

Implementation of a Targeted Inhaled Corticosteroid De-Escalation Process in Patients with Chronic Obstructive Pulmonary Disease in the Primary Care Setting

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ABSTRACT

Purpose: To evaluate the feasibility and success of a pharmacist-led, targeted inhaled corticosteroid (ICS) de-escalation process in patients with chronic obstructive pulmonary disease (COPD) where the risks of ICS therapy outweigh the potential benefits.

Methods: A population health data management tool was leveraged to identify patients who may qualify for ICS de-escalation. Primary care pharmacists clinically reviewed and subsequently contacted patients who were determined to be appropriate candidates. After discussion on the risks and benefits of ICS therapy, a stepwise algorithm was utilized to assist with ICS de-escalation and optimization of bronchodilator therapy. Outcomes analyzed include the proportion of patients for whom ICS was de-escalated, patient acceptability of the intervention, time taken to complete the intervention, barriers to implementation, and the number of additional interventions made by pharmacists.

Results: Of the 126 patients originally identified as potential candidates, 58 (46.0%) were deemed appropriate to proceed with ICS de-escalation and successfully contacted by a pharmacist. Of these patients, 49 (84.5%) were agreeable and ultimately 42 were successfully de-escalated with 37 patients maintained off ICS. The average time required for an encounter was 15.8 minutes.

Conclusion: There is utility in a pharmacist-driven, targeted ICS de-escalation process to facilitate meeting guideline-directed medication therapy goals in patients with COPD, granted the availability of efficient tools to assist in identifying patients that qualify. Such a targeted approach increases pharmacist involvement in medication management of COPD and can expand the primary care pharmacy practice.

Keywords: Medication Therapy Management; Pulmonary Disease, Chronic Obstructive; Risk Assessment; Pharmacists; Population Health Management

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) represents an important public health challenge as this often preventable and treatable disease is a common cause of chronic morbidity and mortality. In fact, COPD is one of the top three causes of death worldwide and can pose a large economic strain on the healthcare system where the estimated annual direct costs of COPD are \$32 billion in the United States alone.¹ Thus, the Global Initiative for Chronic Obstructive Lung Disease (GOLD) seeks to decrease this morbidity and mortality through implementation and evaluation of effective programs for diagnosis and management of COPD.²

To reduce symptoms, reduce the frequency and severity of exacerbations, and improve exercise tolerance and health status of patients with COPD, the GOLD report recommends that treatment regimens are individualized.³ Bronchodilators and inhaled corticosteroids (ICS) have traditionally been the mainstays of therapy, however, recent updates to the GOLD report recommends that ICS should only be used after the possible clinical benefits versus risks have been considered. Not

only do ICS have known adverse effects associated with long-term use such as respiratory infections, diabetes, and osteoporosis, but there may also be instances where ICS are ineffective.³⁻⁷ A number of studies have shown a continuous relationship between blood eosinophils counts and effectiveness of ICS therapy in preventing exacerbations where lower counts, namely if < 100 cells/ μ L, have demonstrated diminished effectiveness of ICS.⁸ Accordingly, as of the 2019 GOLD report, the recommendations highlight that patient specific factors should be taken into consideration when initiating ICS treatment.^{3,9} Significant factors include number and severity of exacerbations, blood eosinophil counts, and comorbidities such as asthma and history of lung infections.

In correspondence with these updated GOLD report recommendations, patients on ICS without an appropriate indication may be at an increased risk of adverse effects without significant benefit. Despite this concern, ICS prescribing rates in COPD have been reported between 36 to 86% when used alone or in combination therapy.⁷ In fact, a cross sectional study that took place within the Veterans Health Administration (VHA) found that nearly one-quarter of 26,536 patients on ICS therapy did not have a history of severe or frequent exacerbations or airflow obstruction.¹⁰ To address these findings, there is a growing interest in ICS withdrawal from such patients. The GOLD report does accordingly highlight

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that discontinuing ICS can be considered in patients with concern for side effects, with an inappropriate original indication (e.g. ICS was used to treat dyspnea in absence of a history of exacerbations), and/or there has been a lack of clinical benefit or response to ICS treatment (Figure 1).³

As medication experts, pharmacists are uniquely equipped with the skills and tools to encourage evidence-based therapy, assist with medication management, and potentially improve health-related outcomes.¹¹ Specifically, previous pharmacist-driven interventions in asthma and COPD have demonstrated a positive impact on medication adherence and inhaler technique education which can lead to improved disease control.¹² Considering recent discussion surrounding ICS therapy and de-prescribing, an opportunity exists to expand ambulatory care pharmacists' involvement in COPD medication optimization. This project seeks to evaluate the feasibility and success of a pharmacist-driven, targeted ICS de-escalation process in patients with COPD who may qualify for de-escalation in the primary care setting.

METHODS

This prospective cohort project was a pilot service implemented within the primary care clinics of a VHA medical center led by clinical pharmacists. Primary care clinics at this institution consist of interdisciplinary teams called patient-aligned care teams (PACTs) which each include a clinical pharmacist. Under the PACT model, clinical pharmacists have scope of practice including prescriptive authority and laboratory ordering privileges for management of chronic disease states such as COPD. In general, PACT pharmacists work with patients through a primary care provider or patient self-referral or by proactive population health management intervention based on chronic disease state metrics through datasets. The ICS de-escalation service was thus incorporated into the PACT pharmacist workflow beginning in September of 2020.

Logistical Integration:

To involve key-stakeholders and ensure effective care coordination, a 30-minute educational session was presented to primary care staff including providers and pharmacists. This session sought to convey updated 2020 GOLD report recommendations as well as present evidence supporting ICS de-escalation in COPD. The purpose, intention, and steps for implementation of this project were discussed.

To assist with the ICS de-prescribing process, an internally created, stepwise de-escalation algorithm based on available literature was prepared prior to implementation of this project and made available to the pharmacists (Figure 2).¹³ A targeted ICS de-escalation note template was created within the electronic medical record (EMR) to aid in documentation of encounters and tracking interventions. The template had functionality to record chart review findings and pharmacists' determination of patient candidacy, as well as the initial ICS risk

versus benefit discussion with the patient and any follow-up visits.

Identifying Potential Candidates:

The pharmacist-led de-escalation process was piloted by four clinical pharmacists and their associated PACT panels which totaled nine primary care providers. A national VHA COPD academic detailing dashboard was leveraged to identify patients who may qualify for ICS de-escalation. The dashboard function is to display quality indicators and identify actionable patient cohorts related to immunization rates, smoking cessation, post-hospital discharge follow-up, and initiating/titrating goal-directed medical therapy in patients with a EMR documented indication of COPD. The dashboard provided pharmacists with an "ICS De-escalation Candidate" report of patients with COPD who did not have a recorded diagnosis of asthma and who did not have a documented COPD inpatient admission or emergency department visit at a VHA facility in the past year.

Determining Candidate Appropriateness:

From the generated list of potential candidates, each patient's EMR was individually reviewed by a clinical pharmacist or a designated pharmacy learner under the supervision of the pharmacist. Patients were excluded from intervention if: COPD was managed by a provider not within the VHA system, ICS was prescribed for a diagnosis other than COPD, the patient was non-decisional (i.e. had an activated power of attorney or resided in a nursing home), the patient was enrolled in hospice/palliative care, or that patient was actively undergoing treatment with chemotherapy.

For patients who did not meet these baseline exclusion criteria, the reviewing pharmacist performed a clinical assessment of patient-specific factors to determine appropriateness for ICS de-escalation. This review was guided by the algorithm in Figure 2, Step 1 and included but was not limited to the following: diagnoses (e.g. confirmed COPD, history of asthma), history of pneumonia or mycobacterial lung infections, history of exacerbations, blood eosinophil counts, and medication adherence via refill history. Throughout the entire de-escalation process, pharmacists had the ability to obtain or update eosinophil counts if determined to be clinically indicated. In addition, interprofessional collaboration was encouraged, and pharmacists would discuss individual patient cases with the patient's primary care provider or e-consult pulmonology services as needed. If the patient was also seeing VHA pulmonology for COPD, the reviewing pharmacist coordinated candidacy determination with the pulmonologist.

Initial Patient Encounter:

Any patient deemed appropriate for de-escalation after the initial chart review was then contacted by the PACT pharmacist or a designated pharmacy learner using either telephone or virtual video visits. Baseline symptom burden was gathered using either the COPD Assessment Test (CAT) questionnaire or

the Modified Medical Research Council (mMRC) dyspnea scale in addition to frequency of rescue inhaler use. Additional information that was previously unavailable or unclear after the chart review could also be ascertained at this initial visit.

If the patient remained an appropriate candidate, the risks and benefits of ICS were discussed, including the patient's specific qualifications for ICS de-escalation. The patient was then asked whether they would be amenable to ICS de-escalation. If the patient declined the intervention, the reason was assessed. If the patient accepted the intervention, the ICS de-escalation algorithm was utilized to assist in de-escalation of the ICS (Figure 2, Step 2).

ICS De-escalation:

The initial ICS dose was established (e.g. high, medium, or low dose) and was generally stepped down to the next dose tier (e.g. medium, low, or none, respectively) or as otherwise specified by the PACT pharmacist. At any point during the de-escalation process, pharmacists could optimize bronchodilator therapy to ensure the patient was meeting guideline-directed goals of therapy with long-acting beta agonists (LABA) and long muscarinic antagonists (LAMA).

A follow-up visit was subsequently conducted 6-12 weeks after each step-down in ICS dose (Figure 2, Step 3). An assessment of COPD symptom control, frequency of rescue inhaler use, recent exacerbation history, and any new eosinophil labs was performed at each encounter. If symptoms were stable, the patient proceeded with ICS de-escalation as indicated. If there was concern for new or worsening symptoms or a recent exacerbation, shared decision making was utilized to determine the appropriate course of action such as resumption of the ICS at the previous dose.

Outcomes:

The primary outcome measures of this project were patient acceptability of the intervention, proportion of patients successfully de-escalated off ICS, and pharmacist time investment needed to perform ICS de-escalation encounters. Secondary outcomes were intended to assist with determining barriers to implementation. They included: rationale for intervention exclusion, patient identified reason for declining, and need to re-titrate the ICS. Secondary outcomes were also used to measure pharmacist interventions. These included: changes in bronchodilator therapy, number of labs ordered, and additional disease state interventions. Data was collected via retrospective chart review using pharmacist's ICS de-escalation documentation in the EMR which included the amount of time spent. Descriptive statistics including measures of frequency, mean, and standard deviation were used to analyze each primary outcome measure. This project was reviewed by the medical center's institutional review board and determined to be an operational activity exempt from review as it fell within the scope of VHA primary care pharmacists.

RESULTS

Population:

A total of 126 patients under the nine PACT panels were identified as potential ICS de-escalation candidates using the VHA COPD dashboard report. After the initial pharmacist chart review, 79 (62.7%) were determined to be potentially appropriate de-escalation candidates and were contacted for an initial pharmacist visit. Ultimately, 58 (46.0%) were successfully contacted, deemed appropriate, and offered the de-escalation intervention. A detailed depiction of the flow of patients throughout the project can be found in Figure 3. Baseline characteristics of both patients offered ICS de-escalation, and the patients who did not receive the intervention were similar (Table 1).

Primary Outcomes:

Of the 58 patients that were offered ICS de-escalation, 49 (84.5%) accepted the intervention. Ultimately 37 (75.5%) of these 49 patients successfully discontinued ICS, with an additional 5 (10.2%) able to reduce the ICS dose. This accounted for 33.3% of the original 126 patients reviewed. The average (\pm standard deviation (SD)) time needed for a pharmacist to complete the initial chart review was 13.0 (\pm 4.4) minutes, 18.3 (\pm 6.0) minutes for the initial patient encounter, and 16.0 (\pm 5.8) minutes for follow-up visits (Figure 4). The average number of visits needed per patient to trial ICS de-escalation was 2.7 (\pm 0.6).

Secondary Outcomes:

Excluded Patients:

In total, 59 patients (46.8% of the original 126) were excluded from the intervention; 47 upon initial chart review and an additional 12 during the initial encounter. The most common reasons for exclusion were clinical inappropriateness, where 35 (59.3%) of the excluded patients were deemed inappropriate candidates for ICS de-escalation and outside provider where another 17 (28.8%) patients had COPD medications managed by a non-VHA provider.

Declined Intervention:

Nine (15.5%) of the 58 patients offered ICS de-escalation declined the intervention, with 2 patients expressing potential future interest after talking with their primary care provider. Predominant reasons for declination were a concern for worsening symptom control or a lack of concern regarding long term adverse effects of ICS (Figure 3).

De-escalation Tolerability:

The ICS was successfully de-escalated and stopped in 37 (80.4%) of the 46 patients in which ICS de-escalation follow-up was performed (Figure 3). An additional 5 (10.7%) patients were able to tolerate an ICS dose reduction, however 3 patients were not able to tolerate any dose step-down. Patients that were not able to tolerate ICS de-escalation either had increased shortness of breath or increased use of their rescue inhaler. Notably, during the project period, one patient was admitted to

the hospital for shortness of breath and hypoxia without changes in chronic cough or sputum approximately 1.5 months after complete withdrawal of ICS. This patient was treated for a potential COPD exacerbation, but mental health was also consulted for frequent panic attacks with severe anxiety. Per patient preference, he remained off ICS on discharge.

Additional Pharmacist Interventions:

In addition to de-escalating the ICS, PACT pharmacists also performed a variety of other interventions to help optimize medication therapy. To assist with ICS de-escalation, a total of 18 eosinophil labs were ordered by pharmacists throughout the process. Among the 49 patients who accepted ICS de-escalation, 44 total bronchodilator therapy interventions were made to improve symptom control, minimize adverse effects/anticholinergic burden, and improve regimen functionality (Table 2). Furthermore, 13 (26.5%) patients were offered additional chronic disease state management by the PACT pharmacist for indications including tobacco use disorder, diabetes mellitus, and hypertension.

DISCUSSION

Most eligible patients were successfully de-escalated off ICS, owing to a high patient acceptance rate and favorable de-escalation tolerability. These results highlight the effectiveness of a pharmacist-driven ICS de-escalation process in the primary care setting to ensure safe and effective medication therapy in patients with COPD. Even though the intervention was a targeted process, the management of ICS de-escalation created opportunities for pharmacists to become involved in COPD medication management. During patient encounters pharmacists made several additional interventions including but not limited to inhaler device education, adherence counselling, and triaging other medication therapy concerns. Such interventions demonstrate the vital role pharmacists can play in population health management. Despite these promising results, there was a relatively small proportion of the original 126 potential candidates reviewed who successfully achieved complete de-escalation. This may put into question the efficiency of identifying patients for a targeted ICS de-escalation process. However, this in part can be attributed to many exclusions related to limitations of the VHA COPD dashboard used to identify potential candidates and inconsistent documentation within the EMR. Certain patient factors such as eosinophil counts, pulmonary function tests, and pneumonia history were not considered in the “ICS De-escalation Candidate” report generated by the dashboard. Additionally, there was no access to outside hospital EMRs, and certain documentation requirements had to be met to identify a history of asthma and/or exacerbations.

Despite the significant amount of pharmacist time that went into reviewing all patient charts to determine initial candidacy, the process of de-escalation was efficient. The time required to complete either a chart review or a patient visit aligned with other PACT pharmacist medication management visits,

facilitating the ability to incorporate into daily practice. Another challenge that was presented to pharmacists during de-escalation visits was how to concurrently de-escalate the ICS dose and optimize bronchodilator therapy. There are a variety of techniques that could be used based on patient adherence, symptom burden, desire to simplify inhaler regimen, and patient or pharmacist preference. Additionally, the use of combination inhalers and inhaler delivery devices needed to be considered. For example, a large majority of patients in this project were on ICS/LABA therapy, leading to a concomitant decrease in LABA dose if the inhaler device was not replaced or changed. It remains unknown which approach is the most effective yet practical and likely varies between patients, thus limiting the ability to create a strict protocol for inhaler tapering technique.

While there has not been a singular adopted method for de-escalation, proposals for ICS management have been suggested.^{7, 13-14} The model used in this project was made using a review of the literature and thus closely reflects previously utilized methods. The success of de-escalating ICS in this project reflects previously reported results in ICS de-prescribing. Many prior studies have found ICS withdrawal to be overall well-tolerated with no difference in exacerbation rates and minimal changes in airflow limitation.¹⁴⁻¹⁸ Additionally, review of the available literature has estimated that the number needed to treat with ICS to improve quality of life ranges from 10-20 patients, which aligns with the proportion of patients unable to tolerate de-escalation over the course of this project.^{15, 17-20} It can be noted that patients who did not tolerate ICS de-escalation often had additional confounding variables such as elevated eosinophils on a repeated lab, active cancer treatment, and abrupt ICS discontinuation rather than de-escalation. The approach to tapering may also play a role in de-escalation tolerance, such as whether bronchodilator background therapy was maximized during de-escalation.

A limitation of this project includes slight differences in ICS de-escalation candidate clinical assessment from the GOLD report recommendations. For example, the algorithm provided to pharmacists did not consider patients who may have lacked a beneficial response to ICS as this may have been difficult to assess via chart review and with recall bias. Secondly, a fair number of patients with severe COPD who were also on oxygen therapy were precluded from de-escalation despite no specific reference to this subset of patients in the GOLD report. The decision to omit these patients was made based on the treating pharmacist’s clinical judgement and review of patient specific factors in a cautionary effort to avoid potential decompensation of symptoms with transient changes in air flow that have been reported in ICS de-escalation.¹⁷⁻¹⁸ Additional limitations involve the timeframe of the project which was set during the Coronavirus Disease 2019 (COVID-19) pandemic. This restricted patient interactions to telephone or virtual video visits and hindered pharmacist ability to order eosinophil labs. As many patients did not have reliable internet

or video technology, the ability for pharmacists to effectively assess and/or teach inhaler technique was significantly diminished. Throughout the course of the project, several patients were unable to be contacted by phone or did not have follow-up with the pulmonary clinic; thus, their status of candidacy and potentially subsequent intervention acceptance and tolerance is unknown. Another identified limitation to implementation of this project was pharmacist comfort level. A variation in the rate of patient's who accepted versus those who declined was noted when the initial visit was performed by different PACT pharmacists. Lastly, the project population consisted of all male patients, and while this is typical of the VHA population, it may limit generalizability.

Despite these findings, the pilot service was overall well-received by providers with several instances of interprofessional collaboration and further referrals of potential ICS de-escalation candidates to PACT pharmacists outside of the project population. Pharmacists' involvement in targeted ICS de-escalation processes can help to raise awareness of the concerns surrounding ICS use, communicate recommendations made by the GOLD report, and ensure that guideline-directed medication therapy goals are met. Advocating for clinical guidance on proper selection of COPD treatment modalities will further increase appropriate ICS prescribing and ensure best practice measure are met. Pharmacists are well positioned to help provide this education to both patients and prescribers while being involved in COPD medication management.

Given the findings of this pilot service, the pharmacist-led ICS de-escalation process will be expanded to the remainder of PACT panels at the medical center for clinical pharmacists to incorporate into their daily workflow. In addition, the COPD provider order menu built within the EMR will be updated to help convey GOLD report recommendations for inhaler prescribing and assist in selection of safe and effective medication therapies.

CONCLUSION

The implementation of a pharmacist-driven, targeted ICS de-escalation process was successful in most patients in terms of patient acceptability and tolerability. Having a comprehensive method for identifying potentially appropriate ICS de-escalation candidates would likely enhance the efficiency of the review process. Once patients are determined to be appropriate candidates, utilizing an evidence-based, stepwise algorithm can assist with ICS de-escalation in a relatively time-efficient manner. However, de-escalation techniques may vary from patient response and comfort which may limit the utility of creating a strict process. Overall, creating an evidence-based, targeted approach to ICS de-escalation increases pharmacist involvement in COPD disease-state management and can expand pharmacy practice roles through encouraging goal-directed medication therapy in the primary care setting.

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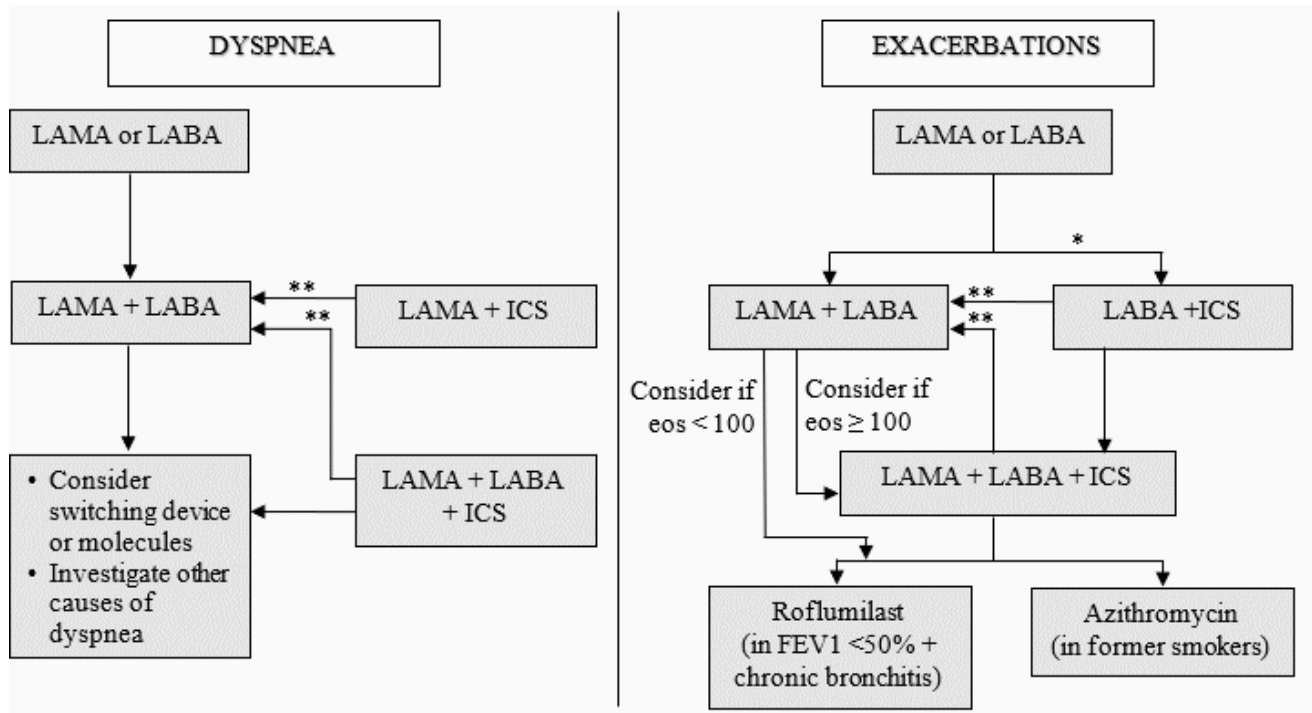
The opinions expressed in this paper are those of the author(s).

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FIGURE 1: GOLD Report Follow-Up Pharmacologic Treatment

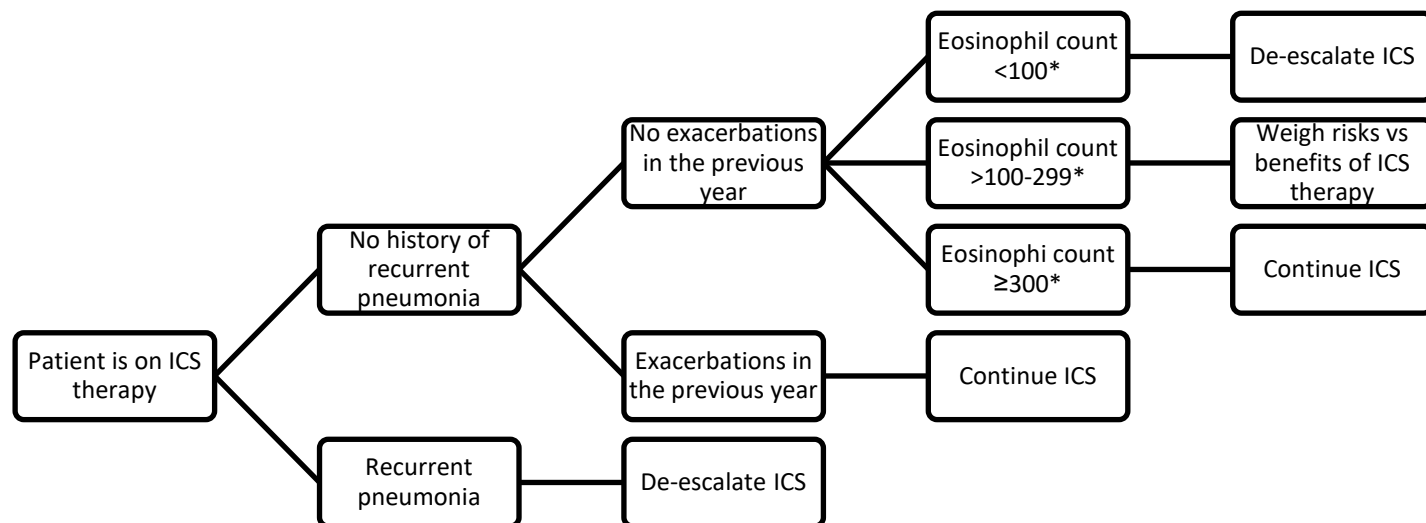


*Consider escalation to LABA/ICS therapy if eos ≥ 300 or eos ≥ 100 AND ≥ 2 moderate exacerbations or 1 hospitalization

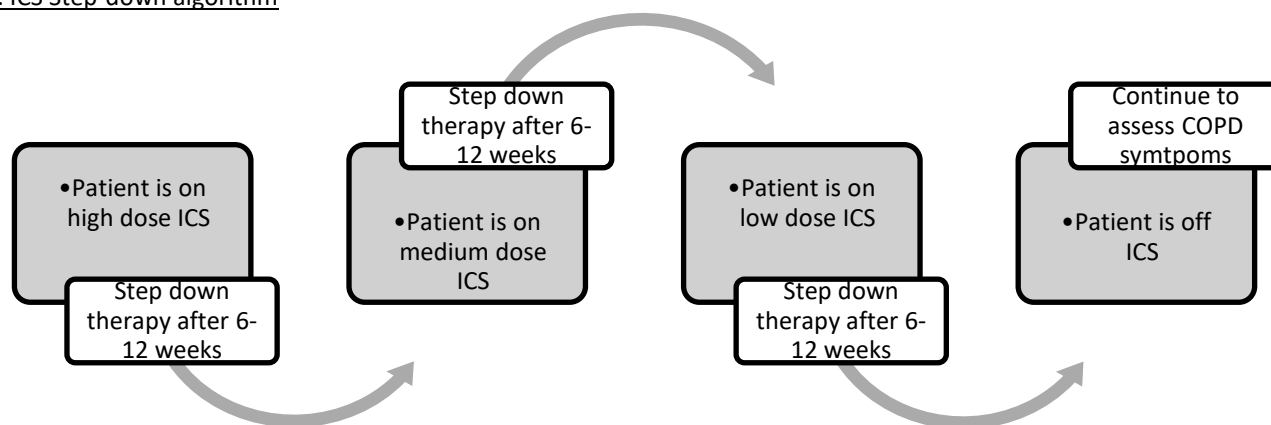
**Consider ICS de-escalation if pneumonia, inappropriate original indication, or lack of response to ICS

Abbreviations: ICS = inhaled corticosteroid, LABA = long-acting beta-agonist, LAMA = long-acting muscarinic antagonist, eos = blood eosinophil count (in cells/ μ L), FEV1 = forced expiratory volume

Note: Reprinted with permission from: Global Initiative for Chronic Lung Disease (GOLD) 2020 Report. Available from www.goldcopd.org. Accessed September 9th, 2020.

FIGURE 2: COPD ICS De-escalation Algorithm¹³Step 1: Determine if the patient is an appropriate candidate for ICS de-escalation

* If eosinophil count is available, otherwise weigh risk vs benefits of ICS therapy.

Step 2: Establish current ICS dosageStep 3: ICS Step-down algorithm**Considerations for COPD Follow-up**

- Assess COPD symptom control at every follow-up before stepping down therapy
 - Assess symptoms of exacerbation (increased mucus production, cough, shortness of breath, etc.)
 - Usage of rescue inhaler
 - Determine if any recent hospitalizations for COPD exacerbation
- Consider obtaining repeat eosinophil count
- If symptoms are stable, continue to step-down ICS as indicated

Step 4: Consider adding/maximizing LABA/LAMA therapy

TABLE 1: Baseline Patient Characteristics

	ICS De-escalation Offered (n =58)	Excluded or Unable to Contact (n=68)
Age [Average (\pm SD)]	71.4 (\pm 7.0)	72.8 (\pm 6.8)
Race [# (%)]	White – 50 (86.2%) Black – 7 (12.1%) Other – 1 (1.7%)	White – 60 (88.2%) Black – 6 (8.8%) Other – 2 (2.9%)
Sex [# (%)]	Male – 58 (100%) Female – 0 (0%)	Male – 68 (100%) Female – 0 (0%)
Baseline COPD [Average (\pm SD)]	Years with documented COPD diagnosis – 7.4 (\pm 4.9) FEV1 – 1.95 (\pm 0.72) FEV1/FVC – 0.58 (\pm 0.13)	Years with documented COPD diagnosis – 6.8 (\pm 4.3) FEV1 – 1.38 (\pm 0.70) FEV1/FVC – 0.51 (\pm 0.16)
Average Eosinophil Count ^a [# (%)]	\geq 300 cells/ μ L – 9 (15.5%) < 300 cells/ μ L – 46 (79.3%) No count available – 3 (5.2%)	\geq 300 cells/ μ L – 19 (27.9%) < 300 cells/ μ L – 37 (54.4%) No count available – 12 (17.6%)
Baseline Short-Acting Inhalers [# (%)]	Albuterol – 37 (63.8%) Ipratropium – 1 (1.7%) Albuterol + Ipratropium – 12 (20.7%) None – 8 (13.8%)	Albuterol – 52 (76.5%) Ipratropium – 0 (0%) Albuterol + Ipratropium – 12 (17.6%) None – 4 (5.9%)
Baseline Maintenance Inhalers [# (%)]	ICS/LABA – 28 (48.3%) ICS/LABA + LAMA – 29 (50.0%) ICS + LABA/LAMA – 0 (0%) Other – 1 (1.7%)	ICS/LABA – 22 (32.4%) ICS/LABA + LAMA – 41 (60.3%) ICS + LABA/LAMA – 2 (2.9%) Other – 3 (4.4%)
ICS Dose [# (%)]	High – 43 (74.1%) Medium – 13 (22.4%) Low – 2 (3.4%)	High – 51 (75.0%) Medium – 14 (20.6%) Low – 3 (4.4%)
ICS Adherence ^b [Average (\pm SD)]	0.62 (\pm 0.29)	0.75 (\pm 0.24)

Abbreviations: ICS = inhaled corticosteroid, SD = standard deviation, COPD = chronic obstructive pulmonary disease, FEV1 = forced expiratory volume, FVC = forced vital capacity, LABA = long-acting beta agonist, LAMA = long-acting muscarinic antagonist

^aAverage Eosinophil Count = Average of up to the previous five recorded blood eosinophil values. Eosinophil values are reported in the EMR as rounded to the nearest hundred

^bICS Adherence = (# of monthly ICS fills over the previous year) / (# of months since first ICS fill up to a maximum of 12 months)

FIGURE 3: Flow of Patients throughout the Duration of the Project

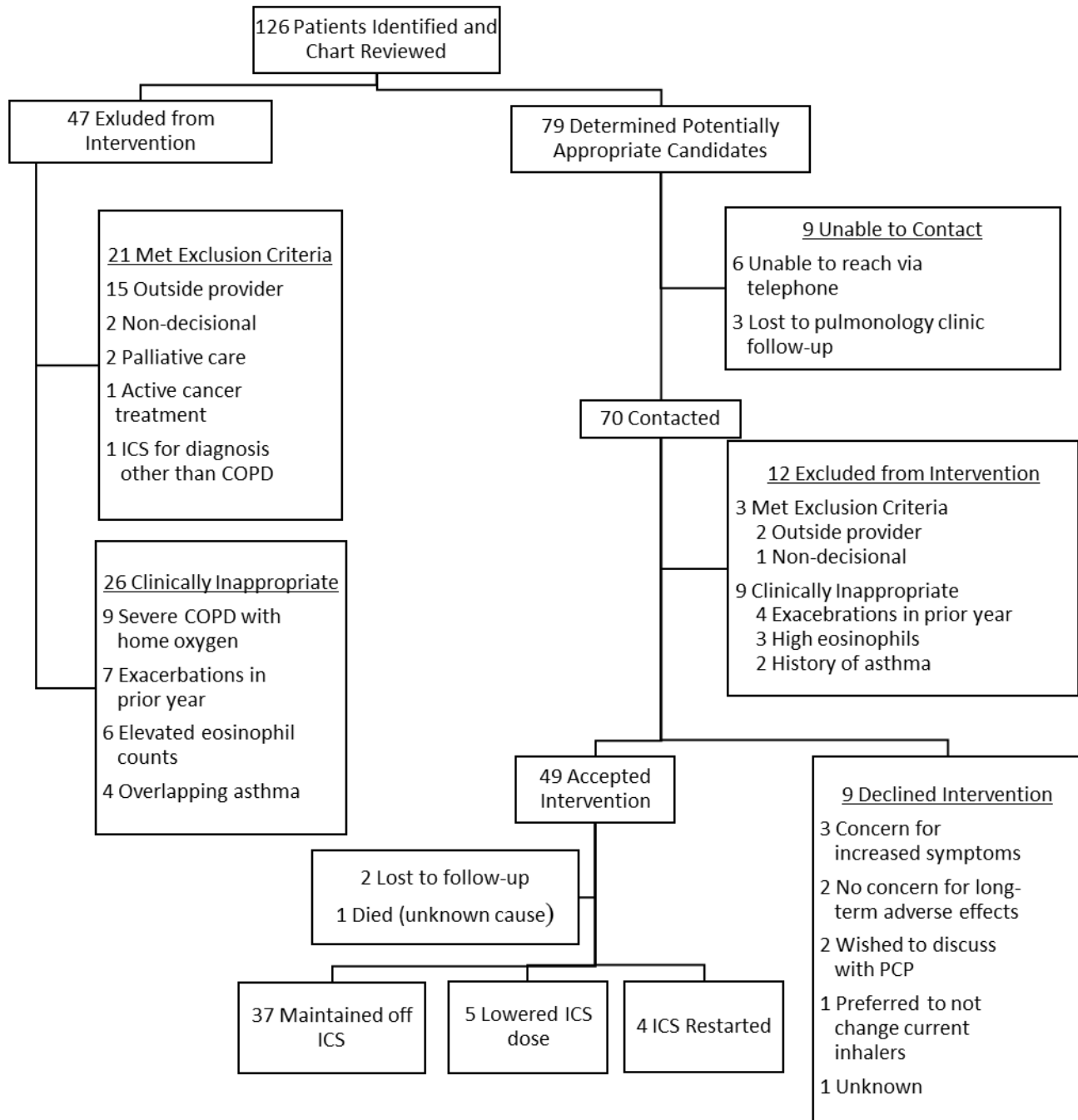
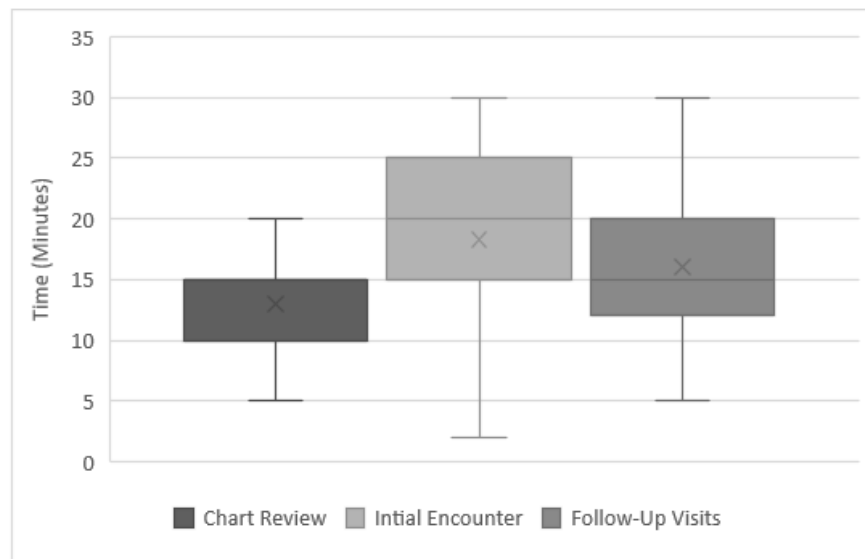


FIGURE 4: Pharmacist Time Investment by Encounter**TABLE 2:** Changes to Bronchodilator Inhaler Regimen

Adjustment to Bronchodilator Regimen	# of Patients with Intervention (n =49)
Addition of LAMA	21 (42.9%)
Removal of LAMA	1 (2.0%)
Addition of LABA	0 (0%)
Removal of LABA	6 (12.2%)
Replace expired SABA	9 (18.4%)
Removal of SAMA	4 (8.2%)
Modified SAMA and/or SABA frequency to as needed	3 (6.1%)

Abbreviations: LABA = long-acting beta agonist, LAMA = long-acting muscarinic antagonist, SAMA = short-acting muscarinic antagonist, SABA = short-acting beta agonist