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Do long periods off work in peak expiratory flow monitoring improve the sensitivity of occupational asthma diagnosis?

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ABSTRACT

Introduction Serial peak expiratory flow (PEF) monitoring is a useful confirmatory test for occupational asthma diagnosis. As weekends off work may not be long enough for PEF records to recover, this study investigated whether including longer periods off work in PEF monitoring improves the sensitivity of occupational asthma diagnosis.

Methods Serial PEF measurements from workers with occupational asthma and from workers not at work during their PEF record, containing minimum data amounts and at least one rest period with ≥ 7 consecutive days off work, were analysed. Diagnostic sensitivity and specificity of the area between the curves (ABC) score from waking time and Oasys score for occupational asthma were calculated for each record by including only consecutive rest days 1–3 in any rest period, including only consecutive rest days from day 4 onwards in any rest period or including all available data.

Results Analysing all available off work data (including periods away from work of ≥ 7 days) increased the mean ABC score by 17% from 35.1 to 41.0 l/min/h (meaning a larger difference between rest and work day PEF values) ($p=0.331$) and the Oasys score from 3.2 to 3.3 ($p=0.588$). It improved the sensitivity of the ABC score for an occupational asthma diagnosis from 73% to 80% while maintaining specificity at 96%. The effect on the Oasys score using discriminant analysis was small (sensitivity changed from 85% to 88%).

Conclusions Sensitivity of PEF monitoring using the ABC score for the diagnosis of occupational asthma can be improved by having a longer period off work.

INTRODUCTION

Serial measurements of peak expiratory flow (PEF) remain the most cost effective confirmatory test in the diagnosis of occupational asthma and are recommended by several guidelines as an important initial confirmatory method, especially in occupational health, primary care and outpatient clinics.^{1–3} Workers performing serial PEF measurements will often do so at a time when they only have weekends off work. However, recovery of PEF may take much longer than 3 days in some workers. Inclusion of longer periods off work may therefore improve the sensitivity of an occupational asthma diagnosis. The potential effect of such longer periods off work on the sensitivity and specificity of PEF monitoring has been unknown. Some specialist centres have encouraged workers to complete PEF measure-

What this paper adds

- ▶ Serial peak expiratory flow (PEF) measurements are an important confirmatory test for occupational asthma, but it is not currently known whether sensitivity can be improved by including a longer period off work within the PEF monitoring period.
- ▶ A greater difference between work day and rest day PEF (illustrated here by the increase in the area between curves (ABC) score from the Oasys program) can be achieved in those with occupational asthma by including a longer period off work.
- ▶ The sensitivity of occupational asthma diagnosis using the ABC score is increased by 7% by including a longer period off work, which means more workers with occupational asthma will be diagnosed using this method.
- ▶ If serial PEF monitoring containing 3 or less consecutive rest days in any rest period fails to show a work-related pattern even though symptoms are suggestive of occupational asthma, it is important to repeat measurements with at least 7 consecutive rest days within the monitoring period.

ments while having at least 1 week off work,⁴ but in many countries such as the UK, this can usually only be achieved during workers' annual leave holidays or during factory shutdown periods without taking unpaid leave, taking the measurements in a longer period off work an important consideration for the worker.

Serial PEF measurements can be analysed by computer based systems such as Oasys.⁵ This system removes the problems encountered when there is variation in expert interpretations of the PEF patterns, which may lead to inconsistencies in diagnosis of occupational asthma.⁶ Oasys computes several outputs, one of which utilises a plot of the maximum, mean and minimum daily PEF values and produces an Oasys score based on comparing each work–rest–work period and rest–work–rest period (complexes). This has been shown to have a sensitivity of 75% and specificity of 94% for the diagnosis of occupational asthma when using a cut-off score of ≥ 2.51 .^{5,7} The updated version of the Oasys program produces a new score from the

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plot of 2-hourly mean PEF measurements plotted separately for work and rest day curves. This score is known as the ABC score and has been shown to have a sensitivity of 69% and specificity of 100% using a cut-off of ≥ 15 l/min/h.⁸ It requires shorter records (with more readings per day) than needed to maintain a similar sensitivity and specificity using the Oasys score.^{8–10} The ABC score is a very suitable method for analysing PEF measurements carried out for 2 weeks at work and 2 weeks away from work as is sometimes recommended,¹ whereas the Oasys score is often unsuitable in this situation. The initial analysis to identify the cut-off point for the ABC score only considered records with ≤ 3 consecutive days off work in any rest period. The ABC plot can be generated according to either clock time or time from waking, but both of these ABC indices had a similar sensitivity and specificity; therefore, only the ABC score by waking time is considered here. It is not currently known whether having a longer period off work increases the sensitivity or reduces the specificity of the occupational asthma diagnosis based on the ABC score.

AIM

The aim of this study was to assess whether serial PEF measurements with only periods of ≤ 3 consecutive days off work in any rest period analysed, are less sensitive and/or more

specific compared to serial PEF measurements that include only consecutive rest days from day 4 onwards in the analysis for the diagnosis of occupational asthma.

METHODS

Study population

A total of 133 serial PEF records from workers with ≥ 7 consecutive days off work diagnosed as having occupational asthma based on independent clinical investigations, that is specific bronchial challenge test, fourfold change in methacholine reactivity or positive specific IgE combined with a strong relevant medical history (referred to as the occupational asthma positive group) were available from patients investigated at the Birmingham Chest Clinic, UK, between 1980 and 2007 after these patients had been referred for suspected occupational asthma. Overall, 117 records from patients diagnosed as having asthma/occupational asthma who were not working during their serial PEF measurement period (to ensure that these records could not demonstrate work-related changes in PEF) (referred to as the occupational asthma negative group) were available from the same time period.⁸ Ethics committee approval was obtained from the Birmingham East, North and Solihull committee; patient consent was not required for this study.

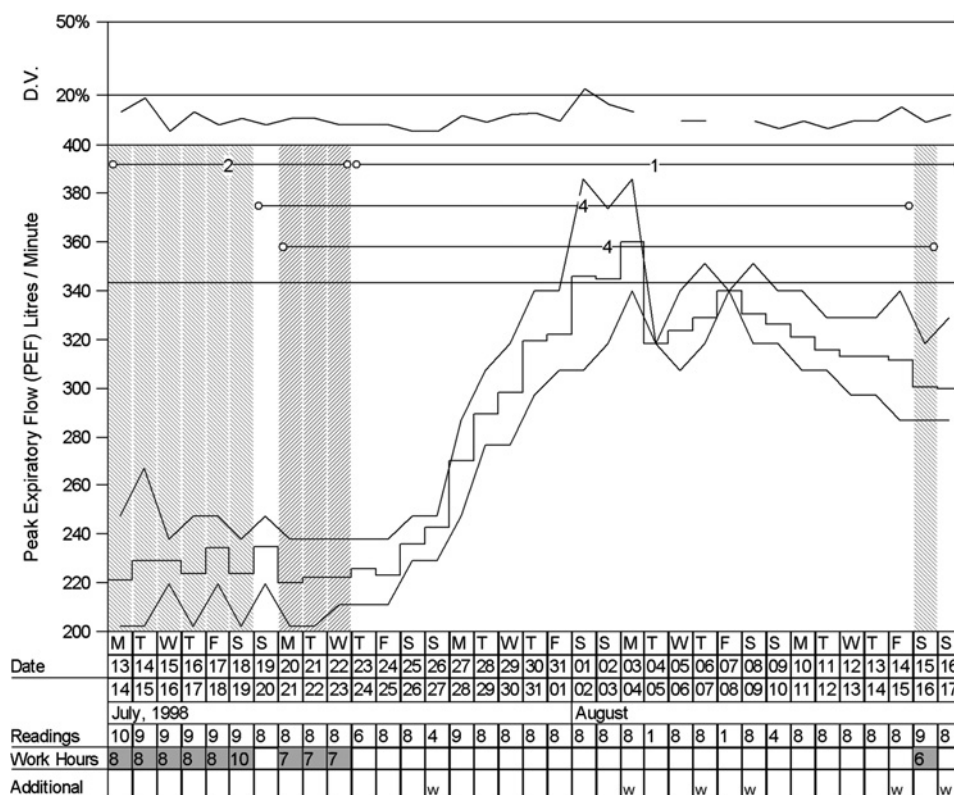


Figure 1 Maximum, mean and minimum peak expiratory flow (PEF) plotted by the Oasys program from an occupational asthma positive worker exposed to cobalt. The top part of the chart shows the diurnal variation (DV) for each day. The middle of the chart shows the maximum, mean and minimum peak flow for each day. The black continuous line is the mean PEF, the upper line the maximum PEF and the lower the minimum PEF for each day. The work periods are the shaded areas (diagonal back slash bars are morning shifts, diagonal forward slash bars are afternoon shifts) and the rest periods are blank areas. The horizontal lines containing numbers in this part of the chart are scores for the work–rest–work and rest–work–rest complexes (four complexes in total in this record). The horizontal line spanning the record indicates the predicted PEF for this worker of 343 l/min. The bottom of the record shows the days and dates of the record. When analysing this record using consecutive rest days 1–3 only, days from 26 July to 14 August would be removed. For analysis using consecutive rest days from day 4 onwards in any rest period, 19 July and 23 to 25 July would be removed. The Oasys score of this record is 2.86 (probable occupational asthma). Using only rest days 1–3, the score changes to 1.80 (interpreted as unlikely to be occupational asthma) and using from consecutive rest day 4 onwards, the score becomes 4.0 (meaning definite occupational asthma). This worker had a fourfold change in methacholine reactivity between when exposed and when away from exposure for at least 1 week.

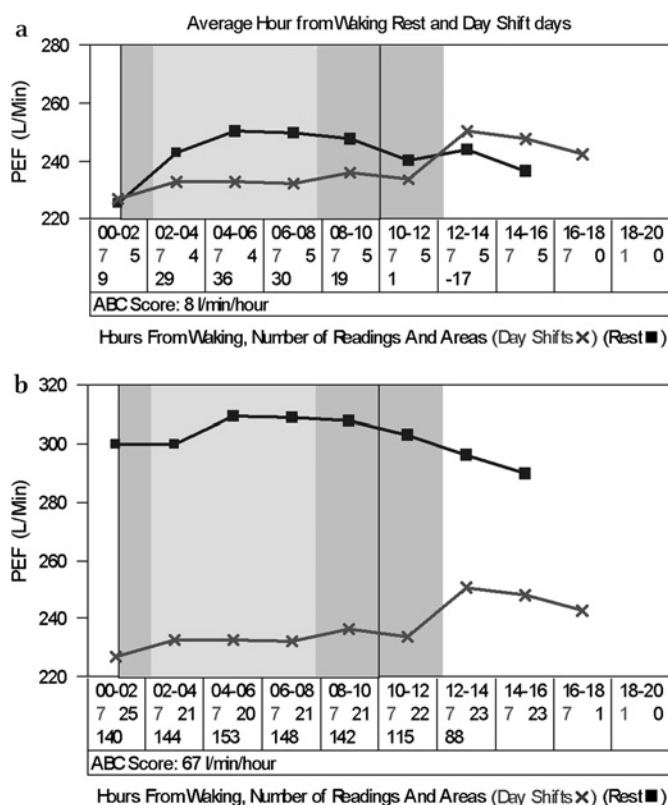


Figure 2 a) A 2-hourly plot of the average peak expiratory flow (PEF) on rest days and work days analysed by the Oasys program for the same worker by analysing rest days 1–3 only. Mean PEF measurements taken at the following times: 0 and 2, >2–4, >4–6 h and so on from the waking time are plotted based on all work days and all rest days. The black upper line (square markers) shows the average peak flow for rest days by 2 h segments from 0 to 24 h from waking. The grey lower line (cross markers) shows the same for work days. The grey area shows information about the times of starting and stopping work (mode, minimum and maximum). The legend shows the start and end of the 2 h time segments, the number of readings used to calculate the work and rest day average PEFs, the area between the rest and work day PEF curves (ABC) on the graph for each time segment and the ABC score. This record gives an ABC score of 8 l/min/h (interpreted as not occupational asthma). (b) The same worker's 2-hourly plot analysed using all available data. The ABC score is now 67 l/min/h (interpreted as definite occupational asthma). Using consecutive rest days from day 4 onwards gives an ABC score of 83 l/min/h (definite occupational asthma).

Data analysis

To enable analysis by the Oasys program, PEF measurements in occupational asthma negative records (recorded while the workers were not being exposed to any occupational agents) made between 09:00 h and 17:00 h from Monday to Friday were analysed as 'at work' and compared with readings on Saturday and Sunday which were analysed as 'off work'. A week off work was chosen for each record of occupational asthma negatives using a random number generator from 1 to 3 (corresponding to the working weeks in the record) for the analyses of all measurements (including a long period off work) and from consecutive rest day 4 onwards only.

Occupational asthma positive and negative records were excluded if they contained less than previously determined minimum data quantity for each score.^{9 10} For the Oasys score, minimum data requirements were ≥ 3 complexes (work–rest–work or rest–work–rest periods) with ≥ 3

consecutive work days in any work period and ≥ 4 readings per day.⁹ Only records with > 8 day shifts were considered for the Oasys score to be comparable with minimum data requirements for the ABC score. For the ABC score, the minimum data quantity criteria were found to be dependent on the number of readings per day the record contained.¹⁰ Therefore, records with a mean number of ≥ 7.5 readings per day required 8 work days and 3 rest days, those with a mean of ≥ 6.5 and < 7.5 readings per day required ≥ 15 work days and 5 rest days and those with ≥ 4.5 but < 6.5 per day required ≥ 15 work days and 8 rest days to maintain sensitivity above 60% and specificity above 90%.

PEF records performed during respiratory tract infections and changes in asthma treatment were excluded as these could have confounded the records. Only one record from any one worker was used in each set to ensure independency of observations.

Only scores for day shifts were considered for the ABC score as these are the only shift type that have been validated previously. Records were analysed in three ways. The first calculated scores for the records (ABC score and Oasys score) including rest days 1–3 only and removing consecutive rest days from day 4 onwards in any rest period (figures 1 and 2a). The second removed rest days 1–3 in any rest period and only analysed consecutive rest days from day 4 onwards (figure 1). The third analysed all available data (including the long period off work) (figures 1 and 2b). The sensitivity and specificity at a cut-off of ≥ 2.51 for the Oasys score and ≥ 15 l/min/h for the ABC score were calculated for each analysis and compared.

Statistical methods

SPSS v 15 was used for all statistical analyses. The χ^2 test was used to investigate differences in occupational asthma negative and positive groups with categorical data. Data were not normally distributed. Where outcome variables were expressed as continuous data and the predictors were categorical, the Mann–Whitney U test or Kruskal–Wallis test was used. An analysis of covariance was used when controlling for confounding factors. As the records of each individual were analysed in three ways, each individual served as his/her own control in the analysis comparing different durations of rest periods on diagnostic PEF scores. Receiver operator characteristic (ROC) curves were used to determine the sensitivity and specificity of the different scores.

RESULTS

A total of 48 occupational asthma positive records and 104 occupational asthma negative records fulfilled all criteria

Table 1 Demographics of the study population

	Occupational asthma positive (n=48)	Occupational asthma negative (n=104)	p Value
Mean age (SD)	44 (10.2)	51 (9.3)	<0.001*
% Males	69.6	61.5	0.345†
% Atopics	42.9	51.1	0.376†
% Current smokers	14.3	20.6	0.308†
% Methacholine reactive	55.3	42.7	0.199†
% Taking ICS	64.1	84.3	0.011†
Mean FEV ₁ % predicted (SD)	86.4 (26.8)	80.6 (24.3)	0.224*
Mean diurnal PEF variation (SD)	22.2 (13.5)	19.7 (13.2)	0.200*

*Analysed using Mann–Whitney U test.

†Analysed using χ^2 test.

ICS, inhaled corticosteroids; PEF, peak expiratory flow.

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Table 2 Differences between occupational asthma (OA) negative and positive workers using records with and without long periods (≥ 7 consecutive days) off work

	Mean ABC score (SD)			Mean Oasys score (SD)		
	OA+ n=45	OA- n=93	p Value	OA+ n=36	OA- n=95	p Value
All available measurements (including long period off work)	41.0 (33.5)	0.4 (8.6)	<0.001	3.3 (0.7)	1.8 (0.6)	<0.001
≤ 3 Consecutive rest days only in any rest period analysed	35.1 (31.2)	0.4 (8.1)	<0.001	3.2 (0.7)	1.9 (0.6)	<0.001
p Value (all rest days compared to ≤ 3 consecutive rest days)	0.331	0.774	NA	0.588	0.612	NA
Consecutive rest days from day 4 onwards in any rest period analysed	48.5 (42.3)	0.3 (12.0)	<0.001	NA	NA	NA
p Value (comparison of ≤ 3 consecutive rest days to consecutive rest day 4 onwards)	0.132	0.442	NA	NA	NA	NA

including data quantity requirements for either score. For the ABC score, 45 occupational asthma positive records and 93 occupational asthma negative records satisfied all criteria and minimum data quantity, and for the Oasys score, 36 occupational asthma positive records and 95 occupational asthma negative records satisfied all criteria, including data quantity. Overall, 64.6% (31/48) of the occupational asthma positive workers were independently diagnosed through specific inhalation challenge testing, 6.3% by a fourfold change in methacholine reactivity (between periods at and away from work for at least 1 week) and 29.2% by specific IgE and a typical symptom history. The majority of workers were exposed to low molecular weight agents (79.2%).

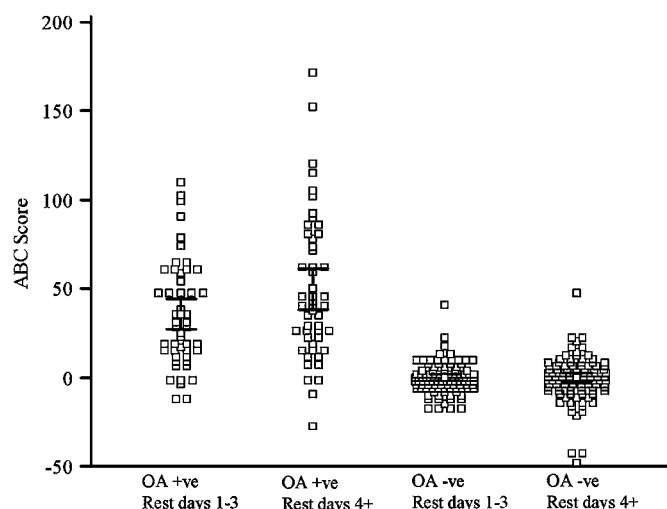
Occupational asthma negative workers were somewhat older than occupational asthma positive workers ($p<0.001$) and more were taking inhaled corticosteroids ($p=0.011$). There were no other significant differences in patient demographics between the occupational asthma positive and negative groups (table 1).

Both the ABC score and Oasys score were significantly higher in occupational asthma positive workers compared with occupational asthma negative workers when using all amounts of data (table 2). Although the ABC score increased by 17% (showing a bigger difference between work and rest day PEF values) when

the long off period was included or by 39% when only consecutive rest days from day 4 onwards were analysed, the differences were not statistically significant. ABC scores are represented graphically when analysing rest days 1–3 and consecutive rest day 4 onwards in figure 3. The ABC score was useful for diagnosing occupational asthma when the analysis was restricted to including consecutive rest days from day 4 onwards, but due to a lack of a sufficient number of complexes (work–rest–work or rest–work–rest periods) Oasys scores could not be computed for most of the records in this latter analysis.

Table 3 shows the sensitivity and specificity of the Oasys score and the ABC score with respect to occupational asthma diagnosis (Oasys score ≥ 2.51 ; ABC score ≥ 15 l/min/h) for the three types of PEF record analyses. Analysis including longer periods off work (≥ 7 consecutive rest days) improved the sensitivity of the ABC score to 80% compared to the analysis that removed rest periods with ≥ 4 consecutive rest days, showing a sensitivity of 73%. Specificity remained high at 96% when all data were used. No records that scored positively using rest days 1–3 became negative when including the long period off work.

Additional analyses were undertaken to investigate if the ABC score differs between occupational asthma positives with different levels of mean PEF, with the hypothesis that those with a low mean PEF level might need a longer period off work to recover. Thus, those with a mean per cent predicted PEF of $\geq 60\%$, 70%, 80% and 100% predicted were compared with those with PEF $<60\%$, 70%, 80% and 100% predicted, analysing from consecutive rest day 4 onwards only. Age, use of inhaled corticosteroids and smoking were controlled for by an analysis of covariance. There were no significant differences when using 60%, 70%, 80% or 100% as a cut-off point ($p=0.885$, $p=0.515$, $p=0.472$, $p=0.744$), suggesting that the influence of the duration of the rest period is not dependent on PEF level.

**Figure 3** A scatter plot of ABC (by time from waking) scores grouped by the analysis based on rest days 1–3 in any rest period and based on consecutive rest days from day 4 onwards in any rest period for the occupational asthma negative and positive records. The mean and 95% CIs are also indicated on the plot.**Table 3** Sensitivity and specificity of Oasys score and ABC score for occupational asthma in records with and without long periods off work

	ABC score		Oasys score	
	% Sensitivity n=45	% Specificity n=93	% Sensitivity n=36	% Specificity n=95
All available measurements	80	96	88	86
≤ 3 Consecutive rest days only	73	98	85	90
Consecutive rest days from day 4 onwards only	78	95	NA	NA

DISCUSSION

We have shown that the ABC PEF score increases from 35.1 to 41.0 l/min/h by including a long period off work in the monitoring period, but this was not a statistically significant improvement ($p=0.331$). The difference in the score between occupational asthma positive workers and negative workers also increases. The Oasys score increased slightly when analysing all data including a long period off work, but not significantly so. This smaller effect on the Oasys score is likely to be explained by the way this score is computed using discriminant analysis^{5 7} which does not require a particular amount of increase in the difference of PEF between work days and rest days. In contrast, the ABC score computes the difference in litres per minute per hour between the mean work and rest day PEF curves plotted in 2-hourly periods (meaning 2-hourly mean PEF values)⁸ and requires a difference of at least 15 l/min/h to achieve a sensitivity of 69% and specificity of 100% for the diagnosis of occupational asthma.

Sensitivity was improved for both scores in all analyses in this group of workers compared to previously published data,^{5 8} although specificity was slightly compromised. Including longer periods off work in the PEF record analysis improved the sensitivity of the ABC score for an occupational asthma diagnosis from 73% to 80%. Specificity was robust, being >95% for the ABC score even when confining the rest day plot to start at consecutive day 4 away from work. Inclusion of longer rest periods had a lesser effect on the sensitivity of the Oasys score. The ABC score was more useful than the Oasys score in situations where there were fewer periods at and away from work. This is due to the Oasys score needing ≥ 3 complexes (rest–work–rest periods or work–rest–work periods) to meet minimum data quantity requirements for a good sensitivity and specificity. It therefore made the analysis of consecutive rest days from 4 onwards inapplicable to the Oasys score as 33 records meeting this minimum data quantity requirement for the Oasys score contained only one rest period with at least 7 consecutive rest days, leading to only one scorable complex. The ABC score does not have this minimum data requirement and can be used in situations where records have been completed for 2 weeks at work and 2 weeks away from work without compromising the sensitivity and specificity of this score.

We found no differences in the ABC score for workers who had a mean PEF per cent predicted $\geq 70\%$ and those with a reduced PEF per cent predicted of $<70\%$ ($p=0.515$). The workers with $\geq 70\%$ predicted PEF had the largest ABC scores (49 vs 38 l/min/h) suggesting that the influence of the duration of the rest period on the ABC PEF score is not restricted to workers with a low mean PEF level.

Although in many countries, such as the UK, PEF measurements during a week off work can only be achieved during workers' holidays, factory shutdown periods or by the worker taking unpaid leave, the extra seven cases identified with this extended time off work may be worth the effort if occupational asthma is not diagnosed from recordings including weekends off alone.

Validity of methods and limitations of the study

We have utilised PEF records of workers whose occupational asthma was confirmed mainly through specific inhalation challenge testing (considered to be the gold standard for occupational asthma diagnosis)³ but have also included workers who had at least fourfold change in non-specific reactivity between when exposed and after at least a week away from exposure, and workers with a positive specific IgE to a relevant occupational agent in combination with a strong

typical work-related symptom history. Some may not agree with using this latter group, but we found no difference in their ABC or Oasys scores compared to the group with specific inhalation challenge test positive occupational asthma ($p=0.741$ and $p=0.582$, respectively). For this reason, we believe that this confirmation method can be used for the purposes of our study. Inclusion of this group extends the spectrum of workers to include the group for whom specific challenge tests are usually thought unnecessary and whose diagnosis of occupational asthma is clearly unrelated to their PEF recording at the time of diagnosis.

Not all of our occupational asthma positive and negative workers had non-specific reactivity outside the normal range. Some centres consider non-specific reactivity to be a requirement for the diagnosis of asthma, but all our occupational asthma positive workers showed a latent interval before symptoms started and were exposed to levels of the agent that were below the level inducing irritant effects. In this study, 13/24 workers who had positive specific challenge tests had normal reactivity. Others have found similar results with regard to the relationship between specific and non-specific reactivity.^{11–14}

Although the ABC score increased by including the long period off work, the difference was not significant. A power calculation revealed the requirement for a 28.1 l/min/h difference between analyses to show significance at 80% power.

Synthesis with previous knowledge

To our knowledge, no other studies have compared PEF records with long periods off work to those with only weekends or up to 3 consecutive days off at any one time. Some studies have requested that workers complete records for at least 2 weeks at work and 2 weeks away from work^{4 15 16} with the idea that this could improve sensitivity to detect occupational asthma. For some workers, it seems to be important to investigate whether it takes longer than 3 days away from exposure for their PEF to recover, as we have shown here that such longer rest periods increase the sensitivity of the ABC PEF score, while maintaining high specificity. In this study, workers with a lower PEF level as per cent of predicted did not require a longer period off work to elicit a positive ABC score compared to those with normal PEF levels, so we were not able to identify any one group of workers whose diagnostics would benefit from such longer rest period.

CONCLUSION

The ABC score computed by the Oasys program to diagnose occupational asthma can be increased in those with occupational asthma by including a long period off work while monitoring PEF for diagnostic purposes. The sensitivity of the peak flow analysis by using the ABC score can also be improved in this way, identifying seven more cases per 100 with independently diagnosed occupational asthma. Specificity was unchanged with inclusion of a long period off work.

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Competing interests None.

Ethics approval This study was conducted with the approval of the Birmingham East, North and Solihull committee.

Contributors All authors were involved in the conception and design of this project. VM, MJ, CB and PSB were involved in the analysis and interpretation of data, with some contribution from AR and CP as well. VM drafted the article and all authors revised it critically and approved the final version to be published.

Provenance and peer review Not commissioned; externally peer reviewed.

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