Patient Adherence in COPD: the Greatest Challenge

David M. Mannino
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DAVID M. MANNINO, MD

Patient adherence to recommended interventions in COPD is complex for a number of reasons. The key interventions in COPD are behavioral and pharmacologic: smoking cessation for patients who are still smoking, adherence to an exercise or pulmonary rehabilitation program, taking medication, and when indicated, using supplemental oxygen. Adherence to pulmonary rehabilitation programs is discussed in more detail elsewhere in this issue of Reviews & Trends in COPD. Nonadherence to recommended interventions may occur because patients may fail to understand or acknowledge the need for the intervention. Those who want to follow treatment protocols may encounter difficulties with the interventions, such as smoking relapses, or problems with medical therapies, such as actuation of inhaler devices or with the sheer number of medications they are prescribed. COPD patients may confuse maintenance and rescue medications and overuse short-acting bronchodilators. Oral dosage forms tend to be more convenient for patients but are not widely used in COPD. Long-term oxygen therapy presents particular adherence problems because of the stigma and inconvenience associated with oxygen equipment.

INTRODUCTION

COPD can be a difficult disease to treat. Available interventions can improve important outcomes such as lung function, quality of life, dyspnea, exacerbation risk, and even mortality risk. However, research studies and clinical trials are often conducted in controlled settings with selected populations and may not reflect the behaviors seen in clinical practice. To fully benefit from these interventions, the patient with COPD must maintain a complex course of management that requires much personal involvement and motivation. Steps for optimal management may include smoking cessation; a daily regimen of several inhaled and sometimes oral medications; pulmonary rehabilitation and/or exercise programs; long-term oxygen therapy (LTOT); preventive measures such as immunizations; and awareness and follow-up of exacerbation warning signs. With regard to adherence, there are many potential pitfalls for patients. Physicians often write prescriptions with little awareness of what does—or does not—happen next. This article will review adherence challenges specific to COPD with an emphasis on helping the patient achieve better self-management practices.

THE PROBLEM OF NONADHERENCE IN COPD

Adherence has been described as “the extent to which a person’s behavior coincides with medical or health advice.” The term “adherence” implies a team approach in which the patient accepts the recommended therapeutic strategy and actively participates in its delivery. This is in contrast to the passive or even obedient tone implied in the term “compliance.”

Adherence to a therapeutic approach is influenced by the nature of the disease, the disease-specific treatments, and the patient’s beliefs and expectations about the therapy. Adherence issues specific to COPD range from relatively simple problems such as difficulty using inhaler devices to more complex challenges relating to nicotine addiction, basic misconceptions about the disease, and why chronic treatment is necessary. The best data on nonadherence in COPD exist with regard to medication use, while less is known about adherence to smoking cessation, LTOT use, and exercise programs by COPD patients.

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Table 1: 5A’s of Smoking Cessation Counseling

1. Ask: Do you smoke?
2. Advise: Urge the patient to quit smoking
3. Assess: Are you ready to quit?
4. Assist: Help patient set goals for quitting
   Provide written materials about quitting
   Refer to a smoking cessation program
   Discuss smoking cessation medications
5. Arrange: Make a follow-up appointment to discuss smoking

Adapted from US Public Health Service. 2000.14

Adherence to smoking cessation involves conquering a very difficult physiologic and psychologic addiction. The Centers for Disease Control and Prevention reported that approximately 70% of smokers want to quit and approximately 40% make an attempt to quit each year, yet approximately 95% of those who attempt to quit on their own have relapsed within a year.5,11 Another source suggests that most of these smokers relapse within just 8 days of an attempt to quit.11 Long-term abstinence rates are also discouraging. Data from the largest smoking cessation trial to date, the Lung Health Study,13 showed an abstinence rate of just 22% after 11 years for those who participated in combined therapy of smoking cessation drugs and counseling techniques. This was an improvement over the 6% abstinence rate for those who did not receive the intervention, but still more improvement is needed in this area. Nationally, however, more than half of the people who have ever been smokers reported that they are currently not smoking, suggesting that there is hope for long-term success.19

Physician advice, individual and group counseling, telephone counseling, and self-help materials have high evidence of efficacy for smoking cessation, with an additive effect when multiple interventions are used simultaneously.14 Yet many physicians still neglect to encourage their patients to quit smoking or provide them with the information and tools needed to do so. Factors cited as limiting the physician’s involvement in smoking cessation efforts include time constraints, lack of expertise in smoking cessation methods, and lack of belief in the patient’s ability to quit.15

The most successful smoking cessation interventions involve a multicomponent approach that addresses the physical, psychologic, and behavioral aspects of tobacco dependence. Physicians can guide the discussion by using the “5A’s method” (Table 1) recommended by the US Public Health Service (PHS) or similar methods.16 Use of pharmacotherapy in smoking cessation has been shown to approximately double long-term cessation rates versus no pharmacotherapy.17 The PHS guideline recommends the use of pharmacotherapy for all smokers attempting to quit, unless contraindicated. Level A evidence supports the efficacy of pharmacologic interventions including nicotine replacements in the form of gum, patch, nasal spray, or inhaler and oral non-nicotine preparations such as bupropion.9

Varenicline, a recent addition to the oral pharmacotherapy repertoire for smoking cessation, has shown promising results in Phase III clinical trials.18,19 A pooled analysis of Phase III studies20 showed that this agent was significantly more effective than bupropion after 12 weeks of treatment (odds ratio [OR] 1.87) as well as after 52 weeks of follow-up (OR 1.56). The recommended duration of therapy is 12 weeks initially, followed by an additional 12 weeks for abstainers to prevent relapse. The most common adverse effects seen with varenicline use include nausea, headache, insomnia, and abnormal dreams. Caution is warranted with use of varenicline in patients with renal impairment.21

Varenicline has not yet been compared directly with nicotine replacement therapies.18 Using this agent in combination with nicotine replacement is not recommended because of the potential for increased side effects, although this has not been evaluated in any studies.21 Bupropion can be used in combination with a nicotine patch; this approach has been shown to increase quit rates compared with either treatment alone.22

Effective smoking cessation interventions combine both pharmacotherapy and counseling. To maximize adherence, behavioral interventions should teach problem-solving skills; help the smoker to set a quit date; identify key motivations for quitting; remove tobacco products from the environment; suggest coping strategies to replace smoking triggers; provide social support; and plan for withdrawal symptoms and/or relapse. Telephone “quitlines” are available in every US state and territory and are accessible via a central toll-free number (1-800-QUIT-NOW).9,10,16

Medication Nonadherence in COPD
Nonadherence to prescribed medications in COPD presents a significant barrier to effective management and has been shown to be a cause of exacerbations and hospitalizations.23-25 In general, adherence to medications and treatment protocols in COPD is
considered low.5,8,14 More data are available on adherence patterns in asthma, but when asthma and COPD are considered together it is estimated that 50% of prescription medications are not taken as prescribed.8

According to the industry report "Noncompliance With Medications"46 compiled in the 1990s, the 5 most common types of medication nonadherence are: (1) failing to have a prescription filled; (2) taking an incorrect dose (ie, either too high or too low); (3) taking the medication at the wrong time; (4) skipping doses; and (5) premature discontinuation of the medication. In primary nonadherence, in which the patient neglects to fill or collect a prescription, cost may be an important consideration, especially for patients taking a large number of prescription medications.26,27 Another reason for primary nonadherence—and one of the most difficult to resolve—relates to the patient's failure to understand or acquiesce to the fact that the medication is needed.

In secondary nonadherence, the medication is misused or prematurely discontinued. Clinical trials have demonstrated that side effects are an important reason for early discontinuation of therapy. Alternatively, some patients may believe they are feeling better and no longer require the medication, or that they have become "immune" to the effects of the medication.8 Specific to COPD, adherence may be influenced by the patient's belief that nothing can be done for the disease, guilt stemming from their smoking history, or, in the case of a continuing smoker, the feeling that smoking might "cancel out" any beneficial effects of the medication.28,29

A US-based study by Dolce and colleagues30 of 78 outpatients highlights the complexity of the typical medication regimen prescribed for COPD. With an average of 6.26 medications per patient, these authors noted that "it was quite common for patients in our sample to be prescribed a combination of 5 to 8 oral and inhaled time-contingent [as needed] medications, with many medications requiring different dosing patterns." When asked the reasons for missed medication doses in the past month, patients often cited forgetfulness and interruptions in their regular routine (Table 2).30

Another form of nonadherence that occurs in COPD and asthma relates to overuse of medications, primarily short-term bronchodilators as "rescue" medications.30-32 This may arise from confusion about the different roles of maintenance and rescue inhalers, or the patient's belief that he or she can use a long-acting bronchodilator "as needed" rather than daily as prescribed.

### Table 2: Top 10 Reasons for Missing Medications During the Past Month

<table>
<thead>
<tr>
<th>% of Patients Reporting</th>
<th>Reason</th>
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<tbody>
<tr>
<td>21.8</td>
<td>Felt good and decided not to dose</td>
</tr>
<tr>
<td>19.2</td>
<td>Felt good and forgot to dose</td>
</tr>
<tr>
<td>16.6</td>
<td>Absorbed in activities and forgot</td>
</tr>
<tr>
<td>15.4</td>
<td>Interrupted prior to dosing and forgot</td>
</tr>
<tr>
<td>14.1</td>
<td>Change in normal routine: planned</td>
</tr>
<tr>
<td>13.0</td>
<td>Side effects</td>
</tr>
<tr>
<td>12.8</td>
<td>Change in normal routine: unexpected</td>
</tr>
<tr>
<td>11.5</td>
<td>Ran out of medicine</td>
</tr>
<tr>
<td>8.9</td>
<td>Believed immune to medication</td>
</tr>
<tr>
<td>8.9</td>
<td>Believed medication was not effective</td>
</tr>
</tbody>
</table>

N=78 outpatients with COPD. Adapted with permission from Dolce JJ, et al. Chest. 1991.26

Overuse of short-acting bronchodilators has been a significant and well-documented problem in both asthma and COPD.1

Fear of systemic corticosteroid effects and confusion with oral glucocorticoids or other types of steroids may also cause patients to underuse maintenance medications.29,33 Fear about developing resistance to a drug or its efficacy wearing off over time is another problem. In a focus group conducted by Jones and colleagues,34 a COPD patient remarked that "sometimes if you're taking a medicine on a regular basis your system can become immune to it."

Most COPD adherence studies have failed to identify any demographic factors such as race, gender, or disease severity that predict adherence patterns.30,33 Rather, personal beliefs and psychologic factors play a major role. Adherence to a treatment protocol requires a trade-off between the patient's social and psychologic needs and the clinical management of the illness.33

In making the decision to use a medication or therapy, patients must weigh the perceived health benefits such as symptom control against the perceived costs, which may include side effects, inconvenience, or fear of long-term dependence on the therapy.33

A study by George and colleagues8 examined how health beliefs and experiences influence adherence patterns by administering questionnaires to 276 outpatients with respiratory disease (90.6% with COPD). Suboptimal adherence was identified in 63% of the sample. When patients were grouped as either more adherent or less adherent, demographic variables and disease characteristics did not predict these groupings. However, the authors
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Table 3: Questions to Consider When Selecting an Aerosol Delivery Device

1. In what device is the drug available?
2. What device is the patient likely to be able to use properly given age and clinical setting?
3. For which device and drug combination is reimbursement available?
4. Which devices are least expensive?
5. Can all types of prescribed inhaled drugs be delivered via the same type of device?
6. Which devices are most convenient for the patient, family, or medical staff to use?
7. Does the patient or physician have any specific device preferences?


We found overall differences between the groups in knowledge about illness, confidence and satisfaction with their treatment and their physicians, and concerns about treatment. The statements most strongly associated with nonadherence were, "I vary my recommended management based on how I am feeling" and "I get confused about my medications."85

Dosage-Form Preferences and Cultural Differences

It stands to reason that patient satisfaction with a device or delivery method is likely to be associated with improved adherence.44 A number of cultural differences are believed to influence patient preferences for certain dosage forms such as oral, injected, or suppository, although these have not been well documented. Some cultural mores proposed in the literature include a tendency among some Latin Americans to associate injected drugs with greater efficacy; for patients from some Asian cultures to halve prescribed medications, believing they are too potent; and a tendency among some patients in developing countries to use medications for only a few days, even those intended for chronic use.35-38 Cultural beliefs may contribute to early discontinuation of a therapy or thinking that a lack of symptoms implies that the disease is cured.85

Data suggest that many patients prefer oral medications to other dosage forms, especially when it comes to convenience. A study by Atkinson and colleagues39 measured patient satisfaction with medications used for chronic diseases and showed preferences according to route of medication, with oral delivery significantly preferred over inhaled delivery in terms of convenience (Figure).39

Another important consideration for adherence is the number of administrations per day. Studies in other disease categories such as asthma showed improved adherence when the number of required daily doses was minimized, with once-daily dosing preferred over twice- or thrice-daily.60-63 Less-frequent dosing can be an advantage for patients whose nonadherence pertains to forgetfulness and convenience issues, but will generally not benefit those who deliberately fail to fill a prescription or discontinue treatment early because they believe they no longer need the drug.8

Adherence to Inhaled Medications

The fact that many drugs for COPD are administered via inhalation further increases the risk of nonadherence. The variety of different inhaler designs, each with different instructions for use, heightens the level of complexity and potential confusion for patients and even physicians.34,44,45 Although newer inhalers are designed to lower the margin of error for users, any type of inhaler can be misused so that little or no drug is deposited in the lungs.44

Mean Satisfaction Scores With Treatments According to Patient-perceived Categories

<table>
<thead>
<tr>
<th>Route of Administration</th>
<th>Effectiveness</th>
<th>Side Effects</th>
<th>Convenience</th>
<th>Total Score</th>
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<tbody>
<tr>
<td>Oral</td>
<td>90</td>
<td>60</td>
<td>70</td>
<td>100</td>
</tr>
<tr>
<td>Topical</td>
<td>80</td>
<td>50</td>
<td>60</td>
<td>90</td>
</tr>
<tr>
<td>Injection</td>
<td>70</td>
<td>40</td>
<td>50</td>
<td>80</td>
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<tr>
<td>Inhaler</td>
<td>60</td>
<td>30</td>
<td>40</td>
<td>70</td>
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</table>

Figure. Patient Preference for Drug Administration Methods

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In 2005, the American College of Chest Physicians and the American College of Asthma, Allergy, and Immunology published joint evidence-based guidelines to aid physicians in the selection of aerosol delivery devices for asthma and COPD. The guideline lists key questions to consider when selecting an inhaled therapy (Table 3) and outlines the advantages and disadvantages of the main inhaler delivery systems (Table 4). Examination of the evidence showed no significant advantages of one inhaler type over another, provided that the particular device was used correctly.

The guideline also highlighted the importance of patient preferences in inhaler selection. Several factors unrelated to the efficacy of the drug itself—such as ease of use, taste of the drug, and portability of the inhaler equipment—are important indicators of patient satisfaction and willingness to use the product. Direct-to-consumer marketing, physician communication or sampling, and the patient’s expectations and prior experiences with an inhaler may also influence patient preference.

Measuring adherence to inhaled therapies presents a number of interesting challenges. Some studies may be biased by excluding patients with unstable disease, cognitive impairment, or those unable to use inhaler devices correctly. Furthermore, real-world patients may not receive the same quality of instruction for inhaler use as that provided in clinical trials. Thus trial results may not reflect adherence or effectiveness of drug delivery in clinical settings.

The Lung Health Study measured a variety of efficacy and adherence outcomes related to both smoking cessation programs and thrice-daily use of an inhaled bronchodilator (ipratropium) in COPD patients aged 35 to 60 years. Patients received an initial 12-week period of counseling and returned for follow-up every 4 months thereafter. Simmons and colleagues used a Nebulizer Chronolog (NC) to electronically record the date and time of each use of inhaled medication during a 5-year follow-up to examine adherence patterns among 231 patients, 129 of whom were aware of the NC’s monitoring function, and 102 of whom were not told about this function. After the first 24 months, these investigators found that mean inhaler use never reached 3 times per day, but was highest for both groups in the first 4 months of the trial and decreased gradually after that. For

<table>
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<th>TABLE 4: ADVANTAGES/DISADVANTAGES OF AEROSOL DRUG DELIVERY SYSTEMS</th>
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<tr>
<td><strong>Summary from American College of Chest Physicians/American College of Asthma, Allergy, and Immunology evidence-based guidelines</strong></td>
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<tr>
<td><strong>Advantages</strong></td>
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<tr>
<td>Pressurized MDI</td>
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<tr>
<td>Holding chamber, reverse-flow spacer, or spacer</td>
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<tr>
<td>Dry powder inhaler</td>
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*Excludes nebulizers.
CFC=chlorofluorocarbon; MDI=metered dose inhaler.

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both groups, adherence to the drug improved immediately after scheduled follow-up visits and then dropped off. Throughout the trial, patients who were aware that their medication use was being monitored demonstrated higher levels of adherence.46

Nebulizers are another delivery option for inhaled COPD drugs but these are best suited for less-mobile patients. Because of a higher complexity of use and longer treatment times, nebulizers are considered by some as mainly full-back devices for most COPD patients.44

ADHERENCE TO LONG-TERM OXYGEN THERAPY IN COPD

Using inhaled and/or oral drugs correctly a few times daily might seem easy compared with the challenges of using LTOT. Data have shown that 18 or more hours of oxygen administration per day may significantly improve survival and exercise tolerance and reduce hospitalizations in patients with COPD.49 However, these benefits clearly come at a high price for the patient. Oxygen equipment can be heavy, cumbersome, and complicated to maintain; the nasal cannula and tubing are uncomfortable, obtrusive, and humiliating to many.46-50

In interviews with 528 oxygen users from the Netherlands,51 20% admitted to using oxygen less than prescribed because of treatment difficulties, perceived lack of symptoms, or fear of oxygen “addiction.” In this study, patient complaints relating to LTOT included restricted autonomy (50%); difficulties with the delivery device (41%); difficulties with the oxygen source (38%); feeling ashamed about needing oxygen (38%); and the treatment duration (8%). Only 33% of patients reported receiving assistance from the oxygen supplier before initiating therapy.51

Formal training in the use of oxygen equipment has been shown to improve adherence. In a study by Peckham and colleagues52 involving patients who participated in an oxygen-use training program, a survey at 6 months showed that 82% reported using their oxygen concentrator more than 15 hours per day compared with 44% of those who did not receive training. Additionally, 93% of the “intervention group” stated that they understood the purpose and hazards of oxygen, versus 41% of the control group.

In a study involving telephone interviews with LTOT users from the National Jewish Medical and Research Center in Denver, Earnest53 identified 3 distinct patterns of adherence to LTOT. "As-needed" users relied on their oxygen equipment as rescue therapy, using it only when they needed a “quick fix” for dyspnea or improved exercise tolerance. “Part-time” users chose to use oxygen at home but omitted it for specific activities outside the home such as attending church, dining out, or shopping. Most part-time users kept a backup source of oxygen handy in their cars. Among “full-time” users, their disease had progressed to the point where they were essentially never without oxygen. For many participants in this study, the pattern of adherence changed with time. Oxygen use increased as the disease progressed and as patients reached a compromise between increased symptoms and the stigma of using oxygen equipment in public. In choosing their level of adherence, patients need to undergo a process of negotiation and compromise, Earnest suggested.53

Barriers to regular LTOT use include embarrassment; self-consciousness; fear of burdening or inconveniencing others; concerns about appearing weak or sick; and a sense of shame about prior smoking and about accepting dependence on oxygen therapy.48,55,53 Other barriers include misconceptions about the therapy that tend to mirror those of inhaled or oral medications, such as patients' fear that they will become addicted or dependent on supplemental oxygen.

Many of these barriers, such as misconceptions and fear of addiction, may be remedied if patients are given more opportunity to discuss these concerns. For example, many patients who believe that they are "all alone" with their fears and concerns can be greatly helped through peer support groups, rehabilitation programs, or

**Table 5: Strategies to Help Increase Adherence to Oxygen Therapy**

- Ensure that patients know how to operate oxygen equipment
  - Have patient demonstrate the process for a staff member
- Review indications for oxygen in writing
  - Have patient write down symptoms, record oxygen use
- Reduce barriers to oxygen use (e.g., misconceptions about dependence or addiction)
  - Ask patient about concerns or fears regarding oxygen
  - Refer to support group if appropriate
- Follow-up oxygen use adherence and problems/concerns
  - Provide positive feedback

Data adapted from Cullen DL, Chronic Respir Dis. 2006.48
counseling. While some patients reported they had a single conversation with the physicians about oxygen therapy at the time of initiation, Callen® recommended ongoing communication and follow-up among the strategies for increasing adherence (Table 5).

CONCLUSION

All of the currently available data on COPD interventions—as well as new research in the pipeline on improved therapies for the disease—is useless if physicians do not know how or whether patients actually use these therapies in the real world. COPD is a chronic inflammatory condition with incidence, morbidity, and mortality rates on the rise, and there is no quick fix or cure when it comes to managing this disease. It is likely that most treatments introduced will be designed for long-term or possibly lifetime use, as the underlying inflammatory process is insidious and ongoing. This article reviewed several issues and challenges pertaining to adherence with COPD therapies. Resolving some of them may require increased responsibility by patients for their own health and self-management. Factors such as older age, multimorbidity, depression, cognitive impairment, cultural beliefs, and social stigmas may hamper this process. Physicians are faced with their own limitations, including lack of time to counsel patients, financial constraints, and organizational difficulties. Still, research has shown that effective partnerships between physicians and patients can increase adherence to therapy and improve outcomes.

REFERENCES


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