



Pregledni članek

Review article

Lung cancer in Slovenia

Pljučni rak v Sloveniji

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Abstract

Lung cancer is the most common type of cancer in males and the leading cause of cancer death worldwide. The highest incidence rates are observed in Eastern Europe and North America for males and in North-West Europe and North America for females. In Slovenia, lung cancer was the most frequently diagnosed cancer in males until 2004. In 2005, when 846 new lung cancer cases were registered, lung became the second most common site of cancer after prostate. With 299 newly diagnosed cases, lung cancer was the fifth most frequent cancer in females in 2005. There are no consistent differences in lung cancer geographical distribution; between 1998 and 2002, the incidence rates were highest in the statistical region of Zasavje. While crude incidence rates of lung cancer have been constantly increasing, in part as a result of the population ageing, the relative increase during the period 1986-2005 was greater in females. In males, the age-standardised incidence rate of lung cancer has been decreasing by 1.6% yearly since 1993, and one year later, mortality rates began to exhibit a downward trend too. Squamous cell carcinoma is the most frequent histological type of cancer in males. Its proportion began to decrease in contrast to adenocarcinomas that shows an upward trend. Adenocarcinoma and small cell carcinoma are the most common histological types among females, with adenocarcinoma also increasing. Five-year relative survival rates based on data from the Cancer Registry of Slovenia have been slowly increasing: from 7% and 10% in male and female patients diagnosed between 1973 and 1977 to 12% and 13% for males and females diagnosed during the period 2001-2005. Even though other risk factors besides tobacco use have been implicated in the aetiology of lung cancer, smoking prevention and control remains the most important measure to decrease the burden of lung cancer.

Key words. Lung cancer, epidemiology, incidence, mortality, risk factors.



Izvleček

Pljučni rak je najpogostejši rak na svetu in najpogostejši vzrok smrti za rakom pri moških. Incidenca je pri moških največja v vzhodni Evropi in Severni Ameriki in severo-zahodni Evropi in Severni Ameriki pri ženskah. V Sloveniji je bil do leta 2004 pljučni rak najpogostejši malignom pri moških; leta 2005, ko je bilo registrirano 846 novih primerov, ga je na prvem mestu zamenjal rak prostate. Pljučni rak je bil pri ženskah leta 2005 po pogostnosti glede na druge rake že na petem mestu; registriranih je bilo 299 novih primerov. Sistematičnih regionalnih razlik v razporeditvi bolnikov sicer ni; v letih 1998–2002 je pri obeh spolih iz slovenskega povprečja izstopala Zasavska statistična regija. Ob tem, ko se groba incidenčna stopnja pri obeh spolih povečuje tudi na račun staranja prebivalcev, je bil v obdobju 1986–2005 relativni porast incidence bistveno večji pri ženskah. Pri moških se starostno standardizirana incidenčna stopnja zmanjšuje od leta 1993 v povprečju za 1,6 % letno, z enoletnim zaostankom ji sledi zmanjševanje starostno standardizirane umrljivosti stopnje. Pri moških je bil v vseh obdobjih najpogostejši ploščatocelični karcinom, vendar se njegov delež v strukturi histoloških vrst zmanjšuje, povečuje pa se delež žlezni karcinomov. Pri ženskah prevladujeta žlezni in drobno-celični karcinom, tudi pri njih se povečuje delež žlezni karcinomov. Podatki Registra raka za Slovenijo kažejo, da se petletno relativno preživetje bolnikov s pljučnim rakom, čeprav sodi med najmanjše, vseeno postopno povečuje, od 7 % pri moških in 10 % pri ženskah, ki so zboleli v letih 1973–1977, se je preživetje povečalo na 12 % pri moških in 13 % pri ženskah, zbolelih v letih 2001–2005.

Čeprav so v nastanek pljučnega raka vpleteni tudi drugi nevarnostni dejavniki, z javnozdravstvenega vidika k njegovemu nastanku največ prispeva kajenje cigaret, zato je omejevanje kajenja najpomembnejše za zmanjšanje bremena te bolezni.

Ključne besede: Pljučni rak, epidemiologija, incidenca, umrljivost, nevarnostni dejavniki.

Introduction

Lung cancer is the most common cancer in males. Even though it is less frequent in females, it remains the leading cause of cancer death in both sexes worldwide. In 2002, there were an estimated 1,400,000 new cases of lung cancer (965,446 in males and 386,875 in females) in the world. The disease killed approximately 1,200,000 people, 848,321 males and 330,753 females (1). In males, the highest incidence rates are observed in Eastern Europe and North America, and in females, in north-west Europe and North America (1).

There are also great differences in lung cancer burden around Europe (1). Hungary has the highest male lung cancer incidence rates (94.6/100,000), followed by Poland, Croatia and Belgium. High rates for females were recorded in Iceland (30.0/100,000) and Denmark, in other northern European countries and in the Netherlands, Hungary and Poland. Iceland and Finland had the lowest male incidence rates (33.4/100,000 and less). Female incidence rates were lowest in the countries

of Southern and Eastern Europe (less than 7.4/100,000). The same rankings for both sexes were seen for both incidence and mortality, an observation indicating a generally poor prognosis; mean age-adjusted five-year relative survival for lung cancer patients is approx. 12% in all European countries (2). As the vast majority of lung cancer cases and deaths in Europe are attributable to tobacco smoking, the rates in each country reflect the current phase of the lung cancer epidemic in terms of past smoking exposure, the dose, duration and type of tobacco consumed (3,4).

Lung cancer in Slovenia

In Slovenia, data on cancer incidence are available from the Cancer Registry of Slovenia, one of the oldest in Europe (5). Cancer mortality data are registered by the Institute of Public Health and are available also from the WHO Statistical Information System (6). These data are a basis for the analysis of the burden of different cancer types, time trends in survival and mortality.



In Slovenia, lung cancer had been the most common cancer type among males until 2004. Since 2005, when 846 new cases were registered, it has ranked second, after prostate cancer. In females, lung cancer was the fifth most common type of cancer, with 299 newly diagnosed cases in 2005 (5). Lung cancer geographical distribution shows no consistent regional variation (7); during the period 1998–2002, the incidence rates were highest in the statistical region of Zasavje (8).

Temporal variation of crude and age adjusted incidence and mortality rates

Crude incidence rates of lung cancer have been slowly increasing in both sexes, mostly as a result of the population ageing. During the period 1985–2005, a relative increase was much higher among females. In 1993, age-standardised rate (world) for males began to decline at an annual rate of 1.6%, and a downward trend in age-standardised mortality rate was noted one year later (Figure 1). As in other European countries (4), different time trends in male and female lung cancer incidence in Slovenia are explainable by smoking habits of successive generations (birth cohorts) (9). Among males, smoking was most prevalent in birth cohorts from 1920 to 1935. In the subsequent period, the prevalence of smoking decreased to rise again in the generation born during the period 1950–1960 (9). Changed levels of risk for different generations are indicated by age-specific rates for different time periods; age-specific incidence rates are increasing for age groups above 70 years. However, changes have also occurred in younger age groups (40–69 yrs) (Figure 2); a further decline in the overall rate is expected to occur when these young generations of men reach old age when lung cancer becomes more common. Before the Second World War cigarette smoking was less popular among females than among males, but its prevalence started to increase in the baby-boom generation born after the war, so we can expect that the rate of lung cancer among females will further increase (10). In females younger than 60 years, the age-specific incidence rate of lung cancer nearly doubled during the period 2001–2005 compared to the period 1986–1990 (Figure 2).

Histological types of lung cancer

In the Cancer Registry of Slovenia, coding of histological cancer type is based on the Interna-

tional Classification of Diseases for Oncology (ICD-O), since 2001 on its third edition (11). For lung cancer the WHO Classification of Tumours is used (12). Between 1986 and 2005, squamous cell carcinoma was the most frequent histological type in males. Its relative frequency, however, was decreasing, whereas the opposite was true for adenocarcinoma (Table 1). Adenocarcinoma and small cell carcinoma are the most frequently diagnosed cancer types in females, with adenocarcinoma showing an upward trend in incidence too (Table 1). The percentage of cases without microscopic diagnosis has been decreasing and has reached 8.7% for males and 9.9% for females.

The time trend in age-standardised incidence rates of different histological types of lung cancer in males indicates that the decrease in the overall rate is primarily due to the decrease in squamous cell carcinoma and in part to a decline in small cell carcinoma; the incidence rate of adenocarcinoma, however, is mounting. In contrast, the most common cancer among females is adenocarcinoma, which is showing an increasing trend and is responsible for the increased overall age-standardised incidence rate of lung cancer in females (Figure 3).

The changing trends in adenocarcinoma observed in Slovenia are similar to those reported by other countries (13,14,15). Between 1980 and 1997, squamous cell carcinoma rates among males declined by over 30% in North America and some European countries, whereas in other areas the decrease was less dramatic and more slowly. Squamous and small cell carcinoma rates among females rose, notably in Norway and in the Netherlands. Adenocarcinoma rates increased in both sexes in virtually all geographical areas.

Differences in histological types and their changes over time may be attributable to differences in smoking habits between males and females, as well as to cigarette composition in different time periods (16). Squamous and small cell carcinomas are most strongly associated with cigarette smoking. Reduction of tobacco consumption in the 1960s has been followed by a recent decrease in the incidence of squamous cell carcinoma, but not by a drop in the rate of adenocarcinoma. After smoking cessation the relative risk of adenocarcinoma has been found to decrease more slowly than that the risk for squamous cell carcinoma (17).

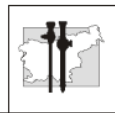


Table 1

Number and percentage of lung cancer cases in Slovenia by histological type/microscopic diagnosis and by sex, 1986–2005.

Time period	1986–1990	1991–1995	1996–2000	2001–2005
Histological type	Number (%)	Number (%)	Number (%)	Number (%)
Males - total	3,496 (100.0)	4,002 (100.0)	4,120 (100.0)	4,253 (100.0)
Squamous cell carcinoma	1,381 (39.5)	1,532 (38.3)	1,661 (40.3)	1,458 (34.3)
Adenocarcinoma	505 (14.4)	619 (15.5)	810 (19.7)	994 (23.4)
Small cell carcinoma	594 (17.0)	680 (17.0)	723 (17.5)	719 (16.9)
Non-small cell and unspecified ca.	384 (11.0)	504 (12.6)	252 (6.1)	232 (5.5)
Other histology type	239 (6.8)	290 (7.2)	342 (8.3)	481 (11.3)
Histologically/cytologically not confirmed	393 (11.2)	377 (9.4)	332 (8.1)	369 (8.7)
Females - total	666 (100.0)	820 (100.0)	1,043 (100.0)	1,406 (100.0)
Squamous cell carcinoma	77 (11.6)	122 (14.9)	180 (17.3)	210 (14.9)
Adenocarcinoma	247 (37.1)	259 (31.6)	418 (40.1)	565 (40.2)
Small cell carcinoma	121 (18.2)	146 (17.8)	189 (18.1)	243 (17.3)
Non-small cell and unspecified ca.	59 (8.9)	89 (10.9)	52 (5.0)	86 (6.1)
Other histology type	45 (6.8)	96 (11.7)	107 (10.3)	163 (11.6)
Histologically/cytologically not confirmed	117 (17.6)	108 (13.2)	97 (9.3)	139 (9.9)

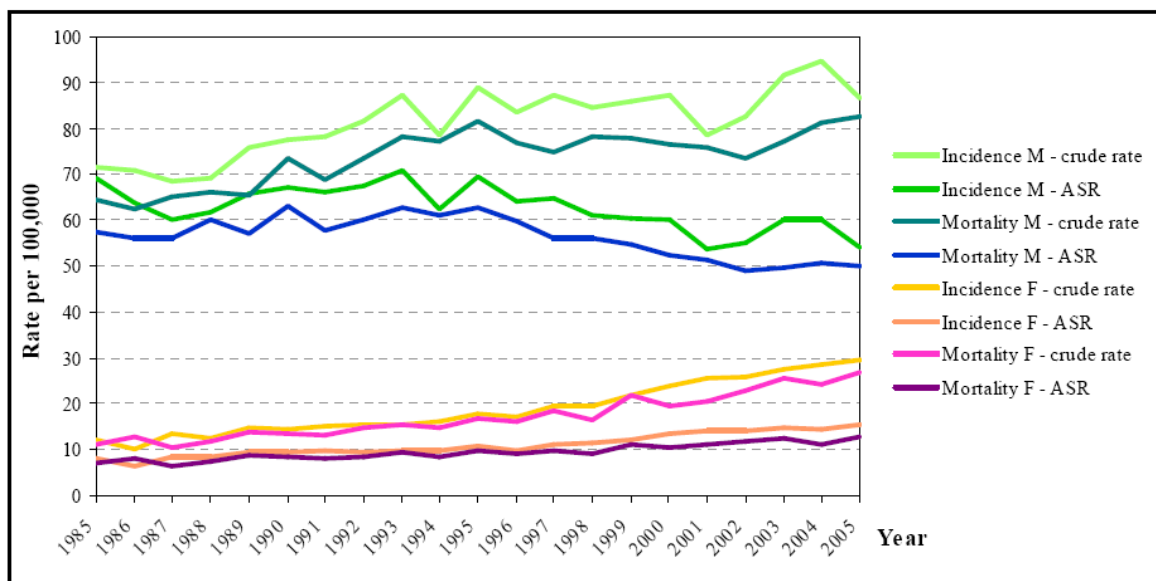


Figure 1

Crude and age-standardised incidence and mortality rates (ASR, world) of lung cancer in Slovenia by sex, 1985–2005.

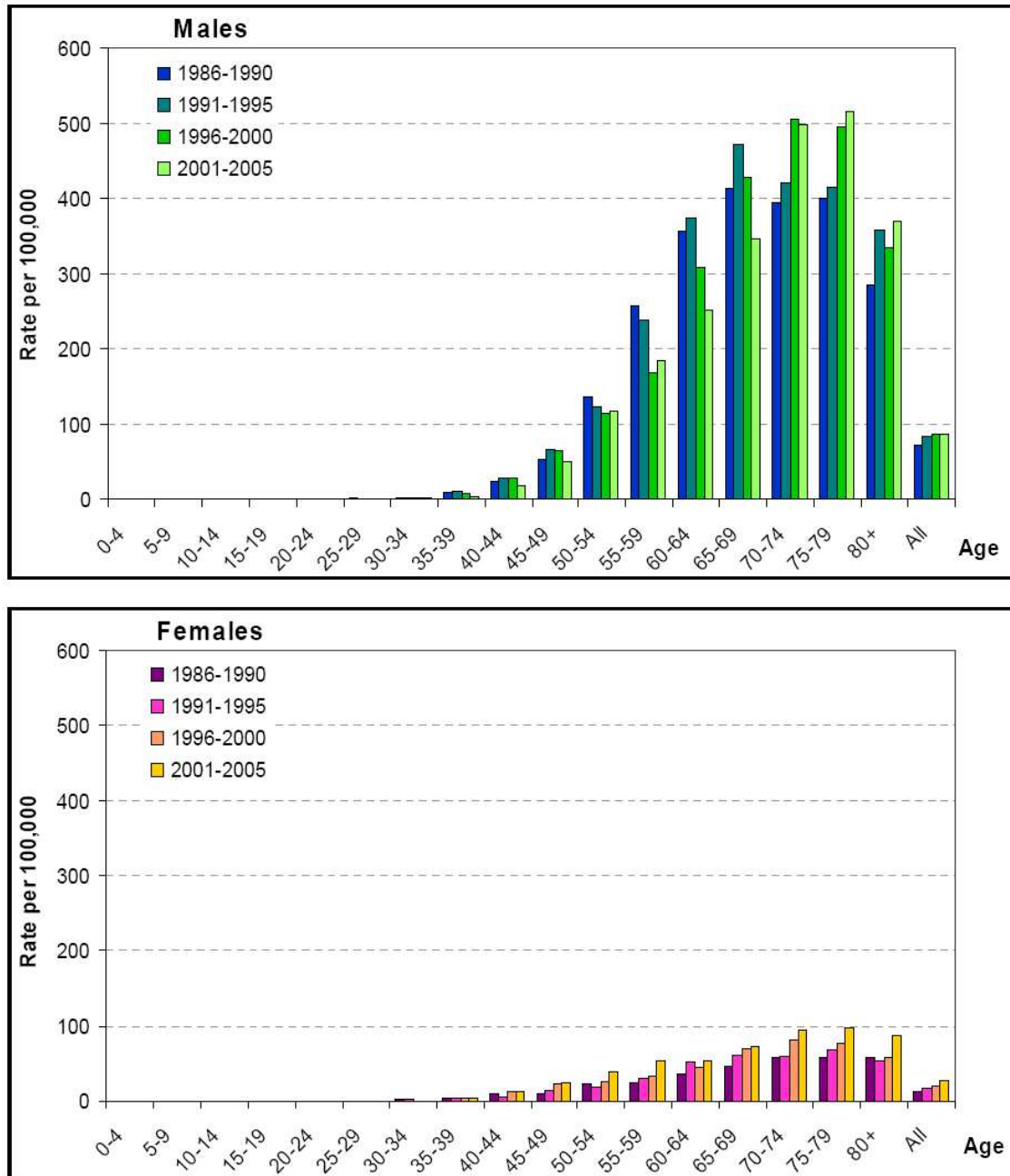


Figure 2
Average age-specific incidence rates of lung cancer in Slovenia by sex, 1986–2005.

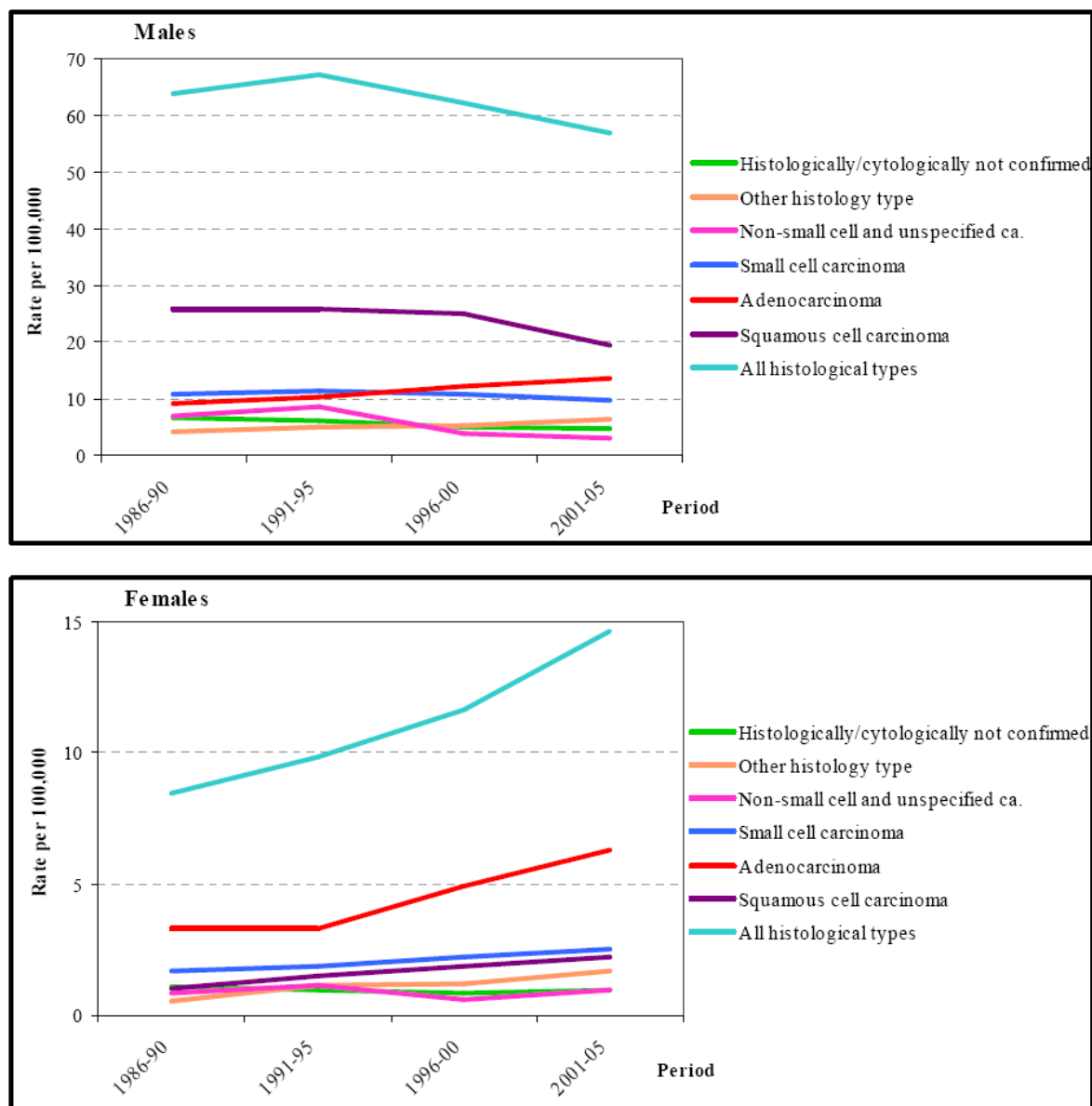


Figure 3
Trends in age-standardised incidence rates (world) of different histological types of lung cancer in Slovenia by sex, 1986–2005.

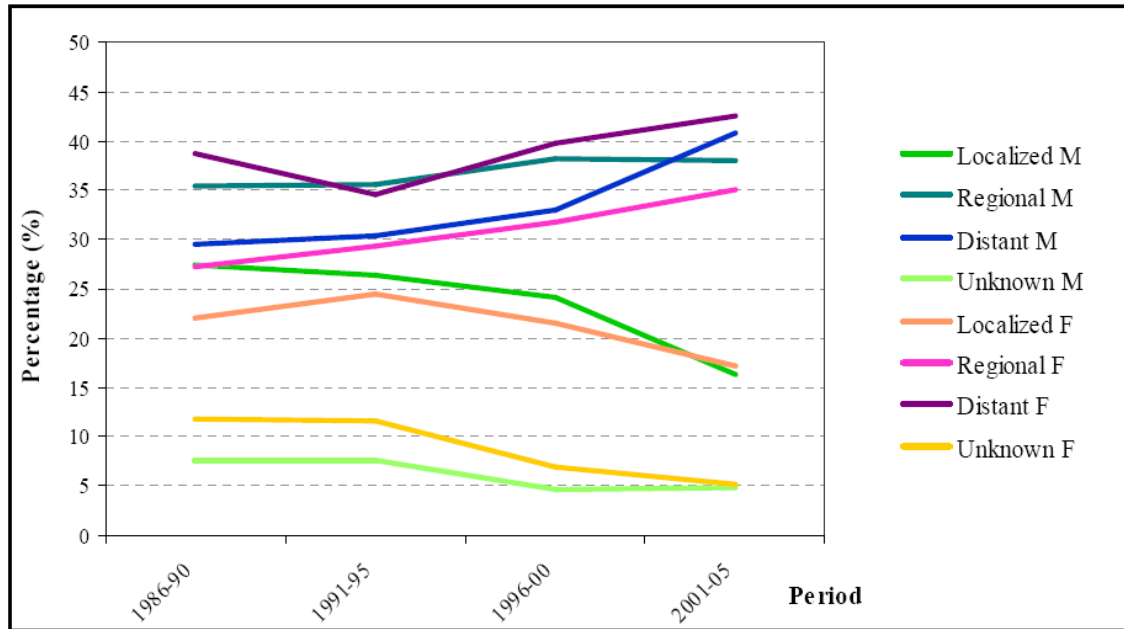


Figure 4
Percentage of lung cancer cases in Slovenia by stage at diagnosis, and by sex, 1986–2005.

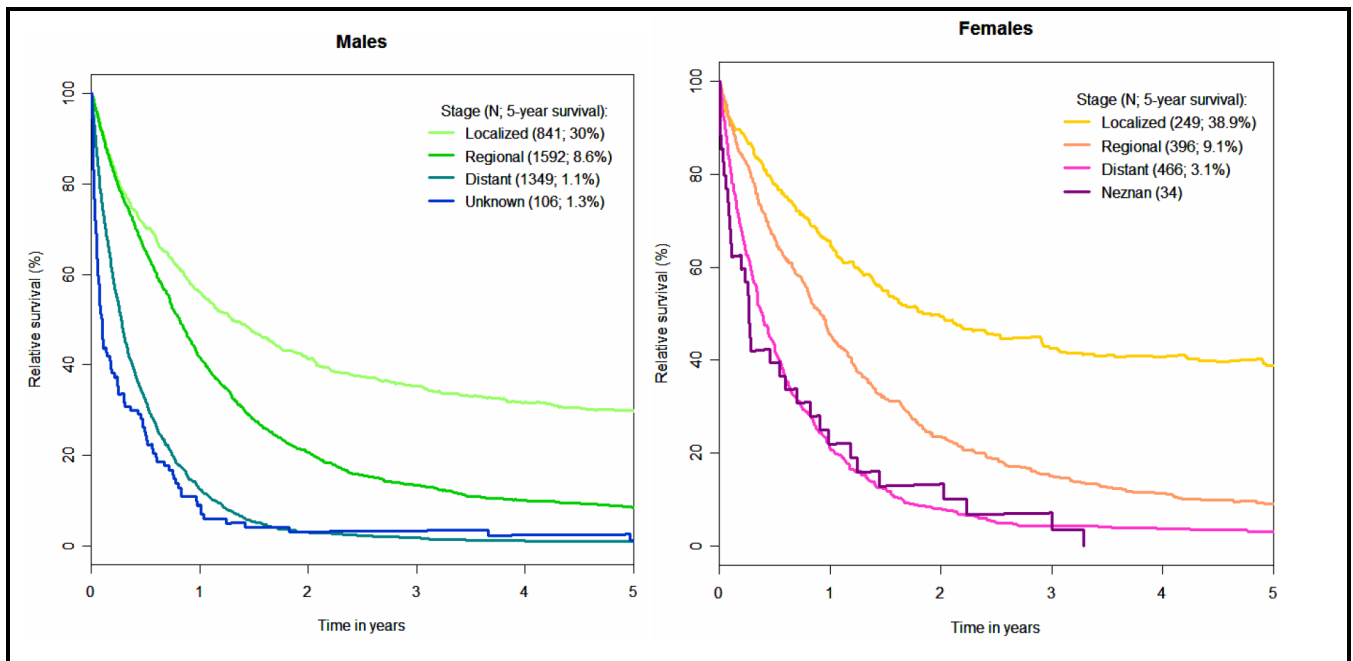
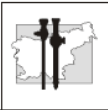


Figure 5
Five-year relative survival of lung cancer patients in Slovenia, diagnosed between 1998 and 2002, by stage at diagnosis and sex.



Variations in the composition of cigarettes smoked in different time periods seem to have played an important role too. With the introduction of filter cigarettes larger particles were removed from cigarette smoke, thus reducing deposition of these particles in the central airway, which is the predilection site for squamous cell carcinoma. The consequence may be an increase in adenocarcinoma that occurs in the peripheral lung regions. Moreover, smokers of filter cigarettes tend to inhale more deeply, which may result in an increased deposition of smoking particles in the small airways, leading to an increase in the incidence of adenocarcinoma. Smokers, especially women, who switched from non-filter to filter cigarettes, increased the number of cigarettes smoked per day, which, again, increases the risk of lung cancer (18). The impact of tar, nicotine level and additives, and their variation still needs to be studied. Between 1978 and 1992, tobacco-specific nitrosamine NNK in cigarette smoke increased by about 45%. It is known to cause adenocarcinoma in rodents and may be responsible for increased incidence rates of adenocarcinoma (18).

Stage at diagnosis

Cancer registries commonly use a simplified staging system, describing the stage of disease as localized with no nodal involvement or distant metastases, regional with regional lymph nodes involvement and distant with distant metastases. In Slovenia, the percentage of regional and distant stages is increasing in both sexes (Figure 4). During the period 2001-2005, more than 40% of all new cancer cases were diagnosed with distant metastases. The proportion of localized stage cancers is decreasing, probably as a result of improved diagnostic methods. On the other hand, this decrease may be attributed in part to changing histological types: adenocarcinoma that grows in the small airways may cause less clinical symptoms, and is discovered later than squamous cell carcinoma.

Survival of lung cancer patients

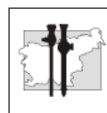
According to data from the Cancer Registry of Slovenia, five-year relative survival of lung cancer patients, though among the lowest, shows an upward trend. It increased from 7% and 10% in male and female patients diagnosed between 1973

and 1977 (19) to 12% and 13% in males and females diagnosed with cancer between 2001 and 2005 (5). As in any other type of cancer, survival depends on the extent of the disease at diagnosis. Patients of both sexes diagnosed with localized stage cancer have better survival (Figure 5). The most recent EURO CARE study shows that survival of lung cancer patients, diagnosed between 1995 and 1999 was poor in all the participating countries: the five-year age-adjusted relative survival in Slovenia was 8.8%, and the European average was 10.2% (2).

Conclusions

Several living and occupational environment related risk factors have been implicated in the aetiology of lung cancer, but from a public health perspective tobacco smoking is the most important causative factor (20). Studies conducted in Europe, Japan and North America have shown that 87% to 91% of lung cancers in men and 57% to 86% of lung cancers in women are ascribable to cigarette smoking (21). In Slovenia, the prevalence of adult male smokers has decreased over the past 30 years, from 48% in 1975 (22) to 26% in 2006 (23), an observation explaining the declining age-standardized lung cancer mortality rate in males noted over the past decade. Lung cancer mortality in females, however, has been increasing at a slow pace, which reflects similar and sustainable smoking habits among women (16% of women in 1975, and 20% in 2006) (22,23).

Tobacco control programme includes a complex set of activities, from promotion of non-smoking and support of smokers to stop smoking, to implementation of anti-smoking legislation. Slovenia's long-term commitment to combat smoking was strengthened by the Act Amending the Restriction of the Use of Tobacco Products, implemented on 5 August 2007 (24). With this Act Slovenia joined Ireland, Italy, Norway, the United Kingdom and some other European countries in prohibiting smoking in all closed public areas and workplaces. Cigarette smoking is permitted only in special smoking rooms that meet strict conditions laid down in a set of rules issued by the Minister of Health, published in September 2007. The amended Act also prohibits selling tobacco products to persons under the age of 18.



In Slovenia, under 18's are not allowed to sell tobacco products either. Within eight months of the implementation of the above mentioned Act, cigarette manufacturers must add the telephone number of the stop-smoking helpline to the existing warning labels on the packaging of tobacco products.

It is hoped that this Act, together with more intensive programmes aimed at reducing smoking, will help to further diminish the prevalence of smoking, and consequently the incidence and mortality of lung cancer in Slovenia.

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