



Adherence to asthma treatments: 'we know, we intend, we advocate'

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Purpose of review

To highlight the state of the art and the current outlook on the adherence to treatment in asthma, starting from the 'Manifesto on Adherence to asthma treatment in respiratory allergy' endorsed by the World Allergy Organization, Allergic Rhinitis and Its Impact on Asthma and Global Allergy, Asthma European Network, and Interasma.

Recent findings

Adherence to the pharmacological treatments of asthma is known to be low: about 50% of those who had been prescribed long-term treatment are nonadherent, at least part of the time. Nonadherence is associated with lack of asthma control, poor health outcomes, and increased costs. The reasons for suboptimal adherence are multifaceted and may be related to the patients, the treatment and asthma features, the physician–patient relationship, and the healthcare resources and facilities.

Summary

Taking into account the multidimensional nature of adherence, no single intervention or strategy is per se able to enhance it, but all players involved in the process (government authorities, patient organizations, scientific societies, stakeholders, and others) are called to work together to develop a combined action plan based on the patient's complexity.

Keywords

adherence, asthma, control, cost, manifesto

INTRODUCTION

The World Allergy Organization (WAO) and Interasma are highlighting via their website (www.wao.org, www.interasma.org) the 'Manifesto on Adherence to asthma treatment in respiratory allergy' endorsed by the above-mentioned organization, as well as by Allergic Rhinitis and Its Impact on Asthma (ARIA) and the Global Allergy and Asthma European Network (Ga₂LEN). The word 'manifesto' is derived from the Latin *manifestum*, which means 'clear' or 'conspicuous'. It is a published verbal declaration of the intentions, motives, or views of the issuer, based on a previously published opinion or public consensus and promotes a new idea with prescriptive notions for carrying out the changes the author believes should be made (www.wikipedia.org). 'We know, we intend and we advocate' constitute the keys points of the document, in which the subscribers summarize the available knowledge, the scientific institution needs, and the claim for partnerships.

The aim of the present review is to highlight and discuss the state of the art and the current outlook

on the adherence to treatment in asthma, on the basis of the recently published literature, in order to propose and adopt significant intervention in improving disease management. Following the 'manifesto' structure, issues concerning what is known, intended, and advocated will be presented.

WE KNOW

Four key points could represent the background for any intervention on nonadherence to asthma treatment: its rate, its relationship with asthma control, its related cost, and the barriers to adherence.

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Rate of medication nonadherence

Patient adherence to medical prescriptions still remains a major problem in the management of all chronic diseases, even with its enhanced recognition in the last few years. According to the WHO, approximately half of the patients with chronic diseases are nonadherent to the treatment prescribed [1], leading to poor health outcomes, lower patient's well being, and increased health costs [2]. The WHO states that increasing adherence may have a more beneficial impact on the health of the population than improving specific treatments [3]. Adherence to the pharmacological treatments for asthma is known to be low: about 50% of those who had been prescribed long-term treatment are nonadherent, at least part of the time [4,5]. The magnitude of the problem becomes particularly worrying in some age groups: children, adolescents, and the elderly are recognized as at increased risk of nonadherence. Data from a recent study [6] involving 5–14-year-old children with persistent asthma showed that adherence rates to beclomethasone propionate (measured through an electronic monitor) were as low as 31.2% after 12 months of treatment.

Among older asthmatic patients (aged ≥ 60 years), only 38.2% were adherent to their controller medication [7]. Apart from age, different factors could be associated with poor adherence. A recent systematic review that aimed to assess the adherence rate to inhaled corticosteroid (ICS) showed a mean level of adherence between 22 and 63%, with improvement up to and after an exacerbation. Poor adherence was associated with youth, having mild asthma, less than 12 years of formal education, and poor communication with the healthcare provider, whereas the prescription of a fixed-combination therapy (ICS and long-acting β_2 agonists) was related to an improvement in adherence [8].

Adherence and asthma control

Good adherence has been shown to be associated with higher lung function, a lower percentage of eosinophils in sputum, reduction in hospitalizations, less use of oral corticosteroids, and lower mortality rate. Overall, 24% of exacerbations and 60% of asthma-related hospitalizations could be attributed to poor adherence [8].

Most studies have reported an increase in adherence following focused interventions. However, it should be mentioned that there are also two studies showing no difference in healthcare utilization: one observed no effect on the symptoms, and one observed more symptoms in individuals in the intervention group compared with the control

group. Even following successful interventions, adherence remains low. Further research is needed to explore the barriers to adherence and interventions for improvement [8].

Poor adherence is clearly undesirable because a large proportion of patients have symptoms that remain suboptimally controlled. However, acceptance of this fact and that poor adherence is endemic might be better than the current practice, in which physicians, believing that the prescribed dose is being taken, are likely to overprescribe (increase the dose or add other medications), adding cost and potential for side-effects, which introduce a further burden on the patients and hinder adherence [9].

Cost of nonadherence

It has been estimated that nonadherence is responsible for more than \$100 billion spent each year on avoidable hospitalizations in the USA [10]. Other authors showed that up to three-quarters of the total costs associated with asthma might be because of poor asthma control [11]. Furthermore, it has been suggested that a significant portion of the healthcare advice and prescriptions dispensed are wasted: over 188 million medical visits prescribed in the USA yearly performed result in patients' failing to adhere to the physician's advice, with an excess cost associated with nonadherence estimated at US\$ 300 billion a year. Even more troubling are the healthcare costs resulting from nonadherence-related disease exacerbations [12]. Both in primary and secondary care, adherence is lower in patients with a history of asthma-related hospitalizations, that are at high risk of readmission and that generally consume a large amount of health-care resources, indicating the need for raising the quality of care provided by generalists and specialists alike [13].

Barriers to adherence

The reasons for suboptimal adherence are multifaceted. Reasons for nonadherence are both intentional and nonintentional, incorporating illness perceptions, medication beliefs, and practical adherence barriers. Nonadherence in children and adolescents deserves special attention because they face unique barriers to adherence that change with age. Young children depend on adults for the delivery of asthma care, and their care is strongly influenced by parental motivation and attitudes and the home environment. As these children enter adolescence, they typically assume responsibility for their asthma care at the same time as they are claiming their

independence and possibly experimenting with high-risk behavior [14]. Family functioning and parental beliefs about asthma and medication treatment demonstrated consistent relationships with treatment adherence [15].

Several forms of research have explored the existing barriers to adherence [15,16]. Treatment-related barriers include prolonged and complex regimens, adverse effects, costs, and delayed onset of action. Clinician-related barriers include difficulty in scheduling, treatment by one different caregiver after another, perceived clinician disinterest, and time constraints. Patient-related barriers include mild or severe asthma, poor understanding of the need for treatment, insufficient confidence in the clinician or medication, the presence of psychological problems, and low motivation to change of behavior. Although all of these factors must be addressed to maximize adherence, patient belief may be most critical [17].

The relationship between beliefs (i.e. necessities and concerns) about ICS and subjectively as well as objectively measuring adherence and the agreement between these measures has been an object of investigation. Higher necessities are associated with higher self-reported adherence, suggesting that it could be more important to focus on the necessities than on concerns in an attempt to improve adherence. Self-reported and refill adherence measurements cannot be used interchangeably, and no relationship was found between adherence and asthma symptoms [18^{***}]. The opinions held by the general population on obstructive lung disease and inhaler devices could influence asthma and chronic obstructive pulmonary disorder (COPD) management and treatment adherence. A public survey on representative group of the Italian population aged 15 years and over has been conducted in order to evaluate the opinions, beliefs, and perceptions with respect to obstructive lung disease as well as their perspectives on the use of inhaler devices. The respondents were asked whether they had recently heard of any of the several diseases, including asthma. Only 51% of the interviewees recognized 'asthma', which ranked fifth among 11 chronic disorders. Although 42% of the interviewees reported a medium-to-high level of asthma awareness, 14% declared that they knew nothing about the disease, whereas 33 and 40% of the respondents reported a poor and a fair knowledge of it, respectively. In conclusion, the awareness of asthma remains, even in a high-income European country, still unsatisfactory and despite its prevalence, asthma remains relatively unknown. The low awareness of the general population may lead to scarce consideration among the asthmatic patients and

healthcare institutions, with a consequent negative impact on asthma care and related treatment adherence [19^{***}].

WE INTEND

The 'Manifesto' clearly underlines that adherence represents a patient's moral responsibility vs. both the healthcare system and the social community. This idea starts from the words of the WHO statement, for which 'poor adherence to long-term therapies severely compromises the effectiveness of treatment making this a critical issue in population health from the perspective of both quality of life and health economics' [20]. Nonadherence in asthma management is a process that depends on different determinants, is influenced by a lot of factors, involve numerous players, and have relevant consequences for patients and society in terms of burden and costs. Taking into account the complexity of the problem and its multidimensional nature, no single intervention or strategy is per se able to enhance adherence.

Nevertheless, key points of the process could be the integration of different strategies to improve education and adherence, taking into account the possibility derived from the use of the new available technologies.

Strategies to improve education

Morisky [21] and Armour [22] performed two studies, in which a disease management program including specific educational interventions was able to improve adherence. Other available researches reported relevant progress in self-management after education, but the effect was not clearly reflected in adherence behavior [23,24]. More recently, the study of Gaude *et al.* [25] evaluated 500 patients suffering from bronchial asthma followed up for a total of 12 weeks for the calculation of nonadherence to the aerosol therapy; in nonadherent patients, various health educational strategies to improve adherence were applied. At the end of the observation period, only 38.6% patients were found to be regularly compliant. After the employment of different educational interventions specifically aimed at improving the level of compliance, the adherence increased in 57.3% among the earlier defaulted patients, whereas the remaining 42.7% were found to be noncompliant even after various educational techniques.

Sometimes, education does not seem to be related to better outcomes. For example, a study by Auger *et al.* [26^{*}] focused attention on caregiver asthma knowledge, beliefs, and reported adherence

to the prescribed medication regimens as potential factors that influence the readmission for childhood asthma exacerbation. The results of a multivariate analysis showed that an improvement in the caregiver's knowledge of asthma was associated with increased readmission risk. In other words, in a multifactorial assessment of risk factors for asthma readmission, both greater asthma knowledge and decreased medication adherence were associated with readmission. The authors suggest that in order to prevent readmission it could be more effective to target medication adherence rather than continuing to primarily provide asthma education.

Strategies to improve adherence

Intervention to improve adherence should be specifically tailored to the patient, taking into account the disease patterns and health-related and-unrelated individual attributes (Fig. 1). For example, starting from the awareness that older adults with asthma show low levels of adherence to their prescribed ICS, an observational study was performed to explore what medication use strategies are associated with good ICS adherence in this age group. Keeping the drugs in a usual location (44.2%), integrating the drug intake with the daily routine (32.6%), taking the medication at a specific time (21.7%) and with other medications (13.4%), using the medication only when needed (13.4%), and using specific reminders (11.9%) were shown to be the strategies that were positively related with adherence. The good adherence rate was greater

among individuals who kept their ICS medication in the bathroom [adjusted odds ratio (OR) 3.05, $P=0.04$] or integrated its use into a daily routine (OR 3.77) [27]. In the same line, other authors showed that women were much more likely to carry an inhaler with them than men (61 vs. 30%, $P<0.0001$) [28]. The severity of asthma directly correlated with an increase in patient inhaler adherence, and a large percentage of patients indicated that they did not feel the need to carry their inhalers even though their physician had specified otherwise [28].

Indeed, research on patient adherence to asthma medications has been limited by imprecise or unsatisfactory measurement tools to estimate the real inhaler use [29,30].

With the aim of overcoming this problem, an inhaler tracker device, which, when clipped onto an inhaler, records each activation of the device itself and that can be programmed to prompt patients to use their inhaler and provide reports to motivate adherence, has been developed and tested [31]. Similarly, some drug-dispensing and drug-delivery devices have been designed to support patients' medication-taking behavior by including dose-memory and dose-reminder functions, which electronically store and visually display dose-history information, enabling the patient to review, monitor, and be actively reminded about their medication doses. These devices are considered valuable in disease management by patients, caregivers and healthcare providers, and they were found to enhance patients' confidence and motivation in managing their reducing forgotten or incorrect

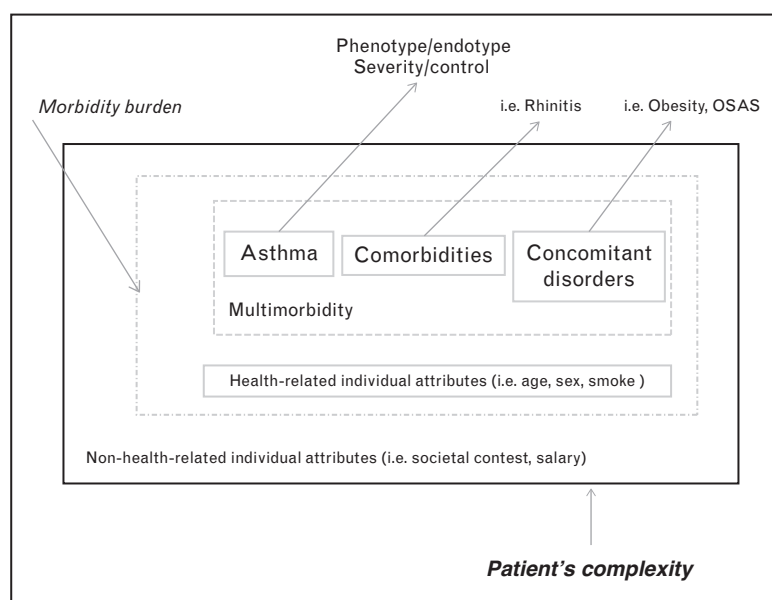


FIGURE 1. Adherence to treatment: conditioning factors. Patient's complexity refers to the overall impact of the different diseases in an individual, taking into account the severity and health, and no health-related individual attributes.

medication dosing [32]. The use of the above-mentioned tools in qualitative and quantitative clinical research, such as in daily practice, could provide useful information about the relation among patient, disease and treatment, and the value and the real impact of different types of intervention on patients' long-term adherence and self-management of treatment.

Although the amelioration of the physician–patient partnership is essential for improving adherence, community pharmacies represent a promising platform for monitoring and enhancing therapy adherence and providing pharmaceutical care. In this sense, the activity performed in the Netherlands by the Medication Monitoring and Optimization (MeMO) program is of note. It starts with structured counseling sessions, with patients at the initiation and follow-up of chronic therapies. This process is followed by a continuous phase, in which patients' therapy adherence is monitored on a monthly basis using standardized search algorithms in the pharmacy database. When the algorithm detects a patient's discontinuation of therapy, tailored interventions are performed to improve adherence and optimize pharmacotherapy [33].

Strategies to implement new technologies

Altering the behavior patterns, first among physicians and then in their patients, may be difficult and time-consuming, and in general, published methods for achieving this goal are complex and

difficult to apply in the primary care setting because of time and other constraints [34].

The use of new technologies represents an unbelievable opportunity. Audiovisual inhaler reminders from the electronic monitor were compared to behavioral intervention; patient-friendly technology was found to be superior to a behavioral approach in improving adherence [35]. Considering that forgetfulness is one of the most common reasons for nonadherence to treatment, daily medication reminder system interventions, in the form of text messages, automated phone calls, and mobile device applications (APPs), can potentially address this problem. Five randomized controlled trials (RCTs) and one pragmatic RCT have been analyzed recently by Tran and colleagues [36[•]] that show how reminder system intervention was associated with greater levels of asthma medication adherence: no changes in asthma-related quality of life or clinical asthma outcomes has been clearly documented.

WE ADVOCATE

Time constraints, insufficient care coordination among healthcare providers, and lack of automation are considered as crucial points in improving adherence to treatment [37]. In fact, the presence of a fragmented healthcare system contributes to creating barriers to medication adherence by limiting the healthcare coordination and the patient's access to care [38]. Moreover, prohibitive drug costs or co-payments also contribute to poor medication

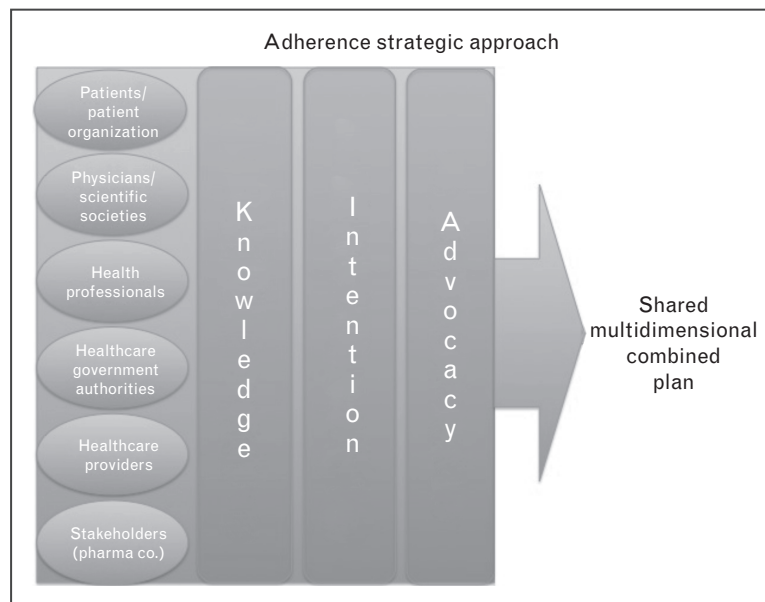


FIGURE 2. Adherence strategic approach. Players of the adherence process should analyze the available knowledge, define their own intentions, and advocate partnership in order to share a multidimensional combined plan.

adherence [39] and health information technology is not widely available yet, preventing physicians from easily accessing information from different patient-care-related venues, which in turn compromises patient care, timely medication refills, and patient–physician communication.

In order to address the above-mentioned issues, the Manifesto claims partnerships to implement adherence to treatment. Government authorities, patient organizations, scientific societies, non-governmental organizations, stakeholders, and all the other actors involved in the adherence process are called to work together, shuffling and integrating different perspectives, in order to find a feasible solution to the problem of nonadherence (Fig. 2). In this sense, research activities such as the Patient Adherence Project (PAP) [19²²] and the Patient Educational Plan [39] developed at a national level or the ‘Adherence, frailty, integrated care and multi-chronic conditions’ framework under development in the contest of the European Community Horizon 2020 project may provide a great opportunity in the future (<http://ec.europa.eu/research/participants/portal/desktop/en/opportunities/3hp/topics/hp-pj-04-2014.html>).

CONCLUSION

The ‘Manifesto on Adherence to asthma treatment in respiratory allergy’ draws attention to the crucial aspects of adherence in asthma management. This review integrates knowledge, intention, and advocacy, stressed by ‘Manifesto’, with new evidence published in the last few years. It becomes increasingly clear that single interventions could not be sufficient to improve adherence. Furthermore, strategies to ameliorate adherence should be tailored not only to disease burdens, but also to health-related and non-health-related individual attributes that contribute to a patient’s complexity. A concrete sharing of aims, actions, and strategies among the involved actors (patients, healthcare providers, institutions, and the pharmaceutical industry) represents the unique way to face the problem of nonadherence.

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Conflicts of interest

There are no conflicts of interest.

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