

Global Antibiotic Resistance Partnership – South Africa Inaugural meeting. Stellenbosch, South Africa 8-9 Feb, 2010

Interventions: Disease Prevention and Antimicrobial Use Reduction - Overview



Global
**Antibiotic
Resistance**
Partnership

Iruka N Okeke

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

Haverford College
Biology Department



Papers cited in the presentation

- Walker et al. Science. 2009 Sep 11;325(5946):1345-6
- <http://www.cgdev.org/section/initiatives/active/drugresistanceglobalhealth/consultationdraftreport>
- van de Sande-Bruinsma N, et al. Antimicrobial drug use and resistance in Europe. *Emerg Infect Dis*. 2008 Nov;14(11):1722-30.
- Källander 2005. Balancing improved access to antibiotics and containment of bacterial resistance. *Paper for discussions at the meeting 'Will we respond to antibiotic resistance in time?' Uppsala Sept 14-17, 2005* <http://soapimg.icecube.snowfall.se/stopresistance/Access.pdf>
- <http://www.who.int/csr/resources/publications/drugresist/en/IAMRmanual.pdf>
- Okeke et al (2007) *Emerg Infect Dis*, 13 (11) 1640-1646
- Taylor et al (2001) *The Lancet*, 357, 1933
- Becker et al (2002) *Lancet Infect Dis*, 2, 325-326
- Okeke and Lamikanra (1995) *Int J. Antimicrob Ag* 5, 245.
- Okeke et al (1999) *Emerg Infect Dis* 5, 18
- Wright et al *Lancet*. 2009 May 30;373(9678):1861-73.
- Scaling up the response to infectious diseases. WHO/CDS/2002.7
- Okeke IN, Klugman KP, Bhutta ZA, Duse AG, Jenkins P, O'Brien TF, Pablos-Mendez A, Laxminarayan R. *Lancet Infect Dis*. 2005 Sep;5(9):568-80
- Okeke, Fayinka and Lamikanra (2000) *Emerg Infect Dis*, 6, 393
- Goldie et al. *N Engl J Med*. 2006 Sep 14;355(11):1141-53
- Mintz ED, Guerrant RL. [A lion in our village--the unconscionable tragedy of cholera in Africa.](#) *N Engl J Med*. 2009 Mar 12;360(11):1060-3.
- Opintan, JA, Newman MJ, Nsiah-Poodoh, OA, and Okeke IN (2008). *J Antimicrob Chemother* 62, 929-933.
- Microbial life.

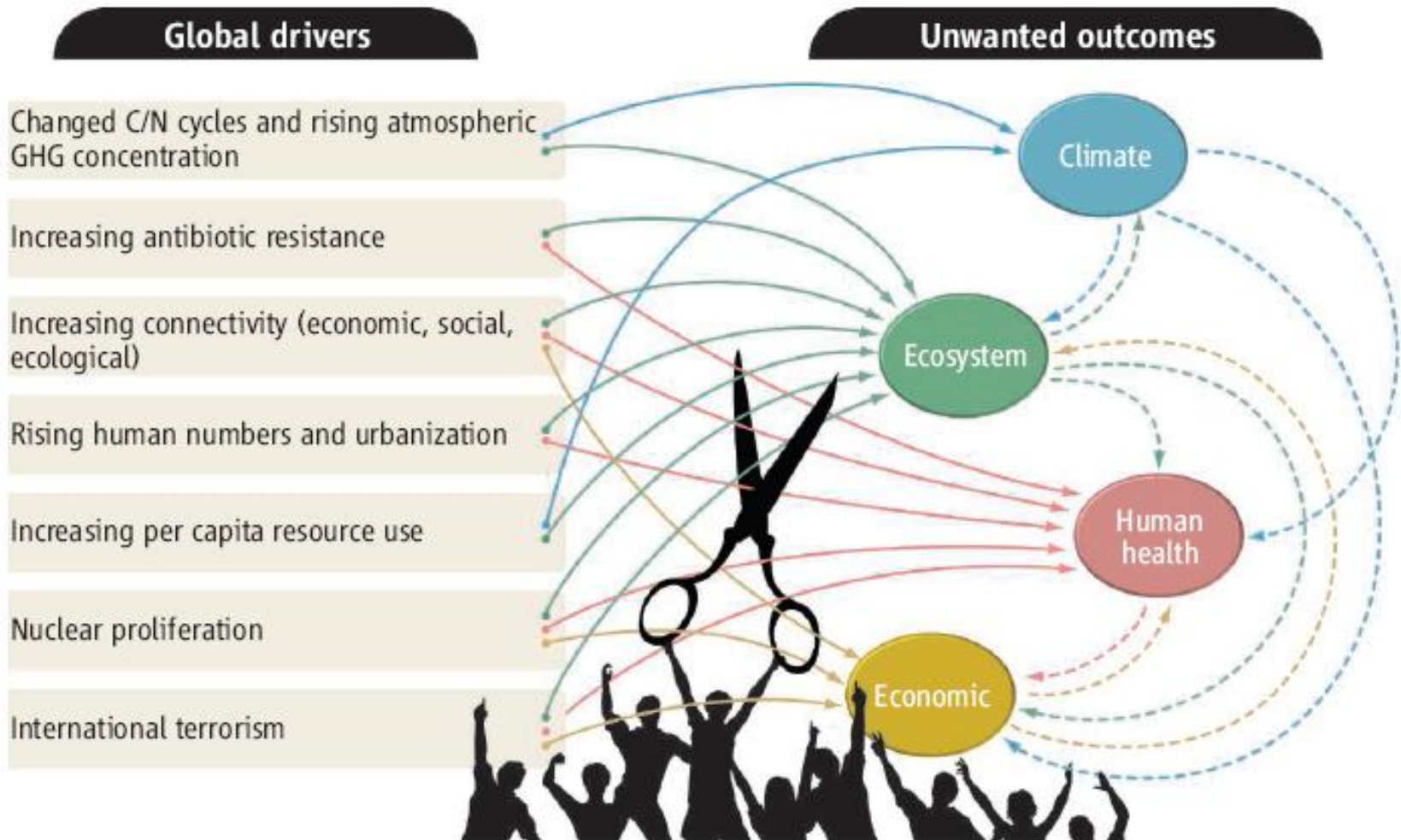


“We need more penicillin and Bibles”.
Miss Sadie Thompson (1953)

García Sánchez JE, et al. Rev Esp Quimioter. 2006;19(4):397-402.

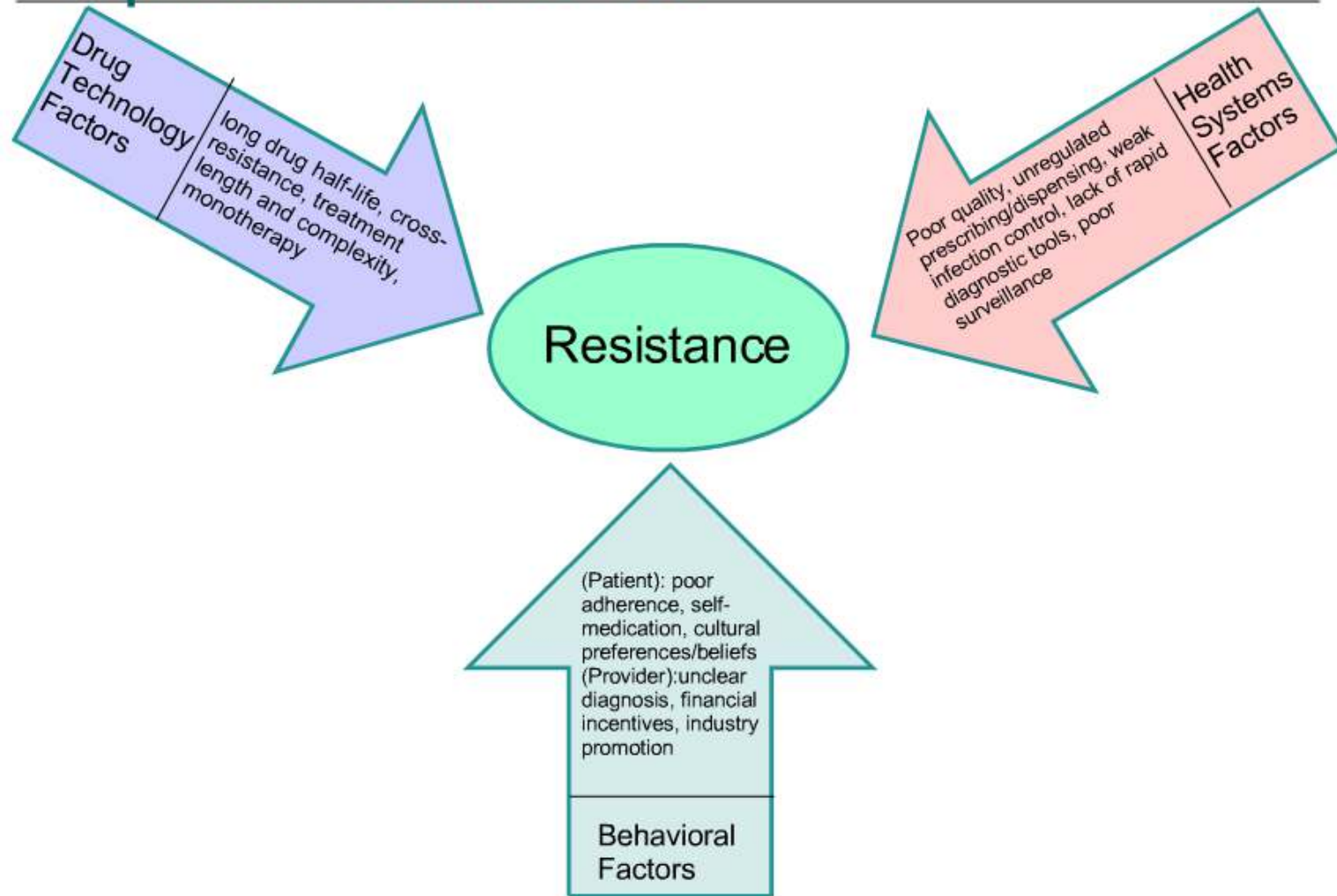
Looming Global-Scale Failures

Walker et al. Science. 2009 Sep 11;325(5946):1345-6.

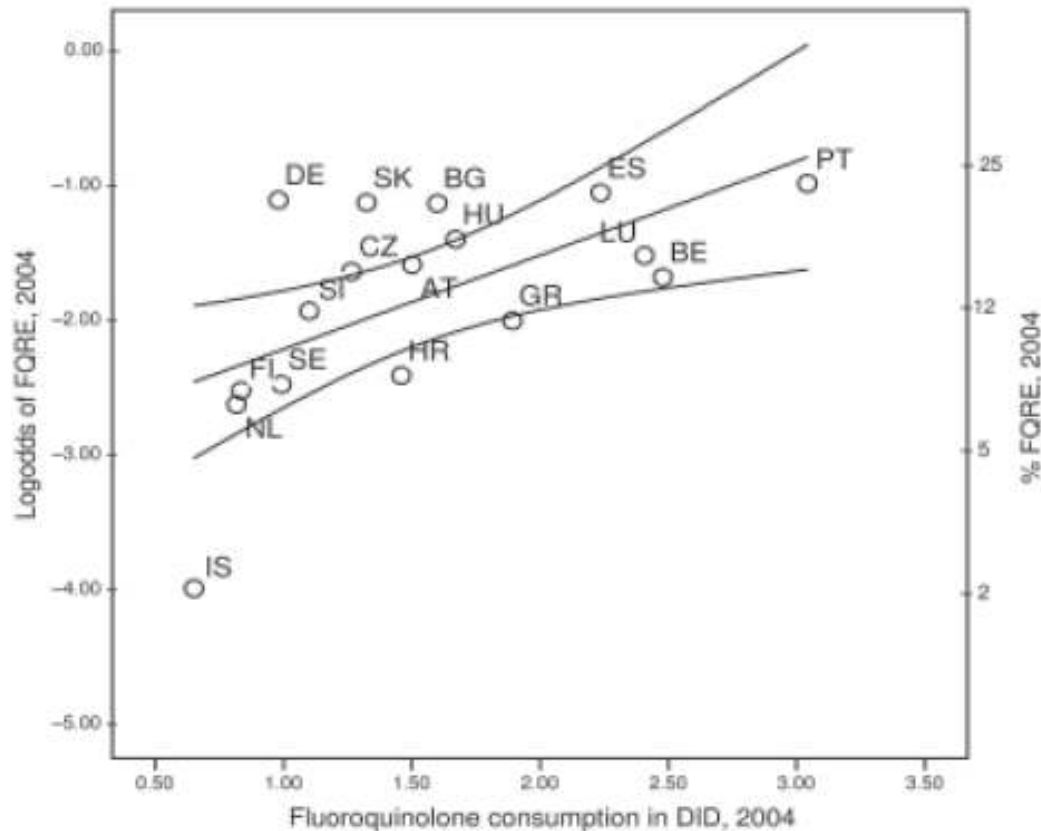


Interactive effects of global drivers on unwanted outcomes in the state of the world. Some outcomes also act as drivers of others (dashed arrows).

Tripartite Framework

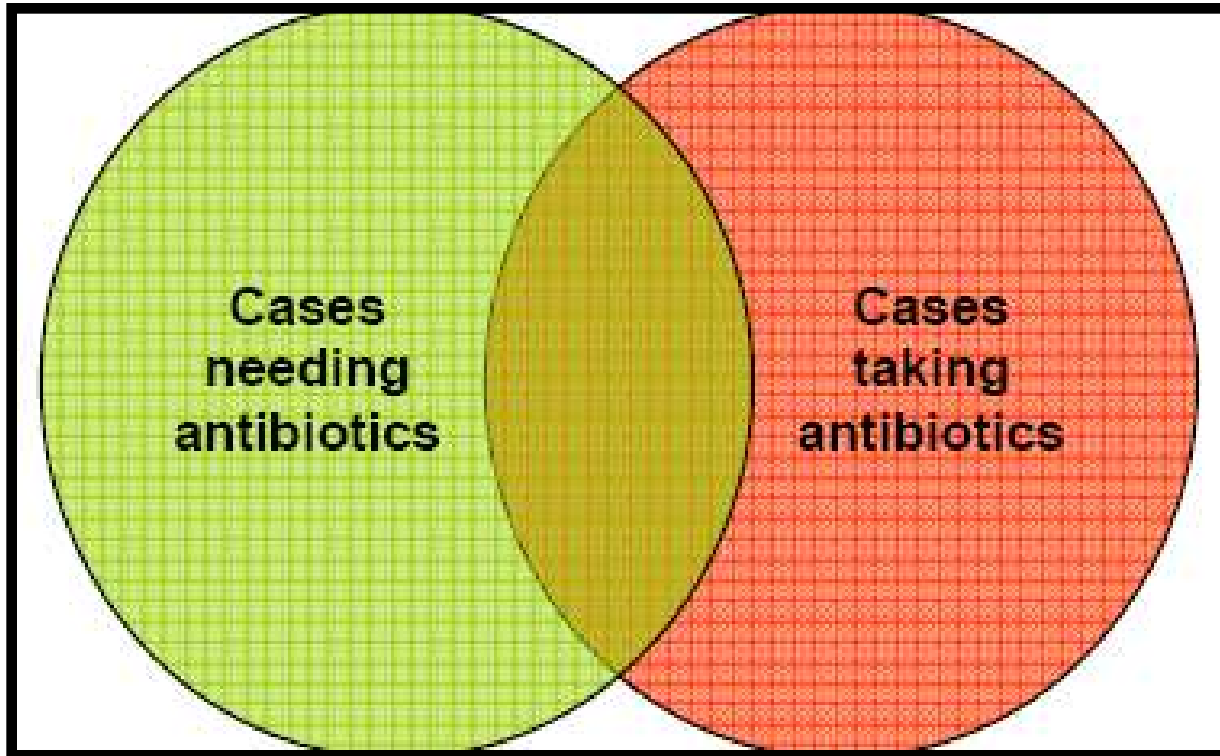


Occurrence of fluoroquinolone-resistant *E. coli* (FQRE) plotted against outpatient use of fluoroquinolone antimicrobial agents in 17 European countries including 95% confidence intervals.



[van de Sande-Bruinsma N, et al.](#) Antimicrobial drug use and resistance in Europe. *Emerg Infect Dis.* 2008 Nov;14(11):1722-30.

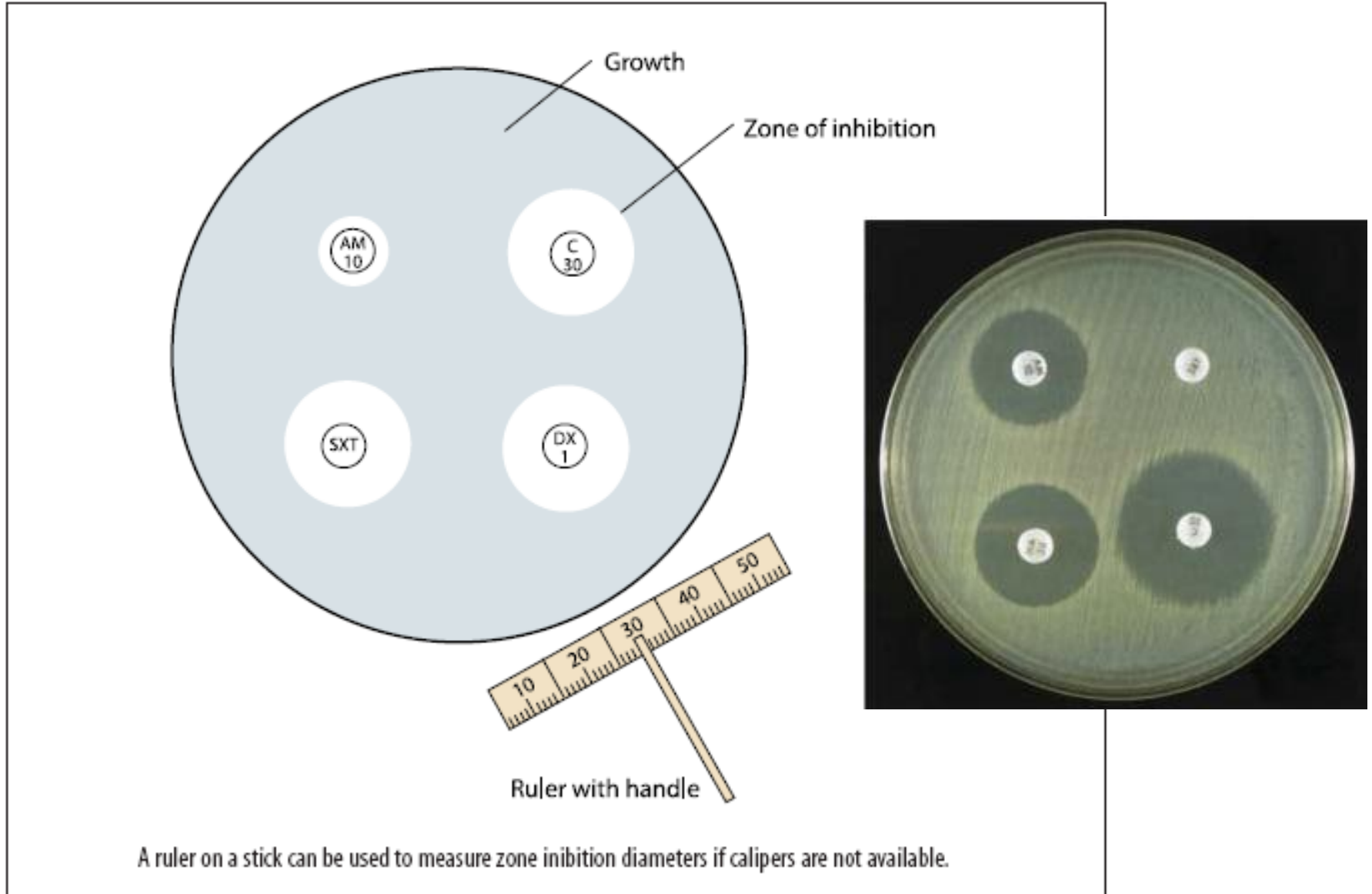
The overlapping relationship b/w patients who need antibiotics and those who take antibiotics.



Källander 2005. Balancing improved access to antibiotics and containment of bacterial resistance. *Paper for discussions at the meeting 'Will we respond to antibiotic resistance in time?' Uppsala Sept 14-17, 2005*

<http://soapimg.icecube.snowfall.se/stopresistance/Access.pdf>

FIGURE 6: The antimicrobial susceptibility disk diffusion test: disk placement and measurement of inhibition zone diameters



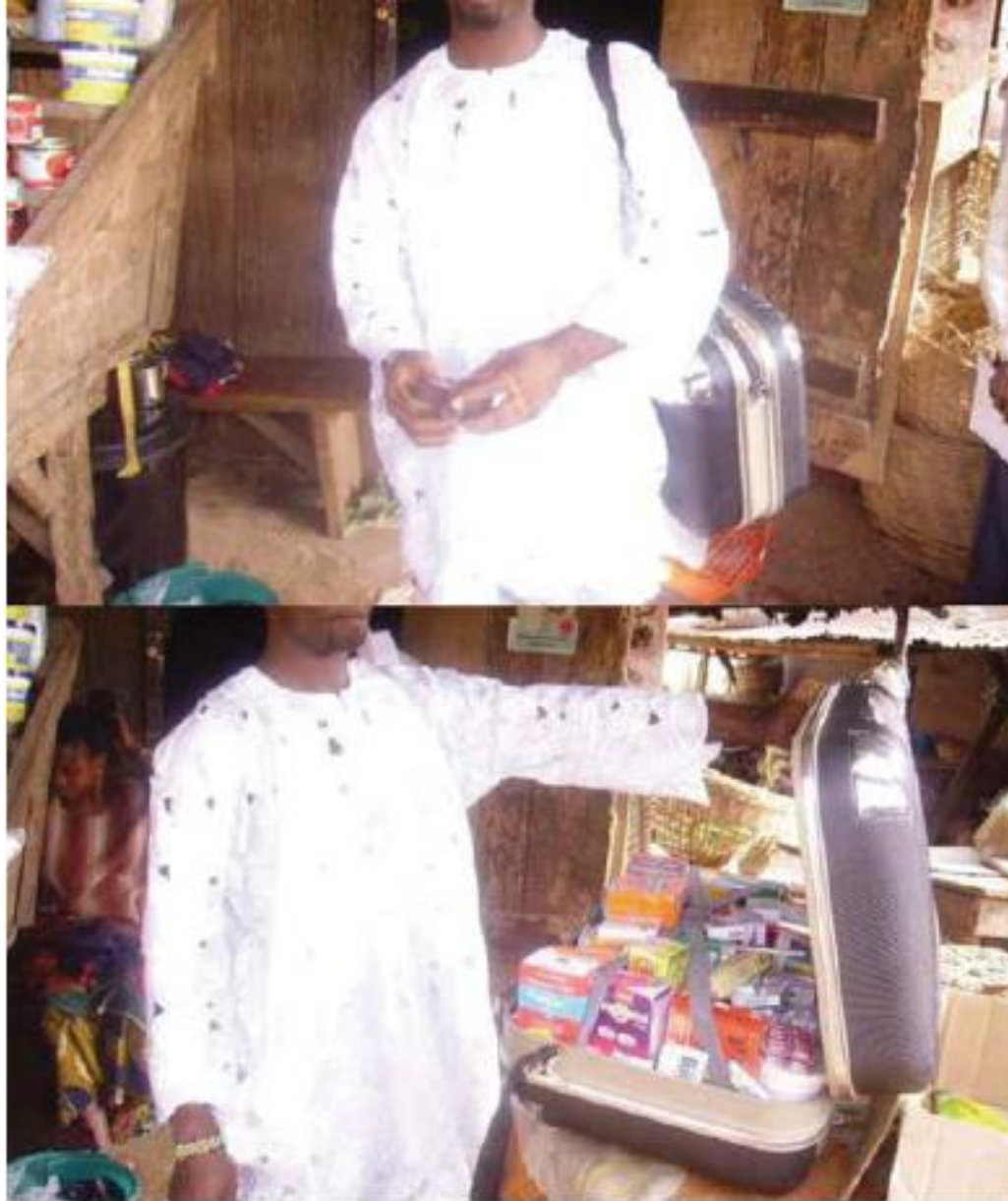


Figure. Itinerant medicine vendor in Oja-tuntun marketplace, Ile-Ife, Nigeria.

Substandard antimicrobial medicines from Nigerian pharmacies

Taylor et al (2001) The Lancet, 357, 1933

	Below Pharmacopoeial limits
Chloroquine phosphate	70-100%
Ampicillin	59-71%
Streptomycin	53%
Isoniazid	100%
Metronidazole	72-100%

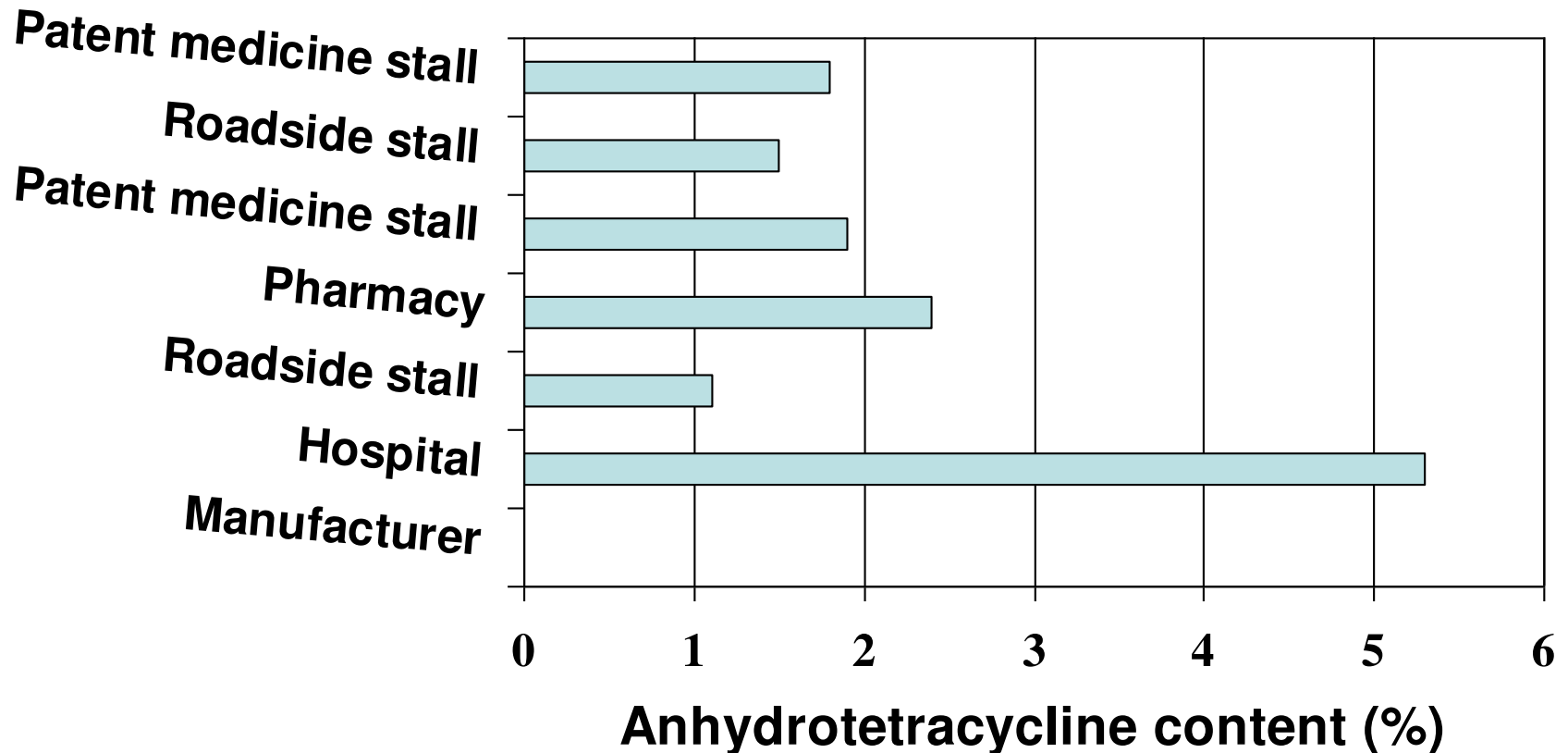
Injectable antibiotics available from market stalls in Kumba, Cameroon

Becker et al (2002) Lancet Infect Dis, 2, 325-326

- Ampicillin
- Benzathine
- Benzylpenicillin
- Gentamicin
- Spectinomycin
- Lincomycin
- Ofloxacin
- Oxacillin
- Cefuroxime
- Ceftriaxone
- Cefotaxime
- Cefepime



Toxic degradation product in dispensed tetracycline capsules



Okeke and Lamikanra (1995) *Int J. Antimicrob Ag* 5, 245.

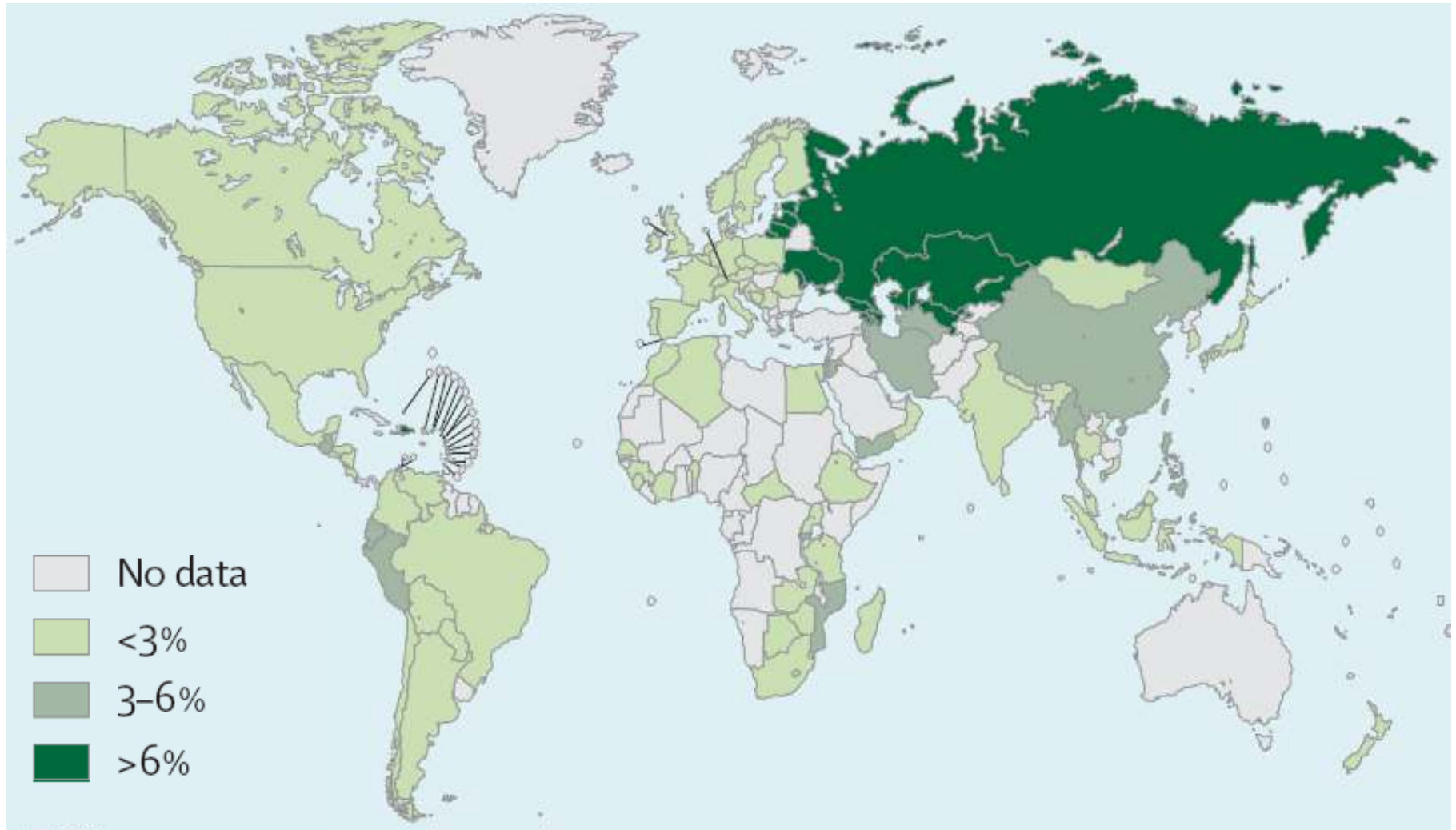
Okeke et al (1999) *Emerg Infect Dis* 5, 18

Medicines made of heat-stable drugs, such as the quinolones, may still be vulnerable to improper storage, which can change physical properties that affect drug absorption.

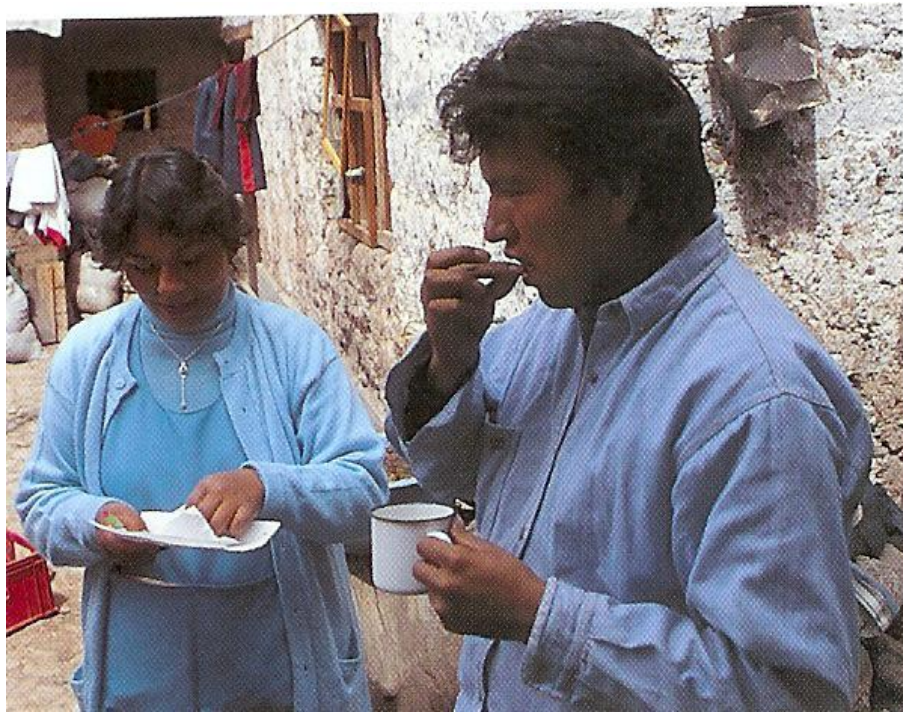
Heat and moisture

- Ambient temperatures in some tropical countries may reach 36-40 C
- Humidity distorts capsule shells and increases permeability to air and moisture, which can degrade the drug
- Elevated temperature and humidity change the physicochemical properties of excipients, affecting drug release
- The packaging of many medicines may be insufficient to protect the medication.
- Air conditioning is not always practicable

Distribution of multidrug-resistant tuberculosis among new cases, 1994–2007



Source WHO, 2008.5. Wright et al Lancet. 2009 May 30;373(9678):1861-73.

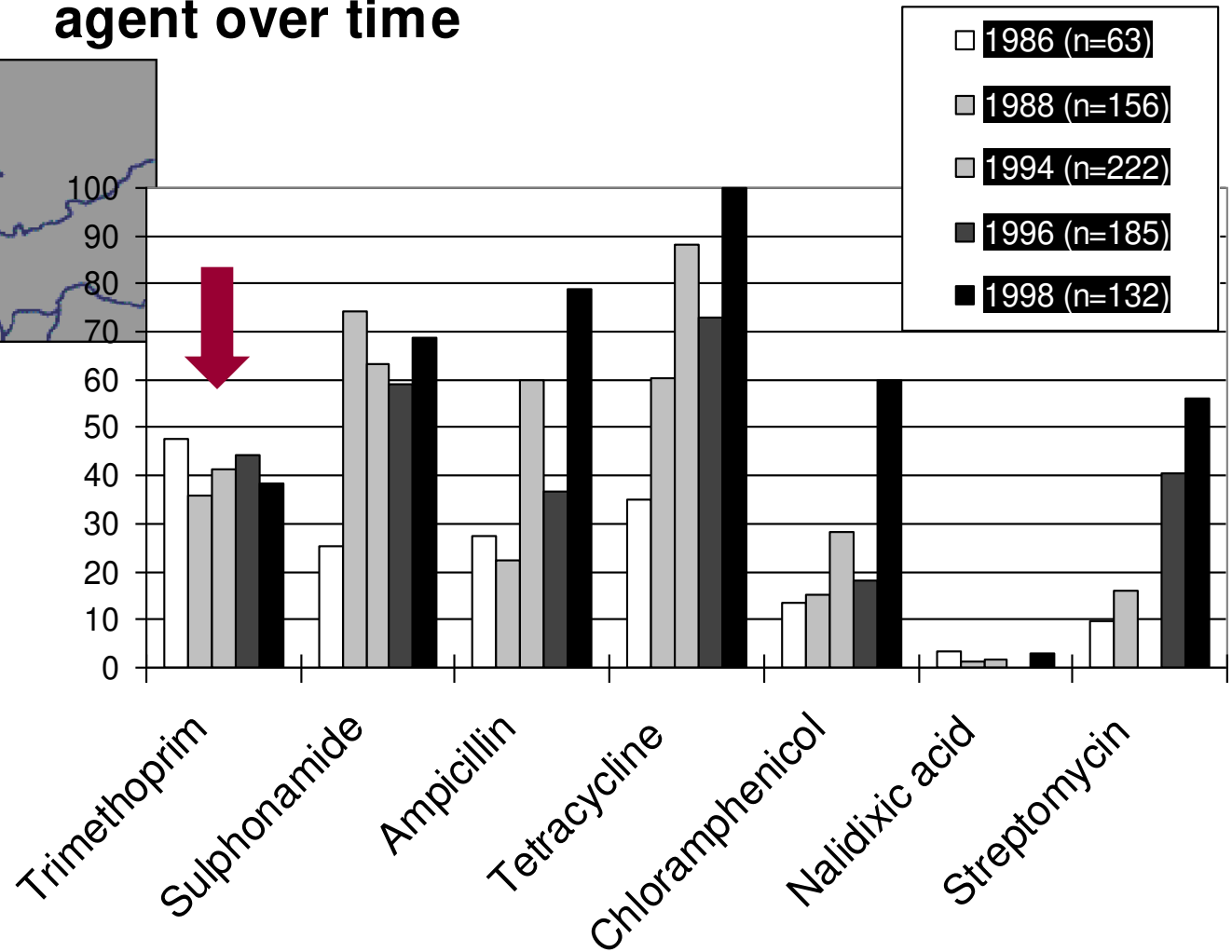


Scaling up the response to infectious diseases. WHO/CDS/2002.7

The elements of DOTS

Elements	Description	Okeke et al LID 2005;5(9):568-80
Case detection	Sputum smear microscopy among self-reporting patients	
Standardised short-course therapy with directly observed therapy	A 6–8-month regimen for smear-positive cases	
Drug supply	A system to ensure an uninterrupted supply of antituberculosis medication	
Recording and reporting	Standardised system to allow for programme assessment	
Political commitment	Initiation, support, and maintenance of the above elements at a national level	

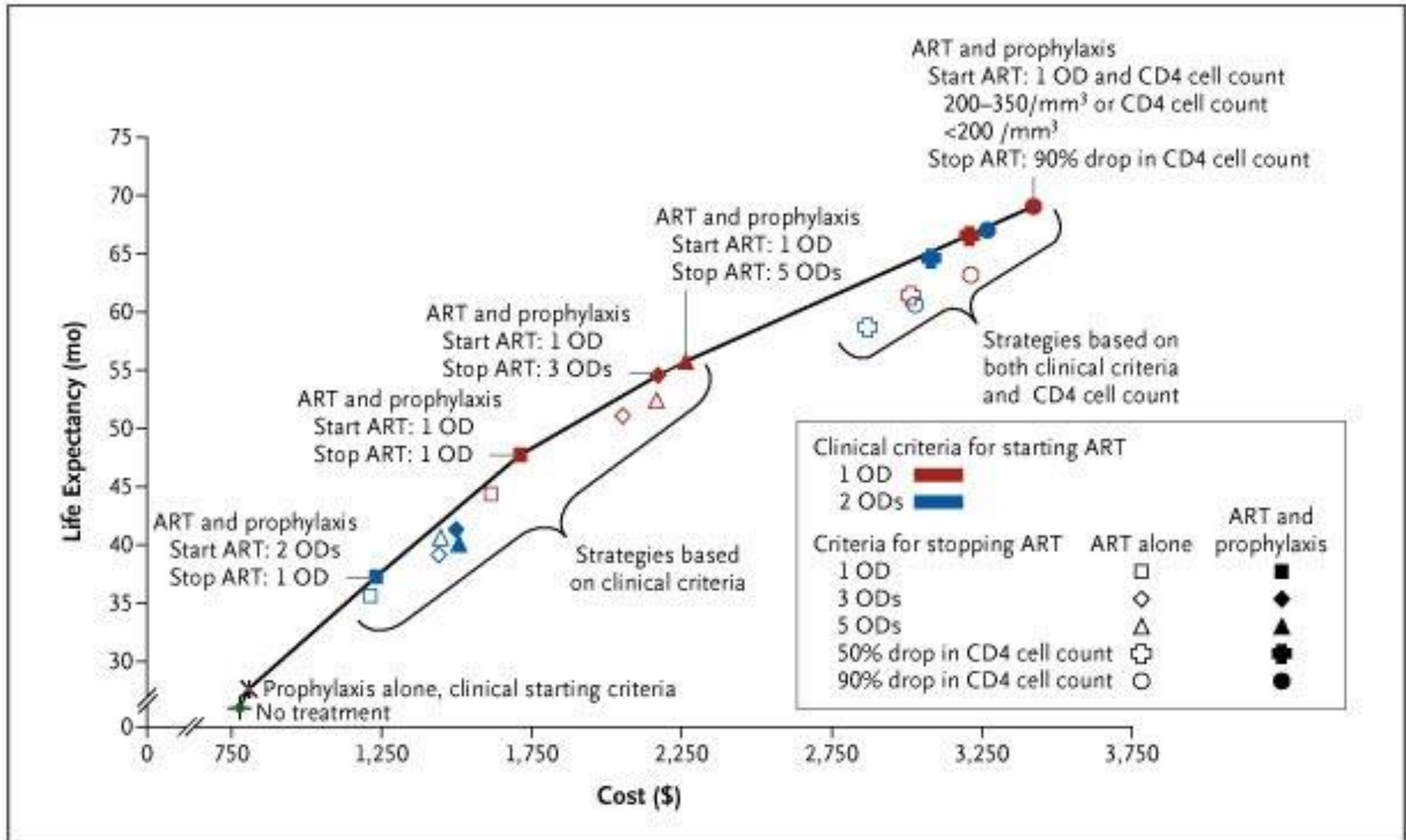
Percentage of isolates resistant to each agent over time



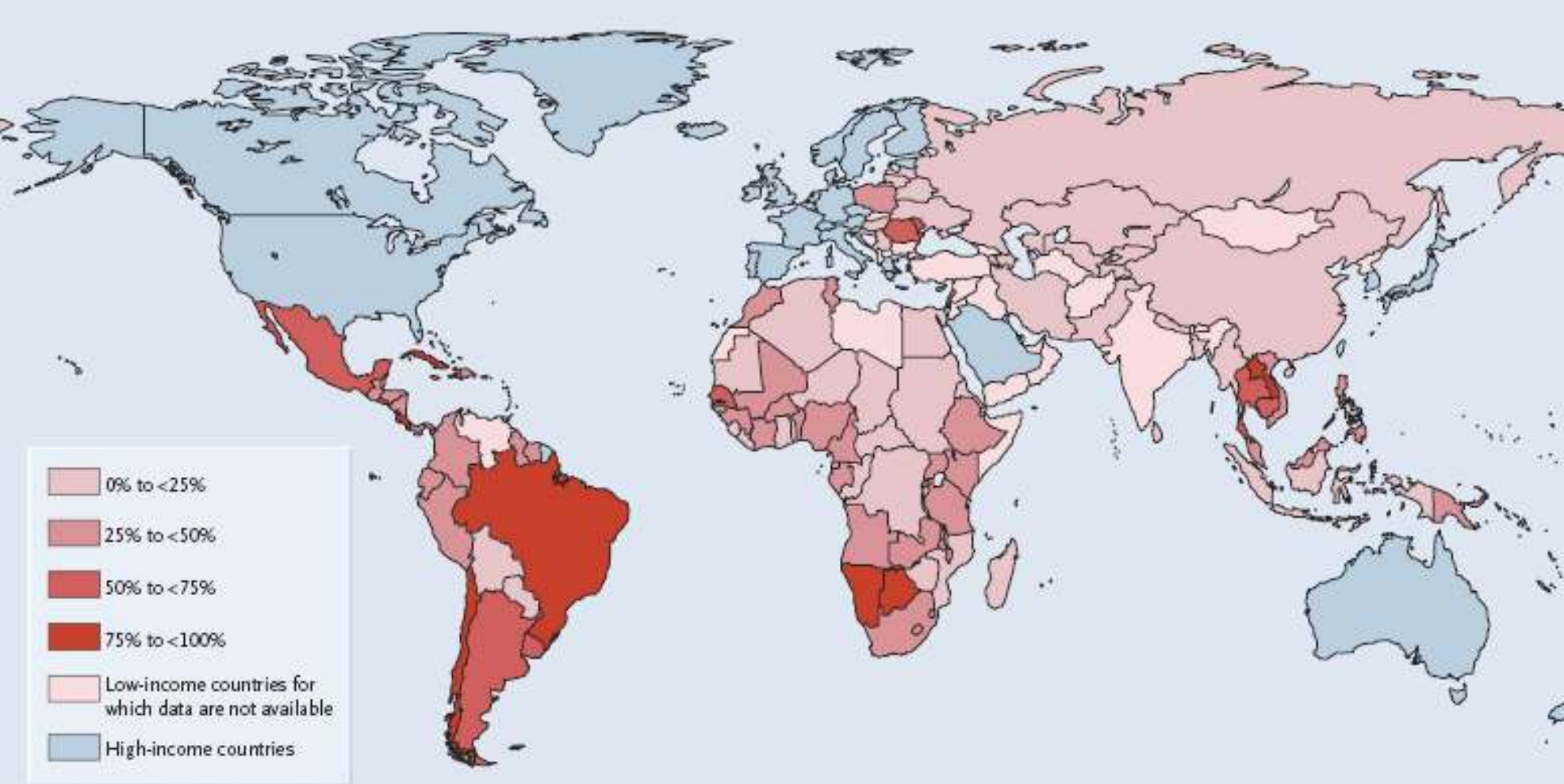
How can we explain a jump in trimethoprim resistance that occurred in commensal *E. coli* sometime between 1998 and 2005?

'Cost-Effectiveness' of Treatment Strategies for HIV-positive patients in resource limited areas.

Goldie et al. N Engl J Med. 2006 Sep 14;355(11):1141-53

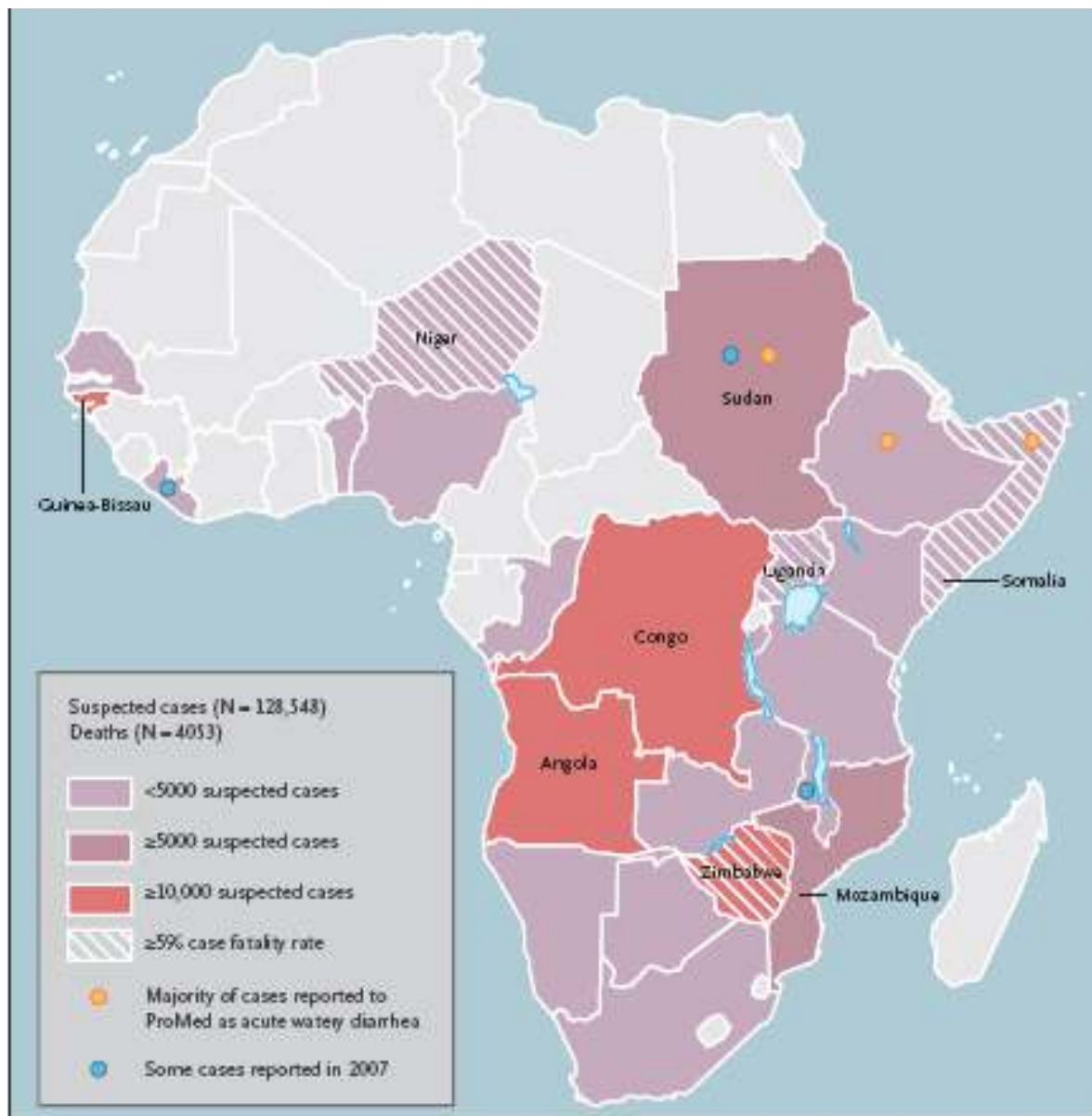


Estimated proportion of persons with HIV infection receiving antiretroviral therapy in low-income and middle-income countries as of December 2007.



Ford N, Mills E, Calmy A. [Rationing antiretroviral therapy in Africa-treating too few, too late.](#) N Engl J Med. 2009 Apr 30;360(18):1808-10.

Mintz ED, Guerrant RL. [A lion in our village--the unconscionable tragedy of cholera in Africa.](#) N Engl J Med. 2009 Mar 12;360(11):1060-3.



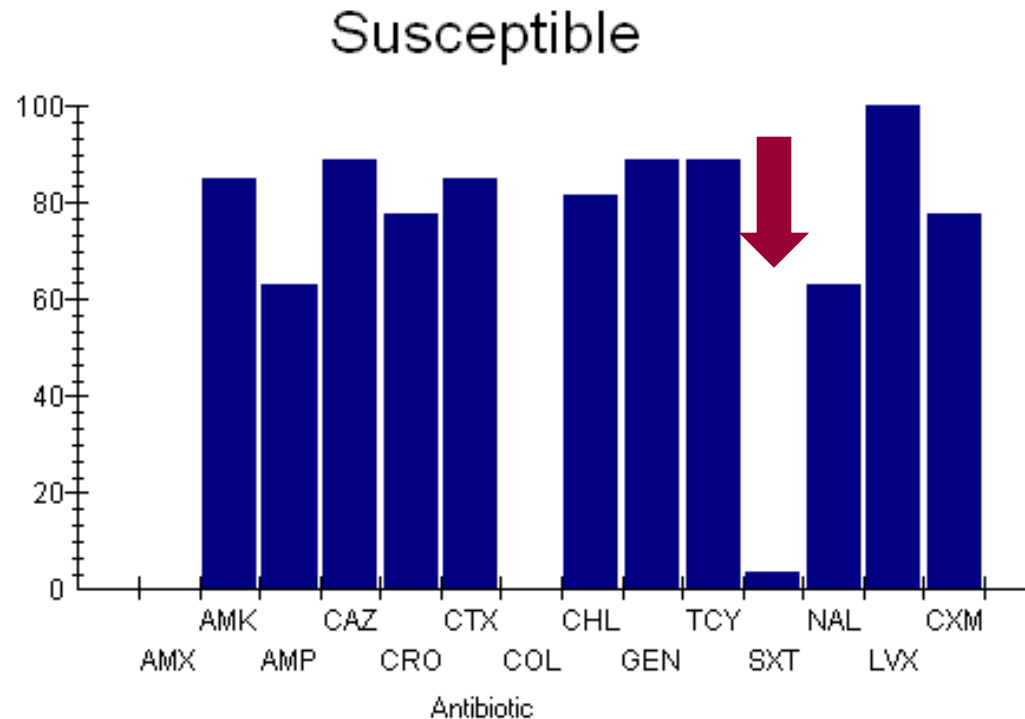
Map of Cholera Outbreaks in Sub-Saharan Africa in 2008, Showing Numbers of Suspected Cases per Country.

Cholera outbreak (Ghana 2006)

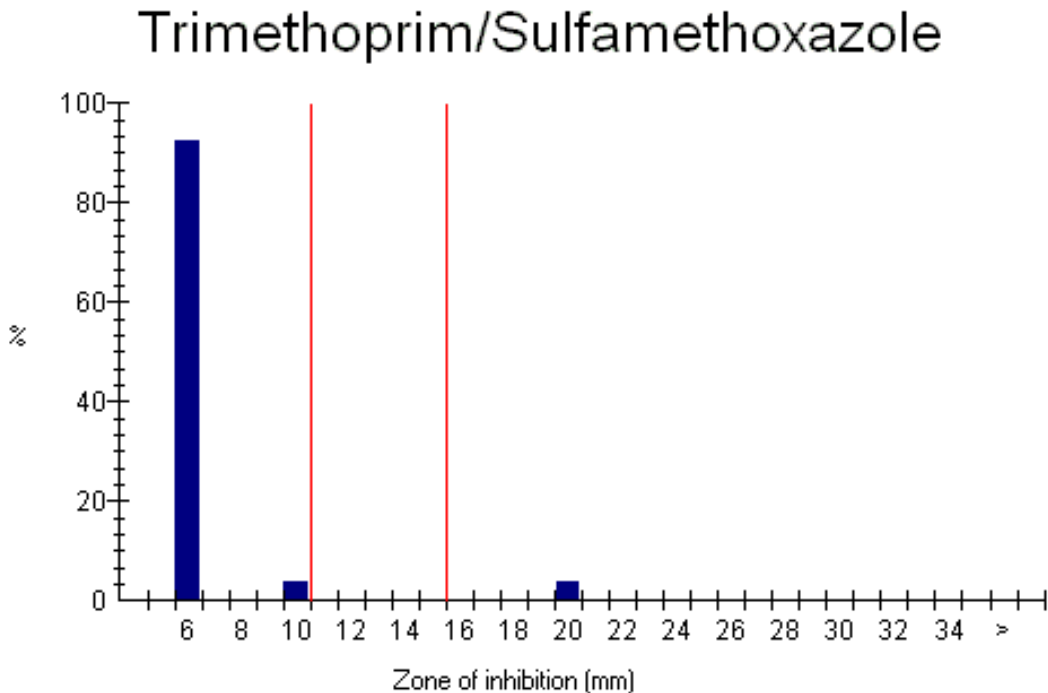
Jan 2-June 25, 2006

Opintan, JA, Newman MJ, Nsiah-Poodoh, OA, and Okeke IN (2008). *J Antimicrob Chemother* 62, 929-933.

- 1869 cases and 79 deaths (4.2% case-fatality rate)
- 27 isolates confirmed *V. cholerae* O1 Ogawa by reference lab



Trimethoprim resistant	26/27
<i>dfrA</i> cassette	19/27
Class 1 integron	0/27
SXT element	23/27
Class 2 integron (<i>dfrA1-sat-aadA</i>)	22/27



We found multiple elements stably bearing resistant *dfr* genes in most of the *V. cholerae* outbreak isolates

Opintan, JA, Newman MJ, Nsiah-Poodoh, OA, and Okeke IN (2008).
J Antimicrob Chemother 62, 929-933.

Public Health Measures and Human Well-Being

Microbial life Box 30.5

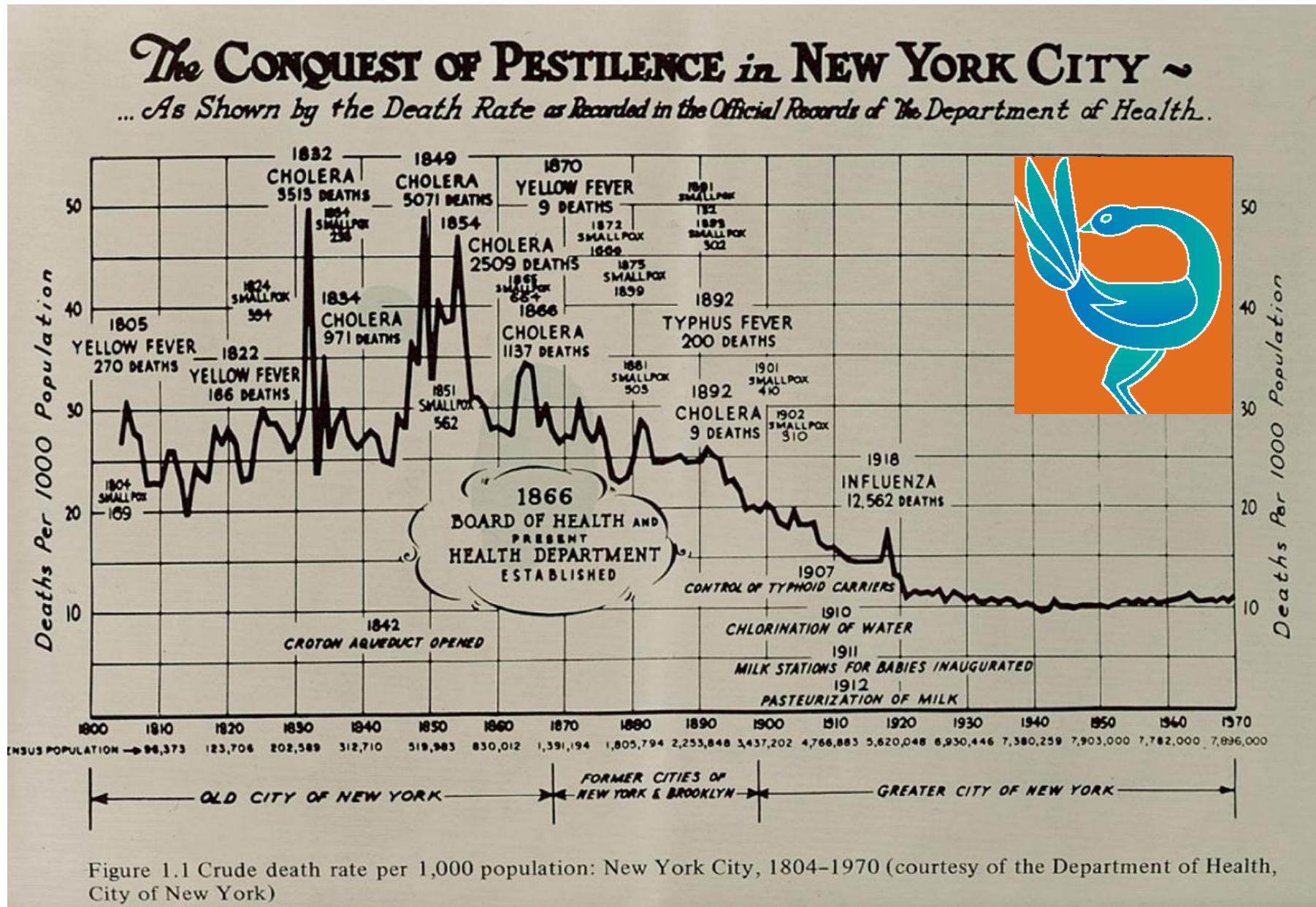


Figure 1.1 Crude death rate per 1,000 population: New York City, 1804–1970 (courtesy of the Department of Health, City of New York)

Public Health Measures and Human Well-Being

Microbial life Box 30.5

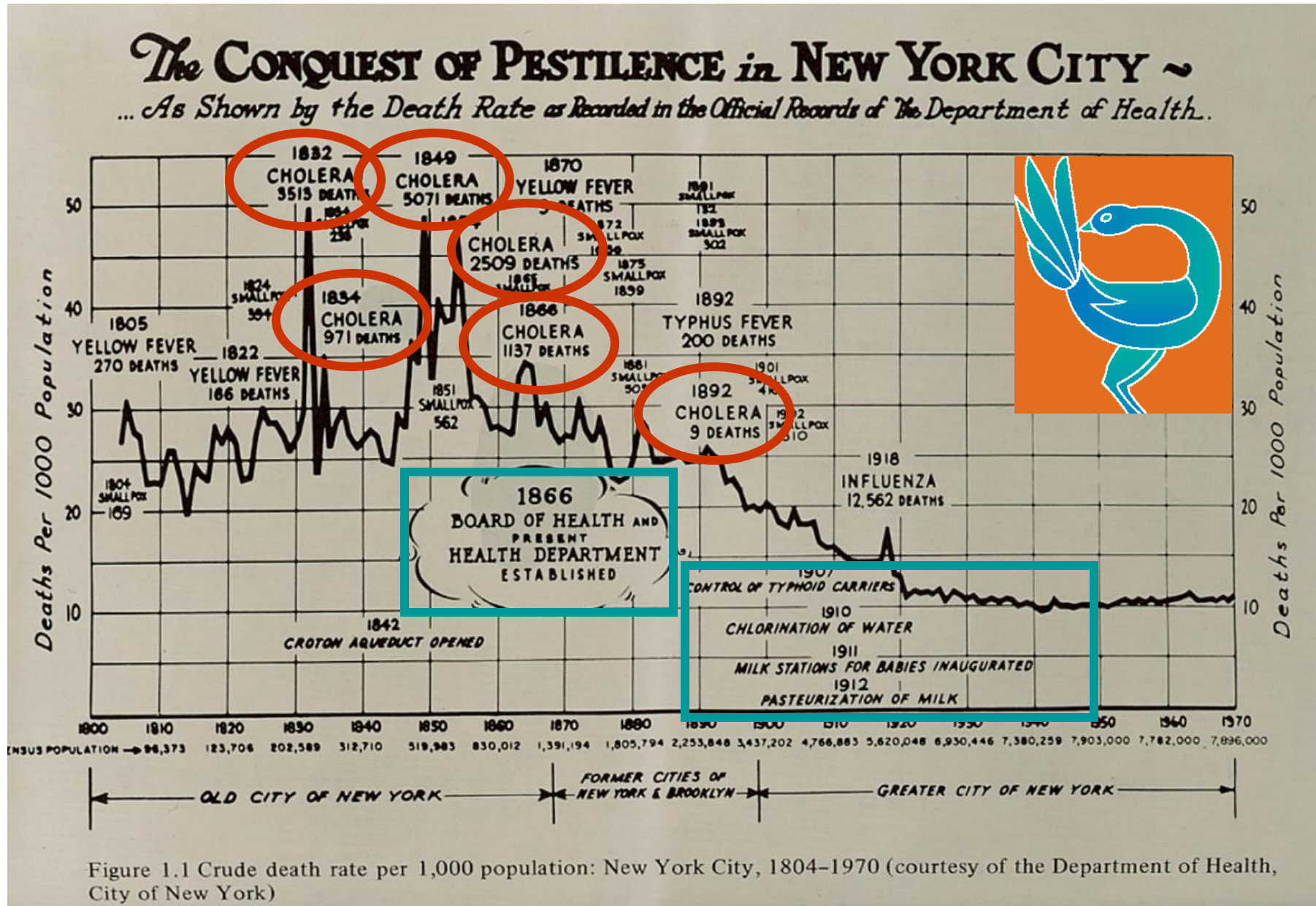


Figure 1.1 Crude death rate per 1,000 population: New York City, 1804–1970 (courtesy of the Department of Health, City of New York)

Disease prevention & antimicrobial use reduction

Adapted from Okeke IN, Klugman KP, Bhutta ZA, Duse AG, Jenkins P, O'Brien TF, Pablos-Mendez A, Laxminarayan R. Lancet Infect Dis. 2005 Sep;5(9):568-80

- **Reducing undesirable selective pressure**
 - Diagnostics
 - Drug quality assurance
 - Treatment guidelines
 - Prescriber education
 - Patient education
- **Treatment strategies**
 - Combination therapy
 - Cycling
 - Drug heterogeneity
- **Reducing spread**
 - Water and sanitation
 - Hand hygiene
 - Vaccination

Acknowledgements

- The Wellcome Trust/ GARP
- Center for Global Development, Disease Control Priorities Project
- Society-in-Science: The Branco Weiss Fellowship
- Koshland Integrated Natural Science Center at Haverford College



The ways and means for putting medicine in order must take account of the conditions of life and work among the people whom it must serve.

Walton H. Hamilton, 1932

