Should I start EN if a patient has gut dysfunction:

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Should I start EN if a patient has gut dysfunction: Can early EN prevent gut dysfunction?

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

JAMA, December 17, 2008—Vol 300, No. 23
Effect of Evidence-Based Feeding Guidelines on Mortality of Critically Ill Adults

A Cluster Randomized Controlled Trial

JAMA, December 17, 2008—Vol 300, No. 23
Evidence-based ICU feeding algorithm

At ICU admission: Should this patient be fed?

- Yes: Can EN be started within 24 hours?
  - Yes: GASTRIC CHALLENGE
    - use full strength concentration
    - Consider prokinetic with challenge
    - GOAL: at least 80% of requirements at 72h
    - assess q12h
    - Will at least 80% of requirements be met by 72h?
      - Yes: Is Goal met?
        - Yes: Increase rate to 100%
        - No: Use prokinetic and/or Use post-pyloric tube
      - No: Use prokinetic and/or Use post-pyloric tube

- No: Acceptable conditions:
  - tolerating adequate oral intake
  - < 24 hours to oral intake
  - palliative care

- No: Acceptable conditions:
  - acute pancreatitis
  - enteric anastomosis
  - ischemic bowel
  - enteric fistula
  - imminent bowel resection
  - imminent endoscopy
  - bowel obstruction
  - high nasogastric losses on admission
  - severe exacerbation of IBD
  - *may still opt for elemental feeds

Begin TPN:
- consider TPN with glutamine
  Reassess q12h for EN eligibility

Continue EN to Max. tolerated
  Supplement with PN
  Continue EN challenges q12h

Is Goal met?
Evidence-based ICU feeding algorithm

At ICU admission: Should this patient be fed?

**YES**
- Can EN be started within 24 hours?

  **YES**
  - GASTRIC CHALLENGE
    - Use full strength concentration
    - Consider prokinetic with challenge
    - GOAL: at least 80% of requirements at 72h
    - Assess q12h

  **NO**
  - Acceptable conditions:
    - Tolerating adequate oral intake
    - < 24 hours to oral intake
    - Palliative care

  **NO**
  - Acceptable conditions:
    - Acute pancreatitis
    - Enteric anastomosis
    - Ischemic bowel
    - Enteric fistula
    - Imminent bowel resection
    - Imminent endoscopy
    - Bowel obstruction
    - High nasogastric losses on admission
    - Severe exacerbation of IBD
    - May still opt for elemental feeds

Will at least 80% of requirements be met by 72h?

**YES**
- Use prokinetic and/or
- Use post-pyloric tube

**NO**
- Begin TPN:
  - Consider TPN with glutamine
  - Reassess q12h for EN eligibility

Is Goal met?

**YES**
- Increase rate to 100%

**NO**
- Is Goal met?

**YES**
- Continue EN to Max. tolerated
  - Supplement with PN
  - Continue EN challenges q12h
Evidence-based ICU feeding algorithm

At ICU admission: Should this patient be fed?

YES

Can EN be started within 24 hours?

YES

GASTRIC CHALLENGE
- use full strength concentration
- Consider prokinetic with challenge
- GOAL: at least 80% of requirements at 72h
- assess q12h

NO

Acceptable conditions:
- tolerating adequate oral intake
- < 24 hours to oral intake
- palliative care

NO

Acceptable conditions:
- acute pancreatitis *
- enteric anastomosis *
- ischemic bowel
- enteric fistula
- imminent bowel resection
- imminent endoscopy
- bowel obstruction
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- *may still opt for elemental feeds

YES

Will at least 80% of requirements be met by 72h?

YES

Begin TPN:
- consider TPN with glutamine
- Reassess q12h for EN-eligibility

NO

Use prokinetic and/or Use post-pyloric tube

YES

Increase rate to 100%

YES

Is Goal met?

NO

Continue EN to Max. tolerated
Supplement with PN
Continue EN challenges q12h

NO

Is Goal met?
Evidence-based ICU feeding algorithm

At ICU admission: Should this patient be fed?

- **YES**
  - Can EN be started within 24 hours?
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      - GOAL: at least 80% of requirements at 72h
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    - Will at least 80% of requirements be met by 72h?
      - **YES**
        - Increase rate to 100%
      - **NO**
        - Use prokinetic and/or Use post-pyloric tube
  - **NO**
    - Is Goal met?
      - **YES**
        - Continue EN to Max. tolerated
      - **NO**
        - Continue EN challenges q12h

- **NO**
  - Acceptable conditions:
    - tolerating adequate oral intake
    - < 24 hours to oral intake
    - palliative care
  - Begin TPN:
    - consider TPN with glutamine
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  - Acceptable conditions:
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Evidence-based ICU feeding algorithm

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    - **NO**
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- **NO**
  - **Acceptable conditions:**
    - tolerating adequate oral intake
    - < 24 hours to oral intake
    - palliative care

**Is Goal met?**

- **YES**
  - Increase rate to 100%
  - **YES**
  - Stop EN
  - Reassess status
- **NO**
  - **Use post-pyloric tube**
  - **NO**
  - **Continue EN to Max. tolerated**
  - Supplement with PN
  - Continue EN challenges q12h

**Will at least 80% of requirements be met by 72h?**

- **YES**
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    - acute pancreatitis*
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Evidence-based ICU feeding algorithm

At ICU admission: Should this patient be fed?
- NO
- YES

Can EN be started within 24 hours?
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- YES

GASTRIC CHALLENGE
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- GOAL: at least 80% of requirements at 72h
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Will at least 80% of requirements be met by 72h?
- NO
- YES

Is Goal met?
- NO
- YES

Use prokinetic and/or Use post-pyloric tube

Increase rate to 100%

Acceptable conditions:
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Acceptable conditions:
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Begin TPN:
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If NO

If YES
- increase rate to 100%

If YES
- is goal met?

If NO
- continue EN to max tolerated supplement with PN
- continue EN challenges q12h
Evidence-based ICU feeding algorithm

At ICU admission: Should this patient be fed?

**NO**

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Acceptable conditions:
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- ischemic bowel
- enteric fistula
- imminent bowel resection
- imminent endoscopy
- bowel obstruction

**NO**

- high nasogastric losses on admission
- severe exacerbation of IBD

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**YES**

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- Reassess q12h for EN eligibility

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Continue EN challenges q12h

Increase rate to 100%

YES

Is Goal met?

NO
Evidence-based ICU feeding algorithm

At ICU admission: Should this patient be fed?

Acceptable conditions:
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Acceptable conditions:
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- imminent bowel resection
- imminent endoscopy
- bowel obstruction
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Excessive vomiting or high losses (>1 to 2 L per day) via gastric tube on free drainage due to obstruction etc.

Increase rate to 100%

Is Goal met?

Continue EN to Max. tolerated Supplement with PN
Continue EN challenges q12h
Evidence-based ICU feeding algorithm

At ICU admission: Should this patient be fed?

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YES

Is Goal met?

NO

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Supplement with PN
Continue EN challenges q12h
"The GI tract is not able to perform digestion and absorption adequately to satisfy the nutrient and fluid requirements of the body”

Gut Dysfunction

“The GI tract is not able to perform digestion and absorption adequately to satisfy the nutrient and fluid requirements of the body”

- high gastric residuals
- vomiting
- diarrhoea
- paralytic ileus

Evidence supporting ANZ Guideline recommendation

**Methods**

**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.
**Methods**

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**Primary analysis**
- Included only methodologically sound RCTs.
Methods

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)

Secondary outcomes reported:

- vomiting/regurgitation, pneumonia, bacteraemia, sepsis and MODS.
Primary electronic search identified Abstracts (N = 4,800)

Potentially relevant papers identified and retrieved (N = 675)

RCTs identified for detailed evaluation (N = 505)

Papers excluded, with reasons (N = 170)
Not RCTs (Letters, observational studies, systematic reviews, narrative reviews, previous meta-analyses)

RCTs excluded, with reasons (N = 475)
329 Did not provide a primary comparison of timing of EN (includes 5 pseudo-randomised trials + 99 trials not reporting clinically meaningful outcomes)
72 Not adult critically ill population
46 Not primary nutritional support intervention (GH etc)
16 Cross-over trials
13 Pre-operative interventions

RCTs evaluating timing of EN (N = 30)

Excluded RCTs (N = 24)
7 - Early EN not started within 24 h of injury or ICU admission
4 - Patient oriented outcomes not reported (no mortality etc)
5 - Not critically ill patient population
2 - Early post-op oral intake, not early EN
2 - EN commenced at same time in both groups
1 - Immuno-enhanced EN (Impact)
2 - Excessive loss to follow-up
1 - Subgroup from a larger trial

Included in primary analysis (N = 6)
On topic, included in primary analysis

Chiarelli, 1990: 20 pts, burns
Kompan, 1999: 36 pts, trauma
Kompan, 2004: 52 pts, trauma
Nguyen, 2008: 28 pts, med/surg critically ill
Chuntrasakul, 1996: 38 pts, trauma
Pupelis, 2001: 60 pts, severe pancreatitis and peritonitis
Chiarelli, 1990: 20 pts, burns
Kompan, 1999: 36 pts, trauma
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Nguyen, 2008: 28 pts, med/surg critically ill
Chuntrasakul, 1996: 38 pts, trauma
Pupelis, 2001: 60 pts, severe pancreatitis and peritonitis

None of these trial excluded patients with pre-existing GI dysfunction.
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>Chuntrasakul 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: 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 (10% absolute reduction, P=0.02)
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

<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>Kompan 2004</td>
<td>9/27</td>
<td>16/25</td>
<td>70.15 [0.09, 0.88]</td>
<td>0.28</td>
<td></td>
</tr>
<tr>
<td>Nguyen 2008</td>
<td>3/14</td>
<td>6/14</td>
<td>29.85 [0.07, 1.91]</td>
<td>0.36</td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>41</strong></td>
<td><strong>39</strong></td>
<td><strong>100.00</strong></td>
<td><strong>0.31</strong></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% absolute reduction, P=0.01)
Results: Primary MA, MODS

Review: Early EN (<24h) vs Standard Care (Primary Anal - delayed EN)
Comparison: 01 early EN vs Control
Outcome: 03 Incidence of MODS, Intention to treat analysis

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment 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>Kompan 1999</td>
<td>12/17</td>
<td>13/19</td>
<td>34.03</td>
<td>1.11 [0.27, 4.60]</td>
<td></td>
</tr>
<tr>
<td>Pupelis 2001</td>
<td>20/30</td>
<td>21/30</td>
<td>65.97</td>
<td>0.86 [0.29, 2.55]</td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>47</strong></td>
<td><strong>49</strong></td>
<td><strong>100.00</strong></td>
<td><strong>0.94 [0.40, 2.23]</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Total events</strong>: 32 (Treatment), 34 (Control)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for heterogeneity: Chi² = 0.08, df = 1 (P = 0.78), I² = 0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 0.13 (P = 0.89)</td>
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<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- No difference in incidence of MODS (68% vs 69% of patients, P=0.78)
- One trial reported a reduction in the severity of MODS (2.5 vs 3.1 organs failed per patient, P=0.057)
Summary

- Evidence supporting the presence of a significant mortality benefit from the provision of early EN (< 24 h of injury or ICU admission) has been present in our literature since 2003.

Summary

- Evidence supporting the presence of a significant mortality benefit from the provision of early EN (< 24 h of injury or ICU admission) has been present in our literature since 2003.

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- Pneumonia may also be significantly reduced.

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  • Suggests reduction in GI dysfunction: reduced micro-aspiration perhaps due to improved gastric motility / lower gastric residual volumes.

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• There were no suggestions of any increase in any adverse events or harms.

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- Pneumonia may also be significantly reduced.
  - Suggests reduction in GI dysfunction: reduced micro-aspiration perhaps due to improved gastric motility / lower gastric residual volumes

- There were no suggestions of any increase in any adverse events or harms.

- Outcomes evaluating GI dysfunction not reported in our published systematic review...

Measures of gut dysfunction

.... three trials did report measures of gut dysfunction:


Measures of gut dysfunction

Post-operative ileus:

- 6.7% (2/30) early EN vs. 20% (6/30) delayed, p=0.25

Measures of gut dysfunction

Post-operative ileus:
• 6.7% (2/30) early EN vs. 20% (6/30) delayed, p=0.25

Vomiting and/or Diarrhea:
• 0% (0/10) early EN vs. 20% (2/10) delayed, p=0.47


Measures of gut dysfunction

Post-operative ileus:
- 6.7% (2/30) early EN vs. 20% (6/30) delayed, p=0.25

Vomiting and/or Diarrhea:
- 0% (0/10) early EN vs. 20% (2/10) delayed, p=0.47

Toxic ileus:
- 10% (1/10) early EN vs. 0% (0/10) delayed, p=0.6


Post-operative ileus:
- 6.7% (2/30) early EN vs. 20% (6/30) delayed, p=0.25

Vomiting and/or Diarrhea:
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Upper Digestive Intolerance:
- GRV > 200mls on two consecutive occasions or vomiting


Measures of gut dysfunction

Post-operative ileus:
• 6.7% (2/30) early EN vs. 20% (6/30) delayed, p=0.25

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• 0% (0/10) early EN vs. 20% (2/10) delayed, p=0.47

Toxic ileus:
• 10% (1/10) early EN vs. 0% (0/10) delayed, p=0.6

Upper Digestive Intolerance:
• GRV > 200mls on two consecutive occasions or vomiting
• 70% (19/27) early EN vs. 80% (20/25) delayed, p=0.52

**Measures of gut dysfunction**

Post-operative ileus:
- 6.7% (2/30) early EN vs. 20% (6/30) delayed, p=0.25

Vomiting and/or Diarrhea:
- 0% (0/10) early EN vs. 20% (2/10) delayed, p=0.47

Toxic ileus:
- 10% (1/10) early EN vs. 0% (0/10) delayed, p=0.6

Upper Digestive Intolerance:
- GRV > 200mls on two consecutive occasions or vomiting
- 70% (19/27) early EN vs. 80% (20/25) delayed, p=0.52

UDI lasted significantly longer in delayed EN patients:
- 1.0 ± 0.9 days vs. 2.2 ± 2.7 days, p =0.045

---


# Novel MA of gut dysfunction

**Review**: Early EN (<24h) vs Standard Care

**Comparison**: 01 early EN vs Standard Care

**Outcome**: 03 Complications (Gut Dysfunction)

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<td>13.65 [0.04, 5.19]</td>
<td>0.47</td>
<td></td>
</tr>
<tr>
<td>Keenan 2004</td>
<td>19/27</td>
<td>20/25</td>
<td>50.49 [0.17, 2.10]</td>
<td>0.60</td>
<td></td>
</tr>
<tr>
<td>Cuesta 2001</td>
<td>2/30</td>
<td>6/30</td>
<td>35.86 [0.07, 1.41]</td>
<td>0.32</td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
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<td><strong>100.00</strong></td>
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**Test for heterogeneity**: Chi² = 0.41, df = 2 (P = 0.81), I² = 0%

**Test for overall effect**: Z = 1.69 (P = 0.09)
**Novel MA of gut dysfunction**

- Meta-analysis suggests the provision of early EN *may* reduce the incidence of gut dysfunction:
  - 33% (22/67) of patients vs. 43% (28/65) of patients, $p=0.09$, no heterogeneity
  - One included trial demonstrated a significantly shorter duration of gut dysfunction ($p=0.045$)

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Early EN n/N</th>
<th>Delayed EN n/N</th>
<th>Peto OR 95% CI</th>
<th>Weight %</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Chiarelli 1990</td>
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Evidence supporting the presence of a significant mortality benefit from the provision of early EN (< 24 h of injury or ICU admission) has been present in our literature since 2003.

Our updated systematic review of the literature suggests early EN may result in an 8 to 10% absolute reduction in mortality (P = 0.02).

Pneumonia may also be significantly reduced.

* Suggests reduction in GI dysfunction: reduced micro-aspiration perhaps due to improved gastric motility / lower gastric residual volumes

There were no suggestions of any increase in any adverse events or harms.

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ANZ Guideline recommends early EN. Recommendation does not specifically exclude patients with pre-existing GI dysfunction.

Effect of Evidence-Based Feeding Guidelines on Mortality of Critically Ill Adults
A Cluster Randomized Controlled Trial
JAMA, December 17, 2008—Vol 300, No. 23
## Table 2. Measures of Nutritional Support Guideline Uptake

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Table 5. Secondary Outcomes and Concomitant Therapies

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Witnessed aspiration (patients receiving EN), events/1000 fed patient-days
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**A Cluster Randomized Controlled Trial**

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Questions?
Immediately after resuscitation:

Stable shock can be defined as:

Shock Index \leq 1 \text{ (heart rate ÷ systolic blood pressure = Shock Index)}

or

Systolic blood pressure > 90 \text{ mmHg or mean blood pressure > 70 mmHg for at least one hour.}
The gut as the motor of MODs

With the onset of critical illness:

- Loss of functional and structural integrity of the intestinal epithelium.

## Detailed reasons for trial exclusion from our MA

<table>
<thead>
<tr>
<th>Trial Name</th>
<th>Reasons for exclusion</th>
<th>DH MA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eyer 1993</td>
<td>1. Excessive ltf: 27% (14/52 pts ltf, missing)</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>2. Early EN not started within 24 h of injury or ICU admit (Early EN average time 31 hours)</td>
<td></td>
</tr>
<tr>
<td>Minard 2000</td>
<td>1. Early EN not started within 24 h of injury or ICU admit (Early EN defined as within 60 hours, average time 33 h)</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>2. Patients received immune-enhanced EN (Impact), not standard EN</td>
<td></td>
</tr>
<tr>
<td>Singh 1998</td>
<td>1. Not conducted in a critically ill patient population</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>2. Early EN not started within 24 hours of injury or ICU</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(EN begun 24 – 48 post-op)</td>
<td></td>
</tr>
<tr>
<td>Ibrahim 2002</td>
<td>1. Enteral nutrition commenced at the same time in both groups</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(Early full goal feeding versus early restricted)</td>
<td></td>
</tr>
<tr>
<td>Schroeder 1991</td>
<td>1. No patient oriented outcomes</td>
<td></td>
</tr>
<tr>
<td>Hasse 1995</td>
<td>1. No patient oriented outcomes</td>
<td></td>
</tr>
<tr>
<td>Watters 1997</td>
<td>1. No patient oriented outcomes</td>
<td></td>
</tr>
<tr>
<td>Seri 1984</td>
<td>1. Not conducted in a critically ill patient population</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2. No patient oriented outcomes</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(No deaths reported as of study day 7, no outcomes reported beyond day 7)</td>
<td></td>
</tr>
<tr>
<td>Taylor 1999</td>
<td>1. Enteral nutrition commenced at the same time in both groups</td>
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<tr>
<td></td>
<td>(Gastric versus post-pyloric feeding)</td>
<td></td>
</tr>
<tr>
<td>Sagar 1979</td>
<td>1. No patient oriented outcomes</td>
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<tr>
<td>Beier-Holgersen 1996</td>
<td>1. Not conducted in a critically ill patient population</td>
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<tr>
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<td>2. Early post-op oral intake, not early EN</td>
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<td>Carr 1996</td>
<td>1. Not conducted in a critically ill patient population</td>
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<td></td>
<td>(elective intestinal resection)</td>
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<td>Heslin 1997</td>
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