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Nutrition and GI

2012 Clinical Congress Presenter Disclosure Slide

American College of Surgeons ♦ Division of Education

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Nothing to disclose

Objectives

- Determine nutritional goals
- Determine when to add parenteral nutrition
- List differences for critically ill bariatric patient
- List advantages of immunonutrition
- Determine optimal site for enteral tube placement
- Describe new methods of diagnosis and treatment for *C. difficile*

Nutritional goals

- Determine energy requirements
- Ideal body weight
  - Men: 50 kg + 2.3 kg for each inch over 5 ft
  - Women: 45.5 kg + 2.3 kg for each inch over 5 ft
- Harris-Benedict equation not accurate in ICU pts
- Indirect calorimetry most accurate
- 25-30 kcal/kg/day
- Protein 1.2-2 g/kg/day
  - If BMI > 30, >2 g/kg/day
  - May be higher in trauma, burns

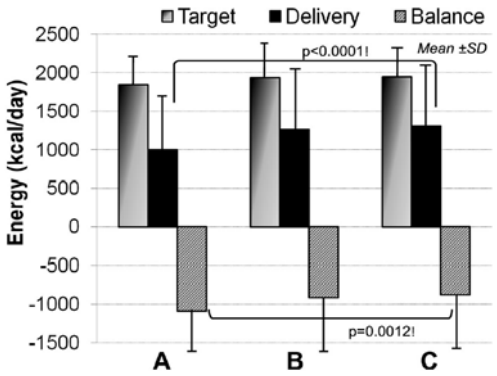
Harris Benedict equation uses basal metabolic rate, Based on weight, height and age, applies activity factor to determine daily energy expenditure
First developed in 1918, revised in 1984

Metabolic cart - determine oxygen consumption (VO_2) and carbon dioxide production (VCO_2) through metabolic measurements

Importance of nutrition support

- Period A: baseline
- Period B: protocol
- Period C: protocol and dietitian

- 80% of ICUs have some type of protocol



Soguel et al, Crit Care Med 2012

Energy deficit and length of hospital stay can be reduced by a two-step quality improvement of nutrition therapy: the intensive care unit dietitian can make the difference.

Prospective time series interventional study, single mixed ICU in Switzerland

Two-step quality program: 1) bottom-up implementation of feeding guideline; and 2) additional presence of an intensive care unit dietitian. The nutrition protocol was based on the European guidelines.

Energy balance was defined as the difference between energy target and the sum of all intakes (nutritional intakes, glucose resulting from glucose, glucosaline or drug infusion, and fat from propofol sedation); it was expressed as crude kcal or kcal*kg^{-1} prehospital body weight*day^{-1}.

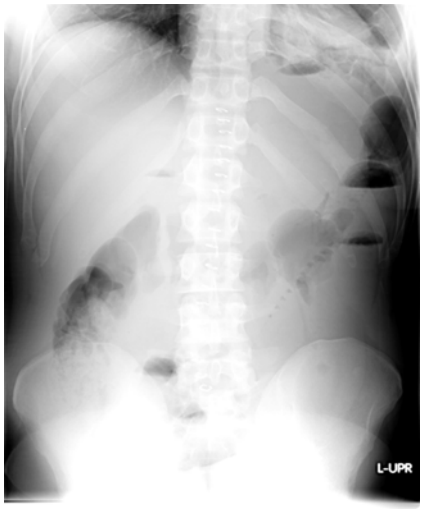
The daily energy balance difference (Fig. 1) was significant between periods A and C with a dietitian (p = .0012), whereas it was not significant between periods A and B. The normalized daily energy delivery (kcal*day^{-1} or kcal*kg^{-1}*day^{-1}) improved significantly in both periods B and C.

Enteral nutrition

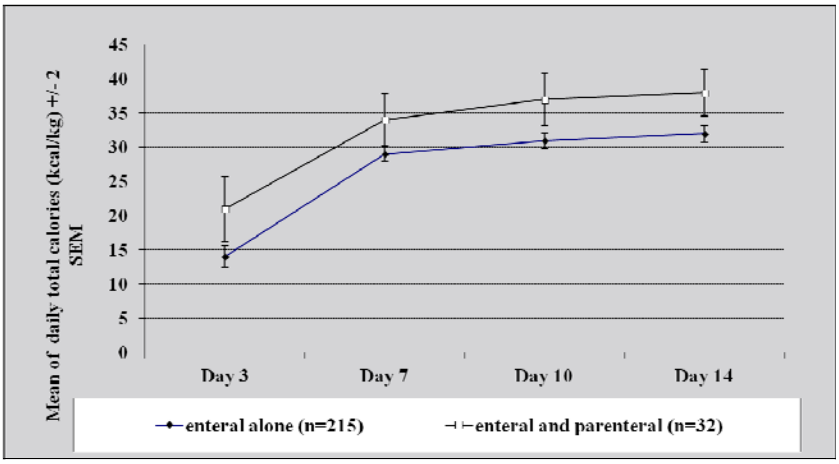
- All the time
- All the patients
- Early

…except when you can't

Ileus



Add parenteral?



Sena et al, JACS, October 2008

Data from the Glue grant

We compared patients receiving PN within 7 days after injury with a control group that did not receive early PN. We then focused on patients who tolerated at least some enteral nutrition (EN) during the first week and evaluated the potential influence of supplemental PN on outcomes in this "enteral tolerant" subgroup. Primary outcomes included occurrence of a nosocomial infection after the first postinjury week. Secondary outcomes included type of infection and hospital mortality.

Of 567 patients enrolled, 95 (17%) received early PN. Early PN use was associated with a greater risk of nosocomial infection (relative risk [RR] = 2.1; 95% CI, 1.6 to 2.6; $p < 0.001$). In the enteral-tolerant subgroup (n = 249), early PN was also associated with an increase in nosocomial infections (RR = 1.6; 95% CI, 1.2 to 2.1; $p = 0.005$) in part because of an increased risk of bloodstream infection (RR = 2.8; 95% CI, 1.5 to 5.3; $p = 0.002$). Mortality tended to be higher in patients receiving additional EN and PN versus EN alone (RR = 2.3; 95% CI, 1.0 to 5.2; $p = 0.06$).

Add parenteral?

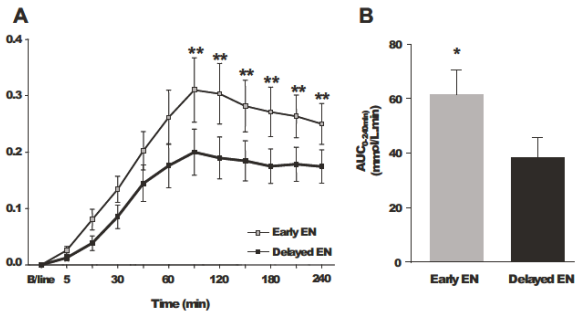
- Randomized multicenter trial comparing early initiation (European guidelines) vs. late initiation (North American Guidelines)
- > 4000 patients randomized to "early" or "late" PN if caloric goal not met day 2
  - "early" day 2
  - "late" PN day 7
- Late initiation of PN associated with lower mortality, fewer infections

Casaer MP, et al. NEJM, June 29, 2011

Trickle tube feeds

- Preserve mucosal integrity
- Do NOT provide adequate nutritional support
- 50-65% of total required

Delaying enteral feeding



- Delayed enteral nutrition decreases plasma glucose levels

Nguyen et al, Crit Care Med, 2012

Patients were randomized to either enteral nutrition within 24 hrs of admission (14 "early feeding": 8 males, 6 females, age 54.9 ± 3.3 yrs) or no enteral nutrition during the first 4 days of admission (14 "delayed feeding": 10 males, 4 females, age 56.1 ± 4.2 yrs).

In the delayed feeding group, both the duration of mechanical ventilation (13.7 ± 1.9 days vs. 9.2 ± 0.9 days; p = .049) and length of stay in the intensive care unit (15.9 ± 1.9 days vs. 11.3 ± 0.8 days; p = .048) were greater.

Tube site

- Retrospective review
- Gastric, duodenal, jejunal
- Aspiration—pepsin in tracheal secretions
- Pneumonia—CPIS
- Multivariate analysis
  - Duodenal vs gastric, OR 0.52
  - Jejunal vs gastric, OR 0.30
- Differences not statistically significant when adjusted for aspiration

Metheny et al, JPEN, 2011

As compared with the stomach, the percentage of aspiration was 11.6% lower when feeding tubes were in the first portion of the duodenum, 13.2% lower when in the second/third portions of the duodenum, and 18.0% lower when in the fourth portion of the duodenum and beyond (all significant at $P < .001$). Pneumonia occurred less often when feedings were introduced at or beyond the second portion of the duodenum ($P = .020$).

NPO and operations

- NPO after midnight
  - <10% achieve caloric goal
- Continuous feeding safe in burn patients
- Jejunal feeds up to time of OR safe for nonabdominal operations
- Pilot study with continuous feeding
  - additional 12 hours of enteral nutrition
  - additional 1065 calories per day

Pearson KS et al, *J Burn Care Rehab* 1992
Moncure M et al, JPEN, 1999
McElroy et al, SCCM 2012

Immunonutrition

- Arginine
- Glutamine
- Chromium
- Selenium
- Fish oil
- Antioxidants
- …

Arginine

- Deficiency occurs due to arginase release from granulocytes
- Results in T cell receptor abnormalities
  - Impaired wound healing
  - Predisposes to infection
- Levels **INCREASE** during sepsis
- ? more harm than good

Bansal et al, JPEN, 2005
Heyland et al, JPEN, 2001
Chiarla et al, Amino Acids, 2006

Different prostaglandins significantly alter the metabolism of arginine. Prostaglandins from omega-6 fatty acids increases arginase I expression. By decreasing arginase I expression, prostaglandins from omega-3 fatty acids may increase available arginine. The specific combinations of dietary fatty acids and arginine should be considered when tailoring dietary regimens.

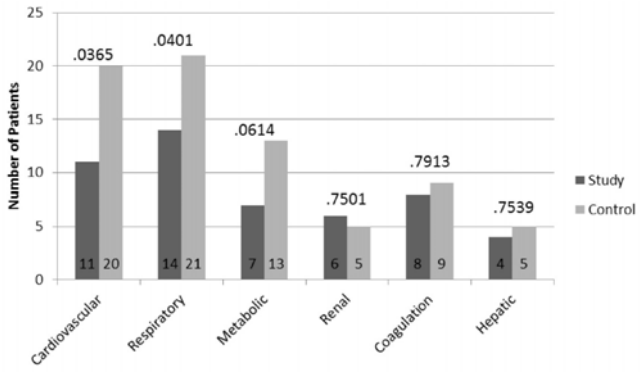
Glutamine

- Rapid depletion of muscle stores
- Benefits
  - Anti-oxidant
  - Maintenance of gut barrier function
  - Enterocyte fuel
- Reduced morbidity and mortality
  - Reduction in infectious complications

Zhou, JPEN 2003
Houdjik, Lancet 1998

Immunonutrition and organ failure

- Ω-3 PUFAs AND γ-linolenic acid



Pontes-Arruda, et al. Crit Care, 2011

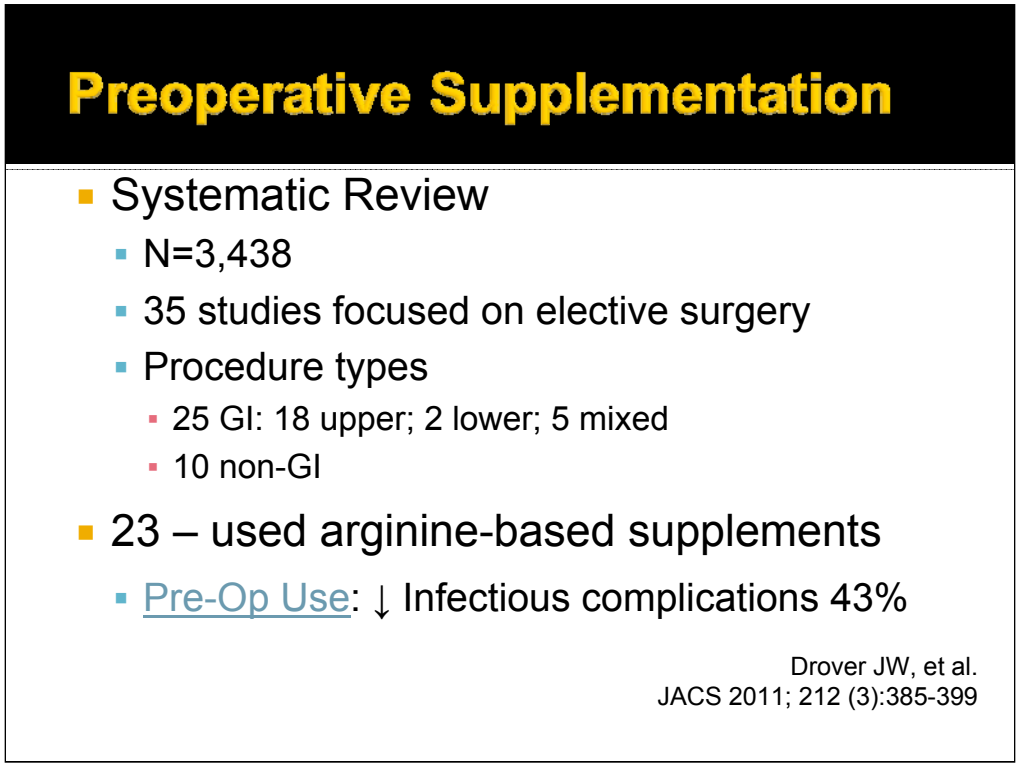
This study was a prospective, multicenter, randomized, double-blinded, controlled trial designed to investigate whether EPA/GLA could have an effective role in the treatment of patients with early sepsis (systemic inflammatory response syndrome with confirmed or presumed infection and without any organ dysfunction) by reducing the progression of the disease to severe sepsis (sepsis associated with at least one organ failure) or septic shock (sepsis associated with hypotension despite adequate fluid resuscitation). Secondary outcomes included the development of individual organ failure, increased ICU and hospital length of stay, need for mechanical ventilation and 28-day all-cause mortality.

Decreased incidence of organ failure, reduced duration ventilation, decreased LOS, no change in mortality

Immunonutrition summary

		CCCPG	ESPEN	ASPEN/SCCM
Trauma	Arginine	No benefit	Benefit	Benefit
	Glutamine	Possible benefit	Benefit	Possible benefit
	Antioxidants			Benefit
Sepsis	Arginine	Harm	Harm	Harm
	Glutamine			
	Antioxidants			Benefit
ALI/ARDS	Arginine	No benefit		
	Glutamine			
	ω-3 fatty acids	Benefit	Benefit	Benefit
	Antioxidants		Benefit	Benefit

Hegazi and Wischmeyer *Critical Care* 2011 **15**:234



there is compelling level 1 evidence that preoperative intervention prior to elective major surgery reduces the morbidity of major morbidities by 40%
In a meta analysis done by Drover, et al. published in 2011. They looked at over 3400 patients through 35 different studies focused on elective surgeries. 25 of these were focused on the GI tract.

These studies looked at supplemental nutritional interventions, where a vast majority looked at Arginine based supplements compared to iso-caloric supplements or standard care controls. Use of these arginine supplemented diets were associated with a 40% reduction in overall infectious complications.

The immune modulating formulas are given 5-7 days prior to surgery 3 times a day.

Metanalysis

7 randomized studies

Look at the risk reduction

Mixed Pre- and Post-op Supplementation

- Meta-analysis: 26 RCTs
- N = 2496
  - 1252 Immunonutrition vs 1244 Control (Isocaloric)

- ↓ infection rates by 46%
- ↓ length of stay ~ 2 days
- No mortality benefit

Marimuthu K, et al.
Ann Surg 2012; 255:1060-1068

Critically ill bariatric patients

- 11-14 kcal/kg/day
- 22-25 kcal/kg/day IBW
- Protein
  - BMI 30-40
    - >2 g/kg/day IBW
  - BMI >40
    - ≥ 2.5 g/kg/day IBW
- Goals
  - Reduce fat mass
  - Improve insulin sensitivity
  - Preserve lean body mass

BMI >30

McClave et al, *JPEN J Parenter Enteral Nutr.* 2009

Some have promoted the notion of hypocaloric, high-protein feeding as a way to minimize the problems associated with overfeeding while allowing for a net positive nitrogen balance and facilitating fat weight loss. In 2009, the Society for Critical Care Medicine and American Society for Parenteral and Enteral Nutrition released a joint consensus statement in which they endorsed the use of hypocaloric enteral feeding for obese ICU patients.[38] In this statement, they suggest providing no more than 60% to 70% of target caloric requirements, or 11 to 14 kcal/kg actual body weight per day. They recommend delivering at least 2.0 g/kg ideal body weight (IBW) per day as protein in class I and II obesity and at least 2.5 g/kg IBW per day for class III obesity. There are relatively few absolute contraindications to this approach, but those with progressive renal and hepatic failure where a high protein load is detrimental, as well as those who require a full caloric load, such as those with recurrent hypoglycemia or severe immunocompromised state, should not be included.

Estimation of target caloric requirements itself is complicated by lack of validated formulas for the critically ill obese patient. Direct calculation using indirect calorimetry may provide useful information but is not practical. When employing the Harris-Benedict equation, for example, there are shortcomings when using IBW as well as actual body weight. Some researchers have advocated the use of an obesity-adjusted weight with a 25% correction of excess weight above the IBW as follows[39]:

Adjusted body weight = (actual weight - IBW) 0.25 + IBW

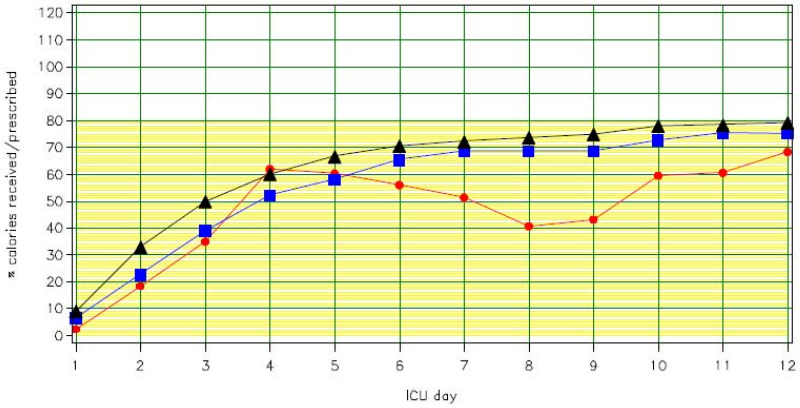
McClave SA, Martindale RG, Vanek VW; ASPEN Board of Directors; American College of Critical Care Medicine; Society of Critical Care Medicine. Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (ASPEN). *JPEN J Parenter Enteral Nutr.* 2009;33(3):277-316.

Timing essential

- Malnourished patients
  - PREoperative nutritional support ≥ 7 days
    - Enteral if possible
- Well-nourished patients
  - Enteral nutrition within 48 hours
  - Parenteral nutrition if >5-7 days without oral intake, adequate enteral nutrition

Benchmarks

Figure 1.1 Adequacy of Calories from Appropriate Nutrition

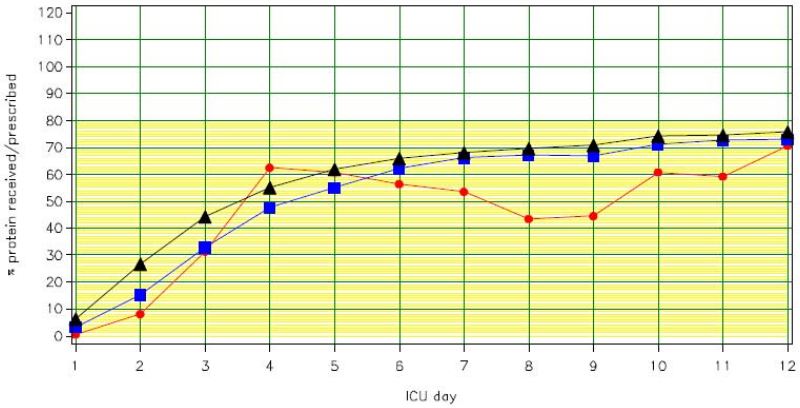


http://www.criticalcarenutrition.com International Nutrition Survey, 2011

Darren Heyland's group, the Clinical Evaluation Research Unit, in Kingston ON
To date, there have been three international period prevalence surveys of nutrition therapies in Intensive Care Units (ICUs), with over 150 ICUs participating each year. This ongoing quality improvement (QI) initiative, aims to compare current nutrition practices in ICUs within and across different countries. The aim of the initiative is to illuminate differences, highlight strengths and weaknesses, and hopefully lead to practice improvements.
Prospective survey of nutrition practices in ICUs throughout the world, 20 sites in canada, 41 in the US
highlighting their strengths and weaknesses in comparison to other ICUs in the database and to the Canadian Clinical Practice Guidelines.

Benchmarks

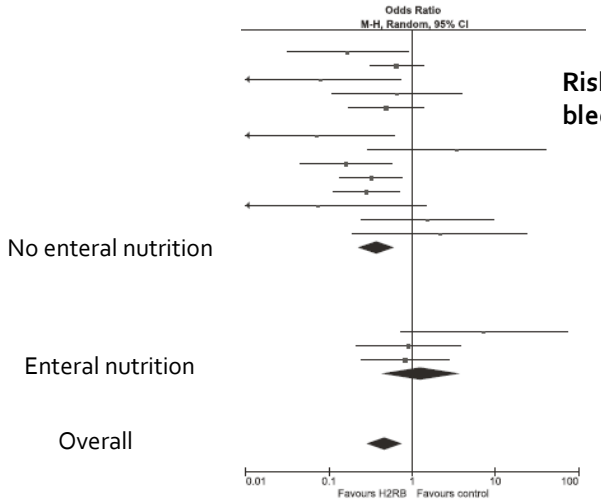
Figure 1.2 Adequacy of Protein from Appropriate Nutrition



http://www.criticalcarenutrition.com International Nutrition Survey, 2011

Go to Criticalcarenutrition.com for more information about how your ICU can participate

Peptic ulcer prophylaxis

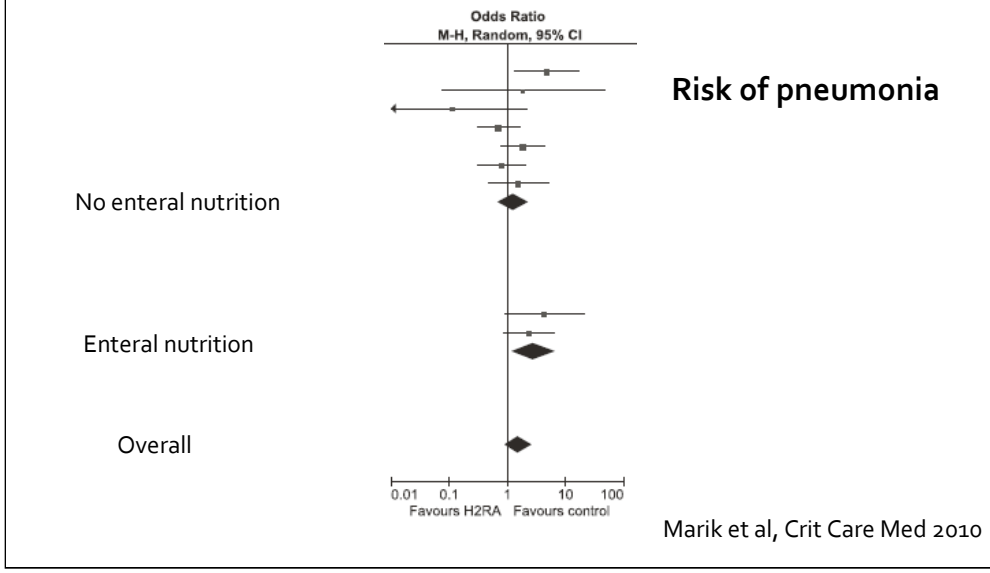


Risk of upper gastrointestinal bleeding

Marik et al, Crit Care Med 2010

Systematic review to determine the benefit and risks of stress ulcer prophylaxis and the moderating effect of enteral nutrition.
Randomized, controlled studies that evaluated the association between stress ulcer prophylaxis and gastrointestinal bleeding. We included only those studies that compared a histamine-2 receptor blocker with a placebo.
Overall, stress ulcer prophylaxis with a histamine-2 receptor blocker reduced the risk of gastrointestinal bleeding (odds ratio 0.47; 95% confidence interval, 0.29-0.76; $p < .002$; $I = 44\%$); however, the treatment effect was noted only in the subgroup of patients who did not receive enteral nutrition.

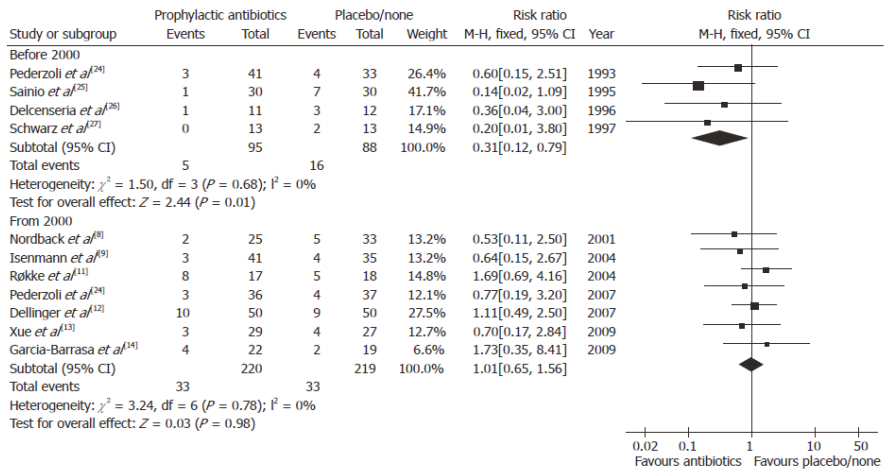
Peptic ulcer prophylaxis



Overall histamine-2 receptor blockers did not increase the risk of hospital-acquired pneumonia (odds ratio 1.53; 95% confidence interval, 0.89-2.61; p = .12; I = 41%); however, this complication was increased in the subgroup of patients who were fed enterally (odds ratio 2.81; 95% confidence interval, 1.20-6.56; p = .02; I = 0%).

Overall, stress ulcer prophylaxis had no effect on hospital mortality (odds ratio 1.03; 95% confidence interval, 0.78-1.37; p = .82). The hospital mortality was, however, higher in those studies (n = 2) in which patients were fed enterally and received a histamine-2 receptor blocker (odds ratio 1.89; 95% confidence interval, 1.04-3.44; p = .04, I = 0%).

Pancreatitis and antibiotics



Study or subgroup	Prophylactic antibiotics Events	Total	Placebo/none Events	Total	Weight	Risk ratio M-H, fixed, 95% CI	Year
Before 2000							
Pederzoli *et al*[24]	3	41	4	33	26.4%	0.60[0.15, 2.51]	1993
Sainio *et al*[25]	1	30	7	30	41.7%	0.14[0.02, 1.09]	1995
Delcenseria *et al*[26]	1	11	3	12	17.1%	0.36[0.04, 3.00]	1996
Schwarz *et al*[27]	0	13	2	13	14.9%	0.20[0.01, 3.80]	1997
Subtotal (95% CI)		95		88	100.0%	0.31[0.12, 0.79]	
Total events	5		16				
Heterogeneity: $\chi^2 = 1.50$, df = 3 ($P = 0.68$); $I^2 = 0\%$							
Test for overall effect: $Z = 2.44$ ($P = 0.01$)							
From 2000							
Nordback *et al*[8]	2	25	5	33	13.2%	0.53[0.11, 2.50]	2001
Isenmann *et al*[9]	3	41	4	35	13.2%	0.64[0.15, 2.67]	2004
Røkke *et al*[11]	8	17	5	18	14.8%	1.69[0.69, 4.16]	2004
Pederzoli *et al*[24]	3	36	4	37	12.1%	0.77[0.19, 3.20]	2007
Dellinger *et al*[12]	10	50	9	50	27.5%	1.11[0.49, 2.50]	2007
Xue *et al*[13]	3	29	4	27	12.7%	0.70[0.17, 2.84]	2009
Garcia-Barrasa *et al*[14]	4	22	2	19	6.6%	1.73[0.35, 8.41]	2009
Subtotal (95% CI)		220		219	100.0%	1.01[0.65, 1.56]	
Total events	33		33				
Heterogeneity: $\chi^2 = 3.24$, df = 6 ($P = 0.78$); $I^2 = 0\%$							
Test for overall effect: $Z = 0.03$ ($P = 0.98$)							

Jiang et al, World J Gastroenterology, 2012

RCTs comparing prophylactic antibiotics for SAP with control or placebo were included for meta-analysis. The mortality outcomes were pooled for estimation, and re-pooled estimation was performed by the sensitivity analysis of an ideal large-scale RCT. significant reduction of mortality rate in the period before 2000, while no significant reduction in the period from 2000 [Risk Ratio, (RR) = 1.01, P = 0.98]. Funnel plot (scatterplot of treatment effect against a measure of study size. It is used primarily as a visual aid to detecting bias or systematic heterogeneity) indicated that there might be apparent publication bias in the period before 2000. Sensitivity analysis showed that the RR of mortality rate ranged from 0.77 to 1.00 with a relatively narrow confidence interval ($P < 0.05$). However, the number needed to treat having a minor lower limit of the range (7-5096 patients) implied that certain SAP patients could still potentially prevent death by antibiotic prophylaxis.

C. Difficile Colitis

- Most laboratories perform toxin testing using an enzyme immunoassay method
  - Sensitivities range from 60-70%, specificity 98%
  - Symptomatic patients with negative tests retested with cell culture cytotoxicity neutralization assays
- PCR method of diagnosis (nucleic acid amplification)
  - Detects gene that encodes Toxin B, not toxin itself
    - Should only test patients that actually have diarrhea
  - Improved sensitivity and specificity to EIA, 2-step
  - Not better than toxigenic culture
  - Rapid turnaround—decreases isolation time

Most laboratories perform toxin testing using an enzyme immunoassay method. In general these tests have sensitivities ranging from 60 to 70% and specificities of 98%. When using these methods, symptomatic patients with negative tests should be tested by another more sensitive method.
Because these assays detect a gene that encodes toxin and not the toxin itself it is important that laboratories test only patients with diarrhea. These molecular assays have been shown to be superior to toxin EIAs, CCNA and 2-step algorithms, but not to toxigenic culture.

C. diff scoring system

TABLE 4. Proposed CDAD Severity Scoring System

1-3 points "mild-moderate disease," 4-6 points "severe" disease, 7 or more points 'severe complicated' disease

Criteria	Points
Immunosuppression and/or chronic medical condition	1
Abdominal pain and/or distention	1
Hypoalbuminemia (<3 g/dL)	1
Fever > 38.5°C	1
Intensive care unit admission	1
CT scan with nonspecific findings of pancolitis, ascites, and/or bowel wall thickening	2
While blood cell count >15,000 or < 1500 and/or band count >10%	2
Creatinine 1.5 fold > baseline	2
Abdominal peritoneal signs	3
Vasopressors required	5
Mechanical ventilation required attributed to CDAD	5
Disorientation, confusion, or decreased consciousness	5

*This scoring system is for patients with a diagnosis of CDAD and is not yet validated.

Neal et al, *Ann Surg* 2011

C. difficile: Novel surgical therapy

- Laparoscopic diverting loop ileostomy and colon lavage as treatment
  - Severe, complicated C. difficile colitis
  - Contraindicated with concurrent abdominal compartment syndrome
  - Loop ileostomy with distal colonic washout
  - Postoperative antegrade Vancomycin enemas
- Reduced mortality compared to historical population (19% vs 50%; odds ratio, 0.24; P = 0.006)
- Preservation of the colon was achieved in 39 of 42 patients (93%).

Neal et al, *Ann Surg* 2011

42 patients diagnosed with severe, complicated ("fulminant") CDAD and were treated at the University of Pittsburgh Medical Center or VA Pittsburgh Healthcare System between June 2009 and January 2011
creation of a loop ileostomy, intraoperative colonic lavage with warmed polyethylene glycol 3350/electrolyte solution via the ileostomy and postoperative antegrade instillation of vancomycin flushes via the ileostomy.
The operation was accomplished laparoscopically in 35 patients (83%). This treatment strategy resulted in reduced mortality compared to our historical population (19% vs 50%; odds ratio, 0.24; P = 0.006). Preservation of the colon was achieved in 39 of 42 patients (93%).

Summary

- How much?
  - 100% probably not necessary
- Don't delay
- Immunonutrition
  - ? overall benefit to arginine, glutamine
  - Benefit to ω-3 PUFAs AND γ-linolenic acid
- Enteral nutrition alone may be all the ulcer prophylaxis needed

Summary

- Currently no role for prophylactic antibiotics in pancreatitis
- New methods for diagnosis, treatment of *C. difficile* colitis