Evidence-based guidance for the assessment of new employees with asthma

A report to the British Occupational Health Research Foundation

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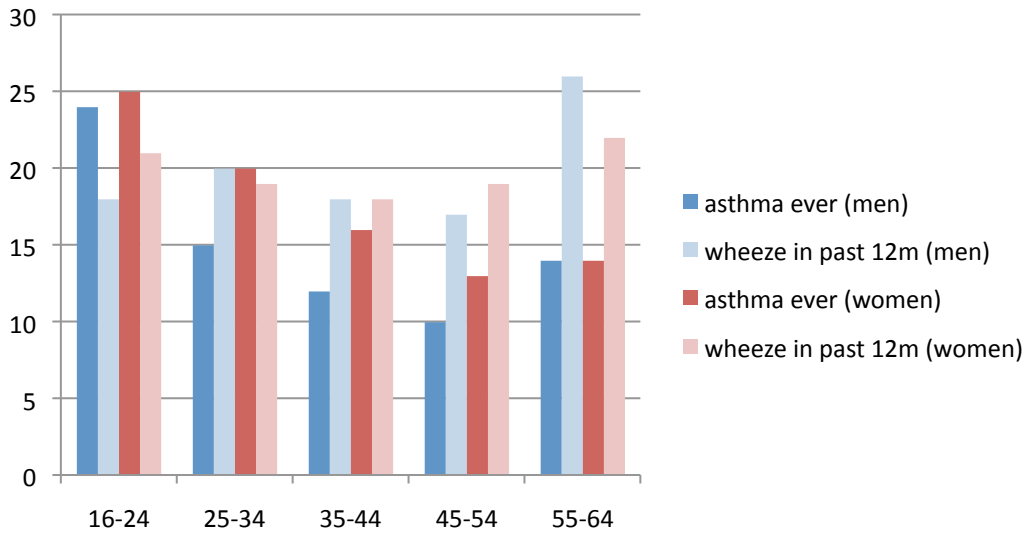
1. **Background**

Asthma

A diagnosis of asthma is common in United Kingdom populations. Findings from the Health Survey for England in 2001, covering 15,647 adults living in private households with an estimated response rate of 67% (1),suggest that about one quarter of men and women aged between 16 and 24 years have at some point been diagnosed with the disease; the proportions are generally lower in older persons (see Figure 1), probably reflecting a birth cohort effect, and at all adult ages are higher in women. In younger adults the frequency of 'ever asthma' is higher than of current wheeze, a pattern which reverses after the age of about 30, reflecting in part other causes of 'wheeze' which tend to increase with age. Since a characteristic of asthma is its tendency to remit (and relapse) and since its symptoms are not specific, none of these figures necessarily reflects the age-specific prevalence of current disease. The incidence of asthma is highest in the first years of life but approximately one third of children with asthma will be asymptomatic by the age of 15.

Figure 1. proportion of working-age adults, by age, reporting either a lifetime diagnosis of asthma or any wheeze within the past year (1).



In those with persisting symptoms in adulthood, there is a range of clinical phenotypes. In the same survey, of all working-age adults who reported wheeze in the previous yearabout half had had fewer than four episodes a year and around three quarters less than one episode a month (Figures 2a and 2b). Forty three percent of these men and 53% of women reportedinterference with daily activities from wheeze; and 11% of working men and 15% of working women that their wheeze had resulted in a day or more away from work over the last year. Among men this last proportion was highest in those aged 16-24 years; in women there was little variation by age until after the age of 54.

Figure 2a. frequency of wheeze, interference in daily activities and absence from work among men with wheeze in the past 12 months (n=1087).

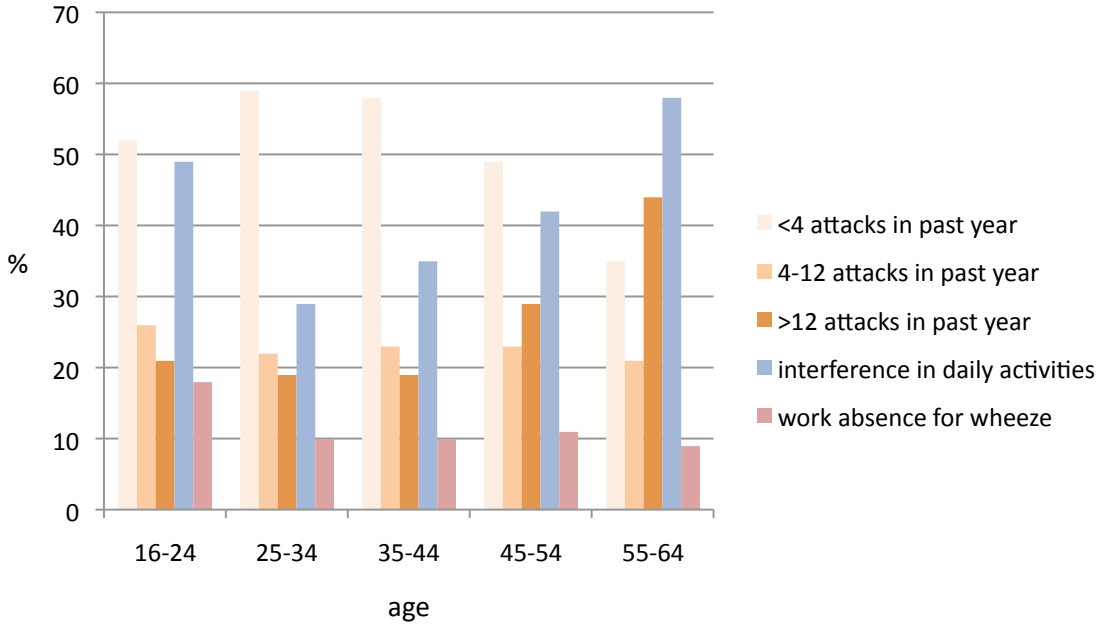
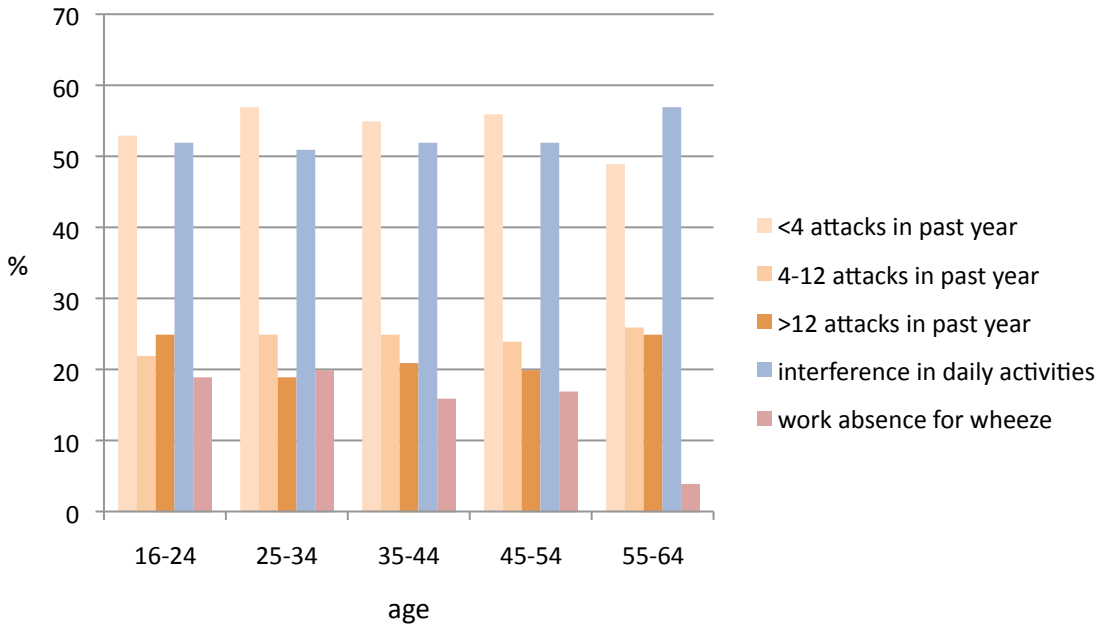


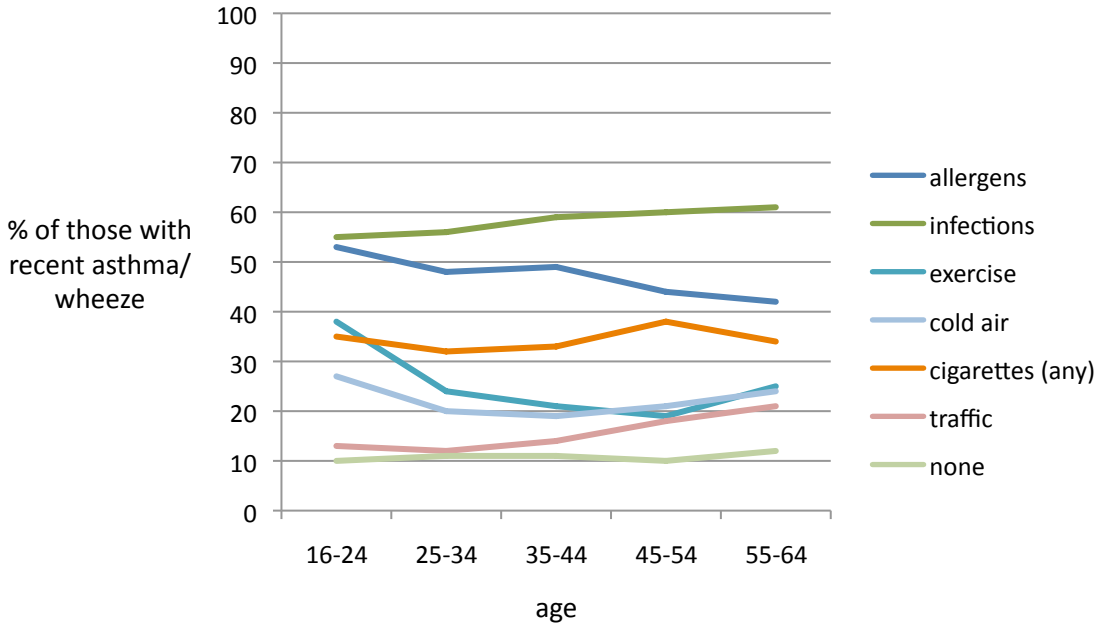
Figure 2b. frequency of wheeze, interference in daily activities and absence from work among women with wheeze in the past 12 months (n=1326).



Most asthma arising in childhood is accompanied by atopy, a tendency to develop immediate-type sensitivity to environmental aeroallergens which frequently persists; in 1995/96, around half of English adults (2) with recent symptoms of asthma reported that these were provoked by specific allergens (Figure 3). Other common precipitants included respiratory infections, cigarette smoke,

exercise and cold air. In this respect, there were comparatively few differences by either age or sex. Around one in ten adults with recent asthma recognised no specific provoking factor(s).

Figure 3 reported precipitating factors among adults with a lifetime diagnosis of asthma or wheeze and the most recent attack(s) within the last five years (2).



The symptoms of asthma are not entirely specific and the disease has no unambiguous or universally accepted definition. Thus diagnoses, and reports of diagnoses, will include alternative respiratory conditions; most authorities, however, consider a doctor's diagnosis to be more specific than otherwise self-reported disease. Conversely, a diagnosis of asthma may not be recalled, especially when it was made in early childhood and the disease has since remitted. Treatments used in asthma are also used for other respiratory diseases, commonly for infection-related wheeze at any age and, later in life, for chronic obstructive pulmonary disease; reports of such treatment are not necessarily confirmation of asthma.

Asthma and employment

In contrast to persons with hayfever, there is little evidence that those with a history of childhood asthma choose employment with any regard to their disease. Thus the proportions of job applicants who have a history of asthma should reflect the frequency of the disease in the general population. Asthma frequently arouses concerns in employers and their health advisors; these concerns are varied, in most cases being specific to the nature of the work. Consequently, questions about asthma are often included in pre-placement health assessments. These screening questions are unstandardised, variable and for the most part unvalidated for such assessment. While some enquire into current or recent disease, others refer to a lifetime prevalence; some ask directly about a medical diagnosis of asthma, others are less specific. Occasionally, the questions are qualified with a measure of disease severity or of current or recent treatment; only rarely is enquiry made into specific precipitating exposures.

Direct discrimination in relation to employment, on the basis of an applicant having a history of asthma, is prohibited by law in the UK. Most employers make decisions about placement of employees using a case-by-case approach. Unsurprisingly there is considerable variation in practice. In some sectors – notably the military and commercial diving – there is standard and tailored guidance designed to reduce such variations. The information produced here and set out below aims to provide guidance, informed by evidence, for use in sectors where none currently exists or where what is available is of uncertain value and/or provenance.

2. Approach

A panel of interested occupational or respiratory specialist clinicians was assembled in 2008. The membership and their affiliations are listed in the Appendix. None reported any conflict of interest.

The tasks of the panel included:

1. The establishment of the range of concerns relating to the employment or placement of persons with asthma. This was achieved through discussion and a survey of occupational health professionals practising in the UK (Part A).
2. The systematic collation and assessment of published evidence relating to each of the identified concerns (Part B).
3. An analysis of UK primary care records of registered adults with asthma (Part C)
4. The writing of a draft report, including a summary of the evidence above.

Early in this process, certain gaps in the published evidence base were identified. The most important of these concerned the 'disease trajectory' - and its determinants - of persons with asthma. To rectify this deficiency, a study of general practice records was undertaken by the Department of Occupational and Environmental Medicine at Royal Brompton Hospital/Imperial College. The summary findings of this study are included in the report below but are to be published more fully elsewhere.

Funding for the panel meetings, for the statistical analyses of general practice records and for preparation of the guidance was provided by the British Occupational Health Research Foundation (BOHRF).

Part A: survey of concerns among UK occupational health practitioners

Ethical approval was sought and obtained for a survey of the membership of a number of professional occupational health organisations[1]. Agreement for a single mailing with anonymised responses was granted. Lists of current members – as far as these were available – were drawn up and each was posted a brief questionnaire enquiring into their qualifications, their current practice and any concerns they might have over the employment and/or placement of new employees with asthma. We received 664 replies, an approximate response rate of 30%. Almost all respondents were of the view that further guidance on the employment of persons with asthma was desirable; the few exceptions felt that the information currently available for their particular spheres of work (the military, commercial; diving) were sufficient.

The identified concerns relating to the employment or placement of persons with asthma were aggregated as follows:

- **how often do employees with asthma report aggravation of their disease at work?**
- **how often do employees with asthma need to take time off work because of their disease?**
- **what proportion of employees with asthma take time off work because of their disease?**
- **how productive at work are employees with asthma?**
- **what is the rate of early retirement among employees with asthma?**
- **what are the costs to an employer of an employee with asthma?**
- **are employees with asthma at an increased risk of developing occupational asthma because of their disease?**
- **what is the risk of an abrupt (unexpected) attack of severe asthma in an employee who has the disease?**
- **what is the risk of relapse in childhood asthma that has remitted?**
- **what are the diagnostic and prognostic values of measurements of airways responsiveness in persons with asthma (current or past)?**
- **are employees with asthma at peculiar risk when they are wearing breathing apparatus?**

In order to understand the relative level of concern for the above we invited those surveyed to consider several occupations (or occupational exposures) separately and within each to apply a score to a list of potential concerns. A summary of our findings is shown in table 1. Particularly high levels of (median) concern were reported for safety critical occupations (firefighting and police work), for exacerbation of asthma in those working in settings of potentially high exposure to biological or chemical dusts or fumes and for the development of occupational asthma in those working with recognised respiratory sensitising agents.

[1] The Society of Occupational Medicine, the Society of Occupational Health Nurses and the Association of Occupational Health Practitioners

Table 1 median scores applied to a series of potential concerns relating to the employment of persons with asthma in different occupations or occupational settings. Those with the highest median scores are shaded.

Scores: 1: not concerned
2: mildly concerned
3: moderately concerned
4: very concerned
5: extremely concerned

	risk of occupational asthma	exacerbation of asthma	sudden attack of asthma	asthma a risk to others	sickness absence for asthma	early retirement for asthma	litigation
firefighter	1	3	3	5	2	1	2
police officer	1	2	4	5	2	2	1
MVRI* employee	3	4	2	2	2	1	3
welder or solderer	4	3	2	2	1–3	2	3
diisocyanate worker	4	4	4	2	2	2	3
animal work	3–4	4	2	2	2	1–2	3
work with flour	3	4	3	1	3	3	3
work with a respiratory sensitizer	5	4	2	1	2	1	2
Work with dust, fumes or vapours	2	4	2	1	2	1	2–3

* MVRI: motor vehicle repair industry

The concerns identified from the survey very largely mapped those we had pre-conceived. Responses to an open question revealed only that other concerns related to the additional costs (logistical and financial) necessary to assess applicants with asthma.

Part B: assessment of published evidence relating to each identified concern.

1. Methods

The concerns identified above were re-formulated as 'questions' and published evidence pertaining to each was sought through a systematic review of all English language PubMed citations through to December 2010.

Few of the questions we asked were readily amenable to automated, key word-based literature searching. Thus, while a very large number of published papers were scanned we found few with information that was useful to us. Further studies were identified from the reference lists of papers we had identified as helpful; and from a variety of systematic and non-systematic reviews. We cannot be sure that we have identified every relevant published study but do not think that we have missed any that would make a significant difference to our conclusions. We have not enumerated those studies which we examined but rejected as unhelpful.

Information was extracted from each selected study by the author, grouped and then if appropriate tabulated and a summary commentary written.

2. Evidence

Workplace aggravation of pre-existing asthma

Question: how often do employees with asthma report aggravation of their disease at work?

This issue has been systematically considered in a recent review by Henneberger et al. (3). Using their findings and our additional survey of the literature, we identified thirteen studies which measured, directly, the proportion of employees with prevalent asthma who reported difficulties with their disease when at work. We omitted studies of new onset asthma attributed casually to work - and those of patients assembled from specialist clinics or surveillance programmes for occupational disease. A summary of the findings of these studies is provided in table 2.

Table 2 Self-reported aggravation of asthma at work. Figures in brackets refer to all surveyed adults with asthma (rather than working adults).

reference	setting	prevalent asthma (n)	response rate	workplace aggravation
Goh 1994 (4)	primary care (Singapore)	802	63%	(27%)
Blanc 1994 (5)	general population (Sweden)	160	65%	(38%)
Axon 1995(6)	adult hospital clinic (UK)	30	97%	31%
Abramson 1995 (7)	general population (Australia)	159	74%	(20%)
Palmer 1997(8)	employees of 4 electronics firms (UK)	21	97%	29%
Tarlo 2000(9)	adult hospital clinic (C)	682	NA	7%

Johnson 2000(10)	general population (Canada)	106	37%	(34%)
Mancuso 2003(11)	primary care (USA)	102	39%	58%
Saarinen 2003(12)	general population of working persons (Fin)	969	79%	20%
Henneberger 2003(13)	general population of working persons (USA)	64	62%	21%
Johnson 2006 (14)	general population (Australia)	694	37%	18%
Henneberger 2006(15)	members of medical insurance plan (USA)	598	61%	22%
Caldeira 2006(16)	birth cohort (Brazil)	227	93%	13%

In surveys of general working populations worsening of asthma at work was reported by between 13% and 38% of those with asthma. Two surveys of patients attending hospital clinics produced figures of 7% and 31%, the latter derived from a very small population. Just one tabulated study was of employees recruited from the workplace: Palmer and Crane (17)reported that among 21 electronic solderers whose asthma preceded their employment, six (29%) had wheeze that was worse at work. This, too, was the only study of a UK population.

Three studies related reports of workplace aggravation to a measure of occupational exposure. In a small US study (18)those in jobs considered by the authors to have a high asthma risk were more likely (50% *vs* 14%) to report that their 'symptoms consistent with asthma' were worse when they were at work. This was not the case for the smaller number with a doctor-confirmed diagnosis of asthma who in fact were less likely to report work-exacerbated symptoms if they were in a high risk job. In a similar but larger US study (19)a matrix of symptoms and probable exposures was created by an expert panel. Of the 243 (41%) employees with asthma who reported work-related symptoms, 12% described symptoms that improved when away from work, 10% that they used their treatment more at work and 34% that there was an asthma trigger in the workplace. On the basis of the matrix, only 136 (56%, or 22% of the total with asthma) were considered to have moderate or strong evidence of work-exacerbated asthma. The findings of a Finnish study (20)provide further information on likely exposures at work and also on the frequency of work-related symptoms. Respondents were more likely to report symptoms at work if they also judged their work to entail exposures to dust, chemical agents, abnormal temperatures, poor indoor air quality or either physical or mental stress. Some confirmation for these findings was provided by an expert evaluation in which those considered to have probable or possible exposure to dusts, gases or fumes (58% of the total) were more likely (54%) to report work-related symptoms than those for whom such exposures were unlikely (32%). Higher rates were also reported by those who used medication on a continual (rather than occasional) basis, those with adult-onset disease and those aged over 45 years. There were no differences between men and women or between smokers and non-smokers. Across the entire study population, of those with symptoms at work (n=371), 48% had them less

than weekly and a further 30% no more than once or twice a week. In an untabulated study of French adults with asthma(21)there was no positive association between asthma severity and exposure to non-sensitising irritants in the workplace.

Katz and colleagues (22)reported on a cohort of 639 recruits to maintenance jobs in the Israeli Defence Forces who had, at the time of their enlistment, 'mild asthma' without the need for daily treatment and evidence of only limited airflow obstruction or bronchial hyperreactivity. The work was characterised by moderate physical activity and exposure to non-specific irritants. Over 30 months of observation, 19% had worsening asthma, a figure no different from that among recruits to sedentary, clerical posts (18.6%). Of 1290 recruits with childhood asthma that had been in clinical remission for at least three years (and with normal spirometry and response to exercise testing) 10% had a relapse during the period of observation, a figure that was higher among those in combat units (13%) than those in maintenance (6%) or clerical posts (5%).

Thus, most studies suggest that around 25% of employees with asthma will report symptoms that are related to their work; it is unclear why two studies (one in Canada, one in Brazil) reported far lower frequencies. Limited evidence (23)suggests that true work-exacerbation is plausible in about half of those reporting relevant symptoms; and that about four fifths will have symptoms less frequently than three times a week and some 10% will need to use more treatment when at work.

Collectively, these findings suggest that reports of work-exacerbation are common but that in most cases they relate to mild or infrequent perturbations. There is disappointingly little information on specific occupations – a clear focus for future research – and none on how reports of exacerbation at work reflect underlying asthma severity or control. Nor, critically, have any of the studies above used a comparator population without asthma.

Sickness absence

"People think that if you employ an asthmatic you're going to have someone who's away sick all the time. And I guess there's a certain amount of the public have a certain amount of baggage about asthma. I've always tried to choose employment that was fairly flexible. If I had a choice between casual and permanent, I always choose casual. When they make the offer to me I will stay casual because that way I can take a day off and it wouldn't matter. I wouldn't worry about sick leave and things". (woman, 30s, clerical/sales/service, chronic severe asthma)(24)

Questions: **how often do employees with asthma need to take time off work because of their disease?**

what proportion of employees with asthma take time off work because of their disease?

Information on sickness absence is summarised in tables2 and 3, expressed by the average number of days absent for asthma (table 3) and by the proportion of employees with asthma taking time off for their disease (table 4). The populations from which this information was collected were various and response rates were often low. The number of absent days over a period of one year ranged from an estimated 1 to 8.6. The proportions of employees with asthma who reported spells of absence for their disease varied more, from just 4% in a US survey of medically insured persons to over half of hospital clinic patients in New Zealand.

The apparent disparity in these data is probably reflective of the very different populations and survey methods employed; of different interpretations of sickness absence; and of the obvious skew

in the distribution of responses, routinely and misleadingly described by mean values. Thus it seems probable that a small proportion of persons with asthma take a lot of time off work while most take little. Ina general population sample of Italian adults with asthma, the authors observed that 16% had taken time off from work over the past year because of their asthma; collectively this group lost an average of 26 days. When spread across the entire population of employees this last figure was 4.1 days.

Further evidence of such variability is provided by three studies in which greater numbers of absent days or higher rates of absence were reported by those with more severe asthma; and by Horn and Cochrane who described a correlation, presumably inverse, between respiratory function and work absence.In contrast, a survey of Spanish patients reported no relationship between asthma severity and work absence; and in a US population, patients adherent to their treatment were no less likely to take sickness absence than those with lower adherence.

There is an unfortunate lack of direct comparative data but what is available suggests little overall difference in sickness absence between employees with and without asthma; or between those with asthma and those with other, chronic diseases. In some contrast, a two-year prospective study of 251 Dutch blue collar and office workers indicated that those with a preceding history of 'asthma complaints' were four times more likely to take time off for a respiratory disorder.

Finally, analysis of 221,249 sick leave periods registered by a Swedish insurance company (25) found that 0.47% were attributed to asthma (3.56% to other airway diagnoses). The findings of a linked postal survey suggested that the label of asthma was, in this context, a sensitive but not a specific indicator of the explanation for sickness absence.

Table 3 Days sickness for asthma

reference	setting	n asthma	response rate	average days sickness in past year
Horn 1989(26)	general practice (UK)	312	58%	8
Jolicoeur 1994(27)	students (US)	51	28%	1.8*
Sørensen 1997(28)	pharmacy customers (DK)	115	NA	~1.5 (estimate)
Ungar 2000(29)	pharmacy customers (C)	386	NA	median 0 mean 4.4
Sauni 2001(30)	construction workers (Fin)	76	71%	6 (=non-asthma)
Godard 2002(31)	hospital clinic (F)	234	NA	0.03 (mild intermittent) 0.58 (mild) 5.38 (moderate) 8.59 (severe)
Taylor 2005(32)	birth cohort (NZ)	176	NA	3.83

Accordini 2006(33)	general population (I)	527		4.1
Lamb 2006(34)	employees of 27 businesses (USA)	797	NA	~1 (estimate) (3.7 all respondents)
Joshi 2006(35)	health-insured state employees (US)	385	25%	5.64 ('high' adherence) 5.42 ('medium' adherence) 4.23 ('low' adherence)
Jansson 2007(36)	general population (S)	115	NA	1.70 (mild intermittent) 3.66 (persistent)

NA = not available

*in one autumn university term; 44 (86%) students were working part-time only

Table 4 Proportion taking sickness absence for asthma

reference	**setting**	**n asthma**	**response rate**	**proportion asthma sickness in past year**
Horn 1989(37)	general practice (UK)	312	58%	47%
McClellan 1990(38)	hospital clinic (NZ)	44	NA	57% (over six months)
Serra-Batlles(39)	Primary/secondary care (E)	333	NA	23% (mild) 28% (moderate) 23% (severe)
Blanc 2001(40)	respondents to telephone survey (US)	72	68%	24% (over four weeks)
Vermeire 2002(41)	respondents to telephone survey (7 European countries)	2050	80% eligible*	16% (UK) 17% (F) 18% (D) 18% (I) 28% (NL) 17% (E) 13% (S)
Erickson 2002(42)	managed care organisation (US)	369	36%	4% (mild, intermittent) 17% (mild) 22% (moderate) 29% (severe)
Cisternas 2003(43)	primary care (US)	401	NA	11% (further 6% lost part days)

Accordini 2006(33)	general population (I)	527	76%	16%
Orbon 2006(44)	general practice (NL)	52	37%	10% respiratory causes (*cf*9% non-asthma) 57% all causes>2d (*cf*44% non-asthma)
Munir 2007(45)	employees in manufacturing/transport/LA sectors (UK)	174	28%	mean 0.65 spells (<5 days) *pa* mean 0.42 spells (≥5 days) *pa*

NA = not available

*of persons with asthma in contacted households

Productivity

Question: how productive at work are employees with asthma?

We found reports of four studies that examined 'productivity' at work, each using a different, self-reported measure (table 5). The high proportion of pharmacy customers in Canada with 'productivity loss days' largely reflected employees who reported continuing to work 'even though (their) breathing problems were worse than usual'. The authors of this paper also pointed out that the distribution of unproductive days was skewed by small numbers of patients reporting large numbers of days. This and one other study found that loss in productivity was directly related to asthma severity; by way of contrast, in a US population of state employees with asthma the average number of unproductive hours per day was unrelated to self-reported adherence to asthma treatments. None of the studies made direct reference to employees without asthma.

Table 5 Work productivity in employees with asthma

reference	setting	n prevalent asthma	response rate	findings
Ungar 2000(46)	pharmacy customers (C)	386	NA	73% reported either absence from, or restriction at work due to asthma • mild: 8.5 days • moderate 11.9 days • severe: 17.3 days mean level of reported function at work when 'restricted' 81%

Blanc 2001(47)	respondents to telephone survey (US)	72	68%	19% reported effectiveness at work ≤90% (*vs* 36% with rhinitis)
Joshi 2006(48)	health-insured state employees (US)	385	25%	mean unproductive hours per working day: 0.9 ('high' adherence) 1.4 ('medium' adherence) 1.1 ('low' adherence)
Williams 2009(49)	general population (US)	2912 controlled asthma 2767 uncontrolled asthma	NA	absenteeism score* • controlled: 4.7 • uncontrolled: 10.4 presenteeism score* • controlled 19.0 • uncontrolled 34.3

*Work Productivity and Activity Impairment questionnaire

Early retirement

Question: what is the rate of early retirement among employees with asthma?

One study only reported rates of early retirement, in an eight year follow-up of 11,000 German construction workers with and without asthma at baseline (table 6). No increase in age-adjusted risk was found; perhaps unsurprisingly there was a low prevalence of asthma (<1%) in this workforce.

Table 6 Early retirement by employees with asthma

reference	setting	n prevalent asthma	response rate	findings
Siebert 2001(50)	Construction workers (D)	757 at baseline	NA	No increase in risk *vs* those without asthma (RR=0.83)

Employer costs

Question: what are the costs to an employer of an employee with asthma?

We found only one study that directly measured the costs of 'asthma' to an employer (table 7). Health insurance claims recorded for employees of a large US corporation were compared between workers with asthma and workers making claims for other disease(s); the groups were matched on age, sex and job type.

Table 7 Annual indirect costs (mean) arising from work absence in employees with and without asthma

	asthma group			**non-asthma group**	
reference	asthma	other respiratory	other	other respiratory	other
Birnbaum 2002(51)	$51	$93	$272	$18	$182

Notably, a large proportion of the incremental costs for employees with asthma was the result of absence for illness other than asthma. The values presented are means with no indication of the spread or distribution of costs.

Societal costs

A systematic review of studies of the economic burden of asthma (Bahadori 2009)(52) found that in 12 (21%) of 57 studies that measured indirect costs, work (or school) absence was the largest single such cost.

Risk of occupational asthma (by sensitisation)

Question: are employees with asthma at an increased risk of developing occupational asthma because of their disease?

Surprisingly, there are very few studies that directly examine the question of whether employees with asthma who are exposed at work to respiratory sensitising agents are, by virtue of their asthma alone, at an increased risk of developing occupational asthma.

There is a broad body of work that demonstrates an increase in risk for employees who are atopic; that is, they have a propensity to produce specific immunoglobulin IgE on ordinary exposure tocommon allergens in their environment. The evidence has been systematically reviewed (53) and summarised as: "atopy increases the risk of developing occupational asthma caused by exposure tomany high molecular weight agents that induce the production of specific IgE antibodies". Most people with asthma – especially that of onset in childhood – are atopic but there is no evidence, either way, that their risk is different from those who are atopic but not asthmatic.

A prospective study of 373 laboratory animal handler apprentices in Canada(54)reported that over a period of follow-up of between eight and 44 months the risk of probable occupational asthma (n=28) was independently increased 2.5-fold in those with any degree of bronchial hyperreactivity at baseline. Such hyperreactivity was measured in 68% of those who developed occupational asthma and 34% of those who did not. There was no detectable increase in risk for those with more marked hyperreactivity; nor, independently, for those who reported asthma at baseline (10% of the cohort).

Abrupt onset asthma

Question: what is the risk of an abrupt (unexpected) attack of severe asthma in an employee who has the disease?

We found no studies that measured the incidence of abrupt-onset deterioration in a general population of persons with asthma. Eight studies reported the proportion of severe attacks (in all cases identified by the need for acute hospital care) that were of rapid onset. These are summarised in table 8. There were no factors predictive of rapid deterioration that were consistently identified in these studies.

Table 8 rates of 'abrupt onset' asthma in patients treated in hospital for asthma

reference	country	n asthma	definition of 'rapid'	proportion with rapid onset
Arnold 1982(55)	UK	261	<1hr	13%
Wasserfallen 1990(56)	CH	34	<3hr	29%
Kolbe 1998(57)	NZ	316		8.5%
Woodruff 1998(58)	US	211	≤3hr	17%
Rodrigo 2000(59)	Ur	403	<6hr	11%
Barr 2000(60)	US	1847	≤3hr	7%
Plaza 2002(61)	E	220	≤2hr	20%

Risk of relapse

Question: what is the risk of relapse in childhood asthma that has remitted?

Studies of the prognosis of childhood asthma suitable for our purpose need:

1. to be representative of the general population
2. preferably, to be prospective, and
3. to have used an unambiguous definition of asthma

Among several we considered, birth cohorts recruited in Dunedin (New Zealand) and Melbourne (Australia) contained the most useful information.

Around two-thirds of children with asthma in childhood will be free of wheeze by early adulthood (62;63). Remission is more common in males, in those whose asthma started after the age of 5, in those without accompanying rhinitis or eczema (64)and in those with no family history of asthma.

There is relatively little published information on either the rates or determinants of asthma relapse; *ie* the return of disease in those whose childhood asthma had remitted. The best available appears to be that derived from the prospective study of a birth cohort in Dunedin. Born in 1972-73, 613 children were followed prospectively and in detail from the age of 9 to 26. One third of those with asthma in remission at age 18 (n=68) had a relapse of their disease by the age of 26 (65). Only two factors were independently and significantly related to the risk of relapse; house dust mite sensitisation at age 13 and a decrease in FEV1/FVC at age 18 (OR 0.90 per 1%increase in ratio). A positive response to a metacholine challenge test at age 15 was associated with a 50% likelihood of subsequent relapse (i.e. a positive predictive value of 50%). A negative test result at that age had a (negative) predictive value of 67%.

Importantly, asthma that represents a relapse of remitted childhood disease appears, in general, to have a mild course:

Table 9 comparison of 'relapsed' with 'persistent' asthma at age 26 (adapted from(66))

	at age 26	
	'relapsed' asthma	'persistent' asthma
FEV_1 %predicted (mean)	97	92
FEV_1/FVC ratio (mean)	79	76
Use of reliever treatment (%)	54	94
Use of preventer treatment (%)	17	64
Hospitalisation age 18-26 (%)	0	11
Work/school absence age 18-26 (mean days)	0.83	3.83

Use of NSBHR measurements

Question: what are the diagnostic and prognostic values of measurements of airways responsiveness in persons with asthma (current or past)?

Measurements of airways responsiveness are made using either 'direct' or 'indirect' methods:

- direct methods, generally using inhaled histamine or metacholine, reflect stimulation of specific airway smooth muscle receptors; they are rarely employed outside hospital or in the setting of epidemiological studies

- indirect methods stimulate one or more intermediate pathways through the release of inflammatory mediators from (non-muscle) airway cells; the results probably reflect current airway inflammation more closely than do those from direct methods of measurement. The most common techniques use exercise, eucapnic hyperventilation (EVH), hypertonic saline or mannitol. Some of these approaches are routinely used in non-hospital, clinical practice.

All of these methods produce results along a continuous scale which can be categorised to identify a state of airways hyperresponsiveness (AHR). AHR is a characteristic but not universal feature of active asthma; the two terms are not synonymous but are often present together.

There is a very large literature on the relationship between AHR and asthma. Most of it is written within the context of hospital practice, drug trials for asthma or epidemiological surveys of general populations; little is easily applicable to occupational health practice.

Direct methods of measuring airways responsiveness:
These are well standardised and widely used in hospital practice; most of the published literature relates to the use of histamine or metacholine.

- the (arbitrary) cut-off points[2], whereby histamine or metacholine provocation tests are categorised as indicative or not of AHR, are set to provide maximum sensitivity at the expense of specificity. Thus the tests have a very high (*c.*100%)negative predictive value but a relatively poor positive predictive value. Thus,
    - in the presence of current symptoms, a negative test effectively rules out current asthma
    - persons with intermittent, allergic asthma, triggered for example by pollens or occupational exposures, may have normal airways responsiveness at times when they are not exposed.
    - if a lower cut-off is used to define AHR, the positive predictive value of the test increases (at the expense of its sensitivity). A test result of ≤1mg/ml, for example, has almost 100% positive predictive value for asthma(67).
    - the high sensitivity of direct methods of measurement is offset by a relatively low specificity. In a general population, fewer than 50% of those with AHR measured in this way will have clinically current asthma(68).
    - most of those who have AHR but no asthma will not have other identifiable disease. Higher rates than normal have however been found in those with COPD and rhinitis or sinusitis; and upper or lower respiratory infections may induce temporary AHR. The condition is probably more common in smokers irrespective of any respiratory disease.
- there are no studies which directly relate either the presence or degree of AHR, measured directly, with clinical responses to irritant exposures in the workplace. In general, however, persons with asthma and marked AHR will be more symptomatic or require more treatment than those with mild AHR(69); and AHR will improve (modestly, and rarely resolve) with inhaled corticosteroid treatment.
- children with asthma whose disease remits may retain their AHR in early adulthood(70); and those who do appear to be more likely to have a relapse of asthma later in life (71).

[2] PC_{20} 8-16mg/ml of histamine or metacholine

Indirect methods of measuring airways responsiveness:

Indirect methods of measuring AHR are more closely reflective of airway inflammation than are direct methods. They tend to be less well standardised than most direct methods and the literature on their interpretation and inter-correlations is somewhat slighter. In the occupational setting exercise testing is most often used.

- exercise provocation tends to be less sensitive in the diagnosis of current asthma than 'direct' challenge with either histamine or metacholine(72;73). The relatively low sensitivity probably reflects the technical and safety constraints that limit the provocation that can practically be achieved through an exercise test; mannitol testing may be an exception in this regard (74).
- the diagnostic performance of exercise testing in asthma equates, roughly, to a direct test cut off of about 1mg/ml histamine or metacholine(75).
- Exercise testing (or EVH) is the challenge of choice for those who may have exercise-induced bronchoconstruction or asthma. Standardised methods for exercise testing are detailed in European (76)and US (77)guidelines.
- the lower sensitivity of exercise testing and other indirect methods is countered by their high specificity – in some cases (such as exercise testing) by definition. They are thus more useful than direct tests in confirming (rather than excluding) a diagnosis of asthma.
- Indirect measurements of AHR are subject to factors that improve (*eg* treatment with inhaled corticosteroids) or exacerbate (*eg* allergen exposure) airway inflammation.

Asthma and Respiratory Protective Equipment

Question: are employees with asthma at particularrisk when they are wearing respiratory protective equipment?

Respiratory protective devices ('respirators') are diverse but broadly may be categorised as:

- filtering facepieces
- half-face (cartridge) masks
- full-face devices with either an external or self-contained supply of (filtered) air

These devices differ not only in the circumstances of their use but also in their ventilatory parameters and physiological consequences.Consequently it is difficult, if not impossible, to reach general conclusions. A further difficulty arises from the fact that most research into the respiratory impacts of respirators has been conducted in healthy persons; very little relates to those with obstructive airways diseases such as asthma.

We located two relevant studies. The first, of only indirect pertinence, compared cardiopulmonary and subjective responses to exercise with added resistance to breathing in 27 men with obstructive airways disease (not defined as 'asthma') and 13 normal volunteers. No important differences were seen, either for those with mild obstruction (FEV_1/FVC ratio <70% but >60%) or moderate obstruction (FEV_1/FVC ratio <60% but >45%).

A study of two types of respiratory protection worn during simulated work tasks included 42 persons with mild asthma, of average age 44 years and mean FEV_1 88%predicted. Numerous device-disease interactions on pulmonary physiology were detected but it is unclear whether (any of) these are of

clinical or functional significance. The authors of this study remarked that the routine evaluation by spirometry may be insensitive for detecting those who will poorly tolerate the use of respirators.

Table 9 studies of respirator use in person with obstructive airways disease.

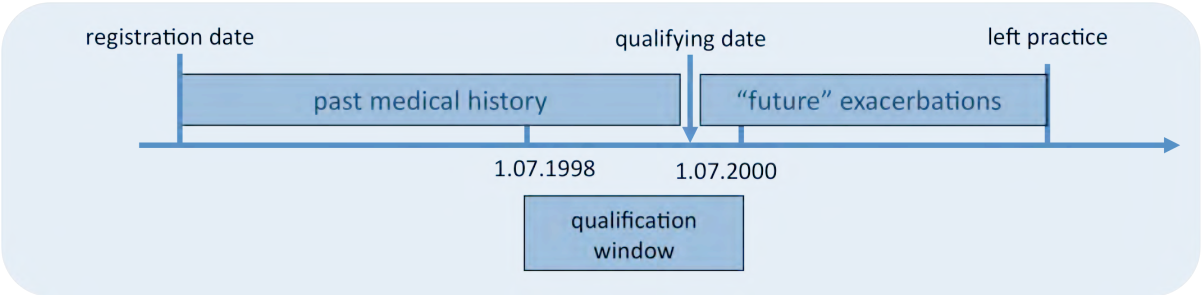
reference	country	n asthma	findings
Hodous 1983(78)	US	17 (mild obstruction) 10 (moderate obstruction)	Cardiopulmonary and subjective responses to short-term sub-maximal exercise with added resistance in those with airflow obstruction similar are similar to those in normal persons
Harber 2010(79)	US	42 (COPD n=14 rhinitis n=17)	Mild disease only. In a comparison of a filtered facepiece with a cartridge half-face mask, small impacts on ventilatory function, of doubtful clinical significance, were related to the presence of asthma. The different effects of the two respirator types varied by disease

Part B: the trajectory of asthma exacerbations in the general population

As expected, we found no useful, published information on this subject. What is available is derived from studies of patients under hospital care, of children or of those enrolled in therapeutic trials. It was necessary, then, to generate primary evidence. Our summary findings are reported here; a full report for publication in 2012 is in preparation.

We used general practice records collated by The Health Improvement Network (THIN) covering about 2.5m registered persons or approximately 3.5% of the UK population. Ethical approval was sought and granted and the relevant data extracted for us by colleagues at the University of Nottingham. We requested the full records of all adults aged 16-40 years old who had been prescribed, at any date between 01.07.1998 and 01.07.2000 (the 'qualifying window'), one or more drugs used in the treatment of asthma (Figure 4): the qualifying date was the first such prescription in the qualifying window.

Figure 4 Scheme for data extraction from THIN records



Of those who fulfilled this criterion almost 75,000 had records of care for one or more years prior to and after their qualifying date.

During this process we defined three types of 'asthma exacerbation' that could validly be identified from the information available from THIN:

- *'hospital exacerbations'* were those asthma events that resulted in attendance at A/E or hospital admission
- *'GP exacerbations'* were asthma events that took place during an out-of-hours consultation or that were suggestive (from the THIN coding) of an acute exacerbation
- *'prednisolone exacerbations'* were those that resulted in a new prescription of prednisolone within 30 days of a prescription for a 'reliever' asthma treatment.

Analysis was carried out by Stephanie MacNeill, biostatistician at the Department of Occupational and Environmental Medicine at Imperial College (NHLI) using Stata software. We enumerated, by year of follow-up, the first exacerbation of each type for each patient and related these to age, sex, and index of asthma severity and the available history prior to qualification.

Findings

Overall incidence rates of exacerbation are summarised in table 10. The annual incidence of an exacerbation requiring attendance at or admission to hospital was low (2-3 per 1000) and, as expected, lower than those needing out-of-hours GP consultation or acute treatment with prednisolone.

Table 10 cumulative annual incidence rates of asthma exacerbations (THIN)

	Cumulative incidence (%)				
years after qualification:	1st	2nd	3rd	4th	5th
hospital/A&E	0.3	0.6	0.8	1.0	1.2
out-of-hours GP	2.4	3.8	5.1	6.5	8.1
prednisolone	8.3	11.8	14.7	17.3	19.9

Table 11relates the incidence of exacerbations in the post-qualification year by age, sex and a crude index of asthma severity (prescription for inhaled corticosteroids at qualification). Rates of each exacerbation type were higher in women and in those whose asthma required also treatment with an inhaled steroid.

Table 11 incidence (%) of exacerbations in the post-qualification year by age, sex and an index of asthma severity

	sex		age			Ics*	
in 12m post qualification:	m	f	16-24	25-34	35-40	no	yes
hospital/A&E	0.2	0.4	0.4	0.3	0.3	0.3	0.5
out-of-hours GP	2.1	2.6	2.4	2.5	2.1	1.7	3.9
prednisolone	7.1	9.2	6.8	8.6	9.9	5.8	14.3

* prescription for inhaled corticosteroids at qualification

In table 12, the incidence of exacerbations in the year after qualification is related to three measures of preceding asthma control. For each type of exacerbation, rates were systematically higher in those with more frequent prescriptions for inhaled steroids or similar exacerbations prior to qualification; and higher in those with more recent exacerbations. Almost half of those who had received three or more acute prescriptions for prednisolone within the past five years required at least one more in the year following qualification.

Table 12 incidence (%) of exacerbations in the year after qualification by measures of preceding asthma control

	# ics* in past year				# events past 5 years				years since last exacerbation			
in 12m post-qualification:	0	1	2	3+	0	1	2	3+	<1	1-2	2-3	3+
hospital/A&E	0.2	0.3	0.5	1.0	0.3	3.3	17.5	18.8	11.8	8.8	6.5	1.9
out-of-hours GP	1.6	3.9	2.6	5.2	1.7	9.0	12.5	30.8	20.5	11.0	9.2	5.8
Prednisolone	6.5	8.2	9.6	15.9	5.9	15.3	24.8	49.5	39.5	22.3	16.2	13.6

* prescription for inhaled corticosteroids at qualification

Having established consistent, relative increases in risk among those with a past history of exacerbations we examined more closely the pattern of absolute risk in the full study population. The findings are displayed in Figure 5 (for exacerbations requiring hospital care) and Figure 6 (exacerbations requiring treatment with prednisolone). The findings for exacerbation requiring out-of-hours GP management were very similar. In both Figures and in each of the five years after

qualification the pattern is one of new incidence; that is, the majority of those affected by exacerbations in each year of follow up were *not* so affected in any of the preceding years.

Figure 5 Schematic depiction of incident exacerbations requiring hospital care in the each of the five years following qualification. Each filled (blue) circle represents an individual patient with an exacerbation.

Figure 6 Schematic depiction of incident exacerbations requiring acute treatment with prednisolone in each of the five years following qualification. Each filled (blue) circle represents an individual patient with an exacerbation.

Discussion

With a prevalence of between 5% and 10%, asthma is common in the UK adult population; a history of asthma is commoner still (25%). Many occupational health providers, however, will not recognise these high figures in job applicants or new recruits. In respect of work that involves exposure to occupational asthmagens there is little if any evidence that individuals with asthma make employment choices based on their disease. In contrast, it seems likely, even if it has not been tested, that they may, on average, make more subtle decisions based on their understanding of the requirements of certain jobs (for example, the physical exertion they entail) or their perceptions of the attitudes of some employers; and that these decisions may in turn relate to their personal experience of their disease. Thus the practice of providers of occupational health services may not reflect either the true prevalence or the full spectrum of asthma in the community.

Nonetheless almost all providers will need to consider the employment and placement of applicants with asthma and will need to do so increasingly as the children of the high-incidence era (1970-2000) seek employment. In this cohort there will be high frequencies of both current and past asthma. Those offering occupational health advice need to establish carefully the particular requirements of the job in question and be sure that, where appropriate, the distinction is made between 'have you ever had asthma' and 'do you have asthma now'; and that the implications of a positive response to each are clearly appreciated. Around two thirds of those with asthma in childhood will experience a remission in their teens; but in about a third of these the disease will return before the age of 30. This incidence is higher than that of true adult-onset asthma. 'Relapsed' asthma tends to be very mild and certainly milder, on average, than disease which has persisted from childhood.

It is plain that a diagnosis of 'asthma' covers both a spectrum of severities and a variety of phenotypes. While the prevalence of the condition is high among professional athletes, others (albeit few) with the disease are severely disabled by breathlessness. While infection is the most commonly reported trigger of an 'attack', many individuals with asthma will report that their difficulties are predictably provoked by exposures to, for example, allergen (commonly those from pets or pollens) or exercise. Indeed, predictability is a hallmark of most asthma since the intra-individual variability of the disease is far lower than its inter-individual variability.

Two conclusions follow from these observations. First, it is unhelpful to consider all asthma as one. This distinction is implicit in recent legislation on equality but in the past has been made too rarely in occupational health policies and, particularly, in published research. Second, the best predictor of the future behaviour of asthma is the past – and in particular the recent past. This pattern is familiar to respiratory clinicians (and of course to most patients) and was apparent in our examination of the trajectory of the disease in patients registered with UK general practices. Thus we found a close relationship between the *relative* risk of disease exacerbations and markers of both disease severity and past experiences, particularly those in the recent past. Importantly however, most incident exacerbations were *not* associated in these ways and most of the absolute burden appears to lie with individuals whose exacerbations could not be thus predicted. This pattern will be familiar to occupational health providers since it is remarkably similar to that observed with musculoskeletal injuries at work and, indeed, with sickness absence from all causes.

Given the above, it is clear that the needs of each new or prospective employee with asthma (current or past) should be considered individually.The necessary focus is likely to be on the severity and stability of an individual's disease and on the impact these will have on their performance in a particular job. Fortunately, most of the necessary information can be collected through a simple history of current and recent symptoms, recent exacerbations and current treatment use. The last of these is commonly used as a measure of asthma severity although this may not be entirely appropriate in an occupational health setting and a distinction between treatment 'use' and treatment 'requirement' needs to be made. Most UK adults with asthma have disease at BTS/SIGN stage 1 or 2(80), requiring only an as-needed ß$_2$ agonist (stage 1) or a regular inhaled corticosteroid at low doses (stage 2). In many workplaces good control at stage 2 may be preferable to incomplete control at stage 1. Beyond a measured history, little seems to be gained by the routine use of 'objective' tests in determining likely performance at work. Spirometry will detect airflow obstruction but is often normal in young adults with well-controlled asthma and in any case is a poor predictor of functional ability. Measurement of residual NSBHR in those whose childhood asthma has remitted has limited utility in predicting a relapse

Among many, three gaps in the published literature stand out:

1. We do not know whether those with asthma (or with asthma in the past) are, as a direct result, at increased risk of respiratory sensitisation when exposed to workplace asthmagens. The available information on the topic fails to distinguish 'asthma' from 'atopy' which frequently accompanies asthma and which is known to increase the risk of sensitisation to high molecular mass (at least) agents. Nor, of course, do we know whether more severe asthma carries a greater risk than milder asthma. Logically, any exclusion of individuals with asthma from work with respiratory sensitising agents ought to be extended to those with (non-asthmatic) atopy, some 15%-40% of the UK adult population depending on how the atopic trait is defined.

   A related matter is the practice in some settings of excluding employees with current asthma from work with respiratory sensitising agents (such as in a bakery) on the grounds that if they were to develop occupational asthma it would be difficult to distinguish this from their constitutional disease. This seems inappropriate except in some individuals with severe asthma prior to employment for whom the development of a further type of asthma would be seriously disabling. In most other cases a distinction between occupational and pre-existing asthma can usually be achieved, even if it requires specialist diagnostic input; in any case it seems unfair to abrogate responsibility for a medical intricacy to the employee.
2. We do not know, in any meaningful detail, the extent and implications of any interaction between asthma and respiratory protective wear, a question that is open to relatively simple investigation. It seems reasonable to take the view that for most individuals with well-controlled asthma the use of most forms of simple equipment will have no important effect on performance. More difficult is the issue of full-face devices with a self-contained or external supply of air, especially where these are worn under conditions of heavy physical exertion as might be expected, for example, in firefighting. The chief determinant of performance under these conditions is likely to be cardiorespiratory and musculoskeletal fitness and those with mild or well-controlled asthma who are otherwise fit are unlikely to perform poorly. It is worth noting here that athletes with exercise-induced asthma are sometimes advised to wear simple, half-face masks to increase the moisture of the air they are breathing during exercise.

3. We do not know in any useful sense how employees with asthma fare in particular workplaces where there is exposure to potential respiratory irritants. The literature on work-exacerbated asthma reviewed above is relatively extensive but just one study was confined to a single occupation (electronic assembly), the remainder covering populations with a wide variety of jobs specified only vaguely, if at all, by reference to 'dust' or 'chemical agents' or 'abnormal temperatures' and the like. Leaving aside its validity, this sort of non-specific information is of little value to the occupational health practitioner. As above, the issue in particular workforces (for example bakeries, firefighting, the Armed Forces) is readily amenable to investigation; and in the meantime, it is likely that most individuals with mild or well-controlled asthma who are otherwise fit will have little difficulty.

Finally, we recognise that not all relevant questions have been answered to our satisfaction. This is largely because the research evidence base is incomplete and in some areas disappointingly so; a number of suggestions as to how it may be enhanced have been made.The information provided above is not intended to be prescriptive. Rather, it is offered as a generic data source to those occupational health practitioners who wish to develop their practice and policies in relation to new recruits with asthma.

Subsequent steps.

In 2012 this report will be presented to the working panel and re-drafted accordingly. An agreed final version will be circulated more widely for consultation before publication.

Appendix

Panel membership and affiliations

Name	Affiliation/representation
Pippa Clark	Occupational health advisor (SME)
Paul Cullinan	Respiratory specialist, Royal Brompton Hospital and Imperial College, London
David Denison	Respiratory specialist, Royal Brompton Hospital and Imperial College, London
Bernie Graneek	Occupational Physician (NHS); Association of National Health Service Occupational Physicians
Angela Jones	Research fellow, Royal Brompton Hospital and Imperial College, London
James Mackie	Occupational Physician (external provider); COPA
Ira Madan	Occupational Physician; NHS-plus;Occupational Health Clinical Effectiveness Unit
Rob Miguel	Trades Union Congress
Paul Nicholson	Occupational Physician (large employers); Society of Occupational Medicine; Faculty of Occupational Medicine
Sam Phillips	Occupational Physician (external provider); Association of Local Authority Medical Advisors
Diane Romano-Woodward	Occupational Health Advisor; Association of Occupational Health Nurse Practitioners, UK
Chris Sharp	Occupational Physician (SME)
Helen Smith	Health and Safety Executive
Alan Swann	Occupational Physician (university); Higher Education Occupational Physicians
Jenny Versnel	lay representative (Asthma UK)
Charles Wilcox	Occupational Physician (armed forces)

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