

Step #1: Make the Diagnosis

COPD is a high burden disease that is easily diagnosed but under-recognized

COPD

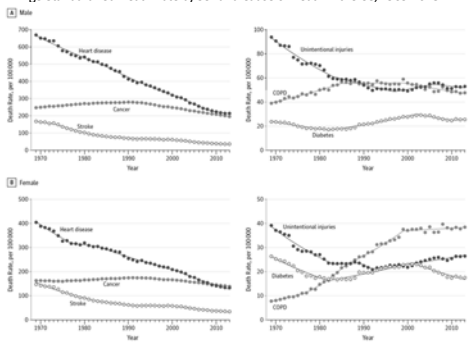
The Facts

- COPD is the 3rd leading cause of death in the United States
- COPD is the only leading cause of death in the US that is *increasing* in prevalence
- In 1990, COPD was ranked 12th as a burden of disease; by 2020 it is projected to rank 5th
- COPD is largely undiagnosed
 - 12 million people in the US diagnosed with COPD, based on NHANES estimates another 12 million *not* diagnosed
- COPD costs health systems (and society) A LOT of money
 - Unscheduled visits, ER visits, hospitalizations, re-hospitalizations, absenteeism
 - 2010: COPD-attributable costs \$36 billion (direct + absenteeism)
 - Illinois costs: ~\$3 billion in 470,400 people being treated for COPD (3.4% total of population)

Ford ES, et al. *Chest* 2015; 147: 31-45

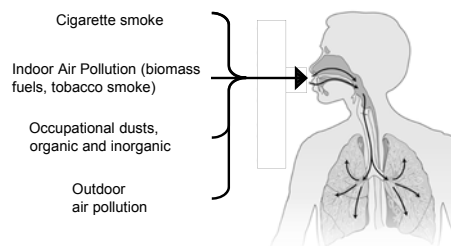
The Rising Burden of COPD

Age-Standardized Death Rate by Sex and Cause of Death in the US, 1969-2013

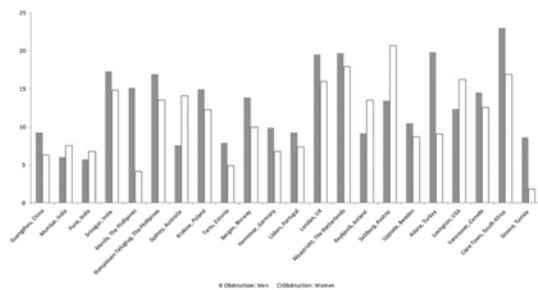


Cumulative Exposure to Noxious Particles is the Major Risk Factor for COPD

Cigarette smoking, but also much more.....



Global Prevalence of COPD



Burney P, et al. *Thorax* 2014; 69: 465-473

COPD Risk Factors – A Global View

- **Smoking**
 - Single biggest risk factor although never-smokers may represent 25-30% of people living with COPD
- **Asthma**
 - Accelerated decline in lung function and/or fixed airflow obstruction
- **Occupational dusts, vapors, chemicals, fumes**
 - Often combined exposure with cigarette smoke
- **Biomass fuel exposure**
 - Cooking and heating homes with open fires/simple stoves
- **Outdoor air pollution**
- **Gender**
 - Women with increasing prevalence due to pattern of smoking, possibly increased susceptibility/accelerated progression, greater biomass exposure
- **Genetics**
 - Alpha-1-antitrypsin deficiency
- **Childhood and chronic respiratory infections**

COPD is Diagnosed by Spirometry

Don't screen for COPD in smokers, but pay close attention to symptoms

Symptoms

Cough
Sputum
Dyspnea

Exposure To Risk Factors

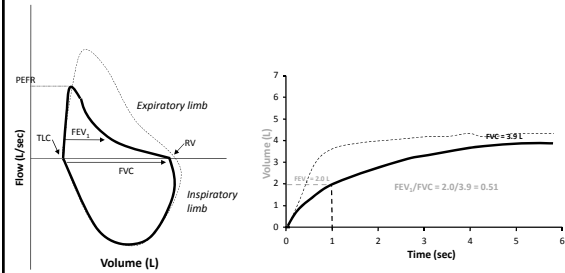
Tobacco
Occupation
Indoor/outdoor pollution



SPIROMETRY

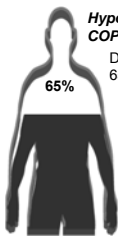
Flow-Volume and Volume-Time Curves in COPD vs. Normal

80% of air *should* come out in the first second of a forced expiration (and and FEV₁/FVC 0.70 after a bronchodilator defines COPD)



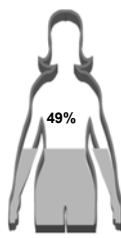
COPD – Misdiagnosed in Women

Despite rising prevalence, recognition remains a major challenge



Hypothetical Male Patient With COPD Symptoms

Diagnosed as COPD by 65% of physicians



Hypothetical Female Patient With COPD Symptoms

Diagnosed as COPD by 49% of physicians

COPD symptoms in women were most commonly misdiagnosed as asthma

Chapman KR, et al. *Chest*. 2001;119:1691-1695

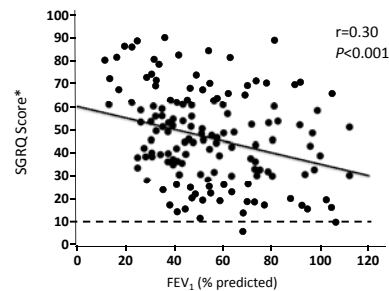
Key Point: Use Lung Function Testing to Diagnose COPD

- Former or current smokers
- Prior or current exposure to occupational vapors/gases/dusts/fumes
- Symptoms:
 - Breathlessness (requires probing questions, NOT “are you short of breath?”)
 - Cough with sputum is NEVER normal
 - “smokers cough” should prompt testing
 - Recurrent bronchitis – requiring antibiotics once a year for “bronchitis” is also NOT normal and should prompt evaluation
- Can be office spirometry OR hospital pulmonary function lab
 - Key is to actually make a diagnosis

Step #2 Perform Objective Clinical Evaluation:

The FEV₁, while important for diagnosis, does NOT tell us all that we want to

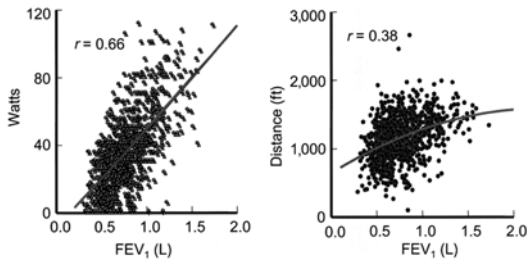
FEV₁ and Quality of Life Do Not Correlate Well in COPD



*Higher scores = worse QoL.
SGRQ = St. George's Respiratory Questionnaire.

Jones PW. *Chest*. 1995;107(suppl):1875-1935.

FEV₁ and Exercise Capacity Do Not Correlate Well in COPD



Cooper CB. *Am J Med* 2006; 119 (suppl): S21-31

Quiet breathing in a healthy individual

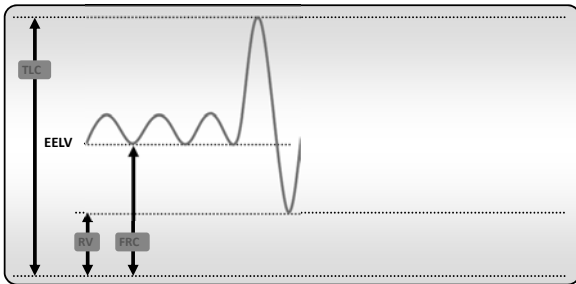
EELV

The graph shows a regular, sinusoidal wave representing tidal volume oscillating around a stable horizontal dashed line labeled 'EELV'. The y-axis ranges from 0 to 3,000.

TLC=total lung capacity; IC=inspiratory capacity; EELV=end expiratory lung volume; RV=residual volume; FRC=functional residual capacity

Adapted from O'Donnell DE, et al. *Am J Respir Crit Care Med*. 2001;164:770-777.

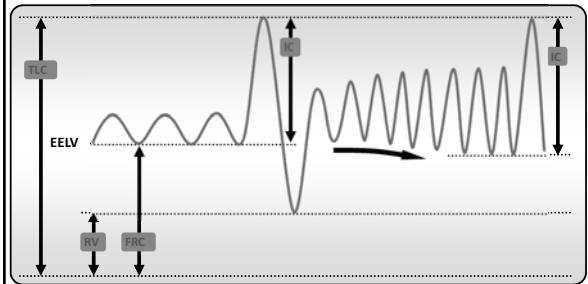
Maximal inspiration and expiration in health



TLC=total lung capacity; IC=inspiratory capacity; EELV=end expiratory lung volume; RV=residual volume; FRC=functional residual capacity

Adapted from O'Donnell DE, et al. *Am J Respir Crit Care Med*. 2001;164:770-777.

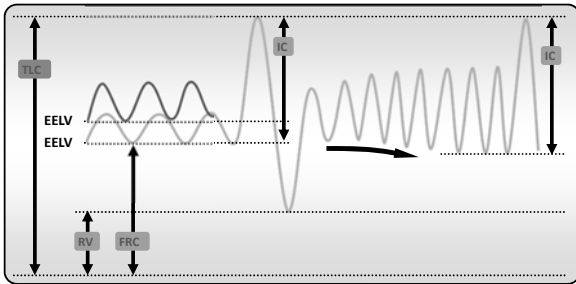
Respiratory response to exercise in health



TLC=total lung capacity; IC=inspiratory capacity; EELV=end expiratory lung volume; RV=residual volume; FRC=functional residual capacity

Adapted from O'Donnell DE, et al. *Am J Respir Crit Care Med*. 2001;164:770-777.

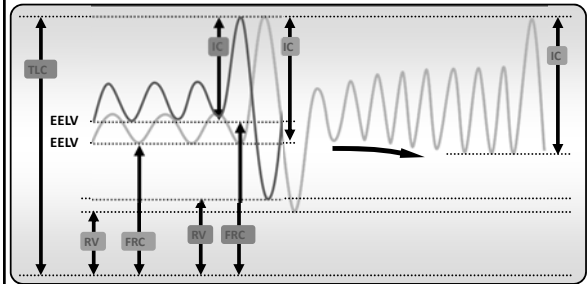
Quiet breathing in COPD



TLC=total lung capacity; IC=inspiratory capacity; EELV=end expiratory lung volume; RV=residual volume; FRC=functional residual capacity

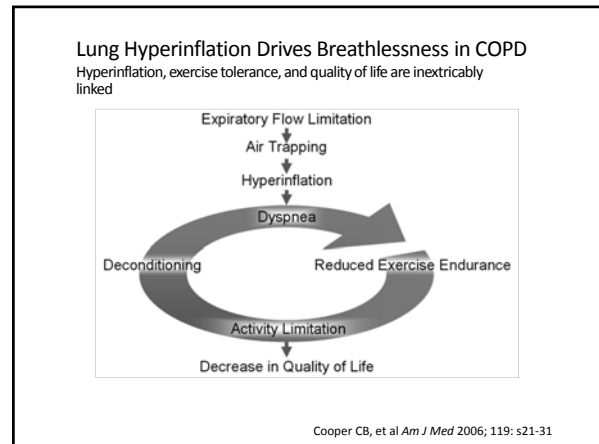
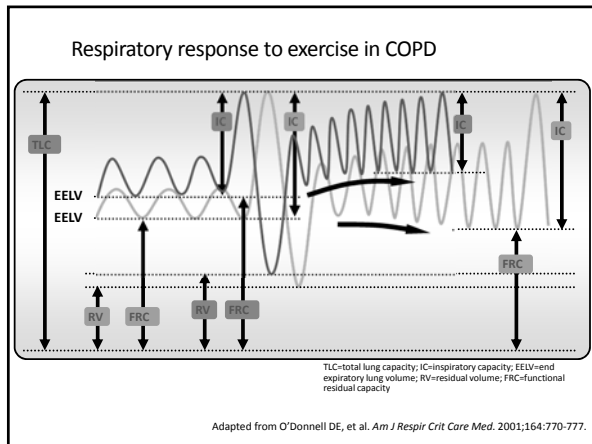
Adapted from O'Donnell DE, et al. *Am J Respir Crit Care Med*. 2001;164:770-777.

Maximal inspiration and expiration in COPD



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Adapted from O'Donnell DE, et al. *Am J Respir Crit Care Med*. 2001;164:770-777.



2015 GOLD Statement – Classify Severity of Airflow Limitation by Spirometry

GOLD Class	FEV ₁ percent predicted (post-BD)
GOLD 1	Greater than 80% of predicted
GOLD 2	50-80% of predicted
GOLD 3	30 – 49% of predicted
GOLD 4	Less than 30% of predicted

Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2015. Available from: <http://www.goldcopd.org/>

2015 GOLD Statement – OBJECTIVELY Evaluate Symptoms

Modified Medical Research Council Dyspnea Scale

mMRC Grade	Description
Grade 0	I only get breathless with strenuous exercise
Grade 1	I get short of breath when hurrying on the level or walking up a slight hill
Grade 2	I walk slower than people of the same age on the level because of breathlessness, or I have to stop for breath when walking at my own pace on the level
Grade 3	I stop for breath after walking about 100 meters or after a few minutes on the level
Grade 4	I am too breathless to leave the house or I am breathless when dressing or undressing

Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2015. Available from: <http://www.goldcopd.org/>
Mahler DA. *Proc Am Thorac Soc* 2006;3:234-238.

2015 GOLD Statement – OBJECTIVELY Evaluate Symptoms

COPD Assessment Test (CAT)

How is your COPD? Take the COPD Assessment Test™ (CAT)

This questionnaire will help you and your healthcare professional monitor the signs of COPD (chronic obstructive pulmonary disease) to help you and your doctor decide on the management of your COPD and the general health of your lungs. For each item below, place a mark (X) in the box that best describes you currently. Be sure to only select one response for each question.

Example: I can not sleep 4 3 2 1 0 I am very well

SCORE

I sleep enough	<input type="radio"/> 0 <input type="radio"/> 1 <input type="radio"/> 2 <input type="radio"/> 3 <input type="radio"/> 4	I cough all the time	<input type="radio"/> 0 <input type="radio"/> 1 <input type="radio"/> 2 <input type="radio"/> 3 <input type="radio"/> 4
I have no phlegm (mucus) coming clear of all	<input type="radio"/> 0 <input type="radio"/> 1 <input type="radio"/> 2 <input type="radio"/> 3 <input type="radio"/> 4	My chest is completely full of phlegm (mucus)	<input type="radio"/> 0 <input type="radio"/> 1 <input type="radio"/> 2 <input type="radio"/> 3 <input type="radio"/> 4
My chest does not feel tight at all	<input type="radio"/> 0 <input type="radio"/> 1 <input type="radio"/> 2 <input type="radio"/> 3 <input type="radio"/> 4	My chest feels very tight	<input type="radio"/> 0 <input type="radio"/> 1 <input type="radio"/> 2 <input type="radio"/> 3 <input type="radio"/> 4
When I walk up a hill or one flight of stairs I am not breathless	<input type="radio"/> 0 <input type="radio"/> 1 <input type="radio"/> 2 <input type="radio"/> 3 <input type="radio"/> 4	When I walk up a hill or one flight of stairs I am very breathless	<input type="radio"/> 0 <input type="radio"/> 1 <input type="radio"/> 2 <input type="radio"/> 3 <input type="radio"/> 4
I am not limited doing any activities at home	<input type="radio"/> 0 <input type="radio"/> 1 <input type="radio"/> 2 <input type="radio"/> 3 <input type="radio"/> 4	I am very limited doing activities at home	<input type="radio"/> 0 <input type="radio"/> 1 <input type="radio"/> 2 <input type="radio"/> 3 <input type="radio"/> 4
I am confident breathing and have no coughing or wheezing	<input type="radio"/> 0 <input type="radio"/> 1 <input type="radio"/> 2 <input type="radio"/> 3 <input type="radio"/> 4	I am not at all confident breathing and have frequent coughing or wheezing	<input type="radio"/> 0 <input type="radio"/> 1 <input type="radio"/> 2 <input type="radio"/> 3 <input type="radio"/> 4
I sleep usually	<input type="radio"/> 0 <input type="radio"/> 1 <input type="radio"/> 2 <input type="radio"/> 3 <input type="radio"/> 4	I have frequent awakenings because of my lung condition	<input type="radio"/> 0 <input type="radio"/> 1 <input type="radio"/> 2 <input type="radio"/> 3 <input type="radio"/> 4
I have lots of energy	<input type="radio"/> 0 <input type="radio"/> 1 <input type="radio"/> 2 <input type="radio"/> 3 <input type="radio"/> 4	I have no energy at all	<input type="radio"/> 0 <input type="radio"/> 1 <input type="radio"/> 2 <input type="radio"/> 3 <input type="radio"/> 4

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Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2015. Available from: <http://www.goldcopd.org/>
Jones PW, et al. *Eur Respir J* 2009;34:648-654.

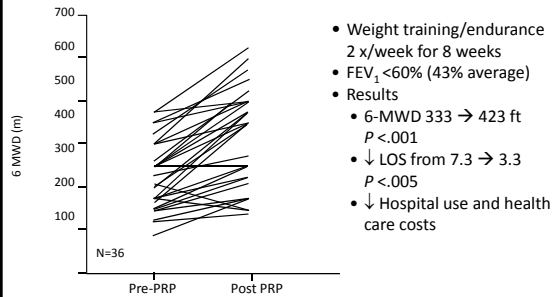
ALL Available Long-acting Bronchodilators for COPD are Effective (and generally safe)

Improved FEV₁ (and FVC), less lung hyperinflation, fewer respiratory symptoms, greater exercise capacity

Drug	Mechanism	Dosing Frequency
Salmeterol	Long-acting β-agonist (LABA)	BID
Formoterol	Long-acting β-agonist (LABA)	BID
Indacaterol	Ultra long-acting β-agonist (ultra LABA)	QD
Olodaterol	Ultra long-acting β-agonist (ultra LABA)	QD
Tiotropium	Long-acting anti-muscarinic (LAMA)	QD
Aclidinium	Long-acting anti-muscarinic (LAMA)	BID
Umeclidinium	Long-acting anti-muscarinic (LAMA)	QD
Vilanterol + Umeclidinium Combination	LABA + LAMA	QD
Olodaterol + Tiotropium Combination	LABA + LAMA	QD

Bronchodilators Will Not Work in COPD without Rehabilitative Exercise

Almost every COPD patient is out of shape and inhalers don't fix that!



- Weight training/endurance 2 x/week for 8 weeks
- FEV₁ <60% (43% average)
- Results
 - 6-MWD 333 → 423 ft $P < .001$
 - ↓ LOS from 7.3 → 3.3 $P < .005$
 - ↓ Hospital use and health care costs

Hui KP, et al. *Chest* 2003;124:94-7

Key Takeaway: COPD is TREATABLE

Treatments work better if coupled with pulmonary rehabilitation

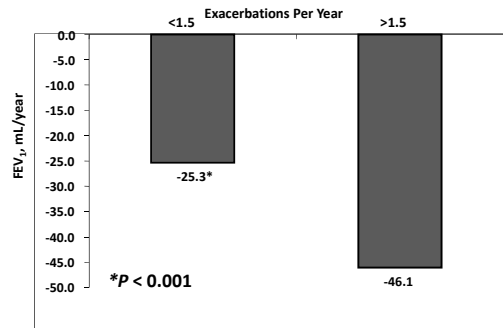
- Every COPD patient with significant symptoms (objectively assessed) should be treated with long-acting bronchodilators
 - MMRC 2 or more
 - CAT 10 or more
- First-line bronchodilators can be a LABA or a LAMA
 - Considerations include device and ease of use, potential side effects (tachycardia, dry mouth), and PBM preferred agents/co-pays
- Combination LABA + LAMAs are available for step-wise increases in medication when symptoms remain uncontrolled
 - If breathlessness is uncontrolled, ensure rehabilitative exercise/PR before increasing pharmacotherapy
 - Inhaled steroid containing regimens should be reserved for patients at risk for exacerbations

Rosenberg SR and Kalhan R. *Med Clin N Am* 2012; 96: 811-26

Step #3 Prevent COPD Exacerbations:

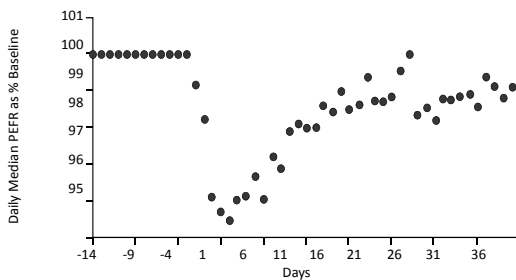
Acute exacerbations of COPD are morbid events and every effort should be made to treat them aggressively and prevent them in the future.

COPD Exacerbations are Associated with Accelerated Decline in Lung Function



Donaldson GC, et al. *Thorax*. 2002;57:847-852.

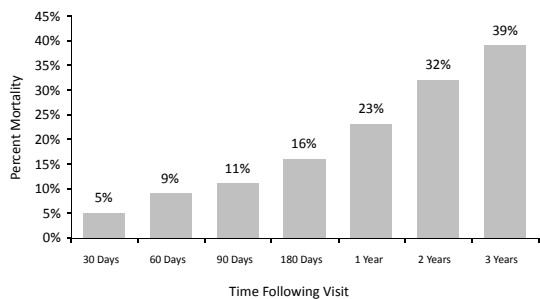
Recovery from COPD Exacerbations is Slow and Often Incomplete



Seemungal TA, et al. *Am J Respir Crit Care Med* 2000;161:1608-13.

COPD Exacerbation are Associated with High Short-term Mortality

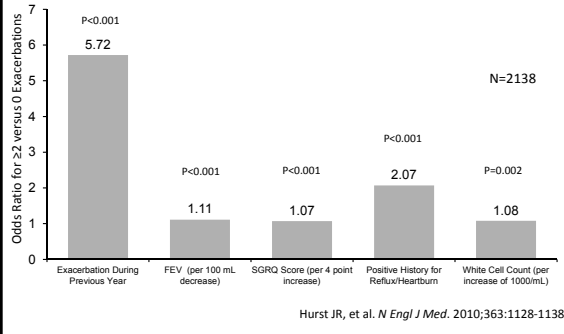
Mortality rates following a single ER visit for COPD exacerbation



Kim S, et al. *COPD*. 2006;3:75-81

COPD Exacerbations Occur Stereotypically in a Subset of COPD Patients

The "frequent exacerbator" phenotype should be targeted for exacerbation prevention strategies



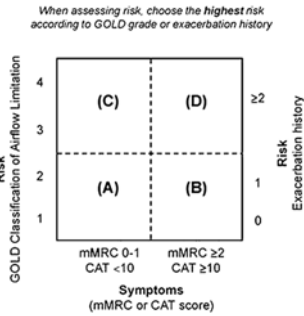
Exacerbation Prevention Strategies

Adding inhaled steroids, considering additional agents

Drug	Population	Exacerbation Risk Reduction
Fluticasone-Salmeterol (50-250 mcg dose)	Prior exacerbation FEV ₁ < 50% predicted	30.5% risk reduction in exacerbations vs. salmeterol
Budesonide-Formoterol (160-4.5 mcg dose – 2 puffs)	FEV ₁ < 50% predicted	37% risk reduction in exacerbations vs. placebo 24.1% risk reduction exacerbations vs. formoterol
Tiotropium (18 mcg)	FEV ₁ < 70% predicted	14% risk reduction in exacerbations vs. placebo
Roflumilast (500 mcg)	Bronchitic symptoms Prior Exacerbation FEV ₁ < 50% predicted	15% - 17% risk reduction in exacerbations vs. placebo
Azithromycin (250mg daily)	COPD with: O ₂ use, exacerbation (steroids/ER/hospital) in prior one year	27% risk reduction exacerbations vs. placebo

Comprehensive Evaluation of COPD – GOLD Framework

Evaluate lung function, objective symptoms, AND prior exacerbations



Comprehensive Evaluation of COPD – GOLD Framework

Individual patient factors drive treatment recommendations

Patient	Characteristics	Risk (spiro or exacs)		Symptoms	
		Spirometry Class	Exacerbations (per year)	CAT	mMRC
A	Low Risk Fewer Symptoms	GOLD 1 or 2	≤ 1	< 10	0 or 1
B	Low Risk More Symptoms	GOLD 1 or 2	≤ 1	≥ 10	≥ 2
C	High Risk Fewer Symptoms	GOLD 3 or 4	≥ 2	< 10	0 or 1
D	High Risk More Symptoms	GOLD 3 or 4	≥ 2	≥ 10	≥ 2

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Non-pharmacologic COPD Therapies

Patient Group	Essential	Recommended	Per Local Guidance
A	Smoking cessation	Physical activity	Flu vaccine Pneumococcal vaccine
B, C, D	Smoking cessation Pulmonary rehabilitation	Physical activity	Flu vaccine Pneumococcal vaccine

Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2015. Available from: <http://www.goldcopd.org/>

Pharmacologic COPD Therapies

Patient	First Line Therapy	Alternate Choices	Other Potential Treatments
A	SABA or SAMA	LAMA or LABA or SABA+SAMA	Theophylline
B	LAMA or LABA	LAMA+LABA	Theophylline SABA +/- SAMA (prn)
C	LABA+ICS or LAMA	LAMA+LABA or LAMA and roflumilast or LABA and roflumilast	Theophylline SABA +/- SAMA (prn) Azithromycin
D	LABA+ICS and/or LAMA	LABA+ICS and LAMA or LABA+ICS and roflumilast or LAMA+LABA or LAMA and roflumilast	N-acetylcysteine Carbocysteine SABA +/- SAMA (prn) Azithromycin Theophylline

Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2015. Available from: <http://www.goldcopd.org/>

Step #4: Personalize COPD care as much as possible

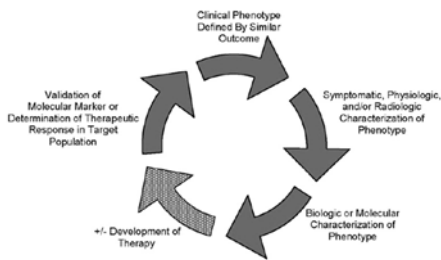
COPD is a disease of multiple phenotypes.....and can get pretty complicated

Operational Definition of a COPD Phenotype

- “A single or combination of disease attributes that describe differences between individuals with COPD as they relate to clinically meaningful outcomes (symptoms, exacerbations, response to therapy, rate of disease progression, or death)”

Han MK, et al. *Am J Respir Crit Care Med* 2010; 182: 598.

Defining a Phenotype

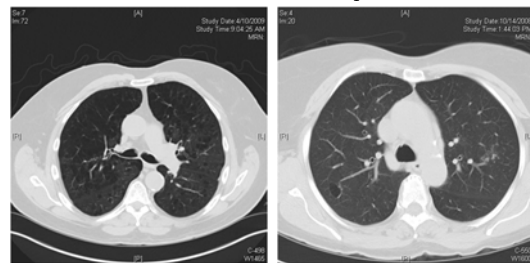


Han MK, et al. *Am J Respir Crit Care Med* 2010; 182: 598.

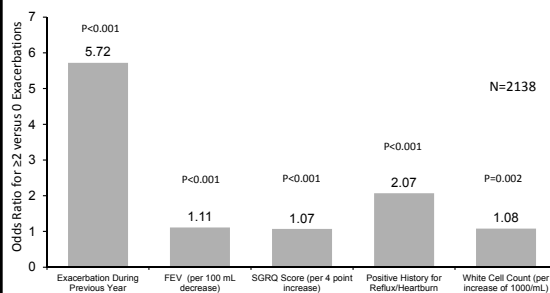
Phenotypic Variation in COPD: Emphysema vs. Airways

64 year old man
FEV₁ = 49% predicted

64 year old woman
FEV₁ = 51% predicted

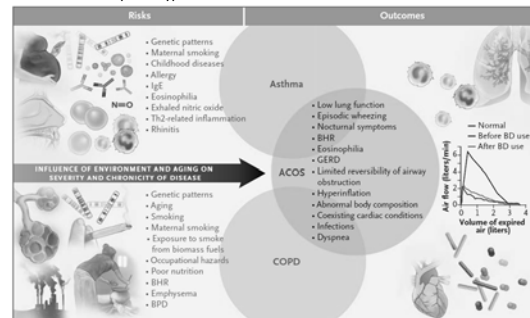


The Frequent Exacerbator Phenotype
Potential targeted therapy: ICS, roflumilast, azithromycin



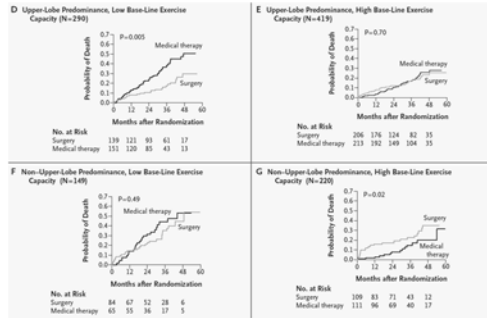
Hurst JR, et al. *N Engl J Med*. 2010;363:1128-1138

Asthma and COPD Overlap Syndrome
The hot new phenotype



Postma DS and Rabe KF. *N Engl J Med*. 2015;373:1241-9

Lung Volume Reduction Surgery Only works in the context of phenotype-directed care



NETT Group. *N Engl J Med.* 2003;384:2059-2073.

Conclusions

- The goals of COPD therapy are to reduce symptoms, reduce the frequency and severity of exacerbations, improve exercise tolerance and health status and reduce mortality.
- Effective treatment of COPD requires that attention be paid to the therapeutic response with objective measurement of symptoms, exacerbations, and exercise capacity on an ongoing basis.
- COPD exacerbations are highly burdensome events which should be prevented.
- Many treatment therapies exist that effectively treat symptoms and/or reduce exacerbations including long-acting beta2 agonists (LABAs), combination LABA- inhaled corticosteroids (ICS), long-acting anti-muscarinics (LAMAs), phosphodiesterase-4 (PDE4) inhibitors and macrolides.
- Phenotype defined and directed care is the the future of how we will approach established COPD