Standard Operating Procedure for case and control recruitment and exposure assessment in the Idiopathic Pulmonary Fibrosis Job Exposure Study (IPF JES)

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1 Scope and applicability

The purpose of this SOP is to describe the instructions for the enrolment of cases and controls, exposure assessment, and genetic testing in the IPF JES.

2 Introduction

The objective of IPF JES is to characterize and measure job exposures as an occupational determinant of Idiopathic Pulmonary Fibrosis (IPF). This will be achieved through a case-control study in which historic job exposures are measured using a validated semi-structured interview. A blood test will also be obtained to investigate interaction between job exposures and IPF genetic susceptibility factors.

3 Recruitment

3.1 Recruitment of cases

See figure 1

Cases will be recruited from male patients with a new diagnosis of IPF made during the study period within the research network.

All clinic patients who meet the case inclusion criteria will be provided with a participant information sheet and participant job history sheet. Patients will be enrolled into the study, blood will be drawn, and a case-report form will be completed. The case-report form and blood samples will be placed into a pre-paid Royal Mail container and put in a postbox. Inclusion and exclusion criteria will be checked as part of enrolment.

The central research team will be updated monthly with details of the number of eligible patients attending clinic, the number of eligible patients approached to participate in the study, and the number of patients agreeing to participate in the study.

Recruitment of cases from a centre stops when the agreed centre target is met or the agreed centre recruitment period ends.

3.2 Recruitment of controls

See figure 2

Controls will be recruited from male patients with a new outpatient department attendance at the same hospital or trust that the cases originate from. Controls will be frequency matched on age to 5-year bands (e.g 50.64, 55-59, 60-64, 65-69, 70-74, 75-79, 80-84, 85+). The overall ratio of cases to controls will be 1:1.

A control clinic will be randomly selected (from all clinics, not limited to respiratory) at each centre. Paediatric clinics and gynaecological clinics will be excluded. This may be achieved by randomly sampling a list of all clinics, by randomly sampling a list of outpatient locations and a time of the week, or by other means. The central research team will provide support for this activity.

The local research team will write to the lead clinician for the selected clinic to obtain permission to recruit patients to the study. If permission is refused then the process is repeated until a lead clinician agrees. Once agreement is obtained this clinic will be the source clinic for all controls at that centre for the duration of the study.

Potential controls will be invited to participate in the study and provided with a patient information sheet when they attend the outpatient department. Patients will be enrolled into the study, blood will be drawn, the participant will be provided with a job history sheet, and a case-report form will be completed. The case-report form and blood samples will be placed into a pre-paid Royal Mail container and put in a postbox. Inclusion and exclusion criteria will be checked as part of enrolment.

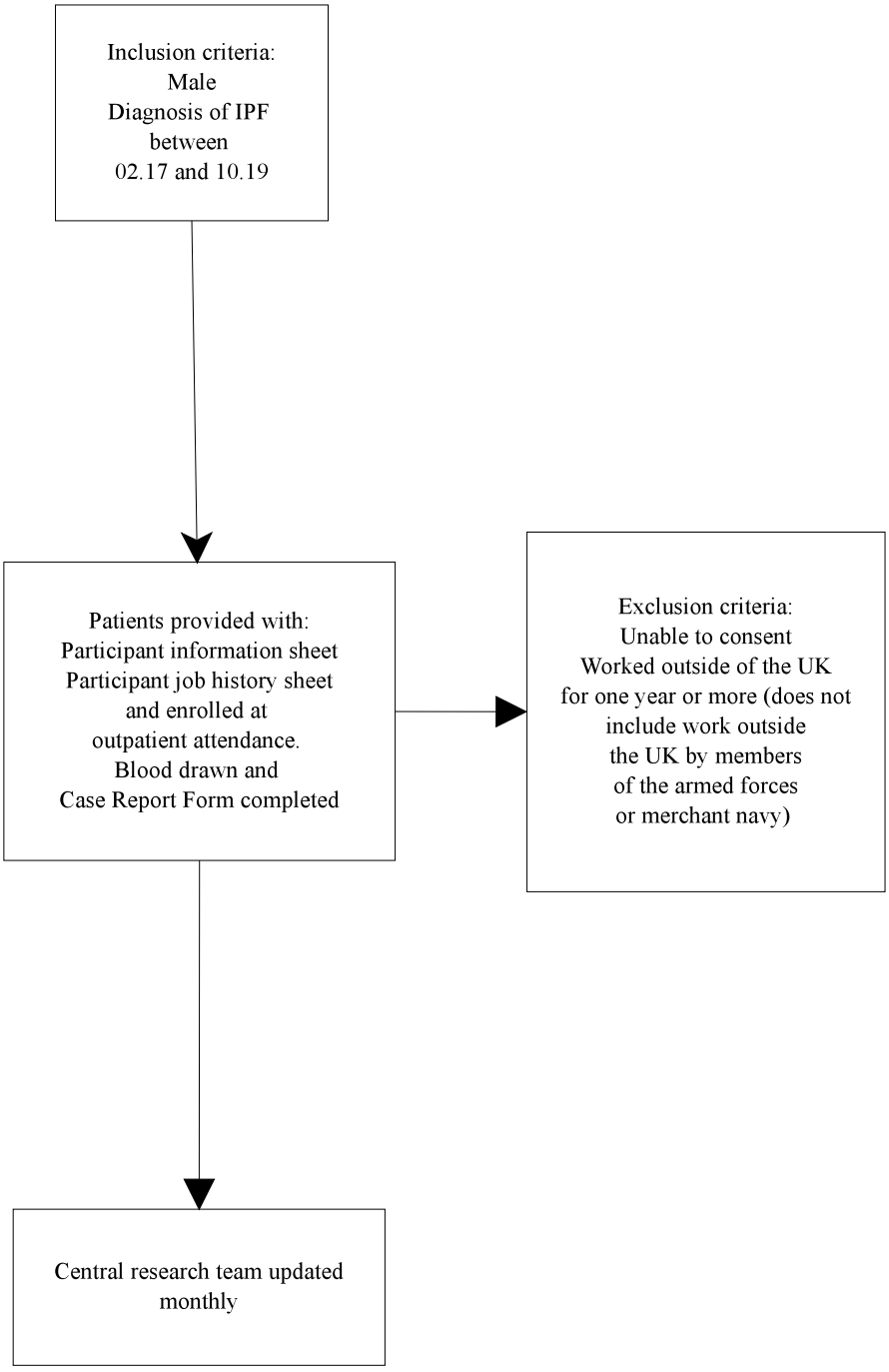

Figure 1: Case recruitment

The central research team will be updated monthly with details of the number of eligible patients attending clinic, the number of eligible patients approached to participate in the study, and the number of patients agreeing to participate in the study.

Recruitment of controls from a centre stops when recruitment of cases stops and one control for each case has been recruited or the agreed centre recruitment period ends.

4 Exposure assessment

The exposure assessment is carried out by the central research team by means of a computer-assisted telephone intereview.

5 Introduction

Hello, my name is **name of researcher**. I am a doctor/nurse/research assistant calling as part of the IPF Job Exposure Study. Is this **name of participant**?

I would like to ask you some questions about the jobs you have had, where you have lived, and smoking. I would also like to record this call for our research if that's ok with you.

Your answers will help us to understand the causes of IPF, make sure people get the right treatment, and ensure that controls of exposures at work are right so that we protect workers and prevent disease in the future.

The interview should take about 30 minutes. Is now a good time to talk?

6 Occupational history

I want you to think about all of the jobs you've had. I know this can be hard, we'll try one at a time.

Do you remember the first job that you had after school?

1. What was the name of your job? (we record SOC2000 job title and map SOC90)
2. What did you do in this job? (we record free text but also have a drop down of activities associated with asbestos exposure)
3. What was the name of the company (if applicable)? (we record name and SIC code, we possibly link to open corporates company house record)
4. What did the company make (if applicable)? (we record free text but also have a drop down of asbestos containing products)
5. In what sort of working area did you spend most of your time? e.g Office, In the Open, Workshop, Construction Site, Factory (Light Industry), Heavy Industry (eg. Power Station), Hospital, School/University, Warehouse, On Location, various buildings, Shop, At Home, Ship/Ship yard, Other (specify)
6. Did you work full time? (if not specify average hours per week)
7. Did you work all year round (if not specify months of the year)

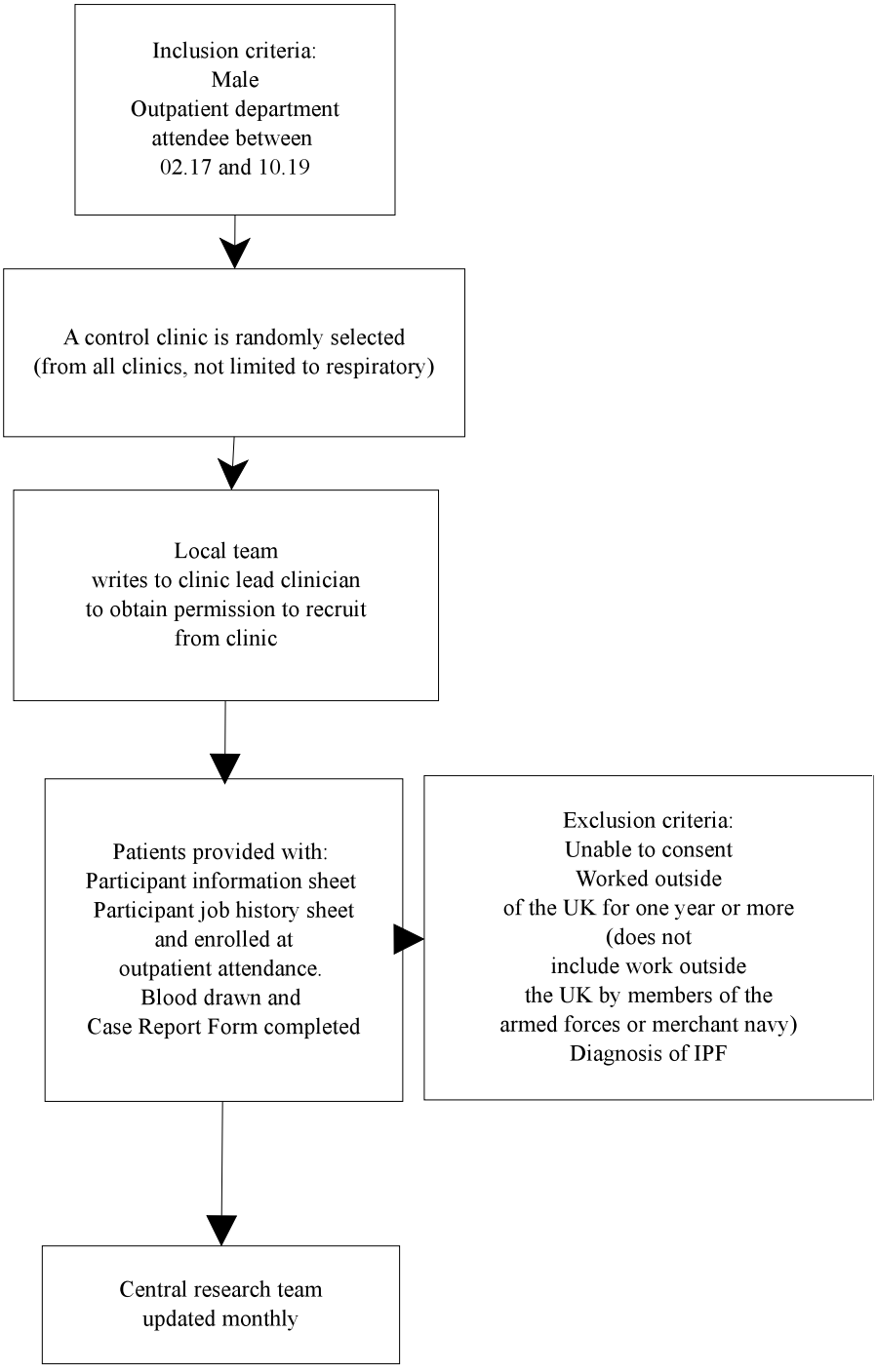

Figure 2: Control recruitment

SOC90	Occupation	PMR
541	Coach & vehicle body builders	528.18
534	Metal plate workers, shipwrights, riveters	416.64
532	Plumbers, heating & ventilating engineers	388.67
570	Carpenters & joiners	382.34
896	Construction & related operatives	359.23
311	Building inspectors	317.83
520	Production fitters (electical/electronic)	300.15
521	Electricians, electrical maintenance fitters	264.12
893	Electrical, energy, boiler & related	252.09
533	Sheet metal workers	245.71
301	Engineering technicians	232.22
506	Floorers, floor coverers, carpet fitters	232.05
913	Mates to metal/electrical & related fitters	230.89
211	Mechanical engineers	217.44
571	Cabinet makers	215.36

Table 1: Standard Occupational Classification 1990 code, Occupation, and Mesothelioma Proportional Mortality Ratio (PMR) for the top 15 significant (95% CI does not include 100) PMRs. HSE data.

8. Do you remember how old you were or what year you started the job?

9. Do you remember how old you were or what year you finished the job?

10. Do you remember what job you had next?

(1 through 10 repeats until lifetime occupational history is complete. Standard occupational classification is used to code occupations)

Any reported contact with asbestos or 'trigger' products (HSE list), industries (construction, factory work, power station work, other heavy industry, ships or ship yards), jobs (see Table 1), and job processes prompts an asbestos exposure history (see later) to be taken.

7 Cohabitation history

I'm going to ask you about people who have lived with you now. I'm specifically interested in people that lived at home with you who went out to work.

1. When you were growing up did anyone who went out to work live at home with you?
2. What was the name of the person?
3. How long did they live with you?
4. Do you remember what their job was?

8 Smoking history

1. Have you ever smoked?
2. What old were you when you started smoking?
3. Do you still smoke?
4. How old were you, or when, did you stop smoking?
5. How many, on average, a day do you/did you smoke?
6. What do you/did you smoke?

9 mMRC dyspnoea questions

I would like to ask you some questions about being short of breath.
Are you:

1. Not troubled by breathless except on strenuous exercise?
2. Short of breath when hurrying on a level or when walking up a slight hill?

Are you someone who:

3. Walks slower than most people on the level, stops after a mile or so, or stops after 15 minutes walking at own pace?
4. Stops for breath after walking about 100 yds or after a few minutes on level ground?

Are you:

5. Too breathless to leave the house, or breathless when dressing/undressing?

10 Drug and medical history

1. Have you ever taken any heart medications such as amiodarone or flecainade, antibiotics such as nitrofurantoin, or immunosupressants and chemotherapy drugs such as, azathioprine, gefitinib, ifosfamide, melphalan, and rituximab?
2. Do you have any other serious illnesses?

11 Family history

1. Does anyone in your family have scarring of their lungs (or pulmonary fibrosis)?
2. If yes, who?

12 Asbestos exposure history

1. Did you, or anyone close to you, ever work with or disturb material you suspected to be made from asbestos? This might include materials such as asbestos lagging, asbestos sprayed coatings, AIB(asbestos insulation board - e.g asbesolux, marinite, shipboard, LDR, turnasbestos etc) or corrugated roofing? (Yes, record what using free text, which job(s) associated with and John Cherrie item/No/Not known)
2. What was done with it? (free text and John Cherrie item)
3. How long did the task take and how often did you do it? (Record % work time on task)
4. Where was the task completed? (free text and drop down e.g inside small room, inside large room, outside)
5. Did you wear a mask? (free text and drop down)

13 (for cases only) how were you diagnosed

1. What took you to the doctor at the beginning of the illness? (e.g cough, breathlessness, incidental finding, other)

14 Ethnicity

For the blood test that we have taken it would be helpful for us to know what ethnicity you are.

To which of the following ethnic groups do you consider you belong?

1. White
2. Black or Black British
3. Mixed

4. Chinese
5. Asian or Asian British
6. Other ethinic group (please specify)

15 Thank-you and updates

Thank-you very much for participating today. Is there anything you'd like to ask us? Would you like to be kept updated on the study? How would you prefer to be updated? (Post or email, capture email if prefers email).

16 Venepuncture, sample storage, transportation, and processing

Venepuncture will be performed by a qualified practitioner. Sites will be provided with one 10ml EDTA tube and one 10ml SST tube per participant to obtain blood. Samples will be labelled with the participants unique research ID and posted using Royal Mail Safebox to a secure lab storage facility at NHLI where they will be kept in a -80 degree centigrade freezer. Royal Mail Safeboxes will be posted into a royal mail postbox by the local researcher; the hospital postal service will not be used. The sender will record the day of delivery and the research team will record receipt of the sample and keep an accurate record of its location. Analysis of samples will include DNA isolation and quantitative PCR taqman assay to investigate pre-defined SNPs of interest.

17 Unique research IDs

Each participant will be assigned a unique research ID which will be used to label the Case Report Form and blood tubes. The ID will be 6 digits long. The first 2 digits will be the assigned centre ID. The subsequent 4 digits can be assigned to cases and controls as the centre wishes so long as there are no repeats.

18 Study documentation and logs

To meet GCP and HTA requirements the local team will maintain a local site study file. The local site file contains:

1. site delegation log (statement of activities document may be used)
2. CVs and GCP certificates for research personnel listed in the delegation log
3. study approvals
4. study protocol
5. study standard operating procedure
6. study recruitment bundle (participant information sheet, consent form, job history sheet, case report form)

Organisation	Centre ID
Heart of England NHS Foundation Trust	01
Morriston Hospital	02
Nottingham University Hospitals NHS Trust	03
Southampton University Hospitals NHS Trust	04
University Hospital of South Manchester	05
Papworth Hospital NHS Foundation Trust	06
Royal Devon and Exeter NHS Foundation Trust	07
Aintree University Hospitals NHS Foundation Trust	08
North Bristol NHS Trust	09
Imperial College Healthcare NHS Trust	10
Aberdeen Royal Infirmary	11
Glasgow Royal Infirmary	12
Royal Infirmary of Edinburgh	13
The Newcastle Upon Tyne Hospitals NHS Foundation Trust	14
Taunton and Somerset NHS Foundation Trust	15
Leeds Teaching Hospitals NHS Trust	16

Table 2: Centre study IDs

7. study training log (ipfjes-tlog.docx)
8. participation (screening) log (ipfjes-plog.xlsx)
9. sample log (ipfjes-slog.xlsx)
10. adverse event log (ipfjes-alog.xlsx)
11. general notes (ipfjes-general-notes.docx)
12. signed consent forms

It is acceptable for some or all of these to be stored electronically. At the end of the study the central research team will be responsible for archiving local site files.

19 Tissue-tracking and communication

The local team will track tissue obtained from research participants by emailing the central research team with the name and research ID of the research participant to inform them when samples are sent.