



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

THE OHIO STATE UNIVERSITY
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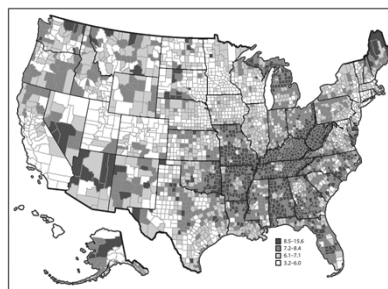
After this lecture, you should be able to:

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.

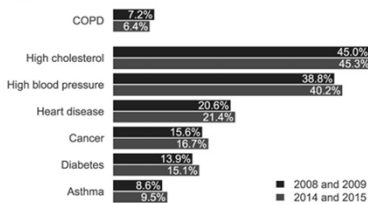
- 15.5 million people diagnosed
- 715,000 hospital admissions per year
- 120,000 deaths/year
- Annual cost up to \$50 billion
 - \$30 billion direct
 - \$20 billion indirect

Prevalence of COPD In The U.S.



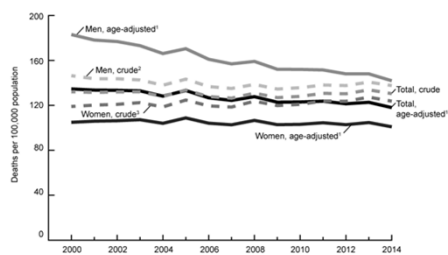
Prevalence of COPD Has Declined as Other Chronic Conditions Have Increased

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



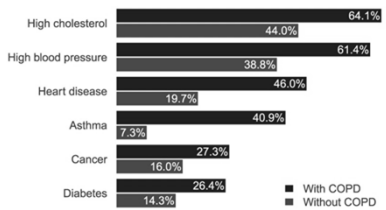
JAMA 2019; 322: 602

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)

Global Initiative on Obstructive Lung Disease (GOLD)

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

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 5th 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
 - ≥ 2 exacerbations/yr
 - ≥ 1 hospitalizations/yr

- Symptoms:
 - Less: MRC 0-1
 - More: MRC ≥ 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

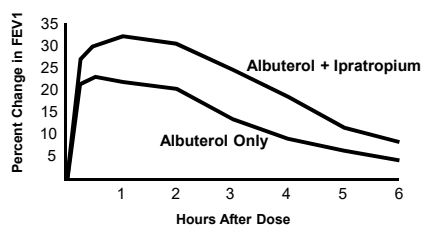
Where do our treatment guidelines come from?

- **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*

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
Generic Albuterol	albuterol	Q 6 Hours PRN	\$18
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
Combivent Respimat	ipratropium + albuterol	Q 6 Hours PRN	\$429
Generic Albuterol*	albuterol	Q 6 Hours PRN	\$21
Generic ipratropium*	ipratropium	Q 6 Hours PRN	\$17
Duoneb*	ipratropium + albuterol	Q 6 Hours PRN	\$32

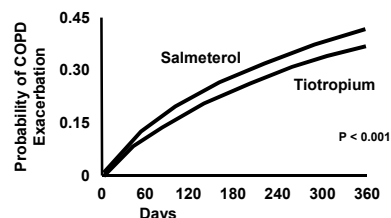
*Nebulized Cost per month: GoodRx



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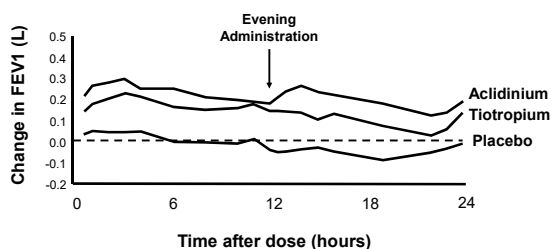
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Tiotropium (LAMA) Is Superior To Salmeterol (LABA) in COPD



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

Acclidinium 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
Perforomist*	formoterol	Twice Daily	\$1,056

*Nebulized formulation

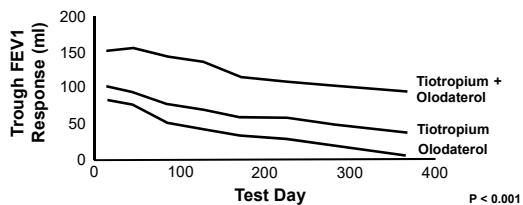
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 - N-acetylcysteine

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

- LABA/LAMA dual therapy preferred over either LAMA alone or LABA alone
- ICS/LABA/LAMA triple therapy recommended for patients with > 1 exacerbation per year requiring:
 - Antibiotics
 - Steroids
 - Hospitalization
- 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	Acclidinium + formoterol	Twice daily	\$990

Cost per month: GoodRx

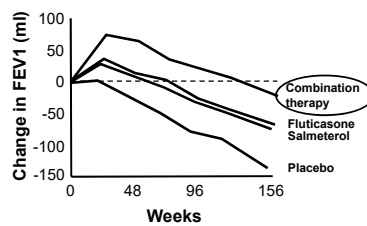


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 - N-acetylcysteine



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



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

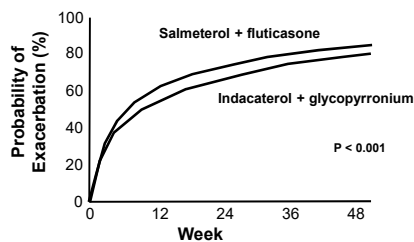
FLAME Study

- 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

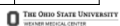


N Engl J Med 2016;374:2222-2234

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

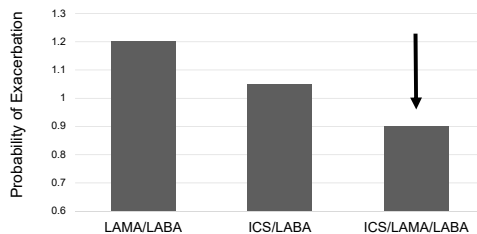
Cost per month: GoodRx



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

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 - Antibiotics
 - Steroids
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3. ICS can be withdrawn if no exacerbations for 1 year

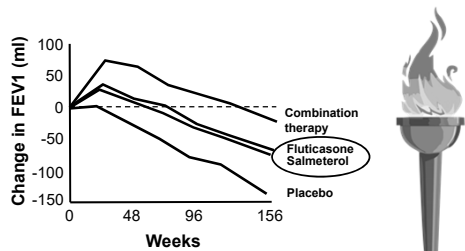
Am J Respir Crit Care Med Vol 201, Iss 9, pp 1039-1049, May 1, 2020

LAMA/LABA/ICS Combination

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

Cost per month: GoodRx

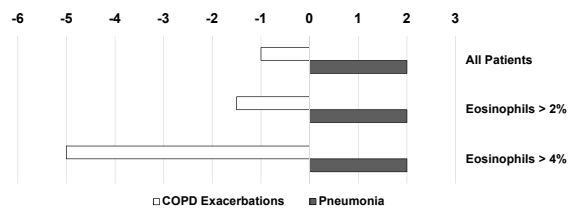
TORCH study: ICS and LABA are equivalent



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

Which patients with COPD should have an inhaled corticosteroid?

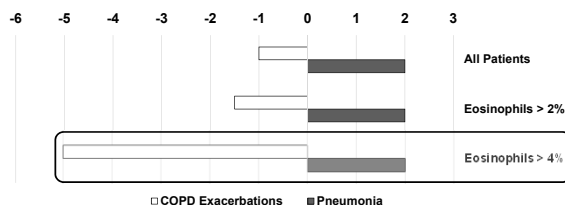
Excess Number Of Patients With A Hospitalization Per 100 Treated In 1 Year:
ICS + LABA versus LABA Alone



Chest 2017; 152:227-231

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 - 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

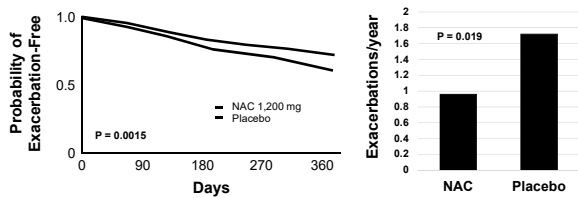
Cost per month: GoodRx



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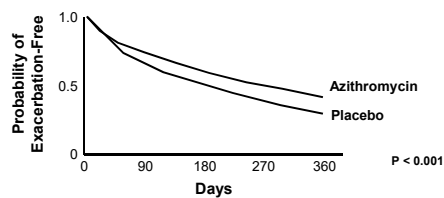
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 - N-acetylcysteine
 - Daily azithromycin
 - Roflumilast

N-acetylcysteine prevents COPD exacerbations



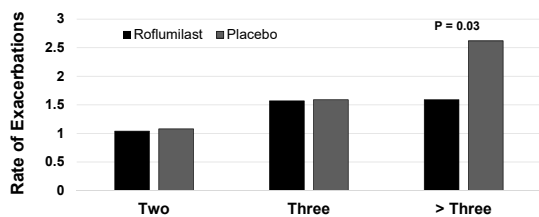
Lancet Respir Med 2014; 2: 187-94

Azithromycin prevents COPD exacerbations



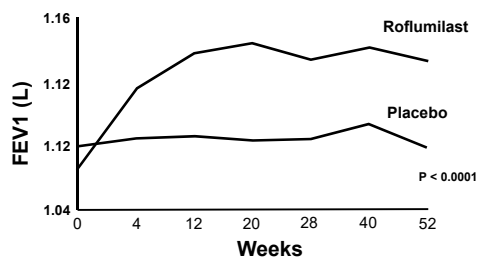
N Engl J Med 2011;365:689-698.

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 LAMA + LABA + azithromycin LAMA + LABA + roflumilast	Albuterol	\$403 \$403 \$775
5	LAMA + LABA + ICS	Albuterol	\$438

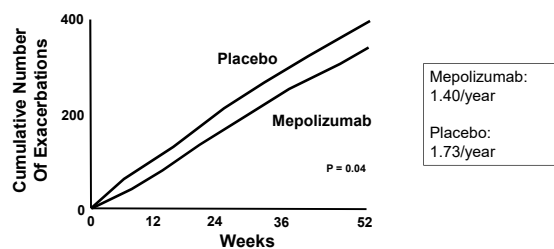
*Cost is monthly cost for least expensive brand alternatives
 LAMA: Long-acting muscarinic antagonist (long-acting anti-cholinergic)
 LABA: Long-acting beta agonist
 ICS: Inhaled corticosteroid

Don't forget inhaler technique training!

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



IL-5 antibody reduces severe exacerbations in eosinophilic COPD

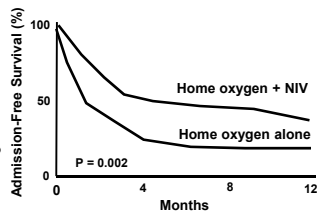


N Engl J Med 2017; 377:1613-1629

Home non-invasive nocturnal ventilation reduces hospital readmission rates

- Baseline PCO₂ > 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



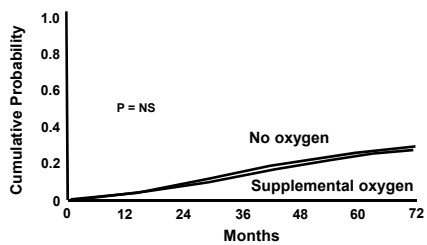
JAMA 2017; 317:2177-86

LOTT: Long-Term Oxygen Treatment Trial



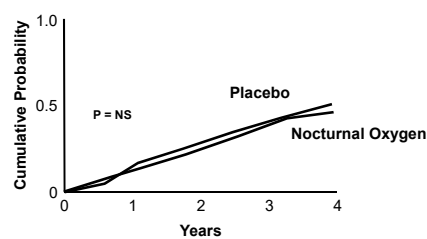
- 738 patients
- 42 medical centers
- Resting sat 89-93%
- 6 MWT sat > 80%
- Randomized to oxygen 2 L versus room air

Probability of Death



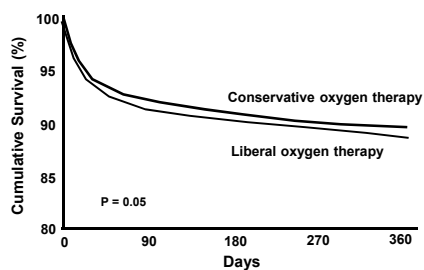
N Engl J Med 2016; 375:1617-1627.

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**

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HEALTH SERVICES

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

70 |

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 SaO₂ 88-92% (but not higher!)
- Non-invasive ventilation when respiratory failure results

Other interventions in very severe COPD:

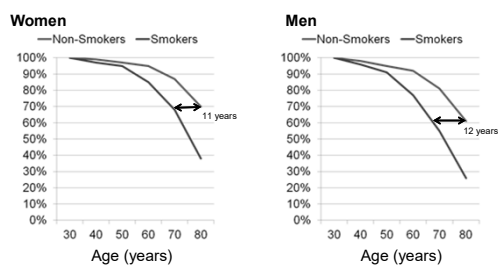
- Lung volume reduction surgery
 - Upper lobe dominant emphysema
- Bullectomy
 - Large bullae
- Endobronchial valves
 - Localized emphysema without collateral ventilation
- Lung transplant
 - Patients not meeting criteria for other interventions

Treatments to avoid in COPD:

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



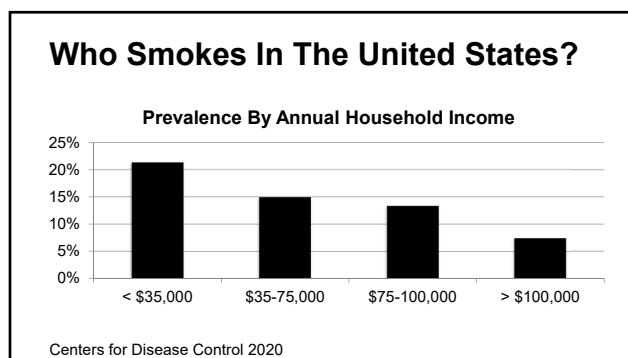
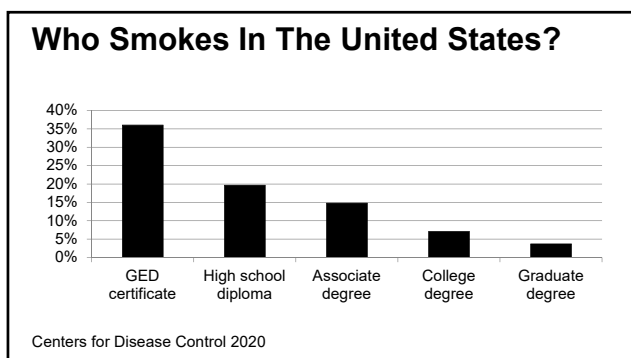
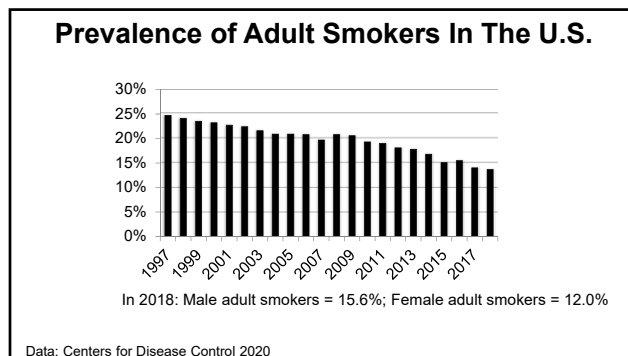
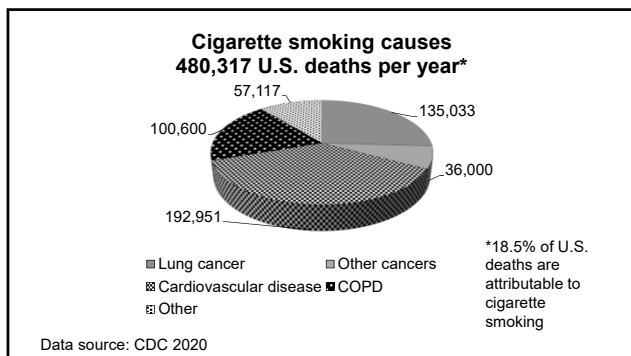
Life expectancy for smokers and non-smokers



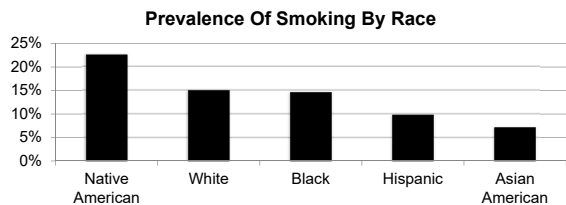
N Engl J Med 2013; 368:341-50

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



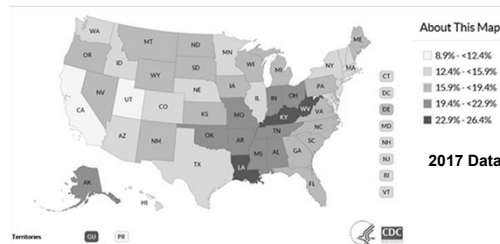


Who Smokes In The United States?



Centers for Disease Control 2020

Who Smokes In The United States?



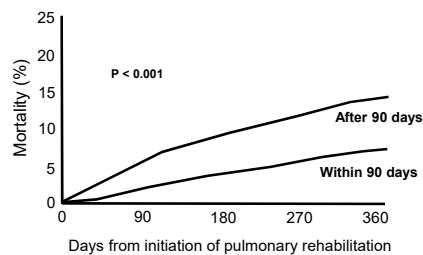
Source: CDC 2020

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

