

Rethinking COPD: New Considerations in Diagnosis and Management

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April 30, 2016

Disclosures

- No financial relationships with a commercial interest.
- Off-label use of azithromycin will be discussed.

What is COPD?

- Common preventable and treatable disease
- Chronic airflow limitation, usually progressive
- Enhanced chronic inflammatory response
- Exacerbations and comorbidities

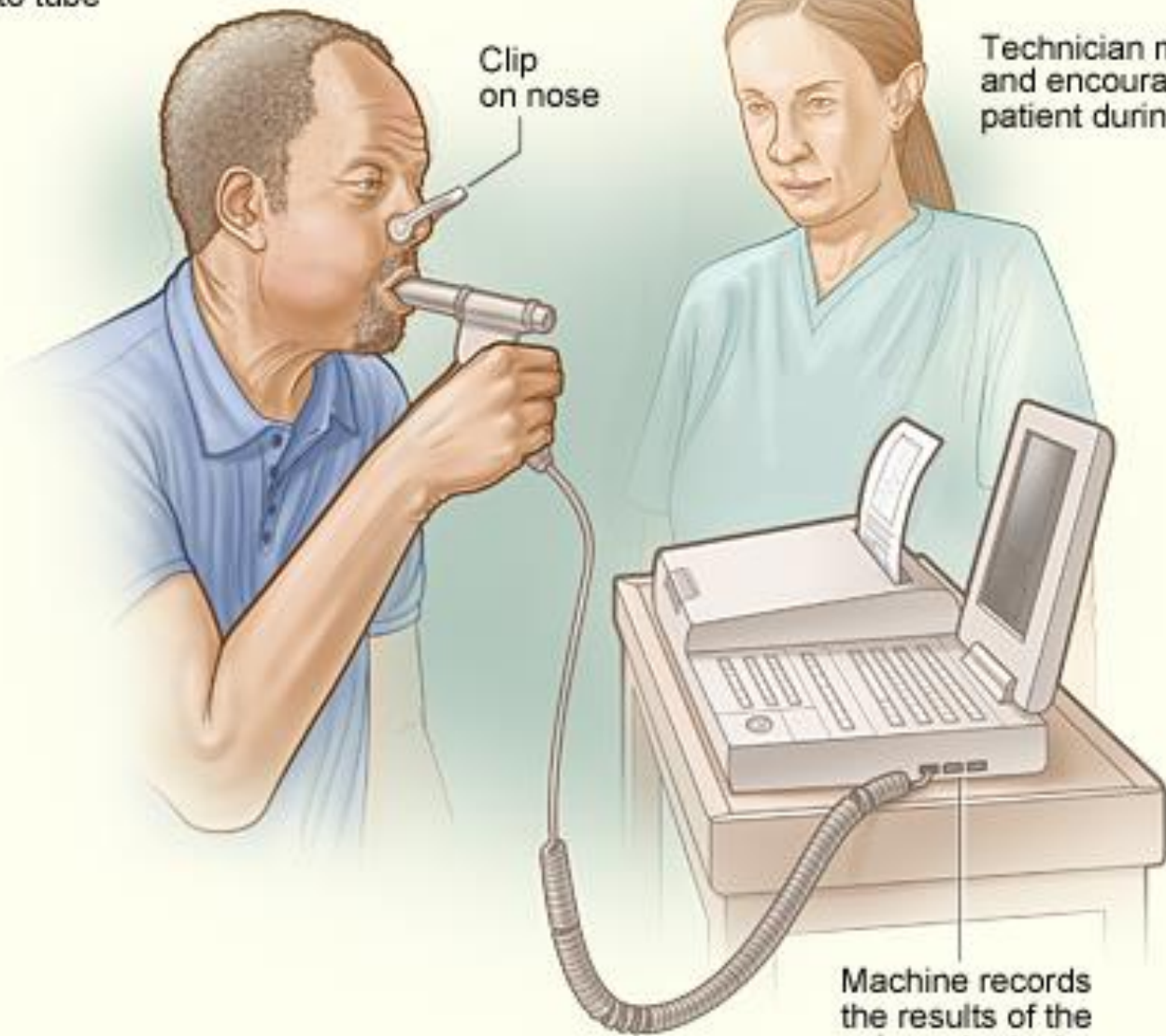


www.goldcopd.org

Patient takes a deep breath
and blows as hard as possible
into tube

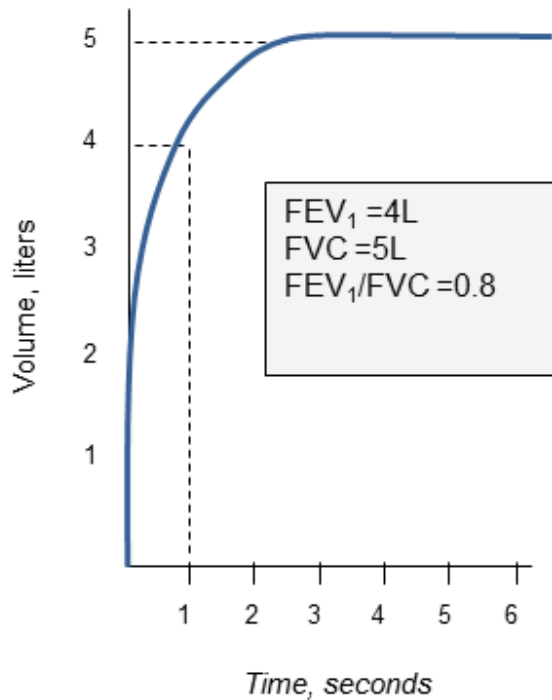
Clip
on nose

Technician monitors
and encourages
patient during test

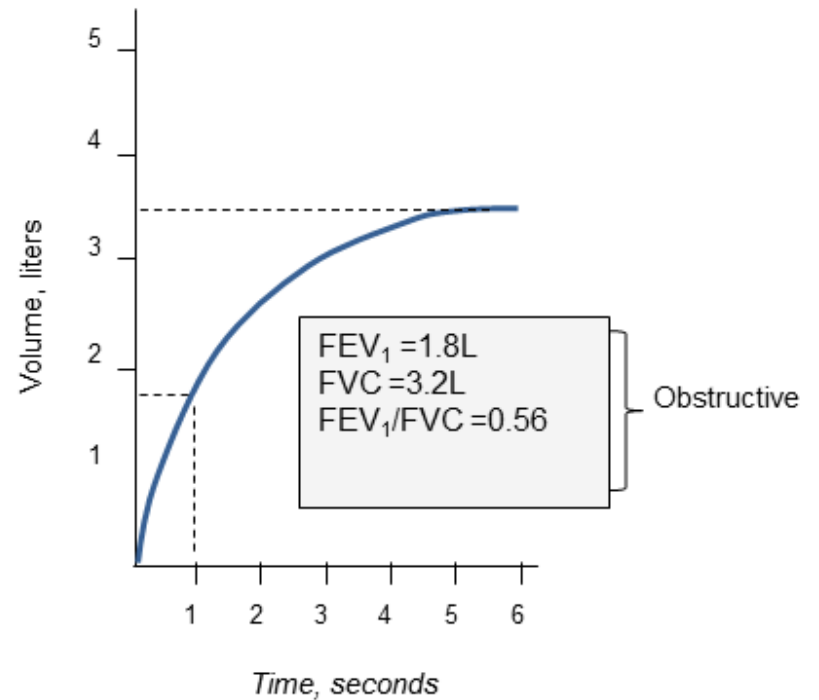


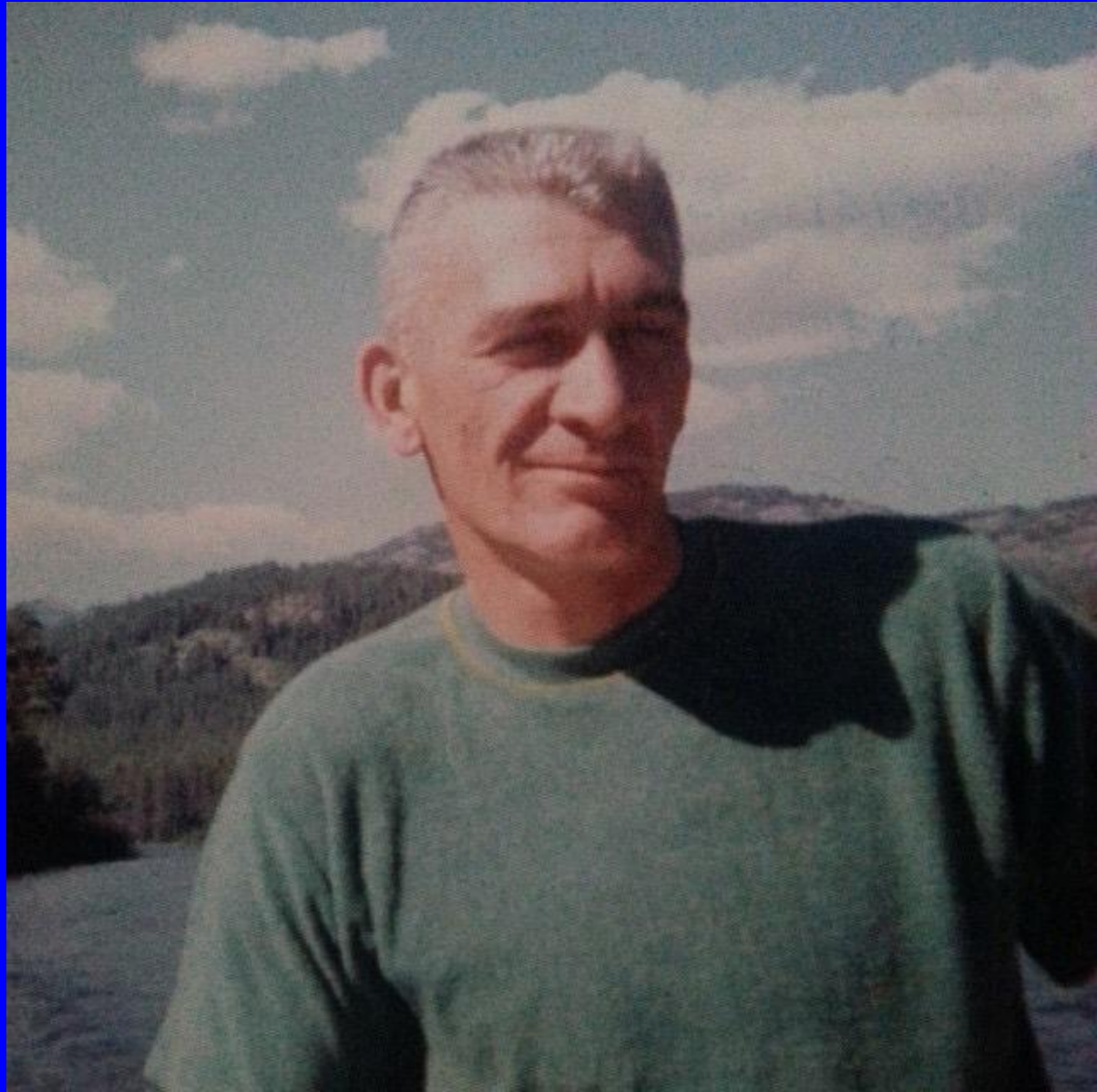
Machine records
the results of the
spirometry test

Healthy patient

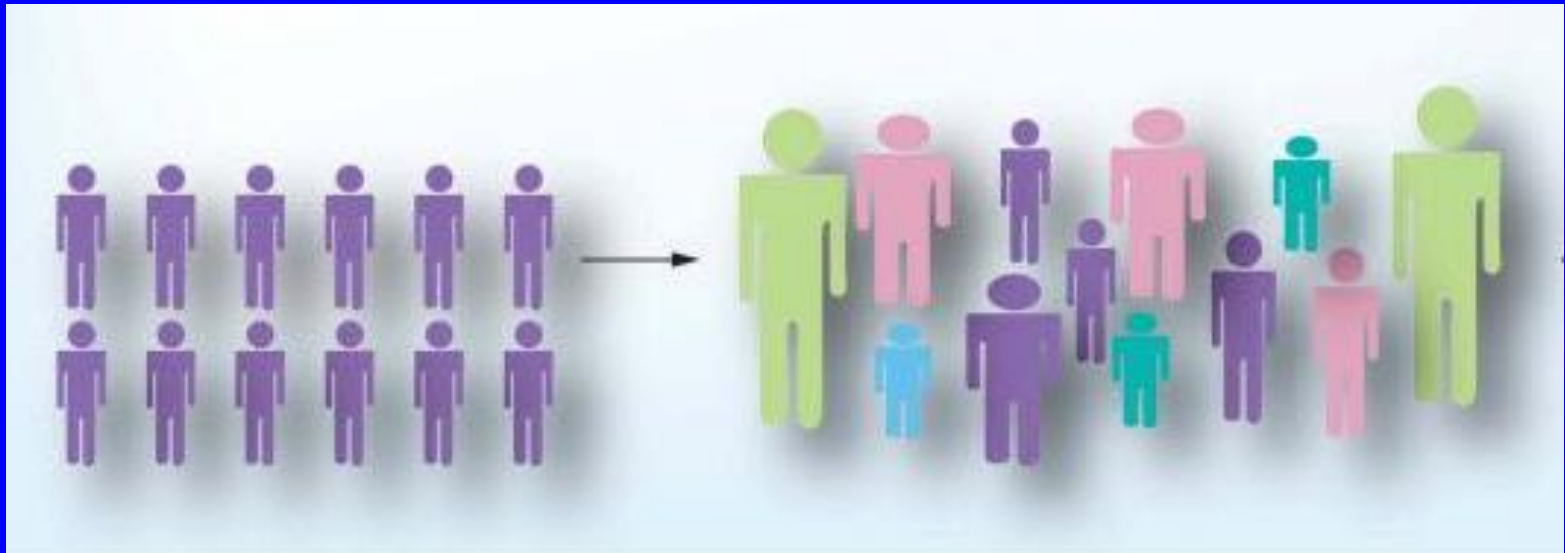


Patient with obstructive lung disease





COPD Heterogeneity



COPD Heterogeneity

Parenchymal destruction
Loss of alveolar attachments
Decreased lung elastic recoil

Small airways disease
Airway inflammation
Airway fibrosis; luminal plugs
Increased airway resistance

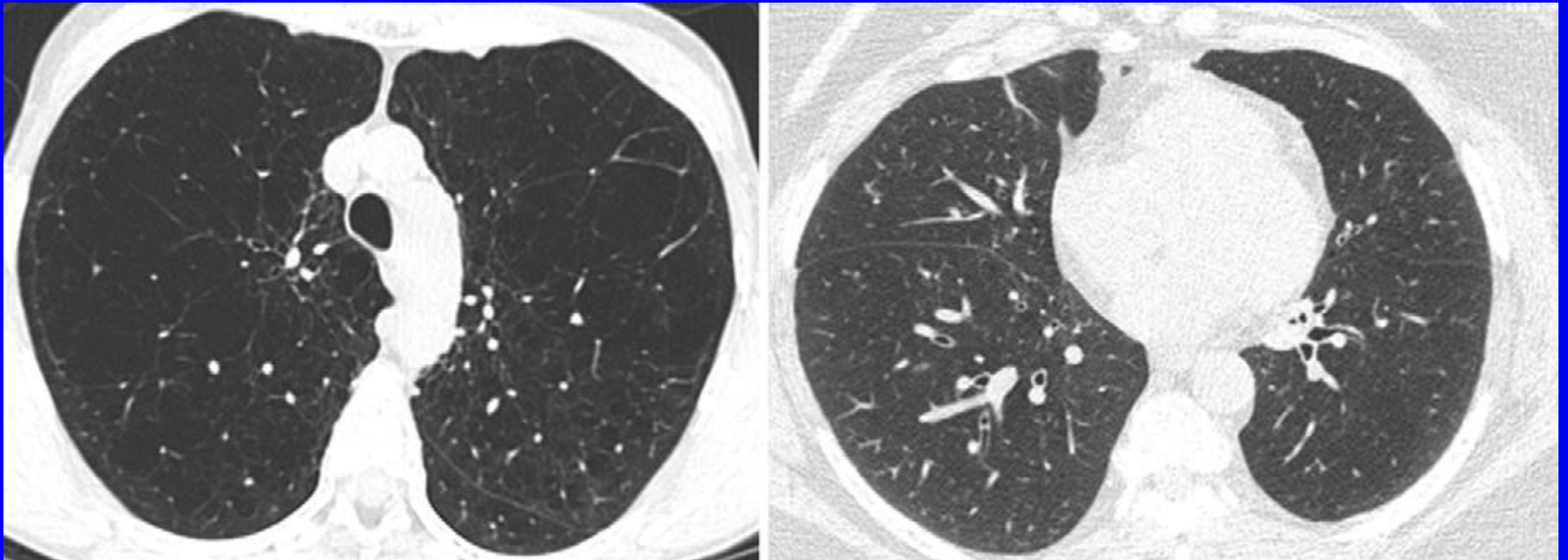
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graph TD; A["Parenchymal destruction<br/>Loss of alveolar attachments<br/>Decreased lung elastic recoil"] --> C["AIRFLOW LIMITATION"]; B["Small airways disease<br/>Airway inflammation<br/>Airway fibrosis; luminal plugs<br/>Increased airway resistance"] --> C;
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AIRFLOW LIMITATION

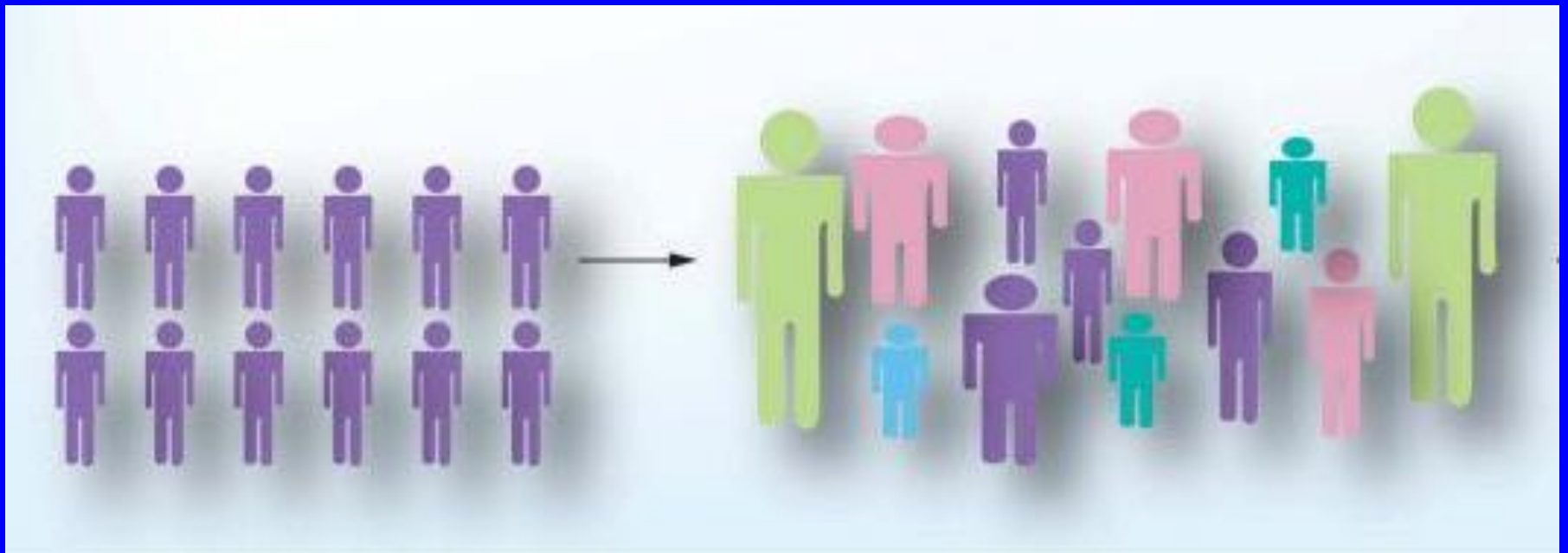
COPD Heterogeneity



COPD Heterogeneity



COPD Heterogeneity



Risk Factors for COPD

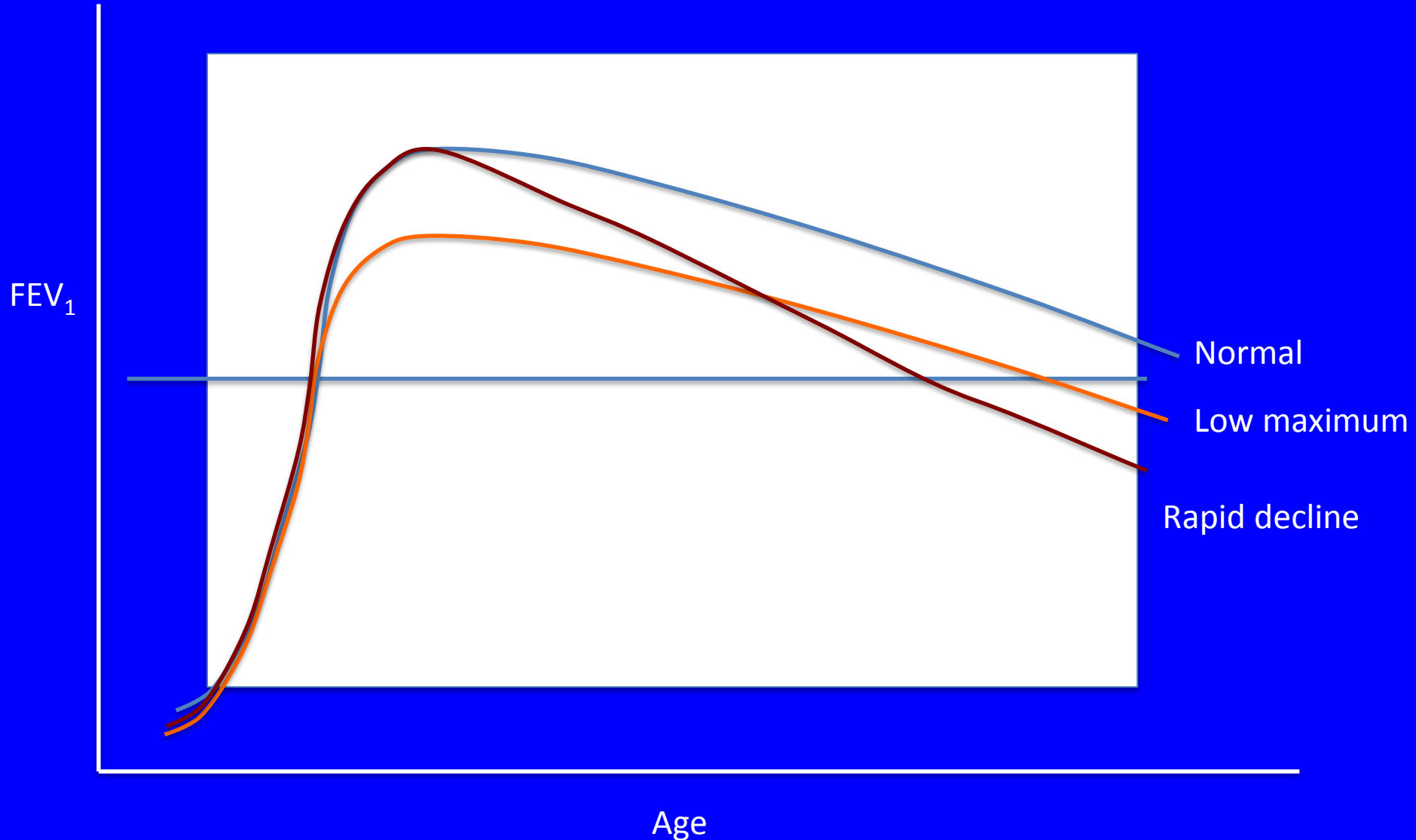
Tobacco smoking



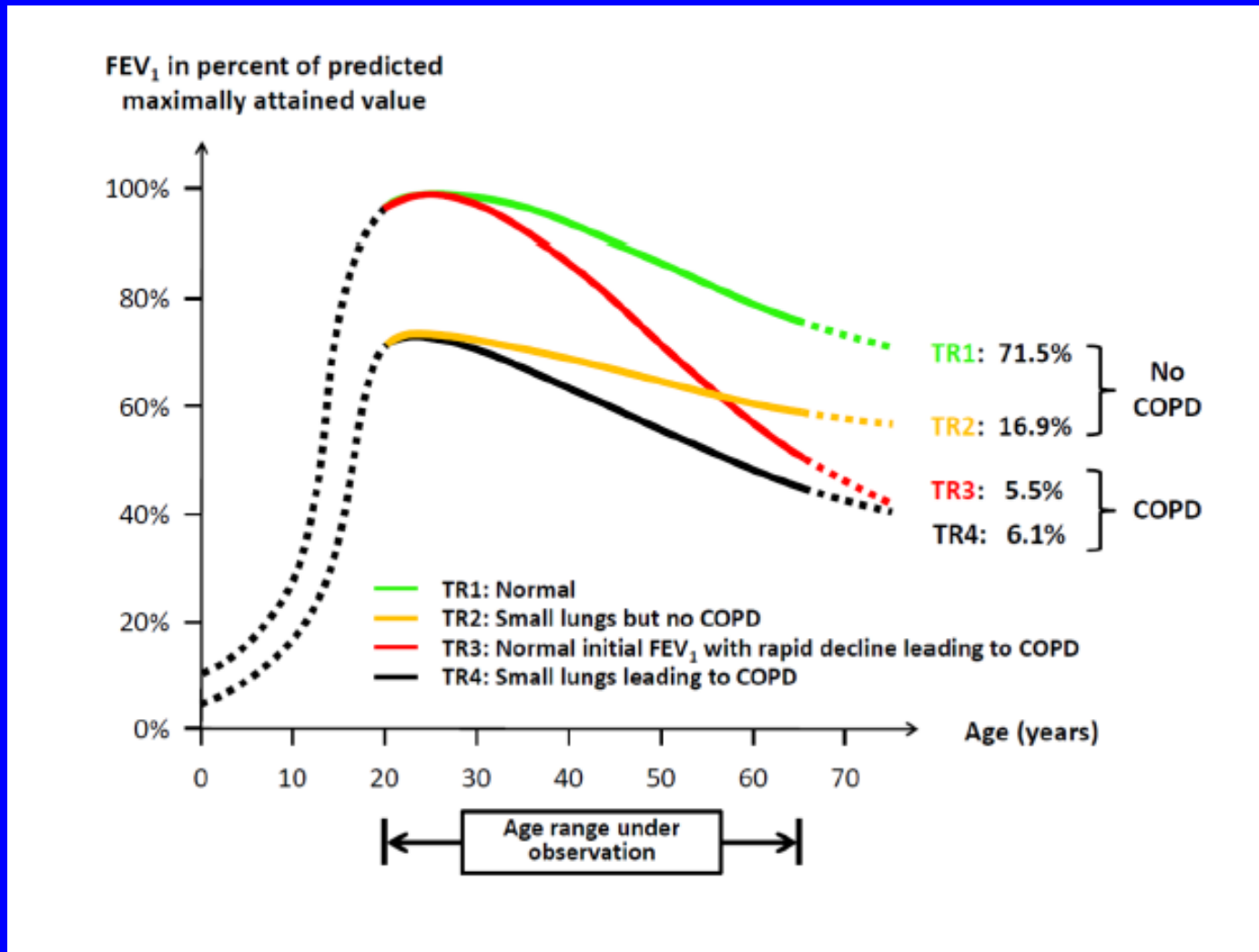
Biomass fuel exposure



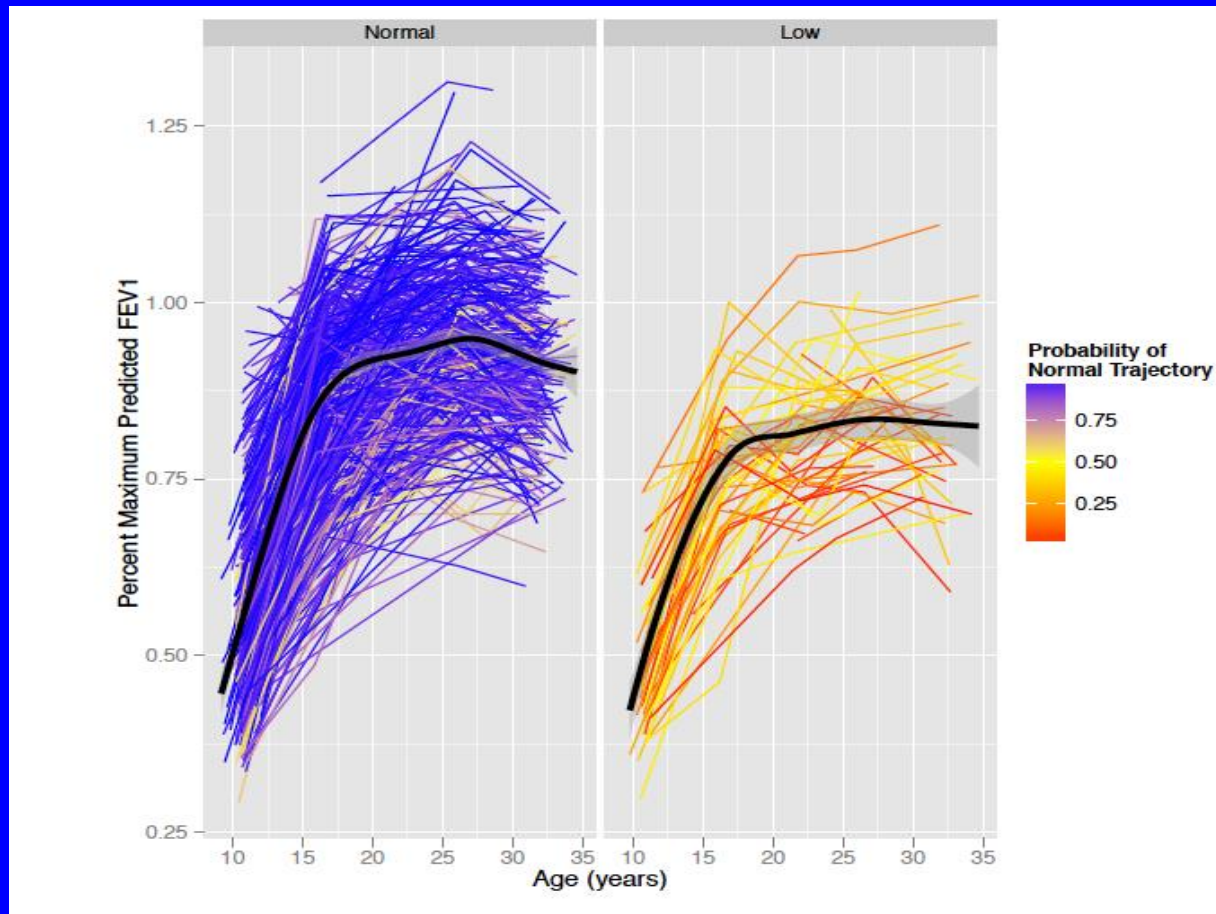
Natural history of lung function



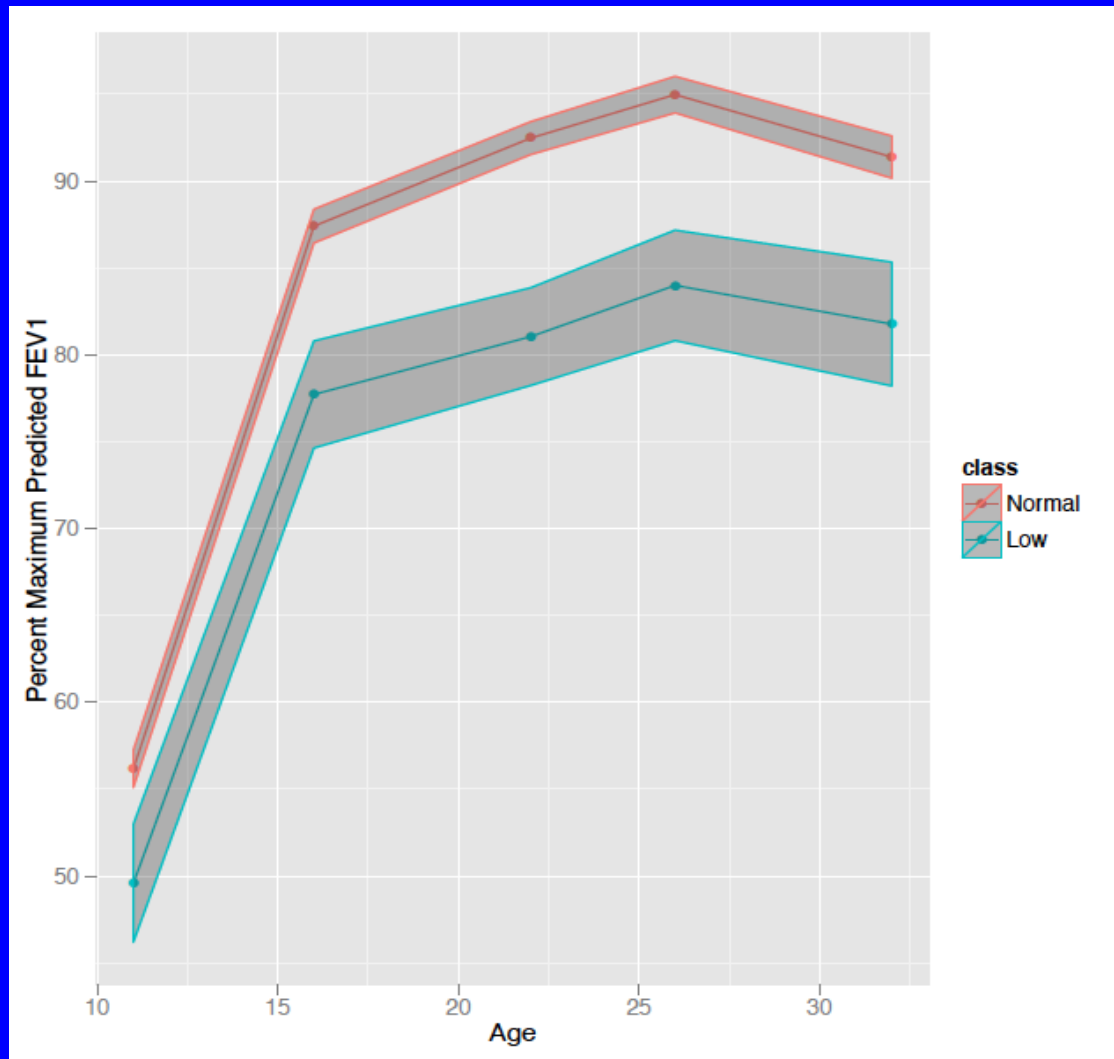
Lung function trajectories



Tucson Children's Respiratory Study

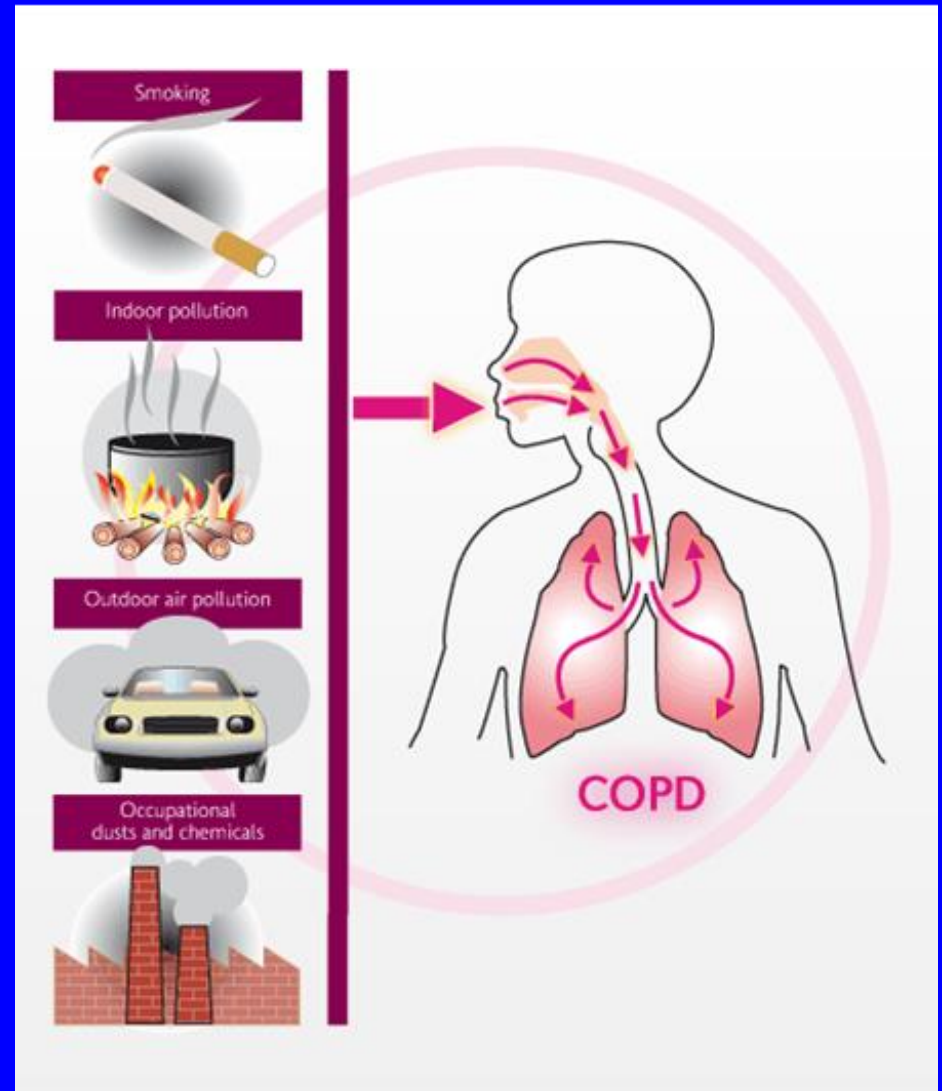


Tucson Children's Respiratory Study

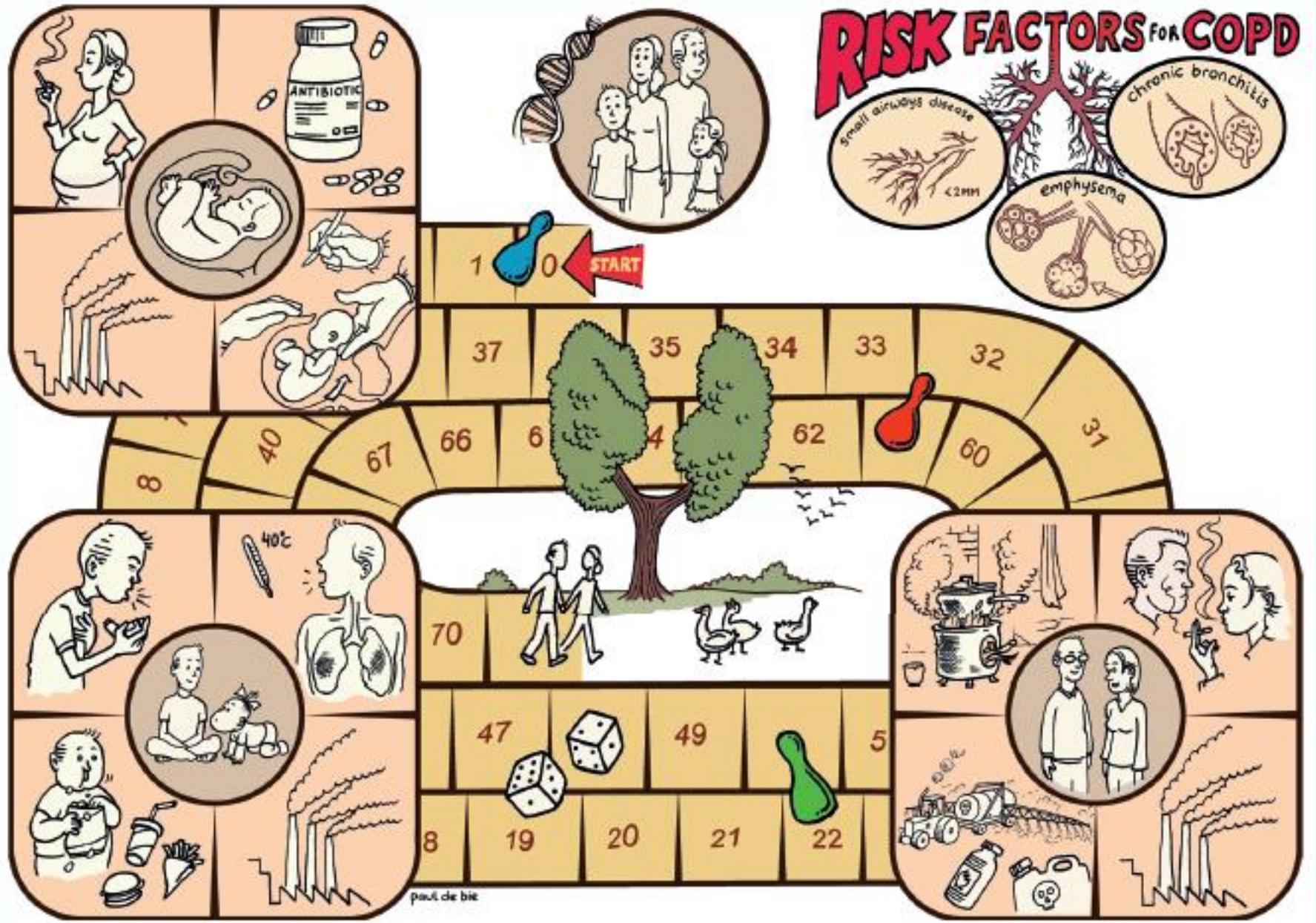


COPD risk factors

- Risk factors:
 - Tobacco smoke
 - Air pollution
 - Occupational dust
 - Family history
 - Genetics (A1AT)
 - Asthma/bronchial hyperreactivity
 - Early life exposures?



RISK FACTORS FOR COPD



paul de bie

COPD Symptoms

COPD symptoms

- Symptoms:
 - Dyspnea
 - Chronic cough
 - Chronic sputum
 - Wheezing
 - Chest tightness
 - Exercise intolerance
 - Low energy



Chronic bronchitis

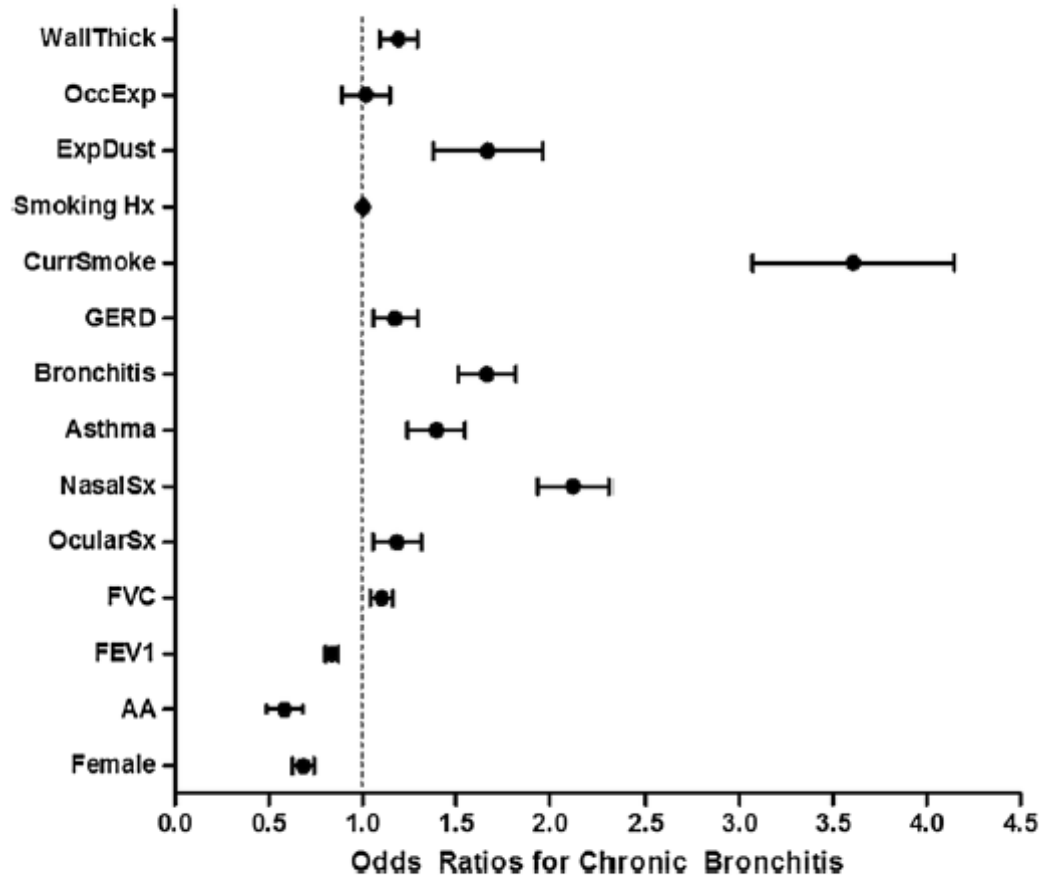


Figure 2 Odds ratios for chronic bronchitis.

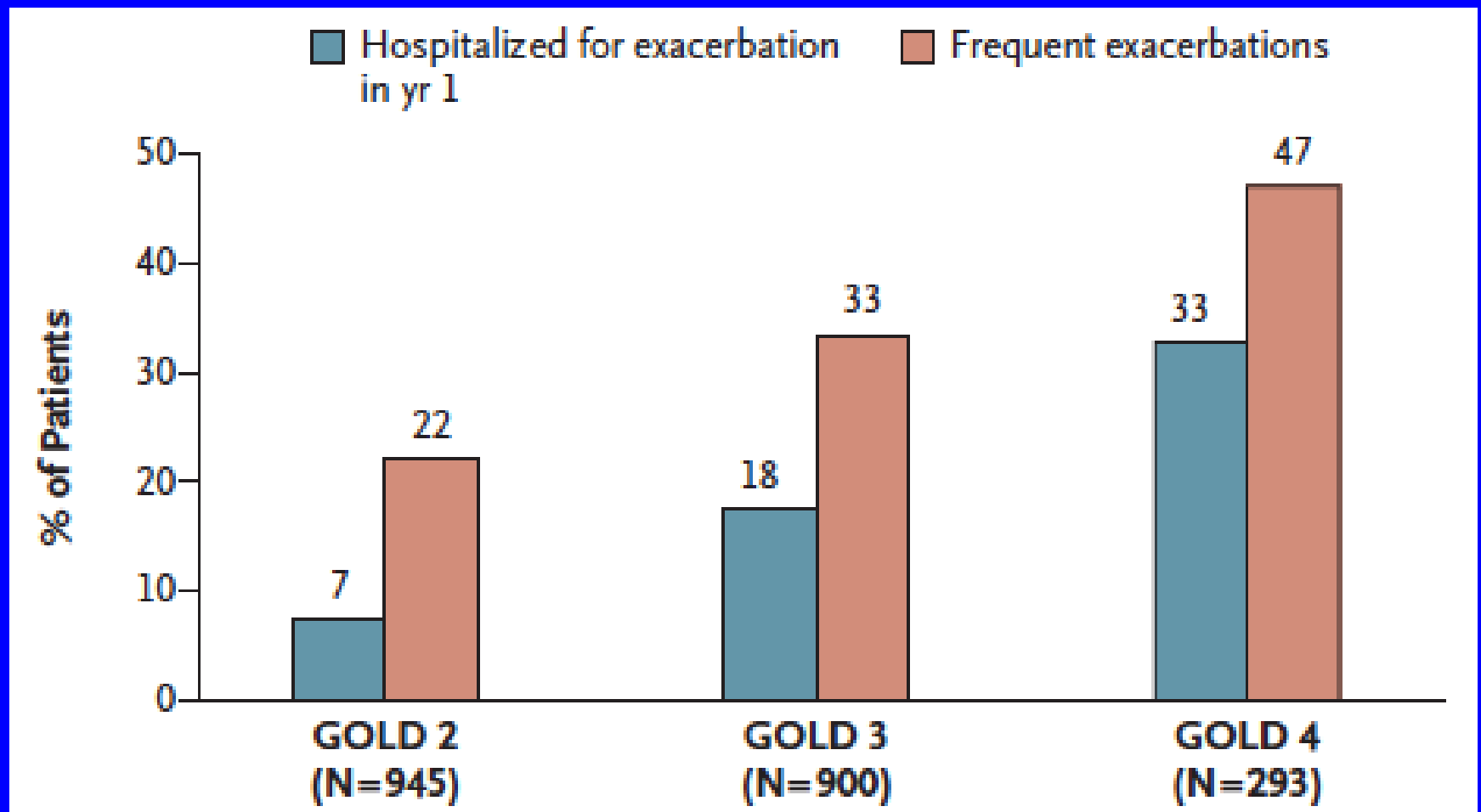
Chronic bronchitis

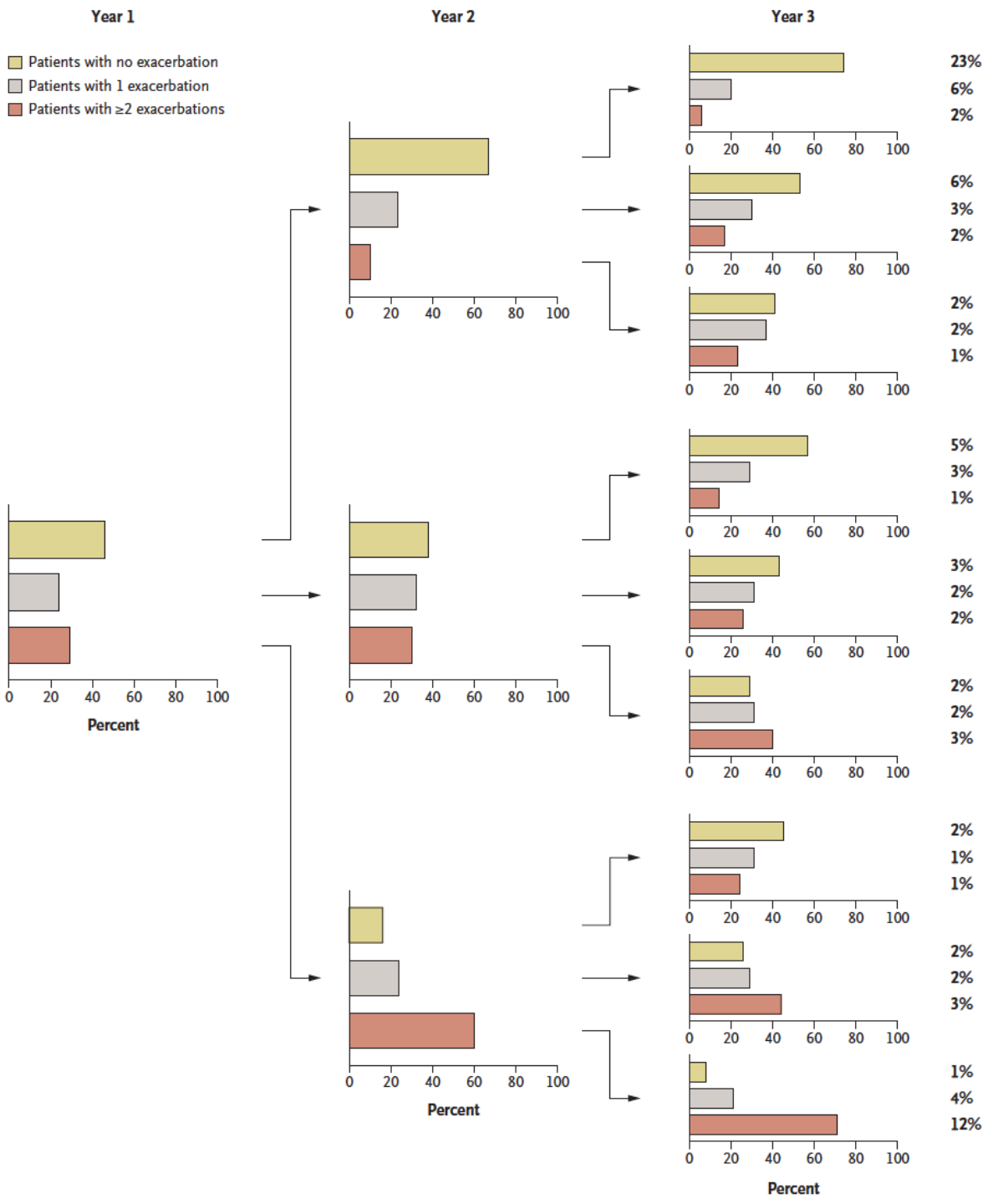
- Reported by 34.6% of ECLIPSE participants
- Higher risk of COPD exacerbations
- Higher risk of COPD hospitalizations
- Worse quality of life
- Faster decline in lung function
- Higher risk of respiratory-related mortality



COPD Exacerbations

COPD exacerbations





Frequent Exacerbations of Chronic Obstructive Pulmonary Disease — A Distinct Phenotype?

Tashkin DP. NEJM 2010; 363: 1183-1184



≥ 2 exacerbations per year

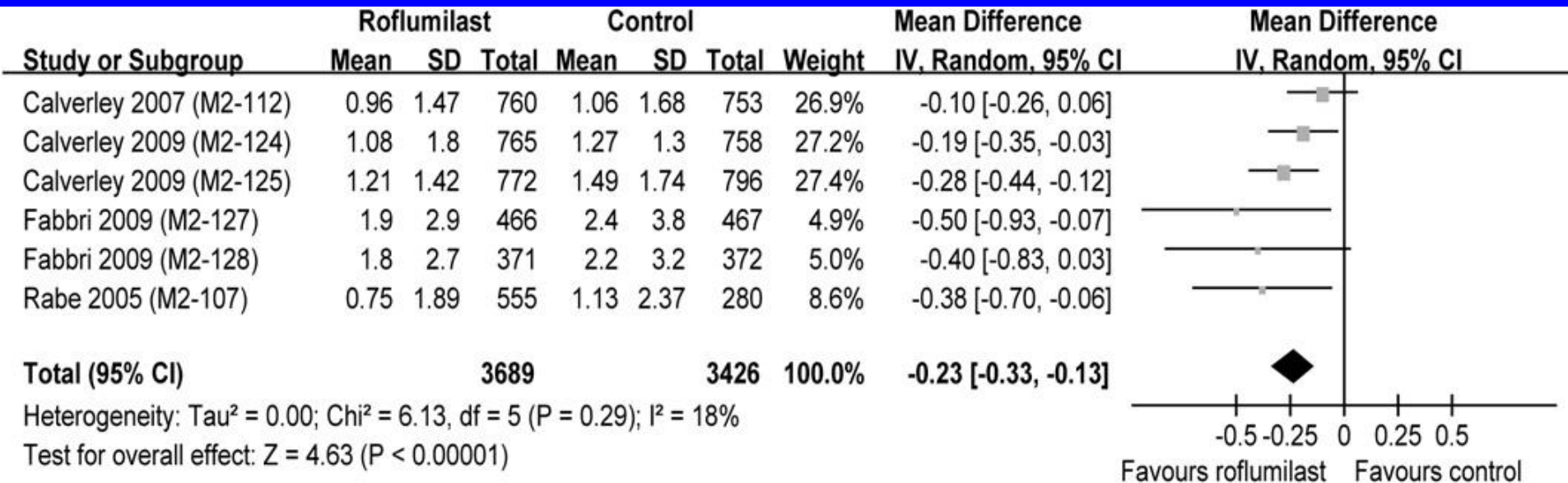
Roflumilast

- Phosphodiesterase 4 inhibitor
- FDA indication “to reduce the risk of COPD exacerbations in patients with severe COPD associated with chronic bronchitis and a history of exacerbations”

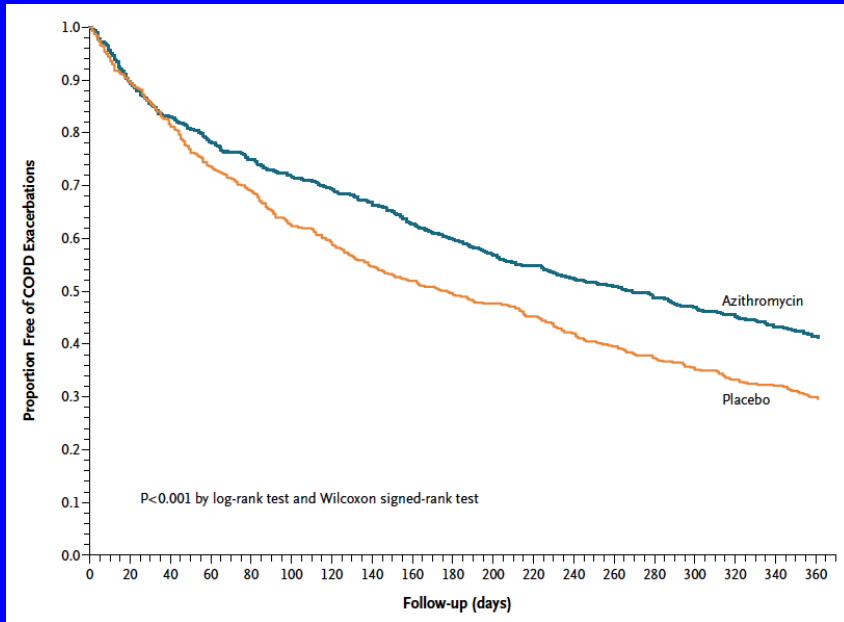


Roflumilast: pivotal trials

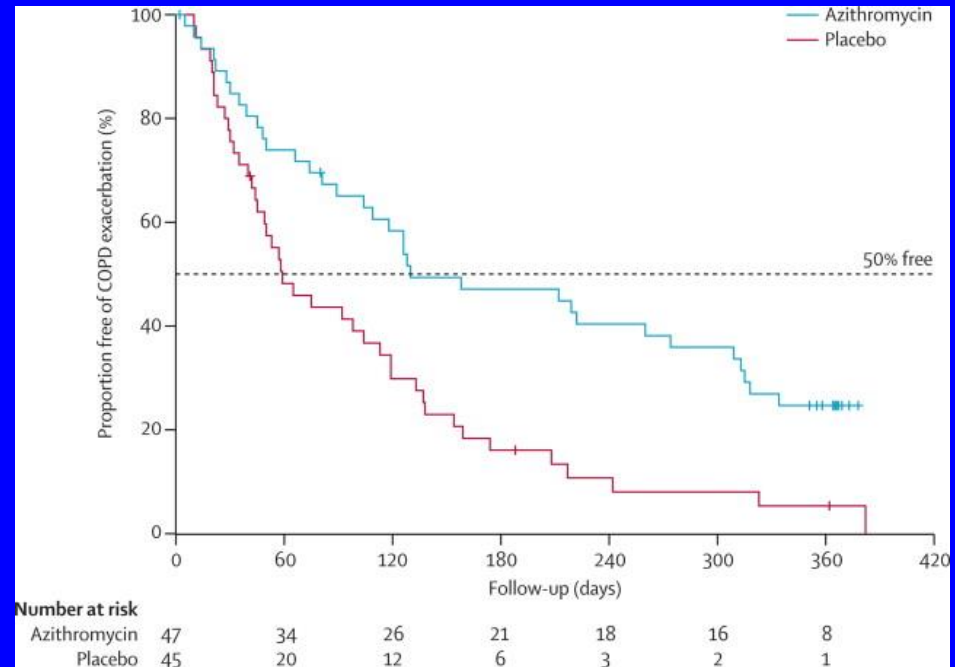
Pooled effect on exacerbation rate



Azithromycin



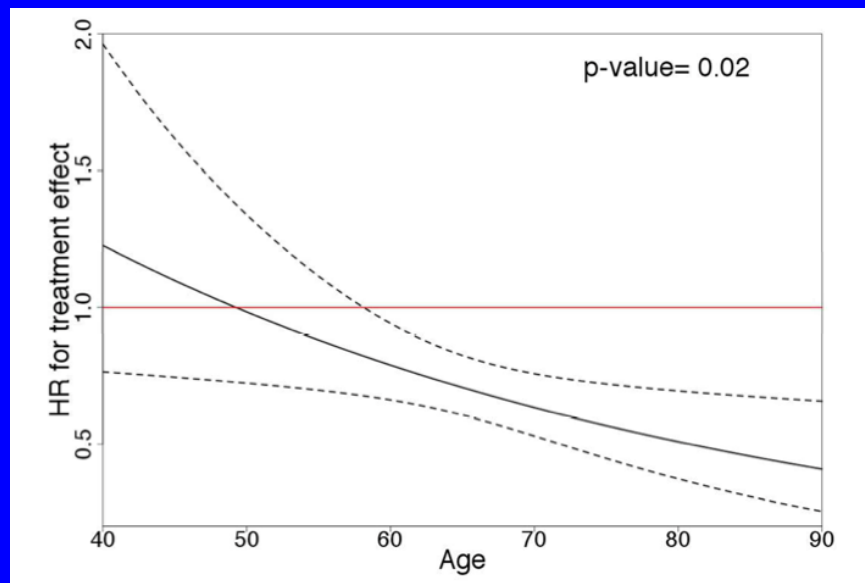
Albert et al. NEJM 2011; 365: 689-698



Uzun et al. Lancet Resp Med 2014; 2: 361-368

Azithromycin

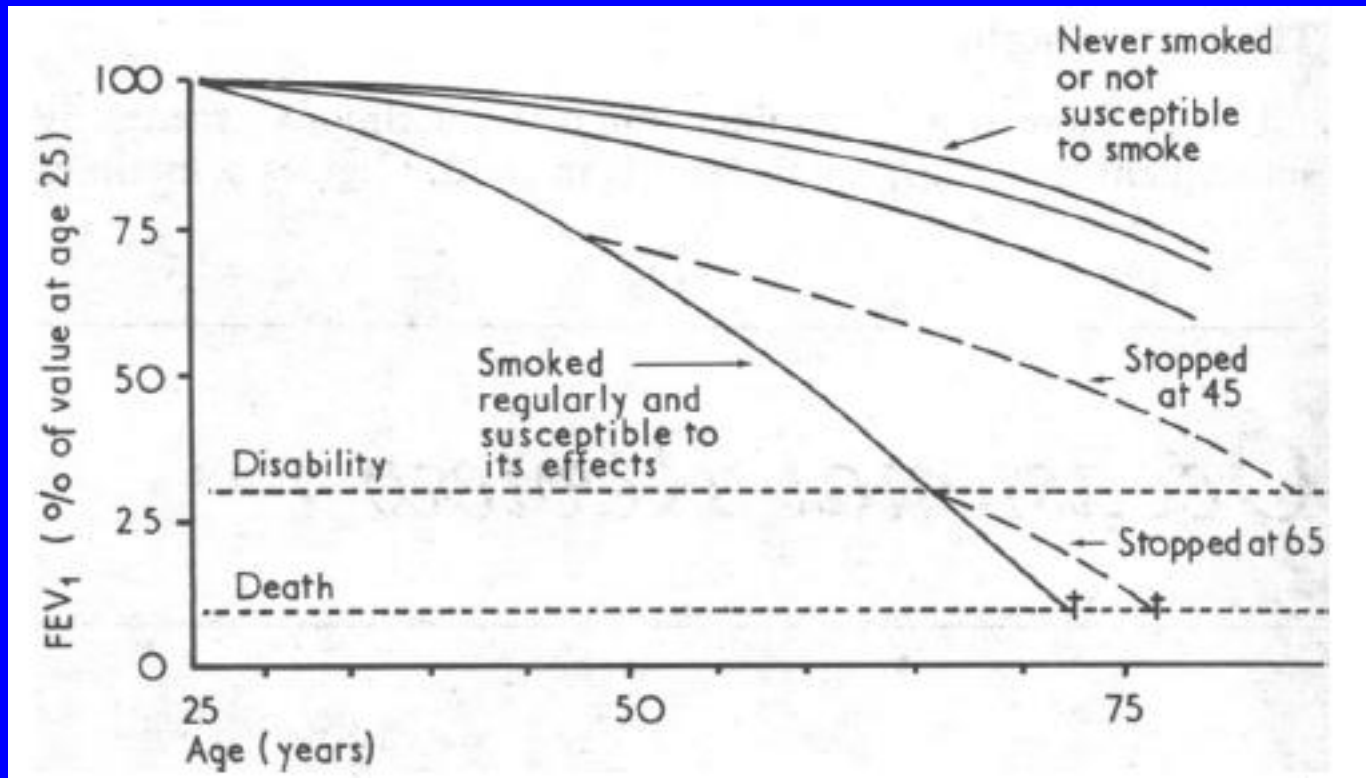
- No apparent benefit in current smokers
- Effective add-on to maximal inhaled therapy
- More effective in milder severity disease
- More effective in older adults



Han et al.
AJRCCM 2014.

COPD Prognosis

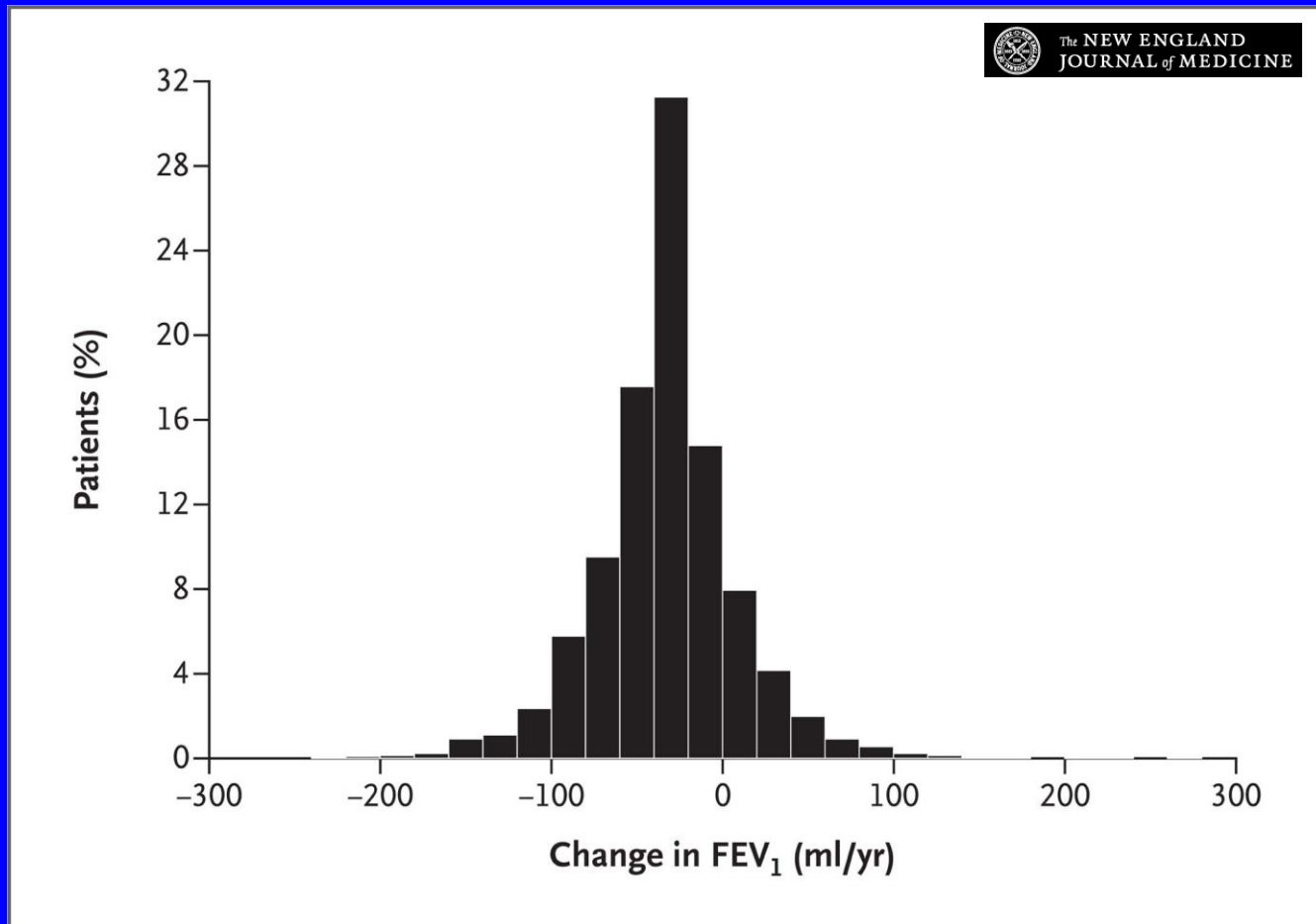
Lung function decline in COPD



The natural history of chronic airflow obstruction

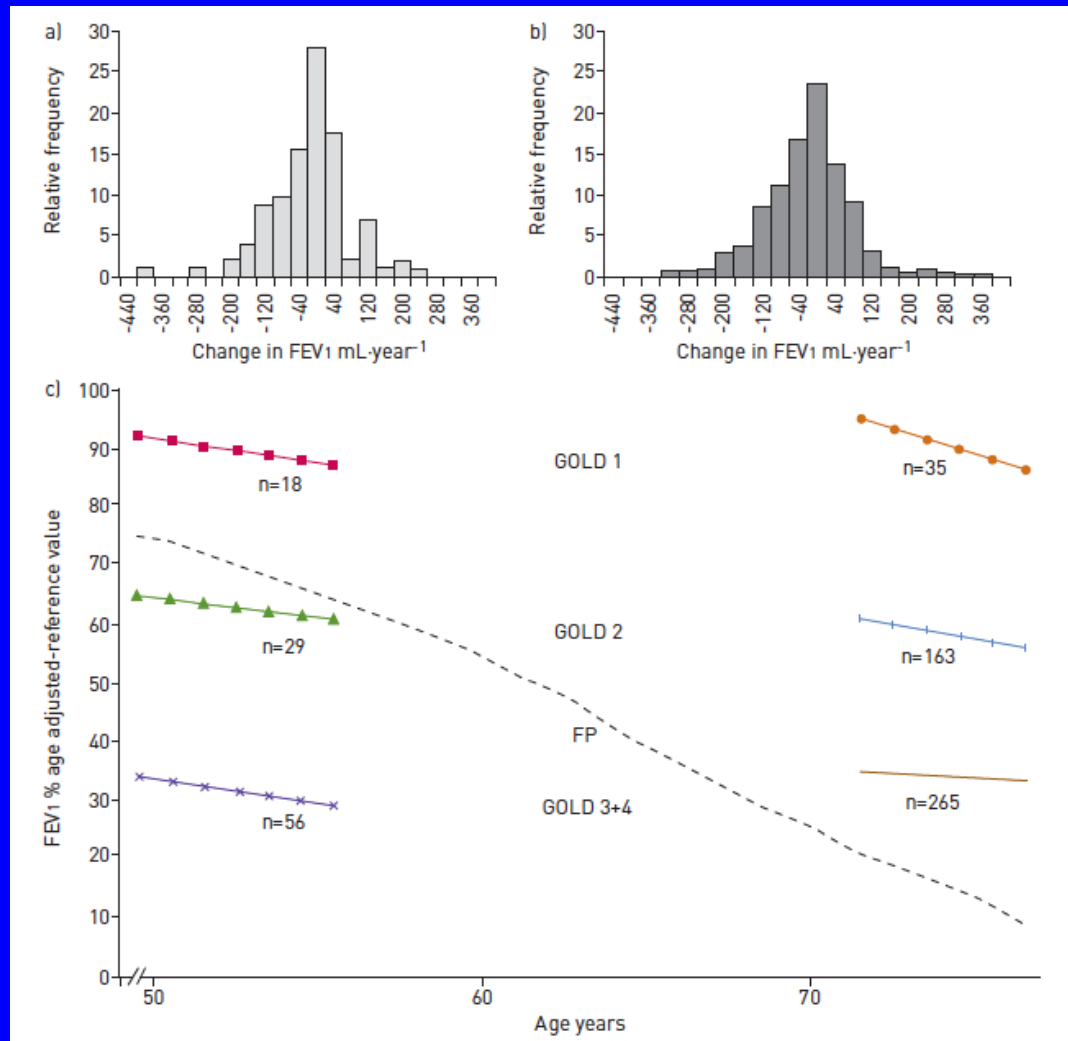
CHARLES FLETCHER, RICHARD PETO

Lung function decline in COPD



Vestbo J et al. N Engl J Med 2011;365:1184-1192

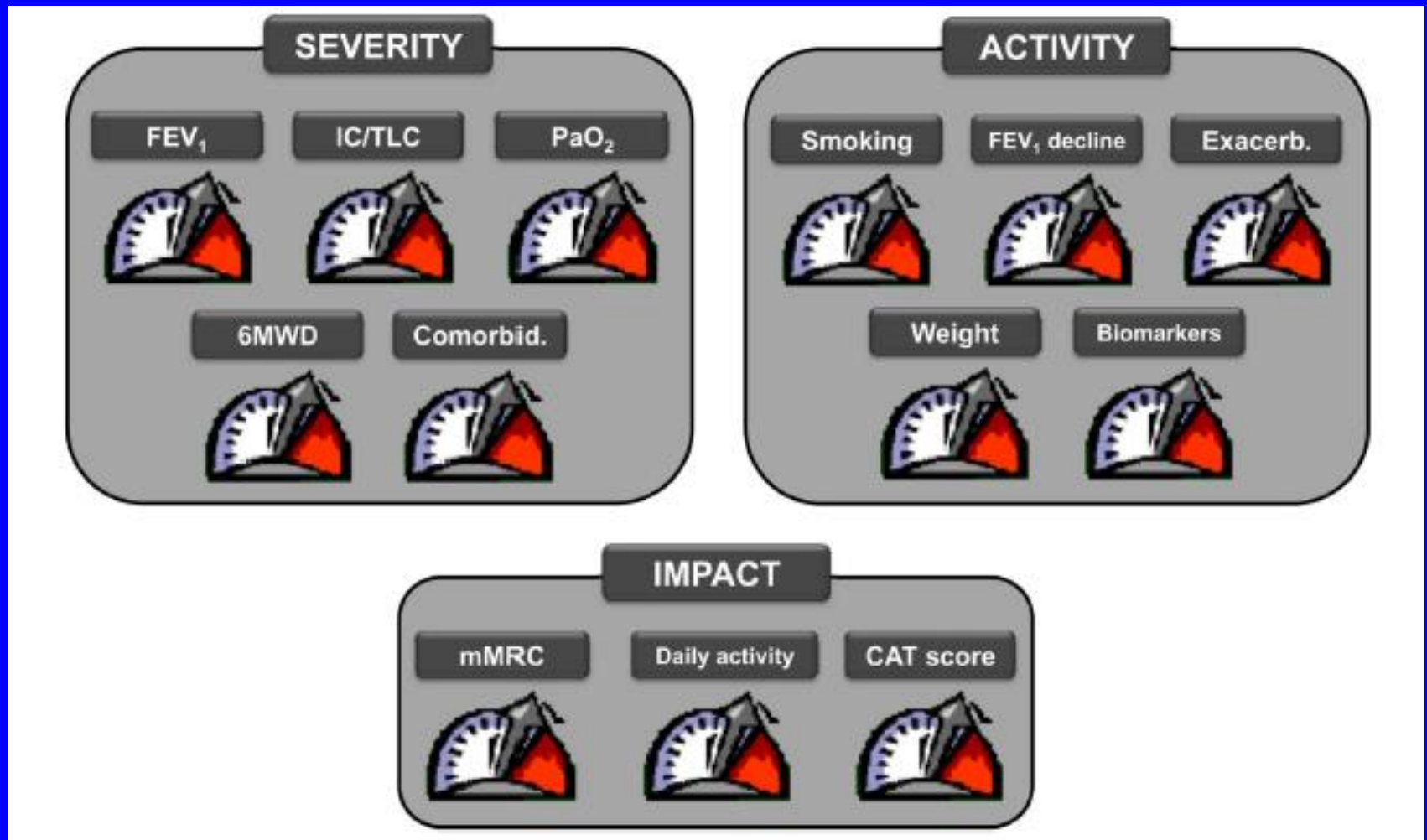
Lung function decline in COPD



COPD heterogeneity in practice

- How should we handle heterogeneity?
- What about chronic bronchitis or emphysema in the absence of airflow limitation?
- How do we use phenotypes in practice?
- What is the role of FEV_1 ?
- Disease activity versus disease severity?

COPD “control panel”



Looking to the future...

All-comers

Stratified
medicine

Personalized
medicine

Evidence-based medicine
Standardized guidelines

Clinical
reality

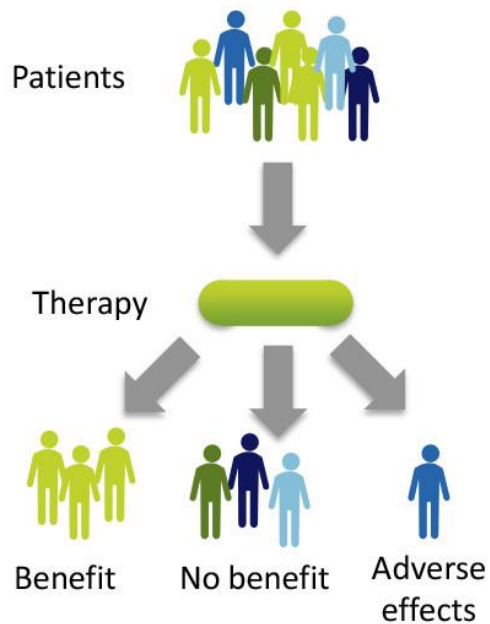
Individualized medicine
Stratification: defining relevant
subgroups of individuals



Looking to the future...

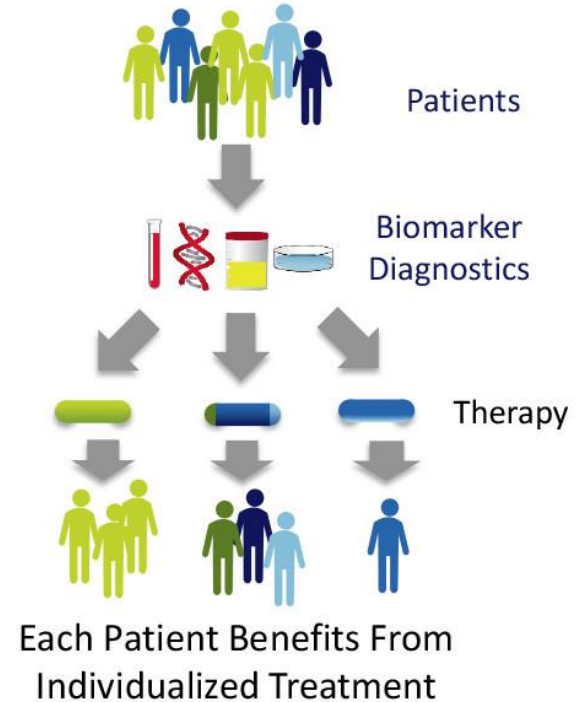
Without Personalized Medicine:

Some Benefit, Some Do Not

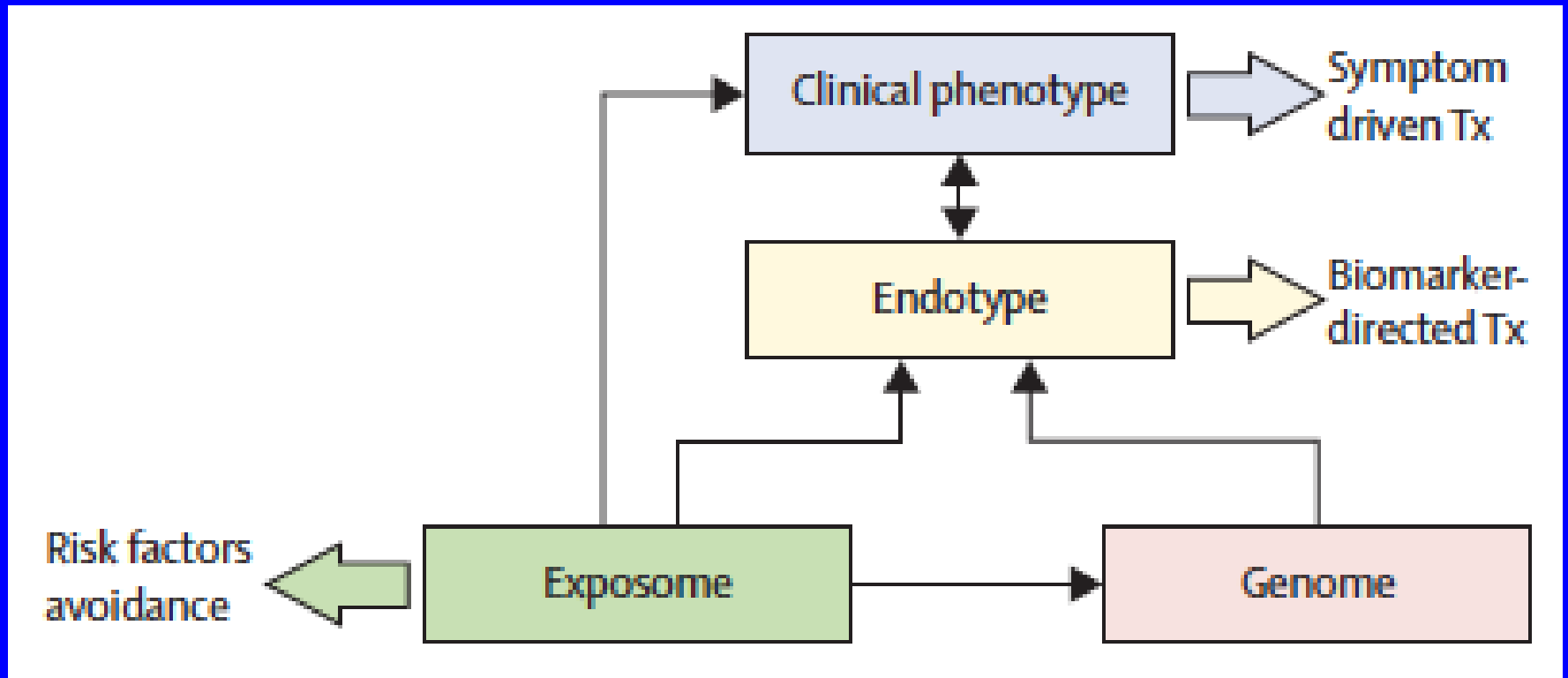


With Personalized Medicine:

Each Patient Receives the Right Medicine For Them



Phenotype → Endotype

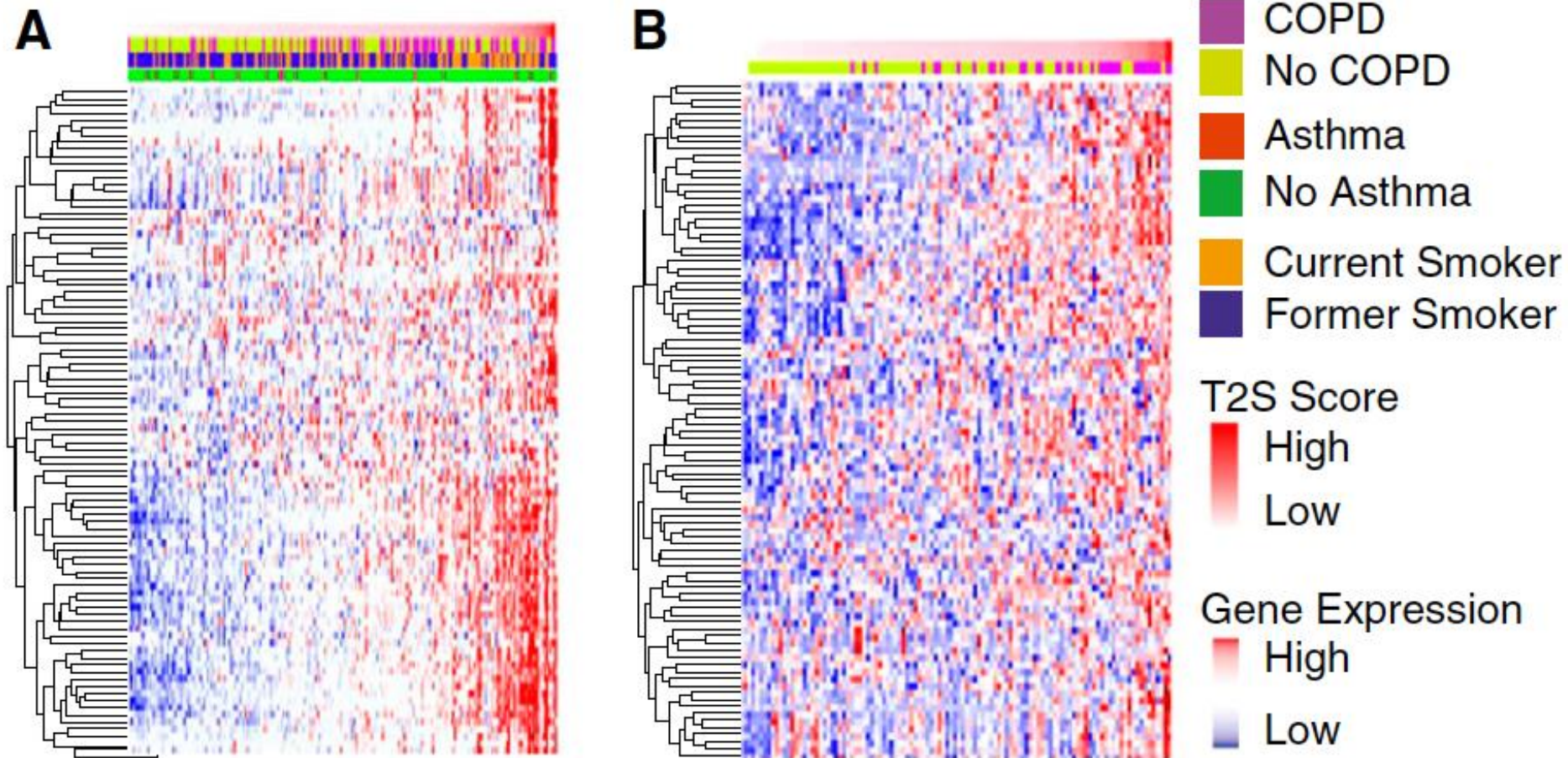


Woodruff et al. Lancet 2015; 385: 1789

Asthma-COPD Overlap

Clinical Relevance of Genomic Signatures of Type 2 Inflammation in Chronic Obstructive Pulmonary Disease

Stephanie A. Christenson^{1,2}, Katrina Steiling^{3,4}, Maarten van den Berge^{5,6}, Kahkeshan Hijazi⁷, Pieter S. Hiemstra⁸, Dirkje S. Postma^{5,6}, Marc E. Lenburg^{3,4,9}, Avrum Spira^{3,4,9}, and Prescott G. Woodruff^{1,2}



Summary

- Heterogeneity is common
- Multiple risk factors for COPD beyond smoking
- Disease severity versus activity versus impact
 - Lung function (FEV_1)
 - Exacerbations
 - Lung function decline
 - Symptoms and physical activity
- Phenotypes may be useful to guide therapy
- Biological endotypes may be employed to predict response to therapy in the future

Questions or comments?

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of Arizona
Health Sciences

