Antibiotic Resistance and Mandatory Screening

Allison McGeer and Elizabeth Bryce
Your profession is....

1. Infectious Disease MD - 27.22%
2. Medical Microbiologist - 21.30%
3. Microbiologist - 8.28%
4. Internal Medicine - 3.55%
5. ICP - 0.59%
6. Laboratory Technologist - 14.79%
7. PhD Microbiology - 4.14%
8. Other - 20.12%

N=169
You work primarily in:

1. An acute care adult facility - 31.08%
2. An acute care pediatric facility - 12.16%
3. Mixed adult and pediatric acute care facility - 14.19%
4. A continuing care or rehab facility - 27.03%
5. An outpatient setting - 0.68%
6. A laboratory setting - 4.05%
7. A private office - 10.81%
8. An academic setting - 10.81%

N=148
You are from

1. Alberta or BC  
2. Saskatchewan or Manitoba  
3. Quebec or Ontario  
4. The Maritimes  
5. Yukon, NWT or Nunavut  
6. A country other than Canada

N=183
Now for the debate about the debate over the debate.
Here’s Liz to explain the rules....

- You will be asked a series of groups of questions related to aspects of mandatory screening
- We’ll highlight some recent relevant studies (you can too)
- The slides with the results will be posted post-conference

Be it resolved that screening and transmission control for antibiotic-resistant organisms should be mandatory components of hospital-based infection control programs.
“Mandatory” to you means.....

1. The government requires it
   - 12.18%
2. Accreditation Canada requires it
   - 12.18%
3. Your provincial government guidelines recommend it
   - 11.54%
4. Your infection control department has decided
   - 8.97%
5. 1 or 2
   - 10.26%
6. 1 or 2 or 3
   - 5.13%
7. 1 or 2 or 3 or 4
   - 39.74%

N=156
What should governments mandate about hospitals and AROs?

1. Reduction or acceptable rate targets for ARO infections (UK)
2. Publicly reporting
3. The existence of control programs, but not content
4. Nothing!
5. 1 and 2
6. 1 and 3
7. 2 and 3
Consequences of mandatory reporting

**Muller M, Detsky AS**  *JAMA* 2010;304;1116  *Hand Hygiene*

- Provides incentive to maximize performance BUT hospitals “overestimate” compliance

**Weber S et al  2007 SHEA Position Statement Legislative Mandates**

- “would exclude local experts…. From the process of risk assessment and resource allocation..”


- Commentary on thinking about fairness and cost-effectiveness in infection prevention targets

**Johnson AP, et al. JAC. 2012;67:802. UK MRSA bacteremia reporting**

- Review of the history and impact of reporting and targets
Control Programs
In your opinion, does your hospital need an ARO control program?

1. No, transmission of ARO’s is not a problem
   - 2.25%
2. No, an ARO control program will not reduce the transmission of AROs
   - 1.12%
3. No, our efforts are better invested in other prevention programs (eg. hand hygiene, CHG bathing)
   - 7.30%
4. Yes, a control program for at least one ARO will reduce patient risk
   - 79.21%
5. Not sure
   - 10.10%

N=178
A control program for an ARO to you means...

1. Admission ARO Screening
2. Additional precautions for infected/colonized patients
3. A combination of prevalence screening, contact screening, response to transmission events
4. 1 and 2
5. 1 and 3
6. 2 and 3
7. None of the above
8. All of the above

N=166
Which organisms does your hospital have specific control programs for currently?

1. MRSA
2. VRE
3. Carbapenemase-producers
4. All of the above
5. 1 and 2
6. 1 and 3
7. 2 and 3
8. None of the above

N=160
What organisms SHOULD your hospital have control programs for?

1. MRSA
2. VRE
3. Carbapenemase producers
4. All of the above
5. 1 and 2
6. 1 and 3
7. 2 and 3
8. None of the above

N = 158
Are we making progress with HAIs?

**CNISP 2006-2011**
- No change in CDI, CLABSI, CSF shunts
- Increasing VRE (0.1-0.7 per 10,000 pt days)
- ?decrease in MRSA (1.7-1.5 per 10,000 pt days)

**US: Magill et al. NEJM 2014; 370:1198**
- Results of point prevalence survey
- Top organisms: CDI (12%), SA (11%), Klebsiella (9.9%)
  - E. coli (9.3%), Enterococci (8.7%)
What are the right infection prevention programs?

- Programs that target an (or >1) organism(s)
- Programs that target transmission of all (or some) organisms
- Programs that target an infection type (CLABSI, SSI)
## CPOs and Outcomes

<table>
<thead>
<tr>
<th>Years of collection and origin</th>
<th>Number of cases</th>
<th>Source of infection</th>
<th>Overall mortality</th>
<th>Mortality</th>
<th>Mortality with most frequent combinations</th>
<th>Mortality with most frequent monotherapy</th>
<th>Risk factors associated with mortality in multivariable analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumbarello et al (2012)⁴³, Italy</td>
<td>125</td>
<td>Unknown (75; 60%), lower respiratory tract (28; 22%), urinary tract (17; 14%), line related (13; 10%), and other (5; 4%)</td>
<td>Crude 30 day mortality: 52 (42%)</td>
<td>27/79 (34%)</td>
<td>Colistin with tigecycline (7/23; 30%), tigecycline with gentamicin (6/12; 50%), and tigecycline with colistin and meropenem (2/16; 13%)</td>
<td>Colistin (11/22; 50%), tigecycline (10/19; 53%), and gentamicin (4/5; 80%)</td>
<td>Septic shock at presentation, inadequate empirical therapy, APACHE score, and triple combination therapy</td>
</tr>
<tr>
<td>Zarkotou et al (2011)⁴⁰, Piraeus, Greece</td>
<td>53</td>
<td>Primary bacteraemia (23; 43%), line related (12; 23%), respiratory tract (7; 13%), urinary tract (6; 11%), soft tissues (4; 8%), and CNS (1; 2%)</td>
<td>30 day attributable mortality: 18/53 (34%), * and crude mortality: 28/53 (53%)</td>
<td>0/20 (0%)†</td>
<td>Colistin with tigecycline (0/9; 0%) and tigecycline with gentamicin (0/2; 0%)</td>
<td>Colistin (4/7; 57%), tigecycline (2/5; 40%), gentamicin (0/2; 0%), and carbapenem (1/1; 100%)</td>
<td>Absence of appropriate antimicrobial treatment combination, APACHE score, and age</td>
</tr>
<tr>
<td>Qureshi et al (2012)⁴¹⁴, New York City and Pittsburgh, USA</td>
<td>41</td>
<td>Line related (13; 32%), pneumonia (10; 24%), urinary tract (7; 17%), and primary bacteraemia (6; 15%)</td>
<td>Crude 28 day mortality: 16 (39%)†</td>
<td>2/15 (13%)‡</td>
<td>Carbapenem with colistin (1/5; 20%) and carbapenem with tigecycline (0/3; 0%)</td>
<td>Colistin (4/7; 57%); tigecycline (4/5; 80%) and carbapenem (2/4; 50%)</td>
<td>Absence of appropriate combination as definitive therapy</td>
</tr>
</tbody>
</table>

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Munoz-Price SL. Lancet Infectious Diseases 2013; 13:785
Surveillance or Screening
What are the components of your hospital’s screening program?

1. Admission screening (some or all) - 14.29%
2. Prevalence screening - 1.30%
3. Roommate/other contact screening - 0.65%
4. All of the above - 40.91%
5. 1 and 2 - 4.55%
6. 1 and 3 - 22.08%
7. 2 and 3 - 2.60%
8. Not relevant to my setting - 13.64%

N=154
What **SHOULD** be the components of your hospital’s screening program?

1. Admission screening (some or all patients)  
2. Prevalence screening  
3. Roommate or other contact screening  
4. All of the above  
5. 1 and 2  
6. 1 and 3  
7. 2 and 3  
8. Not relevant to my setting

N=148
What to you are the right reasons for admission screening?

1. Identifying colonization and preventing cross-transmission to other patients
2. “Benchmark” my facility
3. Improve empiric antibiotics if patient develops an infection
4. All of the above
5. 1 and 2
6. 1 and 3
7. 2 and 3
8. None of the above

N=135
A note on laboratory screening

• Intensity of screening varies
  e.g. Leber et al: Lab based screening of CD stools for VRE – 41% (58) of CDI pos specimens were VRE +

• Screening protocols vary (e.g. CPOs)

• Sensitivity of detection varies (PCR vs traditional)

Mandatory laboratory screening ≠ consistent screening
<table>
<thead>
<tr>
<th>Screening sites</th>
<th>Culture&lt;sup&gt;a&lt;/sup&gt;</th>
<th>PCR rapid test&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of positive</td>
<td>Sensitivity, % (95% CI)</td>
</tr>
<tr>
<td></td>
<td>samples</td>
<td></td>
</tr>
<tr>
<td>Single sites</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nose</td>
<td>1509</td>
<td>48 (46–50)</td>
</tr>
<tr>
<td>Groin</td>
<td>1984</td>
<td>63 (62–65)</td>
</tr>
<tr>
<td>Throat</td>
<td>1923</td>
<td>61 (60–63)</td>
</tr>
<tr>
<td>Combinations of sites</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nose and groin</td>
<td>2475</td>
<td>79 (77–80)</td>
</tr>
<tr>
<td>Nose and throat</td>
<td>2377</td>
<td>76 (74–77)</td>
</tr>
<tr>
<td>Groin and throat</td>
<td>2799</td>
<td>89 (88–90)</td>
</tr>
<tr>
<td>Nose, groin, and throat</td>
<td>3002</td>
<td>96 (95–96)</td>
</tr>
<tr>
<td>Nose, groin, throat, and wounds</td>
<td>3113</td>
<td>99 (99–99)</td>
</tr>
<tr>
<td>Nose, groin, throat, wounds, and others</td>
<td>3137</td>
<td>100</td>
</tr>
</tbody>
</table>

<sup>a</sup> Period, 2006–2009; positive screenings (≥1 positive site), 3137.

<sup>b</sup> Period, 2009; positive screenings (≥1 positive site), 312.
Screening swabs and predicting MR in clinical SA isolates

Table 2: Test characteristics of screening to predict methicillin resistance in clinical isolates of Staphylococcus aureus, stratified by time from screening swab to isolate collection

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Overall</th>
<th>Immediate*</th>
<th>Recent†</th>
<th>Remote‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>True positive, no.</td>
<td>50</td>
<td>20</td>
<td>17</td>
<td>13</td>
</tr>
<tr>
<td>True negative, no.</td>
<td>428</td>
<td>127</td>
<td>203</td>
<td>98</td>
</tr>
<tr>
<td>False positive, no.</td>
<td>3</td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>False negative, no.</td>
<td>29</td>
<td>2</td>
<td>12</td>
<td>15</td>
</tr>
<tr>
<td>Sensitivity, % (95% CI)</td>
<td>63 (52–74)</td>
<td>91 (71–99)</td>
<td>59 (39–77)</td>
<td>46 (28–66)</td>
</tr>
<tr>
<td>Specificity, % (95% CI)</td>
<td>99 (98–100)</td>
<td>100 (97–100)</td>
<td>100 (97–100)</td>
<td>98 (93–100)</td>
</tr>
<tr>
<td>Positive likelihood ratio (95% CI)</td>
<td>91 (29–284)</td>
<td>–§</td>
<td>120 (17–865)</td>
<td>29 (7–120)</td>
</tr>
<tr>
<td>Negative likelihood ratio (95% CI)</td>
<td>0.37 (0.28–0.49)</td>
<td>0.09 (0.01–0.30)</td>
<td>0.42 (0.27–0.64)</td>
<td>0.42 (0.27–0.65)</td>
</tr>
<tr>
<td>Positive predictive value, % (95% CI)</td>
<td>94 (84–99)</td>
<td>100 (83–100)</td>
<td>94 (73–100)</td>
<td>87 (60–98)</td>
</tr>
<tr>
<td>Negative predictive value, % (95% CI)</td>
<td>94 (91–96)</td>
<td>98 (95–100)</td>
<td>94 (90–97)</td>
<td>87 (79–92)</td>
</tr>
</tbody>
</table>

Cl = confidence interval.
*Swab obtained within 48 hours before isolate collection.
†Swab obtained between 48 hours and 14 days before isolate collection.
‡Swab obtained more than 14 days before isolate collection.
§Test characteristics could not be calculated owing to high specificity values.
Getting the balance right

No harm principle

Precautionary approach
What are the important positive consequences of ARO control programs?

1. Ability to reduce cross-transmission (benefit others) - 32.19%
2. Ability to benefit the screened individual - 2.74%
3. Both - 59.59%
4. None - 1.37%
5. Don’t know - 4.11%

N=146
What are the important negative consequences of ARO control programs?

1. Decreased quality of care for isolated patients
2. Uses dollars and resources that could be used for other purposes
3. Isolation “fatigue” of HCWs decreases benefit of precautions
4. All
5. None
6. 1 and 2
7. 1 and 3
8. 2 and 3
Effects of isolation

Abad C JHI 2010;76;97-102
• Lit review 15 studies; majority showed higher depression, anxiety and anger scores, HCWs spent less time with isolated pts, pt satisfaction adversely affected, eight-fold increase in adverse events in isolated pts

Matlow A Peds 2008;122:e411
• 24 isolated/41 nonisolated pts. No difference in interactions with medical team in time spent and organ systems examined

Dhar S ICHE 2014;35:213
• 1013 observations on compliance with HH/barriers for contact isolation. As proportion of pts in isolation in compliance“
Effects of isolation

Confounding
- what makes you sad, anxious, angry is also what gets you an ARO (complex medical condition, long LOS, many interventions)

Goodliffe ICHE 2013 epub ahead of print

- Patient interaction rates:
  - 5.2/hr (4 bed); 4.5/hr (2 bed); 3.8/hr (private); 2.9/hr (private+isolation)
  - Greatest difference with shorter visits without HHO
  - No difference in visits associated with a moment 2/3 HHO
Impact of Screening and Control Programs

Your opinion!
Imagine a non-screening world

Which statement would apply to your hospital?

1. AROs would **not** be a problem for patients in my hospital
2. AROs would cause **less** harm to patients in my hospital
3. AROs would cause **more** harm to patients in my hospital
4. Could go either way

N = 158
Imagine a non transmission based precautions world

Which statement would apply to your hospital?

1. AROs would **not** be a problem for patients in my hospital
   - 4.50%

2. AROs would cause **less** harm to patients in my hospital
   - 17.12%

3. AROs would cause **more** harm to patients in my hospital
   - 42.34%

4. Could go either way
   - 36.04%

N=111
THE DEBATE IS OVER.

Some last thoughts
Problems with the literature on the effect of ARO screening/precautions

• Regional nature of programs makes effective RCTs impossible
• Heterogeneity in the nature of the screening makes interpretation difficult
• Interventions often deployed as part of a “bundle” limiting conclusion re relative value of each intervention

Current debate is whether we should be employing traditional VERTICAL control strategies versus HORIZONTAL PROGRAMS....
“evidence insufficient to reach a conclusion regarding the effectiveness of screening

Mutters NT Dtsch Arztebl Int 2013. VRE

• Insufficient data to make a recommendation for VRE screening...

Huskins WC N Engl J Med 2011 RCT 10 ICUs MRSA and VRE

• Gp 1 = surveillance + reporting of results/precautions
• Gp 2 = surveillance + no results given
• No difference in incidence of MRSA or VRE

Aboelela S AJIC 2006;34:484-94 Barrier precautions

“...not possible to determine whether there is a specific set of interventions that is essential....to reduce risk of transmission.
Targeted versus universal decolonization to prevent ICU Infection

Huang SS NEJM 2013;268;24
Cluster randomized trial in 43 ICUs focusing on MRSA prevention

- **VERTICAL**
  - ACTIVE DETECTION/ISOLATION
  - NO CHANGE IN MRSA RATES

- **MIXED VERTICAL AND HORIZONTAL**
  - ACTIVE DETECTION/ISOLATION AND TARGETED DECOLONIZATION
  - DECREASE IN MRSA RATES

- **HORIZONTAL**
  - UNIVERSAL DECOLONIZATION WITHOUT DETECTION/ISOLATION
  - DECREASE IN MRSA RATES GREATER THAN MIXED PROGRAM

Lack of effectiveness of traditional screening and isolation
Reconsider the pursuit of mandating these measures
Focus efforts on horizontal control programs designed to reduce ALL infections
Dissemination of spa type t104 MRSA in Euregio hospitals, 2005-2008

Ciccolini Int J Med Micro 2013; 303:380
An Ongoing National Intervention to Contain the Spread of Carbapenem-Resistant Enterobacteriaceae

Schwaber CID Mar2014
Right Decision
Wrong Decision
Context is Everything

Need to consider:

• Epidemiology
  – ?Endemic ?Emerging
• Virulence
• Ability to Treat (now and future)
• Ability to Decolonize
• Cost-effectiveness

Isn’t that called Risk Assessment?
References

1. Muller M, Detsky AS. JAMA 2010;304;1116
2. Weber S et al. 2007 SHEA Position Statement
5. MacFadden CMAJ 2013;185:E725
7. Abad C. JHI 2010;76;97-102
8. Matlow A. Peds 2008;122:e411
9. AHRQ Comparative Effectiveness Review #102
10. Mutters NT. Dtsch Arztebl Int 2011
12. Aboelela S. AJIC 2006;34:484-94
13. Huang SS. NEJM 2013;268;24
15. Schwaber. CID Mar 2014