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Original Research

Changes in critical inhaler technique errors in inhaled COPD treatment – A one-year follow-up study in Sweden

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ABSTRACT

Background: Critical inhaler technique errors have been associated with lower treatment efficacy in chronic obstructive pulmonary disease (COPD). We aimed to assess and follow-up critical inhaler technique errors, and to investigate their association with COPD symptoms and exacerbations.

Methods: COPD-diagnosed primary and secondary care outpatients (n = 310) demonstrated inhaler technique with inhaler devices they were currently using. Critical errors in opening, positioning and loading the inhaler device, and exhalation through dry-powder inhalers were assessed and corrected, and the assessment was repeated one year later. COPD Assessment Test, the modified Medical Research Council dyspnoea scale and history of exacerbations were collected at both visits.

Results: The proportion of patients making ≥1 critical inhaler technique error was lower at follow-up in the total population (46% vs 37%, p = 0.01) and among patients with unchanged device models (46% vs 35%, p = 0.02), but not among patients with a new inhaler device model (46% vs 41%, p = 0.56). Not positioning the device correctly was the most common critical error at both visits (30% and 22%). Seventy-four percent of the patients had unchanged COPD treatment from baseline to follow-up. Treatment escalation, de-escalation, and switch was observed in 14%, 11%, and 1% of the patients, respectively. No association was found between critical errors and COPD symptoms or exacerbations.

Conclusions: Assessment and correction of inhaler technique was associated with a decrease in critical inhaler technique errors. This effect was most pronounced in patients using the same device models throughout the follow-up period.

1. Introduction

Chronic obstructive pulmonary disease (COPD) is a serious health concern characterized by persistent respiratory symptoms and a high risk of exacerbations [1]. Pharmacological treatment in COPD is usually delivered as inhalation therapy from handheld inhaler devices [2]. Drug delivery via the inhaled route is complex and prone to errors. Prescribers need to match each patient with an optimal inhaler device model or combination of device models [3], and the patient must learn to use the devices correctly in order to receive the optimal treatment effect [4,5].

Dry-powder inhalers, soft-mist inhalers, and pressurized metered-dose inhalers are different drug formulations [3] commonly used in the treatment of COPD [6–13]. Critical inhaler technique errors, which can be either generic or device-specific, are a result of incorrect device handling [3,14] and should be avoided as they may lead to lower treatment efficacy [4,5]. Unfortunately, incorrect inhaler use is common [4,6–11,13,15] and has been a problem for several decades [16]. Studies with a retrospective study design have found high inhaler error frequencies to be associated with poor disease outcomes in asthma [4,14], unplanned health care contacts related to asthma and COPD [17], and

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severe exacerbations in COPD [11].

Guidelines therefore propose that an assessment of inhaler technique should be part of the management cycle in the adjustment of a patient's pharmacological treatment, alongside a review of the history of exacerbations and symptoms using validated instruments like the COPD Assessment Test (CAT) or the modified Medical Research Council dyspnoea scale (mMRC) [18]. Educational interventions to improve inhaler technique in patients with COPD have been shown to be effective in randomized controlled trials [10,19,20] and observational studies [7,21–25]. However, there are limited data from prospective studies in patients with COPD investigating association of inhaler technique errors with health status and exacerbations [10,19–21,23] after an educational intervention correcting inhaler technique. In addition, previous studies have typically been restricted to studying specific types of device models [10,19–21,23]. The aim of this study was to investigate changes in critical inhaler technique errors in inhaled COPD treatment, in relation to symptom control and exacerbation frequency, in a prospective cohort of Swedish COPD patients.

2. Materials and methods

2.1. Study design and patients

The Tools Identifying Exacerbations (TIE) study is a prospective, observational cohort study in primary and secondary care outpatients with COPD performed in the regions of Dalarna, Gävleborg, and Uppsala in Sweden [6,26,27]. The enrolment of patients started in 2014 with a baseline visit and a follow-up visit one year after study inclusion. Eligible patients had a spirometry-verified COPD diagnosis, were aged ≥40 years, and were able to self-complete the study questionnaires. Exclusion criteria, assessed at the baseline visit, were a history of severe comorbidities, e.g., metastasized cancer, severe heart failure, or severe angina pectoris. The assessment of inhaler technique was performed at the study sites in the regions of Dalarna and Gävleborg. Patients who had completed the 1-year follow-up visit were eligible for inclusion in this study (Fig. 1). As the aim of this study was to assess changes in the handling of inhaler devices and critical errors, we included the 310 patients with inhaled treatment at both baseline and follow-up. The study was approved by the ethics committee of the Regional Review Board in Uppsala, Sweden, on September 25, 2013 (Dnr 2013/358). All patients provided written informed consent prior to study inclusion.

2.2. Patient characteristics and measures

Patient questionnaires provided data on age, sex, current smoking, educational level (elementary school, upper secondary school, or university), health status assessed using the CAT [28], dyspnea assessed using the mMRC scale [29], and exacerbations within the preceding 12 months. Higher CAT and mMRC scores are indicative of worse symptom control. Age was categorized as <65, 65–75, or >75 years. Exacerbations were defined as acute health care visits and/or treatment with a course of oral corticosteroids and/or treatment with antibiotics due to worsening of COPD symptoms, thus including both moderate and severe exacerbations. The exacerbations data were dichotomized into no exacerbations or ≥1 exacerbation within the preceding 12 months. Post-bronchodilatory spirometry was performed with previously described reference values [30,31]. Body mass index (BMI) was calculated based on a patient's weight and height, and the patients were categorized as underweight (BMI <22 kg/m^2), normal weight (BMI 22–30 kg/m^2), or overweight (BMI >30 kg/m^2) [32].

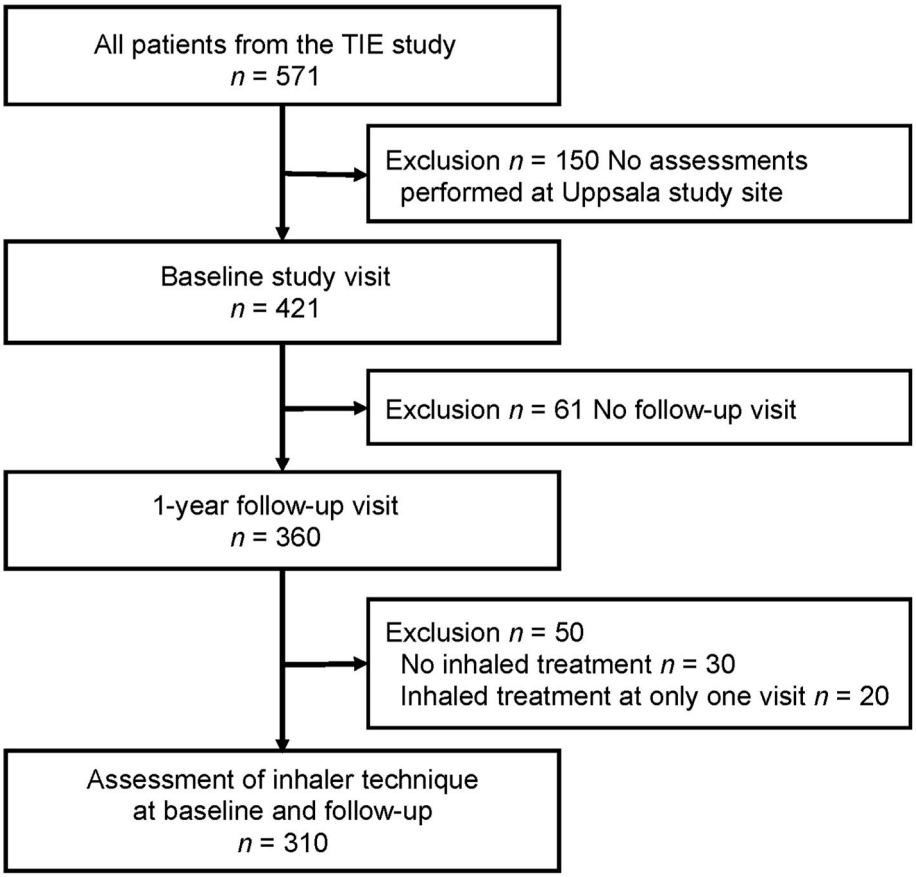

Fig. 1. Flowchart of patients included in and excluded from the study. TIE, Tools for Identifying Exacerbations.

2.3. Pharmaceutical treatment and inhaler devices

Pharmacological treatment categories were as-needed therapy only (regardless of the pharmacological effect of the inhaler), long-acting beta-2-agonists (LABA), long-acting muscarinic antagonists (LAMA), LABA + LAMA, inhaled corticosteroids (ICS), ICS + LABA, ICS + LAMA, and ICS + LABA + LAMA. A change in the pharmacological treatment during the follow-up year was defined as treatment escalation (an additional treatment category was added), unchanged treatment (same treatment category at both visits), treatment de-escalation (discontinuation of one or more treatment categories), and switch (change of treatment categories). Inhaler device treatment was defined as any combination of inhaler device models that a patient was using. Included device models were the single-dose dry-powder inhalers Breezhaler and Handihaler, the multi-dose dry-powder inhalers Diskus, Easyhaler, Genuair, Novolizer, Spiromax, and Turbuhaler, the Respimat soft-mist inhaler, and metered-dose inhalers (MDIs). Breezhaler and Handihaler were considered to be the same device model, as were Genuair and Novolizer, and breath actuated and pressurized metered-dose inhalers, i.e., MDI, due to very similar inhaler handling and critical error assessment. A change from, e.g., Breezhaler to Handihaler was thus not considered to represent a change in inhaler device model. Changes in inhaler device treatment during the follow-up year were defined as: no new device models (unchanged device model combination, or discontinuation of ≥1 device model, i.e., the treatment at follow-up was delivered using the same model/models as at baseline), or ≥1 new device model.

2.4. Critical inhaler technique error assessment and intervention

The patients demonstrated their inhaler technique at baseline and follow-up with each of their device models. The patient's own inhalers were used if possible, otherwise empty demo inhalers with disposable mouthpieces were provided. The inhaler technique was reviewed specifically for errors in opening the device, positioning the device before and during the inhalation manoeuvre, preparing and loading the dose, and exhaling through the device (dry-powder inhalers only) (Table A1), as these were considered as critical errors [4,7–9,11,12,15]. Each assessment was judged by a single assessor using device-specific checklists (Table A1). In total, three assessors were involved, one clinical pharmacist and two asthma/COPD nurses. The checklists were developed from the patient information leaflets for each device, based on available information [4,33–36] and clinical judgement, and described the correct procedure for each inhaler device model. If a patient's technique deviated from what was described in the checklist regarding any of the four possible critical errors, this was judged to be a critical error. No other errors were assessed or corrected during the study visits. Immediately after the assessment, the assessor informed patients with critical errors which errors were observed and with which inhaler device models, and demonstrated the correct technique with each of the device models. The demonstration was repeated until the patients verbally confirmed that they had understood the information. Critical error frequency was calculated based on the observed critical errors at baseline and follow-up, and the patients were categorized as having no critical errors at any visit, ≥1 critical error at baseline but no critical errors at follow-up, no critical errors at baseline but ≥1 critical error at follow-up, or ≥1 critical error at both visits.

2.5. Statistical analysis

Categorical variables are reported as frequencies and percentages and continuous variables as means and standard deviations (SD). There were missing data regarding BMI (n = 2), education (n = 1), CAT (n = 8), and mMRC (n = 5). Pearson's χ^2 test or Fisher's exact test (group size <5) were used for comparison of categorical variables between groups. Comparisons of within-group changes from baseline to 1-year follow-up were performed using the exact McNemar test and paired *t*-tests. The associations between critical errors and CAT score, mMRC score, and previous exacerbations at baseline and follow-up were investigated with a linear mixed model with random intercept (CAT score as outcome), an ordinal logistic regression (mMRC as outcome), and a multiple logistic regression (occurrence of exacerbations within the preceding year as outcome). The frequency of critical errors (≥1 critical error/no critical errors), time of data collection (baseline/follow-up), and the interaction effect between the frequency of critical errors and the time of data collection were included as explanatory variables in all models. Data are presented as coefficient estimates, with standard errors (SEs) and 95% confidence intervals (CIs), or odds ratios (OR) and 95% CIs. Two-sided tests were applied and a p value < 0.05 was considered statistically significant in all analyses. Data management and statistical analyses were performed using R, version 3.4.0 (R Core Team, R Foundation for Statistical Computing, Vienna, Austria, 2017).

Table 1
Baseline demographics and clinical characteristics for all included patients, stratified by critical error (CE) frequency.

	All (n = 310)	No CEs any visit (n = 117)	≥1 CE baseline only (n = 78)	≥1 CE follow-up only (n = 51)	≥1 CE both visits (n = 64)
Sex					
Female	178 (57%)	63 (54%)	51 (65%)	28 (55%)	36 (56%)
Age (years)					
Mean ± SD	69 ± 8	69 ± 8	69 ± 8	70 ± 8	70 ± 8
<65	72 (23%)	36 (31%)	15 (19%)	7 (14%)	14 (22%)
65–75	172 (55%)	60 (51%)	47 (60%)	32 (63%)	33 (52%)
>75	66 (21%)	21 (18%)	16 (21%)	12 (24%)	17 (27%)
Body mass index (kg/m^2)					
<22	37 (12%)	15 (13%)	9 (12%)	9 (18%)	4 (6%)
22–30	194 (63%)	75 (64%)	51 (66%)	33 (65%)	35 (56%)
>30	77 (25%)	27 (23%)	17 (22%)	9 (18%)	24 (38%)
Current smoker	74 (24%)	29 (25%)	22 (28%)	9 (18%)	14 (22%)
Education					
Elementary school	191 (62%)	75 (64%)	45 (58%)	34 (68%)	37 (58%)
Upper secondary school	80 (26%)	24 (21%)	24 (31%)	13 (26%)	19 (30%)
University	38 (12%)	18 (15%)	9 (12%)	3 (6%)	8 (13%)
Severity of airflow limitation					
$FEV_1 \geq 80\%$	20 (6%)	6 (5%)	7 (9%)	6 (12%)	1 (2%)
$50\% \leq FEV_1 < 80\%$	173 (56%)	70 (60%)	43 (55%)	22 (43%)	38 (59%)
$30\% \leq FEV_1 < 50\%$	91 (29%)	32 (27%)	21 (27%)	17 (33%)	21 (33%)
$FEV_1 < 30\%$	26 (8%)	9 (8%)	7 (9%)	6 (12%)	4 (6%)
FEV_1% predicted mean ± SD	55 ± 17	55 ± 16	55 ± 17	55 ± 21	54 ± 15
Level of care					
Primary care	283 (91%)	111 (95%)	73 (94%)	43 (84%)	56 (88%)
Secondary care	27 (9%)	6 (5%)	5 (6%)	8 (16%)	8 (13%)

Data presented as number (%) of patients or mean ± SD; FEV_1, forced expiratory volume in 1 s, SD, standard deviation.

3. Results

Of 360 patients who completed the 1-year follow-up visit, 310 with inhaled treatment at both visits were included in this study (Fig. 1). Table 1 shows demographic information for all included patients, and for the subgroups of patients making no critical errors at baseline or follow-up (n = 117; 38%), making ≥1 critical error at baseline (n = 78; 25%), making ≥1 critical error at follow-up (n = 51; 16%), and making ≥1 critical error at both visits (n = 64; 21%). The typical patient was female, between 65 and 75 years old, of normal weight, with a low education level and moderate airflow limitation (Table 1).

3.1. Changes in inhaled pharmacological treatment and inhaler device models

Triple therapy with ICS in combination with LABA and LAMA was the most commonly used treatment at both baseline (50%) and follow-up (53%) (Table 2). The majority of the patients (229; 74%) had unchanged inhaled pharmacological treatment from baseline to follow-up. Treatment escalation, de-escalation, or switch of pharmacological treatment was observed in 42 (14%), 35 (11%), and 4 (1%) patients, respectively (Table A2). The percentage of patients using Turbuhaler decreased (64% vs 54%, p < 0.0001), whereas the use of Easyhaler (24% vs 35%, p < 0.0001) and Respimat (13% and 19%, p = 0.0003) increased during the follow-up year (Table 2). Most patients had their COPD treatment delivered from a combination of two different inhaler device models at both visits (n = 169; 54% and n = 182; 59%), but some patients combined up to four different inhaler device models (Table 2, Table A3). Treatment with ≥1 new device model was initiated in 95 (31%) patients during the follow-up year (data not shown).

Table 2
Inhaled COPD treatment, planned visits due to COPD, and symptom control and previous exacerbations at baseline and follow-up.

	Baseline n = 310	Follow-up n = 310	P value
Pharmacological treatment			
As-needed only	21 (7%)	20 (6%)	1
LABA	6 (2%)	6 (2%)	1
LAMA	50 (16%)	53 (17%)	0.74
LABA + LAMA	18 (6%)	24 (8%)	0.21
ICS	9 (3%)	6 (2%)	0.55
ICS + LABA	37 (12%)	32 (10%)	0.42
ICS + LAMA	13 (4%)	5 (2%)	0.03
ICS + LABA + LAMA	156 (50%)	164 (53%)	0.30
Inhaler device models used			
Breezhaler and/or Handihaler	158 (51%)	146 (47%)	0.05
Diskus (Accuhaler)	37 (12%)	31 (10%)	0.11
Easyhaler	73 (24%)	107 (35%)	<0.0001
Genuair and/or Novolizer	66 (21%)	72 (23%)	0.34
Spiromax	6 (2%)	6 (2%)	1
Turbuhaler	197 (64%)	167 (54%)	<0.0001
Respimat	41 (13%)	60 (19%)	0.0003
MDI	11 (4%)	10 (3%)	1
Number of device models used			
1	83 (27%)	72 (23%)	0.11
2	169 (54%)	182 (59%)	0.17
≥3	58 (19%)	56 (18%)	0.88
Planned visits in preceding year			
With physician	125 (40%)	100 (32%)	0.03
With asthma/COPD nurse	225 (73%)	168 (54%)	<0.0001
Symptom control and exacerbations			
CAT score	12.2 ± 7.3	12.1 ± 7.2	0.90
mMRC score	1.7 ± 1.2	1.7 ± 1.3	0.54
≥1 exacerbation in preceding year	128 (41%)	106 (34%)	0.07

Data presented as number (%) of patients or mean ± SD. CAT, COPD Assessment Test; COPD, chronic obstructive pulmonary disease; ICS, inhaled corticosteroid; LABA, long-acting beta-2-agonist; LAMA, long-acting muscarinic antagonist; MDI, metered-dose inhaler; mMRC, modified Medical Research Council dyspnea scale. Differences between baseline and follow-up frequencies were tested with the exact McNemar test or paired *t*-test.

3.2. Critical inhaler technique errors

In total, 563 and 584 inhaler technique assessments were performed at baseline and follow-up visits, respectively (Table A4). The proportion of patients in the total population making ≥1 critical error was lower at follow-up than at baseline, 37% vs 46%, p = 0.011 (Fig. 2a). Similar results were seen in the subgroup of patients with unchanged pharmacological treatment (n = 229) (Fig. 2b). A decrease in critical errors was observed in patients who used the same inhaler device models at both study visits, but not in the sub-population of patients who started treatment with ≥1 new inhaler device model during the follow-up year (Fig. 2c and d).

The comparison of the prevalence of patients making ≥1 critical error at baseline and follow-up visits in the total population was tested with Pearson's $\chi 2$ test, and comparisons of within-group changes were performed using the exact McNemar test.

Among the patients making at least one critical error (n = 193), the number of critical errors did not change during the study period in 47 patients (24%), while an increase or decrease in the number of critical errors was identified in 60 (31%) and 86 (45%) patients, respectively (Table 3).

Not positioning the device correctly was the most commonly identified critical error type at both visits (Table 4), contributing to 0–55% of the total critical errors at baseline, and 0–47% at follow-up, depending on device model (Table A4). This was the only error type with a significantly lower prevalence at follow-up (22%) than at baseline (30%) (Table 4). Errors related to preparing and loading the dose correctly were the second most common critical error type identified (Table 4), varying between 0 and 39%, and 0–33% at baseline and follow-up, respectively, depending on device model (Table A4).

3.3. Symptom control and previous exacerbations

Critical errors in inhaler technique, time of data collection (follow-up), and critical errors at follow-up, measured using an interaction effect between critical errors and time of data collection, were not associated with CAT score, mMRC score, or previous exacerbations in the total patient population (Table 5) or in the subgroup of patients with unchanged inhaled pharmacological treatment (Table A5).

4. Discussion

This investigation among primary and secondary care patients with COPD shows that critical inhaler technique errors are common. However, the critical error frequency was significantly lower one year after an initial assessment with a one-time face-to-face educational demonstration and correction of inhaler technique. This effect was observed mainly in patients who did not start treatment with any new inhaler device during the follow-up year.

In this study, the prevalence of patients who made ≥1 critical error in inhaler technique decreased significantly, from 46% at baseline to 37% at 1-year follow-up. Previous studies [7,19–24] in patients with COPD, reporting improvements in inhaler technique after educational activities, have showed somewhat higher reductions in the percentage of patients making inhaler technique errors (10–43%) [7,20–22,24]. However, due to methodological differences, e.g., in the definition of inhaler technique errors, the included device models, and the time of follow-up, direct comparison of intervention effects between studies are difficult. This is reflected for instance in the large variability observed in the baseline error rates, which were either lower (0–43%) [7,21] or higher (64–100%) [20,22,24] compared with those in our study.

The TIE study was designed to be an observational study with a baseline visit and a 1-year follow-up visit. The patients demonstrated their inhaler technique with all their current device models, unlike in

Table 3
Critical inhaler technique errors categorized by number of critical errors at baseline and follow-up.

		Follow-up (n = 310)			
		No CEs (n = 195)	1 CE (n = 98)	2 CEs (n = 16)	4 CEs (n = 1)
Baseline (n =310)	No CEs (n = 168)	117	45	6	0
	1 CE (n = 118)	64	45	8	1
	2 CEs (n = 23)	14	7	2	0
	3 CEs (n = 1)	0	1	0	0

CE, critical error; no critical errors at both visits (light grey), same number of CEs at both visits (black), increased critical error frequency (dark grey with black number), decreased critical error frequency (dark grey with white number).

Table 4
Number (%) of patients at baseline and follow-up categorized by type of critical errors in inhaler technique.

	Baseline (n = 310)	Follow-up (n = 310)	P value
Not opening the device correctly	6 (2%)	2 (0.6%)	0.29
Not positioning the device correctly	94 (30%)	67 (22%)	0.04
Not loading the dose correctly	56 (18%)	53 (17%)	0.91
Exhalation through the device (dry-powder inhalers only)	11 (4%)	12 (4%)	1

Data are presented as n (%) patients. Differences between baseline and follow-up frequencies were tested with the exact McNemar test.

other studies including pre-selected device models [7,22,24] or specific combinations of device models only [7]. The correction of observed critical inhaler technique errors was given through a face-to-face demonstration based on an approach mimicking the COPD care the patients might receive between study visits. In all, 54% of the patients reported having ≥1 planned visit with an asthma/COPD nurse during the follow-up year and 32% with a physician, i.e., it is possible that their inhaler technique was checked and corrected between the study visits as well. Educational interventions similar to the one provided in this study has previously been shown to reduce errors in inhaler technique in COPD patients using the device models Breezhaler [7,21], Diskus (Accuhaler) [7,20,21], Genuair [21], Handihaler [7,20], Turbuhaler [7,20–22], Respimat [21], and pressurized metered-dose inhalers [19–22,24]. In the present study, only one follow-up assessment of inhaler technique was made one year after the baseline assessment. Others have assessed inhaler technique errors only once [7,19,20,23,24] within a time frame of 1–3 months, or up to four times [21,22] within a total study period of 6–12 months. We focused on critical errors in opening the device, positioning the device before and during the inhalation manoeuvre, preparing and loading the dose, and exhaling through the device (dry-powder inhalers only), while others have included other errors, e.g., not exhaling before inhalation [7,19,20,22–24], poor inhalation manoeuvre [7,19–24], not holding breath after inhalation [7,19,20,22–24], or errors in closing the device [20]. This highlights the lack of a standardized method for assessing inhalation errors. Of the critical errors studied, exhaling through a DPI prior to the inhalation was considered a device independent error. The prevalence of this error was found to be 4% at both baseline and follow-up, which is in the lower part of the previously reported range of 3–44% [7,11] when including COPD outpatients using devices they were currently prescribed for the treatment of COPD. However, several studies did not include this general error in the assessment of inhaler technique [8,9,12,19,21].

The prevalence of patients making critical errors was significantly lower at follow-up than at baseline among patients who had not started

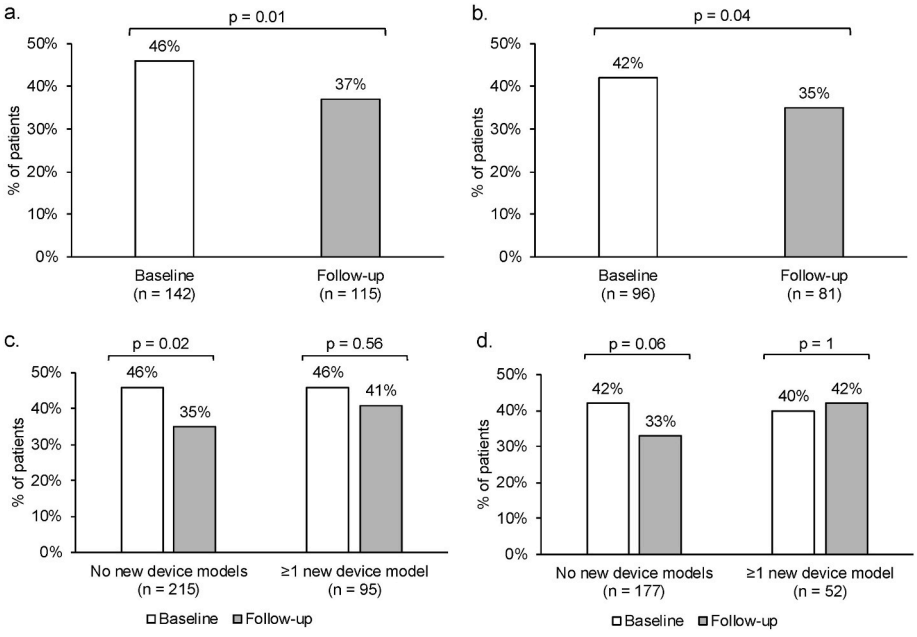

Fig. 2. The proportion of patients with ≥1 critical error in inhaler technique at baseline and follow-up for the total population (n = 310, panels a and c), and the subgroup of patients with unchanged pharmacological treatment (n = 229, panels b and d), categorized into those with and without ≥1 new inhaler device model during the follow-up year.

Table 5
Association of critical errors, time of data collection, and critical errors at follow-up with CAT score, mMRC score, and previous exacerbations.

Variable	CAT score	mMRC score	Exacerbations
	Coefficient estimate (95% CI)	OR (95% CI)	OR (95% CI)
≥1 critical error	−0.15 (−1.21, 0.91)	1.38 (0.92, 2.06)	1.35 (0.86, 2.13)
Time of data collection (follow-up)	−0.36 (−1.18, 0.45)	1.20 (0.50, 2.87)	0.72 (0.26, 1.96)
≥1 critical error at follow-up	0.84 (−0.60, 2.27)	0.90 (0.50, 1.62)	1.05 (0.54, 2.04)

Data are given as coefficient estimates for CAT score as a fixed effect model with 95% confidence intervals (CIs), and odds ratios (ORs) with 95% CI for mMRC score and exacerbations. CAT, COPD Assessment Test; mMRC, modified Medical Research Council dyspnea scale.

treatment with new device models during the follow-up year. Switching device models has previously been associated with poor inhaler technique and loss of asthma control if not accompanied with information about the new medication and device [37]. Device switching occurs in COPD patients for various reasons, e.g., when treatment escalation is needed and the device model the patient is using cannot be used for the new treatment. A switch can also have economic reasons. In Sweden, the regional Drug and Therapeutic Committees regularly update their recommendations of which inhalers should be prescribed, which may be a reason for the decrease in Turbuhaler use and increase in Easyhaler use seen in the present study. Switching of inhaler devices is associated with several disadvantages for the patient [38]. According to the Italian Society of Respiratory Medicine, switching inhaler devices in patients with COPD is recommended only as part of a COPD review where inhaler technique is assessed and patient consent for the switch is obtained. No device switch should occur without patient involvement and follow-up education [39].

No significant association was detected between critical inhaler technique errors and CAT score or mMRC score. This is in line with previous results from studies with a shorter follow-up of 3–6 months [19,21,23]. By contrast, a previous cross-sectional study [40] found higher CAT scores in COPD outpatients with errors in inhaler technique than in patients without errors. Notably, their definition of errors was broader than ours, and they included all errors, not only the ones defined as critical here [40]. Despite the reduction of critical errors and decrease in the proportion of patients with previous exacerbations between baseline and follow-up, no significant association was found between critical errors in inhaler technique and previous exacerbations. In a large 3-month randomized controlled trial, Tommelein et al. [19] found that inhaler technique education significantly reduced severe exacerbations (requiring an emergency department visit or hospitalization) in patients with COPD, but no difference was seen in patients with moderate exacerbations.

A strength of this study was that we included a relatively large cohort of both primary and secondary care patients with varying COPD severity. The information on patients' inhaled pharmacological treatment was based on medication reconciliations performed at the study visits. In addition, we included all device models the patients were currently using in the assessment of inhaler technique. This study also had some limitations. We included four types of critical errors, but not errors related to the inhalation manoeuvre. This was because no training equipment was available to confirm the inspiratory flow. A previously recognised weakness was the lack of standardised methods for assessment of inhaler technique, which makes it difficult to compare the results with those of previous studies.

In conclusion, the results from this observational study in COPD outpatients showed that the proportion of patients making critical inhaler technique errors was lower one year after an initial inhaler technique assessment and correction of specific critical errors. This effect was observed mainly in patients who did not start treatment with any new device models during the follow-up year. However, no association between critical errors in inhaler technique and COPD symptoms or previous exacerbations was found at either baseline or 1-year follow-up. More frequent assessments and training sessions, especially for COPD patients who have started using new device models, might be needed to minimize critical inhaler technique errors and ensure the highest efficacy of inhaled drugs.

Data Availability

Data cannot be made freely available as they are subject to secrecy in accordance with the Swedish Public Access to Information and Secrecy Act, but can be made available to researchers upon request (subject to a secrecy review).

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Declaration of competing interest

KB, MH, AM, HM, and EIN declare that they have no competing interests in this work. JS is an employee at GlaxoSmithKline (GSK), but when this work was done, she was a PhD student at Uppsala university and employed at Region Gävleborg. GSK has not had any influence on the TIE study or this manuscript. BS has received honoraria for educational activities and lectures from AstraZeneca, Boehringer Ingelheim, Meda, Novartis, TEVA, and Chiesi, and has served on advisory boards arranged by AstraZeneca, Novartis, Meda, TEVA, GSK, and Boehringer Ingelheim. KL has received payments for lectures and educational activities from Novartis, AstraZeneca, Boehringer Ingelheim, and TEVA and has served on advisory boards arranged by AstraZeneca, Boehringer Ingelheim, and GSK. CJ has received payments for lectures and educational activities from GSK, Orion, Novartis, AstraZeneca, and Boehringer, and has served on advisory boards arranged by AstraZeneca, Boehringer Ingelheim, Novartis, TEVA, and GSK.

CRediT authorship contribution statement

Johanna Sulku: Conceptualization, Methodology, Formal analysis, Writing – original draft, Writing – review & editing, Funding acquisition. **Christer Janson:** Conceptualization, Methodology, Writing – review & editing. **Håkan Melhus:** Conceptualization, Methodology, Writing – review & editing. **Björn Ställberg:** Conceptualization, Methodology, Writing – review & editing. **Kristina Bröms:** Writing – review & editing. **Marieann Högman:** Writing – review & editing, Funding acquisition. **Karin Lisspers:** Writing – review & editing, Funding acquisition. **Andrei Malinovschi:** Writing – review & editing, Funding acquisition. **Elisabet I. Nielsen:** Conceptualization, Methodology, Writing – review & editing.

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Appendix A. Supplementary data

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