ORIGINAL RESEARCH

Continuity of Care Assessment Within a Vertically Integrated Care Management Organization Before and After COPD-Related Exacerbations

Morgan Justice Fuoco[1]
Richard A Mularski [ID][1]
Benjamin Wu[2]
Chad Moretz [ID][2]
Mary Ann McBurnie [ID][1]
Richard H Stanford [ID][2]
Phillip Crawford [ID][1]
Daniel Gratie[2]
Bianca Salas[1]

[1]Kaiser Permanente Center for Health Research, Science Programs Department, Portland, OR, USA; [2]GlaxoSmithKline, US Value Evidence and Outcomes, Research Triangle Park, Durham, NC, USA

Background: There is currently little research describing patient experience and continuity of care immediately prior, during, and following an acute exacerbation of chronic obstructive pulmonary disease (AECOPD). This analysis examined clinical characteristics, chronic obstructive pulmonary disease (COPD)-related medication patterns and outpatient visits before and after an AECOPD.

Methods: This retrospective analysis used electronic health records, medical claims, and pharmacy dispensing data for patients within the Kaiser Permanente Northwest Health System. Patients with ≥1 AECOPD between January 1, 2015 and December 31, 2017 were identified. The most recent AECOPD was considered the index date. An AECOPD was defined as an inpatient hospitalization with a primary diagnosis of COPD, or respiratory failure with a secondary diagnosis of COPD, or an outpatient visit with a primary diagnosis of COPD and dispensing of respiratory-related antibiotics and/or oral corticosteroids ±5 days of the visit. Eligible patients were: ≥40 years old; ≥2 encounters within 12 months of each other or ≥1 hospitalization with primary or secondary COPD diagnosis, chronic bronchitis, or emphysema prior to index; and continuously enrolled ±90 days relative to index. COPD-related inhaled maintenance medication, rescue inhalers, oral corticosteroid use, and ambulatory visits were assessed 90-days pre- and post-index.

Results: There were 2829 patients included (mean [standard deviation] age: 69.0 [10.5] years) who had an AECOPD (7% severe; 93% moderate). The percentage of patients on inhaled maintenance therapy increased from 60.6% pre-AECOPD to 68.8% post-AECOPD and increased from 60.0% to 87.4% among patients who experienced a severe AECOPD. COPD-related ambulatory visits increased more than four-fold for primary care and more than doubled for pulmonologist visits in the post-AECOPD period.

Conclusion: The low proportion of patients observed with changes to controller and rescue medication (particularly following a moderate AECOPD), yet higher utilization of COPD-related ambulatory visits before and after an AECOPD suggests that there is opportunity to improve pharmacotherapy management.

Keywords: COPD, exacerbation, triple therapy, treatment patterns, quality of care

Introduction

Chronic obstructive pulmonary disease (COPD) is a chronic condition associated with approximately 15.4 million physician visits, 1.5 million emergency department (ED) visits, and 726,000 hospitalizations annually in the United States.[1] Most patients with COPD are also burdened by comorbidities,[2] such as cardiovascular disease and depression.[3] These factors contribute to an estimated annual economic

Correspondence: Morgan Justice Fuoco
Kaiser Permanente Washington Health Research Institute, 1730 Minor Ave, Suite 1600, Seattle, WA, 98101, USA
Tel +1 256-508-4613
Email morgan.j.fuoco@kp.org

burden of $50 billion in the United States in 2010. Nearly two thirds of these costs relate directly to COPD diagnosis, treatment, prevention and rehabilitation, which include physician office visits, hospitalizations, home care, and medications.[4] Indirect costs, relating to reduced productivity or lost days of work due to disease morbidity and mortality, further contribute to the economic burden of COPD.[4]

Many patients suffer from acute exacerbations of COPD (AECOPD), which are defined as an acute worsening of respiratory symptoms that require additional therapy.[5] AECOPDs can be classified as mild (self-managed), moderate (requiring treatment with antibiotics and/or corticosteroids) or severe (requiring hospitalization).[6] Severe AECOPDs can negatively affect patient prognosis, with mortality rates increasing with the frequency of severe AECOPDs.[7] Following discharge from hospitalization due to an AECOPD, nearly one fifth of patients are readmitted within 30 days, further adding to the burden on healthcare systems.[8]

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2020 report states that the goal for treatment of an AECOPD is to reduce the negative impact of the current AECOPD and to prevent subsequent events.[5] Short-acting β_2-agonists (SABA) and/or short-acting muscarinic antagonists (SAMA) are recommended as the initial treatment, with maintenance therapy initiated as soon as possible before hospital discharge.[5] The administration of bronchodilators (anticholinergic agents, β_2-agonists and methylxanthines) within 30 days of a hospital discharge is currently a quality of care measure in the United States.[9] Mortality statistics show that, for a severe AECOPD, the risk of death is highest in the first week following hospital admission.[10] This highlights the importance of prompt and effective intervention for patients admitted to hospital with a severe AECOPD. However, adherence to recommended care is often suboptimal,[11–14] with high levels of under-treatment reported in patients with COPD.[12]

Numerous studies have explored patient characteristics in relation to an AECOPD event or hospital visit/ admission;[15–21] however, they typically focus on one area of care (eg emergency care) rather than using an integrated care delivery network. There is currently little research describing patient experience and continuity of care immediately prior, during, and following an AECOPD. Examining care for patients before and after an AECOPD within an integrated delivery network could

yield information to aid system-level quality improvements. Here we describe the clinical characteristics, COPD-related medication patterns and outpatient medical encounters of patients with COPD, 90 days before and after an AECOPD.

Materials and Methods
Study Design

This retrospective, longitudinal analysis used linked electronic health records, medical claims, and pharmacy dispensing data for patients within the Kaiser Permanente Northwest Health System, an integrated health plan and healthcare organization, which serves over 600,000 people in Oregon and Washington, United States. Ethical approval of this study was provided by Kaiser Permanente – Northwest Region Institutional Review Board (approval number: 1394778) and a waiver of informed consent was granted.

The study design is shown in Figure 1. We examined data for patients with COPD who experienced a moderate or severe AECOPD between January 1, 2015 and December 31, 2017, with follow-up data from 2018 accessed as needed. The date of the most recently identified AECOPD was considered the index date. The index period was defined as the date of the most recent AECOPD to the day before discharge, which applied only to patients who were hospitalized. Using the electronic health records and claims data at the inpatient and outpatient level, descriptive summaries were obtained for each of the periods of interest: 90 days pre-AECOPD, AECOPD (index), and 90 days post-AECOPD.

Study Population

Eligible patients fulfilled the following criteria: ≥40 years old at index; ≥2 independent encounter records at least one day apart and within 12 months of each other or ≥1 hospitalization with a primary or secondary diagnosis of COPD (International Classification of Diseases [ICD]-9:491.xx; ICD-10:J44.x), chronic bronchitis (ICD-9: 492.xx; ICD-10: J41.x; J42.x), or emphysema (ICD-9: 496.xx; ICD-10: J43.x) between January 1, 2008 and December 31, 2017; continuously enrolled for 12 months pre-index using Kaiser insurance gap standards (enrolled at least 10 of 12 months); continuously enrolled for ±90 days relative to the index date; no AECOPD <90 days prior to index. Patients were excluded if, at the time of consent for receipt of
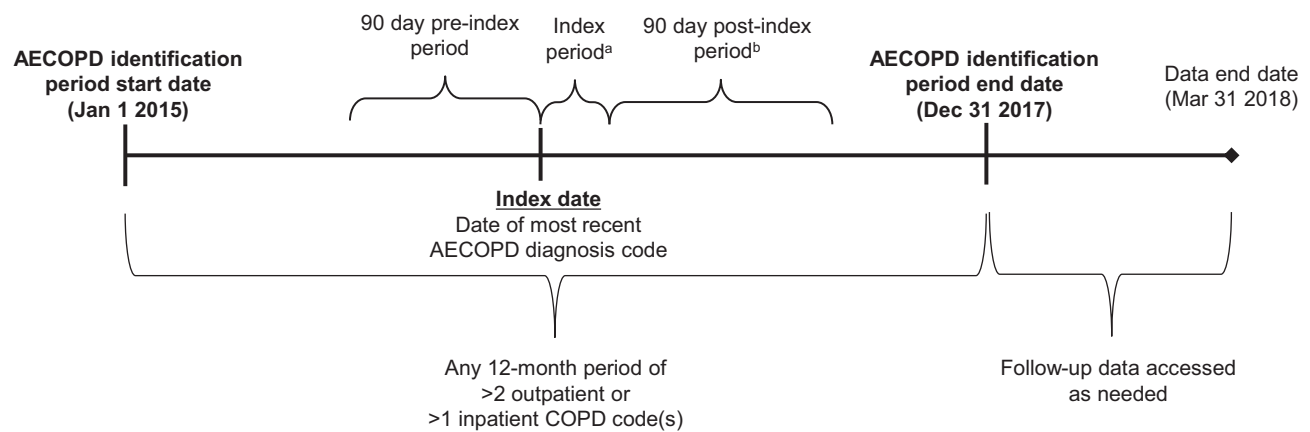
Figure 1 Study design.
Notes: [a]The index period (applying only to hospitalized patients) was defined as the date of the most recent AECOPD until the day before discharge. [b]The post-index period began 1 day after hospitalization discharge or 1 day after outpatient diagnosis code for an AECOPD.
Abbreviations: AECOPD, acute exacerbation of chronic obstructive pulmonary disease; COPD, chronic obstructive pulmonary disease.

medical care within Kaiser Permanente Northwest, they specifically indicated that they did not agree to the use of their health data for research.

A moderate AECOPD was defined as an outpatient visit (ED, physician office, or urgent care) with a primary diagnosis of COPD and dispensing of respiratory-related antibiotics and/or oral corticosteroids ±5 days of the visit. A severe AECOPD was defined as: an inpatient hospitalization with a primary diagnosis of COPD; or respiratory failure with a secondary diagnosis of COPD; or an inpatient hospitalization occurring as a result of an ED visit on the same day or the day following the ED visit with a severe acute AECOPD diagnosis. Each patient only contributed one AECOPD to the analysis.

Outcomes

Variables were gathered using the electronic medical records or dispensing records. COPD-related inhaled maintenance medication, rescue inhalers, oral corticosteroid use, and ambulatory visits were assessed 90 days pre- and post-index AECOPD. Medication overlap was not considered (ie only the medication dispensing date was recorded, regardless of the days covered by that dispensing), and each prescription dispensing must have occurred within the study period. Any changes in therapy that may have occurred at time of discharge from the hospital, ED, or physician office were assessed in the pre-index, index and post-index periods. Outpatient visits were only considered to be COPD related if a primary COPD diagnostic code was associated with the specific encounter. Missing data were not imputed and are reported as missing.

Results
Patient Characteristics at Index

A total of 12,712 patients with COPD were observed during the identification period from January 1, 2015 to December 31, 2017. Of these, 2829 patients (22%) experienced an AECOPD and were included in the study population. Of the patients with an exacerbation, 190 patients (6.7%) had a severe AECOPD and 2639 patients (93.3%) had a moderate AECOPD.

Patient characteristics at index are shown in Table 1. The mean (standard deviation) age was 69.0 (10.5) years and 52.9% of the population were female. The mean (standard deviation) duration of COPD was 4.8 (3.2) years. Overall, 26.0% of patients had concomitant asthma (as defined by encounter diagnosis identified within one year prior to COPD exacerbation), 27.3% were active smokers, 64.5% were former smokers and 7.9% had never smoked.

COPD-Related Treatment at Index

Table 2 describes the medications dispensed at index. Patients could receive either mono-, dual, or triple therapy, or combinations of rescue and controller inhalers. Oral corticosteroids were the most frequently dispensed drugs during an AECOPD (58.6% of patients), followed by SABA rescue inhalers (16.1% of patients). Oral corticosteroids were used slightly more often in patients with a severe AECOPD compared with those who experienced a moderate AECOPD (68.4% versus 58.9%, respectively).

In patients who experienced a moderate AECOPD, SABA rescue inhalers were used nearly six times as

Table I Patient Characteristics at Index

	Overall (N=2829)	Moderate AECOPD (n=2639)	Severe AECOPD (n=190)
Age (years), mean (SD)	69.0 (10.5)	69.1 (10.4)	68.2 (11.7)
Age group, n (%)			
40–49 years	80 (2.8)	70 (2.7)	10 (5.3)
50–64 years	926 (32.7)	857 (32.5)	69 (36.3)
≥65 years	1823 (64.4)	1712 (64.9)	111 (58.4)
Gender, n (%)			
Females	1496 (52.9)	1387 (52.6)	109 (57.4)
Race-ethnicity, n (%)			
White NH	2601 (91.9)	2424 (91.9)	177 (93.2)
Black/African American NH	45 (1.6)	41 (1.6)	4 (2.1)
Native American/Alaskan Native NH	13 (0.5)	13 (0.5)	0
Asian NH	21 (0.7)	21 (0.8)	0
Multi-racial NH	77 (2.7)	73 (2.8)	4 (2.1)
Hispanic	49 (1.7)	46 (1.7)	3 (1.6)
Other	8 (0.3)	8 (0.3)	0
Missing	15 (0.5)	13 (0.5)	2 (1.1)
BMI (kg/m^2), mean (SD)	29.64 (7.8)	29.57 (7.5)	30.51 (10.5)
Weight (kg), mean (SD)	84.06 (24.1)	83.97 (23.8)	85.34 (28.9)
Duration of COPD (years), mean (SD)	4.8 (3.2)	4.8 (3.2)	4.5 (3.4)
<1 year, n (%)	237 (8.4)	212 (8.0)	25 (13.2)
1–5 years, n (%)	1206 (42.6)	1124 (42.6)	82 (43.2)
>5 years, n (%)	1386 (49.0)	1303 (49.4)	83 (43.7)
Smoking status, n (%)			
Current smoker	771 (27.3)	704 (26.7)	67 (35.3)
Former smoker	1824 (64.5)	1720 (65.2)	104 (54.7)
Never smoked	223 (7.9)	206 (7.8)	17 (8.9)
No information	11 (0.4)	9 (0.3)	2 (1.1)
Vaccination status, n (%)			
Pneumococcal (≥50 years of age)[a]	2203 (77.9)	2065 (78.2)	138 (72.6)
Influenza (current season)[b]	1597 (56.5)	1487 (56.3)	110 (57.9)
Influenza (year prior to index)[c]	2042 (72.2)	1899 (72.0)	143 (75.3)
Eosinophil count (cells/µL) – highest value[d]	281.44 (323.1)	279.18 (329.4)	307.76 (236.6)
<150, mean (SD)	531 (18.8)	497 (18.8)	34 (17.9)
150–300, mean (SD)	645 (22.8)	598 (22.7)	47 (24.7)
>300, mean (SD)	518 (18.3)	465 (17.6)	53 (27.9)
No data, n (%)	1135 (40.1)	1079 (40.9)	56 (29.5)
Eosinophil count – most recent value (cells/µL)[e]	217.09 (236.2)	215.59 (237.8)	234.55 (216.7)
<150, mean (SD)	741 (26.2)	690 (26.1)	51 (26.8)
150–300, mean (SD)	592 (20.9)	548 (20.8)	44 (23.2)
>300, mean (SD)	361 (12.8)	322 (12.2)	39 (20.5)
No data, n (%)	1135 (40.1)	1079 (40.9)	56 (29.5)

(Continued)

Table 1 (Continued).

	Overall (N=2829)	Moderate AECOPD (n=2639)	Severe AECOPD (n=190)
Charlson Comorbidity Index score, mean (SD)	2.94 (2.3)	2.92 (2.3)	3.19 (2.4)
Comorbidities, n (%)			
Congestive heart failure[f]	511 (18.1)	462 (17.5)	49 (25.8)
Diabetes[f]	776 (27.4)	716 (27.1)	60 (31.6)
Asthma[f]	736 (26.0)	689 (26.1)	47 (24.7)
Alpha-1 antitrypsin deficiency[f]	5 (0.2)	3 (0.1)	2 (1.1)
Lung function			
FEV_1 (L), mean (SD)	1.68 (0.7)	1.7 (0.7)	1.4 (0.6)
FVC (L), mean (SD)	3.03 (1.0)	3.05 (0.9)	2.76 (1.0)
Most recent reversibility, n (%)			
Patient has no data	1257 (44.4)	1163 (44.1)	94 (49.5)
No	970 (34.3)	920 (34.9)	50 (26.3)
Yes	602 (21.3)	556 (21.1)	46 (24.2)
GOLD Stage, n (%)			
Missing	758 (26.8)	693 (26.3)	65 (34.2)
Stage I	187 (6.6)	185 (7.0)	2 (1.1)
Stage II	759 (26.8)	717 (27.2)	42 (22.1)
Stage III	345 (12.2)	314 (11.9)	31 (16.3)
Stage IV	61 (2.2)	54 (2.0)	7 (3.7)
Patient has post FEV_1/FVC, but not <0.7	219 (7.7)	205 (7.8)	14 (7.4)
Patient has no post FEV_1/FVC or post FEV_1 predicted	500 (17.7)	471 (17.8)	29 (15.3)

Notes: [a]One pneumococcal vaccine within last six years prior to index date for AECOPD. [b]One influenza vaccine during the most recent influenza season (August to March) but not within 14 days of index date. [c]One influenza vaccine within the past year but not within 14 days of index date. [d]Highest eosinophil value within the past year but not within 5 days of index date. [e]Most recent eosinophil value within the past year but not within 5 days of index date. [f]Within one year prior to exacerbation diagnosis.
Abbreviations: AECOPD, acute exacerbation of chronic obstructive pulmonary disease; BMI, body mass index; COPD, chronic obstructive pulmonary disease; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; GOLD, Global Initiative for Chronic Obstructive Lung Disease; NH, non-Hispanic; SD, standard deviation.

often than a combination of SABA and SAMA (15.5% versus 2.8%, respectively). Nebulized SABA rescue therapy was also used more often than nebulized SABA/SAMA concurrent or combination medications in patients with a moderate AECOPD (5.0% versus 1.4%, respectively). In patients who experienced a severe AECOPD, SABA rescue inhalers were used three times less often than the combination of SABA and SAMA (24.7% versus 77.4%, respectively). However, nebulized SABA rescue therapy was used twice as often as nebulized SABA/SAMA concurrent or combination medications in patients with a severe AECOPD (14.1% versus 15.4%, respectively).

Among patients who experienced a severe AECOPD, 31.6% were dispensed a long-acting muscarinic antagonist (LAMA), 27.4% were dispensed an inhaled corticosteroid (ICS)/long-acting β2-agonist (LABA) concurrent or combination medication, 17.9% were dispensed ICS, LABA, LAMA triple therapy and 16.3% were dispensed an ICS

inhaler. However, a maintenance therapy was not dispensed in 31.1% of patients who experienced a severe AECOPD (Table 3). In comparison, patients who experienced a moderate AECOPD were less likely to be prescribed a controller inhaler; 7.6% were dispensed a LAMA, 6.3% were dispensed an ICS/LABA concurrent or combination medication, 1.8% were dispensed ICS, LABA, LAMA triple therapy, and 4.6% were dispensed an ICS inhaler.

COPD-Related Treatment Pre- and Post-AECOPD

The use of controller and rescue COPD medication throughout the study period is shown in Table 3. Prior to an AECOPD, patients showed similar patterns of controller medication use regardless of whether they subsequently experienced a moderate or severe AECOPD. Overall, the percentage of patients using inhaled maintenance therapy

Table 2 COPD-Related Therapy Dispensed in the AECOPD Group at Index[a,b]

	Overall N (%)	Moderate AECOPD n (%)	Severe AECOPD n (%)
Overall, N	2829	2639	190
Controller inhalers			
LAMA	260 (9.2)	200 (7.6)	60 (31.6)
LABA	7 (0.2)	6 (0.2)	1 (0.5)
LAMA+LABA or LAMA/LABA[c]	0	0	0
ICS+LABA or ICS/LABA[c]	218 (7.7)	166 (6.3)	52 (27.4)
ICS+LAMA+LABA or ICS/LAMA/LABA[c]	81 (2.9)	47 (1.8)	34 (17.9)
ICS	153 (5.4)	122 (4.6)	31 (16.3)
Rescue inhalers			
SABA	456 (16.1)	409 (15.5)	47 (24.7)
SAMA	23 (0.8)	15 (0.6)	8 (4.2)
SABA+SAMA or SABA/SAMA[c]	220 (7.8)	73 (2.8)	147 (77.4)
Oral corticosteroid	1657 (58.6)	1527 (57.9)	130 (68.4)
Oral COPD therapy			
Methylxanthines	3 (0.1)	1 (0.0)	2 (1.1)
PDE-4 inhibitors	1 (0.0)	0	1 (0.5)
Nebulized controller therapy			
LAMA	0	0	0
LABA	0	0	0
LAMA+LABA or LAMA/LABA[c]	0	0	0
ICS+LABA or ICS/LABA[c]	0	0	0
ICS+LAMA+LABA or ICS/LAMA/LABA[c]	0	0	0
ICS	2 (0.1)	0	2 (1.1)
Nebulized rescue therapy			
SABA	211 (7.5)	133 (5.0)	78 (41.1)
SAMA	27 (1.0)	13 (0.5)	14 (7.4)
SABA+SAMA or SABA/SAMA[c]	67 (2.4)	38 (1.4)	29 (15.3)

Notes: [a]Medication categories are non-mutually exclusive. [b]Medications dispensed at index, not including therapies a patient was receiving at the time the AECOPD occurred. [c]Classifications with a slash (/) indicate combination medications, a plus (+) indicates simultaneous dispensings.
Abbreviations: AECOPD, acute exacerbation of chronic obstructive pulmonary disease; COPD, chronic obstructive pulmonary disease; ICS, inhaled corticosteroid; LABA, long-acting β_2-agonist; LAMA, long-acting muscarinic antagonist; PDE-4, phosphodiesterase-4; SABA, short-acting β_2-agonist; SAMA, short-acting muscarinic antagonist.

increased from 60.6% pre-AECOPD to 68.8% post-AECOPD. Of note, there was a large increase in the proportion of patients receiving inhaled maintenance therapy post-AECOPD among patients who experienced a severe AECOPD: 60.0% pre-AECOPD versus 87.4% post-AECOPD. In contrast, among patients with a moderate AECOPD, inhaled maintenance therapy use increased from 60.7% pre-AECOPD to 67.4% post-AECOPD.

The use of ICS therapy alone was similar in the pre- and post-index periods (7.3% versus 7.5%, respectively). The use of ICS/LABA+LAMA and ICS+LAMA approximately doubled following an AECOPD event for patients who experienced a severe AECOPD (22.6% versus 42.1%

and 5.3% versus 10.5%, respectively). The increase was much smaller for patients who experienced a moderate AECOPD (19.9% versus 24.7% and 5.1% versus 6.6%, respectively). Overall, the use of multiple-inhaler triple therapy (ICS+LAMA+LABA) increased from 20.1% to 25.9% between the pre-index to the post-index period. The use of rescue inhalers did not markedly change between the pre- and post-index periods (52.4% versus 53.0%, respectively).

Healthcare Utilization
COPD-related healthcare utilization is shown in Table 4. The percentage of patients with at least one COPD-related

Table 3 Treatment Patterns Pre- and Post-AECOPD (Mutually Exclusive)

	90 Days Pre-Index[a]			Index[b,c]			90 Days Post-Index[d]		
	Overall N (%)	Moderate AECOPD n (%)	Severe AECOPD n (%)	Overall N (%)	Moderate AECOPD n (%)	Severe AECOPD n (%)	Overall N (%)	Moderate AECOPD n (%)	Severe AECOPD n (%)
Overall, N	2829	2639	190	2829	2639	190	2829	2639	190
Controller inhalers									
No therapy	1114 (39.4)	1038 (39.3)	76 (40.0)	2220 (78.5)	2161 (81.9)	59 (31.1)	884 (31.2)	860 (32.6)	24 (12.6)
ICS only	207 (7.3)	191 (7.2)	16 (8.4)	125 (4.4)	106 (4.0)	19 (10.0)	213 (7.5)	201 (7.6)	12 (6.3)
LABA only	5 (0.2)	5 (0.2)	0	6 (0.2)	6 (0.2)	0	4 (0.1)	4 (0.2)	0
LAMA only	390 (13.8)	368 (13.9)	22 (11.6)	154 (5.4)	137 (5.2)	17 (8.9)	355 (12.5)	331 (12.5)	24 (12.6)
ICS+LABA or ICS/LABA[e]	382 (13.5)	360 (13.6)	22 (11.6)	218 (7.7)	166 (6.3)	52 (27.4)	433 (15.3)	403 (15.3)	30 (15.8)
ICS/LABA+LAMA[e]	569 (20.1)	526 (19.9)	43 (22.6)	81 (2.9)	47 (1.8)	34 (17.9)	732 (25.9)	652 (24.7)	80 (42.1)
ICS+LAMA[e]	144 (5.1)	134 (5.1)	10 (5.3)	25 (0.9)	16 (0.6)	9 (4.7)	195 (6.9)	175 (6.6)	20 (10.5)
LAMA+LABA or LAMA/LABA[e]	1 (0.0)	1 (0.0)	0	0	0	0	1 (0.0)	1 (0.0)	0
ICS/LAMA/LABA[e]	0	0	0	0	0	0	0	0	0
Other[f]	17 (0.6)	16 (0.6)	1 (0.5)	0	0	0	12 (0.4)	12 (0.5)	0
Rescue inhalers									
Any	1482 (52.4)	1335 (50.6)	147 (77.4)	637 (22.5)	479 (18.2)	158 (83.2)	1498 (53.0)	1347 (51.0)	151 (79.5)

Notes: [a]Pre-index ends the day before index. [b]The index period (applying only to hospitalized patients) was defined as the date of the most recent AECOPD until the day before discharge. [c]Medications dispensed at index, not including therapies a patient was receiving at the time the AECOPD occurred. [d]Post-index starts on discharge date or day after index date for same-day releases. [e]Classifications with a slash (/) indicate combination medications, a plus (+) indicates simultaneous dispensings. [f]Other combinations include simultaneous dispensing of ICS+LABA or LABA+LAMA.
Abbreviations: AECOPD, acute exacerbation of chronic obstructive pulmonary disease; ICS, inhaled corticosteroid; LABA, long-acting β2-agonist; LAMA, long-acting muscarinic antagonist.

Table 4 COPD-Related and Non-COPD-Related Healthcare Resource Utilization Pre- and Post-Index

	90 Days Pre-Index[a]			90 Days Post-Index[b]		
	Overall	Moderate AECOPD	Severe AECOPD	Overall	Moderate AECOPD	Severe AECOPD
Overall, N	2829	2639	190	2829	2639	190
COPD-related ambulatory visits, n	351	325	26	1101	997	104
Primary care, n (%)	170 (6.0)	156 (5.9)	14 (7.4%)	740 (26.2)	660 (25.0)	80 (42.1)
Pulmonologist, n (%)	172 (6.1)	159 (6.0)	13 (6.8%)	457 (16.2)	404 (15.3)	53 (27.9)
Cardiologist, n (%)	3 (0.1)	2 (0.1)	1 (0.5%)	5 (0.2)	5 (0.2)	0
Urgent care, n (%)	12 (0.4)	11 (0.4)	1 (0.5%)	105 (3.7)	105 (4.0)	0
Other, n (%)	26 (0.9)	25 (0.9)	1 (0.5%)	89 (3.1)	81 (3.1)	8 (4.2)
Non-COPD-related ambulatory visits, n	2052	1908	144	2187	2023	164
Primary care, n (%)	1417 (50.1)	1324 (50.2)	93 (48.9)	1526 (53.9)	1396 (52.9)	130 (68.4)
Pulmonologist, n (%)	178 (6.3)	158 (6.0)	20 (10.5)	356 (12.6)	301 (11.4)	55 (28.9)
Cardiologist, n (%)	212 (7.5)	198 (7.5)	14 (7.4)	251 (8.9)	232 (8.8)	19 (10.0)
Urgent care, n (%)	415 (14.7)	380 (14.4)	35 (18.4)	377 (13.3)	360 (13.6)	17 (8.9)
Other, n (%)	1305 (46.1)	1212 (45.9)	93 (48.9)	1392 (49.2)	1290 (48.9)	102 (53.7)

Notes: [a]Pre-index ends the day before index. [b]Post-index starts on discharge date or day after index date for same-day releases.
Abbreviations: AECOPD, acute exacerbation of chronic obstructive pulmonary disease; COPD, chronic obstructive pulmonary disease.

ambulatory visit increased more than four-fold for primary care from the pre-AECOPD to the post-AECOPD period (6.0% versus 26.2% of patients, respectively). The increase in primary care visits was greater among patients who experienced a severe AECOPD (7.4% pre-AECOPD versus 42.1% post-AECOPD) compared with those who experienced a moderate AECOPD (5.9% pre-AECOPD versus 25.0% post-AECOPD, respectively).

The proportion of patients with COPD-related pulmonologist visits also increased from the pre-AECOPD period to the post-AECOPD period (6.1% versus 15.3%, respectively). This increase was also greater for patients who experienced a severe AECOPD (6.8% pre-AECOPD versus 27.9% post-AECOPD) compared with those who experienced a moderate AECOPD (6.0% pre-AECOPD versus 15.3% post-AECOPD). In the post-AECOPD period, 30 (1.1%) patients had a COPD-related hospitalization.

Non-COPD-related healthcare utilization is also shown in Table 4. Overall, 53.9% of patients made at least one non-COPD-related primary care visit and 12.6% of patients made at least one pulmonologist visit in the post-AECOPD period. The proportion of patients with a severe AECOPD making a primary care visit increased from 48.9% pre-AECOPD to 68.4% post-AECOPD. Among patients who had a moderate AECOPD, the proportion of patients who had a primary care visit increased from 50.2% pre-AECOPD to 52.9% post-AECOPD. In total, 104 (3.6%) patients had a non-COPD-related hospitalization in the pre-AECOPD period compared with 122 patients (4.3%) in the post-AECOPD period.

Discussion

This study aimed to describe the COPD-related medication patterns and outpatient encounters 90 days before and after an AECOPD. Most patients identified in our study experienced a moderate AECOPD at index and, consistent with the GOLD 2020 report for patients with an AECOPD,[5] the majority of patients included in the study received systemic corticosteroids during AECOPD events. However, observed dispensing rates suggest that there is room for improvement in care delivery and pharmacotherapy. For example, a high proportion of patients with COPD were not on an inhaled maintenance therapy prior to, and after, an AECOPD. Although the percentage of patients not receiving any COPD therapy decreased slightly in the post-AECOPD period compared with the pre-AECOPD period, almost one third of patients remained without

therapy following an AECOPD. Although the patients who experienced a severe AECOPD were more likely to receive maintenance therapy following their AECOPD, 12.6% of these patients remained without therapy in the post-AECOPD period.

We also observed an increase in the proportion of patients with COPD-related ambulatory visits in the post-AECOPD period compared with the pre-AECOPD period, particularly among patients who had experienced a severe AECOPD. This pattern of increased visits in the post-AECOPD period could suggest either a lack of COPD control following the AECOPD, or increased clinical attention to ensure post-AECOPD care optimization. Coupled with the increased use of inhaled maintenance therapy following a severe AECOPD, the results suggest the latter, that severe AECOPD drives a shift in the pattern of care and pharmacological treatment provided for COPD patients.

Treatment guidelines recommend SABA/SAMA therapy during an AECOPD followed by maintenance therapy as soon as possible before discharge.[5] Our data suggest that the utilization of short-acting inhaled therapy could possibly be improved, as less than a quarter of patients received rescue inhalers at index. The proportion of patients receiving SABA/SAMA rescue medication (both inhalers and nebulized therapy) at index was higher among patients who had a severe AECOPD. In addition, the increased use of controller medications observed in the post-AECOPD period is generally consistent with COPD guideline recommendations. However, guideline adherence assessment at the individual patient level was beyond the scope and intent of this analysis.

Our findings broadly align with previous literature examining lack of optimized maintenance treatment despite a history of AECOPD.[11,12,22] Diette et al found that 36% of patients with COPD were not using inhaled maintenance therapy despite a history of exacerbation,[11] which was similar to our finding for patients in this category (31.2%). In their retrospective cohort study, Price et al observed that 43% of patients with COPD were not prescribed the guideline-recommended treatment in the previous year,[23] while Make et al reported that, among patients hospitalized for COPD, 40.2% of patients with commercial insurance and 29.9% of patients with Medicare remained untreated 45 days following hospitalization.[12] In contrast, we describe a lower proportion of patients untreated 90 days after a severe AECOPD (12.6%), despite using a broader definition for

bronchodilators.[12] It is possible that this difference could be due to a longer post-index period in the present study, which would suggest that a proportion of patients receive therapy between 45 and 90 days post-AECOPD. Alternatively, the lower proportion of untreated patients in our study could reflect standardized care procedures within the Kaiser Permanente Northwest Health System. The lower percentage of untreated patients in our analysis could also potentially be explained by a difference of over 10 years in the observation window and improvements in standards of COPD care over this period.

In a retrospective analysis of inpatient data collected in an administrative database in the United States, the majority of patients with COPD received treatment for an AECOPD in line with GOLD guideline recommendations; 95%, 81%, and 92% of patients received SABAs, systemic corticosteroids, and antibiotics, respectively.[22] However, long-acting bronchodilator maintenance therapy had been initiated in only half of patients (52.2%) before discharge. In contrast, the present study found that only 83.2% of patients with a severe AECOPD received rescue therapy during the AECOPD. However, we identified a higher proportion of patients with a severe AECOPD receiving maintenance therapy during the exacerbation (68.9%) compared with the study by Amin et al.[22] Of note, Amin et al found that patients who did receive maintenance therapy had significantly different characteristics compared with those who did not; for example, patients treated with long-acting bronchodilators had more primary COPD diagnoses, more prior all-cause hospitalizations, longer lengths of hospital stay, fewer comorbidities, and greater spirometry use.[22] This information could be used to identify patient populations with an unmet need for optimized therapy.

We observed that the largest difference in pharmacotherapy management after experiencing an AECOPD was an increased use of ICS+LAMA+LABA triple therapy. Recent clinical trials suggest that ICS+LAMA +LABA triple therapy can improve some post-AECOPD outcomes.[24–27] Lipson et al demonstrated that in symptomatic patients with a history of exacerbations, fluticasone furoate, umeclidinium and vilanterol (FF/UMEC/VI) significantly reduced the annual rate of moderate/severe AECOPD compared with dual therapies (FF/VI and UMEC/VI) and significantly reduced COPD-related hospitalizations compared with UMEC/VI.[25] Additionally, Bogart et al demonstrated that initiation of triple therapy within 30 days of an AECOPD was associated with reduced AECOPD rates and reduced COPD-related healthcare costs compared with delayed therapy.[26] The recently approved triple therapy comprising budesonide/glycopyrrolate/formoterol fumarate (BUD/GLY/FOR) was shown to significantly reduce rates of moderate-to-severe exacerbations compared with dual therapies BUD/FOR and GLY/FOR.[27] In our study, there was a slight increase in the proportion of patients with a moderate AECOPD who received ICS+LAMA+LABA triple therapy, from 19.9% of patients pre-index to 24.7% post-index. Meanwhile, the proportion of patients with a severe AECOPD who received ICS+LAMA+LABA nearly doubled from the pre-index to post-index periods, from 22.6% to 42.1%. Further research is needed to confirm if the potential benefits of triple therapy post-AECOPD are recognized in patients who experience a moderate AECOPD, as well as in those who experience a severe AECOPD. The observed under-treatment and low augmentation to triple therapy, or any inhaled maintenance therapy, following an AECOPD may be an important contributing factor to the increased number of patients with COPD-related outpatient visits in the post-index period of our study.

Our study has a number of strengths that should be mentioned. First, data were obtained from a population of patients served by an integrated delivery network, which captures most aspects of care provided by the healthcare system. Second, the data included clinical metrics from electronic health records that are not found in typical claims databases, for example additional diagnosis data, laboratory test results, lung function data, and dispensed medications. Additionally, our analysis reported medication dispensing, which is expected to be a closer measure of medication use compared with prescriptions. However, the number of dispensed medications is still likely to be higher than actual patient adherence. It is unlikely that COPD medication use was underestimated in our analysis, as sample medications are not provided to patients treated in the Kaiser Permanente Northwest Health System.

The study also has some limitations that should be taken into consideration. As data in the electronic medical records were not originally collected for research purposes, there is potential for data that does not reliably reflect actual patient care. Additionally, only patients who had consistent use of the health system for 10 out of the 12 months prior to their AECOPD were eligible and included in the analysis. Therefore, our findings may not apply to patients who do not routinely access the healthcare system, or who regularly move between systems.

Furthermore, patients with no or low levels of insurance coverage are not well represented in the Kaiser Permanente Northwest Health System. Some important aspects of COPD care were not captured, such as the extent of inhaler device training, smoking cessation counselling or pulmonary rehabilitation after an AECOPD. Additionally, patient adherence to the prescribed therapy could not be verified. The number of post-AECOPD pharmacy dispensings may be higher than actual medication use, depending on the amount of medication patients were dispensed at discharge or had prior to the AECOPD. As the analysis was descriptive, it did not formally test any hypotheses nor draw any causal conclusions, and treatment patterns were not evaluated by patient characteristics (or any other characteristics). A further limitation is that the patient population was homogeneous with respect to geographic region and race/ethnicity groups and so may not apply to other regions or patient demographics. In addition, most COPD patients included in the analysis did not have confirmatory spirometry of their COPD diagnosis, akin to the longstanding <50% rate seen in the Healthcare Effectiveness Data and Information Set measures; this limitation therefore applies to many real-world data analyses and includes the possibility of misdiagnosis or over- or under- diagnosis in the population. Finally, as the study sought to evaluate medication patterns following an AECOPD and thus required 90-day continuous enrollment following the AECOPD, patients who died in this period were not included, introducing a selection bias against those individuals.

Conclusions

Within this vertically integrated care management organization, appropriate increases in therapy aligned with clinical practice guidelines were observed, yet still a third of patients who experienced an AECOPD did not receive maintenance therapy post-exacerbation. These results highlight a continuing need to focus on pharmacotherapy management in patients following an AECOPD, to improve physicians' awareness of COPD treatment recommendations, and to identify factors associated with physician prescribing and patient adherence. This information could be used to inform system-level quality improvements and subsequent population health research. Improving adherence to treatment guidelines post-AECOPD may help to reduce healthcare resource utilization.

Abbreviations

AECOPD, acute exacerbation of chronic obstructive pulmonary disease; BMI, body mass index; COPD, chronic obstructive pulmonary disease; ED, emergency department; FEV1, forced expiratory volume in 1 second; FF, fluticasone furoate; FVC, forced vital capacity; GOLD, Global Initiative for Chronic Obstructive Lung Disease; ICD, International Classification of Diseases; ICS, inhaled corticosteroid; LABA, long-acting β_2-agonist; LAMA, long-acting muscarinic antagonist; NH, non-Hispanic; PDE-4, phosphodiesterase-4; SABA, short-acting β_2-agonist; SAMA, short-acting muscarinic antagonist; SD, standard deviation; UMEC, umeclidinium; VI, vilanterol.

Data Sharing Statement

The data analyzed in this manuscript are contained in a database owned by Kaiser Permanente Northwest and contain proprietary elements. Therefore, it cannot be broadly disclosed or made publicly available at this time.

Ethics Approval and Informed Consent

Ethical approval of this study was provided by Kaiser Permanente – Northwest Region Institutional Review Board (approval number: 1394778) and a waiver of informed consent was granted on the basis that there was minimal risk to the patient associated with the planned data collection. The study was conducted in accordance with the Declaration of Helsinki.

Patient Confidentiality

All patient records included in this analysis were anonymized.

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Author Contributions

All authors made a significant contribution to the work reported, whether that was in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the manuscript; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare the following conflicts of interest during the last three years in relation to this article: CM was an employee of GlaxoSmithKline at the time the study was conducted and owns stocks in GlaxoSmithKline. CM is currently affiliated with Avalere Health, Health Economics and Advanced Analytics, Washington, DC, USA. BW, RHS, and DG were employees of GlaxoSmithKline at the time the study was conducted. RHS and DG are currently affiliated with AESARA Inc, Chapel Hill, NC, USA. MJF, RAM, MAM, PC, and BS received a collaborative grant from GlaxoSmithKline to conduct this analysis. MJF is currently affiliated with Kaiser Permanente Washington Health Research Institute, Seattle, WA, USA. RAM has served on an advisory board for GlaxoSmithKline. The authors report no other conflicts of interest in this work.

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