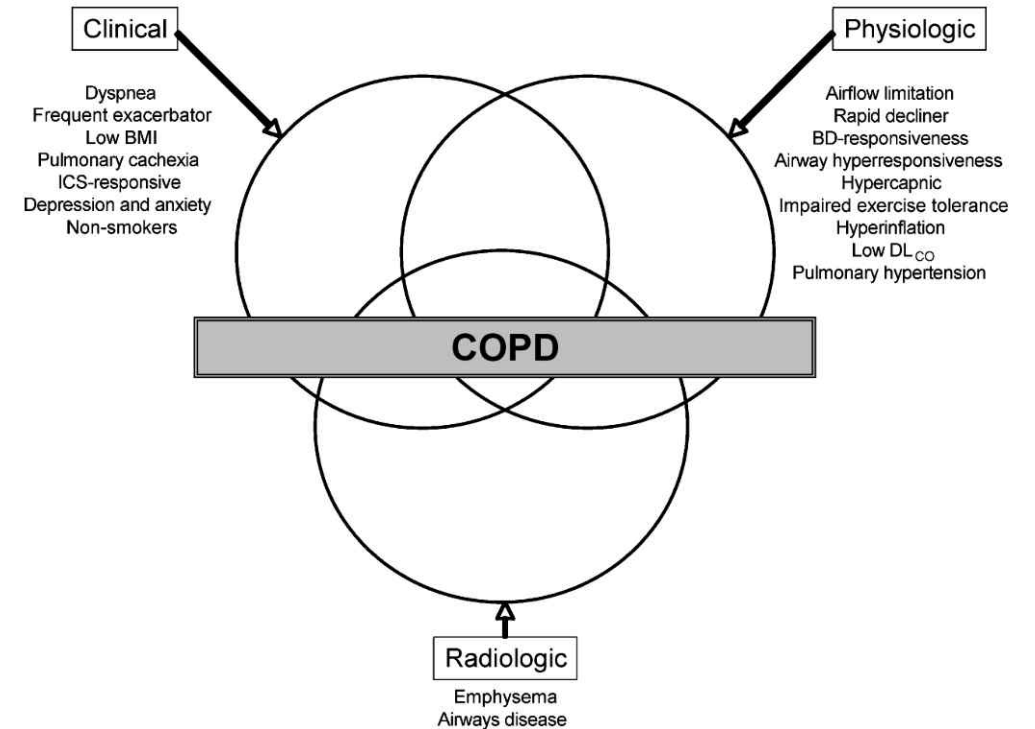
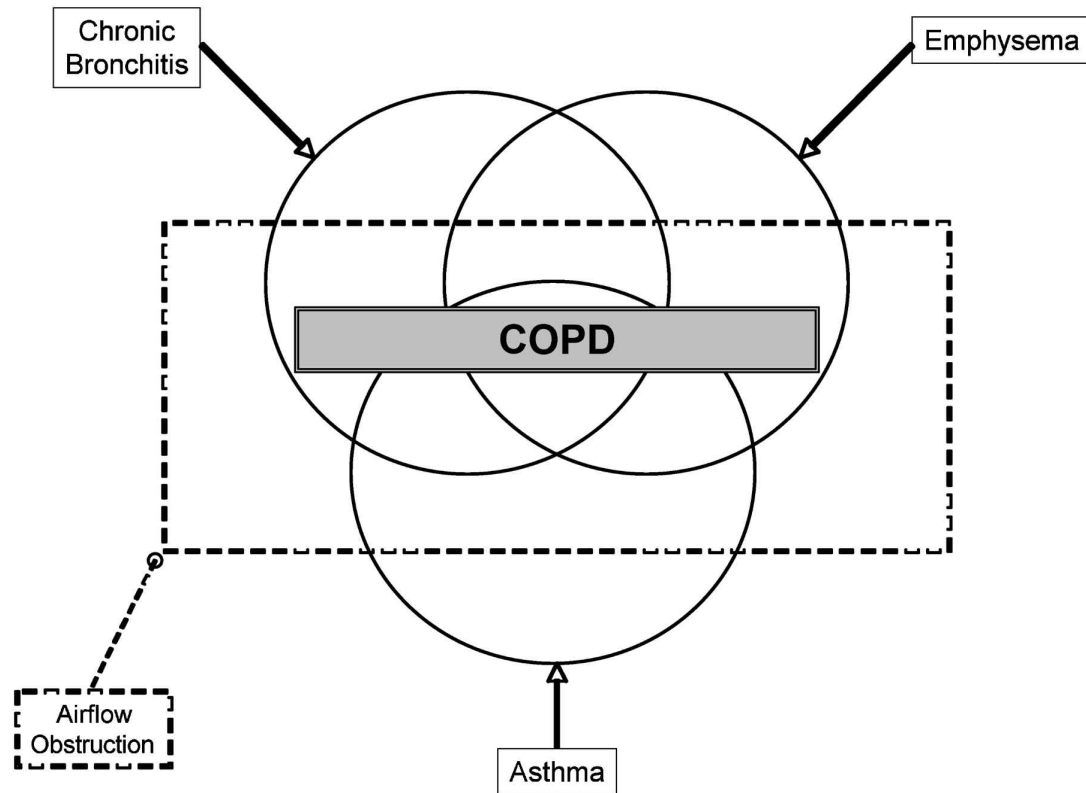


Update of Chronic Bronchitis

가톨릭대학교 인천성모병원
최준영



Heterogeneity of COPD



Poor health-related
quality of life

Kim V. Chest. 2011;140(3):626-633
Meek PM. Chest. 2015;148(2):408-416

Chronic bronchitis (CB)
phenotype

Reduced lung function

Kim V. Curr Opin Pulm Med. 2015;21(2):133-141
Choi JY. IJOPD. 2016;11:1335-1341

Frequent exacerbation

Kania A. IJOPD. 2018;13:1613-1621
Choi JY. IJOPD. 2016;11:1335-1341
Corhay JL. Int J Clin Pract. 2013;67(12):1294-1301.

Higher mortality rate

Lahousse L. Eur Respir J. 2017;50(2).
Meek PM. Chest. 2015;148(2):408-416

Contents

1. Definition of chronic bronchitis
2. Risk factors
3. Pathophysiology
4. Clinical implications
5. Treatments
6. Summary

1. Definition of Chronic Bronchitis

Definitions of CB (Classical)

- CB is usually defined..
 - Frequent cough and sputum production
 - 3 months per year
 - over 2 consecutive years

ATS standardization project (1978)



Problems with Classical Definition

```
graph TD; A[Problems with Classical Definition] --> B[Confusing term ;  
• 3 months per year  
• for 2 consecutive years]; A --> C[Difficult to be applied in  
retrospective cohort studies]; A --> D[Recall bias : 2 year]
```

Confusing term ;

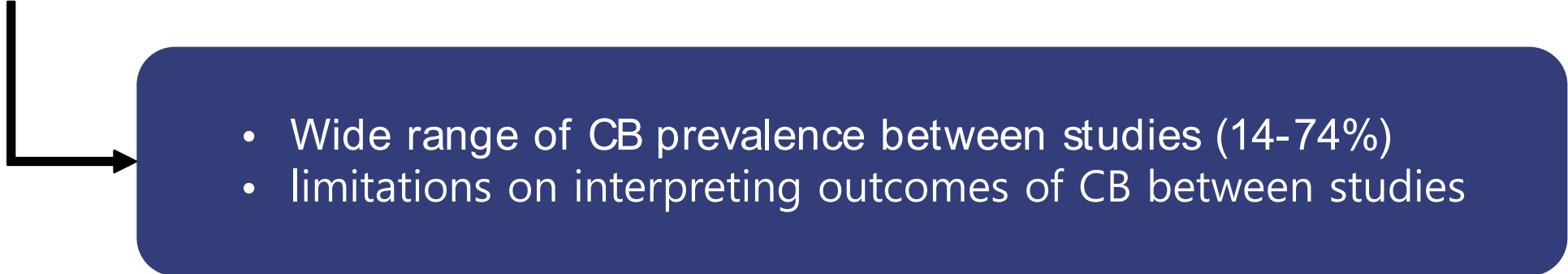
- 3 months per year
- for 2 consecutive years

Difficult to be applied in
retrospective cohort studies

Recall bias : 2 year

Various definitions of CB

Studies	Definitions
Hurst et al (2010)	Chronic cough
Pallasaho et al (1999)	Physician-diagnosed
Vestbo et al (1996)	Cough and sputum lasted 3 months for more than 1 year
Kim et al (2015)	SGRQ based definition
Lim et al (2018)	SGRQ and CAT based definition

- 
- Wide range of CB prevalence between studies (14-74%)
 - limitations on interpreting outcomes of CB between studies

Our works on CAT definition

International Journal of COPD

Dovepress

open access to scientific and medical research

ORIGINAL RESEARCH

Open Access Full Text Article

Alternative definitions of chronic bronchitis and their correlation with CT parameters

This article was published in the following Dove Press journal:
International Journal of COPD

International Journal of Chronic Obstructive Pulmonary Disease

Dovepress

open access to scientific and medical research

ORIGINAL RESEARCH

Open Access Full Text Article

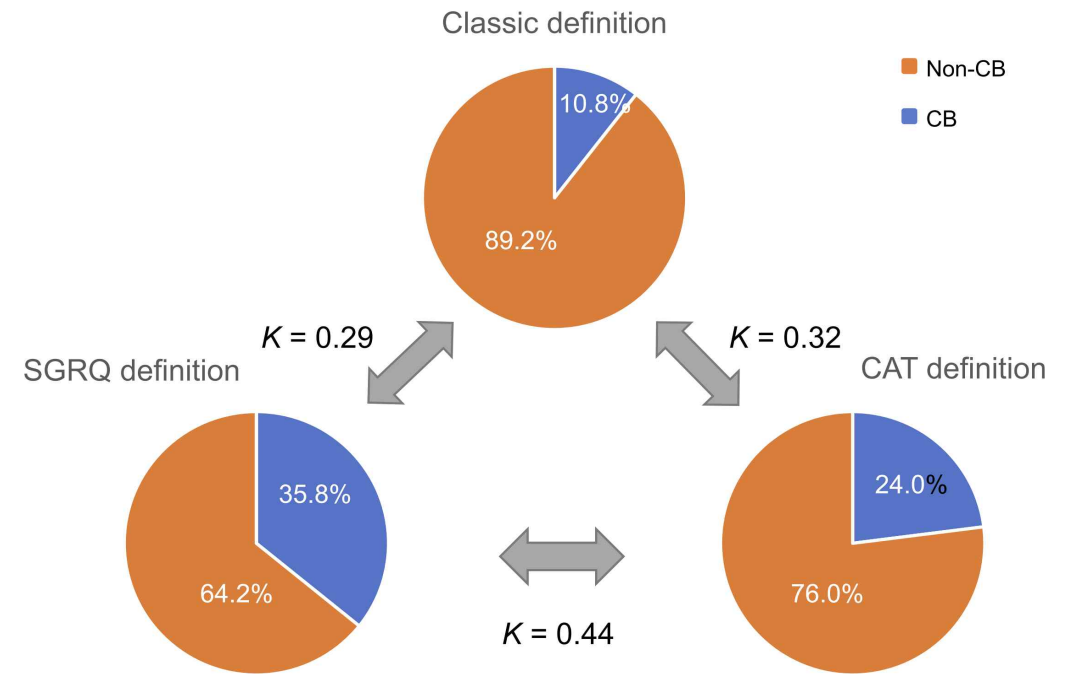
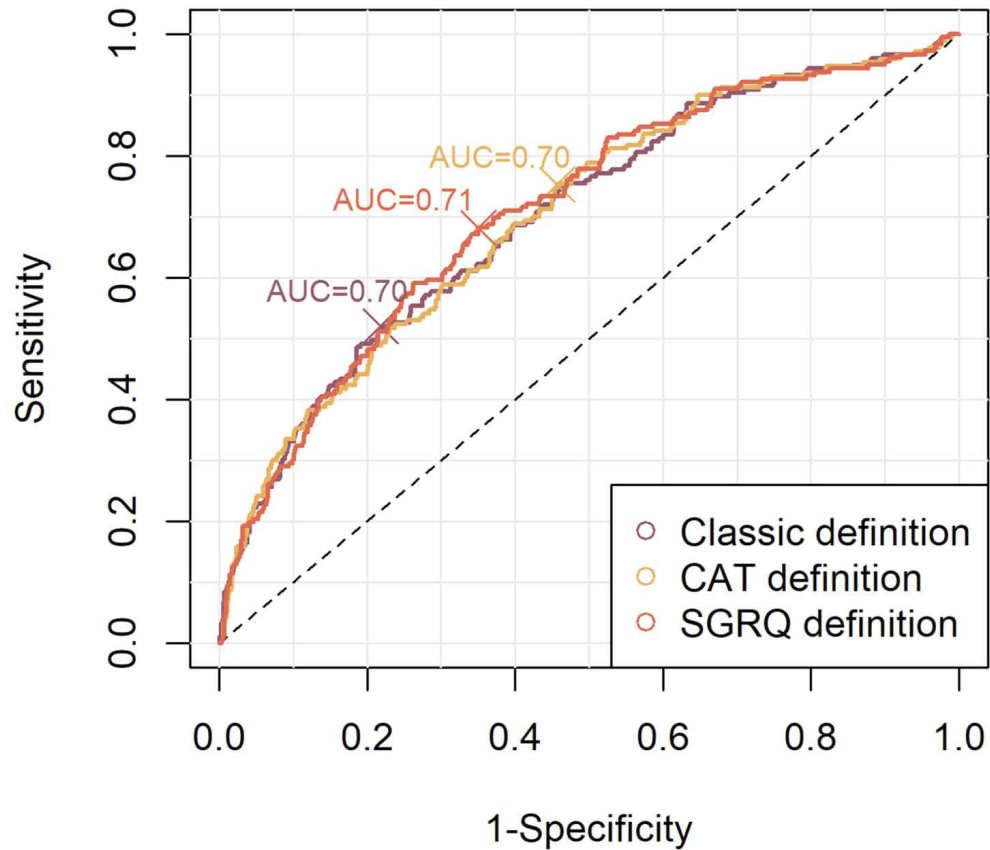
CAT Score and SGRQ Definitions of Chronic Bronchitis as an Alternative to the Classical Definition

This article was published in the following Dove Press journal:
International Journal of Chronic Obstructive Pulmonary Disease

I never cough	0	1	2	3	4	5	I cough all the time	<input type="radio"/>
I have no phlegm (mucus) on my chest at all	0	1	2	3	4	5	My chest is full of phlegm (mucus)	<input type="radio"/>
My chest does not feel tight at all	0	1	2	3	4	5	My chest feels very tight	<input type="radio"/>
When I walk up a hill or a flight of stairs I am not out of breath	0	1	2	3	4	5	When I walk up a hill or a flight of stairs I am completely out of breath	<input type="radio"/>
I am not limited to doing any activities at home	0	1	2	3	4	5	I am completely limited to doing all activities at home	<input type="radio"/>
I am confident leaving my home despite my lung condition	0	1	2	3	4	5	I am not confident leaving my home at all because of my lung condition	<input type="radio"/>
I sleep soundly	0	1	2	3	4	5	I do not sleep soundly because of my lung condition	<input type="radio"/>
I have lots of energy	0	1	2	3	4	5	I have no energy at all	<input type="radio"/>
TOTAL SCORE								<input type="text"/>

CAT 1 & 2 \geq 2 points

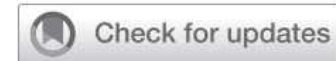
Lim JU et al. IJOPD. 2018 Jun 13;13:1893-1899
Choi JY et al. IJOPD. 2019 Dec 30;14:3043-3052



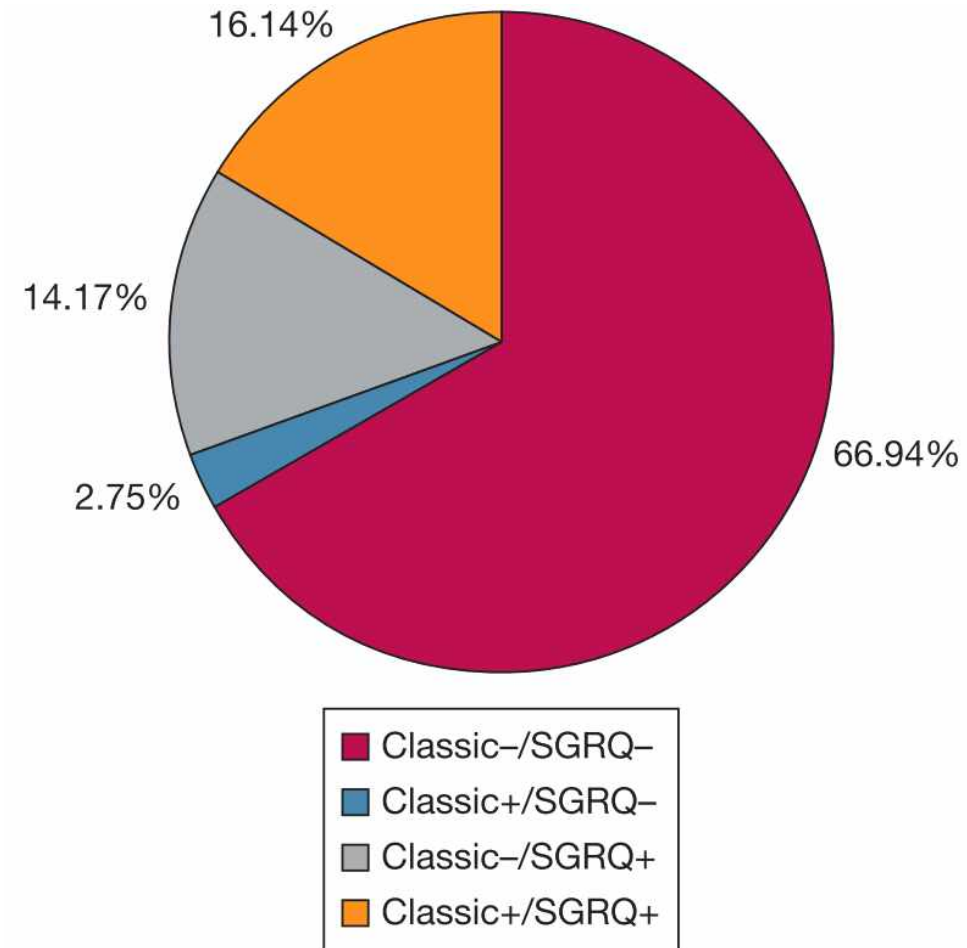
- ROC curve analysis for three different logistic regression model predicting future exacerbation risk by three definitions of CB

- Proportion of CB patients and Cohen's kappa test result for agreement among the three CB definitions

The St. George's Respiratory Questionnaire Definition of Chronic Bronchitis May Be a Better Predictor of COPD Exacerbations Compared With the Classic Definition



*Victor Kim, MD; Huaqing Zhao, PhD; Elizabeth Regan, MD; MeiLan K. Han, MD; Barry J. Make, MD; James D. Crapo, MD; Paul W. Jones, MBBS; Jeffrey L. Curtis, MD; Edwin K. Silverman, MD, PhD; Gerard J. Criner, MD; and the COPD Gene Investigators**



- Percent breakdown of each of the four chronic bronchitis groups

TABLE 4] Multivariable Linear Regression for Exacerbation Frequency

GOLD	Classic CB			SGRQ CB			SGRQ vs Classic
	β Coeff ^a	SE	P Value	β Coeff ^a	SE	P Value	P Value
All	0.083	0.030	.006	0.166	0.026	< .0001	.017
0	0.031	0.035	.366	0.059	0.029	.039	.391
1, 2	0.134	0.045	.003	0.193	0.040	< .0001	.239
3, 4	0.096	0.095	.312	0.310	0.088	< .0001	.038

Probability values in boldface indicate significance. Coeff = coefficient. See [Table 1](#) legend for expansion of other abbreviations.

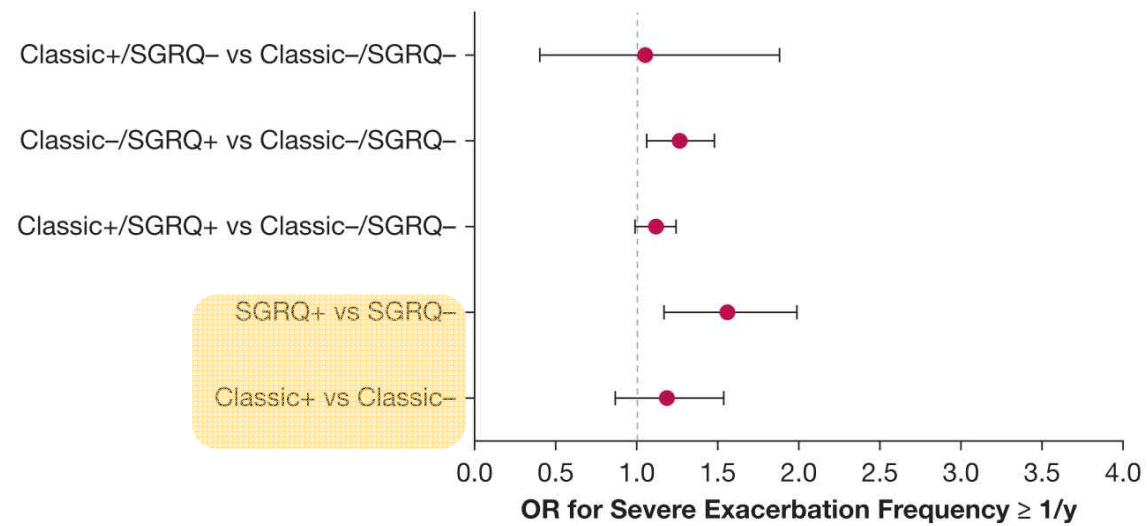
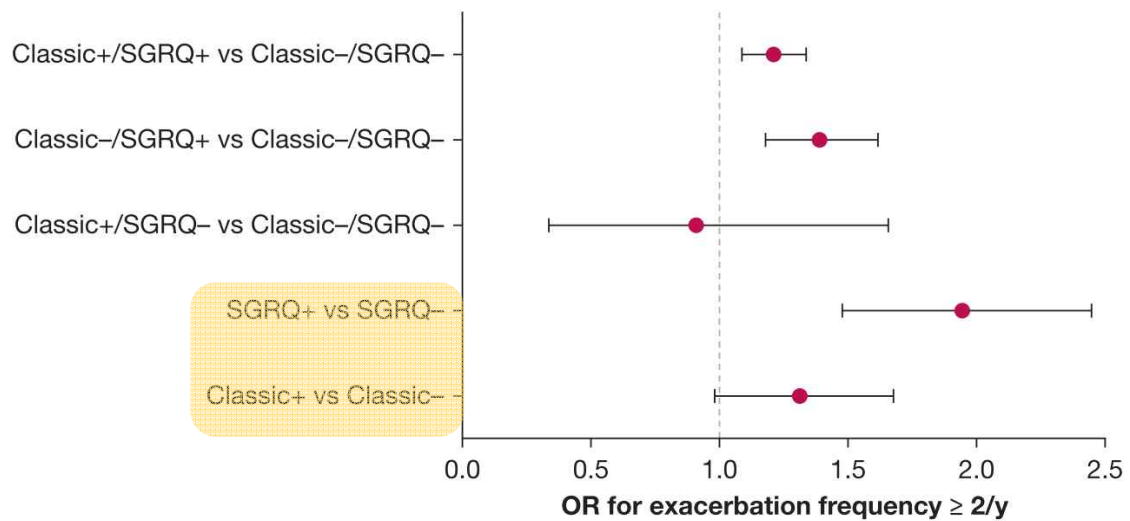
^aAge, race, sex, pack-year history, current smoking, oxygen use, modified Medical Research Council dyspnea score, % emphysema, prior exacerbation frequency, FEV₁% predicted, 6-min walk distance, and BMI as covariates.

TABLE 5] Multivariable Linear Regression for Severe Exacerbation Frequency

GOLD	Classic CB			SGRQ CB			SGRQ vs Classic
	β Coeff ^a	SE	P Value	β Coeff ^a	SE	P Value	P Value
All	0.032	0.016	.054	0.065	0.014	< .0001	.077
0	0.027	0.018	.139	0.035	0.015	.017	.655
1, 2	0.033	0.026	.199	0.054	0.023	.018	.520
3, 4	0.038	0.051	.462	0.121	0.047	.011	.092

Probability values in boldface indicate significance. See [Table 1](#) and [4](#) legends for expansion of abbreviations.

^aAge, race, sex, pack-year history, current smoking, oxygen use, modified Medical Research Council dyspnea score, % emphysema, prior exacerbation frequency, FEV₁% predicted, 6-min walk distance, and BMI as covariates.



Defining Chronic Mucus Hypersecretion Using the CAT in the SPIROMICS Cohort

This article was published in the following Dove Press journal:
International Journal of Chronic Obstructive Pulmonary Disease

Definition	Description
MRC-CMH	Cough on most days for ≥ 3 consecutive months or more during the year AND phlegm from chest on most days for ≥ 3 consecutive months or more during the year
MRC-CB	Cough on most days for ≥ 3 consecutive months or more during the year AND phlegm from chest on most days for ≥ 3 consecutive months or more during the year, with these symptoms for ≥ 2 consecutive years
SGRQ-CMH	Cough for most days or several days a week (option 1 or 2 for the “I cough” question) AND phlegm for most days or several days a week (option 1 or 2 for the “I bring up phlegm [sputum]” question)
CAT-CMH	Multiple permutations of cut-points of 2 or 3 for cough and phlegm questions were explored to determine optimal CAT-CMH definition. Scores spanned 0 to 5, from “I never cough” to “I cough all the time” and from “I have no phlegm in my chest at all” to “My chest is full of phlegm”

Abbreviations: CAT, COPD Assessment Test; CB, chronic bronchitis; CMH, chronic mucus hypersecretion; MRC, Medical Research Council; SGRQ, St. George’s Respiratory Questionnaire.

Table 2 Frequency of CMH by Multiple Definitions

CMH Definition	N	n CMH+	n CMH-
MRC-CMH	1044	398 (38%)	646 (62%)
MRC-CB	1386	326 (24%)	1064 (76%)
SGRQ-CMH	1361	639 (47%)	722 (53%)
CAT-CMH: Cough Q and Phlegm Q both ≥ 3	1407	348 (25%)	1059 (75%)
CAT-CMH: Cough Q and Phlegm Q both ≥ 2	1407	686 (49%)	721 (51%)

Abbreviations: CAT, COPD Assessment Test; CB, chronic bronchitis; CMH, chronic mucus hypersecretion; SGRQ, MRC, Medical Research Council; St. George’s Respiratory Questionnaire.

Table 3 Evaluation of Different CAT Cut-Points Using SGRQ-CMH and MRC-CMH as Gold Standard

CAT vs MRC-CMH	Sensitivity	Specificity	PPV	NPV	Kappa
Cough Q and Phlegm Q both ≥ 3	59%	90%	78%	78%	0.51
Cough Q and Phlegm Q both ≥ 2	87%	72%	66%	90%	0.56
Cough Q ≥ 2 and Phlegm Q ≥ 3	67%	87%	77%	81%	0.55
Cough Q ≥ 3 and Phlegm Q ≥ 2	70%	85%	74%	82%	0.55
Only Cough Q ≥ 3	73%	82%	71%	83%	0.54
Only Phlegm Q ≥ 3	68%	85%	74%	81%	0.54
Only Cough Q ≥ 2	93%	57%	57%	93%	0.44
Only Phlegm Q ≥ 2	90%	64%	60%	91%	0.49
CAT vs SGRQ-CMH	Sensitivity	Specificity	PPV	NPV	Kappa
Cough Q and Phlegm Q both ≥ 3	49%	95%	90%	68%	0.45
Cough Q and Phlegm Q both ≥ 2	80%	78%	77%	82%	0.58
Cough Q ≥ 2 and Phlegm Q ≥ 3	56%	92%	85%	70%	0.48
Cough Q ≥ 3 and Phlegm Q ≥ 2	60%	91%	86%	72%	0.52
Only Cough Q ≥ 3	63%	86%	80%	73%	0.50
Only Phlegm Q ≥ 3	57%	90%	83%	70%	0.48
Only Cough Q ≥ 2	88%	59%	65%	85%	0.46
Only Phlegm Q ≥ 2	85%	69%	71%	84%	0.53

Abbreviations: CAT, COPD Assessment Test; CMH, chronic mucus hypersecretion; MRC, Medical Research Council; NPV, negative predictive value; PPV, positive predictive value; SGRQ, St. George's Respiratory Questionnaire.

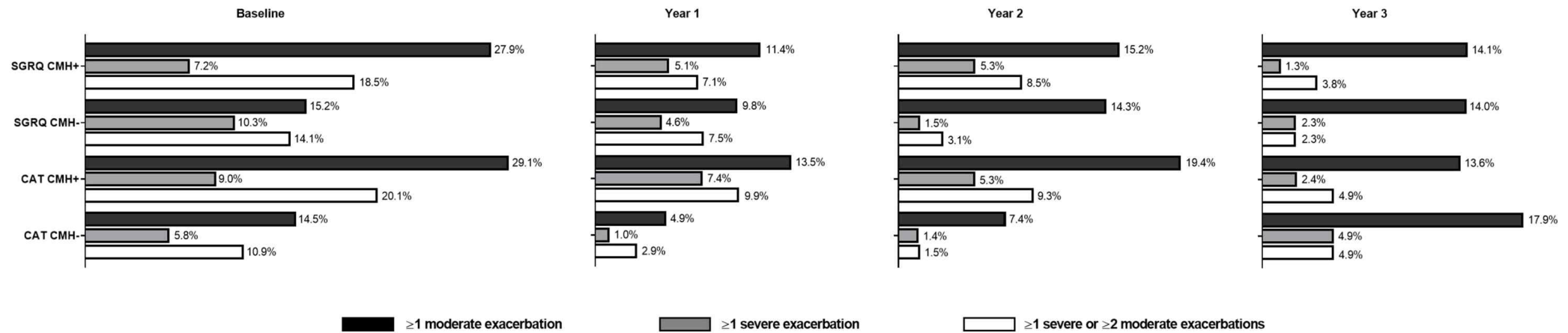


Figure 1 COPD exacerbations (percentage) among current smokers by SGRQ and CAT definitions of CMH 12 months prior to baseline and during first, second and third year of follow-up.

Abbreviations: CAT, COPD Assessment Test; CMH, chronic mucus hypersecretion; SGRQ, St. George's Respiratory Questionnaire.

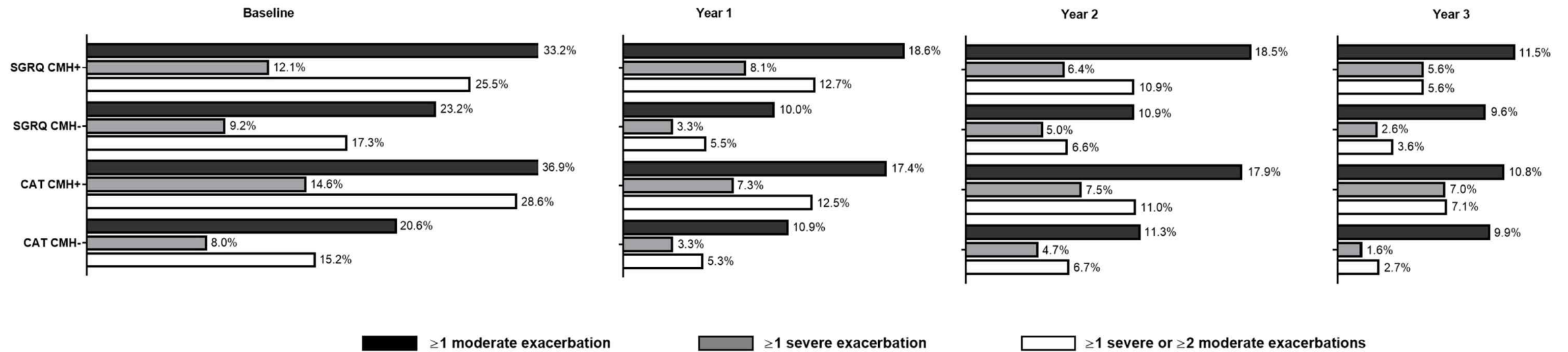


Figure 2 COPD Exacerbations (percentage) among ex-smokers by SGRQ and CAT definitions of CMH 12 months prior to baseline and during first, second and third year of follow-up.

Abbreviations: CAT, COPD Assessment Test; CMH, chronic mucus hypersecretion; SGRQ, St. George's Respiratory Questionnaire.

2. Risk factors

Predictors of chronic bronchitis symptoms in multivariate analysis

	OR (95% CI)	p-value
Male sex	1.25 (0.91–1.71)	0.163
Age per 10-year increase	1.39 (1.22–1.58)	0.001
Education per 1-year increase	0.97 (0.94–0.99)	0.031
Smoking status		
Past smoking	1.12 (0.76–1.68)	0.557
Current smoking	2.74 (1.94–3.87)	0.001
Exposure to passive smoke	1.00 (0.71–1.40)	0.995
Dusty job	1.08 (0.83–1.46)	0.606
Occupational exposure to fumes	1.90 (1.24–2.92)	0.003
Biomass fuel use	0.52 (0.16–1.71)	0.282
Current asthma (self-reported)	7.9 (5.73–10.91)	0.001
Diagnosed heart disease	1.05 (0.70–1.57)	0.818
Ever-diagnosed tuberculosis	0.82 (0.36–1.86)	0.641
Diagnosed lung cancer	6.42 (1.34–30.70)	0.020
Family history of chronic lung disease	1.78 (1.19–2.66)	0.005
Hospitalisation for breathing problems prior to the age of 10 years	1.26 (0.59–2.70)	0.556






ORIGINAL ARTICLE
AIRWAYS DISEASE



CrossMark

Assessment of chronic bronchitis and risk factors in young adults: results from BAMSE

Gang Wang^{1,2,3}, Jenny Hallberg^{3,4}, Petra Um Bergström ^{3,4}, Christer Janson ⁵,
Göran Pershagen^{2,6}, Olena Gruzieva^{2,6}, Marianne van Hage⁷,
Antonios Georgelis^{2,6}, Anna Bergström^{2,6}, Inger Kull^{2,3,4}, Anders Lindén^{2,8} and
Erik Melén ^{2,3,4}

- Swedish BAMSE (Child(Barn), Allergy, Milieu, Stockholm, Epidemiological) cohort
- 4089 infants were included
- 24-year follow-up
- Follow-up questionnaires at age of 1,2,4,8,12 and 16 years

TABLE 1 Characteristics of cohort participants with and without chronic bronchitis (CB)

	CB	No CB	p-value
Subjects	158	2361	
Age years	22.4±0.5	22.4±0.5	0.361
Female	85 (53.8)	1278 (54.1)	0.935
BMI kg·m⁻²	24.03±4.4	23.15±3.8	0.005
Education			0.544
Secondary school	106 (67.1)	1503 (63.8)	
High school	34 (21.5)	514 (21.8)	
University	18 (11.4)	340 (14.4)	
Smoking status			<0.001
Never-smoker	72 (45.6)	1628 (69.1)	
Former smoker	27 (17.1)	289 (12.3)	
Current smoker, sometimes	27 (17.1)	297 (12.6)	
Current smoker, every day	32 (20.3)	142 (6.0)	
Cigarette consumption per day[#]	4.3 (1.1–10.0)	1.4 (0.4–5.0)	<0.001
Electronic cigarette smoking	11 (7.0)	82 (3.5)	0.025

Data are presented as n, mean±SD, n (%) or median (interquartile range), unless otherwise stated. BMI: body mass index. [#]: based on current smokers.

TABLE 3 Distribution of potential risk factors for chronic bronchitis (CB) among young adults from the BAMSE (Child (Barn), Allergy, Milieu, Stockholm, Epidemiological) birth cohort

	CB	No CB	Logistic regression model [#]	
			OR (95% CI)	p-value
Subjects	158	2361		
Electronic cigarette smoking	11 (7.0)	82 (3.5)	1.916 (0.937–3.573)	0.055
Parental occupation				
Unemployed/blue collar	18 (12.9)	212 (10.1)	Ref.	
Low white collar	60 (43.2)	843 (40.0)	0.874 (0.489–1.467)	0.555
High white collar	61 (43.9)	1050 (49.9)	0.705 (0.408–1.219)	0.211
Parental education				
University	71 (44.9)	1365 (57.9)	Ref.	
Primary school/high school	87 (55.1)	993 (42.1)	1.618 (1.167–2.249)	0.004
Parental asthma	33 (21.6)	444 (18.9)	1.174 (0.776–1.730)	0.432
Exclusive breastfeeding for ≥4 months	115 (75.7)	1857 (80.8)	0.743 (0.510–1.107)	0.132
Maternal smoking during pregnancy	21 (13.3)	253 (10.7)	1.249 (0.752–1.979)	0.365
Parental smoking during childhood	65 (41.4)	644 (27.3)	1.822 (1.301–2.563)	<0.001
Premature birth	9 (5.7)	129 (5.5)	1.026 (0.475–1.957)	0.942
Low birthweight	4 (2.5)	84 (3.6)	0.728 (0.220–1.781)	0.541
Respiratory syncytial virus infection/pneumonia during infancy	14 (9.2)	164 (7.1)	1.282 (0.691–2.205)	0.399
Bronchitis during infancy	12 (7.8)	178 (7.8)	0.975 (0.503–1.728)	0.937
Pneumonia at age 0–4 years	16 (10.3)	249 (10.7)	0.950 (0.536–1.576)	0.851
Childhood asthma at age 1–4 years	31 (19.9)	228 (9.8)	2.129 (1.367–3.225)	0.001
Childhood asthma at age 1–8 years	42 (26.9)	275 (11.7)	2.629 (1.773–3.831)	<0.001
Childhood asthma at age 1–16 years	59 (37.6)	367 (15.6)	3.082 (2.166–4.351)	<0.001
Nitrogen oxides $\mu\text{g}\cdot\text{m}^{-3}$				
Age 0–1 years	29.12 (20.3–45.0)	29.3 (18.3–42.5)	1.006 (0.997–1.014)	0.195
Age 1–4 years	25.8 (16.9–37.7)	24.2 (15.3–33.6)	1.011 (1.000–1.022)	0.038
Age 4–8 years	20.5 (13.1–29.8)	18.2 (12.1–27.1)	1.010 (0.994–1.025)	0.192
Age 8–12 years	14.2 (10.0–22.9)	13.8 (10.1–22.2)	1.002 (0.983–1.020)	0.837
Age 12–16 years	11.7 (7.9–17.1)	11.3 (8.3–18.1)	0.997 (0.970–1.022)	0.811
Black carbon $\mu\text{g}\cdot\text{m}^{-3}$				
Age 0–1 years	0.97 (0.8–1.4)	0.97 (0.7–1.3)	1.278 (0.905–1.764)	0.149
Age 1–4 years	0.96 (0.7–1.3)	0.89 (0.7–1.2)	1.575 (1.060–2.289)	0.020
Age 4–8 years	0.87 (0.7–1.2)	0.81 (0.6–1.1)	1.388 (0.849–2.205)	0.177
Age 8–12 years	0.71 (0.6–1.0)	0.70 (0.6–0.9)	1.070 (0.585–1.876)	0.820
Age 12–16 years	0.66 (0.6–0.8)	0.65 (0.5–0.8)	0.916 (0.350–2.249)	0.853

Data are presented as n, n (%) or median (interquartile range), unless otherwise stated. #: results after adjustment for age, sex and body mass index.

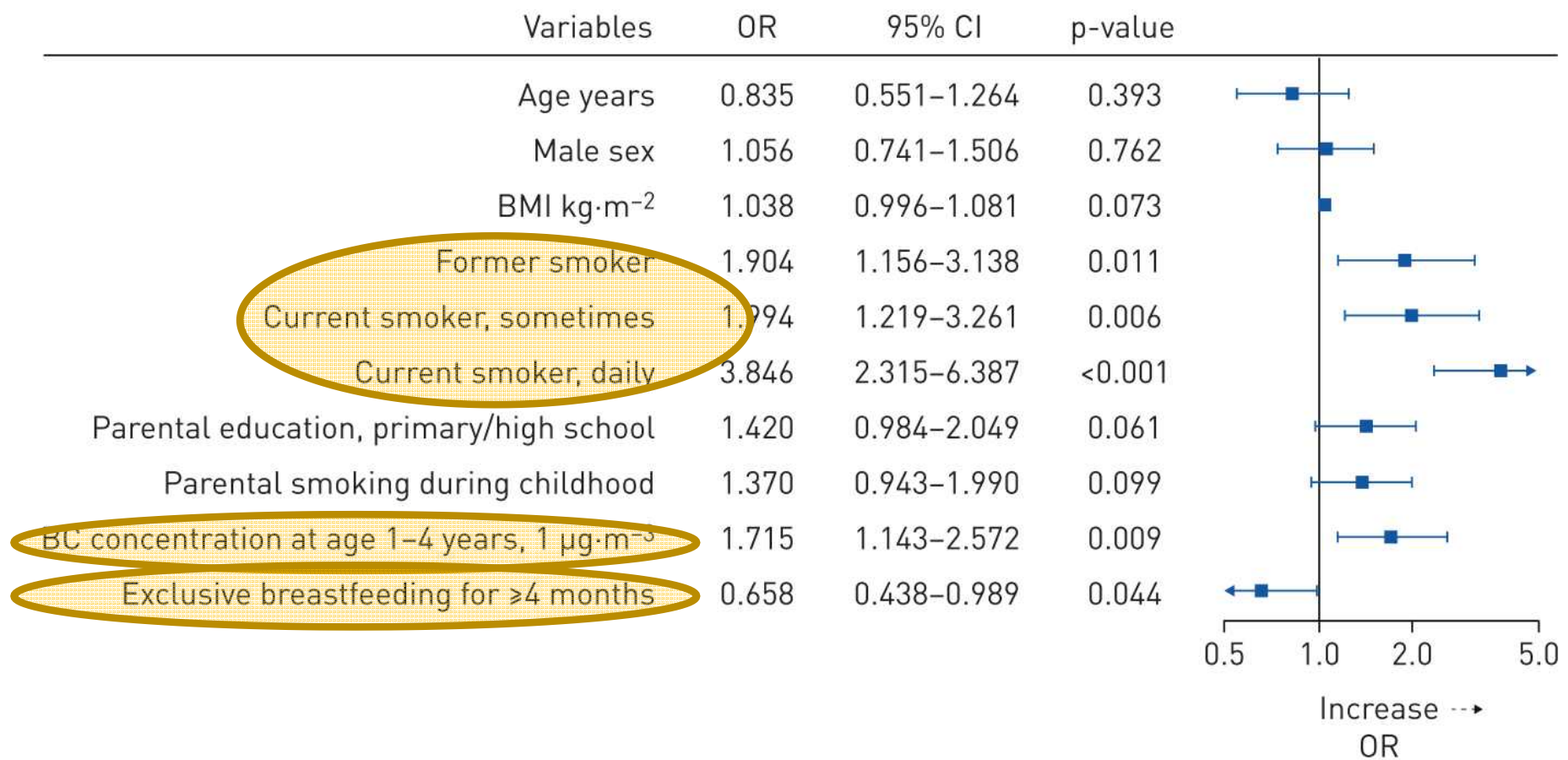
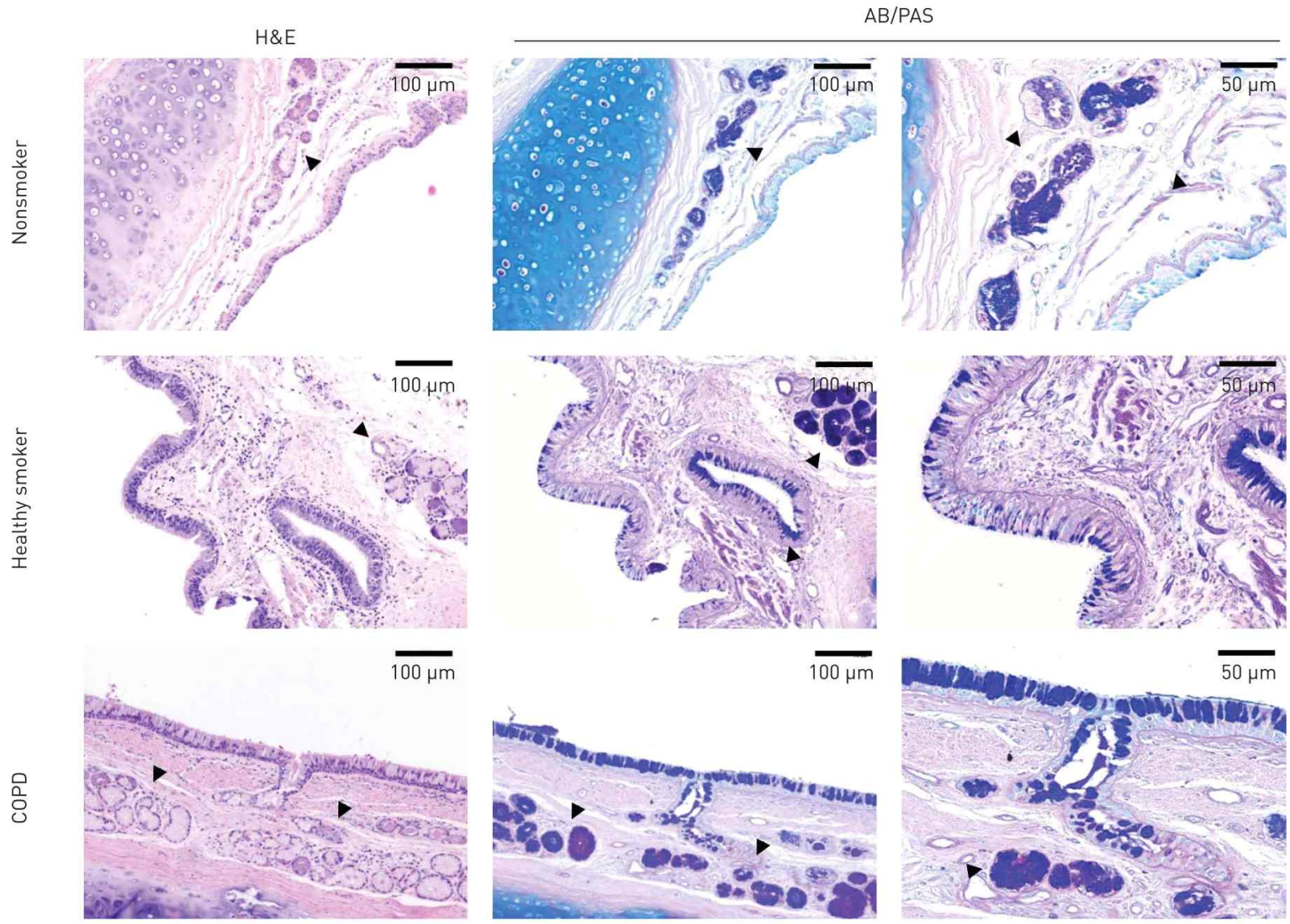
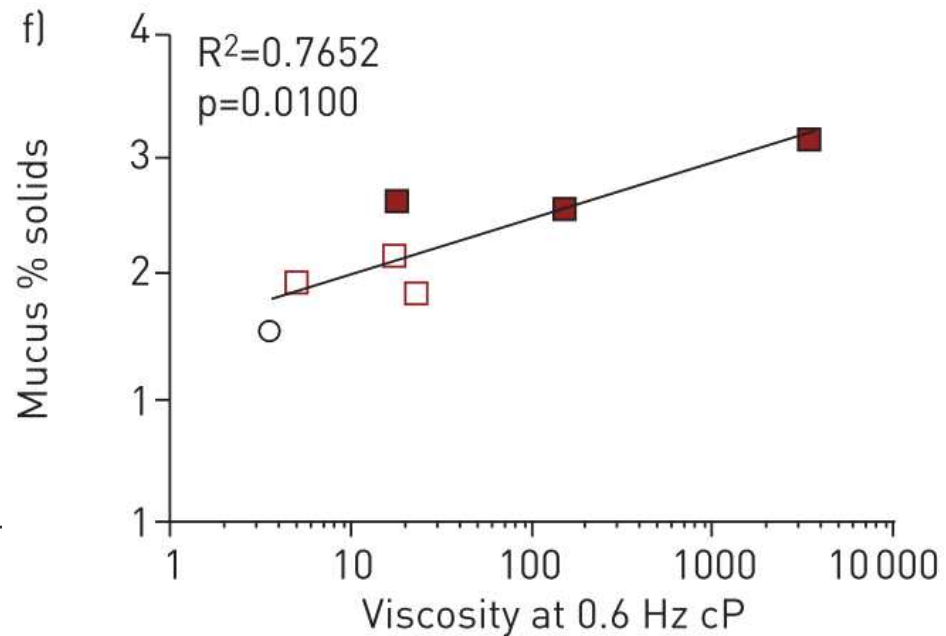
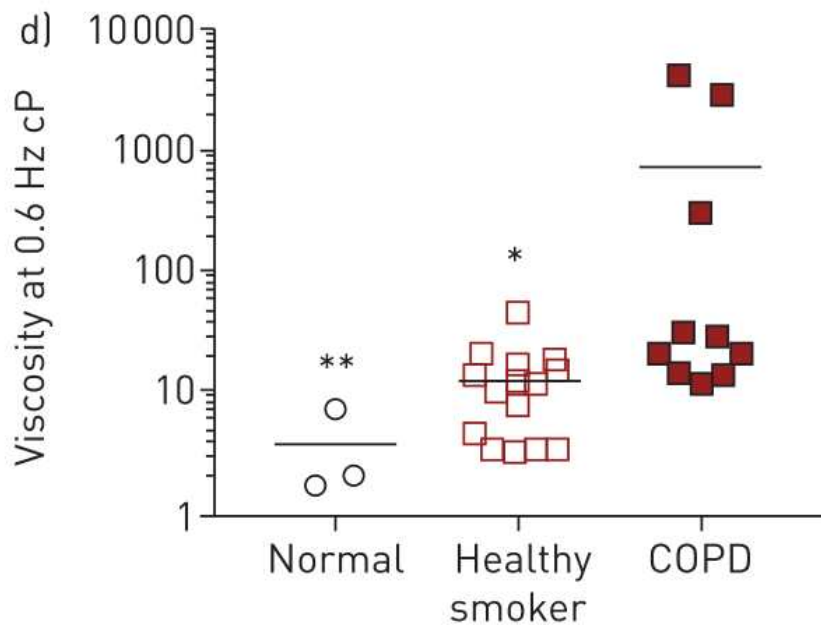
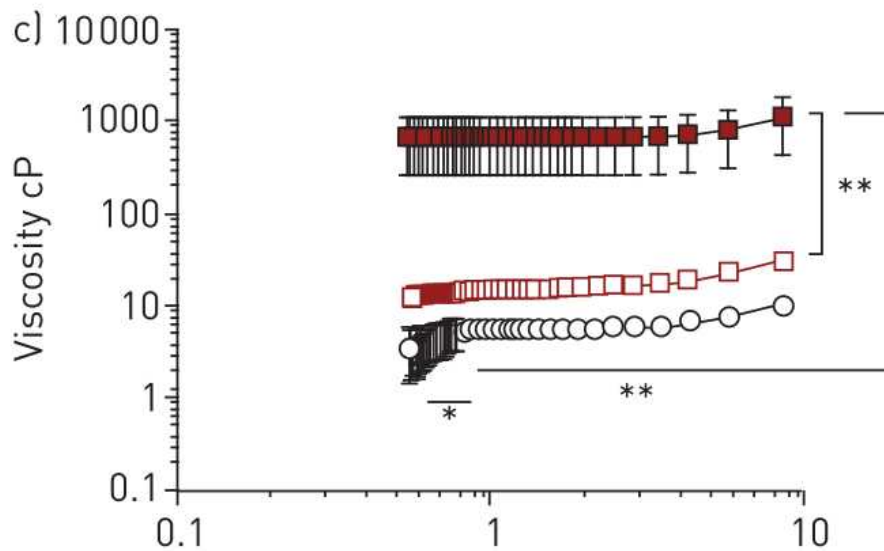
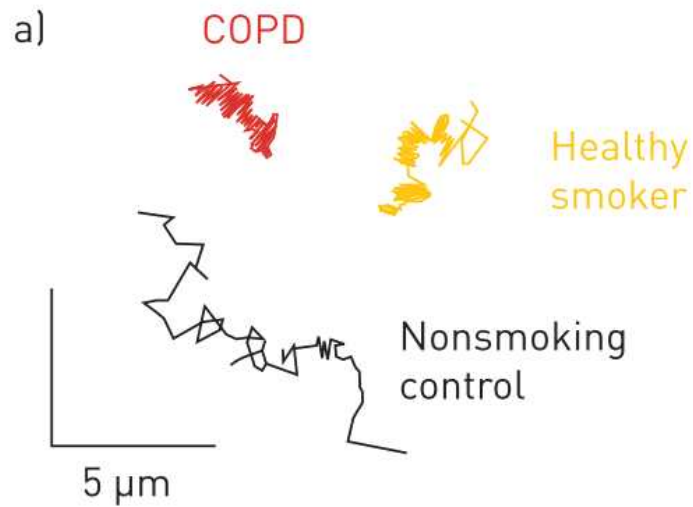


FIGURE 1 Mutually adjusted logistic regression analyses for chronic bronchitis among young adults from the BAMSE (Child (Barn), Allergy, Milieu, Stockholm, Epidemiological) birth cohort. The model included age, sex, body mass index (BMI), smoking, parental education, parental smoking during childhood, air pollution at age 1–4 years (black carbon (BC)) and exclusive breastfeeding for ≥4 months as covariates.





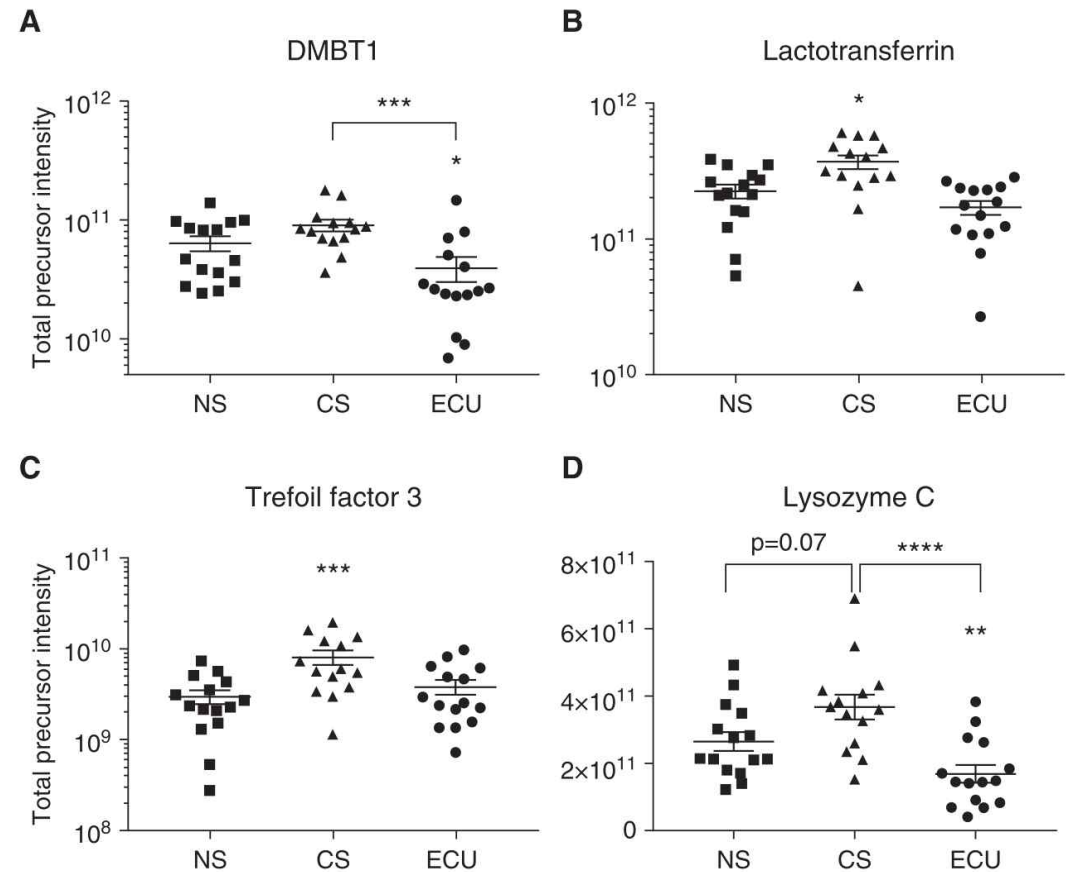
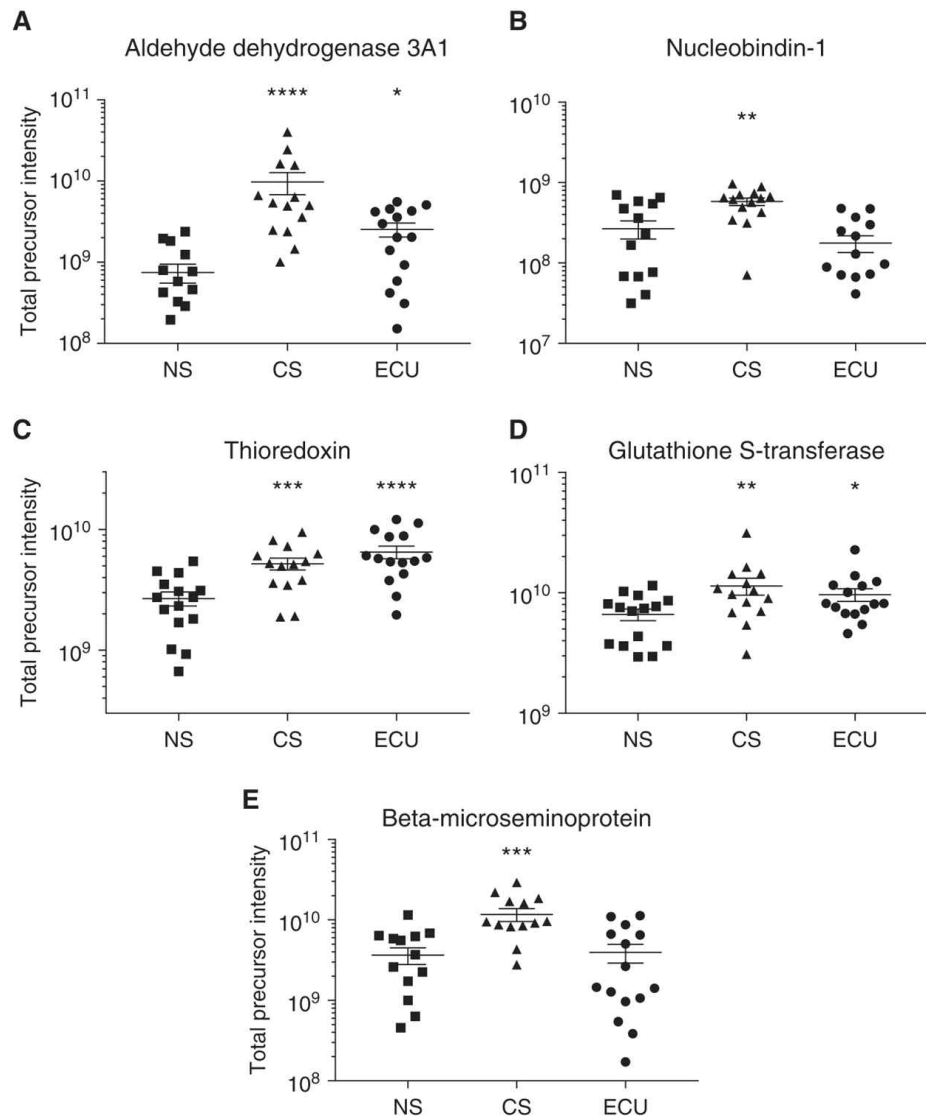
E-cigarette

E-Cigarette Use Causes a Unique Innate Immune Response in the Lung, Involving Increased Neutrophilic Activation and Altered Mucin Secretion

Boris Reidel^{1,2}, Giorgia Radicioni^{1,2}, Phillip W. Clapp³, Amina A. Ford^{1,2}, Sabri Abdelwahab^{1,2}, Meghan E. Rebuli³, Prashamsha Haridass^{1,2}, Neil E. Alexis³, Ilona Jaspers³, and Mehmet Kesimer^{1,2}

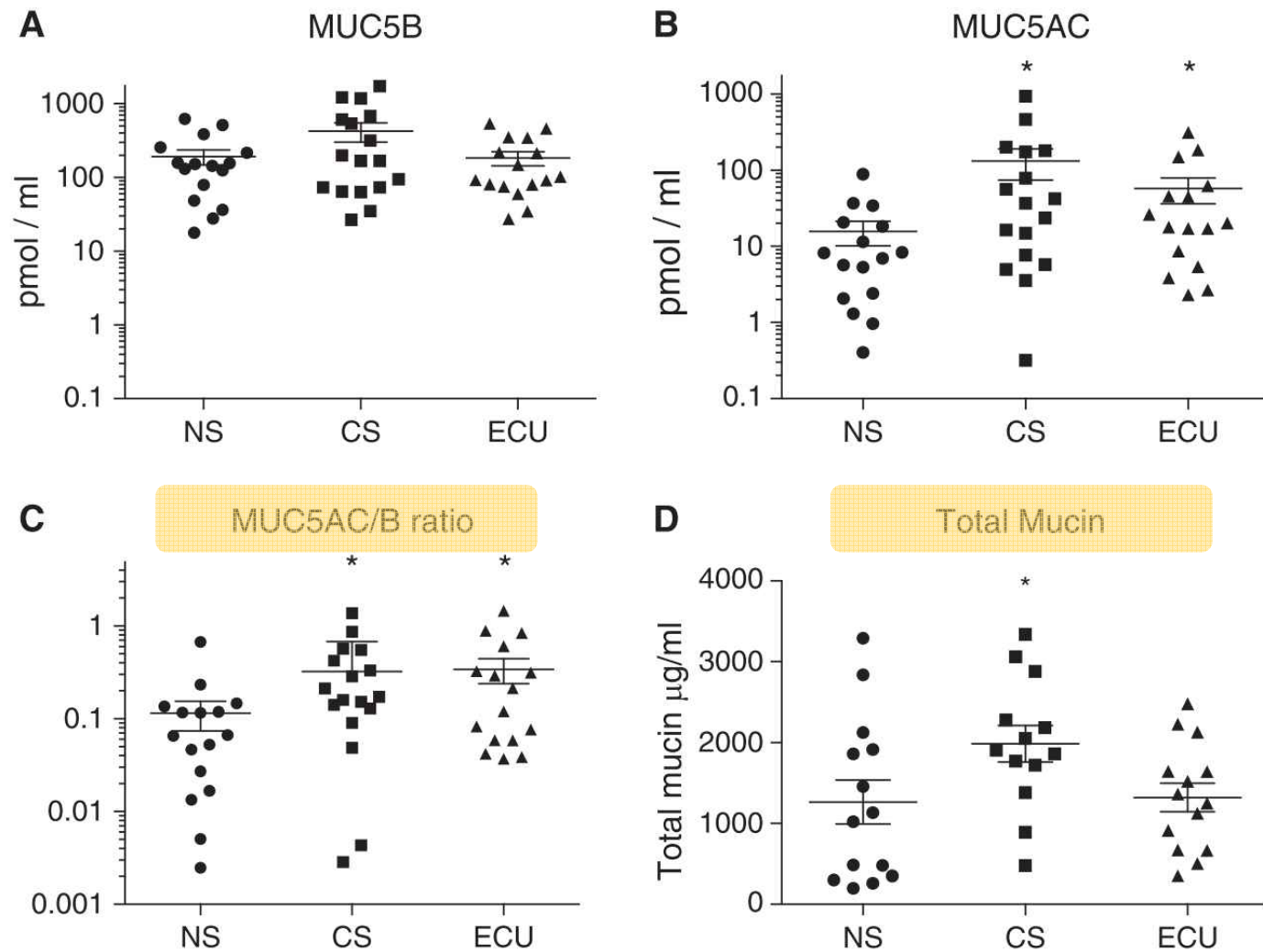
¹Marsico Lung Institute, ²Department of Pathology and Laboratory Medicine, and ³Department of Pediatrics, The University of North Carolina at Chapel Hill, Chapel Hill, North Carolina

- Identification of induced sputum samples of cigarette smokers, e-cigarette users, and non-smokers.



Airway epithelial defense protein levels are significantly altered in tobacco product users.

Levels of proteins known to be affected by cigarette smoke exposure are also altered in e-cigarette users.



The ratio between the major airway mucins MUC5AC and MUC5B is significantly shifted toward MUC5AC in cigarette smokers and follows the same trend in e-cigarette users.

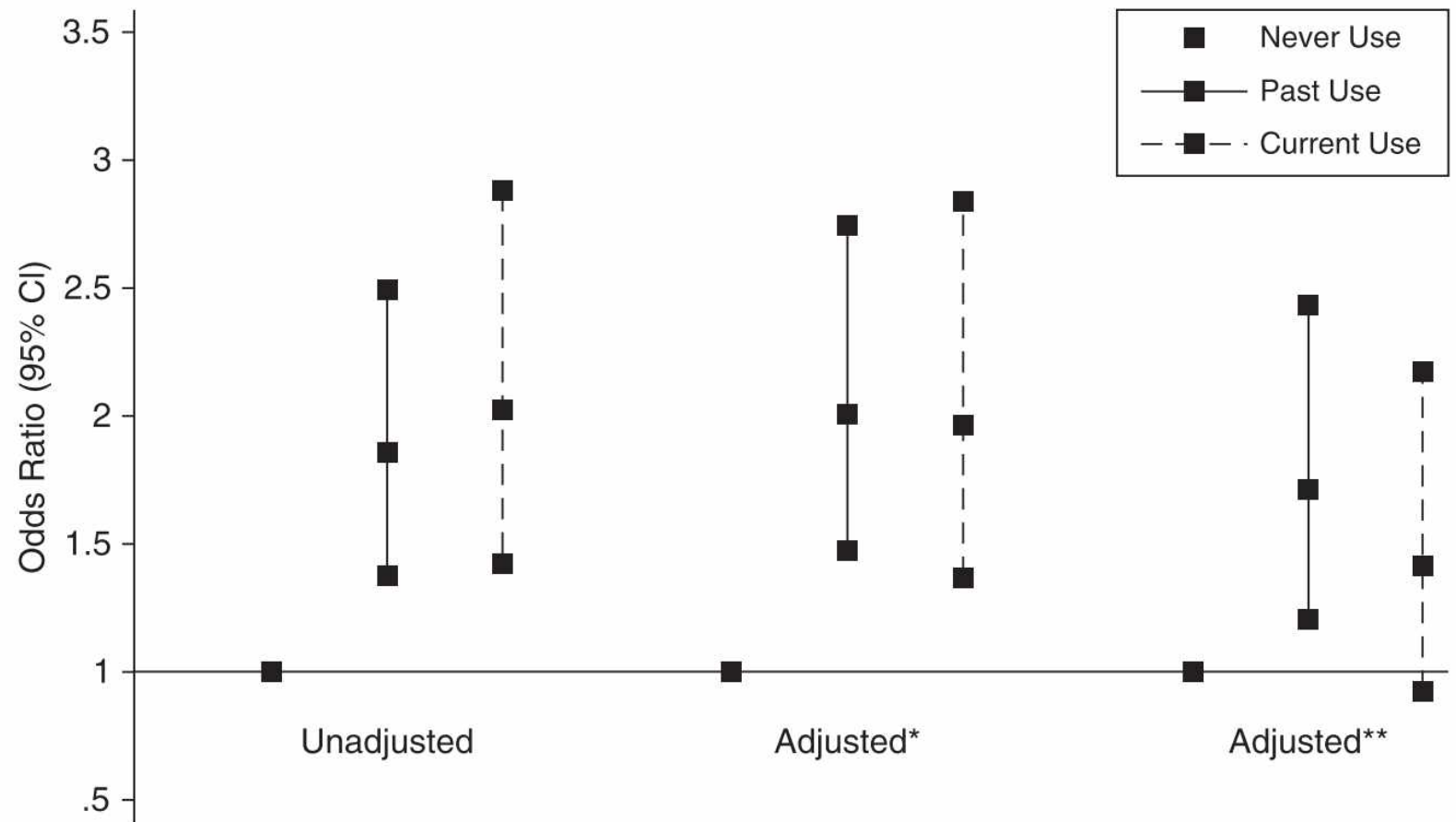
Electronic Cigarette Use and Respiratory Symptoms in Adolescents

Rob McConnell¹, Jessica L. Barrington-Trimis¹, Kejia Wang¹, Robert Urman¹, Hanna Hong², Jennifer Unger¹, Jonathan Samet¹, Adam Leventhal¹, and Kiros Berhane¹

¹Department of Preventive Medicine, Keck School of Medicine, University of Southern California, Los Angeles, California; and ²Division of Pulmonary Medicine, Department of Pediatrics, Children's Hospital Los Angeles, Los Angeles, California

CHS cohort

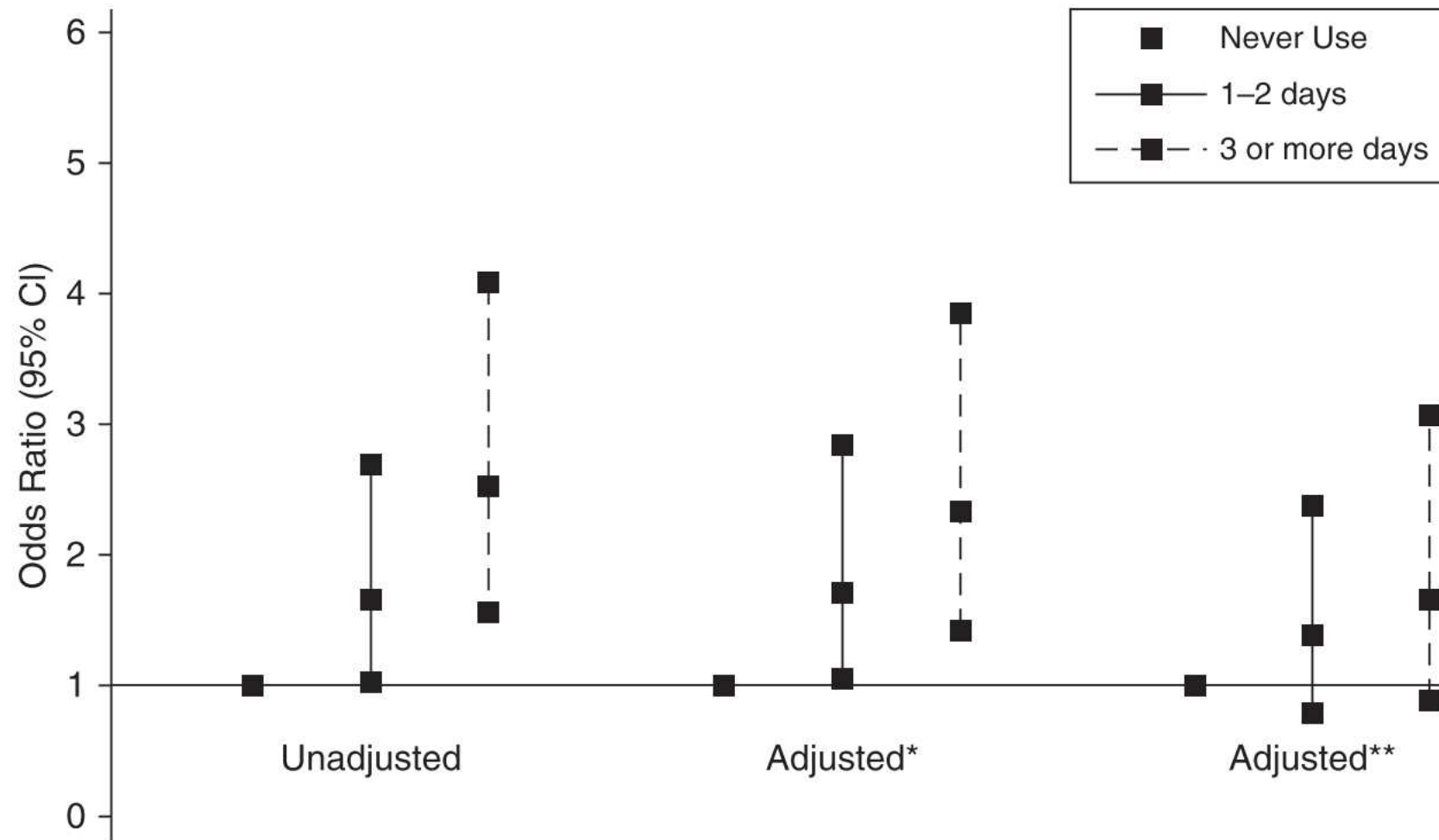
- Recruited in 2002-2003
- Enrolled at kindergarden or first grade
- ~ 11th and 12th grade
- Mean age was 17.3 years



Association of current and past electronic cigarette use with bronchitis

*Adjusted for sex, ethnicity, parental education, and community.

**Adjusted for sex, ethnicity, parental education, community, secondhand smoke, and lifetime number of cigarettes smoked.



Association of number of days of current electronic cigarette use in prior month with bronchitis

*Adjusted for sex, ethnicity, parental education, and community.

**Adjusted for sex, ethnicity, parental education, community, secondhand smoke, and lifetime number of cigarettes smoked.

3. Pathophysiology

The **NEW ENGLAND**
JOURNAL *of* **MEDICINE**

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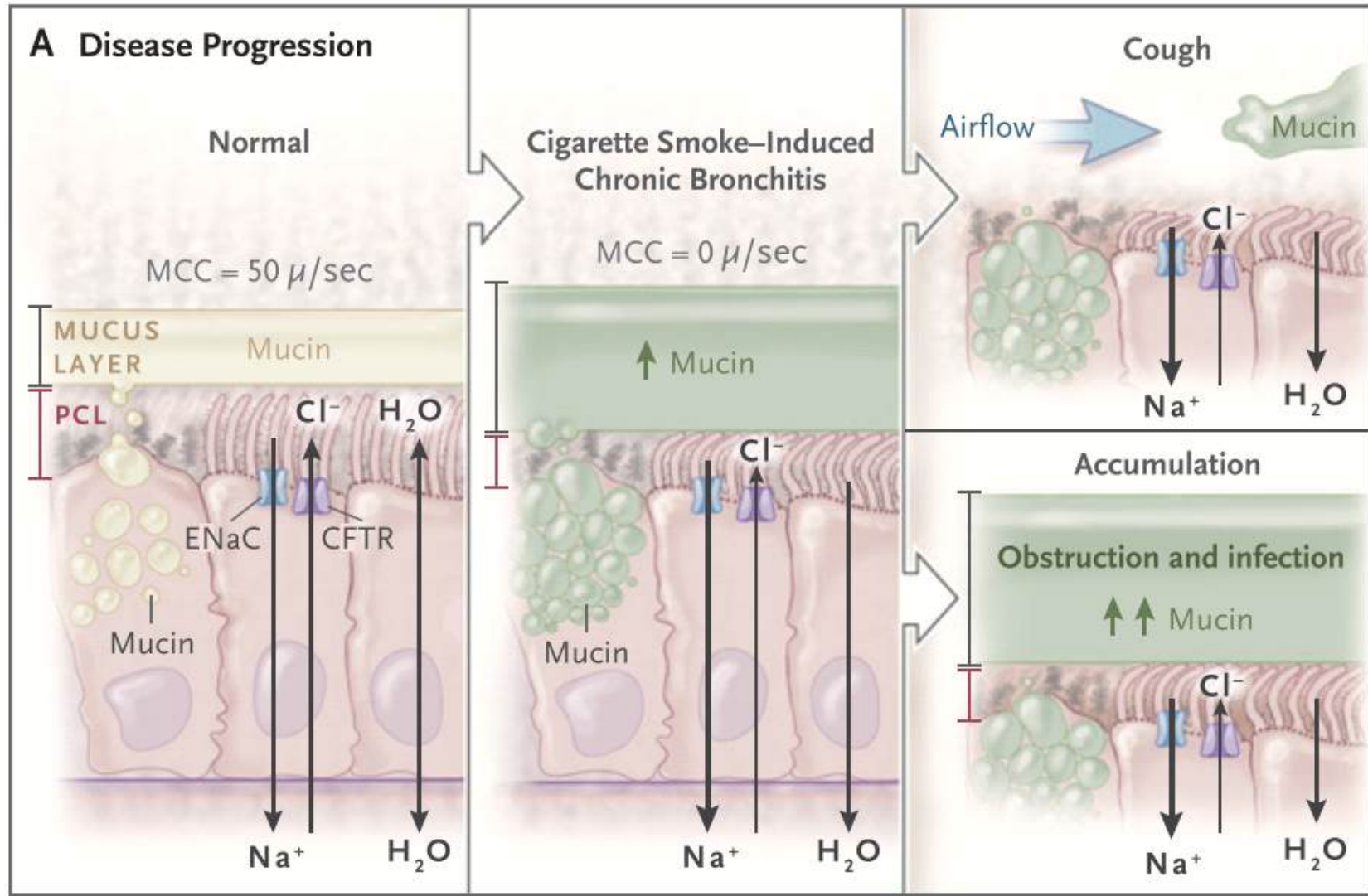
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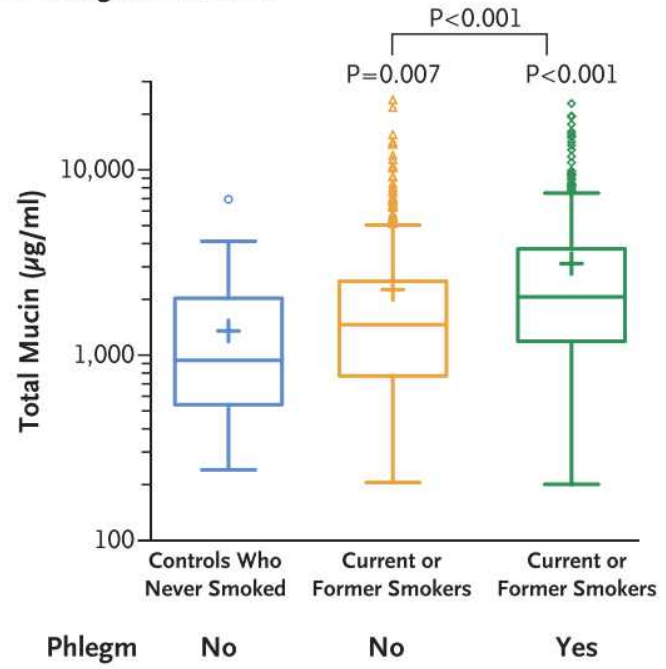
Airway Mucin Concentration as a Marker of Chronic Bronchitis

Mehmet Kesimer, Ph.D., Amina A. Ford, M.S.P.H., Agathe Ceppe, M.S., Giorgia Radicioni, Ph.D., Rui Cao, Ph.D., C. William Davis, Ph.D., Claire M. Doerschuk, M.D., Neil E. Alexis, Ph.D., Wayne H. Anderson, Ph.D., Ashley G. Henderson, M.D., R. Graham Barr, M.D., Dr.P.H., Eugene R. Bleecker, M.D., Stephanie A. Christenson, M.D., Christopher B. Cooper, M.D., MeiLan K. Han, M.D., Nadia N. Hansel, M.D., Annette T. Hastie, Ph.D., Eric A. Hoffman, Ph.D., Richard E. Kanner, M.D., Fernando Martinez, M.D., Robert Paine III, M.D., Prescott G. Woodruff, M.D., Wanda K. O'Neal, Ph.D., and Richard C. Boucher, M.D.

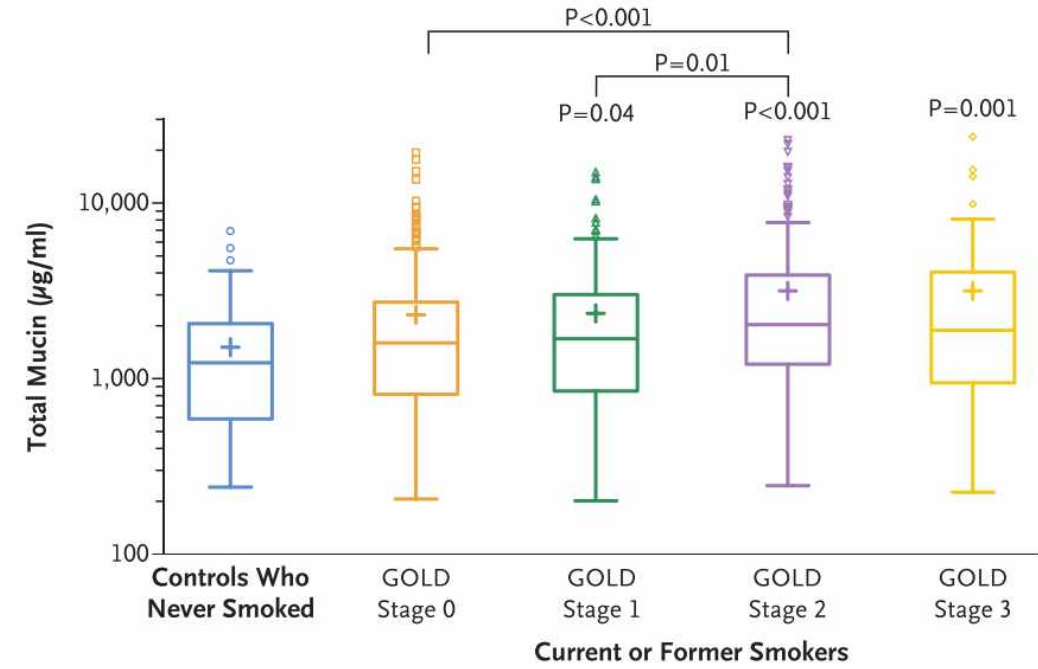
Two Gel Hypothesis



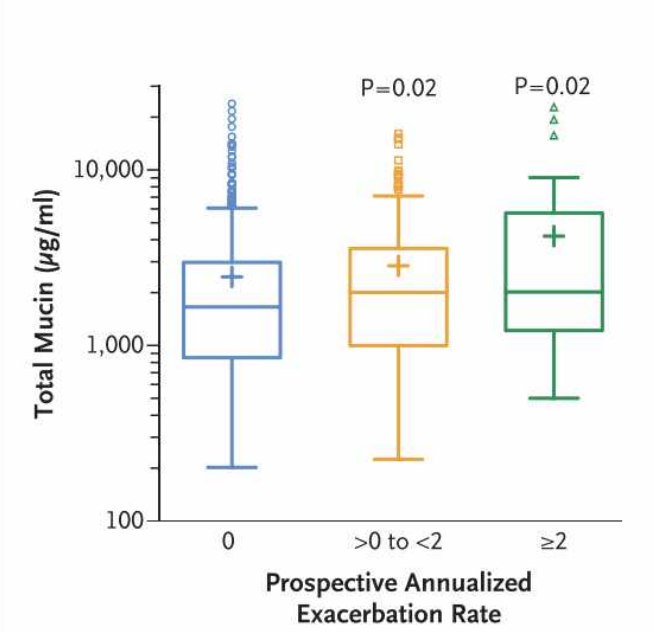
B Phlegm Production



C Severity of COPD



D Respiratory Exacerbations



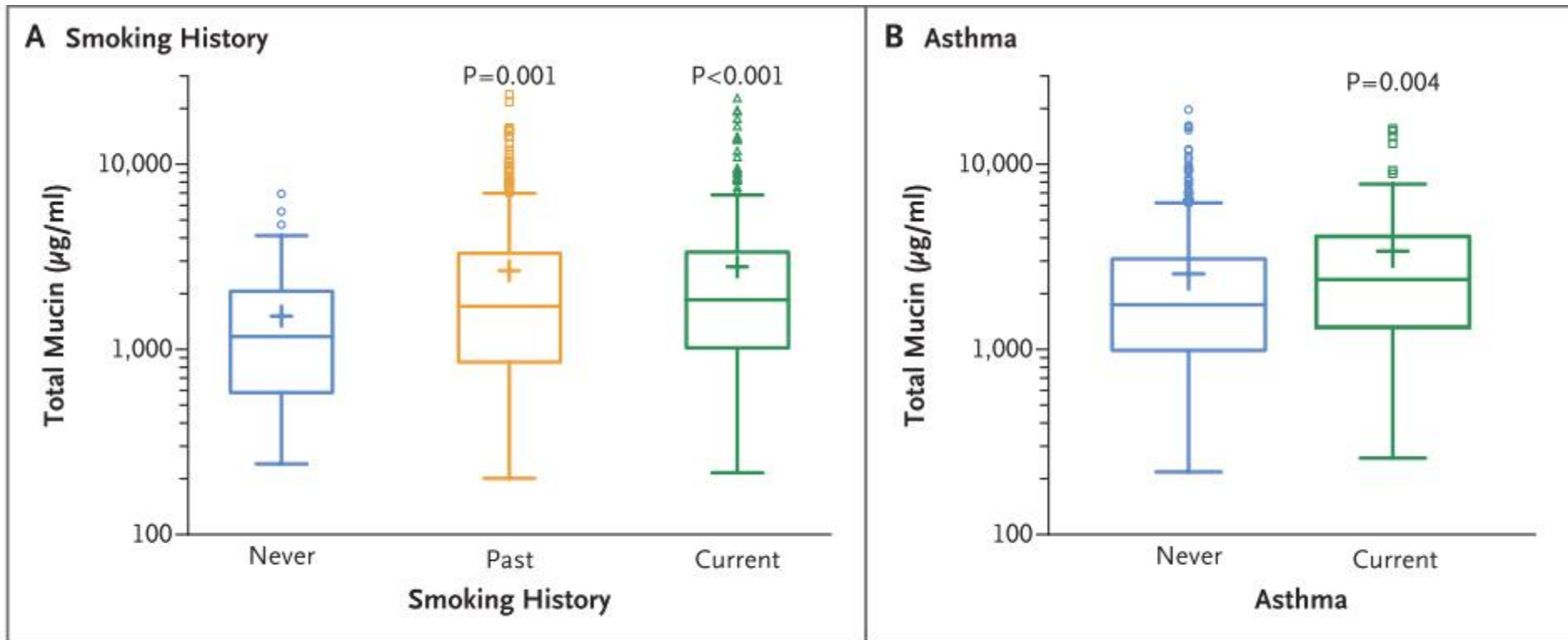


Figure 2. Association between Potential Etiologic Pathways and Total Mucin Concentrations in Sputum.

Panel A shows total mucin concentration and smoking history. Data are for 69 participants who had never smoked, 460 former smokers, and 374 current smokers. Panel B shows total mucin concentration and asthma status in participants with COPD (GOLD stages 1 through 3). Data are for 84 participants with current asthma and 389 participants who had never received a diagnosis of asthma. P values are for the comparison with participants who had never smoked or who had never received a diagnosis of asthma. The horizontal line in the boxes represents the median, the cross represents the mean, and the bottom and top of the boxes represent the 25th and 75th percentiles, respectively. I bars represent the upper adjacent value (75th percentile plus 1.5 times the interquartile range) and the lower adjacent value (25th percentile minus 1.5 times the interquartile range), and the dots outliers. All P values were adjusted for multiple comparisons with the use of the Tukey–Kramer method.

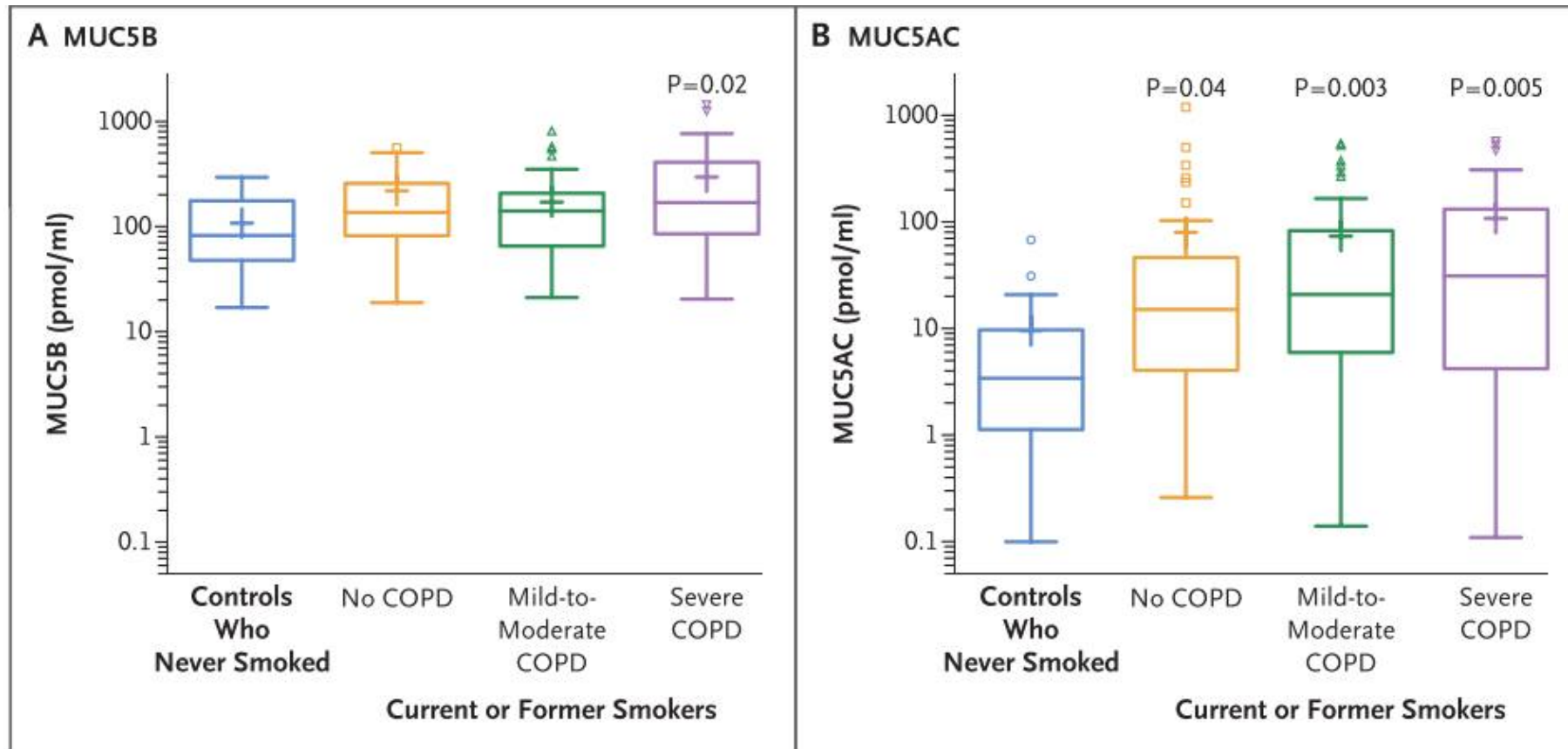


Figure 3. Absolute Concentrations of MUC5B and MUC5AC and Disease Severity.

Panels A and B show absolute concentrations of MUC5B and MUC5AC, respectively, in controls who had never smoked (19 participants), current or former smokers without spirometric evidence of COPD (42 participants), current or former smokers with mild-to-moderate COPD (59 participants), and current or former smokers with severe COPD (28 participants). P values are for the comparison with controls who had never smoked. The horizontal line in the boxes represents the median, the cross represents the mean, and the bottom and top of the boxes represent the 25th and 75th percentiles, respectively. I bars represent the upper adjacent value (75th percentile plus 1.5 times the interquartile range) and the lower adjacent value (25th percentile minus 1.5 times the interquartile range), and the dots outliers. All P values were adjusted for multiple comparisons with the use of the Tukey–Kramer method.

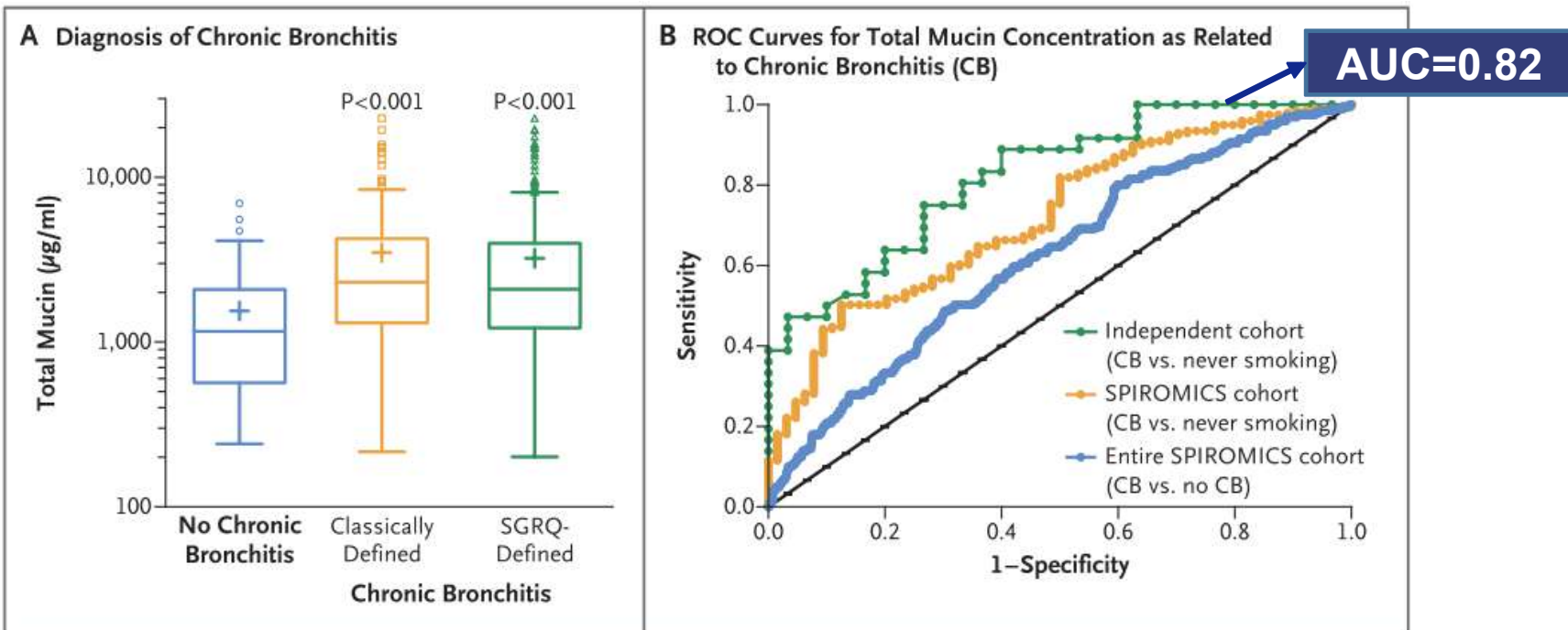


Figure 4. Total Mucin Concentration and Diagnosis of Chronic Bronchitis.

Panel A shows total mucin concentrations in current or former smokers who were identified as having chronic bronchitis by a questionnaire that reflected the classic definition of the disorder (199 participants), current or former smokers who were identified as having chronic bronchitis by the St. George's Respiratory Questionnaire (SGRQ) (382 participants), and controls who had never smoked and were not identified as having chronic bronchitis by either questionnaire (58 participants). P values are for the comparison with healthy controls who had never smoked. The horizontal line in the boxes represents the median, the cross represents the mean, and the bottom and top of the boxes represent the 25th and 75th percentiles, respectively. I bars represent the upper adjacent value (75th percentile plus 1.5 times the interquartile range) and the lower adjacent value (25th percentile minus 1.5 times the interquartile range), and the dots outliers. All P values were adjusted for multiple comparisons with the use of the Tukey-Kramer method. Panel B shows receiver-operating-characteristic (ROC) curves for total mucin concentration in participants with classically defined chronic bronchitis, as compared with controls who had never smoked, in the SPIROMICS cohort (orange curve; area under the curve [AUC], 0.72 [0.65 to 0.79]) and in the independent cohort (green curve; AUC, 0.82 [0.73 to 0.92]). The blue curve represents total mucin concentration in participants with classically defined chronic bronchitis, as compared with all participants without chronic bronchitis, in the entire SPIROMICS cohort (AUC, 0.62 [0.58 to 0.67]).

4. Clinical implications

Poor health-related
quality of life

Kim V. Chest. 2011;140(3):626-633
Meek PM. Chest. 2015;148(2):408-416

Chronic bronchitis (CB)
phenotype

Reduced lung function

Kim V. Curr Opin Pulm Med. 2015;21(2):133-141
Choi JY. IJOPD. 2016;11:1335-1341

Frequent exacerbation

Kania A. IJOPD. 2018;13:1613-1621
Choi JY. IJOPD. 2016;11:1335-1341
Corhay JL. Int J Clin Pract. 2013;67(12):1294-1301.

Higher mortality rate

Lahousse L. Eur Respir J. 2017;50(2).
Meek PM. Chest. 2015;148(2):408-416



ORIGINAL ARTICLE
COPD

Prevalence and burden of chronic bronchitis symptoms: results from the BOLD study

Filip Mejza¹, Louisa Gnatiuc², A. Sonia Buist³, William M. Vollmer⁴, Bernd Lamprecht^{5,6}, Daniel O. Obaseki⁷, Pawel Nastalek¹, Ewa Nizankowska-Mogilnicka¹ and Peter G.J. Burney² for the BOLD collaborators⁸

FEV1: - 1.92%, p<0.001

FEV1: - 4.04%, p<0.001

TABLE 3 Lung function by the presence of chronic bronchitis symptoms, chronic airway obstruction (CAO) and self-reported asthma

	Mutually exclusive categories								p-value [#]
	Without CBS, CAO and asthma	CBS	CAO	CAO+CBS	Asthma	Asthma+CBS	CAO+asthma	CAO+asthma+CBS	
Subjects n	18551	345	1192	129	746	121	257	77	
FEV1 % pred [¶]	89.7±17.1	89.8±17.9	66.6±19.8	56.4±18	86.6±16.4	82.9±17.5	59.8±18.3	55.8±21	<0.001
FVC % pred [¶]	88.1±16.8	90.3±18	86.5±21.8	81.4±18.8	86.8±16	84.3±17.9	82.6±20.1	79.2±20.5	<0.001
FEV1/FVC [¶]	79.4±6.0	77.0±6.4	58.4±8.8	52.3±11	78.1±6.2	76.8±6.5	55.5±10.6	53.2±11.4	<0.001
ΔFEV1 [¶] mL	67.9±14.2	93.7±184.5	110.2±171.0	131.0±141.1	113.9±176.7	127.8±192.8	177.3±184.7	154.9±169.4	<0.001
ΔFEV1 [¶] % of initial value	3.1±7.0	4.0±7.5	7.9±12.4	10.8±12.3	5.6±9.0	6.7±10.3	14±15.3	13.1±13.2	<0.001
Proportion of subjects with ΔFEV1 [¶] ≥12% and >200 mL ⁺	5.3	9.3	18.6	30.2	13.5	19.0	38.9	32.5	<0.001
Proportion of subjects with ΔFEV1 [¶] >15% and >400 mL ⁺	1.4	2.0	4.1	3.9	4.6	5.0	11.7	6.5	<0.001

Data are presented as mean±SD or %, unless otherwise stated. n=21418. CBS: chronic bronchitis symptoms; FEV1: forced expiratory volume in 1 s; % pred: % predicted; FVC: forced vital capacity; ΔFEV1: change in FEV1. #: comparison across mutually exclusive groups; ¶: post-bronchodilator; +: thresholds for significant bronchodilator response suggested in the Global Initiative for Asthma guidelines [28].

TABLE 4 Associations of chronic bronchitis symptoms with other respiratory symptoms, respiratory exacerbations and quality of life

	Total study sample	CAO ⁺	CAO ⁻
mMRC dyspnoea scale ≥ 2	1.54 (1.08–2.22)	2.06 (1.01–4.22)	1.63 (1.06–2.74)
Respiratory exacerbations			
Breathing problems interfering with daily activities or causing subject to miss work in the previous year	4.28 (3.07–5.95)	5.66 (3.08–10.41)	3.66 (2.41–5.55)
Breathing problems causing subject to see a healthcare provider in the previous year	4.93 (3.28–7.41)	3.93 (2.00–7.72)	5.21 (3.06–8.88)
Hospitalisation for breathing problems in the previous year	4.86 (2.67–8.82)	4.54 (1.98–10.44)	4.18 (1.65–10.59)
Quality of life			
SF-12 mental score (lowest quartile)	2.06 (1.52–2.77)	4.04 (2.30–7.08)	1.59 (1.10–2.30)
SF-12 physical score (lowest quartile)	4.00 (2.89–5.53)	5.43 (2.88–10.26)	3.34 (2.26–4.95)

CB - Exacerbation

Original Article

Chronic bronchitis is associated with severe exacerbation and prolonged recovery period in Chinese patients with COPD: a multicenter cross-sectional study

Ying Liang¹, Yahong Chen¹, Rui Wu¹, Ming Lu¹, Wanzhen Yao¹, Jian Kang², Baiqiang Cai³, Xin Zhou⁴, Zheng Liu⁵, Ping Chen⁶, Dejun Sun⁷, Jingping Zheng⁸, Guoyang Wang⁹, Yulin Feng¹⁰, Yongjian Xu¹¹

Table 2 Comparison of frequency and severity of exacerbation between patients with and without CB

Events in the past year	CB+ (n=890)	CB- (n=211)	P
Overall number of exacerbations	2.42±2.50	2.13±2.83	0.134
% Frequency of exacerbations ≥2	530 (59.6)	107 (50.7)	0.019
Overall number of emergency visits	0.69±1.78	0.32±0.98	<0.001
% Emergency visits ≥1	249 (28.0)	35 (16.6)	0.001
Overall number of hospitalizations	0.96±1.34	0.54±1.15	<0.001
% Hospitalizations ≥1	456 (51.2)	59 (28.0)	<0.001
Overall number of ICU stay	0.08±0.35	0.02±0.14	<0.001
% ICU stay ≥1	58 (6.5)	4 (1.9)	0.009

Data are presented as mean ± SD or number (%). CB, chronic bronchitis; ICU, intensive care unit.

Table 4 Risk factors relevant to severe exacerbations of COPD (emergency visits, hospitalization and ICU stay)

Clinical characteristics	Emergency visits			Hospitalization			ICU stay		
	No (n=817)	≥1 (n=284)	P	No (n=586)	≥1 (n=515)	P	No (n=1,039)	≥1 (n=62)	P
Age (year)	65.2±11.1	69.6±11.5	<0.001	63.4±11.2	69.6±10.5	<0.001	66.0±11.3	72.5±9.2	<0.001
Male	534 (65.4)	192 (67.6)	0.492	374 (63.8)	352 (68.3)	0.114	687 (66.1)	39 (62.9)	0.603
Height (cm)	165.1±8.4	165.4±7.9	0.631	164.9±8.3	165.6±8.1	0.145	165.2±8.3	165.9±8.0	0.517
Weight (kg)	62.1±12.1	60.2±12.2	0.023	62.5±12.1	60.5±12.1	0.007	61.7±12.2	60.0±12.1	0.255
BMI (kg/m ²)	22.7±3.8	21.9±4.4	0.004	22.9±3.8	22.0±4.1	<0.001	22.5±4.0	21.8±4.3	0.150
Smoking status			0.209			<0.001			0.810
Current-	193 (23.6)	57 (20.1)		167 (28.5)	83 (16.1)		238 (22.9)	12 (19.4)	
Ex-	366 (44.8)	144 (50.7)		233 (39.8)	277 (53.8)		480 (46.2)	30 (48.4)	
Never-	258 (31.6)	83 (29.2)		186 (31.7)	155 (30.1)		321 (30.9)	20 (32.3)	
Smoking index (pack·year)	22.9±25.7	22.9±23.8	0.966	22.0±24.1	23.9±26.4	0.217	22.6±24.7	26.9±33.3	0.329
CB	641 (78.5)	249 (87.7)	0.001	434 (74.1)	456 (88.5)	<0.001	832 (80.1)	59 (93.5)	0.009
mMRC dyspnea score			< 0.001			<0.001			<0.001
0	86 (10.5)	12 (4.2)		72 (12.3)	26 (5.0)		97 (9.3)	1 (1.6)	
1	319 (39.0)	63 (22.2)		239 (40.8)	143 (27.8)		371 (35.7)	11 (17.7)	
2	242 (29.6)	104 (36.6)		177 (30.2)	169 (32.8)		332 (32.0)	14 (22.6)	
3	117 (14.3)	62 (21.8)		73 (12.5)	106 (20.6)		161 (15.5)	18 (29.0)	
4	53 (6.5)	43 (15.1)		25 (4.3)	71 (13.8)		78 (7.5)	18 (29.0)	
GOLD stage			<0.001			<0.001			<0.001
I	49 (6.0)	11 (3.9)		37 (6.3)	23 (4.5)		60 (5.8)	0 (0)	
II	262 (32.1)	64 (22.5)		220 (37.5)	106 (20.6)		316 (30.4)	10 (16.1)	
III	323 (39.5)	101 (35.6)		227 (38.7)	197 (38.3)		406 (39.1)	18 (29.0)	
IV	183 (22.4)	108 (38.0)		102 (17.4)	189 (36.7)		257 (24.7)	34 (54.8)	

Data are presented as mean ± SD or number (%). COPD, chronic obstructive pulmonary disease; ICU, intensive care unit; BMI, body mass index; CB, chronic bronchitis; mMRC, modified Medical Research Council; GOLD, Global Initiative for Chronic Obstructive Lung Disease.

Table 6 Comparison between patients with well-recovery and poor recovery following the last exacerbation

Clinical characteristics	Recovery status following the last exacerbation ^a		P
	Well-recovery (n=654)	Poor-recovery (n=409)	
Age (year)	64.7±11.8	69.4±10.0	<0.001
Male	412 (63.0)	284 (69.4)	0.032
Height (cm)	165.1±8.5	165.3±7.8	0.747
Weight (kg)	62.8±11.9	59.3±12.2	<0.001
BMI (kg/m ²)	23.0±3.7	21.7±4.3	<0.001
Smoking status			0.042
Current-	143 (21.9)	93 (22.7)	
Ex-	290 (44.3)	207 (50.6)	
Never-	221 (33.8)	109 (26.7)	
Chronic bronchitis	513 (78.4)	351 (85.8)	0.003
MMRC dyspnea score			<0.001
0	65 (9.9)	27 (6.6)	
1	251 (38.4)	111 (27.1)	
2	227 (34.7)	110 (26.9)	
3	80 (12.2)	96 (23.5)	
4	31 (4.7)	65 (15.9)	
GOLD stage			<0.001
I	49 (7.5)	8 (2.0)	
II	222 (33.9)	84 (20.5)	
III	252 (38.5)	157 (38.4)	
IV	131 (20.0)	160 (39.1)	

Table 7 General linear model analysis for recovery period following the last exacerbation

Independent variables in the model ^a	Adjusted regression coefficient (95% CI)	P
Age	0.133 (0.045–0.221)	0.003
GOLD stage	0.316 (–0.884–1.516)	0.606
mMRC dyspnea score	0.802 (–0.160–1.764)	0.102
Chronic bronchitis	2.861 (0.282–5.439)	0.030

^a, including independent variables with statistically significant associations (P<0.1) in univariate analyses. CI, confidence interval; mMRC, modified Medical Research Council; GOLD, Global Initiative for Chronic Obstructive Lung Disease.

CB - Mortality

Rotterdam Study

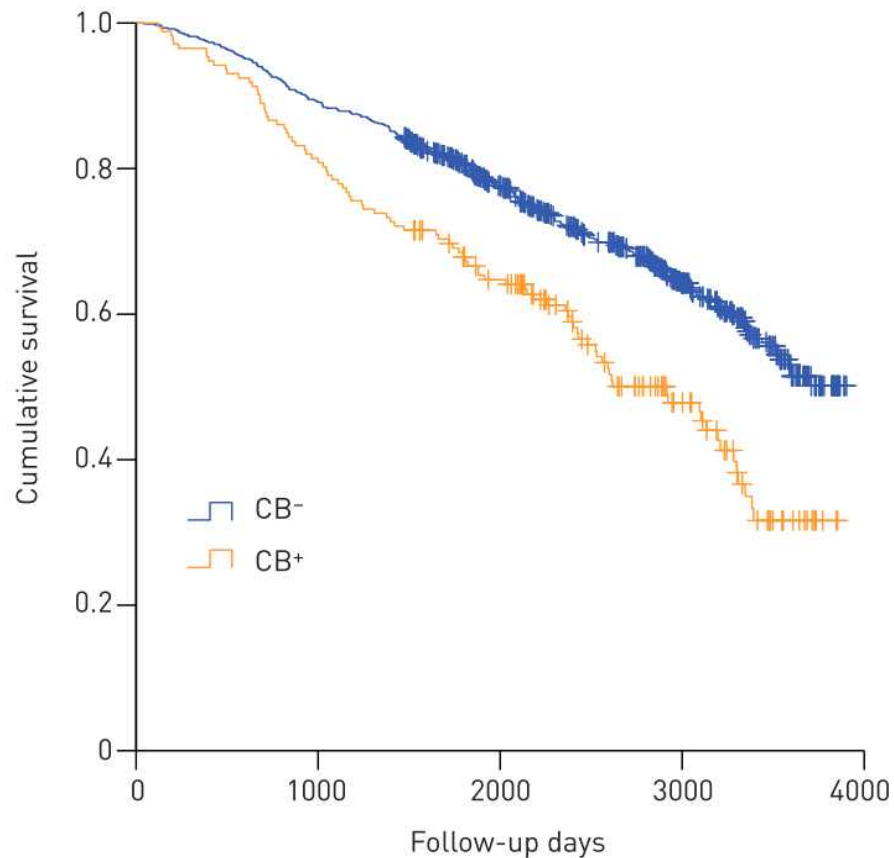


ORIGINAL ARTICLE
COPD

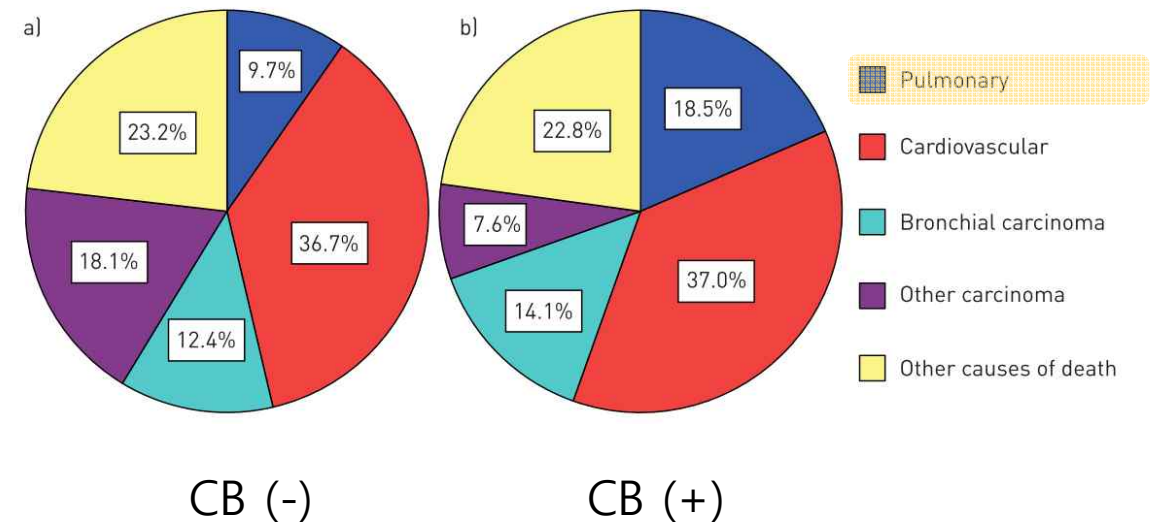
Epidemiology and impact of chronic bronchitis in chronic obstructive pulmonary disease

Lies Lahousse^{1,2}, Leen J.M. Seys^{1,3}, Guy F. Joos¹, Oscar H. Franco², Bruno H. Stricker^{2,4,5} and Guy G. Brusselle^{1,2,6}

- Population-based cohort study comprising almost 15,000 patients
- 1989~

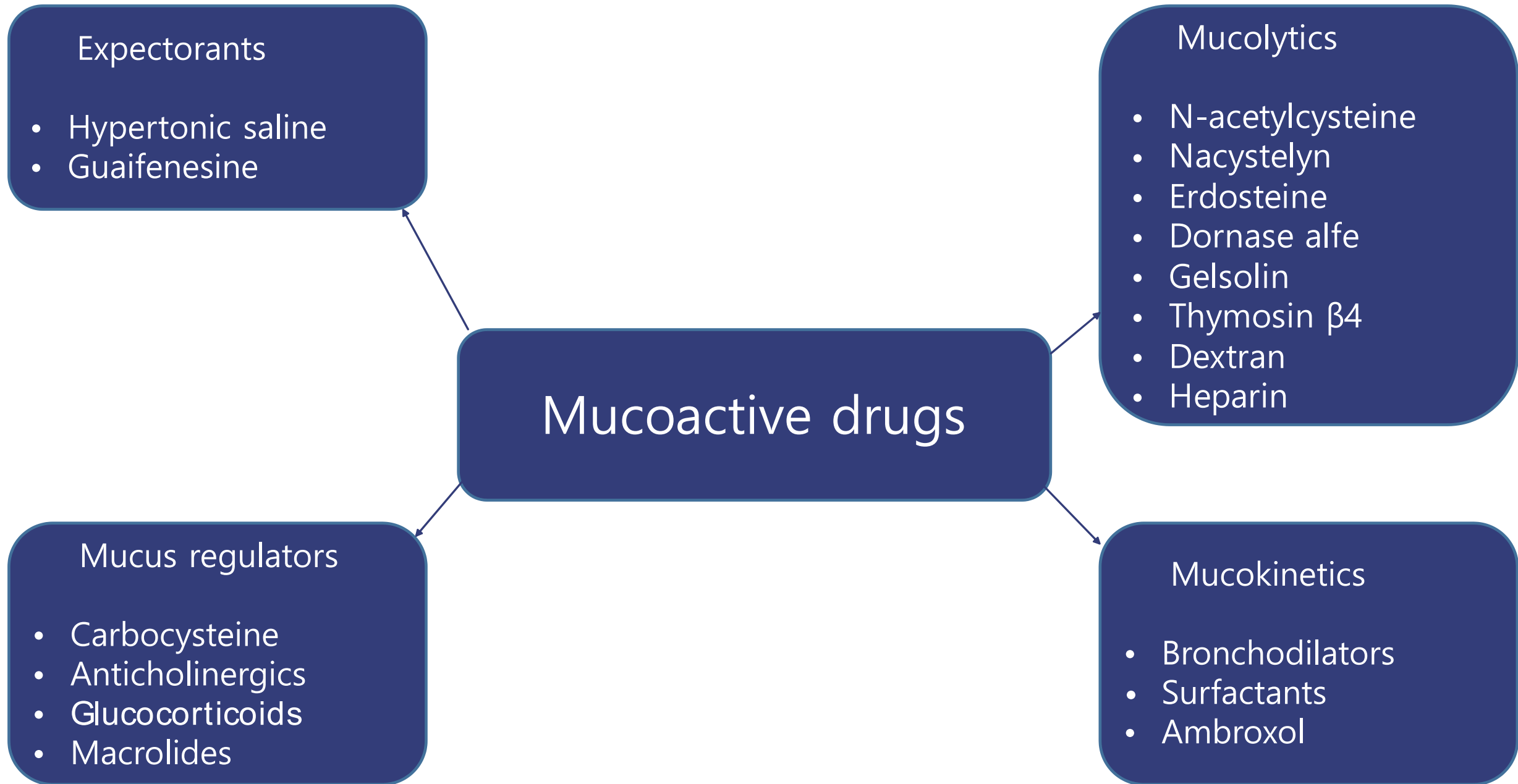


Cause of Death



Kaplan–Meier curve of all-cause mortality according to chronic obstructive pulmonary disease without chronic bronchitis (CB–, n=752) or with chronic bronchitis (CB+, n=172).

5. Treatments

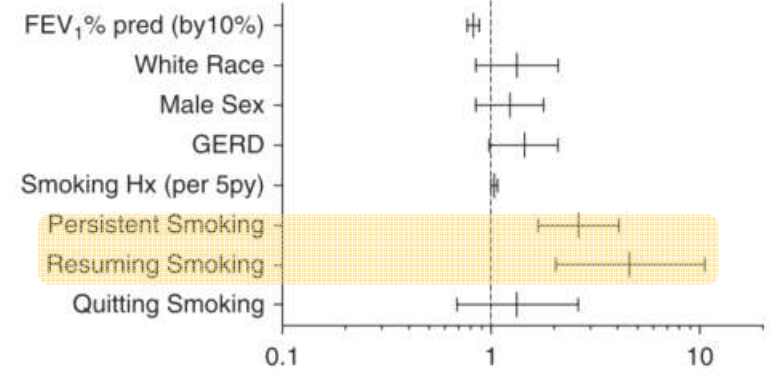


Non-pharmacologic therapies

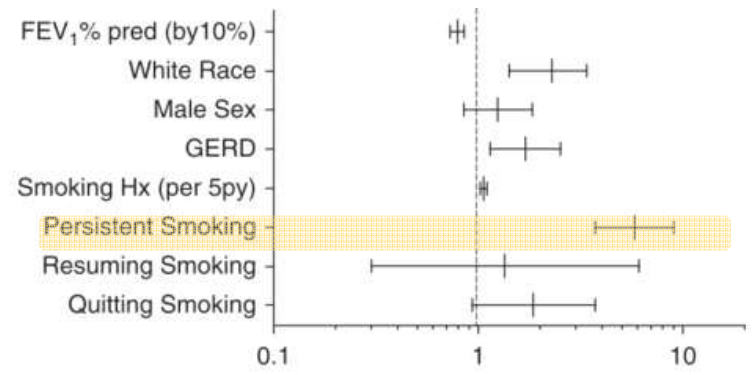
- Smoking cessation

	Resolved Chronic Bronchitis*		New Chronic Bronchitis*		Persistent Chronic Bronchitis+*	
	OR	95% CI	OR	95% CI	OR	95% CI
Univariable						
Quitting smoking [†]	3.436	2.211–5.339	1.120	0.588–2.133	1.362	0.708–2.620
Resuming smoking [†]	1.190	0.364–3.999	3.369	1.679–8.087	0.996	0.232–4.277
Persistent smoking [†]	1.806	1.239–2.634	1.734	1.178–2.551	2.784	1.902–4.074
Smoking, pack-years	1.008	1.001–1.015	1.013	1.007–1.020	1.020	1.014–1.026
GERD	1.429	1.016–2.010	1.361	0.939–1.972	1.563	1.064–2.255
Male sex	1.547	1.110–2.155	1.394	0.976–1.990	1.462	1.021–2.093
White race	1.154	0.799–1.688	1.116	0.751–1.657	1.524	0.994–2.336
FEV ₁ % pred	0.983	0.977–0.989	0.981	0.975–0.988	0.977	0.971–0.984
Multivariable						
Quitting smoking [†]	4.289	2.689–6.842	1.328	0.682–2.585	1.859	0.936–3.691
Resuming smoking [†]	1.449	0.421–4.984	4.585	2.008–10.471	1.350	0.301–6.041
Persistent smoking [†]	2.867	1.872–4.392	2.621	1.677–4.096	5.767	3.702–8.983
Smoking, pack-years	1.001	0.993–1.008	1.007	1.000–1.015	1.013	1.006–1.020
GERD	1.572	1.099–2.249	1.430	0.970–2.109	1.697	1.145–2.515
Male sex	1.493	1.056–2.111	1.227	0.847–1.778	1.242	0.846–1.823
White race	1.651	1.089–2.503	1.327	0.843–2.090	2.287	1.415–3.697
FEV ₁ % pred	0.982	0.975–0.988	0.979	0.972–0.986	0.973	0.966–0.980

New CB



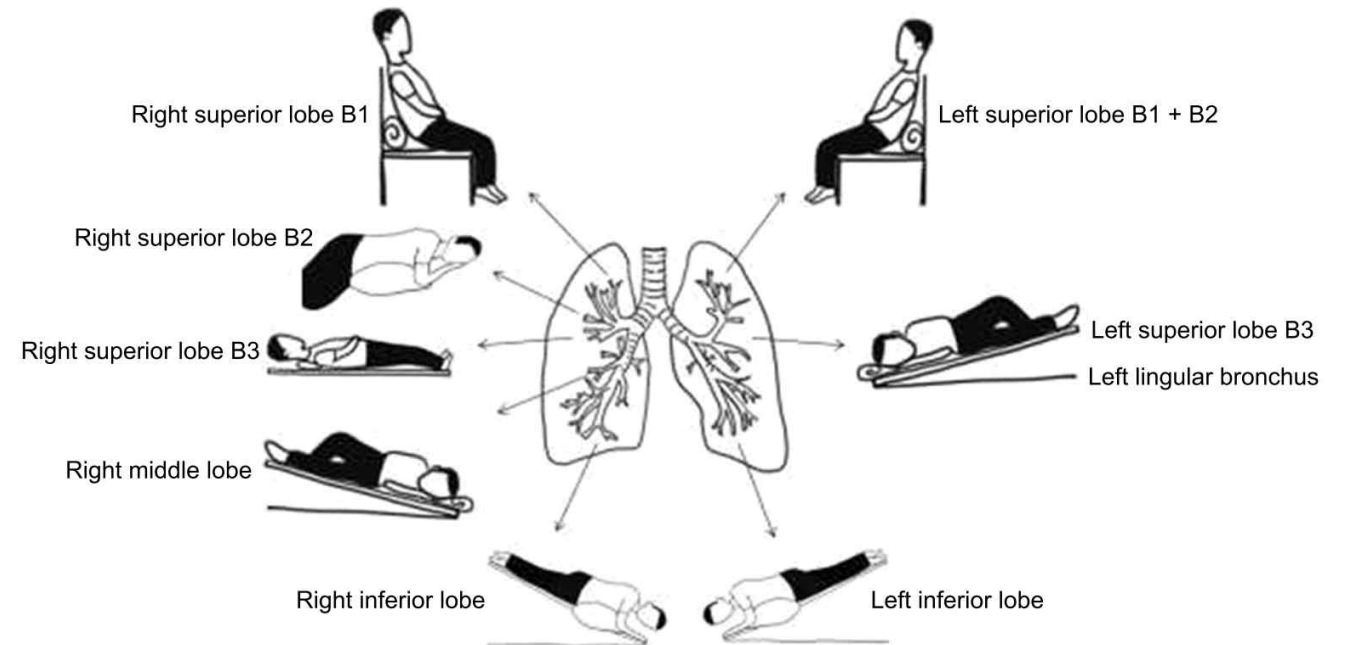
Persistent CB



Non-pharmacologic therapies

- Physiotherapy

- EDBC
- Chest percussion
- Postural expectoration



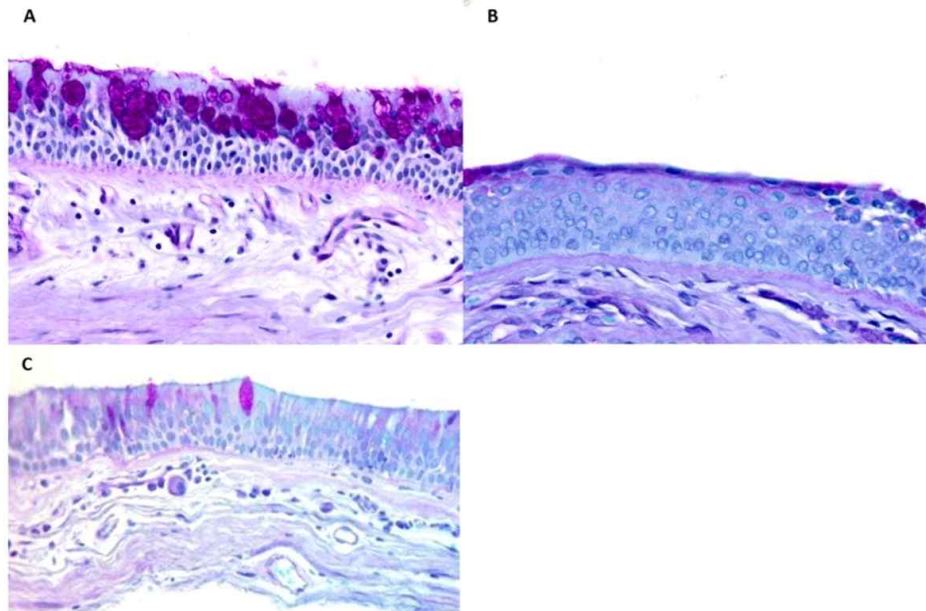
New interventional treatments

- Bronchial rheoplasty
- Metered Cryospray

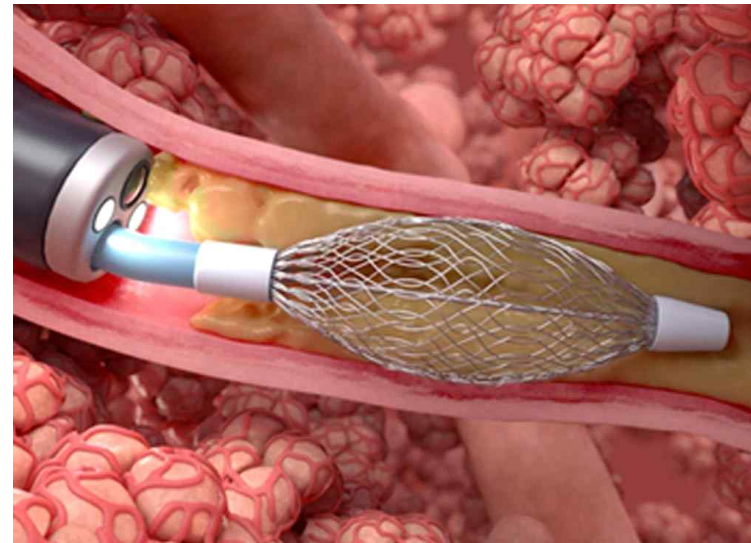
Bronchial Rheoplasty

- Non-thermal, pulsed electric field
→ Ablation of mucus-producing airway cells

Figure 1: Endobronchial histology from a patient treated with Bronchial Rheoplasty



Legend: PAS stained section of the right bronchus intermedius of subject 001-002. The goblet cells are typified by the magenta cytoplasmic vacuoles seen in the most superficial epithelial layer. On Day 0 immediately before therapy (Panel A) significant goblet cell hyperplasia can be seen (semi-quantitative assessment score of 2). At 30 days (Panel B), the epithelium demonstrates squamous metaplasia, indicating a regenerative process. Right bronchus intermedius at 120 days after the initial treatment (Panel C), demonstrating complete regeneration of pseudostratified columnar epithelium with a resolution of goblet cell hyperplasia (semi-quantitative assessment score of 0)



Bronchial Rheoplasty for Treatment of Chronic Bronchitis Twelve-Month Results from a Multicenter Clinical Trial

Arschang Valipour¹, Sebastian Fernandez-Bussy^{2,3}, Alvin J. Ing⁴, Daniel P. Steinfert^{5,6}, Gregory I. Snell⁷, Jonathan P. Williamson⁴, Tajalli Saghaie⁴, Louis B. Irving^{5,6}, Eli J. Dabscheck⁷, William S. Krimsky^{8,9}, and Jonathan Waldstreicher⁹

¹Karl Landsteiner Institute for Lung Research and Pulmonary Oncology, Vienna, Austria; ²Division of Pulmonary Medicine, German Clinic of Santiago, Chile; ³Department of Pulmonary Medicine, Mayo Clinic, Jacksonville, Florida; ⁴MQ Health, Macquarie University Hospital, Sydney, New South Wales, Australia; ⁵Department of Medicine, University of Melbourne, Parkville, Victoria, Australia; ⁶Department of Respiratory Medicine, Royal Melbourne Hospital, Parkville, Victoria, Australia; ⁷Department of Respiratory Medicine, Alfred Hospital, Melbourne, Australia; ⁸Medstar Franklin Square Medical Center, Baltimore, Maryland; and ⁹Gala Therapeutics, Menlo Park, California

- Two prospective, multicenter, single-arm clinical studies under two nearly identical protocols, (Australia, Austria and Chile)

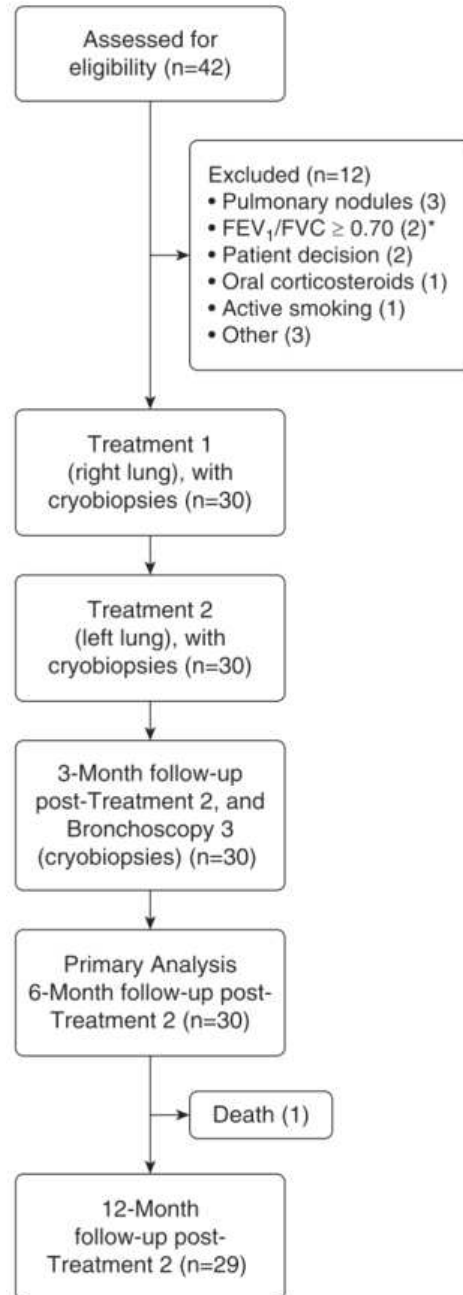
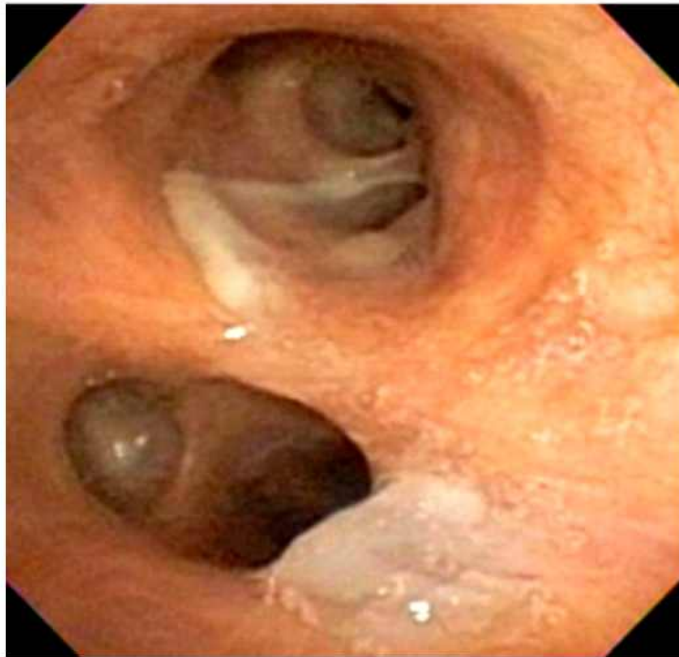


Table 1. Patient Demographics, Baseline Clinical Characteristics, and Medications

Characteristic	Value (N = 30 Patients)
Age, yr	67 (7.4)
Sex, M, n (%)	19 (63.3)
BMI, kg/m ²	27.5 (4.7)
Smoking history, pack-years	40.7 (26.5)
FEV ₁ % predicted*	65.0 (21.2)
FEV ₁ /FVC ratio*	0.53 (0.14)
Airflow obstruction, n (%)	
CB w/o airflow obstruction	4 (13.3)
GOLD I	4 (13.3)
GOLD II	13 (43.3)
GOLD III	9 (30.0)
TLC% predicted*	111.6 (14.2)
RV% predicted*	142.2 (39.8)
RV/TLC*	48.7 (10.1)
Emphysema, % (-950 HU)	8.0 (9.2)
6MWT, m [†]	443.2 (92.4)
CAT total score	25.6 (7.1)
CAT phlegm score	4.1 (0.8)
CAT cough score	3.6 (0.9)
SGRQ total score	59.6 (15.3)
SGRQ symptoms score	76.1 (13.4)
Inhaled pharmacologic treatment, n (%)	
Short-acting only	2 (6.7)
LABA/LAMA/ICS, LABA/LAMA, LABA only, LAMA only	27 (90.0)
ICS only	1 (3.3)
Oral roflumilast, n (%)	3 (10)

Pre-Treatment



1 Month After Bronchial Rheoplasty

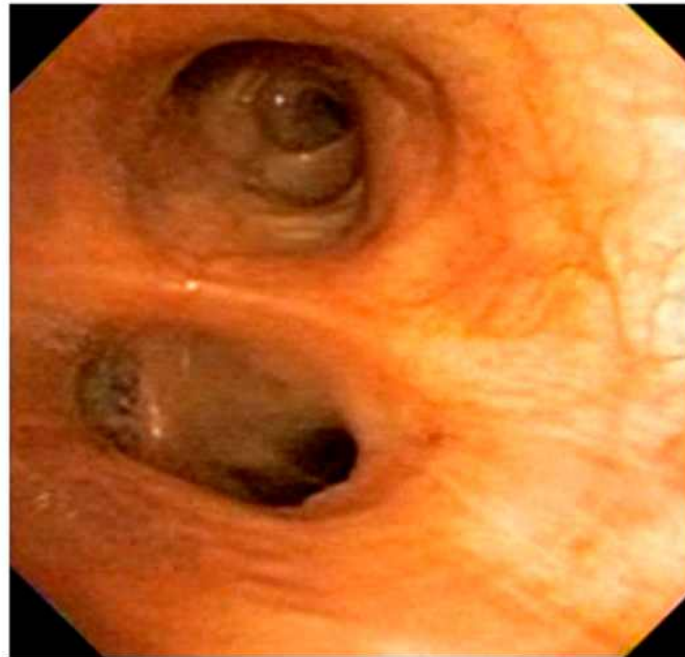
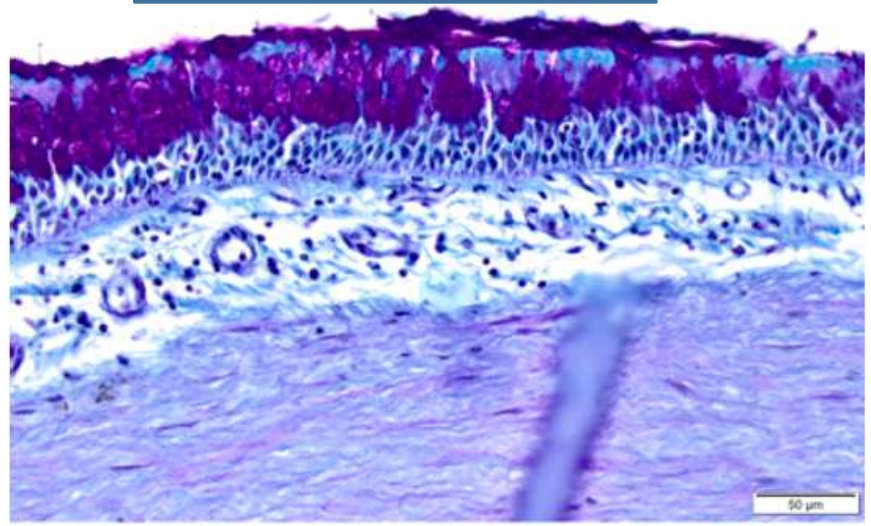


Figure 2. Pre- and post-treatment bronchoscopic images from a study patient. Note the thick mucus before treatment, with resolution after treatment. The images show the endoscopic view of the left upper lobe carina with both upper and lower lobe airways visible.

A Initial



B 120 days later

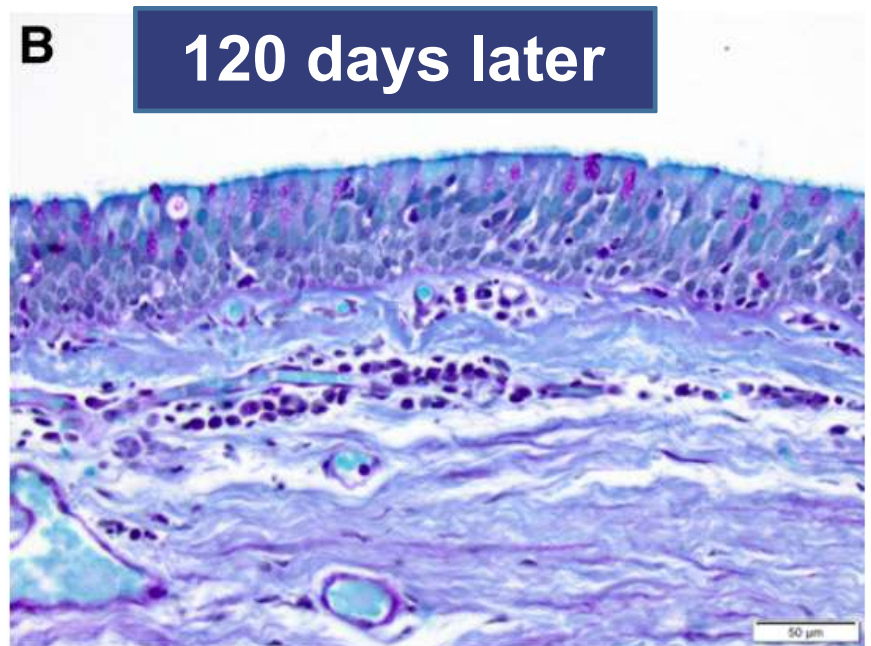


Table 3. Histopathology Results: Goblet Cell Hyperplasia Scores

Statistics	Baseline	Follow-up	Change from Baseline
N (lungs biopsied)	54	54	
Mean score (SD)	1.48 (0.91)	0.91 (0.81)	-0.57*
95% CI	1.23 to 1.73	0.69 to 1.13	-0.83 to -0.32

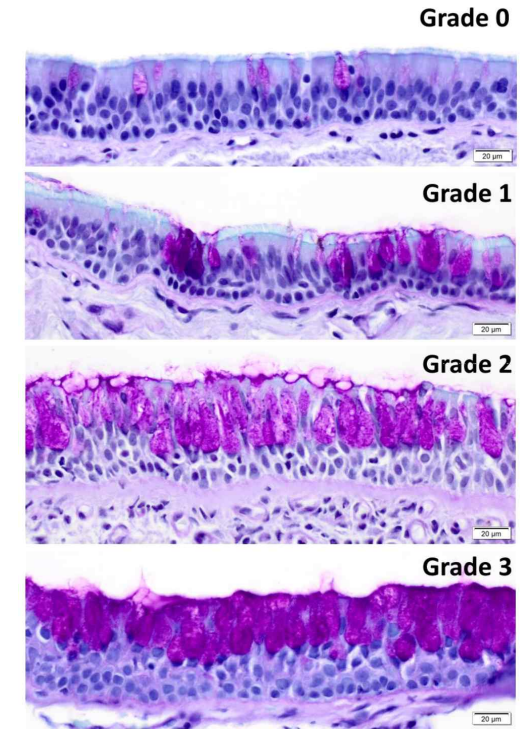


Table 4. Goblet Cell Hyperplasia Score: Change by Baseline Score

Baseline Goblet Cell Hyperplasia Score* (N = 54 Airway Biopsies)	Improved	No Change	Worsened
0	0	5	2
1	6	13	3
2	14	2	1
3	7	1	0

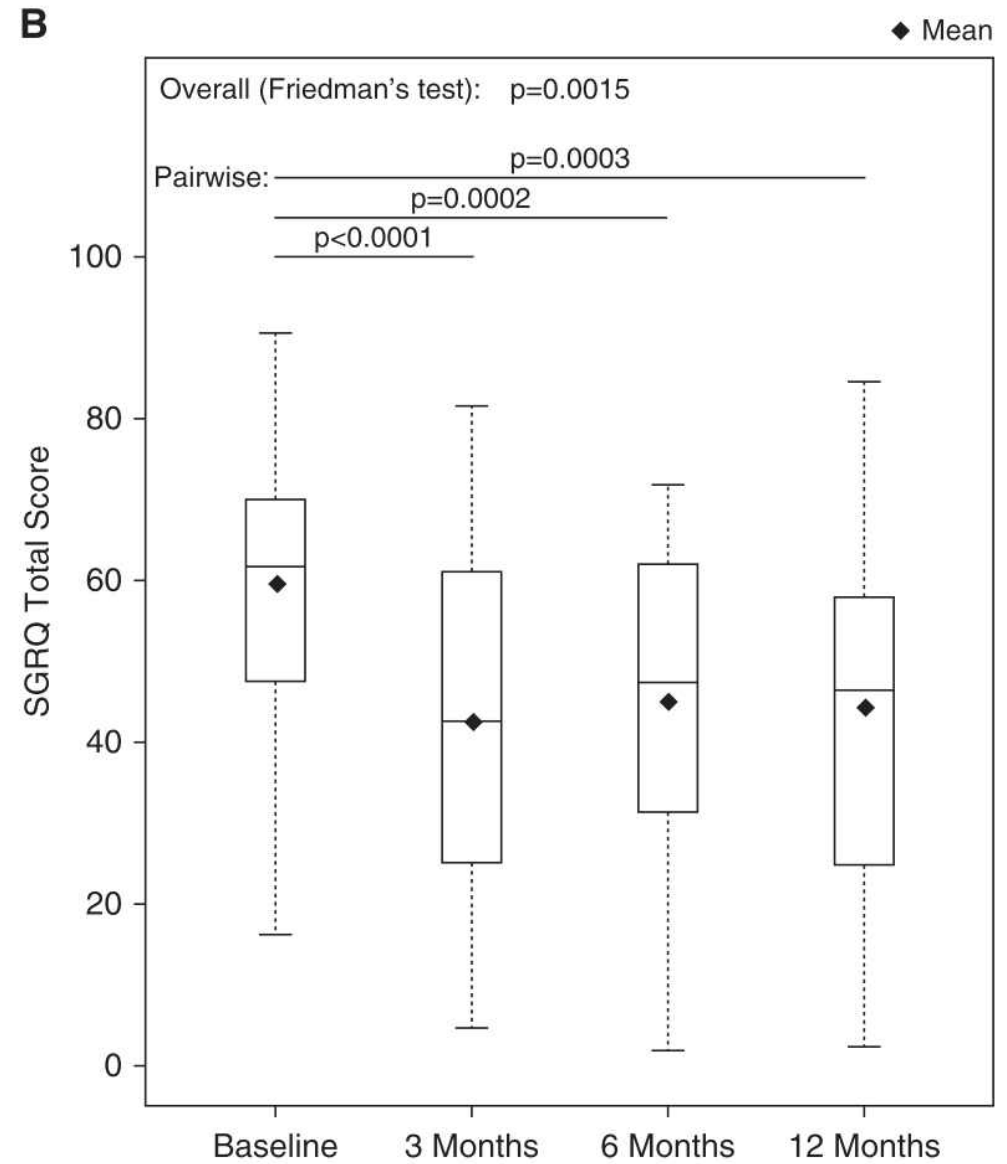
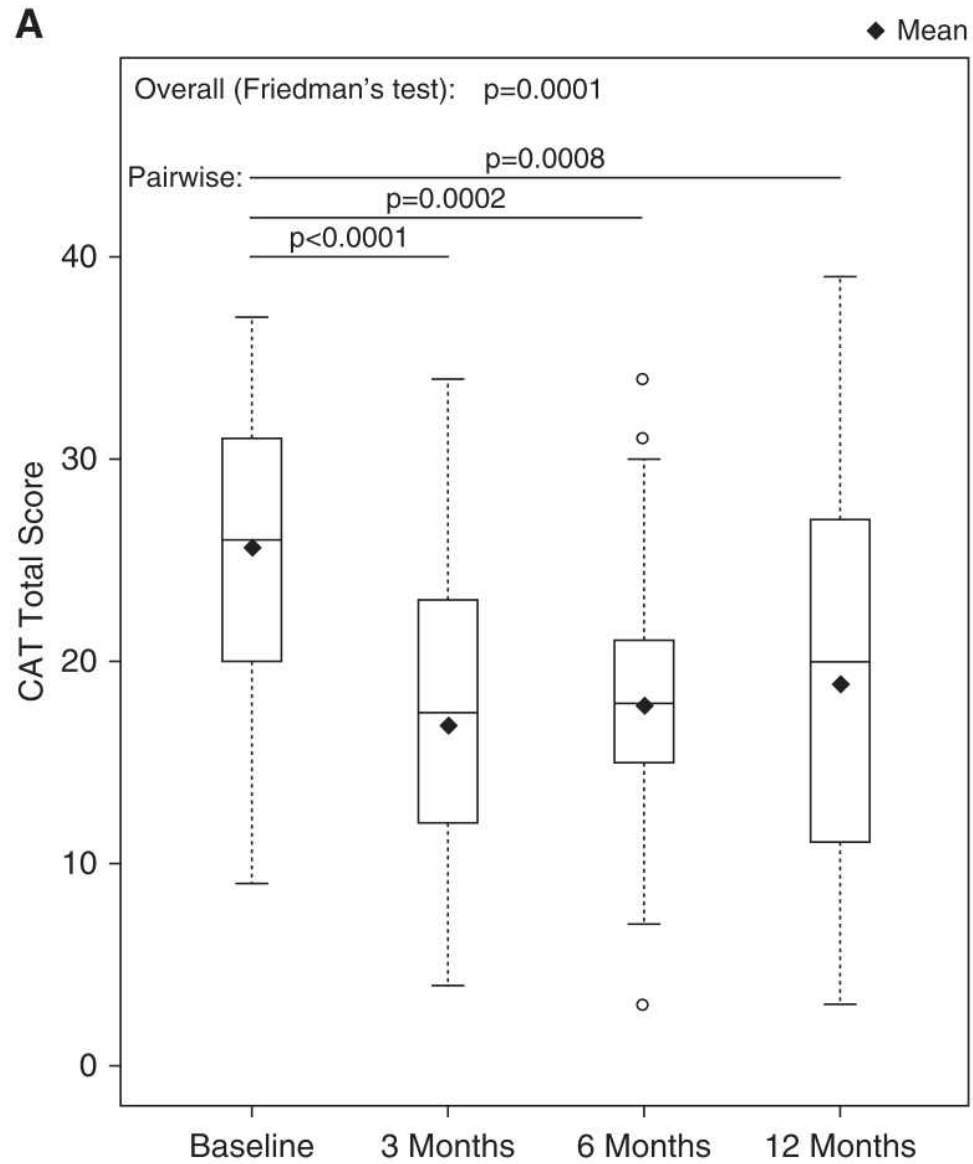
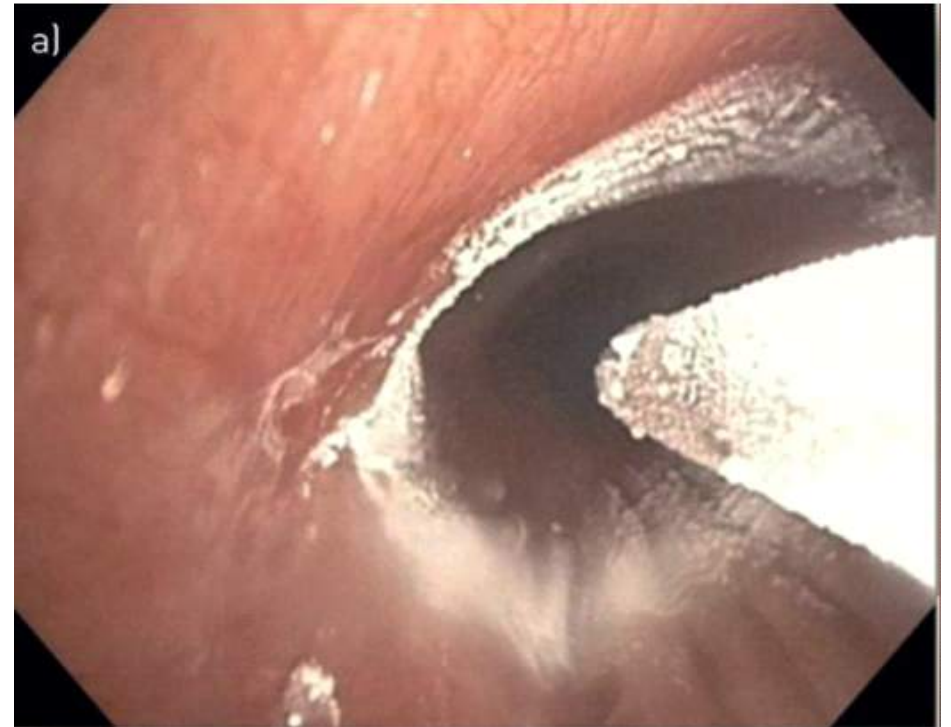


Figure 4. Quality-of-life outcomes. The 3-, 6-, and 12-month time points are in relation to the second treatment procedure. Box plots indicate minimum, first-quartile, median (solid horizontal line), third-quartile, and maximum values. Diamonds indicate mean values. (A) Total CAT score. (B) Total SGRQ score. CAT = Chronic Obstructive Pulmonary Disease Assessment Test; SGRQ = St. George's Respiratory Questionnaire.

Metered Cryospray

- RejuvenAir System Metered Cryospray

- 1) Destroy abnormal surface epithelium with mucin-producing goblet cell hyperplasia
- 2) Promote normal ciliated bronchial epithelium regrowth without goblet cell hyperplasia
- 3) Reduce chronic inflammation and associated airway constriction





ORIGINAL ARTICLE
COPD

A prospective safety and feasibility study of metered cryospray for patients with chronic bronchitis in COPD

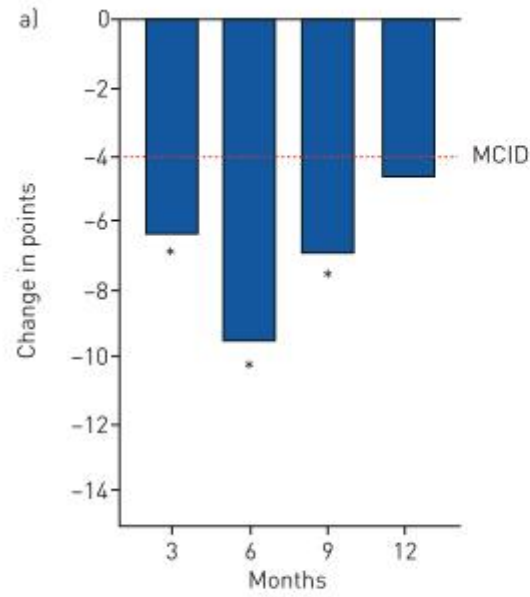
Justin L. Garner^{1,2,3}, Tawimas Shaipanich⁴, Jorine E. Hartman ⁵,
Christopher M. Orton^{1,2,3}, Cielito Caneja^{1,3}, Karin Klooster⁵, John Thornton³,
Don D. Sin⁴, Dirk-Jan Slebos ⁵ and Pallav L. Shah ^{1,2,3}

- Prospective open-label single-arm
- Multicenter study (UK, Neitherland, Canada)

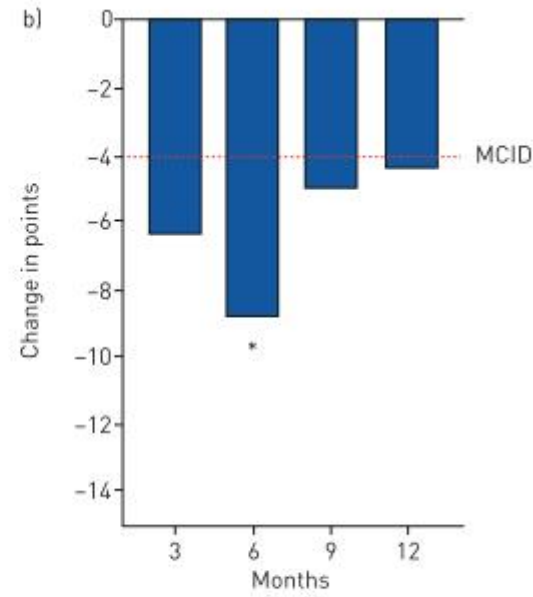
TABLE 1 Baseline characteristics of patients

Demographics		
Age years	35	67.2±7.0
Male %	19	54.3
BMI kg·m ⁻²	35	26.9±5.2
Smoking pack-years	35	45 (33 to 68)
Comorbidities	35	2 (1 to 4)
GOLD grade %		
I	3	8.5
II	10	28.5
III	22	63.0
Baseline medications %		
β-agonist	18	51.4
Anticholinergic	18	51.4
Corticosteroid	17	48.6
Mucolytic	6	17.1
Antibiotic	11	31.4
Lung function		
FEV ₁ L	35	1.4±0.5
FEV ₁ % predicted	35	50.2±14.5
FVC L	35	3.6±1.0
FVC % predicted	35	103.6±16.9
FEV ₁ /FVC % predicted	35	38.5±10.1
FIV ₁ L	25	3.2±0.9
R _{aw} kPa·s·L ⁻¹	27	0.6±0.3
Exercise capacity		
6MWD m	35	400.6±86.8
Symptoms		
mMRC	35	2 (2 to 3)
CAT [#]	34	22.7±7.1
SGRQ		
Total	35	59.2±18.9
Symptoms		66.5±20.5
Impacts		48.3±22.4
Activity		74.1±19.0
LCQ	23	85.0±27.7
VAS [#]		
Rest	34	36.1±28.7
Activity	34	68.6±23.9
Mortality score		
BODE index	35	3 (2 to 4)
Inflammatory marker		
Plasma fibrinogen mg·dL ⁻¹	35	341.1±72.5

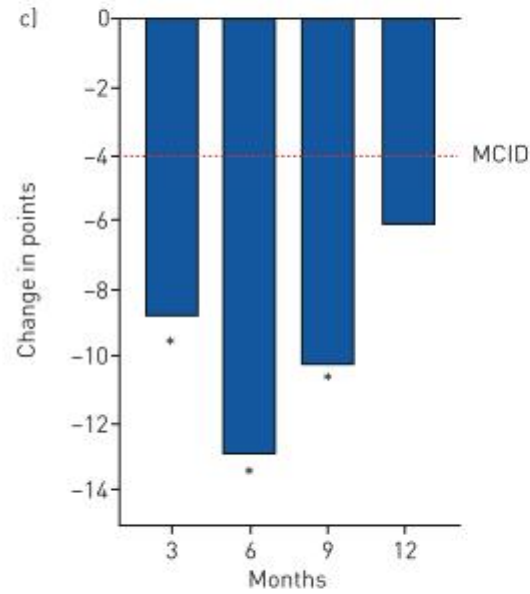
Total
SGRQ



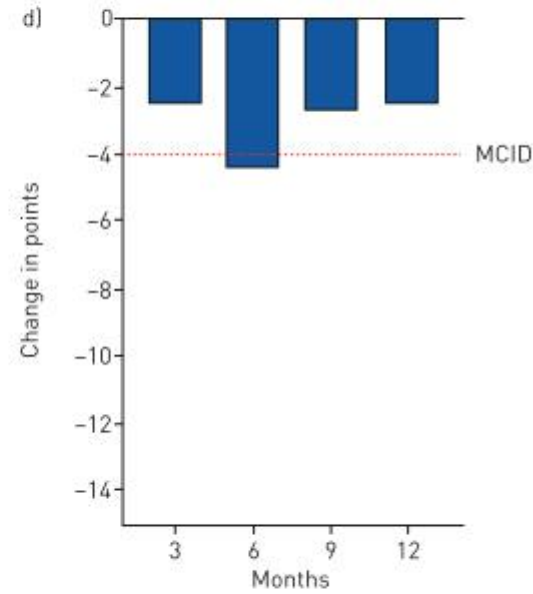
SGRQ
symptom



SGRQ
impact

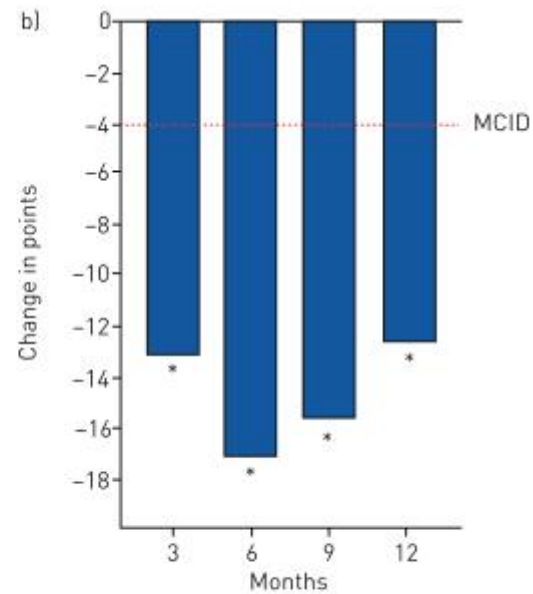
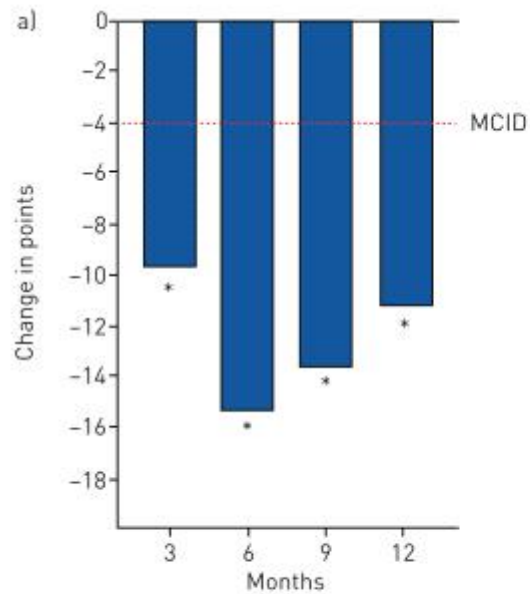


SGRQ
activity



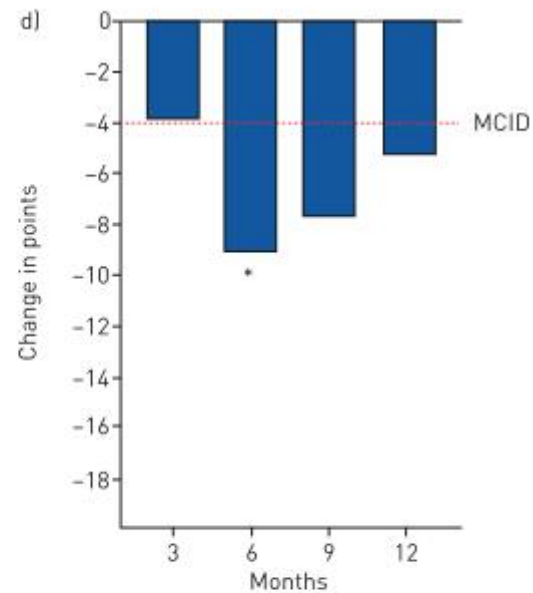
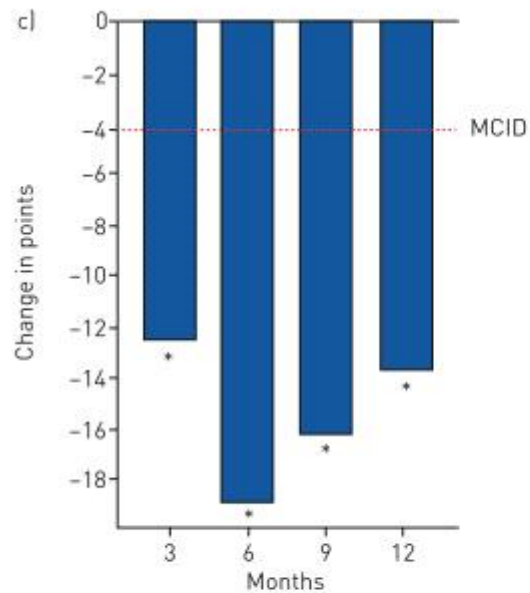
Baseline
SGRQ > 50

Total
SGRQ



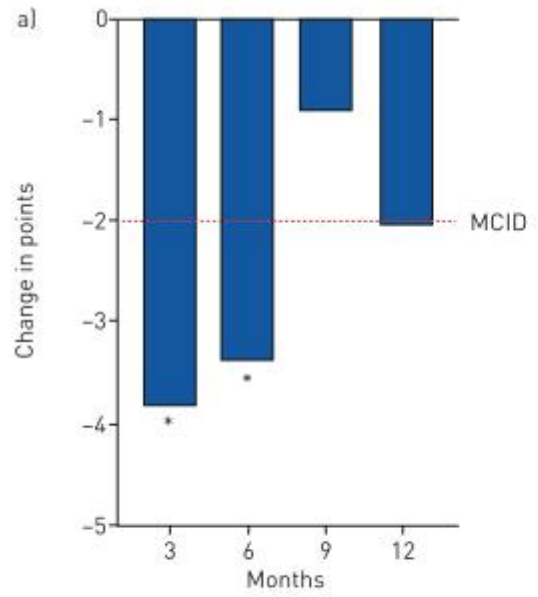
SGRQ
symptom

SGRQ
impact

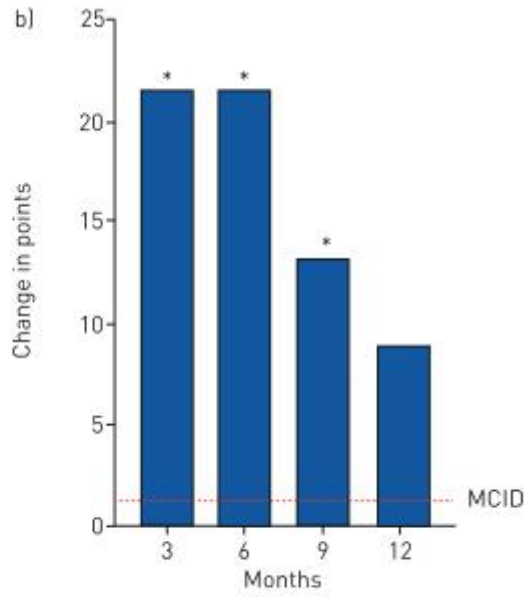


SGRQ
activity

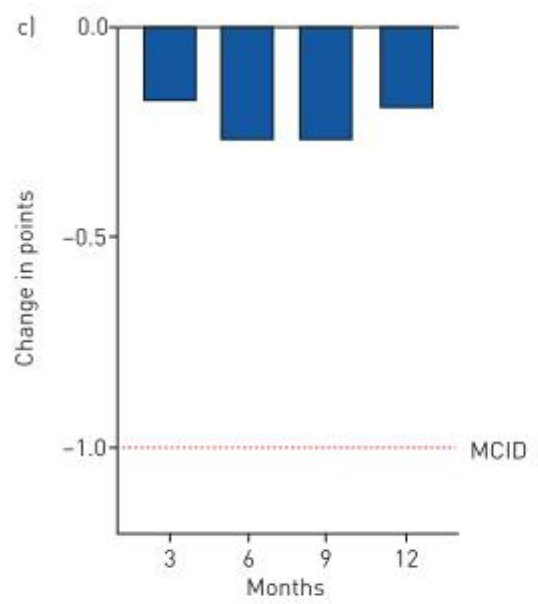
CAT



Leicester Cough Questionnaire



mMRC



Visual analogue scale

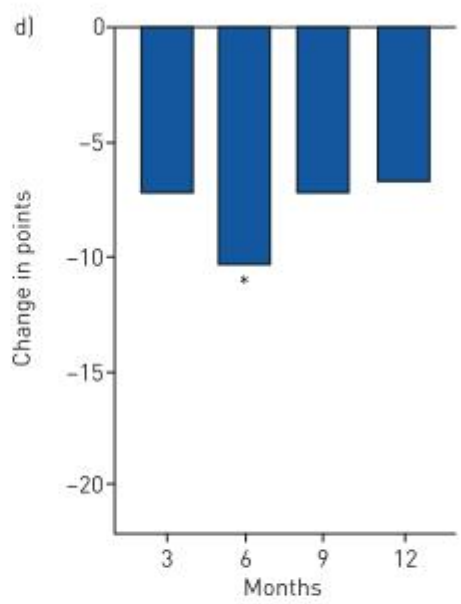


TABLE 2 Changes in clinical characteristics over 12 months

	3 months	p-value	6 months	p-value	9 months	p-value	12 months	p-value
Lung function								
Δ FEV ₁ mL	-33.2±166.9 [-91.5 to 25.0]	0.25					-96.5±197.7 [-169.0 to -23.9]	0.01
Δ FEV ₁ %	-0.7±5.7 [-2.7 to 1.3]	0.45					-2.4±6.5 [-4.8 to 0.0]	0.05
Δ FVC mL	-125.9±330.4 [-241.2 to -10.6]	0.03					-191.3±483.7 [-368.7 to -13.9]	0.04
Δ FVC %	-3.1±9.5 [-6.4 to 0.2]	0.06					-2.8±13.0 [-7.6 to 2.0]	0.24
Δ FEV ₁ /FVC %	0.3±10.6 [-3.5 to 4.0]	0.89					-0.9±3.6 [-2.2 to 0.4]	0.18
Δ FIV ₁ mL	-175.8±389.5 [-340.3 to -11.4]	0.04					-66.2±371.1 [-235.1 to 102.7]	0.42
Δ VC L	1.2±6.6 [-1.4 to 3.9]	0.35					-0.1±0.4 [-0.3 to 0.1]	0.49
ΔR_{aw} kPa·s·L ⁻¹	0.1±0.3 [-0.1 to 0.2]	0.28					0.0±0.2 [-0.1 to 0.2]	0.33

- Device-associated SAE : none

- Exacerbation rate ↓

- GOLD II : 1.29 ← 2.68

- GOLD III : 2.10 ← 3.43

(compared to untreated similarly matched individuals)

Eur Respir J 2003; 22: 931–936

- Effect on HrQOL may be superior compared to mucolytics, prophylactic antibiotics, inhaled bronchodilators and steroids

Cochrane Database Syst Rev 2015; 7: CD001287. Cochrane Database Syst Rev 2018; 10: CD009764.

Cochrane Database Syst Rev 2018; 12: CD012620

Garner J et al. ERJ 2020; 56: 2000556

SUMMARY

1. Definition of chronic bronchitis
 - Classic vs SGRQ vs CAT definition
2. Risk factors
 - Cigarette smoking / E-cigarette
 - Early life disadvantages
3. Pathophysiology
 - Two gel theory / Total mucin/ MUC5AC
4. Clinical implications
 - Poor HrQOL, low lung function, frequent exacerbation, higher mortality
5. Treatments
 - New interventional treatments