Antibiotic Resistance: A Challenge to Public Health in India

Ramanan Laxminarayan

Public Health Foundation of India

Global Antibiotic Resistance Partnership

PUBLIC HEALTH FOUNDATION OF INDIA

THE BRITISH JOURNAL

OF

EXPERIMENTAL PATHOLOGY

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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
...He Will Come Home !

Main Messages

1. Bacterial diseases are still major killers
2. Rising incomes are leading to increased antibiotic consumption
3. Increasing levels of resistance to first line drugs
4. However, many still do not have access to effective drugs
5. Second line drugs may be unaffordable to many low-income families
6. Challenges lie in improving access without destroying drug effectiveness – a global public good

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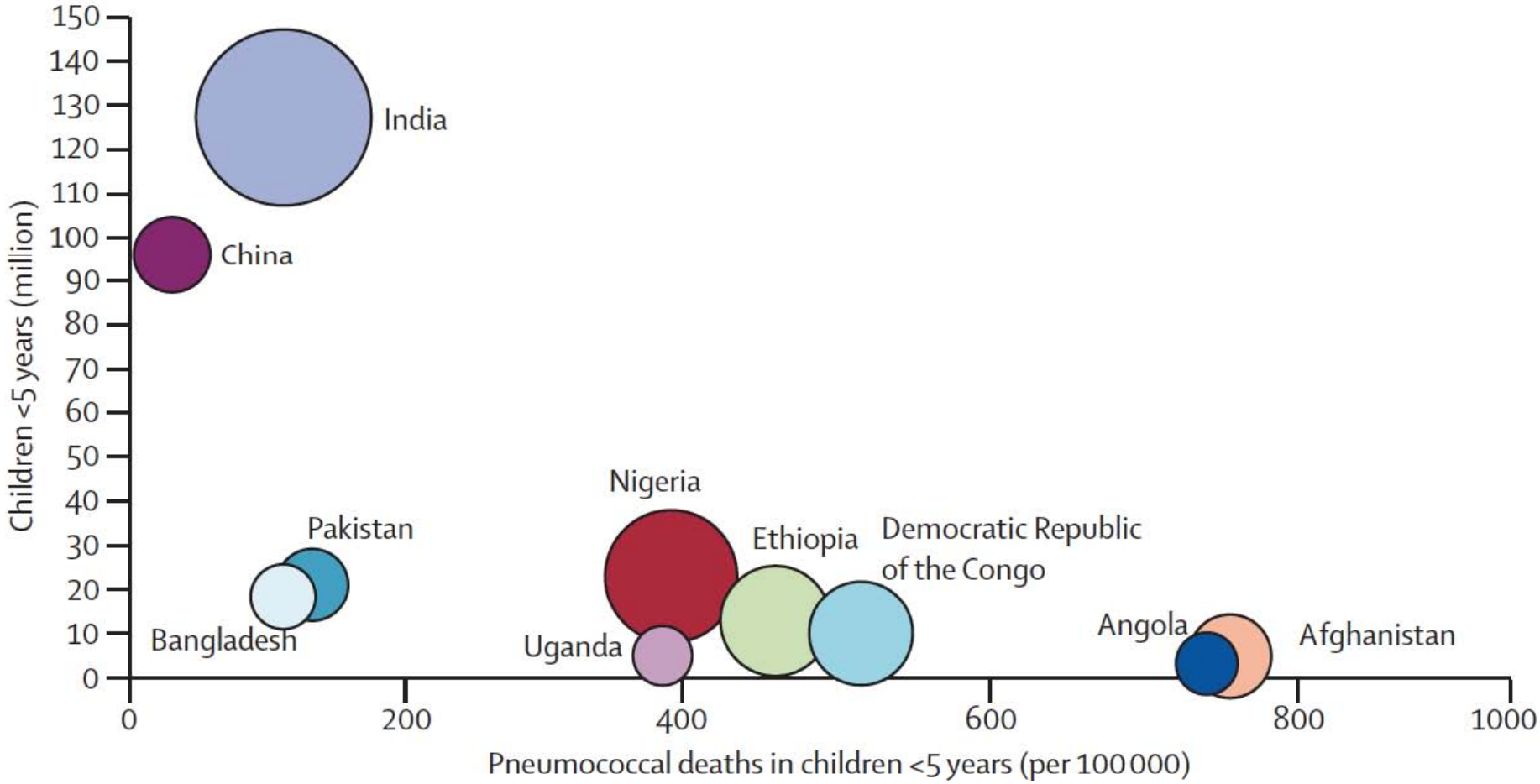
Continuing high burden of pneumococcal deaths in under fives



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O'Brien et al, Lancet 2009

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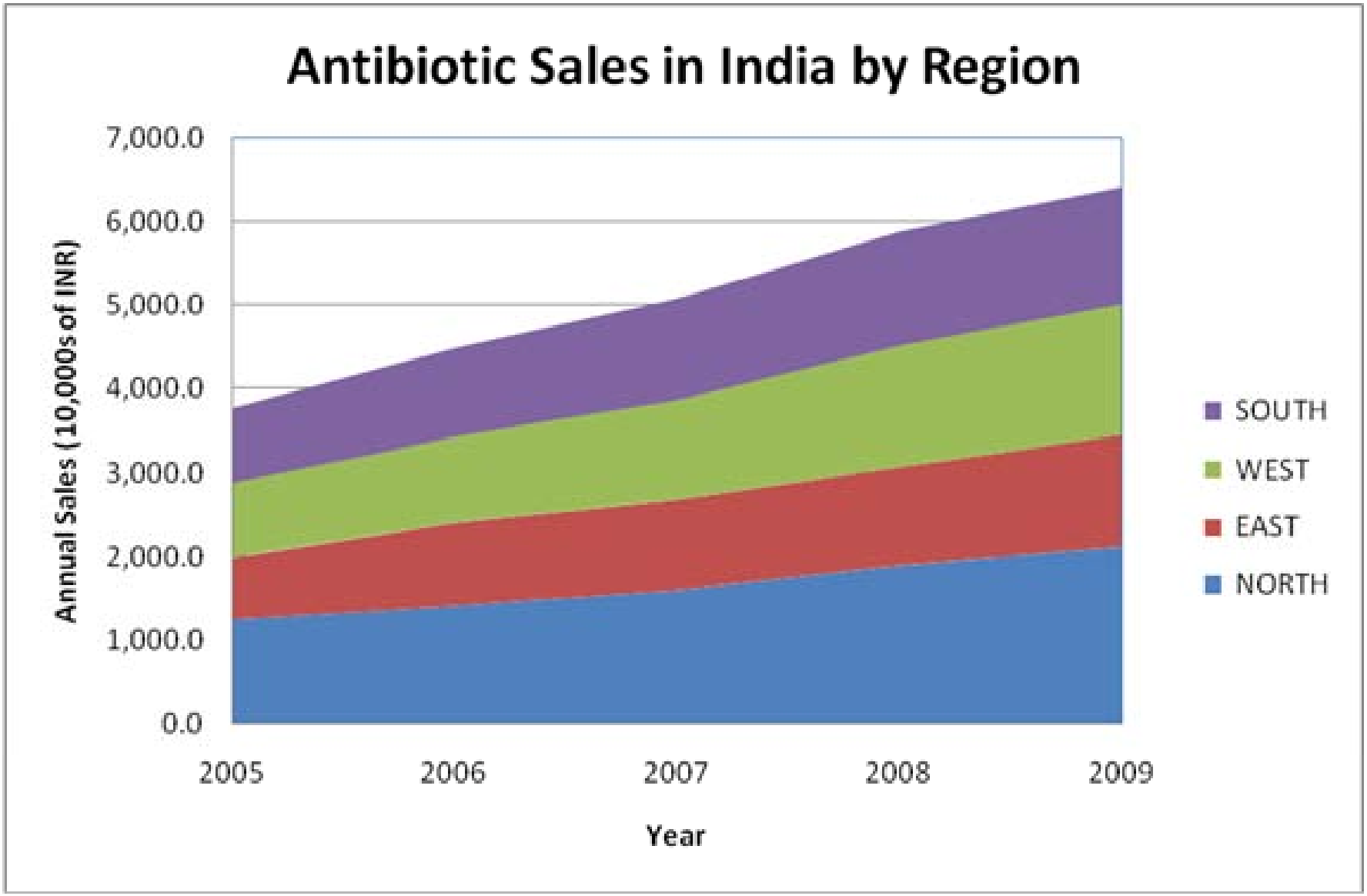

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Source: ORG IMS data from India

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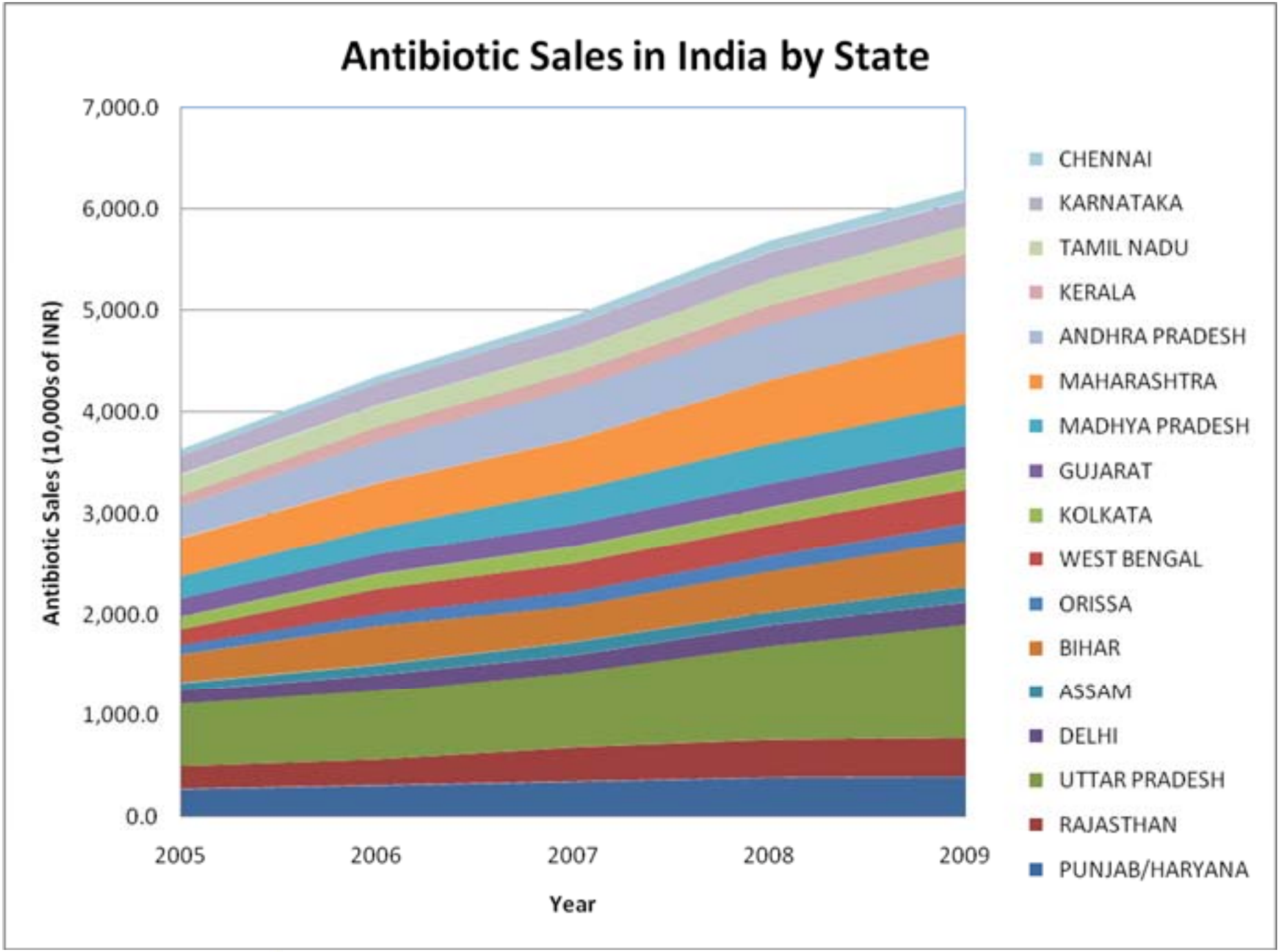
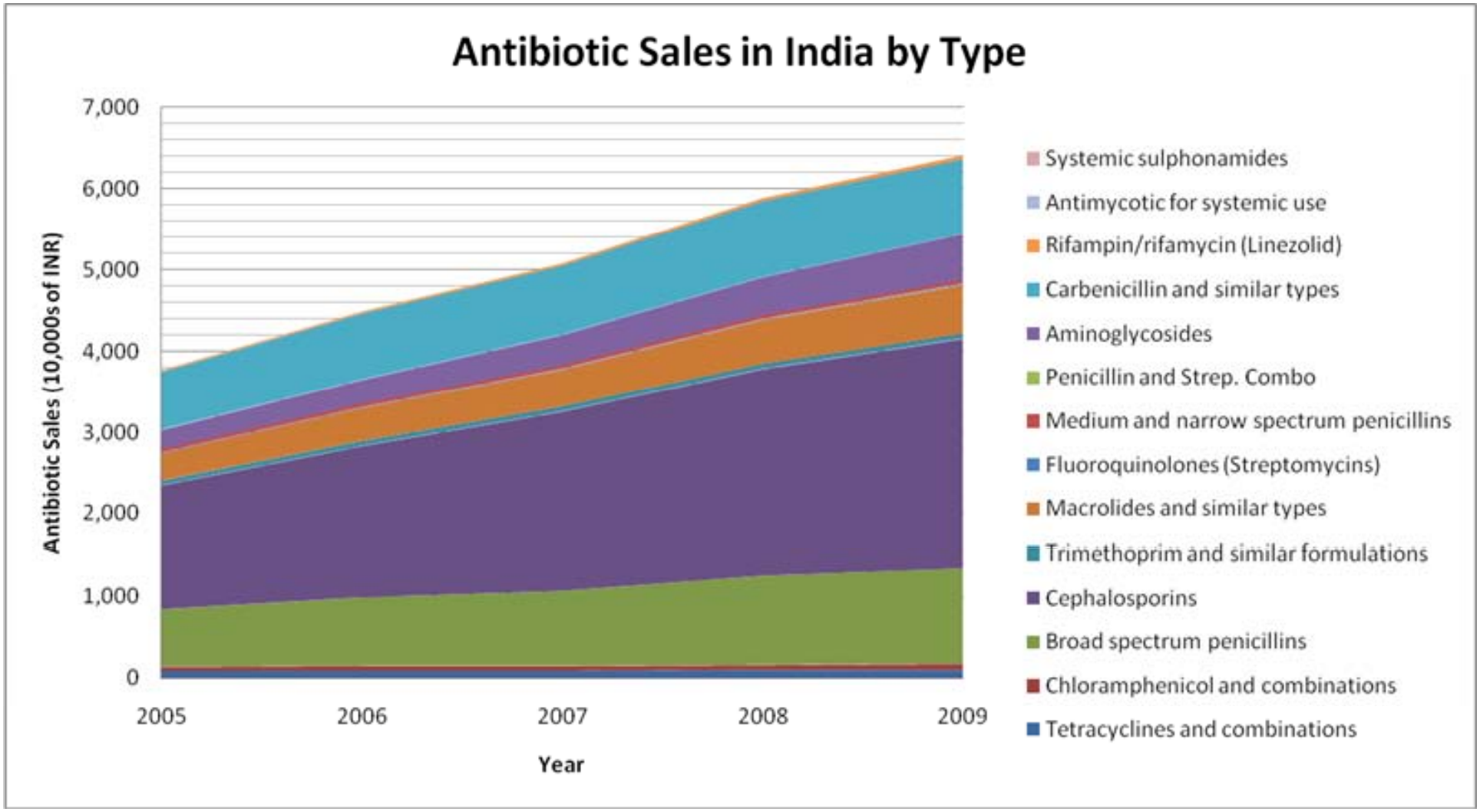

Antibiotic Sales in India by State
7,000.0
6,000.0
5,000.0
4,000.0
3,000.0
2,000.0
1,000.0
0.0
Antibiotic Sales (10,000s of INR)
2005
2006
2007
2008
2009
Year
CHENNAI
KARNATAKA
TAMIL NADU
KERALA
ANDHRA PRADESH
MAHARASHTRA
MADHYA PRADESH
GUJARAT
KOLKATA
WEST BENGAL
ORISSA
BIHAR
ASSAM
DELHI
UTTAR PRADESH
RAJASTHAN
PUNJAB/HARYANA



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Source: ORG IMS data from India

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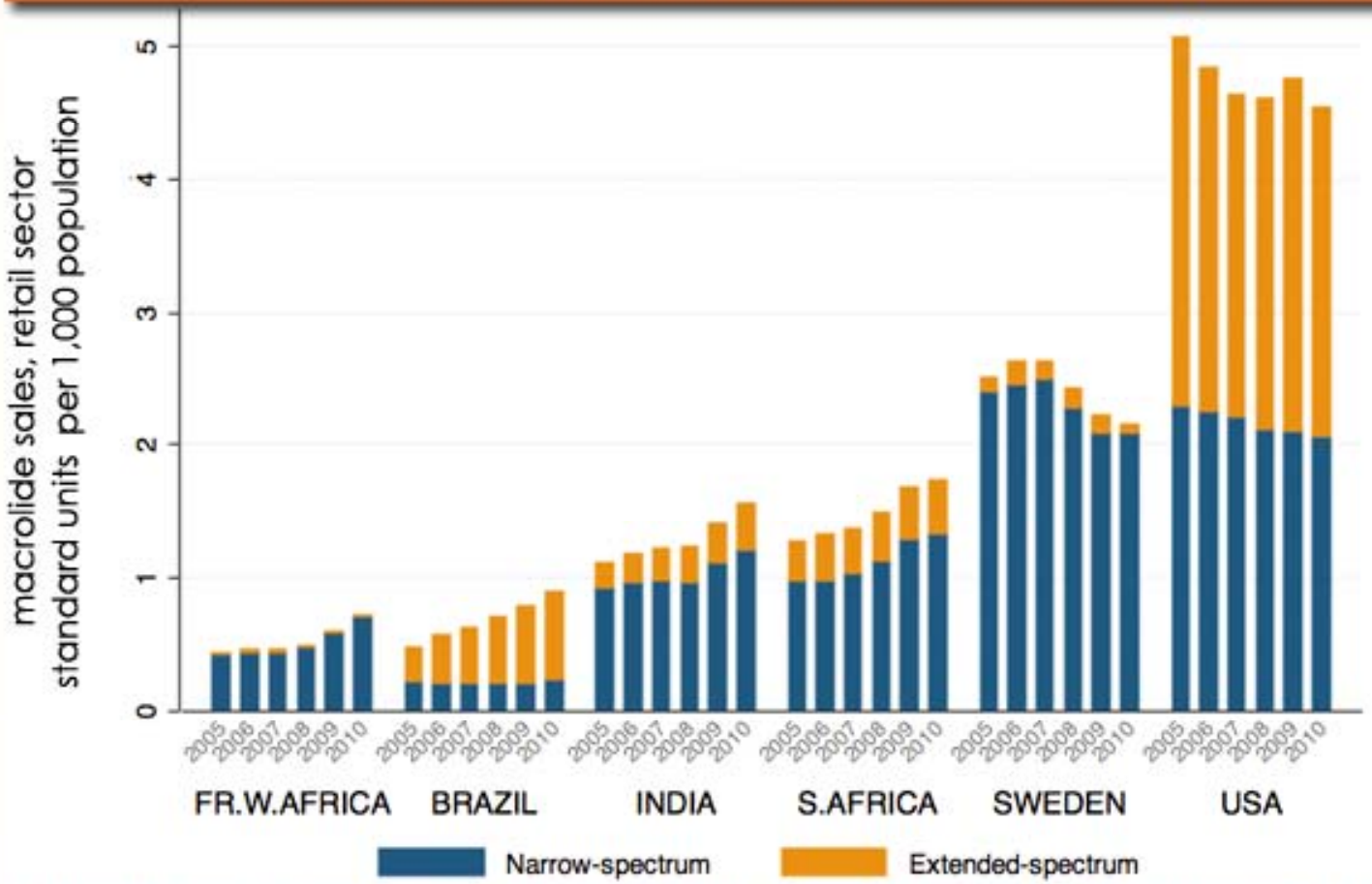
Extended-spectrum macrolide use is highly prevalent in the United States, and increasing in developing countries



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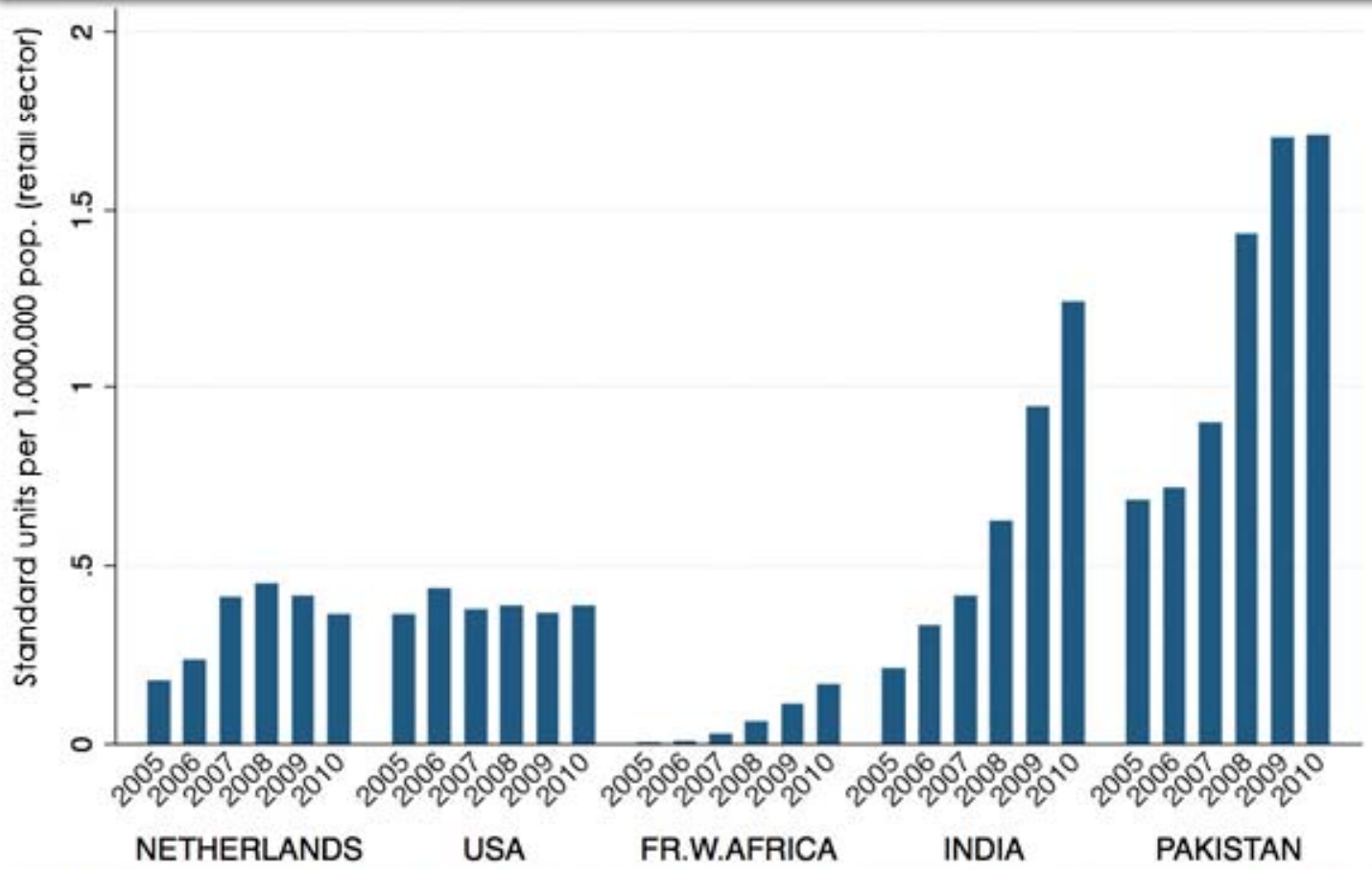
Retail sales of carbapenem antibiotics to treat Gram-negative bacteria are increasing rapidly in India and Pakistan



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Antibiotic use for growth promotion and disease prevention

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ATION

Over half of antibiotics produced in the US are used in agriculture

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Sensitivity to antibiotics in a Delhi hospital (Gram Positives)

GPC	No. of Isolates	Penicillin	Ampicillin	Oxacillin	Ceftriaxone	Clindamycin	Gentamicin	High Dose Gentamicin	Quinolones	Vancomycin/ Teicoplanin	Linezolid	Tigecycline	Daptomycin
Staph. aureus	20	0	-	55	-	75	63	-	5	100	-	100	100
	20	0	-	45	-	65	60	-	26	100	-	100	100
	27	0	-	41	-	44	37	-	11	100	-	100	100
Staphylococci spp. (CONS)	102	6	-	36	-	64	76	-	45	100	-	100	-
	205	4	-	21	-	48	66	-	36	100	-	100	-
	215	1	-	8	-	32	32	-	20	100	-	100	-
Enterococci spp.	7	-	29	-	-	-	-	29	-	57	100	100	100
	25	-	36	-	-	-	-	33	-	56	100	100	100
	47	-	19	-	-	-	-	14	-	72	100	100	100
Strept. pneumoniae	10	90*	-	-	100	-	0	-	100	100	-	-	-
	3	100	-	-	100	-	100	-	100	100	-	-	-
	5	100	-	-	100	-	0	-	100	100	-	-	-

- Not done
** 1 isolate was moderately sensitive*

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GPC	No. of Isolates	Penicillin	Ampicillin	Oxacillin	Ceftriaxone	Clindamycin	Gentamicin	High Dose Gentamicin	Quinolones	Vancomycin/ Teicoplanin	Linezolid	Tigecycline	Daptomycin
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	20	0	-	45	-	65	60	-	26	100	-	100	100
	27	0	-	41	-	44	37	-	11	100	-	100	100
Staphylococci spp. (CONS)	102	6	-	36	-	64	76	-	45	100	-	100	-
	205	4	-	21	-	48	66	-	36	100	-	100	-
	215	1	-	8	-	32	32	-	20	100	-	100	-
Enterococci spp.	7	-	29	-	-	-	-	29	-	57	100	100	100
	25	-	36	-	-	-	-	33	-	56	100	100	100
	47	-	19	-	-	-	-	14	-	72	100	100	100
Strept. pneumoniae	10	90*	-	-	100	-	0	-	100	100	-	-	-
	3	100	-	-	100	-	100	-	100	100	-	-	-
	5	100	-	-	100	-	0	-	100	100	-	-	-

- Not done
** 1 isolate was moderately sensitive*

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Sensitivity to antibiotics in a Delhi hospital (Gram Negatives)

GNB	No. of Isolates	Ampicillin	Cefuroxime	Ceftriaxone	Ceftazidime	Cefepime	Aztreonam	Ampicillin+ Sulbactum	Piperacillin+ Tazobactum	Cefoperazone+ Sulbactum	Co-Trimoxazole	Chloramphenicol	Nalidixic Acid	Quinolones	Gentamicin	Amikacin	Ertapenem	Imipenem / Meropenem	Colistin	Tigecycline
Salmonella typhi	149	93	-	100	-	-	-	-	-	-	91	93	7	73	-	-	-	-	-	-
	80	94	-	100	-	-	-	-	-	-	91	95	8	71	-	-	-	-	-	-
	5	100	-	100	-	-	-	-	-	-	100	100	0	80	-	-	-	-	-	-
Salmonella paratyphi A	69	97	-	100	-	-	-	-	-	-	100	100	0	100	-	-	-	-	-	-
	32	97	-	100	-	-	-	-	-	-	100	100	0	97	-	-	-	-	-	-
	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
E. coli	52	8	22	25	-	27	27	-	79	83	-	-	-	13	42	94	98	98	100	100
	54	8	5	15	-	22	17	-	74	81	-	-	-	9	50	91	90	96	100	98
	40	3	7	8	-	8	8	-	45	54	-	-	-	12	39	75	78	78	100	100
Klebsiella spp.	10	-	43	40	-	50	40	-	80	80	-	-	-	60	60	90	90	100	100	100
	43	-	10	9	-	9	9	-	30	30	-	-	-	12	23	49	50	58	100	63
	104	-	10	10	-	10	10	-	24	22	-	-	-	12	18	42	33	43	100	63
Enterobacter spp.	5	-	40	80	-	80	80	-	60	80	-	-	-	80	80	80	80	80	100	75
	7	-	67	57	-	57	57	-	86	86	-	-	-	57	57	86	86	86	100	100
	14	-	20	7	-	7	7	-	14	8	-	-	-	7	8	21	15	21	100	86
P. aeruginosa	2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	13	-	-	-	42	50	58	-	62	42	-	-	-	62	62	62	-	62	100	-
	30	-	-	-	36	30	24	-	40	23	-	-	-	33	30	33	-	28	100	-
Acinetobacter spp.	7	-	-	50	-	86	43	100	86	86	-	-	-	83	86	86	-	86	100	83
	23	-	-	11	-	26	25	33	43	46	-	-	-	35	30	32	-	36	100	91
	69	-	-	3	-	9	7	17	12	19	-	-	-	13	16	17	-	16	99	84

Sensitivity to antibiotics in a Delhi hospital (Gram Negatives)

GNB	No. of Isolates	Ampicillin	Cefuroxime	Ceftriaxone	Ceftazidime	Cefepime	Aztreonam	Ampicillin+ Sulbactum	Piperacillin+ Tazobactum	Cefoperazone+ Sulbactum	Co-Trimoxazole	Chloramphenicol	Nalidixic Acid	Quinolones	Gentamicin	Amikacin	Ertapenem	Imipenem / Meropenem	Colistin	Tigecycline
Salmonella typhi	149	93	-	100	-	-	-	-	-	-	91	93	7	73	-	-	-	-	-	-
	80	94	-	100	-	-	-	-	-	-	91	95	8	71	-	-	-	-	-	-
	5	100	-	100	-	-	-	-	-	-	100	100	0	80	-	-	-	-	-	-
Salmonella paratyphi A	69	97	-	100	-	-	-	-	-	-	100	100	0	100	-	-	-	-	-	-
	32	97	-	100	-	-	-	-	-	-	100	100	0	97	-	-	-	-	-	-
	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
E. coli	52	8	22	25	-	27	27	-	79	83	-	-	-	13	42	94	98	98	100	100
	54	8	5	15	-	22	17	-	74	81	-	-	-	9	50	91	90	96	100	98
	40	3	7	8	-	8	8	-	45	54	-	-	-	12	39	75	78	78	100	100
Klebsiella spp.	10	-	43	40	-	50	40	-	80	80	-	-	-	60	60	90	90	100	100	100
	43	-	10	9	-	9	9	-	30	30	-	-	-	12	23	49	50	58	100	63
	104	-	10	10	-	10	10	-	24	22	-	-	-	12	18	42	33	43	100	63
Enterobacter spp.	5	-	40	80	-	80	80	-	60	80	-	-	-	80	80	80	80	80	100	75
	7	-	67	57	-	57	57	-	86	86	-	-	-	57	57	86	86	86	100	100
	14	-	20	7	-	7	7	-	14	8	-	-	-	7	8	21	15	21	100	86
P. aeruginosa	2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	13	-	-	-	42	50	58	-	62	42	-	-	-	62	62	62	-	62	100	-
	30	-	-	-	36	30	24	-	40	23	-	-	-	33	30	33	-	28	100	-
Acinetobacter spp.	7	-	-	50	-	86	43	100	86	86	-	-	-	83	86	86	-	86	100	83
	23	-	-	11	-	26	25	33	43	46	-	-	-	35	30	32	-	36	100	91
	69	-	-	3	-	9	7	17	12	19	-	-	-	13	16	17	-	16	99	84

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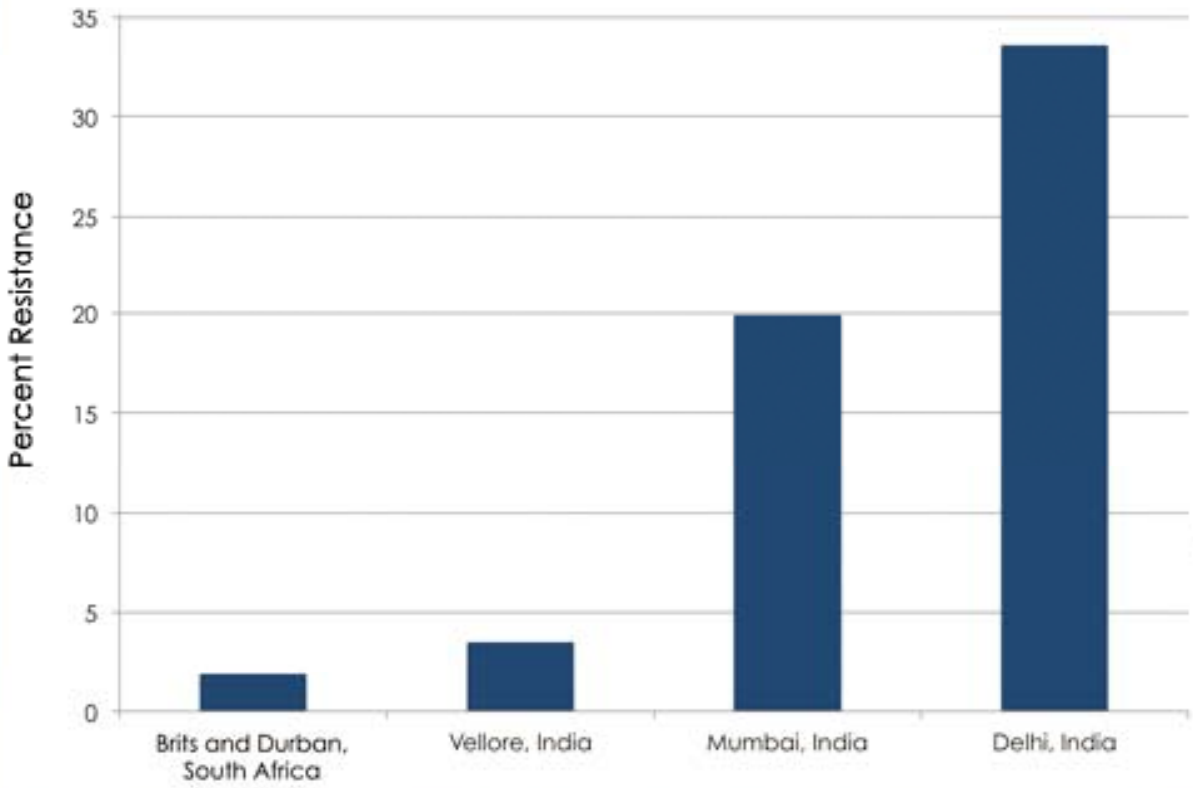
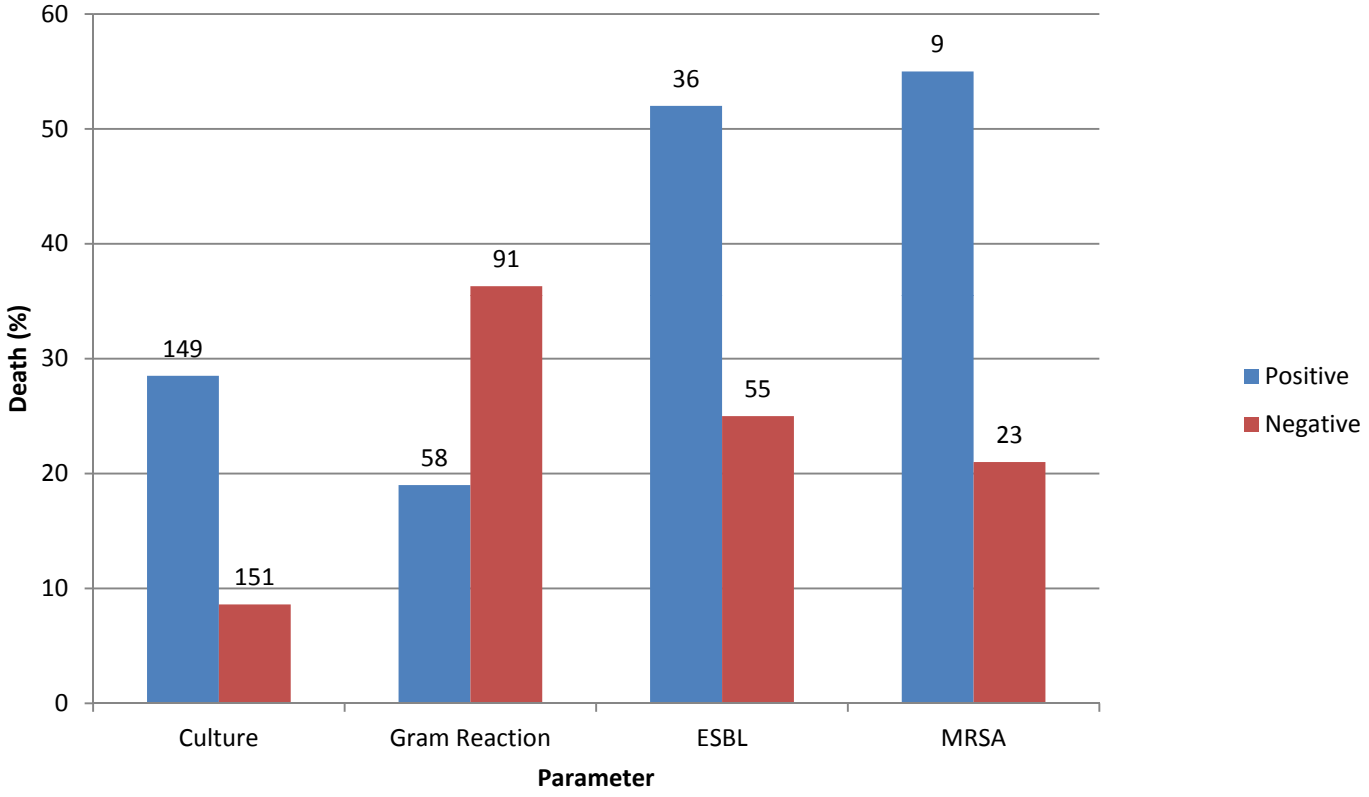
Community-level *E. coli* resistance to ciprofloxacin is high in India, particularly in Delhi



*Note: All cultures sampled from the community setting between 2002 and 2005 from women at risk for UTI infection residing near major hospital centers; Results for India include only commensal bowel isolates; Results for South Africa include commensal bowel and pathogenic urine isolates.

Source: Holloway, K., E. Mathai, et al. (2009). Community-Based Surveillance of Antimicrobial Use and Resistance in Resource-Constrained Settings. Report on five pilot projects. US Agency for International Development. Geneva, World Health Organization.

Mortality outcomes are worse in neonates with resistant infections



Kayange M, Kamugisha E, Mwizamholya DL, Jeremiah S, Mshana SE. 2010. Predictors of positive blood culture and deaths among neonates with suspected neonatal sepsis in a tertiary hospital, Mwanza-Tanzania. BMC Pediatrics 10: 39.

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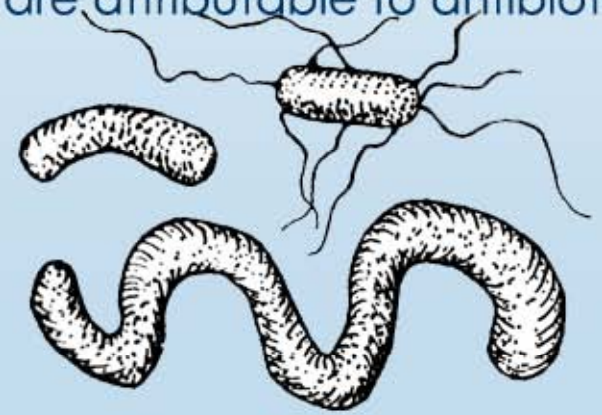
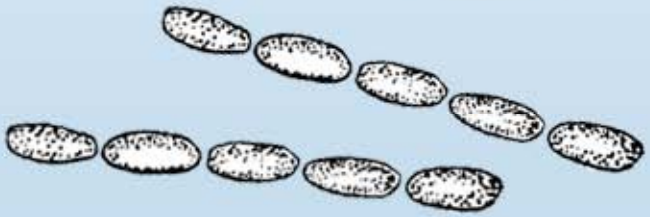
The Burden of Antibiotic Resistance in Indian Neonates

1 million Indian children die in the **first 4 weeks** of life each year...

Of these deaths, **190,000** are caused by sepsis, a bacterial infection that overtakes the bloodstream.

58,319, or **just over 30%**, of neonatal sepsis deaths are attributable to antibiotic resistance.





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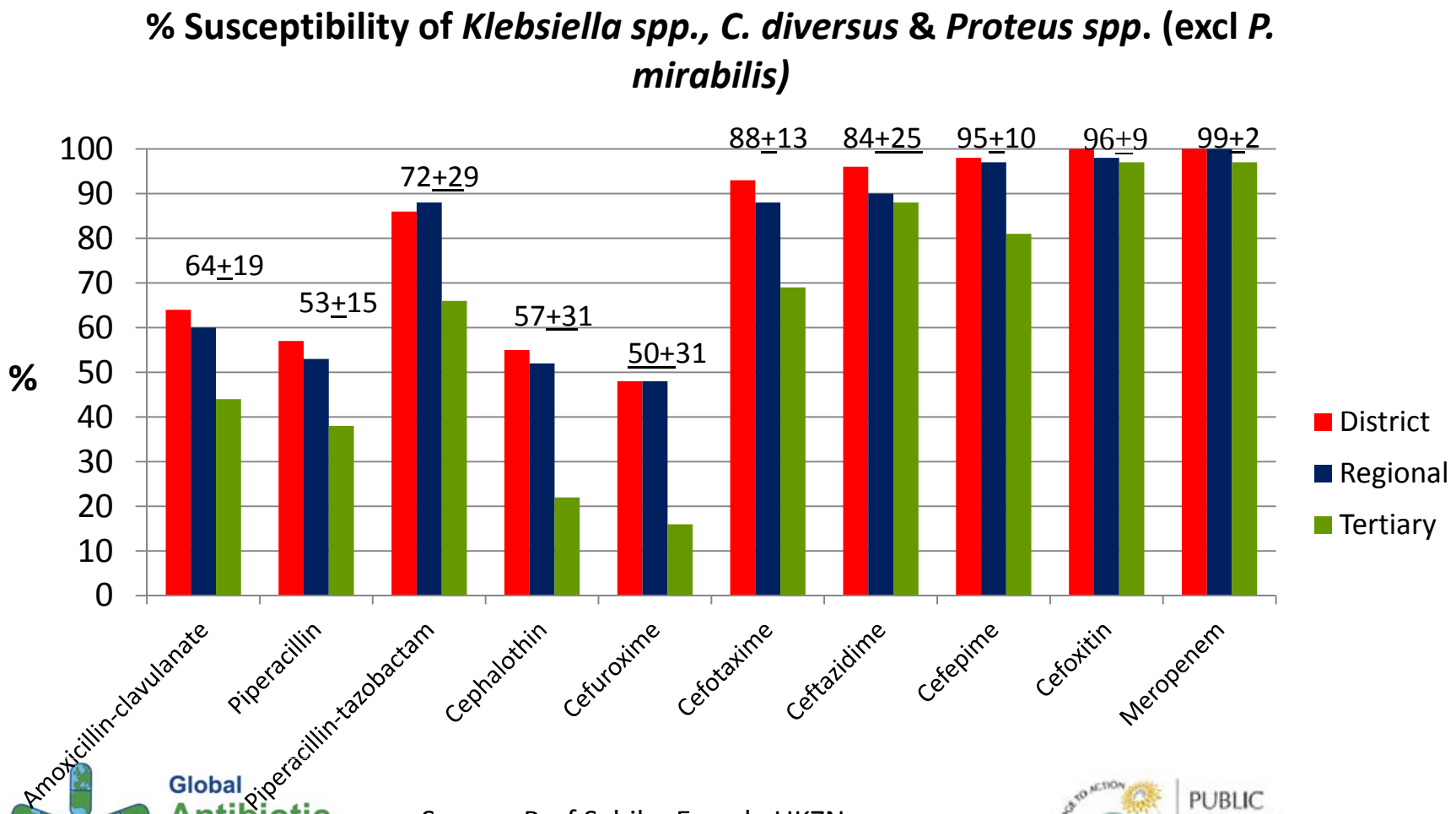
Sources: Sankar, Jeeva M., et al. 2008. Sepsis in the Newborn. AIIMS- NICU protocols. www.newbornwhocc.org.
Kayange, N., et al. 2010. Predictors of positive blood culture and deaths among neonates with suspected neonatal sepsis in a tertiary hospital, Mwanza- Tanzania. *BMC Pediatrics*. (10)39.

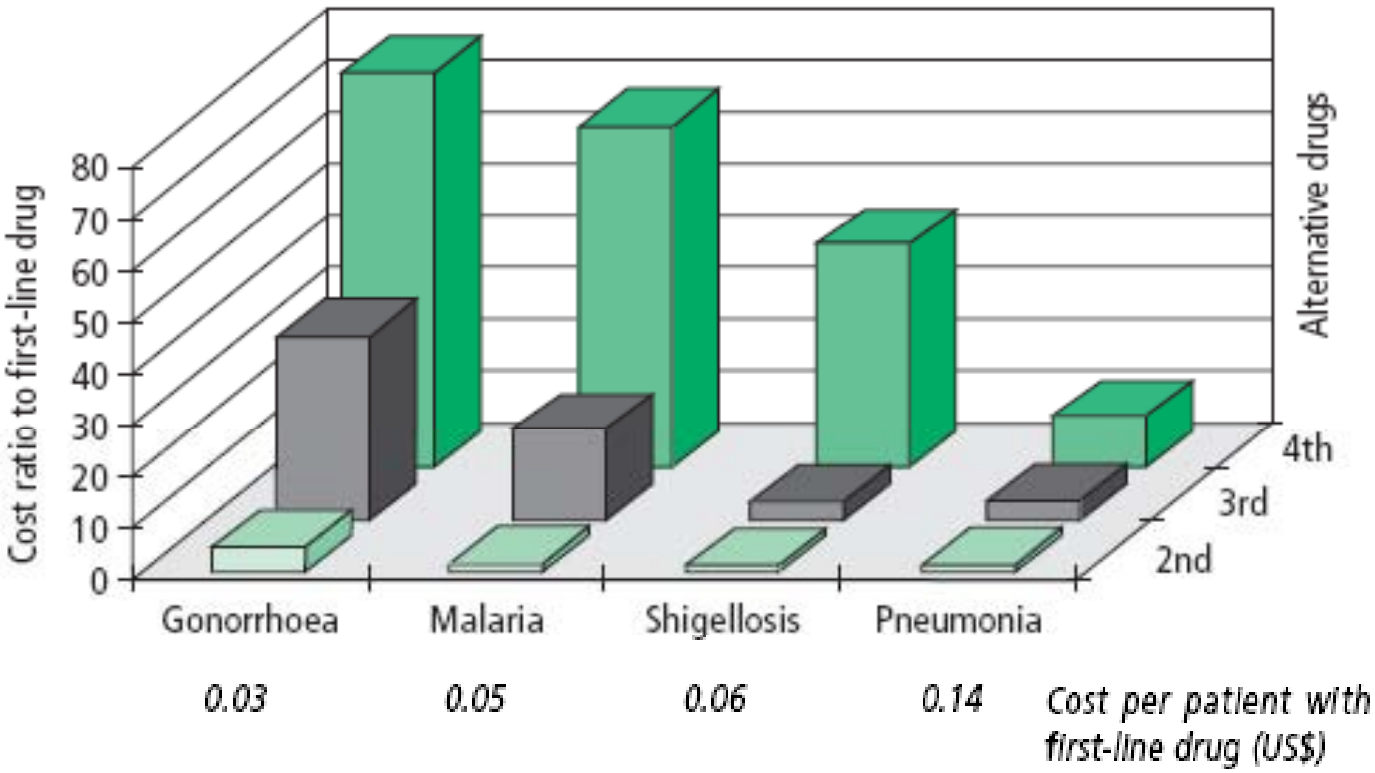
Images: iStock photo, Florida Center for Instructional Technology

Resistance is higher in tertiary facilities



Source: Prof Sabiha Essack, UKZN

Loss of first line drugs increases drug costs



Source: WHO Policy Perspective 2005, adapted from WHO Model Formulary, WHO Clinical Guidelines and Management Sciences for Health's 2004 International Drug Price Indicator Guide (slide courtesy: David Heymann)

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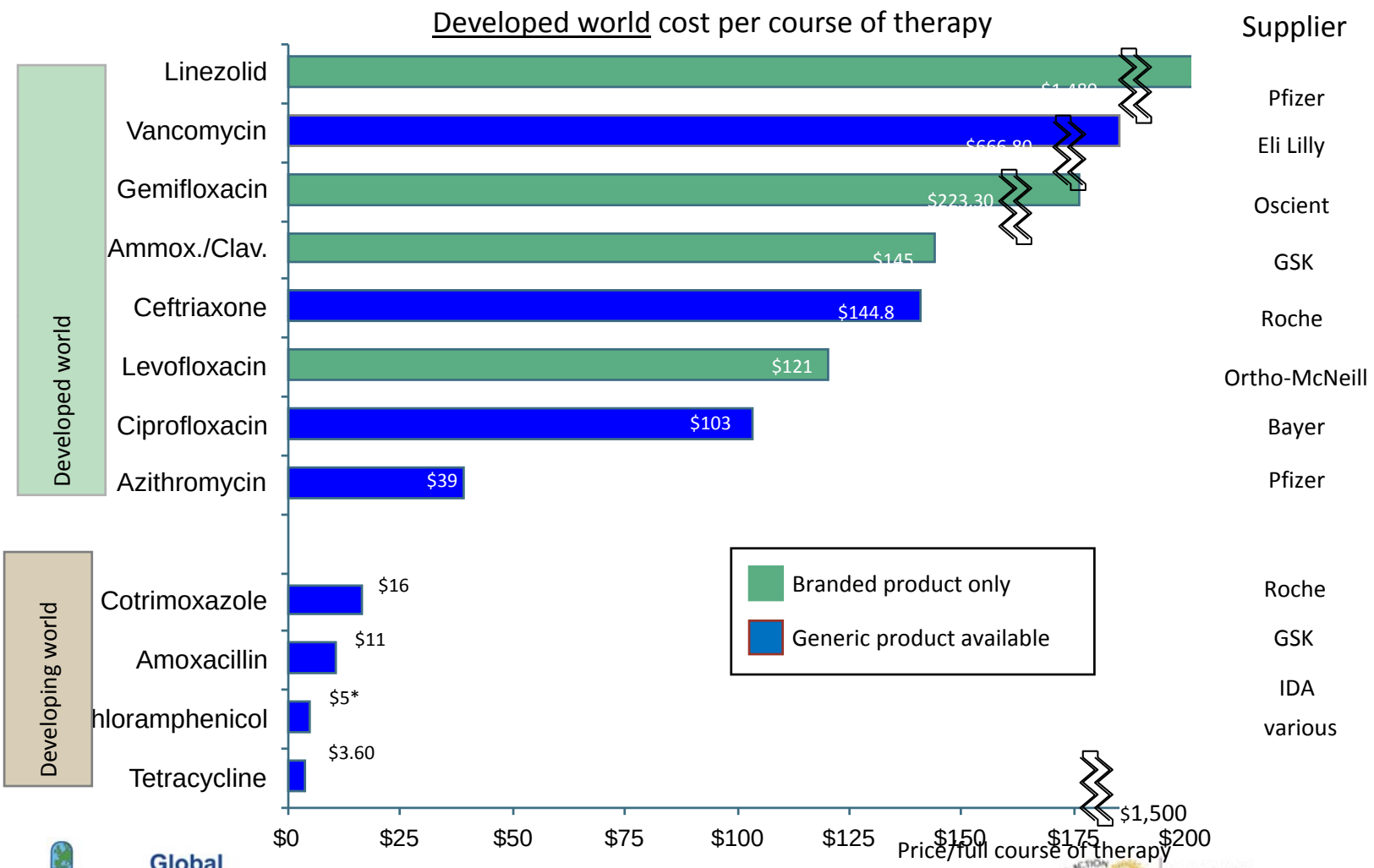
The selection of tools to treat bacterial infections in the developing world is limited by price



Notes: *Chloramphenicol is not available in developed world—price is therefore estimated.
†Ceftriaxone and ciprofloxacin may be available in some tertiary settings in developing world.
Source: The Medical Letter (2006), Disease control priorities in developing countries, Lancet (2006), Expert interviews.

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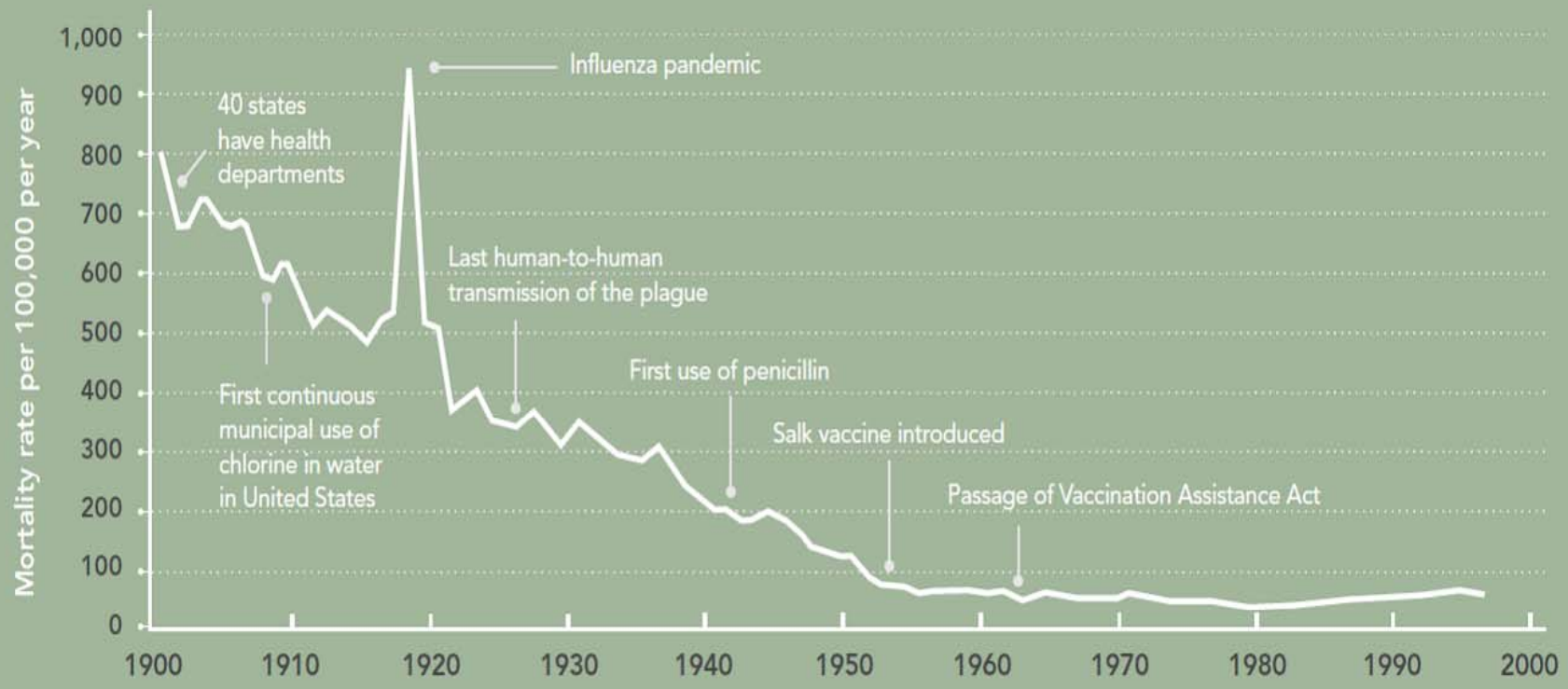
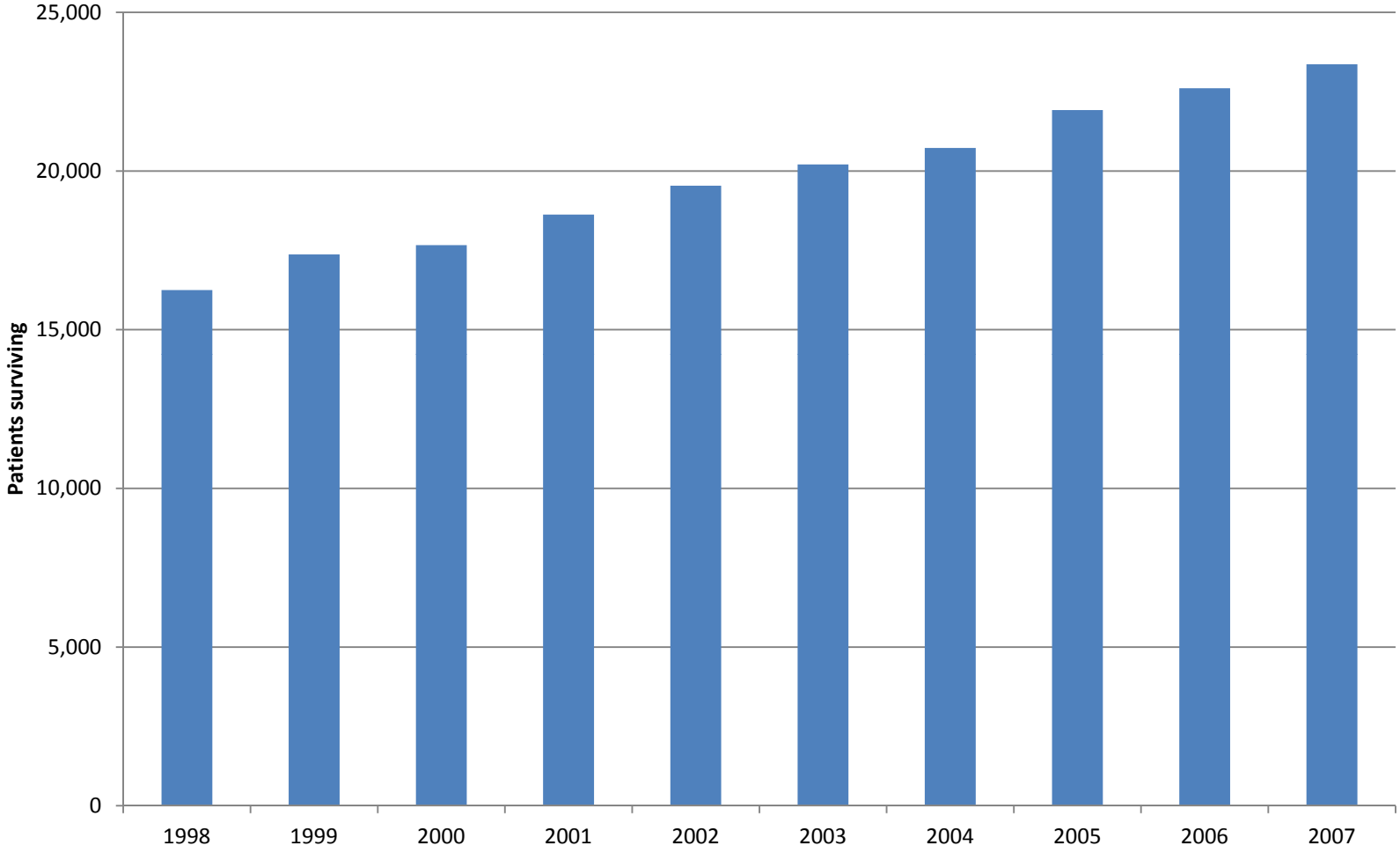
FIGURE 1.1

Crude infectious disease mortality rate in the United States, 1900–1996



Source: Adapted from Armstrong, Conn et al. (1999).

Lives Saved by Organ Transplantation, United States, 1998–2007



Source: United States Health Resources and Services Administration

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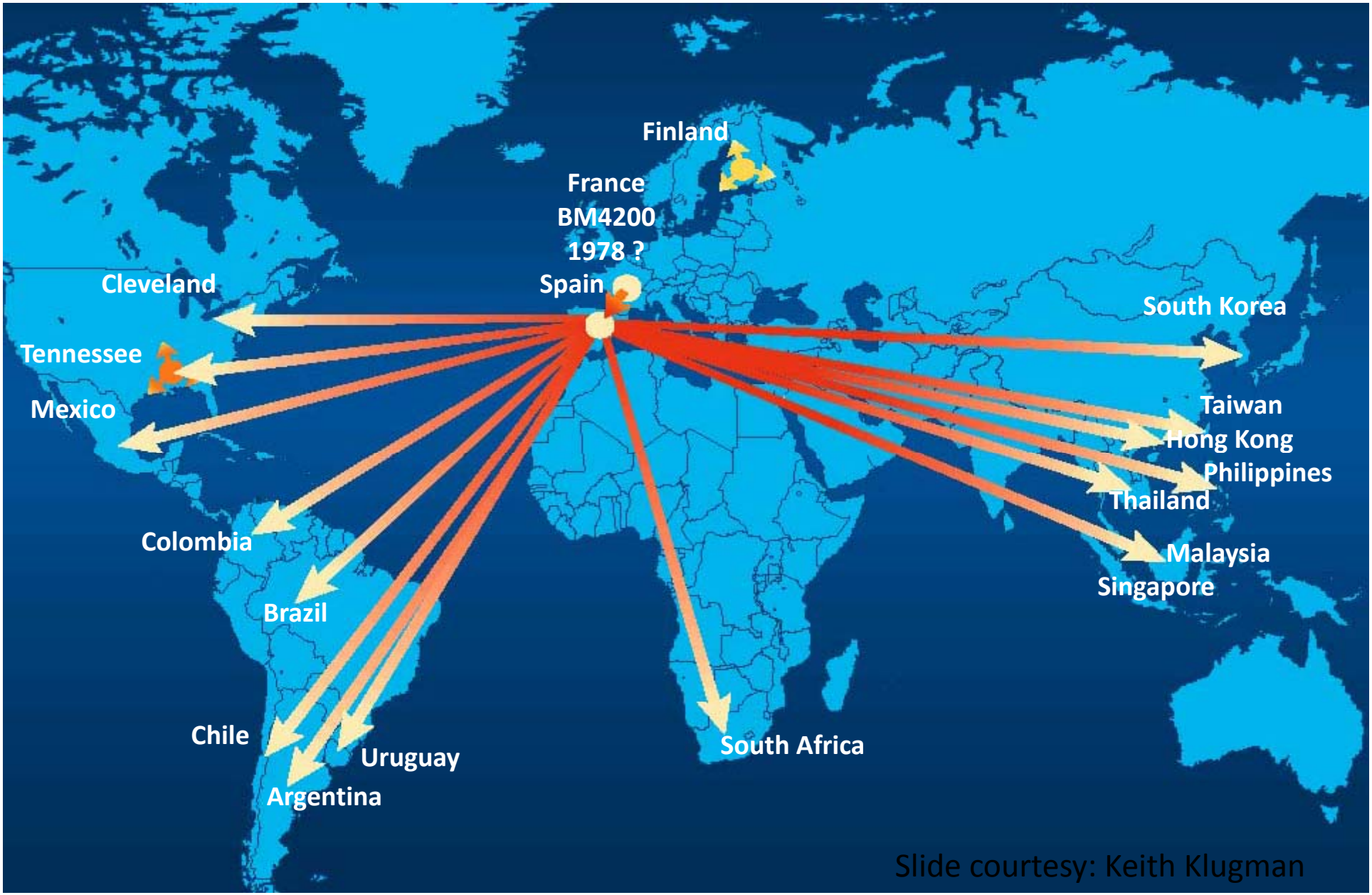
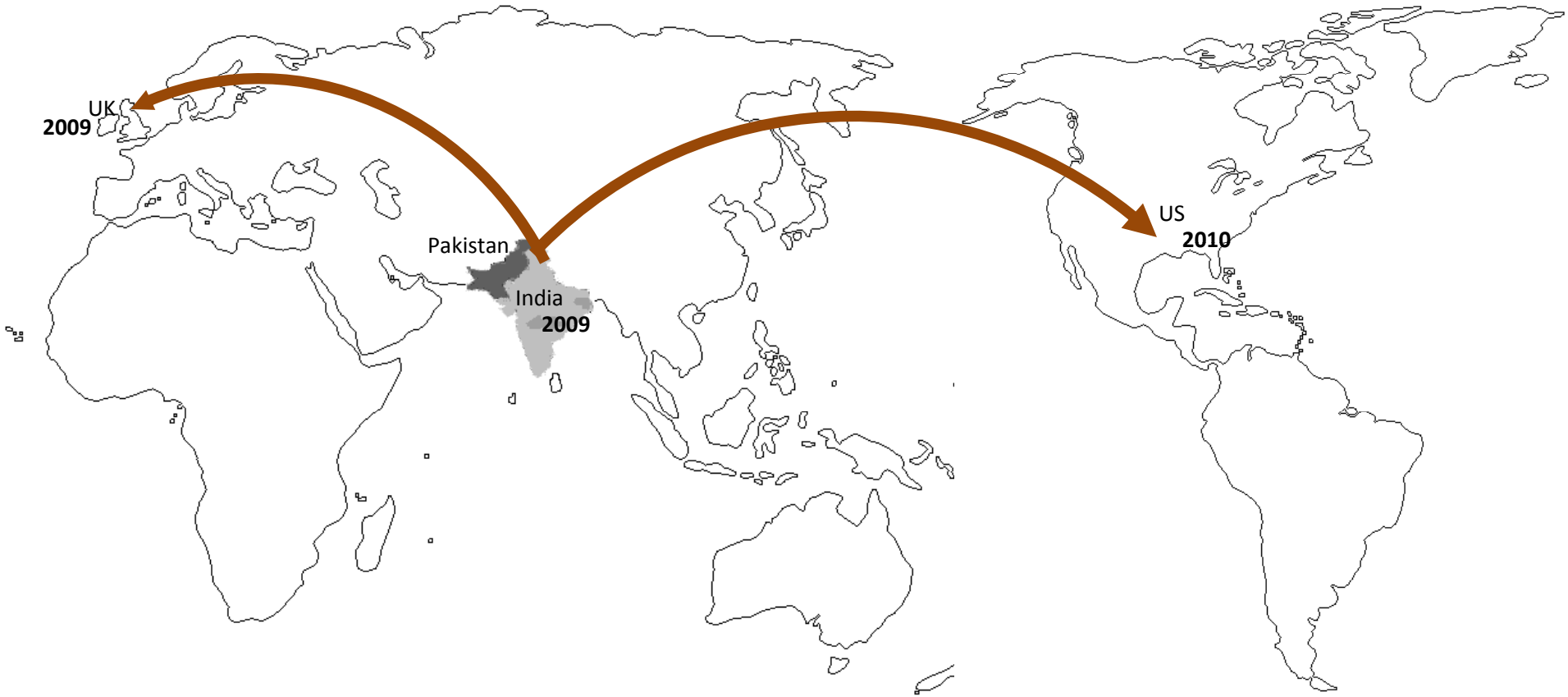
Clonal spread of *S. pneumoniae* 23F

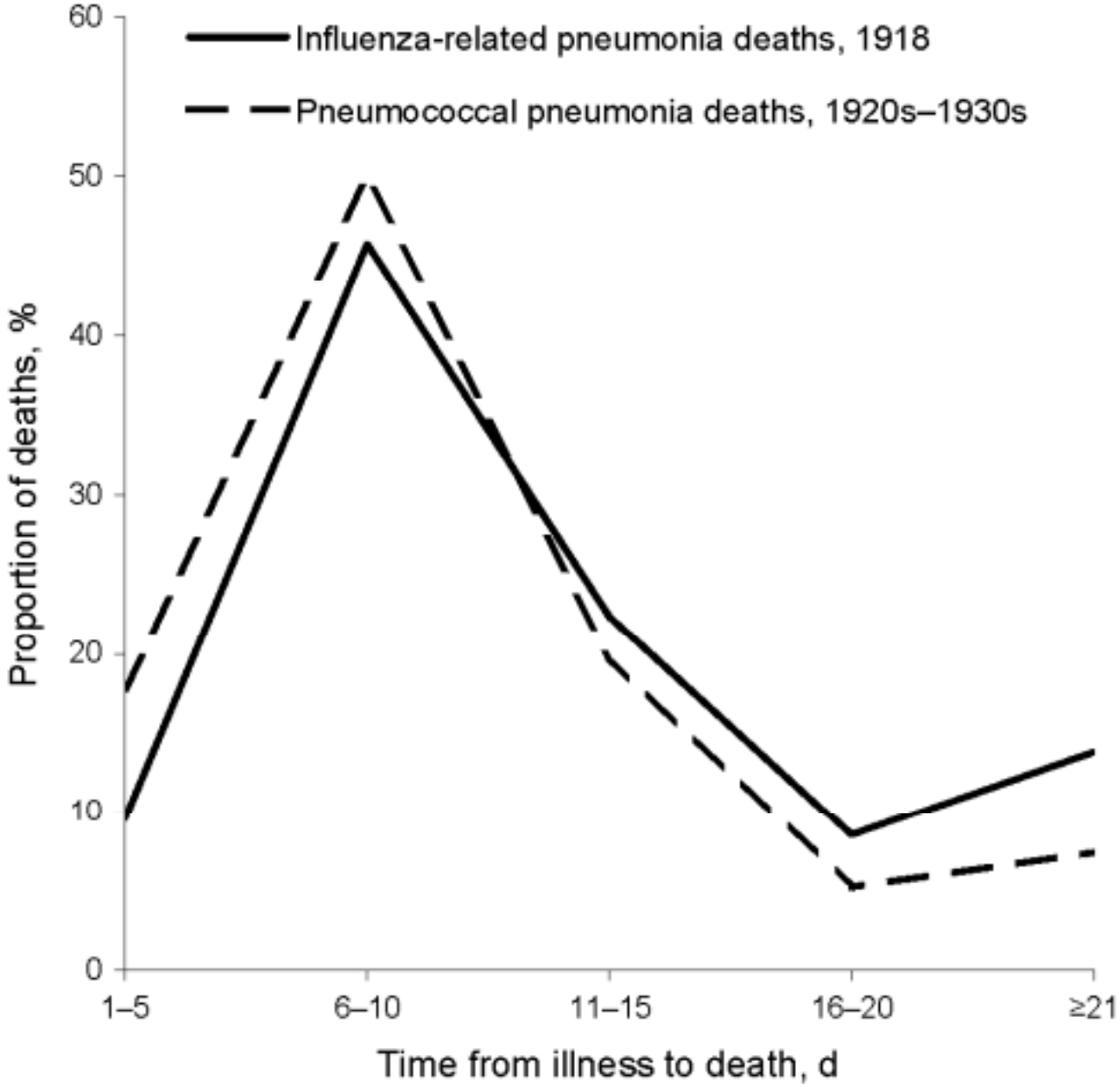


Slide courtesy: Keith Klugman

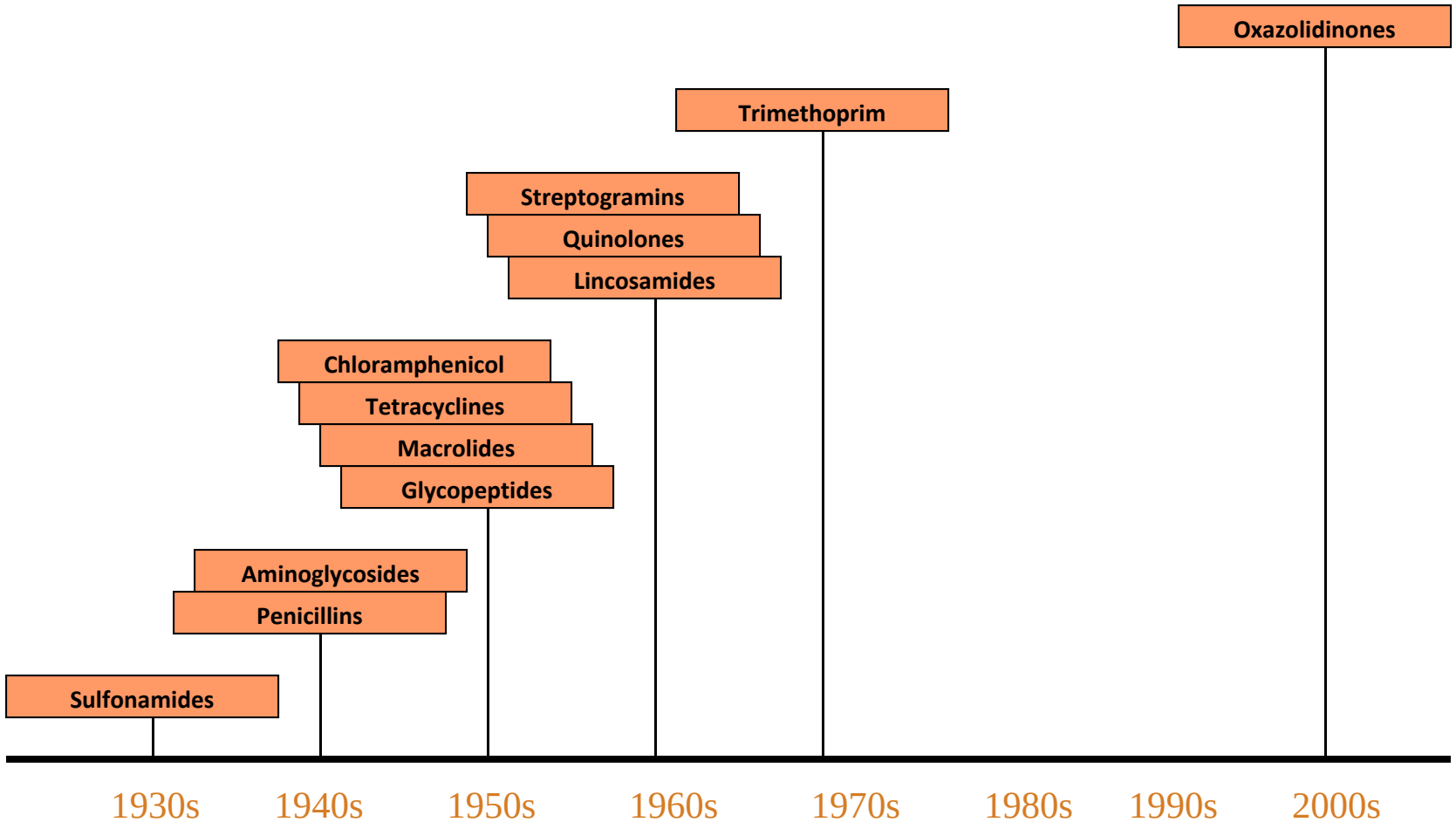
Spread of *Enterobacteriaceae* isolates carrying NDM-1



Center for Disease Control. "Detection of ***Enterobacteriaceae*** Isolates Carrying Metallo-Beta-Lactamase – United States, 2010." MMWR June 25, 2010; 59(24): 750.


Influenza-related pneumonia deaths, 1918
Pneumococcal pneumonia deaths, 1920s–1930s
Proportion of deaths, %
60
50
40
30
20
10
0
1–5
6–10
11–15
16–20
≥21
Time from illness to death, d

Discovery of new classes of antibiotics



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Policy options

- Encourage physician only prescribing?
- Scale up rapid diagnostic tests?
- Improve surveillance?

- Reduce incentives for over prescribing
- Improve access to quality medicines
- Pneumoccocal and HiB vaccination
- Improve hospital infection control