Supplementary methods/results

Inclusion criteria

- Male or Female aged between 18 and 80 years old
- Suspected asthma diagnosis & prescribed a new ICS

Exclusion criteria

- Already using inhaled or oral corticosteroid
- Pregnant females
- Other significant respiratory diagnosis

Study design

ACQ = asthma control questionnaire, ACT = asthma control test, SPT = skin prick test, FE_{NO} = Fractional exhaled nitric oxide level, BHR = methacholine challenge, Blood = full blood count (including differential cell count), Sputum = sputum induction and differential cell count

Study procedures

FE_{NO} was measured using a chemiluminescence analyser (NIOX MINO®; Aerocrine™, Tolna, Sweden) prior to any other study procedures at a flow rate of 50ml/s to provide two approved FE_{NO} measurements as per ATS guidelines(1). Following FE_{NO} measurement subjects were asked to complete the ACQ and ACT questionnaires.

Skin prick tests to a panel of common aeroallergens with normal saline and histamine controls (Alk-Abello™, Berkshire, UK) were performed according to a standard protocol. Participants were requested not to take any antihistamine medications for a minimum of 48 hours prior to the test.

Spirometry was performed using a Vitalograph™ dry wedge bellows spirometer (Vitalograph™ model 2150, Buckinghamshire, England) as per ERS guidelines(2). Airway hyperresponsiveness testing was performed using methacholine as a provocative agent and the tidal breathing method to determine the concentration of methacholine causing a 20% fall in FEV_1 (PC_{20}) as per a standard protocol(3). If subjects attended visit 1a bronchodilator reversibility was assessed 15 minutes after administration of 400 micrograms of salbutamol inhaled via a Volumatic® spacer as per ERS guidelines(2).

Sputum induction was performed using a protocol based on that described by Pin et al(4) and processed to obtain a sputum eosinophil count as previously described(5). Blood samples were also taken at each visit for differential cell count.

Diagnosis and ICS Response Criteria

Diagnosis of asthma was defined as one or both of:

- Reversibility of ≥12% and ≥200 ml of FEV_1 (6, 7)
- Provocative concentration of methacholine (PC_{20}) of ≤8mg/ml(3)

Response to inhaled steroids was pre-defined as a combination of *2* of any of the objective criteria or 1 objective criterion and 1 subjective criterion from the following predetermined criteria:

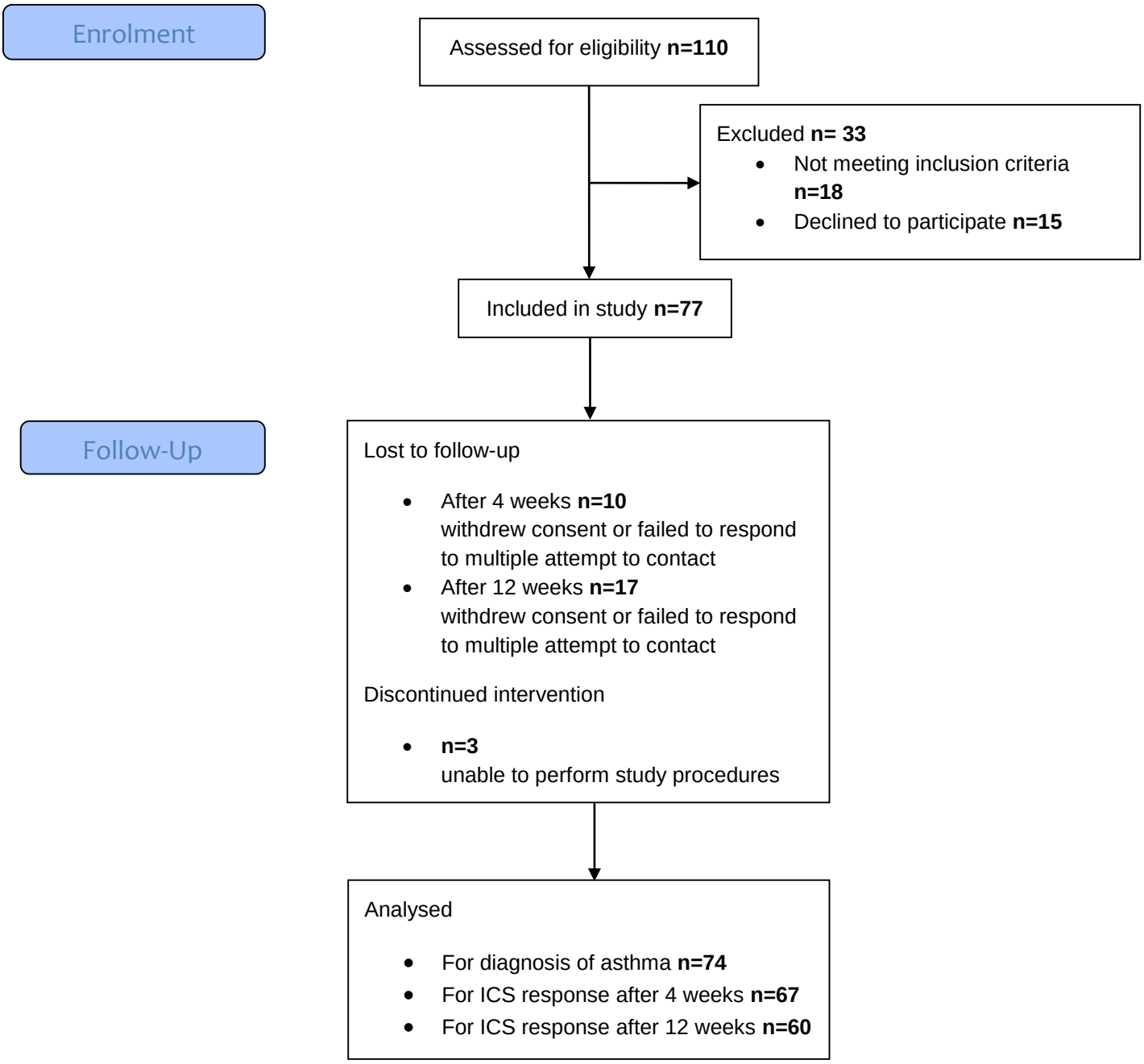
Objective:

- Increase in FEV_1 ≥12% (7)
- Increase in PC_{20} ≥ one doubling dose(8)
- Decrease in FE_{NO} of ≥20% for baseline values > 50 ppb or decrease of ≥10 ppb for baseline values ≤50 ppb (1)

Subjective:

- Decrease in ACQ ≥ 0.5(9)
- Increase in ACT ≥3 points(10)

Consort Diagram



Results

ROC AUC values for other baseline measures as predictors of ICS response

Baseline value	Response Criteria	ROC AUC
PC_{20}	Our defined criteria	0.32
FEV_1	Our defined criteria	0.58
Blood eosinophil count	Our defined criteria	0.67

References for online supplement:

1. ATS/ERS recommendations for standardized procedures for the online and offline measurement of exhaled lower respiratory nitric oxide and nasal nitric oxide, 2005. Am J Respir Crit Care Med. 2005;171(8):912-30.
2. Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, et al. Standardisation of spirometry. Eur Respir J. 2005;26(2):319-38.
3. Crapo RO, Casaburi R, Coates AL, Enright PL, Hankinson JL, Irvin CG, et al. Guidelines for methacholine and exercise challenge testing-1999. This official statement of the American Thoracic Society was adopted by the ATS Board of Directors, July 1999. Am J Respir Crit Care Med. 2000;161(1):309-29.
4. Pin I, Gibson PG, Kolendowicz R, Girgis-Gabardo A, Denburg JA, Hargreave FE, et al. Use of induced sputum cell counts to investigate airway inflammation in asthma. Thorax. 1992;47(1):25-9.
5. Pavord ID, Pizzichini MM, Pizzichini E, Hargreave FE. The use of induced sputum to investigate airway inflammation. Thorax. 1997;52(6):498-501.
6. Standardization of Spirometry, 1994 Update. American Thoracic Society. Am J Respir Crit Care Med. 1995;152(3):1107-36.
7. Pellegrino R, Viegi G, Brusasco V, Crapo RO, Burgos F, Casaburi R, et al. Interpretative strategies for lung function tests. Eur Respir J. 2005;26(5):948-68.
8. Reddel HK, Taylor DR, Bateman ED, Boulet L-P, Boushey HA, Busse WW, et al. An Official American Thoracic Society/European Respiratory Society Statement: Asthma Control and Exacerbations. American Journal of Respiratory and Critical Care Medicine. 2009;180(1):59-99.
9. Juniper EF, Svensson K, Mörk A-C, Ståhl E. Measurement properties and interpretation of three shortened versions of the asthma control questionnaire. Respiratory Medicine.99(5):553-8.
10. Schatz M, Kosinski M, Yarlas AS, Hanlon J, Watson ME, Jhingran P. The minimally important difference of the Asthma Control Test. J Allergy Clin Immunol. 2009;124(4):719-23.e1.