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# Adherence to Therapy in Chronic Obstructive Pulmonary Disease

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## 1. Introduction

Chronic obstructive pulmonary disease (COPD) is a major public health problem for both industrialised and developing countries (Viegi et al., 2001). The prevalence of COPD is increasing worldwide, resulting in a substantial economic burden, including direct and indirect health-care costs (Chapman et al., 2006).

Non-adherence in COPD is common and poses a significant barrier to optimal disease management. According to the World Health Organization (WHO), adherence to long-term therapies averages only 50% (WHO, 2003). Patient adherence in chronic diseases can result in poor health outcomes and increased health-care expenditures (WHO, 2003). Discontinuation of COPD therapy contributes to increasing the frequency of exacerbations, the number of hospitalisations and the mortality rate (Bourbeau & Bartlett, 2008; Regueiro et al., 1998; Vestbo et al., 2011).

Clinical trials may overestimate the level of adherence to medication regimens. Adherence rates in clinical trials have been expected to be approximately 70%–90% among patients with COPD (Kesten et al., 2000; van Grunsven et al., 2000; Rand et al., 1995). In clinical practice, these rates are only in the range of 20%–60% (Agh et al., 2011; Bosley et al., 1994; Dolce et al., 1991; Krigsman et al., 2007a). This difference reflects the fact that patient adherence may be an important explanatory factor of the difference between the efficacy of treatment under experimental conditions and the real-world effectiveness of the treatment (Revicki & Frank, 1999).

Non-adherence in patients with COPD has a number of causes, including factors related to the characteristics of the patient, the disease, the therapies and the health-care provider-patient relationship (Baiairdini et al., 2009; Restrepo et al., 2008; WHO, 2003). Physicians should understand the factors and the strategies that facilitate adherence to improve the effectiveness of the therapy.

The goals of this chapter are as follows: to highlight the importance of adherence in the management of COPD; to introduce the reader to the concepts of adherence, compliance and persistence; to address different methods of measuring adherence; to identify factors related to adherence; and to emphasise strategies to enhance adherence in patients with COPD.

## 2. General overview of adherence

There are a number of terms used to describe the extent to which a patient undertakes the recommendations (medication regimens, lifestyle changes, etc.) of health-care providers. The most commonly used terms are compliance, adherence and persistence.

### 2.1 Terminology: Compliance, adherence and persistence

The definitions used to describe the concepts of compliance, adherence and persistence are not standardised, which causes many difficulties when comparing or combining results of different studies. The definitions from the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) and the WHO are the most widely accepted in the literature.

Medication compliance, as defined by the ISPOR, “refers to the act of conforming to the recommendations made by the provider with respect of timing, dosage and frequency of medication taking” (Carmer et al., 2008). Compliance is expressed as an index number, which is typically given as a percentage and refers to a specified time interval. One of the most commonly used models for calculating medication compliance is the medication possession ratio (MPR). In the model of the MPR, the number of days of medication supplied within the refill interval is divided by the number of days in the refill interval (Peterson et al., 2007). Medication compliance may also be reported as a dichotomous variable, classifying patients into good and poor (or non-) compliance categories (Table 1). The cut-off point of compliance should be determined according to medication and type of disease. However, it is generally set independently at 80%, whether this compliance rate is adequate for disease control or not (Carmer et al., 2008).

Drugs	Months (1 month = 30 days)									Supply (days)	MPR			
	x	x	x	x	x	x								
A	x	x	x	x	x	x				x	x	x	9x30=270	270/360=0.75
B		x	x	x	x		x	x	x	x			8x30=240	240/360=0.66
C			x		x		x	x		x	x	x	7x30=210	210/360=0.58

$\Sigma$  MPR:  $((270+240+210)/3)/360 = 0.66 \rightarrow 66\%^*$

\*:Patient is non-compliant (cut-off point: 80%).

|x| : medication supplied, | | : medication not supplied

Table 1. Calculation of medication compliance: medication possession ratio (MPR)

According to the definition of ISPOR, medication persistence may be described as “the duration of time from initiation to discontinuation of therapy” (Carmer et al., 2008). Persistence analyses must also define a permissible gap period, which specifies the maximum allowable time period between refills without discontinuation of the therapy. Persistence may be counted in days. However, it can also be given as the percentage of the number of persistent patients at the end of a predefined time period (Patricia et al., 2006) (Table 2). A patient’s drug taking behaviour can best be quantified using both parameters: medication compliance and persistence (Carmer et al., 2008).

Although most research in the field has focused on medication compliance and persistence, therapeutic adherence certainly includes other non-drug therapeutic recommendations

Patients	Months (1 month = 30 days)												Days persistent (gap: 30 days)*	Persisted 180 days**	
	[x] : medication supplied,   : medication not supplied														
A	x	x	x	x				x	x	x				120	no
B	x	x	x	x	x	x						x	x	180	yes
C	x	x					x	x				x	x	60	no

\*: Patients persisted an average of 120 days  $((120+180+60)/3)$

\*\* : 33% (1/3) of the patients were persistent for 180 days

[x] : medication supplied, | : medication not supplied

Table 2. Calculation of medication persistence

(following diets, executing lifestyle changes, etc.) as well. Explanation of adherence by the WHO also reflects this concept. The WHO definition of adherence is the following: “the extent to which a person’s behaviour—taking medication, following a diet, and/or executing lifestyle changes—corresponds with agreed recommendations from a health-care provider” (WHO, 2003). This definition accurately highlights the importance of the patient’s active role in their own health-care, which emphasises that the relationship between the patient and the health-care provider should be based on a partnership, instead of a one-sided paternal relationship.

Recently, medication adherence has become the preferred term instead of medication compliance. The primary difference between compliance and adherence is that compliance reflects the patient as a passive recipient of medical advice. Furthermore, compliance has also been viewed as a judgmental term when applied to patient behaviour. Thus, medication adherence will be the preferred term from this point forward.

## 2.2 Methods of measuring adherence

Most studies in adherence research have focused on medication-taking behaviour. Therefore, the following is a brief overview of the methodology of the assessment of medication adherence in COPD. There are a number of ways to assess adherence; nevertheless, there is not a gold standard because each method has strengths and limitations (Table 3).

The easiest way to assess medication adherence within clinical settings is to collect information from the patient themselves through questionnaires or patient diaries (Agh et al., 2011; Dolce et al., 1991; George et al., 2005, 2006a; Laforest et al., 2010). However, it should be mentioned that self-reporting methods may overestimate a patient’s drug-taking behaviour (Dompleing et al., 1992; Rand et al., 1992, 1995). Using postal administration can help to obtain data that are more objective because patients are normally intimidated by their health-care providers and tend to give them the expected answers (Agh et al., 2011). Another commonly used method is the analysis of electronic pharmacy records (Breekveldt-Postma et al., 2007; Cramre et al., 2007; Jung et al., 2009). Retrospective database analysis is rapid and inexpensive. Nevertheless, this approach may also be inaccurate. It evaluates the prescriptions written by physicians or the prescriptions filled by patients, but not the medication intake directly.

	Advantage	Disadvantage
<b>Indirect methods</b>		
<i>Patient self-report: adherence questionnaire, patient diary</i>	Easy to obtain	Unreliable
<i>Pharmacy refill data</i>	Rapid Inexpensive	Inaccurate: <ul style="list-style-type: none"> <li>• Pharmacy database can be incomplete</li> <li>• No indication of ingestion</li> </ul>
<i>Pill count, inhaler weighing</i>	Easy to obtain Inexpensive	Inaccurate: <ul style="list-style-type: none"> <li>• No indication of ingestion</li> <li>• "Dumping"*</li> </ul>
<i>Electronic adherence monitoring</i>	Accurate measure of dosing history	Expensive No indication of ingestion
<i>Therapeutic outcome</i>	Easy to obtain	Clinical outcomes can depend on other factors
<b>Direct methods</b>		
<i>Direct observation of the medication intake</i>	Accurate indication of the ingestion	Unpleasant for the patient Require large human resources
<i>Biological assay</i>	Confirm drug use	Expensive Unpleasant for the patient Limited information regarding use over time Insensitive to inhaled drugs

\*"Dumping": removing most of the medication at one time.

Table 3. Methods of measuring adherence

Pill count (Dompleing et al., 1992; van Grunsven et al., 2000) and canister weighing (Rand et al., 1995; Simmons et al., 2000) are widely used methods of adherence assessment in clinical trials. Pill counts are limited to oral medications, but canister weighing can also be used to monitor inhaled drugs. These approaches assess only the quantity of the medication removed from the canister without indication of ingestion, dose or dose frequency. Electronic compliance monitoring devices can provide more objective information about medication use than the aforementioned methods (Corden et al., 1997; Simmons et al., 1996, 2000). The cap of the pill bottles can be equipped with a microchip that stores data about each opening. Electronic recording devices (chronologs) can be fitted to metered-dose inhalers and nebulisers as well. Electronic monitors provide an accurate measure of dosing history but also cannot confirm ingestion. The major disadvantage of this method is the price; it is relatively costly.

Medication compliance can also be estimated based on direct assessments, such as direct observation of the medication intake or evaluation of blood levels or urinary excretion of the drug or its metabolite or drug-marker (Clark et al., 1996; Hatton et al., 1996). These methods are unpleasant for the patient and expensive. Interestingly, therapeutic drug monitoring may overestimate the actual adherence rate because patients tend to comply shortly before the drug test but not during the whole observation period. Another limitation is that a biochemical drug test is insensitive to inhaled medication.

The assessment of therapeutic adherence seems to be more complicated. However, clinical outcomes can be used to evaluate adherence, as these depend largely on the extent to which a patient undertakes the recommendations of health-care providers.

### 3. Adherence with COPD therapy

#### 3.1 Adherence to medication

Medication non-adherence can take many forms: failure to fill prescriptions (primary non-adherence) or overuse, underuse or alteration of schedule or doses of medication (secondary non-adherence) (Bourbeau et al., 2007; George et al., 2007; Rand et al., 2005).

Only a limited number of studies have evaluated adherence in patients with COPD. Jung et al. (Jung et al., 2009) examined medication adherence and persistence among a sample of COPD patients during their last year of life. The study reviewed the use of inhaled corticosteroids (ICS), long-acting  $\beta_2$  agonists (LABA), anticholinergics (AC) and methylxanthines (MTX), alone and in combination. The overall MPR to COPD medication was 44%. Approximately 30% of the patients persisted with the therapy, and the overall time to discontinuation was 94.2 days. These rates of cooperation are much lower than the drug-taking rates in other chronic diseases. Adherence in hypertension, dyslipidaemia and diabetes is, on average, 72% (MPR), and persistence is 63% (Cramer et al., 2008). In the previously mentioned study, Jung et al. (Jung et al., 2009) found differences between the mean MPRs of COPD drug classes (MTX: 52%, AC: 38%, ICS: 35%, LABA: 34%). Medication adherence was the highest with MTX. One possible explanation of this finding could be that elderly patients may have more difficulty using inhaled medications; therefore, they prefer oral drugs.

Breekveldt-Postma et al. (Breekveldt-Postma et al., 2007) evaluated medication persistence among COPD patients in the first therapy year; new users of tiotropium, ipratropium, LABA and a fixed combination of LABA and ICS (LABA + ICS) were included in their study. The persistence was the highest, 37%, with tiotropium. The COPD patient's drug-taking behaviour was found to be significantly lower with other inhaled medications (ipratropium: 14%, LABA: 13%, LABA + ICS: 17%). Subgroup analysis of persistence data in patients with prior hospitalisation for COPD indicated that hospitalisation may have an enhancing effect on patient cooperation. The one-year persistence rates were increased by 2–3 times in the first year after hospitalisation (tiotropium: 61%, ipratropium: 37%, LABA: 41%, LABA + ICS: 33%). A similar study by Cramer et al. (Cramer et al., 2007) examined trends in patient persistence with inhaled COPD medication. They monitored the refill data of ipratropium, ipratropium + salbutamol, formoterol, formoterol + budesonide, salmeterol, salmeterol + fluticason and tiotropium in a cohort of 31,368 COPD patients. The one-year persistence was considerably higher with tiotropium (53%) compared with other treatments (7%–30%). The significant differences in levels of adherence and persistence between inhaled medications could be partially the result of dosing frequency.

All of the aforementioned studies examined primary adherence, which is based on prescription refill rates. These results represent the maximum possible level of patient cooperation because refill adherence cannot confirm ingestion and does not provide any information on the frequency of medication use. Studies evaluating secondary adherence can provide data about medication use that is more reliable.

The Lung Health Study (Rand et al., 1995) was a double-blind, multicentre, randomised, controlled trial on smoking intervention and bronchodilator therapy (ipratropium or placebo) as early interventions of COPD. Satisfactory adherence was reported by 70% of the participants at the first 4-month follow-up visit, but this rate declined to 60% over the next 18 months. The overall adherence estimated by canister weighing was 72% in the first year and 70% in the second year. Nevertheless, in the first year, only 48% of the participants were classified as adherent with both methods. In an ancillary study within the Lung Health Study, medication adherence rates measured by both self-report and canister weighing were compared with data from electronic medication monitoring (Rand et al., 1992). This study found that self-reporting and canister weighing significantly overestimate adherence: only 15% of the participants used their inhaler 2.5 or more times per day (when three puffs per day were prescribed). In addition, 14% of the patients seemed to be “dumping” medication prior to the clinic visit by removing most of the medication at one time (i.e., actuating inhaler more than 100 times in a 3-h interval) to hide non-adherence. The level of adherence with the prescribed medication regimen was best immediately following each follow-up visit and declined during the interval between follow-up visits. The adherence after each visit was lower for each successive follow-up. These trends could be observed only with electronic medication monitors; self-reporting or weighing could not detect these changes (Simmons et al., 1996).

Studies also suggest that while the underuse of medication seems to be one of the largest problems in the management of COPD, overuse is also common. Symptom-relieving drugs, such as short-acting  $\beta_2$  agonists (SABA), are more often overused than maintenance therapies (Dekker et al., 1993). Krigsman et al. (Krigsman et al., 2007a) evaluated the primary adherence in patients with asthma and COPD. The obtained results indicated that 53% of the patients underused and 18% overused their prescribed medication regimens. In another study by Krigsman et al. (Krigsman et al., 2007b), it was found that 59% of COPD patients had an undersupply and 12% had an oversupply of ICS medication.

Eighty-four percent of COPD patients have one or more co-morbidity (Yeo et al., 2006). For this reason, a question arises about whether the level of a patient's adherence is the same with therapies for different chronic diseases. Krigsman et al. (Krigsman et al., 2007c) investigated refill adherence in patients who suffered from diabetes and COPD. Participants showed higher adherence for their diabetes drugs (68%) than their COPD medications (42%).

Long-term oxygen therapy (LTOT) plays an important role in the management of COPD (Würtemberger & Hütter, 2000). The daily duration of oxygen administration is crucial in the effectiveness of LTOT. Pepin et al. (Pepin et al., 1996) found that only 45% of the COPD patients who were prescribed oxygen therapy for an average of 16 hours per day ( $16 \pm 3$  h/d) used oxygen for 15 hours or more per day. Another study reported that 23% of the patients who had been prescribed LTOT refused to use liquid oxygen away from home and that 12% underused their oxygen (Würtemberger & Hütter, 2000).

Immunisation with both the influenza and pneumococcal vaccines may produce a number of acute exacerbations, hospitalisation and COPD mortality (Nichol et al., 1999; Varkey et al., 2009). However, the vaccination rates in patients with chronic lung diseases are low (Nichol et al., 1999; Tuppin et al., 2011), and the willingness to vaccinate differs by age group. The influenza vaccination status is significantly higher in patients aged 65 years or older (86.2%) than in the younger population (65.7%) (Mehuys et al., 2010).

### 3.2 Adherence to non-drug therapy

Adherence to non-drug therapies, such as respiratory rehabilitation, exercise programs, healthy lifestyle or smoking cessation, is crucial in the management of COPD. Approximately 60% of the patients refuse to take part in rehabilitation programs, and out of those who join, 30% fail to complete the program (Nici et al., 2006). The most important barriers to rehabilitation adherence include exacerbations and progression of COPD (Bourbeau et al., 2007; Brooks et al., 2002). The literature in this field is quite weak; there is a clear need for further research to find out more about the suboptimal adherence to non-drug therapies in patients with COPD.

### 4. Factors associated with adherence in patients with COPD

Non-adherence in patients with COPD is a multidimensional phenomenon. The factors include the characteristics of the patient, the disease, the therapies and the health-care provider-patient relationship; many of these are potentially modifiable (Baiardini et al., 2009; Restrepo et al., 2008; WHO, 2003) (Table 4).

COPD	Treatment
<ul style="list-style-type: none"> <li>• Progressive nature of the disease ↓*</li> <li>• Poor prognosis ↓</li> <li>• Lack of clinical symptoms ↓</li> <li>• Disease severity —</li> <li>• Lung function —</li> </ul>	<ul style="list-style-type: none"> <li>• Polypharmacy ↓</li> <li>• Higher dosing frequency ↓</li> <li>• Higher medication cost ↓</li> <li>• Side effects ↓</li> <li>• Oral administration ↑</li> </ul>
Patient	Health-care provider-patient relationship
<ul style="list-style-type: none"> <li>• Gender -</li> <li>• Demographic factors: old age ↑</li> <li>• Improved quality of life ↓</li> <li>• Social support ↑</li> <li>• Psychiatric co-morbidities ↓</li> </ul>	<ul style="list-style-type: none"> <li>• Higher quality of communication ↑</li> <li>• Type of caregiver: specialist ↑</li> <li>• Closer follow-up ↑</li> <li>• Hospitalisation ↑</li> </ul>

\*Influence on adherence: decrease (↓), improve (↑), no effect (—)

Table 4. Factors associated with adherence in patients with COPD

#### 4.1 Factors related to the characteristics of COPD

COPD is a progressive chronic disease. Adequate cooperation with COPD therapy can improve the patient's quality of life and reduce the frequency of exacerbations but cannot fully control the disease symptoms. A progressive decline in lung function is often interpreted by patients as the medication not helping, so they stop following the recommendations (Chambers et al., 1999). In contrast, a lack of clinical symptoms could also be a reason for suboptimal adherence (DiMatteo, 2004). As implied above, the negative impact of COPD severity or lung function on a patient's adherence is not obvious. Prior studies have shown that disease severity or the post-bronchodilator forced expiratory volume in one second (FEV<sub>1</sub>) percentage may be either not (Agh et al., 2011) or negatively (Turner et al., 1995) related to adherence. The pathologic characteristics of COPD influence



adherence to non-drug therapy as well; a poor COPD prognosis has been identified as one of the most demotivating factors to quit smoking (George et al., 2006b).

#### **4.2 Factors related to the characteristics of the patient**

Most prior studies have found that gender does not influence the level of patient cooperation (Agh et al., 2011; Apter et al., 1998; Corden et al., 1997; Turner et al., 1995). Adherence differences between men and women reported in the literature may be caused by psychological factors (Laforest et al., 2010). The prevalence of anxiety and depression are higher in women with COPD, and these psychiatric comorbidities have been independently linked with non-adherence (Bosley et al., 1995; DiMatteo et al., 2000).

In general, drug-taking behaviour is related to age; older patients seem to be more adherent. Patients of advanced age are more likely to adhere to therapy that requires adjustments in daily life (Agh et al., 2011). However, memory loss and cognitive impairment, which are associated with both age and COPD duration, may adversely affect adherence (Incalzi et al., 1997).

Social support can also influence patient adherence. Stable family life has been found to improve adherence to medication regimens (Tashkin, 1995; Turner et al., 1995). Furthermore, the study by George et al. (George et al., 2006b) indicates that patients with a good relationship with family and friends may live longer and may quit smoking with a higher success rate.

Better quality of life has been considered a trigger for non-adherence (Agh et al., 2011). Decision-making regarding patient adherence is a personal trade-off between the efficacy of the therapy and the negative effects that it generates. Adherence to COPD therapy can reduce the clinical symptoms and improve the patient's quality of life. However, COPD treatment regimens require adjustments in daily life, such as smoking cessation and exercise programs, and can cause side effects as well. Therefore, the interruption of drug therapy can temporarily also increase the patient's quality of life. Therapy in newly diagnosed COPD patients may significantly improve quality of life; however, the change in quality of life may be much smaller in patients treated previously for longer durations (Soumerai et al., 1991). From the patient's perspective, the benefits from the increase in the quality of life during the complication-free period can outweigh the effects of the worsening disease symptoms (Agh et al., 2011).

#### **4.3 Factors related to the characteristics of the therapy**

The number of medications and the dosing frequency have been linked with adherence. According to our evaluations, the dosing frequency of respiratory drugs is one of the most important factors affecting non-adherence in patients with COPD (Agh et al., 2011; WHO, 2003). As a partial result of the daily drug doses, a significant difference has been shown in the adherence rates between the different respiratory drug classes (Apter et al., 1998; Breekveldt-Postma et al., 2007; Laforest et al., 2010). Tiotropium, a once-daily inhaled drug, may enhance adherence compared with other inhaled respiratory medications that are dosed more times daily. We also found that polypharmacy is another common cause of poor adherence (Agh et al., 2011); complicated treatment regimens may frustrate the patients, which may lead to non-adherence (van der Palen et al., 1999).

Patient cooperation is better with oral medication than with inhaled drugs (James et al., 1985; Tashkin et al., 1991). Adherence with inhaled drugs may be compromised by inadequate inhaler technique (Garcia-Aymerich et al., 2000; Shrestha et al., 1996). Furthermore, better adherence with oral theophylline can also be due to the simplicity of the dosing regimens (Kelloway et al., 1995).

Other factors, such as adverse effects and medication costs, are also important. Medication cost is one of the greatest barriers to achieving adequate adherence (Cramer et al., 2007, Jung et al., 2009). Side effects or concerns about side effects from medications can reduce adherence as well (Dolce et al., 1991; Rand et al., 1995). For example, patients with COPD often confuse the side effects of ICS with those of anabolic steroids, which may decrease their cooperation willingness (Boulet, 1998).

#### **4.4 Factors related to the characteristics of the health-care provider–patient relationship**

Effective COPD management requires a good relationship between health-care providers and the patients. Quality of communication is related to adherence. Adherent patients report better overall communication with their providers (Blais et al., 2004). Education during the consultation and providing more information about the therapy may improve adherence (Raynor, 1992), as it reduces the risk of forgetting the providers' recommendations and the likelihood of misunderstandings between providers and patients. Previous studies suggest that immediately after the consultation, patients recall less than 50% of the information conveyed by their provider (DiMatteo, 1991).

The type of caregiver also influences adherence. Medication adherence may increase if the prescribing physician is a specialist instead of a general practitioner (Lau et al., 1996). Furthermore, periodic visits, closer follow-up and hospitalisation may also have increasing effects on patient cooperation (Breekveldt-Postma et al., 2007).

### **5. Adherence enhancing interventions**

Strategies for improving patient adherence have to be formulated based on factors related to adherence. Seventy-six adherence interventions were evaluated in the systematic review by Petrilla and Benner (Petrilla & Benner, 2003).

They identified the following main categories of adherence-enhancing interventions:

- coordination of healthcare: improved linkages between primary care physicians, clinicians and other health professionals;
- live consultation and education;
- changes to the therapy dose, dosage and packaging to enhance the drug-taking convenience;
- patient education materials;
- disease management programs by clinicians;
- reminders: medication refill reminders delivered by mail or telephone;
- self-monitoring;
- social support programs;
- and combinations of these interventions.

Successful adherence-enhancing programs include simplified treatment regimens, facilitation of the physician–patient relationship and patient education methods (Petrilla & Benner, 2003).

While many studies have evaluated strategies to enhance adherence, few of these have focused on COPD. Strategies for improving adherence in COPD include simplifying treatment regimens, improving communication between providers and patients, disease education, optimising inhaler technique, reinforcement and self-management (self-monitoring of symptoms and medication use).

It may be important to prescribe drugs with a fixed combination and/or a low dosing frequency to enhance adherence to COPD medication. Furthermore, the recommended treatment should fit into the patient's limitations and lifestyle. Because many COPD patients are elderly, with the dual risk of cognitive impairment and complex medication regimens, the use of dosing aids and adherence devices, such as medication lists, dosette boxes and timers, should be promoted.

Health-care providers must help their patients understand the progressive nature of COPD and the goals of the comprehensive treatment regimens. Physicians should actively involve patients in decisions regarding their therapy and give strong weight to their personal preferences and concerns. Periodic monitoring, understanding the patient's beliefs and positive reinforcement could also enhance adherence to therapy (Dunbar et al., 1979).

## 6. Conclusion

Suboptimal adherence to medication regimens and to other non-drug therapies are both major problems in the management of COPD. Poor adherence poses a significant health and economic burden in patients with COPD. Non-adherence seems to be influenced by many individual reasons, such as factors associated with the characteristics of the disease, the patient, the therapy and the physician-patient relationship. Among other things, simplified treatment regimens, adequate patient education methods and better communication between caregivers and patients have been found to be critical for overcoming the barriers of poor adherence. However, further research is needed to identify factors related to patient cooperation to develop more effective strategies that can improve adherence.

## 7. References

- Agh, T.; Inotai, A. & Mezsáros, A. (2011). Factors Associated with Medication Adherence in Patients with Chronic Obstructive Pulmonary Disease. *Respiration*, Vol.82, No.4, (September 2011), pp. 328–34, ISSN 0025-7931f
- Apter, A.J.; Reisine, S.T.; Affleck, G.; Barrows, E. & ZuWallack, R.L. (1998). Adherence with twice-daily dosing of inhaled steroids. Socioeconomic and health-belief differences. *American Journal of Respiratory and Critical Care Medicine*, Vol.157, No.6, (June 1998), pp. 1810–1817, ISSN 1073-449X
- Baiardini, I.; Braido, F.; Bonini, M.; Compalati, E. & Canonica, G.W. (2009). Why do doctors and patients not follow guidelines? *Current Opinion in Allergy and Clinical Immunology*, Vol.9, No.3, (June 2009), pp. 228–233, ISSN 1528-4050

- Blais, L.; Bourbeau, J.; Sheehy, O. & LeLorier, J. (2004). Inhaled corticosteroids in COPD: determinants of use and trends in patient persistence with treatment. *Canadian Respiratory Journal*, Vol.11, No.1, (January 2004), pp. 27–32, ISSN 1198–2241
- Bosley, C.M.; Parry, D.T. & Cochrane, G.M. (1994). Patient compliance with inhaled medication. Does combining beta agonists with corticosteroids improve compliance? *European Respiratory Journal*, Vol.7, No.3, (March 1994), pp. 504–509 ISSN 0903–1936
- Bosley, C.M.; Fosbury, J.A. & Cochrane, G.M. (1995). The psychological factors associated with poor compliance with treatment in asthma. *European Respiratory Journal*, Vol.8, No.6, (June 1995), pp. 899–904, ISSN 0903–1936
- Boulet, L.P. (1998). Perception of the role and potential side effects of inhaled corticosteroids among asthmatic patients. *Chest*, Vol.113, No.3, (March 1998), pp. 587–592, ISSN 0012–3692
- Bourbeau, J. & Bartlett, S.J. (2008). Patient adherence in COPD. *Thorax*, Vol.63, No.9, (September 2008), pp. 831–838, ISSN 0040–6376
- Breekveldt-Postma, N.S.; Koerselman, J.; Erkens, J.A.; Lammers, J.W. & Herings, R.M. (2007). Enhanced persistence with tiotropium compared with other respiratory drugs in COPD. *Respiratory Medicine*, Vol.101, No.7, (July 2007), pp. 1398–1405, ISSN 0954–6111
- Brooks, D.; Krip, B.; Mangovski-Alzamora, S. & Goldstein, R.S. (2002). The effect of postrehabilitation programmes among individuals with chronic obstructive pulmonary disease. *European Respiratory Journal*, Vol.20, No.1, (July 2002), pp. 20–29, ISSN 0903–1936
- Caetano, P.A.; Lam, J.M. & Morgan, S.G. (2006). Toward a standard definition and measurement of persistence with drug therapy: Examples from research on statin and antihypertensive utilization. *Clinical Therapeutics*, Vol.28, No.9, (September 2006), pp. 1411–1424, ISSN 0149–1918
- Chambers, C.V.; Markson, L.; Ciomond, J.J.; Lasch, L. & Berger, M. (1999). Health belief and compliance with inhaled corticosteroids by asthmatic patients in primary care practices. *Respiratory Medicine*, Vol.93, No.2, (February 1999), pp. 88–94, ISSN 0954–6111
- Chapman, K.R.; Mannino, D.M.; Soriano, J.B.; Vermeire, P.A.; Buist, A.S.; Thun, M.J.; Connell, C.; Jemal, A.; Lee, T.A.; Miravittles, M.; Aldington, S. & Beasley, R. (2006). Epidemiology and costs of chronic obstructive pulmonary disease. *European Respiratory Journal*, Vol.27, No.1, (January 2006), pp. 188–207, ISSN 0903–1936
- Clark, D.J.; Tan, K.S. & Lipworth, B.J. (1996). Evaluation of plasma and urinary salbutamol levels in COPD. *European Journal of Clinical Pharmacology*, Vol.51, No.1, (September 1996), pp. 91–93, ISSN 0031–6970
- Corden, Z.M.; Bosley, C.M.; Rees, P.J. & Cochrane, G.M. (1997). Home nebulized therapy for patients with COPD: patient compliance with treatment and its relation to quality of life. *Chest*, Vol.112, No.5, (November 1997), pp. 1278–1282, ISSN 0012–3692
- Cramer, J.A.; Bradley-Kennedy, C. & Scalera, A. (2007). Treatment persistence and compliance with medications for chronic obstructive pulmonary disease. *Canadian Respiratory Journal*, Vol.14, No.1, (January 2007), pp. 25–29 ISSN 1198–2241

- Cramer, J.A.; Roy, A.; Burrell, A.; Fairchild, C.J.; Fuldeore, M.J.; Ollendorf, D.A. & Wong, P.K. (2008). Medication compliance and persistence: terminology and definitions. *Value in Health*, Vol.11, No.1, (January 2008), pp. 44–7, ISSN 1098-3015
- Cramer, J. A.; Benedict, A.; Muszbek, N.; Keskinaslan, A. & Khan, Z.M. (2008). The significance of compliance and persistence in the treatment of diabetes, hypertension and dyslipidaemia: a review. *International Journal of Clinical Practice*, Vol.62, No.1, (January 2008), pp. 76–87, ISSN 1368-5031
- Dekker, F.W.; Dieleman, F.E.; Kaptein, A.A. & Mulder, J.D. (1993). Compliance with pulmonary medication in general practice. *European Respiratory Journal*, Vol.6, No.6, (June 1993), pp. 886–890, ISSN 0903-1936
- DiMatteo, M.R. (1991). *Psychology of Health Illness and Medical Care: An Individual Perspective*, Brooks/Cole, ISBN 978-053-4150-48-8, Pacific Grove, California, United States
- DiMatteo, M.R.; Lepper, H.S. & Croghan, T.W. (2000). Depression is a risk factor for noncompliance with medical treatment: meta-analysis of the effects of anxiety and depression on patient adherence. *Archives of Internal Medicine*, Vol.160, No.14, (July 2000), pp. 2101–2107, ISSN 0003-9926
- DiMatteo, M.R. (2004.) Variations in patients' adherence to medical recommendations: a quantitative review of 50 years of research. *Medical Care*, Vol.42, No.3, (March 2004), pp. 200–209, ISSN 0025-7079
- Dolce, J.J.; Crisp, C.; Manzella, B.; Richards, J.M.; Hardin, J.M. & Bailey, W.C. (1991). Medication Adherence Patterns in Chronic Obstructive Pulmonary Disease. *Chest*, Vol.99, No.4, (April 1991), pp. 837–841, ISSN 0012-3692
- Dompeling, E.; van Grunsven, P.M.; van Schayck, C.P.; Folgering, H.; Molema, J. & van Weel, C. (1992). Treatment with inhaled steroids in asthma and chronic bronchitis: long-term compliance and inhaler technique. *Family Practice*, Vol.9, No.2, (June 1992), pp. 161–166, ISSN 0263-2136
- Dunbar, J.; Marshall, G. & Hovel, M. (1979). Behavioral strategies for improving compliance. In: *Compliance in health care*, R. Haynes, D. Wayne, D.L. Sackett, (Eds.), pp. 174–190, Johns Hopkins University Press, ISBN 0-8018-2162-2, Baltimore, United States
- George, J.; Kong, D.C.; Thoman, R. & Stewart, K. (2005). Factors associated with medication nonadherence in patients with COPD. *Chest*, Vol.128, No.5, (November 2005), pp. 3198–3204, ISSN 0012-3692
- George, J.; Mackinnon, A.; Kong, D.C. & Stewart, K. (2006a). Development and validation of the Beliefs and Behaviour Questionnaire (BBQ). *Patient Education and Counseling*, Vol.64, No.1-3, (December 2006), pp. 50–60, ISSN 0738-3991
- George, J.; Kong, D.C.; Santamaria, N.; Ioannides-Demos, L. & Stewart, K. (2006b). Smoking cessation: COPD patients' perspective. *Journal of Pharmacy Practice and Research*, Vol.36, No.2, (June 2006), pp. 107–110, ISSN 1445-937X
- George, J.; Kong, D.C. & Stewart, K. (2007). Adherence to disease management programs in patients with COPD. *International Journal of COPD*, Vol.2, No.3, (October 2007), pp. 253–262, ISSN 1176-9106
- Garcia-Aymerich, J.; Barreiro, E.; Farrero, E.; Marrades, R.M.; Morera, J. & Anto, J.M. (2000). Patients hospitalized for COPD have a high prevalence of modifiable risk factors for exacerbation (EFRAM study). *European Respiratory Journal*, Vol.16, No.6, (December 2009), pp. 1037–1042, ISSN 0903-1936

- Hatton, M.Q.; Allen, M.B.; Vathenen, S.V.; Feely, M.p. & Cooke N.J. (1996). Compliance with oral corticosteroids during steroid trials in chronic airways obstruction. *Thorax*, Vol.51, No.3, (March 1996), pp. 323–324, ISSN 0040–6376
- Incalzi, R.A.; Capparella, O.; Gemma, A.; Landi, F.; Bruno, E.; DiMeo, F. & Carbonin, P. (1997). The interaction between age and comorbidity contributes to predicting the mortality of geriatric patients in the acute-care hospital. *Journal of Internal Medicine*, Vol.242, No.4, (October 1997), pp. 291–298, ISSN 0954–6820
- James, P.N.; Anderson, J.B.; Prior, J.G.; White, J.P.; Henry, J.A. & Cochrane, G.M. (1985). Patterns of drug taking in patients with chronic airflow obstruction. *Postgraduate Medical Journal*, Vol.61, No.711, (Januar 1985), pp. 7–10, ISSN 0032–5473
- Jung, E.; Pickard, A.S.; Salmon, J.W.; Bartle, B. & Lee, T.A. (2009). Medication adherence and persistence in the last year of life in COPD patients. *Respiratory Medicine*, Vol.103, No.4, (April 2009), pp. 525–534, ISSN 0954–6111
- Kelloway, J.S.; Wyatt, R.A. & Adlis, S.A. (1994). Comparison of patients' compliance with prescribed oral and inhaled asthma medications. *Archives of Internal Medicine*, Vol.154, No.12, (June 1994), pp. 1349–1352, ISSN 0003–9926
- Kesten, S.; Flanders, J.; Serby, C.W. & Witek, T.J. (2000) Compliance with tiotropium, a once daily dry powder inhaled bronchodilator, in one year COPD trials. *Chest*, Vol.118, No.4, (October 2000), pp. 1915–1925, ISSN 0012–3692
- Krigsman, K.; Nilsson, J.L. & Ring, L. (2007a). Refill adherence for patients with asthma and COPD: comparison of a pharmacy record database with manually collected repeat prescriptions. *Pharmacoepidemiology & Drug Safety*, Vol.16, No.4, (April 2007), pp. 441–448, ISSN 1053–8569
- Krigsman, K.; Moen, J.; Nilsson, J.L. & Ring, L. (2007b). Refill adherence by the elderly for asthma/chronic obstructive pulmonary disease drugs dispensed over a 10-year period. *Journal of Clinical Pharmacy and Therapeutics*, Vol.32, No.6, (December 2007), pp. 603–611, ISSN 0269–4727
- Krigsman, K.; Nilsson, J.L. & Ring, L. (2007c). Adherence to multiple drug therapies: refi ll adherence to concomitant use of diabetes and asthma/COPD medication. *Pharmacoepidemiology & Drug Safety*, Vol.16, No.10, (October 2007), pp. 1120–1128, ISSN 1053–8569
- Laforest, L.; Denis, F.; Van Ganse, E.; Ritleng, C.; Saussier, C.; Passante, N.; Devouassoux, G.; Chatte, G.; Freymond, N. & Pacheco, Y. (2010). Correlates of adherence to respiratory drugs in COPD patients. *Primary Care Respiratory Journal*, Vol.19, No.2, (June 2010), pp. 148–154, ISSN 1475–1534
- Mehuys, E.; Boussery, K.; Adriaens, E.; van Bortel, L.; de Bolle, L.; van Tongelen, I.; Remon, J.P. & Brusselle, G. (2010). COPD management in primary care: an observational, community pharmacy-based study. *Annals of Pharmacotherapy*, Vol.44, No.2, (February 2010), pp. 257–266, ISSN 1060–0280
- Nici, L.; ZuWallack, R.; Wouters, E. & Donner, C.F. (2006). On pulmonary rehabilitation and the flight of the bumblebee: the ATS/ERS Statement on Pulmonary Rehabilitation. *European Respiratory Journal*, Vol.28, No.3, (September 2006), pp. 461–462, ISSN 0903–1936
- Nichol, K.L.; Baken, L. & Nelson, A. (1999). Relation between influenza vaccination and outpatient visits, hospitalization, and mortality in elderly persons with chronic

- lung disease. *Annals of Internal Medicine*, Vol.130, No.5, (March 1999), pp. 397–403, ISSN 0003–4819
- Pepin, J.L.; Barjhoux, C.E.; Deschaux, C. & Brambilla, C. (1996). Long-term oxygen therapy at home. Compliance with medical prescription and effective use of therapy. ANTADIR Working Group on Oxygen Therapy. *Chest*, Vol.109, No.5, (May 1996), pp. 1144–1150, ISSN 0012–3692
- Peterson, A.M.; Nau, D.P.; Cramer, J.A.; Benner, J.; Gwadry-Sridhar, F. & Nichol, M. (2007). A checklist for medication compliance and persistence studies using retrospective databases. *Value in Health*, Vol.10, No.1, (January 2007), pp. 3–12, ISSN 1098–3015
- Petrilla, A.A. & Benner, J.S. (2003). Critical evaluation of interventions to enhance patient compliance with chronic medications. *Value in Health*, Vol.6, No.3, (May 2003), pp. 200, ISSN 1098–3015
- Rand, C.S.; Wise, R.A.; Nides, M.; Simmons, M.S.; Bleecker, E.R.; Kusek, J.W.; Li, V.C. & Tashkin, D.P. (1992). Metered-dose inhaler adherence in a clinical trial. *American Review of Respiratory Disease*, Vol.146, No.6, (December 1992), pp. 1559–1564, ISSN 0003–0805
- Rand, C.S.; Nides, M.; Cowles, M.K.; Wise, R.A. & Connett, J. (1995). Long-term metered-dose inhaler adherence in a clinical trial. The Lung Health Study Research Group. *American Journal of Respiratory and Critical Care Medicine*, Vol.152, No.2, (August 1995), pp. 580–588, ISSN 1073–449X
- Rand, C.S. (2005). Patient adherence with COPD therapy. *European Respiratory Review*, Vol.14, No.96, (December 2005), pp. 97–101, ISSN 0905–9180
- Raynor, D. (1992). Patient compliance: the pharmacist's role. *International Journal of Pharmacy Practice*, Vol.1, No.3, (March 1992), pp. 126–135, ISSN 0961–7671
- Regueiro, C.R.; Hamel, M.B.; Davis, R.B.; Desbiens, N.; Connors, A.F. & Phillips, R.S. (1998). A comparison of generalist and pulmonologist care for patients hospitalized with severe chronic obstructive pulmonary disease: Resource intensity, hospital costs, and survival. *American Journal of Medicine*, Vol.105, No.5, (November 1998), pp. 366–372, ISSN 0002–9343
- Restrepo, R.D.; Alvarez, M.T.; Wittnebel, L.D.; Sorenson, H.; Wettstein, R.; Vines, D.L.; Sikkema-Ortiz, J.; Gardner, D.D. & Wilkins, R.L. (2008) Medication adherence issues in patients treated for COPD. *International Journal of Chronic Obstructive Pulmonary Disease*, Vol.3, No.3, (October 2008), pp. 371–384, ISSN 1178–2005
- Revicki, D.A. & Frank, L. (1999). Pharmacoeconomic evaluation in the real world: Effectiveness versus efficacy studies. *Pharmacoeconomics*, Vol.15, No.5, (May 1999), pp. 423–434, ISSN 1170–7690
- Shrestha, M.; Parupia, M.; Andrews, B.; Kim, S.; Martin, T.; Park, D. & Gee, E. (1996). Metered-dose inhaler technique of patients in an urban ED: Prevalence of incorrect technique and attempt at education. *The American Journal of Emergency Medicine*, Vol.14, No.4, (July 1996), pp. 380–384, ISSN 0735–6757
- Simmons, M.S.; Nides, M.A.; Rand, C.S.; Wise, R.A. & Tashkin, D.P. (1996). Trends in compliance with bronchodilator inhaler use between follow-up visits in a clinical trial. *Chest*, Vol.109, No.4, (April 1996), pp. 963–968, ISSN 0012–3692
- Simmons, M.S.; Nides, M.A.; Rand, C.S.; Wise, R.A. & Tashkin, D.P. (2000). Unpredictability of deception in compliance with physician-prescribed

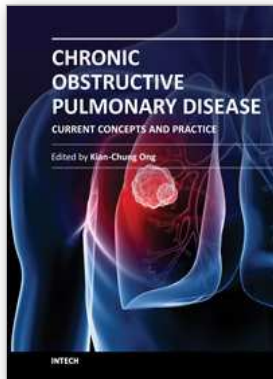
- bronchodilator inhaler use in a clinical trial. *Chest*, Vol.118, No.2, (August 2000), pp. 290-295, ISSN 0012-3692
- Soumerai, S.B.; Ross-Degnan, D.; Avorn, J.; McLaughlin, T. & Choodnovskiy, I. (1991). Effects of Medicaid drug-payment limits on admission to hospitals and nursing homes. *New England Journal of Medicine*, Vol.325, No.15, (October 1991), pp. 1072-1077, ISSN 0028-4793
- Tashkin, D.P.; Rand, C.; Nides, M.; Simmons, M.; Wise, R.; Coulson, A.H.; Li, V. & Gong, H. Jr. (1991). A nebulizer chronolog to monitor compliance with inhaler use. *American Journal of Medicine*, Vol.91, No.4, (October 1991), pp. 33S-36S, ISSN 0002-9343
- Tashkin, D.P. (1995). Multiple dose regimens. Impact on compliance. *Chest*, Vol.107, No.5, (May 1995), pp. 176S-182S, ISSN 0012-3692
- Tuppin, P.; Samson, S.; Weill, A.; Ricordeau, P. & Allemand, H. (2011). Seasonal influenza vaccination coverage in France during two influenza seasons (2007 and 2008) and during a context of pandemic influenza A(H1N1) in 2009. *Vaccine*, Vol.29, No.28, (June 2011), pp. 4632-4637, ISSN 0264-410X
- Turner, J.; Wright, E.; Mendella, L. & Anthonisen, (1995). Predictors of patient adherence to long-term home nebulizer therapy for COPD. The IPPB Study Group. Intermittent Positive Pressure Breathing. *Chest*, Vol.108, No.2, (August 1995), pp. 394-400, ISSN 0012-3692
- van der Palen, J.; Klein, J.J.; van Herwaarden, C.L.; Zielhuis, G.A. & Seydel, E.R. (1991). Multiple inhalers confuse asthma patients. *European Respiratory Journal*, Vol.14, No.5, (November 1999), pp. 1034-1037, ISSN 0903-1936
- van Grunsven, P.M.; van Schayck, C.P.; van Deuveren, M.; van Herwaarden, C.L.; Akkermans, R.P. & van Weel, C. (2000). Compliance during longterm treatment with fluticasone propionate in subjects with early signs of asthma or chronic obstructive pulmonary disease (COPD): results of the Detection, Intervention, and Monitoring Program of COPD and Asthma (DIMCA) Study. *Journal of Asthma*, Vol.37, No.3, (May 2000), pp. 225-234, ISSN 0277-0903
- Varkey, J.B.; Varkey, A.B. & Varkey, B. (2009). Prophylactic vaccinations in chronic obstructive pulmonary disease: current status. *Current Opinion in Pulmonary Medicine*, Vol.15, No.2, (March 2009), pp. 90-99, ISSN 1070-5287
- Vestbo, J.; Anderson, J.A.; Calverley, P.M.; Celli, B.; Ferguson, G.T.; Jenkins, C.; Yates, J.C. & Jones, P.W. (2011). Bias due to withdrawal in long-term randomised trials in COPD: evidence from the TORCH study. *Clinical Respiratory Journal*, Vol.5, No.1, (Januar 2011), pp. 44-49, ISSN 1752-6981
- Viegi, G.; Scognamiglio, A.; Baldacci, S.; Pistelli, F. & Carrozzi, L. (2001). Epidemiology of Chronic Obstructive Pulmonary Disease (COPD). *Respiration*, Vol.68, No.1, (Januar 2001), pp. 4-19, ISSN 0025-7931
- World Health Organization. (2003). *Adherence to long-term therapies: Evidence for action*, World Health Organization, Retrieved from: [http://www.who.int/chp/knowledge/publications/adherence\\_full\\_report.pdf](http://www.who.int/chp/knowledge/publications/adherence_full_report.pdf)
- Würtemberger, G. & Hütter, B.O. (2000). Health-related quality of life, psychological adjustment and compliance to treatment in patients on domiciliary liquid oxygen. *Monaldi Archives Chest Disease*, Vol.55, No.3, (June 2000), pp. 216-224, ISSN 1122-0643



Yeo, J.; Karimova, G. & Bansal, S. (2006). Co-morbidity in older patients with COPD - Its impact on health service utilisation and quality of life, a community study. *Age and Ageing*, Vol.35, No.1, (January 2006), pp. 33-37, ISSN 0002-0729

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## **Chronic Obstructive Pulmonary Disease - Current Concepts and Practice**

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A decade or so ago, many clinicians were described as having an unnecessarily 'nihilistic' view of COPD. This has certainly changed over the years... This open access book on COPD provides a platform for scientists and clinicians from around the world to present their knowledge of the disease and up-to-date scientific findings, and avails the reader to a multitude of topics: from recent discoveries in the basic sciences to state-of-the-art interventions on COPD. Management of patients with COPD challenges the whole gamut of Respiratory Medicine - necessarily pushing frontiers in pulmonary function (and exercise) testing, radiologic imaging, pharmaceuticals, chest physiotherapy, intensive care with respiratory therapy, bronchology and thoracic surgery. In addition, multi-disciplinary inputs from other specialty fields such as cardiology, neuro-psychiatry, geriatric medicine and palliative care are often necessary for the comprehensive management of COPD. The recent progress and a multi-disciplinary approach in dealing with COPD certainly bode well for the future. Nonetheless, the final goal and ultimate outcome is in improving the health status and survival of patients with COPD.

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