Update on COPD

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Questions

1. What is the current definition of COPD?

Emphysema

Chronic Bronchitis

COPD

PHYSIOLOGICAL DIAGNOSIS:
Post-BD $FEV_1/FVC < 0.7$

COPD Definition

COPD, a common preventable and treatable disease, is characterised by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases. Exacerbations and comorbidities contribute to the overall severity in individual patients.

WHO/GOLD 2013 (www.goldcopd.org)

COPD Definition

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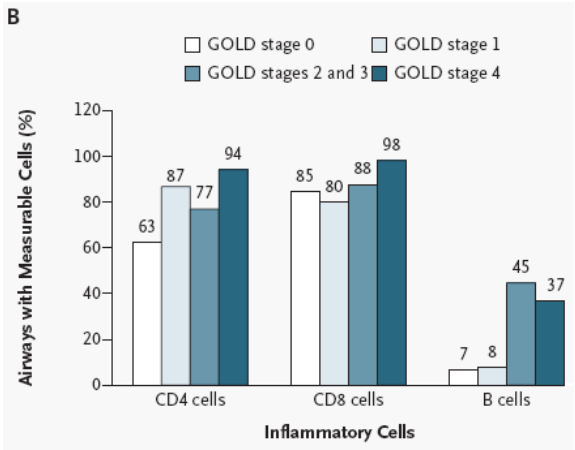
The NEW ENGLAND JOURNAL of MEDICINE

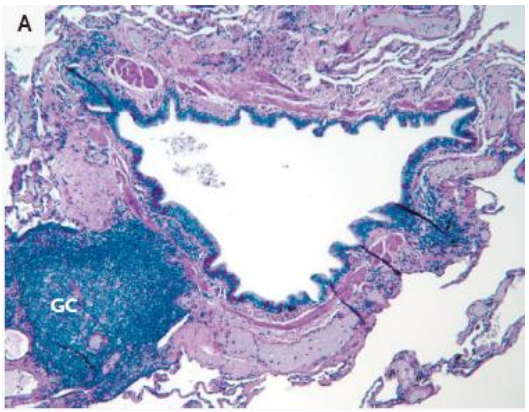
ESTABLISHED IN 1812 JUNE 24, 2004 VOL. 350 NO. 26

The Nature of Small-Airway Obstruction in Chronic Obstructive Pulmonary Disease

James C. Hogg, M.D., Fanny Chu, B.Sc., Soraya Utokaparch, B.Sc., Ryan Woods, M.Sc., W. Mark Elliott, Ph.D., Liliana Buzatu, M.D., Ruben M. Cherniack, M.D., Robert M. Rogers, M.D., Frank C. Sciurba, M.D., Harvey O. Coxson, Ph.D., and Peter D. Paré, M.D.

N Engl J Med 2004;350:2645-53.



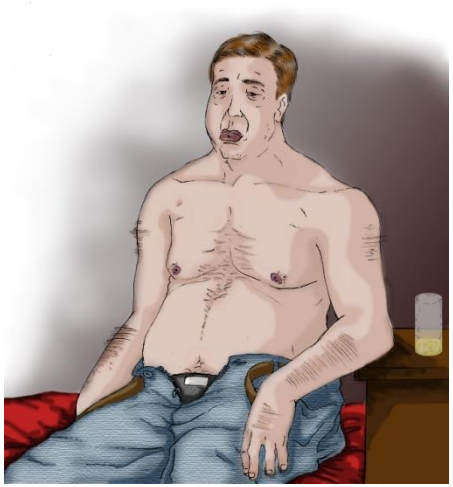


Questions

1. What is the current definition of COPD?
2. What is a COPD ‘phenotype’?

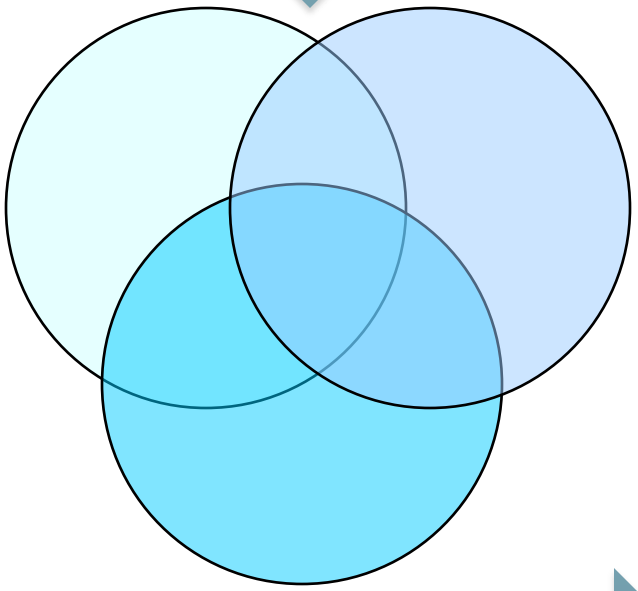
What is a phenotype?

An observable characteristic (trait) of an organism resulting from genes, environment, and gene-environment interaction



Chronic Bronchitis

Emphysema



COPD

PHYSIOLOGICAL DIAGNOSIS:
Post-BD $FEV_1/FVC < 0.7$

Phenotype

Is a problem of defining COPD using a single physiological measure:

FEV_1

Bronchodilator Reversibility

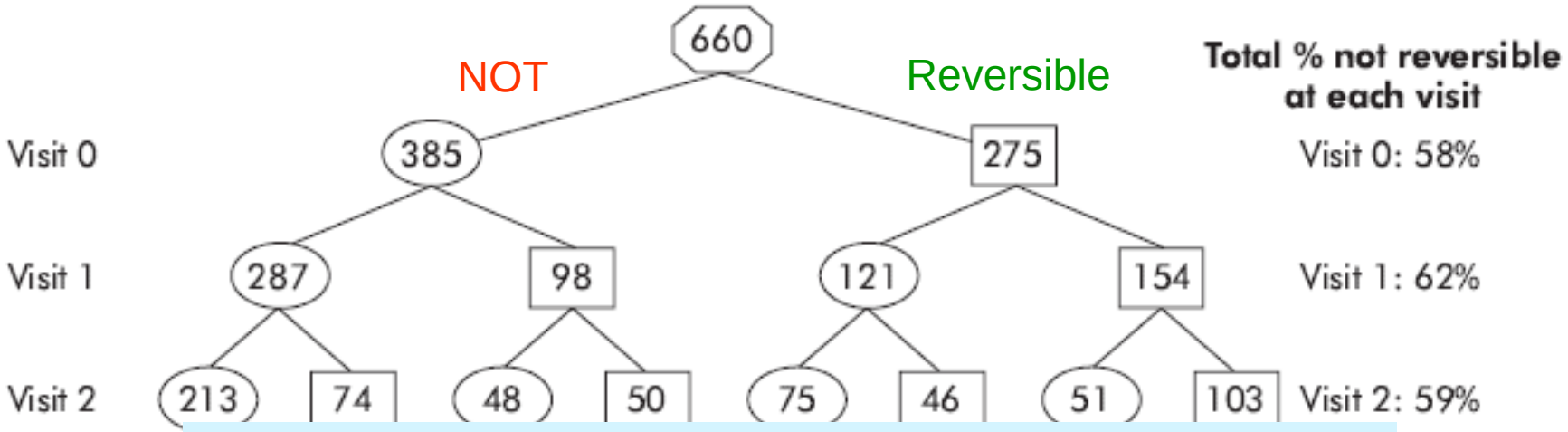
- Do some patients have it and others not?
- Might it be important?

CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Bronchodilator reversibility testing in chronic obstructive pulmonary disease

P M A Calverley, P S Burge, S Spencer, J A Anderson, P W Jones, for the ISOLDE Study Investigators

Thorax 2003;**58**:659–664



Stability

Summary

What is a Phenotype in COPD?

A feature other than FEV_1 that independently predicts a clinical outcome or treatment response and is stable over time

Questions

1. What is the current definition of COPD?
2. What is a COPD ‘phenotype’?
3. What is the point of an alpha-1 service?

The London Alpha-1 Antitrypsin Deficiency Service

Benefits of an Alpha-1 Service

- Joined up, one-stop liver and lung care
- Expert advice
- Training
- Research

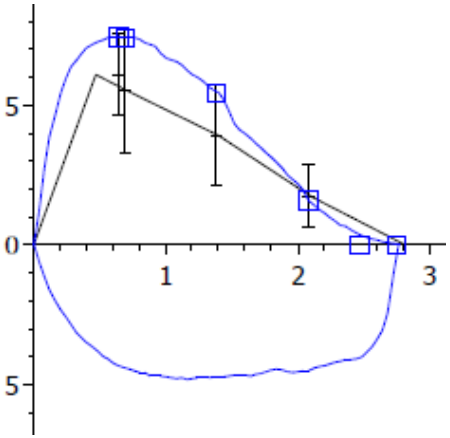
Case History – Mrs A

- ♀ 41 - Iraqi origin living in West London
- Previously fit and well
- May 2013: α-1AT 0.4g/L
  - investigation of left ulnar neuropathy
- Phenotype: “unclear result”
- Genotype: novel variant

Gene	Exon	Nucleotide change	Predicted protein change
SERPINA1	05	c1078G>C homozygous	p.Ala360Pro

α-1 Clinic RFH Jan 2014: Clinical Care

- Confirmed no respiratory, GI or skin symptoms
  - No family history of liver or lung disease
  - parents first cousins
- Fibroscan 6.1kPa (normal), US liver and LFTs all normal
- Lung function normal
- Annual follow-up for monitoring



What is her risk of lung or liver disease?

Academic-Clinical Collaboration

- protein characterisation in Lomas' lab
- Novel variant is polymerogenic

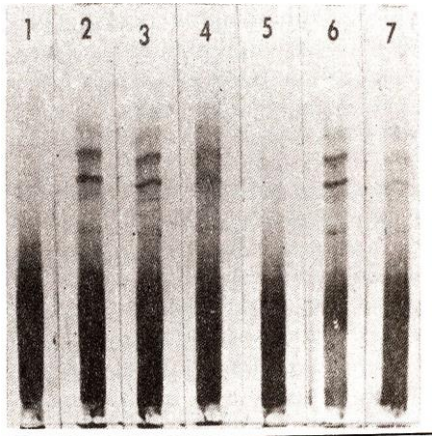
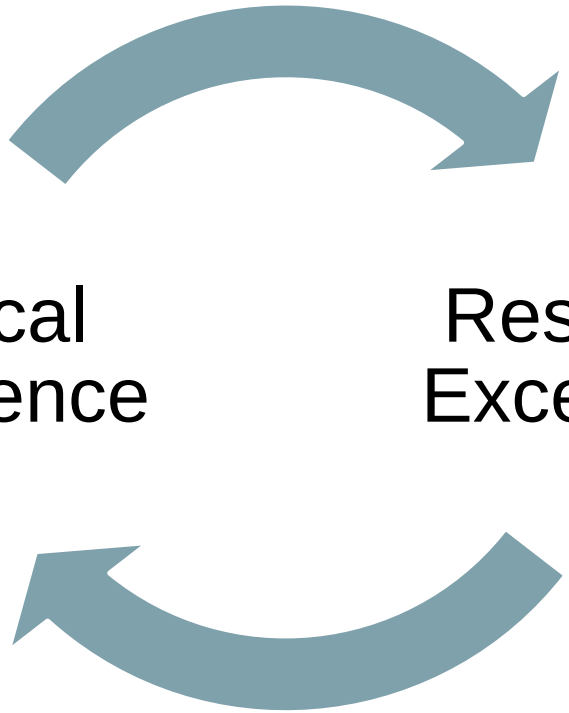


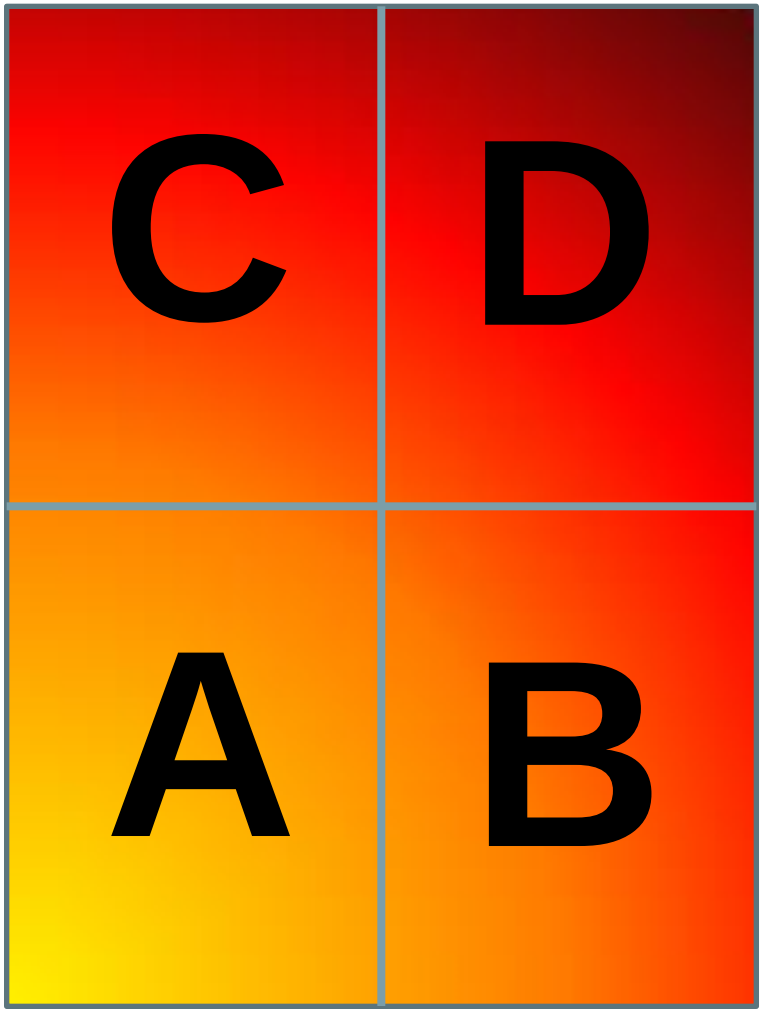
Figure 1. Phenotypes of alpha 1 AT in the family of a duodenal ulcer patient. IEF showing alpha 1 AT phenotypes at pH 4-5 Proband (channel 1), siblings (2-4), son (5), daughters (6,7). Anode at top.


Clinical
Excellence
Research
Excellence

Questions

1. What is the current definition of COPD?
2. What is a COPD ‘phenotype’?
3. What is the point of an alpha-1 service?
4. ICS, LABA and LAMA – for who?

2011 GOLD Revision



SYMPTOMS

mMRC 0-1
CAT<10

mMRC ≥2
CAT≥10

CAT

- To assess the impact of COPD
- May assist in case finding

CAT
COPD Assessment Test

اسمك:

تاريخ اليوم:

ما حالة مرض انسداد الشعب الهوائية المزمن (COPD) لديك؟ قم بإجراء اختبار COPD Assessment Test™ (CAT)

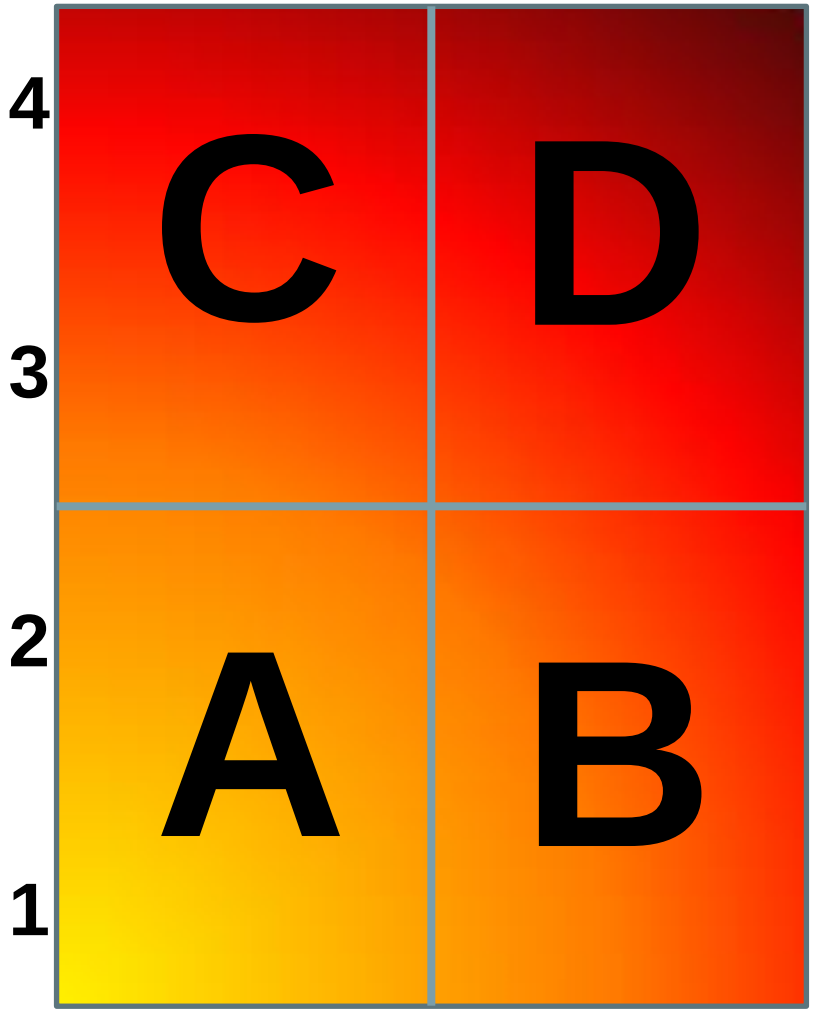
سوف يساعدك هذا الاستبيان أنت وأخصائي الرعاية الصحية على قياس تأثير COPD (مرض انسداد الشعب الهوائية المزمن) على صحتك وحياتك اليومية. ويمكن لك وأخصائي الرعاية الصحية استخدام إجاباتك ودرجاتك في الاختبار للمساعدة في تحسين إدارة مرض الانسداد الرئوي المزمن والحصول على أكبر استفادة من العلاج.

لكل عنصر موجود أدناه، ضع علامة (X) في المربع الذي يصف حالتك حالياً على أفضل نحو. تأكد من اختيارك لرد واحد فقط على كل سؤال.

مثال: أنا سعيد جدًا 0 1 2 X 4 5 أنا حزين جدًا

النتيجة		
	لا أكح مطلقاً 0 1 2 3 4 5 أعاني من الكحة طوال الوقت	
	ليس عندي أي بلغم (مخاط) في صدري 0 1 2 3 4 5 صدري ممتلئ عن آخره بالبلغم (المخاط)	
	لا أشعر بضيق في صدري على الإطلاق 0 1 2 3 4 5 أشعر بضيق شديد في صدري	
	لا تجدني أنهج عند أصعد تل أو عندما أصعد دور واحد من السلم 0 1 2 3 4 5 تجدني أنهج تماماً عند السير لأعلى التل أو عندما أصعد دور واحد من السلم	
	لا يقتصر عملي في المنزل على القيام بأي أنشطة 0 1 2 3 4 5 قدراتي محدودة كثيرا عند القيام بالأنشطة بالمنزل	
	أغادر منزلي في ثقة بالرغم من حالة رئتي 0 1 2 3 4 5 لا أشعر بالثقة مطلقًا في مغادرة منزلي بسبب حالة رئتي	
	أنام بعمق 0 1 2 3 4 5 لا أنام بعمق بسبب حالة رئتي	
	لدي الكثير من الطاقة 0 1 2 3 4 5 ليس لدي طاقة على الإطلاق	
	النتيجة الإجمالية	

2011 GOLD Revision



A: Low Risk, Fewer Symptoms
B: Low Risk, More Symptoms
C: High Risk, Fewer Symptoms
D: High Risk, More Symptoms

GOLD Guideline

- Suggested first line pharmacotherapy

A: Low Risk, Fewer Symptoms

SABA or SAMA PRN

B: Low Risk, More Symptoms

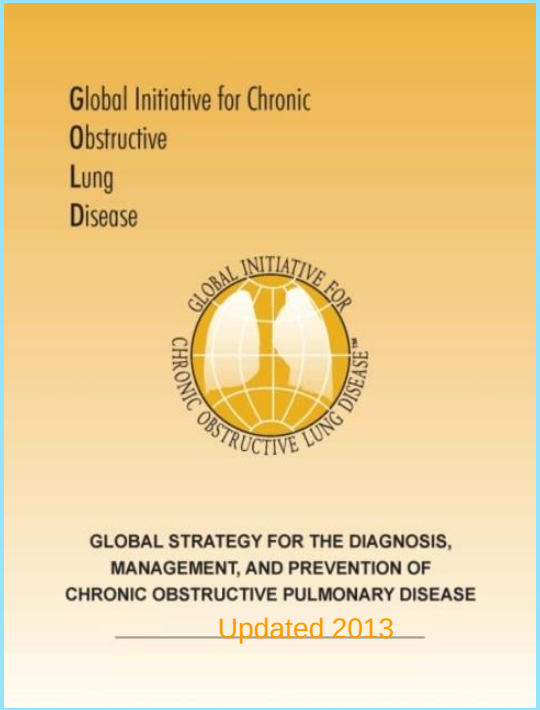
LABA or LAMA

C: High Risk, Fewer Symptoms

ICS/LABA or LAMA

D: High Risk, More Symptoms

ICS/LABA and/or LAMA



Questions

1. What is the current definition of COPD?
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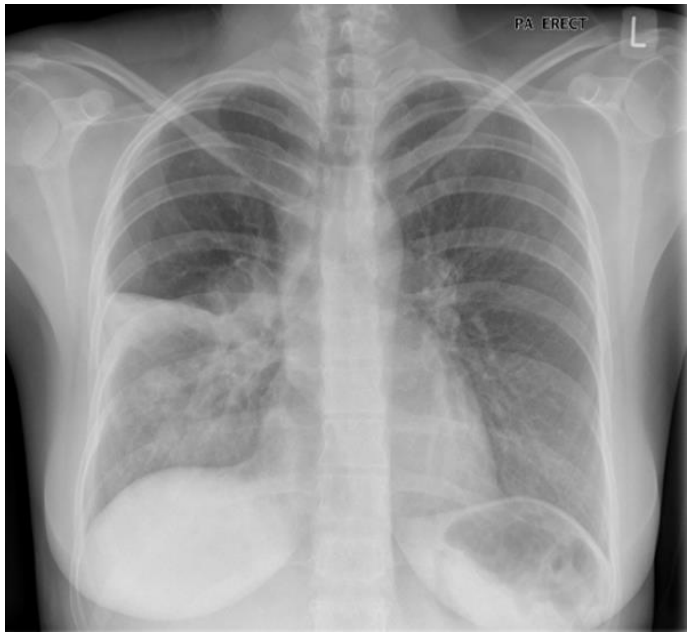
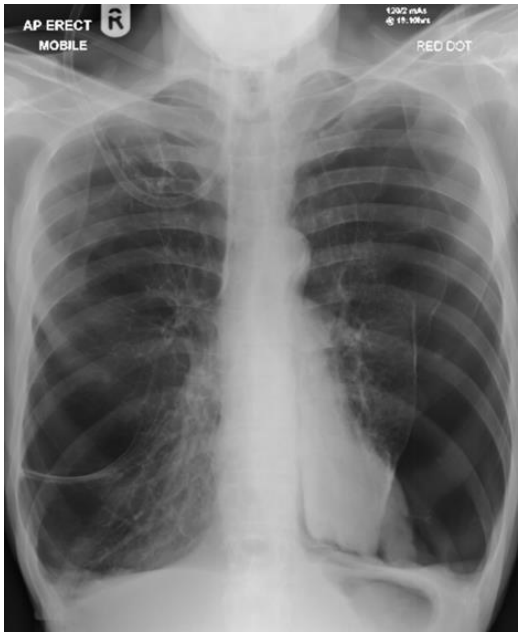
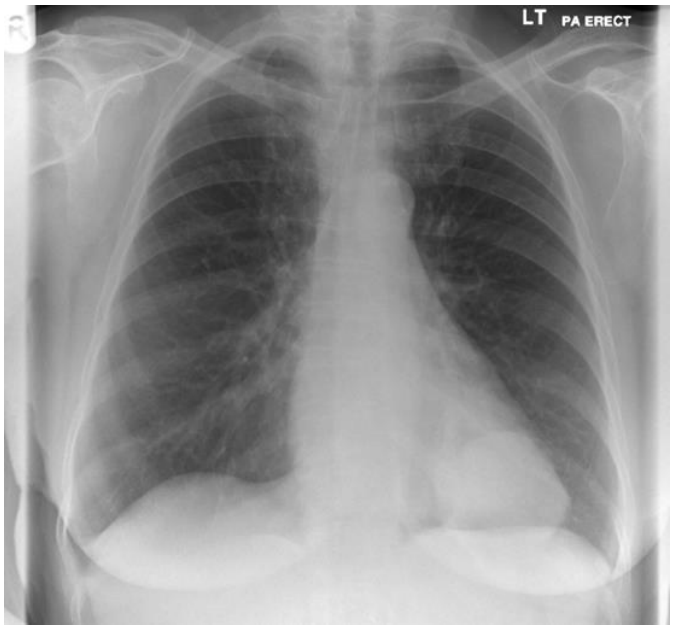
3. What is the point of an alpha-1 service?
4. ICS, LABA and LAMA – for who?
5. What is an exacerbation of COPD?

Which one of these is an exacerbation?

Clinical diagnosis of exclusion (no diagnostic test)







Definition of Exacerbation

an event in the natural course of the disease characterised by a change in the patient's baseline dyspnoea, cough, and/or sputum that is beyond normal day-to-day variations, is acute in onset, and may warrant a change in regular medication in a patient with underlying COPD.

WHO/GOLD Document

Two Definition of Exacerbation in one: SYMPTOMS

an event in the natural course of the disease characterised by a change in the patient's baseline dyspnoea, cough, and/or sputum that is beyond normal day-to-day variations, is acute in onset, and may warrant a change in regular medication in a patient with underlying COPD.

WHO/GOLD Document

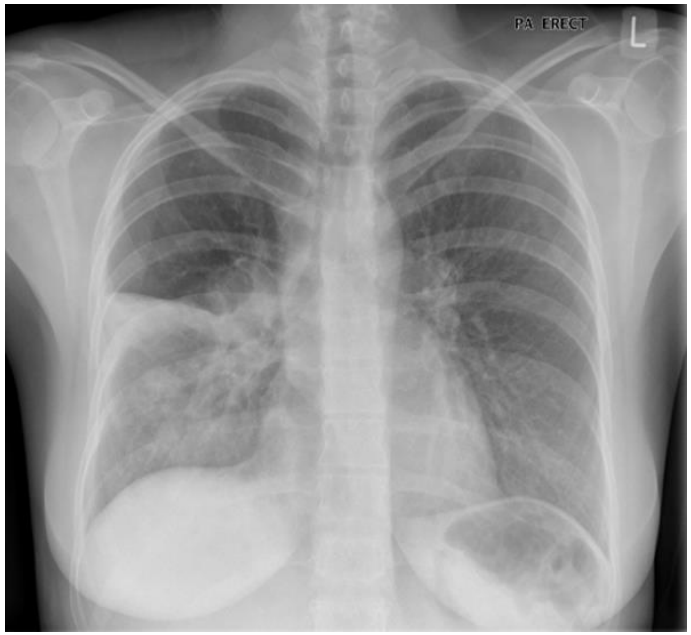
Two Definition of Exacerbation in one: Health-Care Utilisation

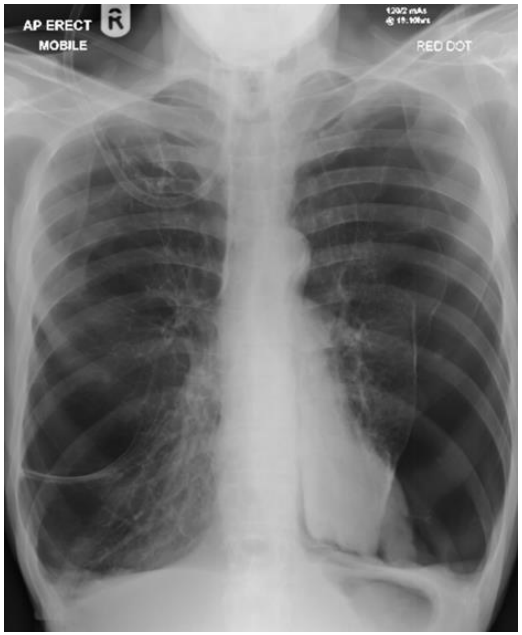
an event in the natural course of the disease characterised by a change in the patient's baseline dyspnoea, cough, and/or sputum that is beyond normal day-to-day variations, is acute in onset, and may warrant a change in regular medication in a patient with underlying COPD.

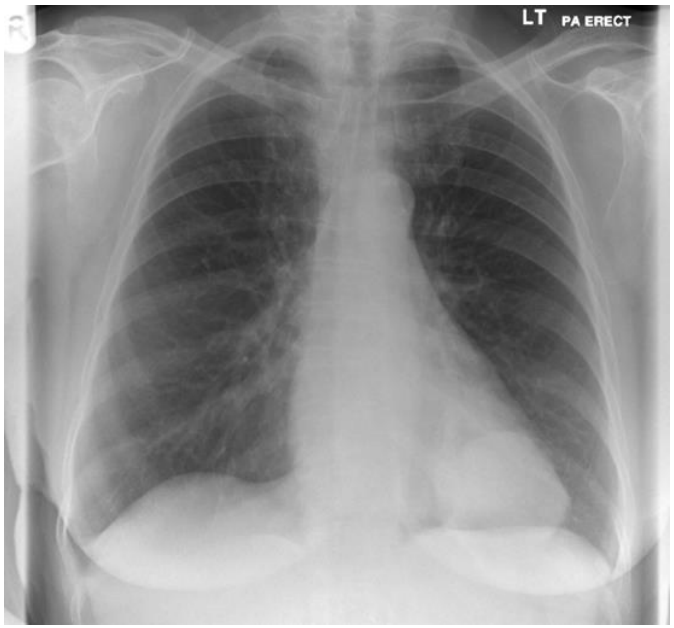
WHO/GOLD Document

Clinical practice

Clinical diagnosis of exclusion (no diagnostic test)







What is a COPD Exacerbation?

"an event in the natural course of the disease characterised by a change in the patient's baseline dyspnoea, cough, and/or sputum that is beyond normal day-to-day variations, is acute in onset, and may warrant a change in regular medication in a patient with underlying COPD"

Not Fit for Purpose?

www.goldcopd.com

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5. What is an exacerbation of COPD?
6. What causes exacerbations?

Respiratory Research

BioMed Central

Research

Open Access

An experimental model of rhinovirus induced chronic obstructive pulmonary disease exacerbations: a pilot study

Patrick Mallia[1], Simon D Message[1], Tatiana Kebadze[1], Hayley L Parker[1], Onn M Kon[2] and Sebastian L Johnston*[1]

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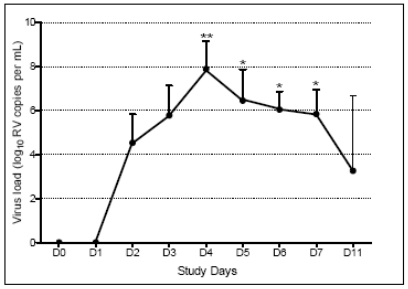


Figure 5
Viral load measured with measured with a real-time quantitative RT-PCR assay. Viral load was significantly increased above baseline on days 4 – 7. ** indicates $p < 0.01$. * indicates $p < 0.05$.

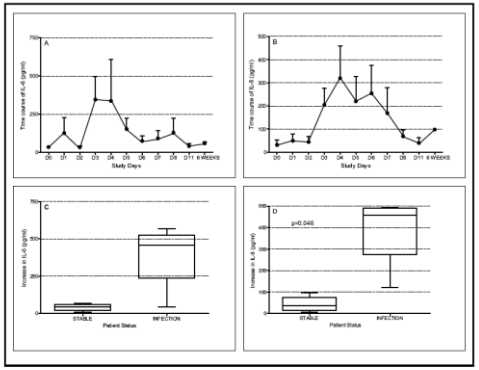


Figure 4
Levels of IL-6 and IL-8 in nasal lavage. (A) Time course of IL-6. (B) Time course of IL-8. (C) Mean levels of IL-6 in nasal lavage when stable and at exacerbation. There was an increase in IL-6 at exacerbation but this was not significant (p = 0.054). (D) Mean levels of IL-8 when stable and at exacerbation. There was a significant increase in IL-8 at exacerbation (p = 0.046).

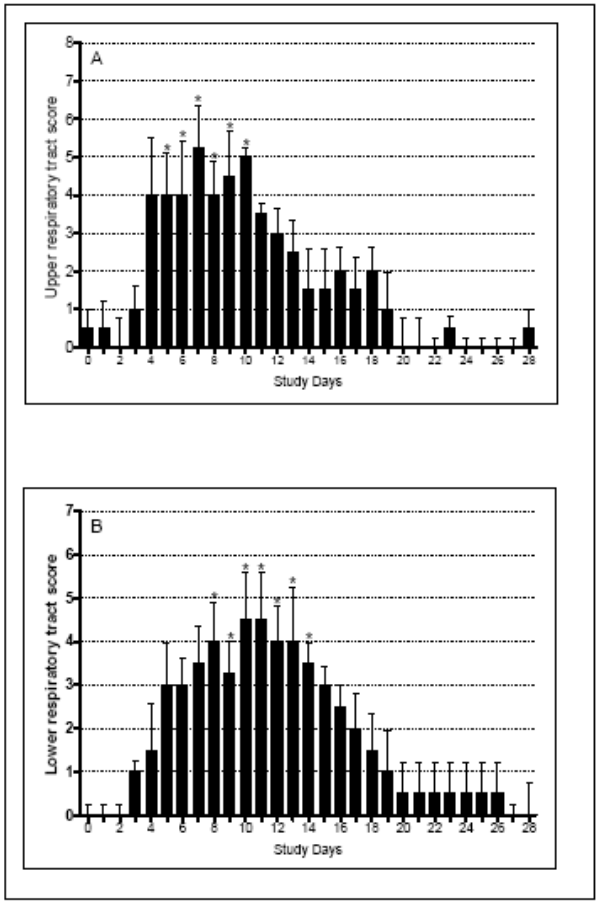
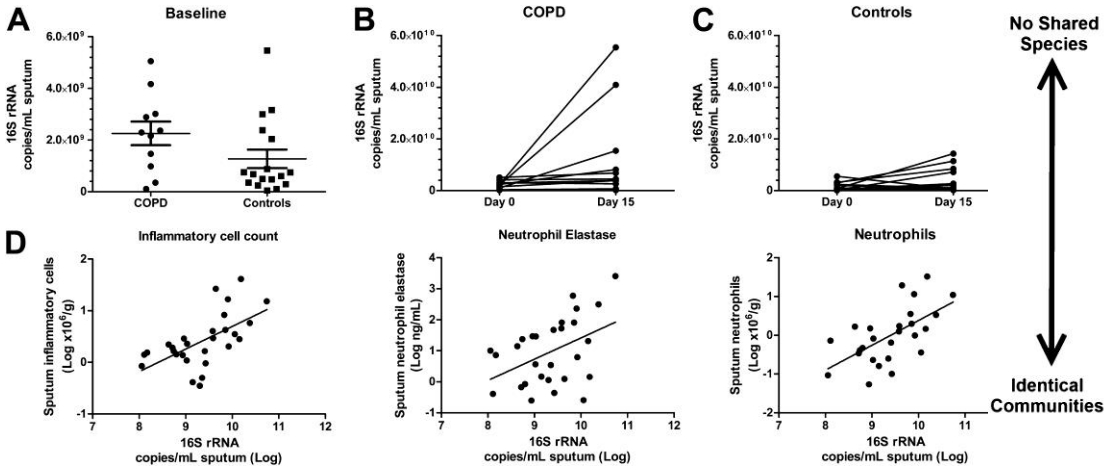
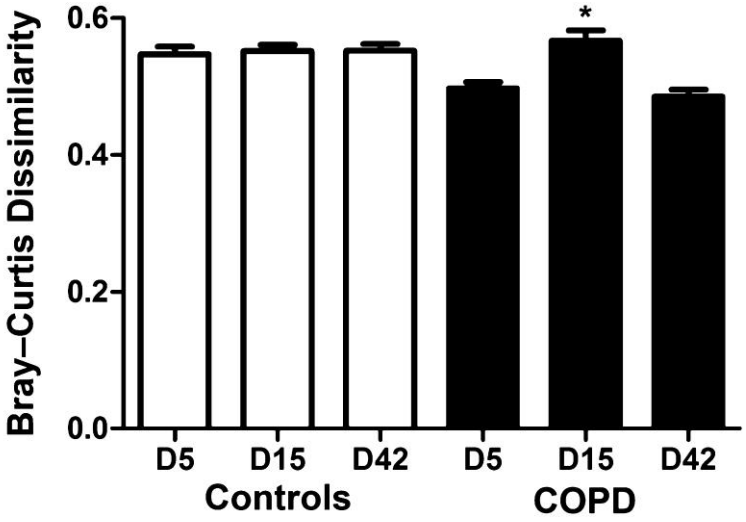


Figure 1
Daily upper and lower respiratory tract scores. (A) Mean total upper respiratory tract symptom scores. Symptoms were significantly increased on days 5 – 10. * indicates $p < 0.05$ compared to baseline. (B) Lower respiratory tract symptom scores. Symptoms were significantly increased on days 7 – 14. * indicates $p < 0.05$ compared to baseline. Mean scores on days -6 to 0 were subtracted from post-inoculation scores for both upper and lower respiratory tract scores.

Viral infection predisposes to secondary bacterial infection



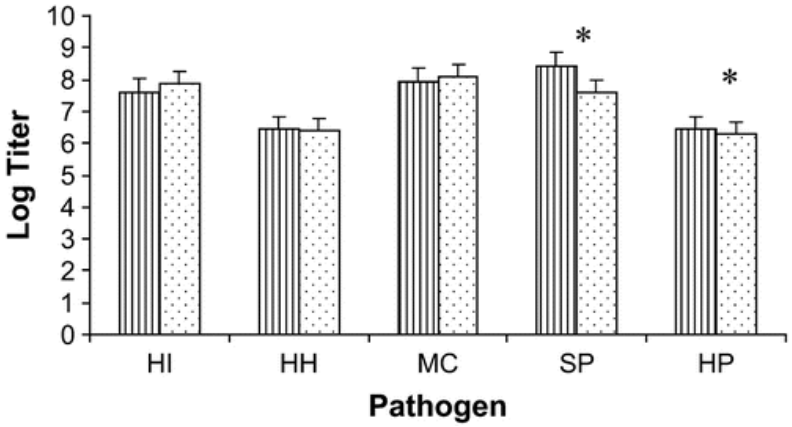


Outgrowth of the Bacterial Airway Microbiome after Rhinovirus Exacerbation of Chronic Obstructive Pulmonary Disease

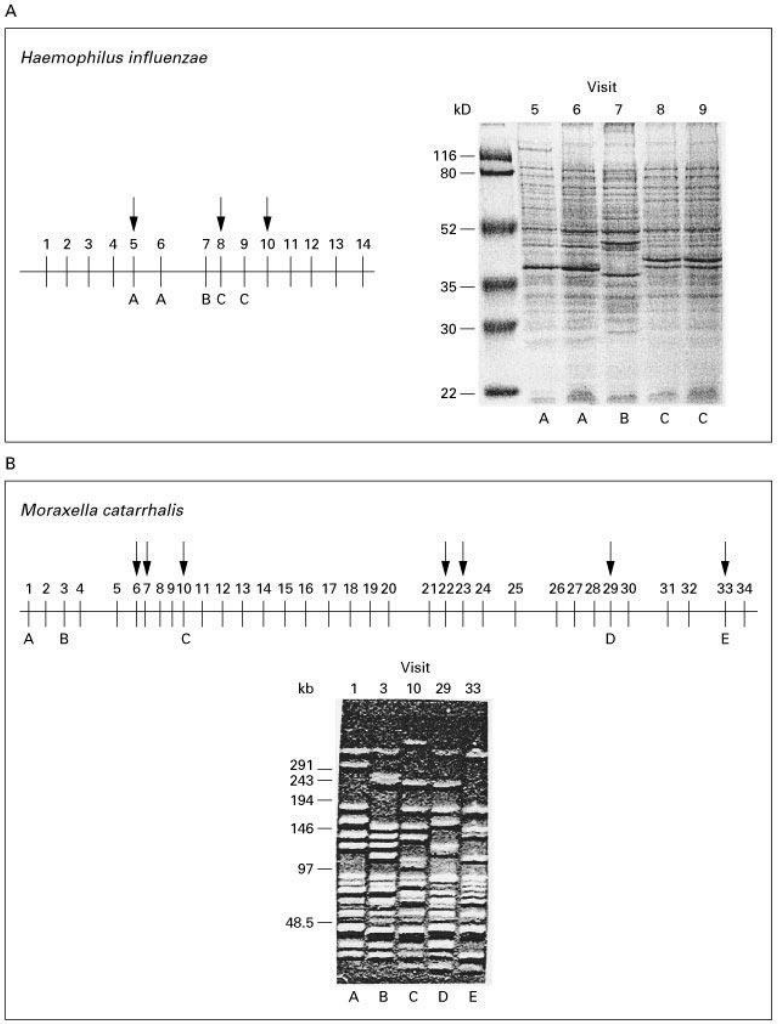
Philip L. Molyneaux[1,2], Patrick Mallia[1,2,3], Michael J. Cox[1,2], Joseph Footitt[1,2,3†], Saffron A. G. Willis-Owen[1], Daniel Homola[1], Maria-Belen Trujillo-Torralbo[1,2,3], Sarah Elkin[1,3], Onn Min Kon[1,2,3], William O. C. Cookson[1,2], Miriam F. Moffatt[1,2*], and Sebastian L. Johnston[1,2,3*]

AJRCCM 2013;188:1224-1231

The Problem isn't load



Sethi S *et al.* *AJRCCM* 2007;176:356-361



Sethi S *et al.* *NEJM* 2002;347:465-471

OPEN ACCESS Freely available online

PLoS one

Disordered Microbial Communities in Asthmatic Airways

Markus Hilty[1], Conor Burke[2], Helder Pedro[3,4], Paul Cardenas[1], Andy Bush[1], Cara Bossley[1], Jane Davies[1], Aaron Ervine[2], Len Poulter[2], Lior Pachter[4], Miriam F. Moffatt[1], William O. C. Cookson[1]*

1 National Heart and Lung Institute, Imperial College London, London, England, 2 Department of Respiratory Medicine, Connolly Hospital, Dublin, Ireland, 3 Instituto Gulbenkian de Ciência, Instituto de Tecnologia Química e Biológica, Oeiras, Portugal, 4 Department of Mathematics, University of California, Berkeley, California, United States of America

Abstract

Background: A rich microbial environment in infancy protects against asthma [1,2] and infections precipitate asthma exacerbations [3]. We compared the airway microbiota at three levels in adult patients with asthma, the related condition of COPD, and controls. We also studied bronchial lavage from asthmatic children and controls.

Principal Findings: We identified 5,054 *16S rRNA* bacterial sequences from 43 subjects, detecting >70% of species present. The bronchial tree was not sterile, and contained a mean of 2,000 bacterial genomes per cm^2 surface sampled. Pathogenic Proteobacteria, particularly *Haemophilus* spp., were much more frequent in bronchi of adult asthmatics or patients with COPD than controls. We found similar highly significant increases in Proteobacteria in asthmatic children. Conversely, Bacteroidetes, particularly *Prevotella* spp., were more frequent in controls than adult or child asthmatics or COPD patients.

Significance: The results show the bronchial tree to contain a characteristic microbiota, and suggest that this microbiota is disturbed in asthmatic airways.

Citation: Hilty M, Burke C, Pedro H, Cardenas P, Bush A, et al. (2010) Disordered Microbial Communities in Asthmatic Airways. PLoS ONE 5(1): e8578. doi:10.1371/journal.pone.0008578

Editor: Olivier Neyrolles, Institut de Pharmacologie et de Biologie Structurale, France

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Competing Interests: The authors have declared that no competing interests exist.

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Introduction

Asthma is a heterogeneous syndrome of intermittent wheeze and airway inflammation that affects 300 million individuals worldwide. Although its causes are unknown, many studies suggest a role for microbiota in its aetiology [4]. Viral infections are important inducers of seasonal exacerbations of asthma [5], but there is circumstantial evidence that bacterial infections may also play a role. Asymptomatic neonates whose throats are colonized with *Streptococcus pneumoniae*, *Haemophilus influenzae*, or *Moraxella catarrhalis* are at increased risk for recurrent wheeze and asthma early in life [6]. These same bacteria have consistently been associated with exacerbations of both asthma [7] and chronic obstructive pulmonary disease (COPD) [8]. The response of asthmatics to antibiotics also suggests the importance of acute and chronic bacterial infections in the pathogenesis of disease [9]. Epidemiological research has consistently indicated that a rich microbial environment in early life confers protection against the development of asthma [1], suggesting the need to understand the extent and nature of normal airway flora.

Apart from asthma, respiratory infections, excluding tuberculosis, cause 6% of the global burden of disease and each year 4.2 million people die of lower respiratory infections. Significantly, death in the 1918–1919, 1957 and 1968 influenza pandemics resulted most commonly from secondary bacterial pneumonia caused by organisms presumed to be previously present in the respiratory tract [10,11].

Chronic Obstructive Pulmonary Disease (COPD) shares many features with asthma and is the fourth leading cause of death worldwide. Infectious exacerbations of the disease are a frequent cause of death, and chronic infection causes a progressive decline of lung function.

Thus, despite strong evidence to implicate bacterial infections in the course and pathogenesis of airway diseases, it is unfortunate that a systematic study of organisms in the airways has been lacking [12].

Only 1% of all bacteria can be cultured in the laboratory [13], so culture is no longer the gold standard for the diagnosis of infections. Culture-independent molecular methods have already shown that the microbiota of humans is far greater in extent than previously recognised [14,15,16]. Humans are recognised to have evolved relationships with their symbiotic bacteria that are essential for health. Ecological changes altering this symbiosis can result in disease [17].

We therefore used molecular analysis of the polymorphic bacterial *16S-rRNA* gene to characterize the composition of bacterial communities from the airways of adult subjects including patients with asthma and COPD. We sought replication of findings from these adults in an additional study of children attending clinics for therapy-resistant asthma.

Results

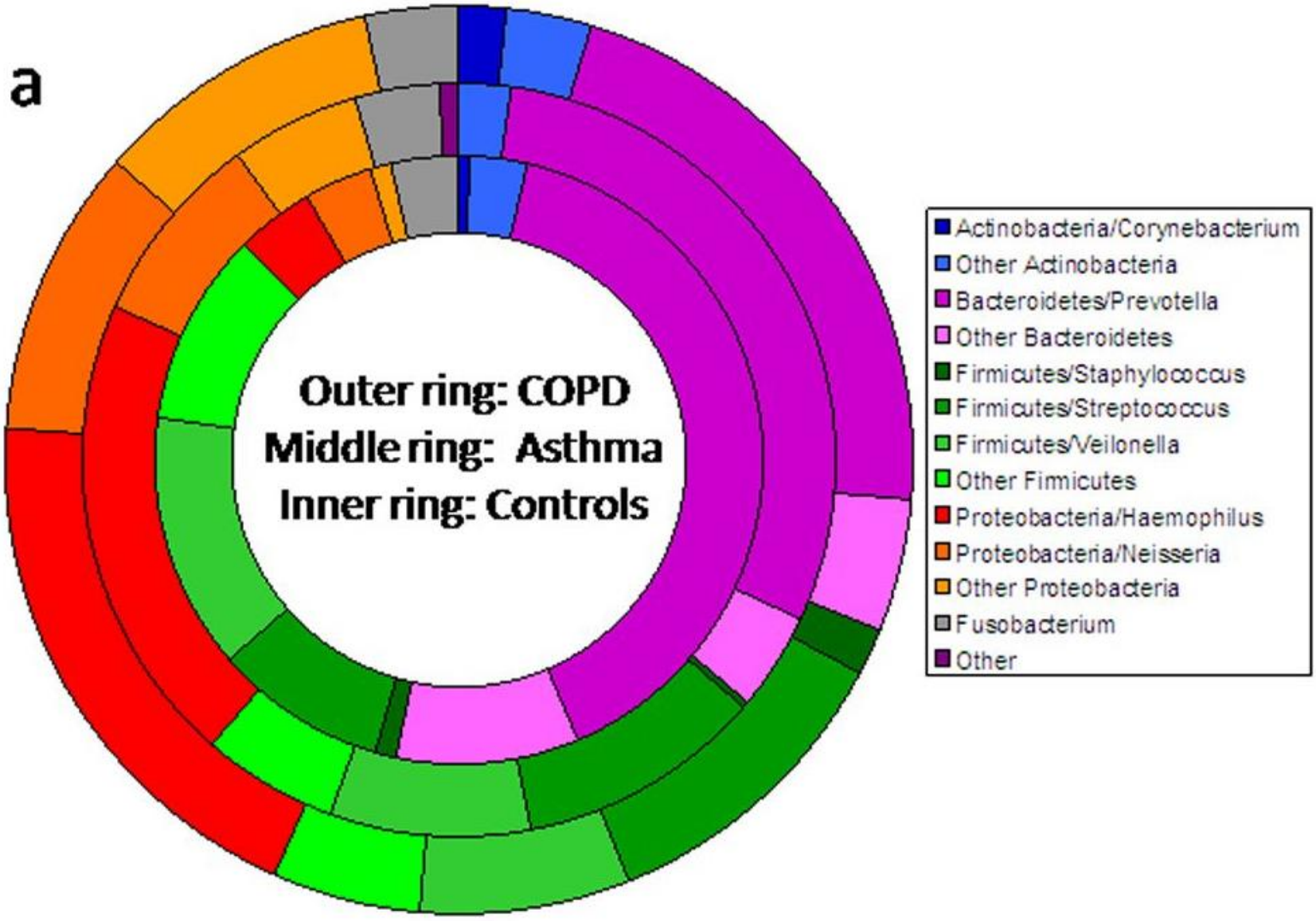
Twenty-four adult subjects were studied, including 5 patients with COPD, 11 patients with asthma and 8 control subjects with no previous history of asthma or COPD and an FEV1≥95%

We identified 5,054 *16S rRNA* bacterial sequences from 43 subjects.

The bronchial tree was not sterile, and contained a mean of 2,000 bacterial genomes per cm^2 surface sampled.

Pathogenic Proteobacteria, particularly *Haemophilus* spp., were much more frequent in bronchi of adult asthmatics or patients with COPD than controls.

Conversely, Bacteroidetes, particularly *Prevotella* spp., were more frequent in controls than adult or child asthmatics or COPD patients.


a
Outer ring: COPD
Middle ring: Asthma
Inner ring: Controls
Actinobacteria/Corynebacterium
Other Actinobacteria
Bacteroidetes/Prevotella
Other Bacteroidetes
Firmicutes/Staphylococcus
Firmicutes/Streptococcus
Firmicutes/Veilonella
Other Firmicutes
Proteobacteria/Haemophilus
Proteobacteria/Neisseria
Other Proteobacteria
Fusobacterium
Other

Pathogenesis: Microbiology

OPEN ACCESS Freely available online

PLoS one

Analysis of the Lung Microbiome in the "Healthy" Smoker and in COPD

John R. Erb-Downward[1], Deborah L. Thompson[1], Meilan K. Han[1], Christine M. Freeman[1,2], Lisa McCloskey[1,2], Lindsay A. Schmidt[1], Vincent B. Young[1], Galen B. Toews[1,2], Jeffrey L. Curtis[1,2], Baskaran Sundaram[1], Fernando J. Martinez[1☯], Gary B. Huffnagle[1*☯]

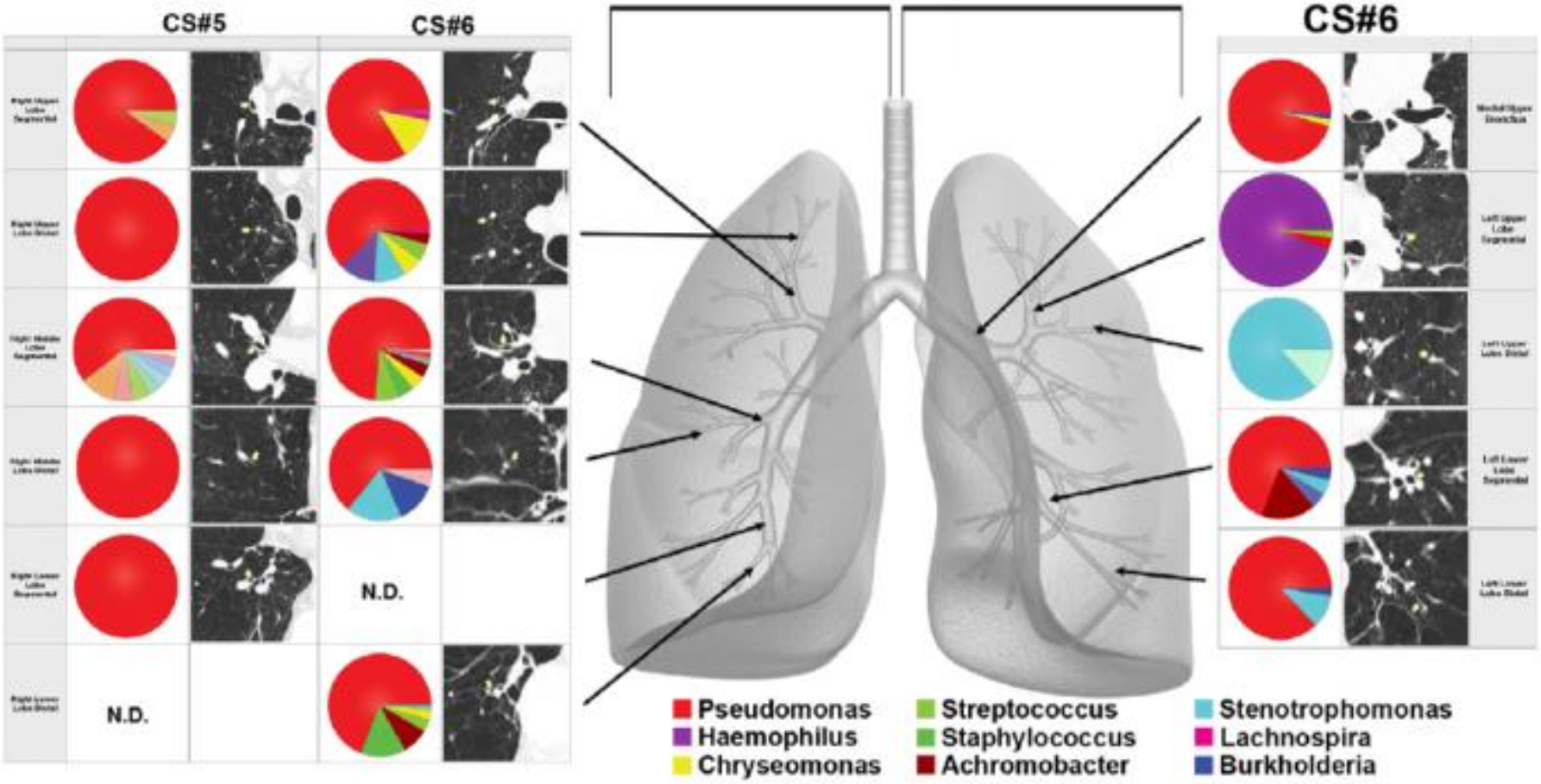
1 University of Michigan, Ann Arbor, Michigan, United States of America, 2 Veterans Affairs Health System, Ann Arbor, Michigan, United States of America

Abstract

Although culture-independent techniques have shown that the lungs are not sterile, little is known about the lung microbiome in chronic obstructive pulmonary disease (COPD). We used pyrosequencing of 16S amplicons to analyze the lung microbiome in two ways: first, using bronchoalveolar lavage (BAL) to sample the distal bronchi and air-spaces; and second, by examining multiple discrete tissue sites in the lungs of six subjects removed at the time of transplantation. We performed BAL on three never-smokers (NS) with normal spirometry, seven smokers with normal spirometry ("heathy smokers", HS), and four subjects with COPD (CS). Bacterial 16 s sequences were found in all subjects, without significant quantitative differences between groups. Both taxonomy-based and taxonomy-independent approaches disclosed heterogeneity in the bacterial communities between HS subjects that was similar to that seen in healthy NS and two mild COPD patients. The moderate and severe COPD patients had very limited community diversity, which was also noted in 28% of the healthy subjects. Both approaches revealed extensive membership overlap between the bacterial communities of the three study groups. No genera were common within a group but unique across groups. Our data suggests the existence of a core pulmonary bacterial microbiome that includes *Pseudomonas, Streptococcus, Prevotella, Fusobacterium, Haemophilus, Veillonella, and Porphyromonas*. Most strikingly, there were significant micro-anatomic differences in bacterial communities within the same lung of subjects with advanced COPD. These studies are further demonstration of the pulmonary microbiome and highlight global and micro-anatomic changes in these bacterial communities in severe COPD patients.

Citation: Erb-Downward JR, Thompson DL, Han MK, Freeman CM, McCloskey L, et al. (2011) Analysis of the Lung Microbiome in the "Healthy" Smoker and in COPD. PLoS ONE 6(2): e16384. doi:10.1371/journal.pone.0016384

Intra-Patient Diversity



Exacerbation Ecology

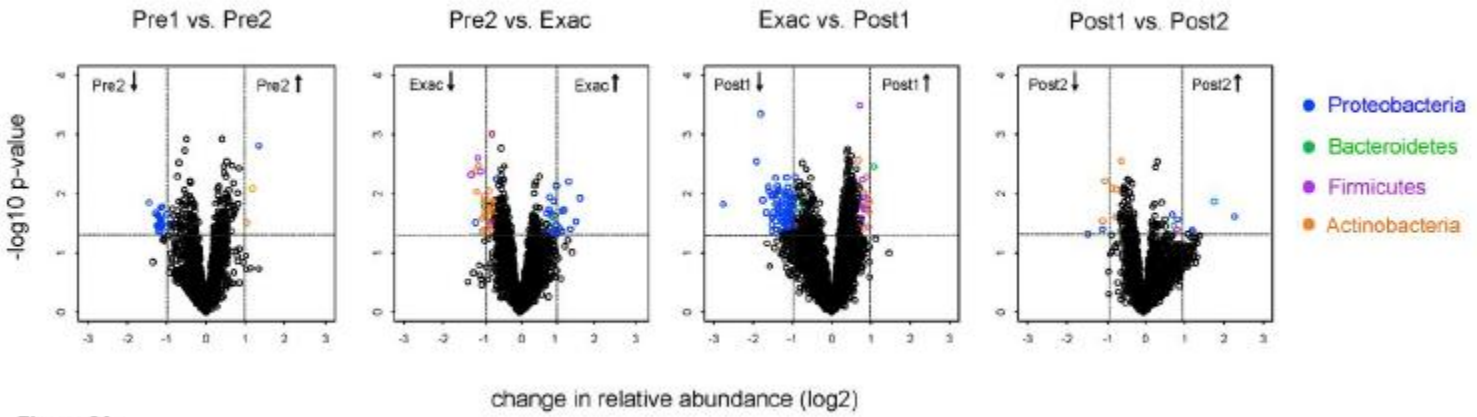


Figure 3A.

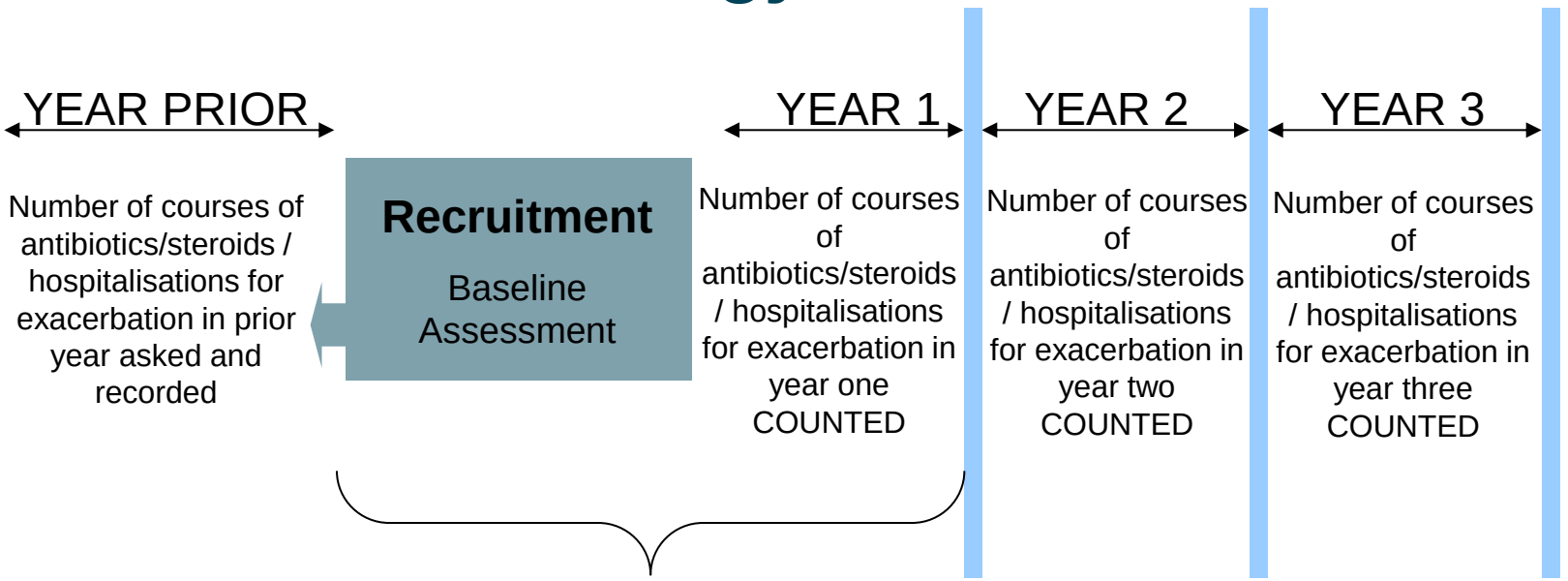
"Volcano plots indicating taxa that are significantly increased (upper right quadrant) or decreased (upper left quadrant) in pair-wise comparisons. Dashed lines indicate significant FDR-adjusted p-values and changes in relative abundance of at least 2-fold. Taxa exhibiting significant changes are coloured by phylum-level classification. Note that in addition to highlighted taxa, many other microbiota members exhibit smaller scale changes in abundance, which cumulatively may contribute importantly to microbiome community function."

Sethi S *et al.* *J Clin Micro* 2014*: in press*

Questions

1. What is the current definition of COPD?
2. What is a COPD ‘phenotype’?
3. What is the point of an alpha-1 service?
4. ICS, LABA and LAMA – for who?
5. What is an exacerbation of COPD?
6. What causes exacerbations?
7. What determines susceptibility to exacerbation?

ECLIPSE Methodology



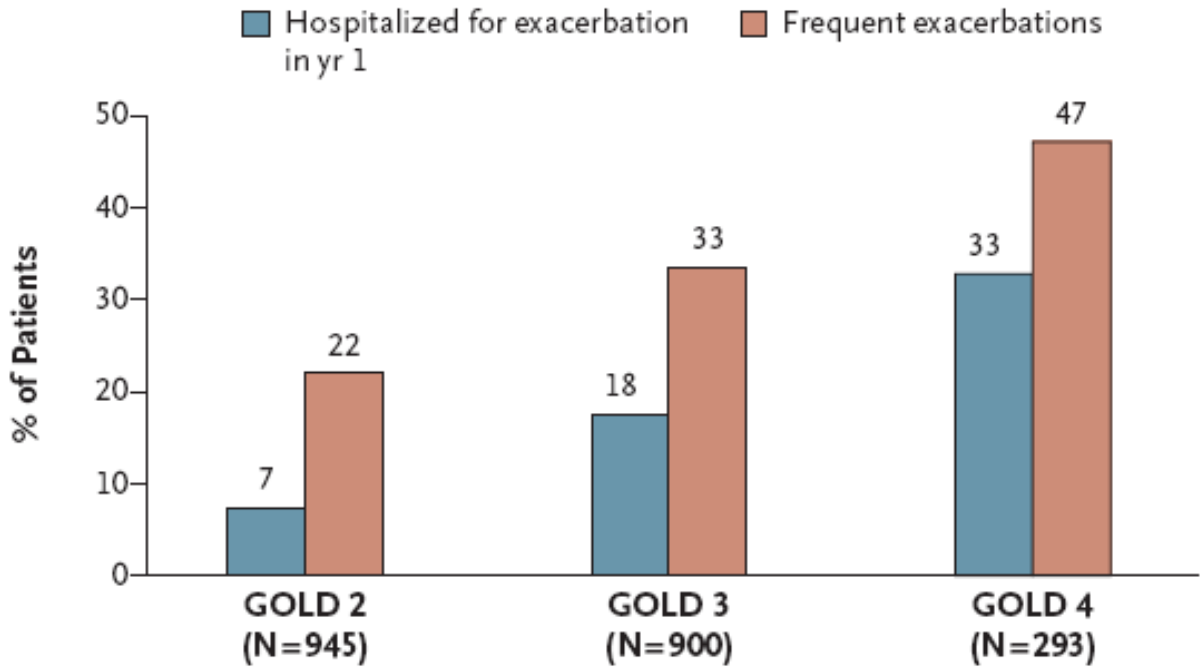
ANALYSIS 1

How do baseline variables relate to observed exacerbations in year 1?

ANALYSIS 2

How stable is exacerbation frequency over 3 observed years, and in relation to patient self report?

Exacerbations and COPD Severity



N Engl J Med 2010;363:1128-38.

Multivariate Analysis

Table 3. Factors Associated with Increased Exacerbation Frequency in the Stepwise Multivariate Model.*

Factor	Number of Exacerbations						P Value for Overall Model
	≥2 vs. 0		1 vs. 0		≥2 vs. 1		
	odds ratio (95% CI)	*P value*	*odds ratio (95% CI)*	*P value*	*odds ratio (95% CI)*	*P value*	
Exacerbation during previous yr — any vs. none	5.72 (4.47–7.31)	<0.001	2.24 (1.77–2.84)	<0.001	2.55 (1.96–3.31)	<0.001	<0.001
FEV_1 — per 100-ml decrease	1.11 (1.08–1.14)	<0.001	1.06 (1.03–1.08)	<0.001	1.05 (1.02–1.09)	<0.001	<0.001
SGRQ score for COPD — per increase of 4 points	1.07 (1.04–1.10)	<0.001	1.01 (0.99–1.04)	0.38	1.06 (1.03–1.09)	<0.001	<0.001
History of reflux or heartburn — yes vs. no	2.07 (1.58–2.72)	<0.001	1.61 (1.23–2.10)	<0.001	1.29 (0.97–1.70)	<0.005	<0.001
White-cell count — per increase of $1\times10^3/mm^3$	1.08 (1.03–1.14)	0.002	1.02 (0.97–1.08)	0.45	1.06 (1.01–1.12)	<0.001	0.007

Hurst JR *et al.* *NEJM* 2010;363:1128-1138

GORD and COPD

- Do exacerbations cause reflux?
- Does reflux cause exacerbations?

Multivariate Analysis

Table 3. Factors Associated with Increased Exacerbation Frequency in the Stepwise Multivariate Model.*

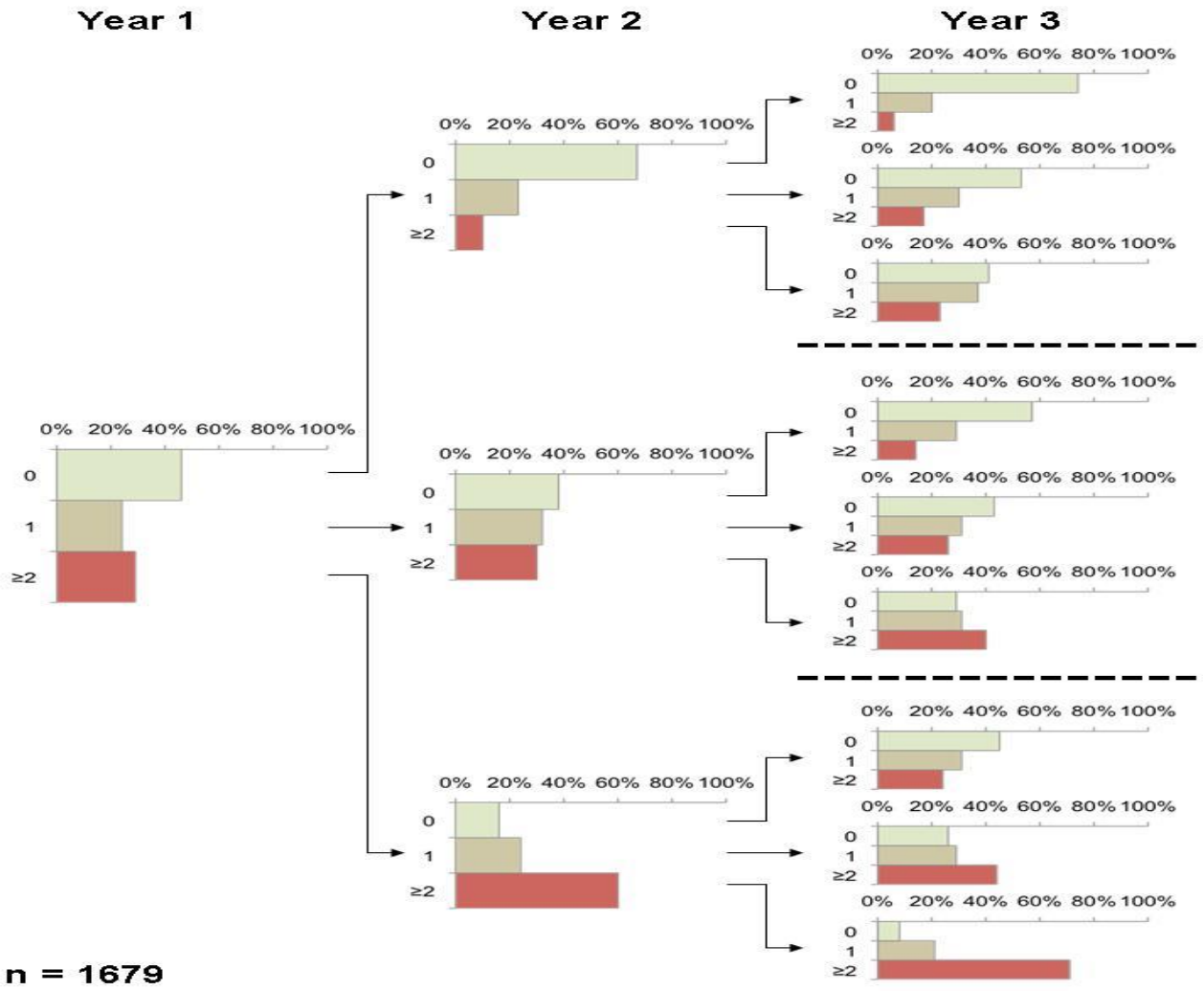
Factor	Number of Exacerbations						P Value for Overall Model
	≥2 vs. 0		1 vs. 0		≥2 vs. 1		
	odds ratio (95% CI)	*P value*	*odds ratio (95% CI)*	*P value*	*odds ratio (95% CI)*	*P value*	
Exacerbation during … any vs. none	5.72 (4.47–7.31)	<0.001	2.24 (1.77–2.84)	<0.001	2.55 (1.96–3.31)	<0.001	<0.001
FEV_1 — per 100-… decrease							
SGRQ score for C… — per increase of 4 po…							
History of reflux or heartbu… yes vs. no							
White-cell count — per increase of $1\times10^3/mm^3$							

Suggests groups of patients or ‘phenotypes’ who are inherently susceptible versus resistant to exacerbations (or at least reporting exacerbations)

IS THIS STABLE OVER TIME?

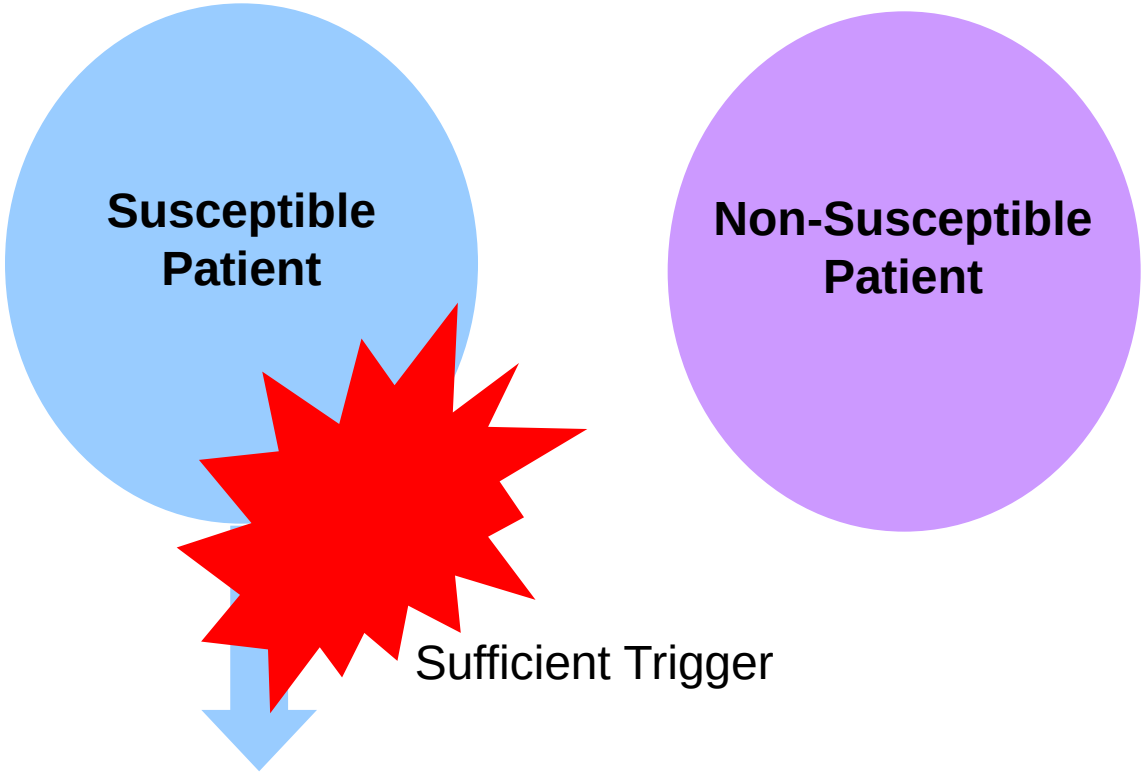
Hurst JR *et al.* *NEJM* 2010;363:1128-1138

“Unstable” COPD?



Hurst JR *et al.* *NEJM* 2010;363:1128-1138

Phenotype Discrepancy?



SUSCEPTIBLE PATIENT + SUFFICIENT STIMULUS = EXACERBATION

$$\mathbf{P_{susc} + S_{suff} = E}$$

Questions

1. What is the current definition of COPD?
2. What is a COPD ‘phenotype’?
3. What is the point of an alpha-1 service?
4. ICS, LABA and LAMA – for who?
5. What is an exacerbation of COPD?
6. What causes exacerbations?
7. What determines susceptibility to exacerbation?
8. What do COPD patients die from?

COPD and Cardiovascular Death

CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Ascertainment of cause-specific mortality in COPD: operations of the TORCH Clinical Endpoint Committee

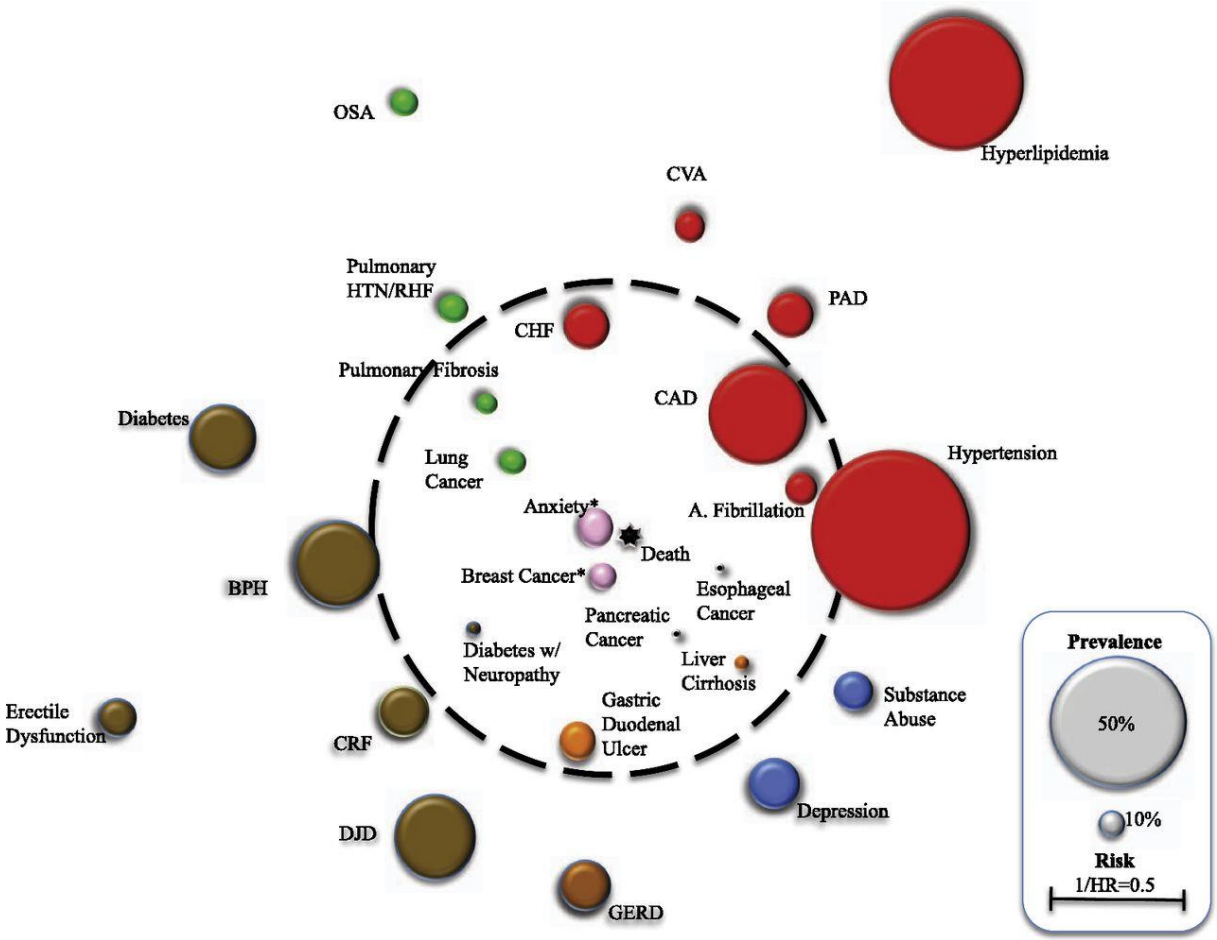
Lorcan P McGarvey, Matthias John, Julie A Anderson, Michael Zvarich, Robert A Wise

Thorax 2007;**62**:411–415. doi: 10.1136/thx.2006.072348

Table 1 Classification of cause-specific mortality (n = 911)

System	%	Subcategory	%
Cardiovascular	26	Congestive heart failure	3
		Myocardial infarction	3
		Stroke	4
		Sudden death	16
Respiratory	35	COPD	27
		Pneumonia	8
		Other	<1
Cancer	21	Lung	14
		Other	7
Other cause	10		
Unknown cause	8		

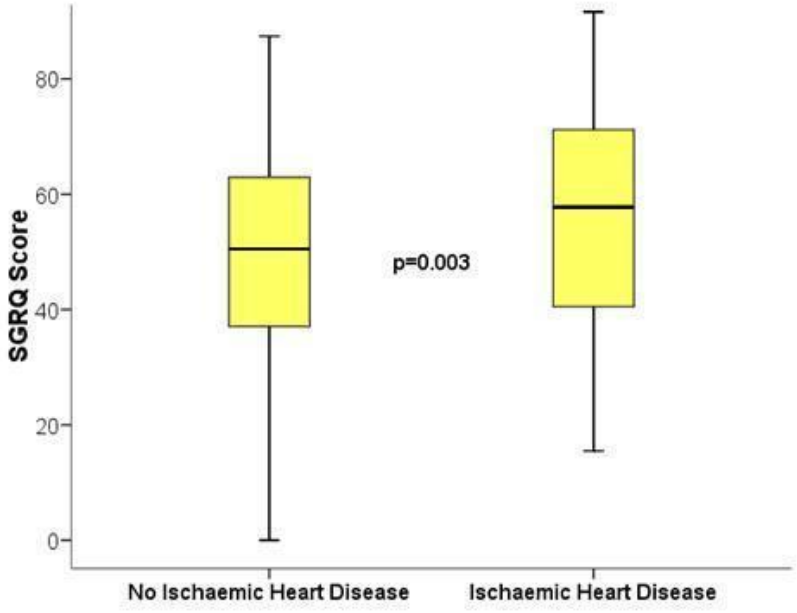
The COPD "Co-Morbidome"

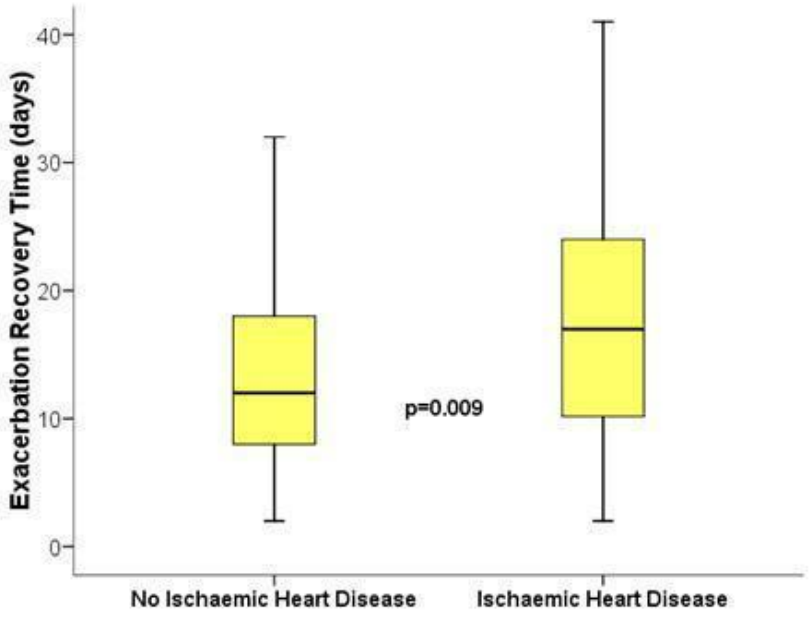


Divo M *et al.* *AJRCCM* 2012;186:pp 155–161

Impact of IHD in COPD

Health Status and Exacerbations

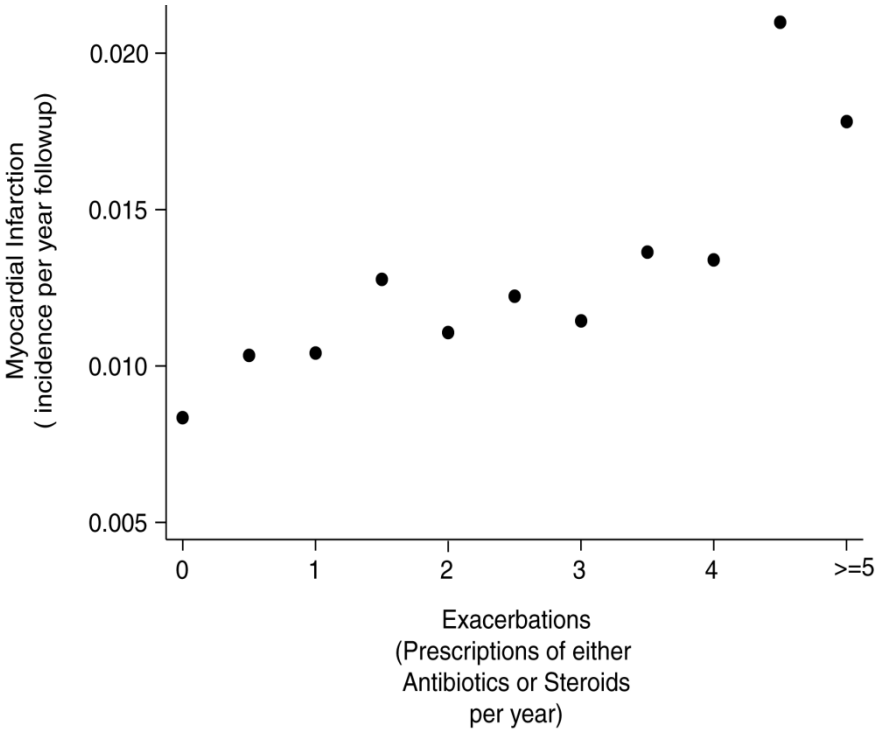




Patel ARC *Chest* 2012;141:851-857

COPD and MI risk

- 2.27 (95% CI 1.1-4.7) fold increased risk of MI in the period 1-5 days following exacerbation
- Patients who did exacerbate had a greater risk of MI than those who did not, and there was a ‘dose response’



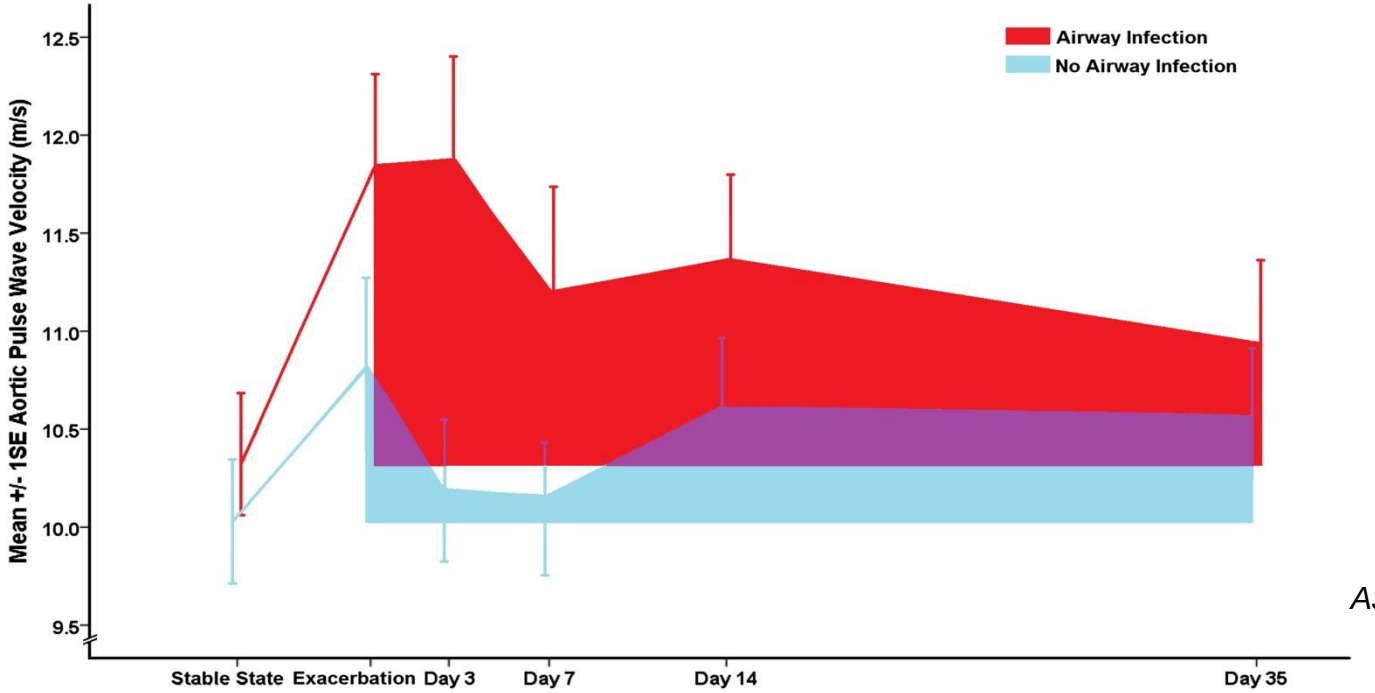
Donaldson GC *et al.* *Chest* 2010;175:1091-1097

CV Risk at Exacerbation

Cardiovascular Risk, Myocardial Injury, and Exacerbations of Chronic Obstructive Pulmonary Disease

Anant R. C. Patel[1], Beverly S. Kowlessar[1], Gavin C. Donaldson[1], Alex J. Mackay[1], Richa Singh[1], Siobhan N. George[1], Davinder S. Garcha[1], Jadwiga A. Wedzicha[1], and John R. Hurst[1]

[1]UCL Respiratory Medicine, University College London, Royal Free Campus, Rowland Hill Street, London, United Kingdom



AJRCCM 2013;188:1091-1099

Key Messages

1. Diagnosis of COPD requires spirometry
2. There is (far too much) interest in patient phenotyping: *right drug, right patient, right time*
3. Please refer patients with alpha-1 to our service!
4. The GOLD revision provides a helpful framework for use of ICS LABA and LAMA
5. An exacerbation is a deterioration in symptoms – in which other causes have been excluded

Key Messages

6. Exacerbations are caused by respiratory viruses, and alterations in bacterial flora
7. Susceptibility to exacerbation appears to be intrinsic
8. Cardiovascular risk is important in COPD: address it and manage it

RESEARCH OPPORTUNITIES:

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URCC

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