status 2: > 8 hours	NR	NR	NR	NR	11.6 (7.7)	15.3 (11.1) (p=<.001)	NR	NR	NR	NR
Kössi 2007[38] NPO status 1: ≤ 6 hours NPO status 2: 6-12 hours NPO status 3: ≥ 12 hours	NR	NR	NR	NR	NR	NR	NR	NR	Difficulty traveling to colonoscopy ≤ 6 hours: 3.8% 6-12 hours: 5.6% ≥ 12 hours: 4.9% P = NS	

Study NPO Status (Intervention/ Control)	Total procedure time, mean (SD)		Cecal intubation time, mean (SD)		Withdrawal time, mean (SD) [a]		Patient adherence to preparation or colonoscopy, % (n/N)		Patient satisfaction, preparation or colonoscopy, % (n/N)	
	NPO group 1	NPO group 2	NPO group 1	NPO group 2	NPO group 1	NPO group 2	NPO group 1	NPO group 2	NPO group 1	NPO group 2
Longcroft-Wheaton 2012[40] NPO status 1: > 3 hours NPO status 2: > 5 hours	NR	NR	NR	NR	NR	NR	N=47 Completed 98%	N=58 Completed 95% P = NS	Interruption of work 0 (median)[b] Sleep disturbed 11 (5/47) Preferred same prep for future 81% (N=NR)	Interruption of work 4 (median)[b] Sleep disturbed 29 (17/58) P = .03 Preferred same prep for future 40% (N=NR)
Manno 2012[41] NPO status 1: 2 hours NPO status 2: > 8 hours	NR	NR	NR	NR	NR	NR	Completed ≥ 75% of prep 96 (162/168)	Completed ≥ 75% of prep 95 (159/168) P = .70	Preferred same prep for future 69 (116/168)	Preferred same prep for future 31 (52/168) P < .001
Matro 2010[44] NPO status 1: 4 hours (am prep only) NPO status 2: 4 hours (pm/am prep)	Median 12.8 min	Median 12.4 min P = .147	NR	NR	Median 8.0 min	Median 7.3 min P = .637	Completed > 90% of prep 84 (52/62)	Completed > 90% of prep 72 (39/54) P = .175	No interference with work day before procedure (only if went to work) 85 (23/27) Slept > 80% of usual hours 71 (44/62) Repeat same prep in future 82 (51/62)	No interference with work day before procedure 55 (12/22) P = .019 Slept > 80% of usual hours 76 (41/54) P = .675 Repeat same prep in future 80 (43/54) P = .814

Study NPO Status (Intervention/ Control)	Total procedure time, mean (SD)		Cecal intubation time, mean (SD)		Withdrawal time, mean (SD) [a]		Patient adherence to preparation or colonoscopy, % (n/N)		Patient satisfaction, preparation or colonoscopy, % (n/N)	
	NPO group 1	NPO group 2	NPO group 1	NPO group 2	NPO group 1	NPO group 2	NPO group 1	NPO group 2	NPO group 1	NPO group 2
Park 2007[46] NPO status 1: 2 hours NPO status 2: > 8 hours	NR	NR	Good compliance[c] 8.0 (5.6) min n=119 Poor Compliance 9.4 (5.8) min n=32	Good compliance[c] 13.0 (7.8) min n=116 P < .01 Poor Compliance 12.7 (5.1) min n=36 P < .05	NR	NR	Good compliance with prep 79 (119/151)	Good compliance with prep 76 (116/152) P > .05	Sleep disturbed 11 (16/151) Overall tolerance of prep 1.01 (1.03)[d]	Sleep disturbed 12 (18/152) P = NS Overall tolerance of prep 1.05 (0.86)[d] P = NS
Park 2010[47] NPO status 1: 2-5 hours NPO status 2: > 8 hours	NR	NR	NR	NR	NR	NR	Compliance > 80% 91 (73/80)	Compliance > 80% 92 (73/79)	Sleep disturbed 28 (22/80) Willing to repeat prep 48 (38/80)	Sleep disturbed 32 (25/79) Willing to repeat prep 62 (49/79) P = .08
Rex 2013[49] NPO status 1: 5-9 hours NPO status 2: > 8 hours	NR	NR	NR	NR	NR	NR	Treatment-emergent adverse event leading to discontinua-tion 0 (0/305)	Treatment-emergent adverse event leading to discontinua-tion 0.7 (2/298)	NR	NR
Varughese 2010[52] NPO status 1: ≥ 3 hours NPO status 2: > 8 hours	*n=68* 19.2 (7.2) min	*n=68* 18.7 (7.2) min P = .73	*n=68* 8.5 (5.5) min	*n=68* 7.4 (4.5) min P = .27	*n=68* 10.6 (5.0) min	*n=68* 11.3 (4.8) min P = .49	Quantity consumed 3.7 (0.5) L (of 4L regimen)	Quantity consumed 3.7 (0.6) L (of 4L regimen) P = .61	Sleep loss 16 (11/68)	Sleep loss 31 (21/68) P = .04

NPO = nil per os; NR = not reported; PC = preparation to colonoscopy; SD = standard deviation
Bowel preparation completed the day before colonoscopy designated as NPO status > 8 hours
[a] Group with shorter NPO status was required to take 3 doses while group with longer NPO status took 2 doses
[b] 5-point Likert scale with 0 = completely unimpaired, 4 = major impact effectively preventing an activity
[c] Study reports time to cecal intubation in minutes (SD) by compliance with preparation (good versus poor)
[d] 4-point scale with 0 = not at all distressing, 3 = severely distressing

Table 5. Hospitalizations, Costs, and Adverse Events

Study NPO Status (Intervention/ Control)	Hospitalizations % (n/N)		Costs		Bowel perforation % (n/N)		Other adverse events[a] (*describe*) % (n/N)	
	NPO group 1	NPO group 2	NPO group 1	NPO group 2	NPO group 1	NPO group 2	NPO group 1	NPO group 2
Barclay 2004[17] NPO status 1: < 3 hours NPO status 2: ≥ 5 hours	NR	NR	NR	NR	NR	NR	Interview 2 days after colonoscopy – no patient in either group developed clinically significant neurologic, cardiac, or other adverse events that were thought to be attributable to colonic purgation	
Church 1998[21] NPO status 1: 5-8 hours NPO status 2: >8 hours	NR	NR	NR	NR	NR	NR	No complications of colonoscopy in either group	
Flemming 2012[26] NPO status 1: ≥ 4 hours NPO status 2: > 8 hours	NR	NR	NR	NR	No documented complications of perforation on discharge from endoscopy unit		No documented complications of bleeding on discharge from endoscopy unit	
Johanson 2007[32] NPO status 1: 2.5-4.5 hours NPO status 2: > 8 hours	NR	NR	NR	NR	NR	NR	0/207	0.5 (1/208) Lower GI bleeding post-colonoscopy
Mathus-Vliegen 2013[43] NPO status 1: Hours unclear (Split-dose, PM exam) NPO status 2: > 8 hours	NR	NR	NR	NR	NR	NR	None reported	1 (1/99) Severe retrosternal pain 3 hours after colonoscopy; anteroseptal infarction diagnosed
Rex 2013[49] NPO status 1: 5-9 hours NPO status 2: > 8 hours	NR	NR	NR	NR	NR	NR	Acute pancreatitis[b] 0.3 (1/305)	Non-cardiac chest pain[b] 0.3 (1/298) Colon cancer 0.3 (1/298)
Voiosu 2013[53] NPO status 1: 1-7 hours NPO status 2: > 8 hours	NR	NR	NR	NR	NR	NR	Reported no serious adverse events throughout the study	

GI = gastrointestinal; NPO = nil per os; NR = not reported

Bowel preparation completed the day before colonoscopy designated as NPO status > 8 hours

[a] Anesthesia-related

[b] Unclear whether event occurred during preparation or colonoscopy

Table 6. Gastric Contents Outcomes

Study NPO Status (Intervention/ Control)	Volume of gastric contents, Mean (SD)		pH of gastric contents, Mean (SD)	
	NPO group 1	NPO group 2	NPO group 1	NPO group 2
Aoun 2005[14] NPO status 1: ≥ 1.5 hours NPO status 2: > 8 hours	No notable difference in the amount of residual gastric fluid between groups		NR	NR
Huffman 2010[31] NPO status 1: ≥ 2 hours NPO status 2: > 8 hours	19.7 (19.1) mL	20.2 (22.4) mL	NR	NR

NPO = nil per os; NR = not reported; SD = standard deviation
Bowel preparation completed the day before colonoscopy designated as NPO status > 8 hours

APPENDIX D. STRENGTH OF EVIDENCE

Outcome Category	Outcome (# of Studies Reporting)	Results, Shorter NPO status vs Longer NPO status	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence
Primary	Aspiration, RCTs (3)	Three moderate sized trials (n=672)[a] reported no aspiration events or no major complications related to sedation	moderate	consistent	direct	imprecise	Low
	Aspiration, Obs. (2)	Two studies (n=1,646), one large and one moderately sized, reported no episodes of aspiration were observed	moderate	consistent	direct	imprecise	Insufficient
	Rescheduled colonoscopies (1)	One moderate sized RCT reported fewer rescheduled colonoscopies with shorter NPO status	moderate	unknown	direct	imprecise	Insufficient
Secondary	Completion rate, RCTs (6)	Pooled results from 5 trials[a,b] (n=1,795) found no difference between NPO status groups (RR 1.00 [95%CI 0.98, 1.01])	moderate	consistent	direct	precise	Moderate
	Completion rate, Obs. (1)	One large retrospective study (n=5175) reported a greater completion rate with a shorter NPO status (OR 1.35 [95%CI 1.03, 1.77])	high	unknown	direct	precise	Insufficient
	Adenoma detection rate, RCTs (1)	A single small trial (n=136)[a] found no difference between NPO status groups	moderate	unknown	direct	imprecise	Insufficient
	Adenoma detection rate, Obs. (3)	Pooled results from 3 studies (n=8,481) found improved adenoma detection rates with a shorter NPO status (OR 1.25 [95%CI 1.13, 1.39])	moderate	consistent	direct	precise	Low
	Diagnostic yield, RCTs (2)	Two moderate sized trials[a,b] (n=254) reported inconsistent results in diagnostic yield of all polyps or lesions	moderate	inconsistent	direct	imprecise	Insufficient
	Bowel perforation, RCT (1)	A single moderate sized trial (n=250) reported no documented complications of perforation	moderate	unknown	direct	imprecise	Insufficient
	False negative colonoscopy (0)	No eligible studies					Insufficient

Obs. = observational studies; RCTs = randomized controlled trials; OR = odds ratio; RR = risk ratio

[a] One additional RCT (n=125) (Matro 2010)[44] of morning-only versus evening before/morning of colonoscopy bowel preparation (all patients NPO for 4 hours with clear liquids allowed until 2.5 hours before colonoscopy) reported one aspiration event requiring 24 hour hospitalization for observations, no significant difference in completion rate, and significantly better adenoma detection rate and diagnostic yield in the morning-only preparation group.

[b] One study (Chiu 2006)[20] was of patients getting follow-up colonoscopy