Global Antibiotic Resistance Partnership

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CDDEP THE CENTER FOR Disease Dynamics, Economics & Policy
WASHINGTON DC • NEW DELHI

RESOURCES FOR THE FUTURE

Objective

Develop actionable national strategies to address the challenge of antibiotic resistance in five low- and middle-income countries

- China
- India
- Kenya
- South Africa
- Vietnam

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Specific Aims

- Develop the evidence base for policy action on antibiotic resistance
- Identify policy opportunities where research dissemination, advocacy, and information can have the greatest impact in slowing the development and spread of resistance.

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Steps

- Create country profiles of baseline resistance, antibiotic use and burden of resistance
- Assess the health and economic consequences of antibiotic resistance
- Develop mathematical models of specific approaches to delay emergence of antibiotic resistance
- Constitute GARP National Working Groups

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Other objectives

- Create an IT platform for a global antibiotic resistance atlas
- International conference to compare policy approaches across the five target countries and to discuss the relevance of these approaches to other countries outside the initial partnership

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Second Phase

- Dissemination of national strategies
- Policy communications
- Further research

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Objectives for this meeting

- How serious a problem is antibiotic resistance in Kenya?
- What are the primary drivers of resistance?
- What policies could both help reduce the
  - Suboptimal use of antibiotics
  - Need for antibiotics
  - Emergence and spread of resistance

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www.extendingthecure.org

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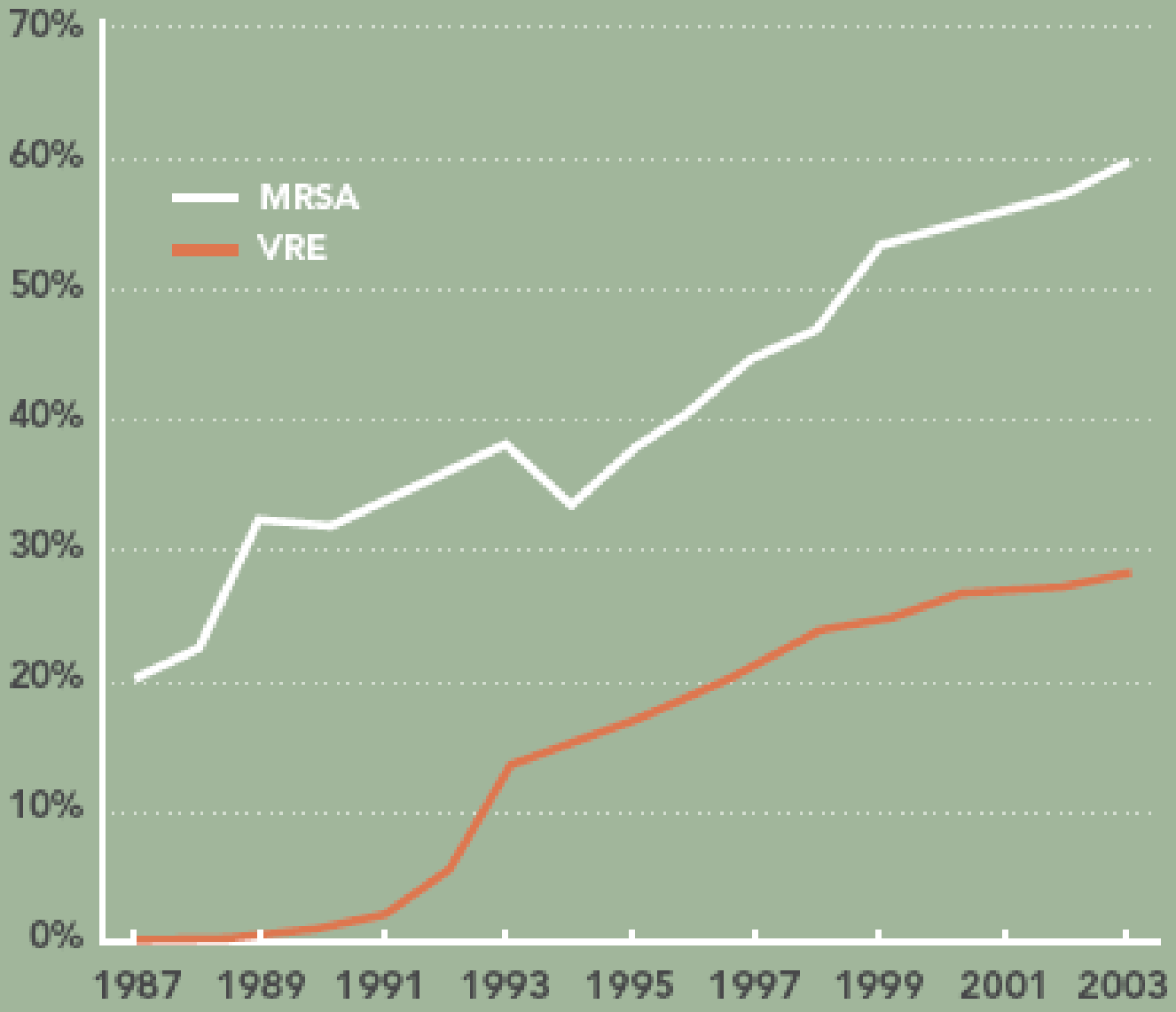
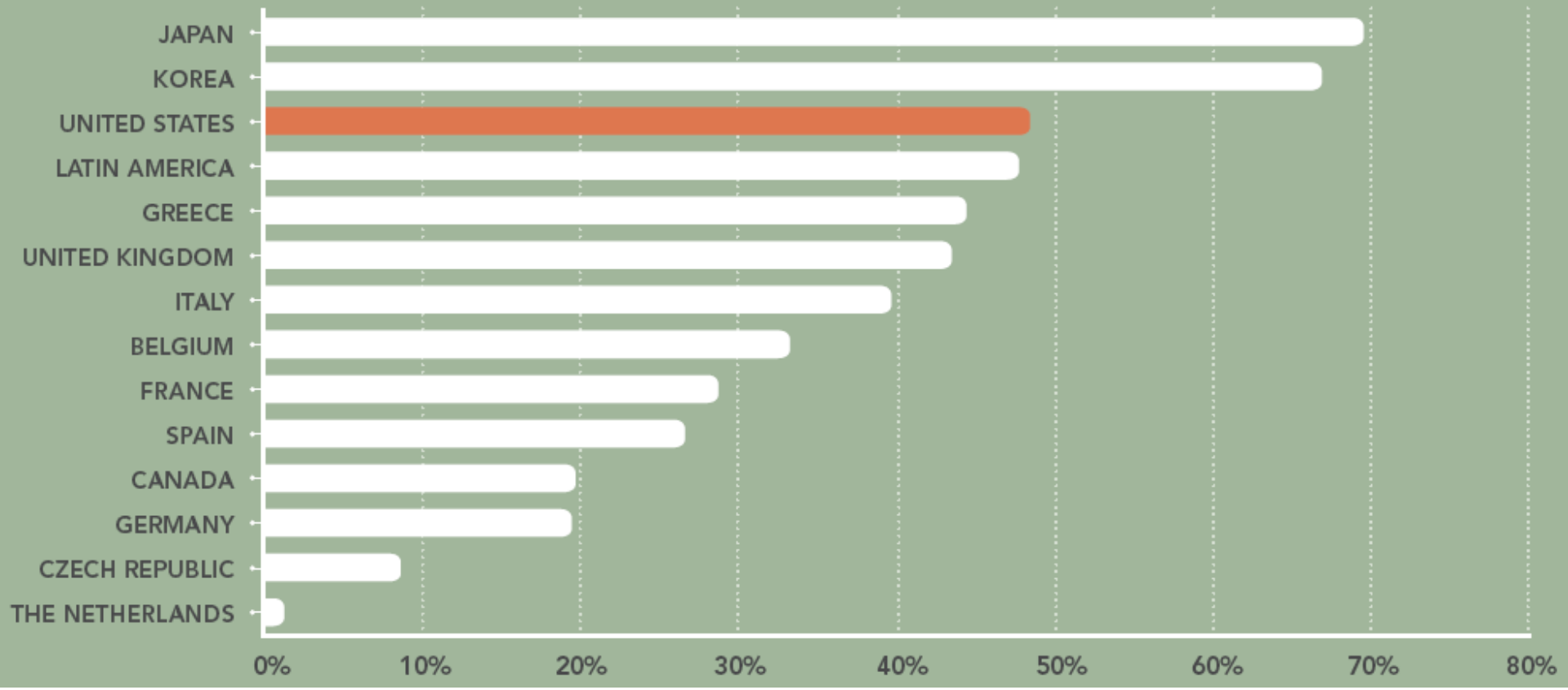
The proportion of methicillin-resistant Staphylococcus aureus and vancomycin-resistant enterococcal infections is increasing (1987–2003)



The proportion of methicillin-resistant Staphylococcus aureus (MRSA) infections in the United States is high compared with other high-income countries (2004)



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Growing resistance combined with an increasing number of Staphylococcus aureus infections has resulted in an increasing number of hospitalized patients who have MRSA infections

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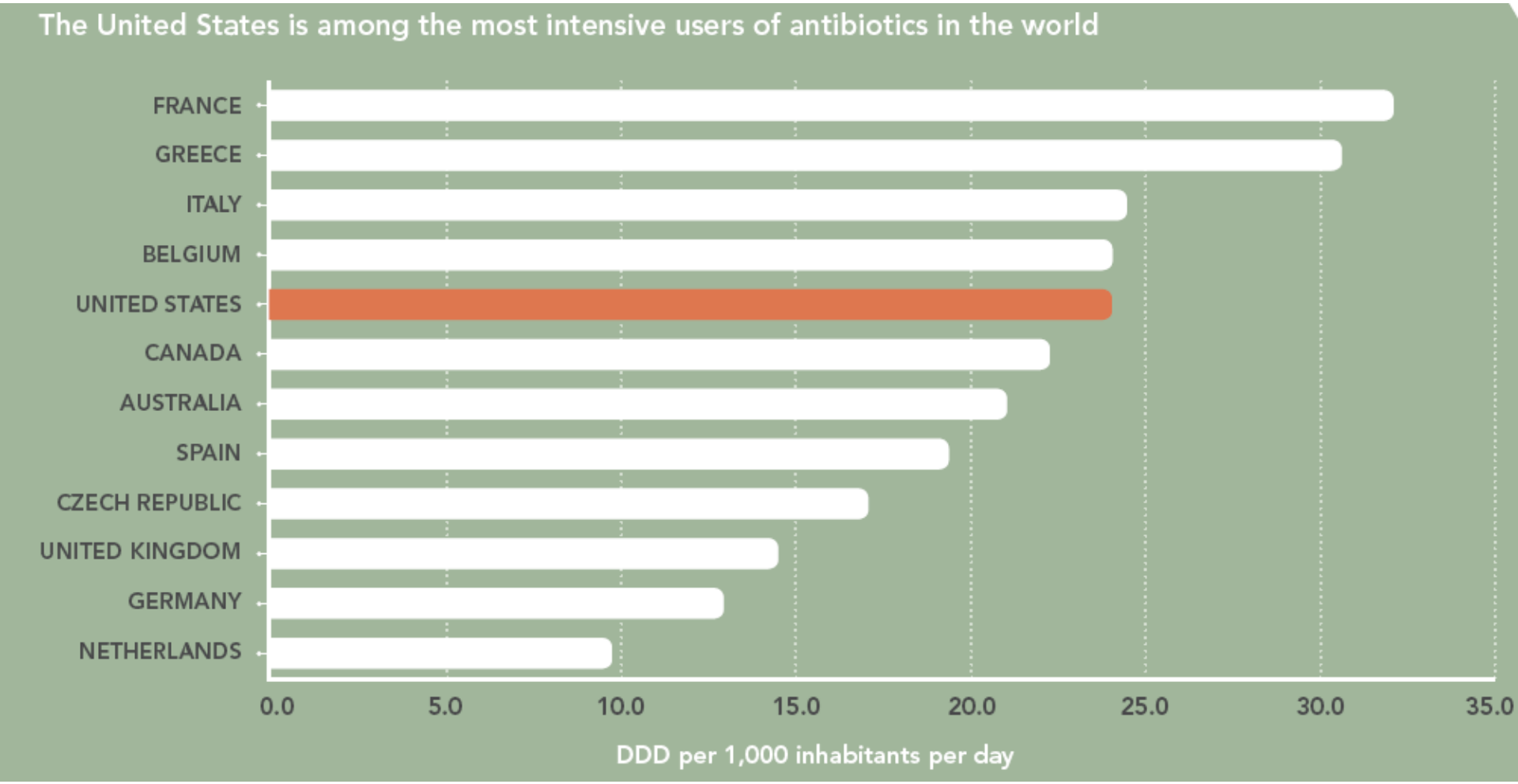

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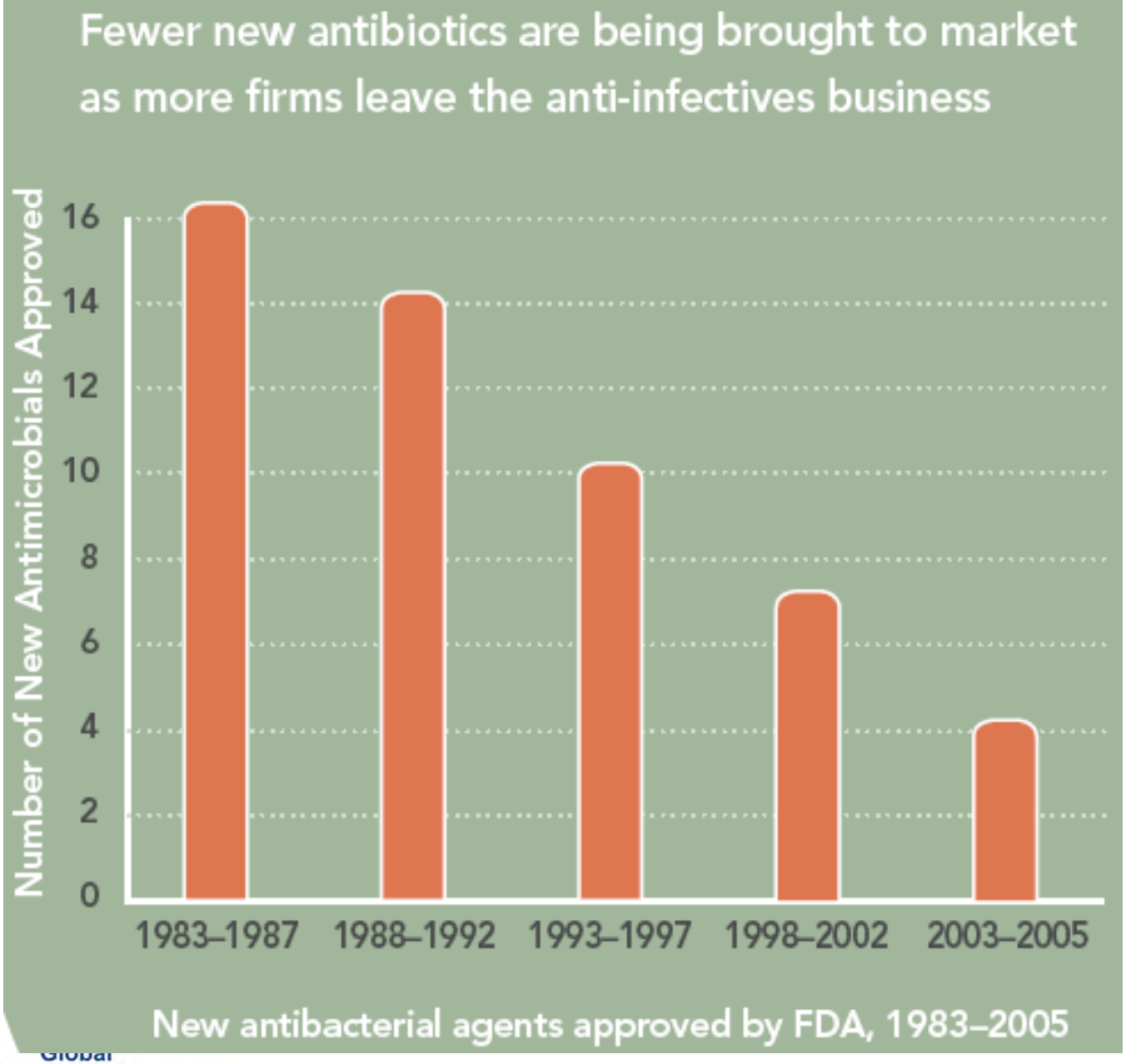

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THE BRITISH JOURNAL

OF

EXPERIMENTAL PATHOLOGY

VOLUME TEN

1929

Reproduced from pages 226–236.

ON THE ANTIBACTERIAL ACTION OF CULTURES OF A PENICILLIUM, WITH SPECIAL REFERENCE TO THEIR USE IN THE ISOLATION OF *B. INFLUENZÆ.*

ALEXANDER FLEMING, F.R.C.S.

From the Laboratories of the Inoculation Department, St Mary's Hospital, London.

Received for publication May 10th, 1929.


Thanks to PENICILLIN
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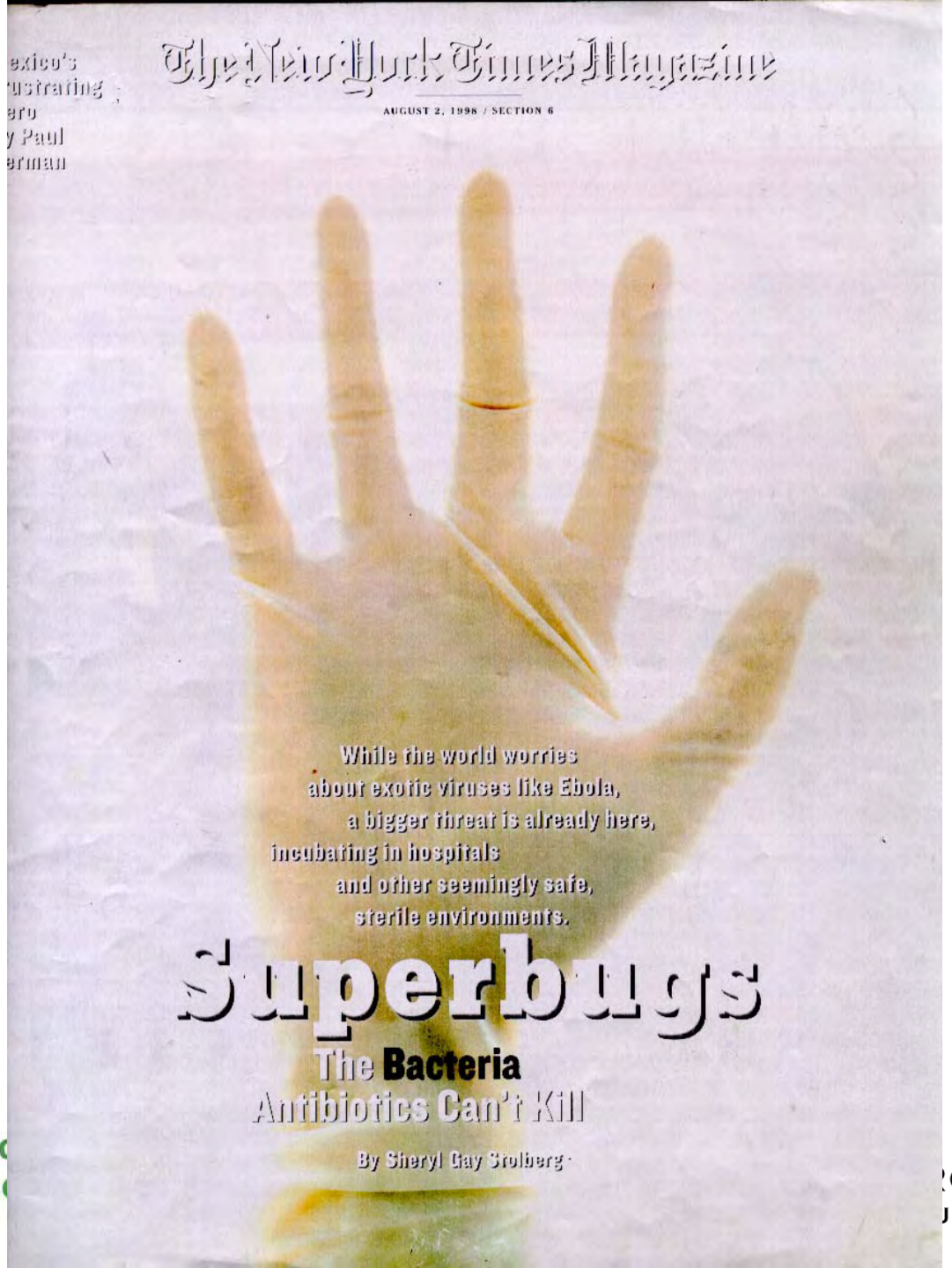
The New York Times Magazine

AUGUST 2, 1998 / SECTION 6



While the world worries
about exotic viruses like Ebola,
a bigger threat is already here,
incubating in hospitals
and other seemingly safe,
sterile environments.

Superbugs

The Bacteria Antibiotics Can't Kill

By Sheryl Gay Stolberg

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The Bug Wars

In the battle of bad bacteria vs. antibiotics, the drugs usually lose.

Infectious diseases give us a startling demonstration of evolution in action. The tiniest bacteria – the ones that survive an antibiotic onslaught – transfer their resistance to new generations and across species. Their ability to fight back usually strengthens with each mutation, allowing them to thwart even the most intelligently designed drugs. Over the past 60 years, deadly bugs like *Staphylococcus aureus*, *Streptococcus pneumoniae*, and *Escherichia coli* have evolved to withstand mechanisms like penicillin, tetracycline, and ciprofloxacin. Do scientists and now planning a flank attack – precisely targeted drug-delivery systems and bacteria-eating nanorobots. But if history repeats itself, the bugs will ultimately win. – **Patrick Di Justo**

BEHIND ENEMY LINES: A LOOK AT RESISTANCE TACTICS

Genetic mutations enable bacteria to adapt to new threats. Here are three ways they evolve to combat antimicrobial agents.

CAMOUFLAGE
A bacterium's protein receptors morph so the antibiotic can't lock into them. (Staph used this method to evade the penicillin family.)

ROADBLOCKS
The cell membrane changes to keep the medicine out. (Bacteria like staph and strep fended off tetracycline this way.)

DISARMAMENT
A bacterium produces enzymes that fend off the active part of the antibiotic. (This is how *E. coli* thwarted cephalosporins.)

Staphylococcus aureus
S. aureus causes everything from skin infections to toxic shock syndrome. More than half of all staph infections found in intensive care units today can be linked to a drug-resistant strain.

Streptococcus pneumoniae
Besides the much-loathed strep throat and the much-feared flesh-eating bacteria, strains of *Streptococcus* cause over 125,000 cases of pneumonia a year that require hospitalization.

Escherichia coli
Dangerous forms of *E. coli* cause all sorts of problems, from GI distress to meningitis. In June 2005, the FDA approved tigecycline, a new type of antibiotic designed to fight resistant *E. coli*.

Antibiotics
More than 110 million antibiotic prescriptions are written annually in the US. The Centers for Disease Control and Prevention discourages the use of antibiotics to treat viral diseases like the flu. The drugs are ineffective against viruses.

Staph resists penicillin
The drug that started it all goes down in just five years, sending scientists back to the lab.

Staph resists methicillin
Staph quickly conquers methicillin, harnessing the era of the "superbug."

Staph resists vancomycin
The drug of last resort, the one deployed when others failed, is finally outwitted.

Staph resists linezolid
The first new class of antibiotic in 35 years takes its firepower within a year.

HOW FAST BACTERIA EVOLVE TO THWART DRUGS

Sources: Alliance for the Prudent Use of Antibiotics; Centers for Disease Control and Prevention; *Emerging Infectious Diseases*; Mark Pendergrast and Elinor Levy, *The New Killer Diseases*; Jeffrey Reiter, *The Plague Makers*; Stuart Levy, *The Antibiotic Paradox*; National Library of Medicine

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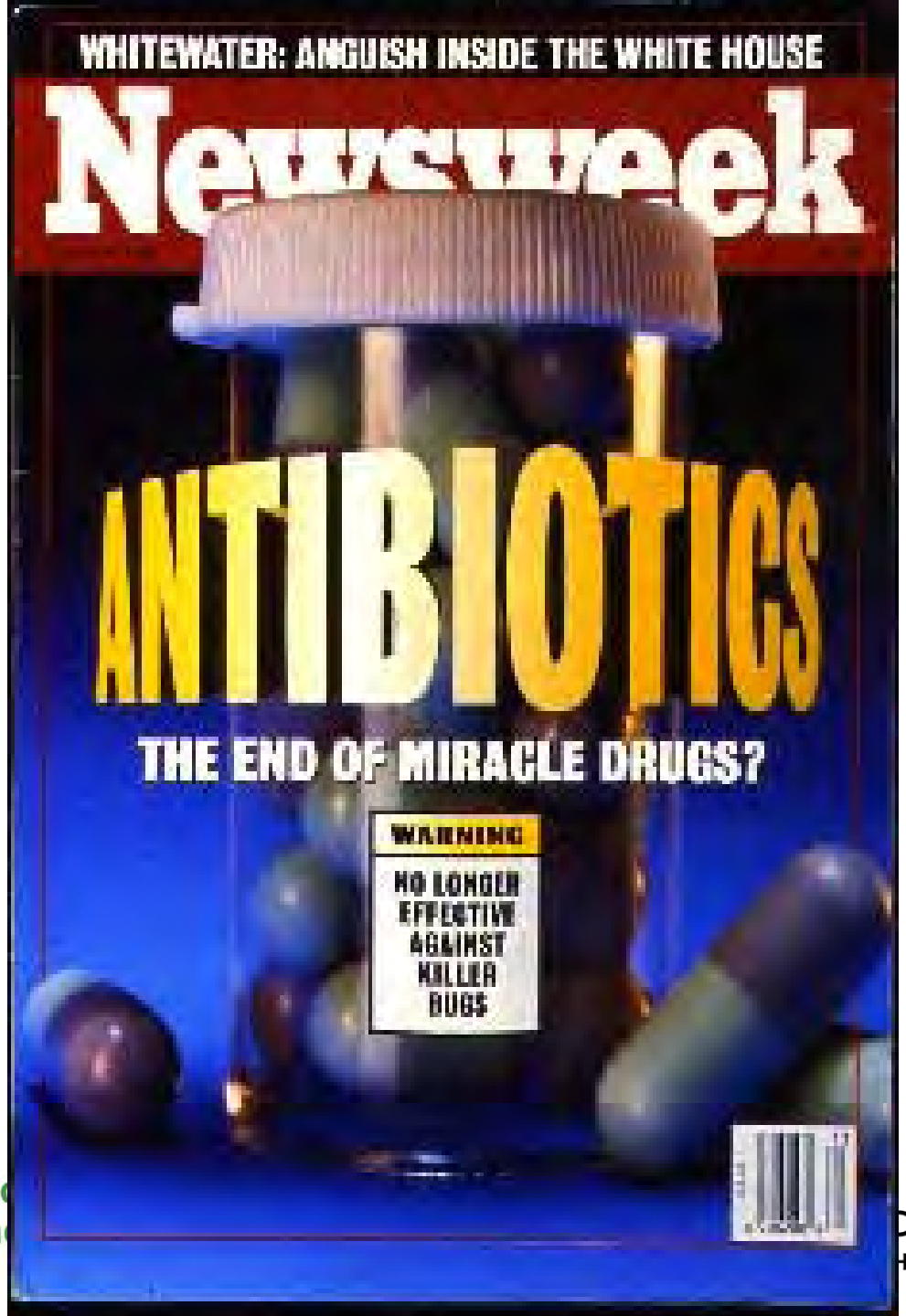

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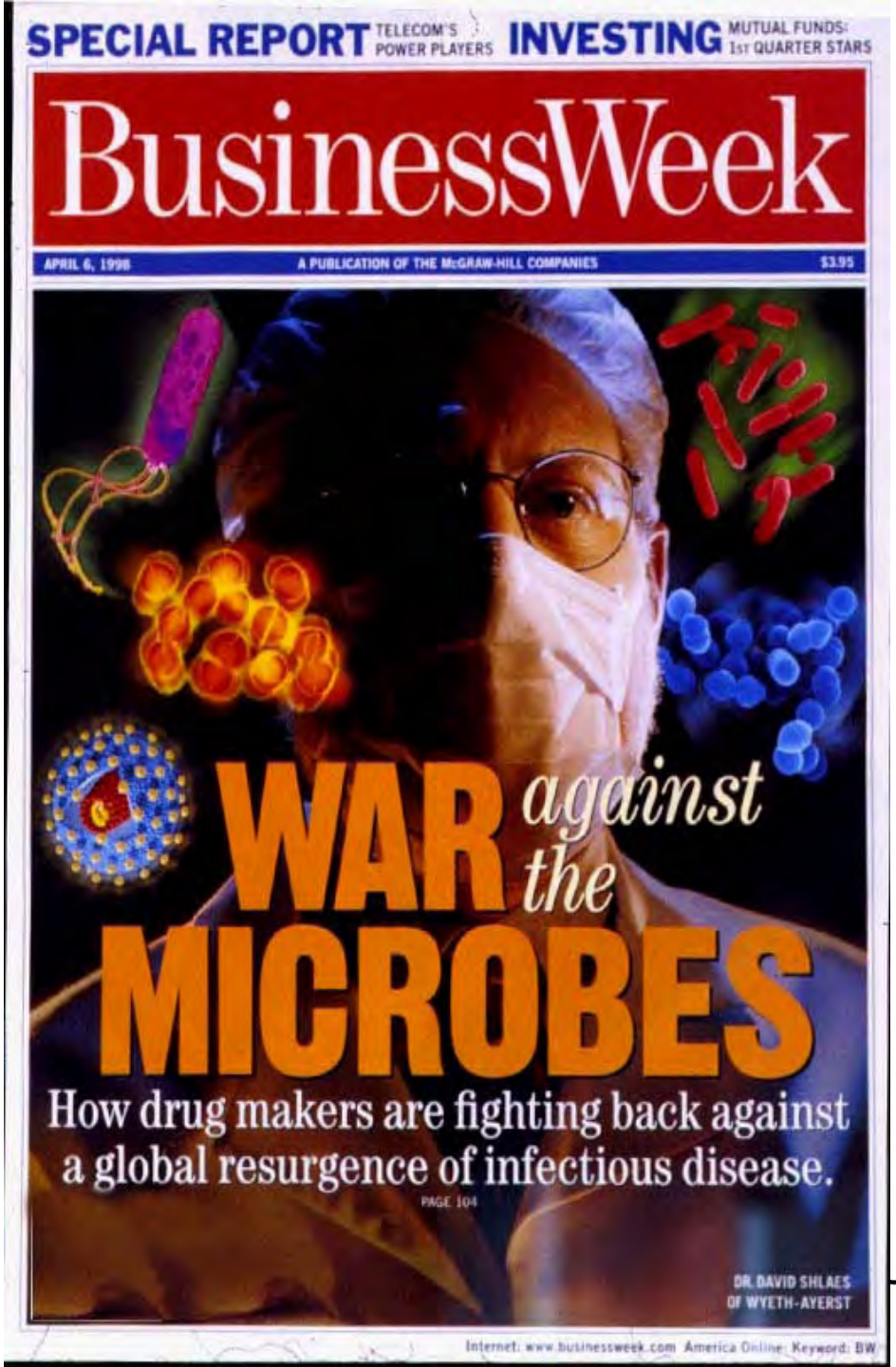

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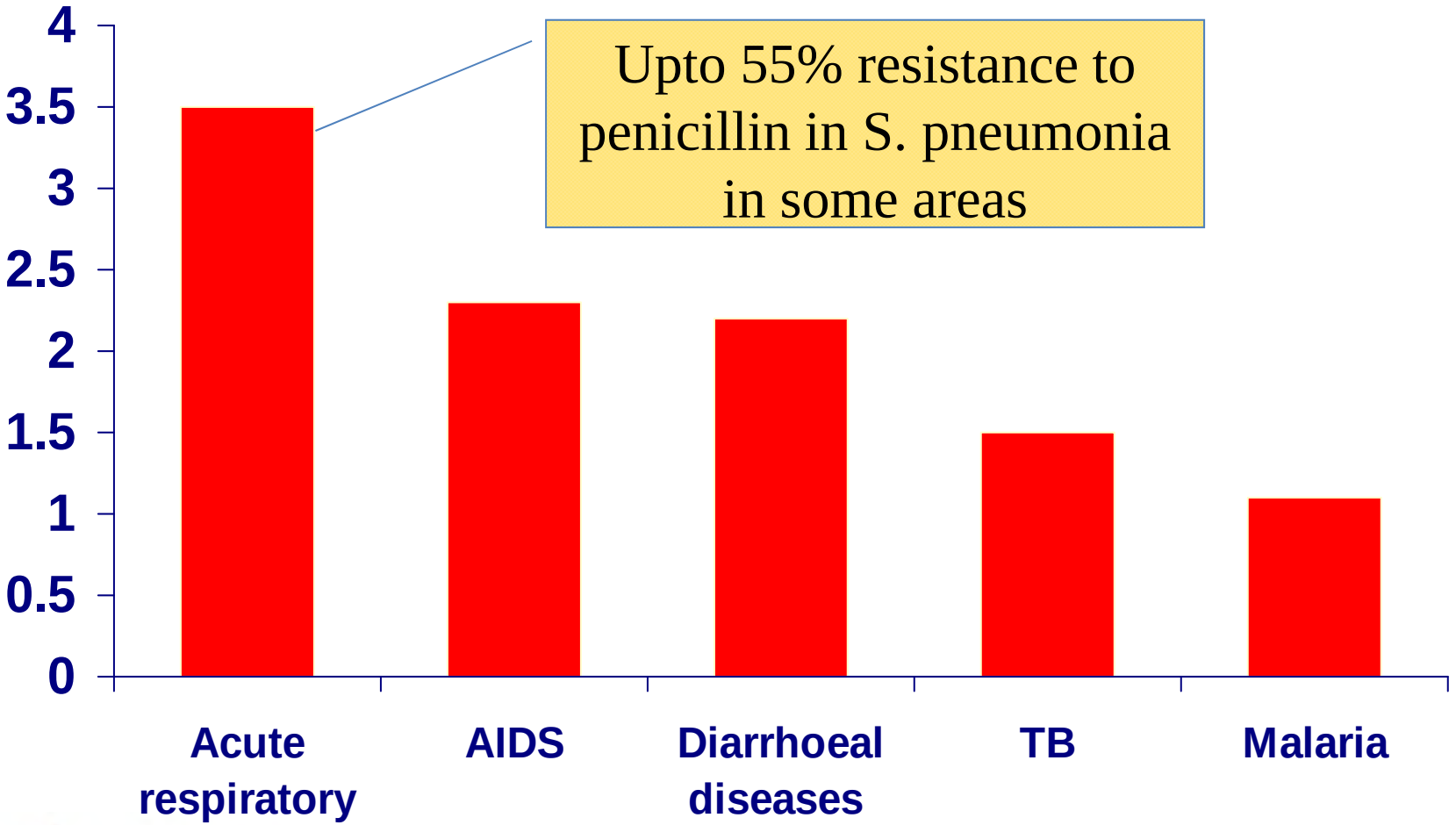
Leading Infectious Killers
Millions of deaths, worldwide, all ages



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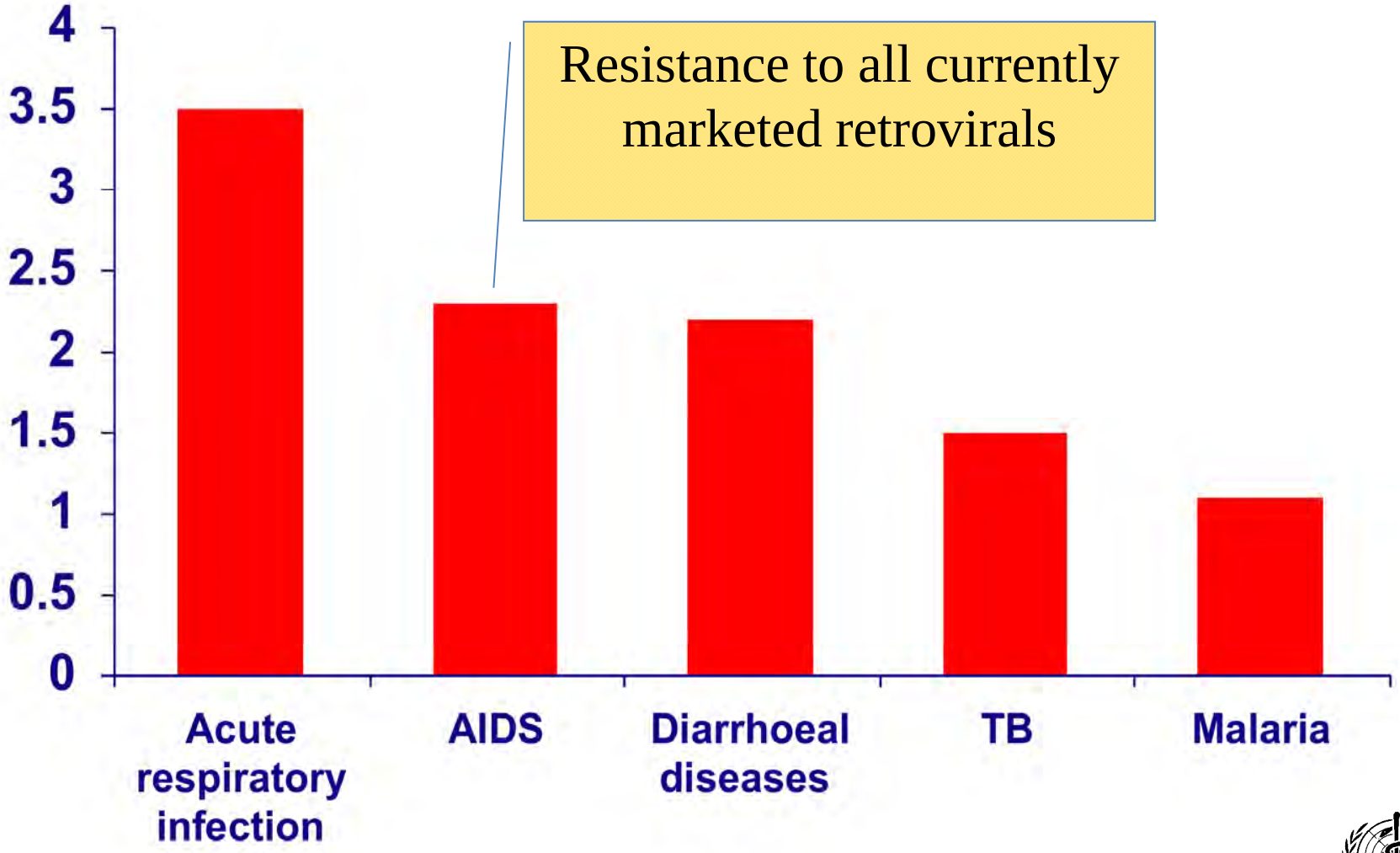

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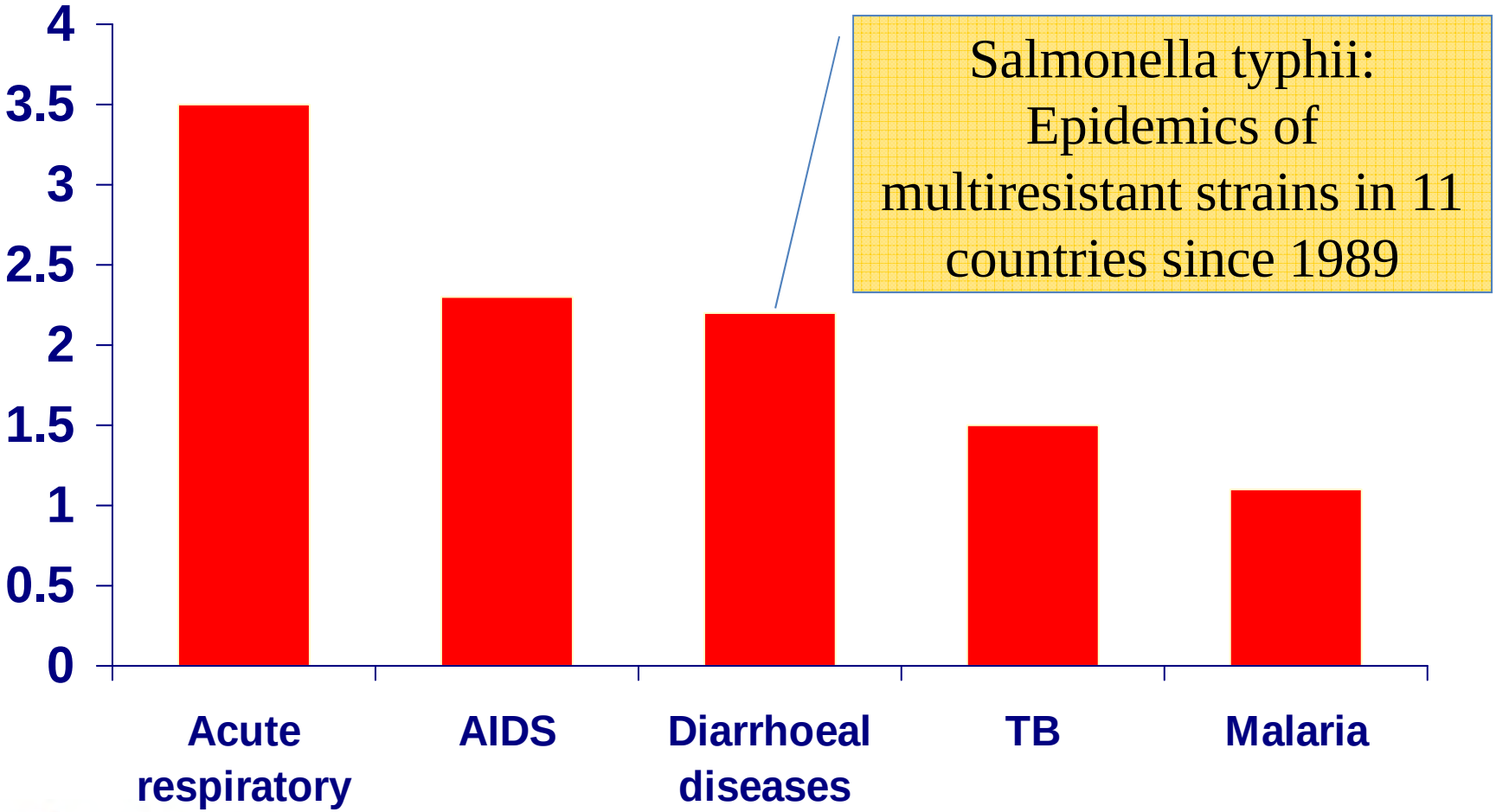

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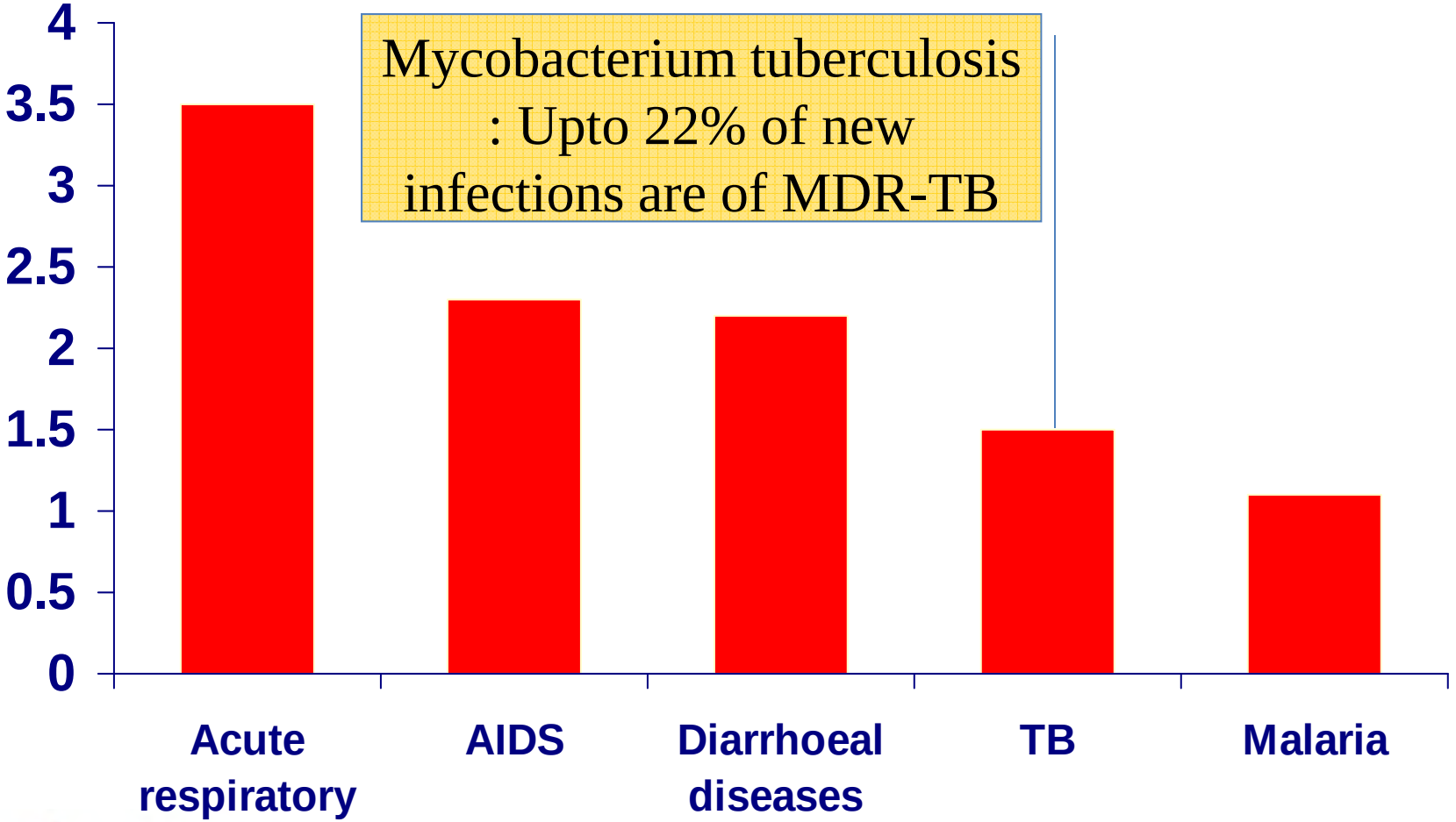

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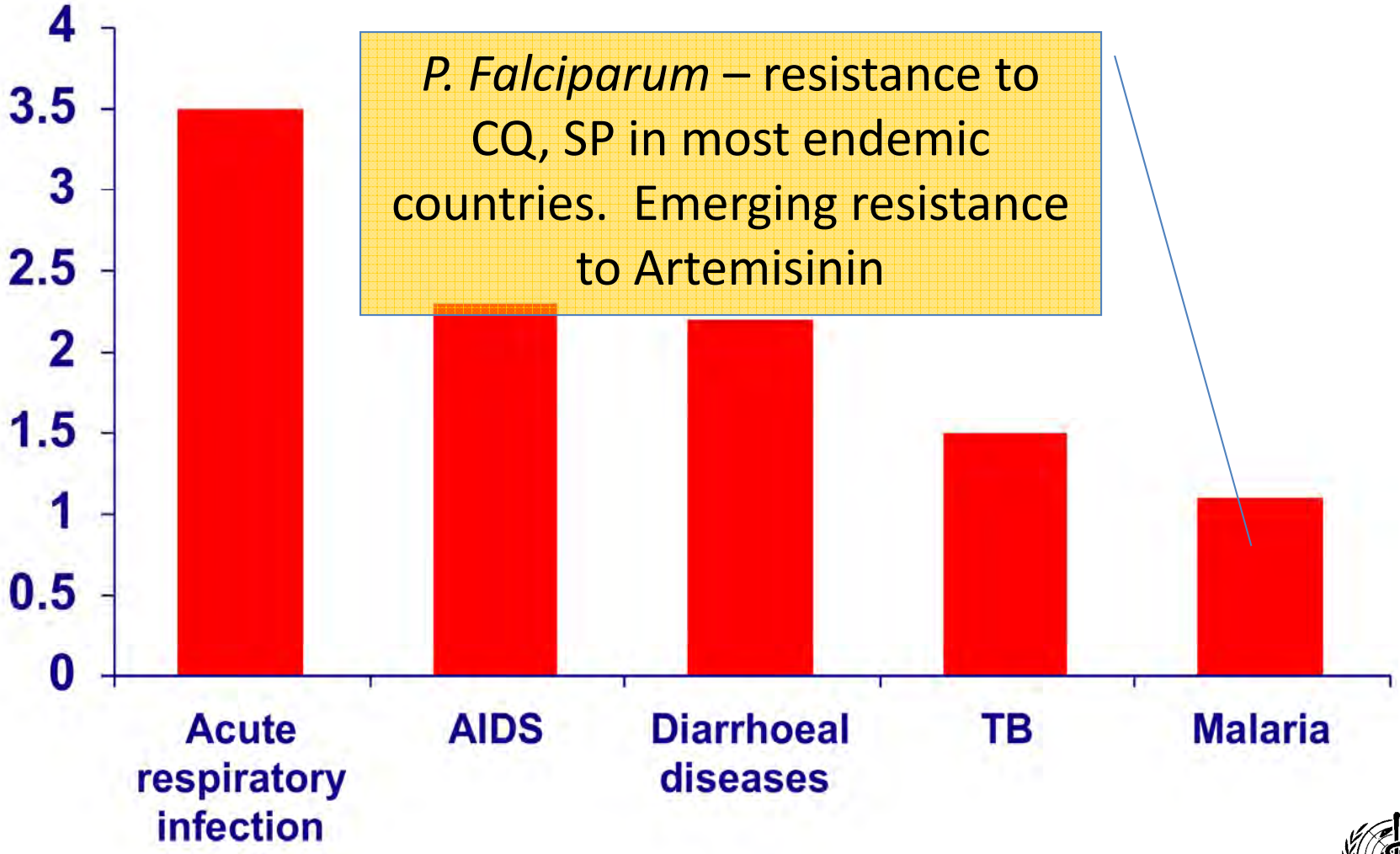

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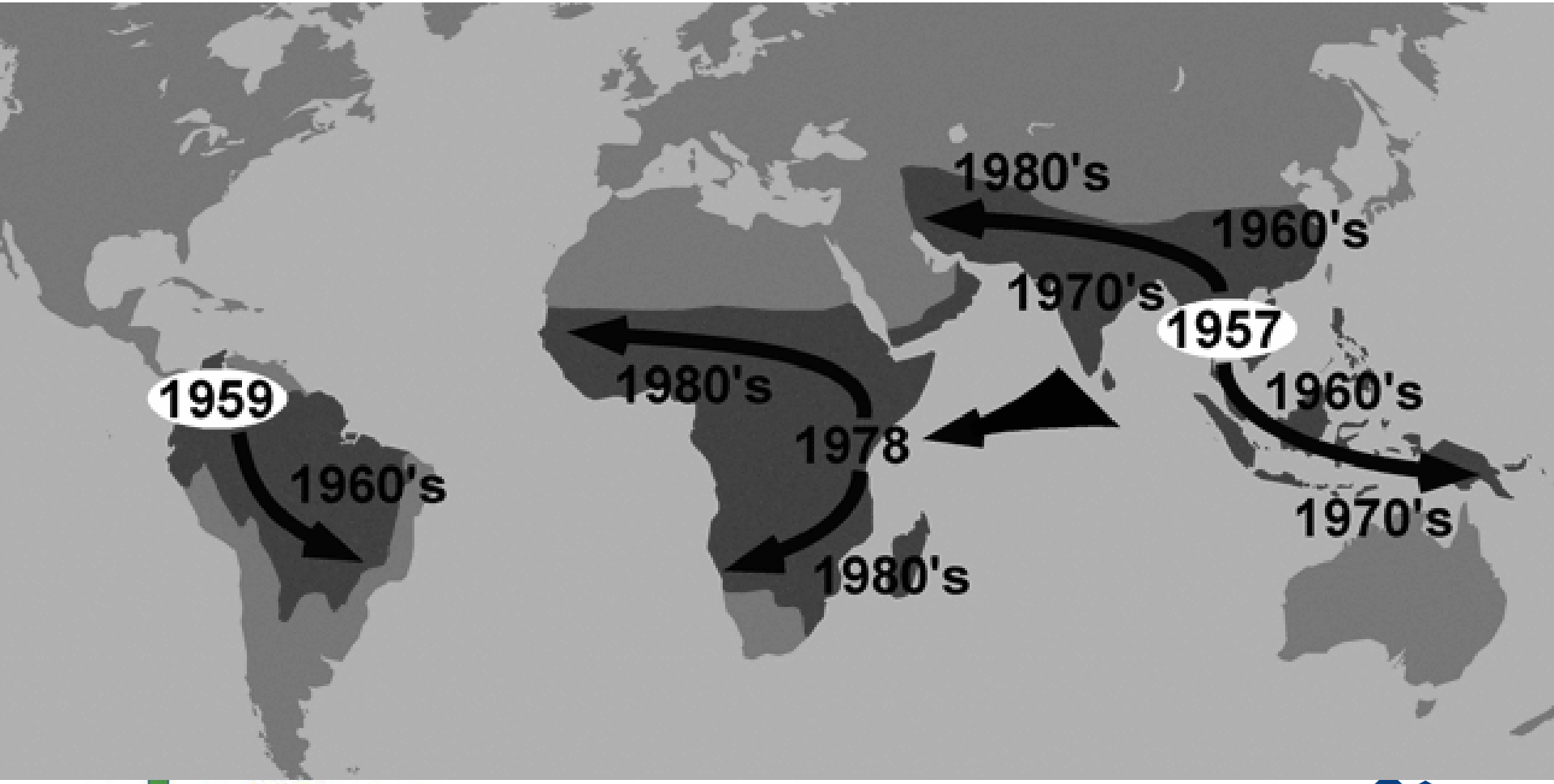
Global spread of chloroquine-resistant strains of *P. falciparum*



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Health Care Consequences

Higher Cost of Care

- Higher prescription cost of newer antibiotics
- Rising insurance premiums

Lower Quality of Care

- Increased risk of morbidity and mortality
- Each year 63,000 deaths attributed to drug resistance in hospital infections by CDC

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Difficulty in Measuring Burden of Resistance

- Resistance-related hospitalizations are not recorded
- Correlation between disease severity and colonization with resistant pathogen
- Not all antibiotic use is bad

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Why is resistance increasing?

Factors internal to the health care system

- Overuse and inappropriate use (for instance, to treat viral infections)
- Sicker patients and longer hospital stays
- Inadequate infection control in hospital settings
- Insufficient treatment compliance
- Widespread use of broad spectrum agents

Factors external to the health care system

- Use in poultry and cattle feed as growth promoters
- Spread of drug resistance from other countries

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What are the incentives to protect antibiotic effectiveness?

Those who use (or manufacture) antibiotics may not have sufficient incentives to consider the impact (cost) of this usage on the rest of society

- Incentives for patients
- Incentives for physicians
- Incentives for hospitals
- Incentives for pharmaceutical companies
- Government?

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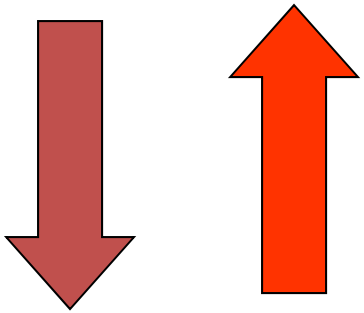
Dealing with resistance

Make better use of existing drugs



Find new drugs

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Incentives for Physicians

- Satisfying patient expectations

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TABLE 5

Frequency of Antibiotic Prescribing by Factors Related to Patients' Expectations of Antibiotics (N = 482)

Factor	No.* (%)	Antibiotic Prescribed No. (%)	OR (95% CI)
Patient expects antibiotic			
Yes	290 (60)	213 (73)	2.6 (1.7-3.9)
No	150 (31)	78 (52)	reference
No answer	42 (9)	28 (67)	
Clinician believes patient expects an antibiotic			
Yes	298 (62)	236 (79)	4.7 (3.2-7.1)
No	182 (38)	81 (45)	reference
No answer	2 (<1)	2 (100)	
Antibiotic helped similar illness in the past			
Yes	284 (59)	212 (75)	4.5 (2.9-6.9)
No	170 (35)	88 (52)	reference
Don't know	19 (4)	12 (63)	
No answer	9 (2)	5 (56)	

NOTE: Because some questions were unanswered, the numbers may not add up to 482.
*In outpatients with nonspecific upper respiratory infections, acute bronchitis, or acute sinusitis.
OR denotes odds ratio; CI, confidence interval.

Dosh, J
Fam Pr 1999

Incentives for Physicians

- Satisfying patient expectations
- Financial (reimbursement) incentives
  - Substitute for repeat visit
- Malpractice liability

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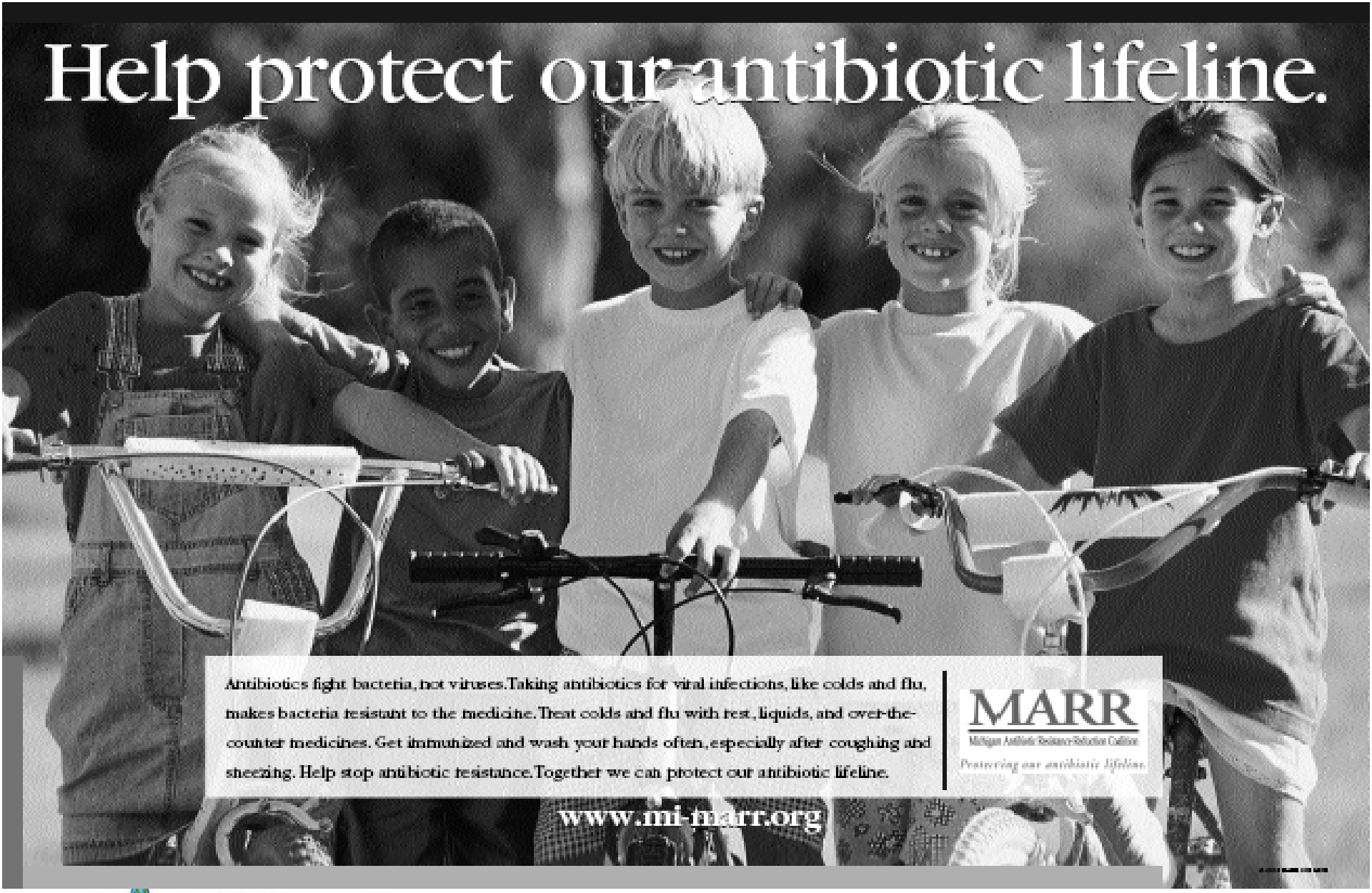

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Campaign to Prevent Antimicrobial Resistance

Centers for Disease Control and Prevention
National Center for Infectious Diseases
Division of Healthcare Quality Promotion

Clinicians hold the solution!

- *Link to: Campaign to Prevent Antimicrobial Resistance Online*
- *Link to: Federal Action Plan to Combat Antimicrobial Resistance*

CDC
Centers for Disease Control and Prevention

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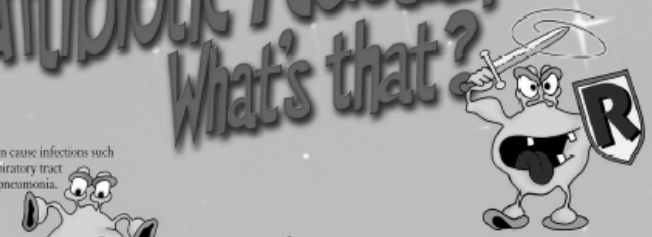
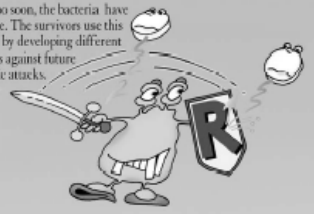
Antibiotic resistance: What's that?



Bacteria often cause infections such as urinary tract or respiratory tract infections, e.g. pneumonia.

Fortunately, there are antibiotics which are usually able to fight these bacteria reliably.

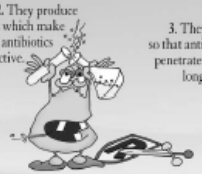
However, bacteria know how to resist antibiotics. Especially when the dose of the antibiotic is too small or treatment is discontinued too soon, the bacteria have the chance to survive. The survivors use this immediately by developing different defence mechanisms against future antibiotic attacks.



Bacteria are tiny, but firmly set on survival.
They can develop four different ways to protect themselves against the deadly effect of antibiotics:

1. They change their vulnerable target, so that antibiotics are unable to find points of attack.

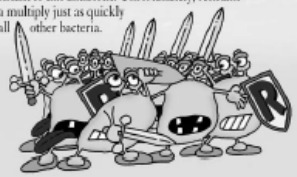
2. They produce enzymes which make certain antibiotics ineffective.



3. They change their outer shell, so that antibiotics cannot penetrate any longer.

4. They simply pump already penetrated antibiotics out again.

If bacteria can repel the attack of an antibiotic by these mechanisms, then they have become resistant to this antibiotic. Unfortunately, resistant bacteria multiply just as quickly as do all other bacteria.



Resistant bacteria can be dangerous. Since certain antibiotics can no longer do them any harm, a simple infection can quickly turn into an illness that is difficult to treat. For this reason it is so important to prevent the emergence of resistance.

What can we do against resistance?

Patients can make an important contribution, by:
- not unnecessarily demanding antibiotics from their physician, e.g. to treat a common cold
- taking the antibiotic dose precisely as prescribed by the physician
- taking the prescribed dose regularly and completely - even if they quickly feel better again

Physicians can prevent the emergence of resistance, by:
- avoiding unnecessary prescription of antibiotics, e.g. for viral infections
- resisting unjustified demands by patients or parents for antibiotics
- prescribing suitable antibiotics which will work the fastest and best

Bayer AG supports physicians and patients through:
- supply of modern, efficient antibiotics
- the LIBRA initiative, which promotes the responsible use of antibiotics and which supports the fight against resistance development
- a broad information offer on this topic under www.librainitiative.com
- providing current data on resistance development - so-called Surveillance data - under www.librainitiative.com

LIBRA
Because our future needs effective antibiotics.

Bayer

Hospital Incentives

- Antibiotics may be a substitute for infection control

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Hospital Incentives

- Hospitals are “sources” for colonization with resistant pathogens
- Health facilities often “share” patients
- Positive external benefits of active surveillance and infection control

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Implications for policy

- Dutch experience: frequency of MRSA infections is < 0.5% after an intensive ‘‘search-and-destroy’’ campaign, compared with 50% in some areas
- In Siouxland (Iowa, Nebraska, S. Dakota), an epidemic of VRE was reversed
- Regionally coordinated response to epidemic

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Who pays for hospital-acquired infections?

- Medicare/Medicaid bear greatest burden of additional cost
- 76% of 11,668 HAIs in 2004 billed to federal Medicare ($1 billion cost)
- Rest to Medicaid ($372 million cost)
- $20 billion burden on Medicare nationwide

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Incentives for Pharma

- Example of Baytril
- Increasing patent scope for antibiotics
  - open access problem of drug effectiveness
  - welfare costs of monopoly power

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The Antibiotics Pipeline

Antibiotics are not a priority for pharmaceutical companies

- Less profitable than drugs for chronic diseases or lifestyle illnesses
- Focus on broad spectrum agents

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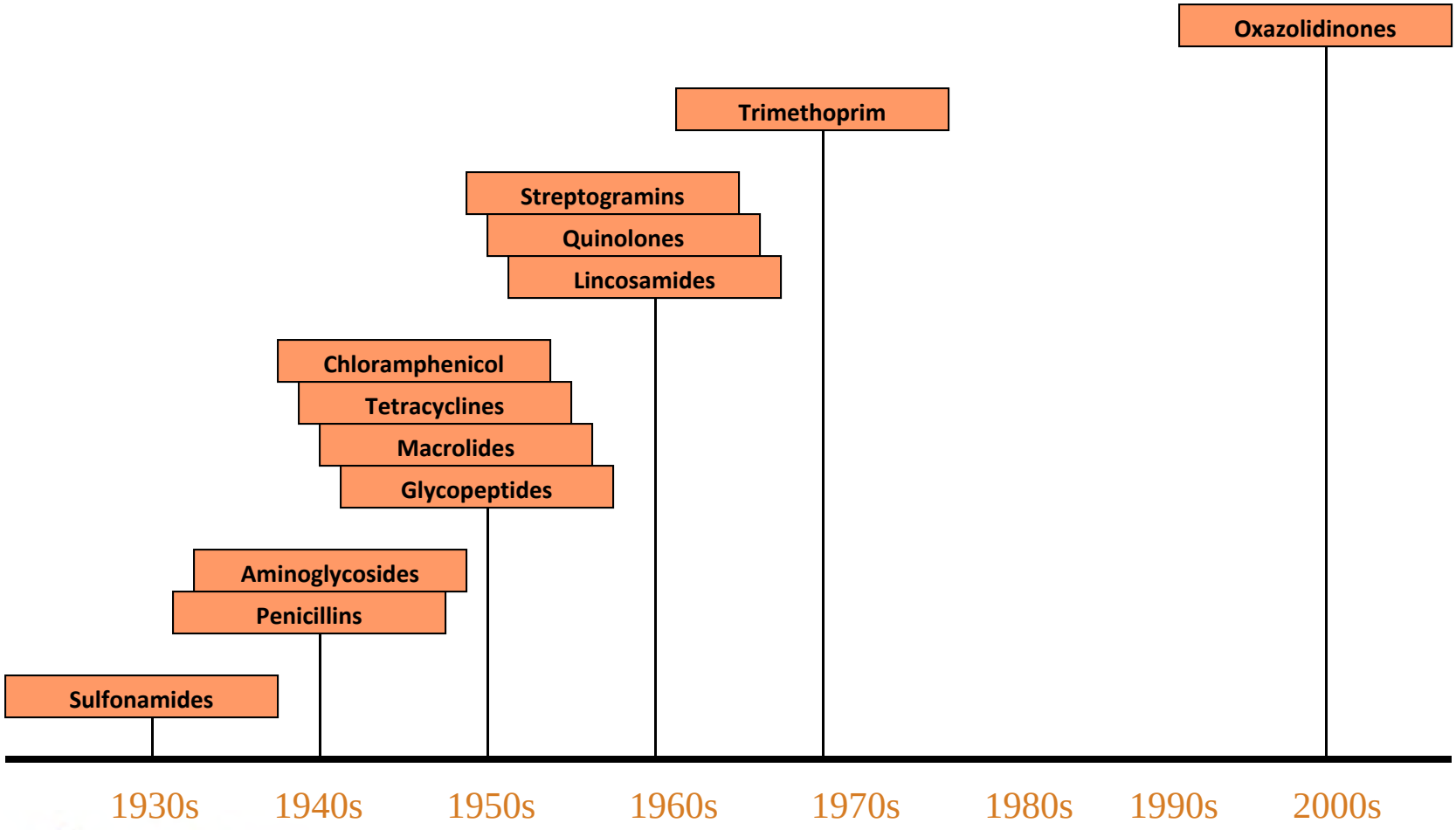
Discovery of new classes of antibiotics



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Role for Government: Vaccinations

- Pnemococcal vaccinations
- Invest in R & D for a MRSA vaccine

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Role for Government: Infection Control

- Require hospital reporting of infections and resistance
- Medicare reimbursement for HAIs
- Regional cooperation in infection control

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Role for Government: Infection Control

- Invest in national surveillance
- Exercise regulatory oversight

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Challenges in developing countries

- Rising incomes – greater access to antibiotics

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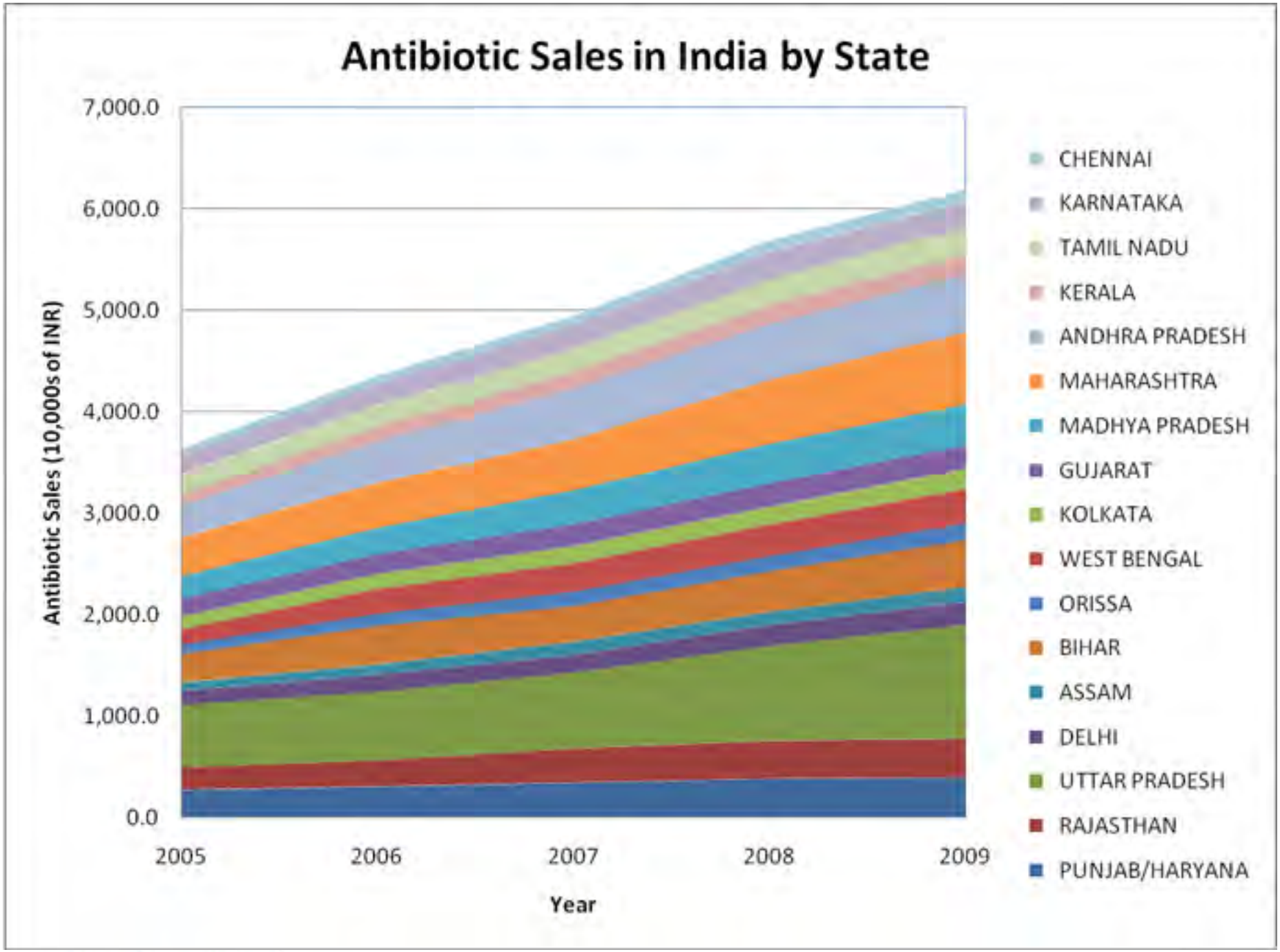
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Antibiotic Sales (10,000s of INR)
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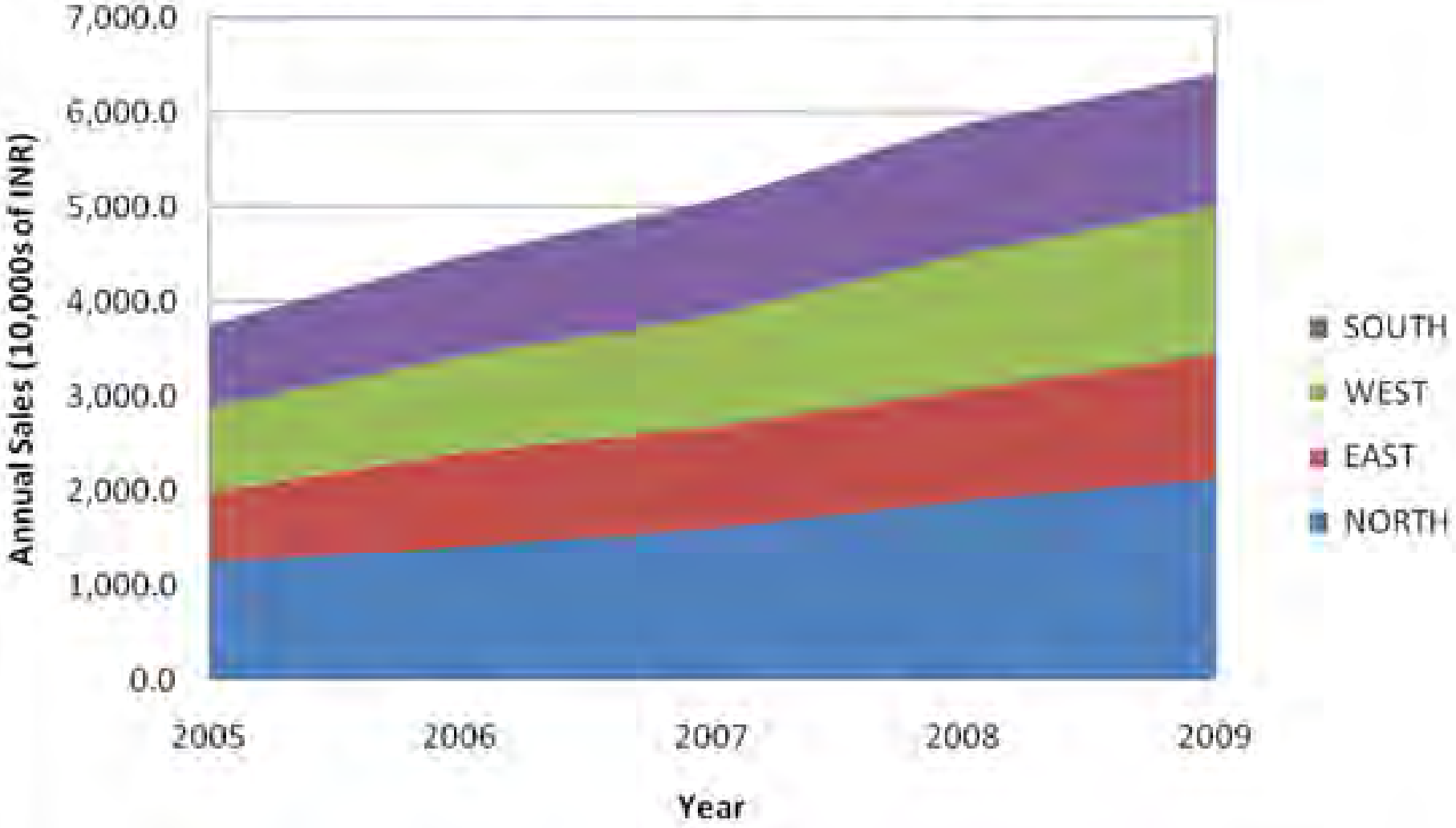
KARNATAKA
TAMIL NADU
KERALA
ANDHRA PRADESH
MAHARASHTRA
MADHYA PRADESH
GUJARAT
KOLKATA
WEST BENGAL
ORISSA
BIHAR
ASSAM
DELHI
UTTAR PRADESH
RAJASTHAN
PUNJAB/HARYANA

Antibiotic Sales in India by Region



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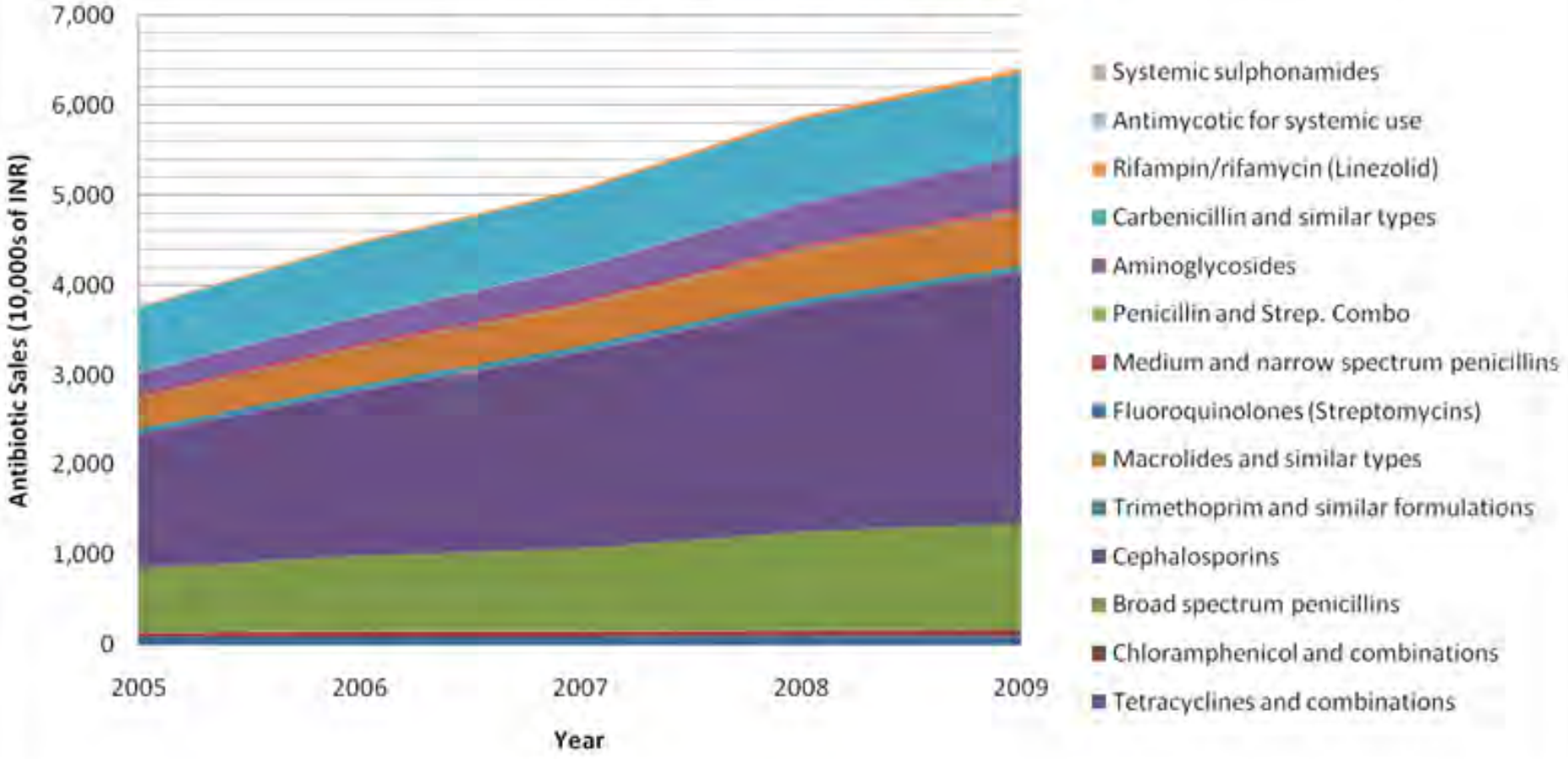
Antibiotic Sales in India by Type



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Challenges in developing countries

- Rising incomes – greater access to antibiotics
- Yet many patients do not have access to effective antibiotics
- Counterfeit or expired antibiotics
- Second line drugs may be unaffordable to many low-income families
- Burden of infectious disease including pneumococcal disease

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