Antimicrobial Resistance:
A Call to Action

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Agenda

- Introduction

- Global perspective

- Elements of an effective ASP

- Measures to monitoring ASP

- Resources to guide development of an ASP

- Regulatory changes

Case

This is a 46 year old female was admitted with hypotension, fever, and flank pain. She has no underlying medical or urologic problems. Her urine showed pyuria and bacteriuria, the peripheral WBC was 16,000/mm^3. She was admitted to the ICU and empirically started on _____.

What would you start?

Introduction

There is without a doubt going to be a lot of attention paid to antimicrobial stewardship!

Birth of Antimicrobial Stewardship

"Microbes are educated to resist penicillin and a host of penicillin-fast organisms is bred out…

In such cases, the thoughtless

person playing with penicillin is

morally responsible for the death of the man who finally succumbs to infection with the penicillin-resistant organism. I hope this evil can be averted."
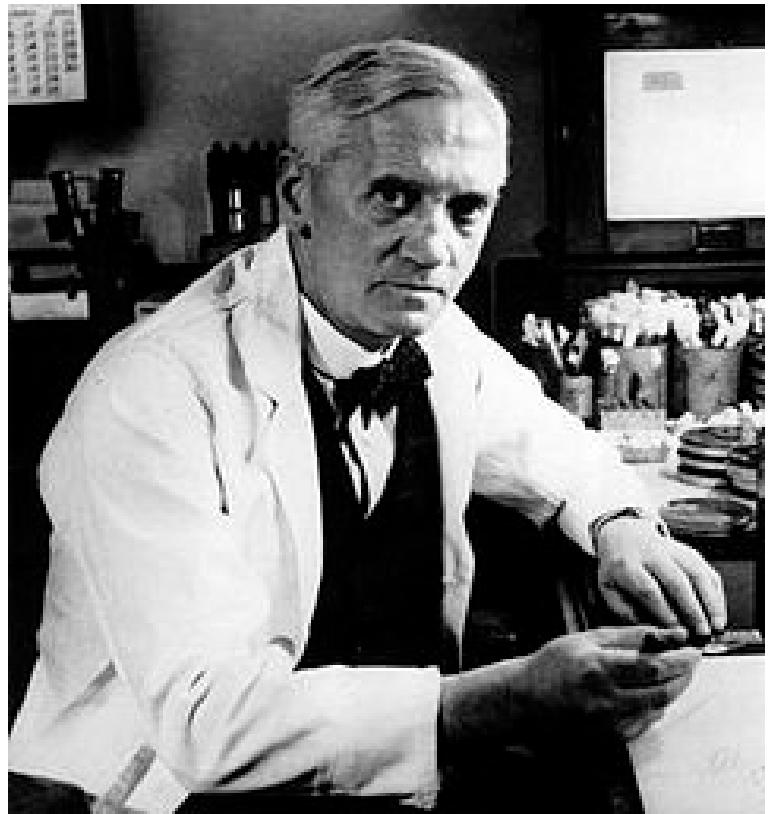
Fleming A. New York Times. 26 June 1945:21.

1994

March 28, 1994

Newsweek

March 28, 1994

$2.95

ANTIBIOTICS
THE END OF MIRACLE DRUGS?

WARNING
NO LONGER
EFFECTIVE
AGAINST
KILLER
BUGS

2015

STRONGER, SMARTER, SEXIER YOU?
WE EVALUATE ANTI-AGING PRODUCT CLAIMS | NEW REFRIGERATORS THAT KEEP YOUR FOOD FRESH LONGER

ConsumerReports

August 2015

HOW TO
STOP A

RETIREMENT RX
Don't Outlive Your Money:
Here's How

SUPERBUG

More and more antibiotics no longer work, and dangerous bugs are making us sicker.
What can we do about it before it's too late?

PLUS **TV, YOUR WAY** A GUIDE TO PICKING
THE BEST PLAN

AUGUST 2015
CONSUMERREPORTS.ORG
$6.99US

Please display at checkout
and mainline until Aug. 3, 2015

We are using a lot of antibiotics worldwide!!

Consumption of antibiotics in 2010 per person (A), and compound annual growth rate of antibiotic drug consumption between 2000 and 2010 (B)


Van Boeckel TP et al. *Lancet Infect Dis*. 2014;14:742-50.
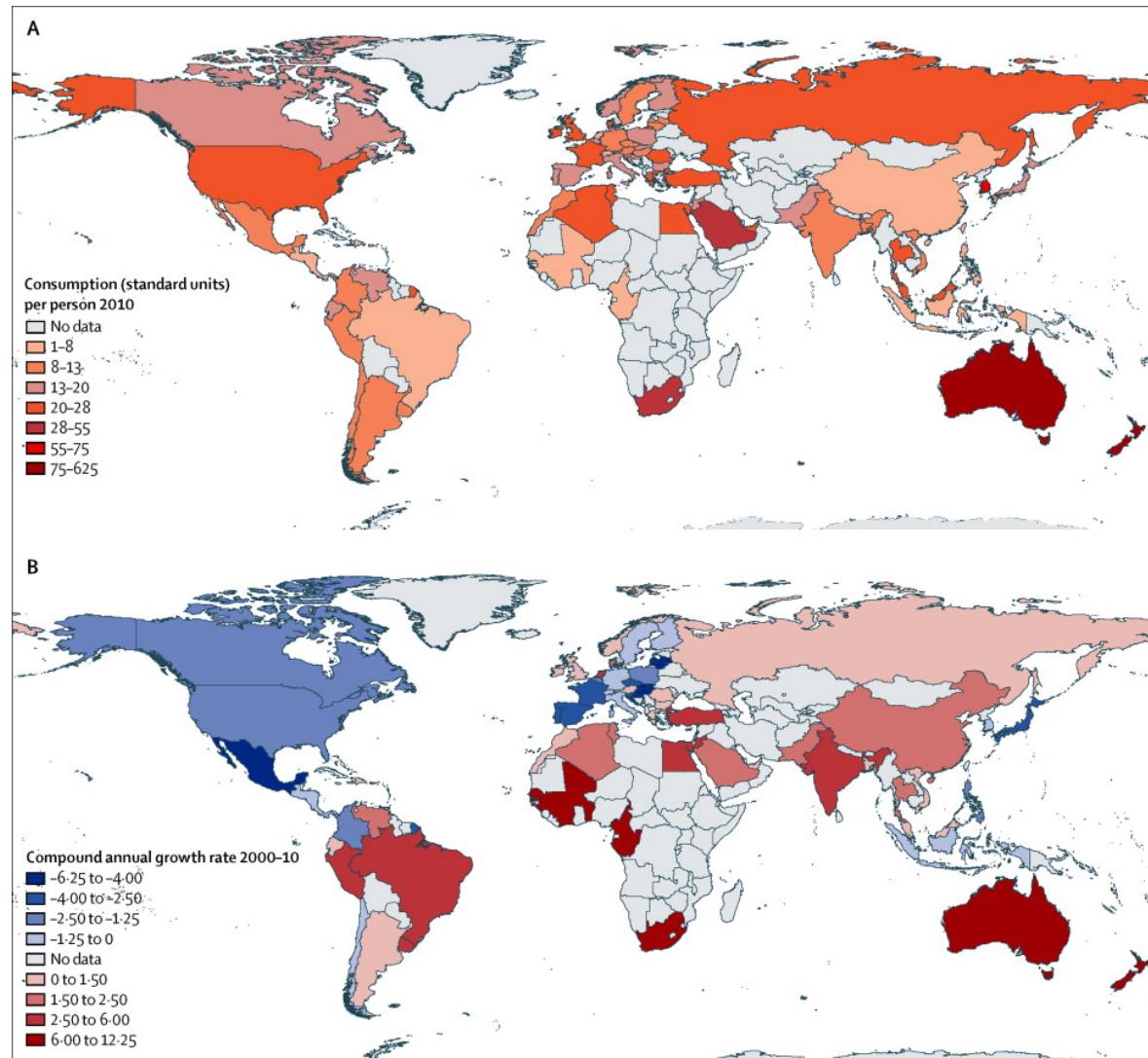
The Perfect Storm Antimicrobial Resistance

Trends in Antimicrobial Resistance

Percentage of Isolates Resistant

1. MRSA
2. VRE
3. Group 2 carbapenem-resistant *Pseudomonas aeruginosa*
4. Group 2 carbapenem-resistant *Acinetobacter* spp.
5. Azole-resistant *Candida* spp.
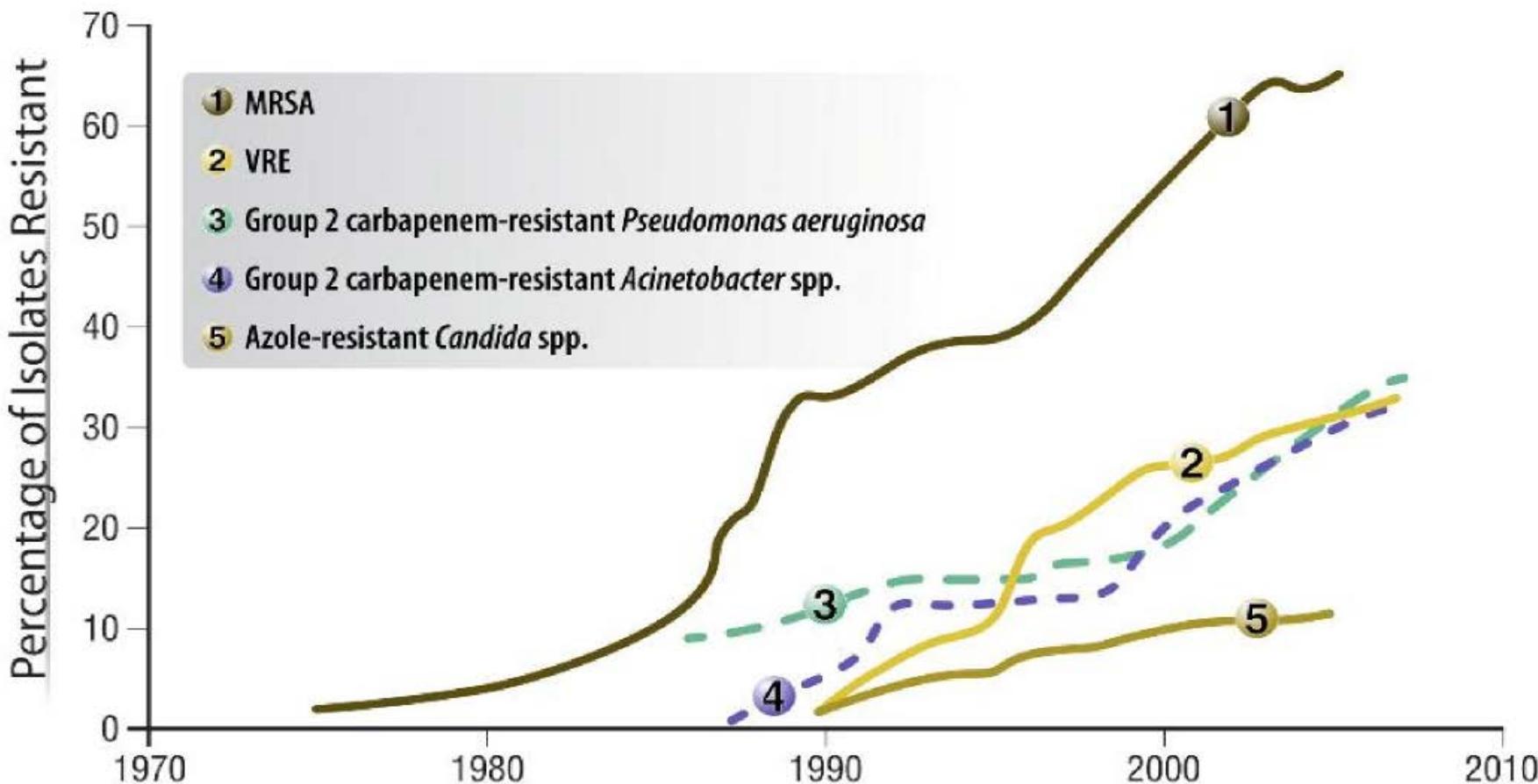
Adapted from Wenzel RP, et al. *Infect Control Hosp Epidemiol.* 2008;29:1012-1018.

Antibiotic Development
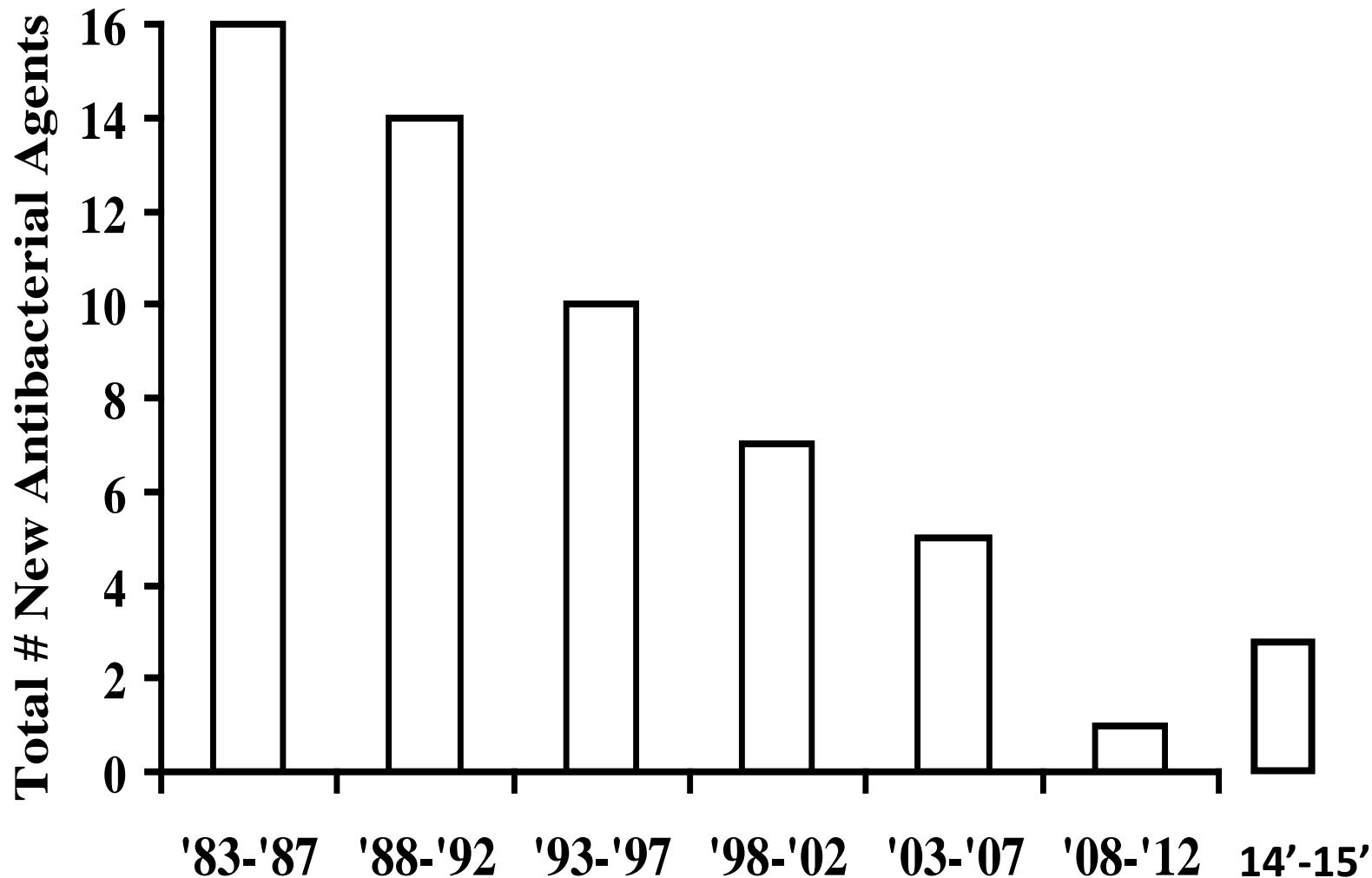
Infectious Disease Mortality in the United States During the 20th Century

US deaths declined by ~ 220 per 100,000 in 15 years

Sulfa

Is this the post antibiotic era?

Penicillin

Other medical technologies reduced deaths by ~ 20 per 100,000 over the next 45 years

?

2014+

US Infectious Disease Death Rate per 100,000 Population

300
200
100
0

1940   1960   1980

Modified from Armstrong, G. L. et al. JAMA 1999;281:61-6.

- $20 billion in excess direct healthcare costs
- Costs to society for lost productivity as high as $35 billion a year (2008 dollars)
- The use of antibiotics is the single most important factor leading to antibiotic resistance
- ↑ *C. difficile* infections[1]
  - **453,000 cases 2011**
  - **29,000 deaths 2011**

Lessa FC et al. *N Engl J Med.* 2015; 372:825-34.

Four Core Actions

- preventing infections and preventing the spread of resistance

- tracking resistant bacteria

- improving the use of today's antibiotics (antimicrobial stewardship)

- promoting the development of new antibiotics and developing new diagnostic tests for resistant bacteria

WHO Report 2014

ANTIMICROBIAL RESISTANCE
Global Report on surveillance
2014
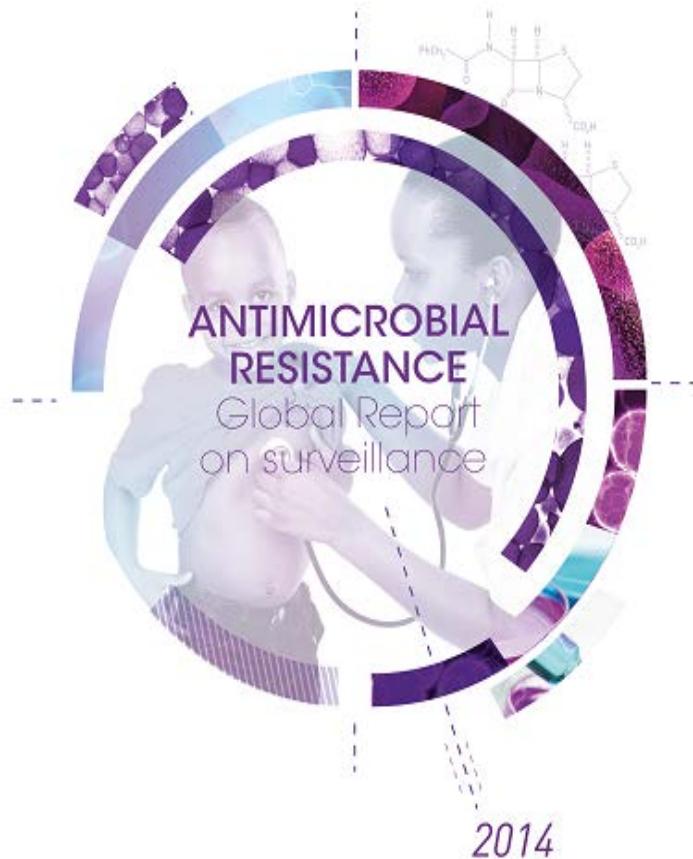
- **All** regions are experiencing resistance to carbapenems

- Resistance to FQ common

- Third-generation ceph ineffective to treat GC in multiple countries including US

- Key measures such as tracking and monitoring are inadequate and more needs to be done in improving appropriate antibiotic use, infection prevention, handwashing, and vaccinations

UK Review on AR 2016

Deaths attributable to antimicrobial resistance every year by 2050

Europe 390,000

North America 317,000

Asia 4,730,000

Africa 4,150,000

Latin America 392,000

Oceania 22,000

number of deaths

Mortality per 10,000 population

5 6 7 8 9 10 >
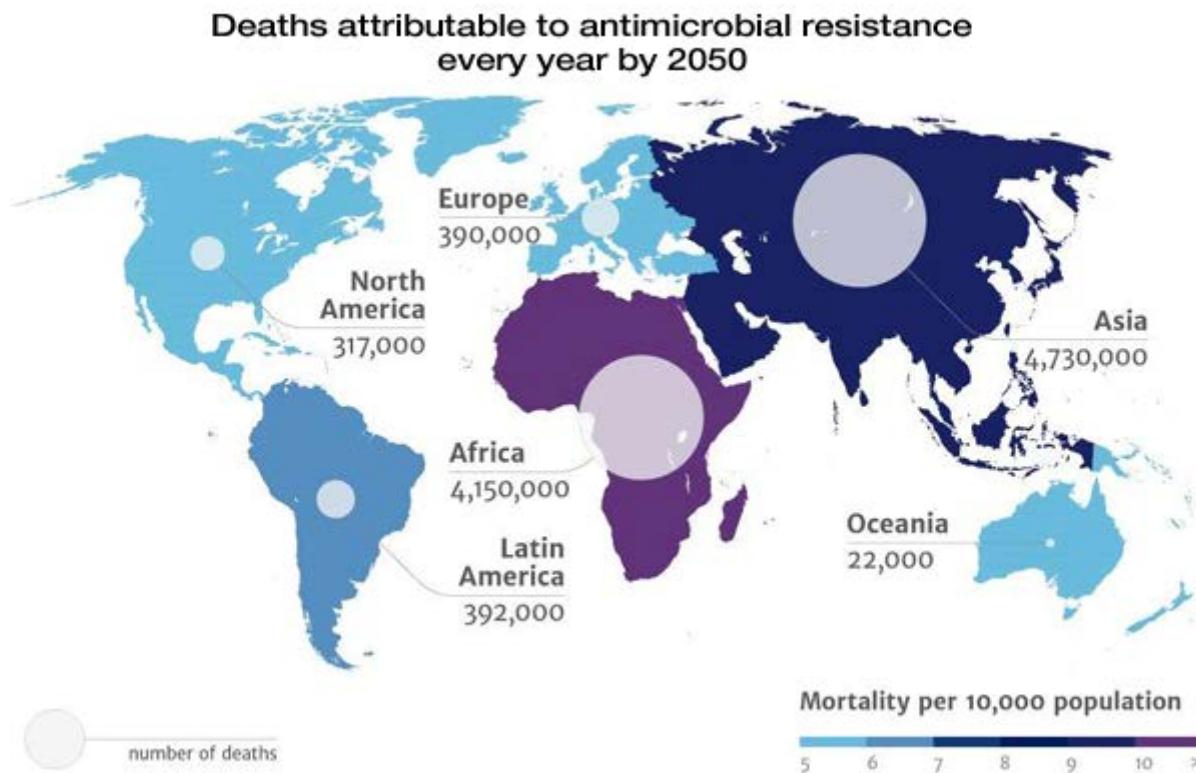
Why We Need to Improve Antibiotic Use

- Antibiotics are misused across the continuum of care
- Use of antibiotics in animals
- Antibiotic misuse adversely impacts patients and society
- Antibiotics are the only drugs where use in one patient can impact the effectiveness in another
- Improving antibiotic use improves patient outcomes and saves money
- Improving antibiotic use is a public health imperative- World Health Organization (WHO) considers AR an emerging threat to global stability

PARTNERS IN ANTIBIOTIC RESISTANCE
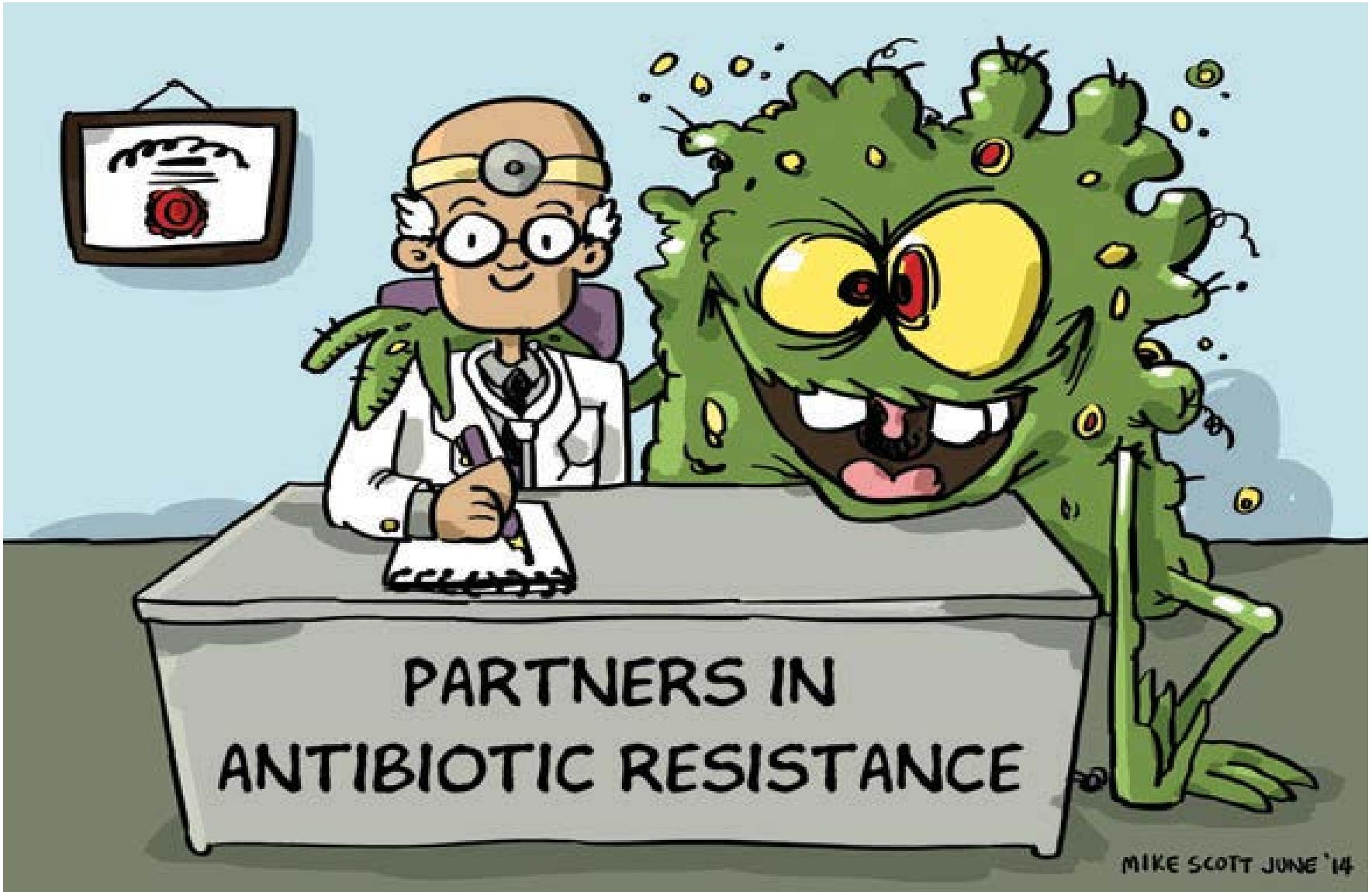
MIKE SCOTT JUNE '14

New Societal Approaches to Empowering AS

"Further improving antibiotic use will require increased accountability and transparency at societal level. A parallel can be drawn between antibiotic stewardship and infection prevention. Hospitals have been required to have infection prevention programs for many decades. Yet no transformative progress in reduction of HAIs occurred until society began requiring public reporting of infection rates and linking such rates to P4P measures. This shift towards greater accountability and transparency in HAIs has led hospitals to vest infection control programs with the authority to implement critical improvements. A similar shift could substantially accelerate efforts to improve antibiotic use."

JAMA 2016; 315:1229-30

Antimicrobial Stewardship
Goals

- Improve patient outcomes

- Optimize selection, dose and duration of Rx

- Reduce adverse drug events including secondary infection (e.g., *C. difficile* infection)

- Reduce morbidity and mortality

- Limit emergence of antimicrobial resistance

- Reduce length of stay

- Reduce health care expenditures

How best can we achieve these goals?

MacDougall CM and Polk RE. *Clin Microbiol Rev.* 2005; 18(4):638-56.
Dellit TH et. al. *Clin Infect Dis*. 2007; 44:159-177.

Initial IDSA/SHEA Antimicrobial Stewardship Guidelines

- A multidisciplinary ASP team should include an **ID physician and pharmacist** and other key stakeholders as determined by the institution
- Two core strategies were recommended
  - Prospective audit with intervention and feedback
  - Formulary restriction and preauthorization
- Other recommended strategies
  - Education
  - Guidelines and clinical pathways
  - Order forms
  - De-escalation
  - Dose optimization
  - IV to PO conversion

IDSA=Infectious Diseases Society of America
SHEA=Society for Healthcare Epidemiology of America

The Challenge

- How to initiate and improve antibiotic stewardship efforts
- Proving that it works
  - Clinical outcomes
  - Decrease resistance
- Changing the antibiotic prescribing culture
- Hardwiring the process
- Continuing to show financial benefit to maintain funding and support of efforts

GUIDELINES

Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America Guidelines for Developing an Institutional Program to Enhance Antimicrobial Stewardship

The Problem with Antimicrobial Stewardship

- Everyone thinks they know what it is

But who knows what it should be?

– Which strategies are most effective?
– How to assess their effectiveness?

Complex problem

Elements of an Effective Antimicrobial Stewardship Program

Team success

- *"The ultimate difference between a company and its competition is, in fact, the ability to execute."*

- Larry Bossidy

One size does not fit all

Core Elements for Antibiotic Stewardship Programs
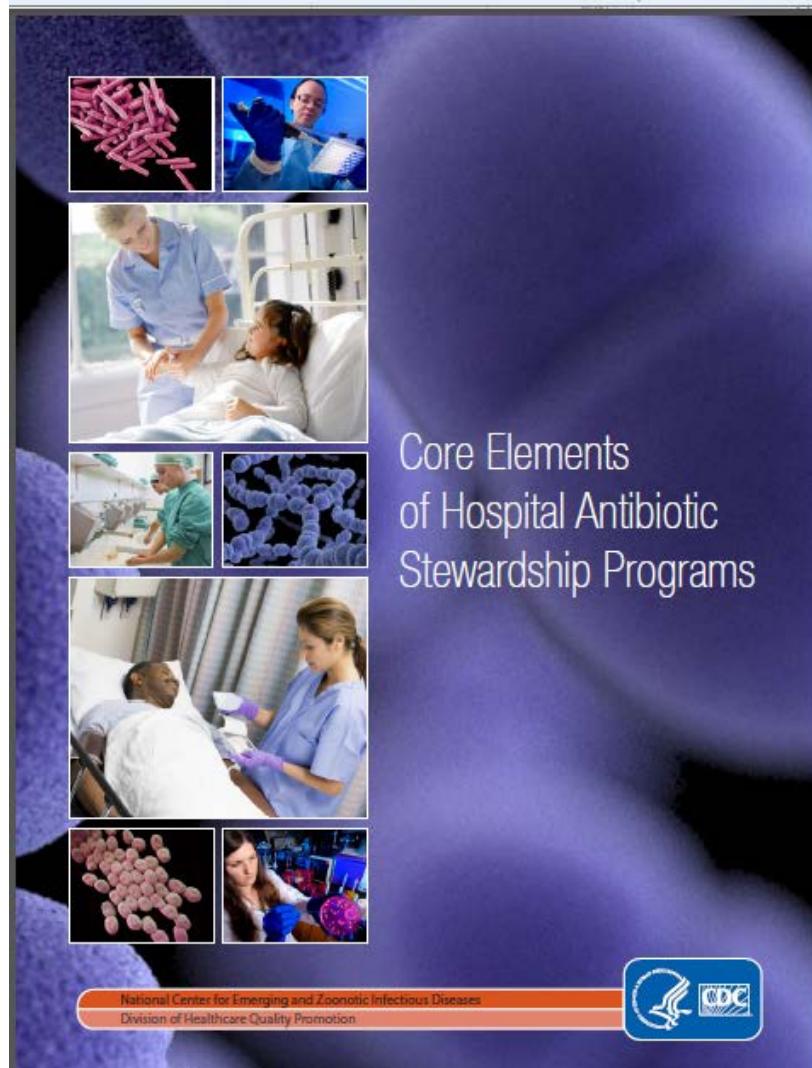
Core Elements
of Hospital Antibiotic
Stewardship Programs

National Center for Emerging and Zoonotic Infectious Diseases
Division of Healthcare Quality Promotion

CDC

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

CDC Antibiotic Treatment in Hospitals: Core Elements

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

2. **Accountability**: Appoint a single leader responsible for program outcomes-this is usually a physician

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

4. **Act**: Take at least one prescribing improvement action, such as "antibiotic timeout"

5. **Track** : Monitor prescribing and antibiotic resistance patterns

6. **Report**: Regularly report to interdisciplinary team the prescribing and resistance patterns, and steps to improve

7. **Educate**: Offer team education about antibiotic resistance and improving prescribing practice

Leadership Commitment

- There should be a formal expression of support for the stewardship program from the facility administration.

- Leadership must ensure that staff have necessary time, education/competencies and resources to implement the stewardship program.

Accountability

- There should be a designated leader of the antibiotic stewardship program.
- Physicians have proven very effective in this role.
  - Prescribing is a <u>medical staff function</u>
  - Often an ID physician, but others have filled this role, especially in hospitals with no ID physicians.
- Leadership by committee is not as effective.

Drug Expertice

- Pharmacy leadership is consistently identified as a must for stewardship in hospitals.

- Pharmacists often play a lead role in implementing improvement interventions and monitoring antibiotic use. Should have some training in infectious diseases. (e.g. MAD-ID. SIDP, SHEA)

- Many programs are co-lead by a physician and pharmacist.

Antibiotic Stewardship Programs in U.S. Acute Care Hospitals: Findings From the 2014 National Healthcare Safety Network Annual Hospital Survey

Infrastructure for antibiotic stewardship		**2298**	**54.9**
1. Hospital leadership commitment: Dedicate human, financial, and IT resources		2508	59.9
23	Written statement of support	2199	52.6
26	Salary support	1326	31.7
23, 26	Both	926	22.1
2. Program leadership (Accountability): Person responsible for outcomes		3016	72.1
24	Pharmacist	1540	36.8
24	Physician	1258	30.1
24	Other	218	5.2
3. Drug expertise: At least 1 pharmacist responsible for improving antibiotic use		3648	87.2
Implementation		**2112**	**50.5**
4. Act: Performance of at least one prescribing improvement action		3926	93.8
28	Facility-specific treatment recommendations	3232	77.3
31	Audit with feedback	3100	74.1
30	Prior-approval	2652	63.4
27	Requirement to document antibiotic indication	1105	26.4
29	Antibiotic time out	979	23.4
5. Track: Monitor prescribing and antibiotic resistance patterns.		3318	79.3
32	Monitor antibiotic use (consumption)	2881	68.9
28[b]	Facility-specific treatment recommendations and monitor adherence to facility-specific treatment recommendations	2203	52.7
27[b]	Requirement to document antibiotic indication and monitor adherence to indication documentation policy	736	17.6
6. Report: Regularly report to staff prescribing and resistance patterns		2822	67.5
33	Feedback to providers on how they can improve prescribing	2478	59.2
32[b]	Reports on antibiotic use shared with prescribers	1861	44.5
7. Educate about antibiotic resistance and improving prescribing practices		2589	61.9
34	Education provided to clinicians and other relevant staff		
Hospitals reporting all 7 core elements of hospital antibiotic stewardship programs		**1642**	**39.2**

TATFAR was created in 2009 with the goal of improving cooperation between the U.S. and the EU in three key areas
1. <u>appropriate therapeutic use of antimicrobial drugs</u> in medical and veterinary communities
2. prevention of healthcare and community-associated drug-resistant infections and
3. strategies for improving the pipeline of new antimicrobial drugs

A Concise Set of Structure and Process Indicators to Assess and Compare Antimicrobial Stewardship Programs Among EU and US Hospitals: Results From a Multinational Expert Panel

Lori A. Pollack, MD, MPH;[1] Diamantis Plachouras, MD, PhD;[2] Ronda Sinkowitz-Cochran, MPH;[1] Heidi Gruhler, MPH;[1] Dominique L. Monnet, PharmD, PhD;[2] J. Todd Weber, MD;[1] Transatlantic Taskforce on Antimicrobial Resistance (TATFAR) Expert Panel on Stewardship Structure and Process Indicators

Anastasia Antoniadou, Bojana Beovic, Franky Buyle, Sara Cosgrove, Peter Davey, Elizabeth S. Dodds Ashley, Catherine Dumartin, Alison Holmes, Winfried Kern, Maria Luisa Moro, Dilip Nathwani, Jeanne Negley, Melinda Neuhauser, Christopher A. Ohl, Jeroen Schouten, Ed Septimus, Marc Struelens, Agnes Wechsler- Fördös

Core indicators - Infrastructure

1. Does your facility have a formal **antimicrobial stewardship programme** accountable for ensuring appropriate antimicrobial use?

2. Does your facility have a **formal organizational structure** responsible for antimicrobial stewardship (e.g., a multidisciplinary committee focused on appropriate antimicrobial use, pharmacy committee, patient safety committee or other relevant structure)?

3. Is an **antimicrobial stewardship team** available at your facility (e.g., greater than one staff member supporting clinical decisions to ensure appropriate antimicrobial use)?

Core indicators – Infrastructure cont

4. Is there a **physician identified as a leader** for antimicrobial stewardship activities at your facility?

5. Is there a **pharmacist** responsible for ensuring appropriate antimicrobial use at your facility?

6. Does your facility provide any **salary support** for dedicated time for antimicrobial stewardship activities (e.g., percentage of full-time equivalent (FTE) for ensuring appropriate antimicrobial use)?

7. Does your facility have the **IT capability** to support the needs of the antimicrobial stewardship activities?

Core indicators - Policy and practice

8. Does your facility have **facility-specific treatment recommendations** based on local antimicrobial susceptibility to assist with antimicrobial selection for common clinical conditions?

9. Does your facility have a written policy that requires prescribers to **document an indication** in the medical record or during order entry for all antimicrobial prescriptions?

10. Is it routine practice for specified antimicrobial agents to be approved by a physician or pharmacist in your facility (e.g., **pre-authorization**)?

11. Is there a formal procedure for a physician, pharmacist, or other staff member to review the appropriateness of an antimicrobial at or after 48 hours from the initial order (**post-prescription review**)?

Measures to Monitoring ASP

Antimicrobial Stewardship Framework

	BEFORE Rx	AFTER Rx
ACTIVE	Antimicrobial Formulary Restriction Order Sets	Prospective Audit with Feedback IV to PO Conversion Dose Optimization
PASSIVE	Audits & Reports Education Guidelines	De-escalation/Streamlining Duration of Therapy
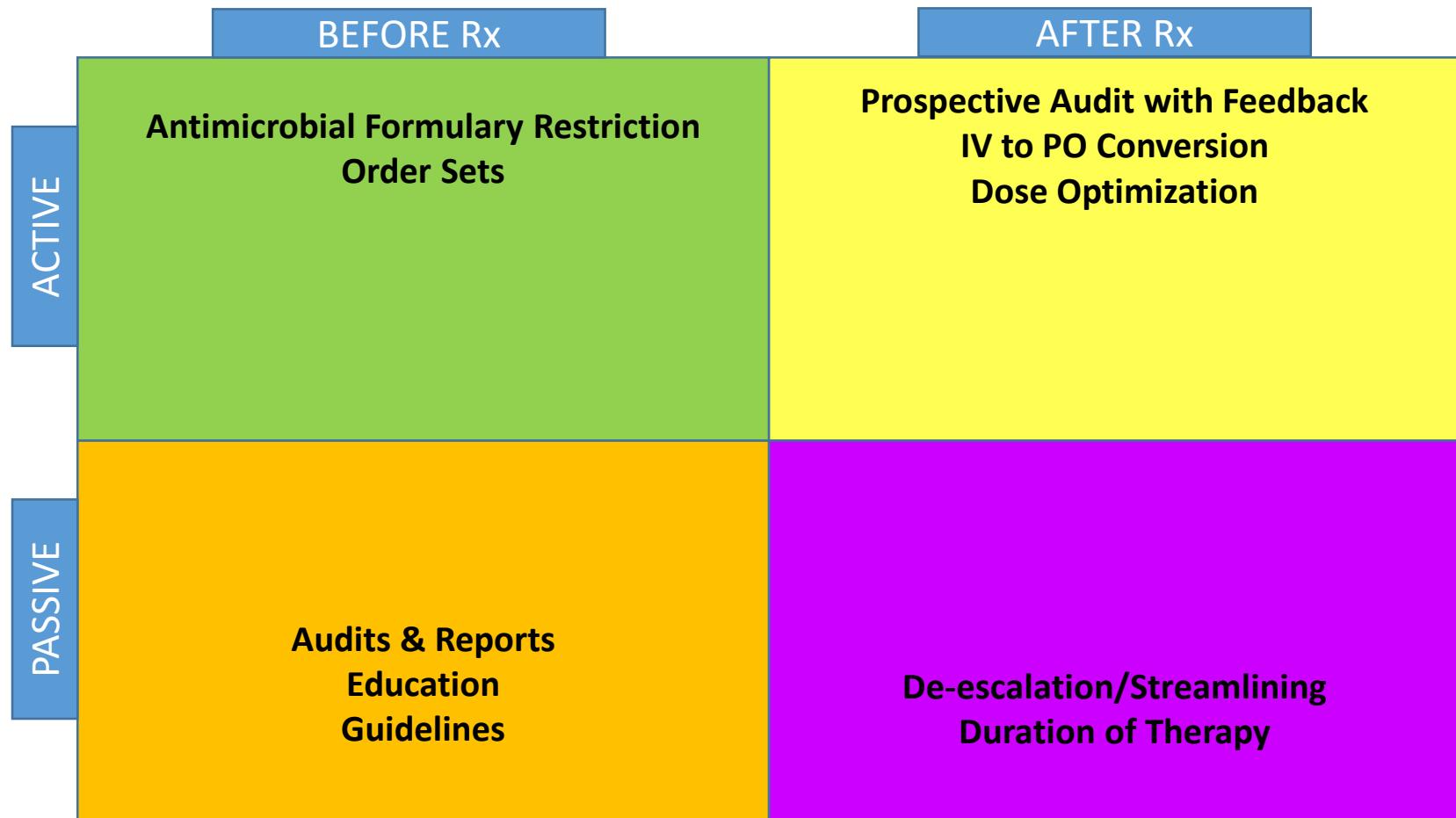
Adapted from Moehring RW et al. *Curr Infect Dis Rep*. 2012; 14(6): 592 – 600.

Suggested Measures

Measurement Area	Measure
Antibiotic consumption	• Days of therapy (DOT) per 1,000 patient days—overall and for specific agents or groups of agents • Defined daily dose (DDD) per 1,000 patient days (if DOT not available) • Standardized Antibiotic Administration Ratio*
Process measures	• Provision of indication with each antibiotic start • Percentage of cases where therapy is appropriate (especially for serious infections, such as sepsis) • Appropriate Treatment of Methicillin-Sensitive Staphylococcus aureus (MSSA) Bacteremia • Frequency at which de-escalation occurs • Timely cessation of antibiotics given for surgical prophylaxis • Antibiotics not prescribed to treat asymptomatic bacteria • Appropriate cultures obtained before starting antibiotics • Adherence to hospital-specific guidelines • Acceptance of ASP recommendations • Frequency of performance of antibiotic time outs or reviews • Timely administration of appropriate antibiotics in cases of suspected sepsis

Suggested Measures continued

Measurement Area	Measure
Outcome measures	• Length of stay • Cure of infection • Risk-adjusted mortality • Hospital readmissions for select infections • Hospital-onset C. difficile infections* • Adverse drug reactions (number/percentage/rate) • Antimicrobial resistance- focusing on hospital onset cases would most likely best reflect the impact of ASPs • Provider-level measures if available (e.g., treatment of *S. aureus* and bloodstream infections)
Financial	• Antibiotic cost per patient day • Antibiotic cost per admission • Total hospital cost per admission

*NQF-endorsed measure

Modified *Curr Infect Dis Rep* 2014; 16:433

NHSN AU Measure NQF Endorsed Standardized Antimicrobial Administration Ratio (SAAR)

SAAR is an Observed-to-Expected (O-to-E) ratio

- **Observed antibacterial use –** Days of therapy reported by a healthcare facility for a specified category of antimicrobial agents in a specified patient care location or group of locations

- **Expected antibacterial use –** Days of therapy predicted on the basis of nationally aggregated AU data for a healthcare facility's use of a specified category of antimicrobial agents in a specified patient care location or group of locations

CMS has posted for comment of potential inclusion of NHSN AU Measure (Standard Antibiotic Administration Ratio or SAAR)

NHSN AU Measure Proposal –
Patient Care Locations

Measure proposal covers antimicrobial use in 6 specified groupings of adult and pediatric patient care locations:

1. Adult medical, surgical, and medical/surgical *intensive care units*
2. Adult medical, surgical, and medical/surgical *wards*
3. Pediatric medical, surgical, and medical/surgical *intensive care units*
4. Pediatric medical, surgical, and medical/surgical *wards*
5. All adult medical, medical/surgical, and surgical *intensive care units and wards*
6. All pediatric medical, medical/surgical, and surgical *intensive care units and wards*

Measure proposal combines each of the 6 patient care location groupings with specified categories of antimicrobial agents. A separate SAAR is calculated for each patient care location-antimicrobial agent combination.

NHSN AU Measure
 Five Antibacterial Agent Categories

High value targets for antimicrobial stewardship programs:

1. **Broad spectrum agents predominantly used for hospital-onset/multi-drug resistant bacteria –** aminoglycosides, some carbapenems, some cephalosporins, some fluoroquinolones, penicillin B-lactam/b-lactamase inhibitor combinations, and other agents
2. **Broad spectrum agents predominarntly used for community-acquired infection –** ertapenem, some cephalosporins, and some fluroquinolones

3. **Anti-MRSA agents –** ceftaroline, dalbavancin, daptomycin, linezolid, oritavancin, quinupristin/dalfopristin, tedizolid, telavancin, in, and vancomycin (IV route only)
4. **Agents predominantly used for surgical site infection prophylaxis –** cefazolin, cefotetan, cefoxitin, cefuroxime (IV route only)

High level indicators for antimicrobial stewardship programs:

5. **All antibacterial agents –** All agents included in NHSN AUR protocol

NHSN AU Measure
Interpreting the SAAR

❑ A high SAAR that achieves statistical significance may indicate excessive antibacterial use.

❑ A SAAR that is not statistically different from 1.0 indicates antibacterial use is equivalent to the referent population's antibacterial use.

❑ A low SAAR that achieves statistical significance (i.e., different from 1.0) may indicate antibacterial under use.

Note: A SAAR alone is not a definitive measure of the appropriateness or judiciousness of antibacterial use, and any SAAR may warrant further investigation

New Resources to Guide Development of an ASP

Implementing an Antibiotic Stewardship Program: Guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America

Tamar F. Barlam,[1,a] Sara E. Cosgrove,[2,a] Lilian M. Abbo,[3] Conan MacDougall,[4] Audrey N. Schuetz,[5] Edward J. Septimus,[6] Arjun Srinivasan,[7] Timothy H. Dellit,[8] Yngve T. Falck-Ytter,[9] Neil O. Fishman,[10] Cindy W. Hamilton,[11] Timothy C. Jenkins,[12] Pamela A. Lipsett,[13] Preeti N. Malani,[14] Larissa S. May,[15] Gregory J. Moran,[16] Melinda M. Neuhauser,[17] Jason G. Newland,[18] Christopher A. Ohl,[19] Matthew H. Samore,[20] Susan K. Seo,[21] and Kavita K. Trivedi[22]

Evidence-based guidelines for implementation and measurement of antibiotic stewardship interventions in inpatient populations including long-term care were prepared by a multidisciplinary expert panel of the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. The panel included clinicians and investigators representing internal medicine, emergency medicine, microbiology, critical care, surgery, epidemiology, pharmacy, and adult and pediatric infectious diseases specialties. These recommendations address the best approaches for antibiotic stewardship programs to influence the optimal use of antibiotics

Infection Prevention and Epidemiology

Select Examples

- Does the Use of Preauthorization and/or Prospective Audit and Feedback Interventions by ASPs Improve Antibiotic Utilization and Patient Outcomes?

  We recommend preauthorization and/or prospective audit and feedback over no such interventions (strong recommendation, moderate-quality evidence).

- Should ASPs Develop and Implement Facility-Specific Clinical Practice Guidelines for Common Infectious Diseases Syndromes to Improve Antibiotic Utilization and Patient Outcomes?

  We suggest ASPs develop facility-specific clinical practice guidelines coupled with a dissemination and implementation strategy (weak recommendation, low-quality evidence)

- Should ASPs Implement Interventions to Improve Antibiotic Use and Clinical Outcomes That Target Patients With Specific Infectious Diseases Syndromes?

  We suggest ASPs implement interventions to improve antibiotic use and clinical outcomes that target patients with specific infectious diseases syndromes (weak recommendation, low-quality evidence)

Table 1. Comparison of Preauthorization and Prospective Audit and Feedback Strategies for Antibiotic Stewardship

Preauthorization	Prospective Audit and Feedback
Advantages	
• Reduces initiation of unnecessary/ inappropriate antibiotics • Optimizes empiric choices and influences downstream use • Prompts review of clinical data/ prior cultures at the time of initiation of therapy • Decreases antibiotic costs, including those due to high-cost agents • Provides mechanism for rapid response to antibiotic shortages • Direct control over antibiotic use	• Can increase visibility of antimicrobial stewardship program and build collegial relationships • More clinical data available for recommendations, enhancing uptake by prescribers • Greater flexibility in timing of recommendations • Can be done on less than daily basis if resources are limited • Provides educational benefit to clinicians • Prescriber autonomy maintained • Can address de-escalation of antibiotics and duration of therapy
Disadvantages	
• Impacts use of restricted agents only • Addresses empiric use to a much greater degree than downstream use • Loss of prescriber autonomy • May delay therapy • Effectiveness depends on skill of approver • Real-time resource intensive • Potential for manipulation of system (eg, presenting request in a biased manner to gain approval) • May simply shift to other antibiotic agents and select for different antibiotic-resistance patterns	• Compliance voluntary • Typically labor-intensive • Success depends on delivery method of feedback to prescribers • Prescribers may be reluctant to change therapy if patient is doing well • Identification of interventions may require information technology support and/or purchase of computerized surveillance systems • May take longer to achieve reductions in targeted antibiotic use

Select examples continued

- Should ASPs Implement Interventions Designed to Reduce the Use of Antibiotics Associated With a High Risk of CDI?

    We recommend antibiotic stewardship interventions designed to reduce the use of antibiotics associated with a high risk of CDI compared with no such intervention (strong recommendation, moderate-quality evidence)

- In Hospitalized Patients Requiring Intravenous (IV) Antibiotics, Does a Dedicated Pharmacokinetic (PK) Monitoring and Adjustment Program Lead to Improved Clinical Outcomes and Reduced Costs?

    We recommend that hospitals implement PK monitoring and adjustment programs for aminoglycosides (strong recommendation, moderate-quality evidence).
    We suggest that hospitals implement PK monitoring and adjustment programs for vancomycin (weak recommendation, low-quality evidence).

Select examples continued

- Should ASPs Implement Interventions to Increase Use of Oral Antibiotics as a Strategy to Improve Outcomes or Decrease Costs?
  > We 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)

- Should ASPs Advocate for Rapid Diagnostic Testing on Blood Specimens to Optimize Antibiotic Therapy and Improve Clinical Outcomes?
  > We suggest rapid diagnostic testing in addition to conventional culture and routine reporting on blood specimens if combined with active ASP support and interpretation (weak recommendation, moderate-quality evidence)

- Should ASPs Implement Interventions to Reduce Antibiotic Therapy to the Shortest Effective Duration?
  > We recommend that ASPs implement guidelines and strategies to reduce antibiotic therapy to the shortest effective duration (strong recommendation, moderate-quality evidence)

Table 2. Meta-analyses and Examples of Randomized Clinical Studies Comparing Shorter Versus Longer Duration of Antibiotics

Reference	Clinical Condition/Population	Treatment Duration, d	Clinical Outcome[a]
Meta-analyses			
Dimopoulos et al, 2008 [123]	Adults and children with CAP	3–7 vs 5–10	Clinical success, relapse, mortality, adverse events
Pugh et al, 2011 [124]	Adults with VAP	7–8 vs 10–15	Antibiotic-free days[b], recurrence[b]
Dimopoulos et al, 2013 [125]	Adults with VAP	7–8 vs 10–15	Relapse, mortality, antibiotic-free days[c]
Randomized clinical trials			
Chastre et al, 2003 [127]	Adults with VAP	8 vs 15	Mortality, recurrent infections[d]
El Moussaoui et al, 2006 [128]	Adults with CAP	3 vs 5	Clinical and radiological success
Greenberg et al, 2014 [129]	Children with CAP	5 vs 10	Treatment failure[e]
Hepburn et al, 2004 [130]	Adults with cellulitis	5 vs 10	Clinical success
Sandberg et al, 2012 [131]	Adult females with acute pyelonephritis	7 vs 14	Clinical efficacy, adverse events
Talan et al, 2000 [132]	Women with acute uncomplicated pyelonephritis	7 vs 14	Bacteriologic and clinical cure[f]
Runyon et al, 1991 [133]	Adults with spontaneous bacterial peritonitis	5 vs 10	Mortality, bacteriologic cure, recurrence
Saini et al, 2011 [134]	Neonatal septicemia	2–4 vs 7 (with sterile culture)	Treatment failure
Sawyer et al, 2015 [135]	Adults with intra-abdominal infection	4 vs ≤10	Composite of surgical site infection, recurrent intra-abdominal infection, or death
Bernard et al, 2015 [136]	Adults with vertebral osteomyelitis	42 vs 84	Cure at 1 y by independent committee and secondary outcomes

Current evidence on hospital antimicrobial stewardship objectives: a systematic review and meta-analysis

- Overall quality of evidence was low, but they concluded there was enough support for some interventions:
    - Following guidelines in administering empiric antibiotics
    - IV to PO
    - Antibiotic restrictions
    - ID consultations
    - therapeutic drug monitoring
    - De-escalation of therapy
- Conclusion: The overall evidence for these interventions shows significant benefits for clinical outcomes, adverse events, costs, resistance rates, or combinations of these. However, the included studies were generally of low quality.

Lancet Infect Dis 2016 published online March 2
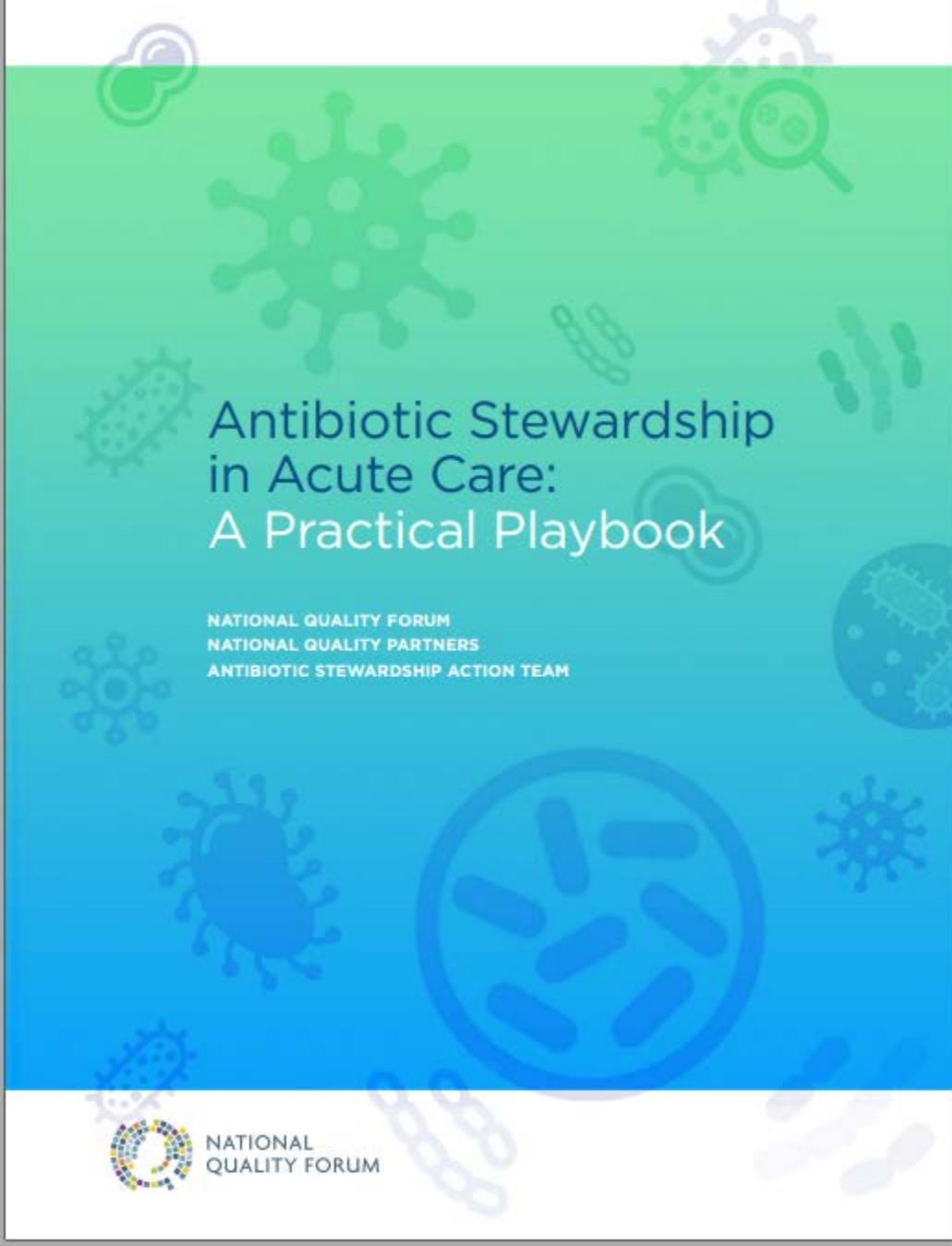
Antibiotic Stewardship in Acute Care:
# A Practical Playbook

NATIONAL QUALITY FORUM
NATIONAL QUALITY PARTNERS
ANTIBIOTIC STEWARDSHIP ACTION TEAM

NATIONAL
QUALITY FORUM

Playbook

- Provide guidance and strategies to implement and sustain a successful ASP

- What successful implementation looks like

- Strategies to address barriers to implementation

- Survey standards to determine if stewardship is based on CDC core elements and is effective
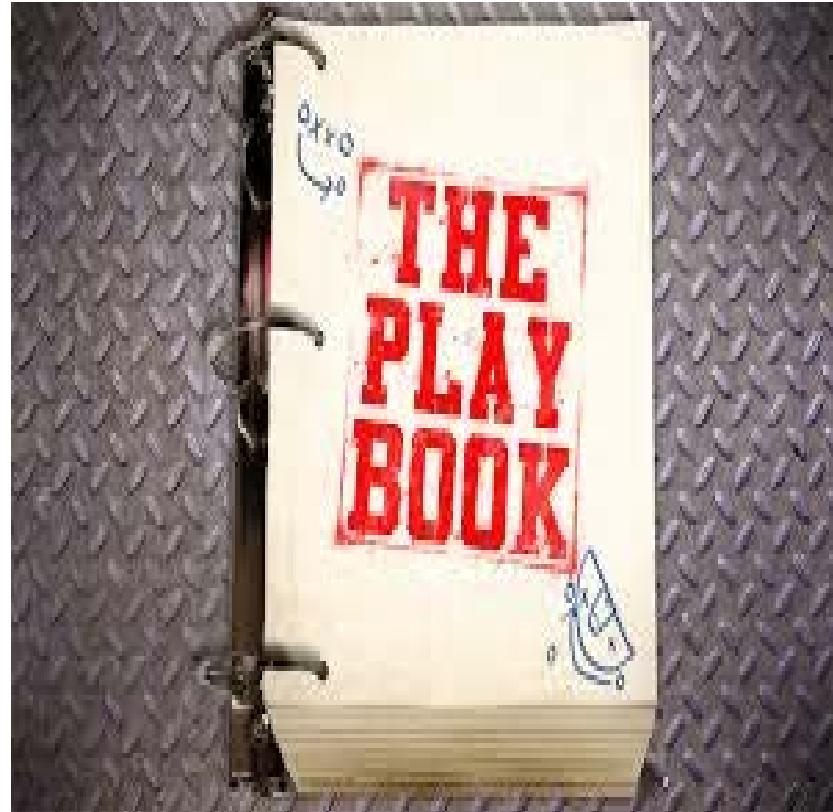
Playbook

- Over the past year, NQP has worked to bring together public and private-sector leaders and experts to develop a common agenda and identify and implement strategies to improve antibiotic practices among providers, healthcare organizations, and local communities.

- The *Playbook* makes recommendations for organizations including hospitals, accreditation bodies, and patient and consumer groups to enhance their stewardship activities to prepare for these changes.

- The *Playbook* attempts to lay out the implementation examples as a broad range of what is possible and achievable while recognizing that what will be effective depends heavily on local circumstances.

Playbook continued

- Based on these *Core Elements*, this *Playbook* provides concrete strategies and suggestions for organizations committed to implementing successful ASPs in acute care hospitals. This *Playbook* has incorporated examples of successful implementation, more specifics concerning the core elements, barriers and solutions for implementation, potential measurement approaches, and future directions.

- The document is **not** a list of "must do's" to be completed. Instead, the *Playbook* attempts to lay out a variety of options from which to choose depending on local context, resources, and needs.

Stewardship Action Team Organizations

- CDC
- HCA
- American Hospital Association
- Soc of Post-Acute and LTC
- AHRQ
- Am Academy of Allergy Asthma
- Am Academy of Emerg Med
- Am Assoc of Nurse Practitioners
- Am Health Care Assoc
- Am Soc Health-System Pharm
- Anthem
- CMS
- Children's Hosp Assoc
- Council for Med Specialty Soc
- Duke University

- IDSA
- IHI
- Intermountain Healthcare
- Johns Hopkins
- TJC
- USC
- Leapfrog
- MGH
- Merck
- NCQ
- Peggy Lillis Foundation
- Pew
- Premier
- SHEA
- SIDP
- Vizient

Value of the Playbook

- Impressive list of national experts with diverse healthcare backgrounds and leading organizations reinforces that antibiotic stewardship is a national priority

- Indispensable tool that aligns perfectly with the CDC's Core Elements and new Joint Commission Accreditation Standards and proposed CMS Conditions for Participation

- Provides examples and suggestions for action for organizations <u>regardless</u> of size or resources
    - Basic > Intermediate > Advanced
    - Barriers and Suggested Solutions
    - Suggested Tools and Resources

The Antimicrobial Stewardship Playbook is a key resource. In addition to distributing the document to 12,000+ individuals and facilities, we hope it will actively integrate it into all acute care hospitals through antimicrobial stewardship collaboratives and with individual hospitals/health systems that are starting or enhancing their ASP program.

Core Element 1: Leadership Commitment

To succeed, antibiotic stewardship programs need clear support from hospital leadership. Leadership commitment can be demonstrated in many ways, and the board, executive team, leadership, and professional staff must all clearly support that commitment. Dedicating necessary human, financial, and information technology resources is a key part of demonstrating an organization's commitment to effective stewardship. Here are examples of core actions that could be taken to demonstrate leadership commitment, examples of implementation, and identified barriers with potential solutions.

- Facility leadership should provide a visible, written statement of support for the antibiotic stewardship program (ASP). Formal statements (e.g., a policy or statement approved by the board) carry more weight with facility staff than less formal communications (e.g., a newsletter column).

- Facility leadership should provide support (financial and time) for training and education on antibiotic stewardship (AS), ensure adequate staffing, and establish a clear communication strategy on AS.

- Facility leadership should provide sustained financial support and ensure that ASP team leaders have time to perform the functions of the program.

Examples of Implementation

Basic

- Issue a formal board-approved statement on the importance of the ASP and include in annual report.

- Develop and distribute a newsletter column from the CEO and CMO and/or chief of the medical staff highlighting the ASP and their commitment to improving antibiotic use.

- Dedicate specific salary support for ASP leaders based on size and population of the hospital.

- Include specific time commitment (%FTE or hours/week, hours/month) in the job description of ASP leaders, and articulate targets and goals.

- Support funding for remote consultation or telemedicine with experts in antibiotic stewardship (e.g., infectious diseases physicians and pharmacists) if local resources are not available.

- Communicate regularly the importance of improving antibiotic use and the hospital's commitment to antibiotic stewardship.

- Share stories, speakers, and other resources that highlight how ASPs can improve patient outcomes.

Intermediate

- Designate or appoint a hospital executive to serve as a "champion" of the ASP.

- Include ASP outcome measures in the facility's strategic dashboard and update leadership regularly on meeting those goals.

- Integrate ASP activities into quality improvement and/or patient safety initiatives and reports to medical executives.

- Include antibiotic stewardship in ongoing provider education programs and annual competencies.

Advanced

- Ensure that ASP leaders have training in measuring and improving antibiotic use.

- Prioritize funding for information technology

Potential Barriers Suggested Solutions

Low Support of ASP by Leaders

Suggested Solutions

- Direct leaders to statements on the importance of antibiotic stewardship programs from groups such as the American Hospital Association, the Institute for Healthcare Improvement, and The Leapfrog Group, which are recognized by hospital C-suite leaders.

- Develop and advance the business case to show that ASPs provide high value by improving patient outcomes, the patient experience, and reducing adverse effects, which in turn decreases costs and results in financial savings.

- Refer to key national reports on the importance of antibiotic stewardship and antibiotic resistance.

- Share data on hospital problem areas such as high antibiotic resistance rates, *C. difficile* infection rates, inappropriate antibiotic use, readmissions due to infections, etc. *C. difficile* rates can be especially influential since they are part of the Centers for Medicare & Medicaid Services Inpatient Quality Reporting Program.

Low Awareness of ASP at Board/C-Suite Levels

Suggested Solutions

- Provide leaders with data, narratives, and expert-led presentations on ASP benefits (e.g., reductions in *C. difficile* infections, improved infection cure rates, and reductions in antibiotic resistance).

- Engage patients and advocates to share stories about *C. difficile* infections and antibiotic-resistant organisms and their impact on patients and families.

Competing Priorities or "Initiative Fatigue"

Suggested Solutions

- Direct leaders to proposed regulatory and accreditation requirements (i.e., from The Joint Commission).

- Emphasize that ASP implementation is a workforce and patient safety issue as well as a patient experience issue.

- Discuss the potential impact on the hospital brand if AS is not prioritized.

- Gain efficiencies by incorporating stewardship efforts into other quality improvement efforts (e.g., *C. difficile*, sepsis).

Suggested Tools and Resources

Hospital Resources

- Centers for Disease Control and Prevention (CDC). Antimicrobial Management Program Gap Analysis Checklist. Atlanta, GA: CDC; 2010.

Evidence on Impact of ASPs

- Schuts EC, Hulscher ME, Mouton JW, et al. Current evidence on hospital antimicrobial stewardship objectives: a systematic review and meta-analysis. *Lancet Infect Dis*. 2016; S1473-3099(16):00065-7. [Epub ahead of print].

Business Case for ASP

- Greater New York Hospital Association (GNYHA), United Health Fund. Appendix M: Theoretical Monthly Savings of an Antimicrobial Stewardship Program. In: Antimicrobial Stewardship Toolkit. New York, NY: GNYHA; 2015:77.

- Anthem. Quality-In-Sights®: Hospital Incentive Program (Q-HIP).

- Kravitz GR. Making the Business Case for ASP: Taking It to the C-Suite [PowerPoint]. St. Paul, MN: St. Paul Infectious Disease Associates; 2015.

- Centers for Disease Control and Prevention (CDC). Get Smart About Antibiotics: Save Money With Antibiotic Stewardship Fact Sheet. Atlanta, GA: CDC; 2015.

- Lynch JB. Antimicrobial Stewardship - A Value-Driven Means to Improved Patient Outcomes and Reduce Costs. *HFM Magazine*. 2016; March: 38-41.

- Rodriguez, AG. A virtual ID Specialist: Antimicrobial stewardship via telemedicine. Becker's Health IT & CIO Review. November 20, 2015.

Key National Resources

- Centers for Disease Control and Prevention (CDC). Core Elements of Hospital Antibiotic Stewardship Programs. Atlanta, GA: CDC: 2014.

- The White House. National Strategy for Combating Antibiotic-Resistant Bacteria. Washington, DC: White House; 2014.

- The White House. National Action Plan for Combating Antibiotic-Resistant Bacteria. Washington, DC: White House; 2015.

- Centers for Disease Control and Prevention (CDC). Get smart for healthcare: overview and evidence to support stewardship.

- Spellberg B, Srinivasan A, Chambers HF. New societal approaches to empowering antibiotic stewardship. *JAMA*. 2016;315(12):1229-1230.

Implementation Tools

- American Hospital Association (AHA), American Hospital Association's Physician Leadership Forum. Appropriate Use of Medical Resources. Antimicrobial Stewardship Toolkit. Washington, DC: AHA; 2014.

- The Society for Healthcare Epidemiology of America. Antimicrobial stewardship: implementation tools & resources.

Regulatory and Accreditation Requirements

- Joint Commission Resources.

Core Element 5: Tracking and Monitoring Antibiotic Prescribing, Use, and Resistance

Monitoring antibiotic prescribing and resistance patterns is critical to identify opportunities for improvement and to assess the impact of improvement efforts.

- Systematic collection of antibiotic use and resistance data allows facilities to assess, monitor, and improve prescribing practices.

Examples of Implementation

Basic:
Process Measures

- Adherence to documentation policies, e.g., requirement to document indications for antibiotic use and requirements to document performance of time-outs.

- Tracking of diagnosis, drug, dose, duration, and de-escalation with antibiotic time-out.

- Adherence to facility-specific treatment recommendations or guidelines.

- Adherence to specified interventions.

- Accurate antibiotic allergy and adverse reaction histories.

Intermediate:
Outcome Measures

- Sequential tracking of antibiotic resistance patterns (e.g., gram negative resistance).

- Tracking of *C. difficile* infection rates.

- 30-day readmission rates for pneumonia and *C. difficile*.

Advanced:
Antibiotic Use Measures

- Number of antibiotics administered to patients per day (i.e., days of therapy, or "DOT"). Hospitals can use the CDC National Healthcare Safety Network (NHSN) Antibiotic Use Option to track and benchmark days of therapy.

- Grams of antibiotics used (defined daily dose, or "DDD") could be used if DOT not available.

- Standardized antibiotic administration ratio (SAAR), an NQF-endorsed quality benchmarking measure for antibiotic use, available to hospitals enrolled in the NHSN Antibiotic Use Option.

- Direct antibiotic expenditures (purchasing costs).

Potential Barriers Suggested Solutions

ASP Does Not Have Resources to Conduct Measurements

Suggested Solutions

- Review organisms on CDC threat report, identify top pathogens relevant to the institution, and monitor one or more of those.

- Standardize data collection in terms of information, recording practices, and timing/frequency.

- Consider choosing one measure of antibiotic use.

- Use shared data to compare with other hospitals.

- Develop relationships with data experts through state collaboratives, health departments, specialty societies, or trade associations.

Lack of Enough Isolates to Produce an Antibiogram

Suggested Solution

- Review antibiotic susceptibility data on a regional basis.

Overwhelming Amount of Antibiotic Use and Resistance Data

Suggested Solution

- Engage units in tracking efforts (e.g., ask every unit to track and report on one syndrome and identified metrics).

- Partner with quality improvement and infection control staff to explore and identify ways to partner for data collection.

Lack of Expertise for Data Collection, Analysis, and Interpretation

Suggested Solutions

- Consider using audit tools or point prevalence surveys to help assess appropriate use (e.g., for urinary tract infections, community acquired pneumonia, and vancomycin).

Lack of IT Infrastructure

Suggested Solution

- Ensure that tracking and monitoring are part of discussions with IT staff and facility administration when engaging their support for stewardship efforts.

Challenges in Defining "Appropriate" or "Optimal"

Suggested Solutions

- Use facility-specific guidelines as the basis for decisions about appropriate use; disregard complex cases that cannot be assessed easily.

- Conduct occasional (e.g., quarterly) structured audits of appropriate use to identify targets for improvement.

- Use standardized audit tools for appropriate use.

Suggested Tools and Resources

Appropriate Antibiotic Use

- Centers for Disease Control and Prevention (CDC). Implementation Resources. Assessment tools for antibiotic use.

- Septimus E. Antimicrobial stewardship—qualitative and quantitative outcomes: the role of measurement. *Curr Infect Dis Rep.* 2014;16(11):433.

- Ibrahim OM, Polk RE. Benchmarking antimicrobial drug use in hospitals. *Expert Rev Anti Infect Ther.* 2012;10(4):445–457.

- National Quality Forum (NQF). Quality Positioning System. NQF-endorsed Standardized Antibiotic Administration Ratio

- CMS. gov. Physician Quality Reporting System. Measure #407: Appropriate treatment of methicillin-sensitive staphylococcus aureus (MSSA) bacteremia – National Quality Strategy domain: effective clinical care.

Modules, Exercises, and Infographics

- Centers for Disease Control and Prevention (CDC). Antimicrobial Use and Resistance (AUR) Module. Atlanta, GA: CDC: 2016.

- Centers for Disease Control and Prevention (CDC); National Healthcare Safety network (NHSN). Antibiogram demo exercise: advanced line list; Demo exercise results: advanced line list. Atlanta, GA: CDC; 2014.

- Centers for Disease Control and Prevention (CDC). Antibiotic Resistance Solutions Initiative Infographic. Atlanta, GA: CDC; 2015.

- Centers for Disease Control and Prevention (CDC). Multidrug-Resistant Organism & Clostridium difficile Infection module. Atlanta, GA: CDC; 2016.

Clinical and Laboratory Standards Institute

- Clinical and Laboratory Standards Institute. M39-A4 QG. Antibiograms: developing cumulative reports for your clinicians quick guide.

Additional Resources

- Premier Safety Institute. Antimicrobial stewardship: Combating antibiotic resistance website.

- Premier Safety Institute. Quest Antimicrobial Collaborative website.

Regulatory Changes

Stewardship Seats at the Table – 3/24/2016
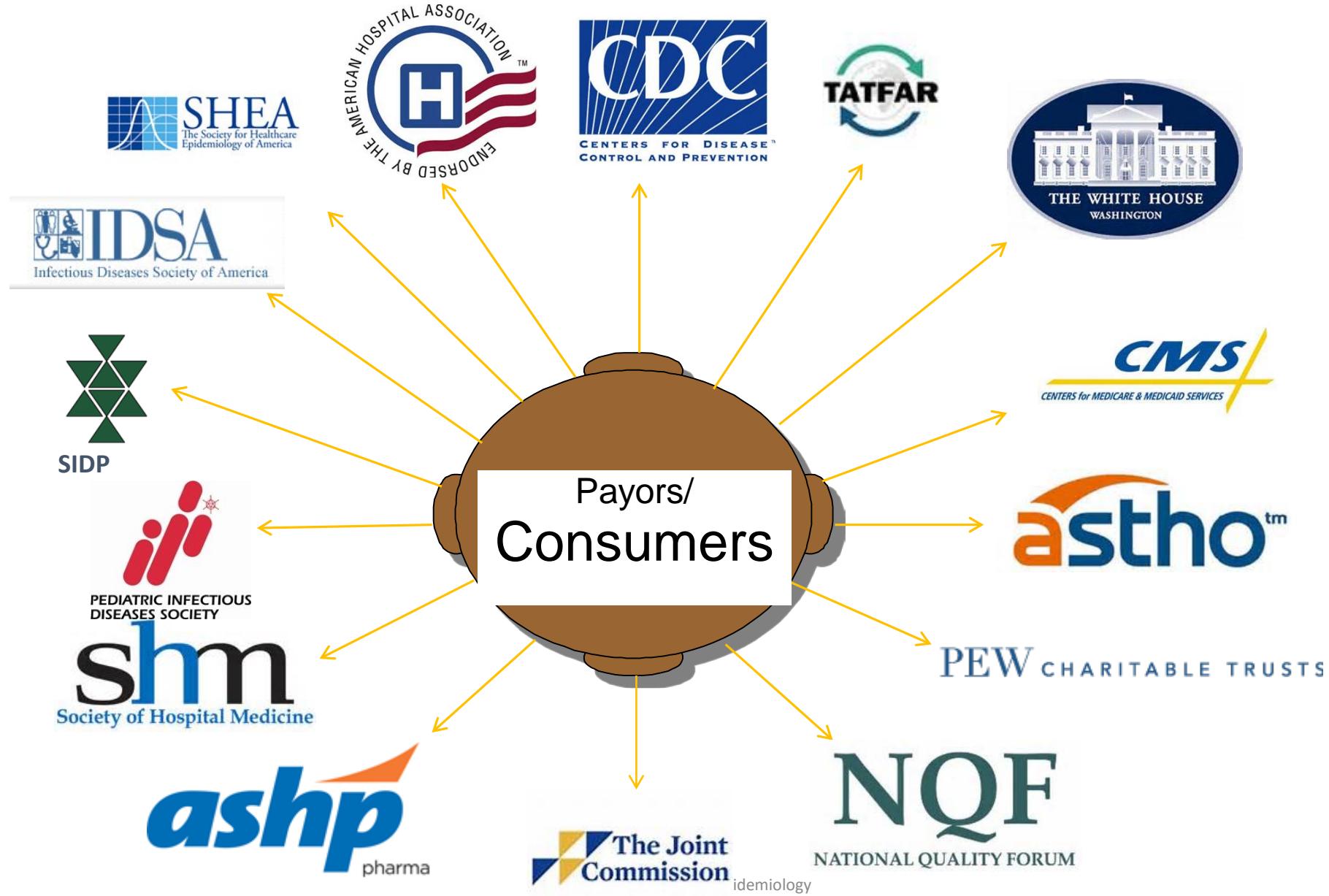
NATIONAL ACTION PLAN FOR COMBATING ANTIBIOTIC-RESISTANT BACTERIA

MARCH 2015

THE WHITE HOUSE
WASHINGTON

Background

- President's Executive Order and National Strategy (Sep 2014)

- PCAST Report to the President (Sep 2014)

- National Action Plan for Combating Antibiotic-Resistant Bacteria (CARB) (Mar 2015)

PCAST-President's Council of Advisors on Science and Technology

National Action Plan highlights

- The plan sets 1-, 3-, and 5-year targets in each of the five overarching goals, which are to:
    - slow the emergence of resistant bacteria and prevent the spread of resistant infections
    - strengthen national one-health surveillance efforts to combat resistance (the "one-health" approach to disease surveillance integrates data from multiple monitoring networks, according to the White House)
    - advance development and use of rapid and innovative diagnostic tests for the identification and characterization of resistant bacteria;
    - accelerate basic and applied research and development for new antibiotics, other therapeutics, and vaccines; and
    - improve international collaboration and capacities for antibiotic resistance prevention, surveillance, control, and antibiotic research and development

National Action Plan continued

- The plan sets goals for eradicating pathogens that have been labeled urgent or serious threats by the Centers for Disease Control and Prevention (CDC). The 2020 targets include:
  - 50% reduction from 2011 estimates in the incidence of *Clostridium difficile*
  - 60% reduction in hospital-acquired carbapenem-resistant Enterobacteriaceae infections
  - 35% reduction in hospital-acquired multidrug-resistant *Pseudomonas* species infections
  - 50% reduction from 2011 estimates in methicillin-resistant *Staphylococcus aureus* bloodstream infections
  - 50% reduction in inappropriate antibiotic use in outpatient settings and a 20% reduction in inpatient settings,
  - The development and wide dissemination of rapid diagnostic tests that can be used in a physician's office or at the hospital bedside to distinguish between viral and bacterial infections, and thus help ensure more appropriate use of therapeutics.

Proposed Policy Changes

- Strengthen antibiotic stewardship in inpatient, outpatient, and long-term care settings
  - **Alignment with CDC Core Elements**
  - **Compliance with Conditions of Participation and The Joint Commission (TJC) Accreditation requirements**
- Implement annual reporting of antibiotic use in inpatient and outpatient settings and identify variation at geographic, provider, and patient levels
- Establish and improve antibiotic stewardship programs across <u>all</u> healthcare settings
- Reduce inappropriate antibiotic use by 50% in outpatient settings and 20% in inpatient settings
- Establish State Antibiotic Resistance (AR) Prevention (Protect) Programs in all 50 states

Joint Commission(TJC) starts January 2017

- **EP 1** : Leaders establish antimicrobial stewardship as an organizational priority
- **EP 2:** The 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.
- **EP 3:** The hospital educates patients, and their families as needed, regarding the appropriate use of antimicrobial medications, including antibiotics

TJC continued

- **EP 4:** The hospital has an antimicrobial stewardship multidisciplinary team that includes the following members, when available: infectious diseases physician, pharmacy, infection prevention, other practitioners

- **EP 5:** The hospital's antimicrobial stewardship program includes the following core elements:
  - **Leadership commitment:** Dedicating necessary human, financial, and information technology resources.
  - **Accountability:** Appointing a single leader responsible for program outcomes
  - **Drug expertise:** Appointing a single pharmacist leader responsible for working to improve antibiotic use

TJC continued

- **EP 5** continued
  - **Action:** Implementing recommended actions, such as systemic evaluation of ongoing treatment need, after a set period of initial treatment (for example, *S aureus* bacteremia, de-escalation, 72 hour time-out).
  - **Tracking:** Monitoring the antimicrobial stewardship program, which may include information on antibiotic prescribing and resistance patterns
  - **Reporting:** Regularly reporting information on the antimicrobial stewardship program, which may include information on antibiotic use and resistance, to doctors, nurses, and relevant staff
  - **Education:** Educating practitioners, staff, and patients on the antimicrobial program, which may include information about resistance and optimal prescribing.

TJC continued

- **EP 6:** The hospital's antimicrobial stewardship program uses organization-approved multidisciplinary
  protocols (for example, policies and procedures).

- **EP 7:** The hospital collects, analyzes, and reports data on its antimicrobial stewardship program

- **EP 8:** The hospital takes action on improvement opportunities identified in its antimicrobial stewardship program.

Antibiotic Stewardship as a Condition of Participation

- By the end of 2017, CMS should have Federal regulations (Conditions of Participation) in place that will require U.S. hospitals, critical access hospitals, and long-term care and nursing home facilities to have in place robust antibiotic stewardship programs that adhere to best practices, such as those contained in the CDC Core Elements for Hospital Antibiotic Stewardship Program recommendations. Similar requirements should be phased in rapidly for other settings including long-term acute care hospitals, other post-acute facilities, ambulatory, surgery centers, and dialysis centers.

CMS Update

- CMS has published proposed conditions of participation(COP)

- CMS has posted for comment of potential inclusion of NHSN AU Measure (Standard Antibiotic Administration Ratio or SAAR)

Case

This is a 46 year old female admitted with hypotension, fever, and flank pain. She has no underlying medical or urologic problems. Her urine showed pyuria and bacteriuria, the peripheral WBC was 16,000/mm^3. She was admitted to the ICU and empirically started on _____.

What would you start?

And Now the Rest of the Story

She was admitted to the ICU and started on cefepime. By day 2, she stabilized and was transferred to the floor. Her urine and blood grew *E. coli* sensitive to all tested antibiotics except ampicillin. The results were not available until after she was transferred to the floor. She was continued on cefepime. On day 11, she spiked a new fever. Blood cultures were drawn and grew_____. Antibiotics were changed to _____. On day 12 her WBC increased to 30,000/mm^3 and she reported unformed stools. Your diagnosis_____

If you want to go Fast, go alone.
If you want to go Far, go together.

THE DOER

THE THINKER
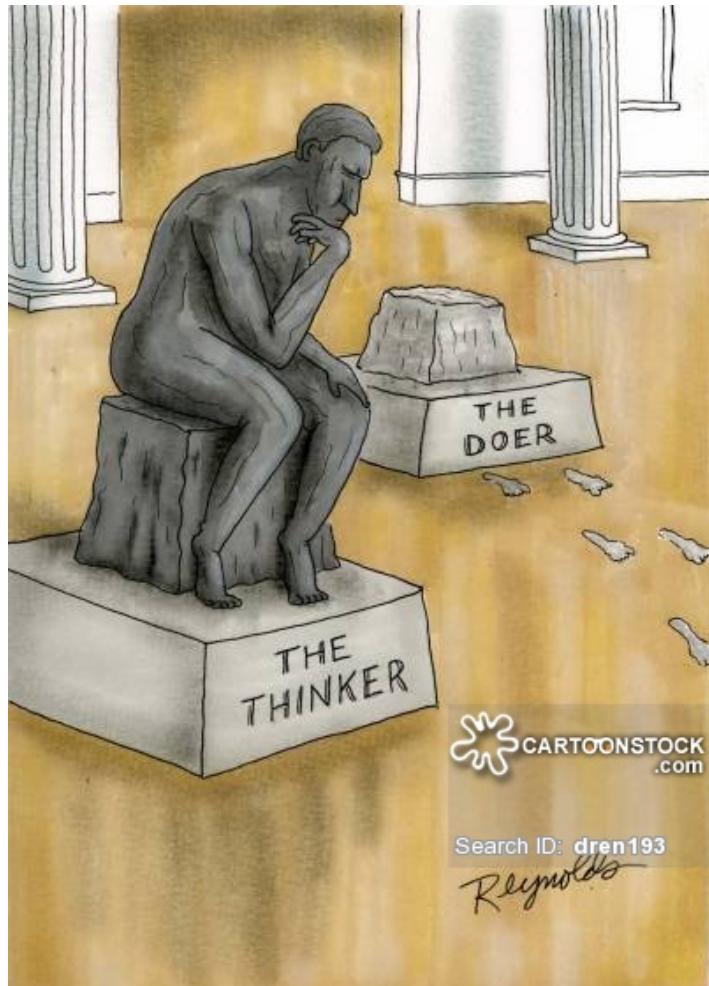
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Infection Prevention and Epidemiology