STUDY TITLE: The healthcare costs associated with comorbidities of refractory asthma and systemic steroid exposure in the UK

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A Respiratory Effectiveness Group Protocol

PROTOCOL

BACKGROUND & RATIONALE

Patients with refractory asthma continue to have poorly controlled asthma and/or frequent exacerbations despite management with high-dose steroid therapy; as such, the present a significant unmet clinical need where (1,2,3). Although the prevalence of refractory asthma is unclear, it is been estimated to account for 5–10% of the total asthma population (1,4,5,6,). Refractory asthma patients pose a significant challenge to healthcare professionals. They suffer significant morbidities, have high levels of healthcare utilization (e.g. unscheduled healthcare visits, frequent exacerbations, hospital admissions) and require significant drug therapies and diagnostic procedures (7,8,9). In addition to the direct cost of refractory asthma to the health service, there are also indirect socio-economic costs to patients and their families in the form of loss of work and days off school and patients are at risk of treatment-related adverse events (particularly those treated with systemic steroids), which may impact on their quality of life.

There remain many unanswered questions about refractory asthma. It is believed that refractory asthma is associated with a substantial economic burden and this warrants further detailed investigation.

Refractory asthmatics continue to have significant symptoms and frequent exacerbations despite high dose treatment and specialised care (10). Currently steroid sparing agents are used infrequently due to risks of adverse events and where they are used they show little effect (11,12). Omalizumab has been shown to have a positive steroid sparing effect in the refractory asthma group (13-16), but it remains one of the few suitable options for therapy. It is probable that new therapies for this group will be more expensive than standard asthma therapies and at a price level similar to omalizumab.

To date no study appears to have looked directly at the cost of refractory asthma or adverse effects of systemic steroids in the refractory asthma group. There is clear evidence to show adverse events in other clinical populations (17-24) (see Table 1) and, with treatment options being limited, it is important to identify the exact cost and adverse effects of systemic steroid use in this subset of asthma. Addressing such questions will help to influence the future management of patients and will be key to informing cost-effectiveness analyses, advances in asthma therapies and steroid sparing strategies which will help reduce the burden of these adverse events as well as the overall burden of refractory asthma.

Table 1: Effects of systemic steroids (17-24)

Disease/Effect
Osteoporosis
Fracture
Diabetes
Hypertension
Ophthalmic effects- cataracts, glaucoma
Gastric conditions- peptic ulcer disease

Psychiatric events- anxiety, depression, agitation
Infections
Sleep disturbances-insomnia
Dyslipidaemia
Weight gain
Skin conditions- bruising, thinning, striae, skin atrophy, acne
Muscle weakness/myopathy
Cardiovascular conditions –MI, heart failure
Oral candidasis
Hyperglycaemia
Adrenal suppression/insufficiency
Osteonecrosis
Cushingoid changes – moon facies, abdominal obesity

OBJECTIVE

This study builds on a cost of illness study for refractory asthma in the UK conducted in 2013 that used data from British Thoracic Society (BTS) Difficult Asthma Registry (manuscript submitted to Thorax 06/13).

This study will use the UK's Optimum Patient Care Research Database (OPCRD) to address a number of objectives relating to refractory asthma in the UK. The findings of the OPCRD evaluations will be compared to those of the BTS Difficult Asthma Registry morbidity prevalence data to help provide best morbidity prevalence estimates for the UK's refractory asthma populations and to inform the development of models to estimate the burden of steroid-induced morbidity.

The OPCRD will be used to:

(1) Evaluate the prevalence of steroid-induced morbidities in patients with refractory asthma compared to the prevalence with patients with well-controlled asthma and among non-asthmatic controls. Morbidity rates will be stratified by:
   a. Asthma severity: refractory asthma vs well-controlled asthma vs non-asthma controls
   b. Age & Gender (12-20;21-30;31-40;41-50;51-60;61-70;70+)

(2) Evaluate the new incidence rate of morbidities in patients with refractory asthma vs well-controlled asthma vs non-asthma controls

Combining data from the OPCRD and the BTS Difficult Asthma Registry:

(3) Morbidity rates in refractory asthma patients will be compared and contrasted.

(4) Using data from (1) and (3), up-to-date UK prevalence rates for potential steroid-induced morbidities will be provided for patients with refractory asthma vs well-controlled asthma.

(5) Based on (2) and (4):
   a. The annual cost associated with the treatment and management of systemic steroid-induced morbidities will be estimated

b. A model estimating the lifetime cost of morbidity attributable to systemic steroid exposure, will be developed.

STUDY DESCRIPTION

Design

There will be two phases to the study:

Phase 1: Cross sectional analysis matched cohort comparison of morbidity rates in refractory asthma, well-controlled asthma and non-asthmatic controls.

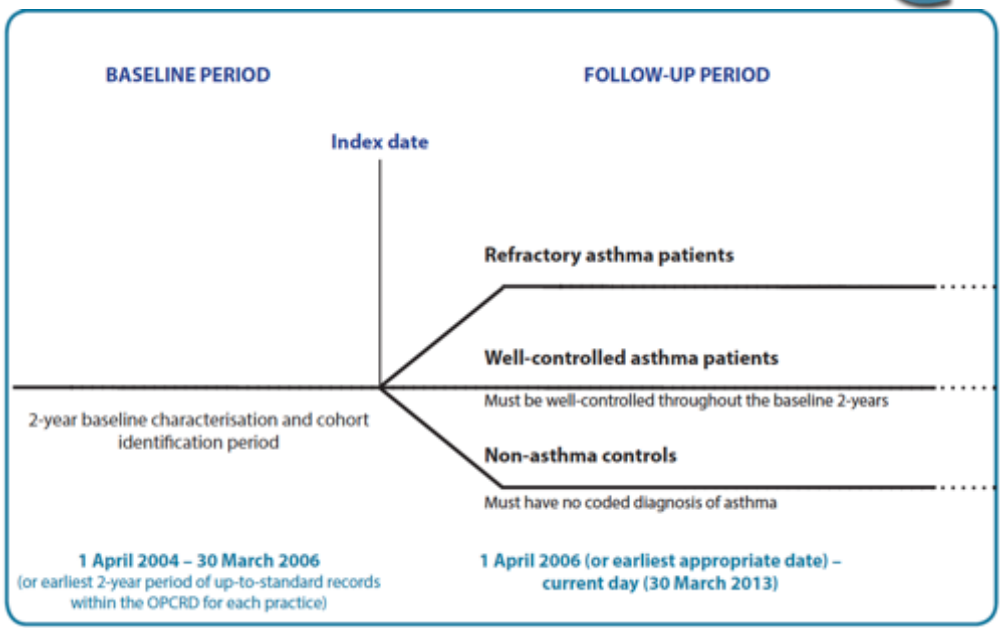
Phase 2: 7-year longitudinal matched cohort comparison of new incidence of morbidities in patients with refractory asthma, well-controlled asthma and non-asthmatic controls.

Study period

Phase 1: The cross-sectional analysis will be evaluated over a 2-year period (necessary for evaluation of cohort eligibility). This will be the latest 2-year period within the OPCRD, i.e. (1 April 2011– 30 March 2013).

Phase 2: The longitudinal study phase will involve:

- A 2-year qualifying period for cohort definition and patient characterization: 1 April 2004 to 30 March 2006 (or the earliest two-year period for which practices have two continuous years of up-to-standard records) prior to the index date (1 April 2006, or earliest period following 2 consecutive years of up-to-standard records)
- A follow-up period running from 1 April 2006 (or earliest appropriate period) to current day (30 March 2013).



Data sources

Optimum Patient Care Research Database

This study will use data from the Optimum Patient Care Research Database (OPCRD).

The **OPCRD** comprises data extracted through the Optimum Patient Care clinical service evaluation. The clinical evaluation involves a combined review of (anonymised) electronic medical records (EMRs) and patients' responses to disease-specific questionnaires (**Appendix 1**)[1] and characterizes patients in terms of their demography, disease control and exacerbation history and makes guideline-based recommendations for possible management changes that may help to optimise control at the lowest possible therapeutic dose and reduce risk of future exacerbations. A full data dictionary for the OPCRD, which indicates the data fields within the dataset, is detailed in **Appendix 2**.

At the time of writing, OPCRD contains anonymised, research-quality data for approximately 300,000 patients with asthma (and 100,000 patients with chronic obstructive pulmonary disease [COPD]) collected from more than 300 practices across the UK that subscribe to OPC for respiratory review service.

BTS Difficult Asthma Registry

In 2006, the BTS Research Committee, in conjunction with physicians with a specialist interest in difficult asthma, established a National Registry for dedicated UK Difficult Asthma services. There are currently seven Specialist Difficult Asthma Services submitting data to the UK Registry - Royal Brompton Hospital, London; Glenfield Hospital, Leicester; University Hospital of South Manchester; Birmingham Heartlands Hospital; Gartnavel Hospital, Glasgow; Stobhill Hospital, Glasgow and Belfast City Hospital.

[1] See **Appendix 1** for a copy of OPC's asthma questionnaire

The Registry is hosted online by Dendrite Clinical Systems and admits password protected anonymised data, after fully informed written consent from patients. The registry records patient demographics including gender, age at diagnosis, occupation and BMI as well as disease characteristics such as asthma medication, exacerbations, and pulmonary function. The Registry is currently used to facilitate numerous research projects. Details of these projects can be found at http://demo.e-dendrite.com/csp/asthma/frontpages/faq.csp.

Patients from across the 7 clinical centres, who after detailed systematic assessment are deemed to receive maintenance systemic steroid therapy, have been selected and screened for any of the comorbidites listed in Table 1. In Belfast City Hospital, all patients receiving maintenance systemic steroid therapy have been selected and their medical notes screened for any comorbidites (Table 2).

Table 2: Steroid induced morbidity Belfast cohort

Disease as per Belfast Cohort	%	(95% CI)
Diabetes	7/93(8%)	(3%-15%)
Impaired glucose tolerance	1/93(1%)	(0%-6%)
Hypertension	17/93(18%)	(11%-28%)
Hypercholesterolaemia	17/93(18%)	(11%-28%)
Osteoporosis/ostopenia	45/85(53%)	(46%-63%)
Obstructive sleep apnoea/OSA	9/93(10%)	(5%-18%)
Sleep disturbance	18/93(19%)	(12%-29%)
Gastric symptoms	67/93(72%)	(62%-81%)
Low mood/depression	44/93(47%)	(37%-58%)
Weight gain	57/93(61%)	(51%-71%)
Obese (BMI >30)	33/93(35%)	(26%-46%)
Cushingoid	27/93(29%)	(20%-39%)
Cataracts	13/93(14%)	(8%-23%)
Glaucoma	3/93(3%)	(1%-9%)
Skin problems	13/93(14%)	(8%-23%)
Myopathy	1/93(1%)	(0%-6%)

Ethics

Optimum Patient Care & planned evaluation

The OPCRD has been approved by Trent Multi Centre Research Ethics Committee for clinical research use, and this study protocol will be submitted to OPCRD's Anonymised Data Ethics Protocols and Transparency (ADEPT) Committee for approval to sanction the use of the OPCRD for the purposes of the proposed study.

BTS Difficult Asthma Registry

ORECNI have given ethical approval to use the BTS Difficult Asthma Registry (10/NIR02/37) for health economic analysis and examination of the prevalence of steroid-induced comorbidity in difficult asthma.

Study population

All patients

Inclusion criteria

To be eligible for inclusion in the study, all patients must meet the following inclusion criteria:

- 2 years of continuous medical records (the latest such period available for each patient)
- Age >12 years:[2]

Exclusion criteria

To minimize the risk of possible confounding of results, the patients with any of the following Read Code diagnosed conditions (for which oral steroid treatment may be prescribed) will be excluded from the study population:

- Crohn's disease
- Ulcerative colitis
- Autoimmune diseases – autoimmune hepatitis
- Joint and muscle diseases – rheumatoid arthritis, polymyalgia rheumatica
- Chronic respiratory conditions other than asthma, i.e. Chronic Obstructive Pulonary Disease (COPD); bronchiectasis; cystic fibrosis; interstitial pulmonary fibrosis; tuberculosis.

Eligibility criteria for comparator groups

In addition to the overall inclusion/exclusion criteria for the study, patients in the different comparator groups must meet the following eligibility criteria:

Refractory Asthma population

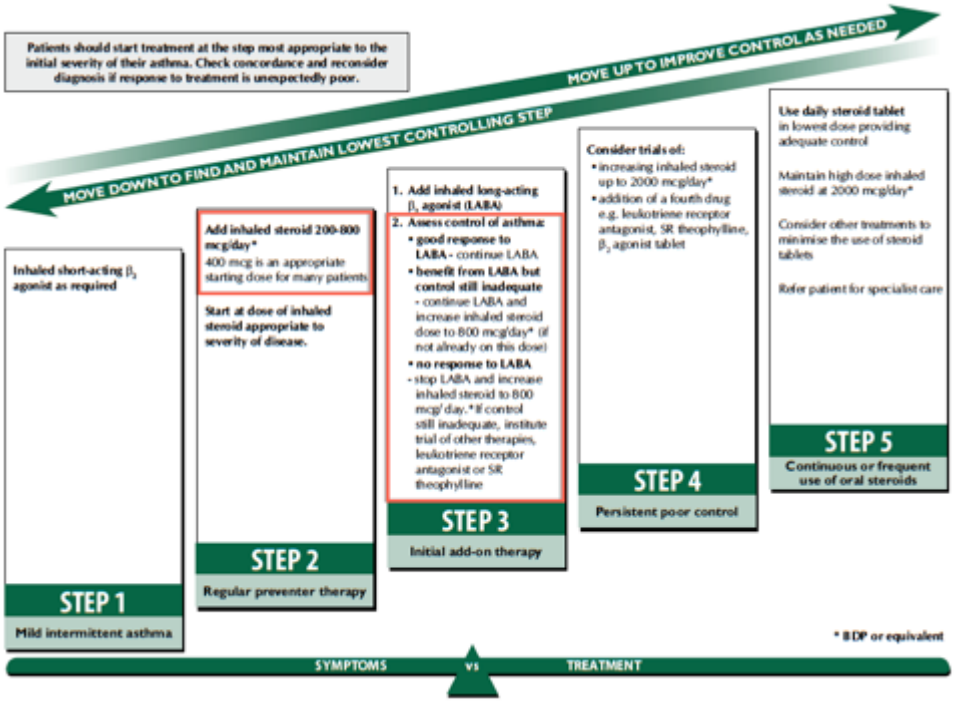
- Have a Read Code diagnosis of asthma
- Prescriptions for Step 5 BTS/SIGN asthma treatment during the 2-year study period (ICS dose of 2000mcg/day- see below)
- Receive ≥4 prescriptions for systemic steroids in each of the two study years (see **Appendix 3**)

Well-controlled asthma population

- Have a Read Code diagnosis of asthma
- Prescriptions for Step 2-3 BTS/SIGN treatment only during the 2-year study period (defined as inhaled corticosteroid therapy ± long-acting beta-agonist therapy; ICS dose of ≤800mcg beclometasone dipropionate equivalent – see below):

[2]Age will be based on each patient's age on day 1 of the 2-year study period

Summary of BTS asthma management guidelines stepwise approach[3]



Control population

- No Read Code diagnosis of asthma
- Diagnosis of rhinitis – either Read Code diagnosis or managed as (i.e. prescriptions for rhinitis therapy in their records).

Subgroup analyses

Morbidity rates will be evaluated for the subgroup of refractory asthma patients who receive maintenance oral steroids quantified by ≥6 oral steroid prescriptions in both years of the study.

Covariates

Prior research in respiratory disease has identified a range of potential confounders that may impact on study outcomes. These include a range of demographic, disease severity, treatment and co-morbid factors. These variables will be extracted, where available, for all patients.

Potential confounders examined at (or closest to) the Phase 1 "Start" date and day 1 of the Phase 2 qualifying period:

- Age of patient
- A marker of socio-economic status where possible, i.e. post codes
- Gender of patient
- Height of patient
- Weight of patient
- Body Mass Index (BMI) (in sub-group where BMI can be evaluated)

[3] British Thoracic Society / Scottish Intercollegiate Guidelines Network. Guideline 101. British Guideline on the Management of Asthma: A national clinical guideline. Available online at: http://www.sign.ac.uk/pdf/sign101.pdf (last accessed 18 July 2013)

- Ethnicity
- Lung function, in terms of percent predicted PEF[4] prior to index date
- Smoking status
- ICS device type
- ICS drug
- Date of first asthma diagnosis
- Duration of asthma
- ICS dose prescribed at index date.

Potential confounders examined over the (a) Phase 1, 2-year cross sectional period and (b) 2-year Phase 2 qualifying period:

- Presence / absence of comorbid rhinitis (diagnosis ever and / or prescriptions)
- Where rhinitis is present, use of nasal steroids for its treatment.
- Presence / absence of comorbid eczema (diagnosis ever and / or prescriptions for eczema)
- Other important unrelated co-morbidities will be expressed using the Charlson Comorbidity Index (CCI)
- Presence of GERD (diagnosis ever and / or prescriptions for GERD therapy over the 2-year analysis period)
- Presence of cardiac disease (diagnosis ever and / or prescriptions for cardiac drugs)
- Number of asthma consultations that did not result in a prescription for an oral steroid
- Number of hospital outpatient attendances where asthma is recorded as the reason for referral
- Number of hospitalisations for asthma or possibly respiratory related (a non-specific hospitalisation code and an asthma / respiratory code within a one week window).
- Number of prescriptions for any antibiotic where the reason for the prescription is LRTI
- Number of prescriptions for any respiratory therapy (split by number of prescriptions for each)
- Number of exacerbations for asthma in year preceding assessment, where an exacerbation is defined as: treatment with oral corticosteroids
- Number of general practice consultations for asthma that did not result in asthma treatment**Error! Bookmark not defined.**
- Number of hospital outpatient attendances in the prior year where asthma and / or other respiratory illness was the reason for referral.
- Number of hospitalisations for asthma and / or respiratory illness in the prior year (including non-specific hospitalisations with an asthma / respiratory code within a one week window).
- Number of short-acting beta-agonist (SABA) prescriptions received (calculated based on total combined dose of refilled prescriptions and averaged over 365x2 days).
- Average ICS daily dose (calculated based on total combined dose of refilled prescriptions and averaged over 365x2 days).

Morbidity evaluations

[4] Calculated using Roberts' Equations for adults

Incidence of the following comorbidities will be evaluated (See table). Rates will reported for each treatment group and (for well-controlled asthma and non-asthmatics controls) compared relative to the refractory asthma patient group rate.

Suggested search term OPCRD*
Diabetes/Type 2 Diabetes - identified by diagnostic codes and diabetic drug prescriptions
Hypertension (On GP hypertension register, Read code for hypertension)
Hypercholesterolaemia (listed as diagnosis or on treatment for hypercholesterolaemia)
Osteoporosis/Osteopenia (diagnosed by DEXA scan or previous fragility fracture)
Obstructive sleep apnoea/Sleep apnoea/OSA (Read code OSA)
GORD (Read code GORD/Heartburn/Reflux)
Depression/Anxiety/Low mood (Read code, GP depression register, on SSRI, attending mental health professional)
Obese/Obesity (BMI >30)
Cushingoid features/Cushings syndrome
Cataracts (Read code, previous surgery)
Glaucoma(Read code, on treatment for glaucoma)
Steroid induced skin complaint e.g. acne, skin thinning, bruising, striae
Myopathy, muscle weakness(Read code)
Cardiovascular disease
Chronic renal disease

METHODS

Statistical analysis

Matching

For both Phase 1 and 2 of the study, well-controlled asthma patients and non-asthmatic controls will be matched to refractory asthma patients. To increase the power of the analysis matching will be on a 5-to-1 basis, with five randomly selected well-controlled asthma patients and five non-asthmatic control patients matched to each refractory asthma patients.

Matching criteria will be patients':

- Age
- Gender
- Year of birth.

Phase 1: cross-sectional evaluation

Frequency of existing morbidities in the 2 year period (2011-2013) will be evaluated and reported separately for each group. Rate ratios will be evaluated for each morbidity (with the refractory asthma rate as the reference rate) with 95% confidence intervals. See **Appendix 3** for dummy output tables.

Comparison with the BTS Difficult Asthma Register: the morbidity prevalence rates obtained in the BTS Difficult Asthma Register will be compared with the

corresponding prevalence rates in the OPCRD refractory asthma on systemic steroids group using indirect standardisation. This will take account of possible differences in age and sex distribution between the groups and will produce a standardised prevalence ratio for each morbidity. It is anticipated that this analysis will only be meaningful for morbidities such as diabetes which are completely recorded in OPCRD.

Phase 2: longitudinal evaluation

The evaluation of the incidence of new morbidities in the period 1 April 2006 – present day will be evaluated for each patient group (refractory asthma, well-controlled asthma and non-asthmatic controls). Survival analyses will be conducted; patients who are lost to follow up (e.g. through leaving the practice or through death) will be censored.

A proportional hazards model will be used with stratification to take account of the matching and the results expressed as hazard ratios with 95% confidence intervals. Death will also be investigated as a competing risk. The analysis will focus on new complications arising during the follow-up period. A code for a chronic condition appearing during follow-up having not been mentioned within a preceding two year period will be considered to be a new diagnosis.

Power calculation

The power of the cross-sectional part of this study to detect excesses of steroid-induced morbidity depends on the size of the groups, the frequency of the morbidity in the comparison group (well-controlled asthmatic population or non-asthmatic population) and the magnitude of the excess expressed in terms of the relative risk/hazard, the ratio of the morbidity rates in the refractory asthma and comparison groups. The following table illustrates the power of a study of 1,000 asthma patients on maintenance steroids to detect various relative risks depending on the prevalence of the morbidity.

Table. Power of a study of 1,000 asthma patients on maintenance steroids to detect a given increase in risk as statistically significant (P<0.05) assuming a comparison group 5-times the size.

Prevalence of morbidity in comparison group	Relative risk				
	x1.25	x1.5	x2.0	x2.5	x3.0
1%	9% †	26%	68%	91%	98%
2%	16%	47%	92%	100%	100%
3%	22%	63%	98%	100%	100%
4%	29%	76%	100%	100%	100%
5%	35%	85%	100%	100%	100%

† Stata command: **sampsi 0.0125 0.01, n1(1000) r(5)**

Statistical tools

(i) All statistical analyses will be carried out using SAS v9.3, SPSS v20, Stata release 12 and EXCEL 2007. In addition to the statistical methods already mentioned, methods that may also be used include:Poisson Regression

models: will be used to determine predictors of future risk in terms of severe exacerbation rates over subsequent 1 & 2 years.

(ii) Ordinal logistic regression models: will be used when annual exacerbations are categorised 0,1 and ≥2.

(iii) The Somers' d statistics: will be used to assess the association between pairs of variables

(iv) Cohen's Kappa Coefficient: will be used to assess inter-rate agreement of measures

(v) Receiver Operating Characteristics (ROC) curves: will be constructed in EXCEL 2007

(vi) Other analyses will use summary statistics: Kruskal Wallis test / Chi Square test.

Limitations of the study design, data sources and analytical methods

As with all database studies a number of limitations exist, such as incomplete coding and recording of events, e.g. diagnoses, reason for prescribing. The effects of this will be minimised by "validating" prevalence rates across two different UK datasets to inform the most appropriate model for evaluating steroid-related morbidity and cost burdens. However, given the inherent limitations of database studies, the study results should be viewed in conjunction with those of other study designs to ensure consideration of the full evidence base.

FUNDING & THE RESEARCH TEAM

Provision of the OPCRD data for the study will be funded through a research grant from the Respiratory Effectiveness Group (REG; www.effectivenessevaluation.org) – a new investigator-led initiative designed to raise the quality and profile of real-life respiratory research. See **Appendix 5** (or visit the group's website) for more information about the REG initiative.

The analysis will be undertaken by researchers at the Centre for Infection and Immunity & Centre for Public Health, Queens University Belfast, Belfast, UK Belfast.

Research Collaborators

Queens University Belfast
Lead Investigator: Liam Heaney, Centre for Infection and Immunity, Queens University Belfast, Belfast, UK
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Respiratory Effectiveness Group
David Price: Primary Care Respiratory Society UK, Professor of Primary Care Respiratory Medicine, University of Aberdeen, UK; Director Optimum Patient Care

Ltd and Research in Real Life Ltd
Alison Chisholm: Respiratory Effectiveness Group Implementation Manager

STUDY TIMELINE

This study will be funded as part of REG's year 1 funding (1 April 2013 and will run through to 31 March 2014).

It is anticipated that the study will be completed within 6 months of provision of data from OPCRD and publications will be completed within a 12 month period.

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APPENDIX LIST

List of Appendices:

- **APPENDIX 1**: Questionnaire used for optimum patient care's asthma service evaluation
- **APPENDIX 2**: OPCRD data dictionary
- **APPENDIX 3:** Glucocorticoid therapies in the british national formulary (section 6.3.2)
- **APPENDIX 4**: Dummy outcome tables for phase 1 of the study
- **APPENDIX 5**: The Respiratory Effectiveness Group

APPENDIX 1: QUESTIONNAIRE USED FOR OPTIMUM PATIENT CARE'S ASTHMA SERVICE EVALUATION

Asthma Questionnaire

Please take a few minutes to complete the whole questionnaire, following the instructions at the head of each section.

In the last week:	0	1	2	3	4	5	6	7	8	9	10+
How many times have you used your reliever inhaler?	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

Thinking about the last 7 days (please tick one box for each question):	0	1	2	3	4	5	6	7
How many days has asthma interfered with your normal activities (eg sport, school, work/housework)?	☐	☐	☐	☐	☐	☐	☐	☐
How many nights have you been affected/woken by asthma symptoms (including cough)?	☐	☐	☐	☐	☐	☐	☐	☐
How many days have you experienced asthma symptoms?	☐	☐	☐	☐	☐	☐	☐	☐

In the past 4 weeks, did you:	Yes	No	Unsure
Miss any work, school, or normal daily activity because of your asthma?	☐	☐	☐
Wake up at night because of asthma?	☐	☐	☐
Believe that your asthma was well controlled?	☐	☐	☐
In general, do you use an inhaler for quick relief from asthma symptoms?	☐	☐	☐

If yes, in the past 4 weeks, what was the highest number of puffs in 1 day you took of the inhaler?

☐ 0 ☐ 1 to 4 puffs ☐ 5 to 8 puffs ☐ 9 to 12 puffs ☐ More than 12 puffs

In the last 12 months:	0	1	2	3	4	5	6	7	8	9	10+
How many times have you needed a course of steroid tablets for worsening asthma?	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
How many days have you had off work/education because of asthma?	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

How many times have you been admitted to hospital with breathing or chest problems? ☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5+

About smoking:

Which best describes you? ☐ Never smoked ☐ Used to smoke, but don't now ☐ Still smoking

	1-5	6-10	11-15	16-20	21-30	31-40	41-50	50+
If you smoke or used to smoke, how many do you/did you smoke per day?	☐	☐	☐	☐	☐	☐	☐	☐
If you smoke, or used to smoke, how many years have you smoked/did you smoke?	☐	☐	☐	☐	☐	☐	☐	☐

Smoking can make asthma worse - if you still smoke, would you like support from your GP or practice nurse to quit? Yes ☐ No ☐

About your nose:

Do you have any of these symptoms: itchy, runny, blocked nose or sneezing when you don't have a cold? ☐ No ☐ Occasionally & little bother ☐ Occasionally & quite a bother ☐ Most days but little bother ☐ Most days & a lot of bother

Do any of the following upset your asthma? Tick all that apply. ☐ Colds ☐ Strenuous activity or exercise ☐ Allergies eg cats, dogs, pollen ☐ Cigarette smoke

Please complete other side

Do you have a preventer inhaler (usually brown, orange, red or purple)? ☐ *Yes* ☐ *No, skip to* ***Section B***

Which statement best describes how you take your regular Asthma treatment. Please tick only one box

☐ *I take it every day* ☐ *I take it some days but others I do not* ☐ *I used to take it, but now I do not* ☐ *I take it only when I have symptoms* ☐ *I never take it*

Please tell us how you well you use your preventer inhaler:

"I think my inhaler technique is very poor" ☐ *1* ☐ *2* ☐ *3* ☐ *4* ☐ *5* ☐ *6* "I think my inhaler technique is excellent"

About your preventer inhaler:	*Strongly disagree*	*Disagree*	*Not Sure*	*Agree*	*Strongly agree*
I need to take my inhaler(s) regularly for my asthma to be well controlled	☐	☐	☐	☐	☐
I find my inhaler(s) difficult to use	☐	☐	☐	☐	☐
Having to take regular asthma medication worries me	☐	☐	☐	☐	☐
I would prefer to take my asthma medications in a once a day dose	☐	☐	☐	☐	☐

Still about your preventer inhaler:	*Never*	*Rarely*	*Sometimes*	*Often*	*Always*
I use it only when I feel breathless	☐	☐	☐	☐	☐
I avoid using it if I can	☐	☐	☐	☐	☐
I forget to take it	☐	☐	☐	☐	☐
I decide to miss a dose	☐	☐	☐	☐	☐
I choose to take it once a day	☐	☐	☐	☐	☐

When you use your preventer inhaler:	*Yes*	*No*
Do you feel a sensation at the back of the throat?	☐	☐
Do you sometimes feel a need to cough	☐	☐
Do you feel your medication is deposited at the back of your throat?	☐	☐

Questions about preventer inhaler side-effects - please tick yes or no for each one

	Yes	*No*		*Yes*	*No*
Continual sore mouth/throat	☐	☐	Hoarse voice	☐	☐
Oral Thrush	☐	☐	Abnormal Weight Gain	☐	☐
Bruising	☐	☐	Cough	☐	☐

Section B: Have you had your inhalers checked in the last 12 months? ☐ *Yes* ☐ *No*

Have you seen a specialist respiratory doctor or nurse outside the practice? ☐ *In the last year* ☐ *More than a year ago* ☐ *Never*

If you have a peak flow meter, please tell us your reading today:

for example: 4 2 0 ☐ *I don't have a peak flow meter*

In the future, would you be willing to participate in further research? If yes, please return your cover letter with this questionnaire ☐ *Yes* ☐ *No*

Practice Ref:

Survey Ref:

APPENDIX 2: OPCRD DATA DICTIONARY

1. Patient

The **Patient** file contains basic patient demographics, patient registration and practice registration details.

Field Name	*Content*
Patient_ID	Anonymised patient identifier
Practice_ID	Unique practice identifier.
Year_Of_Birth	Patient year of birth in format YYYY
Gender	Patient gender
Status	Patient registration status - (R) – Registered, (L) – Left, (D) - Death
Joined_Date	Date joined practice or date first registered on database
Leaving_Date	Date left practice or date first registered on database
Leaving_Reason	Reason for leaving practice
Post_Code	"Out" part of patient postcode and first character of "in" part of patient post code

2. Clinical

The **Clinical** file contains medical history events. This file contains all the medical history data entered on the GP system, including symptoms, signs and diagnoses. This can be used to identify any clinical diagnoses, and deaths. Patients may have more than one row of data. The data is coded using Read codes, which allows linkage of codes to the medical terms provided.

Field Name	*Content*
Patient_ID	Anonymised patient identifier
Event_Date	Date of event
Read_Code	Five byte read code for event including terminal code if available
Read_Term	Rubric associated with read_code
Numeric_1	First numeric value if stored
Numeric_2	Second numeric value if stored
Text	First 50 characters of any text associated with entry

3. Referral

The **Referral** file provides details of all referrals for the defined patient cohort identified by a medical code indicating the reason for referral. This table contains information involving patient referrals to external care centres (normally to secondary care locations such as hospitals for inpatient or outpatient care).

Field Name	*Content*
Patient_ID	Anonymised patient identifier
Event_Date	Date of event in format dd/mm/yyyy
Read_Code	Five byte read code for event including terminal code if available
Read_Term	Rubric associated with read_code
Referral_Type	Referral type e.g. Outpatient
Referral_To	Organisation referred to
Specialism	Referral by e.g. GP referral
Attendance_Type	Attendance type e.g. First visit, follow up

4. Therapy

The **Therapy** file contains details of all prescriptions on the GP system. This file contains data relating to all prescriptions (for drugs and appliances) issued by the GP. Patients may have more than one row of data. Drug products and appliances are recorded by the GP using the Multilex product code system.

Field Name	*Content*
Patient_ID	Anonymised patient identifier
Event_Date	Date of event in format dd/mm/yyyy
Drug_Code	Coding for drug
Drug_Term	Drug term associated with drug code
Form	Formulation e.g. inhaler, tablets etc
Dosage	Usage instructions
Quantity	The quantity supplied
numberpack	Number of packs prescribed
packsize	The units of quantity supplied. (the preparation)
issue_ty	Type of issue where A = Acute Issue, R = Repeat Issue
strength	Drug strength
numberdays	Treatment days
bnf_code	BNF code

5. Practice

The **Practice** file contains details for practices, including region and collection information.

Field Name	*Content*
PracticeID	Unique OPC practice id
Practice_NHS	Unique NHS practice identifier.
Practice_Name	Name of practice
Practice_Address1	Address line 1
Practice_Address2	Address line 2
Practice_Address3	Address line 3
Practice_Address4	Address line 4
Practice_Postcode	Post Code
Practice_list_size	Total practice list size
Last_Extract_Date	Date when practice last did an extract

6. Asthma Questionnaire Data Collection

The **Asthma Questionnaire Data Collection** file contains the data collected from the questionnaires received from patients participating in the OPC Asthma Review Service. The file provides the original response as well as calculated values derived from the patient responses to the questions. Questions currently being surveyed are the following:

Questions	***Answer Options***
In the last week, how many times have you used your reliever inhaler (usually blue).	0–9; ≥10
In the last 7 days, how many days has asthma interfered with your normal activities?	0–7
In the last 7 days, how many nights have you been affected/woken by asthma symptoms (including cough)?	0–7
In the last 7 days, how many days have you experienced asthma symptoms?	0–7

In the last 4 weeks, did you miss any work, school or normal daily activity because of your asthma?	Yes; No; Unsure
In the last 4 weeks, did you wake up at night because of asthma?	Yes; No; Unsure
In the last 4 weeks, did you believe that your asthma was well controlled?	Yes; No; Unsure
In the last 4 weeks, in general, do you use an inhaler for quick relief from asthma symptoms?	Yes; No; Unsure
If yes, in the past 4 weeks, what was the highest number of puffs in 1 day you took of the inhaler?	0 / 1 to 4 puffs; 5 to 8 puffs; 9 to 12 puffs; More than 12 puffs
In the last 12 months, how many times have you needed a course of steroid tablets for worsening asthma.	0–9; ≥10
In the last 12 months, how many days have you had off work/education because of asthma.	0–9; ≥10
In the last 12 months, how many have you been admitted to hospital with breathing or chest problems?	0–9; ≥10
In the last 12 months, how many time have you been treated in accident and emergency or anywhere other than your GP surgery for your asthma?	0–9; ≥10
About smoking, which best describes you?	1 = Never smoked, 2 = Current Smoker, 3 = Ex-smoker
If you smoke or used to smoke, how many cigarettes do you/did you smoke per day?	1-5; 6-10; 11-15; 16-20; 21-30; 31-40; 41-50; >50
If you smoke, or used to smoke, how many years have you smoked/did you smoke?	1-5; 6-10; 11-15; 16-20; 21-30; 31-40; 41-50; >50
Smoking can make asthma worse - if you still smoke, would you like support from your GP or practice nurse to quit?	Yes / No
Do you have any of these symptoms: itchy, runny, blocked nose or sneezing when you don't have a cold?'	No / Occasionally & Little Bother / Occasionally & Quite a Bother / Most days & Little Bother / Most Days & a lot of bother
Do any of the following upset your asthma?	Colds / Strenuous Activity & Exercise / Allergies e.g. cats, dogs, pollen / Cigarette smoke
Thinking about how often you take your regular Asthma treatment during the day:	1 = I always take it exactly at the time prescribed. 2 = I occasionally miss the odd dose. 3 = I often miss or forget to take doses. 4 = I take all once a day- it's easier. 5 = I never take it.
I think my inhaler technique is very poor / I think my inhaler technique is excellent.	An answer from 1 to 6 will indicate which statement best describes how they use their inhaler.
I do not need to take my inhaler(s) for my asthma to be well controlled / I need to take my inhalers(s) regularly for my asthma to be well controlled.	An answer from 1 to 6 will indicate which statement best describes how they use their inhaler.
I find my inhaler(s) easy to use /	An answer from 1 to 6 will indicate which

I find my inhaler(s) difficult to use.	statement best describes how they use their inhaler.
Taking regular asthma medication does not worry me / Taking regular asthma medication worries me.	An answer from 1 to 6 will indicate which statement best describes how they use their inhaler.
I prefer to take my asthma medications in a twice daily dose / I prefer to take my asthma medications in a once a day dose.	An answer from 1 to 6 will indicate which statement best describes how they use their inhaler.
I use it regularly / I use it only when I feel breathless.	An answer from 1 to 6 will indicate which statement best describes how they use their inhaler.
I never avoid using it if I can / I always avoid using it if I can.	An answer from 1 to 6 will indicate which statement best describes how they use their inhaler.
I never forget to take it / I always forget to take it.	An answer from 1 to 6 will indicate which statement best describes how they use their inhaler.
I never decide to miss a dose / I always decide to miss a dose.	An answer from 1 to 6 will indicate which statement best describes how they use their inhaler.
I never choose to take it once a day / I always choose to take it once a day.	An answer from 1 to 6 will indicate which statement best describes how they use their inhaler.
When using preventer inhaler, do you feel a sensation at the back of the throat?	Yes / No
When using preventer inhaler, do you sometimes feel a need to cough?	Yes / No
When using preventer inhaler, do you feel your medication is deposited at the back of your throat?	Yes / No
Experience any side effects for the preventer inhaler?	Yes / No
Perceived Side Effects: Continual sore throat?	Yes / No
Perceived Side Effects: Hoarse voice?	Yes / No
Perceived Side Effects: Oral Thrush?	Yes / No
Perceived Side Effects: Abnormal Weight Gain?	Yes / No
Perceived Side Effects: Bruising?	Yes / No
Perceived Side Effects: Cough?	Yes / No
Have you had your inhaler technique checked in the last 12 months?	Yes / No
Have you seen a specialist respiratory doctor or nurse outside the practice?	Yes / No
Do you have a peak flow meter?	Yes / No
If you have a peak flow meter, please tell us your reading today?	Value
In the future, would you be willing to participate in further research?	Yes / No
Do you have a preventer inhaler?	Yes / No