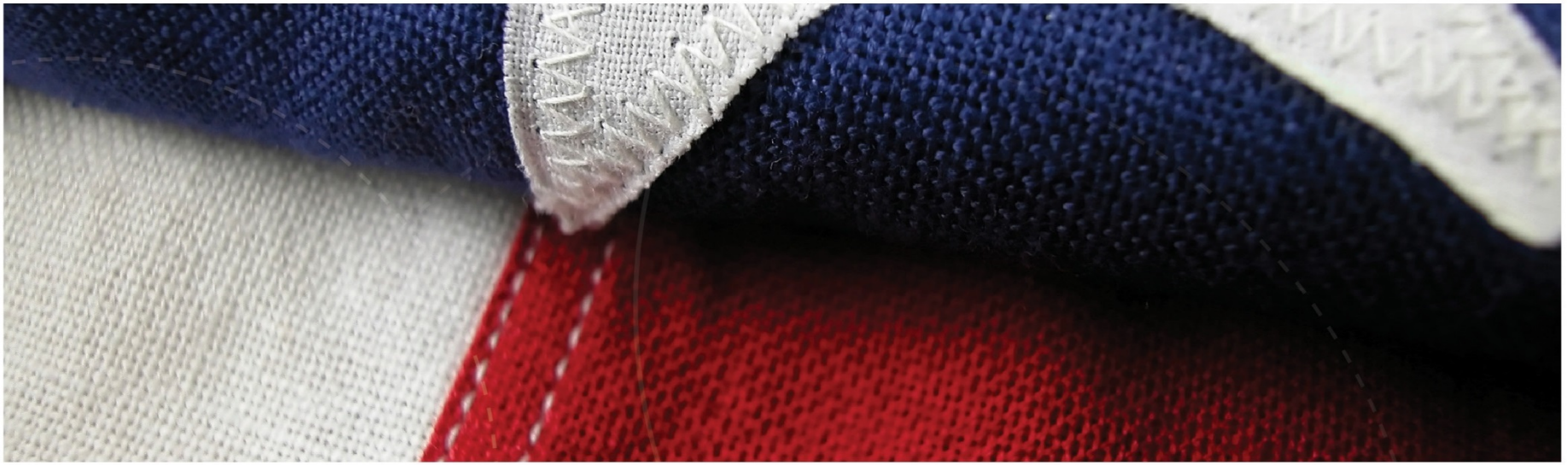

Optimizing Antimicrobial Stewardship Activities Based on Institutional Resources

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Disclosures

- **No disclosures to report**

Learning Objectives

- **Discuss key components of successful antimicrobial stewardship programs**

- **Compare and contrast stewardship activities based on resources available to a hospital**

Antimicrobial Stewardship Definition

"Coordinated interventions designed to improve and measure the appropriate use of antibiotic agents by promoting the selection of the optimal antibiotic drug regimen including dosing, duration of therapy, and route of administration"

Infect Control Hosp Epidemiol 2012;33:322-7.

Goals of Antimicrobial Stewardship

- Primary
  - To optimize clinical outcomes while minimizing unintended consequences of antimicrobial use, including toxicity, the selection of pathogenic organisms (such as *Clostridium difficile*), and the emergence of resistance

- Secondary
  - To improve rates of susceptibilities to targeted antimicrobials
  - To optimize resource utilization

Clin Infect Dis 2007;44:159-77.
Clin Infect Dis 2016;62(10):e51-77.

CDC Core Elements of Hospital Antimicrobial 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

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

CDC Core Elements of Hospital Antimicrobial 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

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

What is the current status of ASPs in the United States?

Antibiotic stewardship programs in U.S. acute care hospitals: findings from the 2014 National Healthcare Safety Network (NHSN) Annual Hospital Survey

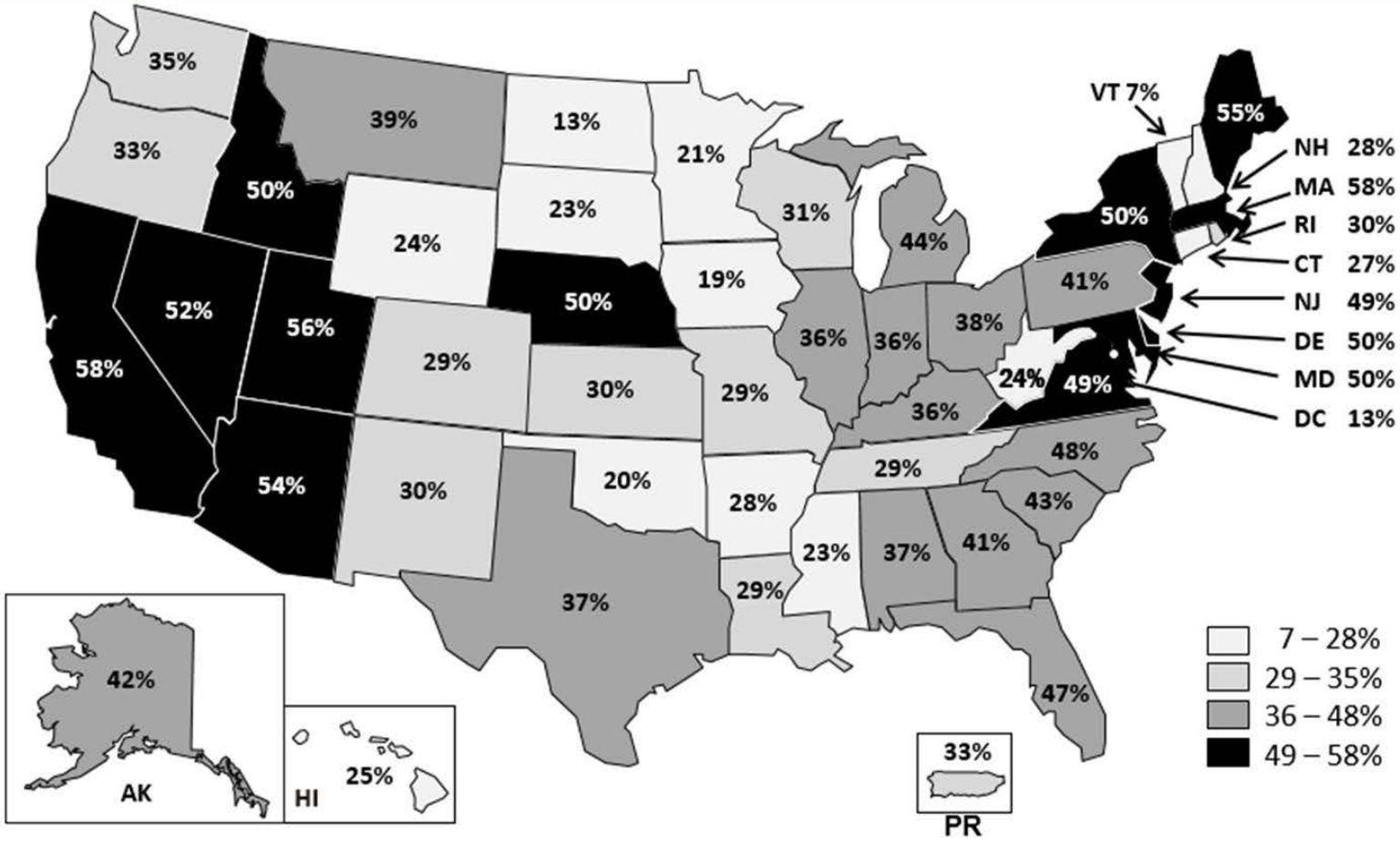
- Analyzed 2014 NHSN Annual Hospital Survey to describe ASPs in U.S. acute care hospitals as defined by the CDC's Core Elements for Hospital Antibiotic Stewardship Programs
- Among 4,184 U.S. hospitals, 39% reported having comprehensive ASPs that met all 7 CDC defined core elements
- Major teaching hospitals (54%) were more likely to have comprehensive ASPs compared to hospitals with undergraduate education or no teaching affiliation (34%)
- Written support (RR 7.2; 95% CI, [6.2-8.4]) or salary support (RR 1.5; 95% CI, [1.4-1.8]) were significantly associated with having a comprehensive ASP

Clin Infect Dis 2016;63(4):443-9.

U.S. Acute Care Hospitals Reporting Implementation of CDC Core Elements

Core Element	Number of Facilities (N=4,184)	%
Infrastructure	**2,298**	**54.9**
Leadership Commitment	2,508	59.9
Accountability	3,016	72.1
Drug Expertise	3,648	87.2
Implementation	**2,112**	**50.5**
Action	3,926	93.8
Tracking	3,318	79.3
Reporting	2,822	67.5
Education	2,589	61.9
Hospitals reporting all 7 core elements	**1,642**	**39.2**

Clin Infect Dis 2016;63(4):443-9.



Clin Infect Dis 2016;63(4):443-9.

IDSA/SHEA Guidelines on Implementing an Antibiotic Stewardship Program

- Recommendation Categories
  - **Interventions**
  - **Optimization of Antibiotic Administration**
  - Microbiology and Laboratory Diagnosis
  - **Measurement and Analysis**
  - Antibiotic Stewardship in Special Populations

Clin Infect Dis 2016;62(10):e51-77.

Interventions
Preauthorization and/or Prospective Audit and Feedback

- **Preauthorization**
  - Strategy to improve antibiotic use by requiring clinicians to get approval for certain antibiotics before they are prescribed

- **Prospective Audit and Feedback (PAF)**
  - An intervention that engages the provider after an antibiotic is prescribed

Clin Infect Dis 2016;62(10):e51-77.

Preauthorization Advantages	PAF Advantages
Reduces initiation of unnecessary/ inappropriate antibiotics	Can increase visibility of antimicrobial stewardship program and build collegial relationships
Optimizes empiric choices and influences downstream use	More clinical data available for recommendations, enhancing uptake by prescribers
Prompts review of clinical data/prior cultures at the time of initiation of therapy	Greater flexibility in timing of recommendations
Decreases antibiotic costs, including those due to high-cost agents	Can be done on less than daily basis if resources are limited
Provides mechanism for rapid response to antibiotic shortages	Provides educational benefit to clinicians
Direct control over antibiotic use	Prescriber autonomy maintained
	Can address de-escalation of antibiotics and duration of therapy

Clin Infect Dis 2016 ;62(10):e51-77.

Preauthorization Disadvantages	PAF Disadvantages
Impacts use of restricted agents only	Compliance voluntary
Addresses empiric use to a much greater degree than downstream use	Typically labor-intensive
Loss of prescriber autonomy	Success depends on delivery method of feedback to prescribers
May delay therapy	Prescribers may be reluctant to change therapy if patient is doing well
Effectiveness depends on skill of approver (ID Pharmacist + ID Physician vs. ID Fellows)	Identification of interventions may require information technology support and/or purchase of computerized surveillance systems
Real-time resource intensive	May take longer to achieve reductions in targeted antibiotic use
Potential for manipulation of system (i.e. presenting request in a biased manner to gain approval)	
May simply shift to other antibiotic agents and select for different antibiotic-resistance patterns	

Clin Infect Dis 2016 ;62(10):e51-77.

Preauthorization and/or Prospective Audit and Feedback

- Preauthorization, PAF, or a combination of those strategies, implementation should serve as the foundation of a comprehensive ASP
- Effective implementation requires the support of hospital administration, allocation of necessary resources for a **persistent effort** by dedicated, well-trained personnel, and ongoing communication with clinicians
- **IDSA/SHEA recommends preauthorization and/or prospective audit and feedback over no such interventions** (strong recommendation, moderate-quality evidence)

Clin Infect Dis 2016 ;62(10):e51-77.

Didactic Education on Antimicrobial Stewardship

- Education is a common tool for ASPs either through didactic lectures or distribution of pamphlets and materials
  - Should include all healthcare disciplines: students, trainees and practitioners
- Education alone can result in unsustainable improvements in antibiotic prescribing
- Most likely effective when combined with other ASP strategies like PAF
- **IDSA/SHEA suggests against relying solely on didactic educational materials for stewardship** (weak recommendation, low quality evidence)

Clin Infect Dis 2016 ;62(10):e51-77.

Facility-Specific Clinical Practice Guidelines for Common Infectious Diseases Syndromes

- Implementation of facility specific clinical practice guidelines can lead to substantial changes in antibiotic use
  - Most evidence in CAP and HAP
  - Interdisciplinary development
  - Dissemination to providers via multiple routes: electronic and hard copies, education, peer champions, PAF, electronic order sets
- Improvements seen with implementation of facility specific guidelines
  - Increase in appropriate initial therapy, use of narrower-spectrum agents, early IV to PO switch, shorter duration of treatment
  - No adverse effects on clinical outcomes

Clin Infect Dis 2016 ;62(10):e51-77.

Michael E. DeBakey Veterans Affairs Medical Center (MEDVAMC) Multispecialty Recommendations for the Diagnosis and Management of Osteomyelitis in the Diabetic Foot

Introduction

Patients with diabetes mellitus comprise at least 70% of the population who experiences non-traumatic limb loss in this country.[1] In addition to the high excess medical costs associated with amputations, limb loss impairs mobility and ability to live independently, and decreases quality-of-life (see review[2]). Efforts at limb preservation not only provide improved outcomes but also cost savings.[3]

A compromised skin barrier is the portal-of-entry for direct bacterial inoculation of the foot. The development of an foot ulcer or other chronic foot wound precedes 85% of above-ankle amputations, and so the occurrence of a foot ulcer has been referred to as a "sentinel event".[4] **Foot ulcers in ambulatory patients – *regardless of the chronicity of the wound or whether acute infection is present* – merit efforts to achieve wound healing (i.e. full re-epithelialization) to reduce the risk of limb loss.**

Three main risk factors have a well-established role in the development of foot ulcers:

1. Patients with diabetes mellitus often develop characteristic **structural abnormalities** of the foot, including prominent metatarsal heads, valgus deviation of the first toe and "hammer toes". These abnormalities often result in an abnormal distribution of pressure on the plantar aspect of the foot during the gait cycle and ulcer formation from repetitive trauma to various parts of the foot.

2. Patients with diabetes mellitus often develop **sensory neuropathy**, also referred to as "loss of protective sensation." This impairs the normal pain response to skin breakdown and lessens the likelihood diabetic patients will notice chronic repetitive trauma and the development of a foot ulcer.

3. Patients with diabetes mellitus have a high prevalence of **peripheral arterial disease**. This characteristically happens at the level of the popliteal and tibial arteries.[5,6] (NOTE: "small vessel disease" or "microvascular disease" is NOT thought to play a causal role in the development of foot ulcers or limb loss; see review[7]). Moderate to severe peripheral arterial disease results in a degree of tissue perfusion that is often adequate for successful wound healing.

Facility-Specific Clinical Practice Guidelines for Common Infectious Diseases Syndromes

- Sustainability of the effects of guideline development are not well established
- Interventions to maintain guideline adherence over time may be needed and outcomes monitored
- **IDSA/SHEA suggest ASPs develop facility-specific clinical practice guidelines coupled with a dissemination and implementation strategy** (weak recommendation, low-quality evidence)

Clin Infect Dis 2016 ;62(10):e51-77.

Reassessment of Antimicrobial Therapy

- Common strategies include antibiotic timeouts and antibiotic automatic stop orders at 48-72 hours of therapy to prompt clinicians to re-evaluate current antibiotic therapy
- Clinicians may require additional prompting from pharmacy or the ASP to comply with these interventions
- Mechanisms should be in place to prevent unintended interruptions in therapy if automatic stop orders are used
- **IDSA/SHEA suggest the use of strategies (eg, antibiotic time-outs, stop orders) to encourage prescribers to perform routine review of antibiotic regimens to improve antibiotic prescribing** (weak recommendation, low-quality evidence)

Clin Infect Dis 2016 ;62(10):e51-77.

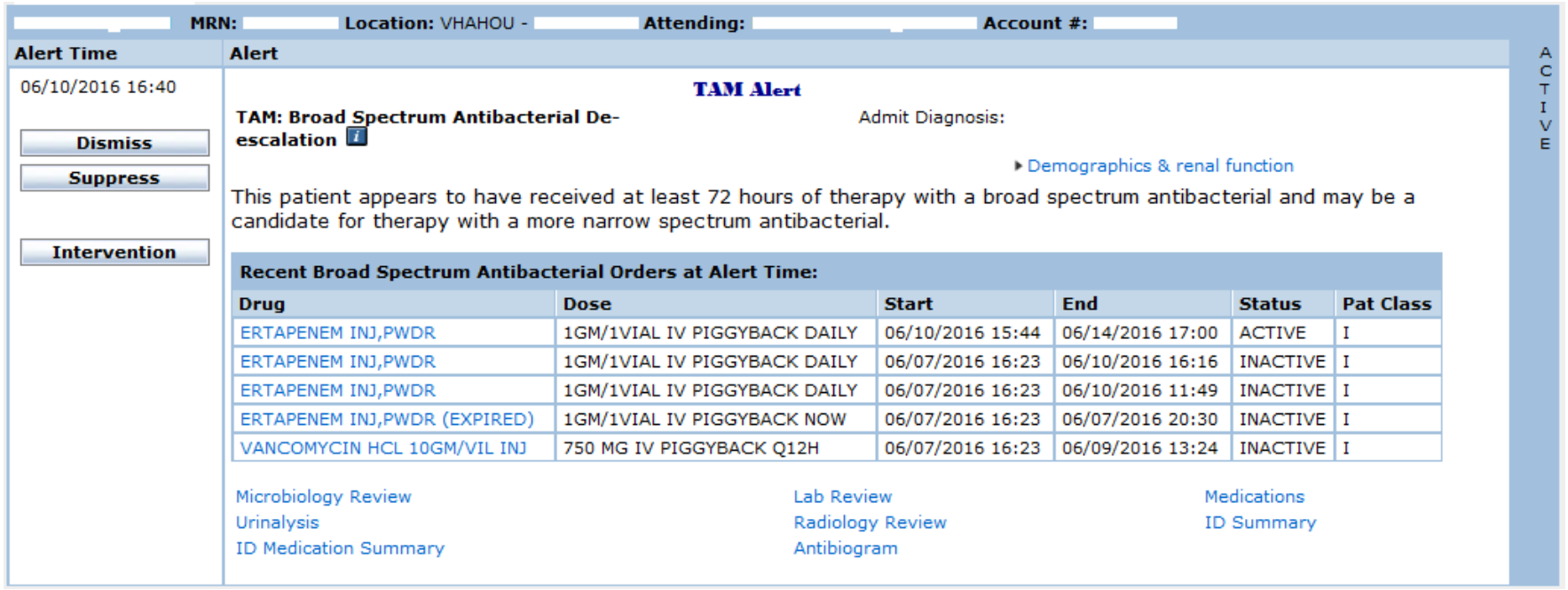
Principles of an Antibiotic Time Out

An Antibiotic Timeout offers the opportunity to modify therapy based upon the clinical course of the patient and preliminary and/or final microbiology results

- This information may lead to one of the following assessments:
  - **An infection requiring antibiotic therapy is no longer present**
  - The patient may have clinically improved to such an extent that **oral antimicrobial therapy can be substituted for parenteral therapy**
  - The infecting micro-organism may be susceptible to an antibiotic that has a more **narrow spectrum or activity** and/or a less toxic antibiotic
  - The infecting micro-organism may be **resistant to the initially selected therapy and require therapy with an antibiotic with enhanced activity**

Slide courtesy of Dr. Chris Graber.

TheraDoc Broad Spectrum De-escalation Alert



Optimization of Antibiotic Administration
Increased Use of Oral Antibiotics (IV to PO)

- Associated with reduced drug costs and hospital length of stay without adverse effects on efficacy or safety
  - Avoidance of IV catheters and associated complications (infection, thrombosis)
- Mandatory Infectious Diseases consultation for Outpatient Parenteral Antimicrobial Therapy has also been shown to facilitate IV to PO conversion or discontinuation of antimicrobial therapy
- IV to PO conversion should be incorporated into routine pharmacy activities
  - Automatic vs. Discussion with Provider
- **IDSA/SHEA recommend ASPs implement programs to increase both appropriate use of oral antibiotics for initial therapy and the timely transition of patients from IV to oral antibiotics** (strong recommendation, moderate-quality evidence)

Clin Infect Dis 2016 ;62(10):e51-77.

MEDVAMC Antimicrobial IV to PO Conversion Criteria

Eligibility Criteria *(pt must meet criteria for ≥ 24 hours)*		
Receiving IV antibiotics	Azithromycin Ciprofloxacin Clindamycin Doxycycline Fluconazole Levofloxacin	Linezolid Metronidazole Minocycline Moxifloxacin Rifampin Trimethoprim/Sulfamethoxazole
Functioning GI tract	Tolerating meds via oral or enteral route, food or enteral feeds	
Hemodynamically stable	HR <100, SBP >90mmHg, RR ≤ 20	
Clinical improvement	T <100°F or <37.7°C, WBC normal/ downtrending	

Exclusion Criteria	
Severe infection	neutropenic fever, CNS infection, endocarditis, fungemia, *Staph aureus* bacteremia, undrained abscess/empyema)
Oral route unavailable/ unreliable	active NPO order, severe N/V, receiving anti-emetics, severe diarrhea, mucositis, malabsorption, ileus, vasopressor therapy, TPN within last 72 hrs, active GI bleed

Dosing Conversions		
Drug	**IV Dose**	**PO Dose**
Azithromycin	500 mg q24h	500 mg or 250 mg q24h *(consult package insert)*
Ciprofloxacin	400 mg q8h 400 mg q12h 200 mg q12h	750 mg q12h 500 mg q12h 250 mg q12h
Clindamycin	600 mg q8h	300-450 mg q8h
Trimethoprim/Sulfamethoxazole (dosing is Trimethoprim component)	320 mg q12h 160 mg q12h	320 mg q12h (2 DS tabs q12h) 160 mg q12h (1 DS tab q12h)
Antibiotics w/ equivalent IV and PO dosing	doxycycline, fluconazole, levofloxacin, linezolid, metronidazole, minocycline, moxifloxacin, rifampin	

Oral/Enteral Administration Considerations		
Drug	**With or without food**	**Chelation medication interaction**
Azithromycin	With or without food. Increased tolerability w/ food	Avoid simultaneous administration
Ciprofloxacin[a]	Give w/ liberal fluids with or without food; should not be taken with dairy products or calcium-fortified juices alone	Administer ciprofloxacin 2 hours before or 6 hours after
Clindamycin	Give w/ full glass of water, with or without food	
Doxycycline[b], Minocycline[c]	Give w/ adequate fluids. If GI irritation occurs, may be given w/ food or milk	Absorption decreased, no specific recommendations
Fluconazole	With or without food	
Levofloxacin[a]	Solution 1 hour before or 2 hours after eating Tablet with or without food	Administer levofloxacin 2 hours before or 2 hours after
Linezolid	With or without food. Avoid foods/drinks w/ tyramine	Administer moxifloxacin 4 hours before or 8 hours after
Metronidazole[c]	With or without food	
Moxifloxacin[a]	With or without food	
Rifampin	1 hour before or 2 hours after a meal w/ full glass of water	Administer rifampin 1 hour before or 2 hours after
Trim/ Sulfa	Give with adequate fluids, with or without food	
Enteral administration	Solutions preferred over tablets; if tablet, must be able to be crushed (not XR or enteric coated) [a]Avoid recommending fluoroquinolones for enteral administration; [b]Doxycycline supplied as a capsule, avoid recommending; [c]Should not be crushed due to slow release	

Reducing Antibiotic Therapy to the Shortest Effective Duration

- Recommendations on duration of therapy can be incorporated into other ASP interventions such as during preauthorization or PAF, education, institutional guidelines or CDSS
- **IDSA/SHEA recommend that ASPs implement guidelines and strategies to reduce antibiotic therapy to the shortest effective duration** (strong recommendation, moderate-quality evidence)

Clin Infect Dis 2016 ;62(10):e51-77.

Measurement and Analysis

Overall Measures to Reflect Impact of ASPs and Interventions

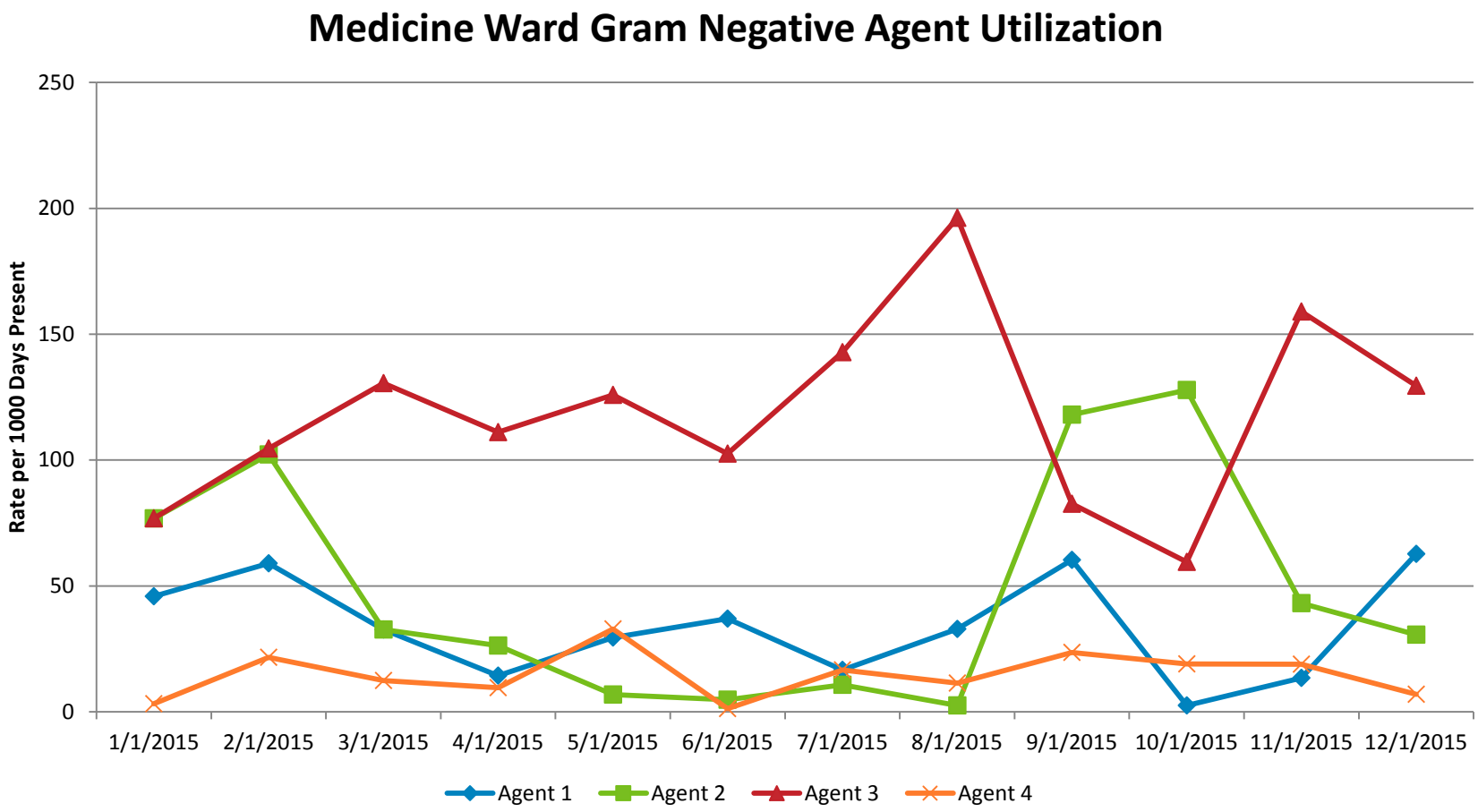
- **Defined Daily Dose (DDD)**
  - WHO definition: Assumed average maintenance dose per day for a drug used for its main indication in adults
  - Total number of grams of antibiotic used divided by DDD gives an estimate of number of days of antibiotic therapy
  - Expressed as DDD per 1000 patient days for benchmarking
- **Days of Therapy (DOT)**
  - Administration of a single agent on a given day regardless of the number of doses administered or dosage strength
  - Expressed as DOT per 1000 patient days for benchmarking

Clin Infect Dis 2007;44:664-70.

CDC NHSN Antimicrobial Use Option

- Provides analysis of antimicrobial utilization data submitted by individual institutions
- Allows institutions to conduct inter- and intra-facility benchmarking of antimicrobial utilization (reported as DOT per 1000 days present)
- Can get utilization for a specific drug administered by a specific route on a specific ward (i.e. Vancomycin IV usage in the MICU)
- Standardized Antimicrobial Administration Ratios (SAAR) are an observed to expected ratio of antimicrobial utilization for a specific category of drugs (i.e. Anti-MRSA Agents)

http://www.cdc.gov/nhsn/acute-care-hospital/aur/index.html


Medicine Ward Gram Negative Agent Utilization
Rate per 1000 Days Present
250
200
150
100
50
0
1/1/2015
2/1/2015
3/1/2015
4/1/2015
5/1/2015
6/1/2015
7/1/2015
8/1/2015
9/1/2015
10/1/2015
11/1/2015
12/1/2015
Agent 1
Agent 2
Agent 3
Agent 4

National Healthcare Safety Network

SAARs Table - All Standardized Antimicrobial Administration Ratios (SAARs) High-Level Indicators and High-Value Targets

As of: November 17, 2015 at 3:10 PM

Date Range: All AU_SAAR

SAAR title

All antimicrobials used in adult ICUs and wards

Denominator

Facility Org ID	Summary Yr/Qtr	SAAR Type	Antimicrobial Days	Predicted Antimicrobial Days	Days Present	SAAR	SAAR p-value	95% Confidence Interval
13860	2014Q1	IND-Adult-1	4416	4421.364	6326	0.999	0.9437	0.970, 1.029
13860	2014Q2	IND-Adult-1	3998	3856.677	5668	1.037	0.0240	1.005, 1.069
13860	2014Q3	IND-Adult-1	3568	3952.912	5765	0.903	0.0000	0.873, 0.933
13860	2014Q4	IND-Adult-1	6835	5731.061	9247	1.193	0.0000	1.165, 1.221
13860	2015Q1	IND-Adult-1	4060	3113.877	5358	1.304	0.0000	1.264, 1.344

Observed Use

Predicted Use

Calculated SAAR Values

Includes data for January 2014 and forward.

Data restricted to medical, medical/surgical and surgical locations.

Source of aggregate data: 2014 NHSN AU Data

Data contained in this report were last generated on November 11, 2015 at 5:57 PM.

http://www.cdc.gov/nhsn/acute-care-hospital/aur/index.html

Overall Measures to Reflect Impact of ASPs and Interventions

- **IDSA/SHEA suggest monitoring antibiotic use as measured by DOTs in preference to DDD** (weak recommendation, low-quality evidence)
- Data on antimicrobial use should be shared with clinicians to inform them of their practices and monitor adherence to institutional guidelines and procedures
- Rates of *C. difficile* infection or antibiotic resistance are complex metrics that can be influenced by factors other than antimicrobial stewardship (patient population, infection control procedures, pathogen and host factors) but can be assessed as **secondary outcome measures**

Clin Infect Dis 2007;44:664-70.

Conclusion

- Antimicrobial Stewardship Programs should be multidisciplinary and include ID Physicians, ID Pharmacists, Infection Control Practitioners and Clinical Microbiologists among others
- Either Preauthorization or Prospective Audit and Feedback should be utilized as the primary mode of antimicrobial restriction
- Antibiotic timeouts for re-evaluation and de-escalation of current antimicrobial therapy at 48-72 hours should be encouraged of all providers

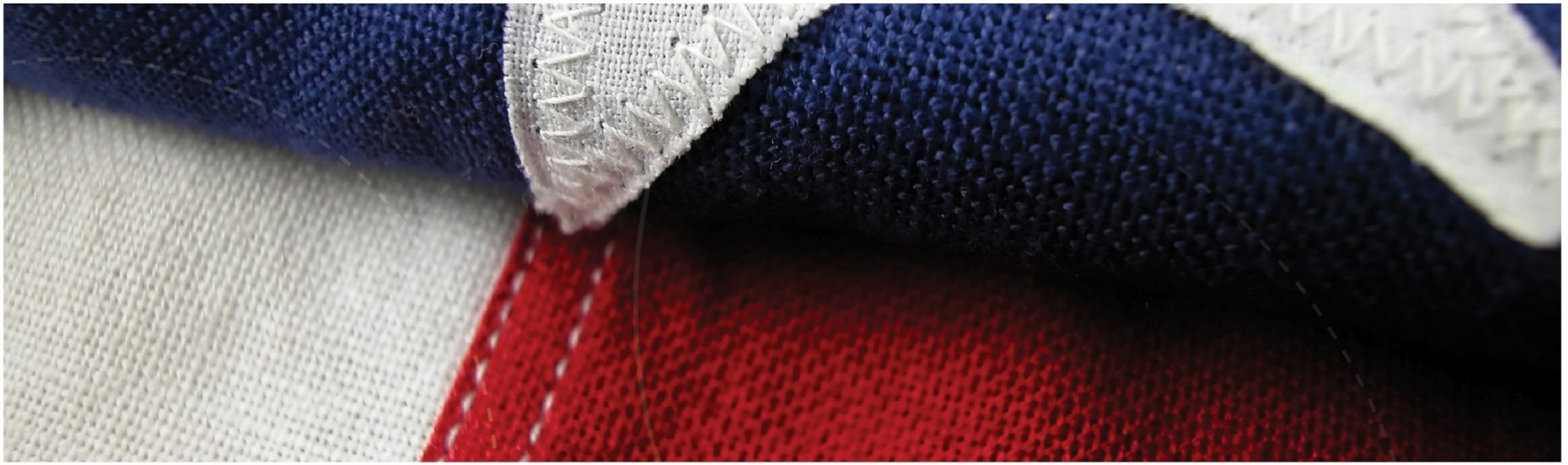
Conclusion

- Antimicrobial Utilization should be tracked and reported as feedback to clinicians on their prescribing practices and adherence to Antimicrobial Stewardship Program guidelines
- Education about Antimicrobial Stewardship should be incorporated into multiple interventions and provided to every clinician and trainee to reinforce Antimicrobial Stewardship Program guidelines
- Tailor the activities of the Antimicrobial Stewardship Program at your institution to include a mixture of more resource intensive (Preauthorization/PAF, Facility Specific Guidelines) and less resource intensive (IV to PO) interventions

Learning Assessment Questions

1. Which of the following intravenous medications would NOT be appropriate for IV to PO Conversion?
   A. Levofloxacin
   B. Fluconazole
   C. Metronidazole
   D. Vancomycin

2. Antimicrobial use should be measured by Days of Therapy rather than by Defined Daily Doses.
   A. True
   B. False



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