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ORIGINAL RESEARCH

# Treatment Patterns and Triple Therapy Utilization in Chinese Patients with Chronic Obstructive Pulmonary Disease: An Analysis of Real-World Data from the Yinzhou Database

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**Purpose:** Triple therapy of chronic obstructive pulmonary disease (COPD), consisting of inhaled corticosteroid (ICS), long-acting β2-agonist (LABA) and long-acting muscarinic antagonist (LAMA) has shown benefits in patients with COPD. However, little is known about the use of triple therapy in Chinese patients. This study aims to describe the treatment patterns and the utilization of triple therapy in COPD patients based on real-world data from China.

**Patients and Methods:** This retrospective study included patients with COPD from the Yinzhou database. Patients aged ≥ 40 years with a diagnosis of COPD were included. Different combinations of ICS, LAMA and LABA prescribed during follow-up were categorized as single, dual, or triple therapies. Descriptive analysis was performed to depict the treatment patterns of each therapy.

**Results:** A total of 7888 patients were prescribed at least one COPD therapy during the follow-up. Among them, 29.1% were prescribed triple therapy (ICS+LABA+LAMA) with a median (IQR) treatment duration of 3.27 (7.17) months. The majority (68.6%) of patients were prescribed dual therapy with ICS+LABA, while 27.3% and 23.3% of patients were prescribed single therapy with ICS or LAMA, respectively. Regarding treatment sequences during follow-up, 30.1% of patients received dual therapy with ICS+LABA, followed by 11.4% receiving only triple therapy and 10.4% receiving single therapy with ICS alone.

**Conclusion:** Our study assessed treatment patterns and triple therapy utilization among patients with COPD in China. The majority of patients were treated with ICS+LABA dual therapy. Triple therapy was also widely used, with most patients transitioning from other treatment modalities.

**Keywords:** COPD, ICS, LABA, LAMA

## Introduction

Chronic obstructive pulmonary disease (COPD) is a heterogeneous lung condition characterized by chronic respiratory symptoms due to abnormalities of the airways and/or alveoli, leading to persistent and usually progressive airflow obstruction.[1] As the third leading cause of mortality worldwide, COPD constitutes a significant global health concern.[2,3] According to World Health Organization (WHO), China has approximately 100 million people living with COPD and accounts for almost one quarter of all COPD cases globally.[4,5] As the population continues to age rapidly in China, the burden of COPD is expected to escalate in the future.[6]

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According to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2017 report,[7] the pharmacologic treatment was recommended based on the severity of the disease. In the intervening years, the GOLD reports, have been further refined to a stepwise approach where triple therapy (ICS+LAMA+LABA) remained a treatment option when patient symptoms and exacerbations persist and where other clinical indicators (e.g., eosinophil values) may indicate additional benefits.[8,9] In China, *the Guidelines for the diagnosis and management of chronic obstructive pulmonary disease (revised version 2021)* largely aligned with the GOLD recommendations for the initiation and use of triple therapy.[10] Fixed-dose inhaled corticosteroid (ICS)/ long-acting β2 agonist (LABA)/ long-acting muscarinic antagonist (LAMA) triple therapies including BREZTRI®, TRELEGY ELLIPTA®, and TRIMBOW® were approved in China in 2019, 2020, and 2022, respectively. Triple therapy has gained wide recognition as an intensive treatment option in COPD management.[11] As demonstrated in the IMPACT, KRONOS, and ETHOS trials, triple therapies for COPD significantly reduce the rate of moderate or severe exacerbations, hospitalizations, and all-cause mortality compared to dual therapies.[12–16]

Despite the robust evidence supporting the effectiveness of triple therapy, medications may not always be prescribed optimally, leading to potential undertreatment or inappropriately prescribed medication in routine clinical practice. Previous studies have revealed discrepancies in the treatment of patients with COPD, between the GOLD report recommendations and actual clinical practice in the United States.[17] Evidence in China has also indicated that treatment patterns in clinical practice may not fully align with the GOLD reports or other national guidelines in China.[18,19] It was shown that approximately one-third of the patients with COPD are never diagnosed nor treated.[20] Poor adherence to respiratory medications has also been documented in patients with COPD on multiple inhalers or complex regimens, compared to patients on single inhalers.[21–23] Moreover, given the rise of triple therapy options in China, there is a lack of research focusing on triple therapy utilization in Chinese patients in recent years with COPD. This study aims to address this gap by investigating the treatment patterns of ICS, LABA, or LAMA, as well as the utilization of triple therapy in COPD patients using real-world data from the Yinzhou region of China.

# Materials and Methods

## Study Design and Data Source

This was an observational retrospective longitudinal cohort study among Chinese patients with COPD, using the Yinzhou regional electronic health records database (Yinzhou database).

Yinzhou is a district of Ningbo, a sub-provincial city in northeast Zhejiang province, located 230 km south of Shanghai. It covers an area of 1346 $km^2$ and has a total population of 1.66 million in 2022, among which 928,000 are permanent residents.[24] Since 2009, the Yinzhou database has covered almost all health-related activities of residents, from birth to death, across all age groups. As of 2017, 98% of all permanent residents in Yinzhou are registered in with a valid healthcare identifier into a health information system.[25] Further details on the Yinzhou database are provided in previous publications.[24]

## Study Population

Screening for patient eligibility was conducted from 1st Jan 2014 to 1st Mar 2022. To be eligible, patients needed to meet specific criteria: a) had ≥ 2 primary diagnosis items/codes for COPD in the outpatient setting or ≥ 1 primary or secondary diagnosis item/code for COPD in the inpatient setting during the screening period; b) were 40 years of age or older at the time of the first COPD diagnosis item/code identification; c) had baseline data available for at least 24 consecutive months before the first COPD diagnosis item/code identification. In addition, patients were excluded if they had a record of Alpha-1 antitrypsin deficiency during the baseline period. The index date was defined as the date of the first identified COPD diagnosis within the screening period. Baseline data was collected from a 24-month lookback period preceding index date. Patients were followed up from the index date until (1) 1st March 2023 (administrative right censoring); (2) loss to follow-up (the last clinical event date recorded in the database); (3) all-cause death (death data was available until 30 Jun 2022), whichever came first (see Figure 1).

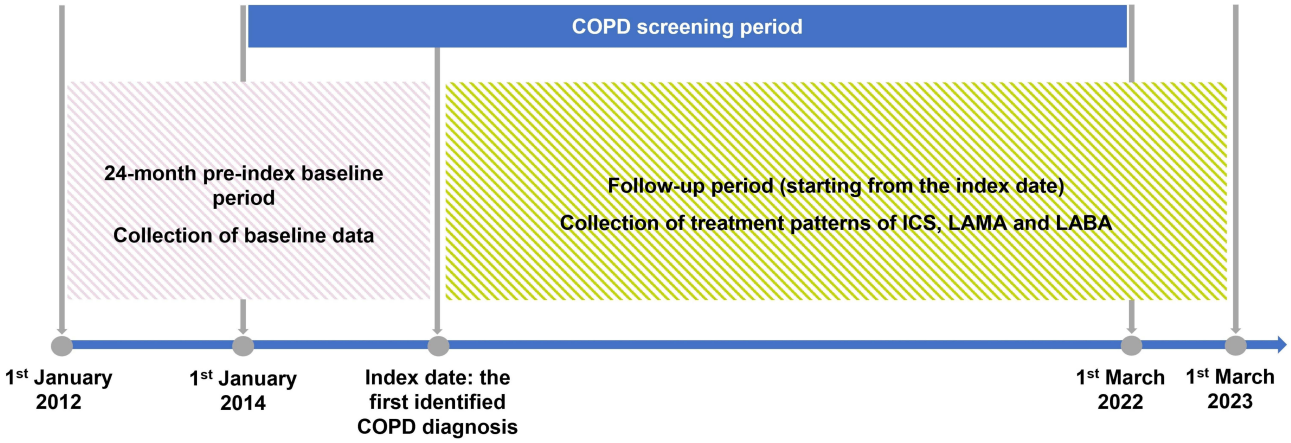


**Figure 1** Study design scheme.
**Abbreviations**: COPD, Chronic Obstructive Pulmonary Disease; ICS, Inhaled Corticosteroids; LAMA, Long-Acting Muscarinic Antagonists; LABA, Long-Acting β2 Agonists.

## Treatment Patterns

The treatment patterns of ICS, LAMA and/or LABA prescribed during the follow-up period were described by grouping different combinations of these medications including single/dual/or triple therapies. Dual and triple therapies involved both fixed-dose combinations and individual medications that were prescribed concurrently.

Single therapy comprised three categories: 1) single therapy with ICS; 2) single therapy with LAMA; and 3) single therapy with LABA. The start date of single therapy regimens was defined as the start date of the first prescription, and the end date was the first of: (a) the end date of the first prescription; (b) the start date of the prescription for another medication if the patient switched to or added any of the other two medications; (c) loss to follow-up; or (d) death. If the gap between two consecutive prescriptions of the same drug class was ≤ 60 days, the prescriptions were combined and counted as one prescription. A valid single therapy should last for at least 30 days.

Dual therapy consisted of combinations including: 1) ICS + LAMA; 2) ICS + LABA; and 3) LAMA + LABA. The start date of dual therapy was the prescription for dual therapy or the addition of a second medication. The end date was the first of: (a) the end date of the first prescription for any of the two medications; (b) the start date of the prescription for a third medication if the patient switched to triple therapy; (c) loss to follow-up; or (d) death. A valid dual therapy consisted of two classes of medications with at least 30 days' overlap.

Triple therapy was defined as concomitant use of ICS, LAMA, and LABA. The start date of triple therapy was the prescription date when the third medication was added, and the end date was the first of: (a) the end date of the first prescription for any of the three medications; (b) loss to follow-up; or (c) all cause of mortality. A valid triple therapy should have the three classes of medications with at least 30 overlapping days (see Figure 2 for examples of valid single/dual/triple therapies).

The treatment duration for single, dual and triple therapies was the complete duration for respective therapy types from the index date until the end of follow-up.

## Statistical Analysis

Descriptive analyses were performed on demographic and clinical characteristics of the entire COPD cohort during the baseline period. Continuous variables were summarized by indicating the mean (standard deviation [SD]), median (interquartile range [IQR]), minimum, and maximum values. For dichotomous or categorical variables, the distribution was expressed as n (%) for each category.

Treatment patterns and treatment duration for each valid therapy type were described throughout the follow-up period. The number (%) of patients with different valid single/dual/triple therapies was reported. The distribution (mean, SD, median, IQR, minimum and maximum) of the treatment duration for each single/dual/triple therapy was summarized and expressed in months.


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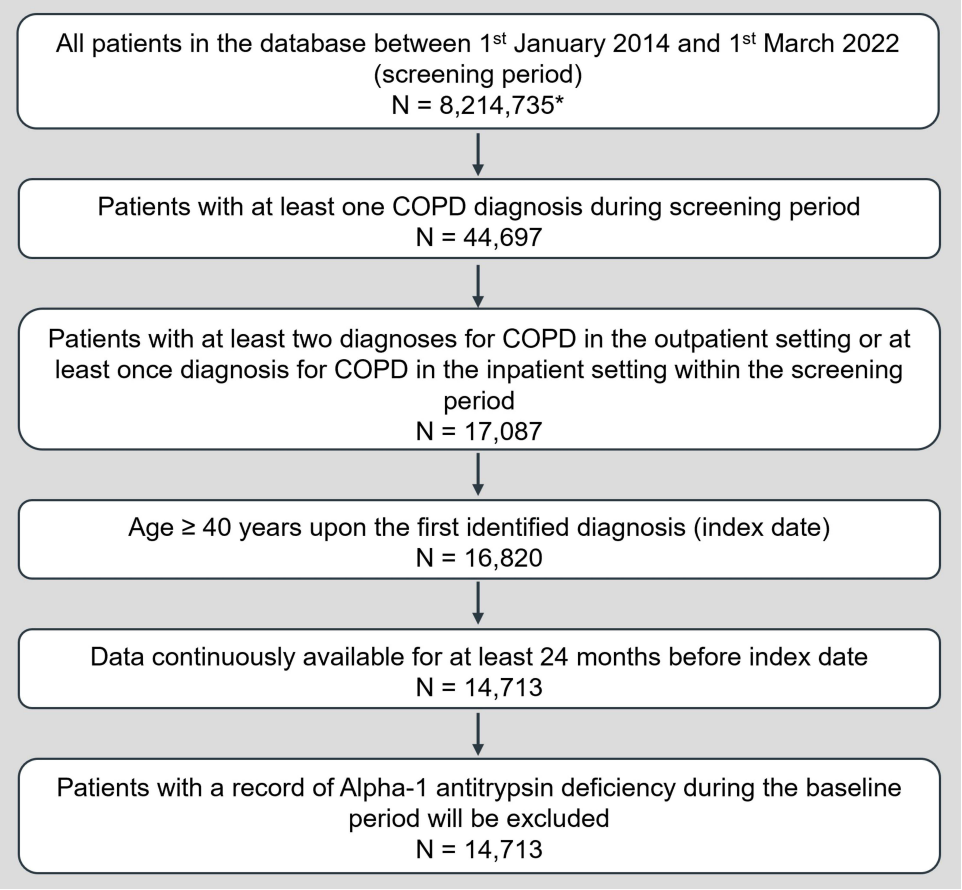


**Figure 2** Patient attrition flow chart.
**Notes**: *8,214,735 is the number of patients that had at least one clinical record in the database during the screening period, including 1,807,835 registered residents of Yinzhou, who had continual contact with the hospital system.

The treatment sequences of all valid single/dual/triple therapies from the index date until the first instance of triple therapy or the end of follow-up (whichever came first) were described. In addition, repeated therapies given in consecutive sequence were collapsed during treatment sequence analysis if the gap in-between was less than 365 days (see Supplementary Figure S1 for examples of treatment sequences).

The statistical program SQL and R Project for Statistical Computing, version 4.2.2 or higher were used.

# Results

## Study Participants and Baseline Characteristics

A total of 14,713 patients with COPD were included in the study during the screening period (from 1st Jan 2014 to 1st Mar 2022) (Figure 2). Of these patients, 43.5% (6,401/14,713) were included between 2014 and 2016, while 56.5% (8,312/14,713) were included later from 2017 to 2022. The mean (SD) age at the index date was 72.0 (11.5) years, and 67.0% (9,862/14,713) of the patients were male. The median (IQR) follow-up period was 41.3 (47.4) months. The majority of patients (71.9%) reported hypertension as a comorbidity at baseline, followed by ischaemic heart diseases (42.8%). Additional cardiovascular-related comorbidities were also noted (Table 1). As for concomitant medications, 34.2% (5,029/14,713) of patients received long-acting COPD treatments at baseline. Among these patients, over half (54.0%, 2,717/5,029) received fixed-dose prescription of ICS+LABA, and 39.2% (1,973/5,029) and 27.1% (1,364/5,029) received prescriptions of ICS and LAMA, respectively. In addition, 24.9% (3,657/14,713) of patients received short-acting COPD treatments at baseline, and 12.8% (1,890/14,713) received oral theophylline. Further details of the baseline characteristics were presented in Table 1.

**Table 1** Baseline Characteristics of the Full COPD Cohort

| Baseline Characteristics | All Patients |
|---|---|
| | N=14,713 |
| | n (%) |
| **Year of cohort entry** | |
| 2014 | 2,891 (19.6%) |
| 2015 | 1,749 (11.9%) |
| 2016 | 1,761 (12.0%) |
| 2017 | 1,536 (10.4%) |
| 2018 | 1,424 (9.7%) |
| 2019 | 1,485 (10.1%) |
| 2020 | 1,879 (12.8%) |
| 2021 | 1,822 (12.4%) |
| 2022 | 166 (1.1%) |
| **Age in years** | |
| Mean [SD] | 72.0 [11.5] |
| Median [IQR] | 73.0 [17.0] |
| Min, max | 40.0, 101.0 |
| **Gender** | |
| Male | 9,862 (67.0%) |
| Female | 4,804 (32.7%) |
| Missing | 47 (0.3%) |
| **BMI (recorded or height / weight derived) at baseline, kg/m²** | |
| Mean [SD] | 23.1 [3.6] |
| Median [IQR] | 22.9 [4.8] |
| Min, max | 9.0, 53.0 |
| Missing | 7,129 (48.5%) |
| **Smoking status** | |
| Smoker | 3,350 (22.8%) |
| Non-smoker or unknown | 11,363 (77.2%) |
| **Education level** | |
| Unknown | 1,736 (11.8%) |
| Illiteracy | 1,832 (12.5%) |
| Elementary school | 5,154 (35.0%) |
| Secondary school and above | 5,991 (40.7%) |

(*Continued*)

**Table 1** (Continued).

| Baseline Characteristics | All Patients |
|---|---|
| | N=14,713 |
| | n (%) |
| **Comorbidities** | |
| Hypertension | 10,572 (71.9%) |
| Ischemic heart diseases | 6,293 (42.8%) |
| Current asthma | 6,142 (41.7%) |
| Any disorders of lipoprotein metabolism and other lipidaemias | 5,902 (40.1%) |
| Cerebrovascular disease | 5,748 (39.1%) |
| Arrythmia | 4,096 (27.8%) |
| Anxiety disorder | 3,437 (23.4%) |
| Heart failure | 3,265 (22.2%) |
| Diabetes mellitus type-1 or −2 | 1,939 (13.2%) |
| **Concomitant medications[a] at baseline** | |
| COPD drug – ICS | 1,973 (13.4%) |
| COPD drug – LAMA | 1,364 (9.3%) |
| COPD drug – LABA | 0 (0.0%) |
| COPD drug – SABA | 2,987 (20.3%) |
| COPD drug – SAMA | 1,766 (12.0%) |
| COPD drug – ICS, LABA | 2,717 (18.5%) |
| COPD drug – LAMA, LABA | 108 (0.7%) |
| COPD drug – ICS, LAMA, LABA | 37 (0.3%) |
| COPD drug – Long-acting treatments[b] | 5,029 (34.2%) |
| COPD drug – Short-acting treatments[c] | 3,657 (24.9%) |
| Theophylline | 1,890 (12.8%) |
| Cardiac drugs[d] | 12,409 (84.3%) |

**Notes**: [a] All COPD drugs presented in the table only contain fixed-dose products. [b] Long-acting COPD treatments: ICS (Inhaled Corticosteroids), LAMA (Long-Acting Muscarinic Antagonists), LABA (Long-Acting β2 Agonists), ICS+LABA, LAMA+LABA, ICS+LAMA+LABA. [c] Short acting COPD treatments: SABA (Short-Acting β2 Agonists), SAMA (Short-Acting Muscarinic Antagonist). [d] Cardiac drugs: Patients had at least one prescription for any of the following categories: antithrombotic and anticoagulants, cardiac therapy, antihypertensives, diuretics, beta blocking agents, calcium channel blockers, statins.

## Treatment Patterns and Treatment Duration

As for treatment patterns of COPD during the follow-up period, 7,888 out of the 14,713 patients were prescribed at least one valid COPD treatment therapy (lasted for ≥ 30 days) during follow-up.

Among these patients, 29.1% (2,293/7,888) were prescribed triple therapy (ICS+LABA+LAMA) with a median (IQR) treatment duration of 3.27 (7.17) months. The majority (68.6%, 5,409/7,888) of patients were prescribed dual therapy with

ICS+LABA during follow-up, with a median (IQR) treatment duration of 4.10 (12.70) months, while 27.3% (2,157/7,888) and 23.3% (1,835/7,888) of patients were prescribed single therapy with ICS or LAMA, respectively. Dual therapy with LAMA +LABA or ICS+LAMA was less common, with only 8.0% (634/7,888) and 1.6% (128/7,888) of patients receiving these treatments, respectively. The treatment duration of each COPD treatment therapy was summarized in Table 2.

## Treatment Sequence

Table 3 summarized the distribution of the top 10 most common treatment sequences of all valid single/dual/triple therapies among the 7,888 patients, including treatments prescribed from the index date until the first instance of triple therapy or the end of follow-up, whichever came first. The most common treatment sequence was "ICS+LABA" alone, accounting for 30.1% (2,371/7,888) of patients. The second most prevalent treatment sequence was "ICS+LAMA +LABA", with 11.4% (902/7,888) of patients receiving only triple therapy during follow-up. Single therapy with ICS was the third most common treatment sequence, reported in 10.4% (823/7,888) of patients. Other treatment sequences

**Table 2** Treatment Duration of COPD Treatment Therapy

| COPD Treatment Therapy | Overall | | |
|---|---|---|---|
| | N = 7,888[a] | | |
| | N[b] (%) | Treatment Duration in Months[c] | |
| ICS | 2,157 (27.3%) | Mean [SD] | 3.53 [4.53] |
| | | Median [IQR] | 2.00 [3.00] |
| | | Min, Max | 1.00, 74.07 |
| LAMA | 1,835 (23.3%) | Mean [SD] | 8.08 [10.10] |
| | | Median [IQR] | 4.37 [7.50] |
| | | Min, Max | 1.00, 77.80 |
| ICS+LAMA | 128 (1.6%) | Mean [SD] | 3.25 [4.97] |
| | | Median [IQR] | 1.72 [2.14] |
| | | Min, Max | 1.00, 33.83 |
| ICS+LABA | 5,409 (68.6%) | Mean [SD] | 10.52 [14.09] |
| | | Median [IQR] | 4.10 [12.70] |
| | | Min, Max | 1.00, 98.67 |
| LAMA+LABA | 634 (8.0%) | Mean [SD] | 3.88 [4.21] |
| | | Median [IQR] | 2.00 [3.95] |
| | | Min, Max | 1.00, 31.03 |
| ICS+LAMA+LABA | 2,293 (29.1%) | Mean [SD] | 6.87 [9.33] |
| | | Median [IQR] | 3.27 [7.17] |
| | | Min, Max | 1.00, 80.13 |

**Notes**: [a] 7,888 (53.6%) patients in the study cohort had at least one valid COPD treatment therapy recorded in the database during follow-up (on or after the index date). [b] The percentage of each COPD treatment therapy is the proportion of patients who ever received that treatment therapy at any point during the study. Therefore, one patient may have received more than one COPD treatment therapy during the follow-up period. [c] Valid treatment duration (lasted for at least 30 days) of the same therapy for a patient during follow-up were summed up.

**Abbreviations**: ICS, Inhaled Corticosteroids; LAMA, Long-Acting Muscarinic Antagonists; LABA, Long-Acting β2 Agonists.


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**Table 3** Distribution of the Top 10 Common Treatment Sequences of All Valid Single/Dual/Triple Therapies

| Treatment Sequence[a] | n (%) N = 7,888 |
|---|---|
| ICS+LABA | 2,371 (30.1%) |
| ICS+LAMA+LABA | 902 (11.4%) |
| ICS | 823 (10.4%) |
| ICS+LABA -> ICS+LAMA+LABA | 598 (7.6%) |
| ICS+LABA -> ICS+LABA | 444 (5.6%) |
| LAMA | 434 (5.5%) |
| LAMA+LABA | 210 (2.7%) |
| LAMA -> ICS+LAMA+LABA | 189 (2.4%) |
| ICS+LABA -> ICS | 181 (2.3%) |
| ICS -> ICS+LABA | 122 (1.5%) |

**Notes**: [a] Treatment sequence included valid single/dual/triple therapies from the index date until the first instance of triple therapy or the end of follow-up, whichever came first. Repeated therapies given in consecutive sequence were collapsed if the gap in-between was less than 365 days.
**Abbreviations**: ICS, Inhaled Corticosteroids; LAMA, Long-Acting Muscarinic Antagonists; LABA, Long-Acting β2 Agonists.

were reported in fewer patients, specifically, the treatment sequences of "ICS+LABA to ICS+LAMA+LABA", "ICS +LABA to ICS+LABA", "LAMA", "LAMA+LABA", "LAMA to ICS+LAMA+LABA", "ICS+LABA to ICS", and "ICS to ICS+LABA" accounted for 5.6% (444/7,888), 5.5% (434/7,888), 2.7% (210/7,888), 2.4% (189/7,888), 2.3% (181/7,888), and 1.5% (122/7,888) of patients, respectively. See Supplementary Table 1 for the distribution of the other treatment sequences that were less commonly reported in patients.

## Discussion

This retrospective longitudinal cohort study described treatment patterns, especially triple therapy use in Chinese patients with COPD. Among the COPD patients who were on respiratory treatment, the most common therapy prescribed was dual therapy with ICS+LABA (68.6%), followed by triple therapy with ICS+LABA+LAMA (29.1%).

It was found that ICS was mainly prescribed as dual (ICS+LABA) or triple (ICS+LABA+LAMA) therapy, which was consistent with results in previous studies and guidelines that do not recommend ICS monotherapy.[8–10,19,26] An observational study in China, which included 4001 patients, suggested that LAMA (39.1%), ICS+LABA+LAMA (39.0%), and ICS+LABA (14.4%) were the top three inhaler dispensed drugs used in COPD.[18] As per the *Guidelines for the diagnosis and management of chronic obstructive pulmonary disease (revised version 2021)* in China,[10] ICS could replace or partially replace systemic corticosteroid due to the related less severe adverse effects of ICS. ICS +LABA dual therapy is associated with more positive outcomes compared with either ICS monotherapy or LABA monotherapy in terms of improved lung function, clinical symptoms and health status, and reduced risk of exacerbations.[27–29] The observed high usage of ICS might also be related to the co-existence of asthma in 41.7% of the study population. Among patients who switched treatment regimen during the follow-up period, the most common treatment sequence was ICS+LABA to ICS+LAMA+LABA noted in 598 (7.6%) patients. This sequence aligns with the international and national guidelines as one of the common combinations of initial and follow-up pharmacological treatments.[7,8,10] It is also worth noting that in addition to approximately 11% of patients started directly on triple therapy,

another almost 60% (17.7%/29.1%) switched to triple therapy treatment from other therapies. This finding was generally consistent with the stepwise treatment approach that recommends triple therapy as the treatment of choice post-exacerbation or when patients experience persistent symptoms.[7,8,10]

Existing evidence showed that triple therapy was associated with a significantly reduced rate of moderate or severe exacerbations compared with dual or single therapy regimens.[12,14,30] Triple therapy has also been found to reduce future hospitalizations following both moderate and severe exacerbations.[12,14,31] Therefore, it is advisable that clinicians consider triple therapy for high-risk COPD patients (e.g., those with an exacerbation history).[32] The use of triple therapy across different countries and in a real-world setting may vary greatly in relation to patient characteristics and health care settings. Results from a Canadian observational study found that over 71% of the 11,318 newly diagnosed COPD patients (50% were classified as GOLD C/D at diagnosis), initiated triple therapy over a mean follow-up period of 55 months.[33] In comparison, a real-world study in Spain, identified 69,668 newly diagnosed COPD patients where the majority were classified as GOLD A/B (72.3%) and where 16.5% initiated triple therapy during the study period.[34] Moreover, a US study found that triple therapy was used in 9.6% of the incident COPD patient population in their study (n=57,141), and 34.3% of these incident COPD patients were treated with other GOLD recommended therapies including LAMA, LABA +LAMA, and ICS+LABA in the year before triple therapy initiation.[17] While prescription data is easier to track in the real-world, patient adherence and compliance to prescribed medication is much more difficult to capture and follow up. One possible reason why there may be reduced adherence and low compliance to triple therapy treatment may be due to the complexity of the dosing regimen, including the use of multiple inhalers with varying daily frequencies or diverse inhalation techniques.[35] In our study, there were only 37 (0.3%) patients at baseline treated with fixed-dose ICS+LABA +LAMA combination therapy, and the number increased to 2,293 (29.1%) during the follow-up period of this study, it is probable that this trend was impacted by the launch of fixed-dose triple therapies in China during this time.[36] It is also believed that the uptake of triple therapy, in combination with the adoption of a single-inhaler device (for delivery of ICS +LABA+LAMA) will increase and potentially expand to a broader population of COPD patients in need.[37] Fixed-dose triple therapy may also improve a patient's health status by facilitating the adherence and persistence of this treatment modality over longer periods of time.

There are limitations to this observational study related to patient mobility and missing data. These limitations are often noted in real-world studies due to where data are collected for reasons other than medical research. Firstly, the data collected for this study were based on the cumulative counts of patients identified during the screening and follow-up periods. These patients may include permanent residents of the region, as well as temporary visitors who may have qualified for entry into our study cohort and who subsequently left during the study period. As a result, it is possible that certain treatment pathways in the long term may not have been fully captured among these temporary visitors. Furthermore, more than 60% of the patients entered the study cohort before the approvals of the fixed-dose triple therapy. Therefore, the treatment patterns were limited by the market access and drug availability. These results may change over time as new products get approved with increased accessibility. Additionally, subgroup treatment pattern assessments were not performed by disease severity, for prevalent and new users of triple therapy. And the effectiveness and safety of these treatments were not assessed in this study. Moreover, there was high missingness in FEV1 and smoking status capture, two factors that are essential in defining the GOLD classification and assessing COPD prognosis.[38,39] Previous literature has demonstrated that the never smokers with COPD are at lower risk of both moderate and severe exacerbations and death than former or current smokers,[40] leading to the occurrence and progression of COPD.[41] Finally, the Yinzhou database contains almost all health-related activities of its permanent residents therefore we believe the findings from this study are strongly representative of the population in Yinzhou. However, differences in clinical practices among physicians across regions could impact the generalizability of the study findings nationwide.

Our study provided valuable insights into the usage of COPD medications, especially triple therapy, in China. Future research may explore the treatment patterns, effectiveness, and safety in different patient groups to refine the identification of high-risk patients who might benefit most from triple therapy. Additionally, adherence and persistence of triple therapy may also be investigated to gain more insights and thus enhance the COPD patient care and improve clinical outcomes.

## Conclusion

Our study assessed treatment patterns and triple therapy utilization among patients with COPD in China using a database consisting of regional electronic health records. Among the patients with valid COPD treatment records during follow-up, the majority (68%) were treated with ICS+LABA dual therapy. Triple therapy was widely used in Chinese patients with COPD, most patients in this study switched to triple therapy from varied other treatment modalities. These findings provide valuable insights into clinical decision-making and evidence-based practice in Chinese COPD patients.

## Abbreviations

BDP/FF/GB, Beclometasone dipropionate + Formoterol fumarate + Glycopyrrolate bromide; BGF, Budesonide + Formoterol fumarate + Glycopyrrolate bromide; COPD, Chronic Obstructive Pulmonary Disease; FF/UMEC/VI, Fluticasone furoate + Umeclidinium bromide + Vilanterol trifenatate; GOLD, Global Initiative for Chronic Obstructive Lung Disease; ICF, Informed Consent Form; ICS, Inhaled Corticosteroid; IQR, Interquartile Range; LABA, Long-Acting β2 Agonists; LAMA, Long-Acting Muscarinic Antagonists; SABA, Short-Acting β2 Agonists; SAMA, Short-Acting Muscarinic Antagonist; SD, Standard Deviation; WHO, World Health Organization.

## Data Sharing Statement

The datasets generated and/or analyzed during the current study are not publicly available due to the protection of personal information and requirements from the data source.

## Ethics Approval and Informed Consent

A protocol for this research was approved by the Peking University Institutional Review Board (IRB) (IRB00001052-23112) and the Medical Ethics Committee (EC) of Zhongshan Hospital, Fudan University (B2023-206(2)).

## Consent for Publication

This retrospective real-world study was conducted using anonymized and de-identified data (existing electronic health records that are available as of the date of the Ethics Committee submission) without any additional prospective components for research purposes. Hence, the process did not necessitate obtaining informed consent since the study did not involve identifiable individuals. Accordingly, permission for the Informed Consent Form (ICF) waiver was obtained from the Peking University Institutional Review Board and the Medical Ethics Committee of Zhongshan Hospital before the initiation of the data collection process for this study.

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## Author Contributions

All authors made a significant contribution to the work reported, whether that is 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 article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and have agreed to be accountable for all aspects of the work.

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## Disclosure

The authors report no conflicts of interest in this work.

## References


1. Celli B, Fabbri L, Criner G, et al. Definition and nomenclature of chronic obstructive pulmonary disease: time for its revision. *Am J Respir Crit Care Med*. 2022;206(11):1317–1325. doi:10.1164/rccm.202204-0671PP
2. Huang Y, Niu Y, Wang X, Li X, He Y, Liu X. Identification of novel biomarkers related to neutrophilic inflammation in COPD. *Front Immunol*. 2024;15:1410158. doi:10.3389/fimmu.2024.1410158
3. Singh D, Han MK, Hawkins NM, et al. Implications of cardiopulmonary risk for the management of COPD: a narrative review. *Adv Ther*. 2024;41(6):2151–2167. doi:10.1007/s12325-024-02855-4
4. Yin P, Wu J, Wang L, et al. The burden of COPD in China and its provinces: findings from the global burden of disease study 2019. *Front Public Health*. 2022;10:859499. doi:10.3389/fpubh.2022.859499
5. Wang C, Xu J, Yang L, et al. Prevalence and risk factors of chronic obstructive pulmonary disease in China (the China Pulmonary Health [CPH] study): a national cross-sectional study. *Lancet*. 2018;391(10131):1706–1717. doi:10.1016/S0140-6736(18)30841-9
6. Liang Y, Sun Y. COPD in China: current status and challenges. *Arch Bronconeumol*. 2022;58(12):790–791. doi:10.1016/j.arbres.2022.04.001
7. From the global strategy for the diagnosis, management and prevention of COPD global initiative for chronic obstructive lung disease (GOLD) 2017: Available from: https://goldcopd.org. Accessed June 19, 2025.
8. From the global strategy for the diagnosis, management and prevention of COPD global initiative for chronic obstructive lung disease (GOLD) 2020: Available from: https://goldcopd.org. Accessed June 19, 2025.
9. From the global strategy for the diagnosis, management and prevention of COPD global initiative for chronic obstructive lung disease (GOLD) 2024: Available from: https://goldcopd.org. Accessed June 19, 2025.
10. Chronic Obstructive Pulmonary Disease Group of Chinese Thoracic S, Chronic Obstructive Pulmonary Disease Committee of Chinese Association of Chest P. [Guidelines for the diagnosis and management of chronic obstructive pulmonary disease (revised version 2021)]. *Zhonghua Jie He He Hu Xi Za Zhi*. 2021;44(3):170–205. Danish. doi:10.3760/cma.j.cn112147-20210109-00031
11. Suissa S, Ariel A. Triple therapy trials in COPD: a precision medicine opportunity. *Eur Respir J*. 2018;52(6):1801848. doi:10.1183/13993003.01848-2018
12. Lipson DA, Barnhart F, Brealey N, et al. Once-daily single-inhaler triple versus dual therapy in patients with COPD. *N Engl J Med*. 2018;378(18):1671–1680. doi:10.1056/NEJMoa1713901
13. Ferguson GT, Rabe KF, Martinez FJ, et al. Triple therapy with budesonide/glycopyrrolate/formoterol fumarate with co-suspension delivery technology versus dual therapies in chronic obstructive pulmonary disease (KRONOS): a double-blind, parallel-group, multicentre, Phase 3 randomised controlled trial. *Lancet Respir Med*. 2018;6(10):747–758. doi:10.1016/S2213-2600(18)30327-8
14. Rabe KF, Martinez FJ, Ferguson GT, et al. Triple inhaled therapy at two glucocorticoid doses in moderate-to-very-severe COPD. *N Engl J Med*. 2020;383(1):35–48. doi:10.1056/NEJMoa1916046
15. Martinez FJ, Rabe KF, Ferguson GT, et al. Reduced all-cause mortality in the ETHOS trial of budesonide/glycopyrrolate/formoterol for chronic obstructive pulmonary disease. a randomized, double-blind, multicenter, parallel-group study. *Am J Respir Crit Care Med*. 2021;203(5):553–564. doi:10.1164/rccm.202006-2618OC
16. Chen Y, Zhou L, Zhang X, et al. Effectiveness of budesonide/glycopyrrolate/formoterol fumarate in Chinese patients with chronic obstructive pulmonary disease. *B52 Evidence Therapeutic Strategies COPD*. 2024. A3818–A.
17. Schabert V, Shah S, Holmgren U, Cabrera C. Prescribing pathways to triple therapy in patients with chronic obstructive pulmonary disease in the United States. *Ther Adv Respir Dis*. 2021;15:17534666211001018. doi:10.1177/17534666211001018
18. Zeng Y, Cai S, Chen Y, et al. Current status of the treatment of COPD in China: a multicenter prospective observational study. *Int J Chron Obstruct Pulmon Dis*. 2020;15:3227–3237. doi:10.2147/COPD.S274024
19. Yang T, Cai B, Cao B, et al. REALizing and improving management of stable COPD in China: results of a multicentre, prospective, observational study (REAL). *Ther Adv Respir Dis*. 2023;17:17534666231178692. doi:10.1177/17534666231178692
20. Balcells E, Gimeno-Santos E, de Batlle J, et al. Characterisation and prognosis of undiagnosed chronic obstructive pulmonary disease patients at their first hospitalisation. *BMC Pulm Med*. 2015;15(1):4. doi:10.1186/1471-2466-15-4
21. Falk J, Dik N, Bugden S. An evaluation of early medication use for COPD: a population-based cohort study. *Int J Chron Obstruct Pulmon Dis*. 2016;11:3101–3108. doi:10.2147/COPD.S123643
22. Ford ES, Mannino DM, Giles WH, Wheaton AG, Liu Y, Croft JB. Prescription practices for chronic obstructive pulmonary disease: findings from the national ambulatory medical care survey 1999-2010. *COPD*. 2014;11(3):247–255. doi:10.3109/15412555.2013.840570
23. Yu AP, Guerin A, Ponce de Leon D, et al. Therapy persistence and adherence in patients with chronic obstructive pulmonary disease: multiple versus single long-acting maintenance inhalers. *J Med Econ*. 2011;14(4):486–496. doi:10.3111/13696998.2011.594123
24. Lin H, Tang X, Shen P, et al. Using big data to improve cardiovascular care and outcomes in China: a protocol for the Chinese electronic health records research in Yinzhou (CHERRY) study. *BMJ Open*. 2018;8(2):e019698. doi:10.1136/bmjopen-2017-019698
25. Liu G, Liu Z, Zhao H, et al. The effectiveness of influenza vaccine among elderly Chinese: a regression discontinuity design based on Yinzhou regional health information platform. *Hum Vaccin Immunother*. 2022;18(6):2115751. doi:10.1080/21645515.2022.2115751
26. Cheng W, Duan J, Zhou A, et al. Real-world effectiveness of inhalation therapy among patients with symptomatic COPD in China: a multicenter prospective study. *Front Pharmacol*. 2021;12:753653. doi:10.3389/fphar.2021.753653
27. Nannini LJ, Lasserson TJ, Poole P. Combined corticosteroid and long-acting beta(2)-agonist in one inhaler versus long-acting beta(2)-agonists for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev*. 2012;2012(9):CD006829. doi:10.1002/14651858.CD006829.pub2
28. Nannini LJ, Poole P, Milan SJ, Kesterton A. Combined corticosteroid and long-acting beta(2)-agonist in one inhaler versus inhaled corticosteroids alone for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev*. 2013;2013(8):CD006826. doi:10.1002/14651858.CD006826.pub2
29. Vestbo J, Leather D, Diar Bakerly N, et al. Effectiveness of fluticasone furoate-vilanterol for COPD in clinical practice. *N Engl J Med*. 2016;375(13):1253–1260. doi:10.1056/NEJMoa1608033
30. Zheng Y, Zhu J, Liu Y, et al. Triple therapy in the management of chronic obstructive pulmonary disease: systematic review and meta-analysis. *BMJ*. 2018;363. doi:10.1136/bmj.k4388

31. Evans KA, Pollack M, Portillo E, et al. Prompt initiation of triple therapy following hospitalization for a chronic obstructive pulmonary disease exacerbation in the United States: an analysis of the PRIMUS study. *J Manag Care Specialty Pharm*. 2022;28(12):1366–1377. doi:10.18553/jmcp.2022.28.12.1366
32. Tamondong-Lachica DR, Skolnik N, Hurst JR, et al. GOLD 2023 update: implications for clinical practice. *Int J Chron Obstruct Pulmon Dis*. 2023;18:745–754. doi:10.2147/COPD.S404690
33. Dhalwani N, Cabrera C, Booth A, Petrella R, Lambrelli D. Characteristics and treatment patterns of newly diagnosed COPD patients in Canada. *Eur Respir J*. 2019;54:PA3385.
34. Monteagudo M, Barrecheguren M, Solntseva I, et al. Clinical characteristics and factors associated with triple therapy use in newly diagnosed patients with COPD. *NPJ Prim Care Respir Med*. 2021;31(1):16. doi:10.1038/s41533-021-00227-x
35. Bogart M, Stanford RH, Laliberté F, Germain G, Wu JW, Duh MS. Medication adherence and persistence in chronic obstructive pulmonary disease patients receiving triple therapy in a USA commercially insured population. *Int J Chronic Obstr*. 2019;Volume 14:343–352. doi:10.2147/COPD.S184653
36. AstraZeneca. AstraZeneca's triple-combination therapy approved in China for patients with COPD. 2019.
37. Mannino D, Bogart M, Wu B, et al. Adherence and persistence to once-daily single-inhaler versus multiple-inhaler triple therapy among patients with chronic obstructive pulmonary disease in the USA: a real-world study. *Respir Med*. 2022;197:106807. doi:10.1016/j.rmed.2022.106807
38. Gülşen A. Pulmonary function changes in chronic obstructive pulmonary disease patients according to smoking status. *Turk Thorac J*. 2020;21(2):80–86. doi:10.5152/TurkThoracJ.2019.18135
39. Doherty DE. A review of the role of FEV 1 in the COPD paradigm. *COPD*. 2008;5(5):310–318. doi:10.1080/15412550802363386
40. Nielsen AO, Lange P, Hilberg O, Farver-Vestergaard I, Ibsen R, Lokke A. COPD and smoking status - it does matter: characteristics and prognosis of COPD according to smoking status. *Chronic Obstr Pulm Dis*. 2024;11(1):56–67. doi:10.15326/jcopdf.2023.0433
41. Song Q, Chen P, Liu XM. The role of cigarette smoke-induced pulmonary vascular endothelial cell apoptosis in COPD. *Respir Res*. 2021;22(1):39. doi:10.1186/s12931-021-01630-1