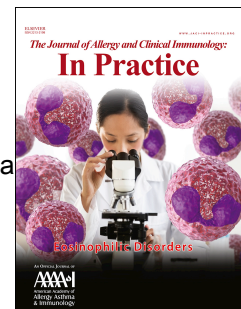


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PII: S2213-2198(20)31004-7

DOI: <https://doi.org/10.1016/j.jaip.2020.09.026>

Reference: JAIP 3136

To appear in: *The Journal of Allergy and Clinical Immunology: In Practice*

Received Date: 22 July 2020

Revised Date: 3 September 2020

Accepted Date: 14 September 2020

Please cite this article as: Haughney J, Lee AJ, McKnight E, Pertsovskaya I, O'Driscoll M, Usmani OS, Peak inspiratory flow measured at different inhaler resistances in patients with asthma, *The Journal of Allergy and Clinical Immunology: In Practice* (2020), doi: <https://doi.org/10.1016/j.jaip.2020.09.026>.

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Peak inspiratory flow measured at different inhaler resistances in patients with asthma

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Declaration of funding and conflicts of interest: The MAPLE Respiratory Service, which provided the specialist nurses for this study, is delivered by National Services for Health Improvement (NSHI) Ltd and funded by Orion Pharma (UK) Ltd as a service to medicine.

JH has received honoraria or consultation fees from AstraZeneca, Boehringer, Cipla, Chiesi, Orion, Sanofi and Teva. AJL received a consulting fee from NSHI to perform the statistical analyses. OSU has received grants and personal fees from AstraZeneca, Boehringer Ingelheim, Chiesi, and GlaxoSmithKline; personal fees from Aerocrine, Cipla, Covis, Menarini, Mereo BioPharma, Mundipharma, Napp, Orion, Sandoz, and Takeda.

Abstract word count: 250; Text word count: 2901

Abstract

Background: Patients' peak inspiratory flow rate (PIFR) may help clinicians select an inhaler device.

Objective: To determine the proportion of patients with asthma who could generate correct PIFRs at different inhaler resistance settings.

Methods: During a UK asthma review service, patients' PIFR was checked at resistance settings matching their current preventer inhaler device, at R5 (high resistance dry powder inhaler (DPI)) and at R0 (low resistance, pressurised metered dose inhaler (pMDI)). Correct PIFR ('pass') was defined for R5 as 30-90 L/min and for R0 as 20-60 L/min. A logistic regression model examined the independent predictors of incorrect PIFR ('fail') at R5 and R0. Asthma severity was assessed retrospectively from treatment level.

Results: A total of 994 adults (female 64.3%) were included, of whom 90.4% currently used a preventer inhaler (71.5% pMDI). PIFR pass rates were: 93.7% at R5 compared with 70.5% at R0 ($p < 0.0001$). All patients failing the R0 PIFR breathed in too fast (> 60 L/min), and 20% of patients currently using pMDI failed for this reason. Independent risk factors for failing R5 were: female gender, older age group and current preventer pMDI; and for failing R0 included: male gender, younger age group, current preventer DPI and mild versus severe asthma.

Conclusions: This study demonstrates that most patients with asthma can achieve adequate inspiratory flow to activate high resistance DPIs, whereas approximately a third of patients breathe in too fast to achieve recommended inspiratory flows for correct pMDI use, including one fifth of patients who currently use a pMDI preventer.

Highlights box

1. What is already known about this topic?

A patient's inspiratory flow together with the internal resistance of a DPI provide the energy to disaggregate the drug formulation and allow effective drug delivery; however, misconceptions remain that inspiratory flow alone determines adequate dose delivery.

2. What does this article add to our knowledge?

This study, using an In-Check DIAL, shows that most patients with asthma in the UK can generate sufficient inspiratory flow to use high resistance DPIs. Additionally, only $\approx 70\%$ achieve the recommended inspiratory flow rate to use a pMDI correctly.

3. How does this study impact current management guidelines?

Clinicians can be reassured that most people with asthma can generate sufficient inspiratory flow to activate a range of DPIs, regardless of internal resistance. Further evidence of some patients' tendency to inhale "too fast" when using a pMDI is provided.

Keywords: Asthma; inhaler resistance; peak inspiratory flow rate

Abbreviations:

BMI: body mass index

CI: confidence interval

DPI: dry powder inhaler

HCPs: healthcare providers

ICS: inhaled corticosteroid

LABA: long-acting β_2 -agonist

- 87 OCS: oral corticosteroids
- 88 PIFR: peak inspiratory flow rate
- 89 pMDI: pressurised metered dose inhaler
- 90

Introduction

Delivery of medications by inhalation is integral to the management of patients with chronic respiratory conditions and is preferred over systemic administration due to their rapid onset of action, high local drug concentrations achieved in the lung and fewer systemic side effects [1-3]. The main classes of portable inhaled delivery systems are pressurised metered dose inhalers (pMDIs), dry powder inhalers (DPIs) and, most recently, soft mist inhalers [2,3]. In order to be effective all types of inhalers rely on correct inhaler technique and adherence to therapy, therefore, choosing the most appropriate device to suit individual patient needs together with clear guidance on their correct use are key elements to successful therapeutic outcomes [3,4].

Breath-actuated DPIs deliver the drug to the respiratory tract as a result of the patient's inhalation triggering the device [5]. The patient's inspiratory flow together with the internal resistance of the flow channel of the device provides the energy required to disaggregate the drug formulation and allow effective delivery to the lungs [5,6]. Higher resistance devices generate more turbulent flow thus contributing proportionately more to the energy available for drug disaggregation, and therefore require less patient inspiratory flow to achieve adequate drug delivery [5,6].

Conversely, devices with lower internal resistance provide less manipulation of the patients' inspiratory flow and rely more on the patient generating higher inspiratory flows to activate the device. This suggests that patients with impaired lung function may benefit from using high resistance devices [5]. A minimum peak inspiratory flow rate (PIFR) of 30 L/min is commonly required to activate DPI devices; that is, to trigger de-aggregation and deliver the dose to the lungs [7-9]. However, misconceptions remain that inspiratory flow alone dictates adequate dose delivery

from DPIs and that some patients may not be able to generate sufficient PIFR to activate devices with high internal resistance [6,10].

An estimation of a patients PIFR may help clinicians select a suitable inhaler device for patients with asthma. The In-Check[®] Dial is a simple tool to estimate PIFR across a range of resistances that reflect the resistances found in different inhaler devices.

The aim of this prospective service evaluation study was to determine the proportion of patients with asthma who were able to generate a correct PIFR at resistance settings representative of 'low' to 'high' resistance devices using the In-Check device, and to describe the phenotypical features of these patients.

Methods

Study design and patient population

This was a multicentre, prospective service evaluation study in which sequential patients were recruited during the conduct of the United Kingdom general practice asthma review service. The reviews were undertaken across 41 sites, conducted at each site by one of ten specialist asthma nurses employed by National Services for Health Improvement Limited, between 1 July and 31 October 2019. Eligible patients were aged ≥ 5 years with a physician-diagnosis of asthma confirmed by the presence of an asthma READ code. Read Codes are a coded thesaurus of clinical terms that are routinely used by clinicians in the UK National Health Service [11]. Patients with chronic obstructive pulmonary disease, other significant respiratory disease or cardiac conditions were excluded. This paper presents the results for adults ≥ 18 years.

As data were collected during routine service evaluation, with no randomised intervention, ethics committee approval and patient written informed consent were not required for this study. All data analysed were completely anonymised.

Patient assessments

During their asthma review, each patient's PIFR was measured using the In-Check DIAL version G16 (Clement Clark International, Harlow, United Kingdom). All nurses had extensive experience in conducting asthma reviews and were trained collectively to standardise and optimise their use of the In-Check device. Inspiratory flow measurements were made according to a standard operating procedure at two or three resistance (R) levels:

1. The resistance corresponding to the patient's current principal preventer/controller inhaler device (if they used one, and if different from options 2 and 3 below)
2. The highest resistance setting (R5)
3. The lowest resistance setting, corresponding to pMDI (R0)

At each resistance setting tested, patients were instructed to breathe out to comfortable exhalation before performing up to three inhalation manoeuvres. If the patient passed, this result was recorded. A 'pass' was defined as a reading with the In-Check DIAL device of 30-90 L/min at settings R1 to R5 or 20-60 L/min at R0 setting, based on published standards (9; Table 1). If the patient failed the assessment, two more attempts could be made. Patients could be taught simple technique and be given encouragement after every effort; for pMDI: "slow and gentle", and for DPI: "fast and hard". Hence, in total, each patient could do a maximum of nine inhalation manoeuvres.

Additional data items collected at asthma review or from patient medical records were: age, gender, body mass index, smoking status, current principal preventer inhaler device, current principal reliever inhaler device, symptom score / control status, number of courses of oral corticosteroids in last 12 months and peak expiratory flow. Asthma severity was assessed retrospectively from the level of treatment required to control symptoms and exacerbations, determined after the patient had been on controller treatment for at least 3 months, and defined as: Mild asthma (well-controlled with as-needed inhaled short-acting beta-agonists or low dose inhaled corticosteroids (ICS), Read code: 663V1); Moderate asthma (well-controlled with low-dose ICS/long-acting beta₂-agonist, Read code: 663V2); Severe

asthma (required moderate or high dose ICS/LABA $\pm$ add-on therapy to maintain asthma control or remained uncontrolled despite this treatment, Read code: 663V3).

Statistical analysis

The sample size for this study was based on a convenience sample with the aim of 1000 sequential patients completing the study assessments.

The proportion of patients able to achieve a correct PIFR ('pass') at each resistance setting were described. Summary statistics (number (%) for categorical factors and mean (standard deviation, SD) for continuous factors) were produced for patient demographic and clinical characteristics and were used to describe the phenotypical features of those patients achieving a PIFR 'pass' or 'fail'.

The chi-squared test was used to examine associations between pass rate at different resistance settings and each categorical demographic/clinical factor. A linear trend test was applied where appropriate. In addition, a logistic regression model with forward conditional approach was used to identify statistically significant independent predictors of PIFR fail at each of R5 and R0. Hence, factors that did not statistically significantly predict failure do not appear in the final logistic model. For each independent predictor, a reference or base group was defined to enable interpretation of the risk of failure at R5 or R0 for each of the other levels (for example using males as the reference group, the odds of failure at R5 for females can be interpreted as compared to that of males). The small number of patients who had missing values for one or more of the potential predictors were excluded from each logistic model in turn. Associations of predictors with failure rate were presented as odds ratio and associated 95% confidence intervals (CI). Boxplots illustrating median (interquartile range) peak inspiratory flow at R5 and R0 using the last value of up to three inhalations and stratified across current preventer resistance

199 groups were produced. All analyses were carried out using IBM SPSS Statistics
200 version 25. Statistically significant results were defined as $p \leq 0.05$.

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Results

Patient population

A total of 1066 asthma patients attending a routine asthma review service were evaluated, the majority of whom were adults (n=994, 93.2%) with 72 children (aged 17 years or under). This report will focus on the 994 adults only. Approximately two thirds of the population were female, 56.6% were aged between 40 and 69 years with 26.8% over 70 years, most patients were either ex-smokers or never smokers (89.3%) and 75.5% were classified as overweight or obese (Table 2). The majority of patients were categorised as having either mild (46.4%) or moderate (47.1%) asthma and 90.4% were currently being prescribed an asthma preventer therapy, most frequently administered via a pMDI (71.5%).

PIFR pass rates

Looking at the whole adult study population of 994 patients, 931 patients (93.7%) achieved a PIFR pass at resistance R5, the highest DPI resistance setting. Patients who failed to achieve a pass rate at this resistance, were more likely to be female, of older age and be a never smoker (Table 3). Patients currently using a pMDI (n=643) were less likely to achieve a pass with R5 (91.6%) compared with those 256 patients currently using a DPI (98.7%).

In the whole adult study population patients achieving a pass rate at R0 (pMDI) setting was 701 (70.5%), statistically significantly fewer than those achieving a pass rate at R5 ($p<0.0001$) (Table 4). All patients failing the R0 test was due to PIFR >60 L/min. Patients failing to achieve a pass rate at R0 were more likely to be male and be using a higher resistance preventer. Patients currently using a pMDI (n=643) were more likely to achieve a pass at R0 (80.2%) compared with those currently using a DPI (n=256) (38.9%). With respect to their current inhaler, only four of 256

patients (1.2%) currently using a DPI failed at the same resistance as their current device. Pass rates by current device resistance were, R5: n=25/25 (100%); R4: n=45/45 (100%); R3: 133/135 (98.5%); R2: n=55/57 (96.5%). No patients had a current device with R1 resistance. By comparison, 19.8% of patients who currently used a pMDI (n=643), failed to achieve a pass rate at R0 resistance.

Independent predictors of PIFR failure rates

A forward conditional logistic regression model showed the independent risk factors of PIFR measurement failure at resistance R5 were gender, age group and resistance of current preventer (Table 5). Females were two and half times more at risk of failing the measurement at R5 compared with male patients, and patients aged ≥ 40 years were more at risk of failing versus those ≤ 39 years, with statistically significantly reduced odds shown in patients ≥ 70 years whose risk of failing was 6 times greater than in patients ≤ 39 years (odds ratio 6.12, 95% CI 1.81-20.77). Compared with patients who currently used a pMDI, patients currently using a medium resistance DPI (R3) had significantly reduced odds for failing the R5 measurement (odds ratio 0.08, 95% CI 0.01-0.59).

The logistic regression model evaluating independent predictors of failure at R0 showed that females had significantly reduced odds of failure compared with males (odds ratio 0.59, 95% CI 0.43-0.81), and patients aged ≥ 40 years were less at risk of failing versus those ≤ 39 years, the difference being statistically significant in patients 55-69 years (odds ratio of 0.55, 95% CI 0.35-0.87) (Table 5). Patients with severe asthma were significantly less likely to fail than those with mild asthma (odds ratio of 0.21, 95% CI 0.09-0.51). Compared with patients who currently used a pMDI, patients using a R2 preventer had more than 5 times the odds (odds ratio 5.46, 95% CI 2.85-10.45) of failing the R0 measurement which increased to twelve

253 times the risk of failing among those currently using an R5 inhaler (odds ratio 12.93,
254 95% CI 4.78-34.92).

255 Figure 1 shows the distribution of peak inspiratory flow at R5 and R0 resistance
256 across different current preventer inhalers. Within each preventer group, there was a
257 wide range of values. Against R0 resistance, patients currently using DPIs fared
258 worse than those currently using a pMDI, with a trend towards higher PIFR with
259 increasing resistance in their current inhaler. Against R5 resistance there was a
260 more homogenous outcome regardless of current inhaler.

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Discussion

This study showed that, irrespective of their current device and with the same level of training as given at a regular asthma review service, the majority of patients with asthma had the capacity to achieve the PIFR required to use a high resistance DPI (R5), and nearly all patients met the PIFR requirements for their current DPI device. By comparison, approximately 30% of the total adult patient population evaluated failed to achieve a PIFR pass rate with the pMDI device (R0). In all patients failing the R0 test, a PIFR > 60 L/min was generated that is, inhaling too fast. Of these failures, roughly 60% were current DPI users and 40% were current pMDI users. However, nearly 20% of patients who currently used a pMDI device failed with R0 even following three attempts with coaching. The factors required to achieve correct inhaler use are well recognised and rely on appropriate training and reinforcement [12,13]. These include correct preparation/handling of the device, a gentle full exhalation away from the mouthpiece before inhaling, ensuring a good mouth seal around the mouthpiece, a correct inhalation manoeuvre ('deep and forceful from the start' for DPI and 'slow and steady over 4-5 seconds' for pMDI) followed by a breath hold for at least 5 seconds [12-14]. Our study examined only PIFR, with the support and guidance of nurses to overcome technique errors. A marked observation in this study was the number of patients failing to achieve the required PIFR for correct pMDI use due to inhaling too fast. Rapid inhalation with a pMDI is associated with increased oropharyngeal deposition and suboptimal drug delivery [12,13] which has potential clinical implications. A previous study evaluating inhaler technique and asthma control as part of the UK IMPACT asthma review service also reported that approximately a third of patients failed the pMDI inspiratory flow criteria (10-50 L/min) after training

and showed a statistically significant association between pMDI misuse (inhaler technique measurements included inspiratory flow, synchronisation of flow/actuation and breath hold) and poor asthma control [15]. Giraud and colleagues, in a general practitioner study, similarly reported that 34% of adult patients failed the 'slow inspiratory flow' criterion and found an association between pMDI misuse (combined criteria) and asthma instability [16]. The CRITIKAL study, based on an asthma review service in Australia and seven European countries including the UK, reported that errors related to inspiratory effort were one of the most common errors made by patients using the Turbohaler (32%), Diskus (38%) and pMDI (47%) [17]. Insufficient inspiratory effort with the DPIs tested was associated with uncontrolled asthma in a multivariate model with other inhaler errors. Whilst "inspiratory effort not slow and deep", was not associated with uncontrolled asthma for pMDI users, other specific pMDI inhaler errors were. In our study, even patients familiar with the pMDI device failed the R0 test, illustrating the difficulties patients have with information retention with regards inhaler device technique. Our data reinforce the importance of inhaler technique training with regular and repeated checks, including clear messaging with respect to the inhalation manoeuvre (DPI: 'Inhale quick and deep'; pMDI: 'Inhale slow and steady'). A recent review of inhaler technique critical errors in the context of asthma management reported that approximately 50% of patients fail to maintain correct inhaler technique over time and drew attention to the importance of patient psychosocial factors, such as motivation, for learning and maintaining good inhaler skills [18].

Only 6% of all patients tested failed the R5 measurement. In this small number, the most significant independent risk factors for failing the test were female gender and age ≥ 70 years. Increasing age and female gender are two factors that have

consistently been shown to be correlated with decreased PIFRs in patients with obstructive airway disease [7,19,20]. The reasons for these findings have not been fully established but others suggest they may include physiological factors such as reduced inspiratory muscle force [19,20]. In this study, asthma severity was not significantly associated with the ability to pass at R5, also consistent with studies that have shown no correlation between PIFR and forced expiratory volume in one-second [7,19,20]. Patient characteristics significantly associated with the risk of failing the R0 measurement were male gender and having mild versus severe asthma and a trend was also observed in younger patients failing versus older patients, but this was not consistently shown across age groups. Although the reasons for this are not fully clear, one explanation may be that milder severity and younger asthma patients more easily 'over-breathe' (breath in too fast) compared to older patients and those with more severe disease. The patient's current preventer device had a significant influence on pass rates for both the R5 and R0 test indicating that those used to using a pMDI were more likely to fail at R5 and those familiar with a DPI device were more likely to fail at R0, the latter being consistently shown across resistances R2 to R5 with the odds of failure increasing with increased device resistance. These findings suggest that a patient's inhalation manoeuvre is learned or imprinted based on the device they are familiar with using. Certainly, others have suggested that past experience with inhalers is important in terms of maintaining correct inhaler technique and disease control [18, 21-23]. This further endorses the message that regular checks of inhaler technique and effective communication between healthcare providers (HCPs) and patients are an important part of asthma management. Training patients to perform correct inhalation manoeuvres leading to activation of their device and optimal drug delivery requires

HCPs to know the techniques required for each device [24]. When selecting a suitable inhaler device for patients, it is also important that HCPs understand the concept that inhalation flow together with the resistance of the DPI provides the energy to cause drug de-agglomeration and delivery of the whole dose to the lungs [24]. Training aids such as the In-Check DIAL can aid suitable device selection. A strength of this study is that we evaluated a real-world asthma population, with few exclusion criteria constraints, and therefore these findings would be expected to be largely generalizable. In this study we didn't evaluate how the inhaler resistance itself affected PIFR (by comparing PIFRs across different device resistances) but we have identified this as an area of future interest.

In conclusion, this study demonstrates in this adult asthma population that most patients can achieve adequate inspiratory flow to activate high resistance DPIs (R5) suggesting very few patients would be unable to use these devices. Nearly a third of patients fail to generate an inspiratory flow for correct pMDI use due to breathing in too fast, including a fifth of patients currently using a pMDI.

Acknowledgements

Medical writing support was provided by Kate Hollingworth of Continuous Improvement Ltd, Devon, United Kingdom and was funded by NSHI Ltd.

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Table 1: In-Check DIAL G16 inhaler resistance range*

Inhaler device	In-Check DIAL G16 resistance setting**	In-Check DIAL G16 flow rate denoting clinically effective range
Handihaler	High	30-90 L/min
Easyhaler (monotherapy)	High	30-90 L/min
NEXThaler	Medium high	30-90 L/min
Twisthaler	Medium high	30-90 L/min
Turbohaler (Pulmicort)	Medium high	30-90 L/min
Turbohaler S (Symbicort)	Medium	30-90 L/min
Clickhaler	Medium	30-90 L/min
Spiromax	Medium	30-90 L/min
GenuAir	Medium	30-90 L/min
Ellipta	Medium low	30-90 L/min
Diskhaler	Medium low	30-90 L/min
Accuhaler	Medium low	30-90 L/min
Breezhaler	Low	30-90 L/min
Respimat	pMDI/none	20-60 L/min
pMDI	pMDI/none	20-60 L/min

*Sanders MJ, et al (9)

**Comprises five representations of DPI device resistance (R5, High; R4, Medium high; R3, Medium; R2, Medium low; R1, Low) and pMDI (R0)

pMDI: pressurised metered dose inhaler; DPI: dry powder inhaler

Table 2: Demographic and clinical characteristics of the patients in the study

	Patients with asthma (N = 994)
Gender	
Male	355 (35.7)
Female	639 (64.3)
Age group (years)	
18-24	38 (3.8)
25-39	127 (12.8)
40-54	200 (20.1)
55-69	363 (36.5)
70+	266 (26.8)
Smoking Status	
Smoker	106 (10.7)
Ex-smoker	307 (30.9)
Never Smoked	581 (58.5)
BMI (Kg/m²)	
Under 18.5	11 (1.1)
18.5 – 24.9	230 (23.1)
25 – 29.9	346 (34.8)
30+	405 (40.7)
Missing, n=2	
Asthma severity	
Mild	461 (46.4)
Moderate	468 (47.1)
Severe	59 (5.9)
Missing, n=6	
Currently using preventer Preventer inhaler device resistance:	899 (90.4)
pMDI R0	643 (71.5)
DPI: R1(Low)	0
R2 (Medium low)	57 (6.3)
R3 (Medium)	130 (14.5)
R4 (Medium high)	44 (4.9)
R5 (High)	25 (2.8)

Data presented as n (%)

BMI: body mass index; DPI: dry powder inhaler; pMDI: pressurised metered dose inhaler

Table 3: Pass rates at R5 resistance by demographic characteristics

	Pass rate n (%)	P-value*
Total sample (n=994)	931 (93.7)	
Gender		0.010
Female	589 (92.2)	
Male	342 (96.3)	
Age group		<0.001
18-24	38 (100.0)	
25-39	124 (97.6)	
40-54	193 (96.5)	
55-69	341 (93.9)	
70+	235 (88.3)	
BMI (Kg/m²)		0.163
Under 18.5	10 (90.9)	
18.5 – 24.9	210 (91.3)	
25 – 29.9	327 (94.5)	
30+	382 (94.3)	
Missing, n=2		
Smoking status		0.037
Current smoker	103 (97.2)	
Ex-smoker	291 (94.8)	
Never smoked	537 (92.4)	
Courses of OCS in past 12 months		0.787
0	683 (93.9)	
1	123 (93.9)	
2+	82 (93.2)	
Missing, n=48		
Severity of asthma		0.168
Mild	426 (92.4)	
Moderate	443 (94.7)	
Severe	56 (94.9)	
Missing, n=6		
Current preventer resistance		0.002
No current preventer	89 (93.7)	
R0/pMDI	589 (91.6)	
R2 (Medium low)	57 (100)	
R3 (Medium)	129 (99.2)	
R4 (Medium high)	42 (95.5)	
R5 (High)	25 (100)	

*Across categories from chi-squared linear trend test

BMI: body mass index; DPI: dry powder inhaler; OCS: oral corticosteroids; pMDI: pressurised metered dose inhaler

Table 4: Pass rates at R0 resistance by demographic characteristics

	Pass rate n (%)	P-value *
Total sample (n=991)	701 (70.5)	-
Gender Female Male Missing, n=3	467 (73.4) 234 (65.9)	0.013
Age group 18-24 25-39 40-54 55-69 70+ Missing, n=3	28 (73.7) 80 (63.0) 136 (68.0) 269 (74.1) 188 (71.5)	0.135
BMI (kg/m²) Under 18.5 18.5 – 24.9 25 – 29.9 30+ Missing, n=5	8 (72.7) 160 (69.9) 242 (70.1) 289 (71.5)	0.676
Smoking status (adults) Current smoker Ex-smoker Never smoked	67 (63.8) 219 (71.6) 415 (71.6)	0.218
Courses of OCS in past 12 months 0 1 2+ Missing, n=51	528 (72.8) 80 (61.1) 63 (72.4)	0.424
Severity of asthma Mild Moderate Severe Missing, n=9	337 (73.1) 311 (66.9) 50 (84.7)	0.804
Current preventer resistance No current preventer R0/pMDI R2 (Medium low) R3 (Medium) R4 (Medium high) R5 (High) Missing, n=3	72 (75.8) 516 (80.2) 25 (44.6) 67 (51.5) 15 (35.7) 6 (24.0)	<0.001

*Across categories from chi-squared linear trend test

BMI: body mass index; DPI: dry powder inhaler; OCS: oral corticosteroids; pMDI: pressurised metered dose inhaler

Table 5: Independent demographic and clinical predictors of failure rate at R5 and R0 resistance

Demographic and clinical characteristic	Failure rate at R0 Odds ratio (95% confidence interval)	Failure rate at R5* Odds ratio (95% confidence interval)
Gender Male Female	Reference 0.59 (0.43-0.81)	Reference 2.46 (1.27-4.76)
Age group (years) ≤ 39 40-54 55-69 ≥ 70	Reference 0.91 (0.55-1.49) 0.55 (0.35-0.87) 0.71 (0.44-1.14)	Reference 1.79 (0.45-7.09) 3.25 (0.94-11.22) 6.12 (1.81-20.77)
Current preventer resistance No current preventer R0/pMDI R2 (Medium low) R3 (Medium) R4 (Medium high) R5 (High)	1.10 (0.64-1.89) Reference 5.46 (2.85-10.45) 5.27 (3.29-8.43) 8.85 (4.37-17.93) 12.93 (4.78-34.92)	0.82 (0.31-2.14) Reference - 0.08 (0.01-0.59) 0.50 (0.12-2.16) -
Severity of asthma Mild Moderate Severe	Reference 0.76 (0.52-1.12) 0.21 (0.09-0.51)	-
Number of courses of OCS in last 12m 0 1 2+	Reference 1.90 (1.24-2.93) 1.29 (0.73-2.28)	-

Factors considered for entry into each logistic model were: gender, age group, BMI group, smoking status, severity of asthma severity, number of courses of OCS in past 12m and current preventer resistance. A forward stepwise procedure was used to identify independent predictors of failure, factors that did not independently predict failure are excluded from the model estimates shown.

*59 patients were excluded from the failure rate at R5 model and 56 from the R0 model due to missing values for one or more of the 7 potential predictors.

No patients with a R2 med low or a R5 high preventer failed at R5 resistance.

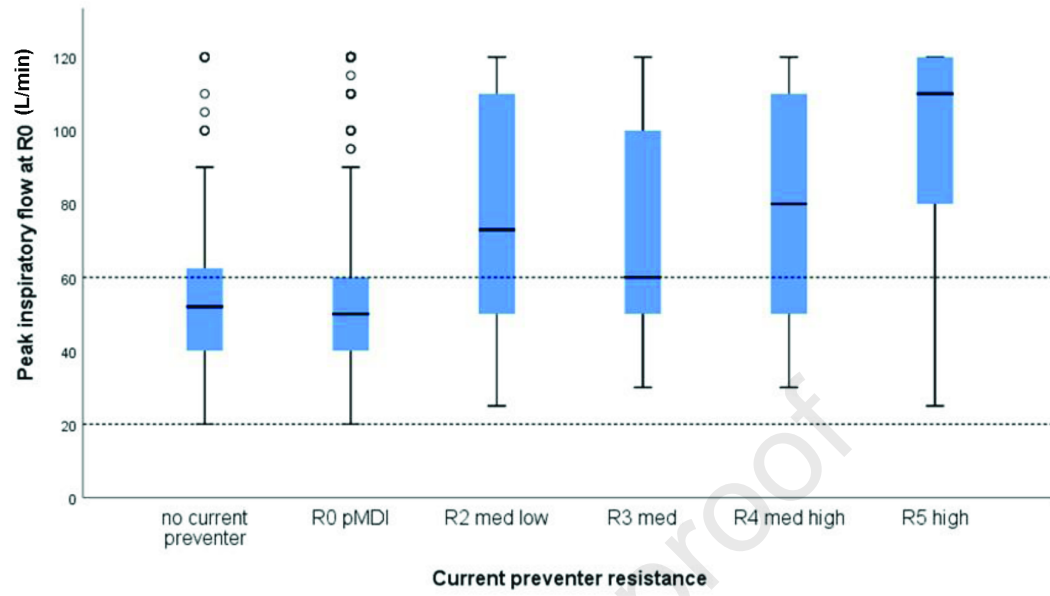
BMI: body mass index; DPI: dry powder inhaler; OCS: oral corticosteroids; pMDI: pressurised metered dose inhaler

Figure legend**Figure 1: Boxplot of peak inspiratory flow by current preventer resistance at A)****R0 and B) R5**

Horizontal bar of each box indicates median whilst upper and lower edges of each box represent the upper quartile and lower quartile respectively. The T-bar extends to 1.5 times the height of the box. An asterisk represents extreme outliers which are values that are more than three times the height of the box. Pass rates for R5 were defined as 30-90 L/min and for R0 as 20-60 L/min, shown as dashed lines on each figure.

pMDI: pressurised metered dose inhaler

A



B

