The Case for Antibiotic Stewardship in Nursing Homes

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“We can look forward with confidence to a considerable degree of freedom from infectious diseases at a time not too far in the future. Indeed ... it seems reasonable to anticipate that within some measurable time... all the major infections will have disappeared.”

T. Aidan Cockburn, 1963
“At the beginning of the 21st century, antimicrobial resistance is common, has developed against every class of antimicrobial drug, and appears to be spreading into new clinical niches.”

Stephan Harbarth & Matthew Samore, 2005

The Antibiotic Pipeline

FDA, New Drug Approvals: Antibiotics

Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America Guidelines for Developing an Institutional Program to Enhance Antimicrobial Stewardship

Antibiotic Stewardship: a set of coordinated strategies to improve the use of antimicrobial medications with the goal of enhancing patient health outcomes, reducing resistance to antibiotics, and decreasing unnecessary costs.
Reservoirs of MDROs: NHs

- NH residents commonly colonized with MDROs

- Resistance imported and created in NHs
  - Furuno et al. Infect Control Hosp Epidemiol 2011; 32(3): 244-9

MDRO Colonization: Health Outcomes

Adjusted HR = 1.38 (1.09 - 1.76)
**MDRO Infections: Health Outcomes**


<table>
<thead>
<tr>
<th>Facilities</th>
<th>Both</th>
<th>FQRB-only</th>
<th>MRSA-only</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.5</td>
<td>0.4</td>
<td>0.3</td>
</tr>
<tr>
<td>1</td>
<td>0.4</td>
<td>0.3</td>
<td>0.2</td>
</tr>
<tr>
<td>2</td>
<td>0.3</td>
<td>0.2</td>
<td>0.1</td>
</tr>
<tr>
<td>3</td>
<td>0.2</td>
<td>0.1</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>0.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>0.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>0.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>0.5</td>
<td>0.4</td>
<td>0.3</td>
</tr>
</tbody>
</table>

**Attributable Mortality of Antibiotic-Resistant Infections:**

<table>
<thead>
<tr>
<th>Infection</th>
<th>MRSA (BSI)</th>
<th>MRSA (SSI)</th>
<th>Resistant PSAE</th>
<th>3rd Gen-R Enterobacter</th>
<th>ESBL E. coli</th>
<th>CRE</th>
</tr>
</thead>
<tbody>
<tr>
<td>DR (red)</td>
<td>22.9</td>
<td>22.9</td>
<td>22.9</td>
<td>22.9</td>
<td>22.9</td>
<td>22.9</td>
</tr>
<tr>
<td>95% CIs (blue)</td>
<td>18.7</td>
<td>18.7</td>
<td>18.7</td>
<td>18.7</td>
<td>18.7</td>
<td>18.7</td>
</tr>
</tbody>
</table>


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**Clostridium difficile**

MDRO Infections: Cost Outcomes

![Chart showing cost outcomes for MDRO infections]

Roberts et al. *Clin Infect Dis* 2009; 49(8): 1175-84

Contact Patterns

- **Nursing homes**
  - Hospital → NH: ~5 million (2010)
  - 30-day Readmission Rate: 23.5% (2006)
  - Overall number of contacts: ???

- **Long-term acute care hospitals (LTACHS)**
  - LTACH → Hosp.: ???

http://hcupnet.ahrq.gov/
Mor et al. *Health Affairs* 2010; 29(1): 57-64
Kahn et al. *JAMA* 2010; 303(22): 2253-9
MDROs: The Healthcare Facility STD?

LTCFs Play an Important Role in the Regional Dissemination of MDROs

Lee et al. PLoS One 2011; 6(12): e29342

Abx & Adverse Drug Reactions

Preventable ADRs

Percentage (%)

20% of all ADRs

New admission
No. of Scheduled Medications
Current Medications


<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>New admission</td>
<td>2.8</td>
<td>(1.5 – 5.2)</td>
</tr>
<tr>
<td>No. of Scheduled Medications</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;5</td>
<td>1.0</td>
<td>(referent)</td>
</tr>
<tr>
<td>5-6</td>
<td>2.0</td>
<td>(1.2 – 3.2)</td>
</tr>
<tr>
<td>7-8</td>
<td>2.8</td>
<td>(1.7 – 4.7)</td>
</tr>
<tr>
<td>≥9</td>
<td>3.3</td>
<td>(1.9 – 5.6)</td>
</tr>
<tr>
<td>Antibiotic</td>
<td>4.0</td>
<td>(2.5 – 6.2)</td>
</tr>
<tr>
<td>Antipsychotic</td>
<td>3.2</td>
<td>(2.1 – 4.9)</td>
</tr>
<tr>
<td>Antidepressant</td>
<td>1.5</td>
<td>(1.1 – 2.3)</td>
</tr>
<tr>
<td>Supplements</td>
<td>0.4</td>
<td>(0.3 – 0.8)</td>
</tr>
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</table>
Abx & Adverse Drug Reactions

Preventable ADRs

Independent Risk Factors of Adverse Drug Events

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<tr>
<td>Current Medications</td>
<td></td>
<td></td>
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<td>(0.3 – 0.6)</td>
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</table>


Antibiotic Script: Time Bomb

- Antibiotic course may be viewed as time bomb that later detonates as *C. difficile* or MDRO infection.
- Intensity of bomb blast > INDIVIDUAL than group level.[Hospital ward, Scottish general practice] Clinical Infectious Diseases 33:1462, BMJ 328:1297
- Important Risk-benefit consideration when considering antibiotic therapy for INDIVIDUAL.
Antibiotic Exposure and Risk of Resistance: Community

Antibiotic Exposure and Risk of Resistance: Nursing Home

**TABLE 3.** Association between antimicrobial exposure and resistance to antimicrobial agents and effect of institutional factors in 50 nursing homes in the United States and Canada, 1998-1999.*

<table>
<thead>
<tr>
<th>Antimicrobial-resistant bacteria</th>
<th>Variables kept in the multivariable model</th>
<th>Unadjusted odds ratio</th>
<th>95% confidence interval</th>
<th>Adjusted odds ratio</th>
<th>95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>TMP-SMX-resistant Enterobacteriaceae</td>
<td>TMP-SMX at the facility level</td>
<td>1.14</td>
<td>1.06, 1.22</td>
<td>1.14</td>
<td>1.06, 1.22</td>
</tr>
<tr>
<td>Use of intravenous therapy in the nursing home</td>
<td>2.83</td>
<td>1.05, 5.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of hard-washing sinks per 100 residents</td>
<td>2.5</td>
<td>1.1, 12.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of occupied beds per 100 residents</td>
<td>0.94</td>
<td>0.90, 0.98</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MRSA*</td>
<td>Vancomycin</td>
<td>0.9</td>
<td>0.80, 1.02</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Use of antimicrobial soap in the nursing home</td>
<td>0.97</td>
<td>0.85, 1.10</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Use of different soaps by staff and residents</td>
<td>0.24</td>
<td>0.13, 0.47</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Use of intravenous therapy in the nursing home</td>
<td>8.55</td>
<td>3.65, 20.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of registered nurses per 100 residents</td>
<td>0.79</td>
<td>0.72, 0.87</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MRSA†</td>
<td>Fluoroquinolones</td>
<td>1.00</td>
<td>0.97, 1.03</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Use of different soaps by staff and residents</td>
<td>0.22</td>
<td>0.13, 0.36</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluoroquinolones-resistant Enterobacteriaceae</td>
<td>Fluoroquinolones</td>
<td>1.08</td>
<td>1.04, 1.11</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>1.04</td>
<td>1.01, 1.07</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Unadjusted odds ratios for antimicrobial exposures and adjusted odds ratios for variables kept in the final multivariable models are shown.
† Odds ratio for antimicrobial exposure per one defined daily dose per 100 resident-days.
‡ TMP-SMX, trimethoprim-sulfamethoxazole; MRSA, methicillin-resistant Staphylococcus aureus.
§ Use of antibacterial soap by staff and use of regular soap by residents.

Costelloe et al. BMJ 2010; 340: c2059

Antibiotic Script: Time Bomb

Greater Explosive Charge in NH
Greater risk of serious infection over 1-2 months
Transmission MDRO: Colonization pressure, Serial Contact Care
Overgrowth MDRO: Pre-existing colonizers

Antibiotics and MRSA

Furuno et al. Infect Control Hosp Epidemiol 2011; 32(3): 244-9
How Common is Emergence of Resistance in Individual?

- 11 of 96 (12%) residents who received antibiotic for suspected UTI developed C difficile diarrhea within 3 weeks. Arch Intern Med, 171:438–443
- Inpatient quinolone therapy prior 30 days increased odds that symptomatic UTI caused by quinolone R organism 16X J Hosp Infec 76: 324
- Outpatient quinolone therapy prior 6 months increased odds that febrile UTI caused by quinolone R organism 17.5X J Antimicrobial Chemotherapy 66:650

How Common is Emergence Resistance

200 residents had C+S within 1 MO. of prior antibiotic- 2/3 R to that antibiotic AJIC 2000;28:8
TMP-Sulfa prophylaxis for 1mo in post-menopausal women increased R E coli in stool from 20 to 85%. Arch Intern Med 172:704
Antibiotic treatment of asymptomatic bacteriuria in young women increased risk of subsequent symptomatic UTI 3X CID 55:771
Antibiotic replaced benign colonizers with virulent bacteria.
Antibiotic Therapy and CDI in NHs

512 Records Screened

172 Cases with Abnormal UA

McGeer (+) (n = 26)

McGeer (-) (n = 146)

Risk versus NH OR = 8.5 (1.7 – 42.2)

Abx (+) (n = 26)

Abx (-) (n = 70)

Abx (-) (n = 76)

CDI (+) (n = 11)

• McGeer Criteria (at least 3 of the following)
  – Temperature ≥ 38°C
  – N/↑ burning/frequency/urgency
  – New flank-suprapubic pain/tenderness
  – Change in character of urine
    • Blood/smell/sediment
    • Pyuria/hematuria
  – Worsening mental or functional status

• Inappropriate therapy (independent of decision to start)
  – Treatment initiated empirically (before culture) in only 27/96 (28%) of residents
  – Empiric antibiotic inappropriate in 56% of cases (FQ when TMP/SMX or NFT reasonable)
  – Dosage (High [21%] / Low [13%] / CI [12%])
  – Duration (Short [3%] / Long [67%])


Antibiotic Usage Patterns in NHs
Antimicrobial Use: NHs

20% of subjects responsible for:
- 48% of antibiotic days
- 60% of antibiotic starts

Relative Frequency of Use: By Metric

Crnich et al. *ID Week 2012*. San Diego, CA.
Inappropriate Antibiotic Use in NHs

- 25 – 80% of use deemed inappropriate

Unpacking Inappropriate Antibiotic Use in NHs: A Systems Problem

- Degree of variation not explained by clinical factors

- Inter-facility > Intra-facility level variation

- Contextual effects seen with other agents prescribed in NHs (i.e., anti-psychotics)
  - Hughes et al. Drugs Aging 2007; 24(2): 81-93
Conclusions

• Antibiotic use in NHs has a societal and individual resident impact
  – Increased risk of ADEs
  – Increased risk of antibiotic resistance

• Inappropriate (both unnecessary and suboptimal) antibiotic use in NHs is common

• Many factors combine to create an “antibiotic prescribing culture” in NHs

• Many opportunities to intervene!