"Trying, But Failing" — The Role of Inhaler Technique and Mode of Delivery in Respiratory Medication Adherence

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Overall Purpose/Goal: To provide excellent reviews on key aspects of allergic disease to those who research, treat, or manage allergic disease.

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Learning objectives:

1. To improve understanding of the discrete components within clinical care that contribute to "good" medication adherence.

2. To understand some of the characteristics of patients with asthma and COPD (and differences between) associated with preference for different inhaled treatment regimens.

3. To improve knowledge of how to tailor different treatment regimens (frequency of delivery, mode of delivery, delivery device) to individual patients.

4. To improve understanding of markers of suboptimal medication adherence that offer opportunity for intervention ahead of referral to specialist care.

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Inhaled therapies are the backbone of asthma and chronic obstructive pulmonary disease management, helping to target therapy at the airways. Adherence to prescribed treatment is necessary to ensure achievement of the clinician's desired therapeutic effect. In the case of inhaled therapies, this requires patients' acceptance of their need for inhaled therapy together with successful mastery of the inhaler technique specific to their device(s). This article reviews a number of challenges and barriers that inhaled mode of delivery can pose to optimum adherence—to therapy initiation and, thereafter, to successful implementation and persistence. The potential effects on adherence of different categories of devices, their use in multiplicity, and the mixing of device categories are discussed. Common inhaler errors identified by the international Implementing Helping Asthma in Real People (iHARP) study are summarized, and adherence intervention opportunities for health care professionals are offered. Better knowledge of common errors can help practicing clinicians identify their occurrence among patients and prompt remedial actions, such as tailored education, inhaler technique retraining, and/or shared decision making with patients regarding suitable alternatives. Optimizing existing therapy delivery, or switching to a suitable alternative, can help avoid unnecessary escalation of treatment and health care resources. **(J Allergy Clin Immunol Pract 2016;4:823-32)**

Key words: *Adherence; Implementation; Initiation; Persistence; Inhaler device; Inhaler technique; Patient preference*

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Abbreviations used
BAI- breath-actuated pressurized metered-dose inhaler
COPD- chronic obstructive pulmonary disease
DPI- dry powder inhaler
iHARP- Helping Asthma In Real People
ICS- inhaled corticosteroid
pMDI- pressurized metered-dose inhaler
RCT- randomized clinical trial
REALISE- REcognise Asthma and LInk to Symptoms and Experience

Inhaled therapies (bronchodilators ± anti-inflammatory therapy) are the cornerstones of obstructive lung disease management approaches.[1,2] The aim of inhaled therapy is to deliver agents directly to the lungs, thereby offering a more rapid onset of action and a lower required dose than systemic administration, minimizing the potential for treatment-related adverse effects. Adherence to obstructive lung disease therapies involves patients initiating their prescribed therapy, implementing it as prescribed (ie, correctly administering the prescribed dose at the physician-directed frequency), and persisting with treatment. Also central to the therapeutic benefit of inhaled therapies is their successful administration, which requires patients to have knowledge and understanding of (and ability to implement) the appropriate inhaler technique required to optimize both the dispensed and administered doses.[3,4]

A wide range of different devices are used to deliver short- and long-acting bronchodilators and inhaled corticosteroid (ICS) drugs (alone or in combination) for the management of asthma and chronic obstructive pulmonary disease (COPD).[1,2] Device types include pressurized metered-dose inhalers (pMDIs), used either alone or attached to spacers or valved holding chambers; breath-actuated pressurized metered-dose inhalers (ie, BAIs); dry powder inhalers (DPIs); or soft mist inhalers. There are more than 200 drug-inhaler device combinations (branded items and generic versions of existing brands) available.[5] The wide variety of inhaler devices available simultaneously presents both opportunities and challenges for patients and prescribers. Each class of device (pMDI, BAI, DPI, soft mist inhaler) is associated with a different approach to inhalation and, in turn, each device within those classes may request specific nuances to the general handling and inhalation technique to optimize delivery and administration. pMDIs, for example, dispense a standardized dose on depression of the canister and require the patients to coordinate the timing of the canister depression and their inhalation. BAIs try to minimize potential coordination errors between the timing of the actuation and breath intake by using the power of the patient's breath to trigger the actuation. Breath control is also key to the successful delivery of pMDIs (whether breathe-actuated or not) as inspiratory flow combines with the energy of the pressurized dose delivery and, if too rapid, can result in oropharangeal deposition of the medication, rather than its delivery to the lungs. In contrast to pMDIs and BAIs, DPIs do not contain a propellant and use the patients' inspiratory flow as both the trigger and the actuation energy for the dispensed dose. While DPIs therefore avoid the coordination issues presented by pMDIs, the fact that they are inspiratory flow—driven means that the dispensed dose is also flow dependent. Furthermore, for each DPI there is a minimum inspiratory flow required to achieve successful dispensing of the prescribed therapeutic dose, something that may present a challenge for patients with compromised lung function, particularly during an exacerbation or, more generally, among elderly patients with COPD and young children with asthma. Inhaled volume is more important for capsule DPIs because the dose needs to be emptied from the capsule during the inhalation.[6] Moreover, a dispensed dose does not equate to a delivered (or administered) dose. Delivery also requires the volume of therapy leaving the device to reach its target—the lungs—requiring appropriate breath control, achievement of which varies substantially between different devices and device types (eg, slow vs sharp; breath-hold).

As such, even when patients are accepting of their treatment, and complicit in its initiation, their ability to implement the prescribed regimen successfully (which has inherent implications for treatment persistence) is dependent on their mastery of the specific inhaler-handling requirements (device positioning/priming, actuation coordination, inspiratory flow rate, and breath control) of their prescribed device(s). The situation is further complicated by the common use of different inhaler device types for reliever and preventer therapies, requiring patients to master (and maintain mastery of) multiple techniques.[6]

Inadequate inhaler instruction and poor inhaler technique represent one of the key determinants of asthma medication adherence identified by the Assessment of the Safety in LABAs in Asthma in Routine Care by combining Health-care databases and direct patient follow up (ASTRO-LAB) through its extensive review of the asthma adherence literature.[7] This article considers the implications of mode of delivery of asthma and COPD therapy on medication adherence (and possible outcomes), in particular the challenges medication inhalation poses to successful implementation of treatment. A number of possible approaches to identifying and addressing inhaler device errors are also suggested.

INHALED THERAPY—"TRYING, BUT FAILING"

The Ascertaining Barriers to Compliance taxonomy for medication adherence was commissioned by the European Union to standardize adherence-related terminology for clinical and research use.[8] It proposes a transparent nomenclature that subdivides the traditional singular overarching research concept of "adherence to medication" into 3 distinct elements, specifically medication (1) initiation, (2) implementation, and (3) persistence. The subdivision summarizes the sequence of events within the medication process that have to occur for patients to take their prescribed medication(s) successfully and consistently (see Figure 1).[8] Each element of the adherence pathway may potentially be affected by prescribed mode of therapy delivery.

Treatment initiation

Although it is often assumed that patients (at least) commence therapy as prescribed, a community-based study of initiation rates of chronic disease medications found that 28% of prescriptions issued to adults for new chronic disease medications were never dispensed and approximately one-quarter of patients prescribed new asthma therapy failed to collect their first prescription.[9]

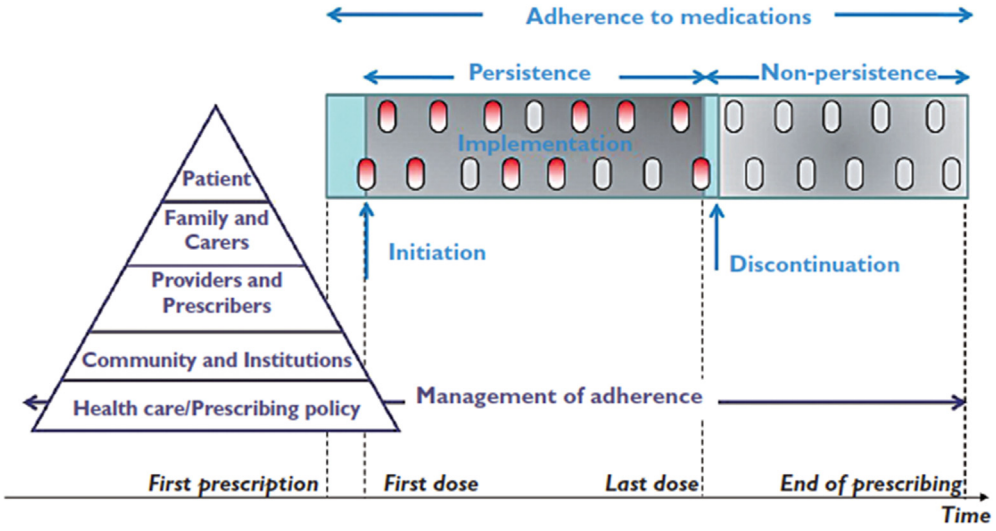


FIGURE 1. Illustration of the 3 key temporal steps involved in medication adherence. Reproduced from Vrijens et al,[8] with permission from the publisher.

In the routine care management of asthma and COPD, treatment initiation can be affected by a range of psychological and practical barriers, among them denial of diagnosis, disease awareness, lack of trust in health care professionals, medication fears, cognitive ability, affordability, and access to therapy.[10-12] In the context of asthma and COPD, mode of therapy delivery can introduce an additional obstacle. Inhaled therapies are the backbone of asthma and COPD management, but there can be substantial stigma around the use of medication inhalers, particularly in certain age and cultural groups. Inhaler stigmas can deter initiation in some and (if collected) subsequent implementation and persistence in others.[13] The recent REcognise Asthma and LInk to Symptoms and Experience (REALISE) Asia study, which assessed patients' perception of asthma control and attitudes toward treatment in a multinational Asian population, found that approximately half of all patients agreed with statements that having inhalers was "embarrassing" or "a nuisance." Patients with uncontrolled asthma, in particular, felt that it was an embarrassment (62.0%) or a nuisance (52.2%) to use or even carry (56.7%) an inhaler in public, representing real psychosocial barriers to initiation (and subsequent implementation and persistence) of inhaled therapy (see Table I).

Treatment implementation and persistence

Although treatment implementation and persistence are 2 distinct concepts—the first relating to the longitudinal accuracy of administration of the prescribed dosing regimen over time and second to the event of therapy discontinuation—these are closely linked when considering the potential implications of therapeutic delivery approach in asthma and COPD. The more challenging the patients find the mode of delivery of their maintenance therapy, the greater their potential barriers to successful implementation (administration and successful delivery) and, in turn, the greater the potential for diminished treatment outcomes.[14,15]

Inhaled medication. When it comes to the management of asthma and COPD, the primary mode of medication delivery is via inhalation. Therefore, in considering successful medication adherence in a holistic way, this requires patients not only to initiate and persist with their prescribed therapy but also to implement it successfully: at the appropriate dose and dosing frequency. This necessitates an understanding of the medication prescribed and the ability to use the inhaled medication correctly.

The REALISE Asia study[13] revealed a distinct lack of understanding of the details and requirements of their treatment regimen: a fundamental necessity to successful implementation and an obvious barrier to successful medication management. More than half (53%) of REALISE Asia patients were aware of the need to use con-troller inhaler regularly to help manage their asthma, but when asked about their controller inhalers only 20% of the patients were able to identify them correctly (31% identified them incorrectly, and the rest did not know). Of those who answered correctly, only 30% reported daily use of their controller inhalers.

To compound the problem, despite continual inhaler redesign and refinement, incorrect (and inadequate) inhalation technique persists,[16-19] resulting in suboptimal medication implementation and compromised asthma and COPD treatment outcomes.[20] In a review of 21 studies of pMDI use, the prevalence of poor inhaler technique ranged from 14% to 90% (with an average of 50%).[21] Furthermore, the use of multiple inhaler devices in an individual patient has been shown to be associated with a higher prevalence of errors than the use of single devices.[22]

The international Implementing "Helping Asthma in Real People" (iHARP) initiative is the largest evaluation of routine care inhaler technique conducted in asthma to date. A total of 5000 structured inhaler technique assessments were undertaken in patients with moderate-to-severe asthma receiving fixed-dose combination ICS and long-acting beta-agonist therapy across 8 participating countries (the United Kingdom, France, Italy, Spain, Sweden, Norway, Australia, and the Netherlands).[23]

The structured inhaler technique assessment was part of a wider iHARP asthma review that included patient questionnaires, lifestyle and current asthma control assessments (including factors that may have an impact on asthma control), and a structured inhaler

TABLE I. Patients' attitudes toward inhalers/inhaler therapy in the REALISE Asia study[12]

Patients who strongly agree or tend to agree with the following statements, n (%)	Overall (N = 2467)	GINA-defined asthma control		
		Controlled (n = 440)	Partially controlled (n = 802)	Uncontrolled (n = 1225)
I feel embarrassed using my asthma inhaler in front of others	1162 (52.5)	140 (40.2)	328 (44.5)	694 (62.0)
I find it a real nuisance having to use my inhaler	1189 (48.2)	187 (42.5)	363 (45.3)	639 (52.2)
I feel embarrassed carrying my asthma inhaler around with me	1294 (47.1)	177 (31.8)	357 (40.9)	760 (56.7)
I ignore my doctor's instructions about when and how often to take my medication (inhaler)	895 (36.3)	101 (23.0)	246 (30.7)	548 (44.7)
I find my inhaler difficult to use	766 (31.1)	109 (24.8)	216 (26.9)	441 (36.0)

GINA, Global Initiative for Asthma.
Reproduced from Price et al,[13] with permission from the publisher.

technique review and inhalation education and retraining, as appropriate. Frequency and inhalation errors were categorized for patients prescribed fixed-dose combinations of a bronchodilator and ICS therapies, formulated in a Diskus or Turbohaler, or pMDI (fluticasone propionate and salmeterol combination; Seretide) with or without a spacer. Analysis of the data revealed a high prevalence (90%) of inhaler technique errors (≥1 error) across all devices: 84% for their Diskus, 91% for Turbohaler, 92% for pMDI, and 91% for the pMDI when used with a spacer. More than 20% of the patients demonstrated at least 4 errors when using their controller inhalers.[24] The 12 most common errors recorded among Diskus users in the iHARP initiative are summarized in Table II. Absence of an inhaler technique review in the previous year was identified as a predictor of error performance among Diskus users, as were asthma-related hospitalization in the previous year, obesity, poor asthma control the previous 4 weeks, and female sex.[25]

Further to this lies a potentially more complex relationship and the clinical significance of inhaler technique errors should not be overlooked. In asthma, research suggests that higher patient satisfaction with their asthma inhaler device is a significant predictor of more favorable clinical outcomes.[26] In a prospective patient and physician survey conducted to evaluate the relationships between asthma outcomes, patient-reported satisfaction with their inhaler device, and physician-reported adherence, more favorable clinical outcomes were significantly associated with greater inhaler satisfaction ($P = .002$) and higher medication adherence ($P = .049$). Attributes associated with device satisfaction in the study included patient perceptions of consistency in the amount of drug delivery to the lungs, ease of use, and feedback about the number of remaining doses.

A similar association between inhaler satisfaction, medication implementation, and clinical outcomes has also been observed in COPD.[27] A multinational real-world survey of clinicians (respiratory specialists and primary care physicians) and patients with COPD (n = 1443) found that patients' overall satisfaction with their maintenance inhaler was significantly associated with their medication implementation (as assessed by their physicians). Patient-reported ease of inhaler use was among the factors that influenced patients' satisfaction with their maintenance therapy delivery device. Significant associations were observed between increasing treatment compliance and fewer exacerbations and hospitalizations. A direct association between inhaler satisfaction and fewer exacerbations was also reported.[26] These results are consistent with research that suggests that motivation for good inhaler technique may be a key factor in long-term correct use.[15]

TABLE II. The 12 most common DPI Diskus errors recorded in the iHARP study[22]

1. Did not slide cover fully open
2. Dose lost after preparation because of holding downward
3. Shook inhaler device after dose preparation
4. Did not breathe out to empty lungs
5. Exhaled into the inhaler before inhalation
6. Did not put Diskus in mouth and seal lips around mouthpiece
7. Did not have head tilted such that chin is slightly upward
8. Insufficient inhalation effort (inhalation is not fast, forceful from the start, and as long as possible)
9. Did not inhale through mouth
10. No breath-hold follow inhalation (or holds breath for <3 s)
11. Patient had expired inhaler or empty inhaler
12. After inhalation did not replace cover

Inhaler device "switching". With the recent and future expiration of patent protections for several longstanding ICS and bronchodilator therapies has come the development of bioequivalent, generic inhaled drugs and the potential for established users of branded inhaled drugs to be switched to generic formulations. Switching can lead to the use of new and/or multiple inhalers and, consequently, new challenges and barriers to effective dose administration and medication implementation.[28-30] Such possibilities will need to be countered by thoughtful training, retraining, and ongoing education to avoid loss of disease control and stability and recognition that switching asthma therapy without an accompanying consultation has been shown to lead to worsening asthma outcomes.[31]

Inhaler device "mixing". Because many patients with asthma and/or COPD are prescribed both inhaled reliever therapy (ie, short-term bronchodilators for symptom relief) and inhaled maintenance therapy (eg, corticosteroids and/or bronchodilators for long-term risk management), the implications of "device mixing" (ie, the prescription of >1 inhaler device type for a single patient) must be considered. Good medication

PATIENT HISTORY

- **Sex:** Female
- **Age:** 56 years
- **Housewife:** Housewife
- **Smoking status:** current smoking
- **Familial:** yes
- **Clinical history:** asthma, bronchitis, COPD (not proven)
- **Atopy:** fog, paint air, perfume air, exertion
- **Exacerbations:** 2 (last year)
- **Disease time course:** since age of 25
- **Medical treatment:**
  - Formoterol 12 ug 2dd1,
  - Ipratropium 20 ug 3dd1
  - Inhaled corticosteroid 400 ug 2dd1

Adherence: uses medication occasionally
Inhalation technique: 4 essential errors instruction given

CLINICAL QUESTIONNAIRE SCORES

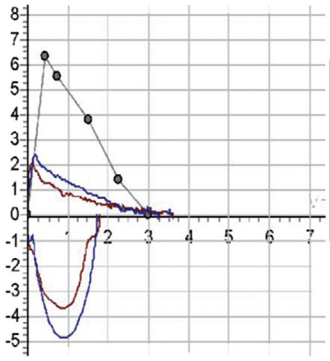
COPD Clinical Questionnaire (CCQ)
Total: 4.8

CCQ1	short of breath at rest	5
CCQ2	short of breath at exertion	6
CCQ3	concerned	5
CCQ4	depressed	6
CCQ5	cough	3
CCQ6	produce phlegm	3
CCQ7	strenuous physical activities	6
CCQ8	moderate physical activities	5
CCQ9	daily activities at home	5
CCQ10	social activities	4

Asthma Control Questionnaire (ACQ)
Total: 4.8

ACQ1	how often wake up at night	5
ACQ2	symptoms in the morning	5
ACQ3	limit of usual activities	5
ACQ4	short of breath	6
ACQ5	wheezing	2
ACQ6	using of rescue medication	2

Medical Research Council (MRC score)
Total: 5



Parameter	Ref.	Pre bronchodilator	% Predicted	Post bronchodilator	% Predicted	% Change
FVC (L)	3.01	3.61	120.2	3.58	119.0	-1.0% (-0.04)
FEV1 (L)	2.56	1.17*	45.6	1.49*	58.4	28.2% (0.33)
FEV1/FVC (%)	78.5	32.2	41.1	41.7	53.2	29.4% (9.5)
PEF (L/s)	6.35	2.10*	33.1	2.39*	37.7	13.9% (0.29)

A CASE OF POOR ICS IMPLEMENTATION ESCALATED TO A SEVERE ASTHMA CLINIC

FIGURE 2. Pre and post bronchodilator spirometry: severe obstructive pattern with significant response to short acting beta 2 agonist.

implementation in the context of multiple devices requires patients to master (and maintain mastery of) more than 1 inhaler technique successfully, something that is further complicated if different classes of device are involved. Indeed, a negative association has been shown between maintenance inhaler number and patients' medication implementation (patients prescribed $\geq$2 maintenance inhaler devices have been shown to be 34% less likely to be "adherent" and to have a 40% higher treatment discontinuation rate than are patients taking a single long-acting inhaled drug),[32] and use of mixed/different inhaler device types for maintenance and reliever therapies is associated with higher rates of severe exacerbations and lower odds of achieving asthma control in patients with asthma initiating ICS therapy.[33]

To mitigate against such challenges in the future, new generations of devices aim to limit the number of inhaler maneuvers necessary and try to support successful administration through visual and auditory feedback systems. In addition, several device manufacturers have developed an inhaler device that will serve as a standard "platform" for all the drugs commercialized by the company, enabling flexibility in terms of drug, and drug dosage, while retaining a standardized inhaler tool across the inhaled therapy portfolio. However, the availability of reliever therapies (eg, salbutamol) in these devices remains limited owing to a lack of commercial viability resulting from regulation of short-acting beta-agonist drug costs.

Oral medication. The challenges patients face in successfully implementing inhaled therapy can be inferred from the results of Price et al's[14] pragmatic single-blind randomized controlled trial and economic evaluation of the use of leukotriene receptor antagonists (LTRAs) in primary care at steps 2 and 3 of the national asthma guidelines (the ELEVATE study, a pragmatic single-blind randomized controlled trial and economic evaluation of the use of leukotriene receptor antagonists in primary care at steps 2 and 3 of the national asthma guidelines). At the primary 2-month outcome period, initiation of LTRAs was equivalent to guideline-recommended ICS therapy in terms of the primary outcome Mini Asthma Quality of Life Questionnaire. By the 2-year secondary outcome period, although true equivalence was not shown, no significant differences were found between LTRAs and ICS for any of the primary or secondary outcome measures.

One of the likely reasons the ELEVATE authors offered for the equivalence finding was the higher rate of adherence to LTRA compared with ICS therapy (median adherence rates of 65% and 41%, respectively). Although ICS is more efficacious than LTRA therapy when implemented optimally in randomized clinical trials (RCTs) environment,[14] the ELEVATE data suggest that starting anti-inflammatory therapy as LTRA is noninferior to ICS when initiated with a less onerous ecology of care than used in classical RCTs. As such, LTRA could be considered as a possible alternative to initiating anti-inflammatory therapy as ICS in patients with asthma, particularly in those with a noted preference for oral over inhaled therapy and/or who struggle to master inhaler device technique.

Dosing frequency. Understanding patient preference is not only important with respect to mode of therapy delivery but also when considering frequency of administration because both are integral to successful medication implementation.[34] Some studies

- **Improved understanding of how adherence and inhaler technique are conceptually related, including:**
  - Longitudinal adherence studies designed to explore the effect of prior clinical contacts and healthcare resource utilization on current and future adherence behaviors

- **Development of generic educational interventions that work across inhaler devices and device categories, including:**
  - Evaluation of the extent to which mode of therapy delivery affects medication implementation (e.g. what are "critical" inhaler errors) and (ultimately) persistence; which are specific to some inhalers versus common to all
  - Optimizing consultation skills & communication, establishing:
    - Establishing effective approaches to patient engagement, education and feedback
    - Understanding how best to tailor interventions to patient adherence behaviors and preference
  - Assessing the value of patient "advocates" in optimizing effective use of medication
  - Assessing the value of "cadence" and repetition of consistent messages across a range of healthcare professionals and healthcare settings to medication initiation, implementation and persistence.

- **Improved understanding of the point at which norms around medication use occur to inform the development of interventions appropriate for different disease stages and disease experiences, involving:**
  - Understanding levels of health literacy and patient interpretation of prescribing instructions
  - Evaluating the effect of mixed versus consistent device use in COPD and older patients with asthma.
  - Understanding the "trade-offs" the patient makes when taking medication to understand their motivation and behavior – benefit/risk ratios – to identify patients in whom adherence interventions might make a difference
  - Assessing the clinical benefit of regimen simplification (e.g. single versus multiple inhalers for the delivery of triple therapy in COPD)

FIGURE 3. Future research needs to support a paradigm shift in obstructive lung disease management—away from consideration of adherence and inhaler technique as discrete entities and toward a more integrated concept of "quality use of respiratory medications."

suggest that simplifying medication regimens, including reducing the frequency of dosing, may improve medication implementation.[35] Such considerations are of particular relevance in patients with comorbidities (and therefore generally more relevant in the management of COPD than asthma) who may already face challenges in coordinating dosing of coexisting therapies. Indeed, in a questionnaire-based assessment of dosing frequency prevalence in 3731 patients with asthma and 2138 patients with COPD, approximately half the patients in each cohort indicated a preference for once-daily controller therapy.[36] Across both asthma and COPD cohorts, preference for once-daily controller medication was significantly associated with poor implementation and higher medication-related concerns. Yet the drivers for patient preference appeared to vary between conditions, with preference for once-daily therapy in patients with asthma being associated with good control and low self-perceived controller medication need while, in contrast, preference among patients with COPD was associated with high self-perceived need for controller medication.

The study findings suggest that there are differences between people with asthma and those with COPD and, moreover, that inherent differences in the nature of asthma and COPD may influence patient perceptions (and behaviors) toward their prescribed therapies. Asthma symptoms are episodic and patients

can experience prolonged symptom-free periods. However, COPD symptoms are constant, progressive, and often debilitating. Furthermore, patients with COPD tend to have multiple comorbidities, which may mean that they are already on a complex cocktail of drugs and are keen to simplify their treatment regimen, where possible.

The limited evidence of the effect of dosing regimen on respiratory medication adherence suggests that once-daily administration may be associated with better implementation than twice-daily therapy in asthma.[35] This is consistent with observations in other chronic conditions, such as diabetes and HIV.[37] Such findings suggest the importance of understanding patients' beliefs about their treatment—in particular their self-perceived necessity and concerns about therapy—in selecting the optimum management approach (including controller therapy and dosing regimen) so as to optimize treatment initiation, implementation, and discontinuation.

ROLE OF THE HEALTH CARE PROFESSIONAL

Patients' medication beliefs and preferences are associated with their adherence to asthma and COPD therapies[38-40] and treatment outcomes depend not only on the availability of medications but also on their appropriate prescribing and successful administration. Poor adherence to asthma and COPD controller medications is associated with higher rates of exacerbations and impaired quality of life, resulting in increased health care costs from unnecessary escalations in therapy and avoidable hospitalizations.[41-44]

Many patients choose not to take their medication because they perceive it to be unnecessary or because they are concerned about potential adverse effects. These concerns are limited not only to the experience of local ICS-related adverse effects but also to more abstract concerns about future medication dependency. Previous work has reported a direct relationship between patients' beliefs about ICS (their need for it and related concerns) and refill-based ICS implementation.[40] Similarly, the odds of ICS implementation have been shown to be higher among patients who felt that using ICS when asymptomatic was important and in patients confident in using their controller therapy, but lower in those who reported concerns about adverse effects of ICS or who felt that their regimen was hard to follow.[34] Similarly, in patients with COPD, patients' conviction of the importance of treatment is reported to have a significant positive influence on adherence.[45]

The health care practitioner has an instrumental role to play in eliciting and addressing patients' attitudes and beliefs about therapy in such a way as to individualize treatment choice and tailor education appropriately with a view to optimizing adherence (see article by van Boven et al[46] in this issue). Despite best efforts, time and resource restrictions may result in patients and/or their caregivers not feeling that they receive all the information they feel they need about their condition and prescribed medications, with the potential for patient disenfranchisement early in the medication adherence pathway.[47]

The concept of patient-centered care is highlighted by the case study described in Figure 2, which summarizes the characteristics of a patient referred to a specialist asthma service in the Netherlands and illustrates how lack of patient engagement and critical interrogation of patient details by primary care clinicians can result in escalation of patients' care and unnecessary use of available health care resources. The 52-year-old female patient has asthma and bronchitis (but COPD is not proven) with very poor Medical Research Council dyspnea, Asthma Control Questionnaire, and Clinical COPD Questionnaire scores of 5, 4.8, and 4.8, respectively. Before presentation at the severe asthma service, she had been prescribed short-acting bronchodilator therapy, ICS, and different long-acting bronchodilator therapies. Although her spirometry readings were also poor, she showed good reversibility and, when asked, she admitted to only occasional use of her medications. Moreover, when assessed she performed 4 inhalation technique errors. A lack of "clinical inertia" within the primary care setting had resulted in an escalation of bronchodilator therapy from short- to long-acting, perhaps reflecting the possible presence of the asthma-COPD overlap syndrome, but overlooking the key issue of poor implementation, with respect to both prescribed treatment frequency and effectiveness of inhaler administration.

TOWARD OPTIMIZED ADHERENCE TO RESPIRATORY MEDICATION

Asthma and COPD guidelines underline the importance of correct inhaler technique training and frequent inhaler technique checks.[1,2,48] Yet assessment of inhaler technique knowledge among health care professionals reveals limited expertise, with 39% to 85% of nurses, doctors, and respiratory therapists unable to demonstrate and brief patients in the proper use of their devices.[49-51] In an assessment of inhaler technique in health care professionals working on a respiratory ward of a major metropolitan hospital in Australia (and the subsequent impact of training on their proficiency), not 1 of the 25 health care professional (pharmacists, n = 11; nurses, n = 16) demonstrated correct inhaler technique before training.[52] The challenge of correct inhaler training by health care professionals is also likely exacerbated by time constraints in clinical practice: it has been reported that 1 in every 4 patients does not receive any verbal instruction and nearly 1 in 2 receives less than 10 minutes of inhaler training.[51]

Ability to successfully administer prescribed therapy has a direct effect not only on medication implementation but also on perceived treatment benefit and patients' willingness to persist with therapy. The importance of optimizing therapy delivery is also stressed in the World Allergy Organization and International Association of Asthmology (INTERASMA) "Manifesto on adherence to asthma treatment in respiratory allergy" (also endorsed by Allergic Rhinitis and Its Impact on Asthma and the Global Allergy and Asthma European Network).[53] The manifesto recommends that adherence be prioritized within patient education and advises that while adherence is considered a "moral responsibility" of the patient, health care professionals should be empathetic rather than condemnatory and provide patients with support and education. In an age of emerging technologies and "smart inhaler" devices and monitors, the World Allergy Organization promotes the use of technology-based adherence interventions, by both patients and health care professionals, to help monitor implementation and motivate improved adherence.[53]

UNMET RESEARCH NEEDS

This review brings together existing evidence on the challenges different modes and approaches to the delivery of asthma and

COPD medications can play on effective therapy administration, treatment satisfaction, medication adherence (initiation, implementation, and persistence), and clinical outcomes. There remain many related research needs that warrant further exploration in well-designed studies (particularly real-life studies) targeted at specific steps of the temporal adherence pathway and using appropriate research methods. Among the future needs identified by Price et al[3] for asthma were the gaps in inhaler education and knowledge; the health economic and clinical outcome evaluations associated with inhaler technique; and the impact of cultural beliefs on inhaler use. Additional research needs relating to asthma and COPD medication delivery and adherence, discussed or implied within this review, are proposed in Figure 3. At their core is the need for a more holistic and integrated approach to treatment optimization that combines generic device education delivered with more targeted interventions to promote overall quality use of medications. To achieve this, there is a need for better understanding of how adherence and inhaler technique are conceptually related (whether they are distinct or should be combined as part of "quality use of medications" approach); a need to develop more generic educational interventions that transcend device-specific challenges, device switching, and combination use, and a need to improve understanding of distinct adherence and technique behaviors within key patient subgroups (eg, pediatrics, adolescents, adults, and elderly) and at different disease stages in order to inform the development of more targeted interventions.

CONCLUSIONS

The efficacy of therapies for asthma and COPD has been repeatedly demonstrated in the RCT setting, yet both conditions are often inadequately managed in everyday routine care.[1,2] The difference in efficacy and effectiveness profiles of respiratory therapies results from strict RCT design. These studies exclude many of the real-life factors that interact with idealized efficacy when therapies are used in the routine care environment, such as comorbid conditions (eg, diabetes, gastroesophageal reflux, and cardiovascular disease), wide ranging lifestyle factors (eg, smoking and trigger exposures), and varying levels of treatment adherence. RCTs may positively bias adherence to therapy through their highly interventional nature, leading to possible "white coat adherence" (improved patient adherence to treatment around clinic visits),[54] Hawthorne effects,[55] and training and retraining of effective technique in the case of inhaled therapies.

As inhaled therapies form the backbone of the therapeutic management of asthma and COPD, it is important to prescribe an inhaler that the patient can and will use.[6] The identification of patients' attitudes (and potential concerns) to inhalers should also be explored to ensure there are no obvious barriers to initiation and use of the prescribed therapy. Thereafter, it is crucial that patients are instructed as to the correct use of their inhalers and that their technique is regularly checked and corrected/retrained, as required. Failure to do so will result in suboptimal implementation (failure to receive the prescribed dose at the frequency intended), suboptimal treatment outcomes, and potential early discontinuation.

Inhaler technique is not always well understood by health care professionals, but clinicians should aim to have knowledge of several inhaler devices (and device types) so that they can tailor device selection to the individual needs, preferences, and capabilities of their patients.[6] The list of common Diskus errors identified by the iHARP investigators[24] can be used by practicing clinicians as an *aide memoire* (or reference checklist) when conducting relevant inhaler technique assessments. Identification of suboptimal inhaler use should prompt retraining and/or a discussion with the patients as to their perceived challenges using their device and alternative treatment options that may be more suitable. Alternatives should include consideration of simplification of treatment regimen (such as use of same type inhalers for reliever and controller medications; move to combination therapies to reduce the number of different inhalers being used; switching to once-daily therapies) or even possible use of oral therapies, in line with guideline recommendations.[1,2]

To optimize adherence to therapy (initiation, implementation, and persistence), treatment decisions should be conducted in collaboration with the patient and should take into consideration their lifestyle factors (eg, work patterns/shifts that may be a barrier to frequent dosing), demographic characteristics (eg, age; see article by Costello et al[56] in this issue), and clinical factors (eg, comorbidities and potentially complex polypharmacy regimens). In this way, treatment choice and its mode of delivery can be tailored to individual patient needs and preferences. Thereafter, it should be frequently assessed (eg, as annual reviews) and, where possible, digitally monitored so as to prompt as-needed education, retraining, and/or adjustment and optimize real-world treatment outcomes.

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