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CONFIDENTIAL

HEALTH OUTCOMES STUDY PROTOCOL - QUALITATIVE RESEARCH

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Description: COPD maintenance treatment patterns in China
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Investigator Protocol Agreement Page

- I confirm agreement to conduct the study in compliance with the protocol.
- I acknowledge that I am responsible for overall study conduct. I agree to personally conduct or supervise the described clinical study.
- I agree to ensure that all associates, colleagues and employees assisting in the conduct of the study are informed about their obligations. Mechanisms are in place to ensure that site staff receives the appropriate information throughout the study.

Investigator Name:

_____

_____ _____

Investigator Signature Date (DD-MMM-YYYY)

PROTOCOL SYNOPSIS

Unique Identifier	213550
Abbreviated Title	COPD maintenance treatment patterns in China
GSK Product	Trelegy
Rationale	Pharmacological treatment of COPD, as perceived by physicians in China, appears very complicated, especially with the increasing number of therapeutic options available and recommendations to personalise treatment of COPD patients to individual needs. Physicians also use different treatment strategies for symptom reduction and exacerbation prevention. For example, many use a step-up approach but some use intensive treatment initially, followed by step down. In addition, treatments depend on the socio-economic condition of the patient such as occupation, educational level, income and environment. A further complication in China is that there are different tiers of hospitals with different formularies and patients move between hospitals and doctors very readily. In addition, the re-attendance rate to the same clinic/physician is low, resulting in little continuity of care. Therefore, this study is conducted to gain an adequate understanding of the complex COPD management environment and doctors' treatment strategy of COPD in China.
Objectives (Primary, Secondary)	**Primary** To quantify the pattern of COPD maintenance treatment prescribing in different patient groups in Tier 2 and 3 hospitals in China **Secondary** • To examine factors (including disease severity and socio-economic factors) that are associated with different patterns of COPD maintenance treatment • To assess the proportion of patients whose prescribed maintenance treatment is stepped up, stepped down, switched, stopped or remains the same across the different study time points • Assess the disease burden of the patients

	• To assess the proportion of patients receiving each treatment class at 3 months.
Study Design	This will be a 3-month, multicentre, prospective, low-interventional study in newly diagnosed and previously diagnosed patients with COPD presenting to clinics, either in stable state or with an acute exacerbation, in Tier 2 and 3 hospitals in China. The study will be conducted at around 35 sites (±5 sites). For the primary analysis, the patients will be categorised into 3 cohorts: 1. Cohort 1: Patients presenting with stable disease 2. Cohort 2: Patients presenting with a moderate exacerbation not requiring hospitalization 3. Cohort 3: Patients requiring hospitalisation for an exacerbation
Study Population	**Inclusion Criteria** Male or female patients with ≥40 years of age at the time of signing the informed consent with a diagnosis of COPD confirmed by spirometry (According to GOLD 2019 criteria). **Exclusion Criteria** • Patients with a current primary diagnosis of asthma, active tuberculosis, bronchiectasis, lung cancer or other active pulmonary disease, other unstable diseases or cognitive behaviour, which could influence COPD assessment test (CAT) and lung function results in the view of their physicians. • Patients who experienced a physician-treated moderate or severe COPD exacerbation within the last 1 month before screening. • Patient participating in another COPD clinical study using investigational medication and/or disease management process.
Data Source	**Primary Endpoints** • The data source will be the study case record form (CRF) • COPD prescription for maintenance therapy (Long-Acting Muscarinic Antagonist [LAMA], Long-Acting Beta-Agonist [LABA]; dual bronchodilator, inhaled corticosteroid [ICS]/ Long-Acting Beta-Agonist [LABA], triple therapy, theophylline and n-acetyl cysteine/carbocysteine) at baseline.

	• COPD prescription for maintenance therapy collected at 3 months (all patients) and at 1 week after a moderate exacerbation or on discharge following hospitalisation. **Secondary Endpoints** • Data source mentioned in primary endpoints • FEV1, exacerbations in previous 1 year, CAT score, Modified Medical Research Council (mMRC) score, co-morbidity, socio-economic status, COPD medication history (within past 1 month)
Data Analysis Methods	The number and percentage of patients who use the maintenance treatment at each visit will be summarized. Moreover, for those who use maintenance treatment, the number and percentage of patients will be summarized for each of the following pattern of maintenance treatment: • Long-Acting Muscarinic Antagonist [LAMA] • Long-Acting Beta-Agonist [LABA] • Dual bronchodilator • Inhaled corticosteroid [ICS]/ Long-Acting Beta-Agonist [LABA] • Triple therapy • Theophylline • N-acetyl cysteine/carbocysteine The results for patients with stable disease and patients with exacerbation at baseline will be analysed separately for the following visits: baseline visit, 1-week follow up (for moderate exacerbations) and discharge follow-up (for hospitalised exacerbations). The results for patients with stable disease and patients with exacerbation will be pooled together for analysis for 3-month follow-up visit.
Sample Size and Power	For this study, around 1500 patients with COPD will be enrolled including stable patients (~50% of the total patients) and patients with exacerbations (~50% of the total patients). All enrolled patients will be included in the analysis. A large overall sample size was chosen to ensure adequate patient representation across China. It is estimated that 750 patients each from tier 2 and tier 3 hospitals will be enrolled to provide adequate representation on healthcare status for COPD in China. After 500 patients have been

	recruited, the numbers will be reviewed to assess whether an adequate number of patients from each of the 3 cohorts have been enrolled for each tier of hospital. Recruitment policy might be changed to ensure an adequate distribution of patients.
Limitations	Potential limitations have been listed below. 1) The study has covered major Chinese provinces as comprehensively as possible, choosed 1-2 sites from major Chinese province but this may not be fully representative of all the Tier 2&3 hospitals in each province. 2) The study includes only those Tier 2 hospitals at a minimum have respiratory department which have LAMA and ICS/LABA and spirometry available; however, this will not fully reflect COPD management in all Tier 2 hospitals, because not all currently have such drugs available. This situation is changing so that all Tier 2 hospitals will have these treatments available relatively soon. 3) It is a 3-month follow-up study and the duration is adequate to measure short-medium term changes, but COPD requires lifelong treatment, so this reflects only a short period of a patient's management. 4) The adherence data is reliant on the patients accurate reporting of which prescribed treatments they are taking, there can be an underestimation or overestimation of adherence to medication.

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ABBREVIATIONS

AE	Adverse Event
BMI	Body Mass Index
CAT	COPD assessment test
CE	Concept Elicitation
CFR	Code of Federal Regulations
CI	Confidence Interval
COPD	Chronic Obstructive Pulmonary Disease
CRF	Case Report Form
CVD	Cardiovascular Disease
DECAF Score	Dyspnoea, Eosinopenia, Consolidation, Acidaemia and atrial Fibrillation (DECAF) Score
eMRCD	Extended MRC Dyspnea Scale
ER	Emergency room
FEV1	Forced expiratory volume in one minute
FSFV	First subject first visit
GCP	Good Clinical Practice
GERD	Gastroesophageal Reflux Disease
GSE	General Self-Efficacy Scale
GP	General Physician
GSK	GlaxoSmithKline
HIPAA	Health Insurance Portability and Accountability Act
ICF	Informed Consent Form

ICH	International Conference on Harmonization
ICS	Inhaled corticosteroid
IEC	Independent Ethics Committee
IHD	Individual human data
IPAQ	International physical activity questionnaire
IRB	Institutional Review Board
LABA	Long-acting beta agonists
LAMA	Long-acting muscarinic antagonist
LSLV	Last subject's last visit
mMRC	Modified Medical Research Council
OR	Odds Ratio
OSAS	Obstructive Sleep Apnea Syndrome
SAMA	Short-acting muscarinic antagonist
SABD	Short acting bronchodilator
OPD	Outpatient department
PHQ9	The patient health questionnaire
PI	Principle Investigator
PII	Personally Identifiable Information
PRO	Patient Reported Outcome
PVP	Pharmacovigilance Program
V	Visit

Trademark Information

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COPD assessment test (CAT)	

1 INTRODUCTION/BACKGROUND

Chronic obstructive pulmonary disease (COPD) is a preventable and treatable disease characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases [GOLD, 2019]. This is associated with increased morbidity and risk of early death [Agusti, 2005; Qaseem, 2011; Rodríguez, 2010].

COPD is the third most prevalent disease in China after hypertension and diabetes [Wang 2018]. A study conducted between 2012-2015 found that 8.6% of Chinese aged ≥20 years met spirometry-defined COPD criteria and the COPD prevalence in adults ≥40 years was 13.7%. This amounts to 99.9 million people with potential COPD in China [Wang, 2018]. Annually, around 8 million Chinese patients are hospitalised due to COPD exacerbations, but a larger but unquantified number of patients experiencing moderate exacerbations are treated as an outpatient. A survey in China, reported that the average exacerbation rate in patients diagnosed with COPD was approximately 2.5 exacerbations per year per patient [Jia, 2018].The frequency of exacerbations may be influenced by patients' level of education and treatment adherence, physicians' treatment decisions and disparity in prescription practice [Cai, 2015; Fang, 2012; Zha, 2019]. The failure of patients and physicians to recognise the significance of exacerbations adds to the challenges in COPD treatment.

Hospitalisation due to COPD exacerbations is associated with high healthcare costs. In China, patients with an acute exacerbation of COPD are admitted to a Tier-3 hospital with an average total cost of $1323 per admission [Yang, 2012]. Reducing hospitalisation through more effective maintenance treatment would greatly reduce healthcare costs in China. Appropriate management of COPD starts with diagnosis. In a study conducted in Beijing, 29% of the patients with high-risk COPD were undiagnosed [Rui, 2014] and many physicians do not consider spirometry as the most appropriate test when a diagnosis of COPD is suspected [Wang, 2018].

In China, there are three tiers of hospital. Tier 1 hospitals have very basic facilities and limited formularies for the long-term management of COPD. Tier 2 hospitals have more facilities and get access to a wider range of treatments, which usually includes the main treatment classes for COPD, but not the latest therapies. The Tier 3 hospitals have the full range of COPD therapies; however, the government is actively encouraging a shift of COPD patients from Tier 3 to Tier 2 hospitals. One more complication in China is that patients move between hospitals and doctors very readily, resulting in very little continuity of care. The experts with an interest in COPD are in a view that the re-attendance rate to the same clinic/physician is very low (approx below 50%).

In a prescription survey conducted between 2010 and 2011 in China, it was observed that, as elsewhere in the world, physicians do not follow GOLD recommendations. [Fang, 2012]. In

addition, the economic burden poses a big challenge, since the social insurance bureau and private companies in China generally reimburse treatment costs due to hospitalisation, rather than maintenance treatment. Such policies are one of the leading causes of under-prescribing of drugs by physicians, because patients fail to receive adequate reimbursement [Li, 2018] and this leads to suboptimal treatment.

Another important factor is the patients' adherence to maintenance therapy, which remains a substantial barrier to optimal disease control. Despite evidence that adherence to inhaled COPD therapy is associated with improved symptom control, lung function and reductions in healthcare resource utilisation and costs, patients non-compliance to treatment remains a major problem [Davis, 2017;

Mäkelä, 2013; Toy, 2011]. Studies in patients with COPD in the Western countries have shown that around 50% patients have suboptimal adherence to treatment [Restrepo, 2008], this is likely to be further low in China, due to low educational qualification of the patient attending COPD units.

Smoking is a major risk factor for COPD. In China, in a study by Jiangna et al, around 82% of the patients recruited in tertiary care hospital were current or ex-smokers. However, there are COPD patients who are never-smokers [GOLD, 2020], due to a range of causes including but not limited to, childhood chest illnesses, passive cigarette, biomass fuel exposure and pollution. Therefore, to ensure an adequate representation of treatment for COPD in China, all patients with a clinical diagnosis of COPD, confirmed on spirometry, will be recruited and their smoking history will be recorded.

Rationale

In recent years, physicians in China have perceived pharmacological treatment of COPD to be very complicated, especially with the increasing number of therapeutic options available and recommendations to personalise treatment. Physicians also use different treatment strategies. A further complication is that treatment will depend on socio-economic factors such as occupation, educational level, income and patients' preference. Besides, patients move between hospitals and doctors very readily, resulting in very little continuity of care. The experts with an interest in COPD are in view that the re-attendance rate to the same clinic/physician is very low (approx. below 50%).

To improve COPD management in China, it is important to understand current patterns of COPD medication prescription and assess the effect of patient characteristics and other factors on treatment decisions made by physicians. Whilst data on physicians' prescribing practises can be obtained through surveys or market research, this can't capture the impact of the broad range of factors that a physician may take into account when deciding on treatment for an

individual patient, hence answers to paper-based scenarios may not accurately reflect behaviour in routine practice. In China, there are currently no databases that would permit analysis of prescribing to well characterised COPD patient groups. A prospective study of actual prescribing at an individual patient level is required, coupled with an assessment of the patient's clinical severity and socio-economic status. This will allow a detailed analysis of the maintenance treatment used for different patient groups and give an insight into the factors that physicians take into account when deciding on treatment.

There are three main clinical scenarios seen in Chinese hospitals:

1. Patients presenting with stable disease
2. Patients presenting with a moderate exacerbation
3. Patients requiring hospitalisation for an exacerbation

In each scenario, the patients may be treated differently, so it is necessary to determine prescribing practices of the physician in each case and identify factors associated with the prescription. It is also necessary to know how the maintenance treatment of the patients changes over time, and the level of the patient's adherence to their prescriptions, as this thought to be low in China, but has not been measured.

In China clinical practice, some patients may be admitted to hospital with an exacerbation but not because of the severity of the exacerbation (i.e. by the request of the patient). To ensure that patients are only recruited to the study because of the severity of the exacerbation, an inclusion criterion of the requirement for intravenous therapy is needed, since this treatment cannot be administered at home.

2 RESEARCH OBJECTIVES

2.1 Primary Objective:

- To quantify the pattern of COPD maintenance treatment prescribing in different patient groups in Tier 2 and 3 hospitals in China

2.2 Secondary Objectives

- To examine factors (including disease severity and socio-economic factors) that are associated with different patterns of COPD maintenance treatment
- To assess the disease burden of patients (using baseline data)
- To assess the proportion of patients whose prescribed maintenance treatment is stepped up (adding another maintenance treatment), stepped down (withdraw any of the maintenance medication but kept the maintenance treatment), switch (between

LAMA+LABA and ICS/LABA), stopped (stop all maintenance treatment) or remains the same across the different study time points

- To assess the proportion of patients receiving each treatment class at 3 months

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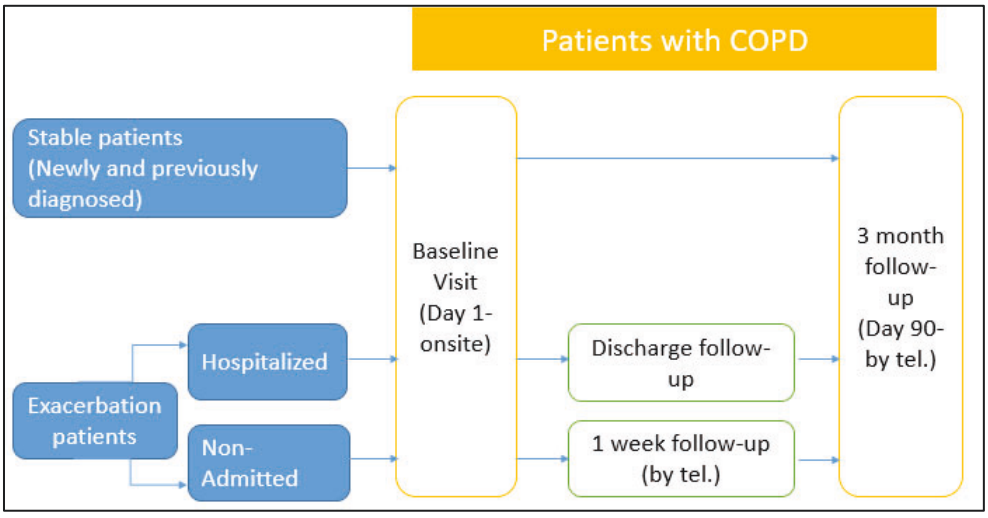
3 RESEARCH METHODOLOGY

3.1 Study Design

This will be a 3-month, multicentre, prospective study in newly diagnosed and previously diagnosed patients with COPD presenting to clinics, either in a stable state, defined as no exacerbation for at least 1 month, or with acute exacerbation, in Tier 2 and 3 hospitals distributed across China. The study will be conducted at around 35 sites (±5 sites). The patients will be categorised into 3 cohorts:

1. Cohort 1: Patients presenting with stable disease (newly and previously diagnosed)
2. Cohort 2: Patients presenting with a moderate acute exacerbation not requiring hospitalization
3. Cohort 3: Patients requiring hospitalisation for an acute exacerbation



Tel.-Telephone

Figure 1: The study schematic

At site evaluation (conducted to evaluate if the sites can be included in the study), the types of medical insurance covered by the hospital, types of COPD maintenance medication available to be supplied to patients and reimbursement rate for each out-patient and in-patient medication will be collected before patient recruitment.

3.2 Study Population

The study population comprises COPD patients in stable status or with acute exacerbation in tier 2 and tier 3 hospitals. Stable status at enrolment is defined as no exacerbation events in the preceding month. An exacerbation of COPD is as an acute worsening of respiratory symptoms that results in additional therapy. Moderate exacerbation is defined as worsening of symptoms for which a patient seeks medical care and is treated by antibiotics and/or systemic corticosteroids /or corticosteroids nebulization, severe exacerbation is defined as patient requires hospitalization or visits the emergency room (ER)

3.2.1 Eligibility Criteria

3.2.1.1 Inclusion Criteria

In order to be eligible to participate in this study, a subject must meet all of the following criteria:

- Patients ≥40 years of age
- Male or female
- A diagnosis of COPD confirmed by spirometry (According to GOLD 2019 criteria) in Tier 2 and Tier 3 hospitals
- In hospitalized patients, recruit only patients who receive any intravenous therapy
- A signed and dated written informed consent must be obtained from the patient prior to study participation
- Patients can communicate normally

3.2.1.2 Exclusion Criteria

A subject who meets any of the following criteria will be excluded from participation in this study:

- Current primary diagnosis of asthma, active tuberculosis, bronchiectasis, lung cancer or other active pulmonary disease
- Other unstable diseases or cognitive behaviour, which could influence CAT and lung function results (judged by physicians)
- Experienced a moderate/severe COPD exacerbation treated by a physician within last 1 month

- Currently participating in another COPD clinical study, which provides the patient investigational medication and/or disease management

3.2.2 Sampling

For this study, around 1500 patients with COPD will be enrolled including stable patients and patients with exacerbations. It is planned that approximately equal number of patients will be recruited from Tier 2 and Tier 3 hospitals. After 500 patients have been recruited a review will be carried out to assess whether an adequate number of patients from each of the 3 cohorts defined in section 3.1 has been enrolled. At this point, recruitment policy might be changed to ensure an adequate distribution across type of hospital and type of patient. Thereafter, recruitment to each cohort will be monitored weekly and further corrective action will be taken if needed.

At least one site in each of the main provinces of China will be selected. There is a variability of spirometry and inhaled therapy availability across Tier 2 hospitals, although this is improving. As the Government is actively encouraging patients to shift from Tier 3 to Tier 2 hospitals, the study will only include Tier 2 hospitals that, at a minimum have respiratory department, supply of LAMA and ICS/LABA, and facilities for spirometry, since this will be the minimum standard of care for patients with COPD in Tier 2 hospitals in the future.

3.2.2.1 Patients presenting with stable disease

Baseline visit (Day 1):

Newly or previously diagnosed patients with stable COPD who attend the clinic will be screened by the study physician. Once eligible patients have been identified, informed consent will be obtained. The physician will then make their treatment decision, before any other study assessments are made.

This visit will be considered as Baseline visit (V1). During the Baseline visit, the following information will be collected;

1. Demography
2. Time since first COPD diagnosis
3. Co-morbidities
4. COPD exacerbation history in prior 12 months
5. COPD medication history (within past 1 month）
6. Concomitant medication
7. COPD medication prescribed at baseline visit (including the drugs prescribed this time and the drugs that the subject needs to continue to use)

8. Smoking history
9. Spirometry (within 7 days of enrollment)†
10. Modified Medical Research Council (mMRC) dyspnea scale, CAT
11. Socio-Economic status (refer to 3.3.2.10)
12. Patient questionnaire and survey ††
13. Physician survey ††
14. Collect spontaneously AE/SAE reports on GSK products
15. Maintenance treatment class availability in hospital internal pharmacy†††
16. Prescribing physician's name†††.

† FEV_1 performed within 6 months before the index date will be acceptable. Index date is the date when physician collect data for baseline. A 7-day time window was set between the time when the V1 lung function results were obtained and the day of enrollment to ensure that there was sufficient time to obtain the lung function report results to deal with the interference of the COVID-19 epidemic on the study.
†† Patient questionnaires include International physical activity questionnaire (IPAQ), The patient health questionnaire (PHQ9), General self-efficacy scale. Patient's survey is developed by the study initiator. The physician's survey is developed by the study initiator.
††† Data will not be collected from patient

3-month Follow-up visit (Day 90 ± 7):

All patients will be followed-up telephonically after 3 months. Following information will be collected:

1. Current COPD medication taken by the patient, including prescription of current treatment and time of prescription, physician and hospital name#.
2. COPD Clinic revisit times and reason
3. Frequency of COPD exacerbation between baseline visit and 3 months follow up
4. Reason for the last hospital visit (i.e. routine or exacerbation)
5. Identify prescribed treatments that the patients did not take on the day of the call*.
6. CAT
7. Patient questionnaire and survey †
8. Collect spontaneously AE/SAE reports on GSK products

A photo of the physician's prescription which includes COPD medication and medical records will provide all that information. If medical records couldn't' be provided, CRC can collect this information by patients' recall.

* This will be evaluated by Clinical research coordinator (CRC) from the photo of the physicians' prescription collected from the patients.
† Patient questionnaire is General self-efficacy scale. Patient's survey is developed by the study initiator

Note: During the 3-month period, there might be changes in prescription, but only the current treatment prescribed to the patient and the patient's use of the treatment on the day or before the day of the call will be documented.

If the patient cannot be contacted telephonically at the first attempt, a minimum of 3 attempts should be made. This should be documented in a medical note. If the subject meets the conditions to withdraw from the project, no further data will be collected from the subject.

3.2.2.2 Patients presenting with a moderate exacerbation (non-hospitalized)

Baseline visit (Day 1)

Data will be collected as per stable patient in section 3.2.2.1- Baseline visit. If a FEV_1 measurement from the last 6 months is not available, spirometry will be performed at the discretion of treating physician, dependent on whether it is possible or reasonable for the patient to do this.

1-week follow-up (Day 8 ± 3)

This follow-up visit will be telephonic on day 8 (+3 days window). The patient will be interviewed to obtain the following details;

1. Any visit to hospital for COPD treatment in the last week? (Yes/No)
    a. If Yes - name of the hospital(s), physician's name, date(s) and physician prescription(s). These can be all collected by taking a picture of the prescription
2. CAT

3. Collect spontaneous AE/SAE reports on GSK products

If the patient cannot be contacted at first attempt, a minimum of 3 attempts should be made. This should be documented in a medical note.

3-month Follow-up (Day 90 ± 7)

Patients will be followed-up telephonically after 3 months. Data will be collected as per section 3.2.2.1- Follow-up visit for stable COPD patients.

Note: During the 3-month period, there might be changes in prescription, but only the current treatment prescribed to the patient and the patient's use of the treatment on the day or before the day of the call will be documented. If the subject meets the conditions to withdraw from the project, no further data will be collected from the subject.

3.2.2.3 Patients requiring hospitalisation for an exacerbation

Baseline visit (Day 1)

Baseline information as per section 3.2.2.1 will be collected on admission to the hospital, but if the patient is too ill, then baseline data will be collected before discharge. In the event that no historical FEV_1 data within 6 months are available, spirometry will be performed if it is possible or reasonable for the patient to *do.*Dyspnoea, Eosinopenia, Consolidation, Acidaemia and atrial Fibrillation (DECAF) Score will be collected for the hospitalized patients during hospitalization period.

Discharge Follow-up (Discharge day ± 1)

At the day of discharge (±1 day) patient will be interviewed face to face for obtaining data as follow;

1. Discharge date
2. COPD prescription at discharge (including the drugs prescribed this time and the drugs that the subject needs to continue to use)
3. CAT
4. Concomitant medication review
5. Total direct cost of the hospitalization
6. Medical insurance reimbursement amount
7. All other data under 3.2.2.1 (if not already collected)
8. Collect spontaneous AE/SAE reports on GSK products
9. Spirometry if no spirometry record within 6 months before baseline

3-month Follow-up (Day 90 ± 7)

Patients will be followed-up telephonically after 3 months. Data will be collected as per section 3.2.2.1- Follow-up visit.

Note: During the 3-month period, there might be changes in prescription, but only the current treatment prescribed to the patient and the patient's use of the treatment on the day or the day before of the call will be documented. If the subject meets the conditions to withdraw from the project, no further data will be collected from the subject.

The sampling plans specified in sections 3.2.2.1-3.2.2.3 are summarised in Table 1.

Table 1: Visit & Observations recording

Patients classification	Baseline Visit	1-week Follow-up or discharge Follow-up ±3 days	3-month Follow-up (Telephonic) ±7 days

Stable patients (Newly and previously diagnosed)	Demography, time since first COPD diagnosis, co-morbidities, COPD exacerbation and medication history, concomitant medication, FEV1%pred, CAT score and mMRC, medicines prescribed at visit, smoking status, socio economic status, patient survey and questionnaire, physician survey, inhaler availability, spontaneous AE/SAE report collection, Maintenance treatment class availability in hospital internal pharmacy, prescribing physician's name.	Not required	**<u>Telephone</u>** CAT score; current treatment taken by patient, the prescription of current treatment and time of prescription (or last hospital visit time and prescription); Name of hospital and name of physician; COPD clinic revisit times and reason, Frequency of COPD exacerbation between baseline visit and 3 months follow up, patient survey, concomitant medication review, spontaneous AE/SAE report collection
Exacerbation Patients (Non-Admitted)	Demography, time since first COPD diagnosis, co-morbidities, COPD exacerbation and medication history, concomitant medication, FEV1%pred*, CAT score and mMRC, medicines prescribed at visit, smoking status, socio economic status, patient survey and questionnaire, physician survey, inhaler availability, spontaneous AE/SAE report collection, Maintenance treatment class availability in hospital internal pharmacy, prescribing physician's name.	**<u>Telephone</u>** CAT score, any visit to hospital(Y/N), If Yes - name of the hospital(s), date(s) and physician prescription(s); spontaneous AE/SAE report collection	
Exacerbation patients (Hospitalized)**	Demography, time since first COPD diagnosis, co-morbidities, COPD exacerbation and medication history, concomitant medication, FEV1%pred*, CAT score and mMRC, medicines	**<u>Onsite</u>** CAT score Prescription at discharge, discharge date spontaneous	

	prescribed at visit, smoking status, socio economic status, Dyspnoea, Eosinopenia, Consolidation, Acidaemia and atrial Fibrillation (DECAF) Score, patient survey and questionnaire, physician survey, inhaler availability**, spontaneous AE/SAE report collection, Maintenance treatment class availability in hospital internal pharmacy, prescribing physician's name.	AE/SAE report collection, Concomitant medication, Total direct cost of the hospitalization, Medical insurance reimbursement amount	

* If FEV1 data is not available, it will be performed at the discretion of treating physician/collected during discharge

** The baseline information can be collected at discharge

3.3 Data Source / Data Collection

3.3.1 Endpoints data source

3.3.1.1 Primary Endpoints

- The data source will be the study case record form (CRF)
- The prescription for COPD maintenance therapy, grouped into one or more of the following treatment classes: (Long-Acting Muscarinic Antagonist [LAMA], Long-Acting Beta-Agonist [LABA], dual bronchodilator, inhaled corticosteroid [ICS]/ Long-Acting Beta-Agonist [LABA], triple therapy, theophylline and n-acetyl cysteine/carbocysteine) at baseline. The categories will be binary, e.g. treatment class used: Yes/No.
- COPD prescription for maintenance therapy collected at 3 months (all patients) and at 1 week after a moderate exacerbation or on discharge following hospitalisation.

3.3.1.2 Secondary Endpoints

- This will include the prescribing data listed in 3.3.1.1
- FEV1, exacerbations in previous 1 year, medication history within 1 month before baseline visit, CAT score, mMRC score, DECAF score in hospitalised patients, co-morbidity, socio-economic status.
- The change in treatment over 3 months, (baseline medication will be used, as described, coupled with current prescribing collected at telephone interview at 3 months).

CCI [redacted]

3.3.2 Exposure and outcomes

3.3.2.1 Demographics

- Sex: Male, Female
- Age, years (below 65 years old vs. 65 years old and above)
- Height, meters
- Weight, kg
- Body mass index (BMI=kg/m^2, BMI<18.5 underweight, BMI18.5~23.9 normal, BMI≥24 overweight, BMI≥28 obesity)
- Smoking status: never a smoker; former smoker (previously smoked and has not smoked for at least 6 months prior to this visit); current smoker (10 pack years and smoked within 6 months of this visit); the number of pack years for former smoker and current smoker should be calculated (round up to the nearest integer)
- Co-morbid diseases: Cardiovascular Disease (CVD defined as ischemic heart disease, heart failure, atrial fibrillation, hypertension), Diabetes, Hyperlipemia, Anxiety, Depression, Gastroesophageal reflux disease (GERD), obstructive sleep apnea syndrome (OSAS), concurrent asthma with COPD, past history of tuberculosis.
- Class of maintenance treatment available at hospital internal pharmacy

3.3.2.2 COPD assessment test (CAT):

The CAT is an 8-item unidimensional measure of health status impairment in patients with COPD. It is applicable worldwide. The development of the CAT has involved well accepted methodologies used to develop psychometric tools [Jones, 2009a; Jones, 2009b]. With CAT, patients are scored on eight items (cough, phlegm, chest tightness, breathlessness, activity limitation, confidence, sleep and energy) on a scale of 0-5 depending on their impact. The sum of scores for each item gives the patient's impact score ranging from 0 CCI [redacted] to 40 CCI [redacted]

After being instructed how to use the CAT (following the COPD assessment test manual www.CATestonline.org), the subjects will complete it by themselves, without supervision or assistance from investigator. If the CAT is normally used by the investigator in their routine clinical work, they should use it as they would do normally; if the investigator does not

routinely use the CAT, it should be completed after the treatment decision has been made. The investigator should check whether the subjects complete all items before the patient leaves.

3.3.2.3 Modified British Medical Research Council (mMRC) Questionnaire

The mMRC was developed in 1960 [Fletcher, 1960], and relates well to other measures of health status [Bestall, 1999] and predicts future mortality risk [Sundh, 2012; Nishimura, 2002]. With mMRC, patients are scored on a scale of 0-4 depending on their disability due to shortness of breath from 0 CCI [redacted] to 4 CCI [redacted]

The mMRC will be completed by each patient by themselves, without supervision, after the CAT. If the mMRC is normally used by the investigator in their routine clinical work, they should use it as they would do normally; if the investigator does not routinely use the mMRC, it should be completed after the treatment decision has been made. The investigator should check whether the patient has completed the mMRC adequately but cannot assist in completing it.

3.3.2.4 Spirometry:

Spirometry data will be obtained for all patients at each site. If lung function data are available within the previous 6 months, this should be recorded, and no test will be required at the study visit. If previous FEV_1 data are not available and the patient cannot perform adequate spirometry because they are being hospitalized for an exacerbation, this will be performed before discharge from hospital.

Subjects should wear a nose clip while performing spirometry maneuvers. For FEV_1 and FVC determinations, at least 3 acceptable spirometry efforts (with no more than 8) should be obtained. Acceptable spirometry efforts should have a satisfactory start of test and end of test (i.e, a plateau in the volume-time curve) and should be free from artifacts due to cough, early termination, poor effort, obstructed mouthpiece, equipment malfunction, or other reasons [

Miller, 2005;Pelligrino, 2005].The largest FEV_1 and FVC from the 3 acceptable efforts should be recorded, even if they do not come from the same effort.

Based on the spirometry results, subjects will be stratified into airflow limitation category (Gold 1 - Gold 4) as per Table 2 .

CCI - This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by third party copyright laws and therefore have been excluded.

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3.3.2.5 Physician survey

Physician will be asked questions on why they follow their prescription practices. The survey will give brief idea on grounds which physicians prescribe treatment to patients.

- In addition to the severity of the patient's disease, which factors have influenced your prescription for THIS patient? (choose one or more options)
  A. Patient or family 's economic condition
  B. Patient's reimbursement position
  C. Drug availability of your hospital
  D. Patient's ability to use the inhaler
  E. Patient's preference

- If none of the above factors applies, which treatment would you choose for THIS patient? (Choose one option)
  A. None
  B. SABA or SAMA (or both)
  C. LAMA or LABA
  D. LAMA+LABA
  E. ICS+LABA
  F. ICS+LABA+LAMA

3.3.2.6 Patient survey and questionnaire

To gain a better understanding of patient-related factors including socioeconomic status, knowledge of COPD and ideas on COPD treatment, a patient survey developed by the study initiator will be administered, together with questionnaires at the baseline visit and at the 3-month visit. The questionnaires will be administered in validated Chinese versions. These are physical activity, assessed using the International Physical Activity Questionnaire (IPAQ), mood state measured with the Patient Health Questionnaire (PHQ9), and self-efficacy using the, General Self-Efficacy Scale (see appendix for full details). The survey and questionnaires will deepen our understanding of the patients' behaviors and beliefs and how they influence adherence to treatment.

3.3.2.7 Exacerbation history and hospitalization for exacerbation in preceding year:

The patient's exacerbation history in the preceding year will be recorded. COPD exacerbation is an acute event characterized by a worsening of the patient's respiratory symptoms that is beyond normal day-to-day variations and leads to a change in medication [GOLD, 2019]. The

standard definition used in clinical studies requires a worsening of respiratory symptoms (including increased cough, sputum, breathlessness, chest tightness or wheeze) for 2 or more days.

The severity of the exacerbation will be determined using the following standard categories:

1. Mild – a worsening of symptoms treated by the patient through an increase in use of their usual medicine, typically increased SABA use
2. Moderate – worsening of symptoms for which a patient seeks medical care and is treated by antibiotics and/or systemic corticosteroids/or corticosteroids nebulization
3. Severe –exacerbation requiring hospital admission.

3.3.2.8 Safety

The data on AE/SAE should not be collected directly by physician. If an AE (serious or non-serious) or complaint with any specifically named GSK product is reported spontaneously by a patient during the course of the study, this will be documented by the site staff.

3.3.2.9 Physician prescription-COPD-Related Medication

This will be collected by treatment class: Long-Acting Muscarinic Antagonist [LAMA], Long-Acting Beta-Agonist [LABA], dual bronchodilator, inhaled corticosteroid [ICS]/ Long-Acting Beta-Agonist [LABA], triple therapy, theophylline and n-acetyl cysteine/carbocysteine. Information which includes such COPD medication and related medical records will be request.

3.3.2.10 Socioeconomic status

The objective questions will be asked to patients understand their socioeconomic status

- Education (illiteracy, primary school, junior mid-school, high-school, university)
- Living area (in city, outside city)
- Marriage condition
- Family total income in the past 12 months
- Individual total income in the past 12 months
- Economic support from others in the past 12 months
- Total health expenditure in the past 12 months
- Out-of-pocket health expenditure in the past 12 months
- COPD expenditure in the past 12 months
- Out-of-pocket COPD expenditure in the past 12 months
- National basic medical insurance
- Commercial insurance

3.3.2.11 DECAF score

The is a 5-point scale that uses items from the MRC dyspnoea scale, together with blood eosinophils (<0.05 x 10^9/L, consolidation (pneumonia) on CXR , moderate or severe acidaemia (pH < 7.3) and presence or history of atrial fibrillation. It has been extensively tested and validated [Echevarria, 2016].

4 SAMPLE SIZE / POWER CALCULATIONS

The primary objective of the study is to understand the prescription pattern of COPD maintenance treatment in Tier 2 and Tier 3 hospitals in China. Around 1500 patients with COPD will be enrolled which includes stable patients and patients with COPD exacerbations (moderate and severe). All enrolled patients will be included in the analysis. This sample size was chosen to ensure adequate patient representation and provide sufficient size for reliable analysis of different patient groups and key subgroups.
It is estimated that 750 patients each from tier 2 and tier 3 hospitals will be enrolled to provide adequate representation on healthcare status for COPD in China. The target number of patients in each tier of hospital and patient groups is shown in Table 3. After 500 patients have been recruited, the numbers will be reviewed to assess whether adequate number of participants have been enrolled for patient in stable state or with COPD exacerbations in each tier of hospital. At this point, recruitment policy might be changed to ensure an adequate distribution of patients. Thereafter, recruitment to different patient groups will be monitored monthly and further corrective action taken if needed.

Table 3: Patient recruitment strategy (estimated distribution ratio)

Patient group	Tier 2 hospital (% of total patients)	Tier 3 hospital (% of total patients)
Stable	25%	25%
Moderate acute or Hospitalized exacerbation	25%	25%

The secondary objective of this study is to examine factors (include baseline disease severity and baseline socio-economic factors) that are associated with different patterns of maintenance treatment. In the secondary analysis, we attempt to find significant association between disease severity (GOLD Group: A&B vs. C&D) and triple therapy at baseline for COPD patients.

Based on a previous study [Brusselle, 2015], about 24% COPD patients in Group A&B were prescribed triple therapy at diagnosis and about 46% COPD patients in Group C&D were prescribed triple therapy at diagnosis. The proportion of patients in Group A&B accounted for

66% of the total. We will use logistic regression to test this association and the parameters mentioned will be used for power calculation.

With a two-sided 5% level of significance and a sample size of 375subjects of each patient group in each Tier of hospital, we will have a power bigger than 98% for demonstrating a statistically significant result for the association between disease severity (GOLD Group: A&B vs. C&D) and triple therapy at baseline for COPD patients.

4.1 Hypotheses

The null hypothesis used to test the association between disease severity and triple therapy will be:

H0: There is no association between disease severity (GOLD grade: A&B vs. C&D) and triple therapy at diagnosis for COPD patients.

The alternative hypothesis will be:

H1: There is association between disease severity (GOLD grade: A&B vs. C&D) and triple therapy at diagnosis for COPD patients.

5 DATA ANALYSIS CONSIDERATIONS

This section summarizes the statistical approaches that will be implemented to assess the study objectives. The descriptive statistical results will be displayed for Tier 2 and 3 hospitals separately for all the analyses. All analyses will be conducted using SAS, version 9.4 or above.

5.1 Primary analyses

The primary objective of this study is to quantify the pattern of maintenance treatment prescribing in different patient groups in Tier 2 and 3 hospitals in China. Firstly, the number and percentage of patients who use the maintenance treatment at each visit will be summarized. Moreover, for those who use maintenance treatment, the number and percentage of patients will be summarized for each of the following pattern of maintenance treatment:

- Long-Acting Muscarinic Antagonist [LAMA]
- Long-Acting Beta-Agonist [LABA]
- Dual bronchodilator
- Inhaled corticosteroid [ICS]/ Long-Acting Beta-Agonist [LABA]
- Triple therapy
- Theophylline
- N-acetyl cysteine/carbocysteine

The results for patients with stable disease and patients with exacerbation at baseline will be analysed separately for the following visits: baseline visit, 1-week follow up (for moderate exacerbations) and discharge follow-up (for hospitalised exacerbations). The results for patients with stable disease and patients with exacerbation will be pooled together for analysis for 3-month follow-up visit. The percentage will be compared between stable and exacerbating patients by maintenance treatment.

5.2 Secondary analyses

The secondary objective of this study is to examine factors (include baseline disease severity and baseline socio-economic factors) that are associated with different patterns of maintenance treatment at baseline. Separate analyses will be performed for stable and exacerbating patients, since it is possible that the factors that influence a physician's choice of treatment may differ between the two conditions.

This part of analysis will be conducted in the group of the patients with stable disease and patients with exacerbation. The number and percentage of patients in each pattern of maintenance treatment will be summarized by the following factors:

- Age
- Gender: female/male
- Smoking history
- Any comorbidity
- Baseline GOLD 2019 grade: A/B/C/D
- Annual income
- Proportion of outpatient medical insurance
- Place of residence (in city, outside city)
- Educational level (illiterate, primary school, junior mid-school, high-school, university)
- Baseline FEV1 stage: I-IV

Multivariate logistic regression will be used to identify adjusted odds ratios (ORs) and 95% confidence intervals (95% CIs) for having a certain maintenance treatment versus none, using the above factors as covariates.
Another secondary objective is to assess the proportion of patients whose prescribed maintenance treatment was stepped up, stepped down, stopped, switched or remained the same across the different study time points. The number and percentage of patients whose prescribed maintenance treatment was stepped up, stepped down, stopped, switched or remained the same will be summarized for each visit.

The results for patients with stable disease and patients with exacerbation will be analysed separately. For those with exacerbation, the results for patients with a moderate exacerbation and patients requiring hospitalisation for an exacerbation will be further analysed separately.

The proportion of who have changed from one pattern of maintenance treatment at baseline to another pattern at 3-month will be summarized separately for the group of patients with stable disease at baseline and those with an exacerbation.

One more secondary objective is to assess the disease burden of the patients. The number and percentage of patients in different mMRC score intervals, CAT score intervals, numbers of historic exacerbation will be summarized according to the usage of different historic treatments. Moreover, mMRC score, CAT score and number of historic exacerbations will be summarized by mean and standard deviation in different patterns of maintenance treatment.

Another secondary objective is to assess the proportion of patients actually receiving each treatment class at 3 months.

5.4 Other analysis

Safety information will be summarized.

6 LIMITATIONS

- At least one site in each of the main province of China will be selected. However, only 1-2 sites per province will be selected and these may not be fully representative of all the Tier 2 and 3 hospitals in each province.
- The study includes only those Tier 2 hospitals which at a minimum to have LAMA and ICS/LABA and spirometry available; however, this will not fully reflect COPD management in all Tier 2 hospitals, because not all currently have such drugs available.
- It is a 3-month follow-up study and the duration is adequate to measure short-medium term changes, but COPD requires lifelong treatment, so this reflects only a short period of a patient's management
- The adherence data is reliant on the patients accurate reporting of which prescribed treatments they are taking, there can be an underestimation or overestimation of adherence to medication.

7 STUDY CONDUCT, MANAGEMENT & ETHICS

7.1 Ethics Committee/IRB Approval

This study will be conducted in accordance with GCP and all applicable regulatory requirements, including, where applicable, the current version of the Declaration of Helsinki.

The investigator is responsible for ensuring that this protocol, the site's informed consent form, and any other information that will be presented to potential subjects (e.g., advertisements or information that supports or supplements the informed consent) are reviewed and approved by the appropriate Independent Ethics Committee (IEC). The investigator agrees to allow the IEC direct access to all relevant documents. The IEC must be constituted in accordance with all applicable regulatory requirements. GSK will provide the investigator with relevant document(s)/data that are needed for IEC review and approval of the study. Before CRFs can be shipped to the site, GSK must receive copies of the IEC approval, the approved informed consent form, and any other information that the IEC has approved for presentation to potential subjects.

7.2 Informed Consent

- The investigator or his/her representative will explain the nature of the study to the participant or his/her legally authorized representative and answer all questions regarding the study.

- Participants will be informed that their participation is voluntary. Participants or their legally authorized representative will be required to sign a statement of informed consent that meets the requirements of 21 CFR 50, local regulations, ICH guidelines,

Health Insurance Portability and Accountability Act (HIPAA) requirements, where applicable, and the IRB/IEC or study centre.

- The medical record must include a statement that written informed consent was obtained before the participant was enrolled in the study and the date the written consent was obtained. The authorized person obtaining the informed consent must also sign the ICF.

- A copy of the ICF(s) must be provided to the participant or the participant's legally authorized representative.

7.3 Data Protection

Subject to participant consent, it is expected that patient number, date of birth, postal code and sex will be the only patient identifiable data that will be included in this transfer.

The data will be housed within secure servers. Access to information is restricted by role and is project specific. Data are analysed on these secure servers, and only the output may be extracted.

The output from this study will not include any individually identifiable data.

7.4 Personally Identifiable Information (PII)

All efforts will be made to ensure compliance with all applicable human subject protection and data protection laws in China and regulations in effect. To this end, all analytical datasets will be in a format that does not allow subjects to be identified, whether directly or through identifiers linked to the subject.

7.5 Adverse Event (AE), Pregnancy Exposure, and Incident Reporting

If an AE (serious or non-serious) or complaint with any specifically with GSK product is reported spontaneously by a subject during the course of the study, the PI or site staff must report to GSK local safety department within 24 hours of first becoming aware of the event in accordance with SOP_54834 Management of Adverse Event, Pregnancy Exposure, and Incident Reports from Human Subject Research.

Per SOP 52214 (Pharmacovigilance Planning for Epidemiology and Health Outcomes human subject research), a Pharmacovigilance Plan (PVP) is required for research with and without safety-related objectives.

7.6 Legal Basis for Processing Individual Human Data

The authors confirm that study data is Individual Human Data (IHD) owned by GSK and that:

The proposed use of the IHD is **Study Use*** as outlined in the patient consent.

* Study Use means - the use of IHD is as stated in the original study protocol and/or aligned with the informed consent form to answer the study objectives and satisfy regulatory requirements and learn more about the product studied and the disease/condition studied. This includes bringing the product to market or maintaining market access, which includes working with government agencies, insurers or health care payers and aiding GSK's understanding of clinical efficacy, safety, or effectiveness of the product.

8 PLANS FOR DISSEMINATING AND COMMUNICATING STUDY RESULTS

8.1 Target Audience

GSK stakeholders will require the information generated by this study, as well as contribute to the published literature. The results will be disseminated externally via manuscripts or presentations.

8.2 Study reporting and publications

Where required by applicable regulatory requirements, an investigator signatory will be identified for the approval of the clinical study report. The investigator will be provided reasonable access to statistical tables, figures, and relevant reports and will have the opportunity to review the complete study results at a GSK site or other mutually agreeable location.

GSK will also provide the investigator with the full summary of the study results. The investigator is encouraged to share the summary results with the study subjects, as appropriate.

The results summary will be posted to the Clinical Study Register no later than 12 months after the last subject's last visit (LSLV) or sooner if required by legal agreement, local law or regulation. In addition, a manuscript will be submitted to a peer-reviewed journal for publication within 18 months of LSLV. When manuscript publication in a peer- reviewed journal is not feasible, further study information will be posted to the GSK Clinical Study Register to supplement the results summary.

A manuscript will be progressed for publication in the scientific literature if the results provide important scientific or medical knowledge.

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10 APPENDICES

10.1 Appendix 1: SCHEDULE OF ACTIVITIES

Procedure	**Baseline Visit**	**Discharge follow-up for admitted patients**	**1-week follow up for non-admitted patients Day 8+3 (Telephone)**	**3 months follow up ±7 (Telephone)**	**Notes**
Informed consent	X				
Inclusion and exclusion criteria	X				
Demography	X				

Full physical examination including height and weight	X				
Co-morbidities	X				
COPD diagnosed history	X				
COPD exacerbation history in prior 12 month	X				
Current COPD disease condition (stable or acute)	X				
Smoking history	X				
Physician name (code)	X				a. will be collected from medical records (will not be collected from patients)
COPD prescription	X	X[a]	X[b]	X[c]	a. COPD prescription when discharge b. the latest COPD prescription at 1-week follow up c. the latest COPD prescription at 3-month follow up
Current COPD medication	X[a]		X	X	a. within past 1 month before baseline visit
Prescription date, physician and hospital of current COPD medication				X[a]	a. will be collected from medical records or patients' recall (the physician's name will not be collected from patients)
Spirometry	X	X[a]			a. the lung function can be collected before discharge if the patient's

					disease is too serious
DECAF score assessment (admitted patients)	X[a]				a. can be assessed during hospitalization period
Physician's survey	X[a]				a. to collect outpatients
Patient's survey and questionnaire	X			X	1. Baseline period: Patient questionnaires include IPAQ, PHQ9, self-efficacy energy scale (GSE); baseline patient survey 2. 3-month follow-up period: patient questionnaires include self-efficacy energy scale (GSE); follow-up period patient survey
CAT	X	X	X	X	
mMRC Dyspnea Scale	X				
Socio-economic	X				
Insurance details	X				
Inhaler availability	X				
Discharge time		X			
COPD Clinic revisit times and reason			X[a]	X[a]	a. If patient visits to clinic
Frequency of COPD exacerbation between baseline visit and 3 months follow up				X	
Concomitant medication review	X	X	X	X	
AE review		----------X----------			*AE data will not be collected directly. A physician can document the adverse event or

			concern reported by the patients.
SAE review		----------X----------	*SAE data will not be collected directly. A physician can document the event or concern reported by the patients.

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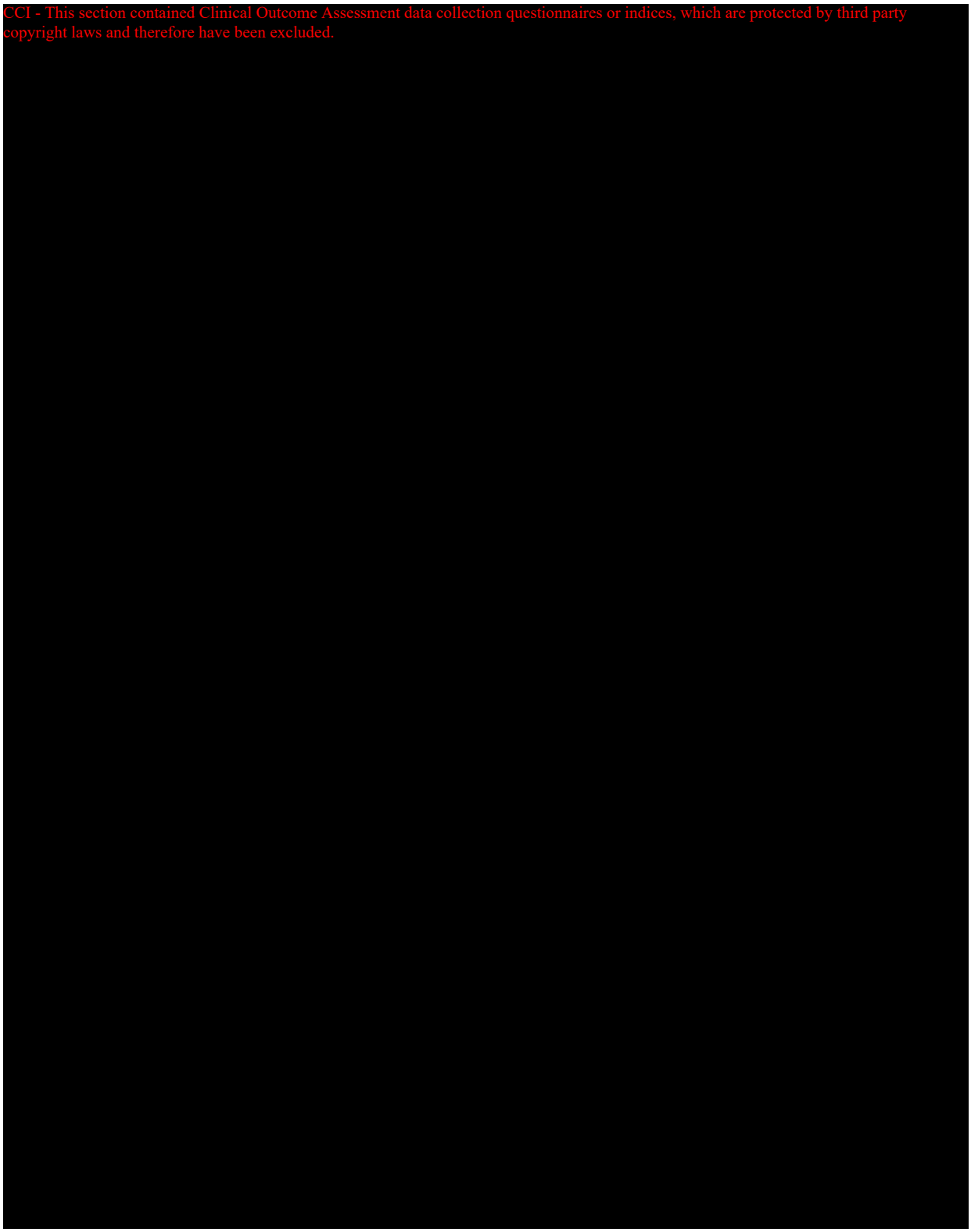
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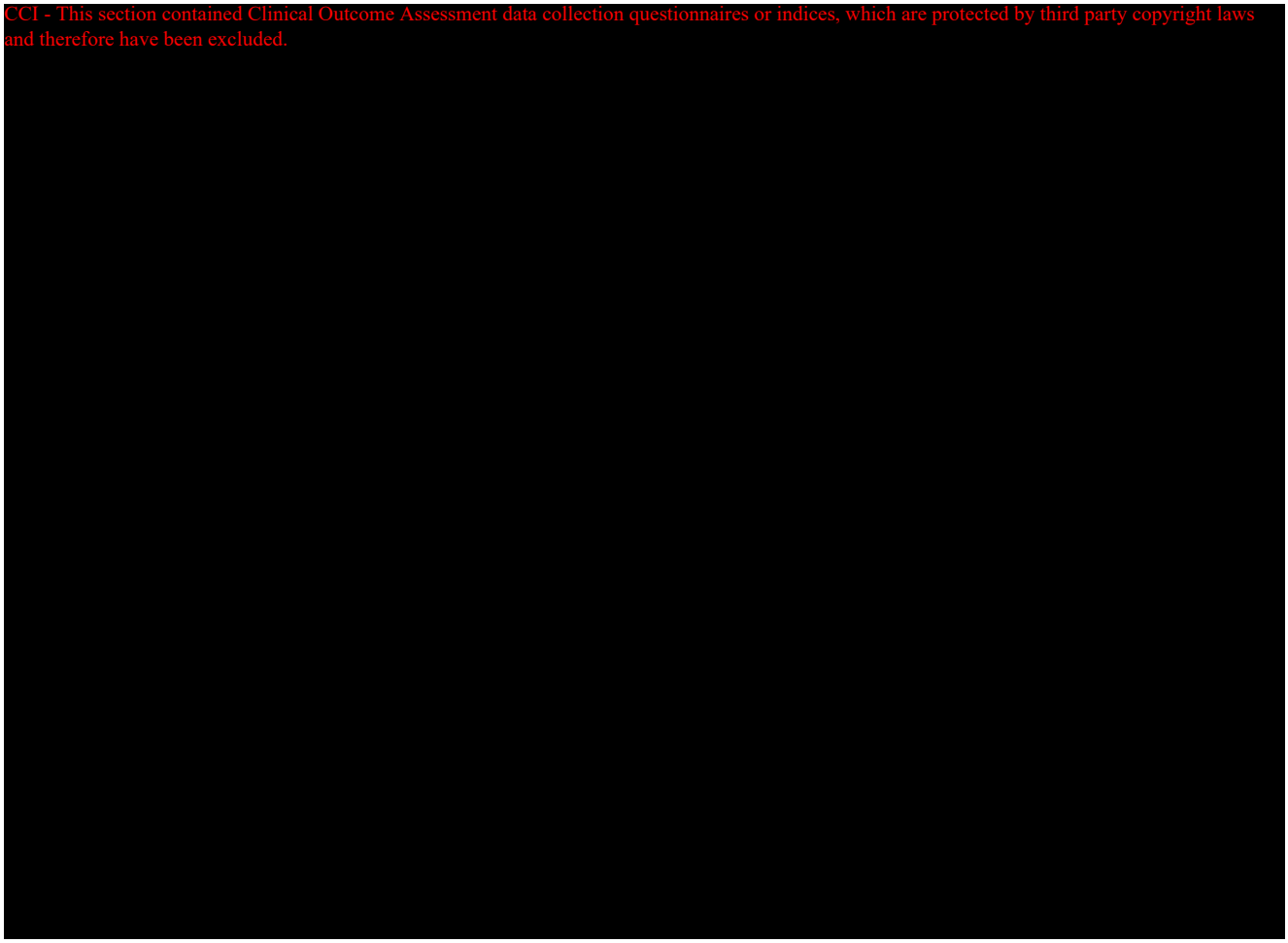
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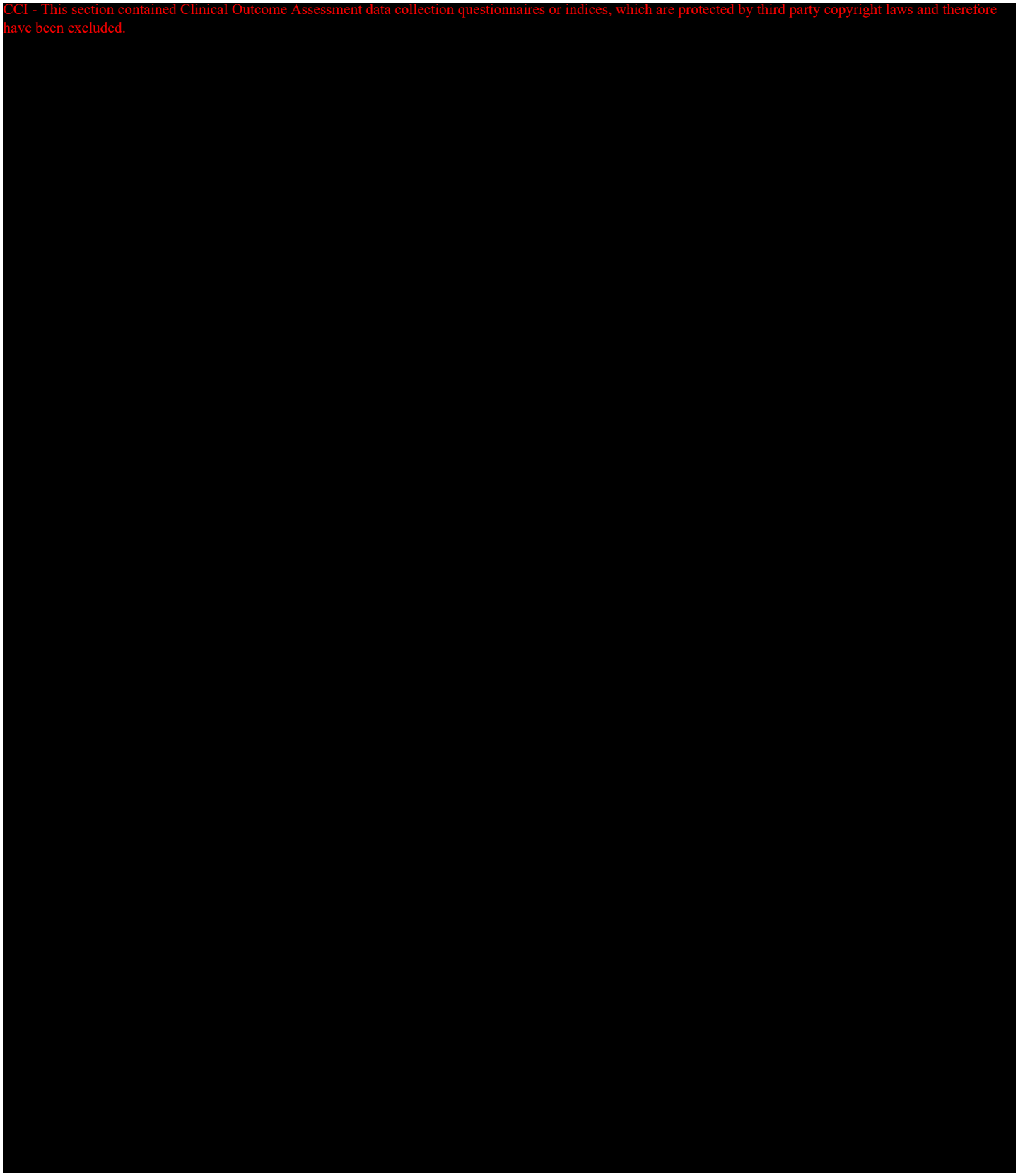

10.6 Appendix 6: sPVP and PVP APPROVAL FORM

Study-Specific Pharmacovigilance Plan (sPVP)

Unique Identifier	213550
Full title of protocol	COPD disease burden, patient characteristics, maintenance treatment patterns and factors influencing treatment decisions in China Tier 2 and Tier 3 hospitals
Abbreviated title of protocol	COPD maintenance treatment patterns in China
Department	China Medical Respiratory TA
Study Accountable Person	PPD
Type of Study (tick type of study that applies)	☐ Interventional (interaction) study with data collection - face-to-face or phone-based interviews
	☐ Interventional (interaction) study with data collection - digital or paper surveys
	☐ Non-interventional study with data collection where data source includes identifiable patient information (e.g., data extraction from medical records, existing registry)
	☒ Other, please describe: Low-interventional study with data collection where data source includes identifiable patient information (e.g., data extraction from medical records, existing registry)
Study-Specific Pharmacovigilance Plan Approval Date	*24-Aug-2020*
Safety and Medical Governance (SMG) Representative:	PPD

Revision Chronology:

Version Date	Document Type	Change(s) since last version
Enter original sPVP approval date	Original	n/a
Enter amended sPVP approval date	*NA*	*NA*

sPVP Element	Study-Specific Pharmacovigilance Plan (sPVP) (tick applicable statements)
Supplier PV training	☐ N/A – No supplier/vendor involved that could identify Human Safety Information (HSI) following exposure of GSK/ViiV products
	☒ Supplier/vendor PV training will be conducted using the agreed method and current, approved content, prior to beginning the study. Training will be completed annually and documented.
Investigator and site staff PV training	☐ N/A – No Investigator and/or site staff involved that could be in receipt of Human Safety Information (HSI) following exposure of GSK/ViiV products
	☒ Investigator and/or site staff PV training will be conducted using the agreed method and current, approved content, prior to beginning the study. Training will be completed annually and documented.
Safety-specific roles	☐ SAP is responsible for the collection, reporting, and reconciliation process for HSI.
	☒ Supplier/vendor is responsible for the collection, reporting, and reconciliation process for HSI.
HSI Collection Processes	☒ The protocol includes details about **collection** of HSI, including all adverse reaction/event, following exposure to any GSK/ViiV product OR ☐ The protocol includes the rationale for **collection** of specific types of adverse reaction/event (e.g. objectives of the study, the stage of the asset development, level of clinical oversight). Required response if second option is selected: ☐ The rationale for the **collection** of data <u>differs</u> from minimum criteria, this has been approved by the Central Safety Department.
HSI Reporting Processes	Please select one of the following options ☒ The protocol includes details about reporting of all HSI following exposure of GSK/ViiV products. OR ☐ The protocol includes details about the rationale for reporting (e.g., objectives of the study, the stage of asset development, level of clinical oversight) targeted follow-up requirements
AE, pregnancy exposure, and	☒ GSK Global Adverse Event, Pregnancy Exposure, and Incident Reporting Form for Epidemiology and Health Outcome studies

sPVP Element	Study-Specific Pharmacovigilance Plan (sPVP) (tick applicable statements)
incident collection forms	☐ Alternative collection form(s) will be utilized (if ticked, please specify the form title here - e.g. standard clinical trial SAE form, Pregnancy Notification Form, and/or any additional study/product-specific safety data collection form, if appropriate)
Frequency of data review	☐ N/A – No batch reviewing of the data.
	☒ Batch review will be conducted (if ticked, please specify the frequency of review) During the visit and follow-ups in this study, once AEs, pregnancy exposures is identified, the investigator will collect and report.
Reviewing and reporting study results	Specify review and timing for the communication of study results to SMG For serious related AE (SADR) or pregnancy exposure safety report sent to local PV team, the report would be forwarded to the global service provider (IQVIA) for their further processing to the drug safety headquarters (CSD) within 24 hours (the next working day in case of weekends); For non serious related AE (ADR), the report would be forwarded to the global service provider (IQVIA) for their further processing to the drug safety headquarters (CSD) within 5 calendar days.

Interim study reports	☒ N/A – No interim study reports are planned.
	☐ Interim study reports will be shared with the SERM product specialist / physician for review of the interim report safety data
Reconciliation process	☐ Reconciliation process defined in protocol ☒ Reconciliation process defined in sPVP, please describe • Study manager is responsible for sending AE reconciliation form to local PV team monthly. • Local PV team will assist in forwarding the AE reconciliation form to the case management group (CMG), CMG is responsible for checking.
PVP monitoring process	☒ SAP will review the sPVP elements and discuss during regular study team and/or supplier meetings to ensure the plan is working effectively.
	☐ Other, please describe
Provision of final study report	☐ Defined in protocol ☒ Defined in sPVP, please describe • All serious and non-serious AEs, pregnancy exposures, and incidents related to any GSK product will be reported in the final report. • Detail table shells will be attached to the research analysis plan.

Study-specific Pharmacovigilance Plan (sPVP)
Approval Page for:
213550

Approval

I confirm that this sPVP is appropriate for the above study and has been completed in accordance with SOP 52214.

Name	Job Title or Role & Qualification	Signature	Date (dd-mmm-yyyy)

Please forward this signed copy by e-mail to the Study Accountable Person and cc the sPVP mailbox: Epi_&_HO_PVP_Queries@gsk.com