

may likely be even higher in burn or multitrauma patients (see sections M and P).

[Quality of Evidence: Very Low]

Rationale: Recent studies in critical illness suggest that provision of protein is more closely linked to positive outcomes than provision of total energy (specifically, delivery of the other macronutrients of fat and carbohydrate). Also, the dose of protein required by critically ill patients appears to be higher than previously thought. A prospective observational study in mechanically ventilated patients demonstrated that achievement of both protein (1.3 g/kg protein provided) and energy targets was associated with a 50% decrease in 28-day mortality, whereas no decrease in mortality was noted when energy targets alone were met (0.8 g/kg protein provided).⁹¹ In another prospective observational study in a mixed MICU/SICU, a stepwise decrease in 28-day mortality was demonstrated with increased protein provision (group 1: 0.79 g/kg, 27% mortality; group 2: 1.06 g/kg, 24% mortality; group 3: 1.46 g/kg, 16% mortality).⁹² Two small RCTs, however, showed no difference in mortality when a higher protein dose was provided.^{93,94} Unfortunately, determination of protein requirements in the critical care setting remains difficult, with most clinicians using simplistic weight-based equations (1.2–2.0 g/kg/d). Use of nitrogen balance or NPC:N (70:1–100:1) is of limited value in the ICU.⁹⁵

D. Monitoring Tolerance and Adequacy of EN

Question: How should tolerance of EN be monitored in the adult critically ill population?

D1. Based on expert consensus, we suggest that patients should be monitored daily for tolerance of EN. We suggest that inappropriate cessation of EN should be avoided. We suggest that ordering a feeding status of nil per os (NPO) for the patient surrounding the time of diagnostic tests or procedures should be minimized to limit propagation of ileus and to prevent inadequate nutrient delivery.

Rationale: Tolerance may be determined by physical examination, passage of flatus and stool, radiologic evaluations, and absence of patient complaints such as pain or abdominal distention. GI intolerance is usually defined by vomiting, abdominal distention, complaints of discomfort, high NG output, high GRV, diarrhea, reduced passage of flatus and stool, or abnormal abdominal radiographs. Metheny et al reported that more than 97% of nurses surveyed assessed intolerance solely by measuring GRVs (the most frequently cited threshold levels for interrupting EN listed as 200 mL and 250 mL).⁹⁶

Less than half of patients ever reach their target goal energy intake during their ICU stay. A number of factors impede the delivery of EN in the critical care setting.^{97–99} Healthcare providers who prescribe EN tend to underorder energy, prescribing only 60%–80% of energy requirements. Patients typically receive approximately 80% of what is ordered. This combination of underordering and inadequate delivery results in patients receiving on average only 50% of target goal energy from one day to the next. Cessation of EN occurs in >85% of patients for an average of 8%–20% of the infusion time (the reasons for which are avoidable in 23% of planned procedures and 65% of all occasions).^{97,99} While patient intolerance accounts for a third of cessation time, only half of this represents true intolerance. Remaining NPO after midnight for diagnostic tests and procedures affects 25%–33% of ICU patients and accounts for up to 25% of cessation time. Technical issues involving the enteral access device, such as maintaining patency or repositioning/replacing the tube, can account for up to 25% of cessation time. In one study, patients randomized to continue EN during frequent surgical procedures (burn wound debridement under general anesthesia) had significantly fewer infections than those patients for whom EN was stopped for each procedure.¹⁰⁰ Ileus may be propagated by repeated and prolonged periods for which patients are NPO.¹⁰¹

Question: Should GRVs be used as a marker for aspiration to monitor ICU patients receiving EN?

D2a. We suggest that GRVs not be used as part of routine care to monitor ICU patients receiving EN.

D2b. We suggest that, for those ICUs where GRVs are still utilized, holding EN for GRVs <500 mL in the absence of other signs of intolerance (see section D1) should be avoided.

[Quality of Evidence: Low]

Rationale: GRVs do not correlate with incidences of pneumonia,^{102,103} regurgitation, or aspiration.¹⁰⁴ Although a study showed that cumulative GRV >250 mL over 24 hours correlated with gastric emptying using scintigraphy studies and (13) C-octanoate breath tests,¹⁰⁵ 3 other trials using the paracetamol (acetaminophen) test showed poor correlation of GRVs done every 4 hours to gastric emptying.^{106–108} In a trial using a highly sensitive and specific marker for aspiration, GRVs (over a range of 150–400 mL) were shown to be a poor monitor for aspiration, with a very low sensitivity of 1.5%–4.1%, a positive predictive value of 18.2%–25%, and a negative predictive value of 77.1%–77.4%.¹⁰⁹ Results from 4 RCTs indicate that raising the cutoff value for GRVs (leading to automatic cessation of EN) from a lower number of 50–150 mL to a higher number of 250–500 mL does not increase the incidence of regurgitation, aspiration, or pneumonia.^{80,102,103,109} Decreasing the cutoff value for

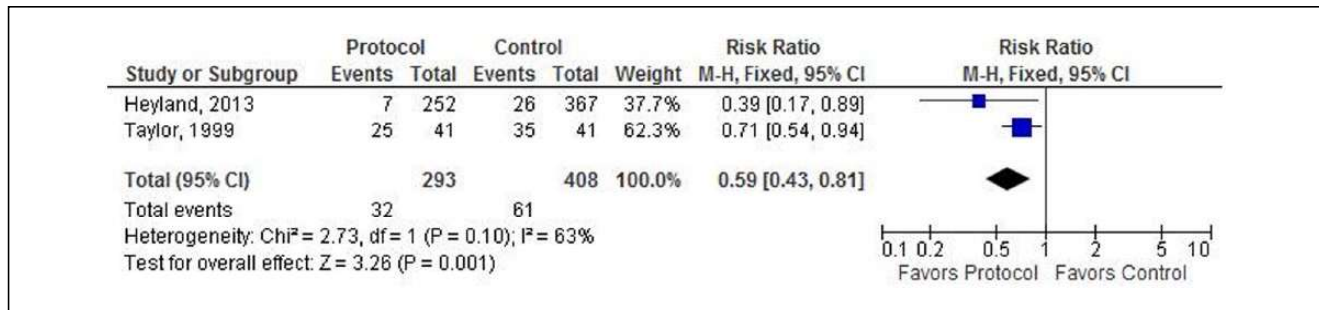


Figure 6. Feeding protocol vs control, infections.

GRVs does not protect the patient from these complications. Use of GRVs leads to increased enteral access device clogging, inappropriate cessation of EN, consumption of nursing time, and allocation of healthcare resources and may adversely affect outcome through reduced volume of EN delivered.¹¹⁰

Three studies have shown that eliminating the practice of using GRVs improves delivery of EN without jeopardizing patient safety.^{110–112} All 3 trials—2 RCTs^{110,112} and 1 prospective before/after implementation trial¹¹¹—showed no significant difference between groups with regard to pneumonia. Two of the trials showed significantly greater EN delivery, by either increased volume of EN infused¹¹¹ or greater reduction in energy deficit.¹¹² One trial showed significantly more vomiting but significantly better overall GI tolerance when GRVs were eliminated,¹¹² while a second trial showed no difference in vomiting between groups.¹¹¹

If the practice of GRVs is eliminated, a number of alternative strategies may be used to monitor critically ill patients receiving EN: careful daily physical examinations, review of abdominal radiologic films, and evaluation of clinical risk factors for aspiration. EN protocols should be initiated, and efforts to proactively reduce risk of aspiration pneumonia should be made (see sections D3 and D4). For those ICUs reluctant to stop using GRVs, care should be taken in their interpretation. GRVs in the range of 200–500 mL should raise concern and lead to the implementation of measures to reduce risk of aspiration, but automatic cessation of EN should not occur for GRVs <500 mL in the absence of other signs of intolerance.^{80,102–104,109}

Question: Should EN feeding protocols be used in the adult ICU setting?

D3a. We recommend that enteral feeding protocols be designed and implemented to increase the overall percentage of goal calories provided.

[Quality of Evidence: Moderate to High]

D3b. Based on expert consensus, we suggest that use of a volume-based feeding protocol or a top-down multistrategy protocol be considered.

Rationale: Use of ICU- or nurse-driven protocols that define goal EN infusion rate, designate more rapid start-ups, and provide specific orders for handling GRVs, frequency of flushes, and conditions or problems under which EN may be adjusted or stopped has been shown to be successful in increasing the overall percentage of goal energy provided.^{80,113–117} In addition, volume-based feeding protocols in which 24-hour or daily volumes are targeted instead of hourly rates have been shown to increase volume of nutrition delivered.¹¹⁶ These protocols empower nurses to increase feeding rates to make up for volume lost while EN is held. Top-down protocols use multiple different strategies simultaneously at the time of initiation of EN to enhance tolerance and increase delivery of EN, removing individual strategies as tolerance improves over the first few days of infusion. Top-down multistrategy protocols typically use volume-based feeding in conjunction with prokinetic agents and postpyloric tube placement initially (among other strategies), with prokinetic agents stopped in patients who demonstrate lack of need.¹¹⁶

By aggregating the data from 2 studies that met our inclusion criteria (Figure 6), use of nurse-driven EN protocols to increase EN delivery positively impacted patient outcome by reducing the incidence of nosocomial infections as compared with controls where no protocol was used (RR = 0.59; 95% CI, 0.43–0.81; *P* = .001).^{80,116}

Question: How can risk of aspiration be assessed in critically ill adults patients receiving EN, and what measures may be taken to reduce the likelihood of aspiration pneumonia?

D4. Based on expert consensus, we suggest that patients receiving EN should be assessed for risk of aspiration and that steps to reduce risk of aspiration and aspiration pneumonia should be proactively employed.

Rationale: Aspiration is one of the most feared complications of EN. Patients at increased risk for aspiration may be identified by a number of factors, including inability to protect the

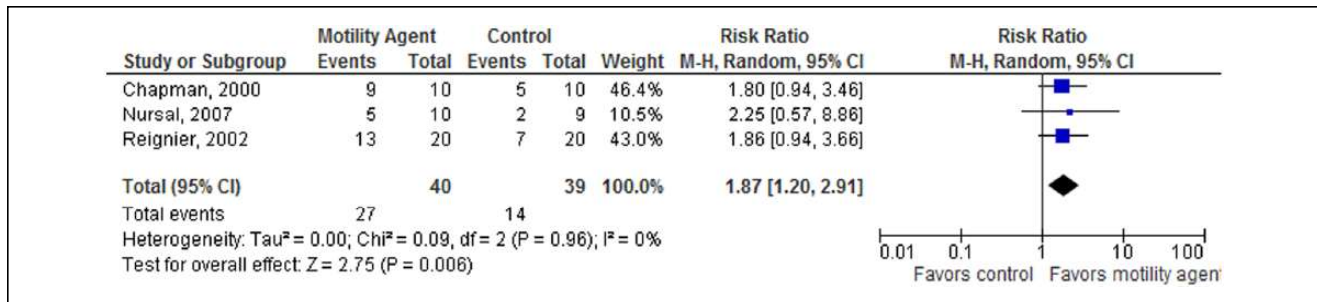


Figure 7. Motility agents vs placebo, outcome lower gastric residual volume.

airway, presence of a nasogastric enteral access device, mechanical ventilation, age >70 years, reduced level of consciousness, poor oral care, inadequate nurse:patient ratio, supine positioning, neurologic deficits, gastroesophageal reflux, transport out of the ICU, and use of bolus intermittent EN.¹⁰⁴ Pneumonia and bacterial colonization of the upper respiratory tree is more closely associated with aspiration of contaminated oropharyngeal secretions than regurgitation and aspiration of contaminated gastric contents.^{118–120}

D4a. We recommend diverting the level of feeding by postpyloric enteral access device placement in patients deemed to be at high risk for aspiration (see also section B5)

[Quality of Evidence: Moderate to High]

Rationale: Changing the level of infusion of EN from the stomach to the small bowel has been shown to reduce the incidence of regurgitation, aspiration, and pneumonia.^{121,122} In 13 RCTs,^{73–84} pneumonia was significantly lower in patients with small bowel EN (RR = 0.75; 95% CI, 0.6–0.93; $P = .01$), even when restricted to studies using evidence of ventilator-associated pneumonia (VAP) (RR = 0.72; 95% CI, 0.55–0.93; $P = .01$), compared with patients on gastric EN. There was no difference in mortality, ICU LOS, hospital LOS, duration of mechanical ventilation, or time to goal EN.

D4b. Based on expert consensus, we suggest that for high-risk patients or those shown to be intolerant to bolus gastric EN, delivery of EN should be switched to continuous infusion.

Rationale: The potential harm from aggressive bolus infusion of EN leading to increased risk of aspiration pneumonia was shown in 1 study.¹²³ An RCT showed a trend toward decreased mortality with continuous EN (13.9% intermittent vs 7.4% continuous; $P = .18$).¹²⁴ Five small RCTs comparing bolus with continuous infusion have shown greater volume with fewer interruptions in delivery of EN with continuous EN but no significant difference between techniques with regard to patient outcome.^{125–129}

D4c. We suggest that, in patients at high risk of aspiration, agents to promote motility, such as prokinetic medications (metoclopramide or erythromycin), be initiated where clinically feasible.

[Quality of Evidence: Low]

Rationale: Adding prokinetic agents such as erythromycin or metoclopramide has been shown to improve gastric emptying and tolerance of EN but has resulted in little change in clinical outcome for ICU patients. A total of 8 RCTs that met our inclusion criteria^{130–137} using metoclopramide and 1 combining erythromycin with metoclopramide were reviewed by meta-analysis. No difference was found in terms of mortality or infection. However, GRVs were lower with prokinetic agents than with control (RR = 1.87; 95% CI, 1.20–2.91; $P = .006$) in 3 RCTs that met our inclusion criteria (Figure 7). Erythromycin doses of 3–7 mg/kg/d have been utilized to treat gastric enteral feeding intolerance. Likewise, metoclopramide, 10 mg 4 times a day, has been shown to be efficacious for elevated gastric residuals; however, dosage adjustments to metoclopramide may be necessary in patients with declining renal function. For both pharmaceutical agents, oral and IV routes may be used. Erythromycin has been associated with undesirable effects, including cardiac toxicity, tachyphylaxis, and bacterial resistance, and should be used cautiously with monitoring. Metoclopramide also has associated adverse complications, including tardive dyskinesia, more frequently in the elderly. Both agents have been associated with QT prolongation, predisposing to cardiac arrhythmias.^{138,139} Combination therapy with erythromycin and metoclopramide did demonstrate improved GRVs, allowing for greater feeding success; however, neither hospital LOS nor mortality was different. Furthermore, the incidence of watery diarrhea was statistically higher in patients receiving combination therapy (54% vs 26.3%; $P = .01$).¹³³ Studies demonstrating improved clinical outcomes from combination therapy without associated increase in risk of adverse effects are needed before this approach can be recommended. Use of naloxone infused through the enteral access device (to reverse the effects of opioid narcotics at the level of the gut to improve intestinal motility) was shown in one study to significantly increase the

volume of EN infused, reduce GRVs, and decrease the incidence of VAP (compared with placebo).¹³² Peripherally acting mu-opioid receptor antagonists, specifically methylnaltrexone and alvimopan, have been shown to facilitate recovery of GI function after surgery; however, to date there are no studies investigating their use as prokinetic agents.

D4d. Based on expert consensus, we suggest that nursing directives to reduce risk of aspiration and VAP be employed. In all intubated ICU patients receiving EN, the head of the bed should be elevated 30°–45° and use of chlorhexidine mouthwash twice a day should be considered.

Rationale: Elevating the head of the bed 30°–45° was shown in 1 study to reduce the incidence of pneumonia from 23% to 5%, comparing supine with semirecumbent position, respectively ($P = .018$).^{140,141} Optimizing oral health with chlorhexidine mouthwash twice daily was shown in 2 studies to reduce respiratory infection and nosocomial pneumonia in patients undergoing heart surgery.^{142,143} While studies evaluating the use of chlorhexidine in general ICU populations have shown little outcome effect, 2 studies in which chlorhexidine oral care was included in bundled interventions showed significant reductions in nosocomial respiratory infections.^{144,145} Other steps to decrease aspiration risk would include reducing the level of sedation/analgesia when possible and minimizing transport out of the ICU for diagnostic tests and procedures.^{104,146}

Question: Are surrogate markers useful in determining aspiration in the critical care setting?

D5. Based on expert consensus, we suggest that neither blue food coloring nor any coloring agent be used as a marker for aspiration of EN. Based on expert consensus, we also suggest that glucose oxidase strips not be used as surrogate markers for aspiration in the critical care setting.

Rationale: Traditional monitors for aspiration are ineffective. Any use of a color monitor (eg, methylene blue, blue food coloring) interferes with other colorimetric tests, such as Hemocult, Gastrocult, and pH testing.^{147,148} High-dose methylene blue may have effects similar to blue food coloring regarding mitochondrial toxicity and interference with oxidative phosphorylation.¹⁴⁷ Blue food coloring, an insensitive marker for aspiration, was shown to be associated with mitochondrial toxicity and patient death.^{147,149} The U.S. Food and Drug Administration (FDA), through a Health Advisory Bulletin (September 2003), issued a mandate against the use of blue food coloring as a monitor for aspiration in patients receiving EN.¹⁵⁰ The basic premise for the use of glucose oxidase (that glucose content in tracheal secretions is solely related to aspiration of glucose-containing formulation) has

been shown to be invalid, and its use is thwarted by poor sensitivity/specificity characteristics.¹⁵¹

Question: How should diarrhea associated with EN be assessed in the adult critically ill population?

D6. Based on expert consensus, we suggest that EN not be automatically interrupted for diarrhea but rather that feeds be continued while evaluating the etiology of diarrhea in an ICU patient to determine appropriate treatment.

Rationale: Diarrhea in ICU patients receiving EN is common but may be serious, as the incidence ranges from 2%–95% and often results in electrolyte imbalance, dehydration, perianal skin breakdown, and wound contamination.¹⁵² If unable to control the diarrhea, clinicians often stop EN, with resulting inadequate nutrition intake. Differences in definition, stool collection, and sampling techniques account for the wide range of incidence in clinical studies; the definitions most commonly used are 2–3 liquid stools per day or >250 g of liquid stool per day.^{153,154}

The following factors may contribute to acute diarrhea: type and amount of fiber in formula, osmolality of formula, delivery mode, EN contamination, medications (antibiotics, proton-pump inhibitors, prokinetics, glucose lowering agents, nonsteroidal antiinflammatory drugs, selective serotonin reuptake inhibitors, laxatives, and sorbitol-containing preparations, in particular), and infectious etiologies, including *Clostridium difficile*.¹⁵² Studies have shown an association between short-chain carbohydrates fermentable oligosaccharides, disaccharides and monosaccharides, and polyols (FODMAPS) and diarrhea, as they are highly osmotic and rapidly fermented by gut bacteria. Formulas with a high content of FODMAPS may play a role in diarrhea, especially if the patient is also receiving antibiotics that have a detrimental effect on intestinal microbiota.¹⁵⁵ Most episodes of nosocomial diarrhea are mild and self-limiting.¹⁵⁶

Assessment of diarrhea should include an abdominal examination, quantification of stool, stool culture for *Clostridium difficile* (and/or toxin assay), serum electrolyte panel (to evaluate for excessive electrolyte losses or dehydration), and review of medications. An attempt should be made to distinguish infectious diarrhea from osmotic diarrhea.¹⁵⁷

E. Selection of Appropriate Enteral Formulation

Question: Which formula should be used when initiating EN in the critically ill patient?

E1. Based on expert consensus, we suggest using a standard polymeric formula when initiating EN in the ICU setting. We suggest avoiding the routine use of all