An evidence-based ICU protocol to address tube feeding associated diarrhoea

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Potential conflicts of interest

Gordon S. Doig

Relevant financial relationships with a commercial interest:

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

• Brief context and background

• Details of the protocol

• Results of a clinical trial

• Summary
The Critical Care Research Network: CCRNet

“CCRNet is a voluntary alliance of Critical Care Units whose mission is to improve patient care and resource utilization through the development, execution and implementation of health services research protocols.”

- established in 1992 by researchers at the University of Western Ontario (WJ Sibbald and CM Martin)
- originally composed of 11 hospitals in South-Western Ontario
- CCRNet has numerous studies to understand care processes and improve patient outcomes
- in 2000, CCRNet included more than 54 hospitals across Ontario
- member hospitals expressed an interest in understanding nutritional support in early 1990’s


Structured literature review to find out ‘what we should be doing’

• the majority of studies demonstrating any benefit of nutrition therapy were performed in severe trauma patients
• there was very little direct evidence to suggest that any form of nutritional therapy improved the outcomes of other groups of critically ill patients

Observational study to find out ‘what we were doing’

• nutrition therapy was started much later than the literature indicated
• EN was frequently stopped due to:
  • diarrhea
  • procedure, and forgot to restart

Structured literature search to find out ‘what we should be doing’

Observational study to find out ‘what we were doing’

We identified an evidence-practice gap

A formal study to find out if improving nutrition therapy resulted in improved patient outcomes was initiated.


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14 teaching and community hospital ICUs were contacted and invited to participate

- all participants were members of CCRNet

- data on baseline feeding practice was collected for 16 weeks (run-in phase)

- mid-way through this run-in period, hospitals were randomized to remain as control hospitals or to improve practice

- practice was improved by the active implementation of an evidence-based guideline

- participants from hospitals randomized to the improve practice were invited to participate in an evidence-based guideline development conference

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Guideline development conference

- an extensive literature search was conducted
  - MEDLINE and EMBASE were searched for controlled trials and overviews of nutritional support (EN and TPN) in critically ill or intensive care patients
  - reference lists of retrieved articles were hand searched for additional articles
  - experts were contacted and asked to search personal files

- evidence was appraised and graded by a content area expert methodologist

- appraisal results were circulated to participants from all hospitals randomized to ‘improve practice’ prior to the conference.

- participants used formal Levels of Evidence to determine guideline recommendations.

- a modified Delphi approach was used to obtain consensus where no evidence existed but a recommendation was still required.


A

At ICU admission: Should this patient be fed?

Yes

Can EN be started within 24 hours?

No

Acceptable conditions:
- Tolerating adequate oral diet
- < 24 h to oral intake
- Palliative care

Yes

Gastric challenge: Use full-strength concentration
Consider prokinetic with challenge
Goal: at least 80% of requirements at 72 h
Assess q12h

Is progression on target to reach at least 80% by 72 h?

No

Acceptable conditions:
- Acute pancreatitis*
- Enteric anastomosis*
- Ischemic bowel
- Enteric fistula
- Imminent bowel resection
- Imminent endoscopy
- Bowel obstruction
- High nasogastric losses
- Severe exacerbation of inflammatory bowel disease

Yes

C

Assess gastrointestinal tolerance to tube feeding q4h

Intolerant patients have:
- Clinically significant stools or
- Readily apparent abdominal distension or
- Increased abdominal girth or
- Multiple emetic episodes or
- Clinically detected aspiration or
- Gastric residuals > 200 mL for nasogastric feeds

Yes

Increase rate to 100% of requirements

Is goal met?

No

Use prokinetic
Use postpyloric tube

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- Liquid stools > 300 mL/d or
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B Is diarrhea present?

- Yes
  - Is stool clinically significant?
    - Yes
      - Continue same enteral feeding
    - No
      - Change medications to tolerate
  - No
    - Does the patient receiving antibiotics?
      - Yes
        - Consider enteral nutrition
      - No
        - Continue same enteral feeding
    - If the diarrhea worsens?
      - Yes
        - Continue same enteral feeding
      - No
        - Digestive care until tolerance improves

C Assess gastrointestinal tolerance to tube feeding q4h

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B

Is diarrhea present?

Yes

Is stool clinically significant? *

No

Continue same enteral feeding

Yes

Are symptoms of the possible cause?

Yes

Change medications needed to tolerance

No

Is the patient receiving antibiotics?

Yes

Seek advice for clinical decision making

No

Consider enteral nutrition

C

Assess gastrointestinal tolerance to tube feeding q4h

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WJ. M. 2004,170(2),197-204.
Is diarrhea present?

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  - Is stool clinically significant? *
    - Yes
      - Continue same enteral feeding
    - No
      - Are medications† the possible cause?
        - Yes
          - Change medications, feed to tolerance
        - No
          - Continue same enteral feeding
  - No
    - Continue same enteral feeding

---

*Clinically significant stools:
- Liquid stools > 300 mL/d or
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†Medications that commonly cause diarrhea:
- Metoclopramide
- Quinidine
- Xylitol
- Magnesium
- Erythromycin
- Aminophylline
- Sorbitol
- Phosphorus

---

Assess gastrointestinal tolerance to tube feeding q4h

Intolerant patients have:
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- Readily apparent abdominal distension or
- Increased abdominal girth or
- Multiple emetic episodes or
- Clinically detected aspiration or
- Gastric residuals > 200 mL for nasogastric feeds
B

Is diarrhea present?

Yes

Is stool clinically significant? *

No

Continue same enteral feeding

Yes

Are medications† the possible cause?

Yes

Change medications, feed to tolerance

No

Is the patient receiving antibiotics?

Yes

Check stool for *C. difficile* toxin, feed to tolerance

No

Consider enteral formula change

C

Assess gastrointestinal tolerance to tube feeding q4h

Intolerant patients have:

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- Readily apparent abdominal distension or
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Is diarrhea present?
  Yes
  Is stool clinically significant? *
    Yes
    Are medications† the possible cause?
      Yes
      Change medications, feed to tolerance
      No
      Is the patient receiving antibiotics?
        Yes
        Check stool for *C. difficile* toxin, feed to tolerance
        No
        Consider elemental formulation
  No
  Continue same enteral feeding

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**B**

- Is diarrhea present?
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        - Yes
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        - No
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            - Yes
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            - No
              - Consider elemental formulation
  - No
    - Continue same enteral feeding

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Assess gastrointestinal tolerance to tube feeding q4h

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- Sorbitol
- Phosphorus
**Algorithm for Diarrhea Management**

1. **Is diarrhea present?**
   - Yes: Continue same enteral feeding
   - No: Is stool clinically significant? *
     - Yes: Change medications, feed to tolerance
     - No: Are medications† the possible cause?
       - Yes: Check stool for *C. difficile* toxin, feed to tolerance
       - No: Consider elemental formulation
         - Is the patient receiving antibiotics? Yes: Continue same enteral feeding
         - No: Decrease rate until tolerance achieved
2. **Is the diarrhea resolved?**
   - Yes: Continue same enteral feeding
   - No: Advance to goal rate as tolerance improves

---

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- Multiple emetic episodes or
- Clinically detected aspiration or
- Gastric residuals > 200 mL for nasogastric feeds
Is diarrhea present?

Yes

Is stool clinically significant? *

No

Continue same enteral feeding

Yes

Are medications† the possible cause?

No

Change medications, feed to tolerance

Yes

Check stool for C. difficile toxin, feed to tolerance

Is the patient receiving antibiotics?

No

Consider elemental formulation

Yes

Is the diarrhea resolved?

No

Decrease rate until tolerance achieved

Yes

Continue same enteral feeding

Assess gastrointestinal tolerance to tube feeding q4h

Intolerant patients have:
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Patient eligibility criteria

All patients expected to remain in the ICU at least three days:

- At time of ICU admission, asked whether the patient was expected to be ‘discharged tomorrow’.


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Baseline outcomes (before practice change)

Guideline development conference

randomization

Study Outcomes (7 ICUs)

Study Outcomes (7 ICUs)

Baseline run-in (16 weeks)

14 ICUs


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Baseline outcomes (before practice change)

<table>
<thead>
<tr>
<th></th>
<th>Control Hospitals</th>
<th>Guideline Hospitals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients enrolled</td>
<td>403</td>
<td>404</td>
</tr>
<tr>
<td>Age (years)</td>
<td>65.1</td>
<td>65.1</td>
</tr>
<tr>
<td>Admission APACHE II</td>
<td>20.6</td>
<td>19.9</td>
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</table>

**Primary outcomes**

<table>
<thead>
<tr>
<th></th>
<th>Control Hospitals</th>
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<tbody>
<tr>
<td>Hospital Mortality</td>
<td>33%</td>
<td>31%</td>
</tr>
<tr>
<td>ICU LOS (days)</td>
<td>13.6</td>
<td>10.0</td>
</tr>
<tr>
<td>Hospital LOS (days)</td>
<td>30.8</td>
<td>28</td>
</tr>
</tbody>
</table>

Percent of patients with LOS greater than 2 days who were enrolled*

76% vs 80%

*At screening, some patients were expected to be ‘discharged tomorrow’, but were not. These patients stayed longer than 2 days, but were not enrolled.

The Critical Care Research Network: CCRNet

Randomized results

14 ICUs

- Guideline development conference
- Baseline run-in (16 weeks)
- Randomization
- Study Outcomes (7 ICUs)
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Randomized results: balance

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<tbody>
<tr>
<td>Patients enrolled</td>
<td>214</td>
<td>248</td>
</tr>
<tr>
<td>Age</td>
<td>67.9 years</td>
<td>64.6 years</td>
</tr>
<tr>
<td>Gender</td>
<td>39% females</td>
<td>39% females</td>
</tr>
<tr>
<td>Admission APACHE II</td>
<td>22.5</td>
<td>20.6</td>
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Percent of patients with LOS greater than 2 days who were enrolled*

|                                | 83%               | 82%                 |

*At screening, some patients were expected to be ‘discharged tomorrow’, but were not. These patients stayed longer than 2 days, but were not enrolled.
### Randomized results: nutrition therapy

<table>
<thead>
<tr>
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<th>Control Hospitals</th>
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<th>p-value</th>
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</thead>
<tbody>
<tr>
<td>ICU admit to EN</td>
<td>2.34</td>
<td>1.53</td>
<td>0.07</td>
</tr>
<tr>
<td>ICU admit to EN/PN</td>
<td>1.99</td>
<td>1.47</td>
<td>0.09</td>
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<tr>
<td>EN delivered</td>
<td>5.31</td>
<td>6.97</td>
<td>0.02</td>
</tr>
<tr>
<td>TPN delivered</td>
<td>1.94</td>
<td>2.25</td>
<td>0.65</td>
</tr>
<tr>
<td>EN or TPN delivered</td>
<td>6.81</td>
<td>8.63</td>
<td>0.01</td>
</tr>
<tr>
<td>Energy delivered</td>
<td>4087</td>
<td>5321</td>
<td>0.23</td>
</tr>
<tr>
<td>Goal achieved</td>
<td>4.1</td>
<td>5.0</td>
<td>0.23</td>
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## Randomized results: Primary outcomes

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<tr>
<td>Hospital Mortality</td>
<td>37%</td>
<td>24%</td>
<td>0.047</td>
</tr>
<tr>
<td>ICU LOS (days)</td>
<td>11.7</td>
<td>10.8</td>
<td>0.65</td>
</tr>
<tr>
<td>Hospital LOS (days)</td>
<td>34.3</td>
<td>25.4</td>
<td>0.006</td>
</tr>
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Percent of patients with LOS greater than 2 days who were enrolled*

- Control Hospitals: 83%
- Guideline Hospitals: 82%

*At screening, some patients were expected to be ‘discharged tomorrow’, but were not. These patients stayed longer than 2 days, but were not enrolled.
Mortality by subgroup

Absolute Risk Reduction for Mortality with 95% confidence interval (test based), accounting for clustering

- All patients n=492
- Medical Admit n=132
- Emerg Dept Admit n=150
- Surgical Admit n=147
- Emergent Sx n=81
- Elective Sx n=66
- From other hospital n=39
- From other ICU n=15

Favours control

Favours Guideline
Active implementation of our evidence-based guideline for nutrition therapy in critical illness resulted in improvements in clinical practice:

• Patients provided EN earlier
• Patients provided EN on more days whilst in the ICU

Evidence supporting benefits from early EN convinced clinicians to start EN earlier.

A practical algorithm for the management of tub feeding associated diarrhoea contributed towards the ability to provide EN on more days whilst in the ICU.

These improvements in clinical practice translated to:

• Reduced mortality
• Reduced hospital stay

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### Canadian vs Australian cRCT

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<tr>
<td>Admit to EN</td>
<td>2.2</td>
<td>1.6</td>
</tr>
<tr>
<td></td>
<td>1.4 days</td>
<td>0.8</td>
</tr>
<tr>
<td>Admit to any feed</td>
<td>1.9</td>
<td>1.5</td>
</tr>
<tr>
<td></td>
<td>2.1 days</td>
<td>0.9</td>
</tr>
<tr>
<td>EN delivered</td>
<td>5.4</td>
<td>6.7</td>
</tr>
<tr>
<td></td>
<td>5.8 days fed / 10 ICU days</td>
<td>7.2</td>
</tr>
<tr>
<td>EN or TPN delivered</td>
<td>6.9</td>
<td>8.5</td>
</tr>
<tr>
<td></td>
<td>6.9 days fed / 10 ICU days</td>
<td>8.1</td>
</tr>
<tr>
<td>Energy delivered</td>
<td>999</td>
<td>1257</td>
</tr>
<tr>
<td></td>
<td>1065 kcal/ICU day</td>
<td>1241</td>
</tr>
<tr>
<td>% of patients never fed</td>
<td>25%</td>
<td>10%</td>
</tr>
<tr>
<td></td>
<td>28%</td>
<td>6%</td>
</tr>
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Guideline implementation strategy

Multifaceted Implementation Strategy

1) Academic detailing

2) Educationally influential opinion leaders

3) Local consensus process
   • local champions

4) Reminders (manual or computerized)
   • active ongoing bedside reminder system
   • educational materials

5) Audit and feedback
   • computer generated, timely
   • should be delivered by peers or opinion leaders

6) Educational outreach process
   • didactic lecture based CME (conferences, lectures)

7) Unsolicited mail
   • educational materials