Pathways to Effective Guidance for Reducing the Use of Antimicrobials in Healthcare Settings

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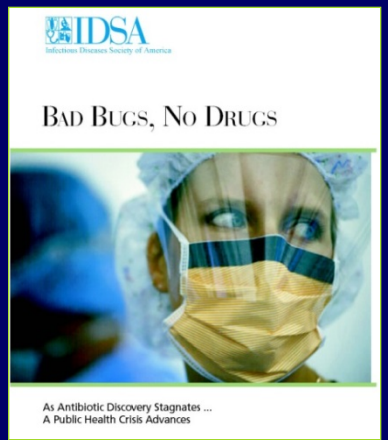
Tufts Medical Center



Disclosures

- Adjudication Committee – NIH
- Data Monitoring Committee
  - Actelion
  - Shire
- Editor
  - ID Clinics of North America
  - Antimicrobial Agents and Chemotherapy
- Treasurer, Infectious Diseases Society of America
- Member, ID Board and ID Test Writing Committee, American Board of Internal Medicine
- Voting Member, Presidential Advisory Council on Combating Antibiotic Resistant Bacteria (PACCARB)

Antimicrobial Stewardship

- How critical are stewardship programs in reducing the use of antimicrobials in healthcare settings?
  - What are the potential economic losses for not having these in place?
- What are the pathways to effective guidance for reducing the use of antimicrobials in healthcare settings
  - e.g., outpatient, ambulatory care, clinic, etc.?
- What kinds of stewardship programs that aim to reduce inappropriate use of antimicrobials in these settings have succeeded and failed, and what kinds of considerations need to be made to ensure that these programs are effective and sustainable?

What is Antimicrobial Stewardship?

- Antimicrobial stewardship involves the *optimal selection, dose and duration* of an antibiotic resulting in the cure or prevention of infection with minimal unintended consequences to the patient including emergence of resistance, adverse drug events, and cost

Ultimate goal is improved patient care and healthcare outcomes

Barlam et al. CID 2016;62(10):e51–e77
Dellit TH, et al. CID 2007;44:159-77,
Hand K, et al. Hospital Pharmacist 2004;11:459-64
Paskovaty A, et al IJAA 2005;25:1-10
Simonsen GS, et al Bull WHO 2004;82:928-34

Nationwide Survey on Antimicrobial Stewardship Program Characteristics

- 8,000 nationwide providers surveyed (5% response rate)
  - Pharmacy directors
  - ID pharmacists
- 51% had formal ASP
- 63% of non-ASP institutions considered implementing a program
  - Common barriers:
    - Staffing constraints
    - Funding constraints
- Institutions with ASPs more likely to have:
  - More admissions
  - Antibiograms
  - ID consult services
  - ID fellowship programs

Doron et al. Clinical Therapeutics 2013; 35(6): 758

Institutions with ASPs: National Survey Results

- Education techniques:
  - Newsletter (56.8%)
  - Grand Rounds (45.9%)
  - Conferences (41.5%)
  - None (6%)
- Stewardship techniques:
  - IV to PO conversion (85.3%)
  - Guidelines and clinical pathways (81.5%)
  - Dose optimization (70.7%)
  - Streamlining/de-escalation (62.5%)
  - Closed formularies (59.8%)
  - Antimicrobial order forms (41.8%)
  - Antimicrobial cycling (3.3%)
- Restriction Methods:
  - “Back end” approach (52.5%)
  - Automatic stop orders (45.9%)
  - ID consult required (44.3%)
  - “Front end” approach (39.3%)
  - None (0%)
- Commonly restricted antimicrobials
  - Antifungals (72.7%)
  - Linezolid (70.5%)
  - Carbapenems (69.9%)
  - Daptomycin (69.4%)
  - Tigecycline (64.5%)
  - Anti-Pseudomonals (57.4%)
  - Fluroquinolones (44.8%)
  - None (0%)

Doron et al. Clinical Therapeutics 2013; 35(6): 758

Antimicrobial Stewardship at TMC
14+ Years and Going Strong

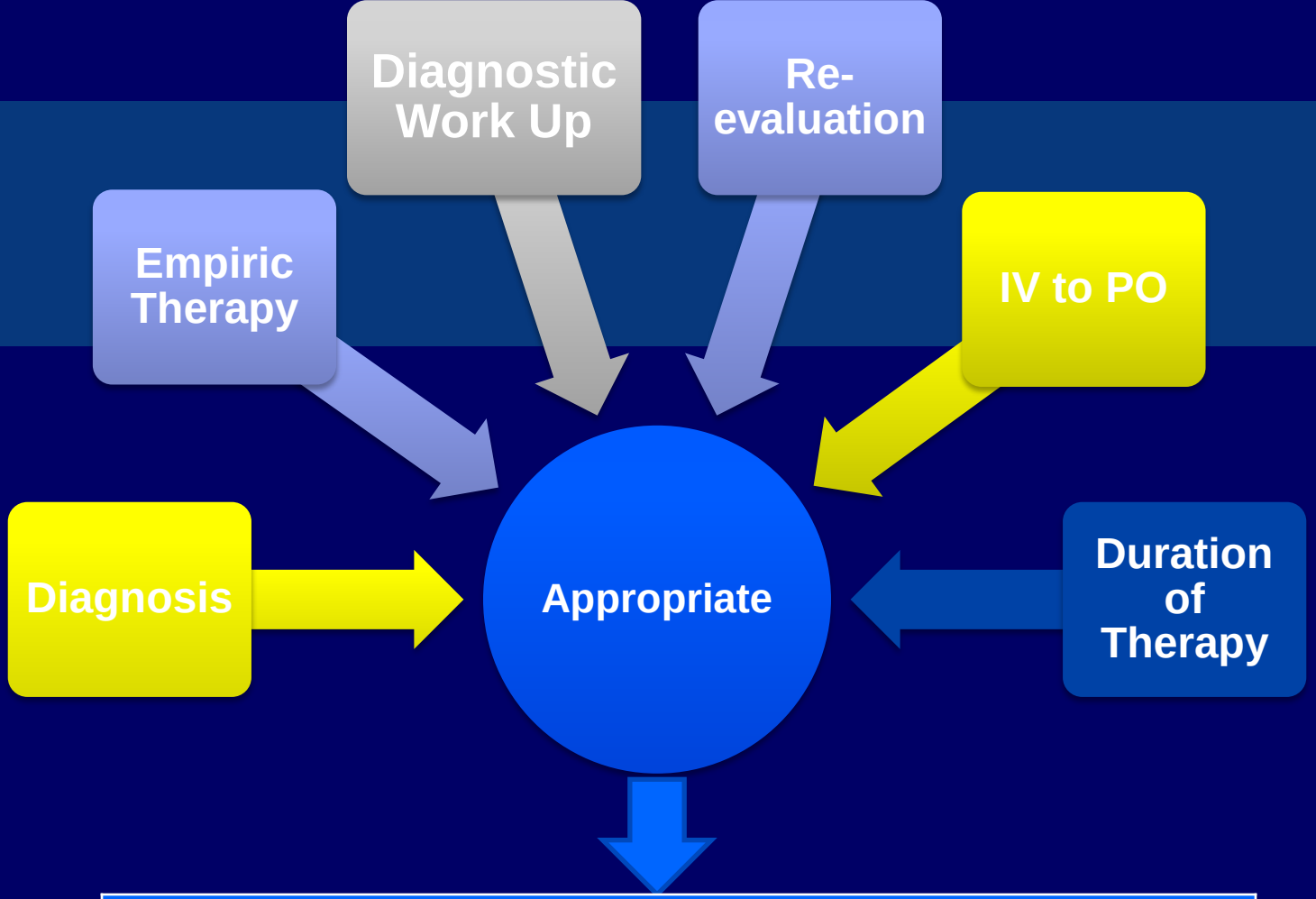
- Improve patient outcomes
- Slow antimicrobial resistance
- Ensure appropriate empirical antimicrobial therapy
  - Antimicrobial choice, dosage, route, and duration
- Educate prescribers on the importance of prudent antimicrobial prescribing
- Reduce medication errors related to antimicrobials
- Reduce cost
  - Duration of treatment
  - IV to PO
  - De-escalation and stopping unneeded treatment
- 2 part-time ID physicians, 1 full time ID PharmD

Antimicrobial Stewardship Strategies at Tufts Medical Center

- Prospective audit with intervention and feedback
- Formulary restriction and preauthorization (dedicated pager)

Supplemental Strategies

- Education: "AMT Question of the Week"
- Guidelines and disease management: "Red Book"
- Dose optimization via PK-PD:
  - extended dosing of Pip-Tazo
- De-escalation/Streamlining
- Antimicrobial order forms/order sets in CPOE
- IV-PO switch: automated by pharmacy
- Computerized decision support
  - Sentri7 and Safety Surveillor



IMPROVED OUTCOMES	
Mortality	Relapse / Readmission
Length of stay	Resistance rates
Adverse Drug Events	*C. difficile infection*

https://www.hhs.gov/sites/default/files/stenehjem.pdf

Improving antibiotic use saves money

- **"Comprehensive programs have consistently demonstrated a decrease in antimicrobial use with annual savings of $200,000 - $900,000"**
  - **Larger academic hospitals and smaller community hospitals**
- **At Tufts Medical Center we estimate the total cost savings to be ~ $400,000 per year**
  - **Over life of program over $ 5.6 million saved**

Dellit et al. CID 2007; 44 (2): 159-177

Impact of Antibiotic Stewardship Program Intervention on Costs

Setting	Intervention	Impact/Savings
Academic Medical Center	AMT	$3MM/3 years
Municipal Hospital	Restriction of cephalexin	29% abx cost reduction
Academic Medical Center	Preset order forms	Non-recommended dosing: 60-90% to 6%, $76,000 annual drug cost savings
VA Hospitals	IV to oral conversion (quinolones)	$4 million/4 years
Academic Medical Center	Batching iv abx	$250,000/year
Academic Medical Center	AMT	> $900,000/year

Issues: Measurements, definitions

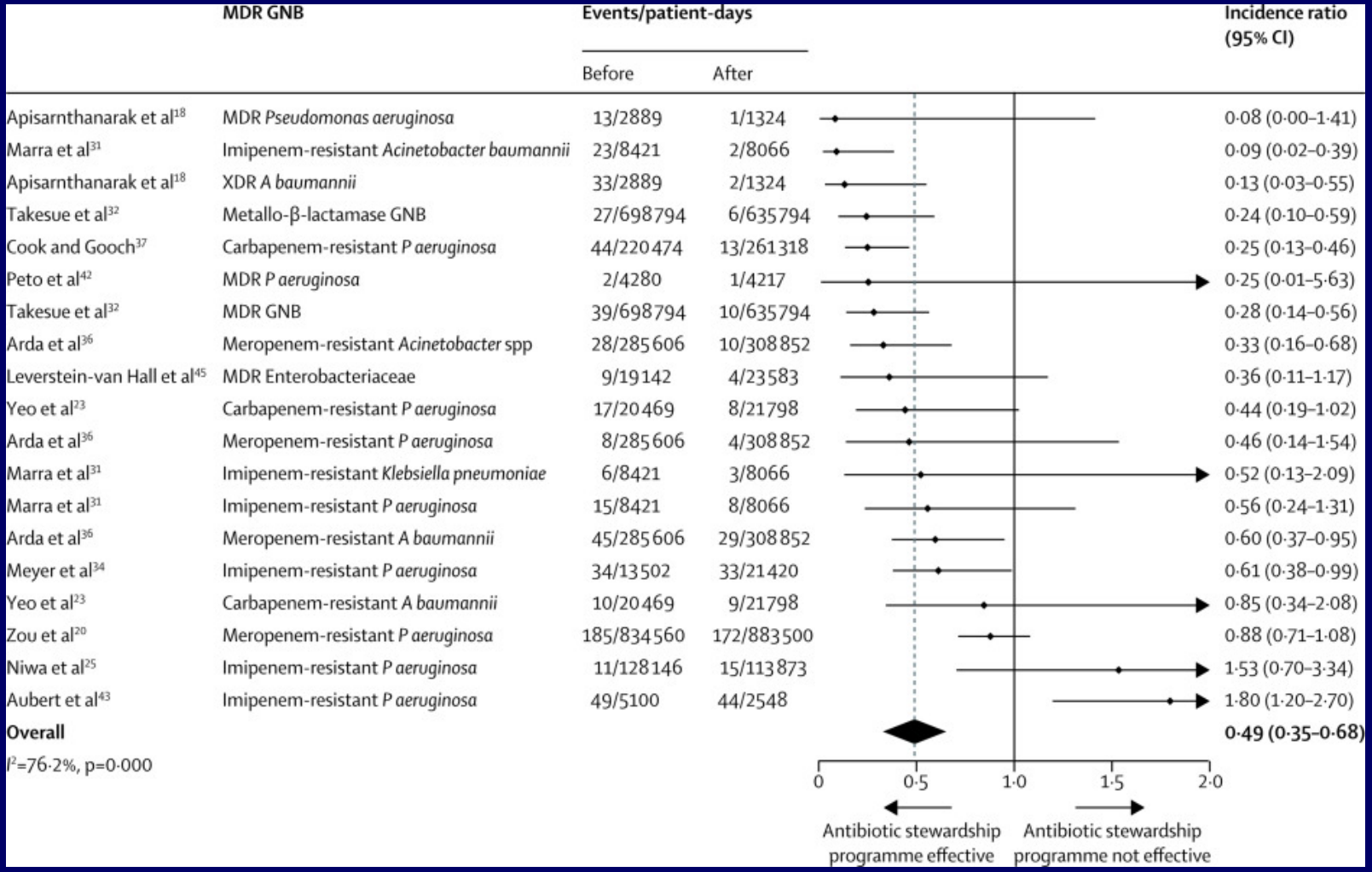
https://www.cdc.gov/getsmart/healthcare/evidence/asp-int-costs.html. Standiford et al. ICHE 2012, 33(4): 338; Seligman SJ. American Journal of Medicine. 1981, 71: 941-944; Archives of Internal Medicine 1988; 148: 1720; Jones et al. ICHE 2012; 33: 362; Bantar, C. et al. Clin Infect Dis 37, 180-6 (2003)

Impact of Antibiotic Stewardship Program Intervention on Other Costs

- Infection and colonization with antibiotic-resistant bacteria, *C. difficile* infection all decreased with antibiotic stewardship
  - Meta analysis
- Adverse Drug Events (ADE)
  - 20% hospitalized patients who receive > 24 hrs abx developed an abx-associated ADE
    - 20% of ADEs attributable to abx prescribed for conditions for which abx not indicated
    - Every 10 days of therapy conferred 3% additional risk of ADE

Baur et al. Lancet Infectious Diseases 2017
Tamma et al. JAMA Internal Medicine 2017

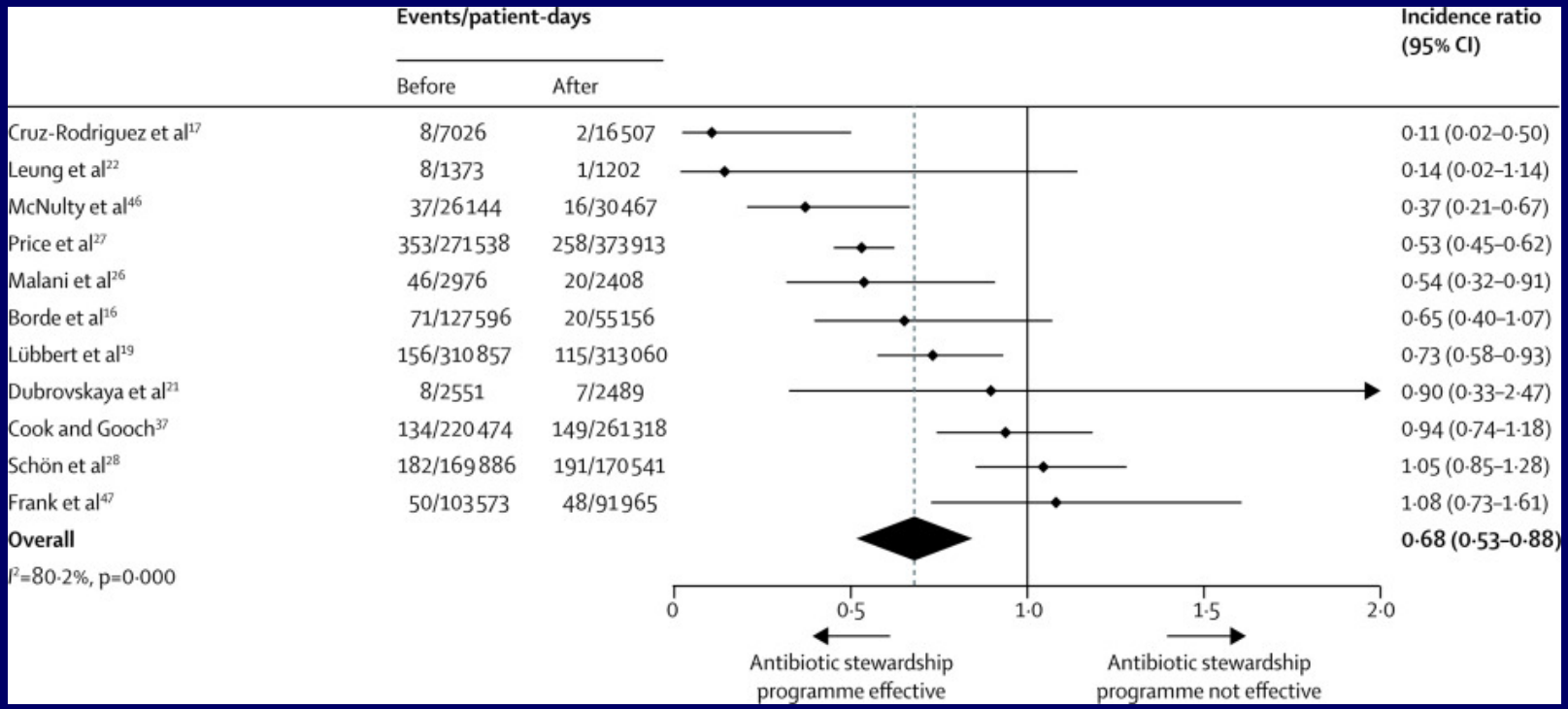
Effect of Antibiotic Stewardship on Incidence of MDR GNB



	MDR GNB	Events/patient-days		Incidence ratio (95% CI)
		Before	After	
Apisarnthanarak et al[18]	MDR *Pseudomonas aeruginosa*	13/2889	1/1324	0·08 (0·00–1·41)
Marra et al[31]	Imipenem-resistant *Acinetobacter baumannii*	23/8421	2/8066	0·09 (0·02–0·39)
Apisarnthanarak et al[18]	XDR *A baumannii*	33/2889	2/1324	0·13 (0·03–0·55)
Takesue et al[32]	Metallo-β-lactamase GNB	27/698794	6/635794	0·24 (0·10–0·59)
Cook and Gooch[37]	Carbapenem-resistant *P aeruginosa*	44/220474	13/261318	0·25 (0·13–0·46)
Peto et al[42]	MDR *P aeruginosa*	2/4280	1/4217	0·25 (0·01–5·63)
Takesue et al[32]	MDR GNB	39/698794	10/635794	0·28 (0·14–0·56)
Arda et al[36]	Meropenem-resistant *Acinetobacter* spp	28/285606	10/308852	0·33 (0·16–0·68)
Leverstein-van Hall et al[45]	MDR Enterobacteriaceae	9/19142	4/23583	0·36 (0·11–1·17)
Yeo et al[23]	Carbapenem-resistant *P aeruginosa*	17/20469	8/21798	0·44 (0·19–1·02)
Arda et al[36]	Meropenem-resistant *P aeruginosa*	8/285606	4/308852	0·46 (0·14–1·54)
Marra et al[31]	Imipenem-resistant *Klebsiella pneumoniae*	6/8421	3/8066	0·52 (0·13–2·09)
Marra et al[31]	Imipenem-resistant *P aeruginosa*	15/8421	8/8066	0·56 (0·24–1·31)
Arda et al[36]	Meropenem-resistant *A baumannii*	45/285606	29/308852	0·60 (0·37–0·95)
Meyer et al[34]	Imipenem-resistant *P aeruginosa*	34/13502	33/21420	0·61 (0·38–0·99)
Yeo et al[23]	Carbapenem-resistant *A baumannii*	10/20469	9/21798	0·85 (0·34–2·08)
Zou et al[20]	Meropenem-resistant *P aeruginosa*	185/834560	172/883500	0·88 (0·71–1·08)
Niwa et al[25]	Imipenem-resistant *P aeruginosa*	11/128146	15/113873	1·53 (0·70–3·34)
Aubert et al[43]	Imipenem-resistant *P aeruginosa*	49/5100	44/2548	1·80 (1·20–2·70)
Overall				**0·49 (0·35–0·68)**
I^2=76·2%, p=0·000				

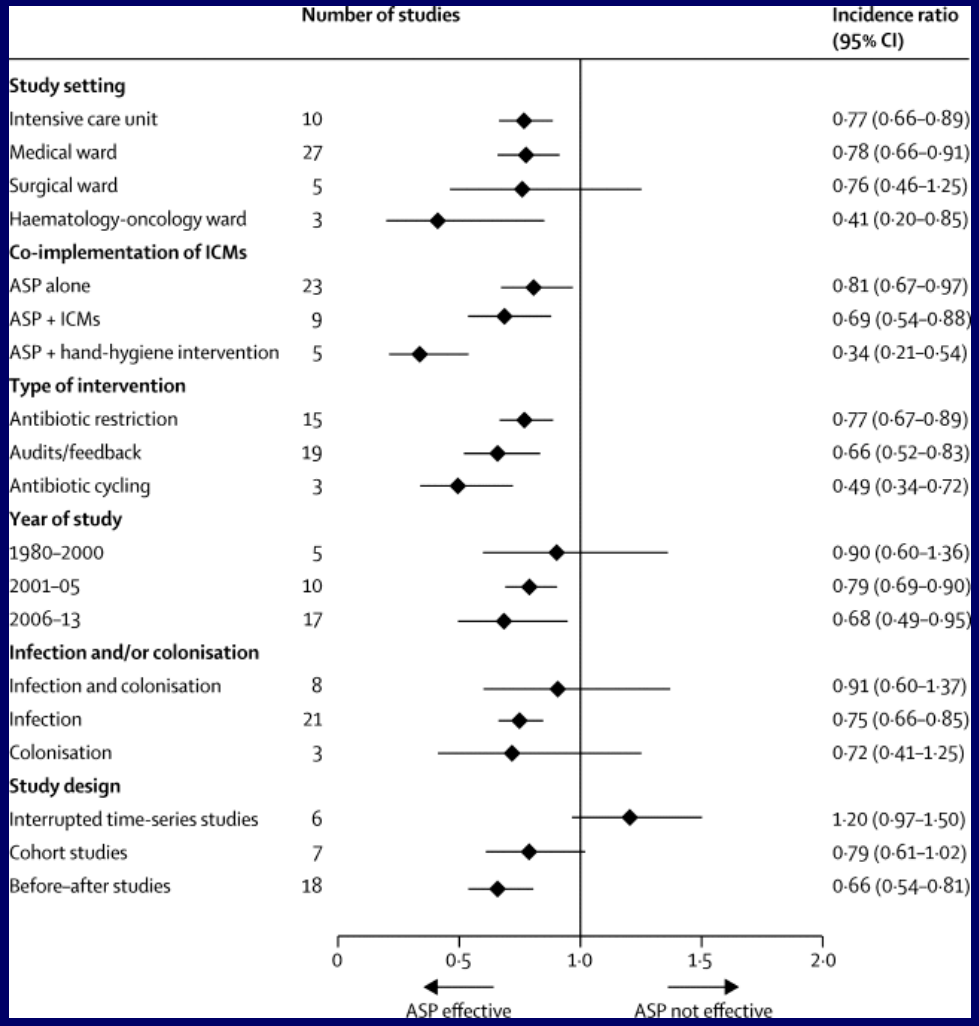
Baur et al. Lancet Infectious Diseases 2017

Effect of Antibiotic Stewardship on Incidence of C. difficile Infections



Baur et al. Lancet Infectious Diseases 2017

Effect of Antibiotic Stewardship on Antibiotic Resistance



Baur et al. Lancet Infectious Diseases 2017

Regulatory Progress: TJC/CMS

Joint Commission Requirement

Official Publication of Joint Commission Requirements

New Antimicrobial Stewardship Standard

Applicable to Hospitals and Critical Access Hospitals

Effective January 1, 2017

Medication Management (MM)

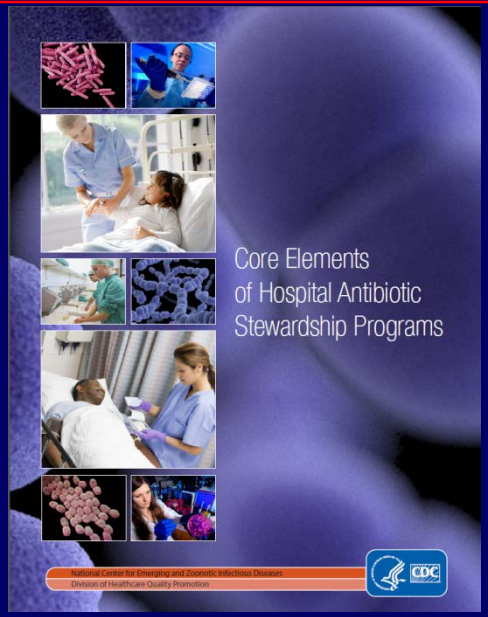
Standard MM.09.01.01
The [critical access] hospital has an antimicrobial stewardship program based on current scientific literature.

Elements of Performance for MM.09.01.01

1. Leaders establish antimicrobial stewardship as an organizational priority. (*See also* LD.01.03.01, EP 5)

   Note: *Examples of leadership commitment to an antimicrobial stewardship program are as follows:*

   - *Accountability documents*
   - *Budget plans*
   - *Infection prevention plans*
   - *Performance improvement plans*
   - *Strategic plans*
   - *Using the electronic health record to collect antimicrobial stewardship data*
2. The [critical access] hospital educates staff and licensed independent practitioners involved in antimicrobial ordering, dispensing, administration, and monitoring about antimicrobial resistance and antimicrobial stewardship practices. Education occurs upon hire or granting of initial privileges and periodically thereafter, based on organizational need.
3. The [critical access] hospital educates patients, and their families as needed, regarding the appropriate use of antimicrobial medications, including antibiotics. (For more information on patient education, refer to Stan-



THELEAPFROGGROUP

Healthcare IT News

TOPICS SIGN UP MA

Proposed CMS rule tackles overuse of antibiotics, aims to boost infection control

New measures could save hospitals up to $284 million annually, officials say.

By Susan Morse | June 15, 2016 | 09:11 AM

SHARE

https://www.hhs.gov/sites/default/files/stenehjem.pdf

Core Elements of Hospital Antibiotic Stewardship Programs

- **Leadership Commitment:**
  - **Dedicating necessary human, financial and information technology resources**

- **Accountability:**
  - **Appointing a single leader responsible for program outcomes**
  - **Experience with successful programs show that a physician leader is effective**

- **Drug Expertise:**
  - **Appointing a single pharmacist leader responsible for working to improve antibiotic use**

https://www.cdc.gov/getsmart/healthcare/implementation/core-elements.html

Core Elements of Hospital Antibiotic Stewardship Programs

- **Action:**
  - **Implementing at least one recommended action, such as systemic evaluation of ongoing treatment need after a set period of initial treatment (i.e. “antibiotic time out” after 48 hours)**
- **Tracking:**
  - **Monitoring antibiotic prescribing and resistance patterns**
- **Reporting:**
  - **Regular reporting information on antibiotic use and resistance to doctors, nurses and relevant staff**
- **Education:**
  - **Educating clinicians about resistance and optimal prescribing**

https://www.cdc.gov/getsmart/healthcare/implementation/core-elements.html

Antibiotic Stewardship Recommendations PACCARB - A One Health Approach

- Implement efforts to promote adoption of antibiotic stewardship in curricula by faculty in colleges of human and veterinary medicine

- Promote a culture of antibiotic stewardship as an integral part of continuing education and clinical practice for practicing providers and professionals
  - Physicians, physician assistants, nurses, nurse practitioners, dentists, pharmacists, health care administrators, and others

https://www.hhs.gov/sites/default/files/paccarb-final-report-03312016.pdf

PACCARB
Antibiotic Stewardship Recommendations

- Ensure development of evidence-based ASPs that are positioned to drive change
- Enlarge and train the ID physician and pharmacist AS workforce
- Enhance collaboration between CMS Quality Improvement Networks and Hospital Engagement Networks and CDC State HAI/AR Prevention Programs
- Increase attention to AS in outpatient settings
- Investigate which educational messages are the most likely to induce behavior change among prescribers and consumers; identify appropriate groups and messengers to deliver the messages
- Ensure sustained funding

https://www.hhs.gov/sites/default/files/paccarb-final-report-03312016.pdf

Continued…

- CDC NHSN survey on national uptake of ASPs
- CDC funding to build core HAI/AR detection and response infrastructure in every state and support State HAI/AR Prevention Programs in up to 25 states
- Continued refinement of CDC NHSN AUR module to collect risk adjusted antibiotic use data
- AHRQ implementation guide for AS in LTCFs
- Active implementation of ASPs in DoD and VA facilities
- Expanded funding to CDC, AHRQ, and NIH for research in development and implementation of interventions to address drivers of the emergence and spread of antibiotic resistance and misuse of antibiotics

https://www.hhs.gov/sites/default/files/paccarb-final-report-03312016.pdf

Research Recommendations

- Fund research on the most effective approaches to perform antibiotic stewardship, to influence and to predict prescriber behavior, and to prevent the spread of antibiotic resistance in acute care, long-term care, and ambulatory settings
- Translate the knowledge gained from research into tools for broad use
- Develop a pipeline of research in this area through funding of investigators to promote a career track in AS/AR activities

Thank You!

- K. Beaulac
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- D. Snydman