Measuring the Efficacy of Antibiotic Therapy in Acute Otitis Media

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Possible Outcomes for Measuring the Efficacy of Antibiotics in Acute Otitis Media

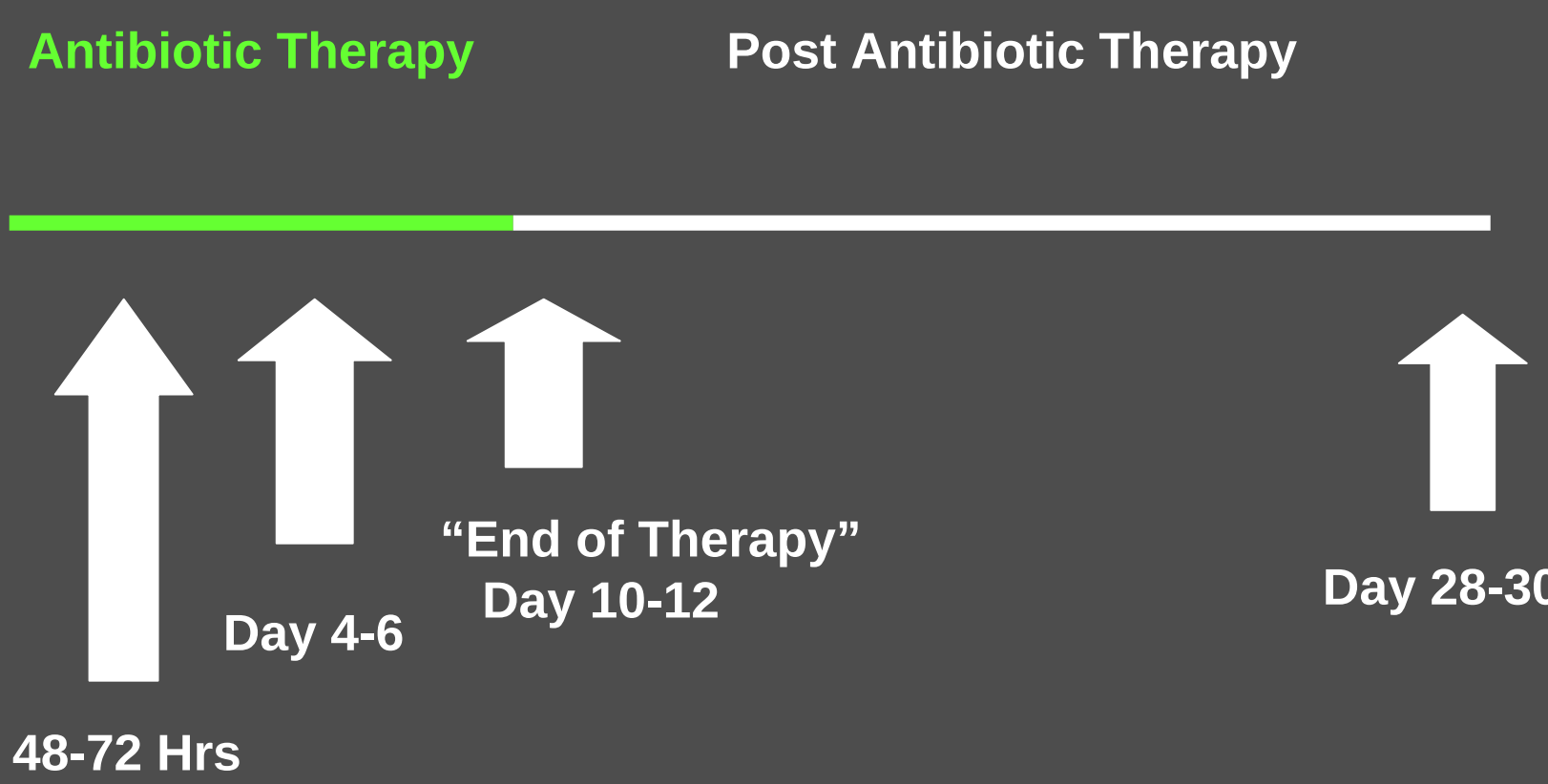
Clinical

- **Symptomatic response** - improvement, persistence, or worsening of earache, irritability and fever
- **Otoscopic evidence of persistent infection** - an opaque, bulging ear drum or otorrhea
- **Middle ear effusion** - by tympanometry, reflectometry or otoscopy (mobility)
- **Compound clinical outcomes** - combinations of the above clinical outcomes

Bacteriologic

- **Eradication of bacteria from the middle ear**

Timing of Clinical Outcomes in Trials of Antibiotic Therapy for Acute Otitis Media



Symptomatic Response and Eradication of Bacteria from the Middle Ear

Bacteriologic and Clinical Outcomes in Acute Otitis Media

	Bacteriologic outcome	
	Eradication	Persistence
Clinical outcome		
Success	236 (93%)	25 (62%)
Failure	17 (7%)	15 (28%)
	253	40

P = 0.001

Carlin et al. Pediatr 1991; 118:178

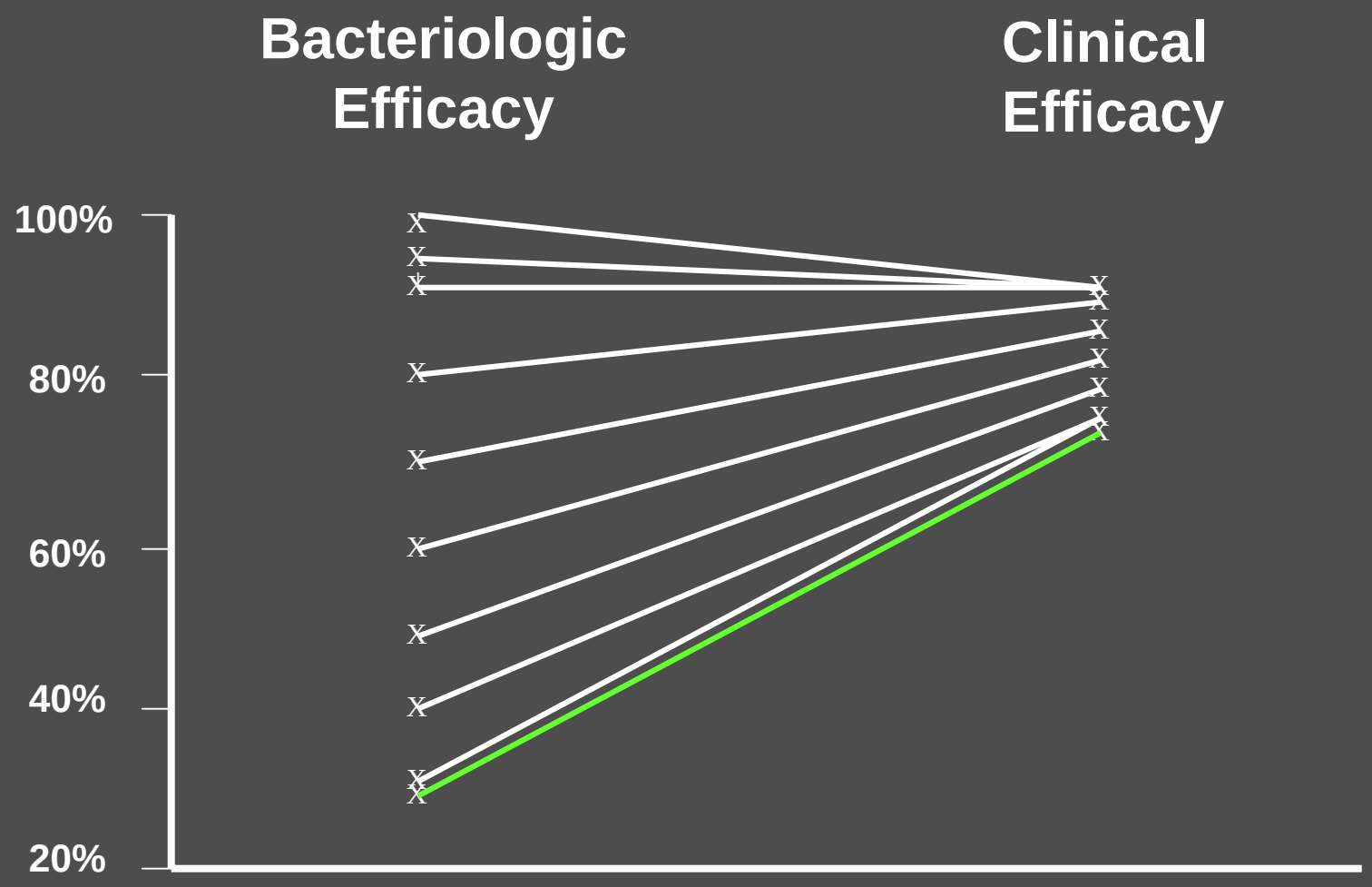
Clinical Success Rates in Acute Otitis Media

- **Bacteriologic Success 236/253 (93.2%)**
- **Bacteriologic Failure 25/40 (62.5%)**
- **Non-Bacterial AOM 124/155 (80.0%)**

*** *P*=0.001, ** *P*=0.013**

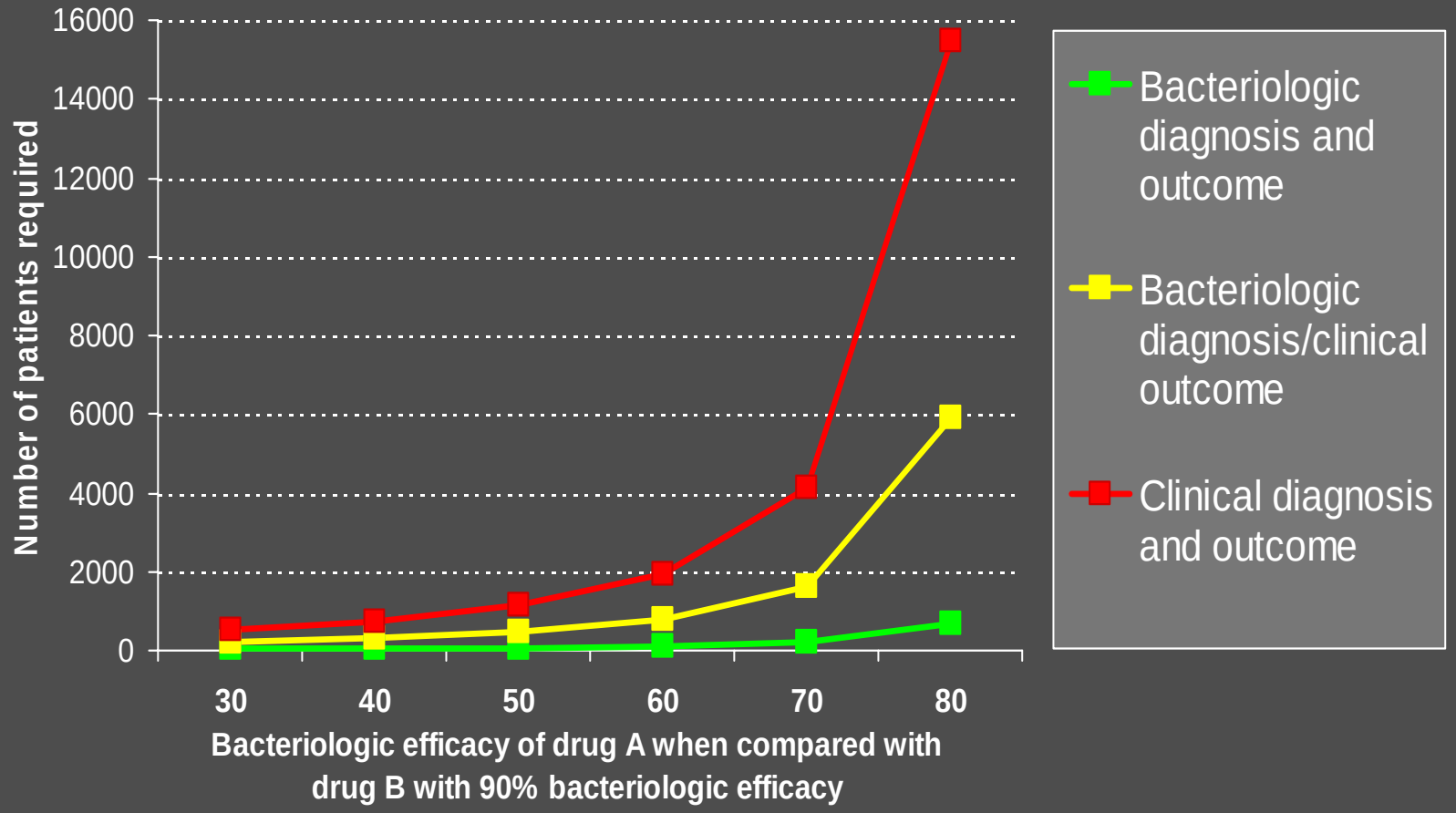
Marchant CD et. al. J Pediatr 1992;120:72

The Pollyanna Phenomenon



Marchant CD et. al. J Pediatr 1992;120:72

Sample Sizes Required to Detect Differences Between Antibacterial Drugs for Acute Otitis Media (AOM): Comparison of Bacteriologic Versus Clinical Outcomes in trial of 2 Drugs With Varying Bacteriologic Efficacy (Half the patients would be in each arm of a study)



Measuring the comparative efficacy of antibacterial agents for acute otitis media: The "Pollyanna Phenomenon." Colin D. Marchant, Susan A. Carlin, Candice E. Johnson, and Paul A. Shurin. *J Pediatrics* 1992;120: 72-77.

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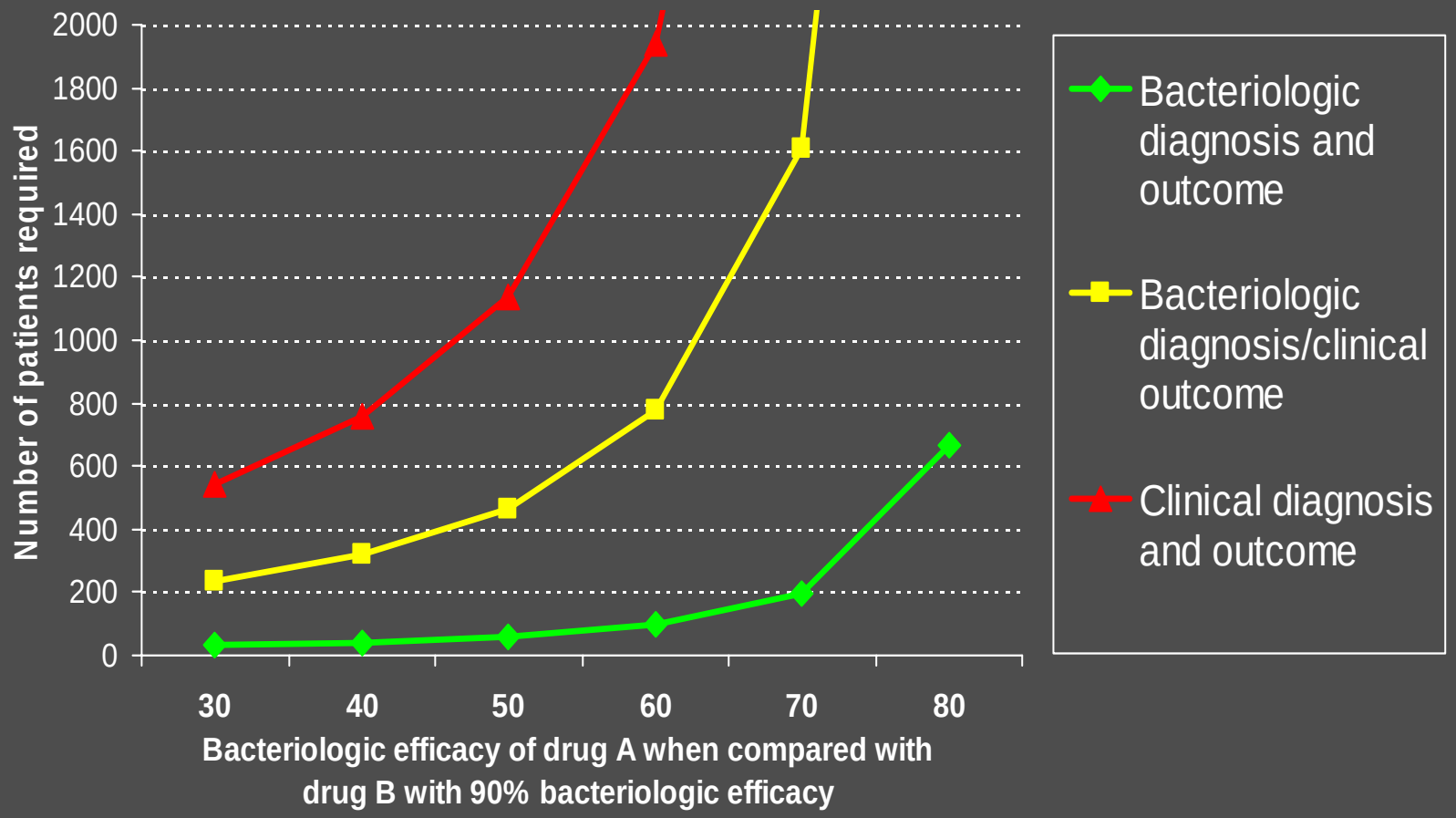

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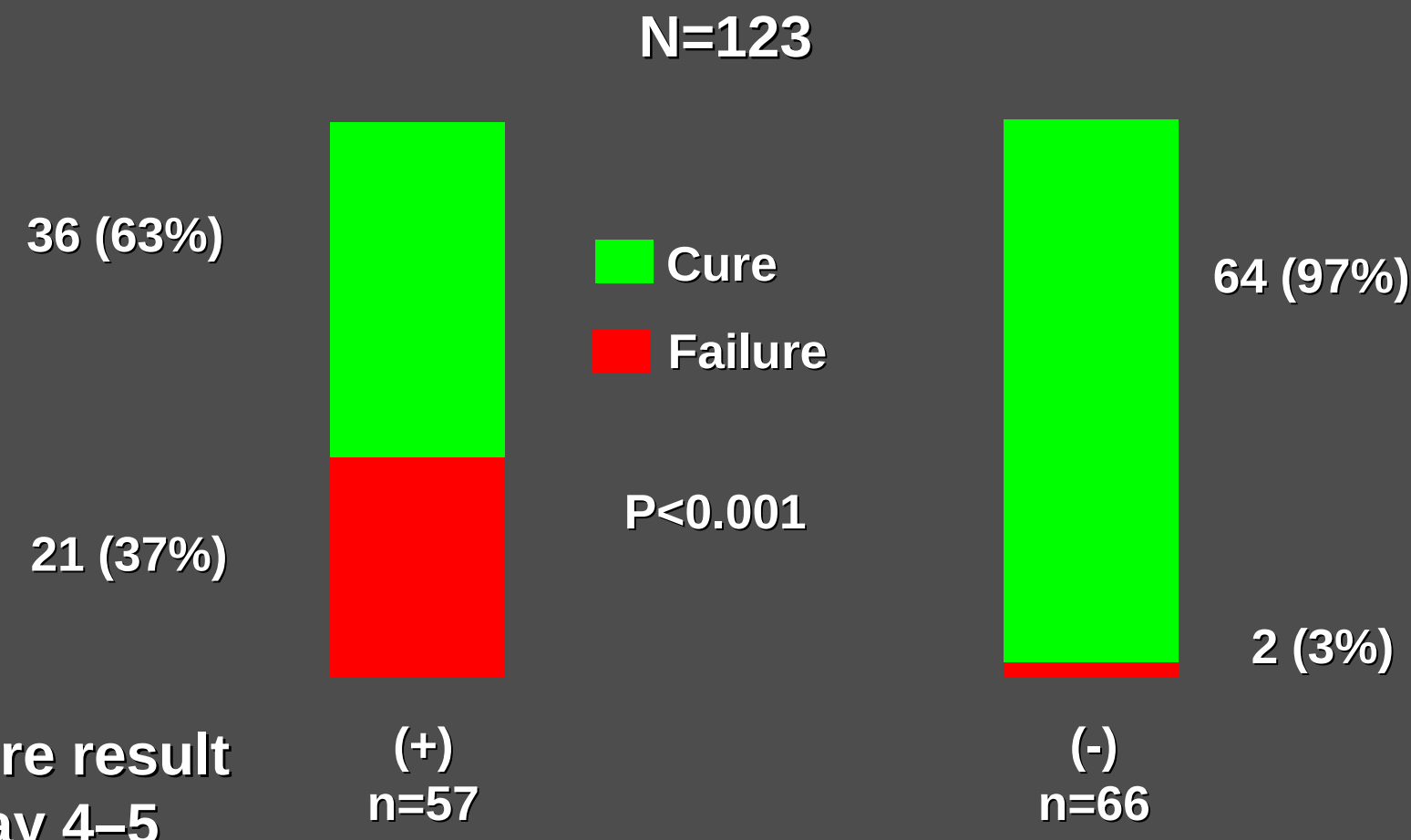
Clinical Versus Bacteriologic Outcome



Dagan et al. Pediatr Infect Dis J 1998;17:776.

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	Eradication	Persistence
Clinical outcome		
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	253	40

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Carlin et al. Pediatr 1991; 118:178

Bacteriology of Acute Otitis Media Unresponsive to Initial Antimicrobial Therapy

Initial therapy	Culture of Middle Ear Exudate		
	Sterile	Sensitive pathogen	Resistant pathogen
Ampicillin/Amoxicillin (N=31)	19 (61%)	5 (16%)	7 (23%)
Other (N=12)	6 (50%)	5 (42%)	1 (8%)
Total	25 (58%)	10 (23%)	8 (19%)

Teele et al, J Ped 1981; 98:537

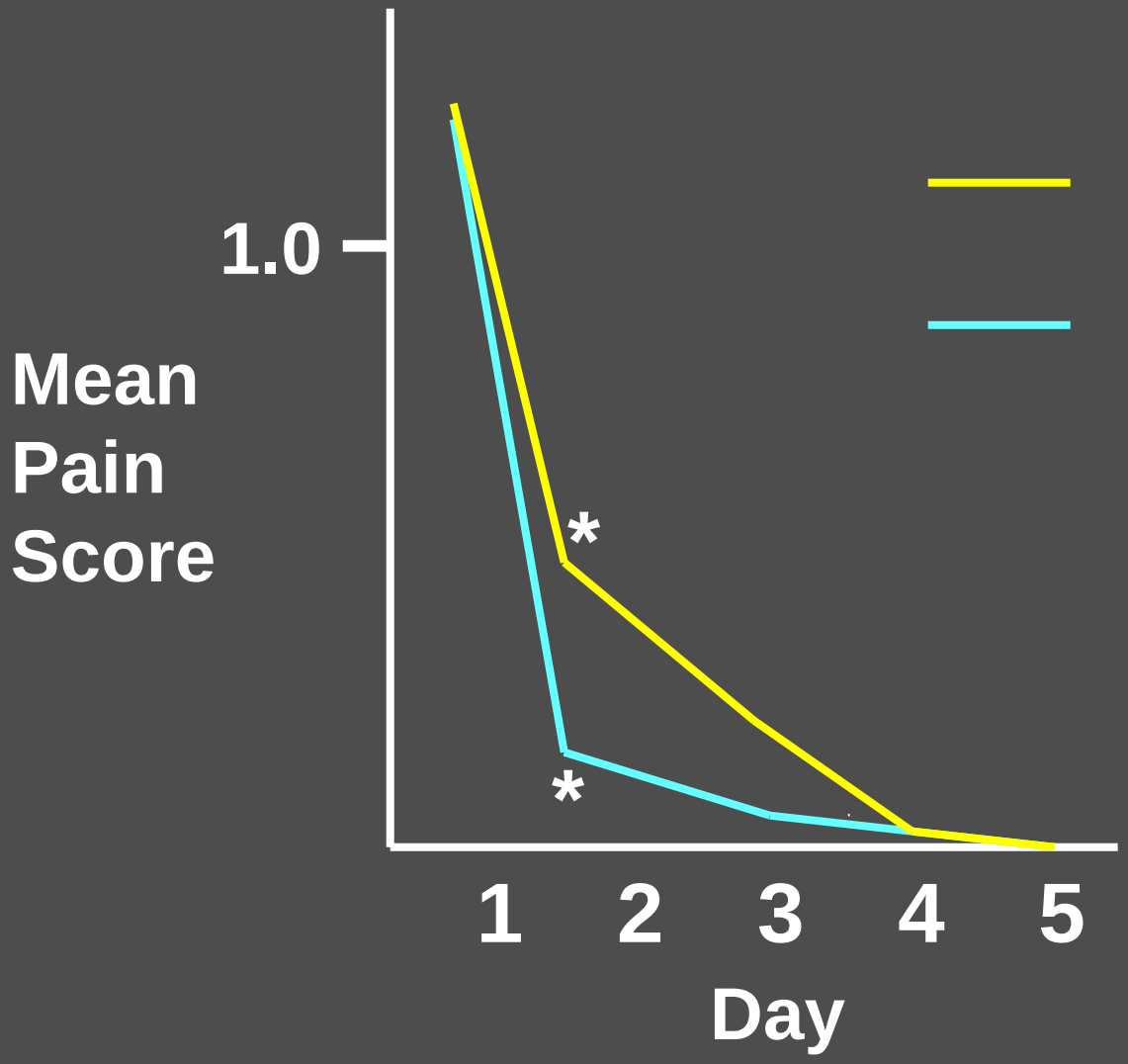
Nasopharyngeal and Middle Ear Viral Infection in Acute Otitis Media vs Nonresponse to Antibacterial Therapy

	Newly diagnosed acute otitis media (N=66)	Symptomatic AOM after 48 hours of antibacterial therapy (N=22)
Adenovirus	1	5
RSV	9	4
Rhinovirus	17	3
Influenza B	1	1
Parainfluenza 3	0	1
Echo II	0	1
Any virus	27 (41%) *	15 (68%) *

Arola et al J Pediatr 1990;116:697

* p<0.05

Effect of Antibiotic Treatment on Earache in Severe AOM



Mygind et al
Clin Otolaryngol
1981;6:5

AGE AND BACTERIOLOGIC OUTCOME IN ACUTE OTITIS MEDIA

BACTERIOLOGIC OUTCOME (DAYS 2 TO 6)

	Success	Failure
N	253	40
Mean Age (Mo)	18.5*	10.6*

Carlin et al, J Pediatr 1987; 118:178

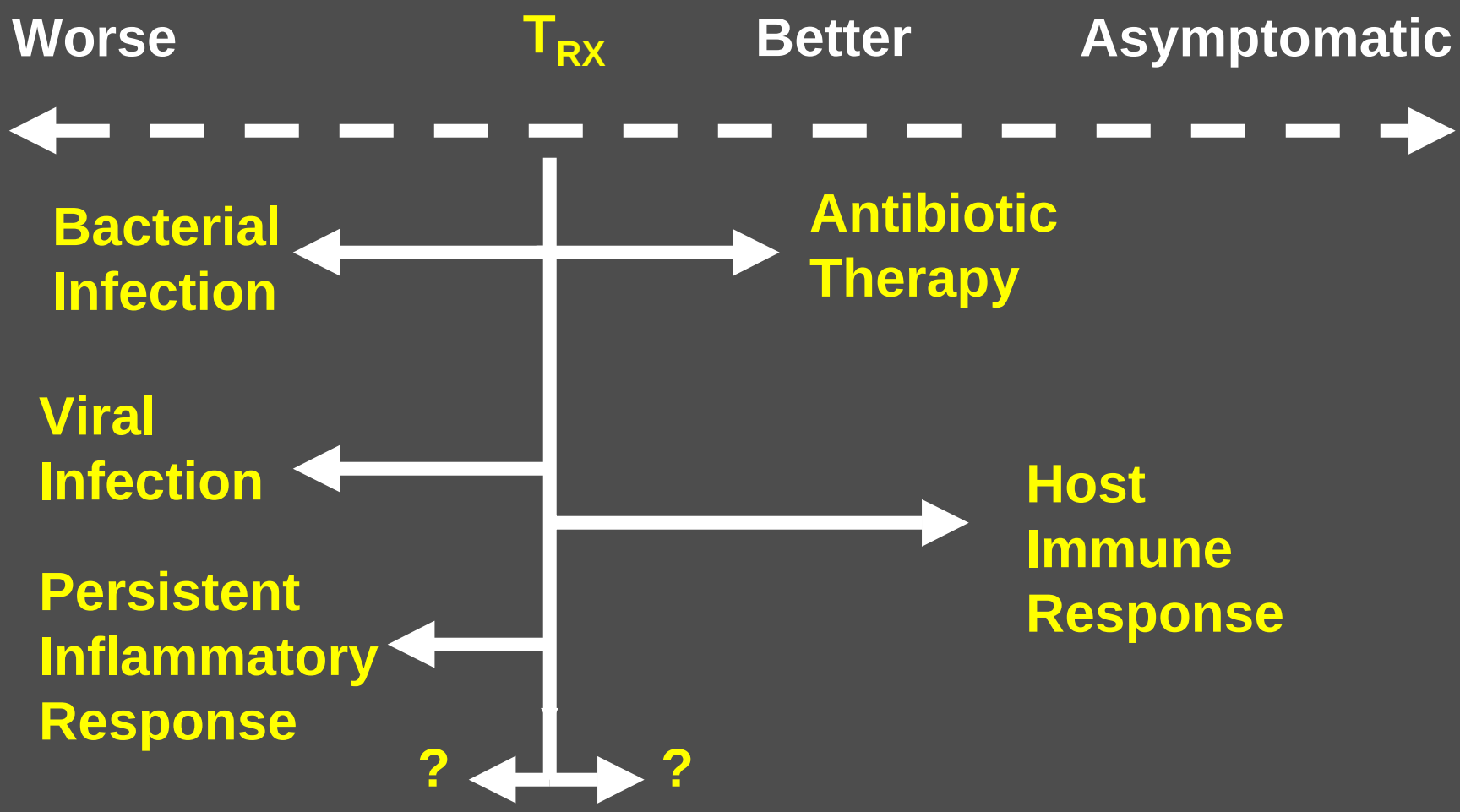
Amoxicillin vs Placebo in AOM

Effect of Age on Initial Clinical Failure

	Initial Rx Failure	
	Amox	Placebo
Age < 2 yrs	6.5%	9.8%
Age > 2 yrs	0.5%	5.5%

Kaleida et. al. Pediatrics 1991;87:466

Symptomatic Response in Acute Otitis Media



Are Recurrences of AOM After Therapy Failures of Therapy ?

or

Should Outcomes After Therapy be Used in Comparative Trials of Antibiotic Therapy for AOM ?

Treatment of Non-severe and Severe AOM

% initial treatment failure

	Placebo (Non-severe) or Myringotomy (severe)	Amoxicillin only
Non-severe AOM	3.9%	7.7% **
Severe AOM	23.5%	9.6% **

** P< 0.01

Kaleida, et al. *Pediatrics, 1991*

Amoxicillin vs Placebo for Non-severe AOM

	Amox N=522	Placebo N=527	P-Value
Initial Rx Failure	3.9%	7.7%	0.009
Effusion 2 wks	46.9%	62.5%	<0.001
Effusion 6 wks	45.9%	51.5%	0.09
Reccurences 2-6 weeks	27.9%	27.6%	0.95

Kaleida et. al. Pediatrics 1991;87:466

Early Recurrences of Acute Otitis Media: Reinfection or Relapse?

Reinfection* (New species or strain)	**12 (41%)**
Relapse* (Same species or strain)	**4 (14%)**
Undefined (Sterile middle ear exudate on first or second culture)	**13 (45%)**
	29

Defined by speciation of bacterial isolates, capsular serotyping of *S. pneumoniae*; biotyping, SDS PAGE OMP patterns and ß-lactamase production by *H. influenzae*; and ß-lactamase production by *M. catarrhalis.*

Carlin et al. *J Pediatr 1987;110:20*

Bacteriologic Relapses After Treatment of AOM (N=4)

Initial Infection	Recurrence (day 1-24 post Rx)
S. pneumoniae (non-viable)	*S. pneumoniae* (19A)
M. catarrhalis (BL+) & *H. influenzae* (BL-)	*M. catarrhalis* (BL+)
M. catarrhalis (BL+)	*M. catarrhalis* (BL+)
S. pneumoniae (6B) & *H. influenzae* (BL-, biotype III)*	*S. pneumoniae* (6B) & *H. influenzae* (BL-, biotype III)*

* paired HI infections also had identical OMP electrophoretic patterns

Carlin et al, J Pediatr 1987;110:20

New Infections After Treatment of AOM (N=12)

Initial Infection	Recurrence (day 1-24 post Rx)
S. pneumoniae	*H. influenzae* (BL-)
S. pneumoniae	*M. catarrhalis* (BL+)
S. pneumoniae	*H. influenzae* (BL-)
S. pneumoniae (14)	*S. pneumoniae* (23F)
S. pneumoniae (9V)	*S. pneumoniae* (23F) & *H. influenzae* (BL-)
M. cattarrhalis (BL+)	*S. pneumoniae*
S. pneumoniae & *M. catarrhalis* (BL-)	*H. influenzae* (BL-) & *M. catarrhalis* (BL+)
S. pneumoniae	*M. catarrhalis* (BL+)
H. influenzae (BL-,biotype III)*	*H. influenzae* (BL-, biotype II)*
H. influenzae (BL-)	*S. pneumoniae*
H. influenzae (BL-)	*S. aureus*
H. influenzae (BL-,biotype V)*	*H. influenzae* (BL-, biotype III)*

* paired HI infections also differed in OMP electrophoretic pattern

Carlin et al, J Pediatr 1987;110:20

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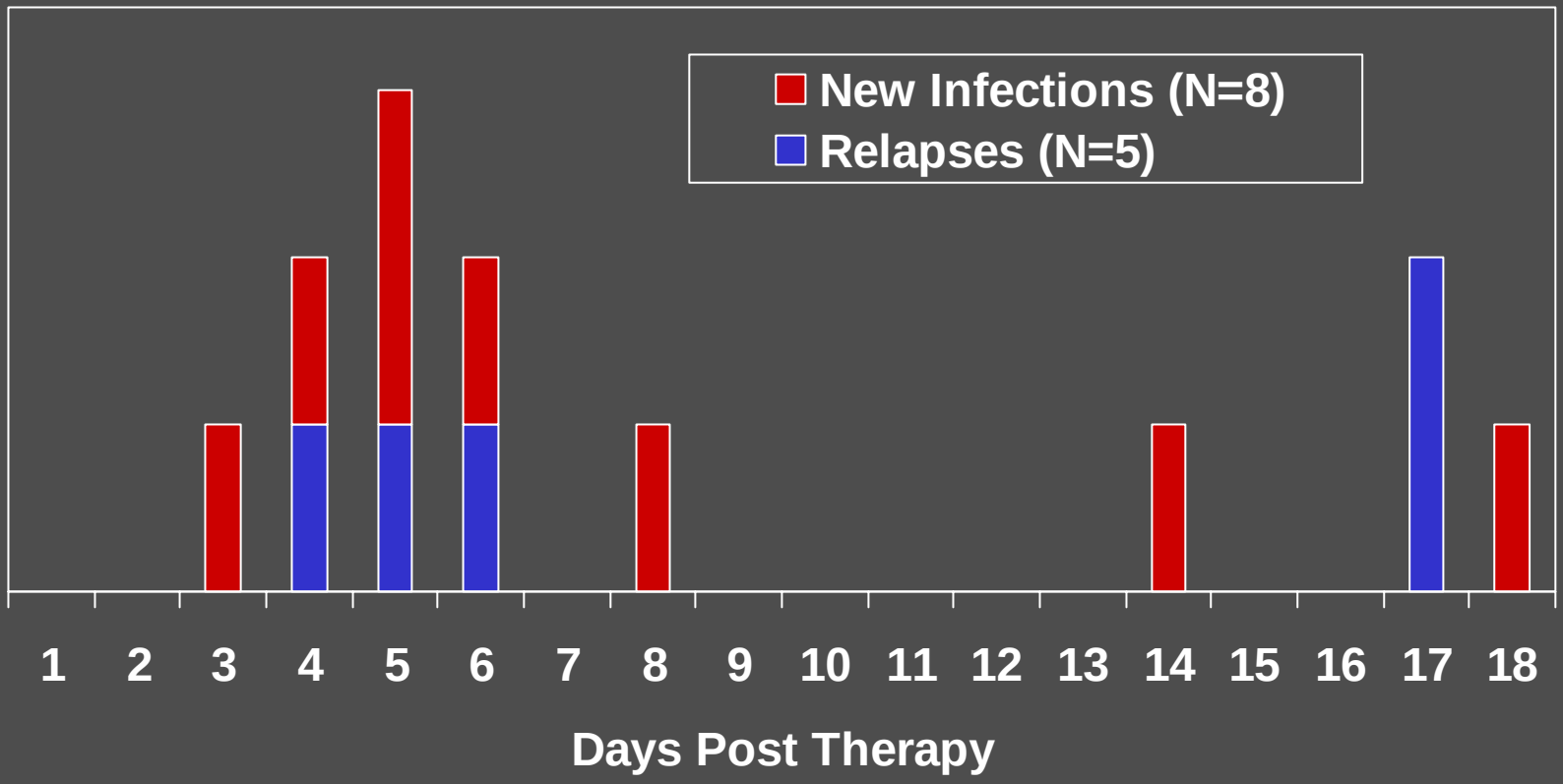
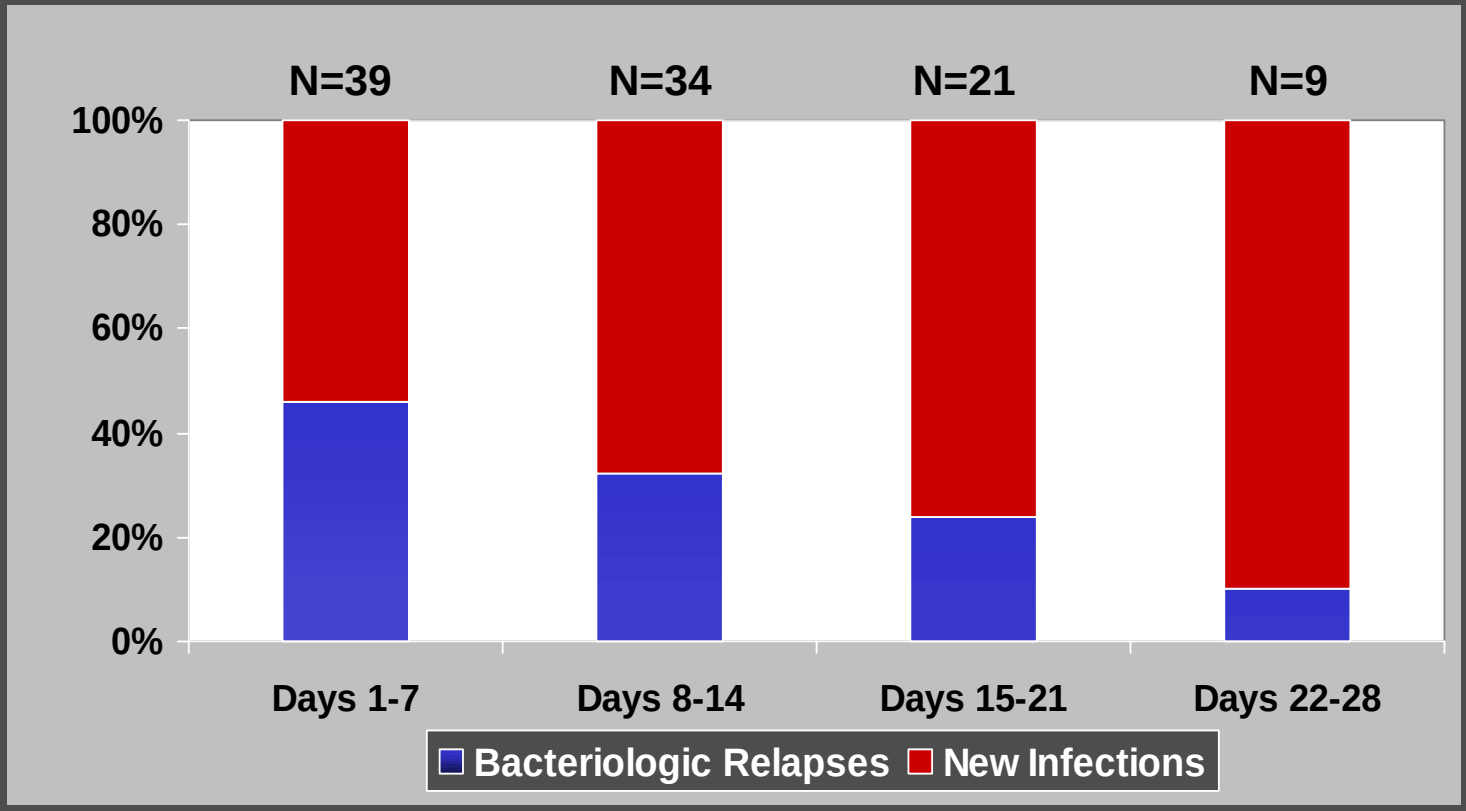
Bacteriology of Initial and Recurrent Episodes of Acute Otitis Media (3-18 Days Post Therapy)



Del Baccaro et al J Pediatr 1992;120:81

Clinical Relapses of AOM 1 Month After Completion of Treatment



Relapses vs New Infections determined for *Streptococcus pneumoniae* by PFGE and serotyping, and for *Haemophilus influenzae* by beta-lactamase production

from Leibowitz et al ICCAC Abstract #1968, Sept 2000

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