Early View

Research letter

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Trends in Non-Receipt of Recommended Chronic Obstructive Pulmonary Disease Medication

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Introduction

Long-acting inhaled medications reduce frequency and severity of exacerbations, decrease number of hospitalizations, improve functional status and reduce mortality for people with COPD¹⁻³. COPD guidelines, including the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines, offer evidence-based recommendations on optimal medication use⁴. However, many COPD patients do not receive these medications.⁵⁻⁷ Previous studies have described appropriate use of long-acting inhaled medications in the COPD population and others have trended medication use over time.^{8,9} However, none that we are aware of, have described or quantified trends in guideline recommended long-acting inhaled medications over time in a large, complete, real world COPD population. This was the focus of the current descriptive study.

There are many ways that medication use can be suboptimal and it is helpful to study each because their causes may differ. While studying overuse and non-adherence to medications has value, we chose to measure receipt of sufficient COPD medications to uncover gaps in treatment.

We conducted a longitudinal, population-based retrospective cohort study using health administrative data from Ontario, the largest province of Canada with a multicultural population of more than 14 million, between 2004 and 2018. Ontario's publicly funded universal health care system covers all medically necessary services provided by physicians and hospitals and

medications for residents age 65 and older. In this setting, we were able to study medication without cost being a significant barrier. This study was approved by the Research Ethics Board of Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada.

Nine Ontario provincial data sources, including those with information on drugs dispensed, physicians services and hospitalizations, were linked using unique encoded identifiers and analyzed at ICES, an independent, non-profit research institute whose legal status under Ontario's health information privacy law allows it to collect and analyze health care and demographic data, without consent, for health system evaluation and improvement. The use of these various databases has been previously validated for respiratory disease health services research and can be found elsewhere.¹⁰

A dynamic cohort of patients aged 66 and older who had physician-diagnosed COPD for at least one year was studied. Age 66 was used because the Ontario Drug Benefit program universally covers medications for Ontario residents starting at age 65 and we required a one year look back period. Individuals were identified as having physician diagnosed COPD if they had three or more ambulatory claims and/or one or more hospitalizations for COPD within two years—a case definition previously shown to have a sensitivity of 66% and specificity of 91% compared to a clinical reference standard¹¹. Although, use of a physician-diagnosed COPD cohort may not perfectly identify patients with COPD, it does indicate patients who physicians believe have COPD and should be considered for treatment.

Minimal optimal medication regimens for patients in a given year were based on exacerbation risk and national and international COPD guidelines in effect during that year.⁴ Patient's exacerbation histories were used to determine those at lower and higher COPD exacerbation risk. COPD patients at low risk had 0 or 1 outpatient exacerbations (COPD emergency department visits or outpatient COPD physician visits for COPD accompanied by receipt of oral corticosteroids and/or respiratory antibiotics within seven days¹²) in the previous year. COPD patients at high risk had two or more outpatient exacerbations or one COPD hospitalization in the previous year.

Since we did not know previous medications patients might have failed to respond to or been intolerant of, since we did not have full knowledge of medication contraindications and since we did not have access to spirometry results or symptoms to know how medications might have been picked, we accepted adequate treatment as being receipt of any of the alternative medication recommended by guidelines from filled prescriptions. Given the overlap of these regimens, we were able to identify minimal medications that, when present, covered several alternatives. Thus, LAMA and/or LABA were deemed sufficient long-term therapy for patients at lower risk of COPD exacerbation; LAMA or LABA/ inhaled corticosteroids (ICS) for patient at higher risk of exacerbation.⁴ Since all patients, including those of low risk, had at least three COPD physician visits within two years or one COPD hospitalization, they likely had, at least, moderate disease—making not being on medication or receiving a short-acting bronchodilator alone insufficient.

To trend yearly proportions of patients receiving appropriate medication from the pharmacy, age-sex direct standardized rates were calculated using the 2018 Ontario COPD population as the reference population. Confidence intervals were calculated using the gamma distribution.

A total of 174,001 individuals were identified with physician diagnosed COPD between April 1, 2004 and March 31, 2018. Of these, 16,592 died and 179 were either ineligible for health insurance or moved out of the province.

Over the study period, the number of individuals at low risk of exacerbation increased from 103,056 to 140,822. An upward trend in standardized proportion receiving recommended medications was observed with an absolute increase of 23.7% (**Figure 1**). Fifty-three percent of patients with COPD at low risk of exacerbation appropriately received a LABA or LAMA in 2018.

From 2004 to 2018, the number of people at high risk of exacerbation increased from 15,874 to 16,408. An upward trend in standardized proportion receiving recommended medications was observed with an absolute increase of 22.8% (**Figure 1**). More than 87% at high risk of exacerbation received recommended medications in 2018.

Our longitudinal, retrospective population based study of recommended medication use for patients with differing severities of COPD, found a marked increase in the proportion of people receiving long-term maintenance therapy over the study period, however 47% and 12% of those at, respectively, low and high risk COPD exacerbation did not receive sufficient therapy in 2018.

Our findings are consistent with previous studies that also found people with COPD to be undertreated.^{13,14} A study of US managed care and Medicare patients with severe COPD found that 59 and 69%, respectively, received no long-term pharmacotherapy⁵. Similarly, an analysis of a large commercial medical and pharmacy claims database in the United States found that only 84% of people with very severe and 66% of people with severe COPD received LABA with ICS⁶. We extend upon this literature by evaluating medication underuse in a complete population of COPD patients over 14 years.

Our study is primarily limited by lack of patient's symptom data, which could lead to misclassification of disease severity. This could have affected our ability to delineate COPD patients at lower risk of exacerbation, however, such potential misclassification was minimized by our COPD case definition that was mostly likely to identify people with symptomatic moderate COPD warranting long-acting inhaled treatment. A second limitation is that we only examined recommended medications until 2018. GOLD 2019 guidelines included prominent suggestions about de-escalation of therapy¹⁵ and future studies should examine how this impacts sufficient medication use. Finally, this study may not be generalizable to healthcare systems where cost is a barrier to accessing medications, however, this would be unlikely to affect trends over time.

In summary, while receipt of sufficient COPD medication is improving, recommended therapy continues to be underused, especially in patients at lower risk of COPD exacerbation. Future strategies should be aimed at optimizing medication receipt with the goal of improving patient's health and reducing burden on health care systems.

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Conflict of Interest: None

Author Contributions

Study concept and design: Gershon and Poon

Acquisition of the data: Gershon

Analysis and interpretation of the data: All

Drafting of the manuscript: Gershon, Poon

Critical revision of the manuscript for important intellectual content: All

Statistical analysis: Pequeno

Study supervision: Gershon

Ms. Pequeno had full access to all the data in the study and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Data Sharing Statement

The data set from this study is held securely in coded form at ICES. While data sharing agreements prohibit ICES from making the data set publicly available, access may be granted to those who meet pre-specified criteria for confidential access, available at www.ices.on.ca/DAS

Figure 1. Age-sex standardized proportion of people with COPD age 66 years and older at A. low risk of exacerbation who received a long-acting beta agonist (LABA) or long-acting anticholinergic bronchodilator, alone or in combination, and B. high risk of exacerbation who received both an inhaled corticosteroid and long-acting beta-agonist (ICS and LABA) or long-acting anticholinergic bronchodilator, in Ontario, 2004 to 2014. Shading indicates 95% confidence intervals.

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