Boehringer Ingelheim

Protocol for non-interventional studies based on existing data

Document Number:	**c30445781-01**
BI Study Number:	1237-0090
BI Investigational Product(s):	Stiolto® Respimat®
Title:	The Role of Inhaler Device in the Treatment Persistence with Dual Bronchodilators in Patients with COPD
Protocol version identifier:	1.0
Date of last version of protocol:	N/A
PASS:	No
EU PAS register number:	Study not registered
Active substance:	Olodaterol and Tiotropium Bromide (ATC R03AL06) Umeclidinium and Vilanterol (ATC R03AL03)
Medicinal product:	Stiolto® Respimat®; Anoro® Ellipta®
Product reference:	N/A
Procedure number:	N/A
Joint PASS:	No
Research question and objectives:	The primary objective of the study is to use US data to determine relative persistence between Olodaterol/Tiotropium Bromide delivered with the Respimat soft mist inhaler and Umeclidinium/Vilanterol delivered with the Ellipta dry powder inhaler using a 1:2 propensity score matched analysis. The secondary objectives of the study are as follows: - Characterize new users of Olodaterol/Tiotropium Bromide and Umeclidinium/Vilanterol in terms of demographics, medication use, comorbidities, and other variables, before and after propensity score matching. - Determine the incidence rate and proportion of patients discontinuing or switching among new users of Olodaterol/Tiotropium Bromide and Umeclidinium/ Vilanterol. - Determine the relative rate and proportion of patients discontinuing between Olodaterol/ Tiotropium Bromide and

	Umeclidinium/Vilanterol. using a standard multivariate analysis (If feasible).
Country(-ies) of study:	United States
Author:	T: Email: T: Email: **BI contact person:**
Marketing authorisation holder(s):	
MAH contact person:	
In case of PASS, add:	N/A
In case of PASS, add:	N/A
Date:	22 November 2019

1. TABLE OF CONTENTS

2. LIST OF ABBREVIATIONS

ACE	Angiotensin Converting Enzyme
AIDS	Acquired Immune Deficiency Syndrome
CCAE	Commercial Claims and Encounters
CDCI	Charlson Deyo Comorbidity Index
CI	Confidence Interval
COB	Coordination of Benefits
COBRA	Consolidated Omnibus Budget Reconciliation Act
COPD	Chronic Obstructive Pulmonary Disease
CT	Computed Tomography
DPI	Dry Powder Inhaler
ENCEPP	European Network of Centres for Pharmacoepidemiology and Pharmacovigilance
ESRD	End Stage Renal Disease
FDC	Fixed Dose Combination
GLP-1	Glucagon-like Peptide-1
GOLD	Global Initiative for Chronic Obstructive Lung Disease
HIV	Human Immunodeficiency Virus
ICD	International Classification of Diseases
ICS	Inhaled Corticosteroid
IP	Inpatient
IQR	Interquartile Range
IRB	Institutional Review Board
LABA	Long-Acting Beta-Agonists
LAMA	Long-Acting Muscarinic Antagonists
NDC	National Drug Code
NSAID	Nonsteroidal Anti-inflammatory Drug
OCS	Oral Corticosteroid
OP	Outpatient
SABA	Short-acting Beta Agonist
SAMA	Short-acting Muscarinic Antagonist
SD	Standard Deviation
SMI	Soft Mist Inhaler

3. RESPONSIBLE PARTIES

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Email:

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Email:

4. ABSTRACT

Name of company: Boehringer Ingelheim International GmbH			
Name of finished medicinal product: Stiolto® Respimat®; Anoro® Ellipta®			
Name of active ingredient: Olodaterol and Tiotropium Bromide (ATC R03AL06); Umeclidinium and Vilanterol (ATC R03AL03)			
Protocol date: 22 November 2019	**Study number:** 1237-0090	**Version/Revision:** 1.0	**Version/Revision date:** NA
Title of study:	The Role of Inhalers In Treatment Persistence With Dual Bronchodilators In Patients With COPD		
Rationale and background	Inhaled therapies are the cornerstone of chronic obstructive lung disease (COPD) management approaches. The aim of inhaled therapy is to deliver therapeutic agents directly to the lungs, optimizing benefits while minimizing the potential for treatment-related adverse effects **(Braido 2016)**. Adherence to COPD therapies involves patients initiating their prescribed therapy, implementing it as prescribed (i.e., correctly administering the prescribed dose at the physician directed frequency), and persisting with treatment **(Braido 2016; Mäkelä 2013)**. Also central to the therapeutic benefit of inhaled therapies is their successful administration, which requires patients to have knowledge and understanding of (and ability to implement) the appropriate inhaler technique required to optimize both the dispensed and administered doses **(Braido 2016)**. Inspiratory capabilities of patients with COPD are affected by increasing static and dynamic hyperinflation and weakening of the respiratory muscles, causing many patients to have peak inspiratory flow rates that are suboptimal to use many dry-powder inhalers (DPIs) **(Sohini 2017)**. This paradoxical situation may lead to improper inhalation that prevents successful drug delivery to the lungs, which may affect treatment efficacy. The question if different devices, DPI and Soft Mist Inhalers (SMI), played a role in treatment persistence remains to be answered. In this study we aim to compare the persistence in using two different medications from the same drug class (LAMA/LABA FDC) which are delivered through different devices, a DPI and an SMI.		

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Protocol date: 22 November 2019	**Study number:** 1237-0090	**Version/Revision:** 1.0	**Version/Revision date:** NA
Research question and objectives:	This study seeks to compare the differences in treatment persistence in using two combinations of two drugs of the same drug class (LAMA/LABA as a fixed dose combination) delivered through different devices (a DPI or an SMI) within an administrative claims database in the US. The primary objective of the study is to use US data to determine relative treatment persistence between patients prescribed Olodaterol/Tiotropium Bromide delivered with the Respimat SMI and Umeclidinium/Vilanterol delivered with the Ellipta DPI using a 1:2 propensity score matched analysis. The secondary objectives of the study are as follows: - Characterize new users of Olodaterol/Tiotropium Bromide and Umeclidinium/Vilanterol in terms of demographics, medication use, comorbidities, and other variables, before and after propensity score matching. - Determine the rate and risk (proportion of patients) of discontinuation among new users of Olodaterol/Tiotropium Bromide and Umeclidinium/ Vilanterol in the 1:2 matched cohort. - Determine the relative rate and risk of discontinuation between Olodaterol/Tiotropium Bromide and Umeclidinium/Vilanterol, using a standard multivariable analysis (Same variables as propensity score model) in the total unmatched cohort.		
Study design:	New-user cohort design with propensity scores used to match up to 2 Umeclidinium/Vilanterol initiators to each Olodaterol/Tiotropium Bromide initiator.		
Population:	Patients initiating Olodaterol/Tiotropium Bromide or Umeclidinium/ Vilanterol between 17 November 2015 and 31 March 2018. Exclusion criteria are: • Aged <40 years. • Enrolment with medical and pharmacy coverage prior to the cohort entry < 180 days. • Never had COPD diagnosis on the cohort entry date or prior to cohort entry.		

<table>
<tr><td colspan="2">Name of company:
Boehringer Ingelheim International GmbH</td><td></td><td></td></tr>
<tr><td colspan="2">Name of finished medicinal product:
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22 November 2019</td><td>Study number:
1237-0090</td><td>Version/Revision:
1.0</td><td>Version/Revision date:
NA</td></tr>
<tr><td></td><td colspan="3">• A record for dispensed Olodaterol/Tiotropium Bromide delivered with Respimat inhalator or Umeclidinium/Vilanterol delivered with the Ellipta Inhaler during the 180-day baseline prior to cohort entry.
• Diagnosis of asthma any time prior to cohort entry.
• Diagnosis of lung cancer any time prior to cohort entry.
• Diagnosis of lung transplant any time prior to cohort entry.</td></tr>
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Protocol date: 22 November 2019	**Study number:** 1237-0090	**Version/Revision:** 1.0	**Version/Revision date:** NA
Variables:	**Exposures** • Olodaterol/Tiotropium Bromide (Stiolto®) delivered via Respimat inhaler • Umeclidinium/Vilanterol (Anoro®) delivered via Ellipta Inhaler **Outcome** • Discontinuation of index treatment (Olodaterol/Tiotropium Bromide or Umeclidinium/Vilanterol), defined as persistence of treatment (no refill claim within 60 days (allowable grace period) after end of <n> days supply). Addition of another drug will not count as a discontinuation. **Covariates** Demographics ● Age on the cohort entry date ● Sex (Male, Female) ● Region (Northeast, North Central, South, West, Unknown, Missing) ● Insurance Type (Commercial, Medicare, Missing) ● Study Year of Cohort Entry (First Year: 17 Nov 2015-30 Nov 2016, Second Year: 01 Dec 2016-30 Nov 2017, Third Year: 01 Dec 2017-31 Mar 2018) Concomitant Medications ● Oral Corticosteroids (OCS) ● Short acting muscarinic antagonist (SAMA) ● Short acting beta agonist (SABA) ● Long acting muscarinic antagonist (LAMA) ● Long acting beta agonist (LABA) ● Inhaled corticosteroid (ICS) ● LAMA / LABA combination (that is not Stiolto or Anoro) ● LABA / ICS combination ● LAMA / LABA / ICS combination ● NSAIDs ● Antihistamines		

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Protocol date: 22 November 2019	**Study number:** 1237-0090	**Version/Revision:** 1.0	**Version/Revision date:** NA
	● Opioids ● Oral antibiotics ● Antidiabetic Agents (not including insulin) ● Insulin (basal or mealtime) ● Methotrexate ● Statins ● Antihypertensives ● Anticoagulants ● Anti-psychotic/anti-depressives/anxiolytic ● Oxygen therapy Comorbidities/Symptoms ● History of All-Cause Hospitalization ● History of Emergency Department Visit ● History of Hospitalization due to Respiratory Condition ● Acute Myocardial Infarction ● Angina Pectoris ● Peripheral Vascular Disease ● Heart Failure ● Hypertension ● Upper Respiratory Infection ● Lower Respiratory Infection ● Cardiac Arrhythmias ● Cerebrovascular Disease ● All cancers (except non-melanoma skin cancer) ● Allergic Rhinitis ● Chronic Sinusitis ● Bronchiectasis ● Pneumonia ● Chronic Bronchitis ● Exertional Breathlessness ● Anxiety ● Dementia ● Depression ● Osteoporosis ● Charlson-Deyo Comorbidity Index			

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1.0</td><td>Version/Revision date:
NA</td></tr>
<tr><td></td><td colspan="3">● Acute Liver Injury or Failure
● Chronic Kidney Disease (without ESRD)
● End Stage Renal Disease
● Rheumatic Disease
● Peptic Ulcer Disease
● Gastroesophageal Reflux Disease
● Type 1 Diabetes Mellitus
● Type 2 Diabetes Mellitus
● HIV/AIDS
● Hemiplegia or Paraplegia

Lifestyle
● Smoking-related claim
● Vaccination for Influenza
● Vaccination for Pneumococcus

Respiratory Function Procedures/Tests Conducted
● Pulmonary function tests
● Six-minute walk test
● Chest X-ray
● High resolution chest CT</td></tr>
</table>

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Protocol date: 22 November 2019	**Study number:** 1237-0090	**Version/Revision:** 1.0	**Version/Revision date:** NA
Data sources:	Truven MarketScan is a claims database that captures longitudinal, individual-level administrative claims data from the United States.		
Study size:	There are 14,751 new users of Olodaterol/Tiotropium Bromide or Umeclidinium/Vilanterol between 17 November 2015 and 31 March 2018 who satisfied the inclusion criteria. Among them, 3,889 initiated Olodaterol/Tiotropium Bromide and 10,862 initiated Umeclidinium/ Vilanterol).		
Data analysis:	For demographic and lifestyle variables, the value recorded on the cohort entry date will be reported, otherwise the most recent known value will be reported. Presence of comorbidities and use of concomitant medication use will be determined based whether they ever occurred within the 180-day baseline period preceding the index date.Differences in the confounder distributions will be inspected for successful confounder balance of measured characteristics. Patients will be followed up until first occurrence of death, discontinuation, disenrollment, end of data, or 365 days. The data will be displayed in a nonparametric fashion on a persistency curve (a Kaplan–Meier curve) with discontinuation considered as elimination. Unmatched Cohort Rates and risks (proportion of patients) with the outcomes for each exposure group will be reported among the unmatched cohort. Matched Cohort Rates and risks (proportion of patients) with the outcomes for each exposure group will be reported among the matched cohort. Logistic regression will be used to calculate the propensity to initiate Olodaterol/Tiotropium Bromide versus Umeclidinium/Vilanterol. The propensity score will then be used to identify up to 2 initiators of Umeclidinium/Vilanterol for each initiator of Olodaterol/Tiotropium Bromide with the same propensity score (± a caliper of 5%) as the corresponding initiator of Olodaterol/Tiotropium Bromide.		

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	Cox proportional hazard regression model will be used to assess the relative rate (or hazard) of the outcome in patients treated with Olodaterol/Tiotropium Bromide compared to patients treated with Umeclidinium/Vilanterol during the one-year follow-up. Crude HRs and 95% CIs will be reported for the matched cohorts. Among the matched cohort, relative risks with 95% CIs will also be reported, as assessed by conditional logistic regression. Relative rates and risks will also be reported using standard multivariable regression. **Sensitivity Analyses** • Restrict the 60-day allowable grace period used to define the discontinuation outcome to 30 days. • Increase the 60-day allowable grace period used to define the discontinuation outcome to 90 days. • Start the patient identification period on 21 May 2015 immediately upon FDA approval. • Exclude patients with ACOS. Patients with asthma only but not COPD are still excluded from cohort.		
Milestones:	- Feasibility assessment Sept 2018 (done) - Draft study protocol Dec 2018 - Final study protocol Apr 2019 - Results tables available May 2019 - 1st Abstract submitted (ERS 2019, ISPOR or AMCP) Jun 2019 - Manuscript submitted Q2 2019		

5. AMENDMENTS AND UPDATES

Not Applicable

6. MILESTONES

Milestone	Planned Date
Draft Protocol	17 December 2018
Protocol Revisions	22 February 2019*
Start of Implementation	01 March 2019
Preliminary Result Tables	15 March 2019
Final Result Tables and Documentation of Implementation	26 April 2019
*Pending time for approval and suggested changes proposed by BI	

7. RATIONALE AND BACKGROUND

Chronic obstructive pulmonary disease (COPD) is a common disease characterized by airway obstruction confirmed by spirometry, often including small airway obstruction, chronic bronchitis and emphysema (**Barnes 2015**). No known medications can reverse COPD, but regular maintenance treatments can help manage symptoms, reduce frequency of COPD exacerbations and improve health-related quality of life. Inhaled therapies are the cornerstone of COPD disease management approaches. The aim of inhaled therapy is to deliver agents directly to the lungs, thereby offering benefits while minimizing the potential for treatment-related adverse effects (**Braido 2016**).

Adherence to obstructive lung disease therapies involves patients initiating their prescribed therapy, implementing it as prescribed (i.e. correctly administering the prescribed dose at the physician directed frequency), and persisting with treatment (**Braido 2016; Mäkelä 2013**). Central to the therapeutic benefit of inhaled therapies is their successful administration which requires patients to have knowledge and understanding of (and ability to implement) the appropriate inhaler technique required to optimize both the dispensed and administered doses (**Braido 2016**). Inspiratory capabilities of patients with COPD are affected by increasing static and dynamic hyperinflation and weakening of the respiratory muscles, causing many patients to have peak inspiratory flow rates that are suboptimal to use many dry-powder inhalers (DPIs) (**Sohini 2017**). This paradoxical situation may lead to improper inhalation that prevents successful drug delivery to the lungs, which may affect treatment effectiveness. On the other hand, soft mist inhalers (SMI) force a metered dose of drug solution through a precise nozzle to deliver consistent and reliable doses to the lungs with each actuation (**Dalby 2004**) and may help preserve benefits in patients with diminished peak inspiratory flow rates.

Stiolto® Respimat®, a combination of Olodaterol and Tiotropium Bromide delivered via soft mist inhaler (SMI), was approved in May 2015 in the US and July 2015 in the EU (marketed

as Spiolto in the EU). Anoro® Ellipta®, a combination of Umeclidinium and Vilanterol delivered via dry powder inhaler (DPI), was approved in December 2013 in the US and in February 2014 in the EU. Both products are maintenance therapies consisting of a combination of long-acting muscarinic antagonists (LAMA) and long-acting beta agonists (LABA). However, the question of whether different devices (DPI and SMI) play a role in treatment persistence remains to be answered.

This study seeks to compare the treatment persistence of two drugs in same drug class (LAMA/LABA as a fixed dose combination [FDC]) delivered through different devices (a DPI and a SMI) within an administrative claims database in the US.

8. RESEARCH QUESTION AND OBJECTIVES

The primary objective of the study is to use US data to determine relative treatment persistence in using Olodaterol/Tiotropium Bromide delivered with the Respimat soft mist inhaler and Umeclidinium/Vilanterol delivered with the Ellipta dry powder inhaler using a 1:2 propensity score matched analysis.

The secondary objectives of the study are as follows:
Characterize new users of Olodaterol/Tiotropium Bromide and Umeclidinium/Vilanterol in terms of demographics, medication use, comorbidities, and other variables, before and after propensity score matching.
Determine the rate and proportion of patients discontinuating among new users of Olodaterol/Tiotropium Bromide and Umeclidinium/ Vilanterol.
Determine the relative rate and proportion of patients discontinuing between Olodaterol/Tiotropium Bromide and Umeclidinium/Vilanterol, using a standard multivariate analysis (If feasible).

9. RESEARCH METHODS

9.1 STUDY DESIGN

The proposed study will utilize data from the Truven MarketScan dataset (US).

The Truven MarketScan databases are comprised of two components: the MarketScan Commercial Claims and Encounters (CCAE) Database and the Medicare Supplemental and Coordination of Benefits (COB) Database. These databases capture longitudinal, individual-level data on healthcare utilization, healthcare expenditures and plan enrollment, and contain integrated records for patient demographics, inpatient events, outpatient events, and pharmacy dispensing of drugs. The CCAE database is a medical and drug insurance claims database on ~150 million patients since from 2008 unique de-identified patients that include active employees, dependents, retirees or recipients of the Consolidated Omnibus Budget Reconciliation Act (COBRA), and data are drawn from large employers, health plans, and public organizations in the United States (Truven Health MarketScan® Research Databases 2015). The MarketScan Medicare Supplemental and Coordination of Benefits (COB) Database contains pooled medical and drug insurance claims data of approximately 13.6 Million unique de-identified patients (since 1996) that are Medicare-eligible retirees with employer-sponsored Medicare Supplemental plans. (**Truven Health MarketScan® Research Databases 2015**).

In principle, in US when a patient goes to a pharmacy and gets a drug dispensed, the pharmacy bills the insurance carrier for the cost of that drug (**Strom 2013**). For billing purposes, the pharmacy has to identify which medication was dispensed along with the dosage strength (e.g. the milligrams per tablet) and quantity (e.g., number of tablets, etc.). Analogously, when a patient goes to a hospital or to a physician for medical care, the providers of care bill the insurance carrier for the cost of the medical care, and have to justify the bill with a diagnosis. Using a common patient identification number for both the pharmacy and the medical care claims, these elements can be linked, and analyzed as a longitudinal medical record (**Strom 2013**).

9.2 SETTING

9.2.1 Definitions

Study Period: the period of time that includes the exclusion criteria assessment period, baseline, cohort entry date, and follow-up period for the study population. This period is the same for all patients.

The study period will be from 1 January 2008 to 31 March 2018, encompassing date of the earliest data availability to the date of the latest data availability.

Patient Selection Period: the period of time for which patients are eligible to enter the cohort. The earliest date of the patient selection period is 17 November 2015, corresponding to 180-days after US approval date of Stiolto Respimat.

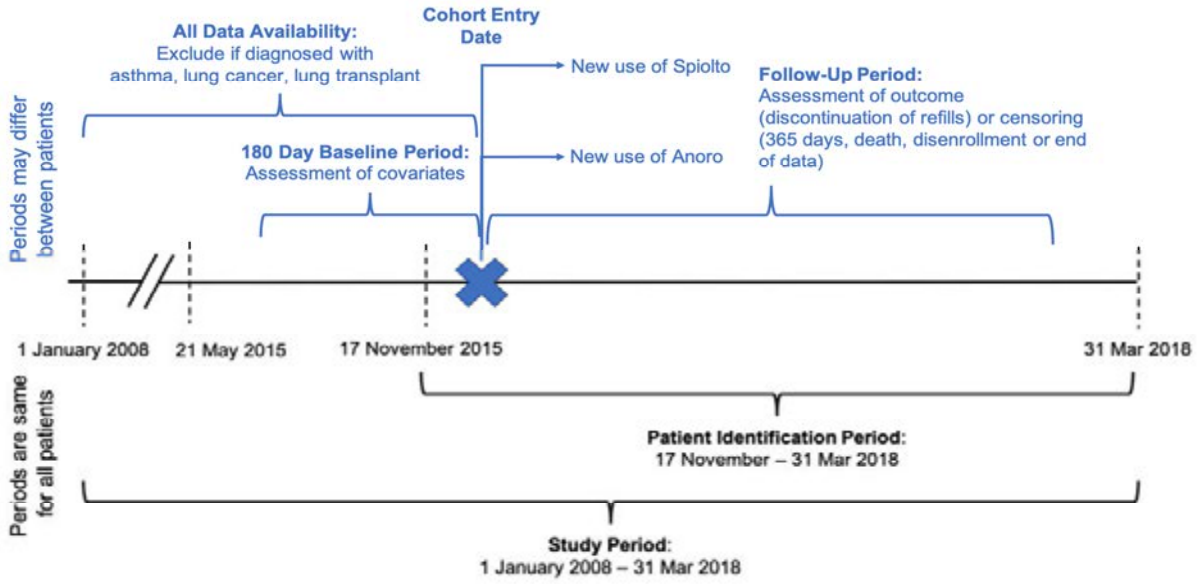
Cohort Entry Date: Date of entry to the initial cohort of Stiolto or Anoro users.

Baseline Period: the 180-day period that ends 1 day prior to the cohort entry date used to assess covariate information. The baseline period will vary between patients depending on these dates. The earliest start of the baseline period would be 21 May 2015, the date of Stiolto approval (i.e. 180 days before November 17, 2015).

Follow-Up Period: the period of time between 1 day after the cohort entry date to the earliest occurrence of the outcome (discontinuation of refills), or any censoring criteria (365 days, death, disenrollment, or end of data). Addition of another treatment in addition to index treatment will not count as discontinuation.

For entry into the study population, patients will be required to have 180 days of continuous enrolment with both medical and pharmacy coverage. Data during the baseline period will be used to confirm study eligibility and classification of incident COPD. The follow-up period will be used for capturing first and second maintenance therapies. This is illustrated in **Figure 1.**

Figure 1 Study timeline for the Primary Study Population

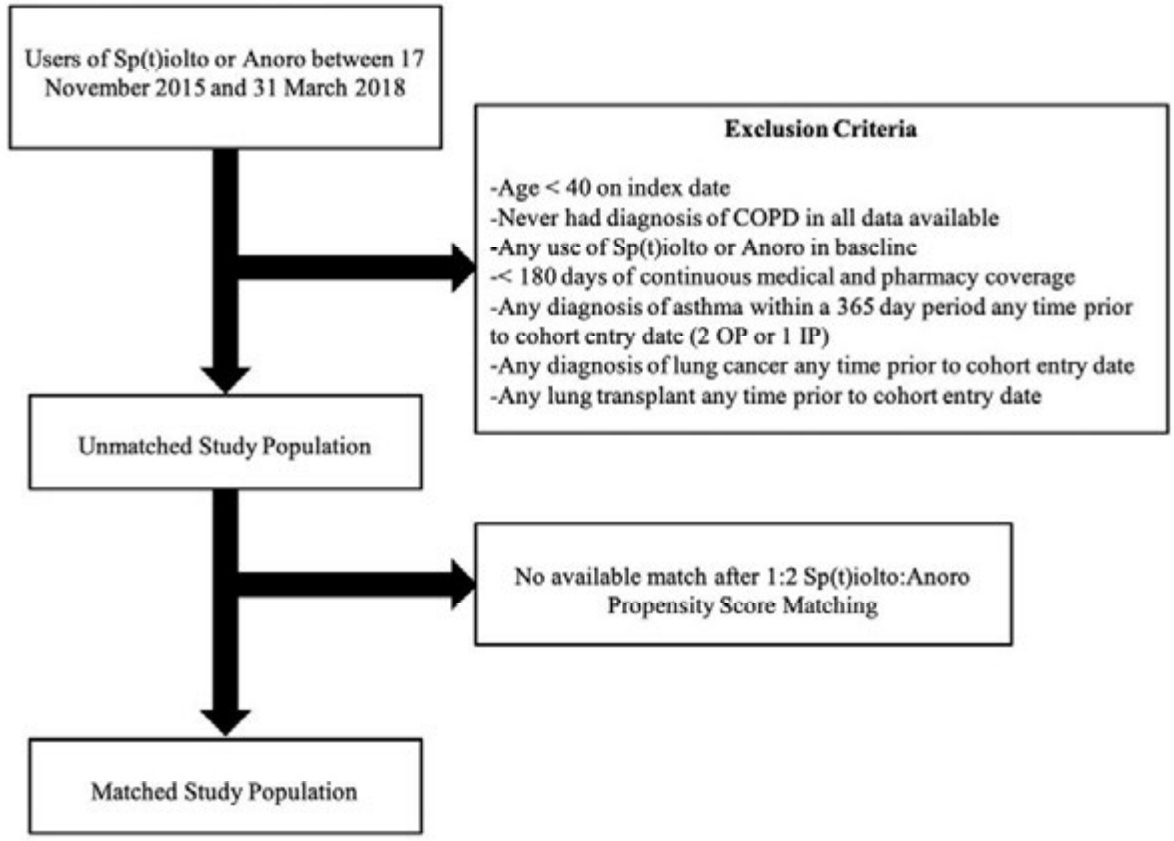


9.2.2 Study population

The pre-matched study cohort will consist of patients initiating Olodaterol/Tiotropium Bromide or Umeclidinium/Vilanterol between 17 November 2015 and 31 March 2018.

The following exclusion criteria will then be applied:
Aged <40 years.
Enrolment with medical and pharmacy coverage prior to the cohort entry < 180 days.
Never had COPD diagnosis on the cohort entry date or prior to cohort entry.
A record for dispensed Olodaterol/Tiotropium Bromide delivered with Respimat inhalator or Umeclidinium/Vilanterol delivered with the Ellipta Inhaler during the 180-day baseline prior to cohort entry.
Diagnosis of asthma any time prior to cohort entry.
Diagnosis of lung cancer any time prior to cohort entry.
Diagnosis of lung transplant any time prior to cohort entry.

Figure 2 Below depicts the flow diagram of patients.



Diagnosis of COPD (ICD-9: 491.*, 492.*, 496.*; ICD-10: J41.0, J41.1, J41.8, J42.*, J43.0, J43.1, J43.2, J43.8, J43.9, J44.0, J44.1, J44.9) will be defined as the presence of an inpatient or outpatient claim.

Diagnosis of asthma (ICD-9: 493.*; ICD-10: J45, J45.20, J45.21, J45.22, J45.90*, J45.99*) will be defined as either 1 inpatient claim or 2 outpatient events 30-365 days apart.

Diagnosis of lung cancer (ICD-9: 162.2, 162.3, 162.4, 162.5, 162.8, 162.9, 231.2; ICD-10: C34.00, C34.01, C34.02, C34.10, C34.11, C34.12, C34.2, C34.30, C34.31, C34.32, C34.80, C34.81, C34.82, C34.90, C34.91, C34.92, C7A.090, D02.20, D02.21, D02.22, Z85.118) will be defined as either 1 inpatient claim or 2 outpatient events 30-365 days apart.

Matched Cohort

A matched propensity score analysis will be used to assess comparative persistence between the two exposure comparison groups. Logistic regression will be used to calculate the propensity to initiate Olodaterol/Tiotropium Bromide versus Umeclidinium/Vilanterol given all covariates (except components of the Charlson Comorbidity index) listed in section 9.3.3, according to the following model:

Logit (Treatment | X1, X2, … , Xn) = $\beta 0 + \beta 1 * X1 + \beta 2 * X2 + \ldots + \beta n * Xn$

Any covariates which are collinear with each other will be dropped from the analysis (if it causes failure of model to converge). The propensity score will then be used to identify up to 2 initiators of Umeclidinium/Vilanterol for each initiator of Olodaterol/Tiotropium Bromide with the same propensity score (± a caliper of 5%) as the corresponding initiator of Olodaterol/Tiotropium Bromide (Austin 2011).

9.3 VARIABLES

9.3.1 Exposures

- Exposure: Olodaterol/Tiotropium Bromide (Stiolto®) delivered with Respimat inhalator
- Active Comparator: Umeclidinium/Vilanterol (Anoro®) delivered with the Ellipta Inhaler

Both exposures will be identified via NDC Generic Name and NDC Brand Name.

9.3.2 Outcomes

9.3.2.1 Primary outcome

Discontinuation
The primary outcome of interest is discontinuation of index treatment (Olodaterol/Tiotropium Bromide or Umeclidinium/Vilanterol), defined as persistence (i.e. no refill claim within 60

days [not involving treatment switch, nor death] (allowable grace period) after end of <n> days supply) during follow-up.

Censoring
Patients will be censoring if they did not discontinue their index treatment but had an occurrence of any of the following: 365 days of follow-up without discontinuation, death, disenrollment, end of data.

9.3.2.2 Secondary outcomes

Not applicable.

9.3.3 Covariates

Covariates will be identified based on data recorded within 180 days prior to or on the index date (date of dispensing/initiation of the exposure), unless otherwise specified. If multiple measurements are made in the baseline period, then the most recent measurement will be used.

Covariates will be used to predict propensity scores in later analyses. Absolute and relative frequencies of each covariate will also be reported in Table Shells 1 and 2 (see Annex 5). Detailed descriptions of the listed covariates can be found in Annex 3 and 4.

Demographics
- Age on index date
- Sex (Male, Female)
- Region (Northeast, North Central, South, West, Unknown, Missing
- Insurance Type (Commercial, Medicare, Missing)
- Year of Cohort Entry (First Year, Second Year)

Concomitant Medications
- Oral Corticosteroids
- Short acting muscarinic antagonist (SAMA)
- Short acting beta agonist (SABA)
- Long acting muscarinic antagonist (LAMA)
- Long acting beta agonist (LABA)
- Inhaled corticosteroid (ICS)
- LAMA / LABA combination (that is not Stiolto or Anoro)
- LABA / ICS combination
- LAMA / LABA / ICS combination
- NSAIDs
- Antihistamines
- Opioids
- Oral antibiotics
- Antidiabetic Agents (not including insulin)

- Insulin (basal or mealtime)
- Methotrexate
- Statins
- Antihypertensives
- Anticoagulants
- Anti-psychotic/anti-depressives/anxiolytic
- Oxygen therapy

Comorbidities/Symptoms

- History of All-Cause Hospitalization
- History of Emergency Department Visit
- History of Hospitalization due to Respiratory Condition
- Acute Myocardial Infarction
- Angina Pectoris
- Peripheral Vascular Disease
- Heart Failure
- Hypertension
- Upper Respiratory Infection
- Lower Respiratory Infection
- Cardiac Arrhythmias
- Cerebrovascular Disease
- All Cancers (except nonmelanoma skin cancer)
- Allergic Rhinitis
- Chronic Sinusitis
- Bronchiectasis
- Pneumonia
- Chronic Bronchitis
- Exertional Breathlessness
- Anxiety
- Dementia
- Depression
- Osteoporosis
- Charlson Deyo Comorbidity Index
- Acute Liver Injury or Failure
- Chronic Kidney Disease (without ESRD)
- End Stage Renal Disease
- Rheumatic Disease
- Peptic Ulcer Disease
- Gastroesophageal Reflux Disease
- Type 1 Diabetes Mellitus
- Type 2 Diabetes Mellitus
- HIV/AIDS
- Hemiplegia or Paraplegia

Lifestyle
- Smoking-related claim
- Vaccination for Influenza
- Vaccination for Pneumococcus

Respiratory Function Procedures/Tests
- Pulmonary function tests
- Six-minute walk test
- Chest X-ray
- High resolution chest CT

9.4 DATA SOURCES

The proposed study will utilize data from Truven MarketScan data (US).

The Truven MarketScan databases capture longitudinal, individual-level administrative claims data from the United States. The data available for the study includes three components of MarketScan: the Commercial Claims and Encounters (CCAE) Database, the Medicare Supplemental and Coordination of Benefits Database (MDCR), and the Medicaid Database. Patients in the databases include active employees, dependents, retirees, COBRA recipients, and Medicare or Medicaid enrollees. Data were drawn from large employers, health plans, and public organizations in the United States. The following tables of the MarketScan databases were available for analysis: Enrollment Detail, Inpatient Admissions, Inpatient Services, Outpatient Services, Outpatient Pharmaceutical Claims, and Long Term Care. These tables provide information on plan enrollment, healthcare utilization and expenditures, demographics, and integrated records for inpatient events, outpatient events, and pharmacy dispensings. Data are available from January 1, 2008 to March 31, 2018, and represent approximately 162 million patients.

9.5 STUDY SIZE

There are 14,751 new users of Olodaterol/Tiotropium Bromide or Umeclidinium/Vilanterol between 17 November 2015 and 31 March 2018 who satisfied the inclusion criteria. Among them, 3,889 initiated Olodaterol/Tiotropium Bromide and 10,862 initiated Umeclidinium/Vilanterol).

9.6 DATA MANAGEMENT

Dataset
The Truven Health MarketScan database is comprised of fully adjudicated and paid claims records of integrated longitudinal enrolment, inpatient, outpatient and drug data from multiple payors that has been standardized and de-identified prior to use for the analysis. The statistical analysis will be conducted using the Evidence Platform.

Drug Duration
Unless otherwise noted, drug event duration was calculated from the "Day's Supply" field, and in cases where this field was 0, the duration was assumed to be 1 day.

Handling of Missing Data
Missing data that occurs in covariates or descriptive variables will be classified as its own level. In addition, a feasibility assessment before beginning the analyses will be done, and variables with >75 % missing values will be excluded from all analyses, other than baseline characteristics. If a variable is left with only one level other than missing, the variable will be excluded completely from all analyses.

9.7 DATA ANALYSIS

9.7.1 Main analysis

For all analyses, variables will be reported as follows:

- Continuous variables (e.g., age) will be presented as means (with standard deviation, SD) and/or medians (with interquartile range, IQR).
- Categorical variables (e.g., sex) will be presented as absolute and relative frequencies.
- All results will have two digits following the decimal point.

9.7.1.1 Descriptive Analysis

All variables specified in section 9.3.3 will be reported. For demographic and lifestyle variables, the value recorded on the cohort entry date will be reported, otherwise the most recent known value will be reported. Presence of comorbidities and use of concomitant medication use will be determined based whether they ever occurred within the 180-day baseline period preceding the index date. Differences in the confounder distributions were inspected for successful confounder balance of measured characteristics.

9.7.1.2 Rates and Risks

- Rate of Discontinuation of Olodaterol/Tiotropium Bromide or Umeclidinium/Vilanterol in the Pre-matched Cohort

Among the pre-matched cohort, rates of discontinuation of Olodaterol/Tiotropium Bromide or Umeclidinium/Vilanterol will be reported as the number of events divided by the number of person-years at risk.

- Risk of Discontinuation of Olodaterol/Tiotropium Bromide or Umeclidinium/Vilanterol in the Pre-matched Cohort

Among the pre-matched cohort, risk (proportion of patients) of discontinuation of Olodaterol/Tiotropium Bromide or Umeclidinium/Vilanterol will be reported as the number of events divided by the number of eligible patients at cohort entry date.

- Discontinuation of Olodaterol/Tiotropium Bromide or Umeclidinium/Vilanterol in the Post-matched Cohort

Among the post-matched cohort, rates of discontinuation of Olodaterol/Tiotropium Bromide or Umeclidinium/Vilanterol will be reported as the number of events divided by the number of person-years at risk.

- Discontinuation of Olodaterol/Tiotropium Bromide or Umeclidinium/Vilanterol in the Post-matched Cohort

Among the post-matched cohort, risk (proportion of patients) of discontinuation of Olodaterol/Tiotropium Bromide or Umeclidinium/Vilanterol will be reported as the number of events divided by the number of eligible patients at cohort entry date.

9.7.1.3 Comparative Persistence

- Relative Rate of Discontinuation of Olodaterol/Tiotropium Bromide vs Umeclidinium/Vilanterol in the Unmatched Cohort

Multivariable Cox proportional hazards models with all variables (except components of the Charlson Comorbidity index) in section 9.3.3. will be used to estimate the hazard ratios (HRs) and 95% CIs for Olodaterol/Tiotropium Bromide compared to patients treated with Umeclidinium/Vilanterol during follow-up for incident discontinuations, according to the following model:

$$h(t \mid \text{Treatment}, X_1, \ldots, X_n) = h(t_0)*\exp(\beta_1*\text{Treatment} + \beta_1*X_2 + \ldots + \beta_n*X_{n+1})$$

Where treatment can be 1=Stiolto or 0=Anoro and t = time to discontinuation

- Relative Risk of Discontinuation of Olodaterol/Tiotropium Bromide vs Umeclidinium/Vilanterol in the Unmatched Cohort

Multivariable logistic regression will be used to assess relative risk of discontinuation and 95% CIs for Olodaterol/Tiotropium Bromide compared to patients treated with Umeclidinium/Vilanterol during follow-up for incident discontinuations, according to the following model using all covariates (except components of the Charlson Comorbidity index) in section 9.3.3.:

$$\text{Logit}(\text{Discontinuation}=1 \mid \text{Treatment}, X_1, X_2, \ldots, X_n) = \beta_0 + \beta_1*\text{Treatment} + \beta_1*X_2 + \ldots + \beta_n*X_{n+1}$$

- Relative Rate of Discontinuation of Olodaterol/Tiotropium Bromide vs Umeclidinium/Vilanterol in the Matched Cohort

Cox proportional hazards models with treatment as the only independent variable will be used to estimate the hazard ratios (HRs) and 95% CIs for Olodaterol/Tiotropium Bromide

compared to patients treated with Umeclidinium/Vilanterol during follow-up for incident discontinuations, according to the following model:

$$h(t \mid \text{Treatment}, X) = h_0(t)*\exp(\beta_1*\text{Treatment})$$

Where treatment can be 1=Stiolto or 0=Anoro and t = time to discontinuation

- Relative Risk of Discontinuation of Olodaterol/Tiotropium Bromide vs Umeclidinium/Vilanterol in the Matched Cohort

Logistic regression will be used to assess relative risk of discontinuation and 95% CIs for Olodaterol/Tiotropium Bromide compared to patients treated with Umeclidinium/Vilanterol during follow-up for incident discontinuations, according to the following model:

$$\text{Logit}(\text{Discontinuation}=1 \mid \text{Matched set}) = \beta_1*\text{Treatment} + \alpha_{\text{stratum(i)}}$$

Where treatment can be 1=Stiolto or 0=Anoro and t = time to discontinuation

9.7.2 Sensitivity Analysis

Four sensitivity analyses will be conducted. For these analyses, in the interest of reducing the number of additional tables, only the descriptive statistics for the matched population (Annex Table 2), and primary results (Annex Tables 4 and 5) will be reported.

Two sensitivity analyses will be conducted to evaluate the robustness of the outcome definition:

1. Use of a 30-day Grace Period

Restrict the 60-day allowable grace period used to define the discontinuation outcome to 30 days to allow a gap of one month. This sensitivity analysis may be useful if the 60-day grace period is too lenient, as the usual day's supply of Stiolto is 30 days.

2. Use of a 90-day Grace Period

Since neither the Olodaterol/Tiotropium Bromide or Umeclidinium/Vilanterol drug products are available as generic formulations, the relatively high price of these medications may lead some patients to space out their doses to greater than the recommended dosing schedule or use one puff instead of two to prolong their medication supply. Patients may also neglect to take their medications due to forgetfulness or because they become less symptomatic. Thus, we will also increase the 60-day allowable grace period used to define the discontinuation outcome, to 90 days.

Two sensitivity analyses will be conducted in an attempt to increase the sample size:

3. Start Patient Identification Period in 21 May 2015

The primary identification period starts 180 days after Stiolto Respimat was approved by FDA for use in the US (21 May 2015) on 17 November 2015. This sensitivity cohort will start the patient identification period immediately upon FDA approval on 21 May 2015.

4. Do Not Exclude Patients with Diagnosis of ACOS from the Cohort

Patients in the primary analysis with diagnosis of asthma (regardless of whether or not they have COPD) will be excluded to restrict to patients with only COPD. It is possible that some patients with COPD may have a claim for asthma prior to their COPD diagnosis as part of their COPD diagnostic work-up, rather than an ongoing asthma diagnosis. Therefore, this sensitivity cohort will not exclude patients with a previous diagnosis of asthma. Note that patients with only asthma but no COPD will still be excluded from this cohort.

9.8 QUALITY CONTROL

will build measures for cohort inclusion, outcomes and covariates. Some of the measure algorithms will be based on those collaboratively developed for another respiratory-related protocol with clinical input from external pulmonology experts. When available, algorithms that have been validated in administrative databases will be used. When validated algorithms are not available, coding criteria will be based on clinical input and through searches of medical claim coding systems.

All measures created, cohorts developed, statistical analyses implemented, and tables completed will undergo quality control review by at least 1 additional analyst or scientist under the supervision of the senior scientist.

This protocol will be strictly followed in the study. However, measure definitions may undergo modification if determined to be scientifically sensible. All changes to this protocol will be documented in protocol amendments.

The study protocol has been written following the Code of Conduct by the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP) [R15-4870] that provides a set of rules and principles for post-authorisation studies with regard to the best practices and transparency, thereby promoting scientific independence of such studies. The study will be registered to the ENCePP's E-register and the results will also be published on the same site.

The study protocol also follows the key elements of the Guideline for Good Pharmacoepidemiology Practices (GPP) by International Society for Pharmacoepidemiology [R11-4318], and the recent draft Guidance for Industry and FDA Staff "Best Practices for Conducting and Reporting Pharmacoepidemiologic Safety Studies Using Electronic Healthcare Data Sets" [R15-4859].

Quality controls include checks for the validity and logical content of codes and checks for missing values and variables. In order to control for potential inconsistencies and errors, all

variables will be tabulated. In addition, the distribution of each variable will be examined. Extreme observations with values larger than ± 3 standard deviations (SD) will be examined as potential outliers and consequently excluded from the dataset.

9.9 LIMITATIONS OF THE RESEARCH METHODS

This study will be conducted using data from insurance claims and is subject to certain limitations. One limitation is that these are based on a large, non-random convenience sample, which may contain biases or lack generalizability to other populations. Data also come mostly from large employers, and although the database also includes a large amount of data from health plans, data from medium and small firms may be underrepresented.

Additionally, the MarketScan database also poses some limitations inherent to administrative claims data. Electronic outpatient pharmacy dispensing records are considered accurate because pharmacists fill prescriptions with little room for interpretation and are reimbursed by insurers on the basis of detailed, complete, and accurate claims submitted electronically (Stergachi 1988, Levy 2003). Pharmacy dispensing information is usually seen as the gold standard of drug exposure information compared to self-reported information (West 1995) or prescribing records in outpatient medical records (West 1994). However, drugs used during hospital stays are not recorded in this data source. Claims data are subject to certain limitations. The presence of a claim for a filled prescription does not indicate that the medication was consumed or that it was taken as prescribed, and any medications filled over-the-counter or provided as samples by the physician will not be observed in the claims data. Furthermore, as with all claims-based analyses, study results may not be generalizable to the overall population as patients who have commercial health insurance may be different from those with non-commercial or without (commercial) health insurance. Finally, patients are required not to have a claim for Olodaterol/Tiotropium Bromide or Umeclidinium/Vilanterol during the baseline period, but use of these medications may have occurred prior to the start of the baseline period.

In the analytical portion of this protocol, propensity score matching will be used to estimate relative persistence between the two exposures of interest. Various covariates are included in the prediction model of the propensity scores, but as with all non-interventional studies, the potential for unmeasured and residual confounding cannot be ruled out.

9.10 OTHER ASPECTS

Not applicable.

9.11 SUBJECTS

9.11.1 Cases

See Section 9.2.2.

9.11.2 Controls

Not applicable.

9.12 BIAS

In principle, electronic outpatient pharmacy dispensing records are considered accurate because pharmacists fill prescriptions with little room for interpretation, and are reimbursed by insurers based on detailed, complete, and accurate claims submitted electronically **(Levy 2003; Stergachis 1988)**. Pharmacy dispensing information is usually seen as the gold standard of drug exposure information compared to self-reported information or prescribing records in outpatient medical records.
The population-based nature of the database will avoid selection bias and ensure external validity. Confounding bias through observable covariates will be controlled for by the design, which includes propensity score matching.
To minimize misclassification of the recorded patient characteristics, previously validated algorithms or code lists will be used whenever available. Code lists will be reviewed by the qualified medical reviewers prior to implementation. Basic plausibility checks will be implemented for continuous variables (e.g. age, etc.).

While this analysis is designed to assess non-persistence as an endpoint. Whether or not the patient actually complied with the prescription cannot be known. For example, a patient may fill a 30-day prescription, but may only comply with the medication for a few days before truly discontinuing, leading to an overestimation of persistence when using claims data. Furthermore, even if a patient did comply, they may administer the doses incorrectly.

The covariates chosen in section 9.3.3. are hypothesized to be confounders in the relationship between exposure and outcome. The range and quantity of variables selected are aimed to make the two exposure groups more comparable so that the interpretation of effect estimates may be more meaningful.

10. PROTECTION OF HUMAN SUBJECTS

As the present study is a non-interventional retrospective cohort study, the most significant potential impact on the participants would be the potential for individual identification and loss of privacy. Patients in the MarketScan dataset are de-identified, such that names are not linked to patient IDs. Thus, the risks to participants are expected to be minimal.

11. MANAGEMENT AND REPORTING OF ADVERSE EVENTS/ADVERSE REACTIONS

Data is anonymized and extracted, analyzed, validated and reported in aggregate.

There is no potential that any employee of BI or agent working on behalf of BI will access individual patient data in which the patient may be identified during data compilation, data reporting or data analysis.

Based on current guidelines from the International Society for Pharmacoepidemiology [R11-4318] and the EMA [R13-1970], non-interventional studies such as the one described in this protocol, conducted using health care records, do not require expedited reporting of suspected adverse events/reactions. Specifically, as stated in section VI.C.1.2.1 of Guideline on Good Pharmacovigilance Practices (GVP), Module VI – Management and Reporting of Adverse Reactions to Medicinal Products, for non-interventional study designs, which are based on use of secondary data, reporting of adverse reactions is not required.

12. PLANS FOR DISSEMINATING AND COMMUNICATING STUDY RESULTS

The results of the study will primarily serve internal decision making for future studies on comparative effectiveness. These baseline results will be published as an abstract and/or manuscript. Conference and Journal to be decided.

13. REFERENCES

13.1 PUBLISHED REFERENCES

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13.2 UNPUBLISHED REFERENCES

Not Applicable

ANNEX 1. LIST OF STAND-ALONE DOCUMENTS

Number	Document Reference Number	Date	Title
1	Annex 1	19 April 2019	List of stand-alone documents
2	Annex 2	19 April 2019	ENCEPP Checklist for study protocols
3	Annex 3	19 April 2019	List of medication measure definitions
4	Annex 4	19 April 2019	List of comorbidity and other measure definitions
5	Annex 5	19 April 2019	Table shells and proposed figures

ANNEX 2. ENCEPP CHECKLIST FOR STUDY PROTOCOLS

Not Applicable

ANNEX 3. LIST OF MEDICATION MEASURE DEFINITIONS

Name	Components
Corticosteroids	Betamethasone, *beclometasone (beclomethasone), cortisone acetate, dexamethasone, hydrocortisone, methylprednisolone, prednisolone, prednisone, triamcinolone, deflazacort, fludrocortisone
Short Acting Beta Agonist	Albuterol, metaproterenol, levalbuterol, pirbuterol, terbutaline
Short Acting Muscarinic Antagonist	Ipratropium
Long Acting Muscarinic Antagonist (LAMA)	Umeclidinium, glycopyrrolate, tiotropium, aclidinium, Incruse, Seebri, Spiriva, Tudorza
Long Acting Beta Agonist (LABA)	Indacaterol, arformoterol, formoterol, salmeterol, olodaterol, Arcapta, Atimos, Brovana, Perforomist, Serevent, Striverdi, Foradil
Inhaled Corticosteroids	Flunisolide, budesonide, mometasone, ciclesonide, fluticasone, beclomethasone, Aerobid, Aerospan, Alvesco, Armonair, Arnuity, Asmanex, Azmacort, Flixotide, Flovent, Pulmicort, Qvar
LAMA / LABA combination	indacaterol/glycopyrrolate, glycopyrrolate/formoterol, Utibron, Bevespi
LABA / ICS combination	Fluticasone/vilanterol, budesonide/formoterol, fluticasone/salmeterol, mometasone/formoterol, Advair, Symbicort, Breo, Dulera
LAMA / LABA / ICS combination	Fluticasone/umeclidinium/vilanterol, Trelegy
NSAIDs	Phenylbutazone, sulindac, tolmetin, diclofenac, etodolac, ketorolac, piroxicam, meloxicam, ibuprofen, naproxen, ketoprofen, fenoprofen, suprofen, flurbiprofen, oxaprozin, mefanamic acid, meclofenamic acid, celecoxib, rofecoxib, valdecoxib, nabumetone, glucosamine sulfate

Opioids	Morphine, hydromorphone, oxycodone, dihydrocodeine, fentanyl, pentazocine, buprenorphine, butorphanol, nalbuphine, tramadol, tapentadol, hydrocodone, codeine
Antihistamines/Antiallergenics	Diphenhydramine, clemastine, carbinoxamine, doxylamine, brompheniramine, dexchlorpheniramine, pheniramine, tripelennamine, promethazine, thiethylperazine, cyclizine, chlorcyclizine, cetirizine, cyproheptadine, phenindamine, triprolidine, azatadine, astemizole, terfenadine, loratadine, ketotifen, azelastine, levocabastine, epinastine, fexofenadine, desloratadine, ephedrine, phenylephrine, oxymetazoline, xylometazoline, naphazoline, nedocromil
Oral Antibiotics	Demeclocycline, doxycycline, chlortetracycline, oxytetracycline, tetracycline, minocycline, tigecycline, chloramphenicol, ampicillin, carbenicillin, amoxicillin, bacampicillin, mezlocillin, piperacillin, ticarcillin, dicloxacillin, cloxacillin, oxacillin, flucloxacillin, nafcillin, sulbactam, tazobactam, cefazolin, cefadroxil, cefoxitin, cefuroxime, cefamandole, cefaclor, cefotetan, loracarbef, cefprozil, cefotaxime, ceftazidime, ceftriaxone, ceftizoxime, cefixime, cefoperazone, cefpodoxime, ceftibuten, cefdinir, cefditoren, cefepime, aztreonam, meropenem, ertapenem, doripenem, trimethoprim, sulfapyridine, sulfanilamide, sulfathiazole, sulfamethoxazole, sulfadiazine, sulfamerazine, sulfapyridine, sulfanilamide, sulfathiazole, sulfadiazine, sulfamethoxazole, sulfachlorpyridazine, sulfamerazine, sulfacetamide, erythromycin, troleandomycin, clarithromycin, azithromycin, dirithromycin, telithromycin, clindamycin, lincomycin, quinupristin/dalfopristin, streptomycin, tobramycin, gentamicin, kanamycin, neomycin, amikacin, netilmicin, paromomycin, ofloxacin, ciprofloxacin, enoxacin, norfloxacin, lomefloxacin, sparfloxacin, grepafloxacin, levofloxacin, trovafloxacin, moxifloxacin, gemifloxacin, gatifloxacin, delafloxacin, cinoxacin, vancomycin, telavancin, dalbavancin, oritavancin, colistin, polymyxin b, metronidazole, tinidazole, nitrofurantoin, fosfomycin, spectinomycin, methenamine, mandelic acid, linezolid, daptomycin, bacitracin, tedizolid, novobiocin
Diabetes Mellitus Medications	Sulfonylureas (chlorpropamide, tolbutamide, tolazamide, glipizide, gliquidone, acetohexamide), biguanides (metformin), thiazolidinediones (troglitazone, rosiglitazone, pioglitazone), alpha-glucosidase inhibitors (acarbose, miglitol), meglitinides (repaglinide, nateglinide, mitiglinide), DPP-4 inhibitors (gitagliptin, vildagliptin, saxagliptin, alogliptin, linagliptin), GLP-1 receptor agonists (exenatide, liraglutide, lixisenatide, albiglutide, dulaglutide, semaglutide), SGLT-2 inhibitors (dapagliflozin, canagliflozin, empagliflozin)
Insulin	Rapid-acting insulin, short-acting insulin, intermediate-acting insulin, long-acting insulin
Methotrexate	Methotrexate
Anticoagulants	Vitamin K antagonists (phenindione, warfarin), heparins (heparin, antithrombin III, dalteparin, enoxaparin, danaparoid, tinzaparin), platelet aggregation inhibitors (clopidogrel, ticlopidine, dipyridamole, epoprostenol, iloprost, abciximab, eptifibatide, tirofiban, treprostinil, prasugrel, cilostazol, ticagrelor, cangrelor, vorapaxar, selexipag), direct thrombin

	inhibitors (desirudin, lepirudin, argatroban, bivalirudin, dabigatran etexilate), direct factor Xa inhibitors (rivaroxaban, apixaban, edoxaban), anticoagulant enzymes (anistreplase, urokinase, reteplase, drotrecogin alfa, tenecteplase), defibrotide, fondaparinux)
Statins	Atorvastatin, fluvastatin, lovastatin, pravastatin, rosuvastatin, simvastatin, pitavastatin, cerivastatin
Antihypertensives	Angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers, beta-blockers, calcium channel blockers, diuretics, alpha-blockers, alpha-beta blockers, vasiodilators
Anti-psychotics/ Anti-depressives/Anxiolytics	Desipramine, clomipramine, trimipramine, amitriptyline, nortriptyline, protriptyline, doxepin, amoxapine, maprotiline, fluoxetine, citalopram, paroxetine, sertraline, fluvoxamine, escitalopram, isocarboxazid, phenelzine, tranylcypromine, tryptophan, trazodone, nefazodone, minaprine, mirtazapine, bupropion, venlafaxine, milnacipran, duloxetine, desvenlafaxine, vilazodone, vortioxetine, selegiline, chlorpromazine, promazine, acepromazine, triflupromazine, fluphenazine, perphenazine, prochlorperazine, trifluoperazine, thioridazine, mesoridazine, pipotiazine, haloperidol, droperidol, molindone, ziprasidone, lurasidone, thiothixene, pimozide, loxapine, clozapine, olanzapine, quetiapine, asenapine, lithium, risperidone, aripiprazole, paliperidone, iloperidone, cariprazine, brexpiprazole, pimavanserin, diazepam, chlordiazepoxide, oxazepam, lorazepam, clobazam, alprazolam, halazepam, hydroxyzine, meprobamate, buspirone
Oxygen Therapy	Oxygen

ANNEX 4. LIST OF COMORBIDITY, SYMPTOMS AND OTHER MEASURE DEFINITIONS

Name	Definition
Comorbidities/Symptoms	
History of All-Cause Hospitalization	All inpatient events
History of Emergency Department Visit	1 Outpatient • **Place of Service** is any of: o Emergency Room - Hospital o Urgent Care Facility
History of Hospitalization due to Respiratory Condition	1 Inpatient **Diagnosis Code (Principal), ICD-9** is any of: { “415.1”, “415.11”, “415.12”, “415.13”, “415.19”, “465”, “465.0”, “465.8”, “465.9”, “466”, “466.0”, “466.1”, “466.11”, “466.19”, “480.0”, “480.1”, “480.2”, “480.3”, “480.8”, “480.9”, “481”, “482.0”, “482.1”, “482.2”, “482.30”, “482.31”, “482.32”, “482.39”, “482.40”, “482.41”, “482.42”, “483.0”, “483.1”, “483.8”, “484.1”, “484.3”, “484.5”, “484.6”, “484.7”, “484.8”, “486”, “487.0”, “488.01”, “488.11”, “488.81”, “490”, “491”, “491.0”, “491.1”, “491.2”, “491.20”, “491.21”, “491.22”, “491.8”, “491.9”, “492.0”, “492.8”, “493.0”, “493.00”, “493.01”, “493.02”, “493.1”, “493.10”, “493.11”, “493.12”, “496”, “515”, “516.3”, “516.30”, “516.31”, “516.32”, “516.8”, “516.9”, “518.81”, “518.83”, “518.84” } **Diagnosis Code (Principal), ICD-10** is any of: { “A01.03”, “A02.22”, “A37.01”, “A37.11”, “A37.81”, “A37.91”, “A40.3”, “A50.04”, “A54.84”, “B01.2”, “B05.2”, “B06.81”, “B77.81”, “B95.3”, “B96.0”, “B96.1”, “I26.9”, “I26.90”, “I26.92”, “I26.99”, “J06”, “J06.0”, “J06.9”, “J09.X1”, “J09.X2”, “J10.0”, “J10.00”, “J10.01”, “J10.08”, “J10.1”, “J11.0”, “J11.00”, “J11.08”, “J11.1”, “J12”, “J12.0”, “J12.1”, “J12.2”, “J12.3”, “J12.8”, “J12.81”, “J12.89”, “J12.9”, “J13”, “J14”, “J15”, “J15.0”, “J15.1”, “J15.2”, “J15.20”, “J15.21”, “J15.211”, “J15.212”, “J15.29”, “J15.3”, “J15.4”, “J15.5”, “J15.6”, “J15.7”, “J15.8”, “J15.9”, “J16”, “J16.0”, “J16.8”, “J17”, “J18”, “J18.0”, “J18.1”, “J18.2”, “J18.8”, “J18.9”, “J20”, “J20.0”, “J20.1”, “J20.2”, “J20.3”, “J20.4”, “J20.5”, “J20.6”, “J20.7”, “J20.8”, “J20.9”, “J21.0”, “J22”, “J39”, “J39.3”, “J39.8”, “J39.9”, “J40”, “J41”, “J41.0”, “J41.1”, “J41.8”, “J42”, “J43”, “J43.0”, “J43.1”, “J43.2”, “J43.8”, “J43.9”, “J44.0”, “J45”, “J45.2”, “J45.20”, “J45.21”, “J45.22”, “J45.3”, “J45.30”, “J45.31”, “J45.32”, “J45.4”, “J45.40”, “J45.41”, “J45.42”, “J45.5”, “J45.50”, “J45.51”, “J45.52”, “J45.9”, “J45.90”, “J45.901”, “J45.902”, “J45.909”, “J45.99”, “J45.991”, “J45.998”, “J47.0”, “J68.0”, “J84.11”, “J84.111”, “J84.116”, “J84.117”, “J84.2”,

	"J85.1", "J96", "J96.9", "J96.90", "J96.91", "J96.92", "J96.0", "J96.00", "J96.01", "J96.02", "J96.1", "J96.10", "J96.11", "J96.12", "J96.2", "J96.20", "J96.21", "J96.22", "J98", "J98.2", "J98.3", "J98.8" }
Acute Myocardial Infarction	1 Inpatient or 1 Outpatient **Diagnosis Code (Position 1), ICD-9** is any of: { "410", "410.0", "410.00", "410.01", "410.1", "410.10", "410.11", "410.2", "410.20", "410.21", "410.3", "410.30", "410.31", "410.4", "410.40", "410.41", "410.5", "410.50", "410.51", "410.6", "410.60", "410.61", "410.7", "410.70", "410.71", "410.8", "410.80", "410.81", "410.9", "410.90", "410.91" } **Diagnosis Code (Principal), ICD-10** is any of: { "I21.09", "I21.11", "I21.19", "I21.29", "I21.3", "I21.4", "I22.0", "I22.1", "I22.2", "I22.8", "I22.9" }
Angina Pectoris	1 Inpatient or 2 Outpatient (30 – 365 days apart) **Diagnosis Code (Any Position), ICD-9** is any of: { "413", "413.0", "413.1", "413.9" } **Diagnosis Code (Any Position), ICD-10** is any of: { "I20.1", "I20.8", "I20.9" }
Peripheral Vascular Disease	1 Inpatient or 2 Outpatient (30 – 365 days apart) **Diagnosis Code (Any Position), ICD-9** is any of: { "440", "440.0", "440.1", "440.2", "440.20", "440.21", "440.22", "440.23", "440.24", "440.29", "440.3", "440.30", "440.31", "440.32", "440.4", "440.8", "440.9", "441", "441.0", "441.00", "441.01", "441.02", "441.03", "441.1", "441.2", "441.3", "441.4", "441.5", "441.6", "441.7", "441.9", "442", "442.0", "442.1", "442.2", "442.3", "442.8", "442.81", "442.82", "442.83", "442.84", "442.89", "442.9", "443.1", "443.2", "443.21", "443.22", "443.23", "443.24", "443.29", "443.8", "443.81", "443.82", "443.89", "443.9", "447.1", "785.4", "38.13", "38.14", "38.16", "38.18", "38.33", "38.34", "38.36", "38.38", "38.43", "38.44", "38.46", "38.48", "39.22", "39.23", "39.24", "39.25", "39.26", "39.29" } **Diagnosis Code (Any Position), ICD-10** is any of: { "I70.0", "I70.1", "I70.209", "I70.219", "I70.229", "I70.25", "I70.269", "I70.299", "I70.399", "I70.499", "I70.599", "I70.8", "I70.90", "I70.91", "I70.92", "I71.00", "I71.01", "I71.02", "I71.03", "I71.1", "I71.2", "I71.3", "I71.4", "I71.5", "I71.6", "I71.8", "I71.9", "I72.0", "I72.1", "I72.2", "I72.3", "I72.4", "I72.8", "I72.9", "I73.1", "I73.81", "I73.89", "I73.9", "I77.1", "I77.71", "I77.72", "I77.73", "I77.74", "I77.79", "I79.8", "I96" }

Heart Failure	1 Inpatient **Diagnosis Code (Any Position), ICD-9** is any of: { “428”, “428.0”, “428.1”, “428.2”, “428.20”, “428.21”, “428.22”, “428.23”, “428.3”, “428.30”, “428.31”, “428.32”, “428.33”, “428.4”, “428.40”, “428.41”, “428.42”, “428.43”, “428.9” } **Diagnosis Code (Any Position), ICD-10** is any of: { “I50”, “I50.9”, “I50.2”, “I50.20”, “I50.21”, “I50.22”, “I50.23”, “I50.3”, “I50.30”, “I50.31”, “I50.32”, “I50.33”, “I50.4”, “I50.40”, “I50.41”, “I50.42”, “I50.43” }
Hypertension	1 Inpatient or 2 Outpatient (30 – 365 days apart) **Diagnosis Code (Any Position), ICD-9** is any of: { “401”, “401.0”, “401.1”, “401.9”, “402”, “402.0”, “402.00”, “402.1”, “402.10”, “402.9”, “402.90”, “403”, “403.0”, “403.00”, “403.01”, “403.1”, “403.10”, “403.11”, “403.9”, “403.90”, “403.91”, “404”, “404.0”, “404.00”, “404.01”, “404.02”, “404.03”, “404.1”, “404.10”, “404.11”, “404.12”, “404.13”, “404.9”, “404.90”, “404.91”, “404.92”, “404.93”, “405”, “405.0”, “405.01”, “405.09”, “405.1”, “405.11”, “405.19”, “405.9”, “405.91”, “405.99” } **Diagnosis Code (Any Position), ICD-10** is any of: { “I10”, “I11.9”, “I12.0”, “I12.9”, “I13.0”, “I13.10”, “I13.11”, “I13.2”, “I15.0”, “I15.8” }
Upper Respiratory Infection (with no sinusitis)	1 Inpatient or 2 Outpatient (30 – 365 days apart) **Diagnosis Code (Any Position), ICD-9** is any of: { “034”, “034.0”, “034.1”, “460”, “461”, “461.0”, “461.1”, “461.2”, “461.3”, “461.8”, “461.9”, “462”, “463”, “464”, “464.0”, “464.00”, “464.01”, “464.1”, “464.10”, “464.11”, “464.2”, “464.20”, “464.21”, “464.3”, “464.30”, “464.31”, “464.4”, “464.5”, “464.50”, “464.51”, “465”, “465.0”, “465.8”, “465.9”, “487”, “487.1”, “487.8” } **Diagnosis Code (Any Position), ICD-10** is any of: { “J03.00”, “J03.01”, “A38”, “A38.8”, “A38.9”, “J00”, “J01”, “J01.9”, “J01.90”, “J01.8”, “J01.80”, “J01.0”, “J01.00”, “J01.01”, “J32.0”, “J01.1”, “J01.10”, “J01.11”, “J32.1”, “J01.2”, “J01.20”, “J01.21”, “J32.2”, “J01.3”, “J01.30”, “J01.31”, “J32.3”, “J02”, “J02.8”, “J02.9”, “J04”, “J04.0”, “J05”, “J05.0”, “J04.1”, “J04.10”, “J04.11”, “J04.2”, “J05.1”, “J05.10”, “J05.11”, “J04.3”, “J04.30”, “J04.31”, “J06”, “J06.9”, “J11.89”, “J11.8”, “J11.1”, “J11”, “J10.89”, “J10.8”, “J10.1”, “J10.00”, “J10.0”, “J10”, “J09.X2”, “J09.X9”,

	"J09.X", "J09" }
Lower Respiratory Infection	1 Inpatient or 2 Outpatient (30 – 365 days apart) **Diagnosis Code (Any Position), ICD-9** is any of: { "466", "466.0", "466.1", "466.11", "466.19" } **Diagnosis Code (Any Position), ICD-10** is any of: { "J20.9", "J21.0", "J21.8", "J22" }
Cardiac Arrhythmias	1 Inpatient or 1 Outpatient **Diagnosis Code (Principal), ICD-9** is any of: { "427", "427.0", "427.1", "427.2", "427.3", "427.31", "427.32", "427.4", "427.41", "427.42", "427.5", "427.6", "427.60", "427.61", "427.69", "427.8", "427.81", "427.89", "427.9" } **Diagnosis Code (Position 1), ICD-10** is any of: { "I46.9", "I47.1", "I47.2", "I47.9", "I48.91", "I48.92", "I49.01", "I49.02", "I49.1", "I49.3", "I49.40", "I49.49", "I49.5", "I49.8", "I49.9", "R00.1" }
Cerebrovascular Disease	1 Inpatient **Diagnosis Code (Any Position), ICD-9** is any of: { "430", "431", "432", "432.0", "432.1", "432.9", "433", "433.0", "433.01", "433.1", "433.11", "433.2", "433.21", "433.3", "433.31", "433.8", "433.81", "433.9", "433.91", "434", "434.0", "434.01", "434.1", "434.11", "434.9", "434.90", "434.91", "435", "435.8", "435.9", "436" } **Diagnosis Code (Any Position), ICD-10** is any of: { "G45", "G45.8", "G45.9", "I60", "I60.0", "I60.00", "I60.01", "I60.02", "I60.1", "I60.10", "I60.11", "I60.12", "I60.2", "I60.20", "I60.21", "I60.22", "I60.3", "I60.30", "I60.31", "I60.32", "I60.4", "I60.5", "I60.50", "I60.51", "I60.52", "I60.6", "I60.7", "I60.8", "I60.9", "I61", "I61.0", "I61.1", "I61.2", "I61.3", "I61.4", "I61.5", "I61.6", "I61.8", "I61.9", "I62", "I62.0", "I62.00", "I62.01", "I62.02", "I62.03", "I62.1", "I62.9", "I63", "I63.0", "I63.00", "I63.01", "I63.011", "I63.012", "I63.019", "I63.02", "I63.03", "I63.031", "I63.032", "I63.039", "I63.09", "I63.1", "I63.10", "I63.11", "I63.111", "I63.112", "I63.119", "I63.12", "I63.13", "I63.131", "I63.132", "I63.139", "I63.19", "I63.2", "I63.20", "I63.21", "I63.211", "I63.212", "I63.219", "I63.22", "I63.23", "I63.231", "I63.232", "I63.239", "I63.29", "I63.3", "I63.30", "I63.31", "I63.311", "I63.312", "I63.319", "I63.32", "I63.321", "I63.322", "I63.329", "I63.33", "I63.331", "I63.332", "I63.339", "I63.34", "I63.341", "I63.342", "I63.349", "I63.39", "I63.4", "I63.40", "I63.41", "I63.411", "I63.412", "I63.419", "I63.42", "I63.421", "I63.422",

	“I63.429”, “I63.43”, “I63.431”, “I63.432”, “I63.439”, “I63.44”, “I63.441”, “I63.442”, “I63.449”, “I63.49”, “I63.5”, “I63.50”, “I63.51”, “I63.511”, “I63.512”, “I63.519”, “I63.52”, “I63.521”, “I63.522”, “I63.529”, “I63.53”, “I63.531”, “I63.532”, “I63.539”, “I63.54”, “I63.541”, “I63.542”, “I63.549”, “I63.59”, “I63.6”, “I63.8”, “I63.9”, “I65”, “I65.0”, “I65.01”, “I65.02”, “I65.03”, “I65.09”, “I65.1”, “I65.2”, “I65.21”, “I65.22”, “I65.23”, “I65.29”, “I65.8”, “I65.9”, “I66”, “I66.0”, “I66.01”, “I66.02”, “I66.03”, “I66.09”, “I66.1”, “I66.11”, “I66.12”, “I66.13”, “I66.19”, “I66.2”, “I66.21”, “I66.22”, “I66.23”, “I66.29”, “I66.3”, “I66.8”, “I66.9” }
All Cancers (except nonmelanoma skin cancer)	1 Inpatient or 2 Outpatient (30 – 365 days apart) **Diagnosis Code (Any Position), ICD-9** is any of: { “140”, “140.0”, “140.1”, “140.3”, “140.4”, “140.5”, “140.6”, “140.8”, “140.9”, “141”, “141.0”, “141.1”, “141.2”, “141.3”, “141.4”, “141.5”, “141.6”, “141.8”, “141.9”, “142”, “142.0”, “142.1”, “142.2”, “142.8”, “142.9”, “143”, “143.0”, “143.1”, “143.8”, “143.9”, “144”, “144.0”, “144.1”, “144.8”, “144.9”, “145”, “145.0”, “145.1”, “145.2”, “145.3”, “145.4”, “145.5”, “145.6”, “145.8”, “145.9”, “146”, “146.0”, “146.1”, “146.2”, “146.3”, “146.4”, “146.5”, “146.6”, “146.7”, “146.8”, “146.9”, “147”, “147.0”, “147.1”, “147.2”, “147.3”, “147.8”, “147.9”, “148”, “148.0”, “148.1”, “148.2”, “148.3”, “148.8”, “148.9”, “149”, “149.0”, “149.1”, “149.8”, “149.9”, “150”, “150.0”, “150.1”, “150.2”, “150.3”, “150.4”, “150.5”, “150.8”, “150.9”, “151”, “151.0”, “151.1”, “151.2”, “151.3”, “151.4”, “151.5”, “151.6”, “151.8”, “151.9”, “152”, “152.0”, “152.1”, “152.2”, “152.3”, “152.8”, “152.9”, “153”, “153.0”, “153.1”, “153.2”, “153.3”, “153.4”, “153.5”, “153.6”, “153.7”, “153.8”, “153.9”, “154”, “154.0”, “154.1”, “154.2”, “154.3”, “154.8”, “155”, “155.0”, “155.1”, “155.2”, “156”, “156.0”, “156.1”, “156.2”, “156.8”, “156.9”, “157”, “157.0”, “157.1”, “157.2”, “157.3”, “157.4”, “157.8”, “157.9”, “158”, “158.0”, “158.8”, “158.9”, “159”, “159.0”, “159.1”, “159.8”, “159.9”, “160”, “160.0”, “160.1”, “160.2”, “160.3”, “160.4”, “160.5”, “160.8”, “160.9”, “161”, “161.0”, “161.1”, “161.2”, “161.3”, “161.8”, “161.9”, “162”, “162.0”, “162.2”, “162.3”, “162.4”, “162.5”, “162.8”, “162.9”, “163”, “163.0”, “163.1”, “163.8”, “163.9”, “164”, “164.0”, “164.1”, “164.2”, “164.3”, “164.8”, “164.9”, “165”, “165.0”, “165.8”, “165.9”, “170”, “170.0”, “170.1”, “170.2”, “170.3”, “170.4”, “170.5”, “170.6”, “170.7”, “170.8”, “170.9”, “171”, “171.0”, “171.2”, “171.3”, “171.4”, “171.5”, “171.6”, “171.7”, “171.8”, “171.9”, “174”, “174.0”, “174.1”, “174.2”, “174.3”, “174.4”, “174.5”, “174.6”, “174.8”, “174.9”, “175”, “175.0”, “175.9”, “176”, “176.0”, “176.1”, “176.2”, “176.3”, “176.4”, “176.5”, “176.8”, “176.9”, “179”, “180”, “180.0”, “180.1”, “180.8”, “180.9”, “181”, “182”, “182.0”, “182.1”, “182.8”, “183”, “183.0”, “183.2”, “183.3”, “183.4”, “183.5”, “183.8”, “183.9”, “184”, “184.0”, “184.1”, “184.2”, “184.3”, “184.4”, “184.8”, “184.9”, “185”, “186”, “186.0”, “186.9”, “187”, “187.1”, “187.2”, “187.3”, “187.4”, “187.5”, “187.6”, “187.7”, “187.8”, “187.9”, “188”, “188.0”, “188.1”, “188.2”, “188.3”, “188.4”, “188.5”, “188.6”, “188.7”, “188.8”, “188.9”, “189”,

	“189.0”, “189.1”, “189.2”, “189.3”, “189.4”, “189.8”, “189.9”, “190”, “190.0”, “190.1”, “190.2”, “190.3”, “190.4”, “190.5”, “190.6”, “190.7”, “190.8”, “190.9”, “191”, “191.0”, “191.1”, “191.2”, “191.3”, “191.4”, “191.5”, “191.6”, “191.7”, “191.8”, “191.9”, “192”, “192.0”, “192.1”, “192.2”, “192.3”, “192.8”, “192.9”, “193”, “194”, “194.0”, “194.1”, “194.3”, “194.4”, “194.5”, “194.6”, “194.8”, “194.9”, “195”, “195.0”, “195.1”, “195.2”, “195.3”, “195.4”, “195.5”, “195.8”, “172”, “172.0”, “172.1”, “172.2”, “172.3”, “172.4”, “172.5”, “172.6”, “172.7”, “172.8”, “172.9”, “196”, “196.0”, “196.1”, “196.2”, “196.3”, “196.5”, “196.6”, “196.8”, “196.9”, “197”, “197.0”, “197.1”, “197.2”, “197.3”, “197.4”, “197.5”, “197.6”, “197.7”, “197.8”, “198”, “198.0”, “198.1”, “198.2”, “198.3”, “198.4”, “198.5”, “198.6”, “198.7”, “198.8”, “198.81”, “198.82”, “198.89”, “199”, “199.0”, “199.1”, “199.2”, “200”, “200.0”, “200.00”, “200.01”, “200.02”, “200.03”, “200.04”, “200.05”, “200.06”, “200.07”, “200.08”, “200.1”, “200.10”, “200.11”, “200.12”, “200.13”, “200.14”, “200.15”, “200.16”, “200.17”, “200.18”, “200.2”, “200.20”, “200.21”, “200.22”, “200.23”, “200.24”, “200.25”, “200.26”, “200.27”, “200.28”, “200.3”, “200.30”, “200.31”, “200.32”, “200.33”, “200.34”, “200.35”, “200.36”, “200.37”, “200.38”, “200.4”, “200.40”, “200.41”, “200.42”, “200.43”, “200.44”, “200.45”, “200.46”, “200.47”, “200.48”, “200.5”, “200.50”, “200.51”, “200.52”, “200.53”, “200.54”, “200.55”, “200.56”, “200.57”, “200.58”, “200.6”, “200.60”, “200.61”, “200.62”, “200.63”, “200.64”, “200.65”, “200.66”, “200.67”, “200.68”, “200.7”, “200.70”, “200.71”, “200.72”, “200.73”, “200.74”, “200.75”, “200.76”, “200.77”, “200.78”, “200.8”, “200.80”, “200.81”, “200.82”, “200.83”, “200.84”, “200.85”, “200.86”, “200.87”, “200.88”, “201”, “201.0”, “201.00”, “201.01”, “201.02”, “201.03”, “201.04”, “201.05”, “201.06”, “201.07”, “201.08”, “201.1”, “201.10”, “201.11”, “201.12”, “201.13”, “201.14”, “201.15”, “201.16”, “201.17”, “201.18”, “201.2”, “201.20”, “201.21”, “201.22”, “201.23”, “201.24”, “201.25”, “201.26”, “201.27”, “201.28”, “201.4”, “201.40”, “201.41”, “201.42”, “201.43”, “201.44”, “201.45”, “201.46”, “201.47”, “201.48”, “201.5”, “201.50”, “201.51”, “201.52”, “201.53”, “201.54”, “201.55”, “201.56”, “201.57”, “201.58”, “201.6”, “201.60”, “201.61”, “201.62”, “201.63”, “201.64”, “201.65”, “201.66”, “201.67”, “201.68”, “201.7”, “201.70”, “201.71”, “201.72”, “201.73”, “201.74”, “201.75”, “201.76”, “201.77”, “201.78”, “201.9”, “201.90”, “201.91”, “201.92”, “201.93”, “201.94”, “201.95”, “201.96”, “201.97”, “201.98”, “202”, “202.0”, “202.00”, “202.01”, “202.02”, “202.03”, “202.04”, “202.05”, “202.06”, “202.07”, “202.08”, “202.1”, “202.10”, “202.11”, “202.12”, “202.13”, “202.14”, “202.15”, “202.16”, “202.17”, “202.18”, “202.2”, “202.20”, “202.21”, “202.22”, “202.23”, “202.24”, “202.25”, “202.26”, “202.27”, “202.28”, “202.3”, “202.30”, “202.31”, “202.32”, “202.33”, “202.34”, “202.35”, “202.36”, “202.37”, “202.38”, “202.4”, “202.40”, “202.41”, “202.42”, “202.43”, “202.44”, “202.45”, “202.46”, “202.47”, “202.48”, “202.5”, “202.50”, “202.51”, “202.52”, “202.53”, “202.54”, “202.55”, “202.56”, “202.57”, “202.58”, “202.6”, “202.60”, “202.61”, “202.62”, “202.63”, “202.64”, “202.65”, “202.66”, “202.67”, “202.68”, “202.7”, “202.70”, “202.71”, “202.72”, “202.73”, “202.74”, “202.75”, “202.76”, “202.77”, “202.78”, “202.8”, “202.80”, “202.81”, “202.82”, “202.83”,

	“202.84”, “202.85”, “202.86”, “202.87”, “202.88”, “202.9”, “202.90”, “202.91”, “202.92”, “202.93”, “202.94”, “202.95”, “202.96”, “202.97”, “202.98”, “203”, “203.0”, “203.00”, “203.01”, “203.02”, “203.1”, “203.10”, “203.11”, “203.12”, “203.8”, “203.80”, “203.81”, “203.82”, “204”, “204.0”, “204.00”, “204.01”, “204.02”, “204.1”, “204.10”, “204.11”, “204.12”, “204.2”, “204.20”, “204.21”, “204.22”, “204.8”, “204.80”, “204.81”, “204.82”, “204.9”, “204.90”, “204.91”, “204.92”, “205”, “205.0”, “205.00”, “205.01”, “205.02”, “205.1”, “205.10”, “205.11”, “205.12”, “205.2”, “205.20”, “205.21”, “205.22”, “205.3”, “205.30”, “205.31”, “205.32”, “205.8”, “205.80”, “205.81”, “205.82”, “205.9”, “205.90”, “205.91”, “205.92”, “206”, “206.0”, “206.00”, “206.01”, “206.02”, “206.1”, “206.10”, “206.11”, “206.12”, “206.2”, “206.20”, “206.21”, “206.22”, “206.8”, “206.80”, “206.81”, “206.82”, “206.9”, “206.90”, “206.91”, “206.92”, “207”, “207.0”, “207.00”, “207.01”, “207.02”, “207.1”, “207.10”, “207.11”, “207.12”, “207.2”, “207.20”, “207.21”, “207.22”, “207.8”, “207.80”, “207.81”, “207.82”, “208”, “208.0”, “208.00”, “208.01”, “208.02”, “208.1”, “208.10”, “208.11”, “208.12”, “208.2”, “208.20”, “208.21”, “208.22”, “208.8”, “208.80”, “208.81”, “208.82”, “208.9”, “208.90”, “208.91”, “208.92”, “V10.82” } **Diagnosis Code (Any Position), ICD-10** is any of: { “C00.0”, “C00.1”, “C00.2”, “C00.3”, “C00.4”, “C00.5”, “C00.6”, “C00.8”, “C01”, “C02.0”, “C02.1”, “C02.2”, “C02.3”, “C02.4”, “C02.8”, “C02.9”, “C03.0”, “C03.1”, “C03.9”, “C04.0”, “C04.1”, “C04.8”, “C04.9”, “C05.0”, “C05.1”, “C05.2”, “C05.9”, “C06.0”, “C06.1”, “C06.2”, “C06.89”, “C06.9”, “C07”, “C08.0”, “C08.1”, “C08.9”, “C09.0”, “C09.1”, “C09.9”, “C10.0”, “C10.1”, “C10.2”, “C10.3”, “C10.4”, “C10.8”, “C10.9”, “C11.0”, “C11.1”, “C11.2”, “C11.3”, “C11.8”, “C11.9”, “C12”, “C13.0”, “C13.1”, “C13.2”, “C13.8”, “C13.9”, “C14.0”, “C14.2”, “C14.8”, “C15.3”, “C15.4”, “C15.5”, “C15.8”, “C15.9”, “C16.0”, “C16.1”, “C16.2”, “C16.3”, “C16.4”, “C16.5”, “C16.6”, “C16.8”, “C16.9”, “C17.0”, “C17.1”, “C17.2”, “C17.3”, “C17.8”, “C17.9”, “C18.0”, “C18.1”, “C18.2”, “C18.3”, “C18.4”, “C18.5”, “C18.6”, “C18.7”, “C18.8”, “C18.9”, “C19”, “C20”, “C21.0”, “C21.1”, “C21.8”, “C22.0”, “C22.1”, “C22.2”, “C22.7”, “C22.8”, “C22.9”, “C23”, “C24.0”, “C24.1”, “C24.8”, “C24.9”, “C25.0”, “C25.1”, “C25.2”, “C25.3”, “C25.4”, “C25.7”, “C25.8”, “C25.9”, “C26.0”, “C26.1”, “C26.9”, “C30.0”, “C30.1”, “C31.0”, “C31.1”, “C31.2”, “C31.3”, “C31.8”, “C31.9”, “C32.0”, “C32.1”, “C32.2”, “C32.3”, “C32.8”, “C32.9”, “C33”, “C34.00”, “C34.10”, “C34.2”, “C34.30”, “C34.80”, “C34.90”, “C37”, “C38.0”, “C38.1”, “C38.2”, “C38.3”, “C38.4”, “C38.8”, “C39.0”, “C39.9”, “C40.00”, “C40.10”, “C40.20”, “C40.30”, “C41.0”, “C41.1”, “C41.2”, “C41.3”, “C41.4”, “C41.9”, “C43.0”, “C43.10”, “C43.20”, “C43.30”, “C43.31”, “C43.39”, “C43.4”, “C43.59”, “C43.60”, “C43.70”, “C43.8”, “C43.9”, “C46.0”, “C46.1”, “C46.2”, “C46.3”, “C46.4”, “C46.50”, “C46.7”, “C46.9”, “C47.8”, “C48.0”, “C48.1”, “C48.2”, “C48.8”, “C49.0”, “C49.10”, “C49.20”, “C49.3”, “C49.4”, “C49.5”, “C49.6”, “C49.8”, “C49.9”, “C50.019”, “C50.029”, “C50.119”, “C50.219”, “C50.319”, “C50.419”, “C50.519”, “C50.619”, “C50.819”, “C50.919”, “C50.929”, “C51.0”, “C51.1”, “C51.2”,

	“C51.9”, “C52”, “C53.0”, “C53.1”, “C53.8”, “C53.9”, “C54.0”, “C54.1”, “C54.2”, “C54.3”, “C54.8”, “C54.9”, “C55”, “C56.9”, “C57.00”, “C57.10”, “C57.20”, “C57.3”, “C57.4”, “C57.7”, “C57.8”, “C57.9”, “C58”, “C60.0”, “C60.1”, “C60.2”, “C60.8”, “C60.9”, “C61”, “C62.00”, “C62.10”, “C62.90”, “C63.00”, “C63.10”, “C63.2”, “C63.7”, “C63.8”, “C63.9”, “C64.9”, “C65.9”, “C66.9”, “C67.0”, “C67.1”, “C67.2”, “C67.3”, “C67.4”, “C67.5”, “C67.6”, “C67.7”, “C67.8”, “C67.9”, “C68.0”, “C68.1”, “C68.8”, “C68.9”, “C69.00”, “C69.10”, “C69.20”, “C69.30”, “C69.40”, “C69.50”, “C69.60”, “C69.80”, “C69.90”, “C70.0”, “C70.1”, “C70.9”, “C71.0”, “C71.1”, “C71.2”, “C71.3”, “C71.4”, “C71.5”, “C71.6”, “C71.7”, “C71.8”, “C71.9”, “C72.0”, “C72.1”, “C72.50”, “C72.9”, “C73”, “C74.90”, “C75.0”, “C75.1”, “C75.2”, “C75.3”, “C75.4”, “C75.5”, “C75.8”, “C75.9”, “C76.0”, “C76.1”, “C76.2”, “C76.3”, “C76.40”, “C76.50”, “C76.8”, “C77.0”, “C77.1”, “C77.2”, “C77.3”, “C77.4”, “C77.5”, “C77.8”, “C77.9”, “C78.00”, “C78.1”, “C78.2”, “C78.39”, “C78.4”, “C78.5”, “C78.6”, “C78.7”, “C78.89”, “C79.00”, “C79.11”, “C79.19”, “C79.2”, “C79.31”, “C79.32”, “C79.49”, “C79.51”, “C79.52”, “C79.60”, “C79.70”, “C79.81”, “C79.82”, “C79.89”, “C80.0”, “C80.1”, “C80.2”, “C81.00”, “C81.01”, “C81.02”, “C81.03”, “C81.04”, “C81.05”, “C81.06”, “C81.07”, “C81.08”, “C81.09”, “C81.10”, “C81.11”, “C81.12”, “C81.13”, “C81.14”, “C81.15”, “C81.16”, “C81.17”, “C81.18”, “C81.19”, “C81.20”, “C81.21”, “C81.22”, “C81.23”, “C81.24”, “C81.25”, “C81.26”, “C81.27”, “C81.28”, “C81.29”, “C81.30”, “C81.31”, “C81.32”, “C81.33”, “C81.34”, “C81.35”, “C81.36”, “C81.37”, “C81.38”, “C81.39”, “C81.40”, “C81.41”, “C81.42”, “C81.43”, “C81.44”, “C81.45”, “C81.46”, “C81.47”, “C81.48”, “C81.49”, “C81.70”, “C81.71”, “C81.72”, “C81.73”, “C81.74”, “C81.75”, “C81.76”, “C81.77”, “C81.78”, “C81.79”, “C81.90”, “C81.91”, “C81.92”, “C81.93”, “C81.94”, “C81.95”, “C81.96”, “C81.97”, “C81.98”, “C81.99”, “C82.90”, “C82.91”, “C82.92”, “C82.93”, “C82.94”, “C82.95”, “C82.96”, “C82.97”, “C82.98”, “C82.99”, “C83.10”, “C83.11”, “C83.12”, “C83.13”, “C83.14”, “C83.15”, “C83.16”, “C83.17”, “C83.18”, “C83.19”, “C83.30”, “C83.31”, “C83.32”, “C83.33”, “C83.34”, “C83.35”, “C83.36”, “C83.37”, “C83.38”, “C83.39”, “C83.50”, “C83.51”, “C83.52”, “C83.53”, “C83.54”, “C83.55”, “C83.56”, “C83.57”, “C83.58”, “C83.59”, “C83.70”, “C83.71”, “C83.72”, “C83.73”, “C83.74”, “C83.75”, “C83.76”, “C83.77”, “C83.78”, “C83.79”, “C83.80”, “C83.81”, “C83.82”, “C83.83”, “C83.84”, “C83.85”, “C83.86”, “C83.87”, “C83.88”, “C83.89”, “C84.00”, “C84.01”, “C84.02”, “C84.03”, “C84.04”, “C84.05”, “C84.06”, “C84.07”, “C84.08”, “C84.09”, “C84.10”, “C84.11”, “C84.12”, “C84.13”, “C84.14”, “C84.15”, “C84.16”, “C84.17”, “C84.18”, “C84.19”, “C84.40”, “C84.41”, “C84.42”, “C84.43”, “C84.44”, “C84.45”, “C84.46”, “C84.47”, “C84.48”, “C84.49”, “C84.60”, “C84.61”, “C84.62”, “C84.63”, “C84.64”, “C84.65”, “C84.66”, “C84.67”, “C84.68”, “C84.69”, “C84.70”, “C84.71”, “C84.72”, “C84.73”, “C84.74”, “C84.75”, “C84.76”, “C84.77”, “C84.78”, “C84.79”, “C84.93”, “C85.80”, “C85.81”, “C85.82”, “C85.83”, “C85.84”, “C85.85”, “C85.86”, “C85.87”, “C85.88”, “C85.89”, “C88.8”, “C90.00”, “C90.01”, “C90.02”, “C90.10”, “C90.11”, “C90.12”, “C90.20”, “C90.21”, “C90.22”, “C90.30”, “C90.31”, “C90.32”, “C91.00”, “C91.01”, “C91.02”, “C91.10”, “C91.11”, “C91.12”, “C91.40”, “C91.41”, “C91.90”, “C91.91”, “C91.92”, “C91.Z0”, “C91.Z1”, “C91.Z2”,

	"C92.00", "C92.01", "C92.02", "C92.10", "C92.11", "C92.12", "C92.20", "C92.21", "C92.22", "C92.30", "C92.31", "C92.32", "C92.40", "C92.41", "C92.42", "C92.50", "C92.51", "C92.52", "C92.90", "C92.91", "C92.92", "C92.Z0", "C92.Z1", "C92.Z2", "C93.00", "C93.01", "C93.02", "C93.10", "C93.11", "C93.12", "C93.90", "C93.91", "C93.92", "C93.Z0", "C93.Z1", "C93.Z2", "C94.00", "C94.01", "C94.02", "C94.20", "C94.21", "C94.22", "C94.30", "C94.31", "C94.32", "C94.80", "C94.81", "C94.82", "C95.00", "C95.01", "C95.02", "C95.10", "C95.11", "C95.12", "C95.90", "C95.91", "C95.92", "C96.0", "C96.4", "C96.9", "C96.A", "C96.Z", "D03.0", "D03.10", "D03.11", "D03.12", "D03.20", "D03.21", "D03.22", "D03.30", "D03.39", "D03.4", "D03.51", "D03.52", "D03.59", "D03.60", "D03.61", "D03.62", "D03.70", "D03.71", "D03.72", "D03.8", "D03.9", "D45", "D03", "D03.1", "D03.2", "D03.3", "D03.5", "D03.6", "D03.7", "C43", "C43.1", "C43.11", "C43.12", "C43.2", "C43.21", "C43.22", "C43.3", "C43.5", "C43.51", "C43.52", "C43.6", "C43.61", "C43.62", "C43.7", "C43.71", "C43.72", "Z85.820" }
Allergic Rhinitis	1 Inpatient or 2 Outpatient (30 – 365 days apart) **Diagnosis Code (Any Position), ICD-9** is any of: { "477", "477.0", "477.1", "477.2", "477.8", "477.9" } **Diagnosis Code (Any Position), ICD-10** is any of: { "J30", "J30.1", "J30.2", "J30.5", "J30.8", "J30.81", "J30.89", "J30.9" }
Chronic Sinusitis	1 Inpatient or 2 Outpatient (30 – 365 days apart) **Diagnosis Code (Any Position), ICD-9** is any of: { "473", "473.0", "473.1", "473.2", "473.3", "473.8", "473.9" } **Diagnosis Code (Any Position), ICD-10** is any of: { "J32", "J32.0", "J32.1", "J32.2", "J32.3", "J32.4", "J32.8", "J32.9" }
Bronchiectasis	1 Inpatient or 2 Outpatient (30 – 365 days apart) **Diagnosis Code (Any Position), ICD-9** is any of: { "011.5", "011.50", "011.51", "011.52", "011.53", "011.54", "011.55", "011.56", "494", "494.0", "494.1", "748.61" } **Diagnosis Code (Any Position), ICD-10** is any of: { "J47.1", "J47.9", "Q33.4", "J47", "J47.0" }

Pneumonia	1 Inpatient or 2 Outpatient (30 – 365 days apart) **Diagnosis Code (Any Position), ICD-9** is any of: { “003.22”, “020.3”, “020.4”, “020.5”, “021.2”, “022.1”, “031.0”, “039.1”, “052.1”, “055.1”, “073.0”, “083.0”, “112.4”, “114.0”, “114.4”, “114.5”, “115.05”, “115.15”, “115.95”, “130.4”, “136.3”, “480.0”, “480.1”, “480.2”, “480.3”, “480.8”, “480.9”, “481”, “482”, “482.0”, “482.1”, “482.2”, “482.3”, “482.30”, “482.31”, “482.32”, “482.39”, “482.4”, “482.40”, “482.41”, “482.42”, “482.49”, “482.8”, “482.81”, “482.82”, “482.83”, “482.84”, “482.89”, “482.9”, “483”, “483.0”, “483.1”, “483.8”, “484”, “484.1”, “484.3”, “484.5”, “484.6”, “484.7”, “484.8”, “485”, “486”, “487”, “487.0”, “487.1”, “487.8”, “517.1” } **Diagnosis Code (Any Position), ICD-10** is any of: { “A01.03”, “A02.22”, “A20.2”, “A21.2”, “A22.1”, “A31.0”, “A37.01”, “A37.11”, “A37.91”, “A43.0”, “A49.2”, “B01.2”, “B05.2”, “B06.81”, “B25.0”, “B37.1”, “B38.0”, “B38.1”, “B38.2”, “B39.0”, “B39.1”, “B39.2”, “B44.0”, “B58.3”, “B59”, “B77.81”, “J09”, “J09.X”, “J09.X1”, “J09.X2”, “J09.X9”, “J10”, “J10.0”, “J10.00”, “J10.01”, “J10.08”, “J10.1”, “J10.8”, “J10.89”, “J11”, “J11.0”, “J11.00”, “J11.08”, “J11.8”, “J11.89”, “J12.0”, “J12.1”, “J12.2”, “J12.3”, “J12.81”, “J12.89”, “J12.9”, “J13”, “J14”, “J15.0”, “J15.1”, “J15.20”, “J15.211”, “J15.212”, “J15.29”, “J15.3”, “J15.4”, “J15.5”, “J15.6”, “J15.7”, “J15.8”, “J15.9”, “J16.0”, “J16.8”, “J17”, “J18.0”, “J18.1”, “J18.8”, “J18.9” }
Chronic Bronchitis	1 Inpatient or 2 Outpatient (30 – 365 days apart) **Diagnosis Code (Any Position), ICD-9** is any of: { “491”, “491.0”, “491.1”, “491.2”, “491.20”, “491.21”, “491.22”, “491.8”, “491.9” } **Diagnosis Code (Any Position), ICD-10** is any of: { “J41”, “J41.0”, “J41.1”, “J41.8”, “J42” }
Exertional Breathlessness	1 Inpatient or 2 Outpatient (30 – 365 days apart) **Diagnosis Code (Any Position), ICD-10** is any of: { “R06.0*” } **Diagnosis Code (Any Position), ICD-9** is any of: { “786.0” }

Anxiety	1 Inpatient or 2 Outpatient (30 – 365 days apart) **Diagnosis Code (Any Position), ICD-9** is any of: { “293.84”, “300.0”, “300.00”, “300.02”, “300.09”, “309.21”, “309.24”, “309.28”, “313.0” } **Diagnosis Code (Any Position), ICD-10** is any of: { “F06.4”, “F41.1”, “F41.8”, “F41.9”, “F43.22”, “F43.23”, “F93.0”, “F93.8”, "F40", "F40.8", "F40.9", "F41", "F41.0", "F41.3" }
Dementia	1 Inpatient or 2 Outpatient (30 – 365 days apart) **Diagnosis Code (Any Position), ICD-9** is any of: { “290.0”, “290.1”, “290.10”, “290.11”, “290.12”, “290.13”, “290.2”, “290.20”, “290.21”, “290.3”, “290.4”, “290.40”, “290.41”, “290.42”, “290.43”, “291.2”, “292.82”, “294.0”, “294.1”, “294.10”, “294.11”, “294.8”, “331.0”, “331.1”, “331.11”, “331.19”, “331.2”, “331.7”, “331.8”, “331.81”, “331.82”, “331.83”, “331.89”, “331.9”, “797” } **Diagnosis Code (Any Position), ICD-10** is any of: { “F01.50”, “F01.51”, “F02.80”, “F02.81”, “F03.90”, “F04”, “F05”, “F06.0”, “F06.8”, “F10.27”, “F19.97”, “G30.9”, “G31.01”, “G31.09”, “G31.1”, “G31.83”, “G31.84”, “G31.89”, “G31.9”, “G93.7”, “G94”, “R41.81”, "F32", "F32.8", "F33", "F33.8" } **Generic Name** is any of: { “DONEPEZIL HCL”, “GALANTAMINE HBR”, “RIVASTIGMINE”, “MEMANTINE HCL” }
Depression	1 Inpatient or 2 Outpatient (30 – 365 days apart) **Diagnosis Code (Any Position), ICD-9** is any of: { “296.2”, “296.20”, “296.21”, “296.22”, “296.23”, “296.24”, “296.25”, “296.26”, “296.3”, “296.30”, “296.31”, “296.32”, “296.33”, “296.34”, “296.35”, “296.36”, “298.0”, “300.4”, “309.0”, “309.1”, “309.28”, “311” } **Diagnosis Code (Any Position), ICD-10** is any of: { “F32.0”, “F32.1”, “F32.2”, “F32.3”, “F32.4”, “F32.5”, “F32.9”, “F33.0”, “F33.1”, “F33.2”, “F33.3”, “F33.41”, “F33.42”, “F33.9”, “F34.1”, “F43.21”, “F43.23” }
Osteoporosis	1 Inpatient or 2 Outpatient (30 – 365 days apart)

	Diagnosis Code (Any Position), ICD-9 is any of: { “733.0”, “733.00”, “733.01”, “733.02”, “733.03”, “733.09”, “733.1”, “733.10”, “733.11”, “733.12”, “733.13”, “733.14”, “733.15”, “733.16”, “733.19” } **Diagnosis Code (Any Position), ICD-10** is any of: { “M80”, “M80.0”, “M80.00”, “M80.00XA”, “M80.00XD”, “M80.00XG”, “M80.00XK”, “M80.00XP”, “M80.00XS”, “M80.01”, “M80.011”, “M80.011A”, “M80.011D”, “M80.011G”, “M80.011K”, “M80.011P”, “M80.011S”, “M80.012”, “M80.012A”, “M80.012D”, “M80.012G”, “M80.012K”, “M80.012P”, “M80.012S”, “M80.019”, “M80.019A”, “M80.019D”, “M80.019G”, “M80.019K”, “M80.019P”, “M80.019S”, “M80.02”, “M80.021”, “M80.021A”, “M80.021D”, “M80.021G”, “M80.021K”, “M80.021P”, “M80.021S”, “M80.022”, “M80.022A”, “M80.022D”, “M80.022G”, “M80.022K”, “M80.022P”, “M80.022S”, “M80.029”, “M80.029A”, “M80.029D”, “M80.029G”, “M80.029K”, “M80.029P”, “M80.029S”, “M80.03”, “M80.031”, “M80.031A”, “M80.031D”, “M80.031G”, “M80.031K”, “M80.031P”, “M80.031S”, “M80.032”, “M80.032A”, “M80.032D”, “M80.032G”, “M80.032K”, “M80.032P”, “M80.032S”, “M80.039”, “M80.039A”, “M80.039D”, “M80.039G”, “M80.039K”, “M80.039P”, “M80.039S”, “M80.04”, “M80.041”, “M80.041A”, “M80.041D”, “M80.041G”, “M80.041K”, “M80.041P”, “M80.041S”, “M80.042”, “M80.042A”, “M80.042D”, “M80.042G”, “M80.042K”, “M80.042P”, “M80.042S”, “M80.049”, “M80.049A”, “M80.049D”, “M80.049G”, “M80.049K”, “M80.049P”, “M80.049S”, “M80.05”, “M80.051”, “M80.051A”, “M80.051D”, “M80.051G”, “M80.051K”, “M80.051P”, “M80.051S”, “M80.052”, “M80.052A”, “M80.052D”, “M80.052G”, “M80.052K”, “M80.052P”, “M80.052S”, “M80.059”, “M80.059A”, “M80.059D”, “M80.059G”, “M80.059K”, “M80.059P”, “M80.059S”, “M80.06”, “M80.061”, “M80.061A”, “M80.061D”, “M80.061G”, “M80.061K”, “M80.061P”, “M80.061S”, “M80.062”, “M80.062A”, “M80.062D”, “M80.062G”, “M80.062K”, “M80.062P”, “M80.062S”, “M80.069”, “M80.069A”, “M80.069D”, “M80.069G”, “M80.069K”, “M80.069P”, “M80.069S”, “M80.07”, “M80.071”, “M80.071A”, “M80.071D”, “M80.071G”, “M80.071K”, “M80.071P”, “M80.071S”, “M80.072”, “M80.072A”, “M80.072D”, “M80.072G”, “M80.072K”, “M80.072P”, “M80.072S”, “M80.079”, “M80.079A”, “M80.079D”, “M80.079G”, “M80.079K”, “M80.079P”, “M80.079S”, “M80.08”, “M80.08XA”, “M80.08XD”, “M80.08XG”, “M80.08XK”, “M80.08XP”, “M80.08XS”, “M80.8”, “M80.80”, “M80.80XA”, “M80.80XD”, “M80.80XG”, “M80.80XK”, “M80.80XP”, “M80.80XS”, “M80.81”, “M80.811”, “M80.811A”, “M80.811D”, “M80.811G”, “M80.811K”, “M80.811P”, “M80.811S”, “M80.812”, “M80.812A”, “M80.812D”, “M80.812G”, “M80.812K”, “M80.812P”, “M80.812S”, “M80.819”, “M80.819A”, “M80.819D”, “M80.819G”, “M80.819K”, “M80.819P”, “M80.819S”, “M80.82”, “M80.821”, “M80.821A”, “M80.821D”, “M80.821G”, “M80.821K”, “M80.821P”, “M80.821S”, “M80.822”, “M80.822A”, “M80.822D”, “M80.822G”, “M80.822K”,

	“M80.822P”, “M80.822S”, “M80.829”, “M80.829A”, “M80.829D”, “M80.829G”, “M80.829K”, “M80.829P”, “M80.829S”, “M80.83”, “M80.831”, “M80.831A”, “M80.831D”, “M80.831G”, “M80.831K”, “M80.831P”, “M80.831S”, “M80.832”, “M80.832A”, “M80.832D”, “M80.832G”, “M80.832K”, “M80.832P”, “M80.832S”, “M80.839”, “M80.839A”, “M80.839D”, “M80.839G”, “M80.839K”, “M80.839P”, “M80.839S”, “M80.84”, “M80.841”, “M80.841A”, “M80.841D”, “M80.841G”, “M80.841K”, “M80.841P”, “M80.841S”, “M80.842”, “M80.842A”, “M80.842D”, “M80.842G”, “M80.842K”, “M80.842P”, “M80.842S”, “M80.849”, “M80.849A”, “M80.849D”, “M80.849G”, “M80.849K”, “M80.849P”, “M80.849S”, “M80.85”, “M80.851”, “M80.851A”, “M80.851D”, “M80.851G”, “M80.851K”, “M80.851P”, “M80.851S”, “M80.852”, “M80.852A”, “M80.852D”, “M80.852G”, “M80.852K”, “M80.852P”, “M80.852S”, “M80.859”, “M80.859A”, “M80.859D”, “M80.859G”, “M80.859K”, “M80.859P”, “M80.859S”, “M80.86”, “M80.861”, “M80.861A”, “M80.861D”, “M80.861G”, “M80.861K”, “M80.861P”, “M80.861S”, “M80.862”, “M80.862A”, “M80.862D”, “M80.862G”, “M80.862K”, “M80.862P”, “M80.862S”, “M80.869”, “M80.869A”, “M80.869D”, “M80.869G”, “M80.869K”, “M80.869P”, “M80.869S”, “M80.87”, “M80.871”, “M80.871A”, “M80.871D”, “M80.871G”, “M80.871K”, “M80.871P”, “M80.871S”, “M80.872”, “M80.872A”, “M80.872D”, “M80.872G”, “M80.872K”, “M80.872P”, “M80.872S”, “M80.879”, “M80.879A”, “M80.879D”, “M80.879G”, “M80.879K”, “M80.879P”, “M80.879S”, “M80.88”, “M80.88XA”, “M80.88XD”, “M80.88XG”, “M80.88XK”, “M80.88XP”, “M80.88XS”, “M81”, “M81.0”, “M81.6”, “M81.8” }

Charlson-Deyo Comorbidity Index	This measure computes a score by summing over the following components: · If the event Acute Myocardial Infarction Occurs within 180 days, set the score to 1.0 Otherwise, set the score to 0.0 · If the event Heart Failure Occurs within 180 days, set the score to 1.0 Otherwise, set the score to 0.0 · If the event Peripheral Vascular Disease Occurs within 180 days, set the score to 1.0 Otherwise, set the score to 0.0 · If the event Cerebrovascular Disease Occurs within 180 days, set the score to 1.0 Otherwise, set the score to 0.0 · If the event Dementia Occurs within 180 days, set the score to 1.0 Otherwise, set the score to 0.0 · If the event Chronic Obstructive Pulmonary Disease Occurs within 180 days, set the score to 1.0 Otherwise, set the score to 0.0 · If the event Rheumatologic Disease Occurs within 180 days, set the score to 1.0 Otherwise, set the score to 0.0 · If the event Peptic Ulcer Disease Occurs within 180 days, set the score to 1.0 Otherwise, set the score to 0.0 · If the event Hemiplegia or Paraplegia Occurs within 180 days, set the score to 2.0 Otherwise, set the score to 0.0 · If the event Renal Disease Occurs within 180 days, set the score to 2.0 Otherwise, set the score to 0.0 · If the event HIV/AIDS Occurs within 180 days, set the score to 6.0 Otherwise, set the score to 0.0 · For the measure Cancer use the value of the measure as the score multiplied by weight 1.0 If the value is missing, set the score to 0.0 · For the measure Diabetes use the value of the measure as the score multiplied by weight 1.0 If the value is missing, set the score to 0.0 · For the measure Liver Disease use the value of the measure as the score multiplied by weight 1.0 If the value is missing, set the score to 0.0
Acute Liver Injury or Failure	1 Inpatient or 1 Outpatient **Diagnosis Code (Any Position), ICD-9** is any of: { “570”, “864.0”, “864.00”, “864.01”, “864.02”, “864.03”, “864.04”, “864.05”, “864.09”, “864.1”, “864.10”, “864.11”, “864.12”, “864.13”, “864.14”, “864.15”, “864.19” } **Diagnosis Code (Any Position), ICD-10** is any of: { “K72.0”, “K72.00”, “K72.01”, “K72.9”, “K72.90”, “K72.91”, “S36.11”, “S36.112”, “S36.112A”, “S36.112D”, “S36.112S”, “S36.113”, “S36.113A”, “S36.113D”, “S36.113S”, “S36.114”, “S36.114A”, “S36.114D”, “S36.114S”, “S36.115”, “S36.115A”, “S36.115D”, “S36.115S”, “S36.116”, “S36.116A”, “S36.116D”, “S36.116S”, “S36.118”, “S36.118A”, “S36.118D”, “S36.118S”, “S36.119”, “S36.119A”, “S36.119D”, “S36.119S” }
Chronic Kidney	1 Inpatient or 2 Outpatient (30 – 365 days apart)

Disease (without ESRD)	**Diagnosis Code (Any Position), ICD-9** is any of: { “585.1”, “585.2”, “585.3”, “585.4” } **Diagnosis Code (Any Position), ICD-10** is any of: { “N18.1”, “N18.2”, “N18.3”, “N18.4” } **Procedure Code (Any Position), CPT and HCPC** is any of: { “G0420”, “G0421”, “G8487”, “G8771” }
End Stage Renal Disease	1 Inpatient or 2 Outpatient (30 – 365 days apart) **Diagnosis Code (Any Position), ICD-9** is any of: { “403.01”, “403.91”, “458.21”, “585.5”, “585.6”, “996.56”, “996.68”, “996.73”, “V42.0”, “V45.1”, “V45.11”, “V45.12”, “V56”, “V56.0”, “V56.1”, “V56.2”, “V56.3”, “V56.31”, “V56.32”, “V56.8” } **Diagnosis Code (Any Position), ICD-10** is any of: { “I12.0”, “N18.5”, “N18.6”, “T86.10”, “T86.11”, “T86.12”, “Z49.01”, “Z49.02”, “Z49.31”, “Z49.32”, “Z91.15”, “Z94.0”, “Z99.2” } **Procedure Code (Any Position),** ICD-9 is any of: { “55.69”, “55.6”, “38.95”, “39.27”, “39.42”, “39.43”, “39.95”, “54.98” } **Procedure Code (Any Position), ICD-10** is any of: { “05HY33Z”, “06HY33Z”, “0TS00ZZ”, “0TS10ZZ”, “0TY00Z0”, “0TY00Z1”, “0TY00Z2”, “0TY10Z0”, “0TY10Z1”, “0TY10Z2”, “3E1M39Z”, “5A1D00Z”, “5A1D60Z” } **Procedure Code (Any Position), CPT and HCPC** is any of: { “36145”, “36800”, “36810”, “36815”, “36825”, “36830”, “36831”, “36832”, “36833”, “50323”, “50325”, “50327”, “50328”, “50329”, “50340”, “50360”, “50365”, “90918”, “90919”, “90920”, “90921”, “90922”, “90923”, “90924”, “90925”, “90935”, “90937”, “90939”, “90940”, “90945”, “90947”, “90951”, “90952”, “90953”, “90954”, “90955”, “90956”, “90957”, “90958”, “90959”, “90960”, “90961”, “90962”, “90963”, “90964”, “90965”, “90966”, “90967”, “90968”, “90969”, “90970”, “90989”, “90993”, “90997”, “90999”, “93990”, “99512”, “A4653”, “A4656”, “A4657”, “A4670”, “A4671”, “A4672”, “A4673”, “A4674”, “A4680”, “A4706”, “A4707”, “A4708”, “A4709”, “A4712”, “A4714”, “A4719”, “A4720”, “A4721”, “A4722”, “A4723”, “A4724”, “A4725”, “A4726”, “A4728”, “A4730”, “A4736”, “A4737”, “A4740”, “A4750”, “A4755”, “A4760”, “A4765”, “A4766”, “A4770”, “A4771”, “A4773”, “A4774”, “A4802”, “A4860”, “A4870”, “A4890”, “A4911”, “A4913”, “A4918”, “A4928”, “A4929”, “C1881”, “E1500”, “E1520”, “E1530”, “E1540”, “E1550”, “E1560”, “E1570”, “E1575”, “E1580”, “E1600”, “E1610”, “E1615”, “E1620”, “E1625”, “E1634”,

	"E1635", "E1636", "E1637", "E1639", "E1699", "G0257", "G0308", "G0309", "G0310", "G0311", "G0312", "G0313", "G0314", "G0315", "G0316", "G0317", "G0318", "G0319", "G0320", "G0321", "G0323", "G0324", "G0325", "G0326", "G0327", "G8727", "G9013", "G9014", "J0635", "J0636", "S2065", "S9335", "S9339", "E1638", "G0322" }
Rheumatologic Disease	1 Inpatient or 2 Outpatient (30 – 365 days apart) **Diagnosis Code (Any Position), ICD-9** is any of: { "135", "183.0", "274.9", "275.49", "279.49", "443.0", "448.9", "530.5", "555.9", "571.42", "571.6", "576.1", "579.0", "696.0", "696.1", "710.0", "710.1", "710.2", "710.3", "710.9", "711.90", "712.19", "714.0", "714.30", "715.09", "715.11", "715.12", "715.13", "715.14", "715.15", "715.17", "715.18", "715.96", "719.42", "719.44", "719.45", "719.47", "719.49", "720.0", "721.90", "725", "729.1", "729.5", "795.79" } **Diagnosis Code (Any Position), ICD-10** is any of: { "D59.0", "D59.1", "D86.9", "D89.89", "E83.59", "I73.00", "I73.01", "I78.9", "K22.4", "K50.90", "K74.3", "K74.4", "K74.5", "K75.4", "K83.0", "K90.0", "L40.0", "L40.1", "L40.2", "L40.50", "L40.54", "L40.59", "L40.8", "M00.9", "M06.9", "M08.00", "M10.9", "M11.9", "M15.0", "M16.0", "M16.10", "M16.11", "M16.12", "M17.9", "M19.019", "M19.029", "M19.039", "M19.049", "M19.079", "M19.91", "M25.50", "M25.529", "M25.559", "M25.579", "M32.10", "M33.90", "M34.0", "M34.1", "M34.2", "M34.81", "M34.82", "M34.83", "M34.89", "M34.9", "M35.00", "M35.01", "M35.02", "M35.03", "M35.04", "M35.09", "M35.3", "M35.9", "M45.9", "M47.819", "M60.9", "M76.0", "M76.11", "M76.12", "M76.8", "M76.9", "M79", "M79.1", "M79.609", "M79.646" }

Peptic Ulcer Disease	1 Inpatient or 2 Outpatient (30 – 365 days apart) **Diagnosis Code (Any Position), ICD-9** is any of: { “531”, “531.0”, “531.00”, “531.01”, “531.1”, “531.10”, “531.11”, “531.2”, “531.20”, “531.21”, “531.3”, “531.30”, “531.31”, “531.4”, “531.40”, “531.41”, “531.5”, “531.50”, “531.51”, “531.6”, “531.60”, “531.61”, “531.7”, “531.70”, “531.71”, “531.9”, “531.90”, “531.91”, “532”, “532.0”, “532.00”, “532.01”, “532.1”, “532.10”, “532.11”, “532.2”, “532.20”, “532.21”, “532.3”, “532.30”, “532.31”, “532.4”, “532.40”, “532.41”, “532.5”, “532.50”, “532.51”, “532.6”, “532.60”, “532.61”, “532.7”, “532.70”, “532.71”, “532.9”, “532.90”, “532.91”, “533”, “533.0”, “533.00”, “533.01”, “533.1”, “533.10”, “533.11”, “533.2”, “533.20”, “533.21”, “533.3”, “533.30”, “533.31”, “533.4”, “533.40”, “533.41”, “533.5”, “533.50”, “533.51”, “533.6”, “533.60”, “533.61”, “533.7”, “533.70”, “533.71”, “533.9”, “533.90”, “533.91”, “534”, “534.0”, “534.00”, “534.01”, “534.1”, “534.10”, “534.11”, “534.2”, “534.20”, “534.21”, “534.3”, “534.30”, “534.31”, “534.4”, “534.40”, “534.41”, “534.5”, “534.50”, “534.51”, “534.6”, “534.60”, “534.61”, “534.7”, “534.70”, “534.71”, “534.9”, “534.90”, “534.91” } **Diagnosis Code (Any Position), ICD-10** is any of: { “K25.0”, “K25.1”, “K25.2”, “K25.3”, “K25.4”, “K25.5”, “K25.6”, “K25.7”, “K25.9”, “K26.0”, “K26.1”, “K26.2”, “K26.3”, “K26.4”, “K26.5”, “K26.6”, “K26.7”, “K26.9”, “K27.0”, “K27.1”, “K27.2”, “K27.3”, “K27.4”, “K27.5”, “K27.6”, “K27.7”, “K27.9”, “K28.0”, “K28.1”, “K28.2”, “K28.3”, “K28.4”, “K28.5”, “K28.6”, “K28.7”, “K28.9” }
Gastroesophageal Reflux Disease	Any of the following criteria: ≥2 medical claims with a primary or secondary ICD-9-CM code for reflux esophagitis (530.11), esophageal reflux (530.81) or heartburn (787.1) or primary or secondary ICD-10-CM code for GERD (K21, K21.0, K21.9) or Heartburn (R12); ≥1 medical claim with a primary or secondary ICD-9-CM 530.11, 530.81 or 787.1 and either (a) ≥1 pharmacy claim for a PPI (esomeprazole, lansoprazole, omeprazole, pantoprazole, rabeprazole), an H2RA (cimetidine, famotidine, nizatidine, or ranitidine) or “other” GERD agent (bethanechol, metoclopramide, sucralfate) or (b) ≥1 medical claim with a primary or secondary ICD-9-CM code for esophageal stricture (530.3) Barrett’s esophagus (530.85), esophageal ulcer (530.2x) or esophagitis (530.1x).
Type 1 Diabetes Mellitus	1 Inpatient or 2 Outpatient (30 – 365 days apart) **Diagnosis Code (Any Position), ICD-9** is any of: { “250.11”, “250.13”, “250.21”, “250.23”, “250.31”, “250.33”, “250.41”, “250.43”, “250.51”, “250.53”, “250.61”, “250.63”, “250.71”, “250.73”, “250.81”, “250.83”, “250.91”,

	"250.93", "250.01", "250.03" } **Diagnosis Code (Any Position), ICD-10** is any of: { "E10", "E10.1", "E10.10", "E10.11", "E10.2", "E10.21", "E10.22", "E10.29", "E10.3", "E10.31", "E10.311", "E10.319", "E10.32", "E10.321", "E10.329", "E10.33", "E10.331", "E10.339", "E10.34", "E10.341", "E10.349", "E10.35", "E10.351", "E10.359", "E10.36", "E10.39", "E10.4", "E10.40", "E10.41", "E10.42", "E10.43", "E10.44", "E10.49", "E10.5", "E10.51", "E10.52", "E10.59", "E10.6", "E10.61", "E10.610", "E10.618", "E10.62", "E10.620", "E10.621", "E10.622", "E10.628", "E10.63", "E10.630", "E10.638", "E10.64", "E10.641", "E10.649", "E10.65", "E10.69", "E10.8", "E10.9" }
Type 2 Diabetes Mellitus	1 Inpatient or 2 Outpatient (30 – 365 days apart) **Diagnosis Code (Any Position), ICD-9** is any of: { "250.00", "250.02", "250.10", "250.12", "250.20", "250.22", "250.30", "250.32", "250.40", "250.42", "250.50", "250.52", "250.60", "250.62", "250.70", "250.72", "250.80", "250.82", "250.90", "250.92" } **Diagnosis Code (Any Position), ICD-10** is any of: { "E11.00", "E11.01", "E11.21", "E11.29", "E11.311", "E11.319", "E11.36", "E11.39", "E11.40", "E11.51", "E11.618", "E11.620", "E11.621", "E11.622", "E11.628", "E11.630", "E11.638", "E11.641", "E11.649", "E11.65", "E11.69", "E11.8", "E11.9", "E13.10" }
Type 1 or Type 2 Diabetes without Complications	1 Inpatient or 2 Outpatient (30 – 365 days apart) **Diagnosis Code (Any Position), ICD-9** is any of: { "250.0", "250.00", "250.01", "250.02", "250.03", "250.1", "250.10", "250.11", "250.12", "250.13", "250.2", "250.20", "250.21", "250.22", "250.23", "250.3", "250.7", "250.70", "250.71", "250.72", "250.73", "249.0", "249.00", "249.01" } **Diagnosis Code (Any Position), ICD-10** is any of: { "E10.1", "E10.6", "E10.8", "E10.9", "E11.0", "E11.6", "E11.8", "E11.9", "E13.0", "E13.1", "E13.6", "E13.8", "E13.9" }

Type 1 or Type 2 Diabetes with Complications	1 Inpatient or 2 Outpatient (30 – 365 days apart) **Diagnosis Code (Any Position), ICD-9** is any of: { “250.4”, “250.40”, “250.41”, “250.42”, “250.43”, “250.5”, “250.50”, “250.51”, “250.52”, “250.53”, “250.6”, “250.60”, “250.61”, “250.62”, “250.63”, “250.3”, “250.30”, “250.31”, “250.32”, “250.33” } **Diagnosis Code (Any Position), ICD-10** is any of: { “E10.2”, “E10.21”, “E10.22”, “E10.29”, “E10.3”, “E10.31”, “E10.311”, “E10.319”, “E10.32”, “E10.321”, “E10.329”, “E10.33”, “E10.331”, “E10.339”, “E10.34”, “E10.341”, “E10.349”, “E10.35”, “E10.351”, “E10.359”, “E10.36”, “E10.39”, “E10.4”, “E10.40”, “E10.41”, “E10.42”, “E10.43”, “E10.44”, “E10.49”, “E10.5”, “E11.2”, “E11.21”, “E11.22”, “E11.29”, “E11.3”, “E11.31”, “E11.311”, “E11.319”, “E11.32”, “E11.321”, “E11.329”, “E11.33”, “E11.331”, “E11.339”, “E11.34”, “E11.341”, “E11.349”, “E11.35”, “E11.351”, “E11.359”, “E11.36”, “E11.39”, “E11.4”, “E11.40”, “E11.41”, “E11.42”, “E11.43”, “E11.44”, “E11.49”, “E11.5”, “E13.4”, “E13.40”, “E13.41”, “E13.42”, “E13.43”, “E13.44”, “E13.49”, “E13.5” }
Mild Liver Disease	1 Inpatient or 2 Outpatient (30 – 365 days apart) **Diagnosis Code (Any Position), ICD-9** is any of: { “571.2”, “571.4”, “571.40”, “571.41”, “571.42”, “571.49”, “571.5”, “571.6” } **Diagnosis Code (Any Position), ICD-10** is any of: { “B18.0”, “B18.1”, “B18.2”, “B18.8”, “B18.9”, “K70.0”, “K70.1”, “K70.10”, “K70.11”, “K70.2”, “K70.3”, “K70.9”, “K71.3”, “K71.4”, “K71.5”, “K71.7”, “K73.0”, “K73.1”, “K73.2”, “K73.8”, “K73.9”, “K74.0”, “K74.1”, “K74.2”, “K74.3”, “K74.4”, “K74.5”, “K74.6”, “K74.60”, “K74.69”, “K76.0”, “K76.2”, “K76.3”, “K76.4”, “K76.8”, “K76.9”, “Z94.4” }
Moderate/Severe Liver Disease	1 Inpatient or 2 Outpatient (30 – 365 days apart) **Diagnosis Code (Any Position), ICD-9** is any of: { “456.0”, “456.1”, “456.2”, “456.20”, “456.21”, “572.2”, “572.3”, “572.4”, “572.8” } **Diagnosis Code (Any Position), ICD-10** is any of: { “I85.0”, “I86.4”, “K70.4”, “K71.1”, “K72.1”, “K72.9”, “K76.5”, “K76.6”, “K76.7” }

Renal Disease	1 Inpatient or 2 Outpatient (30 – 365 days apart) **Diagnosis Code (Any Position), ICD-9** is any of: { “582”, “582.0”, “582.1”, “582.2”, “582.4”, “582.8”, “582.81”, “582.89”, “582.9”, “583”, “583.0”, “583.1”, “583.2”, “583.4”, “583.6”, “583.7”, “585”, “585.1”, “585.2”, “585.3”, “585.4”, “585.5”, “585.6”, “585.9”, “586”, “588”, “588.0”, “588.1”, “588.8”, “588.81”, “588.89”, “588.9” } **Diagnosis Code (Any Position), ICD-10** is any of: { “I12.0”, “I13.1”, “N03.2”, “N03.3”, “N03.4”, “N03.5”, “N03.6”, “N03.7”, “N05.2”, “N05.3”, “N05.4”, “N05.5”, “N05.6”, “N05.7”, “N18.1”, “N18.2”, “N18.3”, “N18.4”, “N18.5”, “N18.6”, “N18.9”, “N25.0”, “Z49.0”, “Z49.01”, “Z49.02”, “Z94.0”, “Z99.2” }
Metastatic Solid Tumors	1 Inpatient or 2 Outpatient (30 – 365 days apart) **Diagnosis Code (Any Position), ICD-9** is any of: { “196”, “196.0”, “196.1”, “196.2”, “196.3”, “196.5”, “196.6”, “196.8”, “196.9”, “197”, “197.0”, “197.1”, “197.2”, “197.3”, “197.4”, “197.5”, “197.6”, “197.7”, “197.8”, “198”, “198.0”, “198.1”, “198.2”, “198.3”, “198.4”, “198.5”, “198.6”, “198.7”, “198.8”, “198.81”, “198.82”, “198.89”, “199”, “199.0”, “199.1” } **Diagnosis Code (Any Position), ICD-10** is any of: { “C77.0”, “C77.1”, “C77.2”, “C77.3”, “C77.4”, “C77.5”, “C77.8”, “C77.9”, “C78”, “C78.0”, “C78.00”, “C78.01”, “C78.02”, “C78.1”, “C78.2”, “C78.3”, “C78.30”, “C78.39”, “C78.4”, “C78.5”, “C78.6”, “C78.7”, “C78.8”, “C78.80”, “C78.89”, “C79”, “C79.0”, “C79.00”, “C79.01”, “C79.02”, “C79.1”, “C79.10”, “C79.11”, “C79.19”, “C79.2”, “C79.3”, “C79.31”, “C79.32”, “C79.4”, “C79.40”, “C79.49”, “C79.5”, “C79.51”, “C79.52”, “C79.6”, “C79.60”, “C79.61”, “C79.62”, “C79.7”, “C79.70”, “C79.71”, “C79.72”, “C79.8”, “C79.81”, “C79.82”, “C79.89”, “C79.9”, “C80”, “C80.0”, “C80.1”, “C80.2” }
HIV/AIDS	1 Inpatient or 2 Outpatient (30 – 365 days apart) **Diagnosis Code (Any Position), ICD-9** is any of: { “042”, “795.71”, “V08”, “V65.44”, “079.53” } **Diagnosis Code (Any Position), ICD-10** is any of: { “B20”, “Z21”, “B97.35”, “O98.7*”, “Z71.7” }
Hemiplegia or Paraplegia	1 Inpatient or 2 Outpatient (30 – 365 days apart) **Diagnosis Code (Any Position), ICD-9** is any of: { “342”, “342.0”, “342.00”, “342.01”, “342.02”, “342.1”, “342.10”,

	"342.11", "342.12", "342.8", "342.80", "342.81", "342.82", "342.9", "342.90", "342.91", "342.92", "344.1" } **Diagnosis Code (Any Position), ICD-10** is any of: { "G81.00", "G81.01", "G81.02", "G81.03", "G81.04", "G81.10", "G81.11", "G81.12", "G81.13", "G81.14", "G81.90", "G81.91", "G81.92", "G81.93", "G81.94", "G82.20", "G81", "G81.9", "I69.05", "I69.051", "I69.052", "I69.053", "I69.054", "I69.059", "I69.15", "I69.151", "I69.152", "I69.153", "I69.154", "I69.159", "I69.25", "I69.251", "I69.252", "I69.253", "I69.254", "I69.259", "I69.35", "I69.351", "I69.352", "I69.353", "I69.354", "I69.359", "I69.85", "I69.851", "I69.852", "I69.853", "I69.854", "I69.859", "I69.95", "I69.951", "I69.952", "I69.953", "I69.954", "I69.959", "G81.0", "G81.1", "G82.2", "G82", "G82.21", "G82.22", "G04.1", "G11.4" }
Lifestyle	
Smoking-related claim	1 Inpatient or 1 Outpatient **Diagnosis Code (Any Position), ICD-9** is any of: { "305.1", "V15.82, "989.84", "649.0x" } **Diagnosis Code (Any Position), ICD-10** is any of: { "F17.2", "T65.2", "Z71.6", "O99.33", "O99.330", "O99.331", "O99.332", "O99.333", "O99.334", "O99.335", "Z72.0", "Z81.2" } **Procedure Code (Any Position), CPT and HCPC** is any of: { "99406", "99407", "G0436", "G0437", "G9016", "S9453", "S4995", "G9276", "G9458", "1034F", "4004F", "4001F"}
Vaccination for Influenza/Pneumococcus	1 Inpatient Service or 1 Outpatient **Procedure Code (Position 1), CPT and HCPC** is any of: { "4040F", "90630", "90653", "90654", "90655", "90656", "90657", "90658", "90659", "90660", "90661", "90662", "90663", "90664", "90665", "90666", "90667", "90668", "90669", "90670", "90672", "90673", "90685", "90686", "90687", "90688", "90732", "G0008", "G0009", "G0919", "G8108", "G8115", "G8864", "G9279", "Q0034", "Q2033", "Q2034", "Q2035", "Q2036", "Q2037", "Q2038", "Q2039", "S0195" }

Respiratory Function Procedures/Tests	
Pulmonary function tests	1 Inpatient or 1 Outpatient **Procedure Code (Any Position), CPT and HCPC** is any of: { “3038F”, “94010”, “94014”, “94015”, “94060”, “94621”, “94720”, “94725”, “94726”, “94727”, “94728”, “94729”, “94750”, “94770”, “94799” } **Procedure Code (Any Position), ICD-9** is any of: { “89.37” } **Procedure Code (Any Position), ICD-10** is any of: { “4A0971Z”, “4A0981Z”, “4A09X1Z”, “4A1971Z”, “4A19X1Z” }
Six-minute walk test	1 Inpatient or 1 Outpatient **Legacy Attribute - Procedure Code (Any Position)** is any of: { “94620” }
Chest X-ray	1 Inpatient or 1 Outpatient **Procedure Code (Any Position), CPT and HCPC** is any of: { “71010”, “71020”, “71021”, “71022”, “71023”, “71030”, “71034”, “71035” }
High Resolution Chest CT	1 Inpatient or 1 Outpatient **Procedure Code (Any Position), CPT and HCPC** is any of: { “71250”, “71270” }

ANNEX 5. TABLE SHELLS AND PROPOSED FIGURES

Table 1. Cohort Selection

	Excluded	Remaining
Eligible Population		
Did not meet cohort entry criteria (use of Tio/Olo or Umec/Vi)		
< 180 days of continuous enrollment		
Prior use of Umec/Vi during 180d washout		
Prior use of Tio/Olo during 180d washout		
Tio/Olo and Umec/Vi both occurring on cohort entry date		
Age <40 years		
No prior diagnosis of COPD any time prior using all available data		
Diagnosis of Asthma any time prior using all available data		
Diagnosis of Lung Cancer any time prior using all available data		
Lung Transplant any time prior using all available data		
Final cohort		

Table 2. Patient Characteristics of the Study Population (Unmatched/ Matched)

	Tio/Olo	Umec/Vi	Standardized Difference (95% CI)
N			
Median Follow-up Time [IQR]			
Demographics			
Age on index date			
Mean (SD)			
Median [IQR]			
Gender			
Male; n (%)			
Female; n (%)			
Region			
Northeast; n (%)			
North Central; n (%)			
South; n (%)			
West; n (%)			
Missing/Unknown; n (%)			
Insurance Type			
Commercial; n (%)			
Medicare; n (%)			
Missing; n (%)			
Year of Cohort Entry, n (%)			
First Year (November 17, 2015 – November 30, 2016); n (%)			
Second Year (December 1, 2016 – November 30, 2017); n (%)			
Third Year (December 1, 2017 to March 31, 2018)			
Concomitant Medications			

	Tio/Olo	Umec/Vi	Standardized Difference (95% CI)
Oral Corticosteroids; n (%)			
Short acting muscarinic antagonist (SAMA), n (%)			
Short acting beta agonist (SABA), n (%)			
Long acting muscarinic antagonist (LAMA), n (%)			
Long acting beta agonist (LABA), n (%)			
Inhaled corticosteroid (ICS), n (%)			
LAMA / LABA combination (not Tio/Olo or Umec/Vi), n (%)			
LABA / ICS combination, n (%)			
LAMA / LABA / ICS combination, n (%)			
NSAIDs, n (%)			
Antihistamines, n (%)			
Opioids, n (%)			
Oral antibiotics, n (%)			
Antidiabetic Agents (not including insulin), n (%)			
Insulin (basal or mealtime), n (%)			
Methotrexate, n (%)			
Statins; n (%)			
Antihypertensives; n (%)			
Anticoagulants; n (%)			
Anti-psychotic/anti-depressives/anxiolytic, n (%)			
Oxygen therapy, n (%)			
Comorbidities/Symptoms			
History of All-Cause Hospitalization; n (%)			
History of Emergency Department Visit; n (%)			
History of Hospitalization due to Respiratory Condition; n (%)			
Acute Myocardial Infarction; n (%)			
Angina Pectoris; n (%)			
Peripheral Vascular Disease; n (%)			

	Tio/Olo	Umec/Vi	Standardized Difference (95% CI)
Heart Failure; n (%)			
Hypertension; n (%)			
Upper Respiratory Tract Infection; n (%)			
Lower Respiratory Tract Infection; n (%)			
Cardiac Arrhythmias; n (%)			
Cerebrovascular Disease; n (%)			
All Cancers (except non-melanoma skin cancer); n (%)			
Allergic Rhinitis; n (%)			
Chronic Sinusitis; n (%)			
Bronchietasis; n (%)			
Pneumonia; n (%)			
Chronic Bronchitis; n (%)			
Exertional Breathlessness; n (%)			
Anxiety; n (%)			
Dementia; n (%)			
Depression; n (%)			
Osteoporosis; n (%)			
Charlson-Deyo Comorbidity Index, continuous			
mean (sd)			
median [IQR]			
Charlson-Deyo Comorbidity Index, categorical			
0; n (%)			
1; n (%)			
2; n (%)			
3+; n (%)			
Acute Liver Injury or Failure; n (%)			
Chronic Kidney Disease (without ESRD); n (%)			
End Stage Renal Disease; n (%)			
Rheumatologic Disease; n (%)			

	Tio/Olo	Umec/Vi	Standardized Difference (95% CI)
Peptic Ulcer Disease; n (%)			
Gastroesophageal reflux disease (GERD); n (%)			
Type 1 Diabetes Mellitus; n (%)			
Type 2 Diabetes Mellitus; n (%)			
Type 1 or Type 2 Diabetes with no chronic complications; n (%)			
Type 1 or Type 2 Diabetes with chronic complications; n (%)			
Mild Liver Disease; n (%)			
Moderate to Severe Liver Disease; n (%)			
Renal Disease; n (%)			
Metastatic Solid Tumor; n (%)			
HIV/AIDS; n (%)			
Hemiplegia or Paraplegia; n (%)			
Lifestyle			
Smoking Related Claim or Intervention; n (%)			
Vaccination for Influenza; n (%)			
Vaccination for Pneumococcus; n (%)			
Respiratory Function Procedures/Tests			
Pulmonary function tests; n (%)			
Six-minute walk test; n (%)			
Chest X-ray; n (%)			
Chest HRCT; n (%)			

Tio/Olo, tiotropium/olodaterol; Umec/Vi, umeclidinium, vilanterol.

Table 3. Absolute Standardized Differences as Measured in the Unmatched vs. Matched Cohorts

	Abs. Std. Diff. (Unmatched)	Abs. Std. Diff. (Matched)	Change	Change (%)
Demographics				
Age on index date				
Gender				
Region				
Insurance Type				
Year of Cohort Entry				
Oral Corticosteroids; n (%)				
Short acting muscarinic antagonist (SAMA), n (%)				
Short acting beta agonist (SABA), n (%)				
Long acting muscarinic antagonist (LAMA), n (%)				
Long acting beta agonist (LABA), n (%)				
Inhaled corticosteroid (ICS), n (%)				
LAMA / LABA combination (not Tio/Olo or Umec/Vi), n (%)				
LABA / ICS combination, n (%)				
LAMA / LABA / ICS combination, n (%)				
NSAIDs, n (%)				
Antihistamines, n (%)				
Opioids, n (%)				
Oral antibiotics, n (%)				
Antidiabetic Agents (not including insulin), n (%)				
Insulin (basal or mealtime), n (%)				
Methotrexate, n (%)				
Statins; n (%)				
Antihypertensives; n (%)				
Anticoagulants; n (%)				

	Abs. Std. Diff. (Unmatched)	Abs. Std. Diff. (Matched)	Change	Change (%)
Anti-psychotic/anti-depressives/anxiolytic, n (%)				
Oxygen therapy, n (%)				
Comorbidities/Symptoms				
History of All-Cause Hospitalization; n (%)				
History of Emergency Department Visit; n (%)				
History of Hospitalization due to Respiratory Condition; n (%)				
Acute Myocardial Infarction; n (%)				
Angina Pectoris; n (%)				
Peripheral Vascular Disease; n (%)				
Heart Failure; n (%)				
Hypertension; n (%)				
Upper Respiratory Tract Infection; n (%)				
Lower Respiratory Tract Infection; n (%)				
Cardiac Arrhythmias; n (%)				
Cerebrovascular Disease; n (%)				
All Cancers (except non-melanoma skin cancer); n (%)				
Allergic Rhinitis; n (%)				
Chronic Sinusitis; n (%)				
Bronchietasis; n (%)				
Pneumonia; n (%)				
Chronic Bronchitis; n (%)				
Exertional Breathlessness; n (%)				
Anxiety; n (%)				
Dementia; n (%)				
Depression; n (%)				
Osteoporosis; n (%)				

	Abs. Std. Diff. (Unmatched)	Abs. Std. Diff. (Matched)	Change	Change (%)
Charlson-Deyo Comorbidity Index, continuous				
Charlson-Deyo Comorbidity Index, categorical				
Acute Liver Injury or Failure; n (%)				
Chronic Kidney Disease (without ESRD); n (%)				
End Stage Renal Disease; n (%)				
Rheumatologic Disease; n (%)				
Peptic Ulcer Disease; n (%)				
Gastroesophageal reflux disease (GERD); n (%)				
Type 1 Diabetes Mellitus; n (%)				
Type 2 Diabetes Mellitus; n (%)				
Type 1 or Type 2 Diabetes with no chronic complications; n (%)				
Type 1 or Type 2 Diabetes with chronic complications; n (%)				
Mild Liver Disease; n (%)				
Moderate to Severe Liver Disease; n (%)				
Renal Disease; n (%)				
Metastatic Solid Tumor; n (%)				
HIV/AIDS; n (%)				
Hemiplegia or Paraplegia; n (%)				
Vaccination for Influenza / Pneumococcus; n (%)				
Respiratory Function Procedures/Tests				
Pulmonary function tests; n (%)				
Six-minute walk test; n (%)				
Chest X-ray; n (%)				
Chest HRCT; n (%)				

Tio/Olo, tiotropium/olodaterol; Umec/Vi, umeclidinium, vilanterol.

Table 4. Unmatched Cohort Discontinuation Rates and Risks for Tio/Olo vs. Umec/Vi.

Parameter	**Tio/Olo**	**Umec/Vi**
Number of patients		
Number of person-years		
Number of events (discontinuations)		
Rate		
Rate per 1,000 person-years		
Rate Difference per 1,000 person-years (95% CI)		1.0 (Reference)
Rate Ratio (95% CI)		1.0 (Reference)
Risk		
Risk per 1,000 patients		
Risk Difference per 1,000 person-years (95% CI)		1.0 (Reference)
Risk Ratio (95% CI)		1.0 (Reference)
Primary Estimates		
Unadjusted Hazard Ratio (95% CI)		1.0 (Reference)
Fully adjusted Hazard Ratio (95% CI)		1.0 (Reference)

Tio/Olo, tiotropium/olodaterol; Umec/Vi, umeclidinium, vilanterol.

Table 5. 1:2 Matched Cohort Discontinuation Risk for Tio/Olo vs. Umec/Vi.

Parameter	**Tio/Olo**	**Umec/Vi**
Number of patients		
Number of person-years		
Number of events (discontinuations)		
Rate		
Rate per 1,000 person-years		
Rate Difference per 1,000 person-years (95% CI)		1.0 (Reference)
Rate Ratio (95% CI)		1.0 (Reference)
Risk		
Risk per 1,000 patients		
Risk Difference per 1,000 person-years (95% CI)		1.0 (Reference)
Risk Ratio (95% CI)		1.0 (Reference)
Primary Estimates		
Matched Hazard Ratio (95% CI)		1.0 (Reference)

Tio/Olo, tiotropium/olodaterol; Umec/Vi, umeclidinium, vilanterol.

APPROVAL / SIGNATURE PAGE

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