



## CASE STUDY 1

### A 52-Year-Old Woman With Asthma...or Is It COPD?

#### Presentation

Diane, a 52-year old, postmenopausal white woman seeks medical treatment because she is—in her words—“having that bronchitis thing again.” She reports having these episodes 1 to 3 times per year during the past 5 years. She denies any fever with this episode. Diane speaks in full sentences and does not appear to be in acute respiratory distress. She is currently a social smoker but previously smoked a pack per day for approximately 10 years. She has a brother with asthma and a grandfather who died of emphysema at the age of 68. She is allergic to shellfish. Diane describes her symptoms as being worse in the morning with lots of coughing and heavy phlegm production. She is also awakened by cough a few times during the night. She is concerned because the illness is recurring more frequently. In the past, she has been treated with a variety of medications, including inhaled corticosteroids (ICS), long-acting beta<sub>2</sub> adrenergic agonists (LABA), oral corticosteroids, and antibiotics. When asked about any changes in her symptoms over time she mentions that they used to be seasonal but now they occur sporadically, year-round. When asked about exercise, she reports that she used to walk 3 times a week with a friend but can no longer keep up because of breathing difficulties; instead, she walks with an older neighbor about once a week. Diane attributes the change to “old age.”

#### Physical Examination

- Height            5 ft 6 in
- Weight           152 lb
- BMI               24.5 kg/m<sup>2</sup>
- BP                 128/74 mm Hg
- HR                74 bpm
- RR                18/min
- Temperature    98.4°F
- HEENT           Normal
- Neck             No jugular venous distention
- Lungs            Decreased breath sounds, scattered end-expiratory wheeze
- Heart             Regular rate and rhythm, no murmurs or gallops

BMI = body mass index; BP = blood pressure; HR = heart rate; RR = respiration rate; HEENT = head, ears, eyes, nose, and throat.

#### Clinical Decision Point

What test should be ordered now?

- Chest X-ray
- Spirometry
- Pulse oximetry
- Allergy testing
- None; refer to pulmonologist

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#### Comment

Diane's respiratory symptoms have never been fully evaluated despite their repeated occurrence and the variety and number of medications that have been prescribed. The symptoms and history presented here most strongly suggest the possibility of asthma or COPD (Table 1).<sup>1,2</sup> As might be expected with asthma, Diane has intermittent symptoms that are worse at night and in early morning, she has a close relative with asthma, and she has a history of allergy.<sup>1</sup> As might be expected with COPD, Diane was in her late forties at onset of symptoms, her symptoms are

progressive in that they now occur year-round, and she has modified her lifestyle to accommodate reduced exercise tolerance.<sup>1,2</sup> Diane's smoking history is not definitive for either disorder. She smokes socially and has a 10 pack-year history, but does not have the 20 pack-year history that is more clearly associated with COPD.<sup>3</sup> Similarly, cough and wheezing are symptoms of both disorders, although a cough producing large amounts of phlegm is more suggestive of COPD.<sup>4</sup> Spirometry is the best tool for differentiating asthma from COPD.<sup>1</sup> Diane is not in acute distress (ie, hypoxic), therefore pulse oximetry is not warranted. Allergy testing or a chest X-ray may be desirable to obtain after a diagnosis is made but will not benefit the diagnosis itself. Because these tests are all available in primary care practice, there is no need to refer Diane to a specialist.

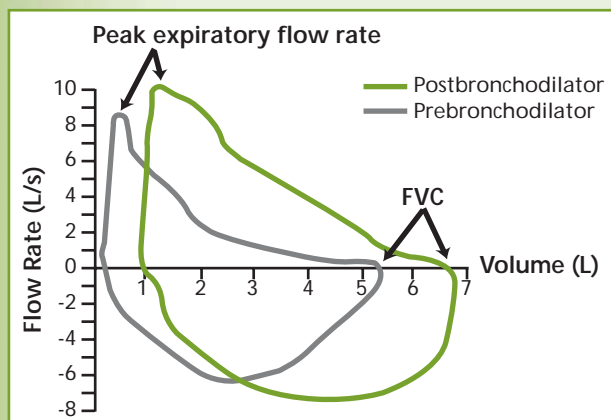
#### Decision: Order spirometry testing.

Prebronchodilator and postbronchodilator testing should be performed to determine the degree of reversibility of any airflow obstruction (Figure 1). Diane's spirometry results are presented in Table 2.

**Table 1. Differential and Overlapping Features of Asthma and COPD**

Diagnosis	Typical Features
COPD	<ul style="list-style-type: none"> <li>➤ Onset in middle age</li> <li>➤ Slowly progressive symptoms</li> <li>➤ History of heavy smoking</li> <li>➤ Dyspnea with exercise</li> <li>➤ Largely irreversible airflow limitation</li> </ul>
Asthma	<ul style="list-style-type: none"> <li>➤ Early onset (often childhood)</li> <li>➤ Variable, intermittent symptoms</li> <li>➤ Nocturnal and early-morning symptoms</li> <li>➤ History of allergy, rhinitis, or eczema</li> <li>➤ Family history of asthma</li> <li>➤ Largely reversible airflow limitation</li> </ul>
Both	<ul style="list-style-type: none"> <li>➤ Wheezing</li> <li>➤ Cough</li> <li>➤ Chest tightness</li> <li>➤ Dyspnea</li> </ul>

*Global Strategy for the Diagnosis, Management, and Prevention of COPD*<sup>1</sup>; Doherty DE.<sup>2</sup>



**Figure 1.** Prototype of spirometry flow-volume loop.

The spirometry tracing must be evaluated initially to determine if it is interpretable: Is there a good rapid start with a 4- to 6-second blow that reaches a plateau without interruptions? An algorithm may guide interpretation of the spirometry results (Figure 2).<sup>5</sup> However, it is important to note that in some cases, asthma may be difficult to distinguish from COPD—even with spirometry. Airflow obstruction can be partially reversible after bronchodilator use in both disorders. The degree of reversibility and other clinical characteristics must be considered. Although the obstruction in asthma may not be fully reversible, it should approach complete reversal. In COPD, postbronchodilator airflow will never return to normal or near-normal values. A postbronchodilator FEV<sub>1</sub>/FVC ratio <.70 indicates COPD.<sup>1,2</sup>

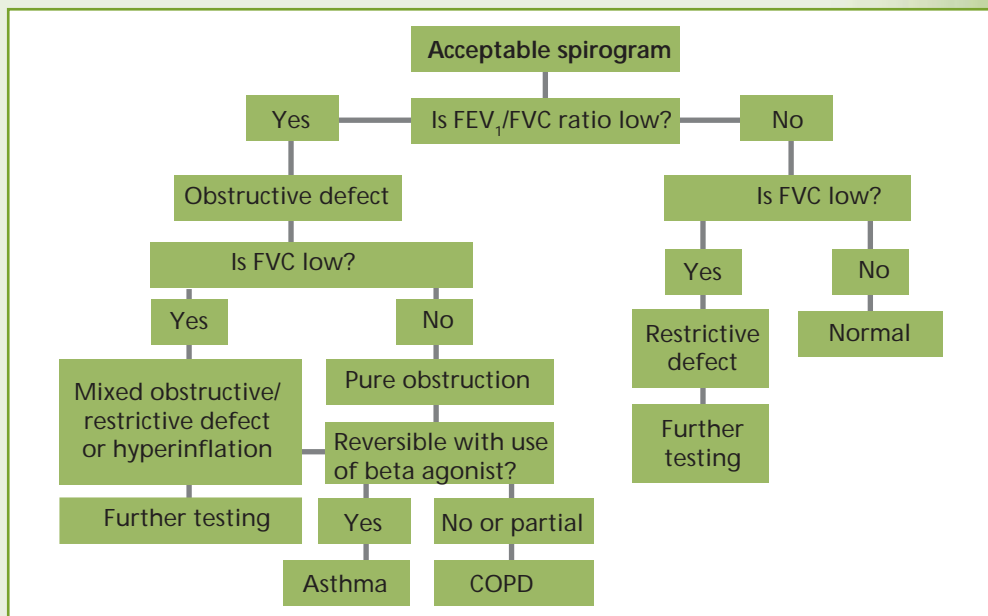
**Table 2. Diane's Spirometry Results**

	Prebronchodilator	Postbronchodilator
FEV <sub>1</sub>	2.02 52% of predicted	2.27 58% of predicted
FVC	3.85 70% of predicted	4.26 87% of predicted
FEV <sub>1</sub> /FVC ratio	52%	53%

**Clinical Decision Point**

What is Diane's diagnosis?

- Bronchitis
- Asthma
- COPD
- Reactive airway disease



**Figure 2.** Algorithm for interpretation of spirometry results. Petty TL.<sup>5</sup>

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Diane's FEV<sub>1</sub>/FVC ratio is low, so we proceed down the left side of the algorithm. Her postbronchodilator FVC is near normal at 87%, suggesting a purely obstructive defect. FVC and FEV<sub>1</sub> were partially reversible with a beta agonist, but are still substantially reduced from normal, and the ratio is <.70. Spirometry results, in conjunction with Diane's signs, symptoms, and history, suggest that COPD is the correct diagnosis.

**Decision: Diane's diagnosis is COPD.**

The frequency of COPD in women has been increasing in recent years, and it is important not to bias diagnostic decisions because of gender. A recent study found that primary care physicians who were presented with medical histories and physical examination data on a hypothetical COPD case were significantly more likely to diagnose COPD in male patients than in female patients, even though they were given identical data with which to make the diagnosis.<sup>6</sup>

In order to proceed with appropriate pharmacotherapy, Diane's clinician must rank the severity of her disease and consults the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines for step therapy in COPD (Figure 3).<sup>1</sup>

Note: GOLD guidelines are not necessarily interpreted strictly as far as FEV<sub>1</sub> threshold values for addition of ICS. Study results indicate that the addition of ICS to LABA may be beneficial in patients who have not yet reached an FEV<sub>1</sub> of <50% of predicted.<sup>7</sup>

**Clinical Decision Point**

Which types of pharmacotherapy do you consider for Diane?

- Short-acting bronchodilators as needed
- Long-acting bronchodilators daily
- Long-acting bronchodilators daily plus short-acting bronchodilators as needed
- Long-acting bronchodilators and ICS daily plus short-acting bronchodilators as needed

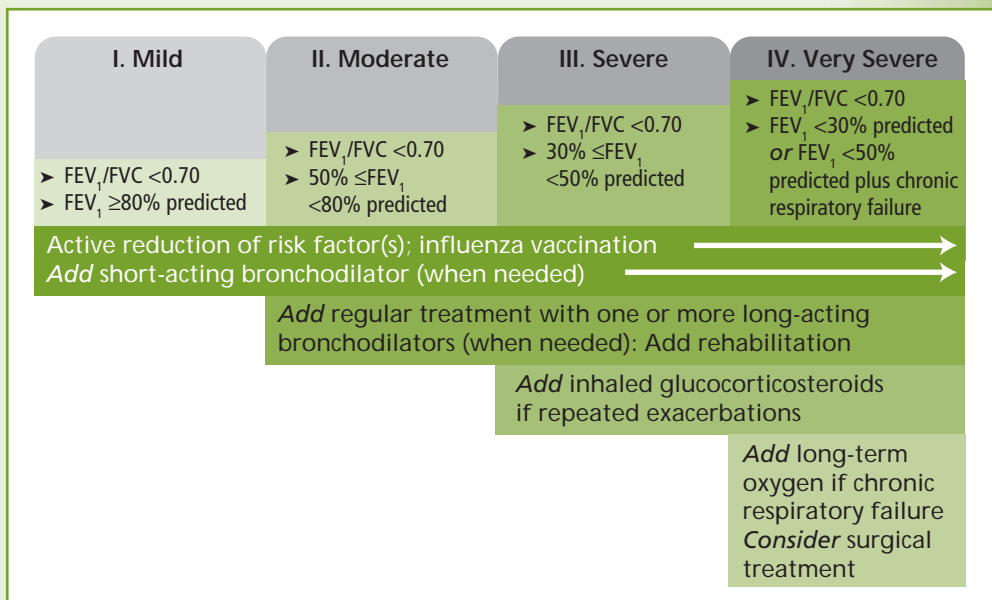
**Background**

Asthma and COPD are common respiratory disorders that result in significant morbidity and mortality. It is estimated that there are over 17 million adults diagnosed with asthma<sup>1</sup> and 10 million adults diagnosed with COPD in the United States.<sup>2</sup> The number of individuals with undiagnosed COPD is estimated to be even higher, according to studies that used spirometry to screen nearly 14,000 adults.<sup>2</sup>

The symptoms of asthma and COPD overlap, and distinguishing between the 2 conditions can be challenging. In order to make the correct diagnosis, the totality of signs, symptoms, risk factors, and patient characteristics must be considered. Correct diagnosis is crucial because optimal management of COPD and asthma require substantially different approaches.

**References**

1. Adult self-reported current asthma prevalence rate (percent) and prevalence (number) by state or territory, BRFSS 2004. Centers for Disease Control and Prevention. <http://www.cdc.gov/asthma/brfss/04/current/current.pdf>. Accessed September 15, 2008.
2. Mannino DM, Homa DM, Akinbami LJ, Ford ES, Redd SC. Chronic obstructive pulmonary disease surveillance—United States, 1971-2000. *MMWR Surveill Summ*. 2002;51(SS-6):1-16.



**Figure 3. GOLD guidelines for step therapy in COPD.** *Global Strategy for the Diagnosis, Management, and Prevention of COPD.*<sup>1</sup>

**Comment**

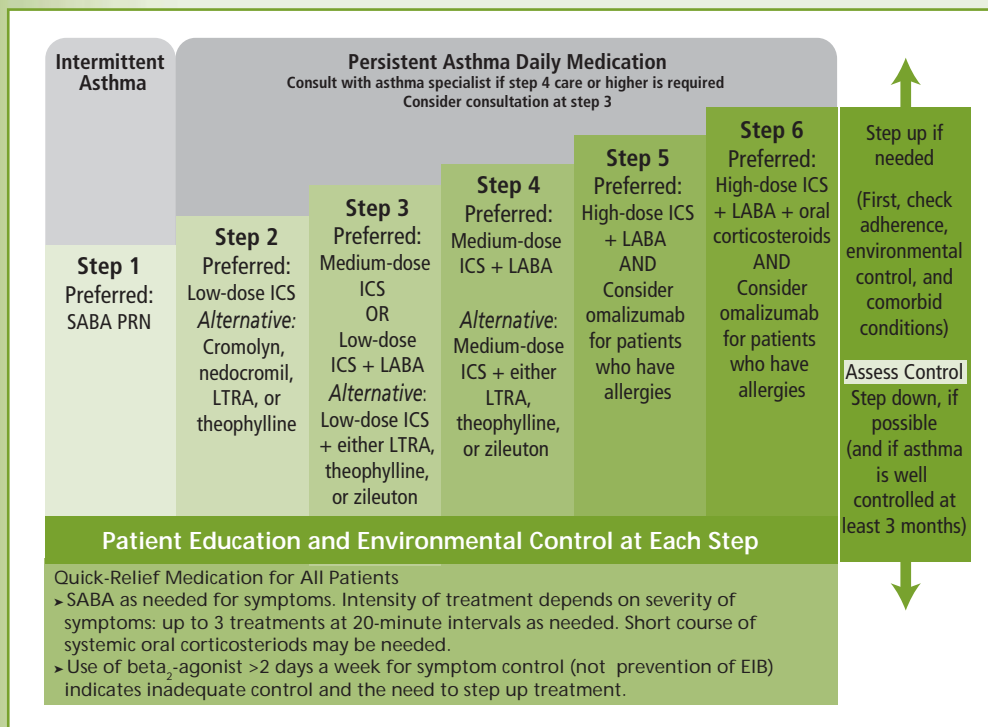
According to the GOLD guidelines, Diane has moderate COPD (FEV<sub>1</sub> is between 50% and 80% of predicted). At this severity of disease, it is appropriate to start Diane on daily inhaled long-acting bronchodilators, which are usually the most effective and convenient treatments.<sup>1</sup> There are 2 types to choose from: LABAs and anticholinergics. Either can be used first; and if the initial therapy does not improve symptoms enough, these therapies can be combined before moving up to the next step in therapy. Additionally, short-acting bronchodilators (short-acting beta<sub>2</sub> agonists [SABAs] or anticholinergics) can be used as needed for symptoms.<sup>1</sup> It is important to note that one of the many reasons that the correct diagnosis is imperative is that the order of therapies used in COPD and in asthma is different. For asthma, the first medication to be added to a short-acting bronchodilator is an ICS, not a LABA (Figure 4).<sup>8</sup>

**Decision: Prescribe daily LABA and a short-acting anticholinergic to be used as needed for symptoms.**

Pharmacotherapy is only one component of effective COPD management. COPD is associated with significant morbidity and mortality, and a multifaceted approach to management is required. It is the 4th-leading cause of death in the United States; and among the top 6 causes, it is the one that is most strongly associated with an increase in mortality over the past few decades.<sup>9</sup> Mortality in women has increased at an even steeper rate than it has in men (Figure 5, page 7).<sup>10</sup> The increase in COPD in women is likely related to an increase in their smoking rates and the potentially higher susceptibility of women to the effects of tobacco smoke in the lungs.<sup>1</sup> Optimal management of COPD should include non-pharmacologic interventions in order to slow the disease process and improve symptoms.

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**Figure 4. National Asthma Education and Prevention Program (NAEPP) guidelines for stepwise management of asthma in adolescents (≥12 years) and adults.** LTRA = leukotriene receptor agonist; EIB = exercise-induced bronchospasm. US Department of Health and Human Services.<sup>8</sup>

**Clinical Decision Point**

What nonpharmacologic approaches should be recommended as a part of Diane's COPD management plan?

- Preventative vaccines and smoking cessation
- Preventative vaccines, smoking cessation, and pulmonary rehabilitation
- Preventative vaccines, smoking cessation, and trigger identification and avoidance
- Preventative vaccines, smoking cessation, pulmonary rehabilitation, and trigger identification and avoidance

**Comment**

Smoking cessation is the single most useful intervention to slow COPD progression and prolong life.<sup>1</sup> All smokers should be offered an intensive smoking cessation intervention. The US Public Health Service recommends a 5-step intervention (Table 3).<sup>1</sup> Numerous pharmacotherapies (including nicotine replacement, bupropion, and varenicline) are now available for patients for whom counseling alone is insufficient.<sup>1</sup> Additionally, the Advisory Committee on Immunization Practices (ACIP) recommends that patients with COPD should receive a flu shot every year and a pneumococcal polysaccharide vaccine.<sup>11</sup> Triggers that worsen symptoms or cause exacerbations

(such as second-hand smoke, air pollution, perfumes, or other irritants) should be identified and avoided if possible. Since Diane is currently experiencing a COPD exacerbation, it may not be appropriate to begin pulmonary rehabilitation just yet, but it should be recommended and briefly discussed for future implementation.

**Decision: Recommend preventative vaccines, smoking cessation, pulmonary rehabilitation, and trigger identification and avoidance.**

Diane returns for follow-up after 4 weeks, to ensure that she understand her diagnosis, is taking the medications as prescribed, that the medications are improving her symptoms and that she is using proper inhaler technique. Diane reports that she is able to walk further, is not coughing at night, and her breathing feels easier. She has been taking her medications and comments that she is glad she has insurance because they are expensive. Upon demonstration, it is noted that Diane's inhaler technique continues to be very good. Diane is reminded that she will need to take these medications (and possibly some additional ones) for the rest of her life because COPD is a chronic condition.

This first follow-up visit also provides an opportunity to discuss pulmonary rehabilitation more thoroughly and refer Diane to a program. Patients with moderate or severe levels of COPD should be strongly encouraged to participate in pulmonary rehabilitation if it is available in the community. Pulmonary rehabilitation programs are important to help address needs that are not addressed by medical therapy, including social isolation, poor mood, exercise deconditioning, muscle wasting, and weight loss. These various negative features of COPD can interact and reinforce each other (Figure 6).<sup>1</sup> Rehabilitation programs vary as far as their particular components, but they generally include exercise training, nutritional counseling, and patient education. Exercise capacity, quality of life,

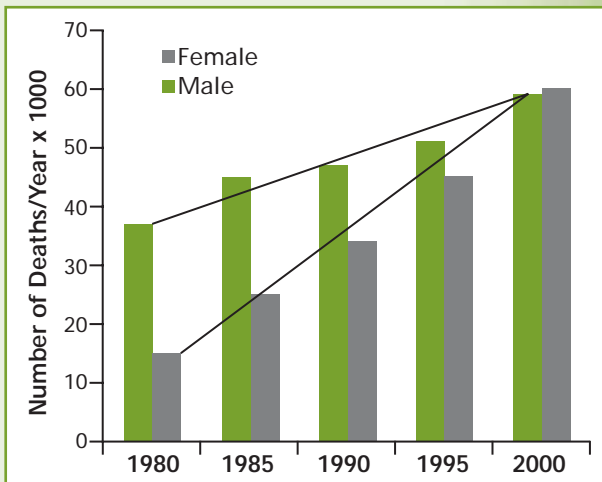


Figure 5. Deaths due to COPD by gender. Mannino DM et al.<sup>10</sup>

**Table 3. Strategies for Encouraging Smoking Cessation**

1. **Ask:** Systematically identify all smokers at every visit and document status.
2. **Advise:** Strongly urge smokers to quit, using a clear, personalized message.
3. **Assess:** Ask the smokers if they are willing to make a quit attempt.
4. **Assist:** Help the smokers quit by providing a quit plan, practical counseling, social support, and supplemental materials for each; recommend use of approved pharmacotherapy, if appropriate.
5. **Arrange:** Schedule follow-up contact.

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muscle strength (respiratory and other muscles), mood, and survival may be improved with pulmonary rehabilitation.<sup>1</sup>

Because Diane's symptoms have improved and she reports no side effects, her medications are not changed. She is referred for pulmonary rehabilitation after a full discussion of its potential benefits. At this and future follow-ups, Diane should be asked about any change in risk factors, including smoking status. Diane reports that she is still smoking socially (approximately a pack each week) and is not willing to try to quit completely.

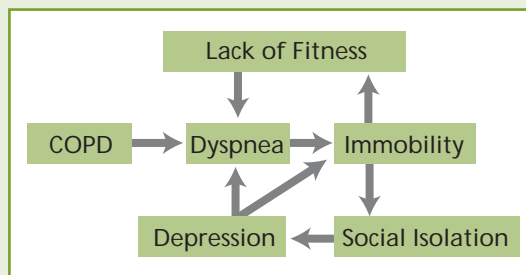
History of exacerbations and changes in comorbid conditions should also be followed up at each visit.<sup>1</sup> Comorbidities, such as cardiovascular disease, bronchial carcinoma, and depression, are common in COPD, in part, because they are indirectly related to the disease and, additionally, because COPD usually occurs in older individuals who tend to have more disorders independent of COPD. Currently, there are no specific guidelines for treating comorbidities in COPD patients. However, they may be more difficult to manage because COPD increases the level of disability and COPD treatments can negatively affect comorbidities. Guidelines for treatment of the particular comorbidity should be followed.<sup>1</sup> Diane's next visit is scheduled for 2 months later, and if she continues to do well, follow-ups will be scheduled for every 3 to 6 months.

Diane returns for routine follow-up and continues to do reasonably well over the next year and a half; however, at a follow-up appointment about 2 years after the initial diagnosis, she reports 3 mild exacerbations in the past 10 months that she self-treated using additional doses of her short-acting anticholinergic. Her current drug regimen includes a LABA and a long-acting anticholinergic daily plus a short-acting anticholinergic as needed. She has reduced her exercise level to her pretreatment baseline, some weeks even less, although she had been quite active for about a year following pulmonary rehabilitation. She blames the backslide on "lack of time". She also reports an increase in daily cough and phlegm production, although she claims to have reduced her smoking to 10 to 15 cigarettes per week. She does not appear to be experiencing acute respiratory distress at the time of her visit. Temperature is 98.5°F; BP, 130/82 mm Hg; HR, 78 bpm; and RR, 19/minute.

**Clinical Decision Point**

In addition to the procedures performed at routine follow-ups, what other procedure(s) should be performed at this visit?

- Arterial blood gases
- Pulse oximetry
- Spirometry
- Chest X-ray and ECG
- No additional tests are needed



**Figure 6.** Interrelation of physical, social, and psychosocial features of COPD. *Global Strategy for the Diagnosis, Management, and Prevention of COPD.*<sup>1</sup>

**Comment**

It is appropriate to obtain pulse oximetry or arterial blood gases for a patient experiencing a severe exacerbation. Chest X-ray and ECG may be necessary to differentiate an exacerbation from other (particularly cardiac-related) diagnoses that may mimic it. However, Diane is not currently experiencing an exacerbation, and only spirometry is indicated. Conversely, spirometry is not usually appropriate during an exacerbation because it is stressful and difficult for a sick patient to complete and therefore unlikely to be accurate.<sup>1</sup>

**Decision: Order spirometry testing.**

Spirometry testing reveals that Diane's current postbronchodilator FEV<sub>1</sub> is 54% of predicted, reduced from 58% at diagnosis and 56% at her 1-year follow-up.

**Clinical Decision Point**

What changes in therapy should be considered, if any?

- Add ICS, intensive smoking cessation counseling
- Add oral corticosteroids, intensive smoking cessation counseling
- Begin O<sub>2</sub> therapy, intensive smoking cessation counseling
- No changes are indicated

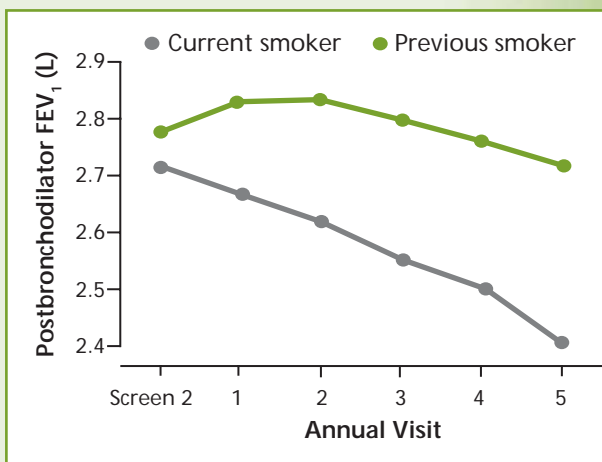
**Comment**

Her FEV<sub>1</sub> value indicates that the severity of her COPD is approaching stage III (severe). Although not stated specifically in GOLD guidelines, in patients who have repeated exacerbations, the addition of ICS may be recommended, even if the FEV<sub>1</sub> has not quite decreased to 50%.<sup>7</sup> Long-term therapy with oral corticosteroids is not recommended because of side effects and lack of proven benefit. Short-term use of oral corticosteroids can be beneficial for exacerbations, however. Oxygen therapy would be indicated if the patient were in chronic respiratory failure.<sup>1</sup>

**Decision: Add ICS to the regimen and initiate intensive smoking cessation counseling.**

ICS can be added as a separate agent, or a combination agent (ICS + LABA) can be prescribed as an alternative to taking ICS and LABA separately. A short-acting bronchodilator should also be available to Diane for use as needed.

The increase in severity of Diane's COPD warrants an even stronger approach to the routine recommendation of smoking cessation. Even though she is smoking very lightly according to her own admission, complete cessation is essential to improve prognosis and potentially reduce exacerbations. Patients typically



**Figure 7.** Decline in FEV<sub>1</sub> in smokers and previous smokers with COPD. Anthonisen NR et al.<sup>13</sup>

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go through several stages of change before they are ready to quit,<sup>12</sup> and Diane may be ready at this point, even though she wasn't earlier. A renewed effort to encourage Diane to stop smoking completely should be undertaken. Additionally, patient education should be continued and tailored to the advancing stage of her disease. Education on self-management skills—including techniques for minimizing breathing difficulty—and recommendations for management of exacerbations—including advice on when to seek medical care—are required.<sup>1</sup> Education pertaining to the effects of smoking on COPD symptoms may also encourage a quit attempt. Specifically, knowledge of the reduced decline in FEV<sub>1</sub> that is associated with smoking cessation may be especially motivating to a patient whose FEV<sub>1</sub> is nearing the threshold for severe COPD (Figure 7).<sup>13</sup> Finally, because Diane's COPD is continuing to advance, consultation with a pulmonologist would be prudent at this point.

Additionally, a recommendation for pulmonary rehabilitation may be appropriate again at this time because Diane is no longer exercising at all. Attacking all the aspects of COPD, both pharmacologically and nonpharmacologically, is at least as important in later stages of COPD as it is during earlier stages of the disease.

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