Strategies in Stewardship and Why Some Antimicrobials Should Be Protected

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Disclosures

- Acted as a consultant
  - Nabriva Therapeutics AG
  - Theravance Biopharma

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Objectives

- Define antimicrobial stewardship
- Discuss current and future strategies for antimicrobial stewardship to promote judicious use of antimicrobials
- Describe the reasons for “protecting” antimicrobials

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Outline

- The Problem
- Antimicrobial stewardship
  - Concept
  - Strategies
    - Passive
    - Active
    - Other (…prevention would be nice)
- Reasons antimicrobials are protected
- Collaboration

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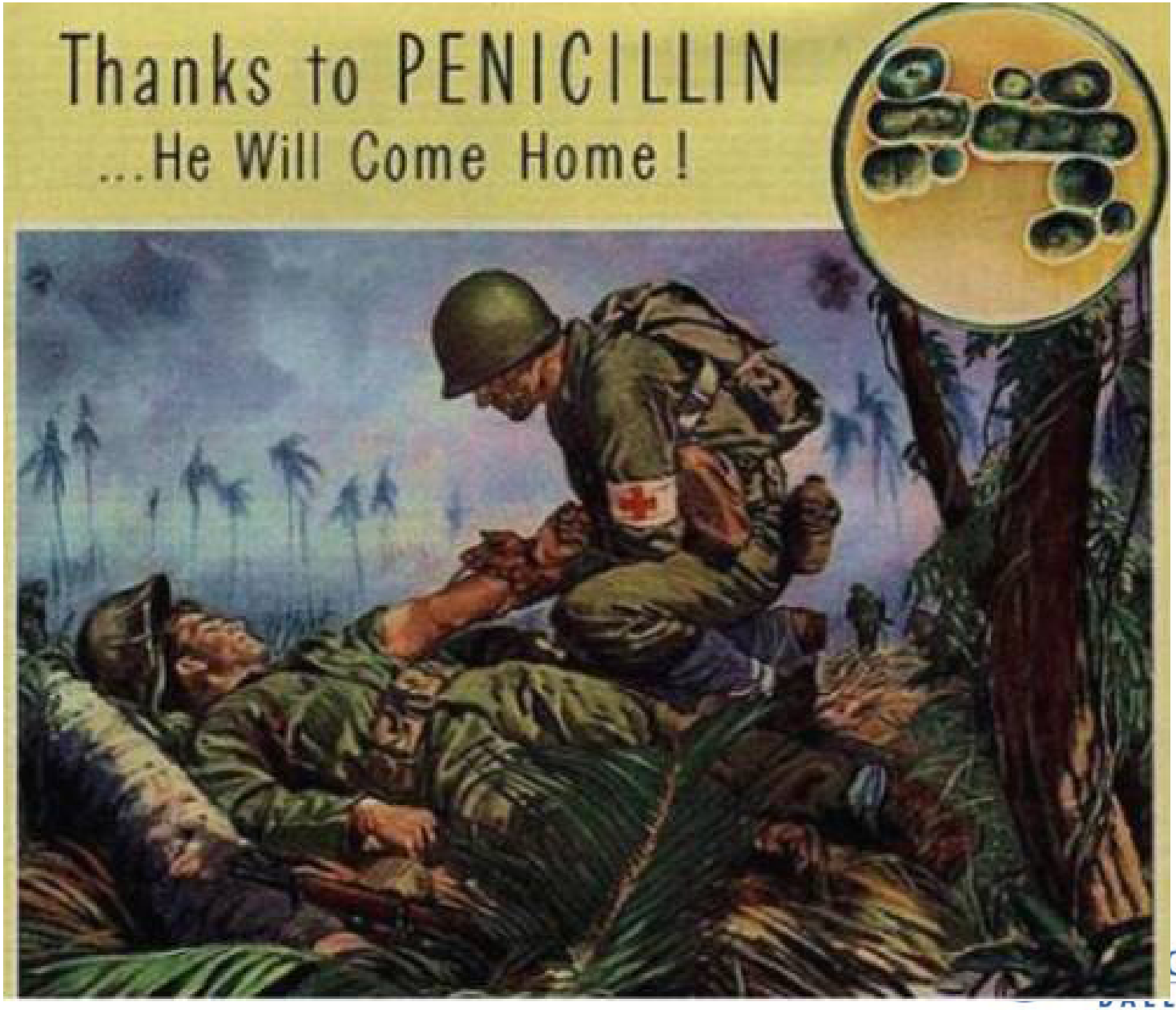
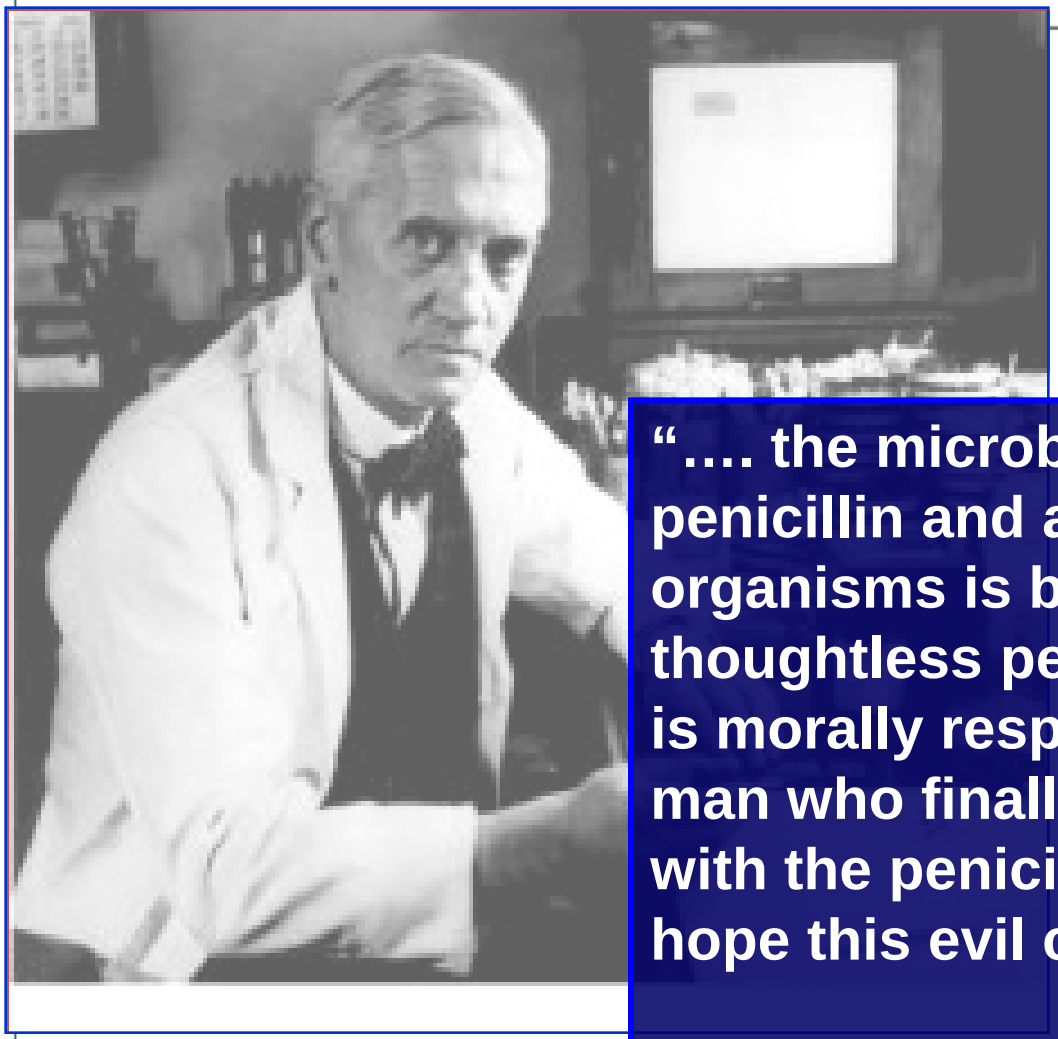

Thanks to PENICILLIN
...He Will Come Home!

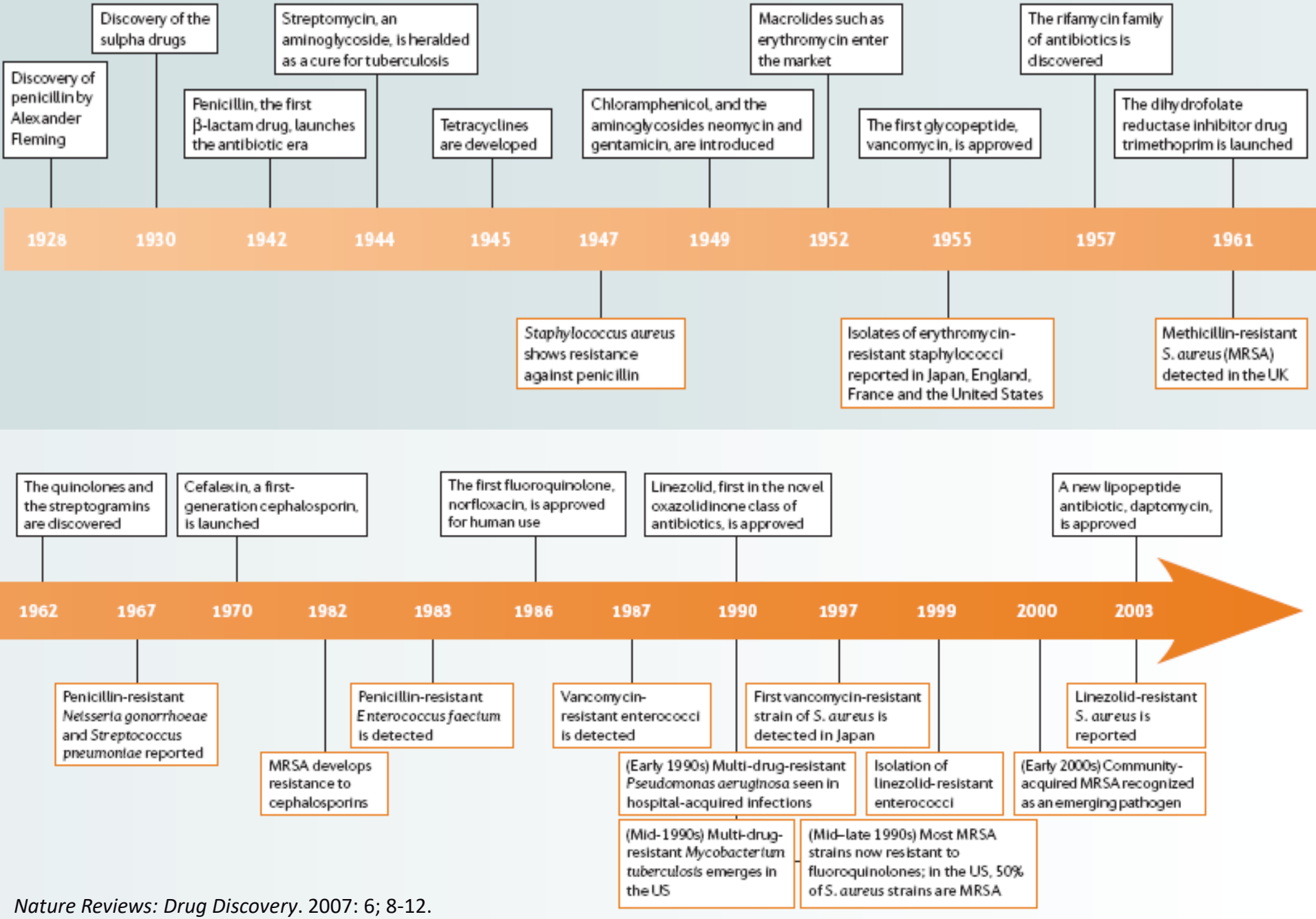
Misuse adversely impacts patients – Resistance



"…. the microbes are educated to resist penicillin and a host of penicillin-fast organisms is bred out… In such cases the thoughtless person playing with penicillin is morally responsible for the death of the man who finally succumbs to infection with the penicillin-resistant organism. I hope this evil can be averted."

- Sir Alexander Fleming, June 1945

Timeline | **Race against time: the introduction of new antibiotic classes and the emergence of resistance**



Nature Reviews: Drug Discovery. 2007: 6; 8-12.

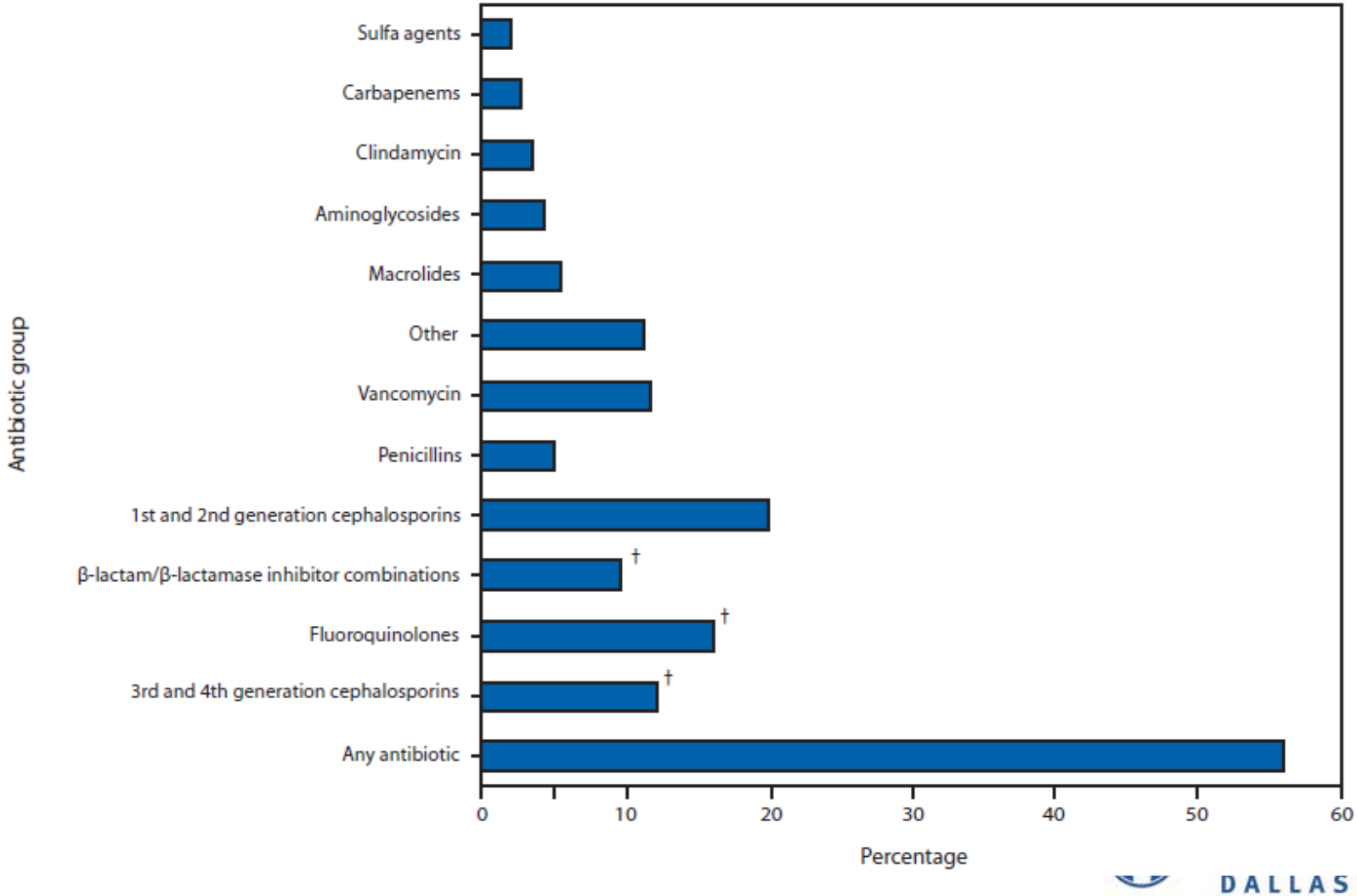
Antibiotics are misused in hospitals

- An estimated **30-50%** of antimicrobial use in hospitals is inappropriate
- Misused in a variety of ways
  - Given when not needed
  - Continued when no longer necessary
  - Wrong dose/drug for infection
  - Broad spectrum for susceptible organisms

IDSA Statement on 'Antibiotic Resistance: Promoting Critically Needed Antibiotic Research and Development and Appropriate Use ("Stewardship") of these Precious Drugs'
-Before the House Committee on Energy and Commerce Subcommittee on Health; June 9, 2010

Antibiotics are misused in hospitals

FIGURE 1. Percentage of hospital discharges with at least one antibiotic day, by antibiotic group — 323 hospitals, United States, 2010*



CDC, MMWR. 2014; 63.

Misuse adversely impacts patients – Adverse Effects

- Perception that there is (almost) no risk and (almost) all benefit to giving an antibiotic
- Antibiotics account for nearly 1 in 5 (19.3%) of drug-related adverse events
  - **>140,000 ED visits/year**
  - **Admission required for 6.1%** of adverse events
- Side effects…

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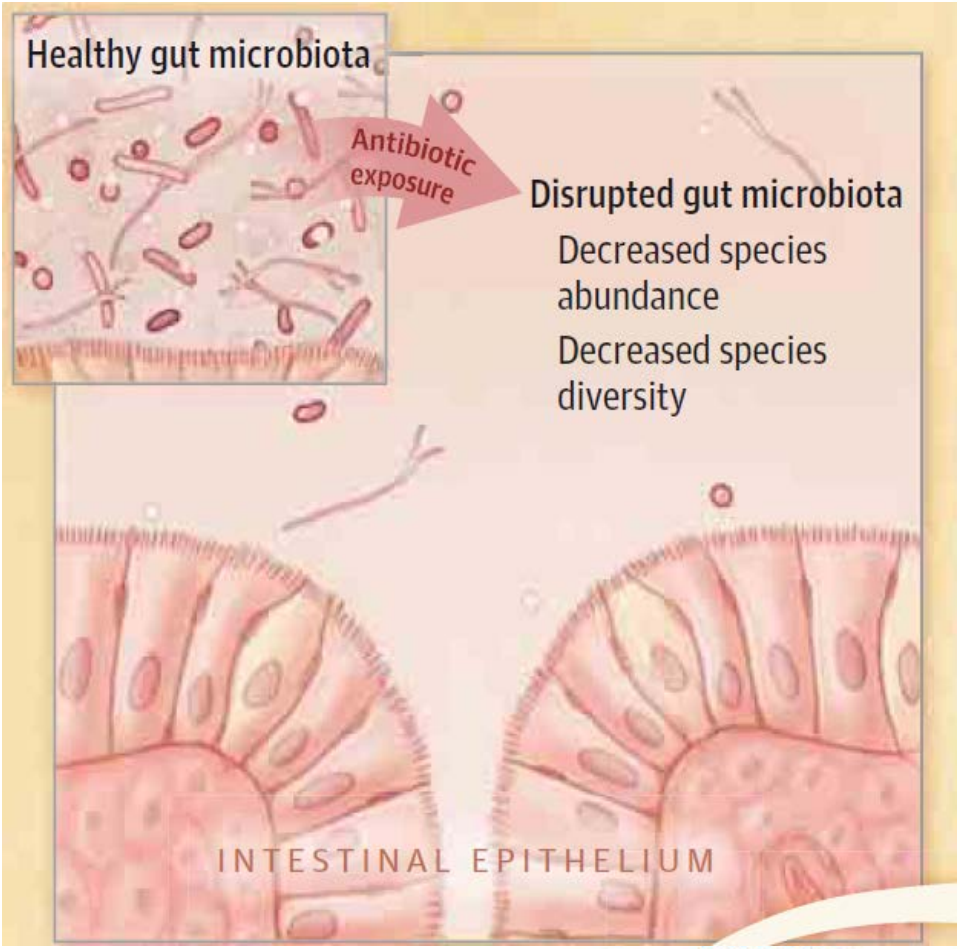
Shehab, et al. Clin Infect Dis. 2008; 47:735.

Misuse adversely impacts patients – *C. difficile*

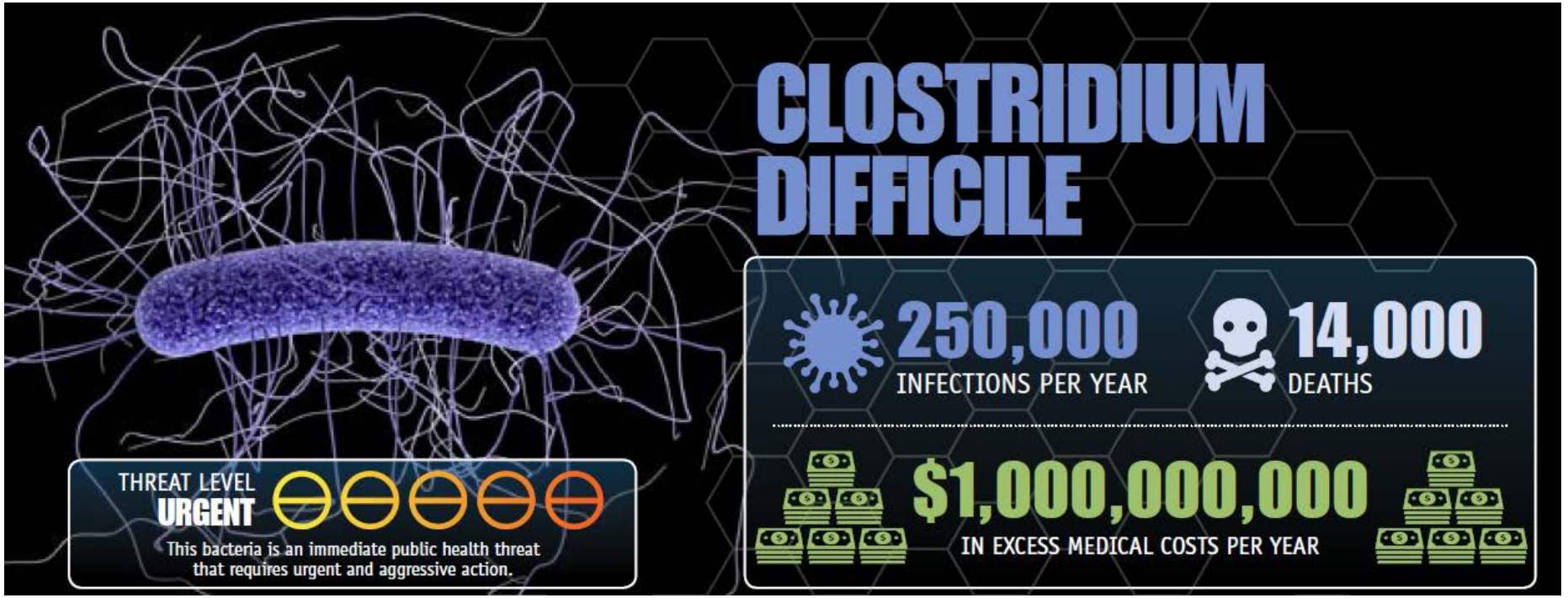
- Antibiotic exposure is single most important risk factor for *Clostridium difficile* associated disease (CDAD)
  - Up to **85%** of patients with CDAD have **antibiotic exposure in the 28 days before** infection



Chang HT, et al. Infect Control Hosp Epidemiol. 2007; 28:926-31.

Bagdasarian N, et al. JAMA. 2015; 313:398-408.

Misuse adversely impacts patients – *C. difficile*



Campbell, et al. Infect Control Hosp Epidemiol. 2009; 30:523-33.
Dubberke, et al. Clin Infect Dis. 2008; 46:497-504.
Dubberke, et al. Emerg Infect Dis. 2008; 14:1031-8.
Antibiotic Resistance Threats in the U.S. 2013.

Misuse adversely impacts patients – Resistance

- Methicillin resistant vs. susceptible *Staphylococcus aureus* (MRSA vs. MSSA)
  - **Mortality is nearly double**
  - Mortality risk with MRSA bacteremia: OR: 1.93; p <0.001
  - Mortality of MRSA infections: RR: 1.7; 85% CI (1.3-2.4)

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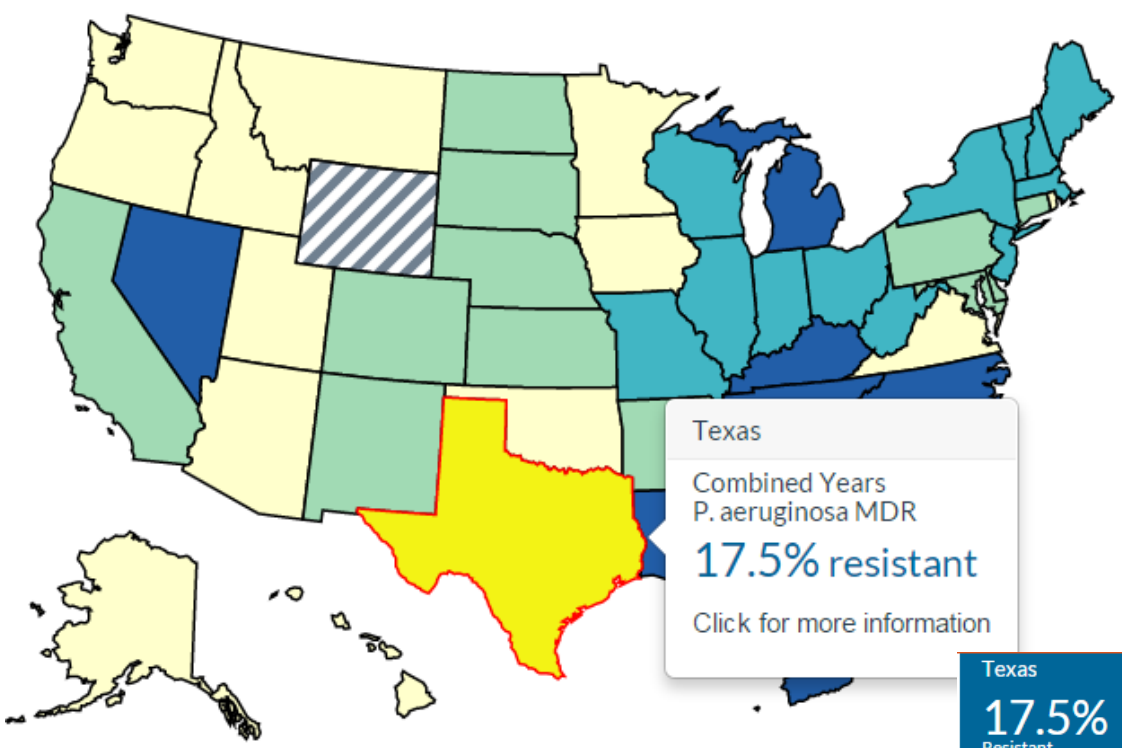
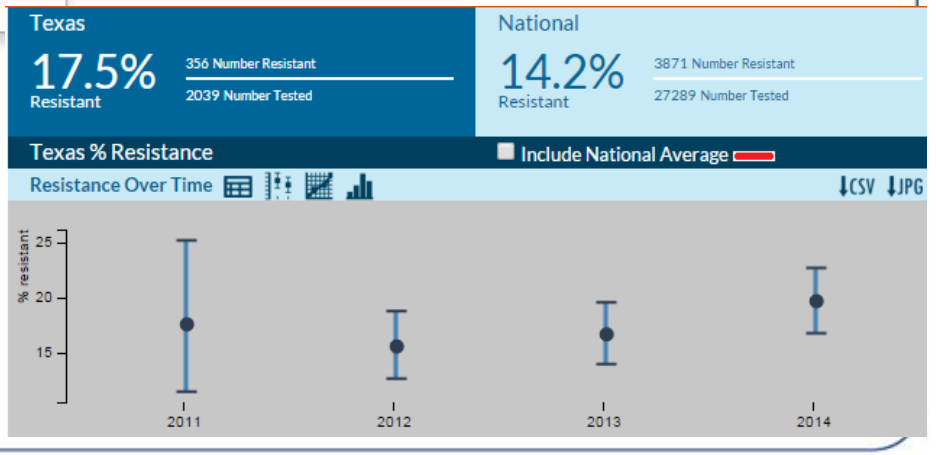
Shurland, et al. Infect Control Hosp Epidemiol. 2007; 28:273-9.

Cosgrove, et al. Clin Infect Dis. 2003; 38:53-9.

MDR *P. aeruginosa* – Regional Epidemiology

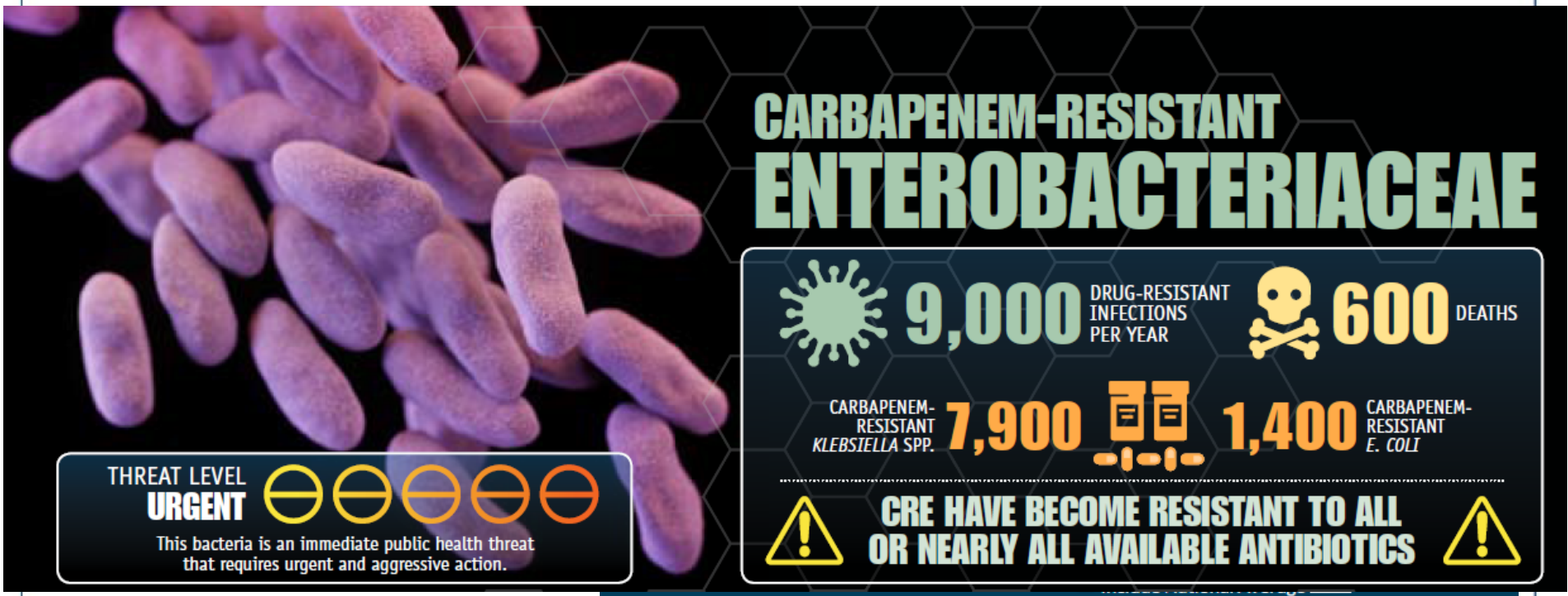
NCHSN (2011 – 2014)

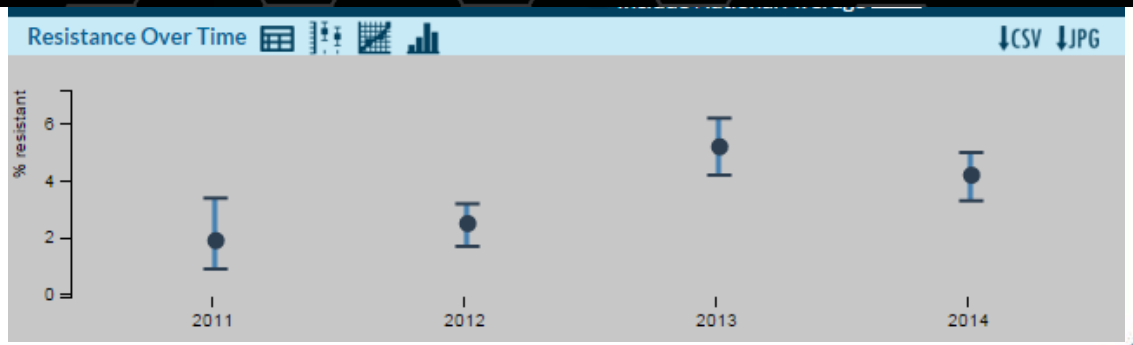




CRE – Regional Epidemiology

NCHSN (2011 – 2014)





Antibiotic Resistance Threats in the U.S. 2013.

Other Threats…

MICROORGANISMS WITH A THREAT LEVEL OF SERIOUS

Multidrug-resistant ***Acinetobacter***

Drug-resistant ***Campylobacter***

Fluconazole-resistant ***Candida*** (a fungus)

Extended spectrum β-lactamase producing **Enterobacteriaceae (ESBLs)**

Vancomycin-resistant ***Enterococcus*** **(VRE)**

Multidrug-resistant ***Pseudomonas aeruginosa***

Drug-resistant **non-typhoidal *Salmonella***

Drug-resistant ***Salmonella*** **Typhi**

Drug-resistant ***Shigella***

Methicillin-resistant ***Staphylococcus aureus*** **(MRSA)**

Drug-resistant ***Streptococcus pneumoniae***

Drug-resistant **tuberculosis**

Antibiotic Resistance Threats in the U.S. 2013.

Improving antibiotic use reduces resistance

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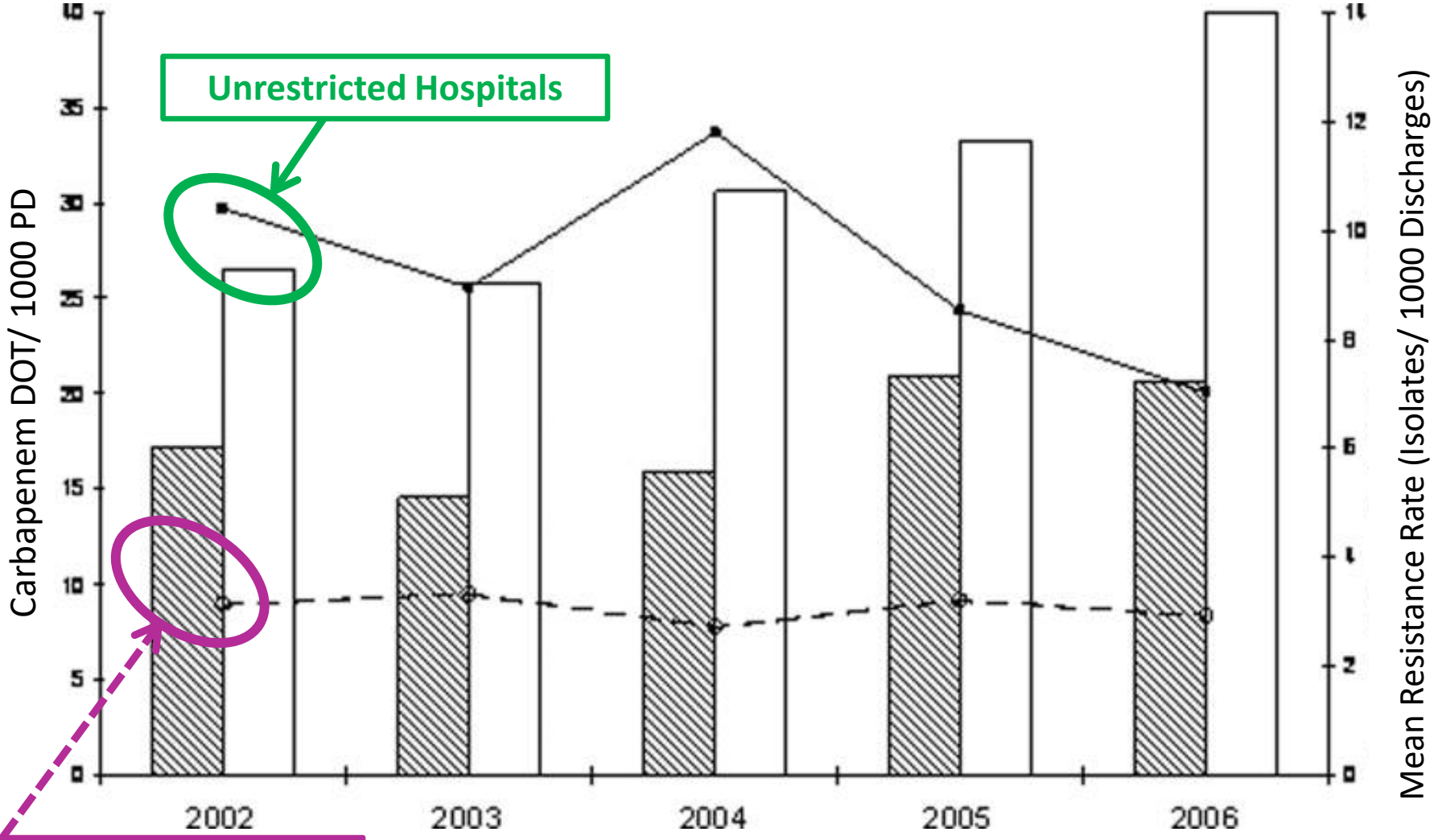
Misuse adversely impacts society



Pakyz, et al. Antimicrob Agents Chemother. 2009; 53: 1983–6.

Improving antibiotic use improves infection cure rates

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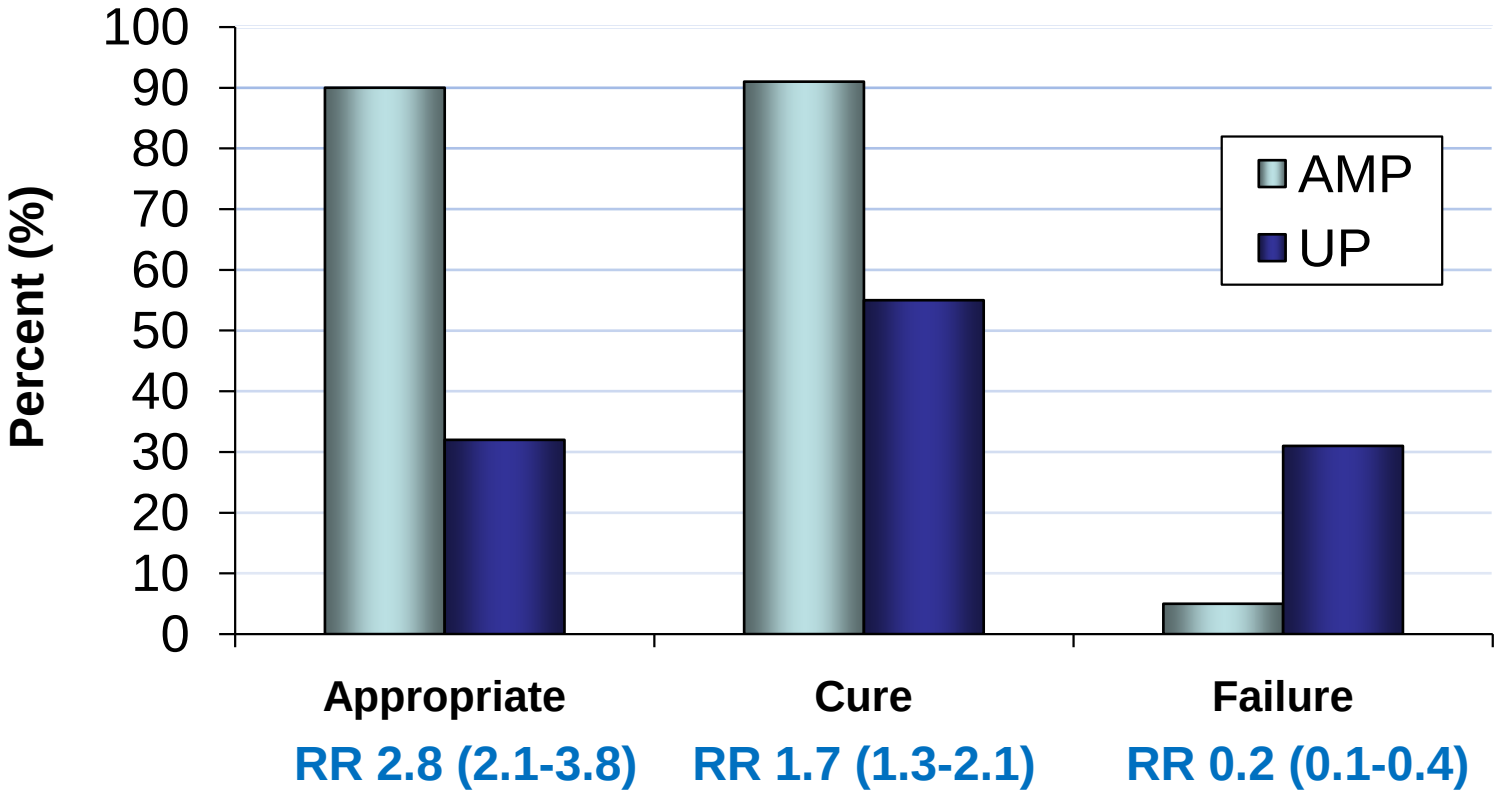
Clinical Outcomes with Antimicrobial Management Program



AMP = Antibiotic Management Program
UP = Usual Practice

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Fishman N. *Am J Med.* 2006;119:S53.

Improving antibiotic use reduces *C. difficile* infections

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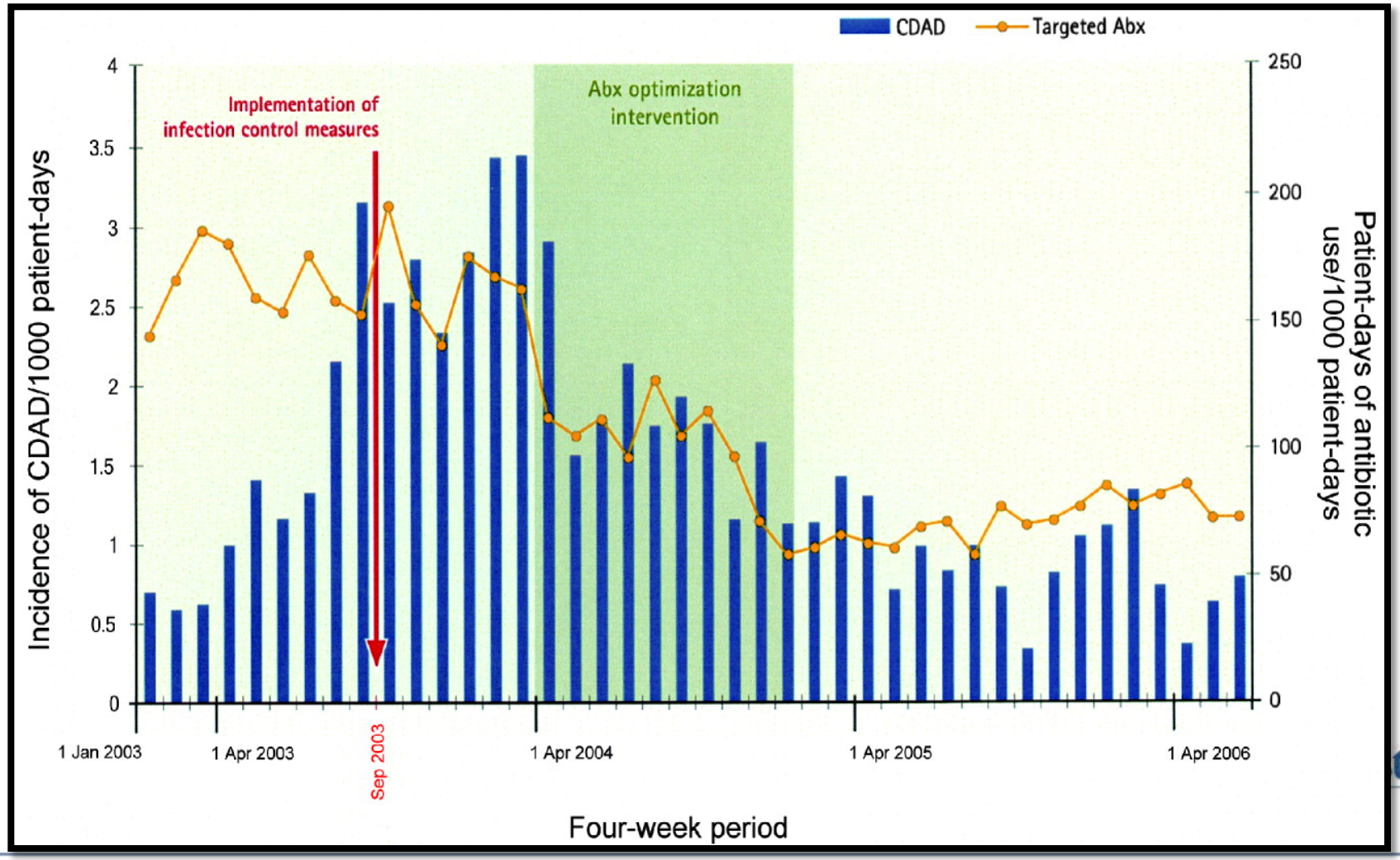
Targeted antibiotic consumption and nosocomial *C. difficile* disease

Tertiary care hospital; Quebec, 2003-2006



Valiquette, et al. *Clin Infect Dis* 2007;45:S112.

Antimicrobial Stewardship

- **A rational, systematic approach to the use of antimicrobial agents in order to achieve optimal outcomes**
  - Most appropriate agent
  - Optimal dosing
  - Appropriate route and duration

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IDSA/SHEA Guidelines for Antimicrobial Stewardship Programs. *Barlam TF, et al. Clin Infect Dis. 2016; 62: e51-77.*

Briefing Room

Your Weekly Address
Speeches & Remarks
Press Briefings
Statements & Releases
White House Schedule
Presidential Actions
Executive Orders
Presidential Memoranda
Proclamations
Legislation
Nominations & Appointments
Disclosures

The White House
Office of the Press Secretary

For Immediate Release September 18, 2014

Executive Order -- Combating Antibiotic-Resistant Bacteria

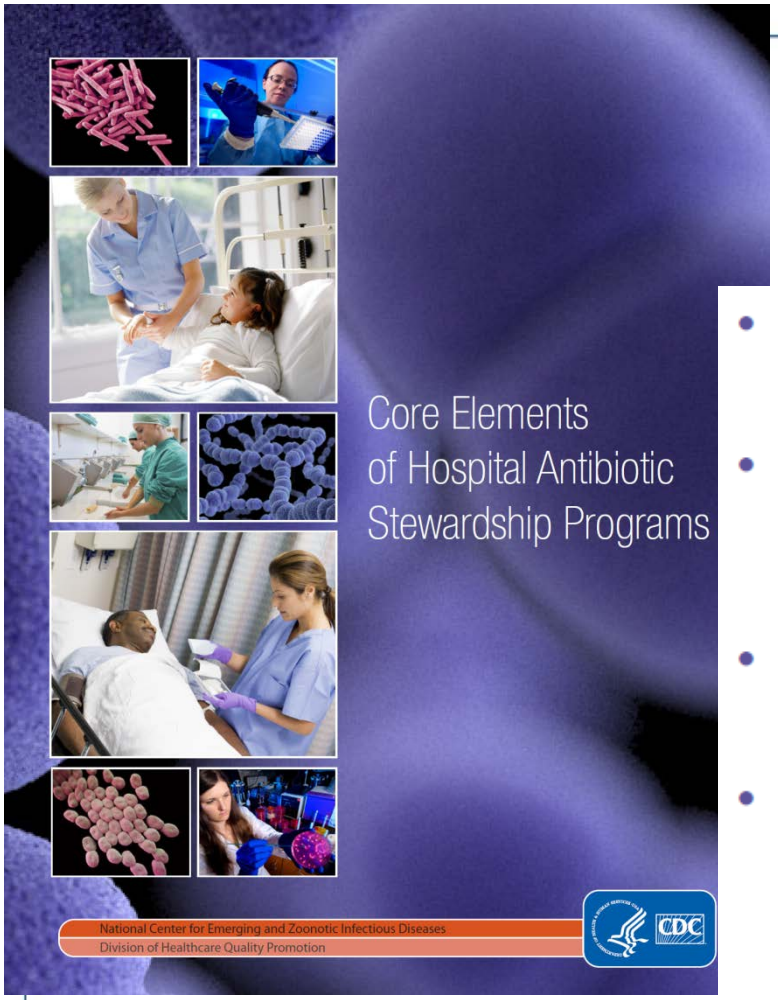
EXECUTIVE ORDER

- - - - - - -

COMBATING ANTIBIOTIC-RESISTANT BACTERIA

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

Section 1. Policy. The discovery of antibiotics in the early 20th century fundamentally transformed human and veterinary medicine. Antibiotics save millions of lives each year in the United States and



- **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.

Joint Commission

Requirement

Official Publication of Joint Commission Requirements

New Antimicrobial Stewardship Standard

APPLICABLE TO HOSPITALS AND CRITICAL ACCESS HOSPITALS

Effective January 1, 2017

Standard MM.09.01.01

The [critical access] hospital has an antimicrobial stewardship program based on current scientific literature.

Elements of Performance for MM.09.01.01

1. Leaders establish antimicrobial stewardship as an organizational priority. (*See also* LD.01.03.01, EP 5)

   Note: *Examples of leadership commitment to an antimicrobial stewardship program are as follows:*

   - *Accountability documents*
   - *Budget plans*
   - *Infection prevention plans*
   - *Performance improvement plans*
   - *ategic plans*
   - *ing the electronic health record to collect antimi-*
   - *bial stewardship data*

2. The [critical access] hospital educates staff and licensed independent practitioners involved in antimicrobial ordering, dispensing, administration, and monitoring about antimicrobial resistance and antimicrobial stewardship practices. Education occurs upon hire or granting of initial privileges and periodically thereafter, based on organizational need.

3. The [critical access] hospital educates patients, and their families as needed, regarding the appropriate use of antimicrobial medications, including antibiotics. (For more information on patient education, refer to Stan-

Continued on page 4

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"We **[propose requiring] a hospital to develop and maintain an antibiotic stewardship program** … to improve hospital antibiotic-prescribing practices and curb patient risk for possibly deadly *Clostridium difficile infections* (CDIs)…and potentially life-threatening, antibiotic-resistant infections."

"We promote **better alignment of a hospital's** infection control and **antibiotic stewardship efforts with nationally recognized guidelines** and heighten the role and accountability of a hospital's governing body in program implementation and oversight."

Goals of Antimicrobial Stewardship

- Optimize clinical outcomes
- Minimize unintended consequences of antimicrobial use
  - Toxicity
  - Emergence of resistance
  - Selection of pathogenic organisms such as *C. difficile*

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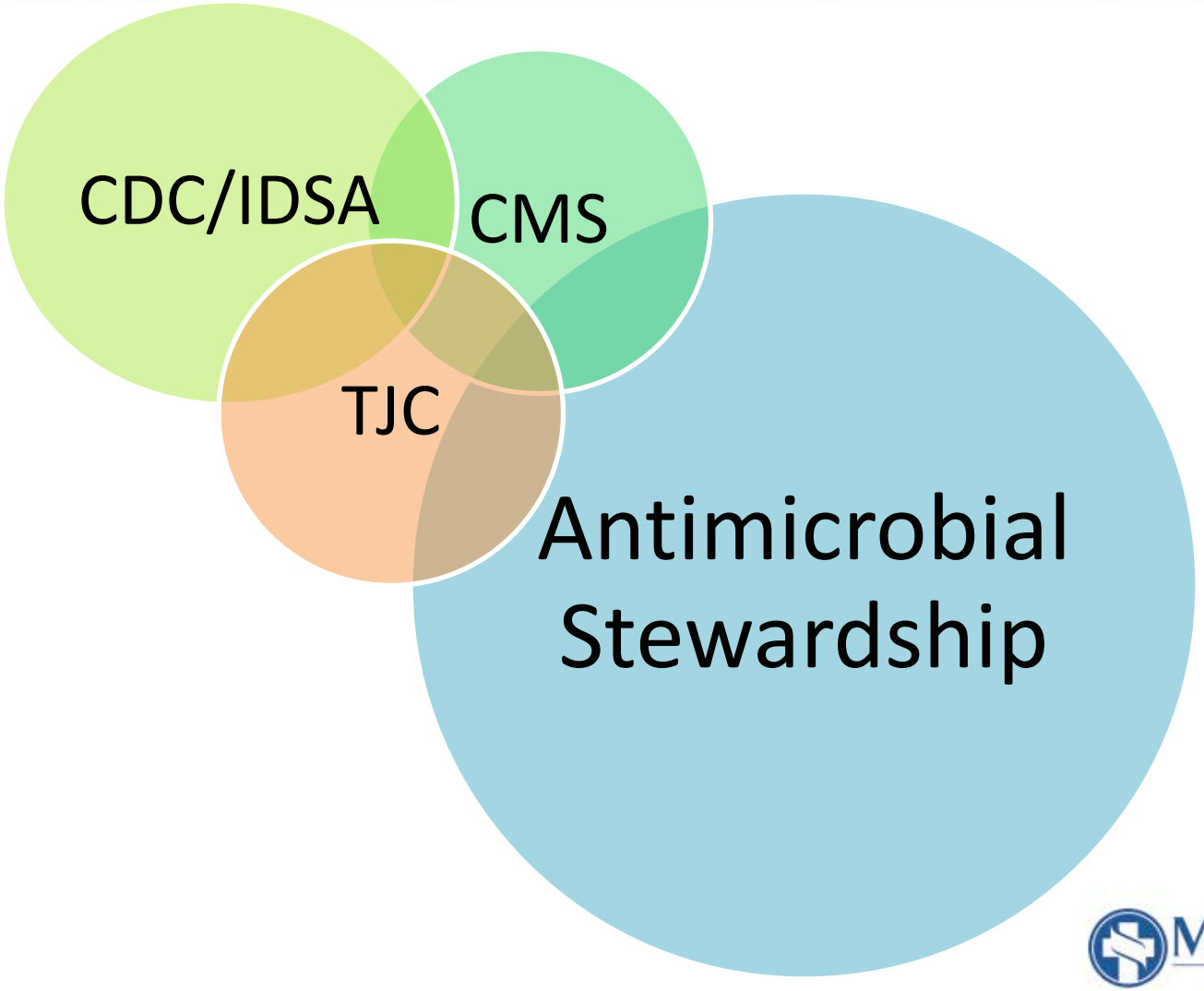
IDSA/SHEA Guidelines for Antimicrobial Stewardship Programs. *Barlam TF, et al. Clin Infect Dis. 2016; 62: e51-77.*

The Landscape of Antimicrobial Stewardship



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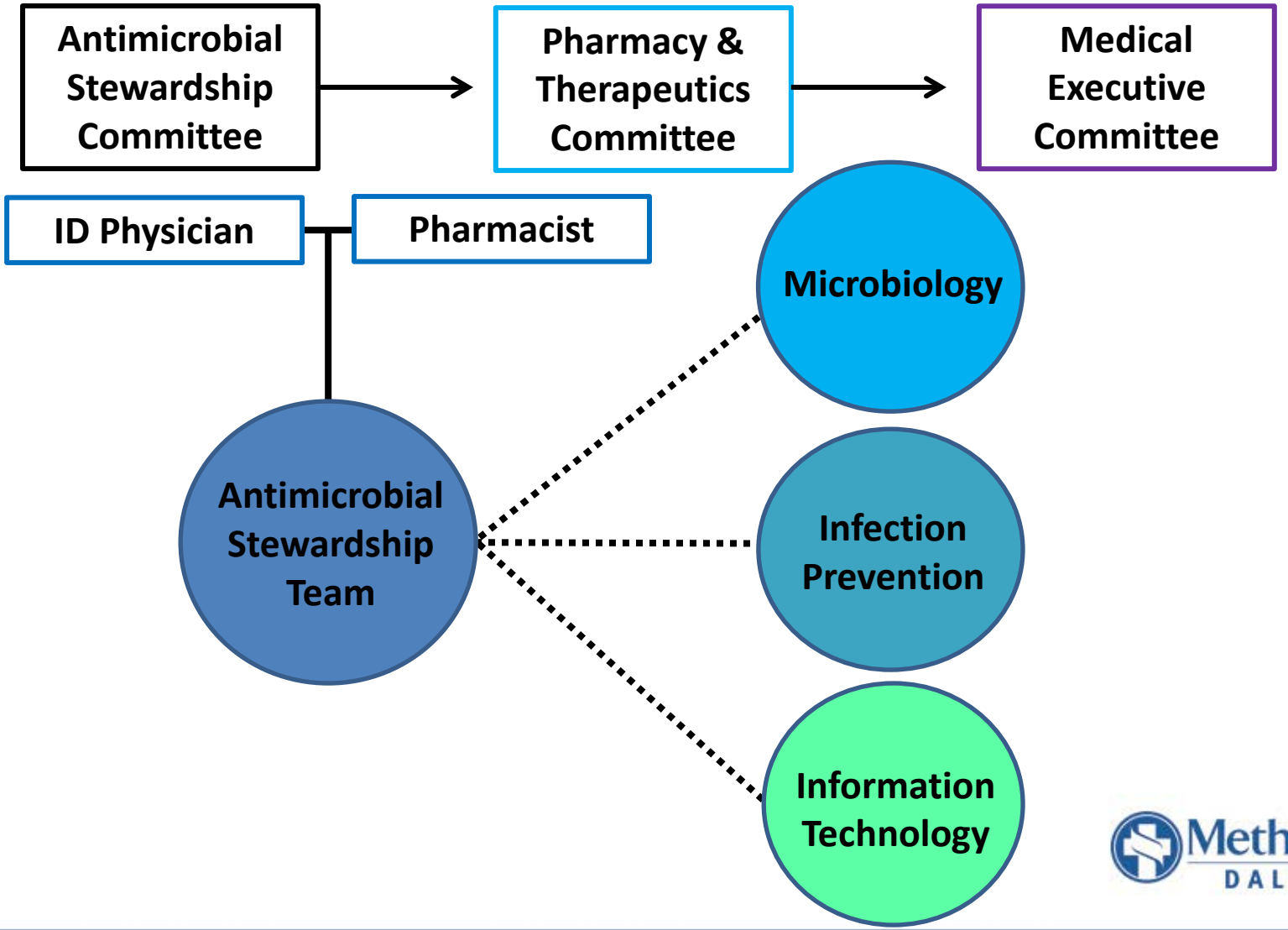
The hospital has an antimicrobial stewardship multidisciplinary team.



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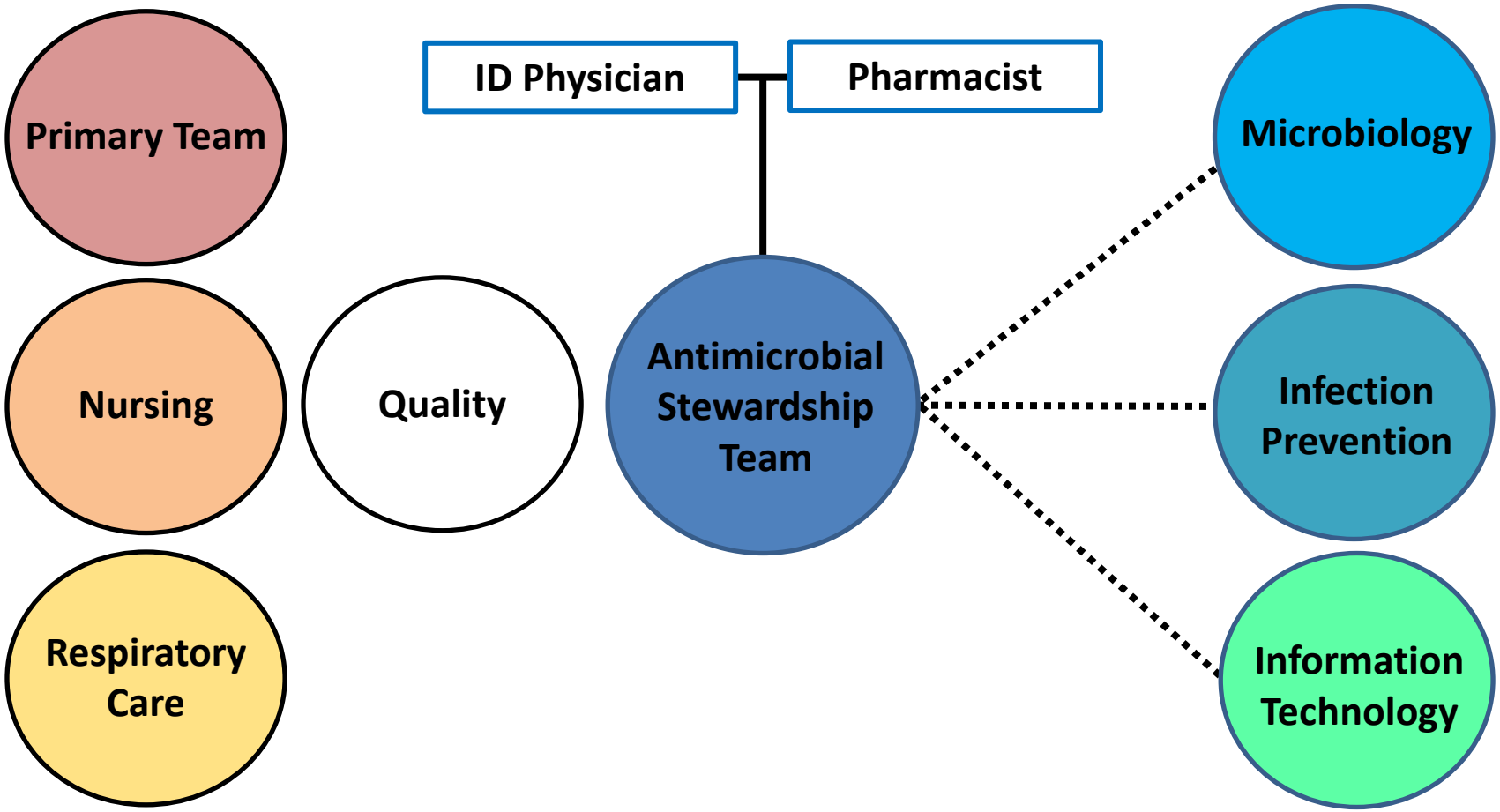

The hospital has an antimicrobial stewardship multidisciplinary team.

Antimicrobial Stewardship Committee

Dr. Dominguez, Chair
Me, Co-Chair
Jon Albrecht
Dr. Barrera
Dr. Ebuh
Marie Hale
Dr. Hunter
Dr. Jaynes
Dr. Lorenzo
Tariro Matsikire
Dr. Momin
Dr. Noori
Joslyn Pribble
Ilka Ratsaphangthong
Dr. Saad
Dr. Schilling
Dr. Thomas
Beth Wallace

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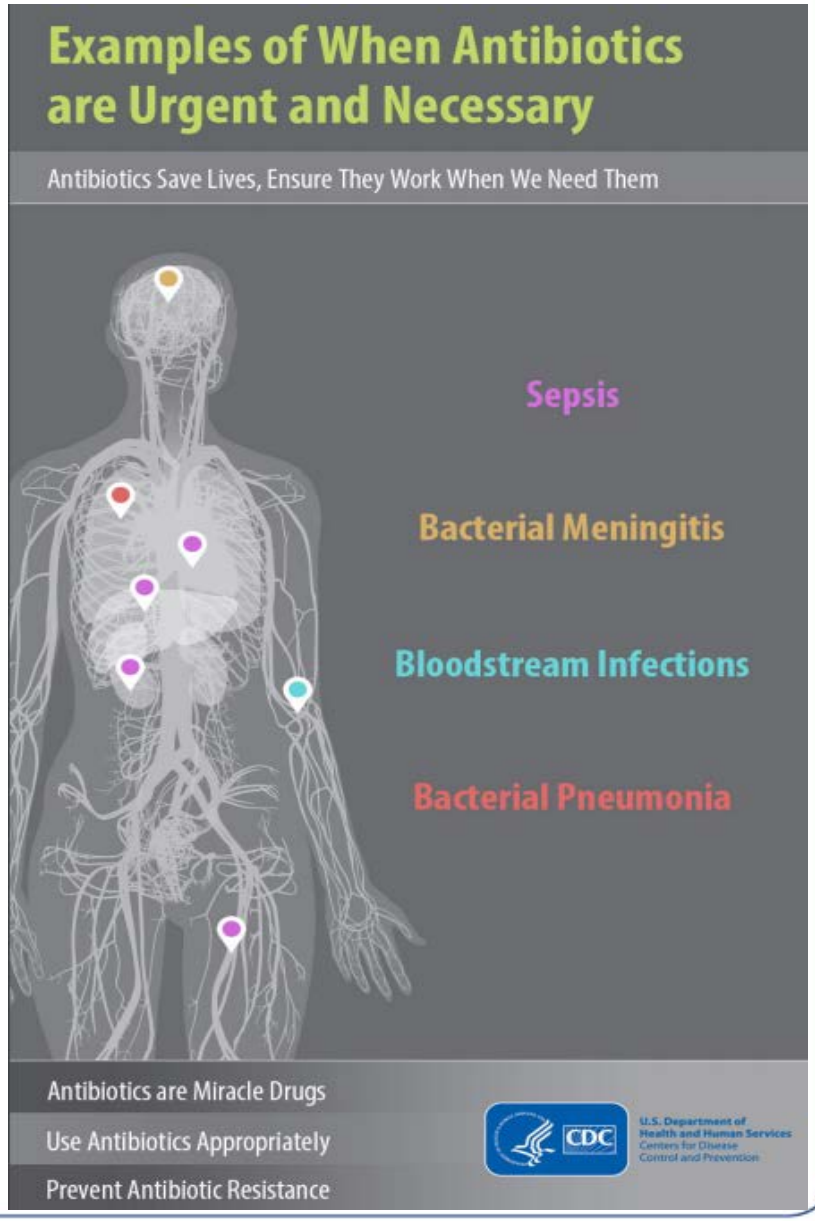
TJC Standards (Effective Jan. 1, 2017)

Strategies for Antimicrobial Stewardship

- How can we improve?
  - Passive
  - Active

  . . . . . Prevent



CDC Getsmart for Healthcare. 2015.

Passive Strategies for Antimicrobial Stewardship (AS)

- Education
  - Providers and staff
  - Patients!
- Guidelines, Pathways, or Protocols

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IDSA/SHEA Guidelines for Antimicrobial Stewardship Programs. *Barlam TF, et al. Clin Infect Dis. 2016; 62: e51-77.*

Hospitals educate patients and families regarding the appropriate use of antimicrobials.

Viruses or Bacteria
What's got you sick?

Antibiotics only treat bacterial infections. Viral illnesses cannot be treated with antibiotics. When an antibiotic is not prescribed, ask your healthcare professional for tips on how to relieve symptoms and feel better.

Illness	Usual Cause		Antibiotic Needed
	Viruses	Bacteria	
Cold/Runny Nose	✓		NO
Bronchitis/Chest Cold (in otherwise healthy children and adults)	✓		NO
Whooping Cough		✓	Yes
Flu	✓		NO
Strep Throat		✓	Yes
Sore Throat (except strep)	✓		NO
Fluid in the Middle Ear (otitis media with effusion)	✓		NO
Urinary Tract Infection		✓	Yes

biotic

infection. Some
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n stop

GET SMART
Know When Antibiotics Work
www.cdc.gov/getsmart

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Antibiotics Aren't Always the Answer

The hospital's ASP uses organizational-approved multidisciplinary protocols.

- Antibiotic Formulary Restrictions: Implementation of antibiotic formulary restrictions have been shown to reduce antibiotic use.
  - We propose replacing the term 'restricted' antibiotics with 'protected.'
  - Specific antimicrobials can be protected in the absence of ID trained specialists with the establishment of use criteria and guidelines

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TJC Standards (Effective Jan. 1, 2017). MM 09.01.01

Passive Strategies: Pathway

***Clostridium difficile* Infection (CDI) Management Guidelines**

Diagnosis

Should be based on combination of clinical and laboratory findings:

- Acute onset of diarrhea (≥ 3 unformed or watery stools occurring in ≤ 24 hours) **AND**
- Positive *C. difficile* toxin test or Pseudomembranous colitis on endoscopy OR high clinical suspicion

Other signs/symptoms associated with CDI include:

- Mild to severe abdominal pain or cramping
- Fever (>38° C or 100° F)
- Leukocytosis
- Dehydration
- Radiographic evidence of toxic megacolon, colonic wall-thickening or pseudomembranous colitis
- Increasing SCr (1.5x baseline)
- Low albumin (≤ 2.5 g/dL)
- Increasing lactate levels

Risk Factors for CDI

- Antibiotic use within past 90 days or currently receiving antibiotics
- Colon disease or underlying cancer
- Previous *C. difficile* infection
- Use of proton pump inhibitors (e.g., Protonix or Nexium)
- Receipt of antiperistaltic drugs (e.g., Lomotil or loperamide)
- Age ≥ 65 year
- Recent or currently hospitalized
- Resident of nursing home or lon
- Underlying immune compromis
- Abdominal procedure or surgery

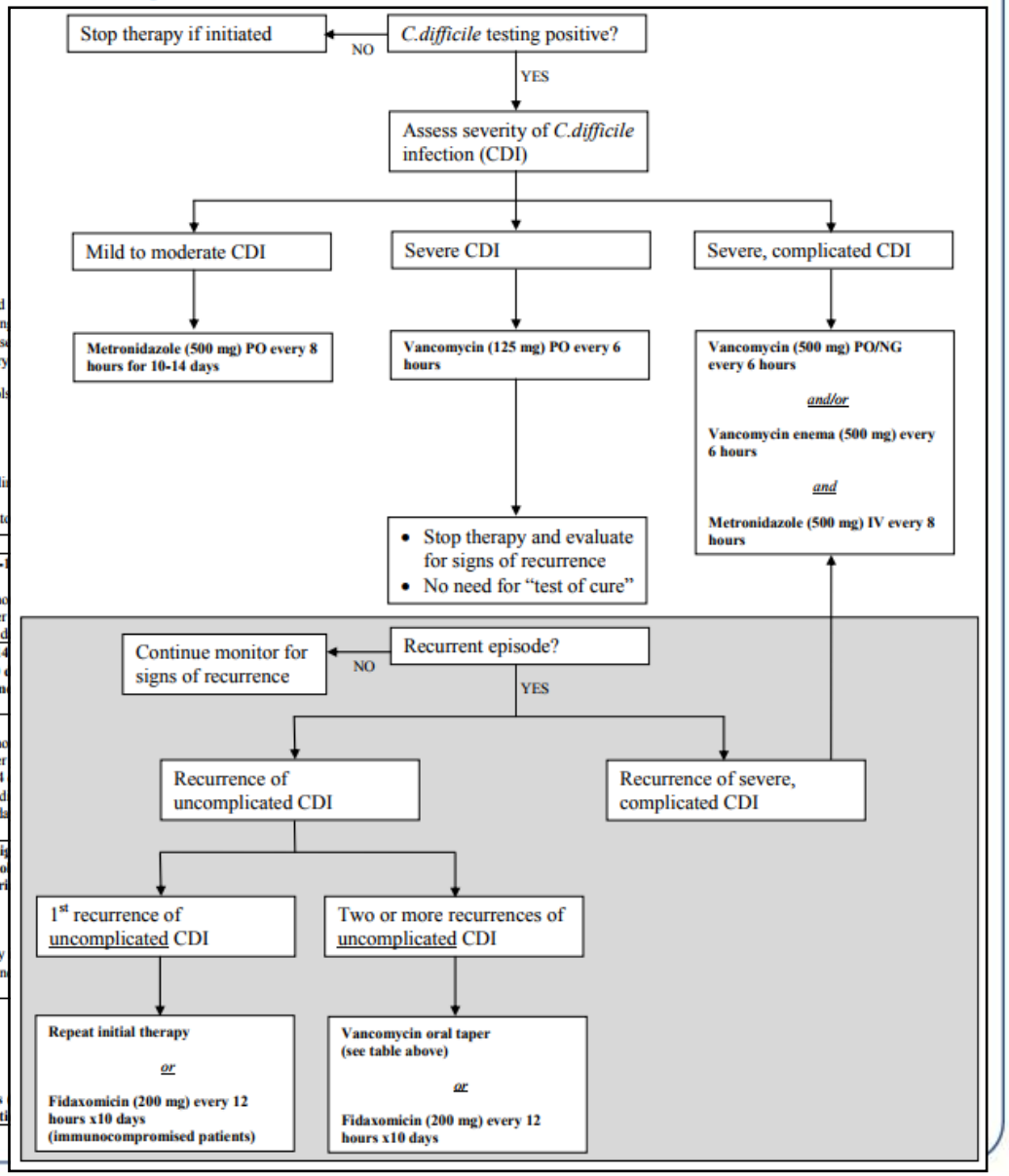
Infection Prevention

- Contact precautions: 1) Gown/gloves to enter room, 2) Continue precautions until treatment complete AND formed stools cleaned, 3) place in contact as soon as suspect *C. difficile* (don't wait for test results)
- Repeat testing NOT necessary after end of treatment. Test can not be repeated within a 7 day time frame.
- Practice hand hygiene with soap and water before and after patient/environmental contact.

General Measures

- Discontinue unnecessary/offending antibiotics or change to a lower risk agent if possible (high risk antibiotics include cli fluoroquinolones, 2nd or 3rd generation cephalosporins)
- Avoid for high risk drugs: proton pump inhibitors, pro-motility agents, antiperistaltic agents, binding agents, laxatives, st

Indication	Criteria	Treatment[1-5]
Mild-Moderate CDI: First episode and first recurrence	• ≥ 3 unformed or watery stools in ≤ 24 hours	• **Metronidazole 500 mg PO every 8 hours for 10-** first recurrence) • If symptoms *worsen or not improving* (diarrhea sho won't be completely resolved) in 4-6 days consider Vancomycin 125 mg PO every 6 hours for 10-14 d
Mild-Moderate CDI: Second recurrence	• Clinical signs/symptoms consistent with mild CDI (see above)	• **Vancomycin 125 mg PO every 6 hours for 10-14** • **Fidaxomicin* 200 mg PO every 12 hours for 10 appropriate initial therapy and duration with m oral vancomycin)**
Severe CDI: First episode and any recurrence	At least 1 of the following criteria: • Admission to ICU due to CDI • Leukocytosis (15,000 cells/μL) • Increasing SCr (1.5x baseline)	• **Vancomycin 125 mg PO every 6 hours** • If symptoms *worsen or not improving* (diarrhea sho won't be completely resolved) in 4-6 days consider Metronidazole 500 mg IV every 8 hours for 10-14 • Consider ID, GI or surgery consult as clinically ind • Fidaxomicin* may be considered following 4-6 da and IV metronidazole
Severe-complicated Disease: First episode and any recurrence	Meets criteria above for severe disease AND has any of the following: • Ileus / Obstruction • Perforation • Toxic megacolon • Colonic wall-thickening • Pseudomembranous colitis • Septic shock/hypotension	• **Vancomycin 500 mg PO/NG every 6 hours (if hig indications – requires ID consult or per protoco reduce dosage to 125mg q6h if only above criteri** *Plus* • **Metronidazole 500 mg IV every 8 hours** • Recommend ID, GI or surgery consult as clinically • If complete ileus, may consider adding retention en mg every 6 hours
Multiple recurrences: ≥ 3 episodes within 3 months	• ≥ 3 unformed or watery stools in ≤ 24 hours • Any of the other signs/symptoms listed above	Vancomycin taper or pulse dosing • 125 mg every 6 hours x 10-14 days • 125 mg every 12 hours x 7 days • 125 mg daily x 7 days • 125 mg every 2-3 days for 2-8 weeks **Fidaxomicin* 200 mg PO every 12 hours for 10 days following 1st recurrence in immunocompromised pati**



The hospital's ASP uses organizational-approved multidisciplinary protocols.

- Anti-MRSA Agents
  - Ceftaroline
  - Daptomycin
  - Linezolid
- Broad-Spectrum
  - Carbapenems
  - Levofloxacin
  - Tigecycline
- Gram-Negative
  - Colistin
  - Ceftolozane-Tazobactam
  - Ceftazidime-Avibactam
- Anti-CDI Agents
  - Fidaxomicin

Antimicrobials with criteria for use at MDMC

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Aren't they all the same?

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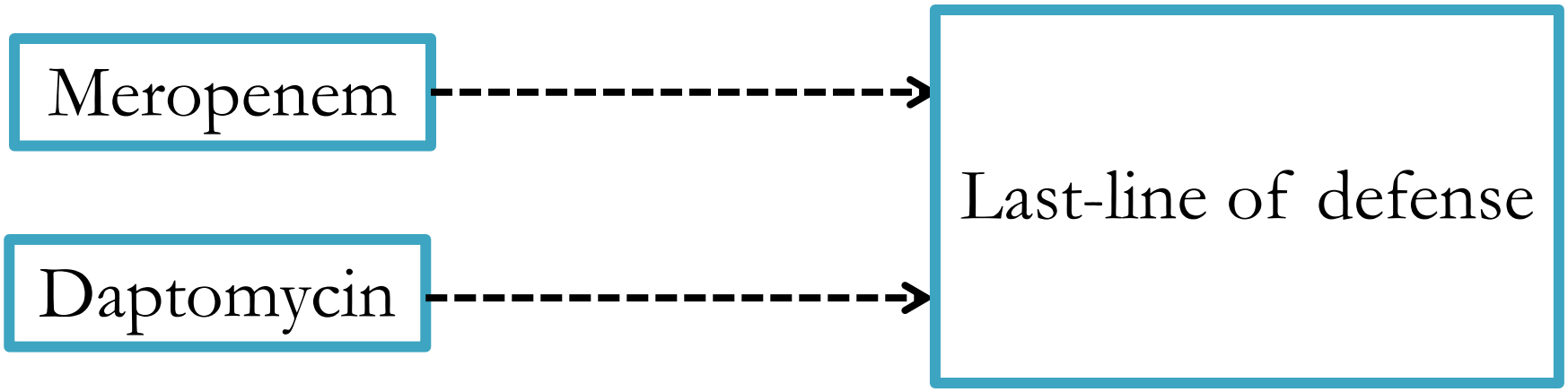
Why "protect" some antibiotics?



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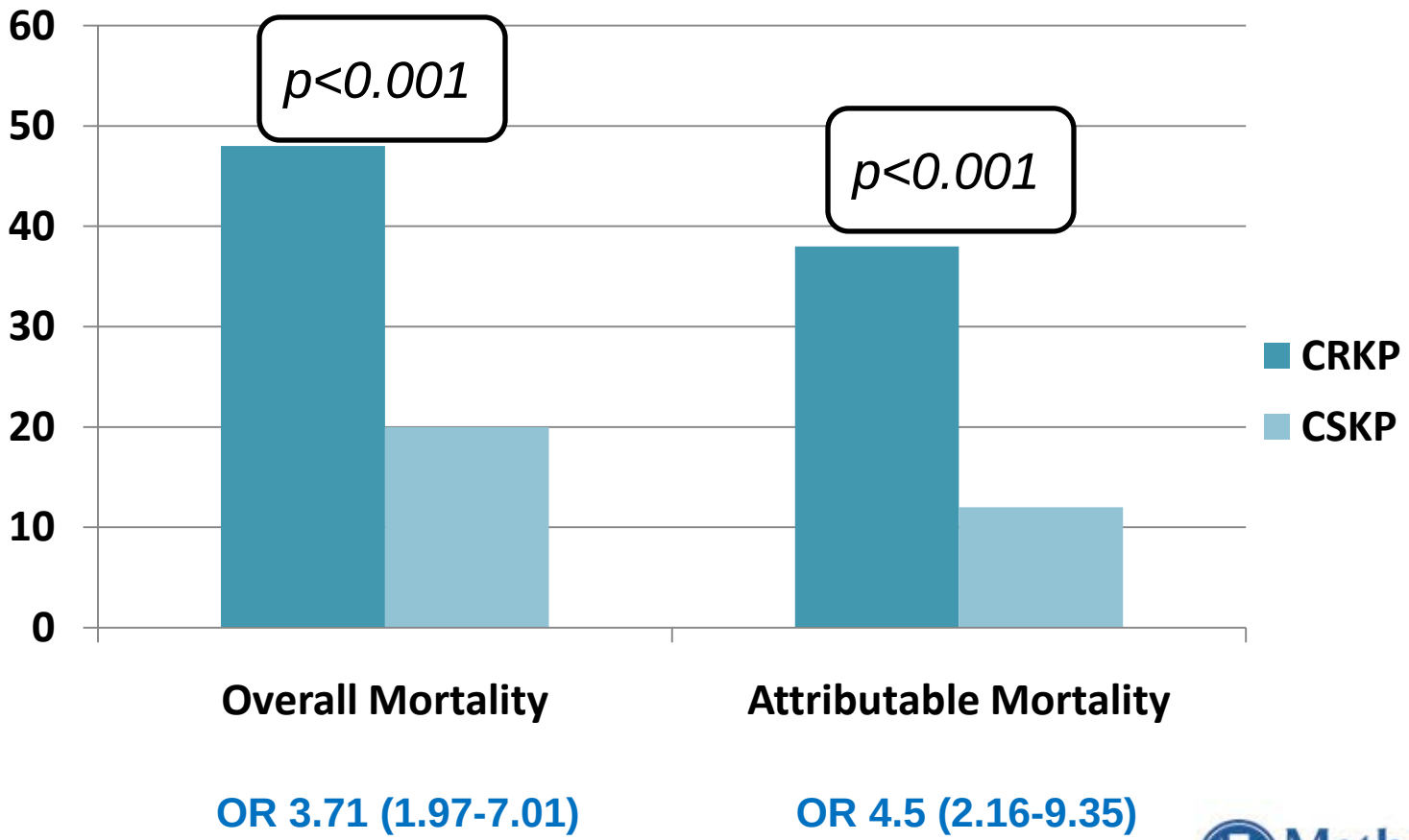
Mortality associated with carbapenem resistant (CR) vs. susceptible (CS) *Klebsiella pneumoniae* (KP)



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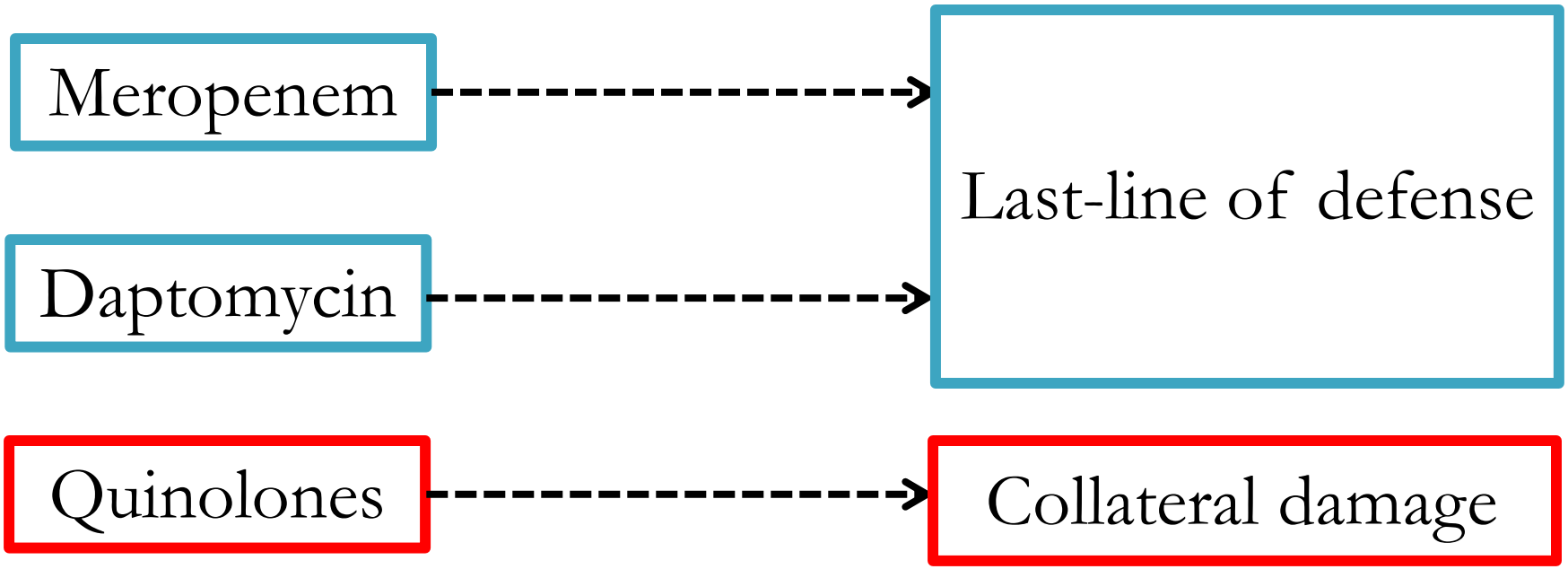
Patel, et al. Infect Control Hosp Epidemiol. 2008; 29:1099-106.

Why "protect" some antibiotics?



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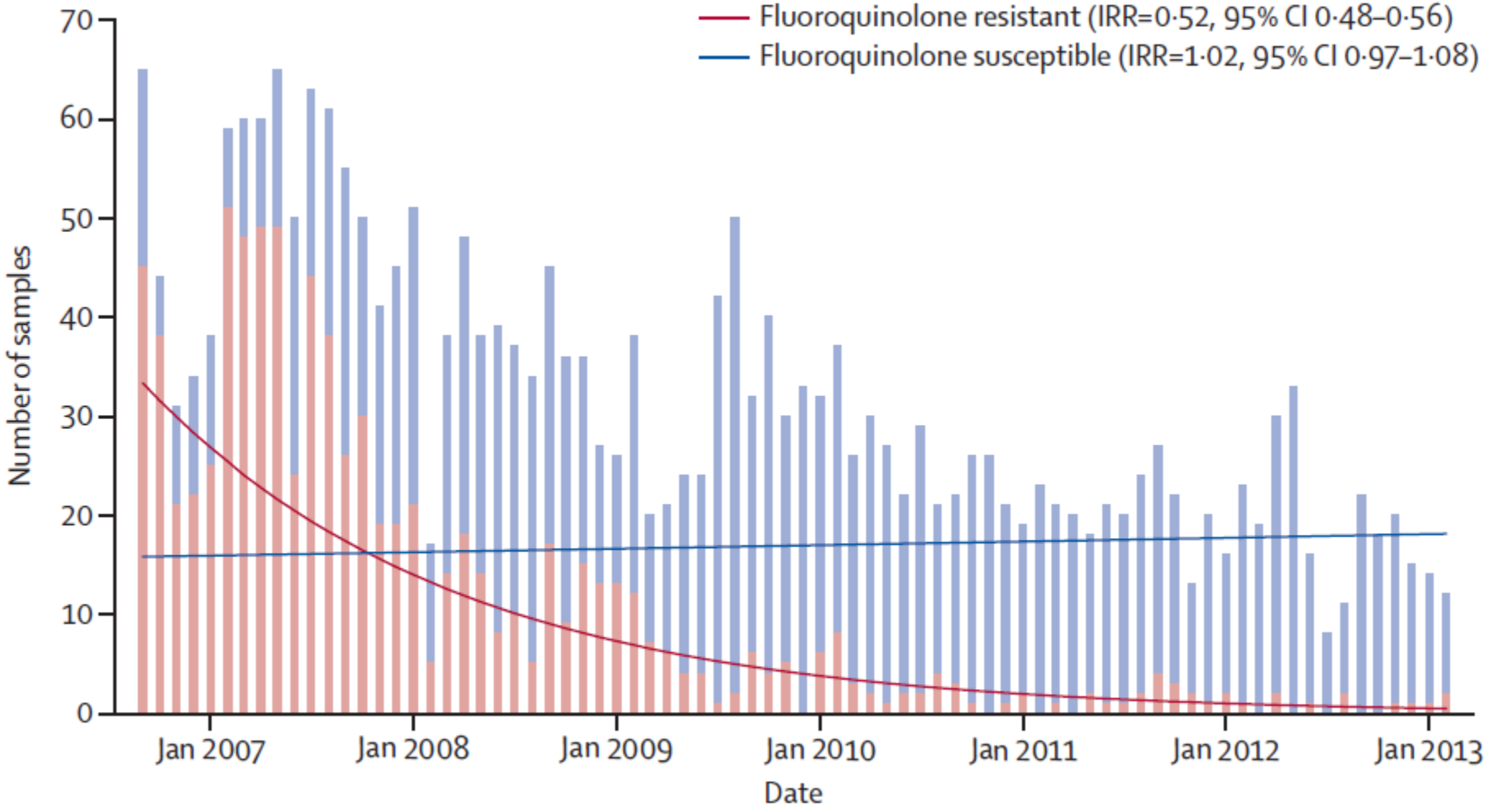
Quinolones & Collateral Damage



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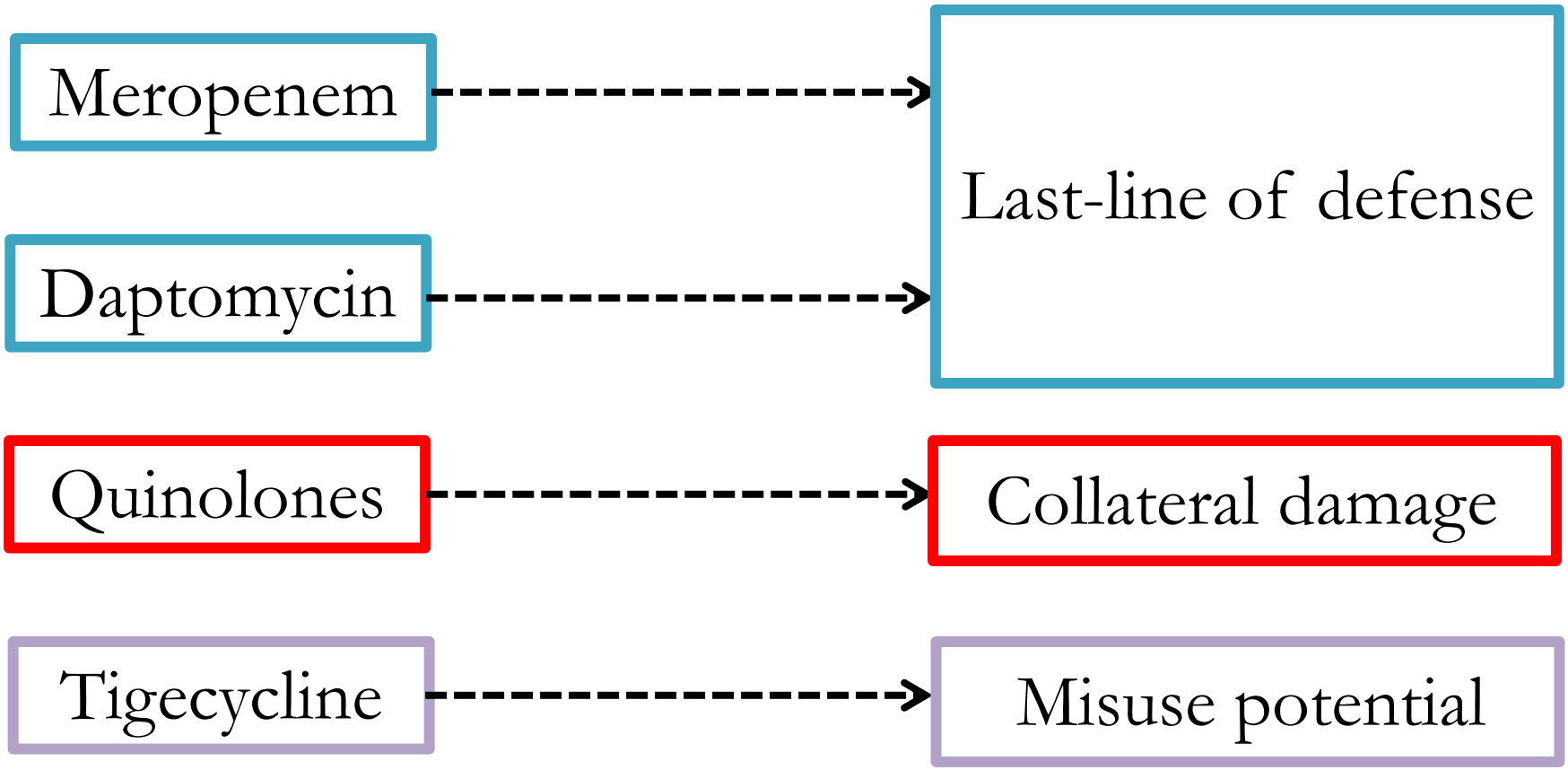
Dingle K, et al. Lancet. 2017;56:1685-94.

Why "protect" some antibiotics?



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FDA Drug Safety Communication: FDA warns of increased risk of death with IV antibacterial Tygacil (tigecycline) and approves new Boxed Warning

"In general, the deaths resulted from worsening infections, complications of infection, or other underlying medical conditions."

non-approved uses. As a result, we approved a new *Boxed Warning* about this risk to be added to the Tygacil drug label and updated the *Warnings and Precautions* and the *Adverse Reactions* sections. A *Boxed Warning* is the strongest warning given to a drug. These changes to the Tygacil label are based on an additional analysis that was conducted for FDA-approved uses after issuing a Drug Safety Communication (DSC) about this safety concern in September 2010.

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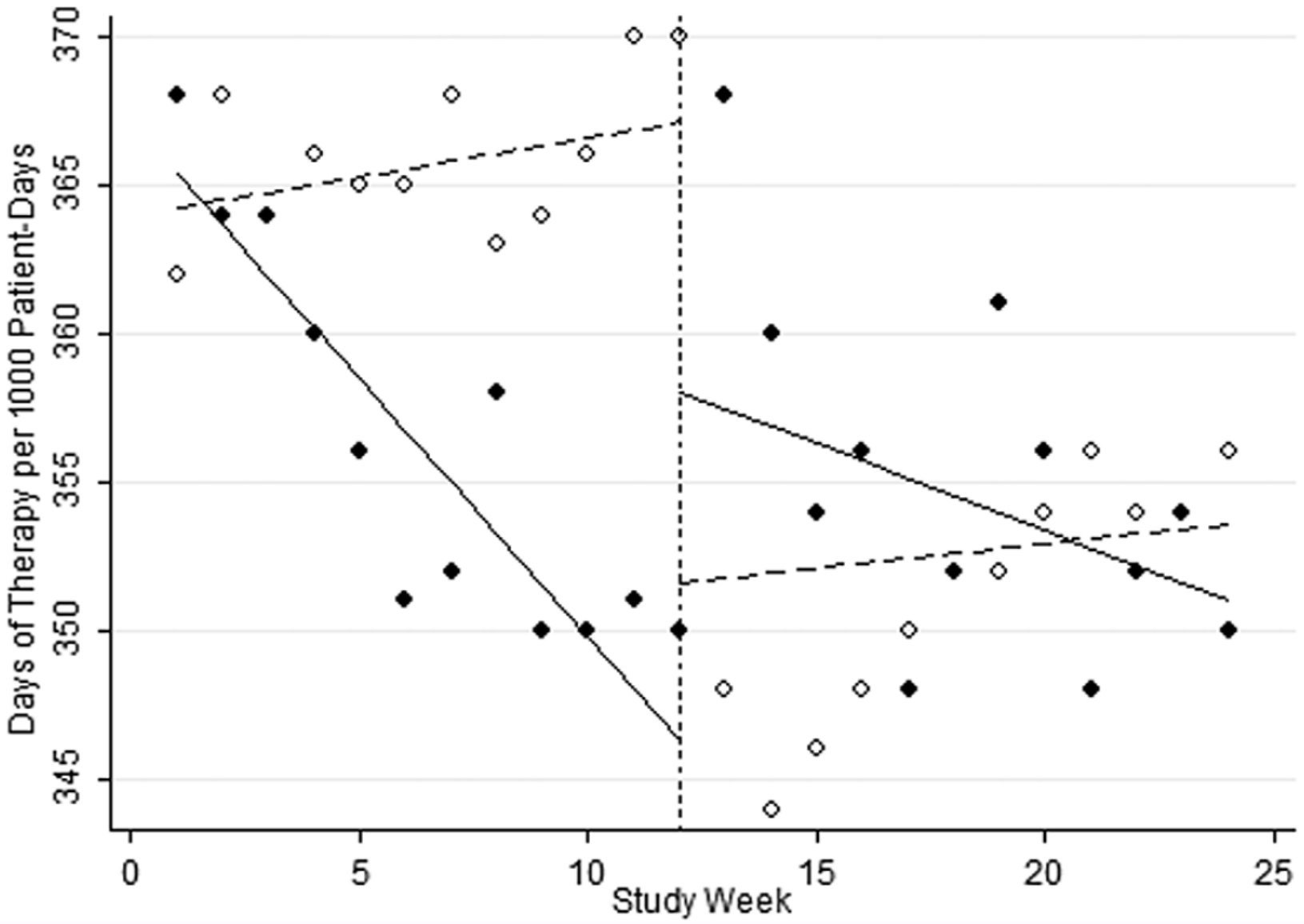
Active Strategies for AS

- Prospective-audit and feedback (PAF)
  - Intervention that engages the provider after an antibiotic is prescribed
  - Labor and time intensive when performed manually
    - Clinical decision-support systems to supply ASP with relevant data and identify patients who should be prioritized for review
- Pre-authorization and restriction (PAR)
  - Prescriber seeks input from stewardship program prior to the first administered dose

Tamma PD, et al. Clin Infect Dis. 2017;64:537–43.
Kullar R, et al. Clin Infect Dis 2013; 57: 1005–13.
Hensgens MP, et al. JAC. 2012; 67: 742–8.
Elligsen M, et al. ICHE. 2012; 33: 354–61.

Which Method is Better?



Tamma PD, et al. Clin Infect Dis. 2017;64:537–43.

Which Method is Better?

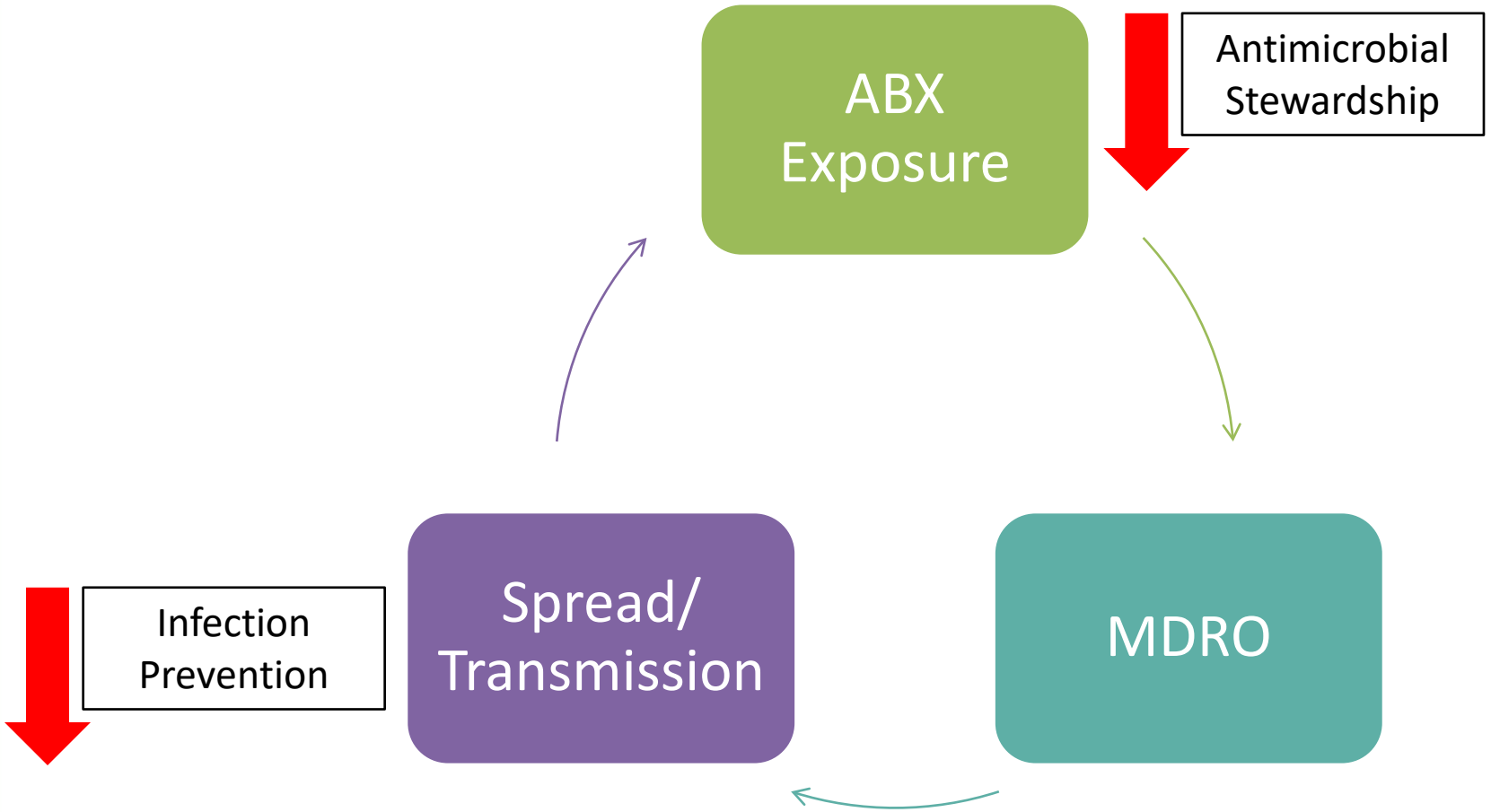
	PROS	CONS
PAR	• Most appropriate agents upfront • Increased likelihood of appropriate culture collection prior to antibiotic initiation • Limit patient exposure to antibiotics when no anti-infective therapy is warranted	• Only select agents • No impact on narrowing, duration • Resource intensive: “on-call”
PAF	• Flexibility of timing (staffing) • More evidenced-based discussion - Micro and clinical data	• Time consuming - More data to review • Uptake is usually optional • Does not address the large burden of empiric antibiotics started unnecessarily

Pre-authorization and restriction (PAR)
Prospective-audit and feedback (PAF)

Any other Strategies?

- Prevention
  - Hand hygiene
  - Terminal cleaning
  - Vaccination

Collaboration



Nagel JL, et al. Infect Dis Clin N Am. 2016;30: 771-84.

Improvement is a public health emergency

Methodist DALLAS

Improving antibiotic use is a public health emergency

- Antibiotics are the only drug where use in one patient can impact the effectiveness in another.
- If everyone does not use antibiotics well, we will all suffer the consequences.

Get Smart for Healthcare – CDC

Methodist DALLAS

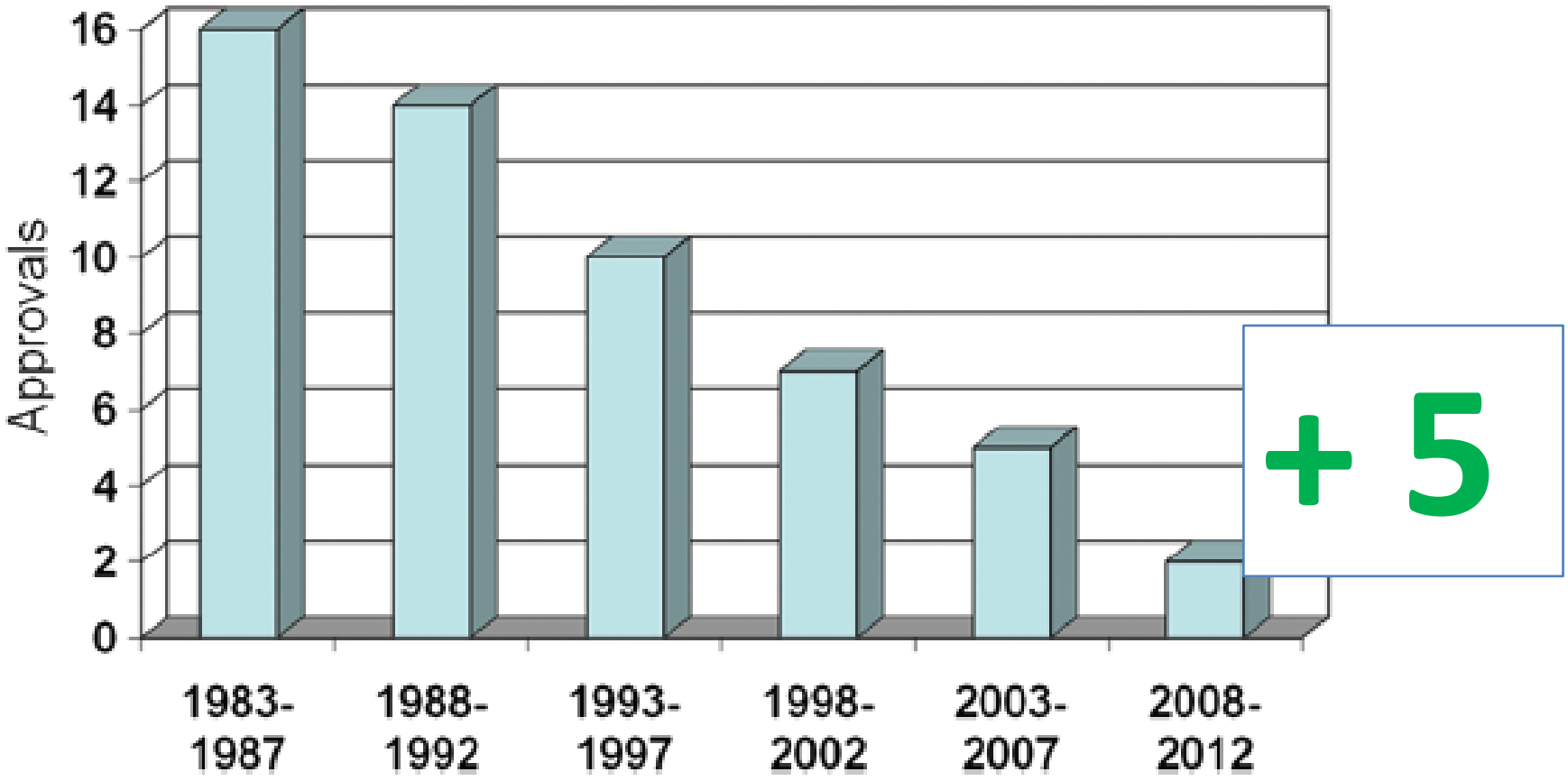
Improving antibiotic use is a public health imperative

- **Antibiotics are a shared resource, (and becoming a scarce resource).**

Get Smart for Healthcare – CDC

Methodist DALLAS

Antimicrobial Drug Development



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Bourcher HW, et al. Clin Infect Dis. 2013;56:1685-94.

Improving antibiotic use is a public health imperative

- Using antibiotics properly is analogous to developing and maintaining good roads.
- Bringing new antibiotics into our current environment is akin to buying a new car because you hit a pot hole, but doing nothing to fix the road.
- Fixing the "antibiotic use road" is part of the mission of public health.

Methodist DALLAS

Summary/Conclusions

- Collaborative goals and strategies
  - Decrease problematic pathogens
  - Determine optimal management of these pathogens
- Collaborative measurement
  - Metrics for success (or failure)
  - Share/report this information to WIDE audience
- **Efforts impact public health and the future of medicine!**

Strategies in Stewardship and Why Some Antimicrobials Should Be Protected

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September 7, 2017

Microorganisms

Aerobic Gram-Positive Cocci (GPC)

***Staphylococcus* spp.**

Staphylococcus aureus
(Skin flora. Hospital and community-acquired pneumonia, SSTIs, osteomyelitis, endocarditis, septic arthritis, blood and catheter infections, MSSA/MRSA)

Staphylococcus epidermidis
(aka Coagulase-negative *Staphylococcus epidermidis*, CoNS)
(Skin flora. Foley (urine) catheter and IV line infections, prosthetic device infections, contaminates blood cultures)

Staphylococcus saprophyticus
(Vaginal flora. UTIs: 2nd to *E. coli* in younger, sexually active females)

***Streptococcus* spp.**

***Streptococcus pyogenes* (Grp A β-hemolytic)**
(Skin flora. Strep throat (pharyngitis), SSTIs, scarlet fever, rheumatic fever, glomerulonephritis)

***Streptococcus agalactiae* (Grp B β-hemolytic)**
(Vaginal flora. Neonatal meningitis, pneumonia, and sepsis)

***Streptococcus pneumoniae* (α-hemolytic)**
(Community-acquired pneumonia (CAP), otitis media, bacterial meningitis)

Viridans Group Streptococci (α-hemolytic)
(GI flora. Dental infections, endocarditis, abscesses)
S. anginosus (aka S. milleri), S. mutans, S. mitis, S. salivarius, S. sanguis, Gamella morbillorum

***Streptococcus bovis* (Grp D Nonenterococcal Strep.)**
(GI flora. Associated with colon cancer)

***Enterococcus* spp.**

Enterococcus faecalis* and *Enterococcus faecium
(GI flora. UTIs, biliary infections, bacteremia, endocarditis, VRE)

Aerobic Gram-Negative Bacilli (GNB)

Enterobacteriaceae ("enteric")

Escherichia coli (Diarrhea, UTIs, neonatal meningitis, sepsis)
***Klebsiella* spp.** (UTIs (foley catheters), nosocomial pneumonia, sepsis)
***Enterobacter* spp.** (Nosocomial infections)
***Citrobacter* spp.** (Nosocomial infections)
Proteus mirabilis (UTIs, nosocomial infections)
***Providencia* spp.**
Morganella morganii
***Serratia* spp.** (UTIs, wound infections, pneumonia)
***Shigella* spp.** (Dysentery. Not GI normal flora – pathogen)
***Salmonella* spp.** (Typhoid fever, diarrhea, sepsis, carrier)
Yersinia enterocolitica (Diarrhea)

Nonenterobacteriaceae

Pseudomonas aeruginosa
(Nosocomial infections: pneumonia, osteomyelitis, sepsis, UTIs, endocarditis)
Acinetobacter baumannii (Nosocomial infections)
Stenotrophomonas (Xanthamonas) maltophilia (Nosocomial infections)
Haemophilus influenzae
(Influenzae, meningitis, epiglottitis, septic arthritis, sepsis)
Legionella pneumophilia (CAP)
Bordetella pertussis (Whooping cough)
Bartonella henselae (Cat scratch disease) and ***Pasteurella multocida*** (Animal bites/scratches)
***Helicobacter pylori* (H. pylori)** (GI ulcers, gastritis)
Brucella spp. (Undulant fevers)
Vibrio cholera (Diarrhea)
Campylobacter jejuni (Diarrhea)

Aerobic Gram-Positive Bacilli

SPORE-FORMING

***Bacillus* spp.**
Bacillus anthracis (Antrax)
Bacillus cereus (Gastroenteritis (food poisoning))

NONSPORE-FORMING

***Corynebacterium* spp.**
(Skin flora . Culture contaminant; non-pathogenic forms are called "diphtheroids"
Listeria monocytogenes
(Meningitis in neonates (3rd after Grp B Strep. and E. coli) and immunosuppressed)
***Nocardia* spp.** (opportunistic pathogen)

***Mycobacterium* spp.**
Mycobacterium tuberculosis

Aerobic Gram-Negative Cocci

***Neisseria* spp.**
Neisseria meningitidis (Meningitis (<1 yo), sepsis)
Neisseria gonorrhoeae (STD - gonorrhea, septic arthritis)

Moraxella catarrhalis (Respiratory infections)

Anaerobic Gram-Positive Bacilli

SPORE-FORMING

***Clostridium* spp.**
Clostridium perfringens (Gas Gangrene - cellulitis/wound infections)
Clostridium difficile
(Antibiotic-induced diarrhea, Pseudomembraneous enterocolitis)

NONSPORE-FORMING

***Actinomyces* spp., *Propionibacterium acnes*, *Lactobacillus* spp.**

Anaerobic Gram-Negative Bacilli

***Bacteroides* spp.**
Bacteroides fragilis (GI/vaginal flora. Abscesses)
Bacteroides melaninogenicus
(GI/vaginal/mouth flora. Aspiration pneumonia, periodontal disease)

***Fusobacterium* spp.**
(Aspiration pneumonia, periodontal diseases, abdominal/pelvic abscesses)
***Prevotella* spp.** (Periodontal diseases)

Anaerobic Gram-Positive Cocci

***Peptostreptococcus* spp. and *Peptococcus* spp.**
(GI/vaginal/mouth flora. Abscesses, aspiration pneumonia)

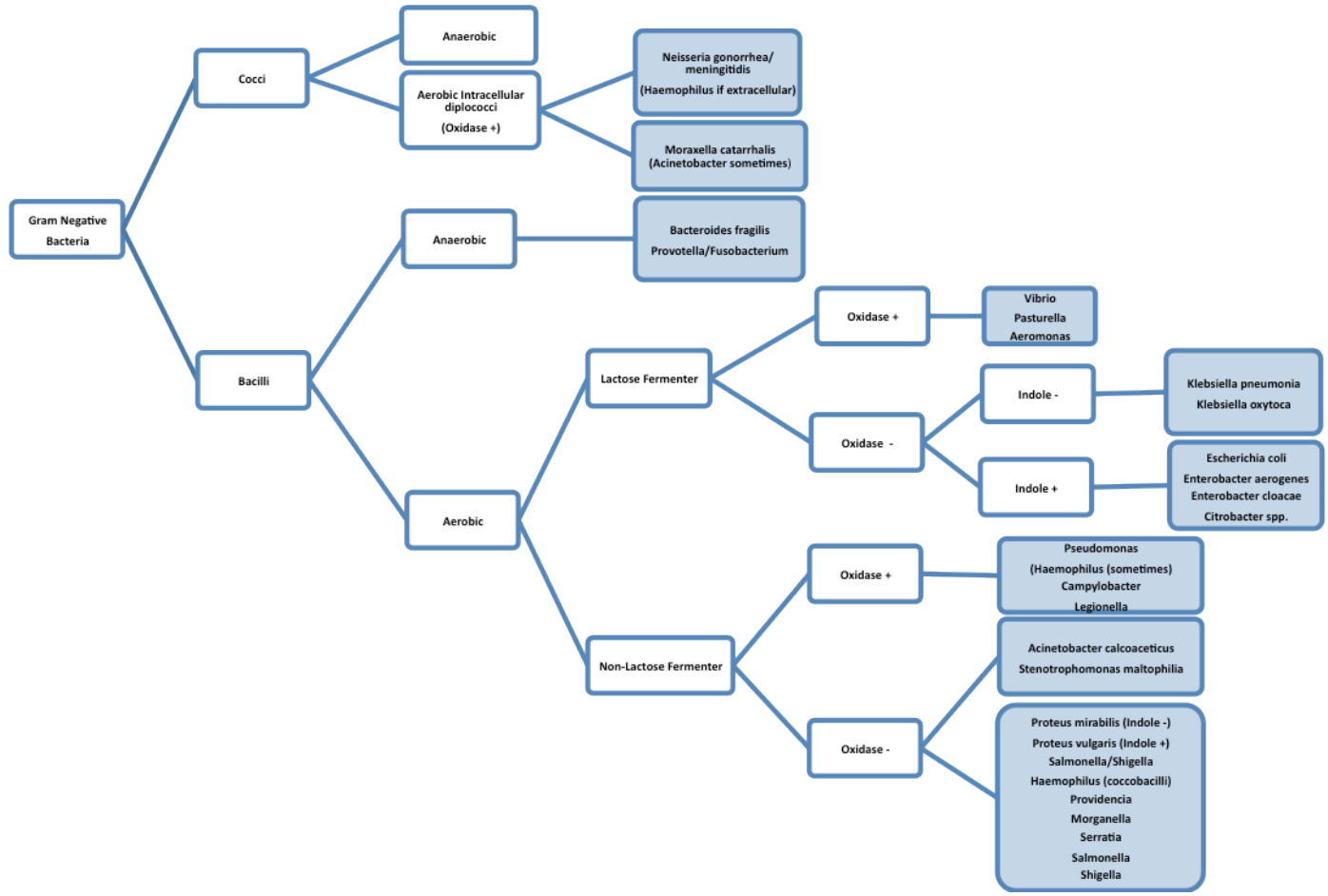
Anaerobic Gram-Negative Cocci

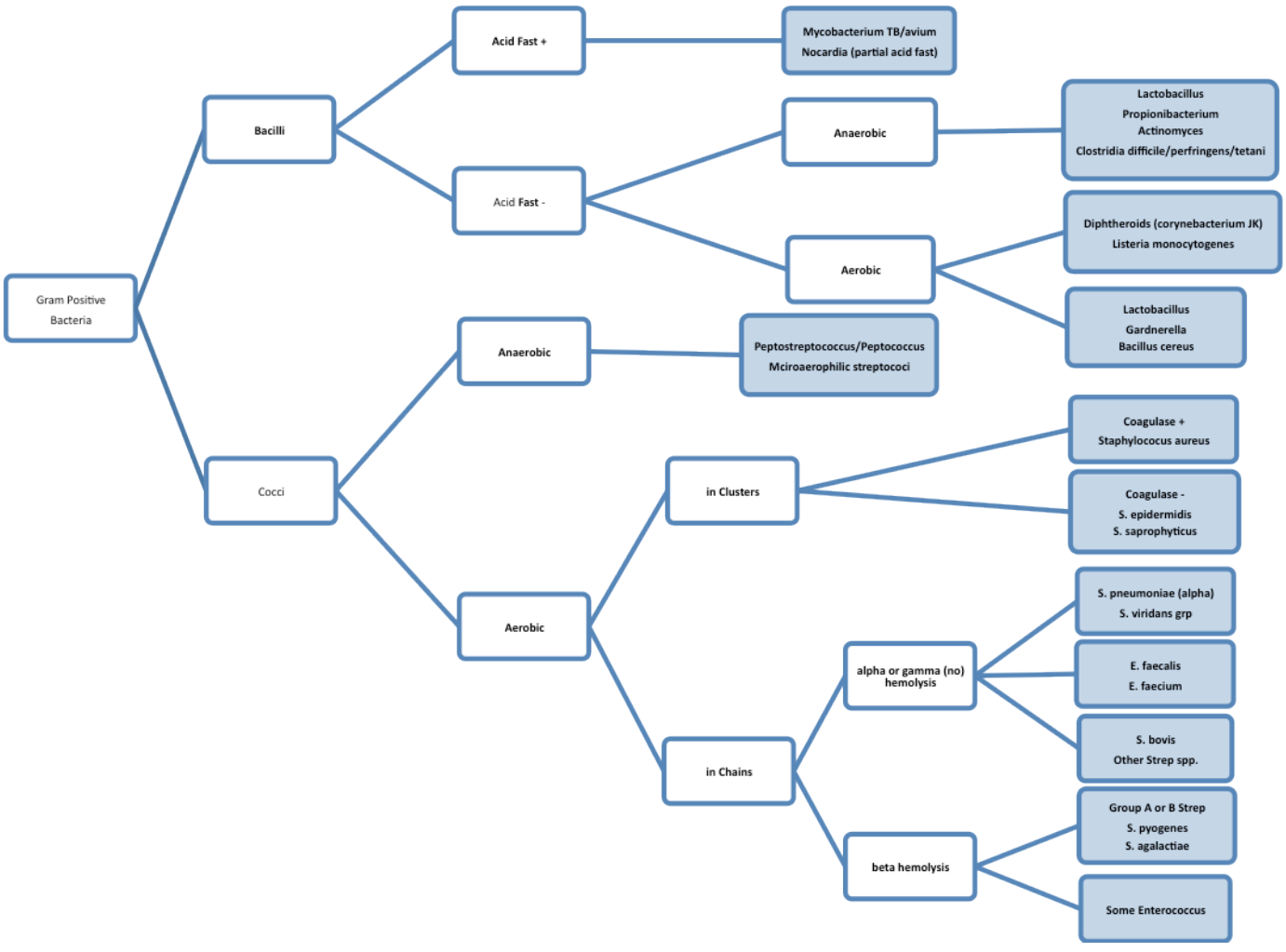
Veillonella spp. (GI normal flora. Rare cases of osteomyelitis and endocarditis)

Miscellaneous

Chlamydia trachomatis (STD)
Chlamydophilia (formerly chlamydia) ***pneumoniae***
(Atypical organism. CAP)
Rickettsia rickettsii (Rocky Mountain Spotted Fever)

Mycoplasma pneumoniae (Atypical organism. CAP)
Borrelia burgdorferi (Lyme disease)
Treponema pallidum (Syphilis)


Gram Negative Bacteria
Cocci
Anaerobic
Aerobic Intracellular diplococci (Oxidase +)
Neisseria gonorrhea/ meningitidis (Haemophilus if extracellular)
Moraxella catarrhalis (Acinetobacter sometimes)
Bacilli
Anaerobic
Bacteroides fragilis Provotella/Fusobacterium
Aerobic
Lactose Fermenter
Oxidase +
Vibrio Pasturella Aeromonas
Oxidase -
Indole -
Klebsiella pneumonia Klebsiella oxytoca
Indole +
Escherichia coli Enterobacter aerogenes Enterobacter cloacae Citrobacter spp.
Non-Lactose Fermenter
Oxidase +
Pseudomonas (Haemophilus (sometimes) Campylobacter Legionella
Oxidase -
Acinetobacter calcoaceticus Stenotrophomonas maltophilia
Proteus mirabilis (Indole -) Proteus vulgaris (Indole +) Salmonella/Shigella Haemophilus (coccobacilli) Providencia Morganella Serratia Salmonella Shigella


Gram Positive Bacteria
Bacilli
Acid Fast +
Mycobacterium TB/avium Nocardia (partial acid fast)
Acid Fast -
Anaerobic
Lactobacillus Propionibacterium Actinomyces Clostridia difficile/perfringens/tetani
Aerobic
Diphtheroids (corynebacterium JK) Listeria monocytogenes
Lactobacillus Gardnerella Bacillus cereus
Cocci
Anaerobic
Peptostreptococcus/Peptococcus Mciroaerophilic streptococi
Aerobic
in Clusters
Coagulase + Staphylococus aureus
Coagulase - S. epidermidis S. saprophyticus
in Chains
alpha or gamma (no) hemolysis
S. pneumoniae (alpha) S. viridans grp
E. faecalis E. faecium
S. bovis Other Strep spp.
beta hemolysis
Group A or B Strep S. pyogenes S. agalactiae
Some Enterococcus

Common Antibacterial Agents

Beta Lactams Penicillins Natural Penicillins *Penicillin G, VK* *Benzathine/Procaine PCNs* Anti-Staphylococcal Penicillins *Nafcillin* *Oxacilin* *Dicloxacillin* Aminopenicillin *Ampicillin* *Ampicillin/sulbactam (Unasyn)* *Amoxicillin* *Amoxicillin/clavulanate (Augmentin)* Anti-pseudomonal Penicillins *Piperacillin/tazobactam (Zosyn)* *Ticarcillin/clavulanate (Timentin)* Cephalosporins 1st generation *Cefadroxil (Duricef)* *Cefazolin (Ancef)* *Cephalexin (Keflex)* 2nd generation *Cefoxitin* 3rd generation *Cefdinir (Omnicef)* *Cefixime (Suprax)* *Ceftibuten (Cedax)* *Cefpodoxime proxetil (Vantin)* *Cefditoren (Spectracef)* *Cefotaxime (Claforan)* *Ceftriaxone (Rocephin)* *Ceftazidime (Fortaz)* 4th generation *Cefepime (Maxipime)* 5th generation *Ceftaroline (Teflaro)* Carbapenems *Imipenem/cilastatin (Primaxin)* *Meropenem (Merrem)* *Ertapenem (Invanz)* *Doripenem (Doribax)*	• Inhibits cell wall synthesis by binding to transpeptidase, the penicillin binding protein (PBPs) • Bactericidal
Monobactam *Aztreonam (Azactam)*	• Inhibits cell wall synthesis by binding to transpeptidase, the penicillin binding protein (PBPs) • Bactericidal
Aminoglycosides *Gentamicin* *Tobramycin* *Amikacin*	• Inhibits protein synthesis by binding to nucleotides in the mRNA decoding region of the 30S subunit of prokaryotic ribosomes and interferes with mRNA translation and translocation • Bactericidal
Fluoroquinolones *Ciprofloxacin (Cipro)* *Levofloxacin (Levaquin)* *Moxifloxacin (Avelox)* *Gemifloxacin (Factive)*	• Inhibits DNA synthesis by binding to DNA gyrase and topoisomerase IV and cleaves DNA in these enzyme-DNA complexes • Bactericidal
Polymixin E *Colistimethate sodium; Colistin (Coly-Mycin-M)*	• Colistimethate in vivo → hydrolyzes to colistin (active drug). • Catatonic detergent. Binds and penetrates cell membrane → interacts with phospholipids in the membrane → disrupts the membrane and alters osmotic barrier → causes leakage of essential intracellular metabolites. • Bactericidal
Glycopeptide *Vancomycin*	• Binds to D-alanyl-D-alanine and interferes with peptidoglycan cross linkage and transpeptidase causing defective cell wall synthesis → cell wall lysis. • Bactericidal

Oxazolidinone *Linezolid (Zyvox)*	• Inhibits protein synthesis by binding to the 23S ribosomal RNA of the 50S subunit → preventing initiation complex formation with the 70S ribosomal subunit. • Bactericidal: Streptococci spp. Bacteriostatic: Staphylococci spp. and Enterococci spp.
Cyclic Lipopeptide *Daptomycin (Cubicin)*	• Interacts with bacterial cell membrane through a calcium-dependent binding mechanism → causes K+ leakage, membrane depolarization, and bacterial cell death → inhibits protein, DNA and RNA synthesis. • Bactericidal
Lipoglycopeptide *Telavancin (Vibativ)*	• Telavancin inhibits bacterial cell wall synthesis by interfering with the polymerization and cross-linking of peptidoglycan. Telavancin binds to the bacterial membrane and disrupts membrane barrier function. • Synthetic derivative of vancomycin • Bactericidal
Streptogramin *Quinupristin/dalfopristin (Synercid)*	• Inhibits protein synthesis: bind to 50S subunits of the 70S ribosome. • Bactericidal: *Streptococcus* spp. and *Staphylococcus* spp. Bacteriostatic: *Enterococcus faecium*
Rifamycins *Rifampin - aka Rifampicin* *Rifabutin (Mycobutin)* *Rifapentine (Priftin)* *Rifaximin (Xifaxan)*	• Inhibits the β-subunit of DNA dependent RNA polymerase in prokaryotic organisms. • Bactericidal
Trimethoprim/Sulfamethoxazole, TMP/SMX; Co-trimoxazole (Bactrim; Septra)	• Two step inhibition of folic acid synthesis and subsequent pyrimidine synthesis in the bacterial cell (inhibits bacterial DNA synthesis). • Bactericidal (combination)
Lincosamide *Clindamycin (Cleocin)*	• Inhibits protein synthesis by binding to the 50S ribosomal unit • Bacteriostatic
Tetracyclines *Tetracycline* *Doxycycline (Vibramycin)* *Minocycline (Minocin)*	• Inhibits protein synthesis by binding to the 30S ribosomal subunit of bacteria and blocks entry of amino-acyl transfer RNA into the A site of the ribosome • Bacteriostatic
Glycylcycline *Tigecycline (Tygacil)*	• Inhibits protein synthesis by binding to the 30S ribosomal subunit of bacteria and blocks entry of amino-acyl transfer RNA into the A site of the ribosome • Structurally similar to minocycline, but overcomes tetracycline resistance • Bacteriostatic
Chloramphenicol	• Inhibits protein synthesis in bacteria by preventing the binding of the amino acid-containing end of the aminoacyl tRNA to the acceptor site on the 50S ribosomal subunit • Inhibits mitochondrial protein synthesis in mammalian cells • Bacteriostatic
Macrolides *Erythromycin (Erythrocin)* *Azithromycin (Zithromax)* *Clarithromycin (Biaxin)*	• Inhibits protein synthesis: binds to 23S rRNA of the 50S ribosomal subunit • Bacteriostatic
Nitrofurantoin (Macrodantin, Macrobid)	• Enzymatic reduction in the bacterial cell → binds to ribosomal proteins and damages bacterial DNA →interferes with bacterial metabolism and cell wall synthesis • Bactericidal
Metronidazole (Flagyl)	• Prodrug; enters cell by passive diffusion and activates. Produces a metabolite that damages bacterial DNA → cell death • Bactericidal
Fosfomycin (Monurol)	• Phosphoric acid derivative, fosfomycin inhibits bacterial wall synthesis by inactivating the enzyme, pyruvyl transferase, which is critical in the synthesis of cell walls by bacteria • Bactericidal