



## COPD Update

**James Allen, MD**

*Medical Director*

*The Ohio State University Wexner Medical Center East Hospital*

*Professor of Internal Medicine*

*Division of Pulmonary and Critical Care Medicine*

*The Ohio State University Wexner Medical Center*

**MedNet21**  
Center for Continuing Medical Education



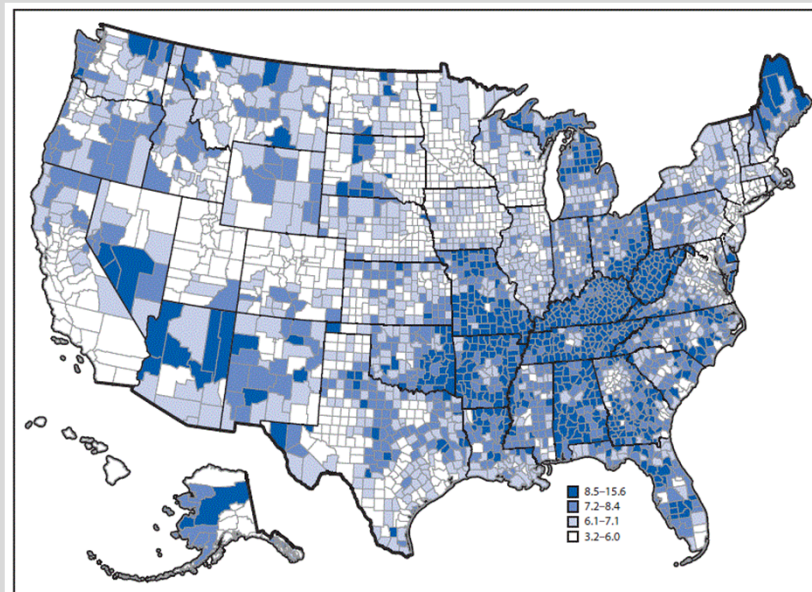
## After this lecture, you should be able to:

1. Diagnose and classify COPD
2. Prescribe step-wise treatment for management of stable COPD
3. Identify patients who would benefit by home oxygen
4. Manage COPD exacerbations
5. Develop strategies to reduce re-admissions for COPD

## Impact of COPD in U.S.

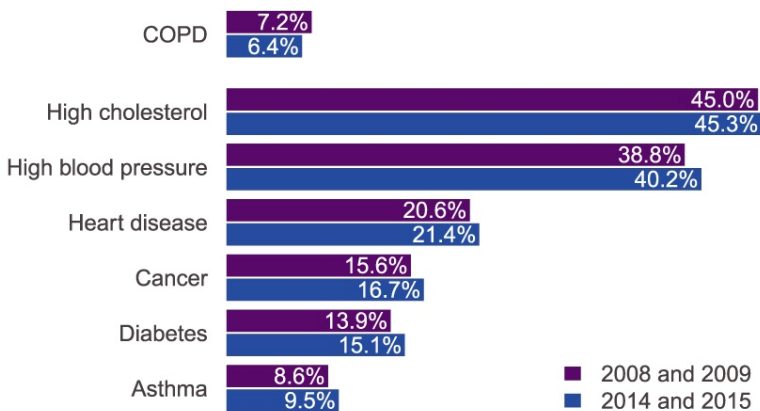
- 15.5 million people diagnosed
- 715,000 hospital admissions per year
- 120,000 deaths/year
- Annual cost up to \$50 billion
  - \$30 billion direct
  - \$20 billion indirect

## Prevalence of COPD In The U.S.



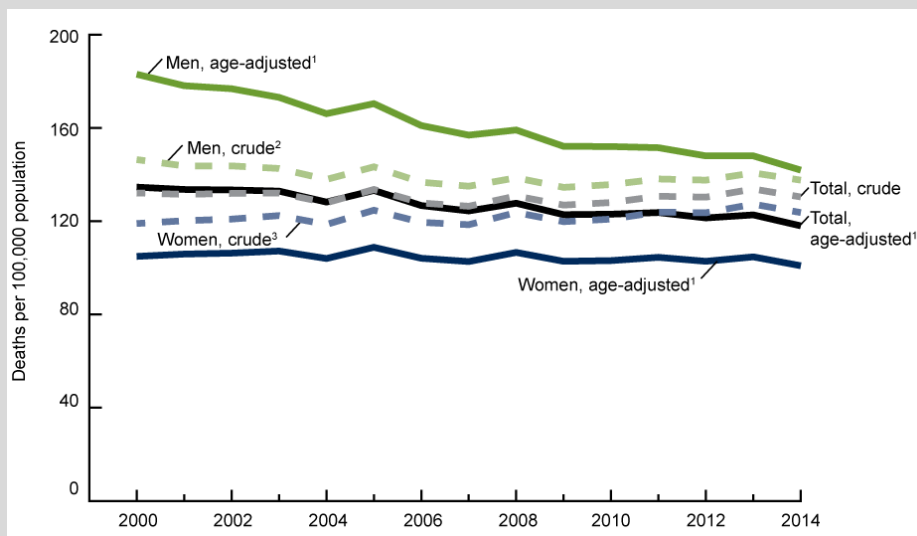
### Prevalence of COPD Has Declined as Other Chronic Conditions Have Increased

Percent of adults aged 40 years or older who reported having been diagnosed with chronic conditions



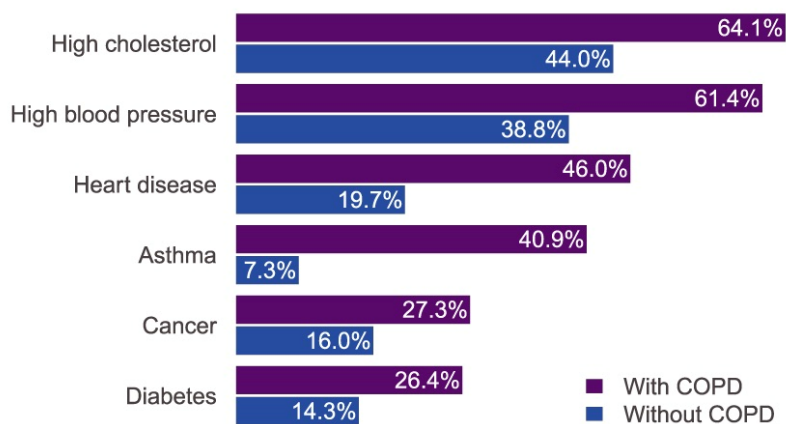
JAMA 2019; 322: 602

## COPD-related deaths in U.S. adults



### Prevalence of Other Chronic Conditions Is Higher Among Adults With COPD

Percent of reported chronic condition diagnoses among adults aged 40 years or older with and without a reported COPD diagnosis, 2014 and 2015



JAMA 2019; 322: 602

## Prevalence of COPD by Age, Income, and Insurance

- **Age:**
  - > 65 years: 10.2%
  - 40-64 years: 4.6%
- **Income:**
  - Poor 13.6%
  - Low 9.9%
  - Medium 6.0%
  - High 3.7%
- **Insurance**
  - Medicare 14.0%
  - Other public 11.1%
  - Commercial 4.3%

## COPD Expenditures Are Increasing

- Percent COPD Patients Using Emergency Department Services:
  - 2008 – 2009: 8.0%
  - 2014 – 2015: 13.2%
- Annual COPD Prescription Drug Costs:
  - 2008 – 2009: \$1,197
  - 2014 – 2015: \$1,768

## Spirometry is essential to diagnosis of COPD



## There are two commonly used scales of obstruction severity:

### American Thoracic Society (ATS)

FEV1 (% predicted)	Obstruction
> 70%	Mild
60-69%	Moderate
50-59%	Moderately Severe
35-49%	Severe
< 35%	Very Severe

### Global Initiative on Obstructive Lung Disease (GOLD)

FEV1 (% predicted)	Obstruction
> 80%	Mild
50-79%	Moderate
30-49%	Severe
< 30%	Very Severe

The ATS defines obstruction as an FEV1/FVC ratio of less than the 5<sup>th</sup> percentile of predicted for that patient's age and this number will vary from patient to patient. The GOLD defines obstruction as anyone with an FEV1/FVC ratio of less than 70% for all patients, regardless of age

## Staging

- Risk:
  - Low:
    - 0-1 exacerbations/yr
    - No hospitalizations/yr
  - High
    - $\geq 2$  exacerbations/yr
    - $\geq 1$  hospitalizations/yr
- Symptoms:
  - Less: MRC 0-1
  - More: MRC  $\geq 2$

## mMRC Score

- 0 – Only breathless with strenuous activity
- 1 – Short of breath when hurrying on ground level or walking up a slight hill
- 2 – Walk slower than people of similar age on level ground or have to stop walking at my own pace
- 3 – Stop for breath after walking 100 yards or a few minutes on level ground
- 4 – Too breathless to leave the house or breathless when dressing

## Can you have emphysema with normal spirometry?

**Yes!**

- Suspect in at-risk patients with dyspnea and either:
  - Hyperinflation or air-trapping by lung volumes
  - Low diffusing capacity
- Confirmation by high resolution chest CT
- 50% of smokers age > 75 with normal spirometry have evidence of emphysema or air trapping by CT

## Alpha-1-Antitrypsin Deficiency

- U.S. prevalence = 1 out of 1,500 to 5,000 people
  - Approximately 100,000 Americans
- World Health Organization recommends all patients with COPD be screened once for alpha-1-antitrypsin deficiency
- Screen with alpha-1-antitrypsin levels
  - Deficiency established with level < 57 mg/dL
  - Do genotyping if level < 100 mg/dL

15

## Where do our treatment guidelines come from?

- **GOLD** (Global initiative for Obstructive Lung Disease)
  - *2020 Guide to COPD Diagnosis, Management, and Prevention*
- **ACCP/CTS** (American College of Chest Physicians; Canadian Thoracic Society)
  - *2015 Prevention of Acute Exacerbations of COPD*
- **ATS** (American Thoracic Society)
  - *2020 Pharmacologic Management of Chronic Obstructive Pulmonary Disease*

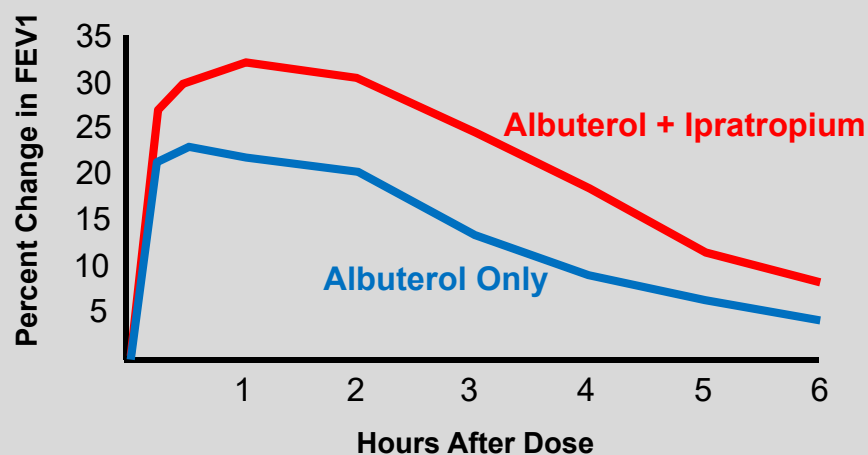
16



## ACCP/CTS Guideline To Prevent COPD Exacerbations:

- Short-acting combination anti-cholinergic plus short acting beta agonist = initial PRN rescue inhaler
- LAMA = first line maintenance therapy
- LAMA/LABA = second line maintenance therapy
- LAMA/LABA/ICS = third line maintenance therapy
- Inhaled steroid alone not recommended
- For patients with exacerbations:
  - Daily azithromycin
  - Roflumilast
  - N-acetylcysteine

## Ipratropium + albuterol is superior to albuterol alone



*Arch Intern Med.* 1999;159(2):156-160

# Short-Acting Bronchodilators

Brand	Component	Frequency	Cost
<b>Generic Albuterol</b>	<b>albuterol</b>	<b>Q 6 Hours PRN</b>	<b>\$18</b>
Proair	albuterol	Q 6 Hours PRN	\$66
Proair Respiclick	albuterol	Q 6 Hours PRN	\$59
Ventolin	albuterol	Q 6 Hours PRN	\$60
Proventil	albuterol	Q 6 Hours PRN	\$86
Generic levalbuterol	levalbuterol	Q 6 Hours PRN	\$33
Atrovent	ipratropium	Q 6 Hours PRN	\$414
<b>Combivent Respimat</b>	<b>ipratropium + albuterol</b>	<b>Q 6 Hours PRN</b>	<b>\$429</b>
Generic Albuterol*	albuterol	Q 6 Hours PRN	\$21
Generic ipratropium*	ipratropium	Q 6 Hours PRN	\$17
Duoneb*	ipratropium + albuterol	Q 6 Hours PRN	\$32

\*Nebulized

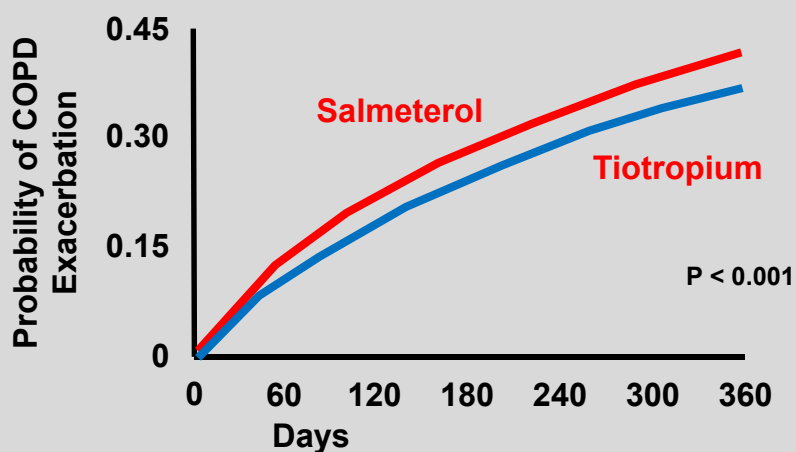
Cost per month: GoodRx



## ACCP/CTS Guideline To Prevent COPD Exacerbations:

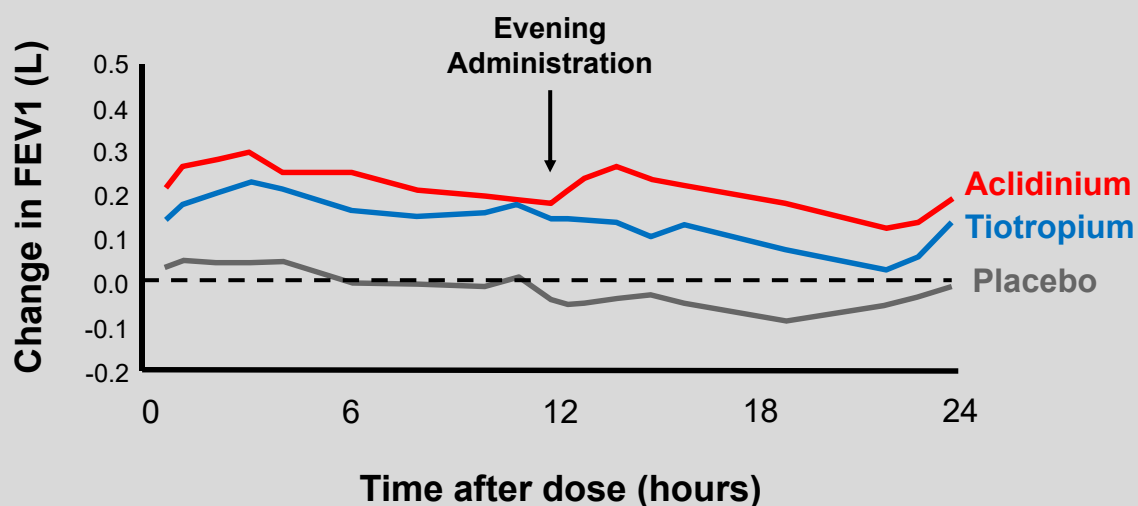
- Short-acting combination anti-cholinergic plus short acting beta agonist = initial PRN rescue inhaler
- **LAMA = first line maintenance therapy**
- LAMA/LABA = second line maintenance therapy
- LAMA/LABA/ICS = third line maintenance therapy
- Inhaled steroid alone not recommended
- For patients with exacerbations:
  - Daily azithromycin
  - Roflumilast
  - N-acetylcysteine

## Tiotropium (LAMA) Is Superior To Salmeterol (LABA) in COPD



Vogelmeier et al. N Engl J Med 2011; 364: 1093-1103

## Aclidinium is similar to tiotropium



Chest 2012; 141:745-52

## Long-Acting Anti-Cholinergics (LAMAs)

Brand	Component	Frequency	Cost
Spiriva Handihaler	tiotropium	Daily	\$457
Spiriva Respimat	tiotropium	Daily	\$440
Tudorza	aclidinium	Twice Daily	\$193
Incruse	umeclidinium	Daily	\$347
Seebri	glycopyrrolate	Twice Daily	\$397
Lonhala Magnair*	glycopyrrolate	Twice Daily	\$1,126
Yupelri*	revefenacin	Daily	\$1,097

\*Nebulized formulation

Cost per month: GoodRx



## Long-Acting Beta Agonists (LABAs)

Brand	Component	Frequency	Cost
Serevent diskus	salmeterol	Twice daily	\$402
Arcapta	indacaterol	Daily	\$263
Striverdi	olodaterol	Twice daily	\$218
Brovana*	arformoterol	Twice Daily	\$1,067
Performomist*	formoterol	Twice Daily	\$1,056

\*Nebulized formulation

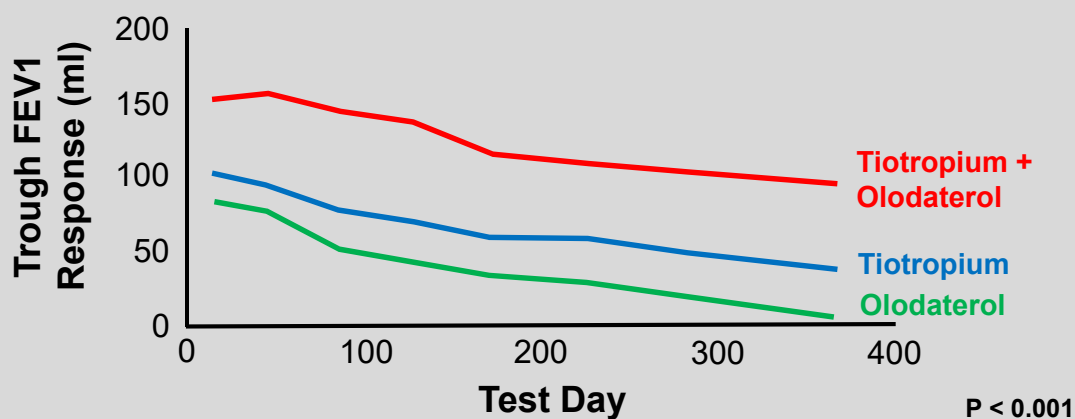
Cost per month: GoodRx



## ACCP/CTS Guideline To Prevent COPD Exacerbations:

- Short-acting combination anti-cholinergic plus short acting beta agonist = initial PRN rescue inhaler
- LAMA = first line maintenance therapy
- **LAMA/LABA = second line maintenance therapy**
- LAMA/LABA/ICS = third line maintenance therapy
- Inhaled steroid alone not recommended
- For patients with exacerbations:
  - Daily azithromycin
  - Roflumilast
  - N-acetylcysteine

## LAMA/LABA combination is superior to LABA alone or LAMA alone



Eur Resp J 2015; 45:969-79

## ATS Guideline on Pharmacologic Management of Chronic Obstructive Pulmonary Disease

1. LABA/LAMA dual therapy preferred over either LAMA alone or LABA alone
2. ICS/LABA/LAMA triple therapy recommended for patients with > 1 exacerbation per year requiring:
  - Antibiotics
  - Steroids
  - Hospitalization
3. ICS can be withdrawn if no exacerbations for 1 year

Am J Respir Crit Care Med Vol 201, Iss 9, pp 1039–1049, May 1, 2020

## LAMA/LABA Combinations

Brand	Component	Frequency	Cost
Stiolto	tiotropium + olodaterol	Twice daily	\$407
Anoro	umeclidinium + vilanterol	Twice daily	\$425
Utibron	glycopyrrolate + indacaterol	Twice daily	\$371
Bevespi	glycopyrrolate + formoterol	Twice daily	\$387
Duaklir	Aclidinium + formoterol	Twice daily	\$990

Cost per month: GoodRx

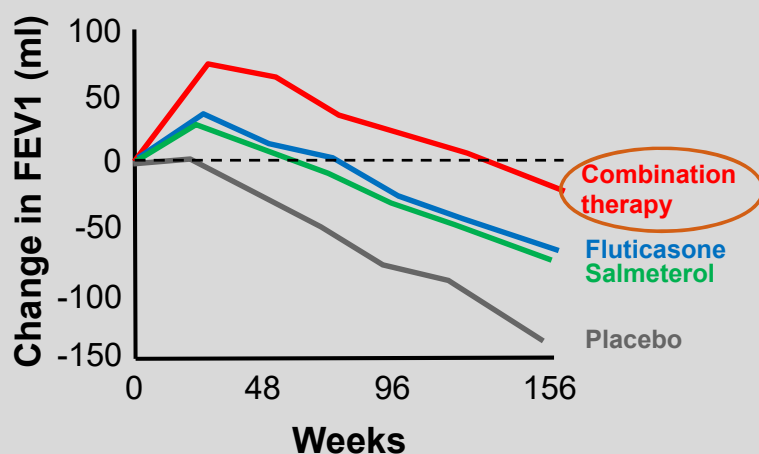




## ACCP/CTS Guideline To Prevent COPD Exacerbations:

- Short-acting combination anti-cholinergic plus short acting beta agonist = initial PRN rescue inhaler
- LAMA = first line maintenance therapy
- LAMA/LABA = second line maintenance therapy
- **LAMA/LABA/ICS = third line maintenance therapy**
- Inhaled steroid alone not recommended
- For patients with exacerbations:
  - Daily azithromycin
  - Roflumilast
  - N-acetylcysteine

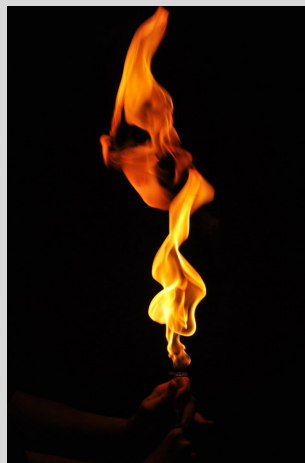
## TORCH study: ICS + LABA are better than either LABA or ICS alone



Calverley P et al. N Engl J Med 2007;356:775-789

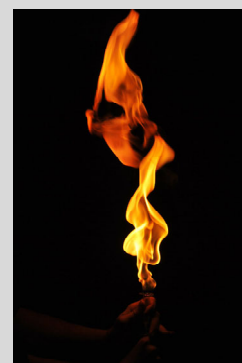
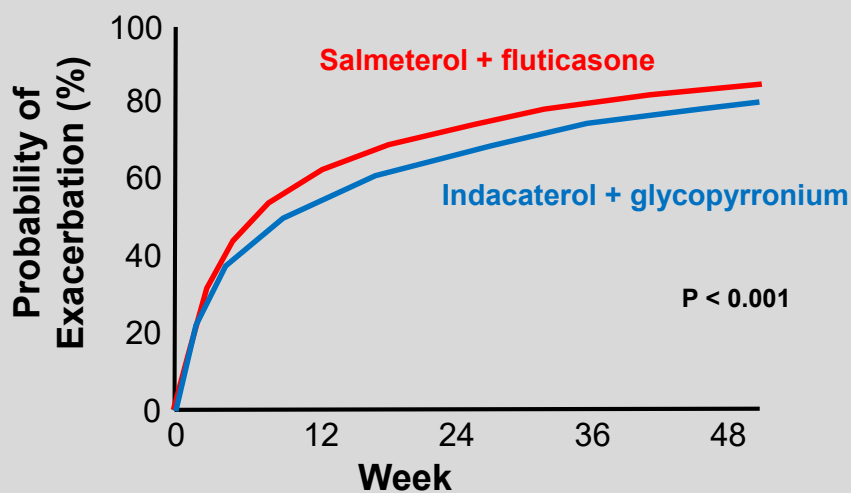
## FLAME Study

- 356 hospitals in 43 countries
- Randomized, double-blind study:
  - 1,680 subjects: LABA/LAMA
  - 1,682 subjects: LABA/ICS
- Subjects followed for 1 year
- LABA/LAMA subjects had:
  - Fewer COPD exacerbations
  - Fewer pneumonias



N Engl J Med 2016;374:2222-2234

## LABA/LAMA is superior to LABA/ICS



N Engl J Med 2016;374:2222-2234

## LABA/ICS Combinations

Brand	Component	Frequency	Cost
Advair Diskus	salmeterol + fluticasone	Twice Daily	\$396
Advair HFA	salmeterol + fluticasone	Twice Daily	\$396
Dulera	formoterol + mometasone	Twice Daily	\$320
Symbicort	formoterol + budesonide	Twice Daily	\$258
Breo	vilanterol + fluticasone	Twice Daily	\$365
Airduo	salmeterol + fluticasone	Twice Daily	\$280
Wixela	salmeterol + fluticasone	Twice Daily	\$100
fluticasone/salmeterol	salmeterol + fluticasone	Twice Daily	\$49
budesonide/formoterol	formoterol + budesonide	Twice Daily	\$258

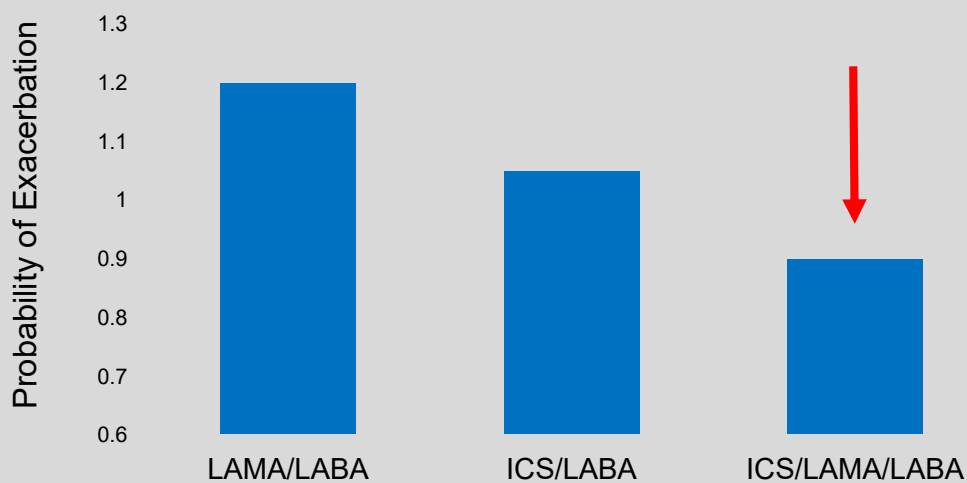
Cost per month: GoodRx



## And now, a LAMA/LABA/ICS!



## IMPACT Trial: Triple therapy inhaler is better than dual therapy inhalers in COPD



N Engl J Med 2018; 378:1671-1680

## ATS Guideline on Pharmacologic Management of Chronic Obstructive Pulmonary Disease

1. LABA/LAMA dual therapy preferred over either LAMA alone or LABA alone
2. ICS/LABA/LAMA triple therapy recommended for patients with > 1 exacerbation per year requiring:
  - Antibiotics
  - Steroids
  - Hospitalization
3. ICS can be withdrawn if no exacerbations for 1 year

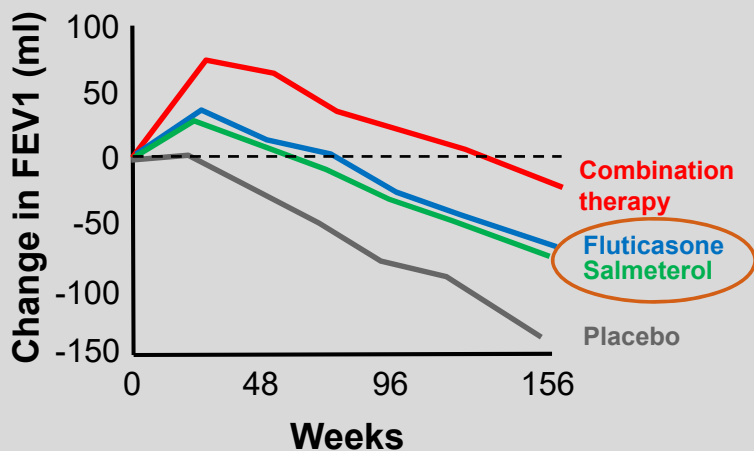
Am J Respir Crit Care Med Vol 201, Iss 9, pp 1039–1049, May 1, 2020

## LAMA/LABA/ICS Combination

Brand	Component	Frequency	Cost
Trelegy	salmeterol + umeclidinium + vilanterol	Once Daily	\$573

Cost per month: GoodRx

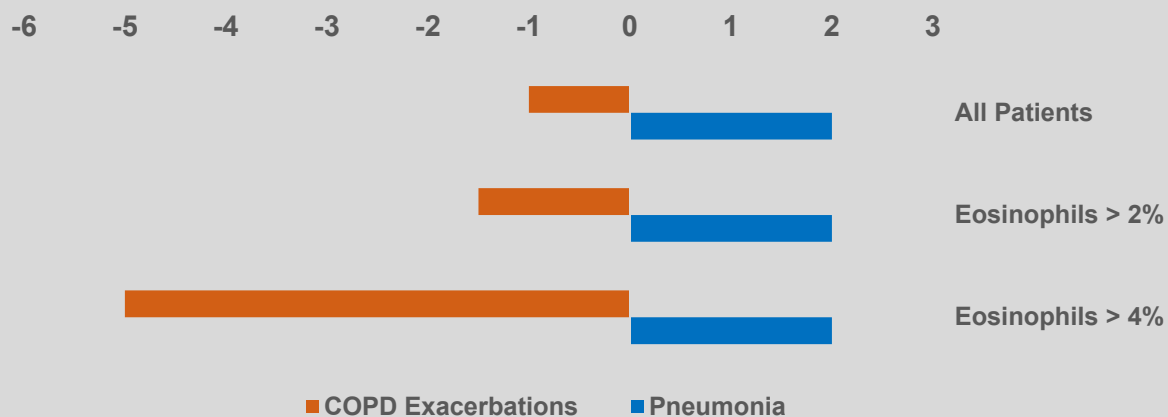
## TORCH study: ICS and LABA are equivalent



Calverley P et al. N Engl J Med 2007;356:775-789

## Which patients with COPD should have an inhaled corticosteroid?

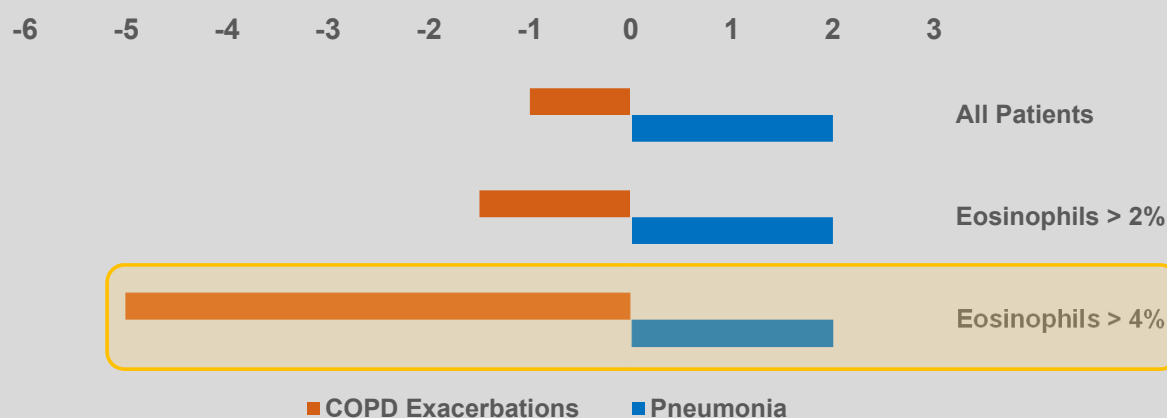
Excess Number Of Patients With A Hospitalization Per 100 Treated In 1 Year:  
ICS + LABA versus LABA Alone



Chest 2017; 152:227-231

## Which patients with COPD should have an inhaled corticosteroid?

Excess Number Of Patients With A Hospitalization Per 100 Treated In 1 Year:  
ICS + LABA versus LABA Alone



Chest 2017; 152:227-231

## ACCP/CTS Guideline To Prevent COPD Exacerbations:

- Short-acting combination anti-cholinergic plus short acting beta agonist = initial PRN rescue inhaler
- LAMA = first line maintenance therapy
- LAMA/LABA = second line maintenance therapy
- LAMA/LABA/ICS = third line maintenance therapy
- **Inhaled steroid alone not recommended**
- For patients with exacerbations:
  - Daily azithromycin
  - Roflumilast
  - N-acetylcysteine

## What Does GOLD Say About Inhaled Steroids?

- Do use:
  - History of COPD exacerbation hospitalizations
  - >2 exacerbations per year
  - Eosinophil count > 300
  - Concurrent asthma
- Consider using:
  - 1 exacerbation per year
  - Eosinophil count 100-300
- Against use:
  - History of recurrent pneumonia
  - Eosinophil count < 100
  - History of mycobacterial infection

## Inhaled Corticosteroids

Brand	Component	Frequency	Cost
Asmanex	mometasone	Twice Daily	\$230
Arnuity	fluticasone	Daily	\$183
Pulmicort flexhaler	budesonide	Twice Daily	\$240
Aerospan	flunisolide	Twice Daily	\$209
Flovent HFA	fluticasone	Twice Daily	\$256
Flovent Diskus	fluticasone	Twice Daily	\$193
Qvar	beclomethasone	Twice Daily	\$223
Alvesco	ciclesonide	Twice Daily	\$132
Armonair	fluticasone	Twice Daily	\$175
Budesonide (generic)*	budesonide	Twice Daily	\$34

\*Nebulized formulation

Cost per month: GoodRx

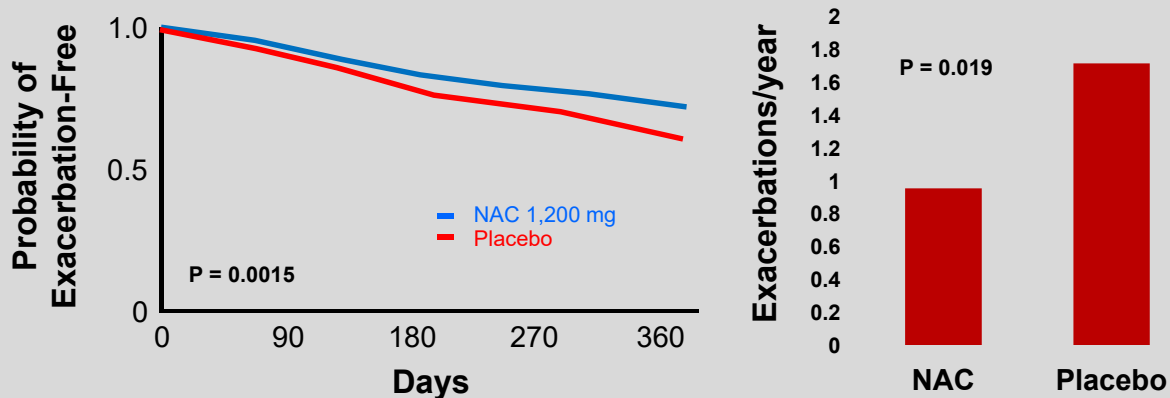




## ACCP/CTS Guideline To Prevent COPD Exacerbations:

- Short-acting combination anti-cholinergic plus short acting beta agonist = initial PRN rescue inhaler
- LAMA = first line maintenance therapy
- LAMA/LABA = second line maintenance therapy
- LAMA/LABA/ICS = third line maintenance therapy
- Inhaled steroid alone not recommended
- For patients with exacerbations:
  - N-acetylcysteine
  - Daily azithromycin
  - Roflumilast

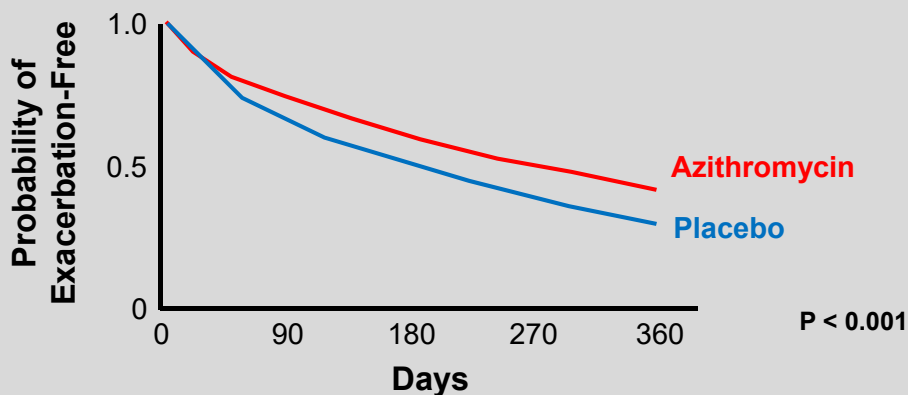
## N-acetylcysteine prevents COPD exacerbations



Chest 2013; 144:106-118

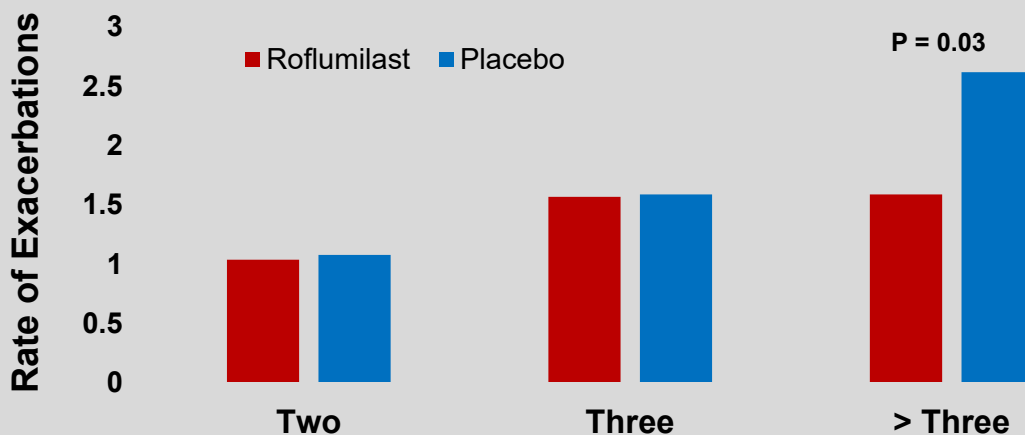
Lancet Respir Med 2014; 2: 187-94

## Azithromycin prevents COPD exacerbations



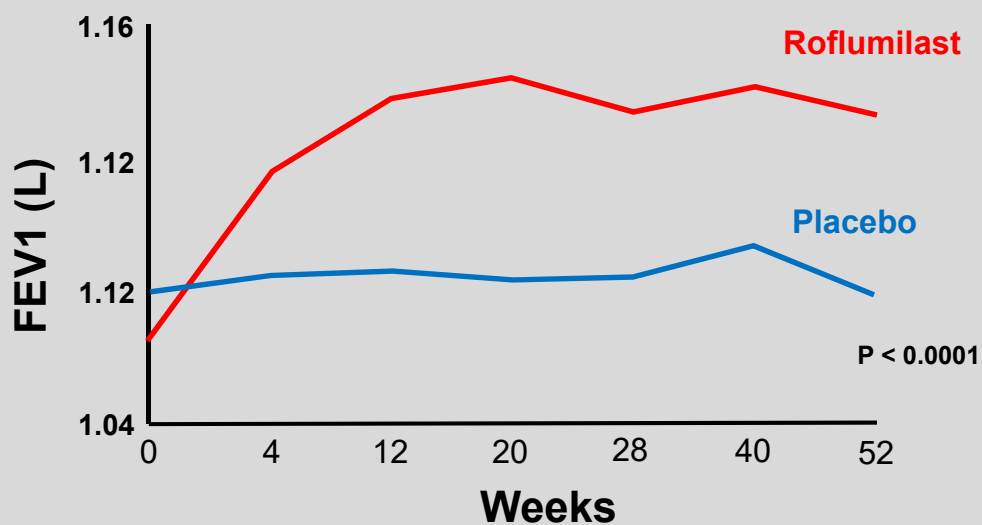
N Engl J Med 2011;365:689-698.

## Roflumilast prevents COPD exacerbations in patients with frequent exacerbations



Am J Resp Crit Care Med 2016; 194:559-67

## Roflumilast improves FEV1



Lancet 2015; 385; 857-66

## Drugs to prevent COPD exacerbations

- N-acetylcysteine
  - Over the counter
  - 600 mg twice daily
  - No monitoring required
- Azithromycin
  - 250 mg daily
  - Check baseline EKG (QTc)
  - Advise patients about hearing loss
  - Not effective in active smokers
- Roflumilast
  - 500 mg daily
  - Check LFTs
  - Monitor weight monthly

## Frequent Exacerbation Medications

Brand	Frequency	Cost
N-Acetylcysteine	Twice Daily	\$14
Azithromycin	Daily	\$14
Roflumilast (Daliresp)	Daily	\$386

Cost per month: GoodRx



## Step-Wise Approach To COPD:

Step	Maintenance Drug	PRN Drug	Total Cost*
1		Combivent Albuterol	\$429 \$18
2	LAMA	Albuterol	\$211
3	LAMA + LABA	Albuterol	\$389
4 (frequent exacerbations)	LAMA + LABA + N-acetylcysteine	Albuterol	\$403
	LAMA + LABA + azithromycin		\$403
	LAMA + LABA + roflumilast		\$775
5	LAMA + LABA + ICS	Albuterol	\$438

\*Cost is monthly cost for least expensive brand alternatives

LAMA: Long-acting muscarinic antagonist (long-acting anti-cholinergic)

LABA: Long-acting beta agonist

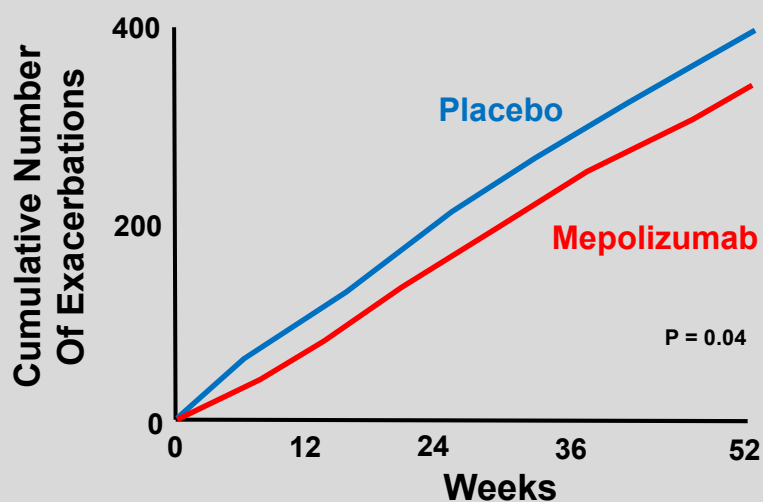
ICS: Inhaled corticosteroid

## Don't forget inhaler technique training!

- CPT code 94664
- Medicare reimbursement:
  - 0.49 RVUs
  - \$18



## IL-5 antibody reduces severe exacerbations in eosinophilic COPD



Mepolizumab:  
1.40/year

Placebo:  
1.73/year

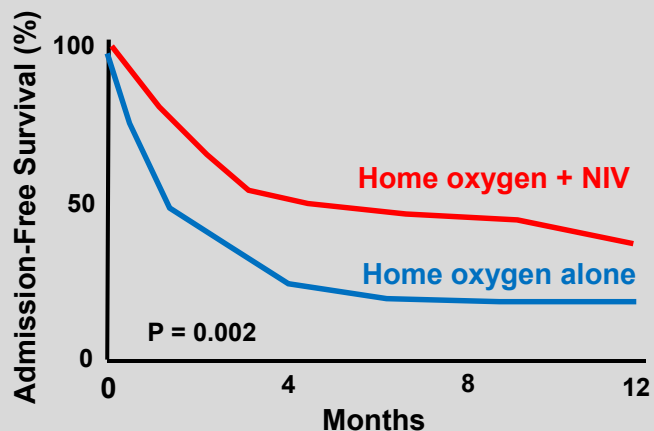
N Engl J Med 2017; 377:1613-1629

## Home non-invasive nocturnal ventilation reduces hospital readmission rates

- Baseline PCO<sub>2</sub> > 53
- Excluded patients with BMI > 35 or known sleep apnea
- 116 patients: oxygen alone versus oxygen plus ventilation
- Typical setting: IPAP 24, EPAP 4, backup rate 14

### Mean time to readmission:

- 4.3 months NIV group
- 1.4 months control group



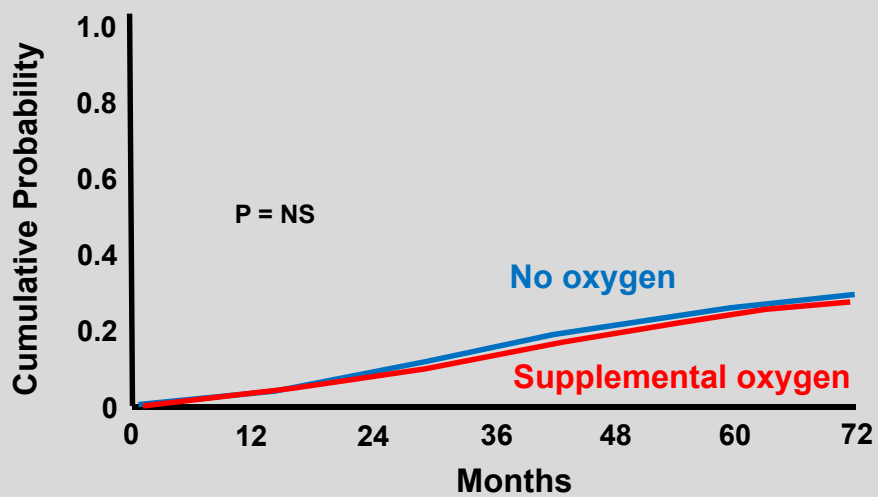
JAMA 2017; 317:2177-86

## LOTT: Long-Term Oxygen Treatment Trial



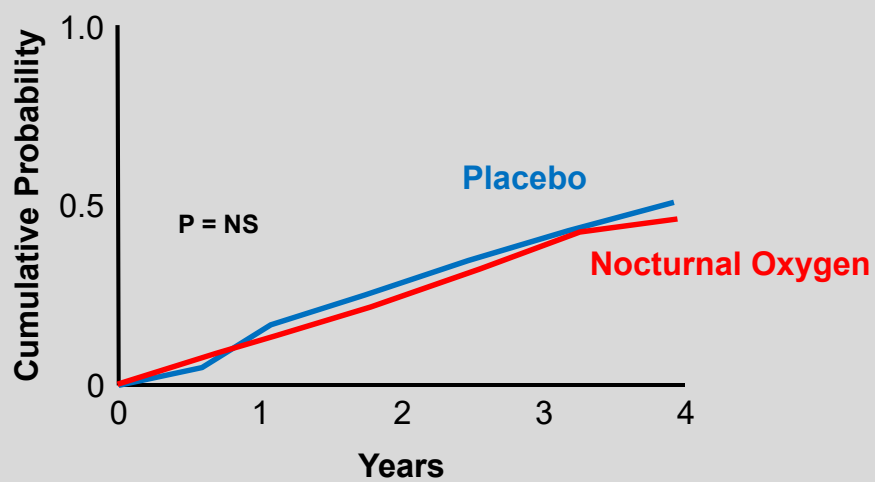
- 738 patients
- 42 medical centers
- Resting sat 89-93%
- 6 MWT sat > 80%
- Randomized to oxygen 2 L versus room air

## Probability of Death



N Engl J Med 2016;375:1617-1627.

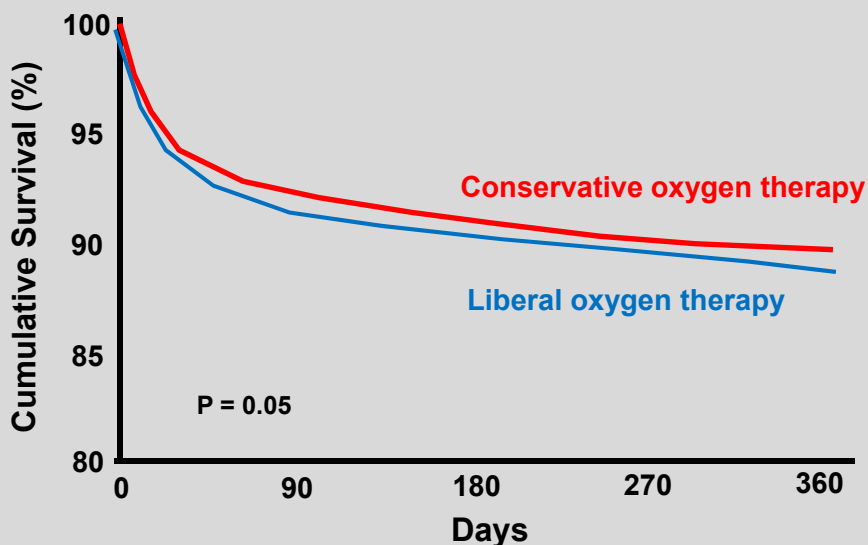
## Probability of Death or Requirement for Long-Term Oxygen



N Engl J Med 2020; 383:1129-1138



## Conservative oxygen therapy is associated with better survival



The Lancet. 391; April 2018: 1693-1705

## So, who should get home oxygen in 2020?

- Resting oxygen saturation  $\leq 88\%$
- Exertional oxygen saturation  $< 80\%$
- Patients who **may** benefit by oxygen with higher saturations:
  - Signs of pulmonary hypertension
  - Dyspnea or fatigue improved with oxygen
  - Nocturnal oxygen saturation  $< 88\%$  for more than 5 minutes total
- For COPD exacerbations: titrate oxygen to 88-92% and not higher

## Home Oxygen Options



## Home Oxygen Options

- Concentrators
  - Standard (5 L continuous flow)
  - High-Flow (10 L continuous flow)
  - Portable (4-6 L pulse flow)
- Compressed oxygen gas
  - E tank (4.4 hours at 2 L continuous flow)
  - D tank (2.5 hours at 2 L continuous flow)
- Liquid oxygen
  - Reservoir (4-6 weeks)
  - Portable tank (8 hours at 2 L pulse low)

## Cost of Oxygen

- Yearly oxygen rental cost: \$2,400
- Purchase options\*:
  - Portable concentrator: \$2,500
  - Home concentrator: \$500
- Yearly electricity cost: \$325

\*Medicare will pay for oxygen rental costs but not purchase costs

## Are Beta Blockers Safe in COPD?

- **Beta-blockers are associated with lower COPD exacerbations when beta-blockers are indicated for cardiovascular conditions**
  - Thorax 2016; 71:8014
- **Beta-blockers do not prevent COPD exacerbations when there is no cardiovascular indications**
  - N Engl J Med 2019; 381:2304-2314

## What about treating exacerbations?

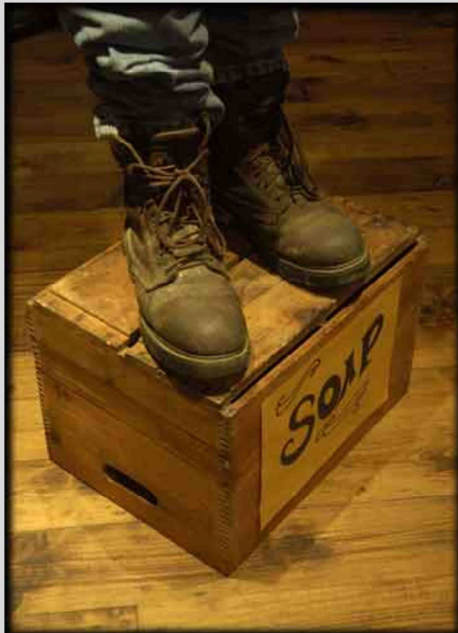
- Short-acting bronchodilators (eg, albuterol and/or ipratropium)
- Initiate maintenance inhaler
- Steroids for 5-7 days (eg, prednisone 40 mg/day)
- Antibiotics for 5-7 days if increased sputum volume/purulence
  - Azithromycin
  - Doxycycline
  - Ampicillin-clavulanate
- Oxygen to keep SaO<sub>2</sub> 88-92% (but not higher!)
- Non-invasive ventilation when respiratory failure results

## Other interventions in very severe COPD:

- Lung volume reduction surgery
  - Upper lobe dominant emphysema
- Bullectomy
  - Large bullae
- Endobronchial valves
  - Localized emphysema without collateral ventilation
- Lung transplant
  - Patients not meeting criteria for other interventions

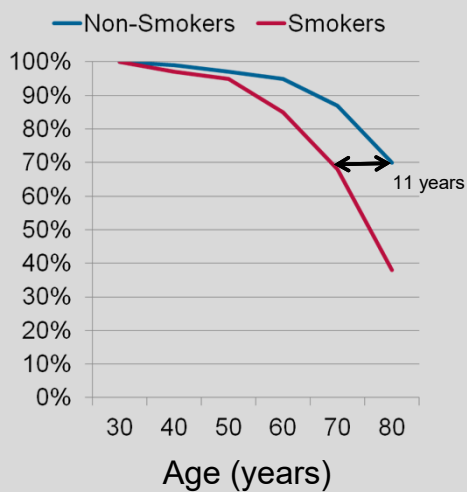
## Treatments to avoid in COPD:

- Inhaled corticosteroid monotherapy
- Long-term oral steroids
- Oral bronchodilators
- Theophylline
- Anti-tussives

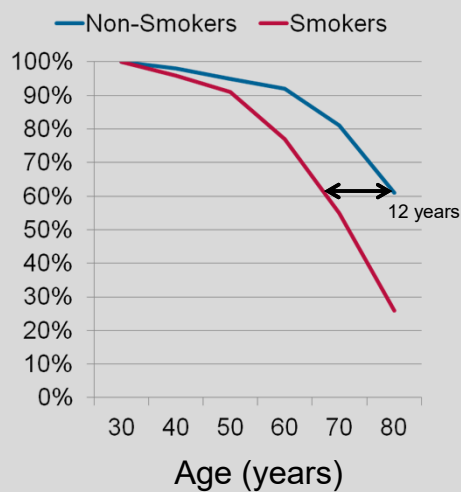


## Life expectancy for smokers and non-smokers

### Women



### Men

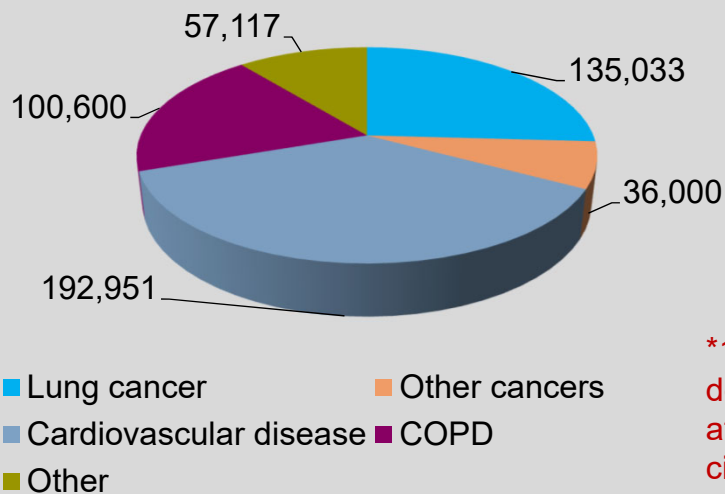


N Engl J Med 2013; 368:341-50

The average smoker loses  
**14 minutes** of life for every  
cigarette smoked



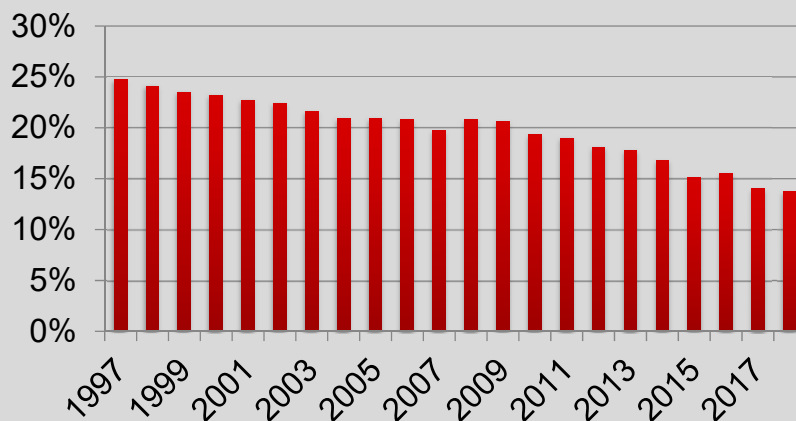
### Cigarette smoking causes 480,317 U.S. deaths per year\*



\*18.5% of U.S. deaths are attributable to cigarette smoking

Data source: CDC 2020

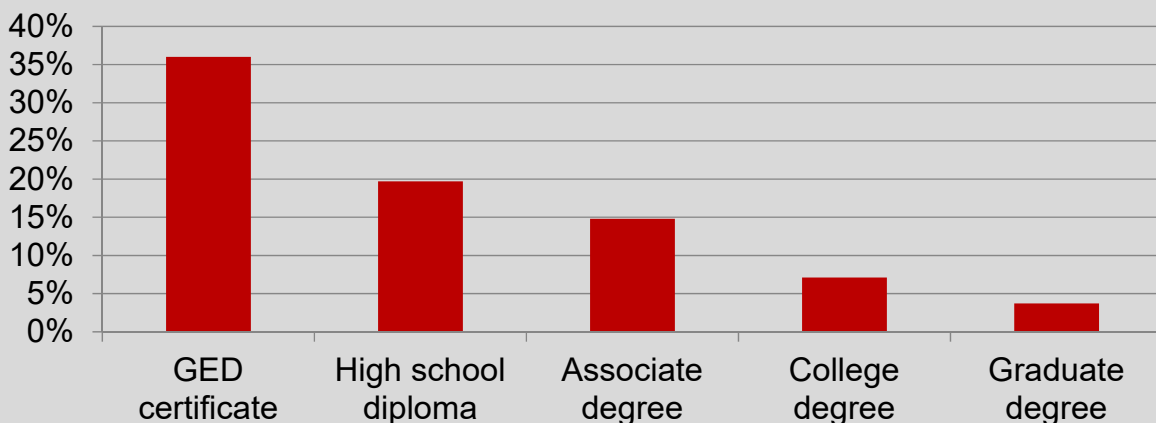
### Prevalence of Adult Smokers In The U.S.



In 2018: Male adult smokers = 15.6%; Female adult smokers = 12.0%

Data: Centers for Disease Control 2020

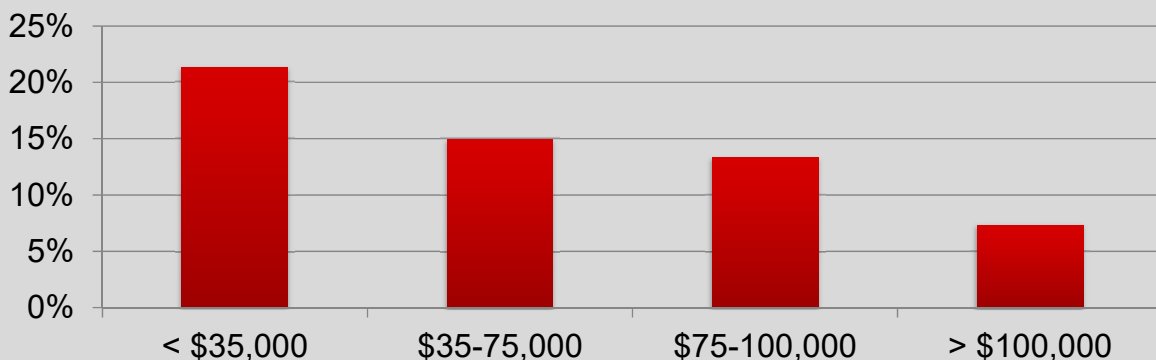
## Who Smokes In The United States?



Centers for Disease Control 2020

## Who Smokes In The United States?

### Prevalence By Annual Household Income

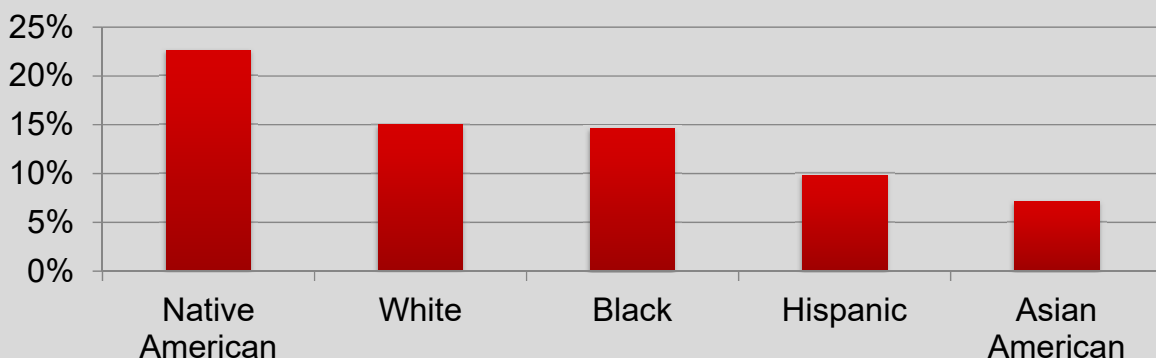


Centers for Disease Control 2020



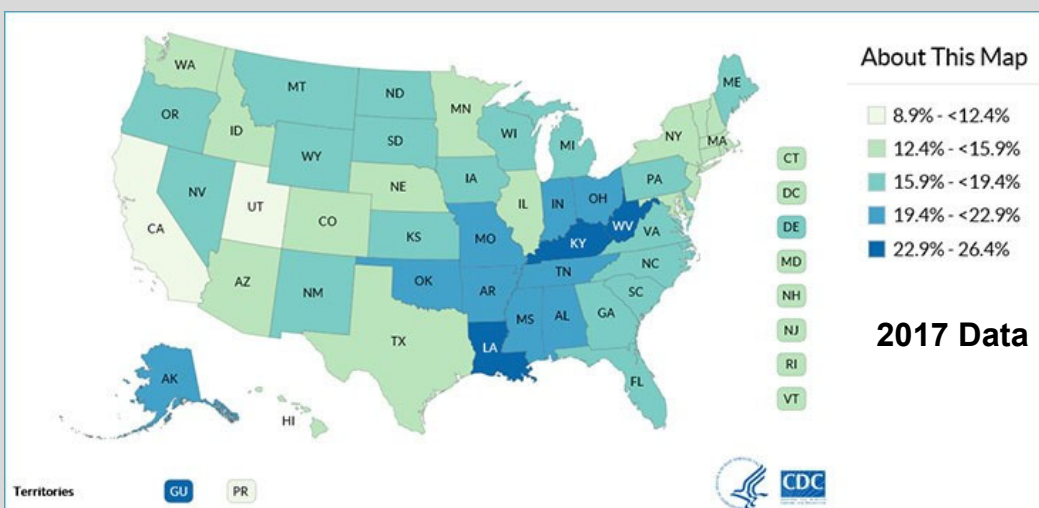
# Who Smokes In The United States?

## Prevalence Of Smoking By Race



Centers for Disease Control 2020

# Who Smokes In The United States?



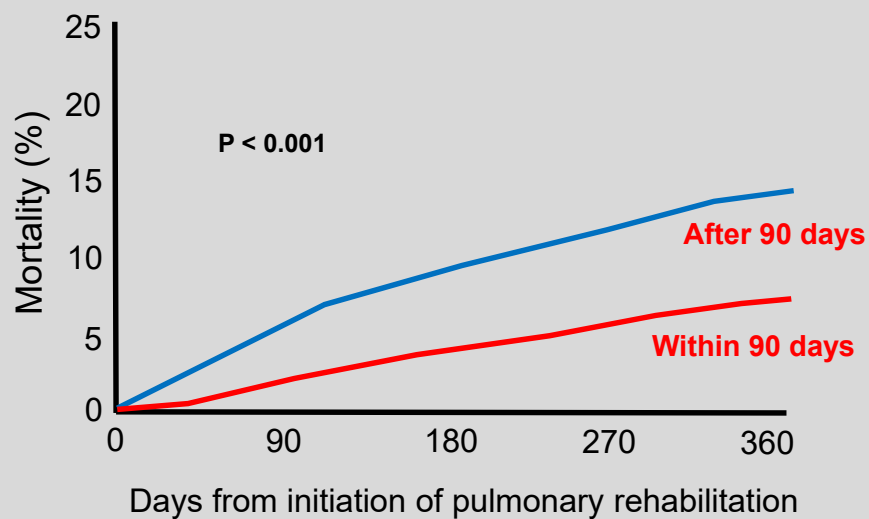
Source: CDC 2020

# Pulmonary Rehabilitation

- 8 week program
- 3 days per week
- 2 hours per session
- Focus on:
  - Education
  - Aerobic conditioning
  - Strength training
  - Quality of life



## Effect of Pulmonary Rehabilitation on Survival



JAMA. 2020;323(18):1813-1823

## **Effects of Pulmonary Rehabilitation on Hospital Readmission for COPD**

**25% reduction in hospital readmission**

*Respiratory Research 2005, 6:54*

## **Medicare 2020 readmission penalty**

- 2,583 hospitals penalized (83%)
- \$563 million in penalties
- Average penalty = 0.57% (\$217,963)
- 2,142 hospitals exempt: veteran's, children's, psychiatric, critical access hospitals

## Why Do COPD Patients Get Readmitted?

- Analysis of 27 million Medicare admissions from 2006-2010
  - 3.5% were for COPD
- 20.2% readmission in 30 days
  - Dual coverage (Medicare + Medicaid) most likely to be readmitted
  - 50% of readmissions occur in the first 2 weeks
- Only 28% of readmissions due to COPD
- 50% due to non-respiratory conditions
  - CHF
  - Sepsis
  - Arrhythmias
  - Fluids/electrolytes
  - Intestinal infection

Shah T. Chest 2015; 147:1219

## So what can we do to prevent readmissions?

1. Guideline-directed ER and hospital management
2. Utilize transition clinics
3. Smoking cessation
4. Inhaler education
5. Exacerbation action plans
6. Provider visit within 1 week
7. Post-discharge phone call at 48 hours
8. Pulmonary rehabilitation
9. Community home care services



89