

Impact of Antibiotic Guidelines at NYPH-CUMC

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- Implementation of NYPH Guidelines for the Empiric Use of Antibiotics in Adult Patients
- Pilot project to evaluate its impact

Antimicrobials

- 20-50% of hospital pharmacy drug expenditures
 - Costs also associated with preparation, administration, and monitoring
- In the U.S., antimicrobial use has resulted in costs >\$7 billion annually
 - Up to \$4 billion used for treatment of more resistant hospital-associated infections
- Antimicrobials may often be unnecessary and inappropriate
- Unnecessary use increases the risk for adverse events

Kubin CJ. *Seminars in Perinatology* 2002; 26 (5): 379-86.

Kunin CM. *J Infect Dis* 1985; 151: 388-98.

Kislak JW et al. *N Engl J Med* 1964; 271: 834-35.

Yates RR. *Chest* 1997; 25: 584-99.

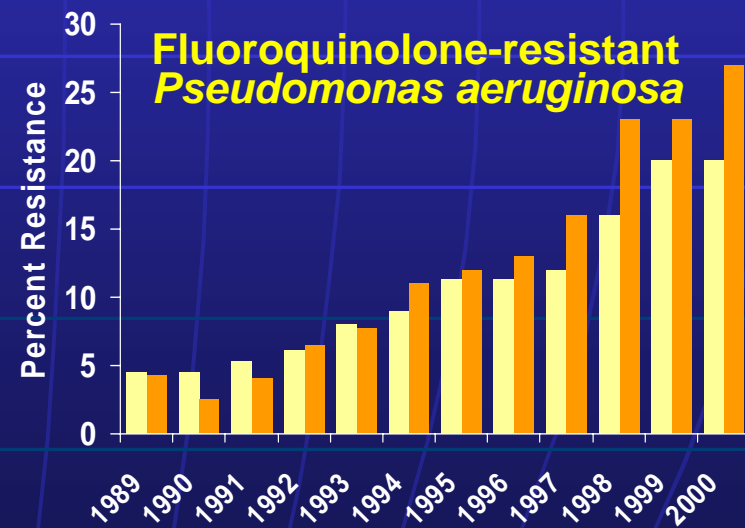
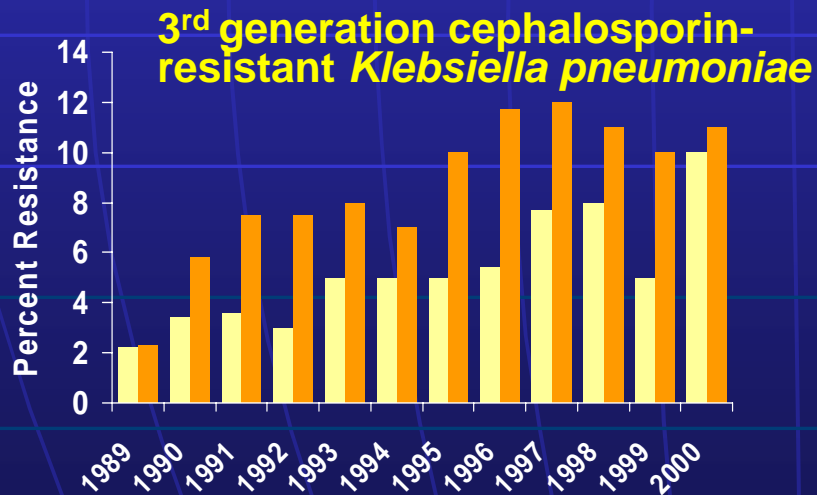
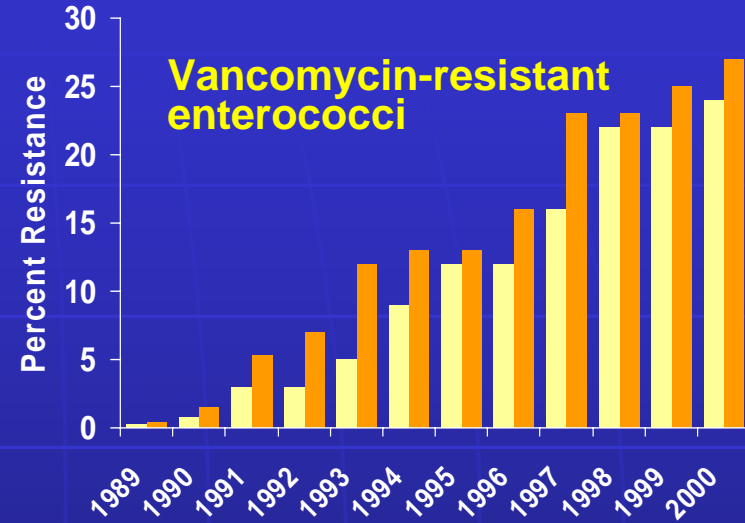
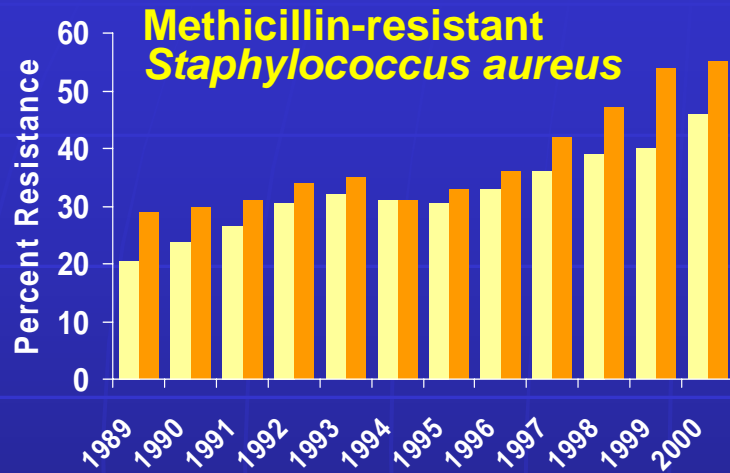
John JF et al. *Clin Infect Dis* 1997; 24: 471-85.

Saez-Llornes X et al. *Pediatr Infect Dis J* 2000; 19: 200-6.

Reasons to Control Antimicrobial Use

- Cost
- Efficacy/safety
- Resistance

Increasing Resistance in ICU Pathogens



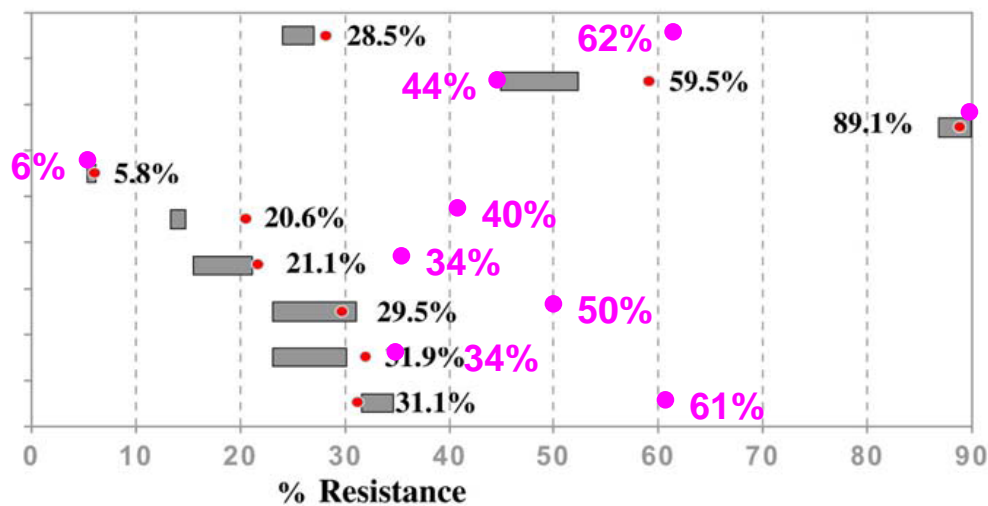
Non-Intensive Care Unit Patients
 Intensive Care Unit Patients

Source: National Nosocomial Infections Surveillance (NNIS) System (www.cdc.gov)

Selected Antimicrobial-resistant Pathogens in ICU Patients – Comparison of 2003 with 1998 through 2002

NYPH-CUMC (2004)

Vancomycin/enterococci
 Methicillin/*S. aureus*
 Methicillin/CNS
 3rd Ceph/*E. coli***
 3rd Ceph/*K. pneumoniae***
 Imipenem/*P. aeruginosa*
 Quinolone/*P. aeruginosa*
 3rd Ceph/*P. aeruginosa*
 3rd Ceph/*Enterobacter* spp.



• January through December 2003
 ■ 1998 through 2002 (+/- standard deviation)*

Jan–Dec 2003 No. of Isolates	% increase in resistance (2003 vs 98-02*)
2048	12%
4100	11%
3336	1%
1355	0%
1068	47%
1392	15%
1825	9%
2119	20%
1411	–6%

Multidrug-resistant *Klebsiella pneumoniae* Outbreak

- ~100 patients infected or colonized with “J” clone since August 2004
- Crude mortality 33%
- Some isolates resistant *in vitro* to all available antibiotics

LIGHT GROWTH OF KLEBSIELLA PNEUMONIAE

METHOD: MICROSCAN MIC

<u>AMI</u>	<u>A/S</u>	<u>CFZ</u>	<u>CPM</u>	<u>CFT</u>	<u>CEZ</u>	<u>CTX</u>	<u>CRM</u>	<u>CIP</u>	<u>GEN</u>	<u>IMP</u>	<u>LVX</u>	<u>P/T</u>	<u>TIM</u>	<u>TOB</u>	<u>T/S</u>	<u>PIP</u>
32 I	>16/8 I	>16 R	>16 R	>32 R	>16 R	>32 R	>16 R	>2 R	>8 R	>8 R	>4 R	>64 R	>64 R	>8 R	>2/38 R	>64 R

LIGHT GROWTH OF KLEBSIELLA PNEUMONIAE

METHOD: E-TEST MIC

<u>IMP</u>	<u>MER</u>	<u>COLISTIN</u>
32 R	>32 R	24 R

Antibiotic Use and Resistance

What we know...


- Resistance can spread via poor infection control practices
- Resistance develops following antibiotic exposure (antibiotic selective pressure)
 - Longer duration of therapy associated with subsequent infections with resistant bacteria
- Certain antibiotics associated with more rapid development of resistance
 - Quinolones
- Antibiotics associated with “collateral damage”
 - Cephalosporins
 - VRE, ESBL-producing *K. pneumoniae*, *C. difficile*, beta-lactam resistant *A. baumannii*
 - Quinolones
 - MRSA, quinolone-resistant organisms including *P. aeruginosa*

Antimicrobial Control Program at NYPH-CUMC


- Current methods of antimicrobial control
 - Formulary restriction
 - Limited effects on stabilizing antimicrobial resistance
- Future methods of antimicrobial control
 - Formulary restriction
 - **Treatment guidelines**
 - De-escalation therapy
 - Limiting duration of therapy
 - Automated epidemiology and antibiotic use

Guidelines for the Empiric Use of Antibiotics in Adult Patients


- Developed by Infectious Diseases, Epidemiology, Pharmacy, Microbiology
- Based on local resistance and antibiotic use patterns
- Implementation May 2005
 - Education
 - Website
- Updated periodically



Division of
Infectious Diseases



New York-Presbyterian
The University Hospital of Columbia and Cornell



COLUMBIA UNIVERSITY
MEDICAL CENTER

EMPIRIC ANTIBIOTIC THERAPY GUIDELINES: CNS

COMMON TYPES OF INFECTIONS	DEFINITIONS / USUAL ORGANISMS	MODIFYING FACTORS	PRIMARY ANTIBIOTIC THERAPY RECOMMENDED	ALTERNATIVE ANTIBIOTIC THERAPY	DURATION OF THERAPY (combined IV + PO therapy)
MENINGITIS^{1a}	<i>S. pneumoniae</i> , <i>N. meningitides</i> , <i>H. influenzae</i>	Community-acquired (18-50 yrs old, not immunocompromised)	Ceftriaxone IV + Vancomycin IV	If PCN-allergic ^{1b} : Vancomycin IV + Aztreonam IV + TMP/SMX IV	10 days
	<i>S. pneumoniae</i> , <i>N. meningitides</i> , <i>Listeria monocytogenes</i> , gram-negative bacilli	Community-acquired (>50 yrs old or immunocompromised or pregnant)	Ceftriaxone IV + Vancomycin IV + Ampicillin IV	If PCN-allergic ^{1b} : Vancomycin IV + Aztreonam IV + TMP/SMX IV	10 days
	<i>S. aureus</i> , <i>S. epidermidis</i> , gram negative bacilli, <i>P. aeruginosa</i>	Post-neurosurgery	Cefepime IV + Vancomycin IV	If PCN-allergic ^{1b} : Vancomycin IV + Aztreonam IV + Levofloxacin IV (OR Tobramycin IV^{1c})	7-14 days

^{1a} An ID Consult should be considered for all patients with meningitis.

^{1b} In patients with less severe PCN-allergies (e.g. mild rash in the absence of both Stevens-Johnson syndrome and anaphylaxis), treatment with a third- or fourth- generation cephalosporin or a carbapenem antibiotic may be possible and in some situations may be necessary. ID Consult recommended to evaluate risk/benefit.

^{1c} Intravenous aminoglycoside penetration into the CSF is generally suboptimal for treatment of gram-negative meningitis/ventriculitis. Intrathecal/intraventricular aminoglycoside administration may be necessary. ID consult recommended.

Basic Principles of Empiric Antibiotic Guidelines

- Optimize antibiotic use based on resistance trends and slow the development of resistance
 - Narrow spectrum of antibiotics where possible
 - Limit duration of therapy
 - Limit the following:
 - Cephalosporins
 - Quinolones
- Serve as an educational tool

Evaluation of Impact of Empiric Antibiotic Guidelines

Impact of Guidelines on:

1. Clinician perception/knowledge of antimicrobial resistance
2. Antibiotics
 - Utilization
 - Cost
3. ****Antimicrobial resistance**
4. Patient outcomes

1. Clinician perception

- 5-minute survey to medical, surgical housestaff
 - Perception of antibiotic resistance at CUMC
 - Knowledge of empiric antibiotic use
- Compare perception and knowledge before and after guideline implementation

2. Antibiotic utilization/cost

- Assess antibiotic utilization as:
 - Usage (defined daily doses/1000 patient-days)
 - Cost (\$)
- Compare pre- and post- guideline implementation
 - t-test
 - Segmented regression analysis in an interrupted time series design
 - Antibiotic usage at 12 monthly time points before intervention will be compared to 12 monthly time points after intervention
 - Least squares regression line will be fit to 2 time periods and t-statistic computed for change in trend

3. Antimicrobial resistance

- Assess % susceptibilities for selected organisms
 - % *Staphylococcus aureus* susceptible to methicillin
 - % gram-negative organisms (*E. coli*, *P. aeruginosa*, *K. pneumoniae*) susceptible to:
 - Quinolones
 - Cephalosporins
 - Piperacillin/tazobactam
 - Aminoglycosides
 - Carbapenems
- Compare pre- and post- guideline implementation
 - Chi-square
 - Segmented regression analysis
 - 4 3-month time intervals before – 4 3-month intervals after

4. Patient outcomes

- Hospital-wide measures
 - In-hospital mortality (# deaths/1000 patient-days)
 - Hospital length of stay
 - ICU mortality
 - ICU length of stay
- Susceptibility-to-antibiotic match-mismatch
 - Computerized query to match all positive cultures to the antibiotic patient received 7 days before culture date
- Selected chart review
 - Patients on empiric therapy
 - Assess adherence to guidelines
 - Ascertain reasons for nonadherence or therapy switches

Preliminary results

1. Clinician perception (baseline)

- Anonymous survey administered to
 - 23 medicine housestaff
 - 9 critical care staff (fellows, residents, PAs, students, pharmacists)
 - As part of conferences on antibiotic resistance and guidelines

Survey on Antibiotics

Medicine Housestaff Survey on Antibiotics Part 1 May 4, 2005

Please mark the most appropriate response for each question:

1. Physicians overprescribe antibiotics.

Strongly disagree 1	Disagree 2	Neutral 3	Agree 4	Strongly agree 5
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2. Physicians at CUMC overprescribe antibiotics.

Strongly disagree 1	Disagree 2	Neutral 3	Agree 4	Strongly agree 5
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3. The current state of antibiotic resistance at CUMC is a serious problem.

Strongly disagree 1	Disagree 2	Neutral 3	Agree 4	Strongly agree 5
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4. When choosing antibiotics for a patient, their impact on future antibiotic resistance in the patient should be taken into account.

Strongly disagree 1	Disagree 2	Neutral 3	Agree 4	Strongly agree 5
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5. When choosing antibiotics for a patient, their impact on future antibiotic resistance in the institution should be taken into account.

Strongly disagree 1	Disagree 2	Neutral 3	Agree 4	Strongly agree 5
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6. Antibiotic management programs are beneficial to hospitals.

Strongly disagree 1	Disagree 2	Neutral 3	Agree 4	Strongly agree 5
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7. The antibiotic preapproval system at CUMC is effective in decreasing antibiotic resistance.

Strongly disagree 1	Disagree 2	Neutral 3	Agree 4	Strongly agree 5
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8. More judicious use of antibiotics would decrease antibiotic resistance.

Strongly disagree 1	Disagree 2	Neutral 3	Agree 4	Strongly agree 5
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Medicine Housestaff Survey on Antibiotics Part 2 May 4, 2005

For each question, please choose the most appropriate antibiotic regimen from the choices listed.

1. A 49-year-old female is admitted for chest pain. In ED, U/A showed +leuk esterase/ nitrites with 15-20 WBC/hpf. On questioning, pt admits to a 5-day h/o dysuria, urinary frequency, and mild suprapubic pain. She is not taking any medications. She is afebrile with stable vital signs and physical exam is unremarkable.

- a) levofloxacin
- b) trimethoprim/sulfamethoxazole
- c) cephalexin
- d) no antibiotics

2. A 68-year-old male was admitted for MI and underwent emergent cardiac catheterization with stenting. On hospital day #5 he complains of urethral discomfort and urine from his foley is sent off. Urinalysis is negative, urine micro showed 3-5 WBC/hpf, and urine culture grew Enterococcus faecalis, sensitive to ampicillin but resistant to vancomycin.

- a) ampicillin
- b) vancomycin
- c) linezolid
- d) no antibiotics

3. A 59-year-old morbidly obese male with COPD, poorly adherent to medications, is admitted with dyspnea and an increased cough productive of thick brownish sputum. T 99.2 BP 148/80, HR 92, RR 32, O2 sat 88% on room air. Physical exam is notable for decreased breath sounds, poor air movement. CXR is a poor quality film due to pt's obesity but is suggestive of slightly increased interstitial markings.

- a) ceftriaxone+azithromycin
- b) levofloxacin
- c) azithromycin
- d) no antibiotics

4. A 71-year-old female nursing home resident with hypertension and COPD was admitted for diverticulitis and treated with piperacillin/tazobactam for 7 days. She was discharged back to the nursing home afebrile and feeling well.

3 days later she is brought back to the ED with fevers, lethargy, and respiratory distress. T 101.2, BP 85/40, HR 112, RR 36, O2 sat 80% on room air. CXR shows a new large RLL infiltrate. She quickly decompensates and is admitted to the MICU intubated and on pressors. You decide to give her vancomycin+imipenem+ 1 dose of tobramycin, given her recent hospitalization and antibiotics. 3 days later she is much improved, still intubated but off pressor support. Her blood cultures are negative but her admission sputum culture shows many polys on gram stain and grows Klebsiella sensitive to piperacillin/tazobactam, imipenem, and tobramycin.

What antibiotic regimen should you give at this point?

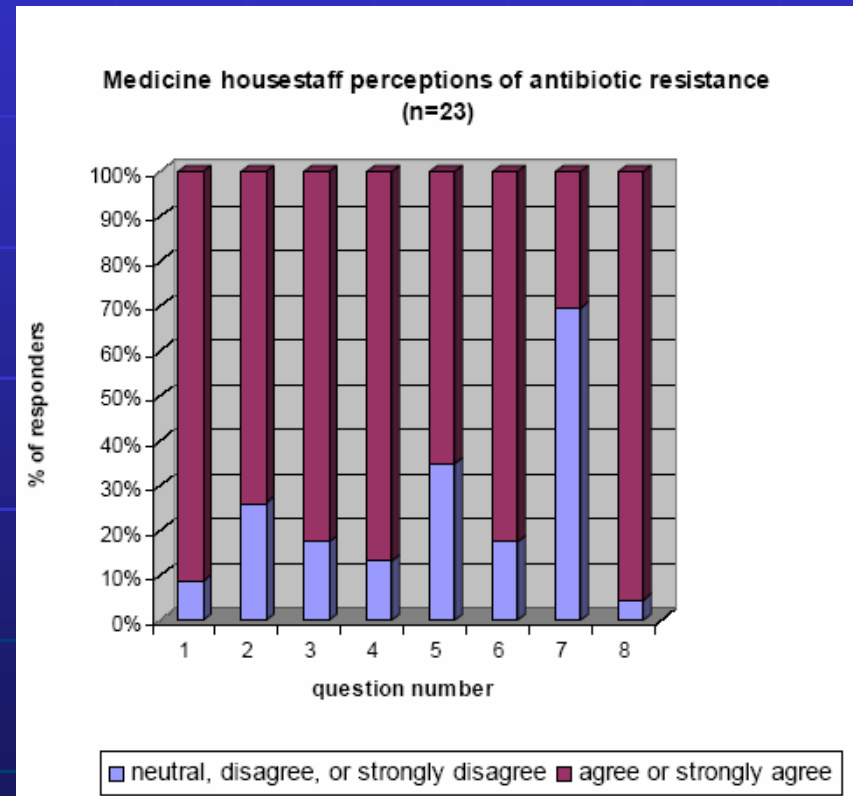
- a) Continue vancomycin + imipenem
- b) Continue imipenem but discontinue vancomycin
- c) Switch to piperacillin/tazobactam alone
- d) Switch imipenem to piperacillin/tazobactam but continue vancomycin

Assuming she continues to respond, how long should you treat her?

- a) 5 days
- b) 7 days
- c) 14 days
- d) until she is extubated

Medicine housestaff survey: perceptions

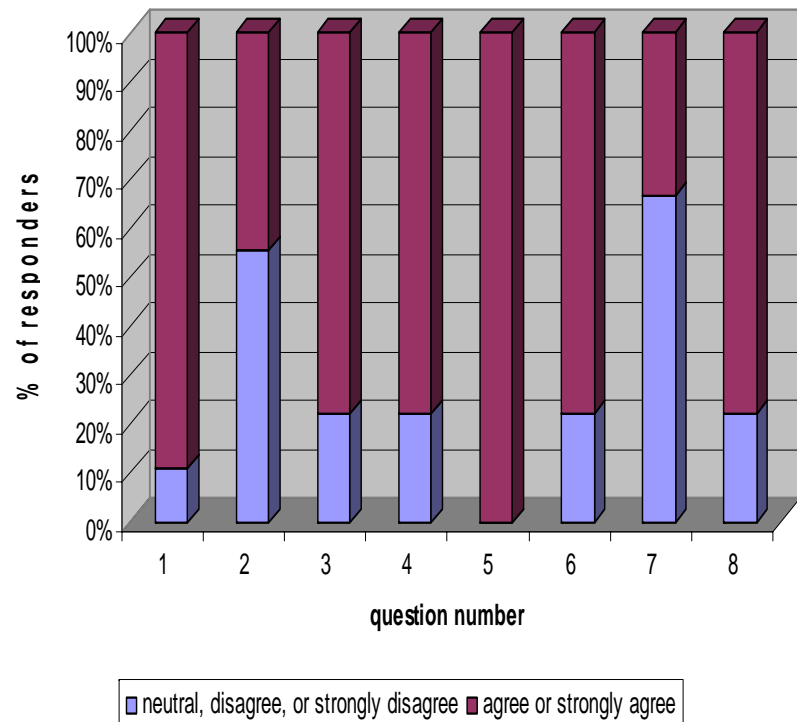
1. Physicians overprescribe antibiotics.
2. Physicians at CUMC overprescribe antibiotics.
3. The current state of antibiotic resistance at CUMC is a serious problem.
4. When choosing antibiotics for a patient, their impact on future antibiotic resistance in the patient should be taken into account.
5. When choosing antibiotics for a patient, their impact on future antibiotic resistance in the institution should be taken into account.
6. Antibiotic management programs are beneficial to hospitals.
7. The antibiotic preapproval system at CUMC is effective in decreasing antibiotic resistance.
8. More judicious use of antibiotics would decrease antibiotic resistance.



Critical care staff survey

1. Physicians overprescribe antibiotics.
2. Physicians at CUMC overprescribe antibiotics.
3. The current state of antibiotic resistance at CUMC is a serious problem.
4. When choosing antibiotics for a patient, their impact on future antibiotic resistance in the patient should be taken into account.
5. When choosing antibiotics for a patient, their impact on future antibiotic resistance in the institution should be taken into account.
6. Antibiotic management programs are beneficial to hospitals.
7. The antibiotic preapproval system at CUMC is effective in decreasing antibiotic resistance.
8. More judicious use of antibiotics would decrease antibiotic resistance.

Critical care staff perceptions of antibiotic resistance
(n=9)



1. Clinician perception (baseline)

- Most surveyed clinicians feel antibiotics are overprescribed (although less so at CUMC)
- Most feel the antibiotic preapproval system is NOT effective in decreasing antibiotic resistance
- Most feel more judicious antibiotic use would reduce resistance

Knowledge of Antibiotic Use

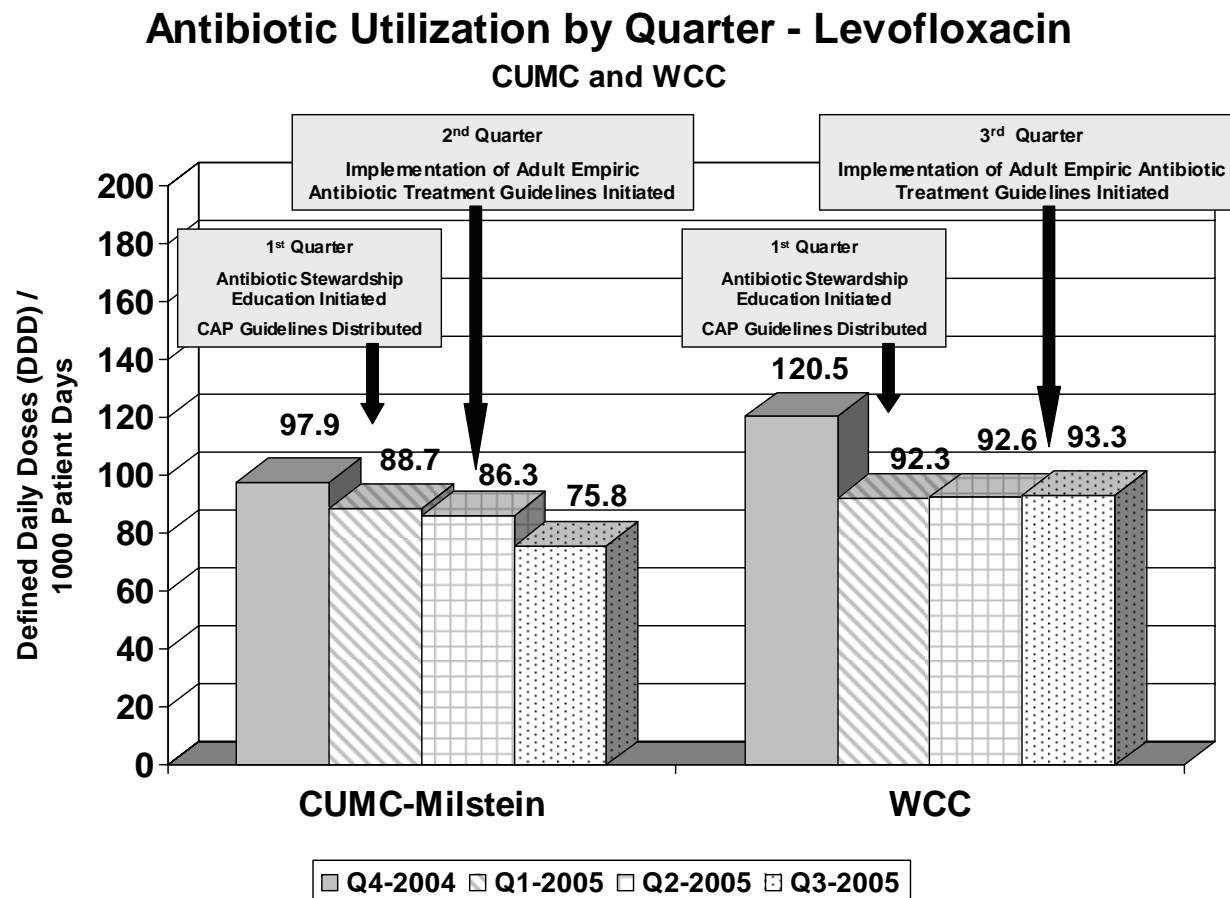
- Questions based on new recommendations in guidelines
- Medicine: 33%
- Critical care: 44%

- Room for improvement at followup survey

2. Impact on antibiotic utilization

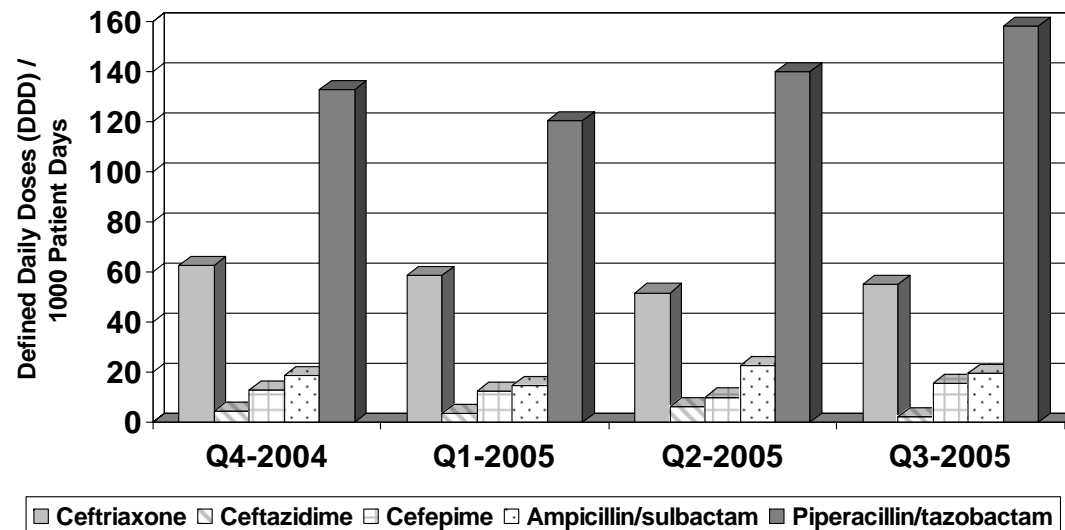
- Currently have partial quarterly results for a number of antibiotics
- Needs to be broken down into smaller intervals for statistical analysis

Antibiotic utilization - levofloxacin



Antibiotic utilization – cephalosporins vs. beta-lactams

Antibiotic Utilization by Quarter -
Broad Spectrum Cephalosporins and
Beta-Lactam/Lactamase Inhibitors
CUMC



Antibiotic utilization

- Guidelines may be having some impact on antibiotic utilization
- Awaiting statistical analysis

Moving forward

- More work to do
- Data gathering, monitoring, and statistical analysis
- Guidelines must be continually publicized and reinforced

Thank you

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