

# Mesothelioma

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## 1. Introduction

### 1.1 General Information and Aetiology

Mesotheliomas are tumours that arise from the mesothelial cells of the pleura, peritoneum, pericardium or tunica vaginalis [1]. Most are pleural mesotheliomas, the peritoneum is the second most common site of mesothelioma development. Pericardial en tunica vaginalis origin is rare [1]. After a peak, it is estimated that the incidence will decline by the year 2018. Exposure to asbestos is a well-documented etiological factor for mesothelioma, with occupational exposure being reported in 70-80% of those affected [2-4]. Mostly the delay is about 20 years although more than 40 years can elapse between exposure to asbestos and the diagnosis of mesothelioma [2-3]. There is also a good known synergistic effect between nicotine smoking and asbestos [5]. Most mesothelioma occur in males between 50-70 years old and the most frequently reported symptoms are dyspnea, thoracic pain and coughing [5].

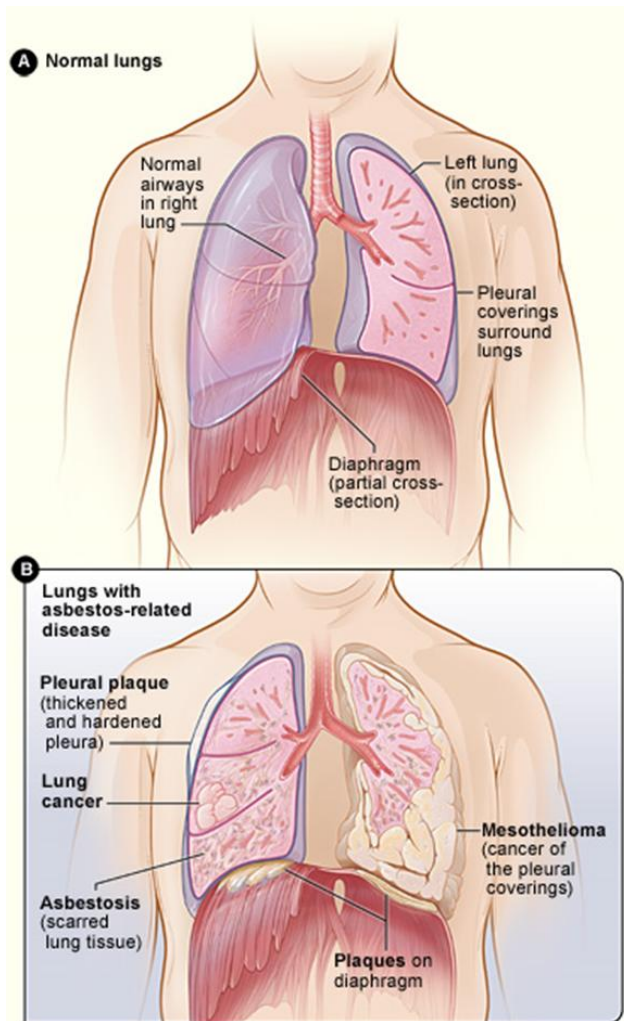


Figure 1. Mesothelioma

## 1.2 Diagnosis and Treatment

Most people initially undergo basic chest X-ray because of their complaints [5]. In case an abnormality is detected, a more detailed imaging (CT-scan, PET-scan or MRI) will be performed. If mesothelioma is suspected, a biopsy will be recommended to confirm the diagnosis. Most frequently a thoracoscopy is done to receive a biopsy for a pleural mesothelioma [5]. When there is assumption of a peritoneal mesothelioma, a peritoneoscopy to receive a biopsy may be performed. Biopsies may also be taken during more invasive surgical procedures [5].

Treatment options for mesothelioma include surgery, chemotherapy and radiation therapy. The treatment-choice depends on the general condition of the patient and the stage of the disease. Where possible, it's preferred to combine two or more of these treatments [6]. In clinical trials, this

multimodal therapy has been shown to improve survival rates [6]. Although early stage cancers may be operated with curative intent, prognosis of mesothelioma is very poor with almost no long term survivors. Sometimes, tumor cells can grow along the tract where biopsy is taken. To prevent painful lesions along the biopsy tract, this area is preventively treated with radiation therapy.

## 2. Data Selection

All mesotheliomas diagnosed between 2004 and 2007 for patients with an official residence in the Flemish Region are selected, resulting in 623 cases (for detailed information on selected topography and morphology codes, see Appendix A). As described in Figure 2, 67 of them are excluded, resulting in 556 patients for whom results are presented in this chapter.

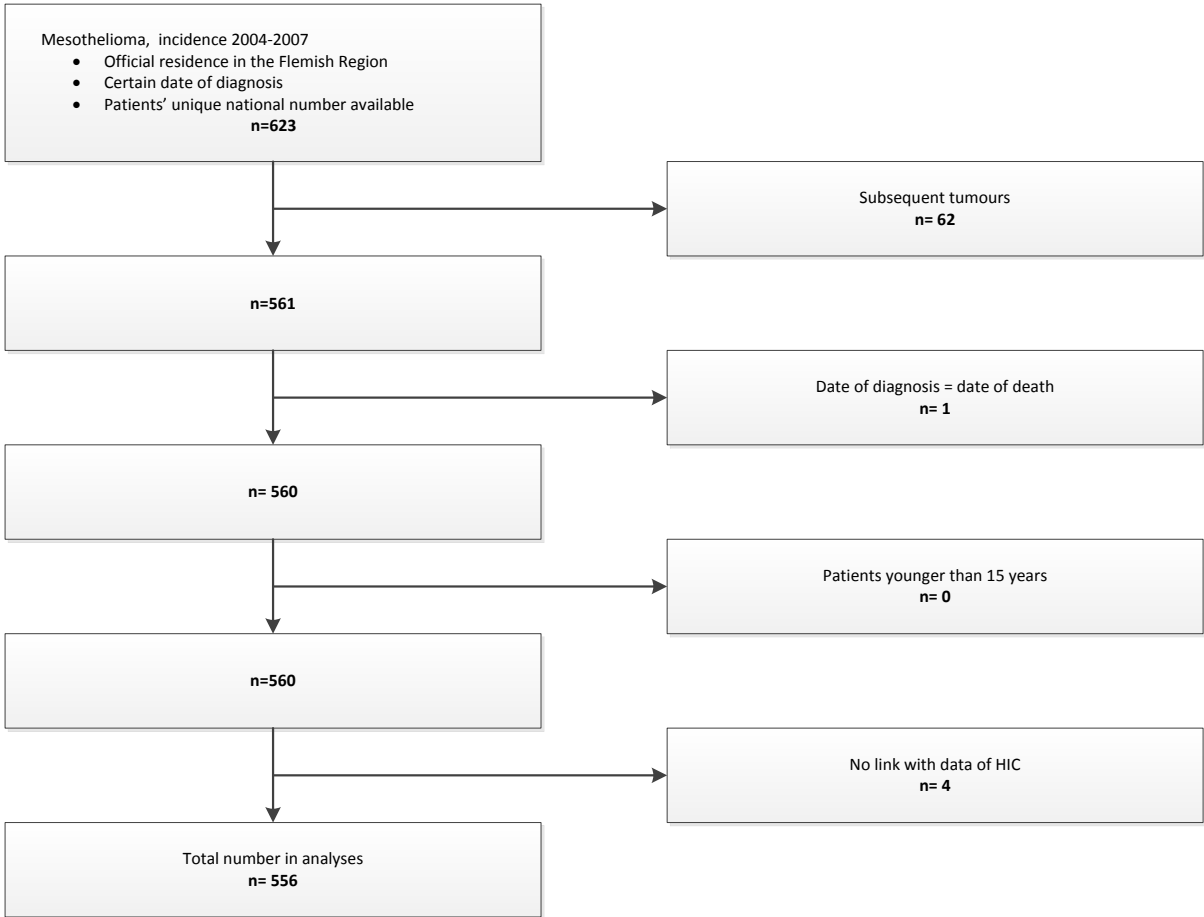


Figure 2. Selection of Mesothelioma (Flemish Region, 2004-2007)

### 3. Patient Characteristics

Mesotheliomas in the Flemish Region are more frequent in males than in females (male/female ratio: 6.08) during the incidence years 2004-2007 (Table 1). No clear trend in the age-standardised rates can be observed in the studied period.

The median age at diagnosis is almost the same for males and females: 70 years in males and 70.5 years in females. The minimum age is 18 years while the maximum is 90 years. For further analyses, patients are divided into three age groups: 15-59 years, 60-74 years and 75 years or older (Table 2).

Table 1. Mesothelioma: Incidence (Flemish Region, 2004-2007)

Incidence year	Males		Females		Total	
	n	ESR	n	ESR	n	ESR
2004	115	3.04	17	0.36	132	1.60
2005	114	3.05	29	0.69	143	1.75
2006	122	3.16	18	0.43	140	1.72
2007	115	2.94	26	0.49	141	1.62
2004-2007	466	3.04	90	0.50	556	1.67

ESR: age-standardised rate, using the European Standard Population (n/100,000 person years)

Table 2. Mesothelioma: Age Distribution (Flemish Region, 2004-2007)

	Males	Females	Total
15-59 years	83	21	104
60-74 years	255	39	294
75+ years	128	30	158

### 4. Tumour Characteristics

Table 3 presents information regarding the sublocalisation, morphology, differentiation grade and stage (clinical, pathological and combined stage) of the selected mesotheliomas. Only two patients are diagnosed with a non-pleural localised mesothelioma. The majority of the tumours have an unknown differentiation grade. However, it should be noted that the relevance of any form of differentiation grading is doubtful for mesothelioma which are not ordinarily graded and for which no prognostic value has yet been attributed to this tumour characteristic [7]. The stage of the

tumours remains unknown for about half of the patients. For the patients with a known stage, stages are more or less evenly distributed. Two tumours (0.4%) could not be staged because their localisation was coded as C45.2 (mesothelioma of pericardium) or C45.7 (mesothelioma of other sites). These tumours are displayed as stage 'NA'.

**Table 3. Mesothelioma: Tumour Characteristics (Flemish Region, 2004-2007)**

	N	% of total	% of known
<b>Localisation</b>			
Mesothelioma of pleura (C45.0)	554	99.6	99.8
Mesothelioma of pericardium (C45.2)	1	0.2	0.2
Mesothelioma of other sites (C45.7)	1	0.2	/
<b>Morphology</b>			
Epithelioid mesothelioma	219	39.4	/
Other morphologies	337	60.6	/
<b>Differentiation grade</b>			
Well differentiated	16	2.9	26.7
Moderately differentiated	11	2.0	18.3
Poorly differentiated	19	3.4	31.7
Undifferentiated	14	2.5	23.3
Unknown	496	89.2	/
<b>Clinical stage</b>			
I	57	10.3	20.9
II	64	11.6	23.4
III	70	12.6	25.6
IV	82	14.8	30.0
Unknown	281	50.7	/
<b>Pathological stage</b>			
I	11	2.0	20.0
II	10	1.8	18.2
III	19	3.4	34.5
IV	15	2.7	27.3

Unknown	499	90.1	/
<b>Combined stage</b>			
I	59	10.6	20.7
II	63	11.4	22.1
III	76	13.7	26.7
IV	87	15.7	30.5
Unknown	269	48.6	/

Note: 2 cases have a localisation for which staging is not applicable (NA)

Stage distribution is comparable for males and females, but the proportion of females with an unknown stage is higher (Figure 3). Younger patients tend to have less stage I cancers, although they also have less stage IV cancers in comparison with older patients (Figure 4). The proportion of tumours with an unknown stage is much higher for patients aged 75 years or older than for the other age groups.

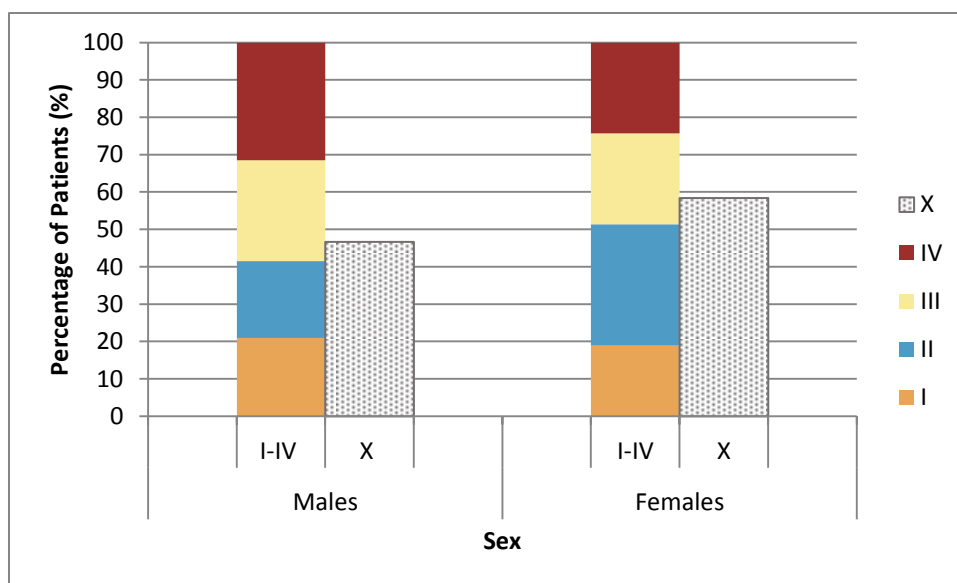


Figure 3. Mesothelioma: Stage Distribution by Sex (Flemish Region, 2004-2007)

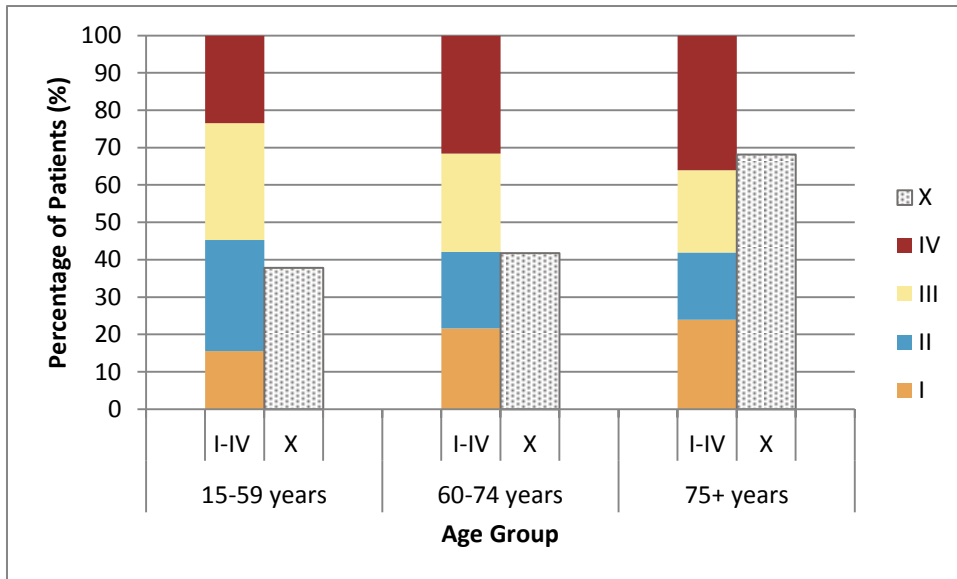


Figure 4. Mesothelioma: Stage Distribution by Age Group (Flemish Region, 2004-2007)

## 5. Diagnostic and Therapeutic Procedures

### 5.1 Diagnosis and Staging

An overview of the diagnosis and staging procedures used for mesotheliomas is shown in Table 4.

Histological examination is performed in almost all patients (98.6%) and most often a cytological diagnosis is also charged.

Only for one patient, no imaging procedure has been charged in the staging procedure. The most frequently used imaging techniques are a CT scan (98.4%) and a X-ray of the thorax (98.7%). MRI scanning is almost never (3.2%) executed during the staging process of mesothelioma. A puncture of the pleura (or ascites) is also performed in about two-third of the patients. Surgical staging by mediastinoscopy or explorative thoracotomy is carried out in about one-third of the patients. PET scanning is performed in almost half of the patients (45.0%).

Table 4. Mesothelioma: Overview of Diagnostic and Staging Procedures (Flemish Region, 2004-2007)

Diagnostic Procedure (-3m<inc<+3m)	Total (N=556)		2004 (N=132)		2005 (N=143)		2006 (N=140)		2007 (N=141)	
	n	%	n	%	n	%	n	%	n	%
<b>Tissue Examination</b>	<b>548</b>	<b>98.6</b>	<b>128</b>	<b>97.0</b>	<b>142</b>	<b>99.3</b>	<b>139</b>	<b>99.3</b>	<b>139</b>	<b>98.6</b>
Histological Diagnosis	545	98.0	127	96.2	141	98.6	139	99.3	138	97.9
Cytology	491	88.3	110	83.3	129	90.2	125	89.3	127	90.1
<b>Imaging</b>	<b>555</b>	<b>99.8</b>	<b>132</b>	<b>100.0</b>	<b>142</b>	<b>99.3</b>	<b>140</b>	<b>100.0</b>	<b>141</b>	<b>100.0</b>
CT	547	98.4	128	97.0	141	98.6	140	100.0	138	97.9
MRI	18	3.2	5	3.8	7	4.9	6	4.3	0	0.0
Chest X-ray	549	98.7	128	97.0	141	98.6	139	99.3	141	100.0
PET Scan	250	45.0	62	47.0	61	42.7	71	50.7	56	39.7
CT/MRI Skull	182	32.7	43	32.6	43	30.1	51	36.4	45	31.9
<b>Punction</b>										
Ascites or Pleural Punction	362	65.1	86	65.2	104	72.7	84	60.0	88	62.4
<b>Surgical Staging</b>	<b>181</b>	<b>32.6</b>	<b>40</b>	<b>30.3</b>	<b>49</b>	<b>34.3</b>	<b>46</b>	<b>32.9</b>	<b>46</b>	<b>32.6</b>
Mediastinoscopy	66	11.9	12	9.1	25	17.5	19	13.6	10	7.1
Explorative Thoracotomy	139	25.0	34	25.8	31	21.7	32	22.9	42	29.8



## 5.2 Multidisciplinary Oncological Consult

Overall, about 66% of all mesothelioma patients have been discussed at a multidisciplinary oncological consult (MOC) within one month before till three months after incidence date. No clear trend can be observed over the incidence years (Table 5).

Table 5. Mesothelioma: Frequency of Multidisciplinary Oncological Consult (Flemish Region, 2004-2007)

Incidence year	MOC	
	n	%
2004 (n=132)	80	60.6
2005 (n=143)	97	67.8
2006 (n=140)	102	72.9
2007 (n=141)	87	61.7
Total (n=566)	366	65.8

## 5.3 Therapeutic Procedures

Two types of surgery are taken into account: pleural resection and pneumonectomy. The surgery type closest to the incidence date is selected. Based on this criterion, 68.2% of the patients who are operated receive a pleural resection while 31.8% receive a pneumonectomy within the timeframe of one month before until six months after the incidence date (Table 6).

Table 6. Mesothelioma: Overview of the Selected Surgeries (Flemish Region, 2004-2007)

Type of Surgery	n	%
Pleural Resection	73	68.2
Pneumonectomy	34	31.8

Some patients without major surgical intervention receive a supportive surgical treatment such as pleurodesis (n=200) or a thoracotomy with intent to resection (n=4).

Almost 20% of the patients undergo surgery in a time-frame of one month before until six months after incidence. Surgery as the sole therapy is seldom ( 3.1%); the majority of the surgically treated patients receive neo-adjuvant and/or adjuvant chemo- and/or radiotherapy.

22.8% of the patients receives concomitant chemoradiotherapy without surgery. Radiotherapy is the only oncological treatment for 15.8% of the patients, while 18.7% of the mesothelioma patients only receive chemotherapy (Table 7).

It should be noted that it is unknown whether irradiation (alone or combined with surgery and/or chemotherapy) is performed with a curative intent, a palliative intent or whether it is an irradiation of the entrance gate of the scoop after an endoscopic intervention.

No primary oncological treatment is found for 23.4% of the patients. This high percentage of untreated patients can at least partly be explained by the lethal character of this cancer type. Certainly in case of advanced disease in older patients, treatment might be restricted to palliation and comfort care.

**Table 7. Mesothelioma: Overview of Treatment Schemes (Flemish Region, 2004-2007)**

Treatment Scheme	n	%
<b>Surgery</b>	<b>107</b>	<b>19.2</b>
No other therapy	17	3.1
Adjuvant radiotherapy	14	2.5
Adjuvant chemoradiotherapy	19	3.4
Adjuvant chemotherapy	27	4.9
Chemotherapy < surgery	2	0.4
Chemotherapy < surgery < chemotherapy	1	0.2
Chemotherapy < surgery < chemoradiotherapy	2	0.4
Chemotherapy < surgery < radiotherapy	10	1.8
Chemoradiotherapy < surgery	4	0.7
Chemoradiotherapy < surgery < radiotherapy	10	1.8
Radiotherapy < surgery < chemoradiotherapy	1	0.2
<b>Radiotherapy</b>	<b>88</b>	<b>15.8</b>
<b>Chemoradiotherapy</b>	<b>127</b>	<b>22.8</b>
<b>Chemotherapy only</b>	<b>104</b>	<b>18.7</b>
<b>No primary treatment registered</b>	<b>130</b>	<b>23.4</b>

## 6. Survival

### 6.1 Observed and Relative Survival

Survival is very poor for all patients diagnosed with a mesothelioma (Table 8). Within one year after diagnosis, more than half of the patients has already died. Relative survival at five years after diagnosis is only 5.0%.

Table 8. Mesothelioma: Observed and Relative Survival (Flemish Region, 2004-2007)

N at risk	Observed Survival (%)					Relative Survival (%)				
	1 year	2 year	3 year	4 year	5 year	1 year	2 year	3 year	4 year	5 year
556	45.9	19.4	9.7	6.1	4.3	47.4	20.6	10.6	6.9	5.0

### 6.2 Relative Survival by Sex

Both males and females have very low 5-year relative survival rates. Survival is somewhat better for females although the absolute differences are small (Table 9).

Table 9. Mesothelioma: Relative Survival by Sex (Flemish Region, 2004-2007)

	N at risk	%	Relative Survival (%)				
			1 year	2 year	3 year	4 year	5 year
Males	466	83.8	46.6	20.6	9.6	6.5	4.5
Females	90	16.2	51.0	20.8	15.4	8.6	7.7

### 6.3 Relative Survival by Age Group

One year after diagnosis, survival is worse for patients aged 75 year and older, but the survival benefit for the younger patients disappears with a longer follow-up (Table 10).

Table 10. Mesothelioma: Relative Survival by Age Group (Flemish Region, 2004-2007)

	N at risk	%	Relative Survival (%)				
			1 year	2 year	3 year	4 year	5 year
15-59 years	104	18.7	54.1	23.3	10.7	5.9	5.9
60-74 years	294	52.9	53.5	23.4	11.6	8.1	4.9
75+ years	158	28.4	30.6	13.2	8.7	5.2	4.8

## 6.4 Relative Survival by Stage

Until three years after diagnosis, survival is remarkably better for the stage I tumours than for the other stages (Figure 5). Thereafter, survival benefit becomes smaller although prognosis remains slightly better.

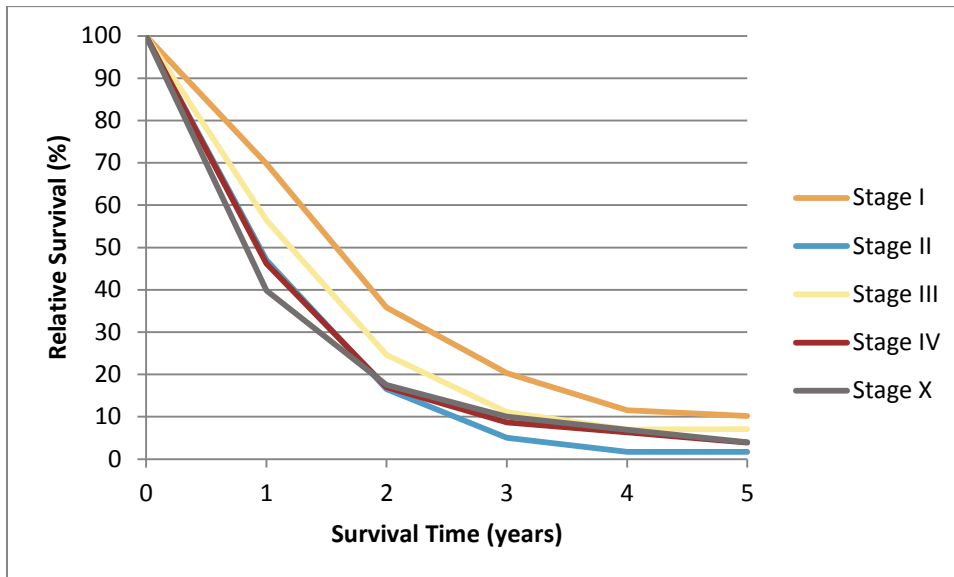


Figure 5. Mesothelioma: Relative Survival by Stage (Flemish Region, 2004-2007)

## 6.5 Relative Survival by Morphology

Patients diagnosed with an epithelioid mesothelioma (n=219) have a relative survival benefit of 20.3% at 1 year after diagnosis, in comparison with patients diagnosed with another morphological type of mesothelioma (n=337, Figure 6). However, relative survival benefit decreases with increasing follow-up time to only 2.1% at 5 years.

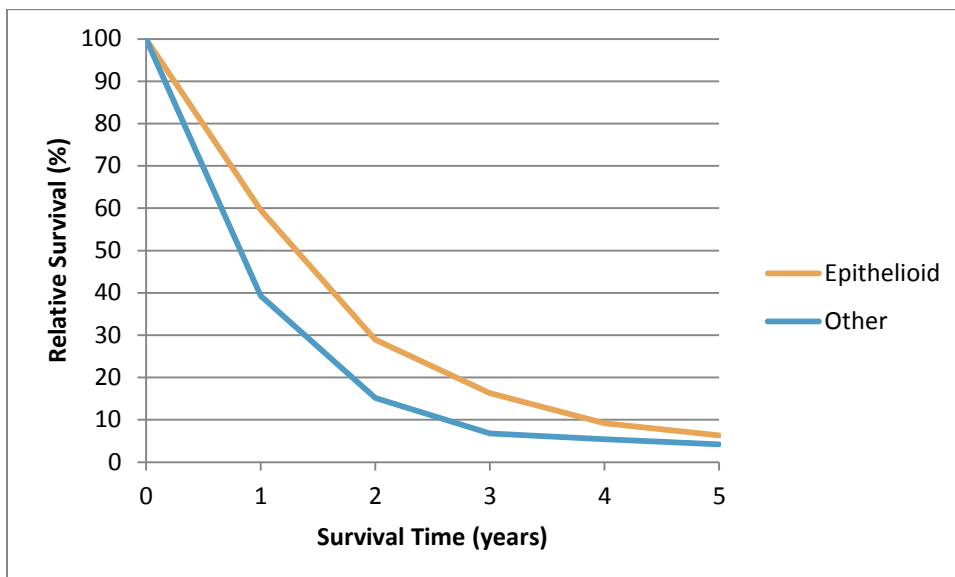


Figure 6. Mesothelioma: Relative Survival by Morphology (Flemish Region, 2004-2007)

## 6.6 Relative Survival by Primary Treatment

Patients who undergo surgery (pleural resection or pneumonectomy, n=107) have a slightly better survival than patients who only undergo radio- and/or chemotherapy or without any registered treatment (n=449, Figure 7). The survival benefit seems to shrink after three years of follow-up: at three years the relative survival rates are 14.8% and 9.6% in favour of surgically treated patients, and at five years the rates are 7.2% and 4.5% respectively.

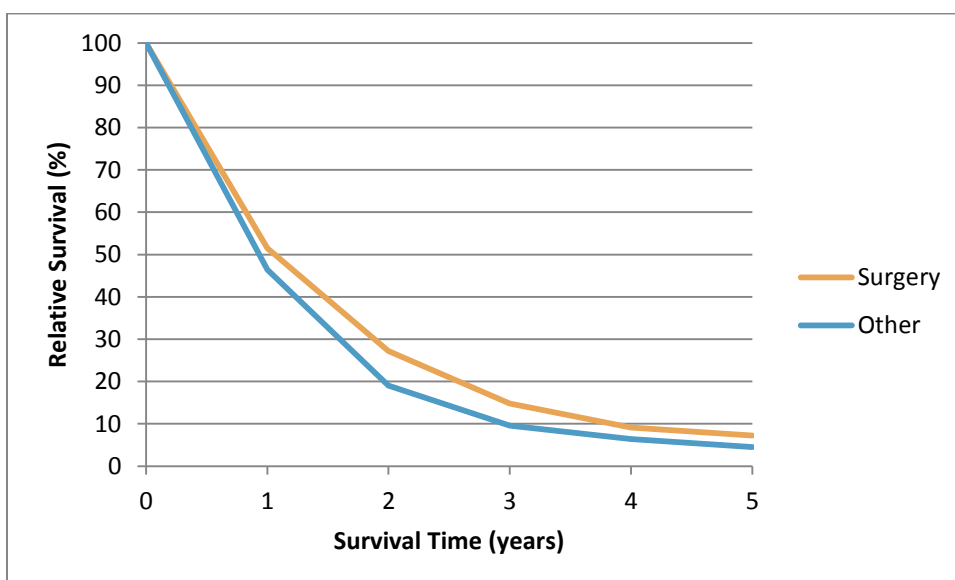


Figure 7. Mesothelioma: Relative Survival by Primary Treatment (Flemish Region, 2004-2007)

## 7. Analyses by Volume

During the period 2004-2007, Belgian patients with mesothelioma are treated in 49 different Flemish hospitals. The mean number of patients (during the period 2004-2007) by hospital is 9.9 and the median number is 4, with a range between 1 and 69. The distribution of the number of patients (=volume) per hospital is displayed in Figure 8.

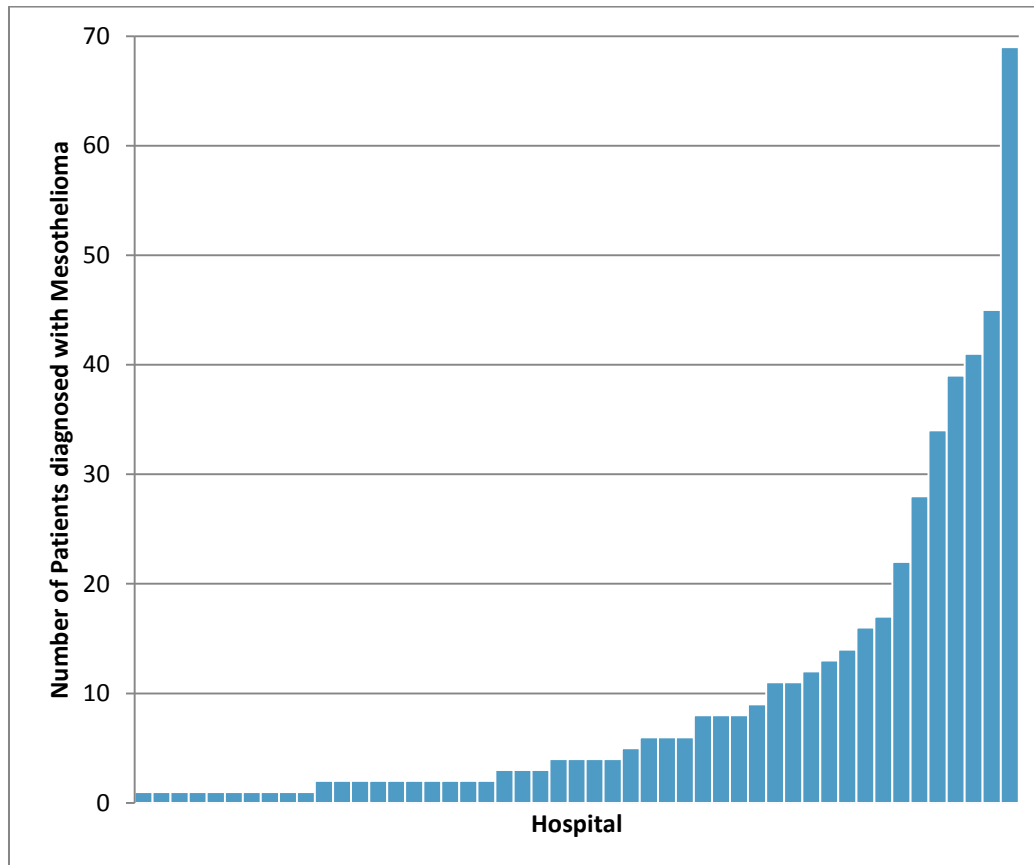


Figure 8. Mesothelioma: Distribution of Patients by Hospital (Flemish Hospitals, 2004-2007)

477 of the Flemish patients (85.8%) can be assigned to a hospital (see Methodology for the rules applied to assign a patient to one hospital). Considering hospitals having taken care of 40 or more patients diagnosed during the period 2004-2007 as high-volume hospitals, 150 patients are assigned to high-volume hospitals and 327 are assigned to low-volume hospitals.

Treatment schemes are different for those considered high-and low-volume hospitals (Figure 9). In high-volume hospitals, 34.0% of the patients is primarily treated with RT and 34.7% with chemoradiotherapy. Surgery (with or without neo- and/or adjuvant treatment) and chemotherapy only, are less frequently used. For low-volume hospitals a larger part of the patients is surgically treated (26.6%). Chemotherapy only and chemoradiotherapy are both used in about one fourth of

the patients (24.8% and 22.9% respectively). Additionally, the number of patients without any oncological treatment is higher in low-volume hospitals (15.0%) than high-volume hospitals (3.3%). It should be noted that the difference in the proportion of patients treated with radio- or chemoradiotherapy in the high-volume versus low-volume hospitals can at least partly be explained by the rules for assignment that give a rather high priority to the hospital where the RT takes place.

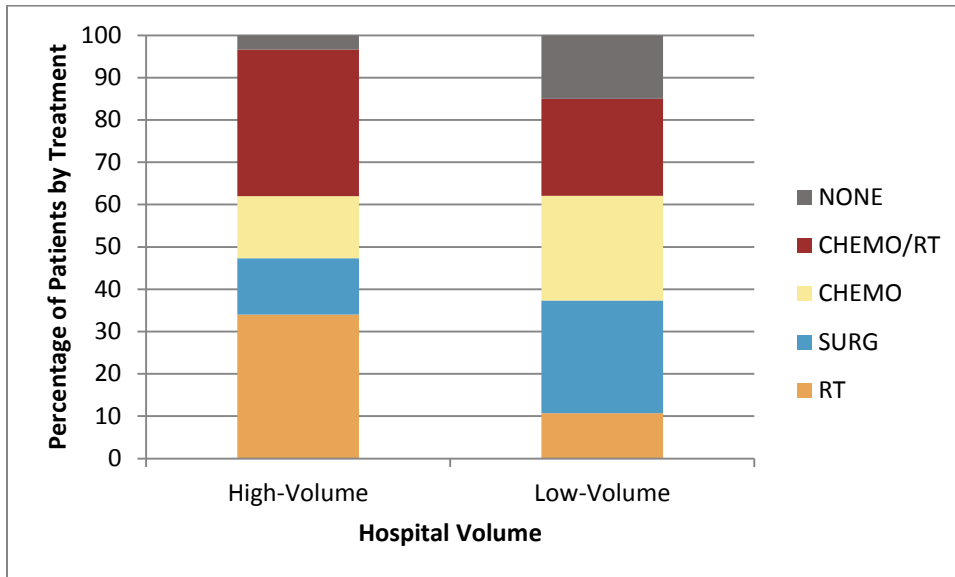


Figure 9. Mesothelioma: Primary Treatment by Hospital Volume (High-Volume versus Low-Volume Hospitals) (Flemish Region, 2004-2007)

## 8. References

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