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Hot Topics in Antimicrobial Stewardship

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Disclosure

P. Brandon Bookstaver

FreeCe.com: Consultant, Developed CE content and delivered material, Other Financial or Material Support; Rockpointe Inc.: Consultant, Developed CE content and delivered material, Other Financial or Material Support

Jason Gallagher

Achaogen: Advisory Board; Allergan: Advisory Board, Speaker's Bureau; Astellas Pharma, Inc. : Advisory Board, Speaker's Bureau; Cidara: Consultant; Merck: Advisory Board, Grant Recipient, Speaker's Bureau; Paratek: Advisory Board; Shionogi: Advisory Board; The Medicines Company: Advisory Board; Theravance: Advisory Board

Susan Davis

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

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Merck: Grant Recipient

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

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Objectives:

- Identify key metrics that can be used to measure antibiotic consumption.
- Discuss strategies for performing and implementing stewardship within specialty groups.
- Describe stewardship interventions in distinct infectious diseases/conditions.
- Summarize national activities related to antimicrobial stewardship.

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Antibiotic Stewardship Legislative Update

Kristi Kuper, Pharm.D., BCPS
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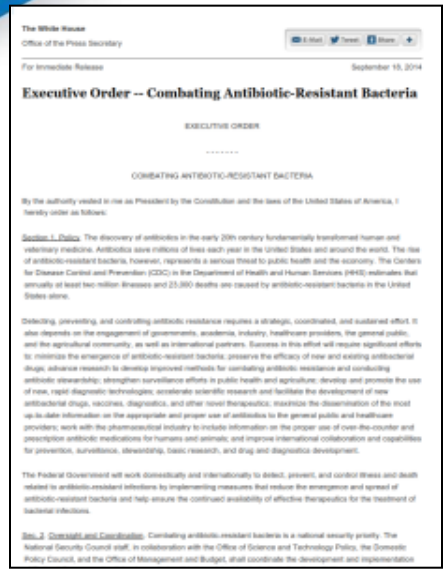
And So It Began… White House (2014-2015)



The White House
Office of the Press Secretary

For Immediate Release

September 10, 2014

Executive Order -- Combating Antibiotic-Resistant Bacteria

EXECUTIVE ORDER

COMBATING ANTIBIOTIC-RESISTANT BACTERIA

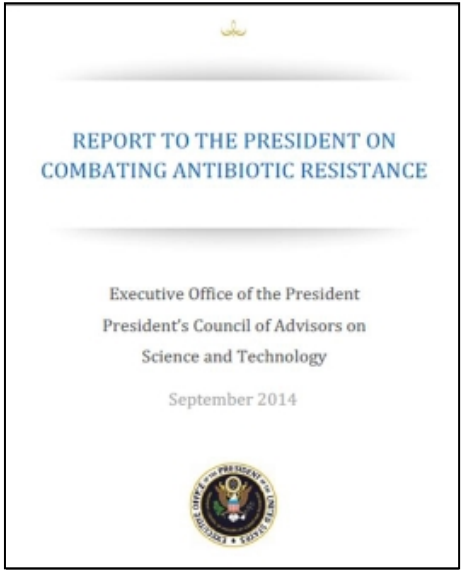
By the authority vested in me as President by the Constitution and the laws of the United States of America, I hereby order as follows:

Section 1. Policy. The discovery of antibiotics in the early 20th century fundamentally transformed human and veterinary medicine. Antibiotics save millions of lives each year in the United States and around the world. The rise of antibiotic-resistant bacteria, however, represents a serious threat to public health and the economy. The Centers for Disease Control and Prevention (CDC) in the Department of Health and Human Services (HHS) estimates that annually at least two million illnesses and 23,000 deaths are caused by antibiotic-resistant bacteria in the United States alone.

Detecting, preventing, and controlling antibiotic resistance requires a strategic, coordinated, and sustained effort. It also depends on the engagement of governments, academia, industry, healthcare providers, the general public, and the agricultural community, as well as international partners. Success in this effort will require significant efforts to: minimize the emergence of antibiotic-resistant bacteria; preserve the efficacy of new and existing antibacterial drugs; advance research to develop improved methods for combating antibiotic resistance and conducting antibiotic stewardship; strengthen surveillance efforts in public health and agriculture; develop and promote the use of new, rapid diagnostic technologies; accelerate scientific research and facilitate the development of new antibacterial drugs, vaccines, diagnostics, and other novel therapeutics; maximize the dissemination of the most up-to-date information on the appropriate and proper use of antibiotics to the general public and healthcare providers; work with the pharmaceutical industry to include information on the proper use of over-the-counter and prescription antibiotic medications for humans and animals; and improve international collaboration and capabilities for prevention, surveillance, stewardship, basic research, and drug and diagnostics development.

The Federal Government will work domestically and internationally to detect, prevent, and control illness and death related to antibiotic-resistant infections by implementing measures that reduce the emergence and spread of antibiotic-resistant bacteria and help ensure the continued availability of effective therapeutics for the treatment of bacterial infections.

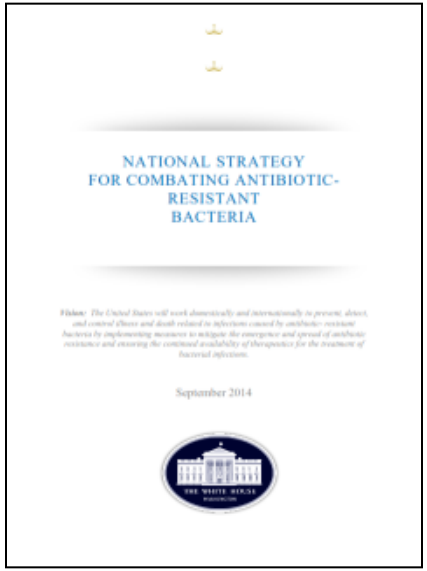
Sec. 2. Oversight and Coordination. Combating antibiotic-resistant bacteria is a national security priority. The National Security Council staff, in collaboration with the Office of Science and Technology Policy, the Domestic Policy Council, and the Office of Management and Budget, shall coordinate the development and implementation



REPORT TO THE PRESIDENT ON COMBATING ANTIBIOTIC RESISTANCE

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

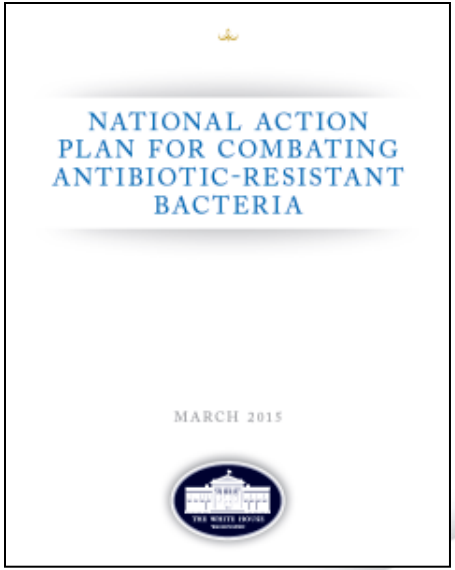
September 2014



NATIONAL STRATEGY FOR COMBATING ANTIBIOTIC-RESISTANT BACTERIA

Vision: The United States will work domestically and internationally to prevent, detect, and control illness and death related to infections caused by antibiotic- resistant bacteria by implementing measures to mitigate the emergence and spread of antibiotic resistance and ensuring the continued availability of therapeutics for the treatment of bacterial infections.

September 2014



NATIONAL ACTION PLAN FOR COMBATING ANTIBIOTIC-RESISTANT BACTERIA

MARCH 2015

https://obamawhitehouse.archives.gov/blog/2014/09/18/pcast-releases-new-report-combating-antibiotic-resistance;
https://obamawhitehouse.archives.gov/sites/default/files/docs/national_action_plan_for_combating_antibotic-resistant_bacteria.pdf

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Antibiotic Stewardship as a CMS 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.

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CMS Condition of Participation (CoP) Update

- Status of CoPs for acute care and critical access hospitals unknown
- Long term CoPs went into effect on November 28, 2016
  - Finalized the requirement that long term care facilities must establish and maintain an Infection Prevention and Control Program that includes an antibiotic stewardship program (ASP).
  - The ASP must include antibiotic use protocols and a system to monitor antibiotic use
  - Part of Phase 2 – Implementation deadline November 28, 2017

https://www.cms.gov/Medicare/Provider-Enrollment-and-Certification/GuidanceforLawsAndRegulations/Nursing-Homes.html

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PAC-CARB

- Advisory Council of experts under the Secretary of Health & Human Services in consultation with the Secretaries of Defense & Agriculture
- Advise on several areas
  - Preserving effectiveness of antibiotics
  - Advancing research for combating resistance and conducting stewardship
  - Strengthening surveillance of resistant infections
  - Preventing transmission of antibiotic resistant bacterial infections
  - Advance development of rapid point of care and agricultural diagnostics
  - Research on new treatments for bacterial infections
  - Develop alternatives to antibiotics for agricultural purposes
  - Maximize the dissemination of up-to-date information on the appropriate and proper use of antibiotics to the general public and human and animal healthcare providers
  - Improve international coordination of efforts to combat antibiotic resistance.

https://www.hhs.gov/ash/advisory-committees/paccarb/about-paccarb/charter/index.html?language=e s

21st Century Cures Act

- Sec. 3041 – Antimicrobial Resistance Monitoring
  - Monitoring of antimicrobial use, resistance and stewardship program implementation in federal facilities
  - 1 year after enactment of “Cures Act” , and annually thereafter, report aggregate national and regional trends of resistance and ASP activities
  - Dissemination of guidance, educational materials and other appropriate materials related to the development and implementation of evidence based stewardship programs at health care facilities
  - Continued support of state based activities to combat antibiotic resistance
- Sec 3042- Limited Population Pathway for antibacterial and antifungal drugs
- Sec. 3044 – Susceptibility test interpretative criteria
  - Includes establishment of a website that contains a list of any appropriate new or updated susceptibility test interpretive criteria

https://www.fda.gov/downloads/MedicalDevices/NewsEvents/WorkshopsConferences/UCM575635.pdf

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Antibiotic Stewardship Meaningful Use 3

- The NHSN Antimicrobial Use (AU) and Antimicrobial Resistance (AR) (AUR) Module reporting has been identified as one option for eligible hospitals to meet Stage 3 of the CMS Meaningful Use Program

https://www.cdc.gov/nhsn/pdfs/cda/MU3-Facility-Guidance.pdf

State Bills

- Missouri SB 579
- All hospitals will have stewardship programs by Aug. 28, 2017
- All hospitals will report antibiotic use and resistance data into NHSN when stage 3 Meaningful Use requirements are finalized
- Antibiotic use and resistance data will be shared with the health department, but will not be reported to the public

State Bills

- California
  - SB 739- Acute care hospitals develop processes around appropriate antibiotic utilization
  - SB 1131 – ASP programs required in acute care facilities by 7/1/15
  - SB 361 - Skilled nursing facilities adopt and implement ASP by 1/1/2017
  - SB 43 – *Currently in committee*
    - Acute care hospitals and clinical labs would have to submit an antibiogram to the State Department of Public Health annually

http://leginfo.legislature.ca.gov/faces/billCompareClient.xhtml?bill_id=201720180SB43; http://www.astho.org/state-legislative-tracking/

Active Federal Legislation*

Bill Title	Description
H.R. 1840 – Reinvigorating Antibiotic and Diagnostic Innovation Act of 2017	Bill allows tax credits for 50% of the clinical testing expenses for "infectious disease products that are intended to treat a serious or life-threatening infection" and in-vitro diagnostic devices that identify in less than four hours the presence, concentration, or characteristics of a serious or life-threatening infection.

* As of October 1, 2017.

Active Federal Legislation*

Bill Title	Description
S. 629 - Preventing Antibiotic Resistance Act of 2017	• **Senate bill** requires the FDA to remove approval for medically important antibiotics in agriculture (exception is if manufacturer demonstrates use does not pose a risk to humans.) It also requires veterinary oversight for medically important antibiotics that are used in livestock. • **House bill** reduces the non-therapeutic use of medically important antibiotics in animal production.
H.R. 1587 – Preservation of Antibiotics for Medical Treatment Act of 2017	

* As of October 1, 2017.

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Key Takeaways

- Key Takeaway #1
  - White House actions in 2014 and 2015 fueled the national interest in antibiotic stewardship
- Key Takeaway #2
  - Accreditation and meaningful use 3 requirements are driving the national conversation around antibiotic stewardship in acute care, not federal policy (e.g. CoPs)
- Key Takeaway #3
  - Most of the active legislation is focused on incentives to promote research and development and reduce veterinary use of medically important antibiotics

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CDC's National Healthcare Safety Network (NHSN) Antimicrobial Use Option

Melinda M. Neuhauser, PharmD, MPH, FCCP, FASHP
Pharmacist- and Acute-Care Lead
Office of Antibiotic Stewardship
Division Healthcare Quality and Promotion
Centers for Disease Control and Prevention

The findings and conclusions in this report are those of the author and do not necessarily represent the official position of The Centers for Disease Control and Prevention.

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NHSN Antimicrobial Use (AU) Option

- Purpose:
  - Provide a mechanism for facilities to report and analyze antimicrobial usage as part of antimicrobial stewardship efforts at their facility

- AU Rate: Days of Therapy/Days Presents

- Standardized Antimicrobial Administration Ratio (SAAR):
  - Provide a set of risk-adjusted AU summary statistics that hospitals can use to compare their AU data with nationally aggregated data

Standardized Antimicrobial Administration Ratio (SAAR)

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

$$\frac{\text{Observed Antimicrobial Days}}{\text{Predicted Antimicrobial Days}}$$

- Calculated for specific groups of antimicrobials & specific location types
  - Modeling used negative binominal regression
- Not a definitive measure of appropriateness or judicious use
  - Starting point or to pinpoint focus & prioritize resources

For full details see AUR Module Protocol: http://www.cdc.gov/nhsn/pdfs/pscmanual/11pscaurcurrent.pdf

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Interpreting the SAAR

- Ratio: Values will always be ≥ 0
- SAAR above 1.0 – **more** antimicrobial use than predicted
- SAAR below 1.0 – **less** antimicrobial use than predicted
- SAAR no different than 1.0 – antimicrobial use is **equivalent** to referent population

Note: A SAAR alone is not a definitive measure of the appropriateness or judiciousness of antibacterial use, and any SAAR may warrant further investigation. For example, a SAAR that is not statistically significant may still indicate under or over use. Likewise, investigation into a statistically significant SAAR may not yield actionable results.

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SAAR Report in NHSN

National Healthcare Safety Network

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

As of: December 20, 2016 at 5:08 PM

Date Range: AU_SAAR summaryYM After and Including 2015M01

SAAR Title

Antimicrobials used for hospital-onset/multi-drug resistant infections in adult wards

Rate Denominator

Facility Org ID	Summary Year/Month	SAAR Type	Antimicrobial Days	Predicted Antimicrobial Days	Days Present	SAAR	SAAR p-value	95% Confidence Interval
13860	2015M01	TAR-Adult-2	97	68.114	583	1.424	0.0010	1.161, 1.730
13860	2015M02	TAR-Adult-2	114	70.801	606	1.610	0.0000	1.334, 1.927
13860	2015M06	TAR-Adult-2	60	122.332	1132	0.490	0.0000	0.378, 0.627
13860	2016M09	TAR-Adult-2	251	130.430	1180	1.924	0.0000	1.697, 2.174
13860	2016M10	TAR-Adult-2	291	133.120	1205	2.186	0.0000	1.945, 2.448

Observed Use

Predicted Use

Calculated SAAR Values

Includes data for January 2014 and forward.

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

Source of aggregate data: 2014 NHSN AU Data

Data contained in this report were last generated on December 20, 2016 at 3:43 PM.

Example data

SAAR by Location

National Healthcare Safety Network
SAARs Table - All SAARs by Location
As of: April 25, 2017 at 11:46 AM
Date Range: AU_SAAR summaryYM 2016M09 to 2016M10

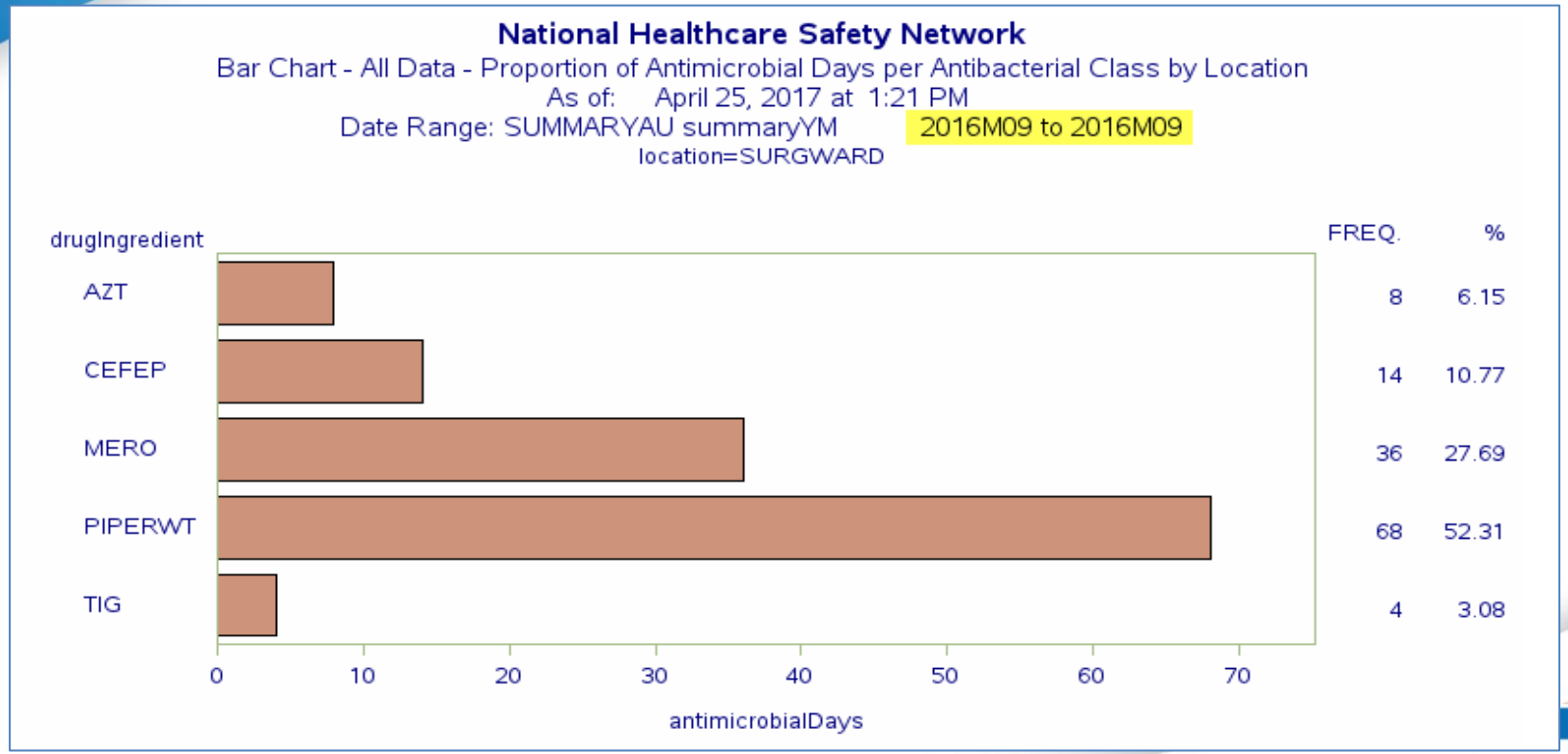
Antimicrobials used for hospital-onset/multi-drug resistant infections in adult wards

orgID	SAARType	location	summaryYM	locCDC	antimicrobialDays	numAUDaysPredicted	numDaysPresent	SAAR	SAAR_pval	SAAR95CI
13860	TAR-Adult-2	MEDWARD	2016M09	IN:ACUTE:WARD:M	121	69.984	599	1.729	0.0000	1.441, 2.058
13860	TAR-Adult-2	MEDWARD	2016M10	IN:ACUTE:WARD:M	120	70.801	606	1.695	0.0000	1.411, 2.019
13860	TAR-Adult-2	SURGWARD	2016M09	IN:ACUTE:WARD:S	130	60.446	581	2.151	0.0000	1.804, 2.545
13860	TAR-Adult-2	SURGWARD	2016M10	IN:ACUTE:WARD:S	171	62.319	599	2.744	0.0000	2.355, 3.179

Includes data for January 2014 and forward.
Data restricted to medical, medical/surgical and surgical locations.
Source of aggregate data: 2014 NHSN AU Data
Data contained in this report were last generated on April 24, 2017 at 2:30 PM.

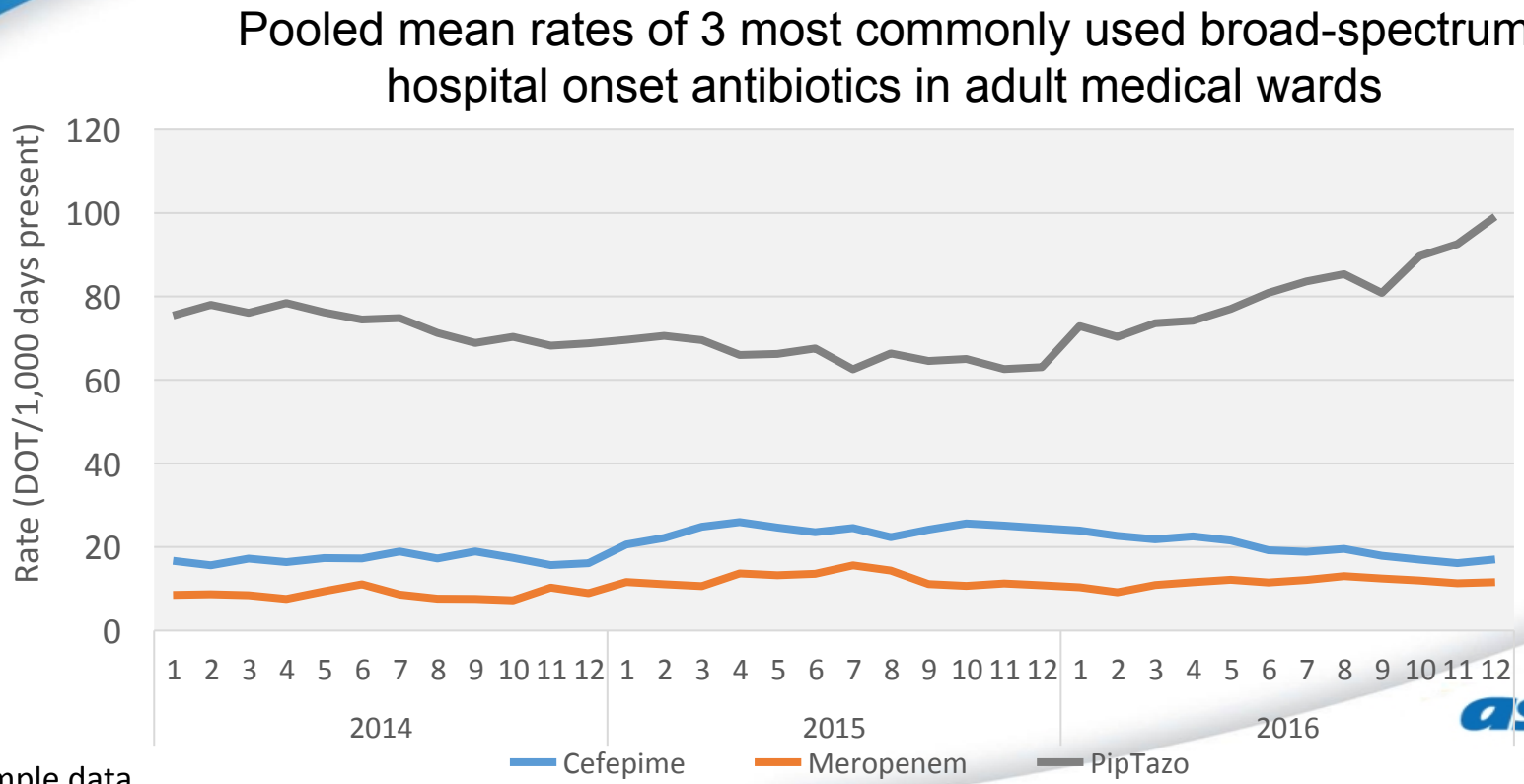
Example data

Example: Drug Composition within the SAAR for Hosp-Onset/MDRO Infxn in Surg Ward



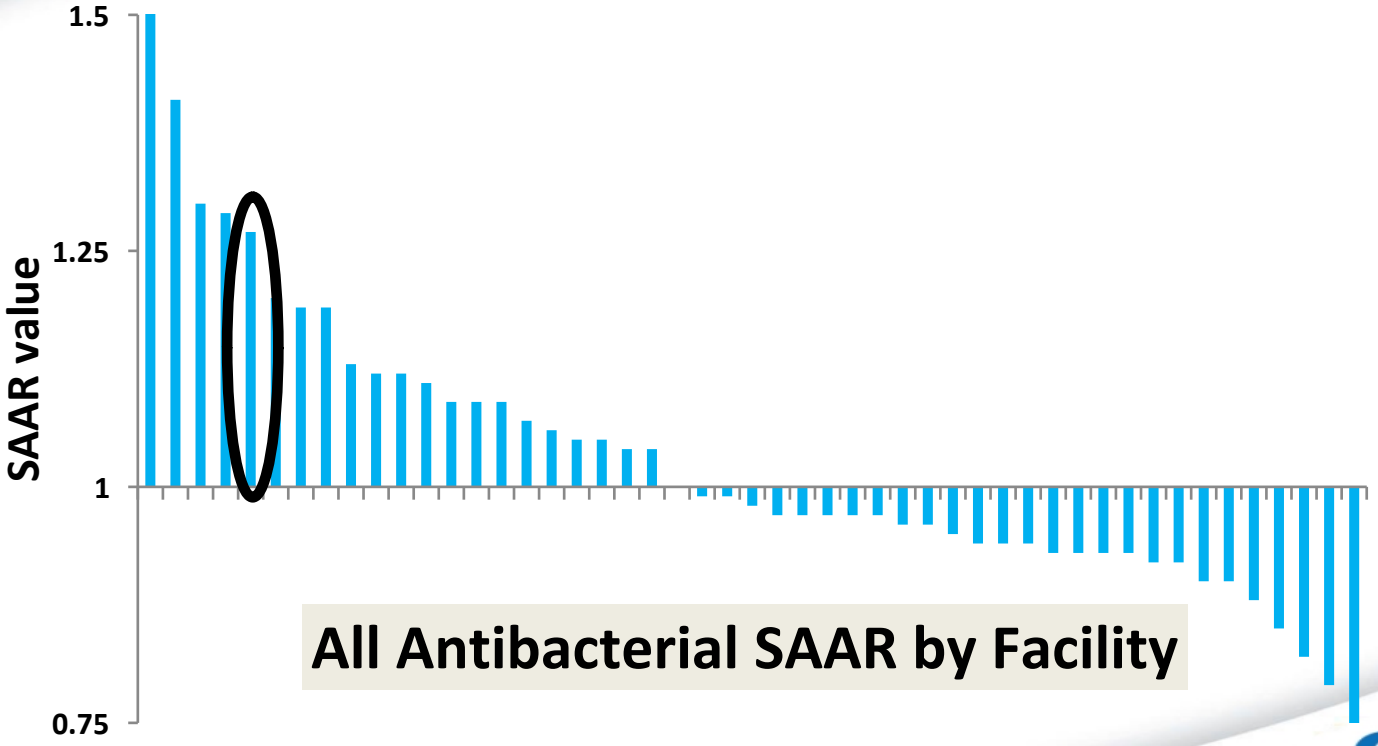
Example data

Investigating the Observed Increase in Broad-Spectrum Hospital-Onset Agent SAAR Values



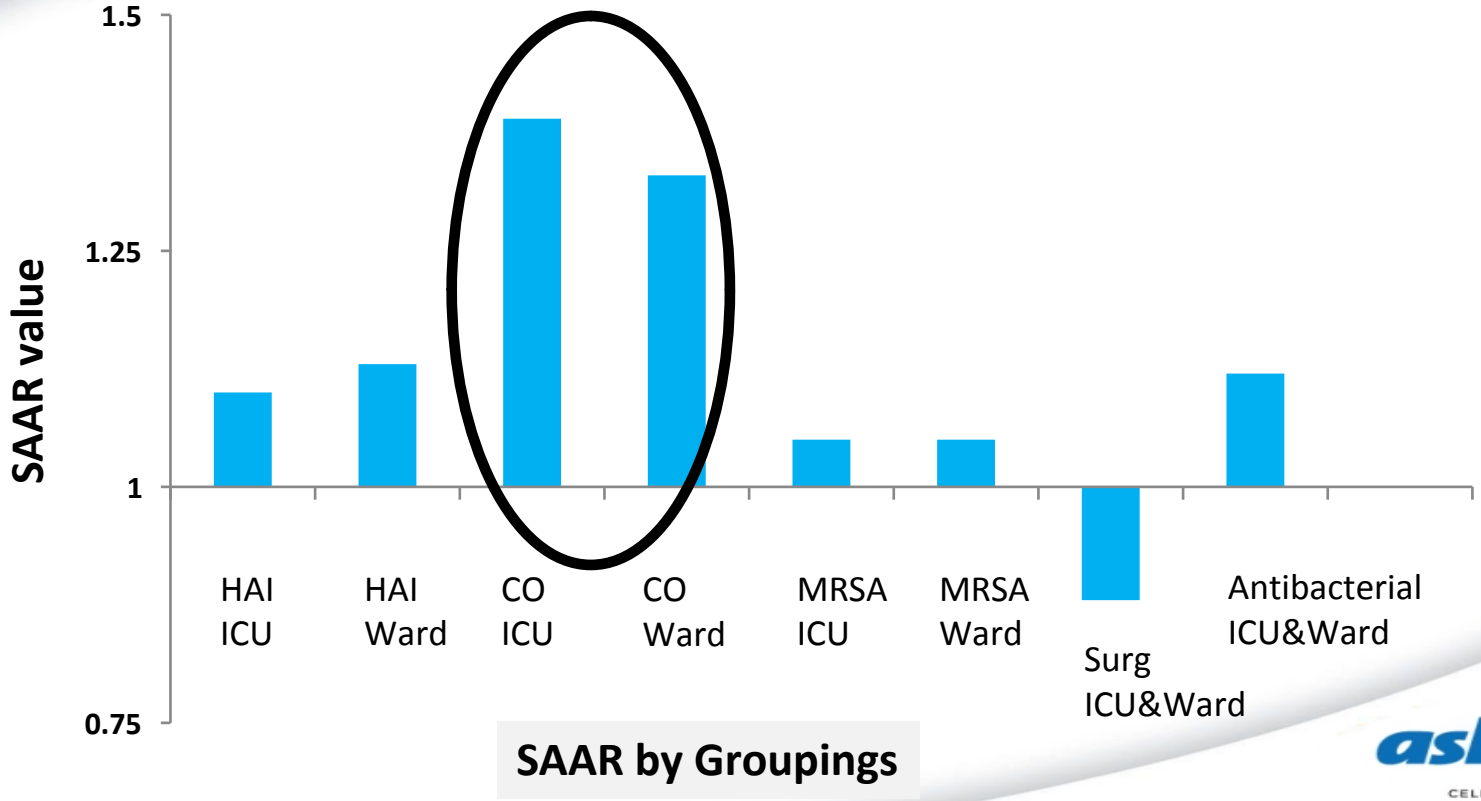
Example data

Using SAAR within a Healthcare Organization



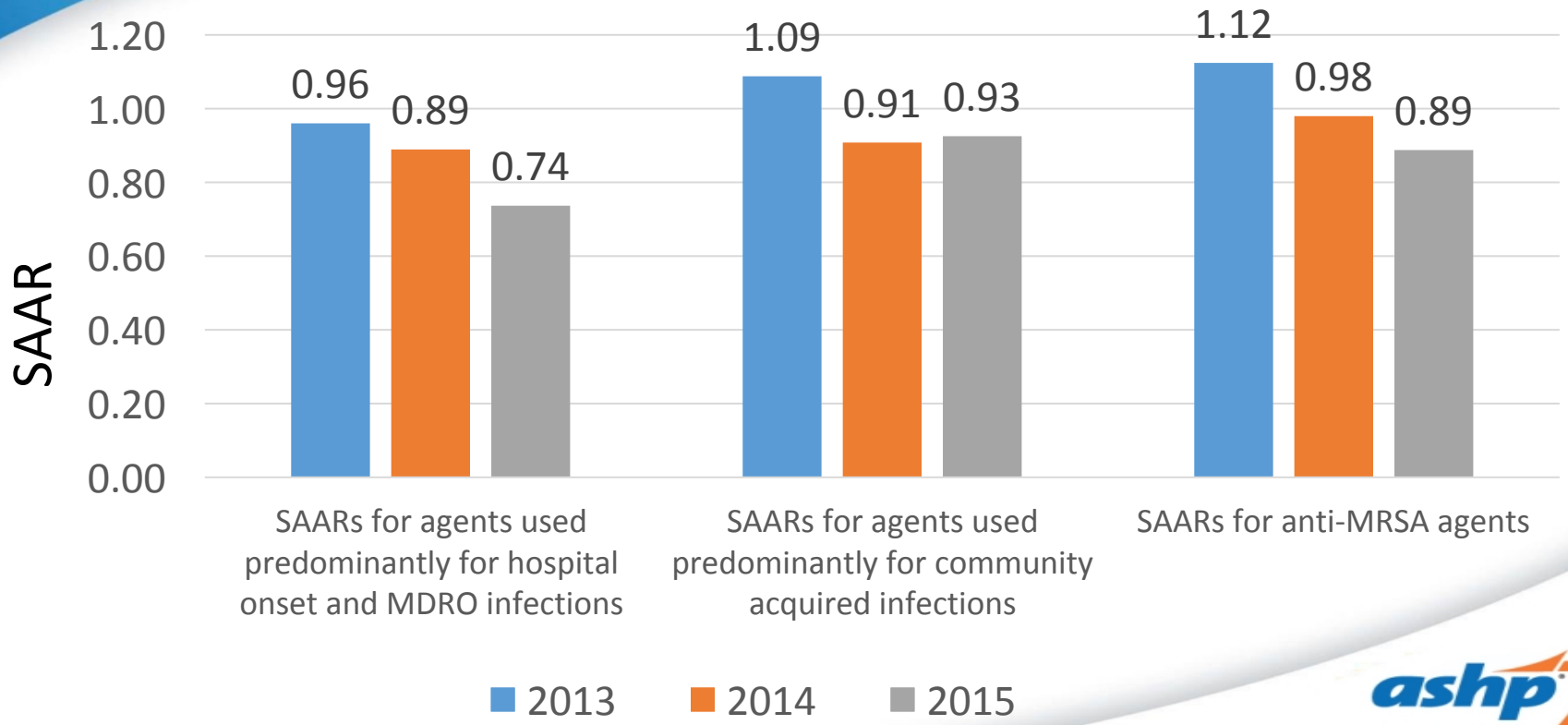
Example data

SAAR Analysis within a Given Facility



Example data

VA Indianapolis, Facility-level SAARs, 2013-2015



Adapted from Daniel Livorsi et al. A Novel Metric to Monitor the Influence of Antimicrobial Stewardship Activities. ICHE2017;38: 721-723

Summary

- Standardized Antimicrobial Administration Ratio (SAAR) is a metric developed by CDC to analyze and report antimicrobial use data in summary form.
- SAARs are generated for five specific antimicrobial groupings, each of which can serve as a high value target or high level indicator for antimicrobial stewardship programs.
- Future iterations of the SAAR can extend its use as a metric to additional patient care locations when aggregate data are sufficient for those purposes.

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CDC's National Healthcare Safety Network (NHSN) Antimicrobial Use Option

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Antimicrobial Stewardship Research: Basics of Conducting Antimicrobial Stewardship Research & Publication

P. Brandon Bookstaver, PharmD, BCPS, FCCP, FIDSA, AAHIVP
Associate Professor & Director of Residency & Fellowship Training
University of South Carolina College of Pharmacy
Palmetto Health Richland & Antimicrobial Stewardship Collaborative of South Carolina (ASC-SC)
Columbia, SC

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Overview for Conducting Stewardship-Related Research

1) Identify research team members & establish roles

2a) Identify gaps in the literature

2b) Discuss institutional goals & stewardship program goals related to research

3) Establish research strategy

4) Execute, evaluate and report out deliverables

Level of Evidence among IDSA Guidelines

Level of Evidence	% of Recommendations	Median % (IQR)
I	14.8	15.8 (5.8-28.3)
II	29.7	30.9 (23.3-43.2)
III	55.5	50.0 (38.1-58.6)
Class of Recommendation		
A	40.2	41.5 (28.7-55.6)
B	37.7	40.3 (27.1-47.9)
C	14.0	8.1 (1.8-14.7)
Other	8.1	0 (0.6.7)

IQR=Interquartile range

Khan AR et al. Clin Infect Dis 2010;51:1147-56.

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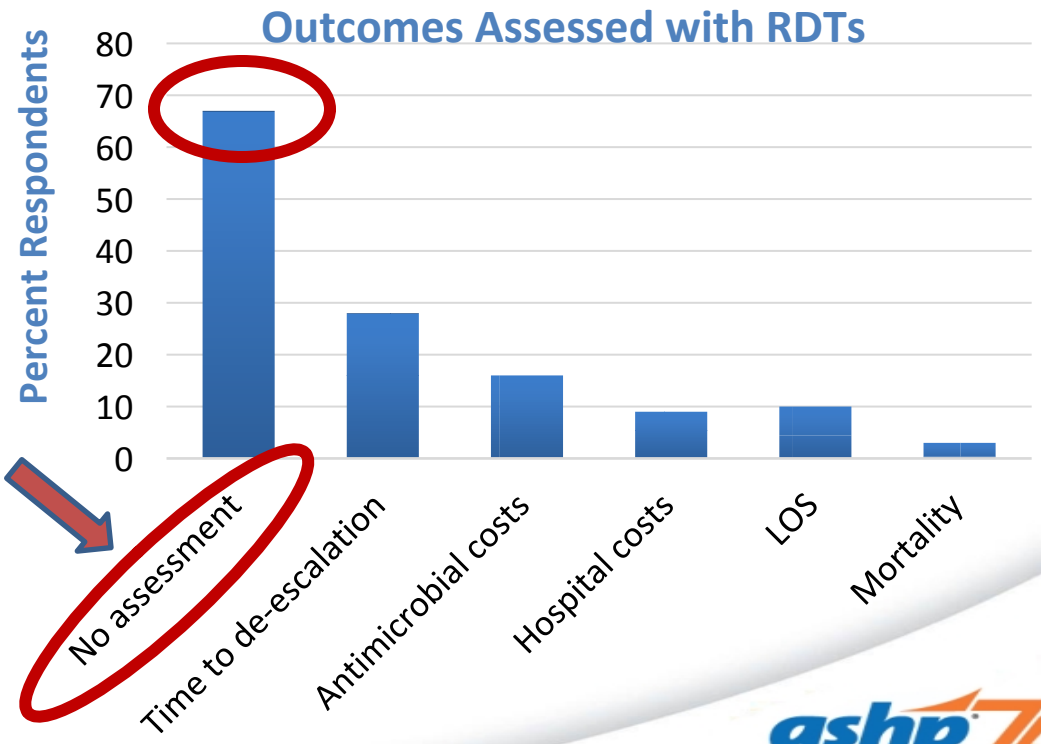
28 Total Recommendations in 2016 IDSA Antibiotic Stewardship Guidelines

8 interventions	6 optimization	6 microbiology & laboratory diagnostics	3 measurement	5 special populations
			2 good practice recs	3 good practice recs
Strength	**Strength**	**Strength**	**Strength**	**Strength**
Strong = 2	Strong = 3	Strong = 0	Strong = 0	Strong = 0
Weak = 6	Weak = 3	Weak = 6	Weak = 1	Weak = 2
Quality	**Quality**	**Quality**	**Quality**	**Quality**
High = 0	High = 0	High = 0	High = 0	High = 0
Moderate = 3	Moderate = 3	Moderate = 3	Moderate = 0	Moderate = 0
Low = 5	Low = 3	Low = 3	Low = 1	Low = 2
Very Low = 0	Very Low = 0	Very Low = 0	Very Low = 0	Very Low = 0

Barlam TF, et al. Clin Infect Dis 2016;62:e51-77.

Reported Assessment of Rapid Diagnostics

- Survey of pharmacists involved in antimicrobial stewardship (n=214)
- Focus was on rapid diagnostic technology (RDT) familiarity/utilization and measuring impact



Foster RA, et al. Infect Control Hosp Epidemiol 2017;38:863-6.

Our Stewardship Research Strategy… It's Simple Really

1) We take clinical questions and look for practical answers using local data.

2) We strive to have objective, evidence-based recommendations (discussions) with our colleagues.

Palmetto Health ASST Evidence-Based Precision Medicine

Strength of association of risk factors & cumulative effect of multiple risk factors

Welcome to the Era of Precision Medicine

"Precision or individualized medicine is an emerging approach for disease treatment and prevention that takes into account individual variability in environment, lifestyle and genes for each person".

National Institute of Health, Precision Medicine Initiative

There is no better example of precision medicine than the selection of empirical antimicrobial therapy in hospitalized patients with serious bacterial infections. The risk of antimicrobial resistance varies widely from one individual to another based on prior use of antimicrobial agents and other healthcare exposures.

Our team has been on a mission to transform empirical antimicrobial therapy from a "one size fits all" approach to an evidence-based selection according to each patient's specific risk of antimicrobial resistance. We invite our colleagues to utilize the Patient-Specific Antibiogram for optimization of empirical antimicrobial therapy. These prediction tools provide objective and precise assessment of the risk of infections due to *Pseudomonas aeruginosa*, ESBL-producing and fluoroquinolone-resistant bacteria. Application of these tools has been demonstrated to increase the adequacy of empirical antimicrobial therapy while reducing utilization of broad-spectrum antimicrobial agents.

Palmetto Health Antimicrobial Stewardship and Support Team

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Scholarship Strategy

Focus your area of study but diversify your approach

"Financial portfolio model"

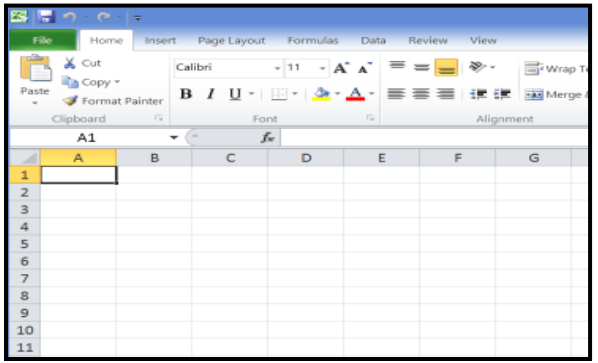
Trainee-driven research

Internal collaborations

External collaborations

Utilize Your Resources

- Utilize (motivated) pharmacy and medical trainees
  - Pharmacy/Medical students, residents
  - ID or non-ID medical fellows
  - ID or non-ID Pharmacy resident/fellow



- Outside collaboration
  - Research networks (eg SHEA, SERGE-45– Southeastern Research Group Endeavor)

- Physician and pharmacists who are excited and engaged in research productivity

- Data already available locally (eg. perpetual databases)

- Mentorship

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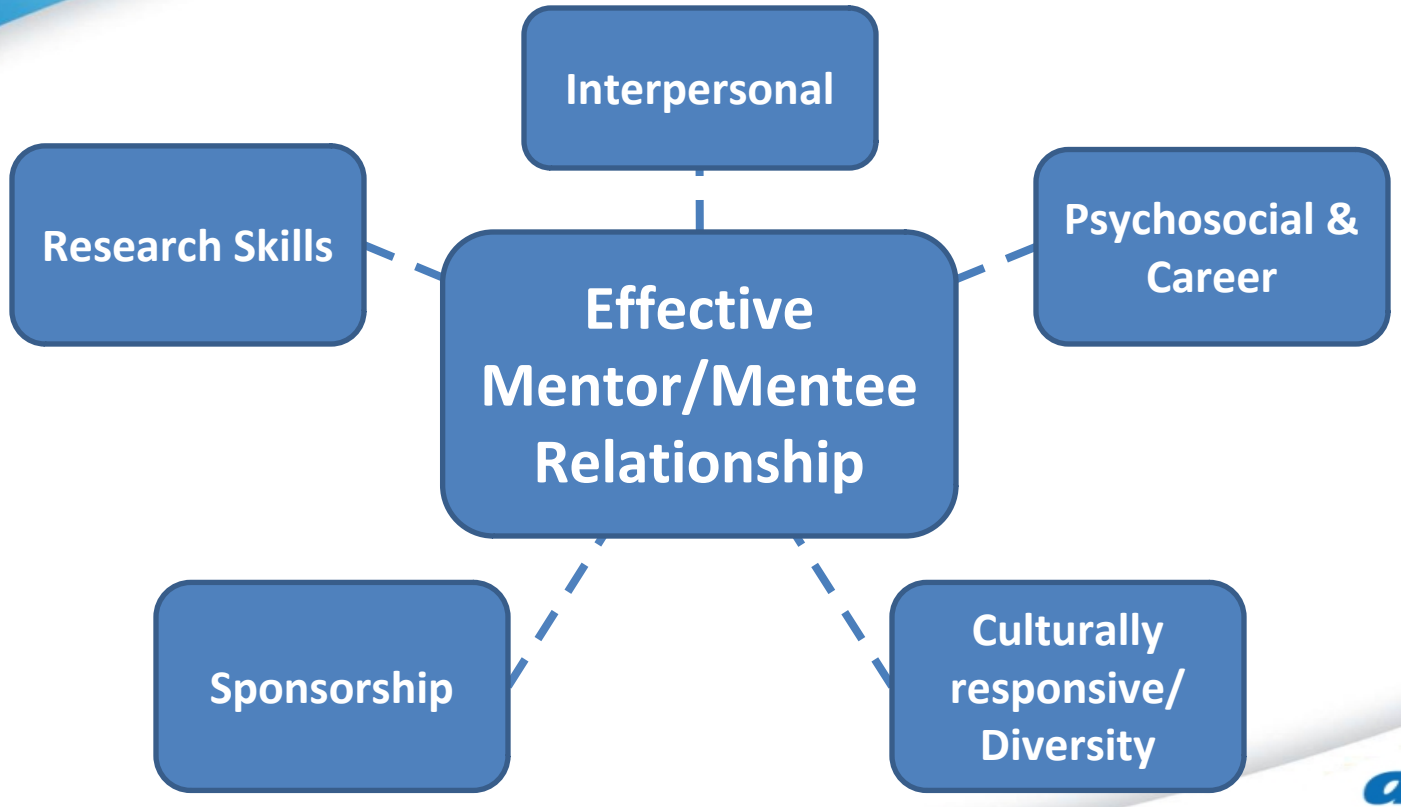
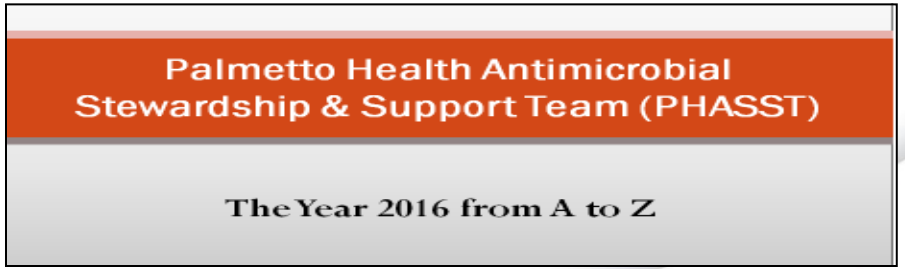
Effective Mentoring in Research



Pfund C, et al. AIDS Behav 2016;20(Suppl 2):238-48.

Scholarship as a Metric

- Presentations, abstracts and publications are metrics for our stewardship program



PHASST 2015 Paper of the Year

AAC
Journals.ASM.org

Stratification of the Impact of Inappropriate Empirical Antimicrobial Therapy for Gram-Negative Bloodstream Infections by Predicted Prognosis

Sarah E. Cain,[a] Joseph Kohn,[b] P. Brandon Bookstaver,[c] Helmut Albrecht,[d] Majdi N. Al-Hasan[d]
University of South Carolina School of Medicine, Columbia, South Carolina, USA,[a] Department of Clinical Pharmacy, Palmetto Health Richland, Columbia, South Carolina, USA,[b] Department of Clinical Pharmacy and Outcomes Science, South Carolina College of Pharmacy, University of South Carolina, Columbia, South Carolina, USA,[c] Department of Medicine, Division of Infectious Diseases, University of South Carolina School of Medicine, Columbia, South Carolina, USA,[d]

Sarah (Cain) Battle, MD
PH/USC SOM

Cain SE, et al. Antimicrob Agents Chemother 2015;49:245-50.

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“How to Successfully Publish a Manuscript”

Step 1:

Write a manuscript

John Bosso, faculty development session (circa 2010ish)

A good idea done well always has a home.

April Miller Quidley (circa 2008)

Scientific literature is not a children’s book.

Paraphrasing John Williamson (circa 2006)

Society of Healthcare Epidemiology of America Publication Series

Series of papers published in Infection Control Hospital Epidemiology (ICHE) from June 2016 – November 2016 highlighting general research principles in stewardship and epidemiology:

- Quasi-experimental studies
- Survey methodology
- Mathematical modeling
- Qualitative analyses

https://doi.org/10.1017/ice.2016.171; https://doi.org/10.1017/ice.2016.91; https://doi.org/10.1017/ice.2016.160; https://doi.org/10.1017/ice.2016.118; https://doi.org/10.1017/ice.2016.117; https://doi.org/10.1017/ice.2016.93 https://doi.org/10.1017/ice.2016.189

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Research & Career Direction

- Participation in research among both pharmacy and medical students increases likelihood of future careers in research & discipline-specific areas of research
- Positive research mentoring leads to increased likelihood of subsequent mentee/mentor experiences for all participants
- Research participation for pharmacy trainees increases critical thinking
- Pharmacy students participating in research are significantly more likely to successfully match for post-graduate residency

Osborne K, et al. Am J Pharm Educ 2017 (In press)
Rosenkranz SK, et al. BMC Med Educ 2015;15:95.

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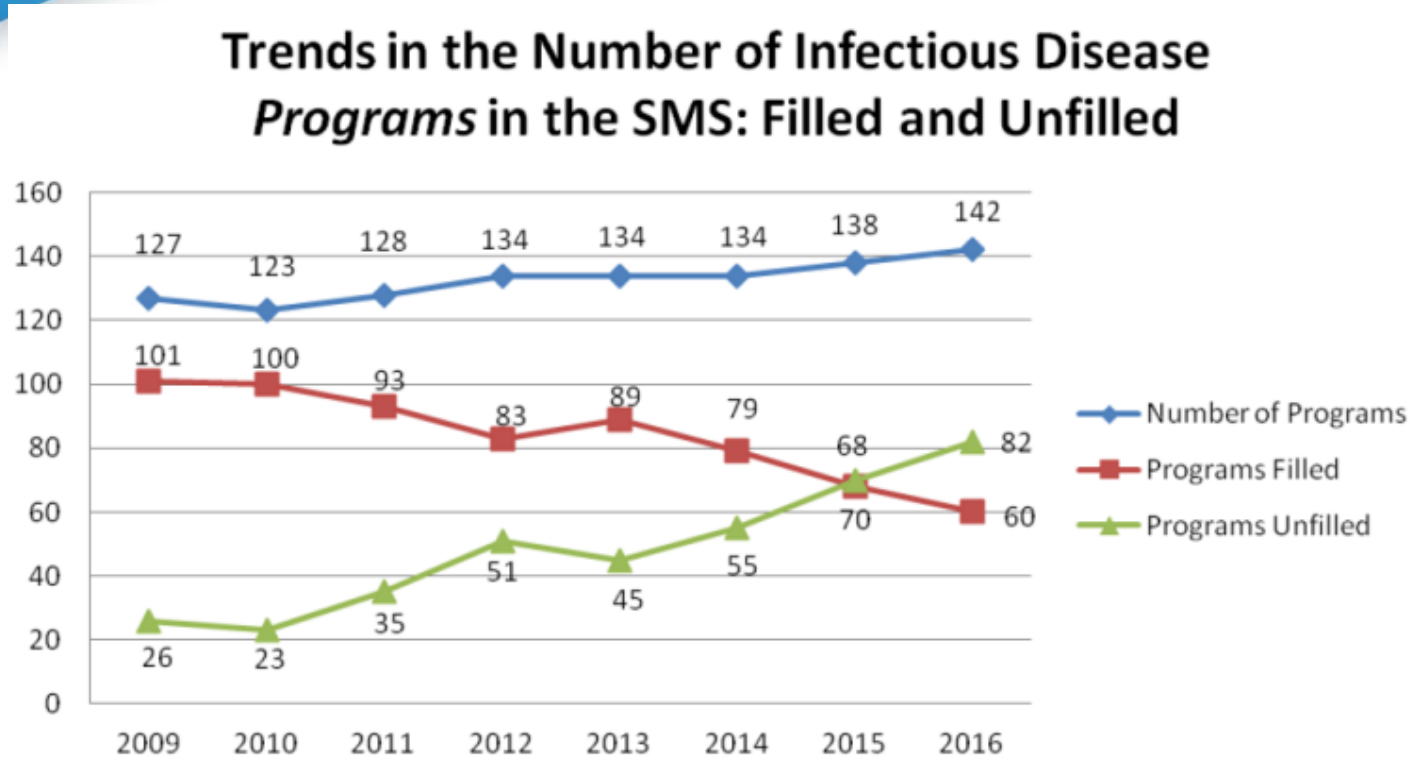
Research & Career Direction



Results and Data Specialties Matching Service, 2016 Appointment Year; NRMP, February 2016

Research & Career Direction

Infectious Diseases Pharmacy Training Programs (2015)

Characteristic	ID PGY2 Programs (%)	ID Fellowship Programs (%)
No. of programs	74	15
No. of positions	75	18
Program location		
West	11 (15)	2 (13)
Midwest	23 (31)	7 (47)
Northeast	14 (19)	3 (20)
South	26 (35)	3 (20)
General/Adult ID focus	71 (96)	14 (93)

Gauthier TP, et al. Clin Infect Dis 2015;60:826-7.

Avoid Distractions, Pitfalls & Barriers

- Not establishing end goal prior to embarking on research
  - Lack of focus
- Lack of "wins"
- Failure to grow network/research base
- Spending excessive time/resources on "outliers"

Available on Twitter®
Included with permission of involved parties

Key Takeaways

- Key Takeaway #1
  - There are significant gaps in the stewardship literature related to intervention, optimization and microlab/diagnostics.
- Key Takeaway #2
  - Establishing a research strategy that matches your institutional goals, local resources and team members is important to success.
- Key Takeaway #3
  - Mentorship, either internal or external, drives success for both mentee and mentor when effective relationships are established.
- Key Takeaway #4
  - Disseminate your stewardship results through abstracts and peer-reviewed publications.

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Antimicrobial Stewardship Research: Basics of Conducting Antimicrobial Stewardship Research & Publication

P. Brandon Bookstaver, Pharm.D., BCPS, FCCP, FIDSA, AAHIVP
Associate Professor & Director of Residency & Fellowship Training
University of South Carolina College of Pharmacy
Palmetto Health Richland & Antimicrobial Stewardship Collaborative of South Carolina (ASC-SC)
Columbia, SC

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But The Computer Told Me To Do It …

(Incorporating Indication Based Dosing in CPOE)

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Clinical Pharmacy Coordinator, Infectious Diseases
Beth Israel Deaconess Medical Center
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What Is It?

Indication Based Dosing

- Requiring prescribers to enter an indication for [antibiotics] at the time of order entry
- Can be programmed to recommend alternative doses based on site/type of infection
- Can incorporate renal/hepatic dosing adjustments
- Out-of-the-box versus home-grown systems

Why Bother?

‡ Cefepime (IV)

	> 60 mL/min	30-60 mL/min	10-30 mL/min	< 10 mL/min	Hemodialysis	CRRT
Bacteremia non-Pseudomonas	2g q12h	2g q24h	1g q24h	500 mg q24h	500 mg q24h	1-2g q12h
CNS Infection	2g q8h	2g q12h	2g q24h	1g q24h	1g q24h	2g q12h
Febrile Neutropenia	2g q8h	2g q12h	2g q24h	1g q24h	1g q24h	2g q12h
Intra-abdominal Infection	2g q12h	2g q24h	1g q24h	500 mg q24h	500 mg q24h	1-2g q12h
Pneumonia non-Pseudomonas	1g q12h	1g q24h	500 mg q24h	500 mg q24h	500 mg q24h	1g q12h
Suspected/confirmed Pseudomonas Pneumonia or sepsis	2g q8h	2g q12h	2g q24h	1g q24h	1g q24h	2g q12h
Skin/Soft Tissue	2g q12h	2g q24h	1g q24h	500 mg q24h	500 mg q24h	1-2g q12h
Urinary Tract	1g q12h	1g q24h	500 mg q24h	250 mg q24h	250 mg q24h	1g q12h

BIDMC Renal Dosing Recommendations

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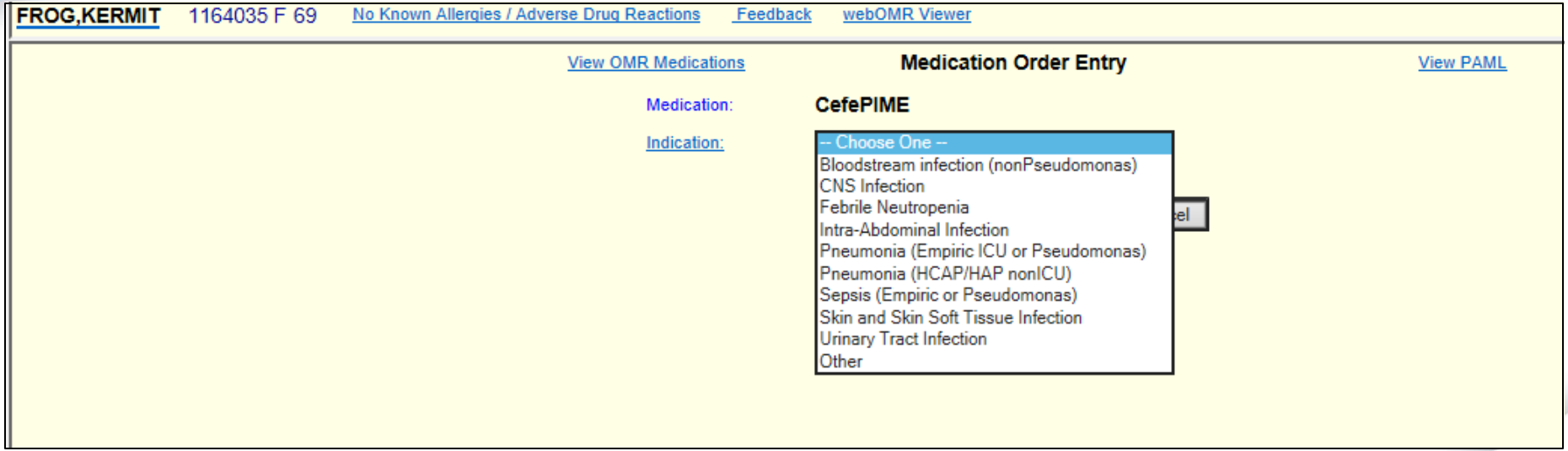
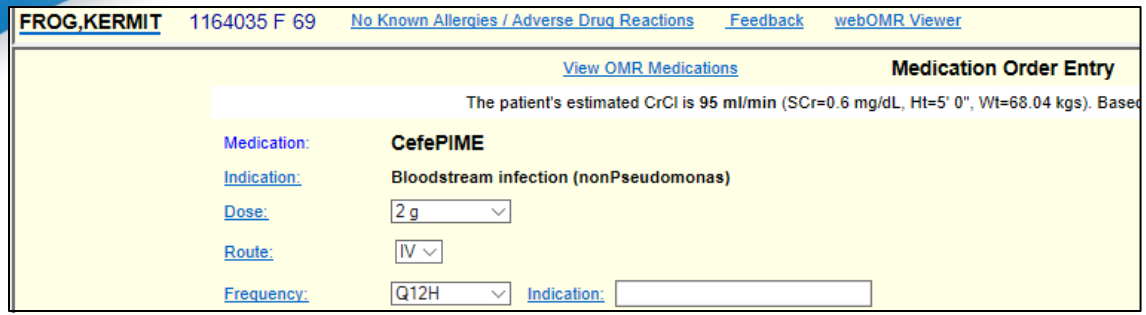
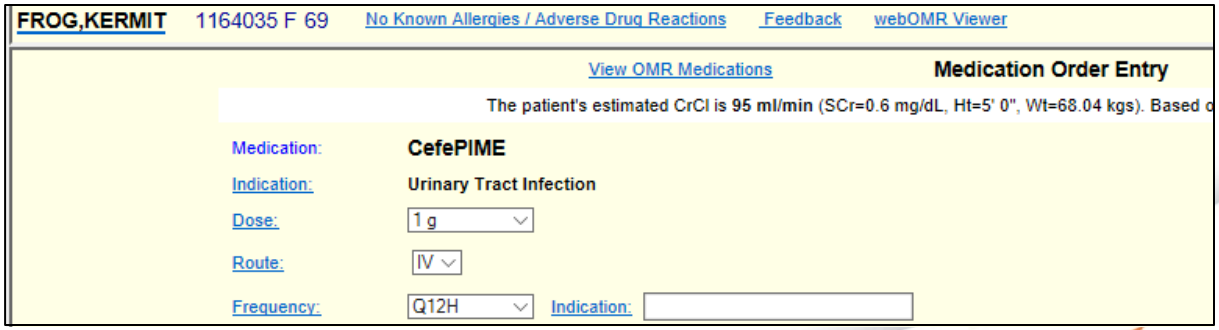
How Does It Work?



How Does It Work?





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Who Supports It?

- IDSA/SHEA Antimicrobial Stewardship Guidelines[1]
- CDC's core elements for antimicrobial stewardship[2]
- NQF's antimicrobial stewardship playbook[3]
- Leapfrog Performance Measure[4]

[1]Barlam et al. *Clin Infect Dis.* 2016;62:51-77
[2]https://www.cdc.gov/getsmart/healthcare/pdfs/core-elements.pdf
[3]http://www.qualityforum.org/Publications/2016/05/National_Quality_Partners_Playbook__Antibiotic_Stewardship_in_Acute_Care.aspx
[4]http://www.leapfroggroup.org/sites/default/files/Files/2017Survey_04052017_v3.3.pdf

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What's The Data?

Reference	Medication(s)	Indication-Infection Concordance
Patel 2012	Prophylaxis (n=50) Treatment (n=50)	100% (50/50) 86% (43/50)
Lee 2017[1]	Cefepime (n=50)	86% (43/50)
Lee 2017[2]	Valacyclovir (n=117)	50% (59/117)

Patel et al. *Infect Control Hosp Epidemiol*. 2012:33:1066-7
[1]Lee et al. ID Week 2017. San Diego, CA. Poster 743
[2]Lee et al. ID Week 2017. San Diego, CA. Poster 761

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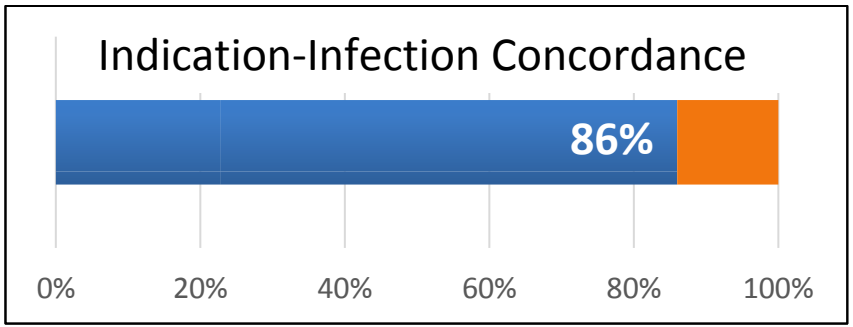
Does Automated ASP Approval Matter?

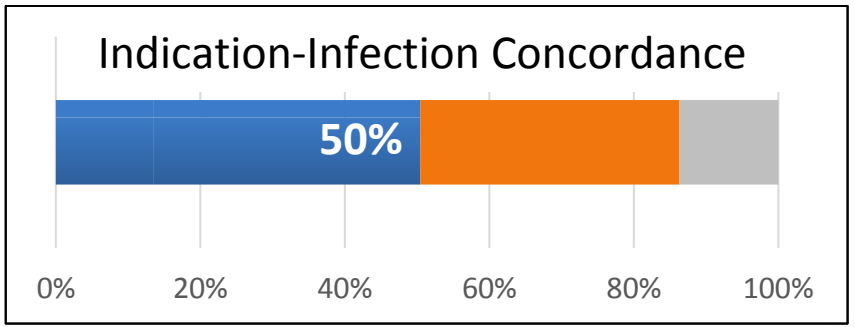
Cefepime[1]

- No automated ASP approval*



Valacyclovir[2]

- Automated ASP approval for 2 indications

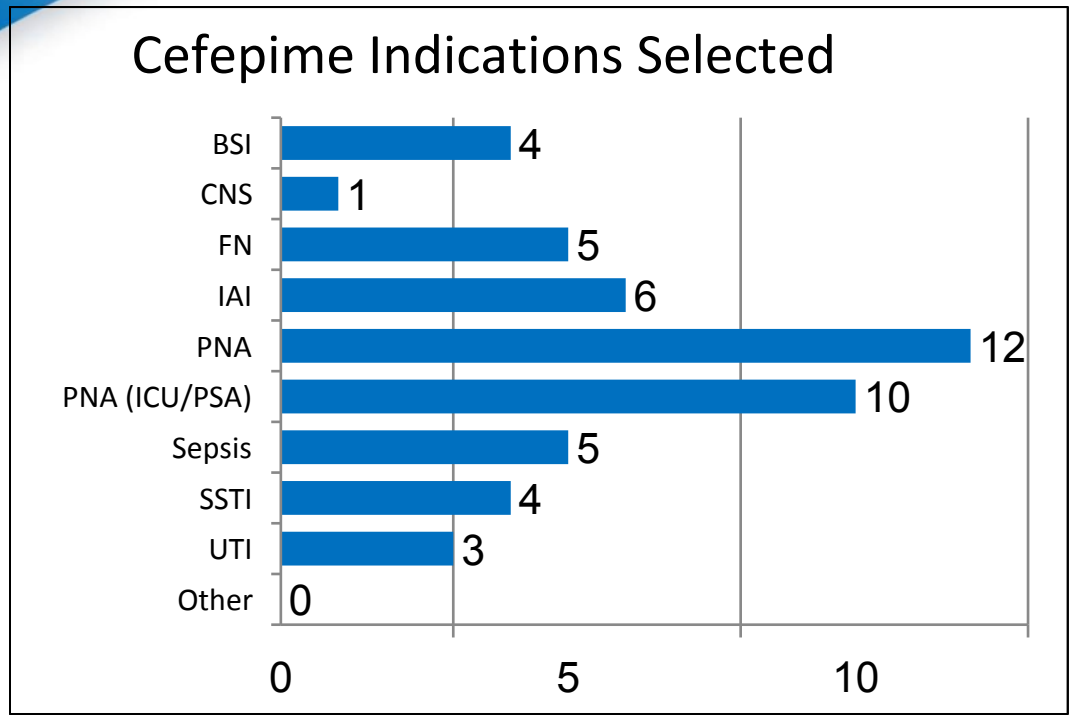


Matched Mis-matched Blank

* Exception: febrile neutropenia (n=5)

[1]Lee et al. ID Week 2017. San Diego, CA. Poster 743; [2]Lee et al. ID Week 2017. San Diego, CA. Poster 761

What Else Can it Do?



- Resulted in 72% (n=36) dosing concordance with institutional renal dosing card
- Discordant doses were mostly higher than recommended (11/14)

Lee et al. ID Week 2017. San Diego, CA. Poster 743

Key Takeaways

- Key Takeaway #1
  - CPOE is a permanent part of the medical record
- Key Takeaway #2
  - Indication based dosing can be a powerful stewardship tool
- Key Takeaway #3
  - Selected indication and suspected/confirmed infection concordance can vary – periodic auditing is recommended, especially if used for automated ASP approval

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But The Computer Told Me To Do It …

(Incorporating Indication Based Dosing in CPOE)

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Antimicrobial Stewardship for the Non-ID Pharmacist

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Infectious Diseases Pharmacist
Henry Ford Health System
Detroit, MI

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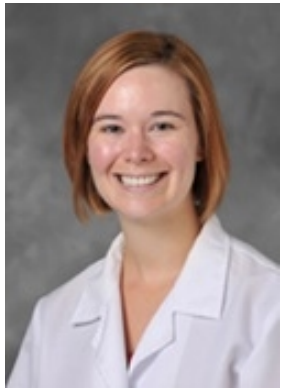
Our Story Begins in Detroit…



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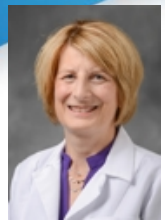
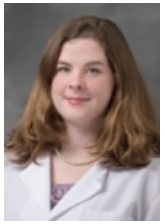
Practice Model Overview





- Patient Care Teams
  - Comprised of pharmacy specialists, generalists, trainees
- Generalist Role
  - Rotate through assignments bedside or drug distribution (monthly)
  - Provide comprehensive pharmacy services

Empowering General Pharmacists in Antimicrobial Stewardship

Carreno JJ et al. AJHP 2015; 72(15):1298-1303

Stewardship Care Bundle

The Stewardship Bundle

1) documentation of indication for antibiotics at initiation
2) collection of appropriate cultures
3) evaluation of appropriateness of empiric therapy
4) de-escalation when microbiologically indicated

Successful bundle implementation requires:

- Patient assessment
- Interpretation of microbiology
- Application of guidelines
- Strong communication skills

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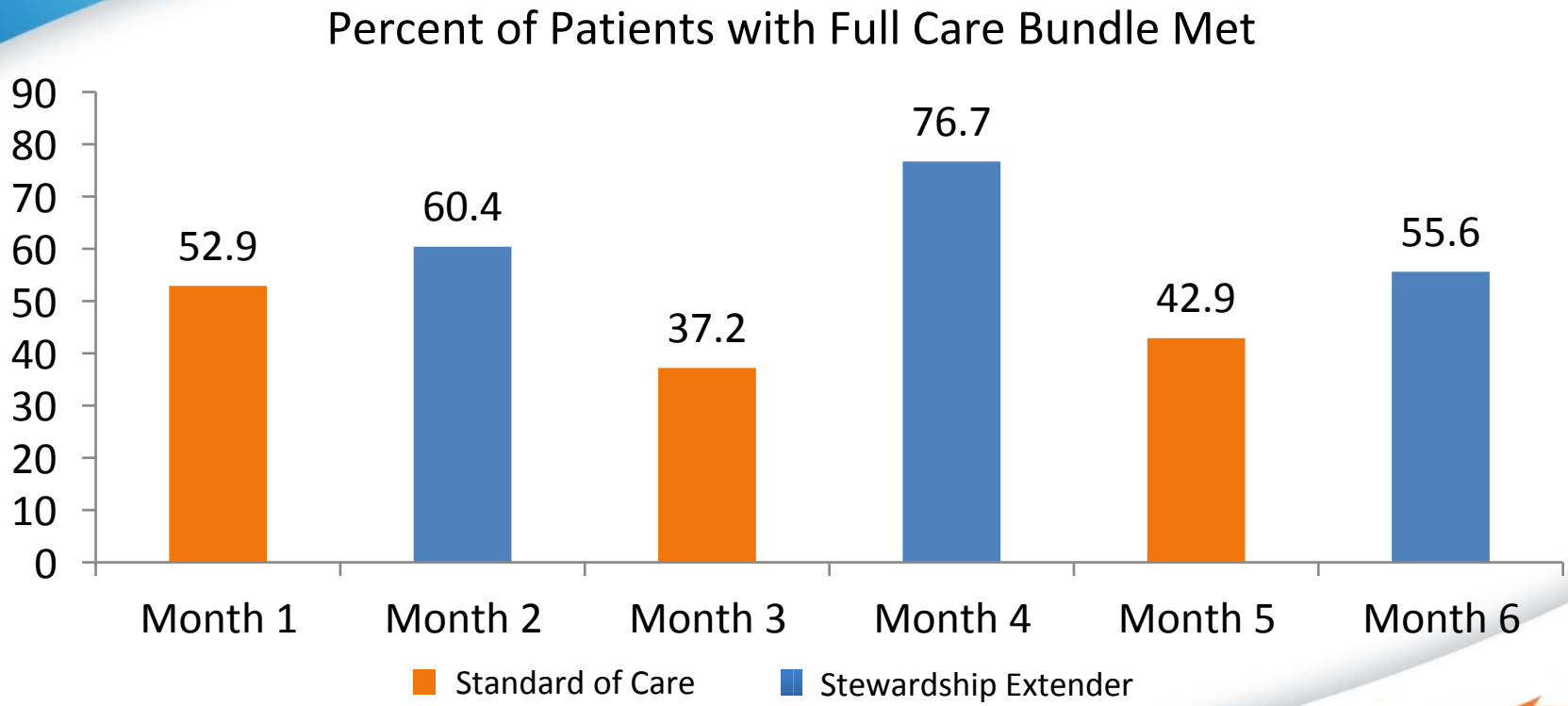
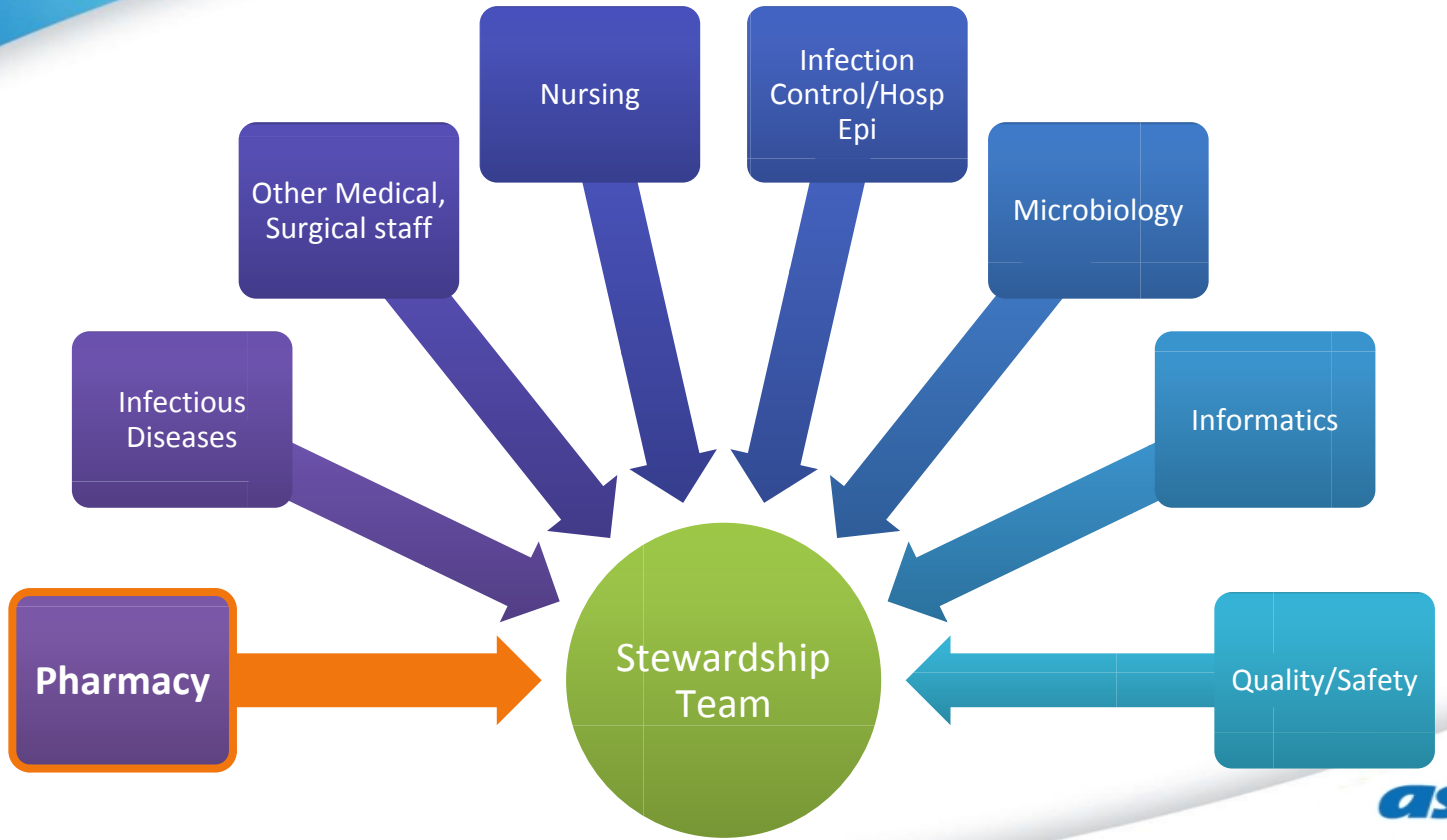
Results



Carreno JJ et al. AJHP 2015; 72(15):1298-1303

Who is on the team?



Dellitt TH et al. *Clin Infect Dis* 2007;44:159-77

Stewardship Core Elements & Pharmacy Roles

Leadership Commitment	ID Pharmacist
Accountability	ID Pharmacist
Drug Expertise	ID Pharmacist
Action	ID Pharmacist
Tracking	ID Pharmacist
Reporting	ID Pharmacist
Education	ID Pharmacist

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

Stewardship Core Elements & Pharmacy Roles

All Pharmacists

All Pharmacists

All Pharmacists

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

Training More Pharmacists in Stewardship??

Basic Training Components

- National/local guidelines
  - Drug selection, dose, duration
  - Appropriate cultures by indication
- Stewardship philosophy, goals, communication

Advanced Training Options

- Consider certificate training programs
  - Intervention implementation
  - Outcomes assessment

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Antimicrobial Stewardship for the Non-ID Pharmacist

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Detroit, MI

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SELF-ASSESSMENT QUESTIONS

Self-Assessment Question 1

Which of the following statements is false?

A. Reporting antibiotic use and resistance data into NHSN can satisfy Meaningful Use 3 requirements.
B. CMS requires long term care facilities to have an antibiotic stewardship program (ASP)
C. CMS requires acute care facilities to have an ASP
D. There are few states that require hospitals to have an ASP

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Self-Assessment Question 2

SAARs are generated for five specific antimicrobial groupings.

A. True

B. False

Self-Assessment Question 3

What percentage of stewardship programs have formally evaluated rapid diagnostic technologies?

A. 90%
B. 30%
C. 60%
D. 10%

Self-Assessment Question 4

Indication based dosing can be a powerful antimicrobial stewardship tool

A. True
B. False

Self-Assessment Question 5

Which of these is NOT part of a basic antimicrobial stewardship care bundle?

A. Documentation of indication for antibiotics
B. Determining collection of appropriate cultures
C. De-escalation to the lowest-cost agent
D. Evaluation of appropriate empiric drug selection

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Stewardshipping the ID Consult Service

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PGY2 Infectious Diseases Residency Program Director
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Madison, WI

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Active Learning Time!

How many programs exempt the ID consult service from common stewardship interventions?

Implementing Antimicrobial Stewardship Programs

- Prospective audit and feedback
- Preauthorization
- Education
- Facility-specific guidelines
  - Disease specific, rapid diagnostic, duration
  - Parenteral to enteral interchange, allergy management
  - PK/PD dose optimization guidelines
- Prescriber-led review strategies (i.e. stop orders, antibiotic timeout)

Barlam TF, et al. Implementing an antimicrobial stewardship program: Guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. *CID*. 2016;62:51-77

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Do Any of These Strategies Apply to Your Interaction with the ID Consult Team?

- Prospective audit and feedback
- 

Preauthorization
- Education
- Facility-specific guidelines
  - Disease specific, rapid diagnostic, duration
  - Parenteral to enteral interchange, allergy management
  - PK/PD dose optimization guidelines
- Prescriber-led review strategies (i.e. stop orders, timeout)

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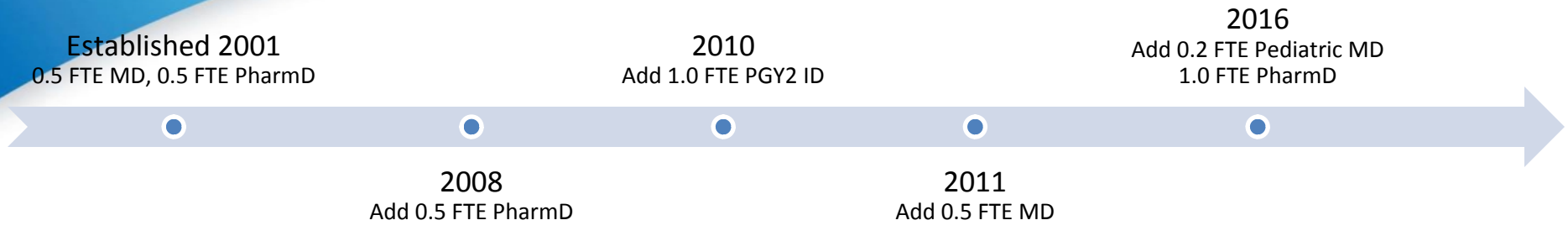
UW Health Antimicrobial Stewardship Program



1.2 FTE ID-trained Physician

2.0 FTE ID-trained Pharmacist

PURPOSE: To provide a collaborative, interdisciplinary system for the optimization of antimicrobial use within the University of Wisconsin Hospital and Clinics to improve drug selection, slow the emergence of antimicrobial resistance, reduce antimicrobial expenditures, and improve patient outcomes.

Stewardship Stakeholders:

Hospitalist, Surgeon, Microbiology, Infection Control, Information Technology, Clinical Pharmacists, Infectious Diseases Physicians

1.0 FTE PGY2 Infectious Diseases Pharmacy Resident

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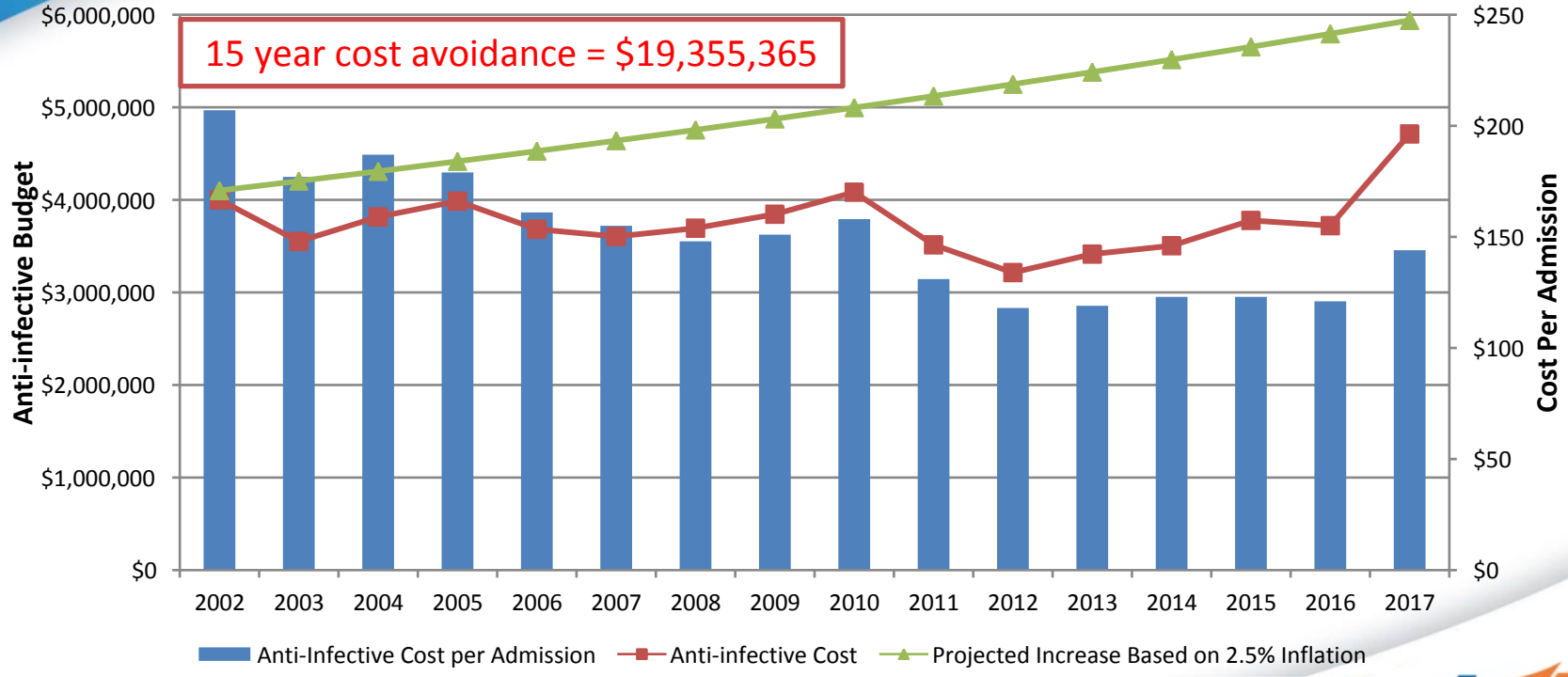
Monitoring Stewardship Effectiveness



excluded drotrecogin alfa, palivizumab, rifaximin, sofosbuvir, daclatasvir and ledipasvir-sofosbuvir from antimicrobial total

Top 1% of Inpatients Administered Antimicrobial Agents Comprising 50% of Expenditures: A Descriptive Study and Opportunities for Stewardship Intervention

- Methods
  - Identified top 1% of expenditures from July 1 through Dec 31, 2014
  - Retrospective chart review
  - Reviewed each case with 2 ID physicians and 1 ID pharmacist
    - Appropriate use: effective, safe, and most cost-effective therapy
    - Inappropriate use: anything not deemed appropriate

Dela-Pena, J; Kerstenetzky L; Schulz L; Kendall R; Lepak A; Fox B. Top 1% of Inpatients Administered Antimicrobial Agents Comprising 50% of Expenditures: A Descriptive Study and Opportunities for Stewardship Intervention. *Infect Control Hosp Epidemiol*. 2016; 1-7

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Who Were the Budget Busters?

- 106 patients accounted for 47.2% of the 6-month budget expenditures
- 2.6± 1.9 hospitalizations per patient
- 85% had ID consult
- 80% were immunocompromised
- 64% of antimicrobial use was for treatment (36% prophylaxis)

Patient Demographics (n=106)	
Male sex – n(%)	68 (64.2)
Age (yrs) – mean (SD)	53.6 (18.7)
BMI (kg/m^2) – mean (SD)	27 (7.0)
Charlson Comorbidity Score – median (IQR)	6 (5,7)
Transfer from referring facility – n (%)	35 (33.0)
Inpatient ID consult – n (%)	85 (80.2)
Post-discharge ID clinic follow up – n (%)	43 (40.6)
Immunocompromised patients – n (%)	80 (75.5)

Dela-Pena, J; Kerstenetzky L; Schulz L; Kendall R; Lepak A; Fox B. Top 1% of Inpatients Administered Antimicrobial Agents Comprising 50% of Expenditures: A Descriptive Study and Opportunities for Stewardship Intervention. *Infect Control Hosp Epidemiol*. 2016; 1-7

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Opportunities for Intervention

57 patients with interventions to improve therapy	Treatment (n)	Prophylaxis (n)	Total (n)
PK/PD dose optimization	20	3	23
Missed opportunity for IV to PO conversion	5	6	11
Double coverage	6	1	7
Allergy consult or improved allergy investigation	5	1	6
Other cost-effective alternative	6	0	6
OPAT convenience continued as inpatient	5	0	5
Missed opportunity to discontinue or deescalate	5	0	5
Error in billing	4	0	4
Discharge delay due to placement issues	3	0	3
Send-out TDM results delayed	1	0	1
Total	**60**	**11**	**71**

Dela-Pena, J; Kerstenetzky L; Schulz L; Kendall R; Lepak A; Fox B. Top 1% of Inpatients Administered Antimicrobial Agents Comprising 50% of Expenditures: A Descriptive Study and Opportunities for Stewardship Intervention. *Infect Control Hosp Epidemiol*. 2016; 1-7

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Key Takeaways

- Antimicrobial stewardship principles and strategies can (and should) apply to all prescribers at your institution.
- Design your program to incorporate and engage all prescribers in the care of patients with infectious diseases complications.
- There are opportunities to intervene on patients, including those followed by the ID consult service.

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Stewardshipping the ID Consult Service

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Echinocandins or Fluconazole for Candidemia?

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Clinical Professor
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Question:
In the treatment of bacteremia caused by MSSA, my preferred agent is:

A Cefazolin or oxacillin

B Vancomycin

C Something else

Question:
In the treatment of candidemia caused by *Candida albicans*, my preferred agent is:

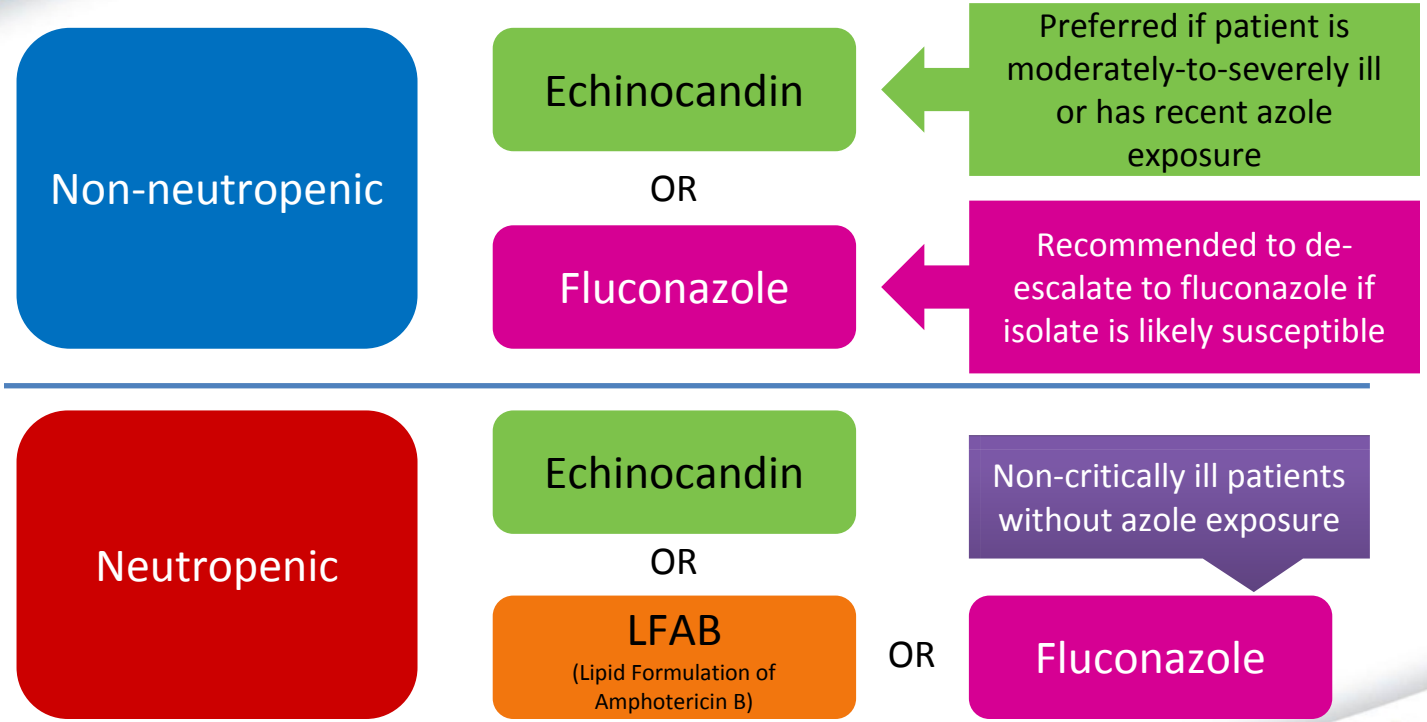
A An echinocandin

B Fluconazole

C An amphotericin B formulation

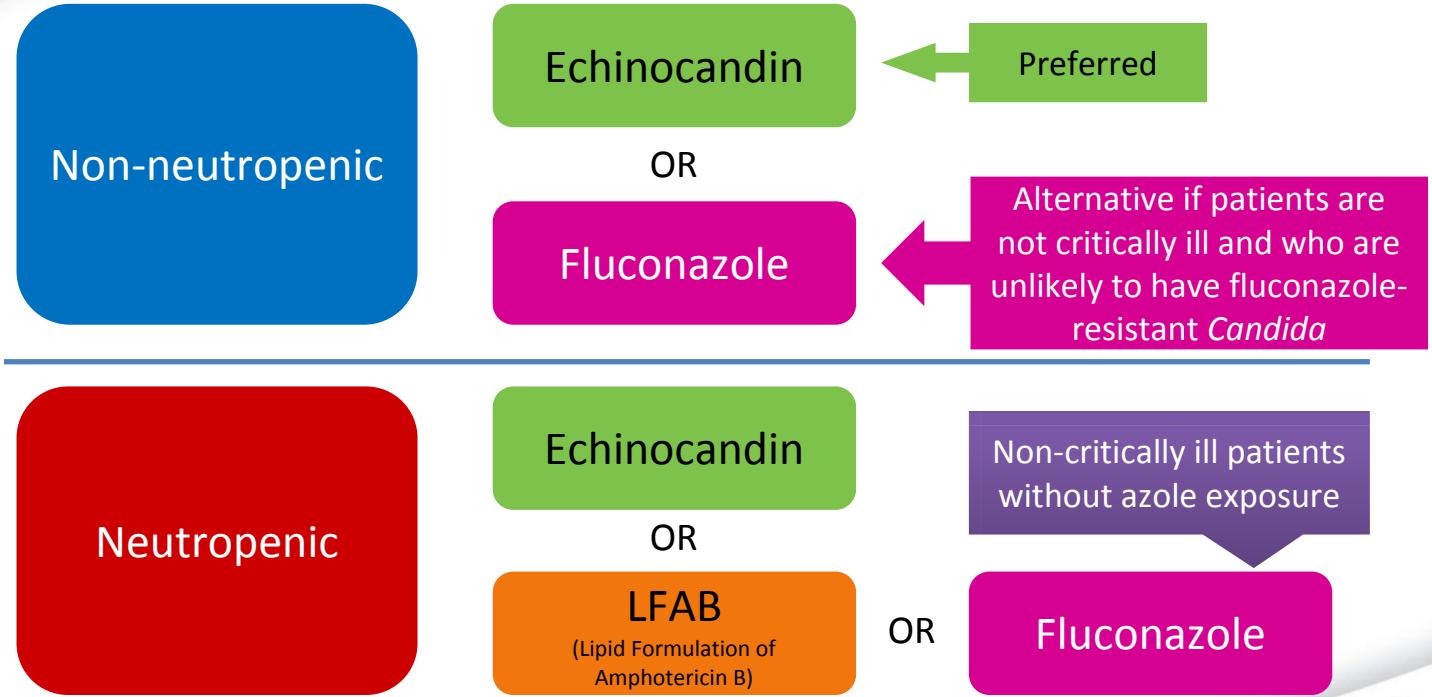
D Voriconazole

Candidemia - 2009 IDSA Guidelines



Pappas PG, Kauffman CA, Andes D, et al. *Clin Infect Dis* 2009;48:503-35.

Candidemia - 2016 IDSA Guidelines



Pappas PG, Kauffman CA, Andes D, et al. *Clin Infect Dis* 2016;62:e1-50.

Candidemia - 2016 IDSA Guidelines

Step-down Therapy

- Transition from echinocandins or AmB to fluconazole in patients who are clinically stable with susceptible isolates and repeat negative blood cultures

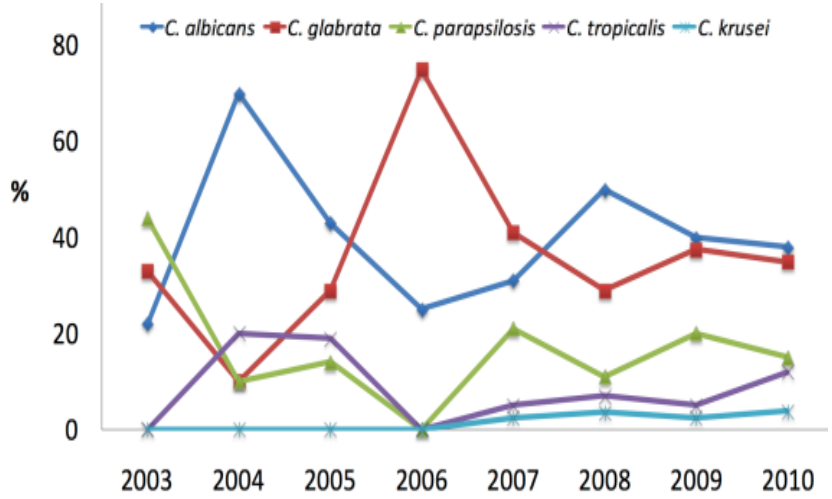
Susceptibility Testing

- Clinically relevant *Candida* isolates should have susceptibility testing for azoles
- Echinocandin testing should be performed if prior exposure and with *C. glabrata or C. parapsilosis* infection

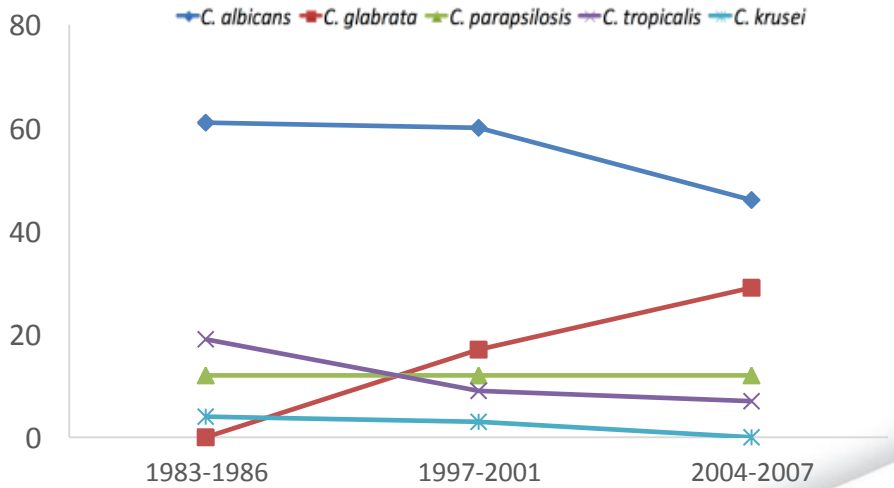
Pappas PG, Kauffman CA, Andes D, et al. *Clin Infect Dis* 2016;62:e1-50.

Shifting Epidemiology

Species causing candidemia,
Temple University Hospital



Species causing candidemia,
University of Iowa Hospitals and Clinics



Le T, Gallagher JC. ACCP 2011. Diekema D, Arbefevile S, Boyken L, et al. *Diag Microbiol Infect Dis* 2012;73:45-8.

The Comparisons

Study	Drug 1	Drug 2	Results
Mora-Duarte 2002	Caspofungin	AmBd	Non-inferiority, less AEs with caspofungin
Kuse 2007	Micafungin	LAmB	Non-inferiority, less AEs with micafungin
Pappas 2007	Caspofungin	Micafungin	Non-inferiority
Reboli 2007	Anidulafungin	Fluconazole	Superiority of anidulafungin

AmBd- amphotericin B deoxycholate LAmB- liposomal amphotericin B

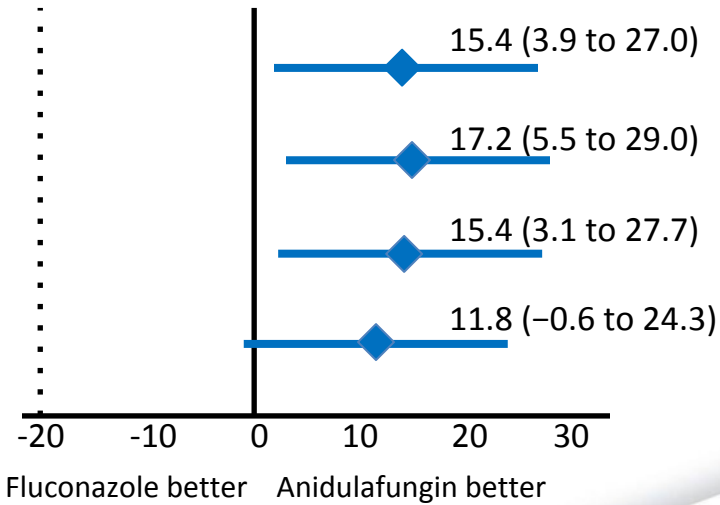
Mora-Duarte J, Betts R, Rotstein C, et al. *N Engl J Med* 2002;347:2020-9. Kuse ER, Chetchotisakd P, da Cunha CA et al. *Lancet* 2007;369:1519-27. Pappas PG, Kauffman CA, Andes D, et al. *Clin Infect Dis* 2009;48:503-35. Reboli AC, Rotstein C, Pappas PG, et al. *N Engl J Med* 2007;356:2472-82.

Anidulafungin vs. Fluconazole

A closer look

Endpoint	Fluconazole (n=118)	Anidulafungin (n=127)
End IV Tx	71 (60.2%)	96 (75.6%)
End Tx	67 (56.8%)	94 (74.0%)
2-week F/U	58 (49.2%)	82 (64.6%)
6-week F/U	52 (44.1%)	71 (55.9%)

Outcome was global response, a composite of microbiological and clinical success



Reboli AC, Rotstein C, Pappas PG, et al. *N Engl J Med* 2007;356:2472-82

Anidulafungin vs. Fluconazole

	Successful Microbiological Response			Successful Global Response		
Pathogen	Anidula	Fluc	P-value	Anidula	Fluc	P-value
Candida albicans	77/81 (95)	57/70 (81)	0.01	60/74 (81)	38/61 (62)	0.02
Candida glabrata	15/20 (75)	18/30 (60)	0.37	9/16 (56)	11/22 (50)	0.75
Candida parapsilosis	9/13 (69)	14/16 (88)	0.36	7/11 (64)	10/12 (83)	0.37
Candida tropicalis	13/15 (87)	7/11 (64)	0.35	13/14 (93)	4/8 (50)	0.04
Other *Candida*	5/6 (83)	3/3 (100)	1.00	3/4 (75)	2/3 (67)	1.00
All *Candida* spp.	119/135 (88)	99/130 (76)	0.02	92/119 (77)	65/106 (61)	0.01

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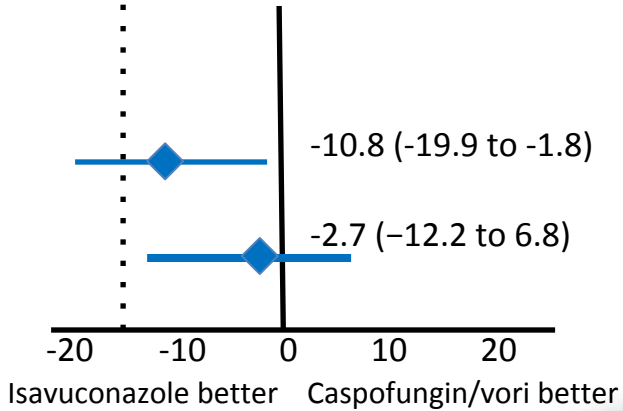
Reboli AC, Rotstein C, Pappas PG, et al. *N Engl J Med* 2007;356:2472-82

Caspofungin vs. Isavuconazole

A Class Effect?

Double-blinded RCT of caspofungin ➔voriconazole vs. isavuconazole (IV➔PO) in 400 patients

Endpoint	Isavuconazole	Caspofungin/ voriconazole
End IV Tx	60.3%	71.1%
2-week F/U	54.8%	57.2%



Basilea Pharmaceutical Ltd. Press Release. July 30, 2015.
http://globenewswire.com/news-release/2015/07/30/756194/10143853/en/Basilea-reports-topline-results-of-isavuconazole-phase-3-study-in-candidemia-and-other-invasive-Candida-infections.html

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Other Studies

Author	Population	Result
Le A, et al.	68 cancer patients with fluconazole S-DD *C. glabrata* candidemia	Echinocandin or LAmB, 30% mortality Azole, 52% mortality (p=0.07) Adjusted HR for mortality= 3.8 (1.6-8.9)
Eschenauer GA, et al.	224 adults with *C. glabrata* candidemia	Echinocandin therapy had OR 2.305 (CI 1.1 -4.7) for 14 day clinical response, no mortality difference
Puig-Asensio M, et al	94 adults with *C. glabrata* candidemia	No difference between echinocandin and fluconazole therapies
Bassetti M, et al.	216 adults with septic shock due to candidemia	No difference between echinocandin and fluconazole therapies

Le A, Farmakiotis D, Tarrand JJ, et al. *Antimicrob Agents Chemother* 2017;61 (early access). Eschenauer GA, Carver PL, Lin S-W, et al. *J Antimicrob Chemother* 2013;68:922-6. Puig-Asensio M, Fernandez-Ruiz M, Aguado JM, et al. *Antimicrob Agents Chemother* 2016;60:3291-3300. Bassetti M, Righi E, Ansaldi F, et al. *Intensive Care Med* 2014;40:839-45.

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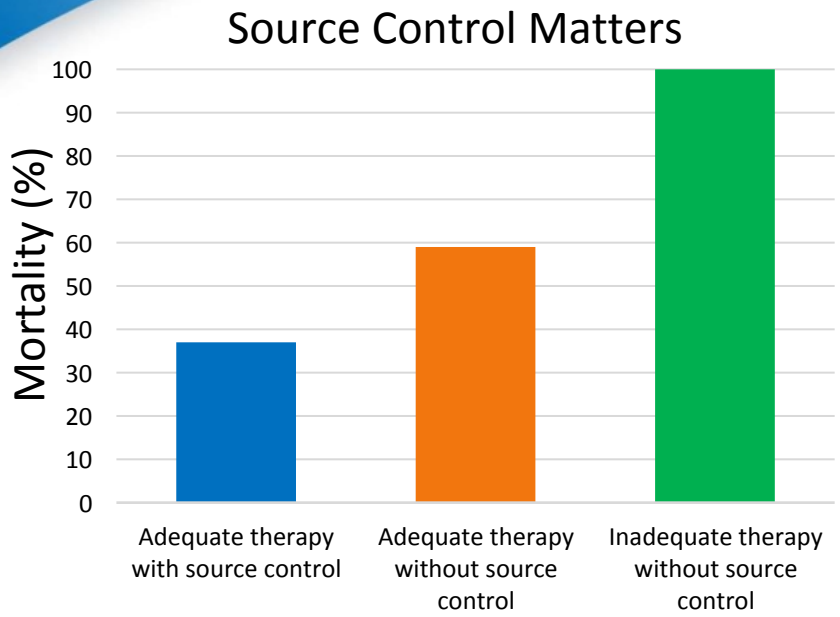
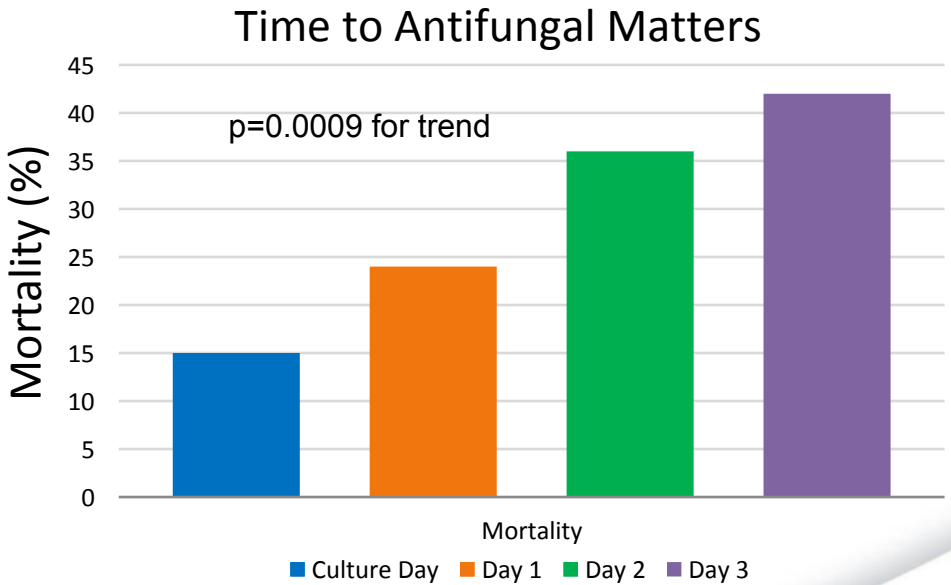
Why Didn't We Know This Already?





Bassetti M, Righi E, Ansaldi F, et al. *Intensive Care Med* 2014;40:839-45.

Garey K, Rege M, Pai MP, et al. *Clin Infect Dis* 2006;43:25-31.

Key Takeaways

- Key Takeaway #1
  - It looks like echinocandins are just better for candidemia
- Key Takeaway #2
  - Fluconazole is likely best used as a stepdown therapy in improving patients
- Key Takeaway #3
  - Susceptibility testing of yeasts is recommended but shouldn't always immediately dictate therapy

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Echinocandins or Fluconazole for Candidemia?

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Clinical Professor
Clinical Specialist, Infectious Diseases
Temple University
Philadelphia, PA

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A Strawberry-Flavored Pearl for *Clostridium difficile* Infection

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Dept of Pharmacy Practice and Translational Research
UNIVERSITY of HOUSTON | COLLEGE OF PHARMACY

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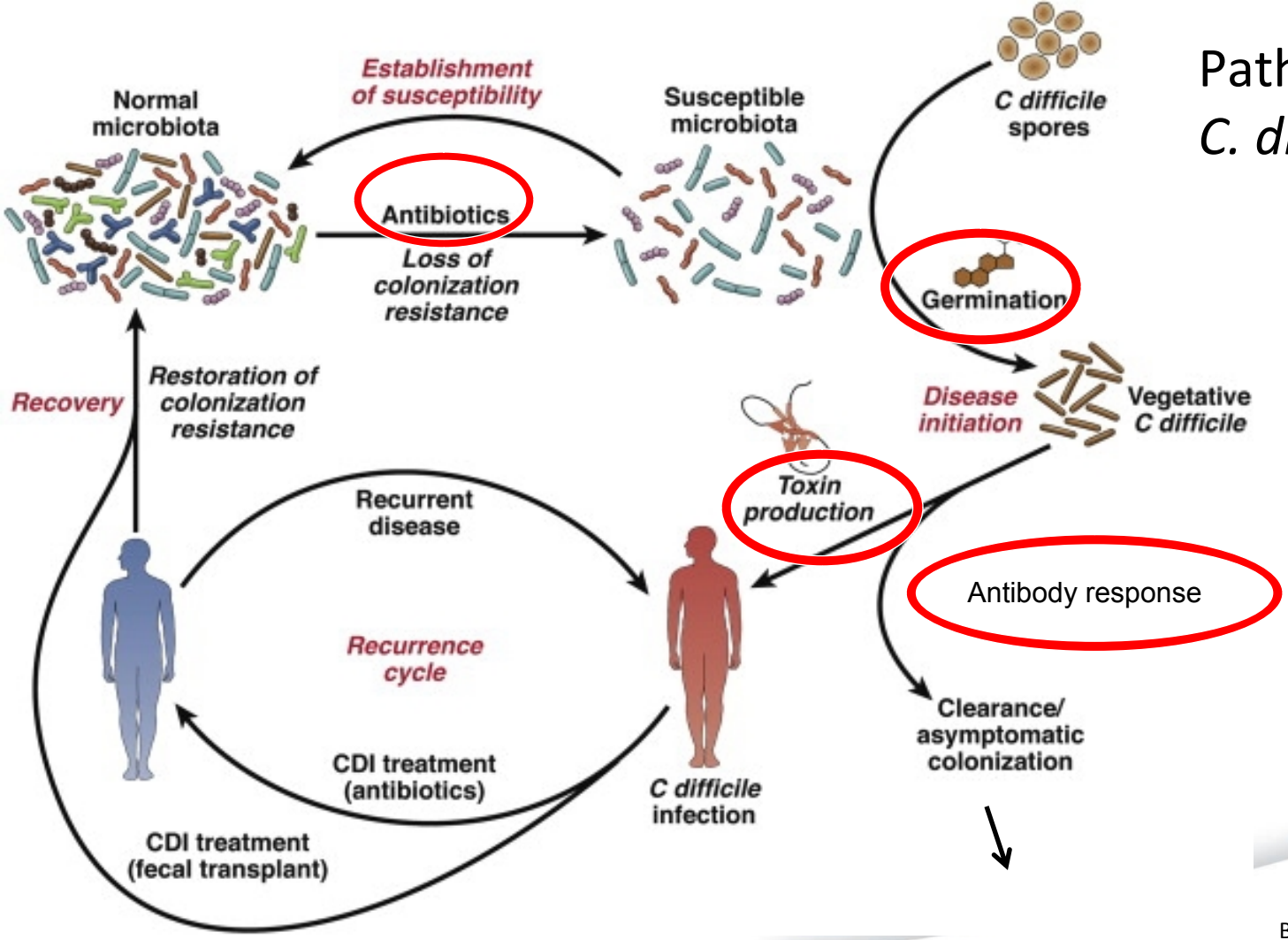
Pathogenesis of *C. difficile* infection

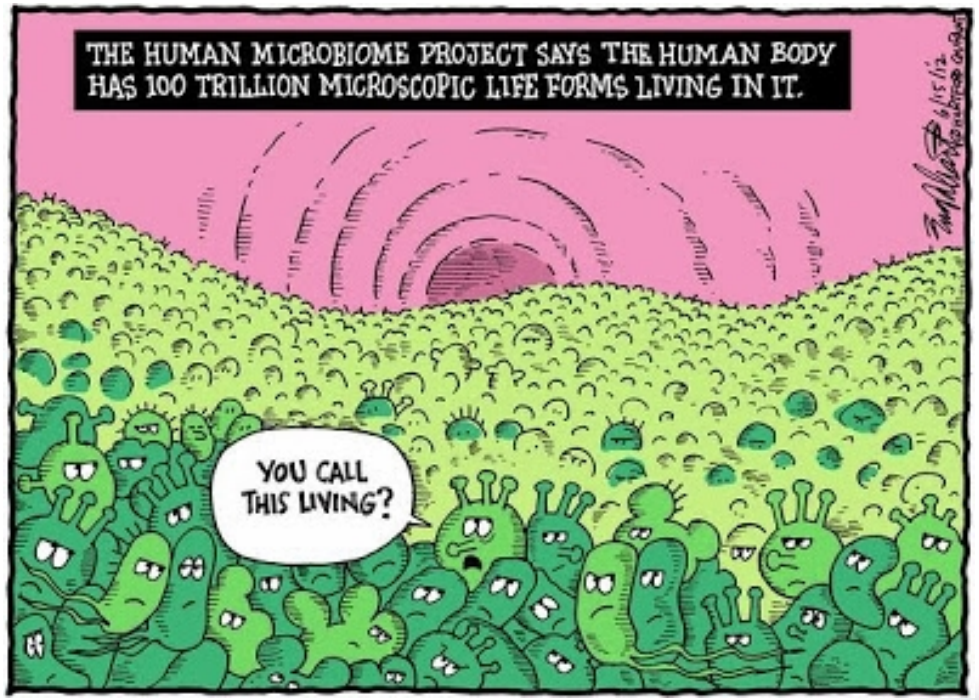


Britton *et al.* 2014

C diff Stewardship Pearl

- Ok, so a damaged microbiome (dysbiosis) starts the whole cascade leading to C. diff infection (CDI).
- Piece of cake, we will stop using antibiotics!! (NOT!!)
- ……..or, is there a way to restore the microbiome after we have damaged it (this will be my pearl)

Welcome to the Wonderful World of the Microbiome!



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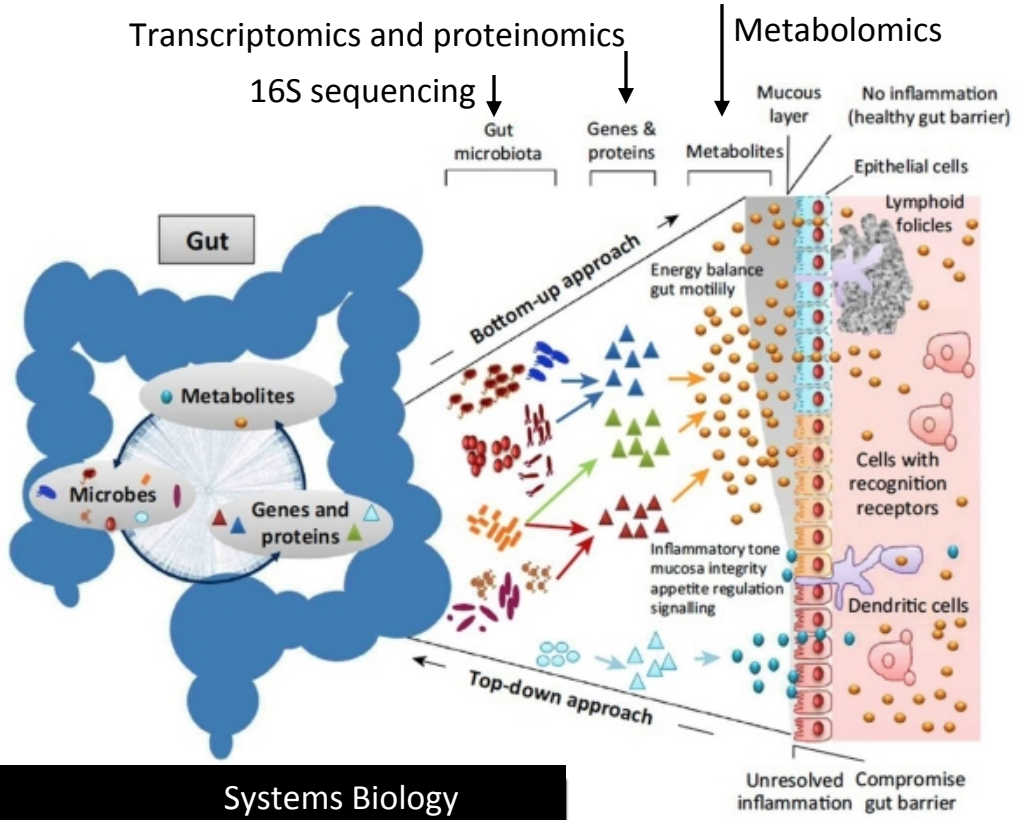
The Microbiome has Opened up a Whole New Area of Science!

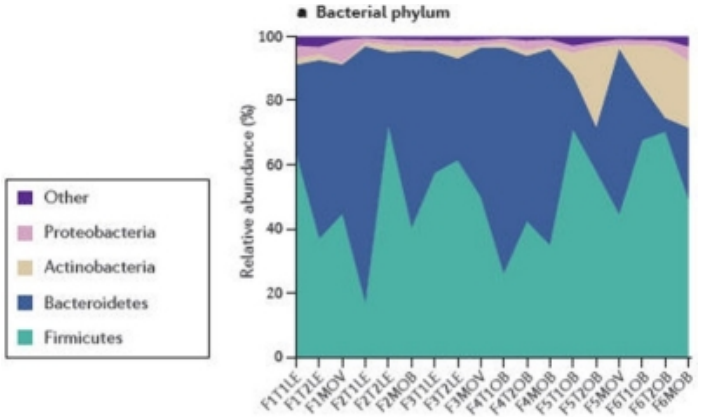


Systems Biology

Gut Microbiota: 16S RNA Sequencing

Firmicutes:
Mostly good (C diff is a firmicute)
Mostly spore formers (think: probiotic)
Usually largest component of microbiota
Bacteroidetes
Mostly good (Bacteroides predominates)
Non-spore forming
Usually tied for largest component
Actinobacteria
Mostly good
Not very common, sort of the ugly stepsister of the healthy microbiota
Proteobacteria
Good in small quantities (this is E. coli, Klebsiella, etc
This is where the 'overgrowth' occurs after antibiotic therapy

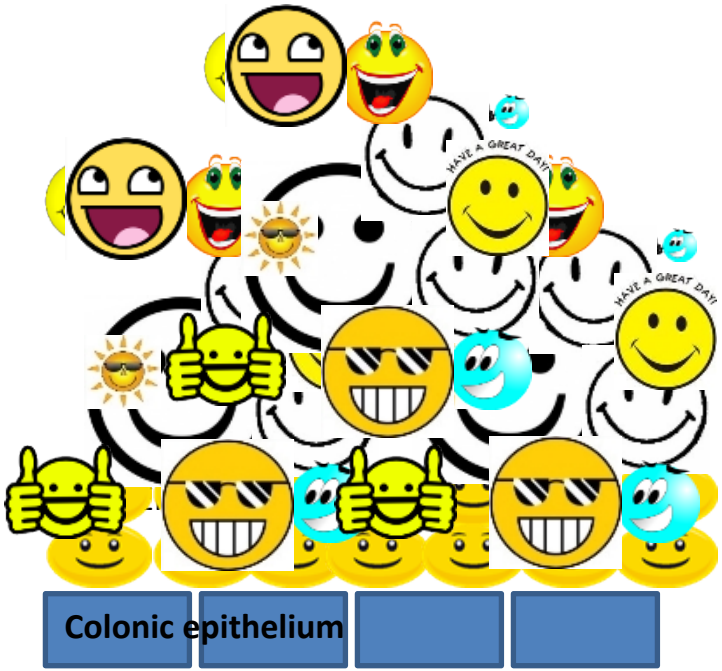
16S sequencing



Cho et al. Nat Rev Genet 2012;13:260-70

Microbiome Analysis is All About Abundance, Diversity, and Types of Organisms Present

Microbiome of non-CDI patients vs. CDI patients

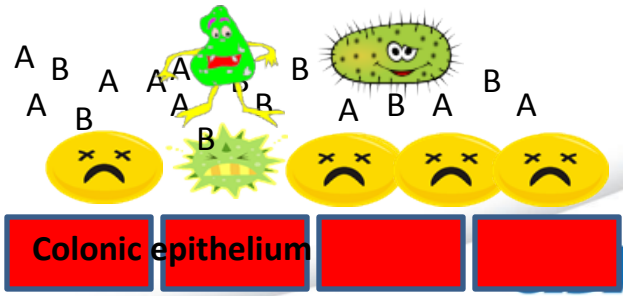


Healthy Microbiome

Total CFU abundance

Diversity of microbiologic species

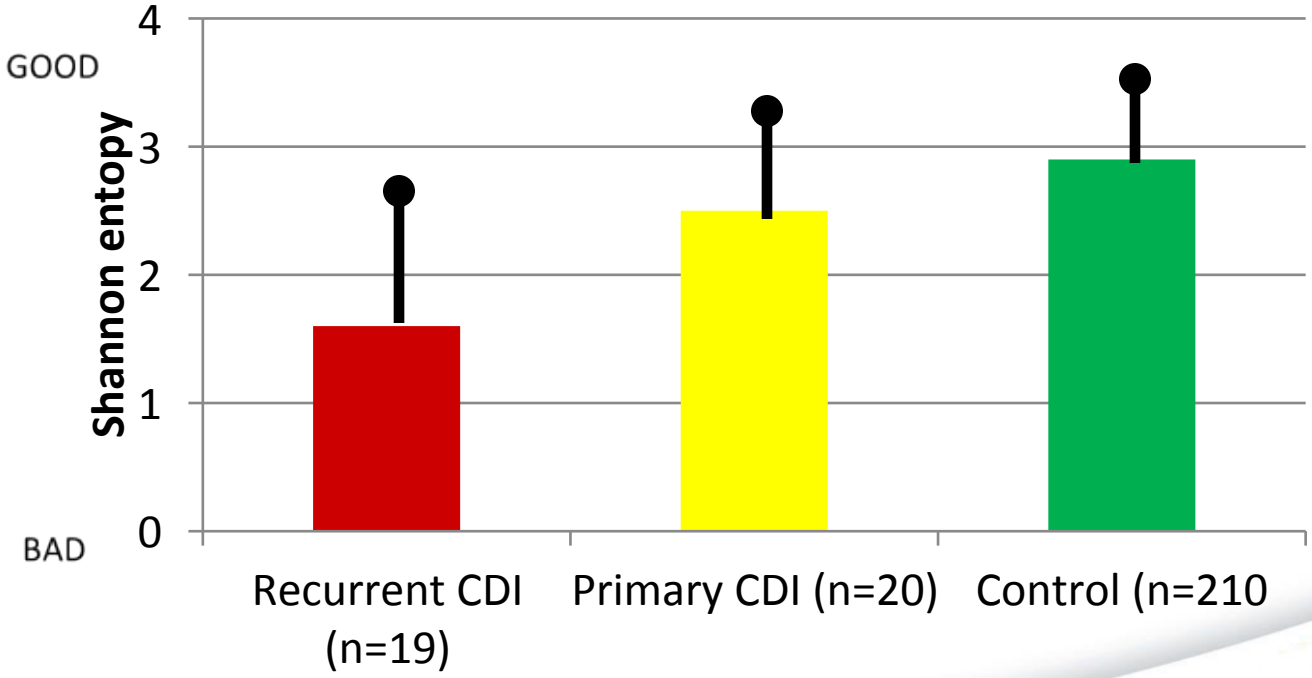
Other pathogenic organisms



Recurrent CDI Microbiome

The Microbiome of Recurrent CDI Patients is Much Less Diverse

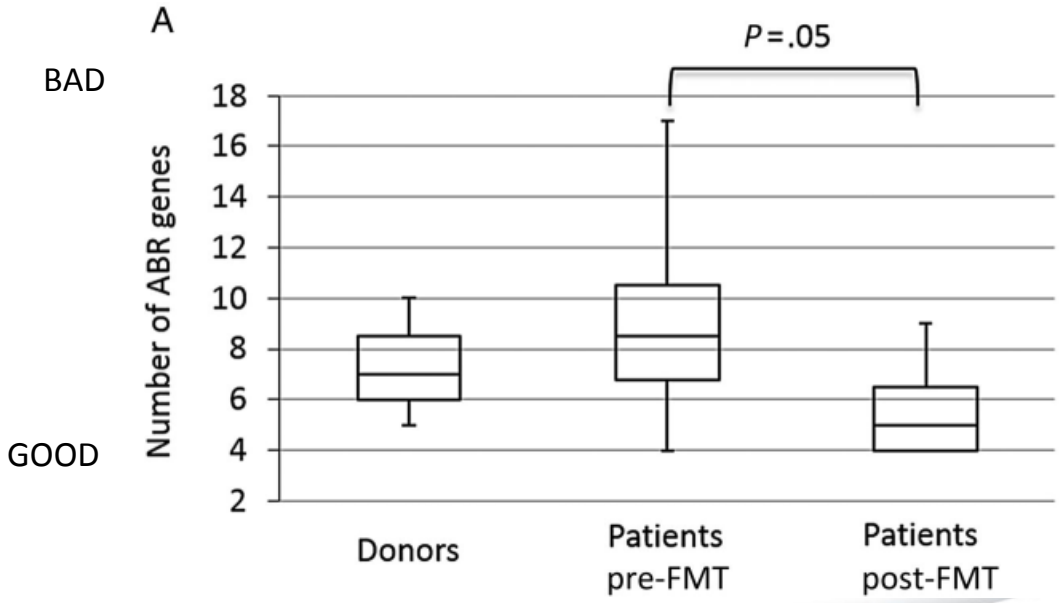
Boston, USA: Decreased microbiome diversity observed in patients with recurrent CDI



Allegretti et al. Aliment Pharmacol Ther 2016;43(11):1142-53

What Else Do We Have in Our Damaged Microbiome?

Canada: Number of antibiotic resistant genes (ABR) present in stool samples from patients with recurrent CDI before and after FMT (n=8)

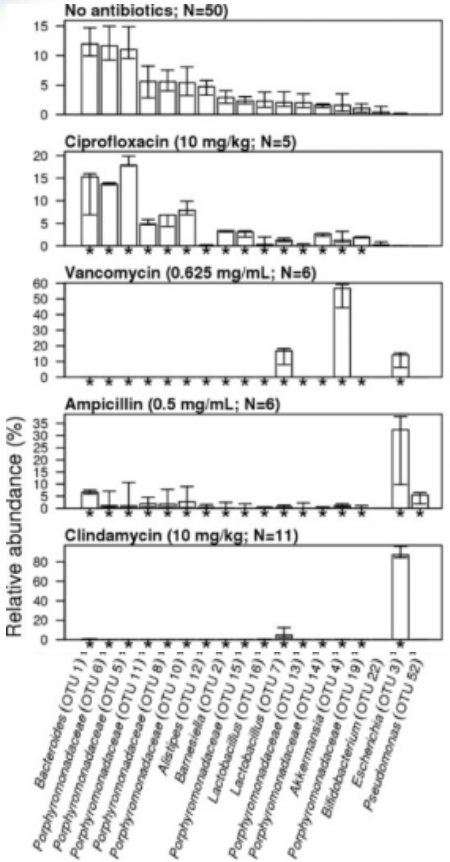


Jouhten et al. CID 2016;63(5):710-11

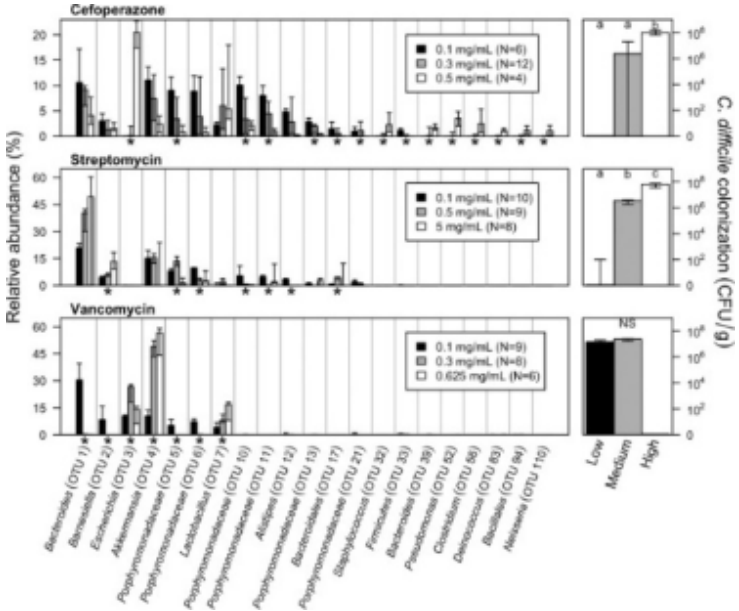
Now that we have an understanding how microbiome studies work, we can apply this technology to better understand how antibiotics kill our microbiota and what we can do about it!

Mice Exposed to a Variety of Antibiotics for 5 Days

5 days of antibiotics are more than enough to completely change the microbiota



….and this disruption is more than enough to support C diff colonization



Schubert et al. mBIO 2015;6:e00974

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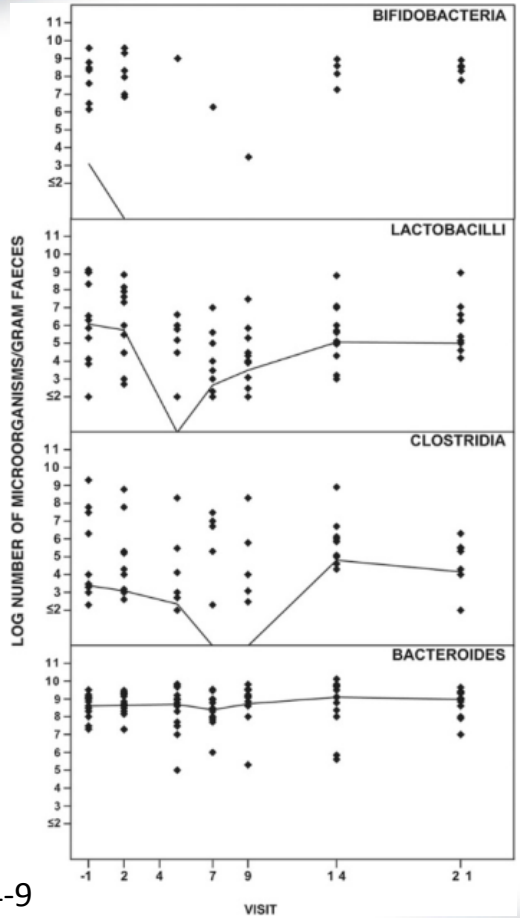
The Effect on the Microbiome Starts Almost Immediately



- 14 healthy volunteers given ceftaroline-avibactam X 7 days
- Changes in microbiota assessed over 21 days

Rashid et al. AAC 2015;59:4504-9

We Are Now Able to Predict What Microbiota is Needed to Protect Against CDI!!

- After seeing this, you can start to understand that fecal microbiota transplantation (FMT) for all may not be a bad idea
  - But this would be totally gross!
- Any antibiotic that kills firmicutes and/or bacteroides will almost immediately increase CDI risk
- Thus: replenishment of this microbiota should protect against CDI

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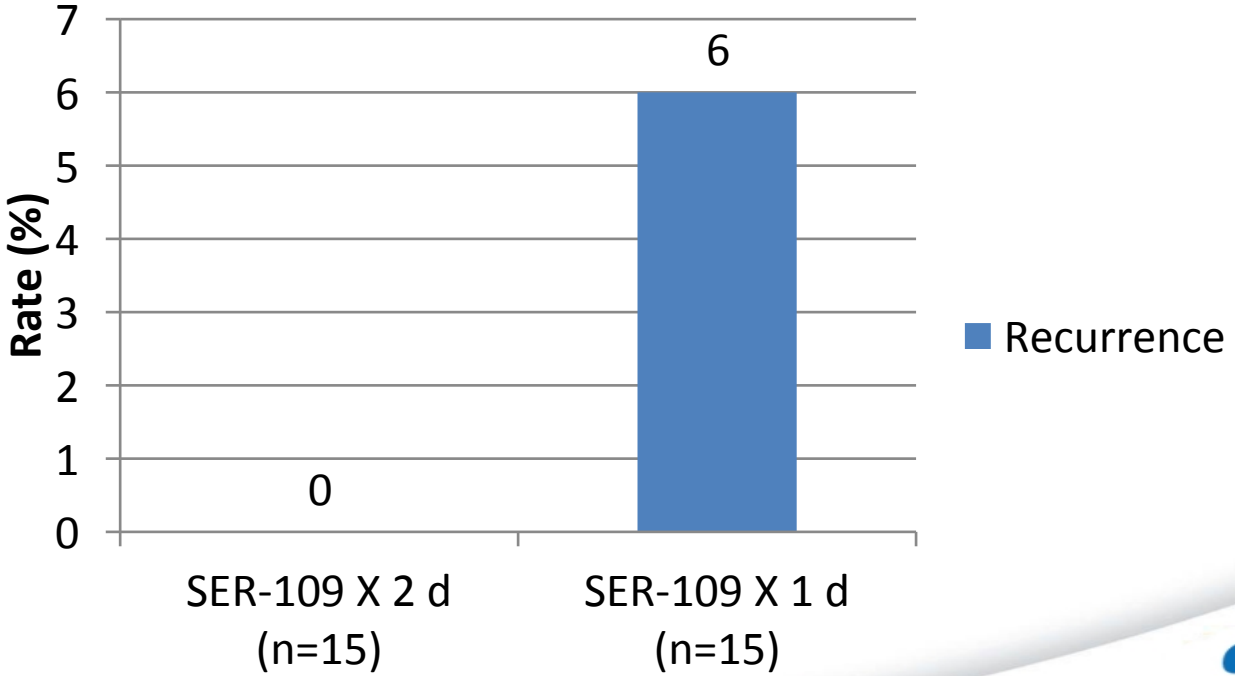
Next Generation FMT

- Designer biotherapeutics
  - Non-toxigenic *C. difficile, SER-109*
- Oral, non-absorbable beta-lactamases to protect gut microbiome from beta-lactam antibiotics
  - Won't present this data, Kaleko et al. Anaerobe 2016 for more info (SYN-004)
- Probiotic cocktails (Kefir)

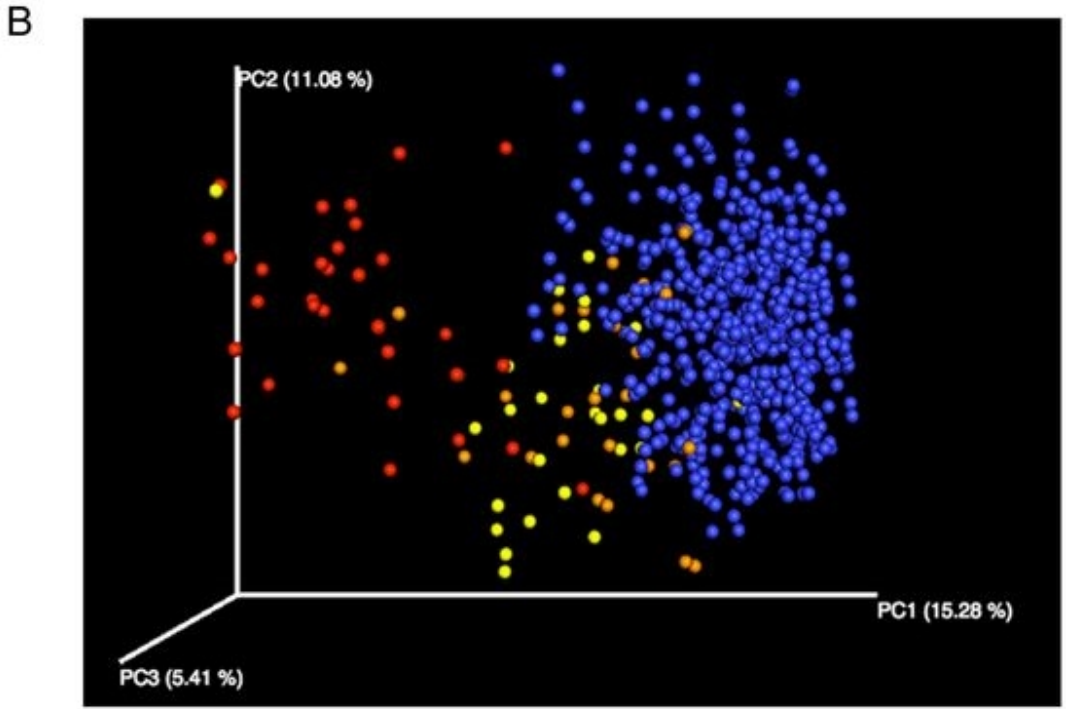
SER-109 (FMT pill). Spores (mainly firmicutes) from Healthy Donor Stools

CDI patients given SER-109 immediately after finishing antibiotic therapy



Khanna et al. JID 2016

Patients Given SER-109 had a Microbiome that Looked like the Average Population



- Microbiome prior to SER-109
- Microbiome after SER-109
- Samples from the human microbiome project

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This is all really sweet science, but……

Where’s my Pearl?

Staggered and Tapered Antibiotics PLUS KEFIR for the Treatment of Recurrent CDI that has Failed to Respond to Standard Antibiotic Therapy

Antibiotic Time Course	Metronidazole Dose/Frequency		Vancomycin Dose/Frequency		Kefir
Weeks 1-2	250 mg Q 6h		125 mg Q 6h		150 mL TID
Weeks 3-4	750 mg Q 72h		375 mg Q 72h		150 mL TID
Weeks 5-6	500 mg Q 72h	OR	250 mg Q 72h	PLUS	150 mL TID
Weeks 7-8	250 mg Q 72h		125 mg Q 72h		150 mL TID
Weeks 9-15					150 mL TID

- 25 patients with recurrent CDI that were not able to perform FMT.
- 21/25 patients (84%) remained free of diarrhea during the following 9 months.
- The 4 patients who relapsed permanently resolved their diarrhea after a conventional 2-week course of PO vancomycin 125 mg 4 times daily followed by a 2-week course of rifaximin 200 mg twice daily.
- All 4 patients remained symptom-free at 12 months of follow-up.

Kefir contains primarily firmicutes!!!!!

Bakken JS Clin Infect Dis. 2014;cid.ciu429

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MY

- For your patients with CDI (or at risk for CDI), counsel these patients to stop at their favorite supermarket on their way home.
- Buy Kefir (flavor with honey if tart) and take 2-3 times per day as directed for at least 30-days. Take up to 3-months if you are enjoying it
- By doing this simple task, you may 1) prevent C diff (recurrence) 2) prevent re-hospitalization, and 3) save a life

Bourrie et al. **The Microbiota and Health Promoting Characteristics of the Fermented Beverage Kefir.** Front Microbiol. 2016; 7: 647.

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A Strawberry-Flavored Pearl for *Clostridium difficile* Infection

Kevin W. Garey, Pharm.D., M.S., FASHP
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Implementation of a Pharmacist-Managed Culture Review Service in the Emergency Department

Jamie Kisgen, Pharm.D., BCPS-AQ ID
Pharmacotherapy Specialist - Infectious Diseases
Sarasota Memorial Health Care System
Sarasota, Florida

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Antimicrobial Stewardship in the Outpatient Setting

- In 2013, approximately 269 million antibiotic prescriptions were dispensed from outpatient pharmacies
- At least 30% of all antibiotic courses prescribed in the outpatient setting are inappropriate
- Patients discharged from the emergency department (ED) on antibiotics, who subsequently have a positive culture, require an intervention up to 25 to 50% of the time

CDC. Outpatient antibiotic prescriptions-US, 2013
Fleming-Dutra, K., et al. *JAMA* 2016;315(17): 1864-1873
Dumkow LE, *Infect Dis Ther.* 2014;3:45-53
Davis LC, *AJHP*. 2016;73: S49-S56

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Impact of a Pharmacist Managed Culture Review Service (CRS)

- Shorter time to culture review and notification of the primary care physician (3 days vs 2 days in each group)
- Decrease in unplanned readmission to the emergency department from 19% to 7%
  - Mostly driven by lower rates of readmission for treatment failure, noncompliance, and drug allergy
- Decrease in ED physician interruptions

Baker SN, et al. *J Pharm Pract* 2012;25(2):190-194
Randolph TC, et al. *Am J Health-Syst Pharm*. 2011; 68:916-9

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Sarasota Memorial Hospital

- 829 bed, community hospital and level II trauma center
- 71-bed ED at main campus, 21-bed free-standing ED, and 6 urgent care centers
- 6.5 FTE Pharmacists provide 24/7/365 pharmacy services
- Pharmacist-managed CRS was implemented in the Fall 2012
- Collaborative practice agreements (CPA) were developed to allow pharmacists to make alterations to empiric antimicrobial therapy as needed for discharged patients

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Collaborative Practice Agreements

- A formal practice relationship between a pharmacist and another health care provider
- Specifies the patient care services provided by the pharmacist beyond the typical scope of practice
- 48 states and D.C. currently allow some degree of CPA between pharmacists and other providers
- Each state may have different requirements/limitations

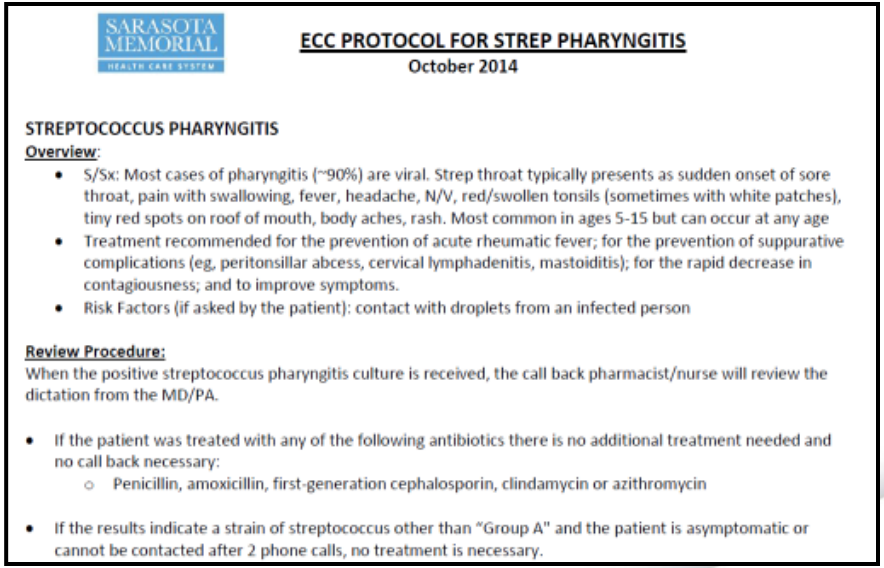
Weaver KK. Policy 101: Collaborative practice empowers pharmacists to practice as providers: https://www.pharmacist.com/policy-101-collaborative-practice-empowers-pharmacists-practice-providers

CPA Development

- A multi-disciplinary group developed the hospital policy and CPA therapeutic protocols
- Key members: ED pharmacy specialist, ED medical director, ED nursing director, ID pharmacy specialist, and ID physician
- Each protocol outlines the procedure for reviewing results, recommended treatment strategies based on culture results, and lists specific criteria for consulting an ED physician

Treatment Protocols

- Pharmacist-Managed CPA:
  - Bacterial vaginosis
  - *Clostridium difficile*
  - Gonorrhea/Chlamydia
  - Streptococcal pharyngitis
  - Urinary tract infections
  - Vaginal candidiasis
  - Wound infections



SARASOTA MEMORIAL HEALTH CARE SYSTEM

ECC PROTOCOL FOR STREP PHARYNGITIS
October 2014

STREPTOCOCCUS PHARYNGITIS

Overview:

- S/Sx: Most cases of pharyngitis (~90%) are viral. Strep throat typically presents as sudden onset of sore throat, pain with swallowing, fever, headache, N/V, red/swollen tonsils (sometimes with white patches), tiny red spots on roof of mouth, body aches, rash. Most common in ages 5-15 but can occur at any age
- Treatment recommended for the prevention of acute rheumatic fever; for the prevention of suppurative complications (eg, peritonsillar abcess, cervical lymphadenitis, mastoiditis); for the rapid decrease in contagiousness; and to improve symptoms.
- Risk Factors (if asked by the patient): contact with droplets from an infected person

Review Procedure:

When the positive streptococcus pharyngitis culture is received, the call back pharmacist/nurse will review the dictation from the MD/PA.

- If the patient was treated with any of the following antibiotics there is no additional treatment needed and no call back necessary:
  - Penicillin, amoxicillin, first-generation cephalosporin, clindamycin or azithromycin
- If the results indicate a strain of streptococcus other than "Group A" and the patient is asymptomatic or cannot be contacted after 2 phone calls, no treatment is necessary.

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Electronic Culture Report

Current List: List - ER Culture Report | Select All Patients | 556 Visit(s) | Save Selected Patients...

ECC Culture Review	Order Name	Organism	Visit Reason	Performed Date/Time	Result Date/Time
*9/15 LVM x 1, strep no abx	Strep Throat Screen and Cult	Streptococcus pyogenes grp A Maj...	SORE THROAT	09/14/2017 04:35	09/15/2017 09:07
*9/15 NoAns UC resis	Culture Urine	Escherichia coli > 100,000 CFU/ml	ABD PAIN/ BLACK STOOL	09/13/2017 20:59	09/15/2017 08:22
*9/15 UC pend	Culture Urine	Gram Negative Bacilli 10,000-50,00...	UTI SX	09/13/2017 19:42	09/15/2017 12:43
*9/15 UC pend	Culture Urine	Gram Negative Bacilli > 100,000 CF...	ABD PAIN	09/14/2017 01:41	09/15/2017 11:33
*9/15 UC pend	Culture Urine	Escherichia coli > 100,000 CFU/ml S...	CATHETER PROBLEMS	09/14/2017 04:29	09/15/2017 11:21
*9/15 UC pend	Culture Urine	Escherichia coli > 100,000 CFU/ml S...	UTI SX	09/14/2017 11:51	09/15/2017 11:50
*9/15 UC pend	Culture Urine	Escherichia coli 10,000-50,000 CFU/...	UTI SX	09/13/2017 11:38	09/15/2017 12:25
*9/15 UC pend	Culture Urine	Escherichia coli > 100,000 CFU/ml S...	UTI SX	09/14/2017 17:18	09/15/2017 12:05
*9/15 UC pend	Culture Urine	Escherichia coli > 100,000 CFU/ml S...	LAB DROP OFF	09/14/2017 15:01	09/15/2017 11:52
*9/15 UC pend	Culture Urine	Escherichia coli 50,000-100,000CFU...	ABDOMINAL PAIN AND...	09/13/2017 18:59	09/15/2017 11:26
*9/15 UC pend	Culture Urine	Escherichia coli 50,000-100,000CFU...	UTI SX	09/14/2017 08:32	09/15/2017 11:15

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CRS Process

Culture Assessment

- Review results of each positive culture
- Assess appropriateness of empiric therapy
- Make alterations as appropriate per CPA
- Discuss with provider if excluded from protocol

Patient Counseling

- Potential side effects of new medication(s)
- MRSA education
- STD counseling
- *C. difficile* counseling

EMR Documentation

- Assessment of finalized cultures
- Patient contact/ counseling
- Antibiotic therapy alterations
- Discussion with ED provider (if applicable)

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Documentation

- Developed standardized documentation for the most common culture types and results
- Utilized an acronym expansion feature in Allscripts® EMR to make documentation more efficient
  - Example: “Gon”

> Patient with a positive Gonorrhea PCR result from lab. Per provider dictation patient was treated with azithromycin 1gm PO and ceftriaxone 250mg IM as single doses. Per CDC guidelines no changes necessary. The patient was called to inform them of positive results, and for standard STD precaution counseling. The patient expressed understanding.

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Barriers to Success

- **Time Concerns**
  - Adequate number of FTEs
  - Constant interruptions
- **Technology**
  - Paper vs electronic reports
  - Missing data, downtime procedures
- **Provider Documentation**
  - Adequate documentation of diagnosis and antibiotics
- **Patient**
  - Incorrect contact info
  - HIPAA concerns

Best Practice Recommendations

- When developing CPS protocols, start with the most common cultures collected in your ED and urgent care centers
- Engage with IT and microbiology early on in the process
- Provide allotted time for ED pharmacist to review cultures
- Make sure that providers are clearly documenting the diagnosis and treatment provided during the ED visit
- Consider incorporating PGY1/PGY2 residents into the CRS as part of their longitudinal service/staffing experience

Key Takeaways

- Key Takeaway
  - Successful implementation of a CRS depends on having dedicated time for ED pharmacists and support from multiple disciplines, including ED clinicians, microbiology, and IT

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Implementation of a Pharmacist-Managed Culture Review Service in the Emergency Department

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Modeling Antimicrobial Consumption

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Midwestern University, Chicago College of Pharmacy
Infectious Diseases Pharmacist
Northwestern Memorial Hospital

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Many good reasons, not the least of which is…

WHY MEASURE ANTIMICROBIAL CONSUMPTION?

…the Joint Commission Says We Should

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

- Antimicrobial stewardship programs:
  - EP 5 Include core elements
    - **Tracking and reporting utilization**
  - EP 7 Collect / analyze data
    - **Use and resistance**
  - EP 8 Act on improvement opportunities
    - **Analyses can identify new opportunities**

https://www.jointcommission.org/assets/1/6/New_Antimicrobial_Stewardship_Standard.pdf

Measuring Consumption

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

$$\text{Metric} = \frac{\text{Days of therapy}}{\text{At-risk bed days}} \times 1000$$

World Health Organization Collaborating Center for Drug Statistics Methodology. http://www.whocc.no/atc_ddd_index
Polk RE, Fox C, Mahoney A, et al. Clin Infect Dis. 2007; 44:664–670.

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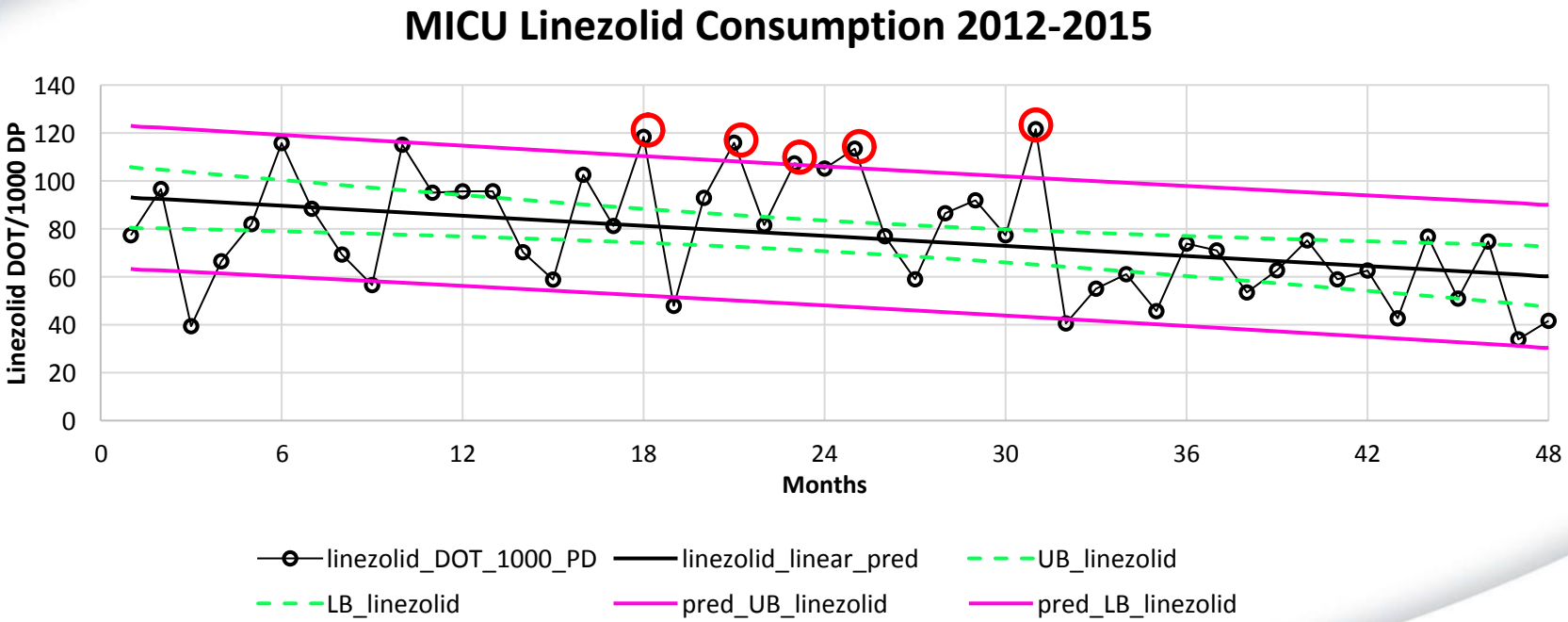
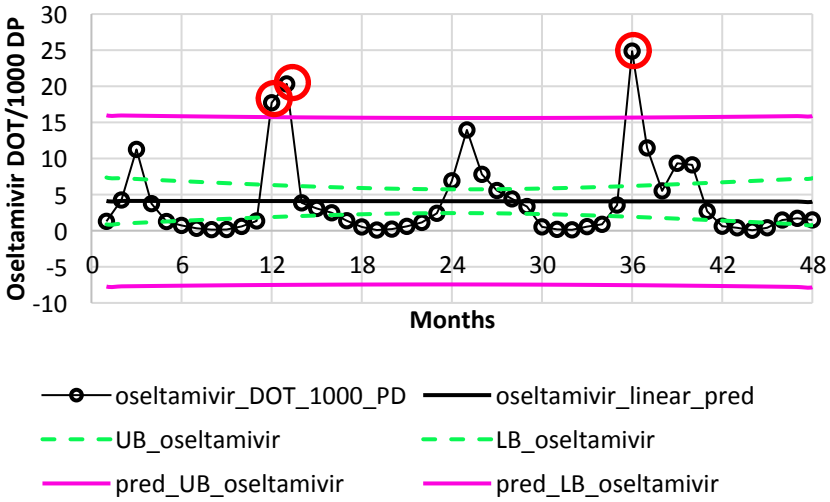
Identifying the "Outliers"



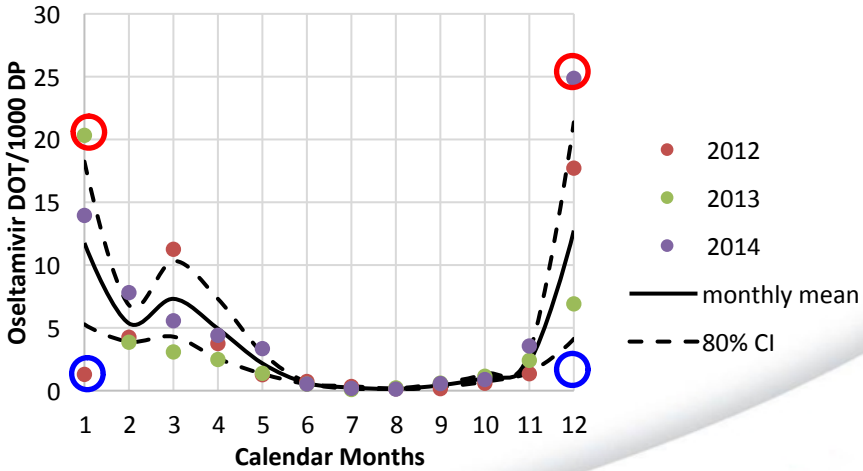
Rhodes NJ. NMH consumption and benchmark data on file. 2017.
Miglis C, Rhodes NJ, Avedissian SN, et al. Infect Control Hosp Epidemiol. 2017;38:860-862

Linear Models Don't Always Work

Facility-wide Oseltamivir Longitudinal Consumption 2012-2015



Facility-wide Oseltamivir Monthly Consumption 2012-2015



Rhodes NJ. NMH consumption and benchmark data on file. 2017.

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

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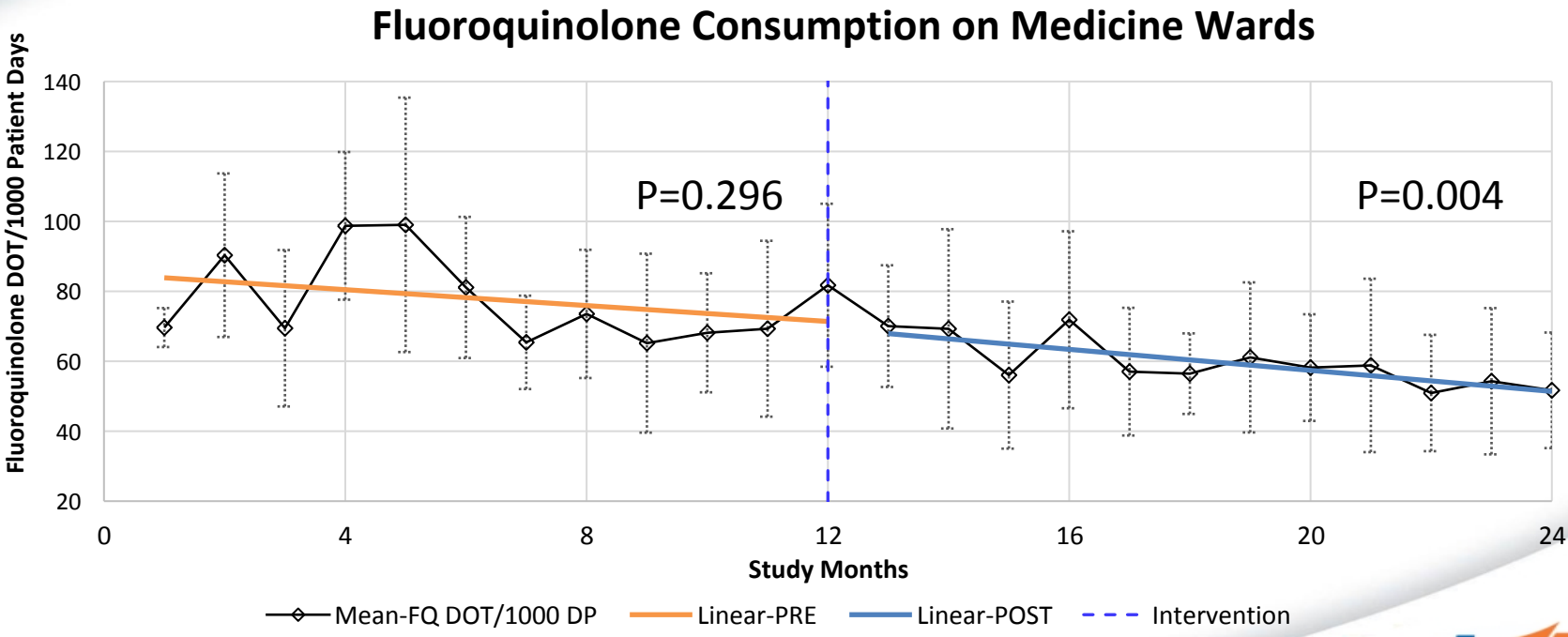
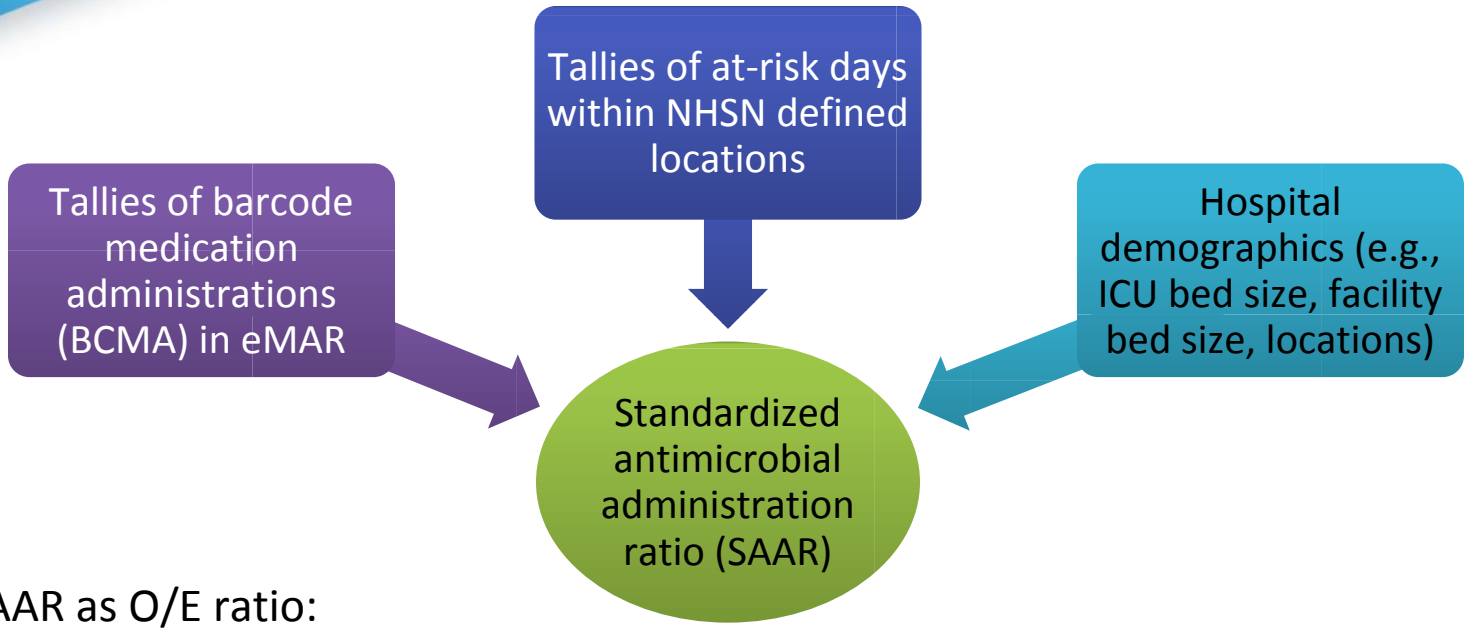
Measuring Process Improvement



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

In Search of a Consistent Measure



Think of SAAR as O/E ratio:

Is observed use > expected use?

Centers for Disease Control and Prevention. National Healthcare Safety Network. Antimicrobial Use and Resistance (AUR) Module. https://www.cdc.gov/nhsn/pdfs/pscmanual/11pscaurcurrent.pdf

van Santen K. National Center for Emerging and Zoonotic Infectious Diseases. Standardized Antimicrobial Administration Ratio (SAAR). March 2017. https://www.cdc.gov/nhsn/pdfs/training/2017/vanSanten_March24.pdf

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The Fault in Our SAARs

- What SAAR **can do**:
  - Tell you if consumption is statistically elevated
  - Whether O/E ratio different from referent population
    - SAAR sig. > 1 may indicate excessive over-utilization
    - SAAR sig. < 1 may indicate under-utilization
- What SAAR **can't** do:
  - Tell you if consumption is clinically meaningfully elevated for your facility
  - Whether antimicrobial use is appropriate or not
    - High SAAR: trigger to look at a specific agent's use?
    - Low SAAR: trigger to look at other agents' use?

Centers for Disease Control and Prevention. National Healthcare Safety Network. Antimicrobial Use and Resistance (AUR) Module. https://www.cdc.gov/nhsn/pdfs/pscmanual/11pscaurcurrent.pdf
van Santen K. National Center for Emerging and Zoonotic Infectious Diseases. Standardized Antimicrobial Administration Ratio (SAAR). March 2017. https://www.cdc.gov/nhsn/pdfs/training/2017/vanSanten_March24.pdf

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Measuring a Moving Target

- General agreement that benchmarks for should consider:
  - Seasonality and trends
    - Intentionally incorporated or
    - Stratified by periods of interest
  - Facility demographics
    - Case-mix / population
    - ICU and ward bed size

Aldeyab MA, McElnay JC, Scott MG, et al. J Antimicrob Chemother. 2014;69:1132-41
Palmay L, Elligsen M, Walker SA, et al. Clin Infect Dis. 2014;59:867-74
Stenehjem E, Hersh AL, Sheng X, et al. Clin Infect Dis. 2016;63:1273-1280
Scheetz MH, Crew PE, Miglis C, et al. Antimicrob Agents Chemother. 2016;60:3265-9

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Key Takeaways

- Key Takeaway #1
  - Antimicrobial consumption measurement is a key element of antimicrobial stewardship and essential for meeting Joint Commission Standard
- Key Takeaway #2
  - Multiple consumption metrics available, but consistency will be key to establishing meaningful benchmarks within centers
- Key Takeaway #3
  - Benchmarks for consumption should account for facility demographics, patient, population, and be robust to seasonal variation

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Modeling Antimicrobial Consumption

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SELF-ASSESSMENT QUESTIONS

Self-Assessment Question 6

There is no additional room for Antimicrobial Stewardship improvement for patients followed by the Infectious Diseases consult service(s)

A. True

B. False

Self-Assessment Question 7

According to the 2016 IDSA guideline, which of the following is preferred (1st line) for empiric treatment of candidemia?

A. Echinocandin – only if neutropenic
B. Echinocandin – regardless of neutropenic status
C. Fluconazole – only if non-neutropenic
D. Fluconazole – regardless of neutropenic status

Self-Assessment Question 8

The probiotic Kefir primarily contains what type of bacterial organisms?

A. Firmicutes
B. Bacteroidetes
C. Proteobacteria
D. Actinobacteria

Self-Assessment Question 9

Which of the following statements is TRUE about implementing a pharmacist-managed culture review service in the ED?

A. Physician workload increases
B. Pharmacist workload decreases
C. Readmission rates will be unchanged
D. Readmission rates may decrease

Self-Assessment Question 10

Which of the following is an emerging nationwide metric for antibiotic consumption?

A. DDD/1000 patient days
B. DOT/1000 patient days
C. The predictive interval of the mean antimicrobial consumption
D. The standardized antimicrobial administration ration

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Hot Topics in Antimicrobial Stewardship

Kristi Kuper

Melinda Neuhauser

P. Brandon Bookstaver

Monica Mahoney

Susan Davis

Lucas Schulz

Jason Gallagher

Kevin Garey

Jamie Kisgen

N. Jim Rhodes

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