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OPTIMIZING BRONCHIAL ASTHMA MANAGEMENT: A COMPREHENSIVE ANALYSIS OF INHALER DEVICE EFFICACY AND PATIENT ADHERENCE

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Abstract

This prospective study evaluated therapeutic adherence and inhalation technique errors in 60 adult asthma patients using either metered-dose inhalers (MDIs) or dry-powder inhalers (DPIs) in real-world clinical practice. Adherence (MMAS-8), inhalation technique (direct observation), and asthma control (ACT) were assessed.

DPI users demonstrated significantly higher adherence and fewer critical mechanical errors compared to MDI users, particularly those using MDIs without spacers. However, DPI effectiveness depended on adequate inspiratory flow. Proper technique and high adherence were strongly associated with better asthma control.

The findings highlight the need for personalized inhaler selection, mandatory spacer use with MDIs, and routine technique verification to improve asthma outcomes.

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Keywords: asthma, inhaler technique, medication adherence, metered-dose inhaler, dry-powder inhaler, spacer, asthma control, MMAS-8, ACT.

Introduction

Bronchial asthma remains one of the most formidable and ubiquitous global healthcare challenges of the contemporary era, representing a highly complex, heterogeneous, and chronic inflammatory disease of the respiratory tract. According to the meticulously compiled epidemiological data provided by the Global Initiative for Asthma (GINA) in its 2024 comprehensive strategy report, alongside the latest global assessments by the World Health Organization, bronchial asthma currently afflicts a staggering population of more than 260 million individuals worldwide [1]. The mortality burden associated with this condition is equally profound, with conservative estimates indicating that over 450,000 people succumb to asthma-related complications annually across the globe. Despite remarkable, paradigm-shifting advancements in the elucidation of asthma pathogenesis—ranging from the intricate cellular mechanics of eosinophilic inflammation to the development of highly potent, targeted pharmacological agents and biologic therapies—the overarching goal of achieving and maintaining optimal disease control in real-world clinical practice remains persistently elusive.

A substantial proportion of the global asthmatic population continues to experience debilitating daytime symptoms, severe restrictions in daily physical activities, disruptive nocturnal awakenings, and acute, life-threatening exacerbations. This chronic lack of optimal control imposes a profound economic burden on healthcare systems through emergency interventions, hospitalizations, and lost productivity, while simultaneously degrading the multidimensional quality of life of the afflicted patient. The contemporary cornerstone of management for persistent bronchial asthma relies predominantly on the localized inhalation of anti-inflammatory agents, primarily inhaled corticosteroids, which

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Eureka Journal of Health Sciences & Medical Innovation (EJHSMI)
ISSN 2760-4942 (Online) Volume 2, Issue 2, February 2026

https://eurekaoa.com/index.php/5

are frequently and synergistically combined with long-acting beta2-agonists. The global pharmaceutical market offers a vast array of highly efficacious combined formulations—such as the widely prescribed budesonide/formoterol, salmeterol/fluticasone, and beclometasone/formoterol—which consistently demonstrate superlative clinical results in the rigorously controlled environments of phase III clinical trials [2].

In real-world observational practice, a profound and critical discrepancy exists between the theoretical efficacy of modern asthma medications and the actual clinical effectiveness achieved by the patient. This paradox is fundamentally rooted in the unique nature of inhalation therapy, which is inherently and entirely "device-dependent"[3]. Unlike oral or intravenous routes of administration, where the systemic delivery and subsequent pharmacokinetic distribution of the active pharmaceutical ingredient are largely independent of the patient's mechanical intervention, inhalation therapy strictly requires the active, precise, and highly coordinated participation of the patient. The intrinsic therapeutic efficacy of the corticosteroid or bronchodilator molecule, once it successfully reaches the distal architecture of the lungs, is scientifically undisputed; the critical failure point lies in the reality that, for a vast majority of patients, the pharmacological agent simply fails to bypass the oropharynx and reach the targeted pulmonary tissue.

Two interconnected human factors serve as the primary barriers to optimal pulmonary drug delivery: suboptimal therapeutic adherence and chronically deficient inhalation technique. Because bronchial asthma is a chronic, fluctuating disease requiring daily, continuous, and often lifelong prophylactic maintenance therapy, sustaining patient compliance is notoriously difficult. The asymptomatic periods that are characteristic of clinical remission frequently generate a deceptive psychological illusion of complete biological recovery, prompting patients to unilaterally and prematurely discontinue their anti-inflammatory baseline therapy. Extensive empirical research and global surveys indicate that

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Eureka Journal of Health Sciences & Medical Innovation (EJHSMI)
ISSN 2760-4942 (Online) Volume 2, Issue 2, February 2026

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real-world adherence to prescribed inhaled corticosteroids frequently hovers between a dismal thirty and fifty percent. This systemic non-adherence inevitably precipitates a gradual recrudescence of airway hyperresponsiveness, culminating in a catastrophic loss of disease control and the sudden onset of acute exacerbations.

Equally, if not more, detrimental to patient outcomes is the widespread prevalence of incorrect inhalation techniques. Diverse multi-center clinical studies consistently demonstrate that an alarming seventy to ninety percent of patients utilizing any form of inhaler device commit at least one observable procedural error during administration [4]. Crucially, up to fifty percent of these mechanical deviations are classified by respiratory specialists as "critical errors." A critical error is rigorously defined as a procedural failure that drastically diminishes or entirely obliterates the fraction of the emitted dose that is successfully delivered to the lungs, effectively neutralizing the therapeutic benefit of the medication even if the patient demonstrates perfect temporal adherence to the prescribed dosing schedule.

These dual challenges of adherence and technique are further complicated by the fundamental mechanical, aerodynamic, and engineering disparities between the two predominant delivery systems currently dominating the global market: pressurized metered-dose inhalers and breath-actuated dry-powder inhalers[5]. Pressurized metered-dose inhalers require intricate, split-second hand-lung coordination, demanding that the patient manually actuate the pressurized canister simultaneously with the exact initiation of a slow, deep, and controlled inhalation. Asynchronous actuation—either too early or too late—or an excessively rapid inspiratory flow results in massive oropharyngeal impaction. In such failure states, more than eighty percent of the emitted dose is deposited harmlessly, or detrimentally, in the oral cavity and posterior throat, leading to localized adverse effects such as oral candidiasis and dysphonia, while yielding negligible pulmonary deposition and zero therapeutic effect.

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Eureka Journal of Health Sciences & Medical Innovation (EJHSMI)
ISSN 2760-4942 (Online) Volume 2, Issue 2, February 2026

https://eurekaoa.com/index.php/5

Conversely, dry-powder inhalers were specifically engineered by the pharmaceutical industry to circumvent this hand-lung coordination barrier by utilizing a sophisticated breath-actuated mechanism. However, this engineering solution inadvertently introduced a novel biomechanical requirement: the patient must independently generate a sufficient peak inspiratory flow rate to successfully deaggregate the active, micronized drug particles from their significantly larger carrier molecules, which are typically composed of lactose monohydrate. Patients with severe, acute airway obstruction, individuals of advanced age with diminished respiratory muscle strength, or pediatric demographics frequently lack the physiological capacity to develop the requisite inspiratory effort, culminating in incomplete dose emission, insufficient particle deaggregation, and ultimate therapeutic failure.

The above determines the relevance of this study. Comparing actual adherence and the frequency of critical errors when using MDIs and DPIs in routine practice will help identify the most vulnerable areas in asthma therapy and develop recommendations for personalized inhalation device selection based not only on diagnosis but also on the patient's individual capabilities.

Study Objective

To study and compare medication adherence and the incidence of critical inhalation technique errors in patients with asthma using metered-dose inhalers (MDIs) and dry powder inhalers (DPIs).

Clinical Study Design: Methodology and Patient Stratification

To empirically evaluate the profound intersection of inhaler device architecture and patient behavior prospective comparative clinical study was executed within the advanced multidisciplinary clinic of the Tashkent State Medical University.

The clinical trial formally enrolled a total of sixty adult patients, spanning an age range from eighteen to sixty-five years. Every selected participant presented with

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Eureka Journal of Health Sciences & Medical Innovation (EJHSMI)
ISSN 2760-4942 (Online) Volume 2, Issue 2, February 2026

https://eurekaoa.com/index.php/5

a formally verified, undisputed diagnosis of bronchial asthma, strictly defined and categorized by the contemporary Global Initiative for Asthma 2023 criteria. To ensure the absolute stability of the baseline data and to eliminate the confounding variables associated with acute drug initiation, all selected participants had been receiving continuous, uninterrupted maintenance therapy—comprising either isolated inhaled corticosteroids or a fixed-dose combination of inhaled corticosteroids and long-acting beta2-agonists—for a minimum contiguous period of three months prior to formal enrollment.

Patients were strictly excluded if they had experienced an acute asthma exacerbation or a severe respiratory tract infection within the four weeks immediately preceding their clinical evaluation visit. Furthermore, individuals presenting with concomitant chronic obstructive pulmonary disease (defined spirometrically by a post-bronchodilator FEV1/FVC ratio of less than 0.7), or those suffering from severe cognitive, neurological, or physical impairments (such as severe rheumatoid arthritis affecting the hands) that would mechanically preclude the proper operation of any inhaler device, were completely excluded from the study cohort.

The sixty eligible participants were then systematically stratified into two equal, parallel cohorts of thirty patients each:

1. **Group 1 (Metered-Dose Inhalers, n=30):** This cohort consisted of patients exclusively utilizing standard, unassisted pressurized metered-dose aerosol inhalers. Crucially, none of the patients in this group utilized a valved holding chamber or spacer device. The pharmacological agents most frequently utilized within this specific group included fixed-dose combinations of salmeterol and fluticasone (widely prescribed as Seretide MDI) and monotherapy fluticasone propionate (prescribed as Flixotide).
2. **Group 2 (Dry-Powder Inhalers, n=30):** This parallel cohort was composed of patients utilizing sophisticated, multi-dose dry-powder inhaler systems. The overwhelming majority of participants in this group operated either the high-

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Eureka Journal of Health Sciences & Medical Innovation (EJHSMI)
ISSN 2760-4942 (Online) Volume 2, Issue 2, February 2026

https://eurekaoa.com/index.php/5

resistance Turbuhaler system (delivering the budesonide/formoterol combination, Symbicort) or the medium-resistance Diskus system (delivering the salmeterol/fluticasone combination, Seretide Diskus).

The comprehensive assessment protocol was structured around three validated clinical instruments: psychological adherence, biomechanical technique, and ultimate physiological disease control.

To evaluate therapeutic adherence, the study utilized the formally validated, Russian-language iteration of the 8-item Morisky Medication Adherence Scale [7].

The evaluation of inhalation technique was conducted through rigorous, direct empirical observation. Patients were instructed. The evaluator utilized standardized, highly specific observational checklists meticulously calibrated to the unique mechanical requirements of each inhaler type (standard MDI, Turbuhaler, and Diskus). Procedural deviations were rigorously recorded and subsequently bifurcated into "critical" and "non-critical" errors. A critical error was stringently defined by the protocol as any mechanical or temporal failure that would confidently result in a greater than fifty percent reduction in the intended pulmonary deposition of the active pharmacological agent, thereby rendering the entire administration sub-therapeutic and clinically useless.

Finally, to correlate these behavioral and mechanical metrics with actual physiological clinical outcomes, overall disease control was quantified utilizing the standardized Asthma Control Test [1]. The ACT provides a numerical score reflecting the frequency of symptoms, rescue medication use, and the impact of the disease on the patient's daily life over the preceding four weeks.

Baseline Demographics and Clinical Homogeneity

As meticulously delineated in Table 1, the cohorts exhibited no statistically significant disparities regarding mean patient age, gender distribution, the chronological duration of the asthmatic disease since initial diagnosis, the specific

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Eureka Journal of Health Sciences & Medical Innovation (EJHSMI)
ISSN 2760-4942 (Online) Volume 2, Issue 2, February 2026

https://eurekaoa.com/index.php/5

therapeutic step assigned according to GINA protocols, or their baseline ACT scores prior to the detailed intervention.

Table 1: Baseline Clinical and Demographic Characteristics of the Study Cohorts

Clinical / Demographic Parameter	Group 1 (Metered-Dose Inhalers, n=30)	Group 2 (Dry-Powder Inhalers, n=30)	Statistical Significance (p-value)
Mean Age, years (M ± SD)	45.2 ± 10.1	47.8 ± 9.5	0.34
Female Patients, n (%)	19 (63.3%)	17 (56.7%)	0.61
Duration of Asthma, years (M ± SD)	8.1 ± 3.4	8.9 ± 4.0	0.42
GINA Therapy Step (Step 2/3/4), n	5 / 16 / 9	4 / 18 / 8	0.81
Baseline ACT Score (M ± SD)	17.5 ± 2.1	18.1 ± 2.5	0.29

Profound Disparities in Pharmacological Adherence

The psychometric evaluation administered via the MMAS-8 instrument revealed a general, systemic landscape of suboptimal therapeutic compliance across the entire study population—a finding that unfortunately, yet accurately, mirrors broader global epidemiological data regarding the management of chronic respiratory diseases. However, a granular, comparative statistical analysis exposed highly significant, actionable divergences between the two device cohorts.

Patients utilizing the breath-actuated dry-powder inhalers demonstrated a demonstrably and statistically superior degree of pharmacological adherence. The mean MMAS-8 score within the dry-powder cohort was calculated at an

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Eureka Journal of Health Sciences & Medical Innovation (EJHSMI)
ISSN 2760-4942 (Online) Volume 2, Issue 2, February 2026

https://eurekaoa.com/index.php/5

impressive 6.8 ± 1.1, which was significantly higher than the mean score of 6.1 ± 1.3 recorded in the metered-dose cohort (p=0.02). This behavioral divergence becomes even more stark and pronounced when examining the extreme ends of the adherence spectrum. The proportion of patients categorized as exhibiting "high adherence"—achieving a perfect, unblemished score of 8 on the MMAS-8 scale—was exactly twice as large in the dry-powder group, comprising 33.3% of the cohort (n=10), compared to a mere 16.7% (n=5) in the metered-dose group (p=0.049). Inversely, instances of dangerously "low adherence" (scores falling below 6) were heavily skewed toward the metered-dose users, occurring in 40.0% of that cohort versus only 23.3% of the dry-powder cohort, although this specific sub-metric trended toward, but did not formally breach, the strict threshold of statistical significance (p=0.15).

The Biomechanics of Failure: Critical Inhalation Technique Errors

While adherence metrics primarily reflect psychological, cognitive, and behavioral parameters, the direct observational analysis of inhalation technique exposes the severe, unforgiving biomechanical vulnerabilities inherent in device-dependent respiratory therapy. The overarching prevalence of simple procedural error was catastrophically high across both delivery systems: 90% of patients operating metered-dose inhalers (n=27) and 80% of those using dry-powder inhalers (n=24) committed at least one observable procedural deviation, a nominal difference that was not statistically significant (*p*=0.28).

The critical, defining differentiator, however, emerged unequivocally during the rigorous classification of these errors. As explicitly detailed in Table 2, the frequency, density, and sheer concentration of *critical* errors—those resulting in massive, therapy-negating dose loss—were heavily and dangerously concentrated in the metered-dose cohort.

Table 2: Comparative Analysis of Therapeutic Adherence and Critical Inhalation Errors

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Eureka Journal of Health Sciences & Medical Innovation (EJHSMI)

ISSN 2760-4942 (Online) Volume 2, Issue 2, February 2026

https://eurekaoa.com/index.php/5

Clinical Parameter	Group 1 (Metered-Dose Inhalers, n=30)	Group 2 (Dry-Powder Inhalers, n=30)	Statistical Significance (p-value)
Psychometric Adherence Metrics (MMAS-8)			
Mean Score (M ± SD)	6.1 ± 1.3	6.8 ± 1.1	0.02
High Adherence (Perfect 8 points), n (%)	5 (16.7%)	10 (33.3%)	0.049
Biomechanical Inhalation Technique Metrics			
Presence of ≥ 1 Critical Error, n (%)	23 (76.7%)	16 (53.3%)	0.03
Mean Number of Critical Errors per Patient	1.9 ± 0.8	1.1 ± 0.6	0.001

Patients prescribed the standard metered-dose inhalers committed critical, therapy-destroying errors at a significantly higher rate (76.7%) than those operating the engineered dry-powder systems (53.3%, p=0.03). Furthermore, the absolute volume of mechanical failure was vastly higher; the mean number of critical errors per individual patient was nearly double in the metered-dose group (1.9 discrete critical errors) compared to the dry-powder group (1.1 errors), yielding a highly significant statistical outcome (p=0.001).

Discussion

The empirical data derived from this comparative clinical analysis unveil profound, deeply concerning insights into the real-world operational challenges of asthma management, generating critical implications for clinical practice, particularly within the rapidly evolving healthcare and pharmaceutical infrastructure of Uzbekistan.

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Eureka Journal of Health Sciences & Medical Innovation (EJHSMI)
ISSN 2760-4942 (Online) Volume 2, Issue 2, February 2026

https://eurekaoa.com/index.php/5

The statistically significant superiority of therapeutic adherence observed within the dry-powder inhaler cohort warrants deep analytical scrutiny. This phenomenon cannot be attributed to the intrinsic efficacy of the pharmacological agents themselves, as the anti-inflammatory and bronchodilatory therapeutic goals were identical across both experimental groups. Rather, the heightened compliance is fundamentally, inextricably linked to the superior user-interface engineering of the dry-powder devices.

First, the integration of objective, mechanical feedback mechanisms is crucial to patient psychology. The majority of modern multi-dose dry-powder inhalers currently available, such as the Turbuhaler and Diskus, are equipped with highly visible, integrated numeric dose counters. This relatively simple engineering feature serves a massive dual psychological function: it acts as a persistent, visual reminder to initiate the daily therapy, and it provides objective, undeniable confirmation of medication consumption, alleviating deep-seated patient anxiety regarding the operation of empty devices. In stark, detrimental contrast, the older-generation standard metered-dose inhalers widely distributed in the region frequently lack this fundamental feature. Patients operating standard MDIs are forced to rely on highly inaccurate estimations, memory, or archaic, scientifically debunked methods such as floating the pressurized canister in a basin of water to deduce the remaining volume. This leads to widespread uncertainty, anxiety, and inadvertent non-adherence when the device secretly empties of active drug while continuing to expel residual propellant.

Furthermore, the distinct sensory feedback provided by dry-powder systems plays a vital, reinforcing role in the psychological habituation of therapy. Formulations utilizing lactose as a micronized carrier molecule impart a distinct, mildly sweet taste upon inhalation, coating the tongue and oropharynx. Patients in the DPI cohort frequently reported this gustatory feedback as definitive, comforting confirmation of a successful dose administration. The metered-dose inhaler, relying solely on the transient, often irritating thermal shock of the

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Eureka Journal of Health Sciences & Medical Innovation (EJHSMI)
ISSN 2760-4942 (Online) Volume 2, Issue 2, February 2026

https://eurekaoa.com/index.php/5

rapidly evaporating hydrofluoroalkane propellant (the "cold freon effect"), provides a vastly less reliable sensory confirmation. This often leads anxious patients to execute redundant, multiple actuations out of uncertainty, thereby depleting the expensive device prematurely and severely disrupting the prescribed temporal dosing regimen. Additionally, the simplified, streamlined dosing regimens often associated with advanced combination DPIs—frequently requiring only once or twice daily administration—dramatically reduce the cognitive and temporal burden placed on the patient, directly and measurably augmenting long-term adherence rates.

Perhaps the most alarming and clinically urgent finding of this investigation is the catastrophic, systemic failure rate associated with the independent operation of metered-dose inhalers. The revelation that 76.7% of patients utilizing an MDI committed at least one critical error implies that over three-quarters of this specific population were effectively receiving sub-therapeutic interventions, rendering them virtually unmedicated despite their formal enrollment in a costly chronic management protocol.

The qualitative profile of these critical errors is strictly dictated by the unforgiving physics of the device. Within the metered-dose group, the most pervasive failure was the catastrophic disruption of hand-lung coordination, observed in a staggering 65% of the entire cohort. These patients actuated the pressurized canister either prematurely, prior to the initiation of inspiratory airflow, or entirely late, after the inspiratory cycle had concluded, effectively firing the high-velocity medication plume into a closed oral cavity. Additionally, 45% of MDI users executed an excessively rapid, forceful inhalation. This action generates massive aerodynamic turbulence within the airway, guaranteeing the immediate impaction of the aerosol plume against the posterior oropharyngeal wall, rather than allowing the microscopic particles to smoothly navigate the glottis into the lower bronchial airways. Furthermore, half of the MDI cohort (50%) failed to vigorously agitate the suspension canister before use. This is a

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Eureka Journal of Health Sciences & Medical Innovation (EJHSMI)
ISSN 2760-4942 (Online) Volume 2, Issue 2, February 2026

https://eurekaoa.com/index.php/5

fatal critical error for suspension formulations like fluticasone, as it leads directly to the inhalation of pure, pharmacologically inert propellant devoid of the active corticosteroid molecule.

A critical, highly consequential contextual observation from this study is the absolute, total absence of valved holding chambers—commonly known as spacers—among the entire MDI cohort. The spacer device was specifically engineered by respiratory scientists to decouple the manual actuation of the canister from the patient's inspiratory effort, entirely neutralizing the formidable hand-lung coordination barrier while simultaneously reducing aerosol velocity to minimize wasteful oropharyngeal impaction. The failure of all thirty patients in the MDI group to utilize a spacer transforms the MDI from a highly reliable, precise delivery system into a high-risk, largely ineffective gamble. This universal omission in the observed clinical setting points to severe systemic deficiencies in patient education, entrenched physician prescribing habits, or potential economic and supply-chain barriers regarding the availability and affordability of spacer devices in the local pharmaceutical market. Prescribing a metered-dose inhaler to patients with demonstrably poor psychomotor coordination without the mandatory inclusion of a spacer is definitively proven by this empirical data to be an inherently flawed and ultimately ineffective clinical tactic.

The Aerodynamic Limitations of Dry-Powder Systems

Conversely, while the engineered dry-powder inhalers successfully circumvented the hand-lung coordination dilemma and resulted in a significantly lower overall critical error rate (53.3%), this failure rate remains unacceptably high for a life-sustaining, prophylactic therapy. The error profile within the dry-powder cohort was characterized entirely by aerodynamic insufficiencies. The most critical failure, noted in 43% of the DPI group, was the sheer physical inability to generate an inspiratory flow of adequate velocity and sustained volume.

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Eureka Journal of Health Sciences & Medical Innovation (EJHSMI)
ISSN 2760-4942 (Online) Volume 2, Issue 2, February 2026

https://eurekaoa.com/index.php/5

This limitation is particularly devastating for devices possessing high internal resistance, such as the widely used Turbuhaler, which demands a peak inspiratory flow approaching 60 liters per minute to effectively shear the active micronized drug particles from the heavy lactose carrier molecules. While newer devices like the Diskus feature lower internal resistance thresholds (requiring approximately 30 liters per minute), failures in flow generation remained highly prevalent across the cohort. This highlights a critical, often ignored flaw in universal prescribing practices: the dry-powder device essentially utilizes the patient's own pulmonary mechanics as its sole power source. Assigning a high-resistance device to a patient suffering from an acute asthma exacerbation, severe chronic obstruction, or generalized muscular frailty guarantees a mechanical failure. The patient physically cannot extract the life-saving medication from the device precisely when they need it most. Furthermore, 30% of DPI users critically compromised their medication by exhaling directly into the device's mouthpiece prior to inhalation. This thoughtless action introduces heavy pulmonary moisture directly into the powder reservoir, causing the highly hygroscopic formulation to rapidly agglomerate into heavy, immovable masses that can no longer be inhaled.

Correlation with Ultimate Disease Control

The final, definitive analytical phase of the study involved the synthesis of behavioral adherence metrics, biomechanical technique proficiency, and the ultimate physiological clinical outcome: overall asthma control as measured by the ACT. The data revealed a profound, undeniable, and direct correlation. Patients occupying the optimal quadrant—exhibiting perfect adherence (an MMAS-8 score of 8) and demonstrating absolute mastery of their device with zero critical inhalation errors—achieved a highly superior mean ACT score of 22.5 ± 1.5, indicating a state of robust, exceptionally well-controlled asthma.

Conversely, patients trapped in the clinical failure quadrant—characterized by low psychological adherence (an MMAS-8 score < 6) compounded by the

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Eureka Journal of Health Sciences & Medical Innovation (EJHSMI)
ISSN 2760-4942 (Online) Volume 2, Issue 2, February 2026

https://eurekaoa.com/index.php/5

presence of at least one critical mechanical error—registered a dismal mean ACT score of 15.1 ± 2.0, signifying a dangerously uncontrolled, high-risk disease state. Reflecting their superior baseline metrics in both behavioral adherence and mechanical technique, the dry-powder cohort as a whole demonstrated a statistically significant trend toward superior overall asthma control at the conclusion of the study, achieving a mean ACT score of 19.8 ± 2.0, compared to the highly suboptimal 17.9 ± 2.4 observed in the metered-dose cohort (p=0.04).

Conclusion

The comprehensive, empirical analysis of therapeutic adherence and inhalation technique among asthmatic patients reveals that the profound efficacy of modern respiratory pharmacotherapy is currently being critically compromised by the biomechanical and psychological barriers inherent in device operation.

The evidence conclusively and statistically demonstrates that engineered multi-dose dry-powder inhalers foster superior pharmacological adherence, largely attributable to the integration of objective dose-counting mechanisms and distinct sensory feedback, which alleviate deep-seated patient uncertainty. Furthermore, dry-powder systems significantly reduce the absolute incidence of critical mechanical failures compared to unassisted metered-dose inhalers.

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Eureka Journal of Health Sciences & Medical Innovation (EJHSMI)
ISSN 2760-4942 (Online) Volume 2, Issue 2, February 2026

https://eurekaoa.com/index.php/5

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