Building a Research Program
From the Ground Up

Deborah Cook
St Joseph’s Healthcare, McMaster University
Canada Research Chair
Using Observational Studies to Inform and Interpret RCTs

Stress Ulceration & The Gastropulmonary Research Program
What is Clinically Important Gastrointestinal Bleeding?

- Overt bleeding 9%
- Clinically important bleeding 2%
- Risk factors for overt bleeding: ventilation & occult bleeding

- .....but given a 2% bleeding rate, to detect a 25% RRR in clinically important bleeding using H2RA with 75% power, N=19,000

Cook et al, J Intensive Care Med 1991
An Integrated Research Program on Stress Ulcer Prophylaxis

- Pilot prognosis study
- Bleeding prognosis/risk factor study
- Bleeding case control study
- First meta-analysis of RCTs
- Second meta-analysis of RCTs
Pre-RCT Observational Studies To Inform A Future RCT

- Pilot prognosis study (for bleeding definitions & incidence)
- Multicenter prognosis study (for bleeding incidence & risk factors)
- Case-control study (for attributable morbidity, mortality & cost of bleeding)
- Meta-analysis of stress ulcer prophylaxis RCTs (for effect on bleeding and pneumonia)
Ranitidine vs Sucralfate Trial
(CCCTG, NEJM 1998)
An Integrated Research Program on SUP

- Pilot prognosis study
- Bleeding prognosis/risk factor study
- Bleeding case control study
- First meta-analysis of RCTs
- Second meta-analysis of RCTs
- VAP case control study
- VAP risk factor study
- VAP diagnosis study
- VAP adjudication study
- Bleeding case control study
- Bleeding risk factor study
7 Problems Averted
By Pre-RCT Observational Studies

1) Non-reproducible bleeding definitions
2) Inaccurate estimates of bleeding incidence
3) Uncertainty about importance of bleeding
4) Randomization of low risk patients
5) Selection of ineffective prophylactic agents
6) Erroneous sample size calculations
7) Irresponsible expenditure of research funds
Several Questions Nested in One Study

2

The Level of Care Study Program
Why this Research Program?

• End of life care was viewed as ‘soft science’
• The value of technology was unchallenged
• Funding was difficult
• We did not have just one question!
• The research archetype was multidisciplinary, modelling critical care medicine
Levels of Care In The ICU:
An International Observational Study

- DNR within 24h of ICU admit
- DNR in ICU
- All bedside clinicians involved
- Life support administered

Discharge
Life Support Withdrawal or Withholding
Death
Determinants of Ventilator Withdrawal

- **pre-ICU**
  - ---

- **in-ICU**
  - Inotropes & vasopressors
  - Predicted ICU survival <10%

- **post-ICU**
  - Predicted poor cognitive function
  - Perceived patient Preference to limit life support
Enrolled
851

- Ventilator weaned
  539
    - ICU death
      3 (2.4%)
    - Hospital death
      57 (10.6%)
    - Hospital discharge
      482 (89.4%)
- Died receiving ventilation
  146
    - ICU death
      146 (100%)
- Ventilator withdrawn
  166
    - ICU death
      145 (87.4%)
    - Hospital death
      160 (96.4%)
    - Hospital discharge
      6 (3.6%)
Reasons for discomfort when life support plan was believed to be too intense

- Fear of legal action
- Fear of family complaint
- Inconsistent with pt/fam wishes
- ICU overestimates QOL
- ICU overestimates survival
- Resources used inappropriately
- Inappropriately prolonging death
- Pt/fam overestimate QOL
- Pt/fam overestimate survival
- Inconsistent with pt/fam wishes
- Fear of family complaint
- Fear of legal action
Products of this Research Program

• Traditional:
  – Publications: 7 abstracts, 1 chapter, 6 papers
    Degrees: 1 PhD, 1 Masters
  – Courses: 1 PhD, 1 Masters

• Intangible:
  – Legitimization of end of life research
  – Promoted reflective practice
  – Optimal engagement with bedside staff
  – Self-funding symbolized commitment
The ‘Full Monty’

3

The Thromboprophylaxis & Knowledge Translation Program
VTE in Critically Ill Patients: Consensus Documents & Guidelines

- 1986: NIH Consensus Conference VTE Prevention
- 1992: European Consensus Statement VTE Prevention
- 1992: Thromboembolic Risk Factors Consensus Group
- 1997: International Consensus Statement VTE Prevention
- 1998: ACCP Consensus Committee Pulmonary Embolism
- 1998: 5th ACCP Antithrombotic Consensus Conference
- 1999: ATS Practice Guideline on Diagnosis of VTE

......Medical-surgical ICU patients not mentioned anywhere!
VTE in Medical-Surgical ICU Research Program

Phase I
- Clinical Examination Systematic Review
- Prophylaxis Systematic Review
- Local Utilization Review

Phase II
- National Practice Survey
- National SICU Utilization Review
- Binational MICU Utilization Review
- VETEC Study of DVT Incidence & Risk Factors
- CRIPTEC Study of Coagulation Risk Profile
- BEHAVE Prophylaxis Study

Phase III
- BITEC Study of VTE Burden of Illness
- Clinically Important DVT Survey
- PROTECT Pilot RCT
- DIRECT Study
- PROTECT
- EPITEC
- PE-METRICS
- HITEC
- E-PROTECT
- CONECKKT-T
Disutility of the Physical Examination For Diagnosing DVT in ICU Patients

Leg Specific Risk Score

AUC 0.59 (0.42, 0.75)  
P = 0.29
Observational Study Differences

<table>
<thead>
<tr>
<th></th>
<th>Audits</th>
<th>Surveys</th>
</tr>
</thead>
<tbody>
<tr>
<td>Directness</td>
<td>Actual practice</td>
<td>Stated practice</td>
</tr>
<tr>
<td>Insights</td>
<td>Patterns and predictors measurable</td>
<td>Knowledge, attitudes, beliefs</td>
</tr>
<tr>
<td>Effort</td>
<td>More effort for participants</td>
<td>Less effort for respondents</td>
</tr>
</tbody>
</table>
10-Step Rigorous Chart Review

1. Write a proposal
2. Submit to REB for expedited review
3. Develop CRFs with analysis in mind
4. Develop an operations manual
5. Personally pilot your CRFs
6. Conduct a reliability exercise
7. Analyze agreement & reasons for disagreement
8. Revise CRFs and operations manual
9. Expand training tool kit as needed
10. Anonymize source data as per GCP

ACCADEMY, McMaster 2006
Franco-Canadian VTE Prophylaxis

![Graph showing comparison between France and Canada for various VTE prophylaxis methods.]

- **UFH**: Comparison shows a higher usage in Canada compared to France.
- **LMWH**: Usage is significantly higher in France, indicated by the star.
- **Antiemb stockings**: Usage is higher in Canada, as indicated by the star.
- **PCD**: Usage is similar in both countries, without the need for a star.
“Pilot Projects”

• Pilot work
  • Work done in preparation for a study (e.g., pretesting a questionnaire)

• Pilot study
  • A stand-alone project in preparation for a study (e.g., development and validation of an instrument for a survey)

Pilot studies are under-discussed, under-used, under-reported.
Prescott & Soeken, 1989
INCLUSION

- ICU patient ≥ 18 yrs
- expected adm > 72h

PROTECT Pilot Study

EXCLUSION

- trauma, ortho, cardiac, neurosurgery, severe HTN, hemorrhagic CVA on adm
- DVT, PE, major bleed on adm, ≤3 mo
- platelets ≤100
- INR ≥2xULN, PTT ≥2xULN
- therapeutic anticoagulation
- HIT
- >2 doses LMWH or UFH in ICU
- pregnant or limited life support
PROTECT Pilot Study Feasibility
Outcomes

Successful if, among 120 patients,
1) ≥115 (98.5%) drug post randomization in 12h & ≥110 (91.7%) have every dose
2) ≥90% necessary dose adjustments made
3) ≥90% admission US within 48h & twice weekly DUS & post ICU discharge
4) ≥1 patient/2 weeks/center
VTE in Medical-Surgical ICU Research Program

**Phase I**
- Clinical Examination Systematic Review
- Prophylaxis Systematic Review
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- EPITEC
- PE-METRICS
- HITEC
- E-PROTECT
- CONECKKT-T
End-of-Grant Knowledge Translation

- CONECCKT-T: Co-operative Network of Critical Care Knowledge Translation: Thromboprophylaxis
- Our mission: PROTECT-ing our patients
- Our newsletter: CONECCKT-Tions
- Our motto: Stop the Clot!
Spectrum of Effort-Related ‘End-of-Grant’ KT

Jonathan Lomas, in the Early KT Days
Goal

To optimize thromboprophylaxis for adult medical-surgical ICU patients from the perspective of the patients, providers and policy makers.

A multi-center, multi-professional, multi-phase, multi-method quality improvement research program.
• Timely, safe, appropriate, cost-effective thromboprophylaxis for medical-surgical critically ill adults in Canada
Meta-analysis & evidence-based med-surg ICU practice guidelines

Phase 1

Retropective practice audit

Analyses of appropriate rates & determinants

Phase 2

Interviews about thrombo prophylaxis prescribing

Analyses of barriers & facilitators

Phase 3

Prospective practice audit = pilot cRCT data collection

Analyses of customized KT strategy

Customized KT

Usual practice

Pilot cRCT
On the Utility of Research Programs

Long-term view is taken to sort out a field
Incremental knowledge is gained
Investigative goals can be complementary
Methodologic advances are made
Research efficiencies are possible
Extensive collaboration is fostered
They are gratifying and make a difference!
<table>
<thead>
<tr>
<th>Outcome</th>
<th>Hazard Ratio (95% CI)</th>
<th># events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital mortality</td>
<td>0.92 (0.80-1.05)</td>
<td>873</td>
</tr>
<tr>
<td>PE</td>
<td>0.51 (0.30-0.88)</td>
<td>67</td>
</tr>
<tr>
<td>DVT</td>
<td>0.92 (0.68-1.23)</td>
<td>299</td>
</tr>
<tr>
<td>VTE</td>
<td>0.87 (0.69-1.10)</td>
<td>340</td>
</tr>
<tr>
<td>HIT</td>
<td>0.47 (0.16-1.35)</td>
<td>17</td>
</tr>
<tr>
<td>Major bleed</td>
<td>1.00 (0.75-1.34)</td>
<td>208</td>
</tr>
</tbody>
</table>
## Decisions From Whose Perspective?

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Perspective</th>
<th>Regarding LMWH.....</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary outcome</td>
<td>Trialist</td>
<td>‘DVT rates were not significantly different’</td>
</tr>
<tr>
<td>Outcomes of interest: PE, HIT</td>
<td>Clinicians</td>
<td>‘PE and HIT rates were 50% lower’</td>
</tr>
<tr>
<td>All clinical outcomes</td>
<td>Patient, family</td>
<td>‘All adverse events were as or less likely’</td>
</tr>
<tr>
<td>All clinical &amp; economic outcomes</td>
<td>Healthcare system</td>
<td>‘Better outcomes for the same resources’</td>
</tr>
</tbody>
</table>
Objectives

- **Phase 1:** to create thromboprophylaxis guidelines
- **Phase 2a:** to record thromboprophylaxis patterns
- **Phase 2b:** to analyze predictors of appropriateness
- **Phase 3a:** to understand barriers & facilitators
- **Phase 3b:** to conduct pilot work toward a future cluster randomized trial of customized KT for thromboprophylaxis
Systematic Review of Heparin Thromboprophylaxis in Medical-Surgical ICU Patients
Alhazzani et al, Crit Care Med 2013

- **Design:** systematic review & meta-analysis
- **Included Studies:** 7 randomized trials
- **Population:** 7313 medical & surgical ICU patients
- **Intervention:** any heparin strategy
- **Comparison:** any other thromboprophylaxis strategy
- **Outcomes:** mortality, PE, DVT, major bleeding, HIT
## Meta-analysis

### Heparin vs No Heparin in Med-Surg Patients

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DVT</td>
<td>0.53 (0.32-0.86)</td>
</tr>
<tr>
<td>PE</td>
<td>0.53 (0.28-0.98)</td>
</tr>
<tr>
<td>Mortality</td>
<td>0.89 (0.78-1.02)</td>
</tr>
<tr>
<td>Major Bleeding</td>
<td>0.82 (0.56-1.21)</td>
</tr>
</tbody>
</table>
Meta-analysis: LMWH vs UFH in Med-Surg ICU Patients

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DVT</td>
<td>0.90 (0.74-1.09)</td>
</tr>
<tr>
<td>PE</td>
<td>0.62 (0.39-1.00)</td>
</tr>
<tr>
<td>Mortality</td>
<td>0.93 (0.78-1.12)</td>
</tr>
<tr>
<td>Major Bleeding</td>
<td>0.97 (0.75-1.26)</td>
</tr>
</tbody>
</table>
CONECCKT-T Audit Methods

• **Design:** Retrospective audit
• **Patients:** med-surg ICU patients admitted in Nov 2011 in 30 centers
• **Data:** demographic & daily data until death, discharge or censored at 90 days
  – Pharmaco & mechanical prophylaxis
  – Prescribing patterns & predictors
  – Confirmatory test results for VTE & HIT
• **REB submissions:** DVT Awareness Month
Thromboprophylaxis Strategy in Medical-Surgical Patients

- Pharm alone: 65.4%
- Mech alone: 15.3%
- Combined: 9.8%
- None: 9.5%
Audit Analysis: Prescribing Patterns & Predictors

- Appropriate thromboprophylaxis measured by guideline concordance, per center and overall

<table>
<thead>
<tr>
<th>ICU days eligible &amp; received</th>
<th>ICU days ineligible &amp; not received</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All ICU days</td>
</tr>
</tbody>
</table>

- Predictors of concordance: hierarchical linear regression to allow concurrent analysis of fixed center factors, and variable patient factors (baseline & time dependent)
Guideline Concordance

- Guideline: Some heparin thromboprophylaxis each day unless legitimate contraindication
- Procedure/surgery
- Bleeding, high risk of bleeding
- HIT/suspected HIT
- Limiting life support
- Late admission, early discharge, etc

- **95.5%** of patient-days (12,181 of 12,756 days) of concordance with guidelines
- **4.5%** of patient-days when patient received no heparin for no reason
Why An Interviewer-Administered Survey?

<table>
<thead>
<tr>
<th>Paper or web-based</th>
<th>Interviewer-based</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less expensive</td>
<td>More expensive, but……</td>
</tr>
<tr>
<td>Non-interactive</td>
<td>Interactive</td>
</tr>
<tr>
<td>Fixed responses</td>
<td>Fixed &amp; free responses</td>
</tr>
<tr>
<td>Lower response rate</td>
<td>Higher response rate</td>
</tr>
<tr>
<td></td>
<td>Chance to clarify</td>
</tr>
<tr>
<td></td>
<td>Encourage reflection</td>
</tr>
<tr>
<td></td>
<td>Explain rationale</td>
</tr>
</tbody>
</table>
CONECCKT-T Survey Methods

• **Design:** Interviewer-administered (in-person or phone)
• **Participants:** ICU director, bedside ICU pharmacist, PROTECT/CONECCKT-T Investigator & Research Coordinator
• **Interviewers:** 6 trained calibrated co-investigators
• **Development Methods:**
  – item generation: literature, RC focus groups
  – item reduction: St Joseph’s/McMaster collaborators
  – domains: barriers and enablers, demographics
• **Test Methods:** clinical sensibility, translation
• **Administration:** response options in advance
Figure 1e: System Facilitators

- Quality Improvement Team Focused on Thromboprophylaxis
- Participation in a Quality Improvement Network
- Analyze Barriers in ICU and Develop Targeted Strategies

- Effective
- Acceptable
- Affordable
<table>
<thead>
<tr>
<th>Barriers to LMWH</th>
<th>Facilitators of LMWH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost of LMWH</td>
<td>Pre-printed orders</td>
</tr>
<tr>
<td>Bleeding concern</td>
<td>Education</td>
</tr>
<tr>
<td>No resident education</td>
<td>Daily reminders</td>
</tr>
<tr>
<td>Renal bioaccumulation</td>
<td>Audit &amp; feedback</td>
</tr>
<tr>
<td>Habit</td>
<td>CQI target</td>
</tr>
</tbody>
</table>
Survey Results

• Participation: Center: 100%; Individual: 99%

• **Affordability** of DGC and CPOE was rated higher in centers with those in place.

• Ratings of **barriers, effectiveness & affordability** of facilitators differed significantly among respondent groups within & across centers (p<0.01).

• Ratings of **acceptability did not differ among respondent groups within center**, but did across centers (p<0.01).
Economic Evaluation

- Economic outcomes are more variable than clinical outcomes
  - Across countries
  - Across centers in a country
  - Over time

- Costs of LMWH are decreasing while UFH are increasing

- LMWH is already cheaper in some centers!

- LMWH associated with similar or improved effects in VTE prevention

- From the acute hospital payer perspective, thromboprophylaxis with LMWH is less costly than with UFH
- Difference: $1,617.22 per patient, robust & significant across sub-groups & in sensitivity analyses

Fowler et al, Heart and Stroke, CICF, U of T, Thrombosis Interest Group of Canada
Meta-analysis & evidence-based med-surg ICU practice guidelines

Phase 1

Phase 1 informing

Phase 2

Retro-spective practice audit

Analyses of appropriate rates & determinants

Phase 3

Interviews about thrombo-prophylaxis prescribing

Analyses of barriers & facilitators

Pilot cRCT

Prospective practice audit = pilot cRCT data collection

Analyses of customized KT strategy

Phase 2 informing

Analyses of barriers & facilitators informing

Analyses of appropriate rates & determinants informing

Interviews about thrombo-prophylaxis prescribing informing

Phase 3 informing

Customized KT informing

Usual practice informing

Analyses of barriers & facilitators informing
Thanks for CONECCKT-T-ing
PROSPECT
PILOT TRIAL
PRObiotics to prevent Severe Pneumonia and Endotracheal Colonization Trial

Jenny Johnstone
Presented by Deborah Cook
CCCTG November 2012
Questions for & Answers from the CCCTG in Nov 2012

• Q: Should this be an external pilot?
• A: Probably
What are Probiotics?

Commercially available microorganisms which, when ingested as individual strains or in combinations, offer potential health benefits to the host

World Health Organization
Research Question

Is it feasible to perform a large RCT in mechanically ventilated critically ill patients to evaluate whether oral *L. rhamnosus* GG prevents VAP, based on

- timely recruitment
- high protocol adherence
- minimal contamination
- an acceptable VAP rate?
4 Feasibility Outcomes
Successful if….

1) Timely recruitment: if $\geq 30$ patients in 6 mos
2) Maximal protocol adherence: if $\geq 90\%$ of prescribed doses are actually administered
3) Minimal contamination: if $\leq 5\%$ of patients receive a dose of open-label probiotics
4) Acceptable VAP rates: if $\geq 10\%$
Clinical Outcomes

1) Diarrhea
Mechanistic Substudy (M Surette)

- **Objective:** to evaluate the microbiologic and immunologic effects of orally ingested *L. rhamnosus* GG on lower respiratory tract and lower gastrointestinal tract colonization with potential pathogens, and the effect on whole-blood endotoxin levels
<table>
<thead>
<tr>
<th>Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Separate hard lumps, like nuts (hard to pass)</td>
</tr>
<tr>
<td>2</td>
<td>Sausage-shaped but lumpy</td>
</tr>
<tr>
<td>3</td>
<td>Like a sausage but with cracks on its surface</td>
</tr>
<tr>
<td>4</td>
<td>Like a sausage or snake, smooth and soft</td>
</tr>
<tr>
<td>5</td>
<td>Soft blobs with clear-cut edges (passed easily)</td>
</tr>
<tr>
<td>6</td>
<td>Fluffy pieces with ragged edges, a mushy stool</td>
</tr>
<tr>
<td>7</td>
<td>Watery, no solid pieces. <strong>Entirely Liquid</strong></td>
</tr>
</tbody>
</table>
Probiotic Meta-analyses

• **AAD:** (RR 0.58, 95%CI 0.50-0.68)
  JAMA 2012

• **GI illness*:** RR 0.58, 95%CI 0.51-0.65)
  PLoS One 2012

• **URTI:** OR 0.67, 95%CI 0.45-0.98
  Cochrane Database Syst Rev 2011

• **AHRQ review:**
  – Overall A/E: RR 1.0, 95%CI 0.93-1.07
  – Critically ill: RR 0.79; 95%CI: 0.51-1.22
  AHRQ 2011

*GI illness* includes pouchitis, infectious diarrhea, IBS, *H. pylori*, CDAD, AAD, Traveler’s diarrhea and necrotizing enterocolitis
# Probiotics in the Critically Ill: A Systematic Review of the Randomized Trial Evidence

**Petrof E, Dhaliwal R, Manzanares W, Johnstone J, Cook D, Heyland D**  
CCM 2012

## Probiotics for prevention of infection

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Experimental Events</th>
<th>Control Events</th>
<th>Total</th>
<th>Weight</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kecskes 2003</td>
<td>1</td>
<td>22</td>
<td>7</td>
<td>23</td>
<td>0.15 [0.02, 1.12]</td>
<td>2003</td>
</tr>
<tr>
<td>Lu 2004</td>
<td>8</td>
<td>20</td>
<td>11</td>
<td>20</td>
<td>0.73 [0.37, 1.42]</td>
<td>2004</td>
</tr>
<tr>
<td>Jain 2004</td>
<td>33</td>
<td>45</td>
<td>26</td>
<td>45</td>
<td>1.27 [0.93, 1.72]</td>
<td>2004</td>
</tr>
<tr>
<td>McNaught 2005</td>
<td>21</td>
<td>52</td>
<td>22</td>
<td>51</td>
<td>0.94 [0.59, 1.48]</td>
<td>2005</td>
</tr>
<tr>
<td>Kotzampassi 2006</td>
<td>22</td>
<td>35</td>
<td>27</td>
<td>30</td>
<td>0.70 [0.53, 0.93]</td>
<td>2006</td>
</tr>
<tr>
<td>Olah 2007</td>
<td>9</td>
<td>33</td>
<td>15</td>
<td>29</td>
<td>0.53 [0.27, 1.02]</td>
<td>2007</td>
</tr>
<tr>
<td>Li 2007</td>
<td>8</td>
<td>14</td>
<td>10</td>
<td>11</td>
<td>0.63 [0.38, 1.03]</td>
<td>2007</td>
</tr>
<tr>
<td>Besselink 2008</td>
<td>46</td>
<td>152</td>
<td>41</td>
<td>144</td>
<td>1.06 [0.75, 1.51]</td>
<td>2008</td>
</tr>
<tr>
<td>Barraud 2010</td>
<td>26</td>
<td>87</td>
<td>29</td>
<td>80</td>
<td>0.82 [0.53, 1.27]</td>
<td>2010</td>
</tr>
<tr>
<td>Ferrie 2011</td>
<td>14</td>
<td>18</td>
<td>16</td>
<td>18</td>
<td>0.88 [0.65, 1.18]</td>
<td>2011</td>
</tr>
<tr>
<td>Tan 2011</td>
<td>9</td>
<td>26</td>
<td>15</td>
<td>26</td>
<td>0.60 [0.32, 1.12]</td>
<td>2011</td>
</tr>
</tbody>
</table>

**Total (95% CI)**  
Total events: 197, 219  
Heterogeneity: $\tau^2 = 0.04; \text{Chi}^2 = 18.00, \text{df} = 10 (P = 0.05); I^2 = 44\%$  
Test for overall effect: $Z = 2.12 (P = 0.03)$
Petrof E et al. CCM 2012
Lack of Efficacy of Probiotics in Preventing Ventilator-Associated Pneumonia

A Systematic Review and Meta-analysis of Randomized Controlled Trials

Wan-Jie Gu, MSc; Chun-Yin Wei, MSc; and Rui-Xing Yin, MD, PhD

• Odds ratio O.82 (0.55-1.24)
• p=0.25
• I² 36%
Bacterial Colonization

• 300+ types of bacteria in the oropharynx
• Dental plaque builds over time & is a reservoir for oral pathogens
• Micro-aspiration of bacteria is common
• Bio-film on ETT also facilitates direct entry of bacteria into the lungs
Cointervention: Toothbrushing to Prevent VAP

Alhazzani et al, CCM 2013
ORAL CARE PROTOCOL

USING A TOOTHETTE AND A 0.12% CHLOROHEXIDINE SOLUTION, SWAB PATIENT'S ORAL SURFACES 4 TIMES DAILY.

FOLLOW BY SUCTIONING PATIENT'S OROPHARYNGEAL CAVITY.

EXCLUSIONS:
1. ALLERGY TO CHLOROHEXIDINE
2. LACK OF ACCESS TO ORAL CAVITY
Cointervention: Toothpaste

- Swabbing the teeth with ‘toothettes’ is not as effective at removing dental plaque as tooth brushing with chlorhexidine or toothpaste.
- Foaming toothpaste inactivates chlorhexidine, so if toothpaste is used, it should be completely suctioned out of the mouth before chlorhexidine is applied.
- Toothpaste should not be applied immediately after chlorhexidine.
Ventilator Associated Pneumonia

It’s All About the Bugs

Material Compiled by Angela Greiter August 2008
Why should the HOB be Elevated?

- Decrease the risk of aspiration
- Decrease the amount of oropharyngeal and nasopharyngeal secretions
- Minimize atelectasis
Contraindications

- Hypotension MAP < 60-70
- Tachycardia > 150
- Cardiac Index < 2.0
- Femoral line
- Interventions and procedures
- Cervical spine instability
- Increased ICP
- Proning
Events Since June 2012

• JJ completed PhD independent study (MM & DJC supervisors)
• CCCTG & NUTRIC endorsement
• JJ relinquished faculty position
• Co-PI model
• JJ taking a year off
• PI change
• Grants submitted for pilot feasibility RCT
• Daren Heyland exploring NIH funding
Questions for the CCCTG

• Should this be an external pilot?
The Publication Fate of Pilot Trials

External Pilot trial

- Published

Internal Pilot trial

- Unpublished
  - Published (blinded)
  - Published (unblinded)
- Roll over