What are we going to do about SDD?
Results of the SuDDICU study

Brian H Cuthbertson
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Sunnybrook Health Sciences Centre
Professor, Critical Care Medicine
University of Toronto
Toronto
Canada
or indeed-

“What is the problem with translating research into practice”
SDD- The background

- Hospital acquired infections significant problem in all hospital
- 20-50% critically ill suffer from HAIs
- Traditionally, HAI in critical illness were from Gram negative enteric bacteria
- This may have changed with the rise of MRSA and other multi-resistant organisms
SDD- History

- First used in neutropenic leukemia patients
- First description in intensive care in 1983
- Flurry of publications from late 80s and 90s
- Large RCTs published in last 7 years
- Used in some areas of NW Europe (Holland)
- Not widely adopted elsewhere in the world
- Not used in ICU practice in North America
What actually is SDD?

- ‘Selective decontamination’ NOT ‘sterilisation’
- Target enteric aerobic Gram negatives
- Gastric overgrowth and subsequent VAP
- Bacterial translocation and metastatic sepsis
- Attempts to not target anaerobes and Gram positive
- Uses polymixin, tobramycin and amphotericin as well as IV antibiotic
It’s not new
SDD is not sexy.....
Antibiotic prophylaxis to reduce respiratory tract infections and mortality in adults receiving intensive care (Review)

Liberati A, D’Amico R, Pifferi S, Torri V, Brazzi L
## SDD and mortality

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Treatment n/N</th>
<th>Control n/N</th>
<th>Odds Ratio M-H,Fixed, 95% CI</th>
<th>Weight %</th>
<th>Odds Ratio M-H,Fixed, 95% CI</th>
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<tr>
<td>Abele-Horn 1997</td>
<td>11/58</td>
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<tr>
<td>Aerds 1991</td>
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<tr>
<td>Bair 1991</td>
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<td>32/170</td>
<td></td>
<td>6.0 %</td>
<td>0.76 [0.42, 1.35]</td>
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<tr>
<td>Boland 1991</td>
<td>2/32</td>
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<td></td>
<td>0.8 %</td>
<td>0.47 [0.08, 2.75]</td>
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<tr>
<td>Cockenill 1992</td>
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<td>3.1 %</td>
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</tr>
<tr>
<td>de Jonge 2003</td>
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<td></td>
<td>25.0 %</td>
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<tr>
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<td></td>
<td>0.8 %</td>
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<tr>
<td>Jacobs 1992</td>
<td>14/45</td>
<td>23/46</td>
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<td>3.5 %</td>
<td>0.45 [0.19, 1.06]</td>
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<tr>
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<td>Palomar 1997</td>
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<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>2025</strong></td>
<td><strong>2050</strong></td>
<td><strong>100.0 %</strong></td>
<td><strong>0.75 [0.65, 0.87]</strong></td>
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</table>

Total events: 496 (Treatment), 614 (Control)
Heterogeneity: Chi² = 15.55, df = 16 (P = 0.49); I² = 0.00%
Test for overall effect: Z = 3.94 (P = 0.000081)

OR 0.75, 95% CI 0.65 to 0.87
SDD and respiratory tract infection

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<td>149/262</td>
<td></td>
<td>11.7 %</td>
</tr>
</tbody>
</table>

Total (95% CI) 1501 1523 100.0 % 0.28 [0.20, 0.38]

Total events: 287 (Treatment), 603 (Control)
Heterogeneity: Tau² = 0.18; Chi² = 33.77, df = 15 (P = 0.004); I² = 56%
Test for overall effect: Z = 8.11 (P < 0.00001)
Effects of selective decontamination of digestive tract on mortality and acquisition of resistant bacteria in intensive care: a randomised controlled trial

Evert de Jonge, Marcus J Schultz, Lodewijk Spanjaard, Patrick M M Bossuyt, Margaretha B Vroom, Jacob Dankert, Jozef Kesecioglu

Summary

Background Selective decontamination of the digestive tract (SDD) is an infection-prevention regimen used in critically ill patients. We assessed the effects of SDD on intensive-care-unit (ICU) and hospital mortality, and on the acquisition of resistant bacteria in adult patients admitted to intensive care.

Methods We did a prospective, controlled, randomised, unblinded clinical trial. 934 patients admitted to a surgical and medical ICU were randomly assigned oral and enteral polymyxin E, tobramycin, and amphotericin B combined with an initial 4-day course of intravenous cefotaxime (SDD group n=466), or standard treatment (controls n=468). Primary endpoints were ICU and hospital mortality and the acquisition of resistant bacteria.

Findings In the SDD group 69 (15%) patients died in the ICU compared with 107 (23%) in the control group (p=0.002). Hospital mortality was lower in the SDD groups than in the control group (113 [24%] vs 146 [31%], p=0.02). During their stay in intensive care, colonisation with gram-negative bacteria was lower in the SDD group (78 [17%] vs 117 [25%], p=0.002). The acquisition of resistance was also lower in the SDD group (40 [9%] vs 66 [14%], p=0.002).

Introduction

Selective decontamination of the digestive tract (SDD) is an infection-prophylaxis regimen that was introduced into intensive-care medicine in 1984. Nosocomial infections contribute substantially to morbidity and mortality of patients treated in intensive-care units (ICUs). Most of these infections are thought to be preceded by oropharyngeal and intestinal colonisation with pathogenic micro-organisms. SDD is based on the concept of colonisation resistance, according to which the indigenous intestinal flora has a protective effect against secondary colonisation with gram-negative aerobic bacteria. The approach aims to eradicate colonisation of aerobic potentially pathogenic micro-organisms from the oropharynx, stomach, and gut, while leaving the indigenous anaerobic flora largely undisturbed. The classic SDD regimen consists of two components. Topical non-absorbed antibiotics, generally polymyxin E, tobramycin, and amphotericin B, are applied orally and through a nasogastric tube, and treatment with parenteral antibiotics, most frequently cefotaxime, is added for the first 4 days to prevent early infections.
Effects of SDD on Survival

Logrank statistic 5.86
p=0.02
Decontamination of the Digestive Tract and Oropharynx in ICU Patients

## Decontamination of the Digestive Tract and Oropharynx in ICU Patients

<table>
<thead>
<tr>
<th></th>
<th>SDD N=2045</th>
<th>Standard Care N=1990</th>
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<tr>
<td>Crude (%)</td>
<td>26.9</td>
<td>27.5</td>
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<tr>
<td>Adjusted</td>
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<td>Odds Ratio 95% CI</td>
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<tr>
<td>SDD vs standard</td>
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<td>0.83 (0.72 – 0.97)</td>
</tr>
</tbody>
</table>
What further evidence do we need?
Effect of Treatment With Low Doses of Hydrocortisone and Fludrocortisone on Mortality in Patients With Septic Shock

Djillali Annane, MD, PhD
Véronique Sébille, PhD
Claire Charpentier, MD
Pierre-Edouard Bollaert, MD, PhD
Bruno François, MD
Jean-Michel Korach, MD
Gilles Capellier, MD, PhD
Yves Cohen, MD, PhD
Elie Azoulay, MD
Gilles Troché, MD
Philippe Chaumet-Riffaut, MD
Eric Bellissant, MD, PhD

Context Septic shock may be associated with relative adrenal insufficiency. Thus, a replacement therapy of low doses of corticosteroids has been proposed to treat septic shock.

Objective To assess whether low doses of corticosteroids improve 28-day survival in patients with septic shock and relative adrenal insufficiency.


Patients Three hundred adult patients who fulfilled usual criteria for septic shock were enrolled after undergoing a short corticotropin test.

Intervention Patients were randomly assigned to receive either hydrocortisone (50-mg intravenous bolus every 6 hours) and fludrocortisone (50-μg tablet once daily) (n=151) or matching placebos (n=149) for 7 days.

Main Outcome Measure Twenty-eight-day survival distribution in patients with relative adrenal insufficiency (nonresponders to the corticotropin test).

Results One patient from the corticosteroid group was excluded from analyses because of consent withdrawal. There were 239 nonresponders to the corticotropin test.
INTENSIVE INSULIN THERAPY IN CRITICALLY ILL PATIENTS

GREET VAN DEN BERGHE, M.D., PH.D., PIETER WOUTERS, M.SC., FRANK WEEKERS, M.D., CHARLES VERWAEST, M.D., FRANS BRUYNINCKX, M.D., MIET SCHEITZ, M.D., PH.D., DIRK VLAESLAERS, M.D., PATRICK FREDINANDE, M.D., PH.D., PETER LAUWERS, M.D., AND ROGER BOUILLON, M.D., PH.D.

ABSTRACT

Background Hyperglycemia and insulin resistance are common in critically ill patients, even if they have not previously had diabetes. Whether the normalization of blood glucose levels with insulin therapy improves the prognosis for such patients is not known.

Methods We performed a prospective, randomized, controlled study involving adults admitted to our surgical intensive care unit who were receiving mechanical ventilation. On admission, patients were randomly assigned to receive intensive insulin therapy (maintenance of blood glucose at a level between 80 and 110 mg per deciliter) or conventional treatment (administration of insulin only if the blood glucose level exceeded 215 mg per deciliter and maintenance of glucose at a level between 180 and 200 mg per deciliter).

Results At 12 months, with a total of 1548 patients enrolled, intensive insulin therapy reduced mortality during intensive care from 8.0 percent with conventional treatment to 4.6 percent (P<0.04, with adjustment for sequential analyses). The benefit of intensive insulin therapy was attributable to its effect on mortality among patients who remained in the intensive care unit for more than five days (20.2 percent with intensive, 17.4 percent with conventional).

Critically ill patients who require intensive care for more than five days have a 20 percent risk of death and substantial morbidity.1 Critical-illness polyneuropathy and skeletal-muscle wasting prolong the need for mechanical ventilation.2,5 Moreover, increased susceptibility to severe infections and failure of vital organs amplify the risk of an adverse outcome.

Hyperglycemia associated with insulin resistance9-8 is common in critically ill patients, even those who have not previously had diabetes. It has been reported that pronounced hyperglycemia may lead to complications in such patients,9-13 although data from controlled trials are lacking. In diabetic patients with acute myocardial infarction, therapy to maintain blood glucose at a level below 215 mg per deciliter (11.9 mmol per liter) improves the long-term outcome.14-16 In nondiabetic patients with protracted critical illnesses, high serum levels of insulin-like growth factor–binding protein 1, which reflect an impaired response of hepatocyes to insulin, increase the risk of death.17,18

CRITICAL INSULIN THERAPY IN CRITICALLY ILL PATIENTS

GREET VAN DEN BERGHE, M.D., PH.D., PIETER WOUTERS, M.SC., FRANK WEEKERS, M.D., CHARLES VERWAEST, M.D., FRANS BRUYNINCKX, M.D., MIET SCHEITZ, M.D., PH.D., DIRK VLAESLAERS, M.D., PATRICK FREDINANDE, M.D., PH.D., PETER LAUWERS, M.D., AND ROGER BOUILLON, M.D., PH.D.

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“There's only two things I hate in this world. People who are intolerant of other people's cultures and the Dutch”
All evidence is equal, but some evidence is more equal than other

MA Kuiper¹, MJ Schultz², PE Spronk³

¹Department of Intensive Care Medicine, Medical Center Leeuwarden, Leeuwarden, The Netherlands
²Department of Intensive Care Medicine, Academic Medical Center, Amsterdam, The Netherlands
³Department of Intensive Care Medicine, Gelre Hospital Apeldoorn, Apeldoorn, The Netherlands

Evidence-based medicine attempts to accurately assess and integrate the weight carried by the various levels of available evidence to certain aspects of medical practice. Specifically, evidence-based medicine seeks to apply judgments on the quality of evidence to those aspects of medicine that depend on rational assessments of risks and benefits of treatments.

Nevertheless, most of the medicine we practice is not backed up by sufficient evidence: only 13% of commonly used treatments can be rated as beneficial, 23% as likely to be beneficial, and 8% as partly beneficial and partly harmful. Six percent can be rated as unlikely to be beneficial, 4% as likely to be ineffective or maybe even harmful, and in the remaining 46%, the effect of the treatment is even “unknown” [1]. So, it seems that most of the medicine that is practiced is not proven to be effective or beneficial. As long ago as 1928, Bernard Shaw wrote that the extent to which beliefs are based on evidence is much less than most believers suppose. This still holds true today.

Contrary to the above, there is also treatment that is backed up by evidence and that is considered beneficial. However, this is not always the case. For example, the use of SDD (systemic decontamination of the digestive tract) has been widely used in intensive care units, but its effectiveness has been debated. A recent study showed that SDD can reduce the incidence of ventilator-associated pneumonia (VAP) and, therefore, has been recommended as a standard of care in many guidelines. However, other studies have shown that SDD does not always reduce the incidence of VAP and can even increase the risk of antibiotic resistance.

Is some evidence a nuisance and do physicians choose to neglect it for as long as they can? Why is there so much hesitation to implement SDD? The argument that there is lack of evidence for its use must be regarded as a rationalization process, thereby obscuring other arguments. In fact, the evidence argument is often primarily used to conceal underlying reasons. Physicians often tend to select and use evidence to defend the standpoint they have already taken.

Because comprehensive examination of relevant clinical studies is not at all easy, physicians may need guidance in the process of deciding what can be regarded as being “enough” or “sufficient” evidence for a change of practice. Moreover, physicians may need to accept the authority of those who can interpret increasingly complicated study designs and statistical methods that provide their conclusions. So, the evidence argument is often a convenient way to resist change.
Evidence-Based Clinical Practice Guideline for the Prevention of Ventilator-Associated Pneumonia

Peter Dodek, MD, MHS; Sean Keenan, MD, MSc(Epid); Deborah Cook, MD, MSc(Epid); Daren Heyland, MD, MSc(Epid); Michael Jacka, MD, MSc; Lori Hand, RRT; John Muscedere, MD; Debra Foster, RN; Nav Mehta, MD; Richard Hall, MD; and Christian Brun-Buisson, MD, for the Canadian Critical Care Trials Group and the Canadian Critical Care Society

Background: Ventilator-associated pneumonia (VAP) is an important patient safety issue in critically ill patients.

Purpose: To develop an evidence-based guideline for the prevention of VAP.

Data Sources: MEDLINE, EMBASE, and the Cochrane Database of Systematic Reviews.

Study Selection: The authors systematically searched for relevant randomized, controlled trials and systematic reviews that involved mechanically ventilated adults and were published before 1 April 2003.

Data Extraction: Physical, positional, and pharmacologic interventions that may influence the development of VAP were considered. Independently and in duplicate, the authors scored the validity of trials; the effect size and confidence intervals; the homogeneity of results; and safety, feasibility, and economic issues.

Data Synthesis: Recommended: The orotracheal route of intubation, changes of ventilator circuits only for each new patient and if the circuits are soiled, use of closed endotracheal suction systems that are changed for each new patient and as clinically indicated, heat and moisture exchangers in the absence of contraindications, weekly changes of heat and moisture exchangers, and semi-recumbent positioning in the absence of contraindications. Consider subglottic secretion drainage and kinetic beds. Not recommended: Sucralfate to prevent VAP in patients at high risk for gastrointestinal bleeding and topical antibiotics to prevent VAP. Because of insufficient or conflicting evidence, no recommendations were made about systematically searching for maxillary sinusitis, chest physiotherapy, the timing of tracheostomy, prone positioning, prophylactic intravenous antibiotics, or intravenous plus topical antibiotics.

Limitations: No formal economic analysis was performed, and patient perspectives were not considered.

Conclusion: If effectively implemented, this guideline may decrease the morbidity, mortality, and costs of VAP in mechanically ventilated patients.


For author affiliations, see end of text.
The guidelines group was evenly split on the issue of SDD, with equal numbers weakly in favor and against recommending the use of SDD (see appendix H). The committee therefore chose not to make a recommendation for the use of SDD specifically in severe sepsis at this time. The final consensus on use of SDD in severe sepsis was achieved at the last nominal committee meeting and subsequently approved by the entire committee (see Appendix H for committee vote).
So....

What is the problem with SDD?
Systematic reviews
**Meta-analysis of SDD and antibiotic resistance - MRSA**

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<th>Study or Subgroup</th>
<th>Intervention</th>
<th>Control</th>
<th>Meta-analysis results</th>
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<td>393</td>
<td>11</td>
</tr>
<tr>
<td>Wiener 1995</td>
<td>2</td>
<td>30</td>
<td>5</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>2780</strong></td>
<td><strong>1753</strong></td>
<td></td>
</tr>
</tbody>
</table>

- Total events: 110
- Heterogeneity: Tau² = 0.19; Chi² = 12.80, df = 8 (P = 0.12); I² = 37%
- Test for overall effect: Z = 1.52 (P = 0.13)
Meta-analysis of SDD and antibiotic resistance- VRE

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Intervention</th>
<th>Control</th>
<th>Odds Ratio</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Events</td>
<td>Total</td>
</tr>
<tr>
<td>Dahms 2000</td>
<td>8</td>
<td>54</td>
<td>102</td>
<td>6098</td>
</tr>
<tr>
<td>De Jonge 2003</td>
<td>4</td>
<td>378</td>
<td>5</td>
<td>395</td>
</tr>
<tr>
<td>De La Cal 2005</td>
<td>16</td>
<td>53</td>
<td>26</td>
<td>54</td>
</tr>
<tr>
<td>De Smet 2008</td>
<td>2</td>
<td>1000</td>
<td>6</td>
<td>1333</td>
</tr>
<tr>
<td>Van Der Voort 2004</td>
<td>1</td>
<td>529</td>
<td>0</td>
<td>513</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>31</td>
<td>139</td>
<td>8393</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

Heterogeneity: $\tau^2 = 3.03$; $\text{Chi}^2 = 38.57$, $df = 4$ ($P < 0.00001$); $I^2 = 90$

Test for overall effect: $Z = 0.35$ ($P = 0.73$)
Meta-analysis of SDD and antibiotic resistance

Aminoglycosides

<table>
<thead>
<tr>
<th>Study of Subgroup</th>
<th>Intervention Events Total</th>
<th>Control Events Total</th>
<th>Weight</th>
<th>Odds Ratio M-H Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Camus 2005</td>
<td>14</td>
<td>130</td>
<td>21</td>
<td>126 13.6% 0.57 [0.28, 1.17]</td>
</tr>
<tr>
<td>De Jonge 2003</td>
<td>33</td>
<td>378</td>
<td>60</td>
<td>395 20.2% 0.53 [0.34, 0.84]</td>
</tr>
<tr>
<td>De Smet 2011</td>
<td>227</td>
<td>1714</td>
<td>104</td>
<td>881 25.8% 1.14 [0.59, 1.46]</td>
</tr>
<tr>
<td>Flaherty 1990</td>
<td>1</td>
<td>51</td>
<td>0</td>
<td>56 1.2% 3.36 [0.13, 84.26]</td>
</tr>
<tr>
<td>Krueger 2002</td>
<td>8</td>
<td>175</td>
<td>12</td>
<td>171 10.2% 0.65 [0.25, 1.59]</td>
</tr>
<tr>
<td>Rocha 1992</td>
<td>2</td>
<td>47</td>
<td>11</td>
<td>54 4.6% 0.12 [0.04, 0.45]</td>
</tr>
<tr>
<td>Vuist 1987</td>
<td>1</td>
<td>19</td>
<td>3</td>
<td>20 2.2% 0.13 [0.03, 0.33]</td>
</tr>
<tr>
<td>Weiner 1995</td>
<td>60</td>
<td>393</td>
<td>29</td>
<td>165 19.3% 0.97 [0.50, 1.83]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>2937</td>
<td>1919</td>
<td></td>
<td>0.73 [0.51, 1.05]</td>
</tr>
</tbody>
</table>

Total events: 346 / 243

Heterogeneity: Tau^2 = 0.12, Chi^2 = 16.51, df = 8 (P = 0.04), I^2 = 52%
Test for overall effect: Z = 1.65 (P = 0.09)

Polymyxins

<table>
<thead>
<tr>
<th>Study of Subgroup</th>
<th>Intervention Events Total</th>
<th>Control Events Total</th>
<th>Weight</th>
<th>Odds Ratio M-H Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Camus 2005</td>
<td>8</td>
<td>130</td>
<td>14</td>
<td>125 5.9% 0.32 [0.21, 1.30]</td>
</tr>
<tr>
<td>De Smet 2011</td>
<td>167</td>
<td>1714</td>
<td>130</td>
<td>881 82.2% 0.62 [0.49, 0.80]</td>
</tr>
<tr>
<td>Flaherty 1990</td>
<td>0</td>
<td>51</td>
<td>4</td>
<td>56 0.6% 0.31 [0.01, 1.26]</td>
</tr>
<tr>
<td>Krueger 2002</td>
<td>16</td>
<td>175</td>
<td>37</td>
<td>171 12.2% 0.34 [0.19, 0.65]</td>
</tr>
<tr>
<td>Vuist 1987</td>
<td>1</td>
<td>19</td>
<td>1</td>
<td>20 0.6% 1.06 [0.05, 18.17]</td>
</tr>
<tr>
<td>Weiner 1995</td>
<td>1</td>
<td>30</td>
<td>1</td>
<td>31 0.6% 1.03 [0.05, 17.33]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>2119</td>
<td>1265</td>
<td></td>
<td>0.58 [0.46, 0.72]</td>
</tr>
</tbody>
</table>

Total events: 193 / 187

Heterogeneity: Tau^2 = 0.00, Chi^2 = 4.00, df = 5 (P = 0.55), I^2 = 0%
Test for overall effect: Z = 4.92 (P < 0.00001)

Fluoroquinolones

<table>
<thead>
<tr>
<th>Study of Subgroup</th>
<th>Intervention Events Total</th>
<th>Control Events Total</th>
<th>Weight</th>
<th>Odds Ratio M-H Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>De Jonge 2003</td>
<td>10</td>
<td>374</td>
<td>44</td>
<td>359 36.0% 0.22 [0.11, 0.44]</td>
</tr>
<tr>
<td>Krueger 2002</td>
<td>3</td>
<td>126</td>
<td>5</td>
<td>171 25.6% 0.58 [0.14, 2.48]</td>
</tr>
<tr>
<td>Vuist 1987</td>
<td>63</td>
<td>383</td>
<td>28</td>
<td>185 38.6% 1.60 [0.66, 1.74]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>946</td>
<td>751</td>
<td></td>
<td>0.52 [0.16, 1.66]</td>
</tr>
</tbody>
</table>

Total events: 76 / 77

Heterogeneity: Tau^2 = 0.88, Chi^2 = 13.66, df = 2 (P = 0.001), I^2 = 85%
Test for overall effect: Z = 1.10 (P = 0.27)

Cephalosporins

<table>
<thead>
<tr>
<th>Study of Subgroup</th>
<th>Intervention Events Total</th>
<th>Control Events Total</th>
<th>Weight</th>
<th>Odds Ratio M-H Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>De Jonge 2003</td>
<td>9</td>
<td>378</td>
<td>21</td>
<td>355 22.8% 0.63 [0.29, 0.95]</td>
</tr>
<tr>
<td>De Smet 2011</td>
<td>78</td>
<td>1714</td>
<td>130</td>
<td>881 52.2% 0.27 [0.20, 0.36]</td>
</tr>
<tr>
<td>Rocha 1992</td>
<td>3</td>
<td>47</td>
<td>16</td>
<td>54 10.9% 0.18 [0.06, 0.60]</td>
</tr>
<tr>
<td>Vuist 1987</td>
<td>8</td>
<td>393</td>
<td>5</td>
<td>185 33.2% 0.75 [0.24, 2.32]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>2532</td>
<td>1515</td>
<td></td>
<td>0.33 [0.20, 0.52]</td>
</tr>
</tbody>
</table>

Total events: 96 / 172

Heterogeneity: Tau^2 = 0.39, Chi^2 = 4.72, df = 3 (P = 0.19), I^2 = 39%
Test for overall effect: Z = 4.54 (P < 0.00001)
Case studies
Aim

To identify and precisely describe the clinical intervention in units and hospitals that deliver SDD
Case studies
Main messages

• Variation in SDD clinical components
• Variation and lack of specification in the behavioural aspects of a clinical intervention
• Delivery of SDD not a problem for nurses
• For a trial, intervention should be clinically and behaviourally specified
The Delphi
Theory

Skills

Knowledge

Social/Role Identity

Beliefs about capabilities

Beliefs about consequences

Motivation and goals

Memory, attention and decision processes

Social influences

Emotion

Behavioural regulation

Envir. context and resources

Michie et al., 2005
# Delphi Study

<table>
<thead>
<tr>
<th>Delphi round</th>
<th>Participant numbers</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>UK</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Australia &amp; New Zealand</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Canada</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td></td>
</tr>
<tr>
<td>R1</td>
<td>47</td>
<td>45</td>
</tr>
<tr>
<td>R2</td>
<td>44</td>
<td>41</td>
</tr>
<tr>
<td>R3</td>
<td>42</td>
<td>34</td>
</tr>
</tbody>
</table>
National survey
Aim

To identify current practice and assess the acceptability of further RCTs in the field of SDD in a wide group of ICU clinicians and medical microbiologists / ID physicians
Synthesized results

Evidence for relevance and topicality of SDD
Relevance and topicality of SDD

“My hospital tries to reduce antibiotic use”

Median = 6, IQR = 8-9, Importance = 8
Relevance and topicality of SDD

“We are addressing VAP using other strategies”

Median = 9, IQR = 8-9, Importance = 7
Relevance and topicality of SDD

“SDD is not on my unit’s list of clinical priorities”

Median= 8, IQR= 7-9, Importance= 6
Relevance and topicality of SDD

“I am opposed to SDD”

Median = 4, IQR = 2-5

N O T R E A L L Y !
Synthesized results

Clinical equipoise and uncertainty with the SDD evidence base
Clinical equipoise

“It is ethically acceptable to conduct further RCTs evaluating the effectiveness of SDD”
Clinical equipoise

“The SDD evidence base is not generalizable to my country”

Mean = 5, IQR = 5-7, Importance = 6
Clinical equipoise

“Overall, SDD benefits the patients to whom it is delivered”

Median= 6, IQR=5-7, Importance
Clinical equipoise

“There is no mortality benefit associated with SDD”
Clinical equipoise

“SDD reduces VAP”

Median=7, IQR= 5-8, Importance= 7
Clinical equipoise

“SDD would increase *C. Difficile* infections”

Median = 5, IQR = 5-5, Importance = 8
Clinical equipoise

“SDD increases antibiotic resistance”

Median= 6 , IQR= 5-7, Importance= 9
### Importance ratings

<table>
<thead>
<tr>
<th>Item stem</th>
<th>Mean (out of 9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Research to date has not adequately addressed concerns about antibiotic resistance and SDD</td>
<td>9</td>
</tr>
<tr>
<td>2. SDD increases antibiotic resistance</td>
<td>9</td>
</tr>
<tr>
<td>3. The decision to adopt SDD requires consensus between my colleagues</td>
<td>8</td>
</tr>
<tr>
<td>4. The decision to adopt SDD requires a review and appraisal of the current best evidence</td>
<td>8</td>
</tr>
<tr>
<td>5. My hospital tries to reduce antibiotic use</td>
<td>8</td>
</tr>
<tr>
<td>6. SDD would increase <em>C. Difficile</em></td>
<td>8</td>
</tr>
<tr>
<td>7. Part of the decision to adopt SDD requires agreement about which patients will receive it</td>
<td>8</td>
</tr>
<tr>
<td>8. We are addressing Hospital Acquired Infections using other strategies</td>
<td>8</td>
</tr>
<tr>
<td>9. We are addressing Ventilator Associated Pneumonia using other strategies</td>
<td>7</td>
</tr>
<tr>
<td>10. The risks of SDD outweigh the benefits</td>
<td>7</td>
</tr>
</tbody>
</table>
Synthesized results

Evidence of willingness to participate in further SDD research
Participation in further research

“Current uncertainties in the evidence base should be addressed in a new study”

I’M PROBABLY IN!
Participation in further research

“I would be prepared for my patients/centre to be randomised to either SDD or control in an effectiveness RCT of SDD”
Participation in further research

“If my colleagues supported my centre participating in a nation-wide effectiveness RCT of SDD I would go along with this”
Participation in further research

“My concerns about antibiotic resistance limit my willingness to participate in future RCT’s of SDD”

Mean= 4, IQR= 3-6

WE’RE SPLIT ON THIS ONE!
Synthesized results

Design features of an effectiveness RCT
Design features of an RCT

“I would be more likely to participate in an RCT if mortality is the endpoint”

Mean = 8, IQR = 8-9
Design features of an RCT

“I would be more likely to participate in an RCT if a cost-benefit analysis was included”

Mean=9, IQR= 8-9
Design features of an effectiveness RCT

“I would be more likely to participate in an RCT if it included pre, during and post-trial monitoring of antibiotic resistance in all patients in the RCT”

Mean = 9, IQR = 9-9
Design features of an effectiveness RCT

“An effectiveness RCT of SDD should include the following components”

- 1. Chlorhexidine control
- 2. VAP bundle control
- 3. Standard practice control
- 4. Monitoring of antibiotic resistance
Synthesized results

Challenges of an effectiveness

RCT
Challenges of an effectiveness RCT

“There are conflicting opinions between microbiologists and Intensive care clinicians”

Mean = 7, IQR = 6-9, Importance = 7
Challenges of an effectiveness RCT

“SDD will not be adopted without a high profile national/international advocate”

Mean = 8, IQR = 7-8, Importance =
“SDD increases nursing workload.”

Challenges of an effectiveness RCT

Mean = 5, IQR = 5-7, Importance = 6
Challenges of an effectiveness RCT

“The skills required to administer SDD fall within the competencies of our ICU nursing staff”

Mean= 9, IQR= 8-9, Importance= 7
Interviews with trialists
Interviewed 12 trialists from around the world
- Including those experienced in ICU effectiveness trials and those experienced behavioural change interventions
- Experts from Canada, UK / Europe, and Australia.
- Topic guide approach
Trialist interviews
Main messages

• Effectiveness trial very demanding (burnout)
• Very large and multinational nature of trial
• Cluster versus individual patient controversial but most favour cluster
• Mortality primary outcome and long term follow-up issues
• Control groups and patient inclusion need agreement
• Ethical / legislative issues – cluster trials challenging in some countries
• Funding problematic
Summary of results

- There is a desire for further effectiveness studies for SDD
- This work should be done in countries who have higher antimicrobial resistance rates who don’t do SDD currently
- Ecology of infection data is just (if not more) important than effectiveness
- Study needs to be large and generalisable
- It will be hard (no really hard!)
The SuDDICU program

Phase 1-
Systematic review of available literature (complete)

Phase 2-
Exploratory study of risks, benefits and barriers (complete)

Phase 3-
Randomised controlled effectiveness trial of SDD and contemporaneous epidemiology of bacterial resistance study (the current proposal)

Phase 4-
KT Implementation study

Phase 5-
Phase IV post-implementation surveillance of effectiveness and microbial resistance patterns study
Thanks for listening