Early parenteral nutrition in critically ill patients with short-term relative contraindications to early enteral nutrition:

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What the evidence really says

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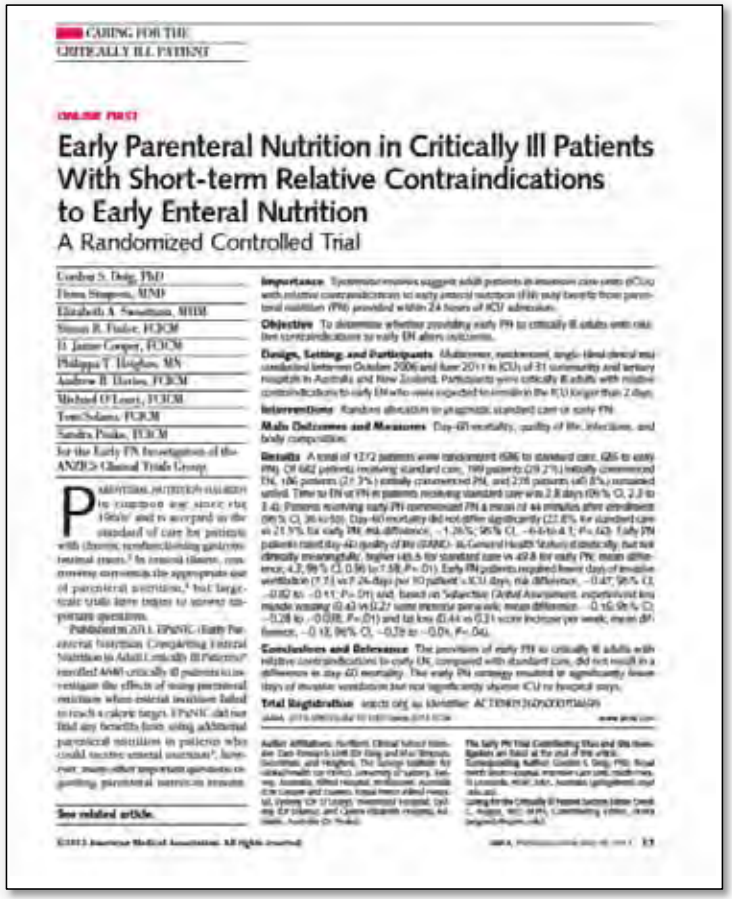

CARING FOR THE CRITICALLY ILL PATIENT

ONLINE FIRST

Early Parenteral Nutrition in Critically Ill Patients With Short-term Relative Contraindications to Early Enteral Nutrition

A Randomized Controlled Trial

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for the Early PN Investigators of the ANZICS Clinical Trials Group

Importance Systematic reviews suggest adult patients in intensive care units (ICUs) with relative contraindications to early enteral nutrition (EN) may benefit from parenteral nutrition (PN) provided within 24 hours of ICU admission.

Objective To determine whether providing early PN to critically ill adults with relative contraindications to early EN alters outcomes.

Design, Setting, and Participants Multicenter, randomized, single-blind clinical trial conducted between October 2006 and June 2011 in ICUs of 31 tertiary and tertiary hospitals in Australia and New Zealand. Participants were critically ill adults with relative contraindications to early EN who were expected to remain in the ICU longer than 2 days.

Interventions Random allocation to usual/specific standard care or early PN.

Main Outcomes and Measures Day-60 mortality, quality of life, infections, and body composition.

Results A total of 1272 patients were randomized (636 to standard care, 636 to early PN). Of 662 patients receiving standard care, 199 patients (29.2%) initially commenced EN, 186 patients (27.3%) initially commenced PN, and 278 patients (40.8%) remained unfed. Time to EN or PN in patients receiving standard care was 2.8 days (95% CI, 2.3 to 3.4). Patients receiving early PN commenced PN a mean of 44 minutes after randomization (95% CI, 36 to 53). Day-60 mortality did not differ significantly (22.8% for standard care vs 21.5% for early PN; risk difference, −1.26%; 95% CI, −6.4 to 3.9; P = .62). Early PN patients rated day-60 quality of life (EQ-5D-3L General Health Status) statistically, but not clinically meaningfully, higher (45.5 for standard care vs 49.8 for early PN; mean difference, 4.2; 95% CI, 0.96 to 7.58; P = .01). Early PN patients required fewer days of invasive ventilation (7.5 vs 9.2 days per 10 patient × ICU days; risk difference, −0.47; 95% CI, −0.82 to −0.11; P = .01) and, based on Subjective Global Assessment, experienced less muscle wasting (0.43 vs 0.27 score increase per week; mean difference, −0.16; 95% CI, −0.28 to −0.038; P = .01) and fat loss (0.44 vs 0.31 score increase per week; mean difference, −0.13; 95% CI, −0.26 to −0.04; P = .04).

Conclusions and Relevance The provision of early PN to critically ill adults with relative 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 days of invasive ventilation but not significantly shorter ICU or hospital stays.

Trial Registration anzctr.org.au Identifier: ACTRN12606000188639

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The Early PN Trial Coordinating Office and the Investigators are listed at the end of the article.

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See related article.

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- Baxter Healthcare, Academic Research Grant, Consultant and Speaker's Honoraria
- Nutricia Pharmaceutical Co Ltd, Speaker's Honoraria
- B Braun Medical Inc, Speaker's Honoraria

Outline

- Brief context and background
- Essential elements of design
- Main results
- Summary


Intensive Care Research Unit University of Sydney
Northern Clinical School

Context

Effect of Evidence-Based Feeding Guidelines on Mortality of Critically Ill Adults

A Cluster Randomized Controlled Trial

Gordon S. Doig, PhD
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Imogen Mitchell, FJFICM
Geoff Dobb, FJFICM
for the Nutrition Guidelines Investigators of the ANZICS Clinical Trials Group

Context Evidence demonstrates that providing nutritional support to intensive care unit (ICU) patients within 24 hours of ICU admission reduces mortality. However, early feeding is not universally practiced. Changing practice in complex multidisciplinary environments is difficult. Evidence supporting whether guidelines can improve ICU feeding practices and patient outcomes is contradictory.

Objective To determine whether evidence-based feeding guidelines, implemented using a multifaceted practice change strategy, improve feeding practices and reduce mortality in ICU patients.

Design, Setting, and Patients Cluster randomized trial in ICUs of 27 community and tertiary hospitals in Australia and New Zealand. Between November 2003 and May 2004, 1118 critically ill adult patients expected to remain in the ICU longer than 2 days were enrolled. All participants completed the study.

Interventions Intensive care units were randomly assigned to guideline or control groups. Guideline ICUs developed an evidence-based guideline using Browman's Clinical Practice Guideline Development Cycle. A practice-change strategy composed of 18 specific interventions, leveraged by educational outreach visits, was implemented in guideline ICUs.

Main Outcome Measures Hospital discharge mortality. Secondary outcomes included ICU and hospital length of stay, organ dysfunction, and feeding process measures.

Results Guideline and control ICUs enrolled 561 and 557 patients, respectively. Guideline ICUs fed patients earlier (0.75 vs 1.37 mean days to enteral nutrition start; difference, −0.62 [95% confidence interval {CI}, −0.82 to −0.36]; $P<.001$ and 1.04 vs 1.40 mean days to parenteral nutrition start; difference, −0.35 [95% CI, −0.61 to −0.01]; $P=.04$) and achieved caloric goals more often (6.10 vs 5.02 mean days per 10 fed patient-days; difference, 1.07 [95% CI, 0.12 to 2.22]; $P=.03$). Guideline and control ICUs did not differ with regard to hospital discharge mortality (28.9% vs 27.4%; difference, 1.4% [95% CI, −6.3% to 12.0%]; $P=.75$) or to hospital length of stay (24.2 vs 24.3 days; difference, −0.08 [95% CI, −3.8 to 4.4]; $P=.97$) or ICU length of stay (9.1 vs 9.9 days; difference, −0.86 [95% CI, −2.6 to 1.3]; $P=.42$).

Conclusions Using a multifaceted practice change strategy, ICUs successfully developed and introduced an evidence-based nutritional support guideline that promoted earlier feeding and greater nutritional adequacy. However, use of the guideline did not improve clinical outcomes.

Trial Registration anzctr.org.au Identifier: ACTRN12608000407392

JAMA. 2008;300(23):2731-2741 www.jama.com

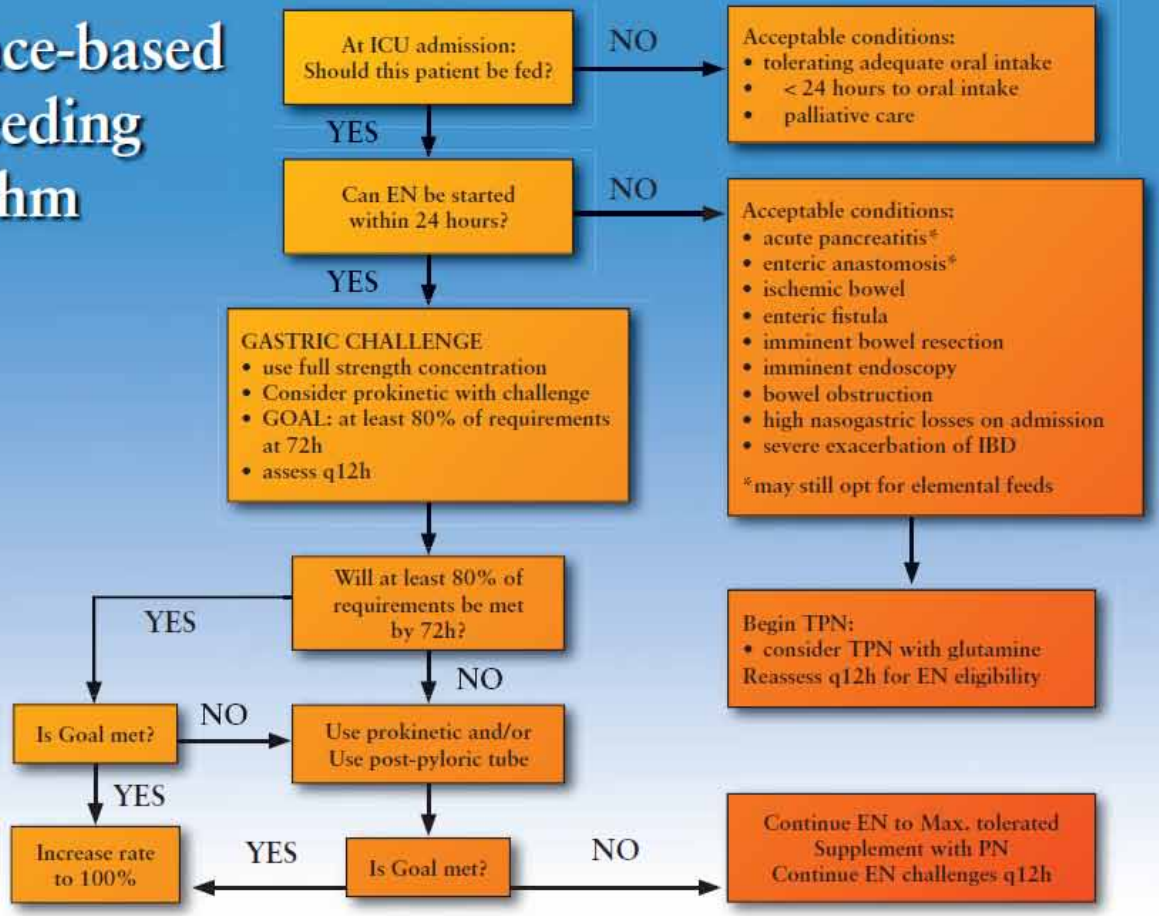
EARLY NUTRITIONAL SUPPORT, provided within 24 hours of injury or intensive care unit (ICU) admission, is a key component in the treatment of critically ill patients and may reduce mortality by 8% to 13%.[1-4] Nevertheless, practice varies widely between ICUs,[5] and up to 40% of eligible patients may remain unfed after 48 hours in the ICU.[6]

Evidence-practice gaps are common in clinical practice, with 30% of hospitalized patients receiving care inconsistent with current best evidence.[7,8] Evidence-based guidelines (EBGs) help reduce evidence-practice gaps by promoting awareness of interventions of proven benefit and discouraging ineffective care.[3,9-11] However, the ICU is a complex multidisciplinary environment, and reducing evidence-practice gaps through the successful

Doig GS, Simpson F, Finfer S, Delaney A, Davies AR, Mitchell I and Dobb G for the Nutrition Guidelines Investigators of the ANZICS Clinical Trials Group. Effect of evidence-based feeding guidelines on mortality of critically ill patients: a cluster randomized controlled trial. *JAMA* 2008 Dec 17;300(23):2731-41.

ICU GUIDELINES

Evidence-based ICU feeding algorithm



Evidence updated by the ANZICS CTG Feeding Investigators Group Oct 28th, 2003.
Chief Investigator: Dr. Gordon S. Doig, University of Sydney. Contact: gdoig@med.usyd.edu.au

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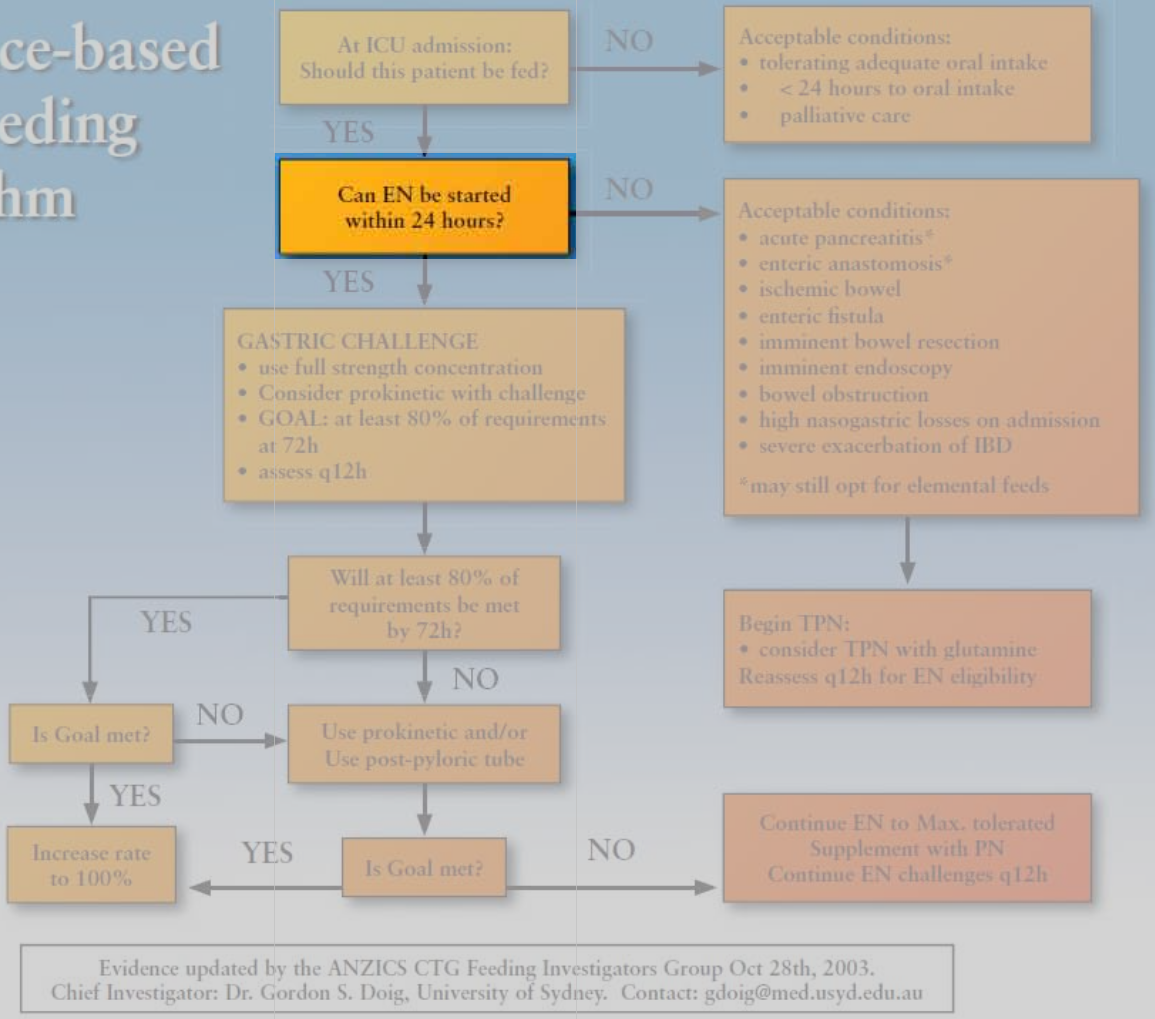

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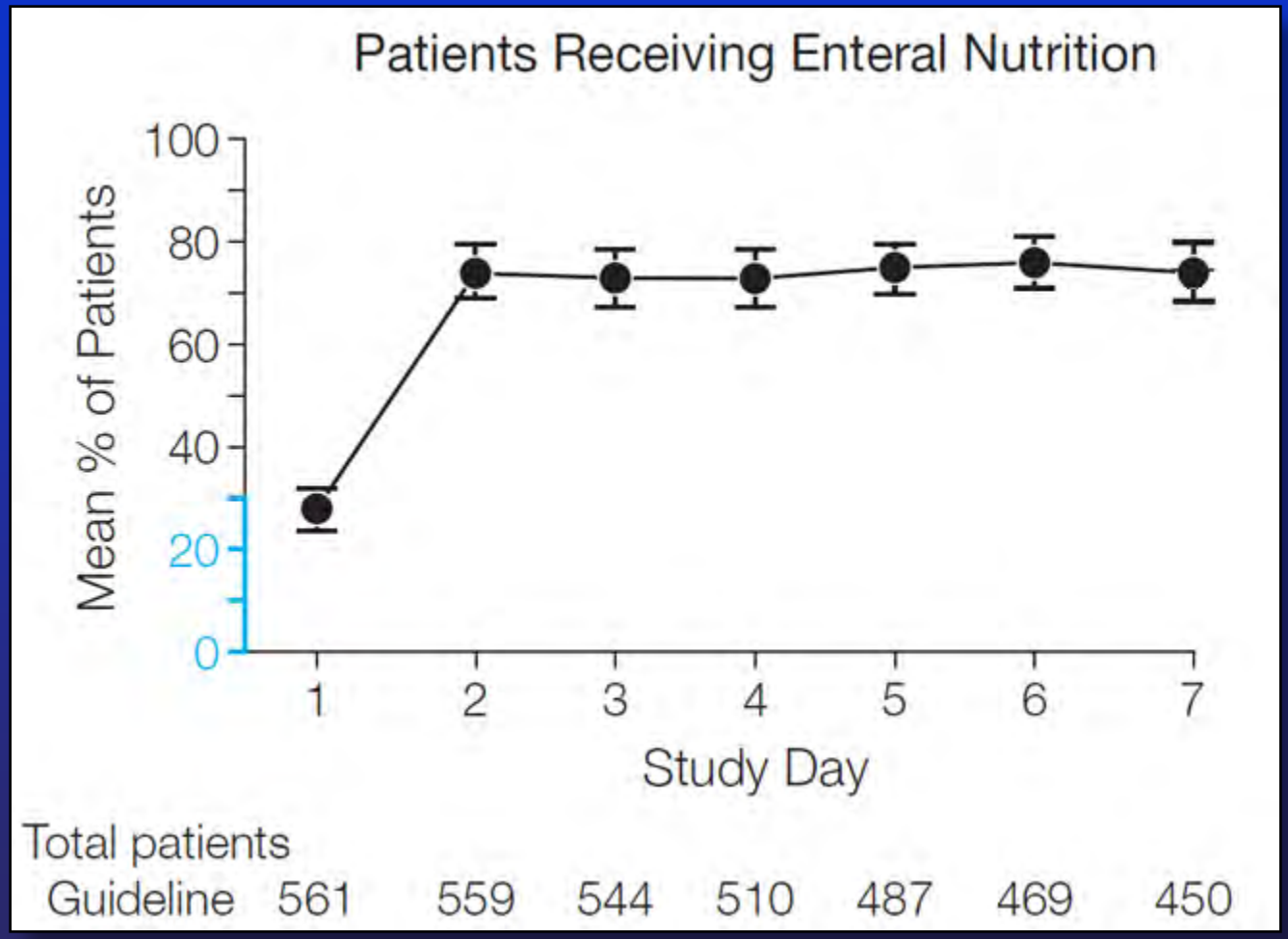

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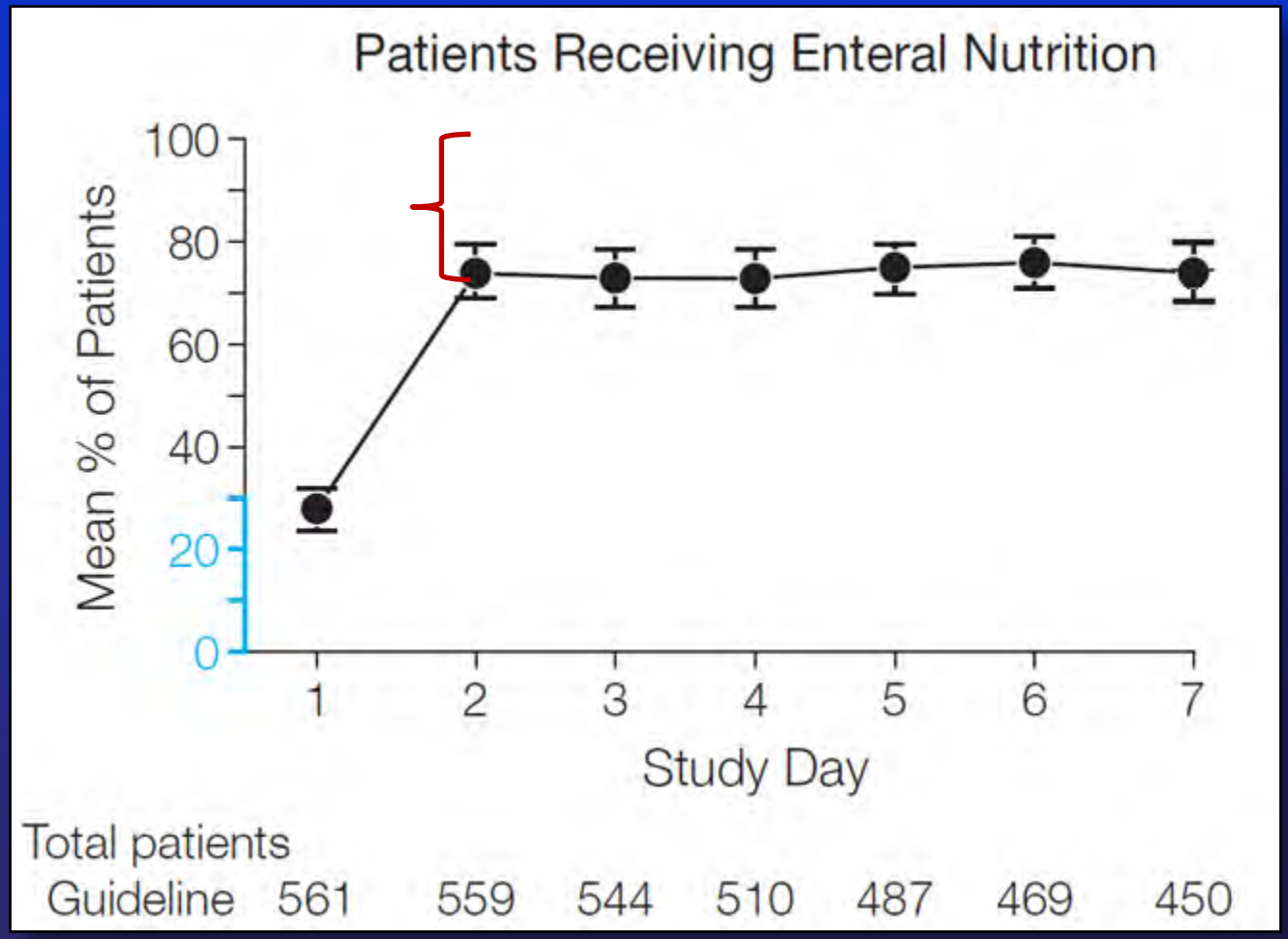

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Intensive Care Med (2005) 31:12–23
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SYSTEMATIC REVIEW

Fiona Simpson
Gordon Stuart Doig

Parenteral vs. enteral nutrition in the critically ill patient: a meta-analysis of trials using the intention to treat principle

Simpson F and Doig GS**.** Parenteral vs. enteral nutrition in the critically ill patient: A meta-analysis of high-quality trials. *Intensive Care Med* 2005;31(1):12-23

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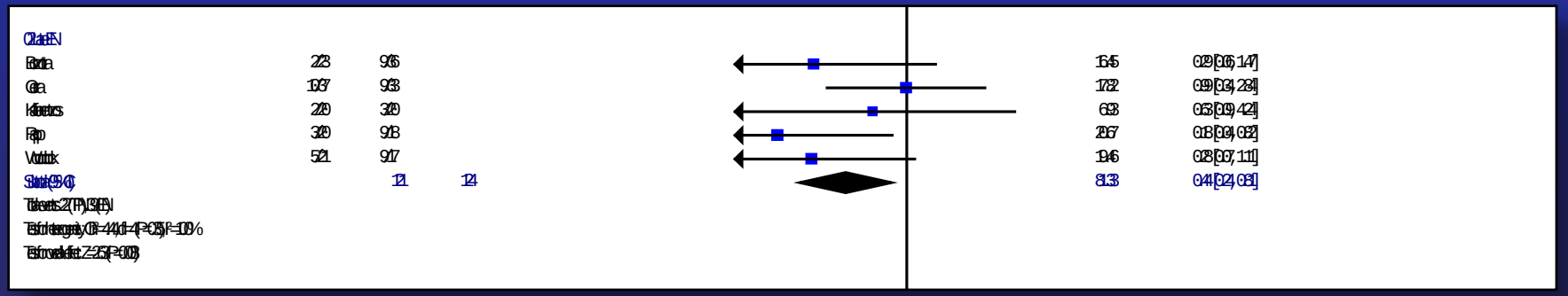

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Equipoise for a large-scale clinical trial

Hypothesis:

In patients who have a short-term relative contraindication to early enteral nutrition, the provision of early parenteral nutrition (within 24 hours of ICU admission) reduces 60-day landmark mortality, and associated measures of morbidity, compared to pragmatic standard care.

A large-scale multi-centre trial

- National Health and Medical Research Council Funded RCT

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- 31 participating hospitals throughout Australia and New Zealand.

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A large-scale multi-centre trial

- National Health and Medical Research Council Funded RCT
- 31 participating hospitals throughout Australia and New Zealand.
- Recruitment ran from 19th October 2006 to 30th June 2011.

  1,363 patients were enrolled and randomised

  682 received pragmatic standard care

  681 received early parenteral nutrition

Eligibility Criteria

Complete inclusion criteria:

- Adult patients admitted to ICU for less than 24 h.
- Expected to remain in ICU today and tomorrow.
- Not expected to receive enteral, parenteral or oral intake today or tomorrow.
- Has a central venous access line through which parenteral nutrition could be delivered.

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Early PN: Study Intervention

- Patients received standard PN
  - ready-to-mix 3-chamber bag containing 34g amino acids, 100g glucose (Glucose 19%), 40g lipid/ 1026mls, 0.9kcal/ml, and electrolytes

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- Starting rates and daily rate increases were defined by study protocols designed to reflect normal care in Australia and New Zealand.

Study PN Protocol A: ALL PATIENTS EXCEPT MALNOURISHED PATIENTS

Feeding Day 1 (first 24 hours of PN)

- Commence TPN at **60ml/hr** (or goal rate, whichever is lower).
- **Consider** trace element, mineral and vitamin needs as clinically appropriate.

Feeding Day 2 (**second 24 hours of PN)**

- Increase TPN to **80ml/hr** (or goal rate, whichever is lower).
- **Consider** trace element, mineral and vitamin needs as clinically appropriate.

Feeding Day 3 (next 24 hours)

- Increase TPN to **goal rate**, as appropriate.
- **Consider** trace element, mineral and vitamin needs, as clinically appropriate.
- **Recommend** trialing enteral/oral nutrition, if clinically appropriate.
- Once the patient tolerates ≥ 475 kcal/day EN, complete remainder of 24 hour TPN infusion and do not hang another bag.
- If patient tolerates any oral caloric intake from food, complete remainder of 24 hour TPN infusion and do not hang another bag.

Feeding Day 4 (next 24 hours) ***plus all additional days after Day 4***

- **May switch** to parenteral nutrition solution tailored to patient's specific clinical needs. Goals not to exceed 25–35 kcal/kg and 1.0–1.5 g protein/kg.
- **Consider** long term needs regarding trace element, mineral and vitamins as clinically appropriate.
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Study PN Protocol B: MALNOURISHED PATIENTS (Ex. BMI ≤ 17 or clinical diagnosis):

Feeding Day 1 (first 24 h of PN)

- Commence TPN at **40ml/hr** (or goal rate, whichever lower).
- **Strongly recommend** administering 100mg thiamine, commencing at least 30 minutes prior to initiation of TPN infusion, as clinically indicated as per product licensing indications.
- **Recommend** daily administration of other vitamins, minerals and trace elements, as clinically appropriate.

Feeding Day 2 (**second 24 hours of PN)**

- Increase TPN to **60ml/hr** (or goal rate, whichever is lower).
- **Recommend** daily administration of vitamins, minerals and trace elements, as clinically appropriate.

Feeding Day 3 (next 24 hours)

- Increase TPN to **goal rate**, as appropriate.
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Feeding Day 4 (next 24 hours) ***plus all additional days after Day 4***

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Early PN: Study Intervention

- Patients received standard PN
  - ready-to-mix 3-chamber bag containing 34g amino acids, 100g glucose (Glucose 19%), 40g lipid/ 1026mls, 0.9kcal/ml, and electrolytes
- Starting rates and daily rate increases were defined by study protocols designed to reflect normal care in Australia and New Zealand.
- Target metabolic needs were calculated using the Harris-Benedict equation.
  - Used total caloric content (including protein calories) of the study PN to calculate PN infusion rates.
  - Metabolic needs for obese patients, defined as a BMI ≥ 30, were calculated based on ideal body weight (BMI = 21).
  - Capped to an upper limit of 35 kcal/kg/day.

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Early PN Trial

Harris-Benedict metabolic goal calculator

Click **here** to read these important instructions.

Equations and adjustment factors as used in the Early PN Trial. Optimized for critically ill patients.

Patient information

Patient Initials		
Date of Birth		dd mm yyyy
Gender		Male or Female
Demi-armspan		cm or Height cm
Current Weight		Kg
Major Active Problem	1.2 Other (Options are ordered from least to most severe)	

Calculate Reset

Results

Age	yrs
BMI	
Ideal Body Weight (if BMI > 30)	kg
Metabolic Goal	kcal per day
Metabolic Goal	kcal per kg per day

[Return to Main Page]

Any questions or comments please contact gdoig@med.usyd.edu.au
Implemented and designed by Gordon Doig
on 30 June 2011
Please accept responsibility for confirming your own calculations.

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www.evidencebased.net/EarlyPN

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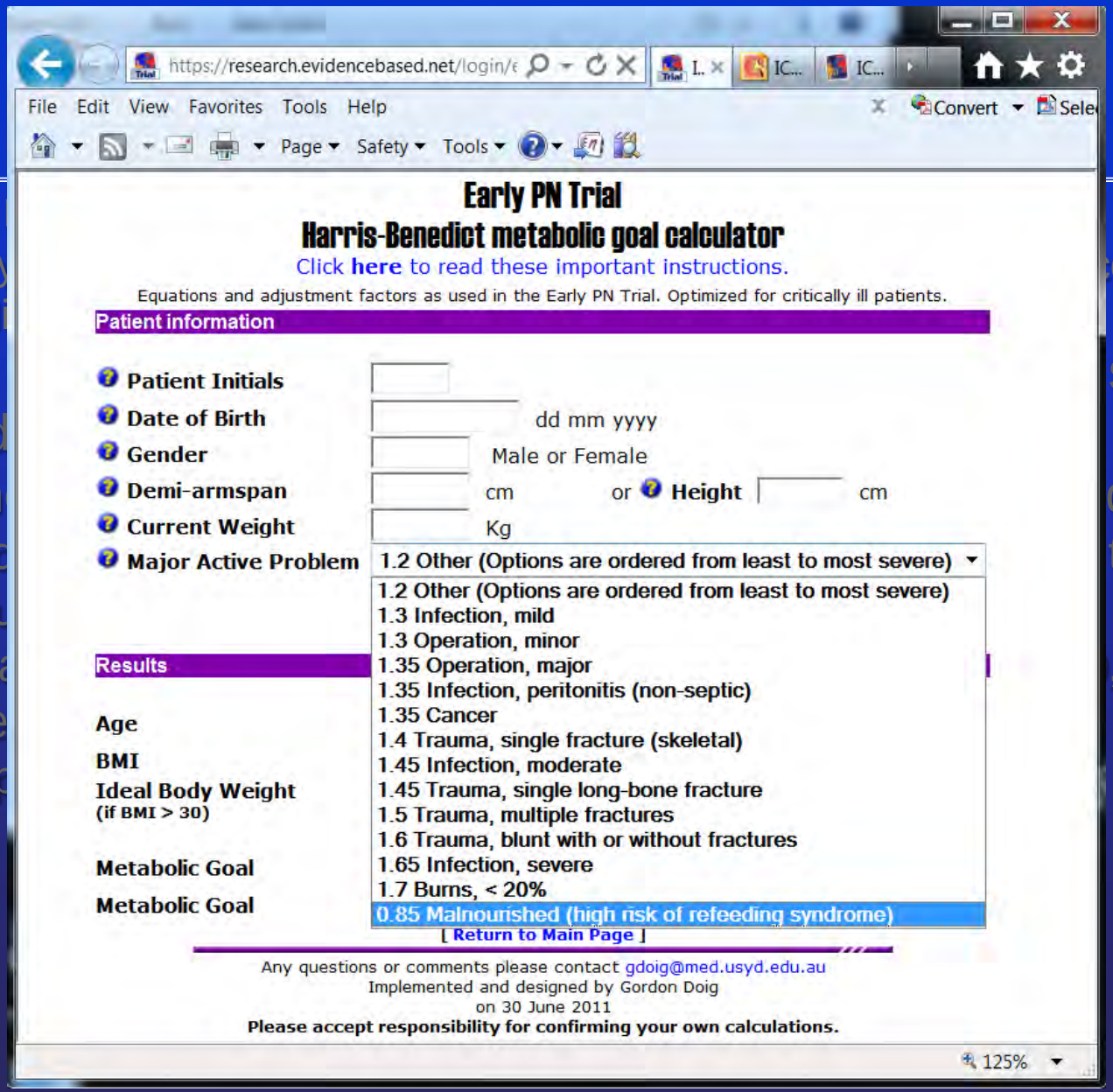

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- *We did not specify the method to be used to re-estimate targets from Day 4 on, however we did recommend that reasonable ranges should be achieved.*

Pragmatic Standard Care

- The attending clinician selected the route, starting rate, metabolic targets, measures of tolerance and composition of feeds to be used in standard care patients based on current practice in *their ICU.*

Who got into the trial:

Main types of patients enrolled:

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

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Overall 65% of patients were surgical and 35% of patients were medical.

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Mortality at Day 60:	301/1358 (22.2%)
Average ICU stay:	8.9 days
Average hospital stay:	25.0 days

This is a critically ill patient population.

Nutrition therapy process measures

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- 278/682 patients (40.8%) never received EN or PN during their 3.72 day ICU stay

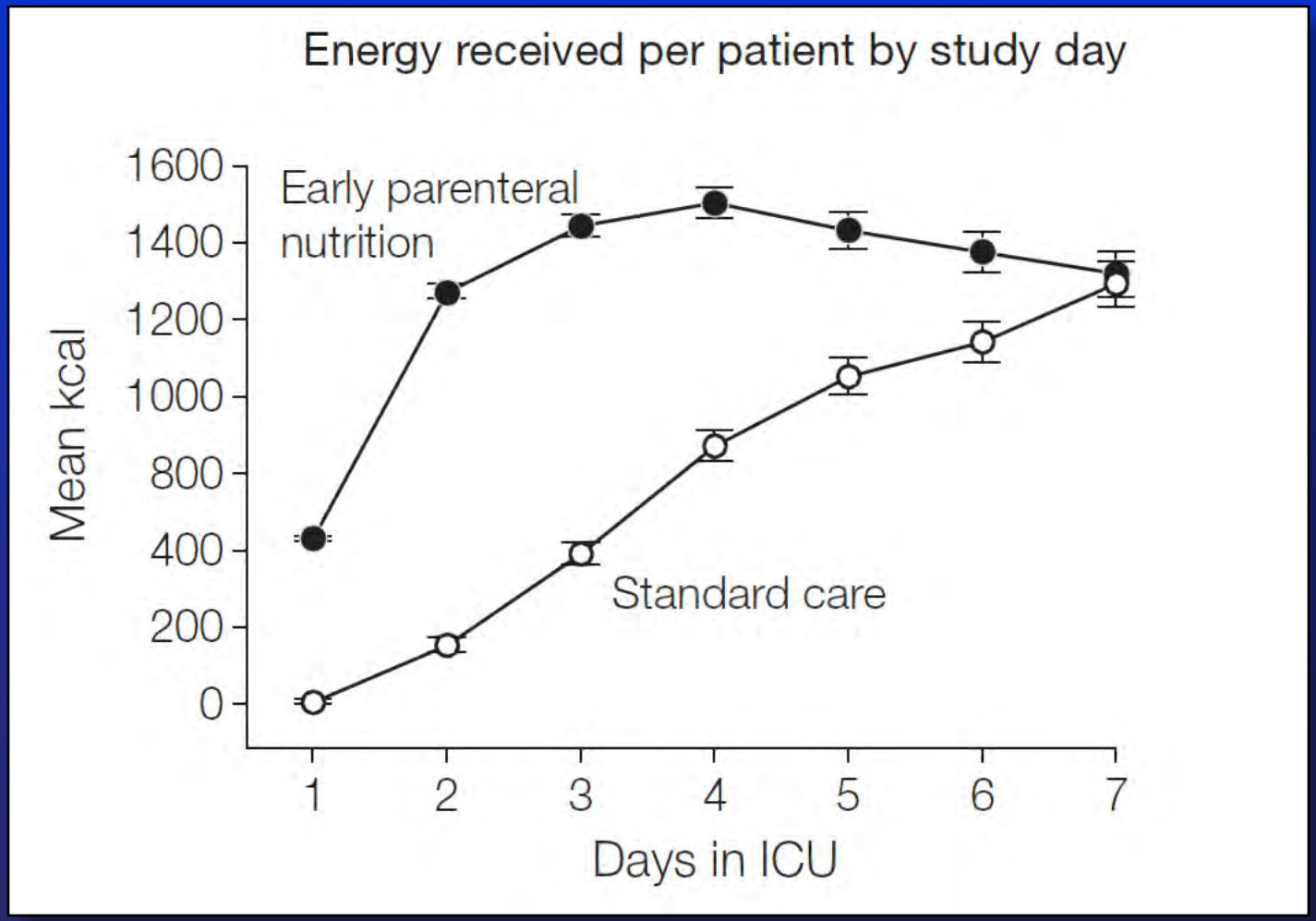

Table 1. Patient Characteristics and Baseline Balance

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)[a,b]	28.5 (6.9)	27.9 (6.8)
APACHE II score, mean (SD)[c,e]	21.5 (7.8)	20.5 (7.4)
Mechanically ventilated, No. (%)	549 (80.6)	572 (83.9)

Pre-specified algorithm was used to identify baseline characteristics for inclusion in a multivariate model to control for confounding.

Final multivariate model controlled for strong predictors and baseline imbalance: **Age, gender, BMI, APACHE 2 score, Chronic Liver, Chronic Respiratory and Source of Admission**.

Table 2. Mortality

	Standard Care (n = 680)[a]	Early PN (n = 678)[a]	Risk Difference, % (95% CI)	*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[b]			0.04 (−4.2 to 4.3)	>.99

[a] 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.

[b] 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.

Table 4. New Infections During Study

Patients With New Infections[a]	No. (%)		Risk Difference (Exact 95% CI)	Exact *P* Value[b]
	Standard Care (n = 682)	Early PN (n = 681)		

[a] new infections based on cultures obtained in the study ICU.

Table 4. New Infections During Study

Patients With New Infections[a]	No. (%) Standard Care (n = 682)	Early PN (n = 681)	Risk Difference (Exact 95% CI)	Exact *P* Value[b]

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[c] venous or arterial catheters

[e] CPIS ≥ 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.

[f] CPIS ≥ 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.

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Patients With New Infections[a]	No. (%) Standard Care (n = 682)	No. (%) Early PN (n = 681)	Risk Difference (Exact 95% CI)	Exact *P* Value[b]
Catheter[c]	32 (4.69)	31 (4.55)	−0.14 (−5.45 to 5.12)	>.99
Catheter tip[c]	28 (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 (4.84)	39 (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[d]	123 (18.04)	101 (14.83)	−3.20 (−8.52 to 2.08)	.12
CPIS-probable pneumonia[e]	96 (14.08)	81 (11.89)	−2.18 (−7.50 to 3.11)	.26
CPIS-confirmed pneumonia[f]	45 (6.60)	43 (6.31)	−0.28 (−5.60 to 5.01)	.91
Any major infection[g]	78 (11.4)	74 (10.9)	−0.57 (−5.89 to 4.72)	.80

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

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Minimally Important Difference = ½ 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.

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Table 3. Concomitant Interventions, Adjusted for Time at Risk (ICU Stay)[a]

	Mean (95% CI), Days per 10 Patient × ICU Days		*P* Value[b]
	Standard Care (n = 682)	Early PN (n = 681)	
Invasive mechanical ventilation	7.73 (7.55 to 7.92)	7.26 (7.09 to 7.44)	.01

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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

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

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- We did not find a difference in any type of infectious complications.
- Early PN patients required significantly fewer ventilator days (1.1 days, p = 0.009) and there was a trend towards a shorter ICU stay (0.75 days, p=0.06).

$1,000,000 question:

HOW could early nutrition reduce duration of ventilation and ICU stay?

Body composition

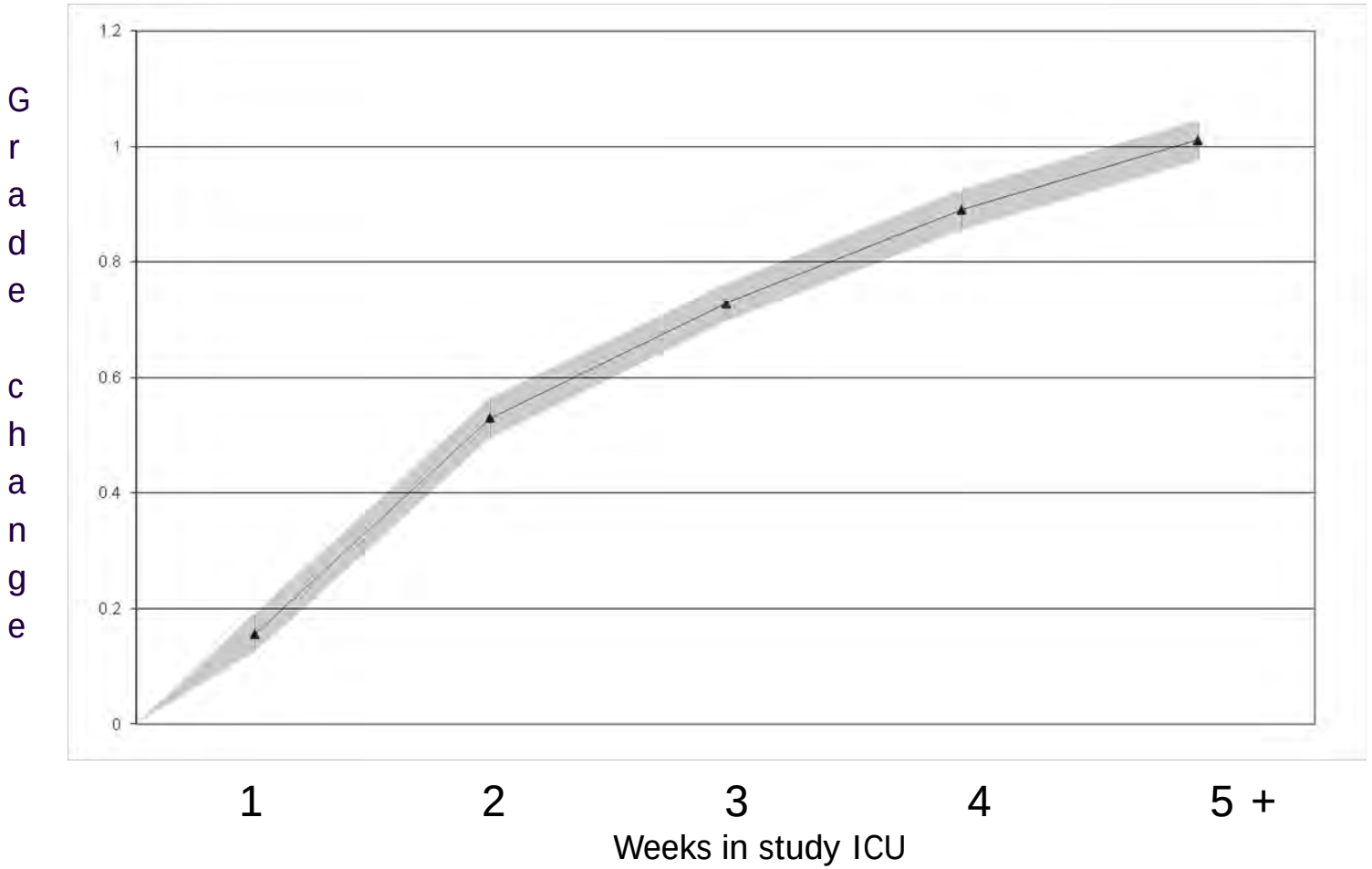
ICU admission:

- Enrolment within 24 h of admit

Body composition measures obtained at enrolment and every Monday and Thursday while in study ICU:

- MAMC, SGA muscle wasting, SGA fat store loss

Subjective Global Assessment: Muscle wasting



Fully factorial repeated measures ANOVA:
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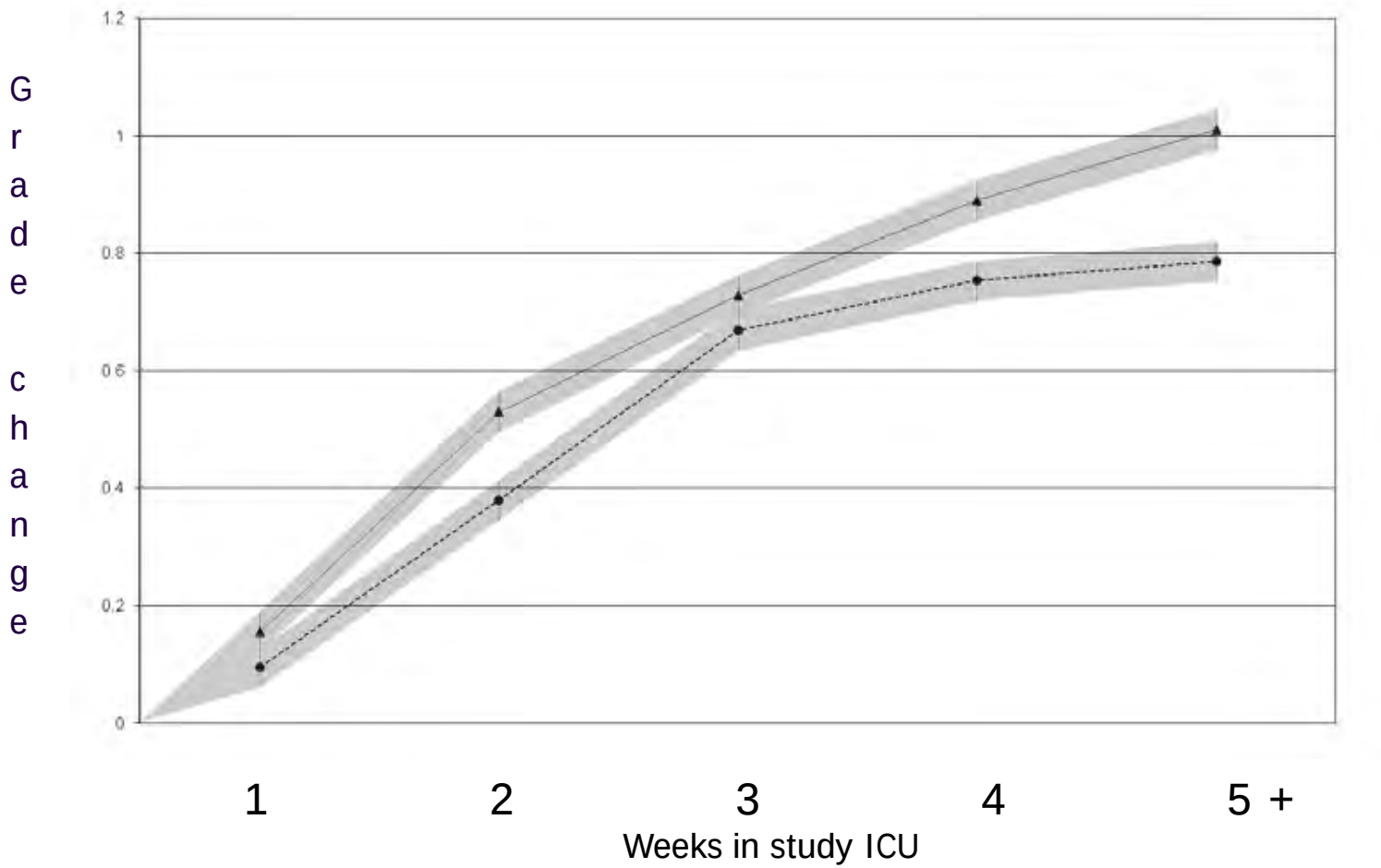
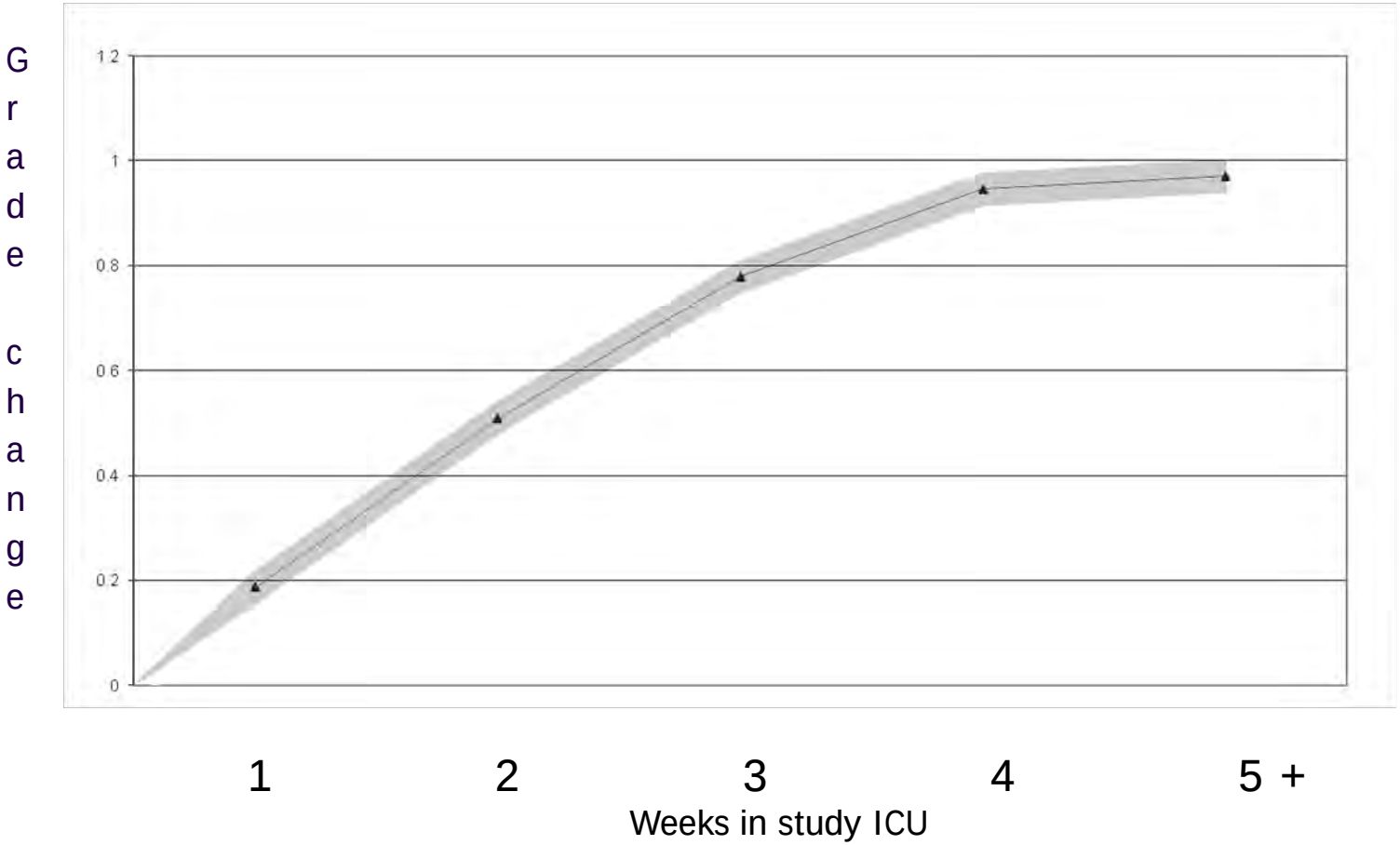


Fully factorial repeated measures ANOVA:
$p < 0.0001$ change over time, $p = 0.014$ difference between groups (0.16 grade per week)

Subjective Global Assessment: Fat loss



Standard care

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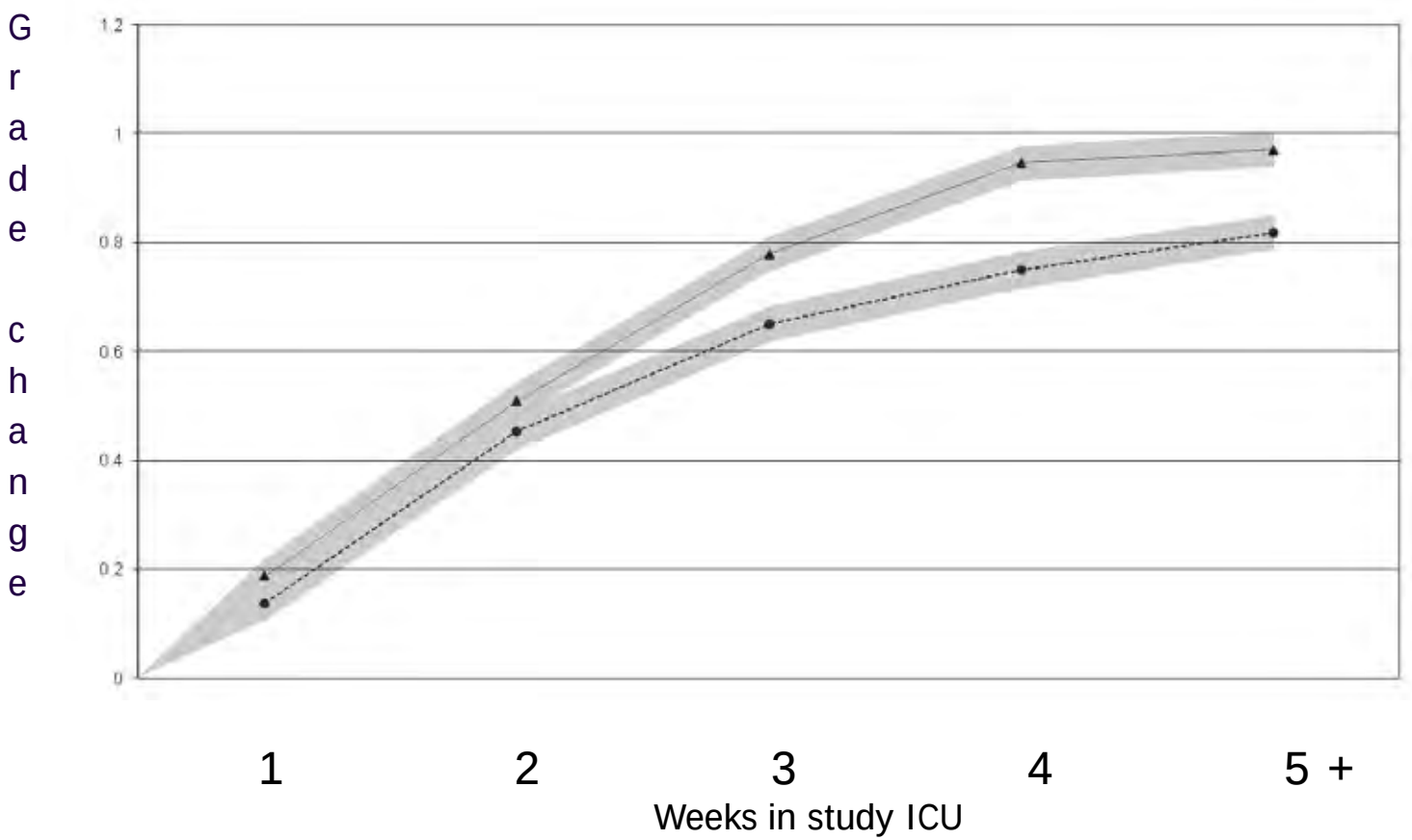

Fully factorial repeated measures ANOVA:
$p < 0.0001$ change over time, $p = 0.045$ difference between groups (0.13 grade per week)

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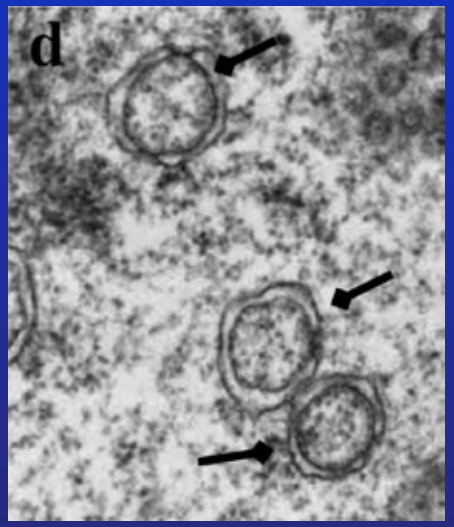

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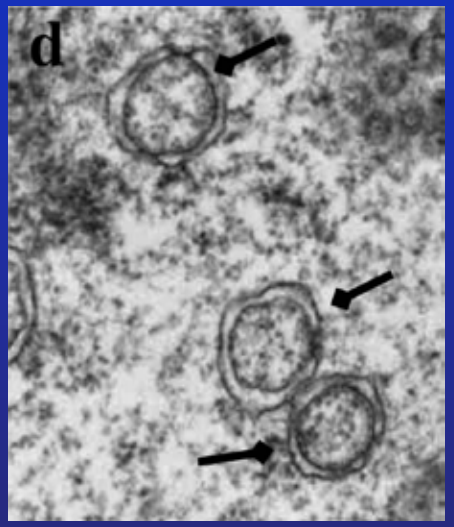

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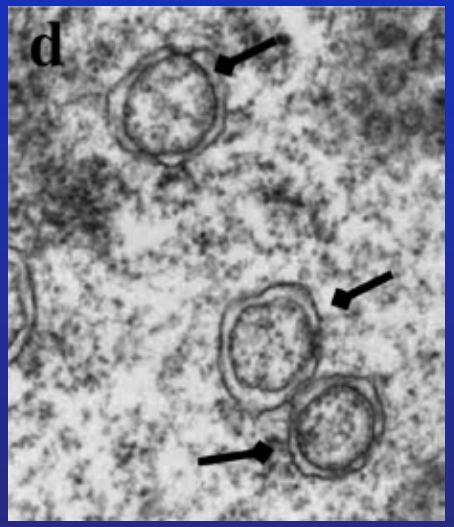

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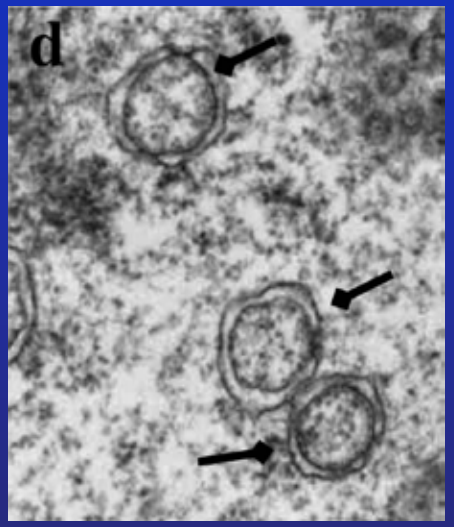

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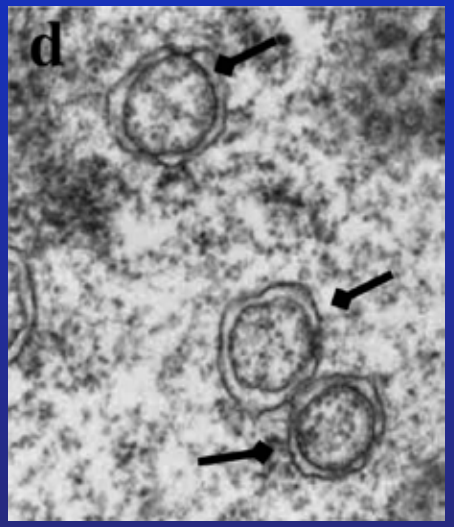

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But what about costs?

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Early parenteral nutrition in critically ill patients with short-term relative contraindications to early enteral nutrition: a full economic analysis of a multicenter randomized controlled trial based on US costs

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On behalf of the Early PN Trial Investigators Group

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Purpose: The provision of early enteral (gut) nutrition to critically ill patients, started within 24 hours of injury or intensive care unit admission, is accepted to improve health outcomes. However, not all patients are able to receive early enteral nutrition. The purpose of the economic analysis presented here was to estimate the cost implications of providing early parenteral (intravenous) nutrition to critically ill patients with short-term relative contraindications to early enteral nutrition.

Materials and methods: From the perspective of the US acute care hospital system, a cost-minimization analysis was undertaken based on large-scale Monte Carlo simulation

Doig GS and Simpson F. Early parenteral nutrition in critically ill patients with short-term contraindications to early enteral nutrition: a full economic analysis of a multicenter randomized controlled trial based on US costs. ***ClinicoEconomics and Outcomes Research*** 2013;5:369-379.

Economic analysis: US costs

Marginal differences in patient outcomes from Early PN Trial:

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

Economic analysis: US costs

Marginal differences in patient outcomes from Early PN Trial:

Costs of ICU care in the US healthcare system:

- Database of 51,009 ICU patients from 253 US hospitals (NDCHealth).
- Costs estimated using hospital specific cost-to-charge ratios

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Marginal differences in patient outcomes from Early PN Trial:

Costs of ICU care in the US healthcare system:

Table 1 Matrix of the distributions of daily costs of care whilst admitted to the intensive care

	Medical patients		Surgical patients		Trauma patients	
	Received MV	No MV received	Received MV	No MV received	Received MV	No MV received
Day 1	$8,141 ($5,584)	$5,357 ($5,584)	$20,582 ($14,319)	$9,916 ($14,319)	$15,625 ($11,955)	$9,062 ($11,955)
Day 2	$6,535 ($4,678)	$4,783 ($4,678)	$7,726 ($6,977)	$5,050 ($6,977)	$7,414 ($6,683)	$4,968 ($6,683)
Day 3 plus	$5,703 ($4,666)	$4,261 ($4,666)	$6,627 ($5,624)	$4,765 ($5,624)	$5,880 ($5,750)	$4,641 ($5,750)

Notes: Mean costs (standard deviation); indexed to 2012 US dollars. Costs of care whilst admitted to the intensive care unit were abstracted from Dasta JF et al.[15]
Abbreviation: MV, mechanical ventilation.

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US costs of PN delivered in the ICU:

- Using the Premier Healthcare Alliance database, Turpin *et al* identified 44,358 hospital patients from 194 hospitals who had at least one transaction level cost recorded for PN.

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Turpin RS, Canada T, Liu FX, Mercaldi CJ, Pontes-Arruda A, Wischmeyer P. Nutrition therapy cost analysis in the US: pre-mixed multi-chamber bag vs compounded parenteral nutrition. *Appl Health Econ Health Policy.* 2011;9(5):281–292.

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US costs of PN delivered in the ICU:

- For the purposes of our study, the costs for providing ready to hang PN were blended with the costs of pharmacy compounded PN to give an estimated cost of US$229.66, with a standard deviation of US$60.44.

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Costs were calculated for *each* of the 1,363 Early PN Trial patient's ICU stay, mechanical ventilation days and PN usage accounting for variability by considering the published *standard deviations of costs using a* Stochastic model with Gamma distributed costs.

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- US$3,150 savings per patient, 95% CI US$1,314 to US$4,990
- *For every $1 spent on PN, $5 are saved in subsequent healthcare costs*

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Discussion

- The Early PN Trial randomised *patients with a short-term relative contraindication to early EN* to receive:

  1) Pragmatic standard care or **2)** PN provided within 24 h of ICU admission.

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www.EvidenceBased.net/EarlyPN