Surgical lung biopsy for the diagnosis of interstitial lung disease in England: 1997-2008

Supplementary material

Additional methods

Selection of codes for interstitial lung disease

ICD-10 codes

- J84.1 Other interstitial pulmonary diseases with fibrosis
- J84.8 Other specified interstitial pulmonary diseases
- J84.9 interstitial pulmonary disease, unspecified
- D86.0 sarcoidosis of lung
- J67.9 hypersensitivity pneumonitis due to unspecified organic dust
- J99.0 rheumatoid lung disease
- J99.1 respiratory disorders in other diffuse connective tissue disorders
- <u>ICD-9 codes</u> used for initial search, but not required as admissions prior to 1997 featuring these codes were dropped
- 515 Post-inflammatory pulmonary fibrosis
- 5163 Idiopathic fibrosing alveolitis
- 517.2 Lung involvement in systemic sclerosis
- 517.8 lung involvement in other diseases classified elsewhere

Exclusion of patients where surgical lung biopsy was not the primary operation coded

The Hospital Episodes Statistics dataset contains records for up to 24 procedures carried out during an inpatient episode. The first operation record is generally the main or most resource intensive procedure. We initially identified all patients with *any* record for a surgical lung biopsy. In the vast majority of cases this was coded as the primary operation, but in some cases it was coded as the second or subsequent operation. In some of these cases, it was clear that surgical lung biopsy was the most significant procedure, despite not being coded in the primary position.

All patients where surgical lung biopsy was not listed as the primary operation were therefore handreviewed by two clinicians to determine if it seemed to be the main procedure or not. Those records where the surgical lung biopsy was likely to be the main procedure were retained, as were those where the surgical lung biopsy seemed a reasonable 'secondary' procedure - for example, alongside a cardiac operation, where a lung biopsy might be performed at the same time. Any cases where there was doubt about the nature of the biopsy - for example, where the primary code was for biopsy of pleural lesion - were excluded.

Details of distinction between 'elective' and 'non-elective' operations

The Hospital Episodes Statistics dataset contains a variable specifying whether procedures are elective or non-elective ('admission method') but this was not available in our extract. We therefore used the 'waiting time' variable as a surrogate: this gives the length of time between the 'decision to admit' and the actual admission date. This variable was only valid for elective admissions: when it was missing, we assumed this was a non-elective admission. These records either had no valid decision-to-admit date or a decision-to-admit date that was identical to the admission date.

Figure E1

How to calculate the updated Charlson score (used with permission of Oxford University Press).

Co-morbidity	Score
Chronic pulmonary disease	1
Rheumatologic disease	1
Renal disease	1
Diabetes with chronic complications	1
Congestive heart failure	2
Dementia	2
Mild liver disease*	2
Hemiplegia or paraplegia	2
Any malignancy†	2
(including leukaemia and lymphoma)	
Moderate or severe liver disease*	4
AIDS/HIV	4
Metastatic solid tumour†	6

^{*}Patients can score for either 'mild liver disease' or 'moderate to severe liver disease'

Quan H et al. Updating and Validating the Charlson Comorbidity Index and Score for Risk Adjustment in Hospital Discharge Abstracts Using Data from 6 Countries. Am J Epidemiol 2011; 173: 676-682

[†]Patients can score for either 'any malignancy' or 'metastatic solid tumour'

Additional results

Table E1 - Number of biopsies per region

Region	Number of	Person-years*	Biopsies per	Crude incidence of
	cases (%)		100,000	IPF per 100,000
			population	
East Midlands	136 (4.8)	51,073,100	0.27	3.92
East of England	378 (13.4)	65,629,300	0.58	4.75
London	356 (12.6)	88,620,000	0.40	3.68
North East	154 (5.5)	30,615,400	0.50	5.66
North West	315 (11.2)	82,006,200	0.38	5.76
South East	307 (10.9)	97,228,900	0.32	<i>3.55</i>
South West	446 (15.8)	60,020,800	0.74	5.89
West Midlands	266 (9.4)	64,073,400	0.42	4.77
Yorkshire & Humber	414 (14.7)	60,501,700	0.68	3.52
Other / Unknown †	48 (1.7)	-	-	-
OVERALL	2,820 (100)	599,768,800	0.47	4.6‡

^{*}Person-years: this was calculated by adding together mid-year population estimates for each region for each year from 1997-2008, rounded to the nearest hundred persons – for example, the mid-year population estimate for the East Midlands for 1997 was 4.1 million, rising to 4.4 million in 2008, giving a cumulative total of 51 million person-years as shown above. Population statistics from the Office of National Statistics, accessed November 2015 from http://www.ons.gov.uk/ons/publications/re-reference-tables.html?edition=tcm%3A77-162632 and http://www.ons.gov.uk/ons/publications/re-reference-tables.html?edition=tcm%3A77-315018.

Biopsies per 100,000 calculated by dividing cases by person-years for each region, then multiplying by 100,000.

^{† &#}x27;Other' includes patients with a postcode from Scotland or Wales who attended English hospitals.

[‡] Overall incidence across *United Kingdom* (ie including Scotland/Wales/N Ireland). Data from Gribbin *et al* (2006) Incidence and mortality of idiopathic pulmonary fibrosis and sarcoidosis in the UK. Thorax. 61:980-985. doi: 10.1136/thx.2006.062836.

Table E2- Multivariable analysis – associations with death within 30 days of surgical lung biopsy for interstitial lung disease

Variables	Cases	Deaths	Unadjusted Odds Ratio (95% CI)	<i>p</i> value	Adjusted Odds Ratio (95% CI)	<i>p</i> value
Sex						
Female	1,274	24	1.00		1.00	
Male	1,546	44	1.53 (0.92-2.52)	0.094	1.40 (0.83-2.35)	0.205
Age						
<44 yrs	576	6	1.00	<0.001	1.00	< 0.001
45-54 yrs	636	12	1.83 (0.68-4.90)	(p for	1.64 (0.61-4.43)	(p for
55-64 yrs	843	16	1.84 (0.71-4.73)	trend	1.53 (0.59-3.97)	trend)
65-74 yrs	588	21	3.52 (1.41-8.78)		2.96 (1.18-7.46)	
>74 yrs	177	13	7.53 (2.82-20.12)		5.23 (1.90-14.39)	
Updated Charlso	n score					
. 0	1,947	45	1.00	0.042	1.00	0.039
1	717	13	0.78 (0.42-1.46)	(p for	0.85 (0.43-1.68)	(p for
2	116	6	2.31 (0.96-5.52)	trend)	1.93 (0.79-4.75)	trend)
3 or more	40	*	4.70 (1.60-13.75)		4.80 (1.58-14.54)	
IMD score	2,760	67	1.00 (0.98-1.02)	0.985	1.00 (0.99-1.02)	0.841
Type of operation	1					
VATS	703	11	1.00	0.154	1.00	0.181
Open	362	12	2.16 (0.94-4.94)		2.14 (0.89-5.15)	
Unclear or	1,755	45	1.66 (0.85-3.22)		1.72 (0.85-3.49)	
not specified						
Provisional diagr	nosis					
J84.1	1,433	47	1.00	0.142	1.00	0.499
J84.9	812	15	0.56 (0.31-1.00)		0.66 (0.36-1.20)	
J84.8	99	*	0.30 (0.04-2.20)		0.37 (0.05-2.75)	
RA-ILD	16	0	-		-	
CTD-ILD	38	*	1.64 (0.38-7.01)		1.48 (0.34-6.55)	
HP	162	*	0.56 (0.17-1.81)		0.84 (0.23-3.05)	
Sarcoidosis	260	0	-		-	

^{&#}x27;*' in this table means a number between 1 and 5 – small numbers hidden to aid confidentiality. Higher updated Charlson score reflects greater degree of co-morbidity.

Table E3— Multivariable analysis – associations with in-hospital death following surgical lung biopsy for interstitial lung disease

Variables	Cases	Deaths	Unadjusted Odds Ratio (95% CI)	<i>p</i> value	Adjusted Odds Ratio (95% CI)	p value		
Sex								
Female	1,274	17	1.00		1.00			
Male	1,546	30	1.46 (0.80-2.67)	0.207	1.29 (0.70-2.38)	0.414		
Age								
<44 yrs	576	*	1.00	0.002	1.00	0.006		
45-54 yrs	636	9	2.05 (0.63-6.70)	(p for	1.91 (0.58-6.31)	(p for		
55-64 yrs	843	13	2.24 (0.73-6.90)	trend	1.98 (0.64-6.15)	trend)		
65-74 yrs	588	14	3.49 (1.14-10.66)		3.10 (1.00-9.58)			
>74 yrs	177	7	5.89 (1.70-20.35)		4.85 (1.37-17.11)			
Updated Charlson	n score							
0	1,947	25	1.00	0.002	1.00	0.002		
1	717	14	1.53 (0.79-2.96)	(p for	1.83 (0.91-3.68)	(p for		
2	116	*	3.46 (1.30-9.22)	trend	2.94 (1.08-8.01)	trend)		
3 or more	40	*	6.23 (1.80-21.56)		6.51 (1.82-23.26)			
IMD score	2,760	47	1.00 (0.98-1.02)	0.876	1.00 (0.98-1.02)	0.803		
Type of operation	1							
VATS	703	*	1.00	0.011	1.00	0.025		
Open	362	9	4.46 (1.36-14.57)		3.89 (1.16-13.06)			
Unclear or	1,755	34	3.45 (1.22-9.76)		3.31 (1.15-9.51)			
not specified								
Provisional diagn	osis							
J84.1	1,433	34	1.00	0.214	1.00	0.508		
J84.9	812	9	0.46 (0.22-0.97)		0.57 (0.27-1.21)			
J84.8	99	*	0.42 (0.06-3.10)		0.52 (0.07-3.86)			
RA-ILD	16	0	-		-			
CTD-ILD	38	*	1.11 (0.15-8.34)		0.88 (0.11-6.75)			
HP Corporidacia	162		0.51 (0.12-2.16)		0.47 (0.10-2.13)			
Sarcoidosis	260	0	-		-			

^{&#}x27;*' in this table means a number between 1 and 5 – small numbers hidden to aid confidentiality. Higher updated Charlson score reflects greater degree of co-morbidity.

Table E4- Multivariable analysis – associations with death within 90 days of surgical lung biopsy for interstitial lung disease – elective patients only

		Deaths	Unadjusted Odds Ratio (95% CI)	<i>p</i> value	Adjusted Odds Ratio (95% CI)	p value
Sex						
Female	1,027	23	1.00		1.00	
Male	1,250	40	1.44 (0.86-2.43)	0.161	1.31 (0.77-2.23)	0.321
Age						
	444	8	1.00	0.169	1.00	0.408
45-54 yrs	521	16	1.73 (0.73-4.07)	(p for	1.42 (0.59-3.41)	(p for
55-64 yrs	702	20	1.60 (0.70-3.66)	trend	1.32 (0.57-3.05)	trend)
65-74 yrs	482	12	1.39 (0.56-3.44)		1.12 (0.45-2.79)	
>74 yrs	128	7	3.15 (1.12-8.87)		2.33 (0.81-6.68)	
Updated Charlson	score					
. 0	1,617	43	1.00	0.112	1.00	0.036
1	553	14	0.95 (0.52-1.75)	(p for	1.21 (0.63-2.33)	(p for
2	79	*	0.95 (0.23-4.00)	trend	1.00 (0.24-4.27)	trend)
3 or more	28	*	6.10 (2.03-18.35)		7.20 (2.28-22.75)	
IMD score	2,226	62	0.99 (0.97-1.01)	0.288	0.99 (0.97-1.01)	0.223
Type of operation						
	583	8	1.00	0.036	1.00	0.039
Open	275	8	2.15 (0.80-5.80)		1.87 (0.65-5.33)	
	1,419	47	2.46 (1.16-5.24)		2.49 (1.15-5.38)	
not specified						
Provisional diagnos	sis					
J84.1	1,151	40	1.00	0.411	1.00	0.568
J84.9	664	20	0.86 (0.50-1.49)		0.94 (0.53-1.66)	
J84.8	81	*	0.35 (0.05-2.56)		0.41 (0.06-3.05)	
	12	0	-		-	
	26	0	-		-	
	125	*	0.45 (0.11-1.89)		0.47 (0.10-2.15)	
Sarcoidosis	218	0	-		-	

^{**} in this table means a number between 1 and 5 – small numbers hidden to aid confidentiality. Higher updated Charlson score reflects greater degree of co-morbidity.

For details on the distinction between 'elective' and 'non-elective' operations, see Additional Methods section.

Table E5- Multivariable analysis – associations with death within 30 days of surgical lung biopsy for interstitial lung disease – elective patients only

Variables	Cases	Deaths	Unadjusted Odds Ratio (95% CI)	<i>p</i> value	Adjusted Odds Ratio (95% CI)	<i>p</i> value			
Sex									
Female	1,027	13	1.00		1.00				
Male	1,250	21	1.33 (0.66-2.67)	0.415	1.31 (0.64-2.67)	0.456			
Age									
<44 yrs	444	*	1.00	0.552	1.00	0.860			
45-54 yrs	521	11	2.37 (0.75-7.50)	(p for	2.09 (0.65-6.67)	(p for			
55-64 yrs	702	10	1.59 (0.50-5.10)	trend	1.31 (0.41-4.25)	trend)			
65-74 yrs	482	*	1.15 (0.31-4.32)		0.94 (0.25-3.58)	ŕ			
>74 yrs	128	*	3.55 (0.87-14.39)		2.74 (0.66-11.42)				
Updated Charlson	1 score								
0	1,617	22	1.00	0.064	1.00	0.046			
1	553	8	1.06 (0.47-2.40)	(p for	1.15 (0.47-2.84)	(p for			
2	79	*	0.93 (0.12-6.98)	trend	0.96 (0.13-7.31)	trend)			
3 or more	28	*	8.70 (2.44-30.96)		9.33 (2.50-34.85)	ŕ			
IMD score	2,226	34	0.99 (0.97-1.02)	0.609	0.99 (0.97-1.02)	0.476			
Type of operation	1								
VATS	583	*	1.00	0.279	1.00	0.281			
Open	275	*	1.71 (0.45-6.40)		1.76 (0.46-6.84)				
Unclear or	1,419	25	2.07 (0.79-5.44)		2.11 (0.79-5.66)				
not specified									
Provisional diagn	osis								
J84.1	1,151	20	1.00	0.987	1.00	0.995			
J84.9	664	11	0.95 (0.45-2.00)		1.09 (0.51-2.33)				
J84.8	81	*	0.71 (0.09-5.33)		0.87 (0.11-6.68)				
RA-ILD	12	0	-		-				
CTD-ILD	26	0	-		-				
HP	125	*	0.92 (0.21-3.98)		1.00 (0.20-5.05)				
Sarcoidosis	218	0	-		-				

^{**} in this table means a number between 1 and 5 – small numbers hidden to aid confidentiality. Higher updated Charlson score reflects greater degree of co-morbidity.

For details on the distinction between 'elective' and 'non-elective' operations, see Additional Methods section.

Table E6- Multivariable analysis – associations with in-hospital death following surgical lung biopsy for interstitial lung disease – elective patients only

Variables	Cases	Deaths	Unadjusted Odds Ratio (95% CI)	<i>p</i> value	Adjusted Odds Ratio (95% CI)	<i>p</i> value
Sex						
Female	1,027	10	1.00		1.00	
Male	1,250	12	0.99 (0.42-2.29)	0.974	1.00 (0.42-2.37)	0.998
Age						
<44 yrs	444	*	1.00	0.522	1.00	0.670
45-54 yrs	521	7	3.01 (0.62-14.56)	(p for	2.59 (0.53-12.71)	(p for
55-64 yrs	702	7	2.23 (0.46-10.76)	trend	1.95 (0.40-9.51)	trend)
65-74 yrs	482	*	1.85 (0.34-10.15)		1.54 (0.28-8.59)	,
>74 yrs	128	*	3.51 (0.49-25.15)		3.05 (0.41-22.67)	
Updated Charlson	n score					
. 0	1,617	11	1.00	0.011	1.00	0.007
1	553	8	2.14 (0.86-5.36)	(p for	2.73 (1.04-7.16)	(p for
2	79	*	1.87 (0.24-14.68)	trend	2.04 (0.25-16.34)	trend)
3 or more	28	*	11.23 (2.37-53.21)		11.81 (2.36-59.01)	,
IMD score	2,226	22	1.00 (0.97-1.03)	0.894	0.99 (0.97-1.02)	0.715
Type of operation	1					
, VATS	583	*	1.00	0.102	1.00	0.083
Open	275	*	2.13 (0.30-15.19)		2.15 (0.29-15.85)	
Unclear or	1,419	18	3.73 (0.86-16.14)		4.02 (0.91-17.76)	
not specified						
Provisional diagr	nosis					
J84.1	1,151	14	1.00	0.916	1.00	0.824
J84.9	664	6	0.74 (0.28-1.94)		0.87 (0.33-2.33)	
J84.8	81	*	1.02 (0.13-7.82)		1.21 (0.15-9.59)	
RA-ILD	12	0	-		-	
CTD-ILD	26	0	-		=	
HP	125	*	0.65 (0.09-5.02)		0.41 (0.05-3.43)	
Sarcoidosis	218	0	-		-	

^{&#}x27;*' in this table means a number between 1 and 5 – small numbers hidden to aid confidentiality. Higher updated Charlson score reflects greater degree of co-morbidity.

For details on the distinction between 'elective' and 'non-elective' operations, see Additional Methods section.

Table E7– Multivariable analysis – associations with death within 90 days of surgical lung biopsy for interstitial lung disease – data from 2005-2008 only

Variables	Cases	Deaths	Unadjusted Odds Ratio (95% CI)	<i>p</i> value	Adjusted Odds Ratio (95% CI)	<i>p</i> value
Sex						
Female	568	17	1.00		1.00	
Male	667	23	1.16 (0.61-2.19)	0.652	0.96 (0.49-1.90)	0.905
Age						
<44 yrs	243	*	1.00	0.001	1.00	0.010
45-54 yrs	255	*	0.95 (0.27-3.33)	(p for	0.93 (0.26-3.32)	(p for
55-64 yrs	373	11	1.45 (0.50-4.22)	trend	1.46 (0.49-4.38)	trend)
65-74 yrs	281	9	1.58 (0.52-4.76)		1.50 (0.48-4.69)	,
>74 yrs	83	10	6.52 (2.16-19.69)		4.97 (1,53-16.19)	
Updated Charlson	n score					
0	798	26	1.00	0.192	1.00	0.077
1	366	9	0.75 (0.35-1.61)	(p for	1.05 (0.47-2.31)	(p for
2	45	*	0.67 (0.09-5.09)	trend	0.62 (0.08-4.84)	trend)
3 or more	26	*	5.40 (1.74-16.79)		6.87 (2.02-23.39)	,
IMD score	1,196	39	1.00 (0.97-1.02)	0.733	1.00 (0.97-1.02)	0.819
Type of operation)					
VATS	631	14	1.00	0.071	1.00	0.119
Open	137	8	2.73 (1.12-6.65)		2.60 (1.01-6.71)	
Unclear or	467	18	1.77 (0.87-3.59)		1.74 (0.83-3.67)	
not specified						
Provisional diagn	osis					
J84.1	548	25	1.00	0.128	1.00	0.531
J84.9	459	14	0.66 (0.34-1.28)		0.83 (0.41-1.68)	
J84.8	43	0	-		-	
RA-ILD	*	0	-		-	
CTD-ILD	14	0	-		-	
HP	73	0	-		-	
Sarcoidosis	93	*	0.23 (0.03-1.70)		0.38 (0.05-2.92)	

^{&#}x27;*' in this table means a number between 1 and 5 – small numbers hidden to aid confidentiality. Higher updated Charlson score reflects greater degree of co-morbidity.

Table E8 – Cox regression model for survival following surgical lung biopsy for ILD (multivariable model adjusted for gender, age, updated Charlson score and type of operation)

Variables	Number of deaths / total	Hazard Ratio (95% CI)	p value	
Gender				
Female	331 / 1,274	1.00		
Male	577 / 1,546	1.52 (1.33-1.74)	<0.001	
Age				
<44 yrs	78 / 576	1.00	<0.001	
45-54 yrs	167 / 636	2.14 (1.63-2.80)	(p for trend)	
55-64 yrs	295 / 843	3.17 (2.47-4.07)		
65-74 yrs	263 / 588	4.80 (3.73-6.19)		
>74 yrs	105 / 177	7.27 (5.41-9.77)		
Updated Charlson scor	r e			
0	640 / 1,947	1.00	0.029	
1	200 / 717	0.92 (0.78-1.08)	(p for trend)	
2	48 / 116	1.40 (1.04-1.88)		
3 or more	20 / 40	2.25 (1.44-3.52)		
Type of operation				
VATS	99 / 703	1.00	<0.001	
Open	133 / 362	1.61 (1.23-2.09)		
Unclear or not specified	676 / 1,755	1.57 (1.26-1.96)		

Higher updated Charlson score reflects greater degree of co-morbidity.

VATS: video-assisted thoracoscopic surgery

For type of operation, 'unclear or not specified' mainly reflects older data from before a specific code for VATS was available. These cases are likely to be a combination of open and VATS procedures, with increasing numbers of VATS in later years.

Thoracic Surgical Centres in England

We could not find a clear definitive universal data source for the number of thoracic surgical centres in England, as there are discrepancies between terminology: one National Health Service trust may run two hospitals; should these be counted as one or two centres? We compiled the following list of centres for our raw estimate of average numbers of procedures per centre.

Southwest

Bristol Royal Infirmary Derriford, Plymouth Royal Devon and Exeter

London

Barts and London Chest Royal Brompton & Harefield Imperial - Hammersmith

UCL Guys Kings St George's

Southeast

Southampton General John Radcliffe, Oxford

East of England

Norwich and Norfolk Papworth, Cambridge Essex Cardiothoracic Centre East Midlands

Nottingham City Hospital Glenfield, Leicester

West Midlands

Heart of England, Birmingham New Cross, Wolverhampton University Hospital Coventry and Warwick Royal Stoke, Stoke-on-Trent

Yorkshire and the Humber Northern General, Sheffield

St James's, Leeds Castle Hill, Hull

Northwest

Liverpool Heart and Chest UHSM, Manchester Victoria Hospital, Blackpool

Northeast

Freeman, Newcastle James Cook, Middlesborough