Review

Personalized Inhaler Selection in COPD and Asthma: Clinical Implications of Aerosol Characteristics and Device Performance

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Review

Personalized Inhaler Selection in COPD and Asthma: Clinical Implications of Aerosol Characteristics and Device Performance

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Abstract

The management of chronic obstructive pulmonary disease (COPD) and asthma depends critically on the effective delivery of aerosolized medications to the respiratory tract. Clinical efficacy is determined not only by the active pharmaceutical ingredient but also by a complex interplay among drug formulation, aerosol particle size, inhaler device characteristics, dosing frequency, and patient-specific factors. This review evaluates the technical specifications and clinical performance of major inhaled therapeutic systems, including the Ellipta platform, the Respimat soft mist inhaler (SMI), conventional pressurized metered-dose inhalers (pMDIs), and dry powder inhalers (DPIs). We examine the impact of particle size and extra-fine formulations on peripheral deposition and small airway disease (SAD), and synthesize comparative clinical evidence linking deposition patterns to symptom control and exacerbation reduction. In addition, we explore clinically relevant determinants of personalized device selection including peak inspiratory flow rate (PIFR) limitations, pneumonia risk, dosing frequency, and rescue inhaler requirements. By integrating inhaler design with real-world clinical considerations, this review provides a practical framework for individualized inhaler selection in obstructive lung disease. A patient-centered approach that accounts for airway phenotype, infection risk, inspiratory flow capability, and adherence patterns is essential to optimize drug delivery and improve long-term outcomes.

Keywords: inhaler devices; pharmaceutical aerosols; COPD; asthma; brochodilators; inhaled corticosteroids; small airway disease

1. Introduction

Chronic Obstructive Pulmonary Disease (COPD) and asthma represent a significant global health burden, ranking among the leading causes of morbidity and mortality worldwide [1]. The goal of medical therapy in these patients is to alleviate symptoms, improve lung function, reduce the frequency and severity of acute exacerbations, while minimizing the adverse effects that may be associated with therapy.

Inhalation therapy is the foundational means for administering those treatments as it allows for direct delivery of bronchodilators and corticosteroids to the airways while minimizing unwanted systemic absorption and associated side effects. As such, the successful management of obstructive airway diseases is intrinsically linked to the advancement of aerosol science. Compared to oral or intravenous drug administration, efficacy of inhaled agents is not only dependent on its active pharmaceutical ingredients. The engineering of the delivery system and a patient's ability to properly use the device is just as crucial. This complex interplay dictates the successful deposition of medication within the respiratory tract and overall clinical efficacy.

Due to technological advancements in aerosol device technology, there is now a diverse array of delivery platforms designed to optimize drug delivery and maximize ease of device usage. This

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review will analyze current major inhaled therapeutic systems, including dry powder inhalers (DPIs) systems such as Ellipta, the Respimat Soft Mist Inhaler (SMI), and various pressurized metered dose inhalers (pMDIs). By analyzing in vivo clinical evidence alongside studies on in vivo scintigraphy and in silico functional respiratory imaging (FRI) that analyze aerosol disposition, this paper will review the specific advantages and disadvantages of different device systems along with their component active pharmacological ingredient.

Understanding these device-specific and drug specific nuances allows personalization of inhaler therapy and enables clinicians to match the right delivery system to the specific physiological and cognitive needs of the patient, thereby optimizing long-term outcomes in asthma and COPD patients.

2. Foundations of Aerosol Science and Drug Delivery

The primary objective of inhalation therapy is to deliver bronchodilators and corticosteroids to the bronchial and alveolar regions while minimizing oropharyngeal deposition and systemic absorption.

The Mass Median Aerodynamic Diameter (MMAD) refers to the midpoint of aerosol particle size distribution by mass. The MMAD is critical for predicting where a medication deposits in the lungs. Deposition of inhaled particles occurs by three primary mechanisms: inertial impaction, gravitational sedimentation, and Brownian diffusion. The mechanisms and interaction with aerosol are summarized in Table 1.

Table 1. Aerosol sizes and Factors Affecting Deposition.

Particle Size Range	Deposition Mechanism	Primary Site of Deposition	Influencing Factors
> 5μm	Inertial Impaction	Oropharynx Large Airways	High flow rates Airway bifurcations
1 - 5μm	Gravitational Sedimentation	Small Airways Bronchioles	Breath-holding time Particle density
< 1μm	Brownian Diffusion	Alveoli	Particle dwell time Respiratory rate

Inertial impaction refers to the deposition of larger, faster moving particles that are unable to follow changes in airflow direction, causing them to impact airway walls at bends and bifurcations. This mechanism mainly affects larger particles ~5 μm in size. Larger particles deposit most in the upper respiratory tract (oropharynx) and the first generations of the tracheobronchial tree. Impaction is strongly velocity dependent and explains why excessively rapid inhalation or high spray velocities increase oropharyngeal deposition. This is particularly relevant for conventional pMDIs which have higher spray velocities.

Conversely, particles with a MMAD less than 5 μm are less susceptible to inertial impaction in the upper airways and can penetrate deeper into the distal bronchi. Accordingly, the fine particle fraction (FPF), defined as the proportion of the emitted dose with an MMAD below 5 μm, is crucial to a device's clinical performance.

Particles in the 1–5 μm range preferentially deposit in the small airways and bronchioles through gravitational sedimentation, which is the time-dependent settling of aerosols under gravity. Breath holding increases dwell time in the airways, thereby enhancing deposition by sedimentation. Particles smaller than 1 μm are capable of reaching the most distal alveolar regions. However, they are as easily exhaled out. For these ultrafine particles, Brownian diffusion—resulting from random molecular motion that causes particles to collide and deposit on the airway wall—becomes the predominant mechanism of deposition. Adequate breath-hold duration ensures that deposition occurs before the particles are exhaled.

Based on the above physical principles, the ideal method of inhaling a drug for many medications is a slow and deep inhalation followed by a breath hold which minimizes oropharyngeal

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inertial deposition, allows for enough drug to enter the distal airways, and allows enough time for deposition via gravitational sedimentation and Brownian diffusion.

Devices that generate a higher fine particle fraction (FPF) generally achieve more efficient distal drug delivery. However, this advantage is accompanied by a trade-off: as particle size decreases, the total delivered drug mass may also decline, potentially necessitating the use of more potent formulations to achieve the desired therapeutic effect. [2] Most inhaled agents used in obstructive lung diseases seek a balance of enough respirable mass to reach distal airways without excessive oropharyngeal deposition to minimize systemic absorption.

3. Measuring Drug Deposition in the Respiratory Tract

The most common method for quantification of inhaled drug deposition is in-vivo gamma scintigraphy. This involves radiolabeling the inhaled formulation with a radioisotope, then capturing images of the lungs using a planar or three-dimensional gamma camera after inhalation. Scintigraphy enables direct measurements of total lung deposition and extrathoracic deposition as well as regional distribution within the lungs. The key advantage of scintigraphy is that it measures actual in vivo deposition within a subject's airway. However, it requires radiolabel modification of a product, involves radiation exposure, and can only capture two-dimensional planar imaging which may underestimate three-dimensional heterogeneity of distribution [3].

Functional Respiratory Imaging (FRI), by contrast, is a computational technique that integrates high-resolution CT-derived three-dimensional airway reconstructions with fluid dynamic modeling to simulate airflow and particle transport. Advanced computational models are used to predict intrathoracic deposition patterns and can generate detailed maps of drug distribution. Input variables such as particle size distribution, drug plume characteristics and inhalation flow can be modified to model multiple inhalation scenarios without repeated human exposure or radiolabeling [4]. Together, scintigraphy and FRI can both be used synergistically to evaluate inhaler performance and understand drug distribution.

4. Engineering Differences of Inhaler Devices

In respiratory medicine, aerosols are generated predominantly by three device families: pressurized metered-dose inhalers (pMDIs), dry powder inhalers (DPIs), and nebulizer/soft-mist systems. Contemporary devices have been engineered to overcome the limitations of early pMDIs, which had environmental concerns with chlorofluorocarbons (CFCs) and used high spray velocities and droplet sizes leading to high oropharyngeal deposition [5]. The key classes of devices will be introduced below and comparison of their deposition rates measured via scintigraphy is shown in Table 2.

Table 2. Inhaler Devices and Studies on Lung and Extrapulmonary Deposition.

Device category	Total lung deposition (%)	Extrapulmonary deposition (%)	Ref
Traditional pMDI	21%	55%	[6]
pMDI with valved holding chamber	~52%	~4%	[7]
Standard jet nebulizer	3%	33.9%	[8]
Respimat SMI	37% -53% (	45 - 56%	[6]
Aerosphere pMDI =	34.5-37.7	62-65.1%	[9]
Ellipta DPI	20.8–22.7%*	Not available	[10]

*Lung deposition for Ellipta is calculated using FRI imaging. The deposition for other devices are measured directly using in-vivo gamma scintigraphy.

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4.1. Pressurized Metered-Dose Inhalers (pMDIs)

pMDIs are propellant driven systems that deliver a fixed metered volume of drug via a high-velocity aerosol plume generated by gaseous propellants. Early CFC propellants were associated with substantial environmental impact. Modern pMDIs using hydrofluoroalkane propellants have significantly reduced this burden; however, their carbon footprint generally remains higher than that of dry powder inhalers [11]. Ongoing technological advances and the development of next-generation propellants are expected to further mitigate the environmental impact [12].

Advantages of pMDIs include compact design, rapid delivery, relative independence from patient inspiratory effort, and broad compatibility with combination formulations, including inhaled corticosteroids(ICS)/long acting beta agonist(LABA) LABA/ long-acting muscarinic antagonists(LAMA), and triple therapy. However, pMDIs require coordination between actuation and inhalation, which is a major limitation in those with cognitive impairment [13]. Suboptimal technique promotes inertial impaction in the oropharynx due to high initial plume velocities. Devices may also require adequate shaking prior to use to ensure dose uniformity.

The addition of a valved holding chamber (VHC) can substantially increase drug delivery and reduce oropharyngeal deposition, but requires carrying an additional device [14].

New developments amongst pMDIs include the formulation of extra-fine pMDIs (e.g., (e.g., Foster, Trimbow). These devices utilize solution-based formulations that are able to generate particles with an MMAD less than 2 μm which have enhanced peripheral lung penetration [15]. Aerosphere Co-suspension Technology, employed in products such as Breztri and Bevespi, represents another novel development. Porous, phospholipid-based particles are co-suspended with active drug crystals which prevents aggregation and sedimentation, allowing for more uniform dosing and consistent aerodynamic performance across actuation events while still achieving relatively high total lung deposition [15,16].

4.2. Dry Powder Inhalers (DPIs)

Dry powder inhalers are propellant-free devices and are actuated by subject breathing. Inspiratory effort disperses drug particles into respirable aerosols. One advantage of DPIs is that they do not require hand-breath coordination, since drug is only released during inhalation.

The principal limitation is that drug delivery is intrinsically dependent on a patient's inspiratory flow rate and the device's internal resistance. Inadequate peak inspiratory flow rates such as in patients with severe COPD or frailty will result in reduced drug delivery [17].

One common DPI platform is the Ellipta device; a medium-resistance DPI engineered to provide consistent doses across a broad range of inspiratory flow rates [18]. The device features a simple open–inhale–close mechanism, incorporates an integrated dose counter, and is available across multiple inhaled therapeutic combinations—including ICS/LABA, ICS/LAMA/LABA, LAMA/LABA, LAMA monotherapy, and ICS monotherapy—all of which are formulated for once-daily administration.

Another novel platform is the Breezhaler, a low-resistance DPI in which a gelatin capsule containing powder is pierced immediately before inhalation. The low internal resistance requires lower patient inspiratory flow rates [18]. The audible capsule "rattles" during inhalation and provides user feedback that inhalation is occurring. However, the requirement to load a capsule for each dose introduces additional handling steps.

4.3. Soft Mist Inhalers (SMIs)

Soft mist inhalers are exemplified by the Respimat platform. These propellant-free devices use stored spring energy to force liquid medication through two microscopic channels that direct opposing liquid jets toward one another. The collision of these jets generates a fine aerosol mist characterized by low plume velocity, prolonged spray duration, and a high fine particle fraction. This profile reduces oropharyngeal impaction and enhances deposition in the distal airways [19]. In COPD

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patients with poor technique, Respimat devices can still achieve up to 53% lung deposition, whereas traditional pMDI deposition only achieves 21% [6].

Although the need for precise hand–breath coordination during the breath cycle is reduced compared with pMDIs, the device still requires a degree of manual dexterity during initial cartridge insertion and mechanical priming before each use.

5. Device Selection

Although inhaler devices vary in deposition profiles and delivery mechanics—and the active pharmaceutical ingredients paired with them differ in half-life and potency—major clinical guidelines are device-agnostic in their recommendations.

Current guidelines for initiating inhaled therapy in obstructive lung disease instead follow a stepwise paradigm. Therapy is escalated based on symptom burden, exacerbation risk, and objective measures of control. For asthma, the Global Initiative for Asthma (GINA) recommends starting with low-dose ICS-containing therapy, preferably as-needed low-dose ICS–formoterol. As disease severity increases, treatment is escalated stepwise by increasing the maintenance ICS dose, adding a LAMA, and considering biologic therapy in severe asthma [20]. Similarly, GOLD guidelines for COPD follow a severity-based escalation model. Initial therapy consists of a single long-acting bronchodilator (LAMA or LABA). This progresses to dual LAMA/LABA therapy in patients with greater symptom burden. For those at increased risk of exacerbations—particularly with elevated blood eosinophil counts—ICS is added [21].

These recommendations are supported by decades of large-scale randomized controlled trials showing that patients with greater disease burden derive additional benefit from stepwise dose escalation and combination therapy. A detailed catalog of all pivotal trials is beyond the scope of this review. Notably, relatively few randomized trials directly compare different inhaler device types within the same pharmacologic class. A foundational principle emerging from the literature is that, when patients are matched for disease severity and treated with equivalent medications, no single inhaler device type is inherently superior to another in terms of clinical efficacy.

A large review of randomized trials has shown no clinical advantage of alternative devices over standard pMDIs for ICS delivery or SABA delivery in asthma [22]. More contemporary systematic reviews similarly report no clinically meaningful differences between pMDIs and non-pMDI devices in asthma and COPD—including DPIs and SMI—across spirometric outcomes, exacerbation rates, reliever use, quality-of-life measures, or major safety endpoints [23]. Comparative analyses of triple fixed-dose combinations in COPD likewise show no significant differences in exacerbation risk, lung function, dyspnea indices, health-related quality of life, serious adverse events, pneumonia, cardiovascular events, or mortality [24].

While large randomized controlled trials and treatment guidelines provide population-level guidance, they are less able to offer precision for individual patient decision-making. Achieving optimal long-term outcomes requires moving beyond a “one-size-fits-all” approach and carefully evaluating patient-specific variables that may favor one device or active pharmacological ingredient over another.

The following sections therefore focus on identifying these patient-specific factors and clarifying how device selection can be individualized in clinical practice.

5.1. Targeting Small Airway Disease

Asthma and COPD are highly heterogeneous diseases. Although patients may share similar symptoms and airflow limitation, inflammation and obstruction are distributed unevenly throughout the bronchial tree. In a substantial subset of patients, pathology predominantly involves the small airways—the distal bronchioles with internal diameters < 2 mm [25]. Functional Respiratory Imaging (FRI) has increasingly validated the clinical importance of this compartment, demonstrating that small airway dysfunction contributes meaningfully to symptoms, air trapping, and disease progression [26].

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In contrast to standard aerosol particles in the 2-5 μm range, extra-fine formulations (MMAD ~1.1 μm) are designed to enhance peripheral deposition. Both Foster (beclometasone/formoterol pMDI) and Trimbow (beclometasone/formoterol/glycopyrronium pMDI) are specifically engineered to generate extra-fine aerosol particles [15,27,28].

In COPD, the rationale for small airway targeting centers on reducing air trapping and hyperinflation. Imaging and physiological studies have shown that switching from non-extra-fine ICS/LABA therapy to extra-fine triple therapy improves distal airway indices and reduces hyperinflation. These physiological improvements were tied to clinically meaningful reductions in symptom and quality of life scores [29]. Randomized trials further support this approach, demonstrating that extra-fine single-inhaler triple therapy reduces moderate-to-severe exacerbations compared with dual bronchodilator therapy [30]. Evidence in asthma is consistent with these findings. Imaging-based studies have shown that treatment with extra-fine BDP/FF increases small airway volume and reduces airway resistance, with structural improvements correlating with better asthma control [31].

Together, these data suggest that specifically targeting peripheral small airway disease translates into measurable physiological and clinical benefit beyond conventional spirometric endpoints. Clinically, extra-fine targeting is most rational in patients with suspected or documented small airway dysfunction—such as abnormal oscillometry indices, radiographic or physiological evidence of air trapping or hyperinflation, disproportionate symptoms relative to spirometry, or recurrent exacerbations despite apparently adequate therapy [32]. In these phenotypes, enhancing peripheral drug delivery may address pathophysiology not fully treated by standard-particle systems.

5.2. Assessing Peak Inspiratory Flow Rate (PIFR) and Its Clinical Consequences

For dry powder inhalers (DPIs), adequate peak inspiratory flow rate (PIFR) is essential to ensure proper powder deaggregation and effective lung deposition. If a patient is unable to generate sufficient inspiratory flow, drug delivery may be suboptimal.

The relationship between PIFR and drug delivery is also strongly influenced by a DPI device's internal resistance. While a minimum PIFR of approximately 30 L/min may allow actuation for some low-resistance DPIs, many devices require flows approaching 60 L/min to achieve optimal fine particle generation Table 3 [33]. In comparative studies, only about half of COPD patients achieved optimal flow for high-resistance DPIs, whereas a greater proportion were able to do so with medium-resistance devices [34].

Table 3. Common DPI Devices and Recommended PIFR [33].

Device	Minimal PIFR(L/min)	Optimal PIFR (L/min)
Turbuhaler	30	60
Diskus/Acculaher	30	60
Ellipta	30	60
Breezhaler	50	50
NEXThaler	35	35

The clinical implications of suboptimal PIFR are significant. Inadequate inspiratory flow has been associated with reduced bronchodilator response, impaired lung-volume improvement, and increased risk of COPD-related readmission [33,35]. In patients with severe COPD and PIFR below 60 L/min against DPI resistance, randomized crossover data demonstrate greater lung-volume responses to nebulized bronchodilators compared with DPI-delivered therapy [36]. These findings underscore that insufficient PIFR is not only a technical issue, but directly impacts clinical outcomes.

Accordingly, assessment of PIFR should be considered when selecting a DPI, particularly in older, frail, or recently exacerbated patients. PIFR can be measured in the ambulatory setting using handheld inspiratory flow devices such as the In-Check DIAL, which can simulate the internal resistance of different specific DPIs allow measurement of inspiratory flow against that resistance

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[37]. When formal PIFR measurement tools are unavailable, surrogate clinical markers such as frailty, and diminished grip strength have all been associated with impaired PIFR [38,39].

If PIFR is insufficient for a chosen DPI, alternative delivery systems should be considered. pMDIs, particularly when used with a spacer or valved holding chamber, reduce coordination dependence and do not rely on high inspiratory flow for drug dispersion. Nebulized therapy may also provide a practical alternative.

5.3. Pneumonia Risk and ICS Molecule Selection in COPD

Patients with COPD have a higher baseline risk of pneumonia. Exacerbations are often infection-triggered and recurrent infections are common. A large meta-analysis of clinical trial data demonstrated that ICS usage significantly further increased pneumonia risk in COPD (OR, 1.43; 95% CI, 1.34-1.53), with higher doses conferring higher pneumonia odds [40].

However, ICS also significantly reduces the risk of acute exacerbation in selected patients. Studies using single inhaler triple therapy emphasizes that ICS benefits for exacerbation prevention increase with higher blood eosinophils, supporting blood eosinophils as a biomarker to guide ICS responsiveness [41]. Contemporary GOLD guidelines acknowledge this and embed eosinophil thresholds into treatment algorithms. Earlier iterations emphasized ICS addition to reduce exacerbations in patients with absolute blood eosinophil counts ≥300 cells/μL, while most recent 2025 guidance recognizes meaningful benefit beginning at ≥100 cells/μL in patients who have had at least one moderate exacerbation [21].

As the therapeutic framework increasingly supports ICS use in appropriate COPD phenotypes, careful attention to safety becomes more important. Because ICS therapy is associated with dose-dependent pneumonia risk, there is a need to mitigate infectious complications through careful patient selection, dose optimization, and molecule choice.

GOLD notes that certain patient characteristics such as active smoking, age ≥55 years, a history of prior exacerbations or prior pneumonia, decreased body mass index <25 kg/m^2, increased symptoms, and worsening airflow obstruction are risk factors for pneumonia [21].

Additionally, different ICS molecules are associated with different pneumonia risk profiles. Large observational analyses have repeatedly found higher pneumonia risk with fluticasone than with budesonide [42]. A large health insurance database study showed a particularly elevated, dose-related risk with fluticasone (RR 2.01; 95% CI 1.93 to 2.10), while budesonide shows a smaller increase (RR 1.17; 95% CI 1.09 to 1.26) [43]. These intraclass differences are also confirmed in a the randomized control trial meta-analysis that found serious pneumonia was significantly increased with fluticasone, but not for budesonide and beclomethasone [40].

Putting this together, a pragmatic selection strategy is to first confirm an ICS indication (exacerbation history plus elevated eosinophil counts, and/or concomitant asthma features), then minimize pneumonia risk by favoring molecules with consistently lower pneumonia signals (budesonide or beclomethasone) in patients with high risk of pneumonia, and reassessing for de-escalation if pneumonia occurs.

5.4. Improving Adherence with Single Daily Dosing

Another key difference among inhaled therapies lies in dosing frequency, which is largely determined by the half-life of the active pharmaceutical ingredient. Some medications only require once-daily administration, whereas others need twice-daily dosing to maintain adequate efficacy.

Across multiple study designs—including electronic inhaler monitoring and large administrative claims analysis—once-daily regimens consistently demonstrate superior adherence compared with twice-daily therapies. In electronically monitored cohorts, once-daily users showed higher median daily adherence in both asthma and COPD populations [44]. Similarly, a real-world database analysis further indicate greater 12-month persistence and a lower likelihood of treatment discontinuation with once-daily regimens [45]. These findings are consistent with patient-reported preferences for simpler dosing schedules and reduced treatment burden.

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Importantly, improved adherence with once-daily therapy is not merely a behavioral observation but has been associated with clinically meaningful outcomes. In a UK observational active-comparator study, comparing two different once-daily agents and a twice-daily agent, initiation of once-daily inhaled therapy has been linked to a reduction in the risk of moderate to severe exacerbations compared with twice-daily regimens [46]. However, it is important to interpret these findings cautiously. Given that different active ingredients were compared, the observed reduction in exacerbation risk may reflect improved adherence associated with simpler once-daily dosing, intrinsic pharmacologic differences between the molecules studied, or a combination of both.

5.5. Avoid Using Multiple Respiratory Inhalers Requiring Different Techniques

Once-daily maintenance regimens offer a clear adherence and convenience advantage. However, most once-daily therapies are delivered via DPIs or SMIs, while most rescue inhalers are more commonly available as a pMDI. For patients who are otherwise on appropriate maintenance therapy yet still experience breakthrough dyspnea, as needed use of a rapid-acting pMDI rescue inhaler remains an essential component of therapy. Although rapid acting agents may be available as a DPI in some regions, reduced peak inspiratory flow during an acute exacerbation may compromise DPI drug delivery [33].

Using a pMDI and DPI properly requires substantially different techniques. This means that patients who use a non-pMDI as maintenance therapy but still require frequent rescue medication use have to master two fundamentally different inhaler techniques. Real-world studies consistently demonstrate that inhaler handling errors are highly prevalent even when just learning a single device type [47].

This issue has also been shown to be associated with clinically significant outcomes. In a matched cohort study comparing patients prescribed maintenance and reliever therapy using the same inhaler device type versus those prescribed different device types, patients in the similar-device cohort experienced a significantly lower rate of exacerbations (RR 0.82, 95% CI 0.80–0.84) and were less likely to require higher doses of rescue agents (OR 0.54, 95% CI 0.51–0.57) [48].

For patients who require frequent rescue medication use, simplifying inhaler technique may therefore offer meaningful advantages. This principle aligns with both COPD and asthma guidance, which emphasize reducing the number of different inhaler types whenever possible, structured patient education, and regular reassessment of inhaler technique to ensure effective and consistent drug delivery [20,21].

Formoterol-based agents are particularly noteworthy because of their unique pharmacologic profile characterized by both rapid onset and sustained bronchodilation [49]. In asthma, ICS–formoterol–based regimens are already validated as a first-line therapy when used as single maintenance and reliever therapy (SMART) [50,51]. The use of formoterol as a reliever has not been formally validated in COPD; however, its rapid onset raises a theoretical advantage in highly symptomatic COPD patients who experience persistent dyspnea throughout the day. In such individuals, twice-daily formoterol-based maintenance therapy (eg. Symbicort, Foster/Fostair, Bevespi, Breztri, Trimbow) may provide perceptible bronchodilation with each scheduled dose, potentially offering symptomatic benefit beyond that of longer-acting but slower onset single daily maintenance bronchodilator. However, it is important to emphasize that this hypothesis has not been prospectively validated in COPD-specific trials, and formoterol-based maintenance therapies are not recommended for use as rescue medications.

6. Conclusions

The clinical success of inhaled therapy is dependent on a complex interplay between the drug's active pharmacological ingredient, the inhaler design, and the way in which the patient uses the device. Although all approved inhaled therapies have demonstrated efficacy in well-conducted clinical trials, meaningful differences remain in particle size, lung deposition, device resistance,

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dosing frequency, and safety profiles. Each drug–device combination carries specific advantages, limitations, and practical nuances that allow clinicians to tailor the right choice to the right patient.

Optimal inhaler selection requires matching device choices to patient-specific factors. These include the presence of small airway disease, peak inspiratory flow capacity, pneumonia risk when considering ICS, preference for once- versus twice-daily dosing, and the need for simple, consistent rescue strategies. As the therapeutic landscape continues to evolve and inhaler technology advances, the emphasis should shift from selecting "the best inhaler" in general to selecting the most appropriate inhaler for a given individual. Personalized inhaled therapy, grounded in an understanding of drug pharmacology, aerosol science, device mechanics, and patient behavior, is essential to improving real-world outcomes in obstructive lung disease

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