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To cite this article: CI Bloom, S Walker & JK Quint (2019): Inadequate specialist care referrals for high risk asthma patients in the UK: an adult population-based cohort 2006-2017, Journal of Asthma, DOI: [10.1080/02770903.2019.1672723](https://doi.org/10.1080/02770903.2019.1672723)

To link to this article: <https://doi.org/10.1080/02770903.2019.1672723>



Accepted author version posted online: 24 Sep 2019.



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Inadequate specialist care referrals for high risk asthma patients in the UK: an adult population-based cohort 2006-2017

Running head: inadequate specialist care referrals

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Keywords: guidelines, high-dose inhaled corticosteroid, oral corticosteroid, hospital admission, electronic healthcare records

Funding: This work was supported by Asthma UK.

Abstract

Objective

To improve asthma morbidity and mortality in the UK, national asthma guidelines recommend referral to specialist care for the following high risk groups, after a hospital admission for asthma, ≥ 3 courses of oral corticosteroids (OCS) in 12-months, an incident high-dose inhaled corticosteroid (ICS) prescription or addition of a fourth asthma drug to a patient's maintenance regimen. We sought to assess the prevalence and temporal change of referrals to identify unmet needs.

Methods

We used UK electronic healthcare records, 2006-2017, to identify high risk asthma patients managed within primary care. Referrals to respiratory clinics in secondary care were measured, within 3 months before or 6 months after, an incident ICS, third OCS in a year, or fourth asthma drug; or 12 months after a hospital admission for asthma. A nested case-control and conditional logistic regression was used to evaluate factors associated with receiving a referral.

Results

246,116 asthma patients were eligible. There was a slight increase in secondary care referrals from 2014 onwards but the percentage remained low with $<20\%$ in each high risk group referred for specialist care. The factors in the past year that were most strongly associated with receiving a referral were a hospital admission or A&E visit for asthma, ≥ 3 OCS courses, ≥ 2 add-on drugs, or high-dose ICS prescription.

Conclusion

The majority of high risk asthma patients were not referred for specialist care, as recommended by national guidelines. Compared to other risk factors, those admitted to hospital were most likely to receive a referral.

Background

Around 5.4 million people in the UK are treated for asthma, approximately 1 in 12 of the population¹. Due to this high prevalence most asthma patients are managed within primary care. But some patients require more specialist care at certain periods during the lifespan of their condition. National and international guidelines propose periods at which patients should receive specialist care. These are advocated when there is uncertainty of the initial diagnosis and when expertise is required to manage their disease. For optimal patient management it is important that guidelines are adhered to fully and consistently.

In the UK, since 2017, there have been two national asthma guidelines, the 'British Thoracic Society (BTS)/Scottish Intercollegiate Guideline Network (SIGN) British guideline on the management of asthma'² and the National Institute for Health and Care (NICE) 'Asthma: diagnosis, monitoring and chronic asthma management'³ (prior to 2017 only BTS/SIGN produced national asthma guidance). The number of deaths from asthma in the UK is increasing and the UK has one of the highest asthma mortality rates across Europe^{1,4}. To understand the reasons behind our high mortality rates a large national review ('Why asthma still kills') was undertaken by the National Review of Asthma Deaths (NRAD) and reported by the Royal College of Physicians in 2014⁵. The review found a large proportion of deaths were potentially avoidable and recommended areas for improving asthma care to prevent asthma attacks and avoidable deaths. Both national guidelines and the NRAD review state several similar recommendations for the point at which an adult with physician-diagnosed asthma must be referred to secondary care for a specialist respiratory review. These include after every hospital admission for asthma, after prescribed higher levels of treatment (including high-dose inhaled corticosteroids (ICS) or adding a fourth asthma drug to a patient's current regimen). In addition, NRAD states all asthma patients must be referred if they have required three or more courses of systemic corticosteroids in the previous 12 months, or attended the emergency department two or more times.

It is unknown in the UK how often referrals are made to specialist respiratory care and which guideline-recommended criteria are more adhered to than others. In this study we assess the annual incidence of referral using guideline-recommended and NRAD criteria, and evaluate the features that are associated with an increased chance of being referred.

Methods

Data source

We used the Clinical Practice Research Datalink (CPRD-GOLD) database, a nationally representative database of de-identified electronic healthcare records. It contains information on clinical diagnoses, prescriptions and test results from over 812 GP practices, on more than 17 million patients, across the UK.⁶ Patient's data were linked to Hospital Episode Statistics (HES), Office of National Statistics (ONS) or Index of Multiple Deprivation (IMD, a socioeconomic marker) for secondary care, mortality and socioeconomic data. HES contains information on all out-patient clinics and hospital admissions in England; therefore only around 60% of all UK practices in CPRD have individual level linkage to HES, ONS and IMD.

Study population

Patients included were identified as having asthma using validated asthma-specific Read codes (the clinical terminology system used by UK GP practices)⁷. Patients were eligible for study inclusion once they had received an asthma Read code, had research acceptable data, were continuously registered in a CPRD GP practice, had HES linked data, and were aged greater or equal to 18 years of age. Study start period was any time from 1st January 2006. Patients were censored on the first date of either death, transfer out of CPRD-linked GP practice, last CPRD or HES data collection date, aged 55 years old or two years after their last asthma Read code or prescribed asthma medication. The study

ended any time before or including 31st December 2017. Patients with COPD were excluded if the diagnosis occurred before or within 2 years of the asthma diagnosis.

A nested matched case-control design was used to assess the association between characteristics and referral to secondary care. Cases were identified as patients who had an incident referral to secondary care, where incident was defined as no referral in the previous 12-months, anytime between 1st January 2006 and 31st December 2017. Four controls were matched by age (10-year age groups), gender and general practice to each case. The index date was the date of the hospital appointment. Controls did not have a referral to secondary care in the previous 12 months or more from the index date.

Variables

A secondary care referral was defined as any appointment with a respiratory clinic in an NHS hospital. This was identified using HES Outpatient Activity data. A course of oral corticosteroids was defined as a prescription of total amount of less than or equal to 300mg not prescribed during an annual asthma review or on days treated for other steroid responsive diseases. A second 'add-on' treatment was defined as a second medication of any of a long-acting beta-agonist (LABA), leukotriene receptor antagonist (LTRA), theophylline or long-acting antimuscarinic (LAMA). A hospital admission was defined as any admission to a NHS hospital for asthma as defined by ICD-10 codes in HES Admissions data. An Accident and Emergency (A&E) admission was defined as any admission to a NHS hospital for asthma in the HES A&E data. Only admission using asthma as the first diagnosis were used. A history of COPD (must have a smoking history and be aged ≥ 35 years), atopy, gastroesophageal reflux (reflux), anxiety, asthma self-management plan, inhaler technique check, annual asthma review, asthma control questionnaire were identified using validated⁸ or appropriate Read codes (available upon request). The level of inhaled corticosteroid (ICS) dose was based on the dose of the highest dose inhaler prescribed in that year using the BTS/SIGN guidelines dosage: low dose ≤ 799 mcg, medium dose 800-1599 mcg, high dose ≥ 1600 mcg. In the regression

model all pharmacological, non-pharmacological and exacerbation variables were measured in the year prior to the index date.

Statistical analysis

All statistical analyses were performed using STATA 14.2. Annual prevalence was calculated as the proportion of patients in each risk group divided by the number of asthma patients with a full year of follow-up in that year. Percentage referred to secondary care was calculated as the number referred divided by the number of patients in that risk group, multiplied by 100. Referral had to be within 3 months before or 6 months after: an incident high-dose ICS prescription (incident was defined as no prescription in the previous 12 months), second add-on therapy or their third OCS prescription; or 9 months after their hospital admission. For all asthma patients the percentage referred was calculated for each calendar year. Incidence density sampling was used to mimic time-to-event analysis. The effect estimate was obtained using conditional logistic regression and adjusted for all variables, excluding the matching variables.

Ethics

The protocol for this research was approved by the Independent Scientific Advisory Committee (ISAC) for MHRA Database Research (protocol number 18_211R) and the approved protocol was made available to the journal and reviewers during peer review. Generic ethical approval for observational research using the CPRD with approval from ISAC has been granted by a Health Research Authority (HRA) Research Ethics Committee (East Midlands – Derby, REC reference number 05/MRE04/87). Linked pseudonymised data was provided for this study by CPRD. Data is linked by NHS Digital, the statutory trusted third party for linking data, using identifiable data held only by NHS Digital. Select general practices consent to this process at a practice level with individual patients having the right to opt-out.

Results

A total of 246,116 asthma patients were eligible to be included in the cohort. The median follow-up time was 3.9 years (IQR 1.8-7.1 years). During the total study follow-up period (1,123,042 person years) there were 73,329 patients prescribed a course of OCS, 19,479 prescribed a high-dose ICS, 94,883 patients prescribed at least two add-on medications, and 8,367 patients that had a hospital admission for asthma.

Annual prevalence of high risk patients

The annual percentage of patients prescribed a high-dose ICS inhaler changed little over the past 10 years, remaining around 5% (Figure 1). However, the percentage prescribed a second add-on therapy has increased from 5% to nearly 9%. Patients receiving three courses of OCS has increased only by 1% but this is nearly a 50% increase over the past decade. Referrals did not change significantly after the publication of NRAD in 2014. The percentage of asthma patients being admitted to hospital has dropped by nearly a quarter of the past decade, and still remains low, around 3-4% each year.

Percentage referred to specialist in secondary care

A low proportion of all risk groups were referred to secondary care, less than 20% of those that should be referred (Figure 2). The risk group with the highest proportion referred was patients that had been admitted to hospital. Patients receiving 3 OCS were also high however after removing those with a hospital admission the percentage almost halved. Over time patients started on a high-dose ICS inhaler or second add-on therapy have had increasing proportion referred to secondary care.

Association between characteristics and referral to secondary care

In the nested case-control there were 5,032 cases (referred to secondary care) and 20,128 matched controls, about two-thirds had mild asthma, one third were current smokers, around half had atopy,

nearly 40% had an annual asthma review but less than 10% had a self-management plan in the previous year, and most did not have a GP or hospital treated exacerbation in the previous year (Supplementary Table 1).

Multiple factors appeared to be associated with increased odds of being referred (Table 1 & 2). The factors mostly strongly and significantly associated were (in decreasing strength of association), hospital admission, 3 or more OCS courses, an A&E visit for asthma, 2 or more add-on treatments, or high-dose ICS prescription, in the previous 12 months. Other factors less strongly associated were having COPD co-diagnosis, reflux disease, an annual review, and being of non-normal BMI, having an annual review in the previous 12 months and being a current smoker. Being given a self-management asthma plan, inhaler technique check or asthma control questionnaire did not appear to be associated with receiving a referral ($p>0.05$).

Discussion

Our study, using nationally representative data, has found that the majority of asthma patients are not high risk (less than 10% in each of the four specified high risk groups) and as such can be well-managed within primary care. However, due to the high prevalence of asthma in the UK, this actually translates to large numbers of people that are at significant risk of worsening asthma control or asthma exacerbations. Yet we have shown here that most of the patients that are identified as high risk, by national asthma guidelines and the NRAD review, are not referred to secondary care where they could be seen by those with expertise in asthma management. Only 1 in 5 patients admitted to hospital for their asthma were referred to secondary care within 9 months of their admission. Troublingly, an even lower proportion of patients on high levels of asthma medication were referred, only around 10% until 2014. Between 2014 and 2016 there did appear to be an increase in referrals which offers some encouragement and could potentially be linked to the publication of NRAD in 2014. However, the only specific additional recommendation NRAD proposed

beyond those in national guidelines, referral after 3 or more OCS in 12 months, did not appear to be temporally influenced by its publication.

The NRAD review found deaths were related to preventable factors, many of which were associated with a lack of referral to specialists. A review in the US of asthma management found that most asthma patients were not well controlled and less than a quarter had ever visited a specialist during their medical care⁹. Yet specialist management has been shown to be associated with more favourable outcomes^{10,11}. The reasons for low referral rates are likely to be complex and differ between GP practice and patient. However, we have shown here that certain factors are more likely to be associated with receiving a referral than others. The variables most strongly associated were hospital admission, more than 3 OCS, an A&E visit, a second add-on therapy and high-dose ICS use in the previous 12 months. This finding is reassuring because these are the factors guidelines recommend should prompt the need for specialist input. Therefore, those that are referred are correctly identified as high risk. This also suggests that in many GP practices there may be either a lack of knowledge, or lack of compliance, with asthma guidelines, leading to the poor referral rate for high risk patients. A UK study in 2009 found a lower than expected knowledge of asthma guidelines, that have been published since 1990, from GPs with a particular interest in respiratory disease¹⁰. Aside from knowledge, GPs may disagree with guidelines on principle¹² but far more likely is the lack of time and staff resources to absorb every published guideline^{13,14}. In addition in some cases there could be financial disincentives to refer patients¹⁵. Lastly the patient may prefer not to access secondary care due to work or financial constraints or lack of understanding of the severity of their asthma.

The benefit of a specialist review is multifaceted. Studies have shown that specialist care reduces hospitalisations, improves asthma management (in part due to more enhanced education), and improves patient's quality of life^{10,11,16-18}. Specialists can also ensure a correct diagnosis as some solely community managed patients may have an incorrect diagnosis, including patients treated with

high levels of medication^{19,20}. Despite the ongoing advances in asthma treatment, both pharmacological and non-pharmacological, in order to improve asthma care we must ensure that those with unmet needs in primary care receive specialist involvement in a timely manner. Better coordination of healthcare between providers is essential. But in the UK our priority now must be to identify the key barriers to referrals in order to develop an effective referral strategy.

Limitations

A potential limitation was misclassification of patients diagnosed with asthma. This misclassification could be due to incorrect GP diagnosis or coding; however, to reduce this only validated asthma diagnostic codes were used to identify patients⁷. Another misclassification could be if patients requested not to be referred to secondary care, this would not be recorded in the hospital data, or were seen in respiratory community clinic only (although community clinics are recorded in CPRD the clinic speciality is not documented). The medications prescribed may not have been used as the data includes prescriptions only, not dispensing information. But as the GP felt the patient required the medication the recommendation of a referral should still apply. Another assumption is that all short courses of OCS were prescribed for an exacerbation, it is possible a small number were prescribed for other disorders but if these occurred on the day of a code for another steroid-treatable disease they were discounted. An NRAD recommendation was to refer patients after a second A&E admission in 12 months. This was not assessed due to the low number of second A&E visits, in part related to incomplete HES A&E data collection before 2015/2016.

Conclusion

Although high risk factors are the strongest indicator for secondary care referral there is a considerable lack of specialist care involvement in all identified high risk asthma patients in the UK. This is of great concern as asthma is one of the most common diseases in the UK and has one of the highest mortality rates in Europe. The lack of referrals needs to be addressed urgently if we are to try to prevent further avoidable asthma deaths.

Declaration of interest: Dr Quint's research group has received funding from The Health Foundation, MRC, Wellcome Trust, BLF, GSK, Insmmed, AZ, Bayer, Chiesi, IQVIA and BI for other projects, none of which relate to this work. Dr Quint has received funds from AZ, GSK, Chiesi, Bayer, Teva and BI for Advisory board participation or travel. Dr Quint's research group received funding from Asthma UK for this work.

Abbreviations

A&E	Accident and Emergency
BTS	British Thoracic Society
CPRD	Clinical Practice Research Datalink
COPD	Chronic obstructive pulmonary disease
GP	General Practice
HES	Hospital Episode Statistics
ICS	Inhaled corticosteroids
IMD	Index of Multiple Deprivation
ISAC	Independent Scientific Advisory Committee
LABA	Long-acting beta-agonist
LAMA	Long-acting antimuscarinic
LTRA	Leukotriene receptor antagonist
NICE	National Institute for Health and Care
NRAD	National Review of Asthma Deaths
OCS	Oral corticosteroids
SIGN	Scottish Intercollegiate Guideline Network
UK	United Kingdom

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Table 1. Association of each characteristic with referral to secondary care. Each variable is adjusted for all other variables. OR=odds ratio. CI=confidence interval.

	Adjusted OR	p-value	95% CI
Clinical characteristics			
Smoking history			
Never	Reference		
Current	1.12	0.02	1.02-1.23
Ex-smoker	0.95	0.25	0.86-1.04
BMI			
Normal	Reference		
Underweight	1.52	<0.001	1.17-1.96
Overweight	1.10	0.07	0.99-1.21
Obese	1.73	<0.001	1.58-1.91
Atopy	0.92	0.03	0.85-0.99
Reflux	1.51	<0.001	1.36-1.68
Anxiety	1.12	0.01	1.03-1.22
COPD	2.01	<0.001	1.69-2.4
Pharmacological management			
SABA canisters			
0	Reference		
1-3	1.54	<0.001	1.39-1.72
>3	1.51	<0.001	1.34-1.7
ICS level			
none	Reference		
Low dose	1.06	0.28	0.95-1.18
Medium dose	1.19	0.01	1.04-1.37
High dose	1.85	<0.001	1.56-2.19
Add-on therapy			
none	Reference		
1 drug	1.45	<0.001	1.31-1.61
>=2 drugs	3.49	<0.001	2.98-4.1
Non-pharmacological			
Self-management plan	0.92	0.32	0.79-1.08
Asthma control questionnaire	0.92	0.63	0.67-1.27
Annual review	1.21	<0.001	1.1-1.34
Inhaler technique check	1.01	0.87	0.9-1.13
Exacerbations			
GP treated (short course OCS)			
0	Reference		
1	2.35	<0.001	1.99-2.78
2	2.50	<0.001	2.18-2.86
≥3	4.60	<0.001	3.96-5.35
A&E visit			
0	Reference		

≥1	3.63	<0.001	2.6-5.07
Hospital admission			
0	<i>Reference</i>		
≥1	30.48	<0.001	21.9-42.41

Table 2. Order of strength of association with referral to secondary care, including all significant variables from the model.

Variable	Adjusted OR
≥1 Hospital admission	30.48
≥3 OCS	4.60
≥ 1 A&E visit	3.63
≥ 2 add-on drugs	3.49
2 OCS	2.50
1 OCS	2.35
COPD co-diagnosis	2.01
High ICS	1.85
Obese	1.73
SABA 1-3	1.54
Underweight	1.52
SABA >3	1.51
Reflux	1.51
1 add-on drug	1.45
Annual review	1.21
Medium ICS	1.19
Anxiety	1.12
Current smoker	1.12

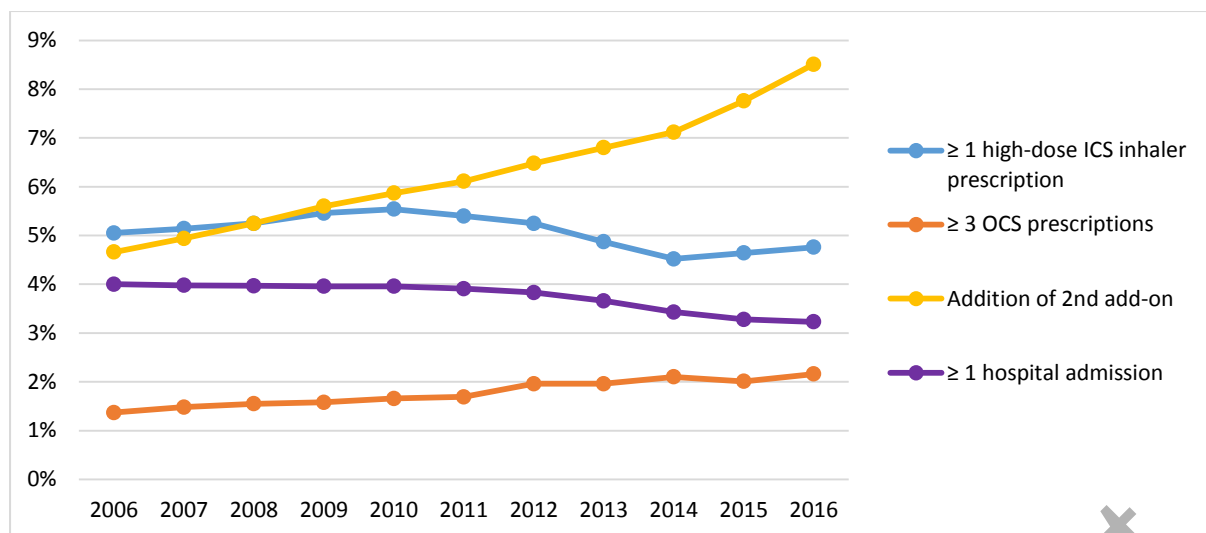


Figure 1. Annual prevalence in asthma population of each high-risk group.

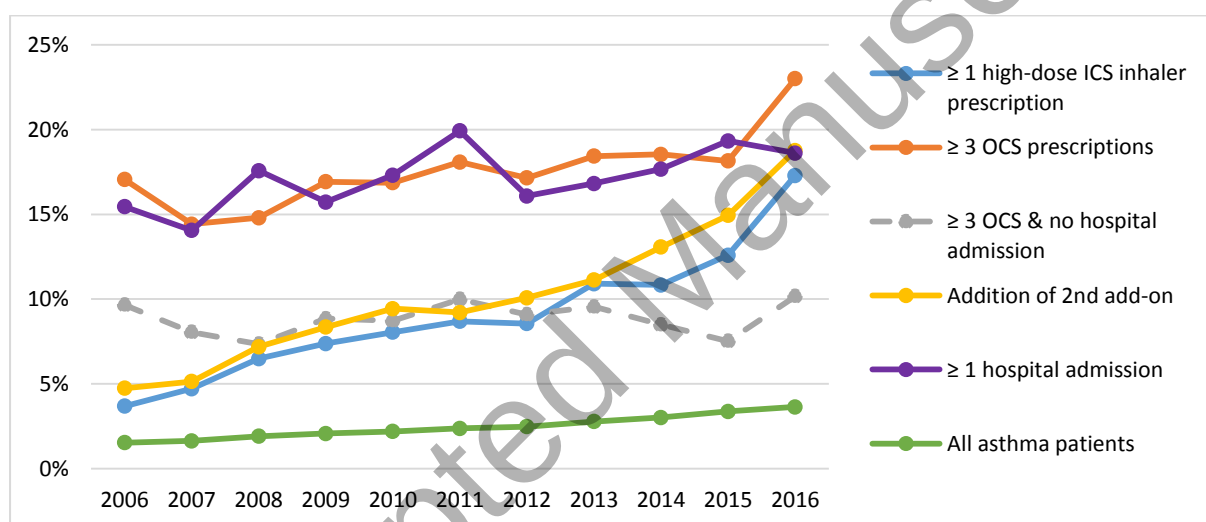


Figure 2. Percentage referred to secondary care in each high-risk group. Time scales used were within 3 months before or 6 months after: an incident high-dose ICS, third OCS in 12-months, addition of second add-on treatment; or 9 months after a hospital admission for asthma; or annual percentage referred in all asthma patients.