

## Cigarette Smoking and Trends in Lung Cancer Incidence in Lithuania: An Analysis by Histological Type

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**Key words:** lung cancer; incidence; trend; smoking.

**Summary.** *Objective.* The aim of this study was to investigate time trends of lung cancer incidence by histological type in Lithuania during the period from 1996 to 2005. The results were evaluated in relation to tobacco smoking trends.

*Material and Methods.* The incidence rates of the most common lung cancer cell types (squamous cell carcinoma, adenocarcinoma, small cell carcinoma, other types, and morphologically not specified cases) were studied using data from the Lithuanian Cancer Registry. The World Standard Population was used for age adjustment. Data on tobacco smoking in Lithuania were obtained from various published sources.

*Results.* Among men, squamous cell carcinoma was the most common type of lung cancer. The age-adjusted rates of squamous cell carcinoma decreased from 25 per 100 000 in 1998–1999 to 19.1 per 100 000 in 2004–2005; the incidence rates for adenocarcinoma and small cell carcinoma rose to around 7 per 100 000 in 2002–2003. Among women, adenocarcinoma was the most common histological type. The incidence rates for adenocarcinoma increased to 1.9 per 100 000 until 2002–2003 and thereafter did not change. The rates of squamous cell carcinoma in women were relatively stable at around 1.1 per 100 000. In 2000, the prevalence of regular smoking among men and women peaked at 51.5% and 15.8%, respectively; there was a significant change from smoking nonfilter cigarettes to filter cigarettes.

*Conclusions.* The decreasing squamous cell carcinoma rates among men and increasing adenocarcinoma rates among men and women are similar to those reported in other European countries and may be due to a shift from nonfilter type cigarettes to filter type.

### Introduction

Lung cancer has been the main cause of death from cancer among men for many decades in Lithuania. Every year more than 1300 patients in Lithuania die of lung cancer (1).

Many studies have proved an association between smoking intensity, duration, and age at the beginning of smoking and lung cancer risk. The relationship between smoking and lung cancer varies by histological type: a stronger association was observed between smoking and squamous cell or small cell carcinoma and weaker between smoking and adenocarcinoma (2–4). Changes in the incidence of different forms of lung cancer have been related to changes in the quality of cigarettes, in particular to the increasing consumption of filter cigarettes. Due to effective tobacco control programs in West European countries and the United States, the prevalence of cigarette smoking among men has declined since the 1960s, and as a result, lung cancer rates decreased 1–2 decades later (4–8). In Central and East European countries,

the prevalence of smoking has increased, and lung cancer rates among men peaked around 1990–1995 (4, 9). Tobacco consumption among women and consequently lung cancer incidence and mortality in many West European countries, Poland, the Czech Republic, and the United States have substantially increased; in some countries, it became the main cause of death from cancer among women. Recently, lung cancer rates among women have leveled out or have begun to decline in younger age groups (5, 6, 8, 10). The incidence of lung adenocarcinoma has increased in Europe, the United States, and Japan among men and women; it is the most common form of lung cancer among women, and in some countries, among men (9, 11). Declining incidence rates for squamous and small cell carcinoma among men were reported in Europe, the United States, and Japan.

In Lithuania, lung cancer incidence rates among men have decreased since 1993; however, they remain among the highest in Europe (5, 12–14). Among women, lung cancer incidence rates have

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been constant since around 1978, and they are the lowest in Europe (5, 14). Trends in lung cancer incidence by histological type in Lithuania have never been reported.

The aim of this study was to investigate the time trends in lung cancer incidence by histological type in Lithuania during the period from 1996 to 2005. As around 85% of all lung cancer cases among men and about 70% among women are caused by smoking, changes in lung cancer incidence are closely related to the prevalence of tobacco consumption in the population a few decades ago. Therefore, trends in incidence were analyzed in relation to tobacco smoking.

### Material and Methods

Incidence data from malignant neoplasms of the trachea, bronchus, and lung (ICD-10 C33 and C34, ICD-9 rubric 162 until 1998) were obtained from the Lithuanian Cancer Registry database. Population data by age, sex, and year were obtained from the Department of Statistics of the Government of the Republic of Lithuania. Age-standardized incidence rates were calculated for all age groups combined for men and women separately for two-year periods: 1996–1997, 1998–1999, 2000–2001, 2002–2003, and 2004–2005. Since the occurrence of lung cancer is rare in the youngest age groups, both male and female, and diagnoses of the disease are less reliable for those aged more than 79 years, the following age groups were formed for the calculation of age-specific incidence rates: 30–49, 50–59, 60–69, and 70–79.

The World Standard Population was used for age adjustment. Because of the availability of reliable data on tumor histological type, time trends for the

period 1996–2005 were evaluated. An annual percentage change (APC) and 95% confidence intervals (95% CI) were calculated for each age group by gender and histological type using a standard log-linear model. The period was too short to use age-period-cohort data analysis.

The incidence rates of the following most common lung cancer cell types were studied: squamous cell carcinoma (ICD-O: 8050–8078, 8083–8084), adenocarcinoma (8140, 8211, 8230–8231, 8250–8260, 8323, 8480–8490, 8550–8551, 8570–8574, 8576), small cell carcinoma (8041–8045, 8246), other (8010–8012, 8014–8031, 8035, 8310, 8800–8811, 8830, 8840–8921, 8990–8991, 9040–9044, 9120–9133, 9150, 9540–9581), and morphologically unspecified.

Data on the prevalence of tobacco smoking in Lithuania were obtained from various published sources, including data for the latest years up to 2007, as it may be of importance for predicting the future trends in lung cancer incidence.

### Results

The total number of lung cancer cases during the 10-year period was 13 639 among men and 2516 among women. The number of cancer cases, age-specific and annual age-standardized incidence rates during the period from 1996 to 2005 is shown in Table. Among men, lung cancer incidence for all histological types combined decreased consistently by 3.7% every two years (95% CI, –6.4% to –1.1%). The incidence rate declined statistically significantly in two age groups among men: the 50–59-year-old group showed a 6.6% decline every two years (95% CI, –11.4% to –1.8%), whereas the 60–69-year-

Table. The Age-Specific and Age-Standardized Incidence Rates per 100 000 Population for Lung Cancer in Lithuania, 1996–2005

Age Group	1996–1997	1998–1999	2000–2001	2002–2003	2004–2005	APC (95% CI)
<b>Men</b>						
30–49	16.3 (160)	17.0 (167)	18.0 (177)	15.4 (151)	12.4 (122)	–6.2 (–18.0; 5.5)
50–59	184.2 (656)	163.4 (560)	151.2 (515)	155.9 (528)	134.1 (464)	–6.6 (–11.4; –1.8)
60–69	397.8 (1157)	401.5 (1164)	358.9 (1029)	357.9 (1017)	346.7 (961)	–3.8 (–6.9; –0.7)
70–79	509.3 (644)	523.4 (750)	511.1 (807)	514.7 (875)	483.3 (844)	–1.2 (–3.9; 1.5)
ASR (95% CI)	66.5 (64.0; 69.0)	66.3 (63.9; 68.8)	61.9 (59.6; 64.3)	62.1 (59.8; 64.5)	56.8 (54.6; 59.1)	–3.7 (–6.4; –1.1)
<b>Women</b>						
30–49	2.9 (30)	4.1 (42)	3.5 (36)	2.9 (30)	3.4 (35)	–0.4 (–16.6; 15.8)
50–59	12.7 (56)	11.1 (47)	13.4 (56)	15.9 (66)	20.0 (84)	13.5 (1.1; 25.9)
60–69	31.9 (136)	31.7 (134)	26.9 (112)	23.5 (97)	26.4 (107)	–6.6 (–15.3; 2.1)
70–79	67.9 (178)	59.5 (175)	59.0 (187)	58.0 (193)	57.4 (193)	–3.5 (–7.9; 0.8)
ASR (95% CI)	6.6 (6.0; 7.3)	6.5 (5.9; 7.1)	6.8 (6.2; 7.5)	6.3 (5.7; 7.0)	6.9 (6.2; 7.6)	0.6 (–3.5; 4.6)

Number of cases in parentheses unless otherwise indicated. ASR, age-standardized incidence rate per 100 000 population (World Standard Population). APC, annual percentage change.

old group showed a 3.8% decline every two years (95% CI, -6.9% to -0.7%). The incidence increased among men aged 30–49 years until 2000–2001 and thereafter declined.

Fig. 1 shows the lung cancer incidence rates by histological type for men. Squamous cell carcinoma was the most common type of lung cancer among men after the exclusion of morphologically unspecified lung cancers. The age-adjusted rates among men peaked at 25 per 100 000 in 1998–1999 and thereafter decreased. The lung cancer rates for adenocarcinoma increased from 5.6 per 100 000 to around 7 per 100 000 in 2002–2003 and afterward did not change. The rates for small cell carcinoma displayed a similar pattern, increasing from 4.9 to 7.3 per 100 000. The incidence of other cancers did not change substantially. There was a large proportion (34%) of unspecified lung cancers; their incidence declined from 29.0 per 100 000 in 1996–1997 to 18.9 per 100 000 in 2000–2001 and thereafter remained constant.

Fig. 2 shows age-specific rates for lung can-

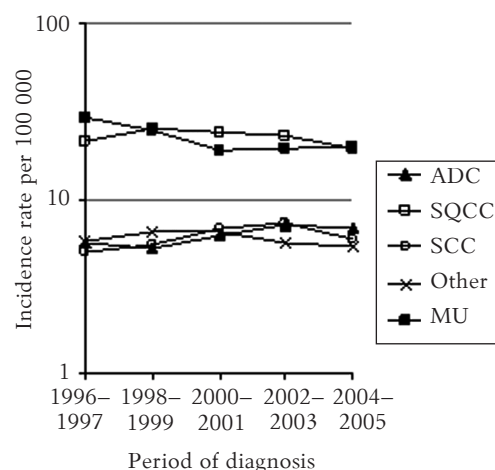


Fig. 1. Lung cancer incidence rates by histological type in men in Lithuania during 1996–2005  
Age-adjusted to World Standard Population. SQCC, squamous cell carcinoma; ADC, adenocarcinoma; SCC, small cell carcinoma; MU, morphologically unspecified.

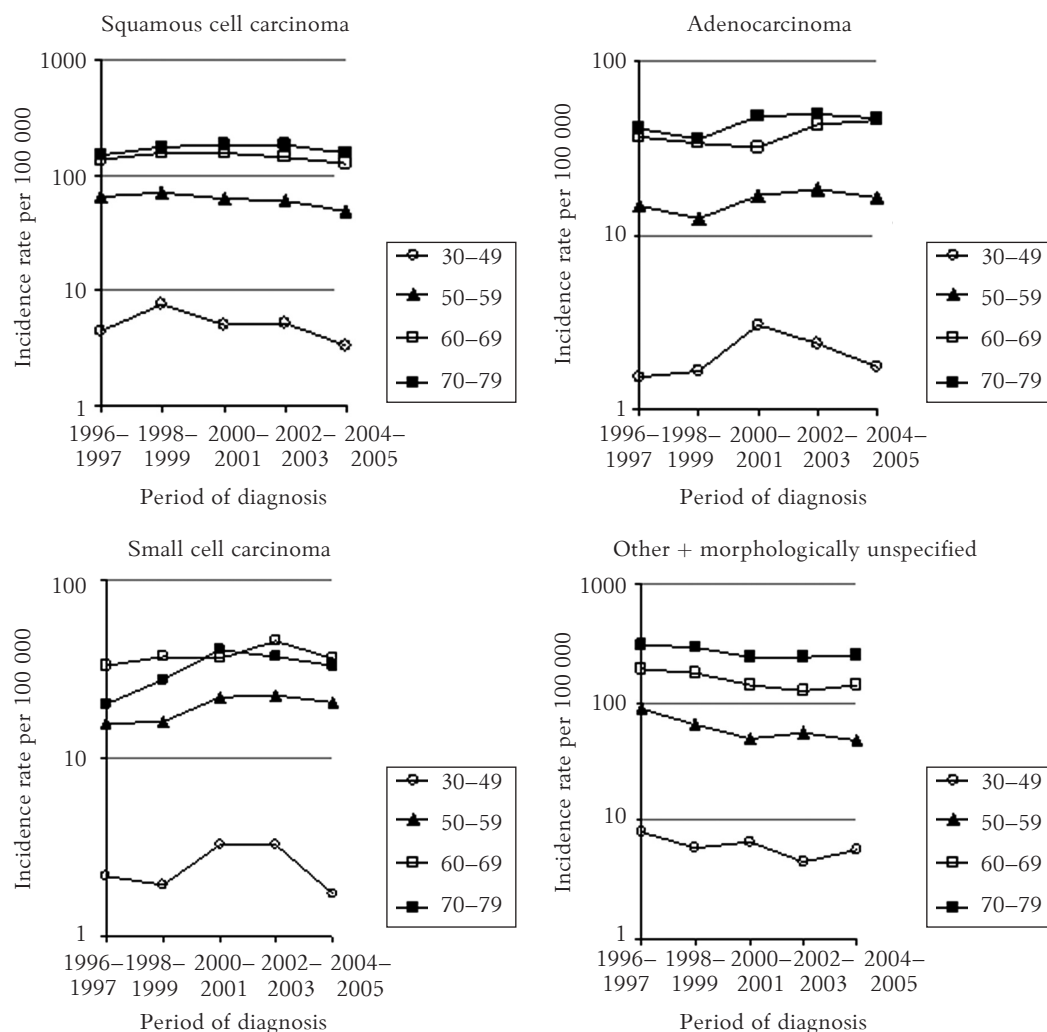


Fig. 2. Trends in age-specific lung cancer incidence rates by period of diagnosis and by histological type in men in Lithuania during 1996–2005

cer by histological type in men. The incidence for squamous cell carcinoma in the age groups below 70 years peaked in 1998–1999 and afterward decreased constantly. In the oldest age group (70–79 years), the rates began to decline later. The rates for adenocarcinoma increased until 2002–2003, then remained constant, except for the 30–49-year-old group, for which an increase until 2000–2001 and thereafter a decrease were observed. The incidence of small cell carcinoma displayed a similar pattern to that of adenocarcinoma. The incidence rates for other and unspecified cancers decreased for each age group.

Lung cancer incidence rates for all histological types combined were stable at around 6.7 per 100 000 among women during the period from 1996 to 2005 (Table). There was a statistically significant increase of 13.5% (95% CI, 1.1% to 25.9%) among 50–59-year-old women. The age-specific rates among the 60–69- and 70–79-year-old groups displayed a statistically insignificant decline. Incidence rates did not change markedly among 30–49-year-old women.

Among women, adenocarcinoma was the most common histological type after excluding morphologically unspecified lung cancers (Fig. 3). Adenocarcinoma incidence rates increased to 1.9 per 100 000 until 2002–2003 and thereafter did not change. Incidence rates of squamous cell carcinoma in women were stable at around 1.1 per 100 000. A statistically significant increase in the rates of small cell carcinoma from 0.4 per 100 000 to 0.8 per 100 000 by 21.5% every two years (95% CI, 11.6% to 31.4%) was observed. The total incidence rates of other lung cancer types in women did not change substantially. The proportion of unspecified lung can-

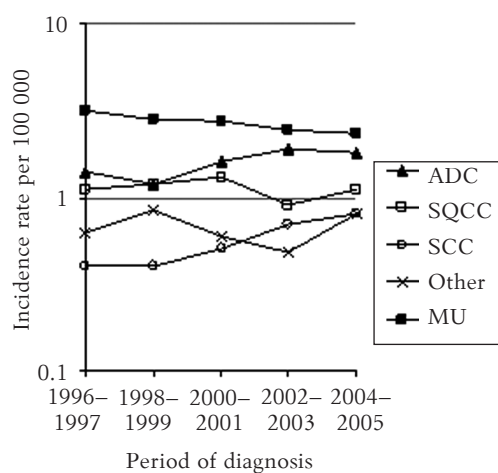


Fig. 3. Lung cancer incidence rates by histological type in women in Lithuania during 1996–2005

Age-adjusted to World Standard Population. SQCC, squamous cell carcinoma; ADC, adenocarcinoma; SCC, small cell carcinoma; MU, morphologically unspecified.

cers (40%) was higher among women than men; the rates showed a decline from 3.1 per 100 000 during 1996–1997 to 2.3 per 100 000 during 2004–2005.

Fig. 4 shows age-specific incidence rates for lung cancer by histological type for women. A slight increase in adenocarcinoma incidence was observed among the 50–59-, 60–69-, and 70–79-year-old groups, and relatively stable rates were documented in the 30–49-year-old group. The incidence rates for small cell carcinoma displayed a similar pattern. Relatively stable age-specific incidence rates were observed for squamous cell carcinoma in all age groups, except the 60–69-year-old group, where the incidence peaked at 7.6 per 100 000 in 1998–1999 and thereafter declined. The other and unspecified lung cancer incidence rates fell among women aged  $\geq 60$  years, whereas the rates in the 50–59-year old group increased slightly.

There are limited data on tobacco consumption before the 1980s. It is known that the prevalence of smoking was high (40%–50%) (15). The results of several studies indicate that the smoking prevalence fluctuated among men in Lithuania during the period 1983–2006: around 38% of men smoked regularly in 1983 and 43% in 2006 (Fig. 5). There was an increase in the percentage of smokers among men in the 1990s; it peaked at 51.5% in 2000 (1, 16–20, 21). The percentage of regular smokers among women increased significantly, more than tripling from 4.1% in 1982 to 15.8% in 2000. Smoking prevalence is high among the younger population, particularly the rural population. Tobacco use among 25–34-year-old rural men was 48.9%, 55.6%, and 51.5% in 1987, 1999, and 2007, respectively, whereas among 25–34-year-old women it was 5.8%, 11.7%, and 33.3% respectively (18–20, 22). There was a significant change from smoking nonfilter cigarettes to filter cigarettes among men and women: 48.9% of male smokers and 13.1% of female smokers reported smoking nonfilter cigarettes in 1994. Only 8.9% of male smokers and 1.4% of female smokers smoked nonfilter cigarettes in 2006 (16, 18).

## Discussion

There was a significant decrease in the overall lung cancer incidence rates among men in Lithuania during 1996–2005. Squamous cell carcinoma was the most common histological type of lung cancer. Decreasing incidence rates for squamous cell carcinoma among men have been observed since 1998–1999. The incidence rates for adenocarcinoma have increased. Similarly, there was an increase in the incidence rates for small cell carcinoma.

Among women, stable overall lung cancer rates and a statistically significant increase in lung cancer rates among the 50–59-year-old group were ob-

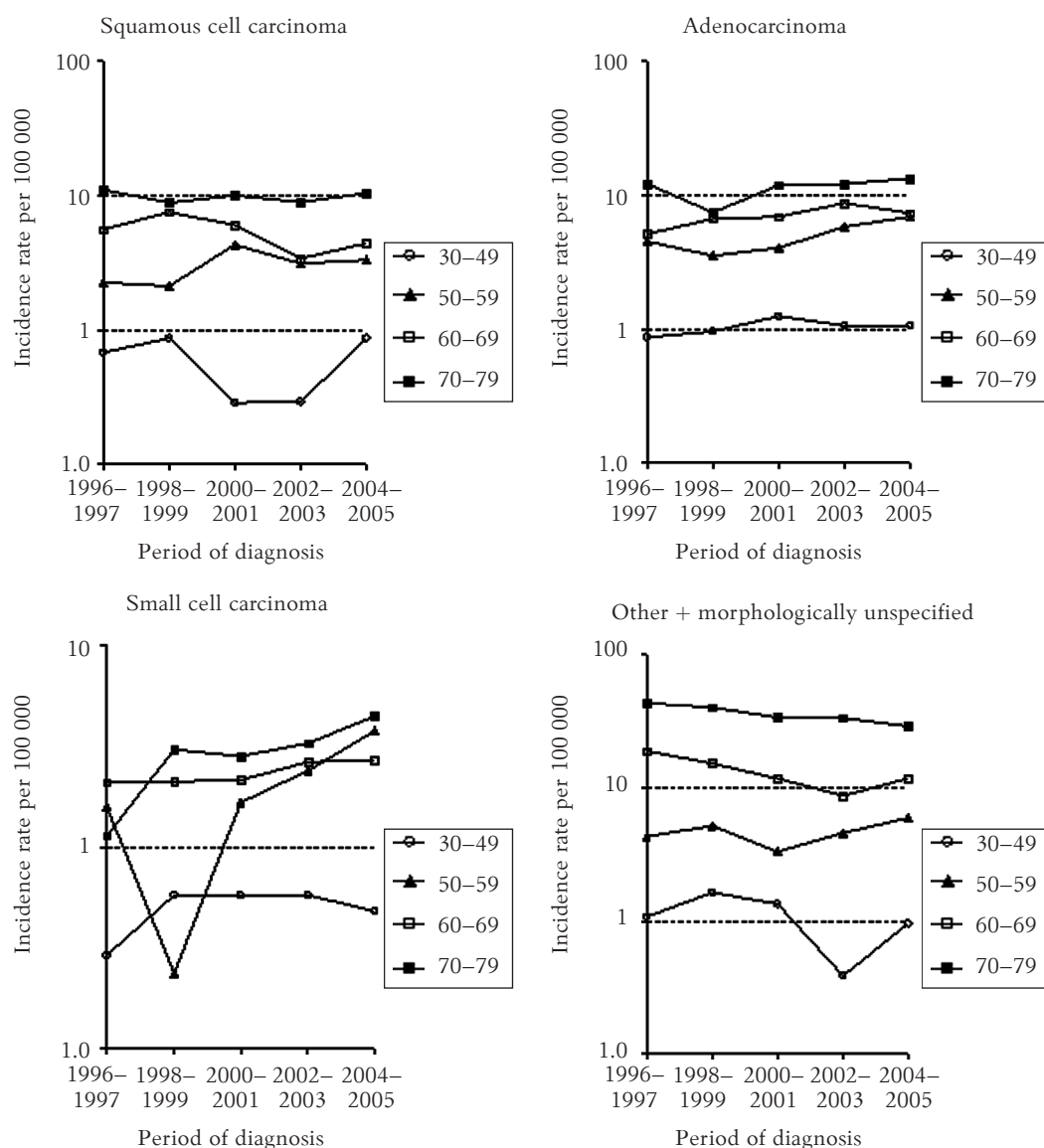


Fig. 4. Trends in age-specific lung cancer incidence rates by period of diagnosis and histological type in women in Lithuania during 1996–2005

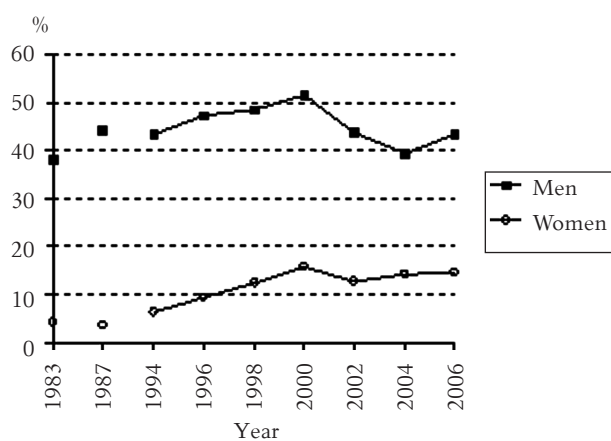


Fig. 5. Smoking prevalence in Lithuania during 1983–2006 (1, 14–18)

served. Adenocarcinoma was the most common type of lung cancer among women in Lithuania. Increasing rates in adenocarcinoma and small cell carcinoma were observed, whereas the incidence of squamous cell carcinoma remained relatively constant.

A decreasing trend in overall lung cancer and squamous cell carcinoma incidence rates and an increasing trend in adenocarcinoma incidence rates among men in Lithuania are in agreement with changes reported in other studies, although in Lithuania the leveling off of lung cancer rates in men began later (7, 8, 23, 24). The declining trends in lung cancer incidence were not parallel with smoking prevalence, which remained high among men. It has been previously suggested that decreasing rates for squamous cell carcinoma and increasing for adenocarcinoma might be the result of switching from nonfilter to filter cigarettes (which were not avail-



able before 1960), when people inhale deeper and smoke more frequently to get the same amount of nicotine (7). Filter cigarettes block the passage of bigger particles of smoke, which lodge in the major bronchi and cause squamous cell carcinoma; however, they allow the passage of small particles, which reach the small airways and cause adenocarcinoma. Due to the extremely high tar content of cigarettes in Lithuania, very high risks were found in comparison with other European countries in the 1980s: the relative risk associated with smoking was 21.2 for smokers and 14.0 for ex-smokers (15). Reductions in tar content could be another explanation for the declining squamous cell carcinoma incidence rates in the present study. However, the increasing tobacco consumption among men suggests that a reversal of the currently declining trends in lung cancer incidence among men may be expected.

The increasing rates of adenocarcinoma among women in Lithuania display a similar pattern to those in many European countries and Japan (7, 10, 25). The comparatively low and stable overall lung cancer incidence rates among Lithuanian women contrast with a rapid increase in rates observed over the last few decades in many European countries, the United States, and Japan (8, 11, 26). Tobacco use among Lithuanian women, particularly the young, has increased, although they smoke less in comparison with women in many European countries, where around 30% of women are smokers (27). The unusual increase in lung cancer incidence among women aged 50–59 years in Lithuania is similar to that documented among women in Belgium. This indicates the need for smoking cessation interventions specifically aimed at middle-aged women (6). The long period of time between the onset of smoking and the occurrence of lung cancer may be the reason for the low and stable lung cancer incidence rates – it is likely that women in Lithuania are still in the early phase of an epidemic. An increasing incidence of lung cancer may be predicted in the near future (5–10 years) if the current unfavorable smoking pattern among women continues. Risk factors other than smoking, including hormonal and infectious factors, were related to the increased risk of lung cancer; however, their effect on trends in lung cancer incidence remains to be elucidated (28, 29).

The present study has several weaknesses. The analysis of trends by histological type is limited by the small number of cancer cases, and particularly by the high proportion of morphologically unspecified

lung cancers. This could obscure the time trends, particularly when the proportion of cases with missing information on histological type declined over time. Changes in classification, improvements in diagnostic techniques, and increasing numbers of tumors that have been morphologically specified may explain some increase in adenocarcinoma incidence; however, to what extent, it remains unknown (23). An increase in the incidence of adenocarcinoma in Lithuania is similar to patterns observed in many countries, which is unlikely to be only due to diagnostic advances and suggest real changes in rates (4, 7, 11, 23). Further studies are needed to investigate the reasons for the observed trends.

### Conclusions

Overall lung cancer incidence rates decreased among men and were stable among women in Lithuania during 1996–2005. Squamous cell carcinoma and adenocarcinoma were the most common types of lung cancer among men and women, respectively. Squamous cell carcinoma incidence rates decreased among men, whereas the incidence rates for adenocarcinoma increased. Among women, the incidence rates for adenocarcinoma increased, and the rates of squamous cell carcinoma remained relatively stable. The decreasing squamous cell carcinoma rates among men and increasing adenocarcinoma rates among men and women are similar to those reported in other European countries and may be due to a shift from nonfilter type cigarettes to filter type. The available data indicate that the tobacco control measures in Lithuania did not result in significant reductions in tobacco use. Therefore, a reversal of the currently declining trend in lung cancer incidence among men and increasing rates of lung cancer among women may be expected if current smoking trends continue. In order to avert these, effective smoking prevention programs and cessation interventions are essential in Lithuania, particularly among men and young and middle-aged women.

### Acknowledgments

We would like to thank Dr. Giedrė Smailytė from the Lithuanian Cancer Registry for the critical review of this manuscript. The authors would also like to express their gratitude to Mr. Joseph Everatt for his help in improving the language.

### Statement of Conflict of Interest

The authors state no conflict of interest.

## Cigarečių rūkymas ir sergamumo plaučių vėžiu pokyčiai Lietuvoje: tyrimas pagal histologinius navikų tipus

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**Raktažodžiai:** plaučių vėžys, sergamumas, rūkymas.

**Santrauka.** *Tyrimo tikslas* – įvertinti sergamumo plaučių vėžiu pokyčius Lietuvoje 1996–2005 m. pagal histologinius plaučių piktybinių navikų tipus. Rezultatai vertinti atsižvelgiant į rūkymo paplitimo pokyčius.

*Medžiaga ir metodai.* Buvo naudoti Lietuvos vėžio registro duomenys apie sergančiuosius piktybiniais trachėjos, bronchų ir plaučių piktybiniais navikais. Buvo vertinamas sergamumas šių histologinių tipų plaučių vėžiu: plokščialąsteline karcinoma, adenokarcinoma, smulkiųjų ląstelių karcinoma, kitais bei nenurodyto histologinio tipo navikais. Sergamumo rodikliai buvo standartizuoti pagal Pasaulio standartinę populiaciją. Duomenys apie rūkymo paplitimą Lietuvoje gauti iš įvairių publikuotų šaltinių.

*Rezultatai.* Vyrams plokščialąstelinė karcinoma buvo dažniausiai diagnozuojamas plaučių piktybinių navikų histologinis tipas. Sergamumas plokščialąsteline karcinoma mažėjo nuo 25 atvejų 100 000 gyventojų 1998–1999 m. iki 19 atvejų 100 000 gyventojų 2004–2005 m.; sergamumas adenokarcinoma ir smulkiųjų ląstelių karcinoma didėjo iki 7 atvejų 100 000 gyventojų 2002–2003 m., vėliau nekito. Adenokarcinoma buvo dažniausias moterų plaučių piktybinių navikų histologinis tipas. Nustatytas moterų sergamumo adenokarcinoma padidėjimas. Sergamumas plokščialąsteline karcinoma išliko stabilus. Reguliariai rūkančių vyrų ir moterų procentas didėjo iki 2000 m. ir buvo atitinkamai 51,5 ir 15,8 proc. Cigarečių be filtro rūkymas sumažėjo, o cigarečių su filtru – padidėjo.

*Išvados.* Mažėjantis vyrų sergamumas plokščialąsteline karcinoma ir didėjantis vyrų ir moterų sergamumas adenokarcinoma yra panašus į nustatytus pokyčius kitose Europos šalyse. Šie pokyčiai, tikėtina, yra susiję su cigarečių su filtru atsiradimu ir jų rūkymu.

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*Received 28 June 2010, accepted 14 April 2011*

*Straipsnis gautas 2010 06 28, priimtas 2011 04 14*