# Nutrition support in the major trauma patient: Open abdomen?? Easy peasy lemon squeezy!!!

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### Faculty Disclosures Gordon S. Doig & Fiona Simpson

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Within the context of a clinical case:

• Consider how the results of recent clinical research might apply to the patient discussed.

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- Review benefits of earlier nutrition (*nutrition = calories + protein + lipids*) in trauma.
- Summary.



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  - open abdomen, scheduled for review next day
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What type of nutritional therapy would this patient receive in *your* hospital?





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- **3.** In our hospital, this patient would have received a postpyloric tube at time of initial surgery and enteral nutrition would be started.





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- **4.** Enteral nutrition begun via gastric tube after initial surgery.
- **5.** Parenteral nutrition begun after initial surgery.





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- 4. If I chose PN, I would be concerned about increasing infectious complications.



### The Open Abdomen



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"deliberately leaving a laparotomy wound open is now the standard of care in clinical situations that require either planned reoperations or decompression of intraabdominal hypertension"

Planned re-operation: Damage control surgery or management of severe abdominal infection



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- Fear of inducing small bowel necrosis by stressing an underperfused bowel.
- Fear of increasing bowel distension, making it harder for the surgeon to obtain fascial closure.

Therefore many open abdomen patients receive no nutrition until fascial closure.



Should we fear enteral nutrition?



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- 72% blunt trauma, ISS 31
- 14% mortality and 31 day hospital stay



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**49%** (292/597) had full thickness bowel injuries, with direct repair, anastomosis or colostomy performed

**39%** (232/597) received EN *before first attempt at closure of the abdomen* 

• Average time to EN start, 3.6 days after injury



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Considering all patients, receiving EN before first attempt at closure resulted in significant improvements in outcome.



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For patients with a bowel injury, mortality effect (OR=0.79) was half the effect for no bowel injury (OR=0.3, previous slide). Perhaps an issue of sample size, however the authors conclude "EN seems to be neither advantageous nor detrimental for these patients"
Burlew CC, Moore EE, Cuschieri J et al. Who should we feed? A Western Trauma Association multi-institutional study of enteral nutrition in the open abdomen after injury. J Trauma Acute Care Surg 2012;73(6):1380-1388.



3 other smaller observational studies in open abdomen patients, comparing EN started prior to fascial closure with delayed nutrition

Dissanaike S, Pham T, Shalhub S et al. Effect of immediate enteral feeding on trauma patients with an open abdomen: Protection from nosocomial infections. *J Am Coll Surg* 2008;207:690-697.
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#### There were no reported adverse events with the use of EN started prior to fascial closure

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- Meta-analysis of all methodologically sound RCT's conducted in:
  - adult trauma patients requiring intensive care and;
  - comparing standard EN fed within 24hrs to standard care (oral intake upon return of bowel sounds, TPN, or TPN + delayed EN).



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Although this meta-analysis does not focus on patients managed with open abdomen, patients with major abdominal trauma were enrolled in the included clinical trials.











Table 2

### Should we fear early enteral nutrition?

Characteristics of eligi	ible studies.			
Study	Patient population	Early EN intervention	Control intervention	
Chuntrasakul 1996	Severe trauma (ISS >20 and <40) Mean ISS $29 \pm 1.5$	Immediately after resuscitation or surgery: 30 mls/h 3/4 strength EN (Traumacal <sup>TM</sup> ) via NGT, concentration increased over time. Goals estimated using modified Harris-Benedict equation. TPN was added if goals were not met	5% dextrose/NSS for maintenance. Oral intake commenced upon return of bowel sounds	
Kompan 1999	Multiple trauma (ISS $>$ 25) Mean ISS 33.6 $\pm$ 10 Mean APACHE II 11.5 $\pm$ 5.8	Immediately after resuscitation: EN (Jevity <sup>TM</sup> ) started at 20 ml/h via NGT. Increased to 50% of estimated goal on Day 1, 75% of estimated goal on Day 2 and 100% of goal on Day 3. Estimated goal was set at 25–35 nonprotein kcal/kg per day and 0.2–0.3 g nitrogen/kg per day at 72 h post-ICU admission. TPN was added to meet estimated requirements	Same protocol as Early EN except EN begun a median 41.4 (33.9–53.6 range) hours after trauma. <i>Note</i> : 50% of goal received via TPN for first 24 h before EN was begun	
Kompan 2004	Multiple trauma (ISS $>$ 20) Mean APACHE II 11.3 $\pm$ 4.8	Immediately after resuscitation: Same protocol as Kompan 1999 except goal set at an average of 25 nonprotein kcal/kg	Same protocol as Early EN except EN begun $38.5 \pm 15.6$ h after trauma. <i>Note</i> : 50% of goal received via TPN for first 24 h before EN was begun	
Moore 1986	Major abdominal trauma (ATI > 15)	Within 12–18 h of surgery: EN (Vivonex HN at 1/4 strength) via NJT at 50 ml/h. Rate and concentration increased at 8 h intervals to target (full strength solution 125ml/h) at 72 h	5% dextrose (approx. 100 g/day) during first 5 days post-op and then TPN if not tolerating oral diet at that time	



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	Study	Patient population	Early EN intervention	Control intervention	
	Chuntrasakul 1996	Severe trauma (ISS >20 and <40) Mean ISS $29\pm1.5$	Immediately after resuscitation or surgery: 30 mls/h 3/4 strength EN (Traumacal <sup>TM</sup> ) via NGT, concentration increased over time. Goals estimated using modified Harris-Benedict equation. TPN was added if goals were not met	5% dextrose/NSS for maintenance. Oral intake commenced upon return of bowel sounds	
	Kompan 1999	Multiple trauma (ISS $>$ 25) Mean ISS 33.6 $\pm$ 10 Mean APACHE II 11.5 $\pm$ 5.8	Immediately after resuscitation: EN (Jevity <sup>TM</sup> ) started at 20 ml/h via NGT. Increased to 50% of estimated goal on Day 1, 75% of estimated goal on Day 2 and 100% of goal on Day 3. Estimated goal was set at 25–35 nonprotein kcal/kg per day and 0.2–0.3 g nitrogen/kg per day at 72 h post-ICU admission. TPN was added to meet estimated requirements	Same protocol as Early EN except EN begun a median 41.4 (33.9–53.6 range) hours after trauma. <i>Note</i> : 50% of goal received via TPN for first 24h before EN was begun	
	Kompan 2004	Multiple trauma (ISS $>$ 20) Mean APACHE II 11.3 $\pm$ 4.8	Immediately after resuscitation: Same protocol as Kompan 1999 except goal set at an average of 25 nonprotein kcal/kg	Same protocol as Early EN except EN begun $38.5 \pm 15.6$ h after trauma. <i>Note</i> : 50% of goal received via TPN for first 24 h before EN was begun	
	Moore 1986	Major abdominal trauma (ATI > 15)	Within 12–18 h of surgery: EN (Vivonex HN at 1/4 strength) via NJT at 50 ml/h. Rate and concentration increased at 8 h intervals to target (full strength solution 125ml/h) at 72 h	5% dextrose (approx. 100 g/day) during first 5 days post-op and then TPN if not tolerating oral diet at that time	



# Review:Early EN (<24h) vs Standard Care (TRAUMA - Primary)</th>Comparison:01 Early (<24 h) EN vs Standard Care</td>Outcome:01 Mortality, Intention to treat analysis

Study or sub-category	Early EN (<24 h) n/N	Standard Care n/N		Peto OR 95% CI		Weight %	Peto OR 95% CI	
Kompan 1999 Kompan 2004 Chuntrasakul 1996	0/17 0/27 1/21	2/19 1/25 3/17	ļ	•••	<u> </u>	29.48 15.20 55.32	0.14 [0.01, 2.38] 0.12 [0.00, 6.31] 0.26 [0.03, 2.06]	
Total (95% CI) Total events: 1 (Early EN ( Test for heterogeneity: Chi Test for overall effect: Z =	65 <24 h)), 6 (Standard Care) <sup>j2</sup> = 0.18, df = 2 (P = 0.91), l <sup>2</sup> 2.09 (P = 0.04)	61 = 0%				100.00	0.20 [0.04, 0.91]	
			0.01 Fave	0.1 1 ors early EN	1 10 Favors Sta	100 ndard Care		

#### Mortality reduced by 8.3%, p=0.04



- Early EN also resulted in:
  - Reduced incidence of pneumonia (33% eEN vs 64%, p=0.050)
  - No significant difference in the *incidence* of MODs, (70% eEN vs 68%, p=0.82) but a trend towards a reduction in the *severity* of MODS (2.5 vs 3.1 organ failures per patient, p=0.057)


## Should we fear early enteral nutrition?

- Early EN also resulted in:
  - Reduced incidence of pneumonia (33% eEN vs 64%, p=0.050)
  - No significant difference in the *incidence* of MODs, (70% eEN vs 68%, p=0.82) but a trend towards a reduction in the *severity* of MODS (2.5 vs 3.1 organ failures per patient, p=0.057)

There were no signs of any harms.

Doig GS, Heighes PT, Simpson F and Sweetman EA. Early enteral nutrition reduces mortality in trauma patients requiring intensive care: A meta-analysis of randomised controlled trials. *Injury* 2011;42(1):50-56





- A Meta-analysis comparing RCT's of early feeding (within 24h) versus no feeding in patients undergoing gastrointestinal surgery.
- 13 studies, 1,173 patients

Lewis SJ, Andersen HK, Thomas S. Early enteral nutrition within 24 h of Intestinal Surgery versus later commencement of feeding: A systematic review and Meta-analysis. *J Gastrointest Surg* 2009;13:569-575.



- A Meta-analysis comparing RCT's of early feeding (within 24h) versus no feeding in patients undergoing gastrointestinal surgery.
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- 13 studies, 1,173 patients
- Early feeding resulted in a significant decrease in:
  - Mortality (2.4% eEN vs 6.9%, p=0.03)
- Early feeding was **not** associated with **any harms**:
  - Wound infections (7.1% eEN vs 9.3%, p=0.26)
  - Anastomotic dehiscence (2.8% eEN vs 4.3%, p=0.27)
  - Pneumonia (2.3% eEN vs 3.3%, p=0.46)



- A Meta-analysis comparing RCT's of early feeding (within 24h) versus no feeding in patients undergoing gastrointestinal surgery.
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  - Pneumonia (2.3% eEN vs 3.3%, p=0.46)

## "There is no obvious benefit for keeping patients "nil by mouth" after gastrointestinal surgery"

Lewis SJ, Andersen HK, Thomas S. Early enteral nutrition within 24 h of Intestinal Surgery versus later commencement of feeding: A systematic review and Meta-analysis. *J Gastrointest Surg* 2009;13:569-575.



In the trauma patient with an open abdomen, starting EN prior to abdominal closure may:

- Significantly reduce time to closure
- Significantly reduce mortality
- NOT result in any increase in complications

Burlew CC, Moore EE, Cuschieri J et al. Who should we feed? A Western Trauma Association multi-institutional study of enteral nutrition in the open abdomen after injury. *J Trauma Acute Care Surg* 2012;73(6):1380-1388.

In the trauma patient with an open abdomen, starting EN prior to abdominal closure may:

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- Significantly reduce mortality
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- In the trauma patient who may be managed with an open abdomen, starting EN within 24 h of injury :
  - Significantly reduced mortality, pneumonia and severity of MODS

Burlew CC, Moore EE, Cuschieri J et al. Who should we feed? A Western Trauma Association multi-institutional study of enteral nutrition in the open abdomen after injury. *J Trauma Acute Care Surg* 2012;73(6):1380-1388.
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It is very unlikely to blow apart a bowel anastomosis.

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#### ..... but ....

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The mean time to abdominal closure for all patients was 6.6 days.



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Do we leave these patients unfed for 6.6 days??



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Do we leave these patients unfed for 6.6 days??

Should we fear parenteral nutrition?



## Should we fear parenteral nutrition?



## Should we fear parenteral nutrition?

CARING FOR THE CRITICALLY ILL PATIENT		
		ΙΛΝΛΛ
ONLINE FIRST		
Early Parenteral	Nutrition in Critically III Patients	
With Short-terr	n Relative Contraindications	The Journal of the American Medical Association
to Farly Enteral	Nutrition	
A Pandomizod Con	trolled Trial	
Cordon S. Doig, PhD Fione Simpson MND	Importance Systematic reviews suggest adult patients in intensive care units (ICUs)	
Elizabeth A. Sweetman, MHM	teral nutrition (PN) provided within 24 hours of ICU admission.	
Simon R. Finfer, FCICM	Objective To determine whether providing early PN to critically ill adults with rela- tive contraindications to early EN alters outcomes.	
D. Jamie Cooper, FCICM Philippa T. Haighay, MN	Design, Setting, and Participants Multicenter, randomized, single-bind dinical trial	GS Dolg and coauthors
Andrew R. Davies, FCICM	hospitals in Australia and New Zealand. Participants were critically ill adults with relative	
Michael O'Leary, FCICM	contraindications to early EN who were expected to remain in the ICU longer than 2 days. Interventions Random allocation to pragmatic standard care or early PN.	Early Parenteral Nutrition in
Tom Solano, FUICM Sandra Peake, FCICM	Main Outcomes and Measures Day-60 mortality; quality of life, infections, and	Critically III Patients With Short-term
for the Early PN Investigators of the	Results A total of 1372 patients were randomized (686 to standard care, 686 to early	
ANZICS Clinical Trials Group	PN). Of 682 patients receiving standard care, 199 patients (29.2%) initially commenced EN, 186 patients (27.3%) initially commenced PN, and 278 patients (40.8%) remained	Relative Contraindications
ARENTERAL NUTRITION HAS BEEN in common use since the	unfed. Time to EN or PN in patients receiving standard care was 2.8 days (95% Cl, 2.3 to 3.4). Patients receiving early PN commenced PN a mean of 44 minutes after enrollment	to Early Enteral Nutrition:
1960s1 and is accepted as the standard of care for natients	(95% CI, 36 to 55). Day-60 mortality did not differ significantly (22.8% for standard care vs 21.5% for early PN: risk difference. – 1.26%; 95% CI. – 6.6 to 4.1; P=.60). Early PN	to Early Entoral Natifition:
with chronic nonfunctioning gastroin-	patients rated day-60 quality of life (RAND-36 General Health Status) statistically, but not clinically meaningfully, higher (45.5 for standard care vs. 49.8 for early PN: mean differ-	A Randomized Controlled Trial
troversy surrounds the appropriate use	ence, 4.3; 95% CI, 0.95 to 7.58; P=.01). Early PN patients required fewer days of invasive ventilation (7.73 vs 7.26 days per 10 patient × ICU days, risk difference0.47; 95% CI.	
of parenteral nutrition,3 but large- scale trials have begun to answer im-	-0.82 to -0.11; P=.01) and, based on Subjective Global Assessment, experienced less muscle wasting (0.43 vs.0.27 score increase ner week: mean difference	
portant questions. Published in 2011. EPaNIC (Early Par-	-0.28 to $-0.038$ ; $P=.01$ ) and fat loss (0.44 vs 0.31 score increase per week; mean dif- ference $-0.13$ ; $95\%$ (1 $-0.25$ to $-0.01$ ; $P=.04$ )	
enteral Nutrition Completing Enteral	Conclusions and Relevance The provision of early PN to critically III adults with	Published online May 20, 2013
enrolled 4640 critically ill patients to in-	readive contraindications to early EN, compared with standard care, did not result in a difference in day-60 mortality. The early PN strategy resulted in significantly fewer	i ublished online May 20, 2015
vesugate the effects of using parenteral nutrition when enteral nutrition failed	days of invasive ventilation but not significantly shorter ICU or hospital stays. Trial Registration arzetr.org.au identifier: ACTRN012605000704695	
to reach a caloric target. EPaNIC did not find any benefits from using additional	JAMA. 2013;309(20):doi:10.1001/jama.2013.5124 www.jama.com	
parenteral nutrition in patients who	Author Affiliations: Northern Clinical School Inten- the Care Research Unit Cir Dole and Miss Strepton, tisators are listed at the end of this article.	
ever, many other important questions re-	Sweetman, and Heighes), The George Institute for Global Health (Dr Finfer), University of Sydney, Syd- North Shore Hospital, Intensive Care Unit, Pacific Hwy,	Available at www.jama.com
garding parenteral nutrition remain.	ney, Australia, Amere Hospital, Meteorume, Australia St. Leonards, NSW 2065, Australia (gdolg@med.usyd (Drs Cooper and Davies); Royal Prince Alfred Hospi- Lial, Svidney (Dro Cluany); Westmead Hospital, Svid- Lial, Svidney (Dro Cluany); Westmead Hospital, Svid- Caring forthe Critically III Patient Section Editor. Denk	•
See related article.	ney (Dr Solano); and Gueen Elizabeth Hospital, Åd- ciaide, Australia (Dr Peake). (angusto@upmc.edu).	
©2013 American Medical Association. All rig	hts reserved. JAMA, Published online May 20, 2013 E1	The JANAA Meturada
		IDE IDE JAMA NEtwork

Doig GS, Simpson F, Sweetman EA et al. Early parenteral nutrition in critically ill patients with short-term relative contraindications to early enteral nutrition: a randomized controlled trial. *JAMA*. 2013 May 22;309(20):2130-8



<b>Table 4.</b> New Infections During Study					
	No. (%	6)			
Patients With New Infections <sup>a</sup>	Standard Care (n = 682)	Early PN (n = 681)	Risk Difference (Exact 95% Cl)	Exact P Value <sup>b</sup>	

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<sup>a</sup> new infections based on cultures obtained in the study ICU.

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	No. (%	<b>(</b> )		
Patients With New Infections <sup>a</sup>	l Standard Care (n = 682)	Early PN (n = 681)	Risk Difference (Exact 95% CI)	Exact <i>P</i> Value <sup>b</sup>
Catheter <sup>c</sup>	32 (4.69)	31 (4.55)	-0.14 (-5.45 to 5.12)	>.99
Catheter tip <sup>c</sup>	28 (4.11)	26 (3.82)	-0.29 (-5.60 to 5.01)	.89

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<sup>a</sup> new infections based on cultures obtained in the study ICU. <sup>c</sup> venous or arterial catheters

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	No. (%	<b>b</b> )		
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Surgical wound	27 (3.96)	22 (3.23)	-0.73 (-6.04 to 4.57)	.56

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Bloodstream	33 (4.84)	39 (5.73)	0.89 (-4.43 to 6.18)	.47

<sup>a</sup> new infections based on cultures obtained in the study ICU.

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Abdominal	3 (0.44)	6 (0.88)	0.44 (-4.89 to 5.74)	.34

F

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Clinically significant UTI	1 (0.15)	2 (0.29)	0.15 (-5.16 to 5.45)	.62

F

<sup>a</sup> new infections based on cultures obtained in the study ICU.

<sup>c</sup> venous or arterial catheters

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Clinically significant UTI	1 (0.15)	2 (0.29)	0.15 (-5.16 to 5.45)	.62	
Airway or lung <sup>d</sup>	123 (18.04)	101 (14.83)	-3.20 (-8.52 to 2.08)	.12	
CPIS-probable pneumonia <sup>e</sup>	96 (14.08)	81 (11.89)	-2.18 (-7.50 to 3.11)	.26	
CPIS-confirmed pneumonia <sup>f</sup>	45 (6.60)	43 (6.31)	-0.28 (-5.60 to 5.01)	.91	

<sup>a</sup> new infections based on cultures obtained in the study ICU.

#### <sup>c</sup> venous or arterial catheters

<sup>e</sup> CPIS  $\geq$  6 plus detection (by staining or culture) of a likely pulmonary pathogen in respiratory secretions (expectorated sputum, endotracheal or bronchoscopic aspirate, or quantitatively cultured bronchoscopic BAL fluid or brush catheter specimen), or the presence of a negative lower respiratory tract culture if collected within 72hrs after starting a new antibiotic regimen.

<sup>f</sup> CPIS  $\geq$  6 (using a Gram stain of a lower respiratory tract sample) plus a definite cause established by the recovery of a probable etiologic agent from **a**) an uncontaminated specimen (blood, pleural fluid, transtracheal aspirate, or transthoracic aspirate); **b**) the recovery from respiratory secretions of a likely pathogen that does not colonize the upper airways (e.g., *Mycobacterium tuberculosis, Legionella* species, influenza virus, or *Pneumocystis jiroveci (carinii*); **c**) recovery of a likely/possible respiratory pathogen in cultures of a lower respiratory tract sample (endotracheal aspirate, BAL, or protected specimen brush); or **d**) positive serology.



	No. (9	%)		
Patients With New Infections <sup>a</sup>	l Standard Care (n = 682)	Early PN (n = 681)	Risk Difference (Exact 95% Cl)	Exact <i>P</i> Value <sup>b</sup>
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Clinically significant UTI	<mark>1 (</mark> 0.15)	2 (0.29)	0.15 (-5.16 to 5.45)	.62
Airway or lung <sup>d</sup>	123 (18.04)	101 (14.83)	-3.20 (-8.52 to 2.08)	.12
CPIS-probable pneumonia <sup>e</sup>	96 (14.08)	81 (11.89)	-2.18 (-7.50 to 3.11)	.26
CPIS-confirmed pneumonia <sup>f</sup>	45 (6.60)	43 (6.31)	-0.28 (-5.60 to 5.01)	.91
Any major infection <sup>g</sup>	78 (11.4)	74 (10.9)	-0.57 (-5.89 to 4.72)	.80

<sup>a</sup> new infections based on cultures obtained in the study ICU.

<sup>c</sup> venous or arterial catheters

<sup>e</sup> CPIS  $\geq$  6 plus detection (by staining or culture) of a likely pulmonary pathogen in respiratory secretions (expectorated sputum, endotracheal or bronchoscopic aspirate, or quantitatively cultured bronchoscopic BAL fluid or brush catheter specimen), or the presence of a negative lower respiratory tract culture if collected within 72hrs after starting a new antibiotic regimen.

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<sup>*g*</sup> Attributable excess case mortality greater than 15%.

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F





Main inclusion criteria:

- Adult patients admitted to ICU for less than 24 h.
- Not expected to receive enteral, parenteral or oral intake 'today' or 'tomorrow'.



F

Main types of patients enrolled:

• 234 (17%) GI perforation (surgical),



F

- 234 (17%) GI perforation (surgical),
- 140 (10%) GI obstruction (surgical or medical management),



F

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- 140 (10%) GI obstruction (surgical or medical management),
- 98 (7%) ruptured aorta (surgical),



F

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F

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- 98 (7%) ruptured aorta (surgical),
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- 91 (7%) other GI (surgical),



F

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- 91 (7%) GI neoplasm (surgical),
- 91 (7%) other GI (surgical),
- 87 (6%) Sepsis other than urinary (med),



F

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- 91 (7%) other GI (surgical),
- 87 (6%) Sepsis other than urinary (med),
- 62 (5%) GI bleeding (med/surg).



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- 234 (17%) GI perforation (surgical),
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- 98 (7%) ruptured aorta (surgical),
- 91 (7%) GI neoplasm (surgical),
- 91 (7%) other GI (surgical),
- 87 (6%) Sepsis other than urinary (med),
- 62 (5%) GI bleeding (med/surg).

Major trauma patient with open abdomen who is NOT going to receive EN today or tomorrow would have been eligible for this trial.



Table 1. Patient Characteristics and Baseline Balance				
Baseline Characteristics	Standard Care (n = $682$ )	Early PN (n = 681)		
Age, mean (SD), y	68.6 (14.3)	68.4 (15.1)		
Female gender, No. (%)	262 (38.4)	281 (41.3)		
BMI, mean (SD) <sup>a,b</sup>	28.5 (6.9)	27.9 (6.8)		
APACHE II score, mean (SD) <sup>c,e</sup>	21.5 (7.8)	20.5 (7.4)		
Mechanically ventilated, No. (%)	549 (80.6)	572 (83.9)		



## Nutrition therapy process measures

Early parenteral nutrition (681 patients):

• 679/681 patients (99.7%) commenced PN 44 minutes after enrolment


### Nutrition therapy process measures

Early parenteral nutrition (681 patients):

- 679/681 patients (99.7%) commenced PN 44 minutes after enrolment
  - 405/679 (59.6%) progressed to EN 3.83 days after PN start



### Nutrition therapy process measures

Early parenteral nutrition (681 patients):

- 679/681 patients (99.7%) commenced PN 44 minutes after enrolment
  - 405/679 (59.6%) progressed to EN 3.83 days after PN start

Pragmatic standard care (682 patients):



### Nutrition therapy process measures

F

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- 679/681 patients (99.7%) commenced PN 44 minutes after enrolment
  - 405/679 (59.6%) progressed to EN 3.83 days after PN start

Pragmatic standard care (682 patients):

 279/682 (40%) standard care patients commenced EN 3.7 days after enrolment



	Standard Care (n = 680) <sup>a</sup>	Early PN (n = 678) <sup>a</sup>	Risk Difference, % (95% Cl)	P Value
Deaths before study day 60, No. (%)	155 (22.8)	146 (21.5)	-1.26 (-6.6 to 4.1)	.60
Covariate-adjusted deaths before study day 60 <sup>b</sup>			0.04 (-4.2 to 4.3)	>.99

<sup>a</sup> 5 patients (2 Standard Care, 3 Early PN) could not be contacted on study Day 60 to determine vital status. Considered 'missing at random' for ITT Primary and Adjusted primary outcome analysis.

<sup>b</sup> Multivariate model controlled for confounding due to baseline imbalance and strong predictors: Age, gender, BMI, APACHE 2 score, Chronic Liver, Chronic Respiratory and Source of Admission.

#Bender R, Vervolgyi V. Estimating adjusted NNTs in randomised controlled trials with binary outcomes: A simulation study. *Contemporary Clinical Trials* 2010;31:498-505.



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<b>Fable 4.</b> New Infections During Study				
	No. (%	<b>()</b>		
Patients With New Infections <sup>a</sup>	Standard Care (n = 682)	Early PN (n = 681)	Risk Difference (Exact 95% Cl)	Exact P Value <sup>b</sup>

F

<sup>a</sup> new infections based on cultures obtained in the study ICU.



#### Table 4. New Infections During Study

No. (%)					
Patients With New Infections <sup>a</sup>	l Standard Care (n = 682)	Early PN (n = 681)	Risk Difference (Exact 95% Cl)	Exact <i>P</i> Value <sup>b</sup>	
Catheter <sup>c</sup>	32 (4.69)	31 (4.55)	-0.14 (-5.45 to 5.12)	>.99	
Catheter tip <sup>c</sup>	28 <mark>(</mark> 4.11)	26 (3.82)	-0.29 (-5.60 to 5.01)	.89	
Surgical wound	27 (3.96)	22 (3.23)	-0.73 (-6.04 to 4.57)	.56	
Bloodstream	33 <mark>(</mark> 4.84)	39 <b>(</b> 5.73)	0.89 (-4.43 to 6.18)	.47	
Abdominal	3 (0.44)	6 (0.88)	0.44 (-4.89 to 5.74)	.34	
Clinically significant UTI	1 (0.15)	2 (0.29)	0.15 (-5.16 to 5.45)	.62	
Airway or lung <sup>d</sup>	123 (18.04)	101 (14.83)	-3.20 (-8.52 to 2.08)	.12	
CPIS-probable pneumonia <sup>e</sup>	96 (14.08)	81 (11.89)	-2.18 (-7.50 to 3.11)	.26	
CPIS-confirmed pneumonia <sup>f</sup>	45 (6.60)	43 (6.31)	-0.28 (-5.60 to 5.01)	.91	
Any major infection <sup>g</sup>	78 (11.4)	74 (10.9)	-0.57 (-5.89 to 4.72)	.80	

<sup>a</sup> new infections based on cultures obtained in the study ICU.

<sup>c</sup> venous or arterial catheters

<sup>e</sup> CPIS  $\geq$  6 plus detection (by staining or culture) of a likely pulmonary pathogen in respiratory secretions (expectorated sputum, endotracheal or bronchoscopic aspirate, or quantitatively cultured bronchoscopic BAL fluid or brush catheter specimen), or the presence of a negative lower respiratory tract culture if collected within 72hrs after starting a new antibiotic regimen.

<sup>f</sup> CPIS  $\geq$  6 (using a Gram stain of a lower respiratory tract sample) plus a definite cause established by the recovery of a probable etiologic agent from **a**) an uncontaminated specimen (blood, pleural fluid, transtracheal aspirate, or transthoracic aspirate); **b**) the recovery from respiratory secretions of a likely pathogen that does not colonize the upper airways (e.g., *Mycobacterium tuberculosis, Legionella* species, influenza virus, or *Pneumocystis jiroveci (carinii*); **c**) recovery of a likely/possible respiratory pathogen in cultures of a lower respiratory tract sample (endotracheal aspirate, BAL, or protected specimen brush); or **d**) positive serology.

<sup>*g*</sup> Attributable excess case mortality greater than 15%.

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	Standard Care (n = 680) <sup>a</sup>	Early PN (n = 678) <sup>a</sup>	P Value
Quality of life and physical function, mean (SD) <sup>c</sup>	(n = 525)	(n = 532)	
RAND-36 general health status <sup>d</sup>	45.5 (26.8) (n = 516)	49.8 (27.6) (n = 52	25) .01

Ware JE, Jr., Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care* 1992;30:473-483.

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Minimally Important Difference =  $\frac{12}{2}$  SD = 13.5

Juniper EF, Guyatt GH, Willan A, Griffith LE. Determining a minimal important change in a disease-specific Quality of Life Questionnaire. *J Clin Epidemiol* 1994;47:81-87.

Norman GR, Sloan JA, Wyrwich KW. Interpretation of changes in health-related quality of life: The remarkable universality of a half a standard deviation. *Medical Care* 2004;41:582-592.

Ware JE, Jr., Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care* 1992;30:473-483.



Table 3. Concomitant Interventions, Adjusted for Time at Risk (ICU Stay) <sup>a</sup>				
Mean (95% CI), Days per 10 Patient $ imes$ ICU Days			D	
	Standard Care (n = 682)	Early PN (n = 681)	Value <sup>b</sup>	
Invasive mechanical ventilation	7.73 (7.55 to 7.92)	7.26 (7.09 to 7.44)	.01	



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	Mean (95% CI), Days per 1	Mean (95% CI), Days per 10 Patient $ imes$ ICU Days	
	Standard Care (n = 682)	Early PN (n = 681)	Value <sup>b</sup>
Invasive mechanical ventilation	7.73 (7.55 to 7.92)	7.26 (7.09 to 7.44)	.01
Pressure ulcer treatment	0.87 (0.74 to 1.02)	0.78 (0.67 to 0.92)	.54
Low serum albumin (<2.5 g/dL)	5.47 (5.28 to 5.67)	5.76 (5.56 to 5.97)	.15
Systemic antibiotic use	7.95 (7.78 to 8.12)	8.05 (7.88 to 8.22)	.55
Witnessed aspiration	1.59 (0.98 to 2.54)	1.96 (1.21 to 3.13)	.66
With new pulmonary infiltrates	0.48 (0.20 to 1.15)	0.71 (0.30 to 1.72)	.65
Renal replacement therapy	0.99 (0.82 to 1.81)	0.80 (0.67 to 0.96)	.25

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Length of Stay	(n = 682)	(n = 681) <i>P</i> Value
ICU stay, mean (95% Cl), d	9.3 (8.9 to 9.7)	8.6 (8.2 to 9.0) .06
Hospital stay, mean (95% Cl), d	24.7 (23.7 to 25.8)	25.4 (24.4 to 26.6) .50



### Daniel C., 42 years, Motor accident



- 186 cm, 72 kg
- Dx:
  - cerebral hematoma
  - multiple rip fractures, rupture of pulmonary artery
  - blunt abdominal trauma, splenic rupture
  - pelvic fracture, massive blood loss
  - Op:
    - drainage of hematoma, repair of pulmonary artery
    - spleen resection, abdominal revision
    - pelvic osteosynthesis
  - 5 hours postoperative
    - open abdomen, scheduled for review next day
    - no post pyloric feeding tube
    - mechanically ventilated, FIO<sub>2</sub> 0.6
    - Temp. 39.2 °C
    - Chest-X-ray:
      - bilateral infiltrates



### Could we consider enteral nutrition?



## Could we consider enteral nutrition?

- 597 patient observational study,
  - Significantly higher fascial closure rates;
  - No difference in complication rates and;
  - Significantly lower mortality.
- 39% received EN before closure of the abdomen, started 3.6 days after injury



### Could we consider enteral nutrition?

#### He could be fed enterally



#### He could be fed enterally



### He could be fed enterally

- Significantly lower mortality
- Reduced pneumonia and severity of MODS
- No signs of harm

Burlew CC, Moore EE, Cuschieri J et al. Who should we feed? A Western Trauma Association multi-institutional study of enteral nutrition in the open abdomen after injury. *J Trauma Acute Care Surg* 2012;73(6):1380-1388.
Doig GS, Heighes PT, Simpson F and Sweetman EA. Early enteral nutrition reduces mortality in trauma patients requiring intensive care: A meta-analysis of randomised controlled trials. *Injury* 2011;42(1):50-56



He could be fed enterally He could be fed *early* (< 24 h from injury) enterally

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He could be fed enterally

He could be fed *early* (< 24 h from injury) enterally

• No impact on mortality



He could be fed enterally

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- No impact on mortality
- No impact on infectious complications



He could be fed enterally

He could be fed *early* (< 24 h from injury) enterally

- No impact on mortality
- No impact on infectious complications
- Significant reduction in duration of mechanical ventilation (1.1 days, p = 0.009)



He could be fed enterally

He could be fed *early* (< 24 h from injury) enterally

- No impact on mortality
- No impact on infectious complications
- Significant reduction in duration of mechanical ventilation (1.1 days, p = 0.009)
- Strong trend towards reduction in ICU stay (0.75 days, p=0.06).



He could be fed enterally

He could be fed *early* (< 24 h from injury) enterally

- No impact on mortality
- No impact on infectious complications
- Significant reduction in duration of mechanical ventilation (1.1 days, p = 0.009)
- Strong trend towards reduction in ICU stay (0.75 days, p=0.06).
- Does not delay eventual EN start time



He could be fed enterally

He could be fed *early* (< 24 h from injury) enterally

If he is not going to be fed early enterally, he could be fed early parenterally!



He could be fed enterally He could be fed *early* (< 24 h from injury) enterally If he is *not going to be fed early* enterally, he could be fed *early* parenterally!

# We are unaware of any published evidence that demonstrates short term fasting (or starvation) is beneficial to any group of critically ill patients.