Cross-sectional observations on the natural history of asthma

RG Neville, C McCowan, G Hoskins and G Thomas

SUMMARY

Background: *Asthma is a major health care problem that affects all ages. It is uncertain whether asthma is a single clinical entity or a grouping of separate clinical syndromes that share a common set of treatment guidelines.*

Aim: *To observe the symptoms, treatment step, and health service utilisation of a population of patients throughout the United Kingdom (UK) listed on an asthma register.*

Design of study: *A cross-sectional study and clinical assessment of asthma patients.*

Setting: *A total of 12 203 patients from 393 general practices throughout the UK.*

Method: *A database was used to observe the symptoms, treatment step, and health service utilisation of the asthma patients.*

Results: *Children aged up to four years had a distinctive profile of symptoms, including night time cough. They also experienced increased health service utilisation including a high hospital admission rate. Symptoms in adults became more common with increasing age. The pattern of symptoms in patients aged 45 years and over suggest many patients on asthma registers may have chronic obstructive pulmonary disease. Patients aged 16 to 30 years showed a different pattern of health service usage to those aged 5 to 15 years and 31 to 45 years, relying more on unscheduled use of health services rather than a review-based management plan. Patients aged 16 to 30 years used less anti-asthma medication than those aged 5 to 15 years and 31 to 45 years.*

Conclusions: *Databases may be a useful tool with which to study the natural history of asthma, but there are problems with bias. Several clinical subgroups exist within the broad diagnosis label of asthma. Knowledge of how these subgroups of doctor-diagnosed asthma use health services may help clinicians to create individual care plans for groups of patients.*

Keywords: *asthma; chronic obstructive pulmonary disease; diagnosis.*

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Introduction

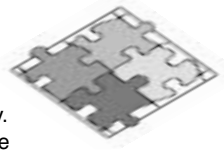
ASTHMA is a major health care problem. It affects all ages, disrupts the lifestyle of sufferers, and is the leading cause of medical admission in childhood.[1,2] There is no single test or diagnostic sign that defines asthma. Some authorities believe that asthma is not one disease, but rather a grouping of diseases with a common set of symptoms and clinical signs.[3,4] The common link between the clinical symptoms that comprise asthma is their response to anti-asthma treatment.

Consensus guidelines on the management of asthma describe different treatment options for different ages.[5] The classification of asthma into age groups of up to four years, 5 to 15 years, and 16 years and above is arbitrary and is based on 'clinical experience' rather than biological phenomena.[6] Some authorities classify adult asthma as age 16 to 44 years, then 45 to 74 years, and 75 years and above to reflect the 'clinical experience' that chronic obstructive pulmonary disease (COPD) is common with increasing age.[7] Work on the natural history of asthma has concentrated on long-term follow-up of cohorts. The 'Melbourne Cohort' has described the clinical features of asthma at ages 7, 14, 21, 28, and 35 years.[8] The work from Aberdeen reported a survey repeated after a 25-year interval.[9] Other studies have demonstrated the changing pattern of symptoms over time when longitudinal methods are used.[10] There are no lifelong cohorts of birth to aged 45 years and beyond, thus other methods must be used to observe the 'natural history' of asthma in middle and late age.[11,12]

It is important to know the natural history of asthma. Patients, and parents of patients, wish to know whether symptoms are likely to improve or deteriorate over time. Clinicians need to weigh up the potential benefits of effective treatments, such as inhaled steroids against concerns about possible side effects. Knowledge about natural history and disease progression is essential when making important therapeutic decisions. One of the difficulties of introducing a screening programme for asthma is the uncertainty about natural history and thus outcome. Wilson's criteria for screening state the importance of understanding the natural history of diseases.[13]

Natural history studies that use longitudinal methods have the advantage of studying individuals over many years, thus enabling the tracking of the response of each subject to a changing environment. Longitudinal studies have the disadvantage that, by definition, they take years to complete and are very expensive. A complete 'cradle-to-grave' study is impossible within the life span of any researcher; thus, study of the natural history of asthma that encompasses all ages of asthmatics is not feasible. A novel approach to the study of natural history is to take a large cohort of all ages of asth-

HOW THIS FITS IN



What do we know?
Asthma is a major health care problem with an unclear natural history. Cross-sectional observations on a large national database is an option for the study of different clinical entities that are labelled as 'ashtma'.

What does this paper add?
1. Children aged under five years have a distinctive profile of symptoms, including night-time cough.
2. Young adults rely more on unscheduled use of health services, rather than a review-based management plan.
3. Many adults aged over 45 years labelled as 'asthmatic' have symptoms suggestive of chronic obstructive pulmonary disease.

ma and observe for a short period of time, e.g. one year. This cross-sectional approach would have the advantage of including all ages of people suffering from asthma in a given year.

The existence of a large United Kingdom (UK) database of all ages, both sexes, and all severities of asthma presented the opportunity to look at the pattern of health-related behaviour using a novel 'cross-sectional' approach.[14] The aim of this paper is to describe the age/sex variation in symptoms and morbidity owing to asthma and thereby make tentative observations on the natural history of the disease in the UK in the 1990s.

Method

In 1994 and 1995, 393 practices from throughout the UK enrolled in a National Asthma Management Initiative.[14,15] Each practice supplied details of 30 patients, selected by a predetermined random number sequence, from their practice asthma registers. Previous work established that 30 patients was a sufficiently large sample on which to compile an audit report, but was small enough to allow a clinical assessment spread over two clinic sessions.[14,15] The selection procedure was piloted and validated.[16] Practice registers, a Family Health Services Authority (Health Board) requirement, consist of all patients who have received an anti-asthma prescription within the past year.[17] Some large practices asked to enroll two sets of 30 patients managed by different GPs. Some patient details were illegible. The total number of patients studied is thus not an exact multiple of 30. The patients were of all ages, both sexes, and formed a complete spectrum of severity of patients diagnosed with asthma, whether managed in hospital, general practice or both. Practices supplied details of each patient's symptoms on their most recent clinical assessment, including cough, wheeze or breathlessness at night, on waking, and on exercise. 'Days lost' from work or school in the last month were recorded. The basic minimum dataset was not dissimilar from that suggested by the recent Royal College of Physicians review.[18]

The anti-asthma medication prescribed for each patient within the past year enabled their British Asthma Guidelines (BAG) treatment step to be calculated.[5] Primary care and hospital outpatient consultations, accident and emergency visits, and admissions owing to asthma were recorded.

The age/sex characteristics, symptoms, medication use, and health service utilisation characteristics of all patients were collated and analysed. Patients were grouped into six-age bands: under five years, five to 15 years, 16 to 30 years, 31 to 45 years, 46 to 64 years, and 65 years and over.

A comparison of a particular age group, for example the under-five years age group, against a combination of other age groups, was made for the occurrence of symptoms (at night, on waking, and on exercise) by means of the occurrence odds between the groups, together with a 95% confidence interval. There would be evidence of some real difference between the two age groups if the 95% confidence interval did not include 1. A similar approach was used to make comparisons for poor compliance, for poor inhaler technique, and for aspects of health service utilisation.

Results

Details of 12 203 patients were available for study. Age/sex, treatment, and health service utilisation data were available for all patients; however, information from a clinical assessment within the past six months was only available in 9625 patients. The number and percentage of patients within age groups for each variable (e.g. treatment, symptom, consultations, etc.) are presented in Table 1. Tables 2, 3, and 4 give odds ratios and 95% confidence intervals for comparing the under-five years age group with the five years and over age groups, the 65 years and over age group with the five to 64 years age groups, and the 16 to 30 years age group with the five to 15 and 31 to 64 years age groups combined, respectively.

Symptoms at night occurred at a significantly higher rate in the under-five years age group than in the other age groups, whereas symptoms on waking and on exercise occurred at a lower rate. General practitioner (GP) consultations and all forms of hospital attendance were also much more common in this group than in the older groups.

Patients in the 65 years and over age group reported symptoms on waking or on exercise more frequently than in the five to 64-year-old group. They had higher compliance rates but poorer inhaler technique. These patients were more likely to be on the highest BAG treatment steps. There was a steady progression of increasing step of BAG with increasing age.

General practice consultations for asthma were very common in children up to four years of age and then declined in frequency until age 31 to 45 years, where they increased and continued to increase with advancing age. Accident and emergency attendance, outpatient attendance, and admission rates showed a similar pattern.

Patients aged 16 to 30 years reported similar symptom levels to those in the adjacent age groups. They had poorer compliance, fewer GP consultations, and fewer outpatient admissions. Additionally, they tended to be on lower BAG treatment steps.

Discussion

This 'cross-sectional' presentation on the natural history of asthma highlights some interesting findings. The results emphasise the considerable burden doctor-diagnosed

Table 1. Symptoms, treatment step, and health service utilisation by age.

	Age groups (years)					
	<5	5–15	16–30	31–45	46–64	65 +
Population size	597	3362	2445	1991	2218	1590
Number of patients assessed for symptoms	469	2742	1634	1514	1881	1385
Night (%)	212 (45)	739 (27)	587 (36)	551 (36)	762 (41)	497 (36)
On waking (%)	168 (36)	808 (30)	676 (41)	715 (47)	943 (50)	788 (57)
Exercise (%)	192 (41)	1360 (50)	890 (55)	844 (56)	1225 (65)	1046 (76)
Compliance assessed	428	2641	1577	1465	1834	1357
Poor compliance (%)	65 (15)	410 (16)	332 (21)	249 (17)	256 (14)	165 (12)
Inhaler technique assessed	406	2637	1564	1454	1821	1335
Poor inhaler technique (%)	57 (14)	181 (7)	122 (8)	118 (8)	168 (9)	154 (12)
British Asthma Guidelines treatment step						
0 (%)	35 (6)	271 (8)	285 (12)	169 (9)	130 (6)	63 (4)
1 (%)	177 (30)	612 (18)	592 (24)	360 (18)	291 (13)	202 (13)
2 (%)	164 (28)	1134 (34)	1099 (45)	825 (41)	812 (37)	585 (37)
3 (%)	164 (28)	884 (26)	329 (14)	432 (22)	559 (25)	341 (21)
4 (%)	55 (9)	436 (13)	116 (5)	175 (9)	325 (15)	287 (18)
5 (%)	2 (1)	25 (1)	24 (1)	30 (2)	101 (5)	112 (7)
Health service utilisation						
Patient-initiated consultations	486 (81)	2107 (63)	1212 (50)	1083 (54)	1316 (59)	948 (60)
Practice review consultations	446 (75)	2426 (72)	1378 (56)	1259 (63)	1551 (70)	1113 (70)
A&E attendance	63 (11)	94 (3)	75 (3)	50 (3)	56 (2)	28 (2)
Hospital outpatient	93 (16)	180 (5)	66 (3)	79 (4)	186 (8)	137 (9)
Hospital admissions	80 (13)	78 (2)	55 (2)	38 (2)	66 (3)	65 (4)
Asthma attacks	221 (37)	697 (21)	437 (18)	401 (20)	509 (23)	388 (24)

Table 2. Odds ratios of patients under five years of age compared with others.

	Age groups (years)		Odds ratio
	<5	5+	
Population size	597	11606	
Number of patients assessed for symptoms	469	9156	
Night (%)	212 (45)	3136 (34)	1.58 [a] (1.31, 1.92)
On waking (%)	168 (36)	3930 (43)	0.74 [a] (0.61, 0.90)
Exercise (%)	192 (41)	5365 (59)	0.49 [a] (0.40, 0.59)
Compliance assessed	428	8874	
Poor compliance	65 (15)	1412 (16)	0.95 (0.72, 1.25)
Inhaler technique assessed	406	8811	
Poor inhaler technique	57 (14)	743 (8)	1.77[a] (1.31, 2.39)
Health service utilisation			
Patient-initiated consultations	486 (81)	6666 (57)	3.24 [a] (2.62,4.02)
Practice review consultations	446 (75)	7727 (67)	1.48 [a] (1.22,1.80)
A&E attendance	63 (11)	303 (3)	4.40 [a] (3.28, 5.90)
Hospital outpatient	93 (16)	648 (6)	3.12 [a] (2.45, 3.97)
Hospital admissions	80 (13)	302 (3)	5.79 [a] (4.42, 7.58)
Asthma attacks	221 (37)	2432 (21)	2.22 [a] (1.86, 2.64)

[a]95% confidence interval, does not include 1.0.

childhood asthma (age up to four years) places on the health service. The level of symptoms of this age group emphasise the disruption to sleep pattern and lifestyle that uncontrolled childhood asthma can cause. Behind these collated statistics are many individual accounts of misery to young children and their families. Modern anti-asthma treatments and innovations in health care delivery may have improved the lives of many sufferers but there remains a substantial burden of morbidity owing to asthma in childhood. The results support the view that childhood asthma is not a homogeneous clinical entity. Silverman and others have argued that asthma in early childhood is a different entity from atopic asthma in the middle-childhood years.[19] The pattern of symptoms experienced by children at different ages suggests that within the diagnostic category 'asthma' there are at least two distinct clinical syndromes. The results of this paper support the BAG division of asthma management in children up to four years of age and then five years and over.

The finding that, in adults, the symptoms of asthma become more common with increasing age is unsurprising. The general practices that contributed patients to the study were asked to include patients from their asthma registers. These registers are usually a pragmatic attempt by practices to list those patients who are receiving anti-asthma medication and might require regular follow-up. It is likely that many

Table 3. Odds ratios of patients aged 65 years and over compared against those aged 5–64 years.

	Age groups (years)		Odds ratio
	65+	5–64	
Population size	1590	10016	
Number of patients assessed for symptoms	1385	7771	
Night (%)	497 (36)	2639 (34)	1.09 (0.96, 1.23)
On waking (%)	788 (57)	3142 (40)	1.94[a] (1.73, 2.19)
Exercise (%)	1046 (76)	4319 (56)	2.47[a] (2.16, 2.82)
Compliance assessed	1357	7517	
Poor compliance	165 (12)	1247 (17)	0.70[a] (0.58, 0.83)
Inhaler technique assessed	1335	7476	
Poor inhaler technique	154 (12)	589 (8)	1.52[a] (1.26, 1.85)
Health service utilisation			
Patient-initiated consultations	948 (60)	5718 (57)	1.11[a] (1.00, 1.24)
Practice review consultations	1113 (70)	6614 (66)	1.20[a] (1.07, 1.35)
A&E attendance	28 (2)	275 (3)	0.63[a] (0.42, 0.95)
Hospital outpatient	137 (9)	511 (5)	1.75[a] (1.43, 2.14)
Hospital admissions	65 (4)	237 (2)	1.76[a] (1.32, 2.35)
Asthma attacks	388 (24)	2044 (20)	1.26[a] (1.11, 1.43)

[a]95% confidence interval, does not include 1.0.

Table 4. Odds ratios of patients aged 16–30 years compared with patients aged 5–15 years and 31–64 years.

	Age groups (years)		Odds ratio
	16–30	5–15, 31–64	
Population size	2445	7571	
Number of patients assessed for symptoms	1634	6137	
Night (%)	587 (36)	2052 (33)	1.12 (0.99, 1.25)
On waking (%)	676 (41)	2466 (40)	1.06 (0.95, 1.19)
Exercise (%)	890 (55)	3429 (56)	0.94 (0.85, 1.06)
Compliance assessed	1577	5940	
Poor compliance	332 (21)	915 (15)	1.46[a] (1.27, 1.69)
Inhaler technique assessed	1564	5912	
Poor inhaler technique	122 (8)	467 (8)	0.99 (0.80, 1.22)
Health service utilisation			
Patient-initiated consultations	1212 (50)	4506 (60)	0.67[a] (0.61, 0.73)
Practice review consultations	1378 (56)	5236 (69)	0.58[a] (0.52, 0.63)
A&E attendance	75 (3)	200 (3)	1.17 (0.88, 1.54)
Hospital outpatient	66 (3)	445 (6)	0.44[a] (0.34, 0.58)
Hospital admissions	55 (2)	182 (2)	0.93 (0.68, 1.28)
Asthma attacks	437 (18)	1607 (21)	0.81[a] (0.72, 0.91)

[a]95% confidence interval, does not include 1.0.

practice registers, and by implication attendances at asthma clinics, have respiratory conditions other than asthma that contribute to symptom prevalence. The true prevalence of COPD is unknown. It is likely that a large proportion of late middle-age and elderly patients on practice asthma registers have COPD, and not asthma, as their dominant condition. There is a case, based on the results presented here, for BAG guidelines to make treatment recommendations for adults aged 65 years and over to take account of COPD.

Apart from children aged under five years, there was a general trend for increased use of health services and increased level of medication as the patients got older. However, the exception to this was patients aged 16 to 30 years who had lower levels of medication and did not use the review services on offer from general practice to help manage their asthma. These patients showed no differences in their use of other health services, suggesting that they seek attention for their asthma when it is a problem rather than simply complying with structured follow-up services.

We opted to separate adult groups into young adults (16 to 30 years), adults unlikely to have COPD (31 to 45 years), and adults aged 46 years up to retirement age. We accept that there are arguments in favour of different classifications. The results presented in this paper do not alter substantially if the age groupings are altered by one or two years at each boundary age.

There are limitations to the use of data collected for one purpose — an Asthma Management Initiative — being used for another, i.e. observations on natural history. We did not survey patients directly; our information is derived from what practices reported. Clearly, the results are thus biased because they are derived from practices that enrolled in a study. Quality control work reported elsewhere shows that the practices are geographically representative of the UK and that they did follow our instructions in enrolling a representative sample of their practice asthma registers.[18] We

have no way of validating each practice's diagnostic accuracy of the term 'asthma'. Many young children with symptoms of cough or wheeze may not have been included in practice registers and hence are excluded from this study. The study is weakened by the rather circular argument that the diagnosis of asthma may be based on symptoms and then symptoms are used to describe asthma. Not all patients enrolled had attended a structured clinical review within the past six months. However, we opted to include these patients in the study. Not all patients take their treatments as intended and some patients with asthma opt not to take treatment at all, the so-called 'Step 0'.[17] We opted to include all these cases. A further weakness of our method was the reliance on a single clinical assessment of symptoms within the past month. Symptoms fluctuate rapidly, particularly in young children.

Databases have become an important feature of modern health care and research. Their use in observational studies is controversial. Natural history should, by definition, be studied in a longitudinal manner, but it would be wrong to disregard the contribution that databases can make to observations on asthma in different age groups. The cross-sectional work presented here gives potentially useful insights into how asthma affects different age groups. The findings may also shed some light on the difficult issue of classifying asthma by subgroup.

In conclusion, if one accepts the principle that database information is a valid tool, observations on the natural history of asthma suggest there are several subgroups within the broad diagnostic category of asthma. These subgroups have differing patterns of symptoms, treatment, and health service utilisation that clinicians need to be aware of.

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