Health economics in ICU nutrition:  
*The time has come*

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

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“... investments in micronutrients have higher returns than those from investments in trade liberalization, in malaria, or in water and sanitation. No other technology offers as large an opportunity to improve lives at such low cost and in such a short time.”
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“... investments in micronutrients have higher returns than those from investments in trade liberalization, in malaria, or in water and sanitation....No other technology offers as large an opportunity to improve lives at such low cost and in such a short time.”

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

Malnutrition: Hospital Perspective
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.
Malnutrition: Hospital Perspective

Malnutrition 'rife in NSW

April 2, 2008
By Vincent Morello

Half the public patients in NSW are malnourished, complications and doubling the time they spend in care services in NSW has been told.

Hospital elderly 'underfed'

May 21, 2000
Jill Stark

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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- 38 – 88% of critically ill patients are malnourished at some time during their ICU stay.

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

*Nutrition* Vol. 12, No. 1, 1996

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

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

*Nutrition* Vol. 12, No. 1, 1996

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

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.
Effect of Evidence-Based Feeding Guidelines on Mortality of Critically Ill Adults
A Cluster Randomized Controlled Trial

<table>
<thead>
<tr>
<th>Process Measure</th>
<th>Control (13 ICUs, 557 Patients)a</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean time from ICU admission to EN, PN, ICU discharge, or death, d&lt;sup&gt;d&lt;/sup&gt;</td>
<td>2.14 (1.73 to 2.66)</td>
</tr>
<tr>
<td>All patients</td>
<td></td>
</tr>
<tr>
<td>Other process measures</td>
<td></td>
</tr>
<tr>
<td>Patients never fed at any time during ICU stay, No. (%)</td>
<td>157 (28.2) [21.2 to 37.5]</td>
</tr>
</tbody>
</table>

Is this delay in feeding due to costs?
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“There is a lack of well-designed studies taking a broad view of relevant comparators, costs and outcomes.”

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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.

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)

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

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

Total events: 8 (early EN (<24 h)), 19 (Control)
Test for heterogeneity: $\chi^2 = 3.20$, df = 4 (P = 0.52), $I^2 = 0$
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)

Results: Primary MA, Pneumonia

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

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<th>OR (fixed) 95% CI</th>
<th>Weight %</th>
<th>OR (fixed) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kompan 2004</td>
<td>9/27</td>
<td>16/25</td>
<td>70.15 0.28 [0.09, 0.88]</td>
<td>70.15</td>
<td>0.28 [0.09, 0.88]</td>
</tr>
<tr>
<td>Nguyen 2008</td>
<td>3/14</td>
<td>6/14</td>
<td>29.85 0.36 [0.07, 1.91]</td>
<td>29.85</td>
<td>0.36 [0.07, 1.91]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>41</td>
<td>39</td>
<td>100.00 0.31 [0.12, 0.78]</td>
<td>100.00</td>
<td>0.31 [0.12, 0.78]</td>
</tr>
</tbody>
</table>

Total events: 12 (early EN (<24 h)), 22 (Control)
Test for heterogeneity: Chi² = 0.06, df = 1 (P = 0.80), I² = 0%
Test for overall effect: Z = 2.47 (P = 0.01)

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

Results: updated MA, ICU length of stay

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

Results: updated MA, duration of MV

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>EEN Mean [days]</th>
<th>EEN SD [days]</th>
<th>Total Mean [days]</th>
<th>SoC Mean [days]</th>
<th>Total</th>
<th>Weight</th>
<th>Mean difference IV, fixed, 95% CI [days]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chuntrasakul et al</td>
<td>5.29</td>
<td>6.28</td>
<td>21</td>
<td>6.12</td>
<td>5.32</td>
<td>17</td>
<td>-0.83 [-4.52, 2.86]</td>
</tr>
<tr>
<td>Kompan et al</td>
<td>12.9</td>
<td>8.1</td>
<td>27</td>
<td>15.6</td>
<td>16.1</td>
<td>25</td>
<td>-2.70 [-9.71, 4.31]</td>
</tr>
<tr>
<td>Nguyen et al</td>
<td>9.2</td>
<td>3.37</td>
<td>14</td>
<td>13.7</td>
<td>7.11</td>
<td>14</td>
<td>-4.50 [-8.62, -0.38]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>62</td>
<td></td>
<td>56</td>
<td>100.0%</td>
<td></td>
<td>-2.49 [-5.05, 0.07]</td>
<td></td>
</tr>
</tbody>
</table>

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)

Results: updated MA, hospital stay

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

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:
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  Journal of Intensive Care Medicine

  [http://jic.sagepub.com/](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


  DOI: 10.1177/0885066608318661

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Conducted in the mixed med-surg ICUs of 3 hospitals in the Netherlands

• 1 University and 2 General Hospitals
• Costed 576 patients, consuming 2,868 ICU days

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  - Average total costs of 1 ventilated-ICU day reported as €2,349

Establishing costs

- Costs of ICU care:
  - Average total costs of 1 ventilated-ICU day reported as €2,349
  - Average total costs of 1 non-ventilated ICU day reported as €1,835
    - indexed to 2012 Euros, using the European Central Bank Harmonised Index of Consumer Prices, Overall Index

Establishing costs

- Costs of 1 day of EN:
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"The cost-effectiveness of different forms of nutrition in different patient groups remains to be established."

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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
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  To account for variability between hospitals, and to allow for a conservative over-estimation of EN costs, the $35 estimate was inflated by 50% to $52.50.
  Converts to €39.30 per day, at 1 USD = 0.748597 EUR (mid-market rates, June 13, 2013 at 2:22 am coordinated universal time [UTC]).

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- To ensure conservative overcosting of the number of extra days of EN support provided by starting EN within 24 hours of ICU admission, the worst performing hospital case was used.
- Assumes that early EN patients received 6.21 *extra days of EN*, compared with standard care patients.

Calculation of crude costs

Crude calculations of costs (based on averages):

\[
6.21 \text{ more days of EN} \times €39.30 = + €244
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Total


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Total savings per treated patient: €5,330


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*savings* per treated patient

............ but ............


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      Difference in ICU stay has mean 2.34 and SD 15.87 days
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  Difference in ICU stay has mean 2.34 and SD 15.87 days

• 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 $\mu$ and shape $\alpha$, where $\alpha = \mu^2 / \sigma^2$, (SAS, ver 6.12)


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• Step 2: generate realistic costs on top of these clinical outcomes, based on estimates of cost variability obtained from the published literature
  • 1,000 patient stochastic model (with costs and consequences)

• Step 3: To allow the calculation of confidence intervals, the stochastic model is re-run 1,000,000 times

Complete model

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• Step 2: generate realistic costs on top of these clinical outcomes, based on estimates of cost variability obtained from the published literature
  • 1,000 patient stochastic model (with costs and consequences)

• Step 3: To allow the calculation of confidence intervals, the stochastic model is re-run 1,000,000 times
  • large scale Monte Carlo simulation

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### Calculation of crude costs

**Crude** calculations of costs (based on averages):

- 6.21 more days of EN
  \[ \times €39.30 = + €244 \]
- 2.34 fewer ICU days,
  \[ \times - €2,349 = - €5,496 \]
- 2.49 less mechanical ventilation days at €514 per day
  \[ \times 2.49 \text{ fewer ICU days} = - €77.10 \]

Total: \[ + €244 - €5,496 - €77.10 = €5,330 \]

*savings* per treated patient

---

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- Complete model required 1 hour 30 minutes computing time
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Revealed a savings of €5,325 per patient in favour of early EN,

95% CI €2,475 to €8,224*

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

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<table>
<thead>
<tr>
<th>Table 1</th>
<th>Matrix of the distributions of daily costs of care whilst admitted to the intensive care unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical patients</td>
<td>Surgical patients</td>
</tr>
<tr>
<td><strong>Medical patients</strong></td>
<td><strong>Surgical patients</strong></td>
</tr>
<tr>
<td>Received MV</td>
<td>Never received MV</td>
</tr>
<tr>
<td>Day 1</td>
<td>$8,141 ($5,584)</td>
</tr>
<tr>
<td>Day 2</td>
<td>$6,535 ($4,678)</td>
</tr>
<tr>
<td>Day 3</td>
<td>$5,703 ($4,666)</td>
</tr>
<tr>
<td><strong>plus</strong></td>
<td></td>
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</tbody>
</table>

*Notes:* Values are expressed as mean costs (standard deviation); indexed to 2012 US Dollars. Costs were abstracted from Dasta et al.!!

*Abbreviation:* MV, mechanical ventilation.

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Calculation of crude costs

**Crude** calculations of costs (based on averages):

- 6.21 more days of EN \( \times \) your cost of EN = costs

- 2.34 fewer ICU days, \( \times \) your cost of an ICU day = savings

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

  \[2.49 \text{ MV days} - 2.34 \text{ fewer ICU days} =
  \]

  \[0.15 \text{ days} \times \text{your cost of MV} = \text{savings}
  \]

Total your total savings per treated patient


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Questions??

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