

Antimicrobial Stewardship Getting Started and Moving Forward

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Objectives

- To distinguish the important elements of developing an Antimicrobial Stewardship Committee (AMSC)
- To describe the potential measurements for your AMSC
- To plan with a gap analysis checklist

Why Should we be Worried about Antibiotic Use?

- Change in antibiotic use in Ontario Hospitals from 2001 to 2003
 - % change in DDD has shown an increase by 10% year over year
- For MRSA, 1 patient every 30 minutes is acquiring MRSA and 1 patient gets an MRSA infection every 1.5 days

CAN-R

- Canadian Antimicrobial Resistance Alliance (CARA) (www.can-r.com)
- Published the CANWARD study in 2007
 - Surveillance data
 - Antibiotic use data
 - Practice guidelines

CANWARD 2008

ESKAPE Pathogens in Canada

- VRE (*E faecium*) 3.1%
- ESBL *K.pneumoniae* 3.2%
- *A. baumannii* (IMP-R) 7.7%
- *P. aeruginosa* (MER-R) 9.6%
- *Enterobacter* spp (CAZ-R) 13.2%
- MRSA 27.0%
- “Bad Bugs”, No Drugs: No ESKAPE

Canadian Bacterial Surveillance Network: Antimicrobial Resistance Data

Data source

- A sample of clinical labs serving Canadian hospitals and communities voluntarily submit bacterial isolates
- Dilution testing is performed at Mount Sinai hospital lab
- CLISI published breakpoints are used to convert MIC values into sensitive, intermediate and resistant categories for each antibiotic
- Data is entered into a central database that is available at:
- <http://microbiology.mtsinai.on.ca/research/cbsn/default.asp>

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The Goal of Antimicrobial Stewardship Programs

- To promote the appropriate use of antimicrobials
 - The right selection, duration, dose, timing and route of administration
- To improve clinical outcomes
 - By reducing the emergence of resistance
 - By limiting drug related adverse effects
 - By minimizing the risk of unintentional consequences
 - Eg *C. difficile* infection
- The combination of effective antimicrobial stewardship with a comprehensive infection control program has been shown to limit the emergence and transmission of antimicrobial-resistant bacteria

Dellit TH et. Al CID 2007; 44(2):159-77,

Drew RH J Manag Care Pharm 2009; 15(2 suppl)S18-23;

Drew RH et al Pharmacotherapy 2009; 29(5):593-607.

Antimicrobial Stewardship

- The goal of antimicrobial stewardship involves more than just selecting the right drug
- Consider
 - Antibiotic activity, toxicity, width of spectrum
 - Medical history and allergies of your patient
 - Organisms commonly seen in your institution
 - Resistance patterns at your practice site
- Manage the costs of treatment

Paradigm

- Pharmacists and other HCP are trained to assess drug-related problems in individuals, recommend interventions in individuals, monitor outcomes in individuals
- Antibiotics are different – their use in individual patients can impact outcomes in population
- Therefore antimicrobial stewardship has to have both individual and population-based components and a CLEAR VISION of program goals and targets

Difficulty of Initiating Antimicrobial Stewardship Programs

- It is easy to quantify the extra cost of ASP
- It is difficult to estimate the incremental benefit

IDSA/SHEA Guidelines

- Guidelines for developing an institutional program to enhance antimicrobial stewardship
- Lists core members
- Elements of the program
- Comments of value of each element of the program

Antimicrobial Stewardship Teams

- Infectious disease physician
- Clinical Pharmacist with ID training
- Support of hospital administration, medical staff leadership
- Infection control
- Hospital epidemiologist
- Information system specialist
- Clinical microbiologist

Antimicrobial Stewardship Teams

- $\frac{1}{4}$ of programs with no MD or Pharm D involved
- Salaries not increased when more antimicrobial stewardship responsibilities were added

Core Elements

- There are 2 core strategies both proactive that provide the foundation for the Antibiotic Stewardship (ABS) program
- Prospective audit with intervention and feedback
- Formulary restriction and preauthorization
- These are not mutually exclusive

Choosing A Primary Approach

Prospective Audit

- Very time intensive
- Provide education to providers
- More consistently evaluated in studies of stewardship

Restriction and preauthorization

- Easier to carry out with only 1 staff
- Sustainable effort that can target resistance at once
- Hard to say NO

Strategies

- Elements that may be considered as supplements to the core active antimicrobial stewardship strategies
 - Education
 - Guidelines and clinical pathways
 - Antimicrobial order forms
 - Combination therapy
 - Streamlining or de-escalation of therapy
 - Dose optimization
 - Parenteral to oral conversions
 - Computer-based surveillance, microbiology lab involvement
 - Process measures (did the intervention result in change) and outcomes measures (did the process reduce or prevent resistance or unintended consequences of antimicrobial use)
- Dellit TH et. Clin Infect Dis 2007; 44(2):159-77

Supplemental Program Elements

- **Education:**
 - Pro: changed behaviour, decrease initial misuse
 - Con: passive, time away from pts, rotation of staff, prescribers fall back into initial poor prescribing habits if education is not continuous
- **Examples**
 - Several pharmacists attended MADD-ID, ISMP
 - Pharmacists educated medical residents and physicians

Supplemental Program Elements

- **Guidelines and Pathways**

- Pro: Improves timely start of appropriate treatment, provider maintains autonomy
- Con: many pts fall off the path, compliance is voluntary, “cookbook” medicine

- **Examples**

- Dr. Quan reviews order sets with antibiotics
- Order sets developed for top infection CMG
- Antibiotic book revised 3 times to incorporate recommendations for empiric therapy
- Antimicrobial order forms
 - Piperacillin/tazobactam, vancomycin, C. difficile

Supplemental Program Elements

- **Computerized methods**
 - Pro: pt-specific data
 - Con: validation, testing and updating takes time
- **Streamlining and de-escalation**
 - Pro: decreases overuse, shortens duration
 - Con: premature de-escalation, undertreatment, reliability of testing
- **Examples**
 - Pharmacists make recommendations once C&S complete
 - Antibiotics reviewed daily at both hospitals by pharmacist specialist

Supplemental Program Elements

- **Dose optimization**
 - Pro: optimizes use and expands options, reduces resistance, can decrease drug cost (but sometimes actually increases cost)
 - Con: Logistics, availability of MIC data, increases pharmacist workload
- **Examples**
 - Pharmacist medical directives for renal dosing, vancomycin and gentamicin dosing
 - Parenteral to oral conversions
 - Pharmacist medical directive

Where to Start with your Antimicrobial Stewardship Committee (AMSC)?

- Before you start writing:
 - Why is the proposal being developed?
 - Do you have administration buy-in?
 - What is the **current state** of infection control/prevention at your institution, including the reporting structure?
 - What baseline data do you have **easy** access to?
 - Have a clear understanding of what is **already being done**

Know What Matters to Administrators

- Public reporting matters
 - Ie C.diff reported provincially
- Safer Healthcare Now bundles
- Antimicrobial Stewardship was proposed for the next set of Accreditation Canada standards
 - Not approved at this time but will probably resurface

Education & PR Ideas

- Stab-It - Staph aureus bacteremia is terrible
- ASP is first to develop app based learning and first to use ipads on rounds to educate health care providers and patients.

Education & PR Ideas

- Frame the problem & create urgency
- Bad bugs, No drugs: No ESKAPE!
 - *Enterococcus faecium*, *Staph aureus*,
Klebsiella pneumonia, *Acinetobacter
baumanii*, *Pseudomonas aeruginosa*,
Enterbacter species
- Opportunistic infections are quite common

Where to Start?

- Step 1: Develop an interdisciplinary team and define the roles and responsibilities of each team member
 - Meet the other team members in your hospital and learn what they do and see what they are collecting
- Step 2: Select strategies by which to execute an antimicrobial stewardship program (ASP).
Select realistic goals.
- Step 3: Start your measurement
- Step 4: Present results of your projects to your committee, medical staff, P&T, MAC, administration

Role of Team Members

- Microbiologist
 - Provides surveillance data on antimicrobial resistance gathered through antibiograms
 - Provides diagnostic testing to help make better antimicrobial choices
 - Rapid MRSA testing, RNA-fish test for yeast
- Infection Control
 - Implement infection control measures
 - Gather and monitor data like hand hygiene and patient outcomes like HAI
 - Determine impact of stewardship on antimicrobial use and resistance patterns
 - Investigation of local outbreaks of infection

Role of Team Members

Pharmacist

- Identify areas for improvement
- Prioritize projects based on resources available and goals of programs
- Makes day to day interventions
- Prepares reports and presents findings
- Education
- Research

Interventions

- Discusses antibiotic changes with physicians
- Documents recommendations
- Monitors antimicrobial therapy to evaluate appropriateness
- Provide PK/PD services
- Reviews yearly antibiogram
- Provides cost effective recommendations

Developing Terms of Reference

- Antimicrobial Stewardship Committee is a subcommittee of P&T
- Committee Members list
- Committee Invitees
- Voting

Responsibilities of AMSC

- Establish an antibiotic formulary
- Produce guidelines for antibiotic usage
- Develop and implement educational programs
- Monitor the efficacies of and compliance with various interventions through audit
- Undertake surveillance of antibiotic use within each specialty providing feedback of prescribers of their own antibiotic practices in relation to peers or standards
- Regularly review interventions

Antimicrobial Stewardship

- Front End – provided at the point of prescribing
 - Formulary restriction and preauthorization
 - Interactive decision support
 - Guidelines, order sets
- Back end – after the antimicrobial has been prescribed
 - Prospective audit and feedback
 - Streamlining or de-escalation
 - Dose optimization
 - Parenteral to oral conversion

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- To illustrate the Windsor experience
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Metrics for Antimicrobial Stewardship Committee

- Safety?
- Microbiology?
- Quality?
- Drug utilization?
- Expenditures?
- Look back to your potential strategies from IDSA

Identify the Problems & Strategize Implementation

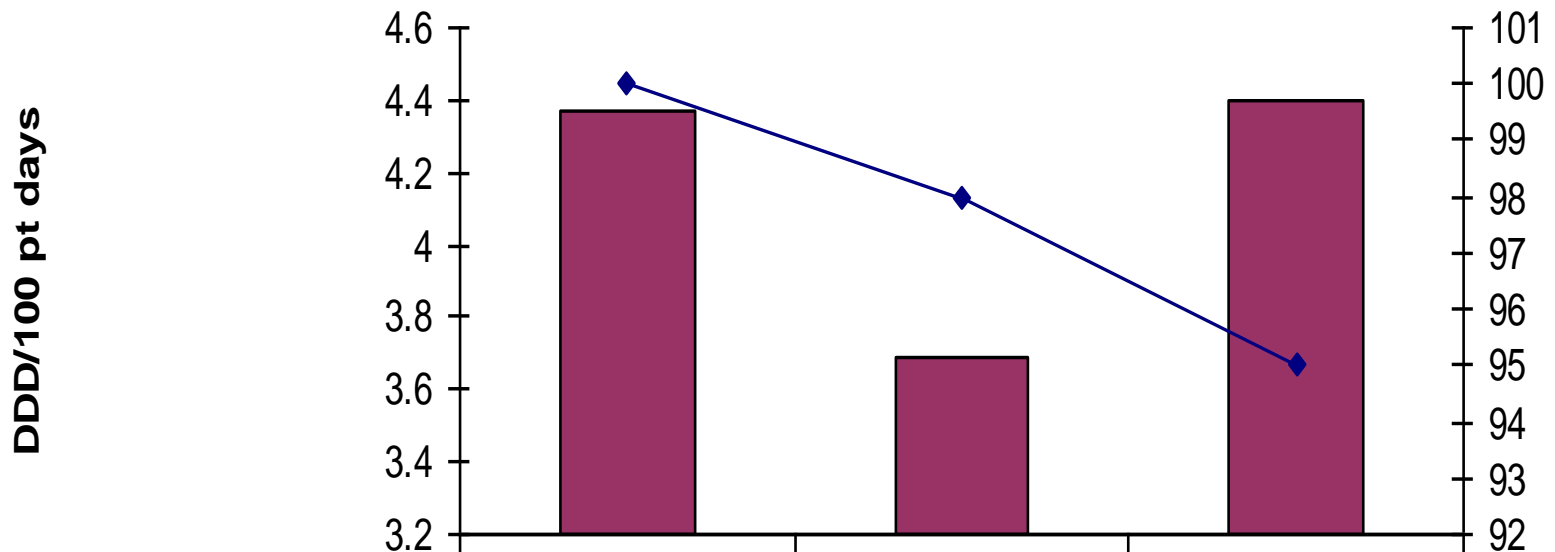
- Barriers to success?
 - Education is not enough as it needs to be repeated
 - Need system wide process improvements
- Strategies
 - Formulary restriction
 - Empiric therapy guidelines
 - Automatic stop orders

Stewardship Targets

- Clinical & microbiologic outcomes
 - Development of resistance
 - Infection related morbidity & mortality
- Appropriateness of anti-infective use
 - Compliance with hospital policy –ORDER SETS
 - Adequacy of therapy
- Cost of care
 - Infection rated costs
 - Anti-infective costs and/or utilization

Example

Levofloxacin Use vs Strep pneumonia susceptibilities



| | | | |
|-----------------------|------|------|-----|
| ■ DDD of levofloxacin | 4.37 | 3.69 | 4.4 |
| ◆ Strep pneumo | 100 | 98 | 95 |

Order Sets

- Piperacillin/tazobactam
- *C. Difficile*
- Vancomycin
- CAP protocol
- COPD
- Surgical prophylaxis

Safety Targets

- Healthcare-associated infection rates
 - Post operative infections
 - *C. difficile* infections – provincial tracking & reporting
- Medication adverse effects
 - Nephrotoxicity – potential target
 - Other less common adverse events

Pharmacist Vancomycin & Gentamicin Dosing

- Dosed by pharmacist
- Initial dosing and follow up
- Protocol for ordering levels, adjusting dose and monitoring

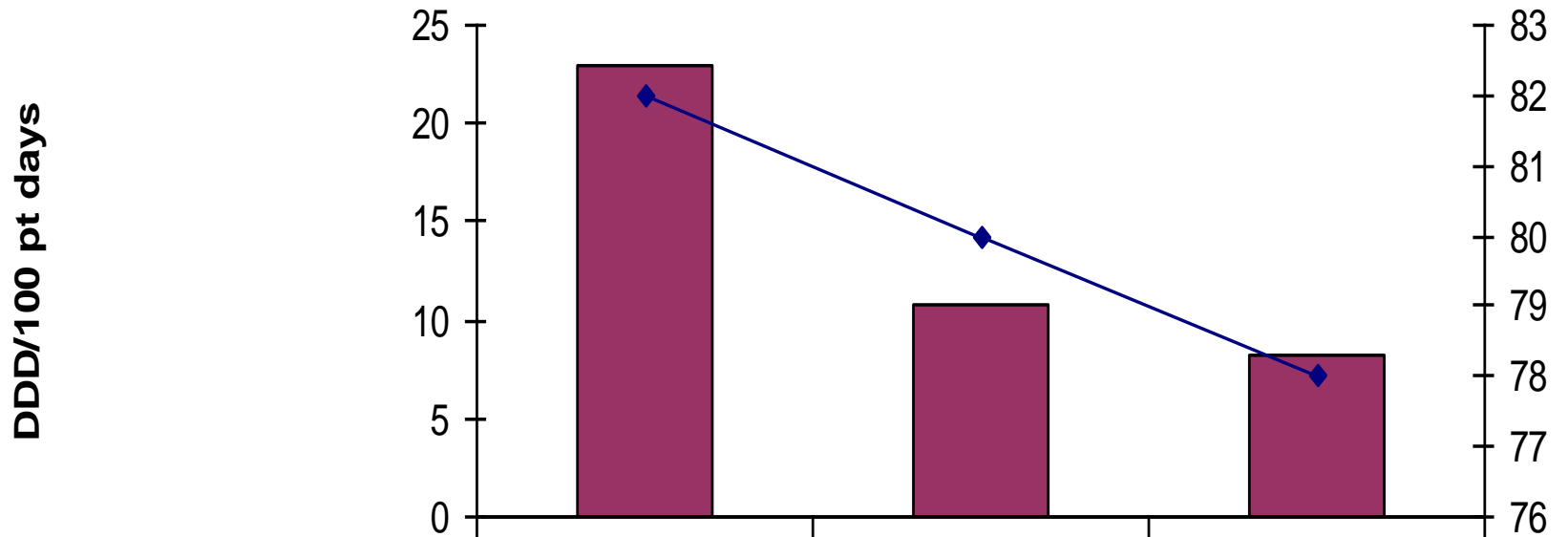
| Drug | 2008 | 2009 | 2010 |
|-------------|-------------|-------------|-------------|
| AMG | 136 | 113 | 102 |
| Vanco | 307 | 500 | 586 |

Microbiology Targets

- Look at resistance patterns
- Resistance takes a long time to reverse back to the wild type (hence the reason why antibiotic cycling does not work)
 - Carbapenem-resistant Enterobacteriaceae
 - FQ resistant *E. coli*
 - Vancomycin resistant enterococci
 - ESBL & *Klebsiella spp* and *E coli*
- Unit specific antibiograms

Example

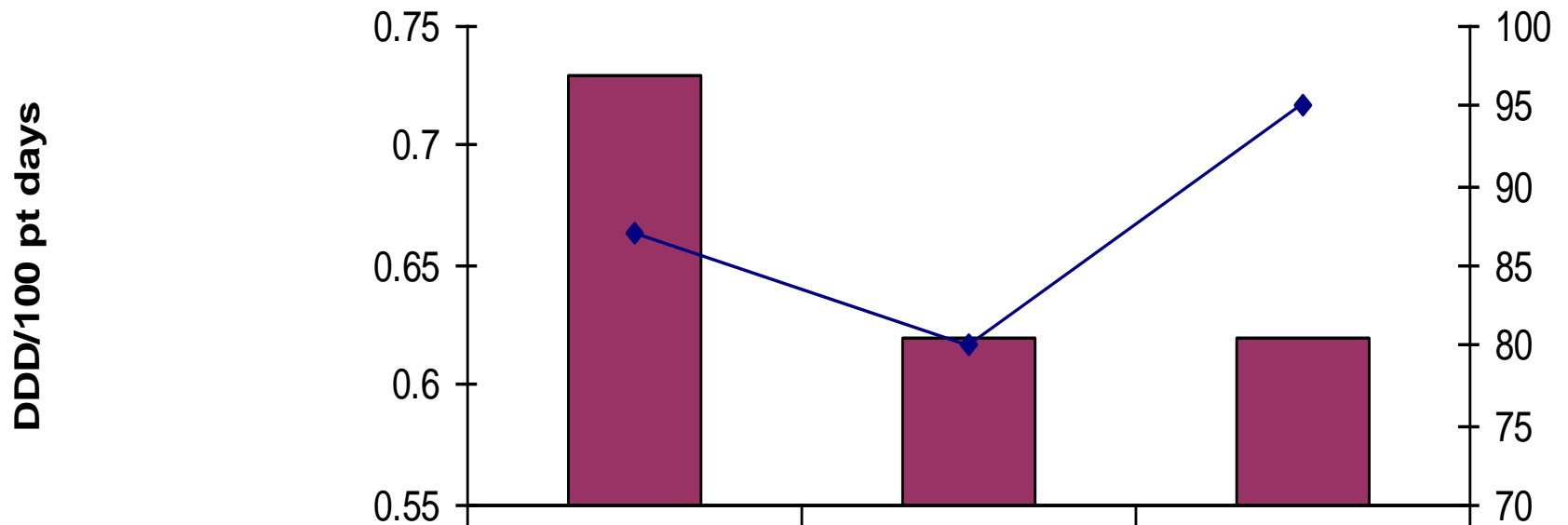
Ciprofloxacin Use vs E coli susceptibilities



| | | | |
|------------------------|-------|-------|------|
| ■ DDD of ciprofloxacin | 22.95 | 10.75 | 8.29 |
| ◆ E coli | 82 | 80 | 78 |

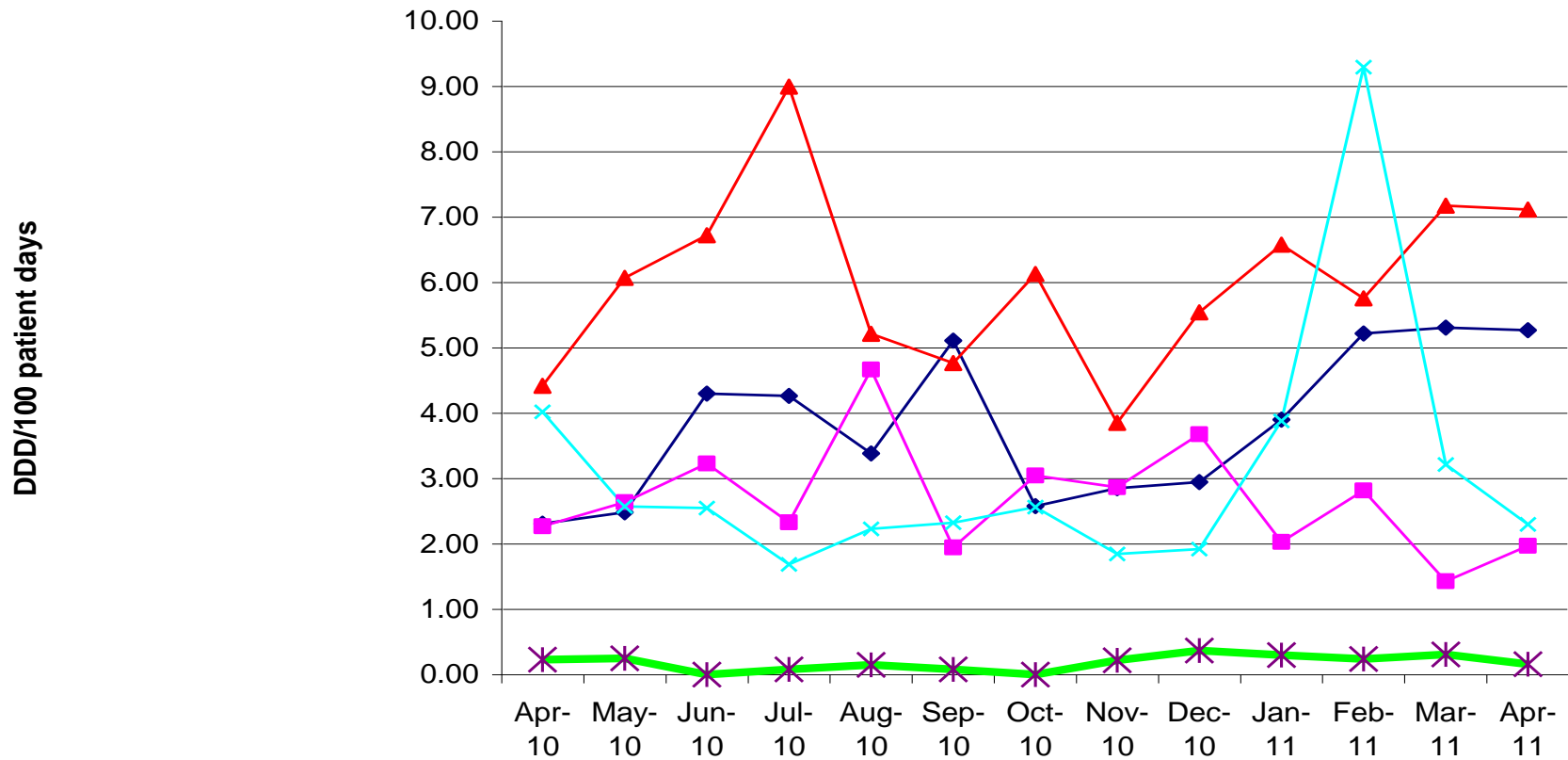
Example

Meropenem Use vs Strep pneumonia susceptibilities HDGH



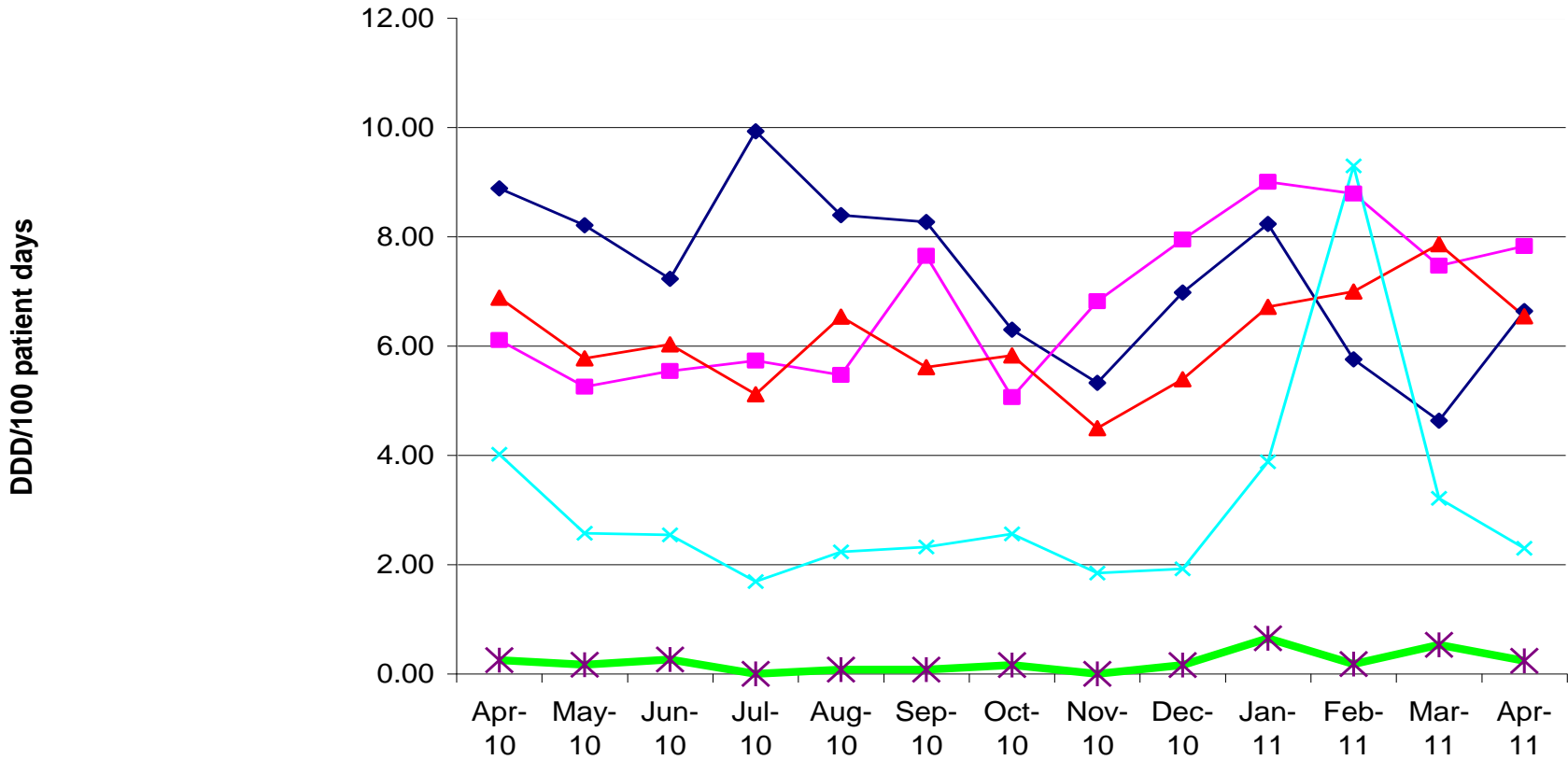
| | | | |
|--------------------|------|------|------|
| ■ DDD of meropenem | 0.73 | 0.62 | 0.62 |
| ◆ Strep pneumo | 87 | 80 | 95 |

VRE rates per 1000 patient days vs Antibiotic use



| | Apr-10 | May-10 | Jun-10 | Jul-10 | Aug-10 | Sep-10 | Oct-10 | Nov-10 | Dec-10 | Jan-11 | Feb-11 | Mar-11 | Apr-11 |
|----------------------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| vancomycin IV | 2.31 | 2.48 | 4.30 | 4.26 | 3.38 | 5.11 | 2.58 | 2.85 | 2.95 | 3.90 | 5.22 | 5.31 | 5.27 |
| ampicillin IV | 2.27 | 2.64 | 3.23 | 2.33 | 4.67 | 1.95 | 3.04 | 2.87 | 3.68 | 2.03 | 2.81 | 1.43 | 1.97 |
| piperacillin tazobactam IV | 4.42 | 6.07 | 6.72 | 8.99 | 5.21 | 4.77 | 6.13 | 3.85 | 5.54 | 6.58 | 5.75 | 7.17 | 7.11 |
| Clindamycin | 4.02 | 2.57 | 2.55 | 1.69 | 2.23 | 2.32 | 2.56 | 1.85 | 1.92 | 3.88 | 9.29 | 3.21 | 2.30 |
| VRE per 1000 pt days | 0.23 | 0.25 | 0.00 | 0.08 | 0.15 | 0.08 | 0.00 | 0.22 | 0.37 | 0.30 | 0.24 | 0.31 | 0.16 |

C diff rates per 1000 patient days vs Antibiotic use



| | Apr-10 | May-10 | Jun-10 | Jul-10 | Aug-10 | Sep-10 | Oct-10 | Nov-10 | Dec-10 | Jan-11 | Feb-11 | Mar-11 | Apr-11 |
|--------------------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| ◆ ciprofloxacin | 8.89 | 8.21 | 7.23 | 9.93 | 8.39 | 8.27 | 6.30 | 5.33 | 6.98 | 8.24 | 5.75 | 4.63 | 6.64 |
| ■ levofloxacin | 6.11 | 5.26 | 5.54 | 5.73 | 5.47 | 7.65 | 5.06 | 6.82 | 7.95 | 9.00 | 8.79 | 7.47 | 7.83 |
| ▲ Ceftriaxone | 6.88 | 5.77 | 6.03 | 5.11 | 6.53 | 5.61 | 5.83 | 4.49 | 5.39 | 6.71 | 7.00 | 7.86 | 6.54 |
| × Clindamycin | 4.02 | 2.57 | 2.55 | 1.69 | 2.23 | 2.32 | 2.56 | 1.85 | 1.92 | 3.88 | 9.29 | 3.21 | 2.30 |
| * Cdiff per 1000 pt days | 0.25 | 0.17 | 0.26 | 0.00 | 0.08 | 0.08 | 0.16 | 0.00 | 0.16 | 0.65 | 0.18 | 0.53 | 0.24 |

Quality Targets

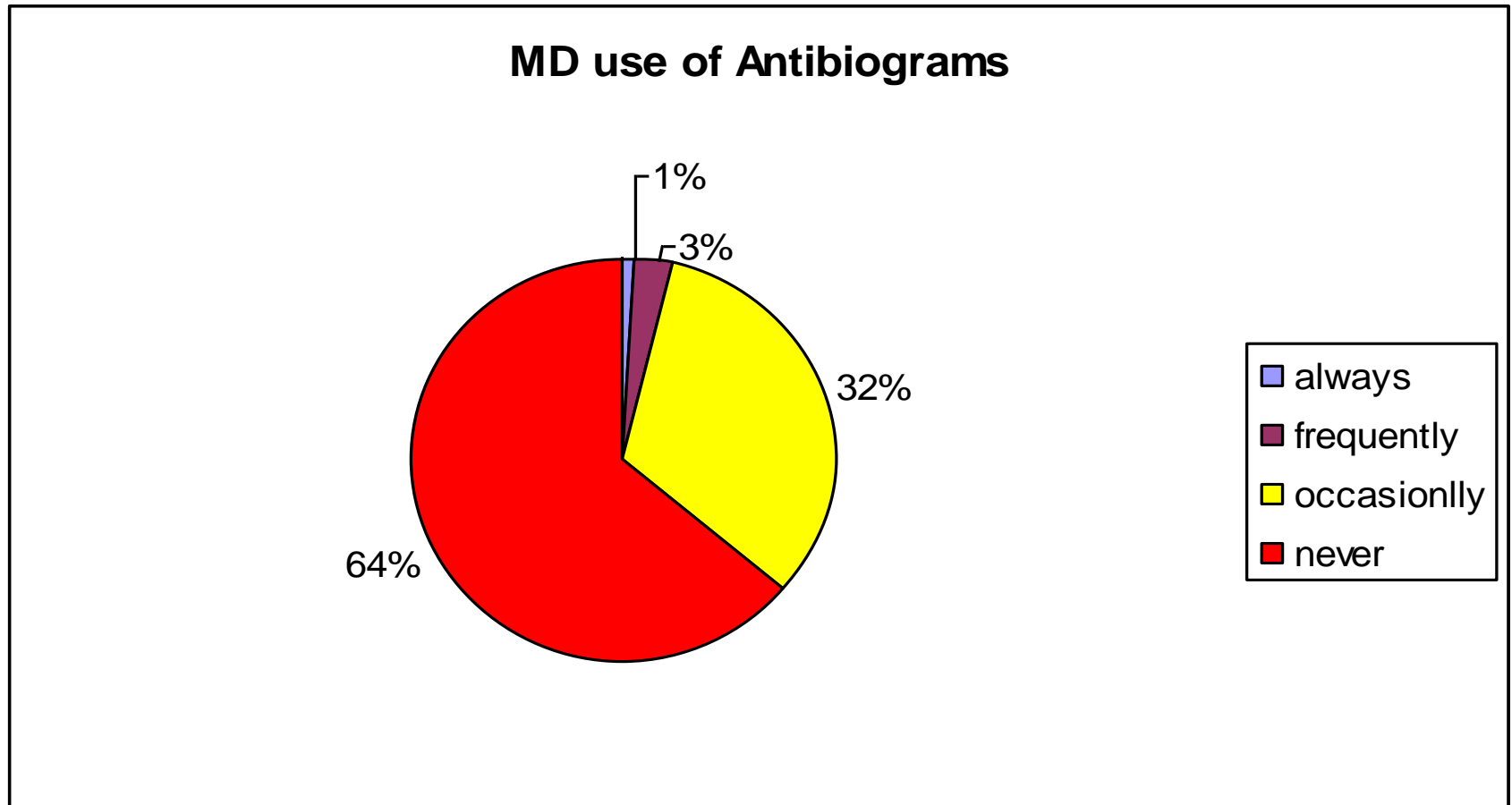
- Compliance with institutional criteria
- Compliance with guideline recommendation
 - Pharmacologic
 - Non-pharmacologic

Pharmacist Measures

| Measure | 2008 | 2009 | 2010 |
|-------------------------------------|-------------|-------------|-------------|
| Renal dosing | 1968 | 1894 | 1905 |
| IV/po stepdown | 828 | 1112 | 1236 |
| Cost savings From IV/po | \$27,000 | \$45,000 | \$46,000 |
| D/C inappropriate antibiotics | 708 | 1522 | 1540 |

Do MD's Use Hospital Antibiofilms?

Online survey of 545 residents at a university teaching hospital

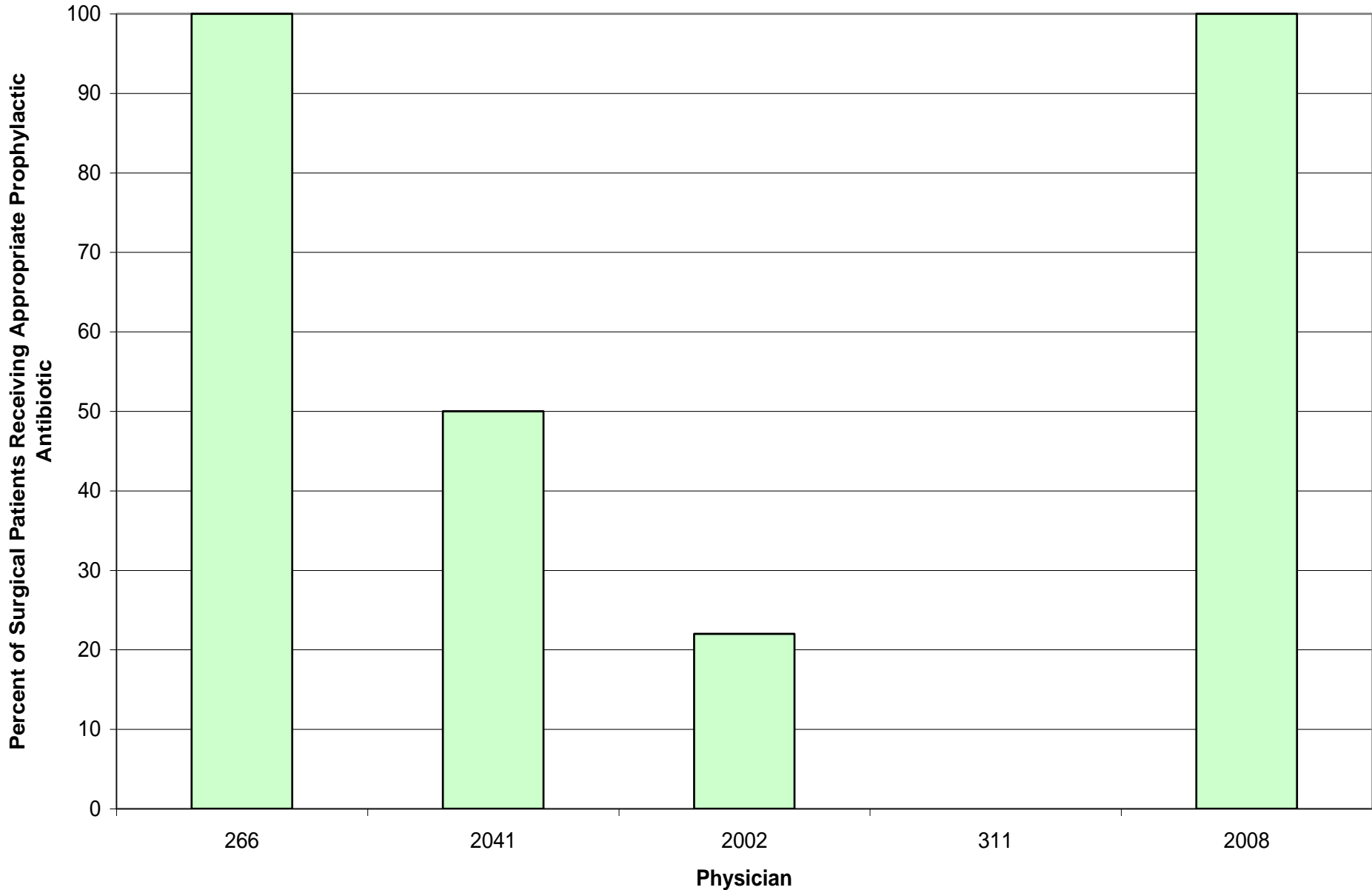


Mermel et al. Clin Inf Dis 2008; 46:1789

Peer to Peer

- Peer pressure can provide incentives that financial reward cannot
- Doctors are very competitive and want to be A students so use those 2 characteristics as levers to motivate behavioural change
- Doctors will try to improve simply as a matter of professional pride when shown data on measures such as infection rates, test utilization, over use of antibiotics

Percent of Surgical Patients Receiving Appropriate Prophylactic Antibiotics - General Surgery



Data from BWH Surgical Site Infection Audit 2006

Drug Utilization Targets

- Target drugs or drug classes
 - High risk drugs like amg or vancomycin
- Restrictions or criteria
 - Meropenem, daptomycin, linezolid, ertapenem, tigecycline are restricted to ID physician and intensivists
 - Voriconazole, caspofungin are restricted to ID, intensivists, oncologists
- Benchmarking of dispensing trends
- DDD tracking quarterly
 - Comparison of WRH and HDGH

Measurement options

- DDD=defined daily doses
- DOT=days of therapy
- Drug costs= cost per patient days
- Costs associated with antibiotics
 - Drug costs
 - Administration and preparation, monitoring, hospital costs (LOS) and ICU vs nonICU
- LOT =length of therapy is NEW

Interhospital Comparisons: Recommendations from IDSA/SHEA

- Drug use data can be standardized using the defined daily dose
- The use of defined daily doses is recommended so that hospitals may compare their antimicrobial use with that of other similar hospitals recognizing the challenges of interhospital comparisons

Defined Daily Dose (DDD)

- Standardized definition of daily antibiotic dose
- Created by World Health Organization
- Correction Factor: $\frac{\text{Total units (eg mg)drug}}{\text{DDD Correction Factor}}$

DDD Pros and Cons

Pros:

- Attempts to convert raw purchase data into utilization data
- Allows comparisons with other institutions
- Easy to calculate

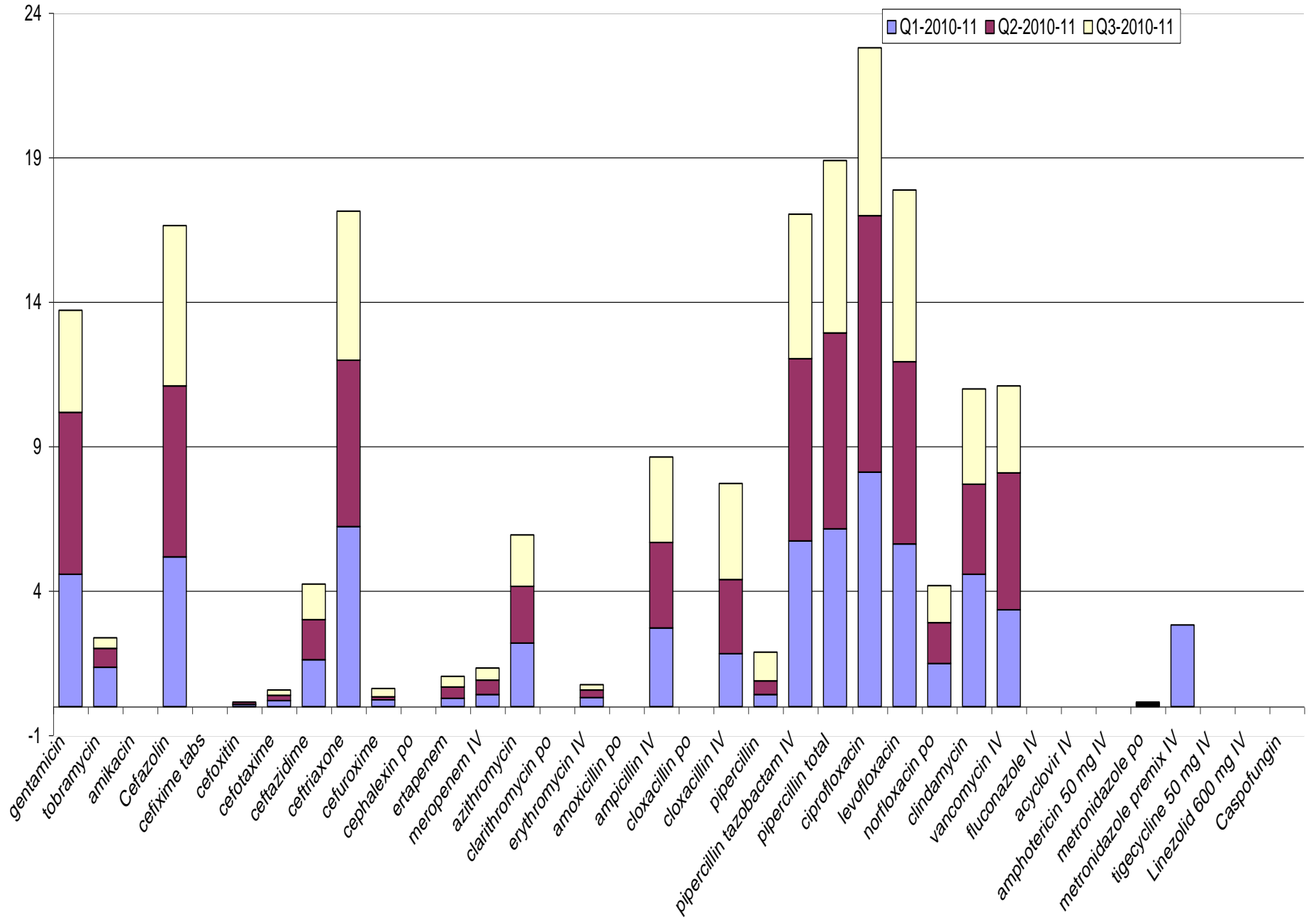
Cons:

- Not everyone agrees with DDD correction factors
- Does not give information about actual patients
- DDD can change with time
- Cannot be used for children, renal dysfunction

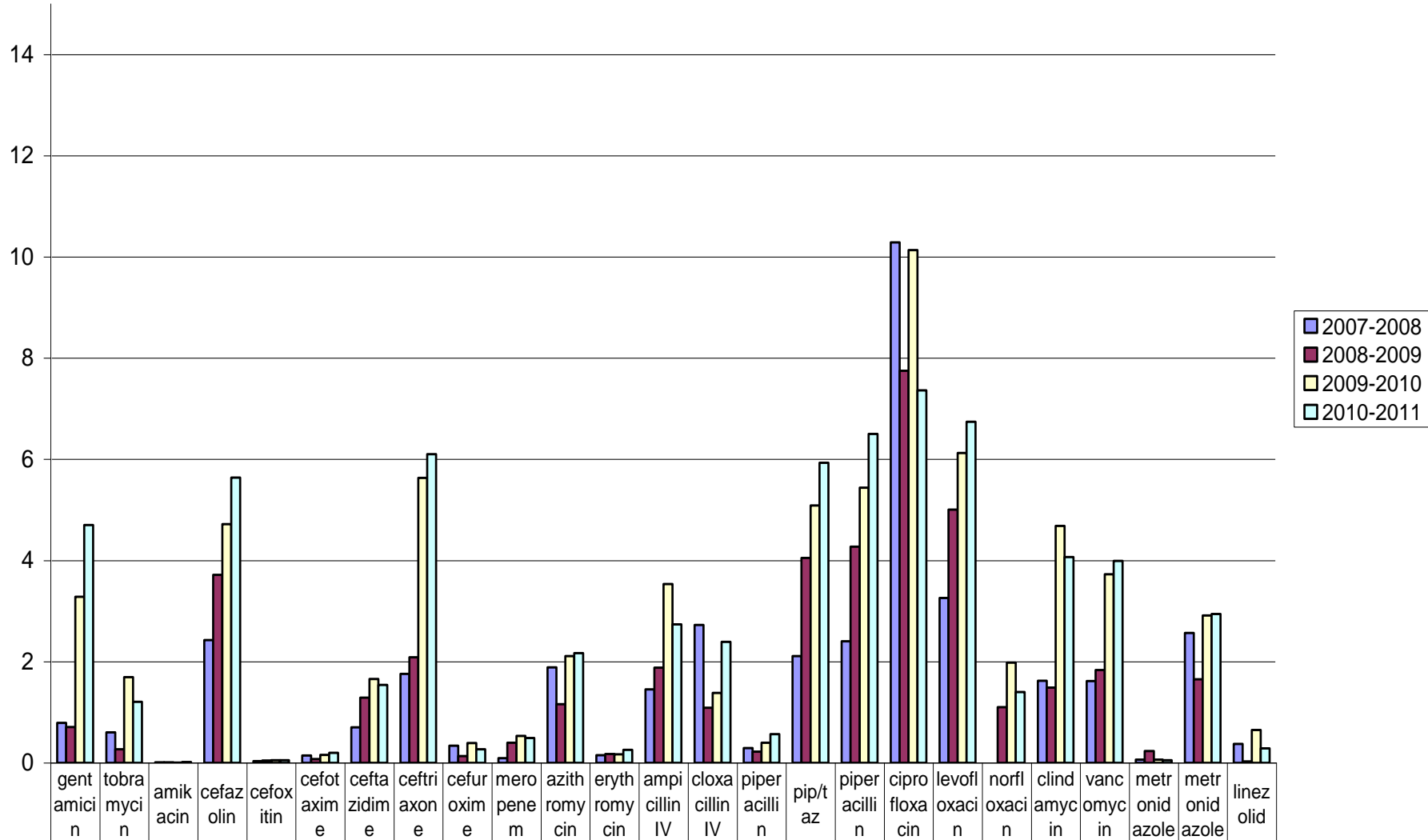
Is DDD/100 patient days the best way to express antibiotic use?

- DDD standardization brought order from chaos but it has a number of shortcomings
 - The WHO DDDs need occasional revision
 - Drugs requiring reduced dosage in renal impairment
 - Best measure to predict resistance?
 - Total DDD is strongly influenced by formulary mix
 - Alternative methods in both numerator and denominator are being explored

WRH Quarterly Review of Antibiotic Load 2010-2011



WRH 2007-2008 vs 2008-2009 vs 2009-2010 vs 2010-2011



| | gentamicin | tobramycin | amikacin | cefazolin | cefoxitin | cefotaxime | ceftazidime | ceftriaxone | cefuroxime | meropenem | azithromycin | erythromycin | ampicillin IV | cloxacillin IV | piperacillin | pip/taz | piperacillin | ciprofloxacin | levofloxacin | norfloxacin | clindamycin | vancomycin | metronidazole | metronidazole | linezolid |
|-----------|------------|------------|----------|-----------|-----------|------------|-------------|-------------|------------|-----------|--------------|--------------|---------------|----------------|--------------|---------|--------------|---------------|--------------|-------------|-------------|------------|---------------|---------------|-----------|
| 2007-2008 | 0.79 | 0.6 | 0.01 | 2.43 | 0.04 | 0.15 | 0.7 | 1.76 | 0.34 | 0.09 | 1.89 | 0.15 | 1.45 | 2.73 | 0.29 | 2.11 | 2.41 | 10.3 | 3.26 | 0 | 1.62 | 1.62 | 0.07 | 2.57 | 0.38 |
| 2008-2009 | 0.71 | 0.27 | 0.01 | 3.72 | 0.05 | 0.08 | 1.29 | 2.09 | 0.13 | 0.4 | 1.16 | 0.18 | 1.88 | 1.09 | 0.22 | 4.05 | 4.27 | 7.75 | 5.01 | 1.1 | 1.49 | 1.83 | 0.24 | 1.66 | 0.03 |
| 2009-2010 | 3.29 | 1.7 | 0.01 | 4.72 | 0.06 | 0.16 | 1.66 | 5.63 | 0.39 | 0.53 | 2.11 | 0.17 | 3.53 | 1.39 | 0.4 | 5.09 | 5.44 | 10.1 | 6.13 | 1.98 | 4.68 | 3.73 | 0.07 | 2.92 | 0.65 |
| 2010-2011 | 4.7 | 1.21 | 0.02 | 5.64 | 0.05 | 0.2 | 1.54 | 6.1 | 0.27 | 0.49 | 2.17 | 0.26 | 2.74 | 2.39 | 0.57 | 5.93 | 6.5 | 7.36 | 6.74 | 1.4 | 4.07 | 3.99 | 0.05 | 2.94 | 0.29 |

Days of Therapy

- A single day of drug administration regardless of number of doses or strength
 - Eg cefazolin 1 gram preop = 1 DOT
- Considered by some as a more realistic estimate of use

Days of Therapy (DOT)

Pros

- Can be used in children
- Not influenced by changes in DDD standards
- Not subject to differences in institutional preference

Cons

- Overestimates use of drugs given multiple times a day
- More difficult to measure without computerized records

Benchmarking Antimicrobial Use

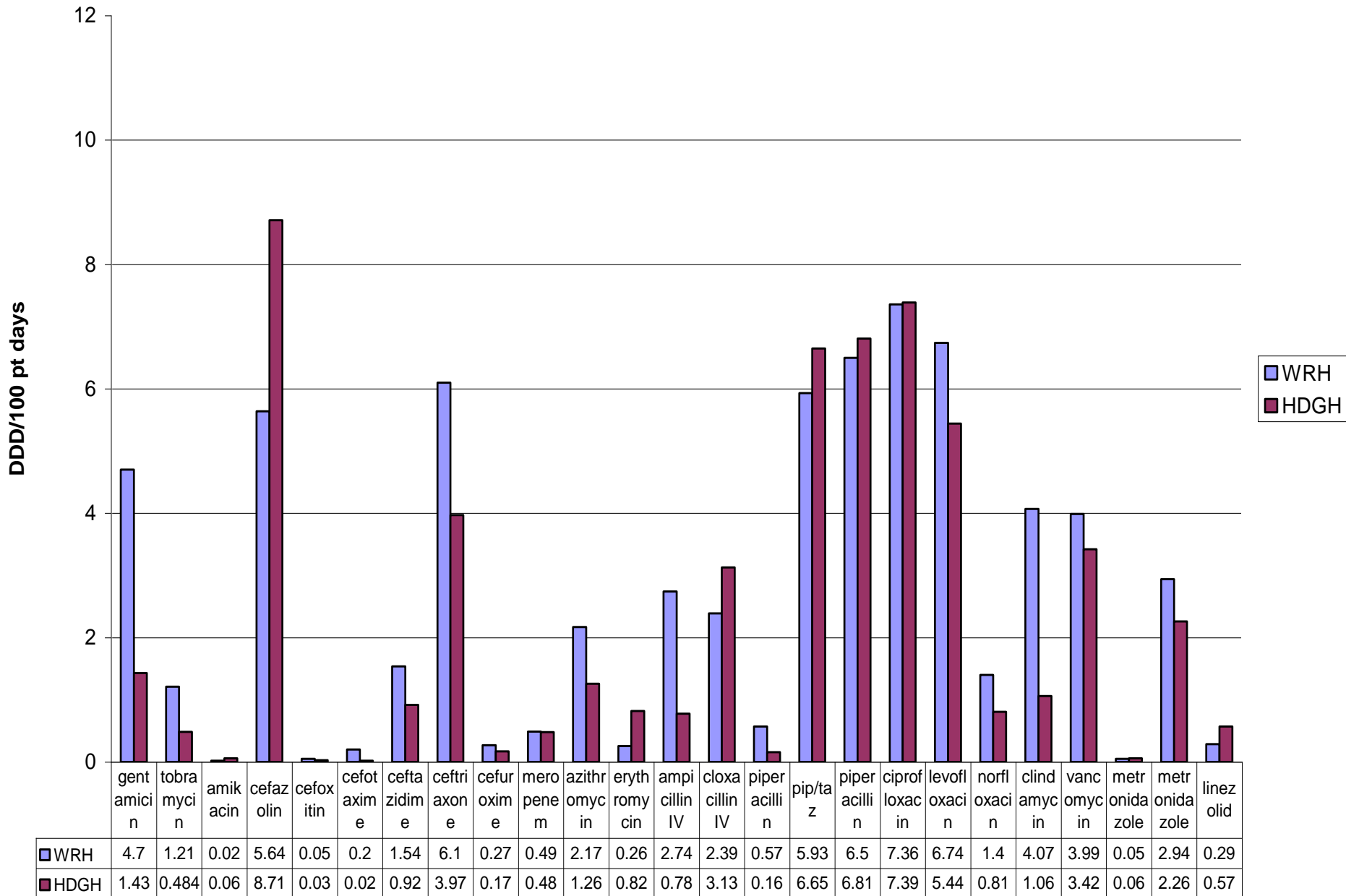
Potential advantages

- Quality improvement strategies to improve use
- Facilitator cooperative stewardship efforts
- Increased power: changes in drug use associated with improved or worsening resistance
- Identify stewardship strategies that work?

Challenges

- How to measure use?
- What are appropriate measures of similarity between hospitals?
- How to measure inappropriate use?
- Will hospitals change usage from benchmarked data?
- Will resistance improve?

WRH vs HDGH 2010-2011 DDD/100 pt days



Financial Targets

- Drug costs
- Drug acquisition
- Administration
- Adjunctive therapy, monitoring
- Length of stay – tough to track
- These are not the easiest targets to get but easiest to explain to hospital administrators

Making a realistic financial estimate

- When comparing to historical data there are several important considerations:
 - Generic cipro (IV and oral)
 - Echinocandin price wars
 - Generic pip/tazo and carbapenems on the horizon
 - Growing attention to CDAD
 - Your baseline is a good place to start

Criteria for evaluation of quality of antimicrobial drug use

- Sufficient data in the records for evaluation
- Indication for antibiotic therapy prophylaxis (is an antibiotic justified?)
- Appropriate choice of antibiotic
- Efficacy (susceptibility, antimicrobial activity)
- Toxicity, allergic reactions
- Cost
- Spectrum (too broad?)
- Appropriate duration? Too long, too short?
- Appropriate pharmacokinetics? Dose, interval, route?
- Appropriate timing? Too early before cultures? Too late after surgical incision?

MUE Elements

- Indications
- Route
- Prescribers for individual feedback
- Doses
- Duration
- Compliance with policy
- Adequacy of therapy – where cultures + and treated appropriately

Dashboard



- Dashboard is summative report providing gauges to assess performance in administrative, financial or clinical goals
- Summary of audit and feedback interventions

Our Dashboard Components

- DDD/100 pt days
- Review of resistance patterns/trends
- Perform DUEs on areas of concern
- Order set development
- Monitoring high risk drugs (amg, vancomycin)
- Vancomycin and VRE rates

Monitoring Outcomes

- **Qualitative Factors**
 - Unit specific antibiogram annually
 - Patient outcomes through MUE
- **Quality indicators**
 - Documentation of rationale, appropriate specimens sent, selection according to policies
 - For continuous daily consideration of de-escalation, IV/PO switch, discontinuation, PK monitoring

Measuring Success

- Compliance with criteria/restriction policies
- Resistance trends – takes awhile
- Appropriate antibiotic use through care bundles
- Administrators want \$ and MD want clinical outcomes
- No perfect measure for success

Appendix

- IDSA antimicrobial stewardship guidelines
- Orientation to antimicrobial stewardship position
- Examples of terms of reference
- Example audit for urine cultures
- Gap analysis checklist

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Gap Analysis Checklist

- AMP-Gap Analysis Checklist from CDC's Get Smart for Healthcare site:
<http://www.cdc.gov/getsmart/healthcare/improve-efforts/resources/>
- There are other useful ASP resources on their website (ie. getting started, successful stories, etc)

Helpful References

- Practice Guidelines and key publications
- IDSA guidelines
- Dellitt TH et al, Clin Infect Dis 2007; 44:159-77
- Owens RC. Diag Microbiol Infect Di 2008; 61:110-28
- Pagani L Clin Infect Dis 2009; 48:626-32
- Perencevich et al. Inf Control Hosp Epidemiol 2007; 28:1121-1133
- Johannsson B et al. Inf Control Hosp Epidemiol 2011; 32(4)

Questions?

