

Karolinska Institutet/ i3 Innovus Benchmarking Report of Lung Cancer Care in selected Countries

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1 Introduction

Cancer causes the second highest number of deaths in Europe after cardiovascular disease. In Europe it is estimated that almost 3.2 million people were diagnosed with cancer in 2006 and, in the same year, 1.7 million people died as a result. With an ageing population the incidence and mortality from cancer is predicted to increase in the future [1].

Poor survival rates make lung cancer the most lethal form of cancer. In 2006, 335,000 people died from lung cancer, which is more than any other form of cancer and 19.7 per cent of all cancer deaths. Lung cancer is the third most common form of cancer with 386,000 new cases annually, or 12.1 per cent of all cancer cases following breast cancer and colorectal cancer.

The incidence rate of lung cancer is mainly a result of smoking [2]. In most countries the incidence has peaked and started to decrease for men, but it is still increasing for women in many countries. The peak in male incidence was in the late 1970s and 80s in Northern and Western Europe, and in the 1990s in Southern and Eastern Europe [3].

Healthcare systems and the strategies for providing the most appropriate cancer care differ from one country to another. To understand the preconditions and strategies for cancer care in general, and lung cancer specifically, it is important to look at each national healthcare system, its organisation and financial structure.

This study will review, compare and discuss the management of lung cancer care and patient access to existing and new treatments in the following countries: Austria, Belgium, the Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Ireland, Italy, the Netherlands, Norway, Poland, Portugal, Russia, Spain, Sweden, Switzerland and the UK in Europe; Brazil and Mexico in Latin America; Australia and New Zealand in Oceania; and Japan in Asia. Comparisons will be made across countries, over time. Main focus will be put on the European countries, and the non-European countries will serve as examples and will be used to put the management of lung cancer in the European countries in a wider perspective. Comparisons will, however still be made and conclusions will be based on all countries included. The reason for placing the main focus on Europe is that these countries have several aspects in common in terms of burden of lung cancer and the organisation of provision and organisation of health care services. Determinants for variations in outcomes of lung cancer treatment will be assessed. These include organisation of lung cancer care, resources available for diagnosis and treatment, the role of treatment guidelines and treatments used.

Unless otherwise stated, throughout the report statistics on lung cancer relate to the ICD C33-34 Cancer in Trachea, Bronchus and Lung according to the International Classification of Diseases (10th revision) [4].

The conditions and organisation of cancer care differs between countries. There is no single reason why some countries are more successful than others in keeping mortality rates down. There are three aspects to the management of lung cancer: prevention, detection and treatment. As the main cause of lung cancer is direct and indirect tobacco smoke, smoking cessation is the natural focus of primary prevention. There are other life-style factors increasing the risk, as well as environmental factors such as exposure to asbestos and radon radiation. Since the success of treatment is highly dependent on the stage of the tumour when detected, patients need to be diagnosed as early as possible. Strategies to develop methods of

earlier detection are therefore very important. Treatment needs to be developed in order to improve survival chances and to minimize pain and discomfort when a cure is not possible.

The major obstacle in comparing lung cancer treatment across countries is the limited availability and reliability of data. Available statistics do not always give full national coverage. Methods of collecting data differ from country to country which means that reported figures are not always comparable across countries. Data for important indicators is often not collected at all. Where does lung cancer treatment stand today and what can be done to improve it? To answer that question and to improve the burden of lung cancer on society, we need systematically collected and reported data.

2 The burden of lung cancer

Lung cancer is one of the most common forms of cancer and because of poor survival rates it is the most lethal. It causes between 15 and 28 per cent of all cancer deaths in Europe. Lung cancer takes a relatively large share of healthcare spending for cancer. The indirect costs of the disease are also high.

2.1 Lung cancer incidence

In Europe each year 47 people out of 100,000, on average, are diagnosed with lung cancer. Table 2-1 shows the age standardized incidence rates in lung cancer per 100,000 inhabitants in the countries of this study, and in Europe as a whole defined as the countries in the study.

For all types of cancer the incidence rates are lower in the Eastern European countries compared to Western and Northern European countries. But the incidence in lung cancer is higher among the Eastern European countries, where rates are very high. For example: Hungary (80.9 per 100,000 inhabitants), and Poland (65.8 per 100,000 inh.). Denmark, with an incidence rate of 56.9 per 100,000 inh and Belgium with 58 cases per 100,000 inh, are exceptions among the Western and Northern European countries, with high incidence rates. In the case of Denmark this is largely based on high incidence among women.

The lowest incidence rates for both men and women are found in Finland, Portugal and Sweden. In all countries the incidence rate is lower among women. In most countries the gender gap is closing because of an increase in the number of women who smoke and a decrease in the number of male smokers. Incidence rates among women are low in the Southern European countries: Portugal, Spain, France, Italy and Greece, as well as in Finland and in the Russian Federation. The highest incidence rates among women are found in Denmark with 48.7 cases and in Hungary with 42.4 cases per 100,000 women.

Lung cancer accounts for about 7 per cent of all new cancer cases in Portugal and Sweden, and more than 16 per cent of all new cancer cases in Hungary, Poland and the Russian Federation. In Greece, Hungary, Poland and Russia lung cancer is the most common type of cancer in absolute numbers. In more than half of the countries lung cancer is the fourth most common type.

The age standardised lung cancer incidence rates in the non-European countries are lower than in most European countries. Lung cancer is also less frequent in relation to other kinds of cancer in these countries, being the third most common cancer form in Brazil, the fourth largest type of cancer in Japan, but only the fifth most common cancer in Australia, New Zealand and Mexico. The largest difference between the European and non-European countries are among men. In New Zealand there are large ethnic differences between the Maori and non Maori population. Among Maori men the incidence is more than two and a half times higher and among Maori women three times higher than in the non Maori population.

Table 2-1 Estimated age-standardized incidence rates in lung cancer (European age standard) per 100,000 inhabitants, 2006

	Male	Female	Total*	Lung cancer share of cancer incidence	Rank in incidence among cancers
Sweden	28.6	23.8	26.2	6.7%	4
Portugal	44.5	11.7	28.1	7.8%	4
Finland	45.8	14.7	30.3	8.4%	4
Austria	54.0	22.3	38.2	10.3%	4
Switzerland	52.7	26.2	39.5	9.1%	4
Germany	61.2	20.8	41.0	10.4%	4
Spain	68.3	13.8	41.1	12.1%	2
Norway	53.8	33.7	43.8	10.4%	4
France	75.5	15.0	45.3	10.6%	4
United Kingdom	57.1	34.6	45.9	12.1%	3
Ireland	60.2	34.1	47.2	10.5%	4
The Netherlands	63.4	32.5	48.0	12.1%	4
Italy	84.7	15.6	50.2	12.2%	3
Greece	88.7	12.7	50.7	14.8%	1
Czech Republic	78.9	22.9	50.9	12.3%	2
Russian Federation	92.7	11.2	52.0	16.0%	1
Denmark	65.0	48.7	56.9	13.3%	2
Belgium	93.0	22.9	58.0	13.1%	3
Poland	103.0	28.6	65.8	17.4%	1
Hungary	119.3	42.4	80.9	16.0%	1
Europe	75.3	18.3	46.8	12.6%	2
Australia **	39.5	16.8	28.2	9.2%	5
New Zealand **	37.3	20.5	28.9	9.1%	5
Japan **	38.1	12.3	25.2	11.1%	4
Brazil **	21.5	7.1	14.3	7.8%	3
Mexico **	17.0	6.7	11.9	7.2%	5

Source: For European countries [1], for non-European countries [5], for Brazil also [6]

* The calculations are made assuming an even distribution of sexes in the populations. This is not an exact measure as the sex specific data are age-standardized in the source.

** World age standard in year 2002,

2.2 Lung cancer mortality

Cancer is the group of diseases causing the second highest number of deaths in Europe after cardiovascular diseases. Lung cancer is the most fatal form of cancer causing from 15 per cent (in Poland) to 28 per cent (in Belgium) of all cancer deaths. The smaller percentage share in Poland should not be mistaken for a low mortality in lung cancer since general cancer mortality rates there are very high.

The survival rates for lung cancer patients in Europe are low. Almost 90 per cent of those diagnosed die within 5 years.[7]. Lung cancer is less common in women and the survival rate in women is slightly higher [7].

As with incidence, the mortality rates are generally higher in Eastern Europe compared to Western and Northern Europe [8]. The age-standardised mortality rates in lung cancer in the countries of this study are shown in Table 2-2. Because of the low survival rates the mortality figures follow incidence. The mortality rates are high in the Eastern European countries of the Czech Republic (48.2 deaths), Hungary (72.3 deaths) and Poland (56.9 deaths), but are also high in the Western European countries of Belgium (57.3 deaths), Denmark (49.8 deaths) and the Netherlands (48.8 lung cancer deaths per 100,000 inhabitants). The lowest mortality rates are found in Finland, Portugal and Sweden with less than 30 cases per 100,000 inhabitants. Following the incidence data, the mortality rates in the non-European countries are lower than in most European countries: the lowest mortality rates are seen in the Latin American countries. The differences in lung cancer mortality rates between European and non-European countries are most pronounced in men.

The incidence, and hence the mortality, in lung cancer mirror smoking habits over several decades. In most countries, the mortality rates reached a peak in the late 1970s and 1980s and have since decreased (Figure 2-1 – 2-10). In the Eastern European countries the peak came in the 1990s [8, 9]. This trend has primarily followed mortality in males but is kept up by increasing mortality rates among women in all countries. In Norway, Portugal and Sweden the increasing mortality in females has led to a still increasing overall mortality rate.

Table 2-2 Estimated age-standardized mortality rates in lung cancer (European age standard) per 100,000 inhabitants, 2006

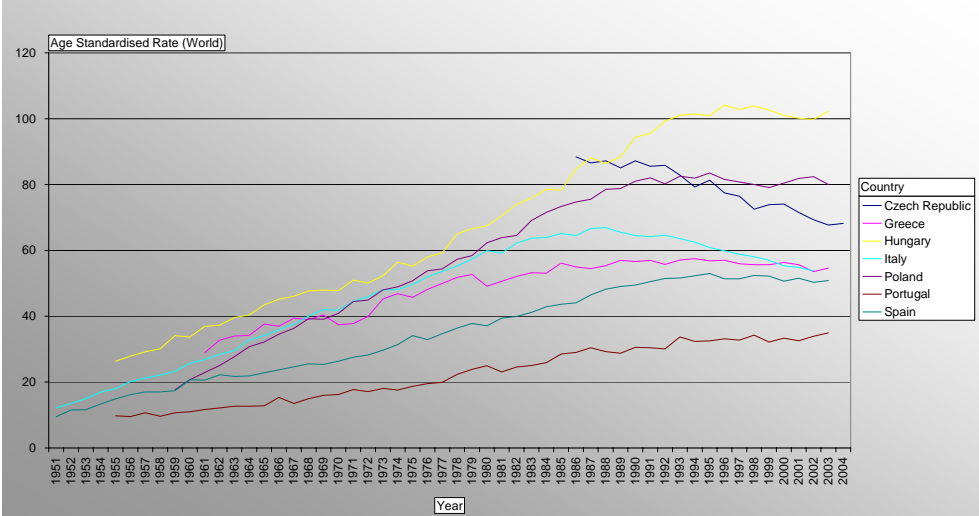
	Male	Female	Total*	Lung cancer share of total cancer mortality
Portugal	43.3	7.9	25.6	22.2%
Sweden	29.7	23.5	26.6	21.4%
Finland	43.5	13.0	28.3	19.9%
Switzerland	43.4	18.1	30.8	19.3%
Austria	51.3	18.2	34.8	19.3%
Germany	53.8	18.0	35.9	24.3%
France	60.0	13.7	36.9	20.7%
Norway	48.4	26.1	37.3	25.1%
Ireland	48.9	26.2	37.6	22.0%
Spain	67.2	8.9	38.1	21.7%
Italy	63.0	14.0	38.5	24.9%
Greece	69.0	11.4	40.2	26.2%
United Kingdom	50.7	29.7	40.2	21.0%
Russian Federation	75.2	8.0	41.6	17.1%
Czech Republic	77.3	19.1	48.2	20.0%
The Netherlands	67.0	30.6	48.8	20.4%
Denmark	57.9	41.6	49.8	22.7%
Poland	92.0	21.8	56.9	15.1%
Belgium	93.8	20.7	57.3	27.7%
Hungary	110.0	34.6	72.3	19.6%
Europe	64.8	15.1	40.0	19.2%
Australia (2005) **	32.7	16.2	23.7	15.9%
New Zealand (2001) **	30.1	19.1	24.9	18.4%
Japan (2005) **	29.8	7.9	18.8	18.7%
Brazil (2002) **	15.2	8.7	12.0	12.3%
Mexico (2002) **	10.9	8.7	9.8	10.7%

Source: [1], except for Australia, New Zealand and Japan [10], Brazil [5, 11] and Mexico [5, 12]

* The total number is calculated by taking the average of men and women, assuming an even distribution of sex in the populations. This is not an exact measure as the sex specific numbers are age-standardised.

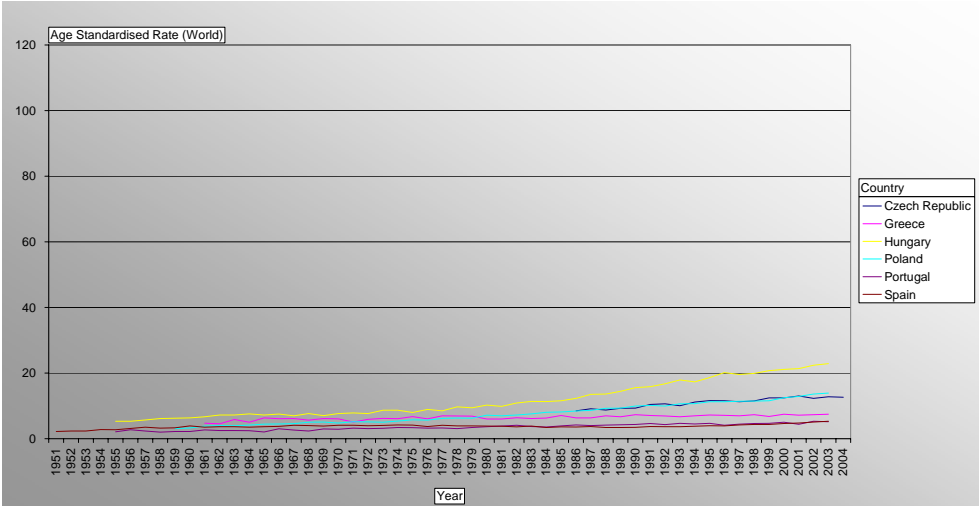
** World age standard

Figure 2-1 Age-standardized lung cancer mortality (European age standard) in Southern and Eastern Europe 1951-2004



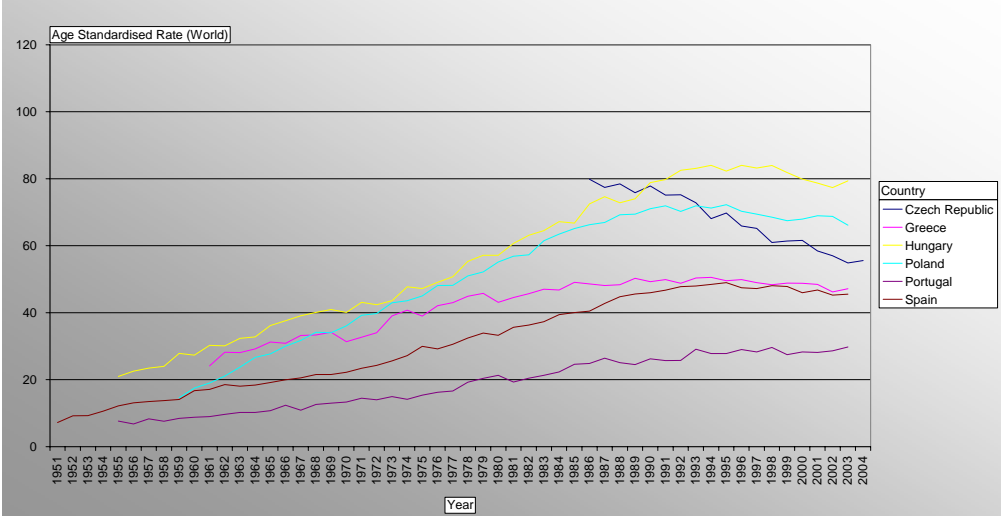
Source: WHO Mortality Database

Figure 2-2 Female age-standardized lung cancer mortality (European age standard) in Southern and Eastern Europe 1951-2004



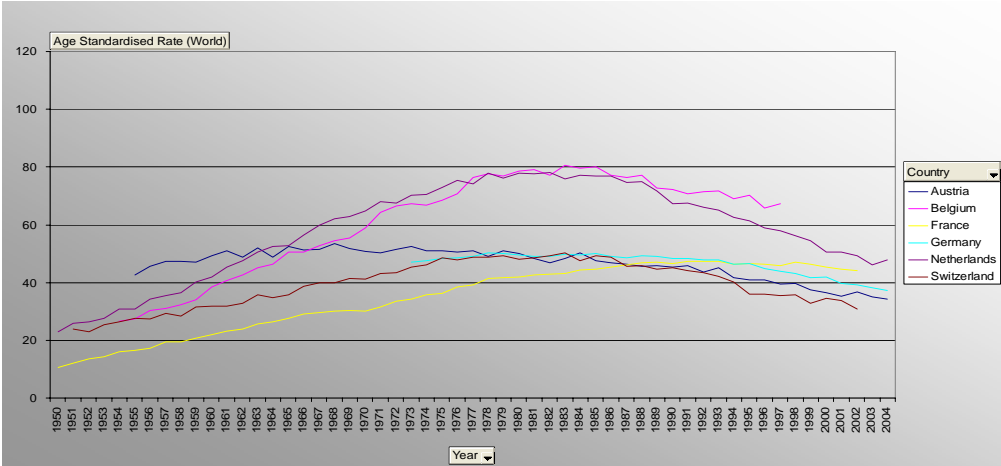
Source: WHO Mortality Database

Figure 2-3 Male age-standardized lung cancer mortality (European age standard) in Southern and Eastern Europe 1951-2004



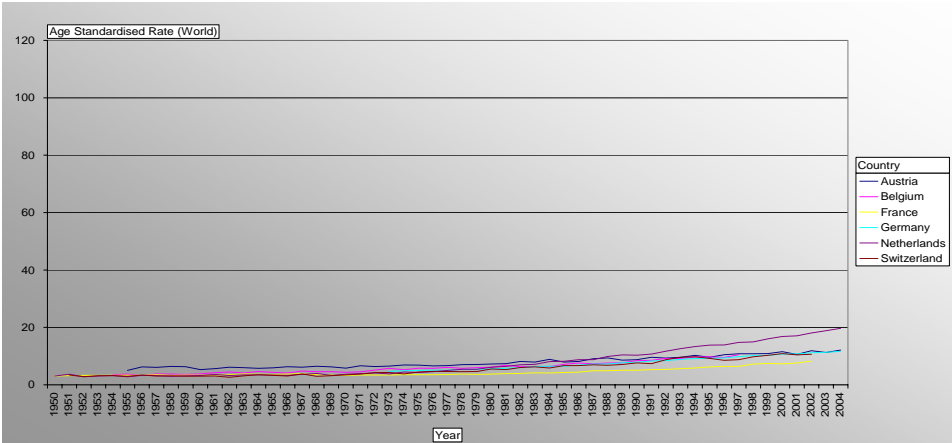
Source: WHO Mortality Database

Figure 2-4 Age-standardized lung cancer mortality (European age standard) in Western Europe 1951-2004



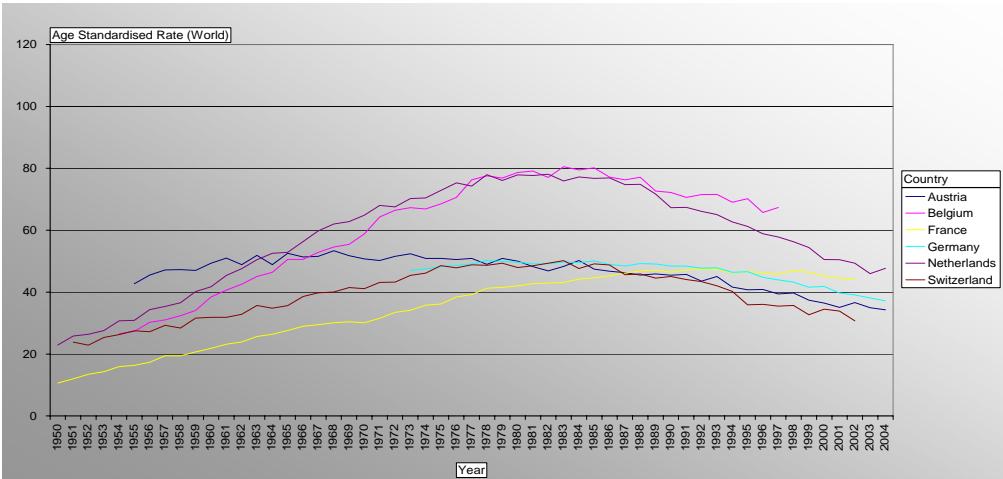
Source: WHO Mortality Database

Figure 2-5 Female age-standardized lung cancer mortality (European age standard) in Western Europe 1951-2004



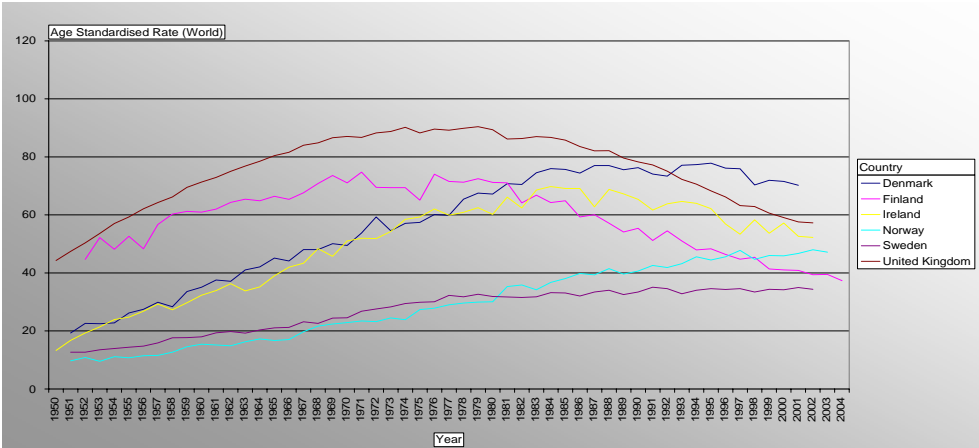
Source: WHO Mortality Database

Figure 2-6 Male age-standardized lung cancer mortality (European age standard) in Western Europe 1951-2004



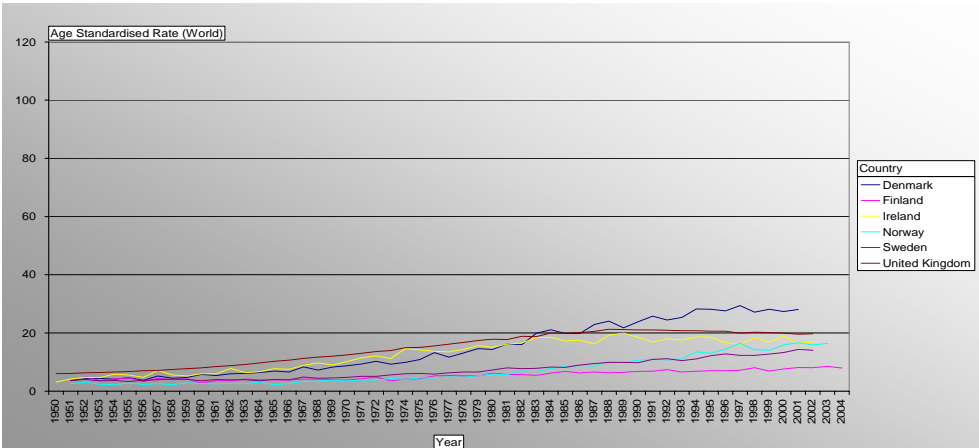
Source: WHO Mortality Database

Figure 2-7 Age-standardized lung cancer mortality (European age standard) in Northern Europe 1951-2004



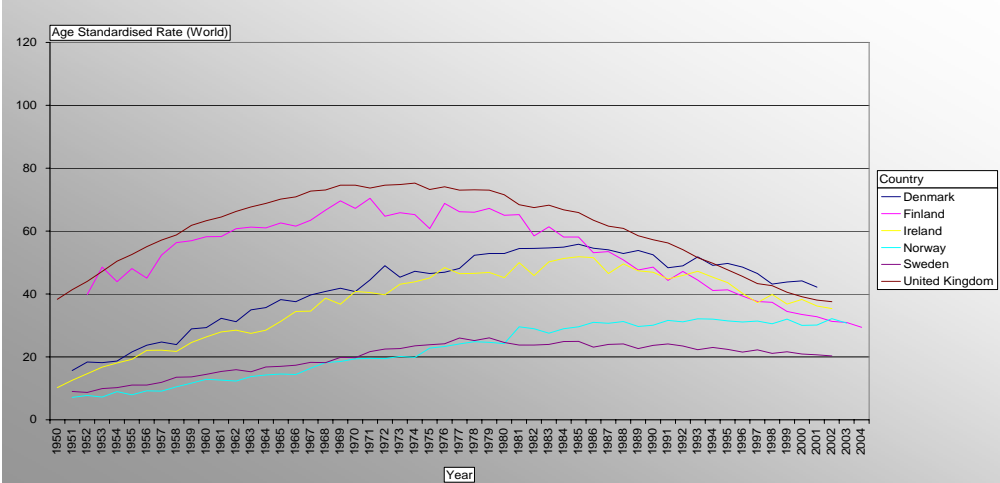
Source: WHO Mortality Database

Figure 2-8 Female age-standardized lung cancer mortality (European age standard) in Northern Europe 1951-2004



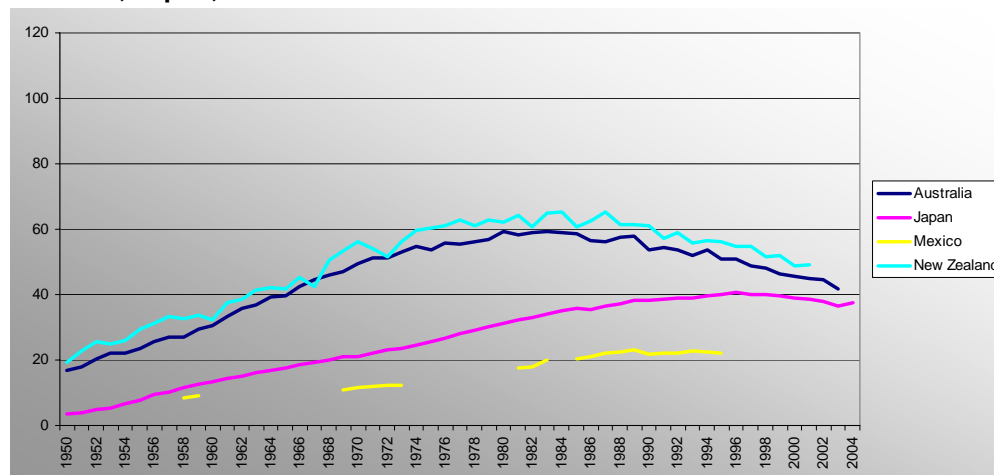
Source: WHO Mortality Database

Figure 2-9 Male age-standardized lung cancer mortality (European age standard) in Northern Europe 1951-2004



Source: WHO Mortality Database

Figure 2-10 Age adjusted (World age standard) lung cancer mortality per 100,000 inhabitants in Australia, Japan, Mexico and New Zealand 1950-2004



Source: WHO Mortality Database

2.3 Disability-Adjusted Life Years lost

The most commonly used measure of the burden of disease is the loss of Disability-Adjusted Life Years (DALYs). This is a term developed by the World Health Organization and the World Bank to measure the number of life years lost due to premature mortality and disability combined.

In the countries of this study the total DALYs lost amounts to 97,000,000 (2002). The largest cause of DALYs lost are due to neuropsychiatric conditions (22.4 per cent) followed by cardiovascular diseases (20.9 per cent), injuries (14.5 per cent), and cancers (13.1 per cent). Lung cancer is the type of cancer causing the most losses of DALYs due to its relative high prevalence and mortality. Lung cancer causes 2,500,000 out of the 12,700,000 DALYs lost by cancer. Lung cancer causes from 2.6 DALYs lost per 1,000 inhabitants in Sweden to 7.5 per 1,000 inhabitants in Hungary. In all countries of this study together, 4.2 DALYs per 1,000 inhabitants are lost due to lung cancer.

The DALYs lost in lung cancer as a share of DALYs lost in all cancers ranges from 13 per cent in Portugal to 25 per cent in Hungary. The countries with the highest lung cancer share of total cancer DALYs lost are also the countries with the highest mortality rates.

Following the lower rates in incidence and mortality in the non-European countries, the DALYs lost due to lung cancer is also smaller than in the European countries. Lung cancer also contributes with a smaller share of the total DALYs lost due to cancer in the non-European countries compared to the European. The difference is most notable in the Latin American countries, where the burden of lung cancer measured in DALYs lost are one fourth to one seventh in Brazil and Mexico respectively of the averages in the European countries in this study (Table 2-3).

Table 2-3 DALYs lost in lung cancer 2002

	DALYs lost in lung cancer per 1,000 inhabitants	Total DALYs lost in lung cancer	DALYs lost in all cancers	Lung cancer share of DALYs lost in all cancer
Austria	3.3	27,000	150,000	18.0%
Belgium	5.3	55,000	226,000	24.3%
Czech Republic	5.1	52,000	264,000	19.7%
Denmark	4.8	26,000	128,000	20.3%
Finland	2.7	14,000	86,000	16.3%
France	4.0	243,000	1,260,000	19.3%
Germany	4.3	354,000	1,807,000	19.6%
Greece	4.4	49,000	214,000	22.9%
Hungary	7.5	76,000	299,000	25.4%
Ireland	3.0	12,000	68,000	17.6%
Italy	4.1	238,000	1,202,000	19.8%
Netherlands	4.5	73,000	335,000	21.8%
Norway	3.3	15,000	84,000	17.9%
Poland	5.6	215,000	920,000	23.4%
Portugal	2.8	29,000	216,000	13.4%
Russian Federation	4.1	576,000	3,211,000	17.9%
Spain	3.6	155,000	785,000	19.7%
Sweden	2.6	23,000	153,000	15.0%
Switzerland	3.4	25,000	126,000	19.8%
United Kingdom	3.8	230,000	1,168,000	19.7%
Europe	4.2	2,487,000	12,702,000	19.6%
Australia	2.7	52,000	306,000	17.0%
New Zealand	2.7	10,000	67,000	14.9%
Japan	2.8	361,000	2,361,000	15.3%
Brazil	1.2	205,000	2,067,000	9.9%
Mexico	0.6	58,000	711,000	8.2%

Source: WHO

2.4 The cost of lung cancer

2.4.1 Direct costs

Cancer treatment is responsible for 5 to 7 per cent of total healthcare costs in Europe [13]. Variations in the overall level of healthcare spending lead to variations in the absolute per capita resources available for cancer treatment in different countries. Taking an average European estimated cancer healthcare expenditure of 6.6 per cent, the per capita direct cost of cancer treatment is € 125 [13].

It follows that countries which spend the most on healthcare generally, spend the most on cancer care: Switzerland (€199) and Norway (€194). Austria (€153), Belgium (€148), Denmark (€141), Germany (€147) and Sweden (€146) are all well above the average.

Far below the European average are the Eastern European countries. The Czech Republic and Hungary spend €50 per capita and Poland €30 per capita on cancer care. These levels are less than half of the European average in the cases of Czech Republic and Hungary and less than one fourth in the case of Poland [13].

Australia (€109) and New Zealand (€102) spend less than the European estimated average, while the Japanese expenditure on cancer care (€155) is only lower than Switzerland and Norway of the countries in this study [13].

Being one of the most common types of cancer, lung cancer takes up a large share of total resources. The availability of data on national costs for lung cancer is poor, both in the European and in the non-European countries. Estimates of direct costs are mostly based on small samples of patients within a region or in a single hospital. These costs are not always representative of an entire healthcare system, and the methods of collecting and estimating data are often unclear [14]. There are, however, some European countries where data is available on different types of cancer.

In Germany, the Netherlands and Sweden, lung cancer takes around 8 per cent of the total expenditure on cancer [15-17]. In Finland it takes 6.6 per cent [18], in France 9.3 per cent [19], and in Hungary 9.9 per cent [20] (Table 2-4). These figures should not be interpreted as directly comparable as the methods for estimating costs vary, and thus what costs are included.

Most direct costs relate to inpatient care. In Germany the share is 93 per cent, in Sweden 86 per cent and in the Netherlands 77 per cent.

Ambulatory, mainly outpatient, care takes 4 per cent in Germany, 13 per cent in Sweden and 9 per cent in the Netherlands.

The cost of drugs in lung cancer care takes 3 per cent in Germany, 1 per cent in Sweden and 3.5 per cent in the Netherlands [15-17]. Compared to direct costs for all cancers, inpatient care uses a relatively large share of the direct costs in lung cancer, while a smaller share is spent on ambulatory care and drugs [13].

Table 2-4 Direct costs of lung cancer

	Direct costs of lung cancer M€	Direct costs of cancer M€	Directs costs of lung cancer as a share of total cancer
Sweden ¹ [17]	128	1,608	8.0%
Finland ² [18]	19	281	6.6%
Germany [16]	1,358	17,673	7.7%
France [19]	1,008	10,858	9.3%
The Netherlands [15]	173	2,164	8.0%
Hungary [21]	49	495	9.9%

2.4.2 Indirect costs

Indirect costs are resources lost due to an inability to work. They include the costs of lost production due to deaths of people of working age (mortality), and the costs due to sickness leave, disability and early retirements (morbidity).

The indirect costs of different kinds of cancer vary greatly. In lung cancer they are high in relation to direct costs because of the poor survival rate.

Estimates from Sweden show that for all cancers indirect costs are about as high as the direct costs. Almost 80 per cent of the indirect costs are due to mortality [13]. In France a study from the *Institute National de Cancer* calculated indirect costs to be 61.6 per cent of the total cost of all cancer [19]. In the US the indirect cost of cancer is estimated at 65 to 75 per cent of the total cost of all cancer [13].

As is the case for all cancers, there are few studies estimating the distribution of direct and indirect cost for lung cancer [14]. The lack of such studies leads to a poor understanding of the burden of lung cancer on society. The numbers of diagnosed lung cancer patients who die from the disease are fairly well known.

In Germany in 1996 indirect costs were estimated to be 89 per cent of the total cost of lung cancer [22]. A more recent study estimated the indirect cost of cancer caused by smoking to be 80 per cent of the total cost [23]. Only half of the cancer cases in that study were lung cancer. This may explain the lower indirect cost as other forms of cancer generally have lower indirect costs.

In Sweden the indirect cost of lung cancer has been estimated to be about 87 per cent of the total cost [17]. Only 5.3 per cent of the indirect cost is due to morbidity, which is 35 per cent of the total cost.

In France the indirect cost of lung cancer is estimated to be 79 per cent of the total cost [19]. The French study also shows that the indirect share of total cost is higher in lung cancer than in other types of cancer. The major part of indirect costs in the countries of this study is the costs of mortality. The morbidity cost is only 1.5 per cent of all indirect costs.

A study in Finland estimated the cost of morbidity to be 29 per cent of total indirect costs [18].

¹ Costs for drugs and secondary prevention not included

² Only costs related to direct inpatient and outpatient care

Methods used to calculate indirect costs vary between countries, and it is therefore not feasible to make further comparisons. However, we can conclude that the vast majority of costs relating to lung cancer are indirect costs, and these are mostly related to production loss due to mortality. The indirect costs are 5-10 times higher than the direct costs related to lung cancer which is higher than most other kinds of cancer (Table 2-5).

Table 2-5 Distribution of direct and indirect costs of lung cancer in selected countries

	Direct Costs			Share of direct costs in lung cancer	Indirect Costs Share in lung cancer
	Inpatient care share of total	Ambulatory care share of total	Drug share of total		
Germany [16]	93	4	3	11	89
Finland[18]				71	29 (morbidity only)
France [19]				21	79
Netherlands [15]	77	9	4		
Sweden [17]	86	13	1	13	87

3 Medical overview of lung cancer

Lung cancer is not one disease but several diseases divided into two main categories: Small Cell Lung Cancer (SCLC) and Non Small Cell Lung Cancer (NSCLC). This section is mainly focused on NSCLC which account for 85 per cent of all cases of lung cancer. Lung cancer is a preventable disease and most cases are caused by smoking. There are few, if any, symptoms in the early stages and most patients are diagnosed with tumours which are already incurable.

3.1 Lung cancer tumours

There are three types of NSCLC:

- Adenocarcinomas are often found in an outer area of the lung.
- Squamous cell carcinomas are usually found in the centre of the lung by an air tube (bronchus).
- Large cell carcinomas can occur in any part of the lung. They tend to grow and spread faster than the other two types.

There are five defined stages of lung cancer:

Stage 0 - the cancer has not spread beyond the inner lining of the lung

Stage I - the tumour is small and has not spread to the lymph nodes

Stage II - the cancer has spread to some lymph nodes near the original tumour

Stage III - the cancer has spread to nearby tissue or spread to far away lymph nodes

Stage IV - the cancer has spread to other organs of the body such as the other lung, brain, or liver.

Stages I-III are often further divided into A and B to reflect differences within the stages.

3.2 Aetiology

80 to 90 per cent of NSCLC cases are caused by smoking, and about 10 per cent of life long smokers develop lung cancer. There are at least 40 components of tobacco smoke that are highly carcinogenic (cancer inducing) and all forms of tobacco smoke, cigarette, cigar, pipe, are equally dangerous. Filtered cigarettes seem to have changed tumour location in the lungs, as filters let smaller particles through. Smoking filtered cigarettes is also associated with more vigorous inhalation. Passive smoking has been identified as the cause of about 25 per cent of NSCLC cases in non-smokers [24].

Other environmental factors as asbestos, silica fibre and radon exposure have also been shown to increase the risk of developing NSCLC. In addition, there seem to be genetic factors that predispose for, as well as protect against, NSCLC.

3.3 Screening programmes, clinical presentation & diagnostic tests

The early stages of NSCLC are often asymptomatic. These tumours are often found when a chest X-ray examination is carried out for other reasons. Patients with more advanced tumours often present with fatigue, cough, dyspnoea, pneumonia, pain and weight loss. Diagnostic tests include bronchoscopy with biopsy, or fine needle biopsy, spirometry and Computerized Tomographic (CT) scans to establish operability and spread to local lymph

glands or other organs. Positron Emission Tomography (PET) and Magnetic Resonance Imaging (MRI) examinations are also being increasingly used. There are no reliable blood tumour markers presently available.

85 per cent of patients are currently diagnosed with tumours in advanced, incurable stages. Screening programmes could therefore have a pivotal role in increasing cure rates. Most of the studies performed so far have not found any evidence of screening benefit. Although in one recent study the value of yearly CT-screening of people at risk for lung cancer was evaluated in a study of over 30,000 people. It showed that 85 per cent of the tumours detected were in a curable stage of the disease [25].

3.4 Prognosis

Prognosis depends mainly on the stage of the tumour at diagnosis. With the exception of a small number of early-stage localised cancers, which can be cured with surgery or sometimes loco-regional radiotherapy, there is no cure. Patients with small tumours, below 3 cm in diameter without metastasis, have a 5-year survival rate of 70 per cent. Patients with larger tumours, with local lymph gland involvement, have a 5-year survival rate as low as 10 per cent. Most patients with metastases to other organs die within 6 months and less than 5 per cent of these patients survive 5 years. Patients with smoking-related NSCLC also have an increased risk of developing second malignancies.

3.5 Prevention

Lung cancer is largely a preventable disease and the strong relationship between smoking and lung cancer has been known for more than half a century. Yet there has been remarkably little public health prevention work in that time. Governments are finally now taking a more active approach to smoking cessation and regulations have recently been imposed to restrict smoking in public spaces. The impact of these measures on cancer incidence cannot, though, be expected to be seen until the mid 2020's.

Preventing lung cancer by medication has also been evaluated. A large retrospective study indicates that statin treatment results in an approximate 55 per cent risk reduction [26]. The value of statin treatment needs to be confirmed in prospective randomized trials. Several trials have also been performed using retinoids as chemoprevention, but these all had a negative outcome. There is reason to be optimistic about future prevention trials because of increased knowledge of the way lung cancer tumours develop. As with other tumours, the identification of cell-surface antigens presents the possibility of future vaccine trials.

3.6 Treatment

Patients with NSCLC can be divided into three groups according to the stage of the disease at diagnosis:

1. Patients with surgically resectable tumours have the best prognosis and a chance of cure. Surgery is, however, associated with 3-6 per cent mortality, and not all patients are suitable for surgery. Radical radiotherapy may be an alternative for patients unfit for surgery. Post-operative chemotherapy provides a moderate survival advantage in patients with stage IB-III A

cancer (all tumours over 3 cm in diameter and regional lymph node involvement on the same side as the tumour but no distant metastasis).

2. Patients with local or regional advanced disease benefit from multimodal treatment. Some patients can be treated with surgical resection in combination with either pre-operative or post-operative chemotherapy or radiation therapy. Patients with unresectable disease are treated with radiation therapy in combination with chemotherapy.

3. Patients with distant metastases may benefit from chemotherapy and local radiation therapy for local control of the disease and related symptoms. In advanced disease palliative chemotherapy offers improvements in median survival time [27] and improvement in disease-related symptoms without adversely affecting the overall quality of life.

3.6.1 Neoadjuvant treatment

The potential value of neoadjuvant (pre-operative) chemotherapy has been evaluated in two small randomized studies of patients with stage IIIA NSCLC and ipsilateral mediastinal lymph node involvement [28, 29]. In both studies patients randomised to three cycles of cisplatin-based chemotherapy before surgery had a median survival time of more than three times as long as patients treated with surgery alone. A large French randomised study of 373 patients also showed a trend in favour of pre-operative chemotherapy, but the difference was not statistically significant [30].

3.6.2 Adjuvant treatment

The first significant positive results concerning increased survival rates using post-operative chemotherapy with cisplatin, were reported in 2003 [31]. Since then similar results have been reported using taxanes and vinorelbine [32, 33]. The overall survival benefit of adjuvant treatment is an increased 5-year survival rate of 5-10 per cent. The value of adjuvant treatment in different stages of the disease varies. Recently, a meta-analysis of trials showed that patients in stage II and III benefit the most, but that there may also be a benefit for patients in stage IB. Patients in stage IA had no benefit from adjuvant chemotherapy [33].

Several studies of patients with unresectable stage IIIB disease have also shown that treatment with cisplatin-based chemotherapy and loco-regional radiotherapy result in improved survival, compared to radiation therapy alone. An analysis of data from several randomised trials indicates that the combination of chemo and radiation therapy results in a 10 per cent reduction in the risk of death compared to radiation therapy alone [34].

3.6.3 Treatment in metastatic disease

Chemotherapy in advanced stages of the disease has been used since the late 1980s, usually based on combinations of cisplatin with other chemotherapies. Currently, standard first-line treatment in most treatment centres uses a combination of cisplatin or carboplatin with gemcitabine, vinorelbine or a taxane, resulting in improved overall survival rates of an average two to three months.

The one-year survival rate increases to approximately 40 per cent compared to 10 per cent for patients who did not receive chemotherapy. Other combinations of chemotherapy such as

cisplatin with docetaxel, gemcitabine, paclitaxel, [35] vinblastine or vinorelbine [36] have resulted in similar responses, as did carboplatin and paclitaxel. Data from meta analyses favour cisplatin, compared to carboplatin-containing regimens, but the difference is relatively small [37, 38].

Recently the largest trial so far in first-line treatment of NSCLC showed that pemetrexed in combination with cisplatin produces similar results to gemcitabine in combination with cisplatin with regards to overall survival, and patients treated with pemetrexed had significantly fewer side effects [39]. When performing sub-group analyses, there was also a significant survival benefit for patient with non-squamous cell lung cancer, who received pemetrexed, compared to those who received gemcitabine.

Recently, it has been shown that levels of messenger RNA (mRNA) may predict which patients would benefit from cisplatin treatment, [40] opening the door to patient selection based on genetic profile.

While combinations of chemotherapy have been successful in improving overall survival, they have had no effect on efficacy survival. Studies combining more than two chemotherapy agents have not resulted in increased efficacy survival. As a second-line treatment, docetaxel or pemetrexed offers a two-month gain in survival [41, 42]. Monotherapy with gemcitabine or vinorelbine is commonly offered to patients with a poor prognosis or to patients who are not suitable for treatment with platinum-based compounds.

More recent therapies specifically target cancer cells, such as the epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor erlotinib. The use of this therapy is increasing, based on a trial which showed increased survival in patients previously treated with chemotherapy [43].

Gefitinib, a similar targeted agent, has mainly demonstrated efficacy in specific subsets of patients, such as those with adenocarcinoma, women, the Japanese and non-smokers. However, both erlotinib and gefitinib have yet failed to demonstrate significant benefit when given in combination with cisplatin/gemcitabine or carboplatin/paclitaxel [44, 45]. Data indicate that non-smokers may benefit from the addition of erlotinib to chemotherapy [44].

There are also indications that patients who would benefit most from EGFR inhibition are those with a particular genetic mutation [46, 47]. Further data is needed in order to have these markers of response fully investigated

Biological research is progressing at a rapid pace and a large number of new targeted agents are currently being investigated in NSCLC

One biological therapy already available is the angiogenesis inhibitor bevacizumab, which in combination with paclitaxel and carboplatin in patients with non-squamous NSCLC has recently been shown to significantly increase response rates from 15 to 35 per cent. Treatment also increased median overall survival from 10 to 12 months with a relatively moderate increase in side effects [48].

In future, combinations of different targeted therapies may offer further improvements. The combination of bevacizumab plus erlotinib has recently been shown to have a value comparable to that of available cytotoxic agents in non-squamous cell NSCLC [49, 50]. A

Phase III study of this combination is on-going. Positive results could herald a coming paradigm shift in the treatment of NSCLC, moving beyond conventional chemotherapy.

In total, approximately 500 clinical trials are registered at www.clinicaltrials.gov in NSCLC, although not all are evaluating new anti-tumour agents. Such trials will provide more information on possible predictive markers of response, which may in the future lead to personalised healthcare.

Table 3-1 Some anti-tumoural agents currently evaluated in clinical trials in NSCLC

Class of drug	Examples of therapeutic agent
EGFR inhibitors	Cetuximab, Panitumomab, Matuzumab
EGFR+ VEGF inhibitors	Vandetenib,
Angiogenesis inhibitors/ multi-targeted agents	Sunitinib, Sorafenib
mTOR inhibitors	Temsirolimus
Proteasome inhibitors	Bortozemib
Antisense Therapeutic vaccines	MAGE A3
COX2 inhibitors	Bexarotene
HER2 inhibitors	Trastuzumab

4 Outcome of lung cancer care

The survival rates for patients diagnosed with lung cancer are low. Almost 90 per cent of all patients in Europe die within 5 years [7]. Lung cancer care and survival rates vary but the gap between the most and the least successful countries is narrowing. There is room for improvement by studying the factors which lead to poor as well as better outcomes. But, as we will discuss in this section, lack of reliable data makes it difficult to assess effectiveness in lung cancer treatment.

In the recent EURO CARE-4 study, the 5-year relative survival rate for lung cancer patients diagnosed between 1995 and 1999 ranged from 7.9 per cent in Denmark to 14.3 per cent in the Netherlands [51]. (EURO CARE is an international collaboration between cancer registries to study the care and survival of cancer in Europe.)

There are also disparities in survival rates within countries. In the UK the 5-year relative survival rate in Scotland for patients diagnosed between 2000 and 2002 was 8.2 per cent compared to 10.7 per cent in Northern Ireland [4]. In Ireland the 5-year relative survival rates ranged from 7.8 per cent in one region to 10.1 per cent in the best performing region [52]

Urban areas tend to have higher survival rates than rural areas. This is evident in Russia, where the geographical distances to health care facilities in the Eastern parts of the country limits access to healthcare [53].

A relationship between socioeconomic status and survival has also been shown as high income earners [54-56] and people with more education [54, 57, 58] have better chances of survival. Chapter 3 reviews the factors related to diagnosis and treatment of lung cancer and their influence on survival.

Figure 4-1 gives a comparative estimate of the outcome of lung cancer treatment. The data is from the GLOBOCAN 2002 database which contains estimates for the incidence, mortality and prevalence of lung cancer in 2002. (GLOBOCAN 2002 is a database built up by the International Agency for Research on Cancer).

In this study, we have chosen to estimate the outcome of lung cancer by the prevalence/incidence measure. This is calculated by dividing the prevalence (the overall number of cases) by the incidence (the number of new cases) multiplied by the number of years of prevalence. The 5-year prevalence/incidence ratio is then the 5-year prevalence divided by the incidence multiplied by 5. The 5-year prevalence is the number of new cases in the past 5 years still being alive.

The reason for using the prevalence/incidence measure is to be able to include all the countries in our study and to present treatment outcomes for the short, medium and long term. They are the best comparable figures available for such a large number of countries. As previously mentioned, lack of more reliable data is a problem in making sound comparisons between countries.

The GLOBOCAN data is estimates based on national or regional cancer registries. Some registries have full national population coverage but others cover only a small share of the population in the country: for example, less than three per cent in Germany and about six per

cent in France and Poland. This means that the numbers are not necessarily representative for the whole country. In addition, registries in different countries use different methods to collect data [59]. For a detailed review of the methods used in the GLOBOCAN data, see [5].

The countries in Figure 4-1 are ranked according to the 5-year ratio. It should be noted that this is not a precise measure of survival. However, our estimate shows which countries perform better and which countries have lower outcomes of lung cancer care.

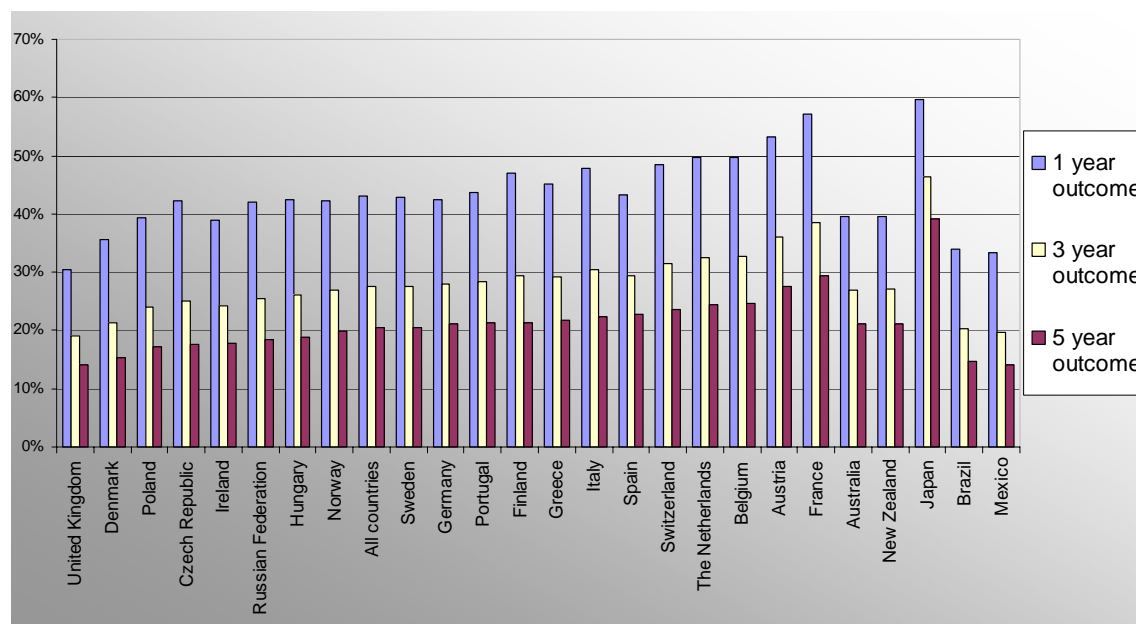
The European countries can be divided into three groups by treatment outcomes: the low performing countries (the United Kingdom, Denmark, Poland, the Czech Republic, Ireland, the Russian Federation, and Hungary), the medium performing countries (Norway, Sweden, Germany, Portugal, Finland, Greece, Italy and Spain) and the countries with the best outcomes of lung cancer care (Switzerland, the Netherlands, Belgium, Austria and France). This division will be used in our analysis of what countries are considered to be more successful in curing lung cancer.

Japan has an outcome of lung cancer care which is much higher than the other countries in this section and the European average; it is even higher than the outcome in the best performing countries in Europe, France and Austria. Australia and New Zealand show an outcome level within the range of the medium performing countries, similar to Norway, Sweden, Germany and Portugal. The outcome in the Latin American countries is within the range of the lowest performing countries in Europe.

As a complement to the outcome data presented in Figure 4-1, table 4-1 presents relative survival rates in 17 European countries from the EURO CARE 4 study. These data largely confirms the picture presented in Figure 4-1 in terms of what countries are performing well and less well. The main exceptions are Germany and Sweden performing relatively better in the EURO CARE study, while France and Spain ranks lower in relation to the highest performing countries. The relative poor performance in the UK countries, Denmark and in the Eastern European countries is confirmed in the EURO CARE study Table 4-1.

The 5-year relative survival rate in lung cancer in Australia is with 14.0 per cent on the same level as the best performing countries in Europe. Only the Netherlands have higher survival rates. It is also higher than in New Zealand, where the corresponding survival rate is 10.8 per cent. The New Zealand survival data is comparable to the average European survival rates. The outstanding performance of lung cancer care in Japan presented in Figure 4-1 is confirmed by registry based survival statistics. For patients diagnosed in 1993-1996 in ten population-based cancer registries, the 5-year relative survival rate was 19.9 per cent. That is by far higher than in any European country. Brazil and Mexico have the lowest 5-year survival rates. There is no statistics on 5-year lung cancer survival on the national level in Brazil and Mexico. Estimates based on data from hospital registries indicate that the 5-year survival is less than 5% in both countries (Table 4-2). There are also socioeconomic and ethnic differences in survival in New Zealand. Lung cancer patients among the Maori population only have half the survival rate of non Maoris [60]. There are studies in progress aiming at finding explanations to these large ethnic differences in survival.

Figure 4-1 Outcome of lung cancer treatment



Source: Calculations based on data from GLOBOCAN 2002 [5]

Table 4-1: 5-year age adjusted relative survival rate for patients diagnosed with lung cancer in selected European countries 1991-1999. Survival measured up to 2003 according to EURO CARE 4.

	Relative survival in % for	
	1991-1994	1995-1999
The Netherlands	12.0	14.3
Austria	14.4	13.9
Switzerland	10.3	13.6
Germany	11.7	13.2
Sweden	10.6	13.1
France	14.0	12.8
Italy	10.8	12.8
Norway	9.7	10.9
Spain	11.4	10.8
Northern Ireland	7.8	10.2
Finland	8.7	9.6
Poland	6.8	9.2
Wales	8.3	9.0
England	7.9	8.6
Czech Republic	7.0	8.2
Scotland	7.4	8.0
Denmark	6.5	7.9

Source: [51].

Table 4-2 5-year age adjusted relative survival rate for patients diagnosed with lung cancer in Australia, New Zealand, Brazil and Mexico

	5-year survival rate in %
Australia 1999-2003 [61].	14.0
New Zealand 1994-2003 [60]	10.2
Japan [62]	19.9
Brazil [63]	0-4
Mexico [64]	5

About half of the countries included in this study, Denmark, Finland, Norway, Sweden, Austria, Belgium, the Netherlands, Ireland, the Czech Republic and Hungary, have a national full population coverage cancer registry or regional registries covering the entire population linked together in a national association. In the other countries there are regional registries covering parts of the population. In international comparisons like GLOBOCAN or EUROCARE, most of the countries are represented by registries covering a small part of the population. In Germany for example the Saarland registry covering 1 per cent of the population is used by EUROCARE. Very small shares of the population are also covered in the Czech Republic (8 per cent) and in Poland (9 per cent) [51].

The use of regional registries alone has been criticized by officials in the Czech Republic as giving an incorrectly negative picture of survival there [65]. Cancer Research UK has criticised the EUROCARE study for showing an unjust negative picture of the UK countries due to the high population registry coverage compared to countries represented by registries in regions expected to have better outcomes than the national averages [66].

It is especially difficult to assess and confirm data in Greece and in Russia. In Greece there are no registries and the estimates in GLOBOCAN are based on data from Italy and Spain. The data on Greece must therefore be interpreted with caution, as the Greek outcome data is probably overestimated. The Russian estimates are based on data from the cancer registry in St Petersburg. This represents a small share of the population and also represents the situation in a large city with better resources than most other parts of the country. The Russian data on outcome is therefore also expected to be over estimated. Great variations in the Russian healthcare system, as well as in the quality and accessibility of cancer treatment, make it very difficult to present a reliable national picture.

5 Organisation of lung cancer care

The organisation of lung cancer care varies from country to country. It generally mirrors the overall organisation of the healthcare system of a particular country but increasingly organisational changes are being made in an attempt to make the best use of more advanced lung cancer care. The most advanced treatment is highly specialised and expensive. Organisation and coordination are therefore important factors in efforts to ensure equal access to the best treatment for all patients.

5.1 National health expenditures

Many studies have found a positive relationship between the outcome of lung cancer treatment and macroeconomic indicators such as GDP or expenditures on health [7]. The health expenditures in the countries of this study, ranked by health expenditures per capita in USD PPP, are presented in Table 5-1 below.

France, Austria, Belgium, the Netherlands, Switzerland, Spain, Italy, Greece, Finland, Portugal, Germany and Sweden are above the European average for treatment outcome as presented in chapter 4. Of these all but the United Kingdom, Italy, Finland, and Spain have a total health expenditure per capita figure higher than 2 900 USD PPP.

The United Kingdom, Denmark, Poland, the Czech Republic, Ireland, the Russian Federation, Hungary and Norway are below the European average for treatment outcome as presented in chapter 4. In the case of the UK, Ireland and Denmark that is despite having overall health expenditures above 2,700 USD PPP per capita.

France, Austria, Belgium, the Netherlands and Switzerland have the best outcome of lung cancer care and are among the six countries with the highest per capita spending on health.

The national health expenditure per capita (PPP) in Brazil and Mexico is lower than in the three other non-European countries, and also lower than most European countries. In Europe only the Russian Federation has a lower per capita spending than Mexico and Brazil. New Zealand and Japan would rank about in the middle of the European countries, while Australia would rank among the top spending countries in health expenditures only outperformed by Norway and Switzerland (Table 5-1).

Table 5-1: Expenditures on health and pharmaceuticals 2005

	Total health expenditure in per cent of GDP	Public expenditure in per cent of total expenditure	Health expenditure per capita in USD PPP	Pharmaceutical expenditure in per cent of total expenditure
Russian Federation	5.3%	61.3%	583	NA
Poland	6.2%	69.3%	867	29.6%
Hungary	8.1%*	70.5%*	1,337*	27.6%
Czech Republic	7.2%	88.6%	1,479	22.0%
Portugal	10.2%	72.3%	2,041	23.2%
Spain	8.3%	71.4%	2,261	22.8%
Finland	7.5%	77.8%	2,331	17.4%
Italy	8.9%	76.6%	2,532	16.3%
United Kingdom	8.3%	87.1%	2,724	21.4%
Sweden	9.1%	84.6%	2,918	12.2%
Ireland	7.5%	78.0%	2,926	12.4%
Greece	10.1%	42.8%	2,981	12.3%
Netherlands	9.2%*	62.5%**	3,094*	9.4%
Denmark	9.1%	84.1%	3,108	14.6%
Germany	10.7%	76.9%	3,287	11.5%
France	11.1%	79.8%	3,374	11.3%
Belgium	10.3%	72.3%	3,389	13.0%
Austria	10.2%	75.7%	3,519	18.9%
Switzerland	11.6%	59.7%	4,177	9.5%
Norway	9.1%	83.6%	4,364	10.4%
Australia	9.5%*	67.5%*	3,128*	14.2%
New Zealand	9.0%	77.4%	2,330	12.5%
Japan	8.0%*	81.7%*	2,358*	19.8%
Brazil	7.9%	46.3%	755	18.0%
Mexico	6.4%	45.5%	724	21.3%

Source: OECD Health Data 2007 except Russian Federation and Brazil WHO, National Health Accounts.

*2004

**2002

5.2 Organisation of healthcare services

European healthcare systems can broadly be described as Beveridgean or Bismarckian. In Beveridgean systems, healthcare is primarily funded through taxation with mainly public providers and staff employed directly by the state. Examples of these systems are found in the UK, the Nordic countries, Spain and Italy. The Bismarckian type of system is based on insurance schemes, and private provision of healthcare. These systems are found in France, Germany and the Netherlands.

With a few exceptions, all the countries included in this report have 100 per cent, or almost 100 per cent, of their population included in the public healthcare system. The Russian system has the intention of providing full coverage, but only 88 per cent of the working population was covered in the year 2000 [67]. In the Netherlands and Germany, people with an income above a certain level may choose private alternative insurances.

All the countries in this study, in common with most industrialised countries, have a combination of private and public involvement in both the financing and provision of

healthcare. The private share of the total health expenditures spans from 11 per cent in the Czech Republic to 48 per cent in Greece. The private share is also low (15-20 per cent) in Denmark, Norway, Sweden and the UK. It is high in Switzerland (42 per cent), the Russian Federation (39 per cent) and the Netherlands (38 per cent)

The share of private health spending in New Zealand and Japan is lower than in most European countries. Australia, on the other hand, would rank Australia among the European countries with the highest private spending.

More than half of health care expenditure in Brazil and Mexico is private spending, the private share of the total health expenditures is 54 per cent both in Mexico and in Brazil, a considerable higher rate than in most European countries of which only five have a private share of total health spending above 30 per cent (Table 5-1).

Healthcare systems mostly follow the political and administrative organisation of a country. These different structures and degrees of centralisation provide the framework for the provision and delivery of lung cancer care.

In federal states like **Russia, Spain, Switzerland, Austria, Belgium** and **Germany**, provision is delegated to regional authorities. They have a certain degree of freedom but are still supervised and regulated by national governments. The Russian healthcare system has been officially decentralised since the fall of the Soviet Union, but in practice power is still highly centralised. Scarce economic resources in the Russian healthcare system, especially in areas outside of the larger cities, has led to large deficits in terms of the availability and quality of health services.

In **the UK** the healthcare system is decentralised to the constituent countries of England, Scotland, Wales and Northern Ireland, though each is itself rather centralised.

In **Portugal** and **Greece** the provision of healthcare is a centralised national responsibility. The Greek healthcare system is fragmented and the provision and quality of services is highly uneven.

In **the Netherlands** a large share of hospitals are run by private non-profit organisations, regulated at a national level.

In **Italy** the provision of healthcare is nationally regulated but delivered by local public health organisations purchasing services from public and private providers.

In **Finland** there are 21 administrative health regions, but the provision of healthcare is highly decentralised to 460 local municipalities responsible for primary and specialist care.

In recent years, some countries have gone through a process of centralisation while others have devolved national responsibilities to regional or local levels. In Denmark, Norway and Ireland healthcare systems are being re-organised to create fewer administrative bodies.

In **Denmark** municipalities and regions have been cut by a third, and the regions now have greater responsibility for the provision of healthcare.

In **Norway** primary care is still a matter for municipalities, but secondary care has been centralised by forming five regional state-owned hospital enterprises.

In **Ireland** a wide range of public authorities and eight regional health boards have been gathered into one Health Service Executive.

In **Sweden** a reduction of the 18 county councils and two regions into a smaller number of regions is currently being discussed, but no decision has yet been made.

Since the 1990s the healthcare system in **France** has been going through a decentralisation process leading to regional government gaining influence from the national government.

In the same time period the central and Eastern European countries of **the Czech Republic, Hungary** and **Poland** have been transformed from highly centralised systems to more pluralist, or regionalised, systems. The reform and decentralisation process in Hungary has been inconsistent due to a lack of political consensus on the level and structure of decentralisation. This has led to poor coordination of healthcare. In the Czech Republic and Poland hospitals are publicly run at a regional level, but university hospitals are managed by the National Ministry of Health.

The responsibilities of healthcare in **Australia** are shared between the Commonwealth on the national level and the six states and two territories on the sub national level. The Australian healthcare system provides universal access to health care through the national *Medicare* program. The States and Territories have the main responsibility of providing public health care services in Australia. They provide public acute and psychiatric hospital services and a wide range of community and public health services. The geographical size of the country and large share of the population living in rural areas poses a challenge in providing access to health services.

The health care system in **New Zealand** covers all citizens and is primarily funded by general taxation. In year 2000, the health care system went through a decentralization reform establishing 21 district health boards (DHBs) with the responsibility to provide health care services to the population in their respective area. These 21 district health boards replaced a national *Health Funding Authority* (HFA) and 23 hospital and health services companies. The DHBs have the responsibility to deliver health care services either themselves or by purchasing services from other providers. The DHBs are cooperating with each other, for example in providing specialist services drawing patients from larger regions. The central government distributes funds for each of the DHBs.

The health care system in **Japan** is a universal health insurance system. All Japanese citizens must be covered by National Health Insurance (NHI). Most of Japanese people have to pay 30 per cent of the medical services that they are offered as co-payment, and rest of the 70 per cent is paid by the NHI. Japan has 47 prefectures which hold the main responsibility for organizing and planning the medical supply system.

The current national health policy in **Brazil** was implemented with the 1988 Brazilian Constitution, making health care a right of every person in Brazil and a responsibility of the state with the goal to establish a welfare state in line with the Beveridgean-type systems existing in Europe. The delivery of public health care in the country is provided through the *Sistema Único de Saúde* (SUS). Management and organization of health services in Brazil is

decentralized; on the federal level, the Ministry of Health oversees the national management of the SUS, while the state and municipal levels manage a complex network of public establishments and subcontracted health care providers. 80 per cent of the hospitals providing services within the SUS are private [68-70]. Approximately 20 per cent of the Brazilian population are covered by private health care plans. Since all inhabitants in Brazil have access to SUS, they may still use public services for procedures not covered by their private plans.

The health care system in **Mexico** follows the Bismarckian model; health care is provided mainly through social security insurance agencies, although (basic) tax-funded health care services are provided for the population not covered by insurance schemes. The two major social insurance agencies, the *Instituto Mexicano del Seguro Social* (IMSS) - for salaried employees of private companies, and the *Instituto de Seguridad y Servicios Sociales de los Trabajadores del Estado* (ISSSTE) - for public sector employees, cover approximately 45% and 10% of the population respectively. For the half of the population not covered by social security, mainly due to not being part of the formal labour market, there are voluntary insurance programmes as well as government schemes that provide health care based on an evaluation of socio-economic status at the time of receiving treatment. The health care system in Mexico can be characterized as being vertically integrated but horizontally segregated with the three institutional groups, social security, public sector, and private sector, functioning separately [71].

For more details on the organisation and financing of health care, please see Appendix 1.

5.3 Organisation of lung cancer care

The organisation of lung cancer care varies from country to country. It often mirrors the organisation of healthcare in a particular country generally but increasingly lung cancer care is crossing traditional administrative and organisational borders.

For patients with lung cancer it is preferable to receive treatment near home. Less advanced treatment such as after-care, palliative care and rehabilitation is therefore carried out in smaller local facilities. However, highly specialised care needs to be organised in treatment centres with high case loads, medical specialties in several disciplines, sufficient equipment and integrated treatment pathways. Such centres are increasingly recognised in many countries as important to ensure accessibility to the highest standard of treatment for all patients, wherever they live. To manage these two objectives there needs to be effective interaction between the smaller local facilities and the specialist treatment centres.

In all countries of the study, initial appointments and less advanced treatment are provided in general hospitals. Specialist care is provided in larger treatment centres, often with a regional area of uptake.

Many countries have realised that if more advanced cancer care is provided at too many hospitals it leads to fragmented treatment paths. This is made worse by a lack of resources in individual hospitals and poor referral systems for sending patients to appropriate treatment centres. This problem is apparent in countries, mainly in Eastern Europe, where less is spent on healthcare. Small units do not have the budget for new innovative drugs, the latest screening and radiotherapy equipment, or the recruitment and training of specialist staff. In recognising the need for such investment, and in trying to use limited resources most

effectively [20], more advanced cancer care is increasingly centralised to fewer treatment centres [72, 73].

The most specialised cancer care is increasingly being brought together in specific organisations or networks of treatment centres. Based on a concept introduced by the US National Cancer Institute, Comprehensive Cancer Centres are recognised as an international standard for treatment institutions. They bring together specialist diagnostic and treatment services, basic and clinical research, clinical trials and education. The purpose of locating clinical care with laboratory, clinical and translational researchers is to create a foundation for the development and application of the latest scientific results.

Several countries have comprehensive cancer centres within single organisations, or operating as networks between treatment institutions. What constitutes a comprehensive cancer centre is not clearly defined and varies from country to country. Even if there are several comprehensive cancer centres, or other specialised treatment centres dedicated to cancer, these do not provide all, or even most, treatment services. They often provide the most advanced treatment alternatives, and perform research and education.

In **France** there are 29 regional hospitals, mostly linked to universities, and 20 comprehensive cancer centres. Extensive cancer care facilities providing surgery, radiotherapy and chemotherapy are also available in all main urban centres. Seven cancer research hubs (*Canceropôles*), bringing together research, cancer care and industry, have also been established to promote research and innovation.

In **the Netherlands** each of the nine healthcare regions has formed a Comprehensive Cancer Centre to coordinate treatment, research and education at institutions within their region.

In **Germany** there are 35 *Tumorzentren* bringing together specialised cancer care with a regional uptake. These may be organised within a single organisation or in a network. The *Tumorzentren* are often, but not always, attached to university hospitals. Four of them are also designated Comprehensive Cancer Centres [74].

Cancer care in **Poland** is organised in a three-tier system. At the top is the Maria Skłodowska-Curie Memorial Cancer Centre, which is also organised as a Comprehensive Cancer Centre, and the Institute of Oncology, Warsaw. The second tier consists of 10 Regional Comprehensive Oncological Centres. In the third tier there are approximately 50 cancer wards and chemotherapy and radiotherapy units in hospitals, many of which are attached to medical faculties at universities. There are also approximately 40 consultation points and outpatient oncological clinics in larger cities.

In **Norway** there is one designated comprehensive cancer centre - a national reference hospital for cancer care. There are also five specialised and well-equipped oncological centres at university hospitals. Initial cancer diagnosis and treatment is mainly carried out in the surgical departments of central or peripheral hospitals in the regions.

In the **Czech Republic** the Czech Oncological Society has designated 18 Complex Cancer Centres, of which one has the status of a comprehensive cancer centre. The Complex Cancer Centres are either single institutions or networks of hospitals collaborating with a medical faculty. The cancer centre operations are coordinated by a National Council of Oncocentres. Only a few years ago cancer care in the Czech Republic was provided at a large number of

often small hospitals with limited resources and insufficient or outdated equipment. This resulted in a lack of coordination within and between hospitals.

Hungary introduced a national cancer plan in 2005. The new organisation of cancer care aimed to pool resources into fewer treatment centres. This plan is replacing a fragmented system in which cancer care was provided at a large number of under-equipped and under-financed treatment facilities [72].

In **the UK** the local primary care trusts in England have formed regional cancer networks. They were introduced in the Calman Hine report in 1995 and now operate under the NHS Cancer plan of 2000. The networks bring together health service commissioners and providers, the voluntary sector, and local authorities. There is also a cancer service collaborative initiative to help the cancer networks organise the delivery of cancer care. Similar networks exist in Scotland, Wales and Northern Ireland.

In **Ireland** cancer care has recently been reorganised into four Managed Cancer Control Networks, each of which has one to three cancer centres. The intention is that each cancer centre should serve a minimum population of 500,000 in order to ensure a sufficient number of cases.

In **Italy** there are seven specialised cancer institutes performing oncological treatment and research. These institutes are financed by, and responsible to, the Ministry of Health. They are therefore largely independent from regional or local authorities and the independent local health companies which are responsible for the provision of healthcare by contracting public and private hospitals. However, most cancer patients are not treated at these institutes but at general hospitals.

In **Portugal** there are three regional Specialised Cancer Institutes offering the most up-to-date cancer treatment in the country. There are also six public radiotherapy centres. Services are also offered at larger urban hospitals and several dozen regional hospitals. Standards at regional and local treatment centres vary significantly because of a lack of resources, staff and equipment in many facilities.

In **Austria** lung cancer patients are mainly diagnosed and treated in general hospitals, including university hospitals which treat about half of the patients. Many district hospitals have oncology boards to ensure multidisciplinary treatment of patients [75].

In **Denmark** lung cancer care is also centred around the university hospitals, though cancer surgery and some chemotherapy is also carried out at the larger central hospitals in the regions. The four university hospitals have specialist oncology departments and radiotherapy facilities. There are also two smaller dedicated oncology centres. Aftercare, palliation and rehabilitation are the responsibilities of local care units and the primary care sector.

The organisation of cancer care in **Belgium** has recently been restructured to improve access and quality. The basis for the new organisation is an oncological care programme focusing on delivery of cancer care by multidisciplinary teams following new clinical guidelines. Cancer care is provided in fewer hospitals which are collaborating in networks. One hospital, *Institute Jules Bordet*, is entirely dedicated to Oncology treatment, research and teaching [73].

In **Spain** cancer diagnosis and treatment is mainly carried out at approximately 150 oncology units in approximately 110 general hospitals and 35 private clinics. The larger public general hospitals have oncology departments. In addition to the general hospital system there are also four specialised oncology centres. These are small, around 100 beds each, so can only treat a limited number of patients.

In **Sweden** the most advanced cancer care, along with other highly specialised care, is coordinated in six healthcare regions. Cancer treatment usually takes place in general hospitals, but the university hospitals serve as regional cancer centres with specialist diagnostic, treatment and research facilities.

University hospitals also serve as specialist cancer centres in **Finland**. In addition, there are radiotherapy units at four other hospitals and at the central hospitals in each of the healthcare regions which also perform oncological surgery. 95 per cent of all lung cancer patients in Finland are treated at the regional hospitals.

Cancer care in **the Russian Federation** is unevenly accessible. There are five cancer institutes, two in Moscow and one each in St Petersburg, Rostov on the Don and Tomsk. There are also three radiology centres. Outside the largest cities there are more than a hundred local cancer hospitals, but the resources in these are very scarce. Outside the large cancer centres the accessibility of modern cancer drugs is poor.

Cancer care services in **Greece** are mostly described as complex, fragmented and inefficient [76]. The lack of national registries and research on the quality of cancer care makes it difficult to assess the effectiveness of lung cancer care. The most advanced cancer treatment is provided at 23 regional hospitals, of which seven are university hospitals.

The organisation of lung cancer care in **Switzerland** follows the general organisation of healthcare, where provision is a regional responsibility of the cantons. There has been a national cancer programme in Switzerland since 2005. One of the main objectives of this plan is to promote a better coordination of cancer care which is made difficult by strong regional independence.

Being a large country with a great part of the population living in remote rural areas, there are great variations in the treatment of lung cancer in **Australia** [77]. As a measure to improve the equity and quality in provision of services, network organisations has been introduced in each of the six states and two territories. However, these networks only cover 8 million out of the total population of 20 million yet.

In order to improve the coordination of cancer treatment services in **New Zealand**, four regional cancer networks was initiated in 2006 covering the entire country. Each of the cancer control networks has one or two specialised cancer centres performing the most advanced cancer treatments. In total there are six specialised cancer centres.

There is one national cancer centre in **Japan** acting as a hub of research, treatment and prevention of cancer in Japan. In addition there are also 28 local cancer centres under the umbrella organization *Japanese Association of Clinical Cancer Centres* (JOCCC). These institutes almost exclusively treat cancer patients, along with clinical research and training of specialists. Some are financed by the central government, while others are financed by the prefectures or from private sources.

Following a recent reorganisation, oncology care in the public sector in **Brazil** is provided by specific health centres for oncology – *Centros de Assistência de Alta Complexidade em Oncologia* (CACONs), and *Unidades de Assistência de Alta Complexidade em Oncologia* (UNACONs) affiliated to the public health system. CACONs and UNACONs are hospital units that offer integral treatment to cancer patients; they are responsible for diagnostics, outpatient and inpatient care, emergency care and palliative care. CACONs offer treatment for all kinds of cancer forms while UNACONs offer treatment for the most prevalent cancer forms. There are currently 365 units under SUS offering oncology care, almost 200 UNACONs, approximately 50 CACONs and in addition a number of specific chemotherapy and radiotherapy units.

Within each regional unit of the largest social insurance agency in **Mexico**, IMSS, there are 1300 *Unidades de Atención Médica* (UAM) which are categorised according to level of care. Of these, approximately 220 are *Hospitales Regionales y Generales de Zona* (HGR/HGZ) where clinical oncology care is provided and 41 are *Unidades de Medicina de Alta Especialidad* (UMAE), in which advanced care such as surgical oncology care is provided [78].

For country specific details on the organisation of lung cancer care, please see Appendix 1.

5.4 National co-ordination and re-organisation of lung cancer services

In a recent review by the OECD Health Committee, lack of co-ordination is identified as a major obstacle to efficient delivery of healthcare, as increased costs and greater complexity leads to growing fragmentation. This trend is most apparent in diseases like cancer where treatment requires a high level of specialisation and high costs require strategies to make the best use of limited resources [79].

Variations in preconditions, treatment and survival in lung cancer are not only noticeable between countries, but also within countries. The reasons for these differences also vary, but the one thing countries with unequal standards share is an inability to provide the best lung cancer care for patients everywhere. These regional variations and inequity in access to the best cancer treatment signals a need for nationally co-ordinated strategies. This has been recognised in several countries and has, together with the burden of cancer disease in society and high death rates, been one of the main drivers of national plans to improve cancer care.

To ensure the best methods are used for screening, referral to specialists and treatment, there are national or regional guidelines on what method or methods to use in any given situation. Such guidelines have also been developed by international societies of oncology, and applied by medical doctors in different countries. National cancer control plans are general whereas treatment guidelines are specific to each type of cancer.

In most countries the organisation of cancer care has been developed without a structured analysis of needs or a strategic plan [80]. However, many countries have realised that to get the most out of cancer care resources, rigorous analysis and extensive reforms, possibly of the entire organisation of cancer care, are required. An effective tool to start such a process is the development of cancer control plans. Of the countries in this study, Belgium, Finland, Greece, Italy, Poland, Russia and Sweden are the exceptions in not having such plans. These countries also lack national coordination of cancer care. In Belgium and Sweden, however, such plans have recently been initiated.

Naturally there is a time lag from realising the need for reform, developing a plan, implementing it and seeing results in improved survival. Large organisations like national healthcare systems, regional health providers or hospital networks require a long time for adaptation and implementation. In addition, national statistics on outcome have a time lag since the effect of any treatment changes on 5-year survival only can be studied 5 years after the change, and even longer to have a sample size large enough to make a reliable assessment. It may therefore be too early to assess the full effects of cancer plans which in most countries were launched in the late 1990s or later.

In many countries the national strategy has been a starting point for scrutinising the strengths and weaknesses of the organisation and delivery of cancer services, and for implementing firm actions and reforms. In countries with a more decentralised organisation of cancer care, a national cancer plan may have less effect, as the power of implementing the strategy is dependent on the will of regional authorities. In Switzerland, for example, the regional cantons have independence to organise healthcare. Cultural differences between cantons have led to a variety of healthcare systems which makes it difficult to develop a comprehensive plan with firm reforms [57]. In Germany, on the other hand, the federal government

programme to coordinate oncology services has shaped the organisation of cancer care throughout the country.

In Spain the decentralised structure has led regional authorities to develop their own cancer plans to cover actions for prevention, diagnosis and treatment within their responsibilities. In the UK, where the constituent countries are responsible for the delivery of healthcare, cancer plans have been developed for each country: England, Wales, Scotland and Northern Ireland.

In many countries the development of cancer plans has resulted in ambitious efforts to reform the organisation of cancer care or other concrete measures to improve cancer treatment. In Ireland the national cancer plan led to the concentration of cancer care in four Managed Cancer Control Networks which aim to enhance the coordination of different parts of the treatment process, and coordination among staff in different disciplines [81]. In France the national cancer control plan introduced a degree of coordinated cancer care in a number of regional cancer centres. Each hospital treating cancer patients has a Cancer Coordination Centre, to ensure that all medical files comply with care standards, or have been discussed in a multidisciplinary consultation meeting. The cancer coordination centres are guided by the National Cancer Institute [82].

Fragmentation of cancer care is a larger problem in countries with more limited resources, such as those in Eastern Europe. Scarcer resources mean those resources have to be used even more efficiently. The large number of hospitals providing cancer care in the Czech Republic are often small with limited resources. This has resulted in a lack of coordination within and between hospitals, and patients not receiving appropriate treatment. Over recent years the establishment of complex cancer centres, nationally coordinated by a Council of Oncocentres, has led to better coordinated care which aims to increasing the equity and accessibility of services.

The importance of the size of cancer treatment centres has been acknowledged in several countries with smaller populations. The importance of a sufficient number of patients to build up and pool experience and knowledge in specialised cancer care has led Belgium, the Czech Republic, Denmark, Hungary, Ireland and Norway to reduce the number of hospitals treating lung cancer.

In Hungary the 2006 National Cancer Control Plan proposed a reorganisation of cancer treatment into regional cancer centres with resources to provide the most appropriate diagnosis and treatment methods.

In Portugal the national cancer plan introduced five regional cancer networks which aim to achieve a better coordination of cancer care, and to execute the actions of the cancer plan.

In 2006 the national authority *Cancer Australia* was established to lead and coordinate the control of cancer. As a part of a reorganisation plan a network system, influenced by network organisations in the UK was introduced. One of the main objectives with the CanNET program is to establish a more integrated path of treatment across organizational and professional boundaries. This will facilitate a multidisciplinary planning and performance of treatment and improve access to treatment for patients living in urban areas [83].

In order to improve the coordination of cancer treatment services, four regional cancer networks were initiated in New Zealand in 2006. These networks are, stretching across the

administrative boundaries of district health boards. The cancer networks will require and formalize cooperation with the district health boards, and other actors providing cancer care.

In addition to the last cancer control plan, launched in 2004, The Japanese government has been pushing an initiative and has validated the new Anti-Cancer Measures Act in 2006 to allocate more funds and resources to cancer care. Following the Act, the government in 2006 established a national action plan on cancer care for the years 2007-2011. One of the top priorities of the action plan is to promote a more integrated care of cancer patients primarily by improving the use of radiotherapy and chemotherapy, and to improve the access to high quality cancer care countrywide.

Brazilian Ministry of Health established in 2005 a National Plan for Cancer Care (*Política Nacional de Atenção Oncológica*) which shall provide direction on cancer prevention and the organisation of cancer care all the way from diagnostics and treatment to rehabilitation or palliative care. The plan emphasises the need to create expert networks of oncologist, to improve the definitions of technical requirement for cancer care and to increased coverage of treatment for cancer patients.

6 Preventive efforts

As smoking accounts for about 90 per cent of all lung cancer cases, smoking cessation is the key focus for prevention. All the countries in this study have information campaigns to warn of the dangers of smoking. Tax levels on tobacco have been raised in most of the countries. More recently many countries have also introduced smoking bans. Efforts to reduce smoking have had an effect. But more than a fifth of the adult population in all countries but Sweden smoke every day.

As described in section 3.3, no screening programmes for lung cancer evaluated in clinical practice has proven any effects on increased survival. One recent study of yearly CT-screening of people at risk for lung cancer did, though, show that 85 per cent of tumours detected were in a curable stage of the disease [25].

The percentage of smokers aged 15 and over ranges from 22 per cent in Sweden to 52 per cent in Greece, with most countries having a rate of between 26 and 40 per cent (Table 6-1). Smoking prevalence is lower in Sweden because of the use of wet snuff (where snuff is placed under the top lip). The question of whether this is a plausible method for smoking cessation is widely debated. The use of snuff and other kinds of smoke-less tobacco definitely keeps cigarette smoking, and hence lung cancer risks, down. But smokeless tobacco contains more than 30 different carcinogens increasing the risk of for example oral, oesophageal and pancreatic cancers [84]. These cause fewer cases and less dangerous forms of cancer although the promotion of snuff as an alternative to smoking is controversial. Sweden is also the only country in the EU where snuff is allowed to be sold, but it is also sold and used in Norway.

As discussed in section 2.1, the incidence of lung cancer among men is decreasing in most countries due to a reduced prevalence of smoking in recent decades. Among women though, many countries show an increasing prevalence of smoking and hence an increased incidence of lung cancer.

In every country of this study there are programmes on how to prevent smoking. The most common method is information campaigns to warn of the dangers of smoking. These are directed towards young people to keep them from starting to smoke, and towards existing smokers to encourage them to stop. In the EU the Commission requires tobacco companies to put labels about the dangers of smoking on every cigarette package. Charities, non governmental organisations and government authorities, all play an important role in communicating the dangers of smoking.

Smoking prevalence has decreased in recent decades. Figure 6-1 shows the trend in smoking prevalence, in people aged 15 or above, in countries with sufficient data to analyse long term trends. We can see that efforts to reduce smoking have had an effect in most countries. But still more than one fifth of the adult population in all countries but Sweden smoke every day.

Table 6-1 Daily smoking prevalence in adult population, 2006

Country	Prevalence of daily smoking in per cent of population aged 15 and over
Sweden	16.3%
Ireland	18.1%
Switzerland *	19.6%
Finland	19.7%
Italy	20.1%
Belgium	20.2%
Czech Republic *	23.5%
Netherlands	24.0%
France **	24.2%
Germany **	24.4%
Norway	24.3%
Denmark *	26.5%
United Kingdom	26.6%
Portugal	27.7%
Spain	28.4%
Poland	29.9%
Hungary **	32.6%
Austria	39.2%
Russian Federation *	42.0%
Australia	18.0%
New Zealand	20.0%
Japan	26.8%
Brazil	12.4%
Mexico	14.1%

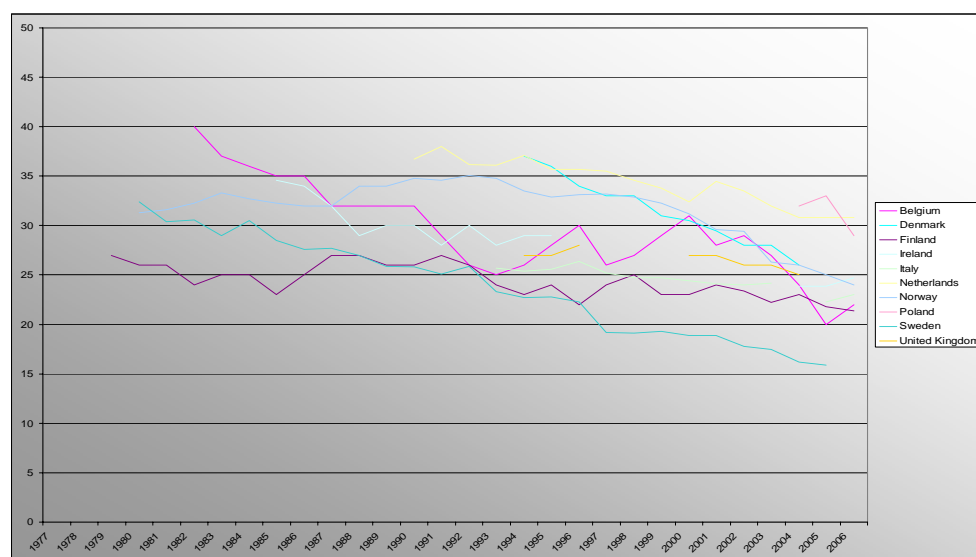
*2004

**2003

*** 2000

Source: [85]

Figure 6-1 Trends in smoking prevalence in adult population in selected countries



Source: WHO, 2007

A traditional direct policy to prevent smoking has been to raise cigarette prices through higher taxes, and restrict tobacco advertising and promotion. Tax levels on tobacco have been raised in most of the countries of study [86].

A more recent strategy to reduce smoking in Europe has been to simply ban smoking in certain places such as the workplace, public areas and restaurants. Establishing smoke free environments also reduces non-smokers exposure to second-hand smoke [87]. Smoking restrictions in public buildings and on public transport have been in place in many countries since the 1980s.

One of the front-runners in expanding smoking bans in recent years has been Ireland where smoking was prohibited in all workplaces, including restaurants and bars, in 2004. Since then smoking bans in restaurants and bars have been introduced in Denmark, Italy, Norway, Sweden, Spain and the UK. In Belgium, the Netherlands and Spain smoking is still allowed, although restricted, in restaurants and bars. The only countries in this study not to have restrictions on smoking in restaurants and bars are Russia and Switzerland. The restrictions vary between countries. In some countries restaurants are allowed to have designated space where smoking is allowed, while some have an absolute ban. In Germany and Austria restaurants have a voluntary restriction in smoking instead of national legislation.

All of the European countries of this study have restrictions on smoking at indoor workplaces, although it is allowed in some circumstances in France, Poland, Russia and Switzerland.

In Brazil advertising of tobacco products are prohibited in TV, radio, newspapers and magazines. Smoking is also prohibited in public transportation since 2000. In Mexico, restrictions in advertising are limited to national radio and TV. Moreover smoking is banned in schools, hospitals, and other published institutions since the beginning of the 1990; however this law is not strictly enforced. From mid-2008, smoking in public places, including bars and restaurants, is prohibited in the capital of Mexico, Mexico City. In Australia there are no national laws establishing smoke free environments in public places and buildings, restaurants and bars or work places. There are however such policies on state and territorial level. Such national restrictions exist in New Zealand prohibiting smoking in public places and buildings, indoor workplaces and restaurants. Advertising in national media is prohibited in both New Zealand and Australia. In Japan there are no restrictions on advertising in media or regulations establishing smoke free environments [85].

There are also policies to help people who wish to stop smoking by supporting different forms of treatments. In an analysis of tobacco control policies in 28 European countries, raising taxation and banning smoking in work places were estimated to have the greatest impact on smoking [86].

7 Lung Cancer Treatment

The treatment of lung cancer is multimodal, requiring several different methods or processes. Successful treatment also requires quick diagnosis. The most important information needed to decide on appropriate treatment is the stage of the disease and the physical status of the patient. The treatment the patient receives is also dependent on the resources available and the organisation of care at treatment centres in each country.

7.1 *Diagnosis of lung cancer patients*

A primary factor behind the poor survival rate in lung cancer is late diagnosis. The disease is often asymptomatic, and symptoms are usually attributed to the common effects of smoking. Lung cancer tumours are also difficult to detect in early stages. No general screening methods have been found to reduce the death rate in lung cancer. It is also advantageous if GPs have experience in lung cancer diagnosis, but this is not always the case. In England GPs see an average of one lung cancer patient a year [88].

Fragmented cancer care organisation may make quick diagnosis more difficult. This issue has been reported in the Czech Republic and Hungary [21, 72, 89]. In England guidelines have been issued to reduce waiting times and geographical variation in referral [90].

7.1.1 Tumour stage at diagnosis

The stage of the tumour when diagnosed is one of the most important factors to influence treatment outcome. In the regions of North Holland and Flevoland in the Netherlands, the 5 year relative survival rate for patients diagnosed between 1999 and 2005 was as follows[91]:

Stage I tumour - 48 per cent survival rate
Stage II tumour - 27 per cent survival rate
Stage III tumour - 7 per cent survival rate
Stage IV tumour - 1 per cent survival rate.

Unfortunately 74 per cent of patients were diagnosed in Stage III or IV and only 26 per cent in Stages I and II.

In Table 7-1 we see that a small percentage of patients are diagnosed in stages I and II. In most countries 75-85 per cent of cases are diagnosed in Stage III or IV. In some of the countries with the least favourable outcomes, such as Ireland, Poland and the Czech Republic, the tumours are detected in later stages, while Switzerland, Austria and Netherlands, which have high outcomes of lung cancer treatment, have a larger share of the patients detected in stages I and II.

In Australia and New Zealand the share of patients diagnosed in stages I or II is larger than in most European countries. As seen earlier, Australia has an outcome of treatment at the level of the best European countries and New Zealand has an outcome at the level of the medium performing countries in Sweden. In the Latin American countries very few patients, 9 per cent or less are diagnosed in the earlier stages I or II. In Brazil, the figure is based on data from only four hospitals. In the country as a whole, the share of patients diagnosed in stages I and

II is expected to be lower. The late diagnosis of lung cancer in Brazil and Mexico results in a poor survival rate and treatment outcome as presented earlier.

As emphasized several times in the report, there are some important factors influencing the stage at which lung cancer is diagnosed:

- Symptom awareness: This has been highlighted in Denmark and in the UK, where efforts have been made to improve public awareness of symptoms.
- Referral routines: Early detection also depends on the experience and training of the physician. Lung cancer has also been marked by a nihilistic attitude by doctors.
- Organisation and infrastructure: A fragmented structure will delay diagnosis.

Table 7-1 Stage at diagnosis percentage of patients

Country	Stage	
	I-II	III-IV
Ireland [52]	12%	88%
Portugal [92]	16%	84%
Czech Republic [93]	19%	81%
Sweden [94]	22%	78%
Denmark [95]	24%	76%
United Kingdom*[96]	24%	77%
Norway [97]	25%	75%
Germany** [98] (NSCLC)	26%	74%
Netherlands*** [91]	26%	74%
Austria^[99]	28%	72%
Switzerland^^ [100](NSCLC)	28%	72%
Australia ^^^[101]	26%	74%
New Zealand [102]	29%	71%
Brazil [63, 103-106]	9%	91%
Mexico [64]	5%	95%

* England

** Land Brandenburg

*** North Netherlands, North Holland and Flevoland

^ Tirol

^^ Zürich

^^^ New South Wales

7.2 Treatment guidelines

Most countries have adopted national and/or regional treatment guidelines for lung cancer. These are generally developed based on scientific evidence of best practices and updated regularly by expert groups. In other countries the medical oncologists refer to guidelines developed by international organisations, such as the European Society for Medical Oncologists (ESMO), the American Society of Clinical Oncology (ASCO) and the American Association of National Comprehensive Cancer Network (NCCN) [107].

In some countries guidelines also give advice on referral routines. Multidisciplinary collaboration is increasingly highlighted to bring a wider perspective to each patient's treatment needs. Such multidisciplinary teams play a central role in the UK lung cancer guidelines [108], but are also highlighted in cancer plans in other countries.

Guidelines have an additional benefit if there is an assessment on whether the recommendations are applied, and whether they have the intended effect. In most countries

treatments are recorded in cancer registries and can be used for evaluation of their effectiveness. In other countries fewer resources and structures means the monitoring of compliance with recommendations is less rigorous. It is essential to analyse the effect of treatment guidelines in order to be able to make updates in the recommendations.

7.3 Specialists treating lung cancer patients

In recent years many countries have made efforts to ensure that each patient is treated by a multidisciplinary team (e.g. surgeons, oncologists, specialist nurses, physiotherapists, occupational therapists, psychologists). This is an integral part of several cancer plans [72, 81, 108] and guidelines [109]. In Hungary, Norway, Spain, Sweden and the UK, treatment choices for at least half of their patients are discussed in multidisciplinary meetings.

Multidisciplinary teams leads to better continuity and coordination of care through all stages of the disease, and better advice on appropriate treatment. It means care is centred on the needs of the individual patient. This is, of course, the ideal situation but there are a number of barriers to implementation. In England, for example, these have included resource shortages, staff shortages and a reluctance among some professionals to work in a multidisciplinary environment [110].

7.4 Treatments and treatment combinations

Treatment in lung cancer involves surgery, chemotherapy, radiotherapy or combinations of all three. Different forms of chemotherapy can also be combined (See chapter 3). The treatment given to lung cancer patients varies greatly between countries. There are several possible explanations for such differences. These include: the organisation of care, equipment and resources available, regulations and restrictions on the use of treatment, and staffing levels. There may also be differences in the population of lung cancer patients, i.e. stage of disease and other factors such as age of patients and co-morbidity.

For early stages removing the tumour through surgery (or in certain cases through radiation therapy) is the first option. The cure rate can be improved by using adjuvant chemotherapy. Lung tumours are only considered resectable in stages I and II, and in a few cases in stage III. In the later stages treatment focuses on prolonging survival and reducing symptoms. Chemotherapy and radiation is often used as palliative treatment, in combination with supportive care.

There is little data at a national level on other treatments used in lung cancer care. Even in countries where information on treatments is available, it is likely to come from smaller regional registries and is not necessarily representative of the country as a whole. The quality of data kept in registries is often not sufficient for proper analysis of treatment patterns.

In the UK and Ireland about half of the lung cancer patients do not receive any active treatment. The numbers of non-treated patients are also high in Hungary. In the Netherlands, Portugal and Sweden about one fifth receive no treatment, while 90 per cent of lung cancer patients in Germany receive active treatment. Of the non-European countries we have data on the share of patients receiving active treatment for Australia and New Zealand. In a study of lung cancer patients in one major regional cancer area in New Zealand, only half of the patients studied received active treatment against their tumour, including a large share (30 per cent) of patients who had limited stage lung cancer [102]. In Australia, a little more than one patient out of four did not receive any active treatment (Table 7-2).

Table 7-2 Patients not receiving treatment

Country	Share of patients receiving no active treatment
Germany* [98]	10%
Netherlands [91]	19%
Portugal[92]	20%
Sweden [94]	21%
Switzerland**[100]	26%
Hungary [111]	32%
United Kingdom*** [96]	48%
Ireland [52]	54%
Australia	27%
New Zealand [102]	50%
*Land Brandenburg	
**Zürich	
***England and Wales	

If a tumour is considered curable the first treatment option is surgery, so the proportion of patients receiving such treatment is an important indicator of the chances of long term survival. In the Netherlands, Switzerland and Germany, between 24 and 35 per cent of all patients are treated with surgery alone or in combination with other therapies. In the UK less than 10 per cent of all patients receive surgery (Table 7-3). Data from regional registries may not be representative for the country as a whole, but the differences between the countries with the lowest and the highest share of patients given surgery are too large to be explained by regional biases.

In Australia almost one out of five lung cancer patients are treated with surgery. This is higher than in many European countries, but still less than some of the best performing European countries. Lung cancer patients in Australia still have relative good chances of survival even compared to the countries with the highest shares of patients treated with surgery.

In the Latin American countries the patient access to surgery is very low compared to the other countries in this study. Only up to 6 per cent of the patients are undergoing surgery. This is a consequence of the low rate of patients diagnosed in stage I-II (Table 7-1), when the tumour may still be resectable. Since surgery is the main treatment option for cure and long term survival in lung cancer, the late diagnosis and consequently a low surgery rate naturally has a negative effect on the patient survival.

Table 7-3 Share of patients treated with surgery

Country	Share of patients undergoing surgery
United Kingdom*[96]	9%
Denmark[95]	17%
Sweden [94]	17%
Norway [97]	17%
Ireland [52]	18%
Portugal [92]	18%
Switzerland ** [100]	23%
Netherlands***[91]	24%
Germany **** [98]	28%
France ***** [112]	34%
Australia [101]	19%
Brazil [63, 103-106]	1.5-6%
Mexico [64]	5%

* England

** Zürich

*** North Holland

**** Land Brandenburg

***** Bas-Rhin

7.5 Factors delaying diagnosis and treatment

In lung cancer care, there are three main reasons why diagnosis and treatment can be delayed [113]:

1. Patient delay: The patient may not have any symptoms or does not suspect a serious condition.
2. Doctor delay: Symptoms do not immediately prompt a doctor to start diagnosis tests.
3. System delay: The waiting time for test or investigation results.

Reducing such delays has been highlighted as the most important factor to improve lung cancer care in the cancer plans and guidelines of many countries [108, 114]. This has led to efforts to detect lung cancers earlier. Clinical trials have not yet shown any significantly positive survival effect on early screening programmes.

In lung cancer the longest delays are generally in the first category when patients do not seek medical attention [115]. There are several reasons why this is often the case. In lung cancer there is a long time period where there are no symptoms. Also, symptoms such as a persistent cough or weight loss are not always associated with cancer. Long distances to a cancer clinic may also delay contact [115]. In a study of the causes of delay in England, two thirds of the delays were due to patients, while one third was attributed to primary care and GPs [90].

Most studies on the impact of delays by doctors, or by a system, find no strong association or even a negative relation between such delays and survival [116-118]. This is of course related to the stage of disease at diagnosis [119]. In the early stages a delay in treatment may have a great impact on survival. A study of lung cancer patients in the UK showed that patients assessed as potentially curable became incurable while waiting for treatment [120].

7.6 Availability of radiation facilities

Radiation is used primarily for palliative treatment to prolong survival and to improve quality of life. But radiation can also be used as part of the potential cure for patients who are not

suitable for surgery. A major obstacle in the treatment of lung cancer is the low access to radiotherapy, due to lack of equipment, staff or inefficient organisation. This is a problem in most countries of this study.

Linear accelerators (linacs) are the device most commonly used for radiotherapy treatment in most countries. In some countries Cobolt machines are more frequently used. Cobolt machines are less modern and less efficient than linear accelerators, but also cost less money. Such machines are more frequently used in countries with less resources available for health care and cancer treatment. The infrastructure and staff needed to make the best use of available radiation equipment varies greatly between countries. There is general acceptance on the need for at least four linear accelerators per million inhabitants. But a European study based on cancer incidence estimated there is a need for up to twice as many: the number of units needed varied from 5 in Ireland to 8 in Hungary [121].

Some of the geographically largest countries in Europe have a notably larger number of treatment centres. Russian Federation which is also larger than Australia has 133 treatment centres, but only 38 linacs. France has 203, Spain has 101, Italy has 146 and Germany has 214 treatment centres. Sweden has 18 and Poland has 22 [122].

There are a large number (920) of radiotherapy centres in Japan, which are generally small with only one or few clinical accelerators. Not all of these centres have any linear accelerators or cobalt machines. With a population of 120 million and approximately 660 linear accelerators gives a provision of 5.5 linacs per million inhabitants. In addition to these, there are also 49 cobalt machines. The access to radiotherapy is limited by a lack of human resources (radiotherapists and relevant co-medicals) [127].

Like European countries with smaller resources spent on health care, Brazil and Mexico both suffer from a lack of radiotherapy equipment. They both have far below four linear accelerators per million inhabitants which is considered an international reference standard. Even though the crude incidence of lung cancer is lower in these countries than in the other study countries, 0.9 linear accelerators and 0.7 cobalt machines per 1 million population in Brazil, and 0.3 linear accelerator and 0.8 cobalt machines per 1 million individuals, are likely low numbers to cover all cancer patients that would benefit from radiotherapy.

Table 7-4 shows the number of linacs in the countries of this study, in absolute numbers and in number per million inhabitants. Countries with the least successful outcome in lung cancer care - Ireland, the UK, Hungary, Czech Republic and Poland - all have well below the minimum recommended number of 4 linacs per million inhabitants. The Southern European countries, Greece, Spain and Portugal, are also relatively under-equipped in radiotherapy machines. The highest numbers of linacs are found in the Nordic countries. Countries with large geographical distances, such as Sweden, Norway and Finland have a need for a larger number of radiotherapy treatment centres and equipment in order to reduce travelling for patients.

Many of the countries with fewer linacs have a large number of Cobalt 60 machines. These are older and less efficient radiotherapy devices. Cobalt machines are often counted as having half the value of a linear accelerator [123]. But even if the Cobalt machines are given the same value as the linacs, there is still insufficient radiation equipment in the Russian Federation, Hungary, Poland, Ireland, Portugal, Spain, Greece and the UK.

Within many countries there is an uneven distribution of equipment. Larger hospitals or cancer centres tend to be sufficiently equipped while smaller institutions are under-resourced. Also, larger hospitals have more resources to invest in new equipment.

There is a need to increase the overall number of radiation machines by investing in new equipment and replacing existing equipment when necessary. The growth in the number of cancer cases, and wider applications for radiotherapy increases the need for equipment and staff. This is a factor often not taken sufficiently into consideration when planning for investments in radiotherapy [124, 125].

The shortage of radiotherapy facilities has been highlighted in cancer plans and strategies in several countries. In some cases this shortage has also resulted in extra money for investment in new linacs. In Denmark, England, France, and Scotland such investment is part of the national cancer strategy [108, 114, 126, 127]. In recent years, large increases in investment have been seen in Denmark, Finland, Greece, Portugal and Spain [122].

Countries with the greatest need for further investment tend to be the ones with the least resources spent on healthcare generally: central and Eastern Europe, Spain, Portugal and Greece. These countries also tend to have a large proportion of the less effective Cobalt machines. In Russia most linear accelerators are found in the larger treatment centres in Moscow and St Petersburg [122]. Treatment centres elsewhere are mainly small with a few Cobalt machines. This provides uneven access to radiotherapy throughout the population. With scarce resources, investments in central and Eastern Europe tend to favour treatment centres in urban areas over more rural areas leading to more uneven access to treatment [20].

It is also important to maximise the use of radiotherapy equipment. The availability of sufficient numbers of trained oncologists, physicists and radiation nurses is a limiting factor in many countries of this study [125].

Radiotherapy is given to lung cancer patients in 34 centres in Australia which have a total of 112 linear accelerators. Given the population of a little more than 19 million, there are 5.9 linacs per million inhabitants which is a rate well above the minimum requirements of 4 per million inhabitants often used in international studies. Given the geographical size of Australia, there should be a larger number of treatment centres than in most European countries in order to provide access to radiotherapy within reasonable travel distance to patients in all parts of the country.

In New Zealand there are 6 treatment centres, with a total of 16 linear accelerators in use. With a little more than 4 million inhabitants in the country this gives 3.8 linacs per million inhabitants. In addition there are also 4 cobalt machines. In total, the number of apparatuses is smaller than in more than half, and best performing, countries in Europe. The small number of treatment centres, allows for a higher caseload of patients, which may provide benefits by a more efficient utilization and specialists to treat a larger number of patients.

Table 7-4 Number of radiotherapy machines

Country	Number of linear accelerators	Linear accelerators per million of population	Number of Cobalt machines	Cobalt machines per million of population	Linear accelerators and Cobalt machines given "half value" of linear accelerators per million of population
Russian Federation	94	0.7	204	1.5	1.5
Poland	53	1.4	17	0.4	1.6
Hungary	20	2.0	12	1.2	2.6
Ireland	9	2.3	4	1.0	2.8
Portugal	23	2.3	7	0.7	2.7
Spain	100	2.5	81	2.0	3.5
Czech Republic	29	2.8	53	5.2	5.4
Greece	33	3.1	16	1.5	3.9
United Kingdom	185	3.3	23	0.4	3.5
Italy	259	4.5	54	0.9	5.0
Switzerland	33	4.5	14	1.9	5.5
Belgium	47	4.6	10	1.0	5.1
Austria	40	4.9	2	0.2	5.0
Germany	403	4.9	33	0.4	5.1
Netherlands	83	5.1	0	0.0	5.1
France	347	5.9	95	1.6	6.7
Finland	34	6.5	0	0.0	6.5
Norway	35	7.7	1	0.2	7.8
Sweden	70	7.9	12	1.4	8.6
Denmark	49	9.1	1	0.2	9.2
Australia	112	5.6	0	0	5.6
New Zealand	16	3.8	4	1.0	4.3
Japan	660	5.5	49	0.4	5.7
Brazil	170	0.9	123	0.7	1.3
Mexico	28	0.3	87	0.8	0.7

Source: Dirac, International Atomic Energy Agency.

There are a large number (920) of radiotherapy centres in Japan, which are generally small with only one or few clinical accelerators. Not all of these centres have any linear accelerators or cobalt machines. With a population of 120 million and approximately 660 linear accelerators gives a provision of 5.5 linacs per million inhabitants. In addition to these, there are also 49 cobalt machines. The access to radiotherapy is limited by a lack of human resources (radiotherapists and relevant co-medicals) [128].

Like European countries with smaller resources spent on health care, Brazil and Mexico both suffer from a lack of radiotherapy equipment. They both have far below four linear accelerators per million inhabitants which is considered an international reference standard. Even though the crude incidence of lung cancer is lower in these countries than in the other study countries, 0.9 linear accelerators and 0.7 cobalt machines per 1 million population in Brazil, and 0.3 linear accelerator and 0.8 cobalt machines per 1 million individuals, are likely low numbers to cover all cancer patients that would benefit from radiotherapy.

8 Market access and uptake of lung cancer drugs

Making the most appropriate treatment available for each patient depends on several factors. For diagnosis, surgery and radiotherapy, investment in equipment and an appropriate organisation and management is crucial. This requires long-term planning and budgeting, balancing short-term costs against investments providing long-term, wider savings and improved outcomes. As we have reviewed in earlier sections, hospitals in many countries are short in necessary investments. This is often due to scarce resources in smaller hospitals and a poor infrastructure in lung cancer treatment.

The process of developing new drugs is long and costly. It can take more than 10 years for a new drug to reach the market. The central registration process also takes time. Price negotiation, carried out at a national level, can also be a lengthy process.

8.1 Pharmaceutical regulation

There is a centralised procedure for the evaluation of safety, efficacy and quality of new drugs before they are made available for use in the EU. The producer submits an application to the regulatory body, the European Medicines Agency (EMA). The Committee for Medical Products for Human Use (CHMP) grants market authorisation for the entire EU. CHMP also grants authorisation for drugs to be used in new indications.

Certain drugs may be given a simplified or accelerated approval procedure. These are usually drugs for serious and life-threatening illnesses, without existing effective treatments. Such exceptional circumstances often apply to drugs for rare cancers or cancers with high mortality, such as lung cancer.

Since 2005 this centralised procedure has applied to new oncology drugs. Authorisation for the 20 anti-cancer drugs assessed since 1995 took an average of 418 days. Almost 30 per cent of this time was used for administration, not related to the approval process itself [129]. By comparison, the average review time for all standard drugs in the US in 2004 was 387 days, and 180 days for priority drugs.

8.2 Reimbursement and pricing of prescription drugs

Drugs take an increasing share of overall healthcare expenditures in all countries although the proportion of direct costs used for drugs is still only about 15 per cent on average. The newest drugs enable clinical results not possible just a few years ago, although at a rapidly increasing cost.

How to contain the cost of new drugs, providing fair access for patients has been a preoccupation of Governments for many years. Countries approach the question of whether or not to subsidise particular drugs (reimbursement) in different ways. Economic evaluation studies have become increasingly important in the processes.

In Belgium, Finland, the Netherlands, Norway, Portugal and Sweden an economic evaluation and the issue of cost-effectiveness is a formal part of the reimbursement processes [130]. In Denmark and Switzerland economic evaluation is not formally required, but is encouraged as

it may assist the reimbursement decision [131, 132]. The Irish Department of Health may request cost-effectiveness studies, but this is not a standard requirement [133].

The reimbursement process is time-consuming in most countries, and is a major delay and barrier for patients' access to new drugs. Table 8-1 shows the average, maximum and minimum time delay due to the reimbursement process in 16 countries. Except for Germany and the UK, where no formal reimbursement decision is needed, the average time delay ranges from 104 days in Ireland to 517 days in the Czech Republic. There are also long delays in Belgium, France, Hungary and Italy, all with a delay exceeding 300 days. The shortest delays are found in Norway, Sweden and Switzerland. Cancer drugs are often used in hospitals, and patient access to these drugs is then not subject to a formal reimbursement decision in many countries, such as Sweden and Netherlands. The restriction in access is more a question of whether hospital budgets allow for use of newer drugs.

Table 8-1 Time delays between approval and market access for pharmaceuticals in a selection countries included in the study

Country	Number of molecules	Average time delay between approval and market access	Maximum time delay between approval and market access	Minimum time delay between approval and market access
Belgium	83	447	1,075	28
Czech Republic	68	517	1,502	60
Finland	89	210	1,310	0
France	75	390	1,001	58
Germany	74	0	0	0
Greece	85	281	863	26
Hungary	80	338	791	79
Ireland	72	104	552	0
Italy	79	431	3,920	28
Netherlands	77	210	711	0
Norway	77	123	416	0
Portugal	82	235	1,071	0
Spain	83	271	662	0
Sweden	89	156	805	0
Switzerland	49	148	816	26
UK	76	0	0	0

Source: [134]

The decisions regarding reimbursement and pricing of a drug are linked together in most countries. Decisions are often made by the same authority or agency, but both decisions are required for a drug to be granted access to the prescription market.

In the EU the pricing process is loosely regulated through the Transparency Directive. This Directive stipulates that national authorities must make a price decision no later than 90 days after market authorisation, and after receiving sufficient information from the producer.

Most countries have some kind of direct price control, for example by direct negotiations with the producer, or by the use of international reference prices. In the countries of this study only Germany and UK have free pricing of patented drugs. In the UK the government has a Pharmaceutical Price Regulation Scheme which prevents excessive manufacturing company profits.

In countries where formal price decisions are made, these are generally negotiated between the producer and a national agency. In most countries a reference price system is applied, comparing the price to other countries or to comparable drugs.

New drugs may not be prioritised in budgets, as they may appear expensive. The economic benefits of new drugs may not be apparent until they are used on a large scale.

8.3 The role of Health Technology Assessments

Health Technology Assessments (HTAs) play an increasing role in the process of granting market access to new health technologies [13]. They are often referred to as the fourth hurdle in market access. HTAs investigate the cost effectiveness of new technologies, along with clinical efficacy. They may facilitate a faster introduction of a new technology, but the process itself can also cause delays.

Cost-effectiveness information is an important part of HTAs. This involves studies of medical, social, ethical and economic implications of the development, distribution and use of a particular health technology. The health technology could be in the area of prevention, rehabilitation, vaccines, pharmaceutical drugs and devices, or medical and surgical procedures.

HTA reports aim to support decision-making in healthcare, improving quality as well as cost-effectiveness in the use of health technologies. Thus, HTAs may have a strong influence on market access. In many cases, there is also a direct link between a positive HTA and funding for the technology appraised. For example, in England there is a direct link between the issuance of a positive guidance on a new therapy by the National Institute for Health and Clinical Excellence (NICE) and reimbursement of this new therapy by the National Health Service (NHS).

In Europe, the Netherlands, Spain, Sweden and the UK are leading the development of HTAs. The vast majority of European HTA reports and economic evaluations, related to lung cancer, are produced in the UK. This reflects the high activity by NICE in producing guidance to the NHS on the use of new and existing drug therapies in England [135]. Of the 20 HTA reports within non-small cell lung cancer, registered in the database organised by the International Network of Agencies for Health Technology Assessment (INAHTA) between 1991 and 2005, 14 were produced in the UK, 2 in Sweden and one each in Denmark, France, the Netherlands and Spain.

The UK also dominates the number of health economic analyses registered in the Health Economic Evaluation Database, developed by the Office of Health Economics and the International Federation of Pharmaceutical Manufacturer's Associations. Of the 39 reports registered between 1991 and 2005, 12 were produced in the UK, 8 each in the Netherlands and Italy, 6 each in Germany and Spain, 5 in France, 3 each in Sweden and Switzerland, 3 in Belgium and one each in the Czech Republic and Finland [13].

HTAs provide evidence on cost effectiveness and can lead to a fast uptake of new, effective, treatments. But the countries which are most active in the production of HTA reports and evaluations are not the countries which are the fastest in making new cancer drugs available to patients [13]. A Canadian study reviewing the impact of HTAs on decision-making processes showed that the practice in the UK and most Scandinavian countries has delayed the adoption of new technologies [136]. A referral to NICE can take up to 18 months, with a minimum of 62 weeks. However, in Scotland evaluations by the equivalent organisation, the Scottish Medicines Consortium, take about three months.

After Health Technology Assessments, there is still the issue of funds for new innovative technologies. The costs of new drugs are concentrated to the budget for medicines in hospitals and ambulatory care. Patients will not have access to new medicines and experience the benefits of these new innovative medicines unless resources are made available.

8.4 Availability of new pharmaceuticals

Most lung cancer drugs are used in hospitals and, in most countries, drug costs are included in hospital budgets. Patient access to these drugs is therefore related to healthcare budgets in general, and hospital budgets in particular.

The costs of drugs used in hospitals are often negotiated between the producer and the healthcare system, either by the hospital directly, by the regional health authority or by a hospital purchasing authority.

To control drug expenditure, many countries (for example Austria, France, the Netherlands and Sweden) issue guidelines with varying degrees of monitoring and penalties, for those who do not comply. In other countries (for example the Czech Republic) drug budgets are separated from the regular hospital budget, and in other countries (for example, Ireland) there are targets or restrictions, sometimes with bonuses or penalties.

Hospital budgets are more restricted and inflexible compared to budgets for ambulatory care. Hospital budgets must be planned several years in advance to make room for the introduction of new treatments. These may look expensive in the short term, but may be an investment which will pay off in the long term. The budgeting process must be able to balance short term costs and investments with long term savings.

A particular issue within hospital budgeting is what has been referred to as “silo budgeting”, an inability or unwillingness to move money between budgets, even if increased costs within one budget could substantially reduce costs in another budget [137]. For example, the extra cost of a new treatment could lead to savings in the ambulatory care budget, reduced costs in the social security system, and reduced losses of income. If budgets were more flexible there would be room for stronger incentives to invest in new treatments.

In some countries there are methods to facilitate the financing of new innovative drugs. For example, France and Germany have separate lists of innovative drugs, which may be funded from outside the regular hospital budget. In Denmark DKK 200 million (€27 million) is set aside each year for the provision of new cancer drugs [138]. In the Czech Republic in 2007, funds were made available to ensure that all patients will have access to the latest innovative drugs, and that specialists in the complex oncology centres are able to prescribe the newest drugs [139].

8.5 Market uptake of lung cancer drugs

There are some studies investigating the overall survival effect of the use of the latest cancer drugs by comparing use and survival across countries and regions. Lichtenberg has studied survival effects from the use of more recent drug vintages across countries, finding a positive correlation [140]. In two studies, Jönsson and Wilking have also shown that countries with a faster uptake of newer drugs had higher survival rates [13, 141]. In a comparison between countries Bernow found a positive mean drug vintage effect in lung cancer patients [142]. Waechter et al found that survival was prolonged for advanced NSCLC-patients, with one-year survival increasing from 19 per cent to 40 per cent in Swiss regions, using third-generation chemotherapy agents after 1997 [143]. Von Plessen et al also found that in patients in Norway with advanced NSCLC, median survival increased from 149 to 176 days in counties using the third-generation drug vinorelbine [144].

Based on prescription surveys in France, Germany, Italy Spain and the UK in 2006, lung cancer is the most common indication for the use of gemcitabine, vinorelbine, pemetrexed, and third to breast and prostate cancer for docetaxel (Table 8-2). Non Small Cell Lung Cancer is also the main indication for the use of erlotinib as monotherapy after failure of at least one prior chemotherapy regimen.

Table 8-2 Use of selected drugs in lung cancer

	Share of use in lung cancer
Gemcitabine,	37.9 %
Vinorelbine,	65.8 %
Paclitaxel,	25.5 %
Docetaxel	15.8 %
Pemetrexed	56.5 %

8.5.1 Market uptake of selected oncology drugs

Until the mid-1990s anti-cancer drugs were not widely used in lung cancer. Many clinicians felt that there was a very limited palliative value of drug treatment and that surgery (for a limited proportion of the patients), and to some extent radiotherapy, were the only valid treatment options available, at least for NSCLC. With the introduction of platinum based combination therapies, including one of the “new” generation lung cancer drugs that became available (vinorelbine; 1991, docetaxel, gemcitabine and paclitaxel; 1998), the scenario changed. One-year survival for patients with metastatic or locally advanced NSCLC increased from 10 per cent with best supportive care only, to 40-50 per cent in clinical trials. An emerging interest in adjuvant therapy also resulted in the initiation of several adjuvant trials, later showing a clear benefit at least in high risk patients undergoing surgery with a curative intent. Several studies also showed that second-line therapy could be of significant value for some patients with advanced NSCLC.

8.5.2 Sales of lung cancer drugs in selected European countries

In the figures below sales for docetaxel and paclitaxel are given in relation to population as these drugs are mainly used outside of lung cancer. Figures are given in relation to mortality for gemcitabine, vinorelbine, erlotinib and pemetrexed since the use of these drugs has until recently been mainly in patients with advanced lung cancer. Y01 Q1 represents the first months of sales since first global approval. As a reference, we have introduced the E13 concept, where E13 represents countries in Western Europe where there is full or almost full IMS coverage of both hospital and prescription sales. E13 includes Austria, Belgium,

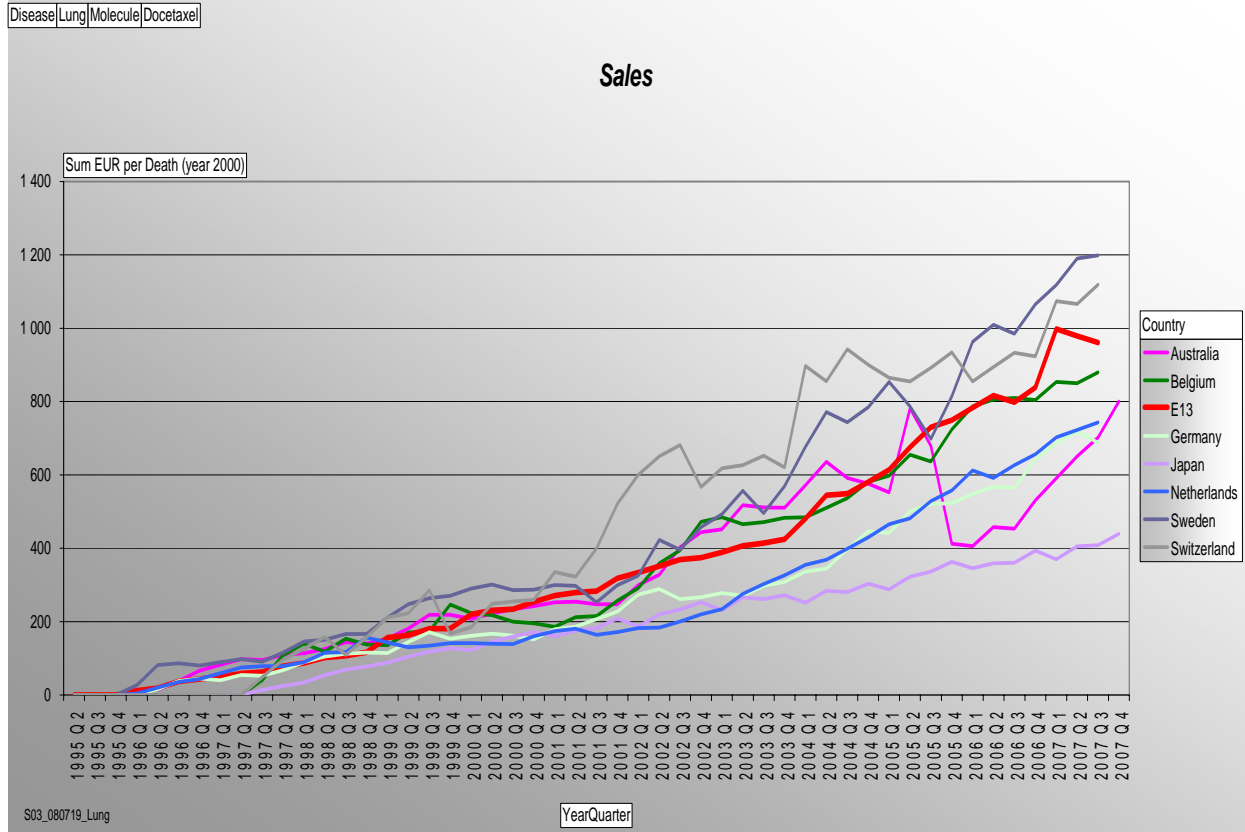
Denmark, Finland, France, Germany, Italy, the Netherlands, Norway, Spain, Sweden, Switzerland and the UK.

The countries have then been grouped according to outcome of lung cancer care. Austria, Belgium, Germany, the Netherlands, Sweden and Switzerland have the best outcome (above 13.0 per cent 5-year survival) according to the EUROCARE-4 study [51]. France, Italy, Norway, Poland and Spain have intermediate outcome. (10.5-13.0 per cent 5 year survival). Denmark, Finland, Ireland and the UK have poor outcome. (below 10.5 per cent 5 years survival). Countries not included in the EUROCARE-4 study (Czech Republic, Greece, Hungary) have been grouped with the countries with poor outcome. Australia and Japan are grouped with the countries having the best outcome and the remaining non European countries are presented with the countries having the lowest outcome following their 5 year survival rate. Sales figures are given below for each of these three groups for each drug.

Figures 8-1, 8-2 and 8-3: Uptake of docetaxel

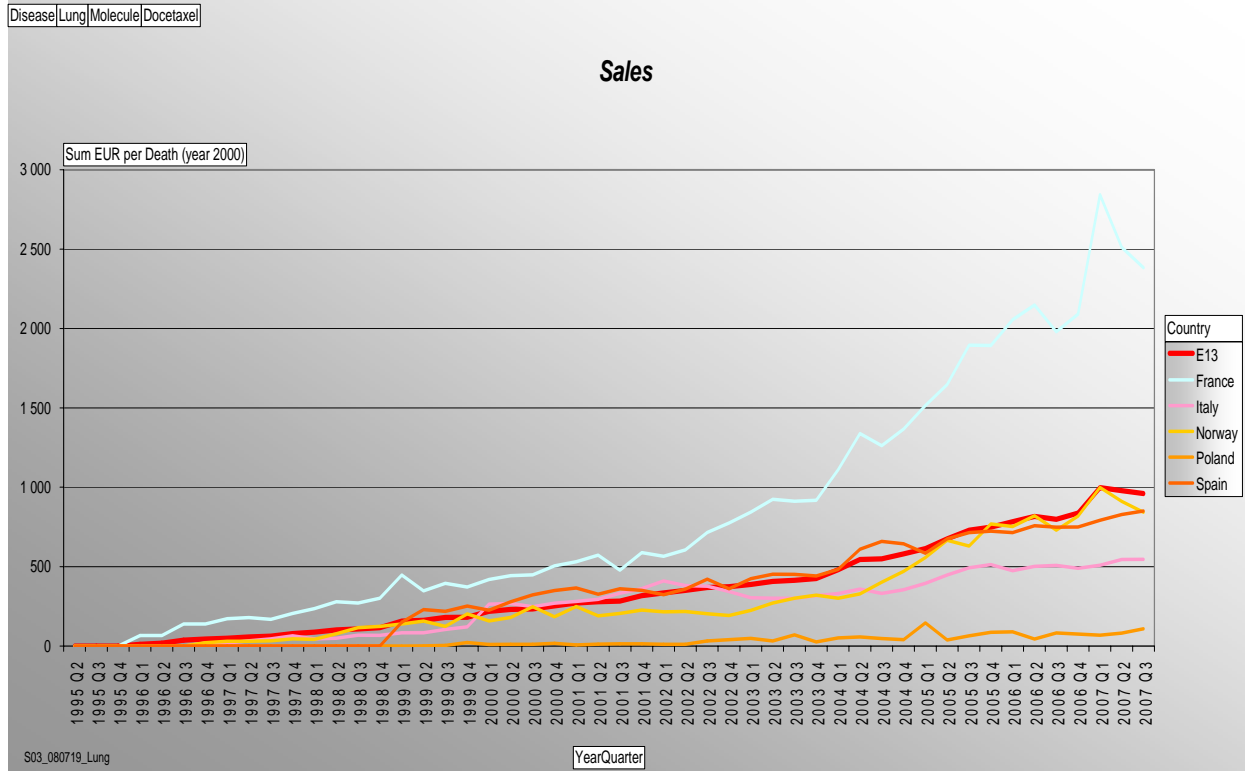
Docetaxel was first introduced in 1995 with metastatic breast cancer as the first indication. Approval for lung cancer came in 1998 as second-line treatment. The drug is now also approved for prostate cancer and gastric cancer. Docetaxel has had the largest sales per capita in France and also high sales in Finland. Data from Ireland does not adequately represent true sales as there is underreporting of sales of hospital drugs. No data for hospital drugs, including docetaxel, is available for Greece. Docetaxel has for many years been considered the standard care for patients suitable for second-line chemotherapy in NSCLC. In general there is a higher than average use of docetaxel in countries with the best outcome in the treatment of NSCLC and a lower than average use in countries with medium or poor outcome of NSCLC patients.

Figure 8-1 Uptake of docetaxel



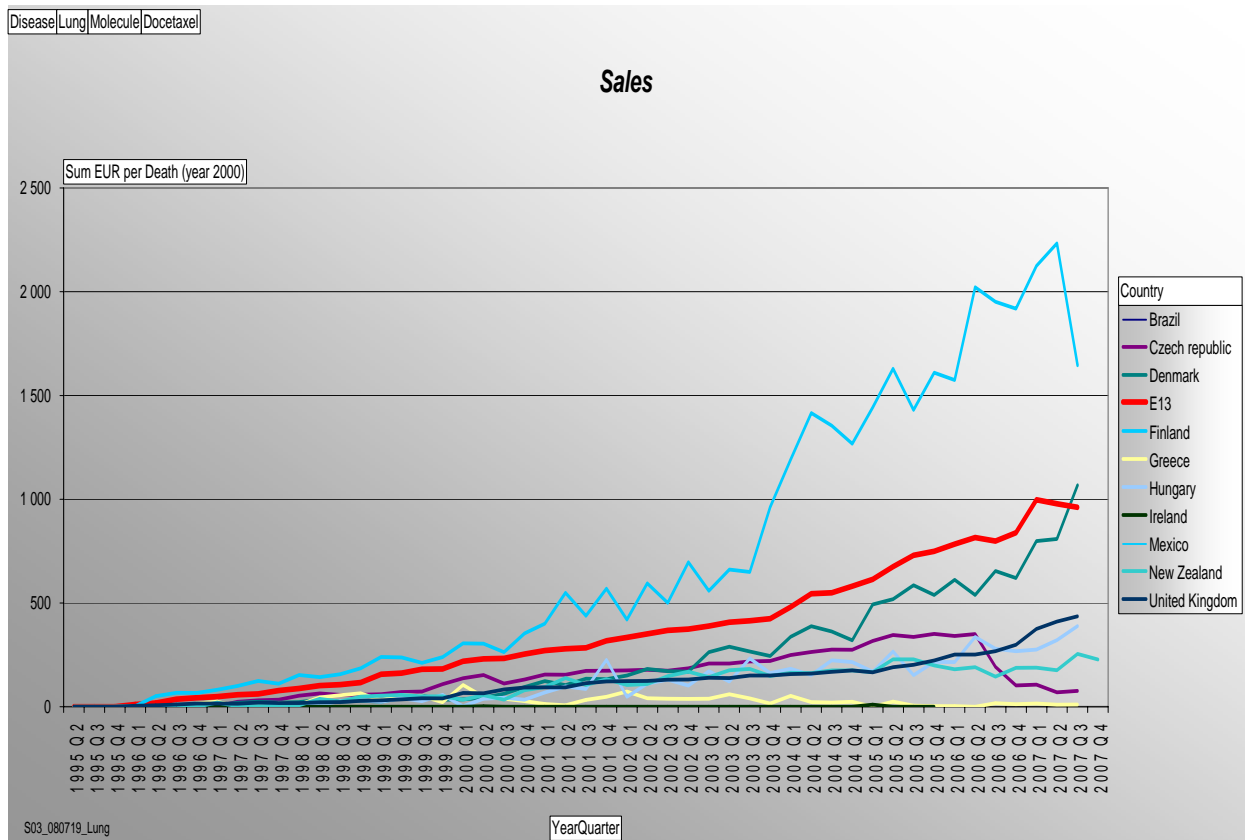
Source: IMS

Figure 8-2 Uptake of docetaxel



Source: IMS

Figure 8-3 Uptake of docetaxel

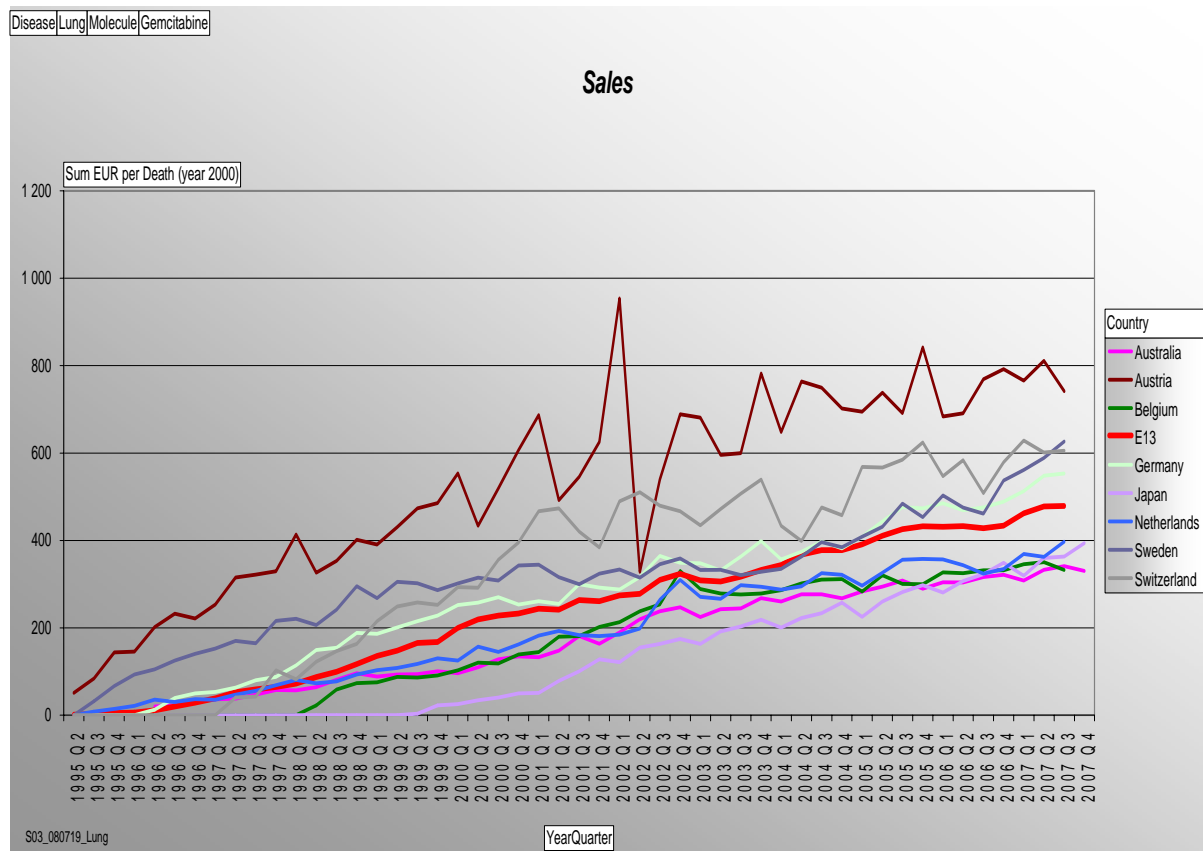


Source: IMS

Figures 8-4, 8-5 and 8-6: Uptake of gemcitabine

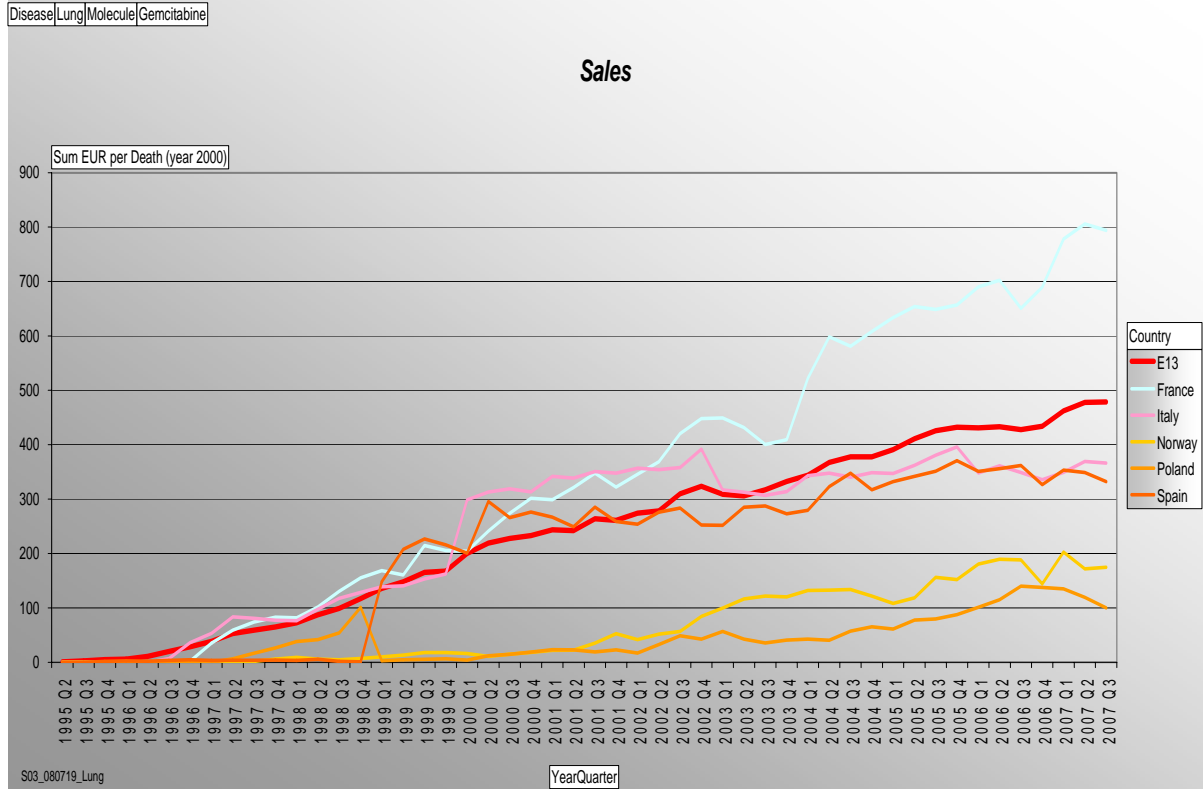
Gemcitabine was first approved in 1995 with pancreatic cancer as the first indication. In 1998 the drug was also approved for lung cancer. Gemcitabine has since been approved for bladder, ovarian and breast cancer. The main use still remains in lung cancer and in most European countries gemcitabine, in combination with cisplatin or carboplatin, represents the most commonly used first-line treatment of NSCLC. Gemcitabine can be considered as an indicator of treatment intensity in NSCLC in many European countries. Gemcitabine use is higher in countries with the best outcome (E13) or close to average outcome. In countries with median outcome the overall use is lower compared to countries with the best outcome. The overall lowest use is seen in countries with the poorest outcome.

Figure 8-4 Uptake of gemcitabine



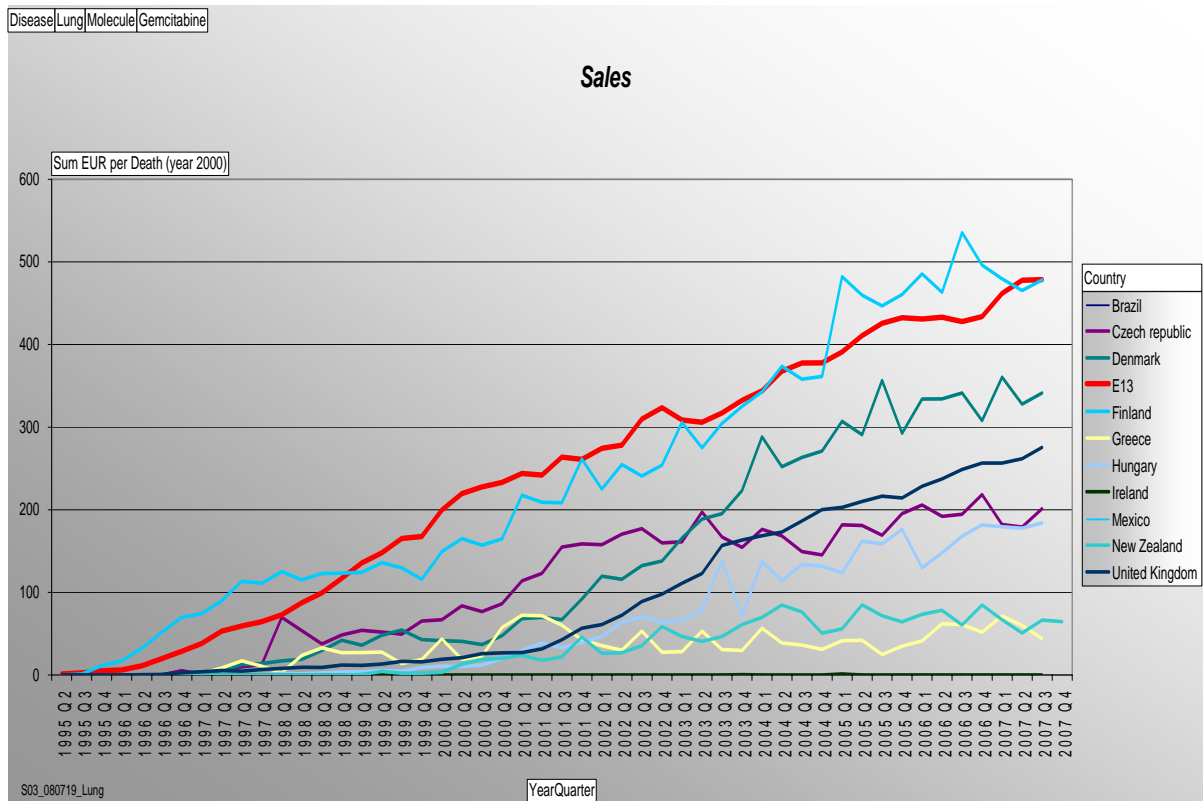
Source: IMS

Figure 8-5 Uptake of gemcitabine



Source: IMS

Figure 8-6 Uptake of gemcitabine

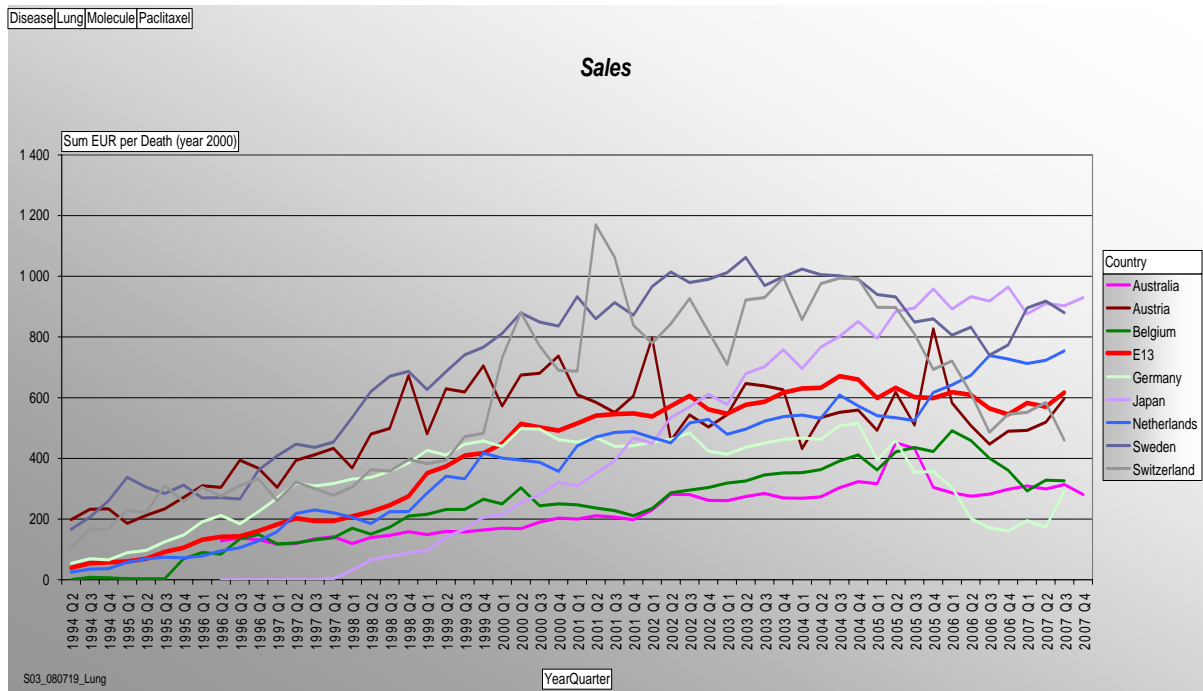


Source: IMS

Figures 8-7, 8-8 and 8-9: Uptake of paclitaxel

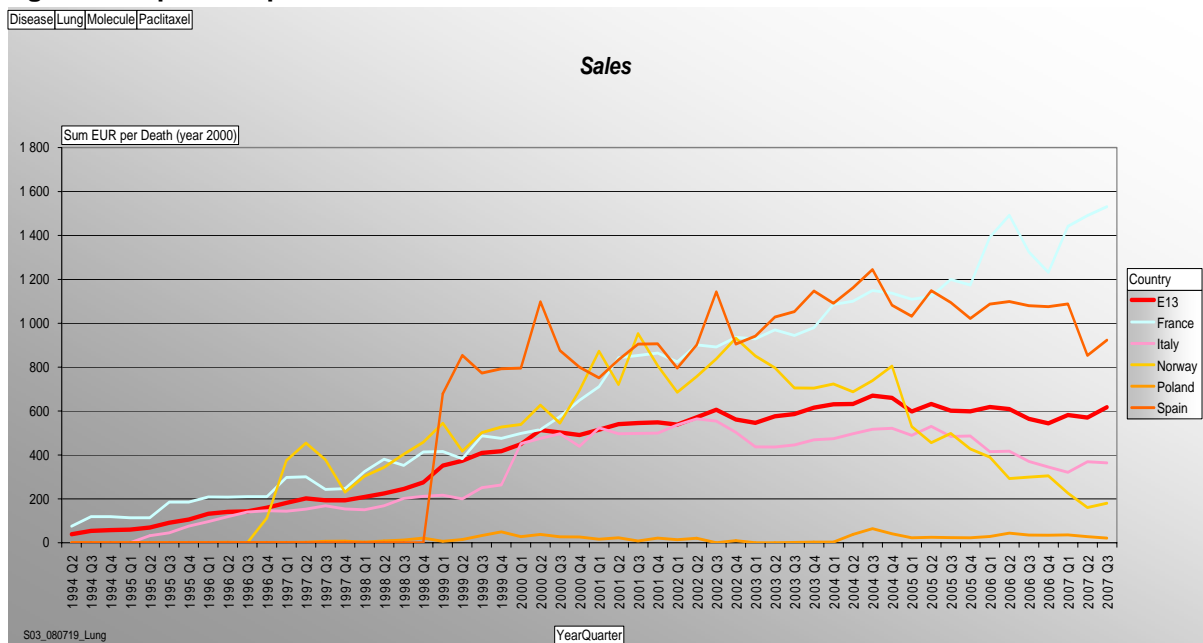
Paclitaxel was first approved in 1993 in ovarian cancer. The lung cancer indication came in 1998 and the drug also has approval in breast cancer. The drug became generic in Europe in 2003. The usage represents a mixture of indications and the share use for lung cancer has been relatively low in Europe. Please note that data from Ireland is not representative of true sales. The only pattern to be observed is the lower than average use in the Czech Republic, Hungary and the UK, all countries with poor outcome.

Figure 8-7 Uptake of paclitaxel



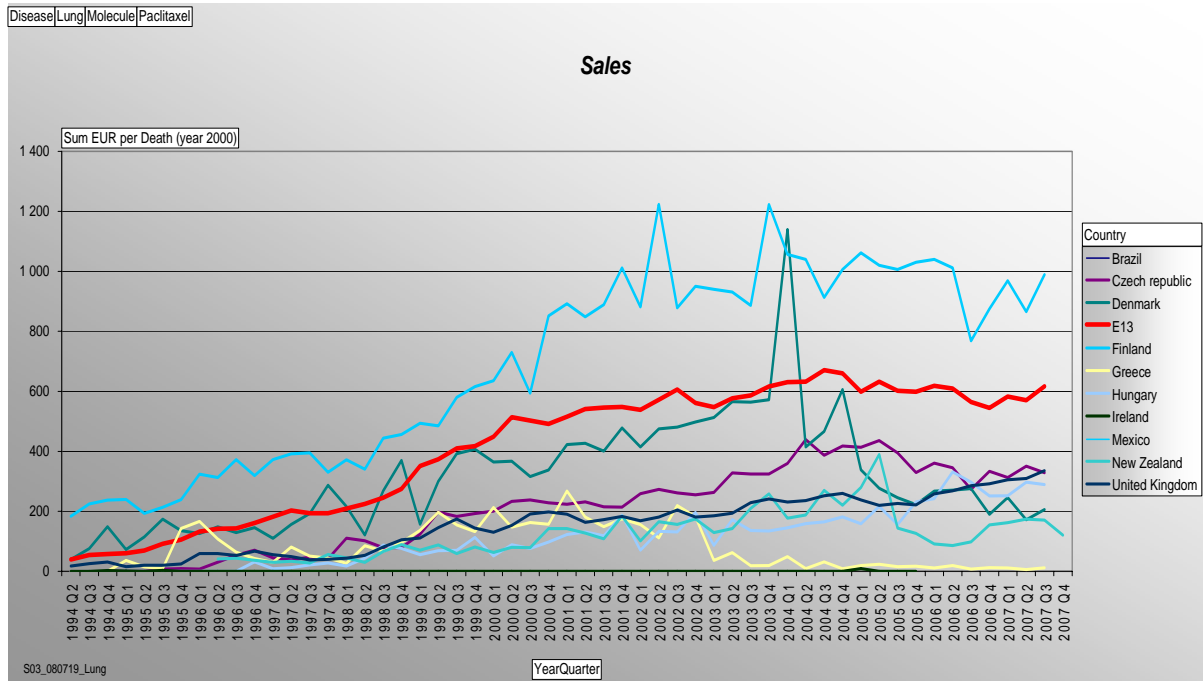
Source: IMS

Figure 8-8 Uptake of paclitaxel



Source: IMS

Figure 8-9 Uptake of paclitaxel

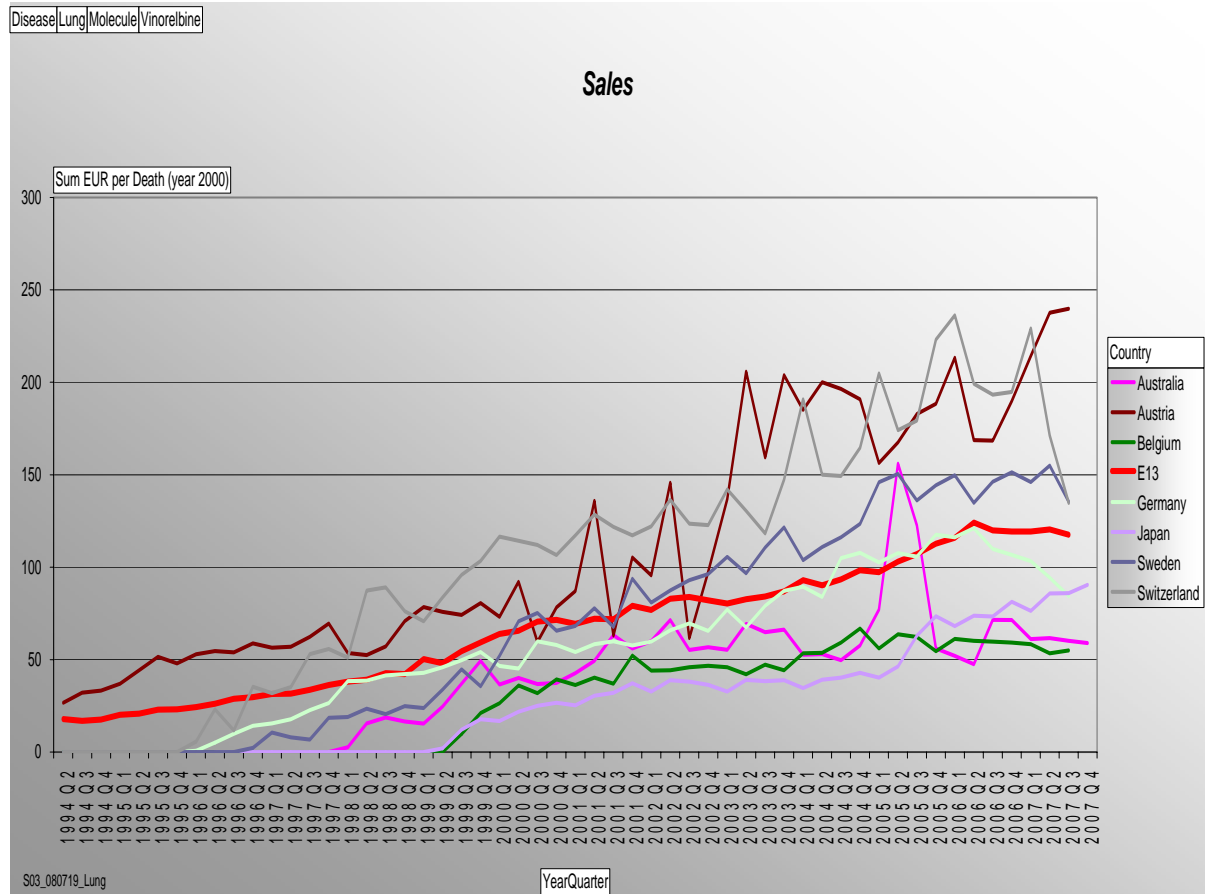


Source: IMS

Figures 8-10, 8-11 and 8-12: Uptake of vinorelbine

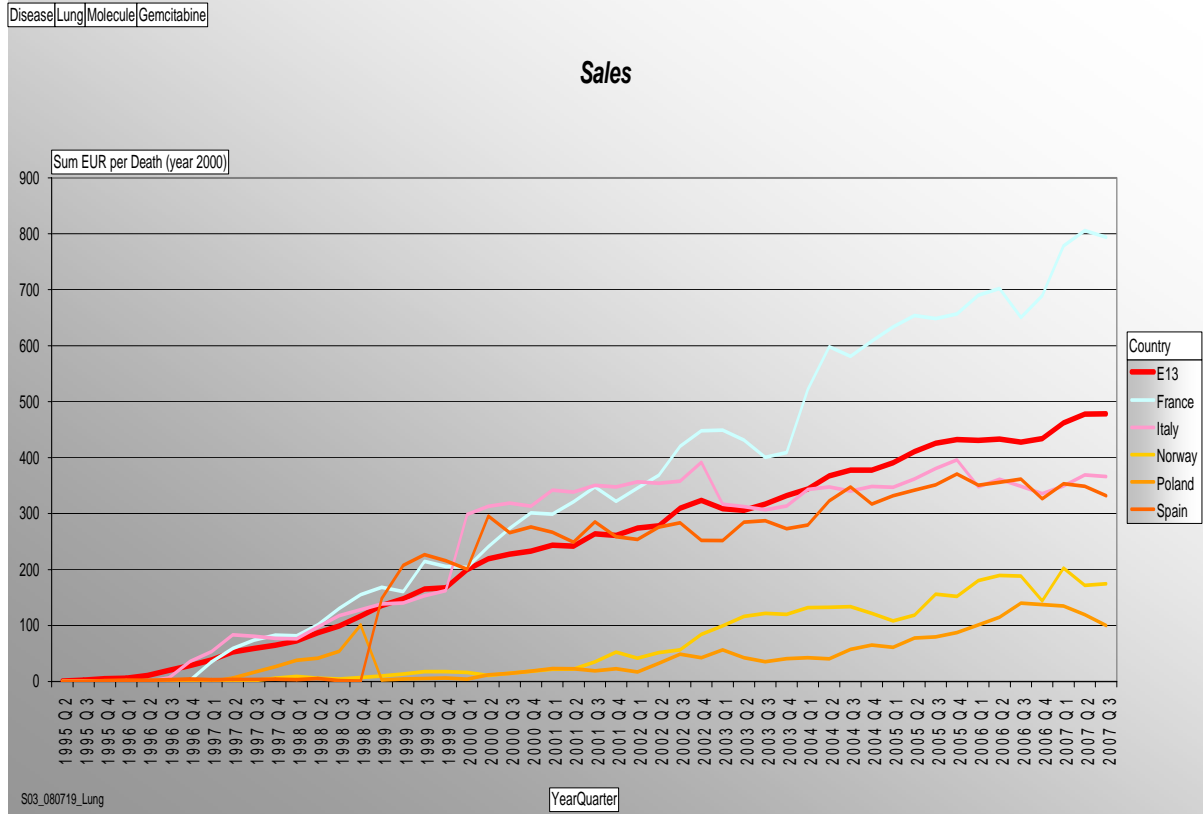
Vinorelbine was first approved in 1991 for use in NSCLC. The drug was considered the first in the new generation of lung cancer drugs during the 1990s. Vinorelbine became part of first line therapy, in combination with a platinum drug in many countries. The drug is now generic. In countries with the best outcome, the use is at or above average. (Please note an underreporting in the Netherlands, not representing the true sales). In countries with medium or poor outcome, sales are at or below average with the exceptions of Finland and France.

Figure 8-10 Uptake of vinorelbine



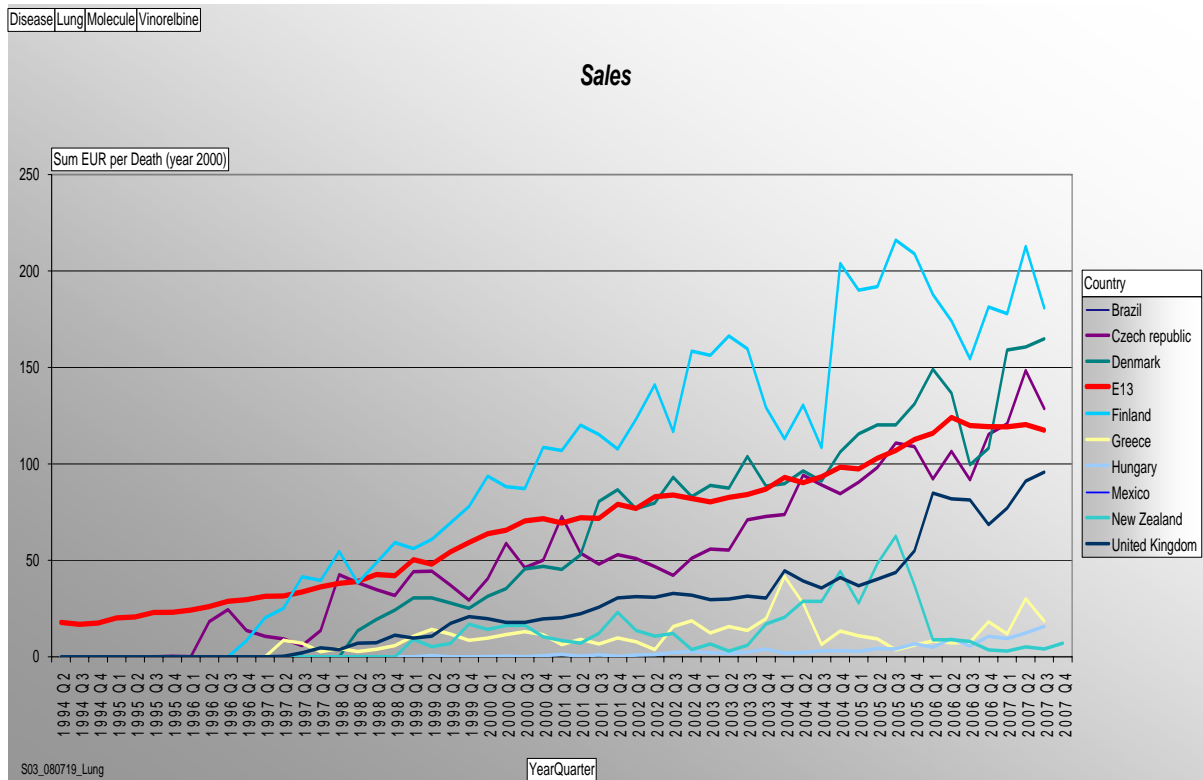
Source: IMS

Figure 8-11 Uptake of vinorelbine



Source: IMS

Figure 8-12 Uptake of vinorelbine

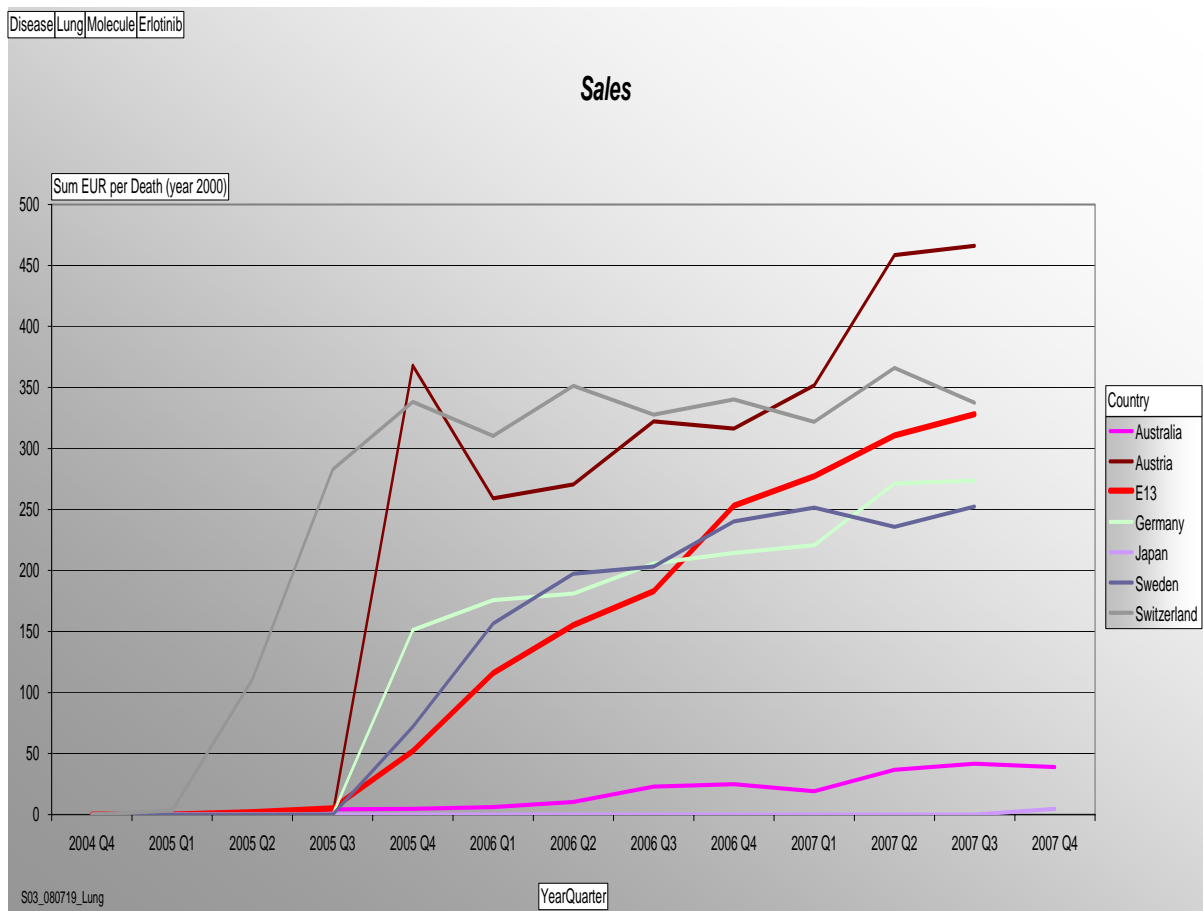


Source: IMS

Figures 8-13, 8-14 and 8-15: Uptake of erlotinib

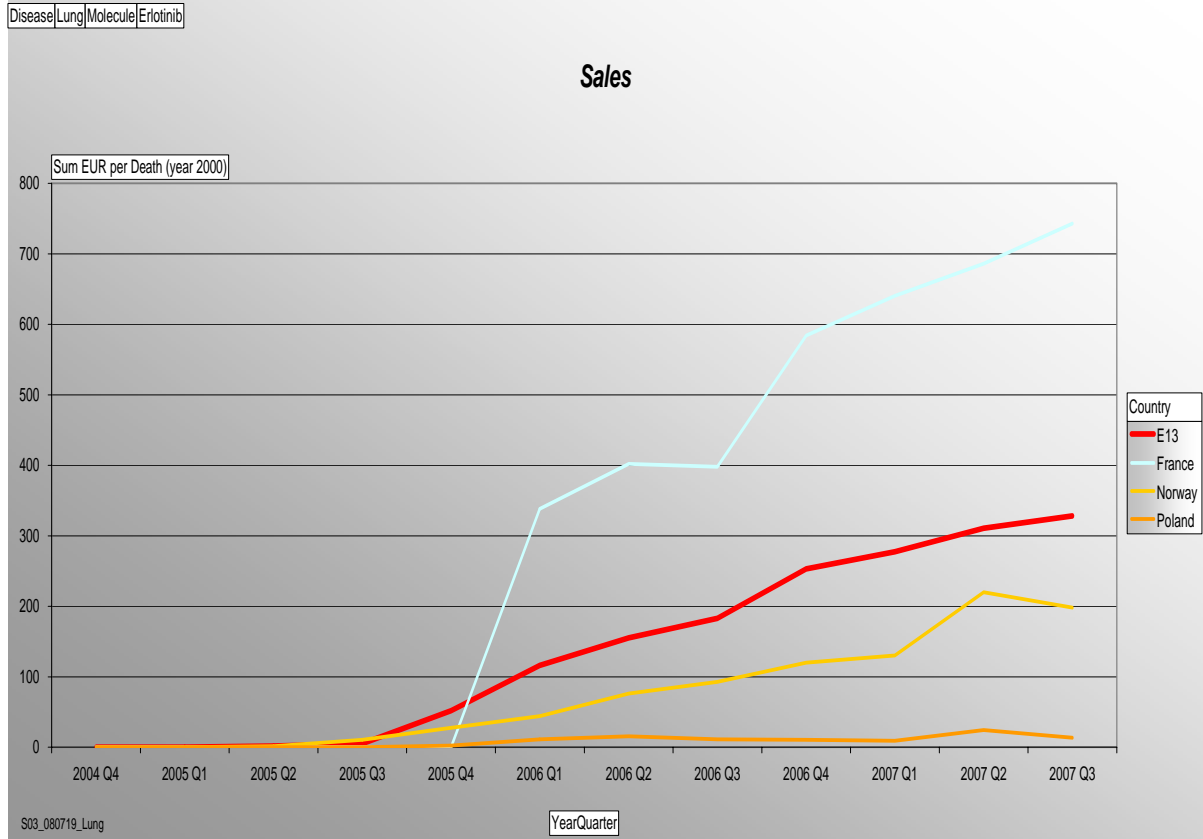
Erlotinib was approved in 2004 with second-line lung cancer as the first indication. Erlotinib has also been approved for pancreatic cancer. The largest use by far is in second-line treatment of patients with NSCLC. In general there is a higher than average or close to average use of erlotinib in countries with the best outcome in treatment of NSCLC. France and Spain have a higher than average (E13) uptake of the drug, while the other countries with medium outcome have a lower than average uptake. In the countries with poor outcome Denmark and Finland have a higher than average uptake of erlotinib. The remaining low outcome countries have lower than average uptake.

Figure 8-13 Uptake of erlotinib



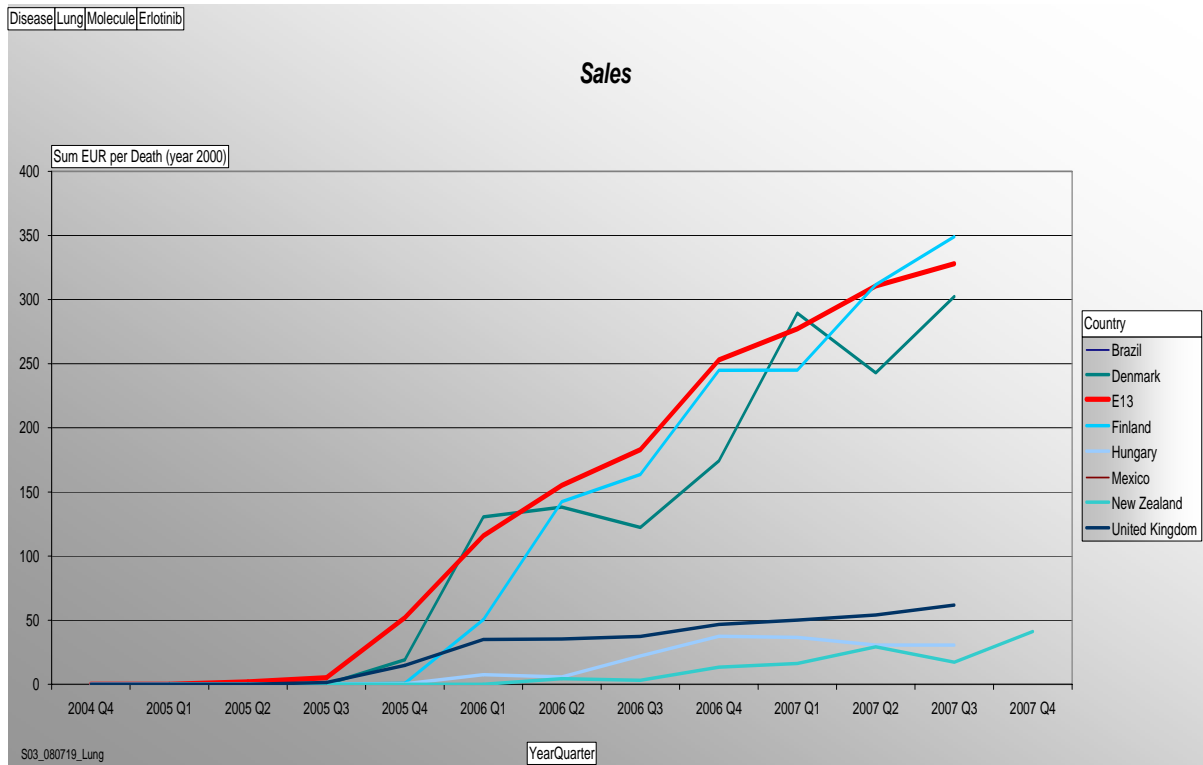
Source: IMS

Figure 8-14 Uptake of erlotinib



Source: IMS

Figure 8-15 Uptake of erlotinib

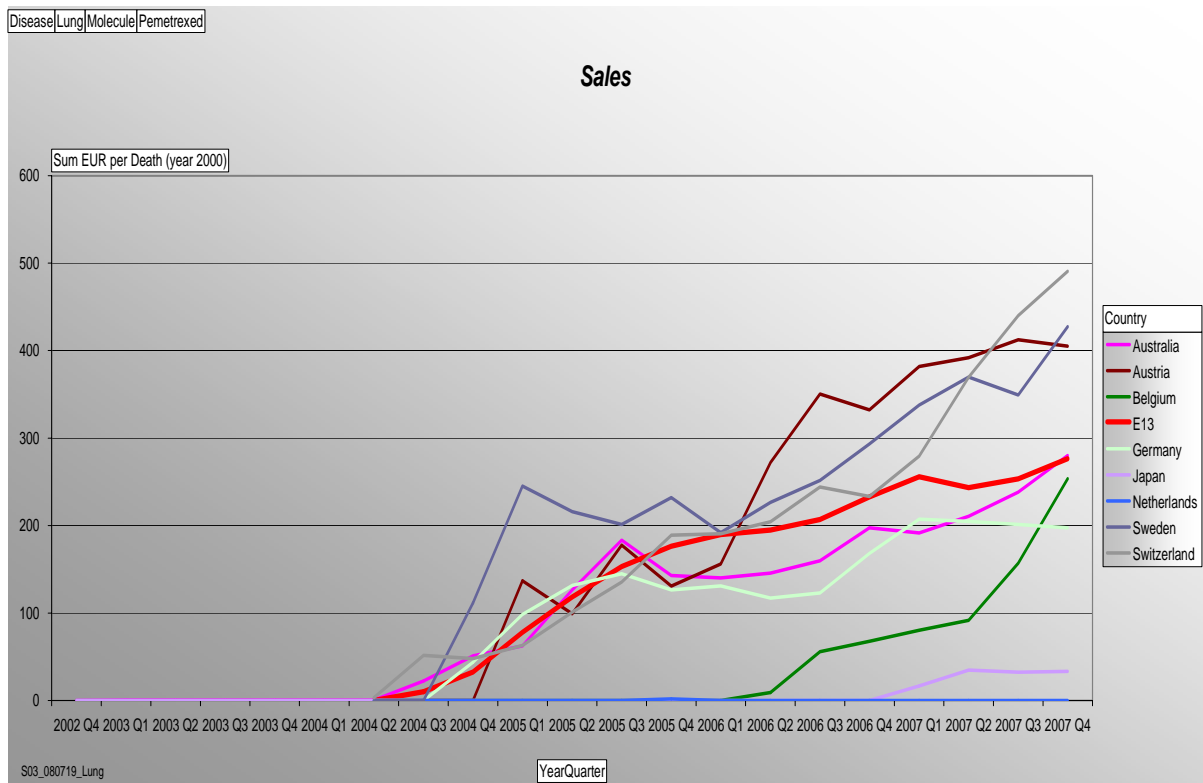


Source: IMS

Figure 8-16, 8-17 and 8-18: Uptake of pemetrexed

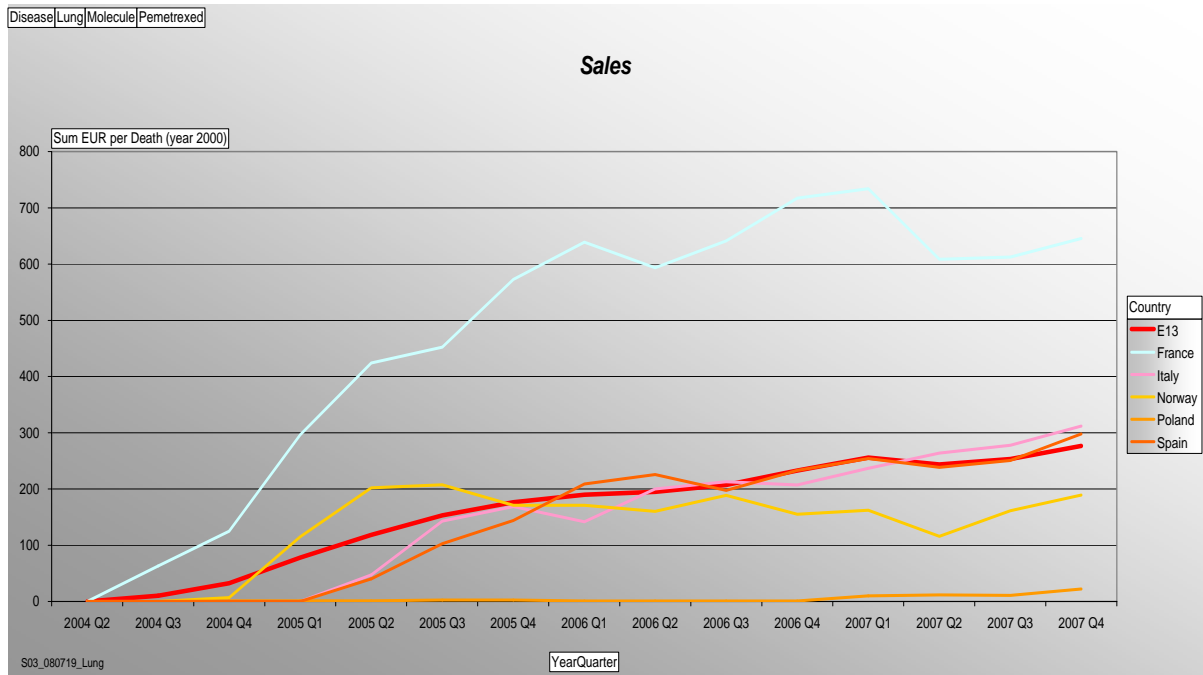
Pemetrexed was initially approved for use in mesothelioma in 2004. It was later approved for second-line as well as first-line use in lung cancer. The use in NSCLC is at present the major market for the drug. Most countries with the best outcome use the drug at the average level (E13) or at a higher level. Among countries with medium outcome the use in France is, by far, the highest. In countries with poor outcome only Finland is above the average use, while the other countries have a lower or much lower than average use.

Figure 8-16 Uptake of pemetrexed



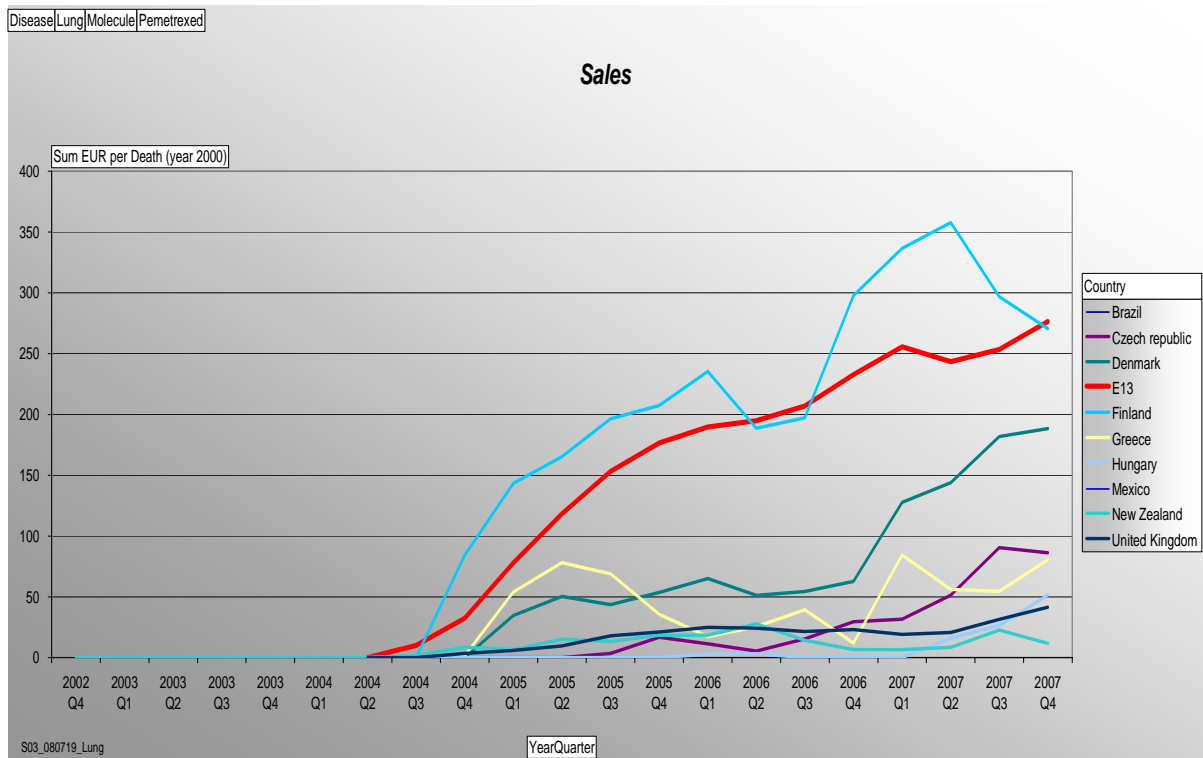
Source: IMS

Figure 8-17 Uptake of pemetrexed



Source: IMS

Figure 8-18 Uptake of pemetrexed



Source: IMS

Summary

France and Austria are the two countries with the fastest uptake and with most patients treated with the studied drugs for NSCLC. Of the five largest European countries, the UK is the lowest user of the drugs studied. Spain is on the E13 average, while Germany and Italy are just below. The Nordic countries, Denmark, Finland, Norway and Sweden, are close to the E13 average. Hungary, the Czech Republic and Poland are at the bottom with hardly any use. Switzerland is generally a fast adopter, but has not had the highest uptake for some years. Belgium and the Netherlands are generally slightly slower compared to the average. Australia has an uptake lower than the E13 average for all drugs but pemetrexed. In Japan the sales per lung cancer death is lower than the E13 average for all of the selected drugs except for paclitaxel. In most cases, where the sales are not above the E13 average, the uptake in Australia and Japan are among the lowest of the best outcome countries. The remaining non European countries, New Zealand, Brazil and Mexico all have an uptake below the E13 average for all of the selected drugs, with Brazil and Mexico having among the lowest of all countries in this study. In many cases they are not even visible on the chart.

9 Discussion and policy conclusion

Lung cancer is the third most common form of cancer in Europe after breast cancer and colorectal cancer. Poor survival rates make lung cancer the most common cause of cancer deaths. The burden of lung cancer is considerable, both in terms of suffering for patients and their relatives, and the economic burden to society. The indirect cost of lung cancer is 80-90 per cent of the total costs.

In this report we have studied management and organisation of lung cancer care in 20 European countries: Austria, Belgium, Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Ireland, Italy, the Netherlands, Norway, Poland, Portugal, Russian Federation, Spain, Sweden, Switzerland and the United Kingdom as well as in five non-European countries: Australia and New Zealand in Oceania, Japan in Asia and Brazil and Mexico in Latin America. We have compared outcomes of lung cancer care, measured by the relation between incidence and prevalence, using data from the GLOBOCAN 2002 database. We have also analysed limitations in patient access to the most appropriate treatment and policies to promote access.

There are large variations between countries in terms of incidence and mortality. Among the countries with the lowest outcomes we find the Eastern European countries, the Czech Republic, Poland, Russian Federation and Hungary, with considerably less overall expenditure on health. Lower overall spending on healthcare also means fewer resources available for cancer treatment, limiting the ability to provide the most appropriate treatment to patients. High incidence and mortality is also found in the UK, Denmark and Ireland. The incidence and mortality is generally lower in the non-European countries, especially in the Latin American countries Brazil and Mexico.

In terms of treatment options used across countries there is no single variable explaining the variations in treatment outcomes. However, if different treatment options are put together, the countries with the best outcomes according to GLOBOCAN data (France, Austria, Belgium, the Netherlands and Switzerland in Europe as well as Japan and Australia outside Europe) tend to have better access to treatment, and countries with the poorest outcomes according to GLOBOCAN data tend to have less access to treatment (the UK, Denmark, Poland, Czech Republic, Ireland, Russian Federation and Hungary as well as Brazil and Mexico in Latin America). The organisation of lung cancer care is fragmented in many countries both on a macro level, in terms of lack of nationally coordinated strategies, as well as on a micro level where treatment is disintegrated and failing to provide the patient with the most appropriate treatment.

In radiotherapy there is lack of investment in equipment and staffing in many European countries: the Russian Federation, Poland, Hungary, Ireland, Portugal, Spain, Czech Republic, Greece and the UK. In all countries with the lowest outcomes, except Denmark, there are fewer than four linear accelerators per million inhabitants, which is an often used standard. This lack of investment is most frequent in countries with fewer resources spent on health care. Countries in Central and Eastern Europe, as well as Spain, Portugal and Greece have a larger share of older Cobalt machines compared to the Nordic countries where most radiotherapy machines are more modern kind linear accelerators.

In the Latin American countries, chances of survival for lung cancer patients are lower and patients have notably less access to treatment than in the other countries of this study. The provision of radiotherapy equipment is considerably lower in Brazil and Mexico. However, it should be noted that the provision is measured in relation to the population and the lung cancer incidence is significantly smaller in these two countries, hence the real need for radiotherapy equipment may be smaller than in the other countries of this study. The uptake of the selected drugs, important in lung cancer treatment, is also considerably lower than in the European countries. Thus, a large share of patients is not offered any active anti-tumour treatment, and only a few per cent of all patients are given surgical treatment which is the first option for curative treatment. The primary explanations for this seem to be lack of resources and late diagnosis. In Brazil and Mexico only a small share of lung cancer cases are detected in stages I or II when lung cancer is normally considered curable. An increased detection rate at earlier stages would likely lead to an increased share of cancer treatment being dedicated to lung cancer, while now, as reported from Mexico, breast cancer and cervix cancer are prioritised over lung cancer since these cancer forms both have higher chances of cure and affect younger individuals. The lower priority of lung cancer may also in turn reduce the efforts and chances of early detection.

Policies, procedures, budgeting systems and economic conditions delay market introduction and restrict patient access to modern lung cancer drugs (docetaxel, gemcitabine, paclitaxel, and vinorelbine). The uptake and use of these drugs is below the European average in countries with poorer outcome. The same is true for the most recently introduced drugs, erlotinib (Denmark being an exception with high uptake) and pemetrexed.

The best performing countries tend to have better patient access to modern lung cancer drugs, as well as better provision of radiotherapy equipment. However, in Australia and Japan where the outcome is among the highest, the uptake of the drugs analysed in this study is generally lower than in the best performing countries in Europe. Also other factors such as the share of patients given treatment with curative intent and patients treated with surgery is higher in the high-outcome countries Switzerland, Netherlands and France as well as the medium performing Germany.

The conclusion of this is that it is very important to ensure that regulations, priorities, funding, and organisation of lung cancer care are coordinated to provide all patients with the most appropriate treatment alternative, ensuring the use of the most cost-effective treatments with minimal delays.

Hospital budgets need to be flexible to accommodate new treatments. Health Technology Assessments and economic evaluations need to be used to guide decision makers in priorities, and to ensure that new treatments that are cost effective to gain market access. It is also important that such evaluations do not delay the introduction of new treatments more than necessary.

The fragmented organisation and management of lung cancer care has been acknowledged by many countries. This has resulted in the analysis and re-organisation of cancer care and the development of nationally coordinated strategies. In some of the countries with the poorest outcomes in lung cancer, comprehensive strategies have been developed. In the UK, there are signs that the problem of long delays has changed, as lately more efficient referral routines and reduced waiting time have been implemented. In Denmark large investments have been made in order to increase radiotherapy capacity. The smaller and medium-sized countries of

Belgium, Denmark, Czech Republic, Hungary and Ireland have reorganised specialised lung cancer treatment to fewer centres in order to improve integration of treatments. These reorganisations also aim to reduce the problems of small treatment centres not having sufficient resource and patient bases to efficiently deliver the most appropriate treatment. In Denmark and the Czech Republic national funds have been made available to ensure that patients gain access to new cancer drugs.

Apart from treatment it is also important to introduce effective measures in prevention and early detection. In recent years new and stronger regulations on smoking in public places, work places and in restaurants and bars have been introduced in most countries. Somewhat slower in introducing tougher restrictions on smoking are the Russian Federation and Switzerland, while Ireland and the Nordic countries have been among the earliest to adopt and extend smoking bans.

The late diagnosis of the disease is the most important factor explaining the low survival rates. There have been several trials aimed at improving early detection in screening programmes, either generally or for groups of people believed to be at risk of lung cancer such as long time smokers. No trials have, however, proved to improve survival even though some recent studies have given new hope.

Organisational changes may take several years before expected improvements are seen. The long-term effects can only be measured many years after actual improvements. Thus, the effects of changes must continuously be followed and monitored. This requires a well structured administration of cancer registries, allowing proper analyses.

Appendix 1: Country review of healthcare systems and cancer care

Austria

The Austrian healthcare system is based on social insurance, administered by 19 sickness funds and their umbrella organisation the *Federation of Austrian Social Insurance Institutions* HVSV. Health insurance is financed by contributions based on the income of individuals. Health insurance contributions account for about half of the health care costs, while private contributions in the form of out-of-pocket expenses and private insurances account for 30 per cent. The remaining 20 per cent is financed by general taxation.

Health services in Austria are federally regulated, but the provision of healthcare is decentralised to the nine *Länder* at regional level. General practitioners, mostly self-employed, offer primary care and act as gatekeepers referring patients to specialist care when needed. Specialist care is either administered in hospitals which are generally public, or in consultation offices. Remuneration of public and non-profit general hospitals is based on a Diagnosis Related Groups system (DRG).

Reimbursement and pricing of pharmaceuticals

The HVSV oversees all Austrian sickness fund schemes and is the formal decision maker on pharmaceutical reimbursement by providing a positive list. The prices of innovative and generic pharmaceuticals are set by the Ministry of Health according to a reference pricing system based on average European prices.

There is no separate budget for expenditure on pharmaceuticals in Austria but there are guidelines issued by the sickness funds which also monitor the adherence. As a last resort, although rarely used in action, the institution of an overspending physician may have to compensate the sickness fund.

In a recently published international comparison of patient access to cancer drugs, Austria is highlighted as one of the fastest countries in Europe to introduce new cancer drugs [13].

Lung cancer care

In Austria lung cancer patients are mainly diagnosed and treated in general hospitals, including university hospitals, which treat about half of the patients. Many district hospitals have oncology boards ensuring a multidisciplinary treatment of patients. Most of these district hospitals provide cancer treatment, and that is also where most patients are treated. There are only a few specialised oncological hospitals mainly concerned with hematological malignancies. In recent years cancer has increasingly been treated in specialised cancer treatment centres primarily at the university hospitals.

Since 1969 every hospital has been required to document its cancer cases in order to keep a nationwide cancer registry. There are also some regional registries collecting more comprehensive data regarding treatment of patients.

In the latest EUROCORE 4 report Austria has the second highest relative survival rate in lung cancer with 13.9 per cent for patients treated between 1995-1999 [51].

The incidence rates in lung cancer are also higher than the European average among women (22.3 per 100,000), but lower among men (54.0 per 100,000). The European average incidence rates were 75.3 per 100,000 for men and 18.3 per 100,000 for women in 2006.

The mortality rates in lung cancer in Austria are higher than the European average among women (18.2 per 100,000), but lower among men (51.3 per 100,000). The European average mortality rates were 64.8 per 100 000 for men and 15.1 per 100,000 for women in 2006.

Belgium

The Belgian healthcare system is based on compulsory social health insurance funded by contributions from employers and employees based on salary and by national taxation. Health insurance is organised by a number of private, non-profit sickness funds. The provision of healthcare is divided between private and public providers. About 80 per cent of the resources spent on hospital services are within the public sector.

Reimbursement and pricing of pharmaceuticals

Decisions on reimbursement of pharmaceuticals are taken by the *Medicines Reimbursement Commission* within the *National Institute for Sickness and Invalidity Insurance* representing the government, the sickness funds, employers, workers and the health care providers.

There is no specific budget or funding for the use of pharmaceuticals in hospitals in Belgium, as such costs are covered by the regular hospital budget.

Cancer care

The organisation of cancer care in Belgium has in recent years gone through a restructuring in order to improve access and quality in cancer care. The basis for the new organisation is an oncological care programme, focusing on delivery of cancer care by multidisciplinary teams following new clinical guidelines. Cancer care is also provided in fewer hospitals which are collaborating in networks. There is also one hospital, *Institute Jules Bordet*, entirely dedicated to treatment, research and teaching within oncology [73].

There are regional registries in the provinces of Limburg and Antwerp. National statistics on cancer are also collected by the *Belgian Cancer Registry Foundation*

Incidence, mortality and survival in lung cancer

Belgium has among the highest relative survival rates in the latest EUROCORE 4 study [51].

The incidence rates in lung cancer are also higher than the European average both among men (93.0 per 100,000) and women (22.9 per 100,000). The European average incidence rates were 75.3 per 100,000 for men and 18.3 per 100,000 for women in 2006. The mortality rates in lung cancer are higher than the European average both among men (93.8 per 100,000) and women (20.7 per 100,000). The European average mortality rates were 64.8 per 100,000 for men and 15.1 per 100,000 for women in 2006.

Czech Republic

The political and economic transformation in the Czech Republic after 1989 and the separation of Czechoslovakia has had a great impact on health care. Most important has been a transfer of responsibility for financing and providing healthcare from the state to nine regional sickness funds who negotiate contracts with health service providers. The health insurance through the sickness funds is mandatory and paid by employers, but the state pays the contributions of certain groups such as children, the retired and unemployed. The health insurance system finances about 80 per cent of all healthcare services. Direct out-of-pocket contributions by patients are required for some medications and account for a little less than 10 per cent of total expenditure on health. The remaining 10 per cent are financed by the state.

Primary care is mostly provided by privately employed GPs within a family physician system while hospitals are predominantly public. Hospitals are run at regional or local level, but university hospitals are managed by the Ministry of Health. The resources at Czech public hospitals are scarce, but a DRG-financed system is being introduced to facilitate appropriate financing and efficient allocation of resources.

Reimbursement and pricing of pharmaceuticals

The decision on the price of new pharmaceuticals in the Czech Republic is taken before the decision on the level of reimbursement. This decision is based on external reference prices. The producer applies for reimbursement after the Ministry of Finance has set the maximum manufacturer price. In general, the drug with the lowest price within a defined group of countries is fully reimbursed. All other pharmaceuticals are partly or fully paid for by patients. Sickness funds only reimburse up to the price of the generic equivalent, i.e. the reference price.

The decision on reimbursement is taken by the Ministry of Health with a categorisation committee, with representatives from the Ministry, the insurance funds and medical and patients associations, which acts as an advisory body.

Restrictions on who is entitled to prescribe certain pharmaceuticals are set during the reimbursement process. For example, newer and more expensive pharmaceuticals are often restricted to prescription by specialists.

In the Czech Republic the physicians have separate budgets for expenditures on pharmaceuticals. These budgets are set by the health insurance companies based on the average cost per specialty in each region. If the physicians overspend they may be punished by cuts in future payments.

Cancer care

Cancer care in the Czech Republic is mainly carried out in 18 so called Complex Cancer Centres. There is also one Comprehensive Cancer Centre located in Brno. The Complex Cancer Centres are either single institutions or networks of hospitals collaborating with a medical faculty. The operations of the cancer centres are coordinated by a National Council of Oncocentres. Until recently, cancer care in the Czech Republic was provided at a large number of hospitals, often small and with limited resources and insufficient or outdated equipment.

Since 1977 there has been a national cancer registry covering the entire population.

The Czech Oncological Society has directed criticism towards the fragmentation of cancer care and the limitations on the use of new cancer drugs. Limited resources have led to inequities in access to cancer care. In 2007, the most expensive treatment in cancer was concentrated to one cancer centre in order to give all patients access to the most appropriate therapies regardless of where they live [89].

Incidence, mortality and survival in lung cancer

In the latest EUROCARE 4 study the Czech relative survival rate of the 8.2 per cent is well below the European average [51]. However, Czech officials claim that their national data used in the study is only a sub sample of a national full coverage cancer registry. This sub sample is not representative for the entire country which they consider to be clearly above average [65].

The mortality rates in lung cancer are higher than the European average both among men (77.3 per 100,000) and women (19.1 per 100,000). The European average was 64.8 per 100,000 for men and 15.1 per 100,000 for women in 2006. The incidence rates in lung cancer are also higher than the European average both among men (78.9 per 100,000) and women (29.9 per 100,000). The European average incidence rates were 75.3 per 100,000 for men and 18.3 per 100,000 for women in 2006. [1].

Denmark

The financing of Danish health care is based on general taxation. Access to health services is guaranteed to all citizens and residents in the country. Primary, secondary and specialist care services are free of charge, but expenditures on drugs are co-financed by the individual.

In January 2007 the Danish health care system was subject to a major municipal reform. The number of municipalities was reduced from 270 to 98 and the 13 counties replaced by five regions. After the reform, the organisation of health care became one of the main responsibilities of the regions. The establishment of the new regions within healthcare is to facilitate a greater specialisation and better utilisation of resources through larger units. As the regions do not collect taxes, healthcare is financed through national (80 per cent) and local (20 per cent) taxation [145].

Except for emergency care, hospital care is subject to referral from a general practitioner, according to a principle that treatment should take place at the lowest effective level possible.

Reimbursement and pricing of pharmaceuticals in Denmark

The Danish Medicines Agency is responsible for decisions on reimbursements as well as pricing of pharmaceuticals. The reimbursement price is set according to a reference price based on the average of European prices. The weight of external reference prices has in recent years been played down in favor of internal reference prices on products in the same substitution or reimbursement group. The reimbursement decision is taken based on the price of the product and the therapeutic value. It is voluntary for the pharmaceutical company to

provide pharmaco-economic studies of a drug, but the decision is facilitated as cost effectiveness is one criteria used in the decision, although given a limited impact [146].

Pharmaceuticals for hospital use only are negotiated directly with the producer by the hospital purchasing agency. The pharmaceuticals used in hospitals are financed within the regional health care budget.

Recently, Denmark has decided to establish additional money in a separate budget for new innovative cancer drugs.

Lung cancer care

The four university hospitals in Copenhagen, Odense and Århus have specialist oncology departments and radiotherapy facilities. There are also oncology centers in Ålborg and Vejle. In addition, cancer surgery and some chemotherapy is carried out at the larger central hospitals in the regions. Aftercare, palliation and rehabilitation are the responsibilities of local care units and the primary care sector.

The *Danish Cancer Registry* is nationwide and population based. Mandatory reporting of cancer was introduced in 1987. In addition to reporting from hospitals, the registry also gets data from the National Patient Discharge Registry.

In 2000 a National Cancer Control Plan was established, updated with a new plan in 2005. The plans were initiated following comparisons in cancer survival with the other Nordic countries which revealed considerably lower rates in Denmark. Following the plan, the Danish government allocates substantial resources to diagnostic and therapeutic equipment, shortening waiting lists and clinical guidelines [114].

Incidence, mortality and survival in lung cancer

Denmark's survival outcomes are in the bottom of the EURO CARE 4 study recently published, below many countries spending significantly less resources on healthcare [1, 7, 51]. The mortality rates in lung cancer are lower than the European average for men (57.9 per 100,000), but the highest among women in the group of countries in this study (41.6 per 100,000). The European average were 64.8 per 100,000 for men and 15.1 per 100,000 for women in 2006. The incidence rates in lung cancer are lower than the European average for men (65.0 per 100,000), but dramatically higher for women (48.7 per 100,000). The European average incidence rates were 75.3 per 100,000 for men and 18.3 per 100,000 for women in 2006 [1].

Finland

The provision of healthcare in Finland is decentralised to the 460 municipalities organising primary care in municipal health centres. The smallest municipalities often run these health centres jointly with other small municipalities. These services can also be purchased from private providers. The municipalities are also responsible for providing the citizens with specialist care. These services are organised in 21 health regions and purchased by the municipalities according to a Diagnosis Related Group system. Each of the 21 healthcare regions have a central hospital, and five of the districts also host a medical faculty and a university hospital, where the most specialised health services are provided.

Reimbursement and pricing of pharmaceuticals

Decisions on reimbursement and the price of pharmaceuticals in Finland are made by the Pharmaceutical Pricing Board (PPB) at the Ministry of Social Affairs and Health. The price is set in negotiation with the producer. The PPB decision is based on a number of factors on which the producer has to provide information in their application: the therapeutic value of the pharmaceutical, prices of major competitors and the price in other European countries, costs for research, development and production of the drug, costs of the pharmaceutical, and a pharmacoeconomic evaluation.

Although the prices in other countries are taken into account when setting the price, there is no formal external reference price system. To keep the expenditures on drugs down there is a system of generic substitution in action.

Pharmaceuticals for hospital use only are not included in the reimbursement system. The prices are negotiated directly between the hospital and the manufacturer. There are no separate budgets to be used for pharmaceuticals, for physicians or in the region budgets.

Lung cancer care

The university hospitals serve as regional cancer centres with specialist diagnostic, treatment and research facilities. There are also radiotherapy units at four other hospitals and at the central hospitals in each of the health care region performing oncological surgery. 95 per cent of all lung cancer patients are treated at the regional hospitals.

Since 1953 a national cancer registry has covered the entire population with compulsory reporting from physicians, hospitals, institutes with hospital beds, and pathology and cytology laboratories, as well as death certificates.

There is no national cancer control plan in Finland, but there are specific treatment guidelines for different types of cancer including lung cancer.

Incidence, mortality and survival in lung cancer

The mortality rates in lung cancer are lower than the European average both among men (43.5 per 100,000) and women (13.0 per 100,000). The European average were 64.8 per 100,000 for men and 15.1 per 100,000 for women in 2006. The incidence rates in lung cancer are also lower than the European average both among men (45.8 per 100,000) and women (14.7 per 100,000). The European average incidence rates were 75.3 per 100,000 for men and 18.3 per 100,000 for women in 2006.

According to the recently published EURO CARE 4 study, the relative 5-year survival for all cancers treated in 1995-1999 in Finland was higher than the mean of the European countries, but the corresponding survival rate for lung cancer was lower than the European mean for patients treated in the same period [51].

France

The French National Health System (Sécurité Sociale) is insurance based and financed by income taxation. The system has universal coverage and uniform healthcare benefits for all citizens.

The provision of healthcare is carried out by both public and private providers. Ambulatory care is mainly private, while hospital care is mainly publicly provided accounting for about 70 per cent of all hospital beds. The provision of healthcare is now organised on a regional basis in order to match spending more closely to the requirements of the population.

Reimbursement and pricing of pharmaceuticals

Reimbursement decisions on pharmaceuticals are made by a transparency committee under the *High Authority of Health*. Reimbursable drugs are priced in negotiation between the producer and the pricing *Comité Economique du Médicament* (CEM) under the French Ministry of Health.

There are policies for new drugs in certain classes. For example there is a fast track procedure for approval and pricing of the most innovative drugs with high therapeutic value, or significant improvement of efficacy and/or reduction of negative side effects. The producer of a pharmaceutical classed as innovative, proposes a price to CEM, which has two weeks to object to the price which otherwise will be accepted. This relates mainly to expensive new innovative drugs, often for cancer treatment.

Pharmaceuticals for use in hospitals only are financed from the general hospital budgets. To control physicians prescriptions, guidelines are issued. There is a possibility to penalise physicians not following these guidelines but these are rarely used.

Lung cancer care

Since the national cancer plan for 2003-2007 was introduced cancer care has been coordinated in 27 regional cancer centres. Each hospital treating cancer patients has a cancer care coordination centre, which ensures that all medical files comply with care standards or have been discussed in a multidisciplinary consultation meeting. The Cancer Coordination Centres are guided by the National Cancer Institute. As a part of the national cancer plan, large investments have been made in diagnostic and therapeutic equipment in order to reduce waiting times. Certain innovative drugs are also promoted by more accessible reimbursement policies.

There are 30 university hospitals and 20 comprehensive cancer centres in France. About 50 per cent of all cancer patients are treated in public hospitals (including some comprehensive cancer centres), while the remaining half are treated in private hospitals. Extensive cancer care facilities providing surgery, radiotherapy and chemotherapy are available in all main

urban centres. As a part of fighting cancer, nine cancer research hubs have also been established to promote research and innovation (Cancerpoles), partnering research, cancer care and the industry.

Cancer registration in France

There are 11 general and nine specialised cancer registries all belonging to the network of French cancer registries (FRANCIM). Registration is active in all cancer registries, with information collected from pathology laboratories, public and private hospitals, social security offices and GPs.

Incidence, mortality and survival in lung cancer in France

The mortality rates in lung cancer are just under the European average both for men (60.0 per 100,000), and for women (13.7 per 100,000). The European average was 64.8 per 100,000 for men and 15.1 per 100,000 for women in 2006. The incidence rates in lung cancer are about the European average among men (75.5 per 100,000), but a little lower among women (15.0 per 100,000). The European average incidence rates were 75.3 per 100,000 for men and 18.3 per 100,000 for women in 2006.

In the recently published EUROCARE 4 data, the relative survival rate in lung cancer in France is well above the average of European countries of study. Nevertheless, the relative survival rate in the period 1995-1999 was lower than in the period 1991-1994 [51].

Germany

The organisation of the German healthcare system is linked to the federal organisation of the country. The authorities responsible for public health services are the Bund at national level, the *Länder* at regional level and the *Gemeinden* at local level.

The financing of the healthcare system is based on social health insurance through nearly 400 *Statutory Health Insurance Funds* (SHIF). The SHIF are financed by income related contributions by employers and employees. Only 8.4 per cent of the total expenditure is financed by taxes. Ambulatory care and hospital care have traditionally been distinct domains with almost no outpatient care delivered in hospitals. Hospital inpatient care is provided by a mix of public and private providers. Private hospitals are mostly run by non-profit organisations.

Reimbursement and pricing of pharmaceuticals

There is no formal mechanism for making national reimbursement decisions for patented pharmaceuticals in Germany, but there is a negative list of drugs not to be prescribed. The physicians can therefore prescribe drugs not on the negative list without such a decision. The physicians have a responsibility to keep the drug costs down as these will be used against the regular budget.

The budget of physicians contracted by the sickness funds is controlled through individual spending targets and through regional agreements on target spending limits and cost-control measures. These control measures are negotiated between the Association of Contracted Physicians and the National Associations of Sickness Funds. The agreements are negotiated

at the regional *Länder* level. The individual spending targets are set for the average prescribing costs per patient each year for each physician. In case of overspending, the individual physician is audited and may be required to re-pay the excess. In the regional agreements on pharmaceutical spending targets, bonuses may be paid out to the physicians if these targets are met.

Cancer care

Cancer care in Germany is coordinated in a federal government programme. In Germany there are about 35 *Tumorzentren* bringing together specialised cancer care with a regional uptake. These may be organised within a single organisation or in a network also involving regional hospitals. A number of regional hospitals also organise cancer treatment themselves. The *Tumorzentren* are often, but not always attached to university hospitals. Four of these centres are also designated Comprehensive Cancer Centres.

There is no single national cancer registry covering the entire population, but the *Länder* are encouraged by the federal government to set up such registries to be coordinated in a national network.

Incidence, mortality and survival in lung cancer

The relative survival rate in lung cancer in Germany is well above the mean in the EURO CARE 4 study [7, 51, 147]. The mortality rates in lung cancer are lower than the European average for men (53.8 per 100,000), but a little higher for women (18.0 per 100,000). The European average was 64.8 per 100,000 for men and 15.1 per 100,000 for women in 2006. The incidence rates in lung cancer are lower than the European average for men (61.2 per 100,000), but higher for women (20.8 per 100,000). The European average incidence rates were 75.3 per 100,000 for men and 18.3 per 100,000 for women in 2006 [1].

Greece

The Greek healthcare system is centralised and national responsibility is assumed by the Ministry of Health and Welfare. The ministry is responsible for the provision and financing of the National Health Service, NHS. In addition to the NHS there is also a system of compulsory insurance funds and some private health care providers. Primary healthcare is mainly provided in about 170 rural health centres run by the NHS and about 350 healthcare units operated by the largest insurance fund, IKA. Hospital care is mainly provided at about 120 NHS hospitals, 13 military hospitals, 5 hospitals run by the IKA, and two university hospitals.

The structure of the NHS is based on the 13 regions, subdivided into 52 districts. Each of the regions should have one regional hospital which is in most cases a university teaching hospital. However, at present only 7 of the 13 regions have large university teaching hospitals, while the remaining regions are served by the regional hospital of the nearest region in the case of tertiary care.

The Greek healthcare system is highly centralised and regulated. Several reforms aimed at decentralising responsibilities to the 13 regional health authorities have not been implemented as the government has kept political control and not provided financial resources. The Social insurance funds are also strictly regulated by the government.

Reimbursement and pricing of pharmaceuticals

The prices of pharmaceuticals in Greece are set by the *Pricing Committee* in the *Ministry of Development* based on the three lowest prices in Europe. When a price is set, the drug is also reimbursable. For certain severe diseases, among these cancer, the drugs are fully reimbursed.

There are no specific budget measures to control prescription by physicians. The prescription habits of the physician have previously not been monitored. The largest insurance fund has started to do such analyses, but there is currently no system of either carrots or sticks.

Lung cancer care

Cancer care services offered in Greece are mostly described as complex, disorganised and inefficient. The most advanced cancer treatment is provided at 23 regional hospitals, of which seven are university hospitals.

There is no national cancer registry and hence a lack of reliable data on treatment and outcomes on the national level.

Incidence, mortality and survival in lung cancer

The mortality rates in lung cancer are higher than the European average for men (69.0 per 100,000), but a little lower for women (11.4 per 100,000). The European average was 64.8 per 100,000 for men and 15.1 per 100,000 for women in 2006. The incidence rates in lung cancer are higher than the European average among men (88.7 per 100,000), but lower among women (12.7 per 100,000). The European average incidence rates were 75.3 per 100,000 for men and 18.3 per 100,000 for women in 2006 [1].

Hungary

After the fall of the communist regime in the late 1980s, the Hungarian healthcare system went from highly centralised to become more pluralist with responsibilities shared between various providers. The previous hierarchical relationships have partly been replaced by contractual relationships and quasi-public arrangements.

A lack of political consensus on the level and structure of decentralisation has led to several changes following changes in national governments. A consequence of this has been a lack of coordination in healthcare.

Health services in Hungary are primarily financed through social health insurance within the Health Insurance Fund (HIF), and in the case of capital costs at hospitals, mainly from taxation. Services are delivered predominantly by local public providers, contracted by the National Health Insurance Fund Administration (NHIFA) administering the insurance funds. The HIF is separated from the government budget.

Reimbursement and pricing of pharmaceuticals

When applying for reimbursement the pharmaceutical company proposes a price along with information regarding benefits compared to already reimbursed pharmaceuticals, internal and

external prices references, expected number of patients treated annually, medical effectiveness studies and pharmacoeconomic studies.

The prescription volume of each individual physician is compared to the average level. If significantly higher than the average the prescription habits are further analysed, but there are no penalties or bonuses in place.

Lung cancer care

To improve the coordination of cancer care previously delivered in a fragmented system at a large number of under equipped and underfinanced treatment facilities, a new organisation has been launched in Hungary aimed at pooling resources into fewer treatment centres.

There is a national cancer registry in Hungary. Historically the quality of data has been low, but efforts have been made in recent years to improve the quality.

Incidence, mortality and survival in lung cancer

In the recently published EURO CARE 4 Study, Hungary had the lowest survival rate of all European countries studied, both in cancer generally and specifically in lung cancer [51]. A fundamental problem is a poorly functioning diagnosis largely due to obsolete instruments and a serious shortage of specialists.

The mortality rates in lung cancer are the highest in this study for men (110 per 100,000), and the second highest for women (34.6 per 100,000). The European averages were 64.8 per 100,000 for men and 15.1 per 100,000 for women in 2006 [1].

The incidence rates in lung cancer are also higher than the European average both among men (119.3 per 100,000) and women (42.4 per 100,000). The European average incidence rates were 75.3 per 100,000 for men and 18.3 per 100,000 for women in 2006.

Ireland

The Irish healthcare system has recently gone through a reform programme launched by the government in 2003. In January 2005 a wide range of national agencies with various responsibilities in the delivery of healthcare was replaced by a single body, the Health Service Executive (HSE). HSE has also replaced the eight regional health boards previously responsible for the direct provision of services. The reform, which concentrates the responsibilities for healthcare, was a response to difficulties in providing national consistency in the delivery of healthcare.

The financing of healthcare in Ireland is a mix of public and private funding with a considerable role for private health insurance, despite the presence of universal public hospital coverage. Healthcare services are provided through a combination of public and private entities. The majority of the providers are public, but they are complemented by a growing number of private providers. The services of the public providers are accessible for all. Even though public healthcare is available for all, about half of the population have additional voluntary health insurance to guarantee themselves more immediate access to some hospital services. Care funded by private insurances is provided both in state and voluntary sector hospitals and in private hospitals.

Reimbursement and pricing of pharmaceuticals

The prices of reimbursable drugs in Ireland are set by *Department of Health and Children* (DoHC) in negotiations with the pharmaceutical industry. The price level is based on external references from five other European countries. The reimbursement decision is made by the product committee of the Ministry of Health and the Health Service Executive based on pharmacological, medical, therapeutic and pharmacoeconomic criteria.

For the decision on reimbursement the DoHC may request a cost benefit study of a new drug, but it is no standard requirement.

For physicians there is a financial incentive scheme giving them a bonus if they keep their prescription below a target level. There are no penalties for doctors not reaching the target. Certain specialists and expensive drugs are excluded from the system.

Lung cancer care

Since 1996 Ireland has had a national cancer control plan. In the updated cancer plan of 2006, a new organisation of Irish cancer care is proposed. Along with this proposal the Minister of Health has announced that cancer care will be concentrated and coordinated by establishing four regional managed Cancer Control Networks providing primary, hospital, palliative, psycho-oncology and supportive care. Patient care should be fully integrated between each of these elements within the networks. Within each of these networks there will be 1-3 specialised cancer centres with a population catchment of at least 500,000 in order to ensure a high case load of patients enabling a more efficient practice of cancer treatment. The development of cancer centres will allow for care to be delivered within a network where diagnosis and treatment planning is directed and managed by multi-disciplinary teams. In such circumstances it can be appropriate for much of the treatment to be delivered in other more local locations.

There is a national cancer registry with full population coverage collecting data on cancer cases, treatment and outcomes.

Incidence, mortality and survival in lung cancer

The relative survival rate is among the lowest in Europe, both for cancer in general and for lung cancer specifically [7, 147]. The mortality rates in lung cancer in Ireland are lower than the European average for men (48.9 per 100,000), but higher for women (26.2 per 100,000). The European average was 64.8 per 100,000 for men and 15.1 per 100,000 for women in 2006. The incidence rates in lung cancer are lower than the European average for men (60.2 per 100,000), but much higher for women (34.1 per 100,000). The European average incidence rates were 75.3 per 100,000 for men and 18.3 per 100,000 for women in 2006 [1].

Italy

The Italian National Health Service (INHS) provides healthcare for all people living in Italy. The system is financed by general taxation at national and regional level, but with a small co-payment by patients seeking primary care. The National Health Service covers the entire population of residents in Italy.

The provision of healthcare is a shared responsibility between the state and the twenty regions. The state defines the essential levels of care while it is a regional responsibility to organise and administer healthcare. While the financing of healthcare in Italy is public, the provision is carried out by both private and public providers in a buyer-provider scheme. Healthcare is delivered by local public health companies (ASL) contracting hospital care of public and private hospitals health services providers. The ASLs are managed independently from local political governments.

Reimbursement and pricing of pharmaceuticals

The Italian Medicines Agency (AIFA) is the agency responsible for classification, pricing and reimbursement decisions. Prices are set in a negotiation with the manufacturer based on external reference prices and cost benefit analyses.

Since 2003 for innovative pharmaceuticals there has been a premium price. There are also additional budget resources available at AIFA to finance these premium prices. There are also plans to introduce certain premium prices if the pharmaceutical companies invest the revenues in research and development in Italy.

The prescription of each individual doctor is monitored by AIFA, but there are no restrictions or individual budget levels. The cost containment ceiling is instead put on the regional level. If the pharmaceutical budgets of the regions are over drafted, the expenditures may be cut correspondingly the following year.

Lung cancer care

There are seven specialist cancer institutes in Italy performing oncological treatment and research. These institutes are financed by and responsible to the Ministry of Health, and therefore largely independent from the regional or local authorities and the ASLs. However, most cancer patients are not treated at these institutes but at general hospitals.

The cancer registries are regionally based and only one fourth of the population is covered.

Incidence, mortality and survival in lung cancer

The mortality rates in lung cancer are just under the European average both for men (63.0 per 100,000), and for women (14.0 per 100,000). The European average were 64.8 per 100,000 for men and 15.1 per 100,000 for women in 2006. The incidence rates in lung cancer are higher than the European average among men (84.7 per 100,000), but lower among women (15.6 per 100,000). The European average incidence rates were 75.3 per 100,000 for men and 18.3 per 100,000 for women in 2006 [1]. The relative survival rate in lung cancer in Italy is, at 12.8 per cent, well above the European mean of 10.8 in the recently published EURO CARE 4 study [51].

The Netherlands

The provision of healthcare in the Netherlands is mainly carried out by private non profit providers. The provision is regulated at the national level as the government sets the framework under which the hospitals operate, what care they can provide and what price they can charge the insurance companies.

In the Netherlands a mix of public and private funding to cover health costs is used. More than 64% of the population is insured for health costs under the Dutch Health Insurance Act via a compulsory insurance policy. Civil servants (nearly 5% of the population) are also insured through a statutory arrangement. The remaining 31% is insured privately.

Reimbursement and pricing of pharmaceuticals

The reimbursement decision and price of pharmaceuticals are set by the Ministry of Health Welfare and Sports. The price is set by reference to the price in four European countries. In recent years the use of pharmacoeconomic evaluations have been highlighted and is now also mandatory in the application of reimbursement.

There is no separate funding for expenditure on pharmaceuticals, but there are guidelines for the doctors and the prescription habits are monitored.

Lung cancer care

Cancer care in the Netherlands is organised in nine Regional Comprehensive Cancer Centres, founded in 1980 with the purpose of coordinating cancer treatment in each region. Central in these regional cancer centres are the university hospitals. The comprehensive cancer centres are also involved in developing and implementing guidelines for cancer treatment and referral, providing postgraduate training in oncology, and increasing psycho-social and palliative care facilities.

Since 2004 there are national guidelines for staging and treatment of lung cancer, issued by the Association of Comprehensive Cancer Centres. For the time period 2005-2010 there is a national cancer control programme based on the guidelines of WHOM.

The Comprehensive Cancer Centres also host the regional cancer registries. The cancer registries collect the minimal data set from clinical records and are increasingly involved in studies on the quality of cancer care.

Incidence, mortality and survival in lung cancer

The relative survival rate in the Netherlands is, according to the recent EURO CARE 4 study, the highest in Europe [51]. The mortality rates in lung cancer are higher than the European average, both for men (67.0 per 100,000), and for women (30.6 per 100,000). The European average were 64.8 per 100,000 for men and 15.1 per 100,000 for women in 2006. The incidence rates in lung cancer are lower than the European average for men (63.4 per 100,000), but much higher for women (32.5 per 100,000). The European average incidence rates were 75.3 per 100,000 for men and 18.3 per 100,000 for women in 2006

Norway

The Norwegian healthcare system is financed through taxation, together with income-related employee and employer contributions and out-of-pocket co-payments. All residents are covered by the National Insurance Scheme, managed by the Norwegian Labor and Welfare Organization. Private medical insurance is rare.

While healthcare policy is controlled centrally, responsibility for the provision of healthcare is decentralised. The 436 municipalities are responsible for organising and financing primary care services according to local demand. The municipalities can produce the health services themselves, together with other municipalities or contract out to private providers. Secondary care and specialised care has since 2002 been nationalised and organised in five regional state-owned health enterprises. Most hospital care is provided by these enterprises, but some private providers exist.

Lung cancer care

Initial cancer diagnosis and treatment are mainly carried out in the surgical departments of peripheral and central hospitals of the regions. In addition to these oncological services, including radiotherapy, are delivered by six specialised and well-equipped oncological centres. There is at least one of these centres in each of the five health regions.

The Norwegian Cancer Registry is nationwide and all new cancer cases in the population must be reported to the registry. The registry has archived all cancer cases diagnosed in Norway since 1953. The registry also receives reports from individual physicians, from pathology and cytology laboratories and from death certificates kept in Statistics Norway.

Incidence, mortality and survival in lung cancer

In the recent EURO CARE 4 Study, Norwegian relative lung cancer survival is above the average of European countries[7]. The mortality rates in lung cancer are lower than the European average for men (48.4 per 100,000), but higher for women (26.1 per 100,000). The European average were 64.8 per 100,000 for men and 15.1 per 100,000 for women in 2006. The incidence rates in lung cancer are lower than the European average for men (53.8 per 100,000), but higher for women (33.7 per 100,000). The European average incidence rates were 75.3 per 100,000 for men and 18.3 per 100,000 for women in 2006 [1].

Poland

Poland has a mixed system for public and private healthcare financing. Contributions to a mandatory social health insurance scheme represent the major public source of healthcare financing. In 2003 the administration of the health insurance schemes was centralised to the National Health Fund (NHF) with regional branches, which replaced a system of 17 sickness funds. The NHF has the responsibility for planning and purchasing public financed health services. Health insurance contributions for certain groups of individuals are not covered by the standard scheme.

The insured have the right to health services including primary healthcare provided by GPs. The sickness fund contracts GPs from which the insured can choose freely for primary care. Hospital services are in general subject to referral from a GP. Non-public health insurance companies also exist and are mostly run by non-profit organisations.

Reimbursement and pricing of pharmaceuticals

Reimbursement decision and prices are set by the Ministry of Health. The prices are based on internal reference prices based on the lowest price of a generic drug, or external reference prices relating to some or all of the other EU countries. Pharmaco-economic analyses have an increasing but still rather small impact on reimbursement decision. There are currently no restrictions or monitoring of prescriptions in place for physicians.

Lung cancer care

Cancer care in Poland is organised in a three-tier system. At the top tier are the *Maria Skłodowska-Curie Memorial Cancer Centre* and *Institute of Oncology, Warsaw*. The second tier consists of 10 Regional Comprehensive Oncological Centres. In the third tier there are about 50 cancer wards and chemotherapy and radiotherapy units in hospitals, many of which are attached to medical faculties at universities. In addition, there are about 40 consultation points and outpatient oncological clinics located in larger cities.

The *National Cancer Registry* covers the whole of Poland and collects and processes data from regional registries. The population-based Warsaw Cancer Registry was established in 1963 and also performs studies of the effects of intervention measures.

Incidence, mortality and survival in lung cancer

In the recent EUROCARE 4 study, the relative survival rates for lung cancer are well below the European average [7, 147]. The mortality rates in lung cancer are higher than the European average, both for men (92.0 per 100,000), and for women (21.8 per 100,000). The European average were 64.8 per 100,000 for men and 15.1 per 100,000 for women in 2006. The incidence rates in lung cancer are also higher than the European average both among men (103 per 100,000) and women (28.6 per 100,000). The European average incidence rates were 75.3 per 100,000 for men and 18.3 per 100,000 for women in 2006 [1].

Portugal

Healthcare in Portugal is provided by the Portuguese National Health System, and planned, monitored and managed by the Ministry of Health. Health services are offered at large urban hospitals, several dozen regional hospitals and numerous health centres providing primary care. All residents in Portugal are entitled to health care paid for out of general taxation. Three systems of health care insurance coexist within the National Health Service: the direct beneficiaries (more than 75 per cent of the population), the health subsystem subscribers (membership based on professional or occupational category) and voluntary private health insurance schemes.

Reimbursement and pricing of pharmaceuticals

The prices of pharmaceuticals are set by the *Director General Enterprise* (DGE) at the average price of four reference countries: Spain, France, Greece and Italy. The producer proposes a price which the DGE has 90 days to oppose. The process is the same for all drugs regardless if they are new or if they are generic.

Lung cancer care

A periodically updated National Cancer Plan has established the main priorities for cancer control in the population. There are also specific treatment guidelines for lung cancer. The treatment is measured against guidelines by the *Government coordination for oncologic disease*. Three regional centers, *Specialized Cancer Institutes*, offer the most up-to-date cancer treatment in the country. There are also six public radiotherapy centres.

Population-based cancer registration has been mandatory since 1988, which led to the establishment of three regional cancer registries coordinated for full national coverage. Cancer registration is compulsory in Portugal in all state hospitals and health centres, and since 1998 private clinics and hospitals are also covered.

Incidence, mortality and survival in lung cancer

In the recently published EUROCARE 4 study, the Portuguese relative survival rate in lung cancer is about the European average [51]. The mortality rates in lung cancer are lower than the European average both for men (43.3 per 100,000), and for women (7.9 per 100,000). The European averages were 64.8 per 100,000 for men and 15.1 per 100,000 for women in 2006. The incidence rates in lung cancer are also lower than the European average both among men (44.5 per 100,000) and women (11.7 per 100,000). The European average incidence rates were 75.3 per 100,000 for men and 18.3 per 100,000 for women in 2006 [1].

Russian Federation

In the Soviet Union the basis for healthcare provision was to ensure universal and free healthcare to all citizens under centralised control by the government. After the fall of the Soviet Union the healthcare system underwent decentralisation to a regional level and, to some extent, local level. In the decentralisation process, the regulatory system in Russia has become somewhat diffuse regarding the division of labor and responsibilities.

As a large country with significantly lower GDP and health expenditure per capita than Western European countries, there are great regional disparities in the quality and provision of healthcare. The most modern and well equipped hospitals are found in the larger urban areas.

Highly specialist care, research and education are mainly provided by federal authorities. Regional health authorities supply health care in larger facilities with specialised medical institutions. At local level, municipalities and cities provide hospital and ambulatory care in smaller hospitals and polyclinics.

Health services are universal and free, financed by a mandatory health insurance system. The insurance is primarily provided by private insurance companies and regional mandatory health insurance funds, financed by tax collection based on employment. The federal mandatory health insurance fund has a responsibility of equalising disparities across the regions and to regulate the regional health insurance fund.

Patient access to drugs has become very limited due to the scarce resources in the Russian healthcare system. Even if the public health system in theory pays for the drugs, in practice patients often have to pay for the drugs themselves.

Lung cancer care

Cancer care in the Russian Federation is very unevenly accessible. There are five cancer institutes, two in Moscow and one each in St Petersburg, Rostov on the Don and Tomsk. There are also three radiology centres. Outside the largest cities there are more than a hundred local cancer hospitals, but the resources in these are very scarce. The accessibility of modern cancer drugs is very poor outside the large cancer centers [53].

There is no national cancer registry in Russia. There is one regional registry in St Petersburg used in, for example, GLOBOCAN and EUROCARE. The size of the country, both in terms of geography and population makes it difficult to get a national overview of the burden of lung cancer and the organisation and provision of cancer services.

Incidence and mortality in lung cancer

The mortality of lung cancer in Russia is higher the European average among men (75.2/100,000), but a little lower among women (8.0/100,000). The European average is 64.8 per 100,000 for men and 15.1 per 100,000 for women (2006). The incidence rates in lung cancer are higher than the European average among men (92.7 per 100,000), but lower among women (11.2 per 100,000). The European average incidence rates were 75.3 per 100,000 for men and 18.3 per 100,000 for women in 2006.

Spain

Spain is organised in 19 autonomous regions each having their own health service structure under a regional health department. Each region is divided into health areas, which are subdivided into health zones. Primary healthcare is a responsibility of the health area. These health areas are also responsible for specialised outpatient care through networks of specialised centres, linked to hospitals and hospital care. There is at least one general hospital in each of the health areas.

Although the regions are fairly autonomous, the financing of health care is organised at the national level under the *National Health Service*. The financing is primarily based on the social security system and on general taxation.

The coverage of the National Health Service is nearly universal and health services are free of charge at the point of use.

Most primary healthcare is public. Hospital beds are 80 per cent public and 20 per cent private. Many of the private hospitals are funded mainly by the National Health Services through reimbursement. Half of the private hospitals are profit making, while the rest are run by non-profit organisations.

A majority of medications are paid for by the National Health Service. The user pays in general cases 40 per cent of the price. Exceptions are retired, handicapped, invalids and people who have suffered occupational accidents, and patients suffering from cancer and other chronic diseases who receive free medications.

Lung cancer care

Cancer diagnosis and treatment is mainly carried out at about 150 oncology units in about 110 general hospitals and 35 private clinics.

There is no national cancer registry in Spain covering the entire population, and no national coordination of the 14 population-based cancer registries and the two specialised pediatric cancer registries. About 10-15 per cent of the Spanish population is covered by cancer registration.

Incidence, mortality and survival in lung cancer

In the recent EUROCARE 4 study the Spanish relative survival rate in lung cancer is slightly above the European average of 10.2 per cent [51]. The mortality rates in lung cancer are higher than the European average for men (67.9 per 100,000), but a little lower for women (8.9 per 100,000). The European averages were 64.8 per 100,000 for men and 15.1 per 100,000 for women in 2006. The incidence rates in lung cancer are also lower than the European average, both among men (68.3 per 100,000) and women (13.8 per 100,000). The European average incidence rates were 75.3 per 100,000 for men and 18.3 per 100,000 for women in 2006 [1].

Sweden

Financing and provision of healthcare in Sweden is decentralised to County Councils at a regional level. The major sources of finance for healthcare are regional taxes supplemented by national taxes. Health services are subject to small point-of-service costs to the patient, and out patient pharmaceuticals are co-financed by the individuals up to a fixed ceiling. Private health insurance plays a marginal role in financing.

Primary care is given by health centres, while secondary healthcare delivery is dominated by public hospitals. In addition, the County Councils are also organised in six Health Care Regions for coordination of highly specialised care, mainly provided by the university hospitals in each region. Private providers play a limited but growing role in provision of healthcare.

The *National Board of Health and Welfare* (SoS) has a supervisory role in monitoring the quality of healthcare provided by county councils, local authorities and private institutions.

The Swedish Council on Technology Assessment in Health Care (SBU) also assists the county councils in their decision making by reviewing and evaluating healthcare technology from medical, economic, ethical and social points of view.

Reimbursement and pricing of pharmaceuticals

Most drugs used to be granted reimbursement, but since 2002 a new public authority *The Pharmaceutical Benefits Board*, LFN, has taken formal decisions on reimbursement of a drug primarily based on cost-effectiveness. If a price suggested by the pharmaceutical firm is considered too high at LFN, the producer may suggest a lower price.

The cost of pharmaceuticals in both in-patient and outpatient care are borne by the county councils, but they receive subsidies from the state for out patient pharmaceuticals, which are also co-financed by the patient. For pharmaceuticals for use in hospitals only, the decision on availability is taken by the county councils. In each county council there is a pharmaceutical

committee supporting physicians in their choice of pharmaceuticals by listing medicines recommended as the first choice treatment for a range of common diseases.

Lung cancer care

Within each of the six healthcare regions there is an oncological centre, coordinating cancer care resources. These regional oncological centres are also responsible for regional cancer registries and the promotion of a series of cancer care and prevention initiatives. There is no nationally coordinated strategy for lung cancer care, but the regional oncological centres have together developed a national treatment programme which is complemented by regional lung cancer guidelines. Within each regional oncological centre, expert groups are also developing clinical treatment guidelines.

Since 1958, a national full coverage cancer registry has used data collected by the regional oncological centres. Since 2001 there is also a specific lung cancer registry in Sweden with a greater level of detail than the general cancer registry.

Incidence, mortality and survival in lung cancer

The 5-year relative survival rate in lung cancer in Sweden for patients treated in 2000-2002 was 13.9 per cent compared to the European mean of 10.9 per cent in the recent EUROCARE 4 study[7]. The mortality rates in lung cancer are lower than the European average for men (53.8 per 100,000), but a little higher for women (18.0 per 100,000). The European averages were 64.8 per 100,000 for men and 15.1 per 100,000 for women in 2006. The incidence rates in lung cancer are far below than the European average for men (28.6 per 100,000), but higher for women (23.8 per 100,000). The European average incidence rates were 75.3 per 100,000 for men and 18.3 per 100,000 for women in 2006 [1].

Switzerland

Switzerland is a federal state with a healthcare system largely decentralised to the 23 regional cantons and local communities. Health insurance regulations, disease prevention and health promotion are federal responsibilities, but the provision is a responsibility of the cantons.

Everyone resident in Switzerland has basic health insurance offered by a large number of insurance companies. Contracts with service providers are negotiated by the Association of Swiss Health Insurance Companies on behalf of its members. The healthcare insurance companies receive money not only from individual premiums but also from federal and canton funds. Switzerland has both private and public providers providing healthcare, and the patient is free to choose his or her doctor.

Reimbursement and pricing of pharmaceuticals

Decisions on reimbursement and pricing of new drugs are taken on a federal level by the Office for Public Health. In the decision, the therapeutic and economic value is taken into account, and the maximum price is limited by prices in some reference countries. In the reimbursement process there is no formal requirement for economic evaluation of new drugs.

In a study comparing the introduction of cancer drugs in different countries, Switzerland is highlighted as one of the fastest countries in Europe for the introduction of new cancer drugs [13].

Lung cancer care

The organisation of lung cancer care in Switzerland follows the general organisation of healthcare, where the provision is a regional responsibility of the cantons. There has been a national cancer programme in Switzerland since 2005. One of the main objectives of this plan is to promote a better coordination of cancer care. The coordination is hindered by regional independence and the differences in the organisation of cancer care.

There is no national full-coverage cancer registry in Switzerland, but nine cancer registries covering about 60 per cent of the Swiss population. All provide data to the Swiss cancer registry network.

Incidence, mortality and survival in lung cancer

In the recent EUROCARE 4 study Switzerland has one of the highest relative survival rates in all cancers in total and specifically for lung cancer[7]. The mortality rates in lung cancer are lower than the European average for men (43.4 per 100,000), but a higher for women (18.1 per 100,000). The European averages were 64.8 per 100,000 for men and 15.1 per 100,000 for women in 2006. The incidence rates in lung cancer are lower than the European average for men (52.7 per 100,000), but higher for women (26.2 per 100,000). The European average incidence rates were 75.3 per 100,000 for men and 18.3 per 100,000 for women in 2006 [1].

The United Kingdom

In the United Kingdom responsibility for healthcare is decentralised to the four constituent countries England, Northern Ireland, Scotland and Wales. In all these countries healthcare is primarily financed by national taxation and delivered by public providers. The responsibility for purchasing health services is being delegated to local bodies in each of the countries, Primary Care Trusts in England, Health Boards in Scotland, Local Health Groups in Wales and Primary Care Partnerships in Northern Ireland. The organisation of healthcare services is basically similar in the different countries. Primary care services are mainly provided by GPs and multi-professional teams in health centres. Hospitals are mainly publicly owned organised as independent trusts. There are also private hospitals providing services mainly to patients with private insurance or paying directly for the services.

Reimbursement and pricing of pharmaceuticals

In the UK prices are regulated by the *Pharmaceutical Price Regulation Scheme* which indirectly regulates the price by capping the profit a company makes on sales to the National Health Services (NHS). If profits exceed the limits, prices have to be lowered or profits repaid to the NHS. All prescription-only medicines are reimbursed by the NHS unless they are on a negative list.

The National Institute for Health and Clinical Excellence (NICE) develops guidelines on clinical effects and cost effectiveness of new treatments for the NHS in England and Wales. In addition, NHS Quality Improvement Scotland (NHS QIS) and the Scottish Intercollegiate

Guidelines Network (SIGN) provide guidance for NHS Scotland. To prevent overlapping work between the UK organisations, NHS QIS overviews and adapts NICE guidelines for Scotland.

In line with the appraisal, new drugs are categorised as either recommended for routine use, recommended for use in clinical trials in order to further value cost effectiveness or not recommended for use at all.

Lung cancer care

The UK has among the lowest relative survival rates in Europe according to the recent EURO CARE 4 study [51] in spite of: more resources spent on cancer research than in any other European country, well analysed shortcomings of cancer care and a high profile cancer control plan, and highly rated health technology appraisal institutions in England and Wales (NICE) and Scotland (Scottish Medicines Consortium). It should, however, be noted here that the EURO CARE 4 survival rates are based on patients treated 1995-1999. Much of the efforts initiated in response to relatively poor outcomes might not have come into full effect in this period of time.

Since 2001 cancer care in England has been organised in geographical cancer networks coordinating resources across care trusts. Cancer care in Scotland is coordinated in three regional managed clinical networks for cancer. Radiotherapy facilities are provided at five main centres but many patients with cancer are diagnosed and receive surgery and chemotherapy at district general hospitals. The Welsh Assembly Government has formed a Cancer Services Coordinating Group (CSCG) setting Minimum Standards for Cancer Care in Wales as well as convening Tumour Site Steering Groups of expert clinicians.

The principal oncology centre in Wales is the Velindre Trust in Cardiff, but there is also an oncological centre at Swansea and a radiotherapy centre in Llandudno. These three areas correspond to the three cancer networks in Wales, which are linked together under the CSCG. The population in the north of Wales is also served by specialist oncology services in Manchester and Liverpool in England.

Cancer care in Northern Ireland is coordinated by the Northern Ireland Cancer Network (NICR). Since 1996, there have been four Cancer Units and a regional Cancer Centre in Belfast. The Cancer Units are now the main focus for the delivery of services for people with the more common cancers.

National clinical guidelines are developed for England and Wales by the National Collaborating Centre for Acute Care at The Royal College of Surgeons of England, commissioned by NICE. The clinical guidelines have also been developed in close cooperation with the *Scottish Intercollegiate Guideline Network*, developing a corresponding guideline for Scotland.

Partly in response to inequalities in cancer care in different parts of the country in the mid 1990s networks of multidisciplinary care teams were established, based in dedicated cancer centres. The aim was to ensure equal access to first-rate specialist services for all patients. The development of these multidisciplinary teams was also central to the NHS Cancer Plan, the first comprehensive national cancer programme, which was published in 2000.

The plan provides a strategy for bringing together prevention, screening, diagnosis, treatment and care for cancer, and the investment needed to deliver these services in terms of improved staffing, equipment, drugs, treatments and information systems. An overriding objective is to have 5-year cancer survival rates at the level of the most successful in Europe by 2010. The Cancer Plan is accompanied by additional funding which will increase staff significantly. The cancer plan is also accompanied with national audits of the care in lung cancer and other kinds of cancer.

Within each of the constituent countries there are regional cancer registries, funded by regional health authorities. In 1993 provision of information to regional cancer registries became mandatory for NHS hospitals. The regional cancer registries are co-ordinated through the UK Association of Cancer Registries (UKACR).

Incidence, mortality and survival in lung cancer

The incidence rates in lung cancer are lower than the European average for men (65.0 per 100,000), but higher for women (57.1 per 100,000). The European average incidence rates were 34.6 per 100,000 for men and 18.3 per 100,000 for women in 2006. The survival rates for lung cancer, like cancer in general in the UK, are among the poorest in Europe in spite of significant resources spent on research and monitoring of cancer care.

Australia

The responsibilities of healthcare in Australia are shared between the Commonwealth on the national level and the six states and two territories on the sub national level. The Australian healthcare system provides universal access to health care through the national *Medicare* program. Medicare, which is mainly financed by general income based taxation, subsidizes access to primary care providers, including medical practitioners, and to a range of specialist and diagnostic services. The Commonwealth also contributes with funding to public hospitals through the Australian Health Care Agreements.

The States and Territories have the main responsibility of providing public health care services in Australia. They provide public acute and psychiatric hospital services and a wide range of community and public health services. The geographical size of the country and large share of the population living in rural areas poses a challenge in providing access to health services.

Public hospitals include hospitals established by governments and in addition hospitals originally established by charities, but now directly funded by government. There is a small number of hospitals built and managed by private firms providing public hospital services under arrangements with State governments. Most acute care beds and emergency outpatient clinics are in public hospitals. Large urban public hospitals provide most of the more complex types of hospital care. Private hospitals are owned by for-profit or not-for-profit organizations such as large corporate operators, religious operators, and private health insurance funds.

Reimbursement and pricing of pharmaceuticals

The National *Pharmaceutical Benefits Scheme* provides subsidized access to pharmaceuticals. Reimbursement decisions are taken by the *Pharmaceutical Benefit Advisory Committee* (PBAC). PBAC considers the therapeutic effectiveness, safety, and cost-effectiveness of each

product, compared to alternative treatments. A separate economics subcommittee reviews the potential economic impacts on government and private spending. The *Pharmaceutical Benefits Pricing Authority* (PBPA) recommends a price for new products, which are then negotiated between the producer and the *Department of Health and Aging*. When reviewing products and considering pricing recommendations, the PBPA evaluates clinical benefits; cost-effectiveness aspects; the price of alternatives; comparisons within therapeutic groups; cost information from the supplier; economies of scale and likely volumes of prescribing and purchasing; the price of the product in similar countries. PBPA may also take the level of activity by the producer in Australia, e.g. investments, production and research, into account.

There are no direct controls placed on prescribing doctors, but there is a national *Quality Use of Medicines* policy actively promoting optimal use of drugs, through guidelines.

Organisation of cancer care in Australia

In 2006 the national authority *Cancer Australia* was established to lead and coordinate the control of cancer. Being a large country with a great part of the population living in remote rural areas, there are great variations in the treatment of lung cancer [77]. As a measure to improve the equity in provision of services, Cancer Australia has developed a program aiming at linking regional with metropolitan cancer services into single networks within the states and territories, within the *Cancer Service Networks National Demonstration Program* (CanNET).

This network model is influenced by the network organisations in the UK. One of the main objectives with the CanNET program is to establish a more integrated path of treatment across organizational and professional boundaries. This will facilitate a multidisciplinary planning and performance of treatment and improve access to treatment for patients living in urban areas [83]. There one network in each state and territory, but they only cover a total population of 8 million out of the total Australian population of 20 million.

As with the case of general health care, the actual provision and organization is primarily a responsibility of the states and territories. Complementing the national strategies, there are also more detailed plans on control of cancer care in the states and territories. More specifically regarding the actual provision of cancer care, there are also strategies on the state/territorial level.

There is no national data available on direct or indirect costs of lung cancer in Australia.

Cancer registries

The states and territories all have their own cancer registry. These are coordinated by the *National Cancer Statistics Clearing House*. The Australian registries are also coordinated with the national cancer registry in New Zealand in the *Australasian Association of Cancer Registries*.

New Zealand

The health care system in New Zealand covers all citizens and is primarily funded by general taxation. In year 2000, the health care system went through a decentralization reform establishing 21 district health boards with the responsibility to provide health care services to the population in their respective area. These 21 district health boards replaced a national

Health Funding Authority (HFA) and 23 hospital and health services companies. The DHBs have the responsibility to deliver health care services either themselves or by purchasing services from other providers. The DHBs are cooperating with each other, for example in providing specialist services drawing patients from larger regions. The central government distributes funds for each of the DHBs.

Reimbursement and pricing of pharmaceuticals

Registration approval for new pharmaceuticals is granted by the national agency *Medsafe*. After Medsafe approval, reimbursement and price is decided by another agency, Pharmaceutical Management Agency, (PHARMAC). The PHARMAC Board makes decisions on whether a drug may be listed on the pharmaceutical schedule. PHARMAC also may determine prescription restrictions, with input from independent medical experts on the *Pharmacology and Therapeutics Advisory Committee* and its specialist sub-committees.

In the reimbursement decision PHARMAC considers the health needs of population, existing products, clinical risks and benefits, the cost-effectiveness of the proposed medicine compared to other treatments, health funding priorities of the government. PHARMAC then negotiates the schedule price with approved manufacturers, who submit a price proposal. The Board is advised by the independent *Pharmacology and Therapeutics Advisory Committee* (PTAC) [148].

PHARMAC uses three pricing strategies when considering additions to the Schedule; reference pricing; tendering; and caps and rebates [149]. PHARMAC applies internal reference pricing involving comparing each drug with other drugs in the same to a therapeutic sub-group. PHARMAC subsidizes each drug at the level of the lowest priced drug in the group. About one-third of the 2,600 drugs on the Schedule are acquired through tender where suppliers bid for a contract to become a sole supplier of a product. PHARMAC may also negotiate reimbursement caps with manufacturers, limiting the price. For hospital drugs PHARMAC is also a monopoly purchaser on behalf of the DHBs, negotiating prices with the manufacturers.

Organization of cancer care in New Zealand

The DHBs play a central role in cancer care through their responsibilities to provide treatment. In recent year measures have been taken to improve the coordination of cancer care. In 2004 the Ministry of Health established an independent Cancer Control Council with the primary role to assume a national leadership in cancer control, and to organize the implementation of the cancer control strategy. The Council formed a Cancer Control Collaborative which will facilitate a national coordination and collaboration of the various actors involved in controlling cancer.

In order to improve the coordination of cancer treatment services, the formation of four regional cancer networks was initiated in 2006. These networks are inspired by the regional networks in the UK, stretching across the administrative boundaries of district health boards. The cancer networks will require and formalize cooperation with the district health boards, non-governmental organisations (NGOs) and community organisations, consumers, Maori and Pacific groups. These networks are intended to be the engine of the implementation of the actions outlined in the cancer strategy. Each of the cancer control networks has one or two specialised cancer centres performing the most advanced cancer treatments. In total there are

six specialised cancer centres. These centres provide surgery, chemotherapy and radiotherapy. Radiotherapy is only offered at these centres, while some surgery and some chemotherapy are also provided at most hospitals.

Although in general detected early, the outcomes of lung cancer treatment in New Zealand is at an average European level. There are indications that the patient access to treatment may have held the outcomes of treatment and relative survival rates down in the past. There has been a shortage of medical oncologists reducing access and delaying care for lung cancer patients. However in only a few years the numbers of medical oncologists has almost doubled. A study of attitudes and treatment practises revealed great variation in preferred treatment options between specialists in different fields of expertise. Nihilistic attitudes and scepticism towards the survival effects of treatments were concluded to be explanatory factors [150]. Previous nihilistic attitudes of doctors towards lung cancer patients may have been improved by newer and younger specialists taking over. Certain initiatives such as an active Lung Cancer Special Interest Sub Group of the New Zealand Association of Cancer Specialists, also points toward increased interest and efforts focused on lung cancer.

Japan

The Japanese health care system

The health care system in Japan is a universal health insurance system. All Japanese citizens must be covered by National Health Insurance (NHI). Most of Japanese people have to pay 30 per cent of the medical services that they are offered as co-payment, and rest of the 70 per cent is paid by the NHI. However, the ratio of the patients' co-payment is 15 per cent in average, because aged patients, patients with low income and hi-tech care are given preferential coverage by NHI. Payments for outpatient care are predominantly on a fee for service basis, and inpatient care is paid through a combination of fixed fee per diem and fee for service. Japanese patients are allowed to freely access to any medical care institution.

Japan has 47 prefectures which hold the main responsibility for organizing and planning the medical supply system. Three major public health insurance programmes are available. Thirty-million employees of large companies and 36 million at smaller companies are covered by corporate insurance societies and one subsidised national insurance scheme, respectively. The remaining 52 million citizens, including farmers, self-employed, etc., are covered by the NHI programme managed by local governments.

Reimbursement and pricing of pharmaceuticals

The regulatory requirements in Japan cause delays in the approval of new drugs. A lack of funding for clinical research also limits investigator-driven trials, including off-label use. However, the Japanese government launched in 2005 a Committee for Faster Access to Innovative Pharmaceuticals. New clinical development guideline was revised to allow the industry to file new drugs with global data, which lead to shortening the delays in introduction of new drugs.

Organisation of cancer care in Japan

There is one national cancer centre in Japan acting as a hub of research, treatment and prevention of cancer in Japan. In addition there are also 28 local cancer centres under the

umbrella organization *Japanese Association of Clinical Cancer Centres* (JOCCC). These institutes almost exclusively treat cancer patients, along with clinical research and training of specialists. Some are financed by the central government, while others are financed by the prefectures or from private sources.

In addition to the dedicated cancer centres, there are also about 100 university hospitals playing an important role in treatment, education and research and about 351 general hospitals providing treatment. The most advanced treatment is offered at the cancer centres or in the university hospitals. The links between the prefectural cancer centres and the university hospitals have often been weak.

In Japan there has since 1983 been national programs for cancer control. The programs have stretched over ten years, and the *Third Term Comprehensive 10-year Programme for Cancer Control* was launched in 2004. This third programme is considered the first to be really recognized by the national health policy management.

In addition to the last cancer control plan, The Japanese government has been pushing an initiative and has validated the new Anti-Cancer Measures Act in 2006 to allocate more funds and resources to cancer care. Following the Act, the government in 2006 established a national action plan on cancer care for the years 2007-2011. One of the top priorities of the action plan is to promote a more integrated care of cancer patients primarily by improving the use of radiotherapy and chemotherapy, and to improve the access to high quality cancer care countrywide. The prefectures are also according to the national action plan obliged to establish regional action plans on cancer care to be coordinated with the health care delivery plans.

In recent years, cancer patients in Japan have been facing difficulties to find reliable care providers. The efforts to improve cancer care have also led to an increase of the resources available for cancer care and cancer research by more than 30 per cent from 2006 to 2007.

In Japan, medical education used to be conducted on organ-oriented basis, and therefore the surgeons have been main treating physicians for solid tumours, even medical treatment. However, the increase of medical oncologists having skills and knowledge in chemotherapy, palliative care and clinical study has been raised as one of the critical issues to improve the patients' access to qualified cancer care. In this context, the certification system has started from 2006, and 205 medical oncologists have been certified as of April 2008.

In lung cancer, however, the medical care has been performed on multi-disciplinary basis between thoracic surgeons and pulmonary internists, and many human resources have been allocated to the care, compared to other solid tumours (7,000 members in Japan Lung Cancer Society). Of 205 certified medical oncologists, 83 are with sub-speciality in lung cancer medicinal treatment. Lung cancer study groups in Japan have been very active and published several outstanding clinical evidences to the globe [151, 152].

Cancer registries

The latest strategy includes several projects aiming at coordination the collection and analysis of data in the prefecture based registries. There is no national cancer registry in operation in Japan. Only since the last comprehensive 10-year program for Cancer control, ambitious efforts have been made to coordinate cancer registration nationally.

Brazil

The current national health policy in Brazil was implemented with the 1988 Brazilian Constitution. The Constitution made health care a right of every person in Brazil and a responsibility of the state under the devices of *universality* and *equality of care* and *completeness of actions*, with the goal to establish a welfare state in line with the Beveridgean-type systems existing in Europe.

The delivery of public health care in the country is provided through the *Sistema Único de Saúde* (SUS). Management and organization of health services in Brazil has been decentralized from the federal to the state and, especially, municipal level. On the federal level, the Ministry of Health oversees the national management of the SUS and university hospitals are managed by the Ministry of Education, while the state and municipal levels manage a complex network of public establishments and subcontracted health care providers. The public establishments cover basic and preventive health care, providing approximately 75 per cent of outpatient services, while the large majority of medical services and inpatient care are contracted out to a network of private and philanthropic hospitals, clinics, and other facilities. 80 per cent of the hospitals providing services within the SUS are private [68-70].

Approximately 37 million Brazilians (20 per cent of the Brazilian population) are covered by private health care plans. This supplementary medical system includes private plans with voluntary affiliation, prepaid health plans and health care insurances. People in this system are mostly employees in the formal economy, mainly in industry and services, who gain coverage through employers. A small share of families also contract directly for private services. Since all inhabitants in Brazil have access to SUS so they may still use public services for procedures not covered by their private plans [153].

The Brazilian health system faces some critical problems. The public system is severely under-funded - financing of the health sector has been insufficient to cover the aims of universality, equity and completeness. Moreover there are some serious incoherencies in the system, for example the public-private segmentation of public health services in Brazil has led to a situation where public sector is responsible for high volume basic health services while the private sector covers more profitable services; the publicly financed, privately provided health system has had a tendency to focus on high-cost curative care. This has led to SUS, which is financed exclusively by public resources, being responsible both for the poorest part of population and for more expensive procedures of the wealthiest part of the population that their supplementary health plans prefer not to cover. This segmentation creates a situation of social injustice and the government health expenditures are not well targeted to the poor. There are also regional inequalities, health manpower and facilities remain more concentrated in the wealthier regions in the south of Brazil [69, 70, 154].

The increasing national health care expenditures have been financed by new taxes, such as a levy on every bank account withdrawal, thus also drawing revenue from the informal economy. A constitutional amendment in 2000 defined a fixed share of the public budget targeted to health care expenditures [153].

Reimbursement and pricing of pharmaceuticals

In 2003 pharmaceuticals represented 18 per cent of total health care expenditure in Brazil [12]. The CMED (*Câmara de Regulação do Mercado de Medicamentos*), established in 2003, is responsible for regulation of the pharmaceutical market and establishes a minimal list of procedures and treatments that insurance companies must offer [155]. Since 2004 prices are updated yearly by CMED based on inflation rate minus a productivity factor, and considering generic participation in the therapeutic class – the higher the market share of generics, the higher the authorised increase. **The principle for price updates is that prices of innovative drugs in Brazil shall be the lowest among a reference list of ten countries.** In 2007, a mandatory discount was set for public-sector drug purchases [156]. It is calculated annually, based on a GDP and human development index comparison among a list of reference countries. In 2007, the mandatory discount was 25 per cent [153].

In 2006, the Brazilian government established a Health Technology Commission, CIETEC. It evaluates the economic value of health care treatments, specifically pharmaceuticals, for both public and private markets. The commission reviews clinical data, cost information and budget impact in both the public and the private sector. Drug bought outside of hospital are not reimbursed by social security in Brazil [153].

The reimbursement of cancer treatment in SUS is governed by *Autorização para Procedimentos de Alta Complexidade* (APAC), Authorisation for High Complexity Procedures. APAC establishes what cancer care treatment procedures are authorised for reimbursement in relation to the localisation and stage of the tumour. However the APAC system does not define the type of medication that shall be used and in what dosage. The APAC system has not been updated for many years so that the most modern treatments are not covered by the public system.

Organisation of cancer care in Brazil

In Brazil a reorganisation of specialised care has taken place in the last years. Following the reorganisation, oncology care is provided by specific health centres for oncology – *Centros de Assistência de Alta Complexidade em Oncologia* (CACONs), and *Unidades de Assistência de Alta Complexidade em Oncologia* (UNACONs) affiliated to the public health system. CACONs and UNACONs are hospital units that offer integral treatment to cancer patients; they are responsible for diagnostics, outpatient and inpatient care, emergency care and palliative care. CACONs offer treatment for all kinds of cancer forms while UNACONs offer treatment for the most prevalent cancer forms. There are currently 365 units under SUS offering oncology care, almost 200 UNACONs, approximately 50 CACONs and in addition a number of specific chemotherapy and radiotherapy units. Advanced cancer treatment is only offered in these units. The referral system for such care is coordinated differently in different regions of the country. The CACONs are responsible for the purchase of medication and are reimbursed by the APAC system (see above).

Brazilian Ministry of Health established in 2005 a National Plan for Cancer Care (*Política Nacional de Atenção Oncológica*) which shall provide direction on cancer prevention and the organisation of cancer care along the line from diagnostics and treatment to rehabilitation or palliative care. The plan emphasised the need to create expert networks of oncologist, to improve the definitions of technical requirement for cancer care and to increased coverage of treatment for cancer patients. The National Cancer Institute of Brazil (INCA) is developing treatment protocols for cancer following directives in the national cancer plan; treatment protocols for lung cancer have not yet been developed. The Brazilian Society of Clinical

Oncology (SBOC) sets the best practices to treat and manage the cancer disease, based on the ASCO and NCCN guidelines. Private clinics that are not governed by the APAC system have internal treatment protocols, based on international best practices. INCA is an organisation under the Ministry of Health responsible for national cancer control initiatives. The organisation present national cancer epidemiology data, provide education, and manage prevention programmes INCA also run five hospital units, with radiotherapy facilities among the best/larges in Latin America. A priority for INCA is also the formation of network of oncology care on the state and regional level.

Since Brazil is such a large country with considerable socioeconomic differences, it is difficult to implement policies that cover the whole country and access to treatment in each state will be depended on the decisions made regionally and locally allocating resources for different kind of diseases and treatment. Moreover, there are some regions of the country with scarcity of cancer care and others with a high concentration of cancer care units [104, 157].

Mexico

In Mexico, health care is provided mainly through social security insurance agencies, as well as by the Ministry of Health (MoH) or state health facilities for those without health insurance. Private insurance in Mexico is limited, only 3 per cent of the population has private insurance, mostly individuals with high incomes. The health care system in Mexico follows the Bismarckian model, although (basic) tax-funded health care services are provided for the population not covered by insurance schemes. The health care system in Mexico can be characterized as being vertically integrated but horizontally segregated with the three institutional groups, social security, public sector, and private sector, functioning separately [71].

Approximately half of the Mexican population is covered by social security insurance. The largest social insurance agency is the *Instituto Mexicano del Seguro Social* (IMSS) that provides coverage for salaried employees of private companies, about 48 million people (45% of the population). The second largest agency, the *Instituto de Seguridad y Servicios Sociales de los Trabajadores del Estado* (ISSSTE), covers public sector employees, approximately 10 million individuals. IMSS and ISSSTE beneficiaries and their dependents are covered for most health care services, and most prescription pharmaceuticals are included in their respective formularies; there is no cost-sharing obligation for prescribed medicines if the drugs are dispensed from a pharmacy operated by the social security agencies.

For the half of the population not covered by social security, mainly due to not being part of the formal labour market (unemployed, agricultural and informal sector workers), there are voluntary insurance programmes as well as government schemes that provide health care based on an evaluation of socio-economic status at the time of receiving treatment. Those outside of the formal labour market people have the option of voluntarily insuring with IMSS, but due to the cost and requirements for doing so, as well as the lack of publicity concerning this option, this is very uncommon. Instead private medical care results the main access to care for those with the fewest resources. There is as growing recognition of the need to improve equity and quality in health care in Mexico. One initiative in this direction is the *Seguro Popular de Salud* (SPS), a voluntary public health insurance scheme, formally implemented in 2004, targeted to low-income families outside the social security system. Patients without social security coverage are provided drugs free of charge while in hospital, but must pay out-of-pocket for drugs after discharge [158].

In 2005 there were 1121 public hospitals in Mexico, with a totality of 78,600 hospital beds. 628 of the public hospitals belong to institutions that care for the non-insured population while the other 428 cover the population with social insurance. There were 3028 private care units; the majority of these have only small hospitalization units, only 6 per cent have more than 25 beds available [159]

Reimbursement and pricing of pharmaceuticals

Pharmaceutical expenditure is a major component of overall health expenditures in Mexico, representing 21 per cent of total health expenditure in 2005 [160]. In volume, pharmaceutical sales in Mexico are in principle split 50/50 between the private market and the public market. However, measured in value the private market accounts for approximately 80 per cent of sales value while the public market accounts for 20 per cent, due to the predominance of patented medicines in the private market while there is a great reliance on generics in the public market [161].

The social security agencies, the Ministry of Health and state health authorities may only purchase pharmaceuticals that are listed in the *Cuadro Básico* (Basic Formulary), for medical care at the primary level or in the *Catálogo de Insumos* (Catalogue of Inputs), for care provided at the secondary and tertiary levels. A request for listing a drug in any of the formularies shall meet three criteria: 1) The drug must have been granted marketing authorisation; 2) The drug must have met all safety and clinical tests; 3) The drug must be cost-effective. With regards to the third criterion, the current regulation states that the applicant must submit with the request for submission all pharmacoeconomic evaluations pertaining to the drug. The cost-effectiveness criterion is currently being revised to make it more explicit and to clarify its implementation. At least half of all requests for inclusion on the formularies are rejected. The social security agencies must use the Basic Formulary but are not obliged to cover all the drugs in the formulary. The formularies of the IMSS, the ISSSTE and the MoH cover approximately 30 per cent fewer drugs than the Basic Formulary. In 2005 IMSS purchased 883 different pharmaceuticals, of which 11 per cent were patented products, 42 per cent interchangeable generics and 53 per cent non-interchangeable generics. In volume terms, only 1 per cent was patented products.

Reimbursement of pharmaceuticals has not been a feature of publicly provided health care services in Mexico. The current, decentralised drug procurement process has been criticised as being lengthy and fragmented, and for consistently leading to supply shortages of necessary medicines in the first quarter of every year. However, as part of its new program, the SPS will be moving to a system of reimbursement. The move to a reimbursement system should lead to greater availability of medicines to patients and avoid the need to accurately predict drug usage and to avoid problems such as expiration or loss of medicines due to poor storage. It may, however, also result in higher costs.

Large private hospitals in Mexico establish their own formularies. Drugs are included in the formulary in accordance with the needs of a particular hospital's different specialties. The formularies of large private hospitals are quite different from the Catalogue of Inputs due to significant differences in patient populations. There is a voluntary maximum price regulation scheme in Mexico, adopted in 2004. The regulation applies only to patent-protected drugs sold in the private-sector market. The principal characteristics of the scheme are as follows:

1) An international reference price serves as a benchmark for establishing a price threshold which the maximum retail sales price of a patented medicine cannot exceed; 2) For new products with no comparators, the manufacturer can set the price, subject to re-evaluation three months after product launch; and 3) Generic drugs and original products whose patents have expired are exempt from price regulation. The fact that most, if not all, manufacturers choose to participate in this voluntary scheme suggests that the system has little impact on price levels. Otherwise manufacturers would face strong economic incentives to not participate. Drug prices in Mexico have been found to be high relative to those of other Latin American countries. Possible explanatory factors include the relative weakness of the maximum price scheme, as well as the influence of the geographic proximity of the United States, as manufacturers take the threat of cross-border trade into account when establishing Mexican prices. Although limited, available evidence indicates a relatively prompt availability of new pharmaceutical products in Mexico, and most new products are adopted within four years after the first world launch [161].

Organisation of cancer care in Mexico

Within each regional IMSS unit, there are *Unidades de Atención Médica* (UAM) which are categorised according to level of care. There are over 1300 UAMs in the country, of these approximately 220 are *Hospitales Regionales y Generales de Zona* (HGR/HGZ), clinical oncology care are provided in these units and 41 are *Unidades de Medicina de Alta Especialidad* (UMAE), these units provide among more advanced care such as surgical oncology care [78].

ISSSTE works with a central decision process. There is a central committee that evaluates the drugs and buys the most appropriate for the Institute. The decision is based on price and efficacy levels. Treatment of patients is based on international guidelines.

Treatment for lung cancer does not have enough resources in Mexico, there are other cancer forms that have higher priority, for example breast and cervical cancer where chances of cure for the patient are higher. The social security has prioritized to procure specialized or biologic treatment to others forms of cancer like cervix cancer and breast cancer.

In general, patients with lung cancer are referred to specialized centres that cover the whole treatment for the patient. However, treatment coverage differs between different hospitals. In hospitals for people without social security the centre may cover radiotherapy and general drugs but the patient needs to cover the specialized drugs.

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