

GOLD COPD Definition Is Not Sufficient



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Disclosures

Advisory board, consultant, multi-center trial, research funding, DSMB, royalties or speaker in the last year on topics related to COPD:

National Heart, Lung, and Blood Institute

Department of Defense

AstraZeneca

Circassia

Phillips

Takeda

Verona

American Lung Association

Boehringer-Ingelheim

GlaxoSmithKline

Sunovion

Up-To-Date

Walters Kluwer

No relationships with tobacco companies

Learning Objectives

- Define COPD using GOLD strategy
- Describe the respiratory abnormalities in smokers without classic airflow obstruction
- Modify your approach to incorporate the new COPDGene® 2019 COPD diagnosis

COPD Definition, GOLD 2020

Is this definition satisfactory for you?

- A common, preventable, treatable disease
- Characterized by persistent respiratory symptoms
- Characterized by persistent airflow limitation
- Due to airway and alveolar abnormalities
- Usually caused by exposure to noxious particles or gases

Primary diagnostic criterion:

airflow obstruction / post BD spirometry

Does Tina have COPD?

54 year old admitted to the hospital with shortness of breath
Can't catch her breath walking up 4 steps into the house
Cough and phlegm for 4 days
Yellow phlegm; cough keeps her awake at night
"Chest cold" once a year; resolve without treatment
Wakes in the morning with some coughing and phlegm
No history of asthma or lung problems
Current cigarette smoker; started at 16 = 38 pack-years
HR 110, RR 25, BP 150/94, O2 sat 88%
Wheezing on exam
No crackles or edema

Tina Is Treated For COPD

ABG: PaO₂ 54, PaCO₂ 32, pH 7.45

EKG – sinus tachycardia. Cardiac echo – normal LVEF.

Chest CT scan – no pneumonia, no PE.

+ emphysema and airway thickening

Treated for COPD exacerbation

Responds to treatment; SaO₂ 92% on RA, wheezes disappear

Discharged after 3 days

Does Tina have COPD?

Spirometry post-bronchodilator one month later:

FEV₁/FVC 0.71

FVC 82% predicted

FEV₁ 77% predicted

No significant bronchodilator response

Interpretation:

No airflow obstruction

Mildly reduced FEV₁

Normal spirometry

COPD Diagnostic Criteria

1 – Persistent airflow limitation

“spirometry post-bronchodilator is required to make a diagnosis”

2 – Risk factors (smoking)

3 – ? persistent respiratory symptoms

4 – ? absence of other diseases

Tina does NOT have COPD by GOLD criteria

▶ PATHWAYS TO THE DIAGNOSIS OF COPD

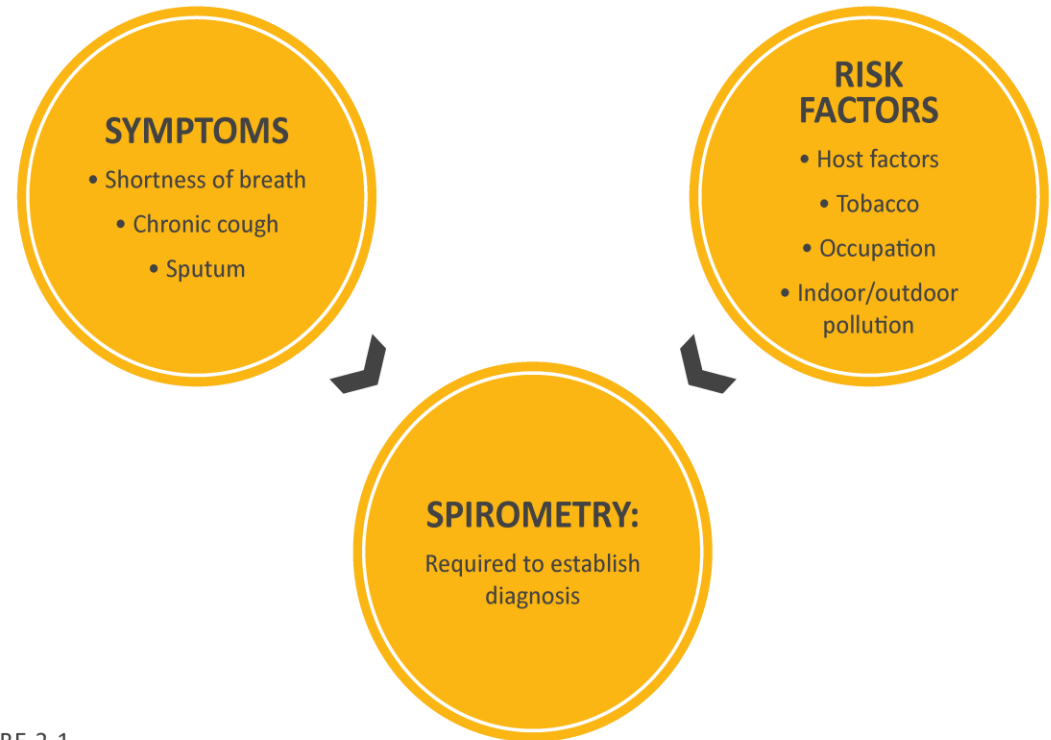


FIGURE 2.1

Barry Make modified from

Global Strategy for Diagnosis, Management and Prevention of COPD. GOLD, 2019. www.goldcopd.com

COPDGene® Participants

A Cohort of Current and Former Cigarette Smokers

Inclusion criteria:

Age 45 – 80

≥ 10 pack-year cigarette smoking history

Non-Hispanic White and African American

Exclusion criteria: minimal to enhance recruitment

Recent COPD exacerbation

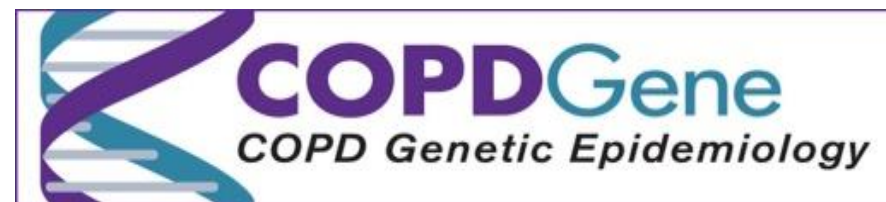
Lung surgery ≥ 1 lobe

Lung cancer, other uncontrolled cancers

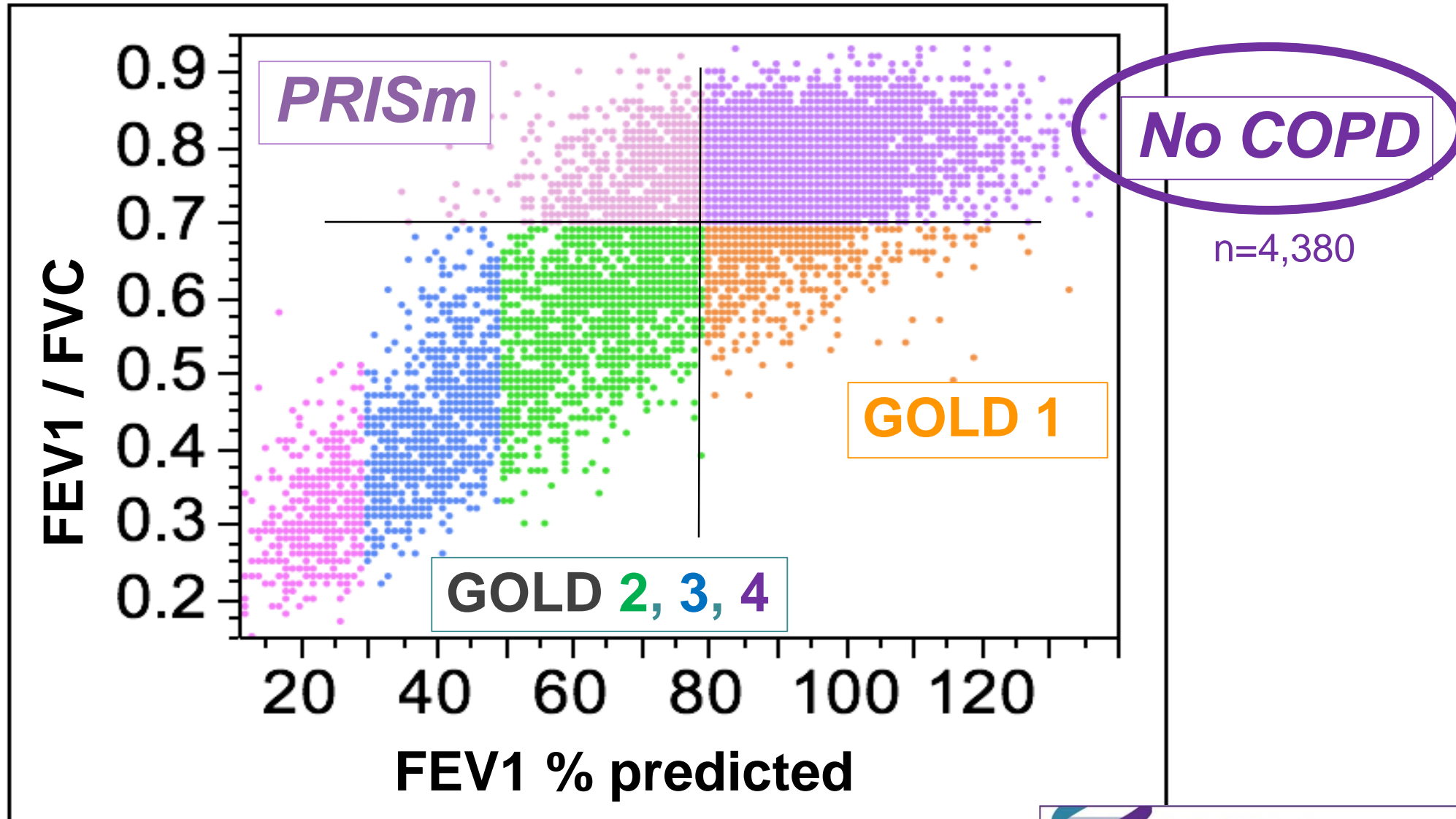
>10,000 subjects enrolled

NHLBI funded

>300 published manuscripts



Spirometry In COPDGene®



Smokers Without Airflow Limitation

Original Investigation

Clinical and Radiologic Disease in Smokers With Normal Spirometry

Elizabeth A. Regan, MD; David A. Lynch, MD; Douglas Curran-Everett, PhD; Jeffrey L. Curtis, MD; John H. M. Austin, MD; Philippe A. Grenier, MD; Hans-Ulrich Kauczor, MD; William C. Bailey, MD; Dawn L. DeMeo, MD; Richard H. Casaburi, PhD, MD; Paul Friedman, MD; Edwin J. R. Van Beek, MD; John E. Hokanson, PhD; Russell P. Bowler, MD; Terri H. Beaty, PhD; George R. Washko, MD; MeiLan K. Han, MD; Victor Kim, MD; Song Soo Kim, MD; Kunihiro Yagihashi, MD; Lacey Washington, MD; Charlene E. McEvoy, MD; Clint Tanner, MD; David M. Mannino, MD; Barry J. Make, MD; Edwin K. Silverman, MD; James D. Crapo, MD; for the Genetic Epidemiology of COPD (COPDGene) Investigators

JAMA Intern Med. doi:10.1001/jamainternmed.2015.2735

Published online June 22, 2015.

Impairment Definition

Symptoms

Chronic bronchitis

MMRC dyspnea ≥ 2

SGRQ health status > 25

Functional

6-minute walk distance $< 350\text{m}$

AECOPD history of ≥ 1 severe AECOPD in last year

Radiologic abnormalities

Emphysema $>5\%$

Gas trapping $>20\%$

No Airflow Obstruction Patients Are Slightly Less Impaired Than GOLD 1

	GOLD 0 (n = 4388)	GOLD 1 (n = 794)
Any Impairment	2375 (54.1)	585 (73.7)
6 Impairments	8 (0.2)	6 (0.8)
5 Impairments	32 (0.7)	17 (2.1)
4 Impairments	156 (3.6)	65 (8.2)
3 Impairments	414 (9.4)	92 (11.6)
2 Impairments	690 (15.7)	204 (25.7)
1 Impairment	1089 (24.8)	201 (25.3)
No Impairment	1990 (45.4)	209 (26.3)

Smoking History With No Airflow Obstruction

54% are impaired - they are ill

Respiratory symptoms: 25%

Impaired health status: 25%

Severe acute respiratory events (AECOPD): >4%

Functional impairment: 15%

Radiologic evidence of lung disease: 20%

Receiving respiratory medications: 20%

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ESTABLISHED IN 1812

MAY 12, 2016

VOL. 374 NO. 19

Clinical Significance of Symptoms in Smokers with Preserved Pulmonary Function

Prescott G. Woodruff, M.D., R. Graham Barr, M.D., Dr.P.H., Eugene Bleeker, M.D., Stephanie A. Christenson, M.D., David Couper, Ph.D., Jeffrey L. Curtis, M.D., Natalia A. Gouskova, Ph.D., Nadia N. Hansel, M.D., Eric A. Hoffman, Ph.D., Richard E. Kanner, M.D., Eric Kleerup, M.D., Stephen C. Lazarus, M.D., Fernando J. Martinez, M.D., Robert Paine, III, M.D., Stephen Rennard, M.D., Donald P. Tashkin, M.D., and MeiLan K. Han, M.D., for the SPIROMICS Research Group*



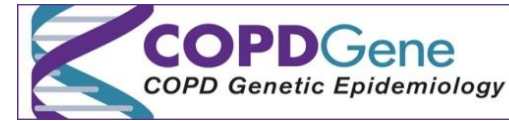
Respiratory Medication Use



Symptomatic ever-smokers with no airflow obstruction

- 42% used bronchodilators
- 23% used inhaled corticosteroids

Chronic Bronchitis / COPD in COPDGene



1061 COPD GOLD Stage 2- 4 subjects
Of first 2500 COPDGene subjects

Chronic bronchitis: cough and sputum for ≥ 3 months a
year for ≥ 2 consecutive years (ATS respiratory
questionnaire)

290 with chronic bronchitis (CB +) and
771 without chronic bronchitis (CB -)

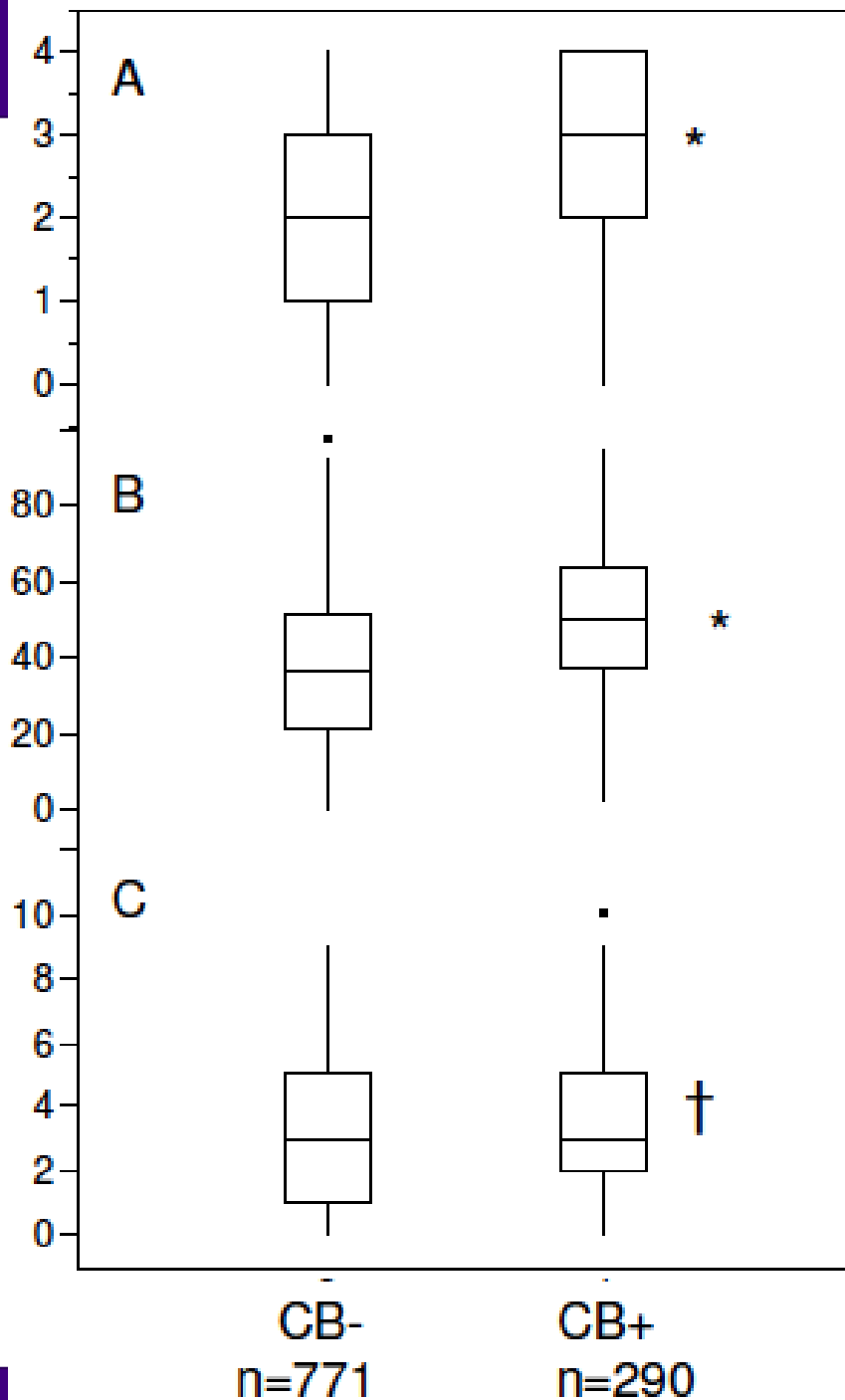
Impact of Chronic Bronchitis with Airflow Obstruction

**MMRC
Dyspnea
(2, 3)**

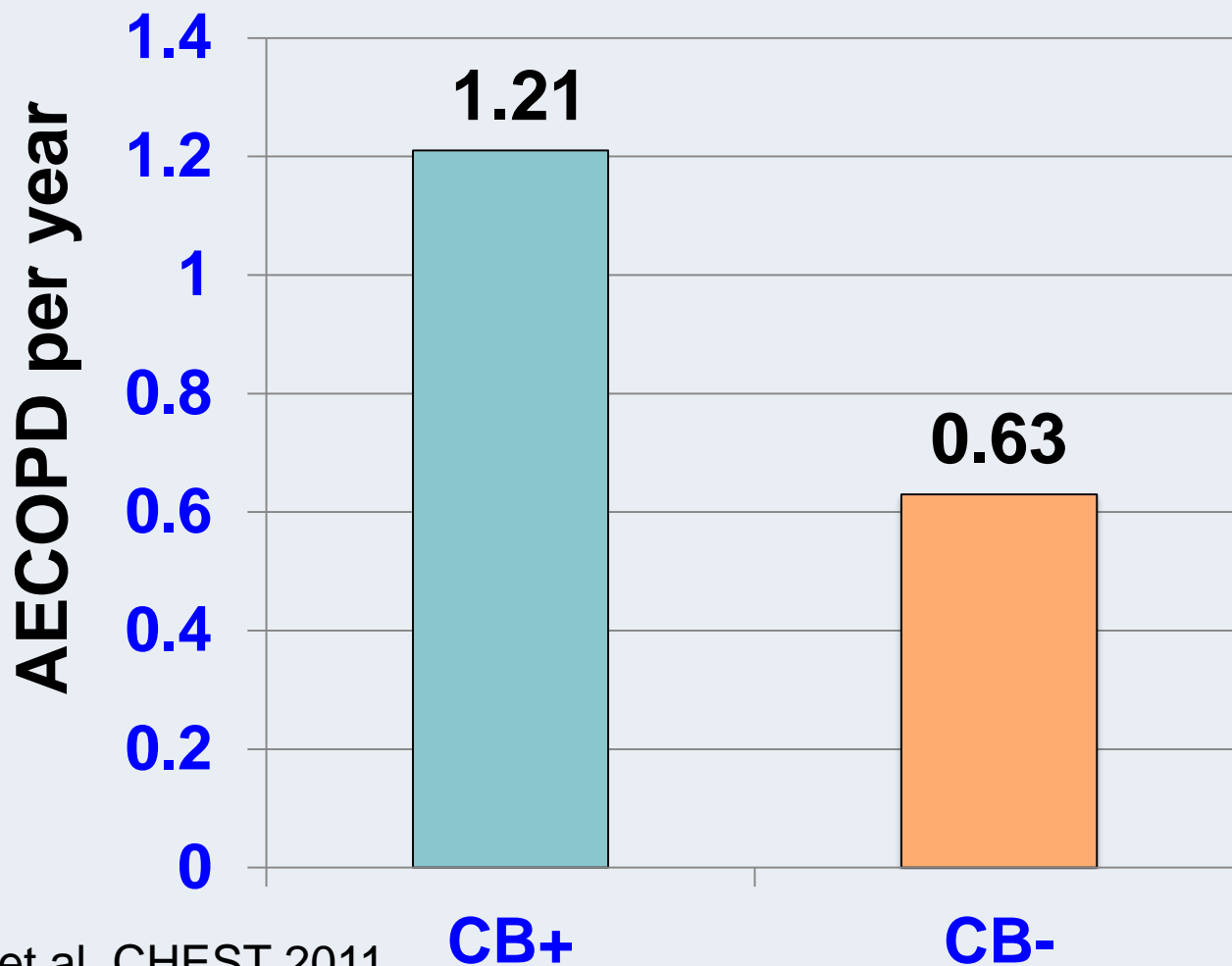
**SGRQ
Health
Status
(37, 50)**

**BODE
Index**

More dyspnea
Worse health status



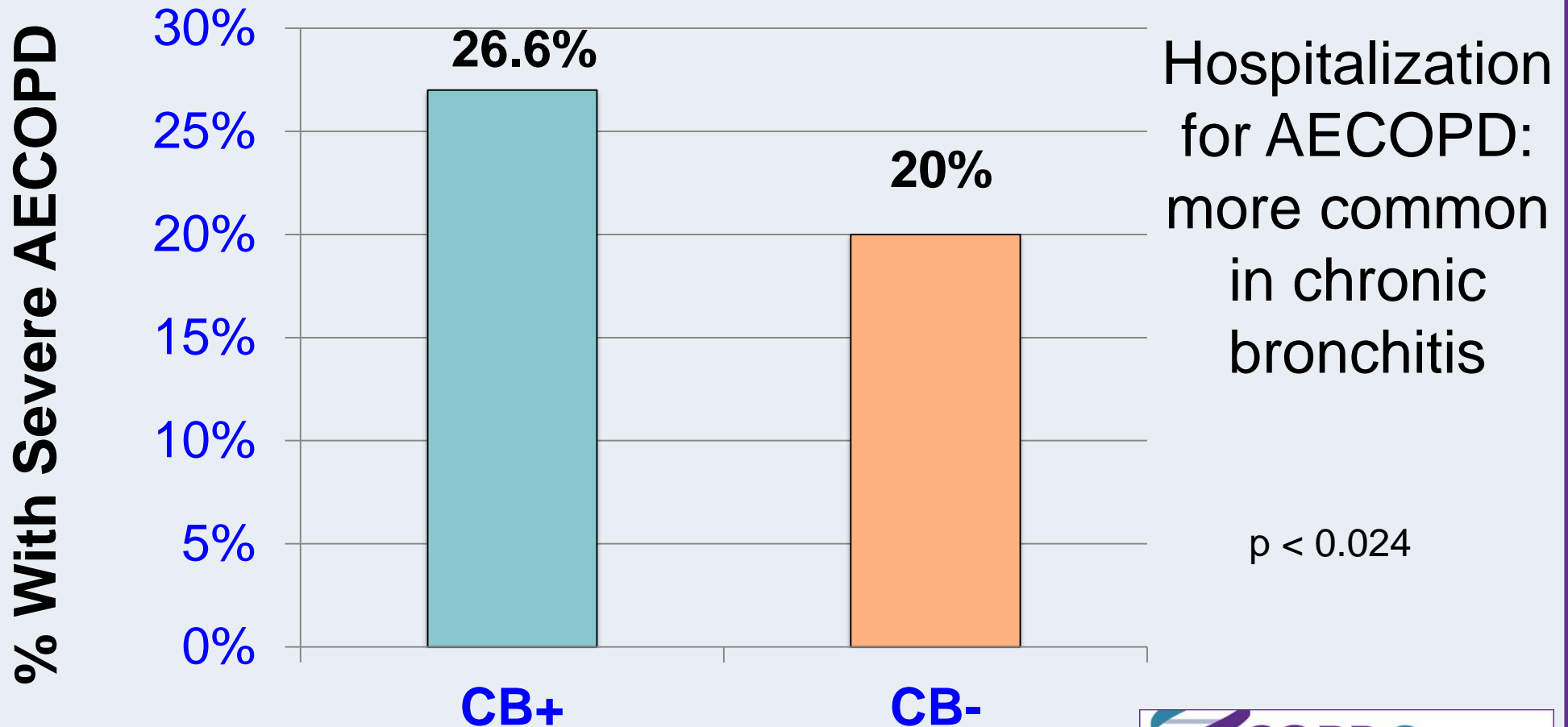
AECOPD Frequency In Chronic Bronchitis



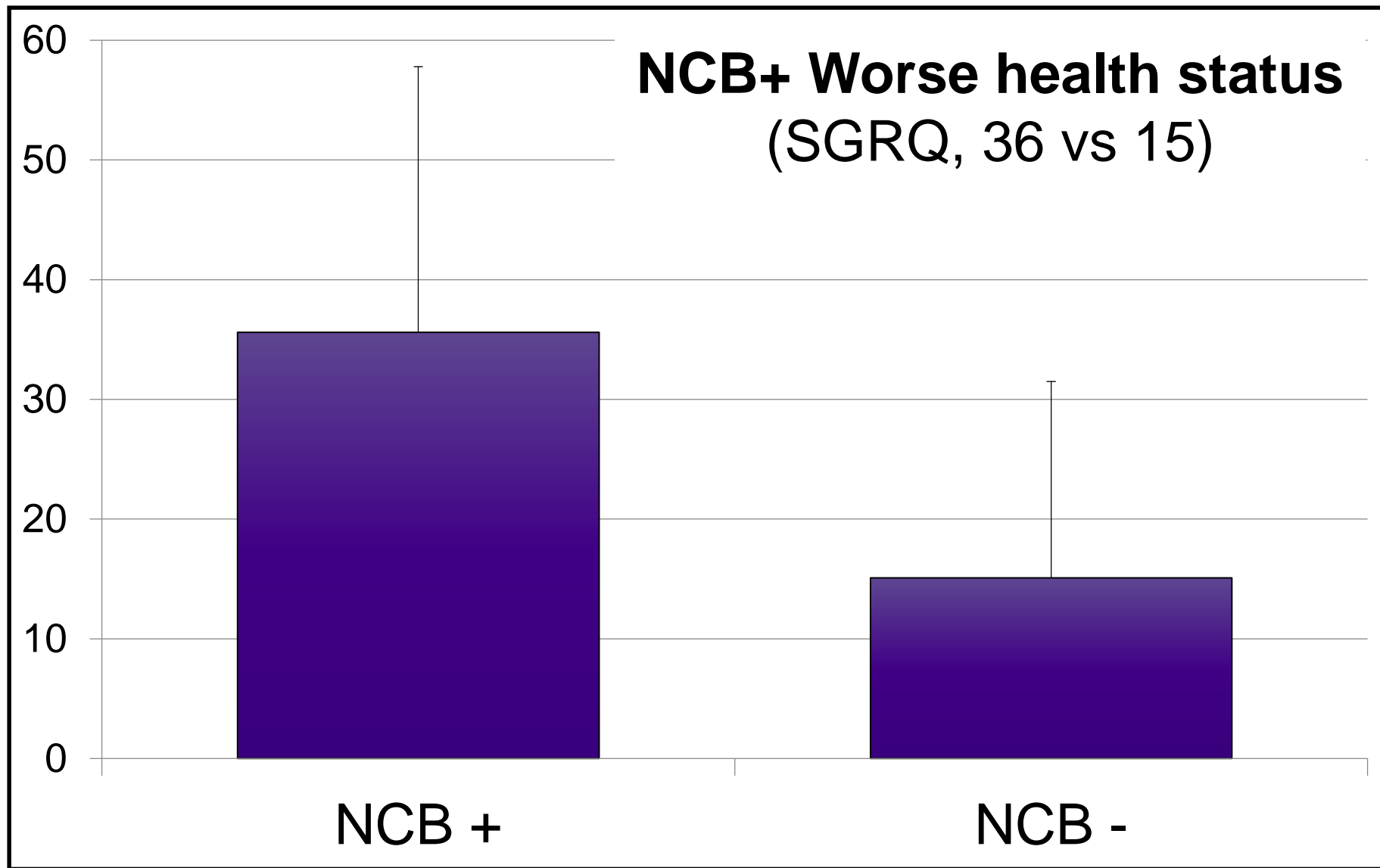
AECOPD:
almost twice as
frequent in
chronic
bronchitis

$p < 0.027$

Percentage of COPD Subjects With Severe AECOPD (hospitalization)



Non-Obstructive Chronic Bronchitis Health Status



Smoking History With No Airflow Obstruction

The Myth of the “Healthy Smoker” - without airflow obstruction:

Respiratory symptoms (chronic bronchitis), structural abnormalities, decreased walk distance, poor health status and exacerbations are common

Do smokers without airflow obstruction have COPD?

- Questions:
 - Do they progress?
 - What are other outcomes, e.g., mortality?
 - How should they be treated?

Hypothesis:

Integrated multi-faceted approach using all four cardinal COPD features

1. environmental exposure (cigarette smoking),
2. clinical symptoms (dyspnea, chronic bronchitis),
3. chest CT imaging (emphysema),
4. spirometry

Better defines disease and

Identifies important outcomes: spirometric progression and mortality



Chronic Obstructive Pulmonary Diseases: Journal of the COPD Foundation

Original Research

COPDGene® 2019: Redefining the Diagnosis of Chronic Obstructive Pulmonary Disease

Katherine E. Lowe, MSc¹ Elizabeth A. Regan, MD, PhD² Antonio Anzueto, MD³ Erin Austin, PhD⁴

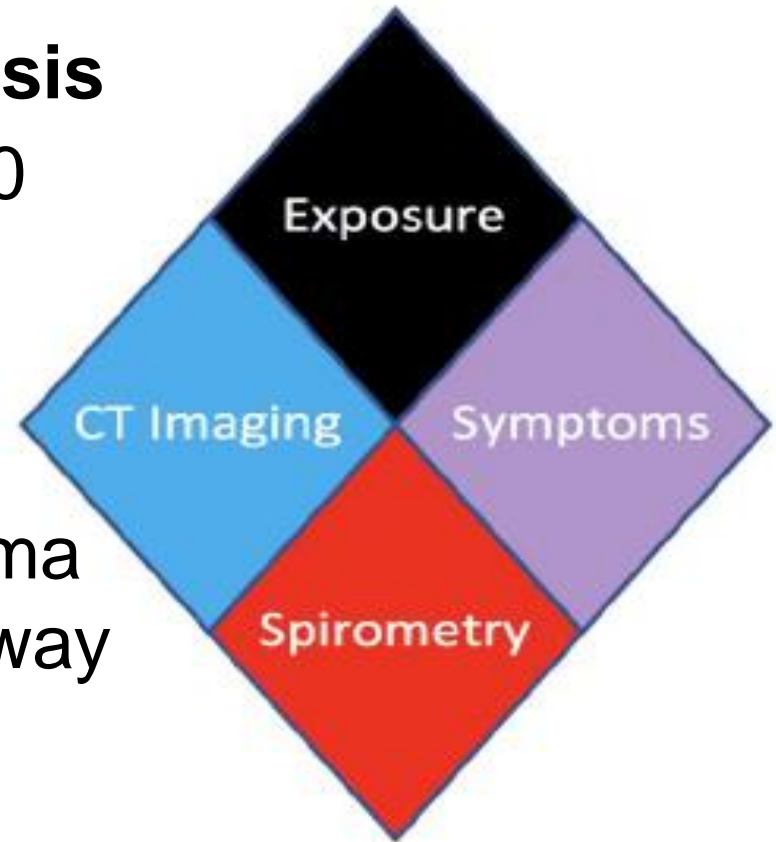
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<https://journal.copdfoundation.org>

Criteria for COPDGene 2019 diagnosis

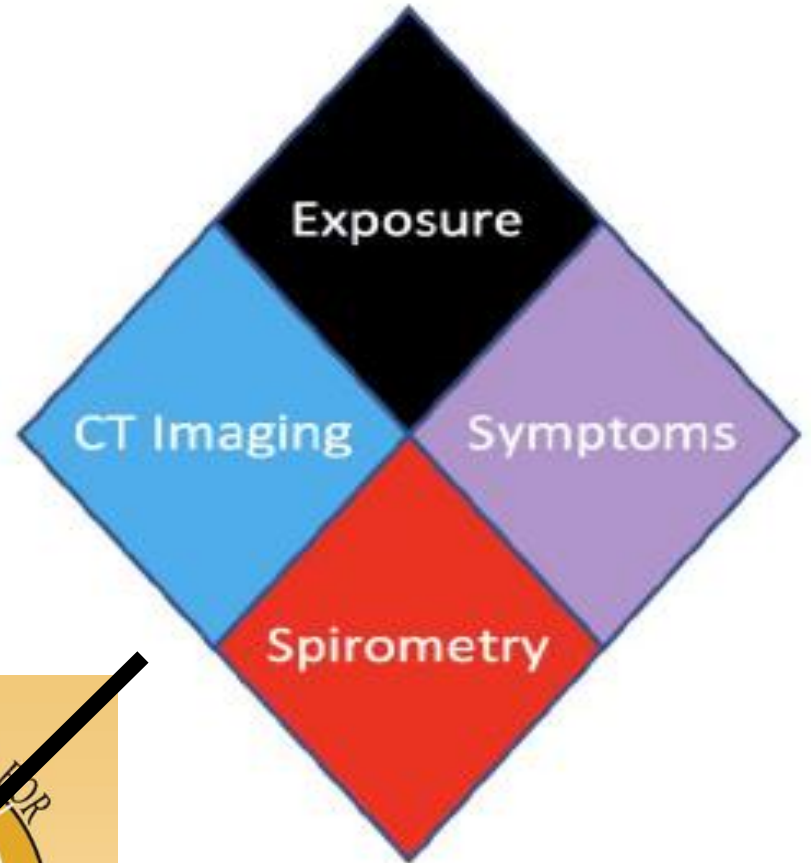
- **Exposure**: Cigarette smoking ≥ 10 pack-years
- **Symptoms**: mMRC dyspnea ≥ 2 or chronic bronchitis (ATS)
- **CT structural disease**: emphysema $\geq 5\%$, gas trapping $\geq 15\%$ or airway thickening
- **Abnormal spirometry**:
PRISm ($FEV_1/FVC < 0.70$, $FEV_1 < 80\%$)



DIAMOND COPDGene® 2019

DIAMOND COPDGene® 2019

”Diamonds are a girl’s best friend”



COPDGene 2019 Subgroups

Category	Description	Disease Features	
A	Exposure	1	
B	Exposure + CT	2	Possible COPD
C	Exposure + Symptoms	2	
D	Exposure + Spirometry	2	
E	Exposure + Symptoms + CT	3	Probable COPD
F	Exposure + Spirometry + Symptoms	3	
G	Exposure + Spirometry + CT	3	
H	Exposure + Spirometry + Symptoms + CT	4	Definite COPD

COPDGene 2019 COPD Progression & Mortality

	Sub-group	Odds FEV ₁ change >350 ml [95% CI]*	Hazard Ratio all-cause mortality (95% CI)#	
	A	1.0 (ref.)	1.0 (ref.)	NO COPD
	B	1.31 (1.04-1.65)	1.05 (0.76-1.44)	Possible COPD
	C	1.42 (1.07-1.88)	1.55 (1.09-2.19)	
	D	0.92 (0.64-1.30)	1.48 (1.03-2.12)	
	E	1.74 (1.28-2.36)	1.90 (1.33-2.71)	Probable COPD
	F	1.02 (0.66-1.60)	2.62 (1.84-3.72)	
	G	2.11 (1.66-2.68)	1.76 (1.36-2.27)	
	H	2.82 (2.18-3.66)	5.18 (4.15-6.48)	Definite COPD

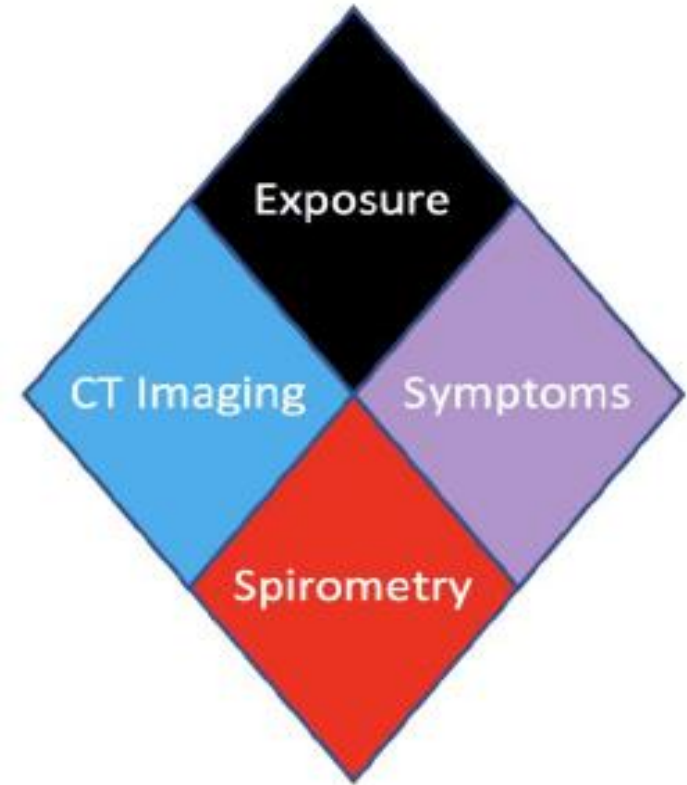
COPDGene 2019 Progression and Mortality

COPDGene 2019 Classification	Change in FEV ₁ >350 ml, odds ratio	All-cause mortality, hazard ratio
Reference	1.0	1.0
Possible COPD	1.26 (1.03-1.53)	1.28 (0.99-1.66)
Probable COPD	1.88 (1.52-2.32)	1.89 (1.48-2.41)
Definite COPD	2.82 (2.18-3.66)	5.18 (4.15-6.48)

Diamond COPD: COPDGene 2019

Integrated approach using

- **environmental exposure,**
- **clinical symptoms,**
- **chest CT imaging** and
- **spirometry**
- Better defines disease than spirometry alone
- Identifies spirometric progression and mortality



Lowe KE et al. COPDGene 2019: Redefining the diagnosis of COPD. J COPD Fndn, in press 2019

Implementing COPDGene 2019

Chronic Obstructive Pulmonary Diseases:
Journal of the COPD Foundation

Perspective

COPD: A New Diagnostic Paradigm

Barry Make, MD¹

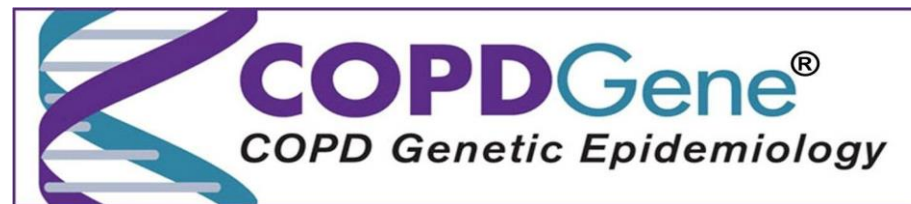
Presents an algorithm to implement COPDGene 2019 in clinical practice.

Suggests further research investigations to simplify the implementation and clinical trials.

Does Tina Have COPD?

- Exposure – cigarette smoking
- Symptoms - chronic bronchitis
- Structural abnormality - emphysema
- PRISm spirometry

Changing the COPD Diagnostic Paradigm



Barry Make, MD

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