Economic Aspects of Disease Epidemiology

Ramanan Laxminarayan
Resources for the Future

Economic Epidemiology

Mathematical conceptualization of the interplay between economics, human behavior and disease ecology to improve our understanding of

- the emergence, persistence and spread of infectious agents
- optimal strategies and policies to control their spread

Overview

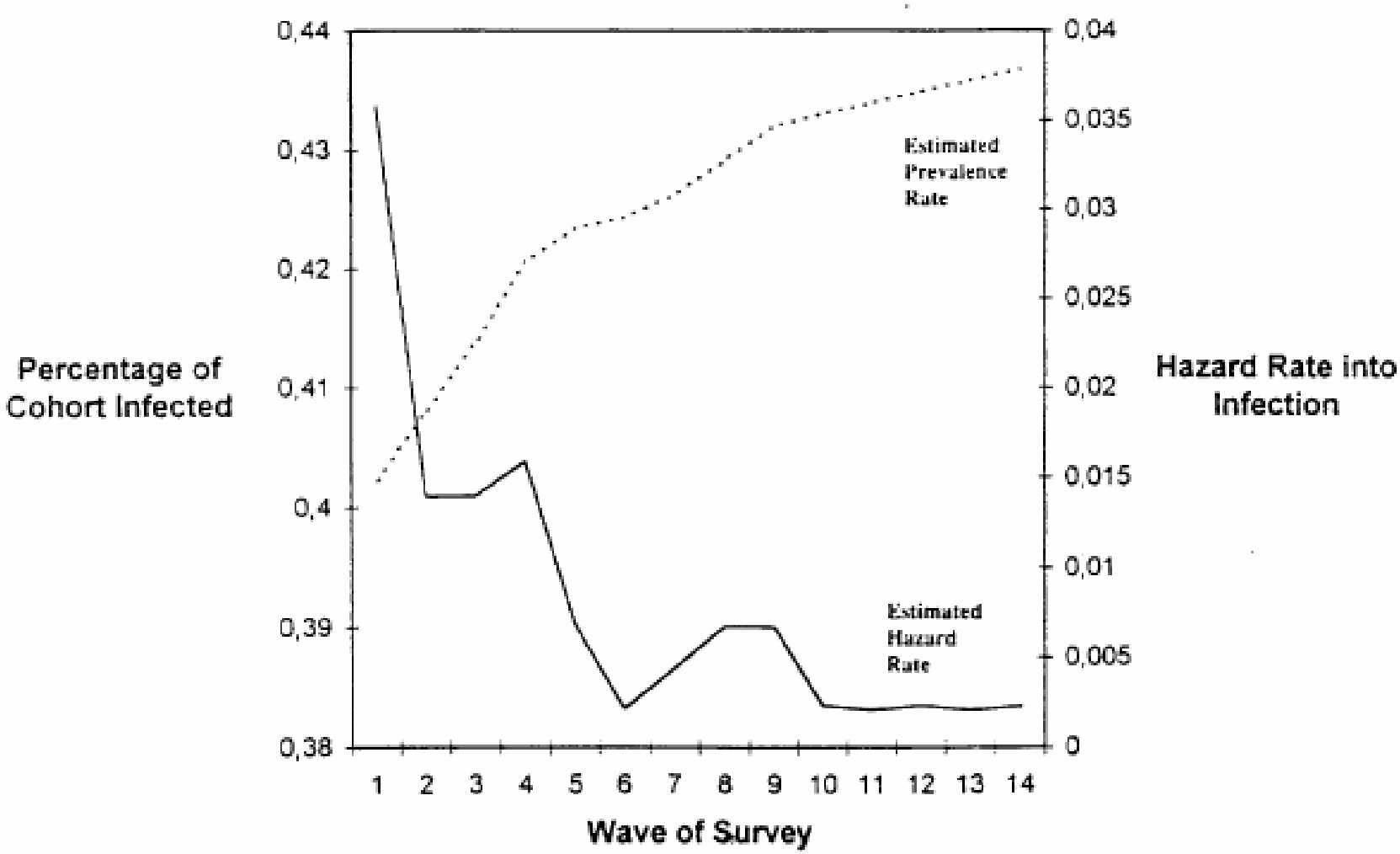
- Individual response and disease
- Incentives of institutions (to invest in hospital infection control)
- Malaria subsidy

Individual response and disease

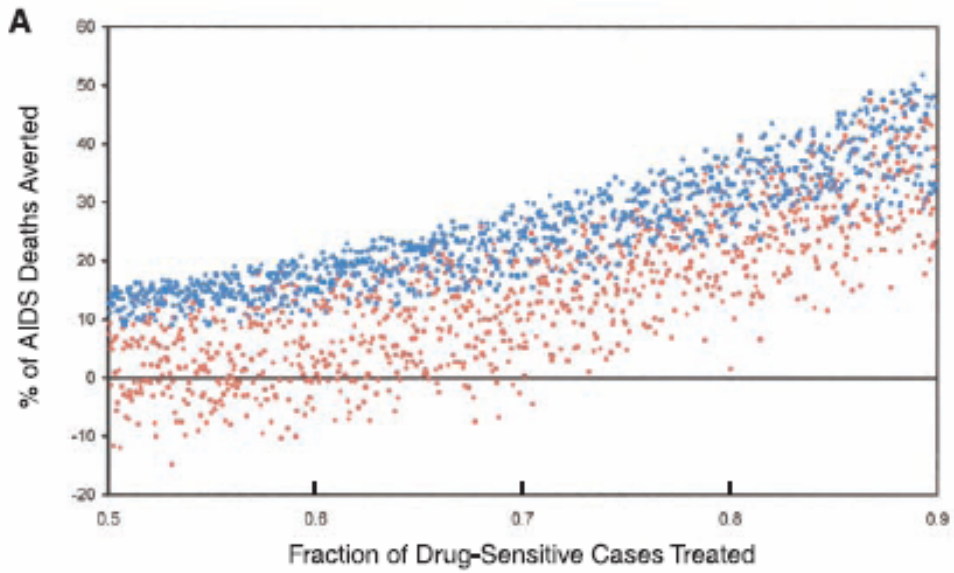
- Vaccinations
  - Insufficient incentives to vaccinate prevent attainment of herd immunity thresholds
- Drug resistance
  - Insufficient incentives to make appropriate use leads to ineffective drugs and increasing prevalence
- Testing
  - Private testing behavior adds to public information on disease prevalence

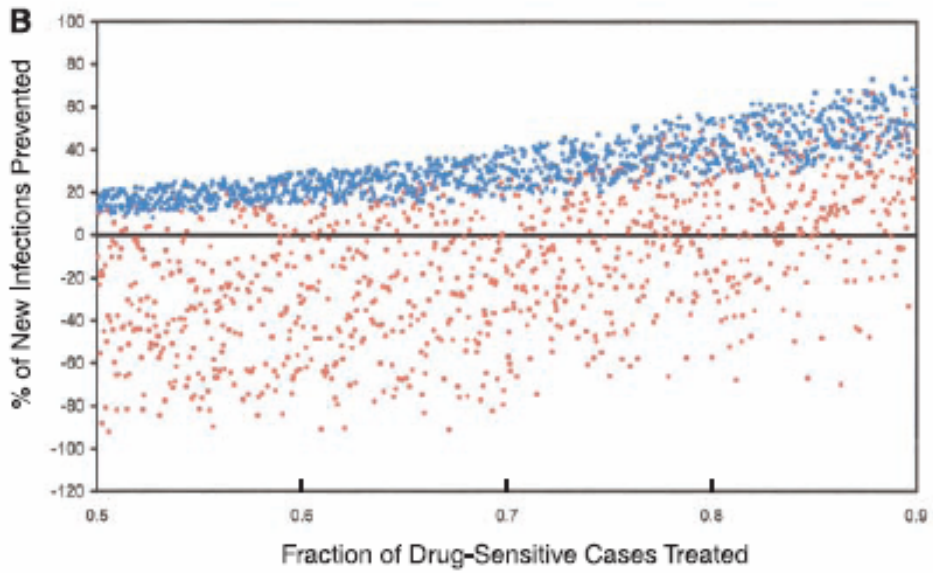
Rational epidemics

- Prevalence response elasticity
  - Hazard rate into infection of susceptibles is a decreasing function of prevalence (opposite of epidemiological model predictions)
  - Application to HIV
  - Application to Measles

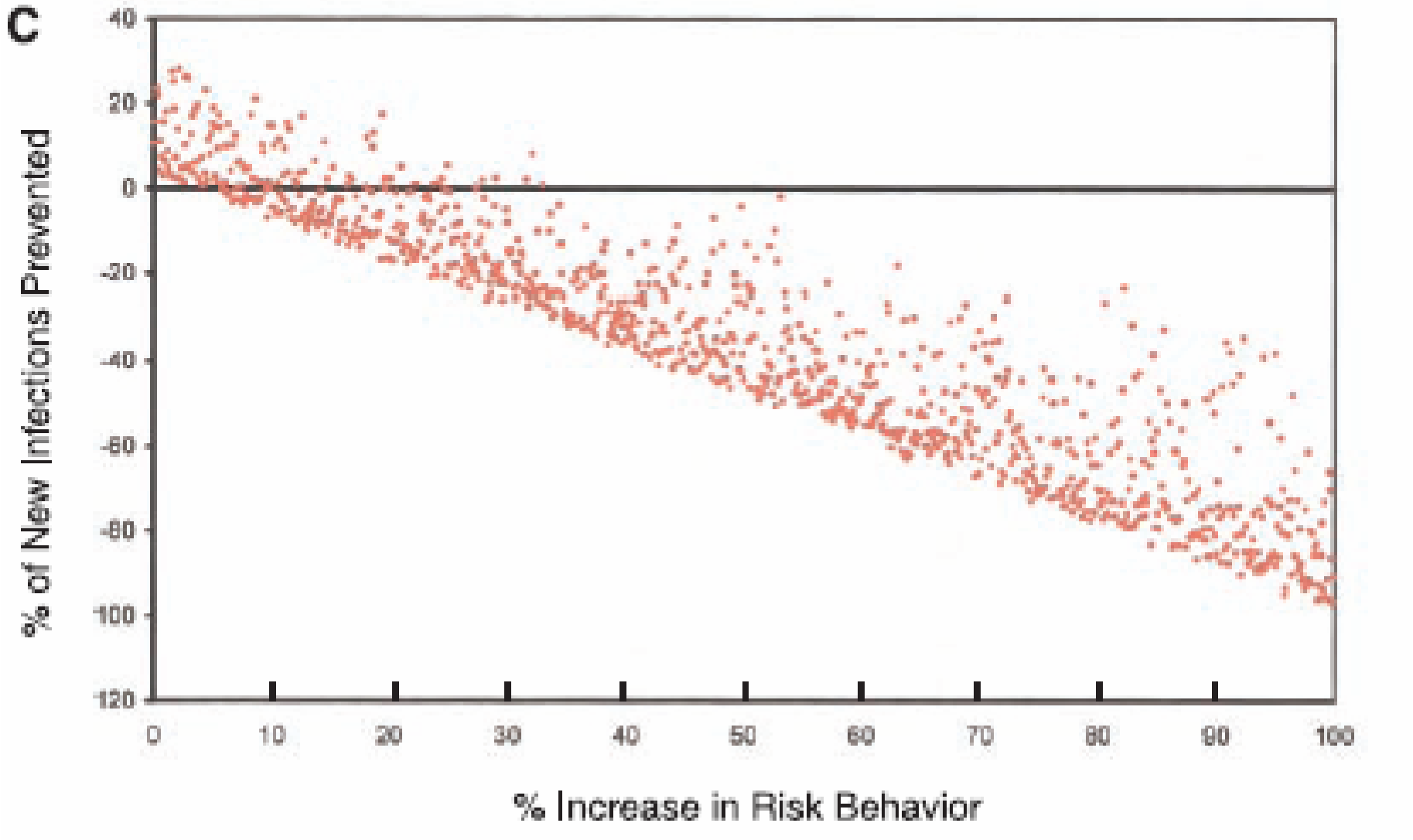


Geoffard and Philipson, Int. Econ. Rev., 1996





Blower et al, Science, 2000



Blower et al, Science, 2000

When should governments intervene?

- Disease prevalence increases adoption of public programs
- Impact of public program may be zero if prevalence has already reached an individual's threshold prevalence
- Paradoxically, the role of government subsidies is lowest when prevalence is highest since individuals will protect themselves regardless

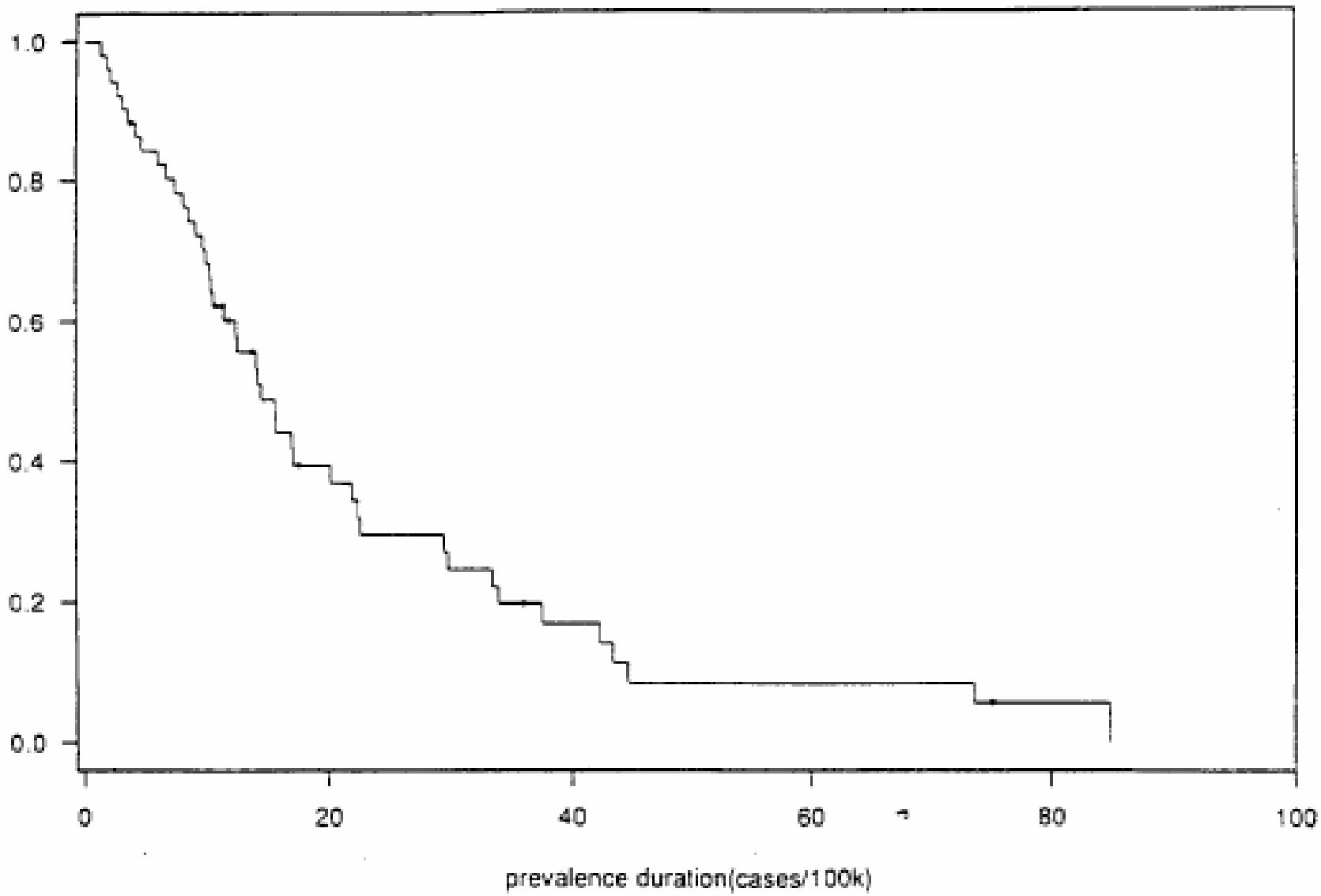


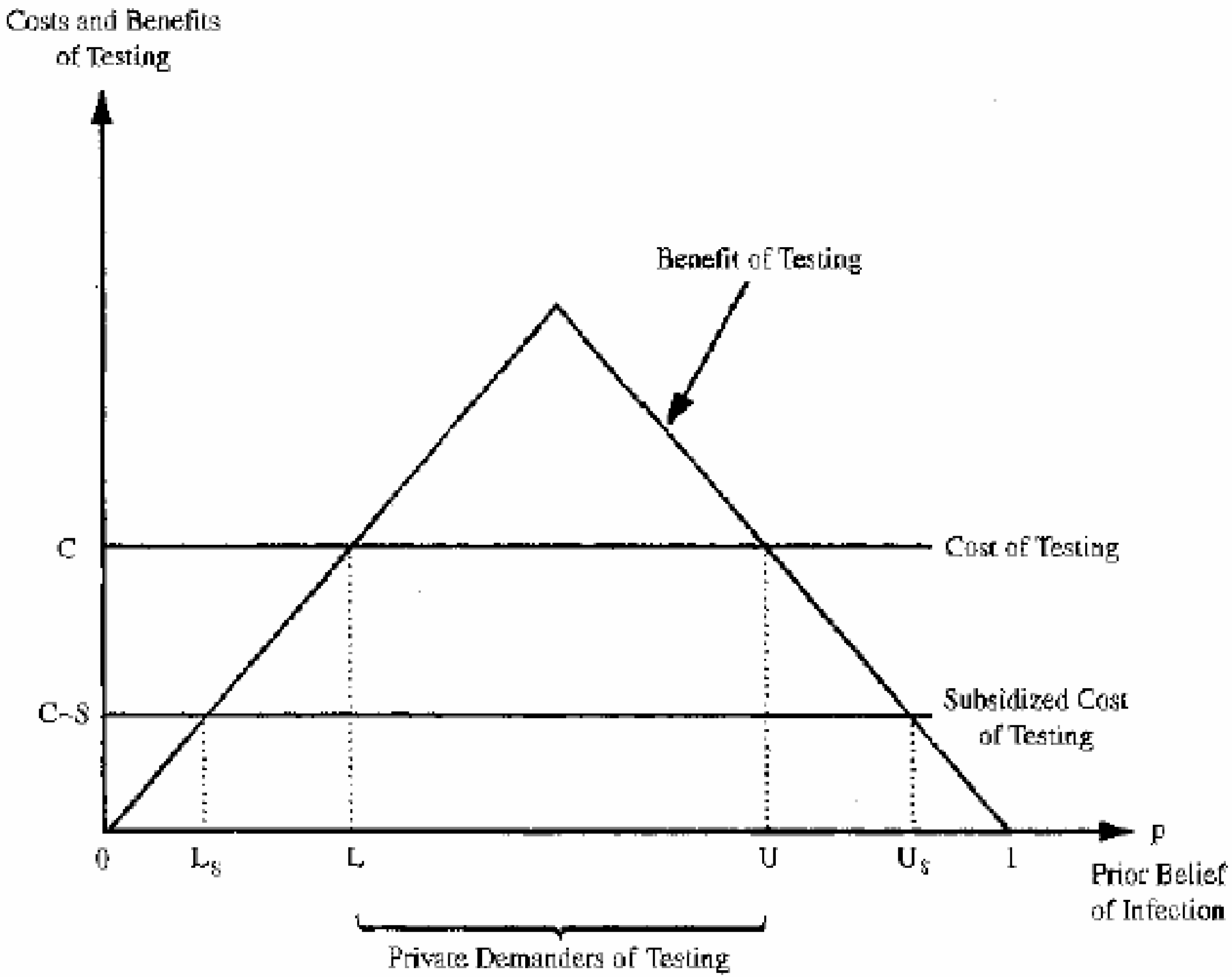
FIGURE 3: Survival in State Government Spending

Philipson, NBER, 1999

Public price subsidies

- Can price subsidies or mandatory programs achieve eradication?
  - Increase in demand by folks covered by the program lowers the incentives to vaccinate for those outside the program
- Do monopolistic vaccine manufacturers have an incentive to eradicate disease?
  - Market for their product would disappear with eradication

Geoffard and Philipson, Int Econ Rev, 1997


Costs and Benefits of Testing
Benefit of Testing
C
Cost of Testing
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0
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U_S
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Prior Belief of Infection
Private Demanders of Testing

Disease Complementarities

- Incentive to invest in prevention against one cause of death depends positively on probability of dying from other causes
- Intervening to prevent mortality not only prevents a death but also increases incentives for the family to fight other diseases

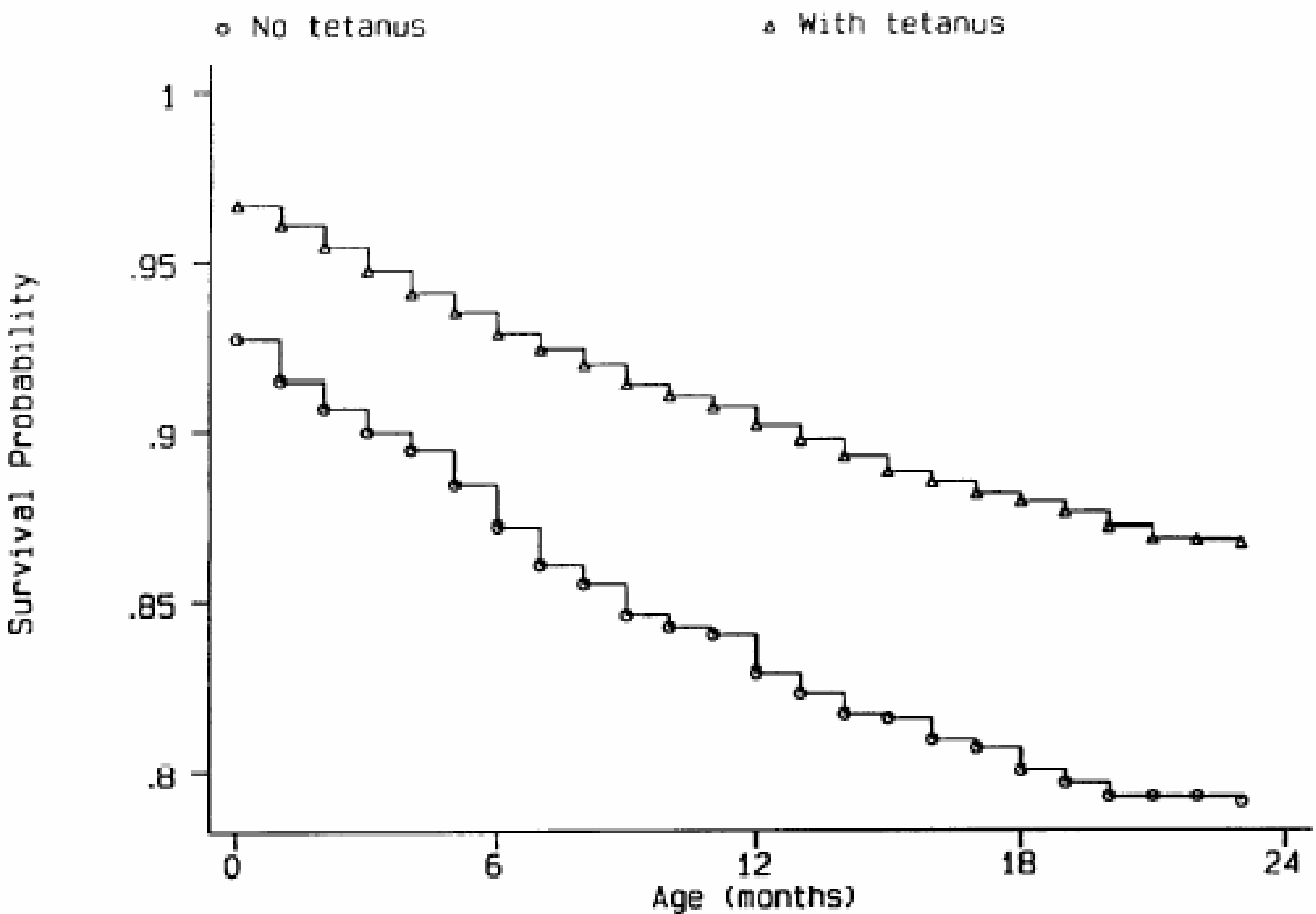
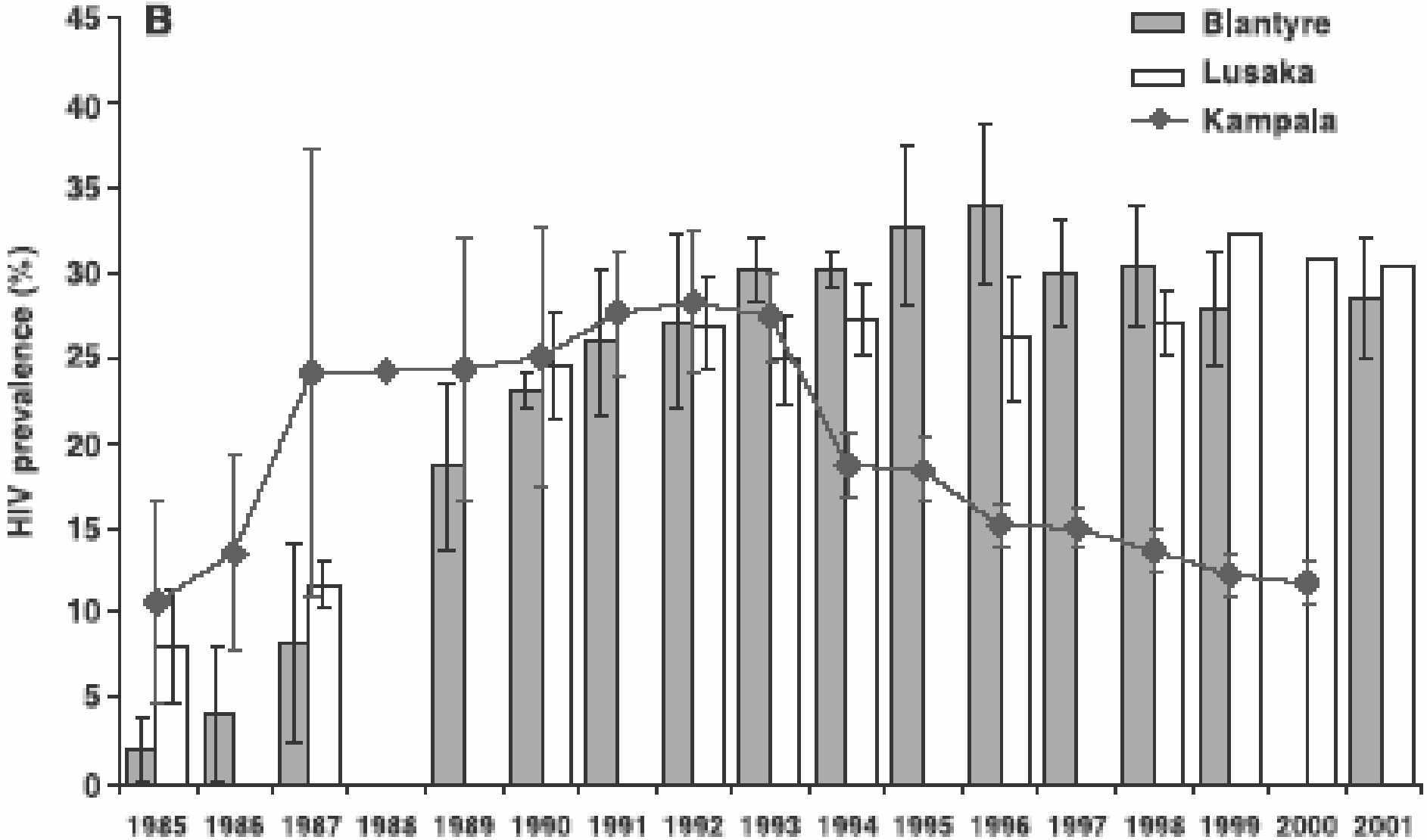


FIGURE 1: Kaplan-Meier Survival Curve to Age 2

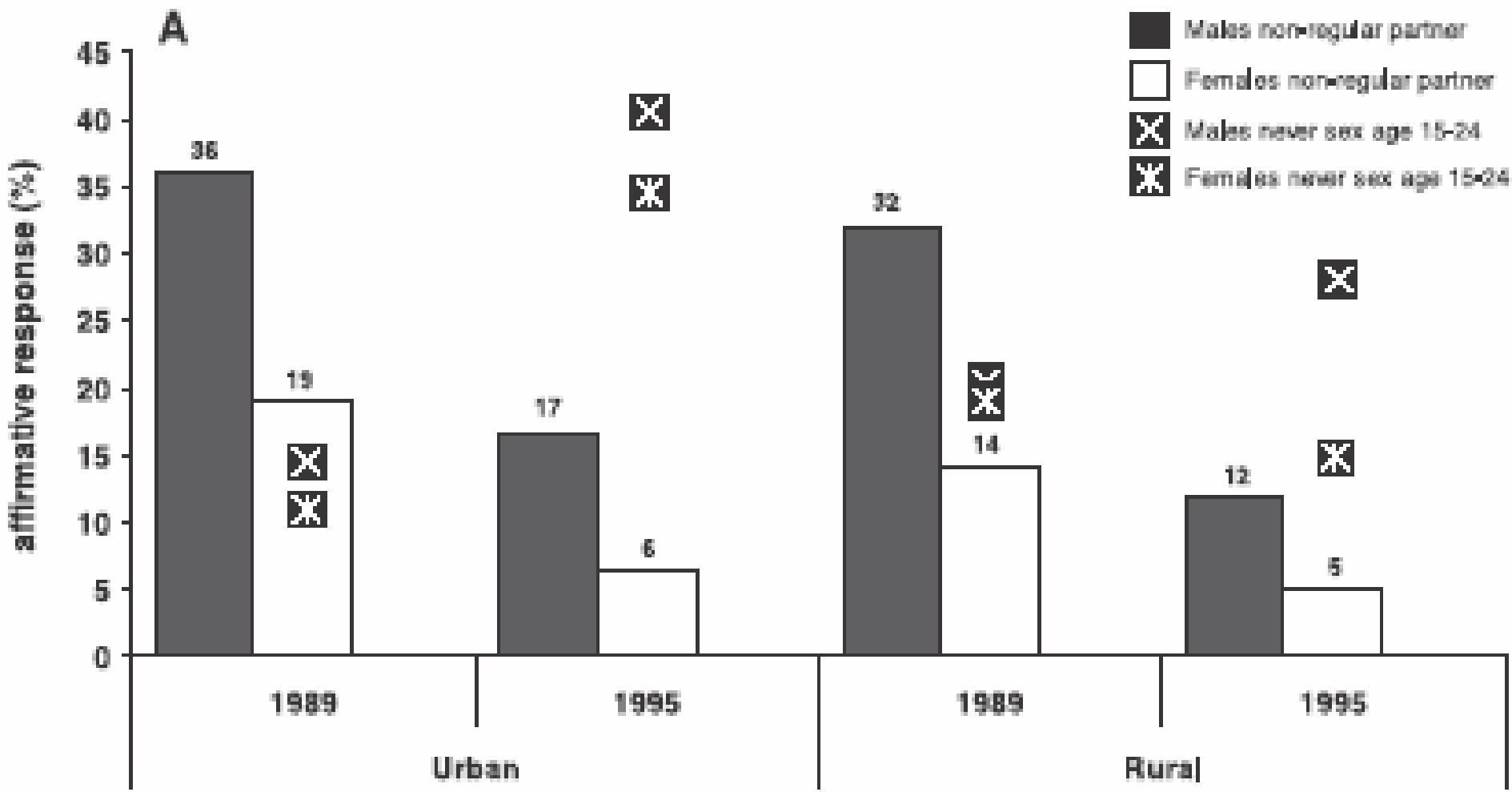
Dow et al, Am Econ Rev, 1999

Does the theory fit the facts?

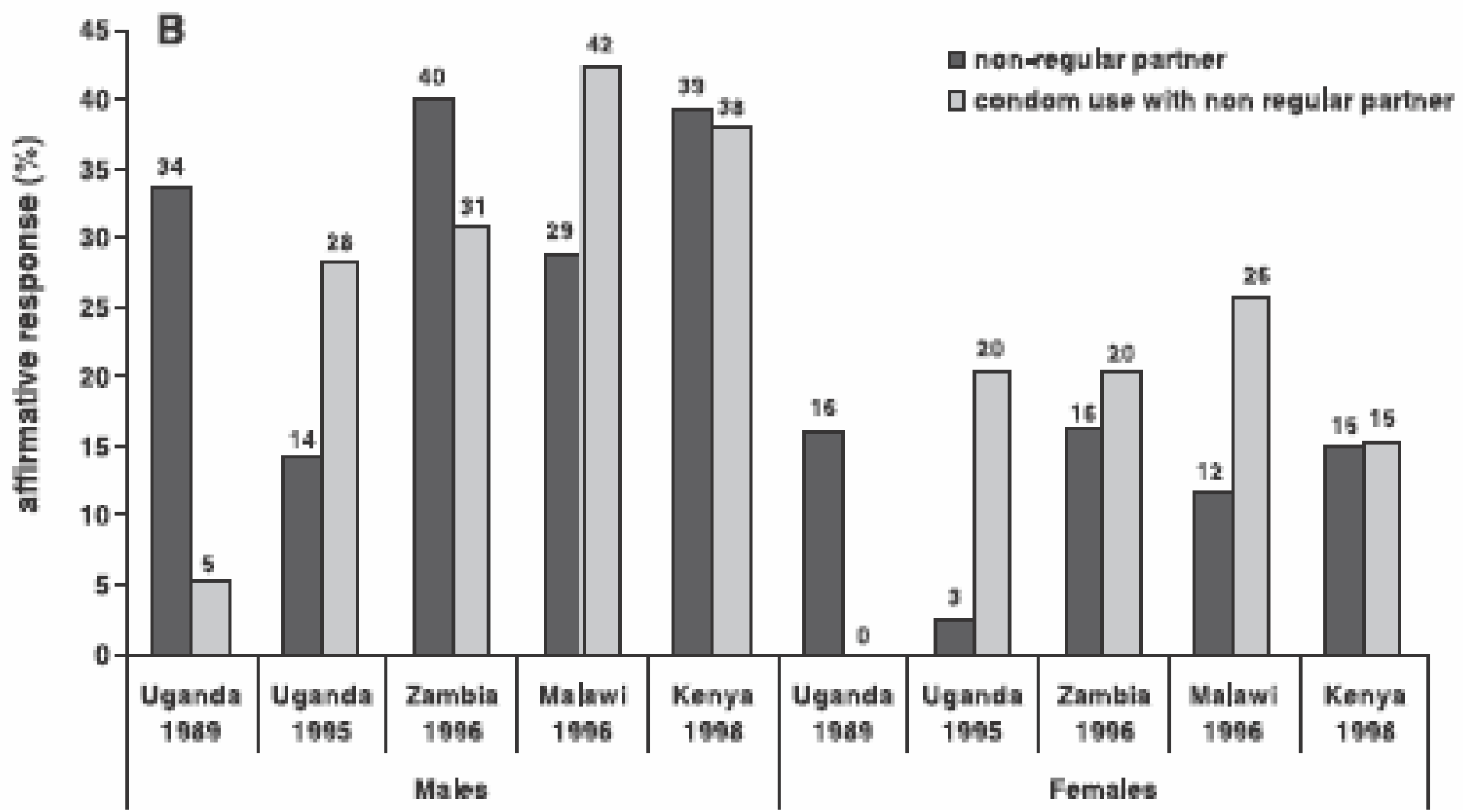
- Do individuals actually observe prevalence?
- Why don’t we see prevalence responsiveness at work everywhere?
- Importance of observational learning (herd behavior)?



Stoneburner and Low-Beer, Science, 2004



Stoneburner and Low-Beer, Science, 2004



Stoneburner and Low-Beer, Science, 2004

THE BRITISH JOURNAL

OF

EXPERIMENTAL

PATHOLOGY

VOLUME TEN

1929

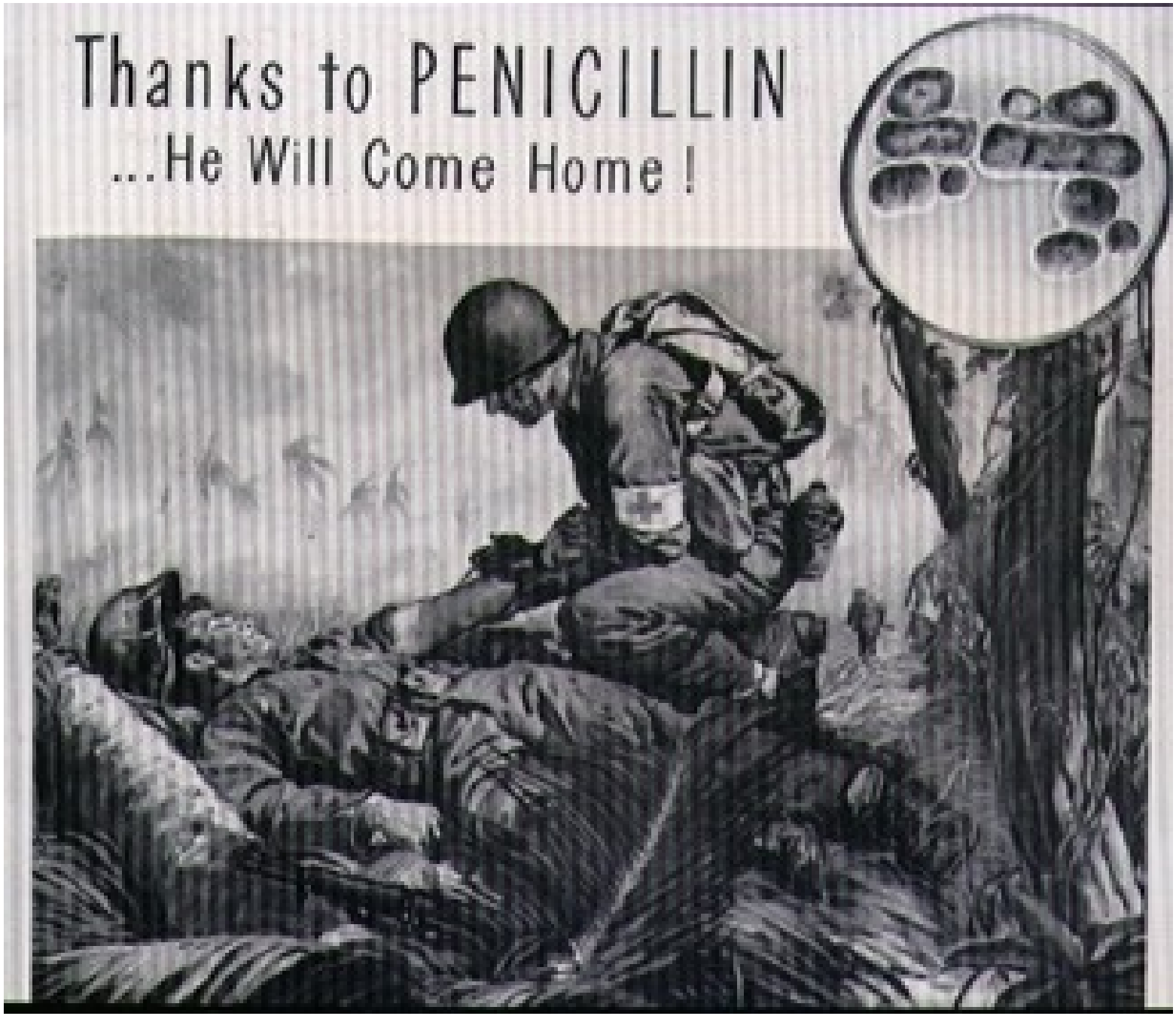
Reproduced from pages 226–236.

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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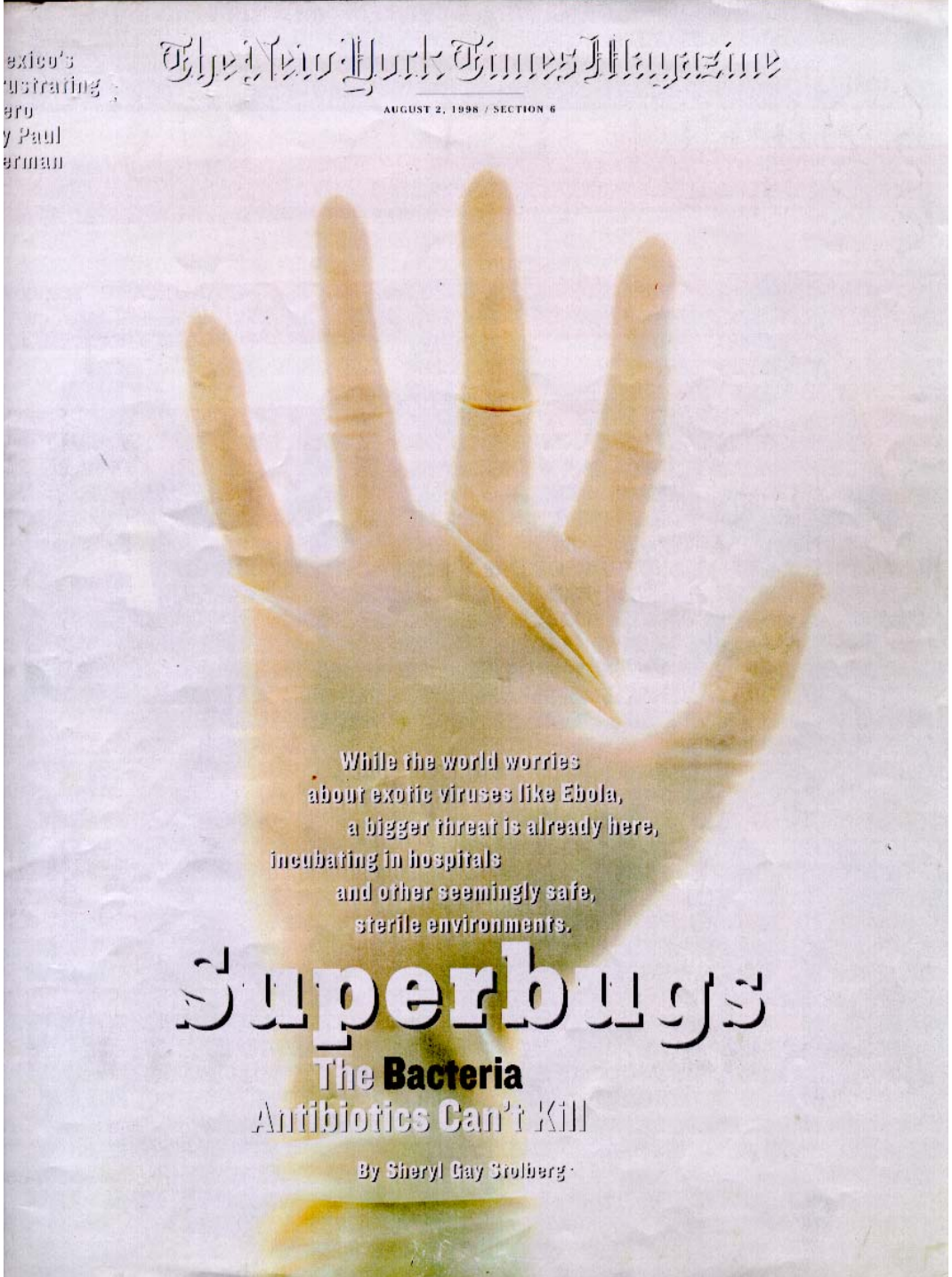
The New York Times Magazine

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

START | infoporn

The Bug Wars

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

Infectious diseases give us a stunning demonstration of evolution in action: The fittest 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 medicines like penicillin, tetracycline, and ciprofloxacin. So scientists are 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 antibiotic out. (Bacteria like staph and strep fended off tetracyclines this way.)

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

HOW FAST BACTERIA EVOLVE TO THWART DRUGS

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.

- **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, heralding the era of the "superbug."
- **Staph resists vancomycin** – The drug of last resort, the one deployed when others failed, is finally defeated.
- **Staph resists linezolid** – The first new class of antibiotic in 35 years loses its firepower within a year.

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.

- Strep resists penicillin
- Strep resists lincomycin
- Strep resists tetracycline
- Strep resists chloramphenicol
- Strep resists cephalosporin
- Strep resists erythromycin
- Strep resists ciprofloxacin
- Strep resists levofloxacin

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

- E. coli resists tetracycline
- E. coli resists chloramphenicol
- E. coli resists streptomycin
- E. coli resists trimethoprim-sulfamethoxazole
- E. coli resists ampicillin
- E. coli resists fluoroquinolones
- E. coli resists cephalosporin
- E. coli resists ciprofloxacin

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.

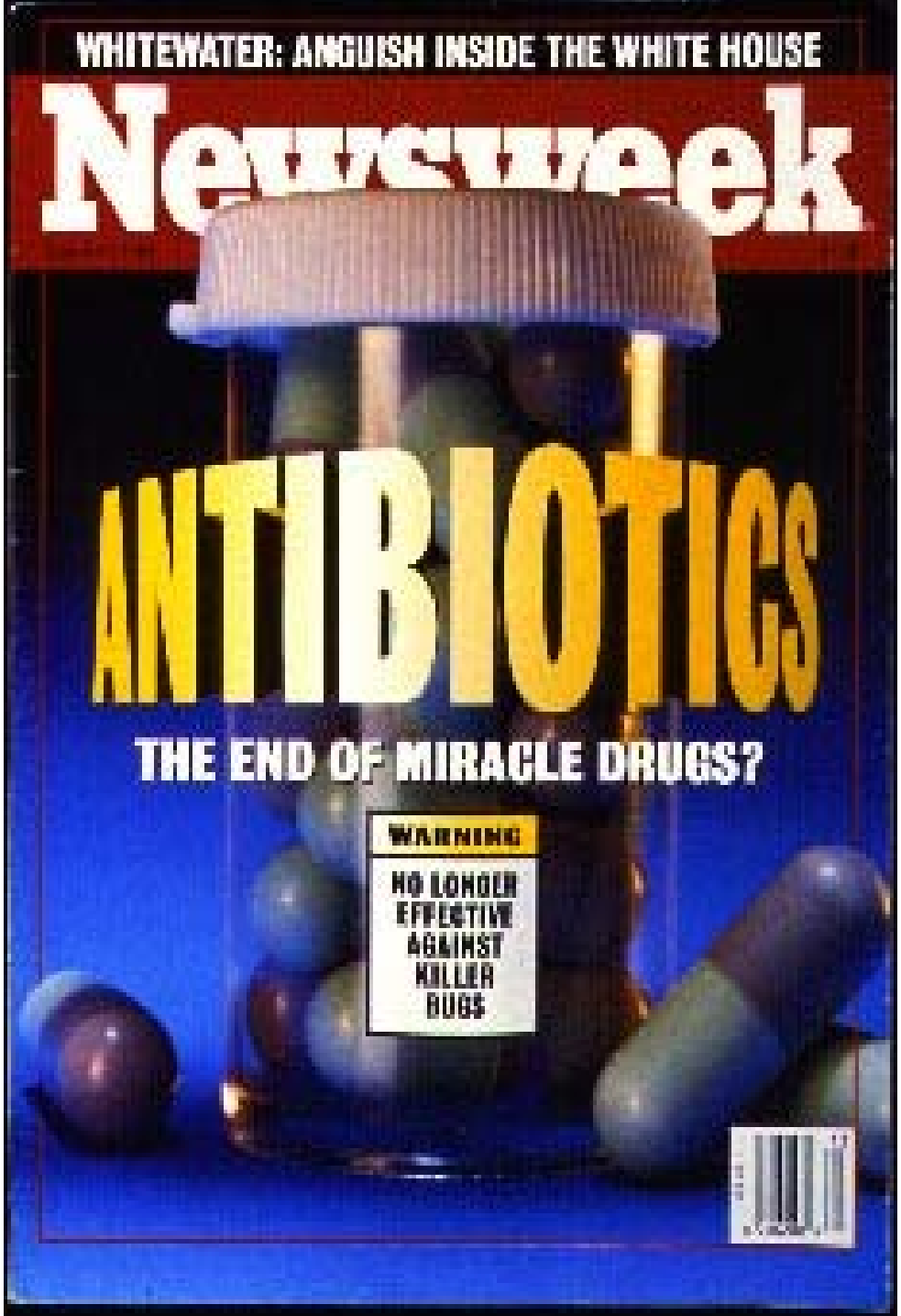
- Penicillin
- Streptomycin
- Chloramphenicol
- Tetracycline
- Erythromycin
- Lincomycin
- Methicillin
- Ampicillin
- Cephalosporin
- Vancomycin
- Trimethoprim-sulfamethoxazole
- Fluoroquinolone
- Ciprofloxacin
- Levofloxacin
- Linezolid
- Tigecycline

1940 · 1945 · 1950 · 1955 · 1960 · 1965 · 1970 · 1975 · 1980 · 1985 · 1990 · 1995 · 2000 · 2005

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

WHITEWATER: ANGUISH INSIDE THE WHITE HOUSE

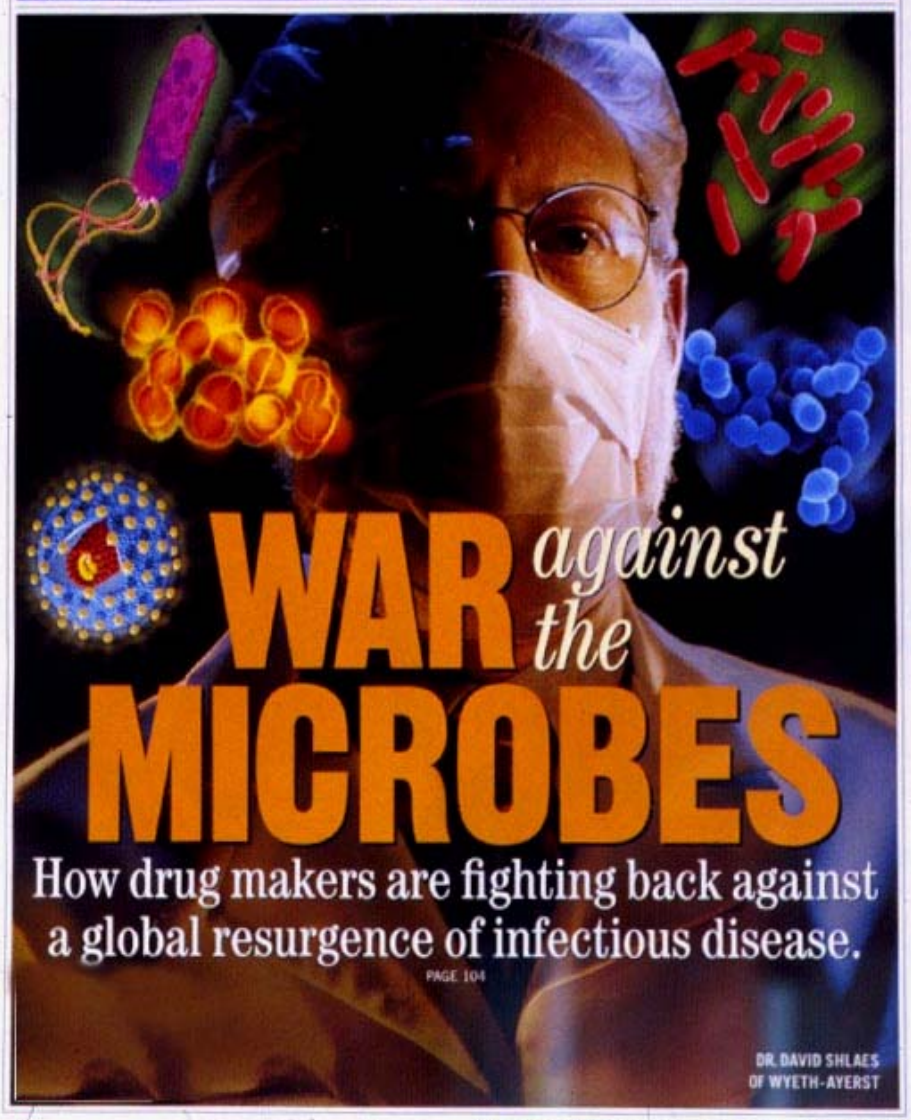
Newsweek



SPECIAL REPORT TELECOM'S POWER PLAYERS **INVESTING** MUTUAL FUNDS: 1ST QUARTER STARS

BusinessWeek

APRIL 6, 1998 A PUBLICATION OF THE McGRAW-HILL COMPANIES $3.95



WAR *against the* MICROBES

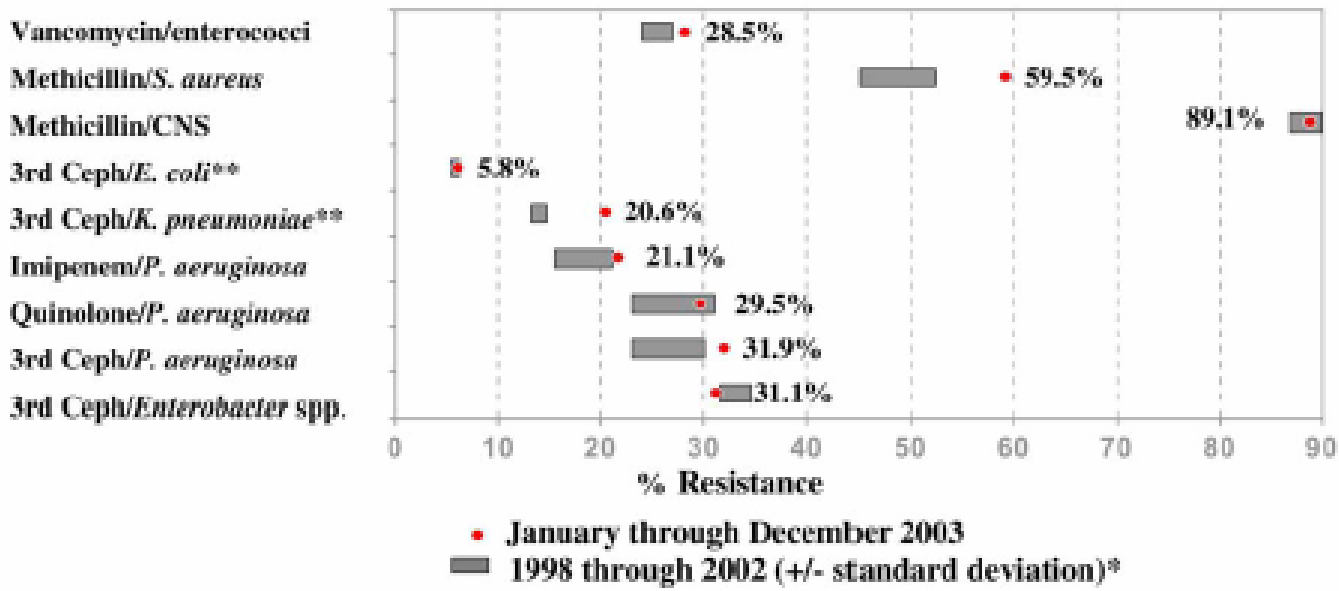
How drug makers are fighting back against a global resurgence of infectious disease.

PAGE 104

DR. DAVID SHLAES OF WYETH-AYERST

Internet: www.businessweek.com America Online: Keyword: BW


COSMOPOLITAN
November 1995
At Last! Something Pleasurable That's Good for You.
The Health Benefits of Sex
The Heart-Pounding Bawdiness of Brad Pitt, Who Couldn't Care Less
Why Marry Instead of Just Fooling Around?
Cosmo's Update on Antibiotics. What's Okay and What's Dangerous
$2.95
Makeup Tricks



Jan–Dec 2003 No. of Isolates	% increase in resistance (2003 vs 98-02*)
2048	12%
4100	11%
3336	1%
1355	0%
1068	47%
1392	15%
1825	9%
2119	20%
1411	–6%

Fig 1. Selected antimicrobial-resistant pathogens associated with nosocomial infections in ICU patients, comparison of resistance rates from January through December 2003 with 1998 through 2002, NNIS System. *CNS*, Coagulase-negative staphylococci; *3rd Ceph*, resistance to 3rd generation cephalosporins (either ceftriaxone, cefotaxime, or ceftazidime); *Quinolone*, resistance to either ciprofoxacin or ofloxacin. *Percent (%) increase in resistance rate of current year (January-December 2003) compared with mean rate of resistance over previous 5 years (1998-2002): [(2003 rate – previous 5-year mean rate)/previous 5-year mean rate] × 100. **"Resistance" for *E coli* or *K pneumoniae* is the rate of nonsusceptibility of these organisms to either 3rd Ceph group or aztreonam.

NNIS Data, 2004

Optimal infection control

Infection dynamics are given by

$$\dot{X} = \beta(c)X(1-X) - \sigma(X-\kappa)$$

Equilibrium prevalence is given by

$$\bar{X}(c) = \frac{S(c)-1+\sqrt{(S(c)-1)^2+4\kappa S(c)}}{2S(c)}$$

Smith, Levin, Laxminarayan (PNAS, 2005)

Objective

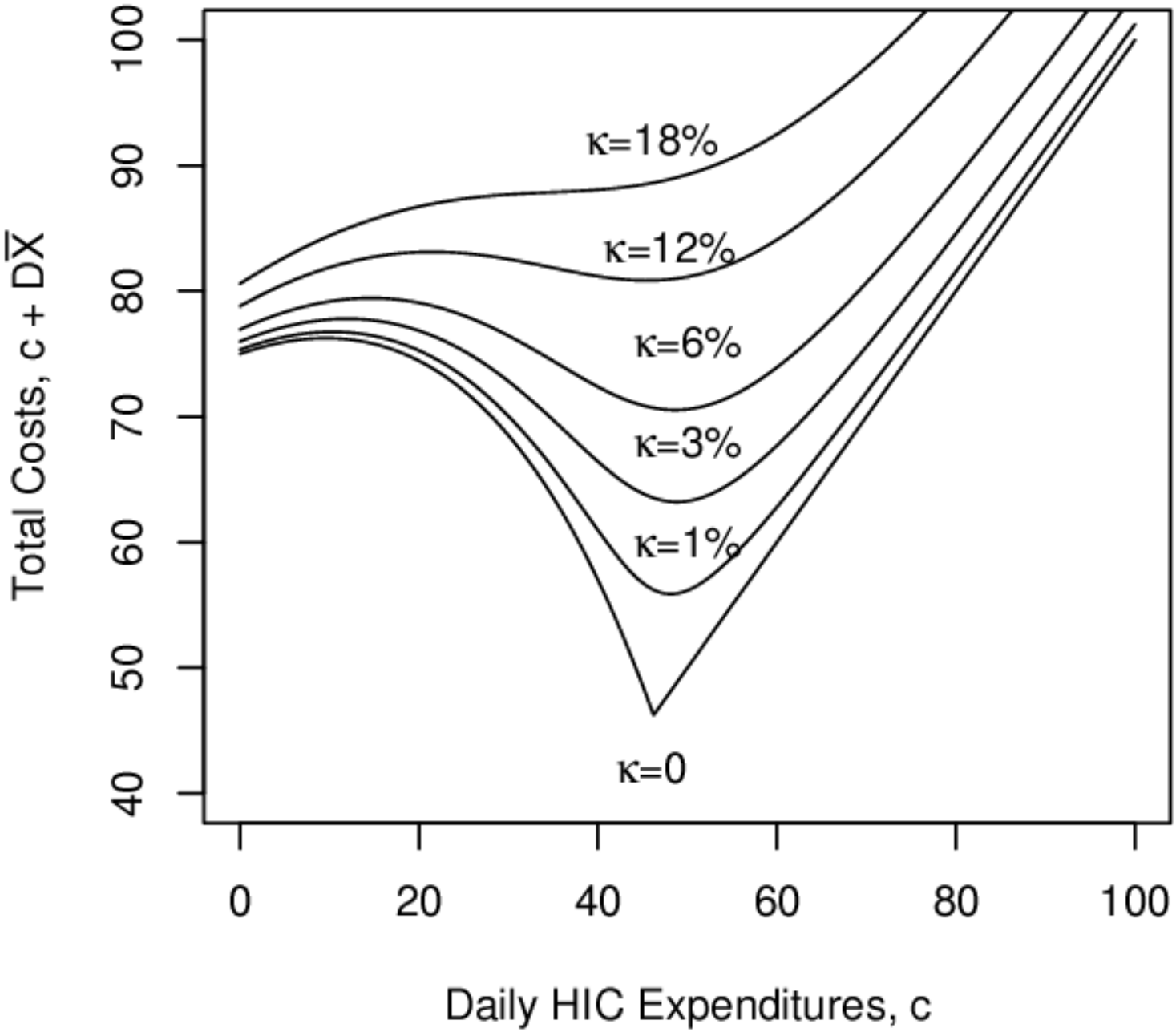
Minimize costs of infection control and infections

$$c + D\bar{X}(c)$$

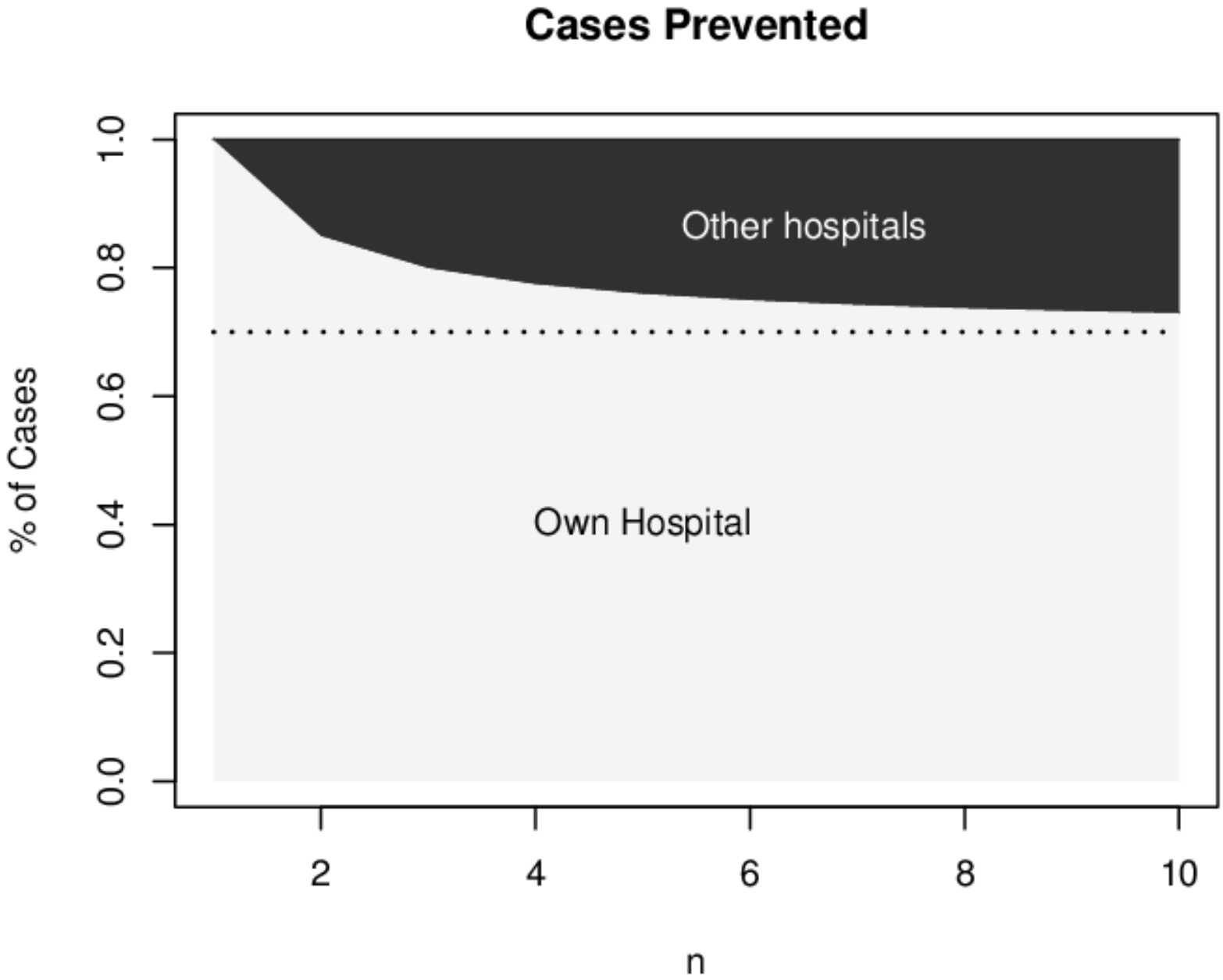
Local minima, if they exist, are solutions to

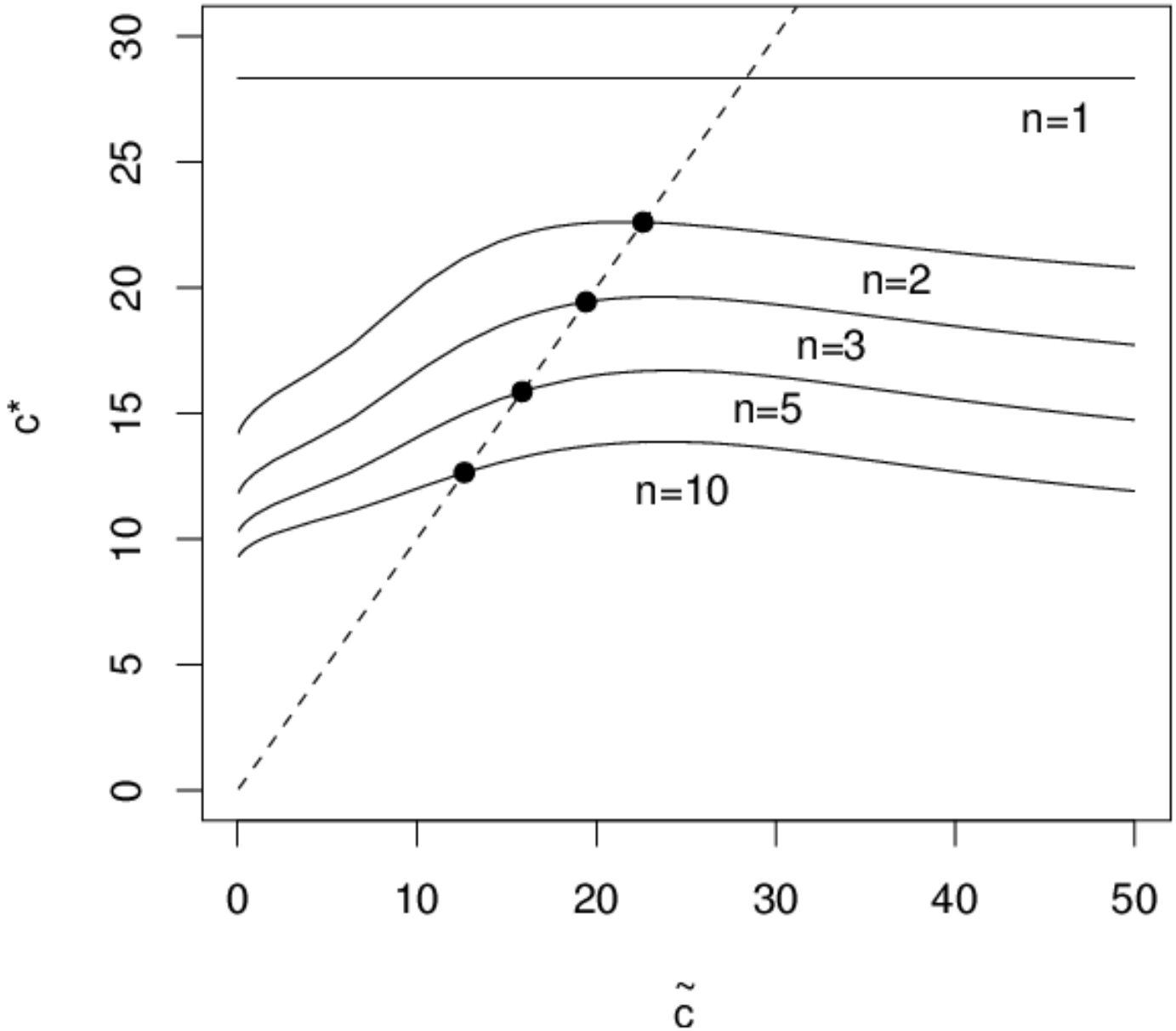
$$1 + D\bar{X}'(c) = 0$$

Smith, Levin, Laxminarayan (PNAS, 2005)



Smith, Levin, Laxminarayan (PNAS, 2005)


Cases Prevented
% of Cases
0.0
0.2
0.4
0.6
0.8
1.0
Other hospitals
Own Hospital
2
4
6
8
10
n


n=1
n=2
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c*
c̃
0
5
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15
20
25
30
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10
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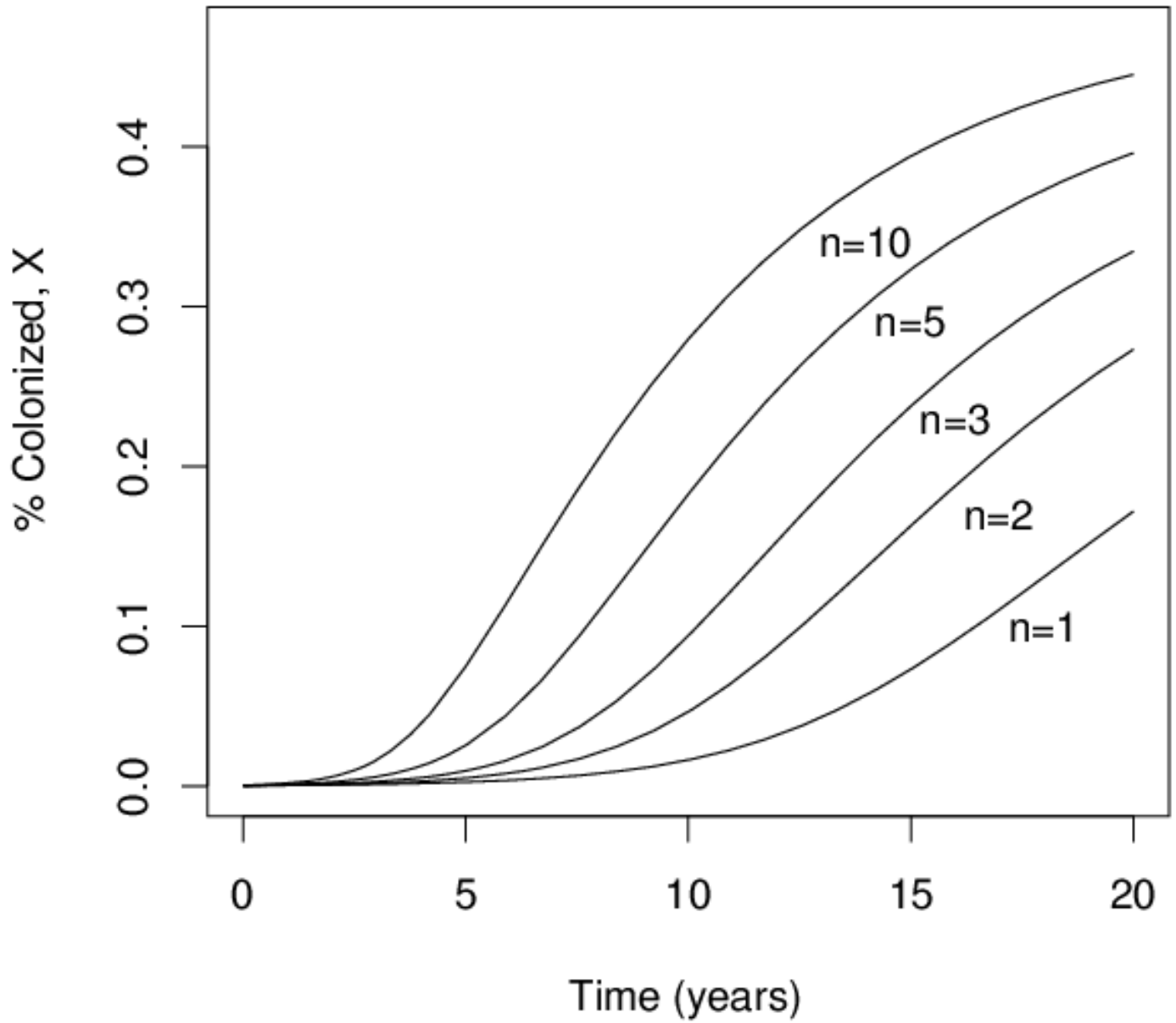
30
40
50


% Colonized, X
0.0
0.1
0.2
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n=10
n=5
n=3
n=2
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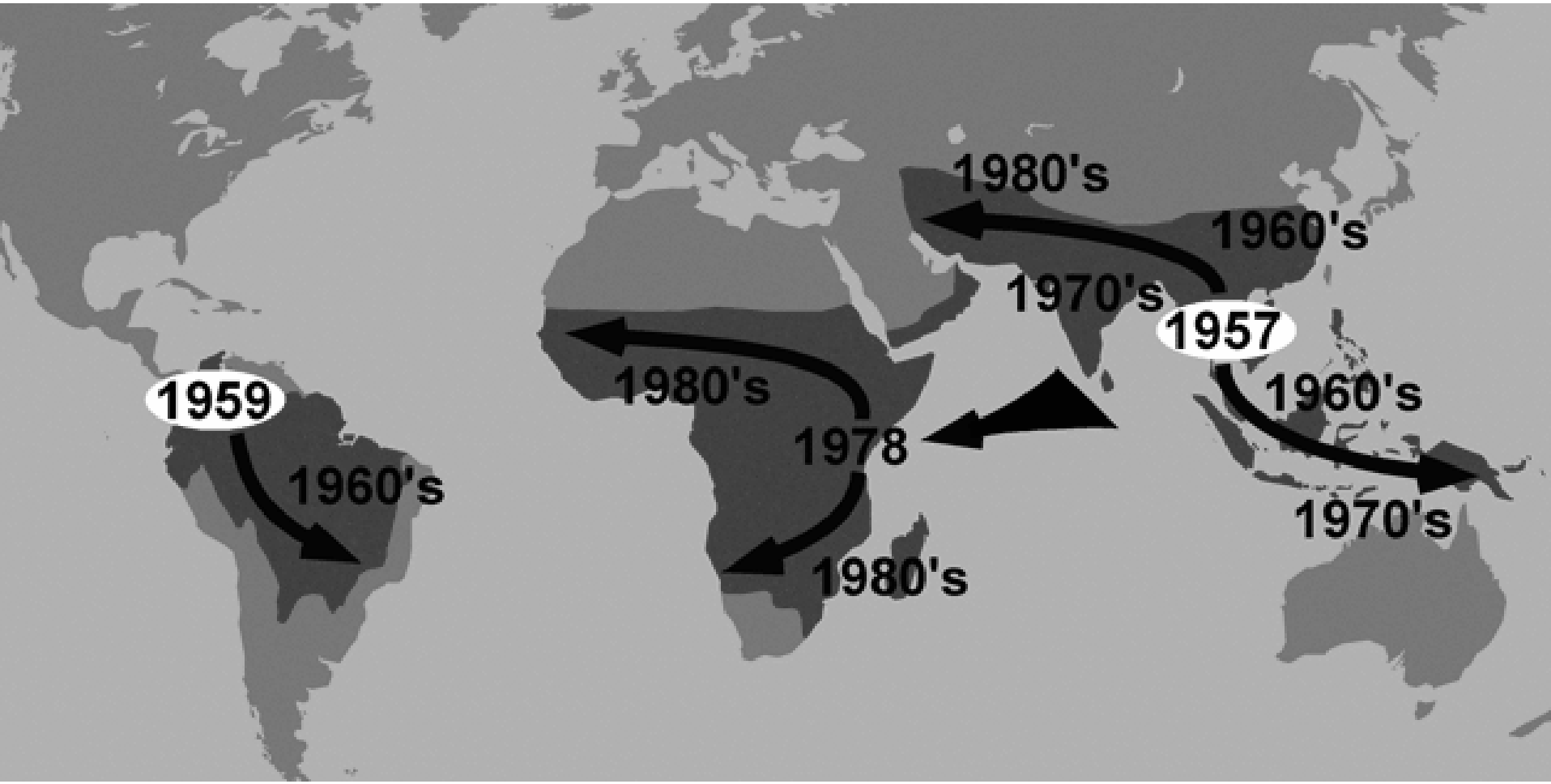
0
5
10
15
20
Time (years)

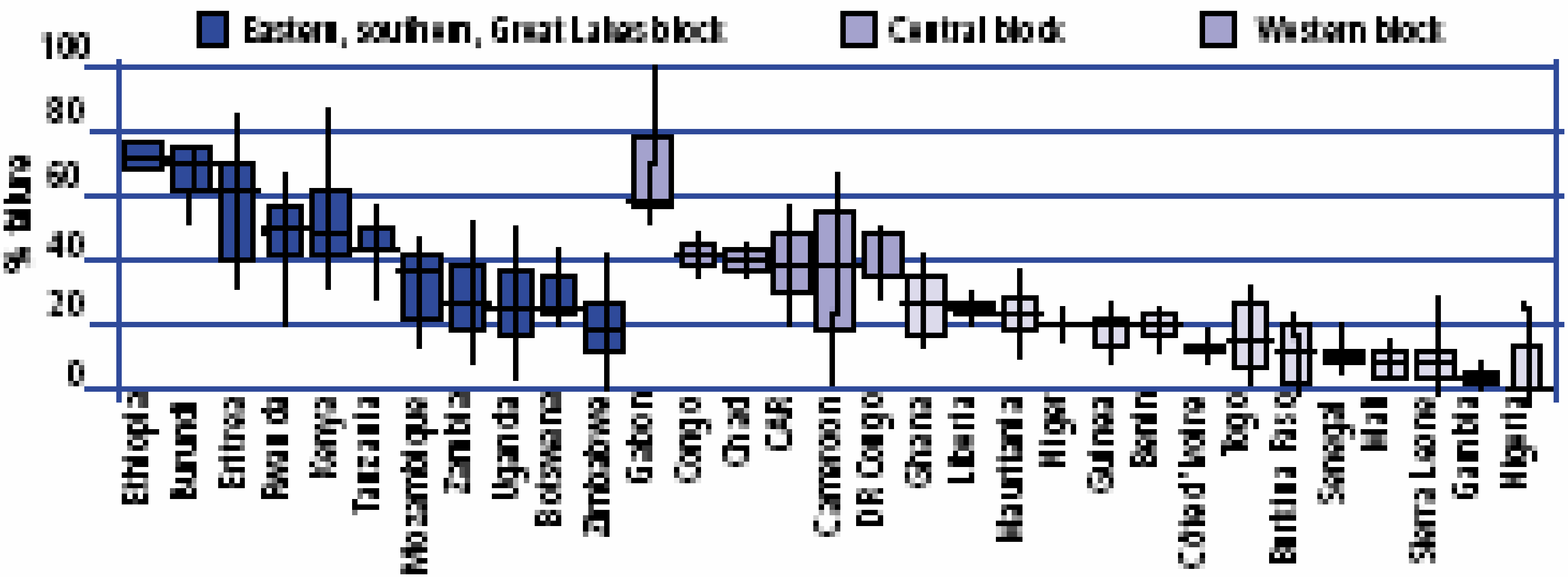
Implications for policy

- 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
- Does this explain higher prevalence of ARB in areas with high concentration of health care institutions?

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



Chloroquine treatment failure in Africa



WHO has established 126 sentinel surveillance sites in 36 African countries that monitor the efficacy of locally used antimalarial drugs by following up patients in clinics. According to standard protocol (13, 14), results are expressed as i) early treatment failure (ETF); ii) late clinical failure (LCF); in the future, late parasitological failure (LPF) will be considered as well. Treatment failure for policy change as shown here consists of the sum of ETF+LCF.

Note: The box indicates the 25th/75th percentile, the line limits lower/upper values, and where the lines cross, the median.

1 in 10^{12} parasites resistant to drug A

One in 10 to 100 patients

1 in 10^{12} parasites resistant to drug B

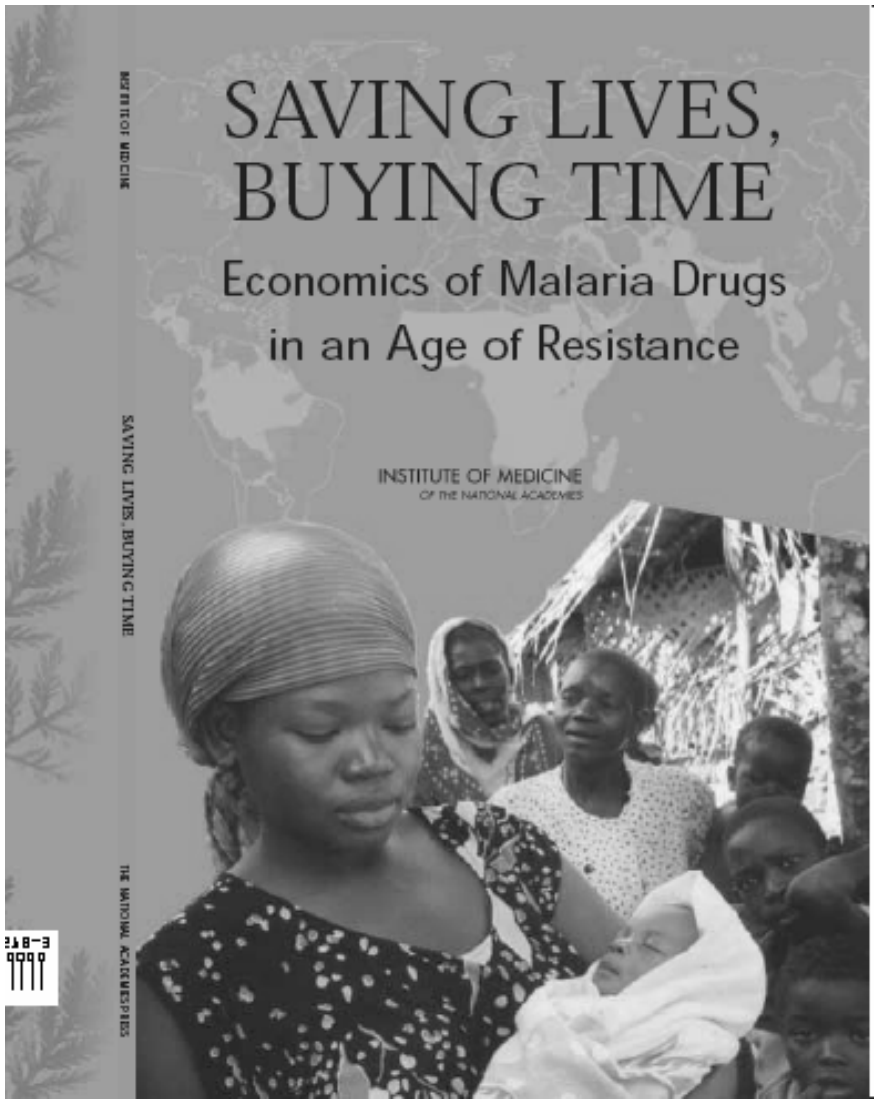
One in 10 to 100 patients

1 in 10^{24} parasites resistant simultaneously to drug A and drug B

Such a parasite would arise once in every 10,000 to 100,000 years

Nick White

Global subsidy for Artemisinin Combinations (ACTs)



- Global subsidy for artemisinin drugs
- Make ACTs as cheap as chloroquine

Central Recommendation

Within five years, governments and international finance institutions should commit new funds of US $300-$500 million per year to subsidize co-formulated ACTs for the entire global market to achieve end-user prices that are comparable to the current cost of chloroquine.

What would a subsidy do?

- Save lives and lower burden of malaria
- Discourage monotherapy by lowering price of ACTs
- Stimulate the ACT market and allow for lower prices by ensuring a stable demand
- Maintain the impetus to produce new antimalarial drugs

Why a global subsidy?

- Allow ACTs to flow through both public and private sector channels
- Give the international community leverage to discourage production of monotherapies
- Minimize administrative costs of subsidy
- Minimize incentives for counterfeit drugs, diversion and smuggling of ACTs

Could a subsidy *increase* the likelihood of resistance?

- Possible if the effect of a subsidy on lowering monotherapies is less than effect on increasing ACT use (and overuse)
- Depends on how ACT use and Artemisinin/partner drug monotherapy change in reponse to the subsidy

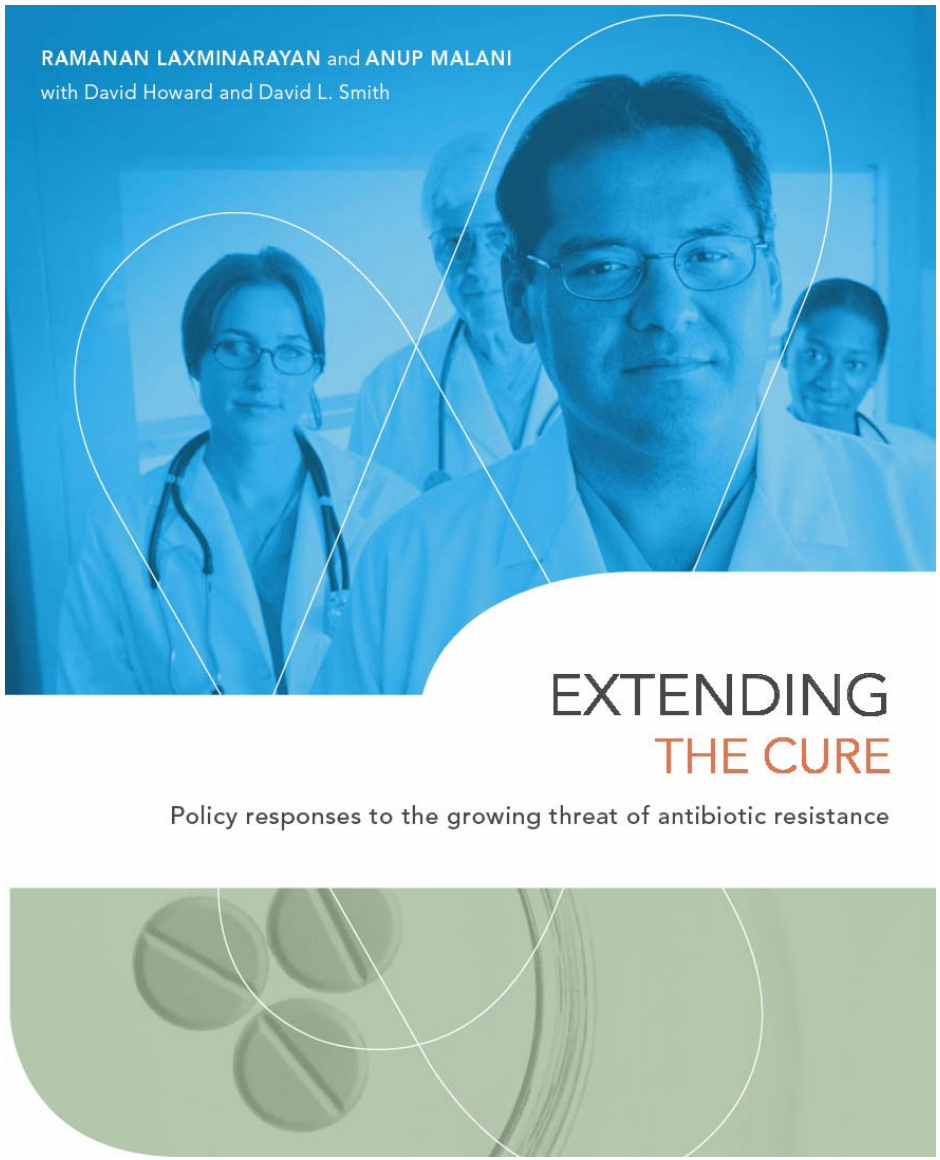
Laxminarayan, Over, Smith, World Bank Policy Research Paper, 2005

EXHIBIT 4
Sensitivity Analysis With Respect To Demand Elasticity For The Six Scenarios For Ten-Year Planning Horizon And One Million Population

	Deaths averted (compared with scenario A)		Treatment cost per death averted ($)[a]		Subsidy cost per death averted ($)[a]	
Scenario	Elasticity −2	Elasticity −4	Elasticity −2	Elasticity −4	Elasticity −2	Elasticity −4
B	2,939	7,732	846	1,698	687	1,180
C	5,246	8,939	1,245	3,625	1,126	3,060
D	3,703	6,724	1,443	3,939	1,301	3,322
E	5,485	12,665	444	1,023	373	720
F	8,141	17,379	802	1,780	736	1,517

Main findings

- Regardless of the degree of responsiveness of antimalarial consumption to price, a subsidy to ACT would save lives even if it hastened the arrival of parasite resistance to artemisinin-based drugs.
- A delay in instituting a subsidy for ACTs would exacerbate resistance would lead to faster resistance to ACTs.
- A global subsidy for multiple ACTs is likely to be far more effective in delaying the onset of resistance and saving lives than reliance on a single or even a limited number of combinations



www.extendingthecure.org

Antimalarial Strategies Project

- Would treating with more than one ACT combination delay emergence of resistance substantially?
- What is the optimal spatial scale for heterogeneity?
- How do these benefits compare with other strategies such as sequential use or cycling?

Opportunities – if you are interested in

- Modeling malaria
- Drug resistance
- Optimization models

Closing thoughts

- Epidemiological models take little or no account of economic constraints or incentives faced by individuals or institutions
- Economic models mostly ignore the spatial and temporal dynamics of disease.