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A study of how workers with occupational asthma breathe out forcefully and quickly (peak expiratory flow)

Submission date 21/04/2023	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 31/05/2023	**Overall study status** Ongoing	
Last Edited 03/07/2024	**Condition category** Respiratory	

Plain English summary of protocol

Background and study aims

This is a research project which aims to improve the quality of the Oasys peak expiratory flow (PEF) analysis system used for the diagnosis of occupational asthma. As the results should be generalizable to any patient with work-related asthma, the project comes within the scope of ethical review. It is a project using existing data only and no new patient contacts are involved. Workers with possible occupational asthma have kept frequent measurements of their breathing using PEF meters over several weeks at work and at home as part of their investigation to confirm their diagnosis, from 1990 onwards. We wish to use these existing PEF records to see if different exposures at work cause different patterns of PEF response. This would include comparing exposures to agents which are thought to act as irritants (such as chlorine-based cleaning agents, mild steel welding fume and diesel exhaust), with those where hypersensitivity is likely (such as flour, isocyanates and acrylates). We will aim to see if different groups of causative agent, grouped by their molecular size, result in different patterns of response. We also wish to identify how big a difference there has to be in PEF to identify a specific cause when a worker is exposed to more than one possible cause. To do this we will use data from days with predominantly one rather than the other exposure. We would also like to compare existing self-reported symptom questionnaire responses with the results from serial PEF records.

Who can participate?

Records from all workers with possible occupational asthma who have kept frequent measurements of their breathing using peak flow meters over several weeks at work and at home as part of their investigation to confirm their diagnosis and who have at least one positive score for occupational asthma, will be identified from the Oasys database on NHS trust computers (derived from- and part of the electronic patient record) from 1990 to the present day

What does the study involve?

We will only use existing data on exposures contained in patients' medical records, as well as any

other confirmatory tests already done such as blood tests for specific IgE or the results of specific inhalation tests. No new data will be collected and no new diagnoses will be made. The results should help us improve interpretation of serial PEF records in the future.

What are the possible benefits and risks of participating?
None

Where is the study run from?
University Hospitals Birmingham NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
June 2019 to August 2026

Who is funding the study?
Investigator initiated and funded

Who is the main contact?
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Contact information

Type(s)
Principal Investigator

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
277792

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
IRAS 277792

Study information

Scientific Title
Analyses of existing peak expiratory flow in workers with occupational asthma

Acronym
OASYS

Study objectives
1. Do different inhaled exposures at work cause different patterns of peak flow response?
2. What is the specificity of self-completed respiratory questionnaire responses using Oasys analysis of PEF as the reference standard?

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 22/05/2023, Brighton and Sussex REC (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0) 207104 8202; brightonandsussex.rec@hra.nhs.uk), ref: None provided

Study design
Retrospective observational study with existing NHS patient data

Primary study design
Observational

Secondary study design
Cross sectional study

Study setting(s)
Hospital

Study type(s)
Other

Participant information sheet
Not applicable (retrospective study)

Health condition(s) or problem(s) studied
Occupational asthma

Interventions
Trial Objectives
1. To determine whether different exposures at work cause different patterns of peak flow response
2. To determine whether exposure to supposed irritants differ from supposed sensitizers in workers reacting to either exposure

3. To determine how big a difference in PEF is needed to identify a specific cause when a worker is exposed to more than one possible cause?
4. To determine whether the specificity of questionnaire responses of work-related asthma symptoms, using positive Oasys analysis of PEF records as the reference standard?

The study design is an observational (cross-sectional) study using retrospective data, collected as part of routine clinical practice. We will select patients with possible occupational asthma who have undergone peak expiratory flow monitoring at the UHB NHS Foundation Trust occupational lung disease unit since 1990, and who have Oasys records available in the unit's clinical database (derived from their electronic patient record). Included patients will be assigned unique study identification numbers (eg. OASYS01, OASYS02, OASYS03 etc. From the whole occupational lung disease clinical database we will gather the following limited data for all patients with occupational asthma diagnosed within the service 1990-2022 (c. 1600-1700):
1. Date of diagnosis
2. Diagnosis (eg. Occupational asthma by sensitization, irritant induced occupational asthma)
3. Causative agent
4. Job role at time of diagnosis
5. Confidence in diagnosis (ie. Diagnosis based upon PEFs or not, any specific challenge test done, or specific IgE done?)

We will collect baseline demographic and diagnostic data:
1. Age
2. Gender
3. Smoking status
4. Atopic status
5. Pre-existing asthma
6. Non-specific reactivity
7. Treatment during the PEF record
8. Presence of work related symptoms (based upon clinical questionnaire filled out by a subgroup of patients identified in workplace outbreaks of asthma, as part of their routine clinical care within the NHS occupational lung disease unit)

and diagnostic data from the PEF record:
1. The causative agent and exposure
2. The ABC score (a score derived from the area between the curves (ABC) of PEF on days at and away from work, calculated automatically when PEFs entered into Oasys software).
3. Diurnal variation on work and rest days (the difference between PEFs in morning and evening)
4. The pattern of reaction (immediate, flat and late) and speed of recovery (1,2,>2 days) from visual inspection of the Oasys records

We will separate those whose exposures are generally regarded as irritant from those generally regarded as due to hypersensitivity. We will also identify a group who have kept records including >1 different exposure. Groups will comprise:

1. High molecular weight allergens (mainly flour, latex, enzymes and laboratory animals)
2. Intermediate agents separately
3. Woods
4. Metal-working fluids
5. Solder fluxes
6. Low molecular weight allergens separately
7. Isocyanates
8. Acrylates

9. Metals (mostly chrome and cobalt)
10. Glutaraldehyde
11. Cleaning agents
12. Agents with exposure in office environments
13. Agents with exposure in school environments
14. Agents encountered in healthcare environments
15. All other low molecular weight agents

Those with records with more than one exposure who have had one agent identified as the cause (for instance from specific inhalation tests), a comparison of days with either exposure will be used for the comparison of PEF responses of different exposures.

The primary outcome will be: differences in ABC score* between groups (ie. irritant or sensitizer exposed individuals)
*where ABC score is a metric outputted from Oasys software and used to diagnose occupational asthma. It is derived from the area between the curves on days at work and days away from work. Secondary outcomes will be:
1. Differences in the pattern of asthmatic reaction (immediate, flat, late) on PEF
2. Recovery time (1,2, >2 days) from asthmatic reactions based upon PEFs
3. Diurnal variation in PEF home vs work
4. Sensitivity and specificity of questionnaire responses (for the questionnaire analysis)

Each of the outcome variables will be compared between relevant groups using T test or ANOVA for normally distributed data, non-parametric comparisons for non-normally distributed data and Chi-squared for categorical data. For the comparison of groups of low molecular weight exposures groups will be matched for the major confounding factors affecting PEF variability, particularly the use of inhaled corticosteroids taken during the record (recorded on the Oasys report). It may be possible to control for exposure during the record (original or reduced) depending on the extent of the data. We will not control for baseline PEF, as this may be affected by the recovery after exposure which is one of the variables we wish to study. For the determination of specificity of work-related asthma symptoms from questionnaires we will use the data from an outbreak of occupational asthma in a car engine factory (2001-6) with occupational asthma from aerosols of metal-working fluid which we have completed, and questionnaires were undertaken as part of routine clinical care. At least one positive score (eg. ABC score) from Oasys analysis will be used as the positive reference.

Intervention Type
Other

Primary outcome measure
The ABC score from the Oasys program for the PEF study measured using patient records

Secondary outcome measures
Measured using patient records at a single time point:
1. Differences in the pattern of reaction (immediate, flat, late)
2. Recovery time (1,2, >2 days)
3. Diurnal variation in PEF home vs work
4. Sensitivity and specificity of questionnaire responses (for the questionnaire analysis)

Overall study start date
01/06/2019

Completion date
01/08/2026

Eligibility

Key inclusion criteria
Records from all workers with possible occupational asthma who have kept frequent measurements of their breathing using peak flow meters over several weeks at work and at home as part of their investigation to confirm their diagnosis and who have at least one positive score for occupational asthma, will be identified from the Oasys database on NHS trust computers (derived from- and part of the electronic patient record) from 1990 to the present day

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
250

Key exclusion criteria
1. Patients for whom PEF records were inadequate for analysis (eg. too few readings, insufficient number of days at work)
2. Records of patients whose occupational exposures are unknown

Date of first enrolment
01/06/2023

Date of final enrolment
01/09/2023

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University Hospitals Birmingham NHS Foundation Trust
Queen Elizabeth Hospital
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Sponsor information

Organisation
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Sponsor type
Hospital/treatment centre

Website
http://www.uhb.nhs.uk/

ROR
https://ror.org/014ja3n03

Funder(s)

Funder type
Other

Funder Name
Investigator initiated and funded

Results and Publications

Publication and dissemination plan
We aim to present the results at the British Thoracic Society Winter Meeting and also the European Respiratory Society Congress. WE will publish the research as a peer-reviewed paper in a subject-specific journal such as Occupational and Environmental Medicine

Intention to publish date
01/06/2024

Individual participant data (IPD) sharing plan
The datasets generated from this study will be stored in a non-publicly available repository and will in principle be available upon request from University Hospitals Birmingham NHS Foundation Trust. Contact: gareth.walters@uhb.nhs.uk

IPD sharing plan summary
Stored in non-publicly available repository, Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version 2.0	10/01/2023	11/05/2023	No	No