Antimicrobial Stewardship Across the Continuum of Care

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Assistant Professor, Infectious Disease
6/5/13

Disclosure

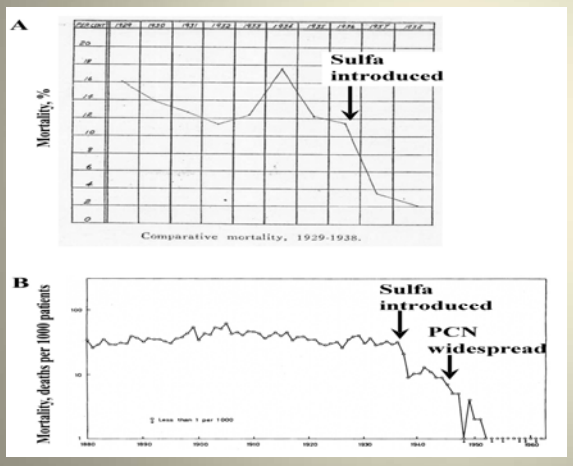
- Trevor Van Schooneveld, MD
  - Nothing to disclose

Objectives

- Describe the forces driving antimicrobial resistance
- Recognize barriers to appropriate antimicrobial use
- Consider implementation of antimicrobial stewardship practices in various healthcare settings

Antimicrobial Impact

(A) Mortality rates for erysipelas at Cook County Hospital 1929-1938
(B) Mortality of erysipelas from Norwegian national registry

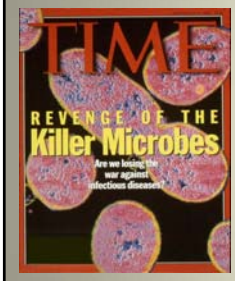


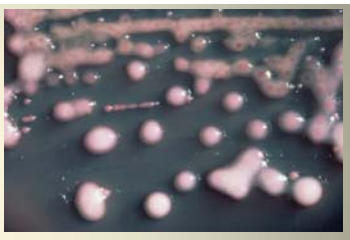
Spellberg, et al. *Clin Infect Dis*. 2009;49:383-91.

Bloomberg

Drug-Defying Germs From India Speed Post-Antibiotic Era

By Jason Gale and Adi Narayan - May 7, 2012
Bloomberg Markets Magazine





guardian.co.uk

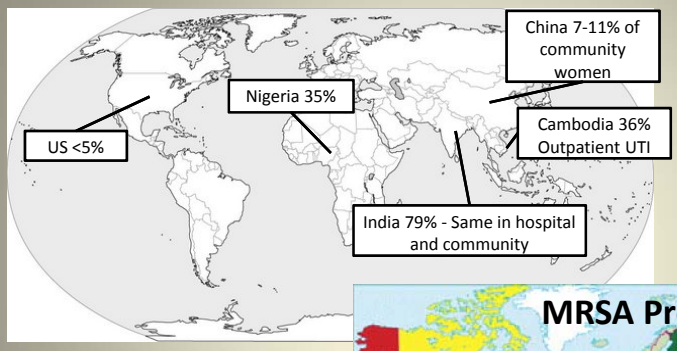
Antibiotics' efficiency wanes due to global spread of drug-resistant bacteria

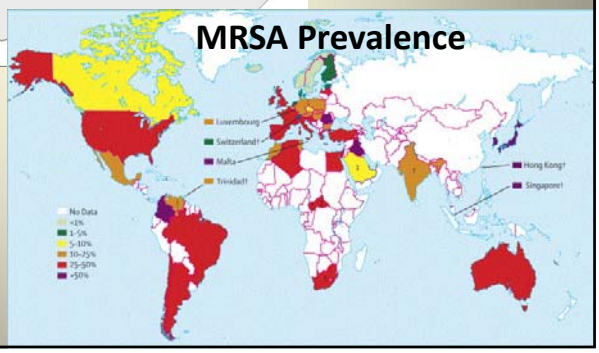
Gene giving high levels of resistance to drugs found in increasingly prevalent intestinal bacteria

Drug-resistant superbugs reach 3 states

The Seattle Times

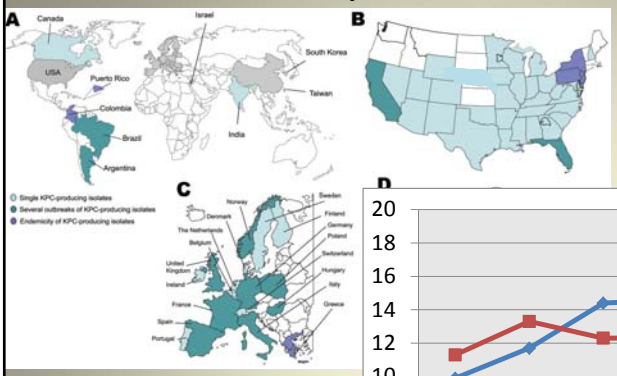
Worldwide ESBL *E. coli*



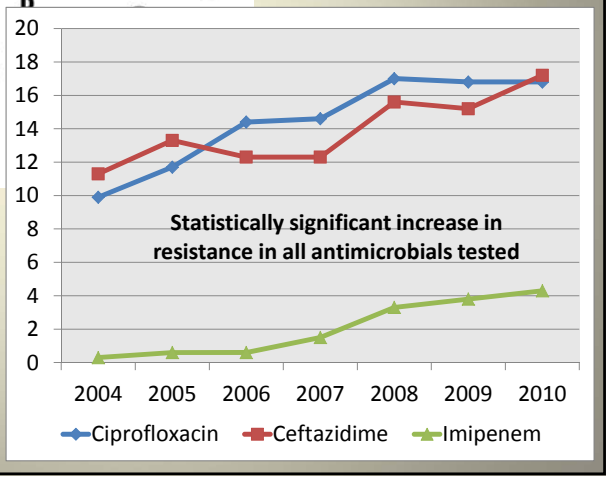


Grundmann. *Lancet* 2006;368:874.

Global KPC Spread

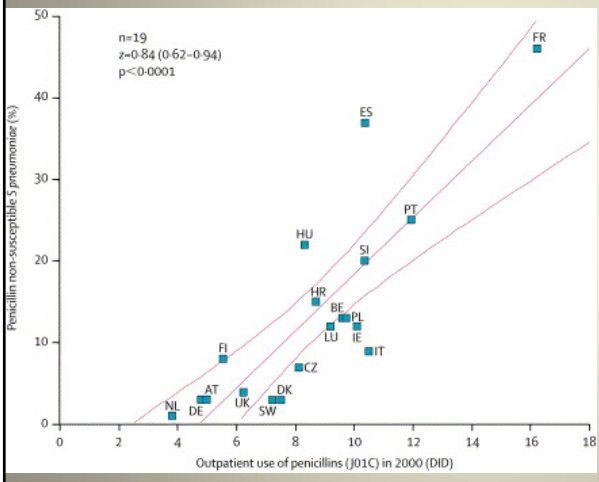


Klebsiella pneumoniae Resistance in Inpatients, USA 2004-2010, TSN Database



Nordmann P. *Emerg Infect Dis*. 2011;17:1791-8.
Sanchez GV. *Emerg Infect Dis*. 2013;19:133-6.

Where Does All This Resistance Come From?

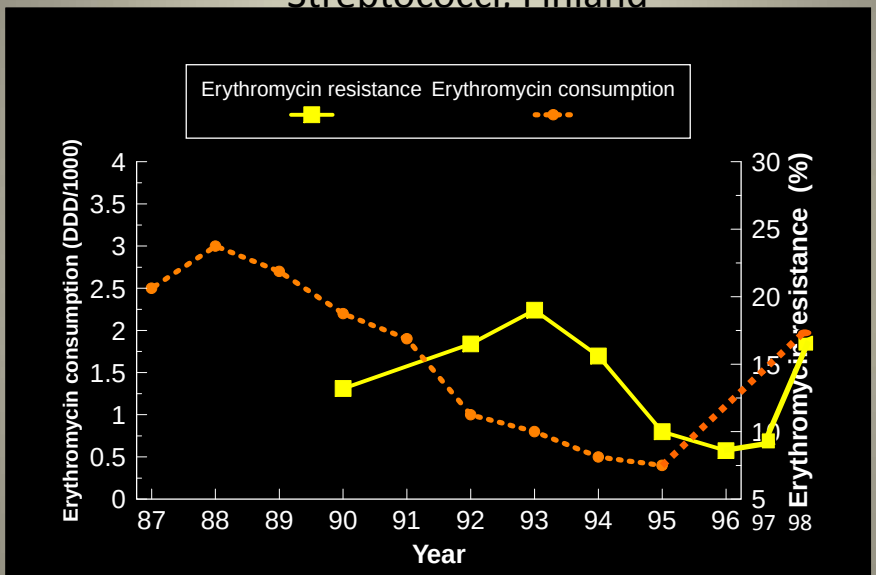


"It is not difficult to make microbes resistant to penicillin… moral: If you use penicillin, use enough."
(Alexander Fleming, Nobel Prize Acceptance Speech, 1945)

"Antibiotic use is the key driver of resistance."
(WHO Global Strategy for Containment of Antimicrobial Resistance, 2000)

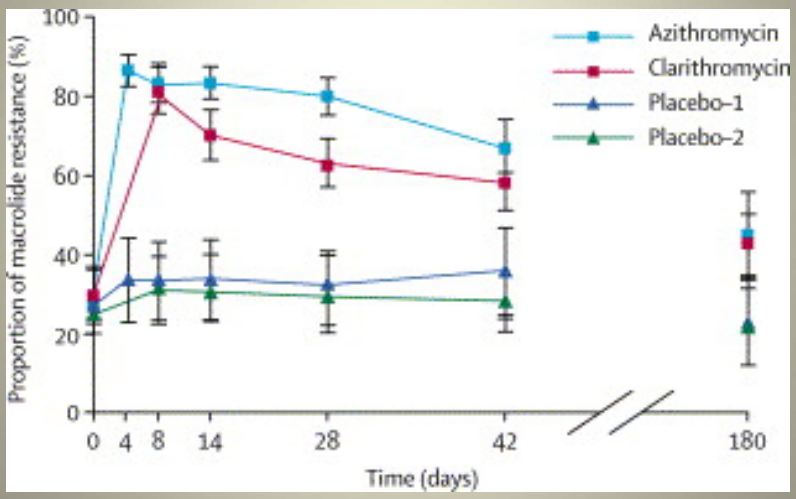
Goossens. *Lancet*. 2005;365:579.

Controlling Erythromycin Resistance in Group A Streptococci, Finland



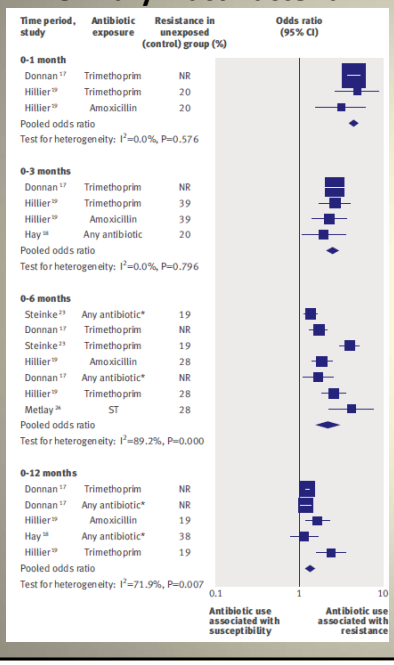
Seppala. *NEJM* 1997;337:441
Post-study data courtesy of Ron Rolk, Pharm.D.

Temporal changes in the proportion of macrolide-resistant streptococci after azithromycin or clarithromycin use

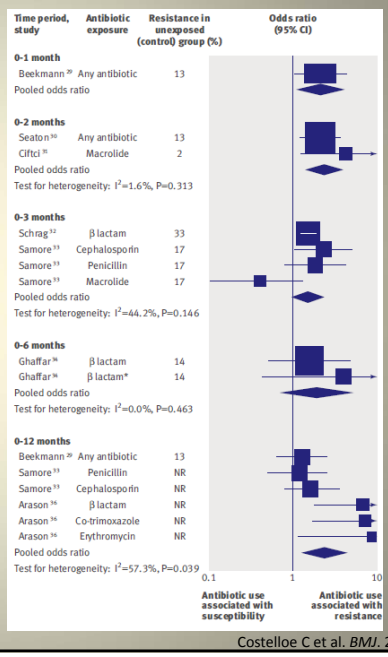


Malhotra-Kumar S. *Lancet*. 2007;369:482-90.

Urinary Tract Bacteria



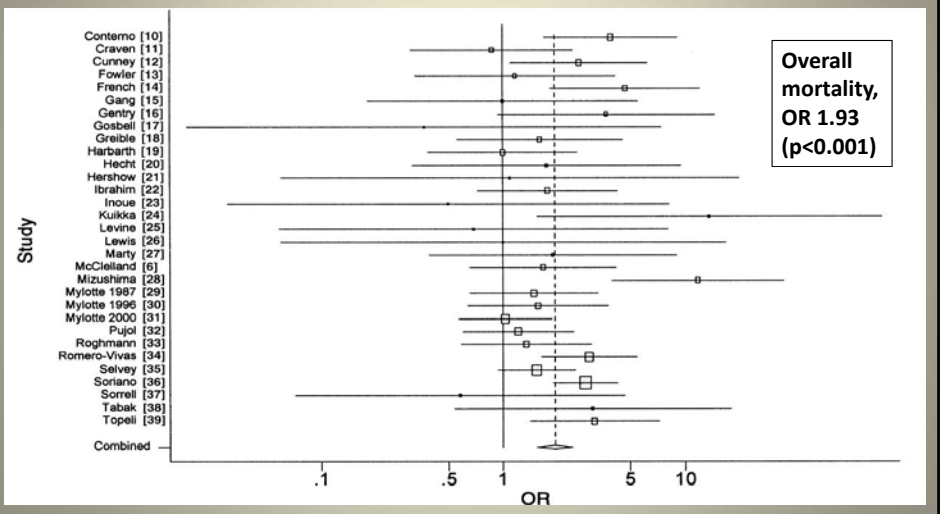
Respiratory Tract Bacteria



Costelloe C et al. *BMJ*. 2010;340

Does Resistance Matter?

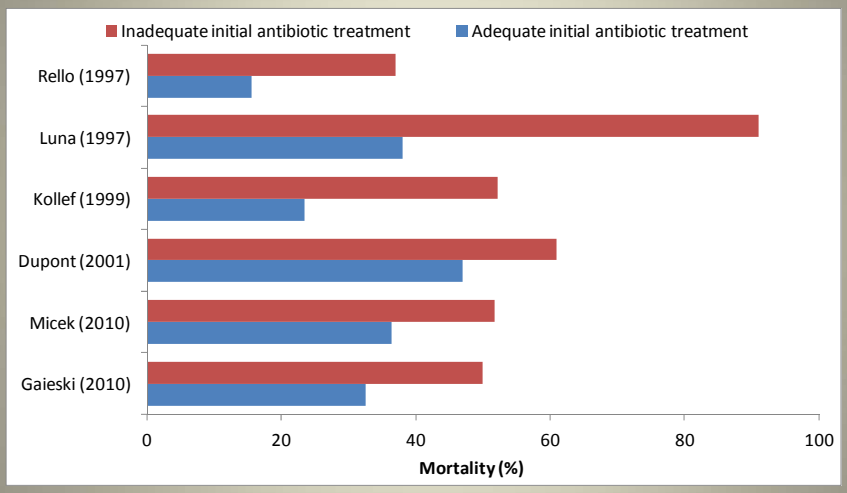
Meta-analysis of 31 Cohort Studies: MSSA vs. MRSA Bacteremia



Overall mortality, OR 1.93 (p<0.001)

Cosgrove. *Clin Infect Dis*. 2003;36:53.

Impact of Antibiotic Resistance



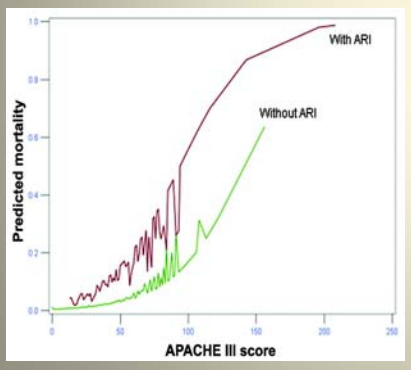
Gaieski DF, et al. *Crit Care Med.* 2010;38:1045-1053.
Dupont H, et al. *Intensive Care Med*. 2001;27:355-362.
Kollef MH, et al. *Chest.* 1999;115:462-474.
Luna CM, et al. *Chest.* 1997;111:676-685.
Rello J, et al. *Am J Respir Crit Care Med*. 1997;156:196-200.
Micek ST, et al. *Antimicrob Agent Chemother.* 2010;54:1742-1748.

The Cost of Resistance:

Bad For Patients, Bad for Healthcare

Analysis of 188 patients with antimicrobial-resistant infections in a group of 1391 hospitalized patients

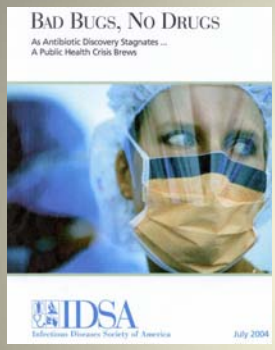
Predicted mortality for patients with/without antimicrobial-resistant infections

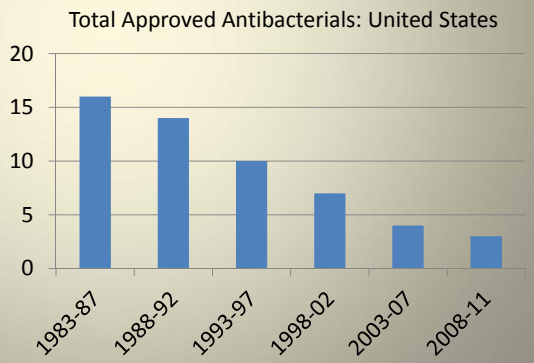


- **Medical Costs** • $18,588 to $29,069 per patient
- **Excess LOS** • 6.4 – 12.7 days
- **Attributable Mortality** • 6.5%
- **Overall Increased Cost 1 year** • $13.35 million

Roberts. *Clin Infect Dis*. 2009;49:1175.

The Impending Crisis!





What Do We Do?

- Options
  1. ~~Create new drugs~~
  2. Learn to use what we have more wisely

ANTIMICROBIAL STEWARDSHIP

Antibiotics Are Unique

- They are the only drugs that lose efficacy over time & must be continually replaced
- They are the only drugs that need to be used sparingly to prolong their efficacy
- They are the only drugs that we actively discourage use of when new drugs are approved
- **They are the only drugs where how I use them affects your patients**

Antimicrobial Facts

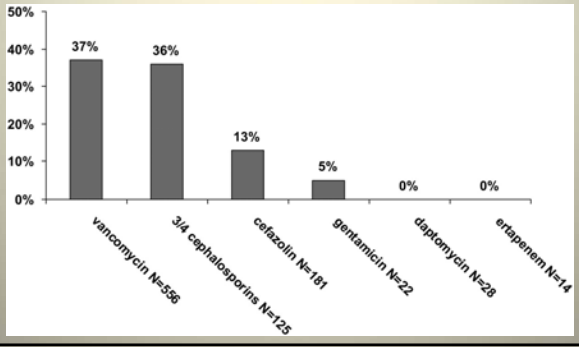
- Nearly 60% of all hospitalized patients will receive an antimicrobial
  - Up to ½ of which are inappropriate or unnecessary
- Inappropriate use leads to
  - Resistance
  - Collateral Damage (*C. difficile*, etc)
  - Toxicity/Side Effects
  - Increased Cost

Antimicrobial Use in Outpatient Hemodialysis Units

Infect Control Hosp Epidemiol. 2013;34:349-57.

Graham M. Snyder, MD;[1] Priti R. Patel, MD, MPH;[2] Alexander J. Kallen, MD, MPH;[2] James A. Strom, MD;[3] J. Kevin Tucker, MD;[4] Erika M. C. D'Agata, MD, MPH[1]

- Two outpatient HD units, 278 patients, 12 mo.
- 1,003 antibiotic doses
  - 29.8% inappropriate
    - No criteria for infection 53%
    - Inappropriately broad 27%
    - Inappropriate surgical prophylaxis 20%



Barriers to Appropriate Use

What is Antimicrobial Stewardship?

- Antimicrobial Stewardship refers to processes designed to optimize the use of antimicrobials
  - Includes interventions to guide clinicians in:
    - Determining **when** antibiotics are needed
    - **What** agent(s) to use
    - **How to** dose, what route and what duration
  - Focus is on **patient and public health** with goals:
    - Cure or prevent infection
    - Minimize toxicity
    - Minimize resistance

Reduce treatment costs

Dellit TH. *Clin Infect Dis*. 2007;44:159-77.
SHEA/IDSA/PIDS. *Infect Control Hosp Epidemiol*. 2012;33:322-7.

ASP Strategies

Primary Strategies

- Multidisciplinary involvement
- **Restriction**
- **Pre-authorization**
- **Prospective audit-feedback**

Additional

- **Use of CPOE/CDS**
- Indication/Duration

Secondary Strategies

- Education
- Institutional guidelines and clinical pathways
- Antimicrobial order forms
- De-escalation
- Dose optimization
- IV to PO conversion
- Antimicrobial Cycling

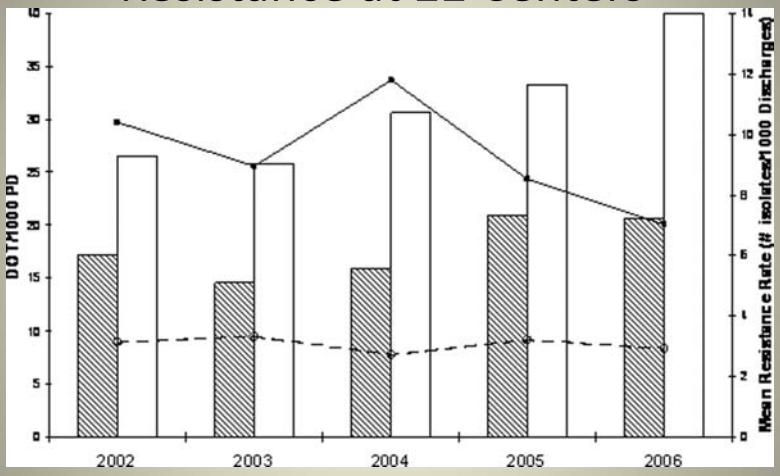
Dellit TH, et al. *Clin Infect Dis*. 2007;44:159-77.

Restriction

- 88% of programs use restrictions in some form
- Advantages
  - Minimal personel needed, will decrease use
- Disadvantages
  - Restrictive, "squeezing the balloon"
- Examples
  - Meropenem is only carbapenem available on formulary
  - Daptomycin is only able to be ordered by ID physicians
  - Vancomycin stopped after 72 hours unless culture positive for MRSA

Johannsson B, et al. *Infect Control Hosp Epidemiol*. 2011;32:367.

Carbapenem Restriction and Resistance at 22 Centers



Mean carbapenem use (DOT/1,000 PD) was significantly lower in hospitals that restricted (shaded bars) versus did not restrict (open bars) carbapenems (P = 0.04)

Pakyz, et al. *Antimicrob Agents Chemother*. 2009;53:1983.

UNMC Restriction

- Allow physicians at bedside to make initial treatment decisions
- Formulary restrictions
  - Ambisome
  - Cephalosporins
- Specific agent restrictions – need to know how to use
  - Fosfomycin
  - Colistin
  - Tigecycline
  - Daptomycin
  - Posaconazole
  - CMV IG

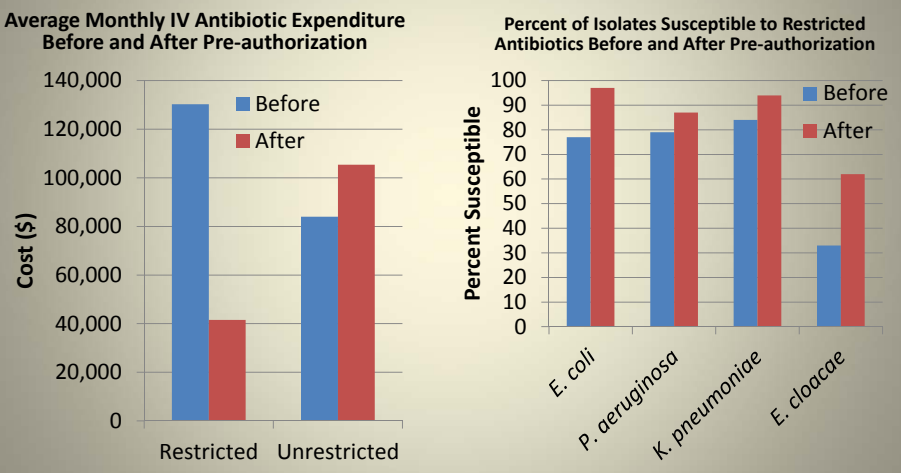
Pre-Authorization

- Advantages
  - Targeted, effective, feedback to clinicians
- Disadvantages
  - Painful, time consuming, info reliability, circumventing

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

Pre-authorization 24 hours a day by ID faculty:

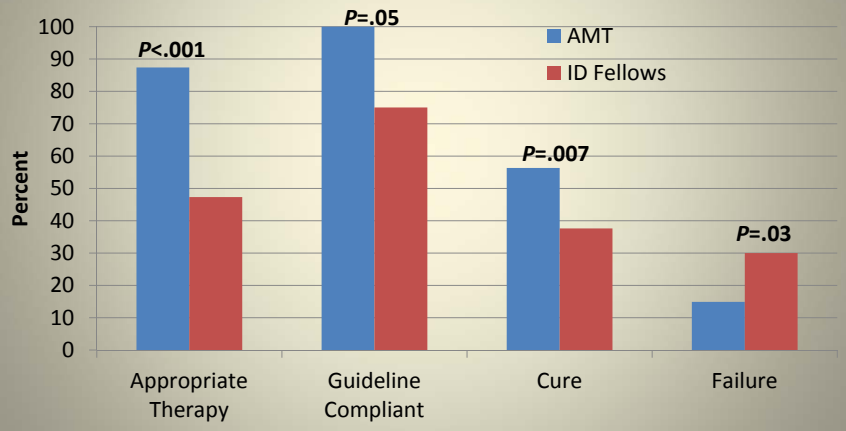
Amikacin, Ceftazidime, Pip/tazo, Imipenem, Ofloxacin, Ciprofloxacin, Fluconazole, Aztreonam



White AC, et al. *Clin Infect Dis.* 1997;25:230.

Impact of a Hospital-Based Antimicrobial Management Program on Clinical and Economic Outcomes

Primary Intervention was Pre-approval



Gross R, et al. *Clin Infect Dis.* 2001;33:289.

Prospective Audit with Intervention and Feedback

- Process of reviewing patients who are receiving antibiotics and giving "unsolicited" advice
- Requires process for identifying patients
  - Software, micro reports, problem areas or units
- Advantages
  - Customization
  - Educational
  - No delays in therapy
- Disadvantages
  - Optional
  - Time intensive
  - Requires broad-based knowledge depending on how applied

Impact

- Single center ICU patients on 3rd or 10th day of broad-spectrum therapy audit/feedback from ID pharmacist
  - Monthly DOT/1000 PD decreased 644→503 (*P*=.0054)
  - No increase mortality
- Inpatients with suspected infection randomized to usual care vs. audit/feedback by ID MD and microbiologist
  - 89% acceptance rat
  - No difference in mortality

	Control (N=125)	Intervention (N=127)	P
LOS from randomization	9 days	5.7 days	<0.001
Antibiotic Costs ($)	2683	2078	0.038
Lab and Radiology Costs ($)	3293	2496	0.032

Elligsen M. *Infect Control Hosp Epi*. 2012;33:354-61.
Gums JG. *Pharmacotherapy* 1999;19:1369–77.

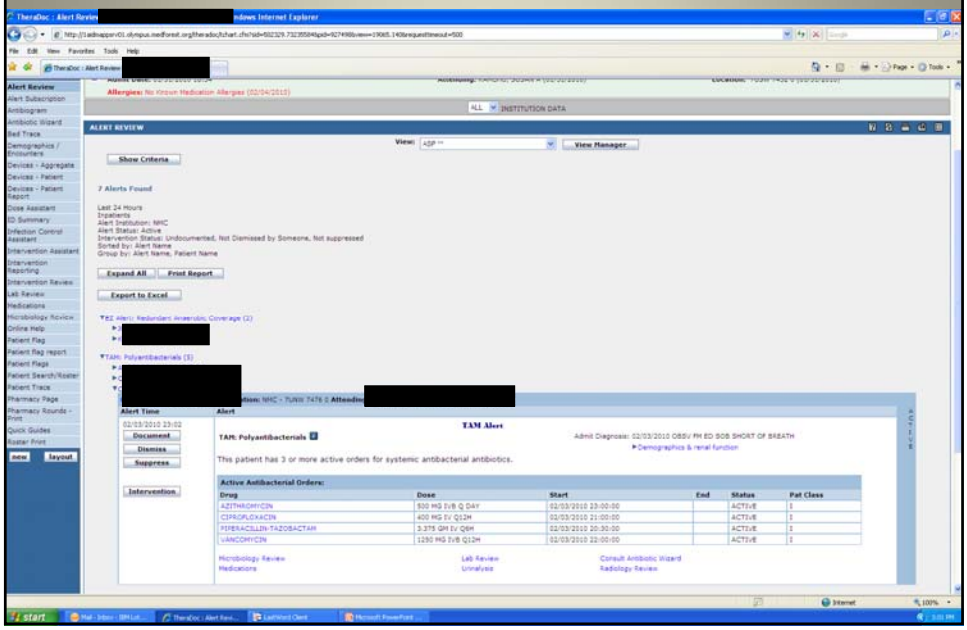
How to Go About Auditing

- What process is used to identify patients?
- Increasing use of computerized physician order entry (CPOE) and electronic medical records
- Clinical decision support software (CDSS) such as Theradoc™ and MedMined™ incorporate microbiology, treatment, and patient-specific information to identify patients requiring intervention
  - Eliminates need for manual review of microbiology and drug reports
  - Can be used for tracking interventions and as a communication tool

Clinical Decision Support Software (CDSS)

- For example, patients can be identified based on:
  - Susceptibility mismatches
    - No therapy
    - Inactive therapy
    - Vancomycin for MSSA
    - Micafungin for fluconazole-susceptible *Candida* spp.
  - Redundant therapy (e.g. double anaerobic coverage)
  - Patients on ≥ 3 anti-infectives
  - Vancomycin for CoNS
  - IV to PO
  - Custom alerts

Theradoc



CDSS in Action

- Real-time microbiology coupled with antibiotic decision support implemented in an ICU

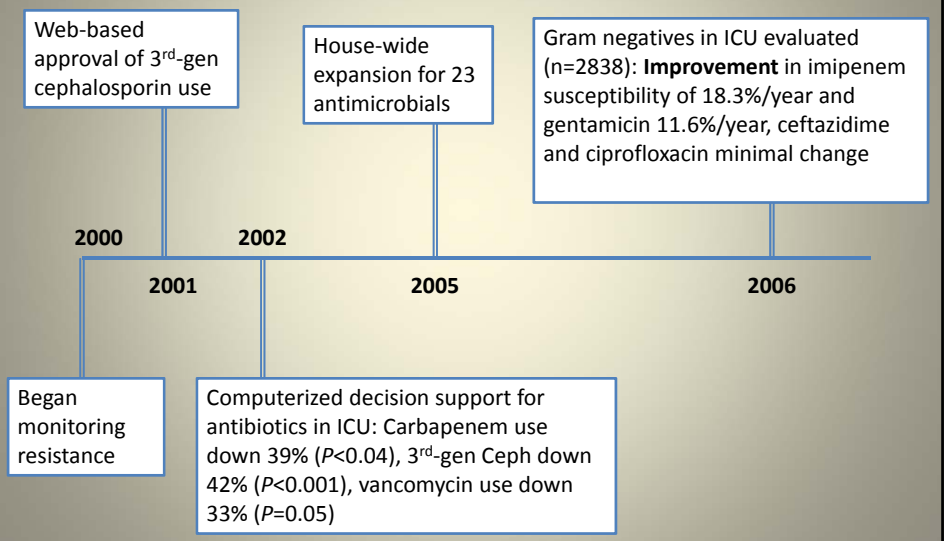
Table 2 Unadjusted odds ratios (ORs) comparing the proportion of patients prescribed antibiotics in the pre-intervention and intervention groups

	Proportion of patients treated (%)			
	Pre-intervention	Intervention	OR (95% CI)	*P*-value
Third-generation cephalosporins	39.1	31.7	0.72 (0.56–0.93)	0.01
Carbapenems	13.4	10.3	0.74 (0.51–1.08)	0.12
Vancomycin	22.1	19.4	0.84 (0.63–1.13)	0.27
Metronidazole	23.3	21.2	0.86 (0.62–1.19)	0.37
First-generation cephalosporins	19.8	20.7	1.02 (0.88–1.18)	0.72
Penicillins[1]	16.2	15.3	0.93 (0.67–1.29)	0.68
Gentamicin	7.0	7.2	1.17 (0.70–1.96)	0.54
Extended spectrum penicillins[2]	3.4	5.0	1.49 (0.81–2.74)	0.20
Ciprofloxacin	4.2	6.0	1.45 (0.83–2.53)	0.19
Macrolides	10.4	17.9	1.83 (1.27–2.64)	0.001

95% CI, 95% confidence interval.
[1]Includes benzylpenicillin, amoxicillin, and flucloxacillin.
[2]Includes ticarcillin/clavulanate and piperacillin/tazobactam.

Thursky KA. *Int J Qual Health Care*. 2006;18:224-31.

CDS and Pre-authorization



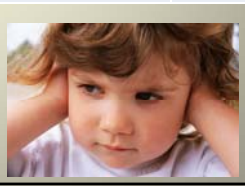
Yong MK, et al. *J Antimicrob Chemother.* 2010;65:1062.

The Problem with CDSS

- Implementation of CDSS at TNMC

Alert	Actionable	Intervention	Intervention Accepted
Polyantibacterial	157/2888 (5%)	118/157 (75%)	102/118 (86%)
Redundant Anaerobic Coverage	68/758 (9%)	60/68 (88%)	50/60 (83%)
Drug-bug Mismatch	85/1688 (5%)	70/85 (82%)	66/70 (94%)
Vancomycin for CoNS	13/259 (5%)	12/13 (92%)	12/12 (100%)
Vancomycin for MSSA	10/139 (7%)	9/10 (90%)	8 /9 (89%)
Overall	333/5732 (6%)	269/333 (81%)	238/269 (88%)

- There is a lot of noise



Hermsen ED. *Infect Control Hosp Epi*. 2012;33:412-5.

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Secondary Strategies

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

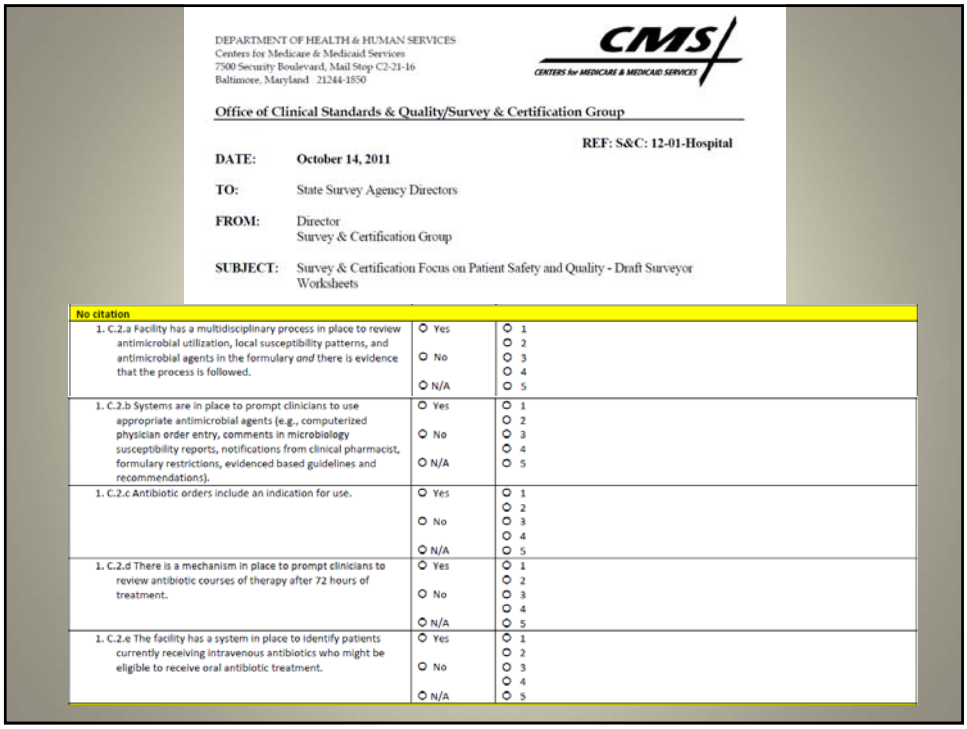
IV-PO Switch

- Patients who meet certain criteria changed to oral form with enhanced bioavailability
- Agents
  - Fluoroquinolones
  - Linezolid
  - Metronidazole
  - Clindamycin
  - Trimethoprim-Sulfamethoxazole
  - Fluconazole
- Mechanisms – what is the process and who is in charge of it
  - Computer reminders
  - Automatic switches
    - Based on pre-determined criteria
  - Pharmacist review

Major Opportunities Exist

- 128 VA medical centers 2006-2010
  - Assessed FQ use (>1.6 million FQ days therapy)
  - Considered IV avoidable if taking oral medication
  - 46.8% FQ days avoidable
  - 90.9% IV FQ days avoidable
  - Estimated cost savings $4 million
- Single center pharmacist lead conversion of IV levofloxacin to oral
  - 37% vs. 92% conversion
  - IV duration 3.5 days shorter
  - LOS 3.5 days shorter

Jones M, et al. *Infect Control Hosp Epi*. 2012;33:362.
Kuti JL, et al. *Am J Health Sys Pharm*. 2002;59:2209.



DEPARTMENT OF HEALTH & HUMAN SERVICES
Centers for Medicare & Medicaid Services
7500 Security Boulevard, Mail Stop C2-21-16
Baltimore, Maryland 21244-1850

CMS
CENTERS for MEDICARE & MEDICAID SERVICES

Office of Clinical Standards & Quality/Survey & Certification Group

REF: S&C: 12-01-Hospital

DATE: October 14, 2011

TO: State Survey Agency Directors

FROM: Director
Survey & Certification Group

SUBJECT: Survey & Certification Focus on Patient Safety and Quality - Draft Surveyor Worksheets

No citation		
1. C.2.a Facility has a multidisciplinary process in place to review antimicrobial utilization, local susceptibility patterns, and antimicrobial agents in the formulary *and* there is evidence that the process is followed.	○ Yes ○ No ○ N/A	○ 1 ○ 2 ○ 3 ○ 4 ○ 5
1. C.2.b Systems are in place to prompt clinicians to use appropriate antimicrobial agents (e.g., computerized physician order entry, comments in microbiology susceptibility reports, notifications from clinical pharmacist, formulary restrictions, evidenced based guidelines and recommendations).	○ Yes ○ No ○ N/A	○ 1 ○ 2 ○ 3 ○ 4 ○ 5
1. C.2.c Antibiotic orders include an indication for use.	○ Yes ○ No ○ N/A	○ 1 ○ 2 ○ 3 ○ 4 ○ 5
1. C.2.d There is a mechanism in place to prompt clinicians to review antibiotic courses of therapy after 72 hours of treatment.	○ Yes ○ No ○ N/A	○ 1 ○ 2 ○ 3 ○ 4 ○ 5
1. C.2.e The facility has a system in place to identify patients currently receiving intravenous antibiotics who might be eligible to receive oral antibiotic treatment.	○ Yes ○ No ○ N/A	○ 1 ○ 2 ○ 3 ○ 4 ○ 5

Potential Quality Measures

1. C.2.a Facility has a **multidisciplinary process** in place to **review antimicrobial utilization**, local susceptibility patterns, and antimicrobial agents in the formulary *and* there is evidence that the process is followed.
1. C.2.b Systems are in place to **prompt clinicians to use appropriate antimicrobial agents** (e.g., computerized physician order entry, comments in microbiology susceptibility reports, notifications from clinical pharmacist, formulary restrictions, evidenced based guidelines and recommendations).
1. C.2.c Antibiotic orders include an **indication for use**.
1. C.2.d There is a mechanism in place to prompt clinicians to **review antibiotic courses of therapy after 72 hours** of treatment.
1. C.2.e The facility has a system in place to identify patients currently receiving intravenous antibiotics who might be **eligible to receive oral antibiotic treatment**.

Proposed National Antimicrobial Stewardship Measure: Time Out

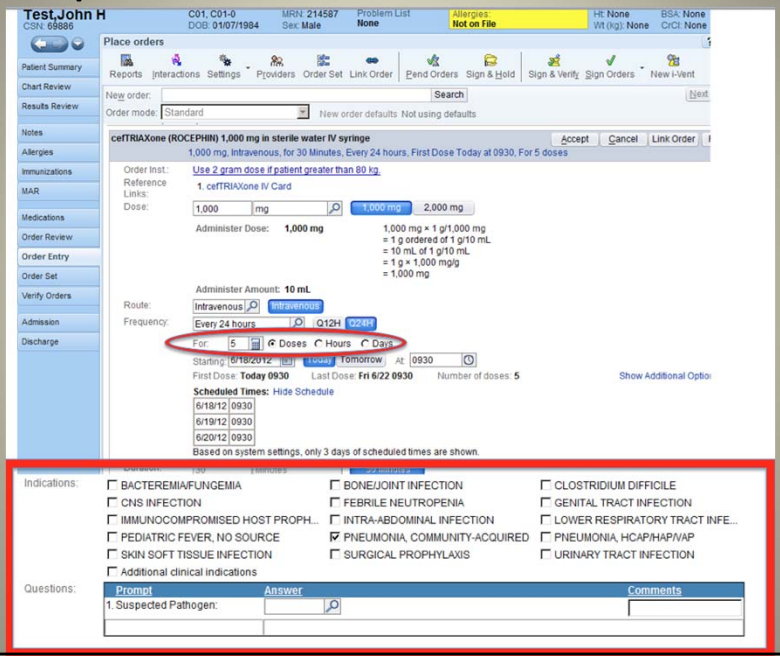
- All antimicrobial orders need:
  - Dose
  - Duration (stop date)
  - Indication
- Get cultures before starting
- Once the culture data comes back, take an antimicrobial time-out: Reassess therapy

http://blogs.cdc.gov/safehealthcare/?p=1026; accessed 3/2/11

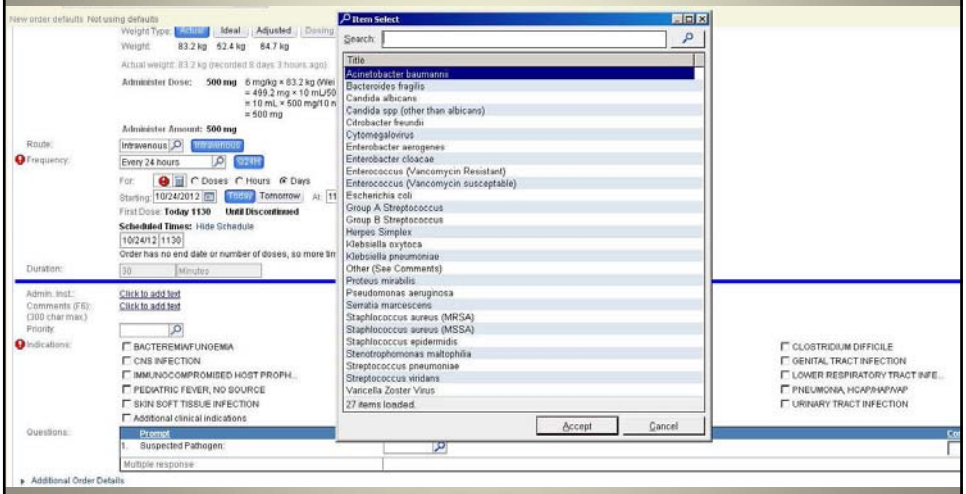
Indication (and Duration)

- Indication data use
  - Communication
  - Use patterns
    - Drug or indication
  - Stewardship analytic tool
  - Prompt therapeutic consideration
  - Regulatory??
- Duration
  - Pre-specified based on indication
  - Ordering physician specified
  - Indefinite

Required Indication and Duration



Pathogen Specific Information

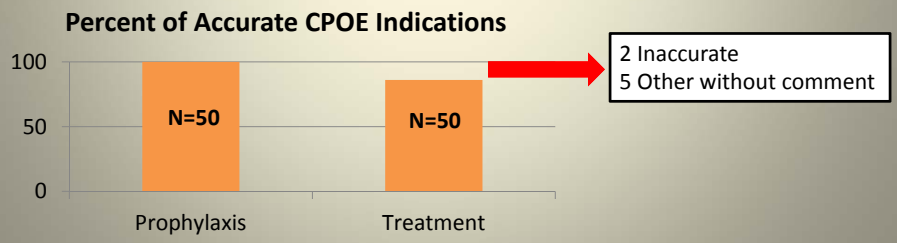


Is the Data Accurate?

- How is data entered
  - Computerized
  - Form
  - Level of Detail
  - Use of Other/fever/sepsis

Use of CPOE Indications at US Medical Center

- Clinical Review Accuracy of Prophylaxis and Treatment Indications

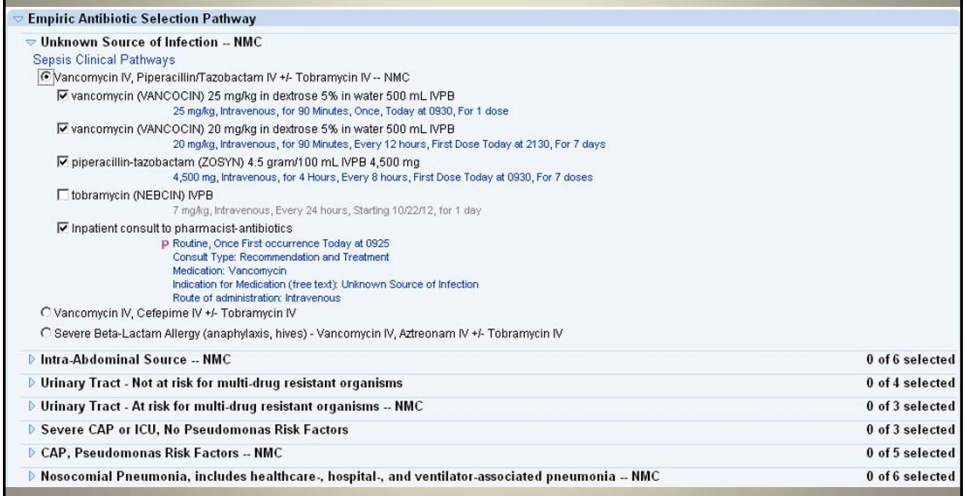


Patel JA, et al. *Infect Control Hosp Epi*. 2012;33:1066.

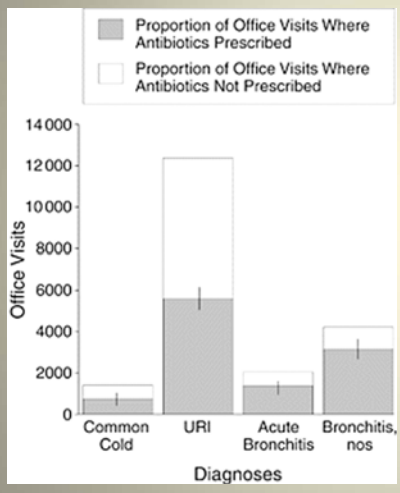
Use of CPOE to Improve Antimicrobial Selection

- Information can be integrated at the point of prescribing
  - Links to institutional/national guidelines
  - Indication/duration prompts consideration of reason and needed duration of antimicrobials
  - Integration of institutional guidelines
    - E.g. order sets for pneumonia, sepsis

Institutional sepsis order set, CPOE integration



Antibiotic Prescriptions for Children with Colds, URI, and Bronchitis

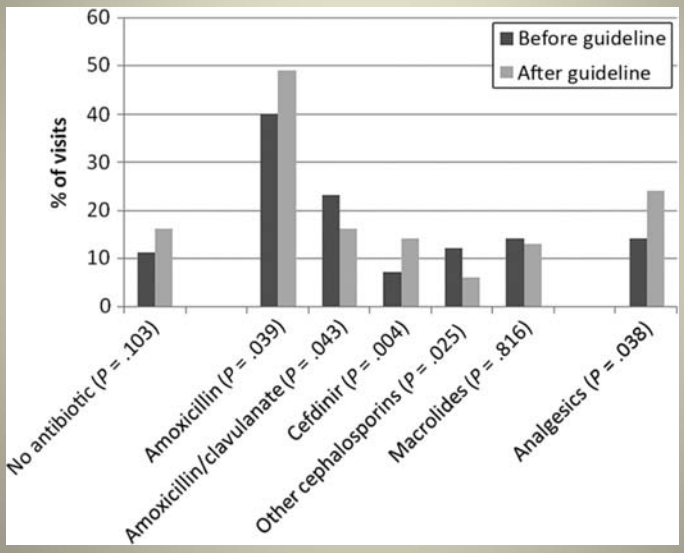


Rate of Antibiotic Prescriptions in Children and Adolescents

- Pediatric office visits for colds, URIs, and bronchitis
  - Antibiotics given in
    - 44% colds
    - 46% URI
    - 75% bronchitis
- Extrapolated to US
  - 6.5 million antibiotic prescriptions for colds and URIs
  - 4.7 million antibiotic prescriptions for bronchitis

Nyquist AC, et al. *JAMA* 1998;279:875-877.

Comparison of prescribing for AOM before and after publication of the AAP/AAFP 2004 clinical practice guideline (N = 1114)

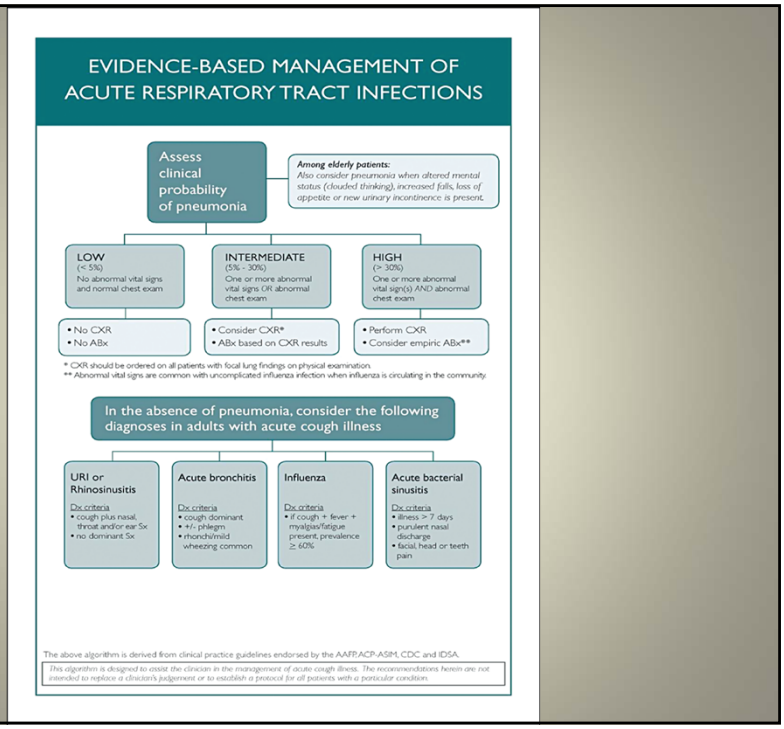


Coco A, et al. *Pediatrics* 2010;125:214-220

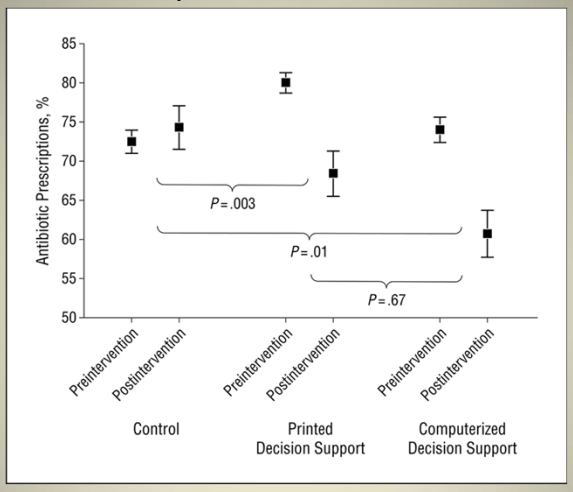
Clinic Guidelines/Education/CDS for Treatment of Bronchitis

- Primary care practices (N=33) randomized to usual care, printed CDS and electronic CDS
  - Intervention groups had education, performance feedback, clinic champion
  - Electronic CDS had specific template, order set to improve history elicitation, documentation and testing
- Adults with bronchitis during Oct-Mar for 3 years (N=9808 visits) before intervention compared to post-intervention period (N=6242 visits)

Gonzales R. *JAMA Intern Med*. 2013;173:267-73.



Antibiotic Prescription Rates for Acute Bronchitis



- Odds of antibiotic prescription decreased 36-43%
- Order set used in 20.5% encounters in CDS group
- Rates of pneumonia were low (~1%) as were ED visits and return visits within 30 days and were not different between groups

What's the Problem?

Acute Cough Illness (Acute Bronchitis)

Acute bronchitis is an acute respiratory infection with a normal chest radiograph that is manifested by cough with or without phlegm production that lasts for up to 3 weeks (*Chest* 2006;129:95S-103S).

Treatment

- Empiric antibiotic treatment is **not** indicated for acute bronchitis.
  - Meta-analyses of randomized, controlled trials all concluded that routine antibiotic treatment is not justified (*BMJ* 1998;316:906; *Chest* 2006;129:95S-103S).

http://www.cdc.gov/getsmart/campaign-materials/info-sheets/adult-acute-cough-illness.pdf

The NEW ENGLAND JOURNAL of MEDICINE

CLINICAL PRACTICE

2006;355:2125-30.

Acute Bronchitis

Richard P. Wenzel, M.D., and Alpha A. Fowler III, M.D.

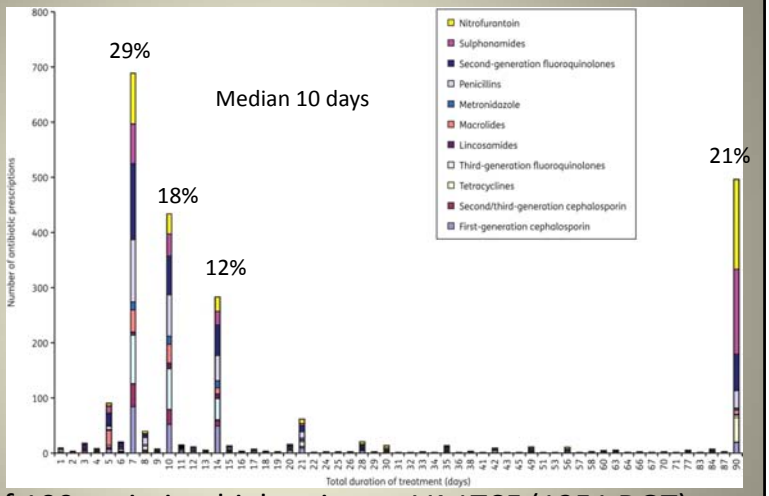
TREATMENT

Antimicrobial Therapy

Antimicrobial agents are not recommended in most cases of acute bronchitis. Systematic analyses of

Antibiotic Use in LTCF

- 5-fold difference in prescribing across facilities
- Longer course more common in high prescribing facilities



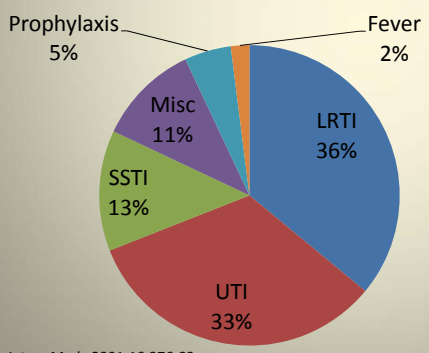
- Review of 100 antimicrobial regimens VA LTCF (1351 DOT)
  - 42 regimens considered completely unnecessary
  - 43% of DOT unnecessary

Daneman N. *J Antimicrob Chemother*. 2011;66:2856-63.
Peron EP. J Am Geriatr Soc. 2013;61:289-90.

Appropriateness of Antibiotics

- 22 LTCF over 1 year
  - 9373 antibiotic course in 2408 patients

Antibiotic Indications



Loeb M. J Gen Intern Med. 2001;16:376-83.

Most Used Agents

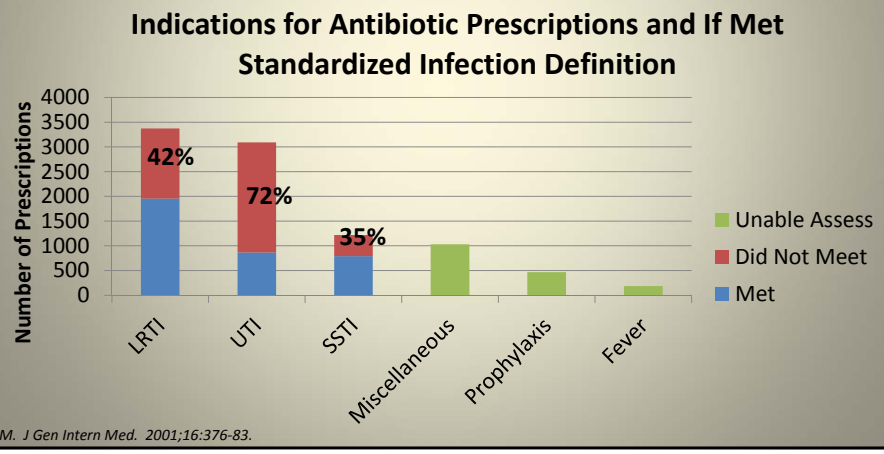
LRTI:
Ciprofloxacin
Amoxicillin
Cefuroxime

UTI:
TMP/SMX
Nor/ciprofloxacin
Amoxicillin

SSTI:
Cloxacillin
Cephalexin
Ciprofloxacin

Were Those Antibiotic Appropriate?

- 22 LTCF over 1 year
  - 9373 antibiotic courses in 2408 patients
  - 49% met surveillance definitions of infection



Loeb M. J Gen Intern Med. 2001;16:376-83.

Education

- Education is key component
- Who to educate
  - Prescribers
  - Nurses (especially in LTCF)
  - Patients??
- What method to use
  - Seminars, lectures, information sheets, guidebooks
  - Academic detailing/social marketing
  - Case-based
  - Clinical pathways

Educational Intervention at a Single LTCF

- Developed and published guidelines for asymptomatic bacteriuria
- Educated
  - Nurses regarding criteria for urine culture
  - MD's regarding appropriate situations for empiric therapy and diagnosis of symptomatic UTI

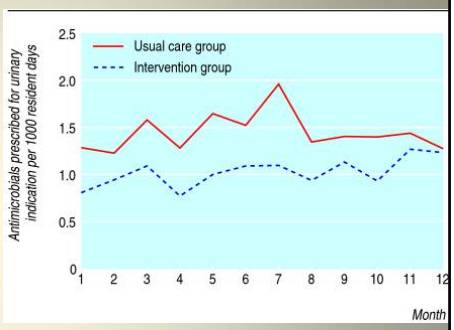
	3-Month Pre-intervention	Initial 6 months post-intervention	7-30 months post-intervention
IC %	69.4%	60.5%	45.7%
IC/1000 pt-days	2.6	0.9	0.6
ASB treated (%)	67.9%	69.2%	44.0%
ASB treated/1000 pt-days	1.7	0.6	0.3

IC=inappropriate culture, ASB=asymptomatic bacteriuria

Zabarsky. *Am J Infect Control*. 2008;36:476-80.

Randomized Trial of Education

- 24 LTCF in US, Canada
  - Randomized usual care vs. intervention
  - Targeted UTI
    - Implementation of UTI diagnostic algorithm
    - Small group training nurses
    - Written material
    - Outreach visits
    - One-on-one MD visits



- 28% reduction abx use and number of antibiotic courses

Loeb. *BMJ*. 2005;331:669-73.

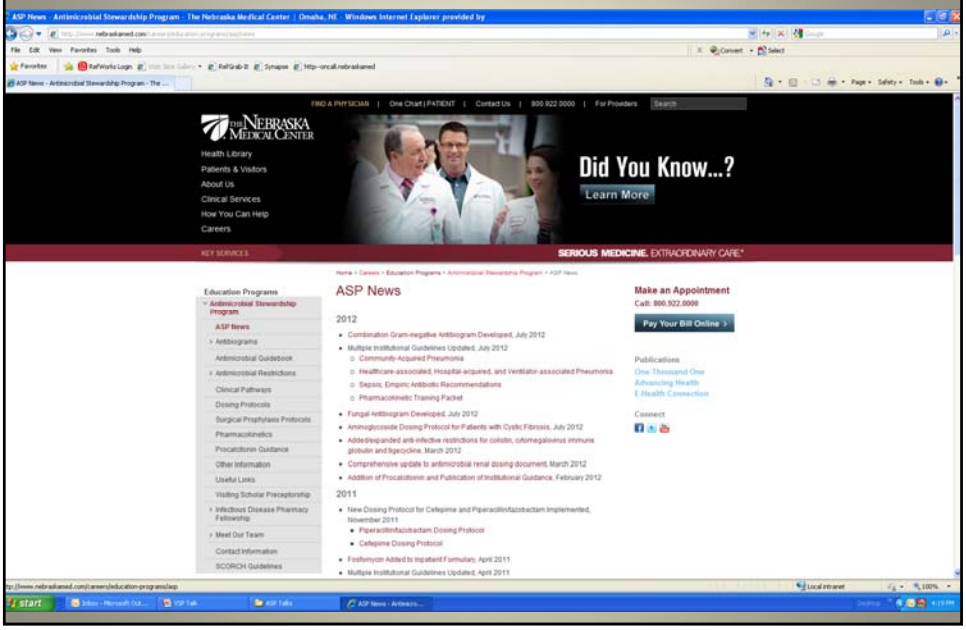
Education + Prospective Review

- Single-center patients with CAP
  - Goal improve choice and duration therapy
- Survey followed by education
  - Local performance data and evidence supporting shorter duration therapy
  - Prospective review CAP with oral feedback

	Preintervention (N=56)	Intervention (N=63)	P
Length of Stay, median, days	4	5	
Duration of Therapy, days	10	7	<.001
Excess Antibiotic Days	241	93	<.001
30-day Readmissions (%)	9 (14.5)	5 (7.7)	.22
C. difficile infection	3 (4.8)	1 (1.5)	.28

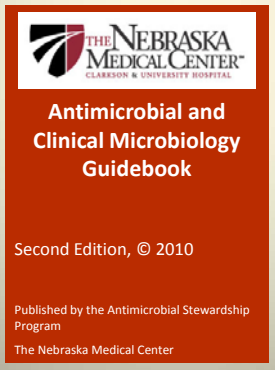
Avdic E, et al. *Clin Infect Dis*. 2012;54:1571.

Web-based



Antimicrobial Guidebook

- Joint venture with microbiology
- Now web-based
  - www.nebraskamed.com\asp

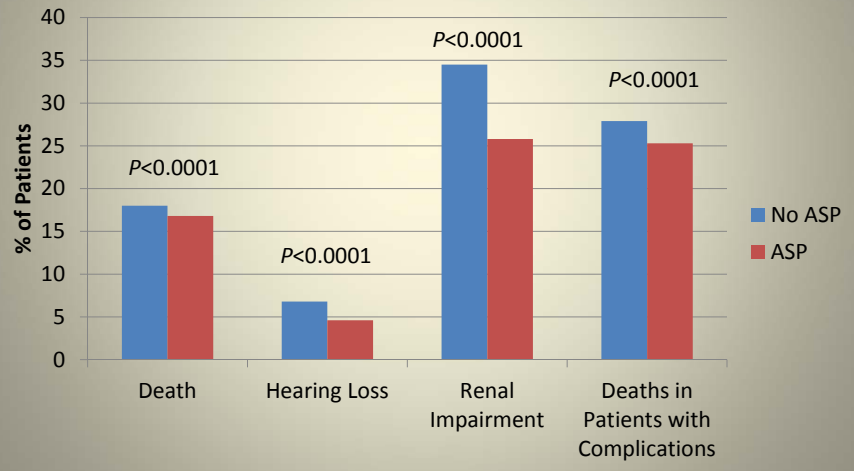


Dosing protocols

- Dose Adjustment Protocols
  - Pharmacy PK consult
  - Once-daily aminoglycoside dosing
  - Anti-infective renal dose adjustment
    - Pharmacist lead
  - Dose substitution
    - Alternate dose of cefepime, meropenem
  - Prolonged infusion
    - Piperacillin/tazobactam

Decreased Toxicity and Improve Clinical Outcomes

Clinical Outcomes for Patients Treated with Aminoglycoside or Vancomycin with and without a Pharmacist-led Antimicrobial Stewardship Program



Bond CA, Raehl CL. *Am J Health-Sys Pharm.* 2005;62:1596-1605.

Local clinical guideline development

- Multidisciplinary
- Evidence-based and integrating local microbiology
- Numerous clinical guidelines
  - Pneumonia, *C. difficile*, sepsis, skin and soft tissue infection, candidemia, surgical prophylaxis, procalcitonin guidance
  - Guidelines can address local prescribing problems

Decreased Antibiotic Utilization After Implementation of a Guideline for Inpatient Cellulitis and Cutaneous Abscess

Arch Int Med. 2011;171:1072-9.

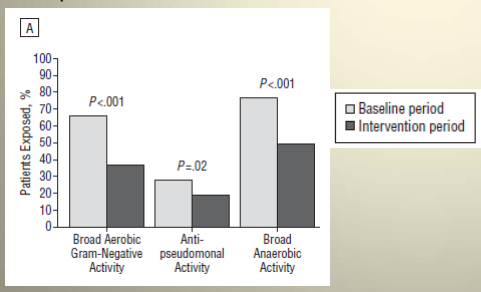
Timothy C. Jenkins, MD; Bryan C. Knepper, MPH, MSc; Allison L. Sabel, MD, PhD, MPH; Ellen E. Sarcone, MD; Jeremy A. Long, MD, MPH; Jason S. Haukoos, MD, MSc; Steven J. Morgan, MD; Walter L. Biffl, MD; Andrew W. Steele, MD, MPH, MSc; Connie S. Price, MD; Philip S. Mehler, MD; William J. Burman, MD

- Streptococci and *Staphylococcus aureus* major pathogens
  - Gram-negative, anaerobic, anti-Pseudomonal antibiotics overuse
  - Duration >14 days unecessary
- Developed treatment guideline
  - Disseminated and educated major users
  - Created CPOE order set
  - 12 months of audit and feedback
- Pre-implementation compared to post
  - Cellulitis and skin abscesses

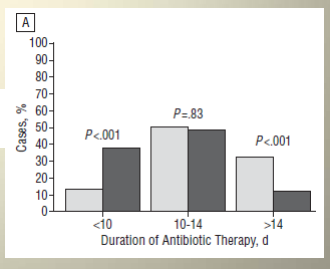
The Impact

- Staphylococci and Streptococci >95% cultures
- Imaging of cellulitis 94%→80% (*P*=.03)
- Median duration therapy 13 → 10 days (*P*<.001)
- Clinical failure no different 7.7% vs. 7.4% (*P*=.93)

Exposure to Antimicrobials



Duration of Antimicrobials



Jenkins TC. *Arch Int Med*. 2011;171:1072-9.

Get local data!

Other studies suggest FQ do not contribute meaningfully to the spectrum of antipseudomonal beta-lactams...

…What about at TNMC?

Pogue JM, et al. *Infect Control Hosp Epidemiol* 2011;32(3):289-292

Combination Antibiogram

- All ICU's
- 7/08 to 7/11
- Pathogens resistant
  - Piperacillin/tazobactam
  - Cefepime
  - Meropenem
  - Aztreonam

Percentage Susceptible to ciprofloxacin or aminoglycosides if resistant to one of the following beta-lactams			
	Pseudomonas aeruginosa	*Escherichia coli*	*Klebsiella oxytoca*
If resistant to piperacillin/ tazobactam	**(n=25)**	**(n=24)**	**(n=23)**
Ciprofloxacin	28%	17%	35%
Gentamicin	52%	71%	100%
Amikacin	76%	92%	100%
Tobramycin	88%	63%	96%
If resistant to cefepime	**(n=52)**	**(n=11)**	**(n=6)**
Ciprofloxacin	39%	0%	17%
Gentamicin	42%	82%	100%
Amikacin	77%	91%	100%
Tobramycin	89%	70%	100%
If resistant to meropenem	**(n=37)**	**0**	**0**
Ciprofloxacin	22%	-	-
Gentamicin	30%	-	-
Amikacin	81%	-	-
Tobramycin	89%	-	-
If resistant to aztreonam	**(n=148)**	**(n=22)**	**(n=35)**
Ciprofloxacin	43%	5%	37%
Gentamicin	49%	86%	100%
Amikacin	73%	-	100%
Tobramycin	86%	76%	100%

E. coli Susceptibility 2011

Organism	Drug	Inpatient % Susceptible	Outpatient % Susceptible
Escherichia coli	Amikacin	99.50%	99.70%
Escherichia coli	Ampicillin/sulbactam	50%	60.10%
Escherichia coli	Aztreonam	93.20%	96.80%
Escherichia coli	Cefepime	95%	98%
Escherichia coli	Ceftriaxone	92.40%	96.70%
Escherichia coli	Cephalothin	32.20%	44.30%
Escherichia coli	Ciprofloxacin	68%	82.30%
Escherichia coli	Ertapenem	100.00%	99.90%
Escherichia coli	Gentamicin	90%	91.80%
Escherichia coli	Piperacillin/tazobactam	89.70%	95.60%
Escherichia coli	Trimeth/sulfa	77.70%	92.20%

Conclusions

- Addition of FQ does not add much coverage (0-43%)
- Tobramycin is the most active agent against *Pseudomonas aeruginosa* (86-89%)
- With *E. coli* (and other *Enterobacteracieae*) gentamicin and amikacin are more active
  - Amikacin is on shortage and thus gentamicin is recommended

Conclusions

- Most patients do not require empiric combination Gram-negative therapy
  - Decision to use should be based on severity of illness, the likelihood of resistance, and potential for drug toxicity
    - Appropriate in severe illness (septic shock), history or resistance
  - Aminoglycoside nephrotoxicity reversible and infrequent with short courses (<5 days)
    - Extended-interval dosing reduces toxicity and maximizes efficacy
  - Fluoroquinolones, while less toxic are less active and associated with *C. difficile* colitis
- Combination therapy should be routinely deescalated to a single agent once susceptibility results are known

Conclusions

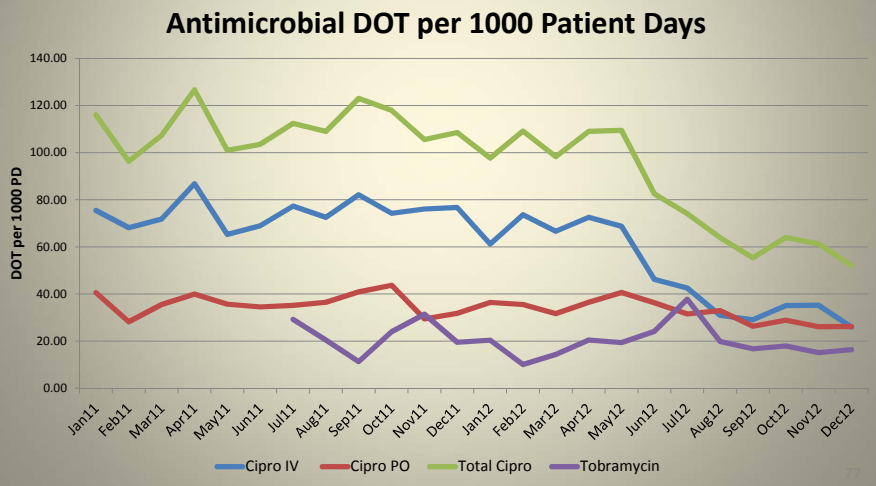
- From our local combination and single drug antibiograms, ciprofloxacin should never be used empirically!!!
- Local data is very compelling to prescribers!
- Guideline development and education of key groups

Sepsis Treatment Guidelines

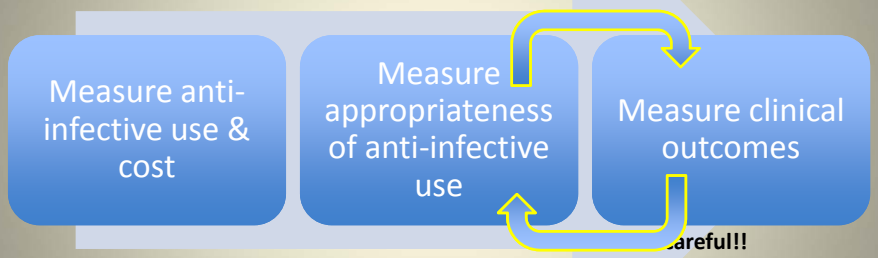
Suspected Source of Infection	Suggested Antibiotics
Unknown (includes catheter related blood stream infection) ‡ ‡Consider Micafungin 100mg IV qday in patients at high risk for invasive candidiasis. Major risk factors predicting candidemia at TNMC include: 1) Broad-spectrum antibiotics, 2) Central venous catheter, 3) Receipt of TPN, 4) Abdominal surgery, and 5) Steroid use. Presence of 2 or fewer of the risk factors suggests a 99.4% chance of **not** developing candidemia, while patients with >2 risk factors have a 4.7% risk of developing candidemia. See Institutional Guidelines for the Treatment of Invasive Candidiasis for further information	Vancomycin IV per pharmacy consult (initial 25mg/kg loading dose) **PLUS EITHER** Piperacillin/tazobactam 4.5g IV q8h, infused over 4 hours **OR** Cefepime 1 gm IV q6hr **+/-** Tobramycin 7 mg/kg IV EIAD Severe beta-lactam allergy (anaphylaxis, hives): Vancomycin IV per pharmacy consult (initial 25mg/kg loading dose) **PLUS** Aztreonam 2 gm IV q8h **+/-** Tobramycin 7 mg/kg IV EIAD
Intra-abdominal Source	Piperacillin/tazobactam 4.5g IV q8h, infused over 4 hours **OR** Cefepime 1g q6h hours **PLUS** Metronidazole 500 mg IV q8h **+/-** Gentamicin **OR** Tobramycin 7 mg/kg IV EIAD **+/-** Vancomycin per pharmacy consult (initial 25mg/kg loading dose) Severe beta-lactam allergy (anaphylaxis, hives): Vancomycin per pharmacy consult (initial 25mg/kg loading dose) **PLUS** Aztreonam 2gm IV q8h **PLUS** Metronidazole 500 mg IV q8h **+/-** Gentamicin **OR** Tobramycin 7 mg/kg IV EIAD

Institutional Sepsis Order Set: CPOE integration

Effect of combination antibiogram, education & new guideline implementation



Antimicrobial stewardship outcome metrics



- Drug purchases
- Anti-infective tonnage
- Anti-infective cost/pt day
- Anti-infective RX rate
- DDD/1000 pt days
- DOT/1000 pt days
- LOT/1000 pt days

- Empiric & definitive therapy
  - Local guideline adherence
  - Susceptibility mismatch
  - Redundant anaerobic
  - Most active therapy
  - Deescalation
- Time to active therapy

Careful!!

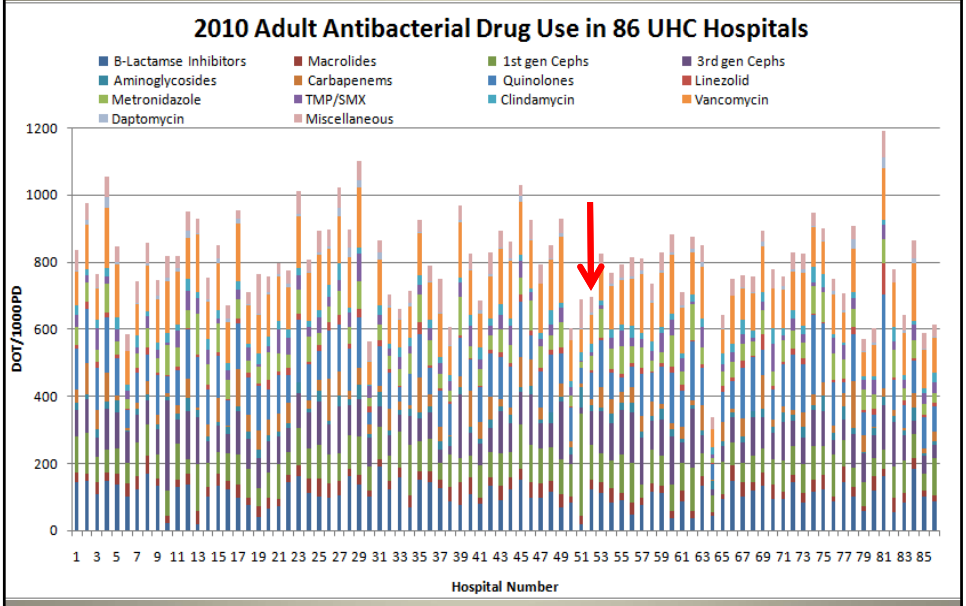
- Mortality
- Length of stay
- Readmission
- Resolution of infection
- Adverse events
- Antibiogram changes
- *C. difficile* infection rates

DDD, defined daily dose; DOT, days of therapy; LOT, length of therapy

Benchmarking

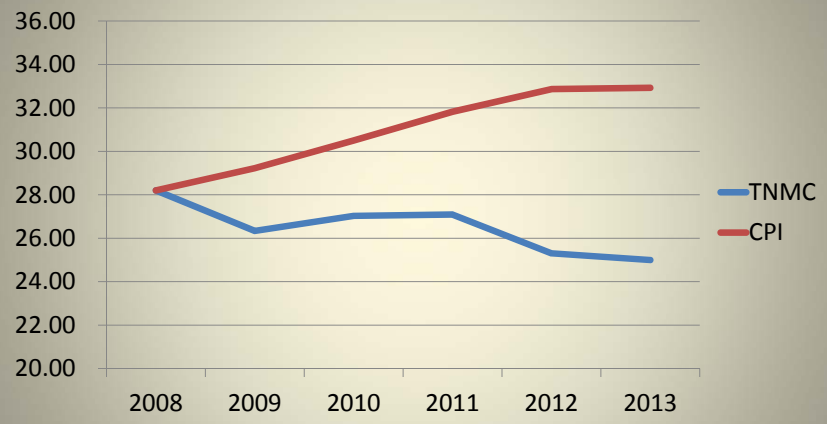
- Tracking local antimicrobial usage and comparing to hospitals with similar patient populations
  - Ideally incorporates risk adjustment
    - Bed size, case mix, patient populations
- DDD/1000 patient days or DOT/1000 patient days
- CDC/NHSN AUR module
  - Goal to provide risk-adjusted intra- and inter-hospital antimicrobial usage benchmarking in DOT/1000 pt days
  - Administered level data
  - No manual data entry

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION



Ron Polk, personal communication
Polk RE, et al. *Clin Infect Dis.* 2011 Dec;53(11):1100-10.

Antimicrobial cost per patient day



- FY 2012 roughly $3,700,000 spent on antimicrobials
- Estimated $1,080,000 in antimicrobial costs compared to CPI (~$8 per PD)

Conclusions

- Antimicrobials use drives resistance and antimicrobial stewardship is essential to maintaining their activity
- Numerous opportunities exist to improve antimicrobial use across the spectrum of care
- Implementation of antimicrobial stewardship practices can improve use


Questions?
DURHAM RESEARCH CENTER II
DURHAM RESEARCH CENTER