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IPF and Asbestos Reserves – Salvation or Damnation?

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Agenda

1. Introduction
2. What is IPF?
3. IPF and Asbestos
4. Ongoing research
5. Potential implications on the Insurance market
6. Questions and Discussions

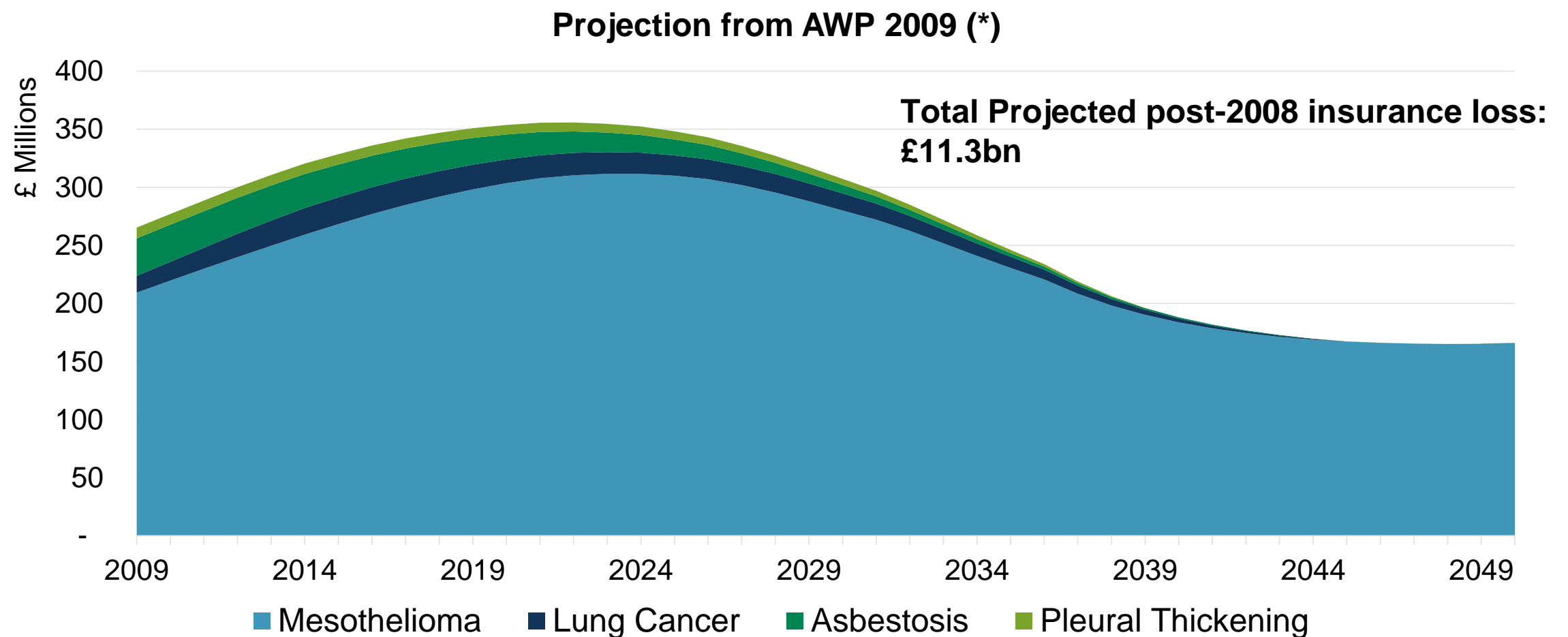


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1. Introduction

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UK Asbestos: Projected market loss split by disease



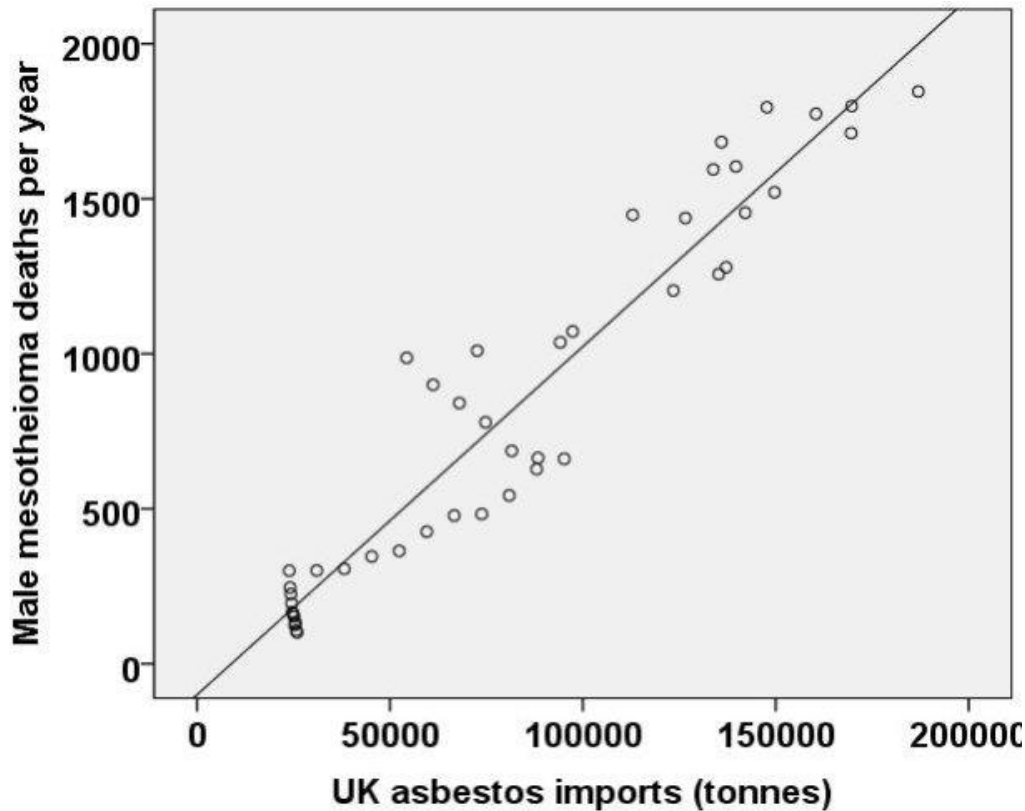
UK Asbestos: Widely-known drivers of loss/ uncertainty to Actuaries

- Mesothelioma losses (c. 90% at 2009)
 - No. of future mesothelioma deaths for males
 - Claims to death ratios
 - Average cost per claim
 - Inflation
 - Legal decisions (eg Decentralisation, LASPO, Ogden)
 - Medical cost
- Other diseases (c. 10% at 2009)
 - Increased costs of Pleural Thickening?

Strong correlation observed between IPF deaths and Asbestos imports* Barber (2015)

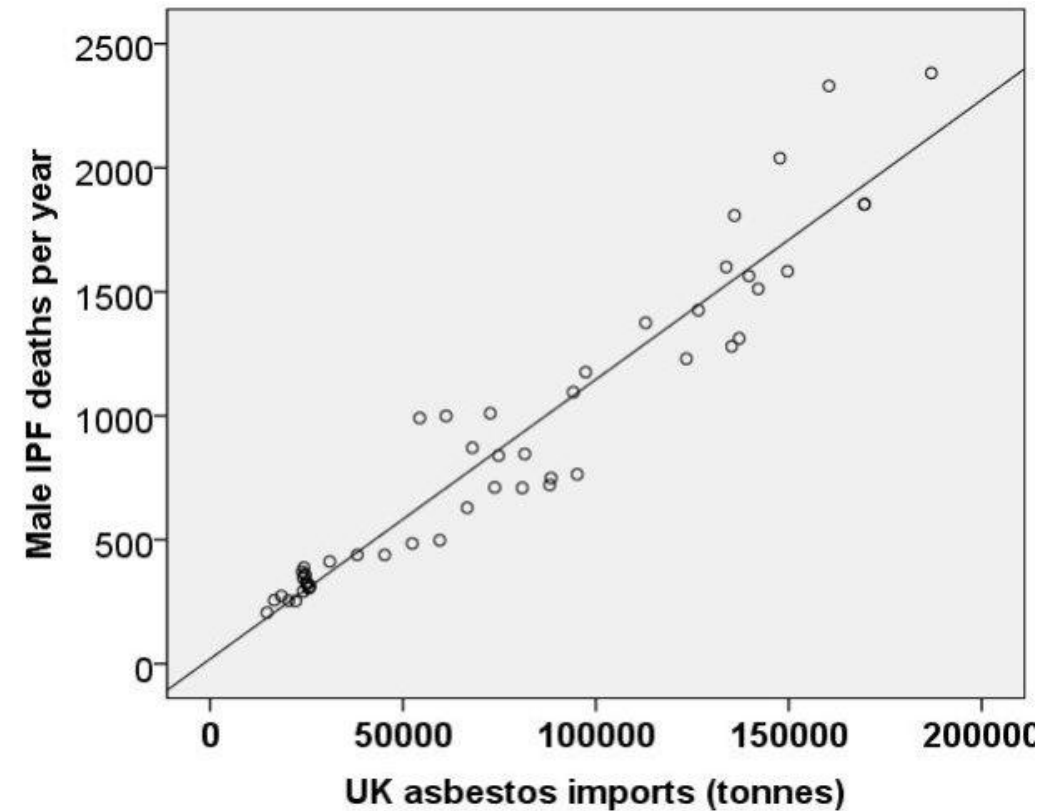
Mesothelioma:

Male annual deaths 1968-2011



IPF:

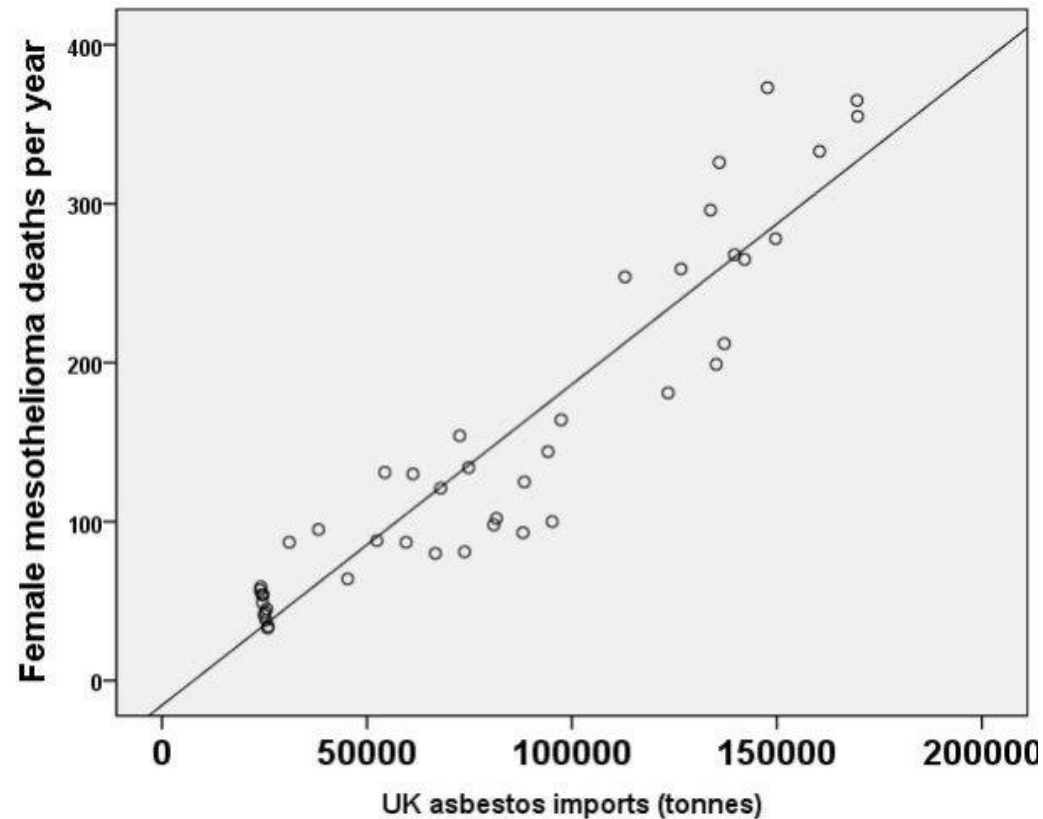
Male annual deaths 1962-2012



IPF has higher incidence of Female Deaths (c. 2:1) compared to Mesothelioma (c. 6:1)

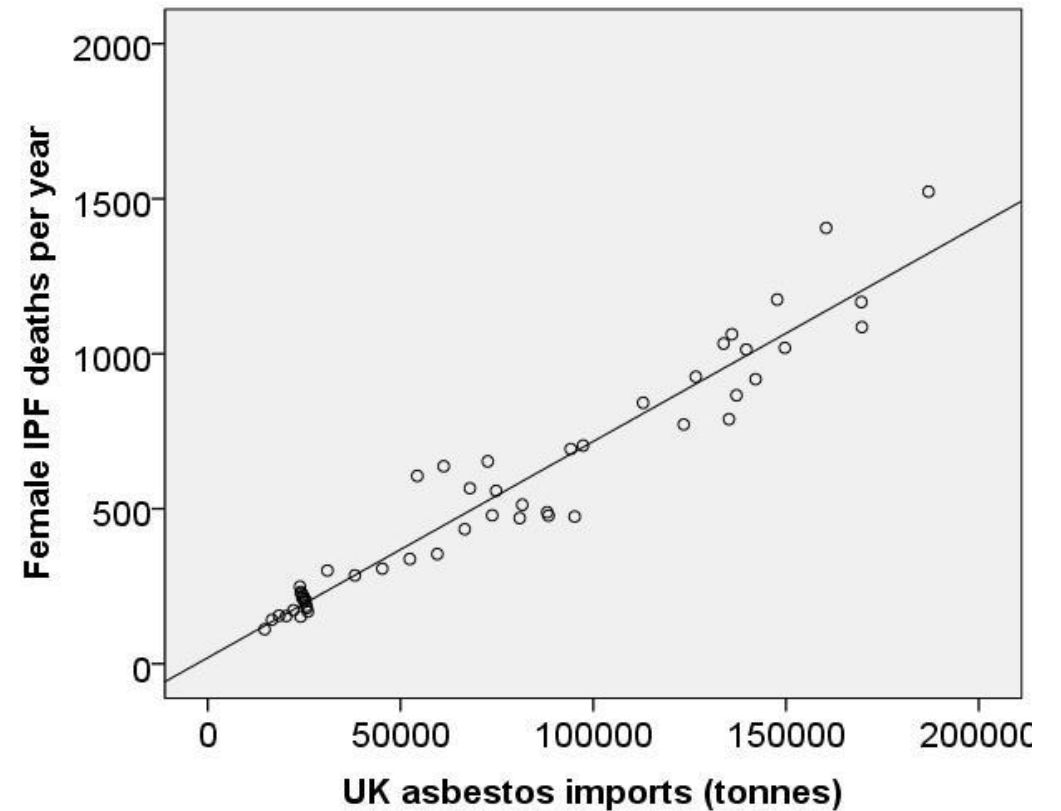
Mesothelioma:

Female annual deaths 1968-2011



IPF:

Female annual deaths 1962-2012



Should we panic?



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2. What is IPF?

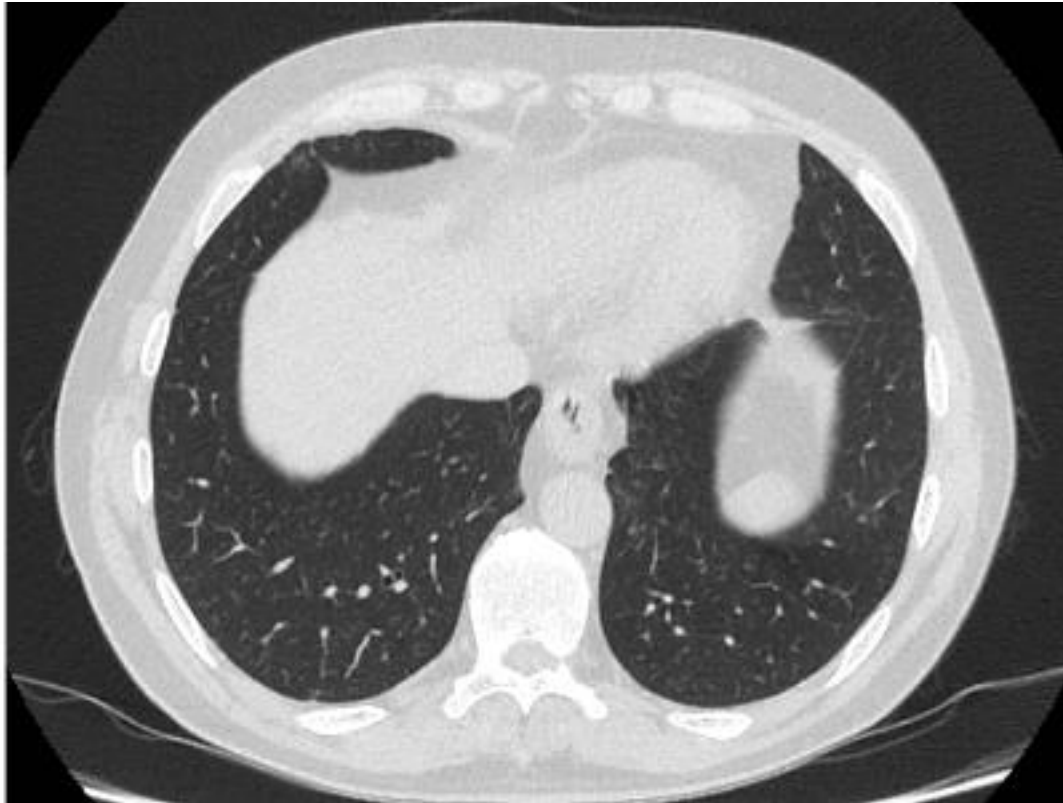
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What is Idiopathic Pulmonary Fibrosis (“IPF”)?

- A form of interstitial lung disease
- Permanent lung scarring of no known cause
- Progressive breathlessness and dry cough
- Typical radiology “UIP pattern” on HRCT
- ~4,000 deaths each year
 - c.f. ~2,500 deaths for mesothelioma
- ~3 years median survival
- Poor prognosis

HRCT Scan

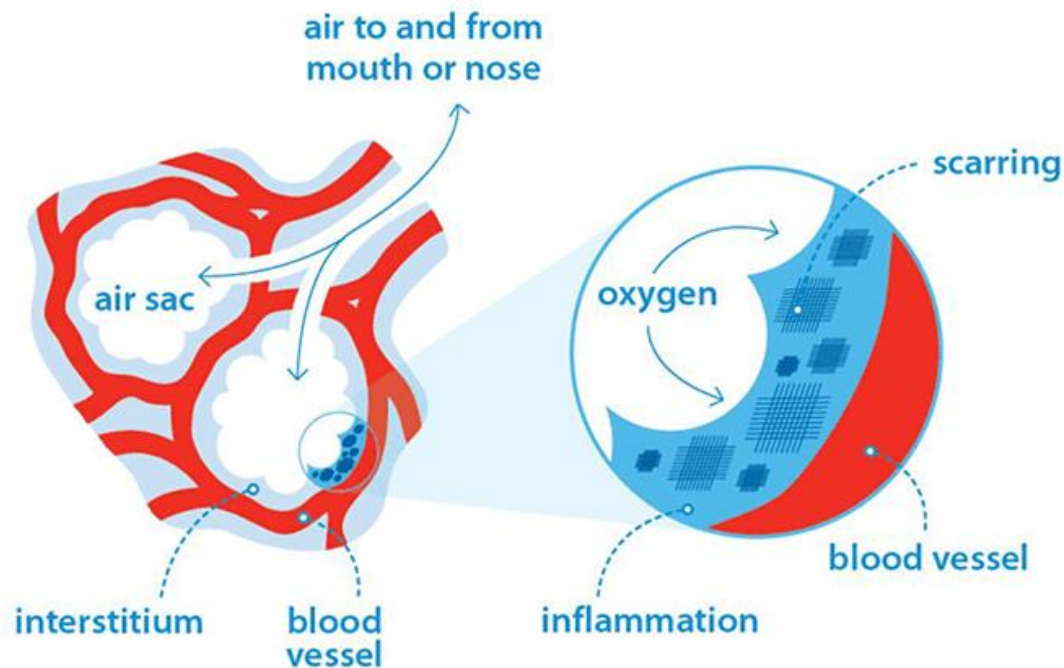
1. Normal lung



2. IPF

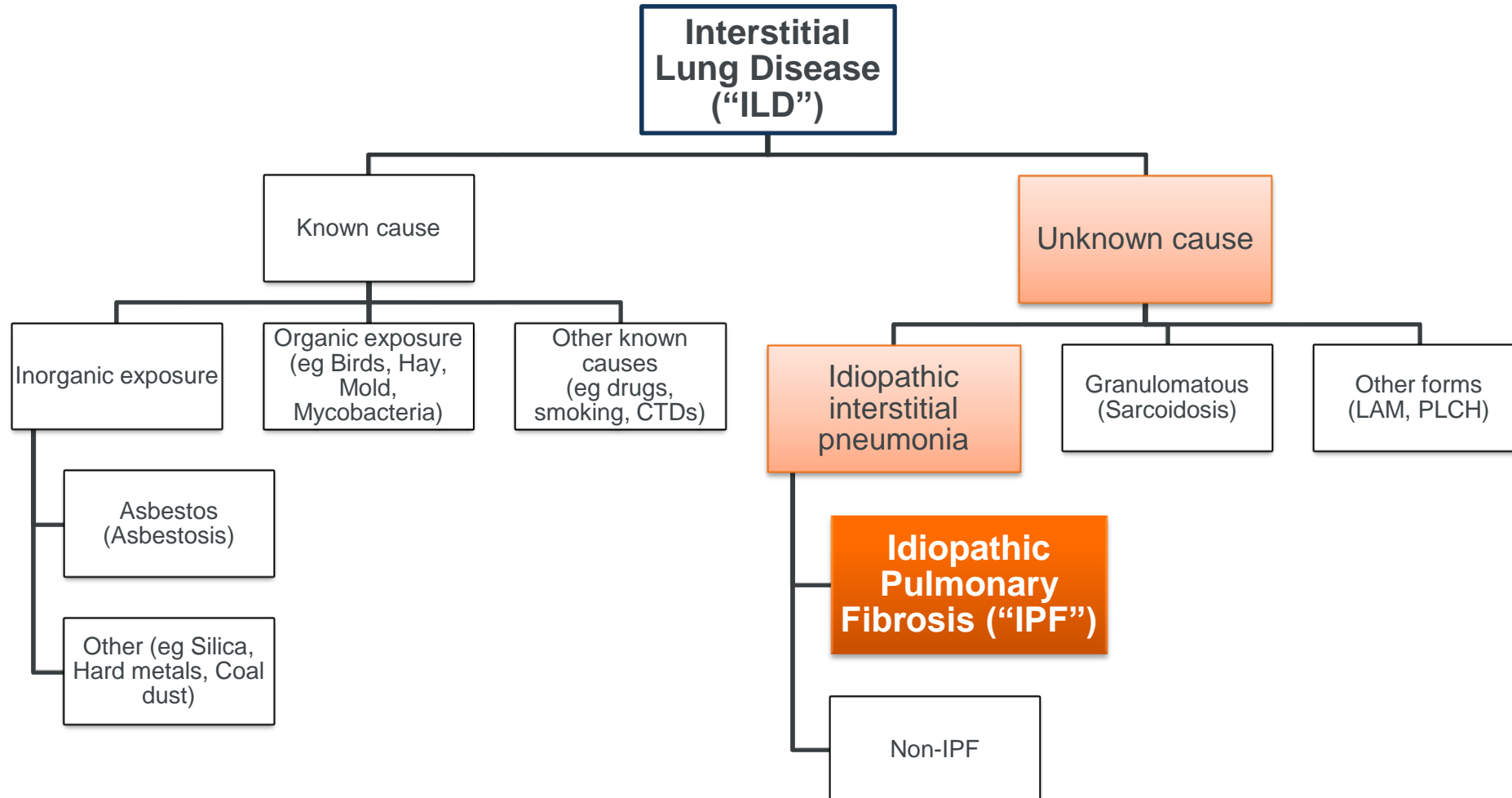


What is Interstitial Lung Disease (“ILD”)?



- Interstitium: lace-like network of tissue providing support to the lung's air sacs (alveoli).
- ILD: causes interstitium to be scarred/thickened, making it more difficult for oxygen to pass into bloodstream

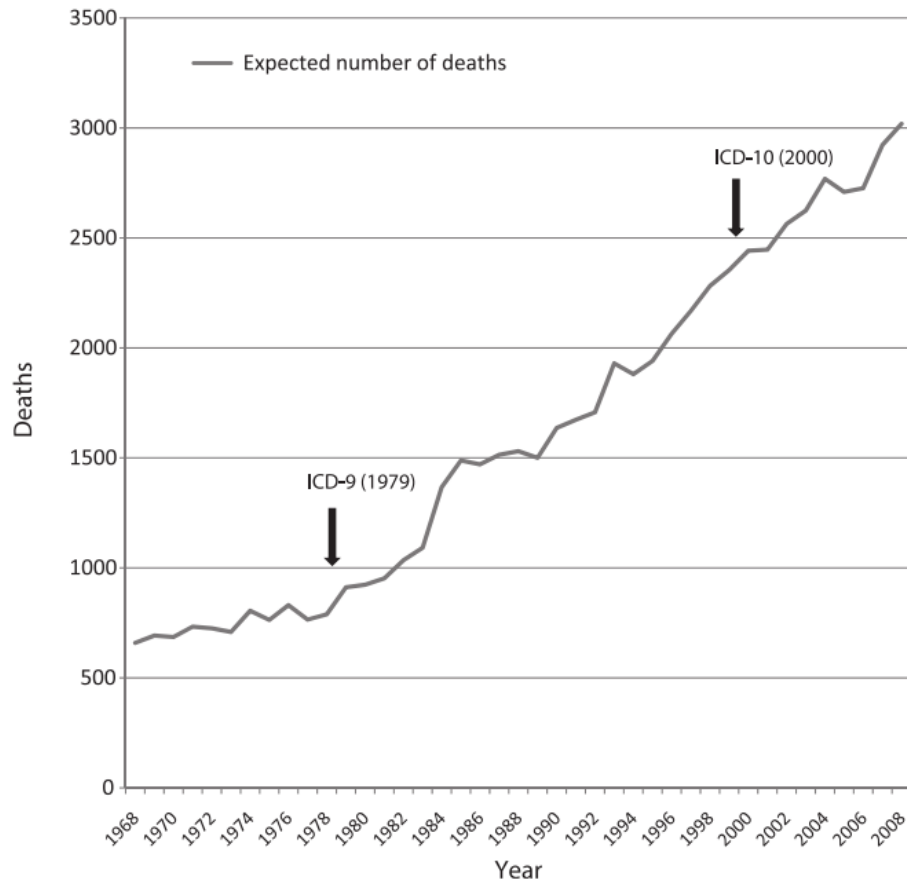
How are ILDs classified?



How is IPF diagnosed?

- IPF is a diagnosis of exclusion
- Identical radiological features in:
 - Connective tissue disease e.g. rheumatoid arthritis
 - Drug side effects e.g. methotrexate
 - Chronic Hypersensitivity Pneumonitis e.g. birdfancier's lung
 - Pneumoconiosis e.g. **asbestosis**
- Some of the conditions above are easier to diagnose eg blood tests, but not for asbestosis, which relies on patient's recollection of asbestos exposures
- No clear guideline on how to estimate a patient's past asbestos exposures

IPF mortality in E+W Navaratnam et al (2011)



“we do not understand what causes IPF-CS, why the incidence is on the rise...”

Figure 1 Estimated number of deaths from idiopathic pulmonary fibrosis clinical syndrome, age standardised to the 2008 population of England and Wales. ICD, International Classification of Diseases.

Why would IPF mortality be rising so rapidly if there is no cause?



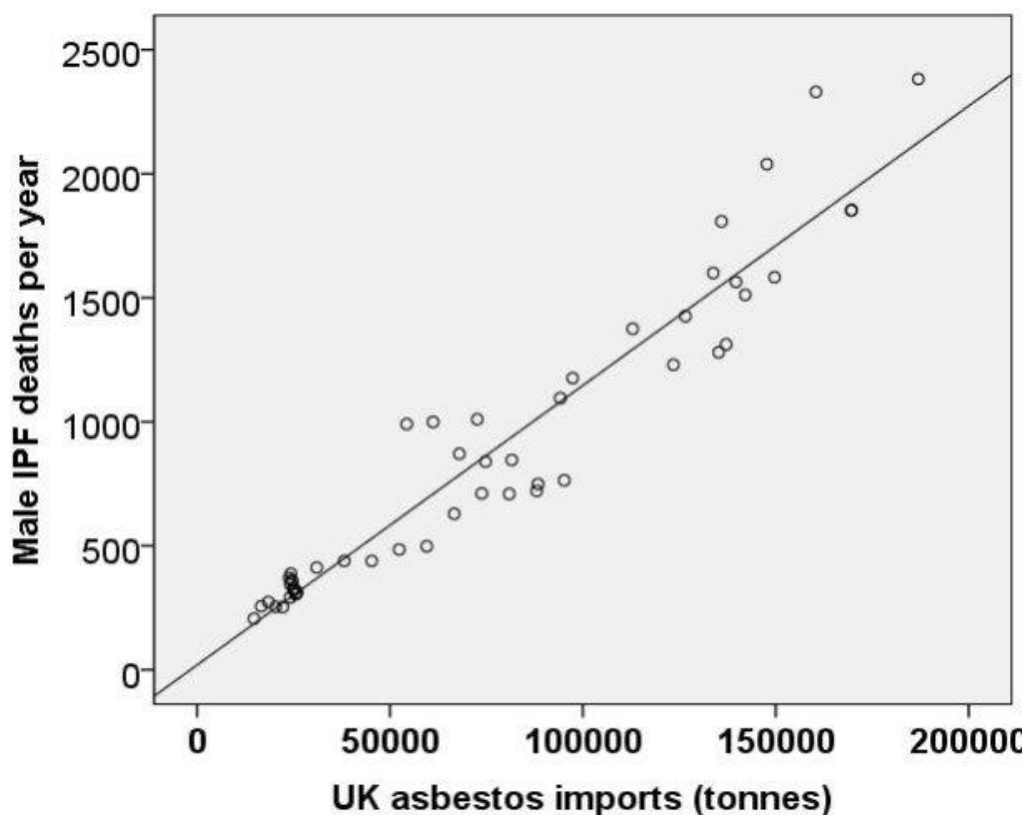
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3. IPF and Asbestos

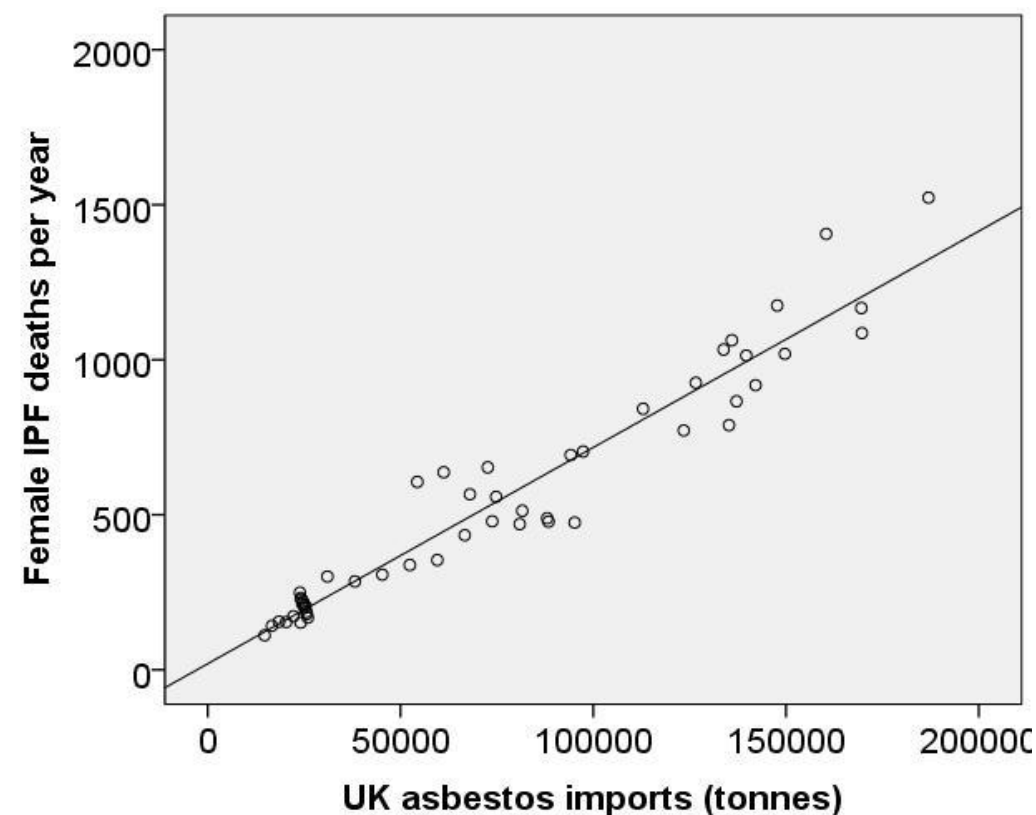
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Number of IPF deaths vs UK Asbestos Imports* Barber (2015)

Male annual deaths 1962-2012
Pearson Coefficient = 0.98



Female annual deaths 1962-2012
Pearson Coefficient = 0.97



IPF and Asbestos: Is there a causation link?

- The unexplained rising mortality in IPF appears similar to the explained rising mortality of mesothelioma Barber (2012)
- Case-control studies linked IPF with wood and metal working, but no link to asbestos exposure Ley (2013)
- BUT occupations linked to IPF risk, have high mortality from an asbestos-related cancer (mesothelioma) Barber (2012)

Could asbestosis be misclassified as IPF?

Comparing IPF and Asbestosis

	IPF	Asbestosis
Condition	Diffuse UIP fibrosis	Diffuse UIP fibrosis
Cause	No known cause	Asbestos
Commoner in smokers?	Yes	Yes
First case occurred in UK	1907	1900
# of cases per year in UK	>5,000 (2010)	985 (2014, IIDB)
Male:Female ratio	~2:1	~10:1
Geographic high-risk areas	Variable, more concentrated in NW, NI, Scotland	Variable, with hotspots (eg shipyards)
Typical age of diagnosis	60-70	60-70
Severity of condition	High: average survival period 3 years after diagnosis	Low-Medium: variable disabling and variable progressive condition

Why is correct diagnosis important to patients?

Compensation

- Asbestosis patients may be eligible, established causation link to asbestos
 - General damages: £12,600 - £88,500 Judicial College (2015)
- IPF patients currently not eligible, no known causes

Treatment

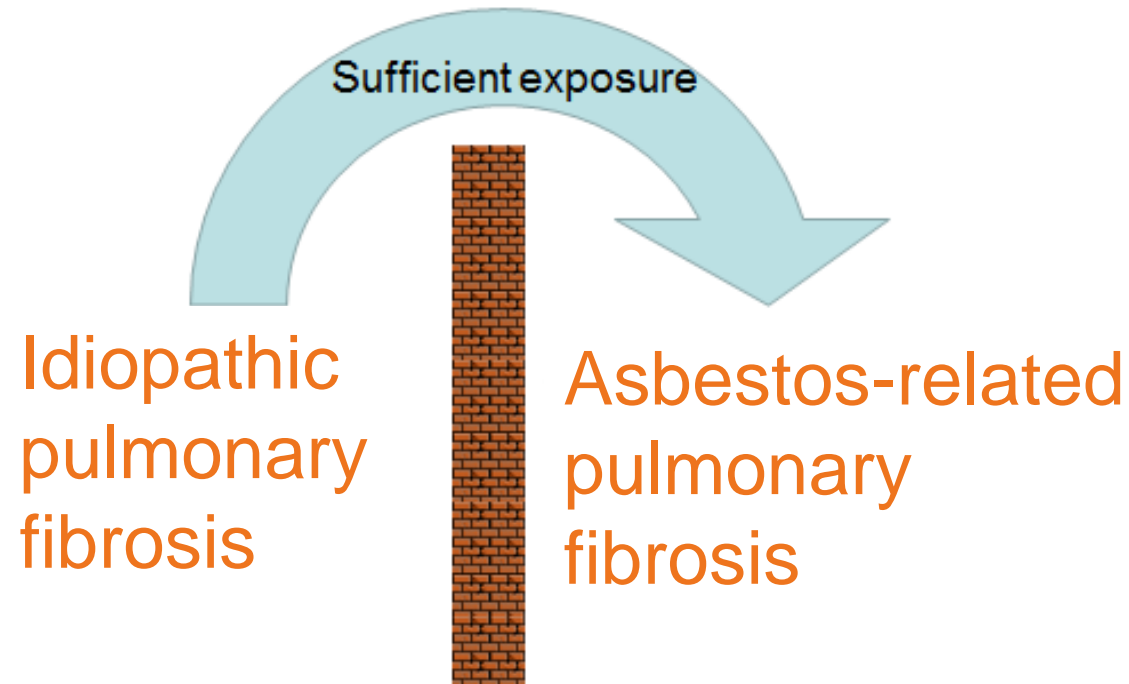
- No treatment currently prescribed for Asbestosis patients
- NHS recently licensed treatment for IPF patients
 - Treatment costs c. £25,000 per year
 - 48% reduction in mortality after 1 year

How easy is it to differentiate IPF from Asbestosis?

- A. History of asbestos exposure
- B. CT scan appearance
- C. Counting fibre burden in lung tissue
- D. Rate of progression

A. History of asbestos exposure: is there a threshold for asbestosis to develop?

Asbestos Exposure Medical/ Legal Threshold in UK
25 fibre/ml-years



A. Is the threshold to develop Asbestosis supported by evidence? ATS 2004

- Asbestosis is commonly associated with prolonged exposure, usually over 10 to 20 years.
- However, short, intense exposures to asbestos, lasting from several months to 1 year or more, can be sufficient to cause asbestosis.
- In one study of former workers from an amosite asbestos insulation factory, that had high levels of asbestos dust, employment for as little as 1 month resulted in a prevalence of 20% of parenchymal opacities 20 years after exposure ceased.

A. Is the threshold to develop Asbestosis supported by evidence? Deng et al 2012

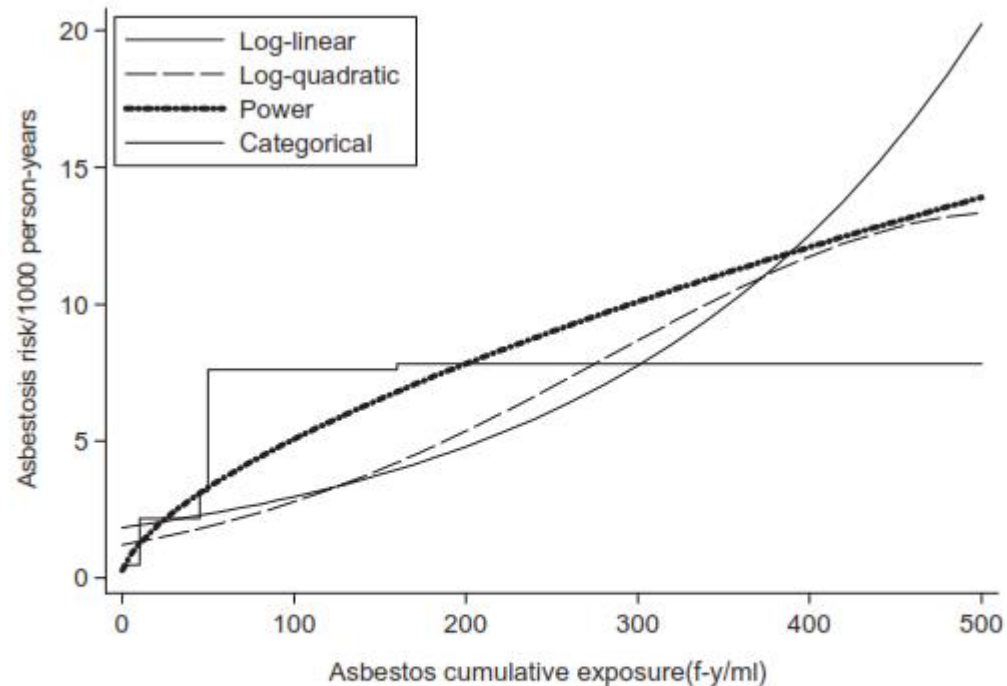


Figure 2 Predicted asbestosis mortality in relation to asbestos exposure in workers aged 50 in 1972–1979, who were also smokers (10-year lag).

Evidence to support a threshold is based on an epidemiological doubling of risk, and not a biological exposure level that is required for disease to occur.

A. Occupational asbestos exposures are often overlooked in UK Peto 2009

- Certain occupations are particularly exposed to asbestos
- Mesothelioma risks within each occupational exposure category were still substantially increased even in men who recalled no substantial asbestos exposure
- Many were exposed indirectly or could not identify the asbestos materials they handled
- The increased risk for “medium-risk” industrial work reflects widespread and often unrecognised contact with asbestos in metal working, electrical trades and assembly line work
- 65% of male and 23% of female controls having worked in occupations that were classified as medium or higher risk

A. Accurately estimating lifetime asbestos exposure is complex and difficult Burgdorf (1999)

Table 2. Risk matrix for historical asbestos exposure in Dutch companies and occupations

Industry/occupation	1946–1955		1956–1965		1966–1975		1976–1985		1986–1995	
	Exp	Pr	Exp	Pr	Exp	Pr	Exp	Pr	Exp	Pr
Primary asbestos industry										
Asbestos insulation	E3	P3	E3	P3	E3	P3		na		na
Asbestos textile	E3	P3	E3	P3	E3	P3	E2	P1		na
Asbestos cement	E3	P3	E3	P3	E3	P3	E2	P2	E1	P1
Asbestos friction materials	E3	P3	E3	P3	E3	P3	E2	P2		na
Asbestos flooring		na		na	E3	P3	E1	P1		na
Asbestos paper and felt	E3	P3	E3	P3	E3	P3	E1	P1	E1	P1
Secondary asbestos industry										
Insulation work	E3	P2	E3	P2	E3	P2	E2	P1	E1	P1
Shipbuilding	E3	P2	E3	P2	E3	P2	E2	P1	E1	P1
Construction	E2	P1	E3	P1	E3	P1	E2	P1	E1	P1
Car service station	E2	P1	E2	P1	E2	P1	E1	P1	E0	P1
Specific occupations										
Loader/sacker	E2	P0	E2	P0	E2	P0	E1	P0	E0	P0
Stripper/demolisher of furnaces & ovens	E3	P2	E3	P2	E3	P2	E2	P1	E1	P1
Engine room worker & stationary engineer	E2	P1	E2	P1	E2	P1	E1	P0	E0	P0
Maintenance worker in power plant	E2	P1	E2	P1	E2	P1	E1	P0	E0	P0
Furnace worker	E2	P2	E2	P2	E2	P2	E1	P1	E0	P0
Electrical fitter	E2	P1	E2	P1	E2	P1	E1	P0	E0	P0
Electrician	E1	P1	E1	P1	E1	P1	E0	P0	E0	P0
Fitter/benchmen, sheet metal worker	E2	P1	E2	P1	E2	P1	E1	P0	E0	P0
Founder, caster	E2	P1	E2	P1	E2	P1	E1	P0	E0	P0

Exp (exposure category): above 5 fibres/cm³ (E3), between 2 to 5 fibres/cm³ (E2), between 0.5 to 2 fibres/cm³ (E1), below 0.5 fibres/cm³ (E0).

Pr (probability of exposure category): each worker exposed (P3), each blue collar worker exposed (P2), specific blue collar workers exposed (P1), only few blue collar workers exposed (P0).

na = not applicable (not present).

An expert system for the evaluation of historical asbestos exposure

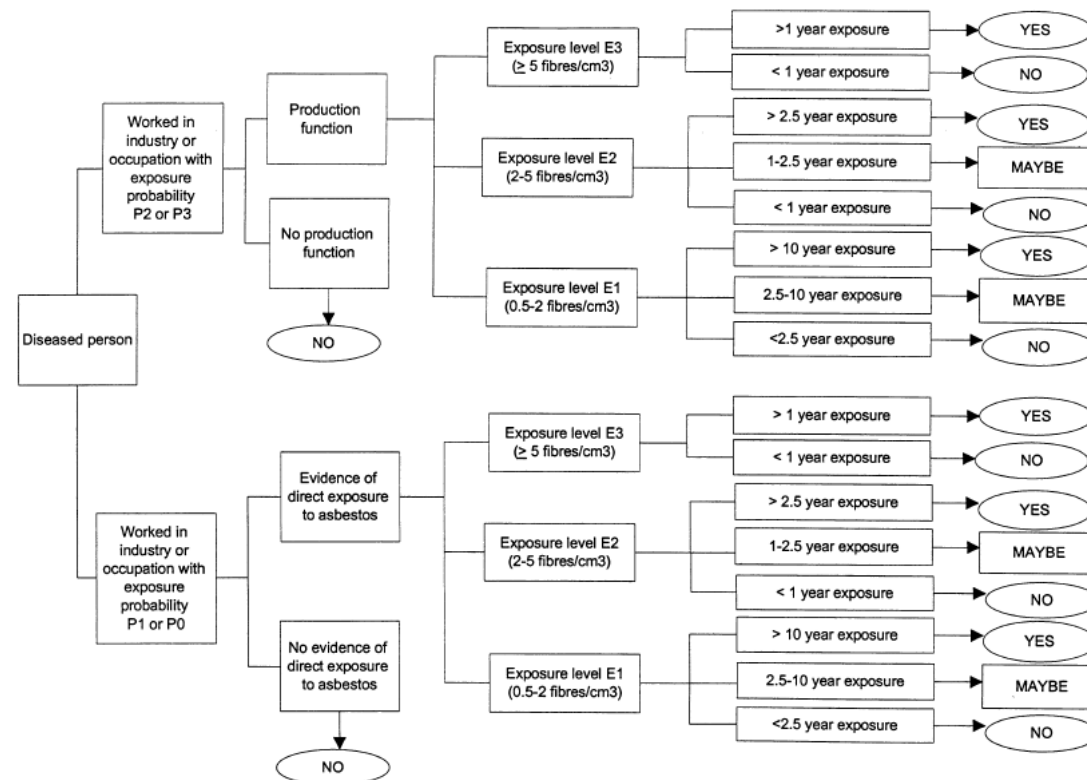


Fig. 1. Stepwise decision tree for historical evaluation of asbestos exposure in ascertainment of asbestosis.

A. Accurately estimating lifetime asbestos exposure is complex and difficult Burgdorf (1999)

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Asbestos textile	E3	P3	E3	P3			P1		na	
Asbestos cement	E3	P3	E3	P3			P2		E1	P1
Asbestos friction materials	E3	P3	E3	P3					na	
Asbestos flooring			na						na	
Asbestos paper and felt	E3	P3								
Secondary asbestos industry										
Insulation work	E3	P2	E3	P2						
Shipbuilding	E3	P2	E3	P2	E3	P1				
Construction	E2	P1	E3	P1	E3	P1				
Car service station	E2	P1	E2	P1	E2	P1				
Specific occupations										
Loader/sacker	E2	P0	E2	P0	E2	P0				
Stripper/demolisher of furnaces & ovens	E3	P2	E3	P2						
Engine room worker & stationary engineer	E2	P1	E2	P1						
Maintenance worker in power plant	E2	P1	E2	P1						
Furnace worker	E2	P2								
Electrical fitter	E2	P1							P0	
Electrician	E1	P1							E0	P0
Fitter/benchmen, sheet metal worker	E2	P1	E2	P1			P0		E0	P0
Founder, caster	E2	P1	E2	P1			P0		E0	P0

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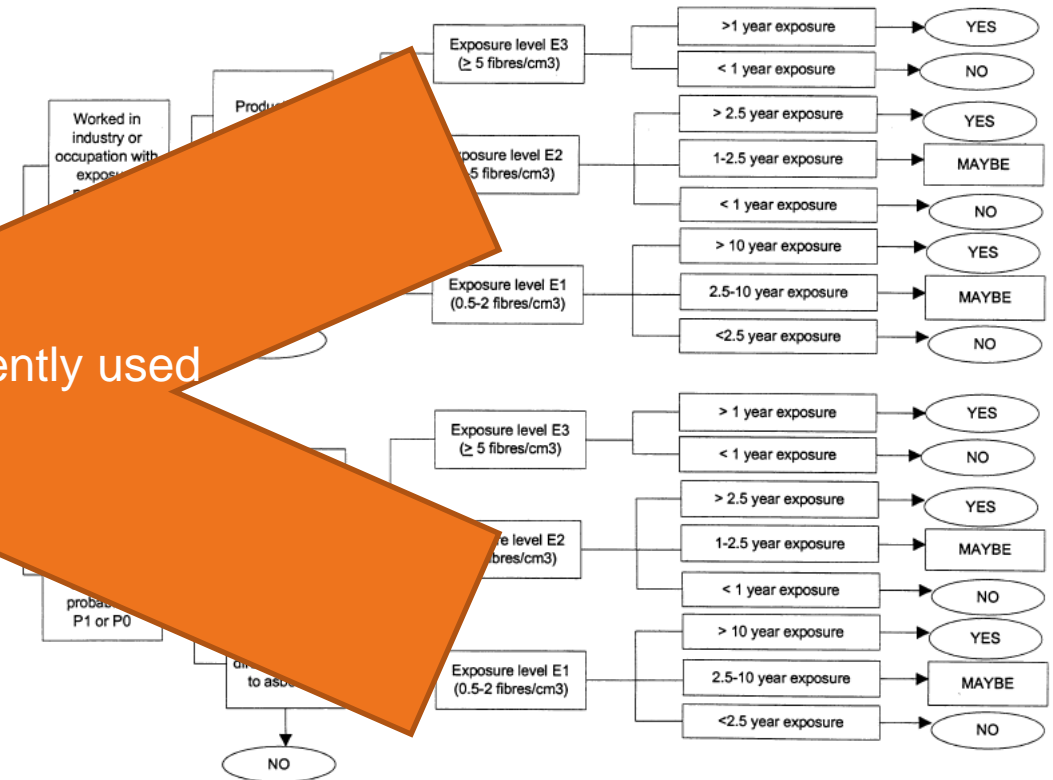


Fig. 1. Stepwise decision tree for historical evaluation of asbestos exposure in ascertainment of asbestosis.

How accurate are UK diagnosis procedures to differentiate IPF from Asbestosis?

Differentiation approach	Accurate approach?	Currently applied?
A. History of asbestos exposure	Potentially, but not as currently applied in UK; history of asbestos exposure often estimated from individuals' recollection	Yes
B. CT scan appearance		
C. Fibre count		
D. Rate of progression		

B. CT Scan Appearance Copley 2003

- The thin-section CT pattern of asbestosis closely resembles that of biopsy-proven UIP (the pattern seen in IPF)
- After adjustment for age, sex, and extent of fibrosis, none of the CT features differed significantly between the patients with asbestosis and those with biopsy-proved UIP

How accurate are UK diagnosis procedures to differentiate IPF from Asbestosis?

Differentiation approach	Accurate approach?	Currently applied?
A. History of asbestos exposure	Potentially, but not as currently applied in UK; history of asbestos exposure often estimated from individuals' recollection	Yes
B. CT scan appearance	No, virtually identical	No
C. Fibre count		
D. Rate of progression		

C. Fibre Counts IIAC 2005

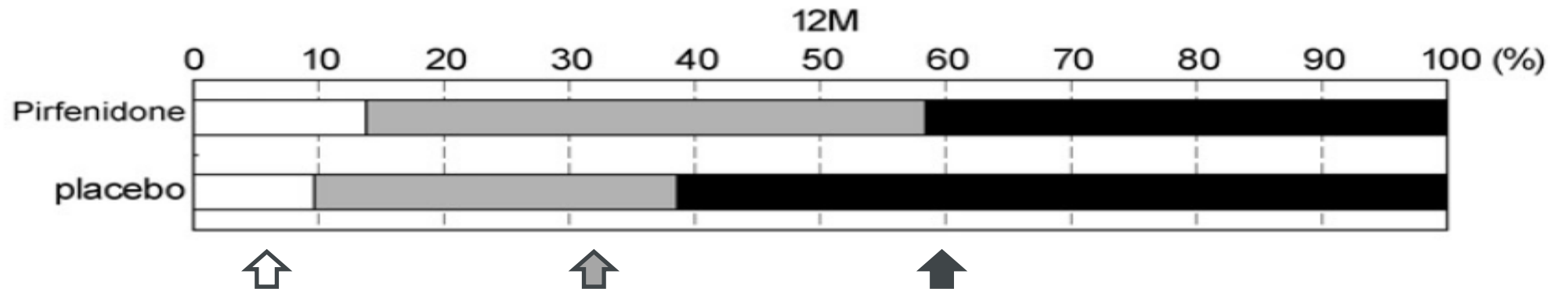
- Biopsy material rarely available in life
- IIAC review (for IIDB) recommend diagnosis based on occupational history not fibre counts
 - Long latency disease
 - T1/2 is years for chrysotile and decades for amphiboles
 - No standardised lab methodology
 - Light microscopy unreliable and misses uncoated fibres
 - More difficult to identify chrysotile even with EM
 - No established UK “normal range”
 - i.e. very difficult (or impossible) to interpret results

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A. History of asbestos exposure	Potentially, but not as currently applied in UK; history of asbestos exposure often estimated from individuals' recollection	Yes
B. CT scan appearance	No, virtually identical	No
C. Fibre count	Potentially, but with limitations and biopsy material rarely available in life	No
D. Rate of progression		

D. Rate of Progression Taniguchi (2011)

- Widely accepted that
 - rapidly progressive disease is expected in IPF
 - slowly progressive or stable disease is typical of asbestosis
- BUT, no head to head studies
- Good evidence that annual rate of progression in IPF is variable



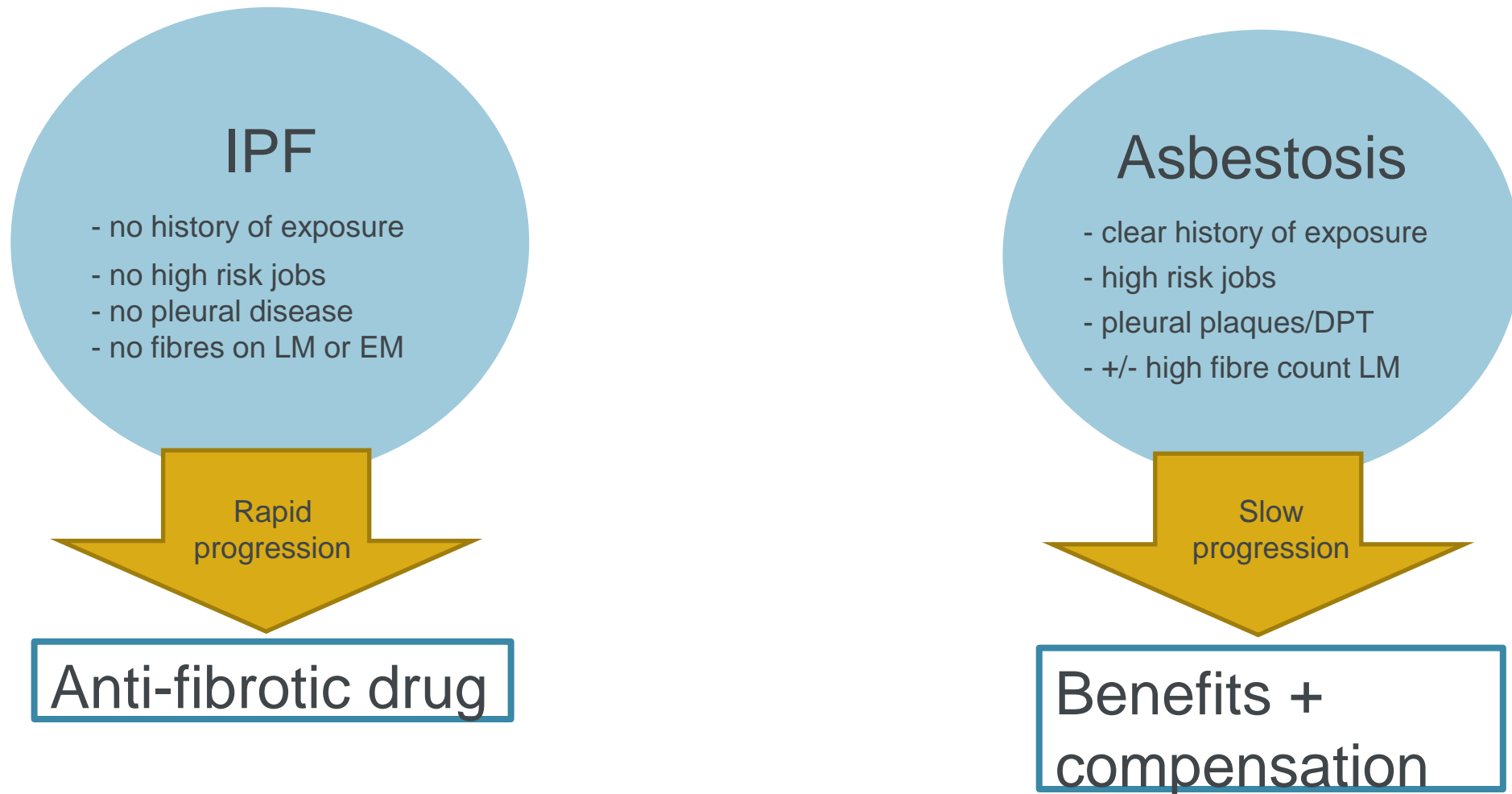
Change in lung function: a) improved $\geq 5\%$ b) stable c) fell by $\geq 5\%$

How accurate are UK diagnosis procedures to differentiate IPF from Asbestosis?

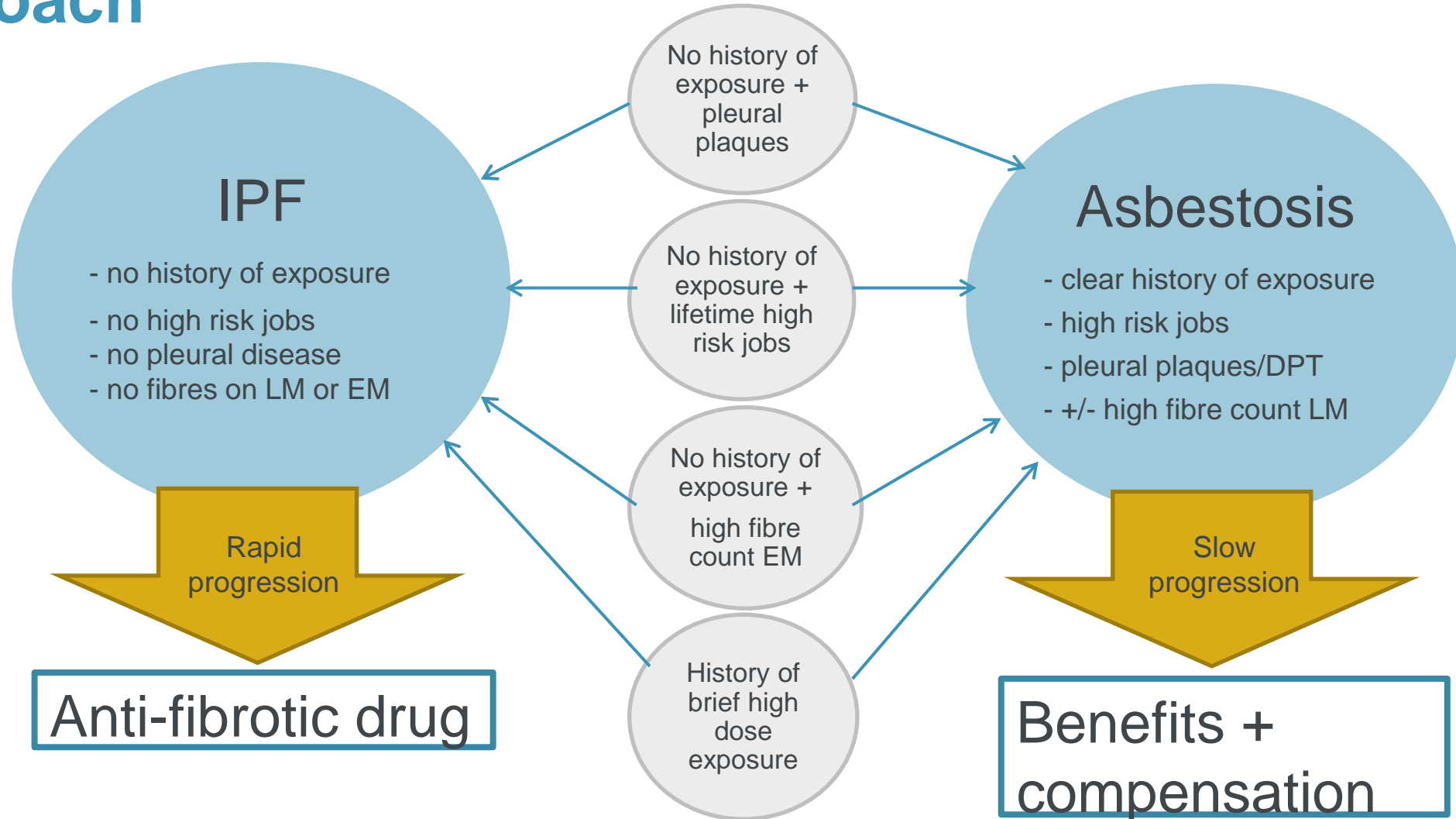
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B. CT scan appearance	No, virtually identical	No
C. Fibre count	Potentially, but with limitations and biopsy material rarely available in life	No
D. Rate of progression	No good evidence to support this	Sometimes

... **probably not very accurate.**

Differentiating IPF from Asbestosis: Current Approach



Cases that could be mis-diagnosed under current approach





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4. Ongoing and Potential Future Research

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Future work

- Potential: A validated approach to estimate lifetime exposure based on job titles in each decade linked to IIDB (Dutch model)
- Ongoing: Better IPF case-control studies using an estimate of life-time asbestos exposures (see next slide)
- Ongoing: Access to anti-fibrotic drugs for UIP based on rate of decline rather than arbitrary name chosen
 - Trial study currently recruiting patients with progressive asbestosis for treatment

Is occupational asbestos exposure a risk factor for “IPF”?

- Wellcome Trust Funded 3-year case-control study
- “Idiopathic Pulmonary Fibrosis Job Exposure Study”
- National recruitment, multi-centre
- Collaboration with Imperial College London
- Lifetime occupational histories of patients with IPF versus controls, genetic polymorphisms



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5. Potential Implications on the Insurance Market

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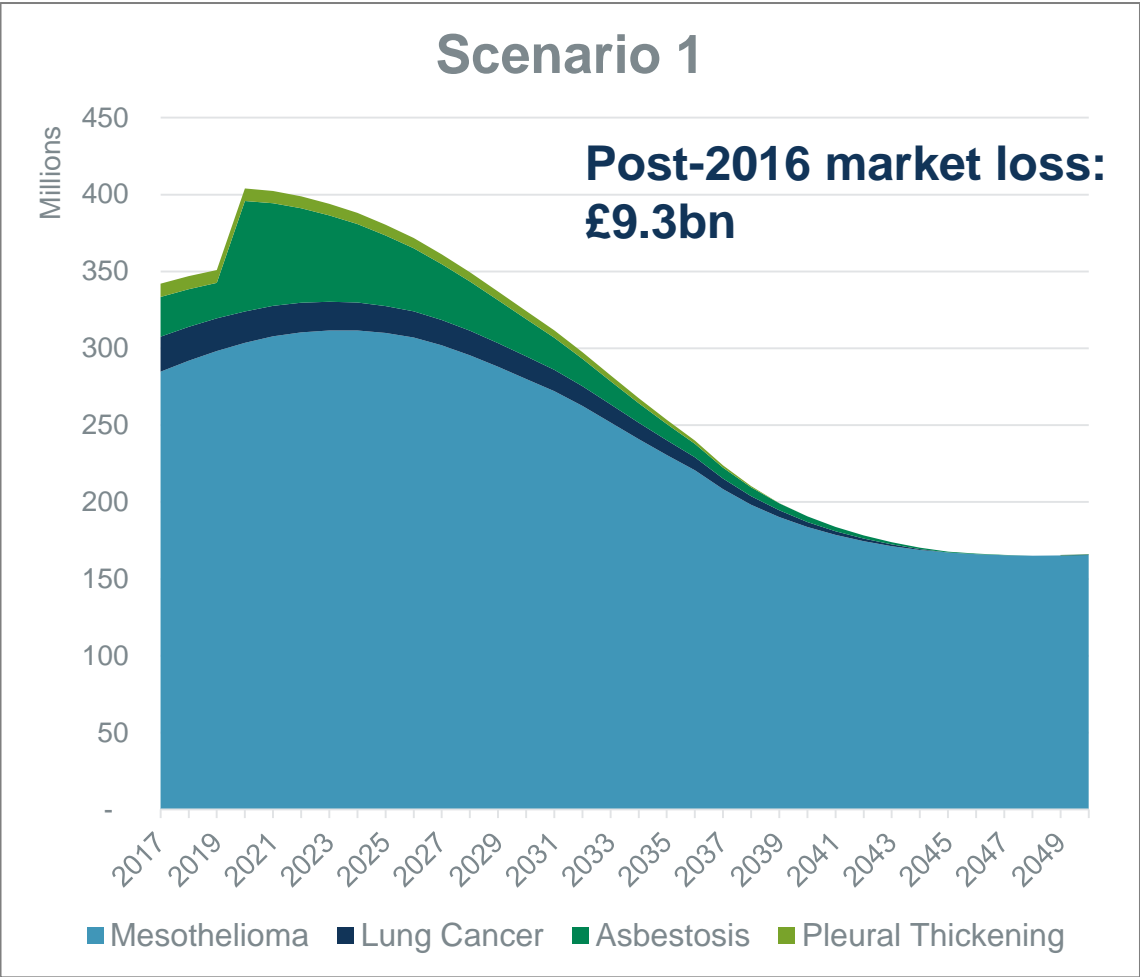
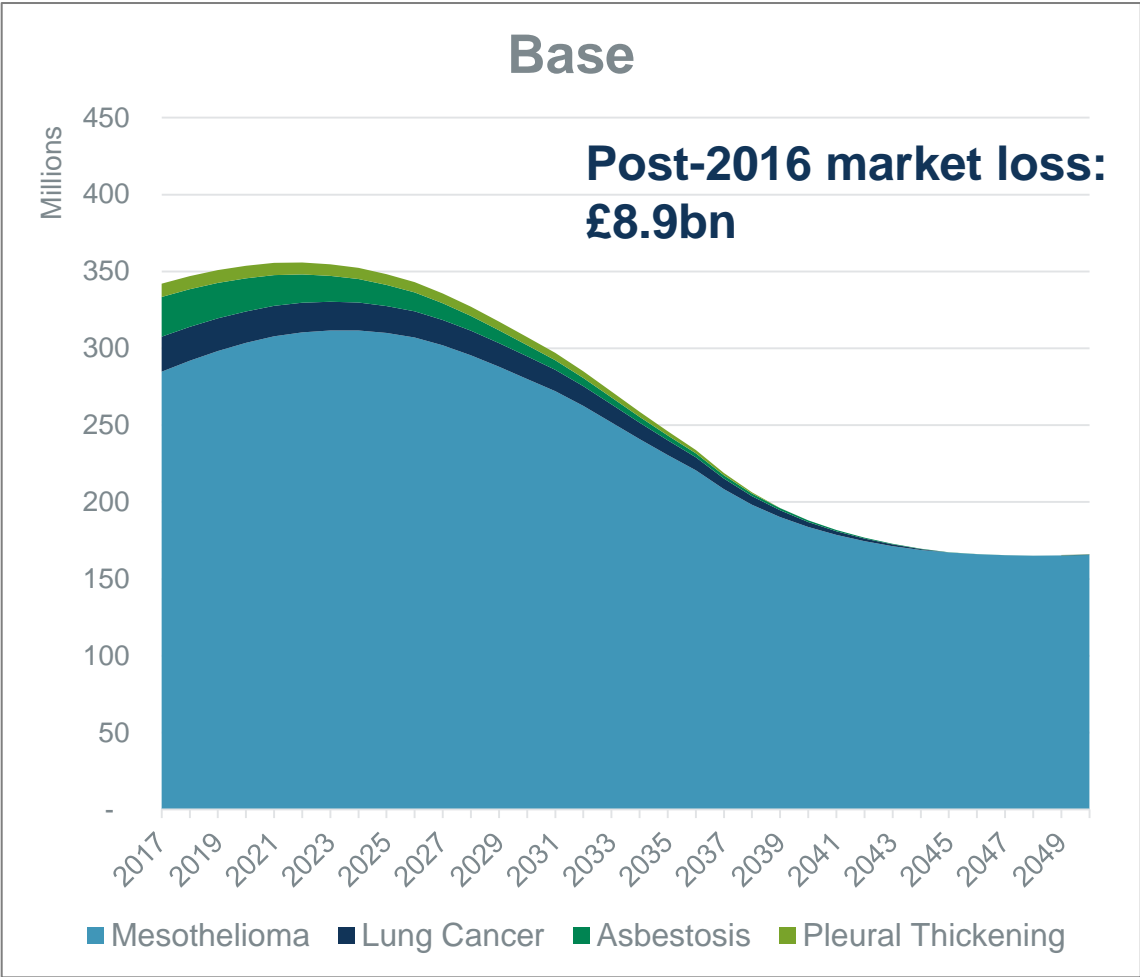
Questions raised

- Early days for research, lots of uncertainty
- Unanswered questions include:
 - Is there a causal link between asbestos and IPF?
 - If there is a causal link, is it due to occupational exposures or general environmental exposures?
 - Are there other contributing/ confounding factors for IPF cases (eg smoking, general industrialisation)?
 - Are most IPF cases in the UK mis-diagnosed asbestosis?
 - Is current IPF treatment effective on asbestosis?

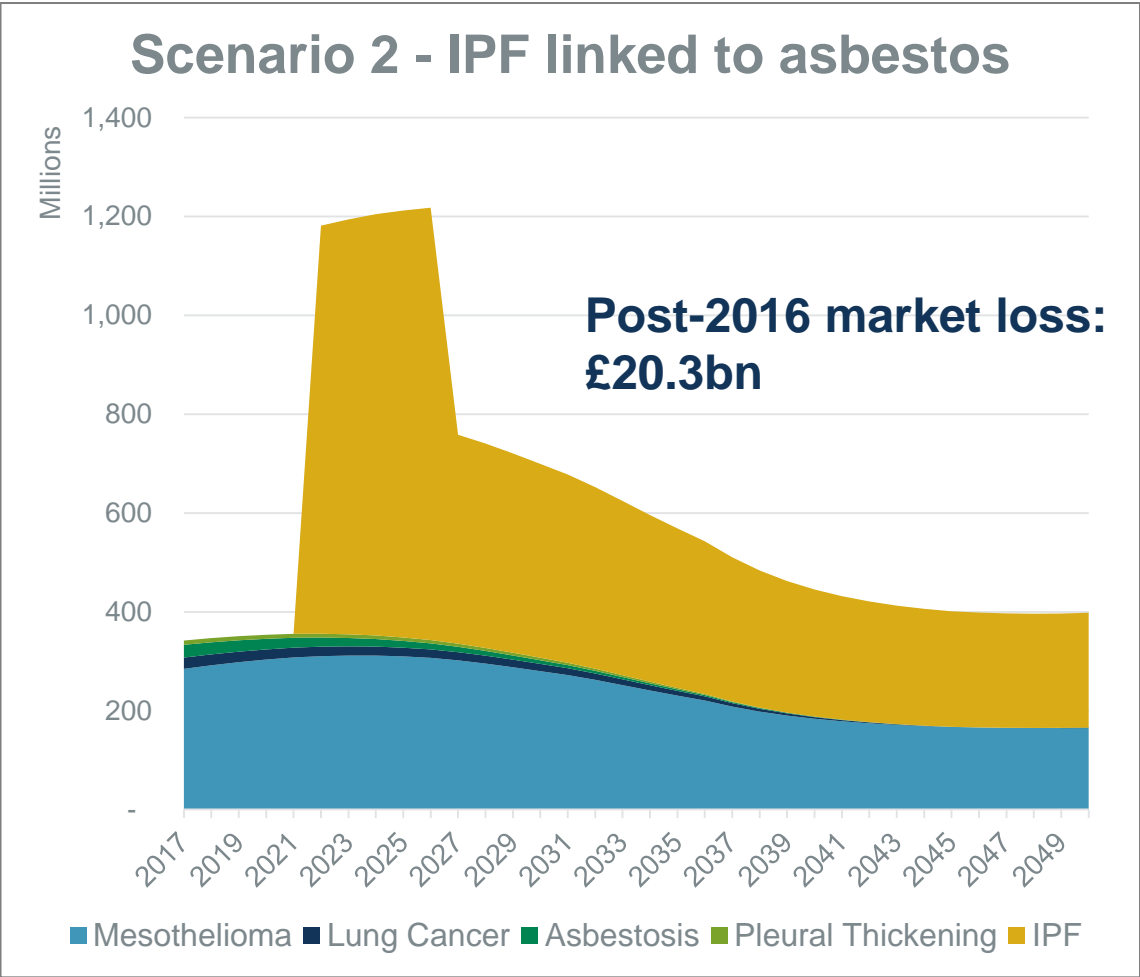
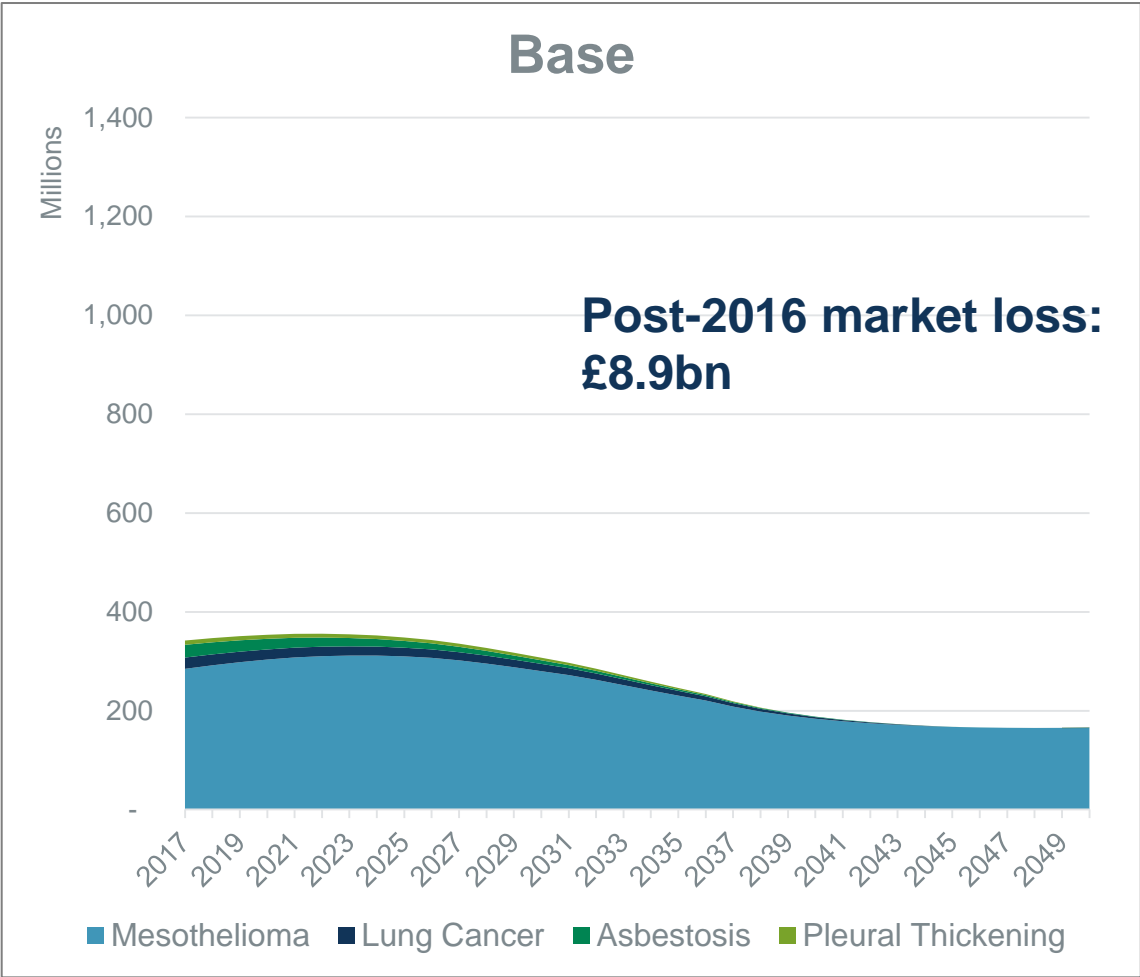
Potential Scenarios

- Illustrative, not intended to be exhaustive or precise
- Projections based on AWP 2009 (Scenario 23 for mesothelioma, Scenario 2B for non-meso)
- **Base:** no casual link between IPF and asbestos
- **Scenario 1:** IPF treatments proven to be effective for asbestosis in 2020
 - 5 years' treatment for 50% of asbestosis cases from 2020, in addition to existing costs
- **Scenario 2:** causal link between IPF and asbestos established in 2022
 - Average cost per claim as per mesothelioma
 - Number of IPF deaths = 1.4 x total number of mesothelioma deaths
 - Claims to death ratio 1/3rd of mesothelioma for 2009-2021, as per mesothelioma thereafter

Scenario 1: IPF treatment prescribed for Asbestosis



Scenario 2: IPF linked to asbestos in 5 years' time





Questions



Comments

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4	Barber CM, Wiggans RE, Young C, Fishwick D. (2016)	UK asbestos imports and mortality due to idiopathic pulmonary fibrosis	Occup Med (Lond). 2016 Mar;66(2) doi: 10.1093/occmed/kqv142 Epub 2015 Oct 28	106-11
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10	Ley B, Collard HR. (2013)	Epidemiology of idiopathic pulmonary fibrosis	Clin Epidemiol. 2013 Nov 25;5 doi: 10.2147/CLEP.S54815	483-92
11	Navaratnam V, Fleming KM, West J, Smith CJ et al. (2011)	The rising incidence of idiopathic pulmonary fibrosis in the U.K.	Thorax. 2011 Jun;66(6) doi: 10.1136/thx.2010.148031 Epub 2011 Apr 27	462-7
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13	Taniguchi H, Kondoh Y, Ebina M et al.; Pirfenidone Clinical Study Group in Japan (2011)	The clinical significance of 5% change in vital capacity in patients with idiopathic pulmonary fibrosis: extended analysis of the pirfenidone trial	Respir Res. 2011 Jul 15;12:93 doi: 10.1186/1465-9921-12-93	93