

# Cancer mortality trends in Lithuania 1978–2005: a joinpoint regression analysis

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The aim of this study was to analyse changes in cancer mortality in Lithuania from 1978 to 2005.

**Materials and methods.** Age-standardised mortality (World standard) rates were calculated for all the malignant neoplasms as well as for stomach, colorectal, lung, prostate, breast and cervical cancers. A joinpoint regression methodology was used to provide estimated annual percentage changes (EAPCs) and to detect points in time where significant changes in the trends occurred.

**Results.** Analysis showed a trend toward mortality reduction for some cancer sites. In males, mortality reduction for all cancer sites combined started from 1995, while in females no significant decrease in mortality trend was revealed for all cancer sites. Colorectal and lung cancer mortality in both sexes as well as female breast cancer mortality rates were increasing and, after a change in trend, started to decrease or levelled off. An increasing trend was observed for female cervical and male prostate cancers, whereas a decreasing one was seen for stomach cancer in both sexes.

**Conclusion.** In Lithuania, reduction and stabilisation in mortality rates occurred during recent years because of causes amenable to primary prevention through reduction of exposures (stomach and lung cancers) and tertiary prevention owing to improved treatment and medical care (breast cancer). Recent introduction of population-based screening interventions for cervix and breast cancers will probably contribute to the downward mortality trends in females over the next years. There is also a need for organized colorectal cancer screening programme in Lithuania.

**Key words:** cancer mortality, age-standardised rates, joinpoint analysis, estimated annual percentage changes

## INTRODUCTION

Cancer is a global problem that is particularly evident in economically developed, industrialized countries such as those of the European Union, where large proportions of the population are elderly and have an elevated risk of cancer. The analysis of mortality trends is an important tool to monitor cancer control and to evaluate the outcomes of modifications in population lifestyle, environmental risks as well as the effectiveness of health care. Examination of trends in cancer mortality in Europe over the past 30 years has shown that, after long-term rises, age-standardised mortality from most common cancer sites has fallen in the EU since the late 1980s (1).

Cancer is the second most frequent cause of death in Lithuania like in other European countries. Cancer mortality in Lithuania has been increasing year by year. However, mortality rates of major cancer sites during the past years showed a decreasing tendency (2). Declining cancer mortality rates could

indicate that cancer prevention activities have been successfully designed and implemented, they could also indicate favourable results of the improved therapeutic procedures applied as well as successful early detection programs. The increase in mortality rates can indicate failures in controlling cancer risk factors and/or appearance of the new ones. Hence, analysis of cancer mortality time trends and patterns in a given population can be helpful in assessing successes, failures and future needs in cancer control programs. A joinpoint regression analysis was employed for this study (a non-linear regression modelling known as piece-wise or segmented regression). This approach was chosen to allow for detecting points in time when significant changes in the direction of a trend occurred as well as to assess average percentage changes in mortality rates.

The aim of this study was to analyze changes in cancer mortality trends in Lithuania during the period 1978–2005 using joinpoint regression models (3).

## MATERIALS AND METHODS

Data of the Department of Statistics for the years 1978–1992 and materials of the Lithuanian Cancer Registry for the years

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1993–2005 were used to analyse cancer mortality trends. Cancer mortality statistics is based on the underlying cause of death as reported on the medical certificate of death by the certifying physician. During the period 1978–1992, cancer mortality statistics was officially reported only for eight individual cancer sites: stomach, colon, rectum, larynx, lung, breast, cervix and prostate. Other cancer sites were combined into broad categories and tabulated. The Department of Statistics is responsible for the publication of the entire mortality statistics of broad categories of the causes of death. The Lithuanian Cancer Registry produces more extensive cancer statistics that is necessary to use as a cancer control measure. The causes of death were coded according to the International Classification of Diseases, 9<sup>th</sup> revision, for the period 1993–1997, and according to the International Classification of Diseases, 10<sup>th</sup> revision, for the period 1998–2005. The corresponding population data, by age, sex and year were available from the Department of Statistic of the Republic of Lithuania.

The mortality rates for all cancer sites – cancers of stomach, colon and rectum, larynx, lung, breast, cervix and prostate – were analyzed for the period 1978–2005. Crude mortality rates and age-standardised rates were calculated for both sexes.

Standardization was performed using the direct method (world standard population).

The joinpoint regression analysis was used to identify the points where a statistically significant change over time in linear slope of the trend occurred (3). Analysis starts with the minimum number of joinpoints and tests whether one or more joinpoints are statistically significant and should be added to the model. The tests of significance use the Monte Carlo permutation method. In the final model, each joinpoint indicates a statistically significant change in trend, and an estimated annual percentage change (EAPC) is computed for each of those trends by means of generalized linear models. A maximum number of 3 joinpoints was allowed for estimations. Joinpoint software version 2.6 was used (4).

## RESULTS

Results of the joinpoint analyses by sex and cancer site, applied to mortality rates in the period from 1978 to 2005, are reported in Table.

For all the sites combined in males a significant joinpoint was found (Fig. 1); standardised rates significantly increased up

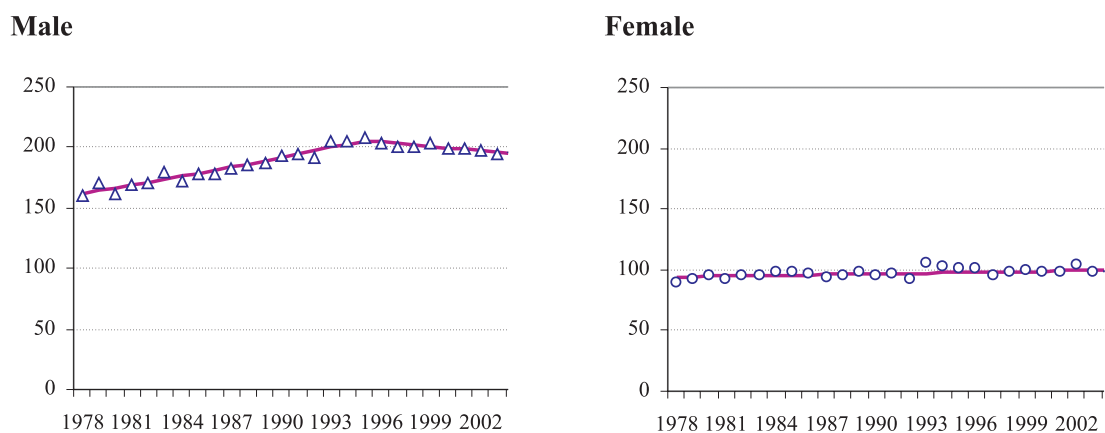


Fig. 1. Observed standardized rates per 100,000 population and 'best' joinpoint model estimates for all cancer sites combined by gender

Table. Joinpoint analysis by sex and cancer site in Lithuania, 1978–2005

Site (ICD-10)	Sex	Period	EAPC	95% Confidence interval	
All sites C00–C99	M	1978–1995	1.42	1.23	1.62
	M	1995–2005	-0.58	-1.02	-0.15
Stomach C16	F	1978–2005	0.23	0.07	0.39
	M	1978–2005	-2.61	-2.81	-2.41
Colon-rectum C18–C21	F	1978–2005	-2.83	-3.8	-2.59
	M	1978–1990	3.89	3.00	4.78
	M	1990–2005	0.82	0.20	1.44
	F	1978–1991	2.32	1.23	3.41
Lung C33–C34	F	1991–2005	-0.73	-1.67	0.22
	M	1978–1993	2.15	1.70	2.59
	M	1993–2005	-1.95	-2.54	-1.35
Breast C50	F	1978–1984	5.26	0.46	10.36
	F	1984–2005	-0.41	-1.12	0.30
Cervix C53	F	1978–1994	1.81	1.23	2.41
	F	1994–2005	-0.51	-1.51	0.50
Prostate C61	F	1978–2005	1.00	0.59	1.41
	M	1978–2005	3.14	2.86	3.43

• Only significant joinpoints ( $p < 0.05$ ) were retained in final models for each site.

to 1995 by 1.42% per year (95% CI from 1.23 to 1.62) and decreased thereafter by  $-0.58\%$  (95% CI from  $-1.02$  to  $-0.15$ ). In females, the rate was increasing on average by  $0.23\%$  (95% CI from 0.07 to 0.39) each year during all the observation period.

Stomach cancer showed decreasing mortality trends in both sexes. It was constantly decreasing in both males and females during all the study period (EAPC =  $-2.61$  and EAPC =  $-2.83$ , respectively) (Fig. 2).

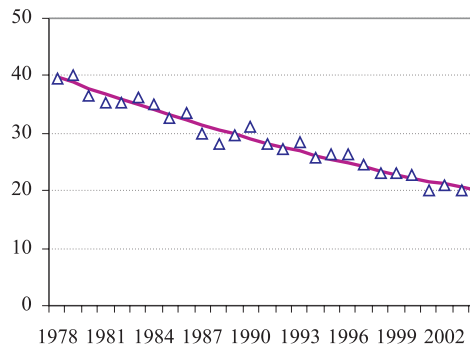
Colorectal cancer mortality trend showed significant joinpoints for both sexes: in females, a significant joinpoint was located in 1991: the curve was first rising by  $2.32\%$  per year and later decreasing insignificantly by  $0.73\%$  per year (Fig. 3). In

males, colorectal cancer mortality increased up to the year 1990 by  $3.89\%$ , the increase slowed down to  $0.82\%$  per year.

A significant joinpoint was found for male lung cancer mortality trend in the year 1993; mortality rates were increasing until 1993 at an EAPC of  $2.15\%$  and decreasing thereafter at an EAPC equal to  $1.95\%$ . Among women, the rates increased over the period 1978–1984 with an EAPC equal to  $5.26\%$  (95% CI from 0.46 to 10.36) and stabilized thereafter, decreasing by  $0.41\%$  (Fig. 4). Only the first slope was statistically significant.

A joinpoint for female breast cancer mortality was detected in 1994 (Fig. 5). Breast cancer mortality increased by  $1.81\%$  (95% CI from 1.23 to 2.41), and in 1994 levelled off (EAPC =  $-0.51\%$ ).

**Male**



**Female**

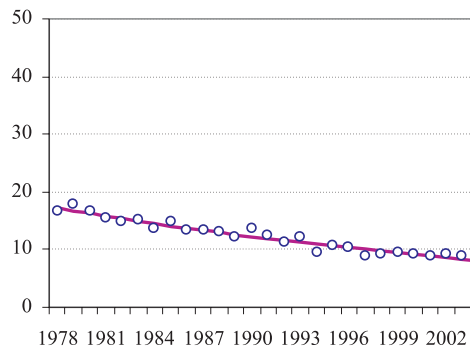
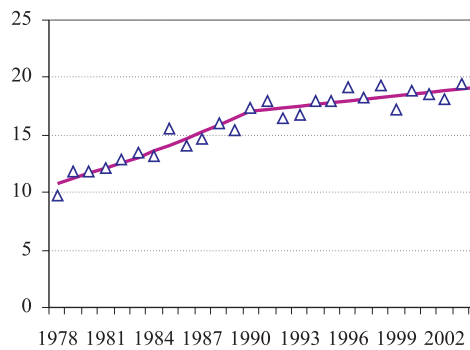


Fig. 2. Observed standardized rates per 100,000 population and 'best' joinpoint model estimates for stomach cancer by gender

**Male**



**Female**

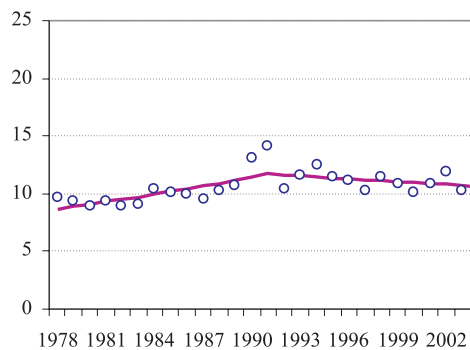
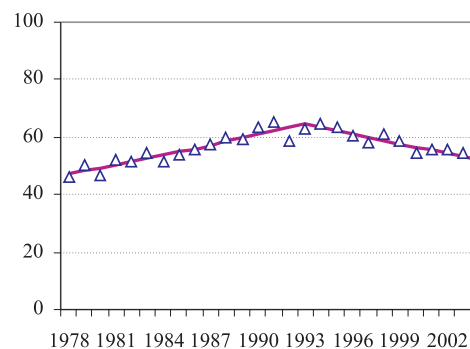


Fig. 3. Observed standardized rates per 100,000 population and 'best' joinpoint model estimates for colorectal cancer by gender

**Male**



**Female**

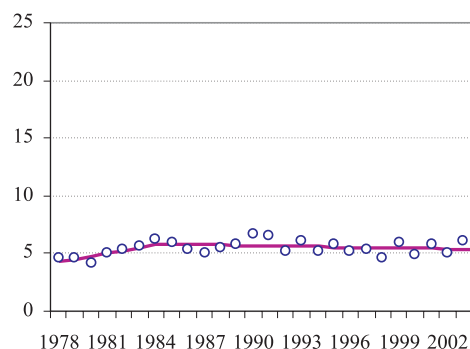


Fig. 4. Observed standardized rates per 100,000 population and 'best' joinpoint model estimates for lung cancer by gender

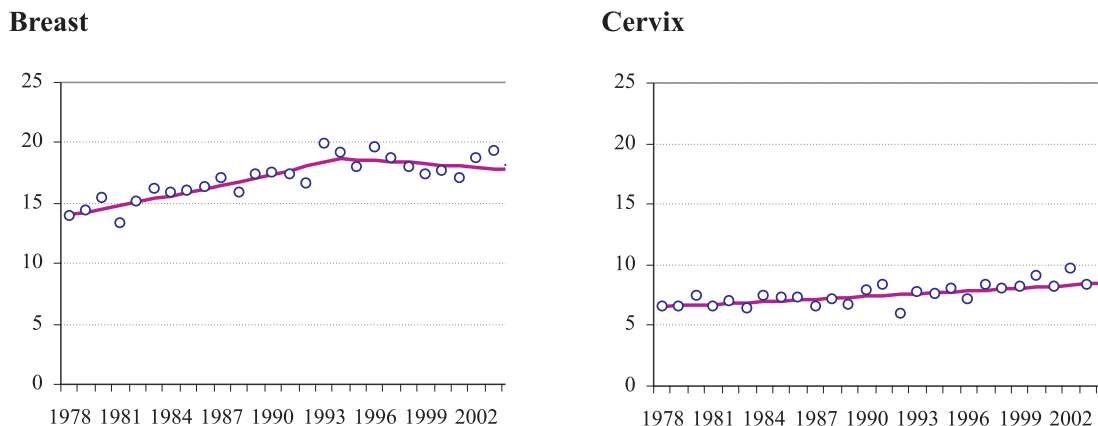


Fig. 5. Observed standardized mortality rates per 100,000 population and 'best' joinpoint model estimates for female breast and cervical cancers

### Prostate

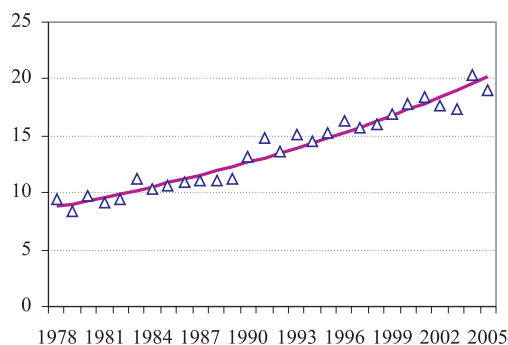


Fig. 6. Observed standardized mortality rates per 100,000 population and 'best' joinpoint model estimates for prostate cancer

Among female cancers, no significant joinpoints were found for cervical cancer (Fig. 5). Mortality rates were linearly increasing (EAPC = 1.00, 95% CI from 0.59 to 1.41).

The prostate cancer mortality was linearly increasing over all the study period by 3.14% per year, and the slope was significant (Fig. 6).

## DISCUSSION

The present analysis showed a trend toward mortality reduction for some cancer sites. In males, a mortality reduction for all the cancer sites combined started since 1995. The observed decrease in male cancer mortality trend is in agreement with the data from other countries (5, 6). In females, no significant decrease in trend was revealed for all sites cancer mortality. Among the selected cancer sites, mortality trends with one joinpoint were detected for colorectal and lung cancers in both sexes and breast cancer in females. Cancer mortality rates were increasing and after a change in trend started to decrease or levelled off. For the remaining study sites a significant, approximately linear (i. e. without joinpoints) trend was observed to be increasing for cervical and prostate cancers and decreasing for stomach cancer in both sexes.

Major reductions in cancer mortality and morbidity are believed to be dependent on the widespread adoption of cancer prevention behaviours and use of early detection services. The mortality rates are affected by changes in cancer incidence be-

cause of the changing exposure to the environmental carcinogens as well as by the improvement in the diagnostic and treatment approaches which were followed by increasing survival and decreasing mortality rates.

The change in the overall cancer mortality is the result of balance of trends for different cancer sites. In most west European countries, total cancer mortality decreases because of the decline in: lung cancer mortality for males; stomach cancer for both sexes; cervical cancer for women as well as some decline in breast and colorectal cancers (7). In Lithuania, decreasing cancer mortality in males was contributed by the decrease of the rates of lung and stomach cancer in males. Concerning females, cancer mortality rate was increasing during all the observation period. Stabilization in female breast, stomach and colorectal cancer mortality has not contributed to the overall cancer mortality trend. Mortality rates were increasing for prostate and cervical cancers.

A substantial decrease in mortality has occurred for stomach cancer in both sexes. The trend, therefore, corresponds to unplanned prevention through the changes in the environmental factors occurring since the middle of the 20<sup>th</sup> century. The exact causes of the decrease of stomach cancer mortality are not well understood, but must include improvements in diet, food storage (e. g. refrigeration) and, possibly, the decline of *Helicobacter pylori* infection (10). Therefore, it cannot be regarded as an outcome of the fight against cancer.

The reduction in the number of lung cancer deaths among males was the major contributor to the overall decline in the number of cancer deaths in males in Lithuania. Trends in lung cancer mortality could reflect the reduced smoking trends in the population. Thus, the decline in lung cancer mortality is due to the slow, but steady, decline in smoking rates among men and to the composition of cigarettes. In contrast, the lack of progress in reducing smoking among females has led to stable lung cancer mortality rates.

Mortality rates for breast cancer, the most common cancer in females in Lithuania, have levelled off recently, partially because of an improved treatment. The fall in breast cancer mortality observed in most European countries over the last decade has to be attributed to the earlier detection and improved treatment (8). The mammography screening programme in Lithuania started in 2005 and has not contributed to the observed stabilization of breast cancer mortality in the years 1994–2005. Treatment

improvements mostly contributed to mortality reduction because a favourable trend appeared before the introduction of the screening program; further improvements are expected as a consequence of introducing the screening (9).

In Europe from 1997 to 2002, appreciable declines were observed in mortality from colorectal cancer in both males and females (1). Colorectal cancer trends have been generally more favourable for females than for males. In Lithuania, mortality rates for male colorectal cancer were increasing during all the observation period. The mortality rates in females were increasing until the year 1991; and remained stable during the years 1991–2005. Changes in dietary habits, diagnostic and therapeutic improvements for precancerous lesions may have contributed to the observed changes in mortality trends.

The cervical cancer mortality in Lithuania is the highest among the EU countries. The drop of the rates in cervical cancer mortality in Europe was mainly due to screening. In Lithuania, the national cervical cancer screening programme started in the year 2004 and has not yet contributed to the cervical cancer mortality rates. The changes in the risk factors, such as sexual behaviour and smoking habits, over the decades might partially explain trends in cervical cancer mortality.

Prostate cancer mortality from 1997 to 2002 decreased in Europe by –1.4% per year (1). However, increase of prostate cancer mortality by 3.14% per year was observed in Lithuania. Both an improvement in the diagnosis and registration, and an increase in risk factors exposure may explain the rising trend in prostate cancer mortality.

In Lithuania, reduction and stabilisation in mortality rates during recent years occurred because of the causes amenable to primary prevention through reduction of exposures (stomach and lung cancers) and tertiary prevention owing to improved treatment and medical care (breast cancer). These changes have not been achieved through the planned interventions.

During the period 1978–2005 there were no nation-wide cancer screening programmes. Some small scale opportunistic activities were established on cervical, breast or colon cancer. The PSA testing became widely available around 2000. Population-wide screening interventions for the prevention of breast and cervical cancer have been introduced since 2005 and 2004, respectively. The introduction of organised cervical and mammographic screening programmes in Lithuania will lead to a reduction in breast and cervical cancer mortality. Similarly, screening for colorectal cancer has been shown to be effective, and there is a need for organized colorectal cancer screening programme in our country.

## CONCLUSIONS

In Lithuania, cancer mortality rates, after an increase in the years from 1978 to 1995, started decreasing since 1995 in the male population but were increasing in female population during the period 1978–2005. Among males, declining mortality due to smoking-related cancers and gastric cancer determined a favourable trend. In Lithuania, reduction and stabilisation in mortality rates during recent years developed because of causes amenable to primary prevention through reduction of exposures (stomach and lung cancers) and tertiary prevention through im-

proved treatment and medical care (breast cancer). The recent introduction of population-based screening interventions for cervix, breast cancers will probably contribute to the downward mortality trends in females over the next years. Besides, there is a need for organized colorectal cancer screening programme in Lithuania.

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## MIRTINGUMO TENDAI LIETUVOJE 1978–2005 M.: LŪŽIO TAŠKŲ REGRESINĖ ANALIZĖ

*Santrauka*

Šio tyrimo tikslas išnagrinėti mirtingumo nuo vėžio pokyčius Lietuvoje 1978–2005 metais.

**Medžiaga ir metodai.** Apskaičiuoti visų piktybinių navikų – skrandžio, storosios žarnos, plaučių, prostatos, krūties ir gimdos kaklelio vėžio – standartizuoti mirtingumo rodikliai (pasaulio standartas). Lūžio taškų regresinės analizės metodu buvo įvertinti vidutiniai metiniai pokyčiai ir nustatyti lūžio taškai, kur įvyksta statistiškai reikšmingi trendo krypties pokyčiai.

**Rezultatai.** Nustatytas mirtingumo nuo kai kurių vėžio lokalizacijų sumažėjimas. Vyrų mirtingumas nuo visų piktybinių navikų pradėjo mažėti 1995 m., moterims nebuvo nustatytas mirtingumo rodiklių mažėjimas. Tarp nagrinėtų piktybinių navikų lokalizacijų mirtingumo tenduose nustatytas vienas abiejų lyčių storosios žarnos ir plaučių vėžio bei moterų krūties vėžio lūžio taškas. Mirtingumo rodikliai didėjo iki nustatyto lūžio taško, o vėliau stebėtas mažėjimas arba stabilizavimasis. Kitiems piktybiniam navikams nustatyti tiesiniai trendai (be lūžio taškų): stebėtas moterų gimdos kaklelio ir vyrų prostatos vėžio atvejų daugėjimas, o vyrų ir moterų skrandžio vėžio – mažėjimas.

**Išvados.** Lietuvoje stebėtas mirtingumo mažėjimas ar stabilizavimasis dėl navikų pirminės profilaktikos priemonių mažinančią ekspoziciją (plaučių ir skrandžio vėžys) ir tretinės profilaktikos priemonių tobulinančią gydymo metodus (krūties vėžys). Pastaraisiais metais pradėtos populiacinės gimdos kaklelio ir krūties vėžio profilaktikos programos turėtų prisidėti ateityje mažinant mirtingumą nuo vėžio. Taip pat Lietuvoje būtina pradėti organizuotą storosios žarnos vėžio patikros programą.

**Raktažodžiai:** mirtingumas nuo vėžio, standartizuoti rodikliai, lūžio taškų analizė, vidutinis metinis pokytis