

Advancing Metrics for Benchmarking in Stewardship Research: is perfection our enemy?

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The authors report no conflicts of interest

Perfection?



LIVE



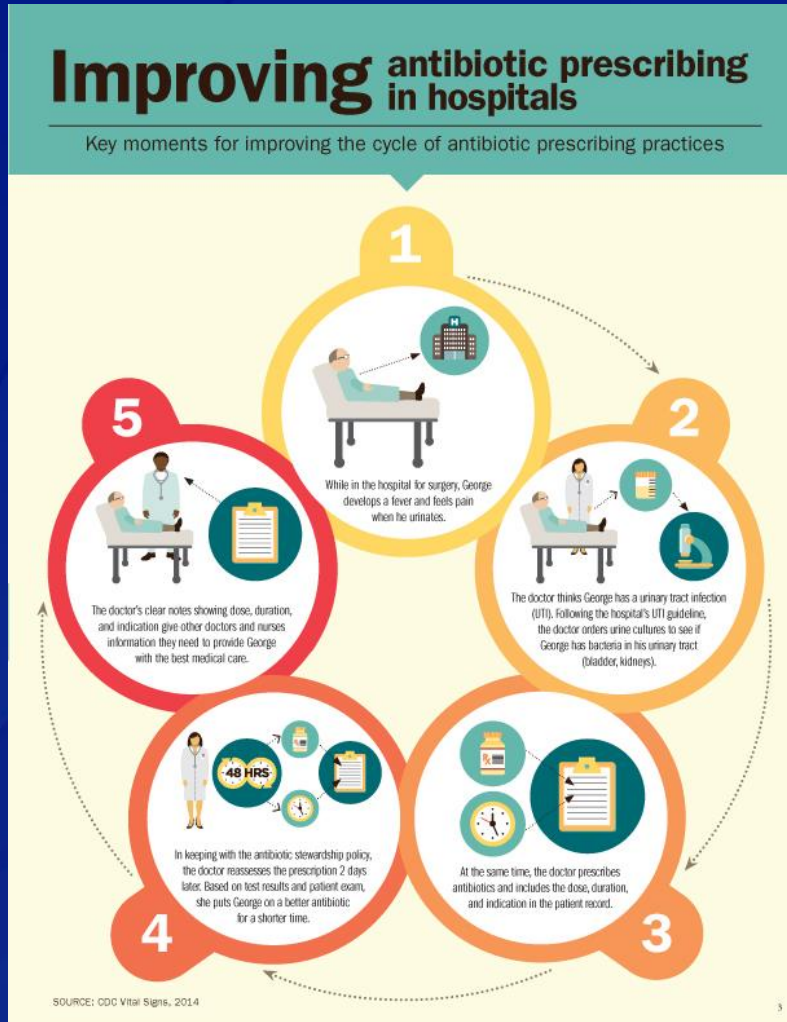
Overview of Presentation

- ❑ Review standard metrics to consider
- ❑ Review drivers of variability observed between inpatient facilities (through benchmarking)
- ❑ What is key research needed around benchmarking
- ❑ Review additional metrics to incorporate

Learning Objectives

- Define common or standard metrics for comparing antibiotic usage in response to a stewardship research project
- Identify likely sources of variation between institutions when comparing antibiotic use between facilities
- List metrics which are most useful to change prescribing practice (sustainably) in response to stewardship interventions.

CDC Recommends All Hospitals Implement Antibiotic Stewardship Programs



- ❑ Leadership commitment
- ❑ Accountability
- ❑ Drug expertise
- ❑ Action
- ❑ Tracking
- ❑ Reporting
- ❑ Education

Summary of Core Elements of Hospital Antibiotic Stewardship Programs

- **Leadership Commitment:** Dedicating necessary human, financial and information technology resources.
- **Accountability:** Appointing a single leader responsible for program outcomes. Experience with successful programs show that a physician leader is effective.
- **Drug Expertise:** Appointing a single pharmacist leader responsible for working to improve antibiotic use.
- **Action:** Implementing at least one recommended action, such as systemic evaluation of ongoing treatment need after a set period of initial treatment (i.e. “antibiotic time out” after 48 hours).
- **Tracking:** Monitoring antibiotic prescribing and resistance patterns.
- **Reporting:** Regular reporting information on antibiotic use and resistance to doctors, nurses and relevant staff.
- **Education:** Educating clinicians about resistance and optimal prescribing.

Stewardship Research Domains

Infrastructure

Interventions

Measures



What Do We Need to Measure?



"Look, we've got to improve our voter-tracking algorithms if we want to make more accurate wild-ass guesses."

ABX Use

What Do We Need to Measure?

- ❑ Antimicrobial Stewardship Programs have “common goal”
 - Measure usage to know if intervention works
 - Measure outcomes related to the use (or change in use)
- ❑ Most measures have been process focused
 - Nationally – no. programs in place, frequency of specific components (e.g., restrictions, audit and feedback, guidelines in place)
 - Facility – consistency with guidelines, documented rational, % patient-days, or cost
- ❑ Justification* for improving patients safety is mostly inferred
 - “concept” AR, ADE, CDI are result of excessive or unnecessary antibiotic use
 - “improved patient outcomes will follow” if we give the right dose, right route, right duration, right indication.....

*McGowan JE Jr.. Antimicrobial Stewardship—State of the Art in 2011: Focus on Outcome and Methods. Infect Control Hosp Epidemiol 2012;33(4)331-337

What Standards Are There?

❑ Quality Indicators of Appropriate Antibiotic Use among Adult Inpatients

- Links to Guidelines
 - Consistent with guideline (empiric)
 - Updated local guidance (3 years) based on national – influenced by local patterns
- Diagnostics
 - 2 BC prior
 - other site prior/rapidly obtained
- Change Plan
 - De-escalate to pathogen directed with culture result
 - Stop empiric after 7 days if evidence lacking
 - Prescribing plan (dose, duration, route, interval) in place
- Dosing improved: tailor to renal function, IV to PO switch, monitoring (if indicated)

Manual

❑ Proxy/Process indicators – summary prescriptions/days/doses (DOT)

What Standards Are There?

One location 4 patients received 1 g/day Cipro for 7 days, 3 patients received both 1g/day ceftriaxone and 0.5 g/day azithromycin for 5 days. Overall 100 patient days in location.

Metric	Calculation	Advantage	Disadvantage	Other
DDD (grams/ref value, for each drug) Per 1000 PD	50.5 DDD/100 PD (28/1 + 15/2 + 7.5/.5)	Easiest, rely on purchase data Valid comparison between drugs	Bias when practice favors dose other than ref value (age, renal)	Variations inpatient dosing make more favorable in outpatient setting
DOT (sum of days each drug is given) Per 1000 PD	58 DOT per 100 PD (4 x 7 + 3 x 5 + 3 x 5)	Valid for wide age range (regardless of dosing)	Bias relates to renal function (skipped dosing) may “favor” single agent broad spectrum usage	Hard to interpret
LOT (no. of days a patient received a drug, regardless of different drugs) Per 1000 PD	43 LOT (or treatment days)/100 PD (4 x 7 + 3 x 5)	Valid for wide age range Reflects duration, regardless of combination therapy	Cannot compare usage of specific drugs	Hard to interpret

Bottom Line Up Front – study impact of stewardship

❑ Minimum metrics

- DOT/1000 Patient-Day (Facility-wide, location specific)
- Cost
- CDI (Clostridium difficile)
- 30 day re-admission rate

❑ Ideal metrics

- SAAR (Fac-wide, location specific)
- Cure or “safety” measure

❑ Minimum comparisons

- Identify problems
 - Track against network if in one
 - Unadjusted facility wide for context
- Impact
 - Track against self (historical)

❑ Ideal comparisons

- External benchmark to national with reasonable risk adjustment
- Audit and feedback among peers

What is Best DOT to Use?

- ❑ By Class of agents, or by standard grouping
- ❑ Facility wide summary, or by location
- ❑ Historical comparison
- ❑ Unadjusted external comparisons
- ❑ Risk adjusted external benchmarking

Best Grouping of Agents?

❑ NHSN Grouping

1. **Broad spectrum agents predominantly used for hospital-onset/multi-drug resistant bacteria** – aminoglycosides, some cephalosporins, penicillin B-lactam/b-lactamase inhibitor combinations, and other agents
2. **Broad spectrum agents predominantly used for community-acquired infection** – ertapenem, some cephalosporins, and some fluoroquinolones
3. **Anti-MRSA agents** – ceftaroline, dalbavancin, daptomycin, linezolid, oritavancin, quinupristin/dalfopristin, tedizolid, telavancin, and vancomycin
4. **Agents predominantly used for surgical site infection prophylaxis** – cefazolin, cefotetan, ceftazidime, cefuroxime

❑ Single Agent (not on first pass)

❑ Intermountain Health

Antibiotic Use in Small Community Hospitals

Edward Steinhilber,^{1,2} Adam L. Herth,³ Xiaoming Sheng,⁴ Peter Jones,¹ Whitney R. Buckel,² James F. Lloyd,⁵ Stephen Howe,⁶ R. Scott Evans,^{5,6} Tom Greene,⁴ and Andrew T. Pavia³

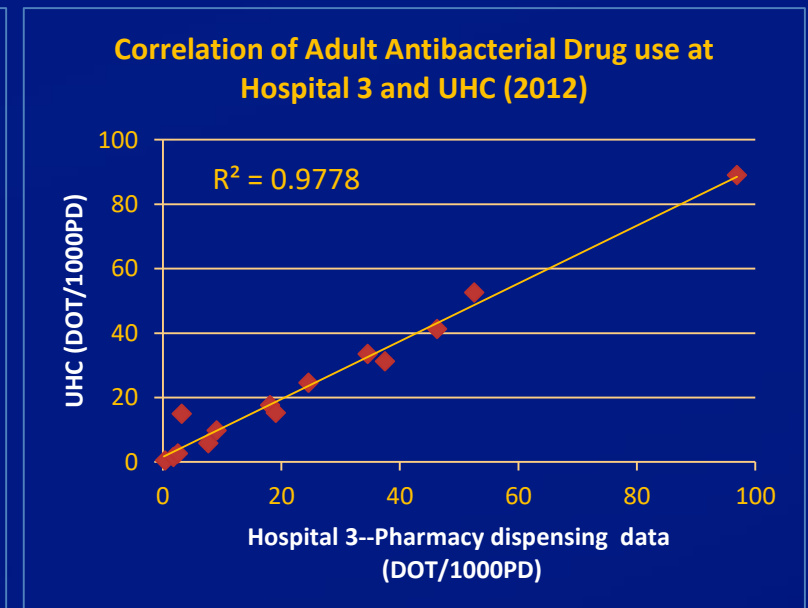
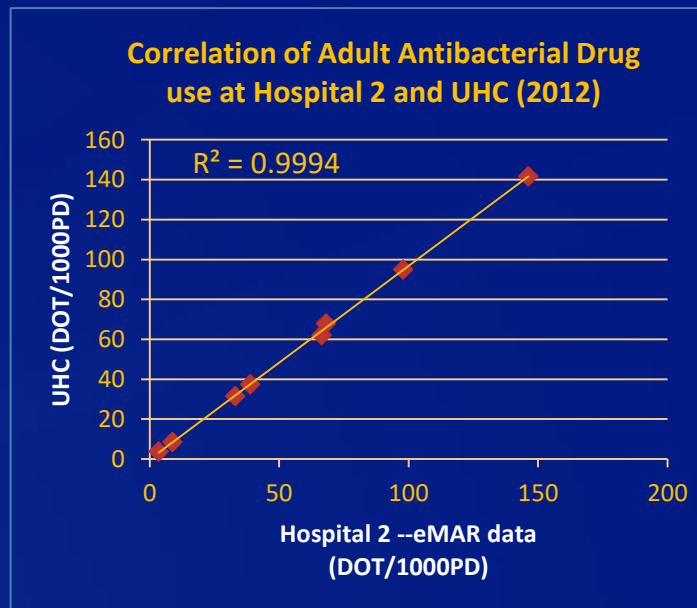
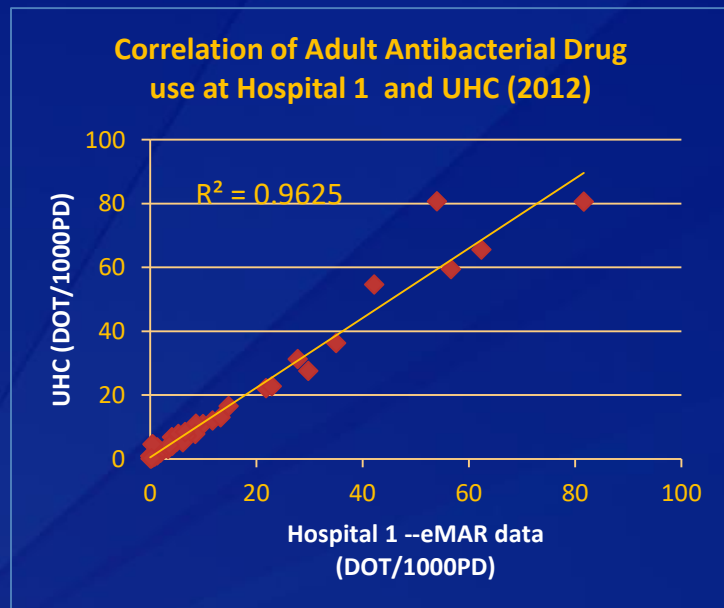
Narrower Broader/MDRO-active				
<ul style="list-style-type: none">• Penicillin• Oxacillin (nafcillin)• Dicloxacillin• Ampicillin• Amoxicillin• Cefazolin• Cephalexin• Nitrofurantoin	<ul style="list-style-type: none">• Tetracyclines• Macrolides• Trimethoprim-sulfamethoxazole• Cefoxitin• Cefuroxime• Clindamycin	<ul style="list-style-type: none">• Amoxicillin-clavulanate• Ampicillin-sulbactam• Ceftriaxone	<ul style="list-style-type: none">• Aminoglycosides• Fluoroquinolones• Aztreonam• Ceftazidime• Cefepime• Ceftaroline• Ertapenem• Vancomycin	<ul style="list-style-type: none">• Imipenem• Meropenem• Piperacillin-tazobactam• Colistin• Daptomycin• Linezolid

❑ Classes

Which grouping is best? – which grouping, when “high” is more likely to best target action steps

What Source is Acceptable for DOT

- ❑ Yes, different sources will provide different values at ward-day or ward-month level (eMAR vs. dispense vs. order vs. charge)
 - Varies by drug/dosing/interval, varies by type of location/patient transfer density
- ❑ Focus on stewardship at your facility source less relevant
 - Ordering data may actually be more relevant than eMAR
- ❑ At Facility-wide level, charge and eMAR are essentially identical



Unpublished data, Ron Polk; personal communication

What is Best DOT to Use?

- ❑ By Class of agents, or by standard grouping
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- ❑ Historical comparison
- ❑ Unadjusted external comparisons
- ❑ Risk adjusted external benchmarking

How much variability must be adjusted for to answer question...
Am I better or worse than them?

Why Experiment around Benchmarking

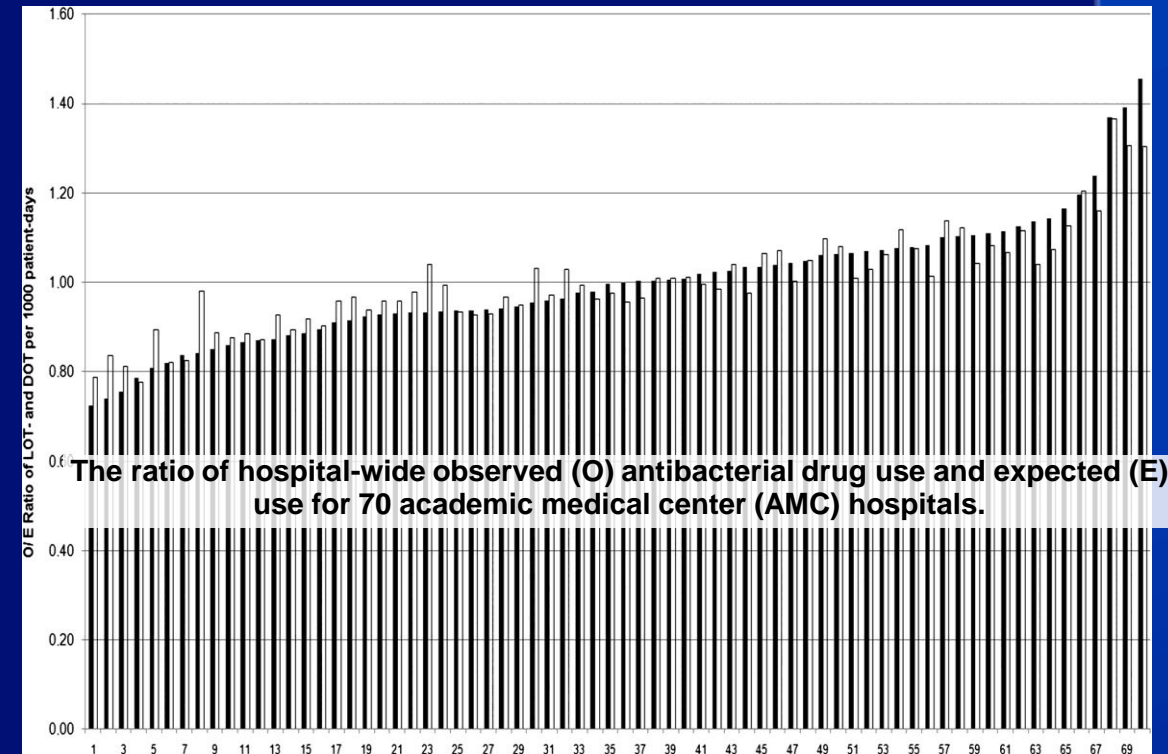
- ❑ **The National Action Plan for Combating Antibiotic Resistance Bacteria**
 - Call for annual reporting of antibiotic use in inpatient settings to identify variations (provider or patient level) that can assist in developing interventions
- ❑ **Local data in context of a fair regional or comparative metric is greatly motivator of change (if done right)**
- ❑ **Research can lead to meaningful and high impact metrics**
 - Inter-hospital comparisons require adjustment to account for differences in patient mix and hospital characteristics
 - Fair comparison, clinically credible, reproducible, ideally accurate
 - Metrics closely aligned with appropriate use will be most clinically meaningful to drive behavior change
 - Uncertain to what degree best adjustment needed for stewardship vs. performance measurement

Benchmark Summary Antibiotic Use Metrics for Performance



Variability in Inpatient Antibiotic Use between Hospitals

- ❑ Early analyses to explain inter-hospital variability in measures of inpatient antibiotic usage have had mixed results
 - European studies
 - Rogues, et al, 84% of variability, DDD / 1,000 PD
 - Kuster, et al, 48%-57% of variability, DDD/100 PD
- ❑ Indirect Standardization using administrative data promising
 - Clinical Service Line allowed comparator by type of patient – clinical sense
 - Introduced O:E (e.g., 10% more than expected)



Ron E. Polk et al. Clin Infect Dis.
2011;53:1100-1110

Clinical Infectious Diseases

Variation in Antibiotic Use Between Inpatient Facilities

- ❑ 130 hospitals, 1 year
- ❑ 87 agents, 1.8 million patients
- ❑ 790 DOT/1000 PD
- ❑ Predicted usage rates (hospital wide)
 - 31% of variation explained by model
 - Hospital beds
 - ICU days/1000 PD
 - Surgeries/100 discharges
 - Pneumonia, BSI,UTI per 100 discharges
- ❑ Residual differences still great

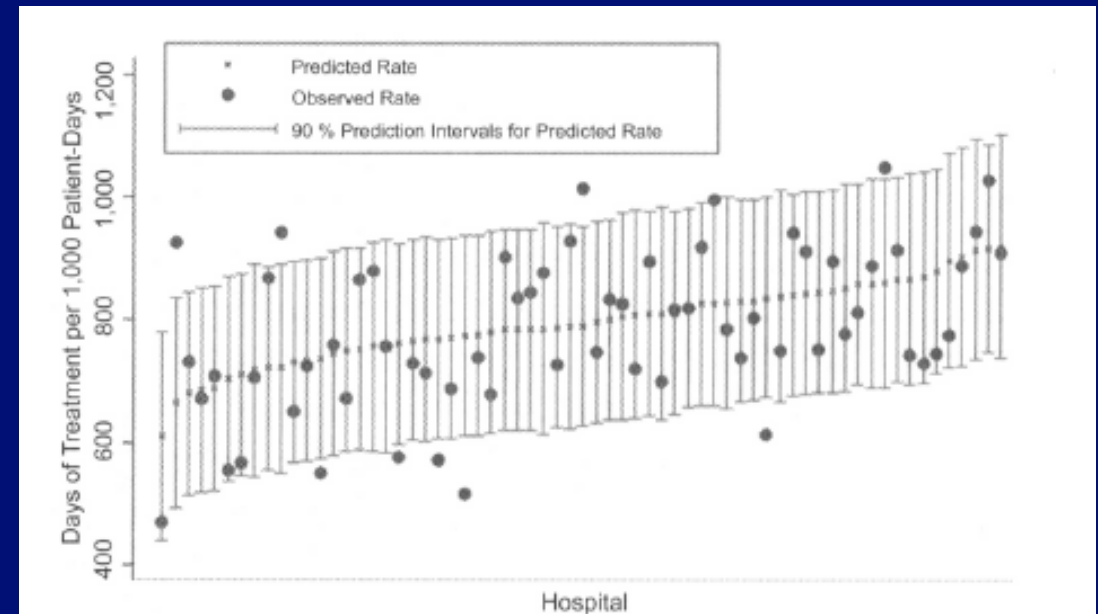


FIGURE. Comparison of observed and predicted total rates of antibacterial use among hospitals in the validation data set. The model used to calculate the predicted rate was as follows: predicted rate of antibacterial use = $0.09(\text{no. of beds}) + 0.74(\text{no. of intensive care unit days per 1,000 patient-days}) + 0.43(\text{no. of surgeries per 1,000 discharges}) + 3.30(\text{no. of cases of pneumonia per 1,000 discharges}) + 6.89(\text{no. of cases of bacteremia per 1,000 discharges}) + 1.68(\text{no. of cases of urinary tract infection per 1,000 discharges}) + 237.08$.

Predictors of Variability in Hospital-wide Use, by Class

Common –

- ICU
- Infection (Pneumonia, BSI, UTI)

Model fit fairly poor

TABLE 4. Multivariable Models of Rates of Antibacterial Use, by Drug Class

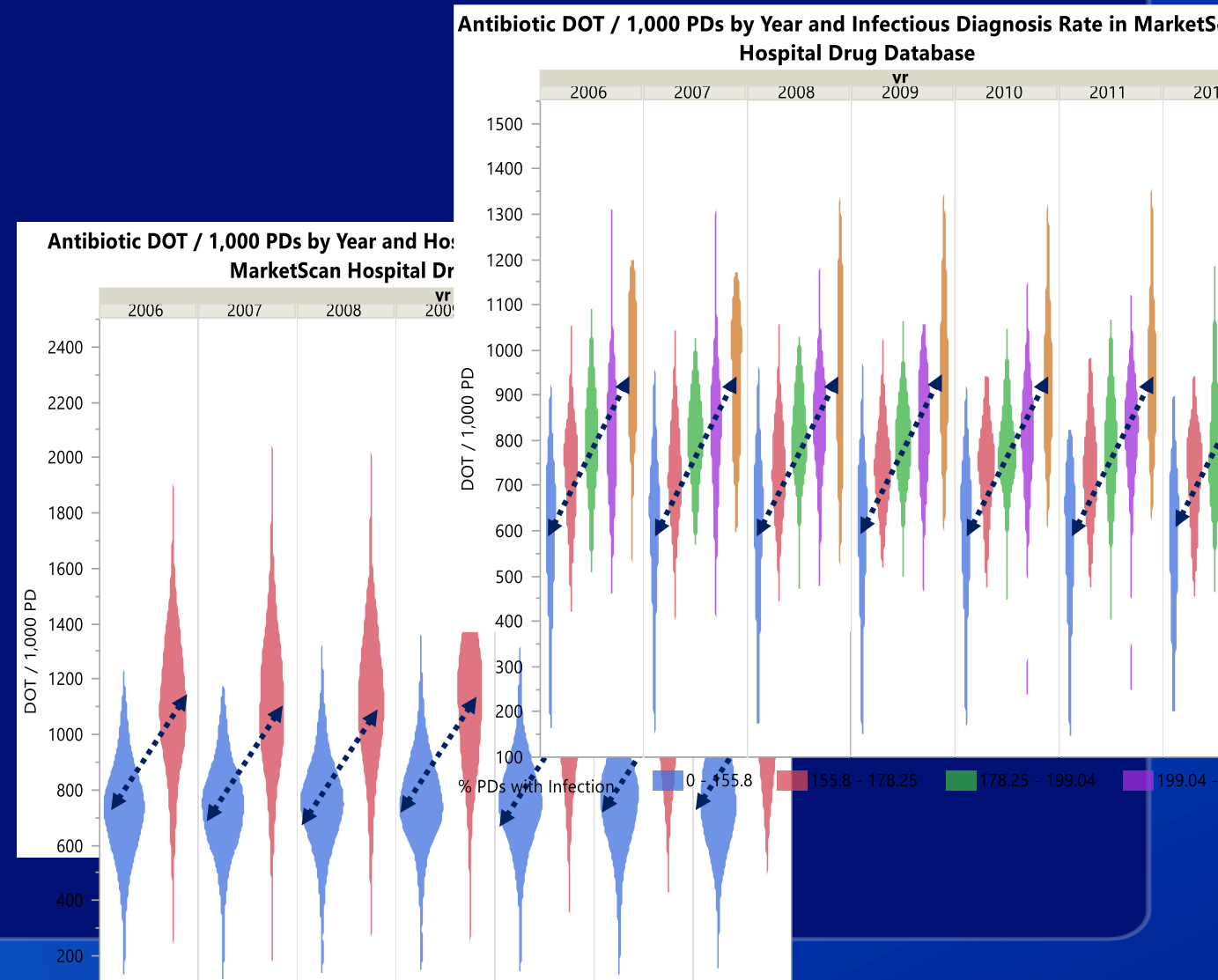
Antibacterial agent or class	Variables in the model	Adjusted R^2	Rate of use, days of therapy per 1,000 patient-days, mean (range)		No. of hospitals with outlying rates	
			Predicted	Observed	Low rate	High rate
All	No. of beds, no. of ICU-days, surgical volume, and no. of cases of pneumonia, UTI, and bacteremia	0.313	794.2 (609.4-919.5)	784.4 (468.4-1,049.3)	5	5
Fluoroquinolones	Teaching status, no. of ICU-days, surgical volume, and no. of cases of pneumonia, UTI, and bacteremia	0.344	196.5 (129.9-286.0)	193.9 (83.9-362.9)	6	7
3G and 4G cephalosporins	No. of ICU-days and no. of cases of pneumonia and bacteremia	0.269	105.46 (66.75-147.74)	97.2 (41.2-161.2)	5	4
Antipseudomonal penicillins	Teaching status, no. of ICU-days, surgical volume, and no. of cases of pneumonia, bacteremia, and UTI	0.063	46.6 (32.7-71.1)	48.9 (0.02-151.2)	0	8
Carbapenems	Case-mix index, surgical volume, and no. of cases of bacteremia and UTI	0.292	15.3 (1.9-45.1)	16.9 (1.2-40.9)	1	8
Vancomycin	No. of beds, case-mix index, and no. of cases of bacteremia and UTI	0.584	50.7 (17.4-87.4)	51.6 (6.3-108.7)	2	6

NOTE. Adjusted R^2 is obtained from derivation data set. Predicted and observed values are for hospitals in the validation data set. ICU, intensive care unit; UTI, urinary tract infection; 3G and 4G, 3rd- and 4th-generation.

Advancing Modeled Usage to Identify Drivers of Variability

- ❑ 500 hospitals, 6 years
- ❑ >100 agents, >10 million patients
- ❑ 775 DOT/1,000 PDs
 - Variability: 10th to 90th percentile range:
 - 546 – 997/1,000 PDs
- ❑ Predicted usage rates (hospital wide)
 - **50-56%** of variation explained by model
 - Two variables explained nearly all the variability (~96%)
 - Hospital location (ICU vs. other)
 - Proportion of PDs with infectious disease diagnosis code
- ❑ Residual differences remain

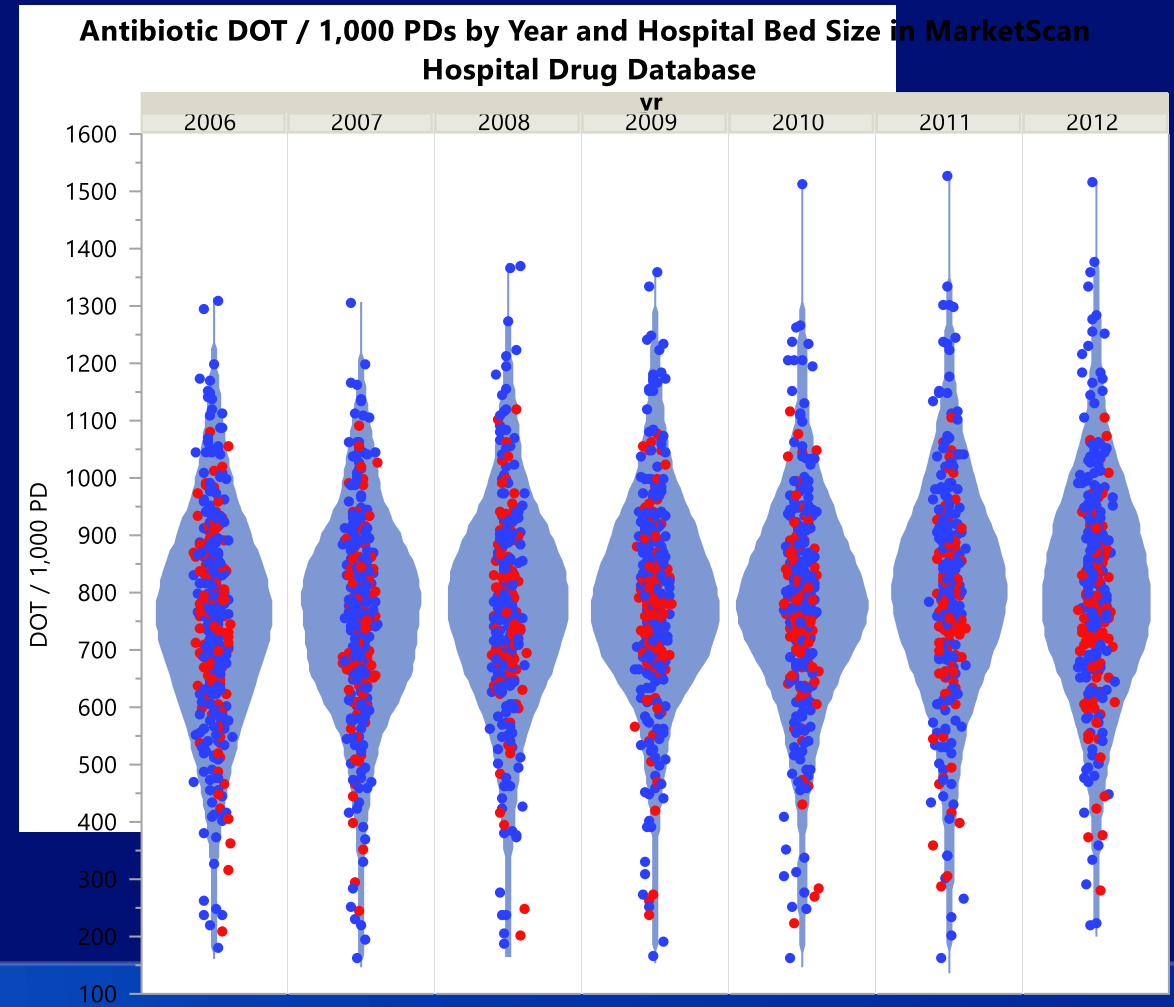
Baggs James IDWeek 2015
Truven Health MarketScan® Hospital Drug Database (HDD): Years 2006-2012



Size doesn't matter

□ Variability often not explained by hospital characteristics

- Red = Large (>300 beds)
- Blue = Small (<300 beds)

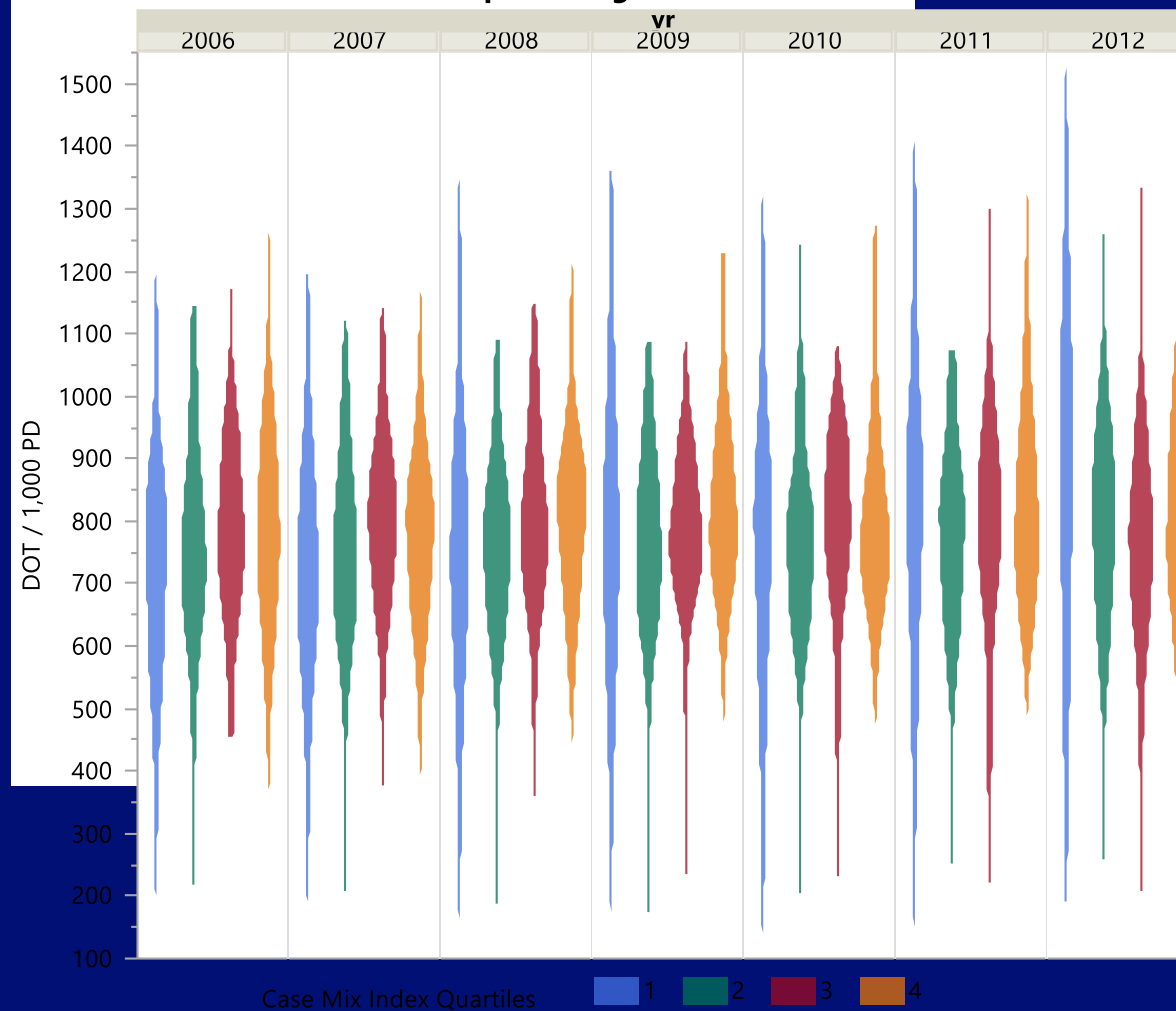


Case-Mix Index didn't matter

□ Variability also not explained by case mix index

- Hospitals divided into quartiles by case mix
 - 1st – Blue
 - 2nd – Green
 - 3rd – Red
 - 4th – Orange

Antibiotic DOT / 1,000 PDs by Year and Case Mix Index Quartiles in MarketScan Hospital Drug Database



Predictors vary by the type of antibiotic

Variables	Type of Antibiotic				
	All Abx	Broad Spectrum I	Broad Spectrum II	Anti-MRSA	"SX PHLX" Types
Hospital-specific location (CC vs. other)	✓	✓	✓	✓	
Proportion of PDs w/ infectious discharge code	✓	✓	✓	✓	
Proportion discharges w/ surgical DRG					✓
Average patient age			✓		
<300 hospitals beds			✓		
Non-teaching status			✓		
Urban location				✓	
Average Case mix index				✓	
Average patient co-morbidity score					

SX PHLX Types = NSGP – Narrow Spectrum Gram Positives, antibacterial agents predominantly used for surgical site infection prophylaxis

Abx – All antibacterial agents

Broad Spectrum I – Broad spectrum antibacterial agents predominantly used for hospital-onset/multi-drug resistant infections

Broad Spectrum II – Broad spectrum antibacterial agents predominantly used for community-acquired infections

NHSN SAAR Risk Adjustment

Building the Models: Part III

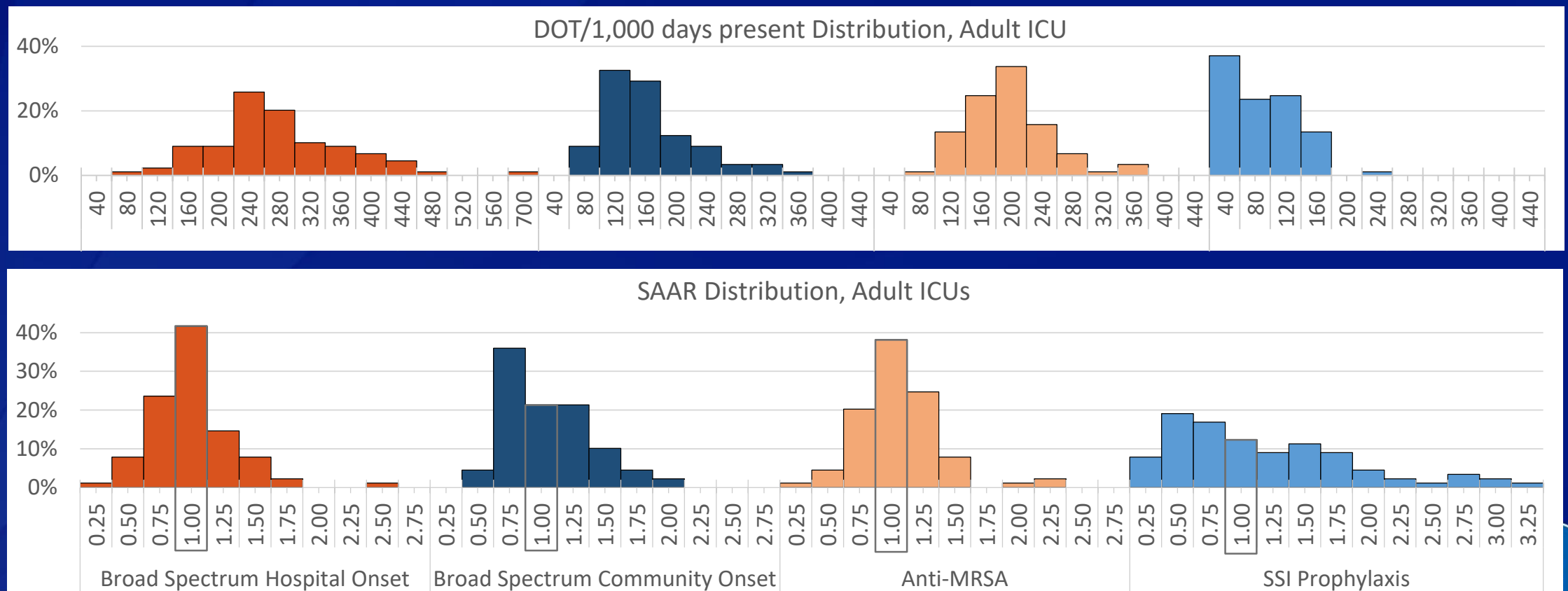
□ Final Models:

- **Model A:** Broad Spectrum Agents Predominantly Used for Hospital-Onset/multi-drug resistant infections
 - ICU, 4 way location-type variable (Levels: Medical Unit, Med/Surg Unit, Surgical Unit, Pediatric Unit*)
- **Model B:** Broad Spectrum Agents Predominantly Used for Community Acquired infections
 - Teaching Status, ICU, Pediatric Location
- **Model C:** Anti MRSA
 - ICU, 4 way location-type variable (Levels: Medical Unit, Med/Surg Unit, Surgical Unit, Pediatric Unit*), Interaction Term: ICU and 4 way location-type variable
- **Model D:** Agents Predominantly used for Surgical Site Infection Prophylaxis
 - ICU, Surgical Location
- **Model E:** All Antibiotic Agents
 - ICU, 4 way location-type variable (Levels: Medical Unit, Med/Surg Unit, Surgical Unit, Pediatric Unit*)

**Referent group in a multi-way variable*

NHSN SAAR Risk Adjustment

- Distribution of antimicrobial use summary measures (top DOT/1000 days present; bottom SAAR), by agent category, adult ICUs reporting to NHSN, 2015



Variation in Antibiotic Use Between Inpatient Facilities

- ❑ Facility-wide measure of “indications” for needing antibiotics (e.g., proportion of PTs with infection), and critical care are MAJOR determinants of antibiotic use – multiple studies
 - Specifics vary by antibiotic class/grouping
- ❑ NHSN SAAR currently limited to account for
 - Surgical, medical, critical care
 - But location specific is big plus
- ❑ However, a large proportion of inter-hospital variability in antimicrobial use remains unexplained (both location specific or hospital-wide)
 - Potentially due to variations in prescribing behavior that may be addressed through antibiotic stewardship
 - OR is it poor risk adjustment - ?

Considerations for Benchmarking Use

- ❑ Even with risk adjustment, be it SAAR or DOT/1000 PD, there is no definitive study metric
- ❑ All proxy/automated metrics just...point...to area needing a deeper dive (e.g., audit/feedback, DUE, Prevalence Survey)
- ❑ Key research needs
 - Refine risk adjustment
 - Additional utilization of “indication metrics” to risk adjust facility usage metrics for benchmarking to advance automated metrics closer to performance metrics
 - Build evidence that high SAAR or DOT/1000 PD correlates with poor prescribing
 - Build evidence that stewardship program (7 core) changes summary metrics
- ❑ These needs must occur before transitions AU reporting to a type of performance measure

Considerations for Benchmarking Use:

Can summary benchmark metrics be used for Stewardship without “Key Research”

- ❑ Yes – use historical comparison to self – similar methods**
- ❑ Yes – can us orders, dispensed, as long as all use similar methods**
- ❑ Yes – reasonable external benchmarks to “Target Action”**
 - NHSN SAAR – O:E ratio summed up across locations**
 - currently not nationally representative, 80 facilities, most advanced adjustment for interfacility comparison
 - Ideally should grow to be more representative of variations in use
 - Ideally should incorporate some adjustment for “indications” for prescribing
 - Facility-wide national comparison – by Class (may expand)**
 - Adjusting proprietary database to reflect US Hospitals overall*

*Estimating National Trends in Inpatient Antibiotic Use Among US Hospitals From 2006 to 2012
JAMA Intern Med. Published online September 19, 2016. doi:10.1001/jamainternmed.2016.5651

From: Estimating National Trends in Inpatient Antibiotic Use Among US Hospitals From 2006 to 2012

JAMA Intern Med. Published online September 19, 2016. doi:10.1001/jamainternmed.2016.5651

Table 3. Extrapolated Estimates of Antibiotic Usage in the Truven MarketScan Hospital Drug Database by Year and Various Characteristics, 2006-2012

Characteristic	DOT/1000 PDs							All Years
	2006	2007	2008	2009	2010	2011	2012	
Antibiotic class								
All	732.5	736.9	755.6	766.8	755.4	770.0	767.5	754.8
Aminoglycosides	30.7	29.2	27.6	25.4	23.3	20.9	19.8	25.3
First- and second-generation cephalosporins	96.8	93.0	90.5	90.0	87.9	85.8	83.1	89.6
Third- and fourth-generation Cephalosporins	90.2	88.1	89.2	93.1	96.7	103.7	105.6	95.2
Lincosamide	23.1	22.9	22.3	21.6	20.4	20.2	19.8	21.5
Fluoroquinolones	143.7	141.0	139.4	134.3	126.6	123.0	117.0	132.3
Macrolides	35.2	34.2	36.9	38.7	37.6	42.0	42.1	38.1
Glycopeptide	72.0	77.1	85.0	91.7	93.6	100.1	103.4	88.8
Sulfa	15.4	16.0	16.5	16.0	15.4	14.5	13.8	15.4
β -Lactam/ β -lactamase inhibitor combinations	75.5	80.5	88.0	93.4	94.5	99.1	102.6	90.4
Carbapenems	22.2	23.8	27.0	29.8	29.6	31.6	32.3	28.0
Penicillins	35.8	34.6	33.0	32.0	30.8	29.1	29.0	32.1
Tetracyclines	8.5	10.1	12.3	14.8	13.7	13.5	13.2	12.3
Metronidazole	53.7	53.1	52.4	51.0	50.0	49.7	49.3	51.3
Other	29.8	33.0	35.4	35.1	35.3	36.8	36.7	34.6

What Additional Metrics Make Stewardship Research Matter?

- ❑ “In this era of diminishing resources for health care, inferential (proxy measures) data likely will not suffice. Providing specific documentation that stewardship programs are [improve outcomes] is necessary.” much of these

-- John E. McGowan Jr. MD

Antimicrobial Stewardship—the State of the Art in 2011: Focus on Outcome and Methods. *Infect Control Hosp Epidemiol* 2012;33(4):331-337

What Do We Need to Measure?

1. Benchmark to Trigger DUE/PPS

- DOT based are O.K.
- O:E or SAAR, by some TBD best grouping
- Unadjusted benchmark not unreasonable to target action

2. Patient safety

- 30 day readmissions – explore risk adjusted benchmarks
- CDI (hospital onset and all comers) – use NHSN LabIDevent required reporting

3. Patient outcomes

- TBD – can there be clinically credible benchmarks here (i.e., cure)

4. AR

- Avoid for now as a promise
- Incidence of clinical culture per 1000 PD and admission (Resistance Option NHSN)

Tracking Readmissions Makes Sense – They are Our Infections

One third of readmissions are infection related;
Of these, most are sepsis, pneumonia or UTI

Infection Categories	Percent Among	
	All Readmissions	Infection-Related Readmissions
1. Sepsis	10.2	29.9
2. Pneumonia	7.8	22.9
3. Genitourinary Infections	5.0	14.6
4. Skin/Soft Tissue Infections	3.1	9.0
5. Post-Operative Infections	1.9	5.4
6. Clostridium difficile Infections	1.4	4.2
...
10. Other	2.0	5.9
Total	34%	100.0%

30 day readmission rates can be risk adjusted:
LOS, SNF admission/discharge, teaching, SOI

Descriptive Variable	Adjusted Odds Ratio	
	All-Cause Readmissions	Infection-Related Readmissions
Male gender	1.14 (1.14–1.15)	1.07 (1.06–1.08)
Length of Stay > 5 days	1.47 (1.46–1.47)	1.97 (1.95–1.98)
Admission from SNF at index admission	0.90 (.89–.91)	1.26 (1.24–1.28)
Discharged to SNF at Index Admission	1.37 (1.36–1.38)	1.95 (1.94–1.97)
Patients living in a Federal Poverty Area	1.04 (1.03–1.04)	1.02 (1.02–1.05)
Academic Hospital Status	1.47 (1.13–1.38)	1.12 (1.95–1.98)
Mean Romano Score	1.15 (1.15–1.15)	1.39 (1.10–1.10)

Gohil et al. Clin Infect Dis. 2015 Oct 15; 61(8): 1235–1243.
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4583583/>

Bottom Line Up Front – study impact of stewardship

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KEEP
CALM
AND DO

ANTIMICROBIAL
STEWARDSHIP

Stewardship Research Funding

❑ NIAID

- Support diagnostics and vaccine development activities
- DEVELOPMENT of such diagnostics
 - small business grants (SBIR/STTR)
 - yearly “partnerships” solicitation for product development <https://grants.nih.gov/grants/guide/rfa-files/RFA-AI-16-034.html>
- VTEUs
<https://www.niaid.nih.gov/about/organization/dmid/researchers/clinical/vteu/Pages/default.aspx>

❑ ARLG has Antimicrobial Stewardship and Infection Prevention one of their four Scientific topic areas

- <http://arlg.org/about-the-arlg/arlg-scientific-agenda>
- <http://arlg.org/how-to-apply>
- <http://cid.oxfordjournals.org/content/58/11/1571.long>

Stewardship Research Funding

□ AHRQ

- <http://www.ahrq.gov/funding/fund-opps/index.html>
- Priority #2. Make Health Care Safer
- AHRQ encourages an interdisciplinary patient safety approach. In addition to health services research, perspectives from organizational theory, human factors, industrial engineering, facilities design, education, and other disciplines can be incorporated in research plans
 - the surveillance, measurement, detection, and reporting of patient safety events
 - diagnostic error; the safe use of medications
 - the challenges inherent in transitions of care and handoffs between health care providers
- hospital, long-term care, ambulatory care, home health care, pharmacy, and transitions of care between settings

Stewardship Research Funding

❑ State HAI AR Programs

- Through CDC's Epidemiology and Laboratory Capacity Cooperative Agreement
- All States (and several Large Metro areas)
- Support for surveillance, detection, response, and prevention including stewardship coordination
- NOT appropriate for research (by design)
 - However, process improvement, targeting action, surveillance improvement