

Original Research

Prevalence of Critical Errors and Insufficient Peak Inspiratory Flow in Patients Hospitalized with COPD in a Department of General Internal Medicine: A Cross-Sectional Study

Gaël Grandmaison, MD¹ Thomas Grobéty² Julien Vaucher^{1,3} Daniel Hayoz¹ Philipp Suter^{1,4}

¹Division of Internal Medicine, University and Hospital of Fribourg, Fribourg, Switzerland

²Division of Physiotherapy, Hospital of Fribourg, Fribourg, Switzerland

³Division of Internal Medicine, Lausanne University Hospital and University of Lausanne, Lausanne, Switzerland

⁴Department of Pulmonary Medicine, Allergology and Clinical Immunology, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland

Address correspondence to:

Gael Grandmaison, MD
Division of Internal Medicine
University and Hospital of Fribourg
2-6 Chemin des Pensionnats
1708 Fribourg, Switzerland
Phone: ++41 26 306 23 68
Email: gael.grandmaison@h-fr.ch

Running Head: Misused Inhaler in Patients Hospitalized With COPD

Keywords: chronic obstructive pulmonary disease; inhaler; hospital; critical error; peak inspiratory flow

Abbreviations:

Funding Support: This work was funded by a HFR grant (grant-2307), HFR Fribourg, Fribourg, Switzerland. The funder of the study was not involved in the study design, data collection, data analysis, data interpretation, and writing of the report.

Date of Acceptance: June 14, 2024 | **Publication Online Date:** June 20, 2024

Citation: Grandmaison G, Grobéty T, Vaucher J, Hayoz D, Suter P. Prevalence of critical errors and insufficient peak inspiratory flow in patients hospitalized with COPD in a department of general internal medicine: a cross-sectional study. *Chronic Obstr Pulm Dis.* 2024; Published online June 20, 2024.

<https://doi.org/10.15326/jcopdf.2024.0505>

This article has an online supplement

Abstract

Background: The suboptimal use of inhalers in the treatment of patients with chronic obstructive pulmonary disease (COPD) is probably a major but poorly documented problem in hospitalized patients. We aimed to describe the prevalence of misused inhalers among patients hospitalized with COPD in a department of general internal medicine.

Method: We conducted a monocentric cross-sectional study in consecutive patients with a diagnosis of COPD and hospitalized between August 2022 and April 2023 in the internal medicine division of Fribourg Hospital, Switzerland. Patients underwent an assessment of their inhaler technique and peak inspiratory flow (PIF) using the In-Check Dial G16®. The primary outcome was the prevalence of misused inhalers, defined as an inhaler used with a critical error and/or insufficient PIF. Secondary outcomes included the prevalence of inhaler unsuitable to patient characteristics and of patients using at least one misused inhaler.

Results: The study included 96 patients and 160 inhalers were assessed at admission. Among these inhalers, 111 (69.4%; 95% confidence interval [CI] 61.6-76.4) were misused; 105 (65.6%; 95% CI 57.7-72.9) due to the presence of a critical error in the inhalation technique and 22 (13.8%; 95% CI 8.8-20.1) due to insufficient PIF. Concerning the secondary outcome, 27 inhalers (16.9%) were unsuitable and 79 patients (82.3%) used at least one misused inhaler.

Conclusion: Among patients hospitalized with a diagnosis of COPD, two-thirds of inhalers were misused. Suboptimal use was mainly due to the presence of critical errors, but also to the presence of an insufficient PIF and unsuitable inhalers.

Introduction

Chronic obstructive pulmonary disease (COPD) is a major cause of morbidity and the third leading cause of mortality worldwide ¹. The pharmaceutical treatment of COPD relies mainly on the administration of medications via inhalation. However, the effectiveness of these treatments is very often hampered by the suboptimal utilization of inhalers, which may arise due to errors in inhalation technique, insufficient peak inspiratory flow (PIF) or the use of unsuitable inhaler devices ¹.

Errors in inhalation technique are remarkably prevalent and associated with an inefficient symptom control, a reduction in quality of life, an upsurge in exacerbations, and an escalated reliance on healthcare systems ²⁻⁵. In addition, specific inhaler types, such as dry powder inhalers, demand a robust and profound inhalation effort to de-agglomerate the medication-containing powder within the inhaler and enable its deposition within the distal airways ^{6,7}. The use of an inhaler with insufficient PIF is also associated with an increase in exacerbations and a higher frequency of hospital admissions ⁸⁻¹⁰. Furthermore, certain patient characteristics, such as lack of manual dexterity or cognitive impairments, impose limitations on the capacity to optimally use inhalers ¹¹.

The prevalence of errors in inhalation technique and insufficient PIF has predominantly been described in the outpatient setting. Furthermore, few studies have simultaneously examined the presence of errors in inhalation technique and PIF, despite the fact that both are critical factors for achieving optimal inhaler utilization ^{12,13}. Finally, there is little information regarding the prevalence of inhalers unsuited to patient characteristics, including those that cannot be used optimally even with proper instruction.

In this cross-sectional study, we describe the prevalence of misused inhalers among COPD patients upon admission to an internal medicine department. An inhaler was considered to be misused if employed with critical errors in inhalation technique and/or insufficient PIF.

Methods

Study Design and Participants

This monocentric cross-sectional study recruited patients in the internal medicine department of the Hospital of Fribourg (HFR), Fribourg, Switzerland, from 1 August 2022 to 3 April 2023. The study was approved by the Ethics Commission of the Canton of Vaud (project #: BASEC 2022-00910) and all participants provided written consent. The results are reported in accordance with the STROBE statement¹⁴.

All adult patients with a COPD diagnosis mentioned in their electronic record admitted to the HFR general internal medicine department and using an inhaler before hospitalization were assessed for eligibility. Exclusion criteria were an inability to complete the initial assessment due to language, physical or cognitive problems, and previous inclusion in the study. Each participant underwent an interview conducted by a research nurse within 72 hours of admission to the internal medicine department to collect demographic data and information concerning the diagnosis and the treatment of COPD and inhaler utilization. Subsequently, each inhaler used upon admission in internal medicine underwent an evaluation by a physiotherapist to assess the inhalation technique, measurement of PIF, and the patient's ability to use correctly their inhaler following a comprehensive therapeutic education. Each physiotherapist conducting the assessment received a 30-minute training session to standardize the evaluation and teaching technique.

The physiotherapist examined the inhalation technique through direct observation using tailored checklists designed for each type of inhaler (Figure S1). Based on the patient information leaflets and previous literature, a critical error was defined as an action or an inaction that could have a detrimental impact on the delivery of the drug to the distal airways³⁻⁵. In the case of critical errors, the patient benefited from a targeted teach-to-goal intervention focused on the specific gaps identified during the initial assessment. The teaching was repeated until the inhalation technique was performed without critical errors. An inhaler was classified as "not teachable" if the patient continued to exhibit critical errors despite receiving three repetitions of the instructions.

PIF was assessed using the In-Check Dial G16® (Alliance Tech Medical, Inc, Hillsborough, NC, USA), a hand-held device designed to replicate the internal resistance profile of the different inhalers¹⁵. PIF was measured at the resistance level corresponding to the inhaler used by the patient. The highest value among three consecutive inspiratory maneuvers was considered as the PIF measurement. If the measured PIF was below the minimum flow for optimal use, the inhaler was considered to be used with an insufficient PIF^{6,15}. As nebulized aerosols are administered by healthcare professionals during hospitalization and do not require a minimum PIF, they were considered to be used optimally and were not included in the study.

Outcomes

The primary outcome was the proportion of misused inhalers. The inhaler was considered misused when used with at least one critical error and/or insufficient PIF measured prior to the teach-to-goal intervention. This composite outcome was chosen because it combines two factors of suboptimal inhaler use associated with poor disease control. The primary outcome was assessed in the following subgroups: male vs. female; <65 years vs. ≥65 years; admission for an acute COPD exacerbation (present vs absent); or for a respiratory problem (present vs

absent). The presence of a COPD exacerbation or hospitalization due to a respiratory complaint was defined by reviewing the patient's admission document and electronic record. A diagnosis of COPD exacerbation was based on information documented in the electronic record by the patient's doctor. A hospitalization with increased respiratory symptoms compared to the usual symptomatology was considered as a hospitalization with a respiratory complaint.

Secondary outcomes included the prevalence of inhalers used with at least one critical error, used with insufficient PIF, unable to be used despite adequate teaching and unsuitable inhalers. An unsuitable inhaler was defined as an inhaler that cannot be used optimally, either because of an insufficient PIF or because of an inability to use an inhaler optimally despite specific teaching. These outcomes were presented for all inhalers, by patient and by type of inhaler.

Statistical Analysis

Data from the literature suggest that 60% of hospitalized patients with COPD make critical errors when handling their device¹⁶. In order to have a margin of error of 10% when assessing the proportion of misused inhaler with a statistical significance level of 5% and considering that each patient uses one inhaler, we estimated that we needed a sample size of 93 patients¹⁷. To allow for intra-patient correlation (cluster=patient), a clustered sandwich estimator was specified to calculate the standard errors. Critical errors, insufficient PIF, and inhalers unable to be used despite adequate teaching and unsuitable inhalers were expressed by proportions with their confidence interval estimated from the above-mentioned statistical model¹⁸. If missing data were less than 5%, the analysis was based on complete cases only¹⁹. Study data were collected and managed using REDCap electronic data capture tools hosted at the University of Fribourg²⁰.

Data are presented as mean +/- standard deviation (SD) for normally distributed values, as median and interquartile range for non-normally distributed values, and as number and percentage for categorical values. Continuous variables were compared with a Student's t-test for normally distributed variables and with a Mann-Whitney U-test for variables with an abnormal distribution. Categorical values were compared using a χ^2 test. The level of statistical significance was defined as a p-value <0.05. Secondary analyses have not been adjusted for multiple comparisons. Statistical tests were performed using STATA version 17 (StataCorp).

Results

Patient Characteristics

The consort flow diagram is shown in **Figure 1**. Of 98 patients included in the study, two were excluded as the physiotherapist assessment could not be completed within 72 hours of admission. Baseline demographic and medical characteristics of patients are shown in **Table 1**. Mean age was 71.6 (SD 9.8 years), 60 (63 %) were men, and 64 (67%) were hospitalized with a COPD exacerbation. Patients used an average of 3.0 inhalers (SD 1.2) and 292 inhalers were assessed. The distribution of inhalers is described in **Table S1**. Nebulizers are considered to be used correctly as they are administered by nursing staff and not reliant on a minimum PIF. Consequently, 132 nebulizers were excluded and a total of 160 inhalers were included in the final analysis (**Fig. 1**).

During the assessment conducted by physiotherapists, 111 (69.4%) inhalers were misused. Among these, 105 (65.6%) were used with at least one critical error and 22 (13.8%) with an insufficient PIF (**Table 2; Fig. 2**). Inhalers were used with a mean of 1.4 errors (SD 1.4) and 1.3 critical errors (SD 1.3). The types of errors made are described in **Table S2**. Over the course of teaching sessions, there was a notable reduction in the number of inhalers being used with critical errors. After one teaching session, 33 inhalers (20.6%) exhibited critical

errors, decreasing to 15 inhalers (9.4%) after two teaching sessions. Even after three teaching sessions, nine (5.6%) inhalers were still being used with at least one critical error and considered not teachable (Fig. 3). Several factors were identified to explain the inability to achieve an adequate inhaler technique, including cognitive disorders (n=5), fine motor disorders (n=2), a lack of coordination between inhaler activation and inspiration (n=4) and the inability to hold one's breath sufficiently (n=2). Moreover, 27 inhalers (16.9%) were deemed unsuitable for optimal use, even after adequate training, due to the persistence of a critical error and/or insufficient PIF.

In the subgroup analysis, the proportion of inhalers used with at least one critical error was lower when patients were hospitalized for a COPD exacerbation or a respiratory cause (Table 3; Table S3). These results were consistent in a sensitivity analysis including all types of inhalers, including nebulizers. Age and gender was not associated with the proportion of misused inhalers, used with at least one critical error or with insufficient PIF. Analysis by patient showed that 79 (82.3%) patients used at least one misused inhaler, 78 (81.3%) used at least one inhaler with a critical error, and 21 (21.9%) with insufficient PIF (Table 3). After three teachings, nine patients (9.4%) continued to use at least one inhaler with a critical error. Twenty-four patients (25%) were using at least one unsuitable inhaler, either because of an inability to use an inhaler without a critical error after three teachings or because of an insufficient PIF. Results by inhaler type are shown in Table S4. Due to the heterogeneous number of inhalers in each category and sometimes the small number of inhalers in each category, a direct comparison between different types of inhalers was not possible.

Discussion

In this study evaluating inhalers used by 96 patients diagnosed with COPD and hospitalized in a department of general internal medicine, 69.4% of inhalers were misused due to a critical error (65.6%) or insufficient PIF (13.8%). Despite adequate instruction, 5.6% of inhalers could not be used without a critical error. When combining inhalers that could not be used adequately after instruction and those used with an insufficient PIF, 16.9% were unsuitable for the patient.

The findings of this study underscore a prevalent issue in the management of patients with COPD within hospital settings, i.e. the widespread occurrence of suboptimal inhaler use. These results align with previous observations in both outpatient settings and limited hospital-based investigations^{2,4,10} and highlight several important issues when considering inhaler use among patients hospitalized with COPD. First, critical errors in inhalation technique are common and require the use of every available opportunity to control inhalation technique. Second, 13.8% of inhalers are used suboptimally due to patients' inability to generate sufficient PIF. This figure rises to 26.5% when focusing solely on dry powder inhalers (DPI) that mandate sufficient PIF for optimal function. Integrating PIF measurements therefore seems necessary to ensure an optimal use of the inhaler. Third, the therapeutic education provided during the evaluation led to a 45% reduction in the number of inhalers used with a critical error after one teaching round, 11.2% after the second lesson, and 3.8% after the third lesson. These results highlight the benefit of repeated therapeutic education. Although, the number of instructions to be given before concluding that the inhaler cannot be used remains to be determined, the literature emphasizes the importance of repeating the instruction over time, and hospitalization seems a good opportunity to do so^{21,22}. Finally, despite repeated and targeted instruction, a significant number of inhalers persistently elude correct usage. Simply demonstrating the correct inhalation technique, even if targeted to the patient's specific errors, does not rectify improper inhalation techniques for

each patient. This inability to perform an optimal inhalation technique despite adequate teaching is explained in our study by the presence of patient-related characteristics, namely cognitive impairment, fine motor impairment, inability to coordinate activation of the inhaler and inspiration when using a pressurized metered-dose inhaler (pMDI), and inability to hold sufficient inspiration. These factors limiting the possibility of using inhalers correctly are consistent with the data in the literature ^{2,11}. This last point underlines the importance of considering patient-specific characteristics when selecting an inhaler and of regularly evaluating the technique of inhalation, given the potential evolution of these characteristics over time ¹¹.

In our study, 82.3% of patients were using at least one of their inhalers in a suboptimal manner, characterized by either one critical error (81.3%) or insufficient PIF (21.9%). A subgroup analysis showed that, paradoxically, the fact of not being admitted to the hospital for a COPD exacerbation or a respiratory complaint was associated with a higher prevalence of suboptimal inhaler use and with a critical error. This association poses a challenge for interpretation as the suboptimal use of inhalers typically correlates with a higher frequency of exacerbations ^{2,4}. As the assessment was carried out during the first 72 hours of hospitalization, it is possible that patients hospitalized for a COPD exacerbation or respiratory problem received more focused attention regarding their inhaler during their stay in the emergency ward or during the early phase of hospitalization. In any case, this observation emphasizes the importance of evaluating the inhalation technique of all patients with COPD using an inhaler and not solely confined to those hospitalized due to a COPD exacerbation or poorly controlled disease.

The inhaler evaluation method employed in this study comprises a three-step approach. First, patients demonstrated their inhalation and the technique was assessed using a checklist specific to each inhaler. Second, the assessment involved measuring PIF using the In-Check

Dial G16®. Finally, targeted education was provided to address any errors identified during the demonstration of the inhalation technique. These steps were conducted by a trained physiotherapist. The expertise required to carry out this evaluation involved a 30-minute training session, while the actual evaluation of the inhalers took between 10 and 15 minutes, depending on the number of inhalers used and the number of identified errors. Involving a person trained in inhaler evaluation seems to be a good strategy to compensate for physicians' lack of knowledge and/or time constraints²³. Consequently, this method presents as an easily implementable approach, not only enabling targeted therapeutic education to be given, but also to identify inhalers that need to be replaced because of an inability to generate a sufficient PIF or to perform an adequate inhalation technique. Considering the established association between suboptimal inhaler usage and adverse outcomes such as poor disease control, more frequent exacerbations, and increased costs, integrating such a strategy should be an integral part of the management of hospitalized patients diagnosed with COPD^{4,10,13}.

It is, however, important to emphasize that our study assessed the inhalers used in the hospital. Therefore, the reason for hospitalization could have played a role in the results obtained by influencing the patient's ability to use their inhaler correctly or to generate a sufficient PIF. For example, two-thirds of the participants in our study were experiencing a COPD exacerbation at the time of their admission. The impact of a COPD exacerbation on PIF is uncertain, and it is possible that PIF could be transiently decreased^{10,24,25}. The information obtained during the initial assessment allows for the selection of an inhaler suitable for the acute phase, but does not determine the patient's ability to use a type of inhaler outside of this context. An evaluation of the inhalation technique and PIF seems to be necessary when the patient's condition changes^{1,10}.

Strengths and Limitations

This study has several strengths. First, it included all patients hospitalized with a diagnosis of COPD and highlighted that the suboptimal use of inhalers is a problem, regardless of the reason for hospitalization. Second, we were able to detail the causes of suboptimal use, namely errors in inhalation technique, insufficient PIF or an unsuitable inhaler. We were also able to specify the reasons why an inhaler might remain unusable despite adequate teaching.

There are also some limitations to this study. First, we explored PIF with the help of the In-Check Dial G16® by asking the patient to inhale as rapidly and forcefully as possible. PIF measurement under these conditions does not necessarily represent the PIF used by the patient when using an inhaler under real-life conditions¹³. Consequently, our results may underestimate the true prevalence of inhalers used with inadequate PIF. Second, the assessment was carried out within 72 hours of admission. Patients, particularly those with respiratory complaints, may have benefited from teaching or adaptation of their inhaler prior to the assessment, again leading to an underestimation of the prevalence of misused inhalers. Third, there is no consensus on which errors should be considered critical. Consequently, the steps defined as critical errors could have an influence on the proportion of inhalers used with a critical error. Fourth, the evaluation relies on a visual assessment by the physiotherapist. Consequently, the evaluation of certain stages of the inhalation technique, such as the coordination between inhaler activation and inspiration when using a pMDI, may lack precision. Similarly, when using a pMDI, it was not taken into account whether the patient was breathing too forcefully. Fifth, the small sample size in our study made it impossible to assess the association between patient characteristics and suboptimal inhaler use. Similarly, the size of our sample does not allow us to comment on the association between different types of inhaler and their misuse. However, our observations confirm that the problem of inhalers used with a critical error affects all types of inhaler and that insufficient PIF is a serious and substantial clinical problem for DPI. Sixth, the diagnosis of COPD was made

based on information found in the patient's electronic file. With pulmonary functions not available for 25% of the patients, it is possible that some diagnoses may be incorrect.

However, a recent study in our department showed that 87% of the COPD diagnoses recorded in our patients' electronic files could be confirmed by pulmonary functions²⁶.

Finally, this is a monocentric study whose results should be confirmed in different centers.

Nevertheless, the results are consistent with the current literature^{10,16,27}.

Conclusion

Misused inhalers in hospitalized patients with COPD is a major problem, irrespective of the reason for hospitalization. Causes are critical errors in inhalation technique, insufficient PIF or an unsuitable inhaler. The assessment of the inhalation technique and the PIF should be part of the standard clinical assessment of patient with COPD during hospitalization, regardless of the reason for hospitalization.

Declarations

Acknowledgments

The authors thank all the patients and their families, as well as the team of investigators involved in this study. Statistical data analysis support, under the direction of the authors, was provided by Mohamed Faouzi, Division of Biostatistics, Center for Primary Care and Public Health (Unisanté), University of Lausanne, Switzerland. Medical writing support, under the direction of the authors, was provided by Rosemary Sudan.

Statement of Ethics

The informed consent forms and study protocol was approved by the Ethics Commission of the Canton Vaud of (project number: BASEC 2022-00910). All patients provided written informed consent prior to inclusion in the study.

Conflict of Interest Statement

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Author contributions

The study was conceived and designed by GG, PS, TG and DH. GG, PS, and TG oversaw conduct of the study. Data were acquired by GG, PS, and TG. Data were analyzed by GG and interpreted by all authors. All authors read and approved the final version.

Data Availability Statement

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

References

1. GOLD. Global strategy for the diagnosis, management, and prevention of chronic lung obstructive disease. 2023.
2. Chrystyn H, van der Palen J, Sharma R, et al. Device errors in asthma and COPD: systematic literature review and meta-analysis. *NPJ Prim Care Respir Med* 2017;27:22.
3. Kocks JWH, Chrystyn H, van der Palen J, et al. Systematic review of association between critical errors in inhalation and health outcomes in asthma and COPD. *NPJ Prim Care Respir Med* 2018;28:43.
4. Usmani OS, Lavorini F, Marshall J, et al. Critical inhaler errors in asthma and COPD: a systematic review of impact on health outcomes. *Respir Res* 2018;19:10.
5. Molimard M, Raherison C, Lignot S, et al. Chronic obstructive pulmonary disease exacerbation and inhaler device handling: real-life assessment of 2935 patients. *Eur Respir J* 2017;49.
6. Ghosh S, Ohar JA, Drummond MB. Peak Inspiratory Flow Rate in Chronic Obstructive Pulmonary Disease: Implications for Dry Powder Inhalers. *J Aerosol Med Pulm Drug Deliv* 2017;30:381-7.
7. Mahler DA. The role of inspiratory flow in selection and use of inhaled therapy for patients with chronic obstructive pulmonary disease. *Respir Med* 2020;161:105857.
8. Loh CH, Peters SP, Lovings TM, Ohar JA. Suboptimal Inspiratory Flow Rates Are Associated with Chronic Obstructive Pulmonary Disease and All-Cause Readmissions. *Ann Am Thorac Soc* 2017;14:1305-11.
9. Chen SY, Huang CK, Peng HC, et al. Peak-Inspiratory-Flow-Rate Guided Inhalation Therapy Reduce Severe Exacerbation of COPD. *Front Pharmacol* 2021;12:704316.
10. Mahler DA, Halpin DMG. Peak Inspiratory Flow as a Predictive Therapeutic Biomarker in COPD. *Chest* 2021;160:491-8.
11. Renaud Y, Suter P, Grandmaison G. Patient Characteristics to Consider When Selecting an Inhaler for the Treatment of Chronic Obstructive Pulmonary Disease and Available Assessment Methods: A Narrative Review. *Respiration* 2023:1-10.
12. J WHK, Wouters H, Bosnic-Anticevich S, et al. Factors associated with health status and exacerbations in COPD maintenance therapy with dry powder inhalers. *NPJ Prim Care Respir Med* 2022;32:18.
13. Leving MT, van Boven JFM, Bosnic-Anticevich SZ, et al. Suboptimal Peak Inspiratory Flow and Critical Inhalation Errors are Associated with Higher COPD-Related Healthcare Costs. *Int J Chron Obstruct Pulmon Dis* 2022;17:2401-15.
14. von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies. *Int J Surg* 2014;12:1495-9.
15. Sanders MJ. Guiding Inspiratory Flow: Development of the In-Check DIAL G16, a Tool for Improving Inhaler Technique. *Pulm Med* 2017;2017:1495867.
16. Batterink J, Dahri K, Aulakh A, Rempel C. Evaluation of the use of inhaled medications by hospital inpatients with chronic obstructive pulmonary disease. *Can J Hosp Pharm* 2012;65:111-8.
17. Eng J. Sample size estimation: how many individuals should be studied? *Radiology* 2003;227:309-13.
18. Norton EC, Miller MM, Kleinman LC. Computing adjusted risk ratios and risk differences in Stata. *Stata Journal* 2013;13:492-509.
19. Lee KJ, Tilling KM, Cornish RP, et al. Framework for the treatment and reporting of missing data in observational studies: The Treatment And Reporting of Missing data in Observational Studies framework. *J Clin Epidemiol* 2021;134:79-88.

20. Harris PA, Taylor R, Minor BL, et al. The REDCap consortium: Building an international community of software platform partners. *J Biomed Inform* 2019;95:103208.
21. Takaku Y, Kurashima K, Ohta C, et al. How many instructions are required to correct inhalation errors in patients with asthma and chronic obstructive pulmonary disease? *Respir Med* 2017;123:110-5.
22. Klijn SL, Hiligsmann M, Evers S, Roman-Rodriguez M, van der Molen T, van Boven JFM. Effectiveness and success factors of educational inhaler technique interventions in asthma & COPD patients: a systematic review. *NPJ Prim Care Respir Med* 2017;27:24.
23. Plaza V, Giner J, Rodrigo GJ, Dolovich MB, Sanchis J. Errors in the Use of Inhalers by Health Care Professionals: A Systematic Review. *J Allergy Clin Immunol Pract* 2018;6:987-95.
24. Price DB, Yang S, Ming SWY, et al. Physiological predictors Of peak inspiRatory flow using Observed lung function resultS (POROS): evaluation at discharge among patients hospitalized for a COPD exacerbation. *International journal of chronic obstructive pulmonary disease* 2018;13:3937-46.
25. Broeders ME, Molema J, Hop WC, Vermue NA, Folgering HT. The course of inhalation profiles during an exacerbation of obstructive lung disease. *Respir Med* 2004;98:1173-9.
26. Tschopp J, Dumont P, Hayoz D. True prevalence of COPD and its association with peripheral arterial disease in the internal medicine ward of a tertiary care hospital. *Swiss Med Wkly* 2017;147:w14460.
27. Press VG, Arora VM, Shah LM, et al. Misuse of respiratory inhalers in hospitalized patients with asthma or COPD. *J Gen Intern Med* 2011;26:635-42.

Table 1. Baseline characteristics

Characteristics	Male (n=60)	Female (n=36)	Patient (n=96)
Age - mean (sd)	72.4 (9.2)	70.3 (10.7)	71.6 (9.8)
BMI [kg/m ²] - mean (sd)	25.6 (5.6)	26.2 (9.3)	25.81 (7.1)
Smoking			
Active - n (%)	26 (43)	14 (39)	40 (41)
Former - n (%)	34 (57)	21 (58)	55 (57)
Comorbidities – n (%)			
Obesity	13 (22)	7 (19)	20 (21)
Ischaemic cardiopathy	28 (47)	6 (17)	34 (35)
Chronic heart failure	22 (37)	7 (19)	29 (30)
Cognitive impairment	2 (3)	0 (0)	2 (2)
Visual impairment	1 (2)	1 (3)	2 (2)
Neurological disease	2 (3)	2 (6)	4 (4)
Rheumatological disease	0 (0)	2 (6)	2 (2)
Anxiety/depression	8 (13)	7 (19)	15 (16)
COPD Classification^a - n (%)			
Grade			
- Grade 1	2 (3)	2 (6)	4 (4)
- Grade 2	17 (28)	9 (25)	26 (27)
- Grade 3	16 (27)	12 (33)	28 (29)
- Grade 4	8 (13)	6 (17)	14 (15)
- Grade Unknown	17 (28)	7 (19)	24 (25)
Group			
- Group A	4 (7)	4 (11)	8 (8)
- Group B	14 (23)	7 (19)	21 (22)
- Group E	22 (37)	14 (39)	36 (38)
- Group Unknown	20 (33)	11 (31)	31 (32)
LTOT - n (%)	16 (27)	13 (36)	29 (30)
mMRC - mean (sd)	3.8 (1.0)	3.7 (1.2)	3.8 (1.1)
CAT score - mean (sd)	17.0 (7.2)	15.7 (8.0)	16.5 (7.5)
Hospitalization – n (%)			
With respiratory complaint	42 (70)	31 (86)	73 (76)
With COPD exacerbation	38 (63)	26 (72)	64 (67)
With ICU stay	15 (25)	6 (17)	21 (22)

^a As reported in the electronic patient record. BMI, body mass index; CAT, COPD assessment test; ICU, intensive care unit; LTOT, long-term oxygen therapy at home; mMRC, modified Medical Research Council dyspnea scale; SD, standard deviation

Table 2. Primary and secondary outcomes

Outcomes by inhalers (n=160)	Inhalers, n (%)	95% CI
Misused inhaler	111 (69.4)	61.6 - 76.4 ^a
Critical error	105 (65.6)	57.7 - 72.9 ^a
Insufficient PIF	22 (13.8)	8.8 - 20.1 ^a
Non-teachable	9 (5.6)	2.6 - 10.4 ^a
Unsuitable	27 (16.9)	11.4 - 23.6 ^a
Outcomes by patients (n=96)	Patient, n (%)	95% CI
Misused inhaler	79 (82.3)	73.2 - 89.3
Critical error	78 (81.3)	72.0 - 88.5
Insufficient PIF	21 (21.9)	14.1 - 31.5
Non-teachable	9 (9.4)	4.4 - 17.1
Unsuitable	24 (25)	16.7 - 34.9

^a The widths of the confidence intervals were adjusted to take into account the cluster analysis at the level of patient. PIF, peak inspiratory flow; CI, confidence interval.

Table 3. Subgroup analysis for misused inhaler

	Misused inhaler		p value for interaction
	n (%)	95% CI	
Total (n=160)	111(69.4)	61.6 – 76.4	
Male (n=97)	67 (69.1)	58.4 – 81.3	0.927
Female (n=63)	44 (69.8)	57.2 – 80.9	
Age < 65 years (n=36)	22 (61.1)	39.3 – 82.9	0.352
Age ≥ 65 years (n=124)	89 (71.8)	63.0 – 80.5	
Absence of COPD exacerbation (n=49)	42 (85.7)	76.4 – 95.1	0.005
Presence of COPD exacerbation (n=111)	69 (62.2)	51.2 – 73.2	
Absence of respiratory complaint (n=34)	28 (82.4)	69.9 – 94.8	0.074
Presence of respiratory complaint (n=126)	83 (65.9)	55.8 – 75.9	

The widths of the confidence intervals and p value for interaction were adjusted to take into account the cluster analysis at the level of patient. COPD, chronic obstructive pulmonary disease; CI; confidence interval.

Figure 1

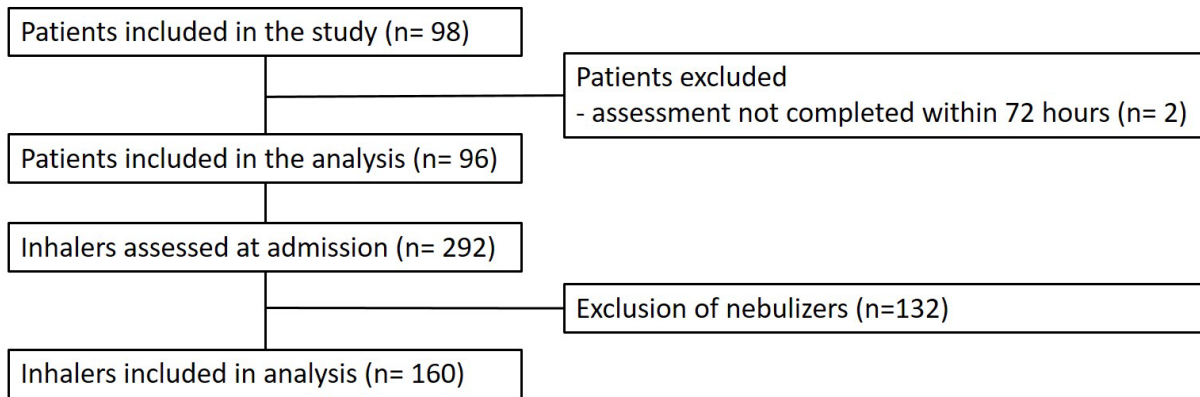


Figure 2

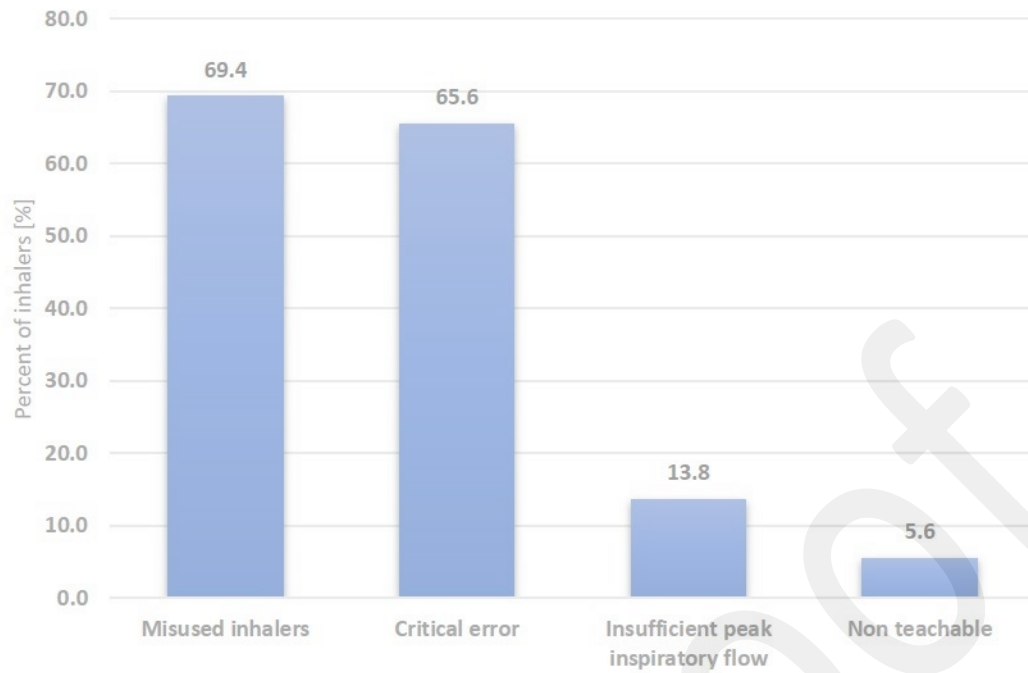
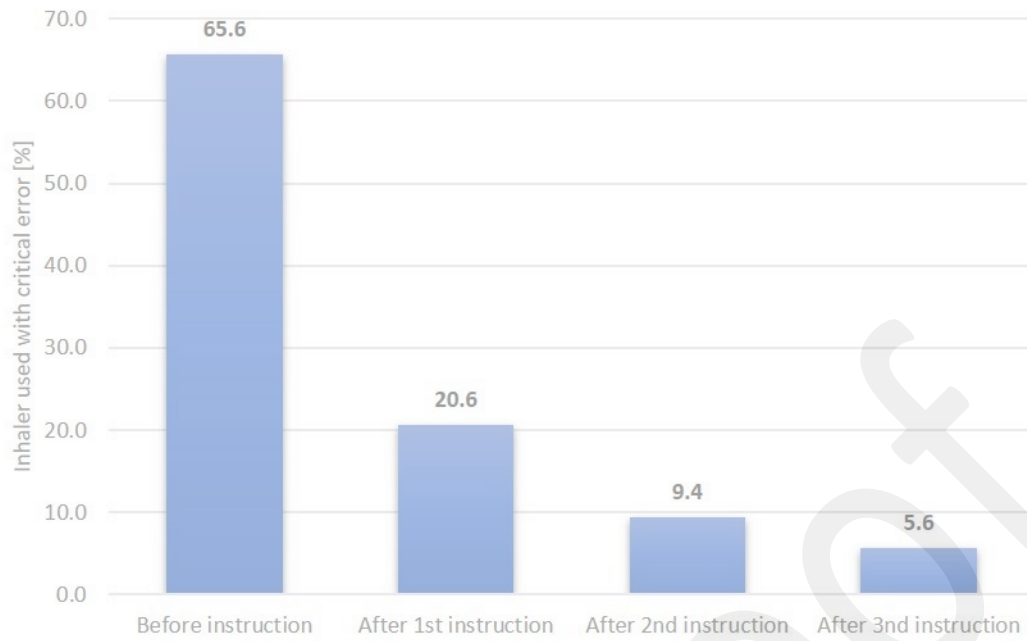


Figure 3



Online Supplement

Figure S1: Checklist for inhaler technique evaluation

	pMDI	pMDI with spacer	BAMDI	Respimat®	Diskus®	Ellipta®	Turbuhaler®	Handihaler®	Breezhaler®	Genuair®
Critical error										
Non-critical error										
Remove cap										
Open lid and mouthpiece and place capsule in chamber										
Check dose counter (if applicable)										
Turn the transparent base of the inhaler until click is heard										
Slide lever until click heard and keep the inhaler upright										
Pierce the capsule once and release the piercing										
Close mouthpiece, ensuring click is heard										
Shake pMDI well										
Flip the red lever on the top up until it flicks into place										
Turn coloured wheel one way, then back until click is heard and keep the inhaler upright										
Insert pMDI well into spacer										
Hold the inhaler horizontally with the coloured button on the top										
Press the button all the way down and release it										
Check that the control window changed to green										
Breathe out normally away from the inhaler										
Hold the inhaler upright (do not cover the air vents at the bottom for BA-pMDI)										
Keep head upright or slightly tilted										
Seal lips around mouthpiece										
Activate pMDI										
Inhale slowly and deeply through the mouth, actuating once during first half of inhalation										
Inhale slowly and deeply through de mouth. Keep breathing in after hearing the click										
Inhale slowly and deeply through the mouth minimum 3 times or hold breath for 5 seconds										
Inhale forcefully and deeply through the mouth										
Continue slow and deep inhalation										
Hold breath for at least 5 seconds										
Breath out gently, away from your inhaler										
Push red lever down										
Check if capsule is empty, if not, repeat steps										
Check the control window has changed back to red, if not, repeat steps										

pMDIs, pressurized metered-dose inhalers; BAMDI, breath-actuated metered-dose inhalers.

Table S1. Inhalers included in the analysis

Type of inhaler	Inhalers, n (%)
pMDI	22 (13.8)
pMDI + spacer	26 (16.3)
BAMDI	1 (0.6)
Respimat®	28 (17.5)
Diskus®	9 (5.6)
Ellipta®	27 (16.9)
Turbuhaler®	13 (8.1)
Handihaler®	17 (10.6)
Breezhaler®	17 (10.6)

pMDI, pressurized metered-dose inhalers; BAMDI, breath-actuated metered-dose inhalers.

Table S2. Frequency of specific critical errors in inhaler technique

	pMDI (n=22)	pMDI with spacer (n=26)	BAMDI (n=1)	Respimat® (n=28)	Diskus® (n=9)	Elipita® (n=27)	Turbuhaler® (n=13)	Handihaler® (n=17)	Breezhaler® (n=17)
	Number of errors (%)								
Remove cap	1 (5)*	1 (4)*	0 (0)*	1 (4)*			0 (0)*		
Open lid and mouthpiece and place capsule in chamber								0 (0)*	1 (6)*
Check dose counter (if applicable)	9 (41)*	8 (31)*	0 (0)*	9 (35)*	2 (22)*	7 (26)*	4 (31)*		
Turn the transparent base of the inhaler until click is heard				1 (4)					
Slide lever until click heard and keep the inhaler upright					2 (22)*	0 (0)*			
Pierce the capsule once and release the piercing								2 (12)*	2 (12)*
Close mouthpiece, ensuring click is heard								0 (0)	2 (12)
Shake pMDI well	13 (59)*	12 (46)*	1 (100)*						
Flip the red lever on the top up until it flicks into place			0 (0)*						
Turn coloured wheel one way, then back until click is heard and keep the inhaler upright							2 (15)*		
Insert pMDI well into spacer		4 (15)*							
Breathe out normally away from the inhaler	3 (14)	2 (8)	0 (0)	3 (12)	1 (11)*	4 (15)*	1 (8)*	2 (12)*	2 (12)*
Hold the inhaler upright (do not cover the air vents at the bottom for BA-pMDI)	0 (0)		0 (0)						
Keep head upright or slightly tilted	0 (0)		0 (0)						
Seal lips around mouthpiece	1 (5)*	2 (8)*	0 (0)*	0 (0)*	1 (11)*	0 (0)*	0 (0)*	0 (0)*	1 (6)*
Activate pMDI		1 (4)*							
Inhale slowly and deeply through the mouth, actuating once during first half of inhalation	12 (55)*			9 (35)*					
Inhale slowly and deeply through the mouth. Keep breathing in after hearing the click			0 (0)*						
Inhale slowly and deeply through the mouth minimum 3 times or hold breath for 5 seconds		11 (42)*							
Inhale forcefully and deeply through the mouth					3 (33)*	6 (22)*	3 (23)*	0 (0)*	1 (6)*
Continue slow and deep inhalation				8 (31)*					
Hold breath for at least 5 seconds	6 (27)*		1 (100)*	10 (38)*	4 (44)*	8 (30)*	6 (46)*	6 (35)*	7 (41)*
Breathe out gently, away from your inhaler			0 (0)		0 (0)	3 (11)	3 (25)	4 (24)	2 (12)
Push red lever down			0 (0)						
Check if capsule is empty, if not, repeat steps								12 (71)*	7 (41)*

* Steps considered as critical error. pMDIs, pressurized metered-dose inhalers; BAMDI, breath-actuated metered-dose inhalers.

Table S3. Subgroup analysis for inhalers used with a critical error

	Critical error		p value
	n (%)	95% CI	
Male (n=97)	67 (69.1)	57.2- 80.9	0.328
Female (n=63)	38 (60.3)	47.5 – 73.1	
Age < 65 years (n=36)	21 (58.3)	36.3 – 80.4	0.428
Age ≥ 65 years (n=124)	84 (67.7)	58.4 – 77.1	
Absence of exacerbation of COPD (n=49)	41 (83.7)	72.7 – 94.7	0.005
Presence of exacerbation of COPD (n=111)	64 (57.7)	46.4 – 69.0	
Absence of respiratory complaint (n=34)	28 (82.4)	69.9 – 94.8	0.027
Presence of respiratory complaint (n=126)	77 (61.1)	50.7 – 71.6	
Total (n=160)	105 (65.6)	57.7 – 72.9	

The widths of the confidence intervals were adjusted to take into account the cluster analysis at the level of patient.

COPD, chronic obstructive pulmonary disease; CI, confidence interval.

Table S4. Misused inhaler, critical error, insufficient peak inspiratory flow, non-teachable and unsuitable inhaler by type of inhaler

	Misused inhaler n (%)	Critical error n (%)	Insufficient PIF n (%)	Not teachable n (%)	Unsuitable n (%)
pMDI (n=22)	17 (77.2)	17 (77.2)	0 (0)	2 (9.1)	2 (9.1)
pMDI+spacer (n=26)	20 (76.9)	20 (76.9)	0 (0)	1 (3.8)	1 (3.8)
BAMDI (n=1)	1 (100)	1 (100)	0 (0)	0 (0)	0 (0)
Respimat® (n=28)	21 (75.0)	21 (75.0)	0 (0)	1 (3.6)	1 (3.6)
Diskus® (n=9)	7 (77.8)	6 (66.7)	5 (55.6)	1 (11.1)	5 (55.6)
Ellipta® (n=27)	19 (70.4)	17 (63.0)	8 (29.6)	1 (3.8)	8 (29.6)
Turbuhaler® (n=13)	10 (76.9)	7 (53.8)	7 (53.8)	2 (15.4)	7 (53.8)
Handihaler® (n=17)	7 (41.2)	7 (41.2)	0 (0)	1 (5.9)	1 (5.9)
Breezhaler® (n=17)	9 (52.9)	9 (52.9)	2 (11.8)	0 (0)	2 (11.8)

pMDI, pressurized metered-dose inhalers; BAMDI, breath-actuated metered-dose inhalers; PIF, peak inspiratory flow.