Research in Real-Life
Study protocol

Study protocol

ICARUS: Inhaled Corticosteroid And Real life Unlicensed Spacer use – stage 1

Examining the real-life unlicensed and licensed use of inhaled corticosteroids with or without spacers in patients with asthma in the United Kingdom

Date:
2nd February 2016

Chiesi contact:
Matthias Ochel

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

Research in Real-Life Ltd
5a Coles Lane
Oakington
Cambridge CB24 3BA
United Kingdom

Phone (+44) 1223 967858
Fax (+44) 0808 2800 792
Web site http://www.rirl.org

Chief Investigator:

Professor David Price, Professor of Primary Care Respiratory Medicine and RiRL Director
Mobile: +44 7787905057
Office number: +44 2081233923
Skype ID: respiratoryresearch
Email: david@rirl.org

Project coordinator:

Simon Yau
Research in Real-Life Ltd
5a Coles Lane, Oakington, Cambridgeshire CB24 3BA, UK
Direct number: 01223 967830
Email: simon.yau@rirl.org

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Study sponsor:

Chiesi Ltd

Primary contact

Matthias Ochel

TITLE	ICARUS
Subtitle	Examining the real-life unlicensed and licensed use of inhaled corticosteroids with or without spacers in patients with asthma in the United Kingdom
Protocol version number	0.4
Medicinal product	Clenil (beclomethasone dipropionate)
Medical device	Aerochamber, Volumatic, Pocket, Able, Optichamber spacer
Marketing authorisation holder	Clenil: Chiesi Limited 333 Styal Road Manchester M22 5LG
Study aims and objectives	The aim of the study is to characterise a cohort of patients prescribed beclomethasone and who are prescribed/not prescribed spacers, to determine whether ICS/spacer guidelines are followed in real life practice
Country of study	UK
Author	RiRL UK Ltd 5a Coles Lane Oakington Cambridge CB24 3BA United Kingdom

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3.0 Background

Treatment of asthma is centered around the use of inhaled corticosteroids, which are recommended in all but the least severe patients with asthma[1]. GINA guidelines recommend patients who require their reliever more than once a fortnight be prescribed inhaled corticosteroids[1]. Inhaled corticosteroids have been shown to require significantly lower doses than oral corticosteroids, reducing the significant risk of glucocorticoid side effects [2](Table 1).

System Class	Adverse Reaction	Frequency
Infections	Oral thrush	Very common
Immune system	Rash, urticarial, pruritus, erthyema	Uncommon
	Oedema	Very Rare
Endocrine	Adrenal suppression, bone density reduction, growth retardation	Very Rare
Psychiatric disorders	Psychomotor hyperactivity, sleep disorder, depression, anxiety, behavioural disorders	Unknown
Nervous system disorders	Headache	Unknown
Eye disorders	Cataracts, glaucoma	Very Rare
Thoracic disorders	Hoarseness, throat irritation	Common
	Cough, bronchospasm, wheezing, dyspnoea	Very rare
Gastrointestinal	Nausea	Unknown

Table 1: Side effects of beclomethasone listed by system [3]

The use of inhaled corticosteroids (ICS) requires meaningful delivery of the drug to the lungs, which requires good adherence and inhaler technique from the patient. Up to 80% of the inhaled drug ends up impacting in the oropharynx, even when good technique is used. Spacer devices are suggested to improve drug delivery[3].

Spacer devices are an extension add on device that allows the aerosol from metered dose inhalers to expand and slow down. This effect changes the actuation spray into a fine mist, allowing more time for the evaporation of the propellant, so a larger proportion of the particles can be inhaled. A fine mist is less likely to impact the oropharynx and reach the target of the lungs. Spacers also help to coordinate the breathing between actuation and breath. The use of bronchodilators and spacers is on par to that of nebulisers in terms of effectiveness[4]. The improved drug delivery can help reduce the amount of inhaled corticosteroid required.

Commented [L2]: In terms of what? Equally frequently? Equally effective? By similar severity patients?

Commented [s3R2]: Added effectiveness

The use of spacers is recommended by NICE for patients aged under 16 with the following guidance [4]:

Inhaler devices for children under 5 years with chronic asthma (August 2000)

A child's needs and likelihood of good compliance should govern the choice of inhaler and spacer device; only then should cost be considered.

- corticosteroid and bronchodilator therapy should be delivered by pressurised metered-dose inhaler and spacer device, with a facemask if necessary;

Inhaler devices for children 5–15 years with chronic asthma (March 2002)

A child's needs, ability to develop and maintain effective technique, and likelihood of good compliance should govern the choice of inhaler device; only then should cost be considered.

- corticosteroid therapy should be routinely delivered by a pressurised metered-dose inhaler and spacer device;
- for other inhaled drugs, particularly bronchodilators, a wider range of devices should be considered;
- children and their carers should be trained in the use of the chosen device; suitability of the device should be reviewed at least annually. Inhaler technique and compliance should be monitored

Figure 1: NICE guidance for spacer use in children

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Also yellow text is not very easy to read

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Spacers are advised for patients who have problems with co-ordinating actuation since they are simpler to use. They are also advised to be used in adult patients using high doses of inhaled corticosteroids (cut off defined as 500 mcg fluticasone/1000 mcg beclomethasone equivalent or higher)[5].

There are several brands of spacers that fit different inhalers as shown in Table 2: Spacer and suitable MDI devices:

MDI	Able spacer	Aerochamber Plus	Optichamber	Pocket Chamber	Volumatic
Beclomethasone (Clenil Modulite)	a	a	a	a	✓
Beclomethasone Dipropionate HFA	a	✓	a	a	×
Fluticasone propionate	a	✓	a	a	✓
Ciclesonide	a	✓	a	a	×
Beclomethasone/ formoterol	a	✓	a	a	×
Fluticasone propionate / formoterol	a	✓	a	a	×
Fluticasone propionate / salmeterol	a	✓	a	a	✓

Table 2: Spacer and suitable MDI devices

a = fits spacer but not licensed for use ✓ = licensed for use × = does not fit spacer

Larger spacers such as the Volumatic spacer have been shown to feature a lower deposition of drug on the filters compared to the use of smaller spacers [2] which may mean that the ICS related adverse events may differ for different spacer devices.

In real life practice, the effectiveness of any device combination depends on the willingness and ability of the patient to use it[6]. Patients may not use the device correctly as in Table 3: Spacer errors [6]:

Errors with spacer devices
Placement of inhaler in the wrong end of the spacer
Failure to exhale slowly
Failure to shake inhaler well
Waiting too long before inhaling
Pressing too many times on the MDI
Rapid inhalation
Exhaling into device
Inadequate breath hold

Table 3: Spacer errors [6]

In addition, primary care physicians who prescribe spacers may not adhere to prescription guidelines given that their patients may be unwilling to carry or use the devices.

The aim of this study is to explore and characterise the demographics of patients prescribed beclometasone within spacer guidelines and, to examine the proportion of patients prescribed of ICS in real life that match current NICE spacer device guidelines.

4.0 Study aims and objectives

4.1 Study aims

The aim of the study is to characterise a cohort of patients with asthma prescribed beclometasone and who are prescribed/not prescribed spacers, to determine whether ICS/spacer guidelines are followed in real life practice

.

4.2 Study objectives

4.2.1 Primary objective

Describe the number of patients with asthma under 65 prescribed non extra-fine beclomethasone with/without different types of spacers and in the following subgroups.

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Commented [L7]: Not sure this is currently reflected in the objectives

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Commented [L9]: This is not very specific. My understanding is that objectives are generally more specific than aims.

4.2.2 Secondary objective

Describe the demographics and disease characteristics of patients prescribed non extra-fine beclometasone and spacers.

4.2.3 Exploratory objective

To describe the number, demographics and disease characteristics of patients over 65 years old

4.3 Sub-analysis

To explore the primary, secondary and exploratory objectives in the following subgroups where applicable:

1) High dose (≤1000 mcg beclometasone per day)
2) Low dose (<1000 mcg beclometasone per day)
3) Under 16 age group
4) Adult population (16 to 65)

5.0 Study design

5.1 Products studied

The medicinal product is Clenil Modulite®, which provides 250µg beclometasone diproprionate per actuation in a pressurised metered dose inhaler (MDI) device.[7]
The devices studied include Volumatic®, Able®, Aerochamber®, Optichamber® and Pocket Spacer®.

5.2 Study design

A historical cross-sectional database study to describe all patients with asthma who are prescribed beclometasone (Clenil Modulite®). Patients with stable therapy beclometasone are described as having ≥2 prescriptions of beclometasone in the year prior to the index date). Patients will be considered spacer users if they have been prescribed a spacer within one year of being prescribed beclometasone. The "index date" is the time of data extraction in the study period.

Commented [L10]: Historical cross-sectional study looking at period prevalence of beclometasone + spacer use among asthma patients aged <65 years.

Period prevalence = you can take first patient/prescription record that occurred in, say, Jan-Dec 2015. So each patient only appears in the study once, and you can analyse more patients because their prescription didn't have to occur on one single date.

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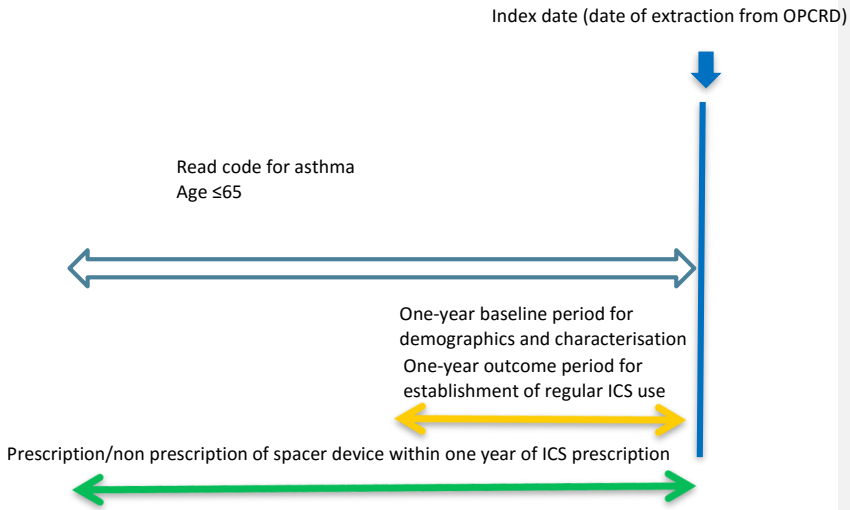


Figure 2: Study design

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5.3 Subanalysis

1. Characterisation by age group (<16, 16-65, all ages, 65+ as an exploratory group)
2. Characterisation by high daily ICS dose (>500mcg fluticasone/1000mcg average daily dose of beclometasone)

6.0 Study Population

6.1 Inclusion and exclusion criteria

Table 4: Inclusion and exclusion criteria

Inclusion criteria
Diagnosis for asthma (confirmed by diagnostic Read code)
Age ≤65 years at index date for main outcomes, all ages for exploratory
Two years of continuous practice data comprising 2-year baseline data
≥2 separate prescriptions of the beclometasone pMDI within one year prior to extraction date
Exclusion criteria
Received beclomethasone in form of FDC ICS/LABA prior to index date

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6.2 Data source

The study will use patient data from the Optimum Patient Care Research Database (OPCRD).[8] The study team work with anonymous data removed of any patient identifiable information. The OPCRD is developed, maintained, and owned by Optimum Patient Care (OPC), a social enterprise company that aims to improve patient outcomes through medical research and services. OPC provides evidence-based recommendations to UK general practices through bespoke software and practice reports.

The OPCRD currently comprises longitudinal medical records for over 2.5 million patients from over 550 primary care practices across the UK. The OPCRD contains two types of data: (1) routinely recorded clinical data and (2) questionnaire responses from over 55,700 patients with respiratory conditions. 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 that complements routinely recorded disease coding and prescribing information with patient-reported outcomes. The OPCRD also links with nationwide practice prescribing data to enable targeted delivery of dataset needs.

A unique dataset is provided for each study with only the variables necessary to inform the study objectives included. Only studies that evaluate risk-benefit profiles of treatment options will report adverse events of treatments, ensuring confidentiality of data at all stages. The study will be performed in compliance with all applicable local and international laws and regulations, including without limitation ICH E6 guidelines for Good Clinical Practices. The database has received a favourable opinion from the Health Research Authority for clinical research use (REC reference: 15/EM/0150). Governance is provided by The Anonymous Data Ethics Protocols and Transparency (ADEPT) committee, an independent body of experts and regulators commissioned by the Respiratory Effectiveness Group (REG, http://www.effectivenessevaluation.org/) to govern the standard of research conducted on internationally recognised databases. All research using OPCRD will be registered on established study databases such as the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP, http://www.encepp.eu/).

7.0 Study variables and study outcomes

Refer to Appendices for detailed variable and outcome definitions, and mock tables of demographic and baseline variables and outcome results.

7.1 Demographic and disease characteristic variables

- Gender (male/female)
- Age of patient (years, at index date)
- Body Mass Index (BMI, at time of index date, calculated from height and weight data if available, otherwise taken from practice-recorded BMI value, detailed definition in Appendix 1)
- Smoking status (identified by Read code, closest to index date)
- SABA daily dose* (closest to index date)
- Percentage predicted peak flow (peak flow predicted, closest to index date)
- FEV_1/FVC ratio (closest to index date)
- ICS daily dose (closest to index date)
- Number of exacerbations (ATS/ERS 2015 consensus definition±, in the year prior to index date)
- Number of oral corticosteroid prescriptions (in the year prior to index date)
- Number of antibiotic prescriptions for lower respiratory tract infections (in the year prior to index date)
- Number of non-extra fine beclometasone prescriptions (in the year prior to index date)
- History of comorbidities related to asthma:
    - Pneumonia (Read code diagnosis in year prior to the index date)
    - Diabetes (Read code diagnosis and/or antidiabetic drugs ever prior to the index date)
    - Ischaemic heart disease (Read code diagnosis ever prior to the index date)
    - Rhinitis (Read code diagnosis, including chronic and allergic rhinitis and prescriptions for nasal steroids in the year prior to index date)
    - Eczema (Read code diagnosis in the year prior to index date)
    - Osteoporosis (Read code diagnosis ever prior to the index date)
    - Charlson Comorbidity Index (based on Read code diagnoses in year prior to index date, detailed definition in Appendix 1)

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Commented [L17]: Footnote definitions are mixed up

* Calculated as average number of puffs per day over the year multiplied by strength (in mcg); i.e. $\frac{Number\ of\ inhalers * doses\ per\ inhaler}{365} * strength$

±See appendix 15.1.2 for definitions

7.2 Primary outcome

Period prevalence of spacer use/non spacer use for patients prescribed non extra-fine beclomethasone in total and within sub-groups.

7.3 Secondary outcomes

Description of patients in each spacer group by demographic and clinical characteristics in total and within sub-groups.

7.4 Exploratory outcomes

Period prevalence of spacer usage and non-extra-fine beclomethasone for patients aged <65 in total and for high/low daily doses (<1000 mcg or ≥1000 mcg)

8.0 Statistical analysis

8.1 Software used

The dataset will be analysed using SPSS version 23, SAS version 9.3, R version 3.1.2, Stata SE version 14 (StataCorp, College Station, TX) and Microsoft Office EXCEL 2013, as appropriate.

8.2 Baseline characterisation

Data preparation and exploratory analysis will include the investigation of potential outliers and missing data for all variables. Plots will be produced where relevant for explanatory and outcome variables. For variables measured on the interval or ratio scale, these will include:

- Frequency plots to illustrate the distribution of the variable and whether categorisation may be necessary (for example, if heavily skewed)
- Box plots to 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.

Skewed data will be transformed or categorised, as appropriate.

8.2.1 Summary statistics

Summary statistics will be produced for all baseline and outcome variables, as a complete dataset, by treatment group and for sub-groups. For variables measured on the interval or ratio scale, these will include:

- Sample size (n)
- Percentage non-missing
- Mean
- Standard Deviation (SD)
- Median
- Inter-quartile range (IQR – 25th and 75th percentiles)

For categorical variables, the summary statistics will include:

- Sample size (n)
- Count and percentage by category

9.0 Regulatory and ethical compliance

This study was 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.

10.0 Data dissemination

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

11.0 Advisory group

No steering committee has been selected for this study.

12.0 Research team

Research Organisation:

Research in Real-Life (RiRL) Ltd

Chief Investigator:

David Price, Professor of Primary Care Respiratory Medicine and RiRL Director
Mobile: +44 7787905057
Office number: +44 2081233923
Skype ID: respiratoryresearch
Email: david@rirl.org

Other RiRL team members:

Commercial and Compliance Director: Catherine Hutton
Project coordinator: Humeyra Erdogan (humeyra@rirl.org)
Project research lead: Simon Yau (simon.yau@rirl.org)
Senior statistician: Vicky Thomas (vicky@crs-ltd.org)
Senior data analyst: Derek Skinner (derek@optimumpatientcare.org)

Study sponsor:

Chiesi Ltd

Primary contact

Matthias Ochel

13.0 Timelines

Table 5: Project timelines

Action	Timeline	Dates
Protocol development	3 weeks	28th February 2016
Chiesi sign off	2 weeks	14th March 2016
Data extraction	4 weeks	14th April 2016
Cross sectional analysis	4 weeks	14th May 2016
Baseline report	3 weeks	9th June 2016
Baseline Chiesi review	1 week	1st July 2016
Sub-analysis	3 weeks	27th July 2016
Final report writing (PowerPoint and Word report)	3 weeks	21st August 2016
Chiesi review	1 week	28th August 2016

Commented [L18]: This could be “cross-sectional” or “period prevalence” or something like that.

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14.0 References

1. Reddel HK, Bateman ED, Becker A, et al. A summary of the new GINA strategy: a roadmap to asthma control. *Eur Respir J.* 2015;46(3):622-639.
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15.0 APPENDIX

15.1 Appendix 1: Definitions

15.1.1 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).

15.1.2 Asthma exacerbation (ATS/ERS consensus definition 2015)

Where an exacerbation is defined as an occurrence* of:

1. Asthma-related†: Unscheduled hospital admission / A&E attendance; OR
2. An acute‡ course of oral steroids; OR
3. Antibiotics prescribed with lower respiratory consultation§.

15.1.3 Comorbidities – Charlson Comorbidity Index (CCI)

The CCI was developed in the US in 1987 as a method of classifying prognostic comorbidity in longitudinal studies.[9] 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.

*Where ≥1 oral steroid course / hospitalisation / antibiotics prescription occur within 2 weeks of each other, these events will be considered to be the result of the same exacerbation (and will only be counted once).

†**Asthma-related Hospitalisations:** consist of either a definite Asthma Emergency Attendance or a definite COPD Hospital Admission; OR a generic hospitalisation read code which has been recorded on the same day as a **Lower Respiratory Consultation**** (see below; (a) – (c) only and excluding where the only lower respiratory code recorded on that day was for a lung function test).

‡ Acute oral steroid use associated with asthma exacerbation treatment will be defined as:

- all courses that are definitely not maintenance therapy, and/or
- all courses where dosing instructions suggest exacerbation treatment (e.g. 6,5,4,3,2,1 reducing, or 30mg as directed), and/or
- all courses with no dosing instructions, but unlikely to be maintenance therapy due to prescription strength or frequency of prescriptions.

where "maintenance therapy" is defined as: daily dosing instructions of <=10mg Prednisolone or prescriptions for 1mg or 2.5mg Prednisolone tablets where daily dosing instructions are not available.

§ **Lower Respiratory Consultations -** consist of the following:

a) Lower Respiratory read codes (including Asthma, COPD and LRTI read codes);
b) Asthma/COPD review codes excl. any monitoring letter codes;
c) Lung function and/or asthma monitoring
d) Any additional respiratory examinations, referrals, chest x-rays, or events.

The weights were revised and updated (for example, mortality due to HIV has fallen) by Dr Foster Intelligence (DFI) in their HSMR Methodology documentation[10] 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 6: 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

15.2 Appendix 2: Mock baseline results tables

Table 7: Summary statistic of baseline variables overall

		Volumatic®	Aerochamber®	Optichamber®	Pocket Spacer®	Able Spacer®	No Spacer
	Total (%)	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**
Age (years)	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Gender, n (%)	Male	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Female	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
BMI (kg/m^2)	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
BMI (categorised), n (%)	Underweight	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Normal	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Overweight	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Obese	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Smoking status, n (%)	Current smoker	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Ex-smoker	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Average SABA daily dose	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Average SABA daily dose (categorised), n (%)	Low	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Medium	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	High	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Medium	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	High	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
FEV_1/FVC ratio	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Exacerbation count	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)

Commented [L20]: You basically have 2 tables – summary statistics of variables of interest, and summary of comorbidities. Isn't it more useful for the protocol just to have these tables in once, and then describe which groups you'll repeat the tables for? Saves loads of pages…

Commented [s21R20]: Happy having millions of tables

Commented [L22]: This is not one of your listed variables…

Commented [s23R22]: included

	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Oral corticosteroids prescriptions	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Antibiotic prescriptions for LRTI	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
% Predicted Peak Flow	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)

Table 8: Summary statistics for diagnoses of co-morbidities at baseline

		Volumatic®	Aerochamber®	Optichamber®	Pocket Spacer®	Able Spacer®	No Spacer
	Total (%)	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**
Pneumonia	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Diabetes	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Ischaemic heart disease	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Rhinitis	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Eczema	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Osteoporosis	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
	0	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	1-4	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)

Charlson comorbidity index, n (%)	5+	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)

		Volumatic®	Aerochamber®	Optichamber®	Pocket Spacer®	Able Spacer®	No Spacer
	Total (%)	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**
Age (years)	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Gender, n (%)	Male	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Female	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
BMI (kg/m^2)	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
BMI (categorised), n (%)	Underweight	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Normal	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Overweight	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Obese	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Smoking status, n (%)	Current smoker	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Ex-smoker	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Average SABA daily dose	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Average SABA daily dose (categorised), n (%)	Low	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Medium	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	High	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Medium	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	High	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
FEV_1/FVC ratio	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)

Commented [L24]: This isn't one of your listed variables

	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Exacerbation count	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Oral corticosteroids prescriptions	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Antibiotic prescriptions for LRTI	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
% Predicted Peak Flow	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)

Table 9: Summary statistics for <16 age group

		Volumatic®	Aerochamber®	Optichamber®	Pocket Spacer®	Able Spacer®	No Spacer
	Total (%)	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**
Pneumonia	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Diabetes	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Ischaemic heart disease	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Rhinitis	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Eczema	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Osteoporosis	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)

	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Charlson comorbidity index, n (%)	0	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	1-4	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	5+	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)

Table 10: Summary statistics for comorbidities in <16 age group

		Volumatic®	Aerochamber®	Optichamber®	Pocket Spacer®	Able Spacer®	No Spacer
	Total (%)	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**
Age (years)	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Gender, n (%)	Male	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Female	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
BMI (kg/m^2)	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
BMI (categorised), n (%)	Underweight	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Normal	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Overweight	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Obese	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Smoking status, n (%)	Current smoker	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Ex-smoker	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Average SABA daily dose	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Average SABA daily dose (categorised), n (%)	Low	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Medium	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	High	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Medium	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	High	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
FEV_1/FVC ratio	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)

Commented [L25]: This isn't one of your listed variables

	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Exacerbation count	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Oral corticosteroids prescriptions	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Antibiotic prescriptions for LRTI	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
% Predicted Peak Flow	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)

Table 11: Summary statistics for mean <1000mcg beclometasone per day

		Volumatic®	Aerochamber®	Optichamber®	Pocket Spacer®	Able Spacer®	No Spacer
	Total (%)	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**
Pneumonia	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Diabetes	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Ischaemic heart disease	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Rhinitis	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Eczema	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Osteoporosis	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)

	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Charlson comorbidity index, n (%)	0	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	1-4	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	5+	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)

Table 12: Summary statistics for mean ICS <1000mcg dose per day

		Volumatic®	Aerochamber®	Optichamber®	Pocket Spacer®	Able Spacer®	No Spacer
	Total (%)	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**
Age (years)	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Gender, n (%)	Male	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Female	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
BMI (kg/m^2)	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
BMI (categorised), n (%)	Underweight	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Normal	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Overweight	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Obese	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Smoking status, n (%)	Current smoker	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Ex-smoker	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Average SABA daily dose	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Average SABA daily dose (categorised), n (%)	Low	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Medium	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	High	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Medium	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	High	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
FEV_1/FVC ratio	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)

Commented [L26]: This isn't one of your listed variables

	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Exacerbation count	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Oral corticosteroids prescriptions	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Antibiotic prescriptions for LRTI	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
% Predicted Peak Flow	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)

Table 13: Summary statistics for 16-65 year olds

		Volumatic®	Aerochamber®	Optichamber®	Pocket Spacer®	Able Spacer®	No Spacer
	Total (%)	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**
Pneumonia	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Diabetes	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Ischaemic heart disease	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Rhinitis	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Eczema	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Osteoporosis	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)

Charlson comorbidity index, n (%)	0	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	1-4	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	5+	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)

Table 14: Summary co-morbidities for 16-65 year olds

		Volumatic®	Aerochamber®	Optichamber®	Pocket Spacer®	Able Spacer®	No Spacer
	Total (%)	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**
Age (years)	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Gender, n (%)	Male	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Female	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
BMI (kg/m^2)	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
BMI (categorised), n (%)	Underweight	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Normal	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Overweight	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Obese	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Smoking status, n (%)	Current smoker	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Ex-smoker	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Average SABA daily dose	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Average SABA daily dose (categorised), n (%)	Low	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Medium	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	High	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Medium	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	High	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
FEV_1/FVC ratio	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)

Commented [L27]: This isn't one of your listed variables

Exacerbation count	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Oral corticosteroids prescriptions	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Antibiotic prescriptions for LRTI	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
% Predicted Peak Flow	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)

Table 15: Summary statistics for mean dose of 1000+ mcg becloemetasone

		Volumatic®	Aerochamber®	Optichamber®	Pocket Spacer®	Able Spacer®	No Spacer
	Total (%)	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**
Pneumonia	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Diabetes	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Ischaemic heart disease	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Rhinitis	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Eczema	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Osteoporosis	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
	0	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	1-4	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)

Charlson comorbidity index, n (%)	5+	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)

Table 16: Summary statistics for mean dose (1000+mcg of beclometasone)

		Volumatic®	Aerochamber®	Optichamber®	Pocket Spacer®	Able Spacer®	No Spacer
	Total (%)	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**
Age (years)	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Gender, n (%)	Male	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Female	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
BMI (kg/m^2)	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
BMI (categorised), n (%)	Underweight	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Normal	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Overweight	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Obese	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Smoking status, n (%)	Current smoker	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Ex-smoker	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Average SABA daily dose	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Average SABA daily dose (categorised), n (%)	Low	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Medium	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	High	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Medium	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	High	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
FEV_1/FVC ratio	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Exacerbation count	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)

Commented [L28]: This isn't one of your listed variables

	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Oral corticosteroids prescriptions	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Antibiotic prescriptions for LRTI	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
% Predicted Peak Flow	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)

Table 17: Summary statistics for <16 and high dose ICS

		Volumatic®	Aerochamber®	Optichamber®	Pocket Spacer®	Able Spacer®	No Spacer
	Total (%)	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**
Pneumonia	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Diabetes	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Ischaemic heart disease	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Rhinitis	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Eczema	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Osteoporosis	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Charlson comorbidity index, n (%)	0	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	1-4	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	5+	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)

Table 18: Summary statistics for <16 and high dose ICS

		Volumatic®	Aerochamber®	Optichamber®	Pocket Spacer®	Able Spacer®	No Spacer
	Total (%)	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**
Age (years)	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Gender, n (%)	Male	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Female	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
BMI (kg/m^2)	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
BMI (categorised), n (%)	Underweight	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Normal	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Overweight	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Obese	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Smoking status, n (%)	Current smoker	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Ex-smoker	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Average SABA daily dose	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Average SABA daily dose (categorised), n (%)	Low	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Medium	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	High	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Medium	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	High	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
FEV_1/FVC ratio	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Exacerbation count	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)

Commented [L29]: This isn't one of your listed variables

Oral corticosteroids prescriptions	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Antibiotic prescriptions for LRTI	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
% Predicted Peak Flow	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)

Table 19: Summary statistics <16 and low dose ICS

		Volumatic®	Aerochamber®	Optichamber®	Pocket Spacer®	Able Spacer®	No Spacer
	Total (%)	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**
Pneumonia	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Diabetes	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Ischaemic heart disease	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Rhinitis	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Eczema	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Osteoporosis	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Charlson comorbidity index, n (%)	0	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	1-4	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	5+	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)

Table 20: Summary co-morbidities for <16 and low dose ICS

		Volumatic®	Aerochamber®	Optichamber®	Pocket Spacer®	Able Spacer®	No Spacer
	Total (%)	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**
Age (years)	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Gender, n (%)	Male	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Female	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
BMI (kg/m^2)	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
BMI (categorised), n (%)	Underweight	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Normal	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Overweight	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Obese	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Smoking status, n (%)	Current smoker	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Ex-smoker	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Average SABA daily dose	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Average SABA daily dose (categorised), n (%)	Low	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Medium	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	High	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Medium	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	High	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
FEV_1/FVC ratio	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Exacerbation count	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Oral corticosteroid	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)

Commented [L30]: This isn't one of your listed variables

s prescriptions	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Antibiotic prescriptions for LRTI	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
% Predicted Peak Flow	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)

Table 21: Summary statistics 16-65 and low dose ICS

		Volumatic®	Aerochamber®	Optichamber®	Pocket Spacer®	Able Spacer®	No Spacer
	Total (%)	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**
Pneumonia	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Diabetes	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Ischaemic heart disease	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Rhinitis	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Eczema	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Osteoporosis	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Charlson comorbidity index, n (%)	0	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	1-4	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	5+	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)

Table 22: Summary co-morbidities 16-65 and low dose ICS

		Volumatic®	Aerochamber®	Optichamber®	Pocket Spacer®	Able Spacer®	No Spacer
	Total (%)	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**
Age (years)	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Gender, n (%)	Male	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Female	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
BMI (kg/m^2)	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
BMI (categorised), n (%)	Underweight	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Normal	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Overweight	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Obese	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Smoking status, n (%)	Current smoker	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Ex-smoker	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Average SABA daily dose	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Average SABA daily dose (categorised), n (%)	Low	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Medium	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	High	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Medium	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	High	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
FEV_1/FVC ratio	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Exacerbation count	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Oral corticosteroid	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)

Commented [L31]: This isn't one of your listed variables

s prescriptions	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Antibiotic prescriptions for LRTI	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
% Predicted Peak Flow	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)

Table 23: Summary statistics 16-65 and high dose ICS

		Volumatic®	Aerochamber®	Optichamber®	Pocket Spacer®	Able Spacer®	No Spacer
	Total (%)	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**
Pneumonia	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Diabetes	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Ischaemic heart disease	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Rhinitis	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Eczema	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Osteoporosis	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Charlson comorbidity index, n (%)	0	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	1-4	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	5+	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)

Table 24: Summary statistics for comorbidities 16-65 and low dose ICS

	Volumatic®	Aerochamber®	Optichamber®	Pocket Spacer®	Able Spacer®	No Spacer

		Total (%)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Age (years)	N (% non-missing)		x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)		x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)		x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Gender, n (%)	Male		x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Female		x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
BMI (kg/m^2)	N (% non-missing)		x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)		x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)		x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
BMI (categorised), n (%)	Underweight		x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Normal		x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Overweight		x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Obese		x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Smoking status, n (%)	Current smoker		x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Ex-smoker		x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)		x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)		x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Average SABA daily dose	N (% non-missing)		x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)		x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)		x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Average SABA daily dose (categorised), n (%)	Low		x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Medium		x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	High		x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Medium		x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	High		x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)		x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
FEV_1/FVC ratio	N (% non-missing)		x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)		x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)		x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Exacerbation count	N (% non-missing)		x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)		x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)		x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Oral corticosteroid	N (% non-missing)		x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)		x (x)	x (x)	x (x)	x (x)	x (x)	x (x)

Commented [L32]: This isn't one of your listed variables

s prescriptions	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Antibiotic prescriptions for LRTI	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
% Predicted Peak Flow	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)

Table 25: Summary statistics 65+

		Volumatic®	Aerochamber®	Optichamber®	Pocket Spacer®	Able Spacer®	No Spacer
	Total (%)	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**
Pneumonia	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Diabetes	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Ischaemic heart disease	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Rhinitis	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Eczema	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Osteoporosis	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Charlson comorbidity index, n (%)	0	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	1-4	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	5+	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)

Table 26: Summary statistics for >65 age group

	Volumatic®	Aerochamber®	Optichamber®	Pocket Spacer®	Able Spacer®	No Spacer
Total (%)	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**

Age (years)	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Gender, n (%)	Male	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Female	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
BMI (kg/m^2)	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
BMI (categorised), n (%)	Underweight	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Normal	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Overweight	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Obese	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Smoking status, n (%)	Current smoker	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Ex-smoker	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Average SABA daily dose	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Average SABA daily dose (categorised), n (%)	Low	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Medium	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	High	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Medium	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	High	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
FEV_1/FVC ratio	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Exacerbation count	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Oral corticosteroids prescriptions	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)

Commented [L33]: This isn't one of your listed variables

Antibiotic prescriptions for LRTI	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
% Predicted Peak Flow	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)

Table 27: Summary statistics for 65+ and low dose ICS

		Volumatic®	Aerochamber®	Optichamber®	Pocket Spacer®	Able Spacer®	No Spacer
	Total (%)	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**
Pneumonia	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Diabetes	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Ischaemic heart disease	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Rhinitis	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Eczema	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Osteoporosis	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Charlson comorbidity index, n (%)	0	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	1-4	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	5+	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)

Table 28: Summary co-morbidities for 65+ and low dose ICS

		Volumatic®	Aerochamber®	Optichamber®	Pocket Spacer®	Able Spacer®	No Spacer
	Total (%)	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**
Age (years)	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)

	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Gender, n (%)	Male	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Female	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
BMI (kg/m^2)	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
BMI (categorised), n (%)	Underweight	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Normal	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Overweight	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Obese	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Smoking status, n (%)	Current smoker	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Ex-smoker	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Average SABA daily dose	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Average SABA daily dose (categorised), n (%)	Low	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Medium	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	High	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Medium	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	High	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
FEV_1/FVC ratio	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Exacerbation count	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Oral corticosteroids prescriptions	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Antibiotic prescriptions for LRTI	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)

Commented [L34]: This isn't one of your listed variables

	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
% Predicted Peak Flow	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)

Table 29: Summary statistics for 65+ and high dose ICS

		Volumatic®	Aerochamber®	Optichamber®	Pocket Spacer®	Able Spacer®	No Spacer
	Total (%)	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**	**x (x)**
Pneumonia	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Diabetes	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Ischaemic heart disease	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Rhinitis	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Eczema	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Osteoporosis	N (% non-missing)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Mean (SD)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	Median (IQR)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)	x (x, x)
Charlson comorbidity index, n (%)	0	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	1-4	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
	5+	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)

Table 30: Summary statistics for 65+ age group and high dose ICS

Commented [L35]: Where are the analysis tables? Your aim is to compare the groups, so what tables will you use to set out your comparison & statistical test results?

Commented [s36R35]: No analysis tables just descriptive