

COPD: Beyond Inhalers

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1

Disclosure

Advisory Board: Solius Labs

Consultant: Neuronic Corporation; Solius Labs

Stock Options: Solius Labs



2

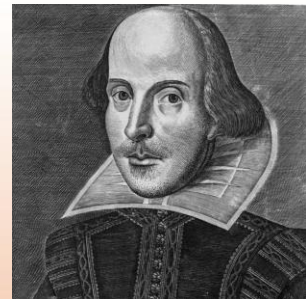


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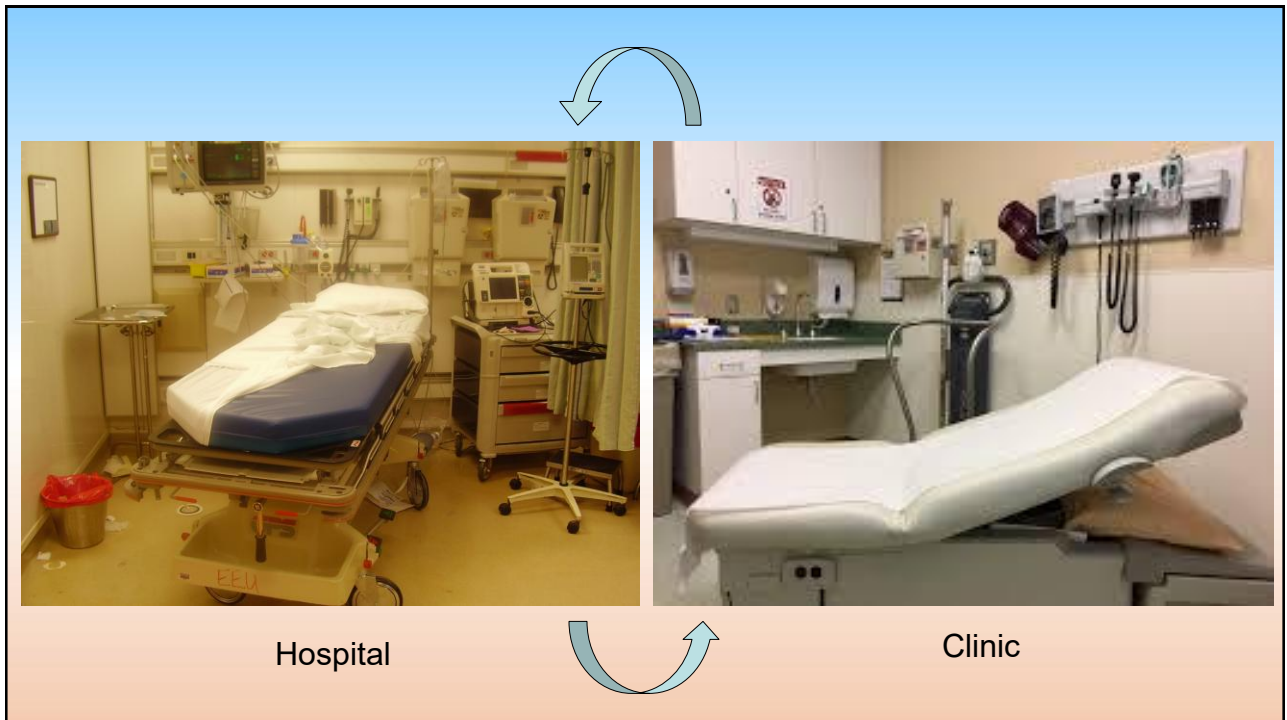
COPD

*“How art thou out of breath when thou hast breath
To say to me that thou art out of breath?”*

Romeo and Juliet, William Shakespeare



4



5

COPD

COPD is a common preventable, and treatable lung disease characterized by persistent airflow limitation that is usually progressive¹

Symptoms include dyspnea, cough, and sputum production¹

COPD includes the lung diseases emphysema and chronic bronchitis²

Risk Factors:

Smoking, occupational dust and chemicals, environmental tobacco smoke, air pollution, genes (A1AT), infections, age and socioeconomic status

1) Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease 2014

2) ATS/ERS Standards for the Diagnosis and Management of Patients with COPD. 2004.

6

COPD

Constriction (obstruction) Emphysema (recoil)

<http://www.allergyasthmazone.com>
<http://library.med.utah.edu/WebPath>

7

COPD

$FEV_1/FVC < 0.7$

Severity FEV_1

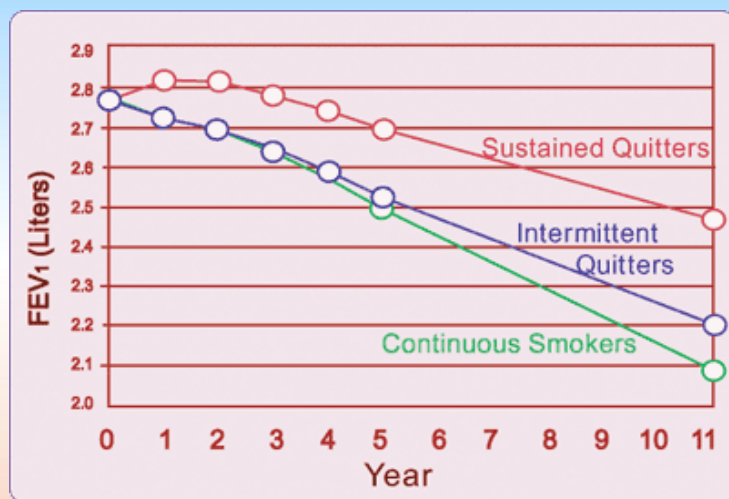
Mild (I)	80-100%
Moderate (II)	50-79%
Severe (III)	30-49%
Very Severe (IV)	0-29%

or $PCO_2 > 45$ mmHg

http://www.medicine.mcgill.ca/physio/vlab/resp/pneumo_exp.htm

8

COPD



<http://www-archive.thoracic.org/sections/copd/for-health-professionals/epidemiology-risk-factors-and-natural-history/natural-history.html>

9

COPD



Symptoms

Dyspnea, cough, sputum

Reduced Exercise Capacity



Inactivity



<http://www-archive.thoracic.org/sections/copd/for-health-professionals/epidemiology-risk-factors-and-natural-history/natural-history.html>

10

COPD

$$\text{COPD} = \text{FEV}_1/\text{FVC} < 0.70$$

	FEV₁ % predicted
COPD I	80-100
COPD II	50-79
COPD III	30-49
COPD IV	0-29 or pCO ₂ > 45 mmHg

11

COPD

Airflow Limitation **	IV	C LAMA/LABA ICS	D Roflumilast Azithromycin	≥2	Exacerbation Risk
	III				
	II	A Any inhaler?	B LAMA/LABA	1	
	I			0	
		CAT < 10 / mMRC 0-1	CAT ≥ 10 / mMRC ≥2		
	Symptoms of SOB				

** New 2017 Gold Guidelines - <http://goldcopd.org>

12

BODE Index (Body mass index, airflow Obstruction, Dyspnea and Exercise capacity.)

FEV1 % Predicted After Bronchodilator

>=65% (0 points)
50-64% (1 point)
36-49% (2 points)
<=35% (3 points)

6 Minute Walk Distance

>=350 Meters (0 points)
250-349 Meters (1 point)
150-249 Meters (2 points)
<=149 Meters (3 points)

MMRC Dyspnea Scale (4 is worst)

MMRC 0: Dyspneic on strenuous exercise (0 points)
MMRC 1: Dyspneic on walking a slight hill (0 points)
MMRC 2: Dyspneic on walking level ground; must stop occasionally due to breathlessness (1 point)
MMRC 3: Must stop for breathlessness after walking 100 yards or after a few minutes (2 points)
MMRC 4: Cannot leave house; breathless on dressing/undressing (3 points)

Body Mass Index

>21 (0 points)
<=21 (1 point)

4 year survival

0-2 Points: 80%

3-4 Points: 67%

5-6 Points: 57%

7-10 Points: 18%

Celli BR, Cote CG, Marin JM, et al. The body-mass index, airflow obstruction, dyspnea, and exercise capacity index in chronic obstructive pulmonary disease. *N Engl J Med.* 2004;350(10):1005-1012. doi:10.1056/NEJMoa021322.

13

COPD

General Approach

GOLD

-control symptoms
-decrease exacerbations
-improve function and QOL

Non Pharmacologic

- 1) Smoking Cessation
- 2) Vaccinations
- 3) Supplemental O₂
- 4) Pulmonary Rehab
- 5) Surgery? Transplant?

Pharmacologic

- 1) β -agonists
- 2) Muscarinic Antagonists
- 3) Inhaled Glucocorticoids
- 4) Theophylline
- 5) PDE-4 Inhibitors
- 6) Others? ABX?

Global Initiative for Chronic Obstructive Lung Disease. Global strategy for prevention, diagnosis and management of COPD: 2026 report. GOLD; 2026.

14

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15

Smoking Cessation

No other discussion is more important.

- it reduces the rate of decline of FEV₁¹
66.1 and 54.2 mL versus 30.2 and 21.5 ml (M/F)
- Which way is best
 - counseling and medication therapy combined²

¹ Am J Respir Crit Care Med. 2002;166(5):675.
² Eur Respir J. 2013 Mar;41(3):727-34. Epub 2012 Aug 30.

16

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17

Vaccinations

Vaccinations are important to prevent infections which are key to preventing exacerbations

- 1) Pneumococcal polysaccharide vaccine
- 2) Annual influenza vaccine (all patients)
 - RPCT of 125 COPD patients, it reduced influenza by 76% regardless of severity.¹
 - influenza vaccine does not increase the rate of influenza²

- 1) Wong et al. Acute respiratory illness in patients with COPD and the effectiveness of influenza vaccination: a randomized controlled study. Chest. 2004;125(6):2011.
- 2) Tata et al. Does influenza vaccination increase consultations, corticosteroid prescriptions, or exacerbations in subjects with asthma or chronic obstructive pulmonary disease? Thorax. 2003;58(10):835.

18

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19

Supplemental Oxygen

Many severe COPD patients are hypoxemic. There is extensive evidence that long term O₂ improves survival and QOL.¹

PaO₂ $\leq$ 55 mmHg or SpO₂ $\leq$ 88%

PaO₂ $\leq$ 59 mmHg or SpO₂ $\leq$ 89% with cor pulmonale

Airline Travel Test (HAST)

-recommended if expected PaO₂ $\leq$ 50 mmHg

-17% oxygen mixture $\sim$ 8000 ft elevation (N₂ mixture)

1) Sin et al. Contemporary management of chronic obstructive pulmonary disease: scientific review. JAMA. 2003;290(17):2301.

20

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21

Pulmonary Rehab

Pulmonary Rehabilitation Programs have been shown to:¹

- 1) Improve exercise capacity
- 2) Improve QOL
- 3) Decrease SOB
- 4) Decrease health care utilization
- 5) reduce mortality?

All in COPD II through IV!



1) Puhan MA et al. Respiratory rehabilitation after acute exacerbation of COPD may reduce risk for readmission and mortality -- a systematic review. Respir Res. 2005;6:54.

22

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23

Lung Volume Reduction Surgery

Tug of War in chest.

- elastic fibers versus chest wall
- in COPD the chest wall wins (large lungs)
- could we improve mechanical advantage if lung were removed?
- National Emphysema Treatment Trial (NETT)¹
 - N = 1218 (surgery vs. Medical treatment)

1) Fishman et al. A randomized trial comparing lung-volume-reduction surgery with medical therapy for severe emphysema. N Engl J Med. 2003;348(21):2059.

24

Lung Volume Reduction Surgery

NETT

- all underwent 6-10 weeks of pulmonary rehab
- results varied but sub group analysis showed trends
- safety monitoring detected increased mortality in:
 - DLCO < 20% of predicted or non-upper lobe emphysema
 - FEV₁ < 20% of predicted

1) Fishman et al. A randomized trial comparing lung-volume-reduction surgery with medical therapy for severe emphysema. N Engl J Med. 2003;348(21):2059.

25

Lung Volume Reduction Surgery

LVRS – who should be considered?

- age less than 75 years
- severe dyspnea despite optimal medical therapy
- smoking cessation > 6 months
- FEV₁ < 45 % of p but not less than 20% of p
- HRCT showing heterogeneous hyperinflation
- DLCO > 20%
- must be able to complete 6-10 weeks of pulmonary rehab

1) Fishman et al. A randomized trial comparing lung-volume-reduction surgery with medical therapy for severe emphysema. N Engl J Med. 2003;348(21):2059.

26

Transplant

Transplant?

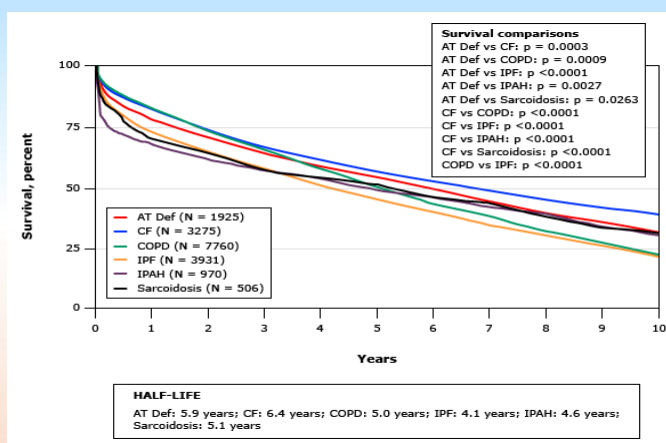
- improves functional capacity
- does it improve survival?
- When to refer?
 - BODE > 5
 - FEV₁ < 25% of p
 - PaO₂ <55 to 60 mmHg
 - PCO₂ > 45 mmHg
 - age less than 65 years typically

Leard LE, Holm AM, Valapour M, et al. Consensus document for the selection of lung transplant candidates: an update from the International Society for Heart and Lung Transplantation. J Heart Lung Transplant. 2021;40(11):1349-1379. doi:10.1016/j.healun.2021.07.005.

27

Transplant

Kaplan-Meier survival by diagnosis for adult lung transplants performed between January 1990 and June 2006



http://www.uptodate.com/contents/image?imageKey=PULM%2F57297&topicKey=PULM%2F1447&rank=1~150&source=see_link&search=copd+management&utdPopup=true

28

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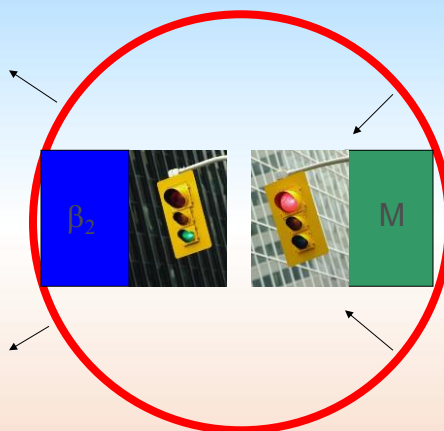
29

Short Acting Bronchodilator

Bronchodilation

 β_2 -agonists

Albuterol
Salmeterol
Fomoterol
Arformoterol
Indacaterol
Vilanterol
Olodaterol



Bronchus

Bronchoconstriction

Anticholinergics

Ipratropium
Tiotropium
Aclidinium
Umeclidinium

30

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31

β -agonists – Short Acting

Albuterol (AccuNeb, ProAir HFA, Proventil HFA, Ventolin HFA)

- short acting
- improve symptoms and lung function
- as needed basis
- if need more than 2-3 times per week consider not controlled
- can have side effects of tachycardia, hypokalemia
- avoid oral β -agonists

Global Initiative for Chronic Obstructive Lung Disease. Global strategy for prevention, diagnosis and management of COPD: 2026 report. GOLD; 2026.

32

β -agonists – Long Acting (LABA)

Salmeterol – Serevent Diskus (BID)
 Formoterol – Foradil Aerolizer (BID)
 Arformoterol – Brovana NEB (BID)
 Indacaterol – Arcapta Neohaler (QD)
 Vilanterol – a component of the Breo Ellipta & Breo Anoro (QD)

TORCH trial (salmeterol)

- n= 6112 patients (FEV₁ mean 44% of p)
- no increase in mortality
- decrease exacerbation rates, improved lung function and QOL

Arrhythmia trial

- retrospective review of 76,661 patients
- no increase when patient with h/o of arrhythmia or heart failure were excluded. Effects waned with longer term use.

Global Initiative for Chronic Obstructive Lung Disease. Global strategy for prevention, diagnosis and management of COPD: 2026 report. GOLD; 2026. Calverley PMA, Anderson JA, Celli B, et al. Salmeterol and fluticasone propionate and survival in chronic obstructive pulmonary disease. N Engl J Med. 2007;356(8):775-789. doi:10.1056/NEJMoa063070.
 Baumgartner RA, Hanania NA, Calhoun WJ, Sahn SA, Sciarappa K, Hanrahan JP. Nebulized arformoterol in patients with COPD: a 12-week, multicenter, randomized, double-blind trial. Clin Ther. 2007;29(2):261-278. doi:10.1016/j.clinthera.2007.02.009.

33

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34

Anticholinergics – Short Acting

Ipratropium bromide (Atrovent HFA)

- short acting
- improved lung function
- increased exercise capacity
- decreased dyspnea
- decreased cough
- combination with albuterol improved lung function more than either one by itself but the combination did not decrease the frequency of exacerbations

35

Anticholinergics – Long Acting (LAMA)

Tiotropium – Spiriva HandiHaler

Aclidinium – Tudorza Pressair

Umeclidinium – a component of the Anoro Ellipta

Tiotropium has been the most studied

- improves lung function and decreases dynamic hyperinflation
- may slow the rate of FEV₁ decline

UPLIFT study

- no significant safety issues over 4 years

36

LABA versus LAMA

Meta-analysis comparing tiotropium with sal, for, indacaterol¹

- no different in QOL
- tiotropium more effective at reducing exacerbations
- no difference in hospitalizations or mortality

Tiotropium versus salmeterol

- tiotropium increased time to first exacerbation

- 1) Chong et al. Tiotropium versus long-acting beta-agonists for stable chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2012;9:CD009157.
- 2) Vogelmeier C et al. Tiotropium versus salmeterol for the prevention of exacerbations of COPD. N Engl J Med. 2011;364(12):1093.

37

LABA PLUS LAMA

“In patients with GOLD stage II-IV COPD whose symptoms are not well controlled with a single long-acting bronchodilator, the addition of a second class of long acting bronchodilator may provide additional benefit.”

Meta-analysis¹ N = 3263 -combination vs monotherapy had

- slightly better QOL
- small increase in FEV₁ over just tiotropium alone

Combination of umeclidinium-vilanterol (Anoro Ellipta)

- greater increases in FEV₁ over mono-components

- 1) Karner et al. Long-acting beta(2)-agonist in addition to tiotropium versus either tiotropium or long-acting beta(2)-agonist alone for chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2012;4:CD008989.

38

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39

Inhaled Corticosteroids (ICS)

Fluticasone propionate (Advair, Flovent)
 Flunisolide (AeroBid)
 Ciclesonide (ALvesco)
 Mometasone (Asmanex)
 Fluticasone furoate (Breo Ellipta)
 Budesonide (Pulmicort)
 Beclomethasone (Qvar)

- can cause osteoporosis, pneumonia, skin thinning, cataracts
- decrease exacerbations
- slow progression of respiratory symptoms
- no impact on lung function or mortality
- never should be used as solo therapy for COPD
- use with COPD III and IV

Global Initiative for Chronic Obstructive Lung Disease. Global strategy for prevention, diagnosis and management of COPD: 2026 report. GOLD; 2026.

40

Combination Therapy with ICS and LABA

-TORCH trial

-significantly improved:

- lung function, health status, rate of exacerbations
- slight but significant reduction in *mortality* versus placebo

-INSPIRE¹

- n= 1323 FEV₁ 39 % of p
- flu/sal (500/50) versus tio
- no difference between exacerbations
- found difference in mortality and health status (pro flu/sal)
- more pneumonias in flu/sal group
- not sufficient to change guidelines stating LABA or LAMA alone and not in combination with ICS²

1) Wedzicha et al. The prevention of chronic obstructive pulmonary disease exacerbations by salmeterol/fluticasone propionate or tiotropium bromide. Am J Respir Crit Care Med. 2008;177(1):19.

2) Welsh et al. Combination inhaled steroid and long-acting beta2-agonist versus tiotropium for chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2010;

41

Triple Therapy?

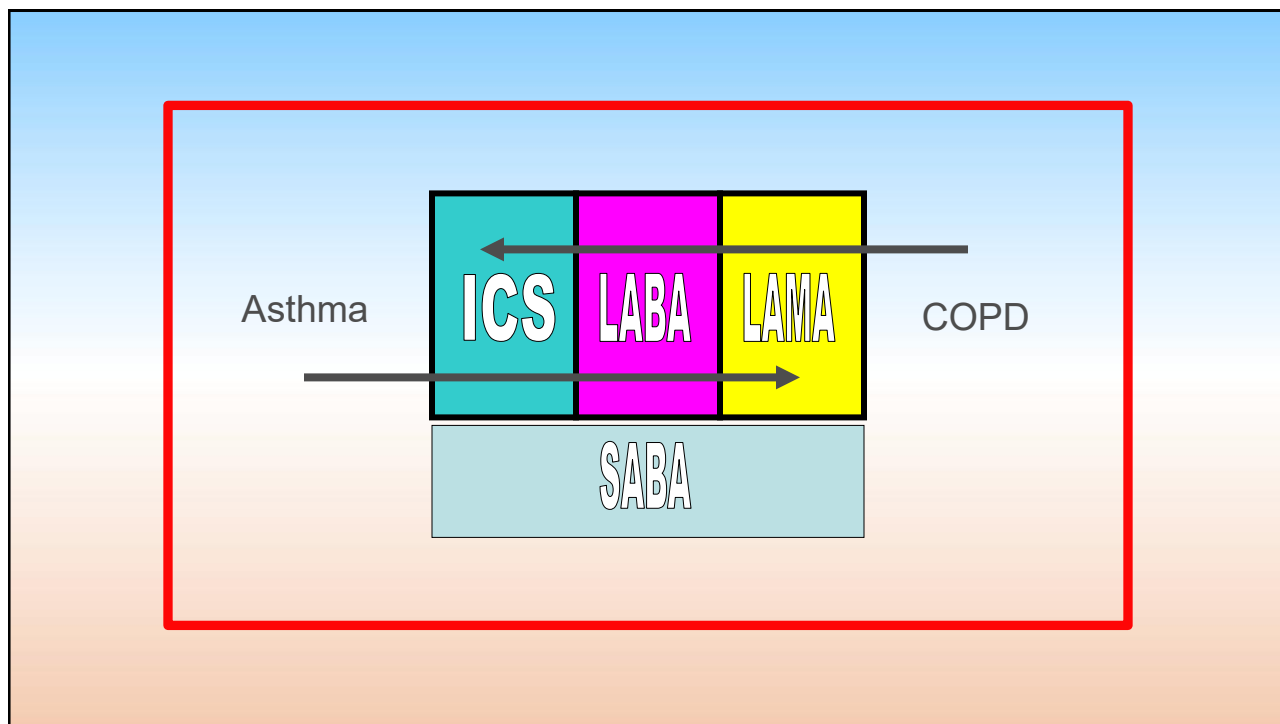
Triple versus Double Therapy

- UPLIFT showed improved airflows, reduced exacerbations
- in a RPCT in comparison to tiotropium alone¹ tio + flu + sal
 - better lung function
 - QOL
 - reduction in all-cause hospitalizations
- in a RPCT in comparison to tiotropium alone² tio +bud+ for
 - less exacerbations
 - better prebronchodilator FEV₁

1) Aaron et al. Tiotropium in combination with placebo, salmeterol, or fluticasone-salmeterol for treatment of chronic obstructive pulmonary disease: a randomized trial. Ann Intern Med. 2007;146(8):545.

2) Welte et al. Efficacy and tolerability of budesonide/formoterol added to tiotropium in patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 2009;180(8):741.

42



43

COPD

Name	Class
(acclidinium bromide)	LAMA
(albuterol sulfate inhalation aerosol)	SABA
(arformoterol tartrate) Inhalation Solution	LABA
(beclomethasone dipropionate inhalation aerosol)	ICS
(budesonide inhalation powder)	ICS
(budesonide and formoterol fumarate) Inhalation Aerosol	ICS/LABA
(fluticasone furoate and vilanterol trifenate)	ICS/LABA
(indacaterol inhalation powder)	LABA
(glycopyrrolate inhalation)	LAMA
(mometasone furoate and formoterol fumarate) Inhalation Aerosol	ICS/LABA
(salmeterol xinafoate/fluticasone propionate powder for inhalation)	ICS/LABA
(tiotropium bromide inhalation powder)	LAMA
(umeclidinium inhalation powder)	LAMA
(umeclidinium and vilanterol inhalation powder)	LAMA/LABA
(fluticasone furoate, umeclidinium and vilanterol trifenate)	ICS/LAMA/LABA

44

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45

Theophylline? Seriously?

Low dose theophylline

- mechanism ? Bronchodilation
- meta-analysis¹ and randomized cross-over trial²
 - improved FEV₁, FVC, and gas exchange
- using an extended-release preparation may reduce nocturnal symptoms
- need to watch levels (8-12 mcg/mL)
 - liver metabolism
 - drug interactions

- 1) Ram et al. Oral theophylline for chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2002;
- 2) Murciano et al. A randomized, controlled trial of theophylline in patients with severe chronic obstructive pulmonary disease. N Engl J Med. 1989;320(23):1521.

46

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47

PDE-4 Inhibitors

Increase cellular cAMP by inhibiting phosphodiesterase
 -type 4 seems to reduce inflammation and promotes
 smooth muscle relaxation¹

Roflumilast (Daliresp) is FDA approved to reduce exacerbations in
 patients with history of a **serious exacerbation in the last year and
 GOLD stage III or IV COPD**

NNT = 4-5 (decreased exacerbations 17%)²

Must be used q day (like a statin for prevention of CAD events)

1) Soto et al. Selective phosphodiesterase-4 inhibitors in chronic obstructive lung disease. Curr Opin Pulm Med. 2005;11(2):129.

2) Calverley et al. Roflumilast in symptomatic chronic obstructive pulmonary disease: two randomised clinical trials. Lancet. 2009;374(9691):685.

48

Ensifentrine

- COPD diagnosis: $FEV_1/FVC < 0.7$
- Post-bronchodilator FEV_1 30-70% predicted normal
- Modified Medical Research Council dyspnea scale ≥ 2
- Current or former smoker (≥ 10 pack-years)
- No asthma diagnosis
- No exacerbation history requirement (other than no steroid-treated exacerbation in past 12 weeks)

Anzueto A, Barjaktarevic IZ, Siler TM, et al. Ensifentrine, a novel phosphodiesterase 3 and 4 inhibitor for the treatment of COPD: randomized, double-blind, placebo-controlled, multicenter phase III trials (ENHANCE). Am J Respir Crit Care Med. 2023;208(4):406-416. doi:10.1164/rccm.202306-0944OC.

49

Ensifentrine

Ensifentrine (3mg NEB BID) is a newly approved nebulized dual PDE3/PDE4 inhibitor for COPD maintenance; Phase III showed modest but real lung-function benefit and fewer exacerbations, with more mixed quality-of-life results.

• **Magnitude of lung function benefit:**

• ENHANCE-1: placebo-adjusted **+87 mL** in FEV_1 AUC_{0–12h} at Week 12 (95% CI 55 to 118, $p < 0.0001$)

• ENHANCE-2: placebo-adjusted **+94 mL** (95% CI 65 to 124, $p < 0.0001$)

• **Exacerbation outcomes over 24 weeks:**

• ENHANCE-1: moderate/severe COPD exacerbation rate ratio **0.64** (95% CI 0.40 to 1.00, $p = 0.050$); time to first exacerbation HR **0.62** (95% CI 0.39 to 0.97, $p = 0.038$)

• ENHANCE-2: exacerbation rate ratio **0.57** (95% CI 0.38 to 0.87, $p = 0.009$); time to first exacerbation HR **0.58** (95% CI 0.38 to 0.87, $p = 0.009$)

Anzueto A, Barjaktarevic IZ, Siler TM, et al. Ensifentrine, a novel phosphodiesterase 3 and 4 inhibitor for the treatment of COPD: randomized, double-blind, placebo-controlled, multicenter phase III trials (ENHANCE). Am J Respir Crit Care Med. 2023;208(4):406-416. doi:10.1164/rccm.202306-0944OC.

50

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51

Others

Steroids:

- not for long term use
- may feel that they work but euphoria may cloud perception
- steroids have use in AECOPD (GOLD, UKNIHCE, ATS/ERS, CTS)
- 30-40 mg prednisone for 10-14 days**

Mucoactive agents – no recommended role in COPD

- NAC
- guaifenesin

52

Chronic Antibiotics

Azithromycin¹

- 250 mg PO QDay or TIW
- 266 days versus 174 days to first exacerbation
- 1.48 versus 1.83 exacerbations per year
- higher macrolide resistant bacteria in nasopharyngeal area
- higher hearing decrements
- must weigh risks and benefits

Hyaluronan aerosol

- decreases severity of elastase induced emphysema in animals and induced reductions in (DI) in preliminary human studies

1) Albert et al. Azithromycin for prevention of exacerbations of COPD. N Engl J Med. 2011;365(8):689.

53

Chronic Antibiotics

Journal Summaries in Pulmonology



Azithromycin during acute chronic obstructive pulmonary disease exacerbations requiring hospitalization (BACE): A multicenter, randomized, double-blind, placebo-controlled trial

American Journal of Respiratory and Critical Care Medicine — Vermeersch K, Gabrovská M, Aumann J, et al. | October 08, 2019

- Multi-center double blinded placebo RCT; N= 301
- AECOPD 10+ pky smoking history (steroids, ABX)
- < 48 hours: Azithromycin 500 mg/d for 3 days then 250 mg/2d for 3 months

6 months f/u	Azithromycin	Placebo
Treatment Failure p=.0526	49%	60%
Treatment Intensification p=.027	47%	60%
Step-up in hospital care p=.002	13%	28%
Mortality rates p=.5075	2%	4%

54

Outcomes in Patients with Chronic Obstructive Pulmonary Disease and Obstructive Sleep Apnea The Overlap Syndrome

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-OSA + COPD more likely to develop PH together versus alone

What are the benefits of CPAP?

Am J Respir Crit Care Med. Vol 182, pp 325-331, 2010
Originally Published in Press as DOI: 10.1164/rccm.200912-1869OC on April 8, 2010
Internet address: www.atsjournals.org

55

Follow-up 9.4 years	COPD OSA + <u>CPAP</u>	COPD OSA + <u>no CPAP</u>	COPD
Number	228	213	210
All cause Mortality (RR)	1	1.79 (1.16-2.77)	1
Hospitalization for Exacerbation (RR)	1	1.70 (1.21-2.38)	1

Controlling for:

Age, sex, BMI, Smoking, ETOH, COPD severity, AHI, daytime sleepiness,

CPAP is associated with a reduction in hospitalizations and mortality

56

FROM THE JOURNALS

Less CPAP time linked to exacerbation in COPD/OSA overlap syndrome

Publish date: September 6, 2019

By [Jake Remaly](#); MDedge News



-Reviewed EMR records to look for COPD + OSA
-found 92 patients with exacerbations and paired them to those without exacerbations

	Exacerbations	No Exacerbations
CPAP time	238.2 min/night	285.4 min/night
Active Smoking	21%	9%
FEV ₁	55.2% of predicted	64.5% of predicted

-Multivariate logistic regression analysis identified independent risks factors above

57

COPD

General Approach

GOLD

- control symptoms
- decrease exacerbations
- improve function and QOL

Non Pharmacologic

- 1) Smoking Cessation
- 2) Vaccinations
- 3) Supplemental O₂
- 4) Pulmonary Rehab
- 5) Surgery? Transplant?

Pharmacologic

- 1) β -agonists
- 2) Muscarinic Antagonists
- 3) Inhaled Glucocorticoids
- 4) Theophylline
- 5) PDE-4 Inhibitors
- 6) Others? ABX?

58

ARS Question #1**All of the Following Are True EXCEPT:**

- A. FEV1/FVC < 0.70 defines the presence of COPD.
- B. The severity of COPD is determined by FEV1 % predicted.
- C. A BODE score of 10 predicts an 18% 4-year survival
- D. alpha-1-antitrypsin deficiency is seen only in males because it is X-linked.
- E. The majority of COPD is caused by smoking.



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ARS Question #2**Which of the Following Patients Would Benefit from Supplemental Oxygen?**

- A. 55 y/o male with severe SOB, resting SpO2 of 92%
- B. 65 y/o female with a resting PaO2 of 58 mmHg and with BLE edema
- C. 75 y/o male with severe SOB and a PaO2 of 58 mmHg
- D. 68 y/o female with resting SpO2 of 90%
- E. 78 y/o male with severe SOB and a resting SpO2 of 92% with BLE edema



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ARS Question #3**Pulmonary Rehab Is Indicated for What Type of Patients with SOB?**

- A. GOLD COPD I-IV
- B. GOLD COPD II-IV
- C. GOLD COPD III-IV
- D. GOLD COPD IV only



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ARS Question #4**What Is an Appropriate Order to Escalate Therapy in Severe COPD Patients (Assume the Patient Already Has a Rescue Inhaler)?**

- A. LAMA → ICS → LABA
- B. ICS → LABA → LAMA
- C. LABA → ICS → LAMA
- D. LAMA → LABA → ICS
- E. ICS → LAMA → LABA

LAMA = long acting muscarinic antagonistLABA = long acting beta agonist

ICS = inhaled corticosteroid



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ARS Question #5**Which Patient Would Benefit from a PDE4 Inhibitor?**

- A. 55 y/o male with FEV1 of 20% and no serious exacerbations in the last 5 years.
- B. 65 y/o female with FEV1 of 60% and a recent hospitalization for COPD 4 months ago.
- C. 75 y/o male with FEV1 of 45% and a recent hospital admission for a flare of his COPD 10 months ago.
- D. 68 y/o female with FEV1 of 40% and a flare of her COPD 2 years ago.



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ARS Question #6**Which of the Following Has Been Shown to Decrease Hospitalizations?**

- A. Azithromycin
- B. CPAP in overlap syndrome
- C. PDE4 inhibitor
- D. All of the above



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64