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The Seven Stages of Man: The Role of Developmental Stage on Medication Adherence in Respiratory Diseases



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Learning objectives:

1. To understand the different patient-related barriers to medication adherence at each developmental stage.
2. To understand the burden and impact of poor adherence for patients with respiratory disease.
3. To increase knowledge on the role of research in developing new adherence strategies.

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The circumstances and drivers of the decision to initiate, implement, or persist with a medication differ for individuals at each developmental stage. For school-age children with asthma,

the social environment of their family's cultural beliefs and the influence of peer networks and school policies are strong determinants of medication adherence. The stage of adolescence

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*Abbreviations used**COPD- chronic obstructive pulmonary disease**ICS- inhaled corticosteroid*

can be a particularly challenging time because there is a reduction in parental supervision of asthma management as the young person strives to become more autonomous. To illustrate the importance of such factors, adherence interventions in children and young adults with asthma have used peer-based supports and social supports, particularly social media platforms. In older patients, it is internal rather than external factors and age-related decline that pose challenges to medication adherence. Seniors face the challenges of polypharmacy, reduced social support, increased isolation, and loss of cognitive function. Strategies to promote adherence must be tailored to the developmental stage and respective behavioral determinants of the target group. This review considers the different attitudes toward medication and the different adherence behaviors in young and elderly patients with chronic respiratory conditions, specifically asthma and chronic obstructive pulmonary disease. Opportunities to intervene to optimize adherence are suggested. © 2016 The Authors. Published by Elsevier Inc. on behalf of the American Academy of Allergy, Asthma & Immunology. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>). (J Allergy Clin Immunol Pract 2016;4:813-20)

Key words: Medication adherence; Implementation; Initiation; Persistence; Elderly patients; Childhood asthma; Adolescents; Cognitive impairment

The European Union—commissioned “Ascertaining Barriers to Compliance” taxonomy for medication adherence outlines 3 key steps in a “temporal sequence” that patients must take to be adherent to their prescribed medication: initiation (picking up and taking a first medication), implementation (using it correctly, as prescribed), and persistence (sustained use).¹ As individuals develop and mature, their social environment, caregiver support, disease characteristics, and cognitive capabilities change dramatically. These factors modify a patient’s ability to manage medications and to adequately initiate, implement, and/or persist with the prescribed regimen.

In childhood and old age, suboptimal adherence to asthma and/or chronic obstructive pulmonary disease (COPD) treatment has important and serious consequences. Asthma is the most common chronic disease in children and a frequent cause of admission to hospital.² Poor adherence to controller therapy has a significant impact on children’s welfare, leading to increased school absence, impaired social development, as well as the clinical adverse effects of increased number of exacerbations.³⁻⁸ In the United Kingdom in 2012-2013, 15% of all asthma deaths were in children and poor adherence was evident in 48% of these cases.⁹

Asthma and COPD are both common conditions in the elderly, yet few studies have specifically investigated the reasons for suboptimal adherence to asthma and COPD treatments in this age group. Early studies indicate that around two-third of elderly patients with asthma or COPD have poor adherence with their inhaled corticosteroid (ICS) treatment, a rate strikingly

similar to that in the younger population.^{10,11} In older/elderly patients, the impact of nonadherence to respiratory medications includes increased rates of morbidity, health care expenditures, hospitalizations, and possibly mortality, as well as unnecessary escalation of therapy and reduced quality of life.^{12,13}

Although there is a substantial body of evidence on patient-level barriers and facilitators to medication adherence (see Dima et al’s article, “Mapping the asthma care process: implications for research and practice,”¹⁴ in this issue), there is a need for a single resource that synthesizes current understanding on how a patient’s life stage may impact the patient’s adherence behavior. Helping clinicians and researchers understand how age may affect patients’ ability to perform the necessary steps required to initiate and implement therapy, in order that they may also persist with it, can help guide more informed adherence decision making and targeted research. In this review, we discuss the determinants of medication adherence that are of particular consequence to children, adolescents, and the elderly, focusing specifically on patients with asthma and COPD.

ADHERENCE TO ASTHMA MEDICATIONS IN CHILDHOOD

Suboptimal adherence to asthma medications has been reported at each step of the adherence pathway. Studies have recorded noninitiation to inhaled therapy in 14% to 20% of children¹⁵ and even higher rates (50%) of noninitiation for those discharged from hospital after an exacerbation.¹¹ Studies using electronic monitoring devices to quantify therapy implementation in pediatric patients with asthma have also reported rates of less than 50%.¹⁶ In the case of asthma—primarily managed by inhaled therapy—observational studies have repeatedly reported poor inhaler technique in children and poor proficiency of inhaler administration by caregivers^{12,17-25} (for more information, see Braido et al’s article, “Trying, but failing’ — the role of inhaler technique and mode of delivery in respiratory medication adherence,”²⁶ in this issue). Even in the more closely monitored interventional clinical trial setting, long-term persistence among children to asthma medications has been shown to drop quite dramatically over time, from around 78% at 3 months to 50% by 2 years.²⁷ Thus, children with asthma demonstrate suboptimal initiation and implementation of inhaled therapies, and poor persistence over the longer term.

DETERMINANTS OF ADHERENCE TO ASTHMA MEDICATION

School-aged children

“Then, the whining school-boy with his satchel

And shining morning face, creeping like snail

Unwillingly to school”²⁸

The social environment for school-age children (5-15 years) primarily consists of their family and peer networks at school, both of which have been shown to affect medication adherence.^{27,29,30} Caregiver attitudes derived from cultural and religious beliefs are strong determinants of medication adherence.³¹ If caregivers have concerns about the side effects of a medication that outweigh their perception of its benefit, they are less likely to administer the medication.^{32,33} Beliefs about the efficacy of the

medication or a misunderstanding about how the medications work may impact both the initiation and persistence phases of adherence. A caregiver may administer medication for the minimal time believed necessary during an exacerbation, but not persist as prescribed thereafter. In addition, depression among caregivers has been shown to have a negative effect on medication adherence among the children they care for and on their overall levels of asthma control.³⁴

With respect to peer networks and school environments, children report concerns of stigmatization of their asthma when they use an inhaler in public. Missing school activities and inability to partake in sports can negatively affect children's emotional state and medication adherence, in particular their adherence to ICS controller therapy.³⁵ School policies or lack of care coordination can result in children having limited access to asthma medications during school hours.³⁶ Increased monitoring and direct observation of medication use by school nurses has been shown to facilitate improved medication implementation.³⁷

Young children are known to have greater difficulty using inhaler devices correctly than do other older children. Spacers are recommended to improve drug delivery and reduce common inhaler technique errors in younger patients, but they are seldom used in practice.³⁸⁻⁴¹ Furthermore, spacer use, as well as inhalers, can add to the stigma around asthma treatment in older children and further reduce their motivation to implement and persist with prescribed therapy.³⁷ Ineffective inhaler use has important clinical consequences because it can negatively affect both the implementation and persistence phases of adherence (through perceived lack of treatment benefit by the child and/or the caregiver) and lead to suboptimal treatment outcomes and possible unnecessary escalation of therapy (eg, referral to severe asthma services, or increased medication dose) by the clinician.

Adolescents

“Full of strange oaths, and bearded like the pard,
Jealous in honour, sudden, and quick in quarrel,
Seeking the bubble reputation”²⁸

Adolescence is a developmental period that is marked by increased interpersonal conflict as individuals seek to separate from their parents and become more independent. It is not surprising, therefore, that medication adherence is a particular casualty during this stage of personal development as adolescents seek to take on more responsibility for their medications without parental monitoring and support. Research has demonstrated, across chronic illness groups, that medication adherence and clinic attendance decline significantly during adolescence.⁴²

There is a known paradox during adolescence with regard to medication adherence. During this time, the patients' knowledge and understanding about their disease and related medications improves, while their adherence to medication declines. One explanation is that adolescence is characterized by changes in reasoning and hypothetical thinking, which, in turn, can affect how information on medications and illness is received (and needs to be communicated) to help optimize adherence to therapy.⁴³ Unless the adolescent has been engaged and involved in the decision to use a medication, and his or her concerns have been addressed, initiation, implementation, and persistence will be at risk.

As adolescents begin to take on more responsibility for their medications, and as they establish autonomy and independence from their parents, they may become less motivated to take medications or may be more likely to forget them than when supervised by a caregiver. As parents begin to withdraw their support and supervision, persistence may fall.⁴² Frequently, this change in responsibility occurs without direct communication between adolescents and parents, which can lead to misassumptions about who is responsible, increased parent/child conflict, and subsequent lower adherence. In adolescence, other psychosocial influences, such as psychological distress, depression, family conflict, and substance abuse, correlate with poor adherence to medications.⁴⁴

THE ROLE OF HEALTH CARE IN FACILITATING ADHERENCE IN CHILDREN AND ADOLESCENTS

The organization of the health care system can influence medication adherence in school-aged children with asthma, with one obvious facilitator being good access to health care coverage. In the United States, for example, children have access to health insurance through Medicaid or state programs, which provide their medications free of charge, or for a nominal fee. Coverage also extends to preventive health care administered through a primary care physician. These features of childhood insurance plans permit continuity of care and offer an opportunity to optimize adherence to therapy in children. For these services to be most effective, it is important that providers use established asthma care guidelines, which recommend the use of objective asthma control questionnaires and ongoing inhaler instruction to improve adherence (all steps) and overall asthma control.⁴⁵

PRACTICAL ADHERENCE INTERVENTIONS IN CHILDHOOD ASTHMA

Adolescents represent a potentially rich resource for adherence research—their engagement in participatory research can help identify and inform developmentally relevant interventions.⁴⁶ The increasing technological sophistication of young adults, often exceeding that of clinicians and clinical investigators, suggests that technology-based solutions could offer a promising opportunity for targeting adherence interventions. Substantive improvements in important asthma outcomes in children, such as increased school attendance, were reported in association with the introduction of electronic reminders to prompt preventer therapy use.⁴⁷ This type of intervention may help children to improve the implementation aspect of their medication adherence, particularly if accompanied by an inhaler technique assessment. Further work is required to understand how best to implement and sustain technology-based adherence interventions in the longer term and in larger populations.

Given the important role that peers play in adherence with childhood asthma therapies, many studies have investigated the potential for peer support to enhance adherence^{43,48,49}; some such studies have demonstrated benefits in terms of improved asthma-related outcomes.^{50,51}

The school environment represents another opportunity to support improved adherence. Schools are places of learning where new skills are taught and developed and, as such, may have a role to play in supporting the delivery of asthma self-management interventions.⁵² Previous research has shown that multilevel interventions that work with both schools and families

can be effective in managing asthma.⁵³ Given that children spend a majority of their day at school, it is imperative that school staff are well trained and prepared to manage asthma symptoms that may arise. Appropriate staff training and access to medications may prevent asthma worsening and poor outcomes.

Asthma is the second most common reason for health care utilization in young adults in America, beaten only by trauma-related events.³¹ Mortality rates among adolescents and young adults (ages 16-21 years) with asthma are 7 times higher than among younger children with asthma. These higher mortality rates may be the result of less frequent use of primary or preventative health care among adolescents and young adults, and/or lower rates of prescription refills and higher use of emergency departments as a substitute for primary care asthma management (particularly among minority groups).

Research in other chronic illness populations has shown that guideline-specific health care transition services (from pediatric to adult care) are associated with reduced medical complications, improved patient-reported outcomes, greater adherence to care, improved continuity of care, positive patient experience, and lower cost.⁵⁴ However, despite the positive effect of transition practices on outcomes, there has been limited focus on the health care transition from pediatric to adult care in asthma.⁵⁵

ADHERENCE TO RESPIRATORY MEDICATIONS IN OLDER PATIENTS

“His youthful hose, well saved, a world too wide
For his shrunk shank, and his big manly voice,
Turning again toward childish treble, pipes
And whistles in his sound.”²⁸

Determinants of respiratory medication adherence in older patients

At present there is little research investigating the specific patient barriers and facilitators to adherence in seniors with asthma and COPD, representing a significant and important gap in the literature. Studies have shown that older people tend to have strong medication views, including distrust of potential side effects, concerns over reduced effectiveness over time (resulting in a desire to postpone taking medications until they are required), concerns over addiction and medication dependency, and a dislike of the burden associated with taking large numbers of medications.⁵⁶⁻⁶³

A number of features distinguish elderly patients from their younger counterparts and can impact their decision to adhere to asthma and COPD treatments. Advanced age often brings multiple comorbidities, multiple medications, and, for many, cognitive deficits, which make medication adherence particularly problematic.⁶⁴⁻⁶⁷ Where cognitive impairment is present, patients may be confused as to why, how, and when to use different treatments. Indeed they may simply forget to take treatments. Moreover, poor motivation and apathy with respect to disease management is common in the elderly perhaps due to fatalism or accepting decline in functionality as part of the normal aging process.

Loss of a partner and poorer mobility may reduce social support, increase isolation, and reduce access to health care



FIGURE 1. Medication hoarding, a consequence of poor adherence. An example of the consequences that arise from poor health literacy and poor patient and physician communication. This photograph was taken in a patient's home by a health care worker visiting a patient with COPD. The patient who had government-funded medications was confused by changing prescriptions between primary and secondary care. He reported being unable to discuss his concerns with either provider and hence simply did not take his medications (photo courtesy of Ms Brenda Deering).

services, all of which can impact the patient's ability to initiate, implement, and persist with prescribed treatments. For a proportion of patients, diagnostic confusion can be an important barrier to adherence. A history of childhood asthma and adult smoking may result in mixed disease in old age⁶⁸ (partially reversible or fixed airflow obstruction and evidence of atopy) and a history of apparently contradictory diagnoses that leave the patient unsure as to the appropriateness of prescribed treatment⁶⁹ and disinclined, or less able, to self-manage their disease.⁷⁰ Furthermore, there are important age-related changes to the structure and function of the respiratory system and a poorer response to treatment that can negatively affect clinical outcomes and confidence in therapy in elderly patients with respiratory problems. These changes contribute to more frequent exacerbations and higher mortality rates in older populations with asthma and COPD and are likely to influence medication adherence negatively as a result of poor perceived treatment effectiveness.⁷¹ This is compounded by a poorer perception and/or habituation to asthma symptoms in older patients with respiratory problems, especially those with long-standing disease.⁷²

One facilitator of adherence in the elderly (as in children) is the availability of reduced cost or free medication, but suboptimal implementation and poor persistence in elderly populations appears to manifest itself by accumulation of unused medication or “hoarding.” An example of medication hoarding is shown in [Figure 1](#). Hoarding of medications underscores that pharmacy refill records may not accurately identify poor adherence.

ROLE OF PATIENTS-HEALTH CARE PROFESSIONAL INTERACTIONS IN FACILITATING ADHERENCE IN THE ELDERLY

Although health care for patients older than 65 years is provided at no or low cost in many countries, such provision does

not necessarily guarantee consistent access to a single health care provider.⁷³ It is plausible that this poor continuity of care may negatively affect respiratory medication adherence. For example, in one study, patients with a single medication prescriber had 30% higher medication persistence than did those with 4 or more prescribers.⁷⁴ Older patients may benefit from access to one health care professional that they trust and who can repeat and reinforce consistent care recommendations to improve motivation and adherence.⁷⁵

Clinicians must be sure to appropriately treat airway inflammation in seniors with asthma and COPD who may be at great risk for lung function decline with undertreatment due to their advanced age. It appears that clinicians may avoid prescribing certain treatments because of diagnostic uncertainty or concerns about safety in seniors, particularly where clinical drug trials have not included elderly populations. Indeed, a Canadian study in those older than 65 years with asthma showed that prescribing of ICS was as low as 40% after an acute exacerbation and lower still in those 80 years or older.⁷⁶

The communication style used by health care professionals (eg, use of technical terms or differences in cultural backgrounds between patients and health care workers) can also affect interactions and medication adherence in older patients.⁷⁷ Furthermore, failing to appreciate the attitudes and health beliefs of older patients can make patients feel that their concerns are not being recognized or addressed. Shared decision making is often underused in therapeutic decision making with seniors, but it can play an important role in patient engagement if it is appropriately tailored to account for possible lower health literacy and/or coexisting cognitive impairment.

ROLE OF THE FAMILY UNIT AND SOCIAL CARE

Evidence suggests a significant relationship between adherence and family cohesion and/or social support. In a meta-analysis of studies that included those in elderly populations, adherence was 1.7-fold higher in cohesive families and 1.5-fold lower in patients from families in conflict.⁷⁸ Marital status and living with another person was also shown to improve adherence modestly. Social support is thought to positively affect adherence behaviors by providing both practical and emotional support (facilitating optimism, self-esteem and protecting the patients from the stresses of being ill while reducing depression, and improving sick role behavior). Such factors may be particularly relevant in the elderly who, through comorbidity, loss, and poorer mobility, may have fewer or more restricted social networks.⁷⁸ Depression and consequently poor motivation are a particular factor that links these life events with poor adherence.⁷⁹

INDIVIDUAL CONSIDERATIONS IN OLDER PATIENTS WITH SUBOPTIMAL RESPIRATORY MEDICATION ADHERENCE

As in younger people, correct inhaler technique has an important role in determining adherence to inhaled therapies prescribed in the elderly (for more information, see Braido et al's article, "Trying, but failing" — the role of inhaler technique and mode of delivery in respiratory medication adherence,"²⁶ in this issue).⁸⁰⁻⁸⁴ Specific inhaler handling errors and poor technique in the elderly can diminish the effective delivery and benefit of treatment and reduce patient's perception of treatment effectiveness and motivation to persist. Elderly patients with advanced

COPD, for example, often have considerable lung hyperinflation and limited ability to generate sufficient inhalational airflow to achieve adequate drug delivery if prescribed a dry powder inhaler. Mild cognitive impairment in patients with COPD (prevalence up to 50% in some studies) or asthma can lead to failures in forward planning and to difficulty in implementing learned tasks.^{85,86} These individuals may quickly forget both how and when to use their inhaler,⁸⁷ and may more readily remember what they have been told *not* to do rather than what they *should* do. Factoring such considerations into education for seniors and tailoring training styles to accommodate cognitive impairment is therefore important.

PRACTICAL ADHERENCE INTERVENTIONS IN OLDER ADULTS

Every step of the adherence pathway is a dynamic process benefiting from regular medication reviews. Nonadherence is a significant determinant of poor control; linking and triangulation of prescribing records (and prescribing and pharmacy dispensing records) can help to identify suboptimal adherence and provide an opportunity to engage the patient and to positively affect adherence.⁸⁸

Clinicians can help to improve adherence in their patients by understanding patients' individual treatment aspirations and tailoring management and management expectations accordingly. Indeed, 2 randomized controlled studies conducted in seniors with asthma compared patient-centered, tailored asthma education (active group) with standard written information or usual care (control) and found that tailoring education improved asthma control and other outcomes such as quality of life or self-care confidence.^{72,89} One of the studies measured adherence and showed a trend toward, but not statistically significantly, better adherence in the intervention versus control group.

The use of appropriate communication skills for adherence is critical.⁹⁰ It is important to ensure the patient does not feel threatened by the clinician. It is better to frame the conversation in such a way that rather than expecting full adherence, suboptimal adherence is regarded as "normal" and that the clinician targets information at the health literacy level of the patient—Assessment of medication adherence should be incorporated into structured clinical reviews such as the holistic SIMPLES (Smoking status, Inhaler technique, Monitoring, Pharmacotherapy Lifestyle, (patient) Education, Support) assessment approach,⁹¹ and potentially integrated into future technology-based solutions to suboptimal adherence to asthma and COPD medications.⁹²

From a community pharmacy perspective, pharmacists can play an important role in optimizing respiratory medication adherence, particularly by reviewing and teaching inhaler technique when patients refill their prescriptions. The pharmacist's role in shared decision-making approaches, however, may need to be adapted for elderly patients because seniors may prefer to depend solely on their physician's advice. However, as the penetration of smartphone devices into the older population increases, the opportunities for interventions that use these technologies, as in younger patients, will increase.

Although more research is needed into the most effective approaches for optimizing medication adherence in seniors with asthma and COPD, Table 1 summarizes a number of practical opportunities (recommended by the authors of this review) for health care practitioners to intervene to support medication adherence.

TABLE 1. Future adherence research needs in relation to age-related determinants of respiratory medication adherence

Childhood and adolescence
<ul style="list-style-type: none"> • “Getting the narrative right”: Assessment of effective communication styles (and health care professional training in them) for supporting adherence • Understanding how to develop and tailor effective adherence interventions that actively engage children (and carer(s) of younger children) • Development of a “behavioral taxonomy” to characterize the role of the parent in optimizing adherence
Adolescence
<ul style="list-style-type: none"> • Assessment of transition-to-adult-care approaches, their effect on medication adherence, and opportunities for improvement • Evaluation of effective adherence support mechanisms for adolescents (online, friends, teachers, general practitioners)
Elderly patients
<ul style="list-style-type: none"> • Investigate the specific attitudes toward medication use and the adherence behaviors of seniors with asthma and COPD • Development of interventions that tackle the adherence barriers specific to older patients (eg, cognition, polypharmacy, and immobility) • Identification of methods for ongoing inhaler technique support outside the professional health care environment • Evaluation of the role of multiple inhaler types prescribing on medication adherence • Evaluation of the role of electronic monitors and reminders for missed doses in elderly patients with COPD • Evaluation of the role of secondary care experiences on medication adherence (ie, direct-to-ward vs to ward via the emergency room)

FUTURE RESEARCH NEEDS IN THE UNDERSTANDING OF AGE-RELATED DETERMINANTS OF RESPIRATORY MEDICATION ADHERENCE

There are many outstanding needs to improve the research understanding and clinical implications and opportunities of medication adherence in asthma and COPD, at both ends of the age spectrum (see Table 1). Most studies outlined above suggest that determinants of medication adherence are likely to differ between age groups and vary between the different steps of the adherence pathway (initiation, implementation, persistence), but well-designed studies are required to confirm and further explore these assertions. There is a particular need for research into the determinants of adherence in elderly patients with respiratory disease and to identify effective adherence interventions in this age group. In adolescents with asthma, there may be significant gaps in access to effective adherence support given the cognitive and developmental changes of this age group as well as the disruptive transition into adult care, and more research is needed to quantify and qualify the additional risk faced by this age group and to mitigate accordingly.

Across all age groups, research is required to identify the barriers and facilitators specific to initiation, implementation, and persistence adherence. The emergence of ever more sophisticated and reliable measurement tools (eg, electronic monitoring devices and linked electronic medical records) may help in this end.

A key requirement for successful implementation of adherence interventions in everyday clinical practice is demonstration of both clinical effectiveness and cost-effectiveness; future studies should be designed to answer both questions and avoid unnecessary barriers to uptake. The most valuable interventions are likely to be those that are “scalable,” that is, complex enough to be effective, but also simple enough for feasible delivery in routine clinical settings. Expensive, complicated, multifaceted interventions that use specialized research teams should be carefully reviewed for ultimate feasibility before work is undertaken.

CONCLUSIONS

This review highlights how nuanced the relationship between patient age and medication adherence can be and the myriad of different age-related considerations that should be taken into account to tailor management style and treatment choice to patients’ stage of physical and cognitive development (or decline). Strategies to promote adherence to medications should start by assessing age-related barriers to initiation, implementation, and persistence and tailoring treatment choice (eg, inhaler device) and consultation style to the health literacy level of the patient. Methods need to be refined for the ongoing monitoring of adherence, as well as for the effective targeting of interventions, at each adherence step and developmental stage (which will be dynamic over the course of a chronic respiratory condition) in each individual patient.

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