Original Research

High Prevalence of Suboptimal Peak Inspiratory Flow in Hospitalized Patients With COPD: A Real-world Study

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Abbreviations
AECOPD: acute exacerbation of chronic obstructive pulmonary disease
COPD: chronic obstructive pulmonary disease
DPI: dry powder inhaler
ICD-9: International Classification of Diseases, Ninth Revision
ICD-10: International Classification of Diseases, Tenth Revision
ICH-GCP: International Council for Harmonisation Good Clinical Practice
LSCMC: Legacy Salmon Creek Medical Center
PIF: peak inspiratory flow
SD: standard deviation

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Abstract

For optimal drug delivery, dry powder inhalers (DPIs) depend on the patient’s peak inspiratory flow (PIF) and the internal resistance of the device to create turbulent energy and disaggregate the powder. A suboptimal PIF may lead to ineffective drug inhalation into the lungs. Our objective was to report the prevalence of suboptimal PIF in patients with COPD hospitalized for any reason using one or more DPIs. In this real-world, observational, single-site, retrospective study, PIF was measured for each DPI using the In-Check™ DIAL set to match the resistance of the DPI used by each patient. PIFs <60 and <30 L/min were considered suboptimal for low to medium-high and high resistance DPIs, respectively. At initial hospitalization, the prevalence of suboptimal PIF was 44.6% in 829 patients (mean age, 71.7 years; 56.8% female); 21.2% were measured during admission for a COPD exacerbation. Suboptimal PIF percentages were 61.0% [38.1±9.5 L/min (mean±SD)] across low to medium-high resistance DPIs and 17.2% (20.7±4.2 L/min) for high resistance DPIs. Overall, 190/829 patients had one or more 30-day all-cause readmission with 253 corresponding PIF measurements. For readmissions, suboptimal PIFs were observed in 49.5% (94/190). Suboptimal PIF percentages were 65.4% (38.4±9.2 L/min) for low to medium-high resistance DPIs and 19.8% (22.4±3.3 L/min) for high resistance DPIs. As the overall prevalence of suboptimal PIFs in hospitalized patients with COPD varied according to the specific internal resistance of the DPI, these findings may have clinical implications for inhaler selection.
Introduction

Inhaled bronchodilators are the mainstay of pharmacological management of chronic obstructive pulmonary disease (COPD) and are delivered using metered-dose inhalers, dry powder inhalers (DPIs), the soft mist inhaler, and nebulizers.\textsuperscript{1,2} Successful delivery of medication to the lungs is dependent upon the drug formulation, delivery system, and various patient-related factors.\textsuperscript{3} One important patient factor is correct inhalation flow,\textsuperscript{2} which is particularly critical when using DPIs because of their structural design and formulation characteristics. With DPIs, patients’ inspiratory flow and the resistance within the DPI are important for the creation of turbulent energy, which is needed for drug-carrier particle disaggregation, optimal drug release, and drug delivery into the airways.\textsuperscript{4,5} Therefore, a low inspiratory flow may result in poor drug-carrier particle disaggregation within the DPI and suboptimal drug delivery into the lungs. Hard and fast inhalation is generally recommended for the optimal delivery of medications with DPIs.\textsuperscript{6}

Peak inspiratory flow (PIF) is the maximal airflow generated during an inspiratory cycle.\textsuperscript{5} Although minimal and optimal PIFs depend on the specific DPI, a PIF of $\geq 60$ L/min is generally considered optimal for low to medium-high resistance DPIs,\textsuperscript{5,7-15} whereas a PIF of $\geq 30$ L/min is generally considered optimal for high resistance DPIs.\textsuperscript{3,15} However, some patients with COPD may not be able to achieve the optimal PIF to derive optimal drug delivery from their prescribed DPI.\textsuperscript{4,16}

The prevalence of suboptimal PIF among patients with COPD has been reported in cohorts of stable outpatients with COPD (19%-100%) and in patients hospitalized for an acute exacerbation of COPD (AECOPD; 32%-52%).\textsuperscript{16-24} However, in these in-patient studies, PIF was measured only against one resistance, regardless of the DPI used by the patient.\textsuperscript{16} Furthermore, data are lacking for broad populations of patients with COPD in real-world settings.
The objective of this observational real-world study was to report the prevalence of suboptimal PIF measured against the simulated resistance of the DPI(s) used prior to admission in hospitalized patients with COPD. Testing was performed at a single medical center in patients admitted for an exacerbation or for a non-exacerbation diagnosis when clinically stable. Furthermore, PIF was measured in this cohort of patients who had a subsequent 30-day all-cause readmission.

Methods

Study design and patients

This observational study was conducted using data from patients diagnosed with COPD admitted to Legacy Salmon Creek Medical Center (LSCMC) for all-cause admission from June 1, 2017, to February 16, 2019 (Figure 1). LSCMC (Vancouver, Washington) serves the southwest Washington state area. A retrospective chart review and collection of patient health information and other data from Epic (the LSCMC electronic health record system) were approved by the Legacy Health Institutional Review Board (#FWA00001280). The study was conducted in accordance with the principles of the Declaration of Helsinki,25 the International Council for Harmonisation Good Clinical Practice (ICH-GCP) guidelines,26 and applicable regulatory requirements.

Patients aged ≥40 years with an International Classification of Diseases, Ninth Revision (ICD-9) or Tenth Revision (ICD-10) code corresponding to a primary or secondary diagnosis of COPD at admission, using ≥1 DPI at the time of admission, and having ≥1 postadmission PIF reading during the study period were included.

PIF assessments and outcomes
PIFs were measured 7 days/week and for 8 hours/day as part of a quality improvement project at LSCMC to optimize therapy for patients admitted with a COPD exacerbation. One measure of PIF was taken during the session. PIFs were measured using the In-Check™ DIAL G16® (Alliance Tech Medical Granbury, Texas, USA) following standard instructions set to match the resistance of the DPI(s) being used at admission, including readmissions, namely, Neohaler® (low); Diskus®, Ellipta® (medium-low); RespiClick®, Aerolizer®, Flexhaler®, Pressair® (medium); Twisthaler® (medium-high); or HandiHaler® (high) as soon as the patients were clinically stable, as assessed by a COPD educator (Supplementary Table S1). If a patient had been using more than one DPI, then PIF was measured against the simulated resistance of each DPI.

Therefore, the number of PIFs available for analyses was greater than the number of patients. A PIF of <60 and <30 L/min was considered suboptimal for low to medium-high resistance DPIs and the high resistance DPI, respectively. Additional information on PIF assessment is presented in Supplementary Information and Supplementary Figure S1.

The primary outcome was the prevalence of suboptimal PIFs in the overall study population and in those readmitted within 30 days of discharge. Suboptimal PIF values were stratified by the DPI internal resistance category. Patient demographics and clinical characteristics included age at first encounter, sex, type of admission (AECOPD related or non-AECOPD related), and the most commonly observed comorbidities in patients with COPD admitted to LSCMC (i.e., diabetes, pneumonia, heart failure, bronchiectasis, pulmonary hypertension, and protein-calorie malnutrition). If a patient had >1 admission during the study period, their age at first admission was used in analyses. Exploratory analyses included the percentage of patients with ≥1 30-day readmission stratified by the PIF category (suboptimal or optimal), DPI internal resistance category, and type of readmission.
Data abstraction and analysis

De-identified data (PIF readings and corresponding patient information) were abstracted from Epic. Comorbidities and 30-day readmission data were abstracted manually from Epic by study personnel. Readmissions were classified as AECOPD related only if COPD was listed as the primary encounter diagnosis (ICD-9 or ICD-10 code). Otherwise, readmissions were classified as non-AECOPD related. Because of the descriptive nature of the study, no statistical hypothesis testing or modeling was planned.

Results

Patient disposition

Overall, 829 patients were admitted to LSCMC for any reason, had COPD as a primary or secondary diagnosis at admission, and met the inclusion criteria during the study period. A total of 1,164 corresponding PIF readings were obtained (Figure 2).

Cohort and dataset characteristics (overall population)

Age at first encounter (mean±standard deviation [SD]) of the 829 patients included in the study was 71.7±10.5 years. The overall study population consisted of more women than men (56.8% vs 43.2%) (Table 1). Most of the corresponding 1,164 PIF readings (collected over the duration of the study) were measured against medium-low resistance (Diskus®, Ellipta®; 439 [37.7%]) or high resistance (HandiHaler®, 577 [49.6%]) DPIs (Figure 3) and during non–AECOPD-related admissions (917 [78.8%]; Table 1). Heart failure (53.3%) and diabetes (41.0%) were the most common comorbidities among those evaluated and were higher in the non-AECOPD group than in the AECOPD group (Table 1).

Suboptimal PIF prevalence
The prevalence of suboptimal PIF was 44.6% (370/829) in the overall study population (Figure 3). The prevalence of suboptimal PIF in patients who never had an AECOPD related admission was 42.5% (265/624) and for patients who had one or more AECOPD related admissions was 51.2% (105/205). Percentages (mean±SD L/min) of suboptimal PIF by inhaler resistance category were 61.0% (PIF: 38.1±9.5 L/min) against low to medium-high resistance and 17.2% (PIF: 20.7±4.2 L/min) against high resistance.

**Characteristics of the suboptimal PIF population**

Age at first encounter of the 370 patients with one or more suboptimal PIF reading was 73.4±10.9 years. This group included 68.6% of women and 31.4% of men (Table 2). Similar to observations from the overall population, most of the 457 corresponding PIF recordings were measured against medium-low resistance (Diskus®, Ellipta®, 234) or high resistance (HandiHaler®, 99; Figure 3) DPIs and during non–AECOPD-related admissions (366 [80.1%]; Table 2). Heart failure (59.3%) and diabetes (36.8%) were the most common comorbidities among those evaluated.

**Thirty-day all-cause readmissions**

Overall, 190 of 829 (22.9%) patients had one or more 30-day all-cause readmissions, with 253 corresponding PIF readings taken during readmissions. Notably, 41 patients had 49 AECOPD-related readmissions, with 52 corresponding PIF readings; 160 patients had 192 non–AECOPD-related readmissions, with 201 corresponding PIF readings (patients could have >1 readmission with a different cause each time; therefore, the number of patients is >190 [41+160]). Of the 190 unique patients who had one or more 30-day readmission, 94 had ≥1 suboptimal PIF reading during the readmission. The prevalence of suboptimal PIF in patients with 30-day all-cause readmissions was 49.5%. Percentages (mean±SD) of suboptimal PIFs at the time of readmission were 65.4% (38.4±9.2 L/min) against low to
medium-high resistance and 19.8% (22.4±3.3 L/min) against high resistance DPIs (Figure 4A). Of the 52 PIFs recorded during AECOPD-related readmissions, 25 and 27 were suboptimal against low to medium-high resistance and high resistance DPIs, respectively (Figure 4B). Of the 201 PIFs assessed during non–AECOPD-related readmissions, 102 and 99 were suboptimal against low to medium-high resistance and high resistance DPIs, respectively (Figure 4C).

**Discussion**

To our knowledge, these data represent the largest real-world study in which PIF was measured against a full range of simulated internal DPI resistance levels in hospitalized patients with COPD. The major findings are that: (1) the overall prevalence of suboptimal PIF was 44.6% among 829 DPI users, (2) most (80.1%) of the suboptimal PIFs were measured during non–AECOPD-related admissions, and (3) the prevalence of suboptimal PIF was 49.5% among 190 patients with one or more 30-day all-cause readmission.

The results of our study provide detailed demographic and clinical characteristics of patients with COPD as well as PIF values that correspond to each DPI’s internal resistance category (Tables 1 and 2). The overall study population consisted of more women than men (56.8% vs 43.2%), and this difference was more pronounced in those with a suboptimal PIF (women: 68.6% vs men: 31.4%). This observation is in line with previously reported studies, in which female patients with COPD were more likely to have suboptimal PIFs than male patients with COPD.16,23 This can be explained, in part, by lower predicted values for lung function in women than men.29

Our study incorporated two unique features. First, PIFs were measured in patients with COPD regardless of the cause of hospital admission. Second, PIFs were measured against the simulated resistance of the DPI(s) that patients were actually using at the time of
admission. In previous studies of patients hospitalized for an exacerbation of COPD, there was a range of 32% to 100% for the prevalence of a suboptimal PIF prior to discharge.\textsuperscript{16,22,24,30,31} The variability in the prevalence of suboptimal PIF may reflect differences in patient populations, as well as differences in methodology, such as the time that PIF was measured relative to discharge and/or the specific instructions given to patients to perform the PIF maneuver.

A unique feature of our study was measurement of PIF in patients readmitted to the hospital within 30 days of their initial enrollment. Overall, 190 of 829 (22.9%) patients had one or more 30-day all-cause readmissions with 253 corresponding PIF readings taken during the readmission. The prevalence of suboptimal PIF was 49.5% among these patients with one or more 30-day all-cause readmission. Our observational study was not designed to identify hospital readmissions in patients based on their initial PIF status.

The findings of this study have clinical implications for both health care professionals (HCPs) and patients with COPD. When prescribing inhaled therapy, HCPs select a medication(s) as well as the delivery system based on individual patient factors. However, an inhaled medication(s) in a DPI may not provide the intended efficacy in patients with a suboptimal PIF. In two prospective clinical trials, in which an inclusion criterion was a suboptimal PIF, there were greater increases in lung function with nebulized therapy compared with a similar class of bronchodilator delivered via a DPI.\textsuperscript{32,33} These findings suggest that patients with a PIF <60 L/min against a medium-low resistance DPI may not achieve optimal inhalation of the powder medication into the lower respiratory tract. An \textit{in vitro} study by Borgström and colleagues\textsuperscript{34} supports this hypothesis. These investigators showed that deposition of radiolabeled budesonide within the Turbuhaler\textsuperscript{®} DPI (Astra Draco AB) nearly doubled (from 15% to 28%) when inspiratory flow was increased from 36 to 58 L/min.\textsuperscript{33}
For optimal use of a DPI, the patient needs to inhale “hard and fast” to create turbulent energy within the device. PIF can be measured to assess the patient’s inspiratory ability to disaggregate the powder into fine particles that can be inhaled deep into the lungs. PIF is considered as a predictive therapeutic biomarker to determine whether the patient is likely, or unlikely, to achieve optimal drug delivery when using a DPI and obtain clinical benefit. The optimal/suboptimal thresholds for PIF are generally based on in vitro studies using lung models to assess dry powder drug delivery. Although information is limited on clinical correlations with a suboptimal PIF, Mahler and colleagues reported that 184 patients with COPD with a suboptimal PIF had a significantly greater symptom burden as measured on the COPD Assessment Test and had significantly more shortness of breath on the modified Medical Research Council scale compared with 219 patients who had an optimal PIF.

The impact of a suboptimal PIF on hospital readmissions is an important consideration for development of discharge pathways/programs aimed to reduce readmission rates. Three studies evaluated readmissions in patients with COPD hospitalized for an exacerbation and had a suboptimal PIF prior to discharge. Loh and colleagues demonstrated a higher rate of 90-day COPD readmissions and fewer number of days before all-cause readmissions in 64 patients with a suboptimal PIF compared with 59 who had an optimal PIF. In contrast, Samarghandi et al. and Sharma et al. found similar readmission rates up to 90 days and 180 days, respectively, between suboptimal and optimal PIF groups. However, in a pay-for-performance management program involving 383 out-patients with COPD in Taiwan, Chen and colleagues reported a significant reduction in severe exacerbations among patients in whom inhaled therapy was guided by PIF measurement using the In-Check™ DIAL G16 compared with any previous inhaler education provided to patients before the PIF-guided approach was instituted.
There are several limitations of this study. First, the study was performed at a single site and the results may be influenced by prescribing behaviors and may not be generalizable to other institutions. Second, PIF was measured when patients were considered stable enough by a COPD educator to perform the maneuver and not at a specific time period prior to discharge as in some other studies. Third, although the class of medication prescribed at discharge was available, the type of inhaler used to deliver the medication and whether patients obtained and/or used their prescribed medication after discharge were not documented. Fourth, PIF values were grouped for low to medium-high DPI resistances because a suboptimal PIF threshold <60 L/min applies to these different internal resistances. This clustering may have introduced a bias as factors such as disease severity were not included in the analysis. Finally, the study was descriptive by design; therefore, analytical comparisons across internal inhaler resistance categories were not conducted.

The strengths of this retrospective observational study include the large, real-world patient population and corresponding number of PIF readings. The overall prevalence of suboptimal PIF was 44.6% in patients with COPD who were hospitalized for any cause and were using at least one DPI at admission. These findings may have implications for inhaler selection as a DPI may not provide the expected clinical efficacy in a patient with suboptimal PIF. Other patient factors, including cognitive function and manual dexterity, should also be considered by HCPs when selecting the right medication in the right delivery device for an individual patient with COPD.
Acknowledgments

Author contributions: All authors contributed equally to the conception or design of the work; the acquisition, analysis, or interpretation of data for the work; and drafting the work or revising it critically for important intellectual content. All authors provided final approval of the version of the manuscript to be published and agree to be accountable for all aspects of the work. The authors meet the criteria for authorship as recommended by the International Committee of Medical Journal Editors (ICMJE). The authors received no direct compensation related to the development of the manuscript. Dr Mahler takes responsibility for (is the guarantor of) all the content in the manuscript, including the data and analysis.

Declaration of Interest

D.A.M. serves on the advisory boards for AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Mylan, Teva, Theravance, and Verona. S.D. and R.H. report grants from Boehringer Ingelheim Pharmaceuticals, Inc. (BIPI), during the conduct of the study. R.H. also received speaker fees from BIPI outside the submitted work. G.G. was an employee of BIPI at the time of study conduct. A.S., C.D.M, and J.E. are employees of BIPI. C.M. reports grants from BIPI during the conduct of the study and has received speaker fees from BIPI outside the submitted work.

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References


Figure Legends

Figure 1. Study design

\(^a\) Patients admitted to LSCMC with relevant problems or diagnoses using the applicable ICD-9 and ICD-10 codes.

\(^b\) Patients did not have clinical support to confirm the COPD diagnosis when assessed by a COPD educator (e.g., PFT ruled out COPD or PFT was not available).

\(^c\) PIF was measured using the In-Check™ DIAL G16 set to the corresponding internal resistance for that inhaler per the LSCMC PIF protocol after admission, including readmissions, as soon as patients were stable enough to undergo a PIF assessment; data noted for 30-day readmissions, including the type of readmission (AECOPD related or non-AECOPD related).

\(^d\) Readmissions were classified as AECOPD related only if the first final discharge ICD-9 or ICD-10 code was for COPD.

AECOPD=acute exacerbation of COPD; COPD=chronic obstructive pulmonary disease; EHR=electronic health record; ICD=International Classification of Diseases; LSCMC=Legacy Salmon Creek Medical Center; PFT=pulmonary function test; PIF=peak inspiratory flow.

Figure 2. Patient disposition

\(^a\) Accounts for patients who were using ≥1 DPI and/or who had ≥1 admission to LSCMC during the study period.

DPI=dry powder inhaler; LSCMC=Legacy Salmon Creek Medical Center; PIF=peak inspiratory flow.
**Figure 3.** PIF classification based on inhaler type and corresponding internal resistance

\(^{a}\)Calculated as the total number of patients using ≥1 DPI and with ≥1 suboptimal PIF reading (370) divided by the total number of patients using ≥1 DPI (829).

\(^{b}\)Defined based on the available reference material.\(^7\)\(^{-14}\)

DPI=dry powder inhaler; PIF=peak inspiratory flow.

**Figure 4.** PIF classification at 30-day (A) all-cause readmission, (B) AECOPD-related readmission, and (C) non–AECOPD-related readmission in patients with suboptimal PIF based on the prescribed inhaler type and corresponding resistance

\(^{a}\)Defined based on the available reference material.\(^7\)\(^{-14}\)

AECOPD=acute exacerbation of chronic obstructive pulmonary disease; DPI=dry powder inhaler; PIF=peak inspiratory flow.
### Tables

**Table 1.** Characteristics of patients with COPD admitted to hospital for any reason who were using ≥1 DPI at the time of admission and had ≥1 postadmission PIF assessment, as well as corresponding encounters

<table>
<thead>
<tr>
<th>Overall population</th>
<th>AECOPD-related admission&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Non–AECOPD-related admission&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unique patients</td>
<td>829</td>
<td>205&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Age at first admission, years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean±SD</td>
<td>71.7±10.5</td>
<td>71.1±10.2</td>
</tr>
<tr>
<td>Median (min, max)</td>
<td>72 (40.0, 97.0)</td>
<td>71 (46.0, 93.0)</td>
</tr>
<tr>
<td>40–60</td>
<td>131 (15.8)</td>
<td>33 (16.1)</td>
</tr>
<tr>
<td>&gt;60</td>
<td>698 (84.2)</td>
<td>172 (83.9)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>358 (43.2)</td>
<td>85 (41.5)</td>
</tr>
<tr>
<td>Female</td>
<td>471 (56.8)</td>
<td>120 (58.5)</td>
</tr>
<tr>
<td>Unique encounters (PIF readings)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>1,164</td>
<td>247 (21.2)</td>
</tr>
<tr>
<td>Number of inhalers used by each patient</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>585 (50.3)</td>
<td>103 (41.7)</td>
</tr>
<tr>
<td>&gt;1</td>
<td>579 (49.7)</td>
<td>144 (58.3)</td>
</tr>
<tr>
<td>Comorbidities&lt;sup&gt;d&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>477 (41.0)</td>
<td>80 (32.4)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>173 (14.9)</td>
<td>34 (13.8)</td>
</tr>
<tr>
<td>Heart failure</td>
<td>620 (53.3)</td>
<td>116 (47.0)</td>
</tr>
<tr>
<td>Bronchiectasis</td>
<td>244 (21.0)</td>
<td>67 (27.1)</td>
</tr>
<tr>
<td>Pulmonary hypertension</td>
<td>171 (14.7)</td>
<td>29 (11.7)</td>
</tr>
<tr>
<td>Protein-calorie malnutrition</td>
<td>307 (26.4)</td>
<td>67 (27.1)</td>
</tr>
</tbody>
</table>

Values are n (%) unless mentioned otherwise.

<sup>a</sup>Confirmed by the discharge code; not included as AECOPD related if the patient had an AECOPD-related code at admission but a different code (e.g., pneumonia) at discharge.

<sup>b</sup>Patients could have been admitted more than once and had an admission of each type.

<sup>c</sup>Accounts for patients who were using ≥1 DPI and/or who had ≥1 admission to LSCMC during the study period. Each unique patient could have had ≥1 admission and, therefore, ≥1 discharge.

<sup>d</sup>Each unique patient could have had ≥1 comorbidity. Comorbidities were collapsed over visits for those patients who had more than one admission.

AECOPD=acute exacerbation of COPD; COPD=chronic obstructive pulmonary disease; DPI=dry powder inhaler; LSCMC=Legacy Salmon Creek Medical Center; max=maximum; min=minimum; PIF=peak inspiratory flow; SD=standard deviation.
Table 2.
Characteristics of patients with COPD admitted to hospital for any reason who were using ≥1 DPI at the time of admission and had ≥1 postadmission PIF assessment and suboptimal PIF, including subsequent hospitalizations

<table>
<thead>
<tr>
<th></th>
<th>Suboptimal PIF population&lt;sup&gt;a&lt;/sup&gt;</th>
<th>AECOPD-related admission&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Non–AECOPD-related admission&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unique patients</td>
<td>370</td>
<td>81&lt;sup&gt;c&lt;/sup&gt;</td>
<td>303&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Age at first admission, years</td>
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<tr>
<td>Mean±SD</td>
<td>73.4±10.9</td>
<td>71.7±10.5</td>
<td>73.8±10.9</td>
</tr>
<tr>
<td>Median (min, max)</td>
<td>74.0 (40.0, 97.0)</td>
<td>73 (46.0, 93.0)</td>
<td>74 (40.0, 97.0)</td>
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<tr>
<td>40–60</td>
<td>49 (13.2)</td>
<td>13 (16.0)</td>
<td>38 (12.5)</td>
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<tr>
<td>&gt;60</td>
<td>321 (86.8)</td>
<td>68 (84.0)</td>
<td>265 (87.5)</td>
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<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>116 (31.4)</td>
<td>20 (24.7)</td>
<td>97 (32.0)</td>
</tr>
<tr>
<td>Female</td>
<td>254 (68.6)</td>
<td>61 (75.3)</td>
<td>206 (68.0)</td>
</tr>
<tr>
<td>Unique encounters (PIF readings)&lt;sup&gt;d&lt;/sup&gt;</td>
<td>457</td>
<td>91 (19.9)</td>
<td>366 (80.1)</td>
</tr>
<tr>
<td>Number of inhalers used by each patient</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>227 (49.7)</td>
<td>40 (44.0)</td>
<td>187 (51.1)</td>
</tr>
<tr>
<td>&gt;1</td>
<td>230 (50.3)</td>
<td>51 (56.0)</td>
<td>179 (48.9)</td>
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<td>Comorbidities&lt;sup&gt;e&lt;/sup&gt;</td>
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<tr>
<td>Diabetes</td>
<td>168 (36.8)</td>
<td>25 (27.5)</td>
<td>143 (39.1)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>70 (15.3)</td>
<td>10 (11.0)</td>
<td>60 (16.4)</td>
</tr>
<tr>
<td>Heart failure</td>
<td>271 (59.3)</td>
<td>41 (45.1)</td>
<td>230 (62.8)</td>
</tr>
<tr>
<td>Bronchiectasis</td>
<td>116 (25.4)</td>
<td>31 (34.1)</td>
<td>85 (23.2)</td>
</tr>
<tr>
<td>Pulmonary hypertension</td>
<td>69 (15.1)</td>
<td>7 (7.7)</td>
<td>62 (16.9)</td>
</tr>
<tr>
<td>Protein-calorie malnutrition</td>
<td>147 (32.2)</td>
<td>26 (28.6)</td>
<td>121 (33.1)</td>
</tr>
</tbody>
</table>

Values are n (%) unless mentioned otherwise.

<sup>a</sup>Patients also had ≥1 suboptimal PIF, which was defined based on the available reference material.<sup>7-14</sup>

<sup>b</sup>Confirmed by the discharge code; not included as AECOPD related if the patient had an AECOPD-related code at admission but a different code (e.g., pneumonia) at discharge.

<sup>c</sup>Patients could have been admitted more than once and had an admission of each type.

<sup>d</sup>Accounts for patients who were using ≥1 DPI and/or who had ≥1 admission to LSCMC during the study period. Each unique patient could have had ≥1 admission and, therefore, ≥1 discharge.

<sup>e</sup>Each unique patient could have had ≥1 comorbidity. Comorbidities were collapsed over visits for those patients who had more than one admission.

AECOPD=acute exacerbation of COPD; COPD=chronic obstructive pulmonary disease; DPI=dry powder inhaler; LSCMC=Legacy Salmon Creek Medical Center; max=maximum; min=minimum; PIF=peak inspiratory flow; SD=standard deviation.
Figure 1

**Inclusion criteria:**
- Primary or secondary diagnosis of COPD at admission to LSCMC, regardless of inpatient admission diagnosis
- Treatment with ≥1 inhaled medication
- ≥1 recorded postadmission PIF assessment (using the In-Check™ DIAL) during the study period. Patients without spirometric evidence of COPD were noted

**Total study period:** June 1, 2017 to February 16, 2019

**Retrospective data sources:**
- EPIC (LSCMC EHR system)
- Manual chart review

**Day 0**
- Visit by COPD educators PIF assessment

Follow-up, including 30-day (all-cause) readmissions
Figure 2

Patients treated with ≥1 inhaled medication at admission
N=1,110

Patients using ≥1 DPI at the time of admission with ≥1 recorded post admission PIF assessment during the study period
- Unique patients, n=829
- Unique encounters (PIF readings), n=1,164

Excluded, n=281
- Patients not using DPIs, n=275
- Patients aged <40 years, n=6
Figure 3

Overall prevalence<sup>a</sup> of suboptimal<sup>b</sup> PIF 44.6%

829 unique patients 1,164 DPI PIFs

Low to medium-high resistance DPI PIFs (587/1,164; 50.4%)

- Low resistance: Neohaler<sup>®</sup> (24/1,164; 2.1%)
- Medium-low resistance: Diskus<sup>®</sup>, Ellipta<sup>®</sup> (439/1,164; 37.7%)
- Medium resistance: RespiClick<sup>®</sup>, Aerolizer<sup>®</sup>, Flexhaler<sup>®</sup>, Pressair<sup>®</sup> (49/1,164; 4.2%)
- Medium-high resistance: Twishafer<sup>®</sup> (75/1,164; 6.4%)

High resistance DPI PIFs

- High resistance: HandiHaler<sup>®</sup> (577/1,164; 49.6%)

Suboptimal<sup>b</sup> PIF <60 L/min

- Low resistance (16/24; 66.7%)
- Medium-low resistance (234/439; 53.3%)
- Medium resistance (44/49; 89.8%)
- Medium-high resistance (64/75; 85.3%)

Suboptimal<sup>b</sup> PIF <30 L/min

- High resistance (99/577; 17.2%)

61.0% (358/587) of low to medium-high resistance DPI PIFs-high–resistance DPI PIFs were suboptimal<sup>b</sup>
Figure 4

190 unique patients with ≥1 30-day all-cause readmission
283 DPI PIFs

Low to medium-high resistance DPI PIFs
(127/253; 50.2%)

High resistance DPI PIFs

66.4% (83/127) of low to medium-high resistance DPI PIFs were suboptimal

Suboptimal PIF <60 L/min

Suboptimal PIF <30 L/min

AECOPD-related readmission
62 DPI PIFs

Low to medium-high resistance DPI PIFs
(25/52; 48.1%)

High resistance DPI PIFs

64.0% (16/25) of low to medium-high resistance DPI PIFs were suboptimal

Non-AECOPD-related readmission
291 DPI PIFs

Low to medium-high resistance DPI PIFs
(102/201; 50.7%)

High resistance DPI PIFs

65.7% (67/102) of low to medium-high resistance DPI PIFs were suboptimal
Supplementary Data

SUPPLEMENTARY TABLE S1. CATEGORIZATION OF DRY POWDER INHALERS BY INTERNAL RESISTANCE, SUBOPTIMAL PIF THRESHOLDS, AND OPTIMAL PIF THRESHOLDS

<table>
<thead>
<tr>
<th><strong>Inhaler internal resistance</strong></th>
<th><strong>Inhalers</strong></th>
<th><strong>PIF threshold, L/min</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Low</strong></td>
<td>Neohaler®,</td>
<td>Suboptimal&lt;60, Optimal≥60</td>
</tr>
<tr>
<td><strong>Medium-low</strong></td>
<td>Diskus®, Ellipta®</td>
<td></td>
</tr>
<tr>
<td><strong>Medium</strong></td>
<td>RespiClick®, Aerolizer®, Flexhaler®, Pressair®</td>
<td></td>
</tr>
<tr>
<td><strong>Medium-high</strong></td>
<td>Twisthaler®</td>
<td></td>
</tr>
<tr>
<td><strong>High</strong></td>
<td>HandiHaler®</td>
<td>&lt;30, ≥30</td>
</tr>
</tbody>
</table>

*Defined based on available reference materials.*7-14

PIF, peak inspiratory flow.
Supplementary Information: Peak inspiratory flow (PIF) assessment protocol (Supplementary figure. S1)

Before June 2018
- Chronic obstructive pulmonary disease (COPD) educators visited patients with a primary or secondary diagnosis of COPD, regardless of admission diagnosis, when an inhaled medication refill was needed.
- COPD educators opened a new inhaler and assessed PIF using the In-Check™ DIAL G16 set to the corresponding internal resistance of the inhaler the patient was using.
- PIF was documented in the patient’s electronic health record (EHR).
- If patients failed to meet the minimum flow required for their prescribed dry powder inhaler (DPI), they were tested for an alternative DPI.

June 2018 to present
- Respiratory therapists visit patients with a primary or secondary diagnosis of COPD, regardless of admission diagnosis, as soon as possible after admission when patients are stable enough to perform a PIF assessment maneuver.
- Respiratory therapists assess PIF using the In-Check™ DIAL G16 set to the corresponding internal resistance for that inhaler before opening any metered-dose inhaler/DPI.
- PIF is documented in patients’ EHRs.
- If patients failed to meet the minimum flow required for their prescribed DPI, they were tested for an alternative DPI.
- PIF protocol
  - COPD educators assessed PIF using the In-Check™ DIAL G16 set to the corresponding internal resistance for that inhaler.
  - Patients using a metered-dose inhaler or soft mist inhaler were coached not to exceed 30 L/min during assessment; therefore, PIFs could not be calculated because maximum inspiratory effort was not applied.

aRefer to the In-Check™ DIAL user manual for further details.27

DPI, dry powder inhaler; LSCMC, Legacy Salmon Creek Medical Center; PIF, peak inspiratory flow; pMDI, pressurized metered-dose inhaler.
E-Figure-1

LSCMC PIF protocol

- Patients were asked to use the In-Check™ DIAL the same way they would use their prescribed inhaler.
  - PIF was then measured for effective flow based on the manufacturer’s recommendations.
- Patients were asked to use the In-Check™ DIAL again after feedback and coaching.
  - Patients were asked to sit up straight if possible, fully exhale until they had no air to push out, and put the mouthpiece in their mouth and keep it level.
  - Patients received instructions on how to use their inhaler.
    - DPIs: breathe in as hard as possible for as long as possible, followed by a breath hold for as long as possible (minimum of 5 seconds; maximum of 10 seconds).
    - pMDIs or Respin®: breathe in slowly and steadily, followed by a breath hold for 5 to 10 seconds if possible; patients were coached not to exceed 30 L/min.
- PIF was then measured for effective flow based on the manufacturer’s recommendations.

A color-coded list, with colors corresponding to the resistance settings reflective of manufacturer-recommended flow for each inhaler, was provided with each In-Check™ DIAL, which are available at each Pyxis®.