Real-world effectiveness of extra-fine Ciclesonide (Alvesco®) versus standard particle inhaled corticosteroid (ICS): effectiveness analysis comparing Ciclesonide, an extra-fine ICS, with other commonly prescribed standard particle ICS therapies in patients from the Netherlands, using the PHARMO database.

Research in Real Life UK Ltd
5 Coles Lane, Oakington, Cambridge, CB24 3BA

Research in Real-Life Pte. Ltd
16 Raffles Quay, #33-03 Hong Leong Building,
Singapore 048581

Phone (+44) 01223 967 874
Fax (+44) 0808 2800 792
E-mail cristiana@rirl.org
Website http://www.rirl.org

Contents

1. FINAL PROTOCOL

1.1 BACKGROUND

Asthma management guidelines recommend long-term, daily anti-inflammatory controller therapy, such as inhaled corticosteroids (ICS), to attenuate chronic airway inflammation in persistent asthma. [i, ii, iii]

Traditional inhaler devices generate particles with a median mass aerodynamic diameter of 2–4 μm. [iv] However, newer pressurized metered dose inhalers (pMDI) have recently been developed that generate an aerosol of smaller particles with a median mass aerodynamic diameter of approximately 1 μm.[iv]

Randomised Controlled Trials (RCT) have shown similar efficacy between extra-fine and standard particles ICS, but extra-fine particles seem to afford a more even lung distribution compared with the larger ones, allowing a more efficient penetration into the distal lung. [iv,v]

Although RCT data are considered the gold standard, due to tightly-controlled inclusion criteria for the selection of study subjects, patients recruited to asthma trials are estimated to represent only a small percentage of the real-world asthma population. [vi,vii,viii] There is, therefore, a need to carry out real-world observational studies to assess the hypothesis that extra-fine ICS are non-inferior to other commonly prescribed ICS therapies in real world clinical practice.

This hypothesis is supported by historic database studies of hydrofluoroalkane beclometasone dipropionate (HFA-BDP) versus fluticasone propionate (FP) using the UK's General Practice Research Database (GPRD) and the USA Ingenix Normative Healthcare Database. [ix,x] These studies showed that extra-fine (EF) HFA-BDP patients achieved equal, or better, asthma outcomes than FP patients (matched on baseline disease severity and demography), but at significantly lower prescribed ICS doses.

1.2 OBJECTIVES

The aim of this study is to evaluate the effectiveness of Ciclesonide, an extra-fine (EF) ICS, compared to standard particle (SP) ICS therapies. This will be carried out in patients receiving asthma therapy in the Netherlands, using the PHARMO database (www.pharmo.nl). Patients will be characterised at baseline (one year) and analysed for treatment effectiveness (in terms of asthma control) over a one-year outcome period.

We will investigate the effects of starting a therapy with either Ciclesonide or SP- ICS (initiation cohort). The effects of increasing doses (≥50%) as either Ciclesonide or SP-ICS may also be evaluated as a separate cohort (step-up cohort), but a decision on whether analysing this cohort or not will be made based on review of the results and strength of signal observed for the initiation cohort.

1.3 DATA SOURCE

The analysis will be carried out using datasets available from the PHARMO Institute (Utrecht, The Netherlands), an independent scientific research organisation funded in 1999 and dedicated to the study of epidemiology, drug utilisation, drug safety, health outcomes, and utilisation of healthcare resources.

The primary database to be used for the proposed analysis is the Pharmacy database, which includes the dispensing records of more than 200 community pharmacies in more than 50 regions throughout the Netherlands and is representative for the Dutch population .[xi]

All patients in the Pharmacy database have data linked with the Hospital database, which include detailed information about admission and discharge dates, primary and secondary discharge diagnoses, diagnostic, surgical and treatment procedures, consultations with medical specialists and length of stay. This database does not include emergency department data, however information on prescriptions related to emergency department attendance are likely to be captured by pharmacy data.

A subgroup of patients also have:
(1) Data linked with the General Practitioner (GP) database (i.e. pharmacy data supplemented by diagnostic data and consultation data, available for approximately 5% of the patients).
(2) Data linked with the Clinical Laboratory Database, which provides spirometry test results (i.e. pharmacy data supplemented by lung function data, available for approximately 30% of the patients).
(3) Data linked to both GP and Clinical Laboratory Databases (i.e. pharmacy data supplemented by both diagnostic and lung function data).

Conditional on data availability within our dataset, a sub-analysis on these subgroups will possibly be conducted as a sensitivity analysis to validate the pharmacy data.

1.4 STUDY DESIGN

This study will be a retrospective, matched cohort effectiveness study consisting of a one-year baseline period, a one-year outcome period and a prescription date.

Prescription date is defined as the date at which asthma patients either:

(i) initiated therapy as (Initiation Cohort):
- Cilcesonide (pMDI), OR
- Standard particle ICS (defined as FP (pMDI) or non-EF BDP (pMDI)).

(ii) increased their baseline ICS therapy (which can be any ICS therapy) by ≥50% as (Step-up Cohort):
- Cilclesonide (pMDI), OR
- Standard particles ICS (defined as FP (pMDI) or non-EF BDP (pMDI)).

We will examine the initiation cohort first and the step-up cohort will be suspended until we review the results for the initiation cohort.

The baseline period is a minimum of one year before and including the prescription date[1] and will be used for confounder definition and patient characterization.

The outcome period is one year following the prescription date and will be used to evaluate the consequences of initiating (or increasing dose of) ICS therapy as Ciclesonide versus SP-ICS (including FP and non-EF BDP). Any change in therapy[2] at any time in the outcome period after prescription date will be considered as a proxy for therapy failure.

Study design is summarised in Figure 1.

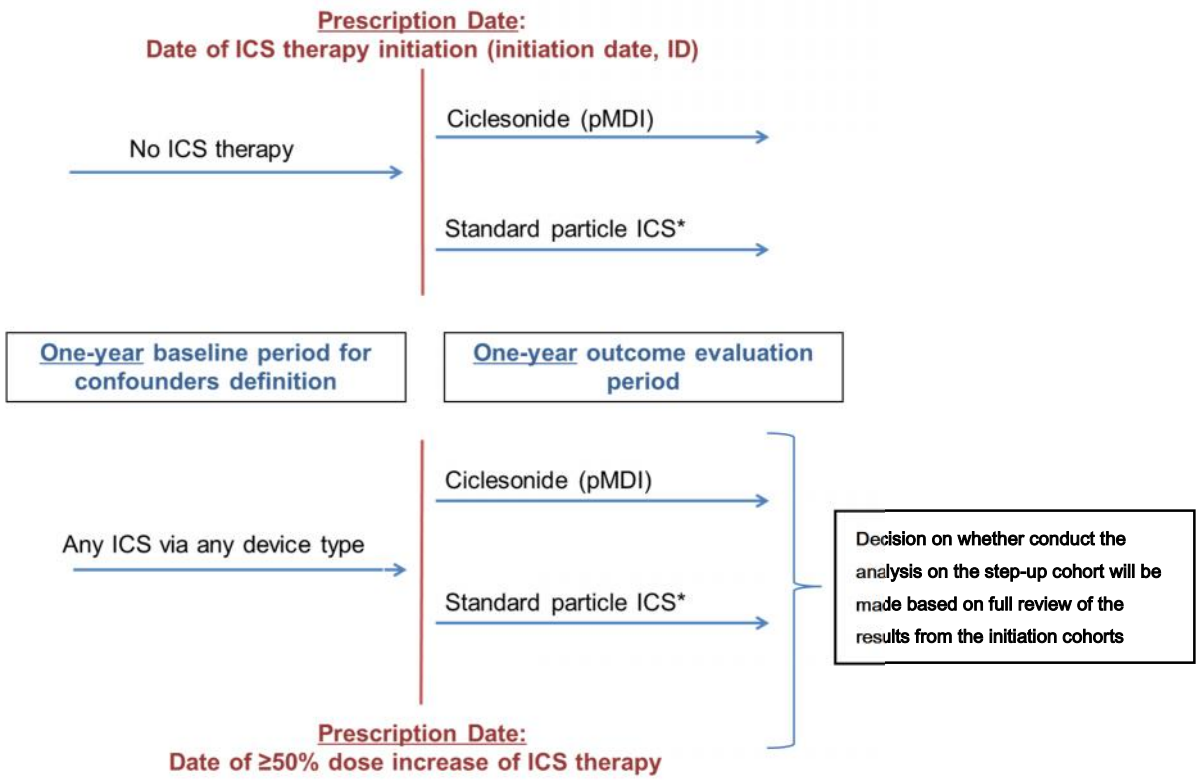

Fig 1. Study design showing baseline and outcome periods. *FP (pMDI) and non-EF BDP (pMDI)

[1] Except for therapy prescribed at prescription date (which is included in the outcome).

[2] Defined as:

- Addition of new therapy, including Leukotriene antagonists (LTRA), Theophyllines or long-acting β2-agonists (LABA) (this may be an add-on or switch, but most likely an add-on) OR,
- Patients who increased their ICS therapy by ≥50 %.

1.5 STUDY PERIOD

The study period will run from September 2005 to the end of December 2012. Patients included in the analysis will have at least one-year data prior to, and post, prescription date (i.e. date of ICS initiation or increase). Thus, prescription date can be at any time between September 2006 and December 2011. A one-year period is estimated to be necessary to identify any measurable change in outcomes such as hospitalisations, and also allows for seasonal changes in respiratory disease and its related conditions.

1.6 STUDY POPULATION

1.6.1 Inclusion criteria

In order to be included in the analysis patients must meet the following inclusion criteria:

- Aged 12-60 years.
- Evidence of asthma:[3]
    - Received ≥2 prescriptions for asthma in their records at any time (asthma therapies are reported in Appendix 1)
- Be receiving current ICS therapy as part of their asthma therapy:
    - ICS prescribed at index date and
    - ≥1 ICS (either Ciclesonide or FP/non-EF BDP pMDI) prescription during the outcome period (not including prescription date)
    - ≥1 ICS (any ICS) prescription during the baseline period (step-up cohort only)[4]
- Have at least one full year of baseline data (prior to the prescription date) and at least one full year of outcome data (following the prescription date).

1.6.2 Exclusion criteria

Patients will be excluded from the analysis if they:

- Have evidence (through prescriptions and/or diagnosis when available) of any chronic respiratory disease at any time other than asthma (diagnostic codes are reported in Appendix 2).
- Are potential COPD patients, i.e. have been prescribed long acting muscarinic antagonists (LAMA) during baseline period and are aged >60 years.
- Are on maintenance oral steroid therapy during baseline, defined as:
    - No evidence of reducing doses instructions, with a prescribed daily dose of <10mg of Prednisolone OR
    - Prescriptions for prednisolone tablets at a strength of 1 mg per day

  With overall script coverage of more than 25% of days in a year.
- Step-up at prescription date with additional therapies to what they had in baseline or have been prescribed multiple ICS therapies at prescription date.

[3] Confirmed by diagnosis where available.

[4] This results in the step-up cohort having 3+ prescriptions for asthma in their records. These patients will possibly be examined in a later phase of the study. Decision will be taken once initiation cohort results have been reviewed.

1.7 OUTCOMES

During the one-year outcome period, the following variables will be compared:

1.7.1 Co-primary endpoints

(i) Number of asthma-related severe exacerbations in the outcome period (Severe Exacerbation Rate), whereby exacerbation is defined based on the American Thoracic Society / European Respiratory Society (ATS/ERS) task force definition:

- Asthma related hospital admissions[5] OR
- Use of acute oral steroid[6].

(ii) Risk domain asthma control during the outcome period, defined as (modified definition)[7] absence of asthma-related:

- Hospital attendance/admission; AND
- Prescriptions for acute courses of oral steroids.

(iii) Overall asthma control[5], defined as (modified definition)[7]:

- Risk domain asthma control AND
- Average daily dose of ≤200mcg salbutamol / ≤500mcg terbutaline.

1.7.2 Secondary outcomes

(i) Change in therapy at any time during outcome period, defined as:
- Addition of new therapy, including Leukotriene antagonists (LTRA), Theophyllines (THEO) or long-acting β2-agonists (LABA) (this may be an add-on or switch, but most likely an add-on) OR,
- Patients who increased their ICS therapy by ≥50%.

(ii) Average daily short-acting β2-agonists (SABA) usage during outcome year, calculated as average number of puffs per day over the year multiplied by strength.

1.7.3 Exploratory outcomes

(iii) Oral thrush: number and percentage of patients who either received a diagnosis of oral candidiasis in their hospital records or received 1 or more topical oral anti-fungal prescriptions.

(iv) Hospitalisations coded with a lower respiratory code, including asthma and LRTI codes.

[5] Asthma-related includes any hospital entry for asthma plus any lower respiratory reason (including lower respiratory tract infections).

[6] Defined as all courses that are definitely not maintenance therapy, whereby "maintenance therapy" is defined as no evidence of reducing doses instructions, with a prescribed daily dose of <10mg of Prednisolone OR prescriptions for prednisolone tablets at a strength of 1 mg per day, with overall script coverage of more than 25% of days in a year.

[7] Both 'risk domain asthma control' and 'overall asthma control' definitions do not include emergency department data and the criteria of "absence of evidence of GP consultations for LRTI" due to PHARMO database not providing this information and/or insufficient linked GP data in PHARMO database. Similarly, emergency department data are not included in the exacerbation definition but emergency department events are likely captured by acute oral steroid use.

1.7.4. Explanatory outcome

(i) Controller-to-reliever[8] ratio, calculated as the number of controller units divided by the total number of controller and reliever units.

1.8 STATISTICAL ANALYSIS

1.8.1 Baseline characterization

The treatment groups will be characterised according to their:

- Age at prescription date
- Sex
- Year of prescription date (exact year)
- Maintenance asthma therapy prior to prescription date (please see appendix 1)
- Baseline use of co-medications known to interfere with asthma control (presence of prescriptions for acetaminophen, NSAIDs, beta blockers)
- Disease control in the year prior to the prescription date
    - Number of asthma-related exacerbations
    - Overall and Risk Domain asthma control
    - Prescriptions for acute oral steroids
    - Number of hospital admissions
    - Reliever medication usage
- Evidence of co-morbidities (diagnosis, when available and/or prescriptions for specific co-morbidities, including rhinitis, eczema, GERD, cardiac disease and hypertension).

1.8.2 Summary statistics

Summary statistics will be produced for all baseline variables and outcome variables, as a complete dataset and by treatment groups.

For variables measured on the interval or ratio scale, these will include:

- Sample size (n)
- Percentage non-missing
- Mean
- Standard Deviation
- Median
- Inter-quartile Range (25th and 75th percentiles and 10th and 90th if sample size is large)

For categorical variables, the summary statistics will include:

- Sample size (n)

[8] Controllers include ICS (including fixed combination ICS/LABA) and LTRA. For ICS a unit is taken to be one inhaler; for LTRA a unit is one prescription. Relievers include SABA, with a unit taken to be one inhaler.

- Percentage non-missing
- Count and Percentage by category (distribution).

Treatment groups will be compared using Mann Whitney U-test for variables measured on the interval/ratio scale and using a chi-square test for categorical variables.

1.8.3 Matching

Where baseline characteristics suggest significant ($p<0.05$) differences between Ciclesonide and comparator patients, matching may be performed to provide a more robust analysis. Patients will be matched on key demographic and asthma-related characteristics during the baseline year to ensure homogeneity. Criteria will be chosen based on baseline differences and clinical experience. The following are suggested matching criteria:

- Age (±3 years aged 12-18 and ±5 years aged >18)
- Gender
- Prescription date year (exact year)
- Exacerbation rate (ATS definition) (0,1,≥2)
- Categorised SABA dosage (categories will be defined following exploratory analysis of the data)
- Baseline LABA use
- Baseline LTRA use
- Baseline diagnosis for oral candidiasis and/or prescriptions definitely for oral thrush

Patients will initially be matched on a 1:1 ratio, but other ratios will be considered based on maximising statistical power for the primary effectiveness outcome.

1.8.4 Analysis of co-primary effectiveness outcomes

Exacerbations rates in the outcome period will be compared between treatment groups using a negative binomial regression model. General estimating equations will be used to account for the correlation within matched pairs. The model will use empirical standard errors for more robust confidence intervals and adjust for potential baseline confounders. The adjusted rate ratio with 95% confidence interval will be reported.

The adjusted odds of achieving asthma control in the 1-year outcome (risk domain and overall definition) will be compared between matched treatment groups using conditional logistic regression models. The dichotomous outcome of asthma control will be used as the dependent variable with treatment and potential confounding factors as explanatory variables. The adjusted odds ratio with 95% confidence interval will be reported.

1.8.5 Confounding factors

In order to minimise biases, potential confounders will be identified based on outcome prediction (through multivariable analysis, $p<0.05$) and residual differences after matching and will be adjusted for in the statistical models.

Prior research in respiratory disease has identified a range of potential confounders that may impact on study outcomes. Based on available variables within the current dataset, these will likely include:

1) Potential confounders examined at (or closest to) the relevant index date:
    - Age of patient
    - Gender of patient
2) Potential confounders examined in the year before the index prescription date:
    - Presence/absence of comorbid rhinitis (diagnosis ever and/or prescriptions of nasal steroid preparations in the baseline/outcome year)
    - Presence/absence of comorbid eczema (diagnosis ever and/or prescriptions for topical steroids tratment in the baseline/outcome year)
    - Presence of GERD (diagnosis ever and/or prescriptions for proton pump inhibitors in the baseline/outcome year)
    - Presence of cardiac disease (diagnosis ever and/or prescriptions for cardiac drugs in the baseline/outcome year)
    - Number of asthma-related hospitalisations or possibly respiratory related (a non-specific hospitalisation code and an asthma / respiratory code within a one week window)
    - Other medications, number of prescriptions for the following:
        - Paracetamol
        - Non-steroidal anti-inflammatory drugs (NSAIDs)
        - Beta-blocker prescriptions
        - Theophylline
        - Statins
        - Tricyclics
    - Number of SABA prescriptions (calculated based on total combined dose of refilled prescriptions and averaged over 365 days).
    - Average ICS daily dose during baseline (calculated based on total combined dose of refilled prescriptions and averaged over 365 days) (in case of step-up cohorts only).
    - Last ICS dose prescribed prior to prescription date (in case of step-up cohorts only).
    - ICS dose prescribed at index date.
    - Controller-to-reliever therapy ratio.
    - Oral thrush.

1.9 LIMITATIONS OF STUDY DESIGN, DATA SOURCES AND ANALYTICAL METHODS

As with all database studies, a number of limitations exist for which it is not possible to adjust and match (e.g., potential confounding factors with the problem of internal validity). Limitations could also arise from

using the PHARMO database, including disease misclassification biases deriving from the almost exclusive use of “asthma prescriptions” to individuate asthmatic patients and the impossibility to fully adjust for confounding factors (e.g., potential confounding by severity for factors indiscernible from patient records or patient reported outcomes). In addition, study findings apply only to those healthier patients who survive at least one year after prescription date. Therefore there may be a potential survival bias.

The methods of adjustment described in the study design will be used to address all factors for which it is possible to account for.

2. ADVISORY GROUP

The advisory group will include a representative of the Small Airways Study Group (SASG):

- Richard Martin, Denver, Colorado, USA,
- Dirkje Postma, Groningen, The Netherlands
- Nicholas Roche, Paris, France
- Wim van Aalderen, The Netherlands

And Dutch experts:

- Richard Dekhuijzen, The Netherlands
- Thys van der Molen, The Netherlands

3. DATA DISSEMINATION

Once a final version of the protocol will be agreed and reviewed by the advisory group, this study will be registered with www.encepp.eu. Initial results will be presented in poster and/or oral format at appropriate thoracic conferences. At least one manuscript containing more detailed results and methodology will be submitted to a journal specialising in respiratory medicine. Submission for publications will be made as soon as the analyses are completed and the results are verified. A list of potential authors for publications will include:
David price as principal investigator, key RiRL staff, including Cristiana Miglio (lead researcher) and Vicky Thomas (lead statistician), Pharmo representative, Takeda staff, including Daniela van Eickels, Javaria Mona Khalid and Matthias Binek and advisory group members as Dutch experts and on behalf of the SASG.

4. TIMELINE

Action	Timeline
Protocol final definition	1 week
Matched Baseline analysis (stage I)	7 weeks
Baseline Report writing	2 weeks
Outcome analysis (stage II)	4 weeks
Final report writing	2 weeks
First draft of paper	4-6 weeks from final report

5. RESEARCH TEAM

5.1 RESEARCH IN REAL LIFE TEAM

1. Professor David Price, General Practice Airways Group Professor of Primary Care Respiratory Medicine, Chief investigator
2. Catherine Hutton, CEO
3. Annie Burden, Senior Statistician
4. Kathryn Richardson and Vicky Thomas, Project Statisticians
5. Julie von Ziegenweidt, Data Manager
6. Cristiana Miglio, Project Researcher

5.2 TAKEDA STAFF

1. Daniela van Eickels, Regional medical Director respiratory, Emerging Markets Medical Affairs, Takeda Pharmaceuticals.
2. Mona Khalid, Associate Director, Global Outcomes and Epidemiology Research.
3. Matthias Binek, Global Medical Head - Medical Affairs Respiratory Takeda Pharmaceuticals.

6. EXAMPLES OF RESULT TABLES

Demographics

		Total population	By treatment		P-value
			Ciclesonide	Standard particle ICS	
Index year (prescription date) n(%)	**2006***				
	2007*				
	2008*				
Sex n(%)	**Male**				
	Female				
Age at prescription date (years)	**N (% non-missing)**				
	Mean (SD)				
	median [IQR]				
Age (categorised) n(%)**	**12-60**				
	>60				
Smoking Status* n(%)**	**Non-smokers**				
	Current smokers				
	Ex-smokers				

* please note that these years have been selected at random and are an example
** please note this is just an example, categorization has been selected at random.
***closest value to prescription date (missing if >5 years either side of prescription date)

Baseline Co-medication

Baseline co-medication n (%)		Total population	Treatment Group		p-value
			Ciclesonide	Standard particle ICS	
Acetaminophen	Yes				
	No				
NSAIDs	Yes				
	No				
Beta blockers	Yes				
	no				

Asthma Control

Asthma Control	Treatment Group		Total
	Ciclesonide	Standard particle ICS	
Controlled n (%)			
Uncontrolled n (%)			
Total n (%)			
Odds Ratio adjusted for baseline confounders * (95% CI)	1.00		

*Adjusted for:

Exacerbations (ATS Definition)

Exacerbations (ATS Definition)	Treatment Group		Total
	Ciclesonide	Standard particle ICS	
None n (%)			
1 n (%)			
2+ n (%)			
Total (n)			

p = 0.xxx (Statistic test used)

7. APPENDIX 1: POSSIBLE ASTHMA THERAPY DRUG TREATMENTS

1 = SABA

2 = SAMA

3 = SAMA + SABA

4 = LABA +/- SAMA +/- SABA

5 = LAMA +/- SAMA +/- SABA

6 = LABA + LAMA +/- SAMA +/- SABA

7 = ICS +/- SAMA +/- SABA

8 = ICS + LABA +/- SAMA +/- SABA

9 = ICS + LAMA +/- SAMA +/- SABA

10 = ICS + LABA + LAMA +/- SAMA +/- SABA

11 = LTRA +/- SAMA +/- SABA

12 = LABA + LTRA +/- SAMA +/- SABA

13 = LAMA + LTRA +/- SAMA +/- SABA

14 = ICS + LTRA +/- SAMA +/- SABA

15 = ICS + LAMA + LTRA +/- SAMA +/- SABA

16 = ICS + LABA + LAMA + LTRA +/- SAMA +/- SABA

17 = ICS + LABA + LTRA +/- SAMA +/- SABA

8. APENDIX 2: DATA DICTIONARY, INCLUDING DIAGNOSTIC AND PRESCRIPTION CODES USED

Variable_Name	Description	Period	Data Type	Length	Definition / Validation Rules	Data present in primary care database	Data present in hospital database	Data present in pharmacy database	Data present in test database
Pharmacy	1 = Pharmacy data available, 0 = Not Available	n/a	Numeric	1				x	
Diagnostic	1 = Diagnostic and Consultation data available, 0 = Not Available for patient	n/a	Numeric	1		x			
Tests	1 = Function Lab data available, 0 = Not Available	n/a	Numeric	1					x
Hospital	1 = Hospital data available, 0 = Not Available	n/a	Numeric	1			x		
Unique_ID	Unique id for each patient row. Possible combination of Cohort, Patient ID and prescription date Date	n/a	Char	100		x		x	
Cohort	Initiation cohort (Initiating ICS), step-up cphprt (Increasing ICS dose), step-up cohort (add on LABA either as separate or as COMBO).	n/a	Char	4		x		x	

Variable_Name	Description	Period	Data Type	Length	Definition / Validation Rules	Data present in primary care database	Data present in hospital database	Data present in pharmacy database	Data present in test database
PatEID	Unique Patient ID - primary key linking same patient across all databases.	n/a	Char	50					
Category	Identifies which category of change occurred at prescription date for each patient: Init_ICS, Increase_ICS, Addon_LABA, Change_COMBO, Change_DEVICE, Change_ICSDrug	n/a	Char	5	Inhaled Corticosteroids (ICS), Long-Acting Bronchodilator (LABA), COMBO (Combination ICS & LABA Inhaler)	x		x	
Category_Code	1 = Initiating ICS, 2 = Increase ICS, 3 = Add on LABA, 4 = Change to COMBO, 5 = Change ICS Device, 6 = Change ICS drug substance.	n/a	Numeric	1					
prescription date_Date	Index prescription date	n/a	Date	10	yyyy-mm-dd	x		x	
Year_of_prescription date	Year of the prescription date_Date	n/a	Numeric	4					
Evidence_of_Asthma	Indicate if patient has either a Asthma diagnosis OR has been on active asthma therapy 1 = Yes, 0 = No.	n/a	Numeric	1	Refer to Asthma_Diagnosis And Active_Therapy variables	x	x	x	

Variable_Name	Description	Period	Data Type	Length	Definition / Validation Rules	Data present in primary care database	Data present in hospital database	Data present in pharmacy database	Data present in test database
Active_Asthma_Therapy	Indicate if patient has had 2 or more Asthma scripts during baseline period. 1 = Yes, 0 = No.	n/a	Numeric	1	≥2 prescriptions for asthma at different points in time during the prior year. (SABA (ATC -R03AC),ICS (ATC -R03BA), LABA (ATC -R03AC), COMBO,(ATC -R03AK), LTRA (ATC -R03DC), THEO(ATC -R03DA))	x		x	
Current_Asthma_Therapy	Indicate if patient has at least 1 more ICS script in outcome period, and, if applicable, at least 1 ICS script in baseline period 1 = Yes, 0 = No	1 Year Prior prescription date and 1Year After prescription date	Numeric	1	Requires ≥2 prescription for "relevant therapy" during the outcome year (i.e. ≥1 prescription in addition to the prescription at index date.)	x		x	
Pharmo_Model_Ind	Indicate if patient matches the definition of an asthma based on their algorithm model.[9]	1 Year Prior prescription date	Numeric	1		x			
Age	Age at prescription date	prescription date	Numeric	3	Ensure age of patient is relevant to study.	x		x	
Gender	0 = FEMALE, 1 = MALE	n/a	Numeric	1		x	x		
Ethnicity	Code to denote ethnicity (if available).	n/a	Numeric	1		x	x		
Reg_Hospital	Number of days patient has been registered on Hospital Database prior to prescription date.	Prior prescription date	Numeric	4	Days registered on database normally to be a **MINIMUM** of 365. or less than 365 for paediatrics aged < 1 year.		x		

[9] New algorithm model indicator variable provided by Pharmo

Variable_Name	Description	Period	Data Type	Length	Definition / Validation Rules	Data present in primary care database	Data present in hospital database	Data present in pharmacy database	Data present in test database
Reg_Diagnostic	Number of days patient has been registered on Diagnostic database prior to prescription date.	Prior prescription date	Numeric	4	Days registered on database normally to be a **MINIMUM** of 365. or less than 365 for paediatrics aged < 1 year.	x			
Reg_Pharmacy	Number of days patient has been registered on Pharmacy database prior to prescription date.	Prior prescription date	Numeric	4	Days registered on database normally to be a **MINIMUM** of 365. or less than 365 for paediatrics aged < 1 year.			x	
Reg_Tests	Number of days patient has been registered on Test database prior to prescription date.	Prior prescription date	Numeric	4	Days registered on database normally to be a **MINIMUM** of 365. or less than 365 for paediatrics aged < 1 year.				x
DeReg_Hospital	Number of days patient has been registered on Hospital Database after prescription date. If still registered, use date of data extract as data end point.	After prescription date	Numeric	4	Days registered on database needs to be a **MINIMUM** of 365		x		
DeReg_Diagnostic	Number of days patient has been registered on Diagnostic database after prescription date. If still registered, use date of data extract as data end point.	After prescription date	Numeric	4	Days registered on database needs to be a **MINIMUM** of 365	x			

Variable_Name	Description	Period	Data Type	Length	Definition / Validation Rules	Data present in primary care database	Data present in hospital database	Data present in pharmacy database	Data present in test database
DeReg_Pharmacy	Number of days patient has been registered on Pharmacy database after prescription date. If still registered, use date of data extract as data end point.	After prescription date	Numeric	4	Days registered on database needs to be a **MINIMUM** of 365			x	
DeReg_Tests	Number of days patient has been registered on Test database after prescription date. If still registered, use date of data extract as data end point..	After prescription date	Numeric	4	Days registered on database needs to be a **MINIMUM** of 365				x
Height	Height (m) - closest to prescription date	Closest to prescription date	Numeric	11,1	Adults - over 16 - Height: > 1.4 metres and < 2.2. Children over 5 and under 16 – Height: > 0.5 metres and < 2.2 Children under 5: Accept current values	x			
Height_Days	Number of Days between closest date of recorded height to the prescription date.	Closest to prescription date	Numeric	10	+/-	x			
Weight	Weight (kg) - closest to prescription date	Closest to prescription date	Numeric	11,1	Adults - over 16 - Weight: > 40kg and < 200kg Children under 5: Accept current values Children over 5 and under 16 - Weight: > 10kg and < 200kg	x			

Variable_Name	Description	Period	Data Type	Length	Definition / Validation Rules	Data present in primary care database	Data present in hospital database	Data present in pharmacy database	Data present in test database
Weight_Days	Number of Days between closest date of recorded weight to the Prescription date.	Closest to prescription date	Numeric	10	+/-	x			
BMI	Calculated BMI for patient - kg / m2	Closest to prescription date	Numeric	3.1		x			
SES	Country specific - Socio Economic Status	n/a	Char	5		x			
Region	Rural / Urban / Inner City if available								
Rank	Country specific SES quintile – 0 is best, 4 is worst	n/a	Numeric	1					
Smoking_Status	2 - Smoker 3 - Ex-Smoker 4 - Passive Smoker -1 - Unknown	Closest prior to prescription date.	Numeric	1	2 - Smoker ICD10 (Z72.0,F17.1),ICD9 3 - Ex-Smoker ICD10 (Z71.6) 4 - Passive Smoker ICD10 (Z758.7)	x	x	x	
Smoking_Status_All	2 - Smoker 3 - Ex-Smoker 4 - Passive Smoker -1 - Unknown	Closest to prescription date.	Numeric	1	2 - Smoker ICD10 (Z72.0,F17.1),ICD9 3 - Ex-Smoker ICD10 (Z71.6) 4 - Passive Smoker ICD10 (Z758.7)	x	x	x	
Asthma_Diagnosis	Indicate if patient had ever had an Asthma Diagnosis: 0 = No, 1 = Yes	At any time	Numeric	1	ICD10 Codes (J45,J46), ICD9 Codes (493)	x	x		
Asthma_First_Diag	Number of days between asthma first	At any time	Numeric	10		x	x		

Variable_Name	Description	Period	Data Type	Length	Definition / Validation Rules	Data present in primary care database	Data present in hospital database	Data present in pharmacy database	Data present in test database
	diagnosed and prescription date.								
Asthma_Year_First_Diag	Year when asthma was first diagnosed	At any time	Numeric	4		x	x		
Asthma_Last_Diag	Number of days between asthma last diagnosed in dataset and date of prescription date.	At any time	Numeric	10		x	x		
Asthma_First_Rx	Number of days between date of first asthma script and date of prescription date.	At any time	Numeric	10		x		x	
Asthma_Diag_Earliest	Identify year which was first; diagnosis or asthma script	At any time	Numeric	4		x	x	x	
COPD Diagnosis	Indicate if patient has ever had a COPD code recorded : 0 = No, 1 = Yes	At any time	Numeric	1	ICD10 Codes (J44) ICD9 Codes (49120, 49121, 49122)	x	x		
COPD_First_Diag	Number of days between date COPD first diagnosed and date of prescription date.	At any time	Numeric	10		x	x		
Rhinitis Diagnosis	Rhinitis Code: 0 = No, 1 = Yes	At any time	Numeric	1	ICD10 Codes (J31.0, J30) ICD9 Codes (4720, 477)	x	x		
Rhinitis_First_Diag	Number of days between date Rhinitis	At any time	Numeric	10		x	x		

Variable_Name	Description	Period	Data Type	Length	Definition / Validation Rules	Data present in primary care database	Data present in hospital database	Data present in pharmacy database	Data present in test database
	first diagnosed and date of prescription date.								
Rhinitis_Dx_Nasal_Spray	Indicate if patient has ever had a Rhinitis Diagnosis and/or Nasal Spray prescribed in baseline or outcome period : 0 = No, 1 = Yes	Baseline and outcome.	Numeric	1	ATC Codes (R01AD,R01AX, R01B)	x		x	
Eczema_Diagnosis	Eczema code recorded: 0 = No, 1 = Yes	At any time	Numeric	1	ICD10 Codes (L20 - L30), ICD9 Codes (6908, 6910, 6918, 6920, 6921, 6922, 6923, 6924, 6925, 6926, 6929, 6930, 6931, 6938, 6939, 6965, 6980, 6981, 6982, 6983, 6988, 6989, 69010, 69011, 69012, 69018, 69281, 69283, 69284, 69289)	x	x		
Eczema_Dx_Drugs	Indicate if patient has ever had a Eczema Diagnosis and/or Topical Steroids prescribed in baseline or outcome period: 0 = No, 1 = Yes	Baseline and outcome.	Numeric	1	ATC Codes - (D07)	x	x	x	
Other_Chronic_Dis	Indicate if patient has ever had any other Chronic pulmonary diseases diagnosed : 0 = No, 1 = Yes	At any time	Numeric	1	ICD10 Codes (J40-J43,J47,J60-J70) ICD9 Codes (500, 5001, 501, 5060, 5062, 5063, 5064, 5069, 5088, 5089, 515)	x	x		

Variable_Name	Description	Period	Data Type	Length	Definition / Validation Rules	Data present in primary care database	Data present in hospital database	Data present in pharmacy database	Data present in test database
GERD_Diagnosis	Indicate if patient has ever had a GERD read code : 0 = No, 1 = Yes	At any time	Numeric	1	ICD10 Codes (K21) ICD9 Codes (53081)	x	x		
GERD_Dx_Drugs	Indicate if patient has ever received drugs for GERD in baseline or outcome period and/or GERD diagnosis : 0 = No, 1 = Yes	Baseline and outcome.	Numeric	1	ATC Codes (A02BC)	x	x	x	
Cardiac_Diagnosis	Indicate if patient has ever had a Cardiac Disease code : 0 = No, 1 = Yes	At any time	Numeric	1	ICD10 Codes (I26-I28) ICD9 Codes (415 - 418)	x	x		
Cardiac_Dx_Drugs	Indicate if patient has ever received any drugs for Cardiac Disease in baseline or outcome period or/and Cardiac Disease Diagnosis : 0 = No, 1 = Yes	Baseline and outcome	Numeric	1	ATC Codes - (C01, C02,C03,C07,C08,C09)	x	x	x	
IHD_Diagnosis	Indicate if patient has ever had Ischaemic Heart Disease : 0 = No, 1 = Yes.	At any time	Numeric	1	ICD10 Codes (I20-I25) ICD9 Codes (411, 413, 410, 42979, 412, 414)	x	x		
Myo_Inf_Dx	Indicate if patient has ever had a Acute Myocardial Infarction. 0 = No, 1 = Yes	1 Year Prior & incl prescription date	Numeric	1	ICD10 Codes (I21, I22, I23, I252, I258), ICD9 Codes (413, 410, 42979, 412, 41402, 41403, 41404, 41405, 41406, 41407, 4142, 4143, 4144, 4148)	x	x		

Variable_Name	Description	Period	Data Type	Length	Definition / Validation Rules	Data present in primary care database	Data present in hospital database	Data present in pharmacy database	Data present in test database
Cancer_Dx	Indicate if patient has Cancer. 0 = No, 1 = Yes.	1 Year Prior & incl prescription date	Numeric	1	ICD10 Codes (C00-C76, C80-C97) ICD9 Codes (140-195,199-209)	x	x		
Cerebro_Dx.	Indicate if patient has Cerebrovascular Disease: 0 = No, 1 = Yes	1 Year Prior & incl prescription date	Numeric	1	ICD10 Codes (G450, G451, G452, G454, G458, G459, G46, I60-I69) ICD9 Codes (43)	x	x		
Congestive_HD_Dx	Indicate if patient has ever had Congestive Heart Disease:0 = No, 1 = Yes	1 Year Prior & incl prescription date	Numeric	1	ICD10 Codes (I50) ICD9 Codes (428)	x	x		
Periph_Vasc_Dis	Indicate if patient has Peripheral Vascular Disease: 0 = No, 1 = Yes.	1 Year Prior & incl prescription date	Numeric	1	ICD10 Codes (I71, I739, I790, R02, Z958, Z959) ICD9 Codes (441, 4439, V4502, V4321, V4322, V4509, V434, V4500)	x	x		
Pulmonary_Dis_Dx	Indicate if patient has Pulmonary Diseases: 0 = No, 1 = Yes.	1 Year Prior & incl prescription date	Numeric	1	ICD10 Codes (J40-J47, J60-J67) ICD9 Codes (490-495, 500-505)	x	x		
Dementia_Dx	Indicate if patient has Dementia: 0 = No, 1 = Yes.	1 Year Prior & incl prescription date	Numeric	1	ICD10 Codes (F00, F01, F02, F03, F051) ICD9 Codes (290, 29410, 29411, 29420, 29421)	x	x		
Conn_Tiss_Dx	Indicate if patient has Connective and Soft Tissue Disease: 0 = No, 1 = Yes	1 Year Prior & incl prescription date	Numeric	1	ICD10 Codes (M05, M060, M063, M069, M32, M332, M34, M353) ICD9 Codes (7141, 71481, 7142, 7140, 7100, 7104, 7101, 5172, 725)	x	x		

Variable_Name	Description	Period	Data Type	Length	Definition / Validation Rules	Data present in primary care database	Data present in hospital database	Data present in pharmacy database	Data present in test database
Diabetes_Dx.	Indicate if patient has Diabetes mellitis: 0 = No, 1 = Yes.	1 Year Prior & incl prescription date	Numeric	1	ICD10 Codes (E101, E105, E106, E108, E109, E111, E115, E116, E118, E119, E131, E136, E138, E139, E141, E145, E146, E148, E149). ICD9 Codes (2500, 2501, 2504, 2507, 2508, 2509, 24910, 24930, 24980, 24990, 24900)	x	x		
Diabetes_Plus_Compl_Dx	Indicate if patient has Diabetes with Complications: 0 = No, 1 = Yes	1 Year Prior & incl prescription date	Numeric	1	ICD10 Codes (E102, E103, E104, E107, E112, E113, E114, E117, E132, E133, E134, E137, E142, E143, E144, E147) ICD9 Codes (25040, 25041, 25043, 2505, 2506, 24950, 36641, 24960)	x	x		
AIDS_Dx	Indicate if patient has Aids: 0 = No, 1 = Yes	1 Year Prior & incl prescription date	Numeric	1	ICD10 Codes (B20, B21, B22, B23, B24). ICD9 Codes (042-044)	x	x		
Mild_Liver_Dx	Indicate if patient has Mild Liver Disease: 0 = No, 1 = Yes	1 Year Prior & incl prescription date	Numeric	1	ICD10 Codes (K702, K703, K717, K73, K74). ICD9 Codes (5712, 5710, 57140, 57141, 57149, 5715, 5719, 5716).	x	x		
Ulcer_Dis_Dx	Indicate if patient has Peptic Ulcer Disease: 0 = No, 1 = Yes	1 Year Prior & incl prescription date	Numeric	1	ICD10 Codes (K25, K26, K27, K28). ICD9 Codes (531, 532, 533, 534)	x	x		
Hemiplegia_Dx	Indicate if patient has Hemiplegia: 0 = No, 1 = Yes	1 Year Prior & incl prescription date	Numeric	1	ICD10 Codes (G041, G81, G820, G821, G822). ICD9 Codes (342, 3441)	x	x		

Variable_Name	Description	Period	Data Type	Length	Definition / Validation Rules	Data present in primary care database	Data present in hospital database	Data present in pharmacy database	Data present in test database
Renal_Dis_Dx	Indicate if patient has Renal Disease: 0 = No, 1 = Yes	1 Year Prior & incl prescription date	Numeric	1	ICD10 Codes (I12, I13, N01, N03, N052-N056, N072-N074, N18, N19, N25). ICD9 Codes (403, 404, 5804, 582, 5831, 5832, 585, 586, 588)	x	x		
Liver_Dis_Dx	Indicate if patient has Moderate/Severe Liver Disease: 0 = No, 1 = Yes.	1 Year Prior & incl prescription date	Numeric	1	ICD10 Codes (K721, K729, K766, K767). ICD9 Codes (5728, 5722, 5728)	x	x		
Meta_Tumour_Dx	Indicate if patient has any Metastatic Tumours: 0 = No, 1 = Yes	1 Year Prior & incl prescription date	Numeric	1	ICD10 Codes (C77, C78, C79) ICD9 Codes (196,197,198)	x	x		
Beta_Blockers	0 = N – none received over period, 1 = Y – received over period	1 Year Prior & incl prescription date	Numeric	1	ATC Codes (C07)	x		x	
NSAIDS	0 = N – none received over period, 1 = Y – received over period	1 Year Prior & incl prescription date	Numeric	1	ATC Codes (M01AB)	x		x	
Paracetamol	0 = N – none received over period, 1 = Y – received over period	1 Year Prior & incl prescription date	Numeric	1	ATC Codes (N02BE01)	x		x	
Statins	0 = N – none received over period, 1 = Y – received over period	1 Year Prior & incl prescription date	Numeric	1	ATC Codes (C10AA)	x		x	

Variable_Name	Description	Period	Data Type	Length	Definition / Validation Rules	Data present in primary care database	Data present in hospital database	Data present in pharmacy database	Data present in test database
Tricyclics	0 = N – none received over period, 1 = Y – received over period	1 Year Prior & incl prescription date	Numeric	1	ATC Codes - (N06AA)	x		x	
BASELINE SPECIFIC VARIABLES - PRE prescription date									
ba_Asthma_Scripts	Count of scripts for asthma ONLY – grouped by patient and date	1 Year Prior prescription date	Numeric	11	ATC Codes (R03A, R03BB, R03DA, R03BA, R03BC, R03DC)	x		x	
ba_Allergy_Scripts	Count of any scripts for ALLERGIES only - grouped by patient and date	1 Year Prior & incl prescription date	Numeric	11	ATC Codes (R01AC, R01AD,R06, D04AA,S01G)	x		x	
ba_Asthma_Consults	Count of consultations where asthma was recorded for GP specific type consultations	1 Year Prior & incl prescription date	Numeric	11		x			
ba_Asthma_Cons_No_OS	Count of asthma consultations where no acute courses of oral steroids were prescribed	1 Year Prior & incl prescription date	Numeric	11		x		x	
ba_prescription date_Consult	Indicate if patient recorded a consultation at prescription date or within 7 days after prescription date.	prescription date or 7 days after	Numeric	1		x			

Variable_Name	Description	Period	Data Type	Length	Definition / Validation Rules	Data present in primary care database	Data present in hospital database	Data present in pharmacy database	Data present in test database
ba_prescription date_Asthma_Consult	Indicate if patient recorded an ASTHMA consultation at prescription date or within 7 days after prescription date.	prescription date or 7 days after	Numeric	1		x			
ba_Surg_Consults	Count of all Primary Care surgery consultations - Using consultation type of ' Follow-up/routine visit', 'Surgery consultation' & ' Emergency Consultation'	1 Year Prior & incl prescription date	Numeric	11		x			
ba_HV_Consults	Count of all Primary Care home visit specific consultations	1 Year Prior & incl prescription date	Numeric	11		x			
ba_NV_Consults	Count of all Primary Care Night visits specific consultations	1 Year Prior & incl prescription date	Numeric	11		x			
ba_OutHrs_Consults	Count of all Primary Care Out of Hours consultations - Using consultation type of ' Night visit, Deputising service', 'Night visit, Local rota', 'Night visit ,	1 Year Prior & incl prescription date	Numeric	11		x			

Variable_Name	Description	Period	Data Type	Length	Definition / Validation Rules	Data present in primary care database	Data present in hospital database	Data present in pharmacy database	Data present in test database
	practice', 'Out of hours, Practice','Out of hours, Non Practice'								
ba_Tel_Consults	Count of telephone conversions recorded with patients - Using consultation type of ' Telephone call from a Patient', 'Telephone call to a patient'	1 Year Prior & incl prescription date	Numeric	11		x			
ba_Clinic_Consults	Count of all clinic (Nurse) consultations	1 Year Prior & incl prescription date	Numeric	11		x			
ba_Comm_Consults	Count of all community nurse consultations	1 Year Prior & incl prescription date	Numeric	11		x			
Ba_Other_Consults	Count of all other type consultations not previously indicated.	1 Year Prior & incl prescription date	Numeric	11		x			
ba_All_Consults	Count of all the Primary Care consultations as specified in the above variables	1 Year Prior & incl prescription date	Numeric	11		x			
ba_Asthma_AE	Count of A & E attendances for Asthma	1 Year Prior & incl	Numeric	11	Ensure that this does include any definite Asthma admissions as well.	x	x		

Variable_Name	Description	Period	Data Type	Length	Definition / Validation Rules	Data present in primary care database	Data present in hospital database	Data present in pharmacy database	Data present in test database
	plus lower respiratory codes (incl LRTI)	prescription date							
ba_Asthma_InP	Count of in-patient hospital admissions for Asthma plus lower respiratory admissions (incl LRTI)	1 Year Prior & incl prescription date	Numeric	11		x	x		
ba_Asthma_InP_Vague	Count of in-patient hospital admissions for any Vague entry.	1 Year Prior & incl prescription date	Numeric	11	Vague defined as any generic hospital admission with an Asthma or Lower Respiratory diagnosis within +/- 7 days of entry. (incl LRTI).	x	x		
ba_Asthma_OPD	Count of out-patient hospital attendances for Asthma plus lower respiratory admissions (incl LRTI)	1 Year Prior & incl prescription date	Numeric	11		x	x		
ba_Acute_OS	Count of total acute oral steroid scripts prescribed to patients to treat exacerbations	1 Year Prior & incl prescription date	Numeric	11	ATC Codes (A07EA)	x		x	
ba_Maint_OS	Count of maintenance steroid courses, defined as dispensings for duration > 10 days	1 Year Prior & incl prescription date	Numeric	11	ATC Codes (A07EA)	x		x	
ba_Maint_OS_Ind	Indicate if patient had maintenance oral steroids in baseline period: 1 = Yes, 0 = No	1 Year Prior & incl prescription date	Numeric	1		x		x	

Variable_Name	Description	Period	Data Type	Length	Definition / Validation Rules	Data present in primary care database	Data present in hospital database	Data present in pharmacy database	Data present in test database
ba_Total_OS	Total number of all oral steroid courses prescribed – acute and maintenance	1 Year Prior & incl prescription date	Numeric	11	ATC Codes (H02AB06, H02AB07)	x		x	
ba_LRTI_Consults	Count of all Primary Care consultations for a Lower Respiratory Tract Infection treated with an Antibiotic	1 Year Prior & incl prescription date	Numeric	11	ICD10 Codes (J20-J22) ICD9 Codes (466) ATC Codes (A07AA)	x	x	x	
ba_Cand_Def	Count of definite oral candidiasis diagnosed	1 Year Prior prescription date	Numeric	11	ICD10 Codes (B37.0) ICD9 Codes (1120)	x	x		
ba_Antifungal_Def	Count of definite antifungal scripts that are only prescribed for oral thrush	1 Year Prior prescription date	Numeric	11	ATC Codes: (Nystatin A07AA02 O, Amphotericin A01AB04 O, Miconazole A01AB09 O, Miconazole A07AC01 O, Clotrimazole A01AB18, Minocycline A01AB23)	x		x	
ba_Cand_Anti_Def	Count of combined dates for definite oral thrush and definite Antifungals	1 Year Prior prescription date	Numeric	11		x	x	x	
ba_Pneumonia	Indicate if patient has had a Pneumonia diagnosis 1 = Yes, 0 = No	1 Year Prior prescription date	Numeric	1	ICD10 Codes (J12-J18) ICD9 Codes (480,481,482 (excl 48284), 483, 4847, 4848, 485, 486)	x	x		

Variable_Name	Description	Period	Data Type	Length	Definition / Validation Rules	Data present in primary care database	Data present in hospital database	Data present in pharmacy database	Data present in test database
ba_Pneumonia_Def	Indicate if patient's Pneumonia diagnosis confirmed by Chest Xray or by referring to hospital	1 Year Prior prescription date	Numeric	1	ICD10 Codes (J12-J18) ICD9 Codes (480,481,482 (excl 48284), 483, 4847, 4848, 485, 486)	X	x		
ba_PF_BE	Typecode – 007R	Last recorded best ever reading prior to prescription date	Numeric	11,1	**For Paediatrics (aged 4-19):**	x			x
ba_PF_BE_ Days	Number of days between Date of best ever reading and date of prescription date.	Last recorded best ever reading prior to prescription date	Numeric	10	The basic equations used are:	x			x
ba_PF_BE_Hgt	Last Height recorded prior to date of best ever	Last recorded best ever reading prior to prescription date	Numeric	11,1	PEFR in litres per second for boys 4-19 years < 162.6 cm (Rosenthal) = (0.073 * (height in cm)) - 5.98	x			x

Variable_Name	Description	Period	Data Type	Length	Definition / Validation Rules	Data present in primary care database	Data present in hospital database	Data present in pharmacy database	Data present in test database
ba_PF_BE_Hgt_Days	Number of days between Date of best ever height recorded AND date of prescription date.	Last recorded best ever reading prior to prescription date	Numeric	10	PEFR in litres per second for boys 4-19 years >= 162.6 cm (Rosenthal) = (0.125 * (height in cm)) - 13.14	x			x
ba_PF_Current	Typecode – 007T	Last recorded current reading prior to prescription date	Numeric	11,1	PEFR in litres per second for girls 4-19 years < 152.6 cm (Rosenthal) = (0.079 * (height in cm)) - 6.79	x			x
ba_PF_Curr_ Days	Number of days between Date of current result and date of prescription date.	Last recorded current reading prior to prescription date	Numeric	10	PEFR in litres per second for girls 4-19 years >= 152.6 cm (Rosenthal) = (0.064 * (height in cm)) - 3.94	x			x
ba_PF_Curr_Hgt	Last Height recorded prior to date of current reading	Last recorded current reading prior to	Numeric	11,1	However, subjects must be > 0.86m tall (girls) or > 0.82m tall (boys) for these equations to be non-negative.	x			x

Variable_Name	Description	Period	Data Type	Length	Definition / Validation Rules	Data present in primary care database	Data present in hospital database	Data present in pharmacy database	Data present in test database
		prescription date							
ba_PF_Curr_Hgt_ Days	Number of days between Date of current height recorded and date of prescription date.	Last recorded current reading prior to prescription date	Numeric	10	The following equation has been used for paediatrics (male & female) <= 1.1m tall:	x			x
ba_PF_Pred	Typecode – 007S	Last recorded pred. reading prior to prescription date	Numeric	11,1	PEFR in litres per second (Robinson from Cotes page 465) = (4.93 * (height in metres)) - 2.9	x			x
ba_PF_Pred_ Days	Number of days between Date of predicted result and date of prescription date.	Last recorded pred. reading prior prescription date	Numeric	10	Subjects must still be > 0.6m tall for a non-negative predicted PEFR.	x			x
ba_PF_Pred_Hgt	Last height taken prior to predicted recording	Last recorded pred. reading prior prescription date	Numeric	11,1		x			x

Variable_Name	Description	Period	Data Type	Length	Definition / Validation Rules	Data present in primary care database	Data present in hospital database	Data present in pharmacy database	Data present in test database
ba_PF_Pred_Hgt_ Days	Number of days between Date of height and prescription date.	Last recorded pred. reading prior prescription date	Numeric	10		x			x
ba_Drug_Treatment	Description to identify asthma therapy	1 Year Prior prescription date	Char	100	See appendix 1	x		x	
ba_Drug_Treatment_Code	Code to identify asthma therapy in baseline period	1 Year Prior prescription date	Numeric	2	See appendix 1	x		x	
ba_SABA_Scripts	No of SABA scripts	1 Year Prior prescription date	Numeric	11		x		x	
ba_SABA_Inhalers	No of SABA inhalers	1 Year Prior prescription date	Numeric	11		x		x	
ba_SABA_Daily_Dose	No of SABA doses per day	1 Year Prior prescription date	Numeric	11,1	(((Count of inhalers * doses in pack) / 365) * mcg strength) / average prescribing dosage for saba (ie 200mcg Salbutamol / 500mcg Terbutaline / 180mcg Albuterol) to get SABA Daily Dose. Ensure that the SABA daily dosage * average prescribing dosage (ie 200mcg Salbutamol) equals SABA Daily Dosage	x		x	

Variable_Name	Description	Period	Data Type	Length	Definition / Validation Rules	Data present in primary care database	Data present in hospital database	Data present in pharmacy database	Data present in test database
ba_SABA_Daily_Dosage	Based on average number of puffs per day over the year x mcg	1 Year Prior prescription date	Numeric	17,2	((Count of inhalers * doses in pack) / 365) * mcg strength	x		x	
ba_ICS_Scripts	No of scripts issued in last 12 months	1 Year Prior prescription date	Numeric	11	Check that ICS scripts is relative to daily dose	x		x	
ba_ICS_Inhalers	No of inhalers issued in last 12 months	1 Year Prior prescription date	Numeric	11	Check that ICS inhalers is relative to ICS scripts.	x		x	
ba_ICS_Daily_Dose	No of ICS doses per day	1 Year Prior prescription date	Numeric	11,1	((Count of inhalers * doses in pack) / 365)	x		x	
ba_ICS_Daily_Dosage	Average mcg daily dose per day – Beclometasone equivalent	1 Year Prior prescription date	Numeric	17,2	((Count of inhalers * doses in pack) / 365) * mcg strength	x		x	
ba_ICS_Total_Dosage	Total dosage in micrograms prescribed in baseline period – bdp	1 Year Prior prescription date	Numeric	11		x		x	
ba_ICS_Duration	Total Pack Days	1 Year Prior prescription date	Numeric	17	Sum (Number doses in pack / Prescribing instructions)	x		x	
ba_ICS_Actual_Period	Actual prescription days.	1 Year Prior prescription date	Numeric	17	(date of last script - date of first script) + Number pack days of last script	x		x	
ba_ICS_Drug_1	Product Name of LAST ICS drug issued prior to prescription date – 1st drug if multiple drugs	1 Year Prior prescription date	Char	200	This is the last ICS prescribed to patient. prior to prescription date. Not applicable for initiation cohort.	x		x	

Variable_Name	Description	Period	Data Type	Length	Definition / Validation Rules	Data present in primary care database	Data present in hospital database	Data present in pharmacy database	Data present in test database
	issued on same day. - 2 = N/A								
ba_ICS_Last_Dose_1	Last prescribed ICS dosage prior to prescription date for ICS Drug 1. - 2 = N/A	1 Year Prior prescription date	Numeric	11		x		x	
ba_ICS_Device_1	ICS Drug 1 device – 0 = MDI, 1 = DPI. - 2 = N/A	1 Year Prior prescription date	Numeric	1		x		x	
ba_ICS_Subst_1	ICS Drug 1 Substance type – 0 = Beclometasone, 1 = Fluticasone, 2 = Mometasone, 3 = Budesonide, 4 = Ciclesonide - 2 = N/A	1 Year Prior prescription date	Numeric	1		x		x	
ba_ICS_Drug_2	Product Name of last ICS drug issued prior to prescription date – 2nd drug if multiple drugs issued on same day. Else indicate a -2 code for N/A.	1 Year Prior prescription date	Char	200	Drug 2 only applicable is patient was prescribed MULTIPLE ICS scripts on the same day immediately prior to prescription date. Not applicable for initiation cohort.	x		x	
_ICS_Device_2	ICS Drug 2 device – 0 = MDI, 1 = DPI. -2 = N/A.	1 Year Prior prescription date	Numeric	1		x		x	

Variable_Name	Description	Period	Data Type	Length	Definition / Validation Rules	Data present in primary care database	Data present in hospital database	Data present in pharmacy database	Data present in test database
ba_ICS_Subst_2	ICS Drug 2 Substance type – 0 = Beclometasone, 1 = Fluticasone, 2 = Mometasone, 3 = Budesonide, 4 = Ciclesonide -2 = N/A	1 Year Prior prescription date	Numeric	1		x		x	
ba_LABA	Indicate if patient received LABA in baseline period : 0 = No, 1 = Yes	1 Year Prior prescription date	Numeric	1	ATC -R03AC	x		x	
ba_LABA_Rx	No of LABA scripts patient was prescribed	1 Year Prior prescription date	Numeric	11	ATC -R03AC	x		x	
ba_LTRA	Indicate if patient received LTRA in baseline period. 0 = No, 1 = Yes	1 Year Prior prescription date	Numeric	1	ATC -R03DC	x		x	
ba_LTRA_Rx	No of LTRA scripts issued to patient	1 Year Prior prescription date	Numeric	1	ATC -R03DC	x		x	
ba_THEO_Rx	No of Theophylline scripts issued to patient	1 Year Prior prescription date	Numeric	11	ATC -R03DA	x		x	
ba_Spacer_Device	Indicate if patients were issued with a spacer device: 1 = Yes, 0 = No. -2 = N/A	1 Year Prior prescription date	Numeric	1	Not applicable to initiation cohort.	x		x	

Variable_Name	Description	Period	Data Type	Length	Definition / Validation Rules	Data present in primary care database	Data present in hospital database	Data present in pharmacy database	Data present in test database
OUTCOME VARIABLE - POST prescription date									
prescription date_ICS_Drug_Name	ICS/COMBO drug product name issued AT prescription date date	**At prescription date**	Char	200		x		x	
prescription date_ICS_Dose	Actual prescribing dosage at prescription date: Prescrib. instructions * strength in bdp-eqv.	**At prescription date**	Numeric	11	**Please Note:** If patient on Self-management Program, assume 2puffs twice daily for MDI device or 1puff twice daily for DPI device.	x		x	
prescription date_ICS_Device	ICS/COMBO Drug device AT prescription date - 0 = MDI, 1 = DPI	**At prescription date**	Numeric	1		x		x	
prescription date_HFA_Type	Indicate if drug is a HFA-BDP and what brand: 0 = No, 1 = QVAR, 2 = CLENIL	**At prescription date**	Numeric	1					
prescription date_ICS_Drug_Substance	ICS drug substance prescribed at prescription date – 0 = Beclometasone, 1 = Fluticasone, 2 = Budesonide	**At prescription date**	Numeric	1		x		x	
prescription date_FDC_Inhaler	If step up in ICS drug is to a Fixed Dose combo Inhaler, indicate which	**At prescription date**	Numeric	1	Applicable to prescription dateA - Change COMBO category.	x		X	

Variable_Name	Description	Period	Data Type	Length	Definition / Validation Rules	Data present in primary care database	Data present in hospital database	Data present in pharmacy database	Data present in test database
	type: - 0 - No, 1 = FP/SAL, 2 = BUD/FOR, 3 = BDP/FOR								
prescription date_LABA_Drug	LABA Drug Product Name AT prescription date date.	At prescription date	Numeric	1	Applicable to step-up cohort only - Addon LABA category.	x		x	
prescription date_LABA_Substance	LABA drug substance - 1 = Salmeterol, 2 = Formoterol.	At prescription date	Numeric	1	Applicable to step-up cohort only - Addon LABA category.	X		x	
out_LABA/ICS_First_Days	Number of days between date of prescription date (LABA rx) and FIRST ICS script.	3 Months After prescription date (incl prescription date)	Numeric	11	Applicable to step-up cohort only - Addon LABA category. If ICS was not prescribed on same day as LABA, then take first ICS rx in 3 months after prescription date. If not found, assume same drug and instructions for last ICS prior prescription date.				
out_ICS_First_Dose	First ICS script dose after prescription date: prescrib. instructions * strength in bdp-eqv.	1 Year After prescription date	Numeric	11		x		x	
out_Asthma_Scripts	Count of scripts for asthma only – grouped by patient and date	1 Year After & incl prescription date	Numeric	11	ATC Codes (R03A, R03BB, R03DA, R03AK, R03BA, R03BC, R03DC)	x		x	
out_Allergy_Scripts	Count of scripts for ALLERGIES only - grouped by patient and date	1 Year After prescription date	Numeric	11	ATC Codes (R01AC, R01AD,R06, D04AA,S01G)	x		x	

Variable_Name	Description	Period	Data Type	Length	Definition / Validation Rules	Data present in primary care database	Data present in hospital database	Data present in pharmacy database	Data present in test database
out_Asthma_Consults	Count of consultations where asthma was recorded for GP specific type consultations	1 Year After prescription date	Numeric	11		x			
out_Surg_Consults	Count of all Primary Care surgery consultations	1 Year After prescription date	Numeric	11		x			
out_HV_Consults	Count of all Primary Care home visit specific consultations	1 Year After prescription date	Numeric	11		x			
out_NV_Consults	Count of all Primary Care Night home visit specific consultations	1 Year After prescription date	Numeric	11		x			
out_Out_Hrs_Consults	Count of all Primary Care Out of Hours consultations	1 Year After prescription date	Numeric	11		x			
out_Tel_Consults	Count of telephone conversions recorded with patients	1 Year After prescription date	Numeric	11		x			
out_Clinic_Consults	Count of all clinic (Nurse) consultations	1 Year After prescription date	Numeric	11		x			
out_Comm_Consults	Count of all Community (Nurse) consultations	1 Year After prescription date	Numeric	11		x			
out_Other_Consults	Count of all Other type of consultations not	1 Year After prescription date	Numeric	11		x			

Variable_Name	Description	Period	Data Type	Length	Definition / Validation Rules	Data present in primary care database	Data present in hospital database	Data present in pharmacy database	Data present in test database
	already specifically catered for.								
out_All_Consults	Count of all the Primary Care consultations as specified in the notes - *See notes for consultation types	1 Year After prescription date	Numeric	11	Ensure that this is the accumulation of all the 'surgery consults', 'Home Visit Consults', 'Night Visits Consults','Out Hrs Consults','Tel Consults','Community Nurse consults','Other Consults' and 'Clinic Consults'.	x		x	
out_Asthma_AE	Count of A & E attendances for Asthma plus lower respiratory codes (incl LRTI)	1 Year After prescription date	Numeric	11		x		x	
out_Asthma_InP	Count of in-patient hospital admissions for Asthma plus lower respiratory admissions (incl LRTI)	1 Year After prescription date	Numeric	11		x		x	
out_Asthma_InP_Vag	Count of in-patient hospital admissions for Asthma plus lower respiratory admissions (incl LRTI) as well as any vague admissions	1 Year After prescription date	Numeric	11	Ensure that this contains the definite Asthma admissions as well.	x		x	
out_Asthma_OPD	Count of out-patient hospital attendances for Asthma plus lower resp admissions (incl LRTI)	1 Year After prescription date	Numeric	11		x		x	

Variable_Name	Description	Period	Data Type	Length	Definition / Validation Rules	Data present in primary care database	Data present in hospital database	Data present in pharmacy database	Data present in test database
out_Acute_OS	Count of all acute oral steroid scripts issued to patient	1 Year After prescription date	Numeric	11	ATC Codes (A07EA)	x		x	
out_Maint_OS	Count of definite maintenance oral steroid courses	1 Year After prescription date	Numeric	11	ATC Codes (A07EA)	x		x	
out_Total_OS	Total number of all oral steroid courses prescribed	1 Year After prescription date	Numeric	11	ATC Codes (A07EA)	x		x	
out_LRTI_Consults	Count of all consultations for a Lower Respiratory Tract Infection treated with Antibiotics	1 Year After prescription date	Numeric	11	ICD10 Codes (J20-J22) ICD9 Codes (466) ATC Codes (A07AA)	x		x	
out_Cand_Def	Count of definite oral candidiasis diagnosed	1 Year After prescription date (inc prescription date)	Numeric	11	ICD10 Codes (B37.0) ICD9 Codes (1120)	x	x		
out_Antifungal_Def	Count of definite antifungal scripts that are only prescribed for oral thrush	1 Year After prescription date (inc prescription date)	Numeric	11	ATC Codes: (Nystatin A07AA02 O, Amphotericin A01AB04 O, Miconazole A01AB09 O, Miconazole A07AC01 O, Clotrimazole A01AB18, Minocycline A01AB23)	x		x	
out_Cand_Anti_Def	Count of combined dates for definite oral	1 Year After prescription date (inc	Numeric	11		x		x	

Variable_Name	Description	Period	Data Type	Length	Definition / Validation Rules	Data present in primary care database	Data present in hospital database	Data present in pharmacy database	Data present in test database
	thrush and definite Antifungals	prescription date)							
out_Pneumonia	Indicate if patient has had a Pneumonia diagnosis 1 = Yes, 0 = No	1 Year After prescription date (inc prescription date)	Numeric	1	ICD10 Codes (J12-J18) ICD9 Codes (480,481,482 (excl 48284), 483, 4847, 4848, 485, 486)	x	x		
out_Pneumonia_Def	Indicate if patient's Pneumonia diagnosis confirmed by Chest Xray or by referring to hospital : 1 = Yes, 0 = No	1 Year After prescription date (inc prescription date)	Numeric	1	ICD10 Codes (J12-J18) ICD9 Codes (480,481,482 (excl 48284), 483, 4847, 4848, 485, 486)	x	x		
out_PF_BE	Typecode – 007R	First recorded best ever reading after prescription date	Numeric	11,1	**For Paediatrics (aged 4-19):**	x			x
out_PF_BE_Days	Number of days between prescription date and Date of best ever reading	First recorded best ever reading after prescription date	Numeric	10	The basic equations used are:	x			x
out_PF_BE_Height	Last Height recorded prior to date of best ever	First recorded best ever reading after	Numeric	11,1	PEFR in litres per second for boys 4-19 years < 162.6 cm (Rosenthal) = (0.073 * (height in cm)) - 5.98	x			x

Variable_Name	Description	Period	Data Type	Length	Definition / Validation Rules	Data present in primary care database	Data present in hospital database	Data present in pharmacy database	Data present in test database
		prescription date							
out_PF_BE_Height_ Days	Number of days between prescription date and Date of best ever height recorded	First recorded best ever reading after prescription date	Numeric	10	PEFR in litres per second for boys 4-19 years >= 162.6 cm (Rosenthal) = (0.125 * (height in cm)) - 13.14	x			x
out_PF_Curr	Typecode – 007T	First recorded current reading after prescription date	Numeric	11,1	PEFR in litres per second for girls 4-19 years < 152.6 cm (Rosenthal) = (0.079 * (height in cm)) - 6.79	x			x
out_PF_Curr_ Days	Number of days between prescription date and Date of current result	First recorded current reading after prescription date	Numeric	10	PEFR in litres per second for girls 4-19 years >= 152.6 cm (Rosenthal) = (0.064 * (height in cm)) - 3.94	x			x
out_PF_Curr_Hgt	Last Height recorded prior to date of current reading	First recorded current reading after prescription date	Numeric	11,1	However, subjects must be > 0.86m tall (girls) or > 0.82m tall (boys) for these equations to be non-negative.	x			x

Variable_Name	Description	Period	Data Type	Length	Definition / Validation Rules	Data present in primary care database	Data present in hospital database	Data present in pharmacy database	Data present in test database
out_PF_Curr_Hgt_ Days	Number of days between prescription date and Date of current height recorded	First recorded current reading after prescription date	Numeric	10	The following equation has been used for paediatrics (male & female) <= 1.1m tall:	x			x
out_PF_Pred	Typecode – 007S	First recorded pred. read after prescription date	Numeric	11,1	PEFR in litres per second (Robinson from Cotes page 465) = (4.93 * (height in metres)) - 2.9	x			x
out_PF_Pred_Days	Number of days between prescription date and Date of predicted result	First recorded pred.reading after prescription date	Numeric	10	Subjects must still be > 0.6m tall for a non-negative predicted PEFR.	x			x
out_PF_Pred_Hgt	Last height taken prior to pf predicted recording	First recorded pred. read after prescription date	Numeric	11,1		x			x
out_PF_Pred_Hgt_Days	Number of days between prescription date and Date of height	First recorded pred. reading after	Numeric	10		x			x

Variable_Name	Description	Period	Data Type	Length	Definition / Validation Rules	Data present in primary care database	Data present in hospital database	Data present in pharmacy database	Data present in test database
		prescription date							
out_SABA_Scripts	No of SABA scripts	1 Year After prescription date (inc prescription date)	Numeric	11	Check that the saba scripts is in relation to saba daily dose.	x		x	
out_SABA_Inhalers	No of SABA inhalers	1 Year After prescription date (inc prescription date)	Numeric	11	Check that the saba inhalers is relative to saba scripts.	x		x	
out_SABA_Daily_Dose	Average no of SABA doses per day	1 Year After prescription date (inc prescription date)	Numeric	11,1	(((Count of inhalers * doses in pack) / 365) * mcg strength) / average prescribing dosage for saba (ie 200 mcg Salbutamol / 500mcg Terbutaline / 180mcg Albuterol) to get SABA Daily Dose. Ensure that the saba daily dosage * average prescribing dosage (ie 200mcg Salbutamol) equals SABA Daily Dosage	x		x	
out_SABA_Daily_Dosage	Based on average number of SABA puffs per day over the year x strength in mcg	1 Year After prescription date (inc prescription date)	Numeric	11,2	((Count of inhalers * doses in pack) / 365) * mcg strength	x		x	

Variable_Name	Description	Period	Data Type	Length	Definition / Validation Rules	Data present in primary care database	Data present in hospital database	Data present in pharmacy database	Data present in test database
out_ICS_Daily_Dose	Average no of ICS doses per day	1 Year After prescription date (inc prescription date)	Numeric	11,1	((Count of inhalers * doses in pack) / 365)	x		x	
out_ICS_Daily_Dosage	Average ICS daily dosage (mcg BDP eqv) - average daily puff of ICS	1 Year After prescription date(inc prescription date)	Numeric	11,2	((Count of inhalers * doses in pack) / 365) * mcg strength	x			
out_ICS_Scripts	No of scripts prescribed in the next 12 months	1 Year After prescription date (inc prescription date)	Numeric	11	Check that ICS scripts is relative to daily dose	x		x	
out_ICS_Inhalers	No of inhalers issued in the next 12 months	1 Year After prescription date (inc prescription date)	Numeric	11	Check that ICS inhalers is relative to ICS scripts.	x		x	
out_ICS_Total_Dosage	Total dosage in micrograms prescribed in outcome period – bdp	1 Year After prescription date (inc prescription date)	Numeric	11		x		x	
out_ICS_Duration	Total Pack Days	1 Year After prescription date (inc	Numeric	17	Sum (Number doses in pack / Prescribing instructions)	x		x	

Variable_Name	Description	Period	Data Type	Length	Definition / Validation Rules	Data present in primary care database	Data present in hospital database	Data present in pharmacy database	Data present in test database
		prescription date)							
out_ICS_Actual_Period *	Actual prescription days.	1 Year After prescription date (inc prescription date)	Numeric	17	(date of last script - date of first script) + Number pack days of last script	x		x	
out_Spacer_Device	Indicate if patients were issued with a spacer device: 1 = Yes, 0 = No	1 Year After prescription date (inc prescription date)	Numeric	1		x		x	
out_ICS_Last_Dose	Indicate last ICS dose prescribed to patient during outcome period. Based on prescribed dose * mcg strength in bdp-eqv.	1 Year After prescription date	Numeric	11		x		x	
out_ICS_DaysDiff	No of days between prescription date and last ICS issued to patient	1 Year After prescription date	Numeric	11		x		x	
out_LABA	Indicate if patient receives any LABA in outcome period	1 Year After prescription date	Numeric	1	ATC -R03AC	x		x	
out_LABA_Rx	Number of LABA scripts issued to patient	1 Year After prescription date	Numeric	11	ATC -R03AC	x		x	

Variable_Name	Description	Period	Data Type	Length	Definition / Validation Rules	Data present in primary care database	Data present in hospital database	Data present in pharmacy database	Data present in test database
out_LTRA	Indicate if patient received any LTRA in outcome period	1 Year After prescription date	Numeric	1	ATC -R03DC	x		x	
out_LTRA_Rx	Number of LTRA scripts issued to patient	1 Year After prescription date	Numeric	11	ATC -R03DC	x		x	
out_THEO_Rx	Number of Theophylline scripts issued to patient	1 Year After prescription date	Numeric	11	ATC -R03DA	x		x	
Change_In_Therapy	Indicate if patient had a change in therapy in the outcome period ie increase in ICS (>=50%) or change in ICS drug or inhaler device or the add on of Theophylline or LTRA: 1 = Yes, 0 = No	1 Year After prescription date	Numeric	1		x		x	
Increase_In_ICS_1st	Indicate if their first change in therapy was as an increase in ICS. Yes, 0 = No	1 Year After prescription date	Numeric	1		x		x	
Increase_In_ICS_Days	Number of days between date of prescription date and date of FIRST change as an Increase in ICS.	1 Year After prescription date	Numeric	10		x		x	

Variable_Name	Description	Period	Data Type	Length	Definition / Validation Rules	Data present in primary care database	Data present in hospital database	Data present in pharmacy database	Data present in test database
Change_in_Drug_1st	Indicate if their first change in therapy was a change in their ICS drug type: 1 = Yes, 0 = No	1 Year After prescription date	Numeric	1		x		x	
Change_in_Drug_Days	Number of days between date of prescription date and date of FIRST change as a Change in ICS drug.	1 Year After prescription date	Numeric	10		x		x	
Change_in_Device_1st	Indicate if their first change in therapy was a change in device: 1 = Yes, 0 = No	1 Year After prescription date	Numeric	1		x			x
Change_in_Device_Days	Number of days between date of prescription date and date of FIRST change as a Change in Device.	1 Year After prescription date	Numeric	10		x		x	
Add_on_Therapy_1st	Indicate if their first change in therapy was the addition of a LTRA or Theophylline: 1 = Yes, 0 = No	1 Year After prescription date	Numeric	1		x		x	
Add_on_Therapy_Days	Number of days between date of prescription date and date of FIRST change	1 Year After prescription date	Numeric	10		x		x	

Variable_Name	Description	Period	Data Type	Length	Definition / Validation Rules	Data present in primary care database	Data present in hospital database	Data present in pharmacy database	Data present in test database
	as the Add on of Therapy.								
Increase_in_ICS	Indicate if change in therapy was an increase in their ICS. Please Note: A patient could have multiple changes: 1 = Yes, 0 = No	1 Year After prescription date	Numeric	1		x		x	
Change_in_Drug	Indicate if change in therapy was a change in their ICS drug type. Please Note: A patient could have multiple changes: 1 = Yes, 0 = No	1 Year After prescription date	Numeric	1		x		x	
Change_in_Device	Indicate if change in therapy was a change in device category ie BAI,MDI,DPI. Please Note: A patient could have multiple changes: 1 = Yes, 0 = No	1 Year After prescription date	Numeric	1		x		x	
Change_in_Device_Type	Indicate if patient changed device type ie Accuhaler to Clickhaler. 1 = Yes, 0 = No. Please Note: does not affect treatment success.	1 Year After prescription date	Numeric	1		x		x	

Variable_Name	Description	Period	Data Type	Length	Definition / Validation Rules	Data present in primary care database	Data present in hospital database	Data present in pharmacy database	Data present in test database
Add_on_Therapy	Indicate if change in therapy was the addition of a LTRA or Theophylline. Please Note: A patient could have multiple changes. 1 = Yes, 0 = No	1 Year After prescription date	Numeric	1		x		x	
Add_Seretide	Indicate if the addition of therapy was as a fixed combination inhaler Seretide. Please note: Patient could have multiple additional therapies. 1 = Yes, 0 = No	1 Year After prescription date	Numeric	1		x		x	
Add_Symbicort	Indicate if the addition of therapy was as a fixed combination inhaler Symbicort. Please note: Patient could have multiple additional therapies. 1 = Yes, 0 = No	1 Year After prescription date	Numeric	1		x		x	
Add_Fostair	Indicate if the addition of therapy was as a fixed combination inhaler Fostair. Please note: Patient could have multiple additional	1 Year After prescription date	Numeric	1		x		x	

Variable_Name	Description	Period	Data Type	Length	Definition / Validation Rules	Data present in primary care database	Data present in hospital database	Data present in pharmacy database	Data present in test database
	therapies. 1 = Yes, 0 = No								
Add_LABA	Indicate if the addition of therapy was a separate LABA inhaler. Please note: Patient could have multiple additional therapies. - 1 = Yes, 0 = No	1 Year After prescription date	Numeric	1		x		x	
Add_LTRA	Indicate if the addition of therapy was as a leukatriene antagonist. Please note: Patient could have multiple additional therapies. 1 = Yes, 0 = No	1 Year After prescription date	Numeric	1		x		x	
Add_THEO	Indicate if the addition of therapy was as a theophylline. Please note: Patient could have multiple additional therapies: 1 = Yes, 0 = No	1 Year After prescription date	Numeric	1		x		x	

9. REFERENCES

[i] Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma. National Heart, Lung, and Blood Institute, National Institutes of Health, 2007. (Accessed March 2008, at http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.pdf.)

[ii] British Guideline on the Management of Asthma, May 2008. 2008. (Accessed 26 June 2008, at http://www.sign.ac.uk/guidelines/fulltext/101/index.html.)

[iii] Global Strategy for Asthma Management and Prevention, updated 2008. 2008. (Accessed at http://www.ginasthma.org.).

[iv] Ivancsó I, Böcskei R, Müller V, and Tamási L. Extrafine inhaled corticosteroid therapy in the control of asthma. J Asthma Allergy. 2013; 6: 69–80.

[v] Shepherd J, Rogers G, Anderson R, et al. Systematic review and economic analysis of the comparative effectiveness of different inhaled corticosteroids and their usage with long-acting beta2 agonists for the treatment of chronic asthma in adults and children aged 12 years and over. Health Technol Assess 2008;12:1-360.

[vi] Herland K, Akselsen JP, Skjonsberg OH, et al. How representative are clinical study patients with asthma or COPD for a larger "real life" population of patients with obstructive lung disease? Respir Med. 2005;99(1):11–9.

[vii] Travers J, Marsh S, Williams M, Weatherall M, Caldwell B, Shirtcliffe P, Aldington S, Beasley R. External validity of randomised controlled trials in asthma: to whom do the results of the trials apply? Thorax. 2007;62(3):219–23.

[viii] Appleton SL, Adams RJ, Wilson DH, et al. Spirometric criteria for asthma: adding further evidence to the debate. J Allergy Clin Immunol 2005;116(5):976–82.

[ix] Price D, Martin RJ, Barnes N, et al. Prescribing practices and asthma control with hydrofluoroalkane-beclomethasone and fluticasone: A real-world observational study. J Allergy Clin Immunol. 2010; 126:511-518.e10.

[x] Colice G, Martin RJ, Israel E, et al. Asthma outcomes and costs of therapy with extrafine beclomethasone and fluticasone. J Allergy Clin Immunol 2013: 132: 45–54 e10.

[xi] Herings RMC. PHARMO: A record linkage system for postmarketing surveillance of prescription drugs in The Netherlands. Pharmaco-epidemiology and - therapy, Utrecht University, Utrecht 1993:232.