Study protocol for TEVA

Training requirements to master inhaler devices available in real-life clinical practice

A prospective evaluation of time required and patient preferences when training patients with asthma and COPD to use inhaler devices available as part of their routine care in the UK

Date:
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TITLE	Training requirements to master inhaler devices available in real-life clinical practice
Subtitle	A prospective evaluation of time required and patient preferences when training patients with asthma and COPD to use inhaler devices available as part of their routine care in the UK
Protocol version number	1.5
Medicinal product	Devices will not contain any active drug
Product code	Not Applicable
Marketing authorisation holder	Not Applicable
Marketing authorisation number	Not Applicable
Study aims and objectives	The aim of this study is to compare different inhaler devices in terms of training required, defined as (a) time required for patient education to device mastery and (b) patients' inhaler device preferences, in patients with asthma and COPD. The primary objective is to measure the time needed for patients to master the required inhaler technique for a specific delivery device available as part of their normal care. The secondary objective is to assess patient preference for inhaler devices
Country of study	UK
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1.0 Background

Chronic respiratory diseases represent a considerable burden on health care services.[1] They contribute to social inequalities in life expectancy, notably through preventable early deaths, as well as to excess winter deaths.[1] Chronic obstructive pulmonary disease (COPD) and asthma are major causes of morbidity.[2,3] In the United Kingdom (UK), COPD alone accounts for 1.4 million general practice consultations per year, and 1 in 8 emergency admissions.[1] Its prevalence is expected to rise between 2010 and 2020.[2,3] It is estimated that around 5.4 million people suffer from asthma in the UK.[4]

Factors that influence treatment benefits include diagnostic inaccuracy, inappropriate treatment choices, smoking, comorbid rhinitis, obesity, adherence to therapy and other psycho-social factors.[5-10] In addition, exploratory work using the UK Clinical Practice Research Database (CPRD) suggests that inhaler device type, and effective inhalation technique, may play an important role in achieving asthma control outcomes.[11]

A large proportion of patients prescribed inhaled medications do not use their inhalers correctly.[12,13] Overall, up to 90% of patients show incorrect technique in clinical studies with either standard pressurised Metered Dose Inhalers (pMDIs)[14,15] or Dry Powder Inhalers (DPIs) such as Accuhaler, Aerolizer, HandiHaler and Turbohaler.[16] Although these newer inhalers were designed to improve ease of use, significant rates of incorrect use among patients with asthma or COPD have been reported for all currently used inhaler designs,[12,16-21] even among regular adult users.[12,17-21] As such, it is important to consider the challenges from a holistic perspective.

One key challenge for many primary care practices is the allocation of personnel and time for patient training in inhaler technique, although the investment in time to provide device training could later save time, resources and adverse patient impact by preventing uncontrolled asthma due to poor inhaler technique. The conventional wisdom is that training patients to use inhalers is time-consuming,[22,23] although there is some evidence to the contrary.[24]

Nonetheless, choosing the most appropriate inhaler for a specific patient and regularly assessing their ability to correctly use their inhaler will likely promote better adherence to therapy with improved disease outcomes, and according to the British Thoracic Society guideline on the management of asthma, is a feature of ‘gold standard’ respiratory patient review clinics.[25] Furthermore, patients' preference for a particular inhaler should be taken into

consideration since it may influence both proper use and adherence. In patients with obstructive airway diseases, inhaler choice is as critical as the choice of medication itself.[26]

Indeed, research on new inhaler devices has attempted to identify desirable attributes of an inhaler. 'Ease of use' is an important characteristic but is often determined after instructed training. Whilst the importance of initial and repeat inhaler technique training cannot be overlooked, a device that is intuitively easy to use may be more beneficial for those patients with poor technique recall or with barriers to access adequate training.[27] Furthermore this may both be preferred by patients, and reduce the time needed to master the device.

To identify ways of addressing this, the International Primary Care Respiratory Group (IPCRG) recommends the use of pragmatic and observational studies to more closely reflect the realities of managing a patient population with widely heterogeneous characteristics.[5]

Within the respiratory market continuously providing improved and more intuitive asthma inhalation devices, there is a need to assess training time in real clinical practice across all available inhalers and to assess patient preferences for those devices.

2.0 Study Aims & Objectives

2.1 Study aims

The aim of this study is to compare different inhaler devices available as part of normal care in terms of training required, defined as time required for patient education to master the device, and patients' inhaler device preferences in patients with asthma and COPD.

2.2 Study Objectives

2.2.1 Primary Objective

The primary objective of the study is to measure the time needed for patients with asthma and COPD to master the required inhaler technique and the number of attempts to achieve mastery for a specific delivery device available as part of their normal care.

2.2.2 Secondary Objectives

- To compare Spiromax to Turbohaler and other commonly prescribed dry powder inhalers with regards to the time taken and number of attempts to achieve device mastery.
- To assess patients' preferences for inhaler devices.

3.0 Study Design

3.1 Devices Studied

During data collection, training on inhaler devices will be based on available devices on practice formulary. For this study the following devices and inhalers will be included:

- Spiromax (DPI)
- Turbohaler (DPI)
- Diskus (DPI)
- Evohaler (pMDI)

3.2 Study Design

This will be a real-world, cross-sectional observational study using prospective inhaler training data collected from best practice asthma and COPD review clinics, captured in the International Helping Asthma in Real Patient (iHARP) database and linked with retrospective patient characterisation data from the Optimum Patient Care Research Database (OPCRD) in the UK.

The time needed to train and achieve correct inhaler technique will be assessed for patients with asthma and COPD, separated by inhaler type.

Patients will be assessed on their current inhaler device* and two sequentially allocated alternative inhaler devices, which will be appropriate alternative devices to their currently prescribed inhaler. Both the devices selected and the order of training will be varied, as selected by the healthcare professional conducting the review clinic.

All patients will receive standard verbal training by the Optimum Patient Care (OPC) healthcare professional (HCP) on how to use their current device and the alternative devices

* Only if their current inhaler device is either Spiromax, Turbohaler, Diskus or Evohaler.

(which will be routinely available on the practice formulary), according to the patient information leaflets. Each patient will then demonstrate use of each device until they reach device mastery*. Trained HCPs will observe a video recording of the inhaler technique section of each patient's review clinic, from which the time taken to teach the patient and for the patient to achieve device mastery will be recorded. The number of attempts to reach device mastery will also be recorded.

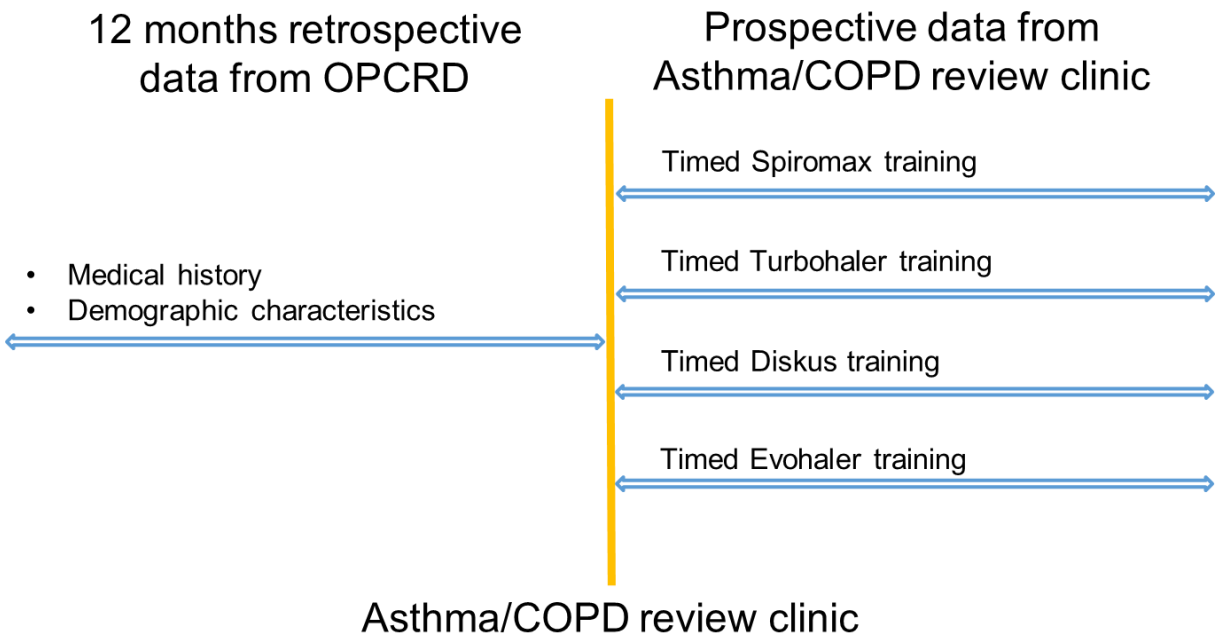

Figure 1: Study design diagram

3.3 Study Period

The data in this study will be provided by data collected via the iHARP review service as part of standard clinical practice from February 2016 to April 2016.

Additional data on medical history and patient demographic characteristics will also be extracted from the OPCRD for the previous 12 months prior to the date of the asthma/COPD review clinic.

* Defined as an error-free demonstration as identified by the clinic nurse during inhaler technique assessment. It is noted that some patients may not be able to achieve device mastery due to medical restrictions (e.g. arthritic hands) or other reasons.

3.4 Study Methods

The following text describes the agenda of best clinical practice asthma and COPD clinics conducted by Optimum Patient Care, highlighting in particular the primary and secondary outcome data collection.

1. Asthma/COPD review clinic, including airway inflammation and lung function tests (FeNO, FEV_1, FVC, PEFR); inspiratory flow measure
2. Patient is asked for consent to be videoed for the duration of the inhaler technique section of the review clinic.
3. Video recording starts. If patients refuse consent, they will receive the same review clinic as detailed below, but will not be videoed. Therefore data capturing the time and number of attempts to achieve device mastery will not be recorded. As will be described in the patient consent form, patients will retain the right to withdraw consent after the review clinic has finished, at which point their video and all subsequent data will be destroyed.
4. Current device:*
    a. Observe real-life technique for preparation and completion of two inhalations;
    b. Clinic nurse verbal instruction, correcting all observed errors if technique was not error free;
    c. Patient demonstrates technique again;
    d. Repeat steps (b) and (c) until device mastery achieved.†
5. Alternative device 1 selected by clinic nurse:‡
    a. Clinic nurse verbal instruction for preparation and completion of two inhalations;
    b. Patient demonstrates technique;
    c. Clinic nurse corrects all observed errors;
    d. Repeat steps (b) and (c) until device mastery achieved.*
6. Alternative device 2 selected at by clinic nurse (clinic proceeds as for step 5).†
7. Video recording ends.

* For patients prescribed a fixed-dose combination (FDC) ICS/LABA therapy, this device will be taken as their 'current device'. For patients not prescribed a FDC therapy, their maintenance therapy device will be taken as their 'current device'. If a patient has more than one maintenance therapy device, their ICS device will be taken as their 'current device'. For patients who are only prescribed a reliever therapy, their reliever device will be taken as their 'current device'.

† Each patient will be permitted to continue to attempt to achieve device mastery (for current and study devices) for as long as necessary, taking into account the patient's state and clinic running time.

‡ Where a patient is unable to master a device, for example due to medical restrictions (e.g. arthritis in the hands), the absence of mastery will be recorded, and the patient will proceed to the next selected device (i.e. there may be a small percentage of patients unable to achieve device mastery). The patient will contribute data regarding their current device, and up to two study devices for which inhalation technique is observed.

8. Patient completes inhaler preference questionnaire (see Section 3313.313.3).

After review clinics are held: video review staff (trained to feedback patient device recommendations according to OPC guidelines) will review inhaler technique videos for each patient, and record time taken and number of attempts to achieve device mastery, according to study definitions (see Section 5.2).

4.0 Study Population

4.1 Patient Inclusion and Exclusion Criteria

Table 1: Patient Inclusion Criteria

Inclusion criteria
Diagnosis of asthma or COPD
Patient is on a maintenance device for asthma or COPD
Patients with an asthma diagnosis: - a diagnostic code and/or ≥2 prescriptions for asthma therapy* during the 12 months prior to the date of the asthma review clinic - age ≥18 years at the date of their asthma review clinic
Patients with a COPD diagnosis: - a diagnostic code and ≥2 prescriptions for COPD therapy* during the 12 months prior to the date of the COPD review clinic - age ≥40 years at the date of their COPD review clinic

Table 2: Patient Exclusion Criteria

Exclusion criteria
Diagnosis of other chronic respiratory disease
Patients who had confirmed respiratory exacerbation or received oral corticosteroids and/or antibiotics for a lower respiratory condition in the 2 weeks prior to the date of the asthma/COPD review clinic

4.2 Data Source

Data will be collected prospectively as part of the iHARP review service in the UK. This data will be linked to medical history and demographic characteristics for each patient via OPCRD.

The iHARP review service and OPCRD are developed and maintained by Optimum Patient Care (OPC), a social enterprise that aims to improve patient outcomes through medical research and clinical review services. OPC provides evidence based recommendations to UK general practices through bespoke patient management tools and tailored practice reports.

* Includes prescriptions for bronchodilators including β2-agonists, anticholinergics, theophylline or combination therapy, inhaled corticosteroids, combination inhaled corticosteroids and bronchodilator therapy

4.3 iHARP Review Service: Prospective Data Capture

The iHARP review service was first set up to offer HCPs a standardised tool and training resource to assist them in delivering gold standard respiratory reviews to their respiratory patients. The service built on the International Primary Care Respiratory Group's 'Helping Asthma in Real People' (HARP) initiative – a practical implementation project that advocated the combined analysis of electronic medical records (from primary care practice) and patients' responses to disease-specific questionnaires. The iHARP database is a unique international database made up of anonymised patient data from patients invited to complete an iHARP asthma review. Data was collected via clinician reviews and included patient reported data such as symptoms, smoking status, comorbidity, treatment, adherence, subjective and objective inhaler technique, lung function, and fractional exhaled nitric oxide (FeNO) readings.

The iHARP asthma review service will continue to cover the precited components, deemed as best practice by the expert steering committee, and a COPD review service will be developed. They will be both adapted to address the current inhaler devices available and training requirements as part of best practice assessment and patient inhaler device preferences.

A revised best practice asthma/COPD review service that will be used in the present study will thus include the items listed in Table 3 and training for patients on available devices within their practice formulary (proposed list of medications and devices suitable for prescription within each region in the UK). The patients will be trained by OPC HCPs. All clinics will be supported by a service coordinator who will arrange for independent videoing of the patient inhaler technique training. Each video will be reviewed by a trained HCP, to inform their recommendation of the most appropriate inhaler device for the patient. They will also record the time taken for the HCP to train the patient on each device and for the patient to reach mastery. The number of attempts made by the patient to master the device will also be recorded to account for patient issues. Finally, as part of the review, patients will be asked for their preferred device and this will be recorded. The question will be presented to the patient in paper format (see Appendix 3: Asthma/COPD device preference questionnaire). Please see **Error! Reference source not found.** for the detailed process of the iHARP Asthma/COPD Review Clinic.

Table 3: iHARP Asthma/COPD Review

Review/Assessment Process	
Routine Data Extraction	
Clinical Data	All GP recorded clinical history and events
Therapy Data	All GP recorded drugs, medications and therapies
Patient Data	All GP recorded patient demographic history
Patient Reported (Questionnaire – Completed prior to clinic)	
Patient Control	RCP/ATAQ/CCQ* (Asthma and COPD questionnaires - Appendix 2)
Patient Status	Steroids/A&E/Hospitalisations (Asthma and COPD questionnaires - Appendix 2)
Smoking Status	Status/Pack Year/ Years (Asthma and COPD questionnaires - Appendix 2)
Rhinitis	Impact of symptoms (Asthma and COPD questionnaires - Appendix 2)
Preventer Inhaler	Adherence/Patient beliefs (Asthma and COPD questionnaires - Appendix 2)
Side Effects	Side effects (Asthma and COPD questionnaires - Appendix 2)
General Care	Inhaler technique reviews/self-management plans
Disease Management (Pre-populated from OPCRD)	
Current Medication	Pre-populated from OPCRD (Asthma and COPD questionnaires - Appendix 2)
Comorbidities	Pre-populated from OPCRD (Asthma and COPD questionnaires - Appendix 2)
Technology Assessment (In asthma and COPD review clinics)	
Airway Inflammation	FeNO
Lung Function	Spirometry (FEV_1, FVC, PEFR)
Inhaler Inspiratory Flow Measurement	Current Device

* RCP: Royal College of Physicians; ATAQ: Asthma Therapy Assessment Questionnaire; CCQ: Common Cold Questionnaire

Inhaler Technique (In asthma and COPD review clinics) – ***NEW***	
Video Observed Inhaler Technique	Current Device and study devices
Inhaler Technique (from video observed inhaler technique) – ***NEW* **	
New: Training & Timing	**Study devices (available at practice)**
New: Patient Inhaler Device Preference	**From all trained above (Asthma/COPD device preference questionnaire - Appendix 3)**

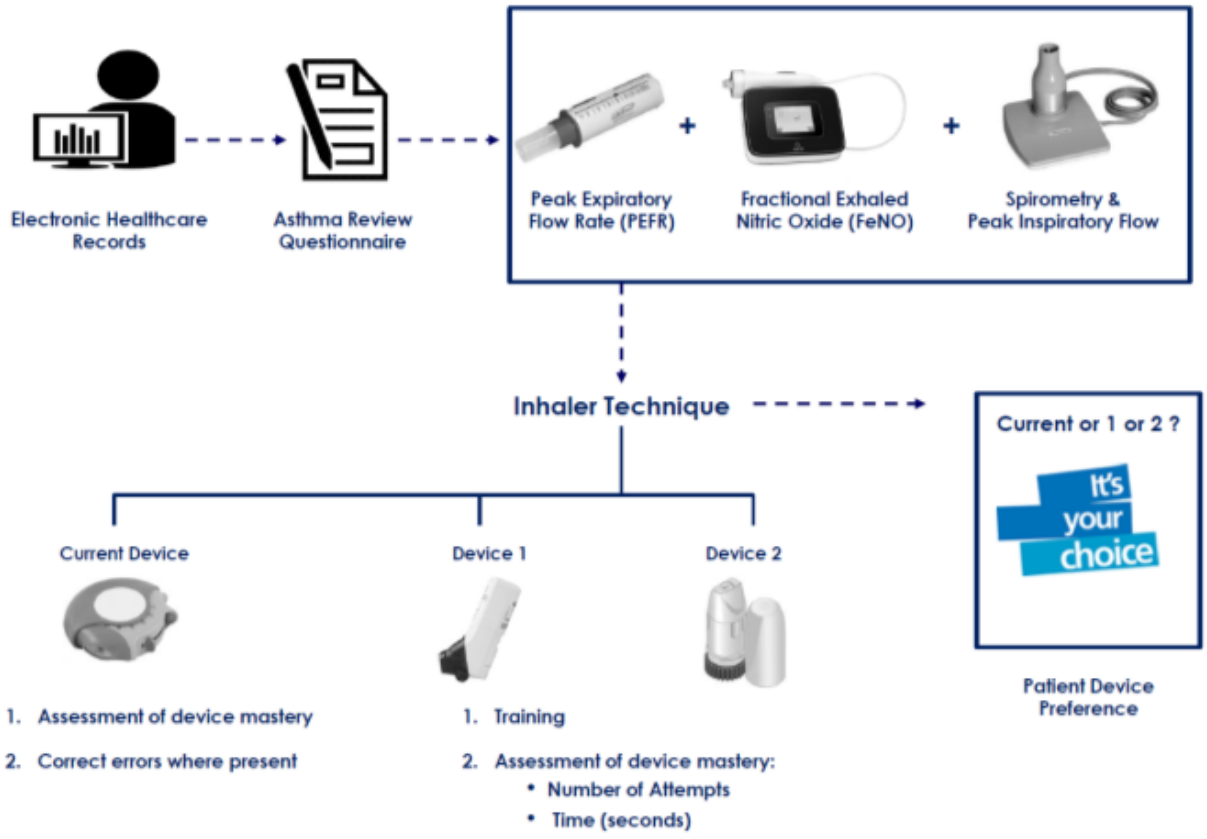

Figure 2: iHARP Asthma/COPD Review Clinic with Inhaler Device Training and Patient Inhaler Device Preference

Information collected during the iHARP review is used to provide personalised feedback to the patients and HCPs on improving a patient's asthma/COPD control and to establish an anonymous database ethically approved for research purposes which can be linked to the OPCRD.

4.4 OPCRD: Linked Retrospective Data Source

In the United Kingdom, the asthma review clinic data (detailed above) is combined with routinely collected health care data from the OPCRD. The OPCRD currently comprises longitudinal medical records for over 2.2 million patients from over 580 primary care practices across the UK.

The OPCRD contains two types of data: routinely recorded clinical data and questionnaire responses from over 40,000 respiratory patients. The OPC questionnaires are a compilation of validated questions covering symptoms, disease control, triggers, side effects, quality of life and unique adherence measures. Indeed the OPCRD is the only database in the UK which compliments routinely recorded disease coding and prescribing information with patient reported outcomes. OPCRD also links with nationwide practice prescribing data to enable targeted delivery of dataset needs.

OPCRD is ethically approved by the NHS Health Research Authority (REC reference: 15/EM/0150) for research use. It is governed by the Anonymous Data Ethics Protocols and Transparency (ADEPT) committee, an independent body of experts and regulators commissioned by the Respiratory Effectiveness Group (REG) to govern the standard of research conducted on internationally renowned databases. All research using OPCRD is registered on recognised study databases such as the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP).

5.0 Study Variables and Outcomes

5.1 Demographic and Baseline Variables

Prior research into respiratory disease has identified a range of potential confounding factors that may impact on asthma and COPD, including education, smoking, medication, comorbid allergic rhinitis and other co-morbid diseases and medications. These variables will be extracted, where available, for all patients (example results tables are presented in Appendix 5).

Potential patient/treatment factors that are reported in the data for descriptive analysis include:

- Age of patient at time of iHARP review
- Gender

- Body Mass Index (BMI)* at time of the iHARP review
- Smoking status at time of iHARP review and packs per year† for current smokers and ex-smokers
- Socio-economic status marker (Highest Education attainment)
- Year and month of iHARP review
- Duration of asthma/COPD (years)
- Peak inspiratory flow (PIF)‡
- Peak expiratory flow rate (PEFR)
- Forced expiratory volume in one second (FEV_1)
- Forced vital capacity (FVC)
- Percentage predicted peak flow
- Co-morbidities expressed using the Charlson Comorbidity Index (CCI)§ and its components
- Presence of patient reported rhinitis and severity**
- Presence of Gastroesophageal Reflux Disease (GERD), self-reported
- Patient reported side effects, including: continual sore mouth/throat, oral thrush, bruising, hoarse voice, abnormal weight gain and cough
- Adherence to therapy††
- Paracetamol use, reported by the patients as: regular, intermittent or not used
- Number and severity of asthma/COPD exacerbations in the year preceding iHARP review‡‡
- Currently prescribed therapy and dose (including SAMA, SABA and inhaled corticosteroids [ICS])
- Number of courses of oral corticosteroids prescribed in the year preceding iHARP review
- Number of courses of antibiotics prescribed for lower respiratory tract infections in the year preceding iHARP review.

* The BMI is a representative measure of body weight based on the weight and height of the subject. Full definition is in Appendix 1
† Pack years – calculated from the (number of cigarettes smoked per day ÷ 20) × number of years of smoking
‡ Assessed using a Vitalograph Spiromax
§ CCI predicts the one-year mortality for a patient who may have a range of comorbid conditions such as heart disease, AIDS or cancer. Each condition is assigned a 'weight' depending on the risk of dying associated with the condition; scores are then summed to give a total score predicting mortality. Full definition and codes available in Appendix 1
** Rhinitis symptoms were recorded in response to the question 'Do you have any of these symptoms: itchy, runny, blocked nose or sneezing when you don't have a cold?' Full definition available in Appendix 5
†† Adherence to therapy was reported using the Medication Adherence Rating Scale (MARS) score. Full definition available in Appendix 5
‡‡ Exacerbations were calculated from questions during the iHARP review about the number courses of oral steroids, and number of hospitalisations and A&E attendances for breathing difficulties

- GP consultations in the year preceding iHARP review

5.2 Primary Outcome

Training required

Where training required is defined as the following per device type:

1. Time taken to achieve device mastery (as recorded in seconds from the beginning of training)

And/or

2. Number of attempts to reach device mastery

Mastery of inhaler technique will be assessed using an error list available for each device type (Appendix 4). The device errors for each inhaler type have been classified according to expert clinical input and on the basis of earlier studies.[28] The lists of errors are incorporated into the iHARP review software or electronic data capture for data entry/collection at the clinics. Device mastery will be reached when no error is identified by the nurse following training.

5.3 Secondary Outcome

Patient Preference Questionnaire

After training and assessment on the devices, the patient will complete an inhaler device preference questionnaire developed by OPC and administered by the HCPs and/or service coordinator on the day of the iHARP asthma/COPD review clinic (Appendix 3: Asthma/COPD device preference questionnaire).

Example results tables are presented in Appendix 6: Example of outcome results tables.

5.4 Exploratory analyses

Training required

Where training required is defined as the following per device type:

1. Time taken to achieve device mastery (as recorded in seconds from the beginning of the patient attempt to demonstrate device use, i.e. excluding nurse instruction time)

Patient population

Analyse the primary and secondary outcomes, stratified by disease group (i.e. analyse asthma patients separately to COPD patients).

6.0 Statistical Analysis

6.1 Statistical Software and Power Calculation

Statistical analysis will be carried out using SPSS version 22 (IBM SPSS Statistics, Feltham, Middlesex, United Kingdom).[29]

Based on data from HCP ELIOT study,[28] Spiromax patients took a mean (SD) number of 2.48 (1.15) steps out of a 6 step training program to achieve device mastery, compared to 3.03 (0.95) on Turbohaler.
However, as the primary objective of this study is exploring median time to mastery and no previous data is available to perform a power calculation, we have used the HCP ELIOT study results as a proxy.

A sample size of 81 will have 90% power to detect a difference in means of -0.550 steps (e.g. Spiromax, μ_1, of 2.48 and other DPI, μ_2, of 3.03), assuming a pooled standard deviation of differences of 1.5,* using a paired t-test with a 0.050 two-sided significance level.

Accounting for a drop-out rate of 20%, a minimum of 102 participants for asthma and 102 participants for COPD will be needed.

6.2 Analysis of Study Outcomes

6.2.1 Primary Outcome

Training required

- The mean/median time required to achieve device mastery between Spiromax and each alternative study device will be compared by using Kaplan-Meier survival curves. Log-rank tests will be carried out and p-values reported.
- The mean/median number of attempts required to achieve device mastery between Spiromax and each alternative study device will be compared by using a paired t-test (means) or Wilcoxon signed rank test (medians), dependent on the data distribution.

* Pooled standard deviation has been inflated as this reference data is not an exact proxy for the primary endpoint, so true variation is unknown

6.2.2 Secondary Outcome

Patient Preference Questionnaire

Results from the patient preference questionnaire will be compared using a paired t-test or wilcoxon signed rank test depending on the data distribution. The 5% level of significance will be used (two-tailed test).

6.2.3 Summary Statistics

Summary statistics will be produced for all explanatory and outcome variables for all patients and for patients using the different types of inhaler devices. Groups will be compared using the following tests:

- Variables measured on the interval/ratio scale:
  - ANOVA
- Categorical variables:
  - Chi-square test

Statistical significance will be set at $p<0.05$

Results will be reported as:

- Variables measured on the interval/ratio scale:
  - Sample size (n) and percentage non-missing
  - Median and inter-quartile range (25th and 75th percentiles)
- Categorical variables:
  - Sample size (n)
  - Count and percentage by category (distribution)

6.2.4 Data Preparation

The data will be prepared for analysis by:

- Investigating potential outliers
- Identifying and creating new variables as necessary:
  - Transformations of skewed data (for example, log transformations)
  - Categorisation of heavily skewed data
- Investigating missing data (type of and reason for absence).

Plots will be produced for all explanatory and outcome variables. For variables measured on the interval or ratio scale, these will include:

- Frequency plots
- Box and whisker plots

Frequency plots will illustrate the distribution of the variable and whether categorisation may be necessary (for example, if heavily skewed). Box plots will illustrate the location and spread of the variable and identify potential outliers. For categorical variables, bar plots will be produced to illustrate distributions and highlight differences between exposure groups.

6.2.5 Predictors of Outcomes

Bivariate analyses will be carried out to identify those explanatory variables that are predictive ($p < 0.05$ or $p < 0.001$ for errors) of outcomes. These will be considered as potential confounders when modelling the outcome variables. In particular, attention will be paid to age, current inhaler and disease group (asthma/COPD) as potential confounders.

7.0 Regulatory and Ethical Compliance

This study is designed and shall be implemented and reported in accordance with the criteria of the "European Network Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP) study" and follows the ENCePP Code of Conduct (EMA 2014). Once a final version of the protocol has been agreed and reviewed by the advisory group, this study will be registered with www.encepp.eu.

8.0 Data Dissemination

Initial results will be presented in poster and/or oral format at appropriate respiratory 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.

9.0 Advisory Group

An independent virtual Steering Committee (SC) has been assembled to oversee the study with the following members:

David Price

Nicolas Roche

Henry Chrystyn

Dermot Ryan

John Haughney

Sinthia Bosnic-Anticevich

10.0 Research Team

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Study sponsor:

TEVA

Primary contact

Hicham Benhaddi

11.0 Timelines

Action	Timescale	Dates
Protocol development	4 weeks	15th February
TEVA/SC sign-off	2 weeks	24th February 2016
Recruitment & Data Extraction	1 week	12th February 2016
Clinic Data Collection	12 weeks	3rd June 2016
Dataset Creation	2 weeks	15th June 2016
Data analysis – explanatory variables	4 weeks	15th July 2016
Data analysis – outcomes analysis	4 weeks	15th August 2016
Slide set and report	4 weeks	15th September 2016
SC review	3 weeks	7th October 2016
TEVA review	1 week	14th October 2016
Manuscript writing	12 weeks	27th January 2017

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13.0 APPENDIX

13.1 Appendix 1: Definitions

13.1.1 Body Mass Index (BMI)

The BMI is a representative measure of body weight based on the weight and height of the subject. It is defined as the weight (in kg) divided by the square of the height (in m) and is measured in kg/m^2. BMI will be categorised as follows: underweight (< 18.5), normal BMI (18.5 - 24.99), overweight (25-29.99), obese (≥30).

13.1.2 Charlson Comorbidity Index (CCI)

The CCI was developed in the US in 1987 as a method of classifying prognostic comorbidity in longitudinal studies.[30] It predicts the one-year mortality for a patient who may have a range of comorbid conditions such as heart disease, AIDS or cancer. Each condition is assigned a "weight" depending on the risk of dying associated with the condition; scores are then summed to give a total score predicting mortality.

The weights were revised and updated (for example, mortality due to HIV has fallen) by Dr Foster Intelligence (DFI) in their HSMR Methodology documentation[31] and calibrated using UK data (due to differences in coding practice and hospital patient population characteristics from the US), using ICD-10 codes. As a result:

- DFI have expanded the coding definition of some conditions;
- Only secondary diagnoses (DIAG02-DIAG14) are now considered;

  There is greater variation in weights between conditions and the Charlson Index (the sum of the weights) can be treated as a continuous variable (limited to the range 0-50) for the purposes of risk adjustment.

The weights, codes and conditions used in this study are summarised in the table below.

Table 4: Co-morbid conditions and scores used in the Charlson Co-morbidity Index (CCI)

Condition	Condition name	ICD-10 codes	Weight
1	Acute myocardial infarction	I21, I22, I23, I252, I258	5
2	Cerebral vascular accident	G450, G451, G452, G454, G458, G459, G46, I60-I69	11
3	Congestive heart failure	I50	13
4	Connective tissue disorder	M05, M060, M063, M069, M32, M332, M34, M353	4
5	Dementia	F00, F01, F02, F03, F051	14
6	Diabetes	E101, E105, E106, E108, E109, E111, E115, E116, E118, E119, E131, E131, E136, E138, E139, E141, E145, E146, E148, E149	3
7	Liver disease	K702, K703, K717, K73, K74	8
8	Peptic ulcer	K25, K26, K27, K28	9
9	Peripheral vascular disease	I71, I739, I790, R02, Z958, Z959	6
10	Pulmonary disease	J40-J47, J60-J67	4
11	Cancer	C00-C76, C80-C97	8
12	Diabetes complications	E102, E103, E104, E107, E112, E113, E114, E117, E132, E133, E134, E137, E142, E143, E144, E147	-1
13	Paraplegia	G041, G81, G820, G821, G822	1
14	Renal disease	I12, I13, N01, N03, N052-N056, N072-N074, N18, N19, N25	10
15	Metastatic cancer	C77, C78, C79	14
16	Severe liver disease	K721, K729, K766, K767	18
17	HIV	B20, B21, B22, B23, B24	2

13.2 Appendix 2: iHARP asthma and COPD questionnaires

Asthma Questionnaire V9.0 10052011

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+
How many times have you been treated in accident and emergency or anywhere other than your GP surgery for your asthma?	☐ 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?	☐	☐	☐	☐	☐	☐	☐	☐

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

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 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*				*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*				*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?	☐	☐

Do you experience any of these side effects from your preventer inhaler? 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 the way you take your inhaler(s) checked in the past 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? ☐ *Yes* ☐ *No*

Practice Ref: _____ Survey Ref: _____

COPD Questionnaire

If you would like **immediate** feedback on your answers to this questionnaire, you can complete it online at **www.copdtrak.org**

PLEASE ANSWER ALL QUESTIONS ON BOTH SIDES

These questions measure the impact COPD is having on your wellbeing and daily life. For each item place a mark(X) in the box that best describes you currently. Please select only one answer for each question.

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

These questions ask your views about your regular COPD treatment. Please show how much you agree or disagree by marking one box for each statement. Please select only one answer for each question.

	Strongly Disagree	Disagree	Not Sure	Agree	Strongly Agree
I need to take my inhaler(s) regularly	☐	☐	☐	☐	☐
I find my inhaler(s) difficult to use	☐	☐	☐	☐	☐
I worry about the side effects of my COPD inhaler(s)	☐	☐	☐	☐	☐
I have enough information about my inhaler(s)	☐	☐	☐	☐	☐
I would prefer to take my regular COPD medications in a once-a-day dose	☐	☐	☐	☐	☐

Thinking about how often you take your regular COPD treatment during the day: please tick one box

☐ I always take it exactly at the times prescribed ☐ I occasionally miss the odd dose ☐ I often miss or forget to take doses ☐ I take it all once a day- it's easier ☐ I never take it

Which statement best describes how you take your regular COPD treatment. Please select only one answer.

☐ 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

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

COPD Questionnaire

COPDQ/V10.4 11052011

Thinking about breathlessness, which statement best describes you? Please select only one answer.

- ☐ Not troubled by breathlessness (except on strenuous exercise)
- ☐ Short of breath when hurrying or walking up a slight hill
- ☐ Slower in walking than others of the same age on the level because of breathlessness, or have to stop for breath when walking at your own pace
- ☐ Stopping for breath after about 100m or after a few minutes on the level
- ☐ Too breathless to leave the house, or breathless when dressing/undressing

How many nights in the last week did you wake up because of your COPD symptoms?

☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7

Overall, how severe would you describe your COPD symptoms at night over the last week?

☐ I did not experience any symptoms ☐ Mild ☐ Moderate ☐ Severe ☐ Very severe

These questions are about smoking. Please select only one answer for each question.

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

If you smoke, or used to smoke: How many cigarettes do/did you smoke per day?

☐ 1-5 ☐ 6-10 ☐ 11-15 ☐ 16-20 ☐ 21-30 ☐ 31-40 ☐ 41-50 ☐ 50+

How many years have you smoked/did you smoke?

☐ 1-5 ☐ 6-10 ☐ 11-15 ☐ 16-20 ☐ 21-30 ☐ 31-40 ☐ 41-50 ☐ 50+

These questions are about what has happened to you during the past year.

In the past year, have you had the way you use your inhalers(s) checked? ☐ Yes ☐ No

In the past year, how many times have you been admitted to hospital with breathing problems? ☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 or more

In the past year, how many times have you had a worsening of your chest symptoms requiring a course of steroid tablets and/or antibiotics? ☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 or more

About your nose: Many people with COPD have trouble with their nose which may interfere with their COPD
Do you have **any** of these symptoms: itchy, runny, blocked nose or sneezing **when you don't have a cold**?

☐ No ☐ Occasionally and little bother ☐ Occasionally and quite a bother ☐ Most days but little bother ☐ Most days and quite a bother

Thinking about exercise, how much time do you spend doing exercise/activity (eg walking) each day?

☐ None ☐ 15mins ☐ 30mins ☐ 45mins ☐ 1 hr ☐ 2 hrs ☐ 3 hrs or more

In the future, would you be willing to participate in further questionnaire based research? ☐ Yes ☐ No

Do you have home oxygen therapy (either cylinders, liquid oxygen or a concentrator)? ☐ Yes ☐ No

Thank you for completing this questionnaire. Please return to us in the freepost envelope provided.

Practice Ref: _____ Survey Ref: _____

13.3 Appendix 3: Asthma/COPD device preference questionnaire

OPTIMUM PATIENT CARE
Supporting Patient Care & Research
Unit 5-6, Old Granary, Westwick, Cambridge, CB24 3AR
Tel: 01223 967 855 | Fax: 01223 967 458
www.optimumpatientcare.org

ASTHMA/COPD DEVICE PREFERENCE QUESTIONNAIRE*

INSTRUCTIONS: Please complete the following questions related to both the new inhalers and your current inhaler that you used during this clinic.

Please tick only one response for each question.

1. Which device do you prefer based on the number of steps needed to take your asthma/COPD medication?

☐ Current inhaler† _____

☐ New inhaler 1† _____

☐ New inhaler 2† _____

☐ No preference

2. Which device do you prefer based on the time needed to take your asthma/COPD medication?

☐ Current inhaler† _____

☐ New inhaler 1† _____

☐ New inhaler 2† _____

☐ No preference

3. Which device do you prefer based on how easy the device is to use?

☐ Current inhaler† _____

☐ New inhaler 1† _____

☐ New inhaler 2† _____

☐ No preference

†Inhaler device name to be added by the HCP

Please feel free to add any general comments:

_____

_____

_____

_____

*Questionnaire adapted from: Clark M, Hofmann A, Tabberer M and Martin S. Development and content validity of the COPD device preference questionnaire. Poster presented at the ISPOR 14th Annual European Congress. November 9, 2011; [abstract] Value in Health. Nov 2011; 14(7):A255.

13.4 Appendix 4: Device Error Lists

Device errors for each inhaler type have been classified according to device type following discussion with clinical advisers, and will be used to determine when device mastery (error-free demonstration) is achieved.

Step type	Spiromax®	Accuhaler®	Turbuhaler®	Evohaler®
Preparation				
1	Does not hold the inhaler with the semi-transparent mouthpiece cover at the bottom	Does not slide outer cover	Does not remove cap	Does not remove cap
2	Does not open cap and a click is not heard when cap is opened	Does not completely slide lever	Inhaler is not held upright when a dose is prepared (upright means mouthpiece skywards ±45°) throughout dose preparation (this includes twisting the base one way and then the other way)	Does not shake before actuation (at least 2 or 3 times)
3	Inhaler is not held between upright and horizontal when the cap is opened (therefore (±90^{o} is OK)	Does not hold device horizontally when sliding lever	Dose preparation: not twisting the base as far as possible, until it clicks and not turning it back to the original position	Does not hold the inhaler upright when pressing canister during an inhalation
4	Points mouthpiece in a downward position after dose preparation (before an inhalation) NB OK to point slightly downwards immediately before placing in the mouth if the head is tilted slightly	Points mouthpiece in a downward position after dose preparation (before an inhalation) NB OK to point slightly downwards immediately before placing in the mouth if the head is tilted slightly	Points mouthpiece in a downward position after dose preparation (before an inhalation) NB OK to point slightly downwards immediately before placing in the mouth if the head is tilted slightly	

Step type	Spiromax®	Accuhaler®	Turbuhaler®	Evohaler®
5	Vigorous shaking before or any shaking after dose preparation	Shakes after dose preparation	Vigorous shaking before or and any shaking after dose preparation	
Inhalation				
6	Does not exhale before taking the dose	Does not exhale before taking the dose	Does not exhale before taking the dose	Does not breathe out gently before an inhalation
7	Exhales into the inhaler before taking dose	Exhaling into the device before inhalation	Exhales into the inhaler before taking dose	Exhales into the inhaler
8	Fails to put in mouth and seal lips around mouthpiece	Fails to put in mouth and seal lips around mouthpiece	Fails to put in mouth and seal lips around mouthpiece	Fails to put in mouth and seal lips around mouthpiece
9	Puts finger (or face) over the air inlet during an inhalation (at front above the mouthpiece)		Puts fingers or mouth around air inlets (positioned around the base and above the mouthpiece)	
10	Inhalation is not as fast as possible (from the start)	Inhalation is not as fast as possible from the start	Inhalation is not as fast as possible (from the start)	Did not actuate a dose at the same time as the start of their inhalation (defined as actuating up to a second after they start to inhale)
11	Inhalation is not as long as possible (>3 seconds)	Inhalation is not as long as possible (>3 seconds)	Inhalation is not as long as possible (>3 seconds)	Inhalation was not steadily and deeply - (defined as lasting at least 3 seconds)
12	Does not hold breath after inhalation (>4 seconds)	Does not hold breath after inhalation (>4 seconds)	Does not hold breath after inhalation (>4 seconds)	Did not hold their breath for at least 3 to 4 seconds after their inhalation

Step type	Spiromax®	Accuhaler®	Turbuhaler®	Evohaler®
After inhalation				
13*	Does not prepare a second dose correctly	Does not prepare a second dose correctly	Does not prepare a second dose correctly	Does not prepare a second dose correctly
14*	Does not inhale a second dose correctly	Does not inhale a second dose correctly	Does not inhale a second dose correctly	Does not inhale a second dose correctly
15	Does not close the cap after taking the last dose	Does not close the cover after taking the last dose	Does not place the cap back on the inhaler after taking the last dose	Does not replace cap after taking the last dose
16	Does not know how to read the dose counter after asking the patient to check the number of doses left	Does not know how to read the dose counter after asking the patient to check the number of doses left	Does not know how to read the dose counter after asking the patient to check the number of doses left	Does not know how to read the dose counter after asking the patient to check the number of doses left Alternatively the method they use to order a new supply. If you are convinced with their response then assess it as correct
17	Expiry: what method do they use to ensure their medicine has not exceeded its use by date - check the expiry date	Expiry: what method do they use to ensure their medicine has not exceeded its use by date - check the expiry date	Expiry: what method do they use to ensure their medicine has not exceeded its use by date - check the expiry date	Expiry: what method do they use to ensure their medicine has not exceeded its use by date - check the expiry date

* Only applicable if patients are prescribed two doses

Step type	Spiromax®	Accuhaler®	Turbuhaler®	Evohaler®
18 **Priming** **MDI ONLY**				Ask what they do when they start a brand new inhaler or do not use their inhaler for >14 days. Correct answer is to prime

Inhalation Steps 1-14 to be assessed by the practitioner and by video
Inhalation Steps 15-18 to be assessed by the practitioner only.
Second inhalation will only be assessed if the patient is prescribed two doses

13.5 Appendix 5: Example of baseline results tables

Example of the demographics results tables

Demographic variable		Inhaler device					
		Spiromax N=x	Turbohaler N=x	Diskus N=x	MDI N=x	Total N=x	p-value[a]
Age (years)*	N (% non-missing) Mean (SD) Median (IQR)	x (x) x (x) x (x, x)	x (x) x (x) x (x, x)	x (x) x (x) x (x, x)	x (x) x (x) x (x, x)	x (x) x (x) x (x, x)	X
Age* categorised, n (%)	18-40 years 41-60 years ≥61 years	x (x) x (x) x (x)	x (x) x (x) x (x)	x (x) x (x) x (x)	x (x) x (x) x (x)	x (x) x (x) x (x)	X
	Total	x (x)	x (x)	x (x)	x (x)	x (x)	
Gender, n (%)	Male Female	x (x) x (x)	x (x) x (x)	x (x) x (x)	x (x) x (x)	x (x) x (x)	X
	Total	x (x)	x (x)	x (x)	x (x)	x (x)	
BMI, (kg/m^2)*	N (% non-missing) Mean (SD) Median (IQR)	x (x) x (x) x (x, x)	x (x) x (x) x (x, x)	x (x) x (x) x (x, x)	x (x) x (x) x (x, x)	x (x) x (x) x (x, x)	X
BMI (categorised), n (%)	Underweight Normal Overweight obese	x (x) x (x) x (x) x (x)	x (x) x (x) x (x) x (x)	x (x) x (x) x (x) x (x)	x (x) x (x) x (x) x (x)	x (x) x (x) x (x) x (x)	X
	Total	x (x)	x (x)	x (x)	x (x)	x (x)	
Peak inspiratory flow (PIF)*	N (% non-missing) Mean (SD) Median (IQR)	x (x) x (x) x (x, x)	x (x) x (x) x (x, x)	x (x) x (x) x (x, x)	x (x) x (x) x (x, x)	x (x) x (x) x (x, x)	X
Peak expiratory flow rate (PEFR)*	N (% non-missing) Mean (SD) Median (IQR)	x (x) x (x) x (x, x)	x (x) x (x) x (x, x)	x (x) x (x) x (x, x)	x (x) x (x) x (x, x)	x (x) x (x) x (x, x)	X
Forced expiratory volume in 1sec (FEV_1)*	N (% non-missing) Mean (SD) Median (IQR)	x (x) x (x) x (x, x)	x (x) x (x) x (x, x)	x (x) x (x) x (x, x)	x (x) x (x) x (x, x)	x (x) x (x) x (x, x)	X
Forced vital capacity (FVC)*	N (% non-missing) Mean (SD) Median (IQR)	x (x) x (x) x (x, x)	x (x) x (x) x (x, x)	x (x) x (x) x (x, x)	x (x) x (x) x (x, x)	x (x) x (x) x (x, x)	X
Duration of asthma (years)	N (% non-missing) Mean (SD) Median (IQR)	x (x) x (x) x (x, x)	x (x) x (x) x (x, x)	x (x) x (x) x (x, x)	x (x) x (x) x (x, x)	x (x) x (x) x (x, x)	X
Duration of COPD (years)	N (% non-missing) Mean (SD) Median (IQR)	x (x) x (x) x (x, x)	x (x) x (x) x (x, x)	x (x) x (x) x (x, x)	x (x) x (x) x (x, x)	x (x) x (x) x (x, x)	X
Smoking status,* n (%)	Non-smoker Current smoker Ex-smoker	x (x) x (x) x (x)	x (x) x (x) x (x)	x (x) x (x) x (x)	x (x) x (x) x (x)	x (x) x (x) x (x)	X
	Total	x (x)	x (x)	x (x)	x (x)	x (x)	
Pack years†	N (% non-missing) Mean (SD) Median (IQR)	x (x) x (x) x (x, x)	x (x) x (x) x (x, x)	x (x) x (x) x (x, x)	x (x) x (x) x (x, x)	x (x) x (x) x (x, x)	X
Highest education level* (categorised), n (%)	Post graduate degree First university degree Any other post-secondary training	x (x) x (x) x (x)	x (x) x (x) x (x)	x (x) x (x) x (x)	x (x) x (x) x (x)	x (x) x (x) x (x)	X

*At iHARP review date
† For current and ex-smokers only

Demographic variable		Inhaler device					p-value[a]
		Spiromax N=x	Turbohaler N=x	Diskus N=x	MDI N=x	Total N=x	
	Completed secondary education	x (x)	x (x)	x (x)	x (x)	x (x)	
	Some secondary education	x (x)	x (x)	x (x)	x (x)	x (x)	
	Completed primary education	x (x)	x (x)	x (x)	x (x)	x (x)	
	Some primary education	x (x)	x (x)	x (x)	x (x)	x (x)	
	None	x (x)	x (x)	x (x)	x (x)	x (x)	
	Total	x (x)	x (x)	x (x)	x (x)	x (x)	
Date of iHARP review (categorised), n (%)	February 2016	x (x)	x (x)	x (x)	x (x)	x (x)	X
	March 2016	x (x)	x (x)	x (x)	x (x)	x (x)	
	April 2016	x (x)	x (x)	x (x)	x (x)	x (x)	
	May 2016	x (x)	x (x)	x (x)	x (x)	x (x)	

[a]p-values will be calculated using the following tests: chi square test for categorical variables and ANOVA for variables measured on the interval scale

Example of the co-morbidities and medications results tables

Co-morbidity variables		Inhaler device					p-value[a]
		Spiromax N=x	Turbohaler N=x	Diskus N=x	MDI N=x	Total N=x	
Charlson comorbidity index, n (%)	0	x (x)	x (x)	x (x)	x (x)	x (x)	X
	1-4	x (x)	x (x)	x (x)	x (x)	x (x)	
	5+	x (x)	x (x)	x (x)	x (x)	x (x)	
	Total	x (x)	x (x)	x (x)	x (x)	x (x)	
Rhinitis severity,* n (%)	No rhinitis	x (x)	x (x)	x (x)	x (x)	x (x)	X
	Mild rhinitis	x (x)	x (x)	x (x)	x (x)	x (x)	
	Significant rhinitis	x (x)	x (x)	x (x)	x (x)	x (x)	
	Total	x (x)	x (x)	x (x)	x (x)	x (x)	
GERD treatment†, n (%)	Yes	x (x)	x (x)	x (x)	x (x)	x (x)	X
	No	x (x)	x (x)	x (x)	x (x)	x (x)	
	Total	x (x)	x (x)	x (x)	x (x)	x (x)	
Patient reported side effects, n (%)	Sore mouth/ throat	x (x)	x (x)	x (x)	x (x)	x (x)	X
	Oral thrush	x (x)	x (x)	x (x)	x (x)	x (x)	
	Bruising	x (x)	x (x)	x (x)	x (x)	x (x)	
	Hoarse voice	x (x)	x (x)	x (x)	x (x)	x (x)	
	Abnormal weight gain	x (x)	x (x)	x (x)	x (x)	x (x)	
	Cough	x (x)	x (x)	x (x)	x (x)	x (x)	
	Total	x (x)	x (x)	x (x)	x (x)	x (x)	

[a]p-values will be calculated using chi square test

* Patients with rhinitis identified by asking the following question: Do you have any of these symptoms: itchy, runny, blocked nose or sneezing when you don't have a cold? Where the answers could be:
1. No
2. Occasionally and little bother
3. Occasionally and quite a bother
4. Most days and little bother
5. Most days and a lot of bother

Classified by:
No rhinitis: 0
Mild Rhinitis = 1 or 3.
Significant rhinitis = 2 or 4

† In the year prior to the iHARP review

Example of treatment adherence and asthma control results tables

Treatment adherence & disease control variables		Inhaler device					
		Spiromax N=x	Turbohaler N=x	Diskus N=x	MDI N=x	Total N=x	p-value[a]
MARS score*	Good	x (x)	x (x)	x (x)	x (x)	x (x)	X
	Borderline	x (x)	x (x)	x (x)	x (x)	x (x)	
	Poor	x (x)	x (x)	x (x)	x (x)	x (x)	
	Total	x (x)	x (x)	x (x)	x (x)	x (x)	
Patient reported paracetamol use, n (%)	Regular	x (x)	x (x)	x (x)	x (x)	x (x)	X
	Intermittent	x (x)	x (x)	x (x)	x (x)	x (x)	
	Not used	x (x)	x (x)	x (x)	x (x)	x (x)	
	Total	x (x)	x (x)	x (x)	x (x)	x (x)	
Number of asthma/ COPD exacerbations†, n (%)	None	x (x)	x (x)	x (x)	x (x)	x (x)	X
	1	x (x)	x (x)	x (x)	x (x)	x (x)	
	≥2	x (x)	x (x)	x (x)	x (x)	x (x)	
	Total	x (x)	x (x)	x (x)	x (x)	x (x)	
Current inhaler device	n (%)	x (x)	x (x)	x (x)	x (x)	x (x)	X

[a]p-values will be calculated using chi square test

* MARS adherence was reported using the Medication Adherence Rating Scale (MARS) score. This measures adherence on a 6-point scale (never, rarely, sometimes, regular, often and always) in response to the following questions about their preventer inhaler use:
    1. I use it only when I feel breathless
    2. I avoid using it if I can
    3. I forget to take it
    4. I decide to miss a dose
    5. I choose to take it once a day

  Adherence was categorised as: poor (any of the questions answered with 'often' or 'always'), borderline (more than one questions with 'sometimes') and good (none of above).

† In the year preceding iHARP review, calculated from questions about the number of courses or oral steroid, hospitalisations and A&E attendances for breathing difficulties.

13.6 Appendix 6: Example of outcome results tables

Example of clinical efficiency results table

Inhaler device	Time to achieve device mastery (seconds)			Number of attempts		
	Mean (SD)	Median	p-value[a]	Mean (SD)	Median	p-value[b]
Spiromax	x (x)	x	x	x (x)	x	x
Turbohaler	x (x)	x	x	x (x)	x	x
Diskus	x (x)	x	x	x (x)	x	x
MDI	x (x)	x	x	x (x)	x	x
Total	x (x)	x	x	x (x)	x	x

[a]p-values will be calculated using log-rank test
[b]p-values will be calculated using paired t-test (mean) or Wilcoxon signed rank test (medians) dependent on the data distribution

Example of patient preference questionnaire results table

Inhaler characteristics	Patient preference					
	Spiromax	Turbohaler	Diskus	MDI	No preference	Total
Number of steps, n (%)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Time needed, n (%)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Ease of use, n (%)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)

Example of risk mitigation strategy table: redefine training time

Inhaler device	Time to achieve device mastery (seconds)*			Number of attempts		
	Mean (SD)	Median	p-value[a]	Mean (SD)	Median	p-value[b]
Spiromax	x (x)	x	x	x (x)	x	x
Turbohaler	x (x)	x	x	x (x)	x	x
Diskus	x (x)	x	x	x (x)	x	x
MDI	x (x)	x	x	x (x)	x	x
Total	x (x)	x	x	x (x)	x	x

[a]p-values will be calculated using log-rank test
[b]p-values will be calculated using paired t-test (mean) or Wilcoxon signed rank test (medians) dependent on the data distribution

Example of risk mitigation strategy table: asthma patient group only

Inhaler device	Time to achieve device mastery (seconds)			Number of attempts		
	Mean (SD)	Median	p-value[a]	Mean (SD)	Median	p-value[b]
Spiromax	x (x)	x	x	x (x)	x	x
Turbohaler	x (x)	x	x	x (x)	x	x
Diskus	x (x)	x	x	x (x)	x	x
MDI	x (x)	x	x	x (x)	x	x
Total	x (x)	x	x	x (x)	x	x

[a]p-values will be calculated using log-rank test
[b]p-values will be calculated using paired t-test (mean) or Wilcoxon signed rank test (medians) dependent on the data distribution

* Where "time to achieve device mastery" is redefined as seconds from the beginning of patient demonstrations (ie excluding clinic nurse instruction time) as per section 5.4.

Example of risk mitigation strategy table: COPD patient group only

Inhaler device	Time to achieve device mastery (seconds)			Number of attempts		
	Mean (SD)	Median	p-value[a]	Mean (SD)	Median	p-value[b]
Spiromax	x (x)	x	x	x (x)	x	x
Turbohaler	x (x)	x	x	x (x)	x	x
Diskus	x (x)	x	x	x (x)	x	x
MDI	x (x)	x	x	x (x)	x	x
Total	x (x)	x	x	x (x)	x	x

[a]p-values will be calculated using log-rank test
[b]p-values will be calculated using paired t-test (mean) or Wilcoxon signed rank test (medians) dependent on the data distribution