Malnutrition: An Emergency in Your Hospital!...

Can PN Improve Outcome?

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Associate Chair of Clinical and Translational Research
Director, Translational PharmacoNutrition Laboratory
Director, Nutrition Therapy Services, UCH
Professor of Anesthesiology, Univ. of Colorado SOM
What risk factor is NUMBER ONE CAUSE of disease burden in world?

A. Unsafe Sex
B. Tobacco
C. Alcohol
D. Malnutrition
E.
What risk factor is NUMBER ONE CAUSE of disease burden in world?

A. Unsafe Sex
B. Tobacco
C. Alcohol
D. Malnutrition
E.
Global distribution of disease burden attributable to risk factors

- Underweight
- Unsafe sex
- High blood pressure
- Tobacco
- Alcohol
- Unsafe water, sanitation, and hygiene
- High cholesterol
- Indoor smoke from solid fuels
- Iron deficiency
- High BMI
- Zinc deficiency
- Low fruit and vegetable intake
- Vitamin A deficiency
- Physical inactivity
- Occupational risk factors for injury
- Lead exposure
- Illicit drugs
-Unsafe health care injections
- Lack of contraception
- Childhood sexual abuse

Attributable DALY (% of global DALY - Total 1.46 billion)
Is malnutrition a neglected disease worldwide?
Nutrition is THE Neglected Disease!
Is malnutrition a neglected disease in the hospital?
Could nutrition possibly be this vital in hospitalized patients?
Joshua T. - a 23 yr. old Male with Crohns Disease Presenting for Elective Colectomy...
Joshua T. - a 23 yr. old Male with Crohns Disease Presenting for Elective Colectomy...

Has SIRS, fever to 39.5...
Productive Cough, SOB...
POD #3 develops septic shock, DIC, and massive abdominal bleeding...

Joshua T. - a 23 yr. old Male with Crohns Disease Presenting for Elective Colectomy...
Joshua T. - a 23 yr. old Male with Crohn's Disease Presenting for Elective Colectomy...

Flown to ER for Management of Septic Shock, Massive Abdominal Hematoma and Ongoing Bleeding...
Acute Lung Injury / ARDS

- American-European consensus definition:
  - Acute onset after 'at risk' dx
  - Bilateral infiltrates on CXR
  - $\text{PaO}_2/\text{FiO}_2 \leq 300$ (ALI)
  - $\text{PaO}_2/\text{FiO}_2 \leq 200$ (ARDS)
  - No left atrial hypertension

- No evidence of CHF, or...

- $\text{PWEDGE} \leq 18$ mm Hg

SIRS/SEPSIS

ARDS/HYPOXIA

STEROIDS!

Poor Nutrition!
23 yo with Crohn's Dz...

NPO for 5 days post-op

Vomiting/ileus when feeds finally started

Off EN 2 days more...

Tolerates ~20-30 cc's/h for next 7 d

Undergoes many procedures...and feeds stopped every time!
23 yo with Crohns Dz...

- 14 day Caloric Debt = \(~20,000\) kCals

- Protein Delivery- 0.65 g/kg/d

- PN Never Started! (Admit BMI: 23)

- Massive loss of lean muscle mass

- Difficult to ween from ventilator

Requires Trach...
23 yo with Crohns Dz...

Discharged from ICU **48 days** post-admit to long term care unit...
Was he a success?
23 yo with Crohn’s Dz...

Following Discharge...

He can not feed himself or swallow...

He can not stand, walk or dress himself...

“I can’t even change the channel with television remote”
23 yo with Crohns Dz...

34 Days Post-Discharge...

Joshua suddenly complains of chest pain and “Feeling of Doom”...

Found in PEA cardiac arrest...

Following 40 minutes of CPR...
Joshua declared dead...

Massive pulmonary embolus found on autopsy
What Happened?
He Should Have Lived....

Right ??
Real Cause of Death...

Malnutrition
Nutrition was neglected!

Was an Emergency in this patient!
Prevalence and Burden of Malnutrition in Hospitalized Adults
Prevalence of Malnutrition in Hospitalized Adults

30-50%

Declines further with prolonged hospital stay

Clinical Nutrition 2008; 27: 5
65%

Pts Undergoing GI Surgery are Malnourished
Is malnutrition related to outcome?
So...

Malnutrition is an Emergency in Many Pts
We Must Do Better!

But How??
ESPEN GUIDELINES

ESPEN Guidelines on Enteral Nutrition: Intensive Care

K.G. Kreymann
G. Kazandjieva
DGEM: ★☆★☆☆

The following article has been published in the special interest issue. Please see the aspen Clinical Guidelines for further information.

Canadian Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.)

Stephen A. McClave, MD; Robert G. Martindale, MD, PhD; Vincent W. Vanek, MD; Mary McCarthy, RN, PhD; Pamela Roberts, MD; Beth Taylor, RD; Juan B. Ochoa, MD; Lena Napolitano, MD; Gail Cresci, RD; the A.S.P.E.N. Board of Directors; and the American College of Critical Care Medicine
ICU Nutrition Guidelines

- Early Oral/EN (start 24-48 h)
- NG tube, std EN product
- 1.3-2.0 g/kg/d Protein
- Tolerate GRV 350-500
- Promotility drugs if EN not tolerated
- PN if EN failing...

ASPEN, ESPEN Guidelines
Right?...
So.. everyone is getting early and successful enteral feeding ... Right??

NO!
New York Hospital Association Survey

43% of pts NPO on survey day
Do We Really Underfeed in ICU?
International ICU Nutrition Survey
Who participated in 2011?  
221 ICUs

- **Canada:** 24
- **USA:** 47
- **Latin America:** 31
- **Europe and Africa:** 26
- **Asia:** 52
  - **China:** 19
  - **Taiwan:** 9
  - **India:** 9
  - **Iran:** 1
  - **Japan:** 9
  - **Singapore:** 3
  - **Philippines:** 1
  - **Thailand:** 1
- **Australia & New Zealand:** 41

Additional participation:
- **Argentina:** 5
- **Chile:** 3
- **El Salvador:** 1
- **Mexico:** 2
- **Brazil:** 4
- **Colombia:** 9
- **Peru:** 1
- **Venezuela:** 2
- **Uruguay:** 4
- **Italy:** 2
- **UK:** 8
- **Ireland:** 6
- **Norway:** 5
- **Switzerland:** 1
- **France:** 1
- **Spain:** 2
- **South Africa:** 1
We Underfeed For 2 Weeks...
Most Pts Fail To Reach 80% of Goal....EVER!

% of Pts NEVER reaching 80% goal kcal in ICU
Average Protein Delivery

0.6 g/kg/d for 2 weeks in ICU!
Why Do We Underfeed?
Where Do Physicians Get Most Nutrition Education?
Oh my God!

My mother was right about everything!
Metabolism in Acute Illness
Continued Effect of Sepsis on Survival

Quartin et al. JAMA 1997; 277:1058-1063
Survival after severe sepsis

Weycker, et al. CCM 2003
> 40% of Mortality at 12 Month Follow-up Occurs Post-ICU Discharge

Shiell AM, Griffiths RD et al Clinical Intensive Care 1990;1 (6): 256-262
Surviving patients recover pre-illness function eventually....

Right??
One-Year Outcomes in Survivors of the Acute Respiratory Distress Syndrome

Margaret S. Herridge, M.D., M.P.H., Angela M. Cheung, M.D., Ph.D., Catherine M. Tansey, M.Sc., Andrea Matte-Martyn, B.Sc., Natalia Diaz-Granados, B.Sc., Fatma Al-Saidi, M.D., Andrew B. Cooper, M.D., Cameron B. Guest, M.D., C. David Mazer, M.D., Sangeeta Mehta, M.D., Thomas E. Stewart, M.D., Aiala Barr, Ph.D., Deborah Cook, M.D., and Arthur S. Slutsky, M.D., for the Canadian Critical Care Trials Group
Physical Role Score (SF-36) Following ICU Discharge

- Physical Role Score (Med):
  - 3 months: 0
  - 6 months: 0
  - 12 months: 25

Normal Value
“Are we creating survivors... or Victims?”
Post-Intensive Care Weakness Survivors....or VICTIMS??

25-50% pts following 4-7 d on ventilator

50-70% pts with sepsis
Post-Intensive Care Weakness
Survivors....or VICTIMS??

50% pts
Not Back At Work At 1 yr

33% pts
Never Return To Work
(including young pts)
But... this must improve after 12 months.... Right??
NO!

Exercise Limitation and Reduced Physical QOL PERSISTS 5-YEARS after ICU discharge
Critically Ill Patients Can Lose As Much As 1 kg of Lean Body Mass Daily!

Loss of lean body mass accelerates in critical illness

Weight change from pre-ICU status

Not Lean Mass Gain!.. Mostly Fat!

Herridge et al. NEJM 2003;348:683-693
Loss of Lean Body Mass is Devastating!

<table>
<thead>
<tr>
<th>% Loss of Total LBM</th>
<th>Complications</th>
<th>Associated Mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>Decreased immunity, increased infections</td>
<td>10</td>
</tr>
<tr>
<td>20</td>
<td>Decreased healing, weakness, infection</td>
<td>30</td>
</tr>
<tr>
<td>30</td>
<td>Too weak to sit, pressure ulcers, pneumonia, no healing</td>
<td>50</td>
</tr>
<tr>
<td>40</td>
<td>Death, usually from pneumonia</td>
<td>100</td>
</tr>
</tbody>
</table>
Joshua T. was a 23 year old Male with Crohn’s Disease s/p Colectomy...
“I Died”
Can We Tell Who Has Low Lean Body Mass?
What Can CT Scans Teach Us About Lean Mass in Elderly?
Physical Characteristics of Elderly Patients

N=149 pts

- Median age: 79 years old
- 57% males
- ISS: 19
- Prevalence of sarcopenia: 71%

Kozar Critical Care 2013 (in press)
## BMI Characteristics

<table>
<thead>
<tr>
<th></th>
<th>All Patients</th>
<th>Sarcopenic Patients (n=106)</th>
<th>Non-sarcopenic Patients (n=43)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (kg/m²)</td>
<td>25.8 (22.7, 28.2)</td>
<td>24.4 (21.7, 27.3)</td>
<td>27.6 (25.5, 30.4)</td>
</tr>
<tr>
<td>Underweight, %</td>
<td>7</td>
<td>9</td>
<td>2</td>
</tr>
<tr>
<td>Normal Weight, %</td>
<td>37</td>
<td>44</td>
<td>19</td>
</tr>
<tr>
<td>Overweight, %</td>
<td>42</td>
<td>38</td>
<td>51</td>
</tr>
<tr>
<td>Obese, %</td>
<td>15</td>
<td>9</td>
<td>28</td>
</tr>
</tbody>
</table>

No Correlation With BMI and Sarcopenia!
Low Muscle Mass Associated with Mortality

<table>
<thead>
<tr>
<th></th>
<th>Proportion of Deceased Patients</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sarcopenic pts</td>
<td>32%</td>
<td>0.018</td>
</tr>
<tr>
<td>Non-sarcopenic pts</td>
<td>14%</td>
<td></td>
</tr>
</tbody>
</table>

Kozar Critical Care 2013 (in press)
Without a CT Scan...How Do We Diagnose Malnutrition?
Can We Tell If Our Nutrition is "Working" At The Bedside?
Can We Assess Lean Body Mass and Muscle Function in ICU?

Yes!
**Lean Body Mass Via UltraSound**

**Why?:**

To assess **LEAN BODY MASS** via Leg Muscle Layer Thickness (MLT) of the M. vastus intermedius and M. rectus femoris

**Whom?:** Can be done by physician, nurse, dietician, specialist, or radiology technician

**How?....**


*Bedside ultrasound is a practical and reliable measurement tool for assessing quadricep muscle layer thickness in the critically ill.*

*JPEN J Parenter Enteral Nutr. Online: Feb 25, 2014*
Can We End Epidemic of Hospital "Victims"
Could This Be Due To Protein/Calorie Malnutrition?...

While in ICU?...

Probably..
Trophic Feeding

“Avoid mandatory full caloric feeding in first week but rather suggest low dose feeding (e.g., up to 500 kcal/d) advancing only as tolerated (grade 2B)”
Trophic Feeding?

What Does Data Say?
Increasing Calorie Debt Associated with Worse Outcomes

Adequacy of EN

↑ Caloric debt associated with:
- ↑ ICU stay
- ↑ Days on mechanical ventilation
- ↑ Complications
- ↑ Mortality

Rubinson CCM 2004;
Villet Clin Nutr 2005;
Dvir Clin Nutr 2006;
Petros Clin Nutr 2006
Impact of energy deficit calculated by a predictive method on outcome in medical patients requiring prolonged acute mechanical ventilation

Mechanically Vent’d Pts >7 d
(Average ICU LOS 28 d)
High Risk Patients!

Mean Energy Debt: > 1200 Kcal/D

Mean Energy Debt: < 1200 Kcal/D
Sick patients not created equal…

Should impact of nutrition be same in all pts?
Whats The Average Age in Your ICU?....
Initial Trophic vs Full Enteral Feeding in Patients With Acute Lung Injury
The EDEN Randomized Trial

The National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network

Mechanically ventilated patients cannot eat normally and if not fed for long periods become malnourished. Because malnutrition is associated with poor outcomes in critically ill patients, artificial nutrition is often provided, especially in those with acute lung injury (ALI) and with expected longer duration of mechanical ventilation. When feasible, enteral nutrition targeting full caloric needs has been advocated over parenteral nutrition. However, feeding intolerance and common care practices (eg, gastric residual volume [GRV] limits) often serve as practical barriers to reaching recommended goals.

Although confounded by indication and severity of illness, several observational studies have shown improved clinical outcomes, including fewer infections, shorter duration of mechanical ventilation, and lower mortality for patients receiving a higher percentage of calculated caloric needs. Nonetheless, the best timing, formulation, and amount of enteral nutrition remain unknown.

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.

Interventions Participants were randomized to receive either trophic or full enteral feeding for the first 6 days. After day 6, the care of all patients who were still receiving mechanical ventilation was managed according to the full feeding protocol.

Main Outcome Measures Ventilator-free days to study day 28.

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, -0.4 to 1.2]; P = .89) or reduce 60-day mortality (23.2% [95% CI, 19.6% to 26.9%] vs 22.8% [95% CI, 18.5% to 27.8%]; difference, 1.0% [95% CI, -2.0% to 4.0%]; 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 = .033). Mean plasma glucose values and average hourly insulin administration were both higher in the full-feeding group over the first 6 days.

Conclusion In patients with acute lung injury, compared with full enteral feeding, a strategy of initial trophic enteral feeding for up to 6 days did not improve ventilator-free days, 60-day mortality, or infectious complications but was associated with less gastrointestinal intolerance.

Trial Registration clinicaltrials.gov identifiers: NCT00609180 and NCT00858948


www.jama.com
Initial Tropic vs. Full EN in Patients with Acute Lung Injury

The Eden Trial

**Table 2. Clinical Outcomes**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Trophic Feeding (n = 508)</th>
<th>Full Feeding (n = 492)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ventilator-free days, No. (95% CI)</td>
<td>14.9 (13.9-15.8)</td>
<td>15.0 (14.1-15.9)</td>
<td>.89</td>
</tr>
<tr>
<td>Failure-free days, No. (95% CI)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>19.1 (18.2-20.0)</td>
<td>18.9 (18.1-19.8)</td>
<td>.75</td>
</tr>
<tr>
<td>Renal</td>
<td>20.0 (19.0-20.9)</td>
<td>19.4 (18.4-20.5)</td>
<td>.43</td>
</tr>
<tr>
<td>Hepatic</td>
<td>22.0 (21.2-22.9)</td>
<td>22.6 (21.8-23.5)</td>
<td>.37</td>
</tr>
<tr>
<td>Coagulation</td>
<td>22.3 (21.4-23.1)</td>
<td>23.1 (22.3-23.9)</td>
<td>.16</td>
</tr>
<tr>
<td>ICU-free days, No. (95% CI)</td>
<td>14.4 (13.5-15.3)</td>
<td>14.7 (13.8-15.6)</td>
<td>.67</td>
</tr>
<tr>
<td>60-d mortality, No. (%) [95% CI]</td>
<td>118 (23.2) [19.6-26.9]</td>
<td>109 (22.2) [18.5-25.8]</td>
<td>.77</td>
</tr>
<tr>
<td>Development of infections, No. (%) [95% CI]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VAP</td>
<td>37 (7.3) [5.0-9.5]</td>
<td>33 (6.7) [4.5-8.9]</td>
<td>.72</td>
</tr>
<tr>
<td><em>Clostridium difficile</em> colitis</td>
<td>15 (3.0) [1.5-4.4]</td>
<td>13 (2.6) [1.2-4.1]</td>
<td>.77</td>
</tr>
<tr>
<td>Bacteremia, No. (%)</td>
<td>59 (11.6) [8.8-14.4]</td>
<td>46 (9.3) [6.8-11.9]</td>
<td>.24</td>
</tr>
</tbody>
</table>

Abbreviations: ICU, intensive care unit; VAP, ventilator-associated pneumonia.

**Figure 3. Survival and Hospital Discharge**

No Difference in Outcomes?

Most All Pts...Young, Well Nourished?

The Eden Trial

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Trophic Feeding (n = 508)</th>
<th>Full Feeding (n = 492)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>52 (17)</td>
<td>52 (16)</td>
</tr>
<tr>
<td>Women, No. (%)</td>
<td>241 (47)</td>
<td>249 (51)</td>
</tr>
<tr>
<td>White, No. (%)</td>
<td>387 (81)</td>
<td>375 (79)</td>
</tr>
<tr>
<td>Medical ICU, No. (%)</td>
<td>309 (61)</td>
<td>309 (63)</td>
</tr>
<tr>
<td>Primary lung injury category, No. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumonia</td>
<td>341 (67)</td>
<td>309 (63)</td>
</tr>
<tr>
<td>Sepsis</td>
<td>82 (16)</td>
<td>63 (13)</td>
</tr>
<tr>
<td>Aspiration</td>
<td>42 (8)</td>
<td>54 (11)</td>
</tr>
<tr>
<td>Trauma</td>
<td>17 (3)</td>
<td>19 (4)</td>
</tr>
<tr>
<td>Transfusion</td>
<td>4 (1)</td>
<td>12 (2)</td>
</tr>
<tr>
<td>Other</td>
<td>21 (4)</td>
<td>34 (7)</td>
</tr>
<tr>
<td>Hours from intubation to randomization, No. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;24</td>
<td>202 (40)</td>
<td>180 (37)</td>
</tr>
<tr>
<td>24-&lt;48</td>
<td>252 (50)</td>
<td>256 (52)</td>
</tr>
<tr>
<td>48-72</td>
<td>50 (10)</td>
<td>53 (11)</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>85.9 (23.5)</td>
<td>87.0 (25.8)</td>
</tr>
<tr>
<td>BMI†</td>
<td>29.9 (7.8)</td>
<td>30.4 (3.2)</td>
</tr>
<tr>
<td>APACHE III score</td>
<td>92 (28)</td>
<td>90 (27)</td>
</tr>
<tr>
<td>Diabetes, No. (%)</td>
<td>136 (27)</td>
<td>142 (29)</td>
</tr>
<tr>
<td>Baseline vasopressor use, No. (%)</td>
<td>188 (37)</td>
<td>190 (39)</td>
</tr>
</tbody>
</table>

Enrolled 12% of Screened Pts

Most All Pts...Young, Well Nourished?

- Average age: 52
- Few Co-morbidities
- Average BMI: 29-30
- All fed w/in 24 h (benefits of early EN)
- Average Duration of Study Intervention: 5 d

No Effect in Young, Overweight Pts with Short Stay!
We All
Underfeed!

Is some it may not matter...

Is some it matters a lot and pts may die as a result...
2013 CPG Recommendation

Trophic Feeding

2013 Recommendation: Based on 2 level 1 studies

In Pts w/ Acute Lung Injury...
Initial Trophic Feeds for 5 d

Should Not Be Considered!
Sick patients not created equal...

Should impact of nutrition be same in all pts?
Patients need different goals...

How do we decide?
International Critical Care Nutrition Survey
Relationship of Caloric Intake, 60 day Mortality and BMI

Calories Delivered

Mortality (%)

0 500 1000 1500 2000

< 20

20-25

25-30

30-35

35-40

> 40

Alberda, C, Heyland D et al
Intensive Care Med. 35:1728-37. 2009
Extra-Protein Reduces Mortality!

Every additional 30 g/d protein given...

Mortality decreased!

Alberda, C, Heyland, D et al
Intensive Care Med. 35:1728-37. 2009
We All Underfeed Protein!!
Aren’t There Some New Trials?
What Can We Learn About Nutrition Delivery From New Trials?

The Evolution of Nutrition in Critical Care: How Much, How Soon?

Paul E Wischmeyer

Critical Care

17 (Suppl 1):S7, 2013
Nutrition must be the complete package...
Carbohydrate, Lipid, Electrolytes, Trace Elements, Protein?
Should We Utilize Lower Energy/High Protein Feeding in Acute Phase of Critical Illness??
Is Sepsis a Hypermetabolic Condition??
No!...Not Early!
Ratio of Measured Resting Energy Expenditure to Predicted Energy Expenditure (REE/REEp) in Sepsis & Trauma

VO₂ in sepsis decreases with severity

Kreymann et al, Crit Care Med 1993

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>VO₂</th>
<th>DO₂</th>
<th>O₂ER</th>
<th>REE (%) normal</th>
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<tbody>
<tr>
<td>sepsis</td>
<td>15</td>
<td>180±19</td>
<td>501±116</td>
<td>0.39</td>
<td>155±14</td>
</tr>
<tr>
<td>sepsis syndrome</td>
<td>11</td>
<td>156±22</td>
<td>515±186</td>
<td>0.33</td>
<td>124±12</td>
</tr>
<tr>
<td>septic shock</td>
<td>8</td>
<td>120±27</td>
<td>404±96</td>
<td>0.29</td>
<td>102±24</td>
</tr>
</tbody>
</table>

(p<0.001) (p=ns) (p=ns) (p<0.01)

During recovery from septic shock REE rose to 161±22% baseline
Protein Requirements in ICU Pts
Energy Expenditure and Protein Requirements

1.8X Increase

4X Increase

Fürst P, Protein and amino acid metabolism: Composition of stressed and nonstressed states, In Cresci G (ed), Nutrition support for the critically ill patient, Taylor & Francis (CRC), Boca Raton, 2005 pg 29
Protein Delivery
(1.2-2.0 g/kg/day)
“EPaNiC Trial”
Early versus Late Parenteral Nutrition in Critically Ill Adults

Michael P. Casaer, M.D., Dieter Mesotten, M.D., Ph.D.,
Greet Hermans, M.D., Ph.D., Pieter J. Wouters, R.N., M.Sc.,
Miet Schetz, M.D., Ph.D., Geert Meyfroidt, M.D., Ph.D.,
Sophie Van Cromphaut, M.D., Ph.D., Catherine Ingels, M.D.,
Philippe Meersseman, M.D., Jan Muller, M.D., Dirk Vlasselaers, M.D., Ph.D.,
Yves Debaveye, M.D., Ph.D., Lars Desmet, M.D., Jasperina Dubois, M.D.,
Aime Van Assche, M.D., Simon Vanderheyden, B.Sc.,
Alexander Wilmer, M.D., Ph.D., and Greet Van den Berghe, M.D., Ph.D.*

Protein Delivery: 0.8 g/kg/d x 2 wk

“Low Protein Study”

No Benefit
Initial Trophic vs Full Enteral Feeding in Patients With Acute Lung Injury
The EDEN Randomized Trial
The National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network*

Mean Protein Delivery: 0.6-0.8 g/kg/d in FULL Energy Group
“Low Protein Study”
No Benefit
Permissive underfeeding and intensive insulin therapy in critically ill patients: a randomized controlled trial

Yaseen M Arabi, Hani M Tamim, Gousia S Dhar, Abdulaziz Al-Dawood, Muhammad Al-Sultan, Maram H Sakkijha, Salim H Kahoul, and Riette Brits

Mean Protein Delivery: 0.6 g/kg/d in BOTH Groups

“Low Protein Study”

No Benefit
The tight calorie control study (TICACOS): a prospective, randomized, controlled pilot study of nutritional support in critically ill patients

Mean Protein Delivery: \(1.0 \text{ g/kg/d}\)

in Supplemental PN Group

“High Protein Study”

Benefit!

Reduced Mortality
Optimisation of energy provision with supplemental parenteral nutrition in critically ill patients: a randomised controlled clinical trial

Lancet, 2013

Claudia Paula Heidegger, Mette M Berger, Séverine Graf, Walter Zingg, Patrice Darmon, Michael C Costanza, Ronan Thibault, Claude Pichard

Mean Protein Delivery: 1.0-1.1 g/kg/d in Supplemental PN Group

“High Protein Study”

Benefit!-
Reduced Infections, LOS
Early Parenteral Nutrition in Critically Ill Patients With Short-term Relative Contraindications to Early Enteral Nutrition
A Randomized Controlled Trial


JAMA, 2013

Mean Protein Delivery: 1.1-1.2 g/kg/d in Early PN Group

“High Protein Study”

Benefit!-
Reduced Time on Ventilator,
Improved QOL!
Data for High Protein Nutrition
Improving ICU Outcome?
Extra-Protein Reduces Mortality!

Every additional 30 g/d protein given...

Mortality decreased!

Alberda, C, Heyland D et al
Intensive Care Med. 35:1728-37. 2009
Has this already been shown in a multi-center RCT?
Effect of Increasing Protein on Infection

Multicenter observational study - 207 pts >72 h in ICU

For increase of 30 g/d:
OR of infection at 28 d

Heyland Clinical Nutrition 2010
Trial of Omega-3 Fatty acid, Gamma-linolenic Acid and Antioxidant Supplementation in the Management of Acute Lung Injury (Omega)

Todd Rice, MD, MSc
Co-chair: NIH NHLBI EDEN-OMEGA
NHLBI ARDS Network of Investigators
Division of Allergy, Pulmonary and Critical Care
Vanderbilt University
OMEGA: 60-Day Mortality

P = 0.05

Omega: 26.6%
Control: 16.3%
FACTT conservative: 25.5%
# N-3 / A-O Supplement vs. Control

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>N-3/A-O Suppl (120mL)</th>
<th>Control (120mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy, cal</td>
<td>240</td>
<td>237</td>
</tr>
<tr>
<td>Osmolarity, kCal / mL</td>
<td>2.04</td>
<td>2.01</td>
</tr>
<tr>
<td>Protein, g</td>
<td>1.9</td>
<td>10</td>
</tr>
<tr>
<td>Carbohydrate, g</td>
<td>2.4</td>
<td>25.6</td>
</tr>
<tr>
<td>Fat, g</td>
<td>22.3</td>
<td>11</td>
</tr>
<tr>
<td>EPA, g</td>
<td>3.42</td>
<td>0</td>
</tr>
<tr>
<td>DHA, g</td>
<td>1.70</td>
<td>0</td>
</tr>
<tr>
<td>GLA, g</td>
<td>2.96</td>
<td>0</td>
</tr>
<tr>
<td>Vitamin C, mg</td>
<td>500</td>
<td>38</td>
</tr>
<tr>
<td>All-natural Vitamin E, IU</td>
<td>220</td>
<td>6</td>
</tr>
<tr>
<td>B-carotene, mg</td>
<td>2.4</td>
<td>0</td>
</tr>
<tr>
<td>Zinc, mg</td>
<td>12.1</td>
<td>2.8</td>
</tr>
<tr>
<td>Selenium, ug</td>
<td>42.6</td>
<td>9</td>
</tr>
<tr>
<td>L-carnitine, mg</td>
<td>90</td>
<td>19</td>
</tr>
<tr>
<td>Taurine, mg</td>
<td>175</td>
<td>19</td>
</tr>
</tbody>
</table>

Daily dosage = 2 Modules
Did 5 x Protein Reduce Mortality in Large RCT?
Optimal Protein and Energy Nutrition Decreases Mortality in Mechanically Ventilated, Critically Ill Patients: A Prospective Observation Cohort Study
Weijs PJM et al. JPEN, 2012

886 MV ICU Pts- EN/PN for > 7 d

Results: Protein Delivery Mean
- No Target Achieved: 0.83 g/kg/d
- Energy Target Only: 1.06 g/kg/d
- Protein/Energy Target: 1.31 g/kg/d
Only Achieving Protein Goals Reduces Mortality in ICU Patients!

PET- Reached Protein/Energy Targets (> 1.2 g/kg/d protein)
ET- Reached Energy Targets Only (< 1.0 g/kg/d protein)

Unadjusted

Adjusted for sex, age, BMI, diag., hyperglycemic index, and APACHE II

Adjusted for PN Use and Time to Goal Nutrition

Weijts PJM et al. JPEN, 2012
Increased Protein Delivery Reduces Risk of Death in ICU

Figure 2. 28-Day survival in the ICU. Kaplan-Meier survival curves for all patients: Mantel log-rank test for trend: P < 0.01.

- High protein & AA
- Medium protein & AA
- Low protein & AA

Log-rank test for trend: P < 0.01

Clinical Nutrition: 31; 462-468, 2012
Increased Protein Delivery Reduces Risk of Death in ICU Patients

ICU Mortality (%)

- Low Protein
- Medium Protein
- High Protein

Protein Alone Reduces Mortality!

2.0 g/kg/day Mortality Decreased!

in 400 pt ICU multi-center RCT of IV protein delivery

Doig and Simpson, ASPEN meeting, 2014
Optimizing energy and protein balance in the ICU

Peter J.M. Weijsa,b,c,d and Paul E. Wischmeyer

Curr Opin Clin Nutr Metab Care 2013, 16:194–201

NO Benefit in Trials Giving

< 1.0 g/kg/d Protein

Such As:

EPaNIC Trial
EDEN Trial
Arabi et al Trial
Optimizing energy and protein balance in the ICU

ALL Trials

> 1.0 g/kg/d

Protein Show Benefit!

Such As:

Early PN Trial, JAMA 2013
Swiss PN Trial, Lancet 2013
TICACOS Trial, ICM 2011
Optimizing energy and protein balance in the ICU

Peter J.M. Weijs\textsuperscript{a,b,c,d} and Paul E. Wischmeyer\textsuperscript{e}

Curr Opin Clin Nutr Metab Care 2013, 16:194–201

Protein is Most Vital Nutrient In ICU!

ESEPN and ASPEN Guidelines: Recommend: 1.2–2.0 g/kg/d
“Are we creating survivors... or Victims?”
Sepsis Deaths Fall By Half...
...Many More Patients to Rehab!

Discharge to Rehabilitation

Adjusted Odds Ratio

Year of ICU admission

No Sepsis

Sepsis

JAMA, Online March 18, 2014
Mortality Related to Severe Sepsis and Septic Shock Among Critically Ill Patients in Australia and New Zealand, 2000-2012

Kirsi-Maija Kaukonen, MD, PhD, EDIC; Michael Bailey, PhD; Satoshi Suzuki, MD; David Pilcher, FCICM; Rinaldo Bellomo, MD, PhD

“Given low ICU mortality... Quality of Life ...will become focus of future trials”
Can Early Protein/Calorie Improve Quality of Life?
“Come Strong or Don’t Come At All”
Increased Protein Improves Physical Function Post-ICU
(REDOXS Study)
First 364 pts w/ SF-36 Score at 3 m

<table>
<thead>
<tr>
<th>(B) Increased protein intake</th>
<th>Model Estimate (CI)</th>
<th>P values</th>
</tr>
</thead>
<tbody>
<tr>
<td>PHYSICAL FUNCTIONING (PF) at 3 m</td>
<td>2.9 (-0.7, 6.6)</td>
<td>P=0.11</td>
</tr>
<tr>
<td>ROLE PHYSICAL (RP) at 3 m</td>
<td>4.4 (0.7, 8.1)</td>
<td>P=0.02</td>
</tr>
<tr>
<td>STD PHYSICAL COMPONENT SCALE (PCS) at 3 m</td>
<td>1.9 (0.5, 3.2)</td>
<td>P=0.007</td>
</tr>
</tbody>
</table>

Presented at ASPEN, 2014
EDEN Trial
Increased Energy Delivery Improves Discharge Home vs. Rehab Center

* - p < 0.04 vs Trophic Feeding
Early PN Reduces Muscle Wasting in ICU

**Legend:** P-values from fully factorial repeated measures ANOVA: $p < 0.0001$ change over time, $p = 0.014$ difference between groups (0.16 grade per week). Grey shaded area represents test based 95% confidence interval from fully factorial repeated measures ANOVA analysis between groups. **ICU:** Intensive Care Unit. **PN:** parenteral nutrition.

Patients: 681

<table>
<thead>
<tr>
<th>Weeks in study ICU</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5 +</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early PN</td>
<td>264</td>
<td>101</td>
<td>44</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>Std Care</td>
<td>254</td>
<td>104</td>
<td>64</td>
<td>38</td>
<td></td>
</tr>
</tbody>
</table>

Doig et al JAMA, Online: May, 2013
Promote Protein Provision!

...and good nutrition will follow...?
We All Underfeed Protein Enterally!!
Use Enteral/Oral Protein Supplements!
Supplement PN Early in At-risk Patients?!?
Failing EN at 2-3 d? Malnourished!
Two New Large Randomized Trials Show....

Standard TPN Does Not Increase Infection Risk in 2014!

Doig et al. JAMA, 2013
Heidegger et al, Lancet, 2013
Standard TPN No Longer Related To Infection in 2014!

- No Longer “Hyperalimentation”
- We Now Control Hyperglycemia
- Higher Protein Delivery
- 3-Chamber TPN Bags
- Better Central Line Care

Improved Lipids?
EN first...as tolerated...

When failing...PN...
What about after the ICU?

What can we do?
Hospital Readmission is a Major Problem!

1 in 5 Medicare patients... readmitted within 30 days of hospital discharge.

At a cost of...

$26 billion per year

Majority of readmissions from...

Congestive Heart Failure (CHF)

Acute MI (AMI)

Pneumonia
These conditions also lead to...

Longer LOS
Greater Hospital Costs

(Pts have more comorbidities and need ICU)

These conditions also lead to...

Longer LOS

Greater Hospital Costs

(Pts have more comorbidities and need ICU)
Can we improve outcomes for these patients?
Hospital Malnutrition...

Contributes to readmission and costs as well?
Role for ORAL Nutrition Supplements? (ONS)
ONS Reduces Hospital Mortality

OR 0.61 [95% CI 0.48–0.78], p < 0.001
Meta-analysis of 11 trials, n = 1965;

Stratton et al, 2003
ONS Reduces Hospital Complications

Stratton et al, 2003

OR 0.31; 95% CI 0.17–0.56, $p < 0.001$

Meta-analysis of 7 trials, $n = 384$
Oral Nutrition Supplements

- Reduce Hospital LOS
- Reduce Hospital Readmission
Reduced Hospital Costs!
Mainly Small Trials...

Limited Data in Large Scale Trials and Elderly Medicare Population

New Data for ONS...

Adults With Any Primary Diagnosis...

\( n = 724,000 \)

ONS patient episodes studied

ONS Improves Outcome...

Reduced Hospital LOS

21%

ONS Reduces Costs...

Reduced Hospital Cost

21.6%

ONS Reduces Costs...

Every $1 spent on ONS...

Saves

$522.63

in hospital costs

ONS Reduces 30 d Readmissions 6.9%

ONS Reduces Costs...

Every $1 spent on ONS...

Saves $2.56 in re-admit costs

Study Objective

Conduct retrospective data analysis of effect of ONS in > 65 y.o. Medicare pts with:

- CHF
- AMI
- Pneumonia
Methods

Premier Research Database

Data from 2000-2010:
- 460 hospitals
- 44 million adult inpatient episodes

14.2 million age ≥65 Medicare episodes!
Methods

Medicare patients ≥ 65 y.o. hospitalized for:

- Myocardial infarction (AMI)
- Congestive heart failure (CHF)
- Pneumonia (PNA)

All Medicare patients aged ≥ 65 y.o. studied as well
Methods

One-to-one matched samples of ONS and non-ONS episodes created using propensity-score matching
Methods

To minimize bias, instrumental variables (IV) regression analyses were applied (only IV results reported)

Instrument used was propensity of hospitals to administer ONS
Results
# ONS Significantly Lowers 30-Day Readmission Rates

Effect of ONS on 30-day readmission in Medicare population (IV estimates)

<table>
<thead>
<tr>
<th>Population</th>
<th>Acute Myocardial Infarction</th>
<th>Congestive Heart Failure</th>
<th>Pneumonia</th>
<th>All Patients Aged 65+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of observations</td>
<td>15,266</td>
<td>30,675</td>
<td>36,829</td>
<td>501,734</td>
</tr>
<tr>
<td>Effect of any ONS use on probability of readmit (SE)</td>
<td>-0.042** (0.014)</td>
<td>-0.038** (0.010)</td>
<td>-0.017 (0.010)</td>
<td>-0.032** (0.003)</td>
</tr>
</tbody>
</table>

**Indicates statistical significance of <0.01
ONS Reduces Probability of Readmission Within 30 Days

- **AMI**: 12.0%
- **CH**: 10.1%
- **Pneumo**: 5.2%
- **All 65**: 8.5%
ONS Significantly Reduces Hospital LOS

AMI: 1.22 Days
CHF: 1.28 Days
Pneumon: 0.76 Days
All 65+: 1.65 Days

** - p < 0.01
# ONS Significantly Reduces Hospital Length Of Stay

Effect of ONS use on length of stay (LOS) in days, IV estimates

<table>
<thead>
<tr>
<th>Population</th>
<th>Acute Myocardial Infarction</th>
<th>Congestive Heart Failure</th>
<th>Pneumonia</th>
<th>All Patients Aged 65+</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number of observations</strong></td>
<td>20,870</td>
<td>38,418</td>
<td>47,477</td>
<td>667,684</td>
</tr>
<tr>
<td><strong>Predicted LOS without ONS</strong></td>
<td>11.12</td>
<td>9.03</td>
<td>8.96</td>
<td>10.35</td>
</tr>
<tr>
<td><strong>Predicted LOS with ONS</strong></td>
<td>9.90</td>
<td>7.75</td>
<td>8.20</td>
<td>8.70</td>
</tr>
<tr>
<td><strong>Change due to ONS use</strong></td>
<td>-10.90%</td>
<td>-14.20%</td>
<td>-8.50%</td>
<td>-15.98%</td>
</tr>
</tbody>
</table>
ONS Significantly Reduces Hospital Costs

** $1,538

** $1,266

** $1,516

** $3,079

** - p < 0.01
## ONS Significantly Reduces Hospital Costs

Effect of ONS use on episode cost in 2010 USD, IV estimates

<table>
<thead>
<tr>
<th>Population</th>
<th>Acute Myocardial Infarction</th>
<th>Congestive Heart Failure</th>
<th>Pneumonia</th>
<th>All Patients Aged 65+</th>
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</thead>
<tbody>
<tr>
<td>Number of observations</td>
<td>20,870</td>
<td>38,418</td>
<td>47,477</td>
<td>667,684</td>
</tr>
<tr>
<td>Predicted episode cost</td>
<td>30,404</td>
<td>16,166</td>
<td>14,261</td>
<td>19,506</td>
</tr>
<tr>
<td>without ONS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Predicted episode cost</td>
<td>28,866</td>
<td>14,900</td>
<td>12,745</td>
<td>16,427</td>
</tr>
<tr>
<td>with ONS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change due to ONS use</td>
<td>-5.10%</td>
<td>-7.80%</td>
<td>-10.60%</td>
<td>-15.78%</td>
</tr>
</tbody>
</table>
Conclusions

Use of ONS in > 65 yo hospitalized pts:

Improves clinical outcomes and reduces costs in AMI, CHF and Pneumonia
Conclusions

Use of ONS in > 65 yo hospitalized pts:

May be inexpensive evidenced-based approach to meet ACA quality targets!
Conclusions

Use of ONS in > 65 yo hospitalized pts:

Significant effect in general population of elderly patients as well
Conclusions

Use of ONS in > 65 yo hospitalized pts:

Reduction of health care costs from AMI, CHF, Pneumonia is vital to reducing overall burden on Medicare
ONS Is Likely...

Most Effective Nutrition Intervention Available in Hospitalized Pts!