

Drivers of Antibiotic Resistance



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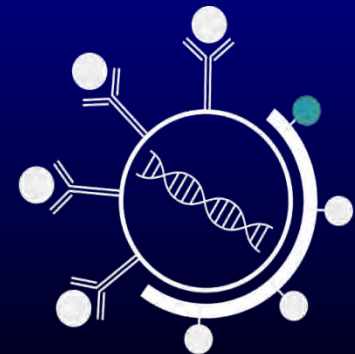
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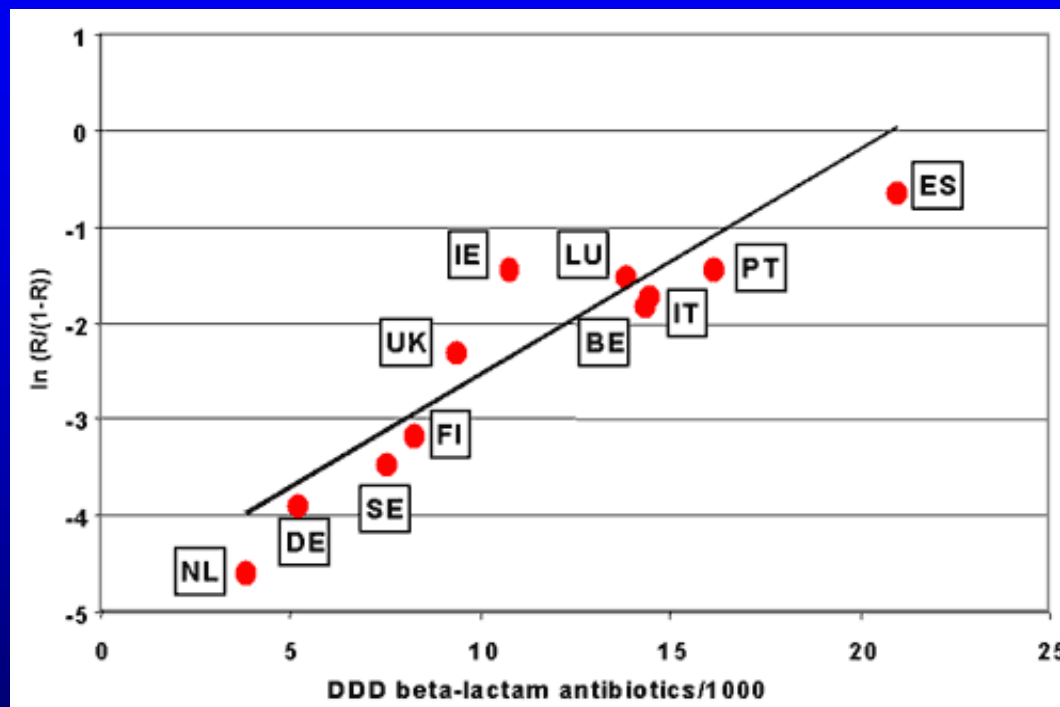


RMPRU

respiratory & meningeal pathogens research unit

Magnitude α Resistance

Association of Antibiotic Use with Resistance in the Pneumococcus

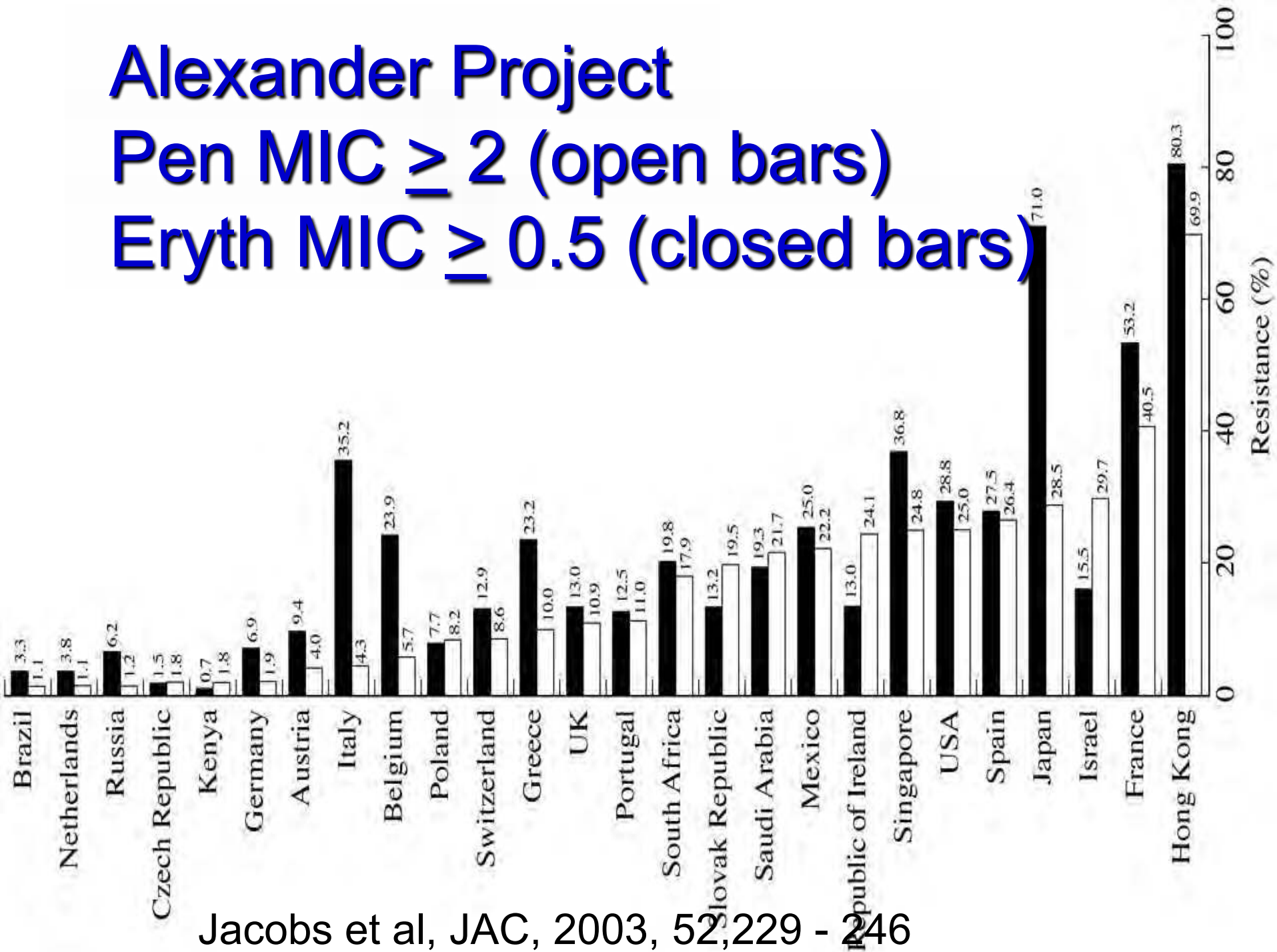


The log odds of resistance to penicillin among invasive isolates of *Streptococcus pneumoniae* (PNSP; $\ln(R/[1-R])$) is regressed against outpatient sales of beta-lactam antibiotics in 11 European countries

Alexander Project

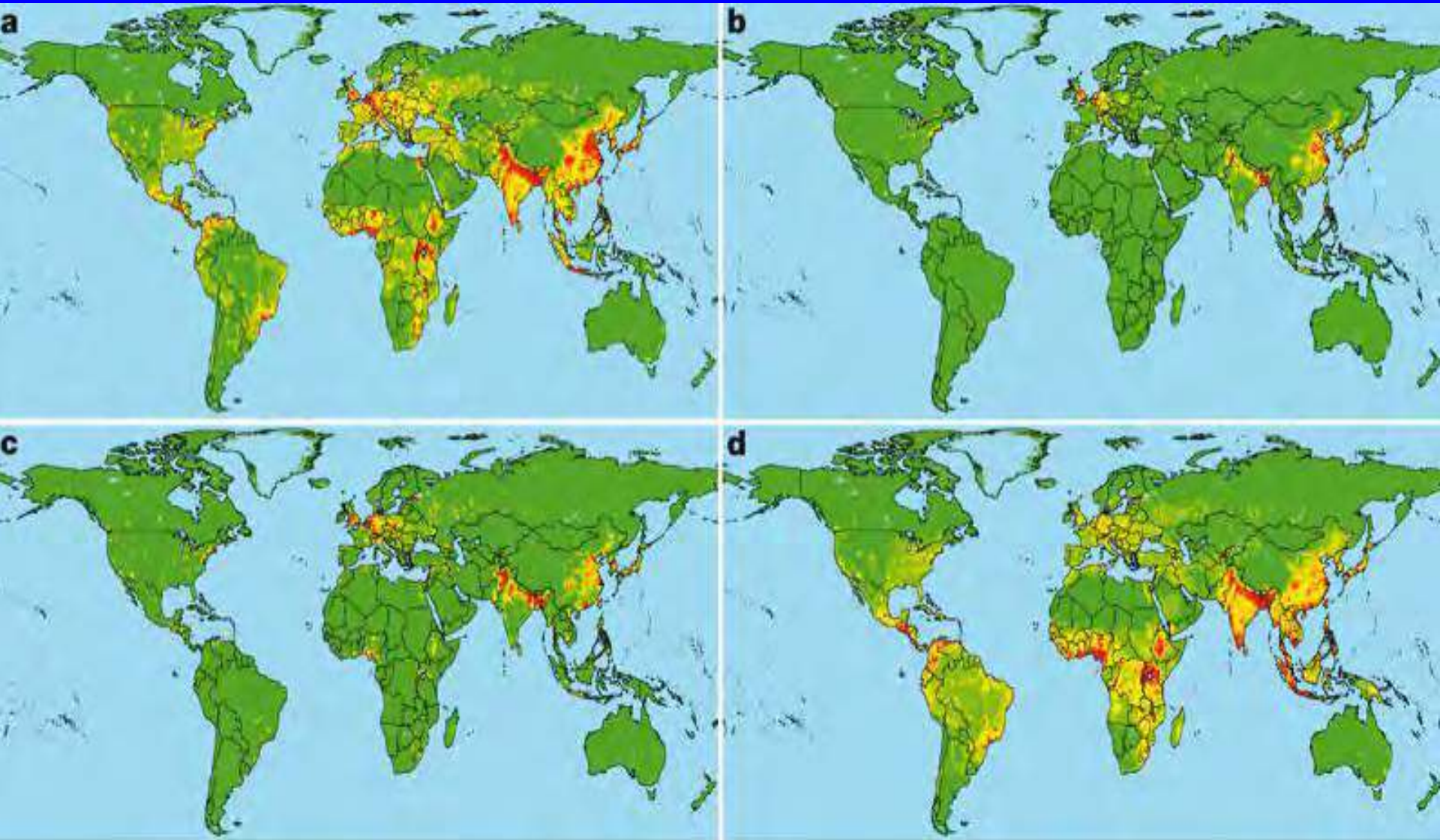
Pen MIC ≥ 2 (open bars)

Eryth MIC ≥ 0.5 (closed bars)



Zoonoses from wildlife

Zoonoses from non - wildlife

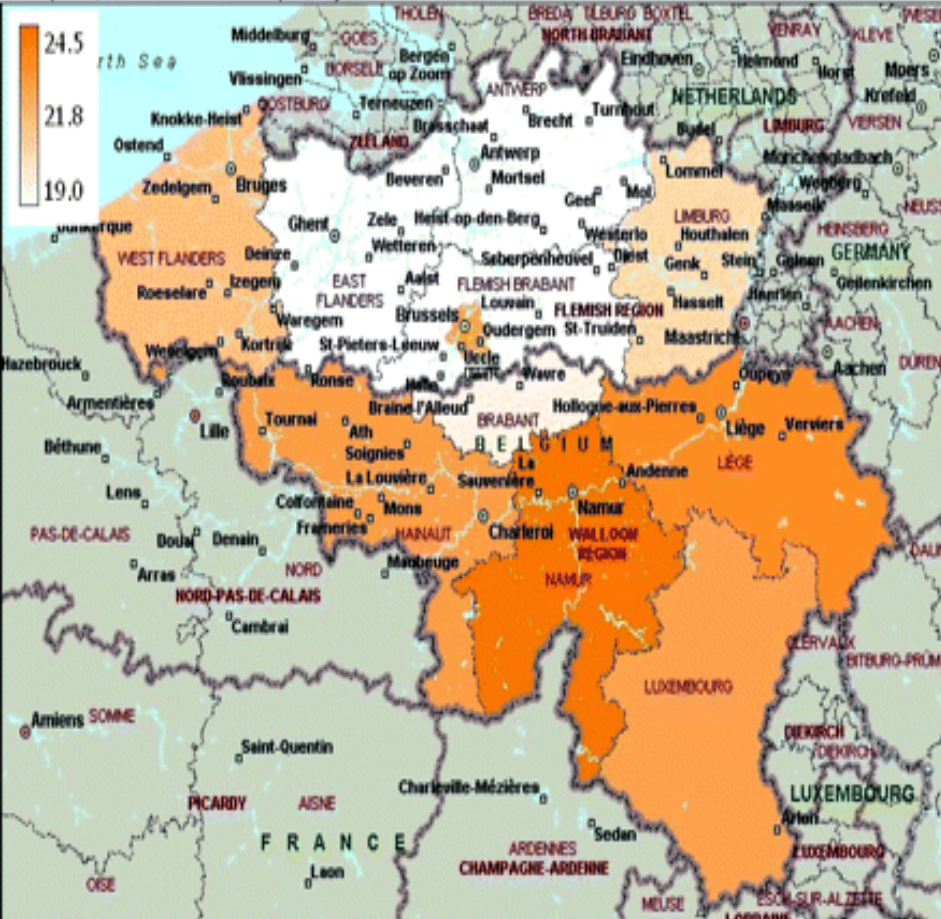


Antibiotic - resistance

Vector borne

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

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



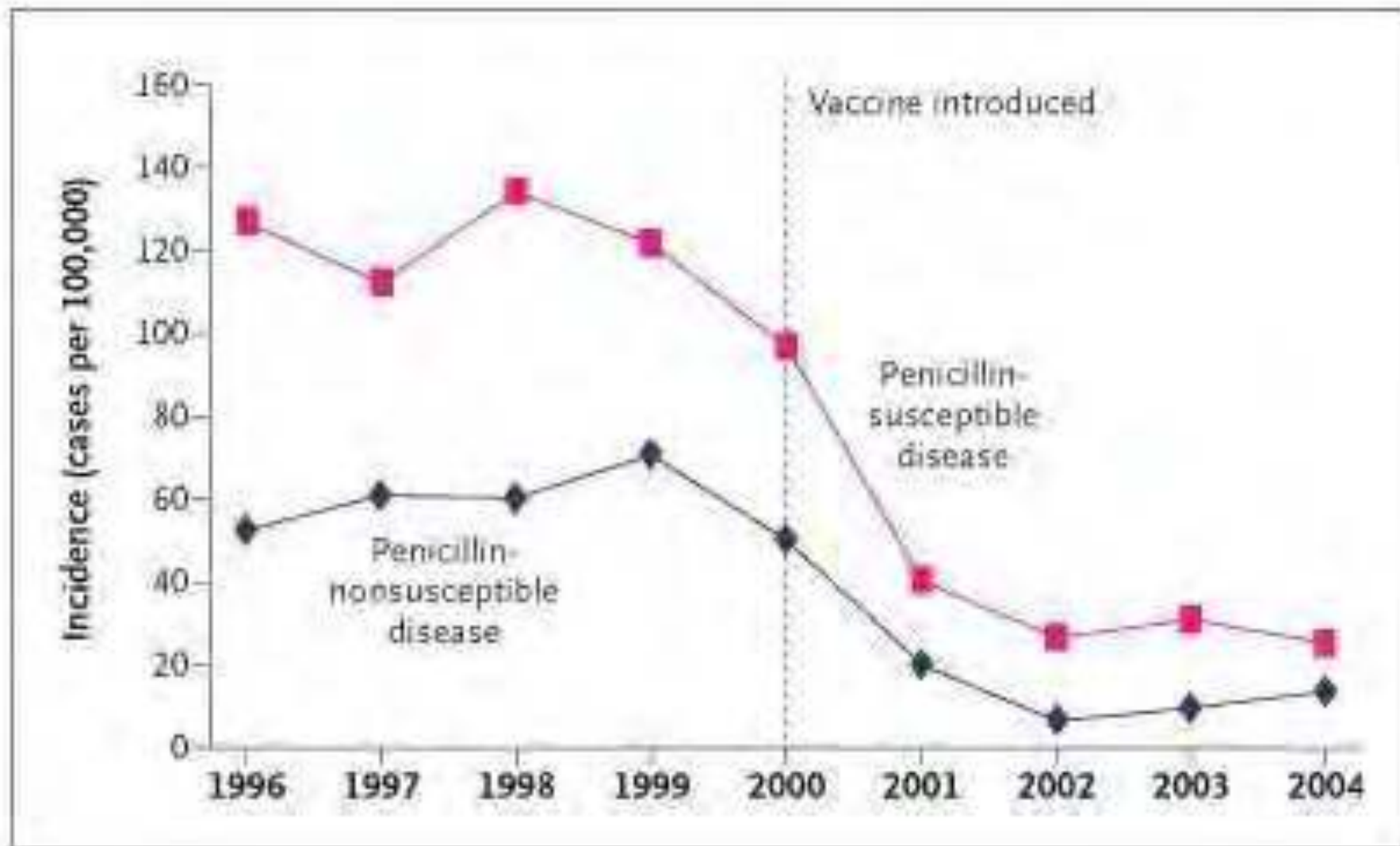
Vaccine efficacy – resistance to antibiotics – all children - ITT

	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

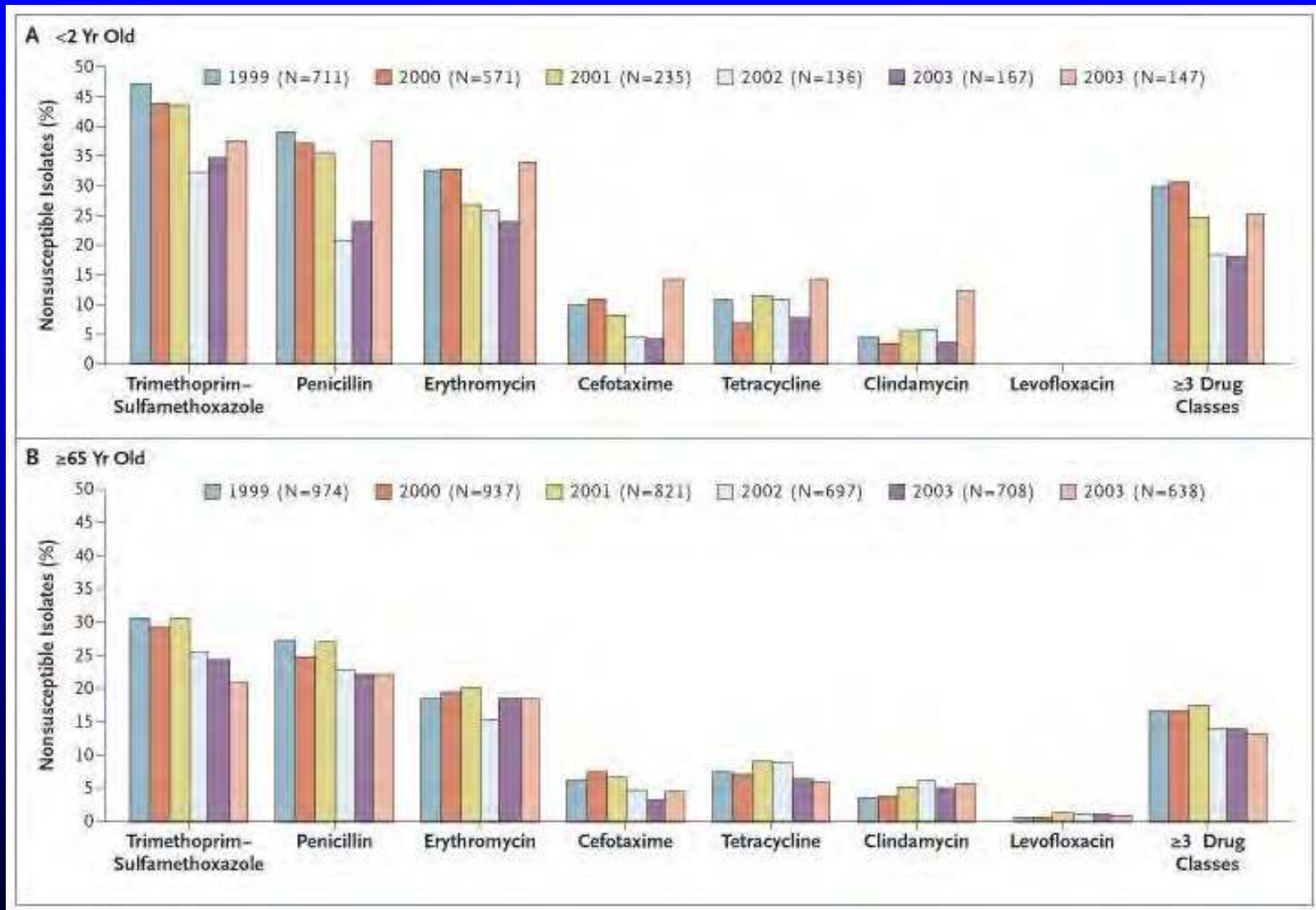
Klugman et al, 2003, NEJM, 349,1341-8

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

Children Less Than Two Years of Age

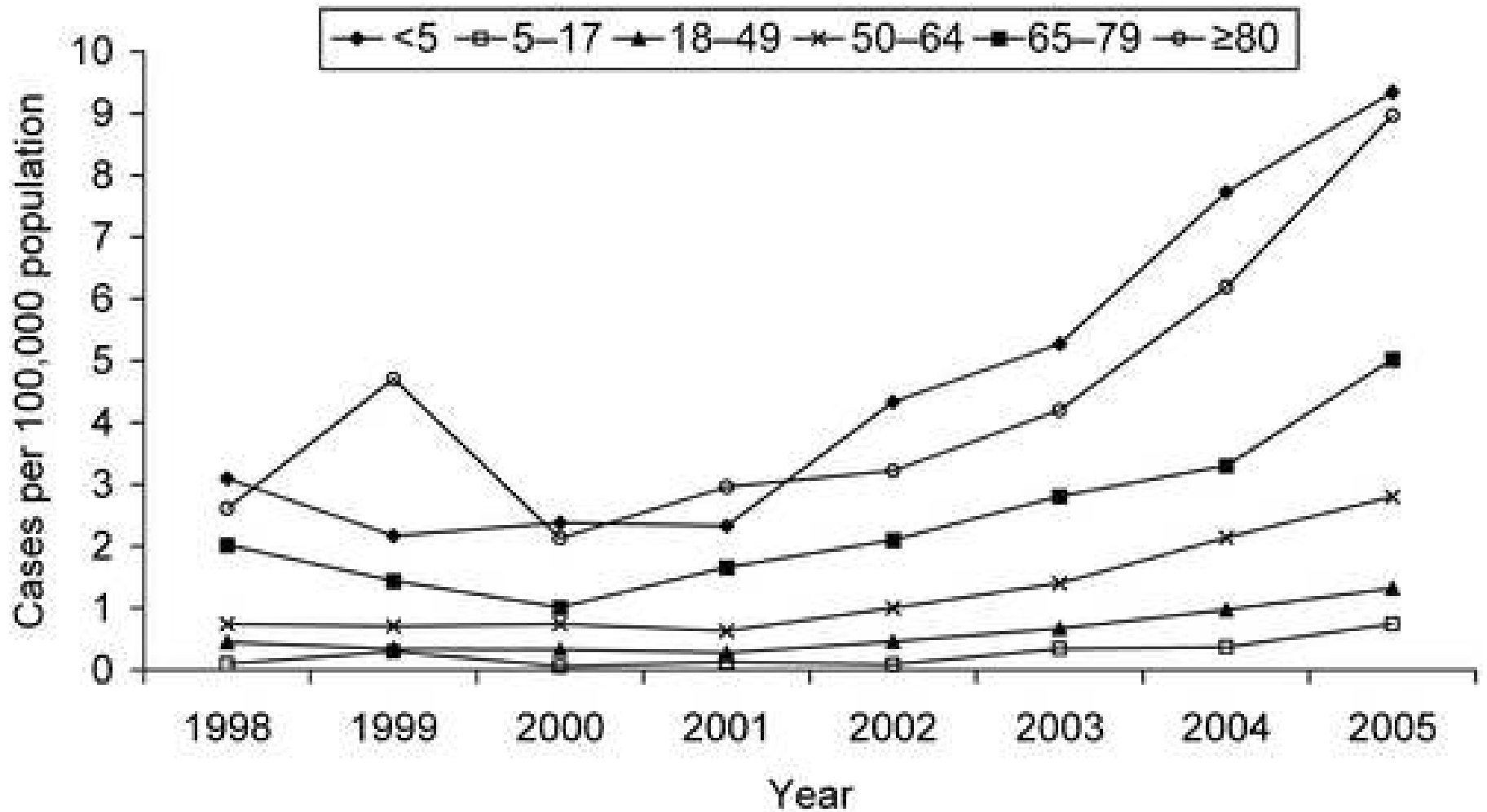


Effect of introduction of PCV-7 on drug-resistant *S. pneumoniae*

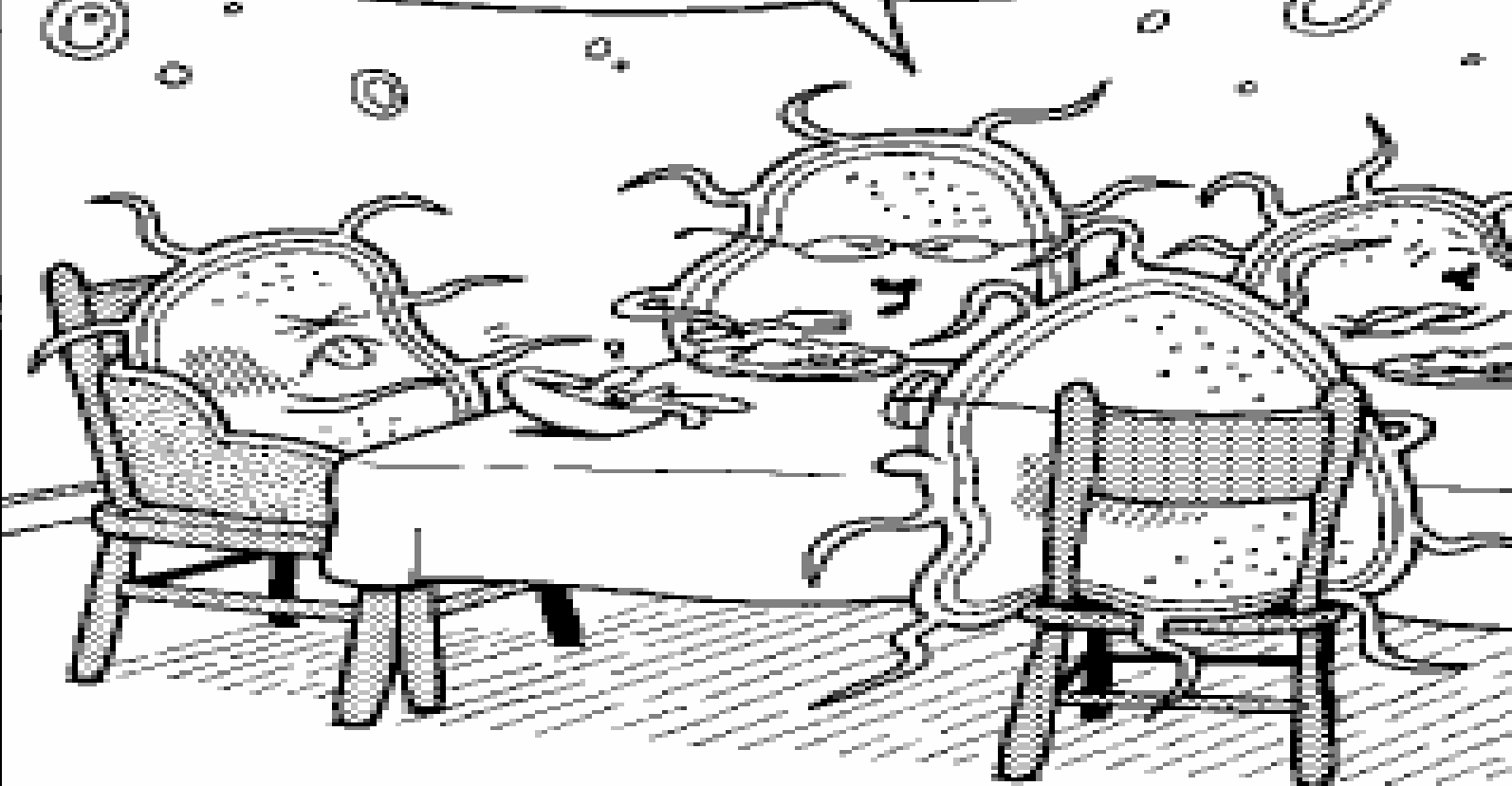




Serotype 19A



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

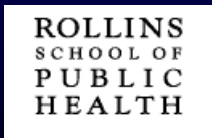


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Slide courtesy John McGowan, Emory U



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