What's new in Antibiotic Stewardship?

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Analysis of data from the National Administrative Database (MarketScan Hospital Drug Database) and CDC’s Emerging Infections Program (EIP) to assess the potential for improvement of inpatient antibiotic prescribing.

Based on representative data obtained from US-hospitals (in 2010):

- 55.7% of inpatients received an AB during hospitalization, and
- 29.8% received at least 1 dose of broad-spectrum ABx
- 39.6% of ABx prescribed for UTIs included a potential error (given for too long, without proper evaluation, unnecessary at all)
- 35.7% of vancomycin prescriptions were also written with a potential error
“Drug resistance follows the drug like a faithful shadow.”

Paul Ehrlich, Nobel prize 1908 -
A PERFECT STORM

Antimicrobial Resistance

Pseudomonas aeruginosa.
History of Antimicrobial Stewardship

In July 2004, IDSA sent a white paper to Capitol Hill stressing the rapidly growing public health crisis in the emergence of bacteria resistant to many, if not all, antibiotics that typically had activity against them.
Guidelines for Improving the Use of Antimicrobial Agents in Hospitals: A Statement by the Infectious Diseases Society of America
Antimicrobial Stewardship: Overview

Updated guidelines for developing programs to enhance antimicrobial stewardship published in 2007

**IDSA/SHEA*consensus guidelines endorsed by**

- American Academy of Pediatrics
- American Society of Health-System Pharmacists
- Infectious Diseases Society for Obstetrics and Gynecology
- Pediatric Infectious Diseases Society
- Society for Hospital Medicine
- Society of Infectious Diseases Pharmacists

**General objective:**

- The optimal selection, dose, and duration of an antimicrobial that results in the best clinical outcome for the treatment of infection, with minimal toxicity to the patient and minimal impact on subsequent development of resistance.

*Infectious Diseases Society of America (IDSA) and the Society for Healthcare Epidemiology of America (SHEA).*

Primary goal
- Optimize clinical outcomes while minimizing unintended consequences of antibiotic use
  - Toxicity
  - Selection of pathogenic bacteria (e.g., Clostridium difficile)
  - Emerging resistance
Secondary goal
- Reduce health care cost without compromising quality of care

*Infectious Diseases Society of America (IDSA) and the Society for Healthcare Epidemiology of America (SHEA).
Guidelines to develop an institutional Antimicrobial Stewardship Program (ASP)

• **Antimicrobial stewardship team:** ID-Physician, Pharmacist ± Microbiologist, IT-Specialist, IC-Professional, Hospital Epidemiologist and administrative support

• **Core Strategies**
  – Active Strategies
  – Supportive Strategies

• **Computer surveillance and decision support**

• **Proactive microbiology lab**

• **Comprehensive multidisciplinary antibiotic management programs**

• **Monitoring of process and outcomes measures**

2007 ASP Guidelines. *CID.* 159-177
Antimicrobial Stewardship Team

As Proposed by IDSA
Practical Guidelines to develop an institutional Antimicrobial Stewardship Program (ASP)

Core Strategies of an ASP

- **Active Strategies:**
  - Prospective audit and feedback
  - Formulary and preauthorization

- **Supportive Strategies:**
  - Education
  - Guidelines
  - Antimicrobial Cycling / Switch
  - Antimicrobial Order Forms
  - Combination therapy
  - Streamlining / De-escalation
  - Dose optimization (PK/PD)
  - Conversion from IV → PO therapy

2007 ASP Guidelines. CID. 159-177
“Education is the most powerful weapon which you can use to change the world.”

- Nelson Mandela

edutoopia.org
Pharmacist level of impact

**Pharmacy**

“Each capsule contains your medication, plus a treatment for each of its side effects.”

**ID-TRAINED**
- Resistance & Case-specific expertise

**GENERAL CLINICAL**
- Clinical practice guidelines

**STAFF**
- Education
- IV to PO
- Renal dosing
ASP-Competency and Training Development for Clinical Pharmacists at a 438-Bed Hospital (University of Arkansas, USA)

- Competency development: Management observation + Intervention review
- Training development: Educational intervention (4 mo‘s)
- Competency and training assessment (after 9 mo‘s)

### Competency Assessment

#### Pretest Score
Range: 19.6-71.2
Mean: 49.7

#### Posttest Score
Range: 56.9-96.3
Mean: 79.3

Mean Δ: 29.6
(95% CI, 23.1-36.0; P <0.01)

Antimicrobial Stewardship Team
- the need for wider engagement:

„All healthcare professionals can be involved in having an active role in recognizing, implementing and sustaining the principal goals of Antimicrobial Stewardship Programmes.“


„The key frontline healthcare professionals who have a role in Antimicrobial Stewardship are physicians, nurses and pharmacists.“
Improving Antibiotic Stewardship by Involving Nurses

Objective:
To assess the influence of nurse education on antibiotic use in clinical practice.

Study sites:
(1) Monash MC-Clayton and (2) Dandenong Hospital; Australia

Study period:
November 2009 (baseline data collection)
Jan.-March 2010 (interventional education)
April-May 2010 (data collection)

Material and Methods:
„Education package“: Slide show presentations, provision of handouts + references, training sessions, collaborative exercises (between pharmacist, nurse and doctor)


Questionnaire

- Use of IV ABx increases risk of CVL infection
- Use of ABx increases risk of VRE
- Use of ABx can promote development of AMR
- Would question a pt’s ABx order if (?) inappropriate
- Understands the switch from IV to PO ABx
- Would consider if AB is necessary before admin
- Able to state the duration pt. will be on ABx
- Unable to state what ABx patient is on

n= 79 Nurses

P< 0.001

P< 0.004

P< 0.003

P< 0.001

P< 0.001

Improving Antibiotic Stewardship by Involving Nurses

Conclusions:
Following education, nurses were able to articulate the risks of treatment with IV ABx and were aware of the benefits to actively promote switching to PO ABx.

Involving nurses in antibiotic stewardship programs should be implemented and monitored to demonstrate an improvement or trends in practice.

Impact of an Educational ASP on Prescribing Practice

Educational, institutionally supported ASP:
Appropriate AB prescription among the top annual objectives linked to economic incentives!

Setting: 1,251-bed tertiary care teaching medical centre

**Step 1:** Institutional agreements; formally accepted by the Medical Directory Board

**Step 2:** Constitution of a multidisciplinary team: ID physician, Pharmacist, Intensivist, Pediatrician, Microbiologist, IT-specialist

**Step 3:** Elaboration of local guidelines

Impact of an Educational ASP on Prescribing Practice

Educational, institutionally supported ASP:
Appropriate AB prescription among the top annual objectives linked to economic incentives!

Setting: 1,251-bed tertiary care teaching medical centre

Step 4: Implementation of ASP
→ Distribution of local guidelines (e-mail; Intranet)
   (pedagogic, non-restrictive methodology)
→ Periodical feedback regarding correct AB use / consumption

Impact of an Educational ASP on Prescribing Practice

Decrease of inappropriate AB treatment

- 53% (176/332)
- 41.6%
- 25.5%
- 26.4% (107/405)

% Inappropriate

1st trimester 2nd trimester 3rd trimester 4th trimester

Inappropriate AB treatment

26.4%
Impact of an Educational ASP on Prescribing Practice in a Tertiary Hospital Centre (University of Seville, Spain)

Decrease of inappropriate AB treatment according to indication

N= 1,206 consults

Impact of an Educational ASP on Prescribing Practice in a Tertiary Hospital Centre (University of Seville, Spain)

Evolution of AB consumption during the 1st year of the ASP

**Conclusion:** The education-based ASP achieved a significant improvement in AB prescriptions and a reduction in AB consumption (even without implementation of restrictive measures).

Multidisciplinary Intervention to Reduce Infections of ESBL/AmpC-Producing Gram-Negative Bacteria at a Danish University Hospital

Antimicrobial Stewardship: Stringent Guidelines for AB Use:

Pocket book (in print and electronically on Intranet)

• Cephalosporins → AB prophylaxis only
• Pip-Tazo (± gentamicin) → Empiric treatment of most febrile conditions
• Fluoroquinolones → Empiric use in septic shock only
  • Carbapenems → Penicillin-allergic patients (ertapenem)
  → Infections due to ESBL/AmpC-producing/ other MDRO

• Maximal Barrier Precautions (gowns, gloves)
• Mandatory, prompt notification of MDRO (electronically)
• Patient room and bed signs
• Insert with ESBL-tick-box for patient’s chart

Knudsen, JD et al.. PLOS ONE, 2014, 9: e86457
Multidisciplinary Intervention to Reduce Infections of ESBL/AmpC-Producing Gram-Negative Bacteria at a Danish University Hospital

after the multidisciplinary intervention

Knudsen, JD et al.. PLOS ONE, 2014, 9: e86457
Conclusion:
The intervention, including ASP, succeeded in a stable statistically significant decrease in the incidence of ESBL/AmpC producing *Klebsiella pneumoniae* infections.

Conclusions:

Antimicrobial stewardship can be a **useful tool** for an institution in its fight against *Clostridium difficile*-Associated Diarrhea (CDAD).

**No single activity** will optimize poor prescribing habits, improve susceptibilities, or control for the development of CDAD in a health care system.

Improved prescribing, monitoring, and analysis of data require a **concerted effort by a multidisciplinary team**.
Impact of an ASP on Reducing the Use of High-Risk ABx and its

Antibiotic guidance aide memoir (mini-version of hospital guidelines, available on

Audit tool (Standardised form for measuring adherence to AB policy)
1. Reassessment of duration of AB-Rx by prescriber (day 3 and 7–10)
2. Stop-order for LRTI and UTI

Formulary and pre-authorization
Restriction of “high-risk” ABx
Exemption forms if AB not included in the policy
Pre-authorization by consultant

Impact of an ASP on Reducing the Use of High-Risk ABx and its Effect on the Incidence of *Clostridium difficile* infection

**ASP:** NHSCT Hospitals, Northern Ireland

Adherence rate % to the AB policy = calculated by dividing the no. of adherent observations by the overall no. of observations (adherent, non-adherent, and indeterminate observations).

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Aldeyab, MA et al. JAC 2012, 67: 2988-2996
Impact of an ASP on Reducing the Use of High-Risk ABx and its Effect on the Incidence of *Clostridium difficile* infection

NHSCT Hospital, Northern Ireland.

**Intervention = Restriction of ABx with high-risk for CDI**

**High-risk ABx**
- 2nd- and 3rd Gen. Cephalosporins
- Fluroquinolones, Clindamycin

**Medium-risk ABx**
- Amoxicillin/Clavulanic acid
- Macrolides

**Low-risk ABx**
- Remaining used ABx

**Methods:** Interventional, retrospective, ecological investigation using time-series analysis (integrating the mean-age-adjusted comorbidity index)

Aldeyab, MA et al.. JAC 2012, 67: 2988-2996
Impact of an ASP on Reducing the Use of High-Risk ABx and its Effect on the Incidence of *Clostridium difficile* Infection

Results:

- Prospective audit
- Feedback
- Preauthorization

Aldeyab, MA et al.. JAC 2012, 67: 2988-2996
Impact of an ASP on Reducing the Use of High-Risk ABx and its Effect on the Incidence of *Clostridium difficile* Infection

**Results:**

**High-risk ABx Group:**

- **Significant change in use of high-risk antibiotics** $(P< 0.0001)$:  
  → Reduction by 0.156 DDD/100 bed-days per month $(P=0.0597)$

- **Significant change in the incidence of CDI** $(P=0.0081)$:  
  → Decrease by 0.0047/100 bed-days per month

- **Variations in the incidence of CDI affected by age-adjusted comorbidity index**  
  → Lag of 1 month (coefficient 0.137051, $P=0.0182$).

- **Significant decreases in slope post-intervention also for medium-risk ABx**

Aldeyab, MA et al.. JAC 2012, 67: 2988-2996
Prospective, one-year study on the efficacy of an Antibiotic Stewardship Program (2 ID-specialists, 3 pharmacists)

- 510 Antibiotic therapies: $63\%$ correct, $18\%$ de-escalated, $12\%$ unaffected
- ID-consults: 344 Patients (Preceeding year: 372 Patients)
- Clostridium difficile Infections ↓ $50\%$ (OR 0.46; 95\%, CI0.25-0.82)
- AB-Costs /treatment day ↓ $13.3\%$ (von $10,16$ to $8,81$)
- DDD’s most important AB ↓ $25.4\%$
- AB Total costs ↓ $15.2\%$
- Cost savings (preceeding year) $228,911$

An analysis of the development and implementation of a smartphone application for the delivery of antimicrobial prescribing policy: lessons learnt

E. Charani¹*, Y. Kyratsis¹, W. Lawson², H. Wickens², E. T. Brannigan², L. S. P. Moore² and A. H. Holmes¹

Study on the development, adoption and implementation process of the Imperial Antimicrobial Prescribing Policy (IAPP) Application across five teaching hospitals in London.

Charani E et al. JAC. 2013; 68: 960-967
Healthcare Information Technology

→ Example: Smartphones

Charani E et al. JAC. 2013; 68: 960-967
Healthcare Information Technology

→ Example: Smartphones

Results:

- 40% (376) of junior doctors with smartphones (primary target user group) downloaded the application within the 1st month,
- 100% (complete target user group) within 12 months
- 1,900 individual access sessions per month (average) compared with 221 hits on the Intranet version
- 71% of clinicians reported using IAPP improved their knowledge on ABx

Charani E et al. JAC. 2013; 68: 960-967
Healthcare Information Technology

→ Example: World Wide Web-based ASP

Study site: Johns Hopkins Children‘s Medical and Surgery Center (JHCMSC)

Healthcare Information Technology

→ Example: World Wide Web-based ASP

Key feature of the WWW-based ASP:
Auto-approval function, allowing for automatic approval of certain ABx for selected predetermined indications.

Outcome of interest:
Antimicrobial approval
Assessment of „gaming“ by studying trends in automatic approval

Methods:
Retrospective analysis of 16,229 ABx requests for 3,542 patients
(June 1, 2005 - June 30, 2009)

Healthcare Information Technology

→ Example: World Wide Web-based ASP

Results:

• **91.3% of ABx requests approved**, with an increase of 6.1% over time (P < 0.01)

• **Renewal requests** more likely approved than primary requests (aOR, 1.72; 95% CI, 1.45-2.04)

• Compared with requests by medical services, requests by surgical services had lower odds of approval (aOR, 0.70; 95% CI, 0.59-0.83); whereas pediatric ICU requests had higher odds of approval (aOR, 1.18; 95% CI, 1.00-1.40)

Conclusion:

The WWW-based ASP allows management of a large number of ABx requests

CDC recommends that every hospital adopts an Antibiotic Stewardship Program with 7 basic elements:

1. **Leadership commitment.** Dedicate necessary human, financial, and IT resources

2. **Accountability.** Appoint a single leader (physician) responsible for program outcomes

3. **Drug expertise.** Appoint a single pharmacist leader to support improved prescribing

4. **Action.** Take at least 1 action to improve prescribing (e.g., implement a universal reassessment within 48 hours to double-check drug choice, dose, duration)

5. **Track.** Monitor AB prescribing and resistance patterns

6. **Report.** Regularly report to staff on AB prescribing and resistance information and what can be done to improve

7. **Educate.** Offer education about AB resistance and best prescribing practice