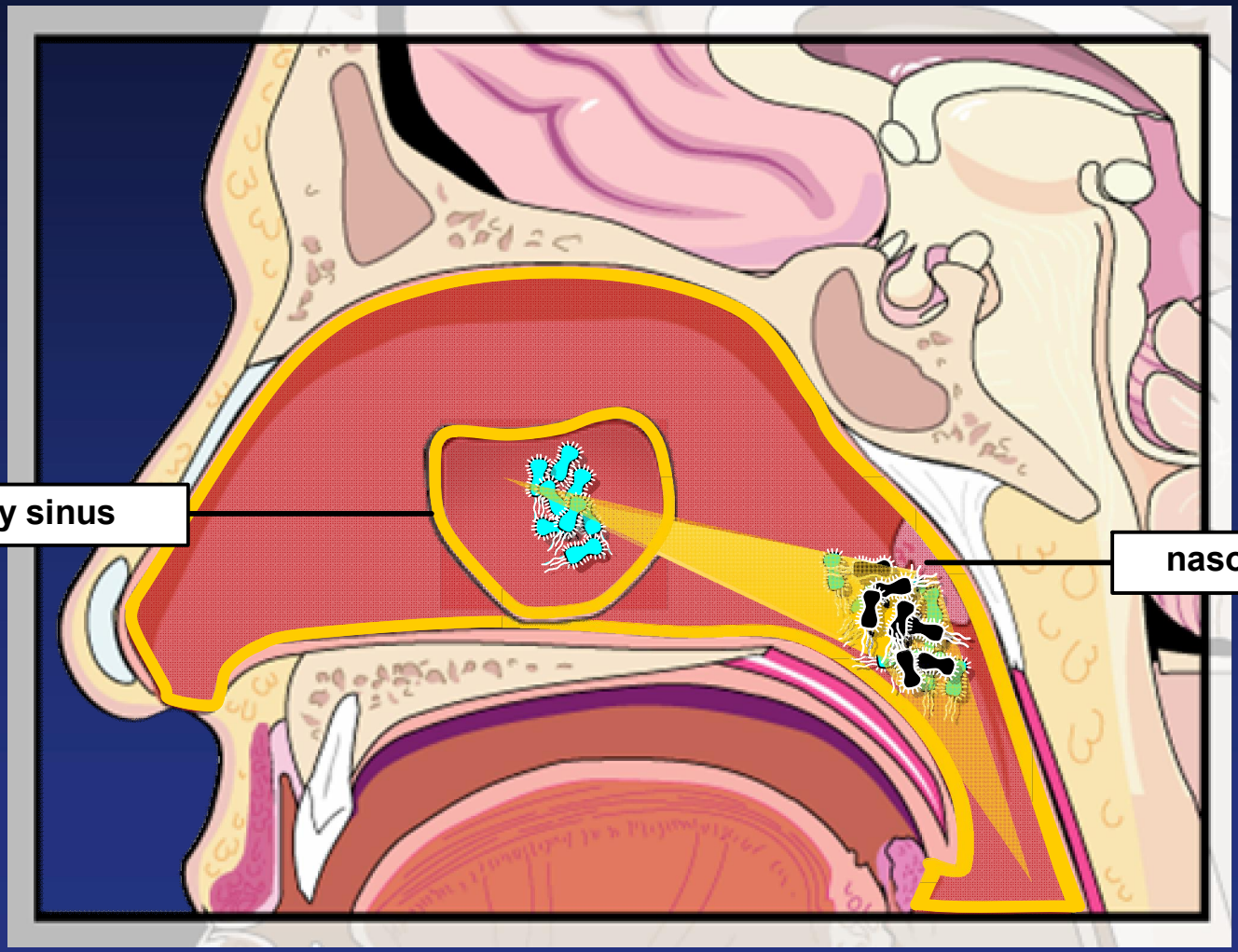
Appropriate Use of Antibiotics in Acute Bacterial Sinusitis: A Strategy to Minimize Resistance in *Streptococcus pneumoniae*

Donald E. Low, MD

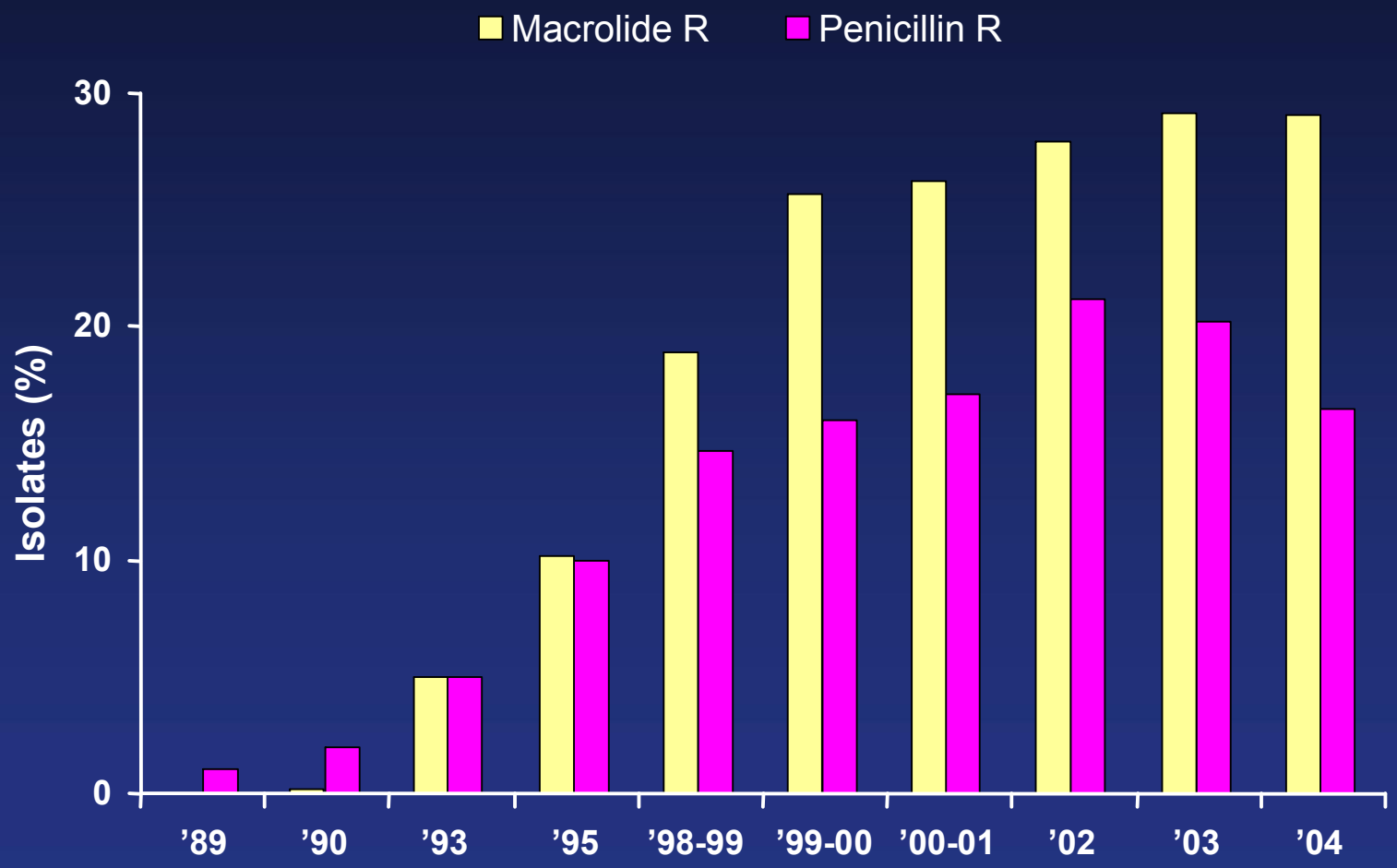
Spread of Resistance Bacteria in ABS



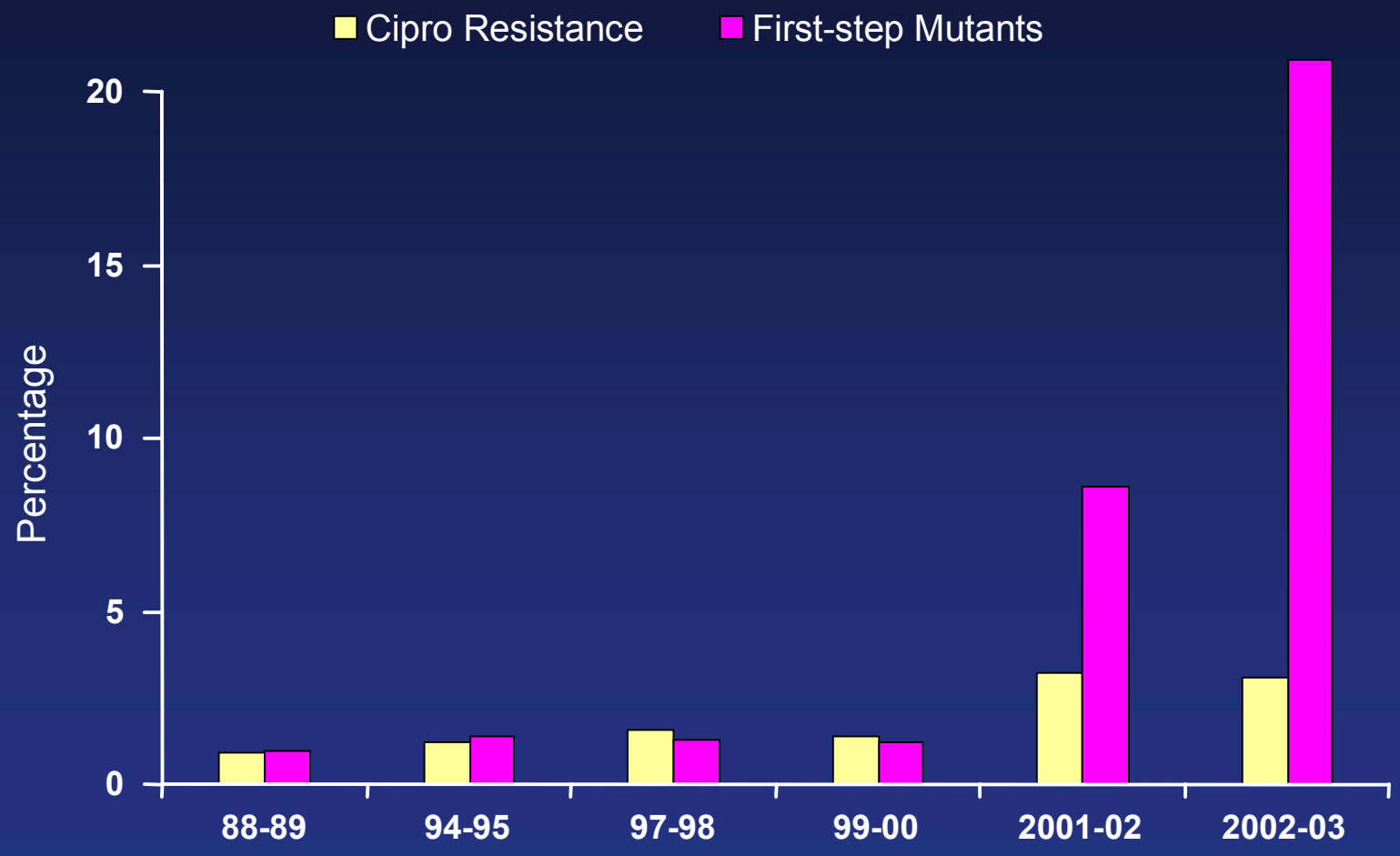
Susceptible bacteria

Resistant bacteria

Penicillin and Macrolide-Resistant *S. pneumoniae* Emerged Rapidly in U.S.



Ciprofloxacin Resistance in *S. pneumoniae* (U.S. data)



Doern et al. CID 2005

Growing Need for Antimicrobials for the Empirical Treatment of Possible Multi-Drug Resistant Pneumococci

n=1,817 Isolates; 44 U.S. Medical Centers, Winter 2002-2003

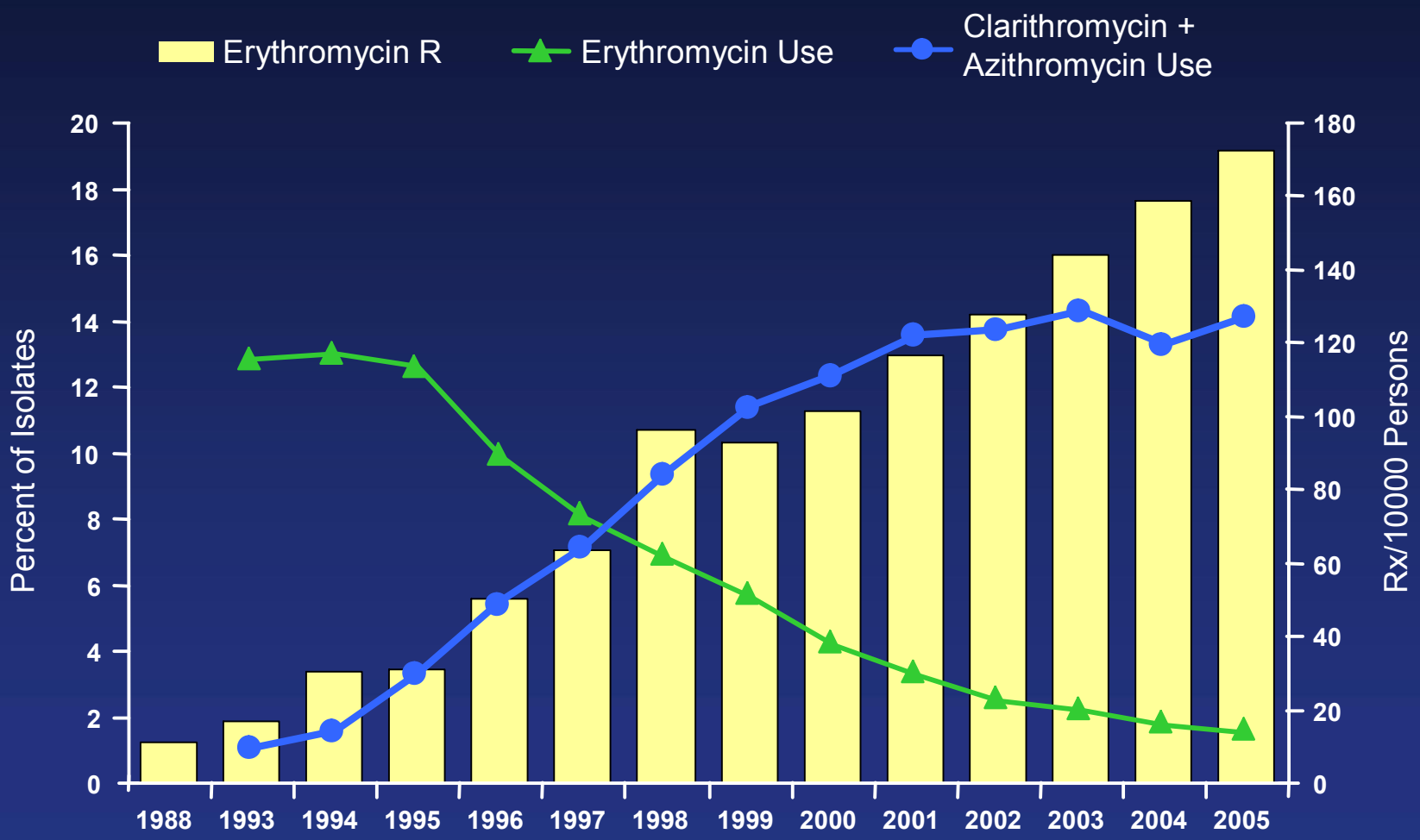
Antimicrobial	Percent Resistant
Macrolides	32.9
Clindamycin	8.6
Tetracyclines	8.4
Chloramphenicol	24.0
TMP-SMX	23.4
MDRSP	**25.2**

Doern et al, Clin Infect Dis, 2005

Canadian Bacterial Surveillance Network:
A Tool for Investigating Resistance Causes & Solutions

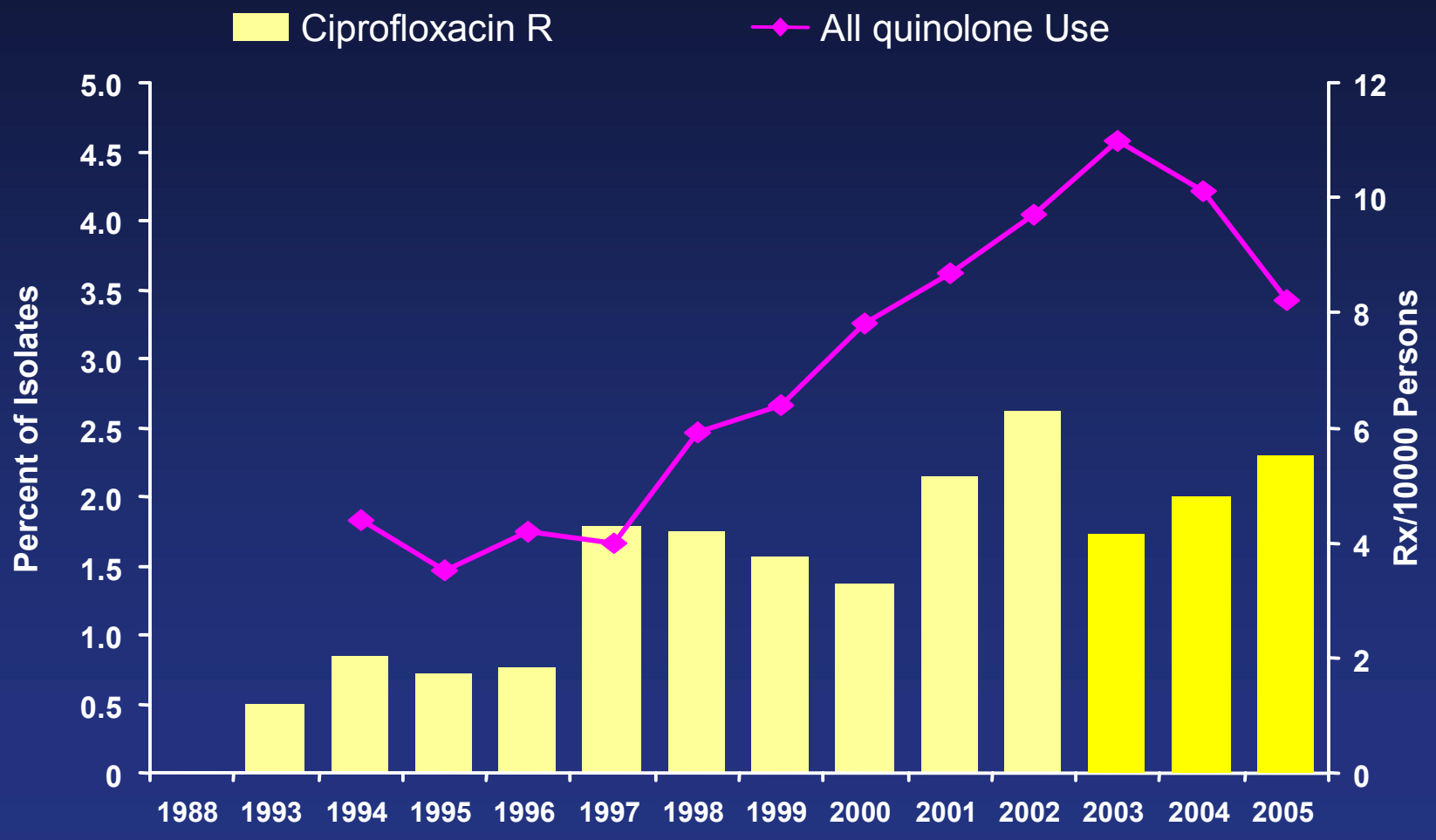
- Helps us understand factors driving resistance
- Made up of ~65 clinical laboratories across Canada
- Shows how long acting & marginally active drugs drive resistance

Use of Longer-Acting Drugs Drove Increase in Macrolide-Resistant SP



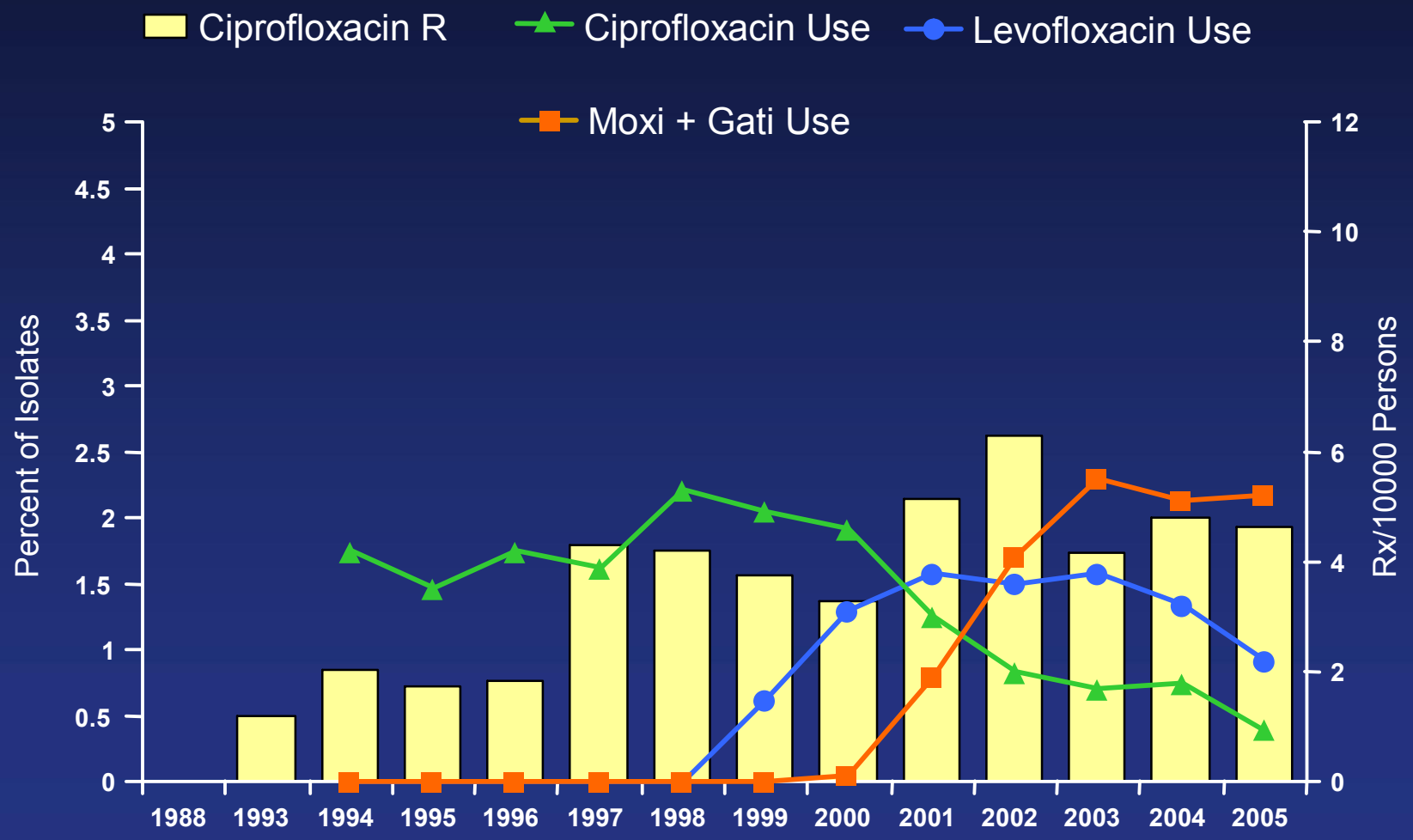
Canadian Bacterial Surveillance Network, Feb. 2006

Why Did Quinolone Resistance Rates Stabilize in Canada in Early 2000s?



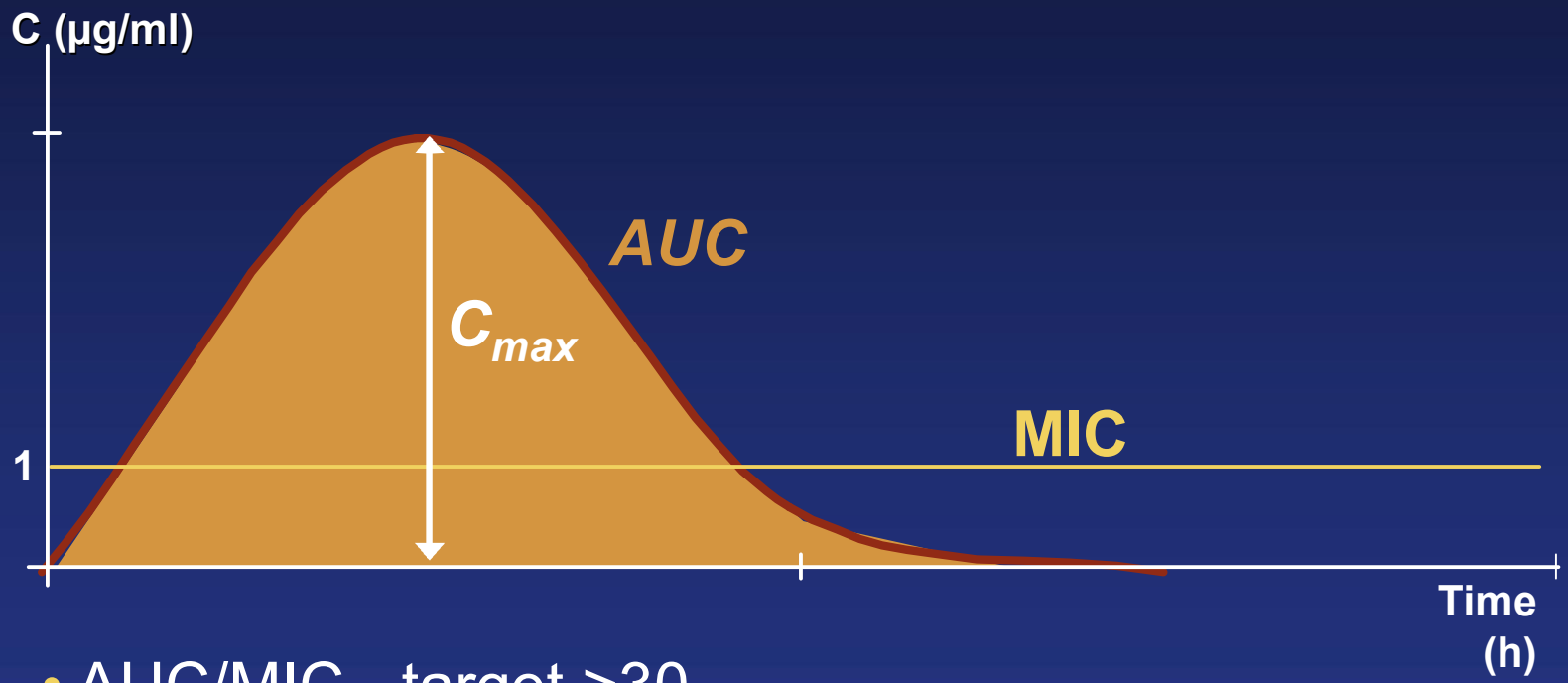
Canadian Bacterial Surveillance Network, Feb. 2006

Resistance Stable Because More Active Quinolones Being Used



PK/PD Parameters Can Predict Activity, Bacterial Eradication & Clinical Efficacy

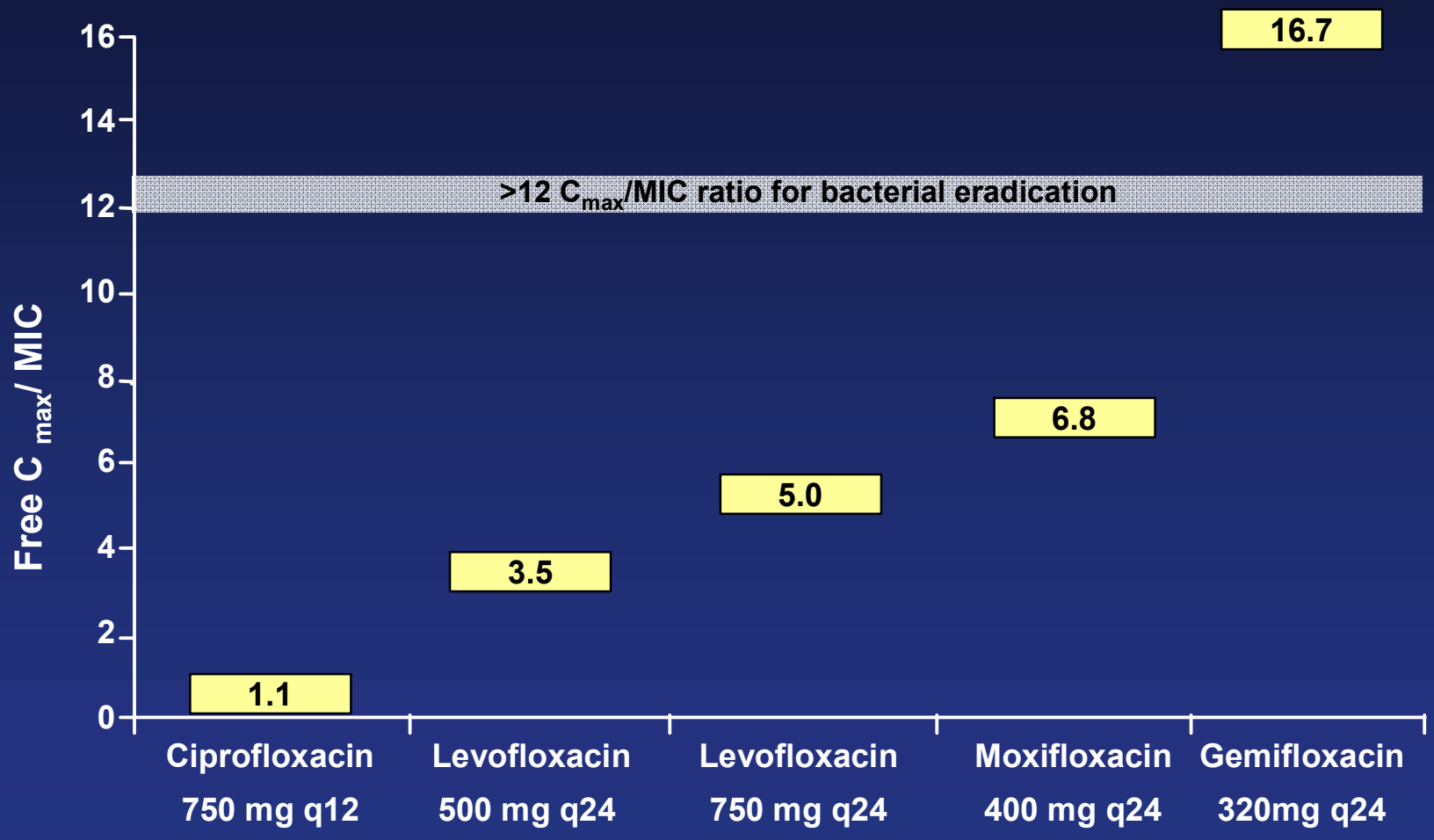
PK/PD Profile for Quinolones



- AUC/MIC - target >30
- C_{max}/MIC - target >12

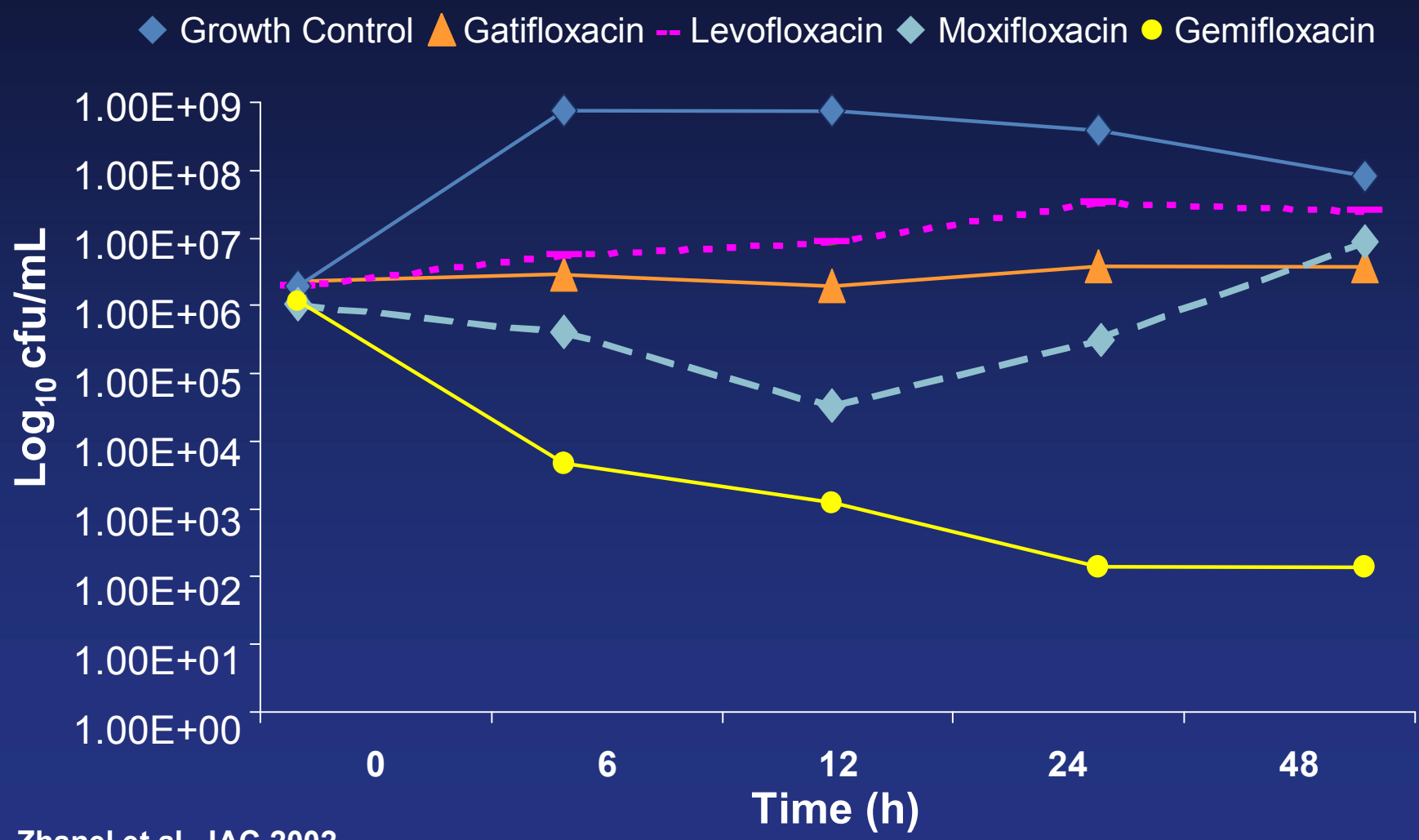
Adapted from Craig, et al. PIDJ 1996; Zhanel. Curr Infect Dis Report 2001

Gemifloxacin is the Most Active Flouroquinolone: C_{max}/MIC



Zhanel and Noreddin, Curr Op Pharm 2001
Preston et al. JAMA 1998

Fluoroquinolone Killing of a Quinolone-Resistant *S. pneumoniae* Isolate Simulating Free AUC/MIC Ratios



Zhanel et al, JAC 2002.

Gemifloxacin Package Insert:

"Gemifloxacin acts by inhibiting DNA synthesis through the inhibition of both DNA gyrase and topoisomerase IV (TOPOIV), which are essential for bacterial growth."

"Gemifloxacin has the ability to inhibit both enzyme systems at therapeutically relevant drug levels in *S. pneumoniae* (dual targeting), and has MIC values that are still in the susceptible range for some of these double mutants."

Microbiological Criteria for Ideal Drug for ABS

- Low potential for resistance induction
- Penetrate tissues rapidly
- Be of appropriate spectrum
- Be rapidly bactericidal
- Have half-life appropriate for once-daily therapy
- Short-term dosing

Sande and Gwatney CID 2004

Gemifloxacin -- Appropriate Treatment Choice for ABS

- Penetrate tissues rapidly
  - Tissue concentrations on average 2- or 3-fold higher than plasma concentration
- Be rapidly bactericidal
  - Concentration dependent bacterial killer
- Be of appropriate spectrum
  - Excellent activity against common respiratory pathogens

Sande and Gwatney CID 2004

Gemifloxacin -- Appropriate Treatment Choice for ABS

- Have half-life appropriate for once-daily therapy
  - 8-hour half-life
- Short-term dosing
  - 5-day course of therapy
- Have low potential for resistance induction

Sande and Gwatney CID 2004