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REVIEW

How to Choose the Right Inhaler Using a Patient-Centric Approach?

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ABSTRACT

There are many different inhaler devices and medications on the market for the treatment of asthma and chronic obstructive pulmonary disease, with over 230 drug-delivery system combinations available. However, despite the abundance of effective treatment options, the achieved disease control in clinical practice often remains unsatisfactory. In this context, a key determining factor is the match or mismatch of an inhalation device with the characteristics or needs of an individual patient. Indeed, to date, no ideal device exists that fits all patients, and a personalized approach needs to be considered. Several useful choice-guiding algorithms have been developed in the recent years to improve inhaler–patient matching, but a comprehensive tool that translates the multifactorial complexity of inhalation therapy into a user-friendly algorithm is still lacking. To address this, a multidisciplinary expert panel has developed an evidence-based practical treatment tool that allows a straightforward way of choosing the right inhaler for each patient.

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Key Summary Points

Many inhalation device options allow an individualized approach for each patient, but increase the complexity of choosing the right device for each patient.

A multidisciplinary expert panel developed an evidence-based practical patient-centric treatment algorithm for choosing an inhaler and for assessing proper inhaler use during patient follow-up.

INTRODUCTION

Asthma and chronic obstructive pulmonary disease (COPD) are chronic respiratory diseases that are associated with significant morbidity and mortality. In the Global Burden of Disease study, it was shown that COPD was the seventh leading cause of years of life lost, and accounted for 81.6 million disability-adjusted life-years worldwide, while asthma accounted for 22.8 million disability-adjusted life-years [24, 75]. As these conditions affect more than 330 million and 250 million people worldwide, respectively, they are considered as a serious global health problem [78]. The cornerstone of asthma and COPD treatment is inhaled therapy that allows a rapid and targeted delivery of medication to the lungs, while limiting systemic exposure and potential side effects. Efficacy and safety of the various inhaled bronchodilators and corticosteroids (ICS) and their adequate dosage are important when choosing appropriate therapy for patients. Although the choice of device is equally important, this aspect of choosing a treatment is too often overlooked by health care professionals in both primary and secondary care [29]. There is a wide variety of inhaler devices that can be grouped into the pressurized metered dose inhalers (pMDI), soft mist inhalers (SMI), dry powder inhalers (DPI), and nebulizers [37]. Each category has its own set of intrinsic characteristics with regard to handling technique, design and inhalation technology, and is associated with specific advantages and disadvantages. Devices can differ significantly within each category. Although the accessibility of these many device options allows an individualized approach for each patient, it also increases the complexity of choosing the right device for each patient. Therefore, several patient-related factors codetermine the potential for a successful therapeutic delivery of drugs, such as the ability to use the device and patient adherence. These are key aspects in achieving better clinical control and improving the quality of life with any device. As such, both the Global Initiative for Asthma and the Global Initiative for Chronic Obstructive Lung Disease guidelines emphasize the importance of the inhalation technique in their management algorithms, and recommend the choice of the device/treatment combination to be the subject of extensive review and education [26, 27].

AIM AND METHODOLOGY

The aim of this paper is to provide a narrative review covering the most important aspects of inhalation therapy devices, and to propose an evidence-based practical treatment algorithm for choosing an inhaler and for assessing proper inhaler use during patient follow-up, with a focus on adults. A multidisciplinary expert panel, including pulmonologists, general practitioners, nurses, and pharmacists, was set up to design a practical tool that allows a straightforward choice. Although the choice of molecule is equally important in the choice of inhalation therapy, this is out of the scope of this paper. This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

OVERVIEW OF INHALATION DEVICES

Metered Dose Inhalers (MDI)

Pressurized metered dose inhalers (pMDI) were introduced in the 1950s and are still the most commonly used inhalation devices. They deliver a plume of aerosolized medicine that is inhaled via a hand–lung coordinated inhalation maneuver. In this regard, the patient has to (1) prepare the device (shake, uncap, and hold inhaler correctly), (2) turn away from the inhaler and breathe out completely, (3) place teeth and lips around the mouthpiece and tilt their head in the correct position, and (4) fire the device while beginning a slow inhalation. They then have to continue the slow and deep inhalation without interruption, after which (6) their breath needs to be held for 5–10 s or as long as possible [31, 39, 59*]. To assure that the pMDI works properly, it is advised to prime it by preparing the device as described before and spraying it into the air before its first use, or in case the inhaler has not been used for more than 14 days. pMDIs have several advantages, including their compact size, user-friendliness, and the fact that most treatment options are available in such format. Another significant advantage of pMDIs is that the dose delivered is reproducible and independent of the inhalation flow. As it does not require a high inspiratory flow, it can be suitable for emergency situations where this is more difficult to achieve. However, the required coordination of inspiration and actuation can be troublesome for patients, and this is indeed a frequently occurring mistake. Similarly, a significant proportion of patients fail to inhale slowly and deeply, stop inhaling immediately after firing, or fail to breath-hold for a sufficient time. Forgetting to shake their inhaler before its use is also a step that is often overlooked, not only by patients but also by healthcare professionals [59, 66*]. This is specifically important in the case of pMDIs formulated as suspensions, where a high variability and inconsistency in the emitted dose is noted when not properly shaken, a risk that is avoided when using solutions [10].

To increase lung deposition of inhaled particles in situations prone to hand–device coordination errors, inhalation chambers were developed, that allow delivery of medication in a slower, controlled fashion. The inhalation chamber slows down the aerosol cloud as it emerges from the pMDI and filters out larger aerosol particles that sediment on the walls. A distinction can be made between spacers and valve-holding chambers (VHC) that trap and hold the aerosol cloud until the patient inhales from the chamber using a one-way valve [38]. To use the chambers, patients have to remove the cap, (1) prepare the device (shake, uncap, and hold inhaler correctly), (2) connect it to the chamber, (3) turn away, exhale gently and completely, and then place teeth and lips around the chamber's mouthpiece to form a seal, (4) fire the pMDI and take one slow and deep breath over 4–5 s, and, finally, (5) hold their breath for 5–10 s or as long as possible [39, 59, 76]. Several types of inhalation chambers exist that vary in size/volume, shape, material of manufacture, tendency to become electrostatically charged, and presence of feedback devices or mechanisms [5, 38, 76]. Importantly, they are not easily interchangeable, due to a variable compatibility and performance with specific pMDIs [20, 38, 73]. An advantage of inhalation chambers is that, in patients where a forced inhalation maneuver is difficult, as is the case for patients with dyspnea, they can be used with tidal breathing and can be administered by a caregiver [76]. Disadvantages include the need for regular cleaning and a lack of portability. In clinical practice, VHCs are only sparsely used.

pMDIs have since their introduction undergone significant technological improvements. When they were first introduced, the pMDIs made use of the ozone-depleting propellant chlorofluorocarbon (CFC). In the 1990s, this propellant was completely replaced by the more environmentally friendly hydrofluoroalkane (HFA), and new developments that further reduce the environmental load are under way and are outlined further on in this article [34, 49]. The HFA-driven pMDIs produce a plume with a lower velocity, improving lung deposition, even when hand–lung coordination

is suboptimal [37*]. Breath-actuated MDIs (BAMDIs) similarly help to solve coordination issues, as they are triggered by airflow upon inspiration. Their use is, however, limited by the restricted number of drugs and combination of medications formulated in BAMDIs. Indeed, none of the currently marketed BAMDIs contain long-acting muscarine antagonists, either alone or in combination with long-acting beta-2-agonist and a triple combination with inhalation corticosteroids is also lacking. Some pMDIs contain a solution rather than a suspension, and hence do not require shaking prior to actuation, such as the pMDIs developed with Modulite® technology [1, 66]. Moreover, a growing number of pMDIs produce a high fine particle fraction, which results in a higher total lung deposition, a better peripheral lung penetration and consequently added clinical benefit, compared to larger particles of equivalent molecules, both in asthma and COPD [66, 71]. Lastly, almost all pMDIs currently on the Belgian market used as controller medications have a dose counter or dose indicator that allows to reliably keep track of the remaining doses.

Dry Powder Inhaler (DPI)

Dry powder inhalers (DPIs) were developed as an inhalation-activated alternative to the propellant-driven pMDIs, aiming to overcome the inherent coordination issues. In this regard, there are three systems that are currently used: single-dose capsule-based inhalers; multi-dose inhalers that make use of blisters; and multi-dose inhalers that make use of a reservoir. Upon a forceful inhalation, the powder de-aggregates or detaches from a lactose carrier resulting in fine particles suitable for inspiration. The effectiveness of inhalation of these drugs depends on the inspiratory flow rate generated by the patient and on the turbulence produced by the intrinsic resistance of the DPI, with the latter depending on technical design. In low-resistance DPIs, the disaggregation of the drug highly depends on the inspiratory flow of the patient, while in medium-resistance DPIs disaggregation is optimal even in the absence of a maximal inspiratory effort [18, 30].

Despite the many differences between DPIs, the steps to use the device generally are the same. Similarly to the pMDI, the patient has to (1) prepare the device (device-specific), (2) turn away from the inhaler and breathe out completely, and (3) place teeth and lips around the mouthpiece to form a seal. In contrast with the pMDI, however, the patient has to (4) breathe in with one brisk, deep inhalation, followed by (5) a breath-hold for 5–10 s or as long as possible [32, 59*]. In the case of single-dose capsule inhalers, two consecutive inhalations are strongly recommended to ascertain inhalation of the complete dose. Moreover, an additional step is required when using the Easyhaler®, which is the sole DPI that requires shaking before use. DPIs can be equally compact and portable compared to pMDIs, and are also available for most treatments [59*]. Moreover, all multi-dose devices have dose counters. Although the DPI overcomes the coordination issues of a pMDI, it also has some drawbacks. As breath actuation is needed for de-aggregation, the device depends on the patient's ability to overcome the internal resistance and generate a strong inspiratory flow. In this regard, the lack of a forceful, deep inhalation is one of the most frequently occurring critical errors, resulting in insufficient drug delivery to the lungs. Therefore, some DPIs have integrated additional auditory feedback mechanisms to assure the patient that a full dose has been inhaled [15]. Other frequent errors related to inhalation technique are the lack of a full expiration before inhalation and not holding breath long enough after inspiration [77]. On a more practical note, DPIs are more sensitive to humidity, necessitating specific storage conditions and, in the case of single-unit devices, the capsule needs to be loaded each time before use, which can be considered a hurdle by some patients.

Soft Mist Inhaler (SMI)

The soft-mist inhaler (SMI) produces a low-velocity cloud by aerosolizing a solution using the energy of a compressed spring inside the inhaler

that pushes the solution through a capillary, without the use of propellants, contrary to what is believed by some healthcare professionals. Similarly to the pMDI, the patient has to (1) prepare the device (prepare dose, uncap, and hold inhaler correctly) (2) turn away from the inhaler and breathe out completely, (3) place teeth and lips around the mouthpiece and tilt their head in the correct position, and (4) fire the device while beginning slow inhalation. They then have to (5) breathe slowly and deeply, without stopping, after which (6) their breath needs to be held for 5–10 s or as long as possible [31, 39, 59*]. The slow-moving cloud somewhat decreases the need for coordination in comparison with pMDIs, while allowing a lower dependence on inspiratory flow rate compared to DPIs [67*]. In addition, the high fine particle fraction allows for a higher lung deposition and a lower oropharyngeal deposition. However, there is only one commercially available SMI to date, and the number of medications that can be delivered through this system is still limited and does not comprise any corticosteroids. This latter fact can be explained by the absence of corticosteroid in aqueous solution in formulations on the market. Moreover, the dose needs to be loaded in this device which can be troublesome for patients with physical limitations [67*].

Nebulizers

Nebulizers convert a liquid containing a medication into an inhalable spray. A mask placed over the nose and mouth or a T-mouthpiece is connected to the nebulizer. The patient can breathe normally through their mouth for 10–15 min to comfortably allow the delivery of high doses of medication contained in ampoules. Several types of nebulizers exist: air-jet nebulizers, ultrasonic nebulizers, and vibrating-mesh nebulizers.

Nebulizers are not as compact as pMDIs and DPIs, require thorough and regular cleaning to avoid contamination, and can potentially transmit respiratory viral infections [26]. Moreover, nebulizer performance is highly variable. Not all nebulizers can generate the necessary range of particle sizes to reach the upper and lower respiratory tracts, and hence some are unsuitable for the regular therapy of obstructive lung disease [14]. There is also a considerable deposition of particles on the nasal mucosa, eyes, and skin when nose–mouth masks are used, potentially leading to unwanted side effects. They all need an external source of energy (compressed gas, electricity). In addition, depending on the nebulizer, there can be a considerable amount of medication volume left in the reservoir at the end of the operation, resulting in an overestimation of the delivered dose [8]. For these reasons, nebulizers are generally not recommended for long-term treatment of asthma and COPD, but only for treatment in small children, disabled people, or elderly patients who are unable to use any other device [26, 27].

CHOOSING THE RIGHT INHALER: A PATIENT-CENTRIC TREATMENT ALGORITHM

Although a personalized approach is necessary, no evidence-based, clinically-validated guidance to help healthcare providers choose an appropriate inhaler exists to date. Several useful choice-guiding algorithms have been developed in recent years [19, 20, 66, 67*], but there is still a lack of a comprehensive algorithm that fully translates the multifactorial complexity of inhalation therapy into a user-friendly guideline. To tackle this, a multidisciplinary expert panel, including pulmonologists, general practitioners, nurses, and pharmacists, was set up to design a practical tool that allows a straightforward choice. Consensus was achieved in a multiple-round process, involving both online and offline revisions. At the core of the resulting treatment algorithm is the continuous evaluation of patients' characteristics as a driver of device choice, followed by the instruction and assessment of inhalation technique, and the evaluation of patient adherence and satisfaction throughout the patient's treatment course (Fig. 1). Each part of the algorithm is further elucidated in the sections below.

CHOOSE

Several patient-related factors codetermine the choice of an inhaler, such as disease severity, comorbidities, level of coordination, manual dexterity, rheumatismal problems, physical properties (sex, height), and cognitive function [2, 4, 57]. To construct a practical tool, the expert panel defined three core questions to which the answers can provide guidance to decide which device types can be used for a specific patient, with a focus on adults.

The first question relates to the inhalation maneuver that is necessary for using a DPI: 'Is a deep, quick voluntary inhalation possible?'. If the patient is not capable of this action, or shows signs of discomfort while performing this maneuver, a DPI is not considered suitable [68*].

In this way, the answer to the first question already gives an indication of the inhaler class that is more appropriate. However, in some patients, the ability to perform this action will not translate into the necessary inspiratory flow, due to a lack of lung volume. A second question therefore relates to the necessary inspiratory flow that is required to operate the different devices: 'Can sufficient inspiratory flow be obtained?'. Indeed, all devices require a minimal inhalation flow to deliver the drug successfully into the lungs. In this regard, a lower inspiratory flow is necessary for pMDIs (> 10 L/min) than for DPIs, with the optimal flow for DPIs varying considerably between devices (> 20–60 L/min) [28]. A lack of sufficient inspiratory flow when using DPIs has been shown to be significantly associated with uncontrolled asthma and exacerbations [56]. The potential decrease in inhalation flow by old age, comorbidities, neuromuscular disease, upper airway obstruction, or exacerbations also codetermines the choice of the inhaler, a particularly important issue when considering rescue medication [33].

Particular attention also needs to be given to patients who are discharged from the hospital after an exacerbation, as a COPD exacerbation can have a negative impact on inspiratory flow due to lung hyperinflation; a suboptimal peak inspiratory flow is indeed common [62, 41]. In this regard, the panel estimates that it is important to evaluate the inspiratory flow at discharge, to determine if the patient can adequately activate a DPI and adapt the choice in device accordingly.

As there is to date no easy, standardized way to measure the inspiratory flow in clinical practice, the analysis or estimation of this parameter is done at the discretion of the physician.

The third question relates to the hand–lung coordination that is required to adequately use pMDIs and SMIs: 'Does the patient have sufficient hand–lung coordination?'. If the patient does not have the ability to fire the device while slowly inhaling over 3–5 s [68*], it is recommended to combine the pMDI with a spacer or to use a BAMDI. Although not recommended, it has been shown that an SMI can be combined with a spacer [47]. This can be a solution in rare cases where the use of a SMI is mandatory, but not advised due to coordination problems. A DPI can be considered when the inspiratory flow is sufficient. Preferably, hand–lung coordination is assessed using a placebo device, but as this is often not readily available, this too can be done by judgement of the physician.

As the prevalence of COPD rises with age, specific challenges are encountered with regard to inhaler device selection for elderly patients [3]. An observational study in primary care has shown that critical errors when using pMDIs and DPIs are particularly frequent in elderly patients (> 65 years) [44]. For these patients, it can be challenging to manipulate the device due to dexterity problems that are linked to comorbidities, such as osteoarthritis, neurological conditions such as Parkinson's disease and stroke, muscle weakness, or cognitive impairment. Also, connecting a spacer to a pMDI or forming a firm seal around the mouthpiece can be difficult to achieve in this patient group [67*]. Moreover, patients might lack the hand strength to generate the minimum force to activate a pMDI or lack the dexterity or strength to coordinate their actions to successfully operate the device [3]. Cognitive dysfunction might also be particularly relevant in elderly patients [3]. Also, in younger patients, the

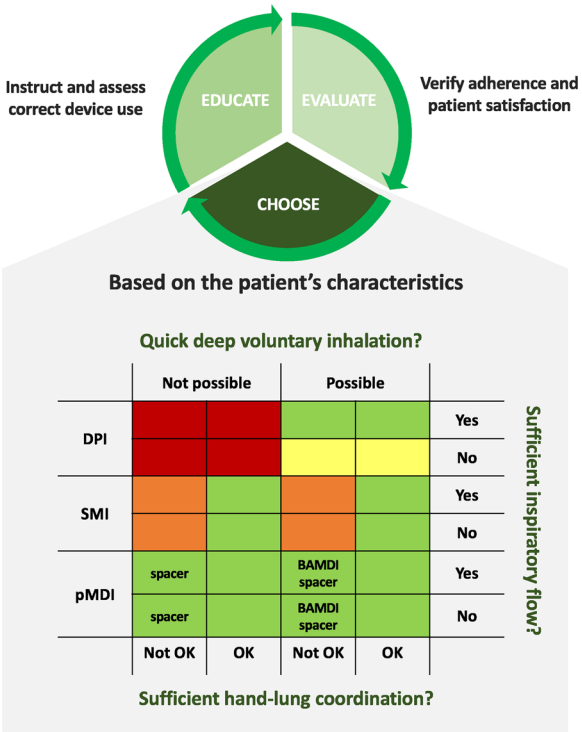

Fig. 1 Treatment algorithm. Choosing an optimal device is guided by three core patient-centric questions. (1) *Is a deep, quick voluntary inhalation possible?* (2) *Can sufficient inspiratory flow be obtained?*, and (3) *Does the patient have sufficient hand–lung coordination?* Based on the answers to these questions an appropriate device can be selected. Green device option possible; Red device option not recommended; Yellow consider a device requiring low inspiratory flow; Orange only in combination with a spacer (not generally recommended). Further explanation is in the text. *DPI* dry powder inhaler, *SMI* soft mist inhaler, *pMDI* pressurized metered dose inhaler, *BAMDI* breath-actuated metered dose inhaler

choice of device is influenced by age-related factors. Depending on the age, children might have an erratic breathing pattern that does not allow a correct breath actuation or have problems with hand–lung coordination. Moreover, even if they have sufficient coordination and strength, they can lack the cognitive ability to understand the complex steps that are required for the correct use of a device [67*].

EDUCATE

In theory, the use of each inhalation device seems relatively straightforward, as it only comprises a limited number of steps. However, due to the plethora of devices, considerable confusion among patients and healthcare professionals exists about their use. When asked about their ability to properly use an inhaler, over a third of patients indicated that they are unsure about their inhalation technique in a study by Hanania et al. [29]. Indeed, clinical practice shows that only a minority of patients use their inhalation device correctly, and poor inhaler technique has been cited as a major reason for ineffective treatment in asthma and COPD [42, 56]. Critical errors that result in limited or no lung deposition of the medication are particularly important, as they render a therapy useless [66*, 45]. A systematic review published in 2018 reported on a total of 10 studies in asthma patients that observed an association between inhaler error frequency and poor disease outcomes, including poor disease control and an increased risk of hospitalization, emergency room visits, and courses of oral steroids [66*]. Inhalation errors in asthma were frequent for both device-specific and generic across devices. The most common errors were not exhaling before use, not holding the breath, insufficient speed of inhalation, and dose preparation errors for DPIs, and coordination problems with pMDIs [56]. Moreover, inhalation errors with DPIs were associated with an increased likelihood of having poorer control of asthma symptoms and an increased exacerbation rate [56]. Similarly, several studies showed that inhalation errors occur frequently, in 60–85% of the patients depending on the device [7, 11, 13] and that misuse is associated with an increased risk for hospital admissions, emergency department visits, and poor disease control in both asthma and COPD [42]. The economic burden of a poor inhalation technique can be considerable, and one study estimated this to be 2–8% of the direct costs of disease management for commonly prescribed DPIs in three European countries, totaling over €100 million in one year [40]. Indeed, the most

expensive inhaler will always be the one that is not used correctly [16]. Consequently, the continuous training of patients' inhalation technique is considered essential to the success of any inhalation treatment by the international treatment guidelines [26, 27].

People often need multiple attempts to achieve successful inhalation, with errors varying between specific devices [58]. A review by the Aerosol Drug Management Improvement Team in European patients published in 2006 showed that up to 50% of the patients are unable to use their inhalers correctly [16]. Moreover, the frequency and type of inhalation errors have not diminished over the past 40 years [59*], highlighting the complexity of inhalation therapy and the strong need for education. Interventions to improve inhaler technique have proven successful [46*]. In this regard, a recent study showed that a single 10-min educational session by a nurse specialist could significantly improve asthma control after 3 months [60]. In agreement, Schulte and colleagues showed that the frequency of inhalation errors decreased significantly after the investigator explained the device handling to the patient compared to a first attempt with only written instructions available, indicating the importance of education when first using the device [61]. However, not only is education at the start of a therapy essential it is also needed during the follow-up to maintain a correct inhaler technique, as this falters over time [48]. Educational tools to improve the patients' knowledge about inhalers should be tailored to the patients' needs, and can include both on- and offline tools, such as instructional leaflets or the MyPuff application launched by the Belgian Respiratory Society that illustrates the correct way to use inhalers with videos.[1] The PHARMACOP study showed that two interventions by the pharmacist focusing on inhaler technique significantly improved inhalation score and was associated with a decrease in the number of hospitalizations, suggesting that different stakeholders may play a role in education regarding device technique [65].

[1] https://www.belgianrespiratorysociety.be/nl/mypuff

Nevertheless, healthcare professionals who are responsible for evaluating a patients' inhalation technique often lack the necessary knowledge themselves. Most physicians focus on the medication class rather than on the type of device when prescribing inhalation therapy [29]. A study by Plaza et al. showed that only 12% of healthcare professionals were able to handle the inhalation devices correctly, prompting the need for education on that level as well [52].

A detailed description of the steps involved in the inhalation maneuver for each device type can be found in the supplementary material.

EVALUATE

Besides inhalation technique, another key factor in determining inhalation therapy success is patient adherence. As seen in other chronic diseases, adherence has been widely reported to be suboptimal in both asthma and COPD [12, 53]. As such, only one-third of asthma patients and half of COPD patients are considered to adhere to their medication [29, 53], but other studies suggest that, even in COPD patients, adherence can be as low as 36% [63]. As for inhalation technique, adherence is shown to be strongly associated with both clinical and economic outcomes, with evidence for increased exacerbations and hospitalizations, mortality, decreased quality of life, and loss of productivity in COPD patients [12, 17, 63, 69, 74]. The evaluation of patients with regard to adherence is therefore considered key [26, 27].

The reasons why patients do not adhere to their inhaled therapies are multiple. A lack of adherence can be intentional or unintentional. Unintentional non-adherence mostly relates to a lack of capacity to take medication, due to cognitive impairment, disease severity, or inhalation errors, which can be particularly relevant in specific age groups. Intentional non-adherence on the other hand is largely associated with patient motivation [63]. Aside from the direct impact of the motivation of a patient to practice a correct inhaler technique, and to maintain correct inhaler use [48], the

misalignment between the priorities of physicians and patients in deciding which inhaler to use can impact adherence. In a study by Dhand and colleagues, a 'minimal effort to inhale the drug' was considered highly important for physicians, while patients gave this item minimal ranking. For patients, the fact that they 'do not need to load the drug before inhaling' was of high importance, as opposed to the ranking by physicians [21]. Patient dissatisfaction with a device and lack of respect for their preferences were linked to poor adherence and clinical outcome, an issue that is often overlooked during decision-making [12, 17]. Attributes influencing inhaler satisfaction were found to be mainly related to sustainability, ergonomics, and ease of use [17]. A recent study by Ruessel and colleagues showed that, within a geriatric treatment-naive population in Germany, people indeed had a clear preference towards the inhaler that was the easiest to use [58].

Several intervention programs have been developed to improve adherence. The concept of shared decision-making, a patient-centric approach in which the treatment is decided taking into account the patient's ideas, concerns, and expectations, has proven to improve adherence and disease outcomes in poorly controlled asthmatics [54]. Educating patients about their disease and informing them about the importance of taking their medication correctly has not only proven to benefit adherence but has also been shown to be cost-saving in COPD [65, 70]. In this regard, multidisciplinary collaboration between physicians and pharmacists allows close monitoring of patients, as community pharmacists can follow-up on the prescription refills and also use their knowledge of treatment administration to educate the patient [70]. Moreover, audiovisual or text reminders as well as simplifying medication regimes, for instance using combination inhalers, can be effective in improving adherence. More recently investigated approaches, like patient empowerment through motivational coaching, have been shown to positively impact disease outcome measures and quality of life in asthma and COPD [25].

There are several ways to measure adherence, but no gold standard exists to date. Although patient- or provider-based reporting is inexpensive and easily applicable in clinical practice, there is only one test that has currently been validated to evaluate adherence specifically for inhalers (TAI®: Test of Adherence to Inhalers) [51]. Dispensing data are unbiased, but cannot confirm actual drug intake. Device-embedded electronic monitors do give objective data on intake, and, although not yet widespread due to their device-specific nature, they could become the norm in the future [25]. Even more interesting is that external factors can influence adherence, as was recently again illustrated by the impact of COVID-19 on the adherence of lung patients, which increased by 15% over a 3-month period [36].

SWITCHING DEVICES

With a vast array of device options available, notable differences, and an optimal patient profile for each device, it appears that an individualized approach will result in the best respiratory outcome. The question then arises whether a patient is currently using the optimal device or whether a switch is necessary. From a clinical point of view, the decisive factor for switching inhalers should be the lack of asthma control or repeated exacerbations or uncontrolled symptoms in COPD [35, 43]. In addition, non-compliance, persistent problems with the inhalation technique, physical limitations, or side effects can prompt the need for a switch in device [35]. Sometimes a switch is involuntary when a step-up or step-down in treatment is necessary due to the evolution in disease pathology, and when the required (combination) medication is not available in the accustomed device.

Several studies have shown that decreasing the complexity of inhalation therapy can improve disease control. As such, the use of separate inhalers was shown to result in higher direct and indirect medical costs compared to a single inhaler that combined treatments [6]. In addition, the use of several devices with mixed inhalation techniques resulted in significantly lower disease control and a higher rate of exacerbations as compared to when devices

with a similar technique were used [9, 55]. The development and widespread use of pMDIs that can be used as both maintenance and reliever therapy in asthma further underscores the benefits of treating with a single inhaler type [26, 50].

Other factors that can come into play are financial constraints, and recently the environmental impact of inhalers, with a strong focus on the propellants used in pMDIs [68*]. However, there has been a development away from CFC propellants towards non-ozone depleting substitutes, such as HFA (such as HFO-1234ze and HFA-152a) and SMIs [23, 49]. Moreover, the elements impacting the environmental load of a device are not only linked to the use of propellants but are also determined by the manufacturing process and waste associated with its use, which necessitates a multifactorial approach when comparing the true ecological footprint of each device [68*]. In this regard, Jeswani and Azapagic recently evaluated the life-cycle environmental impacts of different types of inhalers, and showed that the new propellant, HFA-152a, has the lowest impact on 10/14 analyzed environmental categories compared to older HFAs and DPIs [34, 49]. Anyway, it remains a matter of debate if the environmental factor alone is a sufficient reason to switch a device, especially as switching devices is not without risk [22, 43, 64]. Indeed, the lack of consent of asthma patients in switching devices resulted in inhalation errors, feelings of disempowerment, and loss of personal control over their treatment, which could potentially be associated with an overuse of medication and other resources [22]. Similarly, another study in asthma patients that studied the unconsented switch in ICS devices confirmed that this was associated with worsened asthma control [64]. Any change in inhaler type should be accompanied by a clinical evaluation and patient consultation in which the time necessary to instruct the patient is not underestimated [43, 72].

CONCLUSION

In order to achieve good treatment results, it is crucial to match the inhalation device with the characteristics and wishes of an individual patient. The evidence-based practical treatment tool proposed here allows a straightforward choice of the right inhaler for each patient.

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