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Antimicrobial Stewardship Programs: Are We Measuring Up to Our Full Potential?

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Disclosure

Susan Davis

Allergan: Advisory Board, Speaker's Bureau; The Medicines Company: Advisory Board; Zavante: Advisory Board

Elizabeth Dodds Ashley

HANYS: Consultant; SHEA: Speaker's Bureau

All other planners, presenters, and reviewers of this session report no financial relationships relevant to this activity.

Objectives

- Evaluate strategies to achieve programmatic compliance with current regulatory requirements
- Recommend appropriate analyses to measure antimicrobial consumption
- Interpret the effect of ASP initiatives on clinical outcomes

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Measuring up

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Pharmacist Liaison
Duke Antimicrobial Stewardship
Outreach Network (DASON)

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How to achieve compliance with regulatory mandates

MEASURING UP

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IS STEWARDSHIP REQUIRED?

Our Marching Orders: National Action Plan

TABLE 2: GOALS AND OBJECTIVES: Combating Antibiotic-Resistant Bacteria	
GOAL 1: Slow the Emergence of Resistant Bacteria and Prevent the Spread of Resistant Infections	
Objectives	
1.1	Implement public health programs and reporting policies that advance antibiotic-resistance prevention and foster antibiotic stewardship in healthcare settings and the community.
1.2	Eliminate the use of medically-important antibiotics for growth promotion in food- producing animals and bring other agricultural uses of antibiotics, for treatment, control, and prevention of disease, under veterinary oversight.
1.3	Identify and implement measures to foster stewardship of antibiotics in animals.

Specific goals:

- Within 3 years:
  - Condition of participation from CMS in line with CDC Core Elements of Hospital Antibiotic Stewardship Programs
- By 2020:
  - Establishment of antibiotic stewardship programs in all acute care hospitals and improved antibiotic stewardship across all healthcare settings.
  - Reduction of inappropriate antibiotic use by 50% in outpatient settings and by 20% in inpatient settings.

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So, where are we today?

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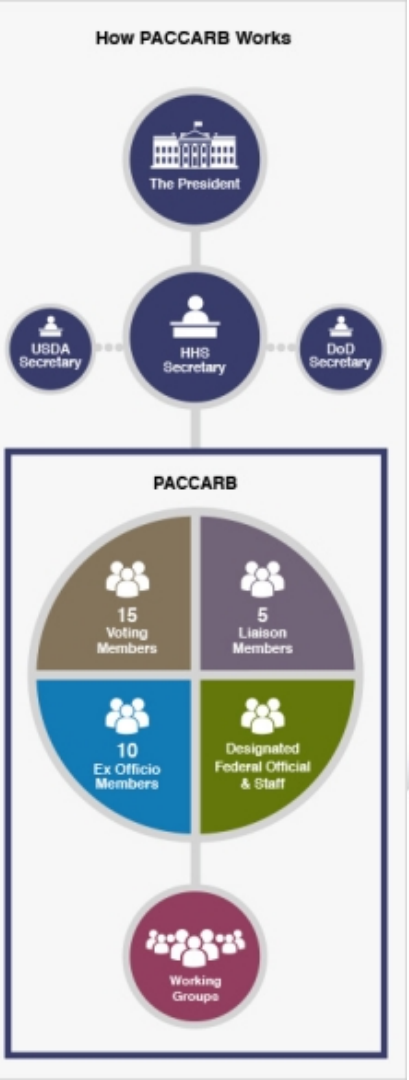
PACCARB

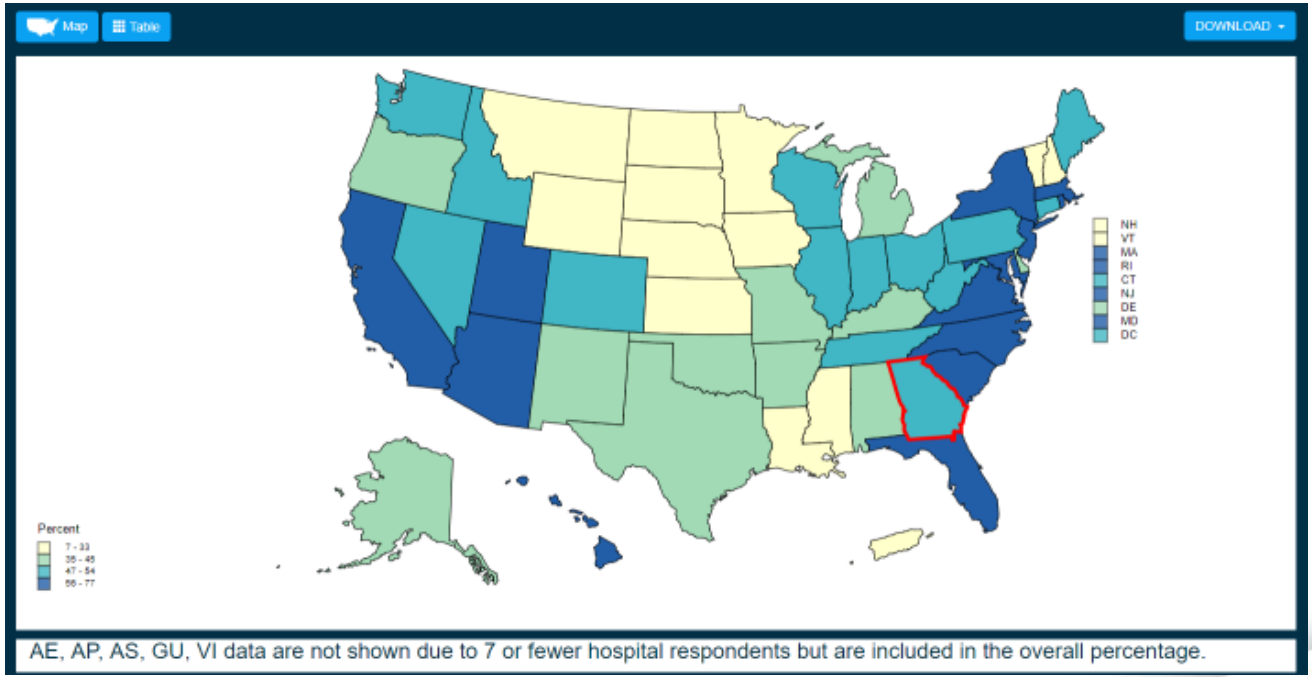
Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria



Current State Stewardship Mandates

- California (SB-1311)
- *Each general acute care hospital, as defined in subdivision (a) of Section 1250, shall do all of the following by July 1, 2015:*
- *(a) Adopt and implement an antimicrobial stewardship policy in accordance with guidelines established by the federal government and professional organizations. This policy shall include a process to evaluate the judicious use of antibiotics in accordance with paragraph (3) of subdivision (a) of Section 1288.8.*
- Missouri (MO-SB579)
- *Additionally, this legislation requires Missouri hospitals and ambulatory surgical centers to establish antimicrobial stewardship programs for surveillance of use and resistance of certain antibiotics by Aug. 28, 2017. Mental health facilities are excluded from the antibiotic stewardship requirement. When federal Stage 3 "meaningful use" regulations take effect, hospitals and ambulatory surgical centers will report through the NHSN Antimicrobial Use and Resistance Module. Hospitals can learn more about establishing an effective antibiotic stewardship program by reviewing resources from the Centers for Disease Control and Prevention.*

AR Patient Safety Atlas- Stewardship Implementation (2015)



https://gis.cdc.gov/grasp/psa

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Key Policy Developments in Stewardship

- July 2015: CMS released revised Conditions of Participation for nursing homes that include a requirement for stewardship programs.
- December 2015: The Joint Commission (TJC) issued proposed accreditation standards requiring antibiotic stewardship programs in all accredited facilities.
- June 2016: CMS released draft revised Conditions of Participation for nursing homes that include a requirement for stewardship programs.
- January 2017: TJC began surveying on antimicrobial stewardship standards.
- November 2017: Stewardship Requirement for nursing homes take effect.

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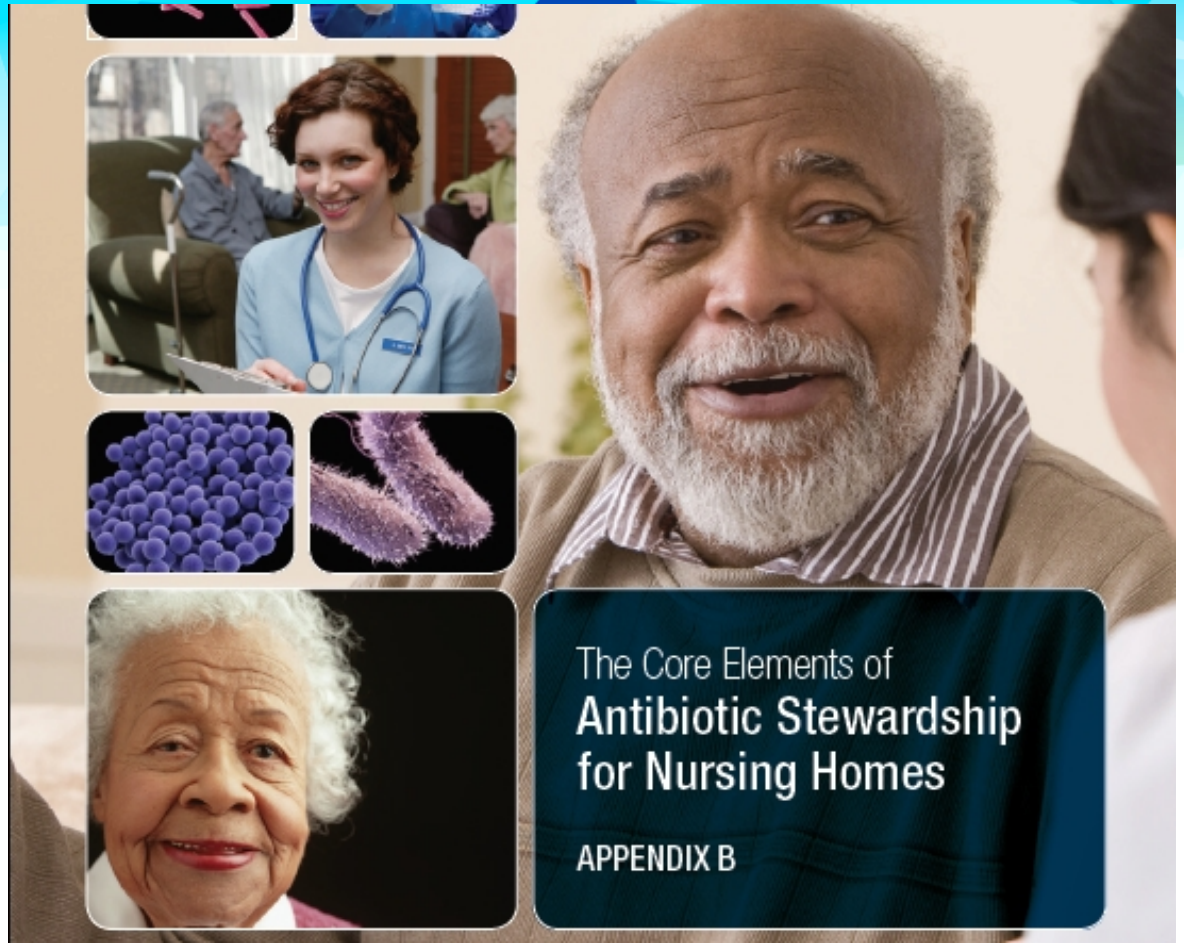
Long Term Care Facility
CMS 2015 Requirements

perform a facility-specific assessment of their resident population and facility (§ 483.70)

- Integration of the infection prevention and control program (IPCP) with the facility's QAPI processes (§ 483.75)
- Revising the description of the infection control program and adding a requirement to periodically review and update the program (§ 483.80)
- Requiring an antibiotic stewardship program that includes antibiotic use protocols and a system for monitoring antibiotic use (§ 483.80)
- Designation of specific infection prevention and control officers (IPCOs) (§ 483.80)
- Written policies and procedures for the IPCP (§ 483.80)
- Education or training related to the infection control program (§ 483.80)

- The stewardship program would be part of the facility's infection prevention and control program.
- CDC has developed "Core Elements for Antibiotic Stewardship Programs in Long Term Care" to help with implementation.



Duke University School of Medicine

dason.medicine.duke.edu

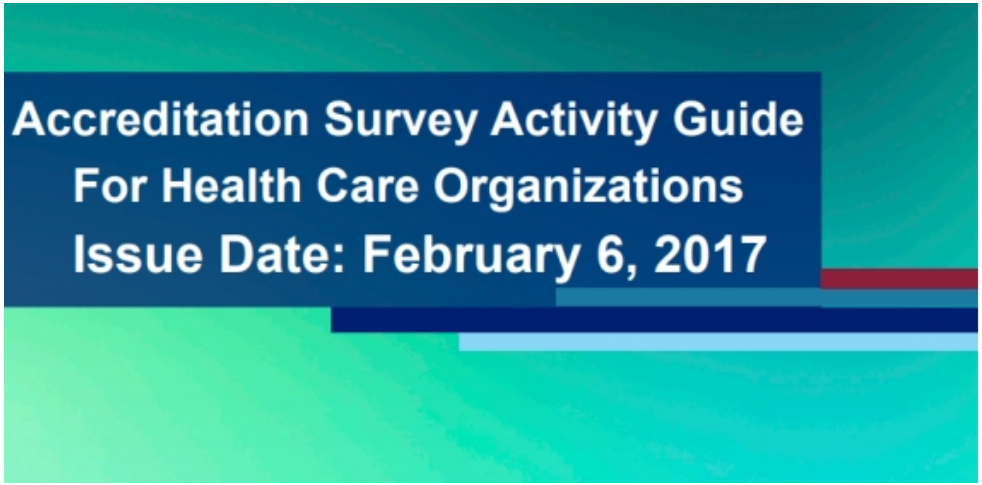
dason DUKE ANTIMICROBIAL STEWARDSHIP OUTREACH NETWORK

Some are Not Waiting: New TJC Standards

Key Points:

- Fall in the Medication Management Section (MM)
- 8 Elements of Performance:
  - Leadership
  - Staff Education
  - ~~Patient and Family Education~~
  - Stewardship Team (MD, RPh, IP)
  - CDC Core Elements
  - Protocols
  - Data
  - Action on improvement opportunities

Are we prepared?

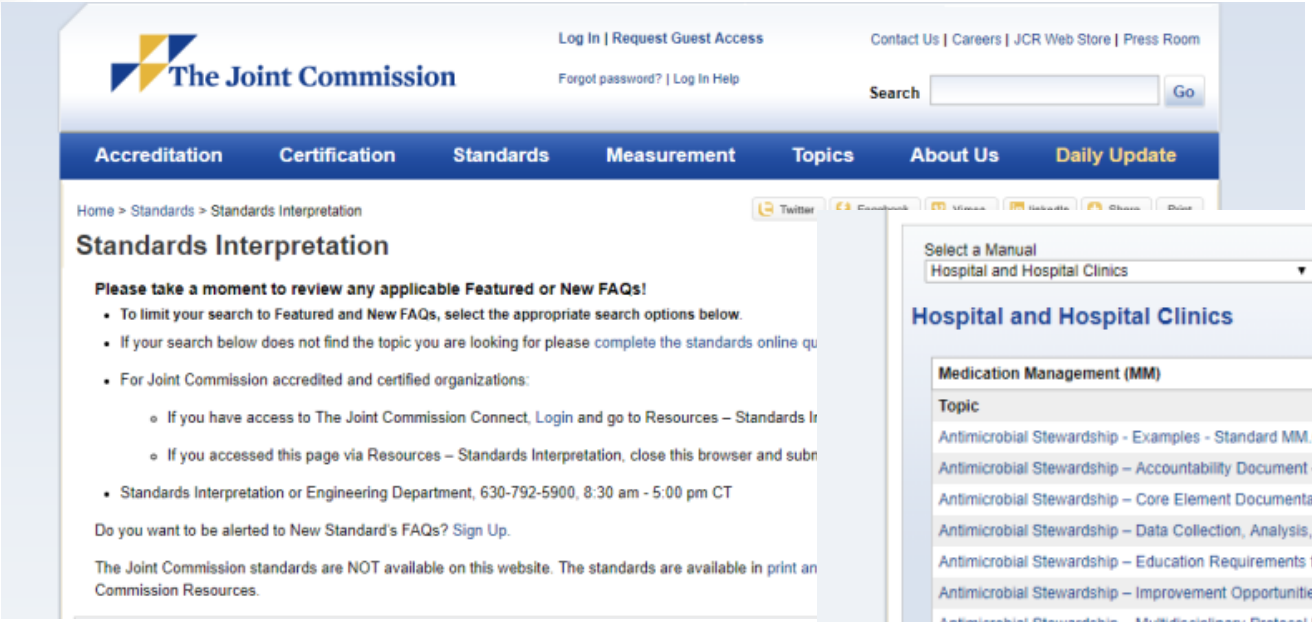


Please ask yourself:

- If I work at an institution with no ID MD will I fail?
- Do I have to implement all of the suggested stewardship interventions?

https://www.jointcommission.org/assets/1/18/2017_Organization_SAG.pdf

Frequently Asked Questions



https://www.jointcommission.org/standards_information/jcfaq.aspx?ProgramId=5&ChapterId=76&IsFeatured=False&IsNew=False&Keyword=

Important Clarifications!

Medication Management (MM) (Hospital and Hospital Clinics / Hospitals)

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Antimicrobial Stewardship – Multidisciplinary Team Requirements - Standard MM.09.01.01, EP 4

If an organization does not have an infectious disease physician on the antimicrobial stewardship multidisciplinary team will it receive a Requirement for Improvement (RFI)?

This depends on the availability of infectious disease physicians to serve in this capacity. The Joint Commission is aware that the composition of this multidisciplinary team may vary based on the type of organization being surveyed as well as the geographic location of the organization. This is the reason MM.09.01.01, EP 4 indicates that the four practitioners listed should be on the multidisciplinary team "when available in the setting." However, it would not be acceptable for an organization to have a team consisting of only a pharmacist and a nurse when physicians and other licensed independent practitioners are available in the organization (e.g., an infectious disease consultation team exists).
Note: Some organizations such as critical access hospitals and nursing care centers may not have the Medication Management System Tracer. In these cases, antimicrobial stewardship will be evaluated during other scheduled activities, such as Orientation to the Organization, Data Use System Tracer, and Individual Patient Tracers.

https://www.jointcommission.org/standards_information/jcfaq.aspx?ProgramId=5&ChapterId=76&IsFeatured=False&IsNew=False&Keyword=

Helpful Tool

Medication Management (MM) (Hospital and Hospital Clinic

Antimicrobial Stewardship – Core Element Documentation - Standard M

What type of documentation is needed for MM.09.01.01 EP 5, the required core program?

The organization needs to have a document indicating how each core element is a This information can be located in a separate document or can be included in othe MM.09.01.01, EP 1). This documentation does not have to be provided in a length elements are addressed in the antimicrobial stewardship program.

Checklist for Core Elements of Hospital Antibiotic Stewardship Programs

The following checklist is a companion to *Core Elements of Hospital Antibiotic Stewardship Programs*. This checklist should be used to systematically assess key elements and actions to ensure optimal antibiotic prescribing and limit overuse and misuse of antibiotics in hospitals. CDC recommends that all hospitals implement an Antibiotic Stewardship Program.

Facilities using this checklist should involve one or more knowledgeable staff to determine if the following principles and actions to improve antibiotic use are in place. The elements in this checklist have been shown in previous studies to be helpful in improving antibiotic use though not all of the elements might be feasible in all hospitals.

LEADERSHIP SUPPORT	ESTABLISHED AT FACILITY
A. Does your facility have a formal, written statement of support from leadership that supports efforts to improve antibiotic use (antibiotic stewardship)?	❑ Yes ❑ No
B. Does your facility receive any budgeted financial support for antibiotic stewardship activities (e.g., support for salary, training, or IT support)?	❑ Yes ❑ No
ACCOUNTABILITY	
A. Is there a physician leader responsible for program outcomes of stewardship activities at your facility?	❑ Yes ❑ No

https://www.cdc.gov/getsmart/healthcare/pdfs/checklist.pdf
https://www.jointcommission.org/standards_information/jcfaq.aspx?ProgramId=5&ChapterId=76&IsFeatured=False&IsNew=False&Keyword=

Important Clarifications

Medication Management (MM) (Hospital and Hospital Clinics / Hospitals)

Antimicrobial Stewardship – Education Requirements for Staff and Licensed Independent Practitioners - Standard MM.09.01.01 EP 2

Will Joint Commission surveyors review human resource records and medical staff credentialing and privileging records to determine if antimicrobial resistance and antimicrobial stewardship education was provided by the organization?

Joint Commission surveyors will not be reviewing staff or medical staff/licensed independent practitioner records on education received regarding antimicrobial resistance and antimicrobial stewardship. Joint Commission surveyors will inquire about the type of education provided by the organization during the Medication Management System Tracer (or other system tracers). During patient tracers, surveyors may ask staff and licensed independent practitioners about the education they have received. Providing written material such as the organization's antibiogram will meet the educational requirement of MM.09.01.01, EP 2.

https://www.jointcommission.org/standards_information/jcfaq.aspx?ProgramId=5&ChapterId=76&IsFeatured=False&IsNew=False&Keyword=

Important Clarifications - Examples are Examples

Medication Management (MM) (Hospital and Hospital Clinics / Hospitals)

Antimicrobial Stewardship – Improvement Opportunities - Standard MM.09.01.01 EP 8

Are there any specific improvement opportunities that surveyors will look for regarding the organization's antimicrobial stewardship pr

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Antimicrobial Stewardship – Multidisciplinary Protocol Requirements - Standard

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Medication Management (MM) (Hospital and Hospital Clinics / Hospitals)

Antimicrobial Stewardship - Examples - Standard MM.09.01.01 EPs 1, 3, 5, 6, and 7

When examples are provided within an EP, are these example considered to be part of the requirement?

No. The examples that are provided in EPs 1, 3, 5, 6, and 7 are not Joint Commission requirements and are provided to assist organizations during their review of the antimicrobial stewardship standard based on the care, treatment, and services provided.

https://www.jointcommission.org/standards_information/jcfaq.aspx?ProgramId=5&ChapterId=76&IsFeatured=False&IsNew=False&Keyword=

Is Reporting to the NHSN AU Option Required?

Medication Management (MM) (Hospital and Hospital Clinics / Hospitals)

Antimicrobial Stewardship – Data Collection, Analysis, and Reporting - Standard MM.09.01.01 EP 7

What type of antimicrobial stewardship data should organizations collect, analyze, and report?

The Joint Commission is not requiring any specific antimicrobial stewardship data in Standard MM.09.01.01. The organization must determine the antimicrobial stewardship data it will collect, analyze, and report. The CDC's Core Elements of Hospital Antibiotic Stewardship Programs at https://www.cdc.gov/getsmart/healthcare/pdfs/core-elements.pdf and The Core Elements of Antibiotic Stewardship for Nursing Homes at https://www.cdc.gov/longtermcare/prevention/antibiotic-stewardship.html provide examples of measures that can be used to collect antimicrobial stewardship data and should be considered by organizations.

Additionally, the National Quality Partners Playbook on Antibiotic Stewardship in Acute Care provides examples of basic, intermediate, and advanced measures.
(http://www.qualityforum.org/Publications/2016/05/National_Quality_Partners_Playbook__Antibiotic_Stewardship_in_Acute_Care.aspx)

https://www.jointcommission.org/standards_information/jcfaq.aspx?ProgramId=5&ChapterId=76&IsFeatured=False&IsNew=False&Keyword=

US Benchmarking Efforts

CDC- Antimicrobial Use and Resistance module

Objective: The primary objective of Antimicrobial Use option is to facilitate risk-adjusted inter- and intra-facility benchmarking of antimicrobial usage.

- Secondary objective: to evaluate trends of antimicrobial usage over time at the facility and national levels.

Primary metric: antimicrobial days/ 1000 days present

Data source: electronic MAR (with or without barcode medication administration)

Standardized Antibiotic Administration Ratio (SAAR)

$$\text{SAAR} = \frac{\text{Observed (O) Antimicrobial Use}}{\text{Predicted (P) Antimicrobial Use}}$$

- Predicted- Calculated by CDC based on predictive models based on nationally aggregated AU data
- Calculated for 5 different drug categories
- 4 different patient care locations
  - Adult/Pediatric medical, medical/surgical and surgical ICUs
  - Adult/Pediatric medical, medical/surgical and surgical wards

NQF: Endorsed Measure

- April 2015:
  - Locations categories
    - Adult and pediatric
    - ICU and ward
  - Agent categories
    - Broad spectrum gram negative agents
      - Primarily active against community pathogens
      - Primarily active against hospital pathogens
    - Anti-MRSA agents
    - Agents primarily for surgical prophylaxis
    - All antibiotics
  - Includes plans to standardized (stay tuned!)

List of Measures under Consideration for December 1, 2015

MUC15-531	National Healthcare Safety Network (NHSN) Antimicrobial Use Measure	Numerous individual studies and systematic reviews provide strong evidence that measurement of antimicrobial use and data-driven interventions by antimicrobial stewardship programs (ASPs) lead to more judicious use of antibiotics, reduced antimicrobial resistance, and other favorable healthcare outcomes (Feazel 2014; Davey 2006; Davey 2013; Kaki 2011). Antimicrobial use measurement enables ASPs to understand prescribing practices, focus efforts on improvement, and determine the impact of their activities (Pollack, 2014). Although standardized metrics have been developed to measure antibiotic use, differences in measurement, limited uptake, and variation among facilities has impeded the ability to compare antibiotic use among hospitals. The measure will serve as a quantitative guide for hospital and health system ASPs, enabling them to benchmark antibiotic use in their facilities and patient care locations against nationally aggregated data. The measure focuses on antibiotic agents that have been shown to be high value targets for antimicrobial stewardship programs activities such as protocols for use or post-prescription reviews to determine need for de-escalation, dose-optimization or oral conversion. Knowledge about antibiotic use patterns of these agents is a primary means to prioritize and evaluate antimicrobial stewardship efforts.

Why Is This Important?

- The items on the Measures Under Consideration list are the ones that CMS is considering making part of some type of reporting and/or payment program.

Slide Courtesy of Arjun Srinivasan, MD

Hospital Inpatient Prospective Payment System
2017 Proposed Rule

- "In the future, we are considering proposing the NHSN Antimicrobial Use measure to advance national efforts to reduce the emergence of antibiotic resistance by enabling hospitals and CMS to assess national trends of antibiotic use to facilitate improved stewardship by comparing antibiotic use that hospitals report to antibiotic use that is predicted based on nationally aggregated data."

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Slide Courtesy of Arjun Srinivasan, MD

Meaningful Use Stage 3

CDC > Meaningful Use > Public Health Options

NHSN Meaningful Use Overview

For 2018, NHSN Antimicrobial Resistance and Antimicrobial Use reporting has been identified as a new option for public health registry reporting under Meaningful Use Stage 3. See https://www.federalregister.gov/articles/2015/03/30/2015-06612/2015-edition-health-information-technology-health-it-certification-criteria-2015-edition-base. See

Some are Not Waiting: New Incentives for Stewardship

- Starting in 2016, Anthem Healthcare added compliance with the CDC Core Elements to its Hospital Quality Incentive Program- more than 1000 hospital eligible.
- The Leapfrog Group is adding questions on CDC Core Elements to their annual survey.
  - Important influence for many C-suites.

Leapfrog Scores

http://www.leapfroggroup.org/compare-hospitals

Key Takeaways

- Key Takeaway #1
  - Antimicrobial stewardship is an essential component of preventing antibiotic resistance
- Key Takeaway #2
  - There is currently no national mandate for antimicrobial stewardship, but several states and other agencies are already requiring proof of a program
- Key Takeaway #3
  - It is important for the stewardship team to stay current with proposed and pending regulations- it is a rapidly shifting landscape

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Setting a standard

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Reporting trends in antimicrobial consumption

SETTING A STANDARD

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Why measure antimicrobial consumption?

- Many good reasons, not the least of which is…

The Joint Commission says it's important

- Medication Management
  - Standard MM.09.01.01
    - Elements for Performance (EP):

- Hospitals with Antimicrobial stewardship programs (ASPs):
  - EP 5 Include core elements
    - Tracking and reporting utilization
  - EP 7 Collect and analyzes data
    - Example: use and resistance
  - EP 8 Act on improvement

Measuring Consumption

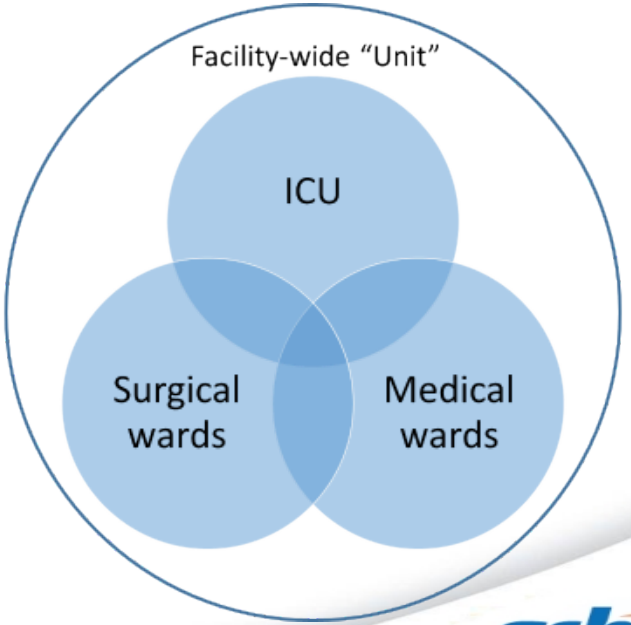
- Consumption metrics
  - Defined daily doses (DDD)
  - Days of therapy (DOT)
- Metric standardization
  - Some measure of occupancy or facility size
  - Should capture number “at-risk”

$$\text{Metric} = \frac{\text{DDD or DOT}}{\text{At-risk days}} \times 1000$$

World Health Organization Collaborating Center for Drug Statistics Methodology. http://wwwwhoccno/atc_ddd_index
Polk RE, Fox C, Mahoney A, et al. Clin Infect Dis. 2007; 44:664–670.

Counting the doses and days

- Knowledge of data sources is essential
  - Where and when are the doses being given?
  - How are the at-risk bedded days counted?



Approach #1:

CORRECT CLASSIFICATION THRESHOLDS

Question 1:

Which of the following will have the largest effect on the positive predictive for an event with a baseline incidence rate of ~10%?

A. Sensitivity increased 5%

B. Specificity increased 5%

C. Incidence increased 5%

D. Incidence decreased 5%

SO YOU HAVE DATA, NOW WHAT?

Is consumption out of control?

- Establishing consumption thresholds
  - Antimicrobial steward reviews consumption data…
    - Asks “Is my antibiotic use out of control (OOC)?”
    - Candidate thresholds can be used to classify whether or not use is OOC

	OOC	Not OOC	Row Total
Use ≥ Threshold	A – true pos	B – false neg	PPV=A/A+B
Use < Threshold	C – false neg	D – true neg	NPV=D/D+C
Column Total	**Sens**=A/A+C	**Spec**=D/D+B	OOC Incidence

Is consumption really out of control?

- Establishing consumption thresholds
  - **Predictive value** of threshold depends on the OOC incidence rate
  - Should prompt deeper look into how/why agents are being used

	OOC	Not OOC	Row Total
Use ≥ Threshold	A – true pos	B – false neg	PPV=A/A+B
Use < Threshold	C – false neg	D – true neg	NPV=D/D+C
Column Total	Sens=A/A+C	Spec=D/D+B	OOC Incidence

Time for a reality check?

- Establishing consumption thresholds
  - Classical detection limits for type I and II error: 5% and 20%

	OOC	Not OOC	Row Total
Use ≥ Threshold	A – 10 month	B – 17 months	27 months; PPV~37%
Use < Threshold	B – 0 month	D – 69 months	78 months; NPV>99%
Column Total	10 months; **Sens: 95%**	86 months; **Spec: 80%**	OOC: 10/96 months (10.4%)

Time for a reality check?

- Establishing consumption thresholds
  - What if we **required higher** specificity from the candidate threshold?

	OOC	Not OOC	Row Total
Use ≥ Threshold	A – 9 months	B – 4 months	13 months; PPV=69%
Use < Threshold	B – 1 month	D – 82 months	83 months; NPV=99%
Column Total	10 months; Sens: 90%	86 months; **Spec: 95%**	OOC: 10/96 months (10.4%)

Time for a reality check?

- Establishing consumption thresholds
  - What if we **accepted a less sensitive** but **more specific** threshold?

	OOC	Not OOC	Row Total
Use ≥ Threshold	A – 7 months	B – 4 months	11 months; PPV=64%
Use < Threshold	B – 3 month	D – 82 months	85 months; NPV=96%
Column Total	10 months; **Sens: 70%**	86 months; Spec: 95%	OOC: 10/96 months (10.4%)

Choosing candidate thresholds

- Maximization of sensitivity of threshold value
  - Improves negative predictive value (NPV) at a fixed incidence
- Maximization of specificity of threshold value
  - Improves positive predictive value (PPV) at a fixed incidence
- Considerations for successful use of this approach:
  - Knowledge of underlying incidence for out of control use needed
  - Access to near real-time consumption data to investigate required

Approach #2:

ESTABLISHING LONGITUDINAL CONSUMPTION THRESHOLDS

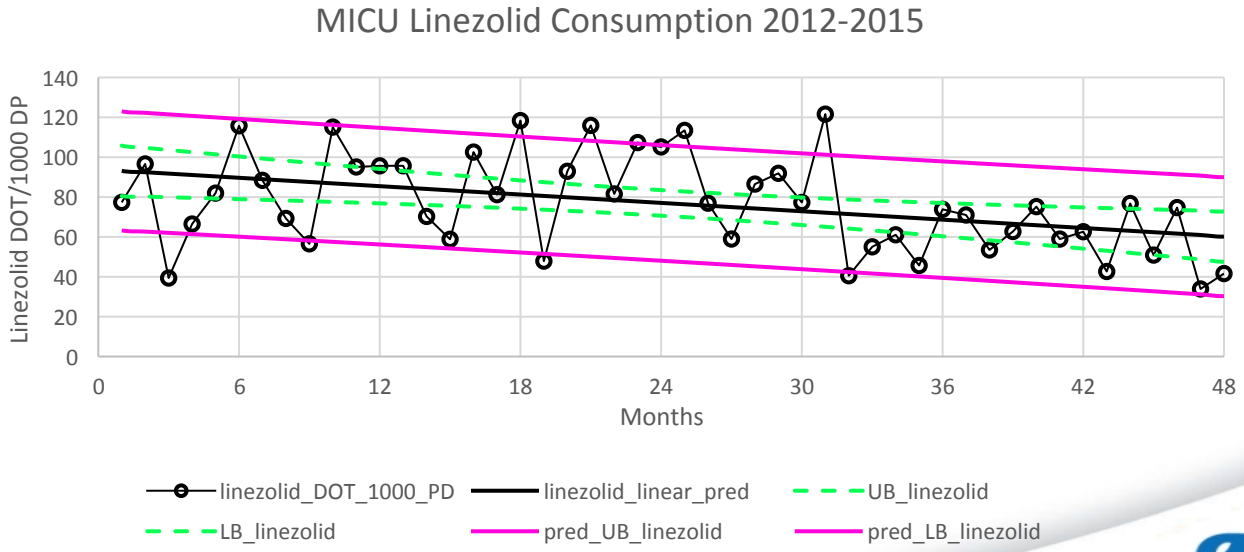
Question 2:
Which of the following best describes the 95% CI?

A. Interval wherein 95/100 predictions of consumption will fall
B. Interval wherein 95/100 predictions of mean consumption will fall
C. Interval wherein mean consumption exists 95% of the time
D. Interval wherein consumption observations will fall into 95% of the time in an 8 year review period

HOW MUCH USE IS TOO MUCH?

Looking back to look forward: How much is too much?

- Longitudinal data can be modeled using least squares regression



Rhodes NJ. NMH consumption data on file. 2017.

Miglis C, Rhodes NJ, Avedissian SN, et al. Infect Control Hosp Epidemiol. 2017;38:860-862

Use of Predictive Interval Thresholds

- 80% Predictive interval (PI)
  - Range that should capture 80% of **future predictions**
- 80% PI requires:
  - SE of the **prediction** (se_pred)
  - Degrees of freedom
  - Critical t value
    - TINV(prob, df=obs-2)* se_pred
  - UB = pred + T-value* se_pred
  - LB = pred – T-value* se_pred

	B	F	G	H	I	J
1	months	se_pred_linezolid	UB_linezolid	LB_linezolid	pred_UB_linezolid	pred_LB_linezolid
2	1	=steyx_drug*SQRT(1+(1/COUNT(months))+((B2-AVERAGE(months))^2/devsq_months))				
3	2	22.90674901	104.7059522	80.22920071	122.251574	62.68357893
4	3	22.85584077	103.6142381	79.92132674	121.4855876	62.04997719
5	4	22.80714055	102.5278419	79.60813482	120.7224722	61.41350453
6	5	22.7606625	101.4473204	79.28906822	119.9622461	60.77414254
7	6	22.71642028	100.3733004	78.96350011	119.204927	60.13187346
8	7	22.67442696	99.30648795	78.63072443	118.4505321	59.48668029
9	8	22.63469507	98.24767841	78.28994586	117.6990775	58.83854675
10	9	22.59723653	97.19776698	77.94026917	116.9505788	58.18745734
11	10	22.56206267	96.15775992	77.58068812	116.2050507	57.53339732
12	11	22.52918419	95.1287856	77.21007433	115.4625071	56.87635279
13	12	22.49861115	94.11210476	76.82716706	114.7229612	56.21631065

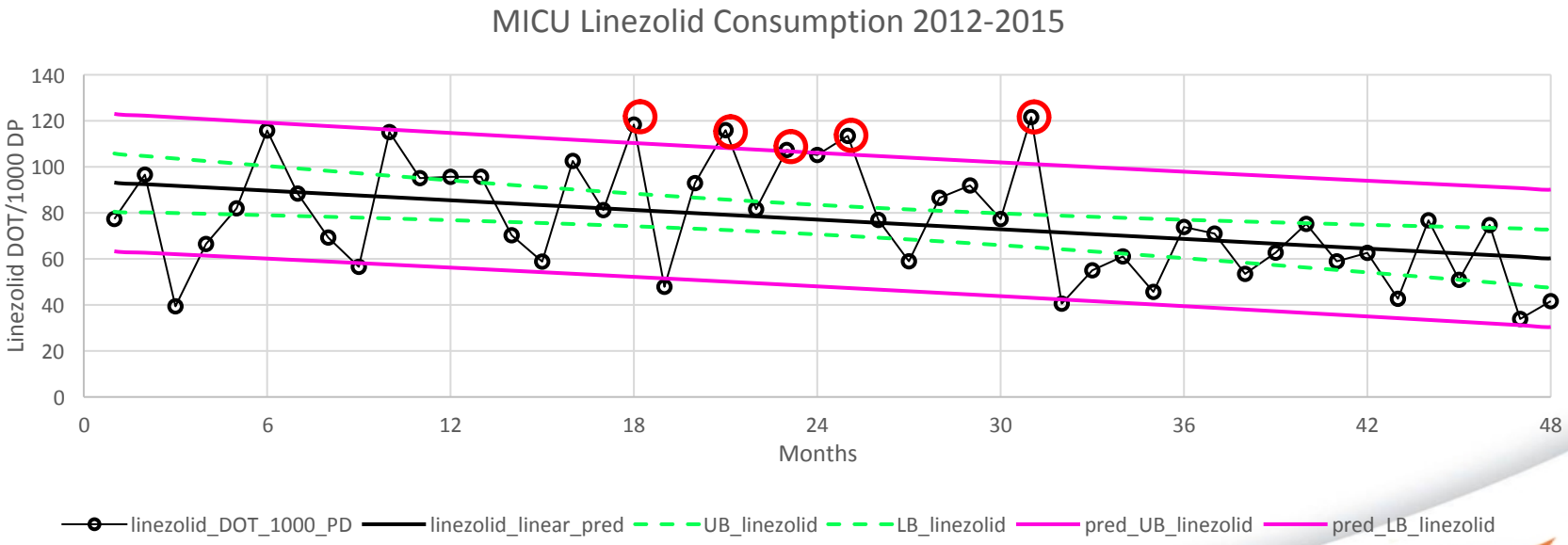
Rhodes NJ. NMH consumption data on file. 2017.
Miglis C, Rhodes NJ, Avedissian SN, et al. Infect Control Hosp Epidemiol. 2017;38:860-862

Calculation of Predictive Intervals

linezolid_DOT_1000_PD	linezolid_linear_pred	se_linezolid	se_pred_linezolid	UB_linezolid	LB_linezolid	pred_UB_linezolid	pred_LB_linezolid
77.34304	93.16737053	6.277086081	22.95985056	105.8024895	80.53225158	123.0204122	63.31432886
96.61355	92.46757647	6.079985352	22.90674901	104.7059522	80.22920071	122.251574	62.68357893
39.39123	91.76778241	5.885280726	22.85584077	103.6142381	79.92132674	121.4855876	62.04997719
66.47673	91.06798836	5.693218042	22.80714055	102.5278419	79.60813482	120.7224722	61.41350453
81.96721	90.3681943	5.504073878	22.7606625	101.4473204	79.28906822	119.9622461	60.77414254
115.77753	89.66840025	5.318159639	22.71642028	100.3733004	78.96350011	119.204927	60.13187346
88.38133	88.96860619	5.135826104	22.67442696	99.30648795	78.63072443	118.4505321	59.48668029
69.27711	88.26881213	4.957468377	22.63469507	98.24767841	78.28994586	117.6990775	58.83854675
56.54102	87.56901808	4.783531203	22.59723653	97.19776698	77.94026917	116.9505788	58.18745734
115.10791	86.86922402	4.614514487	22.56206267	96.15775992	77.58068812	116.2050507	57.53339732
95.0951	86.16942997	4.450978797	22.52918419	95.1287856	77.21007433	115.4625071	56.87635279
95.66075	85.46963591	4.293550475	22.49861115	94.11210476	76.82716706	114.7229612	56.21631065
95.69378	84.76984185	4.142925805	22.47035297	93.10911897	76.43056473	113.986425	55.55325869
70.27027	84.0700478	3.999873484	22.44441837	92.12137553	76.01872006	113.2529101	54.88718552
58.82353	83.37025374	3.865234363	22.42081544	91.15056698	75.5899405	112.5224268	54.21808066
102.5641	82.67045969	3.73991719	22.39955153	90.19852254	75.14239683	111.7949848	53.54593453
81.20438	81.97066563	3.624888911	22.38063332	89.26718857	74.67414269	111.0705928	52.87073846
118.36735	81.27087157	3.521158016	22.36406676	88.35859505	74.1831481	110.3492584	52.19248471
47.86681	80.57107752	3.429749706	22.34985707	87.47480561	73.66734943	109.6309885	51.51116649
92.92929	79.87128346	3.351672335	22.33800877	86.61784995	73.12471697	108.915789	50.82677793
115.94203	79.1714894	3.287875751	22.32852559	85.78964003	72.55333878	108.2036646	50.13931417
81.5739	78.47169535	3.239203851	22.32141057	84.99187452	71.95151617	107.4946194	49.44877126
107.32197	77.77190129	3.206345482	22.31666596	84.22594	71.31786258	106.7886563	48.75514628
105.15672	77.07210724	3.18978937	22.31429328	83.49282022	70.65139425	106.0857772	48.05843725
113.44538	76.37231318	3.18978937	22.31429328	82.79302617	69.9516002	105.3859832	47.3586432
76.92308	75.67251912	3.206345482	22.31666596	82.12655783	69.21848042	104.6892741	46.65576411

Rhodes NJ. NMH consumption data on file. 2017.
Miglis C, Rhodes NJ, Avedissian SN, et al. Infect Control Hosp Epidemiol. 2017;38:860-862

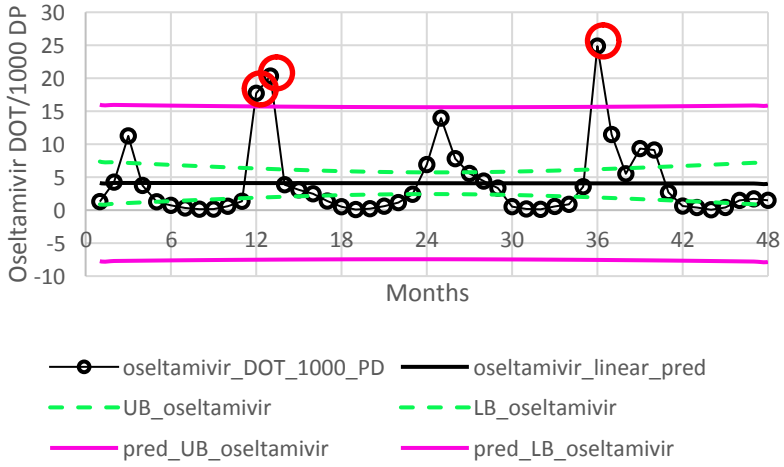
Identifying the “outliers”



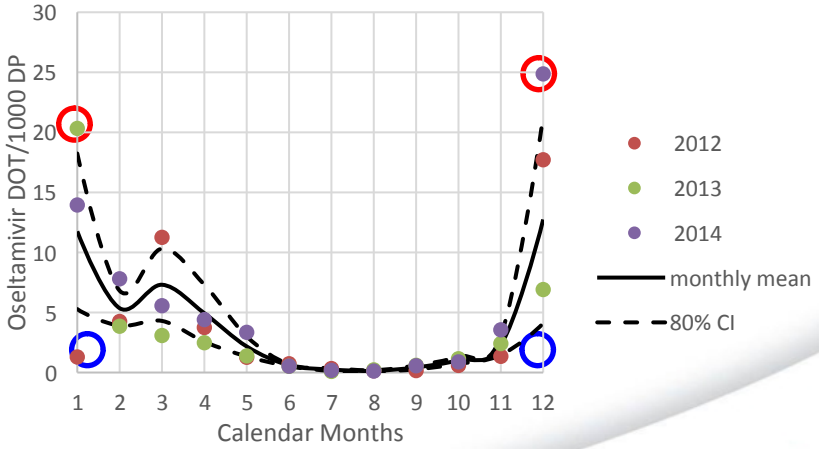
Rhodes NJ. NMH consumption data on file. 2017.
Miglis C, Rhodes NJ, Avedissian SN, et al. Infect Control Hosp Epidemiol. 2017;38:860-862

Important caveat:
Linear models don't always work

Facility-wide Oseltamivir Longitudinal Consumption 2012-2015



Facility-wide Oseltamivir Monthly Consumption 2012-2015



Rhodes NJ. NMH consumption data on file. 2017.

Miglis C, Rhodes NJ, Avedissian SN, et al. Infect Control Hosp Epidemiol. 2017;38:860-862

Choosing candidate thresholds

- Significant deviation from theoretical population mean
  - Confidence interval approach
- Significant deviation from range of theoretical future values
  - Predictive interval approach
- Considerations for successful use of these approaches:
  - Estimation of underlying trends may require 5-7 years of data
  - Seasonal and cyclical patterns will be poorly predicted

Approach #3

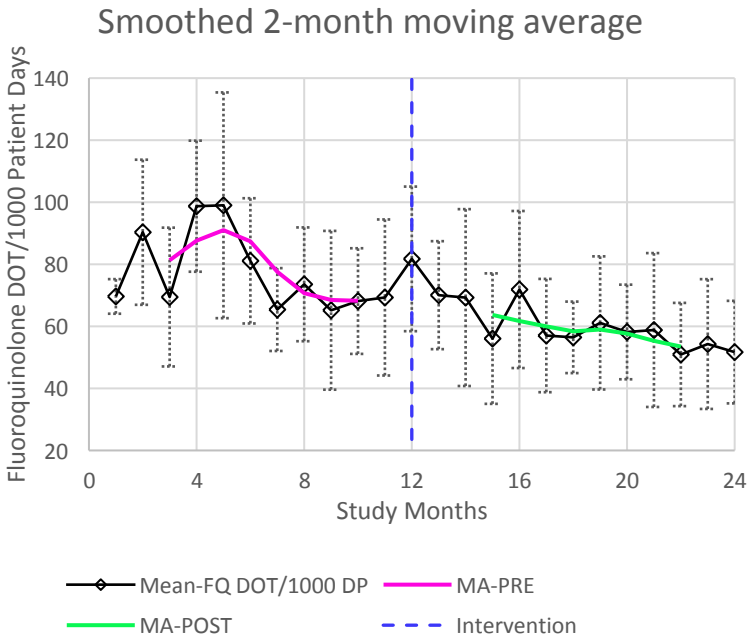
ESTIMATING THE IMPACT OF QUALITY INTERVENTIONS ON CONSUMPTION

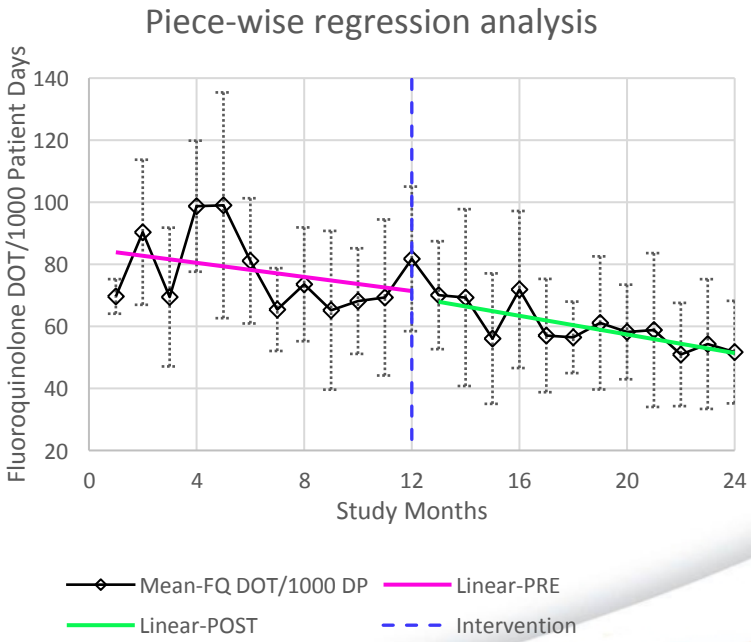
Question 3:
Which of the following is a distinct advantage of quasi-experimental studies?

A. They establish whether or not an intervention was effective
B. They accurately estimate intervention's effect size
C. They are less expensive than randomized controlled trials
D. They are not subject to the biases typical of cohort studies

HOW DO I KNOW IF MY INTERVENTION IS WORKING?

Assessing changes over time

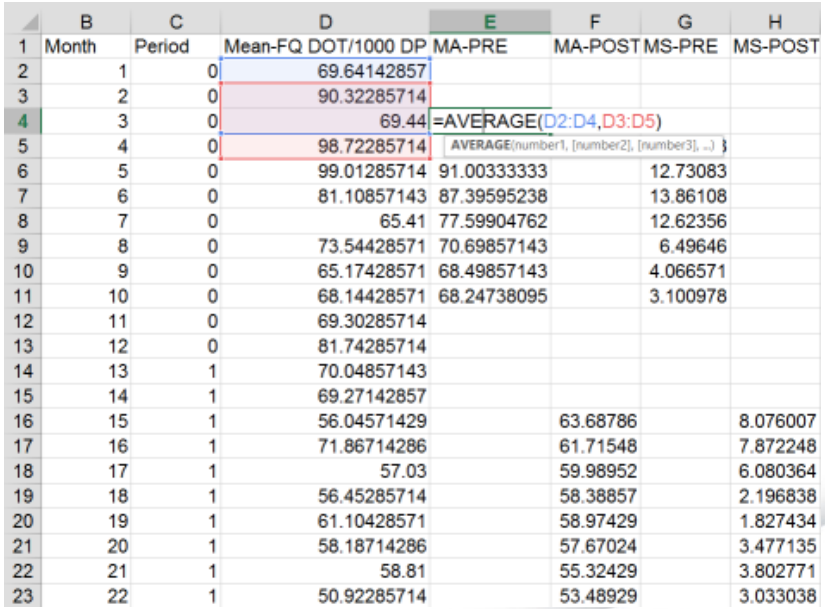




Postelnick MJ, Rhodes NJ, Martin D, et al. ASM Microbe 2017. Session 269. Saturday June 3, 2017.

Moving average (MA)

- Moving average (2-month)
  - Pre/post example
  - Forward MA:
    - Start 2 periods ahead
    - End 2 periods behind
  - Reverse MA:
    - Start 2 periods behind
    - End 2 periods ahead



	B	C	D	E	F	G	H
1	Month	Period	Mean-FQ DOT/1000 DP	MA-PRE	MA-POST	MS-PRE	MS-POST
2	1	0	69.64142857				
3	2	0	90.32285714				
4	3	0	69.44	=AVERAGE(D2:D4,D3:D5)			
5	4	0	98.72285714	AVERAGE(number1, [number2], [number3], ...)			
6	5	0	99.01285714	91.00333333		12.73083	
7	6	0	81.10857143	87.39595238		13.86108	
8	7	0	65.41	77.59904762		12.62356	
9	8	0	73.54428571	70.69857143		6.49646	
10	9	0	65.17428571	68.49857143		4.066571	
11	10	0	68.14428571	68.24738095		3.100978	
12	11	0	69.30285714				
13	12	0	81.74285714				
14	13	1	70.04857143				
15	14	1	69.27142857				
16	15	1	56.04571429		63.68786		8.076007
17	16	1	71.86714286		61.71548		7.872248
18	17	1	57.03		59.98952		6.080364
19	18	1	56.45285714		58.38857		2.196838
20	19	1	61.10428571		58.97429		1.827434
21	20	1	58.18714286		57.67024		3.477135
22	21	1	58.81		55.32429		3.802771
23	22	1	50.92285714		53.48929		3.033038

Piece-wise linear regression

- FORECAST function
  - Least-squares linear regression
  - Pre/post example
    - Pre-intervention
    - Post-intervention
- Piecewise model parameters
  - Estimated using Excel SOLVER

B	C	D	I	J	K
Month	Period	Mean-FQ DOT/1000 DP	Linear-PRE	Linear-POST	STEYX-PRE
1	0	69.64142857	=FORECAST(B2,$D$2:$D$13,$B$2:$B$13)		
2	0	90.32285714	82.74393939		
3	0	69.44	81.60764069		
4	0	98.72285714	80.47134199		
5	0	99.01285714	79.33504329		
6	0	81.10857143	78.19874459		
7	0	65.41	77.06244589		
8	0	73.54428571	75.92614719		
9	0	65.17428571	74.78984848		
10	0	68.14428571	73.65354978		
11	0	69.30285714	72.51725108		
12	0	81.74285714	71.38095238		
13	1	70.04857143		67.90791209	
14	1	69.27142857		66.40536963	
15	1	56.04571429		64.90282717	
16	1	71.86714286		63.40028472	
17	1	57.03		61.89774226	
18	1	56.45285714		60.3951998	
19	1	61.10428571		58.89265734	
20	1	58.18714286		57.39011489	
21	1	58.81		55.88757243	
22	1	50.92285714		54.38502997	

Estimate trends for each period

Date	Month	Period	Mean-FQ DOT/1000 DP	MA-PRE	MA-POST	MS-PRE	MS-POST	Linear-PRE	Linear-POST
May 15	1	0	69.64142857					83.8802381	
Jun 15	2	0	90.32285714					82.74393939	
Jul 15	3	0	69.44	81.315		13.29376		81.60764069	
Aug 15	4	0	98.72285714	87.6102381		14.45458		80.47134199	
Sep 15	5	0	99.01285714	91.00333333		12.73083		79.33504329	
Oct 15	6	0	81.10857143	87.39595238		13.86108		78.19874459	
Nov 15	7	0	65.41	77.59904762		12.62356		77.06244589	
Dec 15	8	0	73.54428571	70.69857143		6.49646		75.92614719	
Jan 16	9	0	65.17428571	68.49857143		4.066571		74.78984848	
Feb 16	10	0	68.14428571	68.24738095		3.100978		73.65354978	
Mar 16	11	0	69.30285714					72.51725108	
Apr 16	12	0	81.74285714					71.38095238	
May 16	13	1	70.04857143						67.90791209
Jun 16	14	1	69.27142857						66.40536963
Jul 16	15	1	56.04571429		63.68785714		8.07600713		64.90282717
Aug 16	16	1	71.86714286		61.71547619		7.87224753		63.40028472
Sep 16	17	1	57.03		59.98952381		6.08036369		61.89774226
Oct 16	18	1	56.45285714		58.38857143		2.19683762		60.3951998
Nov 16	19	1	61.10428571		58.97428571		1.82743424		58.89265734
Dec 16	20	1	58.18714286		57.6702381		3.47713469		57.39011489

<u>OLS estimates from Solver:</u>
b0 = 84.5 (base level)
b1 = -1.13 (base trend)
b2 = -2 (Δ level)
b3= -0.36 (Δ trend)
error = 0.5

b3/b1 x 100 = 32% change

Trend analysis:
P-value $_{pre}$ = 0.296
P-value $_{post}$ = 0.004

$$Y = b0 + b1 * time_{total} + b2 \times period + b3 \times time_{post} + error$$

Evaluating the impact of interventions

- Quasi-experimental and interrupted time series are useful
  - Provide data on performance, though effect sizes less certain
- Piecewise regression analysis can estimate rough “impact”
  - Change in the level by period might be attributable to intervention
- Considerations for successful use of these approaches:
  - Estimation of underlying trends requires at least 12 obs. before/after
  - Adequate control groups / approaches needed

Key Takeaways

- Key Takeaway #1
  - Measuring antimicrobial consumption is a key element of antimicrobial stewardship and essential for meeting Joint Commission Standards
- Key Takeaway #2
  - Consistency in measures recorded over time (e.g., DDD, DOT, NHSN AU days) essential for evaluation of threshold levels for stewardship action
- Key Takeaway #3
  - Quasi-experimental methods can be applied to program interventions using interrupted time series methods but adequate controls required

ashp MIDYEAR 2017
Clinical Meeting & Exhibition

Making an Impact

Susan L. Davis, Pharm.D.
Clinical Associate Professor
Eugene Applebaum College of Pharmacy and Health Sciences,
Wayne State University
Infectious Diseases Pharmacist
Henry Ford Hospital

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Measuring the impact of ASP on clinical outcomes

MAKING AN IMPACT

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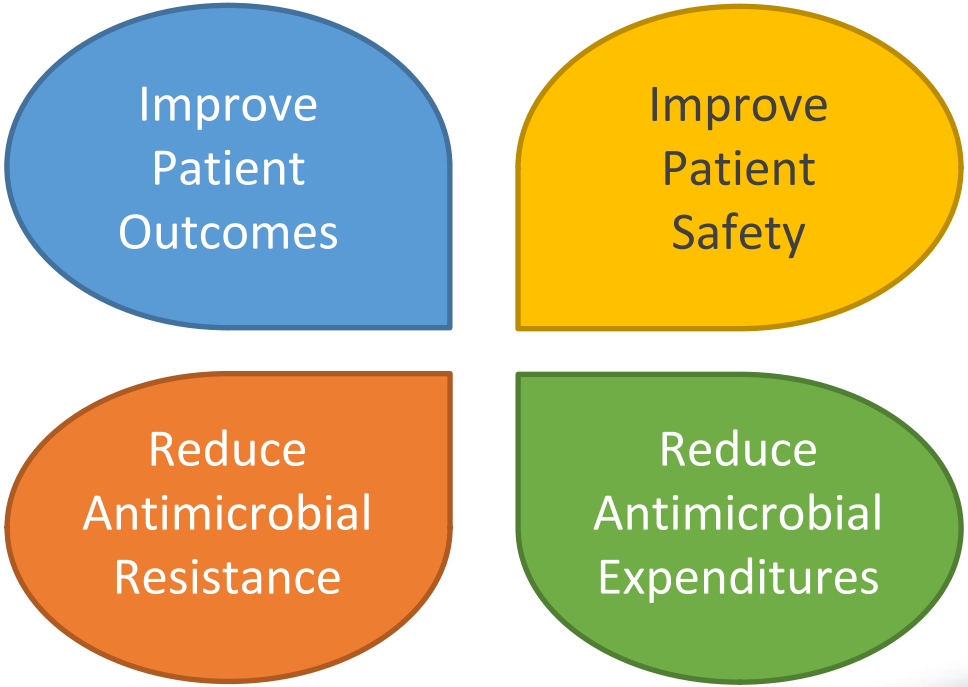
Goals of Stewardship Programs



McGowan JE. *Infect Control Hosp Epidemiol.* 2012; 33:331-337. Wagner B, et al. *Infect Control Hosp Epidemiol.* 2014; 35:1209-1228. Dodds Ashley ES, et al. *Clin Infect Dis.* 2014; 59(S3):S112-S121.

Is There an Ideal Antibiotic Quality Measure?

- Easy to assess compliance
- Will improve practice, change behavior
- Has no unintended consequences
- Practical for any healthcare setting (acute care, long term care, pediatrics)
- Useful to many audiences
  - Stewardship program staff
  - Clinicians
  - Accreditation/regulatory agencies

So many metrics!

- Antimicrobial consumption
- Appropriateness of therapy
- Time to appropriate therapy
- Documented indication for antimicrobial therapy

Process Measures

- Infection-related mortality
- Length of stay
- Readmission rates
- *Clostridium difficile* rates
- Antimicrobial resistance rates
- Clinical success / cure

Outcomes Measures

Structure Measures

- Components of the stewardship program, e.g. Core Elements

Tamma PD. *Infect Dis Clin N Am*. 2011; 25: 245-260.
Toth NR, et al. *Am J Health-Syst Pharm.* 2010; 67:746-749.
Dodds Ashley ES, et al. *Clin Infect Dis*. 2014; 59(S3): S112-S121.

What influences what we measure?

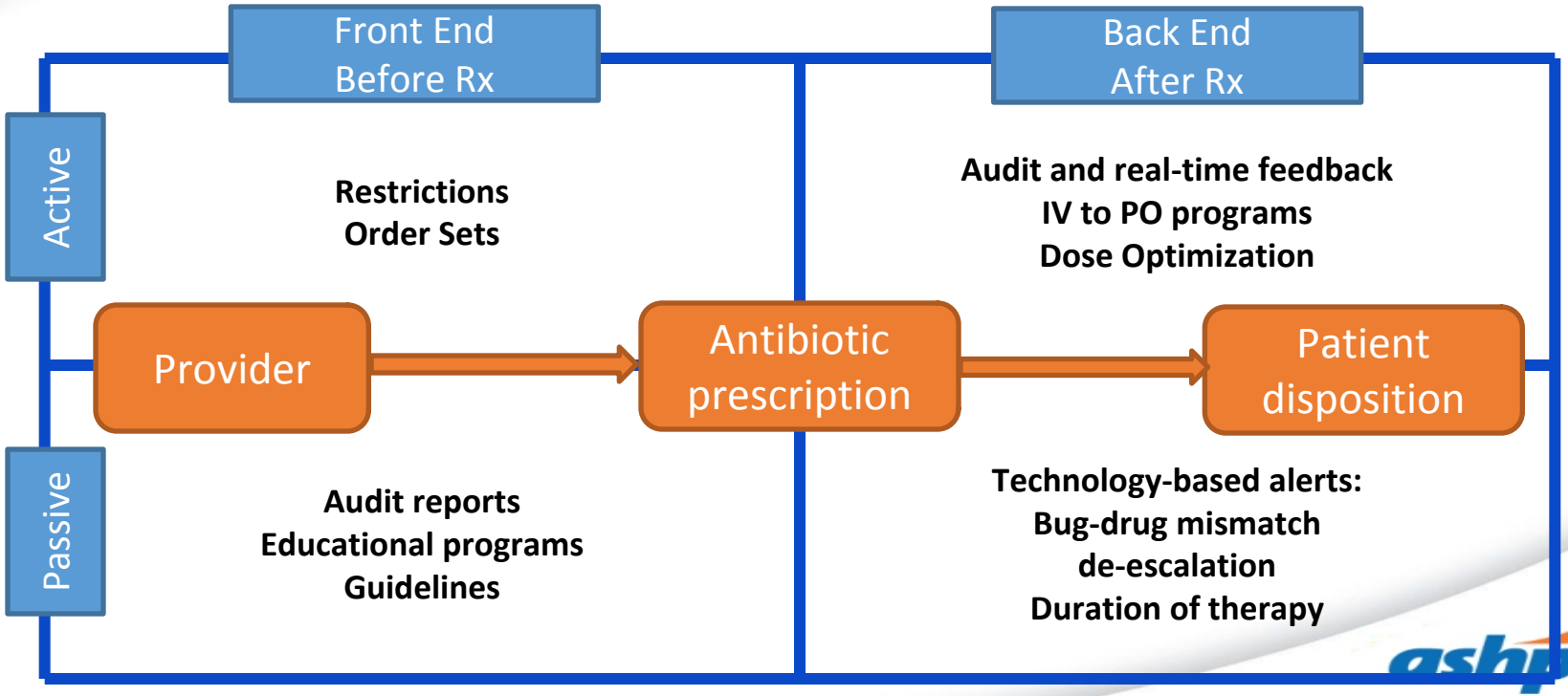
- Expert opinion
- Local preferences, ASP goals
- Ease of measurement
- Regulatory requirements

Core Elements?

Match your metrics to your strategies

CDC. Antibiotic Use in the United States, 2017: Progress and Opportunities. US DHHS, CDC; 2017.

Stewardship Intervention Examples



Adapted from Moerhing RW, Anderson DJ. *Curr Infect Dis Rep* 2012; 14:592-600

Core Element 4. Action

Basic	Intermediate	Advanced
• Implement policy for formulary restriction/authorization • Develop order forms, guidelines	• Establish antibiotic time-out process • Dosing and IV/PO guidelines • Audit and feedback of target drugs	• Implement rapid diagnostics or biomarkers • Implement evidence-based disease state care bundles

NQF. National Quality Partners Playbook: Antibiotic Stewardship in Acute Care. Washington DC, 2016. www.qualityforum.org

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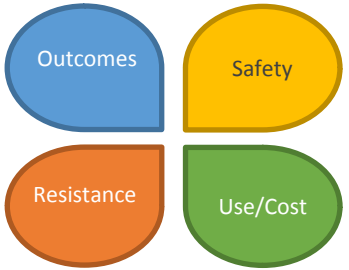


Core Element 5. Tracking and Monitoring

Basic

- Adherence to institutional guidelines
- Acceptance rate for ASP interventions

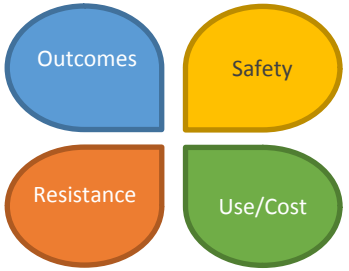
Intermediate

- Resistance for pathogens of interest
- *C. difficile* infections
- readmission

Advanced

- Antibiotic utilization
- Standardized antibiotic administration ratio (SAAR) – NQF endorsed measure

NQF. National Quality Partners Playbook: Antibiotic Stewardship in Acute Care. Washington DC, 2016. www.qualityforum.org



Core Element 6. Reporting

Basic

- Reporting of ASP measures for key committees, staff meetings, web-based reports

Intermediate

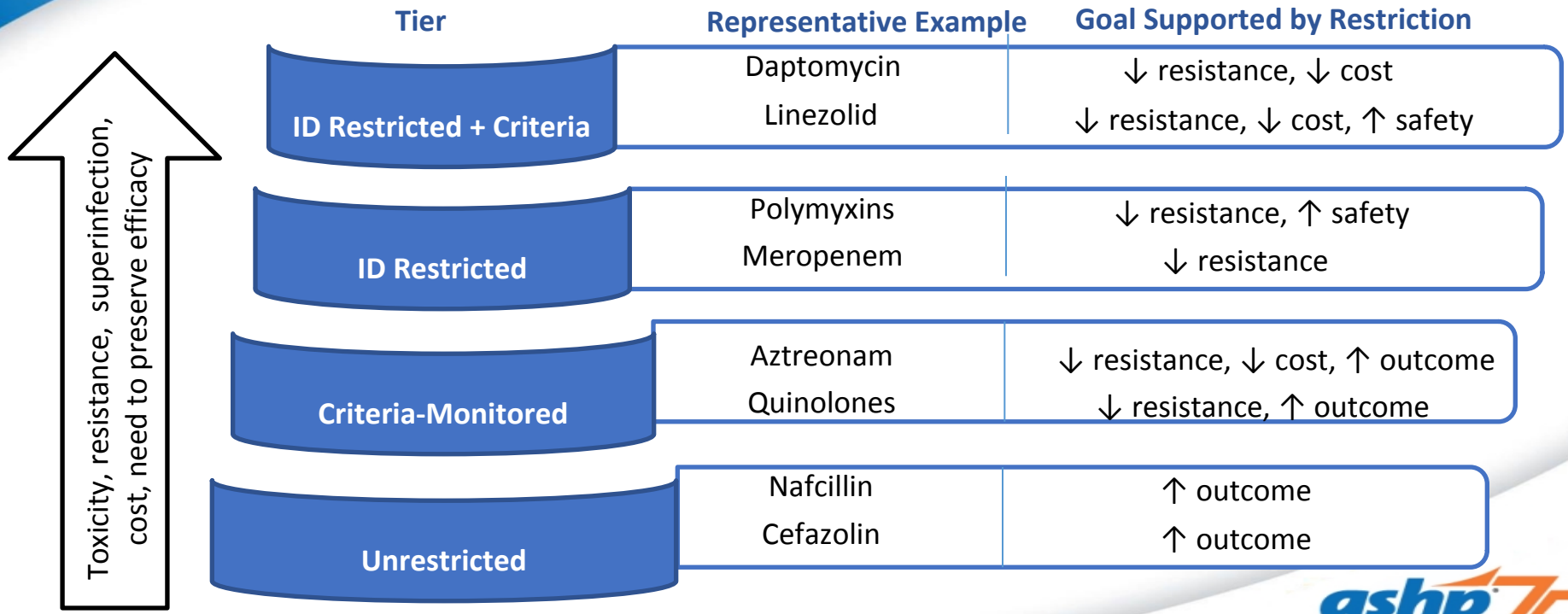
- Reports include suggestions for improvements
- Participate in public reporting
- Present unit-specific data to unit staff

Advanced

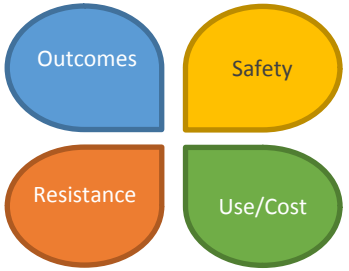
- Distribute provider-level feedback
- Implement a real-time analytics dashboard

NQF. National Quality Partners Playbook: Antibiotic Stewardship in Acute Care. Washington DC, 2016. www.qualityforum.org

Core Strategy:
Rationale for Formulary Restrictions



Athans V, et al. Am J Health-Syst Pharm. 2015; 72:1264-5.



Question:
What metrics would you choose to monitor the success/failure of antimicrobial formulary restrictions?

A. Antibiotic Days of Therapy
B. Antibiotic Expenditures
C. Adverse Drug Events
D. Guideline Compliance/Appropriate Therapy

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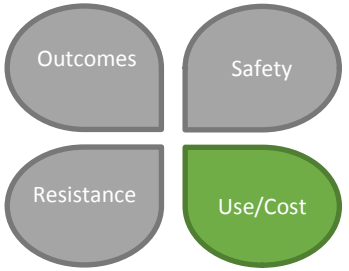

Problems with Cost Measures

- Evaluating drug related cost misses the bigger picture of overall length of stay
- Drug prices are not always comparable over time and between institutions
- Economic endpoints should be used to complement other stewardship goals
- Like drug utilization, cost should be adjusted by census

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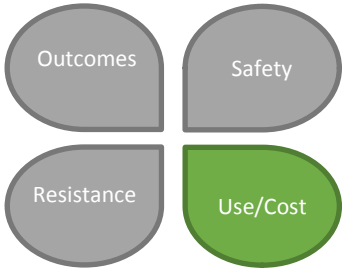


Problems with Antibiotic Consumption

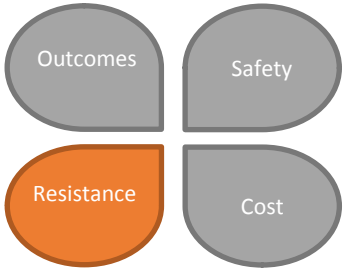
- Heavy restrictions may do more harm than good
  - "restriction" versus "protection"
  - The most expensive antibiotic is the one that doesn't work
- Never focus on just one drug
  - "Squeezing the balloon"
- Consider measuring and aggregating drugs with a common target or feature
  - e.g. MRSA agents, all quinolones
- Some antibiotic use is necessary! "Zero" is not an appropriate goal!

Nicasio AM, et al. *J Crit Care* 2010;25:69-77. Martin CA, et al. *AJHP* 2011; 68:109-10

Using your data: Benchmarks

- There is currently no regulatory or other standard goal for antibiotic use
  - You can set the goal. The goal cannot be zero
- Benchmarking allows comparison of use (not appropriateness) across similar institutions
  - High performers may represent best practices
  - Low performers may represent inappropriate prescribing
  - Need to adjust for confounding factors before making assumptions

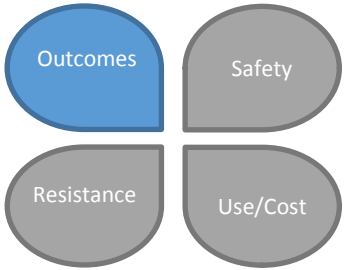
Problems with Resistance



- Difficult to Measure
- Changes can take a long time
- Confounded by multiple factors (e.g. infection control, community endemicity)
- Breakpoint and testing changes over time can bias results

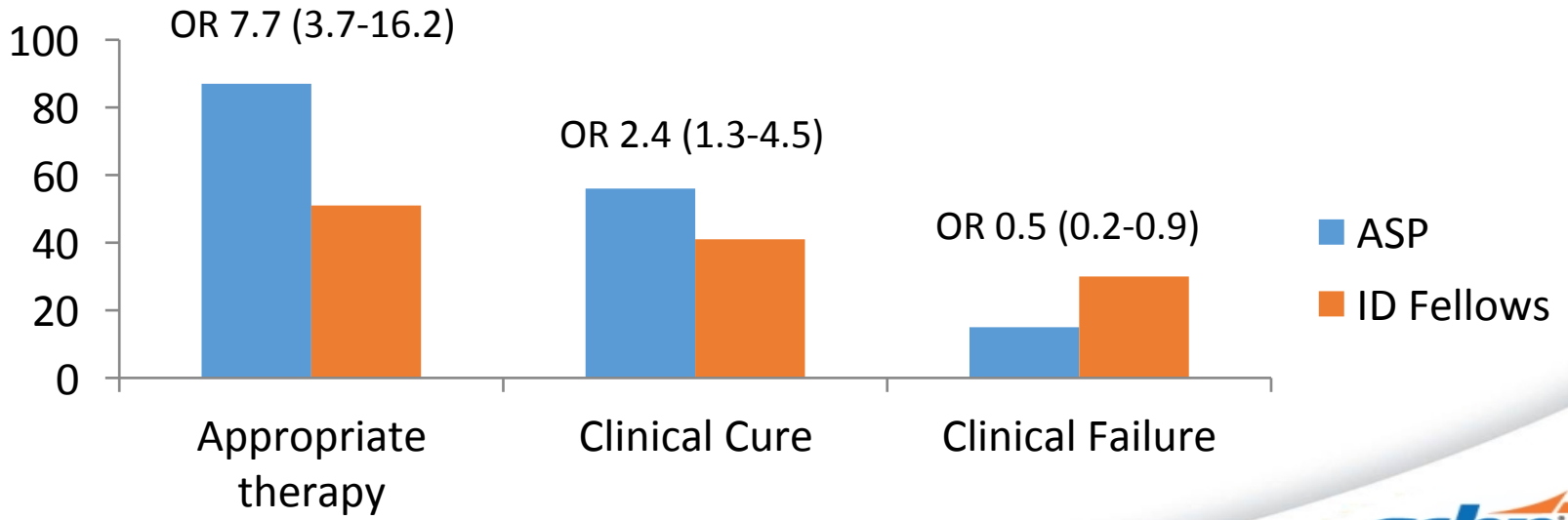
Most of these same problems also apply to measuring clinical outcomes and safety

Philips I. *Clin Infect Dis* 2004;33(Suppl 3):S130-S132. Cook PP, et al. *J Antimicrob Chemother* 2004;53:853-9. MacDougall C, et al. *Clin Microbiol Rev* 2005;18:638-56.

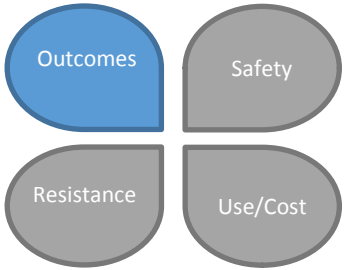


Stewardship Improves Patient Outcomes

RCT: Antimicrobial Management Team (with pharmacist) versus Standard of Care (with ID fellows)



Gross R et al. *Clin Iinfect Dis* 2001;33:289-295

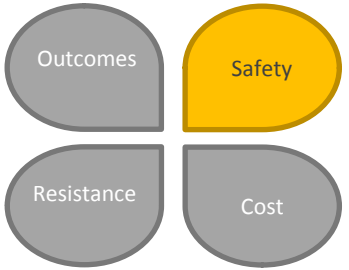


Guideline Adherence Improves Patient Outcomes

Pre-post study of a guideline for management of ventilator associated pneumonia (VAP)

	Pre-VAP Clinical Guideline	Post-VAP Clinical Guideline
Adequate initial therapy	48%	94%
Duration of therapy	14.8 days	8.6 days
VAP recurrence	24%	8%

Ibrahim EH et al. *Crit Care Med* 2001;29:1109-15



Antibiotic Adverse Events: Opportunity for Stewardship

1 in 5 emergency visits

- Allergic reactions (80%)
- Adverse effects (18%)
  - Diarrhea, headache, dizziness
- Most common antibiotics
  - Penicillins (37%)
  - Fluoroquinolones (14%)
  - Cephalosporins (12%)
  - Trimethoprim-sulfamethoxazole (11%)

1 in 5 inpatient/discharge prescriptions

- 30-day ADEs: GI (42%), Renal (24%), Hematologic (15%)

Class	% pts with Rx	% of ADEs
B-lactam	80%	65%
Macrolide	27%	3%
Quinolone	26%	7%
Vancomycin	37%	12%

Shehab D, et al. *Clin Infect Dis* 2008;47:735-43. Tamma PD et al. *JAMA Intern Med.* 2017;177:1308-1315.

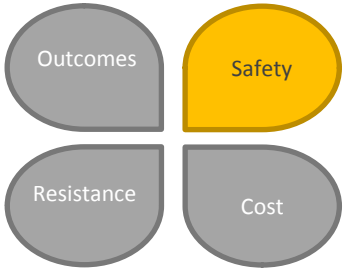


Table 1. Adverse drug events (ADEs) in hospital inpatient settings, 32 states, 2011

Adverse drug event cause[a]	ADEs based on diagnoses present on admission		ADEs based on diagnoses that originated during the hospital stay	
	Number of ADEs per 10,000 discharges	Percent of ADEs[b]	Number of ADEs per 10,000 discharges	Percent of ADEs[b]
Any ADE cause	388.0	100.0	128.7	100.0
Antibiotics and anti-infectives	90.9	23.4	36.1	28.0
Antibiotics	12.5	3.2	12.9	10.0
Clostridium difficile infection[14]	73.1	18.8	21.9	17.1
Other anti-infectives	6.3	1.6	1.7	1.3
Hormones	46.3	11.9	20.7	16.1
Steroids	37.3	9.6	19.7	15.3
Insulin and hypoglycemics	7.1	1.8	0.8	0.6
Other hormones	3.0	0.8	0.3	0.2
Systemic agents	52.8	13.6	8.5	6.6
Antineoplastic drugs	49.2	12.7	7.8	6.0
Antiallergy and antiemetic drugs	3.1	0.8	0.7	0.5
Other systemic agents	0.8	0.2	0.1	0.1
Agents affecting blood constituents	43.9	11.3	8.5	6.6
Anticoagulants	40.6	10.5	6.7	5.2
Other agents that affect blood constituents	3.9	1.0	1.9	1.5
Analgesics	45.5	11.7	16.2	12.6
Opiates/Narcotics	18.8	4.9	11.2	8.7
NSAIDS	28.3	7.3	5.1	4.0

National ADE data

Weiss AJ, Elixhauser A, Bae J, Encinosa W. Origin of Adverse Drug Events in U.S. Hospitals, 2011. HCUP Statistical Brief #158. July 2013. Agency for Healthcare Research and Quality, Rockville, MD. http://www.hcup-us.ahrq.gov/reports/statbriefs/sb158.pdf.

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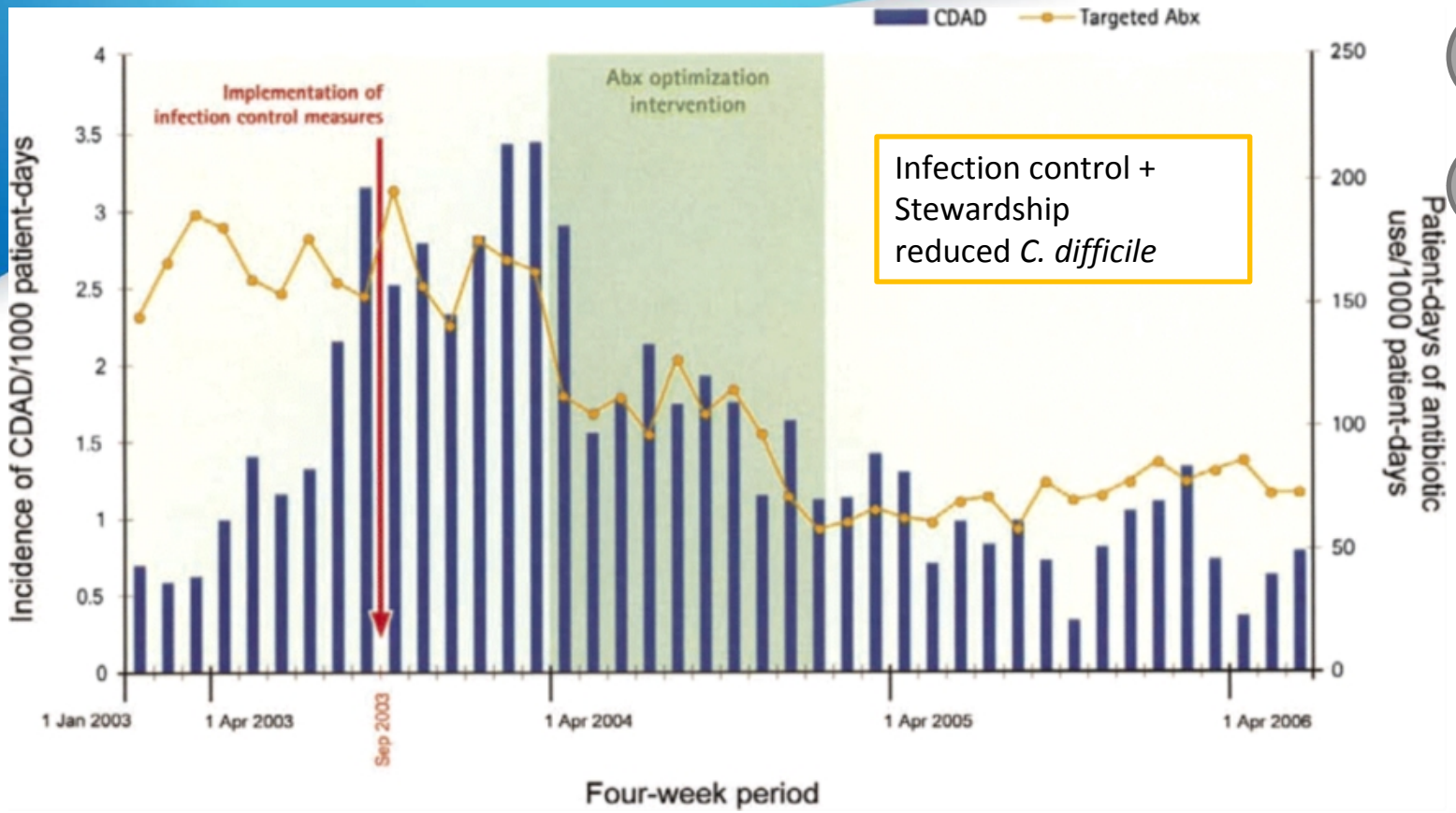
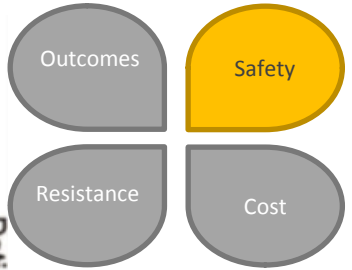


Infection control + Stewardship reduced *C. difficile*



From: Impact of a Reduction in the Use of High-Risk Antibiotics on the Course of an Epidemic of Clostridium difficile-Associated Disease Caused by the Hypervirulent NAP1/027 Strain. *Clin Infect Dis*. 2007;45(Supplement_2):S112-S121. doi:10.1086/519258

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For your chosen ASP problem, what metrics represent the relevant goals?

Stewardship goals	What can you impact?
Improve patient outcome	Mortality Readmission Clinical cure
Improve patient safety	C. difficile Acute kidney injury Adverse drug events
Reduce resistance	Antibiogram trends
Reduce cost	Drug expenditures Drug utilization LOS

What data is available?

Who cares about this measure?

Does it match your ASP interventions?

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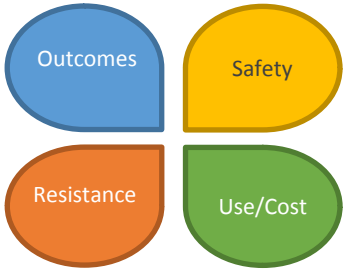

Question: What stewardship metrics do you think are most important to physicians?

A. Antibiotic Days of Therapy
B. Appropriate Therapy
C. Adverse Drug Events
D. Mortality

Importance of ASP Outcomes*

Perceived importance

Outcome	Actually used	Most important*	Admins	Pharmacy Director	P&T Committee	ID Physician
Abx USE	73%	15%	2%	22%	32%	2%
Abx COST	73%	10%	41%	56%	15%	0%
Appropriate	51%	56%	5%	5%	15%	27%
Mortality	7%	34%	2%	5%	2%	37%
LOS	12%	22%	5%	0%	2%	7%

*survey of 94 physicians and pharmacists in acute care hospitals

Bumpass JB, et al. *Clin Infect Dis* 2014;59(S3):S108–11.

Putting it together

comprehensive ASP metrics via Delphi method

Measure	Strong agreement (%)
Domain 1: Consumption	
DOTs	80
DDDs	50
Domain 2: Resistance	
# patients with drug-resistant organisms	78
De-escalation/optimized therapy	70
Domain 3: Outcomes	
Antimicrobial related organism mortality	78
All cause mortality	70
Conservable days of therapy among certain patients	80
Unplanned 30d readmission	100

Morris AM, et al. *Infect Control Hosp Epidemiol* 2012;33:500-506.

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Key Takeaways: Measure Something!

- Key Takeaway #1
  - Antimicrobial consumption measures alone are limited in utility
- Key Takeaway #2
  - Choose a combination of process, outcome and consumption measures to describe the full scope of your ASP impact
- Key Takeaway #3
  - Compelling outcomes like appropriate use, adverse effects, clinical cure, can demonstrate value to targeted audiences

Select resources and readings

- Barlam TF, et al. Implementing an Antibiotic Stewardship Program: Guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. Clin Infect Dis. 2016. doi: 10.1093/cid/ciw118.
- Centers for Disease Control and Prevention. Core Elements of Hospital Antibiotic Stewardship Programs. http://www.cdc.gov/getsmart/healthcare/implementation/core-elements.html
- Centers for Medicare & Medicaid services. https://www.cms.gov/Newsroom/MediaReleaseDatabase/Fact-sheets/2016-Fact-sheets-items/2016-06-13.html
- Joint Commission. https://www.jointcommission.org/assets/1/6/New_Antimicrobial_Stewardship_Standard.pdf

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Acknowledgements

- Society of Infectious Diseases Pharmacists
- Centers for Disease Control and Prevention

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Panel

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