

## Mesothelioma

### Case numbers and cancer sites

Mesothelioma is a rare cancer of the thin lining that mainly covers the lungs and abdominal cavity. An average of 24 cases of mesothelioma was diagnosed per year in Ireland between 1994 and 2010 (Table 1), representing less than 0.2% of all invasive cancers. Over 5 times more frequently diagnosed in men than in women, the main risk factor for mesothelioma is asbestos, largely ascribed to work related exposure in male dominated occupations. It has been estimated that 97% of male and 82.5% of female mesothelioma cases in the UK in 2010 were attributable to occupational exposure.<sup>1</sup> Although information on Irish patient occupation is very incomplete and is unknown for approximately half of all patients, it is worth noting that for those patients with occupational data, 49% of male mesothelioma patients had an occupation in construction, and related trades such as electrical, metal and woodworking, compared to 20% of all male cancer patients. Secondary exposure to asbestos is more probable in women, who are less likely to have direct work-related exposure. 90% of female mesothelioma patients were, or had been, married compared to 81% of female lung cancer patients (where secondary exposure to tobacco is also an important risk factor) and 77% of all female cancer patients.

94% of all male cases and 75% of female cases in Ireland were mesothelioma of the pleura (Table 1). Other sites included the peritoneum and the lining of reproductive organs. The remainder of this report focuses on pleural mesothelioma.

**Table 1. Annual average number of mesothelioma and percentage distribution by site, 1994-2010**

	Females	Males	Total
annual average, all cases	4	21	24
pleura	75%	94%	91%
peritoneum	12%	3%	5%
other specified sites*	5%	2%	3%
unknown primary site	8%	1%	2%

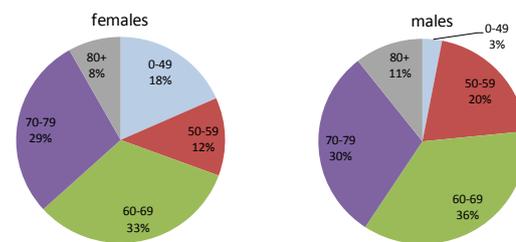
\*lining of reproductive organs/ ill-defined sites

Over 97% of all pleural mesotheliomas were pathologically diagnosed (90% histologically and 7% through cytological examination). The majority of cases were of unspecified subtype (75%), 18% were epithelioid, 5% biphasic and 2% sarcomatoid subtypes.

### Age profile

The majority of pleural mesothelioma patients were between the ages of 60 and 80 when diagnosed, with roughly one third of patients in their 60s and one third in their 70s; this was similar for males and females (Figure 1). 18% of females were aged under 50 at diagnosis compared to just 3% of male patients. Only 10% of all patients were aged 80 or older.

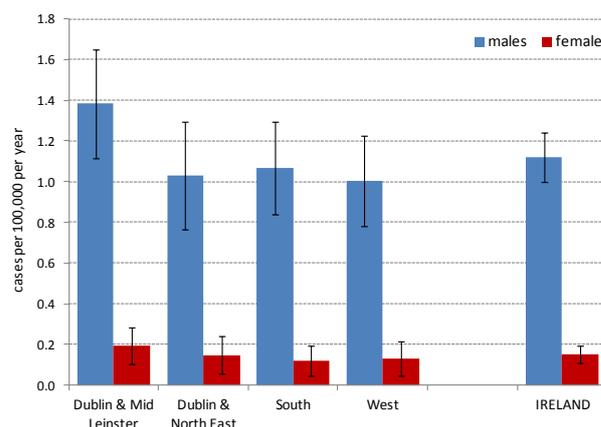
**Figure 1. Age distribution of pleural mesothelioma, females & males, 1994-2010**



### Geographic distribution

The overall incidence of pleural mesothelioma in Ireland was 1.1 cases per 100,000 in men and 0.15 in women per year. Incidence was highest in the Dublin & Mid Leinster area, although this was not statistically significant (Figure 2). Rates in the other 3 HSE regions were about 25% lower.

**Figure 2. Incidence of pleural mesothelioma by HSE region of patient residence, 1994-2010**



Male incidence rates were 31% higher in the most socio-economically deprived areas compared to the least deprived regions (Table 2). However a greater and statistically significant difference was noted between patients living in urban or rural areas, urban dwellers having 49% higher incidence. This may reflect higher proportions of manual workers in construction and related fields in urban populations.

**Table 2. Incidence of pleural mesothelioma in male patients by deprivation index (DI)<sup>2</sup> & urban/rural area<sup>#</sup> of residence 1994-2009**

	cases per 100,000 per year	95% CI
DI-1	0.95	0.69 – 1.22
DI-2	1.19	0.83 – 1.54
DI-3	1.17	0.81 – 1.54
DI-4	1.09	0.79 – 1.40
DI-5	1.25	0.99 – 1.50
rural areas	0.90	0.72 – 1.08
urban areas	1.34	1.14 – 1.54

\*deprivation index range from DI-1 (least) to DI-5 (most) deprived

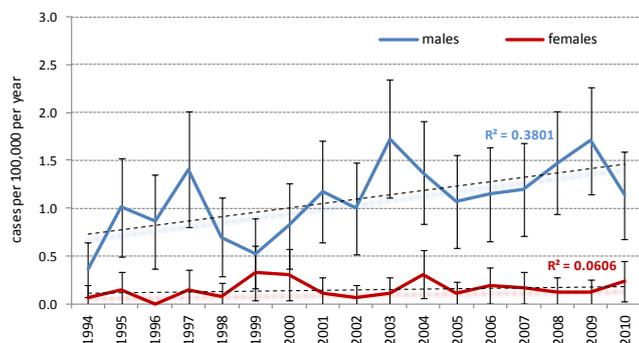
#rural areas defined by population density < 1 person per hectare

### Time trends in incidence

Despite large fluctuations in the number of pleural mesotheliomas diagnosed per year since 1994, incidence rates in men have increased overall by almost 100%, from an average of 13 cases per year in 1994-96, to 36 cases in 2009 (Figure 3). Incidence rates in women, as well as being much lower than in men, varied little

overall with a maximum of 6 women diagnosed in 2004. Increases in mesothelioma incidence in developed countries have been well reported in the literature. With a long latency period between exposure and diagnosis (usually 30 years or more), incidence in the UK is expected to peak in 2020.<sup>3</sup> In Ireland, asbestos was mostly used from the 1960's to the mid 1980's. It was banned on a phased basis under legislation in 1994 and 1998 and a general prohibition on its use was introduced under EU regulations in 2000<sup>4</sup>. Based on incidence trends from 1994 and current population projections, we estimate an annual incidence of 68 cases of male mesothelioma in Ireland in 2020.

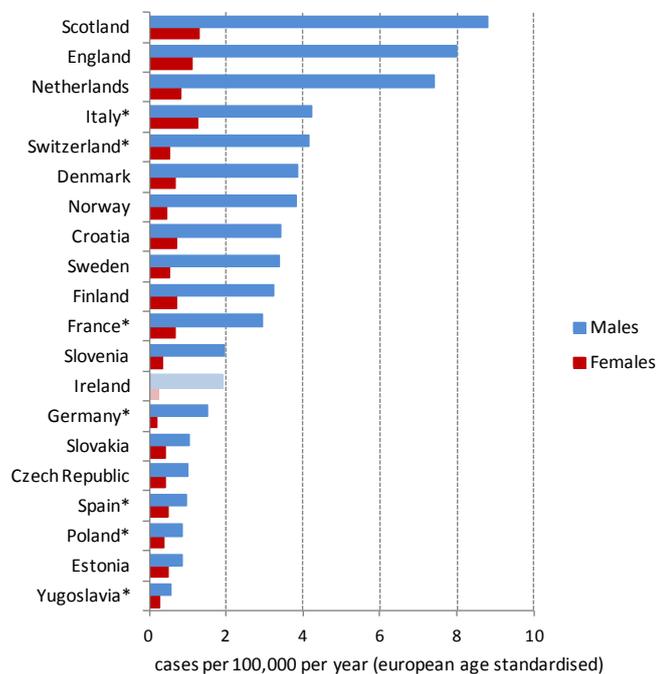
Figure 3. Trends in pleural mesothelioma incidence, 1994–2010



International variation in incidence

Recent directly comparable international incidence data on pleural mesothelioma are difficult to find in the literature. A study published in 2003 indicated that during the 1990's, incidence in males was very variable across Europe, with Irish rates ranked 13th of 20 countries examined (Figure 4).<sup>5</sup> Highest rates were found in Scotland, England and the Netherlands and lowest rates in eastern European countries generally. Irish females ranked 2<sup>nd</sup> lowest in incidence overall and similar to males, highest rates were recorded in Scotland, England and the Netherlands and also in Italy.

Figure 4. Incidence of pleural mesothelioma in Europe, 1990-1997<sup>5</sup>

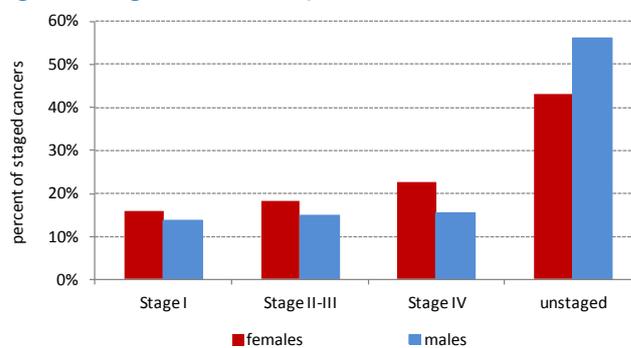


\*selected registries within each country only

Stage at diagnosis

A large proportion of patients had unstaged cancers; 43% of females and 56% of males (Figure 5). Of those cases that were staged, approximately equal proportions of male cases had localised (stage I), regional (stage II-III) and distant (stage IV) tumours. Female patients had a somewhat greater relative proportion of late stage tumours compared to males (23% of all cases) but due to the large volume of unstaged tumours in both sexes, it is difficult to access if there is a real difference in their stage distributions

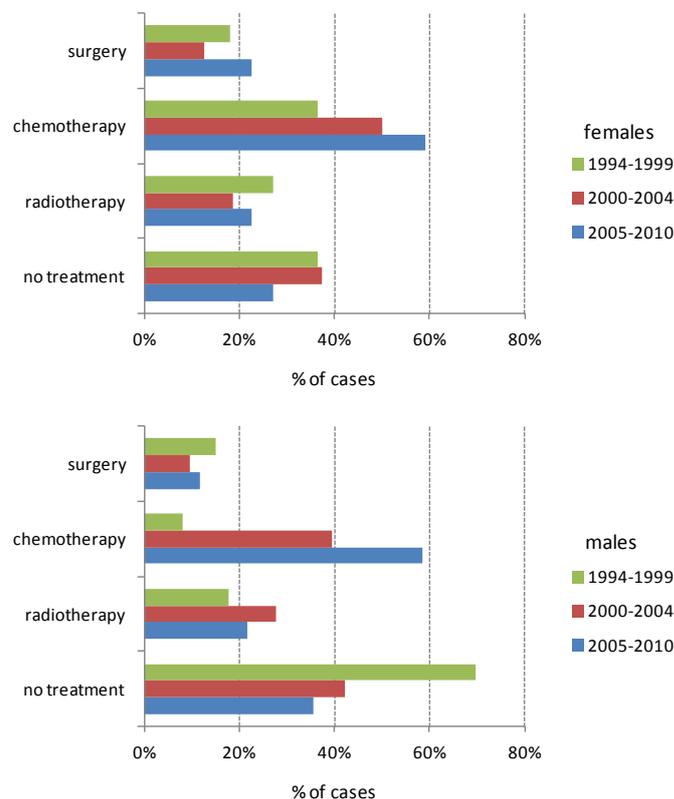
Figure 5. Stage distribution of pleural mesothelioma, 1994-2010



Treatment

Chemotherapy was the most common treatment overall and there was a clear increase in the proportion of patients treated over time - almost 60% of both males and females had chemotherapy during 2005-2010 (Figure 6). Comparatively few patients had tumour-directed surgery and approximately 1 in 5 patients overall had radiotherapy, with no major change in the percentage of patients treated over time. Along with the increase observed in chemotherapy over time was a clear decline in the proportion of patients having no tumour directed treatment, particularly in males, falling from 70% in the 1990's to 36% in recent years.

Figure 6. Treatment of pleural mesothelioma: 1994–2010



Treatment varied considerably with patient age – 71% of male patients aged 80 or older had no tumour directed treatment and only 17% had chemotherapy (Table 3). In contrast, 76% of patients aged between 60 and 69 had chemotherapy and less than 20% were untreated. Rates of tumour-directed surgery were low across all age groups. Many patients not having tumour directed treatment did have other procedures, such as pleurodesis to relieve symptoms.

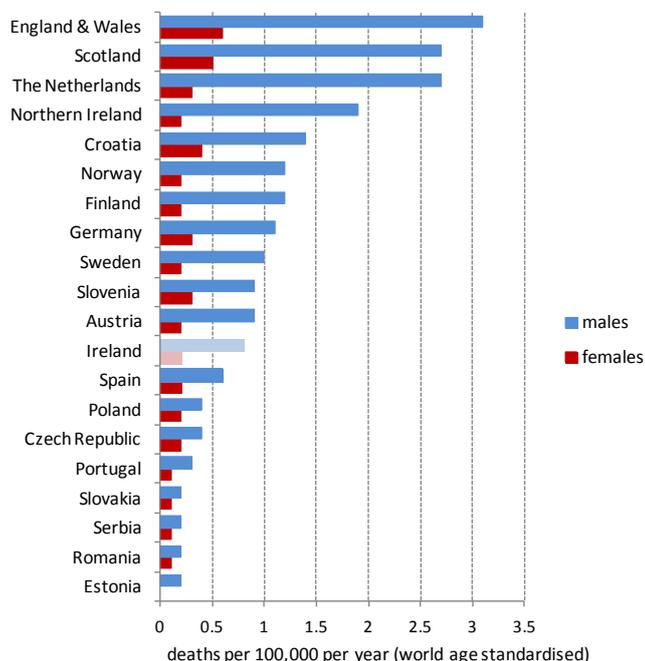
**Table 3. Proportion of male pleural mesothelioma patients treated by age group, 2005-2010**

	<60 years	60-69 years	70-79 years	80+ years
Total cases	25	58	45	24
surgery	20%	14%	2%	17%
chemotherapy	64%	76%	56%	17%
radiotherapy	24%	28%	20%	8%
no treatment	28%	19%	42%	71%

**Mortality**

Between 2007 and 2010 inclusive, there were 17 female and 108 male deaths from mesothelioma (all types) in Ireland<sup>6</sup>. Comparing mortality rates in 2010 across Europe, Ireland ranked 12 highest of 20 countries listed (Figure 7). However mortality rates varied widely with the highest rates in England & Wales, Scotland and the Netherlands all over 14 times higher than the lowest mortality rates recorded in eastern European countries.

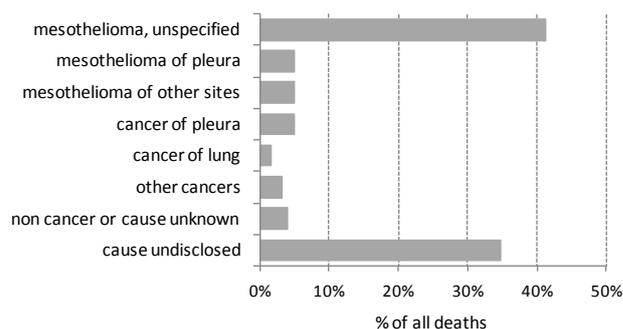
**Figure 7. Mortality rates from mesothelioma in Europe, 2010<sup>6</sup>**



Precise information on pleural mesothelioma mortality has been hampered until recent years by the lack of a specific code (under ICD9). ICD10 coding, in use for death certification in Ireland since 2007, allows for the specification of pleural mesothelioma, of which there were 20 deaths registered between 2007 and 2010 inclusive. However variability in the precision of death certificate coding is likely to be a contributing factor in the wide variation in mortality rates observed internationally and this has been reported in the literature.<sup>7</sup> A review of the cause of death listed for Irish known pleural mesothelioma patients illustrates this point (Figure 8). 51% of deaths were coded as mesothelioma but only 5% precisely as

pleural mesothelioma. A further 7% had their deaths coded either as a non-respiratory cancer, a non-cancer death or cause unknown. 35% of patients who died were the subject of a coroners inquest and so their cause of death was undisclosed.

**Figure 8. Cause of death for known pleural mesothelioma patients diagnosed since 1994, who died between 2007 & 2010**



**Survival**

Pleural mesothelioma has a very poor prognosis and five year relative survival in Ireland, for all patients diagnosed between 1994 and 2009 was 4.5% (2.4%-7.7%). Overall, 71% of patients registered since 1994 are known to have died within 1 year of diagnosis (Table 4). Patients with early stage disease had somewhat better survival, but less than 15% survived for longer than 2 years.

**Table 4. Survival time for pleural mesothelioma patients, diagnosed 1994-2009\* overall and by cancer stage**

	total	stage I	stage II-III	stage IV	unknown
<1 year	71%	61%	77%	77%	8%
1-2 years	19%	24%	15%	16%	19%
2-3 years	5%	6%	2%	4%	5%
3+ years	5%	6%	6%	4%	5%
unknown	1%	2%	0%	0%	1%

\*all patients with minimum follow-up of 1 year (to end 2010)

Recent estimates of survival for thoracic mesothelioma in European populations have shown patients in northern Europe and in the UK and Northern Ireland in particular to have the poorest survival (Table 5). The apparently high survival rate in eastern Europe is likely influenced by low case numbers and diagnostic issues<sup>8</sup>, also likely impacting on international incidence and mortality rankings.

**Table 5. Five year relative survival (period analysis, 2000-02) for thoracic malignant mesothelioma in Europe<sup>8</sup>**

	RS	Std Error
Northern Europe	5.3%	1.1%
Central Europe	6.3%	0.8%
Eastern Europe	12.0%	3.5%
Southern Europe	8.4%	1.1%
UK & Northern Ireland	3.4%	0.5%

**References and notes**

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2. Deprivation Index as per 2002 census. SAHRU ([www.sahrutcd.ie](http://www.sahrutcd.ie))
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6. Source: WHO mortality database. [www.dep.iarc.fr/WHOdb/WHOdb.htm](http://www.dep.iarc.fr/WHOdb/WHOdb.htm)
7. Camidge DR et al 2006. Factors affecting the mesothelioma detection rate within national and international epidemiological studies – insights from Scottish linked cancer registry-mortality data. Br J Cr 95: 649-652
8. Seisling S et al, 2012. Rare thoracic cancers including peritoneum mesothelioma. Eur J Cancer 48: 949-960