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WiredIN

COPD

Tailoring therapy for your patients

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Learning objectives

1. Identify current guidelines for diagnosis and management of COPD.
2. Develop a diagnostic approach for patients with suspected COPD.
3. Construct an individualized management plan for patients with confirmed COPD.

COPD: more Rocky Road than vanilla

- COPD is a complex and *heterogenous* condition with many components to its clinical presentation, including dyspnea, cough (with or without sputum), airflow limitation, reduced exercise capacity/fatigue, weight loss and exacerbations.
- As these components vary in both their presence and severity, *personalization* of the assessment and clinical management of COPD is key to optimizing patient outcomes.

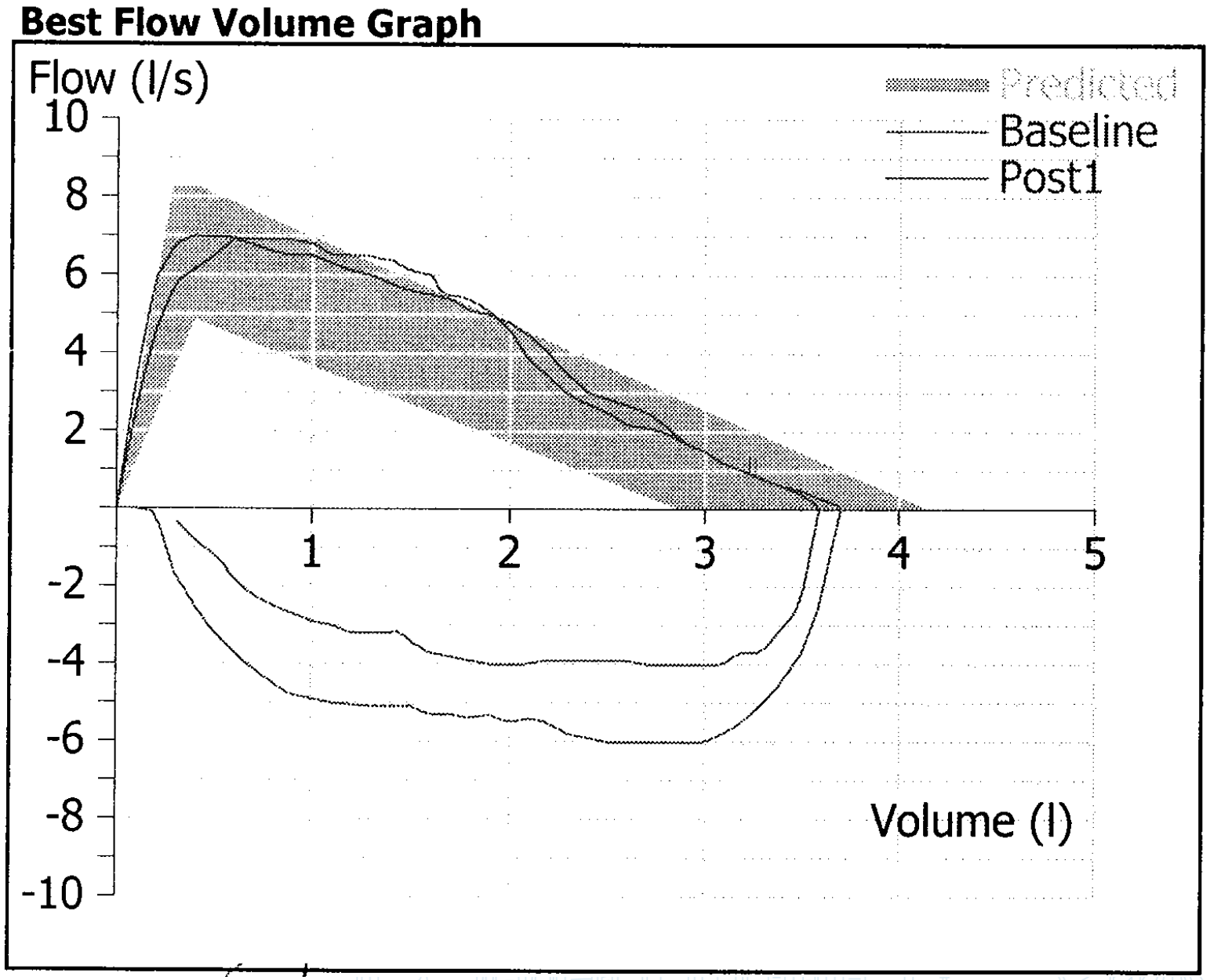
Diagnosis

Classification of Airflow Limitation Severity (GOLD)

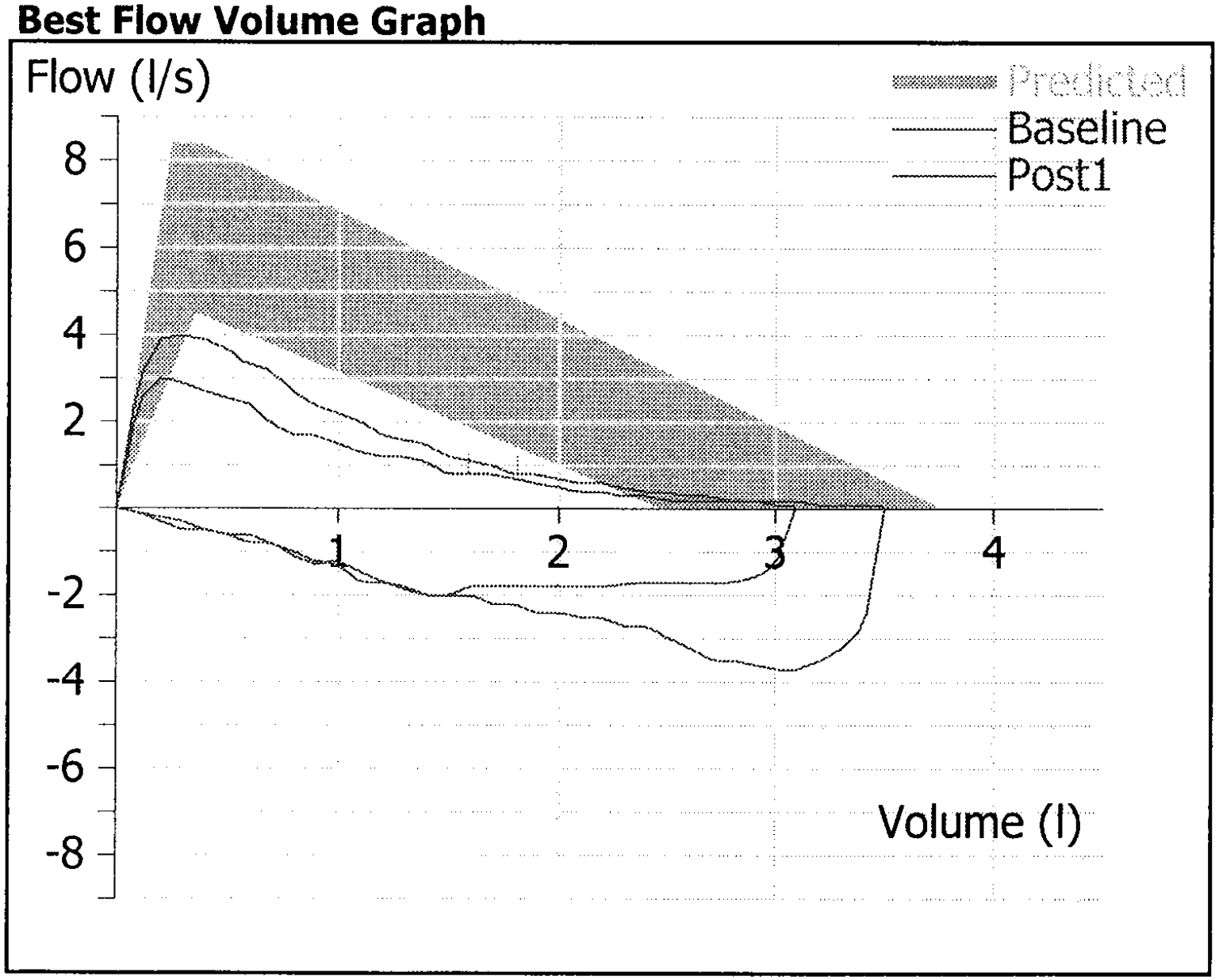
In patients with $FEV_1/FVC < 0.70$, *post-bronchodilator*

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

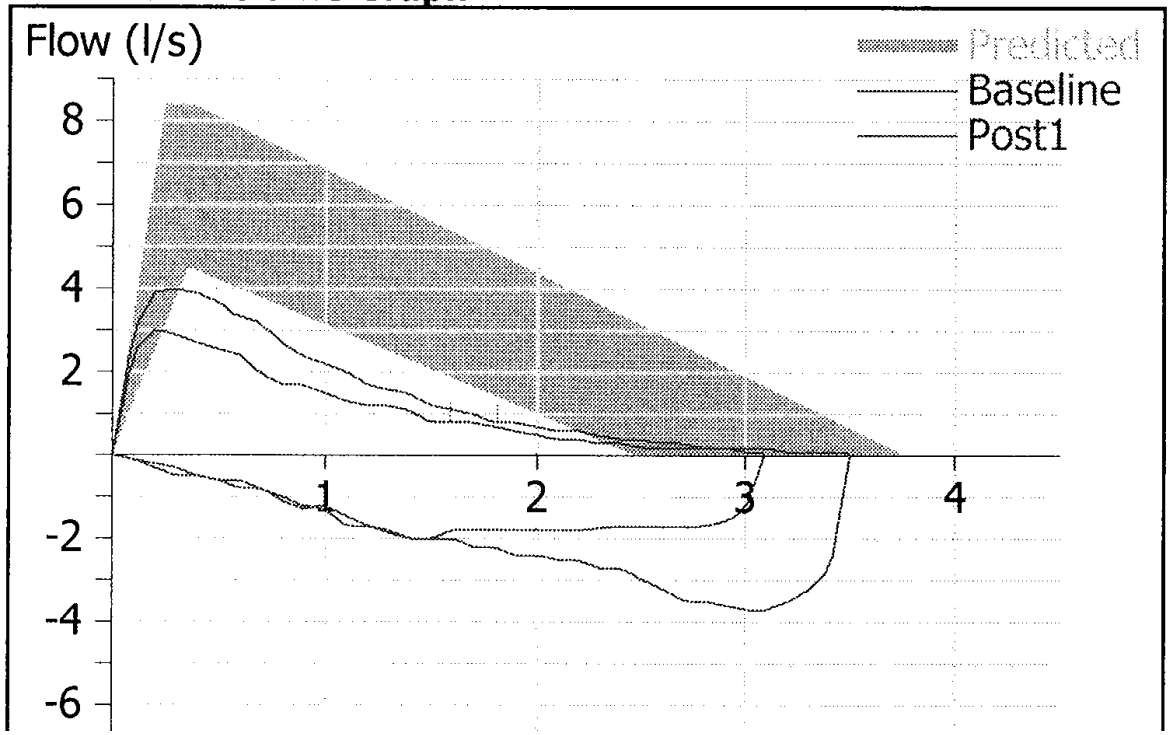
Normal spirometry



Moderate obstruction with significant improvement post-bronchodilator



Best Flow Volume Graph



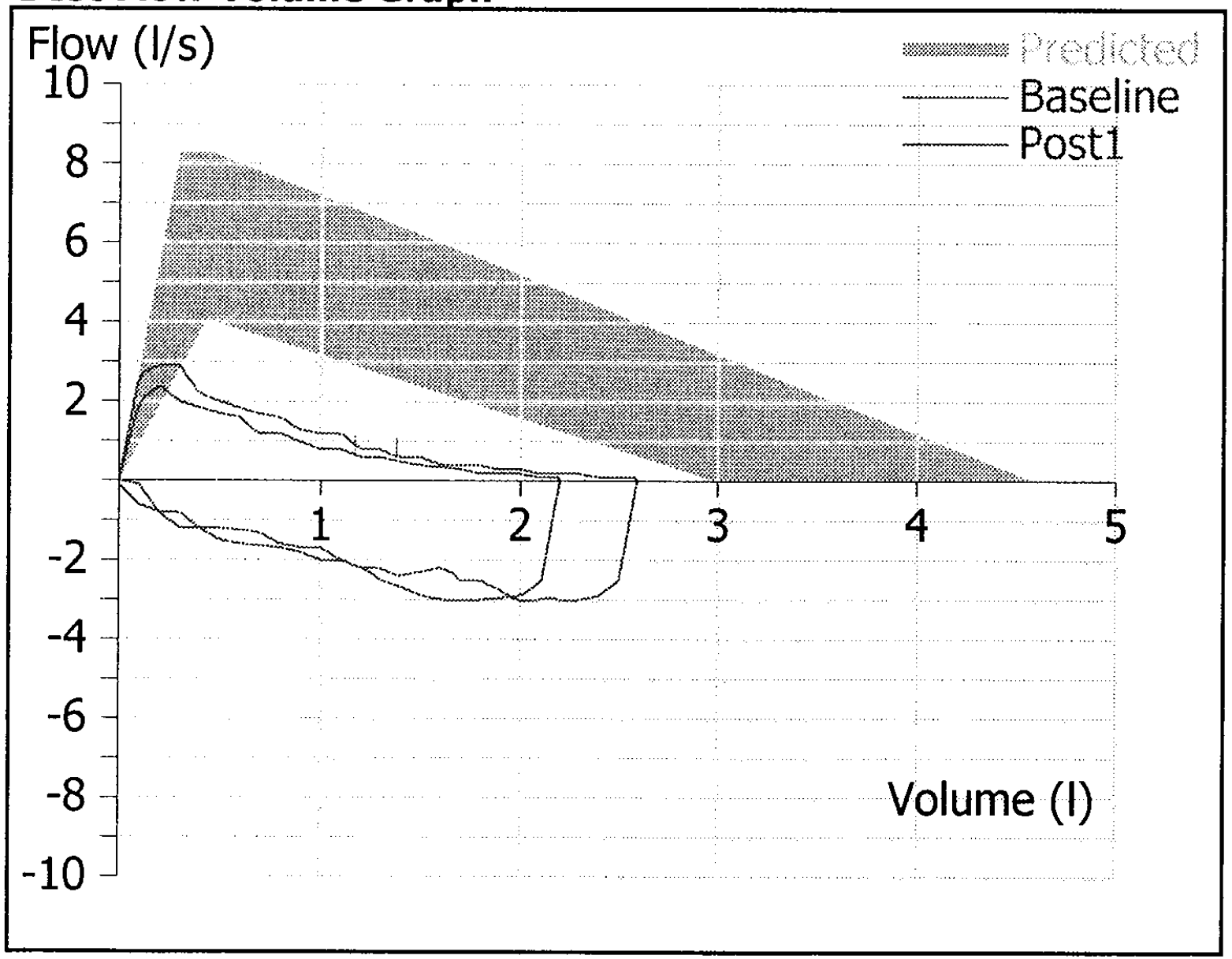
Selected indices of the best blows

Index	Base	%Pred	Zscr	Post1	%Pred	%Chg	Zscr	[Min	Pred	Max]
FEV1	1.59 l	66%	-2.2	1.81 l	75%	14%	-1.6	1.86 l	2.41 l	2.96 l
FVC	3.18 l	102%	0.1	3.38 l	108%	6%	0.6	2.47 l	3.12 l	3.77 l
PEF	2.95 l/s	45%	-3.3	4.08 l/s	62%	38%	-2.2	4.75 l/s	6.57 l/s	8.40 l/s
FEV1/FVC	50%		-4.7	54%		7%	-4.1	68%	78%	88%

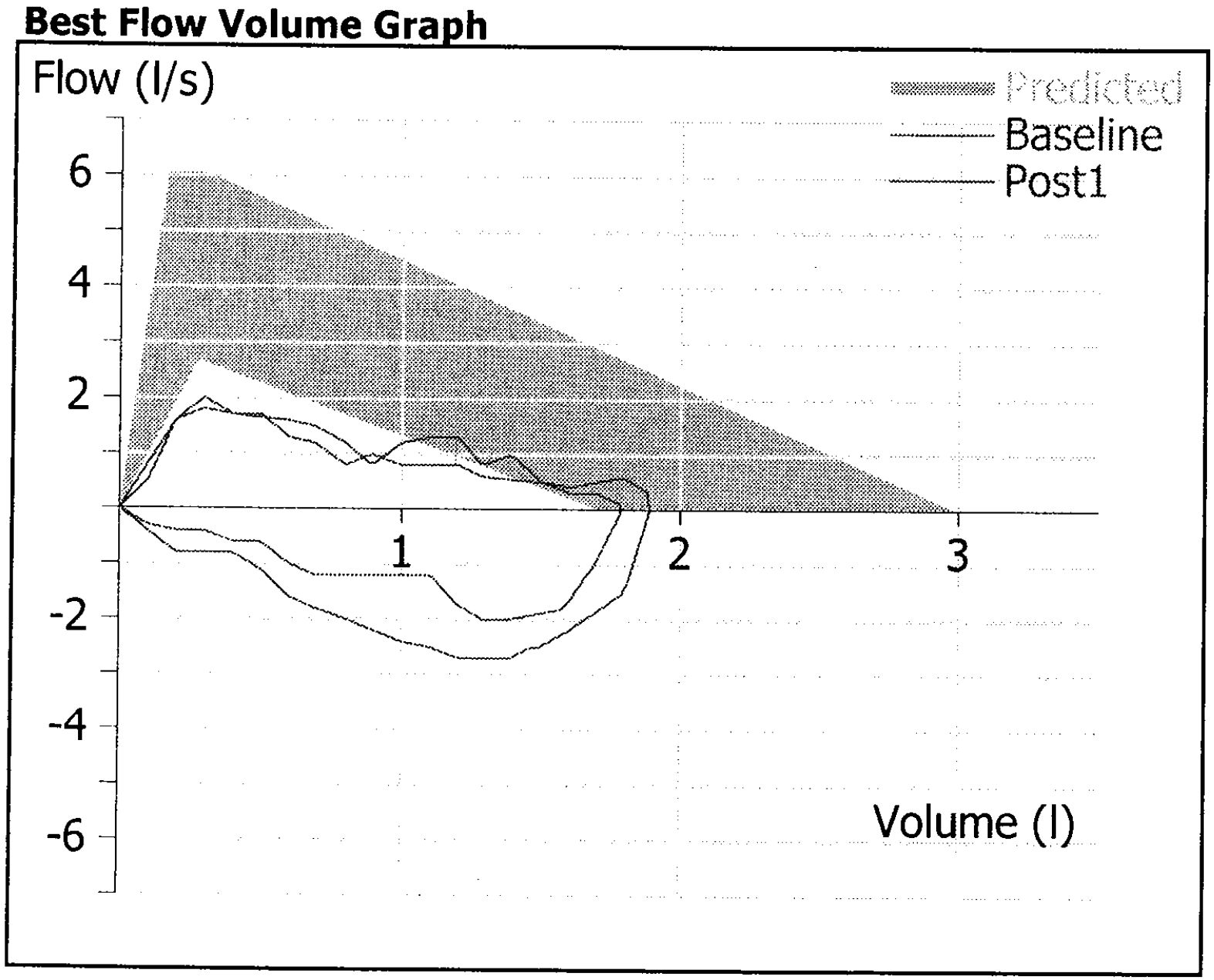
+ 220 ml

≥ 12% AND ≥ 200 ml improvement

Severe obstruction with insignificant improvement post-bronchodilator



Poor quality study



Practice Recommendations

1. Perform spirometry in patients with suspected COPD.

Risk factors

- Although cigarette smoking is the leading cause of COPD, up to *25% of people with the disease have never smoked*.
- Risk of 15% for clinically significant COPD among smokers is commonly cited, but this may be an underestimate.
- Genetic factors also play a role in susceptibility to COPD; the best defined is emphysema related to alpha$_1$-antitrypsin deficiency.

Never-smokers

Risk factors among never-smokers include:

- Exposure to biomass fuels, air pollution, or secondhand smoke
- Workplace exposure to vapors, gases, dust, or fumes
- Asthma
- Maternal smoking in pregnancy
- Low birthweight
- History of respiratory infections during childhood

Screening vs. symptom-based detection

- Epidemiologic data suggest that COPD is *underdiagnosed*.
- The U.S. Preventive Services Task Force recommends *against screening* for COPD in *asymptomatic* adults.
- Patients with COPD may report that they do not have symptoms, but actually limit their daily physical activity to avoid or minimize them, or may attribute their symptoms to physical deconditioning or older age.

When to consider measuring alpha$_1$-antitrypsin level

- All symptomatic patients with fixed airflow obstruction, particularly those with COPD onset in their 50s or earlier
- Family history of alpha$_1$-antitrypsin deficiency
- Emphysema, bronchiectasis, liver disease, or panniculitis in the absence of a recognized risk factor or out of proportion to the culprit exposure

Exertional dyspnea: COPD and HF

- Heart failure and COPD often coexist; risk factors and symptoms overlap.
- Treatment can improve long-term outcomes with HF; few treatments impact long-term outcomes in COPD.
- Normal CXR does not rule out either HF or COPD.
- *Elevated natriuretic peptide(s) are the single most powerful predictor of adverse outcomes in HF, regardless of LVEF.*
- Up to 50% of patients with COPD have elevated plasma NPs – predicts increased mortality risk, even without diagnosis of HF.

HF + COPD = no β-blocker?

- β-blockers improve long-term prognosis of patients with HF, particularly HFrEF.
- Concern for triggering bronchoconstriction or blocking the effect of sympathomimetic bronchodilators may inhibit β-blocker use in HF with COPD. However,
- There is no evidence for worsening symptoms or quality of life in patients with β-blocker use in patients with COPD and HF.
  - Consider a cardioselective β-blocker such as bisoprolol or nebivolol.

Practice Recommendations

1. Perform spirometry in patients with suspected COPD.
2. Consider other diagnoses (particularly heart failure) in patients with exertional dyspnea; do not withhold β-blockers if indicated.

Treatment: stable

Acronyms

- LAMA: long-acting muscarinic antagonist
- LABA: long-acting β_2-agonist
- SAMA: short-acting muscarinic antagonist
- SABA: short-acting β_2-agonist
- ICS: inhaled corticosteroid

GOLD ABCD Staging to Guide Initial Pharmacologic Therapy in COPD

Patient Category	Characteristics	Exacerbations per year	CAT Score	mMRC Dyspnea Scale Score
A	Low risk, fewer symptoms	≤1	< 10	0-1
B	Low risk, more symptoms	≤1	≥ 10	≥ 2
C	High risk, fewer symptoms	≥2 / ≥1 with hospitalization	< 10	0-1
D	High risk, more symptoms	≥2 / ≥1 with hospitalization	≥ 10	≥ 2

COPD Assessment Test (CAT)

catestonline.org

I never cough	0 1 2 3 4 5	I cough all the time
I have no phlegm (mucus) in my chest at all	0 1 2 3 4 5	My chest is completely full of phlegm (mucus)
My chest does not feel tight at all	0 1 2 3 4 5	My chest feels very tight
When I walk up a hill or one flight of stairs, I am not breathless	0 1 2 3 4 5	When I walk up a hill or one flight of stairs, I am very breathless
I am not limited doing any activities at home	0 1 2 3 4 5	I am very limited doing activities at home
I am confident leaving my home despite my lung condition	0 1 2 3 4 5	I am not at all confident leaving my home because of my lung condition
I sleep soundly	0 1 2 3 4 5	I don't sleep soundly because of my lung condition
I have lots of energy	0 1 2 3 4 5	I have no energy at all

Jones et al. ERJ 2009; 34(3); 648-54.

mMRC (Modified Medical Research Council) Dyspnea Scale

mdcalc.com/mmrc-modified-medical-research-council-dyspnea-scale

Symptom severity	Score
Dyspnea only with strenuous exercise	0
Dyspnea when hurrying or walking up a slight hill	1
Walks slower than people of the same age because of dyspnea or has to stop for breath when walking at own pace	2
Stops for breath after walking 100 yards (91m) or after a few minutes	3
Too dyspneic to leave house or breathless when dressing	4

Fletcher CM. BMJ 1960;2:1662.

Initial pharmacologic treatment based on GOLD group

0 or 1 moderate exacerbations (not leading to hospital admission)

A: A bronchodilator (SABA)

B: A long-acting bronchodilator (LABA or LAMA)

≥ 2 moderate exacerbations or ≥ 1 leading to hospitalization

C: LAMA

D: LAMA *or* LAMA+LABA *or* ICS+LABA

GOLD 2023: factors to consider when *starting* ICS

- Strongly favors use:
  - History of hospitalization(s) or ≥ 2 moderate exacerbations per year
  - Eosinophil count ≥ 300
  - History of, or concomitant asthma
- Favors use:
  - 1 moderate exacerbation per year
  - Eosinophil count 100 to < 300
- Against use:
  - Repeated pneumonia
  - Eosinophil count < 100
  - History of mycobacterial infection

Does inhaled therapy containing ICSs reduce all-cause mortality in patients with COPD?

- Yes.

CHEST 2023; 163(1):100-114

Does inhaled therapy containing ICSs reduce all-cause mortality in patients with COPD?

Sixty RCTs enrolling 103,034 patients:

- Inhaled therapy containing **ICSs** (**OR, 0.90**; 95% CI, 0.84-0.97), especially **triple** therapy (**OR, 0.73**; 95% CI, 0.60-0.90), is associated with reduced all-cause mortality risk vs. *inhaled therapy without ICSs*.

CHEST 2023; 163(1):100-114

Does inhaled therapy containing ICSs reduce all-cause mortality in patients with COPD?

Important factors include:

- Treatment duration > 6 months (OR, 0.90)
- Medium-dose ICSs (OR, 0.7)
- Low-dose ICSs (OR, 0.88)
- Budesonide (OR, 0.75)

CHEST 2023; 163(1):100-114

Does inhaled therapy containing ICSs reduce all-cause mortality in patients with COPD?

Predictors of this association:

- Eosinophil counts of ≥ 200/uL or ≥ 2%
- ≥ 2 moderate or severe exacerbations in the previous year
- GOLD stages III or IV
- Age < 65 years
- BMI of ≥ 25

CHEST 2023; 163(1):100-114

Important triple therapy points

- Higher dose steroid does not result in additional risk reduction

- Addition of LAMA to ICS / LABA ~15% reduction in mod-severe exacerbations
- Addition of ICS to LAMA / LABA ~25% reduction in mod-severe exacerbations
  - but the rate is not zero
- If fewer exacerbations, impact of ICS is significantly less.

Should patients with COPD continue treatment with ICS?

11 RCTs with 29,654 patients

- Risk of moderate to severe exacerbation after ICS discontinuation vs. eosinophil count.
- Rate ratios for EOS counts:
  - < 150 cells/µL: 0.88 (12% reduction)
  - 150–300 cells/µL: 0.80 (20% reduction)
  - > 300 cells/µL: 0.57 (43% reduction)

- Continued treatment with ICS is associated with increased risk of pneumonia independent of EOS subgroup (risk ratio: 1.39).

Practice Recommendations

1. Perform spirometry in patients with suspected COPD.
2. Consider other diagnoses (particularly heart failure) in patients with exertional dyspnea; do not withhold β-blockers if indicated.
3. Eosinophil count > 300 cells/µL predicts response to ICS, strongly favors starting ICS per GOLD guidelines.

Exacerbation

COPD exacerbation

The American Thoracic Society (ATS) and European Respiratory Society (ERS) define an exacerbation as an acute change in a patient's baseline dyspnea, cough, or sputum that is beyond normal variability, and that is sufficient to warrant a change in therapy.

- In patients with known COPD, exacerbations occur an average of 1.3 times per year.
- There is no validated diagnostic test or biomarker of COPD exacerbations.

Steroids in COPD exacerbation

Short courses of systemic corticosteroids:

- Increase the time to subsequent exacerbation
- Decrease the rate of treatment failure
- Shorten hospital stays
- Improve hypoxemia and FEV_1

- Oral and IV prednisolone in equivalent dosages (60 mg daily) and 2 vs. 8-week courses show no difference in lengths of hospitalization and rates of early treatment failure.

If steroids, how much?

An RCT of 314 patients presenting to the emergency department with acute COPD exacerbations found no difference between:

- 5-day course of oral corticosteroids, vs.
- 14-day course

- with regard to repeated exacerbation in 6 months.

This supports **prednisone 40 mg/d for 5 days** for patients not requiring admission to the intensive care unit.

Antibiotics in COPD exacerbation

A majority of patients with COPD exacerbations have high concentrations of bacteria in their lower airways.

- Most common: *Streptococcus pneumoniae, Haemophilus influenzae, Moraxella catarrhalis, Mycoplasma pneumoniae*
- The use of antibiotics in moderately or severely ill patients with COPD exacerbations reduces the risk of treatment failure and death.

Antibiotics in COPD exacerbation

- Antibiotics may also benefit patients with mild exacerbations and purulent sputum.
- The optimal choice of antibiotic and length of treatment is not well-supported by existing evidence.
- There is limited evidence that broad-spectrum antibiotics are more effective than narrow-spectrum antibiotics.
- Prophylactic, continuous use of antibiotics does not improve outcomes in patients with COPD.

Practice Recommendations

1. Perform spirometry in patients with suspected COPD.
2. Consider other diagnoses (particularly heart failure) in patients with exertional dyspnea; do not withhold β-blockers if indicated.
3. Eosinophil count > 300 cells/µL predicts response to ICS, strongly favors starting ICS per GOLD guidelines.
4. Treat COPD exacerbations with (short course) steroids and broad(ish)-spectrum antibiotics.

Newer agents

Dupilumab for COPD with type 2 inflammation

- Dupilumab, a monoclonal antibody, blocks the shared receptor component for IL-4 and IL-13, key drivers of type 2 inflammation
- Patients with COPD and eosinophil count $\geq$ 300/uL and elevated exacerbation risk despite standard triple therapy randomized to dupilumab (300 mg SQ q2w) vs. placebo
- Moderate or severe exacerbations:
  - Dupilumab: 0.78 per year
  - Placebo: 1.10 per year; rate ratio 0.70 (i.e., 30% reduction)

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There are different types of inflammation?

- Type 1 inflammation is directed toward *intracellular* invasion by bacteria, viruses.
- Type 2 inflammation is traditionally directed toward *helminthic* infection and triggers an eosinophilic response using multiple mediators, including interleukins.
- Dysregulated type 2 inflammation is seen in 20-40% of patients with COPD and increases risk of exacerbation; also predicts a better response to glucocorticoids.

- These are different from types I-IV hypersensitivity reactions.

Roflumilast

- In patients with chronic bronchitis, severe and very severe airflow limitation (GOLD 3 and GOLD 4), and frequent exacerbations that are not adequately controlled by long-acting bronchodilators, the PDE-4 inhibitor roflumilast [Daliresp; 500 mcg po qd] reduces exacerbations.

- These effects are also seen when roflumilast is added to long-acting bronchodilators.
- There are no comparison studies with inhaled corticosteroids.

Nonpharmacologic

Role of supplemental oxygen

Long-term oxygen therapy *decreases mortality* in patients with severe resting hypoxemia.

Patients with moderate to severe COPD should be periodically evaluated to determine whether they need supplemental oxygen.

Role of pulmonary rehabilitation

- ACP, ACCP, ATS and ERS recommend that clinicians should prescribe *pulmonary rehabilitation* for symptomatic patients with an *FEV_1 <50% predicted* (Grade: strong recommendation, moderate-quality evidence).

- Clinicians may *consider pulmonary rehabilitation* for symptomatic or exercise-limited patients with an *FEV_1 >50%* predicted. (Grade: weak recommendation, moderate-quality evidence).

Practice Recommendations

1. Perform spirometry in patients with suspected COPD.
2. Consider other diagnoses (particularly heart failure) in patients with exertional dyspnea; do not withhold β-blockers if indicated.
3. Eosinophil count > 300 cells/µL predicts response to ICS, strongly favors starting ICS per GOLD guidelines.
4. Treat COPD exacerbations with (short course) steroids and broad(ish)-spectrum antibiotics.
5. Periodically assess need for supplemental oxygen and/or pulmonary rehabilitation.

Thank you for your kind attention.