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Making good antibiotic choices

Sometimes less is more

Giulio DiDiodato MD
November 4, 2015
Topics for Discussion

• Do we have the evidence we need?
• Are we making good antibiotic prescribing choices?
• Can physician prescribing behaviour be changed?
• Summary
• Questions
## Do we have the evidence we need?

<table>
<thead>
<tr>
<th>Clinical syndrome</th>
<th>Reference/Design</th>
<th>Treatment/duration</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellulitis, uncomplicated</td>
<td>Miller LG. et al. NEJM 2015/RCT</td>
<td>Septra vs clindamycin/10 days</td>
<td>77.7% vs 80.3% cure; abscess+/-</td>
</tr>
<tr>
<td>Intra-abdominal infection</td>
<td>Sawyer RG. et al. NEJM 2015/RCT</td>
<td>4 days vs usual care</td>
<td>Composite death/SSI/rIAS 21.8% (I) vs 22.3% (C)</td>
</tr>
<tr>
<td>Hospital-acquired pneumonia</td>
<td>Singh N. et al. AJRCCM 2000/RCT</td>
<td>3 days Cipro + CPIS vs usual care/RCT</td>
<td>Mortality NS MD -6.8 days</td>
</tr>
<tr>
<td>Ventilator-associated pneumonia</td>
<td>Pugh R. et al. Cochrane Database Syst Rev 2015/SR</td>
<td>7/8 days vs 10/15 days</td>
<td>Mortality NS NF-GNB recurrence OR 2.18 (1.14 to 4.16)</td>
</tr>
<tr>
<td>De-escalation in septic shock</td>
<td>Garnacho-Montero J. et al. Int Care Med 2014/Observational</td>
<td>None</td>
<td>De-escalation rate 34.9% Mortality OR 0.58 (95% CI 0.36 to 0.93)</td>
</tr>
</tbody>
</table>
### Do we have the evidence we need?

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<tbody>
<tr>
<td><strong>Uncomplicated cystitis, women</strong></td>
<td>Grigoryan L. et al. JAMA 2014/Review</td>
<td>Septra 3 days NTN 5-7 days fosfomycin 1 dose</td>
<td>early clinical cure &gt;=90% all regimens</td>
</tr>
<tr>
<td><strong>Acute cystitis, men</strong></td>
<td>Grigoryan L. et al. JAMA 2014/Review</td>
<td>7 vs 14</td>
<td>Early recurrence rate NS (3.9% vs 4.2%)</td>
</tr>
<tr>
<td><strong>Community-acquired pneumonia, mild to moderate severity</strong></td>
<td>Dimopoulos G. et al. Drugs 2008/SR</td>
<td>3-7 days vs 7-10 days (adults); 3 vs 5 days (children)</td>
<td>NS difference in clinical success, relapse rate, or mortality</td>
</tr>
<tr>
<td><strong>Sore throat</strong></td>
<td>Spinks A. et al. Cochrane Database Syst Rev 2013/SR</td>
<td>Antibiotic vs placebo</td>
<td>Pain reduced 16 hours OM, quinsy, PIGN rates too low to determine</td>
</tr>
</tbody>
</table>
Do we have the evidence we need?


- Setting: outpatient

- Intervention: prescribing behaviour
  - delayed=use of or advice to use antibiotics >=48 hours after consultation
  - immediate=immediate use of a prescription antibiotic given at time of initial consult
  - none=no prescription of antibiotic at initial consult

- Outcome: patient satisfaction

- Patients: all ages with ARTI

- Period: January 1966 to 2013
Do we have the evidence we need?


- Results
  - N=10 studies; 3157 patients
  - Too much heterogeneity across studies except for comparison of patient satisfaction (measured on Likert scale)
    - immediate (92%) vs delayed (87%) OR 0.52 (95% CI, 0.35 to 0.76)
    - delayed (87%) vs none (83%) NS

- Conclusions
  - Antibiotic use in none (14%) vs delayed (32%) and immediate (93%)
  - Impact of immediate antibiotic use has small but favourable differences in symptoms like fever, pain and malaise
  - No significant differences in complication rates
Topics for Discussion

• Do we have the evidence we need?
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Are we making good antibiotic prescribing choices?

  
  • Acute bronchitis (ICD-9 466.0)
    • cough-predominant acute respiratory illness < 3 weeks duration
    • 'acute LRTI when pneumonia is not suspected'

  
  • Placebo-c or no treatment vs antibiotic RCT, 1966-2014
  • N=17 trials with 5099 patients (excluded COPD patients)
  • Overall risk of bias was low
Are we making good antibiotic prescribing choices?

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Risk Ratio or Days (95% CI)</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cough (Follow-up visit)</strong></td>
<td>0.64 (0.49 to 0.85)</td>
<td>6</td>
</tr>
<tr>
<td><strong>Cough duration (days)</strong></td>
<td>-0.46 (-0.87 to -0.04)</td>
<td></td>
</tr>
<tr>
<td><strong>Illness duration (days)</strong></td>
<td>-0.64 (-1.16 to -0.13)</td>
<td></td>
</tr>
<tr>
<td><strong>Improved according to md</strong></td>
<td>0.61 (0.48 to 0.79)</td>
<td>11</td>
</tr>
<tr>
<td><strong>Adverse events</strong></td>
<td>1.20 (1.05 to 1.36)</td>
<td>5</td>
</tr>
</tbody>
</table>

Smith SM et al. Antibiotics for acute bronchitis. Cochrane Database of Systematic Reviews 2014
Are we making good antibiotic prescribing choices?

  - Acute bronchitis (ICD-9 466.0)
    - cough-predominant acute respiratory illness < 3 weeks duration
    - 'acute LRTI when pneumonia is not suspected'

  - Placebo-c or no treatment vs antibiotic RCT, 1966-2014
  - N=17 trials with 5099 patients (excluded COPD patients)
  - Overall risk of bias was low
  - Conclusions
    - modest benefit of minimal clinical significance
    - selection bias in favour of no benefit given possible under-representation of elderly with multi-morbidities
Are we making good antibiotic prescribing choices?

- Adults 18-64 years
- N=3153 AB visits
- Overall prescribing rate 71% (95% CI, 66% to 76%)
- 75% increase in rate every 10 years (95% CI, 6% to 190%)

Are we making good antibiotic prescribing choices?

  - Between 1980-1999, rate of antibiotic prescribing for AB was 60-80%
  - Significant national education campaigns to curb AB antibiotic use (CDC, NHS)
  - National Committee for Quality Assurance
    - since 2005, reporting metric for AB antibiotic treatment
    - stated that antibiotic prescribing rate should be ZERO
Are we making good antibiotic prescribing choices?

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  - Significant national education campaigns to curb AB antibiotic use (CDC, NHS)
  - National Committee for Quality Assurance
    - since 2005, reporting metric for AB antibiotic treatment
    - stated that antibiotic prescribing rate should be ZERO
  - Conclusions
    - Despite 15 years of educational campaigns and high quality evidence, antibiotic use for AB failed to meet zero target and actually increased during study period
Are we making good antibiotic prescribing choices?

- Hawker JI et al. *Journal of Antimicrobial Therapy* 2014
- Trends in UK primary care
- N=537 practices
  - 1995 to 2011
  - 2.32 million episodes
- SMAC and PHLS guidelines
  - Zero antibiotic prescribing rate for viral sore throats
  - 90% sore throats resolve without antibiotics
Are we making good antibiotic prescribing choices?

- Hawker JI et al. *Journal of Antimicrobial Therapy* 2014
- Trends in UK primary care
- N=537 practices
  - 1995 to 2011
  - 2.97 million episodes
- SMAC and PHLS guidelines
  - Zero antibiotic prescribing rate for cough/colds
Topics for Discussion

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Can physician prescribing behaviour be changed?


• Setting: 2 academic-affiliated veteran affairs community-based hospitals

• Population: hospitalized patients with indwelling bladder catheters

• Design: contemporaneous controlled before and after design

• Outcomes:
  • Primary: number of urine cultures per 1000 patient bed days
  • Secondary: overtreatment of ASB per 1000 patient bed days
  • Secondary: undertreatment of cAUTI per 1000 patient bed days

• Intervention:
  • Year 1: baseline incidence + education/validation materials
  • Year 2: diagnostic algorithm for CAUTI/cASB + case-based audit and feedback (intervention site) versus education (control site)
  • Year 3: case presentation (intervention site) (no further case-based audit and feedback) versus education (control site)
Are we making good antibiotic prescribing choices?

- Trautner BW., et al. *JAMA* 2015

- Primary outcome
  - Urine cultures (I) IRR 0.29 (95% CI 0.26 to 0.32)
  - Control NS

- Secondary outcome
  - ASB IRR (I) 0.24 (95% CI 0.13 to 0.42)
    - Only significant reduction in LTC wards and no change in acute medical wards
  - Control NS

- Secondary outcome
  - cAUTI IRR (NS)
Can physician prescribing behaviour be changed?


• Results
  
  • Proportion of ASB (total urine cultures)
    
    • I ~ 60% vs C ~ 45% (did not change over study period)

  • Rate of ASB overtreatment
    
    • I (medical) 23.4% to 34.2% versus C (medical) 16.8% to 25.3%

• Conclusions
  
  • Despite an extensive educational campaign and stewardship activities, no difference in proportion of patients receiving overtreatment of catheter-associated ASB in medical patients
Can physician prescribing behaviour be changed?


- Setting: single academic centre
- Population: non-catheterized acute medical/surgical patients
- Design: Before-after comparison
- Intervention: reporting of urine culture results upon request

**Results**

- Proportion of urine cultures determined to be ASB
  - 84%-89% (non-catheter) and 90%-93% (catheter)
- Rate of ASB overtreatment
  - Non-catheter: 48% (B) versus 12% (A)
  - Catheter: 42% (B) versus 41% (A)

**Conclusions**

- Structural reporting change reduced rate of overtreatment in non-catheter ASB only
Can physician prescribing behaviour be changed?


• Setting: 2 academic-affiliated veteran affairs community-based hospitals

• Intervention: standardized 30 minute interview antibiotic prescribing habits + 3 clinical vignettes

• UTI vignette

A 72-year-old man presented with a severe *Clostridium difficile* infection, which resulted in both respiratory and acute renal failure. He gradually improved with supportive care, oral *vancomycin*, and IV *metronidazole*. After over a month of being hospitalized in the ICU, his Foley was removed. He was subsequently found to have urinary retention, so he was straight catheterized. The urine obtained from the straight catheterization was cloudy. A urinalysis showed 53 WBCs, positive nitrite, and many bacteria. Urine culture grew >100K *ESBL*-producing *Escherichia coli*. He wasn’t having fevers. He had no leukocytosis and no signs or symptoms attributable to a UTI. What is your diagnosis? What antibiotics would you start?
Can physician prescribing behaviour be changed?


- Intervention
  - After vignette
    - IDSA guidelines were shared with physician
    - Physicians subsequently asked
      - “Would you feel comfortable applying this recommendation to your practice? Are there situations when you would not apply this recommendation?”

- Outcome
  - Thematic analysis of interview to determine concordance with guidelines
Can physician prescribing behaviour be changed?


**Results**

- Median age 34 years old (IQR 30-42)
- Median time in practice 10 years (IQR 3-15)
- 20 physicians (17 hospitalists/3 internists) + 10 senior residents
- General agreement and awareness of guidelines, however, 3 major barriers to implementation
Can physician prescribing behaviour be changed?


**Barriers**

- Lack of awareness of specific recommendations
  - 6/20 prescribed antibiotics for ASB vignette
- Tension between adhering to guidelines and individualized patient care
  - “I would say this is a UTI. I’m sure the guidelines are going to say ‘no,’ but since he was having retention and it wasn’t a urine [culture] obtained from him having a Foley, I have less comfort calling it colonization. I would say that it is probably an infection. You don’t see a lot of fevers in just a bladder infection” (25, attending).

- Skepticism of guideline recommendations
  - Overall, guidelines are easy to follow when they have what to do as opposed to what not to do. . . . We are trained to do something and fix something, so to not do anything is probably the hardest guideline to follow.” (11, resident).
  - “A guy has a catheter in for a month and has a ton of white cells in his urine and is growing something that is clearly pathogenic: he needs treatment. I do not care what the guidelines say” (7, attending).
Can physician prescribing behaviour be changed?


- Results
  - Significant heterogeneity among distribution of barriers among physicians
  - Audit and feedback uncovered disconnect between self-reported practice and guideline adherence
  - Discordant prescribing frequently attributed to patient falling “outside” recommendations
  - Guideline education alone unlikely to influence antibiotic prescribing
Can physician prescribing behaviour be changed?


- Setting: acute care hospitals

- Outcome: antibiotic prescribing

- Update to December 2006 (First review included studies Nov 2003)

- N=89 studies
  - ITSA (56)
  - RCT (25)
  - CBA (5)
  - CCT (3)
Can physician prescribing behaviour be changed?

- n=76 interventions
  - persuasive (44)
    - education, audit and feedback
  - restrictive (24)
    - selective reporting lab results, formulary restriction, prior authorization, automatic stop orders, antibiotic cycling/rotation
  - structural (8)
    - CPOE, rapid lab testing, CDSS, quality monitoring
Can physician prescribing behaviour be changed?

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Design</th>
<th>Persuasive</th>
<th>Restrictive</th>
<th>Structural</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antibiotic prescribing</strong></td>
<td>ITSA</td>
<td>-42.3</td>
<td>-34.7</td>
<td></td>
</tr>
<tr>
<td></td>
<td>cITSA</td>
<td>-31.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>CBA</td>
<td>-17.7</td>
<td>-17.1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>CRCT</td>
<td>-3.5</td>
<td></td>
<td>-23.6</td>
</tr>
<tr>
<td></td>
<td>RCT</td>
<td>-24.7</td>
<td>-40.5</td>
<td>-13.3</td>
</tr>
</tbody>
</table>

ITSA=interrupted time series analysis; cITSA=controlled ITSA; CBA=controlled before-after; CRCT=cluster randomized controlled trial
Can physician prescribing behaviour be changed?

  - Both C-reactive protein (CRP) and advanced communication skills training for physicians each reduced antibiotic prescribing by 20% (Cals J *et al.* BMJ 2009)
  - Multinational, cRCT outpatient physician practices
    - pre-intervention audit October to December 2010
    - randomized to usual care, CRP only, communication only, CRP + communication
    - internet training for interpretation of CRP and communication
    - post-intervention audit February to May 2011, recruitment of up to first 30 patients with LRTI and up to first 5 patients with URTI
    - Primary outcome = antibiotic use
Can physician prescribing behaviour be changed?

  • Results
    • 440 practices approached; 259 agreed to participate
    • pre-intervention period; N=6771 patients
    • randomization
      • usual care (N=53 practices; 870 patients)
      • CRP (N=58 practices; 1062 patients)
      • communication (N=55 practices; 1170 patients)
      • CRP + communication (N=62 practices; 1162 patients)
Can physician prescribing behaviour be changed?

  - Results
    - Adherence to training
      - CRP 87.6%
      - Communication 87%

<table>
<thead>
<tr>
<th>Antibiotic use (LRTI)</th>
<th>Control</th>
<th>CRP</th>
<th>Communication</th>
<th>Both</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Crude %</strong></td>
<td>62</td>
<td>36</td>
<td>44</td>
<td>34</td>
</tr>
<tr>
<td><strong>Basic Risk Ratio</strong></td>
<td>1.0</td>
<td>0.52</td>
<td>0.68</td>
<td>0.44</td>
</tr>
<tr>
<td><strong>Adjusted Risk Ratio</strong></td>
<td>1.0</td>
<td>0.53 (0.35 to 0.74)</td>
<td>0.67 (0.46 to 0.88)</td>
<td>0.35 (0.23 to 0.53)</td>
</tr>
</tbody>
</table>
Can physician prescribing behaviour be changed?


• Systematic overview of systematic reviews

• Intervention: behaviour change interventions as defined by Cochrane Effective Practice and Organisation of Care (EPOC) Review Group
  • Distribution of materials
  • Educational meetings
  • Local consensus processes
  • Educational outreach visits
  • Local opinion leaders
  • Patient-mediated interventions
  • Audit and feedback
  • Reminders
  • Marketing
  • Mass media
Can physician prescribing behaviour be changed?


- Objective: understand social mechanisms by which interventions work as opposed to intervention effectiveness by using theory-led review

- Normalisation process theory (NPT)
  - behaviour change model used to evaluate interventions
  - focuses on action rather than beliefs, attitudes and intentions
  - action based on 4 social mechanisms (16 constructs)
    1. coherence - how do users understand new practices
    2. cognitive participation - how do users engage new practices
    3. collective action - what users do to enact new practice
    4. reflexive monitoring - how do users appraise effects of new practice
Can physician prescribing behaviour be changed?


• Period: 1947 to 2015

• Coding of reviews
  1. guideline implementation
  2. single interventions
  3. multiple interventions
    • NPT-EPOC
      • 'successful', 'unsuccessful', 'not assessed', or 'unclear'
Can physician prescribing behaviour be changed?


• Results
  • N=67 studies
    • n=34 single intervention
    • n=33 multiple interventions
      • 12/33 guideline interventions
  • 3 main strategies
    • persuasive
    • educational and informational
    • action and monitoring
• Results
  • 3 main EPOC strategies that act across most NPT constructs
    • audit and feedback
    • reminders
    • educational outreach
  • Least effective
    • local opinion leaders involved in mass media sessions
Topics for Discussion

• Do we have the evidence we need?
• Are we making good antibiotic prescribing choices?
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Summary

• Do we have the evidence we need?
  • certainly enough to reduce unwarranted prescribing and prolonged durations of therapy for the most clinical syndromes

• Are we making good antibiotic prescribing choices?
  • seem to need more than just evidence

• Can physician prescribing behaviour be changed?
  • antimicrobial stewardship along with adjunctive bio-marker testing may go a long way in changing behaviour
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