

Drivers of Antibiotic Resistance



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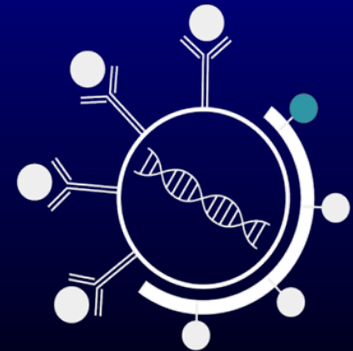
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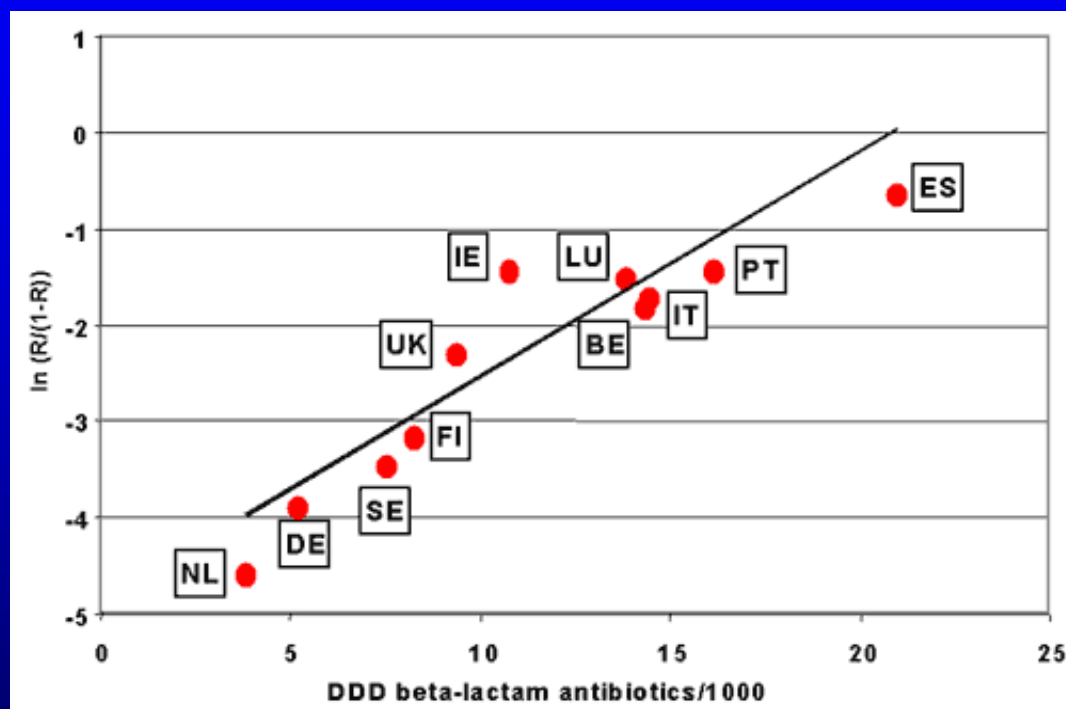


RMPRU

respiratory & meningeal pathogens research unit

Magnitude α Resistance

Association of Antibiotic Use with Resistance in the Pneumococcus

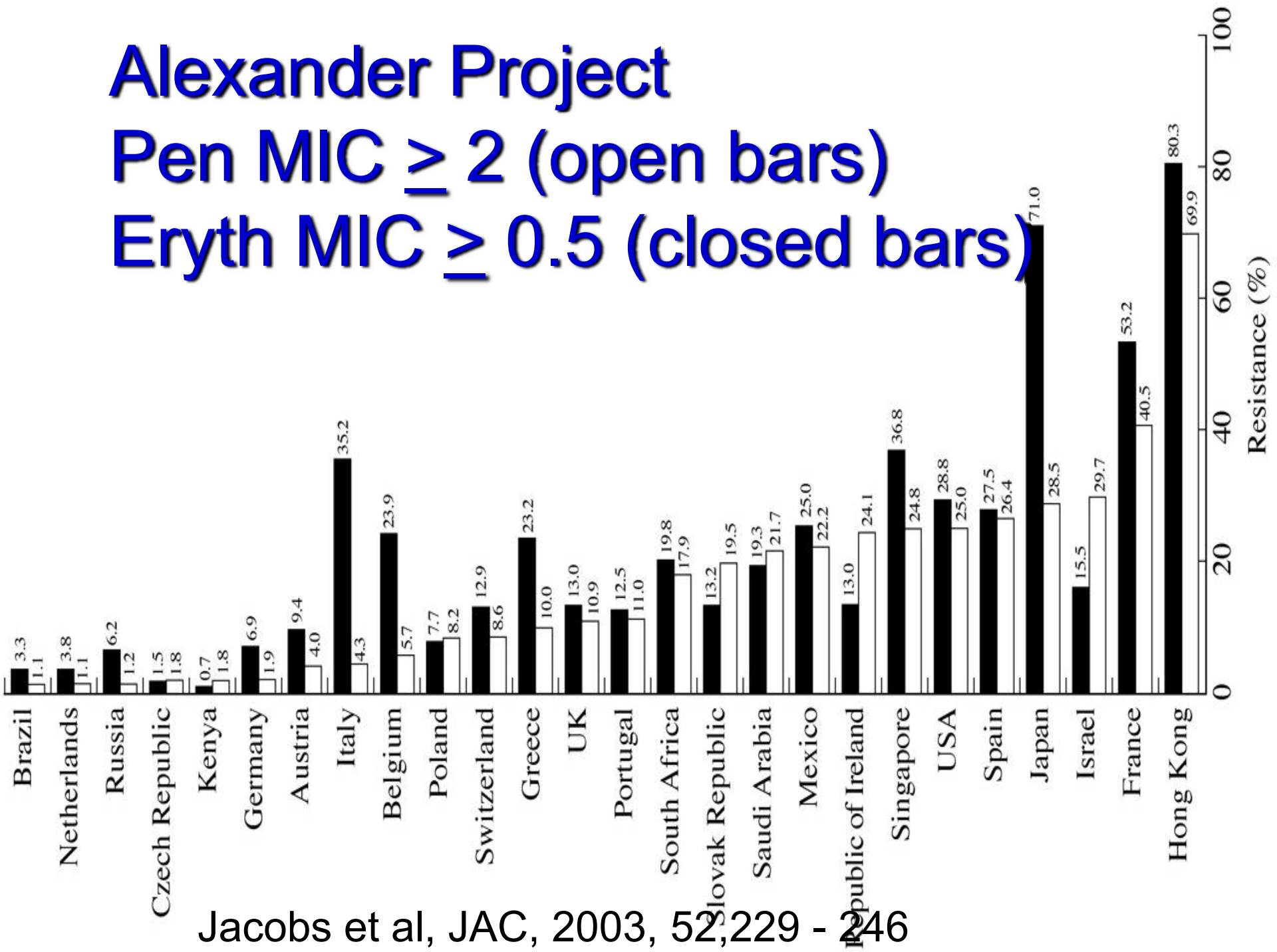


The log odds of resistance to penicillin among invasive isolates of *Streptococcus pneumoniae* (PNSP; $\ln(R/[1-R])$) is regressed against outpatient sales of beta-lactam antibiotics in 11 European countries

Alexander Project

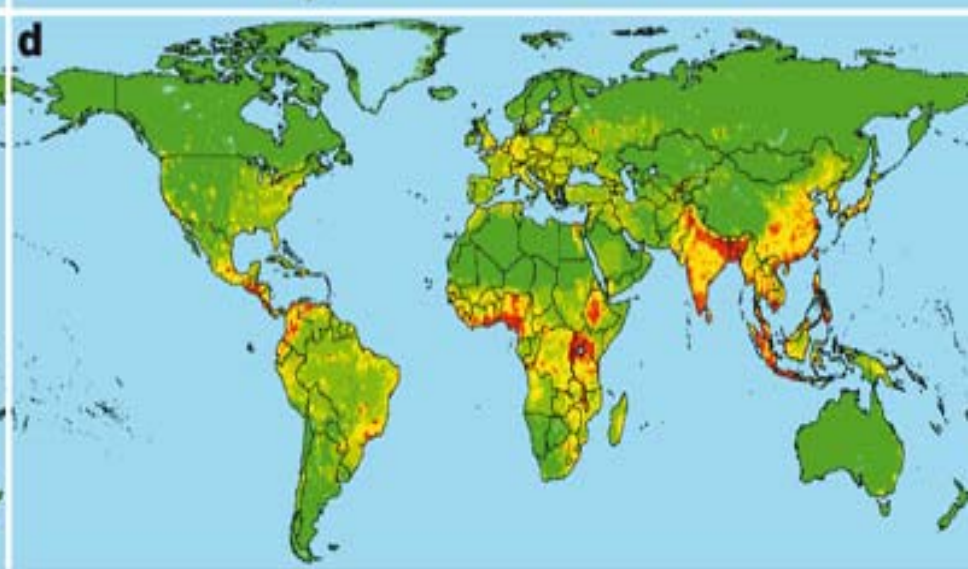
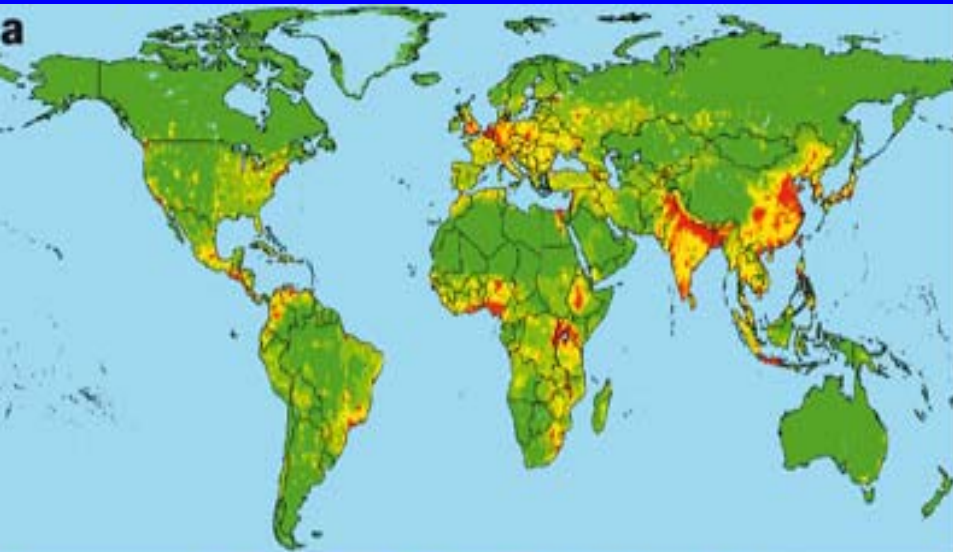
Pen MIC ≥ 2 (open bars)

Eryth MIC ≥ 0.5 (closed bars)



Zoonoses from wildlife

Zoonoses from non-wildlife

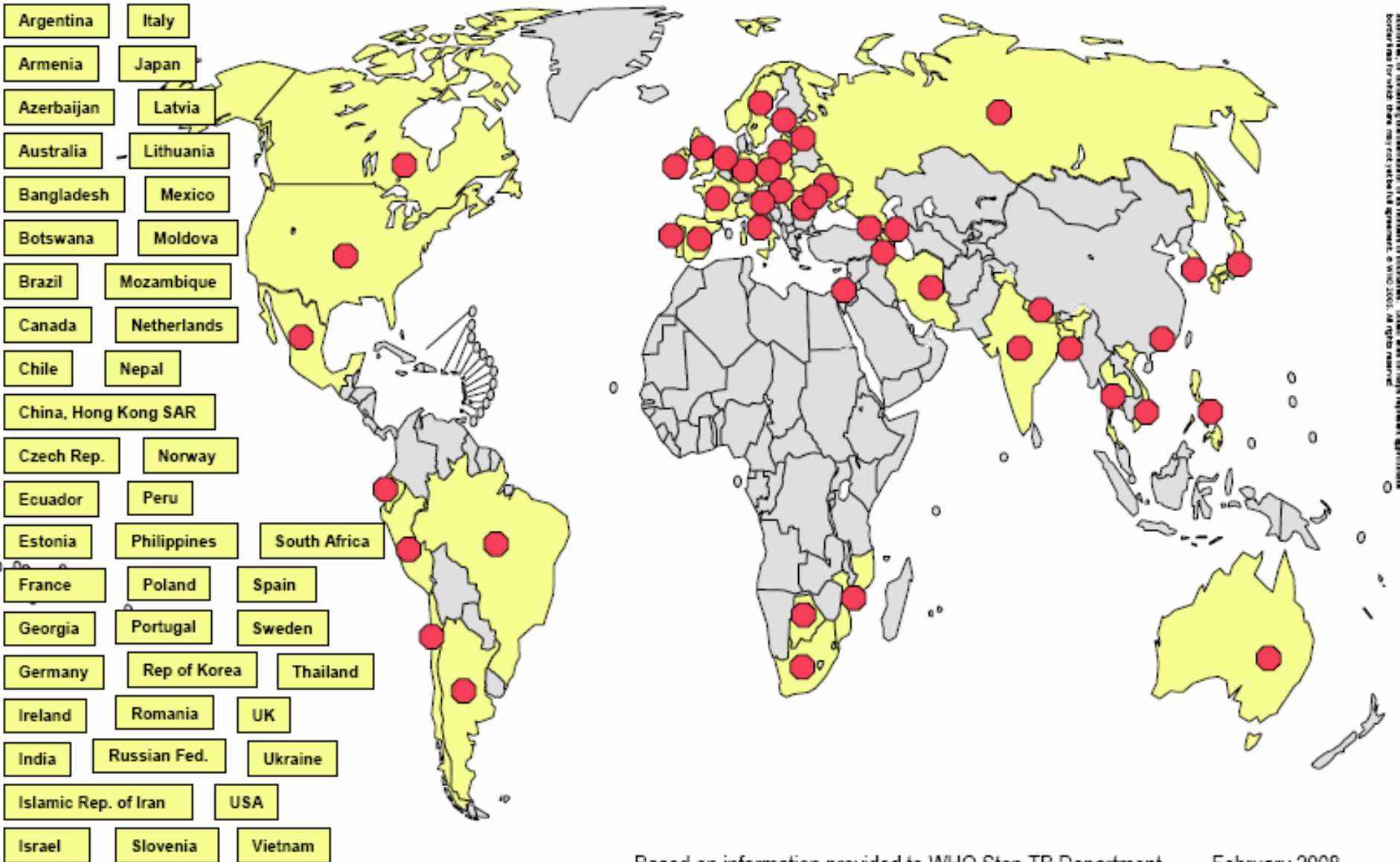


Antibiotic - resistance

Vector borne

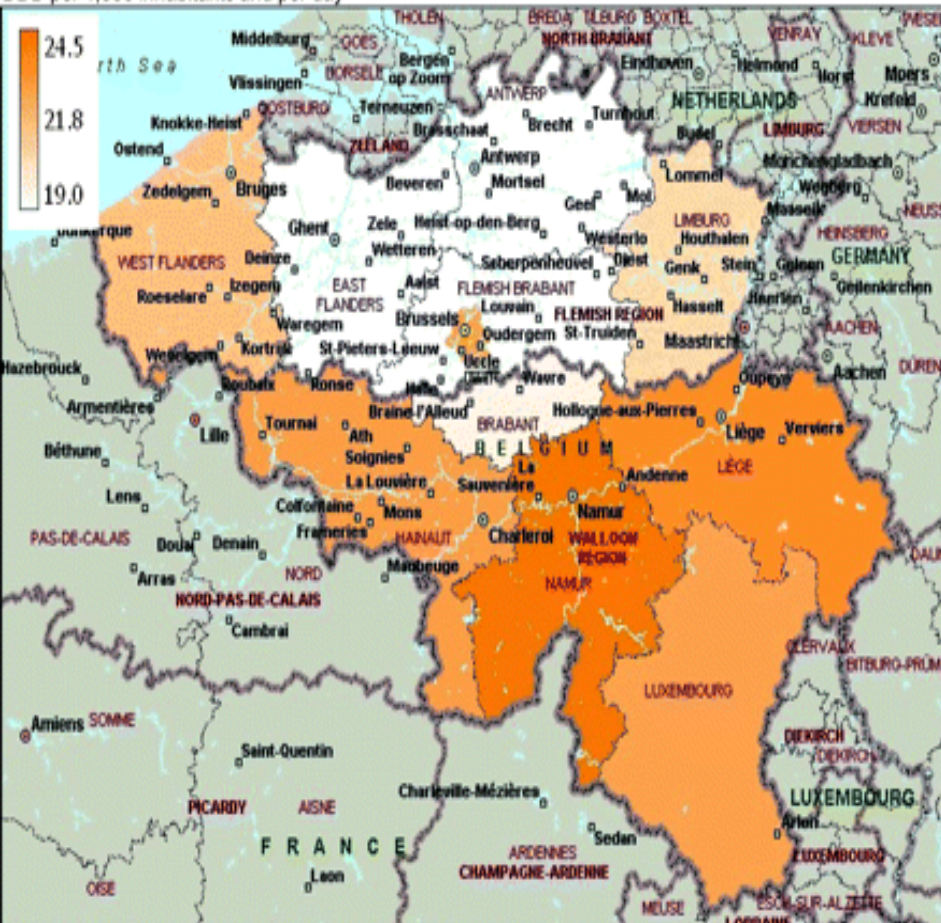
Jones et al (2008) Nature **451**, 990-993

Countries with XDR-TB confirmed cases as of February 2008



The boundaries and names shown on this map are for illustrative purposes only, and do not constitute the expression of any opinion on the part of WHO concerning the legal status of any country, territory, city or area or its authorities, or concerning the delimitation of its frontiers or boundaries. Other names are not meant to be official. The boundaries for which data may not yet be available are shown in grey. © WHO 2008. All rights reserved.

DD per 1,000 inhabitants and per day



Consumption

Van Eldere et al, AAC, 2007, 51,3491-7

Proximity to France as a Risk for Multiple Resistance in Belgium



Clonal spread of *S. pneumoniae* 23F



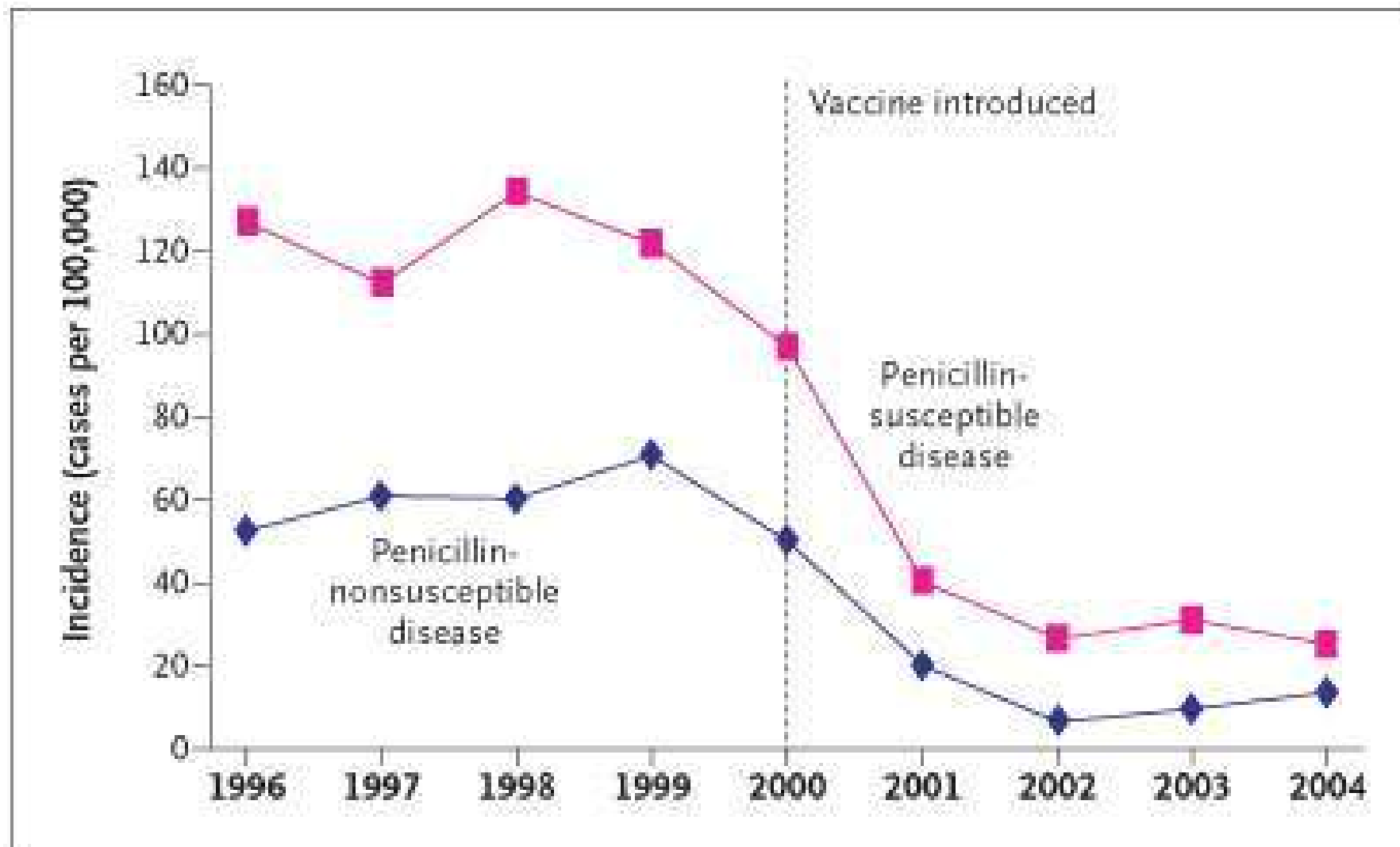
Vaccine efficacy – resistance to antibiotics – all children - ITT

	Cases in control group	Cases in vaccine group	Vaccine efficacy	95% confidence interval
Penicillin	21	7	67	19 - 88
Cotrimoxazole	32	14	56	16 – 78
Any	39	17	56	21 - 77

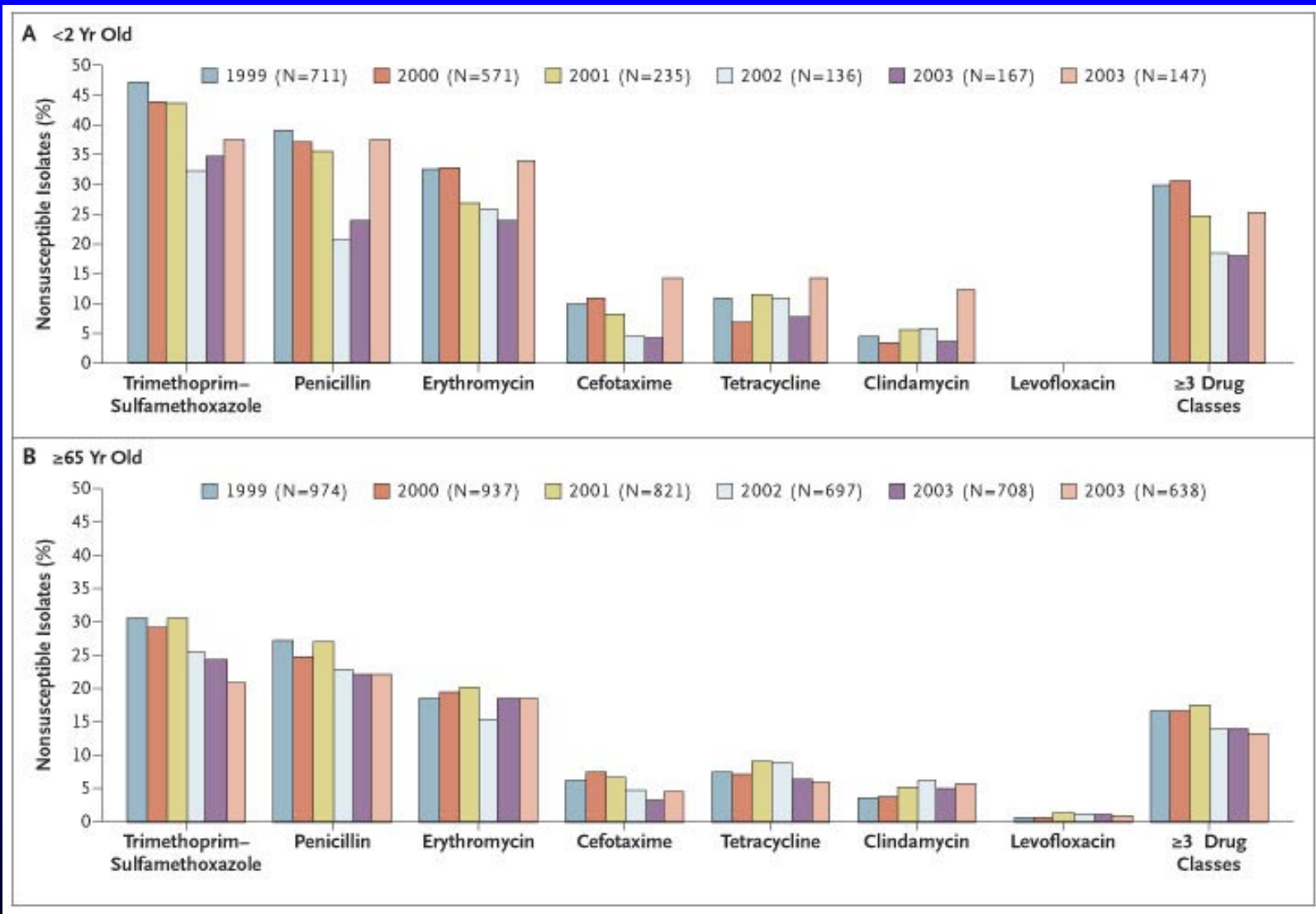
Klugman et al, 2003, NEJM, 349,1341-8

In the cotrimoxazole group
29 and 13 are HIV +ve – VE 55%

Children Less Than Two Years of Age

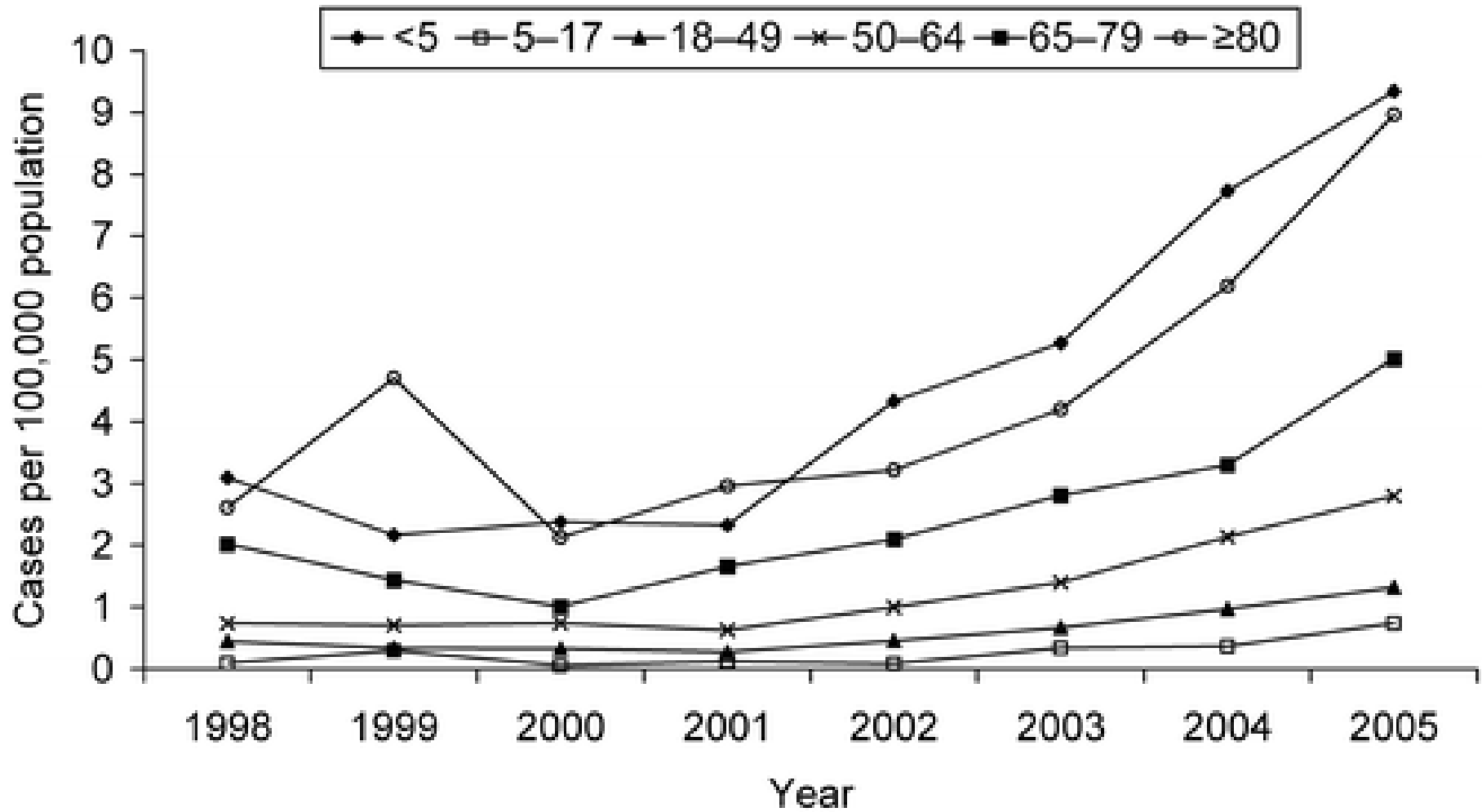


Effect of introduction of PCV-7 on drug-resistant *S. pneumoniae*

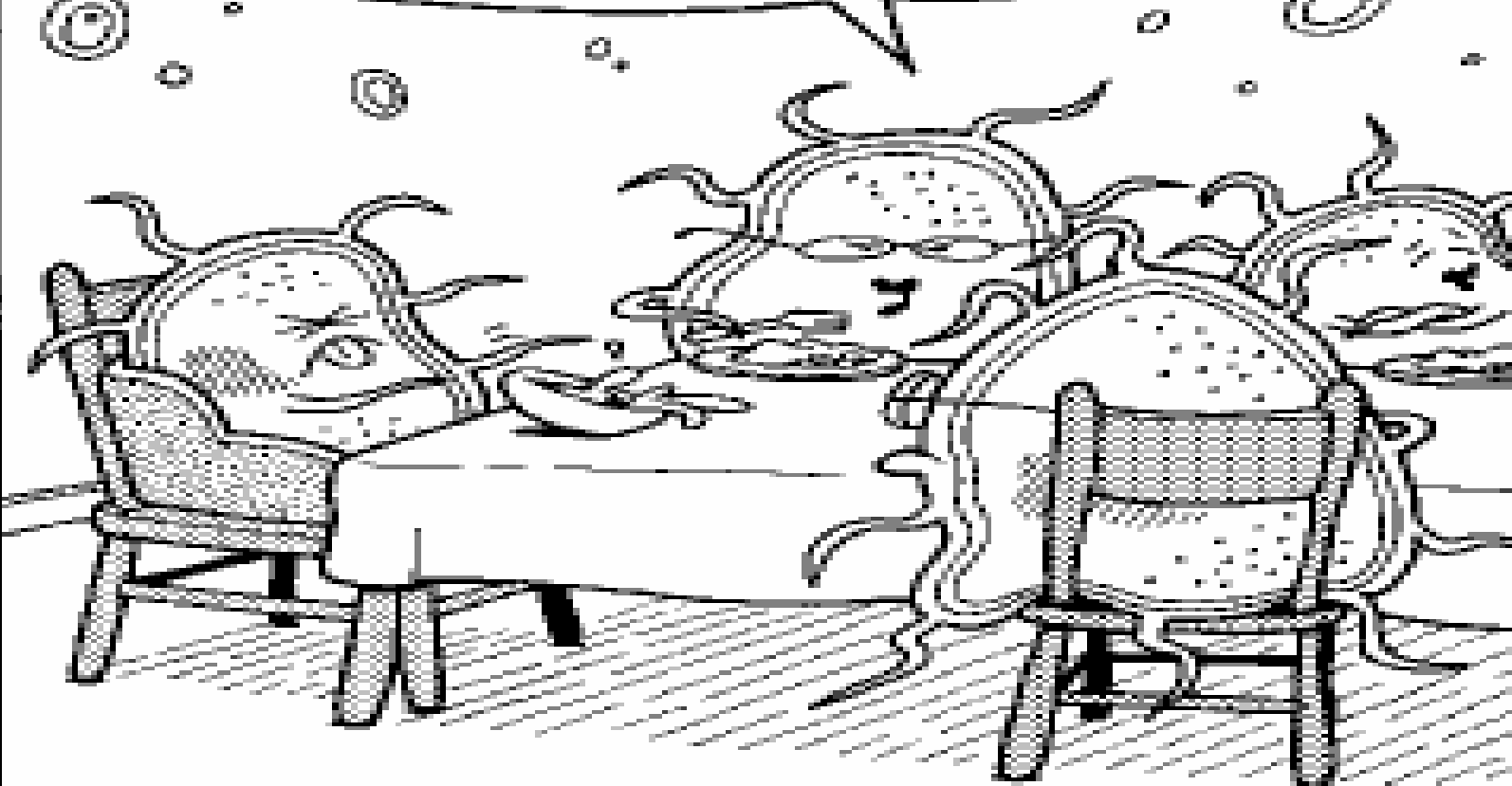




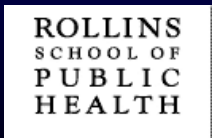
Serotype 19A



IS IT ME, OR DO OUR KIDS SEEM MUCH MORE RESISTANT THAN WE EVER WERE?



Slide courtesy John McGowan, Emory U



Urban vs Rural

- Carriage of resistant strains was compared between a cluster randomized sample of children in rural Lesotho villages, some accessible only by donkey; and similarly aged children from Maseru, the capital.
- Pen R 6.4% urban vs 2% rural (P=0.046)
- Tet R 4.6% urban vs 0.5% rural (P=0.01)
- Urban kids had more recent antibiotic use (OR 8.8, P<0.01); more history of past hospitalization (OR 24.8, P < 0.001); more day care attendance (OR 13.1, P<0.001) but less other children < 5 in the household (OR 0.4, P< 0.001)

Selection of Resistant Pneumococci by High Dose, Short Duration Amoxicillin Rx, Dominican Republic

RELATIVE RISK OF PRSP IN CARRIERS

HIGH DOSE vs LOW DOSE	0.78 (0.65 – 0.95)	P = 0.01
DAY 28 vs DAY 0 HIGH DOSE	1.22 (1.02 – 1.48)	P = 0.03
DAY 28 vs DAY 0 LOW DOSE	1.60 (1.36 – 1.89)	P < 0.001

Schrag et al, JAMA, 2001, 286: 49 - 56