Guidelines are *Not* the Future of Sepsis Management

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12th Congress, WFSICCM
Seoul, Korea
August 31, 2015

St. Michael’s Hospital

University of Toronto
Guidelines for the Management of Severe Sepsis and Septic Shock

Charles I. Sprung, M.D., Gordon R. Bernard, M.D., R. Phillip Dellinger M.D., Guest Editors

Volume 27
Supplement 1
2001

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Surviving Sepsis Campaign: Association Between Performance Metrics and Outcomes in a 7.5-Year Study

Mitchell M. Levy, MD, FCCM¹; Andrew Rhodes, MB BS, MD (Res)²; Gary S. Phillips, MAS³; Sean R. Townsend, MD⁴; Christa A. Schorr, RN, MSN⁵; Richard Beale, MB BS⁶; Tiffany Osborn, MD, MPH⁷; Stanley Lemeshow, PhD⁸; Jean-Daniel Chiche, MD⁹; Antonio Artigas MD, PhD¹⁰; R. Phillip Dellinger, MD, FCCM¹¹

- 29,470 patients
- 218 hospitals, North America, South America, Europe

- Crit Care Med 43:3, 2015
High compliance with bundles was associated with better outcomes ...

<table>
<thead>
<tr>
<th></th>
<th>Resuscitation</th>
<th>Management</th>
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<tbody>
<tr>
<td></td>
<td>29.0 vs 38.6%</td>
<td>32.3 vs 33.8%</td>
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<tr>
<td></td>
<td><em>p</em>&lt;0.0001</td>
<td><em>p</em>=0.04</td>
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Guidelines process

- Questions approached using PICO format
- Systematic review of literature
- GRADE methodology
- Formal process for resolving differences
Okay ...

So what’s the problem?
Okay ...

So what’s the problem?

10 Limitations of Guidelines
1. Their content is inevitably selective

F. Infection Prevention

1a. Selective oral decontamination and selective digestive decontamination should be introduced and investigated as a method to reduce the incidence of ventilator-associated pneumonia; This infection control measure can then be instituted in health care settings and regions where this methodology is found to be effective (grade 2B).

1b. Oral chlorhexidine gluconate be used as a form of oropharyngeal decontamination to reduce the risk of ventilator-associated pneumonia in ICU patients with severe sepsis (grade 2B).
2. They are only as good as the available literature

E. Source Control

1. A specific anatomical diagnosis of infection requiring consideration for emergent source control be sought and diagnosed or excluded as rapidly as possible, and intervention be undertaken for source control within the first 12 hr after the diagnosis is made, if feasible (grade 1C).

2. When infected peripancreatic necrosis is identified as a potential source of infection, definitive intervention is best delayed until adequate demarcation of viable and nonviable tissues has occurred (grade 2B).

3. When source control in a severely septic patient is required, the effective intervention associated with the least physiologic insult should be used (eg, percutaneous rather than surgical drainage of an abscess) (UG).

4. If intravascular access devices are a possible source of severe sepsis or septic shock, they should be removed promptly after other vascular access has been established (UG).
3. They rapidly become dated
Prone Positioning in Severe Acute Respiratory Distress Syndrome

Claude Guérin, M.D., Ph.D., Jean Reignier, M.D., Ph.D., Jean-Christophe Richard, M.D., Ph.D., Pascal Beuret, M.D., Arnaud Gacouin, M.D., Thierry Boulain, M.D., Emmanuelle Mercier, M.D., Michel Badet, M.D., Alain Mercat, M.D., Ph.D., Olivier Baudin, M.D., Marc Clavel, M.D., Delphine Chatellier, M.D., Samir Jaber, M.D., Ph.D., Sylvène Rosselli, M.D., Jordi Mancebo, M.D., Ph.D., Michel Sirodot, M.D., Gilles Hilbert, M.D., Ph.D., Christian Bengler, M.D., Jack Richardeau, M.D., Marc Gaimmier, M.D., Ph.D., Frédérique Bayle, M.D., Gael Bourdin, M.D., Véronique Leray, M.D., Raphaelle Girard, M.D., Loredana Baboi, Ph.D., and Louis Ayzac, M.D., for the PROSEVA Study Group*
4. The data they are based on describes outcomes in populations.
Survival in NICE/SUGAR

5. They assume that the focus is a homogeneous disease, and discourage individualization of care

- 28 year old man with pneumococcal pneumonia
- 87 year old woman with urinary tract infection
6. They provide a false sense of authority
7. Compliance can be confused with competency or quality
8. Not all guidelines are created equal

- Surviving Sepsis Campaign or prevention of DVT
- Hospital-based guidelines for prevention of VAP
9. They can overestimate efficacy
CVP

Mean Arterial Pressure

Fluids

Pressors

ScvO₂

Goals achieved

Transfusion, Inotropes

<8

≥ 8

<65

≥ 65

≥ 70
Early Goal-directed Therapy for Septic Shock

<table>
<thead>
<tr>
<th></th>
<th>Standard (N=133)</th>
<th>Goal-Directed (N=130)</th>
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<tbody>
<tr>
<td><strong>MVO$_2$</strong></td>
<td>65.3±11.4</td>
<td>70.4±10.7*</td>
</tr>
<tr>
<td><strong>APACHE II</strong></td>
<td>15.9±6.4</td>
<td>13.0±6.3*</td>
</tr>
<tr>
<td><strong>Mortality</strong></td>
<td>46.5%</td>
<td>30.5%*</td>
</tr>
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* p<0.02

9. They can overestimate efficacy

ProCESS

ARISE
PROMISE
<table>
<thead>
<tr>
<th>Bundle target</th>
<th>Population</th>
<th>N</th>
<th>OR</th>
<th>p-value</th>
<th>OR</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measure Lactate</td>
<td>All</td>
<td>15,022</td>
<td>0.86</td>
<td>&lt;0.0001</td>
<td>0.97</td>
<td>[0.90, 1.05]</td>
<td>0.48</td>
</tr>
<tr>
<td>Obtain blood cultures before antibiotics</td>
<td>All</td>
<td>15,022</td>
<td>0.70</td>
<td>&lt;0.0001</td>
<td>0.76</td>
<td>[0.70, 0.83]</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Commence broad-spectrum antibiotics</td>
<td>All</td>
<td>15,022</td>
<td>0.78</td>
<td>&lt;0.0001</td>
<td>0.86</td>
<td>[0.79, 0.93]</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Achieve tight glucose control</td>
<td>All</td>
<td>15,022</td>
<td>0.65</td>
<td>&lt;0.0001</td>
<td>0.67</td>
<td>[0.62, 0.71]</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Administer drotrecogin alfa</td>
<td>Multi-organ failure</td>
<td>8,733</td>
<td>0.90</td>
<td>0.26</td>
<td>0.84</td>
<td>[0.69, 1.02]</td>
<td>0.07</td>
</tr>
<tr>
<td>Administer drotrecogin alfa</td>
<td>Shock despite fluids</td>
<td>7,854</td>
<td>0.91</td>
<td>0.30</td>
<td>0.81</td>
<td>[0.68, 0.96]</td>
<td>0.02</td>
</tr>
<tr>
<td>Administer low-dose steroids</td>
<td>Shock despite fluids</td>
<td>7,854</td>
<td>1.06</td>
<td>0.18</td>
<td>1.06</td>
<td>[0.96, 1.17]</td>
<td>0.24</td>
</tr>
<tr>
<td>Demonstrate CVP ≥ 8 mm Hg</td>
<td>Shock despite fluids</td>
<td>7,854</td>
<td>1.08</td>
<td>0.10</td>
<td>1.00</td>
<td>[0.89, 1.12]</td>
<td>0.98</td>
</tr>
<tr>
<td>Demonstrate ScvO₂ ≥ 70%</td>
<td>Shock despite fluids</td>
<td>7,854</td>
<td>0.94</td>
<td>0.24</td>
<td>0.98</td>
<td>[0.86, 1.10]</td>
<td>0.69</td>
</tr>
<tr>
<td>Achieve low plateau pressure control</td>
<td>Mechanical ventilation</td>
<td>7,860</td>
<td>0.67</td>
<td>&lt;0.0001</td>
<td>0.70</td>
<td>[0.62, 0.78]</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
10. They over-simplify the interpretation of clinical research

Clinical trials describe outcomes in highly selected populations, under specific constraints, and at a specific time.

They describe probabilities, not truths.
Guidelines are useful for the non-expert, particularly in the acute setting.
Rigorous, evidence-based syntheses of current data are invaluable. These must be regularly updated, perhaps even in real time.
The Future

- Interactive, web-based tools
- Provide options and alternatives
- Based on specific patient data
- Evaluate response and modify
How should we use guidelines now?

• Develop them
• Refine them
• Learn them
• Question them
Thank you!