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

Evidence-Based Practice Summary
Non-Anesthesia NPO Orders

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BACKGROUND AND RATIONALE

In recent years, NPO (Nil per os or nothing by mouth) orders have been revised, and prolonged preprocedure fasting is considered unnecessary in many settings. Updated NPO order guidelines have been implemented in most countries, recommending clear fluids up to 2 hours before anesthesia and light meals up to 6 hours before (Eriksson 2005). The guidelines for NPO orders are aimed to reduce the risk of pulmonary aspiration of gastric contents. Most of the research done to evaluate pulmonary aspiration and the risk factors leading to this complication has come from the general anesthesia literature (Bahn and Holt 2005). Guideline recommendations are mainly based on evidence from general anesthesia, and have eluded to the fact that controversy still exists for procedures done under deep sedation (Manchikanti 2011). Routine preoperative fasting is regularly imposed on patients, even though there is a lack of evidence on fasting before sedation (Shaukat 2015; Manchikanti 2011). This evidence brief aims to determine if there are benefits and harms associated with NPO orders for patients undergoing invasive procedures and receiving sedation.

ASK THE QUESTION

What are the benefits and harms associated with NPO orders for adult patients undergoing invasive procedures and receiving sedation (NOT general anesthesia)?

SEARCH FOR EVIDENCE

Databases included Ovid MEDLINE <1946 to February Week 4 2018>

Search strategy included:

1. exp Preoperative Care/ (64667)
2. exp Perioperative Period/ (73589)

3. (invasiv* adj3 (procedur* or operat* or therap* or treat* or interven* or diagnos*)).mp. (67046)
4. 1 or 2 or 3 (200342)
5. ((fast or fasting or fasted or fasts or ((abstain* or avoid* or prohibit* or forbid*) adj3 (food* or drink* or eat*)) or npo or nil per os or (nothing adj2 (mouth or oral*))) adj7 (instruct* or order* or recommend* or requir* or educat*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (5665)
6. exp feeding behavior/ (151412)
7. 5 or 6 (156439)
8. exp conscious sedation/ or exp deep sedation/ (8731)
9. exp "Hypnotics and Sedatives"/ad, ae, tu, to (47368)
10. 8 or 9 (53158)
11. 4 and 7 and 10 (28)
12. exp "Outcome and Process Assessment (Health Care)"/ (942749)
13. exp attitude to health/ (364255)
14. exp vital statistics/ (821487)
15. exp epidemiologic studies/ (2119661)
16. 12 or 13 or 14 or 15 (3387824)
17. 7 and 10 and 16 (48)
18. 4 and 7 and 16 (279)
19. 4 and 10 and 16 (1054)
20. (fast or fasting or fasted or fasts or ((abstain* or avoid* or prohibit* or forbid*) adj3 (food* or drink* or eat*)) or npo or nil per os or (nothing adj2 (mouth or oral*))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (293921)
21. 19 and 20 (35)
22. 11 or 17 or 18 or 21 (372)
23. 4 and 7 (889)
24. 4 and 10 (3563)
25. 7 and 10 (235)
26. 20 and 24 (92)
27. 23 or 25 or 26 (1161)
28. limit 27 to (comparative study or controlled clinical trial or evaluation studies or guideline or meta analysis or randomized controlled trial or systematic reviews) (327)
29. 22 or 28 (573)
30. limit 29 to English language (516)

Filters/limits included limited to English language

CRITICALLY ANALYZE THE EVIDENCE

There was limited literature found evaluating the harms and benefits associated with NPO orders for adult patients undergoing invasive procedures and receiving sedation in the adult population. The evidence appraisal tables have been separated based on outcomes reported in the literature. These outcomes include: (1) Aspiration Incidence and Residual Gastric Volume (RGV); (2) Colonoscopy Rescheduling; (3) Nausea and Vomiting; (4) Respiratory Depression; (5) Complications; (6) Success Rate; and (7) Echocardiographic Preload Variables.

1. Aspiration Incidence and Residual Gastric Volume (RGV): One systematic review, one RCT and two non-randomized studies were found reporting on aspiration incidence and residual gastric volume (RGV) regarding NPO timing and/or preprocedural fasting time. These outcomes were combined due to the fact that a higher RGV increases the patient's risk for aspiration. The systematic review (Shaukat 2017) searched the evidence for the relationship between NPO timing and aspiration incidence. Only studies of adults undergoing colonoscopy with moderate or deep sedation in inpatient or outpatient settings were included. The researchers found low-strength evidence that shorter duration of NPO is not associated with a higher incidence rate of aspiration. One RCT (de Aguilar-Nascimento 2014) investigated the gastric emptying of an oral supplement containing carbohydrate plus whey protein consumed before sedation for gastroscopy. Patients were randomized to receive either an overnight fast (minimum of 8 hours; control group) or fast from solids for the same period and drink 200 milliliters mL of an oral nutritional supplement 150 – 210 minutes before the exam (intervention group). Researchers found there was no correlation between the fasting time and the gastric residual volume (RGV) (R = 0.10; p = 0.66). One observational study (Cheng 2017) examined the residual gastric volume (RGV) in colonoscopy after bowel preparations with 3-L polyethylene glycol (PEG). Patients with fasting times of 2 to 3 hours had similar mean RGV and mean RGV per body weight as compared with those with a fasting time > 3 hours (P = 0.25 and P = 0.66, respectively). None of the patients in any group had clinical evidence of pulmonary aspiration or vomiting during their procedures. One non-randomized study (Manchikanti 2011) assessed the need for preoperative fasting and risks without fasting in patients undergoing interventional techniques. The study was performed prospectively on patients without change in their normal course of treatment. No aspirations were reported.
   Quality of Evidence: Low

2. Colonoscopy Rescheduling: One systematic review (Shaukat 2017) searched the evidence for the relationship between NPO timing colonoscopy rescheduling. Researchers found differences in the bowel preparation solutions between groups and imprecise reporting of timing of completion of bowel preparation limited the ability to draw firm conclusions about the role of NPO status on rescheduling. They determined that the strength of evidence was insufficient.
   Quality of Evidence: Very Low

3. Nausea and Vomiting: One non-randomized study (Manchikanti 2011) assessed the need for preoperative fasting and risks without fasting in patients undergoing interventional techniques. The study was performed prospectively on patients without change in their normal course of treatment. There was a lack of preoperative fasting in patients undergoing various types of interventional techniques in managing chronic pain under usual circumstances. Of the 12,000 encounters, overall, 189 or 1.6% of the patients complained of nausea and 3 of them or 0.02% experienced vomiting. Of the 189 patients with nausea, 80 of them improved significantly prior to discharge without further complaints. Thus, 109 patients or 0.9% were minimally nauseated prior to discharge. Postoperative complaints of continued nausea were reported in only 26 patients for 6 to 72 hours.
   Quality of Evidence: Very Low

4. Respiratory Depression: One non-randomized study (Manchikanti 2011) assessed the need for preoperative fasting and risks without fasting in patients undergoing interventional techniques. The study was performed prospectively on patients without change in their normal course of treatment. There was a lack of preoperative fasting in patients undergoing various types of interventional techniques in managing chronic pain under usual circumstances. Of the 11,850 encounters receiving intravenous sedation, brief oxygenation with mask was required in 2 patients without any adverse consequences of nausea, vomiting, aspiration, or other adverse effects.
   Quality of Evidence: Very Low

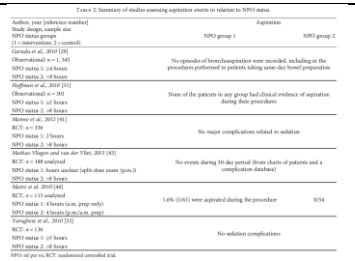
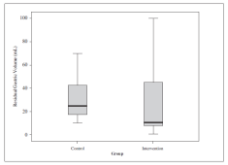
5. Complications: One observational study and one RCT reported complications regarding NPO status for patients receiving sedation. The observational study (Hamid 2014) aimed to demonstrate that percutaneous cardiac catheterization does not require prior fasting. The study included all patients admitted for elective percutaneous coronary intervention (PCI) procedures. Patients are advised to have a light breakfast in the morning without the need for being NPO for 4 hours. No patients developed either intraprocedural or postprocedural aspiration pneumonia. The RCT (de Aguilar-Nascimento 2014) investigated the gastric emptying of an oral supplement containing carbohydrate plus whey protein consumed before sedation for gastroscopy. Patients were randomized to receive either an overnight fast (minimum of 8 hours; control group) or fast for solids for the same period and drink 200 milliliters mL) of an oral nutritional supplement 150 – 210 minutes before the exam (intervention group). The median (range) fasting time was greater ($P < 0.001$) in control group (770 min, ranging from 660-917 min) than in the study group (175min ranging from 150 to 210 min). No complications were reported during any of the exams.
   Quality of Evidence: Low

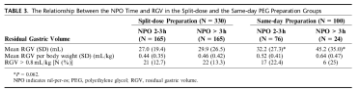
6. Success Rate: One observational study (Hamid 2014) aimed to demonstrate that percutaneous cardiac catheterization does not require prior fasting. The study included all patients admitted for elective percutaneous coronary intervention (PCI) procedures. Patients were advised to have a light breakfast in the morning without the need for being NPO for 4 hours. PCI was technically successful in 95% (1821/1916) of patients.
   Quality of Evidence: Low

7. Echocardiographic Preload Variables: One observational study (Alves 2017) was conducted to determine if fasting causes a change in preload of conscious volunteers or significantly alters their position on the Frank-Starling curve. Thirty-one ASA 1 and ASA 2 volunteers underwent an echocardiographic examination both before and after a fasting period of at least 6 hours. Data from both static and dynamic preload indices were obtained during both periods and compared. Static preload indices exhibited a markedly variable behaviour with fasting. Dynamic indices, however, were far more consistent with one another, all pointing in the same direction, i.e., demonstrating no statistically significant change with the fasting period. The researchers analysed the reliability of dynamic indices to respond to known, intentional preload changes. Aortic velocity time integral (VTI) variation with the passive leg raise maneuver was the only variable that proved to be sensitive enough to consistently signal the presence of preload variation.
   Quality of Evidence: Very Low

In conclusion, there is very low to low quality of evidence that NPO status is not associated with additional harms for adult patients receiving sedation. The studies included in the appraisal were inconsistent, with variation in fasting time before procedure in the different studies. Additionally, some studies were imprecise due to few patients or events included in the analysese. No benefits were reported in the literature on NPO status in patients receiving sedation. Overall, studies demonstrated that reducing the amount of fasting time before an invasive procedure for adult patients receiving sedation does not cause additional harms.

PICO Question: What are the benefits and harms associated with NPO orders for adult patients undergoing invasive procedures and receiving sedation (NOT general anesthesia)?						**Low Quality Rating if:** ☒ Studies inconsistent (*wide variation of treatment effect across studies, population, interventions, or outcomes varied*) ☐ Studies are indirect (*PICO question is quite different from the available evidence in regard to population, intervention, comparison, or outcome)*
Outcome: Aspiration Incidence and Residual Gastric Volume (RGV)						
Study Acronym; Author; Year Published; Location	**Aim of Study; Study Type; Study Size (N)**	**Patient Population**	**Study Intervention (# patients) / Study Comparator**	**Endpoint Results / Outcome (Absolute Event Rates, P values; OR or RR; & 95% CI)**	**Design Limitations**	
Journal: *Gastroenterology Research and Practice* Author: Shaukat, A., et al. Year Published: 2017	**Aim**: To review the evidence for the relationship between NPO timing and aspiration incidence and colonoscopy rescheduling	**Inclusion Criteria**: Studies of any design that reported outcomes following bowel preparation if at least one preparation was completed within	**Intervention**: NPO timing for Colonoscopy	**Results: Researchers found low-strength evidence that shorter duration of NPO is not associated with a higher incidence rate of aspiration.**	**Study Limitations:** ☐ None ***Systematic Review*** ☐ Review did not address focused clinical question	

Location: Veterans Affairs Medical Center, Minneapolis	**Study Type**: Systematic Review **Size**: 40 studies were included (28 RCTs, 2 CCTs, and 10 observational studies), with a total of 22,936 patients	8 hours of the colonoscopy procedure. Only studies of adults, undergoing colonoscopy with moderate or deep sedation, in inpatient or outpatient settings, and reporting outcomes during colonoscopy or recovery from colonoscopy were included. Population-based studies reporting aspiration during colonoscopy were identified.			☐ Search was not detailed or exhaustive ☒ Quality of the studies was not appraised or studies were of low quality ☐ Methods and/or results were inconsistent across studies	☐ Studies are imprecise (*when studies include few patients and few events, and thus have wide confidence intervals, and the results are uncertain)* ☐ Publication Bias (*e.g. pharmaceutical company sponsors study on effectiveness of drug only small, positive studies found)* **Increase Quality Rating if:** ☐ Large effect ☐ Dose-response gradient ☐ Plausible confounders or other biases increase certainty of effect **Quality (certainty) of evidence for studies as a whole:** ☐ High ☐ Moderate ☒ Low ☐ Very Low
Journal: *Nutricion Hospitalaria* Author: de Aguilar-Nascimento, J. E., et al. Year Published: 2014 Location: Federal University of Mato Grosso, Cuiaba, Brazil	**Aim**: To investigate the gastric emptying of an oral supplement containing carbohydrate plus whey protein drunk before sedation for gastroscopy **Study Type**: RCT **Size**: 24; intervention group = 12 and control group = 12	**Inclusion Criteria**: Adult patients scheduled to upper digestive endoscopy **Exclusion Criteria**: Decline to participate, American Society of Anesthesiologists score above II, diabetes mellitus, pregnancy, history of renal or hepatic failure, gastro-esophageal reflux, acute cholecystitis, use of corticosteroids up to 6 months previously, use of an prokinetic drug up to 6 weeks previously, and any noncompliance or violation on the assigned protocol of preoperative fasting.	**Intervention**: Patients were randomized to receive either an overnight fast (minimum of 8 hours; control group) or fast for solids for the same period and drink 200 milliliters (mL) of an oral nutritional supplement (Composition per 200 mL: 0g lipids; 8 g whey protein; 67g carbohydrate being 88% maltodextrin and 12% sacharose; osmolality: 680 mOsm/L; and total energy: 300 kcal; Fresubin Jucy, Fresenius Kabi, Brazil) 150-210 minutes before the exam (intervention group).	**Results**: **There was no correlation between the fasting time and the gastric residual volume (RGV) (R = 0.10; p = 0.66).** Only two cases in each group had a RGV of 60 mL or above (2 cases with 60 mL in each group, one case with 70mL in control group, and one case with 100 mL in the intervention group). A median (interquartile range) of 25 (27) ranging from 10 to 70 mL was found in the control group and 10 (55) ranging from 0 to 100 mL in the intervention group (p = 0.32). 	**Study Limitations:** ☐ None ***RCTs*** ☐ Lack of blinding ☐ Lack of allocation concealment ☐ Stopped early for benefit ☒ Incorrect analysis of ITT ☐ Selective reporting of measures (e.g., no effect outcome) ☐ Large losses to F/U ☐ Difference in important prognostic factors at baseline	
Journal: *Journal of Clinical Gastroenterology*	**Aim**: To examine the residual gastric	**Inclusion Criteria**: Consecutive	**Intervention**: Patients who were scheduled for	**Results**: Patients with fasting times of 2 to 3 hours had similar mean RGV	**Study Limitations:** ☒ None	

Author: Cheng, C.L., et al. Year Published: 2017 Location: Evergreen Hospital, Chang Gung Memorial Hospital and Chang Gung University, Taoyaun, Taipei Medical University Hospital	volume (RGV) in colonoscopy after bowel preparations with 3-L polyethylene glycol (PEG) **Study Type**: Observational Study **Size**: 860 patients; 330 in the split-dose preparation group, 100 in the same-day preparation group, and 430 in the EGD-only group	outpatients scheduled for elective EGD and colonoscopy on the same day. Primary indications for colonoscopy were colorectal polyp/cancer screening and surveillance. **Exclusion Criteria**: Below 18 years, previous gastric or duodental surgery, suspected gastric outlet obstruction, known gastroparesis, known slow gastric emptying, pregnancy, emergent procedure, and ASA classification of physical status grade III or greater. Patients taking metoclopramide or mosapride without gastroparesis by formal testing were not excluded.	morning colonoscopy were instructed to consume 2L of PEG on the evening before the day of their colonoscopy (preparation usually started between 7pm and 8pm) followed by another 1L of PEG the next morning (preparation usually started 5 hours preceding the colonoscopy time). Patients scheduled for afternoon colonoscopy were instructed to consume 3L of PEG on the morning of their colonoscopy (preparation usually started 7h before the colonoscopy time). The time window between the completion of the last PEG dose and the start of the colonoscopy, whether scheduled in the morning or tin the afternoon, was kept to within 3 to 5 hours. **Clear liquids were allowed as desired until 2 hours before colonoscopy. Moderate conscious sedation with fentanyl and midazolam was provided.**	and mean RGV per body weight as compared with those with a fasting time > 3 hours (P = 0.25 and P = 0.66, respectively). **None of the patients in any group had clinical evidence of pulmonary aspiration or vomiting during their procedures.** 	**Non-Randomized Studies** ☐ Failure to develop and apply appropriate eligibility criteria ☐ Flawed measurement of both exposure and outcome ☐ Failure to adequately control confounding ☐ Incomplete or inadequately short follow-up ☐ Differences in important prognostic factors at baseline	

References:

1. Cheng, C. L., Liu, N. J., Tang, J. H., Kuo, Y. L., Lin, C. H., Tsui, Y. N., . . . Chiu, C. T. (2017). Residual Gastric Volume After Bowel Preparation With Polyethylene Glycol for Elective Colonoscopy: A Prospective Observational Study. Journal of Clinical Gastroenterology, 51(4), 331-338. doi:https://dx.doi.org/10.1097/MCG.0000000000000547
2. de Aguilar-Nascimento, J. E., Caporossi, C., Metelo, J. S., Tanajura, G. H., Canevari-de-Oliveira, M., & da Cunha Costa, R. (2014). Safe intake of an oral supplement containing carbohydrates and whey protein shortly before sedation to gastroscopy; a double blind, randomized trial. Nutricion Hospitalaria, 29(3), 681-686. doi:https://dx.doi.org/10.3305/nh.2014.29.3.7161
3. Manchikanti, L., Malla, Y., Wargo, B. W., & Fellows, B. (2011). Preoperative fasting before interventional techniques: is it necessary or evidence-based? Pain Physician, 14(5), 459-467.

4. Shaukat, A., Malhotra, A., Greer, N., MacDonald, R., Wels, J., & Wilt, T. J. (2017). Systematic Review: Outcomes by Duration of NPO Status prior to Colonoscopy. Gastroenterology Research and Practice, 2017, 3914942. doi:10.1155/2017/3914942

PICO Question: What are the benefits and harms associated with NPO orders for adult patients undergoing invasive procedures and receiving sedation (NOT general anesthesia)?

Outcome: Colonoscopy Rescheduling

Study Acronym; Author; Year Published; Location	Aim of Study; Study Type; Study Size (N)	Patient Population	Study Intervention (# patients) / Study Comparator	Endpoint Results / Outcome (Absolute Event Rates, P values; OR or RR; & 95% CI)	Design Limitations
Journal: *Gastroenterology Research and Practice* Author: Shaukat, A., et al. Year Published: 2017 Location: Veterans Affairs Medical Center, Minneapolis	**Aim**: To review the evidence for the relationship between NPO timing and aspiration incidence and colonoscopy rescheduling **Study Type**: Systematic Review **Size**: 40 studies were included (28 RCTs, 2 CCTs, and 10 observational studies), with a total of 22,936 patients	**Inclusion Criteria**: 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, in inpatient or outpatient settings, and reporting outcomes during colonoscopy or recovery from colonoscopy were included. Population-based studies reporting aspiration during colonoscopy were identified.	**Intervention**: NPO timing for Colonoscopy	**Results: Differences in the bowel preparation solutions between groups and imprecise reporting of timing of completion of bowel preparation limited ability to draw firm conclusions about the role of NPO status on rescheduling. Strength of evidence was insufficient.**	**Study Limitations:** ☐ None ***Systematic Review*** ☐ Review did not address focused clinical question ☐ Search was not detailed or exhaustive ☒ Quality of the studies was not appraised or studies were of low quality ☐ Methods and/or results were inconsistent across studies

Low Quality Rating if:
☒ Studies inconsistent (*wide variation of treatment effect across studies, population, interventions, or outcomes varied*)

☐ Studies are indirect (*PICO question is quite different from the available evidence in regard to population, intervention, comparison, or outcome)*

☒ Studies are imprecise (*when studies include few patients and few events, and thus have wide confidence intervals, and the results are uncertain)*

☒ Publication Bias (*e.g. pharmaceutical company sponsors study on effectiveness of drug only small, positive studies found)*

Increase Quality Rating if:
☐ Large effect
☐ Dose-response gradient
☐ Plausible confounders or other biases increase certainty of effect

Quality (certainty) of evidence for studies as a whole:
☐ High
☐ Moderate
☐ Low
☒ Very Low

References:

1. Shaukat, A., Malhotra, A., Greer, N., MacDonald, R., Wels, J., & Wilt, T. J. (2017). Systematic Review: Outcomes by Duration of NPO Status prior to Colonoscopy. Gastroenterology Research and Practice, 2017, 3914942. doi:10.1155/2017/3914942

PICO Question: What are the benefits and harms associated with NPO orders for adult patients undergoing invasive procedures and receiving sedation (NOT general anesthesia)?						
Outcome: Nausea and Vomiting						
Study Acronym; Author; Year Published; Location	**Aim of Study; Study Type; Study Size (N)**	**Patient Population**	**Study Intervention (# patients) / Study Comparator**	**Endpoint Results / Outcome (Absolute Event Rates, P values; OR or RR; & 95% CI)**	**Design Limitations**	**Low Quality Rating if:** ☒ Studies inconsistent (*wide variation of treatment effect across studies, population, interventions, or outcomes varied*) ☐ Studies are indirect (*PICO question is quite different from the available evidence in regard to population, intervention, comparison, or outcome)* ☒ Studies are imprecise (*when studies include few patients and few events, and thus have wide confidence intervals, and the results are uncertain)* ☐ Publication Bias (*e.g. pharmaceutical company sponsors study on effectiveness of drug only small, positive studies found)* **Increase Quality Rating if:** ☐ Large effect ☐ Dose-response gradient ☐ Plausible confounders or other biases increase certainty of effect **Quality (certainty) of evidence for studies as a whole:** ☐ High ☐ Moderate ☐ Low ☒ Very Low
Journal: *Pain Physician* Author: Manchikanti, L., et al. Year Published: 2011 Location: University of Louisville, Louisville, KY	**Aim**: To assess the need for preoperative fasting and risks without fasting in patients undergoing interventional techniques **Study Type**: Prospective, non-randomized study **Size**: 3,179 patients; 12,000 encounters with 18.472 procedures, with patients receiving sedation during 11,856 encounters	**Inclusion Criteria**: Patients receiving interventional techniques **Exclusion Criteria**: Patients undergoing intrathecal implantables	**Intervention**: Study was performed prospectively on patients without change in their normal course of treatment. There was a lack of preoperative fasting in patients undergoing various types of interventional techniques in managing chronic pain under usual circumstances.	**Results**: During 15.4% of the encounters (1,848), patients were given an antiemetic during their stay at the ambulatory surgery center. They were provided with antiemetics based on the feeling of nausea and previous history of nausea or vomiting following sedation, interventional techniques, or general anesthesia. Among the patients receiving antiemetics 72% of the patients received Phenergan, whereas 28% received Zofran. **Of the 12,000 encounters, overall, 189 or 1.6% of the patients complained of nausea and 3 of them or 0.02% experienced vomiting. However, there were no aspirations. Of the 189 patients with nausea, 80 of them improved significantly prior to discharge without further complaints. Thus, 109 patients or 0.9% were**	**Study Limitations:** ☒ None **Non-Randomized Studies** ☐ Failure to develop and apply appropriate eligibility criteria ☐ Flawed measurement of both exposure and outcome ☐ Failure to adequately control confounding ☐ Incomplete or inadequately short follow-up ☐ Differences in important prognostic factors at baseline	

				minimally nauseated prior to discharge. Postoperative complaints of continued nausea were reported in only 26 patients for 6 to 72 hours.		

References:

1. Manchikanti, L., Malla, Y., Wargo, B. W., & Fellows, B. (2011). Preoperative fasting before interventional techniques: is it necessary or evidence-based? Pain Physician, 14(5), 459-467.

PICO Question: What are the benefits and harms associated with NPO orders for adult patients undergoing invasive procedures and receiving sedation (NOT general anesthesia)?

Outcome: Respiratory Depression

Study Acronym; Author; Year Published; Location	**Aim of Study; Study Type; Study Size (N)**	**Patient Population**	**Study Intervention (# patients) / Study Comparator**	**Endpoint Results / Outcome (Absolute Event Rates, P values; OR or RR; & 95% CI)**	**Design Limitations**
Journal: *Pain Physician* Author: Manchikanti, L., et al. Year Published: 2011 Location: University of Louisville, Louisville, KY	**Aim**: To assess the need for preoperative fasting and risks without fasting in patients undergoing interventional techniques **Study Type**: Prospective, non-randomized study **Size**: 3,179 patients; 12,000 encounters with 18.472 procedures, with patients receiving sedation during 11,856 encounters	**Inclusion Criteria**: Patients receiving interventional techniques **Exclusion Criteria**: Patients undergoing intrathecal implantables	**Intervention**: Study was performed prospectively on patients without change in their normal course of treatment. There was a lack of preoperative fasting in patients undergoing various types of interventional techniques in managing chronic pain under usual circumstances.	**Results**: **Of the 11,850 encounters receiving intravenous sedation, brief oxygenation with mask was required in 2 patients without any adverse consequences of nausea, vomiting, aspiration, or other adverse effects.**	**Study Limitations:** ☒ None **Non-Randomized Studies** ☐ Failure to develop and apply appropriate eligibility criteria ☐ Flawed measurement of both exposure and outcome ☐ Failure to adequately control confounding ☐ Incomplete or inadequately short follow-up ☐ Differences in important prognostic factors at baseline

Low Quality Rating if:
☒ Studies inconsistent (*wide variation of treatment effect across studies, population, interventions, or outcomes varied*)

☐ Studies are indirect (*PICO question is quite different from the available evidence in regard to population, intervention, comparison, or outcome)*

☒ Studies are imprecise (*when studies include few patients and few events, and thus have wide confidence intervals, and the results are uncertain)*

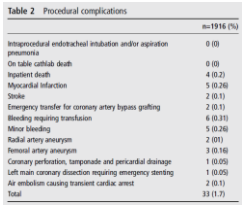
☐ Publication Bias (*e.g. pharmaceutical company sponsors study on effectiveness of drug only small, positive studies found)*

Increase Quality Rating if:
☐ Large effect
☐ Dose-response gradient
☐ Plausible confounders or other biases increase certainty of effect

						Quality (certainty) of evidence for studies as a whole: ☐ High ☐ Moderate ☐ Low ☒ Very Low

References:

1. Manchikanti, L., Malla, Y., Wargo, B. W., & Fellows, B. (2011). Preoperative fasting before interventional techniques: is it necessary or evidence-based? Pain Physician, 14(5), 459-467.

PICO Question: What are the benefits and harms associated with NPO orders for adult patients undergoing invasive procedures and receiving sedation (NOT general anesthesia)?						**Low Quality Rating if:** ☒ Studies inconsistent (*wide variation of treatment effect across studies, population, interventions, or outcomes varied*) ☐ Studies are indirect (*PICO question is quite different from the available evidence in regard to population, intervention, comparison, or outcome)* ☒ Studies are imprecise (*when studies include few patients and few events, and thus have wide confidence intervals, and the results are uncertain)* ☐ Publication Bias (*e.g. pharmaceutical company sponsors study on effectiveness of drug only small, positive studies found)* **Increase Quality Rating if:** ☐ Large effect ☐ Dose-response gradient ☐ Plausible confounders or other biases increase certainty of effect
Outcome: Complications						
Study Acronym; Author; Year Published; Location	**Aim of Study; Study Type; Study Size (N)**	**Patient Population**	**Study Intervention (# patients) / Study Comparator**	**Endpoint Results / Outcome (Absolute Event Rates, P values; OR or RR; & 95% CI)**	**Design Limitations**	
Journal: *Heart* Author: Hamid, T., et al. Year Published: 2014 Location: Royal Albert Edward Infirmary, Wigan, UK	**Aim**: To demonstrate that percutaneous cardiac catheterization does not require prior fasting **Study Type**: Observational Study; Retrospective analysis of database **Size**: 1,916 Percutaneous Coronary Intervention (PCI) procedures	**Inclusion Criteria**: Patients admitted for PCI and acute coronary syndrome (ACS) **Exclusion Criteria**: None included	**Intervention**: All patients at our two institutes, admitted for elective PCI and acute coronary syndrome (ACS), are not kept NBM, and the advice includes that they have a light breakfast in the morning, without the need for being NBM/NPO for 4 h. Patients are listed according to clinical urgency, and go to the catheter laboratory for the procedure as soon as a slot is available. Patients were given sedation as per patient request or operator choice. The sedatives used in our practice are intravenous Diazepam (2.5–10 mg), Midazolam (1–4 mg) or Fentanyl (25–50 mcg).	**Results**: None of the patients were kept NPO/NBM prior to their coronary procedures. No patients developed either intraprocedural or postprocedural aspiration pneumonia 	**Study Limitations:** ☐ None **Non-Randomized Studies** ☐ Failure to develop and apply appropriate eligibility criteria ☐ Flawed measurement of both exposure and outcome ☒ Failure to adequately control confounding ☐ Incomplete or inadequately short follow-up ☐ Differences in important prognostic factors at baseline	
Journal: *Nutricion Hospitalaria*	**Aim**: To investigate the gastric emptying of an oral supplement	**Inclusion Criteria**: Adult patients scheduled to	**Intervention**: Patients were randomized to receive either an overnight	**Results**: **There were no complications during all exams.** The median	**Study Limitations:** ☐ None ***RCTs***	

Author: de Aguilar-Nascimento, J. E., et al. Year Published: 2014 Location: Federal University of Mato Grosso, Cuiaba, Brazil	containing carbohydrate plus whey protein drunk before sedation for gastroscopy **Study Type**: RCT **Size**: 24; intervention group = 12 and control group = 12	upper digestive endoscopy **Exclusion Criteria**: Decline to participate, American Society of Anesthesiologists score above II, diabetes mellitus, pregnancy, history of renal or hepatic failure, gastro-esophageal reflux, acute cholecystitis, use of corticosteroids up to 6 months previously, use of an prokinetic drug up to 6 weeks previously, and any noncompliance or violation on the assigned protocol of preoperative fasting.	fast (minimum of 8 hours; control group) or fast for solids for the same period and drink 200 milliliters (mL) of an oral nutritional supplement (Composition per 200 mL: 0g lipids; 8 g whey protein; 67g carbohydrate being 88% maltodextrin and 12% sacharose; osmolality: 680 mOsm/L; and total energy: 300 kcal; Fresubin Jucy, Fresenius Kabi, Brazil) 150-210 minutes before the exam (intervention group).	(range) fasting time was greater (P < 0.001) in control group (770 min, ranging from 660-917 min) than in the study group (175min ranging from 150 to 210 min). Overall patient satisfaction was excellent, with no difference between groups. The gastroscopist reported that in all cases, the aspiration of gastric contents was very easy and did not increase the time of the procedure. In all cases the gastroscopist was confident on his diagnosis, meaning that he had seen the entire gastric cavity, and the first portions of the duodenum.	☐ Lack of blinding ☐ Lack of allocation concealment ☐ Stopped early for benefit ☒ Incorrect analysis of ITT ☐ Selective reporting of measures (e.g., no effect outcome) ☐ Large losses to F/U ☐ Difference in important prognostic factors at baseline	**Quality (certainty) of evidence for studies as a whole:** ☐ High ☐ Moderate ☒ Low ☐ Very Low

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1. de Aguilar-Nascimento, J. E., Caporossi, C., Metelo, J. S., Tanajura, G. H., Canevari-de-Oliveira, M., & da Cunha Costa, R. (2014). Safe intake of an oral supplement containing carbohydrates and whey protein shortly before sedation to gastroscopy; a double blind, randomized trial. Nutricion Hospitalaria, 29(3), 681-686. doi:https://dx.doi.org/10.3305/nh.2014.29.3.7161
2. Hamid, T., Aleem, Q., Lau, Y., Singh, R., McDonald, J., Macdonald, J. E., . . . Balachandran, K. (2014). Pre-procedural fasting for coronary interventions: is it time to change practice? Heart, 100(8), 658-661. doi:https://dx.doi.org/10.1136/heartjnl-2013-305289

PICO Question: What are the benefits and harms associated with NPO orders for adult patients undergoing invasive procedures and receiving sedation (NOT general anesthesia)?						**Low Quality Rating if:** ☒ Studies inconsistent (*wide variation of treatment effect across studies, population, interventions, or outcomes varied*) ☐ Studies are indirect (*PICO question is quite different from the available evidence in regard to population, intervention, comparison, or outcome)*
Outcome: Success Rate						
Study Acronym; Author; Year Published; Location	**Aim of Study; Study Type; Study Size (N)**	**Patient Population**	**Study Intervention (# patients) / Study Comparator**	**Endpoint Results / Outcome (Absolute Event Rates, P values; OR or RR; & 95% CI)**	**Design Limitations**	
Journal: *Heart* Author: Hamid, T., et al. Year Published: 2014 Location: Royal Albert Edward Infirmary, Wigan, UK	**Aim**: To demonstrate that percutaneous cardiac catheterization does not require prior fasting	**Inclusion Criteria**: Patients admitted for PCI and acute coronary syndrome (ACS) **Exclusion Criteria**: None included	**Intervention**: All patients at our two institutes, admitted for elective PCI and acute coronary syndrome (ACS), are not kept NBM, and the advice includes that they	**Results**: None of the patients were kept NPO/NBM prior to their coronary procedures. **PCI was technically successful in 95%**	**Study Limitations:** ☐ None **Non-Randomized Studies** ☐ Failure to develop and apply appropriate eligibility criteria	

	Study Type: Observational Study; Retrospective analysis of database **Size**: 1,916 PCI procedures		have a light breakfast in the morning, without the need for being NBM/NPO for 4 h. Patients are listed according to clinical urgency, and go to the catheter laboratory for the procedure as soon as a slot is available. Patients were given sedation as per patient request or operator choice. The sedatives used in our practice are intravenous Diazepam (2.5–10 mg), Midazolam (1–4 mg) or Fentanyl (25–50 mcg).	**(1821/1916) of patients**; 88.5% (1697/1916) had transradial approach. Glycoprotein IIb/IIIa inhibitors were used in 8% (158/1916). Pressure Wire studies and Intra-Vascular Ultrasound (IVUS) were used in 13% (258/1916) and 9% (181/1916), respectively. Other devices used included thrombectomy catheters and distal protection devices for vein graft interventions.	☐ Flawed measurement of both exposure and outcome ☒ Failure to adequately control confounding ☐ Incomplete or inadequately short follow-up ☐ Differences in important prognostic factors at baseline	☐ Studies are imprecise (*when studies include few patients and few events, and thus have wide confidence intervals, and the results are uncertain)* ☐ Publication Bias (*e.g. pharmaceutical company sponsors study on effectiveness of drug only small, positive studies found)* **Increase Quality Rating if:** ☐ Large effect ☐ Dose-response gradient ☐ Plausible confounders or other biases increase certainty of effect **Quality (certainty) of evidence for studies as a whole:** ☐ High ☐ Moderate ☒ Low ☐ Very Low

References:

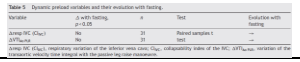
1. Hamid, T., Aleem, Q., Lau, Y., Singh, R., McDonald, J., Macdonald, J. E., . . . Balachandran, K. (2014). Pre-procedural fasting for coronary interventions: is it time to change practice? Heart, 100(8), 658-661. doi:https://dx.doi.org/10.1136/heartjnl-2013-305289

PICO Question: What are the benefits and harms associated with NPO orders for adult patients undergoing invasive procedures and receiving sedation (NOT general anesthesia)?

Outcome: Echocardiographic Preload Variables

Study Acronym; Author; Year Published; Location	Aim of Study; Study Type; Study Size (N)	Patient Population	Study Intervention (# patients) / Study Comparator	Endpoint Results / Outcome (Absolute Event Rates, P values; OR or RR; & 95% CI)	Design Limitations	**Low Quality Rating if:**
Journal: *Brazilian Journal of Anesthesiology* Author: Alves, D.R. and R. Ribeiras Year Published: 2017 Location: Centro Hospitalar de Lisboa	**Aim**: To determine if fasting causes a change in preload of conscious volunteers or significantly alters their position on the Frank-Starling curve	**Inclusion Criteria**: >/= 18 years old; ASA 1 or ASA 2; Acceptance of study conditions **Exclusion Criteria**: Refusal of study conditions; dysrhythmia	**Intervention**: 31 ASA 1 and ASA 2 volunteers underwent an echocardiographic examination both before and after a fasting period of at least 6 hours. Data from both static and	**Results**: All 31 volunteers underwent a longer fasting period than requested, which varied from 7 to 12.5 h (average = 10 standard deviation = 1.4 h) - in accordance with clinical practice.	**Study Limitations:** ☒ None **Non-Randomized Studies** ☐ Failure to develop and apply appropriate eligibility criteria	☒ Studies inconsistent (*wide variation of treatment effect across studies, population, interventions, or outcomes varied*) ☒ Studies are indirect (*PICO question is quite different from the available evidence in regard to population, intervention, comparison, or outcome)*

Ocidental, Lisbon, Portugal	**Study Type**: Observational Study **Size**: 31 volunteers	and/or pacemaker; Systolic dysfunction; Diastolic dysfunction; Valvulopathy; Right ventricular dysfunction; Hyperdynamic states; Compromised renal function; Medication interfering with compensatory hemodynamic mechanisms; Osteoarticular pathology preventing proper positioning and PLR, Inadequate echocardiographic images, Failure to obtain one of the exams	dynamic preload indices were obtained during both periods and compared.	*Static parameters* • A statistically significant decrease of 6.8% in the teledi-astolic area of the left ventricle (PSSAx) (pointing to adecreased preload after fasting), • A statistically significant increase of 9.2% in the Flowtime corrected in the descending aorta (pointing to anincrease in preload after fasting, considering that periph-eral vascular resistance, which is inversely proportionalto the FTcAo dand could complicate the assessment, alsoincreased in this period) • No change in the absolute expiratory diameter of the IVCor in the telediastolic diameter of the LV in PSLAx (M-mode), pointing to the absence of change in preload.  *Dynamic Parameters* • As far as the dynamic preload indices studied are concerned, their behaviour was markedly consistent between different indices, with no statistically significant changeson either the respiratory variations of IVC diameter or in the variation of VTIAo with the PLR manoeuvre. Therefore, they all pointed to the inexistence of a significant	☐ Flawed measurement of both exposure and outcome ☐ Failure to adequately control confounding ☐ Incomplete or inadequately short follow-up ☐ Differences in important prognostic factors at baseline	☒ Studies are imprecise (*when studies include few patients and few events, and thus have wide confidence intervals, and the results are uncertain)* ☐ Publication Bias (*e.g. pharmaceutical company sponsors study on effectiveness of drug only small, positive studies found)* **Increase Quality Rating if:** ☐ Large effect ☐ Dose-response gradient ☐ Plausible confounders or other biases increase certainty of effect **Quality (certainty) of evidence for studies as a whole:** ☐ High ☐ Moderate ☐ Low ☒ Very Low

				preload variation with fasting. 		

References:

1. Alves, D. R., & Ribeiras, R. (2017). Does fasting influence preload responsiveness in ASA 1 and 2 volunteers? Brazilian Journal of Anesthesiology, 67(2), 172-179. doi:https://dx.doi.org/10.1016/j.bjane.2015.11.002

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

Guideline Recommendations:

In 2011, the **American Society of Anesthesiologists (ASA)** Committee on Standards and Practice Parameters stated:

- Both the consultants and ASA members strongly agree that for otherwise healthy infants (younger than 2 yr), children (2–16 yr), and adults, fasting from the intake of clear liquids at least 2 h before elective procedures requiring general anesthesia, regional anesthesia, or sedation/analgesia (i.e., monitored anesthesia care) should be maintained **(Consensus Statement)**

A 2017 updated report by the **American Society of Anesthesiologists Task Force (ASA TF) on Preoperative Fasting and the Use of Pharmacologic Agents** recommended the following be routinely administered before elective procedures requiring general anesthesia, regional anesthesia, or procedural sedation and analgesia in patients to reduce the risk of pulmonary aspiration:

- *Recommendations for Clear Liquids*
  - Clear liquids may be ingested for up to 2 h before procedures requiring general anesthesia, regional anesthesia, or procedural sedation and analgesia **(Category A1-E evidence)**.
- *Recommendations for Solids and Nonhuman Milk*
  - A light meal or nonhuman milk may be ingested for up to 6 h before elective procedures requiring general anesthesia, regional anesthesia, or procedural sedation and analgesia **(Category A3-E evidence)**.
    - Additional fasting time (e.g., 8 or more hours) may be needed in cases of patient intake of fried foods, fatty foods, or meat.
  - Consider both the amount and type of foods ingested when determining an appropriate fasting period.
  - Since nonhuman milk is similar to solids in gastric emptying-time, consider the amount ingested when determining an appropriate fasting period.
- *Recommendations for Gastrointestinal Stimulants*

- Gastrointestinal stimulants may be preoperatively administered to patients at increased risk of pulmonary aspiration **(Category A1-B evidence)**.
- Do not routinely administer preoperative gastrointestinal stimulants for the purpose of reducing the risk of pulmonary aspiration in patients with no apparent increased risk for pulmonary aspiration.

- *Recommendations for Pharmacologic Blockade of Gastric Acid Secretion*
  - Medications that block gastric acid secretion may be preoperatively administered to patients at increased risk of pulmonary aspiration **(Category A1-B evidence)**.
  - Do not routinely administer preoperative medications that block gastric acid secretion for the purpose of reducing the risk of pulmonary aspiration in patients with no apparent increased risk of pulmonary aspiration.
- *Recommendations for Antacids*
  - Antacids may be preoperatively administered to patients at increased risk of pulmonary aspiration **(Category A2-B evidence)**.
    - Only administer nonparticulate antacids
  - Do not routinely administer preoperative antacids for the purpose of reducing the risk of pulmonary aspiration in patients with no apparent increased risk for pulmonary aspiration.
- *Recommendations for Antiemetics*
  - Antiemetics may be preoperatively administered to patients at increased risk of postoperative nausea and vomiting **(Consensus Statement)**.
  - The routine preoperative administration of antiemetics to reduce the risk of nausea and vomiting is not recommended for patients with no apparent increased risk for pulmonary aspiration.
- *Recommendations for Anticholinergics*
  - The administration of preoperative anticholinergics to reduce the risk of pulmonary aspiration is not recommended **(Category A2-E evidence)**.
- *Recommendations for Multiple Agents*
  - The routine administration of preoperative multiple agents is not recommended for patients with no apparent increased risk for pulmonary aspiration **(Category A2-E evidence)**.

In 2018, the **Canadian Anesthesiologists' Society (CAS)** recommended the following in an official position paper:

- The precise requirements for pre-procedural fasting are evolving. In general, patients provided with more profound levels of sedation (RSS 5-6) should fast in accordance with general CAS standards, namely, no lipids or solids for six hours and no clear fluids for two hours. More liberal guidelines may be appropriate for lighter levels of sedation (RSS1-4), but they should be individualized in view of the patients' comorbidities. Some recent research, particularly in the emergency medicine literature, suggests that more liberal guidelines have not been associated with an increased incidence of regurgitation and aspiration of gastric contents. Up to now, these

have been small studies, and while they frequently did not detect complications, they failed to demonstrate safety **(Consensus Statement)**.

The **European Society of Anaesthesiology and European Board of Anaesthesiology (ESA/EBA)** guidelines for procedural sedation and analgesia (PSA) in adults in 2018 recommended:

- Fasting prior to PSA is not evidence-based. A single protocol is used for preoperative fasting prior to surgery should avoid confusion and mistakes **(good consensus: level of evidence C: GoR weak)**.

In 2013, the **American College of Emergency Physicians** stated the following recommendation:

- Do not delay procedural sedation in adults or pediatrics in the ED based on fasting time. Preprocedural fasting for any duration has not demonstrated a reduction in the risk of emesis or aspiration when administering procedural sedation and analgesia **(Level B Recommendation)**.

Guideline Ratings

Guideline Issuer and Date	ASA 2011	ASA TF 2018	CAS 2018	ESA/EBA 2018	ACEP 2013
1. Transparency	B	B	C	A	B
2. Conflict of interest	NR	NR	NR	A	B
3. Development group	B	B	NR	B	A
4. Systematic Review	B	B	C	A	B
5. Supporting evidence	A	A	C	A	A
6. Recommendations	B	B	C	B	A
7. External Review	NR	NR	NR	C	NR
8. Currency and updates	C	B	C	B	B

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

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

Developed by the GRADE Working Group

Grades and interpretations:

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

Type of evidence and starting level

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

Criteria for increasing or decreasing level

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

Appendix B. Trustworthy Guideline rating scale

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

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

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

1. Transparency

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

The grader must refer to any cited methods supplements or other supporting material when evaluating the guideline. Methods should include:

Who wrote the initial draft
How the committee voted on or otherwise approved recommendations

Evidence review, external review and methods used for updating are not addressed in this standard.

2. Conflict of interest

A	Funding of the guideline project is disclosed, disclosures are made for each individual panelist, and financial or other conflicts do not apply to key authors of the guideline or to more than 1 in 10 panel members).
B	Guideline states that there were no conflicts (or fewer than 1 in 10 panel members), but does not disclose funding source.

C	Lead author, senior author, or guideline panel members (at least 1 in 10) have conflict of interest, or guideline project was funded by industry sponsor with no assurance of independence.
NR	Guideline does not report on potential conflict of interests.

For purposes of this checklist, conflicts of interest include employment by, consulting for, or holding stock in companies doing business in fields affected by the guideline, as well as related financial conflicts. This definition should not be considered exclusive. As much as anything, this is a surrogate marker for thorough reporting, since it may be assumed that guideline projects are funded by the sponsoring organization and many authors think it unnecessary to report a non-conflict.

3. Guideline development group

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

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

4. Systematic review

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

In order to qualify as a systematic review, the review must do all of the following:

Describe itself as systematic or report search strategies using multiple databases
Define the scope of the review (including key questions and the applicable population)
Either include quantitative or qualitative synthesis of the data or explain why it is not indicated

Note: this element does not address the quality of the systematic review: simply whether or not it exists. Concerns about quality or bias of the review will be discussed in text, where the analyst will explain whether the weaknesses of the review weaken the validity or reliability of the guideline.

Note: a guideline may be rated B on this domain even if the review on which it is based is not available to us. This potential weakness of the guideline should be discussed in text of the report.

5. Grading the supporting evidence

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

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

6. Recommendations

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

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

7. External review

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

8. Updating and currency of guideline

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

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