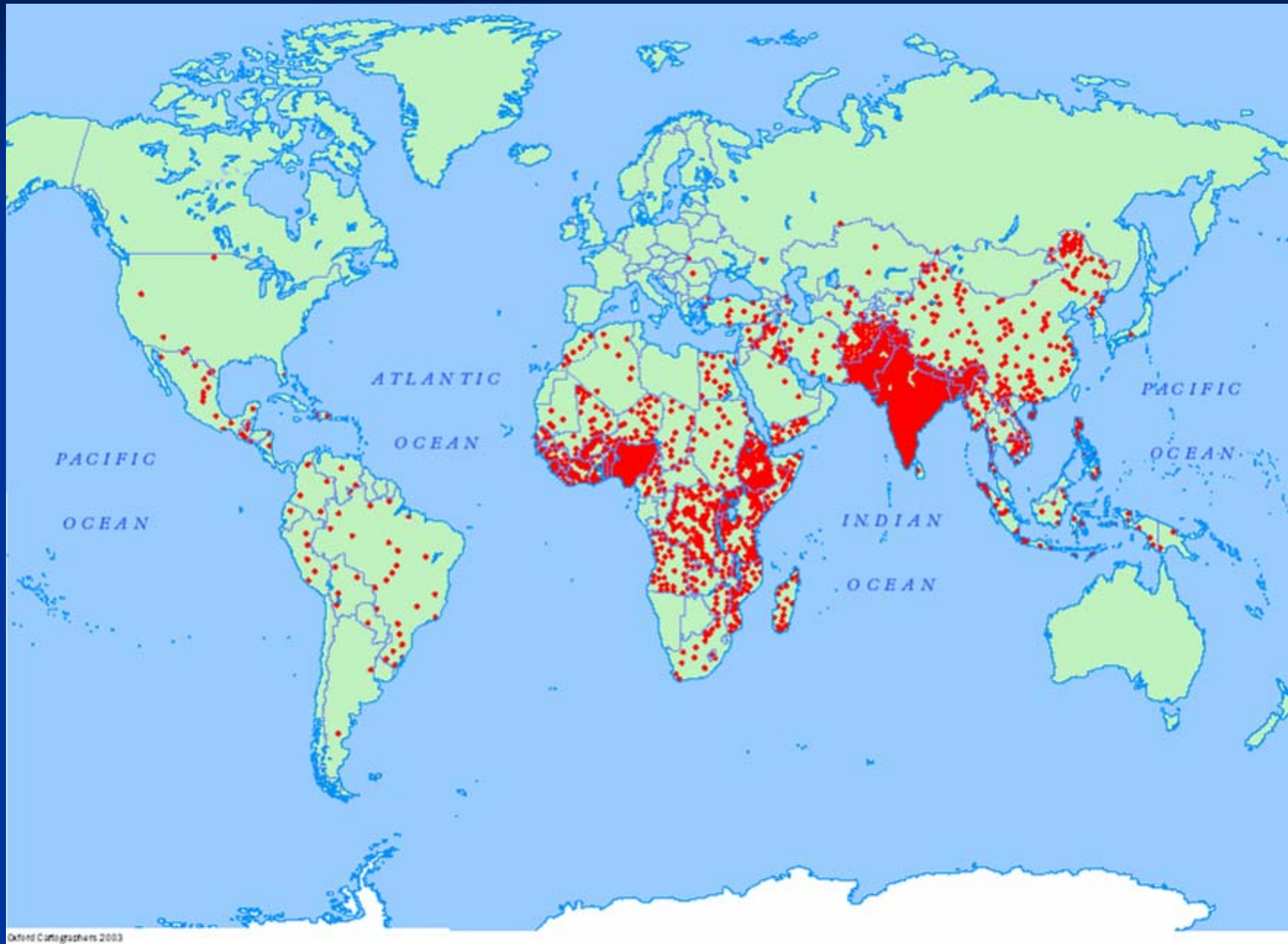


Working for tomorrow's children: impact of antimicrobial resistance on public health

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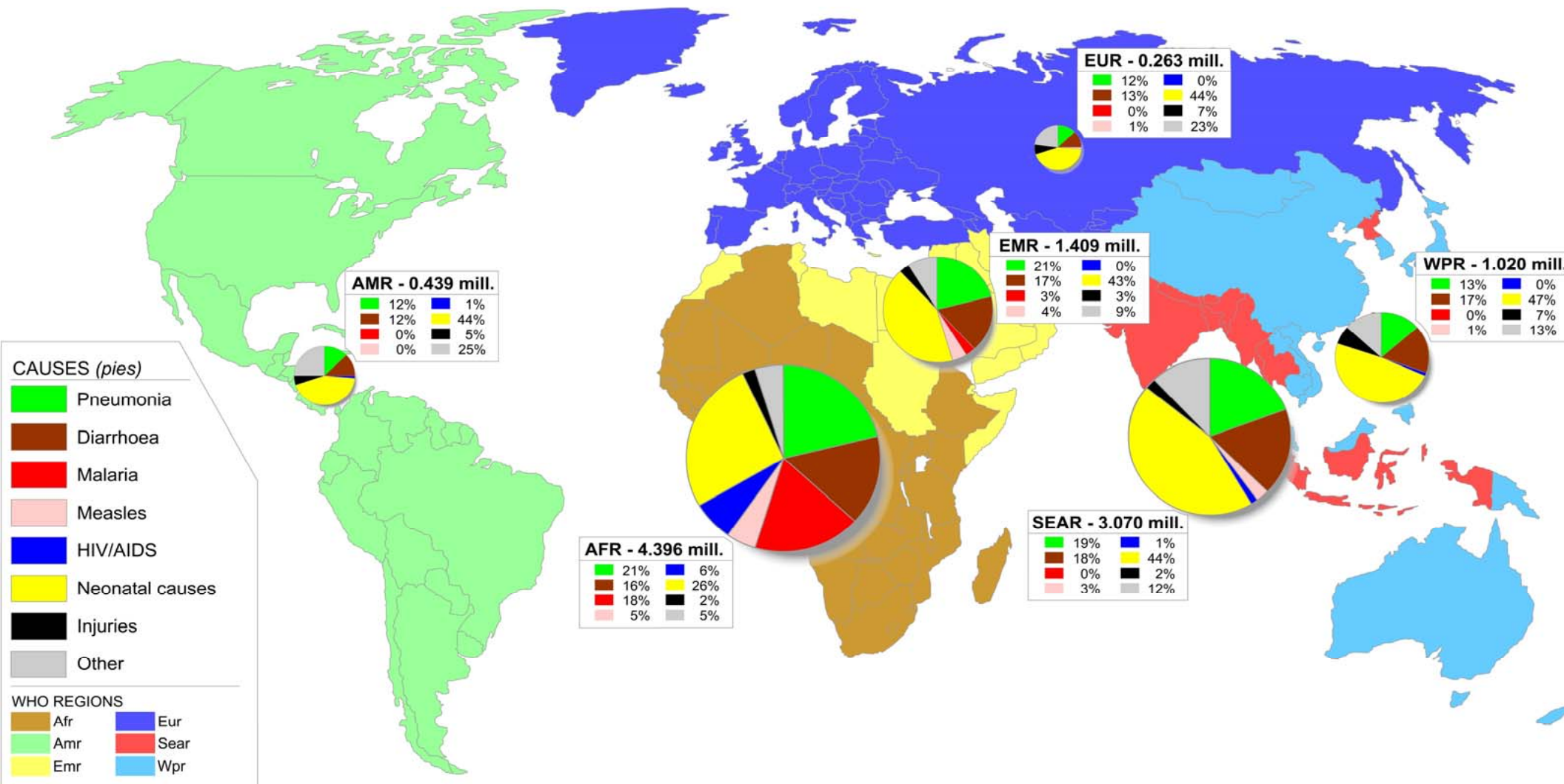
Where are 10 million children dying every year?



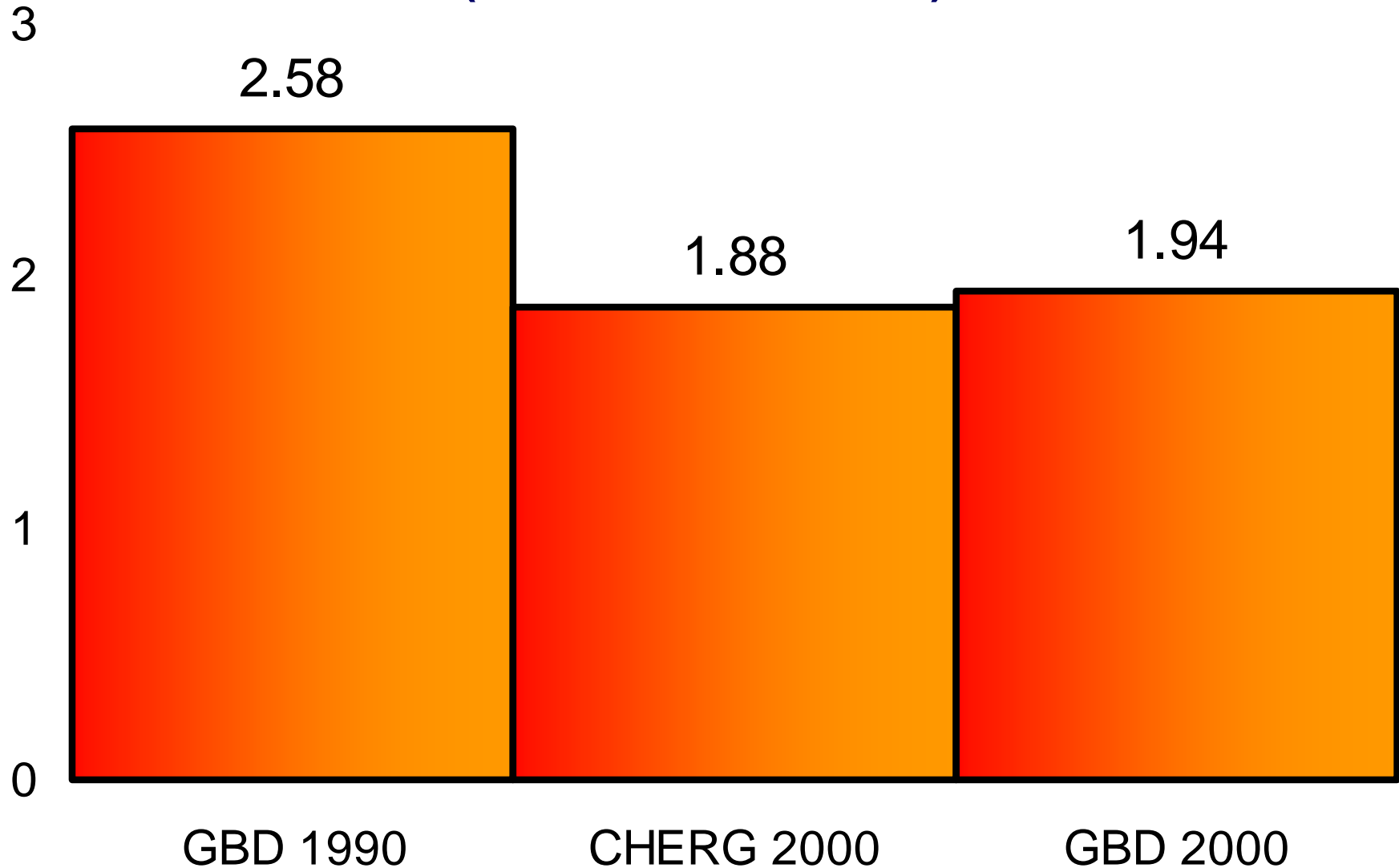
Black et al 2003

Causes of death in children under 5

CHERG Lancet (2005)



Time trends in estimates of ARI mortality (in millions of deaths)

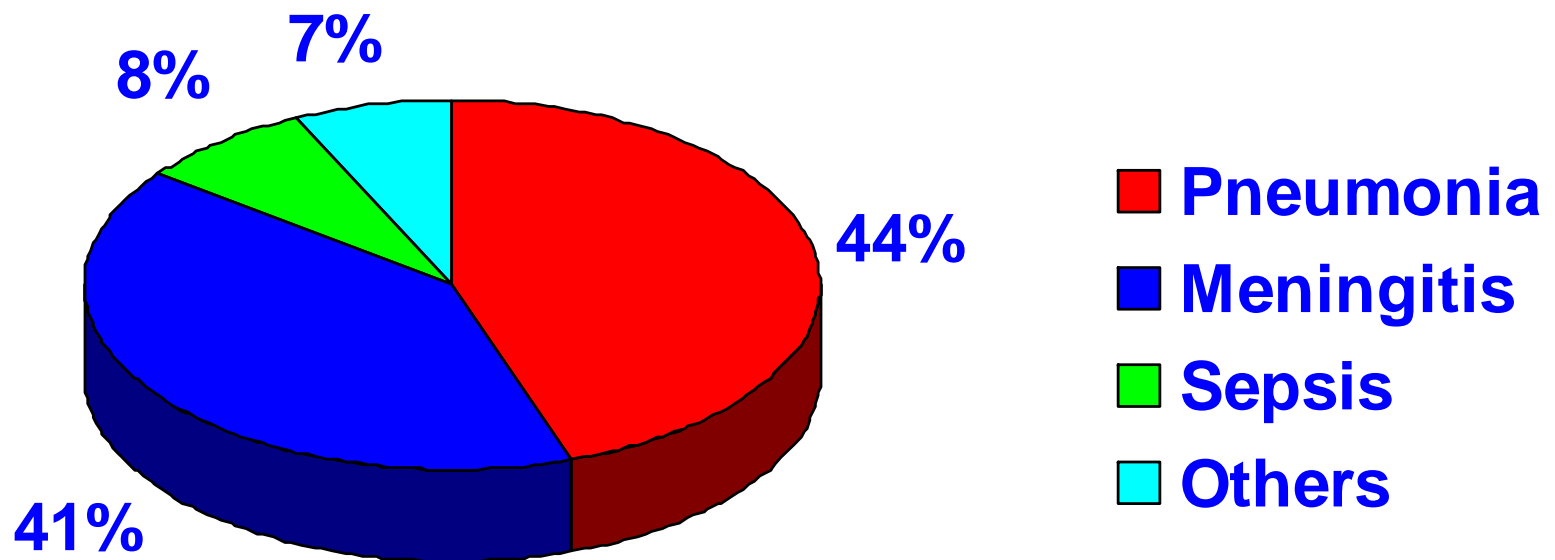


ARI burden of disease

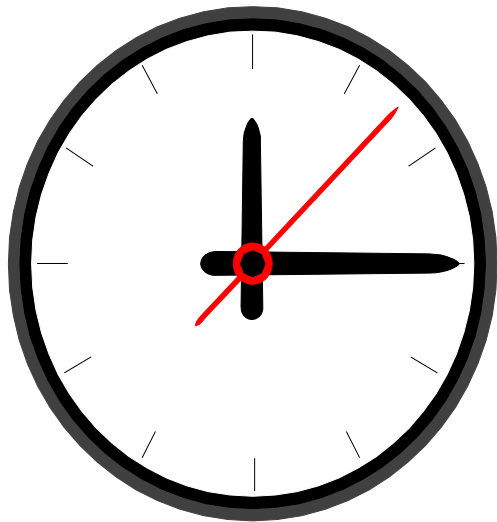
- **5-9 episodes of ARI per year / U-5**
- **1 in 30-50 of these episodes are pneumonia episodes (2-3% of all ARI)**
- **In developing countries**
 - **Most pneumonia is bacterial**
 - **Most ARI deaths are due to pneumonia**

Surveillance of invasive *S. pneumoniae*

Clinical diagnosis



Duration of illness in children who died from pneumonia



Average duration of symptoms of pneumonia before death was 3.5 days (Jumla, Nepal)

In young infants duration of illness was even shorter

Duration of illness before death is often short. Early maternal recognition of signs of pneumonia and prompt care seeking are essential to prevent deaths.

Prescribing practices in childhood diarrhea

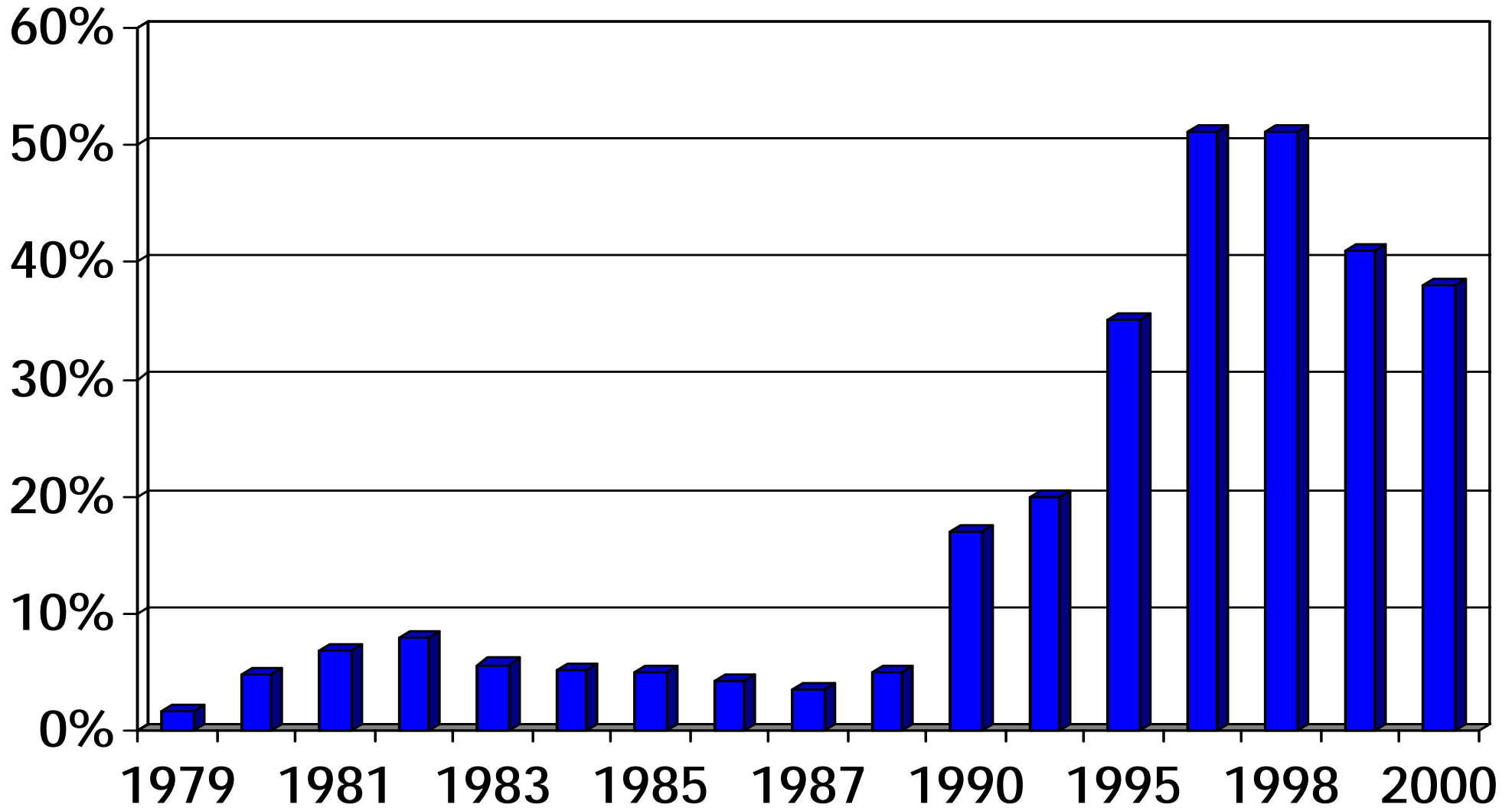
(Nizami & Bhutta, Soc Sci Med 1996;42:1133)

| | General Physicians | Paediatricians |
|--------------------------------|--------------------|----------------|
| Encounters (n) | 613 | 383 |
| Encounter time in minutes (SD) | 3 (2) | 9 (4) |
| Antidiarrheals | 59.7 % | 28.5 % |
| Antibacterials | 66.1 % | 50.0 % |
| Antiamoebics | 38.7 % | 32.1 % |
| Injectables | 32.3 % | 17.9% |

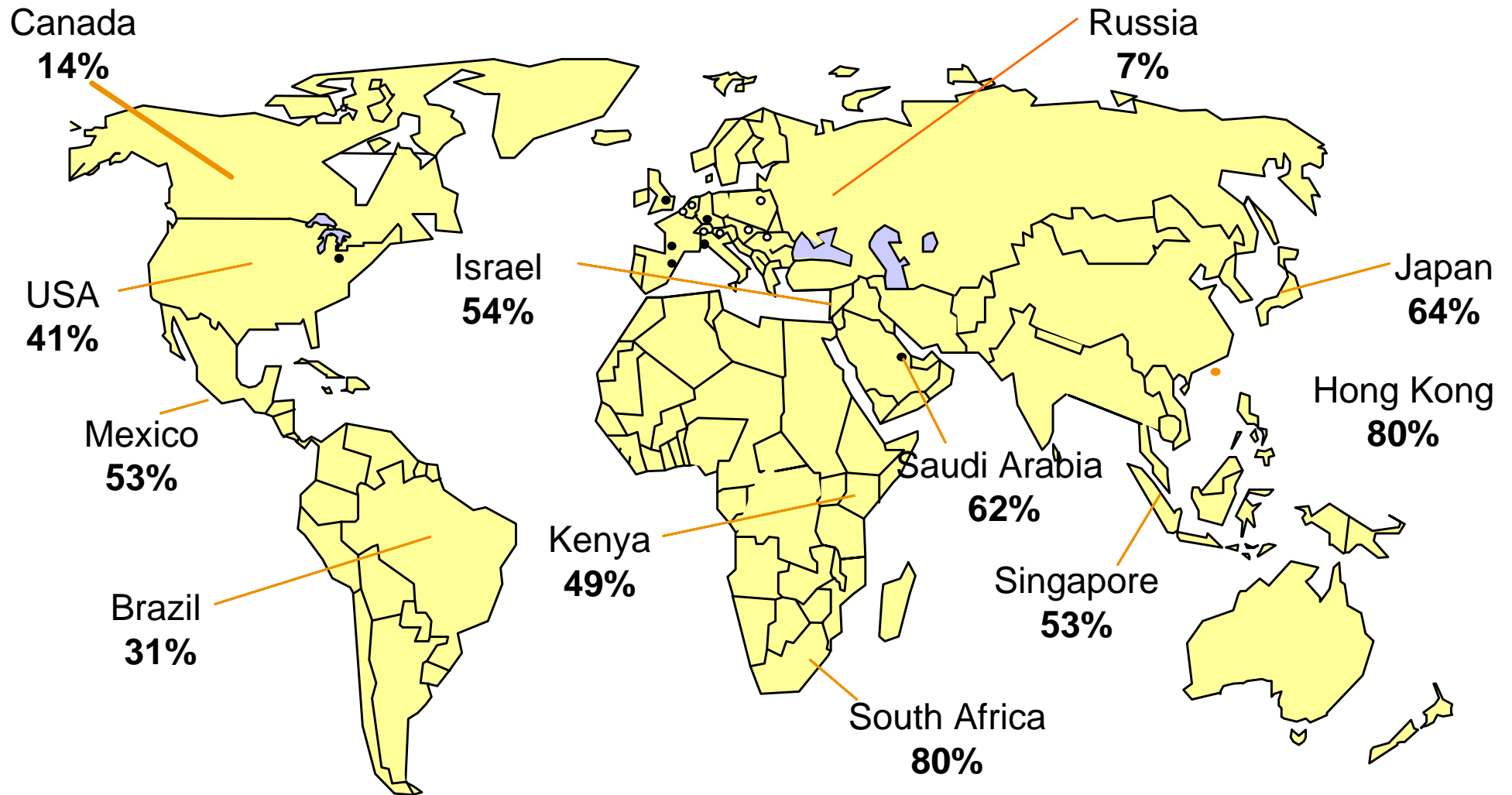
Indiscriminate antibiotic use breeds resistance!



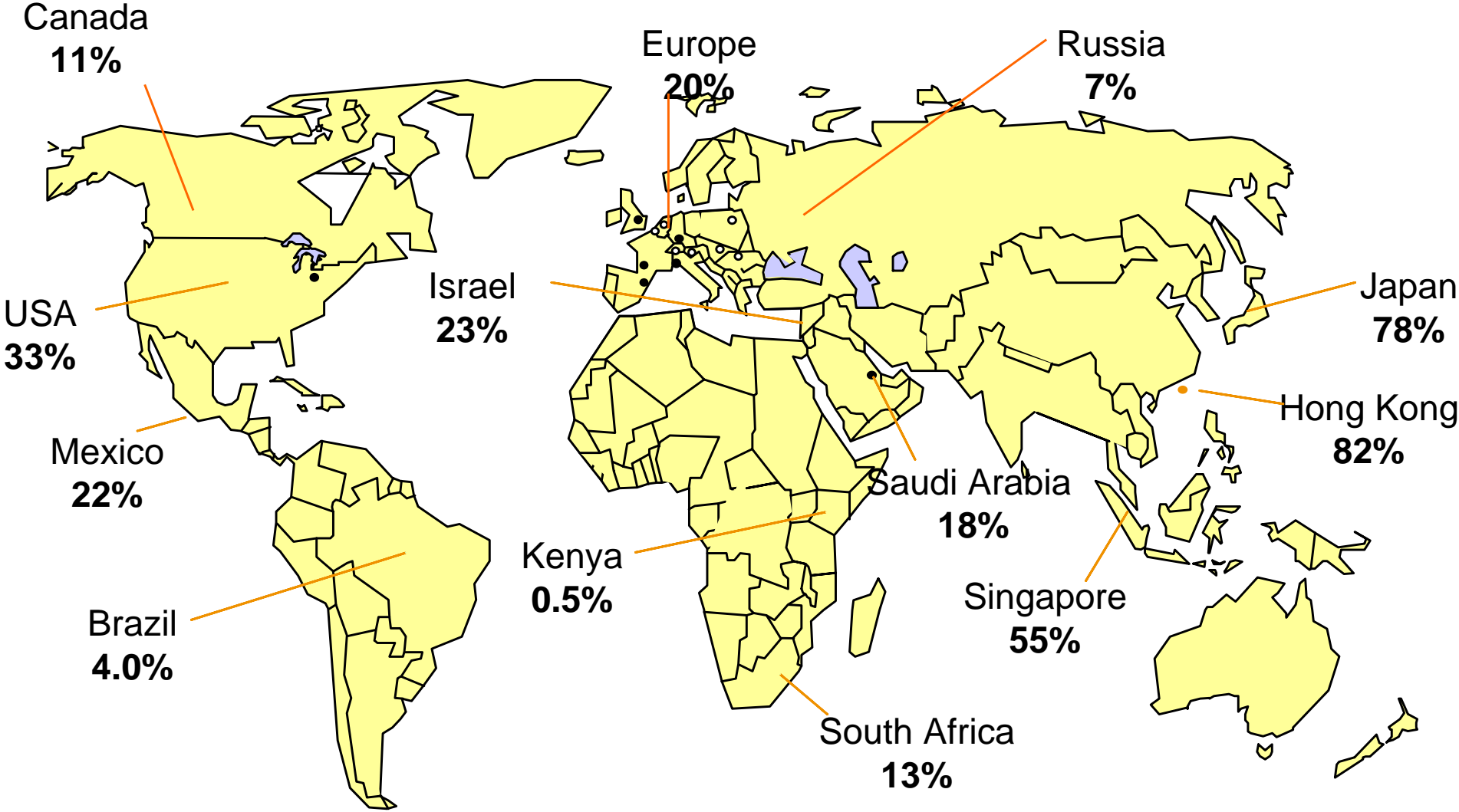
The Emergence of Penicillin Non-Susceptible Pneumococci in the U.S.



Worldwide Distribution of Penicillin Resistant Pneumococci



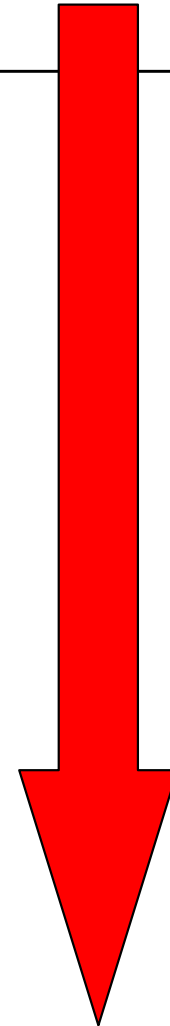
Worldwide *S. pneumoniae* Macrolide Resistance in 2000



Resistance defined as erythromycin MIC ≥ 1 mg/L

RCTs non-severe pneumonia therapy

| RCTs | Therapy regimen and failure rate |
|---|--|
| Keeley et al¹ 1987-88 | 2% Cotrimoxazole (2 doses/d) 1% Procaine penicillin (1 dose/d) |
| Straus et al² 1991-92 | 12% Amoxicillin (3 doses/d) 13% Cotrimoxazole (2 doses/d) |
| COMET³ 1995-96 | 17% Standard dose cotrimoxazole 18% Double dose cotrimoxazole |
| CATCHUP⁴ 1998-99 | 19% Cotrimoxazole (2 doses/d) 16% Amoxicillin (2 doses/d) |
| MASCOT⁵ 1999-2000 | 20% 5-day amoxicillin thrice daily 21% 3-day amoxicillin thrice daily |



Oral amoxicillin vs injectable penicillin in children with severe pneumonia

9 centres in 8 countries n= 1702

| Therapy failure | Penicillin (n = 845) | Amoxicillin (n = 857) | Total (%) |
|------------------------|---------------------------------|----------------------------------|----------------------|
| At 48 h | 161 (19%) | 167 (19%) | 328 (19) |
| At 5 days | 187 (22%) | 186 (22%) | 378 (22) |
| At 14 days | 213 (25%) | 225 (26%) | 438 (25.7) |

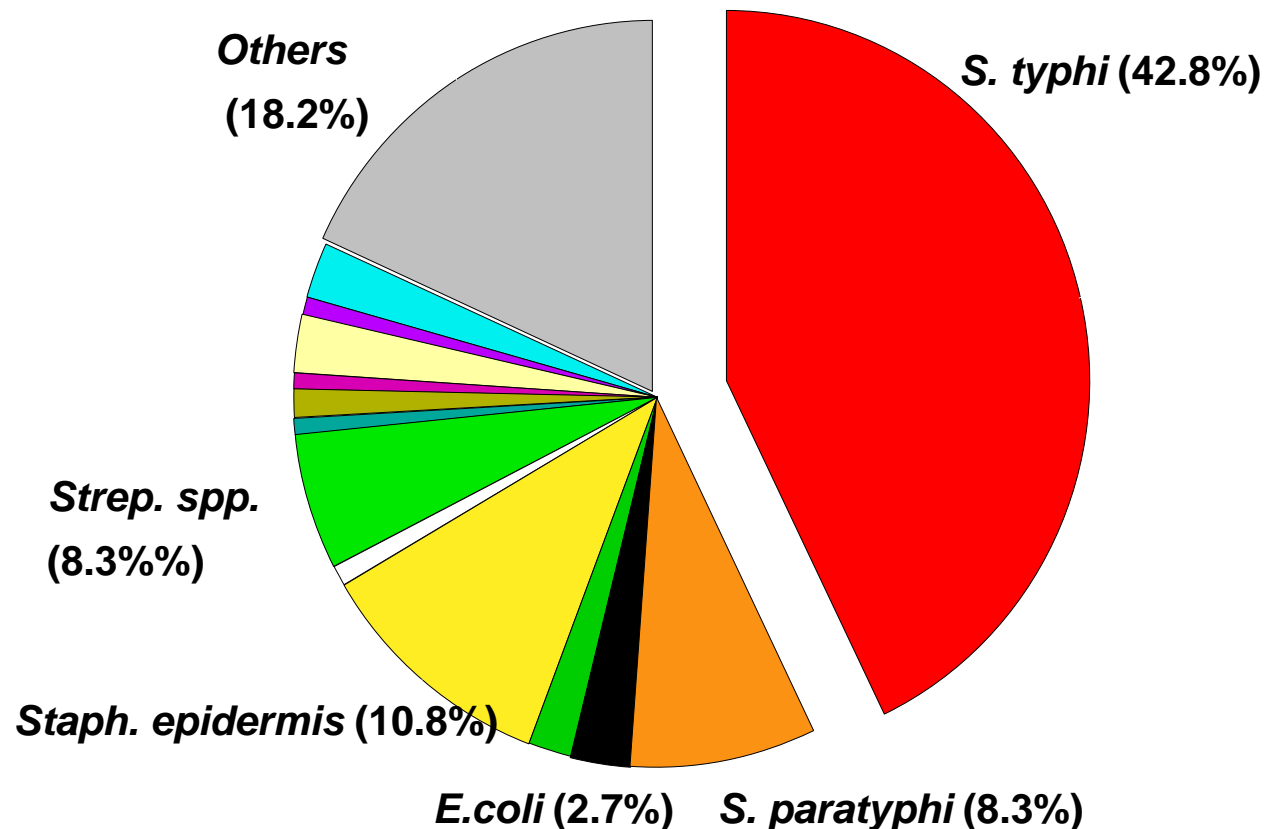
Amoxicillin Penicillin Pneumonia International Study (APPIS)

Typhoid fever

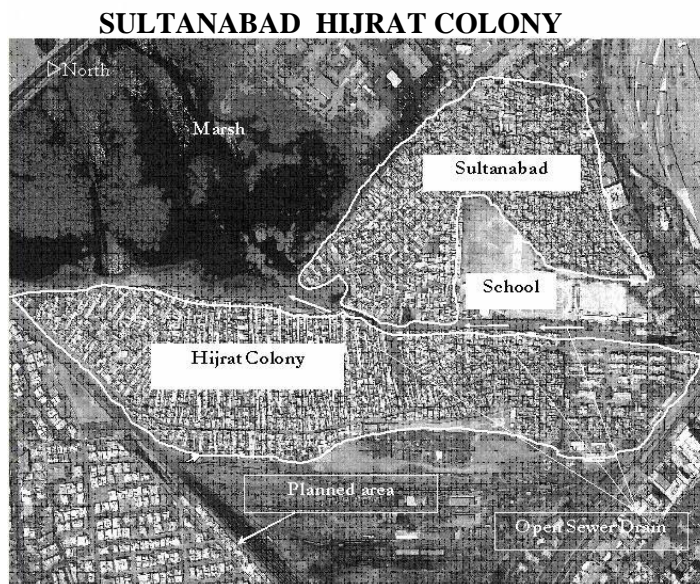
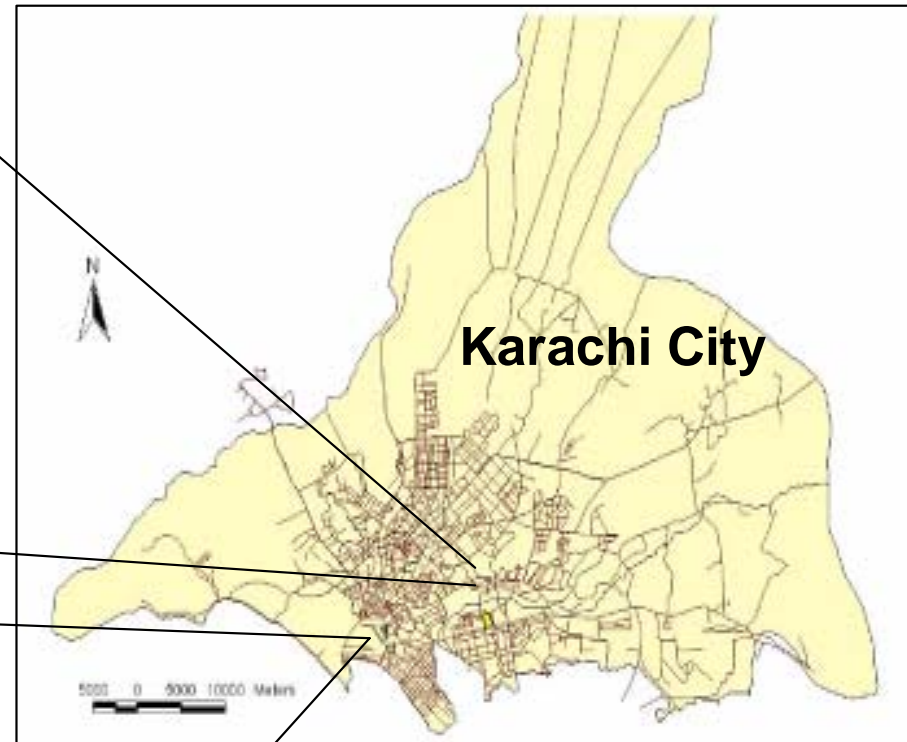
- Typhoid fever is widely regarded as one of the most common causes of morbidity in the developing world.
- In South Asia, this is largely a paediatric disease
- *S. typhi* found to be most common cause of bacteremia among children dying with diarrhea at AKUMC.

Spectrum of paediatric blood culture isolates from AKUMC emergency services (1995-1999)

Ambulatory care and emergency referral data may provide insight into the magnitude of the problem



The Study Sites



The sites were chosen as they are typical of conditions in slum areas of cities throughout Pakistan





Culture Positive Cases

- households
- ▲ S. typhi cases
- Para typhi cases



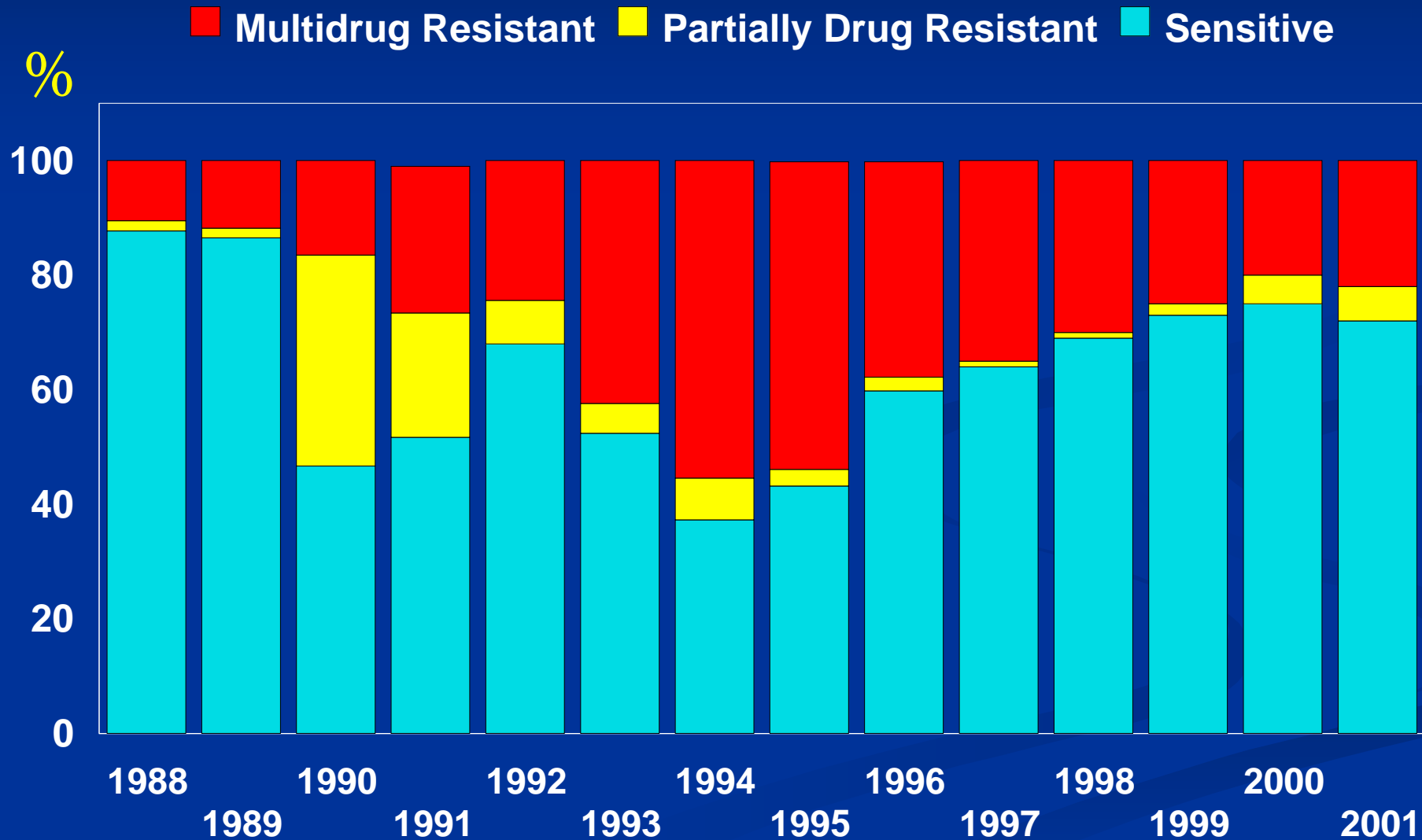
At Health Centre

- <all other values>
- Registered

Incidence of culture proven typhoid fever 2-15 years old

| Incidence (Aug 2002 – July 2003 in Sultanabad and Hirjat Colony) and (Aug 2003 – July 2004 in Bilal Colony) | | | |
|--|-----------------|-------------|---|
| Area | 2001 Population | Total Cases | Annual incidence per 100,000 population |
| Hirjat Colony | 11,609 | 44 | 379 |
| Sultanabad | 9,458 | 68 | 719 |
| Bilal Colony | 25,982 | 262 | 1,008 |
| Total | 47,049 | 374 | 795 |

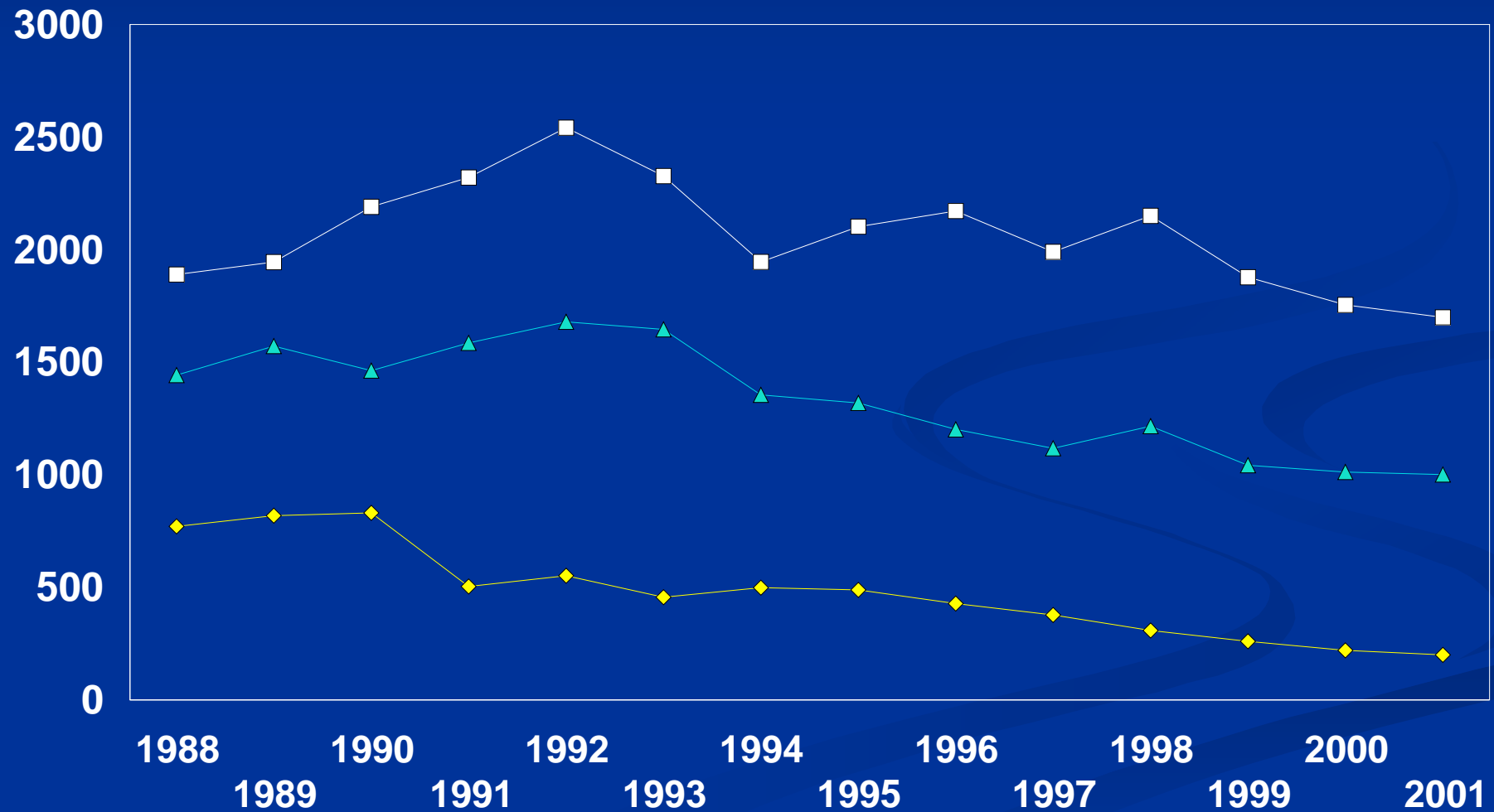
Salmonella typhi



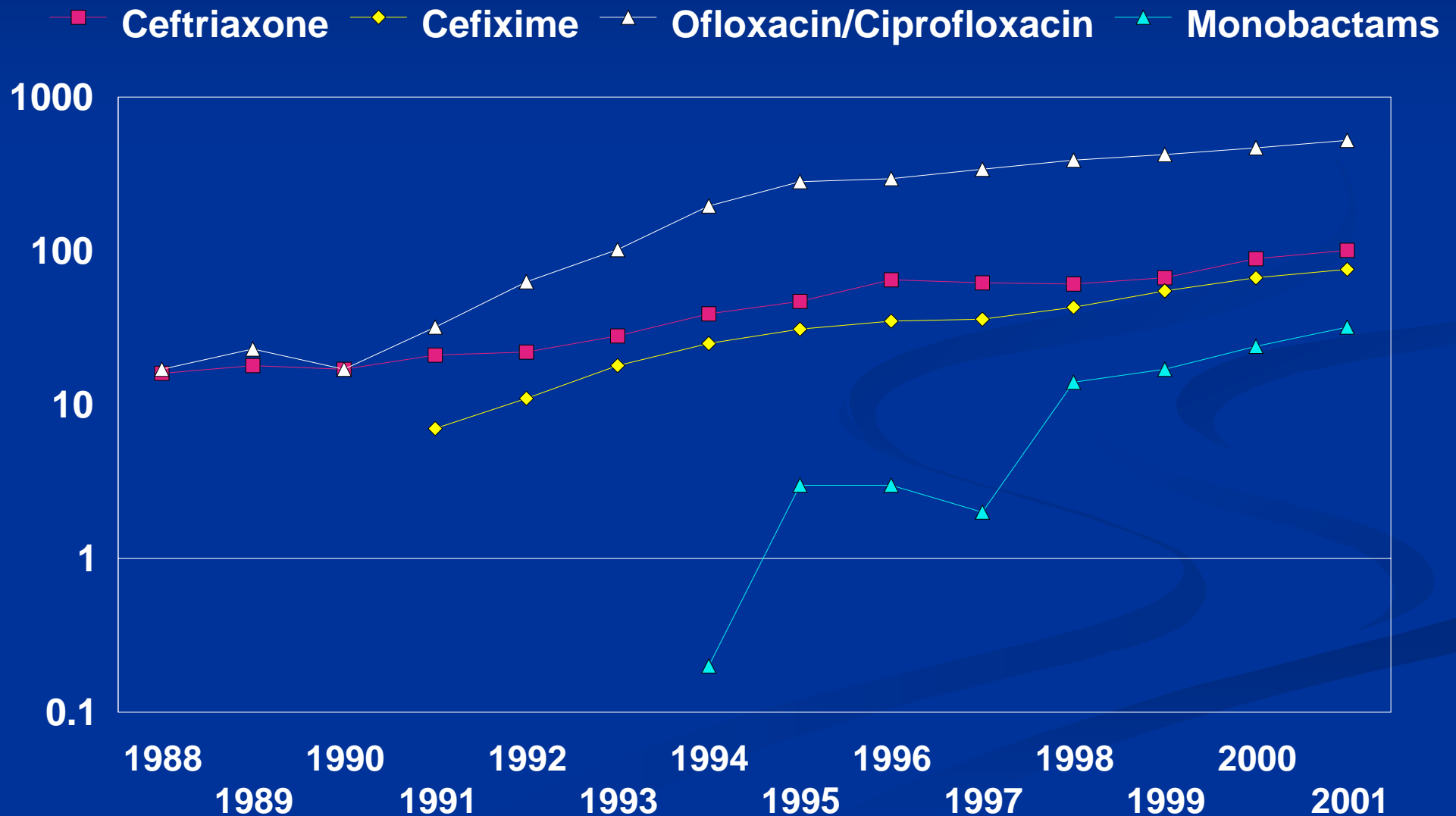
Antimicrobial use in Karachi

(units per 10,000 population)

■ Ampicillin/Amoxicillin ◆ Chloramphenicol ▲ TXP-SX



Antimicrobial use in Karachi (units per 10,000 population)



Implications of growing antibiotic resistance

Average Treatment Costs for Typhoid (US\$)

Child weighing 20 kg using standard treatment guidelines

| | |
|---|----------|
| Course of antibiotics for non-resistant cases | \$3-5 |
| Prolonged fluoroquinolone treatment for quinolone or nalidixic acid resistant cases | \$24-30 |
| Azithromycin | \$35-42 |
| Oral cephalosporins (cefixime) | \$37-42 |
| Parenteral cephalosporins (ceftriaxone) | \$84-104 |

Source: AKU Pharmindex 2004 & WHO guidelines 2003

Implications

- **Increasing antimicrobial resistance to common organisms correlates closely with antimicrobial “pressure” and emergence of resistant strains**
- **Once established these drug resistant isolates are associated with higher rates of treatment failure and increasing cost of therapy**
- **The implications of these findings are much greater for health systems in developing countries**