UCL

Séminaire de Pathologie Infectieuse

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Cliniques Universitaires UCL de Mont-Godinne, Yvoir

NON-CF BRONCHIECTASIS IN ADULTS

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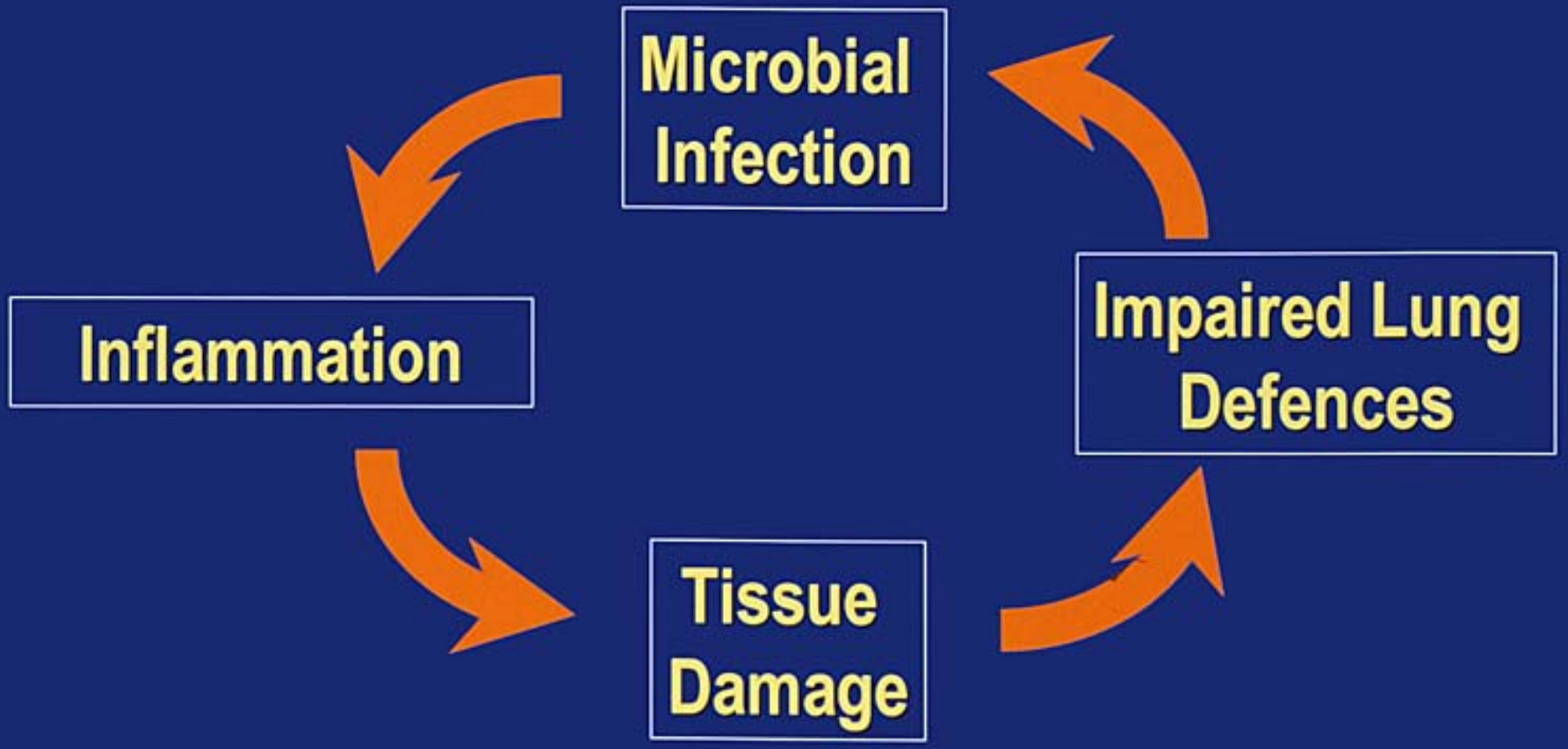
Royal Brompton Hospital, London, UK

A VICIOUS CYCLE OF INFECTION AND INFLAMMATION



Aetiology of bronchiectasis

Cause	n (% of study)
Post infection	51 (32)
Idiopathic	42 (26)
PCD	17 (11)
ABPA	13 (8)
Immune deficiency	9 (6)
Ulcerative colitis	5 (3)
Young's syndrome	5 (3)
Pan bronchiolitis	4 (3)
Yellow nail syndrome	4 (3)
Mycobacterium infection	4 (3)
Rheumatoid arthritis	3 (2)
Aspiration	2 (1)
CF variant	2 (1)
Total	**161**

ABPA = Allergic bronchopulmonary aspergillosis, PCD = Primary ciliary dyskinesia, CF = Cystic fibrosis

Treatable Causes of Bronchiectasis

Immune Deficiency (CVID)

ABPA

Mycobacterial infection (MAC)

Airway obstruction

Inflammatory Bowel Disease

Rheumatoid Arthritis

Aspiration

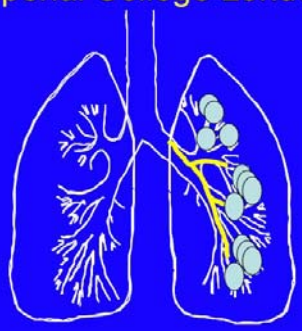
Comparison of patients with idiopathic and post infective bronchiectasis

	Idiopathic group	Post infection group	p value
n	42	51	
Gender - No. males (%)	15(36)	18 (35)	ns
Age at onset (SD)	42 (15)	7 (12)	**<0.01**
Age at referral to Royal Brompton Hospital (SD)	50 (14)	49 (17)	ns
Mean number of lobes involved (SD)	4.1 (1.7)	4.4 (1.7)	ns
Bilateral bronchiectasis (%)	41 (98)	48 (94)	ns
Predominantly lower lobe bronchiectasis (%)	34 (81)	25 (49)	**<0.01**
Chronic rhinosinusitis (%)	35 (83)	25 (49)	**<0.01**
Wheezy bronchitis in childhood (%)	11 (26)	11 (22)	ns
P. aeruginosa (%)	14 (33)	17 (33)	ns
Symptoms chronic since onset	38 (83)	25 (49)	**<0.01**
Smoking history (%)	13 (31)	17 (33)	ns
Lobectomy (%)	1 (2)	5 (10)	ns

Genetic studies implicate altered regulation of natural killer (NK) cells in idiopathic bronchiectasis

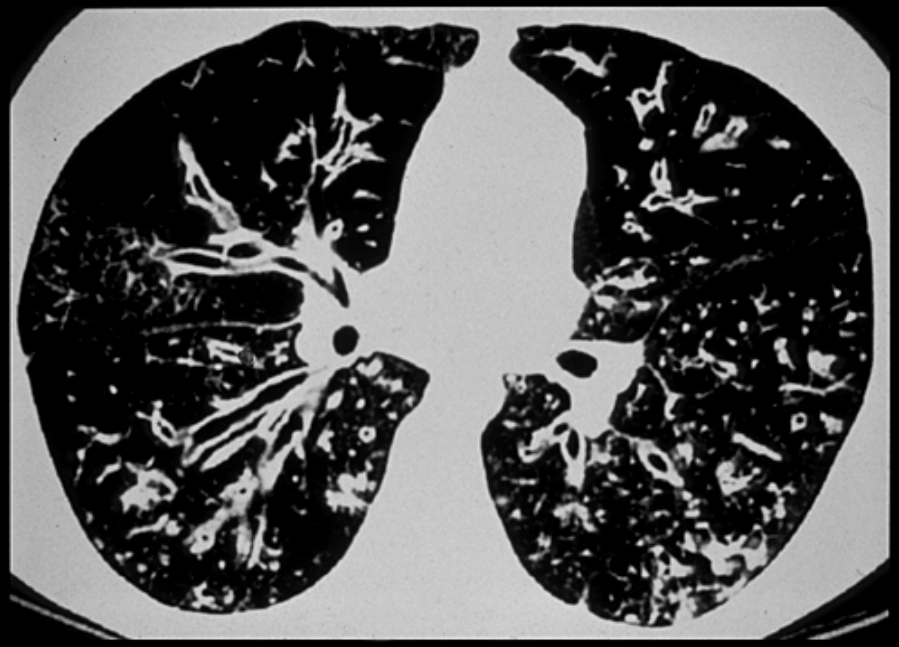
- HLA-Cw*03 and HLA-C group 1 homozygosity associated with idiopathic bronchiectasis
- Analysis of relationship between HLA-C and KIR genes suggest a shift to activated NK cell activity

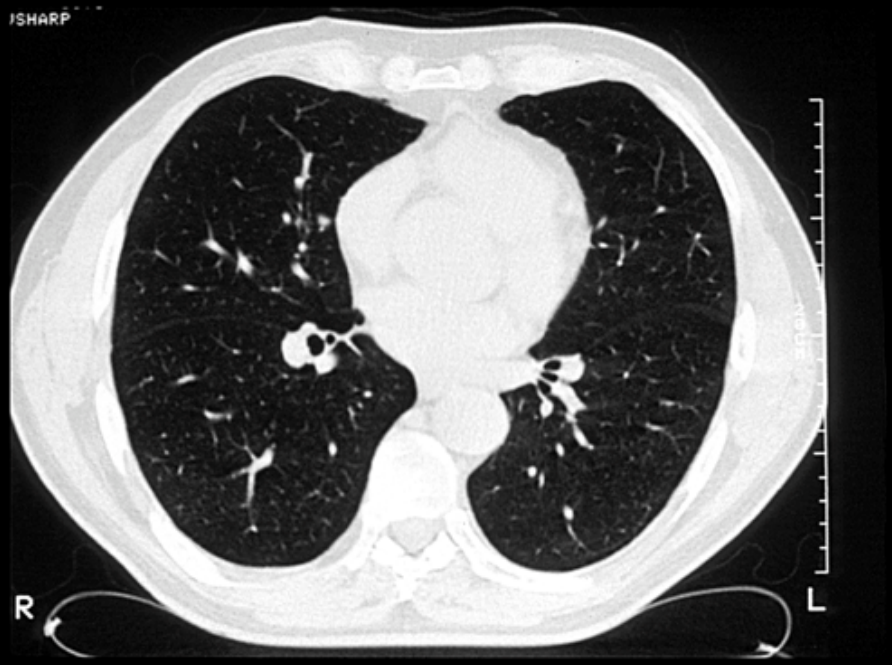
Lung Immunology Group
Imperial College London



HLA-C and killer cell immunoglobulin-like receptor genes in idiopathic bronchiectasis. Boyton et al 2006 Am J Respir Crit Care Med 173, 327-333

MRC Medical Research Council

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SERIAL CHANGE IN BRONCHIECTASIS

Sheehan et al ERJ 2002

- Changes in lung function minor in most patients
- FEV1 correlated with decreased attenuation (mosaic perfusion) of parenchyma (r=0.55); also extent of bx and degree of bronchial wall thickening
- Change in FEV1 correlated with changes in mucus plugging r=0.46 (small and large airways)
- Mosaic perfusion rarely regressed (cf plugging and thickening)
- Changes in severity of bx, bronchial wall thickening and mucus plugging go together

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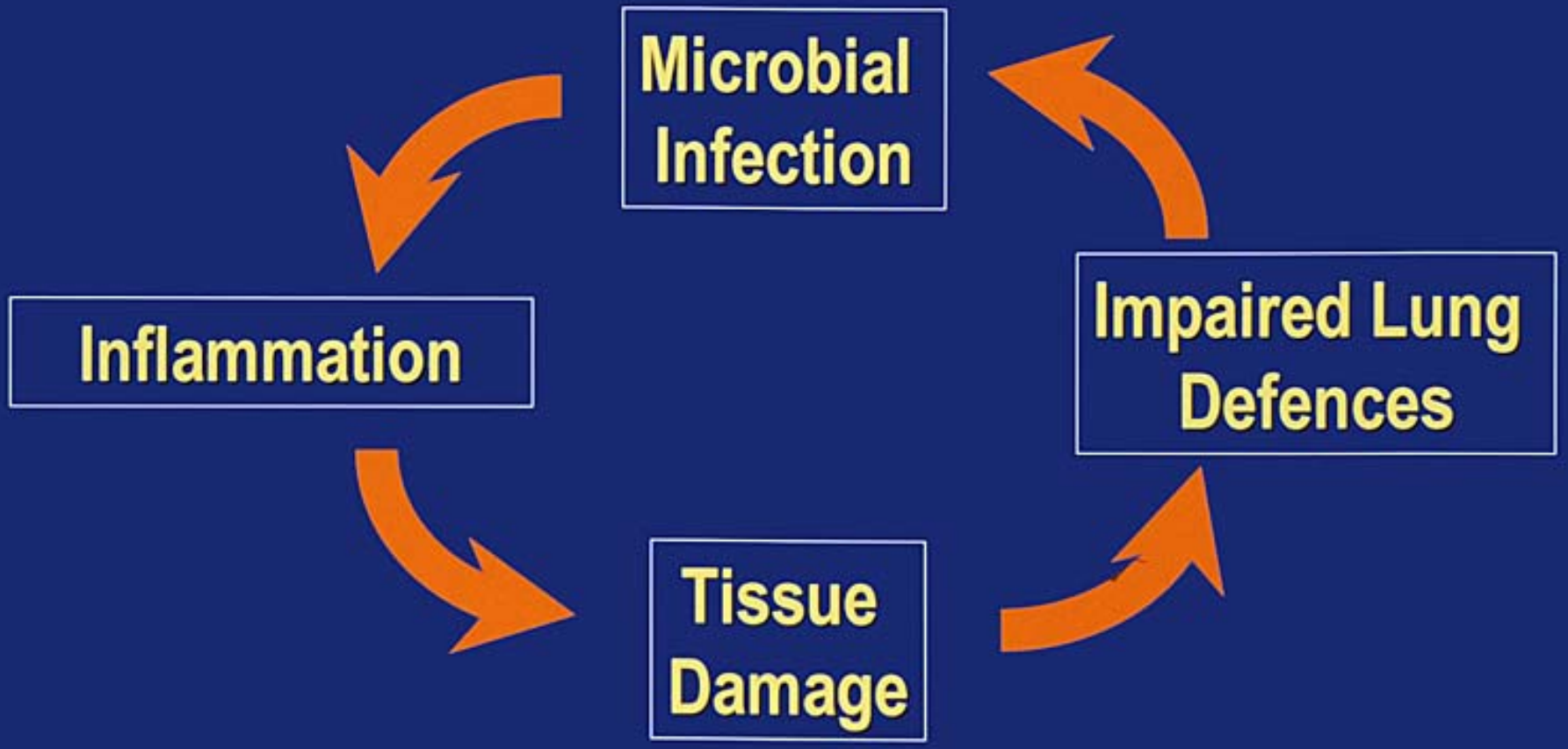


Bronchiectasis exacerbations bacteriology

Common

Haemophilus influenzae

Haemophilus parainfluenzae

Pseudomonas aeruginosa

Less Common

Streptococcus pneumoniae

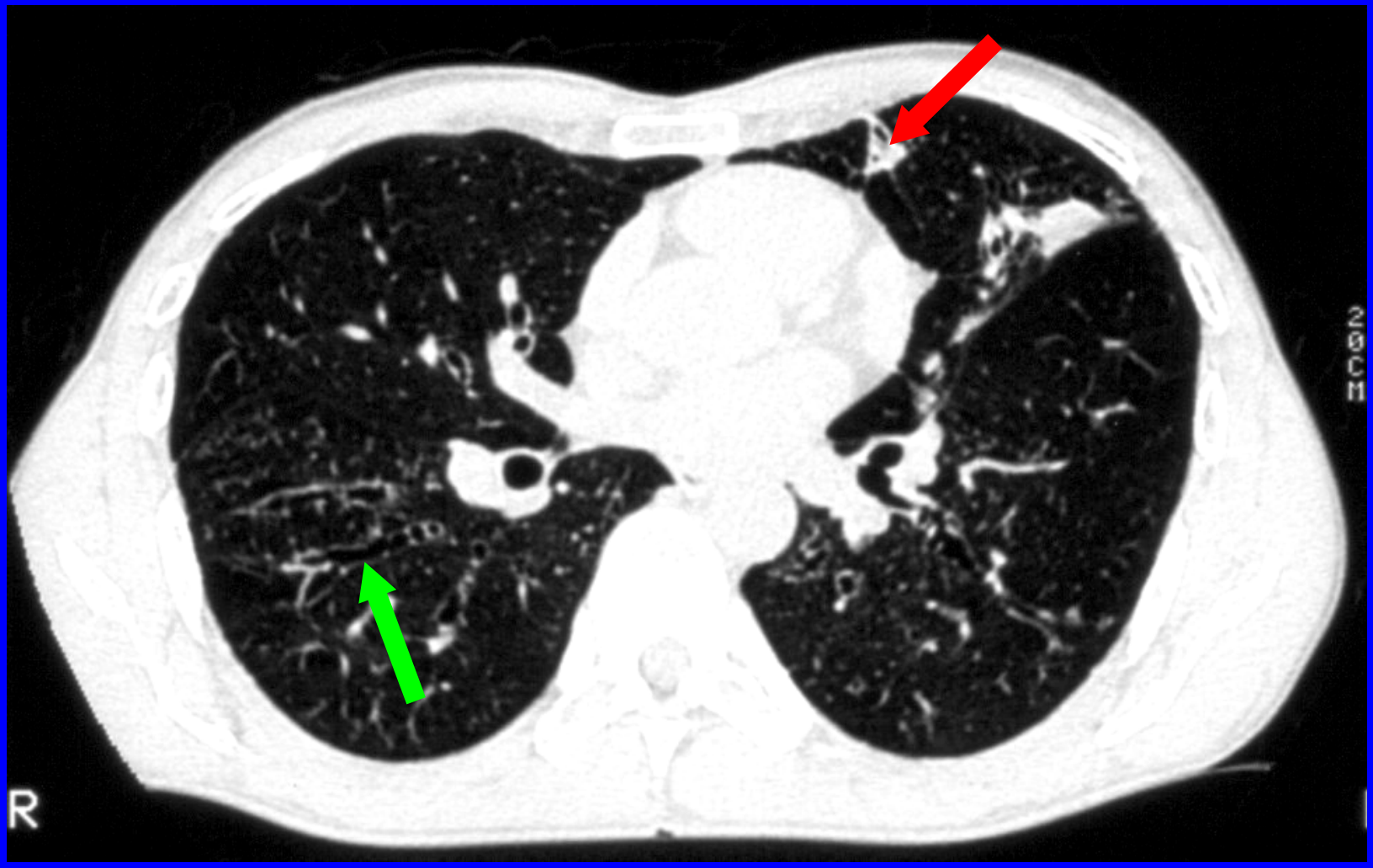
Moraxella catarrhalis

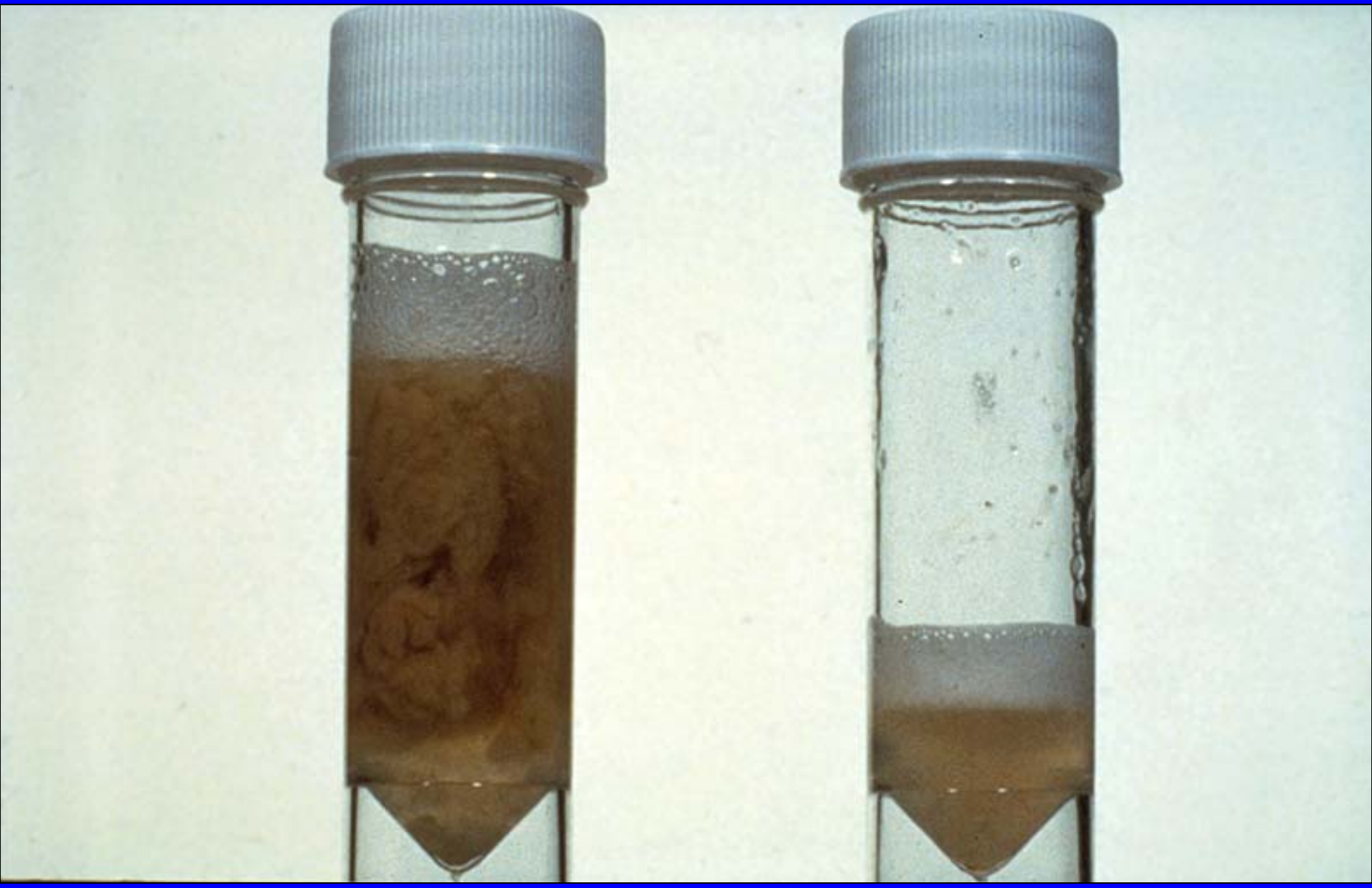
Staphylocccus aureus

Stenotrophomonas maltophilia

GNEB

“Classic” CT of M.avium-intracellulare





Benefits from beta lactam plus aminoglycoside combination

- Only data from CF
- Smith et al J. Pediatr. 1999

  Azlocillin + tobramycin (n=43) v azlocillin + placebo (n=33).

  No difference in clinical response, lung function

  P.a. sputum density decreased more on combination ($p < 0.05$)

  Longer time to readmission ($p < 0.001$)
- Cochrane Review Elphick and Tan 2002 – 8 trials

  Many flawed and /or small numbers

  No difference in clinical response, lung function

  Monotherapy associated with ↑ P.a. resistance

Prolonged antibiotics for purulent bronchiectasis Cochrane review

Evans, Bara, Greenstone 2005

- **6 randomised placebo controlled trials from 447 abstracts reviewed**
- **4 weeks or more**
- **2 nebulised, 4 oral**
- **Limited meta analysis**
- **“Response rate” significant for antibiotics**
- **Exacerbation rate and lung function NS**

Antibiotic prophylaxis in bronchiectasis

Key messages

- **Reduce exacerbation days**
- **Reduce sputum volume/purulence**
- **May ↑ lung function**
- **Side effects**
- **Emergence of resistance (oral)**

Antibiotic prophylaxis in Bx

consider if

Management otherwise optimal

3 sputum samples negative for AFB

Frequent oral antibiotics ≥ 6/year

and rapid relapse after iv without an explanation

≥ 2 hospital admissions per year

Antibiotic prophylaxis in Bx

Approaches

Nebulised (P.aeruginosa)

Long term oral

Rotating antibiotics

Pulsed iv

Macrolides

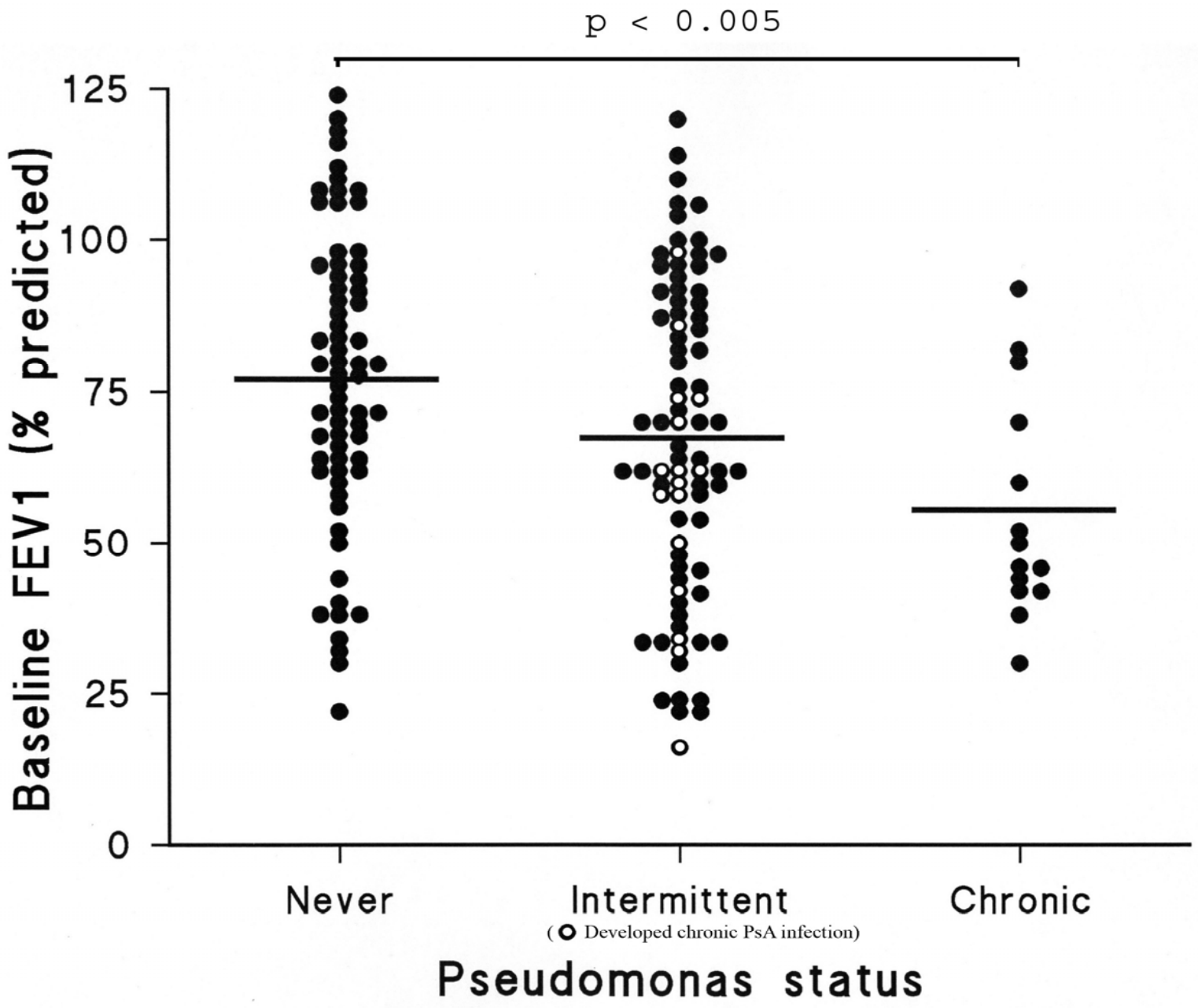
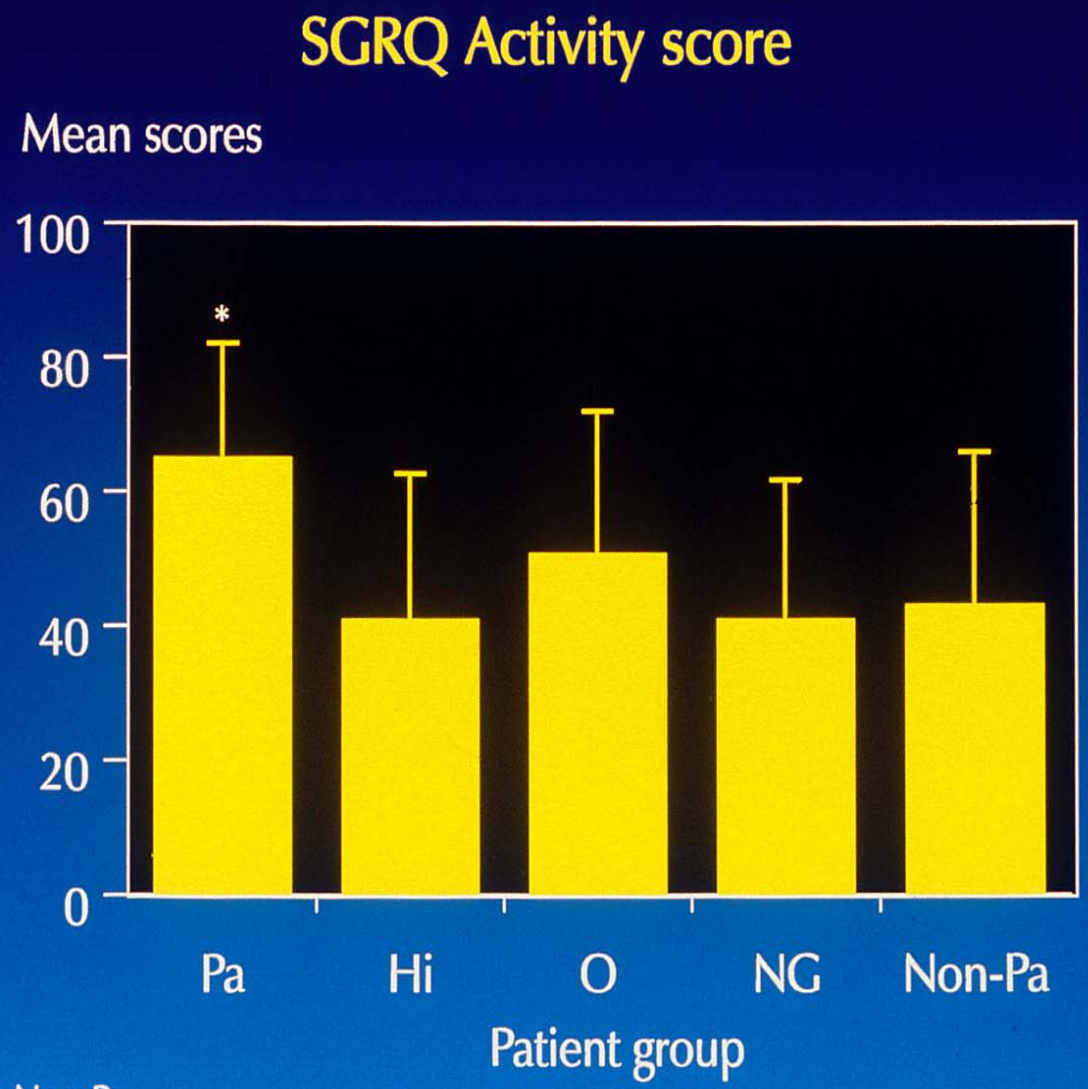


Figure 1. Comparison of baseline FEV1 with pseudomonas status.

Effect of Bacteriology on Quality of Life



*$P<0.01$ cf Hi, NG & Non-Pa

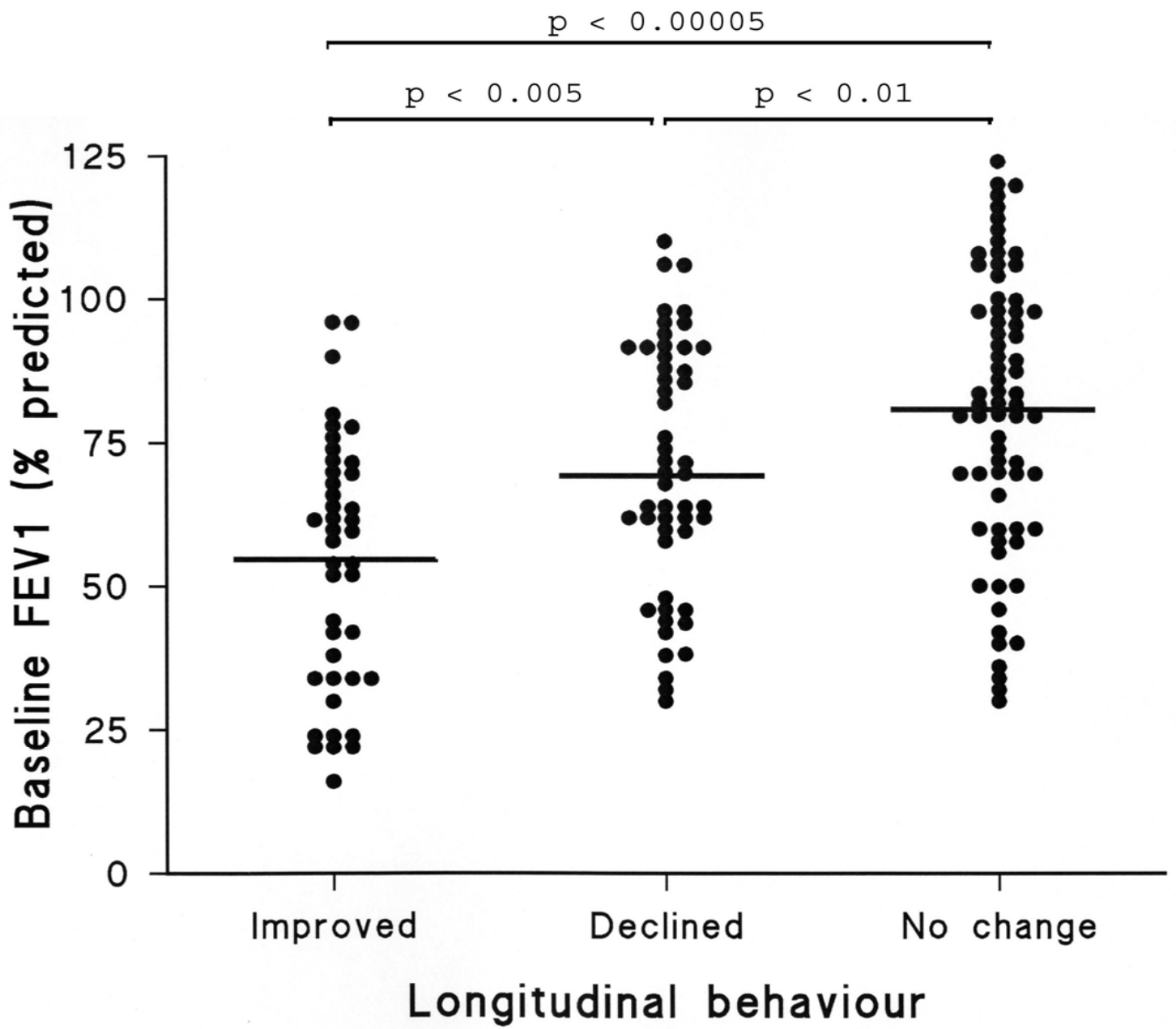


Figure 2. Comparison of baseline FEV1 with longitudinal behaviour, when analysed as decline or improvement of > 10% over time.

Mortality in Bronchiectasis
Loebinger et al ERJ In Press

- 91 patients with moderate to severe bx followed up for 13 yrs
- 29.7% died (70% directly due to bronchiectasis), median age 60 years
- Age, SGRQ activity score, Pseudomonas aeruginosa infection, TLC, RV/TLC and KCO all independently associated with mortality.

Mortality in Bronchiectasis
Loebinger et all ERJ In Press

CT features predicting mortality in multivariate analyses

- Increased wall thickness
- Emphysema

also in univariate analyses

- Bronchiectasis extent
- Dilation severity
- Small and Large airway plugging
- Mosaicism

Prognostic significance of CT signs of raised pulmonary artery pressure in bronchiectasis

Devaraj et al Submitted 2009

- Average RMPA/LMPA diameter strongest predictor of mortality of all other CT features of bronchiectasis

- Diameter greater than 18 mm most strongly predicted mortality

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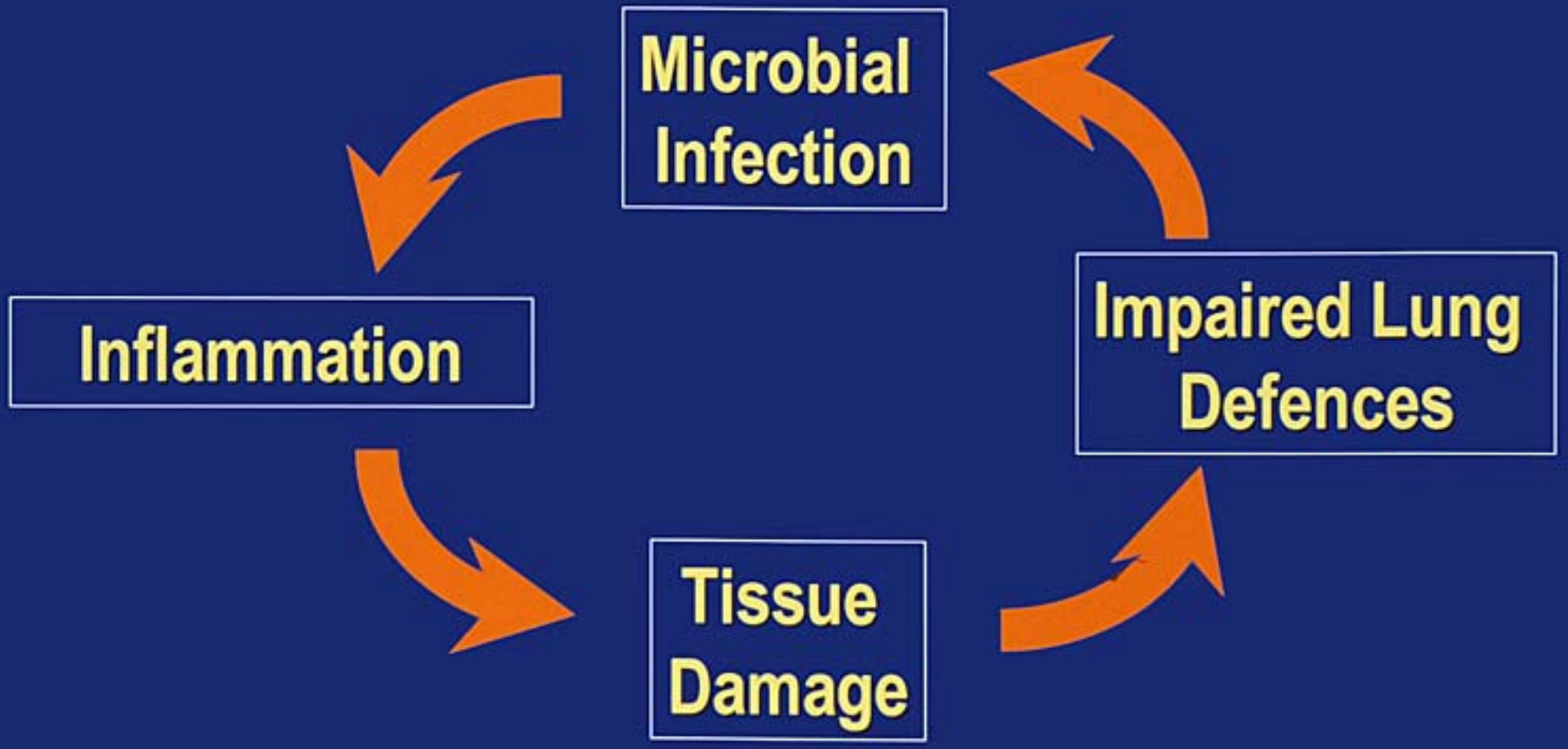


INHALED CORTICOSTEROIDS IN BRONCHIECTASIS

Tsang et al Thorax 2005

Fluticasone 500mg bd versus placebo

No effect on exacerbation frequency or FEV_1

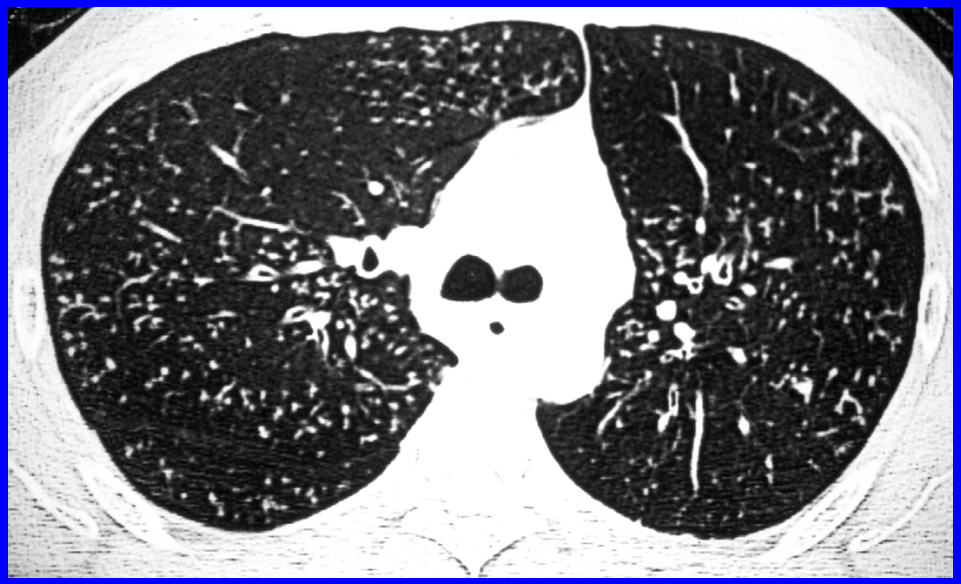
Reduced sputum volume in sub-groups (Pseudomonas)

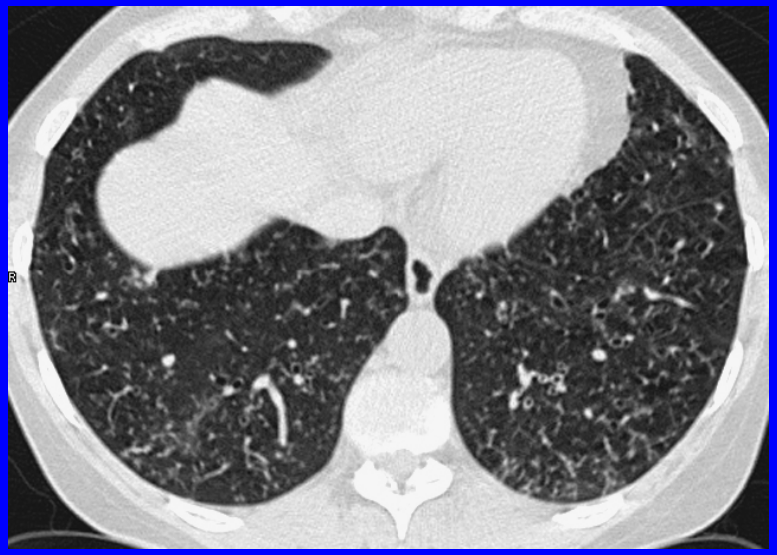
Martinez-Garcia et al Resp Med 2006

Fluticasone 500mg bd versus 250mg bd versus no treatment

No effect on exacerbation frequency or FEV_1

Improved QOL with higher dose





9 months later

Symptoms

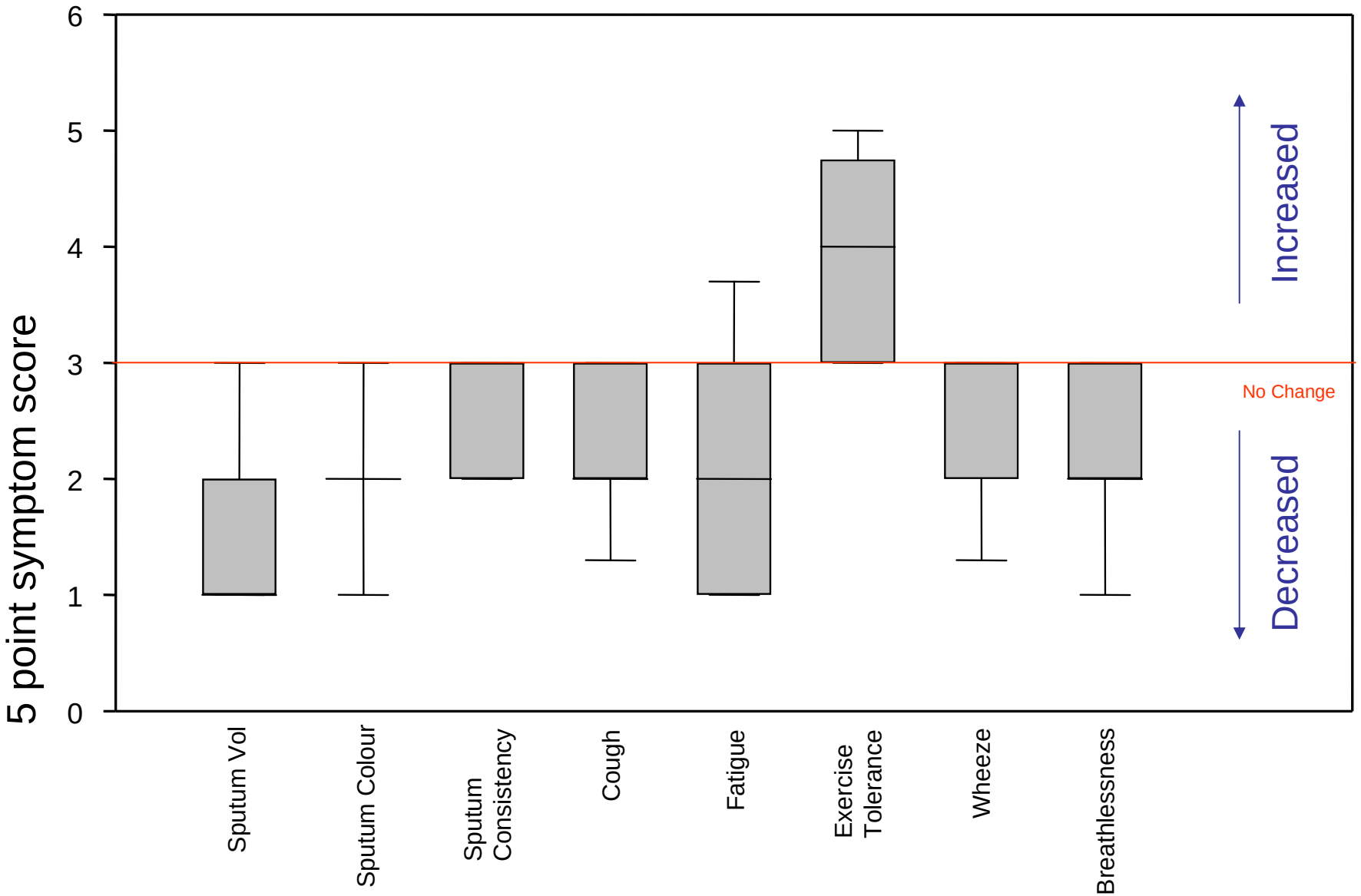


Figure 1. Box plot of symptom scores after Azm prophylaxis on 5 point score with 3 = no change. Median, 25% & 75% percentiles & SD shown

Frequency of Infective Exacerbations

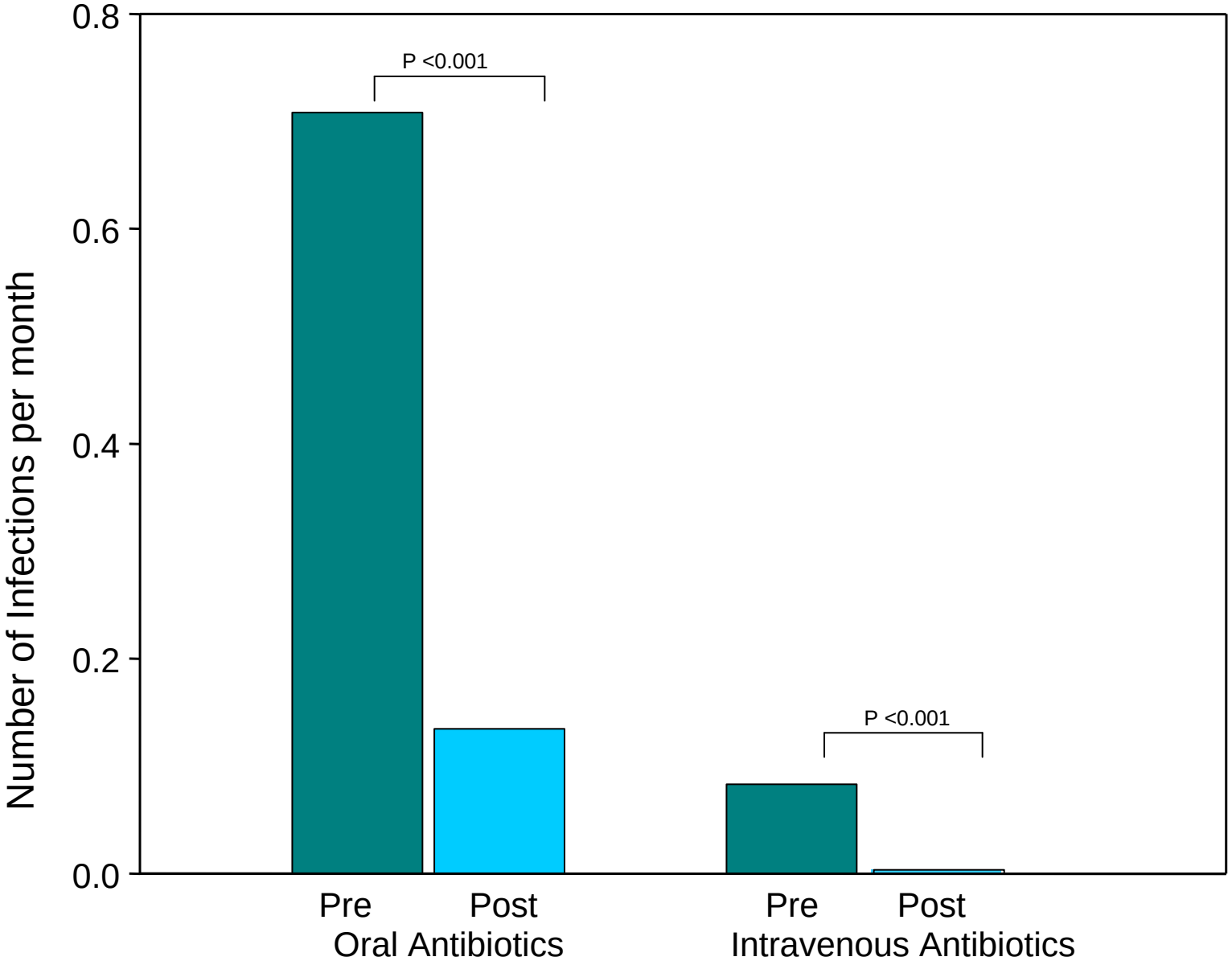


Figure 2. Histogram of number of infections per month in the period prior to Azm prophylaxis and after for both oral & i.v. antibiotics

Azithromycin prophylaxis

500mg 6 days, 250mg 6 days, 250mg Mon, Weds, Fri or alternate days

Side Effects

Liver function, check 2 weeks and 3 monthly

Reduced hearing

Tinnitus

Antibiotic holiday

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