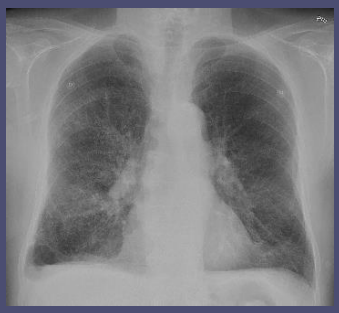

Chronic Obstructive Pulmonary Disease:
Optimizing Outpatient Care & Reducing Exacerbations

Michelle Zeidler, MD, MS
Professor of Medicine, Pulmonary, Critical Care Medicine & Sleep Medicine, VA Greater Los Angeles Healthcare System, David Geffen School of Medicine at UCLA

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Disclosures

- Michelle Zeidler, MD, MS, has no relevant financial relationships with commercial interests to disclose.

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Chronic Obstructive Pulmonary Disease:
Optimizing Outpatient Care & Reducing Exacerbations

- Epidemiology/Pathophysiology
- Diagnosis
- Phenotypes
- Assessment/Stratification
- Outpatient pharmacotherapy
- Exacerbations
  - Risks
  - Treatments

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GOLD Definition of COPD

"COPD is a
- common preventable and treatable disease,
- characterized by airflow limitation that is usually persistent,
- respiratory symptoms and
- airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases."

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Scope of the Problem

- 6.3% of US adults (~ 15 million) have a diagnosis of COPD[1]
  Data obtained from the CDC's Behavior Risk Factor Surveillance System, the world's largest on-going telephone health survey system
- NHLBI estimates that another 12 million Americans have undiagnosed COPD
- In the US, estimated direct costs of COPD are $32 billion and indirect costs $20.4 billion (costs mainly due to exacerbations) [2]

[1] *MMWR* 2012;61(46) [2] *CEOR* 2013;5:235-45 [3] *JAMA* 2013;310(6):591-608

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Scope of the Problem

- COPD is a disease with high mortality and morbidity
  - 4th most common diagnosis among hospitalized U.S. Veterans ages 65-74
  - 3rd leading cause of death worldwide, including the US
    - A person with COPD dies every 4 minutes
    - 120,000 die annually in the U.S. alone
  - 2nd leading cause of disability in the U.S.
    - High resource utilization
      - Frequent office visits
      - Frequent ER visits
      - Frequent hospitalizations
      - Need for chronic therapy
- **COPD is often undertreated with many patients receiving suboptimal or NO treatment!**

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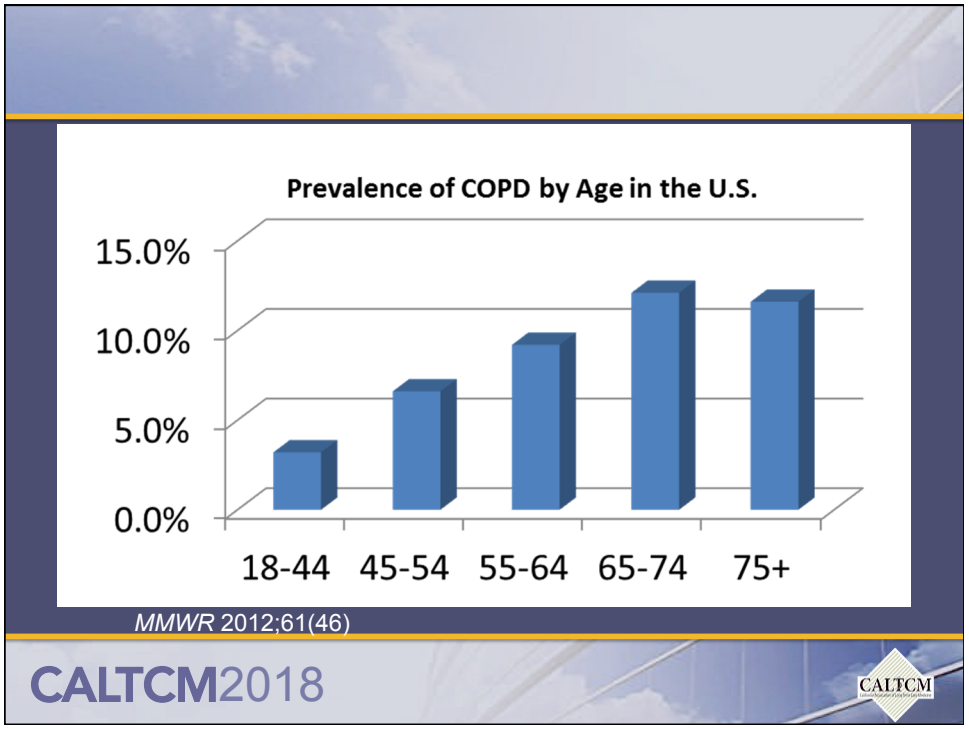

MMWR 2012;61(46)

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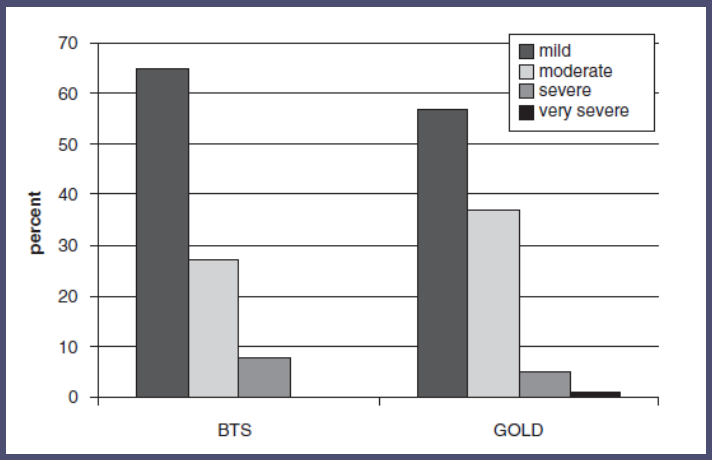
Most cases of COPD are Mild-Moderate



Respiratory Medicine (2006) **100**, 264–272

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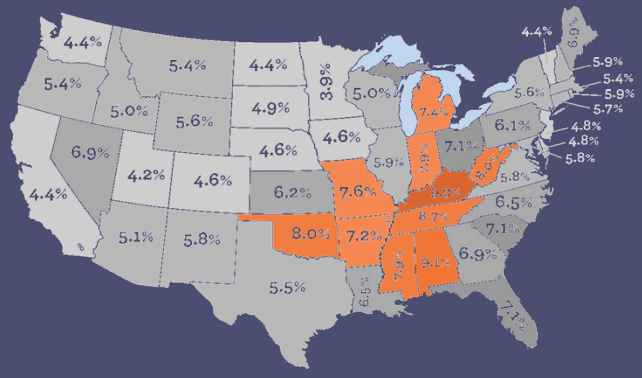
Impact of COPD in the U.S. State Prevalence Rates



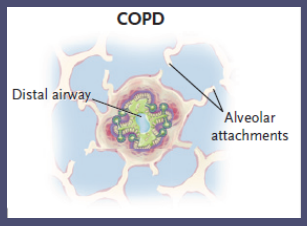
MMWR 2012;61(46)

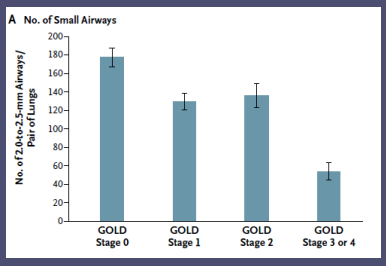
Etiology

- Tobacco smoking
  - Cigarettes, pipe, cigar, environmental tobacco smoke (2nd hand)
- Indoor air pollution
  - Biomass fuel for cooking and heating in poorly ventilated dwellings ("hut lung")
- Occupational dusts and chemicals
  - Vapors, irritants, fumes
- Outdoor air pollution
- Genetic risk factors
  - Alpha-1 antitrypsin*

Pathophysiology

- Chronic inflammation leads to narrowing and reduction in the number of small conducting airways (terminal bronchioles) → airway collapse due to loss of tethering caused by alveolar wall destruction





N Engl J Med 2010;362:1407-16.
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N Engl J Med 2011;365:1567-75.
Copyright © 2011 Massachusetts Medical Society.

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Clinical Manifestations of COPD

- Dyspnea
  - Progressive
  - Worse with exertion
  - Persistent
- Chronic cough
- Wheezing/chest tightness
- Chronic sputum production
- Episodes of acute worsening of these symptoms often occur (exacerbations)

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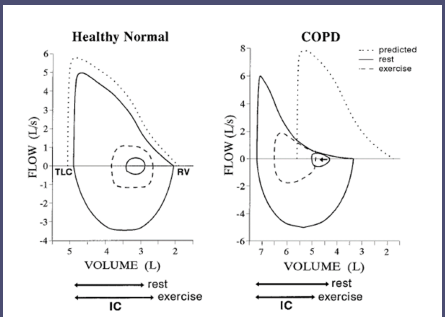
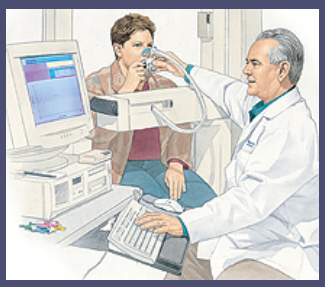
Diagnosis



- Symptoms:
- History of exposure to risk factors
- Spirometry demonstrating a post-bronchodilator FEV1/FVC < 0.70



Laboratory Studies

- Consider CBC to evaluate for anemia as a cause of dyspnea
- Consider BNP to rule out CHF and assess for cor pulmonale
- Consider ABG if bicarbonate is elevated to assess for a compensated respiratory acidosis
- WHO: All symptomatic adults with persistent obstruction on spirometry should have alpha-1 antitrypsin level* checked, especially if young (≤45), non-smokers and basilar predominant emphysema

*Normal AAT is > 11 mmol/L

ORIGINAL RESEARCH

Identification of Five Chronic Obstructive Pulmonary Disease Subgroups with Different Prognoses in the ECLIPSE Cohort Using Cluster Analysis

Table 1. List of variables included in the factor analysis

Demographics	Symptoms	Biochemical	Clinical/Functional
*Age**	*CES-D depression score*	*White blood cell count*	6-minute-walk distance
Sex	FACIT-F fatigue score	*Neutrophil count*	Blood oxygen %
Current smoker (Y/N), pack-year history	*mMRC dyspnea score exacerbation history (>1 V ≤1)*	Eosinophil count Hematocrit C-16 ATS-DLD items	*FEV_1 % predicted* FEV_1 percent reversibility *FVC percent predicted*
	Chronic cough	SP-D	*FEV_1/FVC ratio*
	Chronic sputum	*Fibrinogen*	AX (impulse oscillometry)
	Cardiovascular events	IL-8	R5 (impulse oscillometry)
	Reflux	IL-6	R5–R15 (impulse oscillometry)
	Osteoporosis	TNF-α	Emphysema % LAA (–950 HU)
	Anxiety	CCL18/PARC	Qualitative CT grade
	Diabetes	*CRP*	*BMI*
	Hypertension		Fat-free mass index

AnnalsATS Volume 12 Number 3 | March 2015

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COPD "Phenotypes"

- Cluster A:
  - Mild disease
  - Few deaths and hospitalizations
- Cluster B:
  - Less systemic inflammation at baseline but notable changes in health and emphysema extent
- Cluster C:
  - Many comorbidities
- Cluster D:
  - Low FEV_1
  - Severe emphysema
  - Highest exacerbation rate
  - Highest COPD related hospitalization rate
- Cluster E:
  - Intermediate for most variables
  - May represent a mixed group

AnnalsATS Volume 12 Number 3 | March 2015

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COPD Assessment

1. Assess symptoms
   - COPD Assessment Test (CAT)
   - Modified Medical Research Council (mMRC)
2. Assess degree of airflow limitation
   - Spirometry
3. Assess risk of exacerbations
4. Assess comorbidities

Assess Symptoms: COPD Assessment Test

<10 = Less Symptoms
≥10 = More Symptoms

Assess Symptoms: Modified Medical Research Council

Grade	Patient's description of breathlessness
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 have to stop for breath when walking at my own pace on the level
Grade 3	I stop for breath after walking about 100 yards or after a few minutes on the level
Grade 4	I am too breathless to leave the house or I am breathless when dressing

Fletcher CM. *BMJ* 1960;2:1662

mMRC 0-1 = Less Symptoms
mMRC ≥2 = More Symptoms

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Assess Degree of Airflow Limitation Using Spirometry

In patient's with $FEV_1/FVC < 0.70$:

GOLD Stage	Classification	FEV1
GOLD 1	Mild	$FEV_1 \geq 80\%$ predicted
GOLD 2	Moderate	$50\% \leq FEV_1 < 80\%$
GOLD 3	Severe	$30\% \leq FEV_1 < 50\%$
GOLD 4	Very Severe	$FEV_1 < 30\%$ predicted

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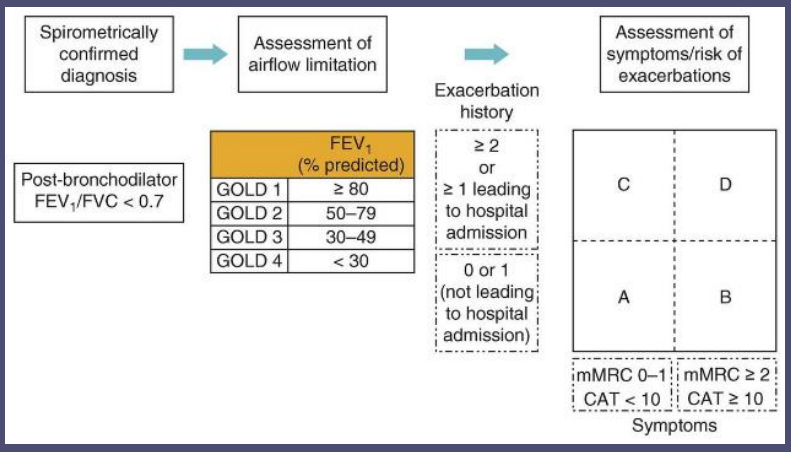
Assess Risk of Exacerbations

- Definition of an Exacerbation
  - An increase in dyspnea, cough or sputum production beyond normal day-to-day variations leading to a change in medication
    - Mild: SABDs
    - Moderate: SABDs plus antibiotics and/or oral steroids
    - Severe: Hospitalization or ER visit
- *Hospitalization for a COPD exacerbation is associated with a poor prognosis and increased risk of death!*

GOLD Combined Assessment for COPD



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Therapies for COPD

- Smoking cessation
- Short acting beta agonists
- Short acting muscarinic agonists
- Long acting beta agonists
- Long acting muscarinic agonists
- PDE4 Inhibitors
- Azithromycin

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Approach to Pharmacotherapy

GOLD 2018 Guidelines

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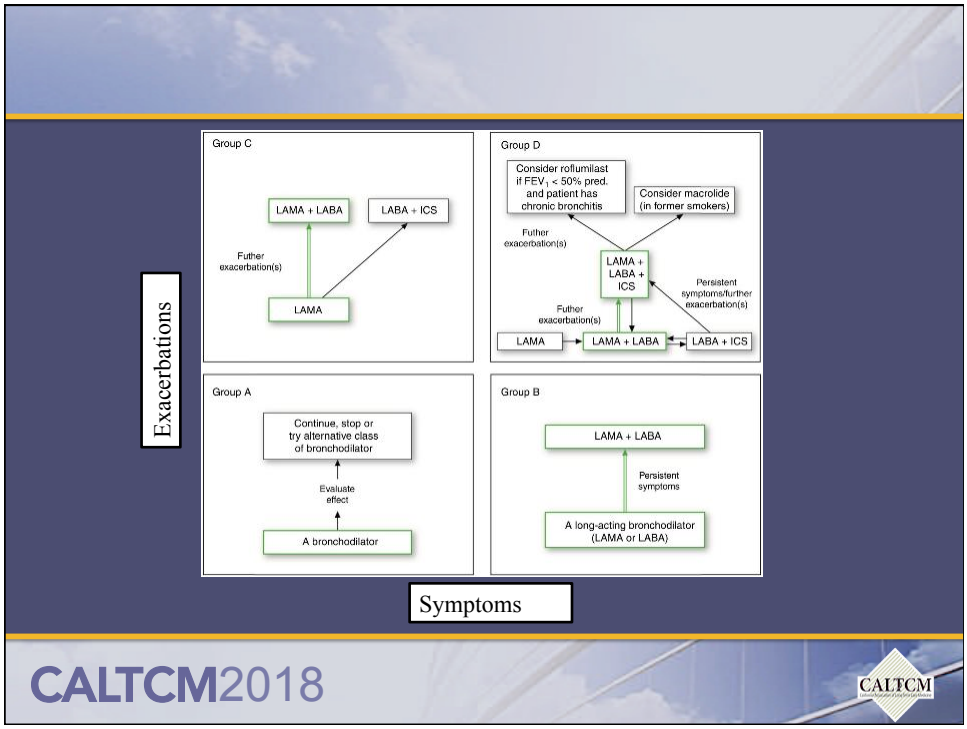

Smoking cessation has the greatest capacity to influence the natural history of COPD

Effects of Smoking Intervention and the Use of an Inhaled Anticholinergic Bronchodilator on the Rate of Decline of FEV_1

The Lung Health Study

Nicholas R. Anthonisen, MD; John E. Connett, PhD; James P. Kiley, PhD; Murray D. Altose, MD; William C. Bailey, MD; A. Sonia Buist, MD; William A. Conway, Jr, MD; Paul L. Enright, MD; Richard E. Kanner, MD; Peggy O'Hara, PhD; Gregory R. Owens, MD; Paul D. Scanlon, MD; Donald P. Tashkin, MD; Robert A. Wise, MD; for the Lung Health Study Research Group

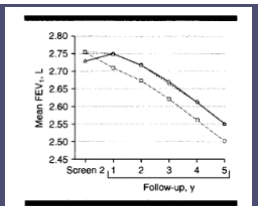

Figure 3.—Mean postbronchodilator forced expiratory volume at 1 second (FEV_1) over the course of the study in all participants in whom the measurement was made. Circles/dotted line represent the smoking intervention and placebo group, triangles/solid lines represent the smoking intervention and ipratropium bromide group, and squares/dashed line represent the usual care group.

N=5887 smokers
Ages 35-60
Mild COPD

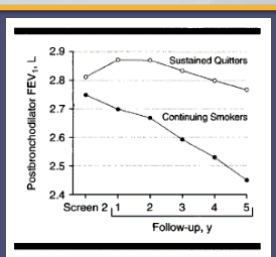

Figure 5.—Mean postbronchodilator forced expiratory volume at 1 second (FEV_1) for participants in the smoking intervention and placebo group who were sustained quitters (open circles) and continuous smokers (closed circles). The two curves diverge sharply after baseline.

Conclusions.—An aggressive smoking intervention program significantly reduces the age-related decline in FEV_1 in middle-aged smokers with mild airways obstruction. Use of an inhaled anticholinergic bronchodilator results in a relatively small improvement in FEV_1 that appears to be reversed after the drug is discontinued. Use of the bronchodilator did not influence the long-term decline of FEV_1.

(*JAMA*. 1994;272:1497-1505)

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Smoking Cessation

- Smoking cessation best accomplished via counseling **AND** pharmacological therapy
  - Counseling:
    - Increases quit rates over self-initiated strategies
    - A brief (3-minute) period of counseling to urge a smoker to quit can result in quit rates of 5-10%
  - Pharmacological agents:
    - Nicotine Replacement Therapy (NRT)
      - Transdermal nicotine patch
      - Nicotine gum
      - Nicotine lozenge
      - Nicotine sublingual tablet
      - Nicotine inhaler
      - Nicotine nasal spray
    - Buproprion (Zyban)
    - Varenicline (Chantix)

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In Chronic Obstructive Pulmonary Disease, a Combination of Ipratropium and Albuterol Is More Effective Than Either Agent Alone

An 85-Day Multicenter Trial

*COMBIVENT Inhalation Aerosol Study Group**

(Chest 1994; 105:1411-19)

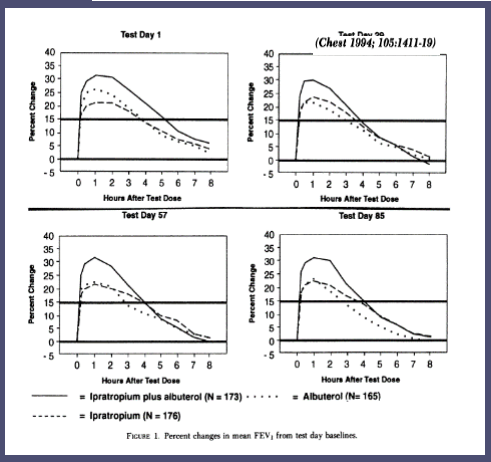

FIGURE 1. Percent changes in mean FEV_1 from test day baselines.

12 week, prospective, double-blind, parallel group evaluation (albuterol, ipratropium or combination)

N=534

Combination demonstrated superior improvement in FEV1, especially over the first 4 hours compared to its mono components

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Long Acting Beta2-Agonists (LABAs) "Controller"

- FDA approved as maintenance treatment of bronchoconstriction in patients with COPD
- Not indicated for acute bronchospasm
- Medications:
  - Long-Acting: last 12 hours
    - Formoterol DPI (Foradil Aerolizer) *** no longer available ***
    - Formoterol solution (Perforomist)
    - Arformoterol solution (Brovana)
    - Salmeterol MDI & DPI (Serevent Diskus)
  - Ultra Long Acting: last 24 hours
    - Indacaterol DPI (Arcapta Neohaler)
    - **Olodaterol SMI (Striverdi Respimat)**
    - Vilanterol (only available in combo therapy with LAMA or ICS)

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THE COCHRANE COLLABORATION®

Long-acting beta$_2$-agonists for chronic obstructive pulmonary disease (Review)

Kew KM, Mavergames C, Walters JAE

- 26 RCTs, n=14,939
- Effective over the medium and long term for patients with moderate to severe COPD
- Improve health related quality of life
- Improve lung function
- Reduce exacerbations, hospitalizations
- No increase in mortality or SAEs

Citation: Kew KM, Mavergames C, Walters JAE. Long-acting beta$_2$-agonists for chronic obstructive pulmonary disease. *Cochrane Database of Systematic Reviews* 2013, Issue 10. Art. No.: CD010177. DOI: 10.1002/14651858.CD010177.pub2.

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Long Acting Muscarinic Antagonists (LAMAs) "Controller"

- FDA approved for the long term maintenance treatment of bronchospasm associated with COPD
- * Tiotropium also FDA approved for reducing the likelihood of COPD exacerbations
- Not indicated for acute bronchospasm
- Medications:
  - **Tiotropium (Spiriva Handihaler; Spiriva Respimat)**
    - Spiriva HandiHaler: 18 mcg daily
    - Spiriva Respimat: 2.5 mcg/actuation daily
  - Umeclidinium (Incruse Ellipta): 62.5 mcg daily
  - Aclidinium bromide (Tudorza Pressair): 400 mcg twice daily
  - Glycopyrronium (Seebri Breezhaler): 50 mcg once daily

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So, do you add a LABA or LAMA first?

Tiotropium versus long-acting beta-agonists for stable chronic obstructive pulmonary disease (Review)

Chong J, Karner C, Poole P

THE COCHRANE COLLABORATION®

- 7 studies; n=12,223
- No difference in mortality
- Tiotropium equivocal with respect to LABAs at improving QOL
- Symptom improvement and lung function improvement similar between the two
- Tiotropium more effective than LABAs in preventing COPD exacerbations and disease related hospitalizations
- Less SAEs with tiotropium

Citation: Chong J, Karner C, Poole P. Tiotropium versus long-acting beta-agonists for stable chronic obstructive pulmonary disease. *Cochrane Database of Systematic Reviews* 2012, Issue 9. Art. No.: CD008157. DOI: 10.1002/14651858.CD008157.pub2.

Combination LABA/LAMA "Controller"

- FDA approved for the long-term maintenance treatment of airflow obstruction in patients with COPD
- Medications:
  - Vilanterol/Umeclidinium (Anoro Ellipta) DPI: once daily
  - Olodaterol/Tiotropium (Stiolto Respimat) SMI: once daily
  - Formoterol/Aclidinium (Duaklir Genuair) DPI: twice daily
  - Indacaterol/Glycopyrronium (Utibron Neohaler) DPI: twice daily
  - Formoterol/Glycopyrrolate (Bevespi Aerosphere) MDI: twice daily

Combination LABA/LAMA

- Compared to LABA or LAMA
  - Improved lung function (FEV1)
  - Improved quality of life (SGRQ)
  - Decreased exacerbations
- Compared to LABA/ICS
  - Decreased exacerbations

Eur Respir J 2015; 45:869-871
Prim Care Respir J 2012; 21(1):101-8
Cochrane Database Syst Rev 2015;10(10):CD008989
FLAME *N Engl J Med* 2016; 374(23):2222-34

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Inhaled Corticosteroids (ICS)

- Inhaled corticosteroids are FDA approved for maintenance treatment of ASTHMA
- Use of inhaled corticosteroids as monotherapy for COPD is OFF-LABEL
- Consider starting first in patients with ACO (+/- LABA)
- Not indicated for acute bronchospasm
- Medications:
  - Beclomethasone (QVAR)
  - Flunisolide (Aerobid)
  - Ciclesonide (Alvesco)
  - Budesonide (Pulmicort Flexhaler)
  - Fluticasone (Flovent HFA or Diskus)
  - Mometasone (Asmanex Twisthaler)
  - Triamcinolone (Azmacort)

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Combination ICS/LABA

- FDA approved for maintenance treatment of airflow obstruction *and* reducing exacerbations* in patients with COPD
- Consider starting first in patients with ACO
- Not indicated for acute bronchospasm
- Medications:
  - Budesonide + Formoterol (Symbicort)
  - Fluticasone + Salmeterol(Advair)*
  - Fluticasone + Vilanterol (Breo-Ellipta)*
  - Mometasone + Formoterol (Dulera)

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Combination LAMA/LABA/ICS aka "triple therapy"

- Compared to ICS/LABA or LAMA monotherapy
  - Improves lung function
  - Improves symptoms
  - Improves health status
  - Reduces exacerbations

Thorax 2008; 63(7):592-8
Thorax 2015; 70(6):519-27
COPD 2016; 13(1):1-10
Lancet 2016: 388(10048): 963-73

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ICS AEs

- Oral candidiasis
- Hoarse voice
- Skin bruising
- Pneumonia
  - Smokers, >55, hx of prior exacerbations/PNA, BMI <25, poor MRC dyspnea score and/or severe airflow limitation

Annals of ATS 2015; 12(1):27-34
SUMMIT trial *Respir Med* 2017; 131:27-34

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AECOPD

- Increased respiratory symptoms (cough, dyspnea, sputum production, purulent sputum, wheezing) resulting in additional therapy
- Classification:
  - Mild: SABDs
  - Moderate: SABDs + Abx and/or steroids
  - Severe: Hospitalization or ER visit
- Etiology: URI, noxious inhalation, non-compliance w/ meds, bad inhaler technique, UACS, GERD, CHF/arrhythmia
- CXR, EKG (?PE), ABG, CBC, BNP, ECHO
- Rx:
  - Oxygen
  - Inhaled short-acting bronchodilators
  - Antibiotics 5-7 days (FQ, macrolides)
    - Shorten recovery time, reduce risk of early relapse, treatment failure and hospital LOS
  - Systemic steroids
    - Shorten recovery time, reduced risk of early relapse, decrease hospital LOS, improves oxygenation and accelerates recovery of FEV1
  - BiPAP if respiratory acidosis (hold if obtunded, vomiting, secretions)
    - Reduces hospital stay
    - Improves mortality in AECOPD with impending respiratory failure
  - Diuresis? Control arrhythmias? Anticoagulation for PE?

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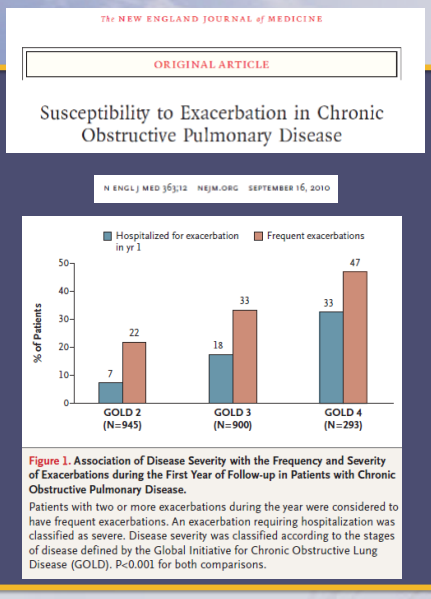

- ECLIPSE study
- N=2138 over 3 years
- Exacerbations more frequent with increased severity of COPD
- Single best predictor of exacerbations (across all GOLD stages) was a history of exacerbations

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Short-term vs Conventional Glucocorticoid Therapy in Acute Exacerbations of Chronic Obstructive Pulmonary Disease

The REDUCE Randomized Clinical Trial

- Double blind, placebo-controlled, non-inferiority trial (n=314)
- Patients presenting to ER in AECOPD and admitted to the hospital
- 40 mg prednisone daily for 5d vs. 14 d
- Outcome: Time to exacerbation within 180d
- 37.2% reexacerbation in the 5d
- 38.4% reexacerbation in the 14d

JAMA, June 5, 2013—Vol 309, No. 21

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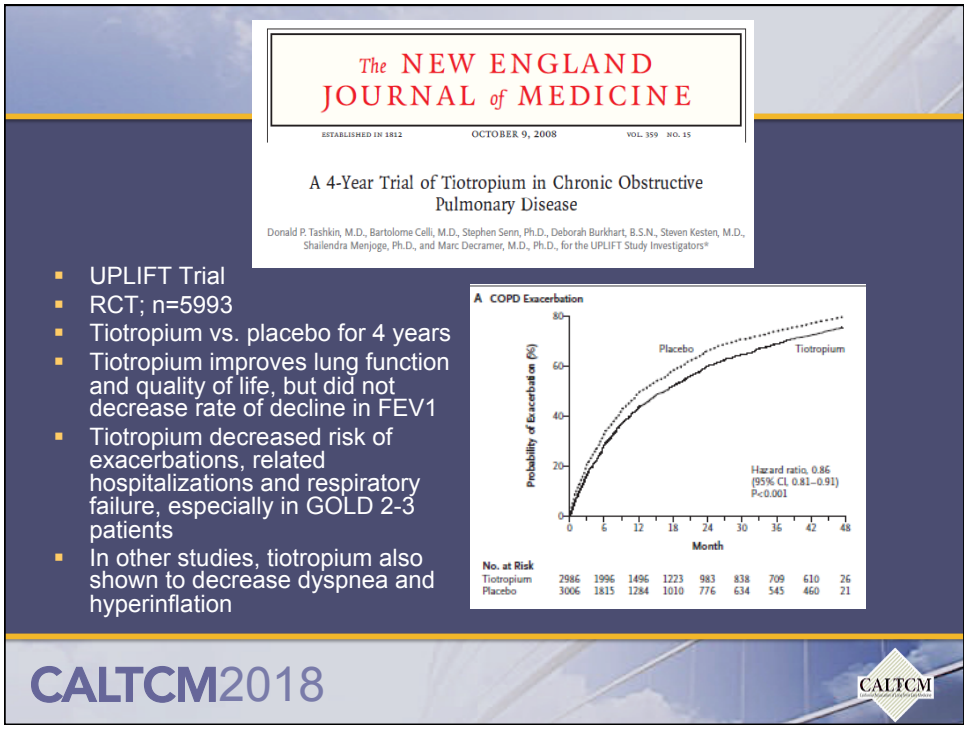
The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 OCTOBER 9, 2008 VOL. 359 NO. 15
A 4-Year Trial of Tiotropium in Chronic Obstructive Pulmonary Disease
Donald P. Tashkin, M.D., Bartolome Celli, M.D., Stephen Senn, Ph.D., Deborah Burkhart, B.S.N., Steven Kesten, M.D., Shailendra Menjoge, Ph.D., and Marc Decramer, M.D., Ph.D., for the UPLIFT Study Investigators*
UPLIFT Trial
RCT; n=5993
Tiotropium vs. placebo for 4 years
Tiotropium improves lung function and quality of life, but did not decrease rate of decline in FEV1
Tiotropium decreased risk of exacerbations, related hospitalizations and respiratory failure, especially in GOLD 2-3 patients
In other studies, tiotropium also shown to decrease dyspnea and hyperinflation
A COPD Exacerbation
Probability of Exacerbation (%)
Placebo
Tiotropium
Hazard ratio, 0.86 (95% CI, 0.81–0.91) P<0.001
Month
No. at Risk
Tiotropium 2986 1996 1496 1223 983 838 709 610 26
Placebo 3006 1815 1284 1010 776 634 545 460 21
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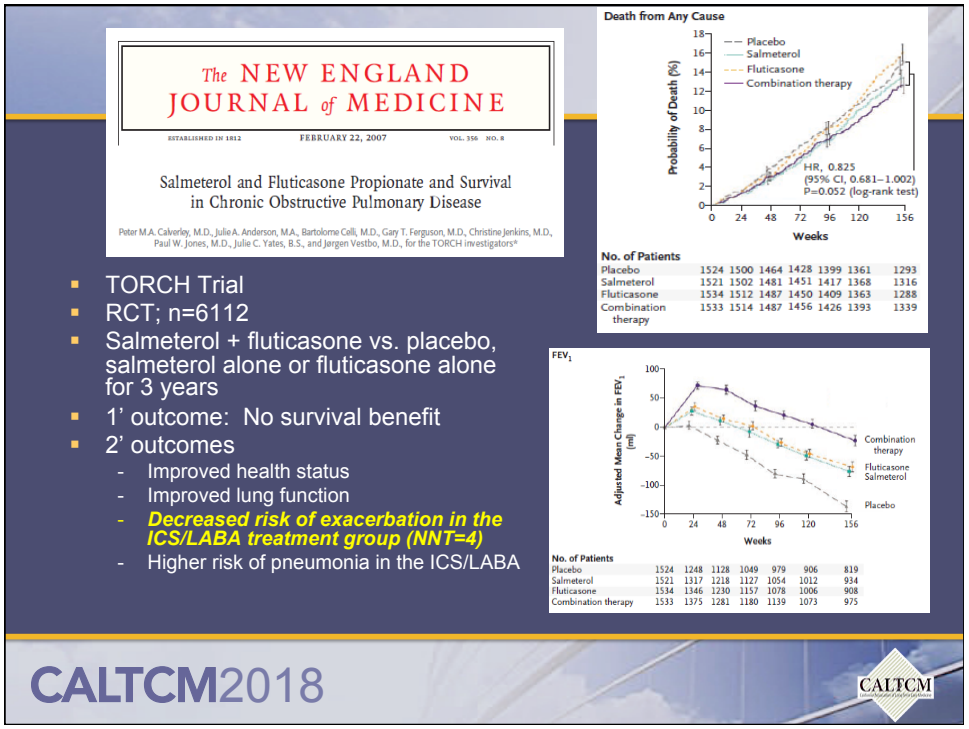
The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 FEBRUARY 22, 2007 VOL. 356 NO. 8
Salmeterol and Fluticasone Propionate and Survival in Chronic Obstructive Pulmonary Disease
Peter M.A. Calverley, M.D., Julie A. Anderson, M.A., Bartolome Celli, M.D., Gary T. Ferguson, M.D., Christine Jenkins, M.D., Paul W. Jones, M.D., Julie C. Yates, B.S., and Jørgen Vestbo, M.D., for the TORCH investigators*
TORCH Trial
RCT; n=6112
Salmeterol + fluticasone vs. placebo, salmeterol alone or fluticasone alone for 3 years
1' outcome: No survival benefit
2' outcomes
- Improved health status
- Improved lung function
- Decreased risk of exacerbation in the ICS/LABA treatment group (NNT=4)
- Higher risk of pneumonia in the ICS/LABA
Death from Any Cause
Placebo
Salmeterol
Fluticasone
Combination therapy
Probability of Death (%)
HR, 0.825 (95% CI, 0.681–1.002) P=0.052 (log-rank test)
Weeks
No. of Patients
Placebo 1524 1500 1464 1428 1399 1361 1293
Salmeterol 1521 1502 1481 1451 1417 1368 1316
Fluticasone 1534 1512 1487 1450 1409 1363 1288
Combination therapy 1533 1514 1487 1456 1426 1393 1339
FEV1
Adjusted Mean Change in FEV1 (ml)
Combination therapy
Fluticasone Salmeterol
Placebo
Weeks
No. of Patients
Placebo 1524 1248 1128 1049 979 906 819
Salmeterol 1521 1317 1218 1127 1054 1012 934
Fluticasone 1534 1346 1230 1157 1078 1006 908
Combination therapy 1533 1375 1281 1180 1139 1073 975
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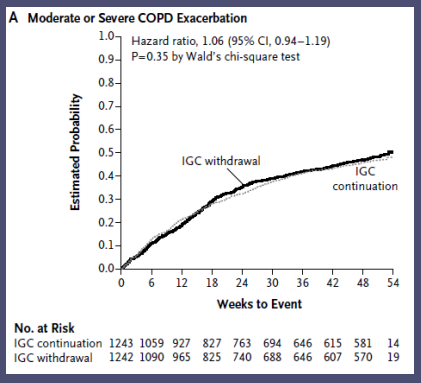
WISDOM Trial

- 12 month, double-blind, parallel-group
- N=2485 w/ hx COPD on LABA + LAMA + ICS; 6 week run in period
- Randomly assigned to continue triple therapy or withdraw ICS in a step-wise fashion over 12 weeks
- 1' endpoint: time to 1st moderate or severe COPD exacerbation
- Results:
  - Risk of exacerbations same
  - Greater decrease in lung function in ICS withdrawal group (~40mL)



N Engl J Med 2014; 371(14):1285-1294

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Phosphodiasterase-4 Inhibitor

- Roflumilast (Daliresp) 500 mcg PO daily
- PD4 inhibitors decrease inflammation and promote smooth muscle relaxation by inhibiting the breakdown of intracellular cyclic AMP
- Indicated as a treatment to reduce the risk of moderate to severe COPD exacerbations in patients with severe COPD to very severe COPD associated with chronic bronchitis and a history of exacerbations (2 or more per year or 1 requiring hospitalization)
- Avoid in patients with unstable mood symptoms, depression, suicidality
- Other AEs: diarrhea, nausea, reduced appetite, weight loss, abdominal pain

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Roflumilast in symptomatic chronic obstructive pulmonary disease: two randomised clinical trials

Peter M A Calverley*, Klaus F Rabe*, Udo-Michael Goehring, Søren Kristiansen, Leonardo M Fabbri†, Fernando J Martinez‡, for the M2-124 and M2-125 study groups‡

- Severe COPD, age >40, bronchitis symptoms, history of exacerbations
- n>2000
- Oral roflumilast vs. placebo for 52 weeks
- ICS were not allowed
- 17% reduction in the risk of moderate (requiring steroids) or severe (requiring hospitalization) exacerbations vs. placebo

Lancet 2009; 374: 685–94

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The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 25, 2011 VOL. 365 NO. 8

Azithromycin for Prevention of Exacerbations of COPD

- RCT, n=1557
- >40, COPD with FEV1<80%, history of exacerbations or O2 dependent
- Azithromycin 250 mg daily vs. placebo + usual care for 1 year
- Decreased median time to first exacerbation
- Decreased frequency of exacerbations
- Improved quality of life
- Decrease in nasopharyngeal colonization with respiratory pathogens, but increased colonization with macrolide-resistant organisms
  - NO effect on exacerbation or pneumonia rates
- Some increased hearing decrement in the azithromycin arm 5%

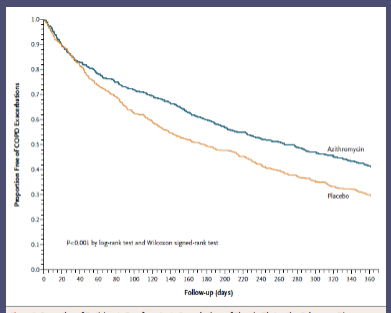

Figure 2. Proportion of Participants Free from Acute Exacerbations of Chronic Obstructive Pulmonary Disease (COPD) for 1 Year, According to Study Group.

N Engl J Med 2011;365:689-98.

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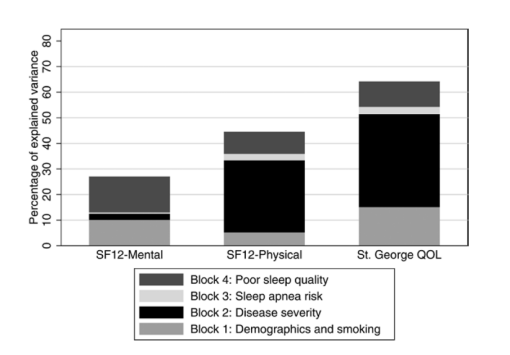
ORIGINAL ARTICLE

Sleep disruption as a predictor of quality of life among patients in the subpopulations and intermediate outcome measures in COPD study (SPIROMICS)



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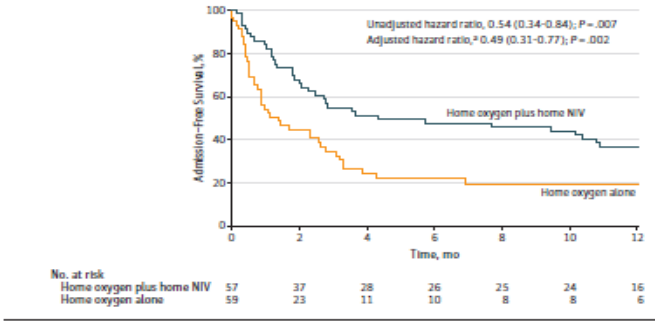
JAMA | Original Investigation

Effect of Home Noninvasive Ventilation With Oxygen Therapy vs Oxygen Therapy Alone on Hospital Readmission or Death After an Acute COPD Exacerbation

A Randomized Clinical Trial

Figure 2. Kaplan-Meier Survival Plot of Time to Readmission or Death From Randomization to the End of Trial Follow-up at 1 Year



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Benefits of Pulmonary Rehabilitation

- Improved dyspnea
- Improved exercise capacity
- Improved health-related quality of life
- Fewer days of hospitalization
- Decreased health care utilization
- Reduces extent of functional decline and hastens recovery after an exacerbation
- May reduce mortality

McCarthy B, Casey D, Devane D, Murphy K, Murphy E, Lacasse Y. Pulmonary rehabilitation for chronic obstructive pulmonary disease. *Cochrane Database of Systematic Reviews* 2015, Issue 2. Art. No.: CD003793. DOI: 10.1002/14651858.CD003793.pub3.

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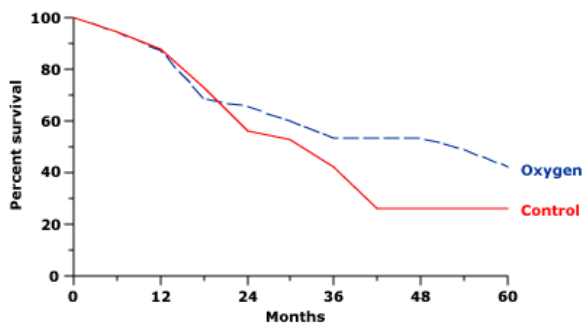

Medical Research Council Trial in which 87 patients with chronic obstructive pulmonary disease, severe hypoxemia, hypercapnia, and a history of heart failure were randomized to treatment with oxygen therapy for at least 15 h/day (blue dashed line) or no oxygen (red line). Continuous oxygen therapy led to a significant survival benefit.
Report of the Medical Research Council Working Party, Lancet 1981; 1:681.

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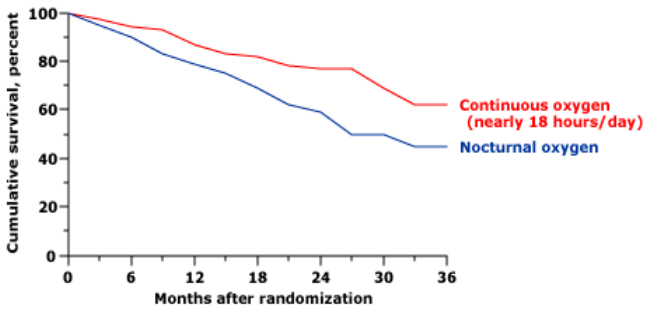
Survival benefit of continuous long-term oxygen therapy in COPD



The Nocturnal Oxygen Therapy Trial randomly assigned 203 patients with chronic obstructive pulmonary disease complicated by hypoxemia to treatment with nearly continuous oxygen therapy (red line) or nocturnal oxygen alone (blue line). Continuous oxygen therapy was associated with a significant survival benefit (p = 0.01). *Redrawn from Nocturnal Oxygen Trial Therapy Group, Ann Intern Med 1980; 93:391.*

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End Stage COPD

- Consider referral to Palliative Care or hospice
- Goals of care discussion, POLST forms
- Rx Short acting opiates (i.e. morphine) for air hunger/dyspnea/anxiety/sleep
- Chest wall vibration, fans blowing face
- Rx Oxygen, irrespective of blood gases, if it improves breathlessness

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