

Choosing the right inhaler for your asthma or COPD patient

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Abstract: Appropriate selection and correct use of inhalation devices is an integral component in the management of asthma and chronic obstructive pulmonary disease (COPD). It is well known that there are many challenges with the use of inhalers, and no one device suits all patients. Challenges can range from difficulties related to lung disease severity and pulmonary function to physical considerations, including manual dexterity and comorbidities such as arthritis. In terms of device selection and adherence, patient engagement and satisfaction are also important factors to consider. Furthermore, problems with inhaler use can be most evident in children and older patients. Here, we discuss aspects for consideration with commonly used devices, including nebulizers, pressurized metered-dose inhalers, dry powder inhalers, and the soft mist inhaler. As each inhaler offers varying technical properties, a tailored and personalized approach to the selection of the most appropriate device for the patient is highly recommended in order to increase the likelihood of achieving improved disease outcomes and enhance persistence with device adherence. Importantly, education and support is crucial, not only to enable patients to recognize the need for optimal disease management, but also to help them develop good inhaler technique. In addition, health care professionals should also aim to increase their knowledge of the devices they prescribe, and develop systems to ensure that they offer comprehensive support to patients in clinical practice. Considering these aspects, this review discusses potential strategies to help address the challenges of inhaler use in asthma and COPD.

Keywords: inhaler, asthma, COPD, adherence

Introduction

Asthma and chronic obstructive pulmonary disease (COPD) are common chronic conditions that comprise approximately 78% of direct health care costs associated with respiratory diseases in the European Union.¹ In the UK alone, 5.4 million patients are currently receiving treatment for asthma; of these, 1.1 million are children.² Over three million people die of COPD worldwide each year, an estimated 6% of all deaths worldwide.³ The delivery of drugs by inhalation is an integral component in the treatment and management of patients with both diseases. Over the past 30 years, there has been unprecedented growth in the market for inhaled therapy, with annual sales having increased from \$7 billion in 1987 to \$36 billion in 2014 and with over 90 billion inhaled doses prescribed to patients in a single year.⁴ Unlike systemic treatments, inhaled medicines are rapidly directed to the airways, allowing for rapid onset. Targeting a drug directly to the lungs allows for lower doses to be administered, limiting potential side effects. There is a large choice of inhalers; in 2011, more than 230 different device-drug combinations were available to prescribers in Europe,⁵ with 48 different inhaler products in the UK alone,⁶ each with its own specific design characteristics.^{7,8} The most common device types sold in Europe in 2011 were pressurized metered-dose inhalers (pMDIs; 47.5%), followed by dry powder inhalers (DPIs; 39.5%)

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and nebulizers (13%), although distribution between inhalers differed considerably between countries.⁵ Therefore, choosing the most appropriate device to meet individual patient needs is an important consideration in clinical practice.

The correct use of inhalation devices and adherence to prescribed therapy are key aspects in achieving better clinical control and improved quality of life.^{9–11} Lack of adherence is an important health challenge, yet both asthma and COPD have lower adherence rates compared with other chronic conditions.¹² The detrimental impact of lack of adherence to COPD medication has been well documented by the TOwards a Revolution in COPD Health (TORCH) study, which found it to be significantly associated with increased risk of death and admission to hospital due to exacerbations.¹³ In patients with COPD discharged from hospital, adherence to medication has been found to be low, with impairment in cognitive function and degree of airways obstruction being key negative influences.¹⁴ It is recognized that a wide range of factors are known to present challenges to patients with respect to inhaler use, including inhalation technique and pulmonary function. In patients with asthma or COPD, incorrect inhaler technique is associated with a 50% increased risk of hospitalization, increased emergency department visits, and increased use of oral corticosteroids.¹⁵ User errors are common, regardless of the device used. A study of 3,393 devices used for continuous treatment of COPD in 2,935 patients has found critical errors in inhalation tests, including with Breezhaler® (Novartis AG, Basel, Switzerland), Diskus® (GlaxoSmithKline, London, UK), Handihaler® (Boehringer Ingelheim Pharma, Ingelheim am Rhein, Germany), pMDIs, Respimat® (Boehringer Ingelheim Pharma), and Turbuhaler® (AstraZeneca, Cambridge, UK) in 15.4%, 21.2%, 29.3%, 43.8%, 46.9%, and 32.1% of patients.¹⁶ A recent systematic review, however, found 299 descriptions for “critical error”, highlighting the need to achieve a consensus on the definition of an inhaler critical error.¹⁷ It is also recommended that patient preferences for devices should be considered when prescribing an inhaler,¹⁰ but physicians must be cognizant that patients often overestimate their ability to handle a device correctly.¹⁸ Factors that influence patient preference include simplicity and convenience (eg, size and durability) and user experience (eg, taste and side effects).¹⁹ Inhaler technique is not necessarily improved due to higher satisfaction with a device, a health care professional’s personal perspective that the patient is engaged in the choice of device, or a patient feeling comfortable using a device in public.²⁰ Given the substantial cost of managing asthma and COPD worldwide, it is important to optimize the use of inhalation devices and technique.²¹ Strategies to achieve this include the provision of high-quality education, both for patients and the

multidisciplinary team (MDT) involved in asthma care, utilization of device technology, and implementation of techniques designed specifically to support adherence.

Scope

This review discusses the factors for consideration when choosing an inhaler device in adults and children with asthma or COPD. It presents evidence to support the selection of the most appropriate device to meet individual patient’s needs, with the aim of optimizing adherence and hence patient outcomes. This is not a systematic literature review, rather an overview of current thoughts, and draws upon clinical experience as well as current literature.

Inhalation devices in asthma and COPD

A variety of different drug and inhaler combinations are available for the management of asthma and COPD, thereby increasing the likelihood of finding an appropriate option for each individual patient. Inhaler devices vary in several ways, including how the inhaler dispenses the medication, whether the treatment is passively or actively generated (eg, using propellant, mechanical, or compressed air), aspects of the drug formulation (eg, solution, dry powder, or mist), whether the inhaler contains medication in a single- or multi-dose, and whether the device is disposable or refillable.²¹ Each inhaler device also has unique design characteristics, meaning that there is the option to tailor choice to meet the patient’s specific needs.²²

However, it can be appreciated that these factors also present the challenge of ensuring that the patient knows how to use their own device, and that they have sufficient education and support to continue to use it properly. This is compounded by the fact that patients are often given multiple devices that work in very different ways. The use of multiple respiratory inhalers requiring different inhalation techniques has been shown to have an adverse effect on clinical outcomes in patients with COPD²³ and asthma.²⁴ Patients who believe using their inhaler is an important part of their asthma management demonstrate higher levels of correct inhaler use.²¹ However, it is recognized that in addition to understanding the need to use an inhaler for disease control, patients must be educated on the necessity of using it properly.²⁵ Thus, from the patient perspective, it is likely that the choice of an inhalation device is often as important as the choice of treatment.²¹ The most commonly used devices include nebulizers, pMDIs, DPIs, and the soft mist inhaler (SMI). The advantages and limitations of the main inhaler devices are overviewed in Table 1. Visual images of the different inhaler types in this article can be found on <http://inhalers4u.org/> and <https://www.rightbreathe.com/>.

Table I Advantages and limitations of commonly used inhalation devices

Inhaler	Advantages	Limitations
pMDI (general)	• Portable • Compact • Multi-dose device • Dose delivered and particle size independent of inhalation maneuver • Quick and easy to use • Less expensive than most other inhalers • Suitable for emergencies • Available for most treatments	• Coordination of inspiration and actuation necessary • Not suitable for young children (without use of spacer) • High oropharyngeal deposition of larger particles (without use of spacer) • Dose counter not available in all devices to assess remaining doses • Propellant required • Needs to be shaken well before each inhalation, and primed if not used within a prespecified time period
pMDI, extra-fine aerosols (mass median aerodynamic diameter, <2 µm)	• Clinically lower doses of drug can be used compared with large particle size drugs • Fewer side effects compared with large particle size drug	• Coordination of inspiration and actuation necessary • Not suitable for young children (without use of spacer) • Dose counter not available in all devices to assess remaining doses • Propellant required • Needs to be shaken well before each inhalation, and primed if not used within a prespecified time period
DPI (general)	• Small and portable • Breath-actuated • Less coordination required • Short treatment time • Available for most treatments	• Moderate to high inspiratory flow required • Not suitable for young children • May not be suitable for emergencies • Partly sensitive to humidity • Need proper dose preparation and loading to achieve optimal available dose for inhalation
DPI, single-dose capsule-based	• Patients can confirm that they have taken their medication by checking the capsule after use	• Need to insert each dose before use • Patient must continue or repeat inhalation until capsule is empty, which can cause dose variability
DPI, multi-unit	• Offers better protection from the environment compared with multiple-dose DPI	• Following dose preparation and actuation, the device needs to be kept horizontal before patient inhalation. Also, patients must not blow into the device before inhalation
DPI, multiple dose (reservoir)	• Built-in mechanism meters out each dose upon actuation	• Requires desiccant inside the powder bed reservoir
SMI	• Portable • Multi-dose device • Low dependence on inspiratory flow rate • Slow velocity aerosol • High fine particle fraction and lung deposition • Long plume duration • Requires less coordination between actuation and inspiration compared with other inhaler devices • No propellant • Dose indicator • Does not require a spacer (in those aged >5 years) • Suitable for use in children	• Dose loaded into the device • Not breath-actuated • Needs to be primed if not in use for over 21 days

Abbreviations: DPI, dry powder inhaler; pMDI, pressurized metered-dose inhaler; SMI, soft mist inhaler.

Nebulizers

Nebulizers are one of the oldest types of device. In general, they are only used in the emergency setting for the acute treatment of patients, or in chronic disease management for children or elderly patients who are unable to use an inhaler with a spacer or who have coordination problems.^{10,26–28}

Once operational, nebulizers are easy to use and offer a convenient way of delivering a higher dose of treatment to the airways if required.²⁶ As nebulizers omit the need for patient coordination between inhalation and actuation, these devices are particularly useful in those with cognitive, neuromuscular, or ventilation impairments.^{26–28} Over 50% of patients

using nebulizers instead of other devices do so because of physical or cognitive disabilities.^{26,27,29} However, most nebulizer devices are generally bulky and inconvenient, require regular maintenance, prolong drug delivery from seconds to 10–15 minutes, and require regular thorough cleaning to sterilize the device.²⁷ It has been shown that in the acute management of disease, nebulizers produced outcomes that were not significantly different than pMDIs with a spacer;³⁰ but compared with DPIs, nebulizers may be beneficial in COPD patients with a suboptimal inspiratory flow.³¹ A new portable nebulizer (Lonhala™ Magnair™, Sunovion Pharmaceuticals Inc., Marlborough, MA, USA), designed to administer glycopyrrolate within 2–3 minutes whilst allowing patients to breathe normally, has recently been approved by the US Food and Drug Administration (FDA).³²

Pressurized metered-dose inhalers

The pMDI is a commonly used device, driven by the wide range of medication that can be delivered via this type of inhaler and the relatively low costs. Recent years have seen the transition from chlorofluorocarbon (CFC) pMDIs, which are almost obsolete, to mainly hydrofluoroalkane (HFA) pMDIs. Available HFA solutions include the long-acting β_2 -agonist formoterol; the corticosteroids ciclesonide (CIC), beclomethasone dipropionate (BDP), and flunisolide; and a drug combination of BDP/formoterol in a single inhaler.³³ BDP and CIC formulations contain extra-fine particles ($<2 \mu\text{m}$ mass median aerodynamic diameter), which are associated with lower oropharyngeal deposition and enhanced deposition in the lung.³³ Preparations with extra-fine inhaled corticosteroids (ICS) have significantly higher odds of achieving asthma control, with lower exacerbation rates at significantly lower doses than fine-particle ICSs.³⁴ Patients stepping up to extra-fine particle ICS preparations experienced lower risk of pneumonia, acute COPD exacerbations, and respiratory events.³⁵ Common user errors with pMDIs include inhaling too fast (and thus not slowly and deeply), failure to tilt head to the correct position, failure to empty lungs prior to inhalation, and failure to hold breath following inhalation.^{11,21} Patients are also not always able to reliably determine the remaining number of doses, as there are still pMDI devices on the market that do not have a dose counter despite FDA guidance in 2003. In a study assessing patient satisfaction with their pMDI, 52% reported that they were “extremely unsure” and 10% “somewhat unsure” of how much medication remained.⁸ While this has been solved by the addition of dose counters in many devices, the patient must be aware of the need to keep track of remaining medication.³⁶

Dry powder inhalers

DPIs were introduced into clinical practice as user-friendly alternatives to CFC- and HFA-driven pMDIs.³⁷ Breath-actuated DPIs are aimed to overcome the difficulties with coordination of inhaler actuation and inspiration.^{15,38} There are three main systems: capsule-based pre-metered single-dose devices; multi-unit dose inhalers (preloaded by the manufacturer with a blister foil); and multiple-dose inhalers that employ an in-built mechanism that meters out a single dose with each actuation from a reservoir of powder.^{38,39} Effective use of a DPI requires that each dose is primed and loaded in the correct manner.⁴⁰ DPIs derive the energy for emptying the drug system from the user's inspiratory flow, and the failure to achieve a forceful inspiratory flow through a device is the most common critical mishandling error with DPIs, occurring in 26%–38% of cases.^{11,15} Common errors for DPIs include not keeping the device in the correct position while loading the dose, failure to tilt head in the correct position, insufficient inspiratory effort, and not emptying lungs before inhalation.^{11,21} It is increasingly recognized that many patients with asthma and COPD find difficulty in generating the necessary optimal inspiratory flow rates for DPIs in order to achieve effective drug delivery and consequent clinical benefit.⁴¹ DPIs are also susceptible to heat and moisture, and special precaution must be taken to avoid humidity. This means that their use in hot and humid climate zones is limited, and care must be taken to store the device in appropriate conditions.^{42,43}

Soft mist inhalers

The SMI provides an alternative option to pMDIs and DPIs, aiming to improve the effective delivery of drug to the lungs in order to benefit the patient and enhance adherence. The Respimat® Soft Mist™ inhaler (Boehringer Ingelheim Pharma), so far the only commercially available SMI for asthma and COPD, was developed with the aim of providing optimal drug delivery to the lungs while avoiding propellants, as well as to reduce the need for patient coordination and inspiratory effort.^{28,37,44} The Respimat® device does not require propellants as it is powered by the energy of a compressed spring inside the inhaler, and individual doses are delivered via a specifically engineered nozzle system as a slow-moving aerosol cloud.²⁸ In addition, as the aerosol is generated from a solution rather than a powder, the Respimat® is resilient to moisture, making it suitable for humid climates.²⁸ While the required inhalation technique is like that used with a pMDI, the aerosol is released very slowly from the device compared with an HFA-driven pMDI.⁴⁵ Dal Negro et al⁴⁶ compared

the instant velocity and the consistency of the emitted cloud from five different pMDIs and the Respimat® at different distances from the nozzle and at different levels of canister filling. Findings suggest that the dynamic characteristics of the SMI result in higher stability of the cloud emitted and hence may contribute to more convenient use to the patient. This is mainly attributed to the slower jet emission and to the more homogeneous composition of the droplet cloud generated. Findings showed that the higher stability of cloud emission from the Respimat® was likely to contribute to easier and more convenient use for patients.⁴⁷ Additionally, the relatively long duration over which the dose is expelled from the Respimat® (about 1.2 s compared with 0.1 s from traditional pMDIs) is thought to largely reduce the impact of poor coordination between actuation and inspiration (a regular patient error still seen with the Respimat® device¹⁶), thus improving the potential for greater lung deposition.⁸ Thus, while coordination between actuation and inhaling is required, the velocity of the Respimat® reduces the potential for drug impaction in the throat. Scintigraphic studies with the Respimat® device have reported that, compared with an HFA-based pMDI, lung deposition is higher (up to 50%) and oropharyngeal deposition is lower.⁴⁸ These findings are attributed to the small particle size emitted by the Respimat®. Overall, the Respimat® Soft Mist™ inhaler offers an alternative option in clinical practice, overcoming some of the limitations of other devices (Table 1).

Inhaler selection in clinical practice

Choice of inhaler depends on a combination of factors,^{49,50} including pulmonary function (ie, inspiratory flow and breathing technique^{22,51}), device handling,^{8,52–55} use of a spacer, required inhaler technique,^{7,11,56,57} and patient preference.^{19,58,59} Correct inhaler technique is important for optimal delivery of the drug to the lungs and peripheral airways, resulting in greater potential for the achievement of disease control.^{36,57,60,61} As treatment efficacy is linked to adherence, addressing patient preferences are essential,⁶² and tailored device selection can help enhance patient satisfaction, treatment adherence, and long-term outcomes.^{22,62}

Physical barriers that affect device handling are well documented.^{8,52–55} Children, the elderly, and those with conditions that may impact on handgrip and manual dexterity require special consideration to ensure selection of the most appropriate inhaler. In older patients, common physical challenges include difficulty manipulating the device due to problems with dexterity, including osteoarthritis, joint pain, stroke, and muscle weakness.^{26,27,60} Difficulty connecting

a pMDI to a spacer and an inability to achieve a firm seal around the mouthpiece when using inhalers alone or with a spacer have also been suggested, particularly for patients with cognitive impairment, facial weakness, or who are missing teeth. In children, the choice of inhaler more specifically depends on the child's age and capability, and challenges with correct handling may be experienced due to manual dexterity and finger size. Successful inhaler use in young children depends on coordination, the technical properties of the inhalation device, and the ability of the child to perform a correct inhalation maneuver with the device.⁵⁵ Spacers are commonly used in children to reduce the need for actuation and breathing coordination.^{52–54} A summary showing the challenges related to the use of inhalation therapy in children and a guide on age-appropriate devices and interfaces are shown in Figure 1. Specific issues related to the use of inhalation therapy in elderly patients and an algorithm for inhaler selection in this patient group are shown in Figure 2.

Inhaled drug deposition in the airways is impacted by the patient's inspiratory flow, the aerosol velocity, and the inhaled drug particle size.^{63–65} These challenges can be particularly evident in young children and older individuals, and, in addition to the difficulties these groups can have with coordination of device actuation with inspiration,³⁷ may lead to a significant reduction in drug deposition in the lungs. The CRITical Inhaler misTakeS and Asthma control study (CRITIKAL)¹¹ is one of the largest studies to investigate inhaler technique. Conducted in a real-life, multinational study population, this study investigated the association between specific inhaler errors and asthma outcomes, and included data from 3,660 patients. Insufficient inspiratory effort was common (made by 32%–38% of DPI users), and was associated with uncontrolled asthma (adjusted odds ratios: 1.30 and 1.56 in those using Turbuhaler and Diskus devices, respectively) and increased exacerbation rate. In pMDI users, actuation before inhalation (24.9% of patients) was also associated with uncontrolled asthma.

Patient factors including preferences and satisfaction can play a significant role in inhaler choice and use.¹⁹ In addition to ease of use, this can be influenced by the portability and compact design of the device, as well as noise, taste, treatment time, and convenience.⁴⁴ Engaging patients in selection of the inhaler that suits them best may help optimize device adherence. In a real-world observational study, Small et al⁶⁶ reported that the higher the level of satisfaction patients had with their device, the more likely they were to be compliant and to experience better outcomes (eg, quality of life and fewer health care challenges), including fewer exacerbations,

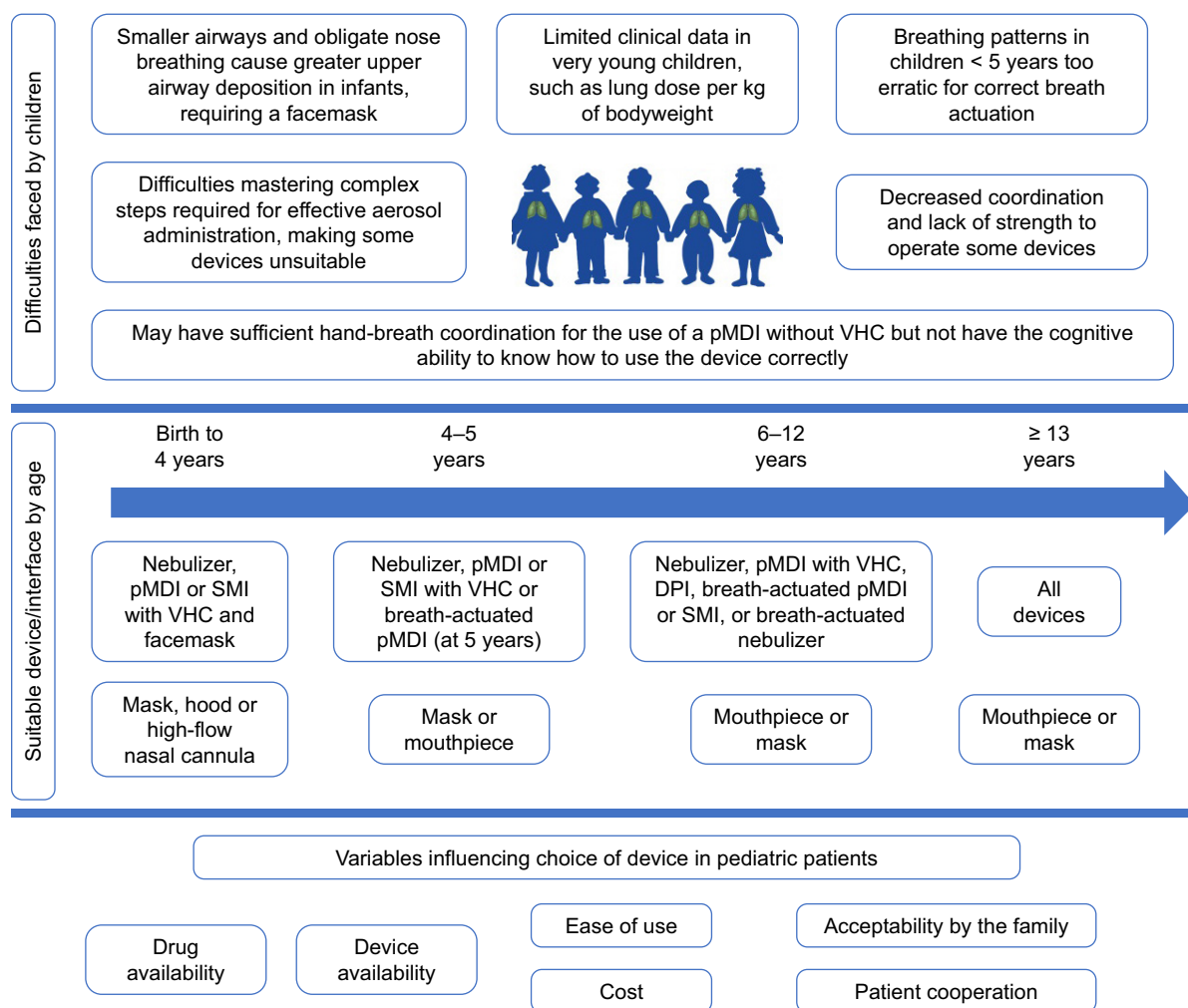


Figure 1 Challenges of inhalation therapy in pediatric patients, and age-appropriate inhaler devices and interfaces.

Note: Data from these studies.^{53,55,90,91}

Abbreviations: DPI, dry powder inhaler; pMDI, pressurized metered-dose inhaler; SMI, soft mist inhaler; VHC, valved holding chamber.

fewer hospital visits, fewer health care visits, and fewer sleep disturbances. In one study in which patients were interviewed to determine their inhaler preferences, it was confirmed that smaller-sized inhalers are desirable due to their portability, and interviewees stated that this characteristic is linked to adherence.⁶⁷ In addition, most participants believed that a dose counter should be an integral part of an inhaler, while the need for proper training with a health care professional was also emphasized.⁶⁷ Patient preference for different inhaler types has been investigated in many studies. Given the wide selection of inhalers available, patient preference for one particular inhaler type has not been demonstrated, and the choice depends on a number of factors, as already discussed.^{20,47,68–72}

Training and education to support the use of inhalers

Inhaler misuse is one of the most commonly reported barriers to adherence. Melani et al¹⁵ observed the strongest and most

significant associations between inhaler misuse with older age, lower schooling, and lack of instruction regarding inhaler technique. It must be acknowledged that even the most user-friendly devices still require education and a demonstration, which has been shown to be lacking in several studies.

Education is the one factor that is modifiable, and health care professionals should seek to tailor advice according to individual patient needs in addition to ensuring that their own education is up to date.⁷ On the introduction of a device into clinical practice, the suggestion that it is user-friendly gives the impression that education and training may not be required. However, a patient will require training and upskilling on any device,^{15,52} and user technique should always be reviewed in patients with poor asthma control, even if they are using a device that is considered easy to use.⁵⁶ However, while training can enhance the ability to use inhalers, it has been reported that many patients revert to an incorrect technique after a short time.^{73,74} The Global Initiative for Asthma

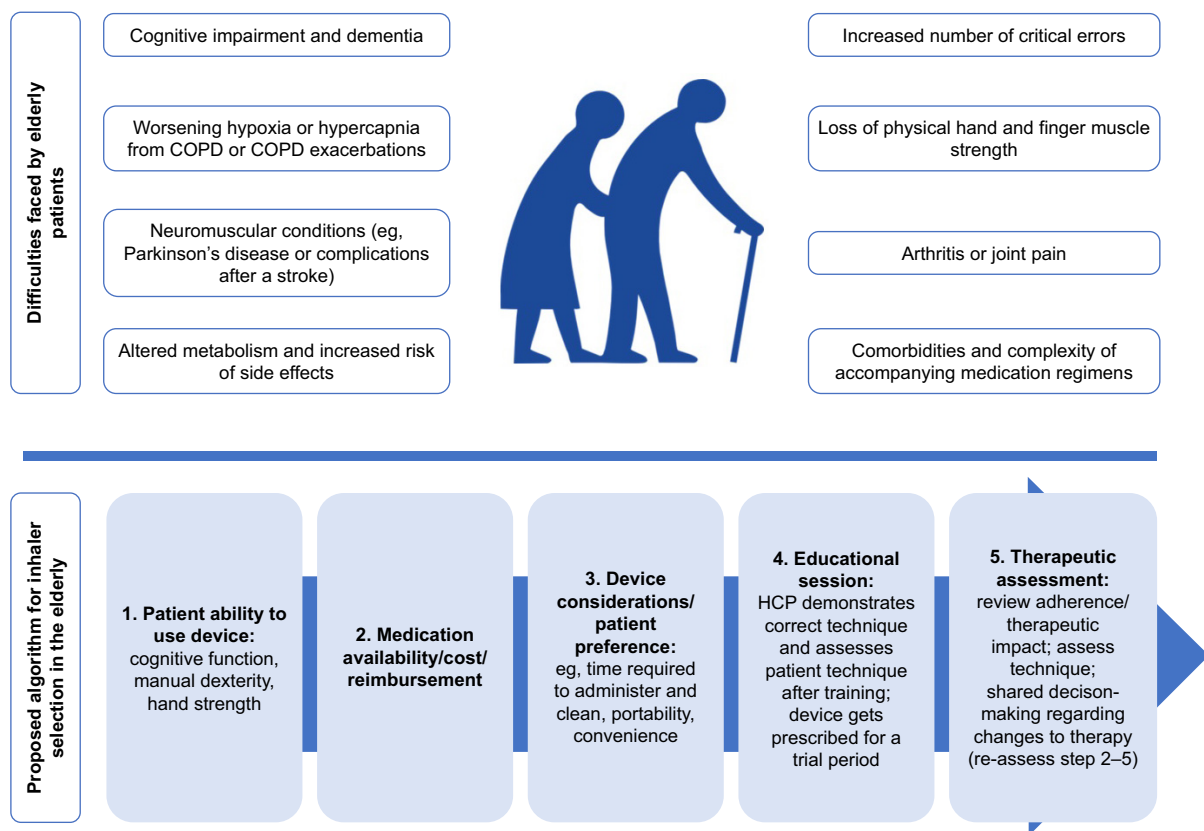


Figure 2 Challenges with the use of inhalation therapy in elderly patients, and an algorithm for appropriate inhaler device selection.^{26,92,93}

Abbreviations: COPD, chronic obstructive pulmonary disease; HCP, health care professional.

(GINA) recommends strategies for helping to ensure effective device use, including a physical demonstration of inhaler technique and patient retraining at follow-up appointments.¹⁰ A Cochrane review evaluated a range of interventions and determined that although many studies demonstrated a post-intervention improvement in the number of individuals with correct inhaler technique, it could not be confirmed whether this translated into clinical benefits.⁵¹ The authors recommended that health care professionals continue to ask their patients to regularly demonstrate their technique and correct this as required, and to refer patients for training as necessary where available.

Patient-related education

The most effective patient training technique has been established as verbal instruction combined with a physical demonstration.⁷⁵⁻⁷⁷ Repeating information over time increases the proportion of patients who maintain the correct technique at follow-up visits.⁷⁷ If poor technique persists, it is essential to elucidate from the patient the challenges they are experiencing, and address any potential lack of understanding around the need for medication and adherence.⁷ Furthermore, treatment decisions should always be taken in

collaboration with the patient and/or their carer in the case of young patients and often elderly individuals.⁷ A selection of educational aids has been developed and are reviewed elsewhere.⁷⁴ In an attempt to improve patient recall of the optimal technique required for use, some device tools provide real-time, interactive sensory feedback of the patient's performance in various aspects of inhalation.⁷⁴ A number of online tools, including videos, also offer patient support, and the Aerosol Drug Management Improvement Team (ADMIT)⁷⁴ provide an online platform offering patients and health care professional educational resources to support the decision-making process regarding which inhaler might be most appropriate and the correct inhaler technique.

Health care professional-related education

The role of the health care professional, whether physician, pharmacist, or other member of the MDT, in inhaler use is central.^{7,52} The wide range of drug and inhaler combinations increases the complexity of inhaler choice for physicians, and may also reduce their experience with each device, hence affecting patient tuition. It has been suggested that up to 67% of clinicians cannot describe the steps involved or demonstrate correct inhaler use.⁵¹ It is recommended that

each health care professional should look to expand their knowledge on inhalation devices and strategies to support their patients, enabling them to offer tailored care that aims to maximize disease control and patient experience while minimizing clinic visits.^{7,77}

When considering pediatric patients specifically, a UK-based study evaluated whether health care professionals were able to counsel this group on use of inhalers, including MDIs and Turbuhaler. Findings were similar to those observed with adults, and concluded that less than 10% of health care professionals were competent with the MDI device. Overall, just 13% of participants provided counseling on all the essential criteria for an MDI inhaler. Pharmacy teams within the hospital and community saw the highest competency levels, with 31% and 30% of staff able to discuss the essential steps, respectively. The physicians or nurses included were not able to identify all the necessary steps. Furthermore, only 10% of participants counseled patients on all essential steps for an MDI with a spacer device, with no nurse or doctor achieving all steps.⁷⁸ Commonly omitted steps included shaking the inhaler and leaving sufficient time between doses.

An improvement in inhaler knowledge and skills has been reported following educational workshops and a small-group lecture format with web-based inhaler tutorials.²¹ Leung et al⁷⁹ tested the usefulness of a physician education implemented as a two-session education program. Attendees were armed with slide decks and access to placebo inhalers so that they could not only teach patients proper inhaler technique, but also raise awareness among other members of the MDT. Before the program, 49% of participants reported providing some form of inhaler teaching in their practices, yet only 10% felt fully competent to teach their patients the inhaler technique. After the program, 98% rated their inhaler teaching as good to excellent, and 83% reported providing inhaler teaching in their practices, either by themselves or by a member of the MDT that they had personally trained. In another study,⁸⁰ health care professionals watched tablet-based multimedia educational videos that demonstrated correct inhaler technique by a clinical pharmacist with teach-back from a patient, before being re-evaluated. Correct inhaler technique was significantly increased among all health care professionals after the training, with the largest increase observed for the RespiMat[®] device; 32% versus 93% demonstrated the correct steps for usage before and after training.

Research has shown that it is necessary to repeat instructions several times to achieve effective inhalation skills in both asthma and COPD patients. A study by Takaku et al⁸¹ designed to evaluate the number of instructions that are

necessary to minimize errors in using pMDI, DPI, and RespiMat[®] concluded that, for every device, at least three instructions were required to achieve less than 10% of errors. As a support strategy to providing verbal instructions, Basheti et al⁸² investigated the effect of the use of inhaler technique reminder labels. Findings demonstrated significantly better inhaler technique after 3 months among those using labels compared with those using initial training alone. The personalized labels highlighted original errors, serving as a reminder of the correct technique; 67% of patients maintained correct technique at follow-up, compared with only 12% of those who received education alone. It was concluded that this is a simple intervention that has the potential to support continued good inhaler technique among patients. Furthermore, the labeling might also help health care professionals with providing instruction during a consultation. The authors also suggested that future research could investigate the potential for inhalers to talk the patient through the steps needed for good medication delivery.

There are many guidelines (eg, GINA and Global Initiative for Chronic Obstructive Lung Disease) to support health care professionals. The UK Inhaler Group have published the “Inhaler Standards and Competency Document”, which provides guidance and recommends that health care professionals are able to demonstrate device use effectively. Furthermore, it has been recommended that health care professionals limit the range of devices they use by balancing the patient’s needs and preferences with prescribing devices that they feel confident explaining.⁸³ Finally, health care professionals should consider the most effective educational tool according to the patient’s needs; for example, younger patients may benefit more from multimedia teaching methods, whereas elderly patients respond well to one-to-one tuition.⁷³

An update on new inhalational therapeutics

Over the past 5–10 years, a number of technological innovations have been introduced that improve the performance of all device types; in addition, new delivery systems have been developed that improve delivery efficacy. Amongst these are “intelligent inhalers”, which carry features to monitor patients’ inhalation and adherence to treatment. Using new technology, pulmonary disposition fractions have been increased up to 40%–50% of the nominal dose compared with 10%–15% of levels achieved in the past, meaning that less drug is required for similar efficacy.⁸ Other innovations (reviewed in more detail by Lavorini et al⁸) include the insertion of microprocessors into pMDIs, novel ways of initiating breath actuation

(including the analysis of inspiratory flow profiles), electronic dose counters, heating elements to reduce aerosol droplet size, and mechanisms that give visual and acoustic feedback to reassure patients that their medication has been taken correctly.

Future developments in inhaler management

Many inhalation products have reached or are approaching patent expiration, leading to a worldwide trend of switching from branded to generic inhalation medicine and the development of new generic inhalers. In the light of this, the European Medicines Agency issued stringent guidelines in 2009 recommending a stepwise approach to demonstrate therapeutic equivalence between two inhaled products. The guidelines stipulate that the generic and reference products must have an identical dosage form containing the same active substance(s). Devices containing generic and reference substances should be equivalent in terms of handling and resistance to airflow, and the delivered dose and particle size should be similar (within 15%) between products. If these *in vitro* criteria are satisfied, the product may be approved without further pharmacokinetic or pharmacodynamic studies to demonstrate equivalence. The FDA has taken a different approach, and has issued separate draft guidance for each specific inhalation product (pMDIs of albuterol sulfate, ipratropium bromide, lev-albuterol tartrate, budesonide/formoterol fumarate, and DPI of fluticasone propionate/salmeterol). To get FDA approval for a generic product, *in vitro* tests and *in vivo* equivalence studies are required, making it much harder to get approval.⁸⁴

Digital health is a growing phenomenon, and offers the potential to help optimize patient care in several aspects of asthma management.⁸⁵ A selection of the digital and electronic options either available or under investigation are reviewed in detail elsewhere.^{86,87} Briefly, one digital platform that has FDA approval (Propeller Health) aims to provide geospatial information on asthma attacks to help health care professionals identify exacerbation triggers. In addition, weekly email reports are considered to help increase disease awareness, as well as to enhance understanding of treatment and preventative measures.⁸⁶ The approach, based on the global positioning system functionality of smartphones and available for the three main device types – pMDI, DPI, and Respimat® – features sensor technology, software, and services; remotely monitors use of inhaled asthma and COPD treatment; analyses patient trends; and provides regular feedback. As technology in this area progresses, it is likely that many additional options to support inhaler use in asthma and COPD will become available. There is also a lot of work

in the innovation of inhaler formulations,⁸⁸ their engineered design,⁸ and also the aerosol form⁸⁹ in order to make inhalers more efficient in their ability to deliver drug to the lungs.

In conclusion, there are a broad range of inhaler devices available for the management of asthma and COPD. Each has varying technical features, and so it is important that the choice of device is tailored to meet individual patient's needs, preferences, and satisfaction, while offering the requisite level of disease control. While there may be no one ideal device for all patients, the range of options available means that there should be a device to suit every patient. Education, both for patients and physicians, is also a key component of optimizing device choice and use.

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References

1. Lewis A, Torvinen S, Dekhuijzen PN, et al. The economic burden of asthma and chronic obstructive pulmonary disease and the impact of poor inhalation technique with commonly prescribed dry powder inhalers in three European countries. *BMC Health Serv Res*. 2016;16:251.
2. Asthma UK. Asthma facts and statistics. Available from: <https://www.asthma.org.uk/about/media/facts-and-statistics/>. Accessed February 12, 2018.
3. World Health Organization. Chronic respiratory diseases. Available from: <http://www.who.int/respiratory/en/>. Accessed October 26, 2017.
4. Stein SW, Thiel CG. The history of therapeutic aerosols: a chronological review. *J Aerosol Med Pulm Drug Deliv*. 2017;30(1):20–41.
5. Lavorini F, Corrigan CJ, Barnes PJ, et al; Aerosol Drug Management Improvement Team. Retail sales of inhalation devices in European countries: so much for a global policy. *Respir Med*. 2011;105(7):1099–1103.
6. Rogueda P, Traini D. The future of inhalers: how can we improve drug delivery in asthma and COPD? *Expert Rev Respir Med*. 2016;10(10):1041–1044.
7. Braido F, Chrystyn H, Baiardini I, et al; Respiratory Effectiveness Group. “Trying, but failing” – the role of inhaler technique and mode of delivery in respiratory medication adherence. *J Allergy Clin Immunol Pract*. 2016;4(5):823–832.

8. Lavorini F, Fontana GA, Usmani OS. New inhaler devices – the good, the bad and the ugly. *Respiration*. 2014;88(1):3–15.
9. Dudvarski Ilic A, Zugic V, Zvezdin B, et al. Influence of inhaler technique on asthma and COPD control: a multicenter experience. *Int J Chron Obstruct Pulmon Dis*. 2016;11:2509–2517.
10. Global Initiative for Asthma. GINA Report: Global Strategy for Asthma Management and Prevention. Available from: <http://ginasthma.org/2017-gina-report-global-strategy-for-asthma-management-and-prevention/>. Accessed August 1, 2017.
11. Price DB, Román-Rodríguez M, McQueen RB, et al. Inhaler errors in the CRITIKAL study: type, frequency, and association with asthma outcomes. *J Allergy Clin Immunol Pract*. 2017;5(4):1071–1081.
12. Brandstetter S, Finger T, Fischer W, et al. Differences in medication adherence are associated with beliefs about medicines in asthma and COPD. *Clin Transl Allergy*. 2017;7:39.
13. Vestbo J, Anderson JA, Calverley PM, et al. Adherence to inhaled therapy, mortality and hospital admission in COPD. *Thorax*. 2009;64(11):939–943.
14. Sulaiman I, Cushen B, Greene G, et al. Objective assessment of adherence to inhalers by patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 2017;195(10):1333–1343.
15. Melani AS, Bonavia M, Cilenti V, et al; Gruppo Educazionale Associazione Italiana Pneumologi Ospedalieri. Inhaler mishandling remains common in real life and is associated with reduced disease control. *Respir Med*. 2011;105(6):930–938.
16. Molimard M, Raherison C, Lignot S, et al. Chronic obstructive pulmonary disease exacerbation and inhaler device handling: real-life assessment of 2935 patients. *Eur Respir J*. 2017;49(2):1601794.
17. Usmani OS, Lavorini F, Marshall J, et al. Critical inhaler errors in asthma and COPD: a systematic review of impact on health outcomes. *Respir Res*. 2018;19(1):10.
18. Press VG, Arora VM, Shah LM, et al. Teaching the use of respiratory inhalers to hospitalized patients with asthma or COPD: a randomized trial. *J Gen Intern Med*. 2012;27(10):1317–1325.
19. Dekhuijzen PN, Lavorini F, Usmani OS. Patients' perspectives and preferences in the choice of inhalers: the case for Respimat® or HandiHaler®. *Patient Prefer Adherence*. 2016;10:1561–1572.
20. Chorão P, Pereira AM, Fonseca JA. Inhaler devices in asthma and COPD – an assessment of inhaler technique and patient preferences. *Respir Med*. 2014;108(7):968–975.
21. Inhaler Error Steering Committee, Price D, Bosnic-Anticevich S, et al. Inhaler competence in asthma: common errors, barriers to use and recommended solutions. *Respir Med*. 2013;107(1):37–46.
22. Bonini M, Usmani OS. The importance of inhaler devices in the treatment of COPD. *COPD Res Pract*. 2015;1(1):9.
23. Bosnic-Anticevich S, Chrystyn H, Costello RW, et al. The use of multiple respiratory inhalers requiring different inhalation techniques has an adverse effect on COPD outcomes. *Int J Chron Obstruct Pulmon Dis*. 2016;12:59–71.
24. Price DB, Colice G, Israel E, et al. Add-on LABA in a separate inhaler as asthma step-up therapy versus increased dose of ICS or ICS/LABA combination inhaler. *ERJ Open Res*. 2016;2(2):00106.
25. Lavorini F, Usmani OS. Correct inhalation technique is critical in achieving good asthma control. *Prim Care Respir J*. 2013;22(4):385–386.
26. Taffet GE, Donohue JF, Altman PR. Considerations for managing chronic obstructive pulmonary disease in the elderly. *Clin Interv Aging*. 2014;9:23–30.
27. Yawn BP, Colice GL, Hodder R. Practical aspects of inhaler use in the management of chronic obstructive pulmonary disease in the primary care setting. *Int J Chron Obstruct Pulmon Dis*. 2012;7:495–502.
28. Wachtel H, Kattenbeck S, Dunne S. The Respimat® development story: patient-centered innovation. *Pulm Ther*. 2017;3:19.
29. Bowles SK, Sketris I, Kephart G; Drug Evaluation Alliance of Nova Scotia. Use of wet nebulized inhaled respiratory medications under criteria-based reimbursement guidelines in a publicly funded Seniors' Pharmacare Program in Nova Scotia, Canada. *Am J Geriatr Pharmacother*. 2007;5(2):120–128.
30. Cates CJ, Welsh EJ, Rowe BH. Holding chambers (spacers) versus nebulisers for beta-agonist treatment of acute asthma. *Cochrane Database Syst Rev*. 2013;(9):CD000052.
31. Loh CH, Peters SP, Lovings TM, Ohar JA. Suboptimal inspiratory flow rates are associated with chronic obstructive pulmonary disease and all cause readmissions. *Ann Am Thorac Soc*. 2017;14(8):1305–1311.
32. BusinessWire. Sunovion Receives FDA Approval for Lonhala™ Magnair™ Inhalation Solution to Treat COPD. Available from: <https://www.businesswire.com/news/home/20171205006502/en/Sunovion-Receives-FDA-Approval-Lonhala%E2%84%A2-Magnair%E2%84%A2-Inhalation>. Accessed February, 2018.
33. Usmani OS. Treating the small airways. *Respiration*. 2012;84(6):441–453.
34. Sonnappa S, McQueen B, Postma DS, et al. Extrafine versus fine inhaled corticosteroids in relation to asthma control: a systematic review and meta-analysis of observational real-life studies. *J Allergy Clin Immunol Pract*. Epub 2017 Sep 20.
35. Sonnappa S, Martin R, Israel E, et al; Respiratory Effectiveness Group, Small Airways Study Group. Risk of pneumonia in obstructive lung disease: a real-life study comparing extra-fine and fine-particle inhaled corticosteroids. *PLoS One*. 2017;12(6):e0178112.
36. Levy ML, Dekhuijzen PN, Barnes PJ, et al. Inhaler technique: facts and fantasies. A view from the Aerosol Drug Management Improvement Team (ADMIT). *NPJ Prim Care Respir Med*. 2016;26:16017.
37. Dalby RN, Eicher J, Zierenberg B. Development of Respimat® Soft Mist™ inhaler and its clinical utility in respiratory disorders. *Med Devices (Auckl)*. 2011;4:145–155.
38. Lavorini F, Pistolesi M, Usmani OS. Recent advances in capsule-based dry powder inhaler technology. *Multidiscip Respir Med*. 2017;12:11.
39. Muralidharan P, Hayes D Jr, Mansour HM. Dry powder inhalers in COPD, lung inflammation and pulmonary infections. *Expert Opin Drug Deliv*. 2015;12(6):947–962.
40. Rau JL. Practical problems with aerosol therapy in COPD. *Respir Care*. 2006;51(2):158–172.
41. Al-Showair RA, Tarsin WY, Assi KH, Pearson SB, Chrystyn H. Can all patients with COPD use the correct inhalation flow with all inhalers and does training help? *Respir Med*. 2007;101(11):2395–2401.
42. Borgström L, Asking L, Lipniunas P. An in vivo and in vitro comparison of two powder inhalers following storage at hot/humid conditions. *J Aerosol Med*. 2005;18(3):304–310.
43. Ganderton D. Targeted delivery of inhaled drugs: current challenges and future goals. *J Aerosol Med*. 1999;12(Suppl 1):S3–S8.
44. Moroni-Zentgraf P. Impact of patient needs on design and usage of an inhalation device in respiratory medicine. *Respir Drug Deliv*. 2013;1:141.
45. Anderson P. Use of Respimat Soft Mist inhaler in COPD patients. *Int J Chron Obstruct Pulmon Dis*. 2006;1(3):251–259.
46. Dal Negro RW, Longo P, Ziani OV, Bonadiman L, Turco P. Instant velocity and consistency of emitted cloud change by the different levels of canister filling with Metered Dose Inhalers (MDIs), but not with Soft Mist Inhalers (SMIs): a bench study. *Multidiscip Respir Med*. 2017;12:13.
47. Dal Negro RW, Povero M. Acceptability and preference of three inhalation devices assessed by the Handling Questionnaire in asthma and COPD patients. *Multidiscip Respir Med*. 2016;11:7.
48. Brand P, Hederer B, Austen G, Dewberry H, Meyer T. Higher lung deposition with Respimat Soft Mist inhaler than HFA-MDI in COPD patients with poor technique. *Int J Chron Obstruct Pulmon Dis*. 2008;3(4):763–770.
49. Pedersen S, Dubus JC, Crompton GK; ADMIT Working Group. The ADMIT series – issues in inhalation therapy. 5) Inhaler selection in children with asthma. *Prim Care Respir J*. 2010;19(3):209–216.
50. Vincken W, Dekhuijzen PR, Barnes P; ADMIT Group. The ADMIT series – issues in inhalation therapy. 4) How to choose inhaler devices for the treatment of COPD. *Prim Care Respir J*. 2010;19(1):10–20.
51. Normansell R, Kew KM, Mathioudakis AG. Interventions to improve inhaler technique for people with asthma. *Cochrane Database Syst Rev*. 2017;3:CD012286.

52. Fink JB, Rubin BK. Problems with inhaler use: a call for improved clinician and patient education. *Respir Care*. 2005;50(10):1374–1375.
53. Ari A, Fink JB. Guidelines for aerosol devices in infants, children and adults: which to choose, why and how to achieve effective aerosol therapy. *Expert Rev Respir Med*. 2011;5(4):561–572.
54. Melani AS, Bracci LS, Rossi M. Reduced peak inspiratory effort through the Diskus® and the Turbuhaler® due to mishandling is common in clinical practice. *Clin Drug Investig*. 2005;25(8):543–549.
55. Kamin W, Frank M, Kattenbeck S, Moroni-Zentgraf P, Wachtel H, Zielen S. A handling study to assess use of the Respimat® Soft Mist™ inhaler in children under 5 years old. *J Aerosol Med Pulm Drug Deliv*. 2015;28(5):372–381.
56. Westerk JA, Carter V, Chrystyn H, et al. Characteristics of patients making serious inhaler errors with a dry powder inhaler and association with asthma-related events in a primary care setting. *J Asthma*. 2016;53(3):321–329.
57. Levy ML, Hardwell A, McKnight E, Holmes J. Asthma patients' inability to use a pressurised metered-dose inhaler (pMDI) correctly correlates with poor asthma control as defined by the global initiative for asthma (GINA) strategy: a retrospective analysis. *Prim Care Respir J*. 2013;22(4):406–411.
58. Hodder R, Price D. Patient preferences for inhaler devices in chronic obstructive pulmonary disease: experience with Respimat Soft Mist inhaler. *Int J Chron Obstruct Pulmon Dis*. 2009;4:381–390.
59. Perriello EA, Sobieraj DM. The Respimat Soft Mist inhaler, a novel inhaled drug delivery device. *Conn Med*. 2016;80(6):359–364.
60. Darbà J, Ramírez G, Sicras A, Francoli P, Torvinen S, Sánchez-de la Rosa R. The importance of inhaler devices: the choice of inhaler device may lead to suboptimal adherence in COPD patients. *Int J Chron Obstruct Pulmon Dis*. 2015;10:2335–2345.
61. Usmani OS. Small-airway disease in asthma: pharmacological considerations. *Curr Opin Pulm Med*. 2015;21(1):55–67.
62. Scichilone N. Asthma control: the right inhaler for the right patient. *Adv Ther*. 2015;32(4):285–292.
63. Verbanck S, Ghorbaniasl G, Biddiscombe MF, et al. Inhaled aerosol distribution in human airways: a scintigraphy-guided study in a 3D printed model. *J Aerosol Med Pulm Drug Deliv*. 2016;29(6):525–533.
64. Verbanck S, Kalsi HS, Biddiscombe MF, et al. Inspiratory and expiratory aerosol deposition in the upper airway. *Inhal Toxicol*. 2011;23(2):104–111.
65. Usmani OS, Biddiscombe MF, Barnes PJ. Regional lung deposition and bronchodilator response as a function of beta2-agonist particle size. *Am J Respir Crit Care Med*. 2005;172(12):1497–1504.
66. Small M, Anderson P, Vickers A, Kay S, Fermer S. Importance of inhaler-device satisfaction in asthma treatment: real-world observations of physician-observed compliance and clinical/patient-reported outcomes. *Adv Ther*. 2011;28(3):202–212.
67. Jahedi L, Downie SR, Saini B, Chan HK, Bosnic-Anticevich S. Inhaler technique in asthma: how does it relate to patients' preferences and attitudes toward their inhalers? *J Aerosol Med Pulm Drug Deliv*. 2017;30(1):42–52.
68. Miravittles M, Montero-Caballero J, Richard F, et al. A cross-sectional study to assess inhalation device handling and patient satisfaction in COPD. *Int J Chron Obstruct Pulmon Dis*. 2016;11:407–415.
69. Schürmann W, Schmidtman S, Moroni P, Massey D, Qidan M. Respimat Soft Mist inhaler versus hydrofluoroalkane metered dose inhaler: patient preference and satisfaction. *Treat Respir Med*. 2005;4(1):53–61.
70. Hodder R, Reese PR, Slaton T. Asthma patients prefer Respimat Soft Mist Inhaler to Turbuhaler. *Int J Chron Obstruct Pulmon Dis*. 2009;4:225–232.
71. Lenney J, Innes JA, Crompton GK. Inappropriate inhaler use: assessment of use and patient preference of seven inhalation devices. *EDICI. Respir Med*. 2000;94(5):496–500.
72. Molimard M, Colthorpe P. Inhaler devices for chronic obstructive pulmonary disease: insights from patients and healthcare practitioners. *J Aerosol Med Pulm Drug Deliv*. 2015;28(3):219–228.
73. Crompton GK, Barnes PJ, Broeders M, et al; Aerosol Drug Management Improvement Team. The need to improve inhalation technique in Europe: a report from the Aerosol Drug Management Improvement Team. *Respir Med*. 2006;100(9):1479–1494.
74. Lavorini F, Levy ML, Corrigan C, Crompton G; ADMIT Working Group. The ADMIT series – issues in inhalation therapy. 6) Training tools for inhalation devices. *Prim Care Respir J*. 2010;19(4):335–341.
75. Melani AS, Zanchetta D, Barbato N, et al; Associazione Italiana Pneumologi Ospedalieri Educational Group. Inhalation technique and variables associated with misuse of conventional metered-dose inhalers and newer dry powder inhalers in experienced adults. *Ann Allergy Asthma Immunol*. 2004;93(5):439–446.
76. Basheti IA, Reddel HK, Armour CL, Bosnic-Anticevich SZ. Counseling about turbuhaler technique: needs assessment and effective strategies for community pharmacists. *Respir Care*. 2005;50(5):617–623.
77. Bosnic-Anticevich SZ, Sinha H, So S, Reddel HK. Metered-dose inhaler technique: the effect of two educational interventions delivered in community pharmacy over time. *J Asthma*. 2010;47(3):251–256.
78. Goodwin R, Chander T, Shah N, Tomlin S. Inhaler counselling, the real deal or just fresh air? *Arch Dis Child*. 2016;101(9):e2.
79. Leung J, Bhutani M, Leigh R, Pelletier D, Good C, Sin DD. Empowering family physicians to impart proper inhaler teaching to patients with chronic obstructive pulmonary disease and asthma. *Can Respir J*. 2015;22(5):266–270.
80. Mulhall AM, Zafar MA, Record S, Channell H, Panos RJ. A tablet-based multimedia education tool improves provider and subject knowledge of inhaler use techniques. *Respir Care*. 2017;62(2):163–171.
81. Takaku Y, Kurashima K, Ohta C, et al. How many instructions are required to correct inhalation errors in patients with asthma and chronic obstructive pulmonary disease? *Respir Med*. 2017;123:110–115.
82. Basheti IA, Obeidat NM, Reddel HK. Effect of novel inhaler technique reminder labels on the retention of inhaler technique skills in asthma: a single-blind randomized controlled trial. *NPJ Prim Care Respir Med*. 2017;27(1):9.
83. Goodwin R, Heraghty J. Do healthcare professionals understand asthma devices? *Arch Dis Child Educ Pract Ed*. 2015;100(6):302–305.
84. Hou S, Wu J, Li X, Shu H. Practical, regulatory and clinical considerations for development of inhalation drug products. *Asian J Pharm Sci*. 2015;10:490–500.
85. Simpson AJ, Honkoop PJ, Kennington E, et al. Perspectives of patients and healthcare professionals on mHealth for asthma self-management. *Eur Respir J*. 2017;49(5):1601966.
86. Kikidis D, Konstantinos V, Tzovaras D, Usmani OS. The digital asthma patient: the history and future of inhaler based health monitoring devices. *J Aerosol Med Pulm Drug Deliv*. 2016;29(3):219–232.
87. Carpenter DM, Roberts CA, Sage AJ, George J, Horne R. A review of electronic devices to assess inhaler technique. *Curr Allergy Asthma Rep*. 2017;17(3):17.
88. Usmani OS. New developments in inhaled drugs: within and beyond the lungs. *Respiration*. 2014;88(1):1–2.
89. Biddiscombe MF, Usmani OS, Barnes PJ. A system for the production and delivery of monodisperse salbutamol aerosols to the lungs. *Int J Pharm*. 2003;254(2):243–253.
90. Berlinski A. Pediatric aerosol therapy. *Respir Care*. 2017;62(6):662–677.
91. Hamelmann E, Szeffler SJ. Efficacy and safety of tiotropium in children and adolescents. *Drugs*. 2018;78(3):327–338.
92. Barrons R, Wheeler J, Woods JA. Opportunities for inhaler device selection in elderly patients with asthma or COPD. *Patient Intelligence*. 2015;7:53–65.
93. Scichilone N, Braidò F, Lavorini F, Levy ML, Usmani OS. Routine use of budesonide/formoterol fixed dose combination in elderly asthmatic patients: practical considerations. *Drugs Aging*. 2017;34(5):321–330.

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