Antibiotic Resistance

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- North Carolina Division of Public Health

- Communicable Disease Conference – April, 2015

Antibiotic Resistance

- Wake AHEC requires all speakers to disclose any relevant financial conflicts of interest.
- Zack Moore has no relevant financial conflicts of interest to disclose.

The Life-Saving Benefits of Antibiotic Use

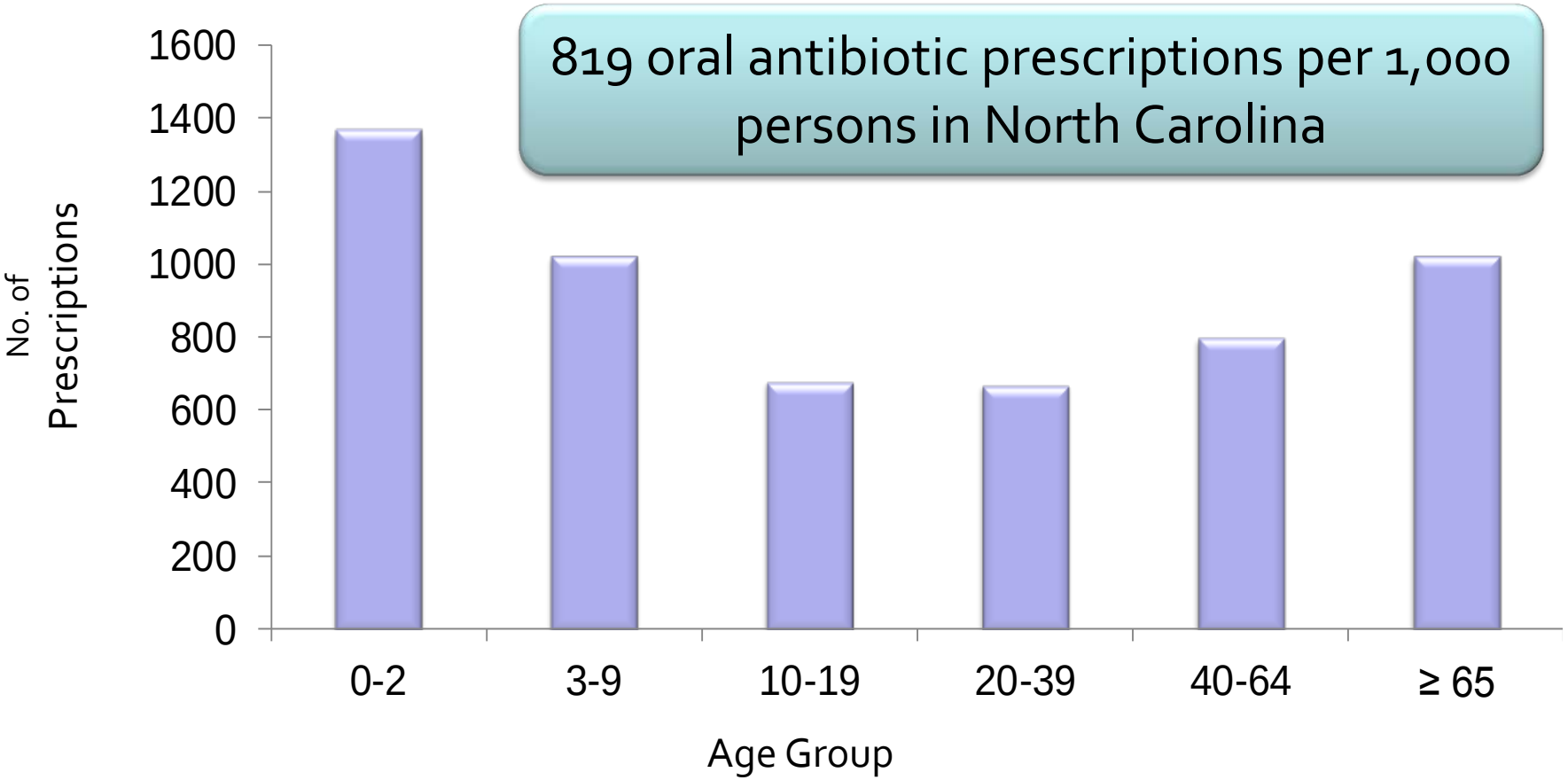
- Once deadly infectious diseases treatable, substantially reducing deaths compared to the pre-antibiotic era
- Important adjunct to modern medical advances
  - Surgeries
  - Transplants
  - Cancer therapies

The End of the Antibiotic Era?

- No new types of antibiotics developed in over 10 years
- More toxic antibiotics being used to treat common infections
- Must treat antibiotics as precious and finite resource

Lauri Hicks, CDC: "Call to Action: Improving Antibiotic Use"

Volume of Antibiotic Prescriptions, 2010



Hicks LA et al. N Engl J Med 2013;368:1461-1462 and
http://www.cddep.org/resistancemap/use

Antibiotic Prescriptions: Adults

- Acute respiratory infection most common reason adults receive an antibiotic
  - More than one out of four antibiotic prescriptions for adult outpatients are for conditions for which antibiotics are not needed
  - Even when antibiotics were indicated, the wrong drug was frequently prescribed
- Providers in the South more likely to prescribe for conditions that do not warrant antibiotic use

Shapiro et al. J Antimicrob Chemother 2013 Jul 25

Antibiotic Prescriptions: Children

- **Good news**
- **Bad news**

Lauri Hicks, CDC: "Call to Action: Improving Antibiotic Use"
CDC. MMWR. 2011;60:1153-6

Unintended Consequences of Antibiotic Use

- Adverse drug events
  - Hypersensitivity/allergy
  - Antibiotic associated diarrhea/colitis
  - Other side effects
  - Clostridium difficile infection
- Antibiotic resistance
- Increased health-care costs

Ohl CA, Luther VP. J. Hosp. Med. 2011;6:S4

Unintended Consequences of Antibiotic Use

- >140,000 Emergency Department visits/year
  - ~20% of all visits for drug-related adverse events
  - 6.1% required hospital admission
- Most common cause of drug-related ED visits for children

2004-2005 NEISS-CADES project; Shehab N et al. Clin Infect Dis. 2008;47:735

Unintended Consequences of Antibiotic Use: *Clostridium difficile*

- *C. difficile* diarrhea occurs as a result of disruption of normal gut bacteria due to antibiotic use

Lauri Hicks, CDC: "Call to Action: Improving Antibiotic Use"

Unintended Consequences of Antibiotic Use: *Clostridium difficile*

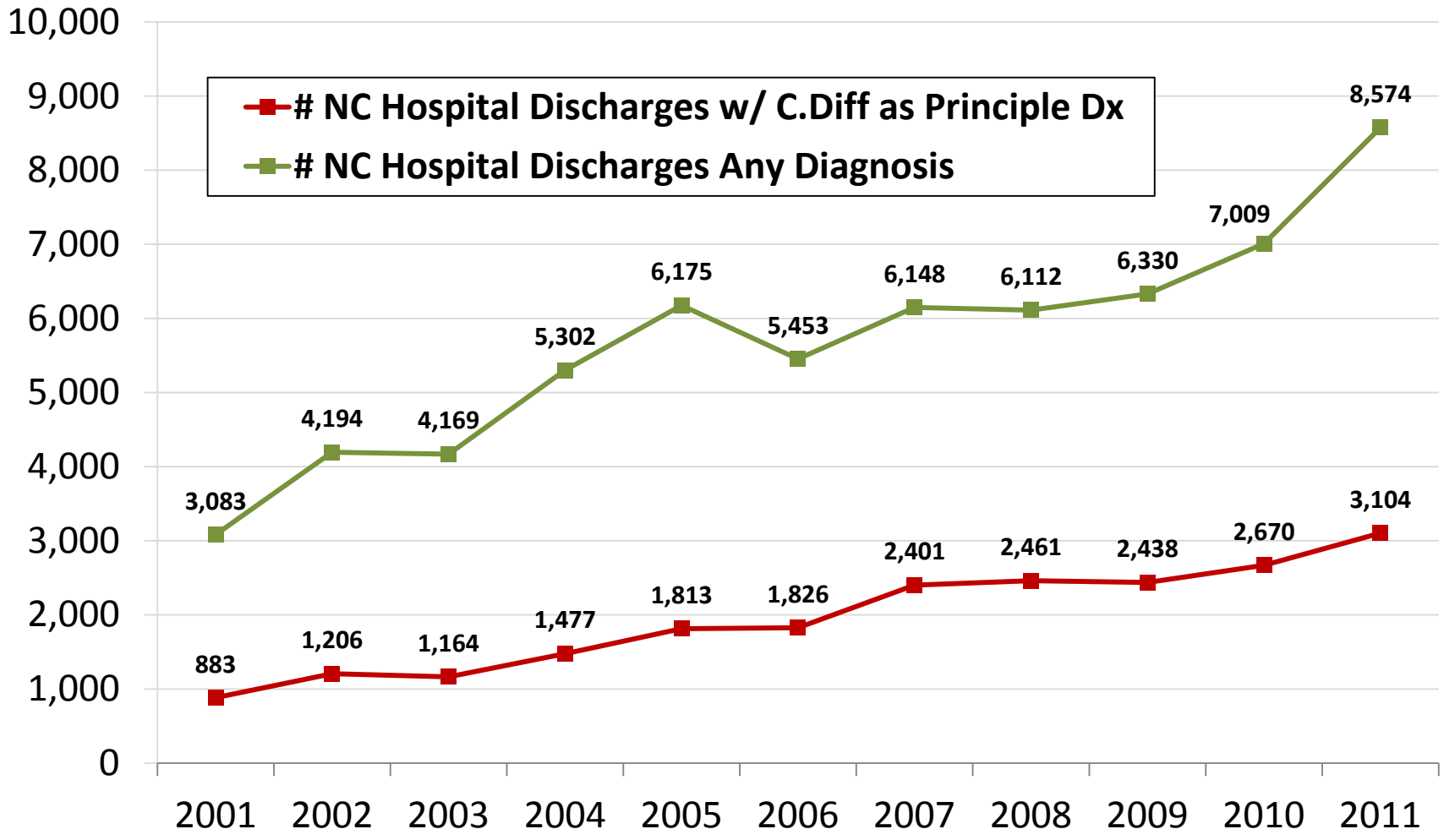
- Antibiotic exposure is the single most important risk factor for the development of *Clostridium difficile*-associated disease (CDAD)
- Up to 85% of patients with CDAD have antibiotic exposure in the 28 days before infection[1]

Unintended Consequences of Antibiotic Use: *Clostridium difficile*

- Emergence of the NAP-1/BI or "epidemic" strain of C. difficile has intensified the risks associated with antibiotic exposure.
- Epidemic strain of C. difficile is associated with increased risk of morbidity and mortality.
- Epidemic strain is resistant to fluoroquinolone antibiotics, which confers a selective advantage.

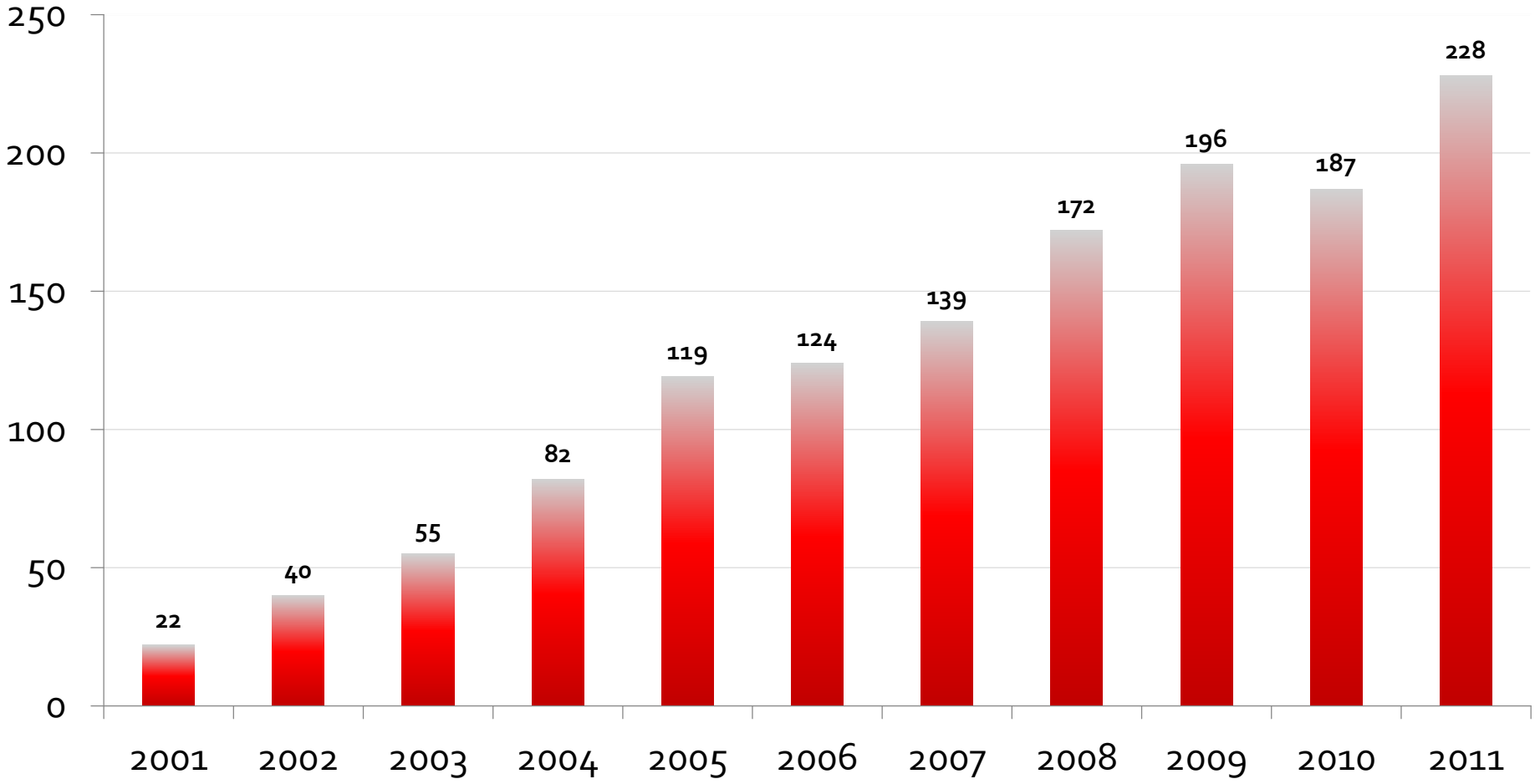
McDonald LC et al. *New England Journal of Medicine* 2005;353:2433-41

Clostridium difficile Hospitalizations — North Carolina, 2001–2011



Source: http://hcup.net.ahrq.gov

Clostridium difficile-Related Deaths — North Carolina, 2001–2011



Source: NC Vital Statistics at http://www.schs.state.nc.us/schs/data/vitalstats.cfm

Unintended Consequences of Antibiotic Use: Antibiotic Resistance

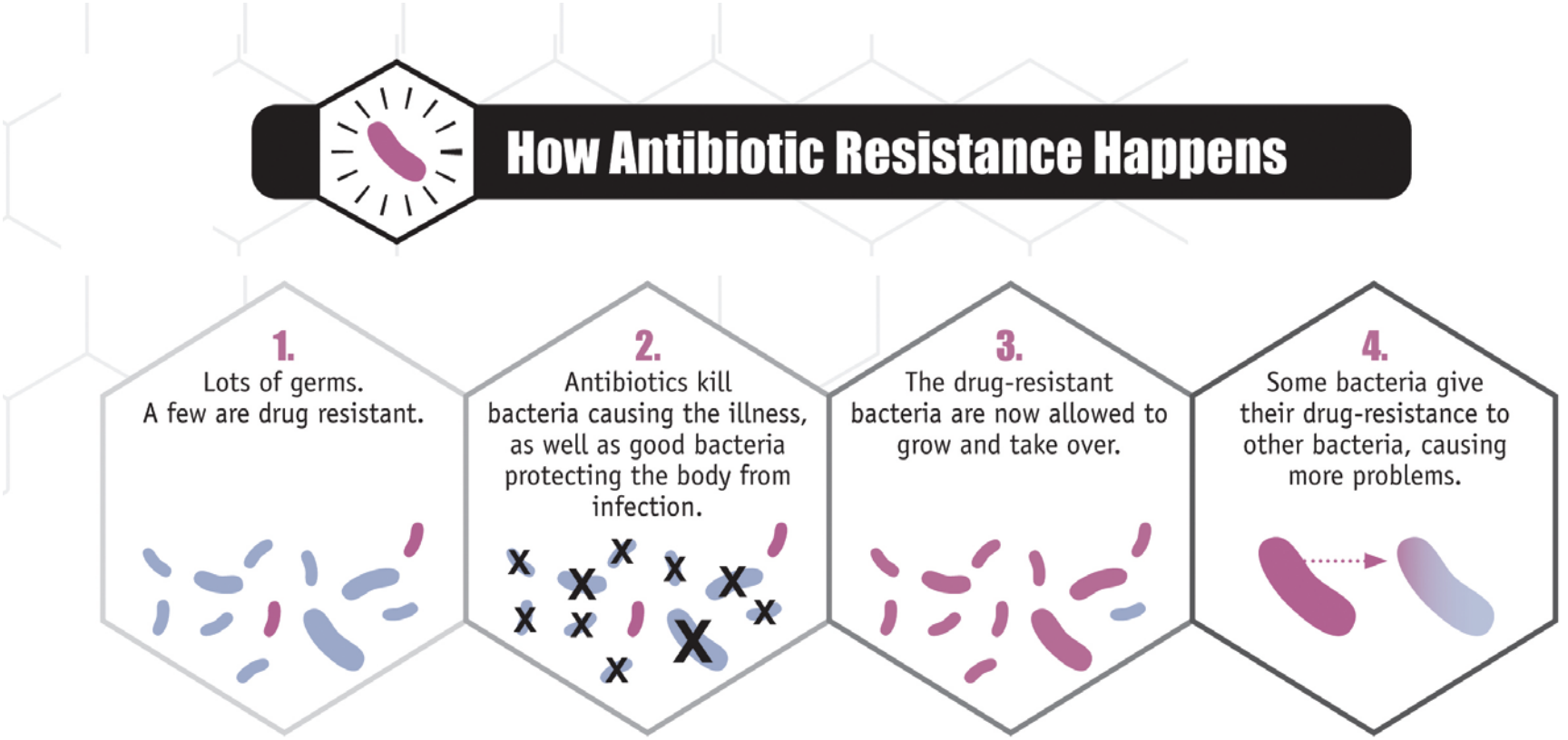
- Getting an antibiotic increases a patient's chance of becoming colonized or infected with a resistant organism.

Principles of Antibiotic Resistance

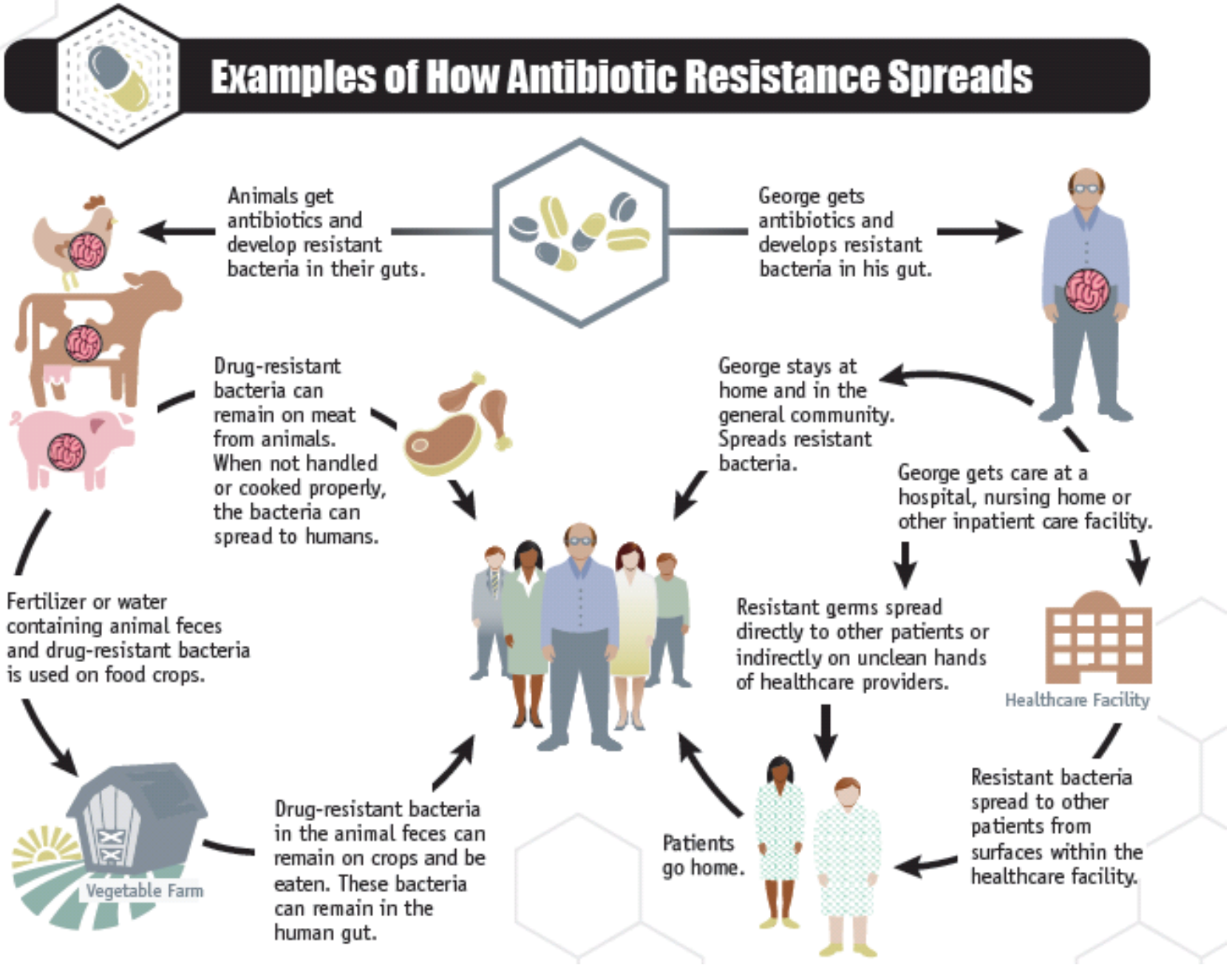
1. Given sufficient time and drug use, antibiotic resistance will emerge.
2. Resistance is progressive, evolving from low levels through intermediate to high levels.
3. Organisms resistant to one antibiotic are likely to become resistant to other antibiotics.
4. Once resistance appears, it is likely to decline slowly, if at all.
5. The use of antibiotics by any one person affects others in the extended as well as the immediate environment.

Slide by David Weber, adapted from Levy SB. NEJM, 1998

Unintended Consequences of Antibiotic Use: Antibiotic Resistance



CDC. Antibiotic resistance threats in the United States, 2013.
www.cdc.gov/drugresistance/threat-report-2013/



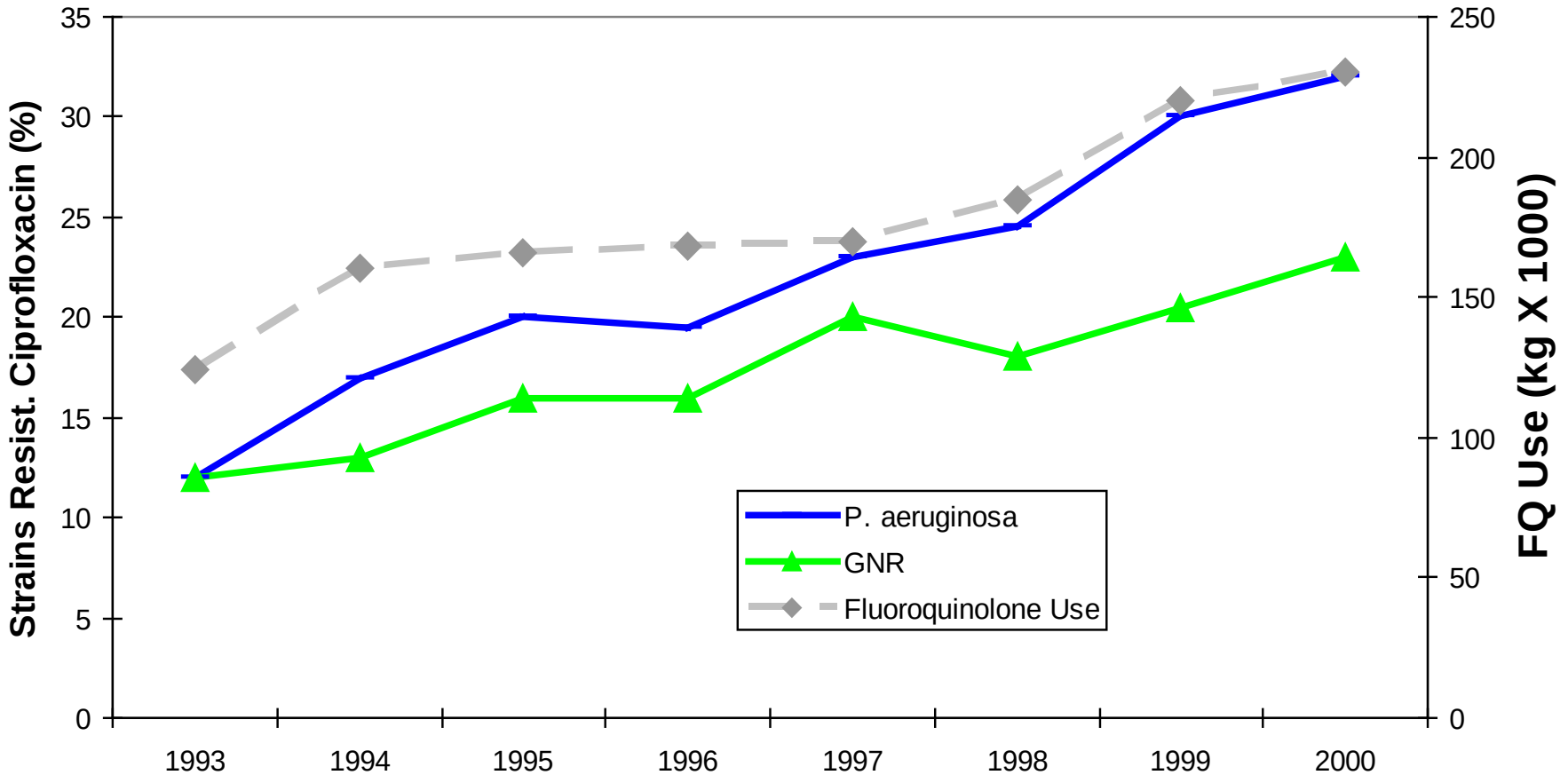
http://www.cdc.gov/drugresistance/threat-report-2013/

Antibiotic Exposure Increases the Risks of Resistance

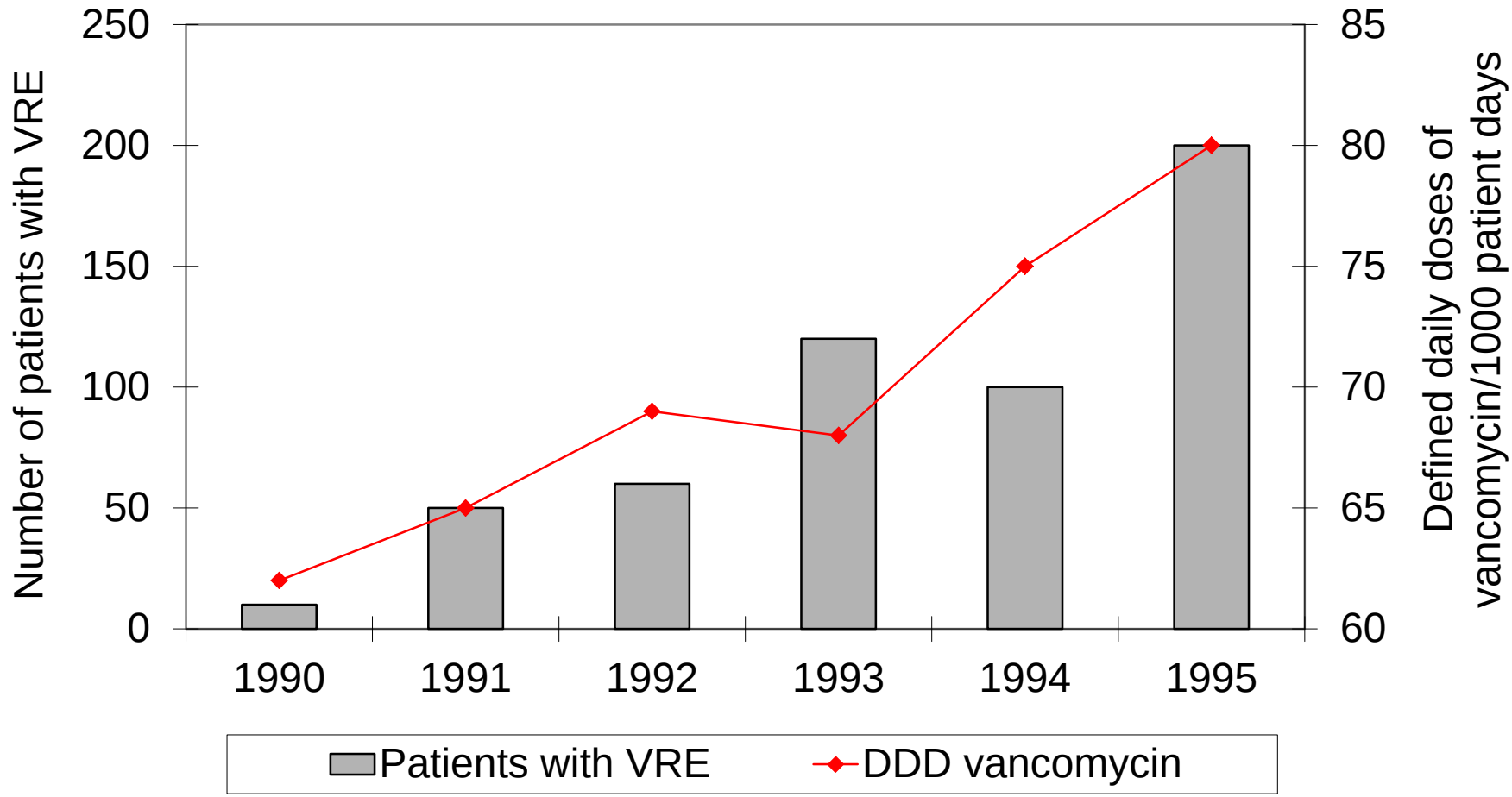
Pathogen and Antibiotic Exposure	Increased Risk
Carbapenem Resistant Enterobactericeae and Carbapenems	15 fold
ESBL producing organisms and Cephalosoprins	6–29 fold

Patel G et al. *Infect Control Hosp Epidemiol* 2008;29:1099-1106
Zaoutis TE et al. *Pediatrics* 2005;114:942-9
Talon D et al. *Clin Microbiol Infect* 2000;6:376-84

Fluoroquinolone Use and Resistance, 1993–2000



Association of Vancomycin Use with Resistance

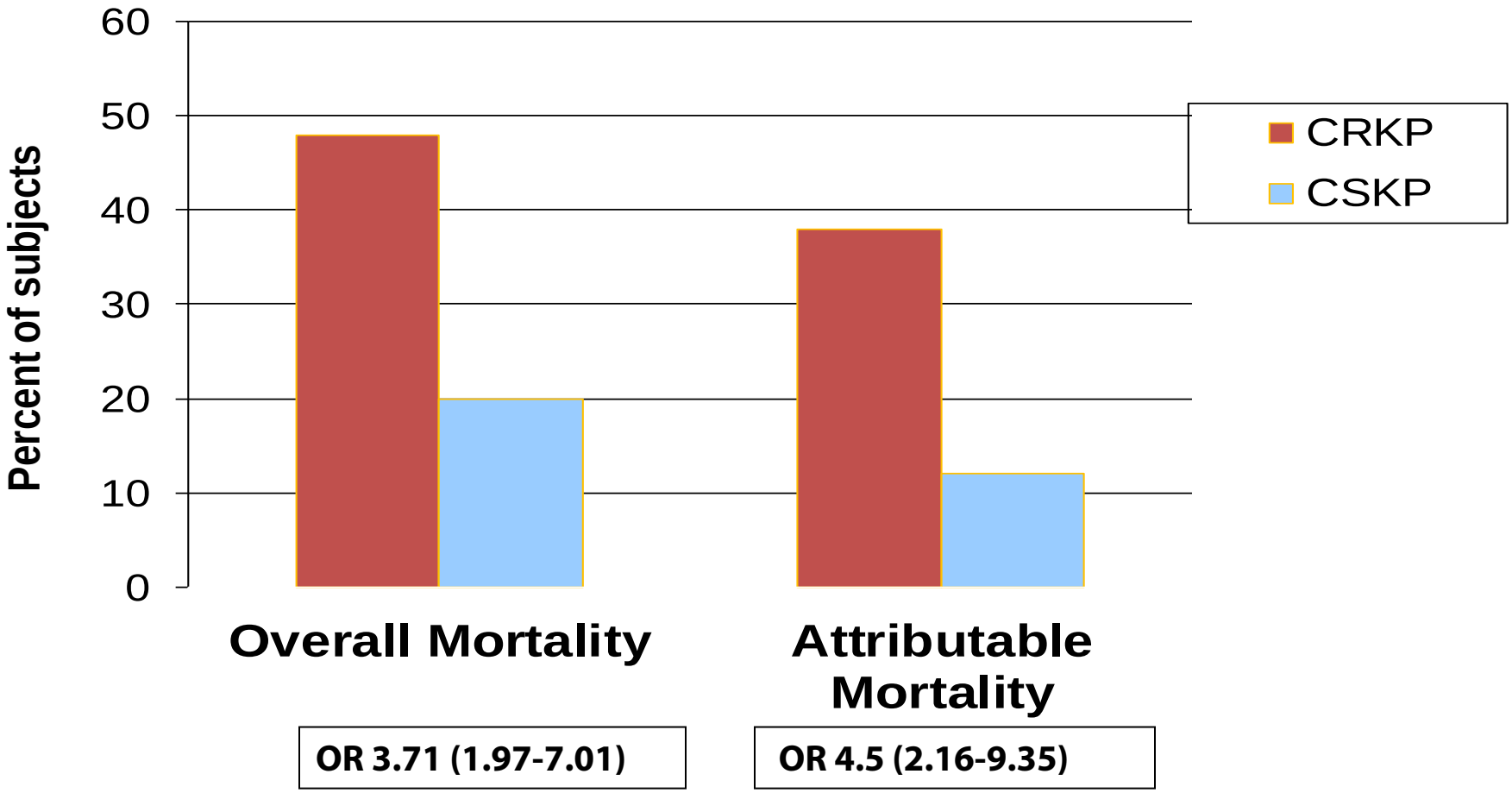


JID 1999;179:163

Unintended Consequences of Antibiotic Use: Antibiotic Resistance

- Getting an antibiotic-resistant infection increases a patient's risk of severe illness or death.

Mortality from Carbapenem Resistant vs. Susceptible *Klebsiella pneumoniae*



Patel G et al. *Infect Control Hosp Epidemiol* 2008;29:1099-1106

Mortality of Resistant (MRSA) vs. Susceptible (MSSA) *S. aureus*

- Mortality risk associated with MRSA bacteremia, relative to MSSA bacteremia: OR: 1.93; $p < 0.001$.[1]
- Mortality of MRSA infections was higher than MSSA: relative risk [RR]: 1.7; 95% confidence interval: 1.3–2.4).[2]

1. *Clin. Infect. Dis*.36(1),53–59 (2003).
2. Infect. Control Hosp. Epidemiol.28(3),273–279 (2007).

Carbapenem-Resistant Enterobacteriaceae (CRE)

Enterobacteriaceae:

- Family of bacteria that normally live in water, soil, and the human gut
- Common cause of healthcare and community infections (*E. coli, K. pneumoniae*)

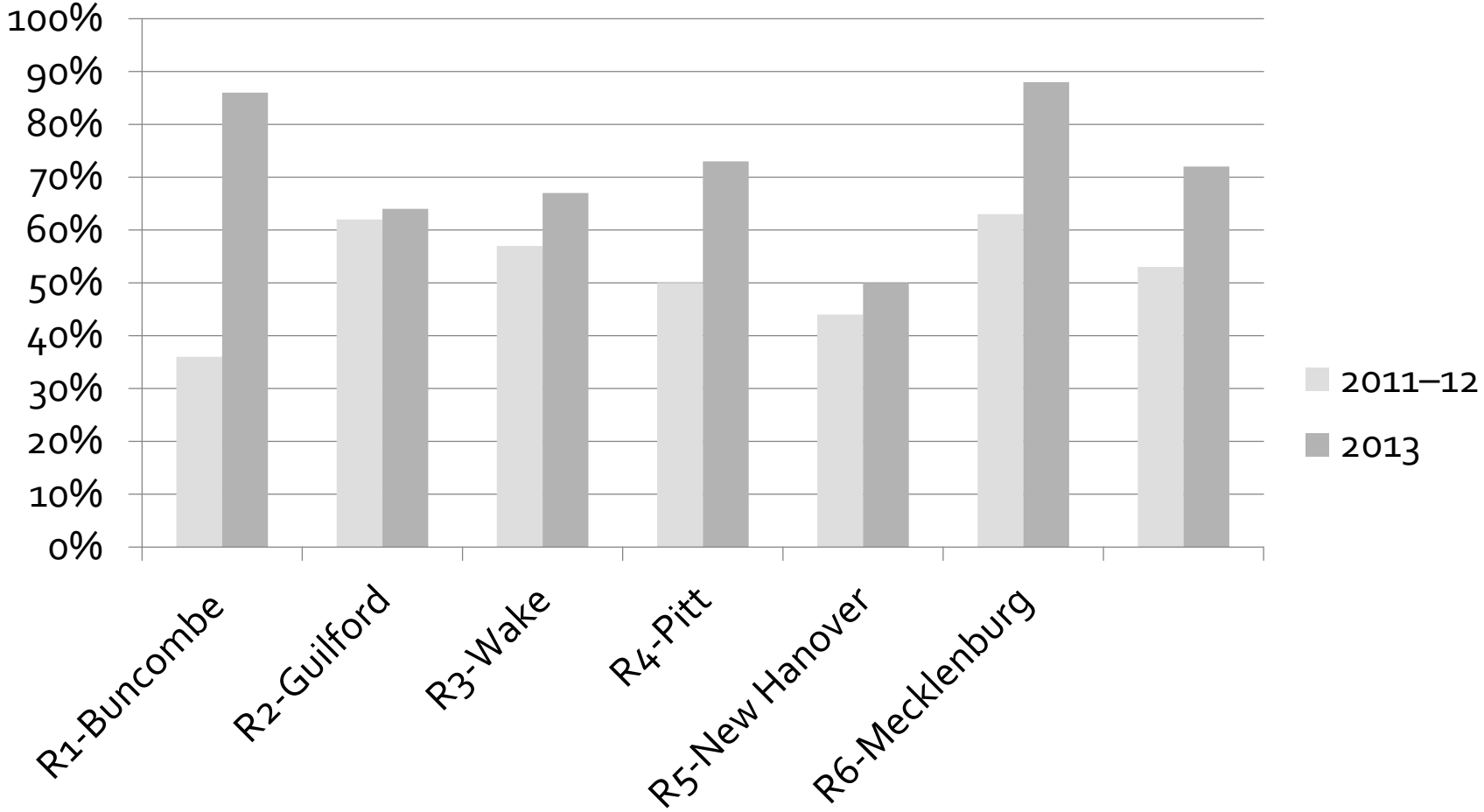
Carbapenems:

- Class of broad-spectrum antibiotics considered the "last resort" for treatment of serious gram-negative infections

CRE: Importance

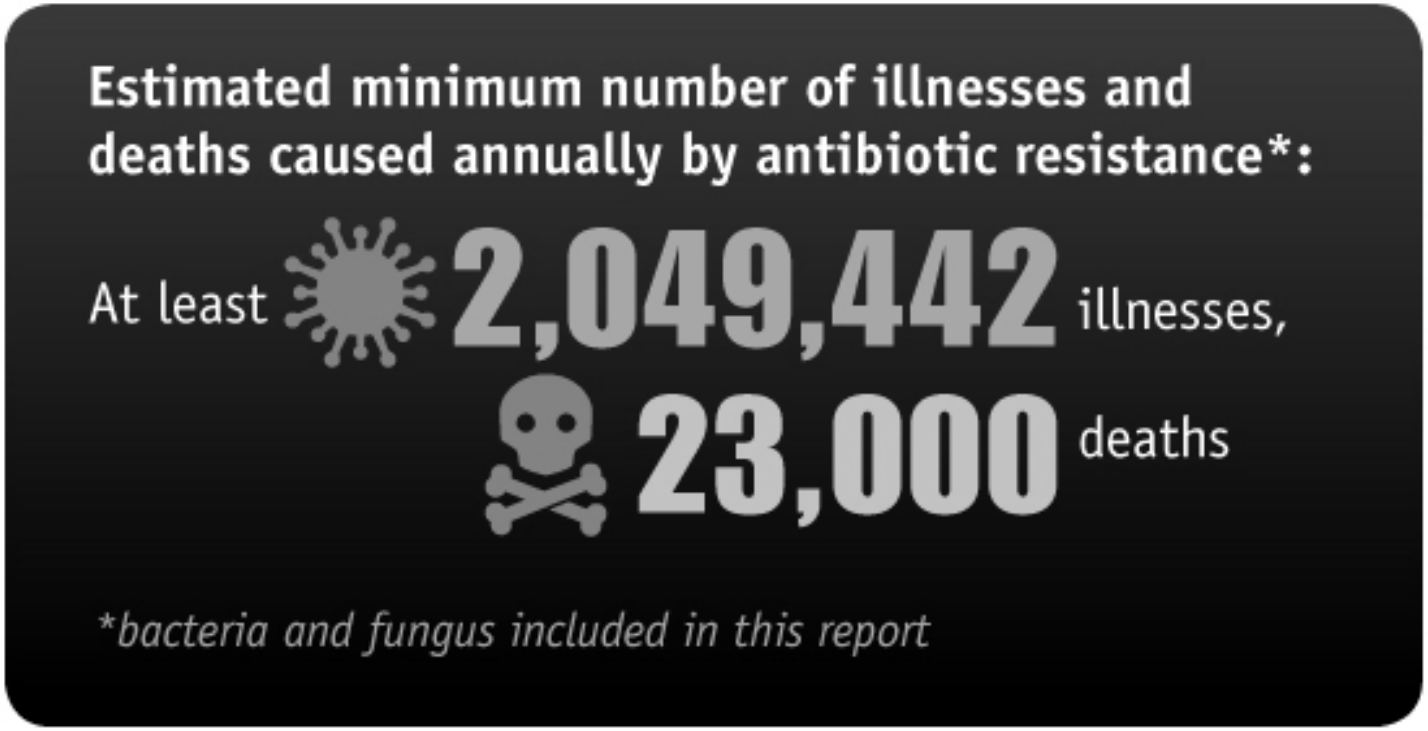
- Multidrug-resistant, limited treatment options
- Capable of transferring resistance
- High mortality rates for invasive infections
- Potential to spread out of healthcare settings

Proportion of NC Hospitals Identifying CRE at Once per Year



N.C. Division of Public Health, unpublished data

Unintended Consequences of Antibiotic Use: Antibiotic Resistance



Estimated cost of $30 billion annually
(range $20-$35 billion, 2008 dollars)

Lauri Hicks, CDC: "Call to Action: Improving Antibiotic Use"

Costs of Antibiotic Resistance

- Prolonged and costlier treatments
- Extended hospital stays
- Additional provider visits and healthcare use
- Greater disability and death compared to infections that are easily treatable with antibiotics

Lauri Hicks, CDC: "Call to Action: Improving Antibiotic Use"

"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"

CDC. "Get Smart for Healthcare: Know When Antibiotics Work"

DETECT AND PROTECT

Stop Deadly Drug Resistant Infections

Emerging healthcare-associated infection pathogens, especially highly drug resistant pathogens, pose a significant public health threat. CDC must detect highly drug resistant "superbugs" such as carbapenem-resistant Enterobacteriaceae (CRE) and protect patients from their spread.

Threat:

Drug resistant infections are on the rise

Some of these infections are virtually untreatable with currently available drugs

In the past decade, one type of drug resistant infection, CRE has increased from

1% to 4%

42

CRE infections have been reported in medical facilities in 42 states during the last 10 years

Solution:

Implementing "detect and protect" strategies that identify pathogens and stop transmission within and between facilities in a region.

DETECT if Patients Have Drug Resistant Infections

1. Use electronic data sources like CDC's National Healthcare Safety Network to detect superbugs
2. Request alerts every time the lab identifies a patient infected with a superbug
3. When receiving or transferring patients, find out if the patient has a drug resistant infection

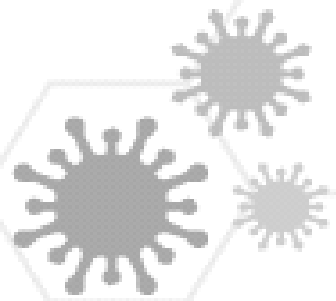
PROTECT Patients from Drug Resistant Infections

1. Follow contact and other precautions when treating patients with drug resistant infections
2. Dedicate rooms, equipment, and staff to patients with highly drug resistant infections
3. Take out temporary medical devices like catheters as soon as possible
4. Prescribe antibiotics carefully; monitor antibiotic use with tools such as CDC's National Healthcare Safety Network's Antimicrobial Use module

http://www.cdc.gov/hai/pdfs/cre/CDC_DetectProtect.pdf

Four Core Actions to Prevent Antibiotic Resistance

1 PREVENTING INFECTIONS, PREVENTING THE SPREAD OF RESISTANCE



Avoiding infections in the first place reduces the amount of antibiotics that have to be used and reduces the likelihood that resistance will develop during therapy. There are many ways that drug-resistant infections can be prevented: immunization, safe food preparation, handwashing, and using antibiotics as directed and only when necessary. In addition, preventing infections also prevents the spread of resistant bacteria.

2 TRACKING

CDC gathers data on antibiotic-resistant infections, causes of infections and whether there are particular reasons (risk factors) that caused some people to get a resistant infection. With that information, experts can develop specific strategies to prevent those infections and prevent the resistant bacteria from spreading.

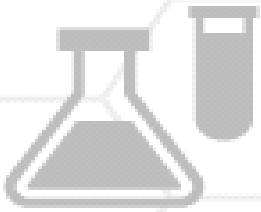
http://www.cdc.gov/drugresistance/threat-report-2013/

Four Core Actions to Prevent Antibiotic Resistance

3 IMPROVING ANTIBIOTIC PRESCRIBING/STEWARDSHIP

Perhaps the single most important action needed to greatly slow down the development and spread of antibiotic-resistant infections is to change the way antibiotics are used. Up to half of antibiotic use in humans and much of antibiotic use in animals is unnecessary and inappropriate and makes everyone less safe. Stopping even some of the inappropriate and unnecessary use of antibiotics in people and animals would help greatly in slowing down the spread of resistant bacteria. This commitment to always use antibiotics appropriately and safely—only when they are needed to treat disease, and to choose the right antibiotics and to administer them in the right way in every case—is known as antibiotic stewardship.

4 DEVELOPING NEW DRUGS AND DIAGNOSTIC TESTS



Because antibiotic resistance occurs as part of a natural process in which bacteria evolve, it can be slowed but not stopped. Therefore, we will always need new antibiotics to keep up with resistant bacteria as well as new diagnostic tests to track the development of resistance.

http://www.cdc.gov/drugresistance/threat-report-2013/

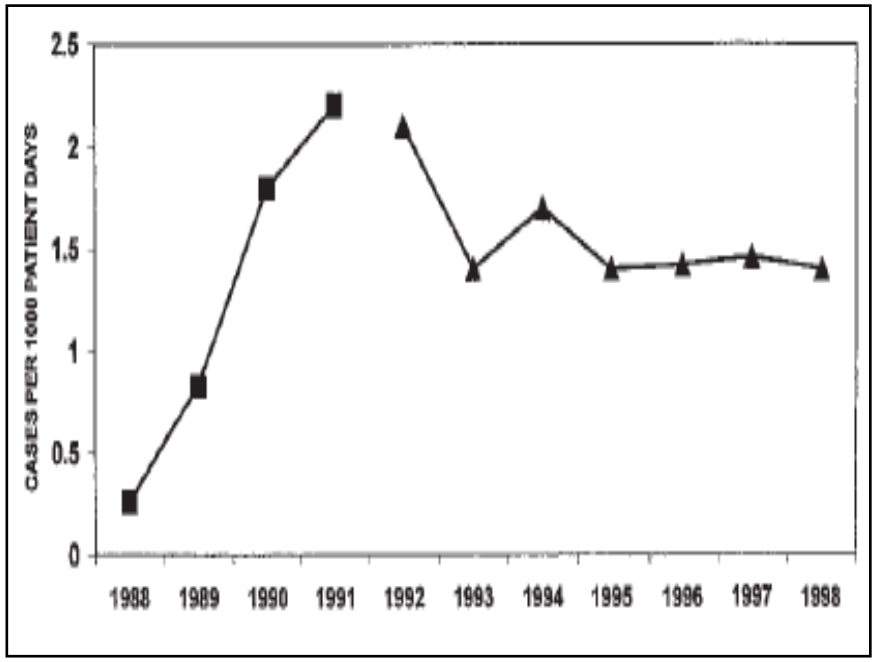
Antimicrobial Stewardship

- A system of informatics, data collection, personnel, and policy/procedures which promotes the optimal selection, dosing, and duration of therapy for antimicrobial agents throughout the course of their use
- Purpose:
  - Limit inappropriate and excessive antibiotic use
  - Improve and optimize therapy and clinical outcomes for the individual infected patient

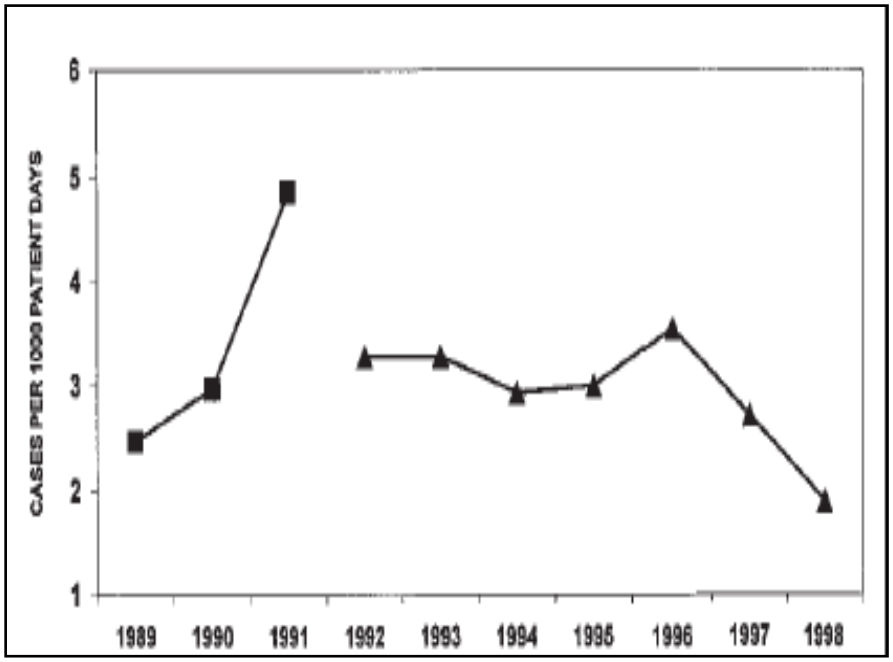
Ohl CA. *Seminar Infect Control* 2001;1:210-221; Ohl CA, Luther VP. J. Hosp. Med. 2011;6:S4; Dellit TH, et. al. Clin Infect Dis. 2007;44:159-177

Antibiotic Stewardship Reduces CDI and Gram Negative Resistance

Rates of CDI

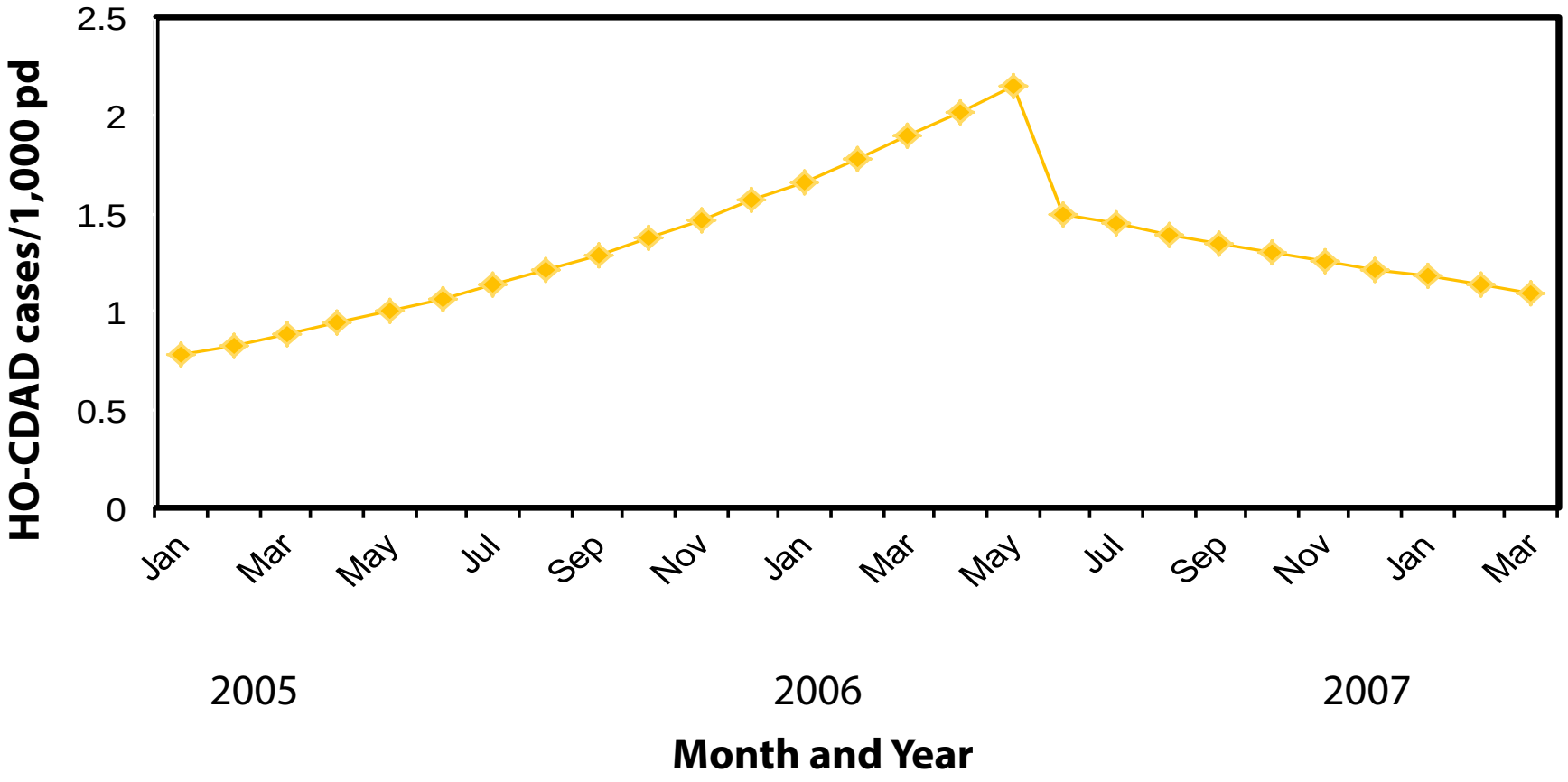


Rates of resistant Enterobacteriaceae



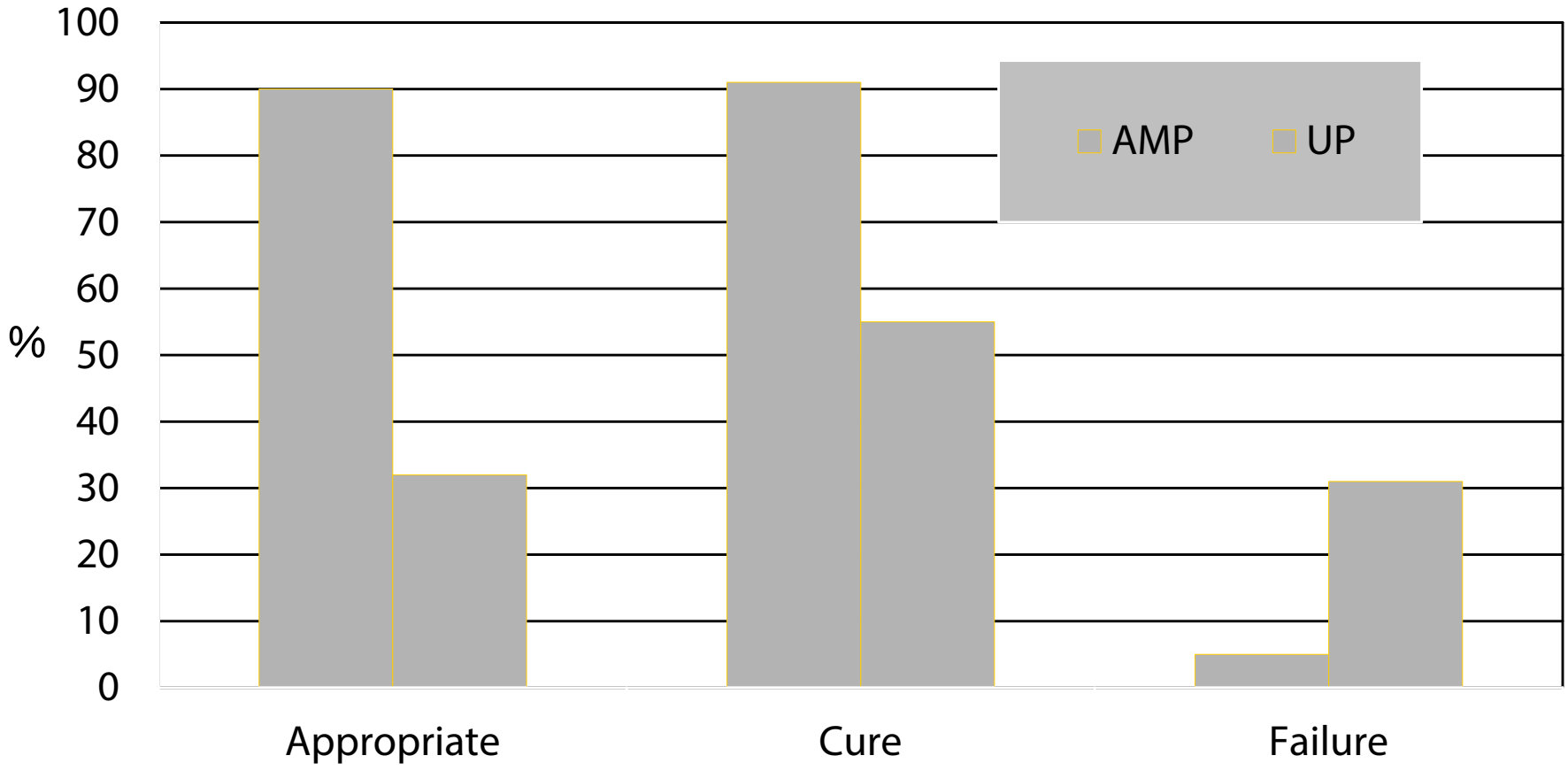
Carling P et al. Infect Control Hosp Epidemiol. 2003;24(9):699-706.

Impact of Fluoroquinolone Restriction on *C. difficile* Infection



Infect Control Hosp Epidemiol. 2009 Mar;30(3):264-72.

Antibiotic Stewardship Improves Clinical Outcomes



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

AMP = Antibiotic Management Program
UP = Usual Practice

Get Smart Campaign

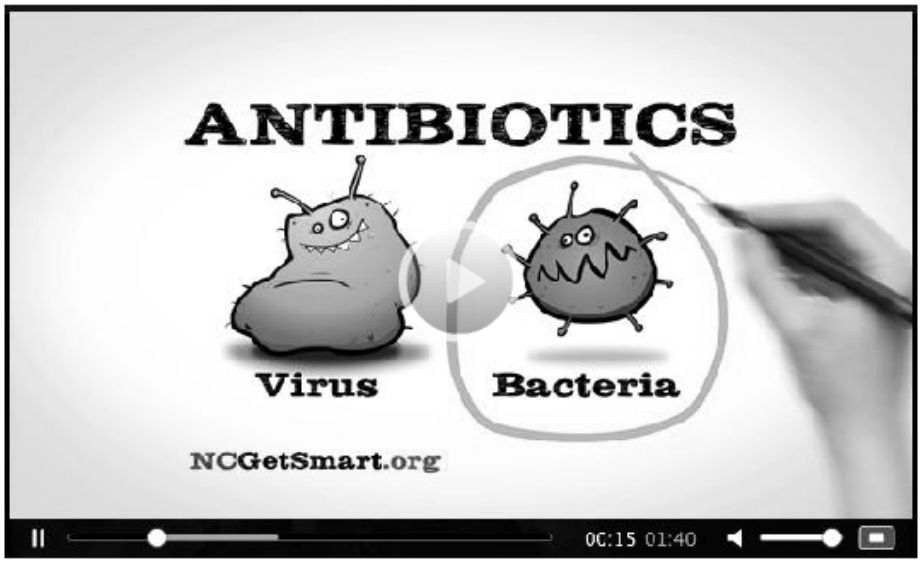
Know
When
Antibiotics
Work

Get Smart Campaign: Goals

- Improve patient safety through better treatment of infections.
- Reduce the emergence of anti-microbial resistant pathogens and *Clostridium difficile*.
- Heighten awareness of the challenges posed by antimicrobial resistance in healthcare and encourage better use of antimicrobials as one solution.

Get Smart NC – Activities

- Media campaign (November – March)



Get Smart NC – Activities

- Working to improve appropriate antimicrobial use education in NC health science programs (medicine, nursing, pharmacy)
- Working to improve antimicrobial stewardship programs in NC hospitals

What Can You Do?

- Work with DPH and healthcare partners to investigate cases and outbreaks of highly-resistant infections
- Promote appropriate antibiotic use education in your community

Conclusions

- Antibiotic misuse adversely impacts society and individual patients
- Improving antibiotic use improves patient outcomes and saves money
- Improving antibiotic use is a public health imperative