



Hamilton Health Sciences

# **IS THIS YOUR STOP? Antimicrobial Stewardship**

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Chair Antimicrobial Stewardship Team



CHEDOKE • CHILDREN'S • GENERAL • JURAVINSKI • McMASTER • ST. PETER'S

16<sup>th</sup> CHICA-HANDIC ANNUAL EDUCATION DAY

# Objectives

- 1) Consequences of antibiotic (over)use
- 2) Goals of Antimicrobial Stewardship
- 3) Urinary tract infections: Stewardship needed?





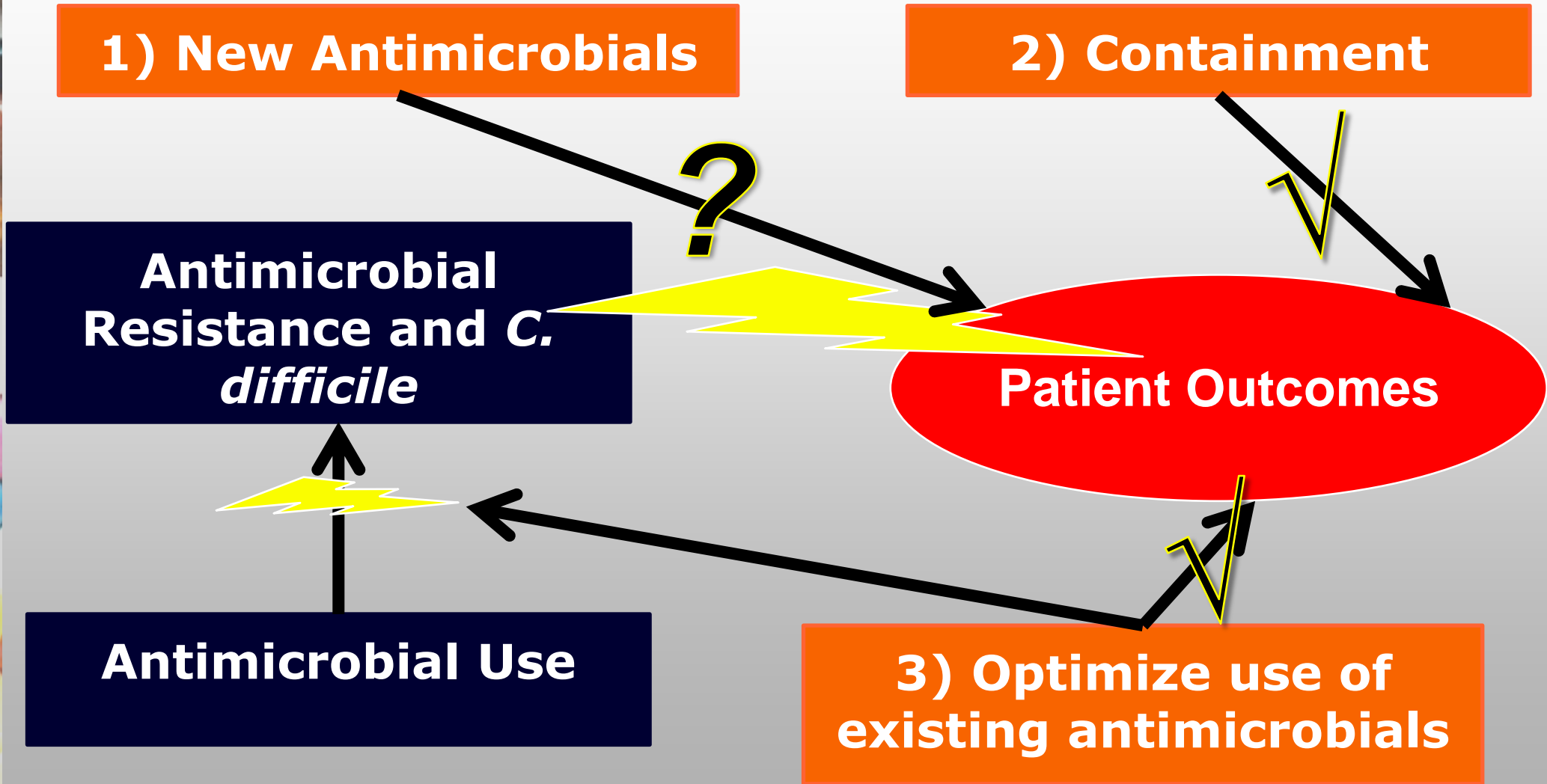
# Consequences of Antimicrobial (over) use

# Goal

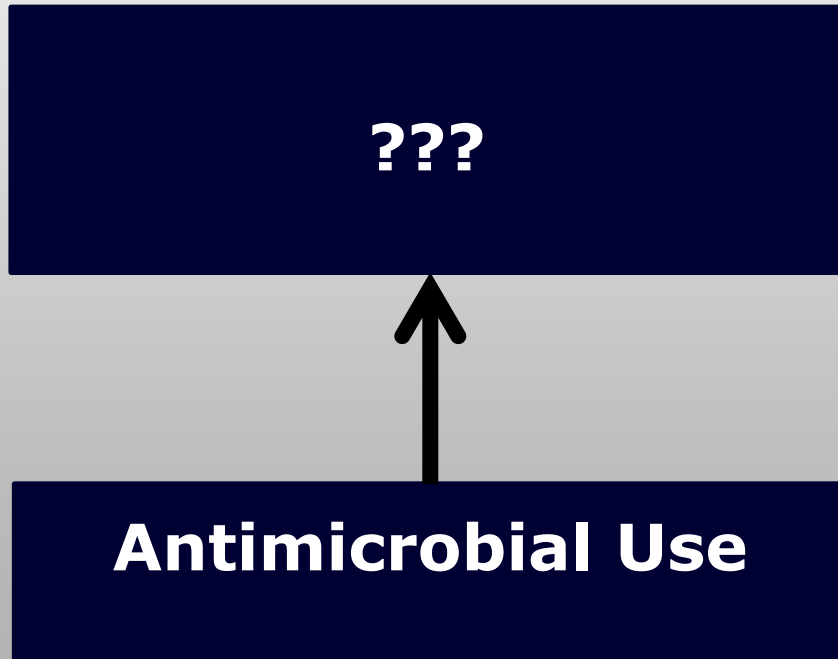


**To improve  
patient outcomes**

# Common Goal



# Collateral damage



# Juravinski Hospital ramps up C. diff measures outbreak

## Six patients affected, but no new cases in unit

BY NICOLE O'REILLY

Juravinski Hospital has implemented C. difficile control measures in one of its units, after an outbreak affecting six patients was declared June 17.

None of those patients remains in the affected unit — four are in other areas of the hospital, one has transferred to Brantford and one has died, though not from C. diff.

All are believed to have contracted the infection while in the F3 medicine unit.

The hospital didn't have its face-to-face meeting with public health until Monday, said Dr. Dominik Mertz, medical director of the infection prevention and control program at Hamilton Health Sciences. For that reason and since there have been no new cases on the unit since June 10, the hospital didn't notify the public about the outbreak until Tuesday, he said.

Legislation does not require hospitals to notify the public about outbreaks of the infection, rather they report to public health and some numbers are disclosed at designated intervals through the Ministry of Health and Long-Term Care website.

The patients in the unit became ill between June 6 and 10. Some pa-

tients who were transferred out didn't develop symptoms until June 14 and 15, Mertz said.

Four of the patients didn't develop symptoms until being transferred, including the one who went to Brantford.

However, Mertz said there "is no sign of any ongoing outbreaks anywhere else in the hospital ... we don't have any new cases potentially linked to those cases."

The Juravinski is taking special precautions to contain the outbreak, including hand-cleaning audits, and ramping up its cleaning to include an anti-sporicide.

C. difficile is a spore-forming bacteria that causes diarrhea and fever. The elderly, those with underlying medical conditions and those taking antibiotics are the most vulnerable because antibiotics kill "good bacteria," allowing the infection to grow.

The bacteria are spread through inadequate hand and environmental cleaning.

Recent provincial statistics found that Juravinski workers only wash their hands about half the time before caring for a patient. This is the lowest rate among area hospitals and well below the provincial average.

The hospital posted a 36 per cent hand washing rate in 2008-09.

That improved to 49 per cent the next year and went up to 55 per cent this year.

"In general, hand washing is needed to prevent C. difficile from spreading, but I can't say specifically in this case," said Dr. Chris Mackie, an associate medical officer of health in Hamilton.

Mertz agreed, adding he believes the outbreak may help raise awareness about hand washing and improve overall practices across the hospital.

Public health is testing to see if the patients were made ill by one strain — passed among them — or by separate strains.

Mackie said he doesn't know why the hospital to announce the outbreak made it clear that the infection would be generally, the number of cases considered to be over the unit return number of cases: one and two.

St. Catharines is battling its own outbreak that has affected 10 patients since May 28. There are 10 reported on

noreilly@thespec 905-526-3199

thespec.com



## Married couple dies from C. Diff 10 weeks apart

July 2, 2011

At 85, Thomas Dawson accepted he would die from lung cancer.

He'd lived a good life and believed he had enough time left to see his granddaughter's wedding in August and his 65th wedding anniversary in December.

He died April 8, only a couple of weeks after his diagnosis. But it wasn't cancer that killed him — it was C. difficile.

And he had no idea the same gruesome disease would also claim his wife — 84-year-old



# Antibiotics and Resistance



Antibiotic utilization = major driver for resistance:

**Table 2. Causal associations between antimicrobial use and the emergence of antimicrobial resistance.**

Changes in antimicrobial use are paralleled by changes in the prevalence of resistance.
Antimicrobial resistance is more prevalent in health care-associated bacterial infections, compared with those from community-acquired infections.
Patients with health care-associated infections caused by resistant strains are more likely than control patients to have received prior antimicrobials.
Areas within hospitals that have the highest rates of antimicrobial resistance also have the highest rates of antimicrobial use.
Increasing duration of patient exposure to antimicrobials increases the likelihood of colonization with resistant organisms.

**Ecological studies**

- Association over time
- Cross-sectional

- $\Delta$  in resistance is paralleled by  $\Delta$  in antimicrobial use
- Resistance is more prevalent in the health care setting
- Hospital areas with highest antimicrobial use have the highest rates of resistance



# Antibiotics and Resistance



Antibiotic utilization = major driver for resistance:

**Table 2. Causal associations between antimicrobial use and the emergence of antimicrobial resistance.**

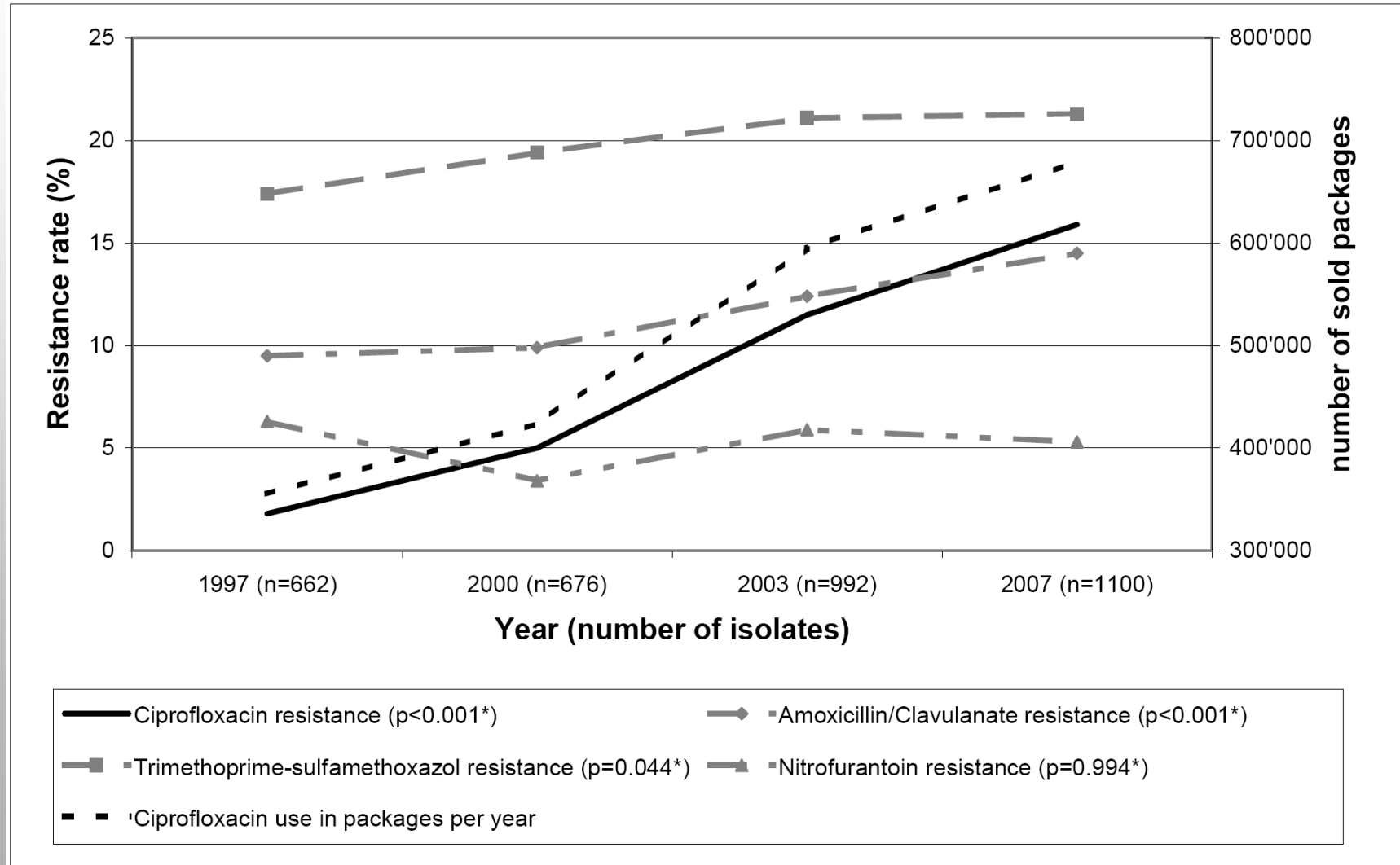
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Increasing duration of patient exposure to antimicrobials increases the likelihood of colonization with resistant organisms.

Individual level studies

- Exposure
- Duration of exposure

- Prior exposure to antimicrobials associated with risk for resistance in health-care associated infections
- Duration of exposure associated with higher likelihood of colonization by resistant pathogens

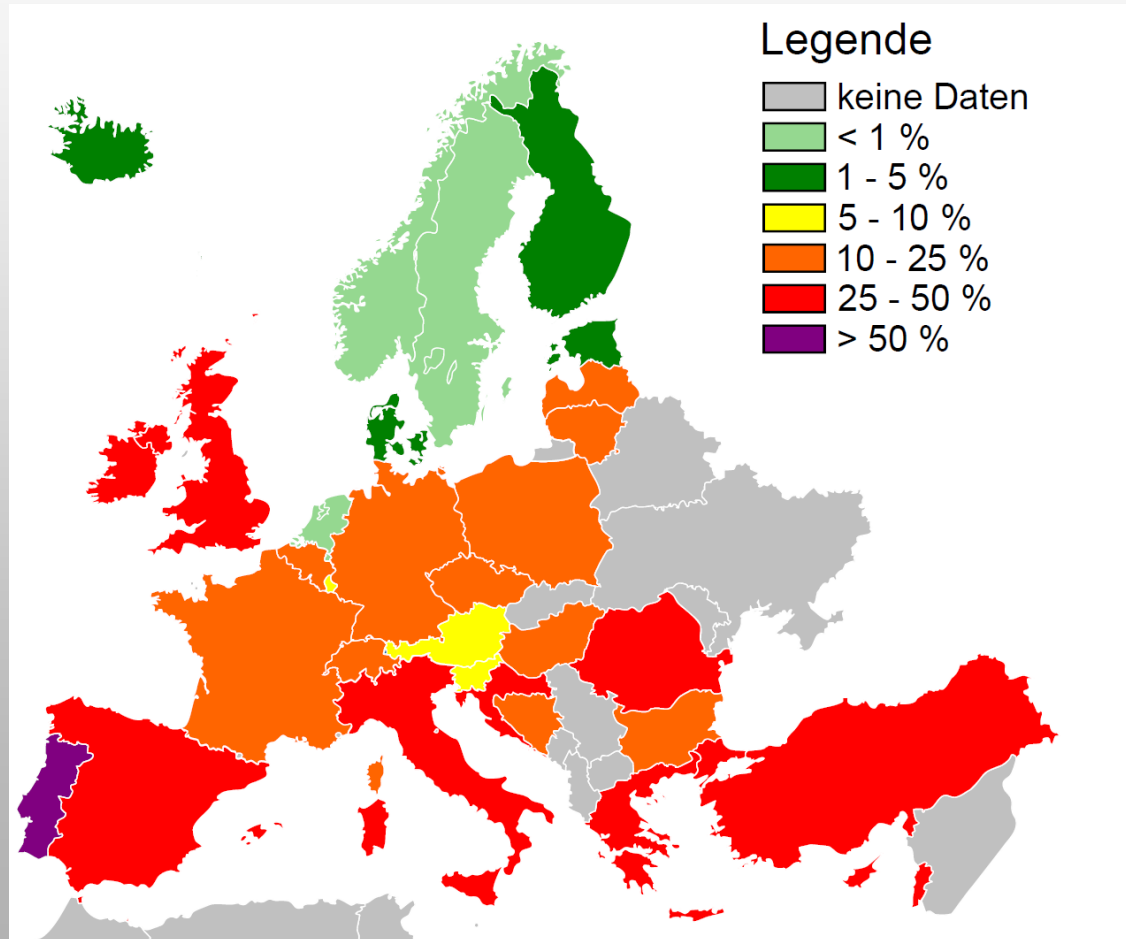
# Collateral damage



# Antibiotics and Resistance



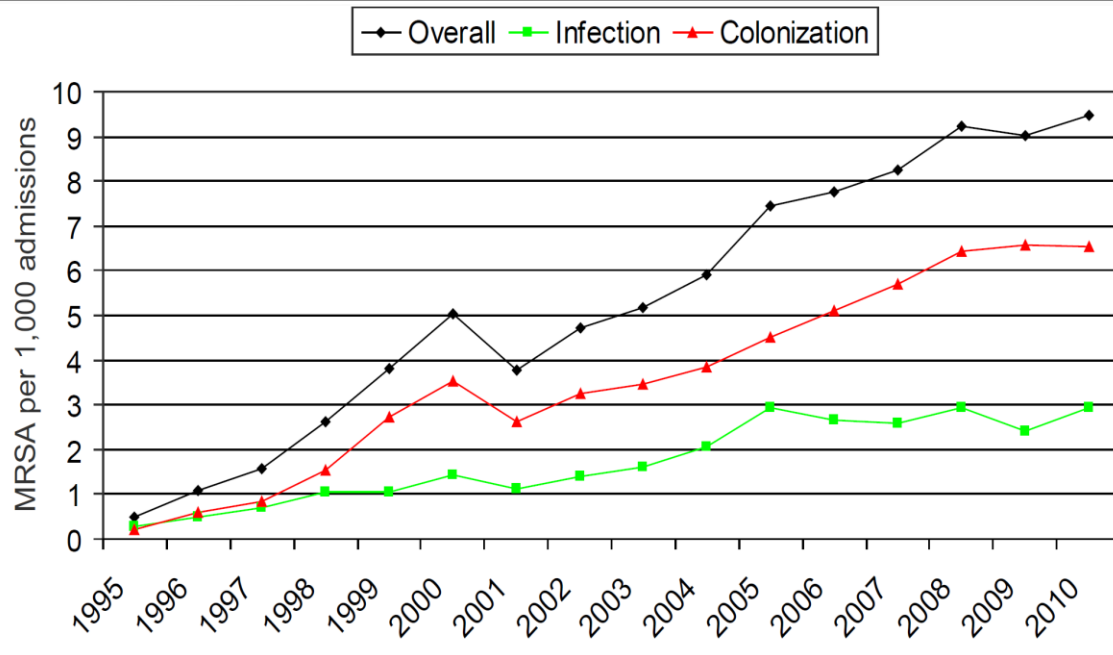
% MRSA in *S. aureus*



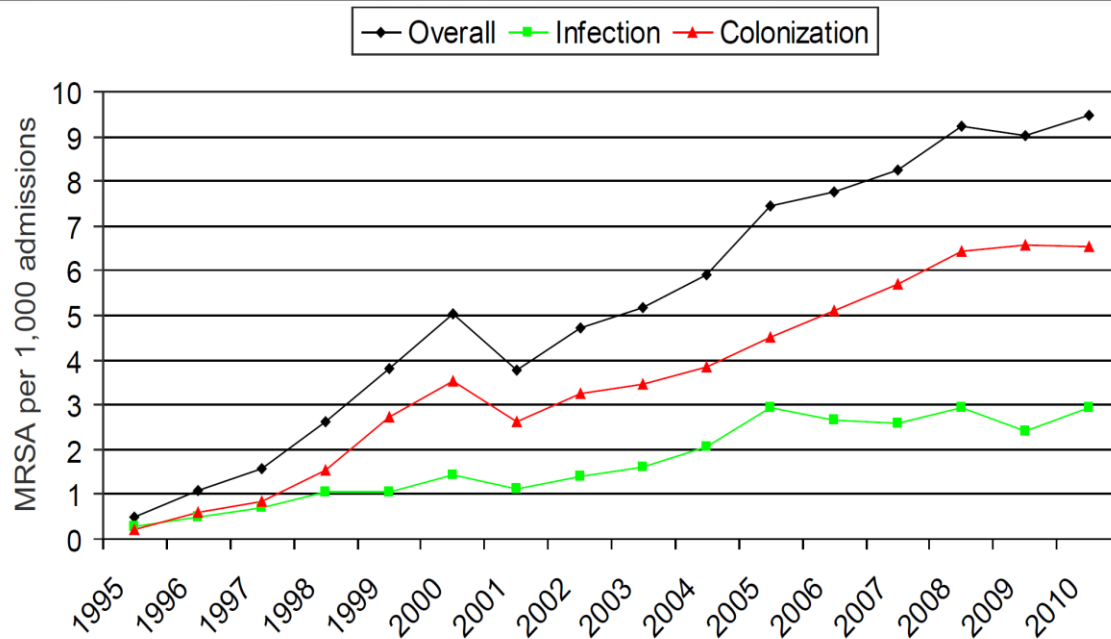
Portugal, Spain, Italy, Greece, and Turkey:

- Highest MRSA rates
- Highest utilization of Antimicrobials
- Antimicrobials over the counter

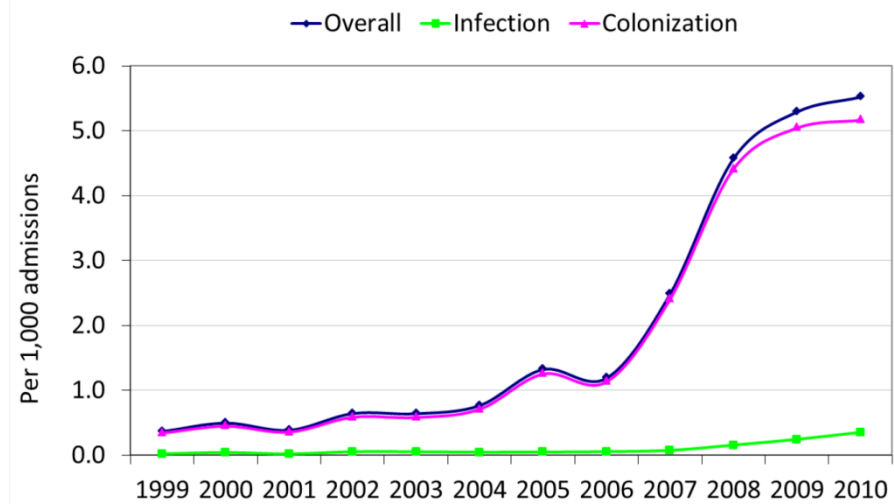
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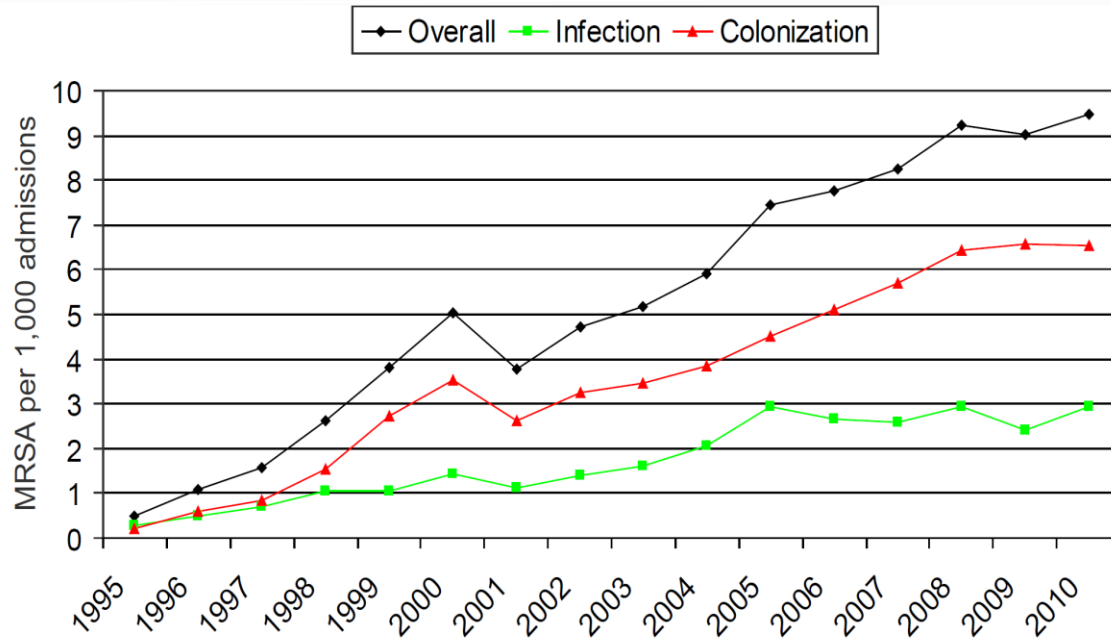
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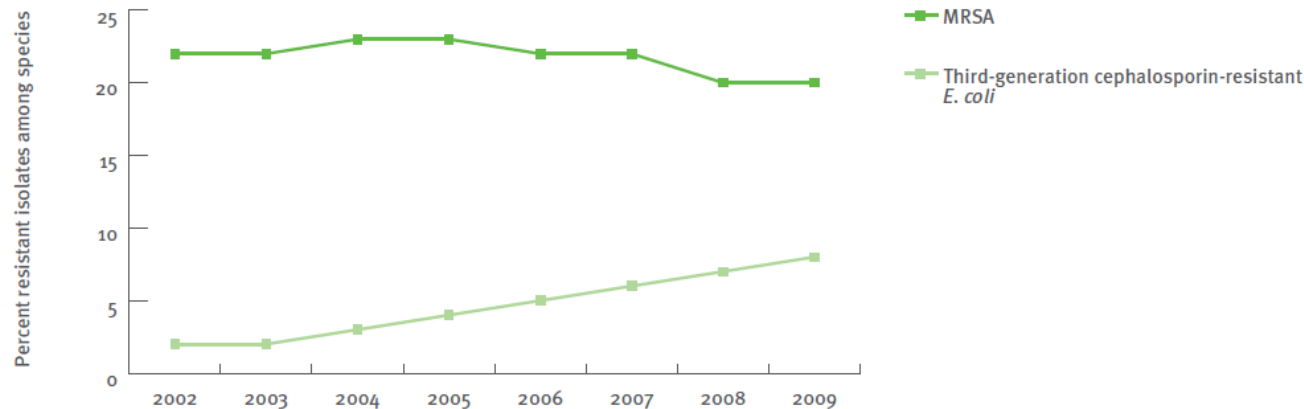
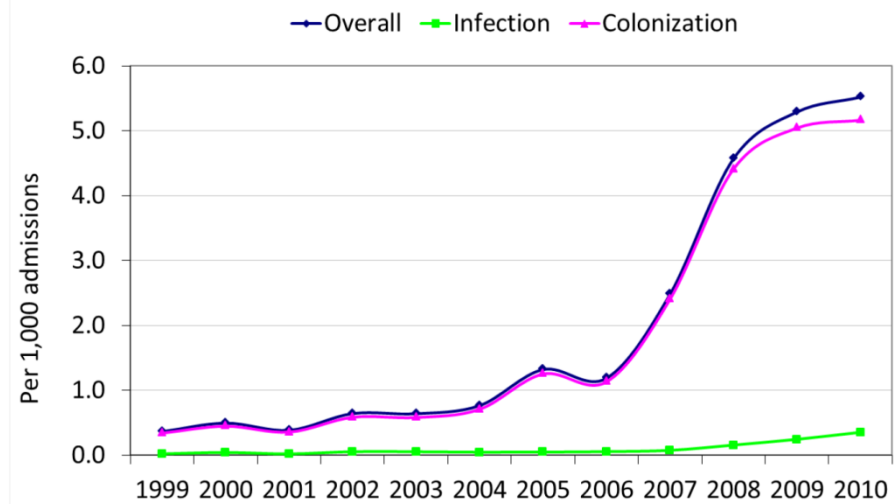
Overall VRE incidence rates per 1,000 patient admissions, 1999-2010



# Collateral damage



Overall VRE incidence rates per 1,000 patient admissions, 1999-2010

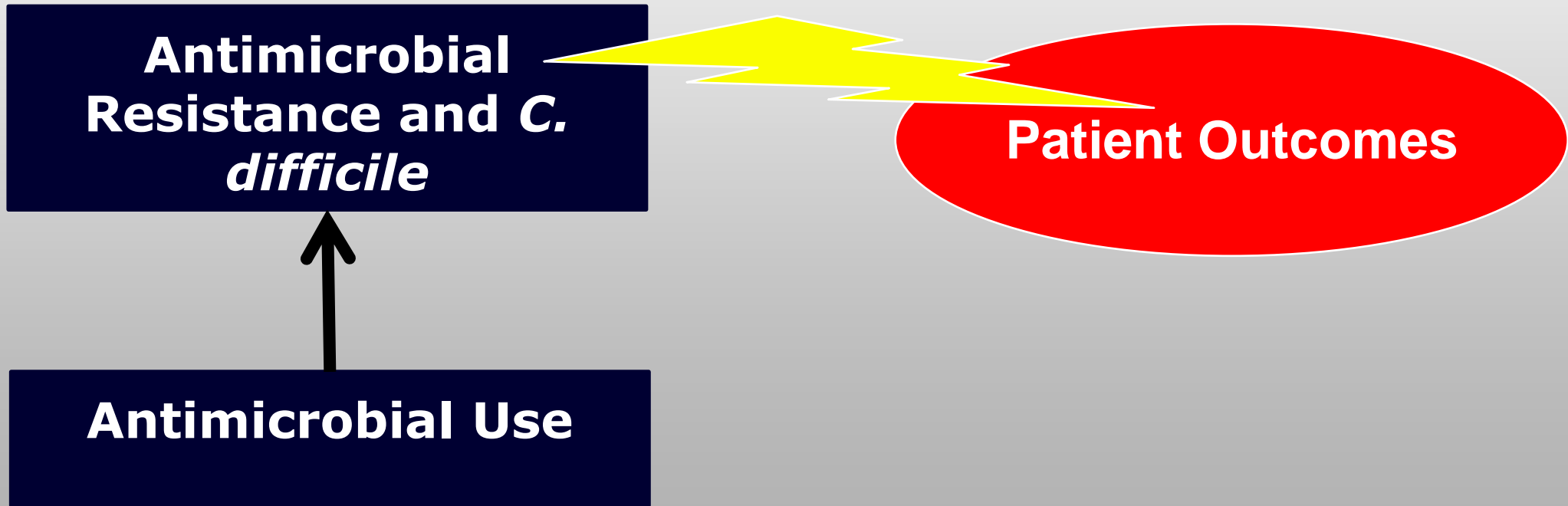


Only laboratories reporting susceptibility results for specific antimicrobials continuously during the period 2002–2009 are included in the analysis.



**Antimicrobial Resistance is one of three  
greatest threats to human health**

# Goal





# Collateral damage



## Clinical implications of resistant bacteria:

- Worse outcomes
  - Higher mortality rates
  - Longer length of stay
  - Greater costs
- as compared to their susceptible counterparts

# Collateral damage



## Clinical implications of *Clostridium difficile*:

- Worse outcomes
- Higher mortality rates
- Longer length of stay
- Greater costs

# Solutions

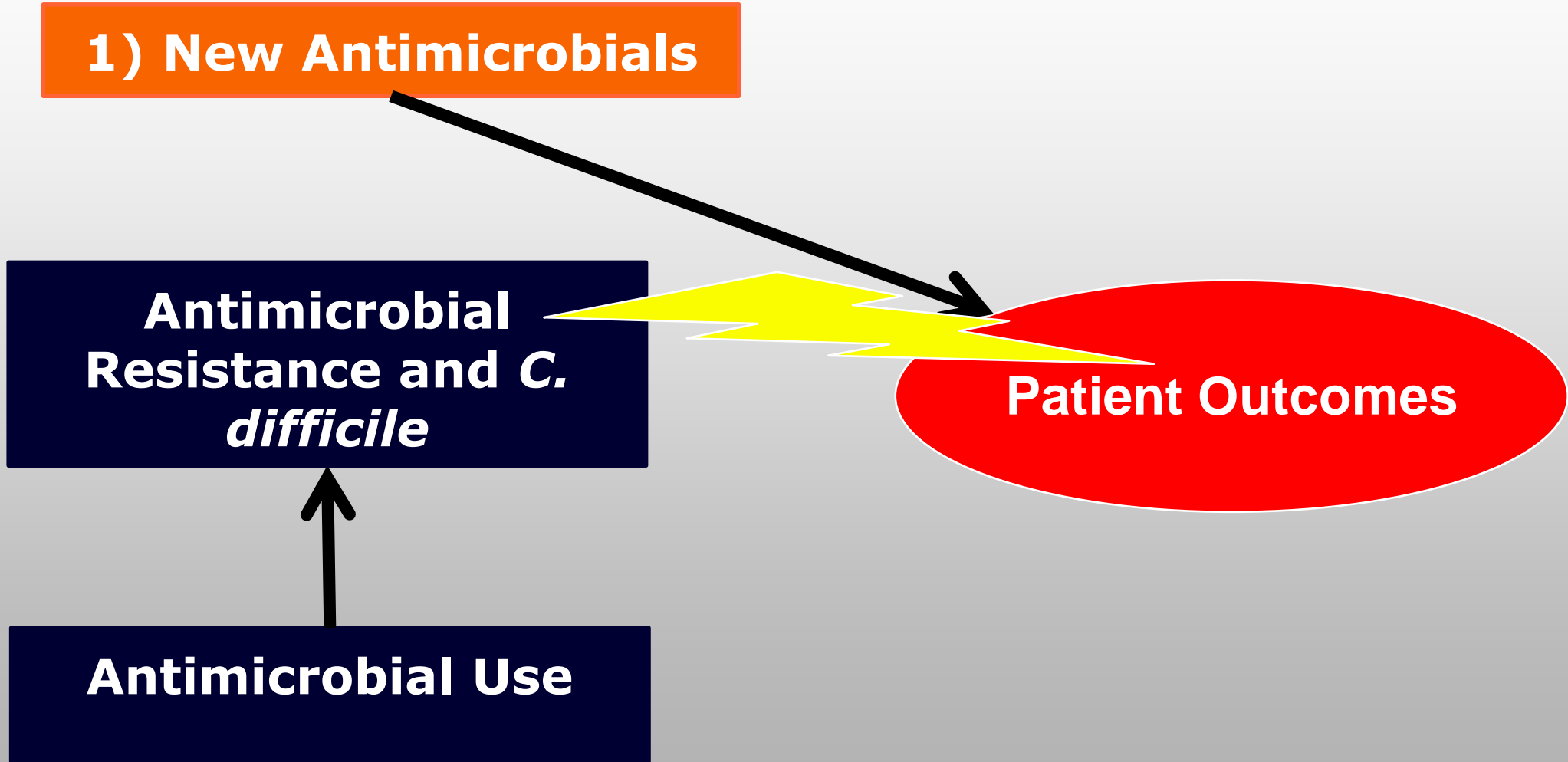


## 1) New Antimicrobials

**Antimicrobial  
Resistance and *C. difficile***

**Patient Outcomes**

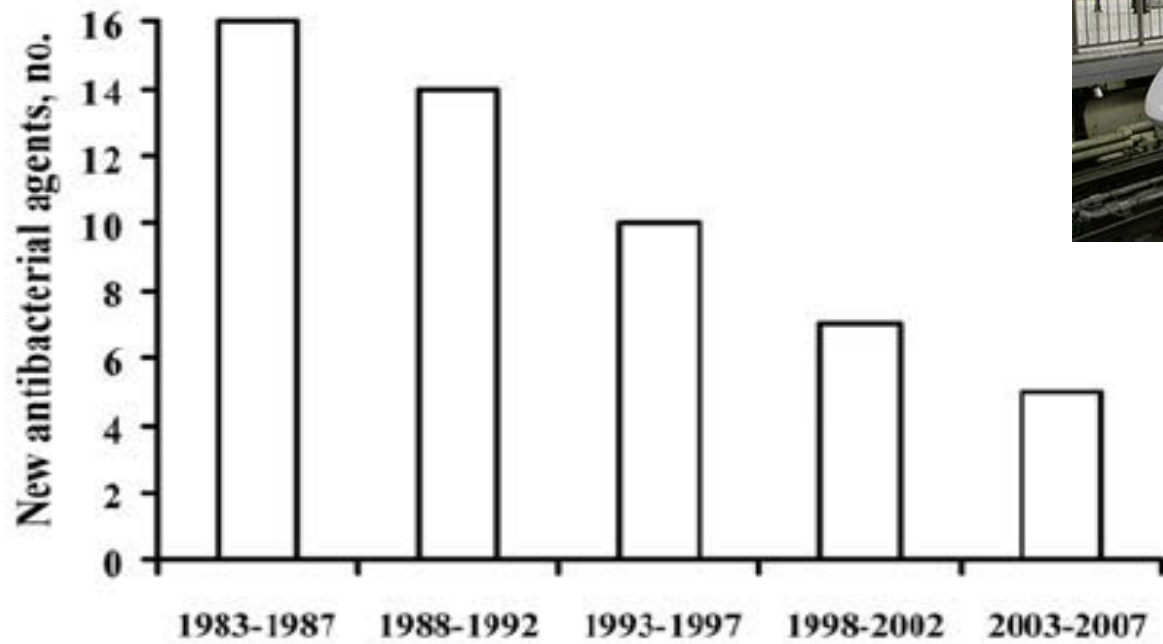
**Antimicrobial Use**



# The solution



## 1) New Antimicrobials

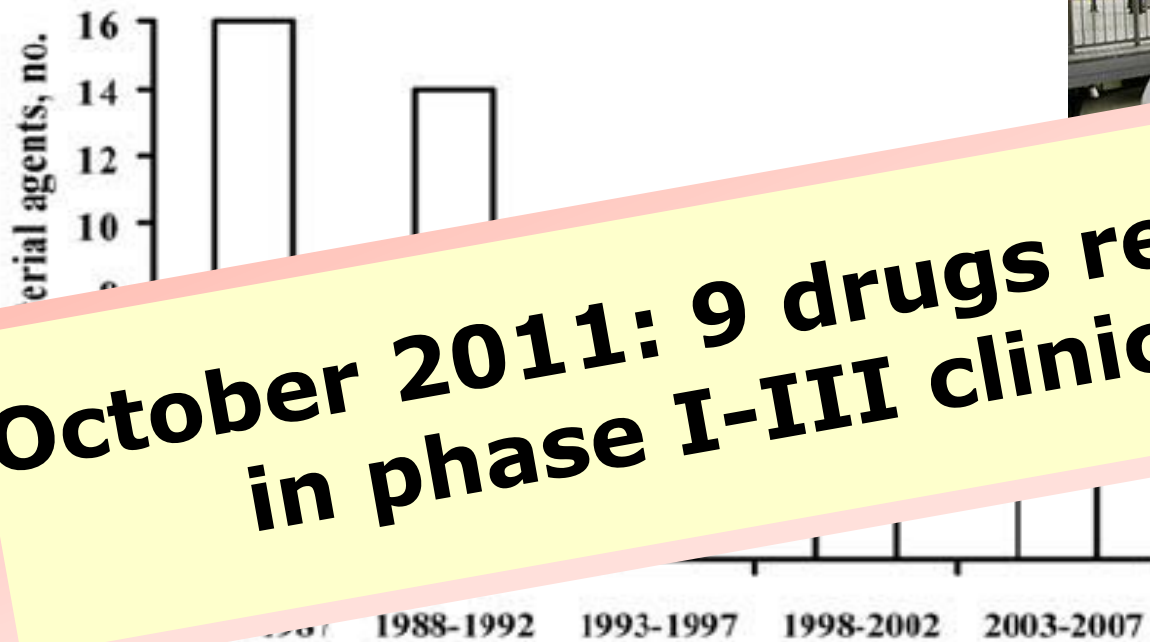


**Figure 1.** New antibacterial agents approved in the United States, 1983–2007, per 5-year period [2, 3].

# The solution



## 1) New Antimicrobials



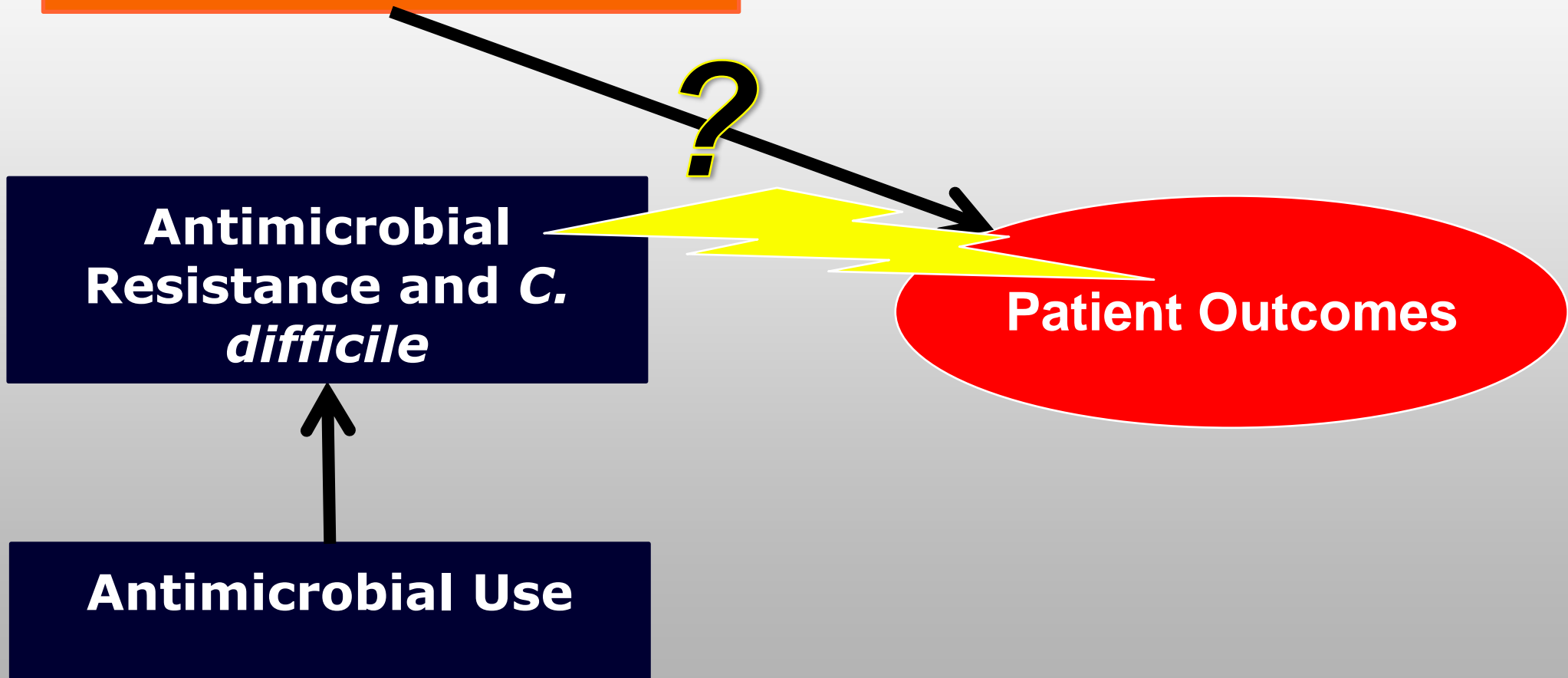
**October 2011: 9 drugs reported to be in phase I-III clinical trials**

**Figure 1.** New antibacterial agents approved in the United States, 1983–2007, per 5-year period [2, 3].

# Solutions



## 1) New Antimicrobials



# Solutions



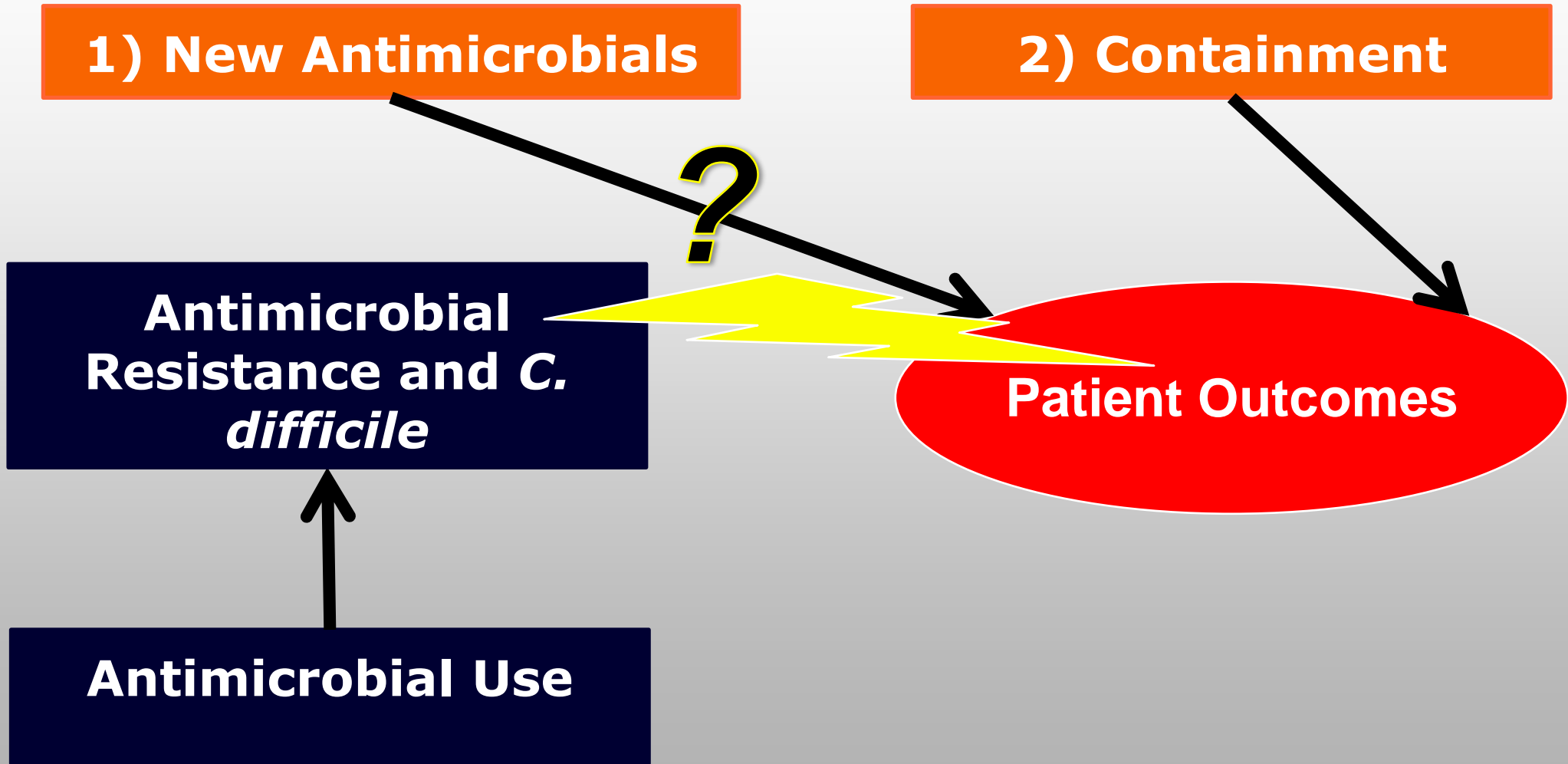
**1) New Antimicrobials**

**2) Containment**

**Antimicrobial  
Resistance and *C. difficile***

**Antimicrobial Use**

**Patient Outcomes**



# The solution



# STOP

## CONTACT PRECAUTIONS



**Use With Routine Practices**

**Dedicate or Clean & Disinfect Shared Equipment**

OVER

## 2) Containment

### Infection Prevention & Control

#### Challenges:

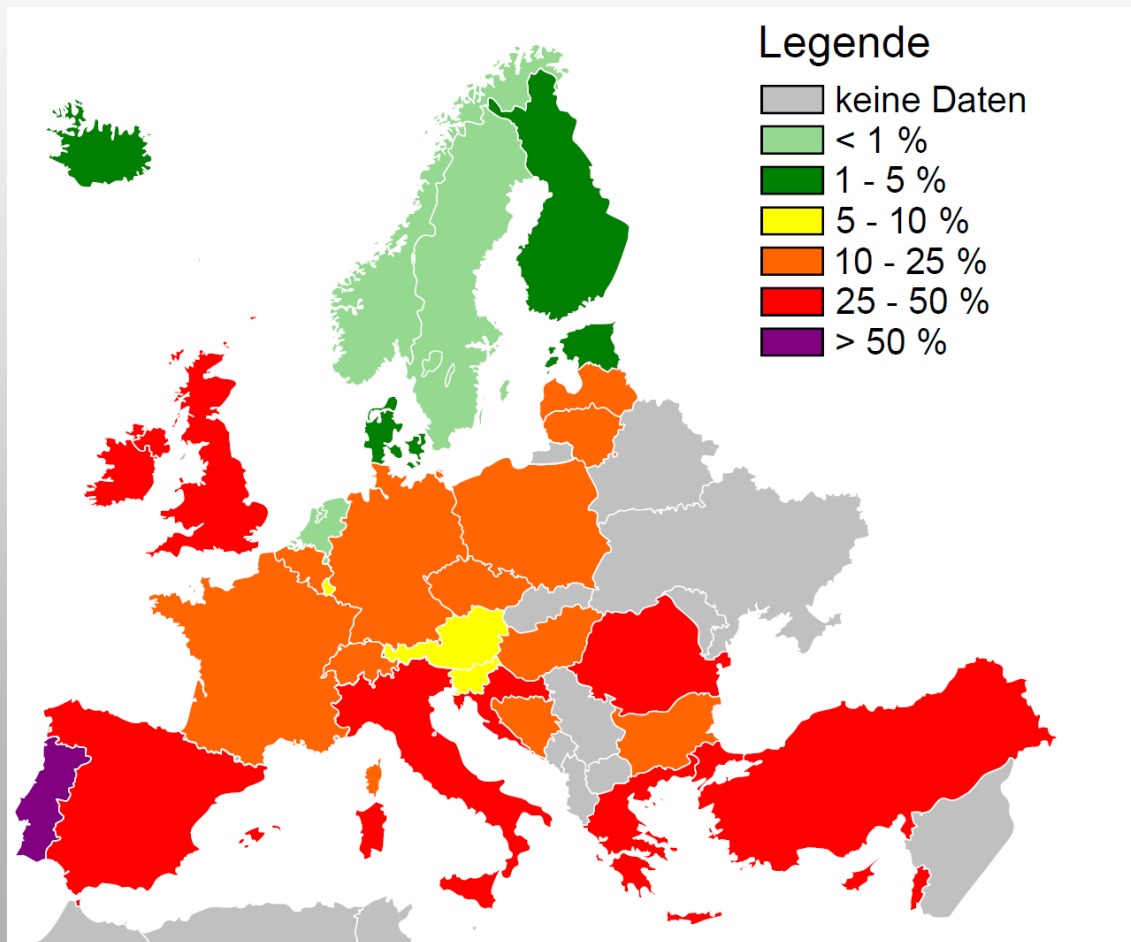
- Screening
- Compliance
- Private rooms
- Costs
- Community...



# The solution



% MRSA in *S. aureus*



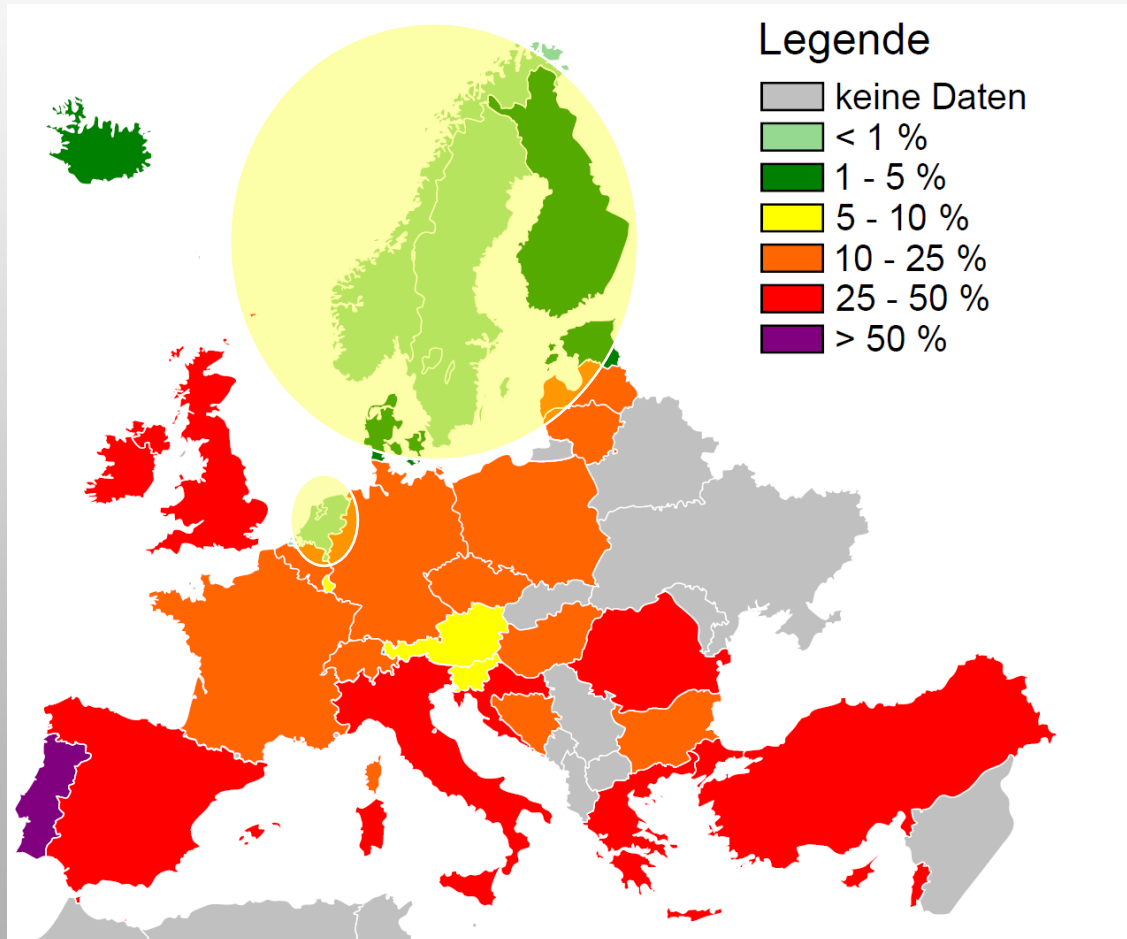
## 2) Containment

From the European Antimicrobial Resistance Surveillance System

# The solution



## % MRSA in *S. aureus*



## 2) Containment

MRSA Search & Destroy strategy successful:

- Netherlands
- Scandinavian Countries

# Common Goal



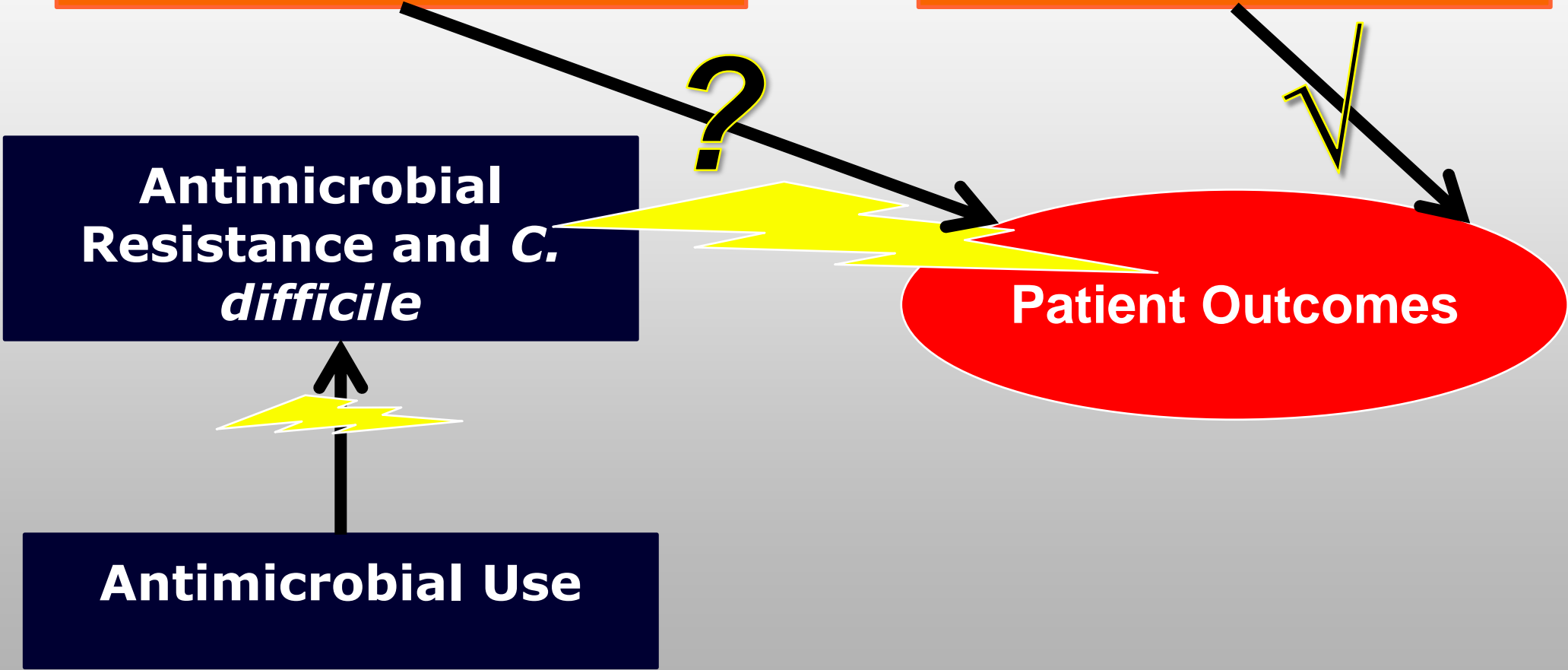
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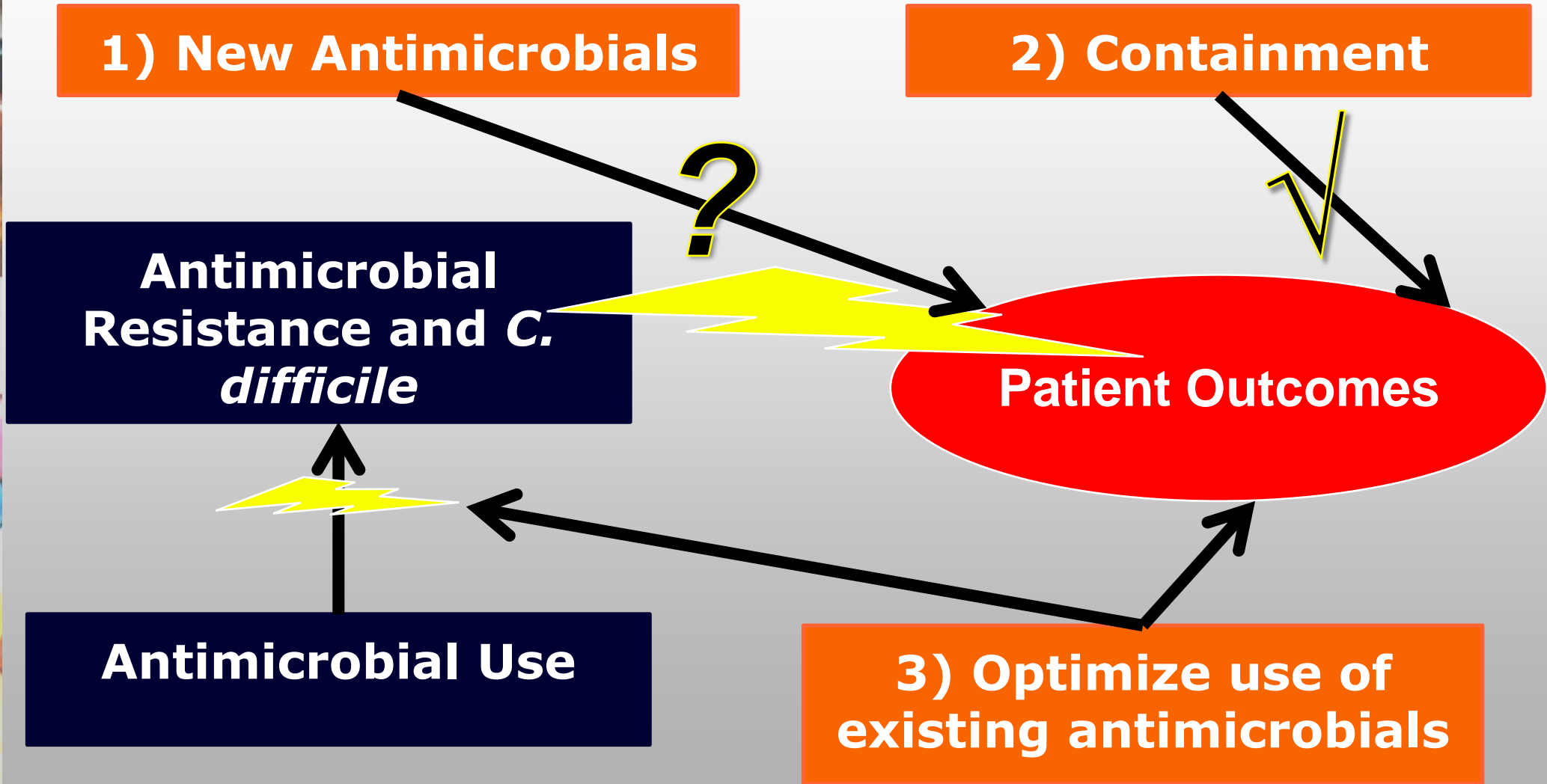
Antimicrobial Resistance and *C. difficile*

Patient Outcomes

Antimicrobial Use



# Common Goal





# Goals of Antimicrobial Stewardship Programs (ASP)

# Anti-Infectives: Facts



- 2<sup>nd</sup> most commonly prescribed class of drugs in US (likely similar here in Canada)
- Account for at least 20% of hospital pharmacy budgets
- > 40% of all hospitalized patients receive antibiotics
- **Repeatedly demonstrated that up to 50% of antimicrobial use is *inappropriate***

# What is ASP?



- Optimization of antimicrobial therapy via appropriate:
  - ✓ Choice
  - ✓ Dose
  - ✓ Route
  - ✓ Duration

# What is ASP?



- Optimization of antimicrobial therapy via 4 steps:

- ✓ Choice

- ✓ **"I am not sure whether we have a problem with inappropriate use of antibiotics here"**

- ✓ D



# Goals of ASP



## Quality improvement and patient safety initiative

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

# Goals of ASP



## Quality improvement and patient safety initiative

- Optimize clinical outcomes
- Minimize unintended consequences of anti-infective use
  - Toxicity
  - Selection of pathogenic organisms (such as *C. difficile*)
  - Emergence of resistance
- Also shown to reduce costs...

# Goals of ASP



Quality improvement and patient safety initiatives

- Optimize clinical outcomes
- Minimize

**Win - Win - Win**  
**(patient - resistance - costs)**

... (such as C. difficile) ...  
... of resistance

- Also shown to reduce costs...

# Elements of ASP



The single best element of ASP?

‘Multi’: multiple elements and multidisciplinary

- Prospective audit & feedback (AI)
- Restrictions (All)
- Guidelines & clinical pathways (All)
- Dose optimization (All)
- Streamlining (All)
- IV to PO switch (All)
- Antibiotic order forms (BII)
- Education (AIII)
- Microbiology consultations
- Rapid diagnostics
- MDR surveillance
- Adverse effects surveillance
- Process measure
- Outcome measure
- Decision support systems

# Urinary tract infections: Stewardship needed?



# Definitions



- Urinary tract infection (UTI)

= ???

- Asymptomatic bacteriuria

= ???

# Definitions

- Urinary tract infection (UTI)  
= positive culture + signs/symptoms
  
- Asymptomatic bacteriuria  
= positive culture in the absence of signs/symptoms

# Definitions

- Urinary tract infection (UTI)

= positive culture + signs/symptoms

'Positive urine culture'

- Women:  $>10(5)$  cfu/ml bacteria clean catch voided urine (x2)
- Men:  $>10(5)$  cfu/ml bacteria clean catch voided urine  
or 1x  $>10(2)$  cfu/ml in a catheterized specimen

signs/symptoms



# Definitions

- Urinary tract infection (UTI)

= positive culture + signs/symptoms

Symptoms:

Dysuria, frequency, urgency, suprapubic pain, hematuria

- Acute pyelonephritis: and/or: Fever, chills, flank pain, costovertebral angle tenderness, nausea/vomiting

signs/symptoms

# Clinical implications



- Urinary tract infection (UTI)

= positive culture + signs/symptoms

**TREATMENT**

- Asymptomatic bacteriuria

= positive culture without signs/symptoms

**NO TREATMENT**  
(with few exceptions)

# Clinical implications



- Urinary tract infection (UTI)

= positive culture + si

Implications of urine analysis?

- No clinical implications due to lack of predictive value:
  - Nitrite: sensitivity ~20-30%, specificity ~ 94-100% (for positive culture)
  - Leukocyturia: specificity ~60-70% (for UTI), positive culture in patient with no Lc in urine most likely contamination

# Asympt. bacteriuria: Epidemiology



## Women:

- 1% in schoolgirls to >20% >80 years
- Diabetics: 8-14%
- Pregnant women: 7%

## Men:

- Rare in the young, 6-15% >75 years

# Microbiology



Uncomplicated UTI:

*E. coli* 75-95%

Other enterobacteriaceae (*P. mirabilis*, *K. pneumoniae*), *S. saprophyticus*

Complicated UTI:

Plus *Pseudomonas*, *Serratia*, and *Providencia* species, enterococci, staphylococci, and fungi

# Microbiology



Organism	Number of Isolates	Ampicillin	Cefazolin	Ceftriaxone	Ceftazidime	Piperacillin	Piperacillin-Tazobactam	Imipenem	Ertapenem	Meropenem	Gentamicin	Tobramycin	Amikacin	Nitrofurantoin (urine only)	TMP/SMX	Ciprofloxacin
<i>E. coli</i>	706	62	90	96			97	100	100	na	93	93	100	95	76	74
<i>Klebsiella pneumoniae</i>	162	0	96	99			96	100	100	na	99	99	100	28	94	95
<i>Enterobacter spp</i> ##	38							97	95	na	100	100	100	13	92	95
<i>Proteus mirabilis</i>	70	93	97	97			100	93	100	na	100	100	100	0	93	97
<i>Pseudomonas aeruginosa</i>	58				93	97	95	89	na	91	83	95	97			74

# Antimicrobial Treatment



## Uncomplicated UTI:

- Cystitis (female):
  - Nitrofurantoin (100mg BID x 5 days)
  - TMP/SMX (1 DS tablet BID x 3 (-7) days)
  - Ciprofloxacin (500mg BID x 3 days)
  - Betalactams: amoxi/clav, cefpodoxime, cefaclor, cephalexin
  - Fosfomycin (n/a)

# Antimicrobial Treatment



## Uncomplicated UTI:

### - Cystitis (male):

- ~~Nitrofurantoin (100mg BID x 5 days)~~
- TMP/SMX (1 DS tablet BID **x 3** (-7) days)
- Ciprofloxacin (500mg BID x **3 days**)
- ~~Betalactams: amoxi/clav, cefpodoxime, cefaclor, cephalexin~~
- ~~Fosfomycin (n/a)~~

7-14 days  
(nobody knows...)

Insufficient tissue levels (prostatitis) / lack of data



# Antimicrobial Treatment



## Complicated UTI:

### - Cystitis:

- ~~Nitrofurantoin (100mg BID x 5 days)~~
- ~~TMP/SMX (1 DS tablet BID x 3 (-7) days)~~

**1<sup>st</sup> choice:** Ciprofloxacin (500mg BID x 3 days)

- ~~Betalactams: amoxi/clav, cefpodoxime, cefaclor, cephalexin~~
- ~~Fosfomycin (n/a)~~

5-14 days

Resistance rates in complicated UTI

# Catheter-related: Definition



Symptomatic catheter related bacteriuria:

- fever, suprapubic tenderness, costovertrabral angle tenderness, or otherwise unexplained systemic symptoms (altered mental status, hypotension, SIRS)

AND

- $>10(5)$  cfu/ml irrespective of urine specimen
- $>10(3)$  cfu/ml with evidence of pyuria

While indwelling catheter or 48h after removal

# Catheter-related: Epidemiology



- Most common hospital-acquired infection
- Bacteriuria in 3-10% per catheter day
- 10-25% of these will become symptomatic
- Risk factors for symptoms: female sex, diabetes, prolonged catheterization, errors in catheter care
- Pathogenesis: mostly extraluminal (2/3 of cases)

# Catheter-related: Treatment



- Who to treat?
- All patients with significant pyuria and bacteriuria?
- Empiric treatment indicated?
- Spectrum of antibiotics?
- Duration?
- Management of indwelling catheter?

# Catheter-related: Treatment



- ONLY SYMPTOMATIC PATIENTS
- Pyuria and bacteriuria per se does not need to be treated
- Symptomatic patients:
  - Treatment according to susceptibility results
  - If needed, empirically ceftriaxone, ciprofloxacin, ceftazidime
  - Duration 14 days
  - Remove or replace catheter whenever possible



In-house data

Hamilton Health Sciences

# Stewardship initiative UTI



Problem: treatment of asymptomatic bacteriuria

Methods: review all patients with positive urine cultures

Assessment of symptoms: charts and discussion with teams

Outcome: appropriate management of positive urine culture

# Stewardship initiative UTI



Problem: treatment of asymptomatic bacteriuria

Methods: review all patients with positive urine cultures

Assessment of symptoms: charts and discussion with teams

Outcome: appropriate management of positive urine cultures

Results:

- >100 patients with positive urine cultures
- about 50% obtained from asymptomatic patients
- >50% of asymptomatic patients were treated



# Take Home Messages



- Order urine cultures only if there is an indication for treatment:
  - **Signs or symptoms of UTI**
  - **Pregnancy or urological intervention**
- >20% of *E. coli* isolates resistant to FQ or TMP/SMX
- Consider nitrofurantoin in non-complicated UTI

# Take Home Messages



- Order urine culture

- **Abx can harm**

- **Abx indicated if potential benefit > potential harm**

- **Need to treat patients, not lab results**