Health economics in ICU nutrition:
The time has come

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Faculty Disclosures

Gordon S. Doig

Relevant financial relationships with a commercial interest:

- Fresenius Kabi, Academic Research Grants (Past), Consultant and Speaker's Honoraria (Current)
- Baxter Healthcare, Academic Research Grant (Current), Consultant and Speaker's Honoraria (Current)
- Nestle Healthcare, Academic Research Grant (Current), Consultant and Speaker's Honoraria (Current)

Overview

- Perspectives on *malnutrition*
- Understanding costs of nutrition in the ICU
- Describe the current study
  - a large scale Monte Carlo simulation of stochastic model based on European costs
- Briefly review financial implications of providing early nutrition to critically ill patients

Malnutrition: Global Perspective

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"Nearly 4 million people die prematurely in India every year from malnutrition and related problems."

Repositioning Nutrition as Central to Development: A Strategy for Large-Scale Action. The World Bank, **2006**.
Hoddinott, Rosegrant and Torero, *Copenhagen Consensus Challenge Paper*, Copenhagen Consensus **2012**.

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"Nearly 4 million people die prematurely in India every year from malnutrition and related problems."

"The portion of the global burden of disease (mortality and morbidity, 1990 figures) in developing countries that would be removed by eliminating malnutrition is estimated as 32 percent."

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"Every $1 invested in nutrition generates as much as $138 in better health and increased productivity."

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Malnutrition: Hospital Perspective

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Malnutrition 'rife in NSW hospitals'

April 2, 2008

By Vincent Morello

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Half the public patients in NSW are malnourished, making them more vulnerable to complications and doubling the time they spend in "error-filled" hospitals, an inquiry into acute care services in NSW has been told.

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Hospital elderly 'underfed'

May 21, 2008 Read later

Jill Stark

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MORE than 90% of elderly hospital patients suffer malnutrition or are at risk of it but most are not being diagnosed, a new study has found.

Dietitians say a focus on obesity and a lack of screening means a "silent epidemic" of malnutrition has been forgotten.

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Half of hospitals 'failing to feed elderly patients properly'

Staff forgetting to give food and water, while dignified care is lacking at 40% of hospitals, Care Quality Commission says

Staff and agencies
guardian.co.uk, Saturday 8 October 2011 08.08 BST

The Care Quality Commission found 40% of hospitals did not offer dignified care for elderly people and half had problems with nutritional standards in aged care. Photograph: Rex Features

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Malnutrition: ICU Perspective

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- Up to 37% of critically ill patients are moderately or severely malnourished at the *time of admission* to the ICU.

Kim H, Stotts N, Froelicher E, Engler M & Porter C. Why patients in critical care do not receive adequate enteral nutrition? A review of the literature. *J Crit Care* **2012**;27: 702-713.

Malnutrition: ICU Perspective

- Up to 37% of critically ill patients are moderately or severely malnourished at the *time of admission* to the ICU.
- 38 – 88% of critically ill patients are malnourished at *some time during their ICU stay*.

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In 1995 a Correlation Between Malnutrition and Poor Outcome in Critically Ill Patients Still Exists

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129 critically ill patients: 74 (57%) Well Nourished and 55 (43%) Malnourished

Giner M, Laviano A, Meguid M and Gleason J. In 1995 a correlation between malnutrition and poor outcome in critically ill patients still exists, *Nutrition* **1996**;12 (1): 23-29.

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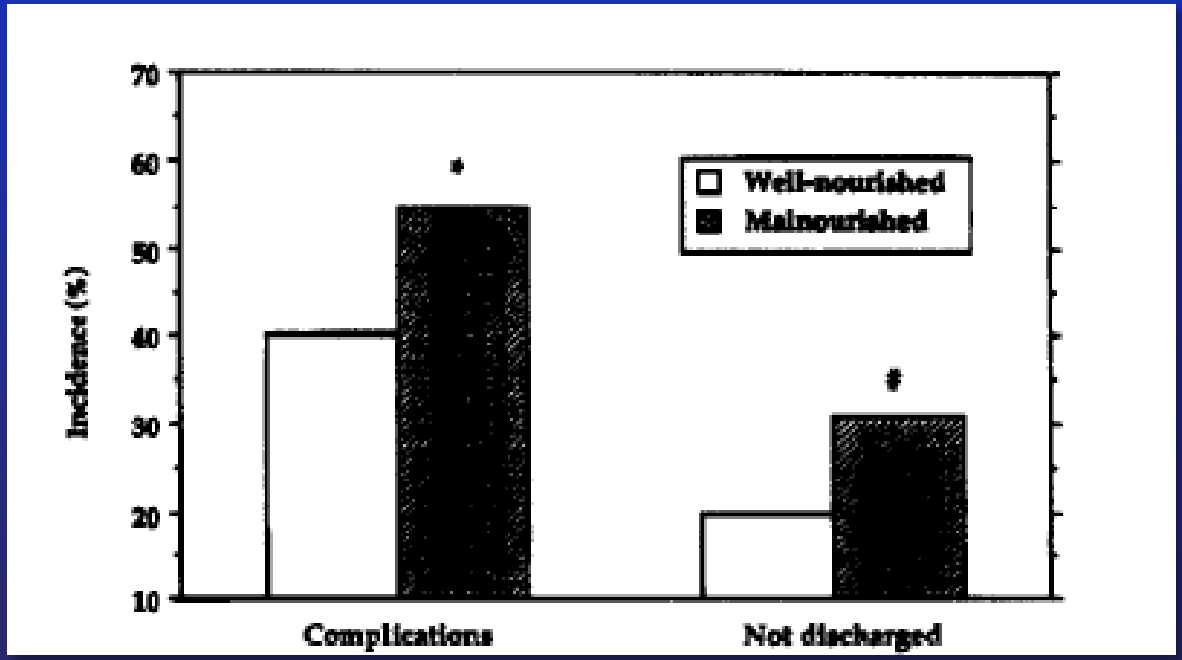

40% vs 55% (p<0.01) / 20% vs 31% (p<0.05)

Giner M, Laviano A, Meguid M and Gleason J. In 1995 a correlation between malnutrition and poor outcome in critically ill patients still exists, *Nutrition* **1996**;12 (1): 23-29.

Meta-analysis of early EN in critical illness

Intensive Care Med (2009) 35:2018–2027
DOI 10.1007/s00134-009-1664-4

SYSTEMATIC REVIEW

Gordon S. Doig
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Fiona Simpson
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Early enteral nutrition, provided within 24 h of injury or intensive care unit admission, significantly reduces mortality in critically ill patients: a meta-analysis of randomised controlled trials

Doig GS, Heighes PT, Simpson F, Sweetman EA and Davies AR. Enteral nutrition within 24 h of ICU admission significantly reduces mortality: A meta-analysis of RCTs. *Intensive Care Medicine* **2009** Dec;35(Issue 12):2018-2027.

CARING FOR THE CRITICALLY ILL PATIENT

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

A Cluster Randomized Controlled Trial

Process Measure	Control (13 ICUs, 557 Patients)[a]
Mean time from ICU admission to EN, PN, ICU discharge, or death, d[d]	
All patients	2.14 (1.73 to 2.66)
Other process measures	
Patients never fed at any time during ICU stay, No. (%)	157 (28.2) [21.2 to 37.5]

Doig G, Simpson F, Finfer S, Delaney A, Davies AR, Mitchell, I et al. 2008, Effect of evidence based feeding guidelines on mortality of critically ill adults: a cluster randomized controlled trial. *JAMA* **2008**;300:2731-2741.

Is this delay in feeding due to costs?

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Review

Enteral Nutrition and Oral Nutrition Supplements: A Review of the Economics Literature

Clive Pritchard, PhD*; Steven Duffy, PGDip†; Jackie Edington, PhD‡; and Francis Pang, PhD§

Pritchard C, Duffy S, Edington J, Pang F. Enteral nutrition and oral nutrition supplements: a review of the economics literature. *JPEN* **2006** Jan-Feb;30(1):52-9.

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"The cost-effectiveness of different forms of nutrition in different patient groups remains to be established."

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Purpose of this project

- Full economic analysis involves the comparison of alternative courses of action in terms of both costs (resource use) and consequences (patient outcomes, adverse effects).

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- Full economic analysis involves the comparison of alternative courses of action in terms of both costs (resource use) and consequences (patient outcomes, adverse effects).

- A well-conducted meta-analysis based on a systematic review of randomized trials is the *least-biased* source of data to establish treatment consequences (resource use, patient outcomes, adverse effects) for use in an economic model.

Methods for the Economic Evaluation of Health Care Programmes. By M Drummond, MJ Sculpher, GW Torrance, BJ O'Brien and GL Stoddart. Oxford University Press, Oxford **2005**.

Cochrane Handbook for Systematic Reviews of Interventions, Version 5.0.0. Higgins JPT, Green S (editors). [updated February **2008**]. The Cochrane Collaboration, 2008. Available from www.cochrane-handbook.org.

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Meta-analysis of early EN in critical illness

Comprehensive Literature search

- MEDLINE (http://www.PubMed.org) and EMBASE (http://www.EMBASE.com)
- Academic and industry experts were contacted,
- Reference lists of identified systematic reviews and evidence-based guidelines were hand searched by at least two authors.
- The search was not restricted by Language.

Primary analysis

- Included only methodologically sound RCTs.

Primary outcome

- clinically meaningful patient oriented outcomes: (mortality / physical function / quality of life)

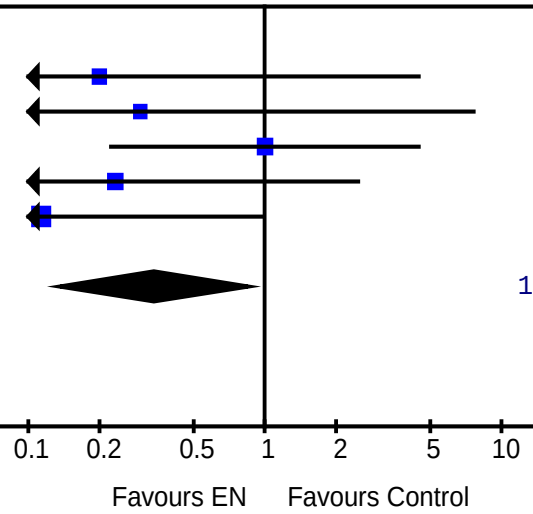
Doig GS, Heighes PT, Simpson F, Sweetman EA and Davies AR. Enteral nutrition within 24 h of ICU admission significantly reduces mortality: A meta-analysis of RCTs. *Intensive Care Medicine* **2009** Dec;35(Issue 12):2018-2027.

Results: Primary MA, mortality

Review: Early EN (<24h) vs Control (Primary Analysis)
Comparison: 01 early EN vs Control
Outcome: 01 Mortality, Intention to treat analysis

Study or sub-category	early EN (<24 h) n/N	Control n/N	OR (fixed) 95% CI	Weight %	OR (fixed) 95% CI
Chiarelli 1990	0/10	0/10			Not estimable
Kompan 1999	0/17	2/19		13.40	0.20 [0.01, 4.47]
Kompan 2004	0/27	1/25		8.89	0.30 [0.01, 7.63]
Nguyen 2008	6/14	6/14		19.95	1.00 [0.22, 4.47]
Chuntrasakul 1996	1/21	3/17		18.38	0.23 [0.02, 2.48]
Pupelis 2001	1/30	7/30		39.38	0.11 [0.01, 0.99]
Total (95% CI)	119	115		100.00	0.34 [0.14, 0.85]

Total events: 8 (early EN (<24 h)), 19 (Control)
Test for heterogeneity: Chi² = 3.20, df = 4 (P = 0.52), I² = 0%
Test for overall effect: Z = 2.31 (P = 0.02)

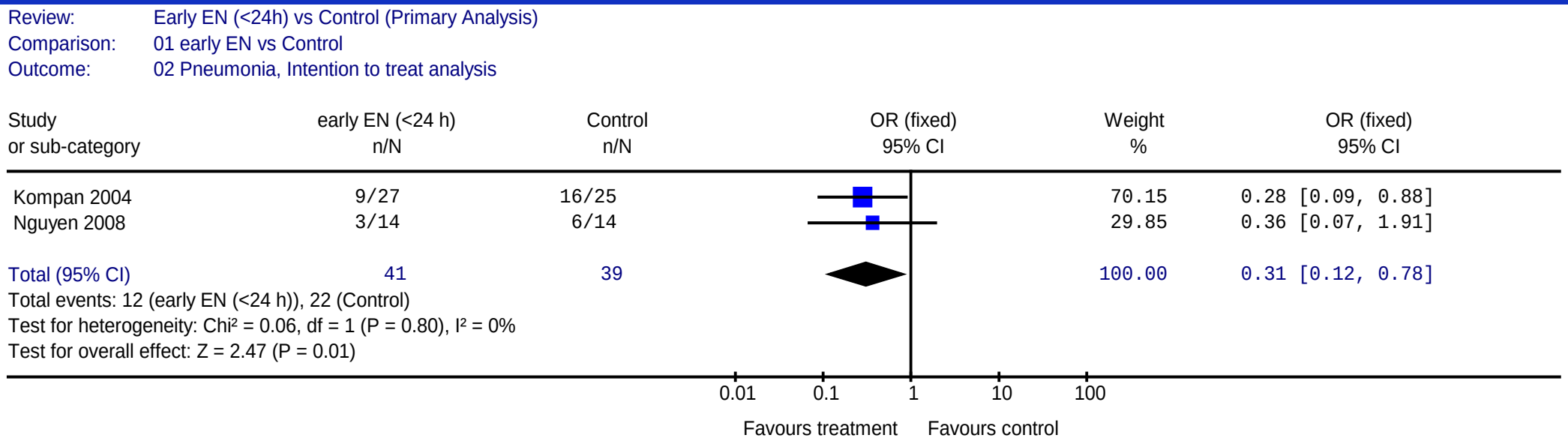


Significant reduction in mortality with early EN (95%CI 8.6% to 17.2%, P=0.02)

Doig GS, Heighes PT, Simpson F, Sweetman EA and Davies AR. Enteral nutrition within 24 h of ICU admission significantly reduces mortality: A meta-analysis of RCTs. *Intensive Care Medicine* **2009** Dec;35(Issue 12):2018-2027.

Results: Primary MA, Pneumonia

Review: Early EN (<24h) vs Control (Primary Analysis)
Comparison: 01 early EN vs Control
Outcome: 02 Pneumonia, Intention to treat analysis



Significant reduction in pneumonia with early EN (27% reduction, P=0.01)

Doig GS, Heighes PT, Simpson F, Sweetman EA and Davies AR. Enteral nutrition within 24 h of ICU admission significantly reduces mortality: A meta-analysis of RCTs. *Intensive Care Medicine* **2009** Dec;35(Issue 12):2018-2027.

Results: updated MA, ICU length of stay

Doig et al — Dovepress

Study or subgroup	EEN Mean [days]	EEN SD [days]	EEN Total	SoC Mean [days]	SoC SD [days]	SoC Total	Weight	Mean difference IV, fixed, 95% CI [days]	Year
Chuntrasakul et al[18]	8.14	6.28	21	8.35	4.78	17	47.7%	−0.21 [−3.73, 3.31]	1996
Pupelis et al[19]	13.9	14.6	30	16	20.5	30	7.3%	−2.10 [−12.86, 8.66]	2001
Kompan et al[20]	15.9	9.7	27	20.6	18.5	25	8.9%	−4.70 [−12.82, 3.42]	2004
Nguyen et al[21]	11.3	2.99	14	15.9	7.11	14	36.1%	−4.60 [−8.64, −0.56]	2008
Total (95% CI)			92			86	100.0%	−2.34 [−4.76, 0.09]	

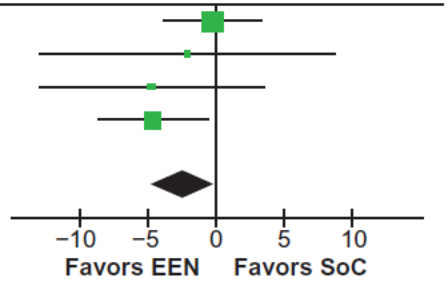


Figure 1 Meta-analysis of ICU length of stay: early enteral nutrition vs standard care.
Notes: Heterogeneity: $\chi^2 = 2.94$, $df = 3$ ($P = 0.40$); $I^2 = 0\%$. Test for overall effect: $Z = 1.87$ ($P = 0.06$).
Abbreviations: CI, confidence interval; EEN, early enteral nutrition; ICU, Intensive Care Unit; IV, inverse variance; SD, standard deviation; SoC, standard of care.

Trend towards reduced length of ICU stay with early EN (2.34 days, P = 0.06)

Doig GS, Chevrou-Severac H and Simpson F. Early enteral nutrition in critical illness: A full economic analysis using US costs. *ClinicoEconomics and Outcomes Research* **2013**;5:429-436.

Results: updated MA, duration of MV

Study or subgroup	EEN Mean [days]	EEN SD [days]	EEN Total	SoC Mean [days]	SoC SD [days]	SoC Total	Weight	Mean difference IV, fixed, 95% CI [days]
Chuntrasakul et al[18]	5.29	6.28	21	6.12	5.32	17	48.1%	−0.83 [−4.52, 2.86]
Kompan et al[20]	12.9	8.1	27	15.6	16.1	25	13.3%	−2.70 [−9.71, 4.31]
Nguyen et al[21]	9.2	3.37	14	13.7	7.11	14	38.6%	−4.50 [−8.62, −0.38]
Total (95% CI)			62			56	100.0%	−2.49 [−5.05, 0.07]

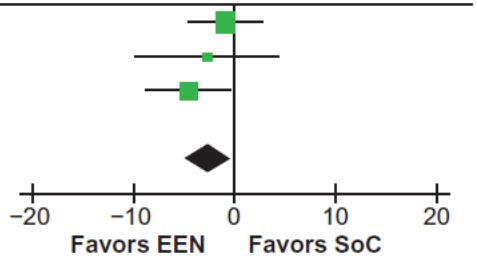


Figure 2 Meta-analysis of duration of mechanical ventilation: early enteral nutrition vs standard care.
Notes: Heterogeneity: $\chi^2 = 1.69$, $df = 2$ ($P = 0.43$); $I^2 = 0\%$. Test for overall effect: $Z = 1.91$ ($P = 0.06$).
Abbreviations: CI, confidence interval; EEN, early enteral nutrition; IV, inverse variance; SD, standard deviation; SoC, standard of care.

Trend towards reduced mechanical ventilation with early EN (2.49 days, P = 0.06)

Doig GS, Chevrou-Severac H and Simpson F. Early enteral nutrition in critical illness: A full economic analysis using US costs. *ClinicoEconomics and Outcomes Research* **2013**;5:429-436.

Results: updated MA, hospital stay

Study or subgroup	EEN Mean [days]	EEN SD [days]	EEN Total	SoC Mean [days]	SoC SD [days]	SoC Total	Weight	Mean difference IV, fixed, 95% CI [days]	Year	Mean difference IV, fixed, 95% CI [days]
Chiarelli et al[22]	69.2	32.89	10	89	59.77	10	10.2%	−19.80 [−62.08, 22.48]	1990	
Pupelis et al[19]	35.3	22.9	30	35.8	32.5	30	89.8%	−0.50 [−17.50, 16.50]	2001	
Total (95% CI)			40			40	100.0%	−2.46 [−15.95, 11.02]		

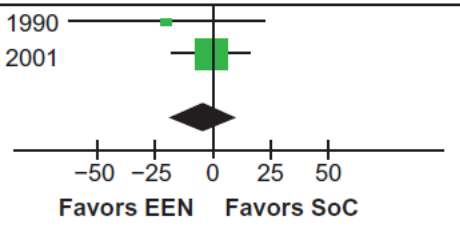


Figure 3 Meta-analysis of hospital length of stay: early enteral nutrition versus standard care.
Notes: Heterogeneity: $\chi^2 = 1.69$, $df = 1$ ($P = 0.41$); $I^2 = 0\%$. Test for overall effect: $Z = 0.40$ ($P = 0.72$).
Abbreviations: CI, confidence interval; EEN, early enteral nutrition; IV, inverse variance; SD, standard deviation; SoC, standard of care.

No difference in hospital stay (2.46 days, P =0.72).

Doig GS, Chevrou-Severac H and Simpson F. Early enteral nutrition in critical illness: A full economic analysis using US costs. *ClinicoEconomics and Outcomes Research* **2013**;5:429-436.

Summary of the consequences of early EN use

- Significant reduction in mortality (95%CI 8.6% to 17.2%, P=0.02)
- Trend towards reduction in length of ICU stay (2.34 days, P=0.06)
- Trend towards reduction in mechanical ventilation (2.49 days, P=0.06)
    - Significant reduction in VAP (27%, P=0.01)

Establishing costs

- Costs of ICU care:

Establishing costs

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Journal of Intensive Care Medicine
http://jic.sagepub.com/

Review of A Large Clinical Series: A Microcosting Study of Intensive Care Unit Stay in the Netherlands

Siok Swan Tan, Leona Hakkaart-van Roijen, Maiwenn J. Al, Clazien A. Bouwmans, Marga E. Hoogendoorn, Peter E. Spronk and Jan Bakker

J Intensive Care Med 2008 23: 250 originally published online 28 May 2008
DOI: 10.1177/0885066608318661

Tan SS, Hakkaart-van Roijen L, Al MJ, et al. Review of a large clinical series: a microcosting study of intensive care unit stay in the Netherlands. *J Intensive Care Med*. **2008**;23(4):250–257.

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- Average total costs of 1 non-ventilated ICU day reported as €1,835
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Establishing costs

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JOURNAL OF PARENTERAL AND ENTERAL NUTRITION
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Review

Enteral Nutrition and Oral Nutrition Supplements: A Review of the Economics Literature

Clive Pritchard, PhD*; Steven Duffy, PGDip†; Jackie Edington, PhD‡; and Francis Pang, PhD§

"The cost-effectiveness of different forms of nutrition in different patient groups remains to be established."

Pritchard C, Duffy S, Edington J, Pang F. Enteral nutrition and oral nutrition supplements: a review of the economics literature. *JPEN* **2006** Jan-Feb;30(1):52-9.

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Is the Use of Specialized Nutritional Formulations a Cost-Effective Strategy? A National Database Evaluation

Adrien Strickland, Anita Brogan, Janis Krauss, Robert Martindale and Gail Cresci

JPEN J Parenter Enteral Nutr 2005 29: S81

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- Considered purchase costs, supplies used for delivery, and professionals' time
- $35 per day
  - indexed to 2012 US dollars using US Consumer Price Index, Medical Consumers

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- Assumes that early EN patients received 6.21 extra days of EN, compared with standard care patients.

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Calculation of crude costs

Crude calculations of costs (based on averages):

6.21 more days of EN	x	€39.30	=	+ €244

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  Ex. Cost of 1 non-ventilated ICU day has mean €1,835 and SD €1,688

  Difference in ICU stay has mean 2.34 and SD 15.87 days

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- The total accumulated costs is the sum of a series of cross products of sets of numbers, each with considerable variability
- In addition, costs and length of stay are known to have long tailed distributions
  - Gamma distributed random numbers are generated with mean μ and shape α, where $\alpha = \mu^2 / \sigma^2$, (SAS, ver 6.12)

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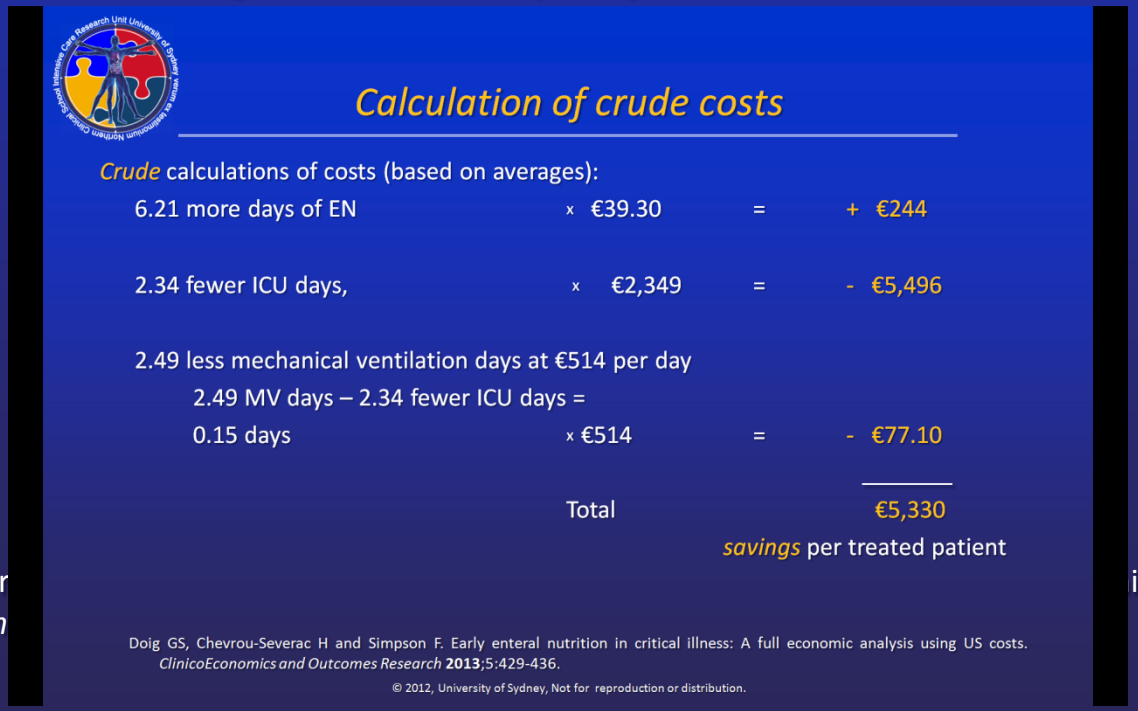

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*95% CI obtained via the Percentile method (non-parametric)

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

	Medical patients		Surgical patients		Trauma patients	
	Received MV	**Never received MV**	**Received MV**	**Never received MV**	**Received MV**	**Never received MV**
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: Values are expressed as mean costs (standard deviation); indexed to 2012 US Dollars. Costs were abstracted from Dasta et al.[11]
Abbreviation: MV, mechanical ventilation.

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  - For every $1 spent, $45.40 are returned!!
- *And* we conducted a similar cost analysis for patients evaluating early PN in patients who could not receive early EN:
  - Early PN reduces costs ($3,150 per patient, 95% CI $1,314 to $4,990)
  - For every $1 spent, $5 are returned!!

Doig GS and Simpson F. 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. *ClinicoEconomics and Outcomes Research* **2013**;5:369-379.

Doig GS, Chevrou-Severac H and Simpson F. Early enteral nutrition in critical illness: A full economic analysis using US costs. *ClinicoEconomics and Outcomes Research* **2013**;5:429-436.

Calculation of crude costs

Crude calculations of costs (based on averages):

6.21 more days of EN x *your cost of EN* = costs

2.34 fewer ICU days, x *your cost of an ICU day* = savings

2.49 less mechanical ventilation days at *your cost of MV* per day

2.49 MV days – 2.34 fewer ICU days =

0.15 days x *your cost of MV* = savings

Total *your total savings* per treated patient

Doig GS, Chevrou-Severac H and Simpson F. Early enteral nutrition in critical illness: A full economic analysis using US costs. *ClinicoEconomics and Outcomes Research* **2013**;5:429-436.

Questions??

- The provision of early enteral nutrition to critically ill patients *dominant*:
  - Early EN reduces mortality (95%CI 8.6% to 17.2%) *and*
  - Early EN reduces costs (€5,325 per patient, 95%CI €2,475 to €8,224)
  - For every €1 spent, €22.8 are returned!!
- We re-ran the Monte Carlo simulation with a complex database of US cost:
  - Early EN reduces costs ($14,462 per patient, 95% CI $5,464 to $23,669)
  - For every $1 spent, $45.40 are returned!!
- *And* we conducted a similar cost analysis for patients evaluating early PN in patients who could not receive early EN:
  - Early PN reduces costs ($3,150 per patient, 95% CI $1,314 to $4,990)
  - For every $1 spent, $5 are returned!!

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