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

Contents

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 suceptibility 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.

Centres within the research network will provide the research team with a list of the hospital numbers for all patients newly diagnosed with IPF in the preceding month, on a monthly basis.

For each centre the research team will randomly select a sample from the provided list on a monthly basis. The size of the sample N_{centre} will be calculated as follows

$$N_{centre} = tp \times (1/nm)$$

Where tp = total number of patients on list provided, nm = number of months in the study period.

The research team will request that centres write to these patients inviting them to participate in the study and enclosing the patient information sheet. Patients will be enrolled into the study at their next outpatient department, blood will be drawn, and a telephone interview will be scheduled. Inclusion and exclusion criteria will be checked as part of enrolment.

Recruitment of cases from a centre stops when (460/number of centres) cases are recruited.

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 cases originate from. Controls will be frequency matched on age and the ratio of cases to controls will be 1:1.

Centres within the research network will provide the research team with a list of the outpatient clinics (exluding female only clinics and paediatric clinics) that take place each month and an estimate for the number of new male patients seen in each clinic. (n.b this list is provided to the research team only once, it is anticipated that the administrative information needed to create the list will be readily available).

The research team will list each clinic alphabetically and serially assign an integer range equal to the expected number of new male patients per clinic per month. The full integer range will then be randomly shuffled and used to derive a list of clinic leads to be approached sequentially as necessary.

The research team will write to the lead clinician for the selected clinic to obtain permission to recruit patients to 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 at their next outpatient department attendance, blood will be drawn, and a telephone interview will be scheduled. Inclusion and exclusion criteria will be checked as part of enrolment. (n.b once a control clinic is selected it is used throughout the study).

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

4 Exposure assessment

4.1 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 your lifetime smoking history. I would also like to record this call for our research if that's ok with you.

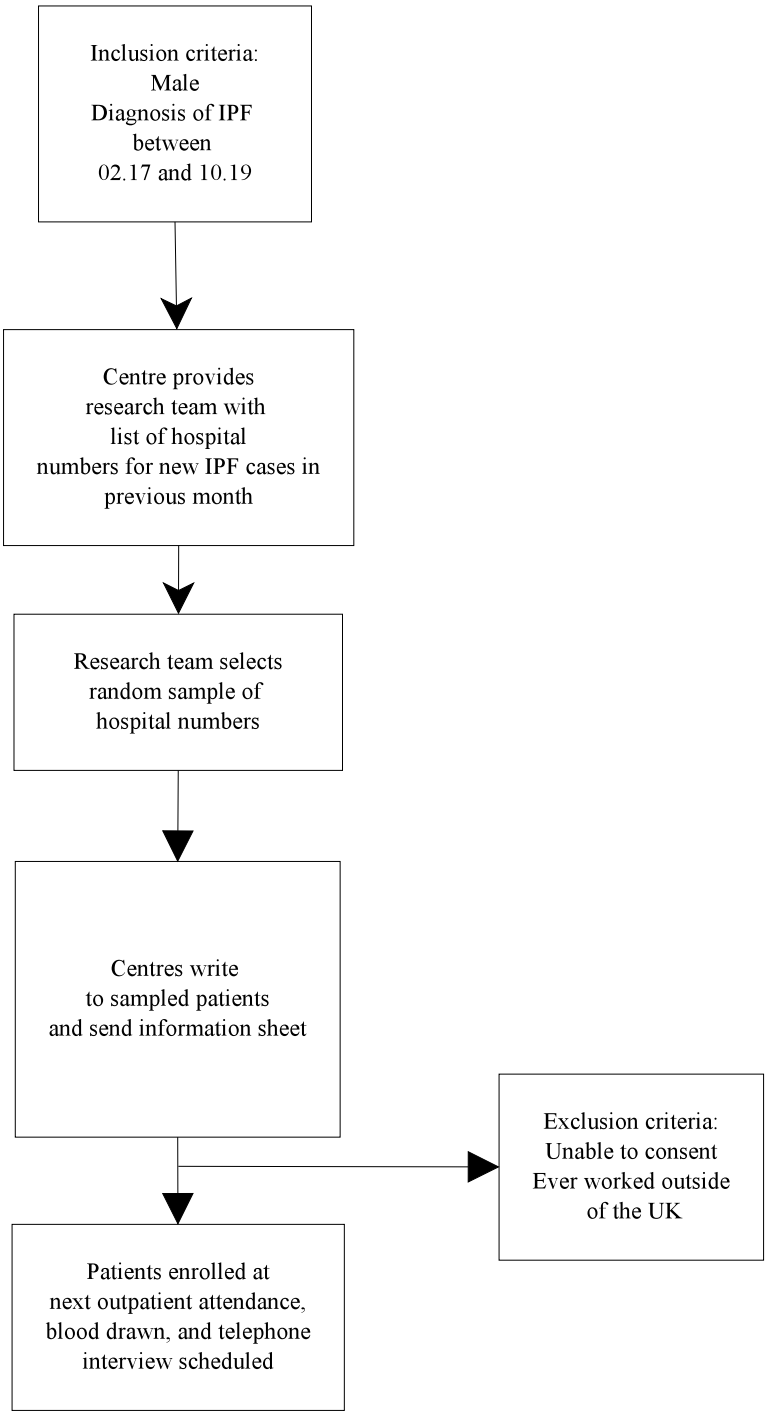

Figure 1: Case recruitment

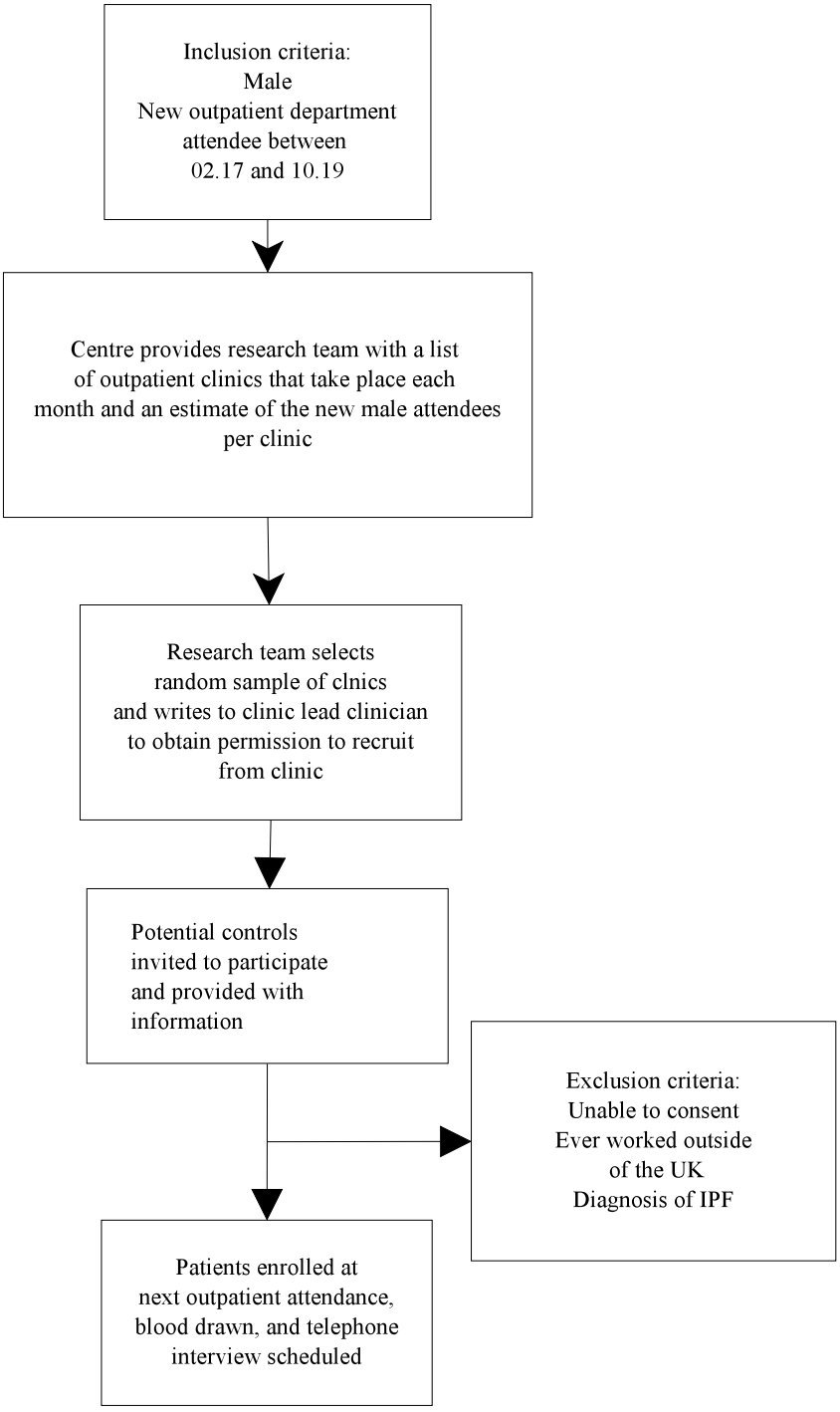

Figure 2: Control recruitment

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.

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?

4.2 Occupational and residential 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?
2. What did you do in this job?
3. What did the company make (if applicable)?
4. Do you remember how old you were or what year you started the job?
5. Do you remember how old you were or what year you finished the job?
6. Do you remember where you lived when you had that job?
7. Do you remember what job you had next?

(1 through 7 repeats until lifetime occupational history is complete. Standard occupational classification is used to code occupations)

'Trigger' jobs (see Table 1) table prompt more detailed questioning regarding job process(es), materials used, and control measures (according to validated semi-structured job process based historic job exposure assessment tool developed by John Cherrie)

I'm going to ask you about places that you've lived now. I know it might be difficult to remember, don't worry.

8. What country were you born in?
9. What place were you born in?
10. Do you remember the places you lived when you were growing up? (until you finished school)
11. When you were growing up who lived at home with you?
12. How long for?
13. Do you remember what their job was?

4.3 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?

4.4 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?

4.5 Drug and medical history

1. Do you take any regular medications?
2. What do you take these for?
3. Do you have any other serious illnesses?

4.6 (for cases only) how were you diagnosed

1. What took you to the doctor at the beginning of the illness?

5 Venepuncture, sample storage, transportation, and processing

Venepuncture will be performed by a qualified practitioner. The number of blood tubes to be drawn depends on the volume of the tubes used. A total of 14mls of blood will be obtained using purple top EDTA tubes and a total of 10mls of blood using gold top SST tubes for each participant. 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. 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.