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## Original Research Article

# Prostate cancer trends in Latvia during 1990–2012: Incidence, prevalence, mortality, and survival rates

Juris Plonis<sup>a</sup>, Kristaps Bokums<sup>a,\*</sup>, Vinita Cauce<sup>b</sup>, Edvins Miklasevics<sup>c</sup>, Peteris Vaganous<sup>a</sup>, Arvids Irmejs<sup>c</sup>, Janis Gardovskis<sup>a,c</sup>, Egils Vjaters<sup>a,c</sup>

<sup>a</sup> Center of Urology, Pauls Stradins University Hospital, Riga, Latvia

<sup>b</sup> Medical Faculty, Riga Stradins University, Riga, Latvia

<sup>c</sup> Institute of Oncology, Pauls Stradins University Hospital, Riga, Latvia

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## ABSTRACT

**Background and objective:** Prostate cancer (PCa) is one of the most common form of cancer in males worldwide. One of the highest PCa-related mortality rates in the world is observed in Latvia.

**Materials and methods:** Our study included male patients diagnosed with PCa between 1990 and 2012. We analyzed incidence, prevalence and mortality trends using joinpoint analysis. Kaplan–Meier analysis was performed for 5-, 10-, 15- and 20-year overall survival and cancer-specific survival rates.

**Results:** A total of 14,083 PCa patients with a mean age of initial PCa diagnosis being 70.1 (SD 8.6) was registered. The standardized incidence rates (per 100,000) increased from 18.9 in 1990 to 74.7 in 2012, while the standardized prevalence rates (per 100,000) increased from 69.9 in 1990 to 437.6 in 2012. Standardized PCa mortality rates (per 100,000) also rose from 13.2 in 1990 to 27.2 in 2006 followed by statistically insignificant decrease continuing up to 2012. The mean 5-year cancer-specific survival rates increased from 43.6% in 1990 to 70.7% in 2007, and the mean 10-year cancer-specific survival rates from 32.9% in 1990 to 40.5% in 2001. **Conclusions:** This study revealed that the incidence, prevalence and mortality rates increased between 1990 and 2012, and although the 5- and 10-year overall and cancer-specific survival rates improved over the reviewed period they still needed to get better.

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\* Corresponding author at: Center of Urology, Pauls Stradins Clinical University Hospital, Pilsonu 13, 1002 Riga, Latvia.

E-mail address: [bokumsk@gmail.com](mailto:bokumsk@gmail.com) (K. Bokums).

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## 1. Introduction

Over the last two decades, prostate cancer (PCa) has become one of the most common forms of cancer worldwide. In 2012, despite improved early diagnosis and innovative treatments, there were 28,000 PCa-related deaths in the United States only [1]. In fact, because of improved early diagnosis, population aging and environmental pollution, PCa will be first diagnosed in twice as many males in the next two decades as were diagnosed in 2008, when PCa was found in about 899,000 males worldwide [2]. The accumulated data show that, along with age and genetics, race is a very important factor affecting PCa incidence [3]. In some regions such as Northern Africa and South America, the incidence of PCa is less frequent. Usually the PCa incidence rates, as well as PCa-related mortality rates, are higher in the developed world: the United States, Canada, Australia, and some European countries [4]. There have been several publications analyzing PCa incidence and mortality data for Europe, as well as the world in general, where some information on Latvia is given [5,6]. The data provided testify to the fact that PCa mortality rates for Latvia (as well as other Baltic states) are the highest in Europe [5,6].

Our current study is based on the first comprehensive PCa epidemiology analysis carried out in Latvia over the 23-year period. It reveals trends in PCa incidence, prevalence and mortality, 5-, 10-, 15-, and 20-year overall survival (OS) and cancer-specific survival (CSS) rates.

## 2. Materials and methods

Our study included 14,805 PCa patients diagnosed between 1990 and 2012. The data on PCa were collected from a database in the Latvian Center for Disease Prevention and Control (LCDPC) which in its turn had inherited the database of the Latvian Cancer Register founded in 1973. The LCDPC has been accumulating and regularly updating all cancer-related information for the whole country with a population of about 2 million. The LCDPC data on PCa were subjected to retrospective analysis. The study was approved by the Riga Stradins University Research Ethics Committee. The youngest patient diagnosed with PCa was 25 years old, the oldest, 97 years old. Six patients aged from 1 to 24 years, diagnosed with embryonic prostate cysts in the last 20 years and also included in the LCDPC register, were excluded from our study.

PCa patients were grouped and categorized in 10-year age bands within which age-specific incidence, prevalence and mortality rates were analyzed. As there were only 31 patients younger than 45 years, they were excluded from the age-specific analysis as a statistically insignificant group and therefore we ended up having the following groups: <60, 60–69, 70–79, 80+. We standardized our data on incidence, prevalence and mortality rates proceeding from the World Health Organization (WHO) data published for the standard world population in 2000 [7]. The data on the Latvian population were obtained from the Central Statistical Bureau of Latvia (CSB) updated after the latest Population and Housing Census of 2011.

## 2.1. Statistical methods

Values for continuous variables were reported as the mean  $\pm$  standard deviation. Performing descriptive analysis, 95% confidence intervals were reported for PCa groups. We examined trends in PCa incidence, prevalence, and mortality using joinpoint regression analysis (Joinpoint Regression software, version 4.04, of May 2013, available through the Surveillance Research Program of the US National Cancer Institute). The log-transformation was used to analyze the trends of, age standardized and age specific rates. A number of joinpoints were set between 0 and 4. Grid Search method was selected. The permutation test was used to select the best joinpoint models. Significance level was of 0.05 and the number of permutation was 4499 as default [8]. Kaplan–Meier analysis was performed for 5-, 10-, 15- and 20-year OS and CSS rates. Over the said period there were 754 PCa cases (5% of the total PCa number) diagnosed *post mortem* and not included in the OS and CSS analyses. To avoid OS and CSS year-to-year fluctuations these rates were calculated as three year average values.

SPSS 20.0 was applied for all data analyses.

## 3. Results

From 1990 to 2012, there were 14,083 patients first diagnosed with PCa whose mean age was 70.1 years (SD 8.6) with the mean age at death being 74.8 years (SD 9.0) (Fig. 1). Of the 8161 PCa patients who died over the period under review, 72% ( $n = 5864$ ) had PCa-related deaths.

The standardized incidence rates (per 100,000) increased from 18.9 in 1990 to 74.7 in 2012. There were three join points observed indicating 2 periods with a statistically significant annual percentage change (APC): 10.2% from 1994 to 2005 and 4.7% from 2008 to 2012 (Table 1). As far as PCa incidence rates by age groups are concerned, APC for the <60 age group remained stable at 10.2% during the whole of the reviewed period. The largest fluctuations occurred in the 70–79-year-old group. The greatest APC of 13.0% was registered in the 60–69-year-old group from 1997 to 2006 (Table 1).

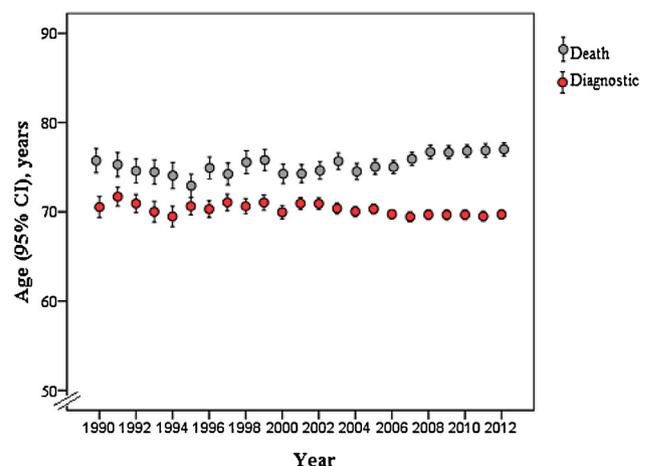


Fig. 1 – Mean age with 95% confidence interval at PCa diagnosis and death.

**Table 1 – Prostate cancer incidence, prevalence and mortality trends in Latvia 1990–2012 (joinpoint analysis: ASR, by age group).**

	Trend 1		Trend 2		Trend 3		Trend 4		AAPC
	Years	APC	Years	APC	Years	APC	Years	APC	1990–2012
<b>Incidence</b>	1990–1994	0.3 <sup>†</sup>	1994–2005	10.2 <sup>†</sup>	2005–2008	–2.4	2008–2012	4.7 <sup>†</sup>	5.9 (4.5–7.3) <sup>*</sup>
Age group, years									
<60	1990–2012	10.2 <sup>*</sup>							10.2 (9.0–11.4) <sup>*</sup>
60–69	1990–1997	3.5 <sup>*</sup>	1997–2006	13.0 <sup>*</sup>	2006–2012	4.2 <sup>†</sup>			7.5 (6.2–8.9) <sup>*</sup>
70–79	1990–1994	2.6 <sup>†</sup>	1994–2005	9.3 <sup>†</sup>	2005–2009	–4.6	2009–2012	6.3 <sup>†</sup>	5.0 (3.3–6.8) <sup>*</sup>
80+	1990–2003	8.1 <sup>†</sup>	2003–2012	0.5 <sup>†</sup>					4.9 (3.3–6.6) <sup>*</sup>
<b>Prevalence</b>	1990–1997	5.4 <sup>†</sup>	1997–2005	11.4 <sup>†</sup>	2005–2012	8.0 <sup>†</sup>			8.4 (7.5–9.2) <sup>*</sup>
Age group, years									
<60	1990–1997	3.4 <sup>†</sup>	1997–2012	14.8 <sup>*</sup>					11.1 (8.8–13.4) <sup>*</sup>
60–69	1990–1997	4.4 <sup>†</sup>	1997–2012	13.6 <sup>*</sup>					10.6 (9.0–12.2) <sup>†</sup>
70–79	1990–1996	3.1 <sup>†</sup>	1996–2005	10.8 <sup>*</sup>	2005–2012	7.6 <sup>*</sup>			7.6 (6.6–8.7) <sup>†</sup>
80+	1990–2004	9.1 <sup>†</sup>	2004–2012	4.0 <sup>†</sup>					7.2 (6.7–7.6) <sup>*</sup>
<b>Mortality</b>	1990–2006	4.8 <sup>†</sup>	2006–2012	–0.9					3.2 (2.1–4.3) <sup>*</sup>
Age group, years									
<60	1990–2012	1.9 <sup>†</sup>							1.9 (0.2–3.7) <sup>†</sup>
60–69	1990–2012	2.8 <sup>†</sup>							1.6 (1.2–4.0) <sup>†</sup>
70–79	1990–2006	4.7 <sup>†</sup>	2006–2012	–2.5					2.7 (1.5–3.9) <sup>*</sup>
80+	1990–2012	4.9 <sup>†</sup>							4.9 (4.0–5.9) <sup>*</sup>

APC, annual percent change; AAPC, average annual percent change; ASR, age standardized rate per 100,000.

<sup>\*</sup> P < 0.05.

The standardized prevalence rates (per 100,000) increased from 69.9 in 1990 to 437.6 in 2012 with AAPC 8.4% during the whole period, and 2 join points were observed in 1997 and 2005 (Table 1). Concerning PCa prevalence rates by age groups, the largest AAPC occurred in those under 70 (Table 1).

Standardized PCa mortality rates (per 100,000) also increased from 13.2 in 1990 to 27.2 in 2006 with APC 4.8% followed by statistically insignificant decrease up to 2012 (Table 1). The 70–79-year-old group was the only one showing a statistically insignificant decrease in the mortality rate from 2006 to 2012 (Table 1).

Over the whole period in question, the median CSS was 9.7 years (95% CI, 9.1–10.3) (Fig. 2). The 5- and 10-year OS and

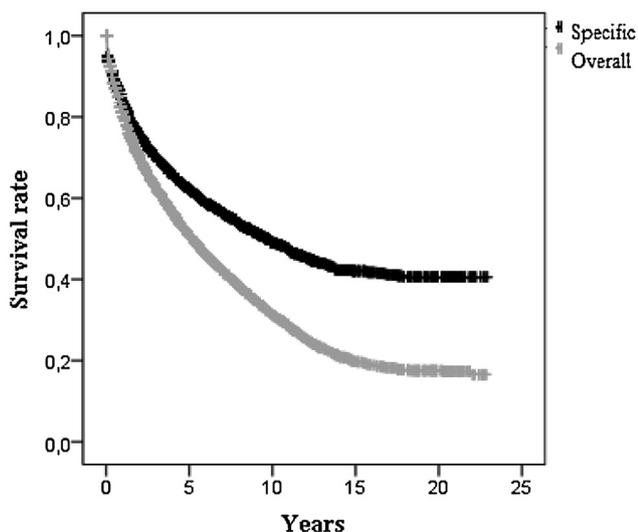
CSS rates calculated from the year of diagnosis are shown in Table 2. The mean 15-year OS rate was 16.7% (95% CI, 14.0%–19.4%) at the beginning compared to 8.5% (95% CI, 6.7%–10.3%) at the end of the reviewed 1990–1997 period. The 20-year OS rate was 15.0% (95% CI, 12.5%–17.5%). The mean 15-year CSS rate was 29.4% (95% CI, 25.7%–33.1%) at the beginning vs. 24.0% (95% CI, 20.7%–27.3%) at the end of the reviewed 1990–1997 period. The 20-year CSS rate (1990–1992) was 28.8% (95% CI, 25.1%–32.5%).

#### 4. Discussion

PCa is one of the most common forms of male cancers worldwide. There are a lot of publications on PCa epidemiology; however as far as Latvia is concerned there has been no comprehensive and detailed study to reflect PCa epidemiology over a period as long as 23 years. The study presented in this article is the largest of its kind ever to be carried out in Latvia, as well as one of the largest ones undertaken in Northern Europe. Apart from that, this research may be of particular interest in the light of the fact that it shows trends in PCa epidemiology for Latvia after the country regained its independence and started applying the European Urology Association guidelines.

And, according to the CSB database of 2012, there were more than 385,000 male deaths in Latvia over the period under review, with 1.5% of them being PCa-related deaths. By comparison, in 1990 PCa-related deaths constituted 5.6% of all cancer death cases, whereas in 2009 the share of PCa-related mortality had already reached 10.8%.

The PCa incidence rates increased over the whole period under review, and the said growth registered since 1994 has resulted from introduction of the PSA test as part of a routine



**Fig. 2 – Overall survival and cancer-specific survival rates.**

**Table 2 – 5- and 10-year survival rates.**

Survival rates		1990–1992	1993–1995	1996–1998	1999–2001	2002–2004	2005–2007
5-year (95% CI)	OS	35.1 (31.8–38.4)	33.2 (29.9–36.0)	41.5 (38.4–44.6)	41.1 (38.2–44.0)	50.6 (48.1–53.1)	58.3 (56.3–60.8)
	CSS	43.6 (39.9–47.3)	40.3 (36.8–43.8)	51 (47.3–54.7)	54 (50.7–57.3)	63.4 (60.9–65.9)	70.7 (68.9–73.2)
10-year (95% CI)	OS	20.7 (17.8–23.6)	19.9 (18.2–21.6)	23.6 (20.5–26.7)	24.4 (21.9–26.9)	–	–
	CSS	32.9 (29.2–36.6)	29.3 (25.8–32.8)	37.7 (33.8–41.6)	40.5 (37.2–43.8)	–	–

practice. However, the speed of incidence growth slowed down after 2006 when the PCa population screening in Latvia was cancelled. As well as in the case of Latvia, the PSA test introduction resulted in globally observed PCa incidence growth, although in the USA, Canada, Australia, and New Zealand, as well as in a number of North-European and Asian countries, the incidence rates have lately stabilized with no statistically significant incidence decrease in the above countries [1,5,6]. We observed higher AAPC in the under-70 patients' group over the whole period in question, which may be attributed to the fact that PSA test, widely used in younger males for early PCa diagnostics, was not so common in case of 70+ patients demonstrating a tendency to avoid testing older males.

In 1990–2012 the PCa prevalence rates showed the same steady increase as that of the incidence rates which can be accounted for by growth in the number of newly diagnosed cases, as well as higher 5- and 10-year OS rates. Forman et al. analyzed the PCa prevalence in the United Kingdom and Scotland, reporting prevalence rates of 210 cases (per 100,000) in the United Kingdom in 1992, and 198 cases (per 100,000) in Scotland in the same year [9]. Another study by Micheli et al. reporting on PCa prevalence in Europe for 1992 showed that Sweden had the highest PCa prevalence rates of 574.8 cases (per 100,000) with the average PCa prevalence rates in Europe being 206.6 cases (per 100,000) [10], whereas prevalence in Latvia was under 100 cases (per 1,000,000) until 1996. With the introduction of PSA test as part of a routine PCa diagnostic procedure there was observed a worldwide PCa prevalence rise. As far as Europe is concerned, in 2012, in accordance with the International Agency for Research on Cancer (IARC), the highest prevalence rates were registered in Scandinavia and France.

Mortality in Latvia showed stable growth until 2006, with mortality rates in Latvia, as well as other Baltic, Scandinavian and Caribbean countries being the highest in the world [4–6]. McDavid et al. reported that the US mean mortality rate in 1991 was 29.4 cases (per 100,000) [11] which is twice as high as the mortality rate of 12.8 cases (per 100,000) in 1991 in Latvia. However, unlike Latvia, the US showed the highest AAPC decrease in the world in 1996–2005 [6]. AAPC decrease was also observed in most of North and South American countries, as well as Western and Northern Europe [4–6]. It is noteworthy that since 2006 there has been mortality rates' decrease, albeit statistically insignificant. Common use of PSA screening was linked with the PCa incidence and prevalence increase, which in its turn was followed by mortality decrease; however, the

screening process resulted in overdiagnosis [12,13]. Our data shows how relatively low OS and CSS rates are. Usually, the 5-year CSS rates exceed 90% having improved significantly since the PSA test implementation [13]. There is a tendency towards survival rates improvement in Latvia too, although 5- and 10-year CSS do not exceed 70% and 40% respectively (Table 2). A study carried out in central Sweden shows high survival rates [14]. However, if compared with the survival data for Latvia, 15- and 20-year OS rates differ only by 3%–5%, whereas 15- and 20-year CSS rates are 2–3 times higher in Sweden. As the main reason for the above difference we would mention low average life expectancy observed in the Latvian male population, which, during the whole period under review, varied between 63 and 67 years of age according to the existing CSB data. It is noteworthy that the above life expectancy is by 3–8 years lower than the mean age of the initial PCa diagnosis. As far as limitations of the study are concerned, the data for the first 3 years of the reviewed period may be incomplete due to the fact that Latvian cancer register inherited the data collected before the country regained its independence. Mortality and CSS data are to be treated with caution, as in some cases the reported cause of death could be disputed. Besides, migration (the hidden one including) could skew figures for the Latvian male population.

## 5. Conclusions

The increase in PCa incidence, prevalence, and mortality rates was observed during the whole period in question, although a statistically insignificant decrease in mortality rates was registered from 2006. The 5- and 10-year survival rates improved over the reviewed period, but they still remain relatively low in Latvia.

## Conflict of interests

The authors declare that they have no competing interests.

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