Should we use feeding guidelines in the ICU?
A review of the evidence

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Abstract - Objective: The appropriate and timely provision of nutritional support to the critically ill hospitalized patient is recognized as an important quality benchmark. However, daily practice is not consistent with best evidence practice. The purpose of this review was to identify and appraise the available evidence to determine whether guidelines for nutritional support can bridge the gap between best evidence and actual practice in the intensive care unit (ICU). Search strategy: Medline (www.PubMed) was searched to detect cluster randomized controlled trials evaluating the benefits of implementing a clinical practice guideline for nutritional support in the ICU. Reference lists of retrieved articles were hand searched. Summary of findings: Three hundred and seventy-six potentially eligible studies were reviewed. Three multi-centre cluster randomized trials were identified. In two of these trials, significant practice change was achieved in the ICU through the active implementation of a clinical practice guideline. In one trial, these improvements in practice translated to a significant reduction in mortality and hospital length of stay. No harm was documented. Conclusions: Evidence-based clinical practice guidelines may be used as a vehicle to change practice and improve patient outcomes in the intensive care unit. Use of a multifaceted practice change strategy, composed of as many specific change interventions as practicable, may be required to overcome ICU-specific barriers to change.

Keywords - Nutrition, Intensive Care, Critical Care, Critically ill, Guidelines, Review

Introduction
The appropriate and timely provision of nutritional support to the critically ill hospitalized patient is recognized as an important quality benchmark [1] and has been proposed for consideration as a 'standard of care' [2].

Numerous systematic reviews demonstrate potential clinical benefits arising from the provision of appropriate nutritional support in critical illness [3-6]. Meta-analyses evaluating timing consistently demonstrate a reduction in mortality that can be attributed to early nutritional support [7-9]. Despite documented clinical and patient oriented benefits, daily practice is not consistent with best evidence practice.

Data from control arms of clinical trials reveals up to 37.5% of eligible patients may never receive nutritional support during their ICU stay, while 40% of the patients who are fed do not have their nutritional support started for 48 hours or longer after ICU admission [10]. Furthermore, nutritional goals are achieved on only 50% of feeding days [10,11]. Clinical practice guidelines may help reduce evidence-practice gaps by promoting awareness of interventions of proven benefit and discouraging ineffective care [12,13].

The purpose of this review was to identify and appraise the available evidence evaluating the implementation of nutrition guidelines in the intensive care and to provide expert comment on their potential utility.

Study selection and search methods
Cluster randomized controlled trials (cRCT) comparing the effects of implementing guidelines for nutritional support in critically ill patients were sought. A previously published definition was used to identify critically ill patient populations [14].

The primary search was conducted using Medline via PubMed (www.PubMed.org). The search was not limited by language. A sensitive search statement designed to detect cluster randomized trials [“(cluster randomized” or “cluster randomised”) OR (cluster) AND ((clinical[Title/Abstract] AND trial[Title/Abstract]) OR clinical trials[MeSH Terms] OR clinical trial[Publication Type] OR random*[Title/Abstract] OR random allocation[MeSH Terms] OR therapeutic use[MeSH Subheading])] was crossed with the MeSH term ‘Nutrition’. Reference lists of retrieved articles were reviewed for eligible papers. Recognized academic experts were contacted. The closing date for the search was 3 August 2009.

Only truly randomized controlled trials evaluating the impact of the implementation of a nutrition guideline or protocol were eligible for inclusion. Because observational studies, pseudo-randomized trials and non-randomized trials (Ex. before-and-after studies) have been accepted as being susceptible to serious forms of bias, they were not eligible for inclusion.

Eligible papers were appraised with regards to methodological quality as determined by the three most commonly accepted key methodological attributes: 1) the maintenance of allocation concealment; 2) the use of blinding and; 3) presentation of intention to treat results [14]. Eligible papers were described with regards to basic elements of study design, guideline development, guideline content and guideline evaluation. The search, appraisal and data extraction was conducted independently by both authors. Meta-analysis was not attempted nor intended.
Results

Three hundred and seventy six potentially eligible abstracts were identified. Hand searching of abstracts, review of reference lists and contact with experts revealed three potentially eligible papers [10,15,16]. The review of the reference lists of these potentially eligible papers and contact with recognised experts did not reveal any additional studies.

All three potentially eligible papers qualified for inclusion. These three papers evaluated the impact of implementing nutrition guidelines or protocols across multiple sites. No single centre cRCTs or individual patient randomized controlled trials were identified. Table 1 presents a comparison of the key aspects of the three different guidelines that were evaluated.

Methodological quality

All three included trials reported using a randomization process such that allocation concealment would have been maintained. Participating sites were required to consent to participation before they were informed whether or not they would be allocated to develop and implement the guideline.

None of the three included trials reported using any form of blinding.

Two included trials presented results from an intention to treat analysis. The third trial presented results from a per protocol analysis but outcome reporting was complete such that intention to results could be calculated [15].

The Canadian ACCEPT Nutrition Guideline Trial

The ACCEPT trial, published in 2004, was conducted by a collaborative network of community and metropolitan teaching hospital ICUs throughout South-western Ontario, Canada [15]. Participating sites used an explicit and repeatable process to develop a novel nutritional support guideline, which was then evaluated in a cRCT.

After development of the guideline, seven hospitals were randomly allocated to implement the guideline and seven remained as controls. The evaluation phase was initiated at each of the seven active sites by an educational outreach visit (EOV), conducted by a study chief investigator (academic opinion leader). The chief investigator visited each participating site and presented the contents of the guideline at grand rounds or a dinner meeting. These formal didactic educational sessions were followed-up with one-to-one interactions with interested parties (academic detailing), conducted by the chief investigator. The purpose of the EOVs was to provide education on the guideline content and study design in order to communicate the need for practice change to the ICU staff and stakeholder clinicians, and to empower the ICU site investigator as the local opinion leader champion for change.

The ICU site investigator, which was a local ICU dietician, was primarily responsible for implementation of the guideline recommendations. The guideline implementation strategy included active reminders (short friendly bedside chats with clinicians) supported by passive reminders (posters etc).

Although investigators from the seven control hospitals participated in the development of the guidelines, they received no active implementation support. No constraints were placed on practice change in the control hospitals.

Four hundred and ninety nine patients were enrolled at the 14 participating hospital ICUs during the guideline evaluation phase. Follow-up was complete. Due to a failure in the randomization process (one hospital refused to implement the guideline), results were presented for both appropriately randomized hospitals and for all hospitals. Active implementation of the study guideline resulted in significant improvements in the delivery of nutritional support. Patients in guideline ICUs received enteral nutrition (EN) (5.4 vs. 6.7 EN days per 10 day ICU stay, p=0.042) and enteral and/or parenteral nutrition (PN) (6.9 vs. 8.5 EN and/or PN days per 10 day ICU stay, p=0.02) significantly more often. Controlling for minor imbalances in patient populations, hospital discharge mortality was significantly reduced in appropriately randomized guideline ICUs (10% absolute reduction, p=0.035).

Jain et al.’s Canadian Nutrition Guideline Trial

Published in 2006, Jain et al conducted a cRCT at 50 ICU sites throughout Canada [16]. This study evaluated the impact of a nutritional support guideline that had been developed and published prior to the commencement of the trial [6].

Dietician site investigators randomized to implement the published ICU guideline, received support via a study website. They were provided with a link to access the guideline, supporting documents, educational tools (nutrition algorithms including an evidence-based feeding protocol, flow sheets, sample order sheets), and training kits to assist them in their leadership role. Dieticians were instructed to implement an enteral feeding protocol or modify their existing one in order to reflect the guideline recommendations. Posters and pocket cards that summarized the guideline recommendations were also distributed to the sites.

Site-specific benchmarking reports were prepared to provide a form of audit and feedback. Each dietician was instructed to conduct at least one interactive workshop with relevant ICU staff to review the site reports, discuss the site’s strengths and weaknesses in current practice, and formulate strategies to improve practice. Dieticians were encouraged to conduct ongoing audits of their practice change strategies to affirm that appropriate changes were occurring. Site specific EOVs were not undertaken by the chief investigators.

Control ICU study dieticians received a copy of the published guideline in the mail, but no other support material.

Six hundred and twelve patients were enrolled in the 50 ICU sites during the guideline evaluation phase. Follow-up was complete. Eighty-four percent of active guideline sites held one or more interactive workshops compared to 16% of control sites. Fifty percent of active sites adopted revisions to their existing feeding protocols as a result of these workshops, compared to 28% of control sites. There were no significant differences between groups during the evaluation phase with regards to the primary outcome, adequacy of enteral nutrition support, or any
secondary measures of the provision of nutritional support. There were no between group differences in mortality or length of stay.

**Australian and New Zealand (ANZ) Guidelines Trial**

The ANZ Nutrition Guidelines Trial was conducted by a collaborative network of 27 community and metropolitan teaching hospital ICUs throughout Australia and New Zealand and was published in 2008 [10].

Fourteen participating hospitals were randomly selected to participate in the guideline development process and then implement the guideline. An explicit and repeatable process was used to develop the evidence-based guideline. Thirteen hospitals remained as controls. The guideline evaluation phase was initiated at each of the 14 active sites by an EOV, conducted by the study chief investigators. The chief investigators visited each participating site and presented the content of the guideline at grand rounds or a similar meeting. These formal didactic educational sessions were followed up with one-to-one interactions with interested parties (academic detailing), conducted by the chief investigators. The purpose of the EOVs was to provide education on the guideline content in order to communicate the need for practice change to the ICU staff and stakeholder clinicians, and to empower the site co-investigators as the local opinion leader champions for practice change.

The co-investigators, which included a local ICU dietitian and ICU clinician at each site, were primarily responsible for implementation of the guideline recommendations. At the study start-up meeting, site investigators received formal instruction and training on the use of each of the following interventions to support guideline implementation: 1) active reminders (short friendly bedside chats with clinicians); 2) peer-to-peer academic detailing; 3) a formal survey to identify and co-opt nursing, surgical and ICU-based educationally influential opinion leaders; 4) timely web-enabled performance feedback, allowing comparisons between guideline hospitals; 5) multiple in-service sessions for all ICU staff and; 6) passive reminders (posters etc).

Control hospital investigators did not participate in the development of the guideline nor did they receive copies of the guideline. In an attempt to minimize contamination, active study guideline hospitals were instructed not to disseminate study guideline content outside of their own participating site and control hospitals were requested not to implement new feeding guidelines during the study evaluation phase.

One thousand one hundred and eighteen patients were enrolled at the 27 participating sites during the guideline evaluation phase. Follow-up was complete. Successful implementation of the guideline resulted in numerous significant improvements to key measures of nutritional support. At guideline hospitals, significantly more patients were fed during their ICU stay (71.2% vs. 94.3% of eligible patients fed, p<0.001), patients were fed significantly earlier (2.14 vs. 0.91 days to feeding start, p<0.001), patients received nutritional support more consistently (6.9 vs. 8.1 fed days per 10 day ICU stay, p<0.002) and nutritional goals were met more often (5.0 vs. 6.1 days per 10 day ICU stay, p=0.03). Hospital discharge mortality and length of stay did not differ between groups.

**Discussion**

This review identified three cRCTs that evaluated the impact of implementing a guideline for nutritional support across multiple ICUs. In two of the cRCTs, significant practice change was achieved as a result of active implementation of the guideline [10,15]. In one cRCT, successful implementation translated to a significant reduction in mortality and hospital length of stay [15]. None of the cRCTs reported any harm associated with implementation of the guideline. Measures of physical function, quality of life and costs were not reported in any of the three trials.

**Does nutrition support improve patient outcomes?**

Clinical trials of nutritional support in critical illness tend to be small in size and are known to have numerous methodological shortcomings [14,17,18]. Despite these deficiencies, meta-analyses that focus on clinical trials that are free from major flaws demonstrate significant mortality benefits attributable to the early provision of nutritional support in critical illness [7-9]. In vitro and in vivo experimental evidence reveal a physiological bases for this mortality benefit [19,20].

No reviews of the provision of early standard EN formulae substantiate the presence of clinically important harm to patients [21], with the most recent meta-analysis suggesting that ventilator associated pneumonia may actually be decreased [8]. Furthermore, although meta-analysis of clinical trials of PN demonstrate an increase in infectious complications [9], this has been attributed to an increase in catheter related bloodstream (CRB) infections (absolute increase 3.5%, 95% CI from 1.2% to 5.8%) [22]. With heightened awareness and prompt treatment [23], an increase in CRB infections may be of lesser clinical importance when considered in the context of the mortality benefit attributable to early PN use [9,24,25].

We concede that the meta-analyses of nutritional support interventions demonstrating improvements in mortality are based on small, methodologically weaker trials; however, we find the balance between potential benefit and possible harm weighs in favour of the provision of timely and appropriate nutritional support. We recognize other clinicians may require better evidence [26].

Large-scale multi-centre clinical trials evaluating various aspects of nutritional support in critical illness are currently ongoing (Ex. Early vs. delayed EN and borage oils in acute lung injury, ClinicalTrials.gov NCT00609180; Glutamine and anti-oxidants, ClinicalTrials.gov NCT00609180; Early parenteral nutrition in patients with contraindication to EN, Australian Clinical Trials Registry Number: 012605000704695). Results from these clinical trials may provide more convincing evidence of a need to change daily practice.

**Changing daily practice in the ICU**

The ICU is a complex multi-disciplinary environment that necessitates a cooperative team based approach to patient care. The success of an evidence-based guideline initiative may be related to a combination of local ICU-level characteristics, measures of inter- and intra-profession communication, factors intrinsic to the...
individual guideline [27] and properties of the practice change strategy used to implement the guideline [28,29]. Complex multidisciplinary environments may necessitate the use of a comprehensive, multi-faceted practice change strategy that addresses the needs of the individual, the team, the department and the system within which departments interact [30].

The clinical practice guidelines implemented in the three cRCTs reviewed in this paper do not differ substantially in their key recommendations (Table 1). It is likely that differences in practice change achieved in the three trials is attributable to differences in the active practice change strategies that were employed, not differences in guideline content. The ANZ Nutrition Guidelines Trial employed the most comprehensive practice change strategy, which resulted in the largest difference in practice between groups.

The ANZ Nutrition Guideline was supported by seven main practice change interventions which were delivered by external academic opinion leaders (EOVs) and a local team composed of up to five individuals (ICU dietician and ICU clinician co-investigators and a peer-nominated educationally influential opinion leader ICU nurse, ICU clinician and surgeon). In a follow-up survey of participating sites, all seven types of practice change interventions were reported as ‘successful’ in overcoming barriers to change [29]. Furthermore, respondents identified a wide variety of barriers to practice change that were shared between hospitals, and listed additional barriers that were unique, but commonly encountered, within particular hospitals.

The use of a multifaceted practice change strategy to actively implement and maintain guidelines across multiple sites is assumed to be time consuming and resource intensive [28]. Each site participating in the ANZ Guideline Trial reported using a different and unique combination of practice change interventions ‘most frequently’ to address their own unique combination of barriers [29]. It is possible that the comprehensive nature of the practice change strategy employed in the ANZ Guideline Trial decreased workload because sites were able to identify and use subset-combinations of change interventions they found to be most effective in their particular environment.

**Characteristics of successful guidelines**

If a guideline recommendation is simple and has a clear, unambiguous advantage supported by strong evidence, the recommendation is more likely to be adopted and implemented into practice [31-33]. By definition, the relative advantage of an opinion-based recommendation is open to interpretation. If potential users do not share the expert’s opinion, and thus do not believe the expert recommendation holds a clear advantage, they may not consider it further [33].

All three guidelines evaluated in the cRCTs included, made recommendations that were relatively uncomplicated and easy to understand. However, only the ANZ Guideline was wholly evidence-based. For example, because the clinical trials addressing starting rates and nutritional goals do not provide strong evidence of a clear, unambiguous patient benefit of one approach over any other, the ANZ Guidelines did not contain specific recommendations concerning starting rates and goals.

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**Table 1. Key Elements of Nutrition Guidelines evaluated in cRCTs**

<table>
<thead>
<tr>
<th>CANADIAN ACCEPT GUIDELINE</th>
<th>JAIN’S CANADIAN GUIDELINE <a href="http://WWW.CRITICALCARENUTRITION.COM">WWW.CRITICALCARENUTRITION.COM</a> 2003 PUBLISHED VERSION</th>
<th>AUSTRALIAN AND NEW ZEALAND GUIDELINE <a href="http://WWW.EVIDENCEBASED.NET">WWW.EVIDENCEBASED.NET</a></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type of guideline</strong></td>
<td>Evidence-based and expert-opinion recommendations.</td>
<td>Evidence-based recommendations.</td>
</tr>
<tr>
<td>Preference for EN</td>
<td>Yes.</td>
<td>Yes.</td>
</tr>
<tr>
<td>Recommend early EN</td>
<td>Yes, &lt; 24 h of ICU admission.</td>
<td>Yes, within 24 to 48 h of ICU admission.</td>
</tr>
<tr>
<td>Start PN at same time as EN</td>
<td>No recommendation.</td>
<td>No recommendation.</td>
</tr>
<tr>
<td>Start PN if EN not tolerated</td>
<td>After attempting prokinetics and post-pyloric feeding.</td>
<td>After attempting prokinetics and post-pyloric feeding.</td>
</tr>
<tr>
<td>Start PN if EN contraindicated</td>
<td>Yes, &lt; 24 h of ICU admission.</td>
<td>Yes, &lt; 24 h of ICU admission.</td>
</tr>
<tr>
<td>PN composition</td>
<td>No recommendations.</td>
<td>Recommend glutamine.</td>
</tr>
<tr>
<td>Recommend intensive insulin therapy</td>
<td>No recommendations.</td>
<td>Recommended in surgical patients.</td>
</tr>
</tbody>
</table>

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Successful implementation of the ANZ Guideline resulted in significantly shorter times from ICU admission to starting EN, but the starting rates and advancement rates used by both guideline and control ICUs did not differ and similar nutritional goals were eventually achieved. In effect, each guideline ICU was able to start and advance EN at the rates with which they were already familiar: they just focussed on starting earlier in more patients. Developing a sparse guideline that allows hospitals to retain familiar local practices where evidence is unclear, such as EN starting rates, may increase the acceptance and uptake of aspects of the guideline where evidence of objective benefit is clear [33-35].

Strengths and weaknesses of this overview

Our search focussed on evidence generated from multi-centre cRCTs. When a study intervention involves a significant educational component that may change a clinician’s approach to standard care, such as education provided on the contents of a clinical practice guideline, use of a cluster randomized design helps protect against changes in standard care [36]. In a cRCT, entire ‘units of practice’ (E.g.. an entire ICU) are randomized to receive the intervention or remain as controls. Although there are well conducted single-centre before-and-after studies demonstrating the benefits of implementing evidence-based guidelines for nutritional support [37], multi-centre cRCTs are more generalizable and are considered to be less prone to internal bias [38].

Although the guidelines evaluated in each of the three included cRCTs were similar with regards to key recommendations, they did differ on a number of minor recommendations. It is also important to note that each trial used a distinctly different combination of practice change interventions to implement the guideline under study. As a result, each trial serves as an evaluation of a unique guideline and practice change strategy combination. The success or failure of any single trial cannot be traced to one specific guideline component or implementation intervention.

Conclusions

Two of the three cRCTs identified by this review documented significant improvements in the delivery of nutritional support as a result of the active implementation of a clinical practice guideline [10,15]. In one cRCT, these practice changes translated into improvements in patient outcomes [15]. Practice change lessons learnt from these three projects may inform others attempting to improve care in the ICU.

The potential to change practice using a clinical guideline may be related to a combination of local ICU-level characteristics, communication structures and pathways, guideline content and presentation and properties of the practice change strategy used to implement the guideline. Guideline recommendations that are simple and clear, with an obvious advantage to patient outcomes supported by strong evidence, are more likely to be adopted into daily practice. Expert opinion based recommendations that are not supported by evidence, may be more likely to cause local dissension. Whilst evidence-based guidelines may impart knowledge, passive dissemination alone is unsuccessful in achieving sustained behaviour change.

Use of a multifaceted practice change strategy, composed of as many specific change interventions as practicable, may be required to overcome site-specific barriers to change. The selection of individual practice change interventions for inclusion in the strategy should be based on: an assessment of available resources; a recognition of the importance of different types of barriers to different sites; research evidence supporting the effectiveness of combinations of interventions and; recognition that workload may be reduced by using certain interventions in combination.

References


