Outpatient Antimicrobial Stewardship

Jeffrey S Gerber, MD, PhD
Division of Infectious Diseases
The Children’s Hospital of Philadelphia
Overview

- The case for outpatient antimicrobial stewardship
- Interventions that work
- Some future directions
Case Presentation

• 14 year-old male presents to clinic with cough
• 10 days ago had slight fever, runny nose, sore throat
• Now without fever, but has nasal congestion and persistent cough – says he “feels it in his chest”
• T= 37.8; RR = 18; HR = 78; 02 sat = 98% (RA)
• Well appearing, occasional cough, lungs clear

• What do you do?
US Outpatient Antibiotic Prescribing Variation According to Geography, Patient Population, and Provider Specialty in 2011

Lauri A. Hicks,¹ Monina G. Bartoces,¹ Rebecca M. Roberts,¹ Katie J. Suda,² Robert J. Hunkler,³ Thomas H. Taylor Jr,¹ and Stephanie J. Schrag¹

- IMS Health Xponent database
- 262.5 million antibiotic prescriptions dispensed in 2011
- 842 prescriptions per 1000 persons

Clinical Infectious Diseases 2015;60(9):1308–16
<table>
<thead>
<tr>
<th>Provider Specialty</th>
<th>Prescriptions, No. in Millions (%)</th>
<th>Providers, No.</th>
<th>Prescriptions per Provider, Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Providers</td>
<td>262.5</td>
<td>911 814</td>
<td>289</td>
</tr>
<tr>
<td>Persons &lt;20 y</td>
<td>73.8 (29)</td>
<td>. . .</td>
<td>. . .</td>
</tr>
<tr>
<td>Persons ≥20 y</td>
<td>102.6 (71)</td>
<td>. . .</td>
<td>. . .</td>
</tr>
<tr>
<td>Family practice</td>
<td>64.1 (24)</td>
<td>96 073</td>
<td>667</td>
</tr>
<tr>
<td>Persons &lt;20 y</td>
<td>12.9 (21)</td>
<td>. . .</td>
<td>. . .</td>
</tr>
<tr>
<td>Persons ≥20 y</td>
<td>49.7 (79)</td>
<td>. . .</td>
<td>. . .</td>
</tr>
<tr>
<td>Dermatology</td>
<td>8.2 (3)</td>
<td>11 329</td>
<td>724</td>
</tr>
<tr>
<td>Pediatrics</td>
<td>32.4 (12)</td>
<td>54 228</td>
<td>598</td>
</tr>
<tr>
<td>Otolaryngology</td>
<td>4.1 (2)</td>
<td>95 36</td>
<td>430</td>
</tr>
<tr>
<td>Emergency medicine</td>
<td>13.8 (5)</td>
<td>32 346</td>
<td>427</td>
</tr>
<tr>
<td>Internal medicine/pediatrics</td>
<td>1.4 (1)</td>
<td>33 29</td>
<td>421</td>
</tr>
<tr>
<td>Internal medicine</td>
<td>32.1 (12)</td>
<td>83 841</td>
<td>383</td>
</tr>
<tr>
<td>Physician assistants</td>
<td>17.5 (7)</td>
<td>63 467</td>
<td>276</td>
</tr>
<tr>
<td>Infectious diseases</td>
<td>1.3 (1)</td>
<td>61 66</td>
<td>211</td>
</tr>
<tr>
<td>Dentistry</td>
<td>25.6 (10)</td>
<td>122 706</td>
<td>208</td>
</tr>
<tr>
<td>Obstetrics/gynecology</td>
<td>6.7 (3)</td>
<td>37 590</td>
<td>178</td>
</tr>
<tr>
<td>Nurse practitioners</td>
<td>19.5 (7)</td>
<td>109 741</td>
<td>178</td>
</tr>
<tr>
<td>Surgery (general)</td>
<td>6.9 (3)</td>
<td>69 536</td>
<td>99</td>
</tr>
<tr>
<td>Pediatric subspecialty</td>
<td>0.8 (&lt;1)</td>
<td>8 273</td>
<td>97</td>
</tr>
<tr>
<td>Medical subspecialty</td>
<td>6.9 (3)</td>
<td>74 424</td>
<td>93</td>
</tr>
<tr>
<td>Other</td>
<td>8.2 (3)</td>
<td>113 783</td>
<td>72</td>
</tr>
<tr>
<td>Urology</td>
<td>6.0 (2)</td>
<td>10 131</td>
<td>59</td>
</tr>
</tbody>
</table>
Antibiotic Use: Outpatient Children

Chai G et al. *Pediatrics* 2012;130:23-31
Antibiotic use for ARTIs

- acute respiratory infections (ARTIs) constitute about 10% of all ambulatory care visits in the United States and account for 44% all antibiotic prescriptions

- 21% of all ambulatory visits for children, 72% for ARTI

Grijalva *JAMA* 2009;302(7):758-766
Hersh *Pediatrics* 2011;128;1053
But is there Room for Improvement?

- although prescribing rates for ARTIs have declined significantly, this has been modest, and antibiotic use for ARTIs remains common and most are caused by viruses
- use of broader-spectrum antibiotics for ARTI has increased
- the most commonly prescribed individual antibiotic agent was azithromycin
- “40 years of randomized controlled trials, as well as more recent guidelines and performance measures, indicate that antibiotics are not beneficial for acute bronchitis and that the right antibiotic prescribing rate is zero.”

– J. Linder

Grijalva JAMA 2009;302(7):758-766
Hersh Pediatrics 2011;128;1053
Antibiotic Prescribing for Adults With Acute Bronchitis in the United States, 1996-2010

Figure. Antibiotic Prescribing for Acute Bronchitis in the United States by Site of Care, 1996-2010

Michael L. Barnett, MD
Jeffrey A. Linder, MD, MPH
Antibiotic use across populations

Figure 1. Antibiotic Prescriptions per 1000 Persons of All Ages According to State, 2010.
Off-Guideline Antibiotic Prescribing

Excluding: preventive visits, CCC, antibiotic allergy, prior antibiotics
Standardized by: age, sex, race, Medicaid

Gerber, JPIDS, 2014
So What?

- we use a LOT of antibiotics
- we use them variably
- but ... so what?
Adverse Effects of Antibiotic use

• use drives resistance
• bacteria have shown the ability to become resistant to every antibiotic that has been developed
• antibiotic-resistant infections:
  – $20 billion in excess healthcare costs
  – $35 billion in societal costs
  – 8 million additional hospital days
NATIONAL SUMMARY DATA

Estimated minimum number of illnesses and deaths caused by antibiotic resistance*:

At least 2,049,442 illnesses, 23,000 deaths

*bacteria and fungus included in this report

Estimated minimum number of illnesses and death due to *Clostridium difficile* (*C. difficile*), a unique bacterial infection that, although not significantly resistant to the drugs used to treat it, is directly related to antibiotic use and resistance:

At least 250,000 illnesses, 14,000 deaths

WHERE DO INFECTIONS HAPPEN?

Antibiotic-resistant infections can happen anywhere. Data show that most happen in the general community; however, most deaths related to antibiotic resistance happen in healthcare settings, such as hospitals and nursing homes.
Resistance Aside. . .

- 5\%–25\% diarrhea
- 1 in 1000 visit emergency department for adverse effect of antibiotic
  - comparable to insulin, warfarin, and digoxin
- 1 in 4000 chance that an antibiotic will prevent serious complication from ARTI

Shehab N. *CID 2008:47*; Linder JA. *CID 2008:47*
So what can we do?
FIGHTING BACK AGAINST ANTIBIOTIC RESISTANCE

Four Core Actions to Prevent Antibiotic Resistance

1. PREVENTING INFECTIONS, PREVENTING THE SPREAD OF RESISTANCE
   Avoiding infections in the first place reduces the amount of antibiotics that have to be used and reduces the likelihood that resistance will develop during therapy. There are many ways that drug-resistant infections can be prevented: Immunization, safe food preparation, handwashing, and using antibiotics as directed and only when necessary. In addition, preventing infections also prevents the spread of resistant bacteria.

2. TRACKING
   CDC gathers data on antibiotic-resistant infections, causes of infections and whether there are particular reasons (risk factors) that caused some people to get a resistant infection. With that information, experts can develop specific strategies to prevent those infections and prevent the resistant bacteria from spreading.

3. IMPROVING ANTIBIOTIC PRESCRIBING/STEWARDSHIP
   Perhaps the single most important action needed to greatly slow down the development and spread of antibiotic-resistant infections is to change the way antibiotics are used. Up to half of antibiotic use in humans and much of antibiotic use in animals is unnecessary and inappropriate and makes everyone less safe. Stopping even some of the inappropriate and unnecessary use of antibiotics in people and animals would help greatly in slowing down the spread of resistant bacteria. This commitment to always use antibiotics appropriately and safely—only when they are needed to treat disease, and to choose the right antibiotics and to administer them in the right way in every case—is known as antibiotic stewardship.

4. DEVELOPING NEW DRUGS AND DIAGNOSTIC TESTS
   Because antibiotic resistance occurs as part of a natural process in which bacteria evolve, it can be slowed but not stopped. Therefore, we will always need new antibiotics to keep up with resistant bacteria as well as new diagnostic tests to track the development of resistance.

ANTIBIOTIC STEWARDSHIP IN YOUR FACILITY WILL

DECREASE
- ANTIBIOTIC RESISTANCE
- C. DIFFICILE INFECTIONS
- COSTS

INCREASE
- GOOD PATIENT OUTCOMES

PROMOTE ANTIBIOTIC BEST PRACTICES—A FIRST STEP IN ANTIBIOTIC STEWARDSHIP

- ENSURE ALL ORDERS HAVE DOSE, DURATION, AND INDICATIONS
- GET CULTURES BEFORE STARTING ANTIBIOTICS
- TAKE AN “ANTIBIOTIC TIMEOUT” REASSESSING ANTIBIOTICS AFTER 48–72 HOURS

ANTIBIOTIC STEWARDSHIP PROGRAMS ARE A “WIN–WIN” FOR ALL INVOLVED

A UNIVERSITY OF MARYLAND STUDY SHOWED ONE ANTIBIOTIC STEWARDSHIP PROGRAM SAVED A TOTAL OF $17 MILLION OVER EIGHT YEARS

ANTIBIOTIC STEWARDSHIP HELPS IMPROVE PATIENT CARE AND SHORTEN HOSPITAL STAYS, THUS BENEFITING PATIENTS AS WELL AS HOSPITALS
Antimicrobial Stewardship Programs recommended for hospitals

• most antibiotic use occurs in the outpatient setting

• is outpatient “stewardship” achievable?

Antimicrobial Stewardship

• Core Strategies
  – prior authorization
  – prospective audit & feedback
  – formulary restriction

• Supplemental Strategies
  – education
  – clinical guidelines
  – IV to PO conversion
  – dose optimization
  – antimicrobial order forms
Antimicrobial Stewardship

• Core Strategies
  – prior authorization
  – prospective audit & feedback
  – formulary restriction

• Supplemental Strategies
  – education
  – clinical guidelines
  – IV to PO conversion
  – dose optimization
  – antimicrobial order forms
What has been done?
Clinical Decision Support
LESS IS MORE

A Cluster Randomized Trial of Decision Support Strategies for Reducing Antibiotic Use in Acute Bronchitis

Ralph Gonzales, MD, MSPH; Tammy Anderer, PhD, CRNP; Charles E. McCulloch, PhD; Judith H. Maselli, MSPH; Frederick J. Bloom Jr, MD; Thomas R. Graf, MD; Melissa Stahl, MPH; Michelle Yefko; Julie Molecavage; Joshua P. Metlay, MD, PhD

• **3-arm cluster RCT**: 33 primary care practices within integrated health care system
• **11 sites**: print-based decision support
• **11 sites**: computer-assisted (EHR) decision support
• both intervention sites also received:  
  – clinician education and feedback on prescribing practices  
  – patient education brochures at check-in
• **11 control sites**
Education of Clinicians and Patients
Impact of a 16-Community Trial to Promote Judicious Antibiotic Use in Massachusetts

Jonathan A. Finkelstein, MD, MPH\textsuperscript{a,b}, Susan S. Huang, MD, MPH\textsuperscript{a,c}, Ken Kleinman, ScD\textsuperscript{a}, Sheryl L. Rifas-Shiman, MPH\textsuperscript{a}, Christopher J. Stille, MD, MPH\textsuperscript{d}, James Daniel, MPH\textsuperscript{e}, Nancy Schiff, MPH\textsuperscript{f}, Ron Steingard, MD\textsuperscript{g}, Stephen B. Soumerai, ScD\textsuperscript{a}, Dennis Ross-Degnan, ScD\textsuperscript{a}, Donald Goldmann, MD\textsuperscript{h}, Richard Platt, MD\textsuperscript{a}

- clinician guideline dissemination, small-group education, frequent updates and educational materials, and prescribing feedback
- parents received educational materials by mail and in primary care practices, pharmacies, and child care settings
- using health-plan data, measured changes in antibiotics dispensed among children aged 3 - 72 months

*Pediatrics* 2008;121;e15-e23
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control</th>
<th>Intervention</th>
<th>Intervention Impact ( ^{c} )</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Unadjusted Rate, Baseline Year 1(^{a} )</td>
<td>Unadjusted Rate, Baseline Year 1(^{a} )</td>
<td>Adjusted % Change(^{b} )</td>
<td>Adjusted % Change(^{b} )</td>
</tr>
<tr>
<td>Overall</td>
<td>2.8</td>
<td>2.9</td>
<td>-20.7</td>
<td>-21.2</td>
</tr>
<tr>
<td>3 to &lt;24 mo</td>
<td>1.7</td>
<td>1.7</td>
<td>-10.3</td>
<td>-14.5</td>
</tr>
<tr>
<td>24 to &lt;48 mo</td>
<td>1.4</td>
<td>1.4</td>
<td>-2.5</td>
<td>-9.3</td>
</tr>
<tr>
<td>48 to &lt;72 mo</td>
<td>1.4</td>
<td>1.4</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Audit and Feedback
Effect of an Outpatient Antimicrobial Stewardship Intervention on Broad-Spectrum Antibiotic Prescribing by Primary Care Pediatricians
A Randomized Trial

- cluster-RCT of 18 practices, 170 clinicians
- common EHR
- focused on antibiotic choice for encounters for bacterial infections with established guidelines
  - streptococcal pharyngitis
  - acute sinusitis
  - pneumonia
- all should get penicillin or amoxicillin
Broad spectrum antibiotics use for acute visits

Rate (95% CI) of prescribing before, during, and after intervention

- Control Practices
- Intervention Practices

Standardized Rates (% of Prescribing)

Month before(-) and after intervention

JAMA. 2013;309(22):2345-2352
Broad spectrum antibiotics use for acute visits

Rate (95% CI) of prescribing before, during, and after intervention

- Control Practices
- Intervention Practices

Start audit and feedback

End of audit and feedback

JAMA. 2013;309(22):2345-2352
What do Clinicians Think?
Clinician Perceptions: Pediatrics

• most did not believe that their prescribing behavior contributed to antibiotic overuse

• reported frequently confronting parental pressure, sometimes acquiescing to:
  – appear competent
  – avoid losing patients to other practices that would “give them what they want”

Szymczak, ICHE, 2014, vol. 35, no. s3
“We have lots of parents who come in and they know what they want. They don’t care what we have to say. They want the antibiotic that they want because they know what is wrong with their child.”
Clinician Perceptions: Pediatrics

- interviewed 10 physicians, 306 parents

- physician perception of parental expectations for antimicrobials was the only predictor of prescribing antimicrobials for viral infections
  - when they thought parents wanted antimicrobial:
    - 62% vs. 7% prescribed antibiotic

- prescribing behavior was not associated with actual parental expectations for receiving antimicrobials

Mangione-Smith et al. *Pediatrics* 1999;103(4)
Clinician Perceptions: Adults

• semi-structured interviews of 13 PCPs in Boston
• all clinicians agreed with guidelines and felt that clinicians other than themselves were responsible for overprescribing
• barriers to adherence included:
  – perceived patient demand
  – lack of accountability
  – saving time and money
  – other clinicians misperceptions about bronchitis
  – diagnostic uncertainty
  – failing to meet patient expectations

Dempsey et al. BMC Family Practice 2014, 15:194
What do parents think?
What do Parents Think?

- direct parental request for antibiotics in 1% of cases
- parental expectations for antibiotics not associated with physician-perceived expectations
- parents who expected antibiotics but did not receive them were more satisfied if the physician provided a contingency plan
- failure to meet parental expectations regarding communication events during the visit was the only significant predictor of parental satisfaction
  - NOT failure to provide expected antimicrobials

What do Parents Think?

• 5 focus groups (31 parents) – knowledge/attitudes surrounding antibiotic use in 2011
  – considerable concern for antibiotic resistance
  – expressed desire to use antibiotics only when necessary
What do Parents Think?

• interviewed >100 parents of kids presenting with ARTIs from waiting rooms

• parents **did not plan to demand an antibiotic** for their child
  – deferred to medical expertise about the need for antibiotic therapy
  – parents are aware of the downsides of antibiotics and may be willing to partner to improve appropriate use

Szymczak; ID Week, San Diego; 2015
Communication
Communication

- parent and clinician surveys after 1,285 pediatric ARTI visits to 28 pediatric providers from 10 practices in Seattle

- **positive treatment recommendations** (suggesting actions to reduce child’s symptoms) were associated with decreased risk of antibiotic prescribing

Mangione-Smith et al. *Ann Fam Med* 2015;13:221-227
Effects of internet-based training on antibiotic prescribing rates for acute respiratory-tract infections: a multinational, cluster, randomised, factorial, controlled trial

Paul Little, Beth Stuart, Nick Francis, Elaine Douglas, Sarah Tonkin-Crine, Sibyl Anthierens, Jochen W L Cals, Hasse Melbye, Miriam Santer, Michael Moore, Samuel Coenen, Chris Butler, Kerenza Hood, Mark Kelly, Maciek Godycki-Cwirko, Artur Mierzecki, Antoni Torres, Carl Llor, Melanie Davies, Mark Mullee, Gilly O’Reilly, Alike van der Velden, Adam W A Geraghty, Herman Goossens, Theo Verheij, Lucy Yardley, on behalf of the GRACE consortium

- 246 practices, 4264 patients in 6 European countries

- training in enhanced communication skills – gathering information on patient concerns/expectations; exchange of information on symptoms, natural disease course, and treatments; agreement of a management plan

- communication training led to a >30% reduction in antibiotic prescribing for ARTI
Novel Socio-Behavioral Strategies
QI interventions often neglect psychosocial and professional factors that may affect clinical decisions.

simple, low-cost behavioral “nudge” in form of a public commitment device: a poster-sized letter signed by clinicians and posted in their examination rooms indicating their commitment to reducing inappropriate antibiotic use for ARTIs.

20% reduction in antibiotic prescribing for viral infections.
Case Presentation

• 14 year-old male presents to clinic with cough
• 10 days ago had slight fever, runny nose, sore throat
• Now without fever, but has nasal congestion and persistent cough – says he “feels it in his chest”
• T = 37.8; RR = 18; HR = 78; O2 sat = 98% (RA)
• Well appearing, occasional cough, lungs clear

• What do you do?

• reassure the patient (and parents) that he probably has a viral infection that is improving, but that the cough might persist even through the second week
• give clear directions about when to return
Final Thoughts

• many investigators and public health entities have implemented promising strategies to improve antibiotic use in the ambulatory setting, such as education, audit with feedback, and decision support
• have made some progress, but lots of effort with relatively modest benefits
• novel socio-behavioral approaches, such as improving communication and holding clinicians accountable are needed
• one size might not fit all
What We Need

- national mechanism for tracking antibiotic use to allow benchmarking/goal setting/feedback
- studies powered to compare clinical outcomes between groups, including those that are patient-centered
- studies that identify optimal behavioral change strategies to leverage, which might differ by subspecialty, setting, and provider role
- additional targets:
  - duration of Tx (UTI, CAP, AOM)
  - hospital discharge (OPAT, oral)
  - Emergency Department
  - ambulatory surgery
Thank You