

**IPFJES SITE  
INITIATION VISIT  
DR CARL REYNOLDS AND MISS  
RUPA SISODIA**

**IDIOPATHIC  
PULMONARY  
FIBROSIS JOB  
EXPOSURES STUDY**

this talk is available online

*<http://carlreynolds.net/ipfjes-siv>*

this studies documentation is available online

*[https://github.com/drcjar/ipfjes  
/blob/master/README.md](https://github.com/drcjar/ipfjes/blob/master/README.md)*

**TODAY WE WILL  
COVER WHY, WHAT,  
AND HOW**

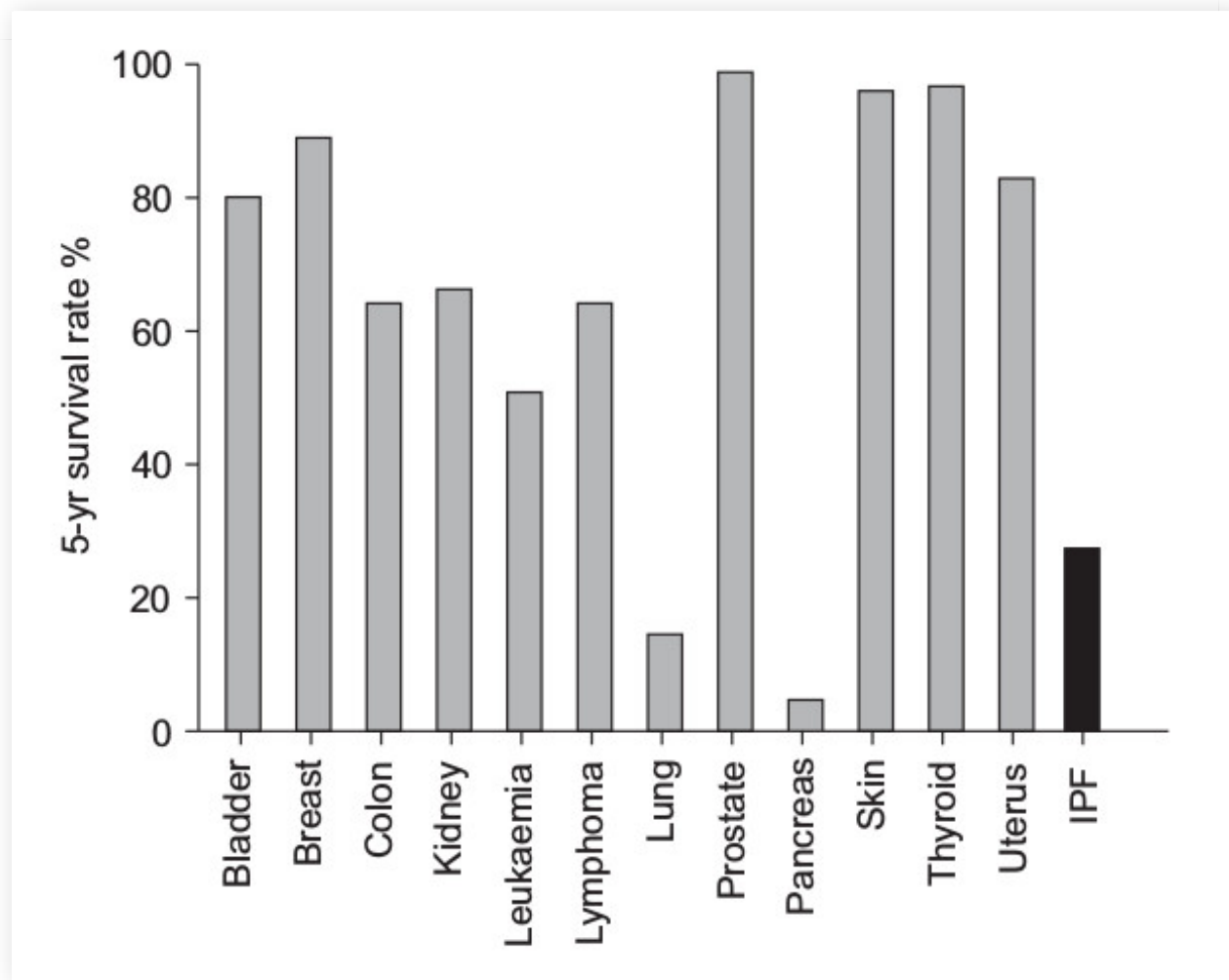
**WHY ARE WE DOING  
IPF JES?**

- It's bad to not know the cause of a killer disease that is becoming more common
- There is ongoing asbestos exposure globally (including the UK)
- There is reason to think some IPF is due to asbestos, potentially we can better understand and prevent IPF

**IPF CAUSES  
SIGNIFICANT  
MORBIDITY AND  
MORTALITY**

- c.4000 deaths in 2012 for England & Wales
- median survival of three years; worse than several cancers
- more common in men, manual workers, those living in industrial regions
- incidence increasing 5% pa since 2000; don't know why





C. Vancheri et al. IPF: a disease with similarities and links to cancer biology. Eur Respir J, Mar 2010

**ASBESTOS RELATED  
DISEASE REMAINS A  
PROBLEM**

- 2 million metric tons per year of asbestos consumed per year
- 125 million people around the world work in environments in which they are exposed to asbestos
- 107,000 people die from occupational exposure to asbestos / year



# Pleural mesothelioma and lung cancer risks in relation to occupational history and asbestos lung burden

Clare Gilham,<sup>1</sup> Christine Rake,<sup>1</sup> Garry Burdett,<sup>2</sup> Andrew G Nicholson,<sup>3</sup> Leslie Davison,<sup>4</sup> Angelo Franchini,<sup>1</sup> James Carpenter,<sup>1,5</sup> John Hodgson,<sup>6</sup> Andrew Darnton,<sup>6</sup> Julian Peto<sup>1</sup>

► Additional material is published online only. To view please visit the journal online (<http://dx.doi.org/10.1136/oemed-2015-103074>)

<sup>1</sup>London School of Hygiene and Tropical Medicine, London, UK

<sup>2</sup>Health and Safety Laboratory, Buxton, UK

<sup>3</sup>Department of Histopathology, Royal Brompton and Harefield Hospitals NHS Foundation Trust, and National Heart and Lung Institute, Imperial College, London, UK

<sup>4</sup>Department of Cellular Pathology, Leeds Teaching Hospitals NHS Trust, Leeds, UK

<sup>5</sup>Medical Research Council Clinical Trials Unit, Kingsway, London, UK

## ABSTRACT

**Background** We have conducted a population-based study of pleural mesothelioma patients with occupational histories and measured asbestos lung burdens in occupationally exposed workers and in the general population. The relationship between lung burden and risk, particularly at environmental exposure levels, will enable future mesothelioma rates in people born after 1965 who never installed asbestos to be predicted from their asbestos lung burdens.

**Methods** Following personal interview asbestos fibres longer than 5  $\mu\text{m}$  were counted by transmission electron microscopy in lung samples obtained from 133 patients with mesothelioma and 262 patients with lung cancer. ORs for mesothelioma were converted to lifetime risks.

**Results** Lifetime mesothelioma risk is approximately 0.02% per 1000 amphibole fibres per gram of dry lung tissue over a more than 100-fold range, from 1 to 4 in the most heavily exposed building workers to less than 1

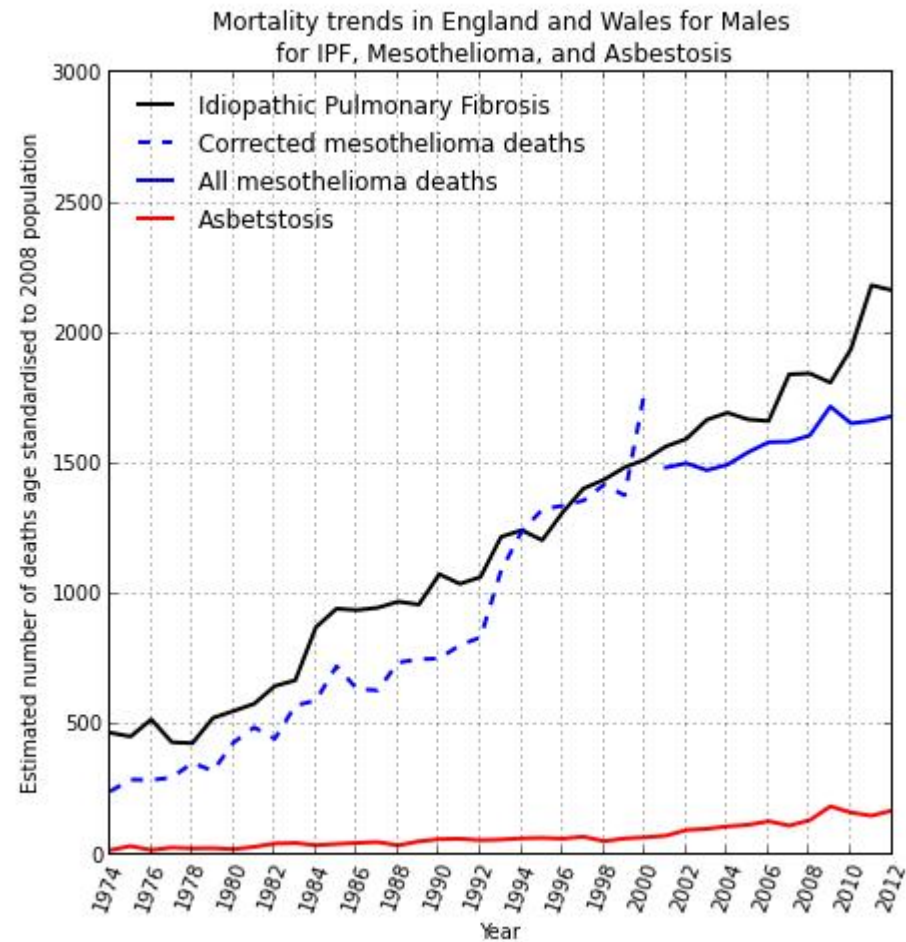
## What this paper adds

- Britons born before the 1960s have the highest mesothelioma death-rate worldwide, reflecting high occupational asbestos exposure in men and widespread environmental exposure in both sexes before 1980, when asbestos use virtually ceased in Britain.
- The risk to younger people from asbestos still present in many buildings is not known but could be substantial.
- We have shown that lifetime mesothelioma risk is approximately 0.020% per 1000 asbestos fibres per gram of dry lung tissue over a more than 100-fold range, from 1 to 4 in the most heavily exposed building workers to less than 1 in 500 in most of the population.
- This will enable the risk from current asbestos

**THERE IS REASON TO  
THINK SOME IPF IS  
DUE TO ASBESTOS**

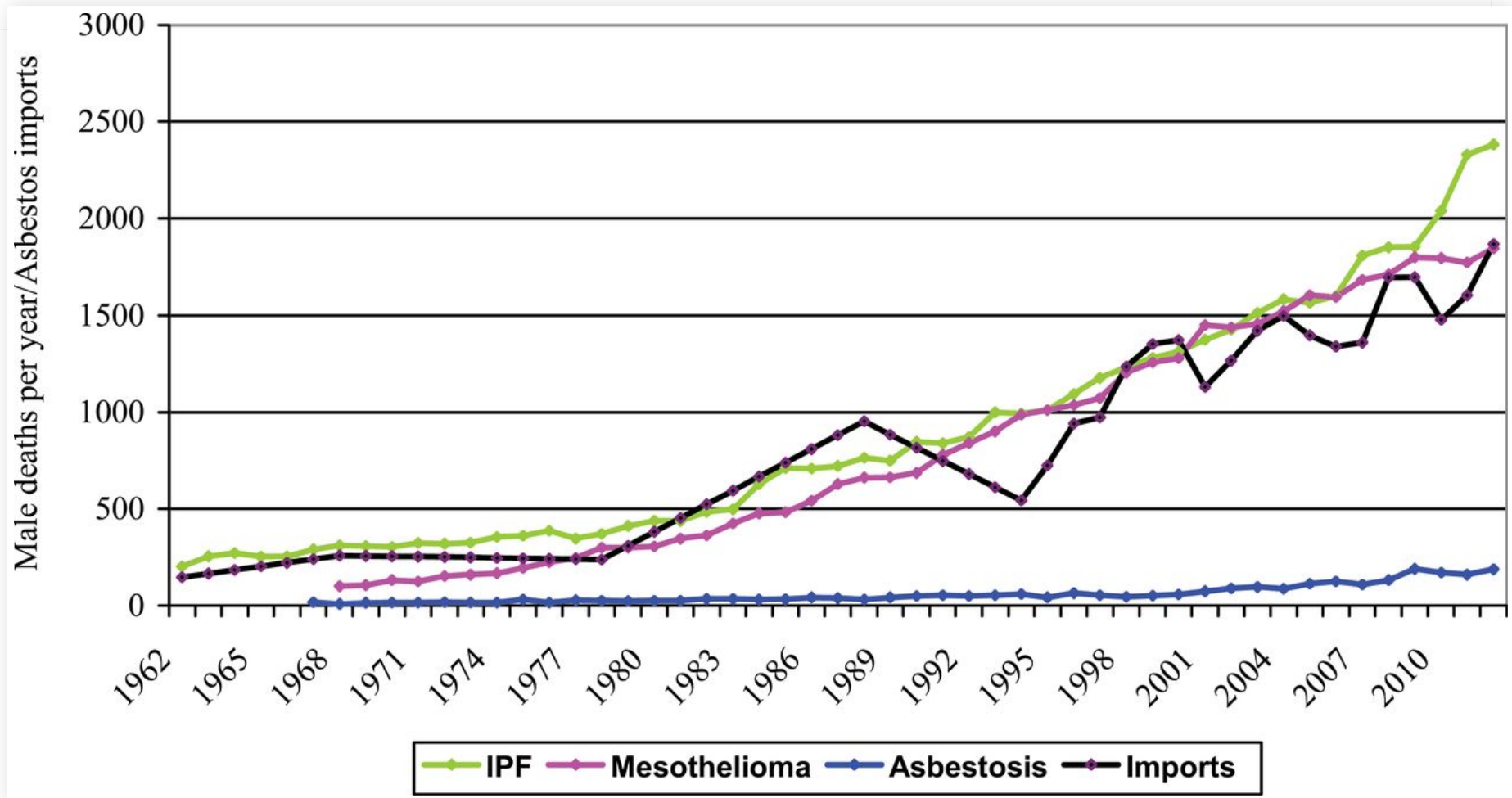
- Clinical Plausibility
- Observed epidemiological patterns
- Fibre studies and existing case-control data

- Clinical presentation can be similar
- Radiologically and histopathologically both give rise to UIP - no differentiating biomarkers
- Doctors may not elicit previous asbestos exposure and patients may not recall it; unclear what dose is needed



Reynolds et al. IPF, Mesothelioma, and Asbestosis mortality trends for England and Wales, BTS 2014





Barber et al. UK asbestos imports and mortality due to idiopathic pulmonary fibrosis. Occ Medicine, 2015

## Lung dust content in idiopathic pulmonary fibrosis: a study with scanning electron microscopy and energy dispersive x ray analysis

E Monsó, J M Tura, J Pujadas, F Morell, J Ruiz, J Morera

### Abstract

Examination with an optical microscope and polarised light is not sensitive enough to detect low diameter asbestos fibres. This limitation implies that some cases of asbestosis can be erroneously diagnosed as idiopathic pulmonary fibrosis (IPF) if asbestos bodies are not found in the standard examination of abnormal tissue. To determine whether IPF is over-diagnosed, a study was carried out with scanning electron microscopy (SEM) and energy dispersive x ray analysis (EDXA) on 25 samples

A lung sample showing pulmonary fibrosis and inorganic particles allows the diagnosis of pneumoconiosis. Absence of inorganic particles in a fibrotic lung sample of a patient with diffuse interstitial lung disease, if no other cause is determined, usually gives a diagnosis of idiopathic pulmonary fibrosis (IPF). It is well known, however, that examination with an optical microscope and polarised light is not sensitive enough to detect low diameter inorganic particles, especially asbestos fibres. For lung samples from patients previously diagnosed by optical microscopy as having IPF, an

# PREVIOUS STUDIES

- 14 case-control studies to date
- 8 find an association with metal dust; 4 with wood; 2 with stone
- Most use community controls and self-reported exposure measures; none quantify asbestos exposure
- Occupational overlap with mesothelioma case-control studies
- (meta-analysis and analysis of occupational data from Navaratnams 2014 study - unpublished)

# WHAT WE'RE DOING

- (another) hospital-based case-control study
- lifetime occupational histories combined with occupational proportionate mortality ratios for mesothelioma and a job-process based asbestos exposure assessment..
- blood test for susceptibility genetics to investigate gene-exposure interactions
- basically a telephone-interview + blood test for 920 patients at 16 centres

# HOW IPF JES WORKS

- Funded by Wellcome Trust and in the NIHR portfolio. All regulatory approvals in place.



- Central research team: full-time clinical research fellow + research assistant, supervised by Prof Cullinan, Chris Barber, and Sara De Matteis. Advisory board of the great and the good. Study management and coordination + one site locally.

- Local research centres: PI + research nurse.  
Identification and recruitment of cases and controls.

- All the study documents are online  
<https://github.com/drcjar/ipfjes/blob/master/README.md>

**LOCAL CENTRES  
IDENTIFY AND  
RECRUIT  
PARTICIPANTS**

# **KEY DOCUMENTS && EVENTS**

- The SOP
- The bundle
- The box with blood and CRF
- The email with name and research ID

# WHAT'S IN THE SOP

- how to identify cases and controls
- how to recruit them
- how to record the process and communicate with us



# **IDENTIFYING CASES AND CONTROLS**

- men with an incident diagnosis of IPF from Feb 2017 - Oct 2019 from the ILD clinic
- (age-matched) men without a diagnosis of IPF from not-the-ILD-Clinic
- never worked abroad

# **SELECTING NOT-THE-ILD-CLINIC**

- randomly selected
- using a list of all clinics / services / consultants / clinic locations and times
- we're not rigid about how as long as it's 'fair', we're happy to support
- local team asks the clinic lead if its ok to recruit from their clinic, if it's not then we select again

**RECRUITING CASES  
(AND CONTROLS)  
FROM CLINIC**

- Record number of eligible participants
- Record number of eligible participants approached who refuse to participate
- Complete case-report form for participants + take or arrange blood sample collection
- Post case-report form and blood samples to us in the provided prepaid Royal Mail specimen box
- Email us about the number of eligible participants, number of refusals, and the research ID and name of the samples you're sending us

# ON RESEARCH IDS

- used to label samples and the CRF
- together with recruitment and tissue tracking clinic email allows us to telephone people
- 6 integers, first 2 integers identify centre, remaining four integers allocated however you like (as long as no duplicates)



# **WHAT'S IN THE BUNDLE**

- participant information sheet (contains enough information for a competent person to consent someone for the study)
- consent form
- case report form
- job history sheet

# ANY QUESTIONS?

- [carl.reynolds@imperial.ac.uk](mailto:carl.reynolds@imperial.ac.uk) | [r.sisodia@imperial.ac.uk](mailto:r.sisodia@imperial.ac.uk)
- [drcjar](#) | [ipfjes](#)
- [www.carlreynolds.net](http://www.carlreynolds.net) | [www.ipfjes.org](http://www.ipfjes.org)