

# ~~Macrolides for Asthma~~

## Appropriate anti-microbial coverage for chronic asthma

**Richard J. Martin, M.D.**  
**Prior Chair, Department of Medicine**  
**Edelstein Professor of Medicine**  
**National Jewish Health**

**Professor of Medicine**  
**National Jewish Health**  
**University of Colorado Denver**  
**Mount Sinai School of Medicine**

## **Disclosures:**

**AstraZeneca – consultant**

**Merck – consultant**

**Global Life Science - consultant**

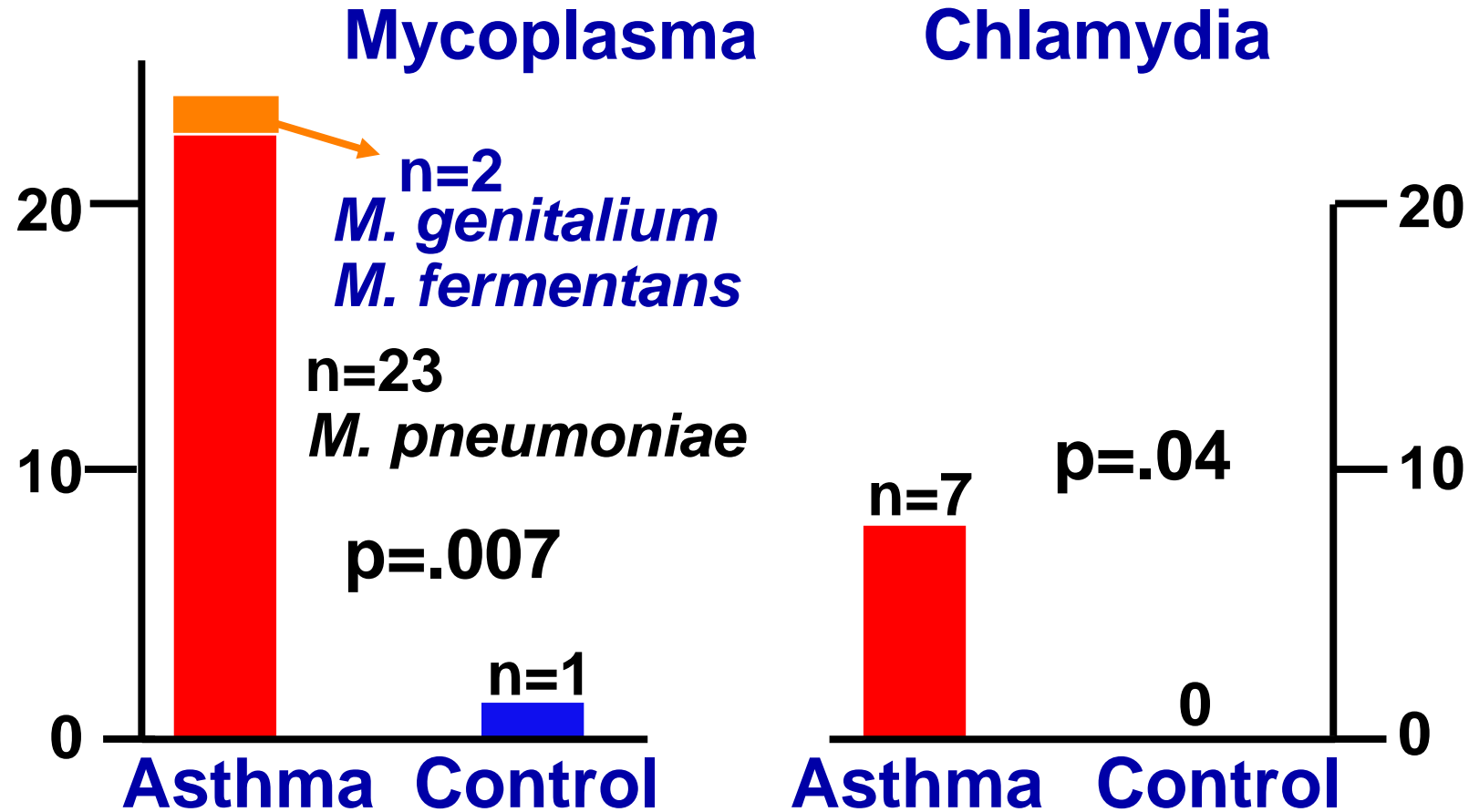
# Learning objectives

Upon completion of this learning activity, participants should be able to:

- **To recognize the phenotype of subacute bacterial infection (SBI) in asthma**
- **To manage SBI in asthma**
- **To assess response to therapy**

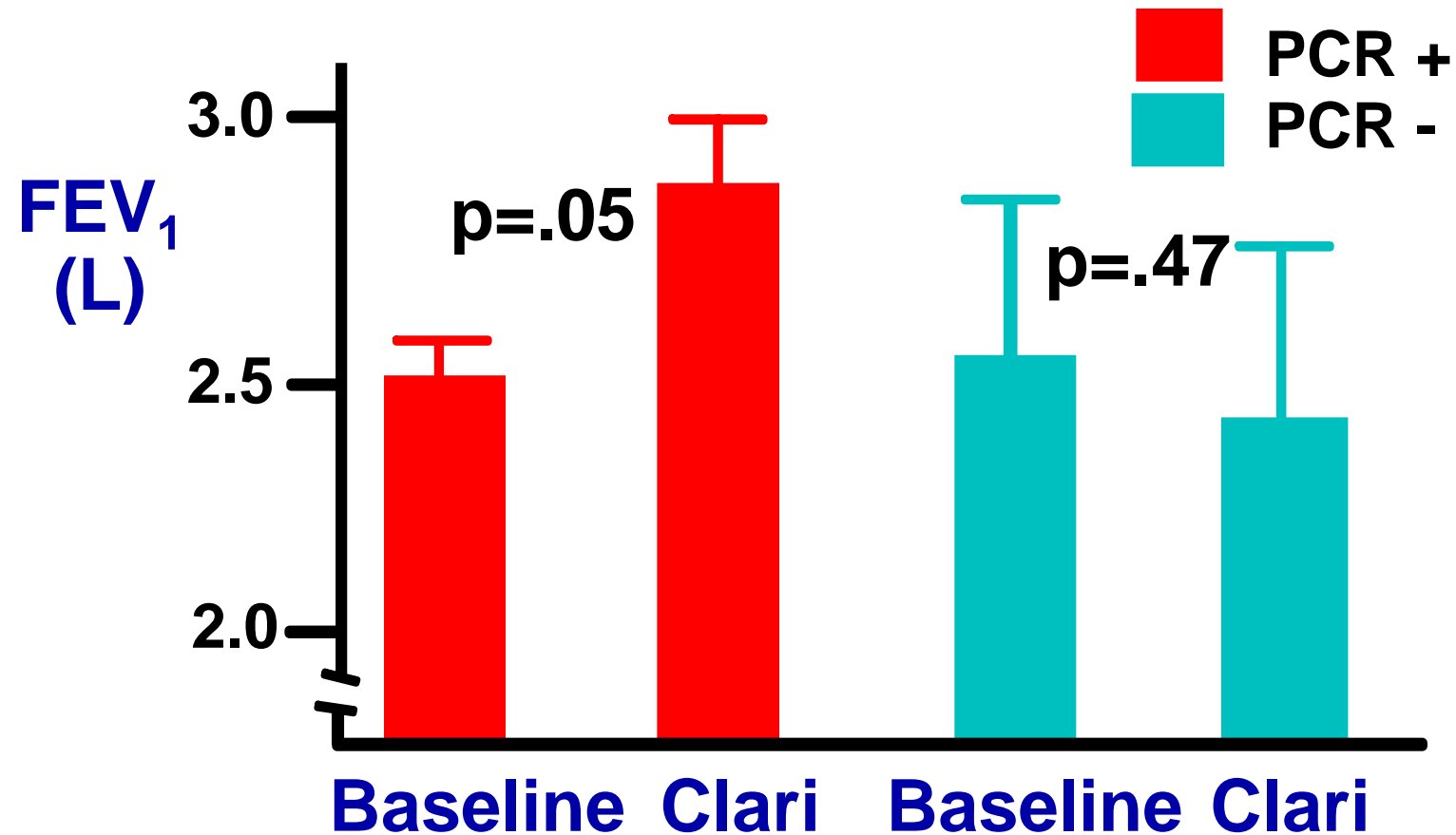


# PCR + Asthma (n=55) and Controls (n=20)



Martin R, et al. JACI 2001;107:595-601.

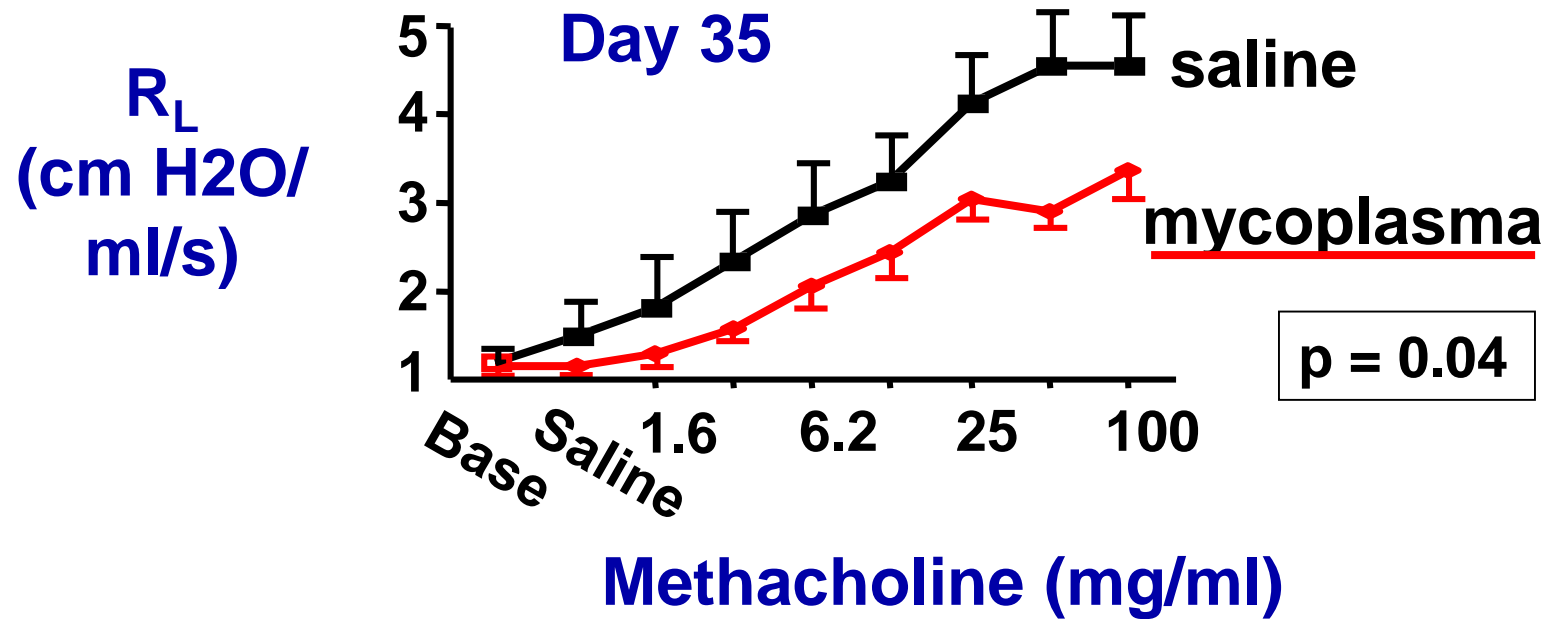
# Change in FEV<sub>1</sub> after treatment depends on PCR positivity



# Hygiene Hypothesis

**The immune system in newborn infants is skewed toward Th2 cells and needs timely and appropriate environmental stimuli (e.g. infection) to create a balanced immune response.**

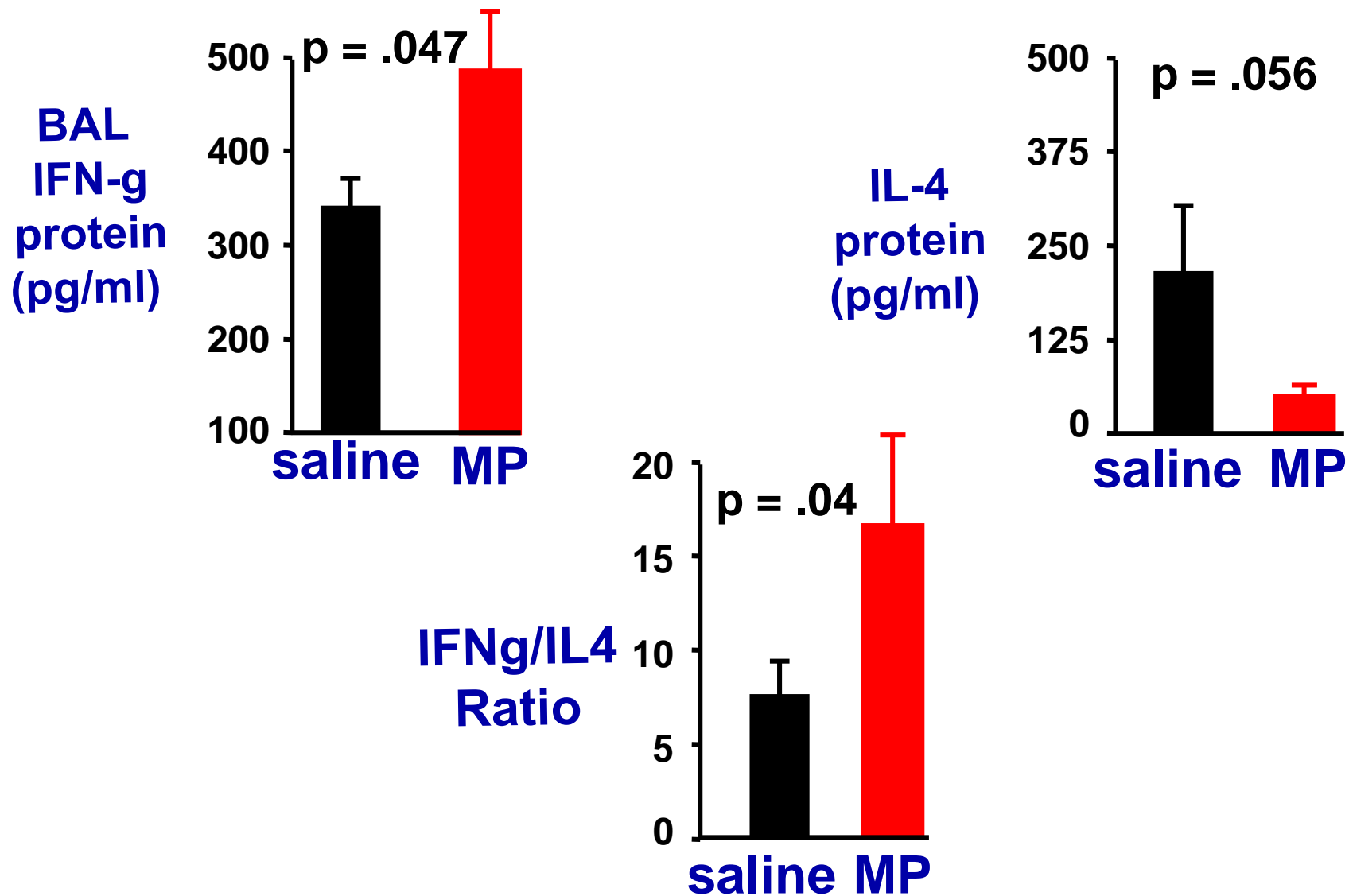
# Model: Infect-Sensitize-Challenge



Chu, et al. Infect Immun; 71:1520-1526, 2003.

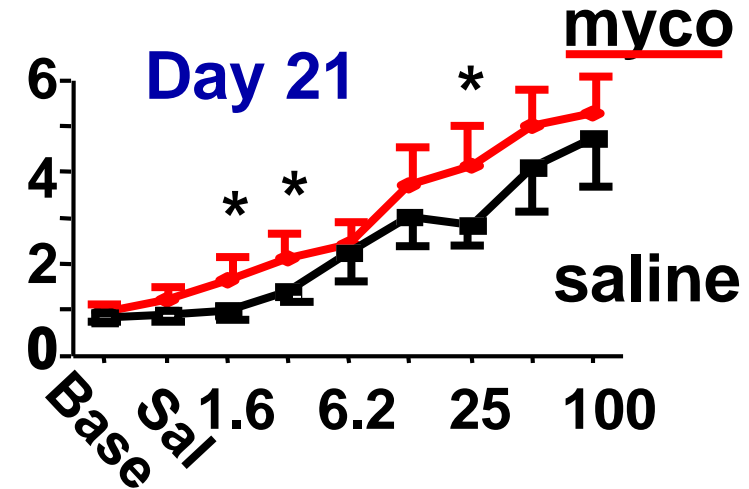
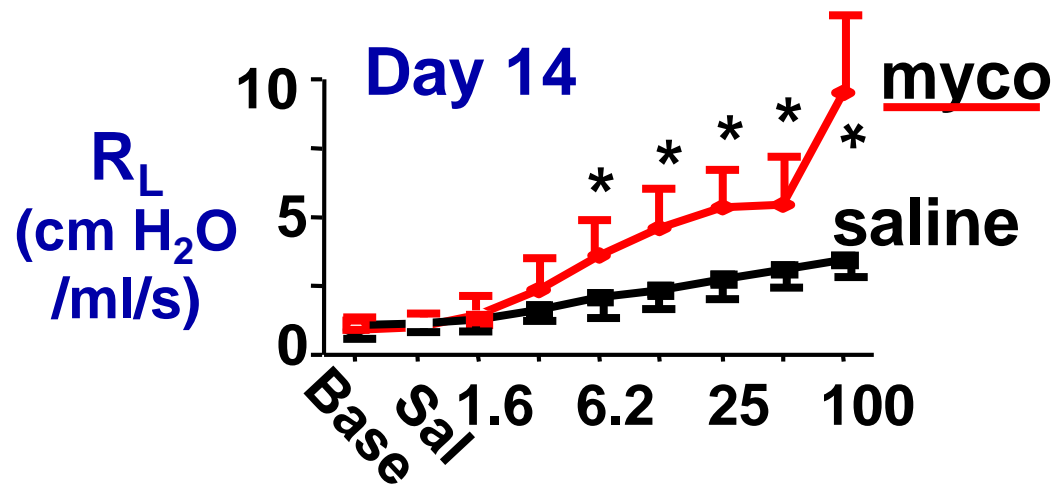
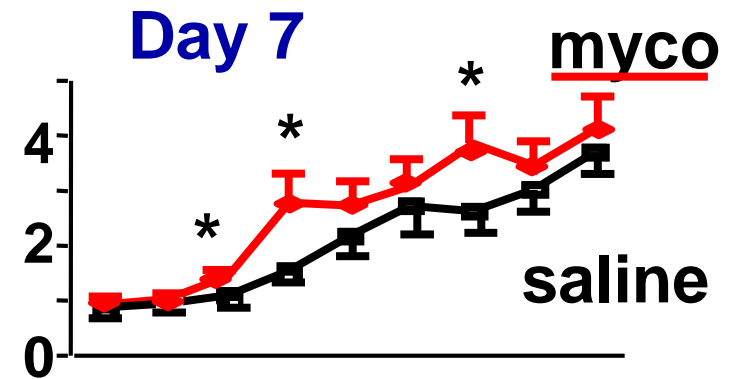
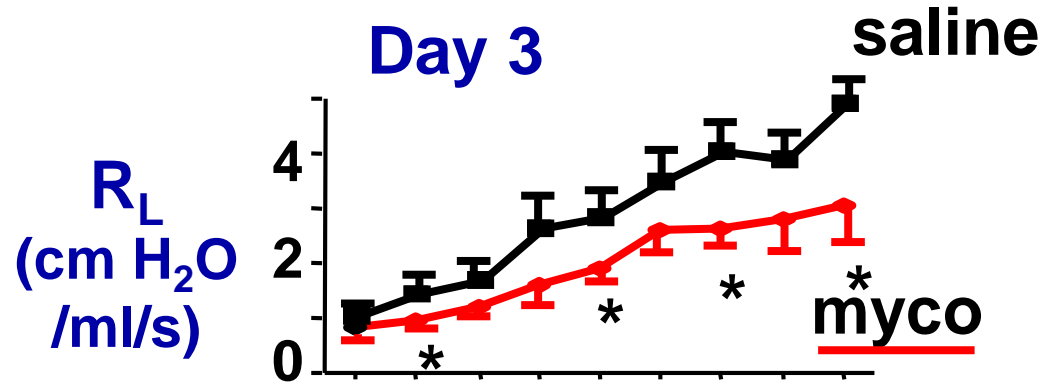


# MP-OVA-OVA (Day 35)



**What is the Effect of “Seeing” Allergen Prior to Infection?**

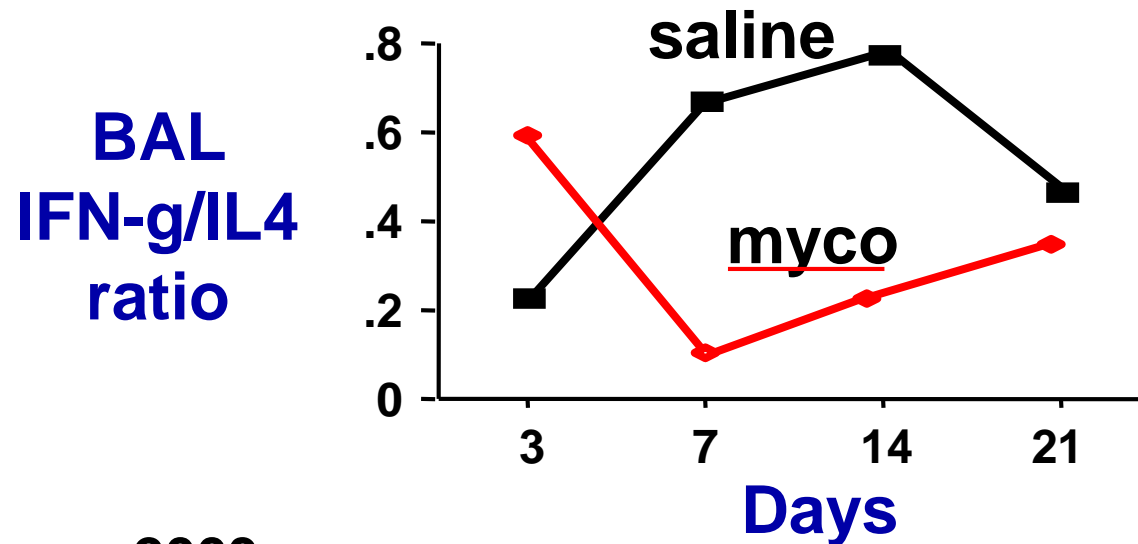
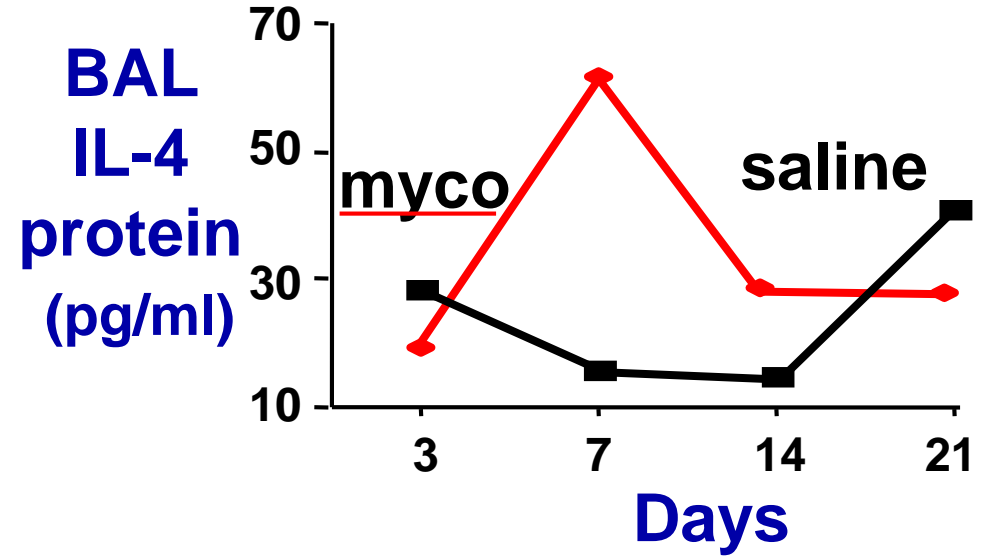
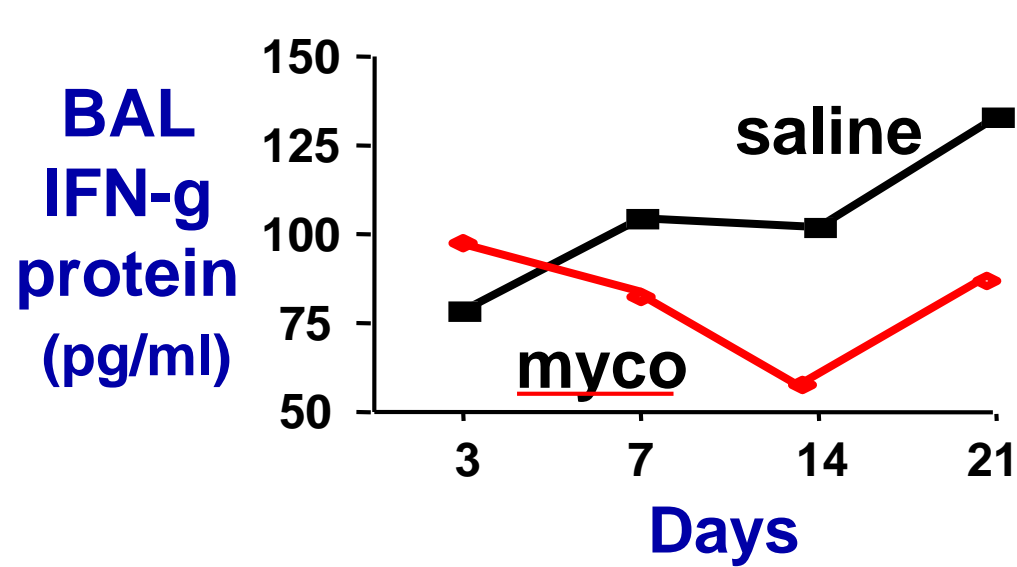
# Model: Sensitize - Challenge - Infect



Methacholine (mg/ml)

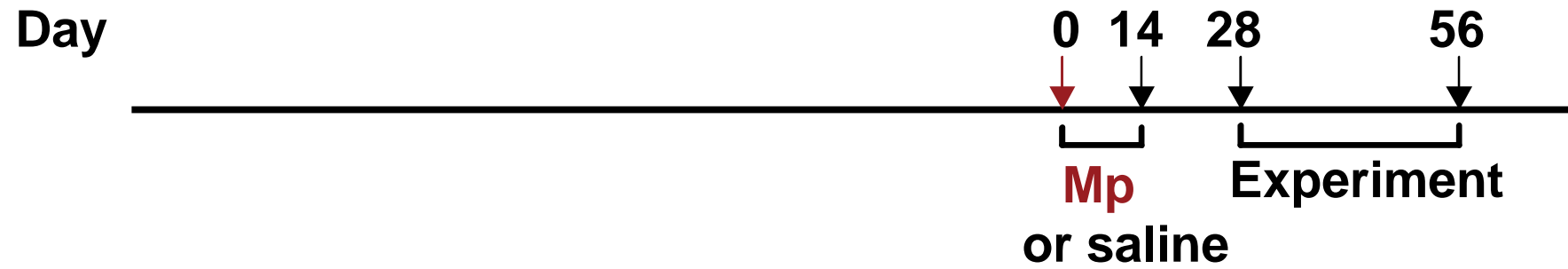
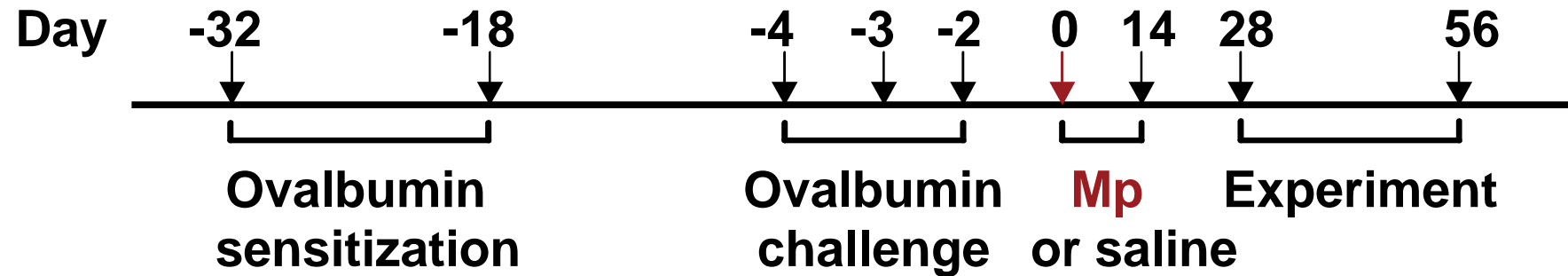
Methacholine (mg/ml)

# Model: Sensitize - Challenge - Infect

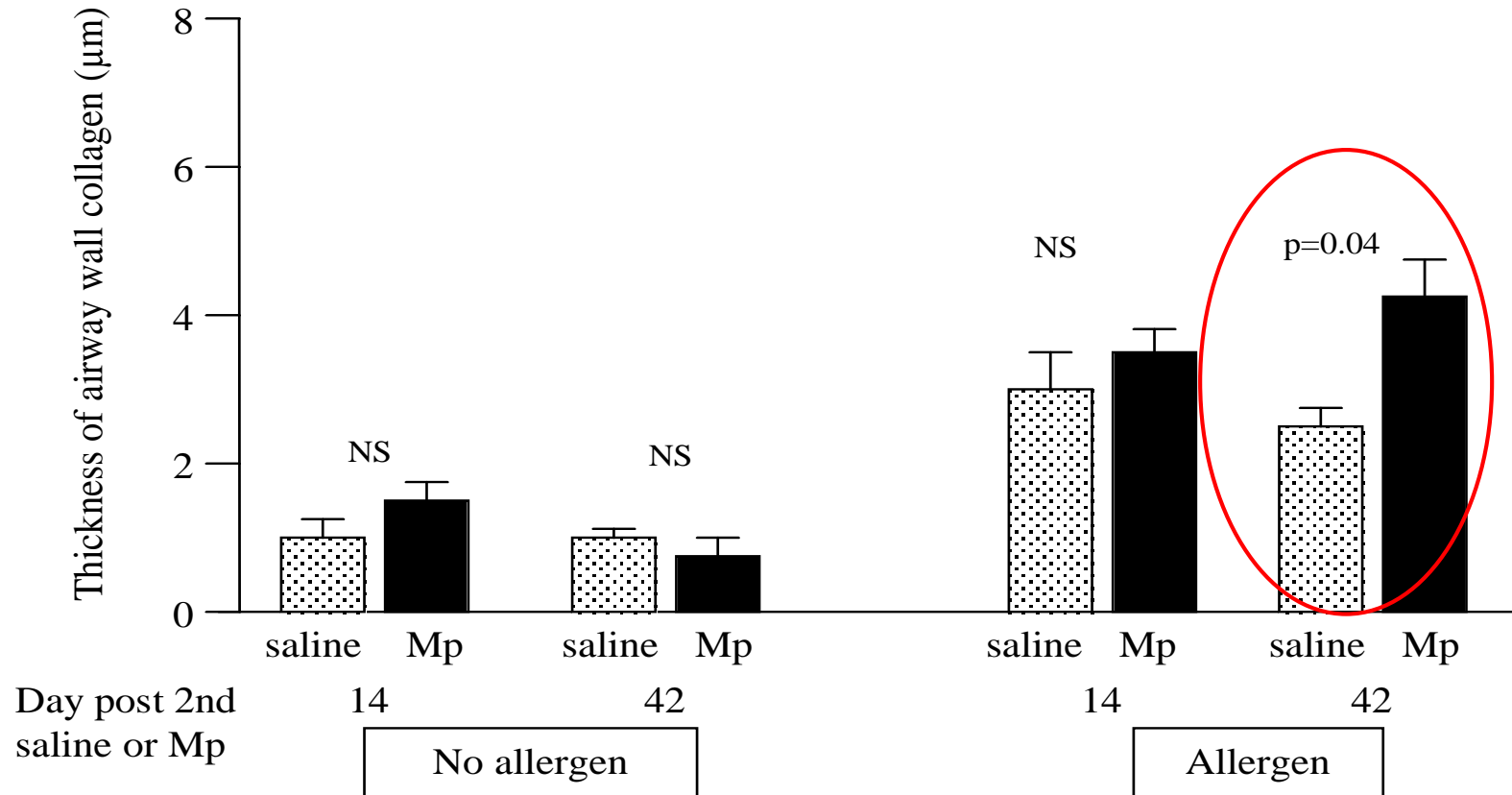


**Does mycoplasma infection increase  
airway collagen deposition in asthma?**

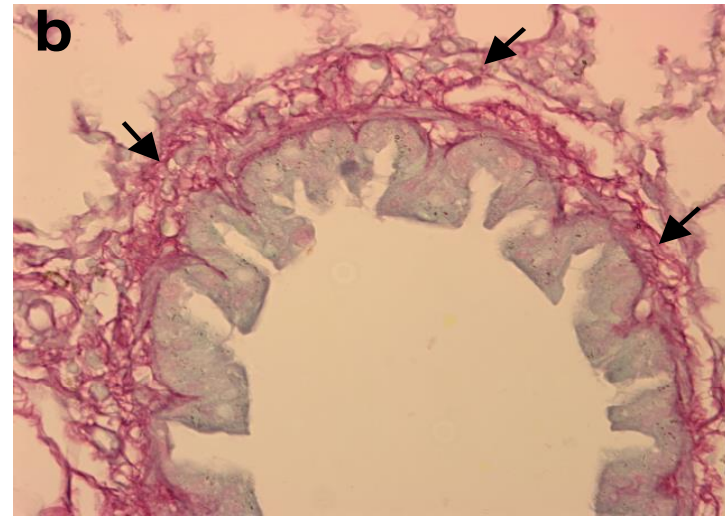
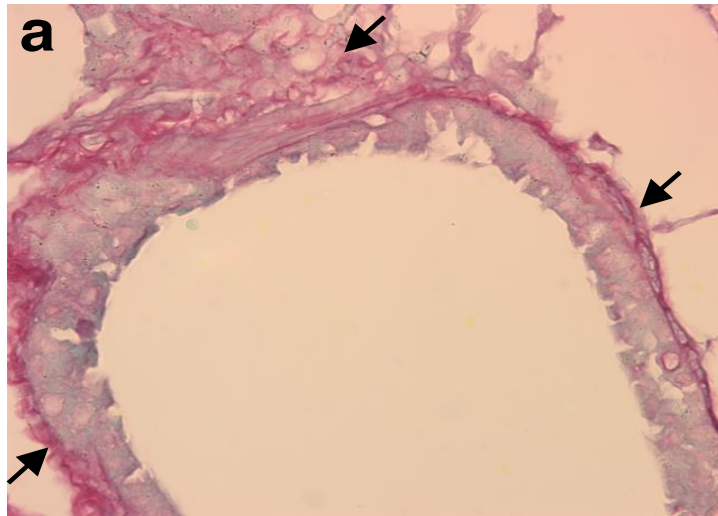
# Multiple mycoplasma infections in a murine model of asthma



# Airway collagen increased in response to multiple mycoplasma infections in a murine model of asthma



# Increased airway collagen deposition in mice with allergen challenge and mycoplasma (Day 42)



**Saline**

**Mycoplasma**

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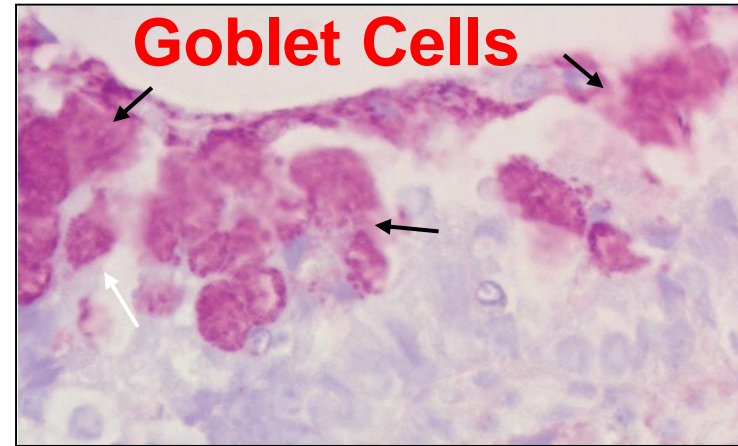
**Allergen**



## Mucin MUC5AC Staining (day 7)



Allergen +  
Saline

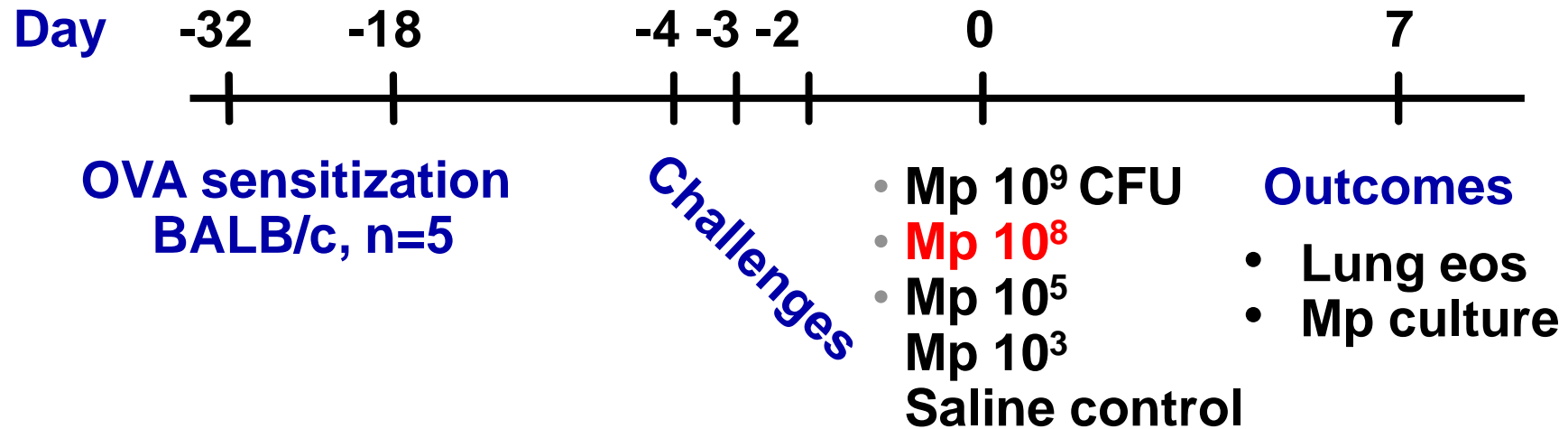


Allergen +  
*M. pneumoniae*

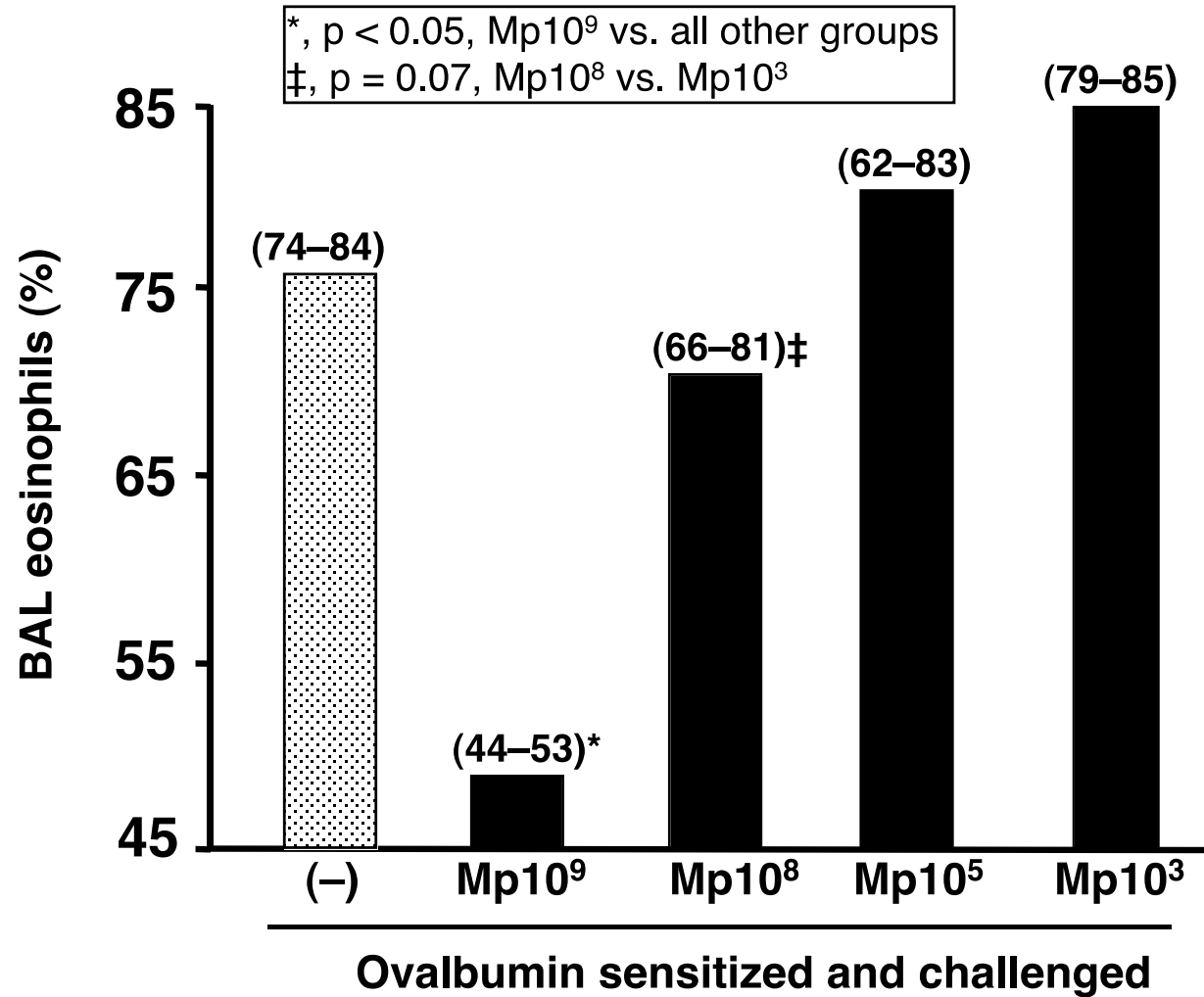
Magnification  
x400

**Does a higher or lower  $M_p$  respiratory load  
cause more or less immunomodulatory  
effect?**

# Mp concentration - Inflammation

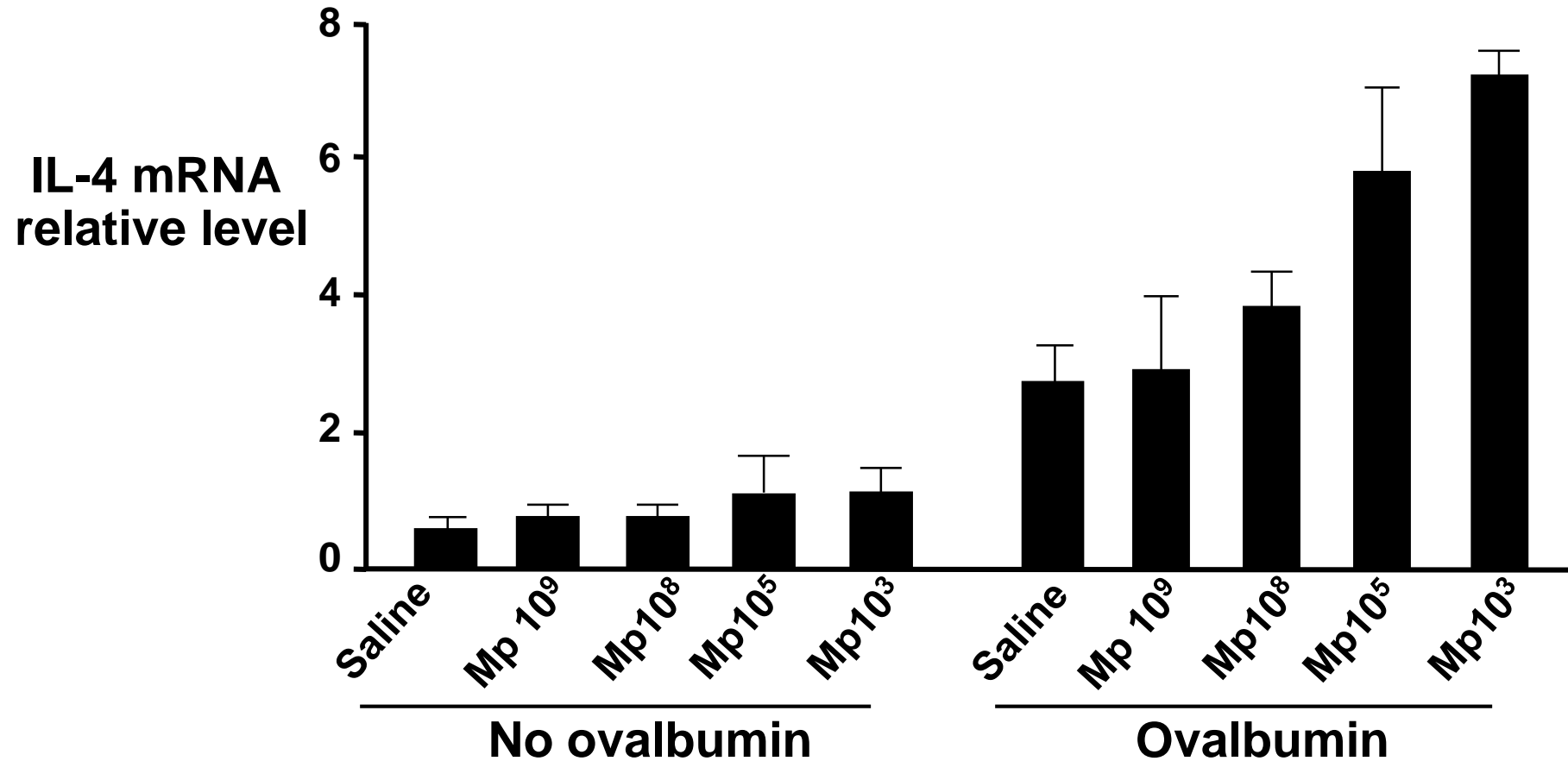


# Inflammation - eosinophils



# IL-4 mRNA expression by purified lung CD4+ T-cells

BALB/c mice n = 6/group



**In patients with refractory asthma,  
does infection play a role?**

# Subacute bacterial infection

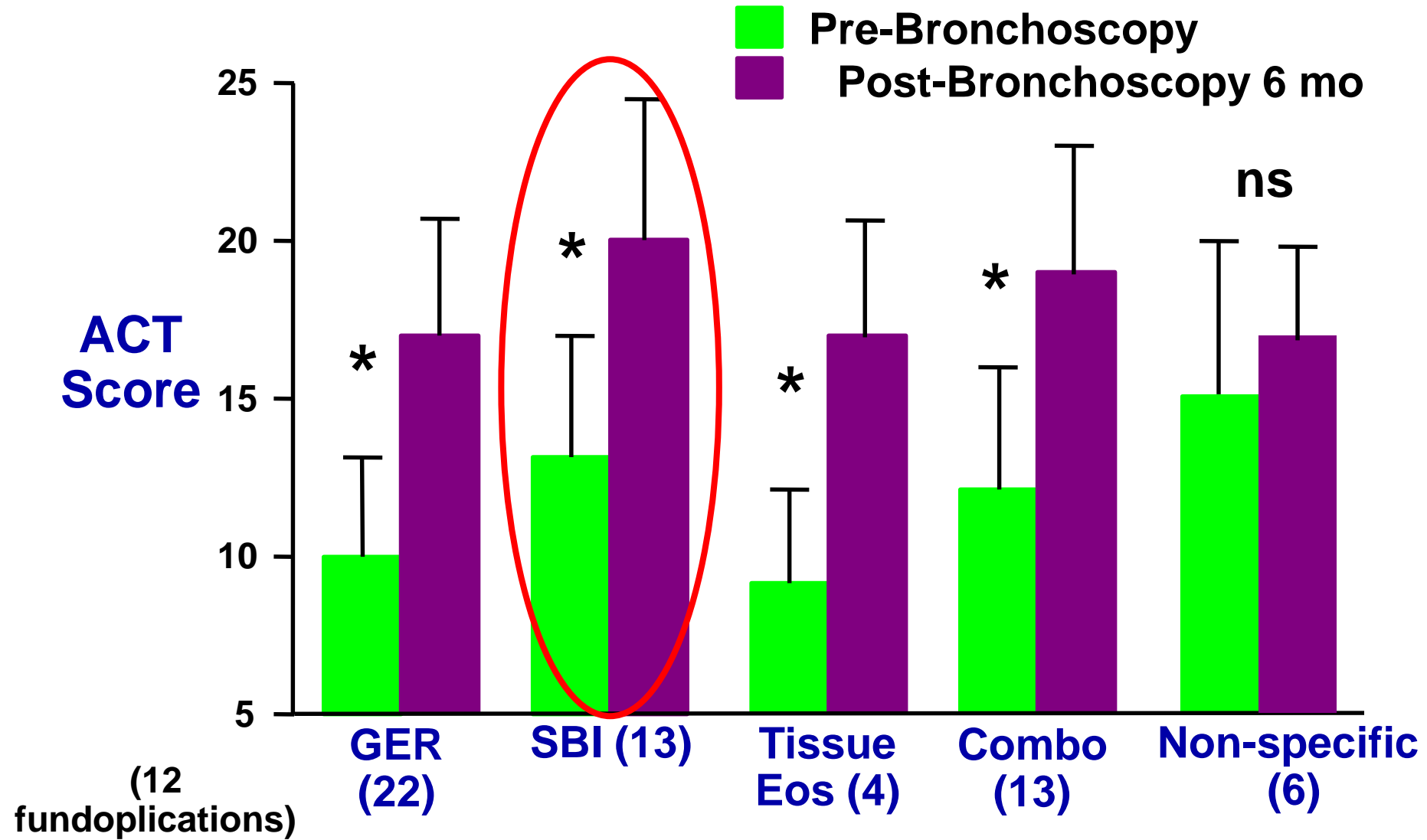
- 25 total patients (43%)
  - BAL neutrophils > 20% always associated with SBI
  - BAL neutrophils could also be < 20% with SBI
- Mp on Cp n = 13
- **Other bacteria** n = 12
- Sole phenotype n = 13    combination n = 12

# Subacute bacterial infection - Organisms

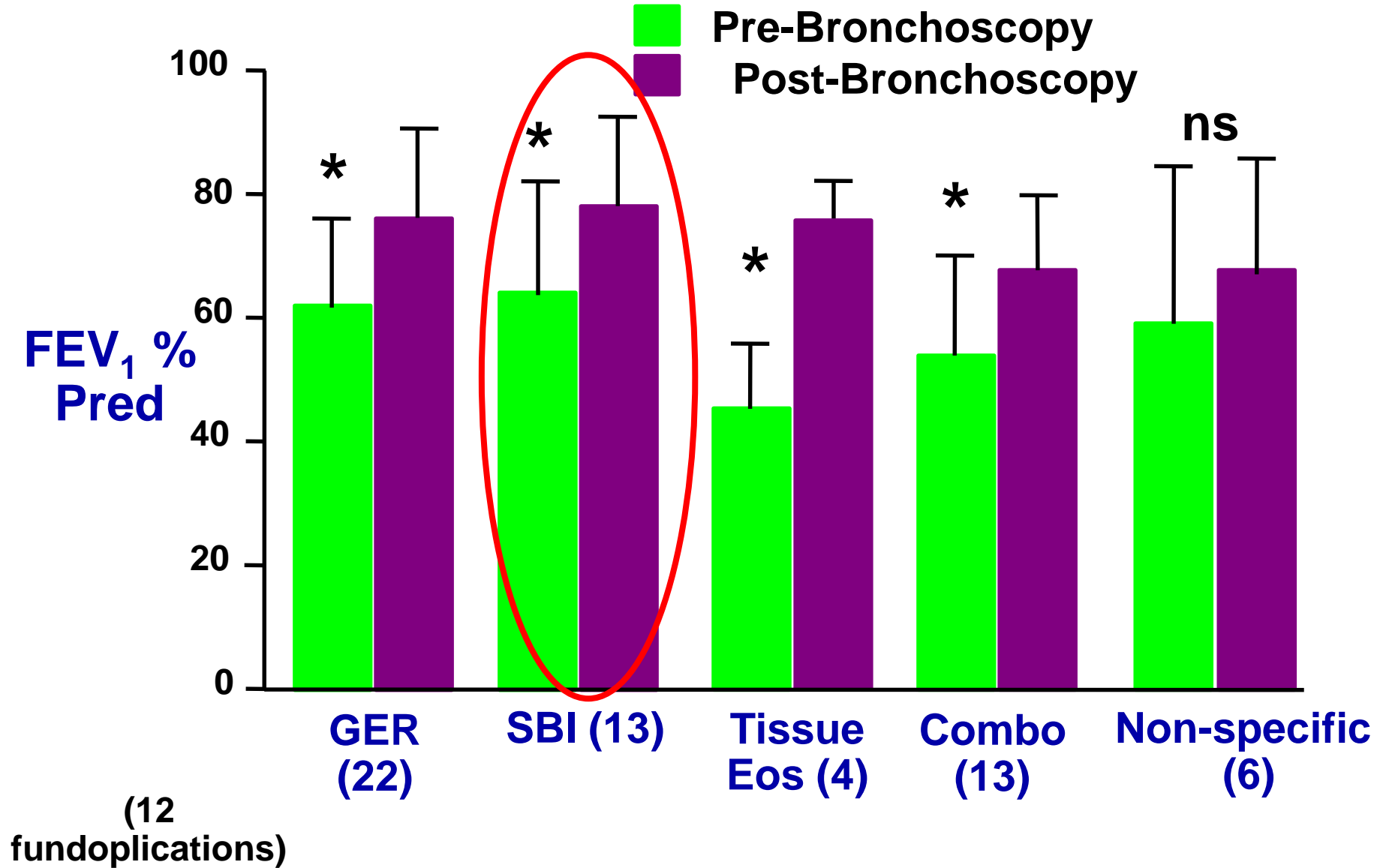
<b># of Pts</b>	<b>Bacteria:</b>
1	Acinetobacter
1 each	Methicillin resistant/sensitive Staph aureus
1	Alcaligenes xylosoxidans
1	Moraxella catarrhalis
2	Alpha hemolytic streptococci
2	Stenotrophomonas maltophilia
3	Pseudomonas aeruginosa
3	Haemophilus influenza
3	Chlamydia pneumoniae
10	Mycoplasma pneumoniae



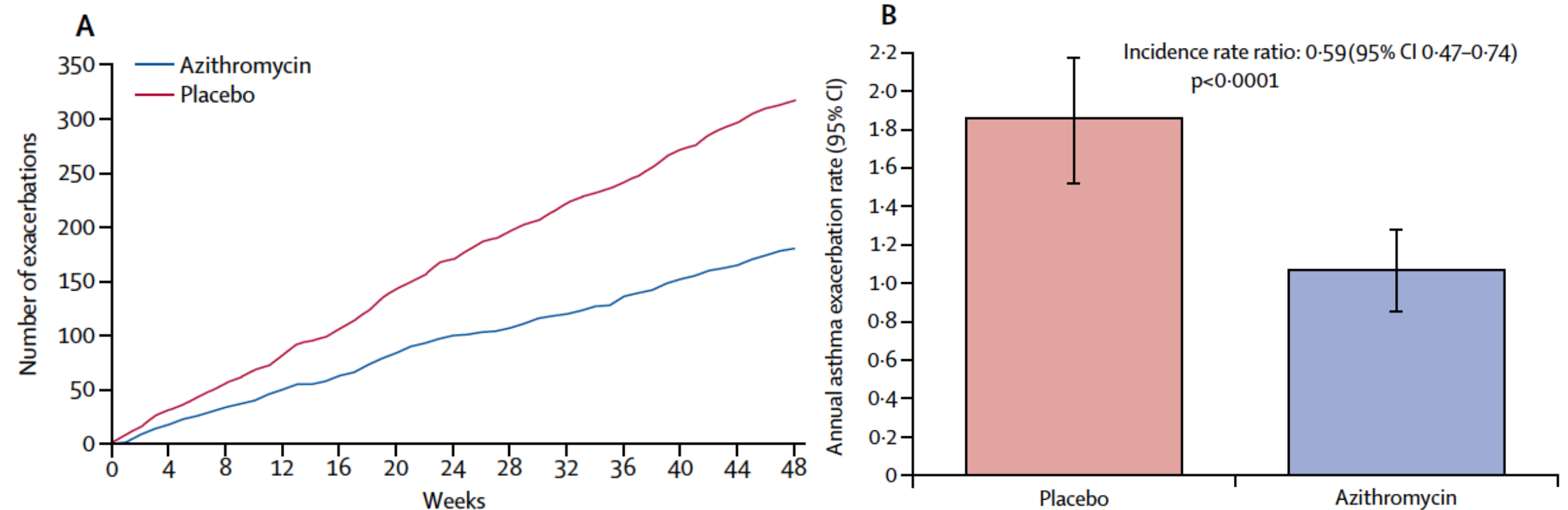
# Asthma Control Test n = 58



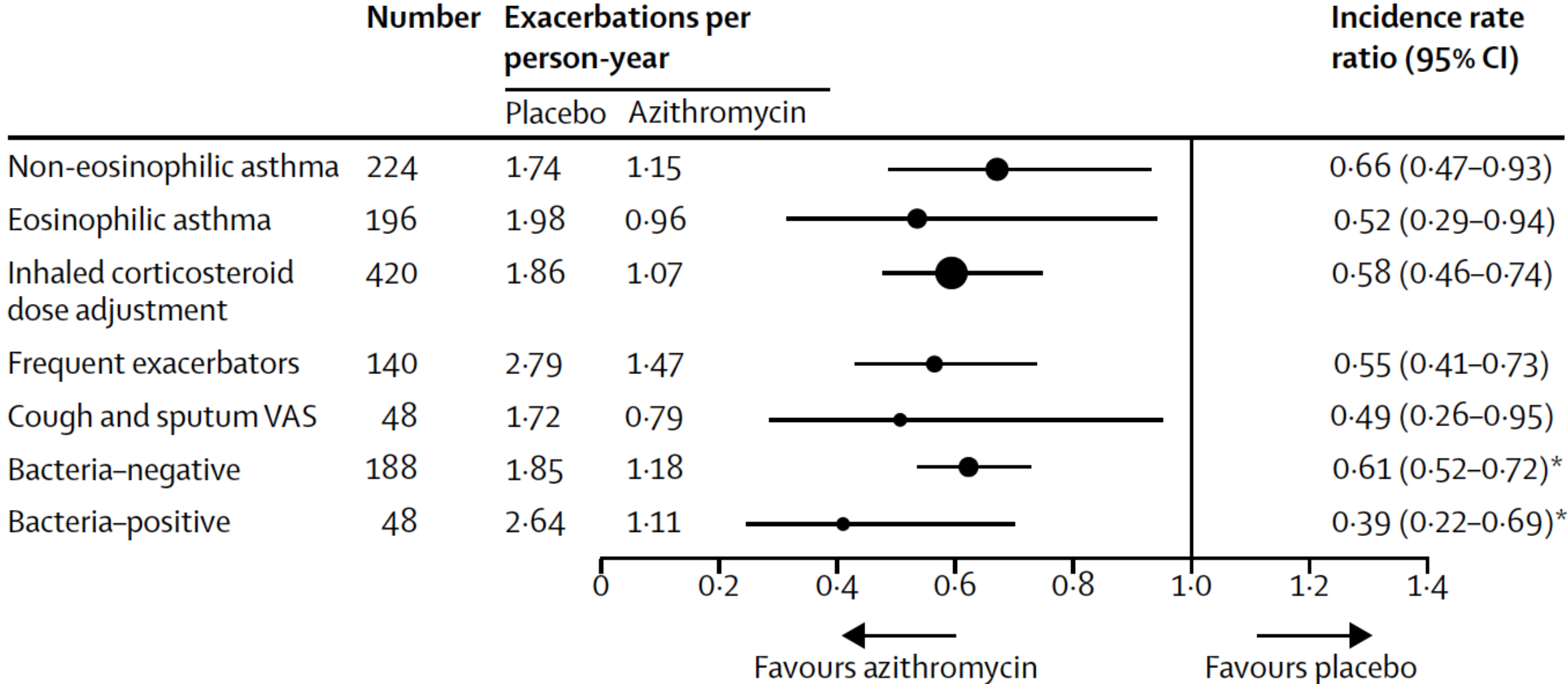
# FEV<sub>1</sub>% Predicted n = 58



# Asthma exacerbations (severe and moderate) over 48 weeks azithromycin 500 mg, 3X/week



# Exacerbation rate – per year



# **Are anti-microbials important in asthma?**

**A subacute bacterial infection is involved in a large percent (25-40%) of patients with refractory asthma which can propagate disease. Directed antimicrobial therapy of appropriate duration will improve lung function and asthma control.**