Challenges to Diagnosing Enteral Feeding Intolerance

Mark. H DeLegge, MD
Medical University of South Carolina
DeLegge Medical

HOSPITAL MALNUTRITION: FREQUENCY AND COST OF CARE

1 in 3

COST OF MALNUTRITION AMONG HOSPITALIZED PATIENTS FOR SAME DRG[2]

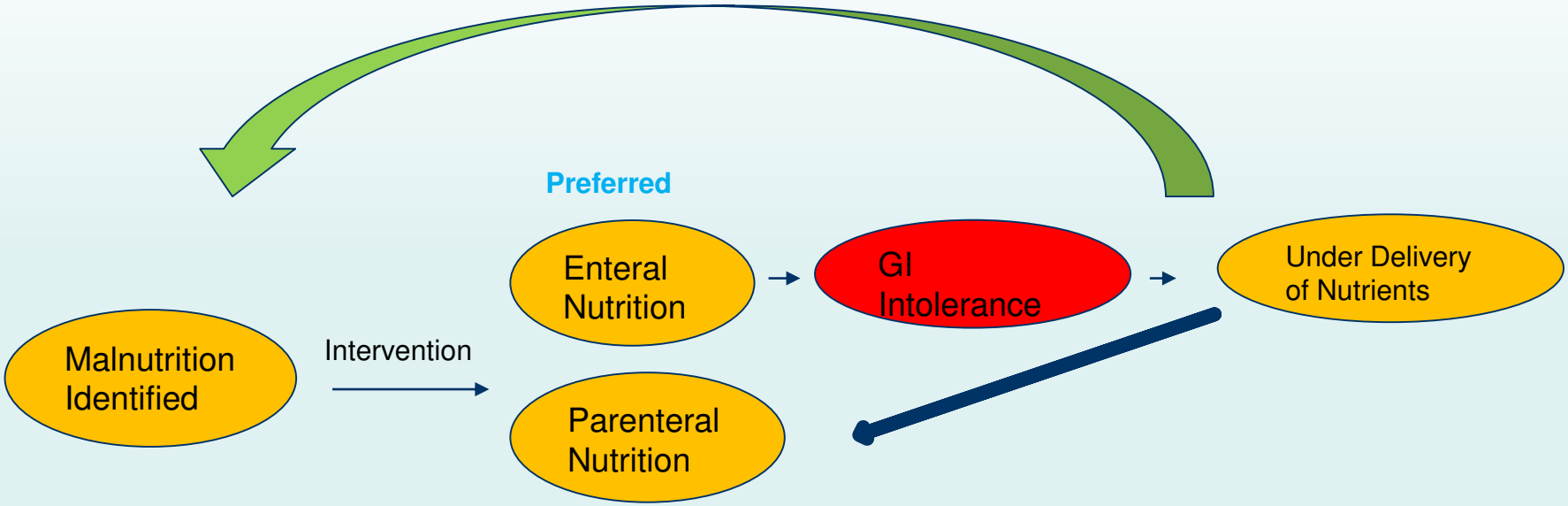
↑ 30%

Annual direct medical costs of disease-associated malnutrition in the US[3]

>15.5 billion

1. Sauer AC JPEN 2019 ahead of print. **2.** Robinson JPEN 1987; 11: 49-51. **3.** Goates S PLoS One. 2016;11:e0161833.

The Malnutrition Paradox



GI Intolerance is the “BRAKE” on Effective *Enteral Nutrition Delivery

*Enteral Nutrition is Oral Nutrition Supplement or Tube feeding

Goals and Objectives

- Define enteral nutrition intolerance
- Analyze the clinical reasons for interrupting enteral nutrition
- Determine the relevancy of data supporting the identified “reasons” for interrupting enteral nutrition

Tolerate Definition

Verb

Allow the existence, occurrence, or practice of (something that one does not necessarily like or agree with) without interference.

- accept or endure (someone or something unpleasant or disliked) with forbearance.
- be capable of continued subjection to (a drug, toxin, or environmental condition) without adverse reaction

Synonyms

Allow, permit, authorize, sanction, condone, agree to, accede to, approve of

Enteral Feeding “Interruption”

*Derived From ICU Studies

- Nausea and vomiting (OS)
- High gastric residuals (O)
- Diarrhea (O)
- Abdominal pain (S)
- Bowel sounds (O)
- Bloating (S)
- Abdominal distention (O)

O – Objective S - Subjective

Nursing Survey of Enteral Intolerance

- Survey of 2298 US Nurses on GI Intolerance
- 42% University-Based Nurses
- 6 Assessment Tools Used to Determine GI Intolerance
  - Gastric Residual Volume (97.1%)
  - Abdominal Distention (88.5%)
  - Vomiting (86%)
  - Bowel Sounds (79.7%)
  - Nausea (79.6%)
  - Abdominal Discomfort (79.3%)

64% use all 6 assessment tools

5% use 1 assessment tool

Methany et al: Am J Crit Care 2012

Gastric Residuals:

- Enteral Nutrition Held:
  - < 200 ml – 24.9%
  - > 200 ml - 36.5%
  - > 250 ml – 21.4%
  - > 500ml – 12.6%

- ASPEN Guideline:
  - Gastric residual volumes 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 feeding should not occur for GRVs < 500 mL.

Hospital-Wide Study
Enteral Nutrition Enteral Feeding Intolerance (2015)

Rx	Total	ICU	Non-ICU
Anti-emetic Pro-kinetic	47%	46%	48%
Anti-diarrheal	3%	4%	1%
Anti-Motility	2%	0%	5%
Combo	5%	4%	5%
Decrease TF Rate	31%	28%	35%
Hold TF < 24 Hours	25%	23%	29%
Stop TF	5%	4%	5%
Change NG to NJ	15%	20%	5%
Change to PN	15%	12%	20%

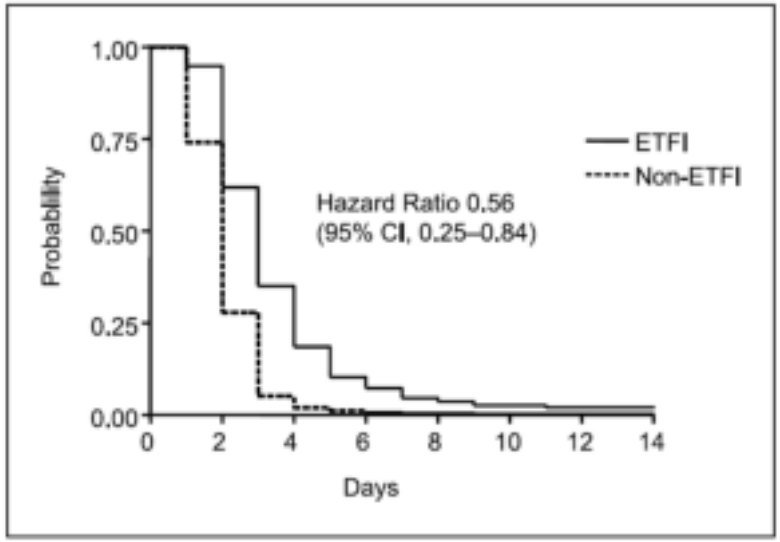
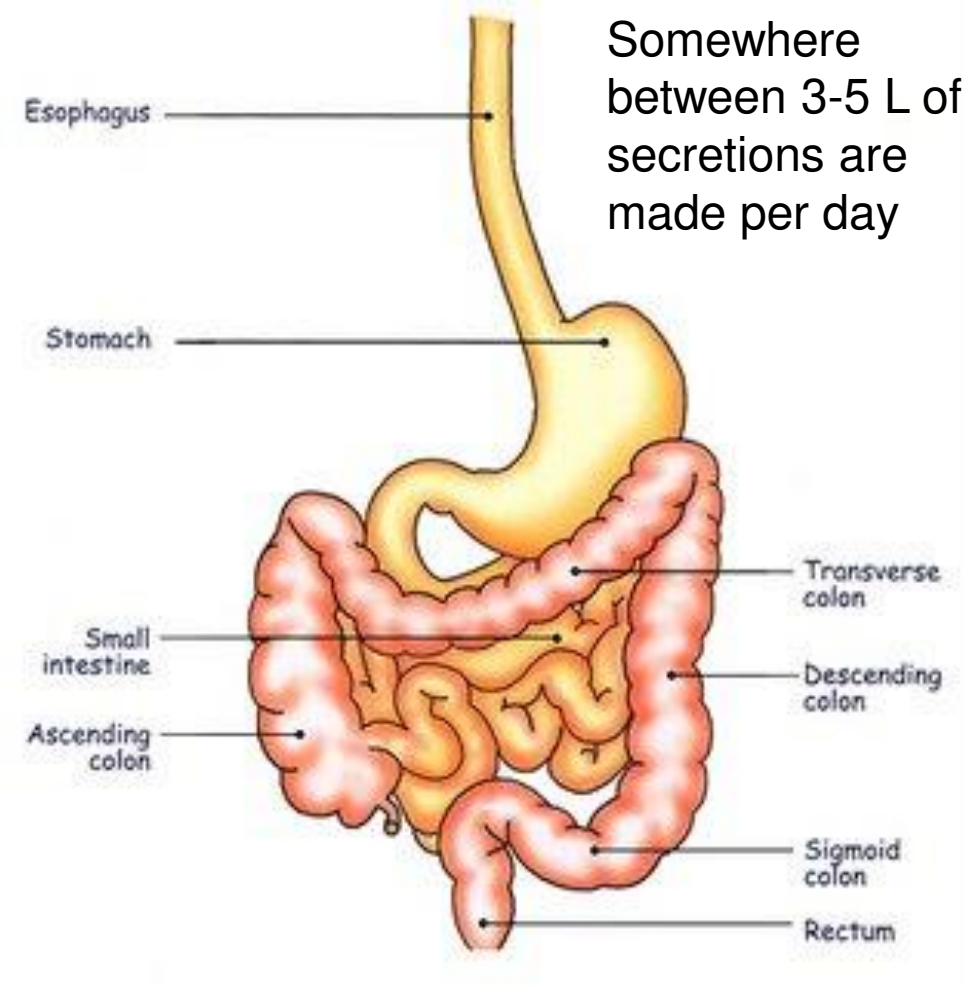


Figure 3. Kaplan-Meier curves showing proportion of patients not achieving goal rate as a function of time in days after commencement of feeding. ETFI, enteral tube feeding intolerance.

Wang et al: JPEN 2015

Gastrointestinal Gut Secretions

Even When NPO



Somewhere between 3-5 L of secretions are made per day

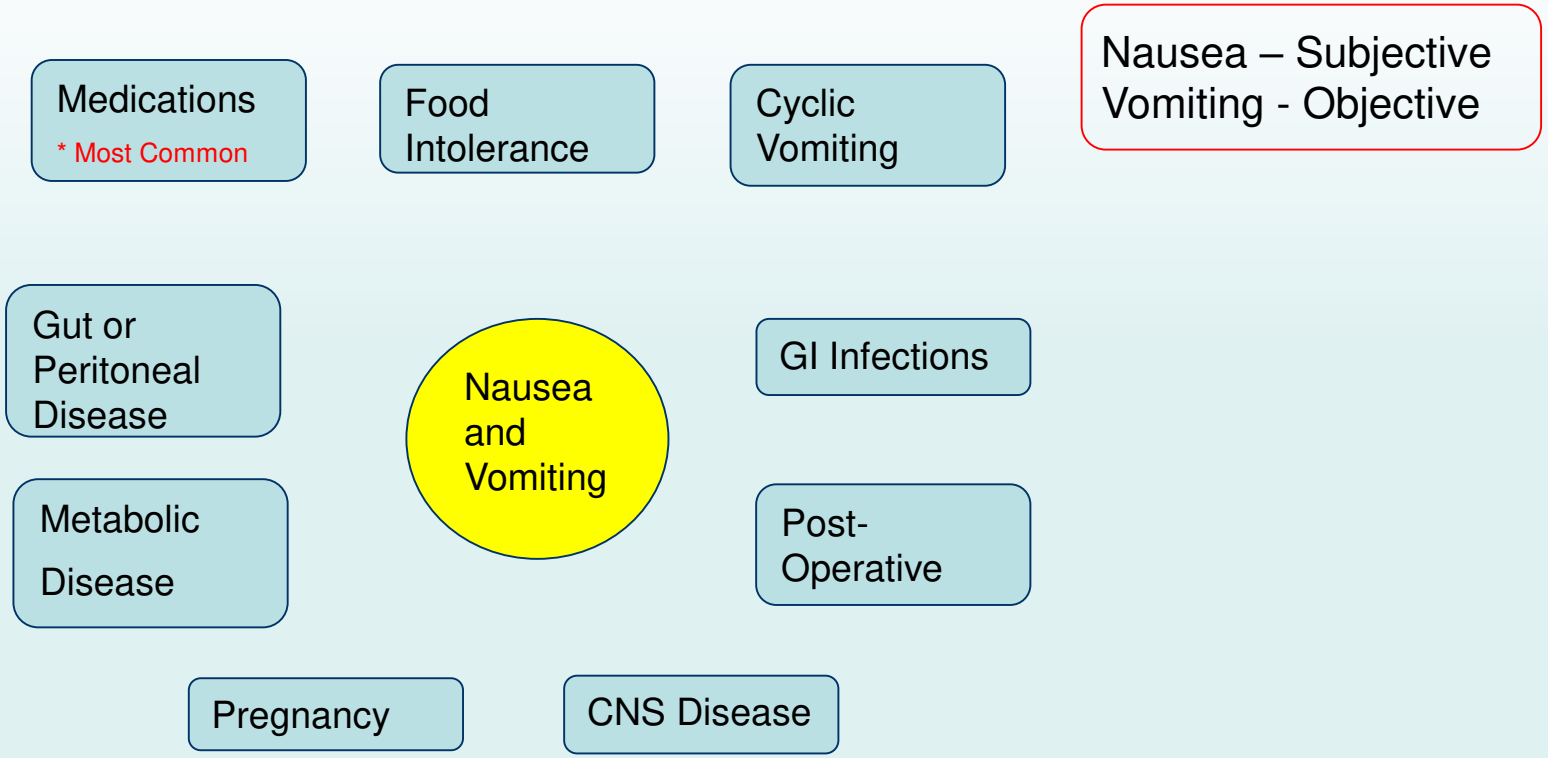
Enteral Feeding Intolerance "Biomarkers"

- Nausea and Vomiting
- Diarrhea
- Presence of Bowel Sounds
- Abdominal Distention
- Bloating
- Gastric Residual Volumes

Nausea and Vomiting

There Are No Data Evaluating the Use of Nausea and Vomiting For Determination of Enteral Nutrition Tolerance

Differential Diagnosis of Nausea and Vomiting



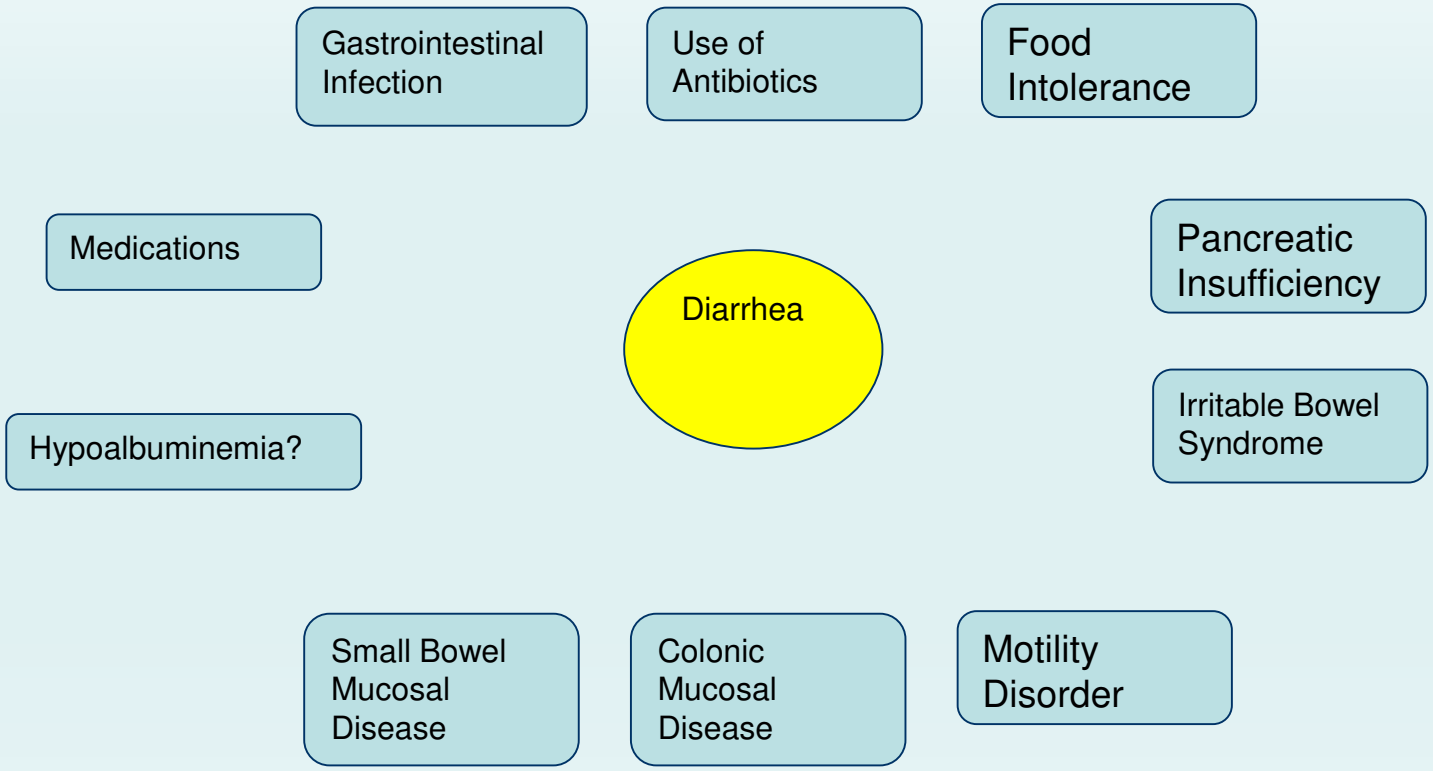
The Differential Diagnosis Needs to be Vetted in a Step-Wise; Time Efficient Manner

Diarrhea

Limited Data Investigating its Use as a Meaningful Tool for Clinicians

Diarrhea With Enteral Nutrition

Diarrhea - Objective



The Differential Diagnosis Needs to be Vetted in a Step-Wise; Time Efficient Manner

Diarrhea
Definition Difficulty

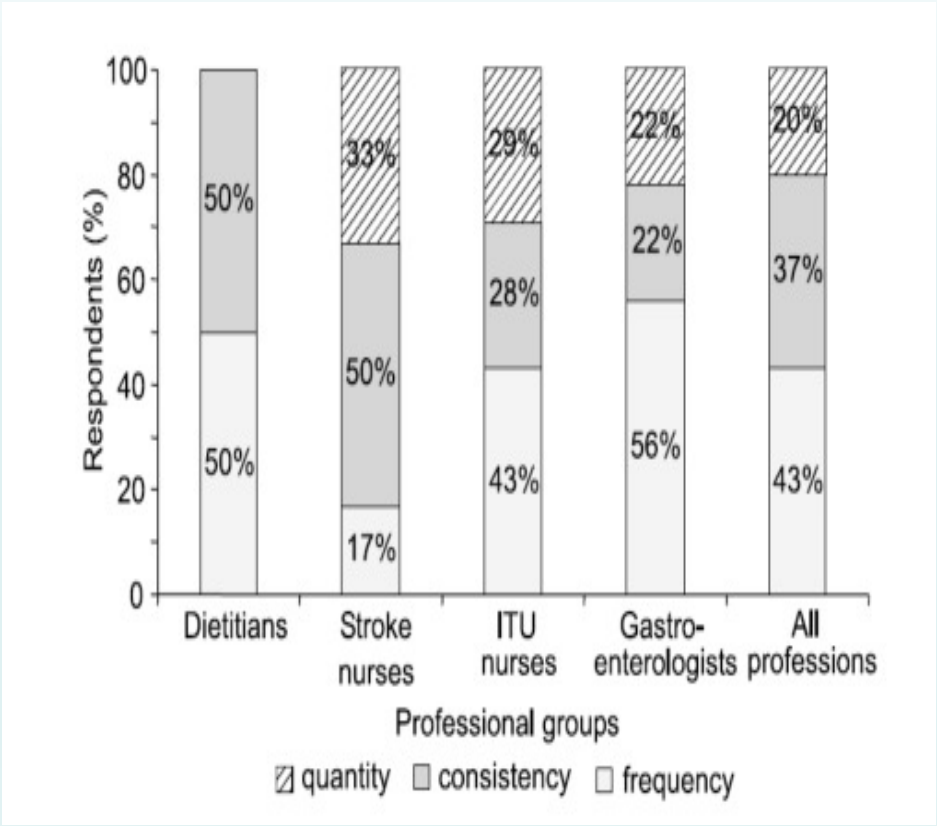
Survey for Factors That Influence Diagnosis of Diarrhea to Interrupt Tube Feedings

- 8 Dietitians
- 7 Stroke Nurses
- 7 ICU Nurses
- 11 GI Physicians

Agreement of 3 Risk Factors

- Stool Frequency – 43%
- Stool Consistency – 37%
- Stool Quantity – 20%

Whelan et al; J Human Nutr Dietet 2003



The Term Diarrhea Has More Than 33 Definitions in the Literature

Bernard et al; Nutr Clin Pract 2004

Impact of Fiber and Probiotics on Diarrhea with Enteral Nutrition

Table 2 Randomized controlled trials that measure the preventive impact of fiber on stool output or diarrhea

Reference	Patient group	Number	Fiber studied	Results
Vandewoude *et al.* [14]	Geriatrics	155	Cellulose, hemicelluloses, pectin, inulin	Reduced number of stools, improved stool consistency
Hart and Dobb [15]	ICU	68	Ispaghula husk	No effect
Homann *et al.* [16]	Medicine/surgery	100	Partially hydrolyzed guar gum	Reduced diarrhea incidence
Spapen *et al.* [17]	ICU (sepsis)	25	Partially hydrolyzed guar gum	Reduced diarrhea incidence
Schultz *et al.* [18]	ICU	44	Pectin/fiber mixture[a]	No effect
Belknap *et al.* [19]	Medicine/surgery/ICU	60	Psyllium	No effect
Dobb and Towler [20]	ICU	91	Soy polysaccharides	No effect
Frankenfield and Beyer [21]	ICU	9	Soy polysaccharides	No effect
Guenter *et al.* [22]	ICU	100	Soy polysaccharides	No effect
Reese *et al.* [23]	Postoperative	80	Soy polysaccharides	Reduced diarrhea incidence in men only
de Kruif and Vos [24]	Postoperative	60	Soy polysaccharides	Reduced diarrhea score
Khalil *et al.* [25]	Postoperative	16	Soy polysaccharides + oat fiber	No effect

[a] Oat, soy, gum arabic, carboxymethylcellulose, fructooligosaccharides.

Table 3 Randomized controlled trials that measure the impact of probiotics on stool output or diarrhea in patients receiving enteral nutrition

Reference	Patient group	Probiotic intervention and placebo	Sample size	Results	*P* value
Heimburger *et al.* [38]	41 adults starting EN	*Lactobacillus acidophilus* and *L. bulgaricus* (3 g/day)	18	31% developed diarrhea	0.21
		Placebo	23	11% developed diarrhea	
Alberda *et al.* [39]	28 adults starting EN on ICU	VSL#3 – live cells (9×10^{11} bacteria/day)	10	14% of days with diarrhea	NS
		VSL#3 – DNA only (9×10^{11} bacteria/day)	9	12% of days with diarrhea	
		Placebo	9	23% of days with diarrhea	
Bleichner *et al.* [40]	128 adults starting EN on ICU	*Saccharomyces boulardii* (2 G/D)	64	14% of days with diarrhea	0.0069
		Placebo	64	19% of days with diarrhea	
Frohmader *et al.* [41••]	45 adults starting EN on ICU	VSL#3 (9×10^{11} bacteria/day)	20	0.5 liquid stools/day	0.03
		Placebo	25	1.1 liquid stools/day	
Ferrie and Daley [42••]	36 adults with diarrhea during EN on ICU	*L. rhamnosus* GG (2×10^{10} cells/day) and inulin (560 mg/day)	18	3.8 days duration of diarrhea	0.08
		Inulin (560 mg/day)	18	2.6 days duration of diarrhea	
Barraud *et al.* [43••]	167 adults starting EN on ICU	Ergyphilus (2×10^{10} cells/day)	87	55% developed diarrhea	NS
		Placebo	80	53% developed diarrhea	

Both Fiber and Probiotics Have Not Consistently Been Shown to Improve Diarrhea

Whelan et al; Curr Opin Gastro 2011

Bowel Sounds and Enteral Nutrition

- Limited Data Investigating its Use as a Meaningful Tool for Clinicians

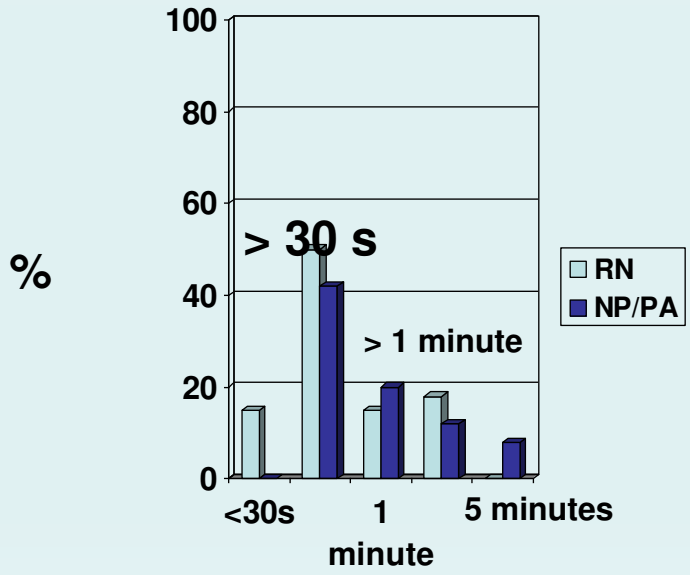
Bowel Sounds

Bowel Sounds - Objective

- Changes of GI motility following abdominal surgery first noted on X-ray in the 1890's
- One century ago the practice of listening for bowel sounds was initiated (nurses)
- Belief that bowel sounds correlate with bowel function

Bowel Sounds Survey Hospital-Based

- **RN (19) and (54) NP/PA surveyed**
- **How long do you listen for bowel sounds?**



- Madsen et al; Am J Nurs 2005

Correlation of Bowel Sounds With Bowel Function

- 38 patients following colon surgery
  - Early fed group – 5.2 day LOS
  - Traditional fed group – 8 day LOS
  - Ileus group – 10.6 day length of stay

- *Neither bowel sounds nor flatus production were a good indicator of oral tolerance.

- **Bufo et al; Dis Colon Rectum 1994**

Abdominal Distention and Bloating

Limited Data Investigating its Use
as a Meaningful Tool for Clinicians

Intraluminal Gas

- Total volume at any one time is 100 – 200 ml
- Complicated process of gas input and output
- Gas in GI tract
  - Swallowing
  - Chemical reactions
  - Fermentation
  - Diffusion (from blood)

Bloating – Subjective
Distention - Objective

Abdominal Distention and Bloating

- 30% of people in a US survey had a regular feeling of bloating
- 75% of these people quantified their bloating as severe

- Thompson et al; Functional Intestinal Disorders, 2000

Pathophysiology of Bloating/Distention Four Factors

- Subjective sensation
- Objective girth changes (distention)
- ? Dependent on volume of intra-abdominal contents
- Abdominal wall muscular activity

Objective Abdominal Distention May Not Correlate to Symptoms of Boating

Does Bloating Equal Abdominal Distention?

Study	Device	Y/N
Poynard et al	Tape measure	No
Maxton et al	Tape measure	Yes
Sullivan et al	CT scan	Yes
Lea et al	Plethysmography	Yes

Poynard et al, J Neurogastro Motility 2013
Maxton et al; Gut 1991
Sullivan et al; ISRN Gastro, 2012
Lea et al: Gastro, 2003

Do Patients With Bloating Have More Intestinal Gas?

Study	Method	Y/N
Lasser et al	Washout	N
Serra et al	Washout	N
Calderella et al	Washout	N
Chami et al	X-ray	Y
Koide et al	X-ray	Y
Poynard et al	X-ray	Y
Maxton et al	CT scan	N

Lasser et al; NEJM 1975
Serra et al: Gastro 1998
Calderella et al, Gastro 2000
Chami et al; Am J Gastro 1991
Poynard et al, J Neurogastro Motility 2013
Maxton et al; Gut 1991

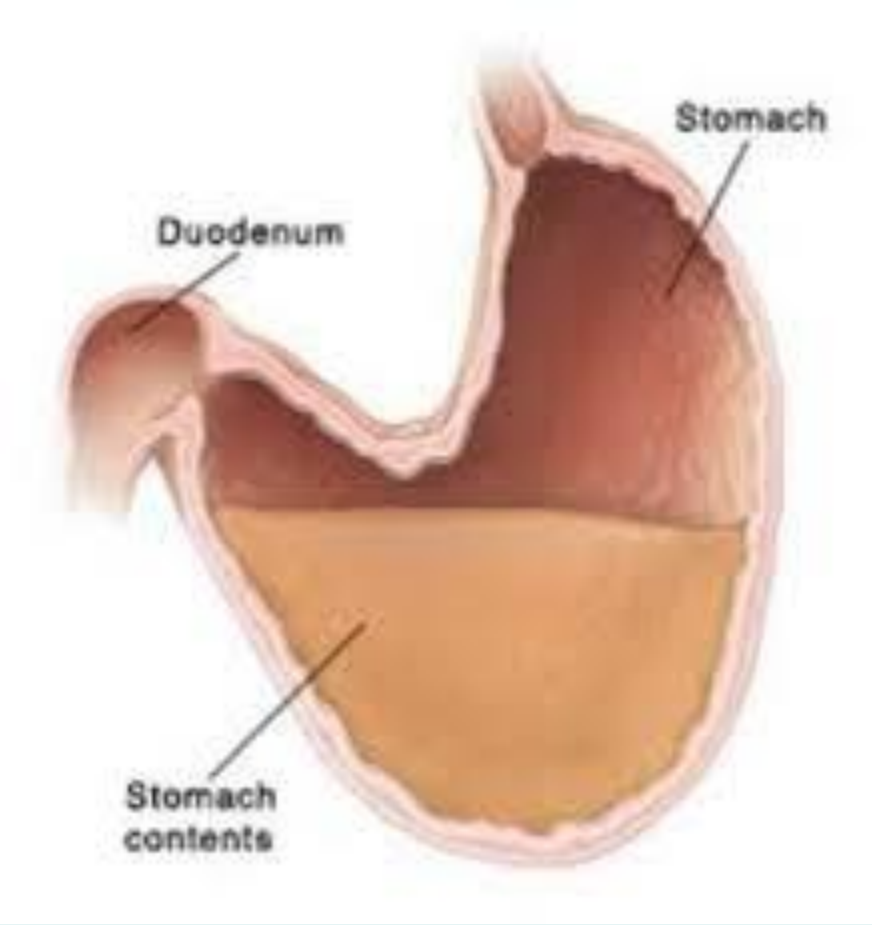
Abdominal Wall

- Shape of abdominal wall influenced by the vertebral column, anterolateral muscles, diaphragm and pelvis.

- Even without volume changes in the gut, subtle changes in body position can create new abdominal distention.

Gastric Residual Volume

GRV - Objective



Gastric Residual Volume

- The Impact of Measuring GRV on Aspiration Events Has been Studied in the ICU
- The Impact of GRV on Aspiration Events on the Hospital Floor Has Not Been Studied
- The Impact of Checking GRV on the Ability to Deliver Nutrition on the Hospital Floor Has Not been Studied

Gastric Residual Volume

Table 2. Randomized Controlled Trials on the Use of Monitoring GRV.

Study	N	Surgical Patients, %	GRV	Type/Size of Tube	Method[a]	Primary End Point[b]	Main Result
GRV higher vs lower thresholds							
Pinilla et al, 2001[68]	96 (80 in final analysis)	50	>150 mL vs >250 mL[c]	NG: 14–18 Fr: n = 41 10 Fr: n = 25 n = 14: alternations of the 2 sizes	Aspiration every 4 h	Frequency of GI intolerance: high GRV, emesis, or diarrhea	No statistical difference, trend of improved EN, and reduced time to reach goal rate with GRV >250 mL[d]
McClave et al, 2005[69]	40	62.5	>200 mL vs >400 mL	NG: n = 21 12 Fr: n = 19 8 Fr: n = 2 PEG: n = 19	NA	Frequency of regurgitation/ aspiration	No statistical difference
Montejo et al, 2010[70]	329 (322 in final analysis)	17.2	>200 mL vs >500 mL[e]	NG: <8 Fr: 3% 8 Fr: 6% 10 Fr: 14.8% 12 Fr: 34% >12 Fr: 42%	Gravity drainage for 10 min or aspiration (50-mL syringe)[f]	Diet volume ratio[g]	First week of ICU stay: mean EN volume ratio 200 mL: 84.5% 500 mL: 88.2% (P = .0002) No between-group difference after second week
Monitoring vs not monitoring GRV							
Reignier et al, 2013[71]	449	NA (93% medical)	>250 mL vs no GRV measurement	NG: no size reported	Aspiration (50-mL syringe)	VAP	No difference
Regular vs variable time interval of monitoring GRV							
Williams et al, 2014[72]	357	NA (28% trauma)	GRV aspiration 4 hourly (control) vs variable regimen (up to 8 hourly, intervention)[h]	NG: 12–14 Fr[i]	Aspiration	Number of gastric tube aspirations per day	More tube aspirations per day in the control group (5.4 vs 3.4 in the intervention group, P < .001)

Elke et al: Nutr Clin Pract, 2015.

Gastric Residual Volume

Table 3. Current Guideline Recommendations on the Use of GRV Monitoring.

Guidelines[a]	DGEM 2013[85]	CCPG 2013[1]	A.S.P.E.N. 2009[2] **and 2016
GRV	For patients, especially those who are admitted with a medical diagnosis, units that can safely handle a concept of not monitoring GRV should do so, thereby reducing nurses' workload. EN delivery rate should be modified in the event of vomiting (A; strong consensus). In (abdomino)surgical patients, GRV should be measured regularly (every 4–6 hours), and a threshold of 200 mL should be considered to adjust the EN delivery rate. If threshold is reached, the EN delivery rate should be modified (strong consensus). The use of lower GRV thresholds is unnecessary.	There are insufficient data to make a recommendation for not checking GRVs and for establishing a specific gastric residual volume threshold. Based on 1 level 2 study, a gastric residual volume of either 250 or 500 mL (or somewhere in between) is acceptable as a strategy to optimize delivery of EN in critically ill patients.	Holding EN for gastric residual volumes <500 mL in the absence of other signs of intolerance should be avoided (grade B).

A.S.P.E.N., American Society for Parenteral and Enteral Nutrition; CCPG, Canadian Clinical Practice Guidelines; DGEM, German Society for Nutritional Medicine; EN, enteral nutrition; GRV, gastric residual volume.
[a]No specific information on the use of GRV monitoring in the currently available ESPEN (European Society for Clinical Nutrition and Metabolism) guidelines on EN in intensive care medicine.[3,47]

Elke et al: Nutr Clin Pract, 2015

Tube Feeding
The Rate "Truth"

- 10 cc/hr = 1 cc every 6 minutes
- 20 cc/hr = 1 cc every 3 minutes
- 30 cc/hr = 1 cc every 2 minutes

Going Forward

- **Content of Enteral Formulations**
  - Alternative Osmolarities
  - Alternative Fats
  - Small Peptide
  - Low Carbohydrate
  - Plant-Based, Non-GMO

Intolerance Tool

Symptom	Mild	Moderate	Severe
Diarrhea	1	2	3
Abdominal pain	1	2	3
Nausea or Vomiting	1	2	3
Regurgitation	1	2	3
Bloating	1	2	3

Mild – 2x or less per week and generally does not interfere with enteral nutrition or oral supplement intake
Moderate – 3x-7x episodes/week and intermittently interferes with delivery of enteral nutrition or oral supplement intake
Severe – 7x or greater per week and usually interferes with delivery of enteral nutrition or oral supplement intake

Conclusion

- Enteral tolerance is under the microscope by clinicians
- We have more reasons to stop EN than we do to initiate it
- Bowel sounds and gastric residual volume are poor biomarkers of enteral intolerance
- There is limited data validating the importance of abdominal distention, bloating, nausea and diarrhea as a biomarker of GI intolerance
- We need a standardized tool to diagnose enteral feeding intolerance