Asthma and COPD

WA-ACP Internal Medicine Board Review Course

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Case 1: 55 year-old man

History

Routine follow-up for hypertension
No dyspnea, chest pain, cough
Still able to keep up with his work as a janitor
40 pack-year history of smoking

Exam

No crackles or wheezes
No murmur or lower extremity edema

Spirometry

Test	Actual	Predicted	% Predicted	Z-score	LLN
FVC (L)	3.50	4.32	81	-1.40	--
FEV_1 (L)	2.30	3.37	68	-1.75	--
FEV_1/FVC	0.66	0.79	---	--	0.69

LLN: Lower limit of normal

A Question

Which of the following is the most appropriate next step for this patient?

1. Start inhaled albuterol prn
2. Start scheduled tiotropium
3. Start inhaled budesonide
4. Start inhaled fluticasone / salmeterol
5. Do not start any medications

Do Not Screen Asymptomatic Individuals *

Likely to identify mild airflow obstruction that does not require treatment in absence of symptoms

Reserve spirometry for people with chronic respiratory symptoms and risk factors for COPD

CAPTURE questionnaire may identify occultly symptomatic patients who warrant evaluation with spirometry

* Up to 20% of people with severe airflow obstruction do not report symptoms
Source: Martinez et al. Am J Respir Crit Care Med 2017. 195(6): 748

Case 2: 67 year-old woman

History

Six months of progressive dyspnea on exertion

Can walk 50 m at own pace before stopping to catch her breath

50 pack-year history of smoking

Never admitted to hospital for respiratory issues

Spirometry

Test	Actual	Predicted	% Predicted	Z-Score	LLN
FVC (L)	3.29	4.58	72	-1.72	--
FEV_1 (L)	1.90	3.60	53	-2.10	--
FEV_1/FVC	0.58	0.79	---	--	0.67

LLN: Lower limit of normal

A Question

Which of the following medication regimens would be appropriate at this time?

1. Inhaled prn albuterol and ipratropium alone
2. Inhaled tiotropium plus prn albuterol
3. Inhaled formoterol and tiotropium
4. Inhaled fluticasone
5. Inhaled fluticasone plus salmeterol

Basic PFT Patterns: Obstructive Lung Disease

Required For Diagnosis

Low FEV_1/FVC *

Characterize Physiology

<u>Lung volumes</u>

High TLC: hyperinflation

High RV: air-trapping

<u>Bronchodilator Response</u>

FEV_1 or FVC increase by 10% from predicted value **

* Specific criteria vary based on which resource you consult

** The criteria for a bronchodilator response have recently been revised but the new criteria are too young for the boards

Diagnosing COPD: Three Essential Elements

Risk Factors

Tobacco
Indoor air pollution
Occupation

Chronic Symptoms

Cough
Sputum Production
Dyspnea
Wheezing

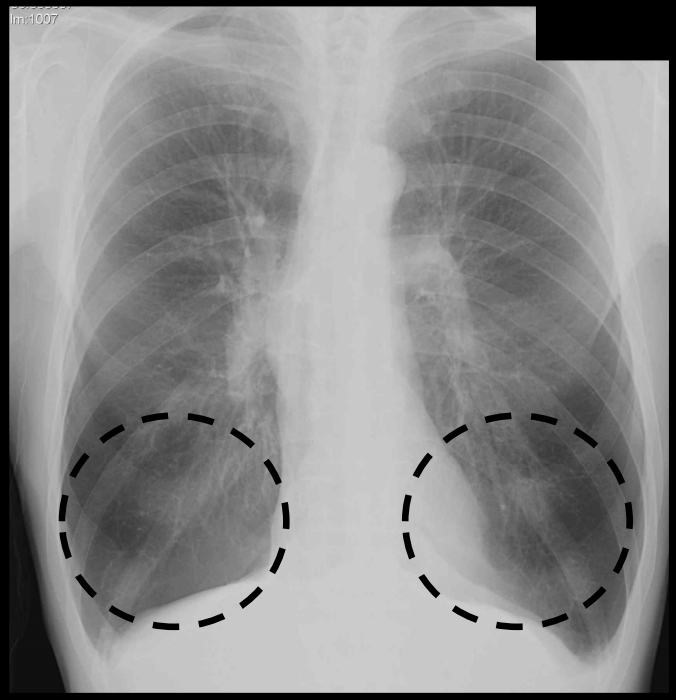
Spirometry

Decreased FEV_1/FVC

This is required for the diagnosis!!!

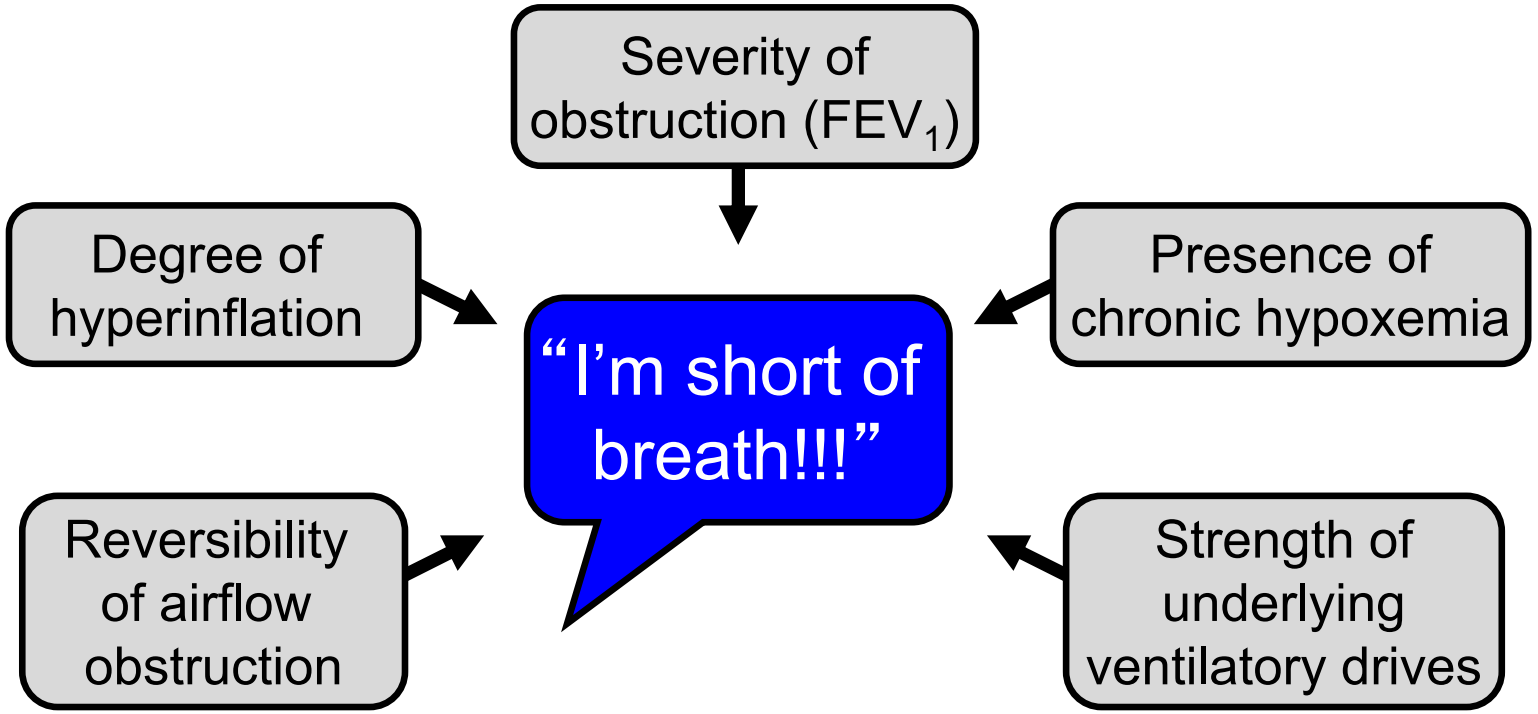
Be Able To Recognize This Presentation

40 year-old man with 30 pack-year history of smoking presents with worsening dyspnea on exertion. Pulmonary function testing shows an obstructive pattern with an FEV_1 52% predicted.



The Diagnosis: Alpha-1 Antitrypsin Deficiency

Many Factors Affect Symptom Severity In COPD

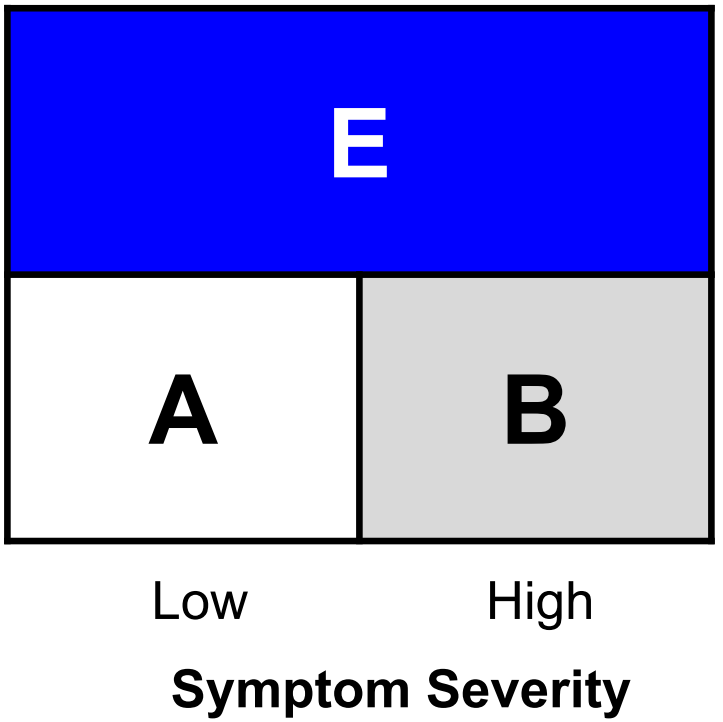


The GOLD Categories In COPD

Exacerbations history

≥ 2 moderate exacerbations or ≥ 1 leading to hospitalization

0-1 moderate exacerabations (no hospitalization)



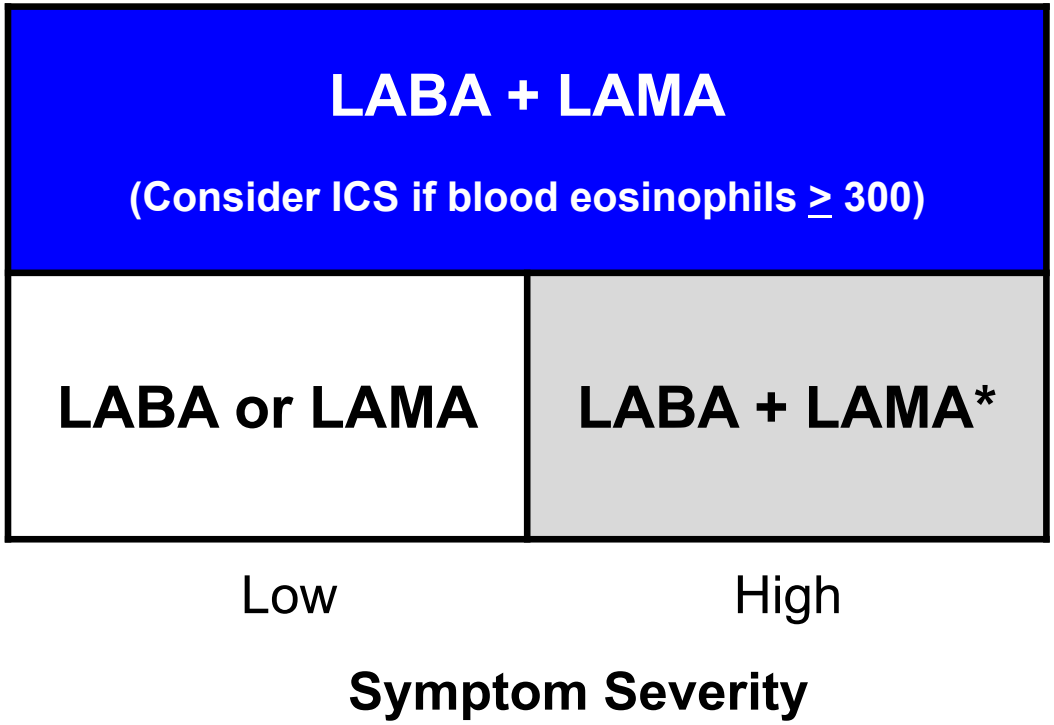
Symptom severity assessed using either of two scoring tools:
- mMRC Dyspnea Scale (> 2 considered “high”)
- CAT Score (≥ 10 considered “high”)

Initial Pharmacologic Treatment In COPD

Exacerbations history

≥ 2 moderate exacerbations or ≥ 1 leading to hospitalization

0-1 moderate exacerabations (no hospitalization)



LABA: long-acting beta-agonist; LAMA: long-acting anti-muscarinic
ICS: inhaled corticosteroid
* A single inhaler may be more effective and convenient than multiple agents

Key Points On Inhaled Bronchodilators

- SABA-SAMA combinations are superior to either medication alone (changes in FEV_1 and symptoms)
- LABA vs LAMA:
  - Both reduce symptoms and exacerbations, improve lung function
  - LAMA likely have greater effect on exacerbations, hospitalizations
- LABA-LAMA combinations are superior to monotherapy for lung function, symptoms and exacerbations

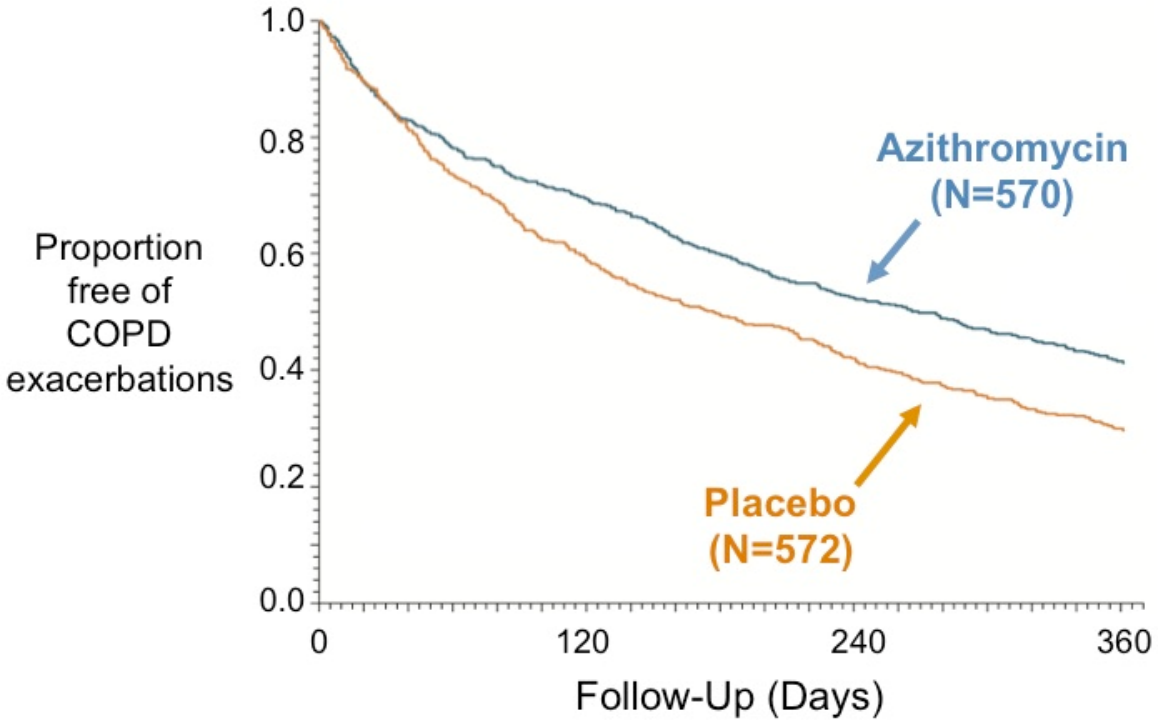
Issues seen with LABA monotherapy in asthma not present in COPD;
Cardio-selective beta-***blockers*** are okay in patients on beta-agonists

Key Points On Inhaled Corticosteroids

Category	Summary of Data
Benefit	Decrease exacerbations Modest slowing of symptom progression
No clear benefit	Lung function Mortality
Concerns	Regular use increases risk of pneumonia, especially in those with severe disease

Reserve for persistent symptoms or exacerbations despite LABA+LAMA;
Benefit likely highest in those with peripheral eosinophils ≥ 300 cells/μL

For Patients With Frequent Exacerbations: Macrolides (Azithromycin)



Source: Albert et al. New Engl J Med 2011. 365: 689

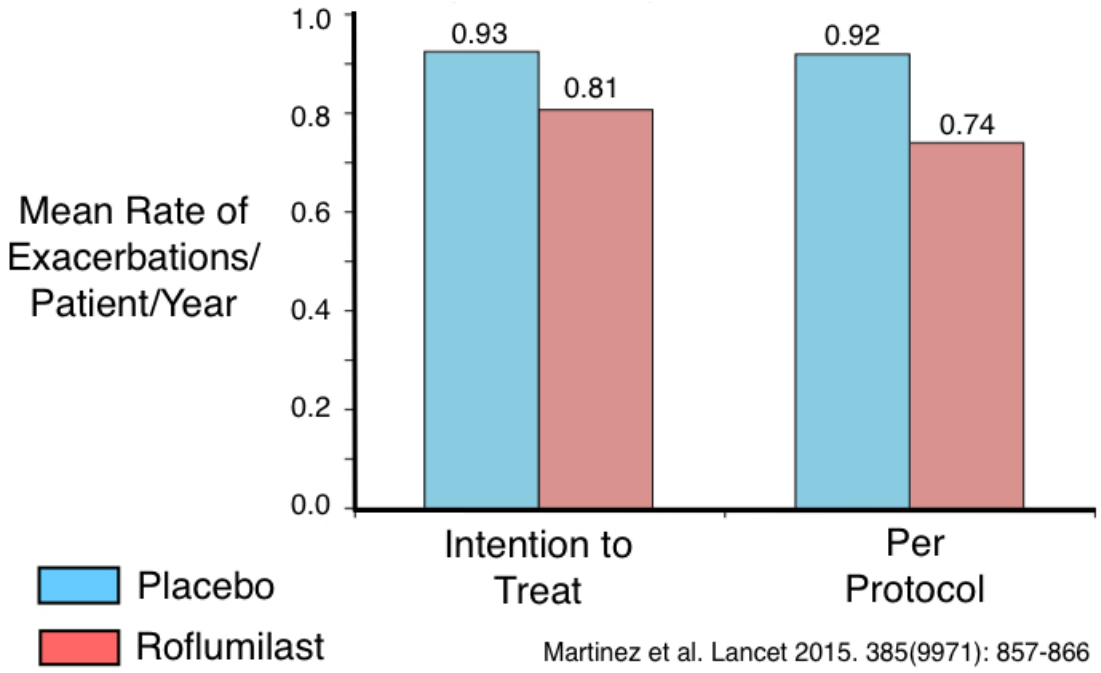
Decreases exacerbations

May be less effective in current smokers

Risk of hearing impairment

Avoid in patients with QT prolongation

Another Option For Frequent Exacerbators: PDE4 Inhibitors (Roflumilast)



Martinez et al. Lancet 2015. 385(9971): 857-866

Along with bronchodilators, modest effect on exacerbations

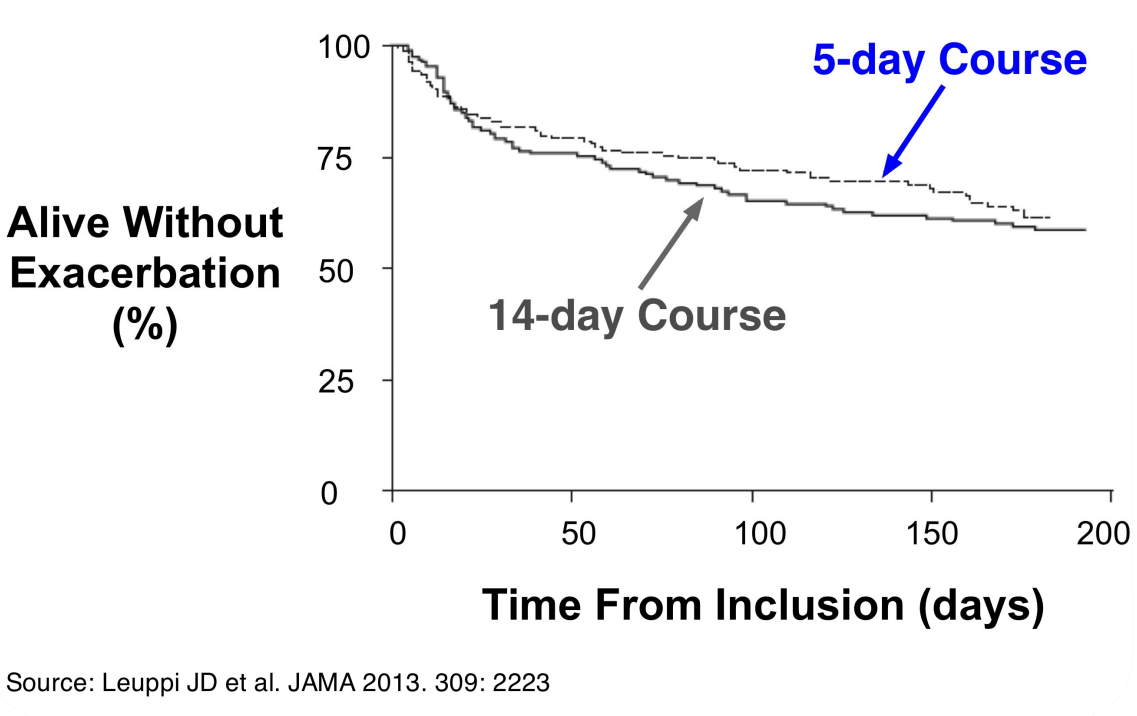
Limited effect on lung function

Use with caution in those with depression

Weight loss, diarrhea are important side effects

PDE-4: Phosphodiesterase 4

Length of Steroid Course In Exacerbations



Source: Leuppi JD et al. JAMA 2013. 309: 2223

5-day prednisone course has same 6-month re-exacerbation rate as 14-day course with lower glucocorticoid exposure

Case 3: 66 year-old man

History	Diagnosed with COPD 5 years ago FEV_1: 30% predicted Worsening dyspnea despite using medications
Medications	Umeclidinium Formoterol Fluticasone
Other Data	CT Chest: upper and lower lung zone emphysema ABG: P_aO_2 67 mmHg breathing air

A Question

Which of the following is indicated for this patient at this time?

1. Referral for lung volume reduction surgery
2. Referral for lung transplantation
3. Referral for pulmonary rehabilitation
4. Start long-term continuous oxygen therapy
5. Start oral theophylline

Options For Very Severe COPD

Lung Volume Reduction

Survival benefit:
Upper lobe predominant
Low exercise capacity

Avoid with:
$FEV_1 \leq 20\%$ predicted
& (DLCO $\leq$ 20% or
homogeneous disease)

Refer for Lung Transplant

Progressive disease

FEV_1 ~ 25% predicted *

BODE Index 5-6

Not an LVRS candidate

Resting $P_aO_2 < 60$ mmHg

$P_aCO_2 > 50$ mmHg

Long-Term O_2 Therapy

$P_aO_2 \leq 55$ mmHg or
$S_aO_2 \leq 88\%$
or
$P_aO_2 \leq 59$ mmHg with
cor pulmonale or
hematocrit > 55%

Must be used on
continuous basis

Pulmonary rehab indicated for stable Group B and E COPD

*Post-bronchodilator

Case 4: 20 year-old woman

History

Presenting for follow-up for asthma
Using prn albuterol 5 times/week
prn albuterol at night up to 4 times/month
No clear precipitants
Negative allergy testing in past

Spirometry

Test	Actual	% Predicted	Z-score	LLN	Post-BD	% Change
FVC (L)	3.59	82	- 1.05	--	3.70	3
FEV_1 (L)	2.44	75	-1.72	--	2.99	16
FEV_1/FVC	0.68	---	--	0.73	0.75	--

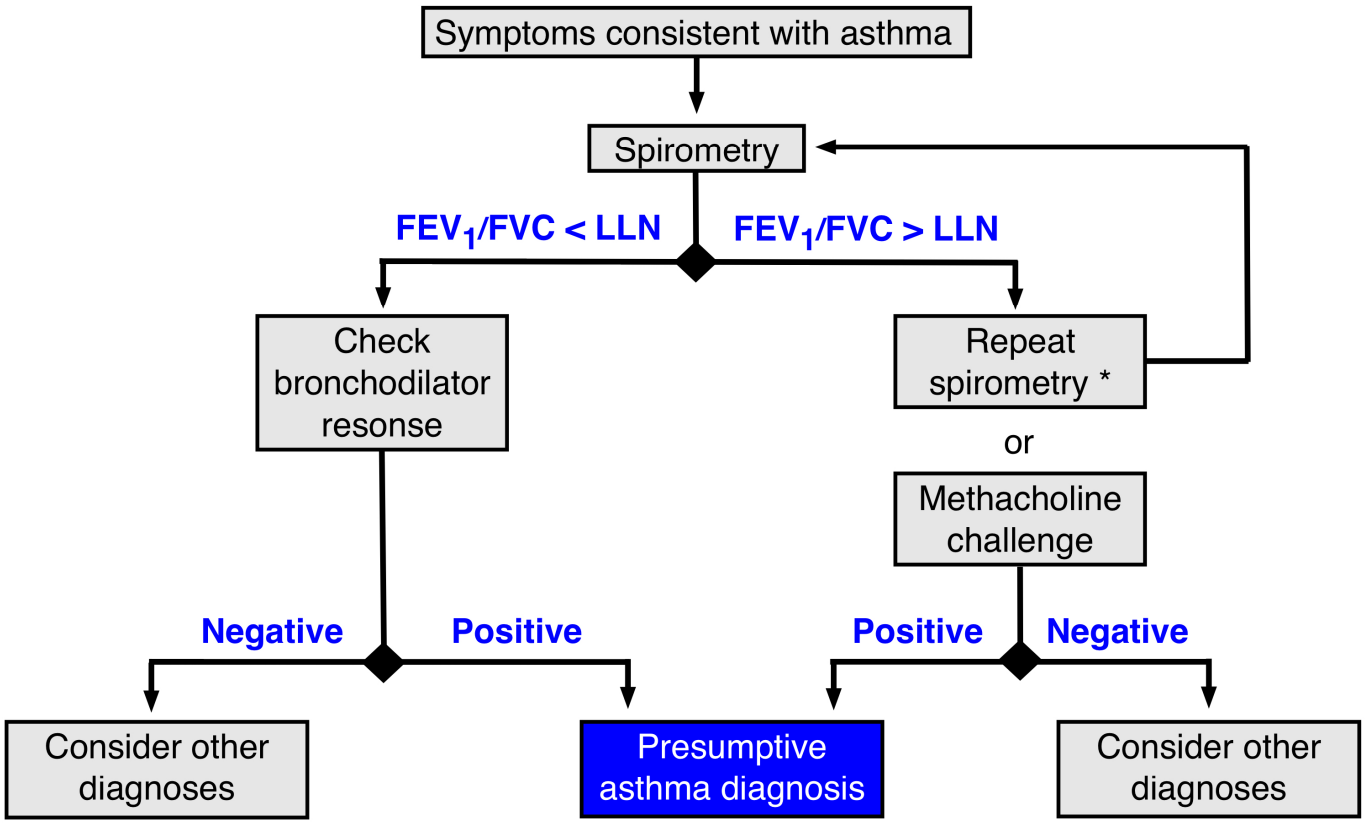
BD: Bronchodilator

A Question

Which of the following changes in her asthma medications is indicated at this time?

1. Add inhaled ipratropium prn
2. Start budesonide-formoterol
3. Start formoterol
4. Start montelukast
5. Refer for methacholine challenge

A Diagnostic Algorithm For Asthma



* At a different time

McCracken et al. JAMA 2017. 318(3): 279

Asthma Mimic: Paradoxical Vocal Cord Motion *

Mechanism	Paradoxical adduction of vocal cords on inhalation
Big Clues	Frequent intubations with rapid recovery Poor response to appropriate asthma treatment Stridor (usually inspiratory)
Diagnosis	Flattened inspiratory limb of flow volume loop Otolaryngology for flexible laryngoscopy
Treatment	Speech therapy

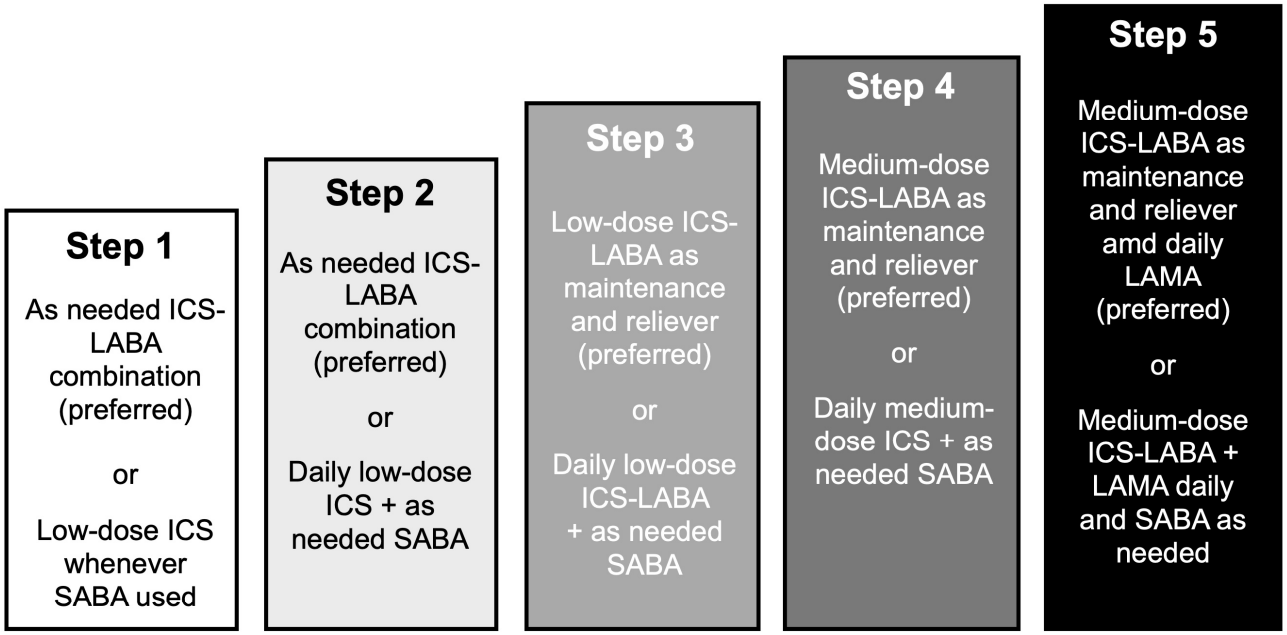
* Can be seen in patients with asthma

Rating Asthma Severity

Severity	Symptom frequency	Nocturnal awakening	Other
Intermittent	< 2 times/week	--	--
Mild persistent	≥2 times/week but < 4-5 days/week	--	--
Moderate persistent	Most days	≥ 1 time/week	Risk factors for exacerbations
Severe persistent	Daily	≥ 1 time/week	Low lung function

National Asthma Education and Prevention Program: Expert Panel Report III, 2007
Global Strategy for Asthma Management and Prevention, Global Initiative for Asthma (GINA)

The Stepwise Approach To Treatment

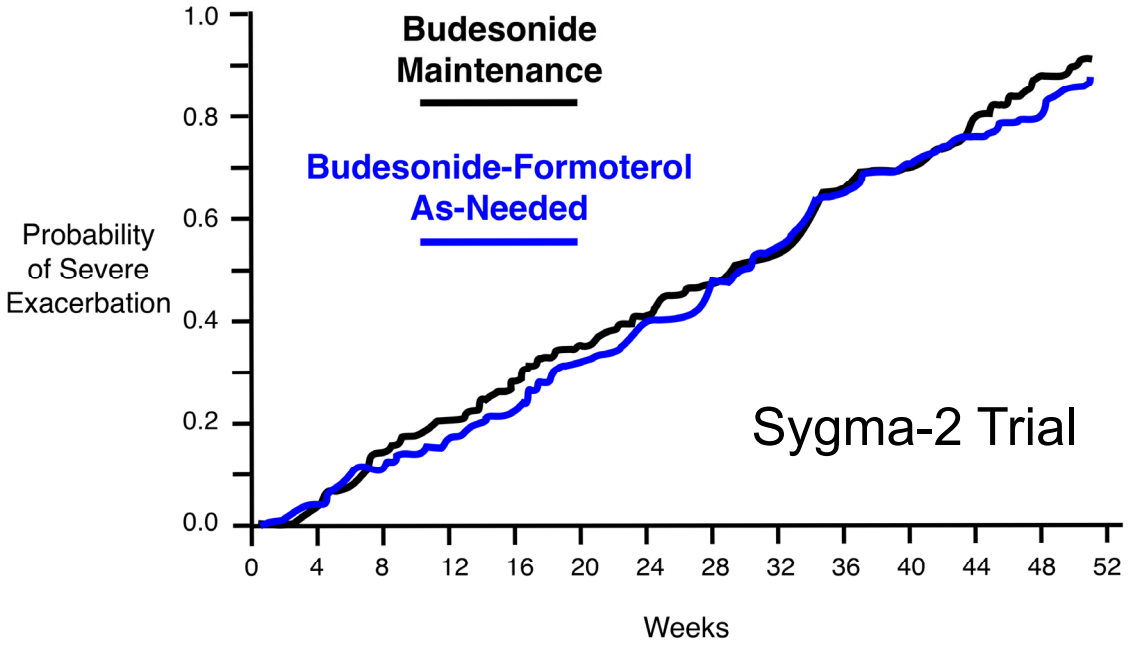


The NAEPP guidelines also use a step-wise approach with some differences in medication choices at each step

Key: ICS: inhaled corticosteroid; LABA: long-acting beta-agonist; LAMA: long-acting beta-agonist
SABA: short-acting beta agonist

Source: 2023 GINA Guidelines: ginaasthma.org
NAEPP: National Asthma Education and Prevention Program

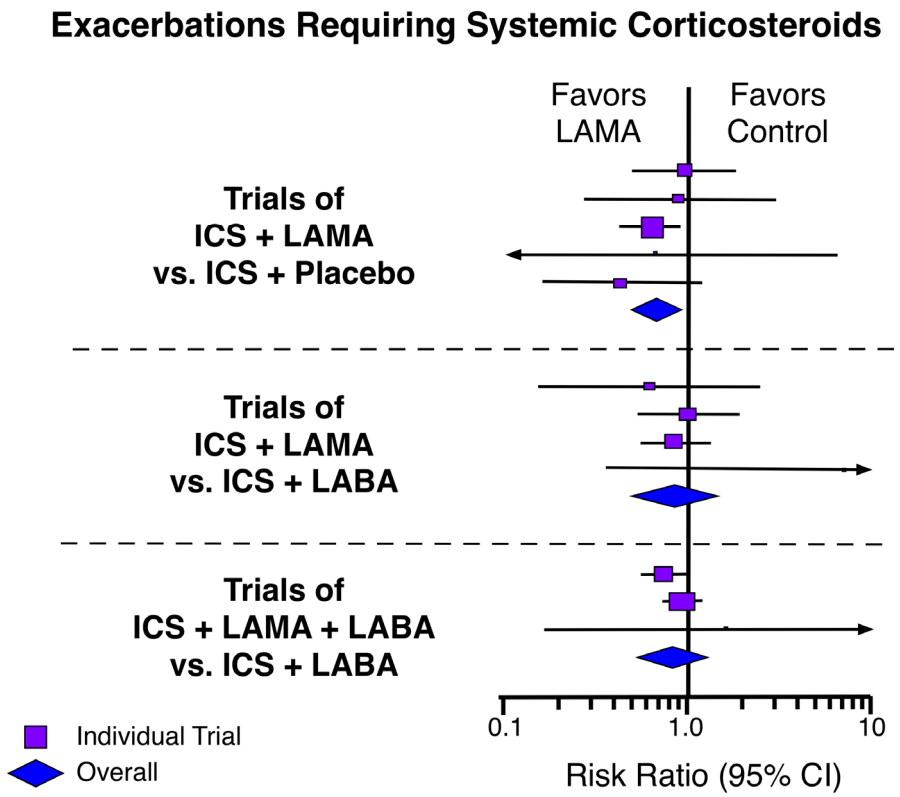
The Shift In Practice With Rescue Inhalers Was Driven By The Sygma 1 and 2 Trials



Sygma-1 showed similar results: worse symptom control but similar exacerbation rates with the prn ICS-LABA combination

Batemen et al. NEJM. 2018. 378: 1877

The Other Shift In Practice: Tiotropium



LAMA decreases risk of exacerbations when added to steroids

May not offer benefit over LABA when added to ICS

Now included as part of later steps in GINA and NAEPP guidelines

Sobieraj et al. JAMA 2018. 319(14): 1473

LAMA: long-acting anti-muscarinic; LABA: long-acting beta agonist; ICS: inhaled corticosteroid

Case 5: 35 year-old woman

History

Severe asthma requiring prednisone

Presenting with one month of fevers, weight loss, malaise

Medications

Fluticasone
Salmeterol
Montelukast (added 2 months ago)
Prednisone (recently decreased to 15 mg/d)

Studies

CBC: WBC 10 x 10^3 cells/μL; 40% eosinophils

Chest Radiograph: Scattered alveolar opacities

A Question

Which of the following laboratory findings is most likely in this patient?

1. Decreased complement levels
2. Elevated antinuclear antibody titre
3. Positive P-ANCA
4. Positive anti-glomerular basement membrane antibody
5. Positive serum cryoglobulins

Problems In Difficult-To-Control Asthma

Feature	ABPA	EGPA **
Also seen with	Cystic fibrosis	Atopy, allergic rhinitis
Clinical features	Fevers, malaise, expectorate plugs	Multisystem eosinophilic infiltration then vasculitis
Imaging	Finger in glove opacities Perihilar opacities *	Lobar or segmental opacities *
Labs	Elevated eosinophils, IgE Ab to aspergillus	Elevated eosinophils, IgE Positive P-ANCA
Treatment	Systemic steroids +/- antifungal therapy	Systemic steroids +/- immunosuppression

* Multiple other imaging patterns possible
** Formerly Churg Straus Vasculitis
ABPA: Allergic Bronchopulmonary Aspergillosis EGPA: Eosinophilic Granulomatosis With Polyangiitis

Biologics In The Management of Asthma

Feature	Omalizumab	Mepolizumab or Reslizumab	Dupilumab
Mechanism of action	Anti-IgE monoclonal antibody	Anti-IL-5 monoclonal antibody	Anti-IL-4 receptor subunit antibody
Route	Subcutaneous injection	Mepolizumab: SQ Reslizumab: IV	Subcutaneous infection
Criteria for use	Elevated IgE (30-1000) Allergic sensitivity	Increased eosinophil counts *	Eosinophil counts > 150 cells/μL
Main Benefit	Less exacerbations Less need for steroids	Less exacerbations Less need for steroids	Less exacerbations Less need for steroids

* Mepolizumab: > 150 eosinophils / μL
Reslizumab: : 400 eosinophils / μL

Case 5: 25 year-old man

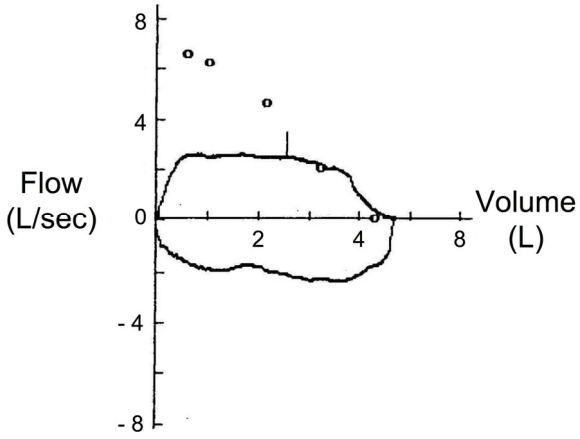
History Increasing dyspnea over several weeks

Worse when he lays down at night

Exam Expiratory wheezes over central chest

Spirometry

Test	Actual	% Predicted	Z-score	LLN
FVC (L)	2.38	83	-1.10	--
FEV_1 (L)	1.65	74	-1.85	--
FEV_1/FVC	0.69	---	---	0.74



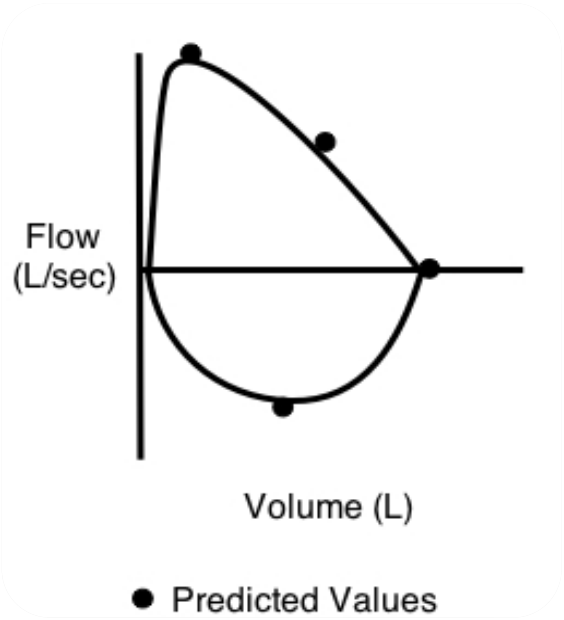
LLN: Lower limit of normal

A Question

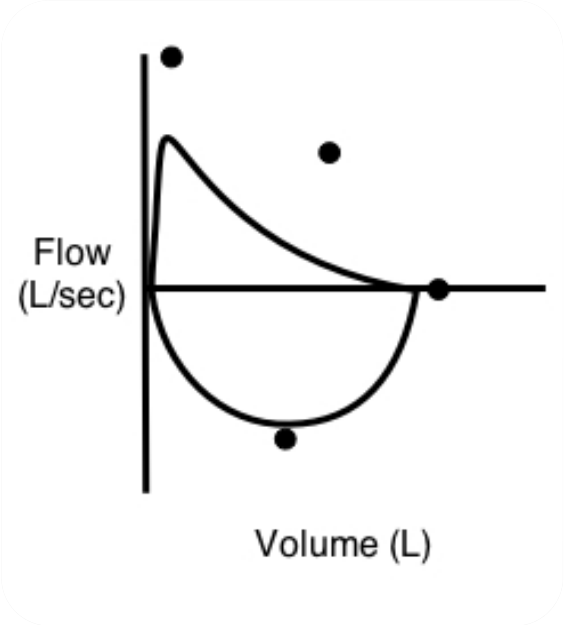
Which of the following is the most appropriate next step for this patient?

1. CT scan of the neck and chest
2. Referral to Otolaryngology for laryngoscopy
3. Referral to Pulmonary for bronchoscopy
4. Start inhaled corticosteroids and short-acting prn bronchodilators
5. Start short-acting prn bronchodilators

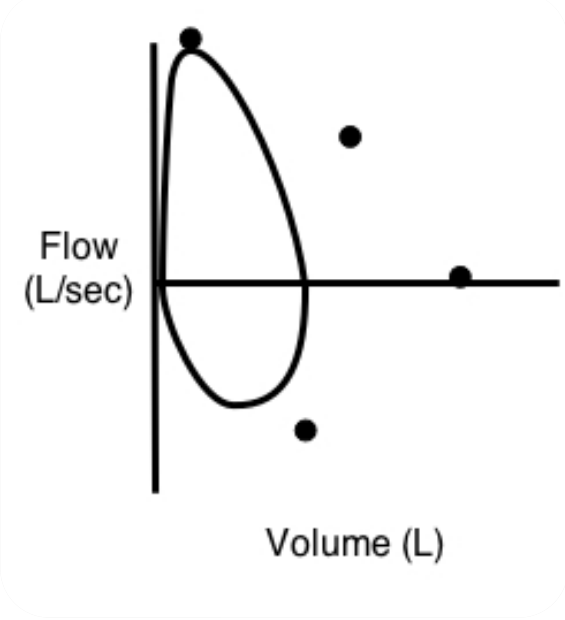
Don't Forget To Look At The Flow-Volume Loops



Normal

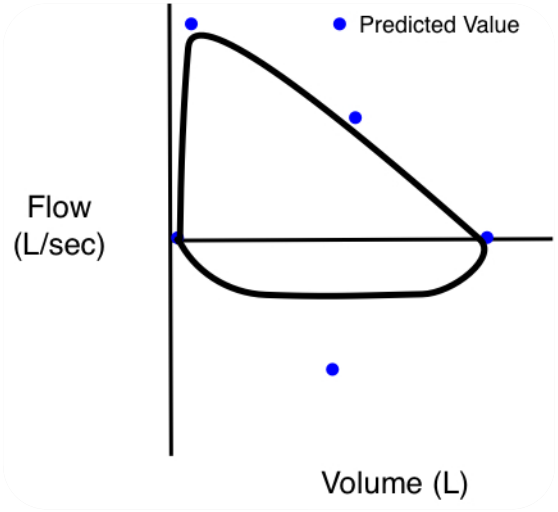


Obstruction

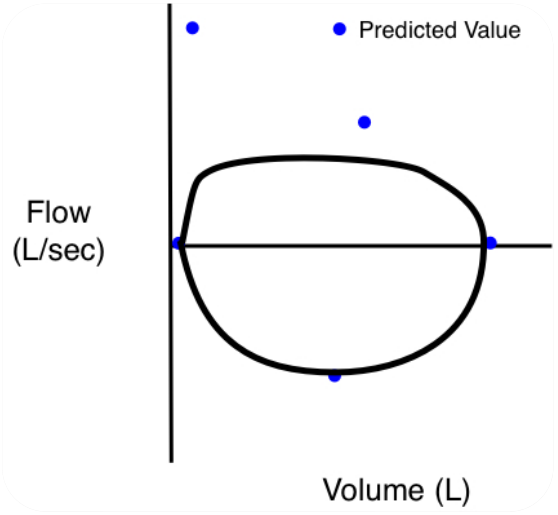


Restriction

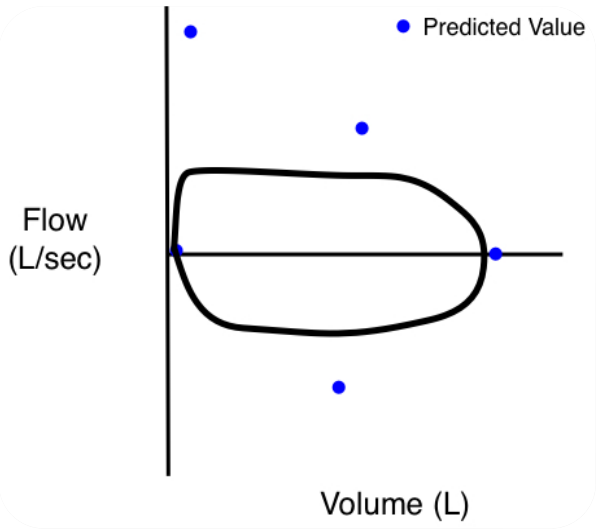
Upper Airway Obstruction On Flow Volume Loops



Variable Extrathoracic
(e.g., thyroid mass)



Variable Intrathoracic
(e.g., tracheomalacia)



Fixed Upper Airway
(e.g., tracheal stenosis)

Thanks For Listening!

Questions?

aluks@uw.edu

Answer Key

Question	Answer
1	5
2	2
3	3
4	2
5	3
6	1