

# Pediatric Specialists *of Virginia*

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**Children's National**™



**I have no financial interests to disclose**

**1 out of 2 children receive  
a macrolide agent in the U.S.**

# **Macrolides: Managing Medicines and Myths**

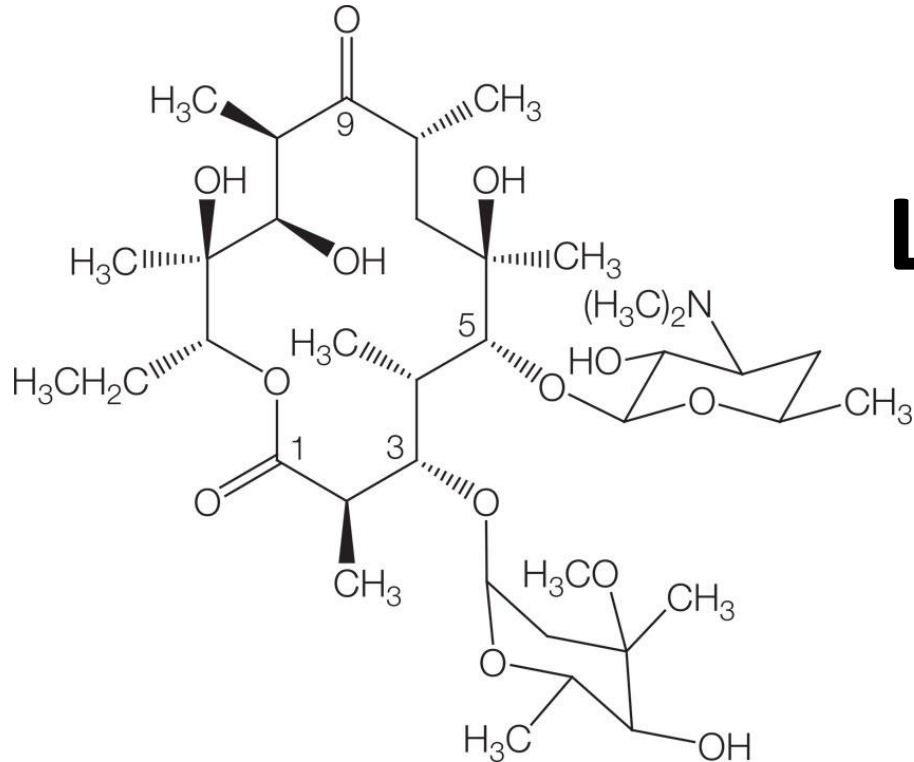
**Andrew Nuibe, MD, MSCI**

# Dr. Abelardo Aguilar



# *Streptomyces erythreus*

## Erythromycin

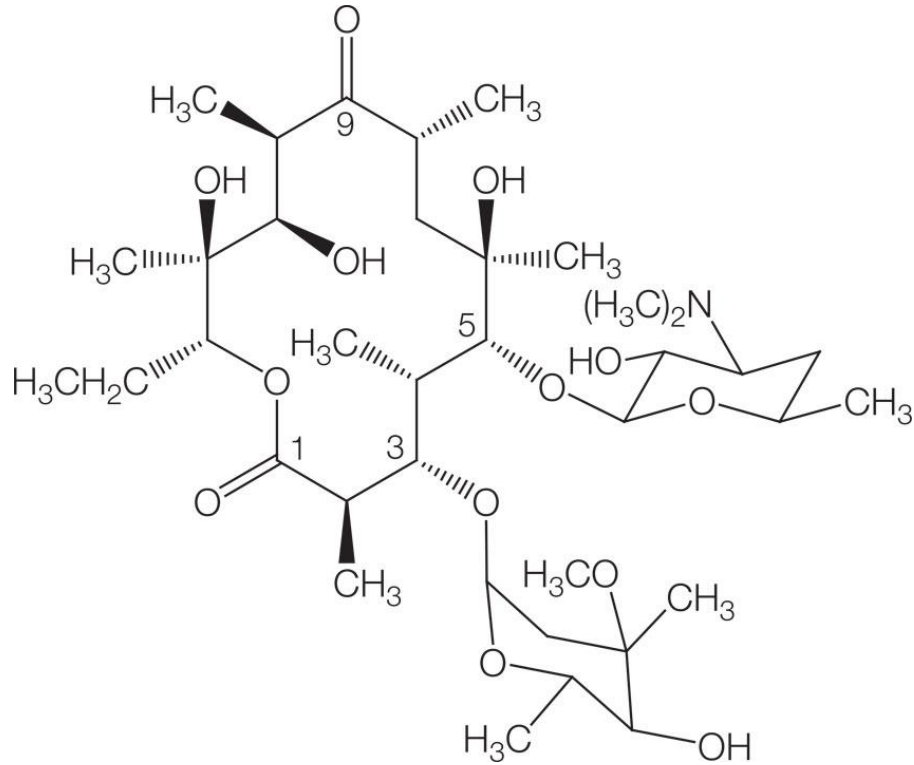


**Lactone ring = -olide**

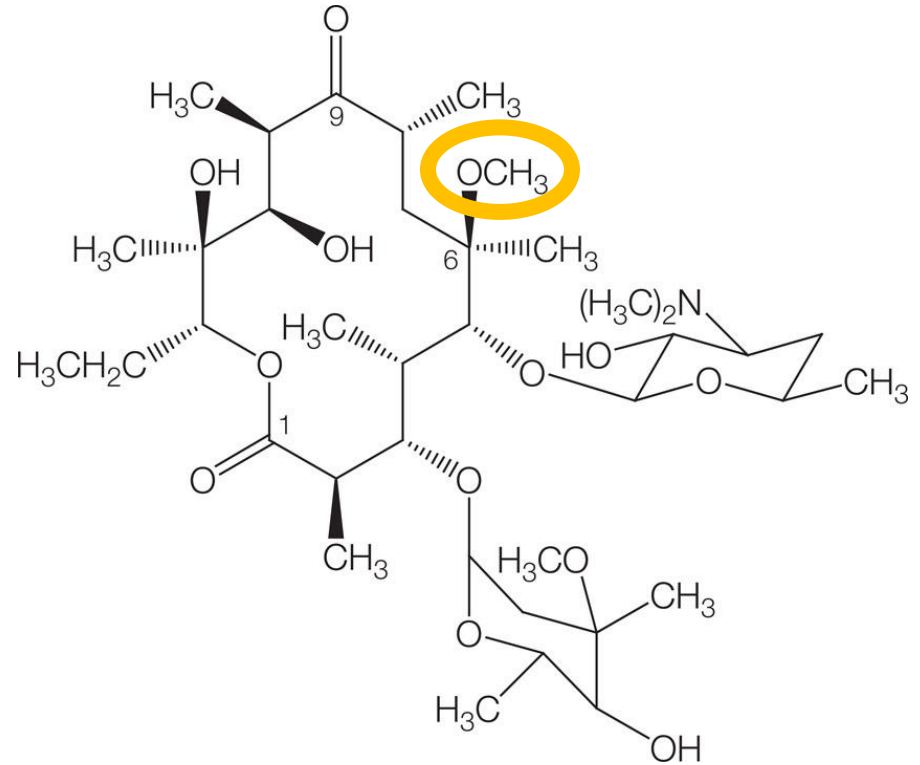
**Macrolide**

1980

# Erythromycin

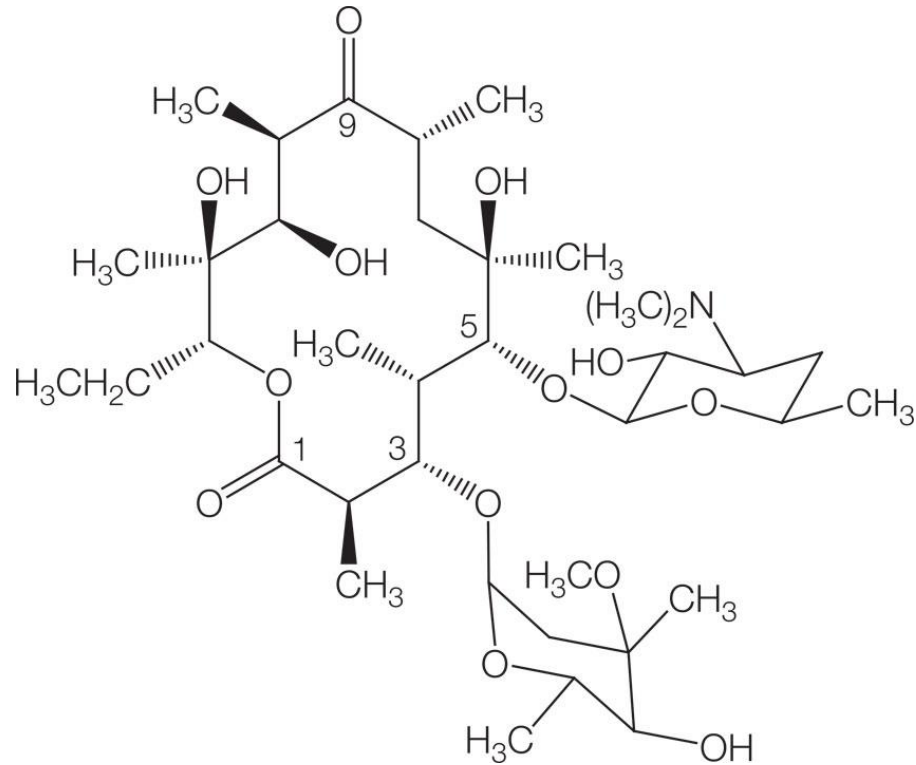


# Clarithromycin

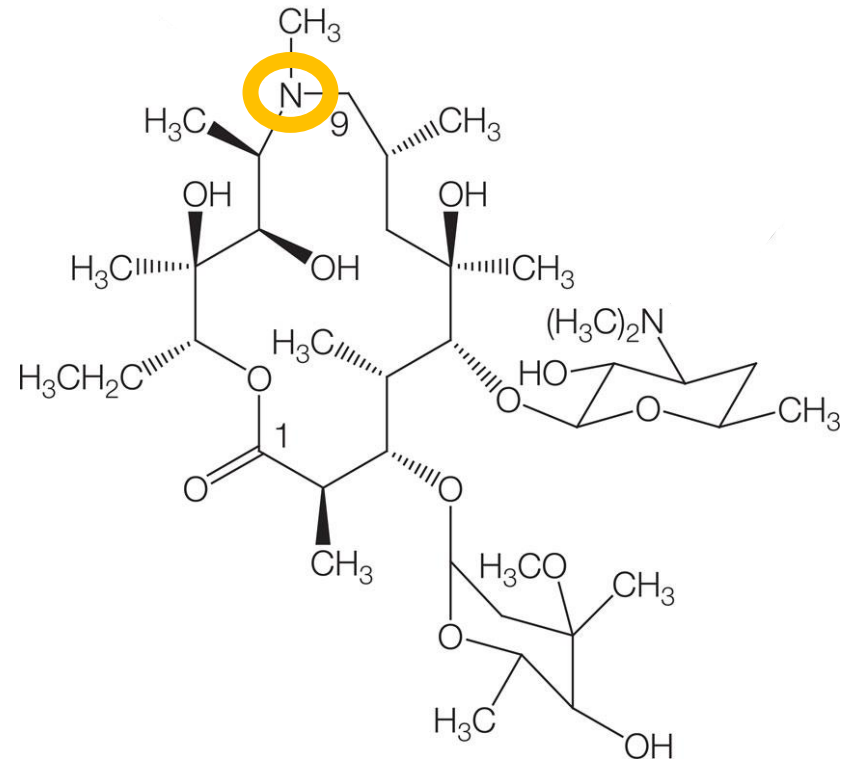


1988

# Erythromycin



# Azithromycin





**Erythromycin**

**Clarithromycin**

**Azithromycin**

**Erythromycin****Clarithromycin****Azithromycin****Acid stable****No\*****Yes****Yes****Absorption  
with food****Decreased\*****No affect\*****No affect****CYP450  
interaction****High****Moderate****Low****Serum  $t_{1/2}$** **4 hours****7 hours****~3 days**



**Erythromycin > Clarithromycin > Azithromycin**



**32%**



**13%**



**12%**



**Erythromycin**

**Clarithromycin**

**Azithromycin**

## Neonatal exposure

## Pyloric Stenosis Outcome

**Erythromycin**

For < 14 days old:  
**0.003 /patient year → 0.01 /patient year**

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For 14 - 120 days old:  
**0.003 /patient year → 0.005 /patient year**

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**Clarithromycin**

**No increased risk**

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**Azithromycin**

For ≤ 14 days old:  
**0.2% → 1.7%**

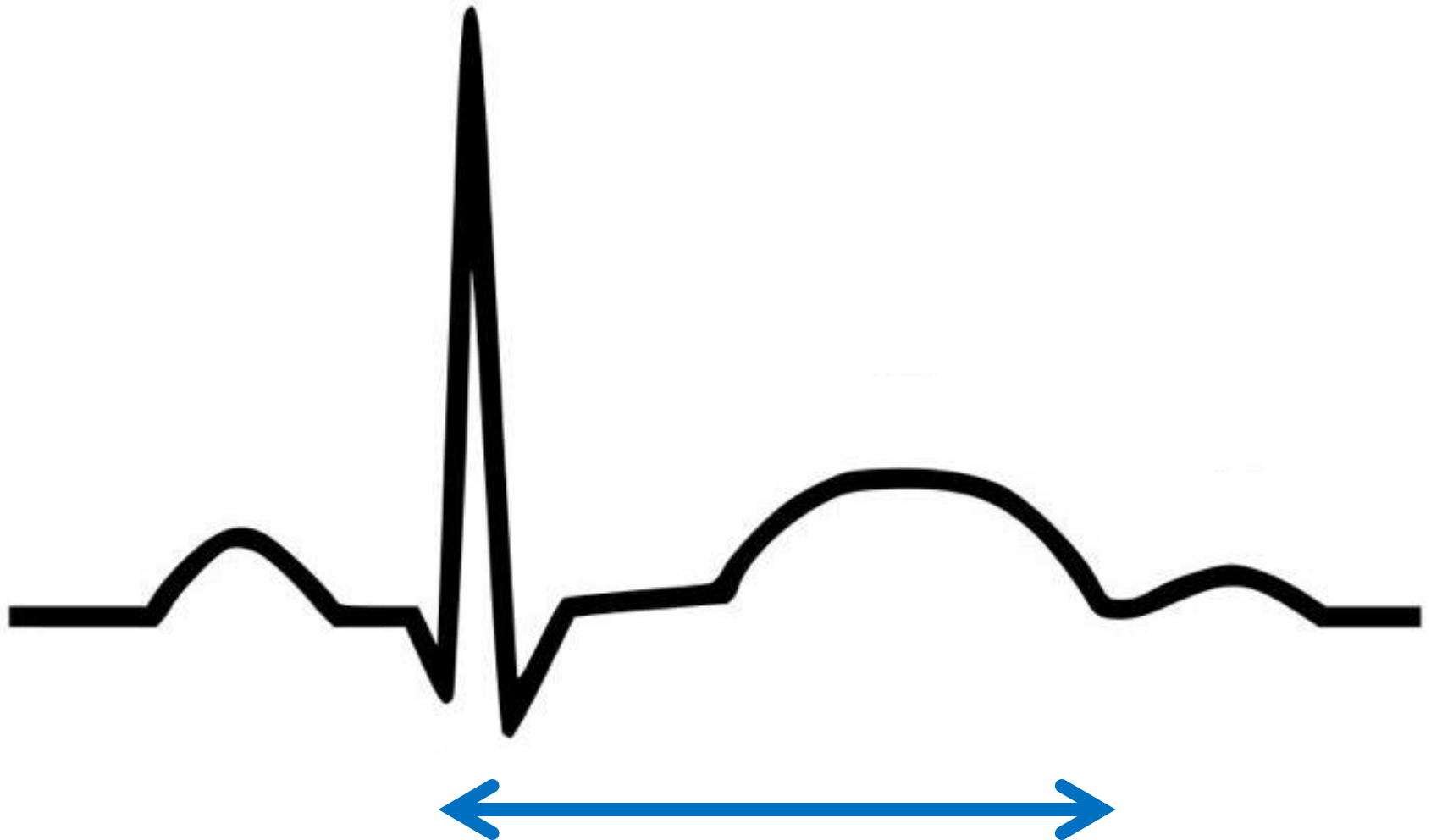
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For 15 - 42 days old:  
**0.2% → 0.6%**

**Pyloric stenosis is rare**

**Erythromycin or azithromycin in the first 2 weeks of life give the highest risk for pyloric stenosis**

# 1980s: Case reports of cardiac arrhythmia with erythromycin & clarithromycin





	No antibiotic	Azithromycin
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<b>Number of cases</b>	<b>1,319,810</b>	<b>347,795</b>
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<b>Mean score for CVD risk</b>	<b>9.2</b>	<b>9.2</b>
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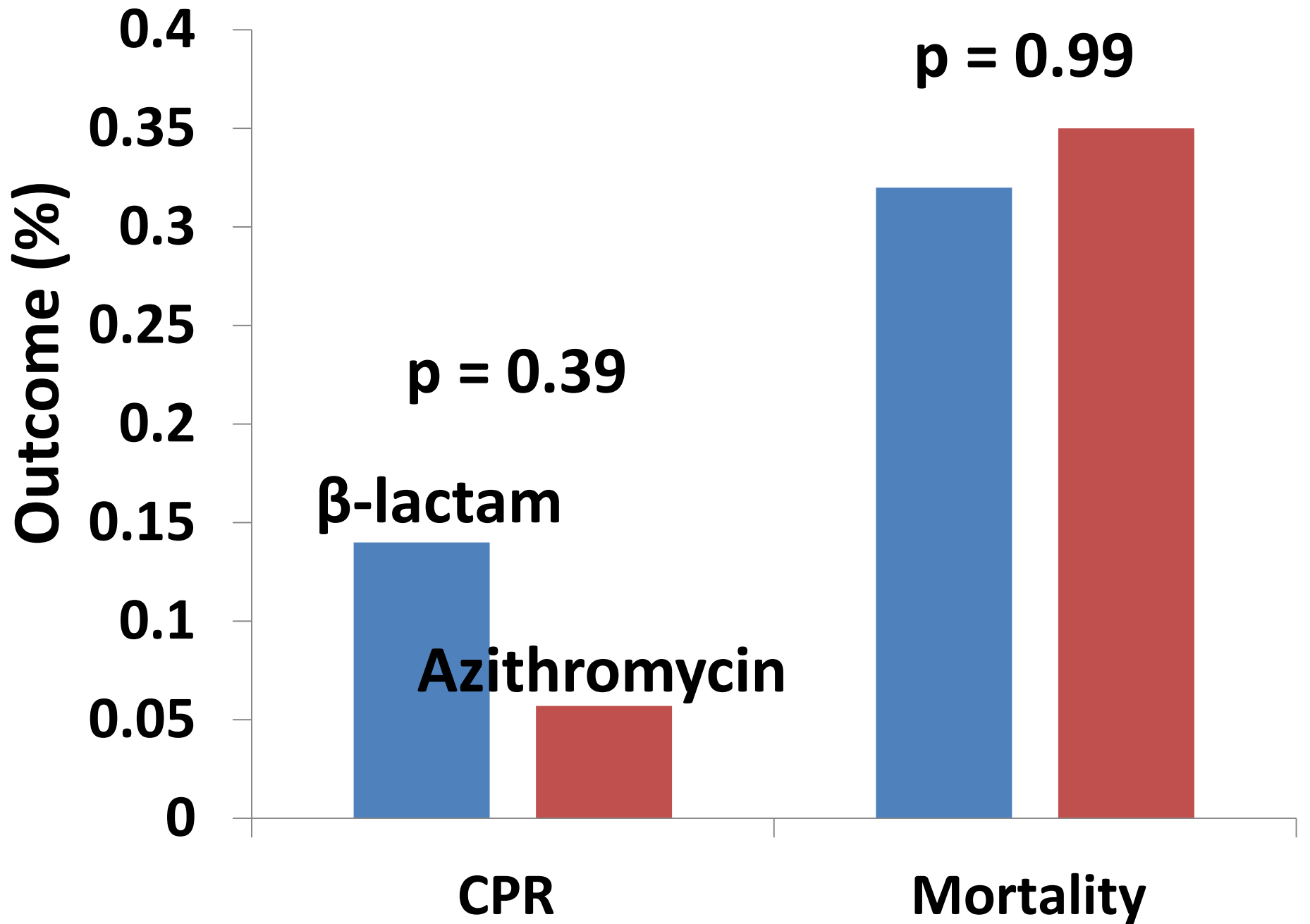
<b>Sudden cardiac death HR</b>	<b>1</b>	<b>2.71 (95% CI: 1.6-4.6)</b>
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**Did not record EKGs**

**Azithromycin cohort mean age:  
~50 years old**

**Azithromycin cohort: ~75% female**

**Concurrent medications unclear**



**Azithromycin does not increase the  
risk of pediatric cardiac arrest  
compared to beta-lactams**



**Erythromycin**



**Clarithromycin**  
**Azithromycin**



# Erythromycin

**Alternate therapy for  
*Corynebacterium diphtheriae***

# Clarithromycin

*Helicobacter pylori*

**Some non-tuberculous  
Mycobacterial infections**



# Azithromycin

**Atypical pneumonia**

***Bordetella pertussis***

***Campylobacter jejuni* and *Salmonella*  
species**

***Chlamydia trachomatis***

**Some non-tuberculous  
Mycobacterial infections**

**Azithromycin is not recommend  
for *S.pneumoniae* lower  
respiratory tract infection**

**AAP does not recommend  
azithromycin as first-line  
treatment for AOM**



# **Diffuse panbronchiolitis**

**Chronic erythromycin use  
prolonged the lifespan of diffuse  
panbronchiolitis patients**





**2007: Clarithromycin &  
Rheumatoid arthritis**



**59% got better  
vs 33% ( $p < 0.01$ )**

**2016: Clarithromycin &  
CV inflammation**



**1.9X greater MI risk  
with clarithromycin  
(95% CI: 1.2-2.7)**

**2008: Clarithromycin &  
Crohn's disease**



**26% with remission  
vs 27% ( $p > 0.99$ )**

**2013: Macrolides  
& pediatric asthma**



**Improved FEV1 and  
less oral steroid use  
69 children  
Benefit only with  
troleandomycin**

**2016: Azithromycin  
& pediatric  
asthma-like illness**



**Recovered 3 days faster  
1-3 years old  
Only looked at 1 episode**



**2003: Azithromycin &  
pediatric cystic fibrosis**



**Better FEV1 and  
less exacerbations  
HR 0.65  
(95% CI: 0.44-0.95)**

**2012: Azithromycin &  
pediatric cystic fibrosis**



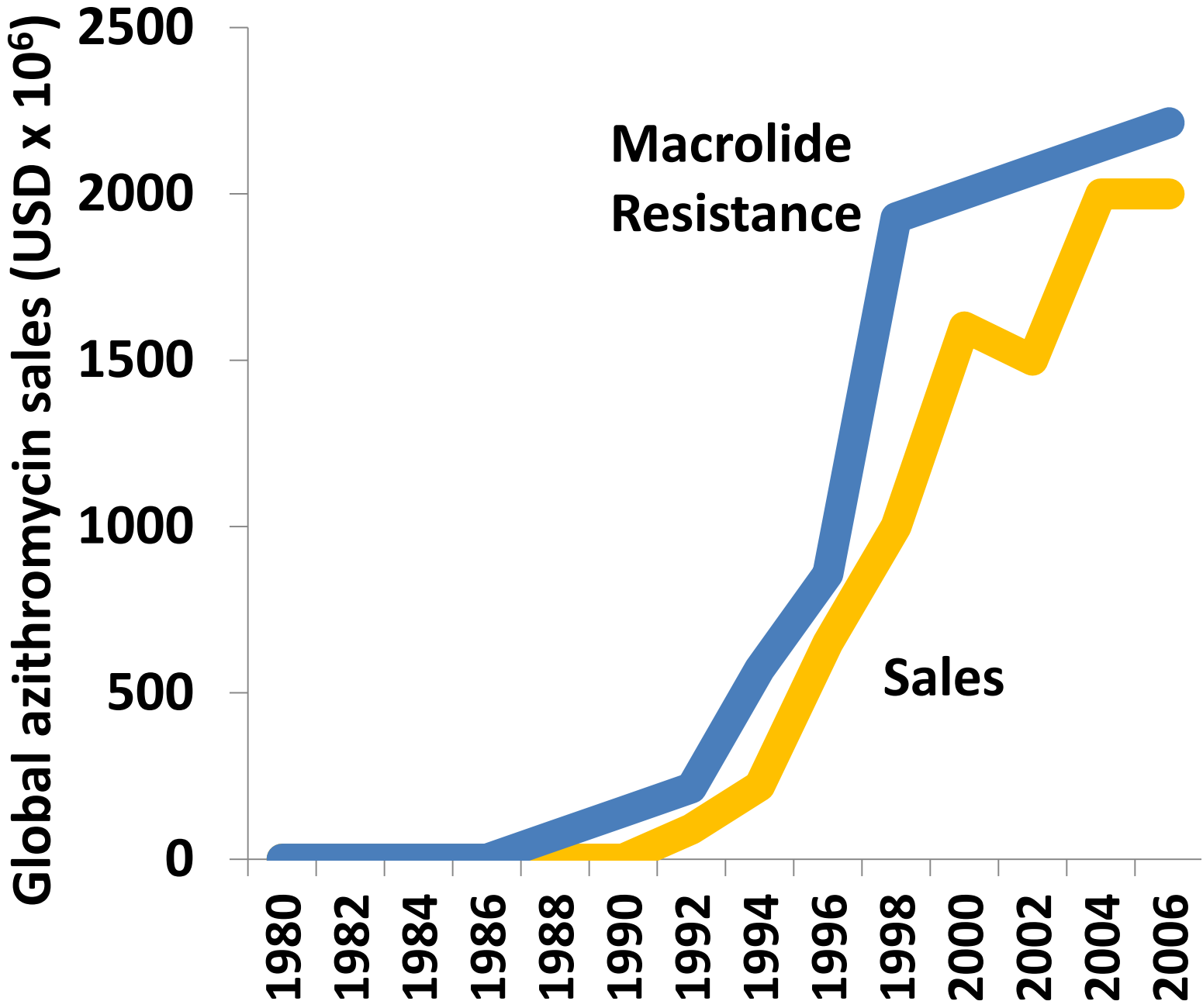
**2X lower risk of  
exacerbation  
(95% CI: 1.2-3.3)**

**2017: Azithromycin &  
pediatric cystic fibrosis**



**Triggered  
*Pseudomonas*  
tobramycin resistance**

**Best evidence of pediatric macrolide  
anti-inflammatory effect in cystic  
fibrosis but it is not risk-free**



**Each macrolide agent is unique**

**Macrolides can do a lot  
but they are not a harmless panacea**

**Carefully consider your macrolide  
prescribing**