

Antibiotic Stewardship

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Disclosures

- None

Learning objectives

- Describe what an antibiotic stewardship program (ASP) does and its benefits
- Learn strategies to use when establishing an ASP
- Identify at least one ASP intervention that could be implemented or enhanced at your facility

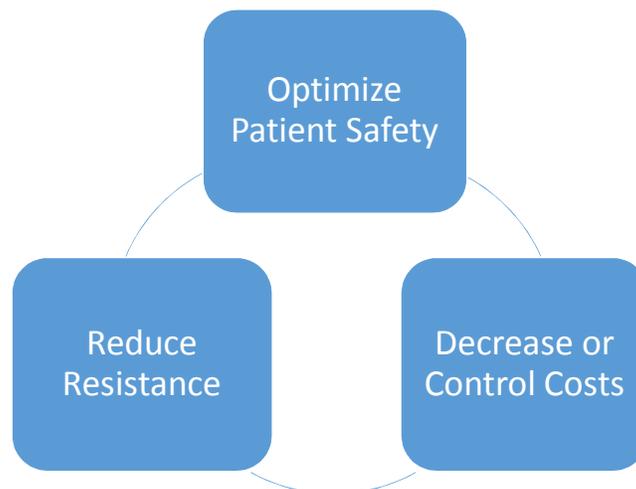
Framing the Issue

- Antibiotics are life-saving agents but their use is not without risks
- Antibiotic use promotes bacterial resistance at the level of the individual patient and of the population
- At least 5% of hospitalized patients experience an adverse reaction
 - Rash
 - Nephrotoxicity
 - *C. difficile* infection
- Very few new antibiotics are being developed

What is Antibiotic Stewardship?

- Coordinated interventions to **improve and measure the appropriate use of antibiotics** by promoting the selection of the optimal antibiotic drug regimen, dose, duration of therapy and route of administration or ensuring every patient gets an antibiotic only when one is needed and if needed, the antibiotic is the right agent at the right dose for the right duration

Goals of Antibiotic Stewardship Programs



National recognition of the need for stewardship

- White House announced a national effort to combat antibiotic resistance in bacteria.
- Three key items released on that day:
 - Report from the President's Council of Advisors on Science at Technology (PCAST)
 - National Strategy for Combatting Antibiotic Resistant Bacteria
 - Executive Order
- Stewardship prominent in all three because it *works*.

The image shows the cover of a report titled "REPORT TO THE PRESIDENT ON COMBATING ANTIBIOTIC RESISTANCE". At the top center is a small gold emblem. Below it, the title is written in blue capital letters. Underneath the title, the text "Executive Office of the President" and "President's Council of Advisors on Science and Technology" is centered. Below that, the date "September 2014" is centered. At the bottom center is the official seal of the Executive Office of the President.

REPORT TO THE PRESIDENT ON COMBATING ANTIBIOTIC RESISTANCE

Executive Office of the President
President's Council of Advisors on
Science and Technology

September 2014



Regulatory agencies are getting on board

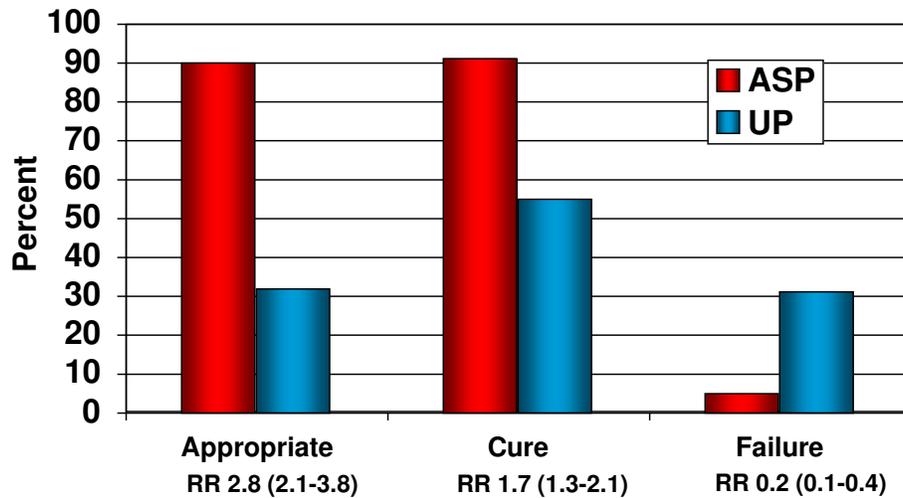
- Centers for Medicare and Medicaid services have proposed a new standard that requires hospitals (and other health facilities like LTCF) to have “policies and procedures for, and to demonstrate evidence of, an active and hospital-wide antibiotic stewardship program” as a Condition of Participation (published 6/16/2016 with a 60-day comment period).

<https://www.federalregister.gov/articles/2016/06/16/2016-13925/medicare-and-medicare-programs-hospital-and-critical-access-hospital-cah-changes-to-promote>

- The Joint Commission a new standard requiring hospitals to have an antibiotic stewardship program to educate, monitor, track and measure antibiotic use. (6/22/2016)

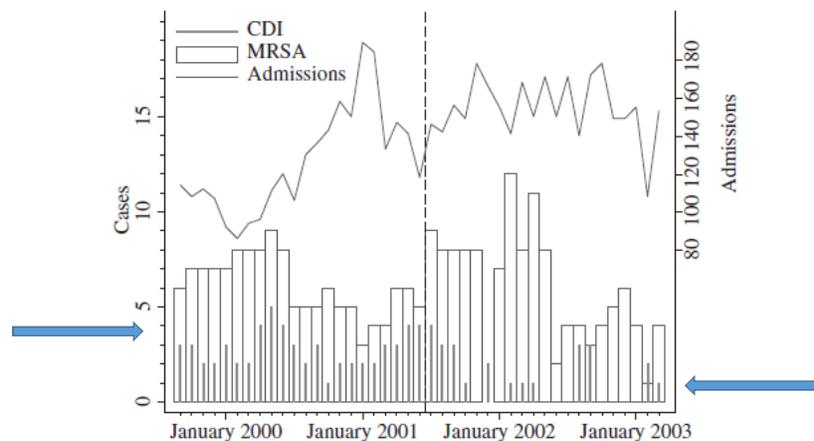
https://www.jointcommission.org/assets/1/6/HAP-CAH_Antimicrobial_Prepub.pdf

Stewardship optimizes patient safety: improved clinical outcomes



Fishman N. Am J Med 2006;119:S53

Stewardship optimizes patient safety: reduce *Clostridium difficile* infections



Fowler S et al. J Antimicrob Chemother. 2007;59:990.

Stewardship reduces antibiotic resistance

	Cipro	Standard
Antibiotic duration	3 days	10 days
LOS ICU	9 days	15 days
Antibiotic resistance/ superinfection	15%	35%

Singh N et al. *Am J Respir Crit Care Med.* 2000;162:505-11.

Stewardship Decreases Costs

Strategy	Type of Institution	Annual Cost Savings
Pre-prescription approval	County teaching hospital	\$803,910
	Tertiary care hospital	\$302,400
Post-prescription review	Tertiary care hospital	Decrease antimicrobial charge per patient (\$1287 vs. \$1873, p<0.04)
	VA hospital	\$145,942
	Community hospital (175 beds)	\$200,000-250,000
	Community hospital (120 beds)	\$177,000
	Argentinean hospital (250 beds)	\$913,236

White AC et al. *Clin Infect Dis.* 1997;25:230-239. Fishman N. *Am J Med.* 2006;119:S53-S61.
 Fraiser GL et al. *Arch Intern Med.* 1997;157:1689-94. Gentry CA et al. *Am J Health Syst Pharm.* 2000;57:268-74.
 LaRocco A. *Clin Infect Dis.* 2003;37:742-3; Bantar C et al. *Clin Infect Dis.* 2003;37:180-6.
 Carling P et al. *Infect Control Hosp Epidemiol.* 2003;24:699-706.

Essential Team Members

Physician

- Role
 - Physician leadership critical as most interactions are with the medical staff
 - Settling disagreements
 - Determining program goals
- Qualifications
 - Ideally trained in infectious diseases
 - Interest in antibiotic use and patient safety
 - Diplomatic and collegial

Pharmacist

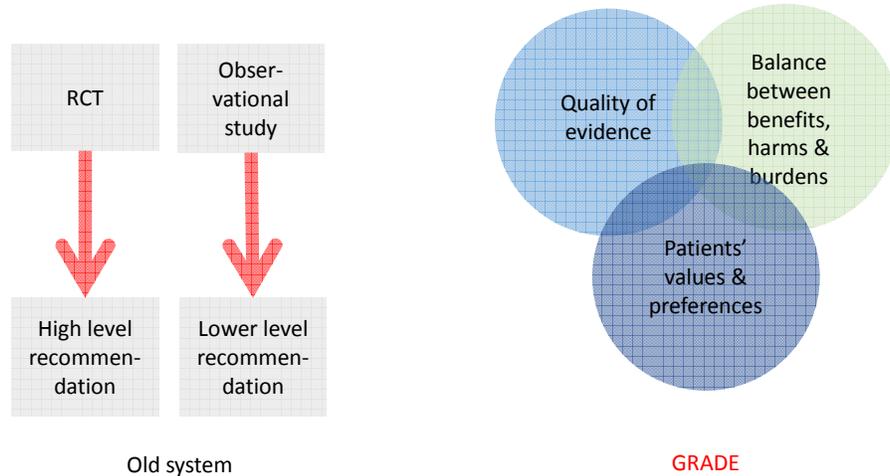
- Role
 - Bridge to pharmacy and other pharmacists
 - Interventions
 - Determining program goals
- Qualifications
 - Same as for physician
 - Comfortable advising physicians and other providers

Referred to: CDC Core elements of hospital antibiotic stewardship programs. 2014 Available from: <http://www.cdc.gov/getsmart/healthcare/pdfs/core-elements.pdf>

A tale of two guidelines

- Former guideline:
 - Dellit TH, Owens RC, McGowan JE et al: IDSA and SHEA Guidelines for Developing an Institutional Program to Enhance Antimicrobial Stewardship (Clinical Infectious Diseases 2007;44:159)
- New guideline:
 - Increase the focus on implementation
 - Expand scope
 - e.g. pharmacologic optimization, the role of microbiology-relevant interventions, and metrics by which to assess program
 - Attempt to improve relevance to all stakeholders
 - Reference special populations, settings
 - <http://cid.oxfordjournals.org/content/62/10/e51.full.pdf+html>

From evidence to recommendations



Slide courtesy of Dr. Yngve Falck-Ytter

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Organization of guideline

- Intervention strategies
- Optimization
- Microbiology
- Measurement
- Special populations

Interventions

- Preauthorization and/or prospective audit and feedback
- Didactic education
- Clinical practice guidelines
- Syndrome-specific ASP
- Interventions to reduce rates of *C. difficile* infection
- Prescriber-led antibiotic review
- Computerized clinical decision support
- Antibiotic cycling and mixing

Interventions

- Preauthorization and/or prospective audit and feedback
- The core of any ASP
 - Include one or both strategies, based on resources for consistent implementation
- Previous guideline preferred PAF over preauthorization, we did not
 - Meta-analysis of restrictive vs persuasive: restrictive worked better and faster on prescribing, CDI, ABR but two strategies became equivalent at 12 months
 - Switch of preauthorization to PAF
 - Increased days of therapy
 - Increased hospital length of stay

Davey et al, Cochrane DSR 2013;4:CD003543
Mehta et al, ICHE 2014;35:1092

Interventions

- Didactic education: Lectures alone are not stewardship. Inappropriate prescribing is often not due to a lack of knowledge. Can be effective when combined with other strategies
- Clinical guidelines: Simple algorithms that direct prescribers towards preferred agents can be very helpful
 - Based on local formulary and resistance pattern

Interventions

Syndrome-specific ASP

- Wanted to emphasize the benefit of this approach
 - Focused
 - Reinforces clinical guidelines and algorithms
 - Improves sustainability
- Possible targets
 - Skin and soft tissue infection (SSTI)
 - Community and nosocomial/ventilator pneumonia (CAP, VAP)
 - Asymptomatic bacteriuria
 - Positive sterile site cultures (primarily blood cultures)

Interventions

Clostridium difficile

- One of the top three most urgent threats in the 2013 CDC report on antibiotic resistance
 - CDC "Antibiotic Resistance Threats in the United States. 2013," available at <http://www.cdc.gov/drugresistance/threat-report-2013/>
- A consideration of CDI should be incorporated when crafting interventions

Optimization

- Dedicated pharmacokinetic monitoring and adjustment program
- Pharmacokinetic/Pharmacodynamic (PK/PD)-driven dosing schemes
- IV to PO
- Addressing history of antibiotic allergy (penicillin)
- Duration of therapy

Optimization

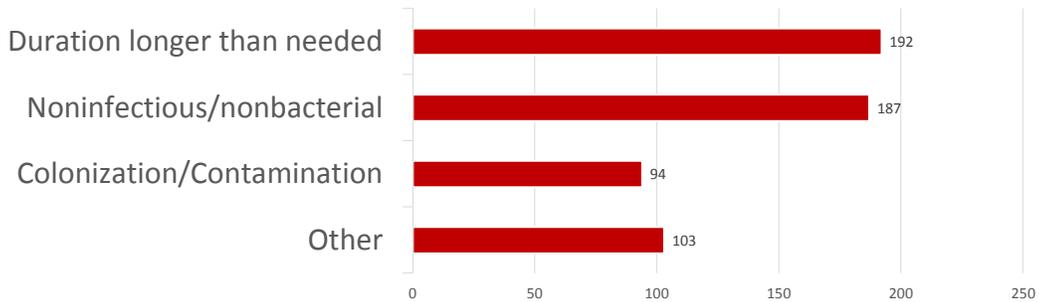
- Many interventions incorporated into routine pharmacy activities
 - Gentamicin, vancomycin monitoring
 - IV to PO
 - ASP input more appropriate when an IV agent does not have an oral formulation
 - Alternative dosing based on PK/PD principles
 - Once daily dosing for Ags
 - Extended infusion β -lactam antibiotics – limited data, may improve outcomes or adverse effects but inadequate evidence. However, it will save money on antibiotic costs
- Allergy testing – can enhance use of first-line agents
 - Collaboration with allergists

Optimization

- Duration of therapy
 - Important ASP activity
 - Incorporate into clinical guidelines, interventions
 - RCTs, prospective studies
 - VAP
 - CAP
 - SSTIs
 - Intra-abdominal abscess
 - Pyelonephritis

Duration and inappropriate use

Days of unnecessary antibiotic therapy
576/1941 days of therapy (30%)



Hecker et al, Unnecessary use of antimicrobials in hospitalized patients. Arch Intern Med 2003;163:972

Microbiology

- Antibiograms – stratification, unit- or site-specific, adult vs pediatrics
- Susceptibility-reporting strategies-censoring broad-spectrum agents when narrow-spectrum agents are active
- Molecular testing for respiratory pathogens-influenza, comprehensive respiratory panels
- Rapid diagnostics for blood specimens
- Procalcitonin use to reduce / improve antimicrobial use
- Fungal markers

Rapid testing

- PNA-FISH: peptide nucleic acid fluorescence in situ– Staphylococci, Enterococci, Candida species
- PCR: available for many organisms e.g. MRSA/*S. aureus*, pan-fungal PCR, *C. difficile*, multiplex PCR
 - PCR results in 1-2 hours; can give information on resistance, can rapidly identify fastidious bacteria, fungi
- Matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF) identifies bacteria, mycobacteria and yeast from a single agar colony in minutes

ASP implications

- Can help micro prioritize which tests to institute
- ASP involvement can maximize benefit.
 - PCR
 - Significant reduction in time to appropriate therapy – less unnecessary MRSA therapy; faster β -lactam therapy for MSSA (initiation 5.2 h vs 49.8 h) Parta et al ICHE 2010;31:1043
 - Good results with ASP Bauer et al CID 2010;51:1074 but same results not seen without ASP Carver et al J Clin Micro 2008;46:2381
 - RCT with rapid multiplex PCR with either templated comments or real-time ASP audit and feedback in addition to templated comments resulted in decreased broad-spectrum and increased narrow-spectrum β -lactam use compared with control
 - Time to appropriate de-escalation or escalation was shortest when ASP was involved Banerjee et al CID 2015;61:1071

Procalcitonin

- Procalcitonin
 - Released in response to bacterial toxins and mediators
 - Correlation between PCT and extent or severity of infection
 - Increases within hours of infection and decreases when infection is controlled
- Respiratory tract infections: can reduce initiation of antibiotics and duration without adversely impacting outcomes Schuetz et al JAMA 2009;302:1059
- Sepsis: did not reduce antibiotic initiation but duration was significantly lessened without a change in mortality or recurrence of infection. Nobre et al Am J Respir Crit Care Med 2008;177:498

Measurement

- Days of therapy (DOT) vs defined daily dosing (DDD)
- Measuring expenditures
- Targeted interventions
 - Cellulitis
 - Urinary tract infections and asymptomatic bacteruria
 - Community-acquired pneumonia

Measurement

- DOT not impacted by dose adjustments
- Useful in both adult and pediatrics
- CDC will use DOT for antibiotic usage reporting
- DDD does not require patient-level data as does DOT and may be only option for many facilities
- Still a useful way to measure overall use, specific use by unit, provider or hospital service

Measurement

- Antibiotic costs ideally measured based on prescriptions or actual administrations rather than by purchasing data and normalized by patient census
- Cost savings wane as ASP continues so must measure what the costs would be in the absence of the ASP intervention and compare to the actual costs with the intervention.

Possible Metrics for syndrome-specific ASP interventions

Process Measures

Excess days of therapy (i.e., unnecessary days of therapy avoided based on accepted targets and benchmarks)

Duration of therapy

Proportion of patients compliant with facility-based guideline or treatment algorithm

Proportion of patients with revision of antibiotics based on microbiology data

Proportion of patients converted to oral therapy

Outcome Measures

Hospital length of stay

30-day mortality

Unplanned hospital readmission within 30 days

Proportion of patients diagnosed with hospital-acquired CDI or other adverse events related to antibiotic treatment

Proportion of patients with clinical failure (e.g., need to broaden therapy, recurrence of infection)

Special populations

- ASP for cancer patients
 - Clinical pathway guidelines for fever and neutropenia
 - Antifungal clinical pathways
 - De-escalation in persistently neutropenic patients
- ASP for Neonatal ICUs
- ASP in long-term care facilities
- ASP for terminally ill patients with pneumonia

Closing comments

- We sought to create a guideline more focused on practical aspects of implementation of ASP
- We did not create a tiered list of interventions
 - Each site must decide what will work for them
 - The comments for each PICO was intended to give more context for those choices

Acknowledgments

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- | | |
|-----------------------------------|---------------------|
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