Observational Study Protocol

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Real-world use of Breztri/Trixeo for the management of COPD in a UK primary care population

An observational, historical cohort study to evaluate the acceptability of budesonide/glycopyrrolate/formoterol (Breztri/Trixeo) for the management of chronic obstructive pulmonary disease using the OPCRD database

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List Of Abbreviations And definition of terms

Abbreviation or special term	Explanation
ADEPT	Anonymised Data Ethics & Protocol Transparency Committee
AZ	AstraZeneca
BMI	Body Mass Index
CAT	Chronic obstructive pulmonary disease Assessment Test
COPD	Chronic obstructive pulmonary disease
ENCePP	European Network of Centres for Pharmacoepidemiology and Pharmacovigilance
FEV_1	Forced Expiratory Flow in one second
FVC	Forced Vital Capacity
GOLD	Global Initiative for Chronic Obstructive Lung Disease
ICS	Inhaled Corticosteroids
LABA	Long Acting β adrenoceptor Agonists
LAMA	Long-Acting Muscarinic Receptor Antagonists
MACRE	Major cardiac and respiratory events
mMRC	Modified Medical Research Council dyspnoea questionnaire
NICE	National Institute for Health and Care Excellence
OCS	Oral Corticosteroids
OPC	Optimum Patient Care
OPCRD	Optimum Patient Care Research Database
OPRI	Observational and Pragmatic Research Institute
PRO	Patient-reported outcome
SABA	Short-Acting Beta-Agonists
SAMA	Short-Acting Muscarinic Antagonist
UK	United Kingdom

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PROTOCOL SYNOPSIS

An observational, historical cohort study to evaluate the acceptability of budesonide/glycopyrrolate/formoterol (Breztri/Trixeo) for the management of chronic obstructive pulmonary disease using the OPCRD database

Background/Rationale:

The current, stepwise management approach of patients with stable chronic obstructive pulmonary disease (COPD) involves the use of long-acting beta-agonists (LABA), long-acting muscarinic antagonists (LAMA), and/or inhaled corticosteroids (ICS) depending on patients' disease severity and symptomatology. In particular, dual therapies, namely LAMA+LABA or ICS+LABA, are recommended for highly symptomatic patients with moderate to severe COPD. Nonetheless, some patients remain symptomatic and suffer from exacerbations despite using dual therapies. Hence, recent years have seen the emergence of triple therapies (LABA+LAMA+ICS), such as budesonide/glycopyrrolate/formoterol (Breztri/Trixeo). Following demonstration of efficacy by randomized controlled trials, Breztri/Trixeo has been approved by the United States' Food and Drug Administration on 23rd July 2020,7 and by the European Medicines Agency on 9th December 2020. Nevertheless, as a new medication, real-life evidence underlying the safety, acceptability, and efficacy of Breztri/Trixeo is lacking. Given that findings from randomized controlled trials may only be applicable to a subset of patients in real life, this study seeks to investigate the patient acceptability and describe clinical outcomes of Breztri/Trixeo amongst patients with COPD in the early period after launch using a large general practice database in the United Kingdom.

Objective: To describe the acceptability and clinical outcomes of Breztri/Trixeo amongst patients with COPD.

Methodology:

Data source(s)

The most recent extraction of Electronic Medical Record (EMR) data from Optimum Patient Care Research Database (OPCRD) general practices will be used for this analysis, as well as EMR data from 11 general practices which were early adopters of Breztri/Trixeo from England National Prescribing Data and were recruited as part of the targeted Breztri/Trixeo site recruitment by the Optimum Patient Care (OPC). A subset of patients further received telephone consultation and completed the OPC Questionnaire, thus generating patient-reported outcome (PRO) data.

Study design

This is a historical cohort study of COPD patients who are early adopters of Breztri/Trixeo within the OPCRD and recruited general practice. The index date will be the date of Breztri/Trixeo initiation. Data will be right censored at the end of data availability, which is expected to be November 2022 at the latest.

Study Population

Inclusion Criteria

1. Received at least one prescriptions of Breztri/Trixeo from the start of data availability up to 90 days prior to the date of data extraction, which is expected to be in November 2022 by the latest; and
2. Ever record with any diagnostic code for COPD; and
3. Aged at least 40 years old at index date; and
4. Ever recorded to be an ex-smoker or current smoker; and
5. With at least one year of continuous practice data prior to index date; and
6. Had 90-day medication persistence, as defined by having received at least one further prescription of Breztri/Trixeo without any other LABA- / LAMA- / ICS-containing prescription within 90 days of the first prescription of Breztri/Trixeo.

Exclusion Criteria

1. Patients who were ever recorded with any diagnostic code for other chronic lower respiratory conditions will be excluded, with the exception of asthma.

Exposure

Exposure will be defined as at least one prescription of Breztri/Trixeo.

Outcomes

Primary outcome

The primary outcome will be medication success assessed at 90 days (early medication success) after Breztri/Trixeo initiation, which will be a binary, composite outcome that is defined as fulfilling all of the following:

1. No major cardiac and respiratory events (MACRE), defined as not having any of the below events:
    - New diagnosis of heart failure; or
    - Hospitalization for heart failure; or
    - Myocardial infarction; or
    - Hospitalization for respiratory events; or

- Complicated COPD exacerbations, as defined by exacerbations which require hospitalization or treatment with acute doses of oral corticosteroids and/or antibiotics between 8 and 28 days after the start of the initial event (i.e. the date of coding for COPD exacerbation); or
- All-cause mortality.

2. No pneumonia, defined as a physician diagnosed pneumonia that was confirmed with a chest radiograph or hospital admission within one month of diagnosis

Medication success will be claimed if the proportion of patients who meet the primary outcome of medication success is demonstrated to be ≥70% (i.e. if the lower 95% confidence limit for the percentage is ≥70%), which has been considered in previous publications to be a clinically significant limit. Medication success at 90 days (primary) will be termed "early medication success" and, at 180 days (exploratory), "sustained medication success".

Exploratory outcomes

Exploratory outcomes include and will be defined as the following:

1. Patient demographics and clinical characteristics at Breztri/Trixeo initiation and during follow-up
2. In a subset, for patients with CAT score available at both baseline and follow-up, changes in CAT score will be analysed as both a continuous variable and a categorical variable (with or without clinically significant changes in CAT score), stratified by whether patients switched to Breztri/Trixeo from another triple therapy regimens or stepped up from non-triple therapy. Significant changes in CAT score will be defined as changes by at least 2 points in CAT score.
3. Factors associated with the primary outcome (early medication success) and with change in CAT score after 90 days
4. Medication success assessed at 180 days. The definition of medication success will be the same as the above.
5. Amount of short-acting beta-agonist (SABA) use based on collected prescriptions, and calculated as $\frac{Count\ of\ inhaler\ doses\ (pack\ mg\ strength)}{duration\ of\ follow{-}up\ in\ days}$, and expressed as salbutamol equivalent in mg/day.
6. Acceptability of medication change, as defined by the percentage of patients receiving at least one additional prescription for Breztri/Trixeo during the follow-up period.
7. Adherence, as represented by the MPR which will be calculated as the ratio of total Breztri/Trixeo pack days (i.e. total number of days' equivalent of Breztri/Trixeo prescribed) to the number of prescription days (i.e. total number of days from Breztri/Trixeo initiation to the last day of prescription), and which was expressed as a percentage.
8. The overall number of inhalers used (fixed triple, free triple, or SABA).
9. Change in COPD control assessed at a minimum of 90 days after index date. Definitions and measurements of COPD control are detailed in Appendix 1: Potential PRO data from the OPC quality improvement program.

10. Change in exercise capacity assessed at a minimum of 90 days after index date. Definitions and measurements of exercise capacity are detailed in Appendix 1: Potential PRO data from the OPC quality improvement program.

The number of missing records will be recorded for each variable. Additionally, the time between the date of baseline data availability and index date will be described for all patients.

Feasibility

As of 10th August 2022, 449 patients in OPCRD were prescribed Breztri/Trixeo. After applying the inclusion and exclusion criteria, 198 patients were eligible for this study, with 180 days' follow-up data available for 136 patients. The median follow-up time of these 198 patients was 248 days [interquartile range 160-294 days]. Fifty of these patients had CAT score available in the year prior to Breztri/Trixeo initiation, and 37 had CAT score available at 1-year post-initiation.

Patients using other fixed triple therapies (Trelegy and Trimbow) were analysed with the specified inclusion and exclusion criteria using data as of 17th October 2022. Of the 16,294 and 19,462 eligible patients on Trelegy and Trimbow, respectively, 90.1% and 87.4% achieved medication success by 90 days, respectively. Survival analysis also estimated 90.2% and 82.9% of patients on Trelegy achieving medication success by 90 and 182 days, respectively; the corresponding values for patients on Trimbow were 87.9% and 79.4%, respectively.

As of 24th October 2022, the number of patients eligible for this study in OPCRD has increased to 285.

Statistical Analysis

Primary and exploratory outcomes will be summarised as means, medians or percentages as appropriate with 95% confidence intervals. For the primary outcome, medication success will be claimed if the lower 95% confidence limit for the percentage achieving success is ≥ 70%, assessed at 90 days after Breztri/Trixeo initiation. Exploratory outcomes will be summarised separately for 90 days and 180 days. Additionally, an exploratory analysis will be carried out to try to identify factors associated with the primary outcome (early medication success) and with change in CAT score at 90 days.

Amendment history

Date	Section of study protocol		Amendment or update	Reason
11/07/22	Various	v1	Initial protocol	Initial protocol
2/8/2022	Various	v2	Revision 1	Following statistical review and initial reviewing by AZ team
15/8/2022	Various	v3	Revision 2	Following second reviewing by AZ team
26/8/2022	Various	v4	Revision 3	Following third reviewing by AZ team
11/9/2022	Various	v5	Revision 4	Following senior AZ protocol review
21/10/22	Various	v6	Revision 5	Following further feasibility analyses and AZ review
26/10/22	Various	v6.1	Revision 5.1	Following minor comments from AZ and further statistical review

MILESTONES

Milestone	Planned date
Draft Protocol to AZ	July 2022
Dataset Created: OPCRD electronic medical records-only	July 2022
Analysis of OPCRD electronic medical records-only dataset	Sep 2022
Dataset Created: OPCRD enhanced with PRO data	Nov 2022
Analysis of OPCRD enhanced with PRO data	Dec 2022

1. BACKGROUND AND RATIONALE

1.1 Background

Chronic obstructive pulmonary disease (COPD) is a prevalent public health problem, affecting an estimated 10.3% of all people aged 30-79 years old globally in 2019 which translated to 391.9 million patients with COPD.[1] In 2010 alone, COPD incurred USD32 billion in direct costs and USD20.4 billion in indirect costs in the United Sates.[2] Current management of stable COPD takes a stepwise approach, with regimens consisting of long-acting beta-agonists (LABA), long-acting muscarinic antagonists (LAMA), and/or inhaled corticosteroids (ICS) depending on patients' disease severity as measured by the numbers of moderate exacerbation or COPD hospitalization, and symptomatology as measured by the COPD Assessment Test (CAT) or the modified Medical Research Council dyspnoea questionnaire (mMRC).[3] Dual therapies, namely a combination of LAMA+LABA or ICS+LABA, are recommended for highly symptomatic (CAT score ≥10 or mMRC ≥2) patients with at least two moderate exacerbations or any COPD hospitalization in a year.[3] The National Institute for Health and Care Excellence (NICE) guidelines largely echoed the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guideline in that dual therapies are to be used for more severe patients.[4]

Nonetheless, some patients remain symptomatic or continue to suffer from COPD exacerbations despite using dual therapies. Although "open triple" therapies, referring to separate prescriptions of LABA+LAMA+ICS have been used clinically by some clinicians, "fixed triple" therapies, where LABA+LAMA+ICS are available as a single medication such as budesonide/glycopyrrolate/formoterol (Breztri/Trixeo), have been explored as a potential option for these patients. In 2018, the KRONOS trial first demonstrated superiority of Breztri/Trixeo over corresponding dual therapies in terms of lung function improvement in patients with moderate to very severe COPD.[5] This was followed by the ETHOS trial in 2020 which reported significant superiority of Breztri/Trixeo over monotherapies and dual therapies in patients with moderate to very severe COPD, resulting in significantly less COPD exacerbation without significant differences in adverse events.[6] Following these, Breztri/Trixeo was approved by the United States' Food and Drug Administration for maintenance treatment of patients with COPD on 23rd July 2020,[7] followed by approval by the European Medicines Agency for maintenance treatment in adult patients with moderate to severe COPD not adequately treated by a combination of ICS and LABA or LABA+LAMA on 9th December 2020.[8]

1.2 Rationale

It has been shown that due to the highly controlled and experimental settings of randomized controlled trials, findings from these trials may not be applicable for a subset of patients in real life.[9,10] Hence, despite strong evidence from the KRONOS and ETHOS trials indicating the clinical efficacy of Breztri/Trixeo, real-life evidence of the acceptability and clinical outcomes of Breztri/Trixeo remains an important area of investigation. As a relatively new medication, real-life evidence for Breztri/Trixeo is exceedingly scarce, further highlighting the need for observational studies evaluating the acceptability and efficacy of Breztri/Trixeo.

2. OBJECTIVES

2.1 Primary objective

To evaluate medication success at 90 days after Breztri/Trixeo initiation.

2.2 Exploratory objectives

1. To describe patient characteristics at Breztri/Trixeo initiation and during follow-up
2. To compare CAT scores before Breztri/Trixeo use and 90 days after Breztri/Trixeo initiation in a subset of patients for whom CAT scores are available at both baseline and follow-up
3. To identify factors associated with the primary outcome (early medication success) and with change in CAT score after 90 days
4. To explore medication success at 180 days after Breztri/Trixeo initiation
5. To describe the amount of short-acting beta-agonists (SABA) used during the first 90 days after Breztri/Trixeo initiation
6. To describe acceptability of medication change at 90 days after Breztri/Trixeo initiation
7. To describe adherence, as represented by the medication possession ratio (MPR), during the first 90 days after Breztri/Trixeo initiation
8. To describe the overall number of inhalers used (fixed triple, free triple, or SABA) during the first 90 days after Breztri/Trixeo initiation
9. To explore changes in COPD control assessed at a minimum of 90 days after index date
10. To explore changes in exercise capacity assessed at a minimum of 90 days after index date

3. METHODOLOGY

3.1 Data Sources

Patients' electronic medical records will be extracted from general practices from the Optimum Patient Care Research Database (OPCRD). In addition, 11 general practices which were early adopters from England National Prescribing Data in the United Kingdom (UK) were recruited as part of the targeted Breztri/Trixeo site recruitment by the Optimum Patient Care (OPC). This recruitment was done as part of the quality improvement program by OPC. Selected patient-reported outcome (PRO) data can be extracted from the data collected as part of the quality improvement program where available (Appendix 1: Potential PRO data from the OPC quality improvement program).

The OPCRD comprises data extracted through the OPC Clinical Service Evaluation. At the time of writing, OPCRD contains anonymized, research-quality data for approximately 16.4 million patients across the UK. The OPCRD encodes diagnostic, prescription and procedural data using

SNOMED-International codes, SNOMED-UK codes, Read codes v2 and v3, and ICD-10 codes. The OPCRD database is approved by the Health Research Authority for clinical research use (Research Ethics Committee reference: 15/EM/0150), is governed by the Anonymised Data Ethics & Protocol Transparency (ADEPT) Committee, and offers a high-quality data source that is used regularly in clinical, epidemiological and pharmaceutical research.

3.2 Study Design

This is a historical cohort study of COPD patients of Breztri/Trixeo within the OPCRD and recruited general practice from the start of data availability up to an expected data extraction in November 2022 at the latest.

The **index date** will be the date of Breztri/Trixeo initiation.

The **baseline period** will encompass the entire period available for each patient prior to the index date and will be of at least one year.

The **enrolment period** will start at the date of Breztri/Trixeo launch in the UK and will end 90 days before the end of data availability. For exploratory objective 4 the enrolment period will end 180 days before the end of data availability.

The **follow-up period** will start at the date of Breztri/Trixeo launch in the UK and will end at the end of data availability, which is expected to be in November 2022 by the latest. The study design is briefly illustrated in Figure 1.

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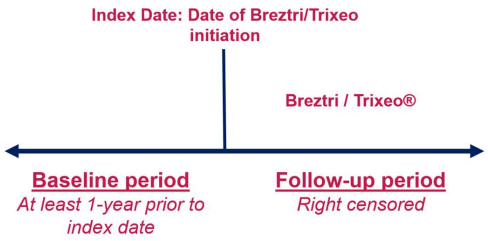
Figure 1 Study design



3.3 Inclusion and exclusion criteria

The inclusion and exclusion criteria below will result in the patient flow depicted in Figure 2.

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3.3.1 Inclusion Criteria

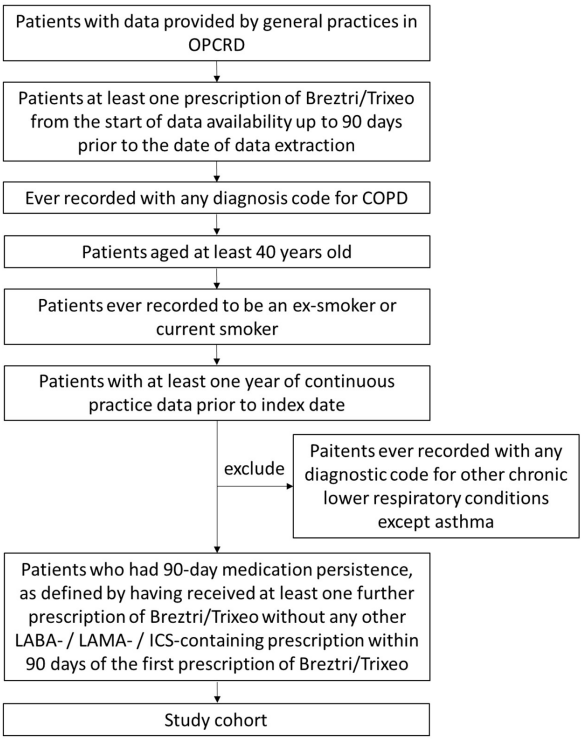
Patients fulfilling all of the following inclusion criteria will be identified:

1. Received at least one prescription of Breztri/Trixeo from the start of data availability up to 90 days prior to the date of data extraction, which is expected to be in November 2022 by the latest; and
2. Ever recorded with any diagnostic code for COPD during baseline; and
3. Aged at least 40 years old at index; and
4. Ever recorded to be an ex-smoker or current smoker during baseline; and
5. With at least one year of continuous practice data prior to index date; and
6. Had 90-day medication persistence, as defined by having received at least one further prescription of Breztri/Trixeo without any other LABA- / LAMA- / ICS-containing prescription within 90 days of the first prescription of Breztri/Trixeo.

3.3.2 Exclusion Criteria

Patients who were ever recorded with any diagnostic code for other chronic lower respiratory conditions will be excluded, with the exception of asthma.

Figure 2 Patient flow diagram



4. VARIABLES AND EPIDEMIOLOGICAL MEASUREMENTS

4.1 Exposures

Exposure will be defined as prescription of Breztri/Trixeo.

4.2 Outcomes

4.2.1 Primary outcomes

The primary outcome will be medication success assessed at 90 days (early medication success) after Breztri/Trixeo initiation, which will be a binary, composite outcome that is defined as fulfilling all of the following:

1. No major cardiac and respiratory events (MACRE), defined as not having any of the below events:
    - New diagnosis of heart failure; or
    - Hospitalization for heart failure; or
    - Myocardial infarction; or
    - Hospitalization for respiratory events; or
    - Complicated COPD exacerbations, as defined by exacerbations which require hospitalization or treatment with acute doses of oral corticosteroids and/or antibiotics between 8 and 28 days after the start of the initial event (i.e. the date of coding for COPD exacerbation; Figure 3); or
    - All-cause mortality.
2. No pneumonia, defined as a physician diagnosed pneumonia confirmed with a chest radiograph or hospital admission within one month of diagnosis[11]

The cardiovascular component of MACRE here is a derivation and subset of the classical, core components of major adverse cardiovascular events as recommended by both the Food and Drug administration of the United States of America and the European Medicines Agency, i.e. cardiovascular mortality, myocardial infarction, and stroke.[12,13] Stroke was omitted from MACRE in this study, as recommended by AstraZeneca, due to an apparent lack of mechanisms via which Breztri/Trixeo may influence the risk of stroke. Multiple components of MACRE, and pneumonia may occur to the same patient, and the number of patients who experience each of these components will be described; however, as this is a primary outcome, each of these patients will only be counted once when evaluating the primary outcome, regardless of how many components these patients each experience.

The definition of pneumonia included here has been used in prior work as a specific definition of pneumonia.[11]

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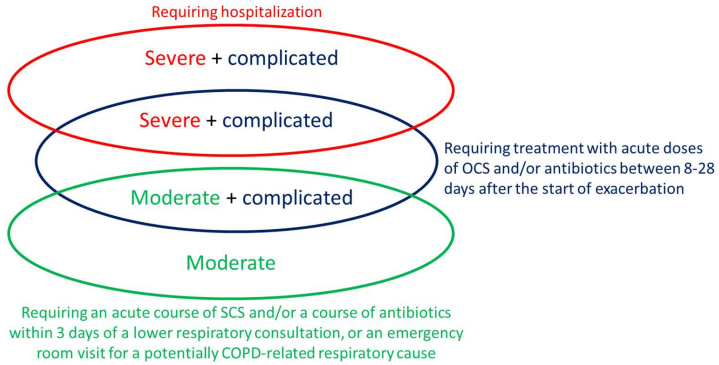
Figure 3 Relationship between categories of COPD exacerbation severity



Medication success will be claimed if the proportion of patients who meet the primary outcome of medication success is demonstrated to be ≥70% (i.e. if the lower 95% confidence limit for the percentage is ≥70%), which has been considered in previous publications to be a clinically significant limit.[14] Medication success at 90 days will be termed "early medication success" and, at 180 days, "sustained medication success".

4.2.2 Exploratory outcomes

Exploratory outcomes will be assessed at both 90 and 180 days. These included and were defined as the following:

1. Patient demographics and clinical characteristics at Breztri/Trixeo initiation and during follow-up
2. In a subset, for patients with CAT score available at both baseline and follow-up, changes in CAT score will be analysed as both a continuous variable and a categorical variable (with or without clinically significant changes in CAT score), stratified by whether patients switched to Breztri/Trixeo from another triple therapy regimens or stepped up from non-triple therapy. Significant changes in CAT score will be defined as changes by at least 2 points in CAT score.
3. Factors associated with the primary outcome (early medication success) and with change in CAT score after 90 days
4. Medication success assessed at 180 days. The definition of medication success will be the same as the above.
5. Amount of short-acting beta-agonist (SABA) use based on collected prescriptions, and calculated as $\frac{Count\ of\ inhaler\ doses\ (pack\ mg\ strength)}{duration\ of\ follow\text{-}u\ \ in\ days}$, and expressed as salbutamol equivalent in mg/day.
6. Acceptability of medication change, as defined by the percentage of patients receiving at least one additional prescription for Breztri/Trixeo during the follow-up period.

7. Adherence, as represented by the MPR which will be calculated as the ratio of total Breztri/Trixeo pack days (i.e. total number of days' equivalent of Breztri/Trixeo prescribed) to the number of prescription days (i.e. total number of days from Breztri/Trixeo initiation to the last day of prescription), and which was expressed as a percentage.
8. The overall number of inhalers used (fixed triple, free triple, or SABA).
9. Change in COPD control assessed at a minimum of 90 days after index date. Definitions and measurements of COPD control are detailed in Appendix 1: Potential PRO data from the OPC quality improvement program.
10. Change in exercise capacity assessed at a minimum of 90 days after index date. Definitions and measurements of exercise capacity are detailed in Appendix 1: Potential PRO data from the OPC quality improvement program.

Patient treatment satisfaction may also be assessed as part of the quality improvement program.

4.3 Covariates

Baseline characteristics of all patients will be described, as summarized in Table 1. The number of missing records will be recorded for each variable for the entire cohort, as well as specifically for patients with fully characterised baseline (initiation visit) and follow-up PRO data. Additionally, the time between the date of each baseline variable availability and index date will be described for all patients, expressed as median with interquartile range. Furthermore, the maintenance treatment used by patients at the time of initial CAT score assessment will be described, with comparison of subgroups stratified by the maintenance regimens.

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Table 1 Variables to be measured at baseline. Selected variables will also be measured on follow-up as specified.

Patient characteristics

Age	Age in years on index date, expressed as mean ± standard deviation and/or median with interquartile range. This is to be analysed and described as both a continuous and categorical variable, with the following categories: • 40-59 years old • 60-79 years old • 80 years old or above
Sex	Female or Male
Body Mass Index (BMI)	Defined as the ratio of weight (kg) to squared height (m^2) closest to Breztri/Trixeo initiation. This is to be analysed and described as both a continuous and categorical variable, with the following categories: • Underweight (BMI <18.5) • Normal weight (BMI 18.5 to <25)

	• Overweight (BMI 25 to <30) • Obese (BMI 30 and over)
Smoking status	The status prior to and closest to Breztri/Trixeo initiation will be used. This will be analysed and described as categories, with the following categories: • Active smoker • Ex-smoker
Socioeconomic status	This will be analysed and described as categories, based on the deciles of Index of Multiple Deprivation of the patient's corresponding general practice. The Index is based on national statistics for the postcode in which the general practice is situated.
Ethnicity	This will be analysed and described as categories, with the following categories: • White • Black • Asian • Mixed / others • Unknown
Comorbidities	
Asthma	Active / inactive / never diagnosed Active asthma is defined by ongoing codes for asthma within a year before or after Breztri/Trixeo initiation.
Validated COPD diagnosis	This is defined as a post-bronchodilator forced expiratory volume in 1 second (FEV1) to forced vital capacity (FVC) ratio that is less than 0.7 on spirometry: yes / no
Evidence of asthma before the age of 40	Yes / no
Rhinitis	Any diagnosis, ever: yes / no
Eczema	Any diagnosis, ever: yes / no
Nasal polyps	Any diagnosis, ever: yes / no
Chronic sinusitis	Any diagnosis, ever: yes / no
Gastroesophageal reflux disease	Any diagnosis, ever: yes / no

Diabetes mellitus	Any diagnosis, ever: yes / no
Osteoporosis	Any diagnosis, ever: yes / no
Hypertension	Any diagnosis, ever: yes / no
Ischaemic heart disease	Any diagnosis, ever: yes / no
Heart failure	Any diagnosis, ever: yes / no. This will also be recorded on follow-up as part of the outcomes.
Chronic kidney disease	Any diagnosis, ever: yes / no
Depression or anxiety	Any diagnosis, ever: yes / no
Sleep apnoea	Any diagnosis, ever: yes / no
Sleep disorder	Any diagnosis, ever: yes / no
Clinical characteristics	
Time since COPD diagnoses, years	The date of first validated COPD diagnosis will be determined, and the time between that and Breztri/Trixeo initiation will be determined. This will be analysed as a continuous variable, expressed as mean ± standard deviation and/or median with interquartile range.
FEV1	The value within 24 months prior to and closest to Breztri/Trixeo initiation will be used. FEV1 in litre, expressed as mean ± standard deviation and/or median with interquartile range
Percentage predicted FEV1	The value within 24 months prior to and closest to Breztri/Trixeo initiation will be used. Percentage predicted FEV1 in percent, expressed as mean ± standard deviation and/or median with interquartile range. This is to be analysed as a continuous variable, as well as a categorical variable according to the GOLD stage of airflow limitation: • GOLD 1 (mild): ≥80% • GOLD 2 (moderate): 50% to <80% • GOLD 3 (severe): 30% to <50% • GOLD 4 (very severe): <30%

Ratio of FEV1 to FVC <0.7	The value within 24 months prior to and closest to Breztri/Trixeo initiation will be used. Patients with recorded FEV1/FVC <0.7
mMRC score	The value within 24 months prior to and closest to Breztri/Trixeo initiation will be used. This is to be analysed as a categorical variable, with each integer score value constituting a separate category. This will also be recorded on follow-up. The definitions of individual scores of the mMRC score are detailed in Appendix 2: mMRC score.
GOLD groups[3]	The grouping within 24 months prior to and closest to Breztri/Trixeo initiation will be used. This is to be analysed as a categorical variable, with each treatment group (A / B / C / D) constituting a separate category. Definitions of individual GOLD groups are detailed in Appendix 3: GOLD treatment groups. An alternative GOLD classification to A/D groups will be applied as a secondary one shall it arise during the protocol development.
CAT score	The value within 24 months prior to and closest to Breztri/Trixeo initiation will be used. This is to be analysed as a continuous variable, expressed as mean ± standard deviation and/or median with interquartile range. This will also be recorded on follow-up as part of the outcomes. The CAT questionnaire and calculation of CAT score are detailed in Appendix 4: CAT questionnaire. Additionally, the number of patients with multiple CAT score assessments will be recorded, as well as the number of assessments per patient. This variable will be described with stratification by maintenance therapies.
Number of COPD exacerbations	This is to be measured in the year prior to the index date, and to be analysed and described as both a continuous and categorical variable, with the following categories: • None • 1 exacerbation • 2 exacerbations • 3 exacerbations • ≥4 exacerbations Additionally, the severity of exacerbation will be recorded. Complicated COPD exacerbations have been defined above as part of the outcomes. Moderate COPD exacerbations will be defined by the requirement for an acute course of systemic corticosteroids and/or a course of antibiotics within 3 days of a lower respiratory consultation, or an emergency room visit for a potentially COPD-related respiratory cause. Severe COPD exacerbations will be defined by COPD-related

	hospitalizations. Moderate and severe exacerbations are mutually exclusive, but there may be overlaps between severe and complicated exacerbations, and between moderate and complicated exacerbations (**Error! Reference source not found.**). The respective numbers of patients with moderate, severe, and complicated COPD exacerbations will be described, with multiple categories allowed for the same patient. This variable will also be recorded on follow-up as part of the outcomes.
Number of acute OCS courses	This is to be measured in the year prior to the index date, and to be analysed and described as both a continuous and categorical variable, with the following categories: • None • 1 course • 2 courses • 3 courses • ≥4 courses Acute OCS courses are short course of OCS prescriptions related to respiratory exacerbations as identified and defined by an OPRI algorithm which has been used in previous studies of OCS prescriptions. The algorithm is briefly described in Appendix 6: OPRI algorithm for acute OCS courses.
Number of antibiotic courses with lower respiratory consultations	This refers to courses of antibiotic prescriptions accompanied by consultations for lower respiratory conditions in the baseline period (year prior to index date). This is to be analysed and described as both a continuous and categorical variable, with the following categories: • None • 1 course • 2 courses • 3 courses • ≥4 courses
Average daily SABA dose, mcg/day	This is to be measured in the year prior to the index date, and to be analysed and described as both a continuous and categorical variable, with the following categories: • No SABA use • 1-100 • 101-200 • 201-300 • 301-400 • >400
COPD-related general practice consultations	This is to be measured in the year prior to the index date, and to be analysed and described as both a continuous and categorical variable, with the following categories:

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	• None • 1 consultation • 2-4 consultations • 5-7 consultations • ≥8 consultations
All-cause general practice consultations	This is to be measured in the year prior to the index date, and to be analysed and described as both a continuous and categorical variable, with the following categories: • 0-1 consultation • 2-4 consultations • 5-8 consultations • 9-13 consultations • 14-17 consultations • 18-22 consultations • ≥23 consultations
Maintenance COPD treatment immediately prior to Breztri/Trixeo initiation	This refers to the last combination of maintenance COPD treatments that is to be recorded in the year prior to the index date. It is to be analysed and described as a categorical variable, with the following categories: • LAMA only • LABA only • LABA+LAMA • ICS+LABA • ICS+LABA+LAMA as separate prescriptions (i.e. free triple) • ICS+LABA+LAMA as a single, combined prescription (i.e. fixed triple) In addition to the regimen used by patients immediately before initiating Breztri/Trixeo, the maintenance treatments used by patients during the year prior to Breztri/Trixeo initiation, and the pattern of these treatments will be described.
Maintenance COPD treatments during the year prior to Breztri/Trixeo initiation	This refers to all combinations of maintenance COPD treatments observed in the year prior to the index date. The following combinations will be recorded: • LAMA only • LABA only • LABA+LAMA • ICS+LABA • Free triple • Fixed triple The number of patients with each combination recorded during the year prior to the index date will be described; a patient may have multiple combinations recorded. Additionally, the pattern of these combinations will be described.

Number of SABA inhalers used	This is to be measured in the year prior to the index date, and to be analysed and described as both a continuous and categorical variable, with the following categories: • None • 1-2 inhaler(s) • 3-6 inhalers • 7-10 inhalers • 11-16 inhalers • ≥17 inhalers
Blood eosinophil count, 10^9cells/L	This refers to the highest blood eosinophils in the year prior to index date; if no measurement is available within a year prior to index date, the closest value within the 5 years prior to index date will be used. This is to be analysed and described as both a continuous and categorical variable, with the following categories: • <50 • 50-349 • ≥350

The above baseline variables will also be described for patients who were excluded because of having had Breztri/Trixeo initiated less than 90 days before data extraction. Additionally, the proportion of patients with the following events will be described for these patients:

- New diagnosis of heart failure
- Hospitalization for heart failure
- Myocardial infarction
- Hospitalization or hospital admittance for respiratory events
- Complicated COPD exacerbations
- Pneumonia
- Death

5. STATISTICAL ANALYSIS PLAN

5.1 Statistical Methods – General Aspects

The variables listed in Table 1 will be summarised as numbers of patients with data, means (standard deviation (SD)), medians (inter-quartile range (IQR)) or percentages, as appropriate, along with the number of patients with missing values for these measures. For each characteristic, the median (IQR) time since data collection and the patient's index date will also be presented. Where it is specified that these will be collected at more than one time point, each timepoint will be summarised separately. Each characteristic will be described with stratification by the availability of CAT data at 90 and 180 days, respectively. For all analyses,

p-values <0.05 will be considered significant. For all analyses, the numbers of patients excluded (due to missing data or other reasons) will also be summarised.

5.1.1 Primary outcome

The primary outcome (early medication success) will be presented as the number of patients achieving medication success at 90 days and also as a percentage of all patients included, together with a 95% confidence interval (CI). Overall medication success will be claimed if the lower 95% confidence limit for the percentage achieving early medication success is ≥ 70%.

5.1.2 Exploratory outcomes

Exploratory outcomes will be summarised separately for 90 days and 180 days as follows: (Summaries will include all patients with available data for the appropriate timepoint and percentages will be of all patients with available data for the appropriate timepoint, together with the number of patients not included due to missing data).

- Acceptability of medication change (patients receiving at least one additional prescription for Breztri/Trixeo) – the number and percentage (95% CI) (180 days only).
- Adherence (medication possession ratio), SABA usage (salbutamol equivalent in mg/day), and overall number of inhalers – the mean (SD), if normally distributed, or median (IQR), if non-normally distributed will be presented, along with a 95% CI.
- For patients with data available, change in CAT score will be assessed using a paired t-test (if normally distributed) or Wilcoxon's matched pairs test (if non-normally distributed). Change in CAT score will also be summarised as the mean change (SD), if normally distributed, or median change (IQR), if non-normally distributed, together with a 95% CI and also as the number and percentages of patients who had a clinically significant increase (≥2 points increase), clinically significant decrease (≥2 points decrease) or no clinically significant change (≤ 1 point change). This analysis will be stratified by prior asthma status (yes / no).
- The above analyses (acceptability of medication change, adherence, and change in CAT score) will be repeated for groups defined by whether the patient switched to Breztri/Trixeo from another triply therapy *vs.* stepped up from a non-triple therapy, and by baseline CAT score ≥10 *vs.* baseline CAT score <10.
- Sustained medication success – this is defined as for the primary outcome but will be assessed at 180 days after Breztri/Trixeo initiation. It will be analysed as described for the primary outcome.
- COPD control at baseline and follow-up will be summarised as the percentage of patients with control at each timepoint, and the change between baseline and follow-up will be assessed using a McNemar test.
- Exercise capacity at baseline and follow-up will be summarised as the percentage of patients in each category and also the median (IQR) category. The change between baseline and follow-up will be assessed using a Wilcoxon's matched pairs test.

Furthermore, stratified analysis of the primary outcome will be performed, as described above, including but not limited to for sub-groups defined by patients (a) with vs without prior asthma status; (b) who switched to Breztri/Trixeo from another triple therapy regimen *vs.* stepped up from non-triple therapy; (c) by prior exacerbation history; and (d) by prior maintenance medication adherence level.

Additionally, an exploratory analysis will be carried out to try to identify factors associated with the primary outcome (early medication success) and with change in CAT score.

Associations between the primary outcome (early medication success) and baseline values of each of the variables listed in Table 1 will be tested individually using logistic regression models. Considering the results from these univariable models, exploratory attempts may be made to create a multivariable prediction model using lasso and / or stepwise regression, to identify patient characteristics independently associated with success of the Breztri/Trixeo treatment. Consideration will be given to omitting variables from the multivariable model if they are highly correlated or have too many missing values. Clinical opinion will also be used to identify groups (e.g., above and below specified cut-offs) who might be expected to benefit least / most from the treatment and their effect tested using logistic regression models. This would also allow us to investigate interactions between specified characteristics. It is likely that the final choice of models and / or sub-groups of interest will need to take into account the distribution of patient characteristics in the sample and the total number who do not experience medication success.

A similar approach will be used for change in CAT score using linear regression to identify the baseline factors most associated with change. This analysis is likely to be limited by the number of patients for whom we have data on changes in CAT scores as well as the other covariates.

5.2 Missing Data

Values will be imputed where possible to maximise the number of patients who can be included in each analysis using the methods detailed in Table 2.

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Table 2 Missing data handling

Missing value	Rule(s)
Date (days & months)	- Impute 15th of the month for missing days - Impute July 1st for missing days and months
Strength from generic active ingredient read codes	- Affects < 1% observations - Impute strength of branded/generic drug of the same active ingredient (by Read code) that is most frequently prescribed
Invalid quantity (number of units prescribed)	- Up to 35% invalid observations. Mostly quantity = 0 1. Impute most common strength of the same drug (by strength & Read code) for the patient

	2. Impute most common quantity of drug of the same strength (by strength & Read code) prescribed for the OCS-related condition 3. Impute based on clinical input
Dose information	- Missing dose information for Breztri/Trixeo will assume two inhalations twice daily as per the defined in the summary of product characteristics. - Missing dose information for other drug such as SABA will be derived using the dose text data where possible. If this is not possible the dose will be imputed using the most common quantity of drug of the same strength.
BMI	- Patients BMI will be calculated using individual height and weight measurements if available.
Patient registration details	- Missing or incorrect patient join dates (dates in the future or distant past) will utilise the first clinical or therapeutic record as a proxy start date.

5.3 Sample size calculation

The sample size calculation is based on the primary outcome of medication success. If 80% of patients have success, 285 patients will be sufficient to give us 97.6% power to demonstrate a medication success rate ≥70% at the p<0.025 (one sided) level of significance.

6. FEASIBILITY

As of 10th August 2022, 449 patients in OPCRD were prescribed Breztri/Trixeo. After applying the inclusion and exclusion criteria, 198 patients were eligible for this study, with 180 days' follow-up data available for 136 patients. The median follow-up time of these 198 patients was 248 days [interquartile range 160-294 days]. Fifty of these patients had CAT score available in the year prior to Breztri/Trixeo initiation, and 37 had CAT score available at 1-year post-initiation.

Patients using other fixed triple therapies (Trelegy and Trimbow) were analysed with the specified inclusion and exclusion criteria using data as of 17th October 2022. Of the 16,294 and 19,462 eligible patients on Trelegy and Trimbow, respectively, 14,679 (90.1%) and 17,011 (87.4%) patients achieved medication success by 90 days, respectively. Survival analysis was also performed (Figure 4), with 90.2% and 82.9% of patients on Trelegy estimated to achieve medication success by 90 and 182 days, respectively; the corresponding values for patients on Trimbow were 87.9% and 79.4%, respectively.

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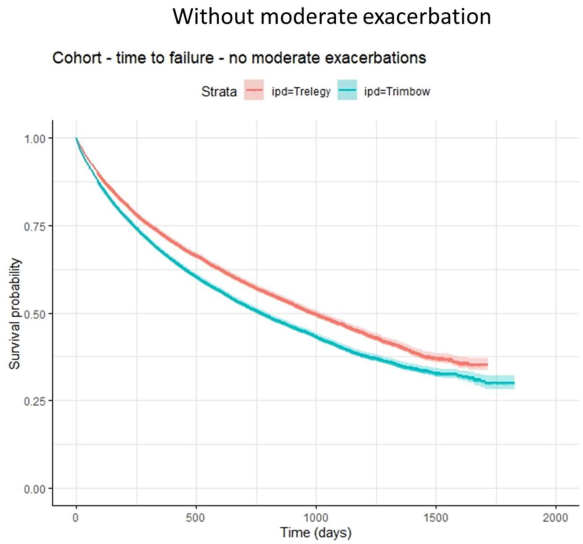
As of 24th October 2022, the number of patients eligible for this study in OPCRD has increased to 285.

Figure 4 Kaplan-Meier survival curve and risk tables for medication success in patients taking Trelegy and Trimbow



Trelegy

Time	At risk	Event	Survival	lower 95% CI	upper 95% CI
90	14710	1597	0.902	0.897	0.907
182	12682	2744	0.829	0.823	0.835
365	9454	1497	0.724	0.717	0.731
720	5517	1588	0.583	0.574	0.591
1096	2523	855	0.472	0.462	0.481
1460	507	310	0.375	0.362	0.388

Trimbow

Time	At risk	Event	Survival	lower 95% CI	upper 95% CI
90	17121	2357	0.879	0.874	0.883
182	14537	3968	0.794	0.788	0.799
365	10379	2054	0.673	0.666	0.68
720	5418	1989	0.519	0.511	0.527
1096	2280	940	0.406	0.397	0.415
1460	467	250	0.336	0.325	0.348

7. STRENGTHS AND LIMITATIONS

This study will use all eligible patients in a large real-world database. The real-life design of this study provides high generalisability of the results to primary care patients managed in actual primary care practice. Additionally, the availability of patient-reported outcomes allows for in-depth exploration of disease state.

It is worth providing the caveat that patient-reported outcome data is missing for some patients, potentially predisposing to selection bias, e.g. patients who are more health-conscious may be more willing to provide such data, which may confound the study results. The primary outcome, medication success, is also novel and not necessarily well-validated, possibly requiring further evaluation. Additionally, no control group is included in this study, meaning that no conclusion

may be made as to whether Breztri/Trixeo provides incremental benefits to patients with COPD, compared to or on top of standard therapies. Furthermore, the observational nature of this study predisposes to residual and unmeasured confounders. This was partially mitigated by using a pre-post design. Lastly, the dataset represents information collected for clinical and routine use rather than specifically for research purposes. The validity and completeness of individual patient records cannot be assessed.

8. STUDY CONDUCT AND REGULATORY DETAILS

8.1 Data Management

Database construction and analyses of data will be performed by OPRI.

8.2 Study Conduct

Analyses will be performed by the Observational & Pragmatic Research Institute. A steering committee of respiratory research experts will be established to advise on the study. Suggested members of the steering committee are:

- Prof David Price
- Dr James Kreindler
- Prof Dave Singh
- Dr Katherine Hickman

8.2.1 Study Flow Chart and Plan

TIMELINE PROJECTION TO STUDY COMPLETION		
Department/Activity	**Estimated Delivery Time**	**Contracted Timeline**
Draft Protocol to AZ	July 2022	
Dataset Created: OPCRD electronic medical records-only	July 2022	
Analysis of OPCRD electronic medical records-only dataset	Sep 2022	
Dataset Created: OPCRD enhanced with PRO data	Nov 2022	
Analysis of OPCRD enhanced with PRO data	Dec 2022	
Study report with results from OPCRD electronic medical records-only dataset	Nov 2022	
Final Study Report Delivery	Dec 2022	

8.2.2 Procedures

8.2.3 Quality Control

All code for dataset generation, dataset preparation and analyses will be reviewed by a second researcher. All data will be reviewed for correctness and completeness, and the data will be cleaned appropriately. All code lists used for this study will be reviewed by a clinician or a pharmacologist.

8.3 Protection of Human Subjects

The Observational Study will be performed in accordance with ethical principles that are consistent with the Declaration of Helsinki, ICH GCPs, GPP and the applicable legislation on Non-Interventional Studies and/or Observational Studies.

The Investigator will perform the Observational Study in accordance with the regulations and guidelines governing medical practice and ethics in the country of the Observational Study and in accordance with currently acceptable techniques and know-how.

8.4 Communication Plan

8.4.1 Publication Plan

The results will be presented in at least in one national/international conference and a manuscript will be submitted to a journal.

8.4.2 Compliance with Study Registration and Results Posting Requirements

The study will be registered at ENCePP (http://www.encepp.eu/).

8.4.3 Compliance with Financial Disclosure Requirements

Any information that may be seen as a conflict of interest in terms of compensation or financial interests will be disclosed for each investigator.

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10. APPENDICES

10.1 Appendix 1: Potential PRO data from the OPC quality improvement program

The OPC quality improvement program is a free service provided by OPC to participating general practices. As part of the program, some patients may have completed the OPC questionnaire (Supplementary Table 1), which includes assessment of the CAT score. Treatment satisfaction may be assessed by relevant measures as part of the quality improvement program as well.

Supplementary Table 1. Domains of the OPC Questionnaire.

OPC Questionnaire Domains	Number of Questions
CAT	8
Cough Severity	1
Sputum	1
Breathing Problems	1
Breathlessness/ mMRC	5
Physical Activity	1
Exacerbation QOF	2
Flare-up treatment	3
Hospital Admittance	2
Reliever Inhaler	1
Maintenance Medication	1
Medication Adherence	1
Inhaler technique	1
Smoking	3
Action Plan	1
Rescue Pack	2
Goal Setting	2
TOTAL	**36**

Specifically, responses to the question for the domain "physical activity" constitute the outcome data for exploratory outcome 4 (exercise capacity). Patients are asked to respond to the question "thinking about exercise, how much time do you spend doing exercise or activities per day (e.g. walking)" with one of the following categories which thus constitute the nominal categories for exploratory outcome 4:

- None
- 15 minutes
- 30 minutes
- 45 minutes

- 1 hour
- 2 hours
- 3 hours or more

Additionally, the OPC quality improvement program uses the COPD control tool, the data from which constitutes the outcome data for exploratory outcome 3 (COPD control). The COPD control tool was developed and validated to help define the current clinical situation of a patient and therefore support individualized evaluation and management.[15,16] Clinical impact (relating to the patient's current clinical situation) and stability (how this situation compares to previous visits or assessments) are the two components that make up the tool (Figure 5). The tool describes a patient's COPD status as 'controlled' if they have low clinical impact and are stable in terms of subjective assessment and exacerbation frequency. Patients are described as 'not controlled' if either clinical impact is 'high' or they are 'unstable' according to tool parameters. These categories ('controlled' and 'not controlled') thus constitute the data categories for the binary exploratory outcome 3.

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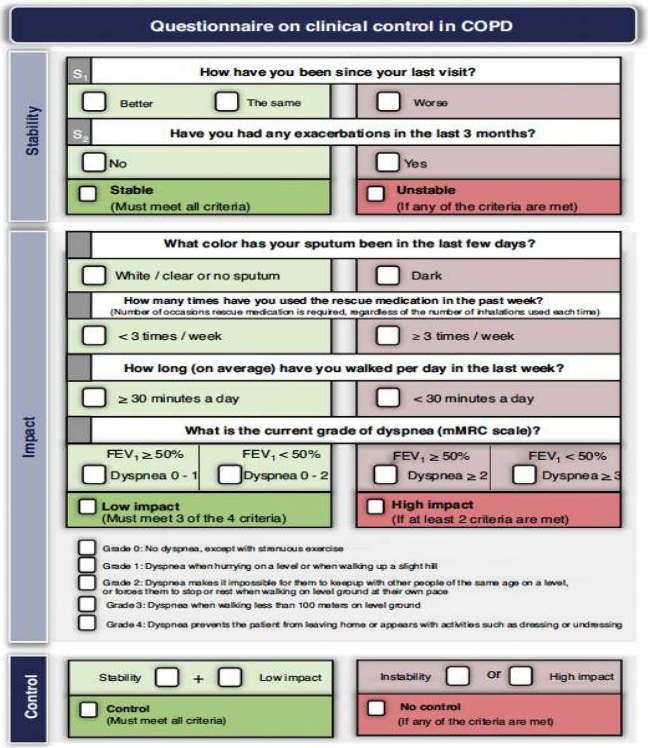
Figure 5 The COPD control tool



10.2 Appendix 2: mMRC score

The mMRC score is measured in a scale of 0-4:

0 - Dyspnea only with strenuous exercise

1 - Dyspnea when hurrying or walking up a slight hill

2 - Walks slower than people of the same age because of dyspnea or has to stop for breath when walking at own pace

3 - Stops for breath after walking 100 yards (91 m) or after a few minutes

4 - Too dyspneic to leave house or breathless when dressing

10.3 Appendix 3: GOLD treatment groups

Definitions of GOLD treatment groups are summarized in Figure 6.

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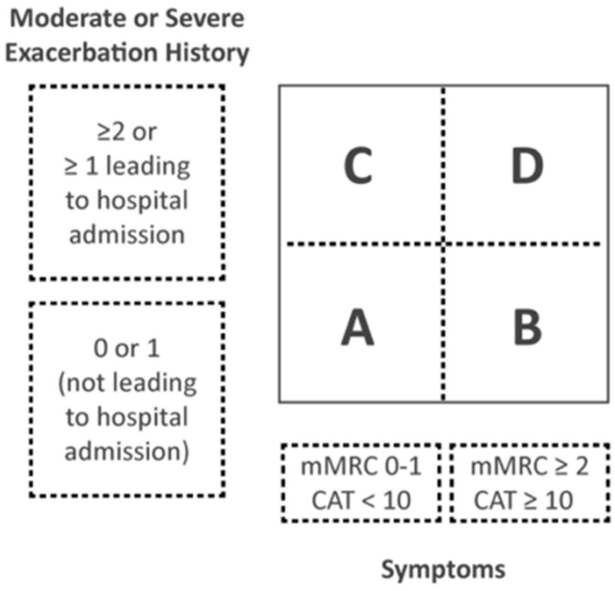
Figure 6 Definition of GOLD treatment groups



10.4 Appendix 4: CAT questionnaire

The CAT questionnaire contains 8 items, each of which adopts a Likert-type scale of 0-5 scores. The items are as follows (bracketed number indicates the corresponding score):

1. "I never cough" (0) to "I cough all the time" (5)
2. "I have no phlegm (mucus) in my chest at all" (0) to "My chest is completely full of phlegm (mucus)" (5)
3. "My chest does not feel tight at all" (0) to "My chest feels very tight" (5)
4. "When I walk up a hill for one flight of stairs I am not breathless" (0) to "When I walk up a hill or one flight of stairs I am very breathless" (5)
5. "I am not limited doing any activities at home" (0) to "I am very limited doing activities at home" (5)
6. "I am confident leaving my home despite my lung condition" (0) to "I am not at all confident leaving my home because of my lung condition" (5)
7. "I sleep soundly" (0) to "I don't sleep soundly because of my lung condition" (5)
8. "I have lots of energy" (0) to "I have no energy at all" (5)

The CAT score is calculated as a sum of the score from all 8 items above.

10.5 Appendix 6: OPRI algorithm for acute OCS courses

Acute courses of OCS prescriptions are identified and defined using the algorithm depicted in Figure 7.

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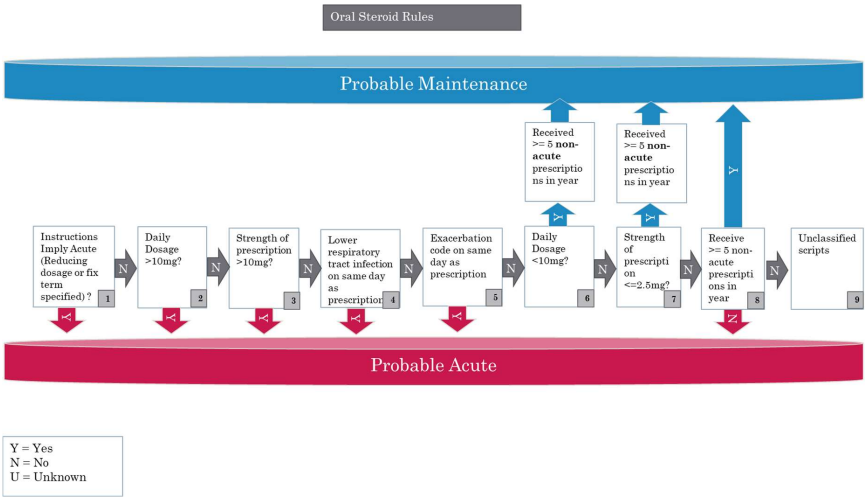
Figure 7 OPRI algorithm for acute OCS courses



10.6 SABA Read Codes

read_code	MX_PRODUCT_NAME
c12w.	SALBUTAMOL inh 100micrograms/inhalation
c131.	ASMAVEN inh 100micrograms
c133.	SALBULIN inh
c134.	VENTOLIN inh 100micrograms/inhalation
c136.	VENTOLIN rcap 200micrograms
c137.	VENTOLIN rcap 400micrograms
c13C.	SALBUTAMOL disc 200micrograms
c13D.	SALBUTAMOL disc 400micrograms
c13E.	VENTODISKS disc 400micrograms/blister
c13F.	VENTODISKS disc 200micrograms/blister
c13G.	VENTODISKS disc 400micrograms/blister
c13H.	SALAMOL inh 100micrograms/actuation
c13I.	AIROMIR cfc free inh 100micrograms/inhalation
c13J.	VENTOLIN inh 100micrograms/inhalation
c13K.	SALAMOL EASI-BREATHE breath act inh 100micrograms/actuation
c13L.	VENTOLIN ACCUHALER 200micrograms/actuation
c13M.	VENTOLIN ACCUHALER 200micrograms/actuation
c13N.	SALBUTAMOL vortex inh 100micrograms/inhalation
c13P.	SALBUTAMOL spacehaler 100micrograms/inhalation
c13Q.	SALBUTAMOL CYCLOCAPS inh caps 200micrograms [APS]
c13R.	SALBUTAMOL breath act pwdr inh 200micrograms/actuation
c13S.	SALBUTAMOL breath act pwdr inh 95micrograms
c13T.	VENTOLIN inh 100micrograms/inhalation
c13U.	SALBUTAMOL breath act inh 100micrograms/actuation
c13V.	SALBUTAMOL inh 100micrograms/inhalation
c13Y.	SALAMOL inh 100micrograms/actuation
c13c.	AEROLIN AUTOHALER breath act inh 100micrograms/actuation
c13d.	VENTODISKS disc 200micrograms/blister
c13e.	VENTODISKS disc 400micrograms/blister
c13f.	VENTODISKS disc 200micrograms/blister
c13g.	VENTODISKS disc 400micrograms/blister
c13h.	SALBUVENT inh 100micrograms/actuation
c13l.	AEROLIN AUTOHALER breath act inh 100micrograms/actuation
c13n.	AEROLIN AUTOHALER breath act inh 100micrograms/actuation
c13p.	MAXIVENT inh 100micrograms/inhalation
c13q.	SALBUTAMOL inh caps 200micrograms
c13r.	SALBUTAMOL inh caps 400micrograms
c13v.	SALBUTAMOL inh 100micrograms/inhalation
c13x.	SALBUTAMOL inh caps 200micrograms

c13y.	SALBUTAMOL inh caps 400micrograms
c144.	BRICANYL inh
c145.	BRICANYL refill canister
c146.	BRICANYL spacer inh
c14f.	BRICANYL TURBOHALER 500micrograms
c14g.	BRICANYL TURBOHALER 500micrograms
c14j.	BRICANYL TURBOHALER 500micrograms
c14t.	TERBUTALINE inh 250micrograms/actuation
c14u.	TERBUTALINE inh 250micrograms/actuation
c14v.	TERBUTALINE inh 250micrograms/actuation
c151.	BEROTEC inh 200micrograms/actuation
c153.	BEROTEC inh 100micrograms/actuation
c154.	FENOTEROL inh 100micrograms/actuation
c15y.	FENOTEROL inh 200micrograms/actuation
c173.	BRONCHODIL inh 500micrograms/dose
c17y.	REPROTEROL inh 500micrograms/dose
c181.	PULMADIL inh
c182.	PULMADIL inh
c183.	PULMADIL AUTO inh
c18z.	RIMITEROL inh
c1E1.	SALAMOL EASI-BREATHE breath act inh 100micrograms/actuation
c1E2.	PULVINAL SALBUTAMOL breath act pwdr inh 200micrograms/actuation
c1E3.	VENTODISKS disc 200micrograms/blister
c1E4.	VENTODISKS disc 400micrograms/blister
c1E5.	VENTODISKS disc 200micrograms/blister
c1E6.	VENTODISKS disc 400micrograms/blister
c1E7.	EASYHALER SALBUTAMOL breath act pwdr inh 100micrograms/actuation
c1E8.	EASYHALER SALBUTAMOL breath act pwdr inh 200micrograms/actuation
c1E9.	SALBULIN inh
c1EA.	SALBUTAMOL breath act pwdr inh 100micrograms/actuation
c1EC.	SALBUTAMOL disc 400micrograms
c51A.	DUOVENT inh 40micrograms + 100micrograms/actuation
c51B.	FENOTEROL + IPRATROPIUM BROMIDE breath act inh 100micrograms + 40micrograms/actuation
c51C.	IPRATROPIUM BROMIDE + SALBUTAMOL inh 20mcg + 100mcg
c51D.	COMBIVENT inh 20mcg + 100mcg
c51i.	DUOVENT inh 40micrograms + 100micrograms/actuation
c51x.	DUOVENT AUTOHALER breath act inh
c621.	VENTIDE inh
c622.	VENTOLIN rcap 200micrograms
c623.	VENTIDE paed rcap
c722.	AEROCROM inh

c72y.	SODIUM CROMOGLICATE + SALBUTAMOL inh & spacer
c72z.	SODIUM CROMOGLICATE + SALBUTAMOL inh
i966.	VENTOLIN inh 100micrograms/inhalation
x00Af	SALBUTAMOL inh 100micrograms/inhalation
x02Xr	COMBIVENT inh 20mcg + 100mcg
x02qI	SALAMOL inh 100micrograms/actuation
x02uD	VENTOLIN ACCUHALER 200micrograms/actuation

10.7 SAMA Read Codes

read_code	MX_PRODUCT_NAME
c311.	ATROVENT inh 20micrograms/actuation
c312.	ATROVENT UDVs neb soln 500micrograms/2ml
c313.	ATROVENT FORTE inh 40micrograms/actuation
c314.	ATROVENT UDVs neb soln 0.25mg/ml
c315.	ATROVENT AUTOHALER breath act inh 20micrograms/actuation
c316.	STERI-NEB IPRATROPIUM unit dose neb soln 250micrograms/ml
c317.	STERI-NEB IPRATROPIUM unit dose neb soln 250micrograms/ml
c318.	ATROVENT AEROCAPS 40mcg
c319.	ATROVENT AEROHALER 40mcg
c31A.	IPRATROPIUM BROMIDE inh caps 40mcg
c31B.	IPRATROPIUM BROMIDE caps + inh 40mcg
c31C.	RESPONTIN NEBULES 250micrograms/ml
c31D.	RESPONTIN NEBULES 250micrograms/ml
c31F.	TROPIOVENT STERIPOULE unit dose neb soln 250micrograms/ml
c31G.	ATROVENT cfc free inh 20micrograms/actuation
c31t.	IPRATROPIUM BROMIDE cfc free inh 20micrograms/actuation
c31u.	IPRATROPIUM BROMIDE inh 20micrograms/dose
c31v.	IPRATROPIUM BROMIDE unit dose neb soln 250micrograms/ml
c31w.	IPRATROPIUM BROMIDE unit dose neb soln 250micrograms/ml
c31x.	IPRATROPIUM BROMIDE inh 20micrograms/dose
c31y.	STERI-NEB IPRATROPIUM unit dose neb soln 250micrograms/ml
c31z.	IPRATROPIUM BROMIDE inh 40micrograms/metered inhalation
c51A.	DUOVENT inh 40micrograms + 100micrograms/actuation
c51B.	FENOTEROL + IPRATROPIUM BROMIDE breath act inh 100micrograms + 40micrograms/actuation
c51C.	IPRATROPIUM BROMIDE + SALBUTAMOL inh 20mcg + 100mcg
c51D.	COMBIVENT inh 20mcg + 100mcg
c51E.	COMBIVENT UDVs neb soln 2.5ml
c51F.	IPRATROPIUM BROMIDE + SALBUTAMOL unit dose neb soln 500micrograms + 2.5mg/2.5ml

c51H.	SALBUTAMOL + IPRATROPIUM BROMIDE unit dose neb soln 2.5mg + 500micrograms/2.5ml
c51i.	DUOVENT inh 40micrograms + 100micrograms/actuation
c51v.	DUOVENT UDVs neb soln
c51w.	IPRATROPIUM BROMIDE + SALBUTAMOL unit dose neb soln 500micrograms + 2.5mg/2.5ml
c51x.	DUOVENT AUTOHALER breath act inh
c531.	IPRAMOL STERI-NEB unit dose neb soln 500micrograms + 2.5mg/2.5ml
x02Uk	ATROVENT AEROCAPS 40mcg
x02Xr	COMBIVENT inh 20mcg + 100mcg

10.8 ICS Read Codes

read_code	MX_PRODUCT_NAME
c611.	BECLOFORTE inh 250micrograms/actuation
c612.	BECOTIDE 50 inh 50micrograms/actuation
c613.	BECOTIDE rcap 100micrograms
c614.	BECOTIDE rcap 200micrograms
c617.	BECOTIDE 100 inh 100micrograms/actuation
c619.	BECODISKS disc 100micrograms
c61A.	BECODISKS disc 200micrograms
c61B.	BECOTIDE rcap 400micrograms
c61C.	BECODISKS disc 100micrograms
c61D.	BECODISKS disc 200micrograms
c61E.	BECLOMETASONE breath act inh 250micrograms/actuation
c61F.	BECLOMETASONE breath act inh 100micrograms/actuation
c61G.	FILAIR inh 50micrograms/actuation
c61H.	FILAIR inh 100micrograms/actuation
c61J.	FILAIR FORTE inh 250micrograms/actuation
c61K.	BECLAZONE inh 50micrograms/actuation
c61L.	BECLAZONE inh 100micrograms/actuation
c61M.	BECLAZONE inh 250micrograms/actuation
c61N.	BECLOFORTE disks (refill pack) 400micrograms/actuation
c61O.	BECLOMETASONE breath act inh 100micrograms/actuation
c61P.	BECLOMETASONE disc 100micrograms
c61Q.	BECLOFORTE INTEGRA inh/compt spacer 250micrograms/actuation
c61R.	BECLOFORTE INTEGRA inh/compt spacer 250micrograms/actuation
c61S.	BECLOMETASONE inh/compt spacer 250micrograms/actuation
c61T.	BECLOMETHASONE breath act inh 250micrograms/actuation [APS]
c61V.	BECLOMETASONE vortex inh 50micrograms/actuation
c61W.	BECLOMETASONE inh caps 100micrograms
c61X.	BECLOMETASONE inh 100micrograms/actuation

c61Y.	BDP spacehaler 100micrograms/actuation
c61Z.	BECLOMETASONE vortex inh 250micrograms/actuation
c61a.	BECODISKS disc 200micrograms
c61b.	BECOTIDE rcap 400micrograms
c61c.	BECODISKS disc 100micrograms
c61d.	BECODISKS disc 200micrograms
c61e.	BECODISKS disc 400micrograms
c61f.	BECODISKS disc 400micrograms
c61g.	FILAIR inh 50micrograms/actuation
c61h.	FILAIR inh 100micrograms/actuation
c61i.	BECOTIDE 200 inh 200micrograms/actuation
c61j.	AEROBEC AUTOHALER 50micrograms/actuation
c61k.	AEROBEC forte AUTOHALER 250micrograms/actuation
c61l.	AEROBEC AUTOHALER 100micrograms/actuation
c61m.	BECLOFORTE DISKHALER 400micrograms/actuation
c61n.	BECLOFORTE disks (refill pack) 400micrograms/actuation
c61p.	BECLOMETASONE disc 100micrograms
c61q.	BECLOMETASONE disc 200micrograms
c61r.	BECLOMETASONE inh 100micrograms/actuation
c61s.	BECLOMETASONE disc 200micrograms
c61t.	BECLOMETASONE inh 250micrograms/actuation
c61u.	BECLOMETASONE inh 200micrograms/actuation
c61v.	BECOTIDE 50 inh 50micrograms/actuation
c61w.	BECLOMETASONE inh caps 100micrograms
c61x.	BECLOMETASONE inh caps 200micrograms
c61z.	BECOTIDE 100 inh 100micrograms/actuation
c621.	VENTIDE inh
c641.	PULMICORT inh 200micrograms
c643.	PULMICORT refill canister 200micrograms
c644.	PULMICORT LS inh 50micrograms
c645.	PULMICORT LS refill canister 50micrograms
c647.	PULMICORT inh 200micrograms
c648.	PULMICORT TURBOHALER breath act pwdr inh 200micrograms/actuation
c649.	PULMICORT TURBOHALER breath act pwdr inh 400micrograms/actuation
c64A.	BUDESONIDE inh 200micrograms/actuation
c64B.	BUDESONIDE inh 50micrograms/actuation
c64C.	PULMICORT inh 200micrograms
c64D.	PULMICORT LS inh 50micrograms
c64E.	PULMICORT inh 200micrograms
c64F.	BUDESONIDE dry pdr inh cart ref 200micrograms
c64G.	NOVOLIZER BUDESONIDE inh pdr (refill) 200micrograms
c64H.	EASYHALER BUDESONIDE breath act pwdr inh 100micrograms/actuation

c64I.	EASYHALER BUDESONIDE breath act pwdr inh 200micrograms/actuation
c64J.	EASYHALER BUDESONIDE breath act pwdr inh 400micrograms/actuation
c64K.	BUDESONIDE inh 100micrograms/actuation
c64L.	BUDESONIDE inh 100micrograms/actuation
c64M.	PULMICORT inh 200micrograms
c64N.	BUDESONIDE inh 200micrograms/actuation
c64c.	PULMICORT TURBOHALER breath act pwdr inh 100micrograms/actuation
c64d.	BUDESONIDE breath act pwdr inh 100micrograms/actuation
c64e.	PULMICORT inh 200micrograms
c64g.	BUDESONIDE breath act pwdr inh 200micrograms/actuation
c64h.	BUDESONIDE breath act pwdr inh 400micrograms/actuation
c64m.	BUDESONIDE inh caps 200micrograms
c64n.	BUDESONIDE inh caps 400micrograms
c64o.	BUDESONIDE inh 200micrograms/actuation
c64p.	NOVOLIZER BUDESONIDE inh pdr + device 200micrograms
c64u.	BUDESONIDE dry pdr inh cart+dev 200micrograms
c64v.	BUDESONIDE inh 200micrograms/actuation
c64x.	BUDESONIDE inh 200micrograms/actuation
c64y.	BUDESONIDE inh 50micrograms/actuation
c64z.	BUDESONIDE inh 200micrograms/actuation
c651.	FLIXOTIDE disc 50micrograms
c652.	FLIXOTIDE disc 100micrograms
c653.	FLIXOTIDE disc 250micrograms
c654.	FLUTICASONE disc 500micrograms
c655.	FLUTICASONE disc 100micrograms
c656.	FLUTICASONE disc 250micrograms
c657.	FLIXOTIDE disc 50micrograms
c658.	FLIXOTIDE disc 100micrograms
c65A.	FLUTICASONE disc 50micrograms
c65B.	FLIXOTIDE disc 100micrograms
c65C.	FLIXOTIDE disc 250micrograms
c65D.	FLIXOTIDE inh 25micrograms/actuation
c65E.	FLIXOTIDE inh 50micrograms/actuation
c65F.	FLIXOTIDE inh 125micrograms/actuation
c65G.	FLUTICASONE inh 25micrograms/actuation
c65H.	FLUTICASONE inh 50micrograms/actuation
c65I.	FLUTICASONE inh 50micrograms/actuation
c65J.	FLUTICASONE inh 250micrograms/actuation
c65K.	FLIXOTIDE inh 250micrograms/actuation
c65L.	FLIXOTIDE disc 500micrograms
c65M.	FLIXOTIDE disc 500micrograms
c65N.	FLUTICASONE disc 500micrograms

c65O.	FLUTICASONE disc 500micrograms
c65P.	FLUTICASONE breath act pwdr inh 50micrograms/inhalation
c65Q.	FLUTICASONE breath act pwdr inh 100micrograms/inhalation
c65R.	FLIXOTIDE ACCUHALER 250micrograms/inhalation
c65S.	FLUTICASONE breath act pwdr inh 500micrograms/inhalation
c65T.	FLIXOTIDE ACCUHALER 50micrograms/inhalation
c65U.	FLIXOTIDE ACCUHALER 100micrograms/inhalation
c65V.	FLIXOTIDE ACCUHALER 250micrograms/inhalation
c65W.	FLIXOTIDE ACCUHALER 500micrograms/inhalation
c65b.	FLUTICASONE cfc free inh 125micrograms/actuation
c65c.	FLUTICASONE cfc free inh 250micrograms/actuation
c65d.	FLIXOTIDE EVOHALER 125micrograms/actuation
c65e.	FLIXOTIDE EVOHALER 250micrograms/actuation
c65f.	FLUTICASONE cfc free inh 50micrograms/actuation
c65g.	FLUTICASONE inh 25micrograms/actuation
c661.	ASMABEC spacehaler 250micrograms/actuation
c662.	BECOTIDE EASI-BREATHE breath act inh 50micrograms/actuation
c663.	BECOTIDE EASI-BREATHE breath act inh 100micrograms/actuation
c664.	BECLOFORTE EASI-BREATHE breath act inh 250micrograms/actuation
c665.	QVAR cfc free inh 50micrograms/actuation
c666.	QVAR cfc free inh 100micrograms/actuation
c667.	QVAR AUTOHALER cfc/free b/act inh 50micrograms/actuation
c668.	QVAR AUTOHALER cfc/free b/act inh 100micrograms/actuation
c669.	BECLAZONE inh 200micrograms/actuation
c66A.	BECLOMETASONE breath act inh 50micrograms/actuation
c66B.	BECLOMETASONE breath act pwdr inh 100micrograms/actuation
c66C.	BECLOMETASONE breath act inh 250micrograms/actuation
c66D.	ASMABEC CLICKHALER dry pdr inh 50micrograms
c66E.	ASMABEC CLICKHALER dry pdr inh 100micrograms
c66F.	BECLOMETASONE breath act pwdr inh 250micrograms/actuation
c66G.	BECLOMETASONE breath act pwdr inh 400micrograms/actuation
c66H.	BECLOMETASONE breath act pwdr inh 200micrograms/actuation
c66I.	PULVINAL BECLOMETASONE DIPROPIONATE breath act pwdr inh 100micrograms/actuation
c66J.	PULVINAL BECLOMETASONE DIPROPIONATE breath act pwdr inh 200micrograms/actuation
c66K.	PULVINAL BECLOMETASONE DIPROPIONATE breath act pwdr inh 400micrograms/actuation
c66L.	BECLOMETASONE CYCLOCAPS inh caps 100micrograms [APS]
c66M.	BECLOMETASONE CYCLOCAPS inh caps 200micrograms [APS]
c66N.	BECLOMETASONE CYCLOCAPS inh caps 400micrograms [APS]
c66P.	BECODISKS disc 100micrograms

c66Q.	BECODISKS disc 200micrograms
c66R.	BECODISKS disc 400micrograms
c66S.	BECODISKS disc 100micrograms
c66T.	BECOTIDE 200 inh 200micrograms/actuation
c66U.	BECODISKS disc 400micrograms
c66V.	BECLOMETASONE EXTRAFINE PARTICLE cfc free inh 50micrograms/actuation
c66W.	BECLOMETASONE EXTRAFINE PARTICLE cfc free inh 100micrograms/actuation
c66X.	BECLOMETASONE breath act inh 50micrograms/actuation
c66Y.	BECLOMETASONE breath act inh 100micrograms/actuation
c66Z.	QVAR EASI-BREATHE cfc/free b/act inh 50micrograms/actuation
c66a.	QVAR EASI-BREATHE cfc/free b/act inh 100micrograms/actuation
c66b.	EASYHALER BECLOMETASONE breath act pwdr inh 200micrograms/actuation
c66c.	CLENIL MODULITE cfc free inh 50micrograms/actuation
c66d.	CLENIL MODULITE cfc free inh 100micrograms/actuation
c66e.	CLENIL MODULITE cfc free inh 200micrograms/actuation
c66f.	CLENIL MODULITE cfc free inh 250micrograms/actuation
c66g.	BECLOMETASONE cfc free inh 200micrograms/actuation
c66h.	BECLOMETASONE cfc free inh 250micrograms/actuation
c681.	MOMETASONE FUROATE dry pdr inh 200micrograms/actuation
c682.	MOMETASONE FUROATE dry pdr inh 400micrograms/actuation
c683.	ASMANEX TWISTHALER dry pdr inh 200micrograms/actuation
c684.	ASMANEX TWISTHALER dry pdr inh 400micrograms/actuation
c691.	ALVESCO cfc free inh 160micrograms/actuation
c692.	ALVESCO cfc free inh 80micrograms/actuation
c69y.	CICLESONIDE cfc free inh 80micrograms/actuation
c69z.	CICLESONIDE cfc free inh 160micrograms/actuation
p436.	BECLOFORTE VM pack 250micrograms/actuation
x00Hz	BECODISKS disc 200micrograms
x00I0	BECODISKS disc 400micrograms
x00QU	PULMICORT inh 200micrograms
x00gE	PULMICORT TURBOHALER breath act pwdr inh 100micrograms/actuation
x00gF	PULMICORT TURBOHALER breath act pwdr inh 200micrograms/actuation
x00gG	PULMICORT TURBOHALER breath act pwdr inh 400micrograms/actuation
x01MQ	BECLOMETASONE inh 100micrograms/actuation
x02Mk	BUDESONIDE inh 200micrograms/actuation
x02ct	FLIXOTIDE ACCUHALER 100micrograms/inhalation
x03d9	PULMICORT inh 200micrograms

10.9 LABA & ICS/LABA Read codes

read_code	MX_PRODUCT_NAME
c19..	SALMETEROL inh 25micrograms/actuation

c191. SALMETEROL inh 25micrograms/actuation
c192. SEREVENT inh 25micrograms/actuation
c193. SEREVENT DISKHALER 50micrograms
c194. SEREVENT DISKHALER 50micrograms
c195. SALMETEROL disc 50micrograms
c196. SALMETEROL disc 50micrograms
c197. SALMETEROL disc 50micrograms
c198. SEREVENT ACCUHALER 50micrograms/actuation
c199. SEREVENT inh 25micrograms/actuation
c19A. SALMETEROL inh 25micrograms/actuation
c19B. SALMETEROL inh 25micrograms/actuation
c19z. SALMETEROL disc 50micrograms
c1C1. FORMOTEROL FUMARATE inh caps 12mcg
c1C2. FORADIL inh caps 12mcg
c1C3. FORMOTEROL FUMARATE breath act inh 6 micrograms/actuation
c1C4. FORMOTEROL FUMARATE breath act inh 12micrograms/actuation
c1C5. OXIS 6 TURBOHALER 6 micrograms/actuation
c1C6. OXIS 12 TURBOHALER 12micrograms/actuation
c1C7. ATIMOS MODULITE cfc free inh 12micrograms/actuation
c1C8. FORMOTEROL FUMARATE breath act inh 12micrograms/actuation
c1Cz. FORMOTEROL FUMARATE breath act inh 12micrograms/actuation
c1D1. SERETIDE 100 ACCUHALER
c1D2. SERETIDE 250 ACCUHALER
c1D3. SERETIDE 500 ACCUHALER
c1D4. SERETIDE 50 EVOHALER 25micrograms + 50micrograms/actuation
c1D5. SERETIDE 125 EVOHALER 25micrograms + 125micrograms/actuation
c1D6. SERETIDE 250 EVOHALER 25micrograms + 250micrograms/actuation
c1D7. SIRDUPLA 25micrograms/125micrograms inhaler
c1D8. SIRDUPLA 25micrograms/250micrograms inhaler
c1D9. AIRFLUSAL FORSPIRO 50micrograms/500micrograms pdr inhaler
c1Du. FLUTICASONE + SALMETEROL cfc free inh 50micrograms + 25micrograms/actuation
c1Dv. FLUTICASONE + SALMETEROL cfc free inh 125micrograms + 25micrograms/actuation
c1Dw. FLUTICASONE + SALMETEROL cfc free inh 250micrograms + 25micrograms/actuation
c1Dx. FLUTICASONE + SALMETEROL dry pdr inh 100micrograms + 50micrograms/inhalation
c1Dy. FLUTICASONE + SALMETEROL dry pdr inh 250micrograms + 50micrograms/inhalation
c1Dz. FLUTICASONE + SALMETEROL dry pdr inh 500micrograms + 50micrograms/inhalation
c1b1. ONBREZ BREEZHALER capsules for inhalation + inhaler 150micrograms [NOVARTIS]
c1b2. ONBREZ BREEZHALER capsules for inhalation + inhaler 150micrograms [NOVARTIS]
c1b3. ONBREZ BREEZHALER capsules for inhalation + inhaler 300micrograms [NOVARTIS]
c1b4. ONBREZ BREEZHALER capsules for inhalation + inhaler 300micrograms [NOVARTIS]
c1c1. Flutiform Cfc-free inhaler 50 micrograms + 5 micrograms/dose 120 doses
c1c2. Flutiform Cfc-free inhaler 125 micrograms + 5 micrograms/dose 120 doses

c1c3.	Flutiform Cfc-free inhaler 250 micrograms + 10 micrograms/dose 120 doses
c1cx.	Flutiform Cfc-free inhaler 250 micrograms + 10 micrograms/dose 120 doses
c1cy.	Flutiform Cfc-free inhaler 125 micrograms + 5 micrograms/dose 120 doses
c1cz.	Flutiform Cfc-free inhaler 50 micrograms + 5 micrograms/dose 120 doses
c1d1.	STRIVERDI RESPIMAT 2.5micrograms inhaler
c1d2.	OLODATEROL 2.5micrograms inhaler
c671.	SYMBICORT TURBOHALER 100micrograms + 6micrograms/actuation
c672.	SYMBICORT TURBOHALER 200micrograms + 6micrograms/actuation
c673.	SYMBICORT TURBOHALER 400micrograms + 12micrograms/actuation
c674.	DUORESP SPIROMAX 160mcg/4.5mcg breath-act dry powder inhaler
c675.	DUORESP SPIROMAX 320mcg/9mcg breath-act dry powder inhaler
c67x.	BUDESONIDE + FORMOTEROL breath act pwdr inh 400micrograms + 12micrograms/actuation
c67y.	BUDESONIDE + FORMOTEROL breath act pwdr inh 200micrograms + 6micrograms/actuation
c67z.	SYMBICORT TURBOHALER 100micrograms + 6micrograms/actuation
c6A1.	FOSTAIR cfc free inh 100micrograms + 6micrograms/actuation
c6A2.	FOSTAIR NEXTHALER 100micrograms + 6micrograms powder inhaler
c6A3.	FOSTAIR 200micrograms/6micrograms inhaler
c6A4.	FOSTAIR NEXTHALER 200micrograms/6micrograms powder inhaler
c6Aw.	BECLOMET DIPROP+FORMOTERL FUMARATE DIHYD 200mcg/6mcg pdr inh
c6Ax.	BECLOMET DIPROP+FORMOTERL FUMARATE DIHYD 200mcg/6mcg inhaler
c6Ay.	BECLOMET DIPROP+FORMOTERL FUMARATE DIHYD 100mcg/6mcg pdr inh
c6Az.	BECLOMETASONE + FORMOTEROL 100 micrograms + 6 micrograms/dose
c6B1.	RELVAR ELLIPTA 184micrograms/22micrograms inhaler
c6B2.	FLUTICASONE FUROATE+VILANTEROL 184mcg/22mcg dry pdr inhaler
c6B3.	RELVAR ELLIPTA 92micrograms/22micrograms inhaler
c6B4.	FLUTICASONE FUROATE+VILANTEROL 92mcg/22mcg dry pdr inhaler
x02qr	SEREVENT ACCUHALER 50micrograms/actuation
x04xm	SERETIDE 100 ACCUHALER
x0594	SERETIDE 125 EVOHALER 25micrograms + 125micrograms/actuation
x05J2	SYMBICORT TURBOHALER 100micrograms + 6micrograms/actuation

10.10 LAMA Read codes

read_code	MX_PRODUCT_NAME
c33..	TIOTROPIUM inh caps 18 micrograms
c331.	TIOTROPIUM inh pdr cap (refill) 18 micrograms
c332.	TIOTROPIUM inh caps 18 micrograms
c333.	Spiriva Respimat Solution For Inhalation 2.5 micrograms/puff 60 puffs

c33x.	Spiriva Respimat Solution For Inhalation 2.5 micrograms/puff 60 puffs
c33y.	SPIRIVA inh pdr caps+dev 18 micrograms
c33z.	SPIRIVA inh caps 18 micrograms
c341.	EKLIRA GENUAIR inhalation powder 322micrograms
c342.	Aclidinium Bromide Dry Powder Inhaler 375 micrograms/dose
c351.	Incruse Ellipta 55micrograms/dose dry powder inhaler
c352.	UMECLIDINIUM 55micrograms/dose dry powder inhaler
o323.	SEEBRI BREEZHALER 44micrograms inhalation capsules
o324.	GLYCOPYRRONIUM 44micrograms inhalation capsules
x05gG	SPIRIVA inh pdr cap (refill) 18 micrograms

10.11 LABA/LAMA Read codes

read_code	read_term
c1e..	INDACATEROL+GLYCOPYRRONIUM
c1e1.	ULTIBRO BREEZHALER 85mcg/43mcg inh powder capsules+inhaler
c1e2.	INDACATEROL+GLYCOPYRRONIUM 85mcg/43mcg inh powder caps+inh
c51I.	ANORO ELLIPTA 55micrograms/22micrograms dry powder inhaler
c51J.	UMECLIDINIUM+VILANTEROL 55mcg/22mcg dry powder inhaler
c51K.	DUAKLIR GENUAIR 340micrograms/12micrograms powder inhaler
c51L.	ACLIDINIUM+FORMOTEROL FUMARATE DIHYD 340mcg/12mcg pdr inh
c51M.	SPIOLTO RESPIMAT 2.5micrograms/2.5micrograms inhaler
c51N.	TIOTROPIUM+OLODATEROL 2.5micrograms/2.5micrograms inhaler

10.12 ICS/LABA/LAMA Snowmed codes

snomed	nm
34681611000001100	Trimbow 87micrograms/dose / 5micrograms/dose / 9micrograms/dose inhaler
34683311000001106	Generic Trimbow 87micrograms/dose / 5micrograms/dose / 9micrograms/dose inhaler
34952211000001104	Trelegy Ellipta 92micrograms/dose / 55micrograms/dose / 22micrograms/dose dry powder inhaler
34955111000001103	Generic Trelegy Ellipta 92micrograms/dose / 55micrograms/dose / 22micrograms/dose dry powder inhaler

10.13 OCS Read codes

read_code	read_term

fe3..	DEXAMETHASONE [ENDOCRINE]
fe31.	DEXAMETHASONE 500micrograms tablets
fe32.	DEXAMETHASONE 2mg tablets
fe33.	DECADRON 500micrograms tablets
fe36.	*ORADEXON 500microgram tablets
fe37.	*ORADEXON 2mg tablets
fe3A.	DEXSOL 2mg/5mL oral solution
fe3B.	DEXAMETHASONE 10mg/5mL oral solution
fe3C.	MARTAPAN 2mg/5mL oral solution
fe3r.	DEXAMETHASONE 500micrograms/5mL solution
fe3s.	DEXAMETHASONE 2mg/5mL sugar free solution
fe3u.	DEXAMETHASONE 2mg/5mL liquid
fe4..	HYDROCORTISONE
fe41.	HYDROCORTISONE 10mg tablets
fe42.	HYDROCORTISONE 20mg tablets
fe43.	*HYDROCORTISTAB 20mg tablets
fe44.	*HYDROCORTONE 10mg tablets
fe45.	*HYDROCORTONE 20mg tablets
fe4e.	PLENADREN 5mg m/r tablets
fe4f.	HYDROCORTISONE 5mg m/r tablets
fe4g.	PLENADREN 20mg m/r tablets
fe4h.	HYDROCORTISONE 20mg m/r tablets
fe5..	METHYLPREDNISOLONE [ENDOCRINE]
fe51.	MEDRONE 2mg tablets
fe52.	MEDRONE 4mg tablets
fe53.	MEDRONE 16mg tablets
fe5f.	MEDRONE 100mg tablets
fe5m.	METHYLPREDNISOLONE 100mg tablets
fe5n.	METHYLPREDNISOLONE 2mg tablets
fe5o.	METHYLPREDNISOLONE 4mg tablets
fe5p.	METHYLPREDNISOLONE 16mg tablets
fe6..	PREDNISOLONE [ENDOCRINE]
fe61.	PREDNISOLONE 1mg tablets
fe62.	PREDNISOLONE 5mg tablets
fe64.	*DELTA-PHORICOL 5mg tablets
fe65.	DELTACORTRIL ENTERIC 2.5mg tablets
fe66.	DELTACORTRIL ENTERIC 5mg tablets
fe67.	*DELTALONE 1mg tablets
fe68.	*DELTALONE 5mg tablets
fe69.	*DELTASTAB 1mg tablets

fe6a.	*DELTASTAB 5mg tablets
fe6c.	*PRECORTISYL 1mg tablets
fe6d.	*PRECORTISYL 5mg tablets
fe6e.	PRECORTISYL FORTE 25mg tablets
fe6f.	*PREDNESOL 5mg tablets
fe6g.	*SINTISONE 5mg tablets
fe6h.	PREDNISOLONE 2.5mg e/c tablets
fe6i.	PREDNISOLONE 5mg e/c tablets
fe6j.	PREDNISOLONE 5mg soluble tablets
fe6k.	PREDNISOLONE 50mg tablets
fe6l.	DILACORT 5mg gastro-resistant tablets
fe6m.	DILACORT 2.5mg gastro-resistant tablets
fe6t.	PREDNISOLONE 10mg tablets
fe6v.	*PREDNISOLONE 2.5mg tablets
fe6w.	*PREDNISOLONE 2.5mg tablets
fe6z.	PREDNISOLONE 25mg tablets
fe7..	PREDNISONE
fe71.	*PREDNISONE 1mg tablets
fe72.	*PREDNISONE 5mg tablets
fe73.	*DECORTISYL 5mg tablets
fe74.	*ECONOSONE 1mg tablets
fe75.	*ECONOSONE 5mg tablets
fe76.	Prednisone 20mg tablet
fe77.	LODOTRA 2mg m/r tablets
fe78.	LODOTRA 5mg m/r tablets
fe79.	LODOTRA 1mg m/r tablets
fe7x.	PREDNISONE 5mg m/r tablets
fe7y.	PREDNISONE 2mg m/r tablets
fe7z.	PREDNISONE 1mg m/r tablets
x00yP	Oral prednisolone
x01Mh	Oral dexamethasone
x01Na	Oral hydrocortisone
x01Nb	Oral methylprednisolone

10.14 Height, weight, BMI Read Codes

Read code	Read term
229..	Height
22A..	Weight
22K..	BMI

10.15 Blood Eosinophil Count Read codes

Read code	Read term
42K..	Eosinophil count
42K1.	Eosinophil count normal
42K2.	Eosinopenia
42K3.	Eosinophil count raised
42KZ.	Eosinophil count NOS
42b9.	Percentage eosinophils
4E32.	Sputum: eosinophilia
D403	Hereditary eosinophilia
D403.	Eosinophilia
D4033	Allergic eosinophilia
D4034	Secondary eosinophilia NOS
D403z	Eosinophilia NOS
H583.	Pulmonary eosinophilia
H5831	Tropical eosinophilia
H583z	Pulmonary eosinophilia NOS
J08z	Oral mucosa eosinoph.granuloma
X00l1	Eosinophil non-allergic rhinit
X102G	Asthmatic pulm eosinophilia
X102H	Cryptogenic pulm eosinophilia
X3009	Eosinophilic oesophagitis
X80VM	Eosinophil
Xa0kb	Tropical pulm eosinophilia
Y02Rr	Eosinophil non-allergic rhinit
Y108t	Eosinophilic pneumonia
Y108u	EP - Eosinophilic pneumonia
Y108v	Pulm infiltrate + eosinophilia
Y108w	PIE - Pul infil + eosinophilia
Y108z	Acute eosinophilic pneumonia
Y1090	Simple pulmonary eosinophilia
Y1094	Asthmatic pulm eosinophilia
Y1095	Cryptogenic pulm eosinophilia
Y1096	Chronic eosinophilic pneumonia
Y1097	Crypt eosinophilic pneumonia
Y1098	Chronic pulmonary eosinophilia
Y1099	Tropical pulm eosinophilia
Y20fq	Eosinophilic disorder
Y3017	Eosinophilic oesophagitis
Y80lD	Eosinophil
Ya14p	EP-Acute eosinophil pneumonia

Read code	Read term
Yaeib	Percentage eosinophil count
YakcK	Eosinophil count - observation

10.16 Spirometry measurement Read codes

Read code	Read term
3396.	Forced vital capacity - FVC
33960	FVC - forced vital capacity normal
33961	FVC - forced vital capacity abnormal
3397.	Forced expiratory volume - FEV
3398.	FEV1/FVC ratio normal
3399.	FEV1/FVC ratio abnormal
339a.	FEV1 before bronchodilation
339b.	FEV1 after bronchodilation
339e.	FEV1 pre steroids
339f.	FEV1 post steroids
339h.	FVC after bronchodilation
339j.	FEV1/FVC ratio pre steroids
339k.	FEV1/FVC ratio post steroids
339l.	FEV1/FVC ratio before bronchodilator
339M.	FEV1/FVC ratio
339m.	FEV1/FVC ratio after bronchodilator
339O.	Forced expired volume in 1 second
339O1	Forced expired volume in one second/vital capacity ratio
339P.	Expected FEV1
339R.	FEV1/FVC percent
339s.	Forced vital capacity before bronchodilation
339S.	Percent predicted FEV1
339S0	Percentage predicted FEV1 after bronchodilation
339T.	FEV1/FVC > 70% of predicted
339U.	FEV1/FVC < 70% of predicted
X77Qu	Forced expired volume in 1 second
X77Ra	Forced expired volume in one sec/forced vital capacity ratio
XaCJK	Expected FEV1
XaEFy	FEV1/FVC percent
XaEFz	Percent predicted FEV1
XaIxQ	FEV1 before bronchodilation
XaIxR	FEV1 after bronchodilation
XaIxU	FEV1 pre steroids
XaIxV	FEV1 post steroids
XaJ3K	FVC after bronchodilation
XaJ9B	FEV1/FVC ratio pre steroids
XaJ9C	FEV1/FVC ratio post steroids
XaJ9D	FEV1/FVC ratio before bronchodilator

Read code	Read term
XaJ9E	FEV1/FVC ratio after bronchodilator
XaPpI	Forced vital capacity before bronchodilation
XaVx3	Percentage predicted FEV1 after bronchodilation

10.17 Peak Expiratory Flow Read codes

Read code	Read term
339..	Respiratory flow rates
3391	Resp. flow rate measured
3392	Resp. flow rate not measured
3393	Resp. flow rate normal
3394	Resp. flow rate abnormal
3395	Peak exp. flow rate: PEFR/PFR
339A.	PFR - before bronchodilation
339B.	PFR - after bronchodilation
339C.	PFR - expected
339D.	PFR - best ever
339E.	PFR >80% of predicted
339F.	PFR 60-80% of predicted
339G.	PFR <60% of predicted
339H.	Predicted peak flow
339I.	Expected peak flow rate x 50%
339J.	Optimal peak flow rate
339K.	Expected peak flow rate x 30%
339L.	Expected peak flow rate x 80%
339V.	Recorded/predicted PEFR ratio
339W.	Worst peak flow rate
339X.	Percentage of best ever PEFR
339Y.	Percentage of PEFR variability
339Z.	Respiratory flow rates NOS
339c.	PEFR pre steroids
339d.	PEFR post steroids
339g.	Serial peak expirat flow rate
339n.	Serial PEFR abnormal
339o.	PEFR using EN 13826 device
339p.	Predict PEFR using EN13826 std
339u.	Peak inspiratory flow rate
745C0	Measure peak expirat flow rate

11. SIGNATURES

Authoring Instructions

- *The following signature pages for an Observational Study protocol may be required and further details on who is required to sign can be found in the SOP 8-P102-CV-C Design, Execution, and Reporting of AstraZeneca Sponsored Observational Studies:*
  - *Global Medical Affairs Lead or Global Clinical Lead/Delegate for global studies*
  - *MC Medical Director/Delegate for local studies*
  - *Global Epidemiologist /Local Study Leader*
  - *Optional signature from Biostatistician or Delivery Director*
  - *Always print the names and addresses.*

ASTRAZENECA SIGNATURE(S)

<<Study Description>>

<<This Observational Study Protocol >> <<has/have>> been subjected to an internal AstraZeneca review>>
I agree to the terms of this Study protocol.

AstraZeneca representative

<<Name, title>>	Date (Day Month Year)
<<Email address and telephone number>>	

Page 5: [1] Deleted **Johann Castaneda** **16/11/2022 10:40:00**