# Should patients be fed to achieve full caloric goals rapidly? If so, does the route matter?

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# *Disclosures*
## *Gordon S. Doig*

Relevant financial relationships over past 5 years:

- Nestle Healthcare, Academic Research Grant, Consultant and Speaker's Honoraria
- Fresenius Kabi, Academic Research Grants, Consultant and Speaker's Honoraria
- Baxter Healthcare, Academic Research Grant, Consultant and Speaker's Honoraria
- Nutricia, Speakers Honoraria

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2. If so, does the route matter?

*Yes.*

# *Conclusions*

1. Should patients be fed to achieve full caloric goals rapidly?

*No. You actually might kill critically ill patients by trying to achieve goals too rapidly.*

2. If so, does the route matter?

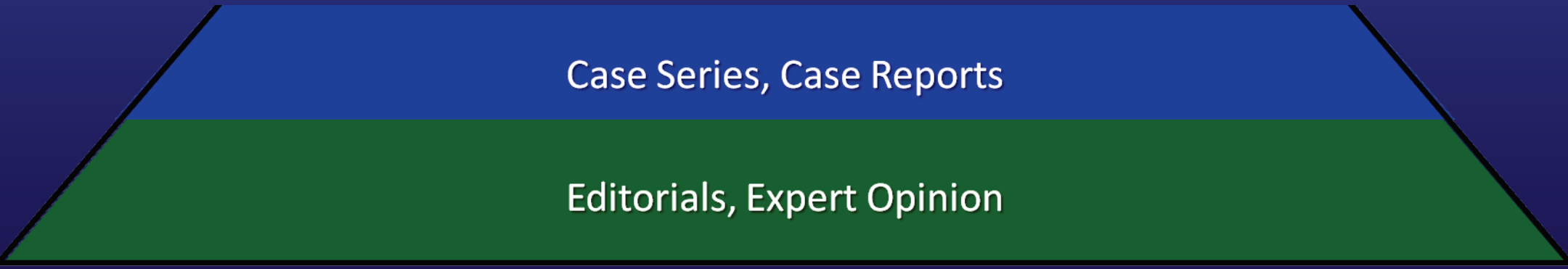
*Yes. Early EN is cheaper than Early PN whilst Early PN is cheaper than not feeding at all!*

# *Summary of this talk*

- Understand Levels of Evidence.
- Investigate the concept of ‘caloric / energy debt’ in critical illness.
- Review the most recent clinical evidence on the topic.
- Investigate costs.
- Conclude, with succinct evidence-based recommendations.

Editorials, Expert Opinion

The Oxford 2011 levels of evidence. Oxford: Oxford centre for evidence based medicine; 2011.

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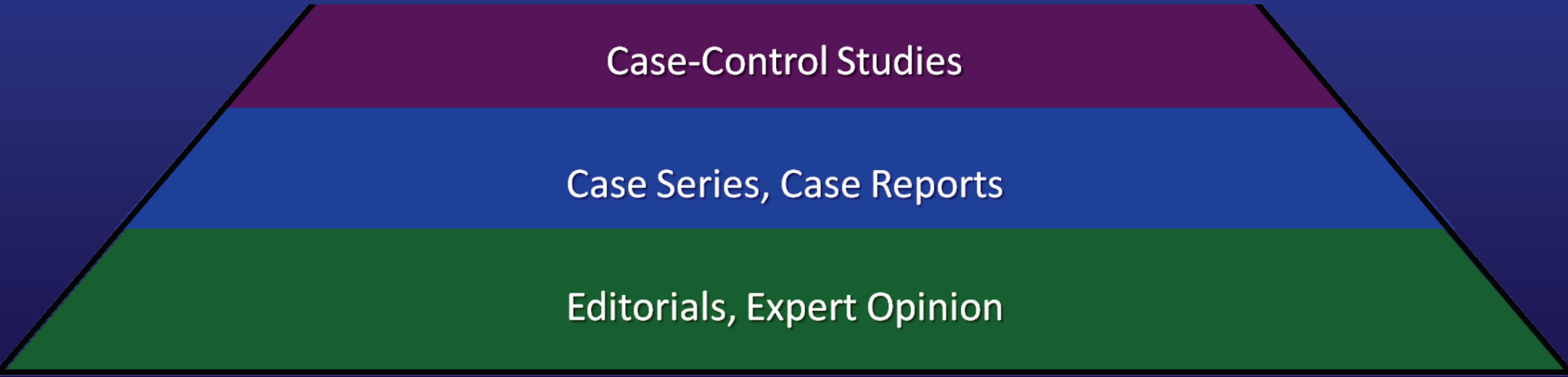


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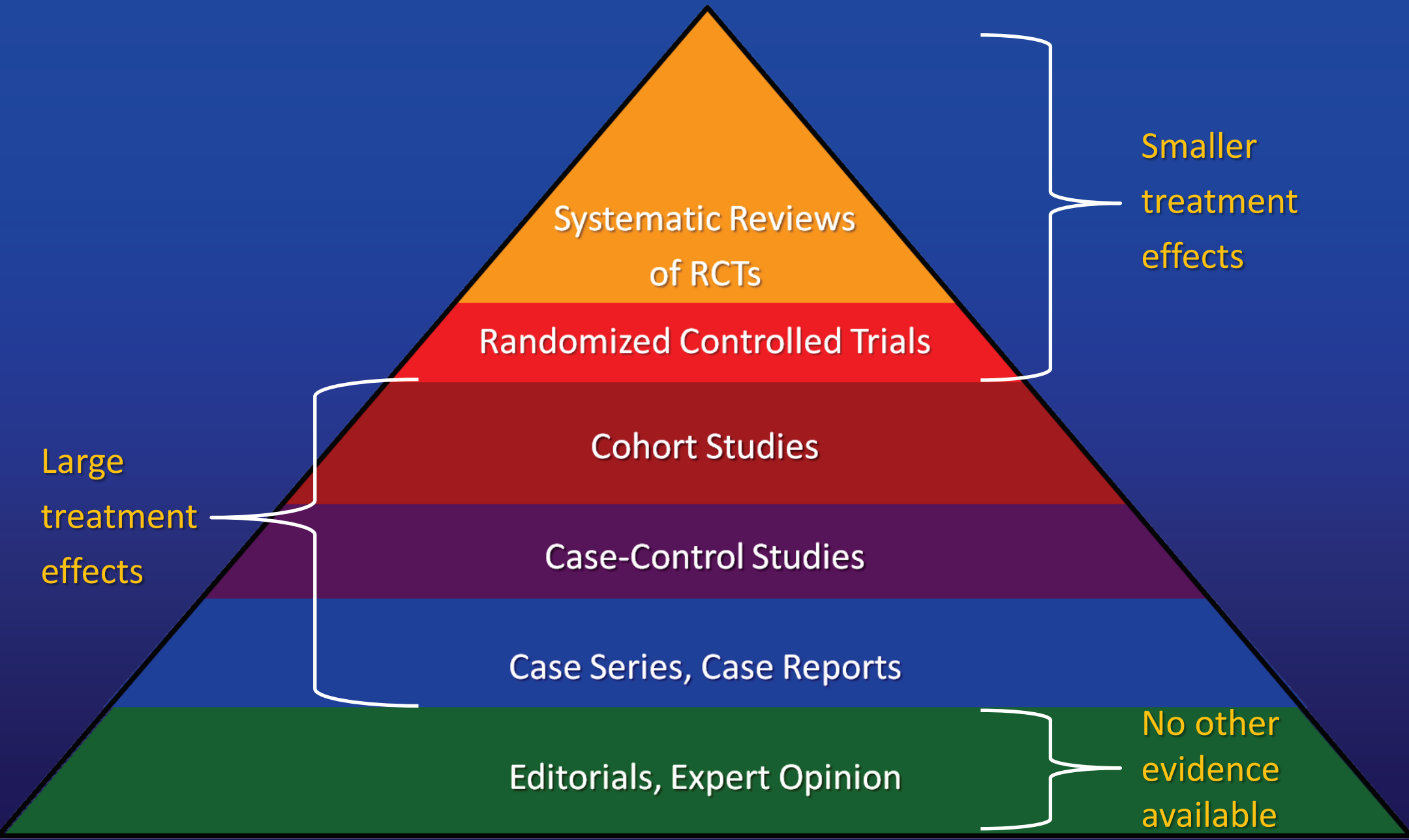


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# *Finding the evidence:*

Intensive Care Medicine
December 2003, Volume 29, Issue 12, pp 2119-2127

## Efficient literature searching: a core skill for the practice of evidence-based medicine

Gordon Stuart Doig, Fiona Simpson

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Doig GS, Simpson F. Efficient literature searching: a core skill for the practice of evidence-based medicine. Intensive Care Med. 2003 Dec;29(12):2119-27.

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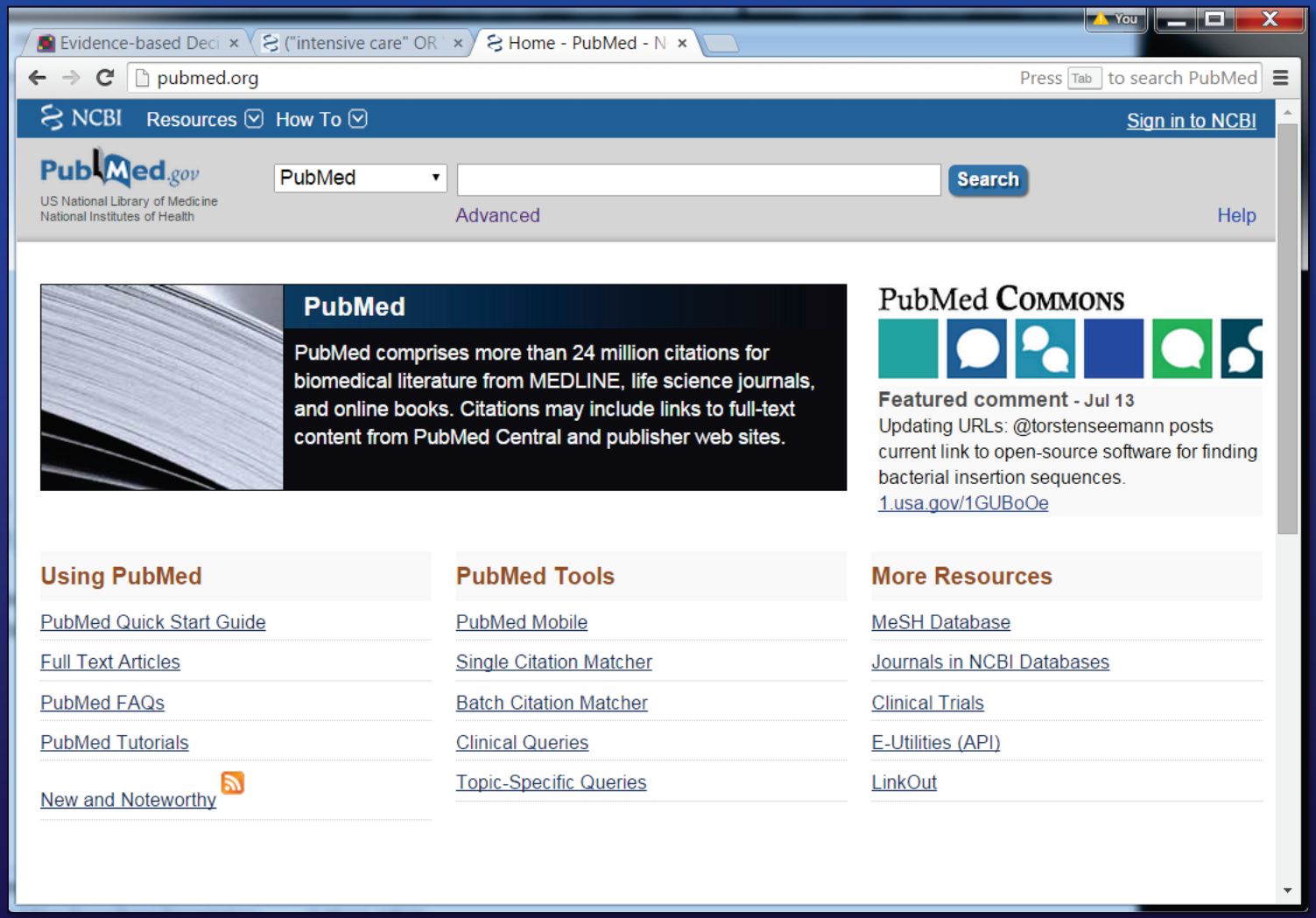


# *Simple PubMed Search:*

("intensive care" OR "intensive care units" OR "intensive therapy" OR "critically ill" OR "critical care")

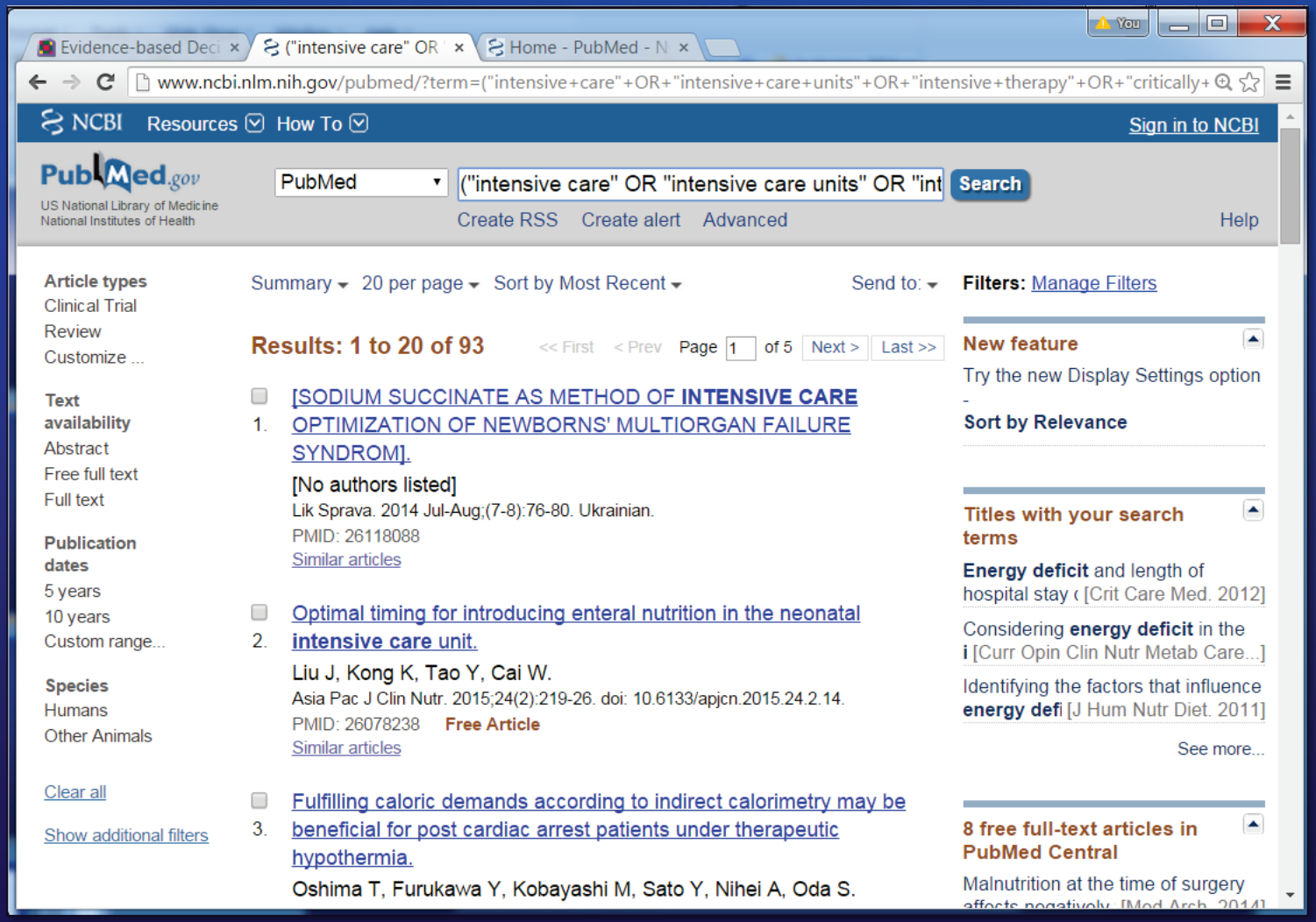
AND

energy deficit

OR

energy debt

# www.PubMed.org



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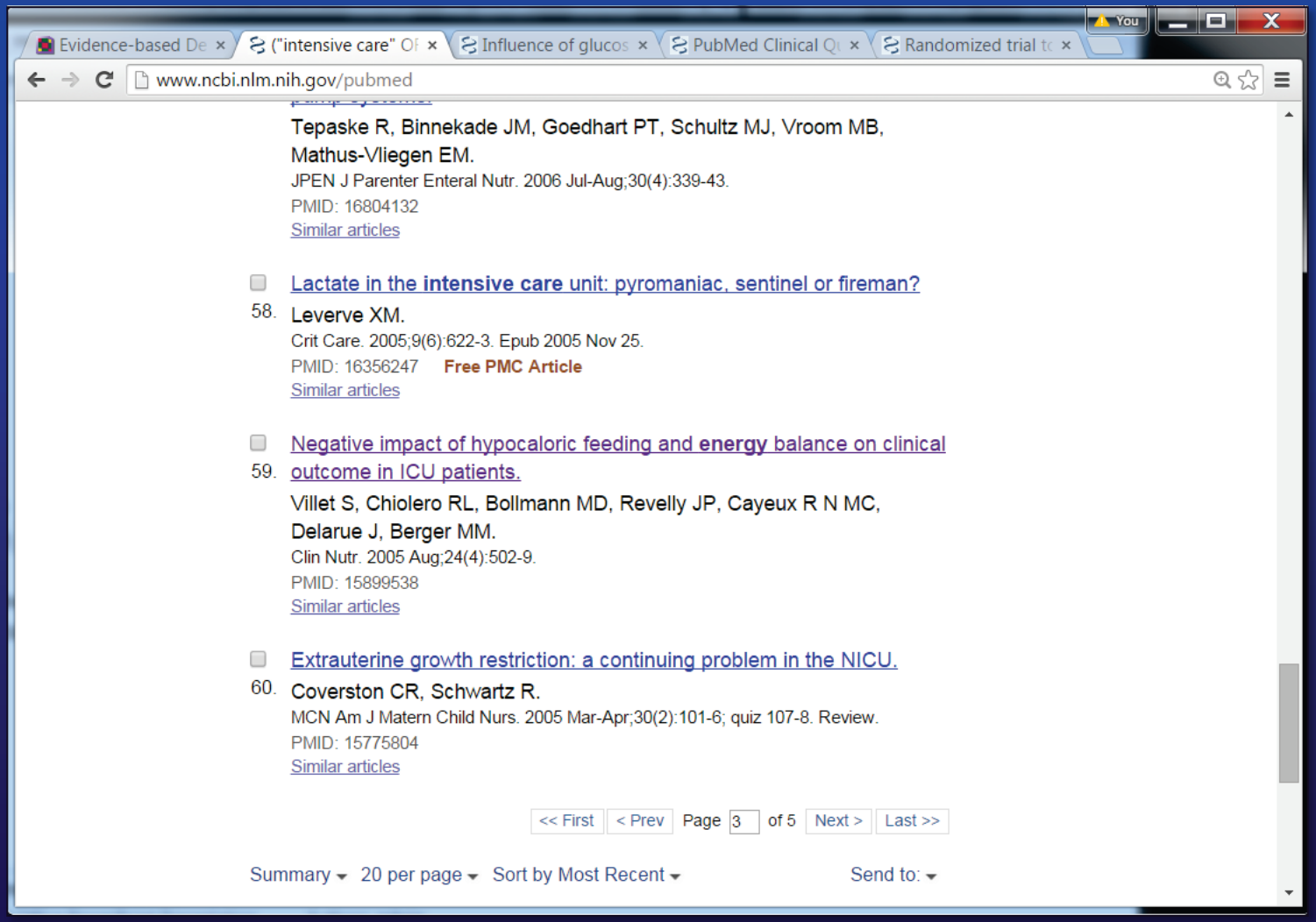

Abstract Send to:

Clin Nutr. 2005 Aug;24(4):502-9.

# Negative impact of hypocaloric feeding and energy balance on clinical outcome in ICU patients.

Villet S[1], Chiolero RL, Bollmann MD, Revelly JP, Cayeux R N MC, Delarue J, Berger MM.

Author information

## Abstract

**BACKGROUND AND AIMS:** Critically ill patients with complicated evolution are frequently hypermetabolic, catabolic, and at risk of underfeeding. The study aimed at assessing the relationship between energy balance and outcome in critically ill patients.

**METHODS:** Prospective observational study conducted in consecutive patients staying > or = 5 days in the surgical ICU of a University hospital. Demographic data, time to feeding, route, energy delivery, and outcome were recorded. Energy balance was calculated as energy delivery minus target. Data in means+/-SD, linear regressions between energy balance and outcome variables.

**RESULTS:** Forty eight patients aged 57+/-16 years were investigated; complete data are available in 669 days. Mechanical ventilation lasted 11+/-8 days, ICU stay 15+/-9 was days, and 30-days mortality was 38%. Time to feeding was 3.1+/-2.2 days. Enteral nutrition was the most frequent route with 433 days. Mean daily energy delivery was 1090+/-930 kcal. Combining enteral and parenteral nutrition achieved highest energy delivery. Cumulated energy balance was between -12,600+/-10,520 kcal, and correlated with complications ($P < 0.001$), already after 1 week.

**CONCLUSION:** Negative energy balances were correlated with increasing number of complications, particularly infections. Energy debt appears as a promising tool for nutritional follow-up, which should be further tested. Delaying initiation of nutritional support exposes the patients to energy deficits that cannot be compensated later on.

## Comment in


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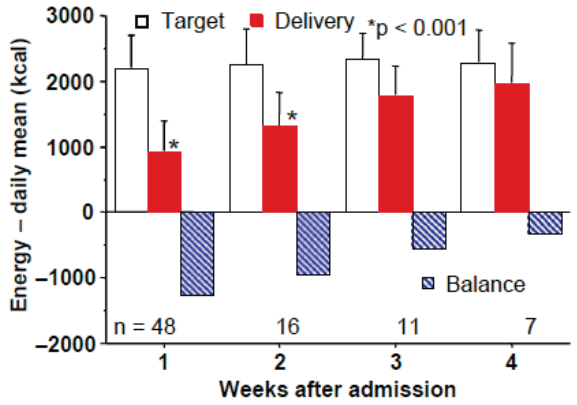


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# *Finding the evidence:*

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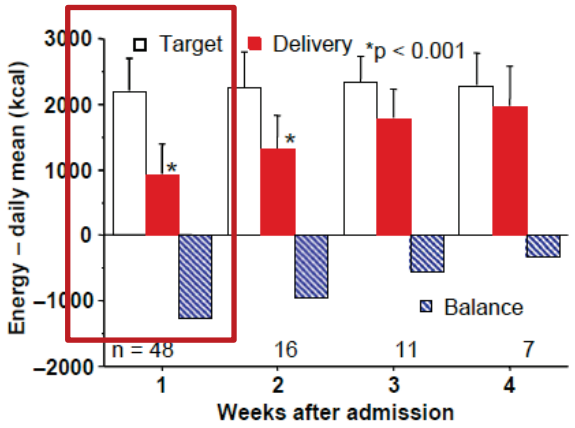


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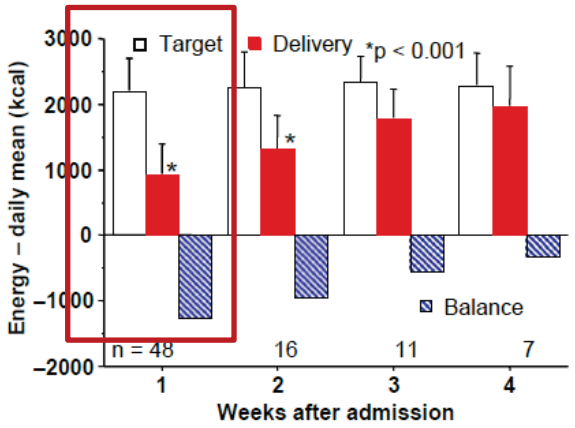


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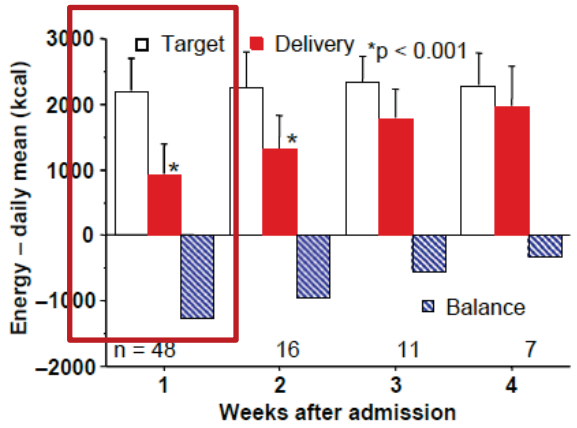


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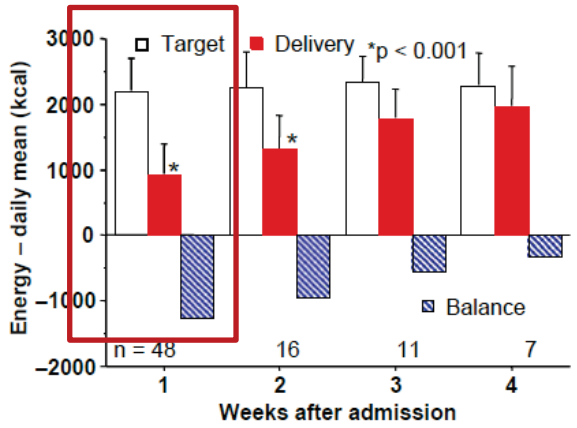


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# Initial trophic vs full enteral feeding in patients with acute lung injury: the EDEN randomized trial.

National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network, Rice TW, Wheeler AP, Thompson BT, Steingrub J, Hite RD, Moss M, Morris A, Dong N, Rock P.

**Collaborators (210)**

## Abstract

**CONTEXT:** The amount of enteral nutrition patients with acute lung injury need is unknown.

**OBJECTIVE:** To determine if initial lower-volume trophic enteral feeding would increase ventilator-free days and decrease gastrointestinal intolerances compared with initial full enteral feeding.

**DESIGN, SETTING, AND PARTICIPANTS:** The EDEN study, a randomized, open-label, multicenter trial conducted from January 2, 2008, through April 12, 2011. Participants were 1000 adults within 48 hours of developing acute lung injury requiring mechanical ventilation whose physicians intended to start enteral nutrition at 44 hospitals in the National Heart, Lung, and Blood Institute ARDS Clinical Trials Network.

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**RESULTS:** Baseline characteristics were similar between the trophic-feeding (n = 508) and full-feeding (n = 492) groups. The full-feeding group received more enteral calories for the first 6 days, about 1300 kcal/d compared with 400 kcal/d (P < .001). Initial trophic feeding did not increase the number of ventilator-free days (14.9 [95% CI, 13.9 to 15.8] vs 15.0 [95% CI, 14.1 to 15.9]; difference, -0.1 [95% CI, -1.4 to 1.2]; P = .89) or reduce 60-day mortality (23.2% [95% CI, 19.6% to 26.9%] vs 22.2% [95% CI, 18.5% to 25.8%]; difference, 1.0% [95% CI, -4.1% to 6.3%]; P = .77) compared with full feeding. There were no differences in infectious complications between the groups. Despite receiving more prokinetic agents, the full-feeding group experienced more vomiting (2.2% vs 1.7% of patient feeding days; P = .05), elevated gastric residual volumes (4.9% vs 2.2% of feeding days; P < .001), and constipation (3.1% vs 2.1% of feeding days; P = .003). Mean plasma glucose values and average hourly insulin administration were both higher in the full-feeding group over the first 6 days.

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**TRIAL REGISTRATION:** clinicaltrials.gov Identifiers: NCT00609180 and NCT00883948.

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N Engl J Med. 2015 Jun 18;372(25):2398-408. doi: 10.1056/NEJMoa1502826. Epub 2015 May 20.

# Permissive Underfeeding or Standard Enteral Feeding in Critically Ill Adults.

Arabi YM[1], Aldawood AS, Haddad SH, Al-Dorzi HM, Tamim HM, Jones G, Mehta S, McIntyre L, Solaiman O, Sakkijha MH, Sadat M, Afesh L; PermiT Trial Group.

⊕ Collaborators (44)

⊕ Author information

## Abstract

**BACKGROUND:** The appropriate caloric goal for critically ill adults is unclear. We evaluated the effect of restriction of nonprotein calories (permissive underfeeding), as compared with standard enteral feeding, on 90-day mortality among critically ill adults, with maintenance of the full recommended amount of protein in both groups.

**METHODS:** At seven centers, we randomly assigned 894 critically ill adults with a medical, surgical, or trauma admission category to permissive underfeeding (40 to 60% of calculated caloric requirements) or standard enteral feeding (70 to 100%) for up to 14 days while maintaining a similar protein intake in the two groups. The primary outcome was 90-day mortality.

**RESULTS:** Baseline characteristics were similar in the two groups; 96.8% of the patients were receiving mechanical ventilation. During the intervention period, the permissive-underfeeding group received fewer mean (±SD) calories than did the standard-feeding group (835±297 kcal per day vs. 1299±467 kcal per day, P<0.001; 46±14% vs. 71±22% of caloric requirements, P<0.001). Protein intake was similar in the two groups (57±24 g per day and 59±25 g per day, respectively; P=0.29). The 90-day mortality was similar: 121 of 445 patients (27.2%) in the permissive-underfeeding group and 127 of 440 patients (28.9%) in the standard-feeding group died (relative risk with permissive underfeeding, 0.94; 95% confidence interval [CI], 0.76 to 1.16; P=0.58). No serious adverse events were reported; there were no significant between-group differences with respect to feeding intolerance, diarrhea, infections acquired in the intensive care unit (ICU), or ICU or hospital length of stay.

**CONCLUSIONS:** Enteral feeding to deliver a moderate amount of nonprotein calories to critically ill adults was not associated with lower mortality than that associated with planned delivery of a full amount of nonprotein calories. (Funded by the King Abdullah International Medical Research Center; PermiT Current Controlled Trials number, ISRCTN68144998.).

PMID: 25992505 [PubMed - indexed for MEDLINE]

N Engl J Med. 2015 Jun 18;372(25):2398-408. doi: 10.1056/NEJMoa1502826. Epub 2015 May 20.

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**BACKGROUND & AIMS:** High supply of protein and energy has been introduced to very-low-birth-weight infants to improve growth and cognitive development. The aim of this study was to compare two different feeding strategies on postnatal growth and clinical outcome during neonatal hospitalization.

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**CONCLUSION:** Our study implies that enhanced feeding may induce electrolyte imbalances in VLBW infants, and that deleterious side effects similar to those seen in refeeding syndrome may occur. ClinicalTrials.gov, number NCT01103219 and the EudraCT number is 2010-020464-38.



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Turk J Med Sci. 2014;44(3):369-74.

# Refeeding hypophosphatemia: a potentially fatal danger in the intensive care unit.

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## Abstract

**AIM:** To determine the overall and comparative incidence of refeeding hypophosphatemia (RH) between enteral and parenteral nutrition in general adult intensive care unit (ICU) patients.

**MATERIALS AND METHODS:** This study was performed as a retrospective analysis. A total of 117 patients who received enteral and parenteral nutrition were included in the study. Demographic characteristics, type of nutrition, daily energy intake, and serum phosphorus levels before and after the initiation of the nutrition were recorded for 7 days.

**RESULTS:** The mean age of the patients was 65.8 ± 16.7 years. RH was found in 61 patients (52.14%). There was no significant difference in RH with regard to nutrition type (P = 0.756). The duration of the ICU stay was longer in the patients with RH compared with the patients without RH [median: 12 (3-68) and 8.5 (3-41) days, respectively; P = 0.025]. The mortality rate was higher in patients with RH compared with patients without RH (P = 0.037).

**CONCLUSION:** The incidence of RH was quite high in our medical ICU. The mortality rate and the duration of ICU stay were higher in the patients with RH than those without RH.

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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[1], Heighes PT, Simpson F, Sweetman EA, Davies AR.

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**METHODS:** Medline and EMBASE were searched. Hand citation review of retrieved guidelines and systematic reviews were undertaken, and academic and industry experts were contacted. Methodologically sound randomised controlled trials (RCTs) conducted in critically ill patient populations that compared the delivery of standard EN, provided within 24 h of intensive care unit (ICU) admission or injury, to standard care were included. The primary analysis was conducted on clinically meaningful patient-oriented outcomes. Secondary analyses considered vomiting/regurgitation, pneumonia, bacteraemia, sepsis and multiple organ dysfunction syndrome. Meta-analyses were conducted using the odds ratio (OR) metric and a fixed effects model. The impact of heterogeneity was assessed using the I (2) metric.

**RESULTS:** Six RCTs with 234 participants were analysed. The provision of early EN was associated with a significant reduction in mortality [OR = 0.34, 95% confidence interval (CI) 0.14-0.85] and pneumonia (OR = 0.31, 95% CI 0.12-0.78). There were no other significant differences in outcomes. A sensitivity analysis and a simulation exercise confirmed the presence of a mortality reduction.

**CONCLUSION:** Although the detection of a statistically significant reduction in mortality is promising, overall trial quality was low, trial size was small, and the findings may be restricted to the patient groups enrolled into included trials. The results of this meta-analysis should be confirmed by the conduct of a large multi-centre trial enrolling diverse critically ill patient groups.

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*There is no evidence from RCTs that demonstrates IF feeding is delayed, 'catching up' on caloric intake improves outcome.*

Abstract Send to:

Clin Nutr. 2005 Aug;24(4):502-9.

# Negative impact of hypocaloric feeding and energy balance on clinical outcome in ICU patients.

Villet S[1], Chiolero RL, Bollmann MD, Revelly JP, Cayeux R N MC, Delarue J, Berger MM.

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## Abstract

**BACKGROUND AND AIMS:** Critically ill patients with complicated evolution are frequently hypermetabolic, catabolic, and at risk of underfeeding. The study aimed at assessing the relationship between energy balance and outcome in critically ill patients.

**METHODS:** Prospective observational study conducted in consecutive patients staying > or = 5 days in the surgical ICU of a University hospital. Demographic data, time to feeding, route, energy delivery, and outcome were recorded. Energy balance was calculated as energy delivery minus target. Data in means+/-SD, linear regressions between energy balance and outcome variables.

**RESULTS:** Forty eight patients aged 57+/-16 years were investigated; complete data are available in 669 days. Mechanical ventilation lasted 11+/-8 days, ICU stay 15+/-9 was days, and 30-days mortality was 38%. Time to feeding was 3.1+/-2.2 days. Enteral nutrition was the most frequent route with 433 days. Mean daily energy delivery was 1090+/-930 kcal. Combining enteral and parenteral nutrition achieved highest energy delivery. Cumulated energy balance was between -12,600+/-10,520 kcal, and correlated with complications ($P < 0.001$), already after 1 week.

**CONCLUSION:** Negative energy balances were correlated with increasing number of complications, particularly infections. Energy debt appears as a promising tool for nutritional follow-up, which should be further tested. Delaying initiation of nutritional support exposes the patients to energy deficits that cannot be compensated later on.

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Negative impact of hypocaloric feeding and energy balance on clinical outcome in ICU patients.
Villet S[1], Chiolero RL, Bollmann MD, Revelly JP, Cayeux R N MC, Delarue J, Berger MM.
Author information
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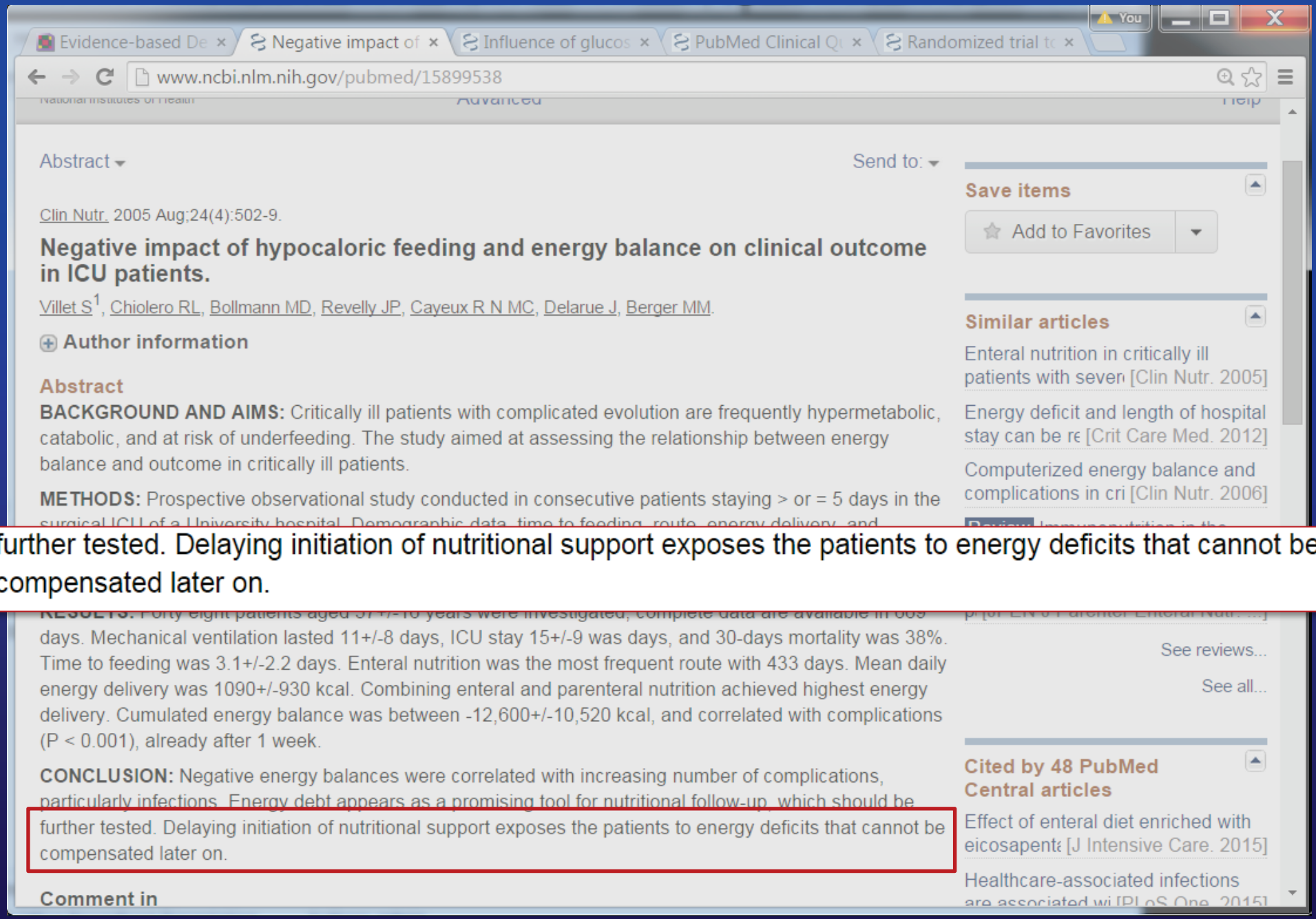


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# Early EN vs Early PN

N Engl J Med. 2014 Oct 30;371(18):1673-84. doi: 10.1056/NEJMoa1409860. Epub 2014 Oct 1.

## Trial of the route of early nutritional support in critically ill adults.

Harvey SE, Parrott F, Harrison DA, Bear DE, Segaran E, Beale R, Bellingan G, Leonard R, Mythen MG, Rowan KM; CALORIES Trial Investigators.

Collaborators (138)

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**CONCLUSIONS:** We found no significant difference in 30-day mortality associated with the route of delivery of early nutritional support in critically ill adults. (Funded by the United Kingdom National Institute for Health Research; CALORIES Current Controlled Trials number, ISRCTN17386141.).

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