



Improving adherence to asthma therapies

Andrew G. Weinstein

Purpose of review

Adherence to asthma therapies is poor leading to unnecessary morbidity and increased use of emergency and hospital resources. Strategies to improve adherence have not been successful.

Recent findings

Asthma adherence disease management is a clinical method to improve adherence for asthma patients. The method includes: diagnosing adherence status; identifying patient barriers leading to nonadherence; selecting specific strategies for the clinician for each barrier identified; use of patient-centered communication skills to enhance the effectiveness of the strategies employed. This approach is now being tested in multiple controlled trials.

Summary

Clinicians may want to consider these strategies, in whole or in part, to improve asthma patient adherence.

Keywords

adherence, asthma child/adult, communication skills, health beliefs, outcomes

INTRODUCTION

Asthma is a common disease in the US population affecting 8% of the adults (18.7 million individuals) [1] and 9.3% of the children under 18 years (6.8 million) [2]. Asthma consumes a significant amount of healthcare resources: in 2010, there were 1.8 million emergency visits [3] and 439 000 hospitalizations with the average length of stay of 3.6 days [4]. The annual economic costs of asthma, including direct medical costs from hospital stays, are \$50.1 billion [5]. The indirect costs, such as lost school and work days, amount to more than \$56 billion annually [5]. It is estimated that 20–30% of asthma patients have severe persistent asthma [6]. Patients with severe asthma have more frequent symptoms, lower lung function, poorer quality of life, increased utilization of physician and hospital care, as well as increased cost [6–8]. The largest amount of direct costs was that allocated to in-patient hospitalization [9]. These difficult-to-treat asthma patients accounted for 67% of the overall asthma-related costs [10]. Patients with severe asthma have a greater incidence of nonadherence leading to increased emergency care, hospitalization and rescue oral corticosteroid use [11–13]. Given that patients with severe asthma have the greatest morbidity, cost, reduced quality of life and reduced adherence rates, it would make sense to apply adherence programs for this high-risk sub-population and improve outcomes [14].

Clinicians are at a disadvantage in promoting adherence because they lack the following:

- (1) Diagnostic tools to measure adherence: Electronic monitors are expensive and not routinely available, and prescription information cannot provide accurate information over brief time frames when the patient is ill. Many patients are not truthful about medication use and receive unnecessary medication, laboratory studies, medical imaging, consultation and sometimes in-patient care (Fig. 1).
- (2) Templates to identify patient adherence barriers.
- (3) Strategies to overcome each barrier.
- (4) Patient-centered communication skills to effectively deliver the adherence strategy: The focus of this review will examine how clinicians can implement an effective asthma adherence disease management strategy and reduce unnecessary utilization and cost. Because inhaled corticosteroids (ICS) are the primary treatment for asthma and recommended by both National

Correspondence to Andrew G. Weinstein, Associate Clinical Professor of Pediatrics, Thomas Jefferson Medical University, President, Asthma Management Systems, P.O. Box 247, Rockford, DE 19732, USA. Tel: +1 302 893 5455; e-mail: agwmd@aol.com

Curr Opin Pulm Med 2015, 21:86–94

DOI:10.1097/MCP.0000000000000128

KEY POINTS

- All asthma patients should be evaluated for adherence at the time of consultation with an asthma specialist.
- Providers should not rely solely on patient report for adherence history.
- Adherence is simultaneously influenced by several factors: characteristics of the disease; treatment type; socioeconomic; healthcare system; personal. Each must be evaluated preferably at the initial evaluation.
- When a patient states they have been nonadherent, believe them. When a patient is identified as nonadherent, they should be supported, not blamed.
- Patient-centered communication skills will enhance patient adherence. Assessing the readiness of a patient to accept a medical recommendation is essential. Physician extenders (nurse practitioners, physician's assistant, nurses) can work with physicians to promote adherence.

Heart Blood and Lung Institute and Global Initiative for Asthma guidelines, adherence data and studies will focus on this class of treatment [15,16].

DEFINITION

The term compliance has been used to define 'the extent to which patients follow physician instructions, prescriptions and proscriptions'. It implies that treatment decision-making was entirely the physician's responsibility and the patient must obey or acquiesce [17]. Adherence is defined by the WHO as 'the extent to which a person's behavior – taking medication, following a diet, and/or executing lifestyle changes – corresponds with agreed recommendations from a healthcare provider' [18]. The main difference between adherence and compliance is that adherence is consensual: it requires the patient's agreement to the recommendations, that patients should be active partners with health professionals in their own care, and that good communication between patient and health professional is a must for an effective clinical practice [18].

THE EXTENT OF NONADHERENCE

Nonadherence can be classified as: primary (failure to get the prescription refilled), secondary (underuse of therapy) and premature discontinuation of treatment. Primary nonadherence may range from 7 to 44% [19,20]. Examples of primary and secondary nonadherence only determine that the medication

was received, but does not provide information regarding the actual use. Rates of secondary ICS adherence in both children and adults are approximately 50%, but may change over time [21]. Bender *et al.* [22] examined refills of fluticasone/salmeterol over 12 months in over 5500 patients. On an average, patients filled enough medication to cover 22.2% of days, and more than half of the patients filled a 30-day prescription only once over the 1-year period [22]. Using electronic adherence monitors, Onyirimba *et al.* [23] found that adherence to ICS decreased by 50% in 1 week and dropped by as low as 20% after 12 weeks. Krishnan *et al.* [24] also found a 50% decrease in ICS usage after discharge from the hospital ICU. Jonasson *et al.* [25] found that adherence to inhaled budesonide administered to 163 children was 70% after 6 months and dropped to 60% after 1 year.

SIGNIFICANCE OF NONADHERENCE AND CLINICAL OUTCOMES

Nonadherence is related to adverse outcomes. In a review of an epidemiologic database, Suissa *et al.* [11] found that patients treated regularly with ICS for at least 16 days and as long as 6 months were 40% less likely to be readmitted for asthma. In another study, Suissa *et al.* [26] compared the deaths of a known asthma population to a control group of individuals who died from asthma. The rate of death from asthma during the first 3 months after discontinuation of ICS was higher than the rate among patients who continued to use the drugs. Milgrom *et al.* [13] placed electronic adherence monitors on ICS metered dose inhaler (MDI) for 24 children aged 8–13 years with moderate-to-severe asthma in an outpatient setting and monitored them for 3 months. Children with low adherence (median 11%) required oral steroid bursts, whereas the adherent group (median 64%) did not require any oral steroids.

Williams *et al.* [21] found that less adherent adult patients treated in a health maintenance organization (HMO) were more likely to be seen in the emergency department, be hospitalized, and receive more oral corticosteroid during the study period. Similarly, Krishnan *et al.* [24] found that patients discharged from an ICU who were subsequently nonadherent with both ICS and oral corticosteroid had reduced asthma control measured by asthma control test.

METHODS TO ASSESS ADHERENCE

There are a variety of methods to assess a patient's adherence.

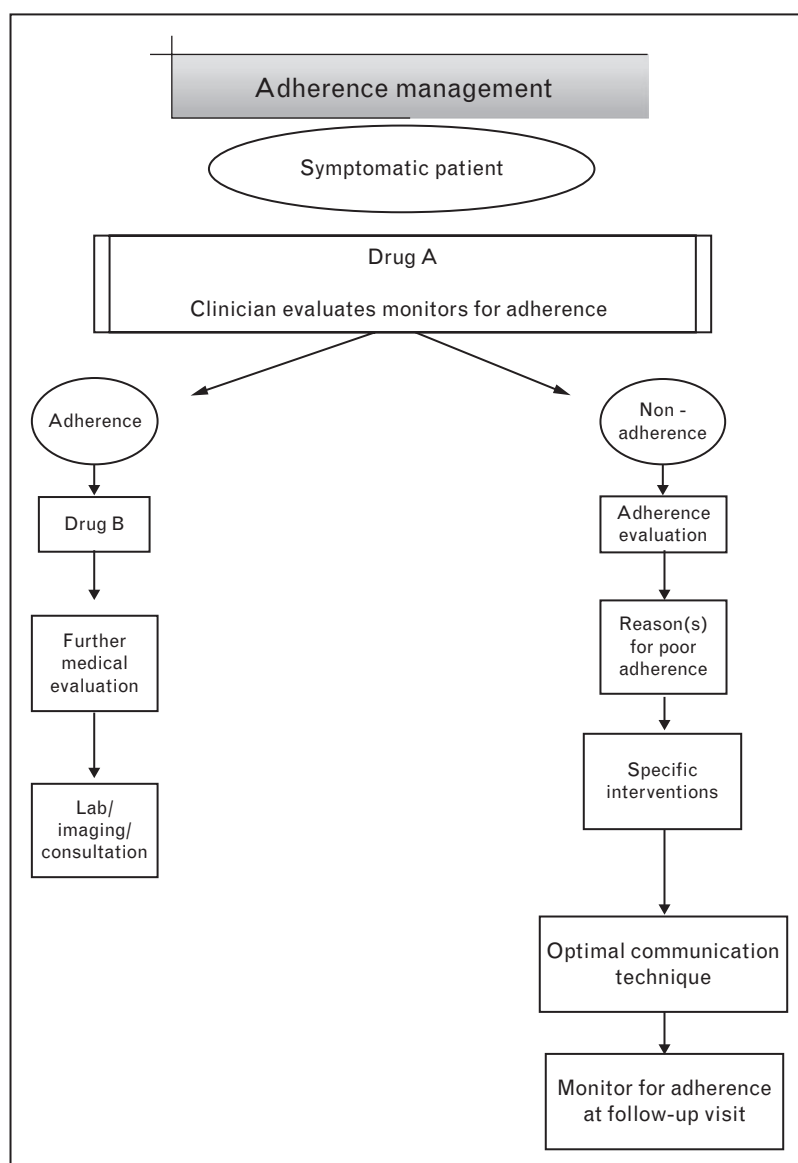


FIGURE 1. Adherence management. Adherence management is appropriate for any chronic disease that requires continuous pharmacologic therapy. Once an individual is identified as nonadherent, an evaluation is performed identifying the cause(s); the specific strategies to be implemented; and the appropriate communication technique [14].

Self-report

Self-report measures, asking a patient about medication use or keeping a diary, are not accurate. Patients may not want to disappoint a provider and thus overestimate medication use [27]. As a result, clinicians tend to overestimate patient adherence [27]. Studies comparing patient diary with electronic adherence devices demonstrate the weakness of patient report [13].

The validity of self-reported nonadherence was demonstrated by Choo *et al.* [28] who compared patient report, pill count, and electronic monitoring device, and automated pharmacy records. Non-adherence reported by patients can serve as a qualitative indicator and predictor of reduced adherence.

Direct measures

Direct measures such as blood and saliva measures of theophylline, an oral bronchodilator, were commonly used to evaluate patient adherence in the 1970s and 1980s in the USA before anti-inflammatory medication became the standard of care. Their advantage is identification of the medication [29]. Problems with theophylline monitoring include: absorption and excretion affected by medication, food and smoking; value is accurate for only one point in time; and patient can anticipate monitoring and alter medication use.

Electronic monitors for MDIs have become more prevalent in research and practice. They are able to identify the pattern of medication use for more than

a month giving the opportunity to review these results with the patient in relation to symptoms and lung function measures at home [14]. Their disadvantage is cost. The Doser computed tomography (CT) is less expensive, but records only 30–45 days of data and does not generate an electronic record for the clinician showing date and time of use [30]. Two electronic monitoring devices – SmartInhaler [31] and Propeller technology [32] – are more expensive and provide documentation of the patient's adherence record and can be applied to a greater number of MDIs currently in use. Both include wireless capability to permit remote monitoring. The SmartInhaler provides audible feedback [31].

Patient questionnaires

Patient questionnaires have been used to assess adherence for multiple diseases by identifying patient barriers to medication use. Recent questionnaires have been used to assess asthma adherence. Patients can self-identify concerns about need for medication, effectiveness of treatment, cost and so on. Schatz *et al.* [33] enrolled 440 adult asthma patients receiving ICS and followed them for 1 year. They studied the relationship of a 20-item questionnaire developed by Weinstein *et al.* [34] to two adherence measures: history of self-reported non-adherence and ICS prescription refill data. They identified five questions: I follow my medication plan; I do not need preventive treatment; I forget at least one dose per day; my ICS causes side-effects; and I cannot afford my medication. All five questions are related to asthma control, and the specific barrier questions are related to subsequent adherence or asthma-related healthcare utilization [33].

Pharmacy refill data

Pharmacy prescription refill databases have proved valuable in assessing adherence. Some local pharmacies may be helpful in giving prescription refill data. Although refill information does not provide daily medication use, it does give primary adherence data showing whether the medicine was obtained by the patient. One learns how 'persistent' the patient is about continuing the prescription over time, as well as computing average daily 'adherence' of medication dispensed from the inhaler [35]. Prescription refill data are becoming more available for clinicians in the USA.

TYPES OF NONADHERENCE

Patients may be categorized by types of behavior and nonadherence [18]. 'Erratic' patients have difficulty

following treatment because of the complexity of treatment or the chaos of their lives. They tend to be forgetful, to be too busy with changing schedules, and frequently run out of medication. Their priorities do not match the requirements to follow the regimen recommended by their provider. 'Unwitting' patients misunderstand the dosing regimen or forget instructions. They fail to understand the rationale for therapy and do not distinguish acute from preventive therapies. There may be language barriers or health literacy issues. 'Intelligent' patients frequently believe that they know more about the appropriate treatment than the provider does. They may say that they do not need treatment or it is ineffective; they are concerned about drug dependence, side-effects or addiction; or they have a different cultural belief from the provider.

FACTORS OR BARRIERS RELATED TO NONADHERENCE

Barriers can be categorized as related to the characteristics of the disease, the therapy required, the individual patient, the clinician, the practice and health system or general societal conditions [18]. A patient's barrier(s) may change over time and a review of these barriers should be made at each visit. Below are common barriers affecting asthma management.

Therapy-related factors

Regimen factors that may affect adherence include: duration, frequency, complexity, cost, efficacy and real or perceived concerns about side-effects [36]. Correct use of MDI is a key, and an incorrect technique may be considered a form of poor adherence. Patients must also differentiate when to supplement daily ICS use with as needed use of rescue medication. Individuals may not use ICS inhalers because they do not perceive the immediate bronchodilation effect with beta-2 agonists.

Patient-related factors

According to WHO, 'patient-related factors' represent the resources, knowledge, beliefs, perceptions, and expectations of the patient [18]. Poverty may lead to decreased access to medication and healthcare providers. Individuals in poverty may have lower adherence since they have a greater incidence of depression and stresses that can influence understanding of instructions, beliefs and expectations about treatment. Age may be a factor affecting adherence. Older individuals may forget to take their medicine. Adolescents may be reluctant to follow medication recommendations because of

body image, peer pressure or autonomy issues. Knowledge of asthma care instructions may be a barrier secondary to poor literacy or poor instruction from the provider.

Health beliefs are associated with adherence. Individuals who do not believe that the treatment is effective will not follow through with recommendations [37]. Distrust of the healthcare provider leads to less adherence [38]. In asthma, low literacy has been associated with improper use of metered dose inhalers [39]. One aspect of literacy may be particularly important: ability to understand and use numerical concepts. Poor numerical scores have been shown to be related to Emergency Department and hospitalizations [40]. This suggests that comprehension of numerical concepts can affect outcomes.

Patient beliefs about ICS directly affect adherence and outcomes. Patients who are concerned about steroid use may under-dose or discontinue long-term use in an effort to be 'steroid-sparing' [18]. A survey of over 600 adult asthma patients was conducted to find outpatients' perceptions about the role of ICS in the treatment of asthma and the potential side-effects of asthma. Among them, 40% believed that ICS were bronchodilators and 25% were aware that ICS reduced inflammation [41]. This would suggest that physicians identify these concerns before prescribing ICS.

Provider-related factors

Physician communication skills are appreciated by patients and can influence adherence and outcomes [42]. A significant body of research supports the concept that providers who are friendly and empathetic; have the ability to earn the trust of patients; can relate to the patient at their level of comprehension; and have the sensitivity to assess and overcome patient barriers will have enhanced adherence and outcomes [43].

Disease-related factors

The role of asthma management is to achieve adherence. Unfortunately, the following characteristics of asthma are associated with poor adherence: the disease is chronic requiring continuous medication administration; there may be periods when patients may be asymptomatic; and a portion of the patients have difficulty appreciating the bronchoconstriction requiring bronchodilator therapy [18].

Practice and system-related factors

Studies have shown that the organization of the practice clinic affects adherence to asthma treatment. Fewer patients seen per hour, appointment length, evening hours, multilingual staff, consistency of care,

ease of making appointments, ease and effectiveness of telephone communication, as well as use of telephone for reminders and follow-ups – all promote adherence [44]. At a system level, physicians have more access to pharmacy refill data to identify patient adherence. Increasing co-payments for visits and medication are responsible for nonadherence. By reducing co-payments to ICS one can increase adherence by 5.88% [45].

INTERVENTIONS TO IMPROVE ADHERENCE

Interventions should be focused on individual barriers identified by the patient. The approach to overcome these barriers can be focused on the regimen, the patient and the providers of care, and then tailored to the individual patient [18].

Regimen interventions

Attempts to decrease the complexity of regimen to once daily, and combining medications into one MDI to decrease the number of medicines to be taken, has been reported to be helpful in increasing adherence [46]. Patients frequently report that forgetting is a common cause of nonadherence. One should carefully assess if forgetting is the 'real reason' for missing medication [36]. Patients use 'forgetting' as a reason when the individual may have one or more concerns about the medication prescribed. Incorrect inhaler use is a common reason for treatment failure when the patient has been 'adherent' using a faulty technique. The techniques of inhaling aerosol and dry powder are significantly different. Review of MDI use and correcting when needed are essential.

Patient interventions

Gibson *et al.* [47], in the Cochrane Airways group, reviewed adherence articles related to asthma interventions that focused on self-management programs. Successful programs that involved self-monitoring of either peak expiratory flow rates, symptoms, combined with regular medical review and written action plans, had marked improvement in health outcomes (including reduction in nocturnal asthma, hospitalizations, physician visits, missed days at school and work) for adults with asthma [48,49]. These superior outcomes were achieved for patients with written asthma action plans who had the ability to adjust their medication.

In another Cochrane review of adherence to multiple chronic illnesses, Haynes *et al.* [50] reported that the most effective interventions for patients included providing reinforcement for patients' efforts to change health-related behaviors,

giving feedback on progress, tailoring the education intervention to the specific needs of the patient, teaching self-management skills, and providing the patient with educational resources. McDonald *et al.* [51] found that, despite the effectiveness in improving adherence, most strategies were too costly, complex, labor-intensive, and of variable effectiveness.

Providing patients with feedback about medication use has been shown to be helpful in increasing adherence to asthma therapies. Onyirimba *et al.* [23] used electronic monitors on ICS on adult inner city women and found that those who were given feedback about medication use had higher (78%) adherence during the 10-week outpatient study than those in the control group who received no feedback. Weinstein *et al.* [52] employed theophylline monitoring in the outpatient phase of an uncontrolled trial of 59 children with severe asthma who were initially treated in a 10-day rehabilitation protocol. There were marked reductions in hospital and emergency utilization, as well as cost, during the 4-year follow-up. These results were duplicated in a 5-day outpatient rehabilitation program [53].

Patient-centered communication

Patient-centered communication strategies have recently been introduced to help patients be more consistent with their medication regimen. Patient-centered approaches are associated with better patient retention, adherence, and treatment outcomes, all without increased time and cost [42]. Motivational interviewing is a patient-centered counseling approach that can be briefly integrated into patient encounters and is specifically designed to enhance motivation to change among patients not ready to change [43]. Existing asthma management approaches (e.g. education and self-management) increase resistance among patients not ready or willing to follow medical recommendations. Motivational interviewing helps patients resolve their ambivalence about behavior change and builds their intrinsic motivation before being provided education. Wilson *et al.* [42] used a patient-centered counseling approach – Shared-Decision-Making (SDM) – to determine its effectiveness in increasing adherence and asthma control in 612 adults with asthma. Practitioners in the study were nonphysicians. The focus of SDM is negotiation of a treatment regimen that accommodates patient goals and preferences. During this 2-year study, patients had increased adherence with ICS and long-acting beta-2 agonists; improved asthma-related quality of life, lower use of rescue medication, better asthma control and lung function, as well as decreased clinic visits. These outcomes support the conclusion that

negotiating patients' treatment decisions significantly improves adherence to asthma pharmacotherapy and clinical outcomes.

Providers' acquisition of communication skills is related to adherence. Studies have examined how to improve communication skills of physicians caring for asthma patients. Clark *et al.* [54] and Cabana *et al.* [55] have provided training in communication skills, as well as in asthma management, to primary care physicians, and have demonstrated increased filling of anti-inflammatory prescriptions, decreased nonemergency visits, and increased patient satisfaction persisting over 2 years.

Healthcare system interventions

The 2003 World Health Report emphasizes the need to think beyond clinicians as the sole intervener to promote adherence to a large population [18]. Clinicians can no longer afford the time to provide personal interventions. In a response to increasing cost of care, the USA has turned to disease management companies to improve management. The Asheville Project – a widely cited disease management program – studied 207 adult asthma patients [56]. Each received multiple one-to-one visits of an education intervention by a pharmacist every 3 months for 1 year. The study demonstrated significant reduction in emergency department and hospitalizations; and more patients had less severe National Asthma Education and Prevention Program asthma severity classification and spirometry from baseline. Adherence was determined by the amount of spending on medication.

Healthcare information technology

Because of low cost and the ability to reach large populations, disease management and population health studies are utilizing interactive voice recognition (IVR). IVR has been used to collect adherence and other health data [57]. IVR systems use voice-processing technology to link individuals with a computer database. Prerecorded voice files generally prompt the caller to press telephone buttons to answer questions or request information. The IVR system can then retrieve appropriate health or resource information by accessing the host computer's database and providing it to the patient.

A study of poorly controlled asthma patients from an HMO evaluated the effectiveness of IVR in promoting asthma adherence [58]. There were 50 adults who had been prescribed ICS in the poorly controlled group. Calls were completed in less than 5 min and included content designed to inquire about asthma symptoms, deliver core educational

Table 1. Factors affecting adherence to asthma treatment and interventions to address these barriers

Factors affecting adherence	Interventions to improve adherence
Drug-related factors	
Difficulties with inhaler devices	Identify appropriate device for patient. Demonstrate use and have patient demonstrate technique in turn.
Awkward regimens, for example, 4 times daily, or multiple drugs	Simplify regimen or tailor to patient preference [15,16] .
Fears about side-effects	Determine whether concern is theoretical or specific. If specific, relate the persistence of the symptoms vs. likelihood of side-effects. Use motivational interviewing to assess 'pros and cons' and reduce ambivalence. Consider referral to support group [43].
Cost of medication	If patient has prescription plan, select least expensive drug. If not, refer to discount pharmacy plans or pharmaceutical programs [60].
Dislike of medication	Reduce allergic or irritant exposure to decrease symptoms or medication [60]. Use motivational interviewing to assess 'pros and cons' and reduce ambivalence [43].
Distant pharmacies	Identify capability of receiving prescription by mail [60].
Nondrug-related factors	
Misunderstanding or lack of instruction	If lack of instruction, provide instruction. Assess level of literacy. If low, provide suitable education strategy. Review pathophysiology and rationale for treatment as well as consequences of no treatment. Provide instruction and have patient demonstrate technique [15,16] .
Dissatisfaction with healthcare professionals	Have patient speak to administrator regarding issue. May require patient to see another provider if interactions do not improve [61].
Unexpressed/undisclosed fears or concerns	Identify concerns and address each. Determine if they are theoretical or actual. Consider referral to a support group. May require psychological intervention if fears or concerns persist [43,60].
Inappropriate expectations	Clarify expectations from a medical perspective. If patient expects greater or quicker improvement, attempt to reset expectations. Review role of allergen/irritant exposure as factor [18].
Poor supervision, training, or follow-up	Encourage supervision for children/elderly. Review use of medication in office. Schedule appropriate follow-up [18].
Anger about condition or its treatment	Identify reason for anger. Express that treatment may improve condition. Assess ambivalence about treatment and review possible alternatives [43].
Underestimation of severity	Relate symptoms with pulmonary function or use exercise challenge to demonstrate severity of condition [60].
Cultural issues	Appreciate that varying cultures have different concepts of development of asthma, factors that exacerbate it, and treatment choices. Take advantage of community health workers to clarify issues [18].
Concerns about stigmatization	Assess patient reaction to diagnosis. Understand the patient's concerns and refer to support group if the concerns persist [43].
Forgetfulness or complacency	Determine whether the problem is forgetting to follow treatment vs. other reasons. Consider tailoring medication use to patient's daily activities. Address complacency by withdrawing treatment to determine actual need for treatment [18].
Attitudes toward ill health	Assess patient's health beliefs about asthma and treatment. For patients who question the diagnosis or efficacy of treatment, consider stopping treatment and having patient monitor lung function at home [60].
Religious issues	Clarify how patient's religious beliefs may affect attitudes about diagnosis and treatment. Discussing this with patient's religious leader may give insight and source of support for the patient [18].
Patient behaviors	
Erratic nonadherence: Forgetfulness, busy lives, changing schedules	Simplification of the regimen; tailoring treatment to a specific daily activity (tooth brushing); memory aids [15,16].
Unwitting nonadherence: Failure to understand the specifics of the treatment or the necessity for adherence	Provide clear communication and use patient-centered communication techniques to verify comprehension [43].

Table 1 (Continued)

Factors affecting adherence	Interventions to improve adherence
Intelligent nonadherence: Deliberate choice to not follow treatment; patients no longer feel the need; concern about side-effects; believe that variation in regimen works better than prescribed	Use communication skills (open-ended questions, active listening) to identify patient concerns and motivational interviewing to address patient ambivalence [43].

Adapted with permission from [61]. Reference adapted from [59[■]].

messages, encourage refilling of inhaled corticosteroid prescriptions, and increase communication with providers. Adherence was 32% higher in the intervention group.

Weinstein [59[■]] has created an asthma adherence disease management model that was developed while caring for children with severe asthma. It consists of four sequential steps when evaluating symptomatic patients: objective measure of medication use; increase medication if adherent, identify patient barriers if nonadherent; select appropriate intervention(s) for specific barrier(s); and use the appropriate patient-centered communication technique(s). The same investigator has developed a web-based asthma adherence clinical decision support system for disease management to promote adherence to asthma treatments for children and adults. Patients identify barriers to treatment and receive written and video responses to each barrier. Providers review the barrier(s) and are given specific recommendations for these patients as well as patient-centered counseling techniques to achieve optimal adherence (Table 1). This system is being tested telephonically by disease management clinicians trained in motivational interviewing (MI) technique. These clinicians follow patient medication use from remote electronic adherence monitors and deliver interventions over the telephone, tailored to the concerns of the patients [62].

CONCLUSION

Adherence to medication is an essential part of asthma care and can be achieved following the four sequential management principles presented: diagnosis of patient adherence status, identification of barriers to treatment, application of strategies to address barriers, and use of effective patient-centered communication strategies. Careful attention to these adherence management principles should increase adherence, enhance outcomes, and reduce unnecessary morbidity and cost.

Acknowledgements

None.

Financial support and sponsorship

None.

Conflicts of interest

Dr Weinstein has received Research Support from The National Institutes of Health. Dr Weinstein is the President of Asthma Management Systems (AMS) LLC.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- of outstanding interest

- Blackwell DL, Lucas JW, Clarke TC. Summary health statistics for U.S. adults: National Health Interview Survey, 2012. National Center for Health Statistics. Vital Health Stat 10.
- Summary Health Statistics for U.S. Children: national health interview survey. 2012. http://www.cdc.gov/nchs/data/series/sr_10/sr10_258.pdf. [Cited 8 October 2014]
- National Hospital Ambulatory Medical Care Survey: 2010 Emergency Department summary tables, table 12. http://www.cdc.gov/nchs/data/ahcd/nhamcs_emergency/2010_ed_web_tables.pdf. [Cited 8 October 2014]
- National Hospital Discharge Survey: 2010 table. Average length of stay and days of care: number and rate of discharges by first-listed diagnostic categories. http://www.cdc.gov/nchs/data/nhds/2average/2010ave2_first_list.pdf.
- Centers for Disease Control and Prevention Asthma in the U.S. Vital signs. 2011. <http://www.cdc.gov/vitalsigns/asthma/>. [Cited 8 October 2014]
- Dolan CM, Fraher KE, Bleeker ER, et al. Design and baseline characteristics of the epidemiology and natural history of asthma: Outcomes and Treatment Regimens (TENOR) study: a large cohort of patients with severe or difficult-to-treat asthma. *Ann Allergy Asthma Immunol* 2004; 92:32–39.
- Vollmer WM, Markson LE, O'Connor E, et al. Association of asthma control with healthcare utilization: a prospective evaluation. *Am J Respir Crit Care Med* 2002; 165:195–199.
- Ivanova J, Bergman R, Birnbaum H, et al. Effect of asthma exacerbations on healthcare costs among asthmatic patients with moderate and severe persistent asthma. *J Allergy Clin Immunol* 2012; 129:1229–1235.
- Weiss KB, Gergen PJ, Hodgson TA. An economic evaluation of asthma in the United States. *N Engl J Med* 1992; 326:862–866.
- Bahadori K, Doyle-Waters MM, Marra C, et al. Economic burden of asthma: a systematic review. *BMC Pulmonary Medicine* 2009; 9:24.
- Suissa S, Ernst P, Kezouh A, et al. Regular use of inhaled corticosteroids and the long term prevention of hospitalisation for asthma. *Thorax* 2002; 57:880–884.
- Williams LK, Peterson EL, Wells K, et al. A cluster-randomized trial to provide clinicians inhaled corticosteroid adherence information for their patients with asthma. *J Allergy Clin Immunol* 2010; 126:225–231.
- Milgrom H, Bender B, Ackerson L, et al. Noncompliance and treatment failure in children with asthma. *J Allergy Clin Immunol* 1996; 98:1051–1057.
- Weinstein AG. Should patients with severe persistent asthma be monitored for medication adherence? *Ann Allergy Asthma Immunol* 2005; 94:251–257.
- Guidelines for the Diagnosis and Management of Asthma (EPR3) 2007. NIH, NHLB August 2007. NIH publication no. 08-4051:52.
- Global Strategy for Asthma Management and Prevention, Global Initiative for Asthma (GINA) 2008. <http://www.ginasthma.org>.
- Haynes RB, Taylor DW, Sackett DL. Compliance in healthcare. Baltimore: Johns Hopkins University Press; 1979.

18. Rand C, Weinstein A, Bender B, *et al.* Asthma. In Sabate E, editor. Adherence to long-term therapies: evidence for action. World Health Organization: Geneva; 2003. p. 47–58.
19. Watts RW, McLennan G, Bassham I, el-Saadi O. Do patients with asthma fill their prescriptions? A primary compliance study. *Aust Fam Physician* 1997; 26 (Suppl1):S4–S6.
20. Kelloway JS, Wyatt RA, Adlis SA. Comparison of patients' compliance with prescribed oral and inhaled asthma medications. *Arch Intern Med* 1994; 154:1349–1352.
21. Williams LK, Pladevall M, Xi H, *et al.* Relationship between adherence to inhaled corticosteroids and poor outcomes among adults with asthma. *J Allergy Clin Immunol* 2004; 114:1288–1293.
22. Bender BG, Pedan A, Varasteh LT. Adherence and persistence with fluticasone propionate/salmeterol combination therapy. *J Allergy Clin Immunol* 2006; 118:899–904.
23. Onyirimba F, Apter AJ, Reisine ST, *et al.* Direct clinician-to-patient feedback of inhaled steroid use: its effect on adherence and asthma outcome. *Ann Allergy Asthma Immunol* 2003; 90:411–415.
24. Krishnan JA, Riekert KA, McCoy JV, *et al.* Corticosteroid use after hospital discharge among high-risk adults with asthma. *Am J Respir Crit Care Med* 2004; 170:1281–1285.
25. Jonasson G, Carlsen K, Mowinckel P. Asthma drug adherence in a long term clinical trial. *Arch Dis Child* 2000; 83:330–331.
26. Suissa S, Ernst P, Benayoun S, *et al.* Low-dose inhaled corticosteroids and the prevention of death from asthma. *N Engl J Med* 2000; 343:332–336.
27. Adams SA, Matthews CE, Ebbeling CB, *et al.* The effect of social desirability and social approval on self-reports of physical activity. *Am J Epidemiol* 2005; 161:389–398.
28. Choo P, Rand C, Inui T, *et al.* Validation of patient reports, automated pharmacy records, and pill counts with electronic monitoring of adherence to antihypertensive therapy validation of patient reports. *Med Care* 1999; 37:846–857.
29. Weinstein AG, Cusky W. Theophylline compliance in asthmatic children. *Ann Allergy* 1985; 54:19.
30. O'Connor SL, Bender BG, Gavin-Devitt LA, *et al.* Measuring adherence with the Doser CT in children with asthma. *J Asthma* 2004; 41:663–670.
31. Burgess SW, Sly PD, Devadason SG. Providing feedback on adherence increases use of preventive medication by asthmatic children. *J Asthma* 2010; 47:198–201.
32. propellerhealth.com.
33. Schatz M, Zeiger R, Yang S-J, *et al.* Development and preliminary validation of the adult asthma adherence questionnaire. *J Allergy Clin Immunol* 2013; 1:280–288.
34. Weinstein AG, Schatz M, Laurenceau JP. Preliminary analysis of an adherence survey for adult asthma patients. *J Allergy Clin Immunol* 2009; 123:S72.
35. Vink NM, Klungel OH, Stolk RP, Denig P. Comparison of various measures for assessing medication refill adherence using prescription data. *Pharmacoepidemiol Drug Saf* 2009; 18:159–165.
36. Bender B, Milgrom H, Rand C. Nonadherence in asthmatic patients: Is there a solution to the problem? *Ann Allergy Asthma Immunol* 1997; 79:177–186.
37. Osman LM, Russell IT, Friend JA, *et al.* Predicting patient attitudes to asthma medication. *Thorax* 1993; 48:827–830.
38. George M, Freedman TG, Norfleet AL, *et al.* Qualitative research enhanced understanding of patients' beliefs: results of focus groups with low-income urban African-American adults with asthma. *J Allergy Clin Immunol* 2003; 111:967–973.
39. Williams MV, Baker DW, Honig EG, *et al.* Inadequate literacy is a barrier to asthma knowledge and self-care. *Chest J* 1998; 114:1008–1015.
40. Apter AJ, Cheng J, Small D, *et al.* Asthma numeracy skill and health literacy. *J Asthma* 2006; 43:705–710.
41. Boulet LP. Perception of the role and potential side effects of inhaled corticosteroids among asthmatic patients. *Chest* 1998; 113:587–592.
42. Wilson S, Strub P, Buist A, *et al.* The Better Outcomes of Asthma Treatment (BOAT) Study Group. Shared treatment decision making improves adherence and outcomes in poorly controlled asthma. *Am J Respir Crit Care Med* 2010; 181:566–577.
43. Borrelli B, Riekert K, Weinstein A, Rathier I. Brief motivational interviewing as a clinical strategy to promote asthma medication adherence. *J Allergy Clin Immunol* 2007; 120:1023–1030.
44. Lowe RA, Localio AR, Schwarz DF, *et al.* Association between primary care practice characteristics and emergency department use in a Medicaid managed care organization. *Med Care* 2005; 43:792–800.
45. Chernew M, Shah M, Wegh A, *et al.* Impact of decreasing copayments on medication adherence within a disease management environment. *Health Aff* 2008; 27:103–112.
46. Stoloff SW, Stempel DA, Meyer J, *et al.* Improved refill persistence with fluticasone propionate and salmeterol in a single inhaler compared with other controller therapies. *J Allergy Clin Immunol* 2004; 113:245–251.
47. Gibson PG, Powell H, Wilson A, *et al.* Self-management education and regular practitioner review for adults with asthma (review). *Cochrane Database Syst Rev* 2003; CD001117.
48. Koteses H, Bernstein IL, Bernstein DI, *et al.* A self-management program for adult asthma. Part I: development and evaluation. *J Allergy Clin Immunol* 1995; 95:529–540.
49. Taitel MS, Koteses H, Bernstein IL, *et al.* A self-management program for adult asthma. Part II: cost-benefit analysis. *J Allergy Clin Immunol* 1995; 95:672–676.
50. Haynes RB, Yao X, Degani A, *et al.* Interventions to enhance medication adherence. *Cochrane Database Syst Rev* 2005; CD000011.
51. McDonald HP, Garg AX, Haynes RB. Interventions to enhance patient adherence to medication prescriptions: scientific review. *J Am Med Assoc* 2002; 288:2868–2879.
52. Weinstein AG, McKee L, Stapleford J, Faust D. An economic evaluation of short-term inpatient rehabilitation for severe asthmatic children. *J Allergy Clin Immunol* 1996; 98:264–273.
53. Weinstein AG, Sheslow D, Wasserman P, *et al.* Outpatient vs. inpatient rehabilitation for severe asthmatic children: morbidity and economic outcomes. *J Allergy Clin Immunol* 1998; 101:S178.
54. Clark NM, Gong M, Schork MA, *et al.* Long-term effects of asthma education for physicians on patient satisfaction and use of health services. *Eur Respir J* 2000; 16:15–21.
55. Cabana MD, Slish KK, Evans D, *et al.* Impact of physician asthma care education on patient outcomes. *Pediatrics* 2006; 117:2149–2157.
56. Bunting B, Cranor C. The Asheville Project: long-term clinical, humanistic, and economic outcomes of a community-based medication therapy management program for asthma. *J Am Pharm Assoc* 2006; 46:133–147.
57. Kaplan B, Farzanfar R, Friedman RH. Personal relationships with an intelligent interactive telephone health behavior advisor system: a multimethod study using surveys and ethnographic interviews. *Int J Med Inform* 2003; 71:33–41.
58. Bender BG, Apter A, Bogen D, *et al.* Test of an interactive voice response intervention to improve adherence to controller medications in adults with asthma. *J Am Board Fam Med* 2010; 23:159–165.
59. Weinstein AG. Asthma adherence management for the clinician. *J Allergy Clin Immunol*: In Practice 2013; 1:23–28.
- This study provides a four-step process in promoting adherence to asthma therapy.
60. Weinstein AG. Clinical management strategies to maintain drug compliance in asthmatic children. *Ann Allergy* 1995; 74:304–310.
61. Weinstein AG. The potential of asthma adherence management to enhance asthma guidelines. *Ann Allergy Asthma Immunol* 2011; 106:283–291.
62. NIH grant #R43HL115846. An asthma adherence telehealth system to improve asthma management. PI: Weinstein AG.