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Association between inhaler device type and therapeutic adherence in Belgium: a retrospective cohort study

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Abstract

Background

Despite its importance for asthma and COPD outcomes, therapeutic adherence remains suboptimal. Evidence largely focuses on dry powder and pressurised metered-dose inhalers (DPIs and pMDIs) in corticosteroid-based therapies, with limited data on other devices and pharmacological classes.

Methods

We conducted a retrospective cohort study using dispensing data from the Belgian Independent Health Insurance Funds. Adults aged 19–80 years with ≥ 2 dispensations of ICS-, LABA- or LAMA-based mono-, dual- or triple therapy between 2020 and 2023 were included. Adherence was measured using CMA3, calculated for each patient–device–class combination and dichotomised at CMA ≥ 0.8. Mixed-effects logistic regression models with patient-level random intercepts were used.

Results

A total of 77,237 patients contributed to CMA3 exposures. DPIs showed higher adherence (41.4%) than pMDIs (32.5%) and nebulizers (13.1%). SMIs showed the highest adherence (48.6%) but were limited to LAMA and LABA/LAMA therapies. In adjusted analyses, inhaler device type remained independently related to adherence. DPIs showed higher odds of adherence than pMDIs in the main model (OR 1.64; 95% CI 1.57 1.71). In the restricted LABA/LAMA model, DPIs also showed higher adherence than SMIs (OR 4.65; 95% CI 4.25–5.09). This pattern was consistent across all pharmacological classes.

Conclusions

Inhaler device type is associated with therapeutic adherence. Across therapeutic classes, DPIs were associated with higher adherence than pMDIs and SMIs. Device choice should be considered alongside inhaler training to improve adherence.

Background

A major challenge in the management of asthma and COPD is poor therapeutic adherence (1). Suboptimal adherence has been consistently associated with worse symptom control, reduced quality of life, increased risk of exacerbations, higher morbidity and mortality, and substantial healthcare cost (2–7). Despite the availability of effective inhaled therapies, long-term adherence remains disappointingly low in both asthma and COPD, highlighting a critical gap between therapeutic efficacy and real-world effectiveness (8).

Several studies in the respiratory field have reported that the inhaler device type may influence therapeutic adherence (1, 9). Pressurized metered-dose inhalers (pMDIs) and dry-powder inhalers (DPIs) are the recommended devices for asthma and COPD, whereas soft-mist inhalers (SMIs) are available mainly for COPD treatment. Nebulizers can also deliver bronchodilators and inhaled corticosteroids (ICS), but they are no longer recommended for the chronic management of asthma or COPD (10, 11). In various analyses, DPI use was associated with improved adherence and lower risk of treatment discontinuation (1, 12–14). Real-world dispensing studies have shown that patients receiving ICS, long-acting beta-agonists (LABA), or LABA–long-acting muscarinic-antagonists (LAMA) therapies via DPIs were more adherent than those using pMDIs (1). To date, no real-world studies have assessed therapeutic adherence to SMIs, despite their increasing utilisation in COPD management.

Beyond adherence, real-world dispensing data also show higher overall consumption of DPI-based therapies compared with pMDIs, trough consistently higher acquisition rates for DPIs (15). However, between 2013 and 2016, pMDIs were still predominantly dispensed for ICS (1). Because pMDIs rely on propellants, which have a measurable environmental impact, ecological considerations are increasingly emerging as an additional factor influencing inhaler prescribing patterns worldwide(16). In this context, understanding whether device type plays an independent role in therapeutic adherence has become particularly relevant.

Despite these insights, the independent effect of inhaler device type on adherence remains unclear. Most existing refill-based studies assess adherence at the patient level, which does not capture the complexity of real-world use where individuals may receive multiple pharmacological classes and inhaler devices over time. In addition, few analyses have simultaneously considered device type, pharmacological class, and sociodemographic factors, or accounted for repeated observations within the same patient. This limitation is particularly important when assessing adherence in real-world settings, where patients are frequently exposed to multiple devices and pharmacological classes over time.

To address these gaps, this retrospective cohort study evaluates adherence across all major inhaler types -including SMIs- and examines the independent association between device type and therapeutic adherence using a high-granularity real-world dataset structured at the patient–device–pharmacological-class level. By applying mixed-effects logistic regression models adjusted for pharmacological class and demographic and socio-economic factors, and accounting for within-patient clustering, we aimed to assess whether inhaler device type was independently associated with adherence.

Methods

Study Participants and Data Source

This study used administrative claims data from the Belgian Independent Health Insurance Funds (Mutualités Libres), capturing all reimbursed community-pharmacy dispensations of ATC R03

medications for insured beneficiaries.

Patients were eligible if they received ≥ 2 dispensations of inhaled drugs for obstructive airway diseases (ATC R03) between January 2020 and December 2023 and were aged 19–80 years at first dispensing.

Inhaled pharmacological classes recommended by Global Initiative for Asthma (GINA) and for Chronic Obstructive Lung Disease (GOLD) guidelines were included: ICS for asthma; LABA, LAMA and LABA/LAMA for COPD; and combination therapies (LABA/ICS and LABA/LAMA/ICS) indicated in both asthma and COPD.

Study Design

The study covered the period from January 2020 to December 2023 (1,460 days). To minimise edge effects at the start and end of follow-up, an Observation Window (OW) was defined as the 1,370-day period beginning 45 days after each patient's first dispensing.

Adherence Measurement

Adherence was quantified using the Continuous Multiple interval Measure of Medication Availability (CMA3) metric implemented in the AdhereR package (v0.8.1), defined as the sum of medication-covered days (excluding the last dispensing) divided by the time interval between the first and last dispensing, with values capped at 1 (17). CMA3 was selected to minimise overestimation of adherence by excluding post-refill coverage and limiting stockpiling bias.

Because prescribed dosing information was unavailable, treatment duration was estimated using WHO Defined Daily Doses (DDD). CMA was computed for each patient–device–pharmacological class combination, allowing patients using multiple devices or classes to contribute multiple observations. To avoid artificial underestimation of adherence due to administrative product code changes, CMA was not calculated at the CNK (Code National(e) Kode) level; instead, device type and pharmacological class were derived from CNK codes and used as the unit of analysis. When the same pharmacological class was delivered via different devices, each device–class combination was considered a distinct exposure.

Only patients with at least three dispensations within the OW contributed to the calculation of CMA3, as a minimum of two refill intervals is required once the window begins 45 days after the first dispensing. For individuals with fewer than three dispensations, CMA3 could not be derived and was therefore recorded as missing. These missing values were excluded from the dataset used for descriptive adherence analyses, and no imputation procedures were applied. No missing data were present for the covariates included in the models.

Descriptive Analysis

Adherence was defined as a CMA ≥ 0.8 (18). The proportion of adherent individuals was calculated overall and stratified by inhaler device type, pharmacological class, age group, sex, socio-economic status (beneficiaries of increased reimbursement, BIM, used as a proxy), and region of residence.

Statistical Model Specifications

To estimate adjusted associations between patient characteristics and therapeutic adherence, we fitted mixed-effects logistic regression models. Because individual patients could contribute multiple observations if they used more than one device type and/or pharmacological class, a random intercept for patient ID was included to account for within-patient correlation.

To explore crude associations with adherence, we first fitted univariate mixed-effects logistic regression models for each covariate. We then developed a series of multivariable mixed-effects models, each including a random intercept for patient ID to account for clustering of repeated observations within individuals.

Modelling strategy

Because inhaler devices are not uniformly available across pharmacological classes, two complementary multivariable logistic regression models were developed. In the primary model, all pharmacological classes were included and the analysis was restricted to DPIs and pMDIs. SMIs were excluded from this model because they are only available for LAMA and LABA/LAMA, which would have introduced structural non-comparability across classes.

A second, restricted model was therefore limited to the classes for which SMIs are available (LAMA and LABA/LAMA), allowing adherence to be compared between SMIs and DPIs within a more homogeneous therapeutic context. Nebulised formulations were excluded from both models because they apply almost exclusively to ICS and do not allow meaningful comparison with handheld devices used for chronic asthma and COPD management.

In addition, class-specific multivariable logistic regression models were fitted for each pharmacological class to assess device-related adherence patterns within classes and minimise residual confounding by treatment category.

All multivariate models were adjusted for age category, sex, BIM status, and region. All analyses were performed in R 4.4.1 using data.table and dplyr for data processing and lme4 for mixed-effects modelling.

Reference categories were selected based on clinical relevance and interpretability, and to ensure comparability across models. Detailed reference categories for each variable are provided in Table 4.

Sensitivity Analysis

As a sensitivity analysis, the main and restricted models were repeated using an alternative adherence threshold of CMA ≥ 0.50. Consistent findings across both thresholds supported the robustness of the primary results.

Results

Sample characteristics

A total of 77,237 adult patients met the inclusion criteria and were included in the adherence analysis. Baseline characteristics, including age, sex and BIM status, are shown in Table 1.

Table 1
Characteristics of unique patients included in the adherence analysis

Variable	Category	Count	Percentage
Sex	Female	41,028	53.1
	Male	36,209	46.9
Age Category	19–40 years	15,249	19.7
	41–64 years	36,994	47.9
	65–80 years	24,994	32.4
BIM	No	62,284	80.6
	Yes	14,953	19.4
Region	Brussels-Capital Region	12,393	16
	Flemish Region	32,904	42.6
	Walloon Region	31,940	41.4
Number of class-device combination(s)	1	59,939	68.6
	2	21,096	24.1
	>=3	6,325	7.2

Table includes unique patients for whom CMA could be calculated. BIM: Beneficiaries of Majored Intervention (BIM); CMA3: Continuous Multiple-interval Measure of Medication Availability

Treatment patterns, including the number of pharmacological class–device combinations per patient and the distribution of patient–device–class exposures, are summarised in Table 2.

Table 2
Distribution of CMA exposures by inhaler device and pharmacological class

Variable	Category	Count	Percentage
Device Type	DPI	66,135	70.9
	Nebulizer	4,978	5.3
	pMDI	17,778	19.1
	SMI	4,339	4.7
Pharmacological class	ICS	10,210	11.0
	ICS/LABA/LAMA	7,657	8.2
	LABA	2,556	2.7
	LABA/ICS	61,644	66.1
	LABA/LAMA	5,680	6.1
	LAMA	5,483	5.9
Device -Pharmacological class	DPI-ICS	2,884	3.1
	pMDI-ICS	2,348	2.5
	Nebulizers-ICS	4,978	5.3
	DPI-ICS/LABA/LAMA	3,819	4.1
	pMDI- ICS/LABA/LAMA	3,838	4.1
	DPI-LABA	2,427	2.6
	pMDI-LABA	129	0.1
	DPI-LABA/ICS	50,181	53.8
	pMDI-LABA/ICS	11,463	12.3
	DPI-LABA/LAMA	3,920	4.2
	SMI-LABA/LAMA	1,760	1.9
	DPI-LAMA	2,904	3.1
	SMI-LAMA	2,579	2.8

DPI: Dry Powder Inhalers; pMDI: Pressurized Metered Doses Inhalers; ICS: Inhaled Corticosteroids; LABA: Long-Acting Beta-Agonist; LAMA: Long-Acting Muscarinic Antagonist.

Adherence Overview

Adherence levels varied markedly across inhaler devices (Table 3). Among the most frequently used devices, adherence was higher for DPIs than for pMDIs, with 41.4% of exposures classified as adherent, compared with 32.5% for pMDIs and 13.1% for nebulizers. SMIs also displayed relatively high adherence (48.6%), although comparisons remain limited by their use in specific pharmacological classes, such as LAMA and LABA/LAMA (Fig. 1). Marked differences were also observed across pharmacological classes, ranging from 18.2% adherence for ICS monotherapy to more than 70% for triple therapy (ICS/LABA/LAMA) and 74% for LAMA alone. Similar patterns were observed when examining device–class combinations, where DPI-based therapies were consistently associated with higher adherence within each pharmacological class (Table 1).

Table 3
Distribution of Adherence Percentage

Variable	Category	% Adherent-Patients	% Non-Adherent Patients
Global	N/A	38.5	61.5
Device Type	DPI	41.4	58.6
	pMDI	32.5	67.5
	Nebulizers	13.1	86.9
	SMI	48.6	51.4
Pharmacological class	ICS	18.2	81.8
	ICS/LABA/LAMA	71.4	28.6
	LABA	63.7	36.3
	LABA/ICS	31.8	68.2
	LABA/LAMA	58.1	41.9
	LAMA	74.0	26.0
Device - Pharmacological class	DPI-ICS	25.4	74.6
	pMDI-ICS	20.2	79.8
	Nebulizers-ICS	13.1	86.9
	DPI-ICS/LABA/LAMA	74.9	25.1
	pMDI-ICS/LABA/LAMA	67.8	32.2
	DPI-LABA	65.4	34.6
	pMDI-LABA	31.8	68.2
	DPI-LABA/ICS	33.8	66.2
	pMDI-LABA/ICS	23.2	76.8
	DPI-LABA/LAMA	76.9	23.1
	SMI-LABA/LAMA	16.1	83.9
	DPI-LAMA	76.9	23.1
	SMI-LAMA	70.7	29.3

A single patient may appear multiple times if they were dispensed medications from more than one pharmacological class and/or device during the OW. DPI: Dry Powder Inhalers; pMDI: Pressurized Metered

Doses Inhalers; ICS: Inhaled Corticosteroids; LABA: Long-Acting Beta-Agonist; LAMA: Long-Acting Muscarinic Antagonist.

Multivariable Models

Primary multivariable model (DPI vs pMDI)

Device type remained strongly and independently associated with adherence after adjustment for all covariates. Patients using DPI had significantly higher odds of being adherent compared with those using pMDI (OR = 1.64; 95% CI 1.57–1.71, p < 0.001) (Fig. 2).

Global Type III Anova tests indicated that inhaler device type, pharmacological class, age category, sex and BIM status made significant contributions to the adjusted model (all p < 0.001) explaining adherence, whereas region showed only a weak global contribution. Region was nevertheless retained as an adjustment variable based on its clinical relevance in the Belgian healthcare context, irrespective of statistical significance.

Restricted SMI model (LAMA and LABA/LAMA only)

In this subset, DPI use was associated with significantly higher adherence compared with SMI (OR = 4.65; 95% CI 4.25–5.10, p < 0.001). This effect was highly consistent and remained robust after full adjustment (Fig. 2).

In the restricted multivariable model, Type III ANOVA tests indicated that inhaler device type, pharmacological class and age category made a statistically significant contribution to the adjusted model explaining adherence (all p < 0.001), whereas sex, BIM status and region did not contribute significantly (p > 0.001). Sex, BIM status and region were retained in the restricted model to maintain consistency with the primary model analysis.

Class-specific stratified models

Across all pharmacological classes, DPI was consistently associated with higher odds of adherence compared with pMDI and SMI. All class-specific estimates showed odds ratios greater than 1, with confidence intervals excluding unity and p-values < 0.001 (Fig. 3).

The magnitude of the DPI effect varied across classes. In the LABA class, DPI use was associated with substantially higher adherence compared with pMDI (OR 3.96; 95% CI 2.69–5.83), while an even stronger association was observed in the LABA/LAMA class (OR 17.54; 95% CI 15.12–20.34), relative to SMI.

Overall, these stratified analyses confirm that the adherence advantage associated with DPI was consistently observed within each therapeutic class and was not driven by a single pharmacological category.

Full results of the class-specific multivariable models, including estimates for all adjusted covariates, are presented in Table 4.

Table 4
Adjusted Odds Ratios and 95% Confidence Intervals from the Multivariate Models

	Details	Category	p-value	OR* 95% [CI]
primary Model	Device (Ref: pMDI)	DPI	< 0.001	1.64 [1.57–1.71]
	Class (Ref: ICS)	ICS/LABA/LAMA	< 0.001	7.26 [6.67– 7.90]
		LABA	< 0.001	4.26 [3.83– 4.75]
		LABA/ICS	< 0.001	1.44 [1.34–1.54]
		LABA/LAMA	< 0.001	7.34 [6.62–8.14]
		LAMA	< 0.001	7.24 [6.47–8.10]
	Sex (Ref: Female)	Male	< 0.001	1.19 [1.15–1.23]
	Age Category (Ref: 19–40 years)	41–64 years	< 0.001	1.49 [1.42– 1.56]
		65–80 years	< 0.001	2.25[2.15–2.36]
	Region (Ref: Flemish Region)	Wallonia	0.09	0.97[0.94–1]
		Brussels-Capital	0.002	0.93[0.89–0.97]
	BIM (Ref: No-BIM)	BIM	< 0.001	1.26[1.21–1.31]
Restricted Model	Device (Ref: SMI)	DPI	< 0.001	4.65 [4.25–5.09]
	Class (Ref: LABA/LAMA)	LAMA	< 0.001	3.03[2.76–3.31]
	Sex (Ref: Female)	Male	0.70	1.02[0.93– 1.11]
	Age Category (Ref: 19–40 years)	41–64 years	0.12	1.38[0.92– 2.07]
		65–80 years	0.01	1.72[1.15–2.58]
	Region (Ref: Flemish Region)	Wallonia	0.05	0.91[0.83–1.00]
		Brussels-Capital	1.00	1.00[0.87–1.14]
	BIM (Ref: No-BIM)	BIM	0.09	0.91[0.83–1.00]
Class Models	ICS (Ref: pMDI)	DPI	< 0.001	1.33[1.17–1.52]
	ICS/LABA/LAMA (Ref: pMDI)	DPI	< 0.001	1.44[1.30–1.59]
	LABA (Ref: pMDI)	DPI	< 0.001	3.96[2.69–5.83]
	LABA/ICS (Ref: pMDI)	DPI	< 0.001	1.71[1.63–1.79]

OR: Adjusted odds ratios from the multivariable mixed-effects logistic regression model, adjusted for age, sex, pharmacological class, BIM status and region area; CI: confidence interval; ICS: Inhaled Corticosteroids; LABA: Long-Acting Beta-Agonist ; LAMA: Long-Acting Muscarinic Antagonist*

	LABA/LAMA (Ref: SMI)	DPI	< 0.001	17.54[15.12 – 20.34]
	LAMA (Ref: SMI)	DPI	< 0.001	1.38[1.22–1.56]

OR: Adjusted odds ratios from the multivariable mixed-effects logistic regression model, adjusted for age, sex, pharmacological class, BIM status and region area; CI: confidence interval; ICS: Inhaled Corticosteroids; LABA: Long-Acting Beta-Agonist ; LAMA: Long-Acting Muscarinic Antagonist*

Sensitivity Analysis

Sensitivity analyses using an alternative adherence threshold (CMA ≥ 0.5) yielded results consistent with the primary analyses (Supplementary Material, Table A1). In both the main and restricted models, the direction of the association between inhaler device type and adherence remained unchanged: DPIs were consistently associated with higher odds of adherence compared with pMDI in the main model and compared with SMI in the restricted LABA/LAMA model (Supplementary Material, Table A2).

Taken together, these findings indicate that inhaler device type is a major and highly consistent determinant of adherence. Across all analytical models, DPI use was consistently associated with significantly higher odds of adherence compared with both pMDI and SMI, independent of pharmacological class, demographic and socio-economic characteristics.

Discussion

This large real-world analysis shows that inhaler device type is consistently associated with therapeutic adherence in asthma and COPD. Across all analytical approaches, DPI use was associated with higher adherence than pMDI and SMI, independent of pharmacological class, demographic and socio-economic factors.

Unlike most previous real-world studies focusing on selected device types or pharmacological classes—mainly DPIs versus pMDI within ICS-based therapies (13, 15)—our study provides an integrated assessment of adherence across all major inhaler devices and pharmacological classes, reflecting the complexity of real-world inhaler use.

Differences in adherence across inhaler devices likely reflect a combination of technical and behavioural factors (19). Devices differ in their coordination requirements, handling complexity, and inspiratory demands, all of which may influence sustained use (9, 20, 21). pMDIs are particularly prone to coordination errors (19, 22, 23), whereas DPIs avoid hand–breath coordination but require sufficient inspiratory flow, which may limit their use in advanced disease (22, 24). SMIs offer an alternative independent of inspiratory flow but may be associated with handling errors, particularly at treatment initiation, as well as higher costs (24–26), and limitations related to their fixed metered volume, which restricts use to adequately soluble drugs (25). Refill-based adherence measures do not capture inhaler technique, which may differ across devices and contribute to the observed patterns.

Nebulisers showed lower adherence than handheld inhalers in our study. Although no longer recommended as first-line therapy for adults (10, 11), their use remained substantial between 2020 and 2023 (Table 2), possibly reflecting perceptions of greater effectiveness despite higher treatment burden, costs and contamination risk (27, 28). By contrast, DPIs—associated with higher adherence—were the most frequently used devices in this cohort, which may be reassuring from a primary care perspective.

Beyond device-related characteristics, several clinical and prescribing factors may also contribute to the adherence patterns observed in this study. In mild asthma, inhaled therapies are often prescribed as-needed only (e.g., ICS–formoterol combinations). This intermittent use pattern may not be fully captured by refill-based adherence measures such as CMA3, as it results in more sporadic medication dispensing. Consequently, adherence may be underestimated in these patients despite appropriate use, particularly for ICS–LABA therapies delivered via DPI or pMDI (10). This variability limits the ability to accurately infer adherence from dispensing data based on a single DDD. In contrast, patients with COPD are more frequently treated with regular maintenance therapies, which may favour higher refill-based adherence estimates (11).

Disease severity may also influence both device selection and adherence patterns. Patients with more severe disease or more persistent symptoms may be more likely to use their medication more regularly, resulting in higher adherence estimates (29). Dosing regimen complexity may further contribute to this relationship, as once-daily treatments are generally associated with better adherence than multiple daily dosing schedules (30, 31). Conversely, patients with milder or moderate symptoms may use their inhalers less consistently and only when symptoms appear, contributing to lower observed adherence. In addition, prescribing practices and patient characteristics not captured in the available data — such as comorbidities (particularly depression and anxiety), inhaler preference, lung function parameters and overall treatment burden — may also influence both device choice and medication use (32, 33). Taken together, these factors highlight the complexity of interpreting adherence differences across device types in observational data.

A key finding of this study is that the association between device type and adherence was observed consistently within each pharmacological class, indicating that the association observed for DPIs was not driven by a single therapeutic category. The observed differences for the LABA class should be interpreted with caution. The number of patient–device exposures in the pMDIs group was relatively small compared with the DPIs group (Table 2), which likely limits the robustness of this comparison and may partly explain the magnitude of the observed effect. In addition, the distribution of LABA formulations across device types reflects prescribing practices, as most LABA therapies are delivered via DPIs, while only a limited number of pMDI formulations are available. Consequently, patients receiving LABA via pMDIs may represent a more selected population, potentially including long-term users or patients with specific clinical profiles, particularly in COPD, where LABA monotherapy remains in use.

A marked difference in adherence was observed between LABA/LAMA delivered via SMI and DPI, with substantially lower adherence for SMIs, a pattern not observed for LAMA monotherapy. This suggests that the finding may reflect treatment instability and higher rates of discontinuation or switching in patients receiving LABA/LAMA SMI, rather than a device effect alone.

Finally, these findings suggest that inhaler device type is an important factor associated with treatment adherence, beyond pharmacological class. However, given the observational nature of the data and limited clinical information, residual confounding cannot be excluded. These results support considering inhaler device choice as an integral component of strategies aimed at optimizing adherence in routine care.

Clinical and public health implications

These observations may have implications for clinical decision-making, suggesting that inhaler device choice could be more explicitly considered alongside pharmacological class, and supported by systematic assessment of inhaler technique and device-specific training. However, further research incorporating detailed clinical data and patient outcomes is required to determine whether observed differences in adherence translate into meaningful clinical benefits.

Importantly, emerging evidence suggests that differences in inhaler device type may also translate into clinically meaningful outcomes. A recent observational study in COPD reported that LABA/LAMA combinations delivered via DPIs were associated with a lower risk of first exacerbation compared with pMDI formulations (38).

Beyond clinical performance, the transition toward more environmentally sustainable inhalers represents an increasingly important public health objective, particularly given that hydrofluorocarbon propellants used in pMDIs alone are estimated to account for approximately 0.03% of annual global greenhouse gas emissions (39). Recent evidence suggests that clinicians are beginning to incorporate environmental considerations into prescribing decisions; healthcare providers have been shown to prefer inhalers with a lower environmental footprint even when associated with higher costs, although more polluting devices may still be favoured when perceived to offer superior protection against exacerbations (16). In our study, adherence was higher for propellant-free devices—namely DPIs and SMIs— which may be relevant in light of the established relationship between adherence and disease control (9). Taken together, these findings highlight the potential alignment between clinical and environmental considerations and suggest that inhaler device characteristics may be meaningfully considered as part of shared decision-making in routine care.

In conclusion, inhaler device characteristics appear to play a meaningful role in therapeutic adherence and may represent a point of convergence between clinical effectiveness and environmental sustainability. Integrating device choice into shared decision-making may therefore support both improved adherence and more sustainable respiratory care.

Strengths and Limitations

This study benefits from a large, nationally representative cohort covering approximately 20% of the Belgian population, based on a comprehensive healthcare database with longitudinal records of reimbursed controller medications for asthma and COPD. The proportion of BIM patients (~ 20%) was consistent with national data across Belgian health insurance funds (34), supporting the representativeness of the study population. The availability of detailed socio-economic and demographic variables strengthened adjustment for key determinants of therapeutic adherence (35, 36).

Additional strengths include the inclusion of all major inhaled pharmacological classes, reflecting the complexity of real-world treatment, and the novel assessment of adherence to SMIs compared with DPIs. Adherence was assessed using a standardized approach and analysed with multivariable mixed-effects models accounting for repeated measures at the patient level.

This study also has limitations. Dispensing data do not confirm actual medication use or inhalation technique, an important determinant of treatment effectiveness (37). The absence of diagnostic information precluded clear differentiation between asthma and COPD [10,11]. CMA-based adherence reflects medication availability rather than effective use and may overestimate adherence. The requirement of at least three dispensations may have introduced selection bias, although it reduced misclassification of sporadic users. Finally, treatment coverage was estimated using the DDD, which may not fully reflect prescribed or clinically optimal dosing.

Conclusions

In this large real-world cohort, inhaler device type was consistently associated with therapeutic adherence across pharmacological classes. DPIs showed higher adherence compared with pMDIs and SMIs, independent of pharmacological class and demographic and socio-economic characteristics. While causal inference cannot be established, these findings highlight the potential relevance of inhaler device choice as part of strategies aimed at optimising adherence in routine asthma and COPD care.

Abbreviations

ATC
Anatomical Therapeutic Chemical classification
BIM
Beneficiaries of Increased Reimbursement
CI
Confidence Interval
CMA
Continuous Multiple-interval Measure of Medication Availability
CNK

Code National(e) Kode

COPD

Chronic Obstructive Pulmonary Disease

DDD

Defined Daily Dose

DPI

Dry-Powder Inhaler

GINA

Global Initiative for Asthma

GOLD

Global Initiative for Chronic Obstructive Lung Disease

ICS

Inhaled Corticosteroids

LABA

Long-Acting Beta-Agonist

LAMA

Long-Acting Muscarinic Antagonist

OW

Observation Window

OR

Odds Ratio

pMDI

Pressurised Metered-Dose Inhaler

SMI

Soft-Mist Inhaler

WHO

World Health Organization

Declarations

Clinical trial number

Not applicable

Ethics approval and consent to participate

Ethical approval and informed consent were not required for this study, as it was based on pseudonymised administrative dispensing data collected for reimbursement purposes, with no direct patient identification by the investigators.

Consent for publication

Not applicable

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Author Contribution

Conceptualization, A.R., G.B., S.R. and C.D.V.; methodology, A.R. software, A.R.; validation, A.R., S.R., and C.D.V.; formal analysis, A.R., S.R.; investigation, A.R.; resources, W.K., G.K.; data curation, W.K., G.K., A.R.; writing—original draft preparation, A.R.; writing—review and editing, A.R., S.R., S.P., G.B., W.K., G.K. and C.D.V.; visualization, A.R.; supervision, C.D.V.; project administration, A.R. All authors have read and agreed to the published version of the manuscript.

Data Availability

The data that support the findings of this study are not publicly available due to legal and data protection restrictions, as they are based on administrative health insurance data. Access to the data may be granted by the Belgian Independent Health Insurance Funds, subject to applicable regulations and approval.

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Figures

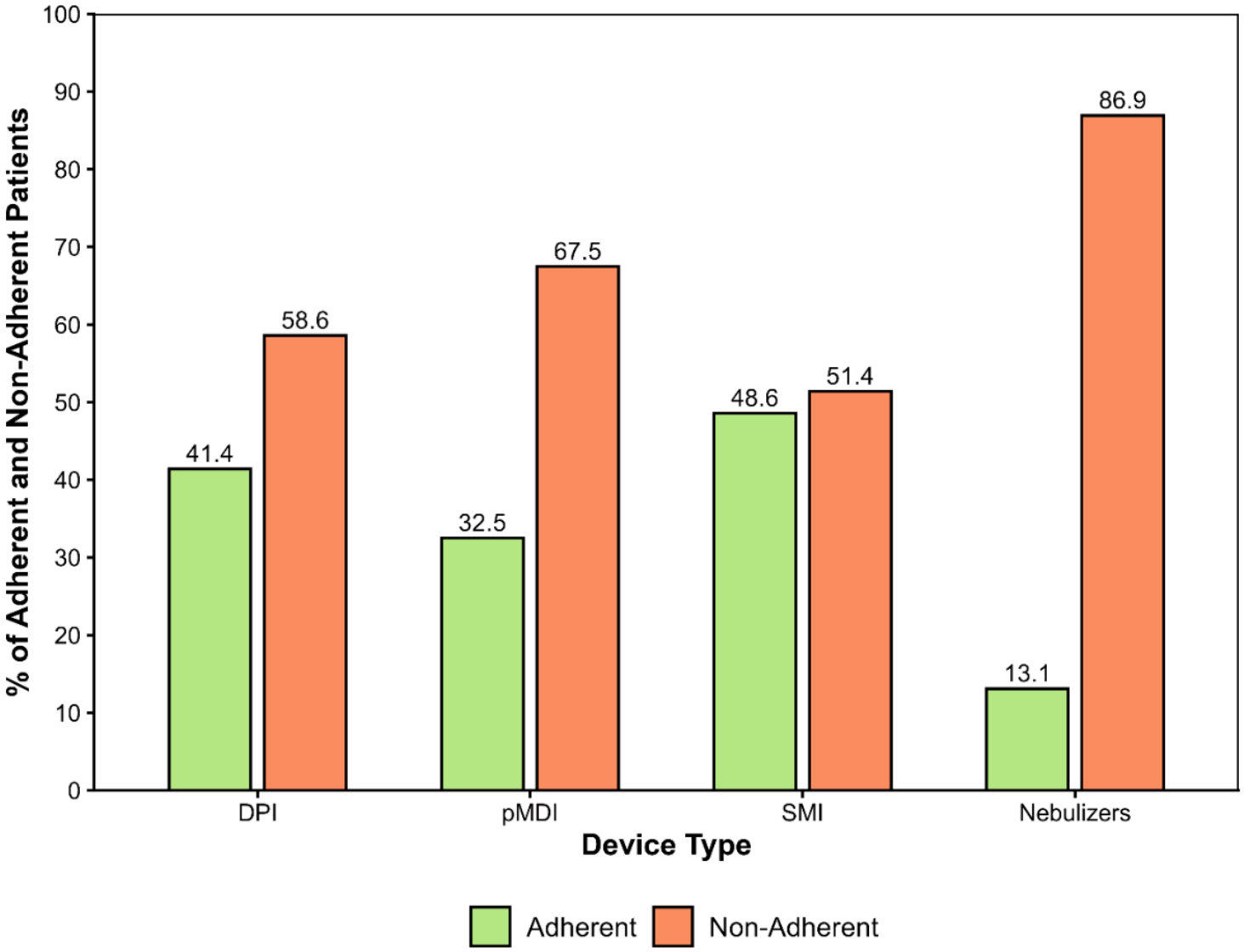


Figure 1

Distribution of Adherent and Non-Adherent patients across inhaler device types.

Percentage of adherent (CMA ≥ 0.8) and non-adherent patients for each device type. DPI: dry-powder inhaler; pMDI: pressurised metered-dose inhaler; SMI: soft-mist inhaler. One patient may contribute multiple exposures if treated with more than one device and/or pharmacological class.

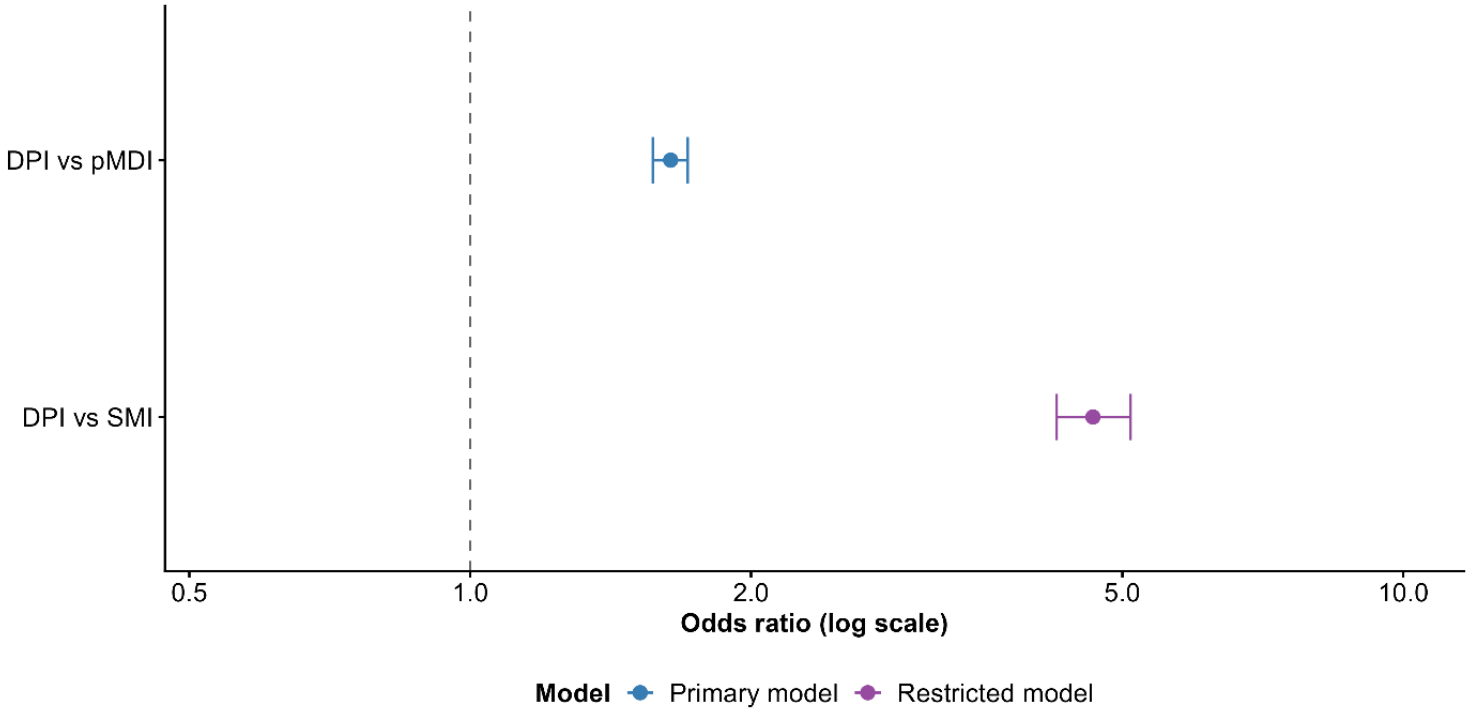


Figure 2

Adjusted odds ratios from the primary and restricted mixed-effects models

Odds ratios (OR) with 95% confidence intervals from two independent multivariable mixed-effects logistic regression models. The primary model estimates the adjusted effect of DPI versus pMDI across all classes. The restricted model includes only LAMA and LABA/LAMA therapies and provides the adjusted effect of DPI versus SMI. Both models were adjusted for age, sex, BIM status, region, and pharmacological class. The vertical dashed line indicates the null value (OR = 1).

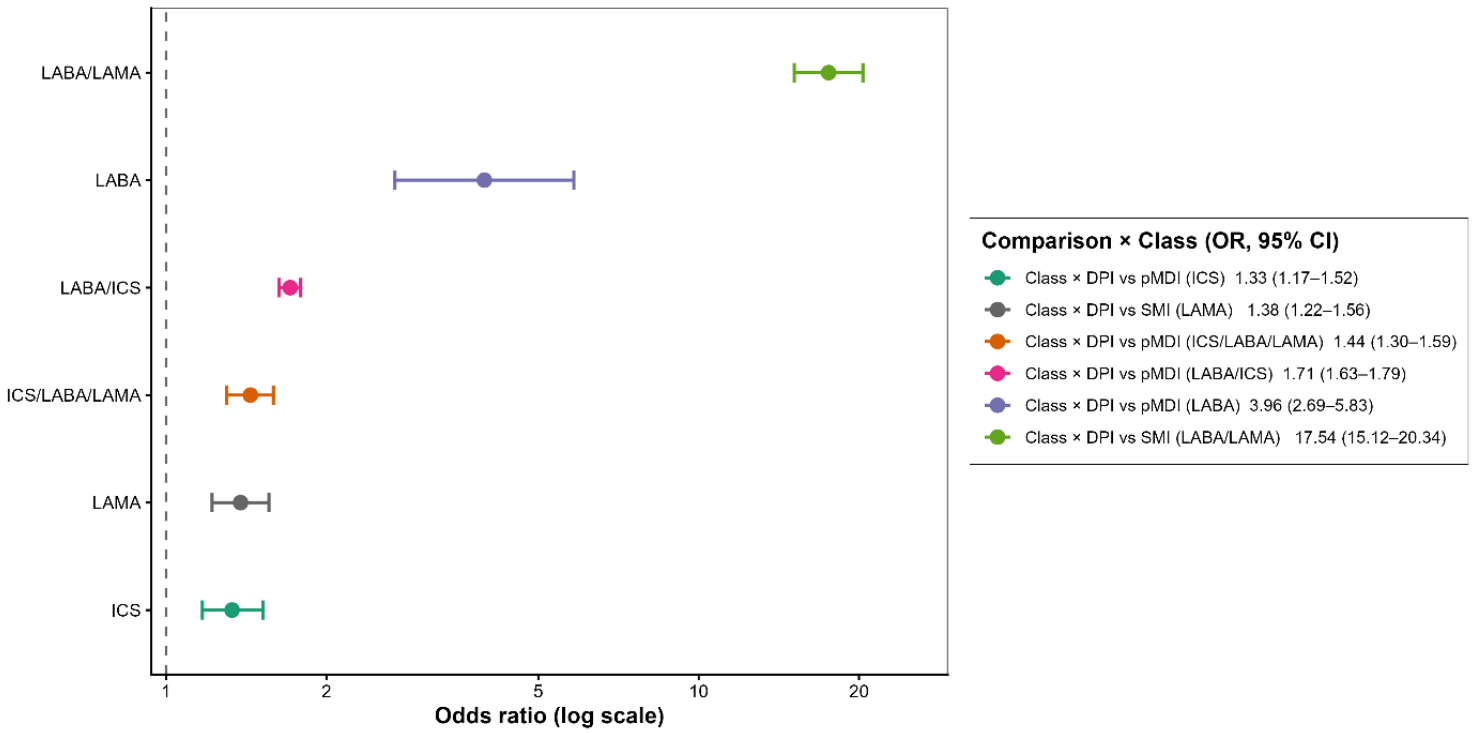


Figure 3

Adjusted odds ratios for DPI versus pMDI device effects within each pharmacological class

Adjusted odds ratios (OR) and 95% confidence intervals from class-specific mixed-effects logistic regression models. For ICS, ICS/LABA/LAMA, LABA/ICS and LAMA, the comparison reflects DPI versus pMDI, as both devices were available within these classes. Except for LABA and LABA/LAMA: the comparison reflects DPI versus SMI. All models were adjusted for age, sex, BIM status and region. The vertical dashed line indicates OR = 1 (no difference in adherence).

Supplementary Files

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