Trends in Prostate Cancer Survival in Switzerland

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Introduction

In most Western societies, prostate cancer has become one of the most frequent incident cancers among males. In Switzerland, it is now the most frequent incident cancer among males with approximately 5,700 new cases per year, accounting for 30% of all cases [1], and the incidence has been increasing since the mid 1980s. Most of this increase is attributed to more frequent prostate cancer screening by measuring prostate-specific antigen (PSA) and/or palpation of the prostate. Since the use of PSA testing is more common among men younger than 70 years of age, the mean age of prostate cancer diagnosis has shifted towards a lower age at diagnosis. In contrast to the increase in the incidence rate, prostate cancer mortality rates started decreasing in the mid 1990s dropping by 19% between the five-years periods 1993-1997 and 2003-2007 [1]. Despite this decrease, however, prostate cancer is the second most common cause of cancer deaths among men in Switzerland with about 1,300 deaths per year (15% of cancer deaths). Given these trends in prostate cancer incidence and mortality rates in Switzerland during the last 30 years, the aim of our analysis was to examine prostate cancer survival between 1989 and 2009 with particular focus on changes by age groups as PSA screening has most strongly affected incidence rates among men less than 70 years of age.

Methods

The present study is based on the National Cancer Dataset managed by the Foundation National Institute for Cancer Epidemiology and Registration (NICER) for the purpose of national cancer monitoring in Switzerland. Fifteen Swiss cantons register cancer long enough to study time trends. A pooled dataset including data from eleven cantons was used for this report: Basel City and Basel Land (BS/BL), Fribourg (FR), Geneva (GE), Grison and Glarus (GR/GL), St. Gallen, Appenzell Outer-Rhodes and Appenzell Inner-Rhodes (SG/AR/AI), Ticino (TI) and Valais (VS). Of the remaining cantons, Zurich could not be included because active as well as passive follow-up was incomplete for prostate cancer, whereas the cantons of Neuchâtel, Jura and Vaud do not provide survival information to the National Cancer Dataset.

Cancer registries recorded all incident cancer cases diagnosed in their resident population and assessed cases' survival until at least 31.12.2009. The incidence date refers to the date of confirmation of diagnosis or the date of hospitalization if it preceded the diagnosis and was related to prostate cancer. We selected 33,440 cases with primary malignant prostate cancer (C61.9 ICD-O, 3rd edition) [2], aged 35-99 years (which excluded 13 cases) and diagnosed 1980-2009. For BS/BL the latest available year of diagnosis was 2008. All morphologies were included. Prostate cancer cases that were preceded by a primary cancer of a different topography were included [3]. We excluded all cases diagnosed at death or with a death certificate as only source of information (N=1,720). Completeness of case ascertainment for prostate cancer could be assessed in GE, GR/GL, SG/AR/AI, TI and VS and was found to be higher than the international standard of at least 90% within three years after the date of diagnosis [4].

Recent active follow-up was lacking for 923 (12%) cases in BS/BL, 499 (17%) in GR/GL, 168 (2%) in SG/AR/AI and 347 (10%) in VS. Based on the assumption that passive follow-up was complete for these cases, survival status was set to living as of 31.12.2009. For BS/BL this assumption was questionable for diagnoses earlier than 1.1.2002 (388 or 5% of cases) so the given date of last contact was used instead.

Observed (OS) and relative survival (RS) probabilities were derived for consecutive years after diagnosis during which the hazards were assumed to remain constant. RS was calculated as the ratio of the observed probability of survival of cancer cases and the expected survival of persons in the general population matching in age, sex and calendar year of death (i.e. estimation of mortality due to prostate cancer by accounting for competing risks of death) [5]. Expected cancer survival proportions were estimated using the Ederer II method applied to combined all-cause mortality tables for the cantons included in the present work as supplied by the Swiss Federal Statistical Office [6]. All-cause death probabilities, transformed from age-, sex-and calendar year-specific death rates, were interpolated and smoothed using the Elandt-Johnson formula [7]. RS ratios were estimated using the strs com-

Cantons	Diagnosis period	Number of Patients in Age-groups				Person-years	% of pooled person-years
		35-64 years	65-74 years	75-84 years	85-99 years		
GE	1980-2009	1569	2238	1471	495	32047	19.5
SG/AR/AI	1980-2009	1528	3054	2613	611	43779	26.7
BS/BL	1981-2008	1619	2880	2171	446	43833	26.7
GR/GL	1989-2009	602	1108	1013	253	13834	8.4
VS	1989-2009	904	1392	880	236	18556	11.3
TI	1996-2009	660	978	676	179	10190	6.2
FR	2006-2009	223	316	171	40	1970	1.2
Total		**7105**	**11966**	**8995**	**2260**	**164209**	**100.0**

Table 1: Overview of Swiss cantons contributing prostate cancer cases to the pooled dataset.

mand (version 1.3.7) [8] written for the Stata Statistical Software [9]. Complete analysis was used for the diagnosis period 1995 to 1999 and period analysis for 2005 to 2009 in order to derive the most up-to-date survival estimates [10]. In brief, complete analysis describes the survival experience of cases defined by dates of diagnosis, whereas period analysis defines cases by follow-up dates. The latter is achieved by left truncation of person-times at risk at the beginning of the specified follow-up period in addition to right censoring at its end. RS estimates were age-standardized using weigths specific for prostate cancer from the International Cancer Survival Standards (ICCS) [11]. Standard weights for age-groups were: 0.42 (35-64 years), 0.29 (65-74 years), 0.23 (75-84 years) and 0.06 (85-99 years). Ninety five percent confidence intervals (95% CI) were estimated using Greenwood's method [12] in complete analysis and in period analysis by applying the delta method to a transformation of the cumulative hazard. For age-standardized RS, 95% CI were estimated as described in [11].

To test for linear time trends of one- and five-year RS in age strata, piecewise Poisson regression models for the logarithm of excess number of deaths were fitted as linear functions of the logarithm of person-time (offset) and calendar period of follow-up (numeric variable). The p-value for inclusion of calendar period as explanatory variable, based on the Wald test, indicated the significance of a linear trend . The significance of a linear trend in RS for all age groups (age-standardized RS) was tested by additionally adjusting the Poisson model for age. Average annual percentage change (AAPC) was estimated as

$$AAPC = 100((RS_{lastyear} - RS_{firstyear})/RS_{firstyear})\Delta t^{-1}.$$

Results

Table 1 lists by cantons the diagnosis years, number of prostate cancer cases by age-group, the total person-years and the contribution of person-years per canton to the pooled dataset. The pooled dataset represents approximately one-third of the total at-risk population in Switzerland and accumulated more than 164,000 person-years of follow-up by more than 30,000 prostate cancer patients. Table 2 lists age-specific as well as age-standardized OS and RS for two five-year calendar periods. The RS estimates are plotted in Figure 1.

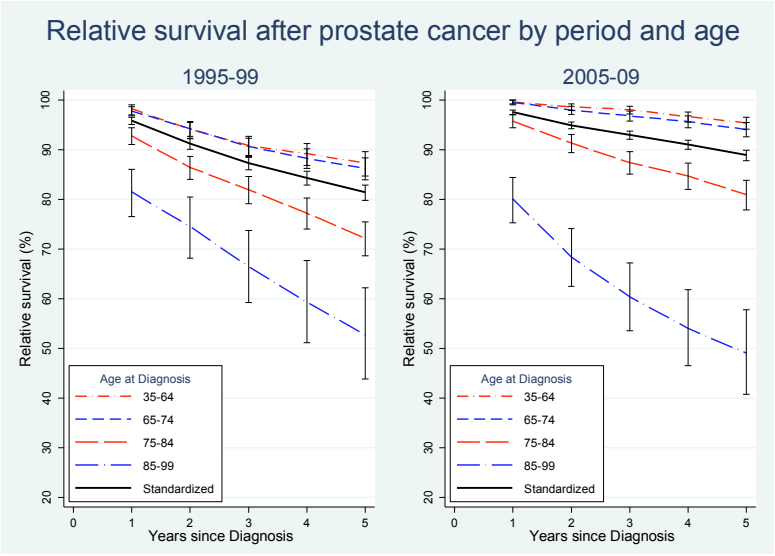

Figure 1: Age-specific and age-standardized relative survival curves with 95% confidence intervals in two calendar periods: 1995-1999 and 2005-2009. Prostate cancer cases were pooled from eleven Swiss cantons.

		Calendar period for analysis					
		1995-1999			2005-2009		
Age in years	Years since diagnosis	Observed Survival %	Relative Survival %	95% CI	Observed Survival %	Relative Survival %	95% CI
35-64	1	97.2	98.2	[97.0, 99.1]	98.9	99.7	[99.2, 100]
65-74		95.2	97.8	[96.8, 98.7]	97.6	99.6	[99.0, 100]
75-84		86.5	92.8	[91.0, 94.4]	90.8	95.8	[94.4, 97.0]
85-99		68.5	81.5	[76.5, 86.1]	69.2	80.1	[75.3, 84.4]
35-64	5	82.3	87.3	[84.7, 89.6]	91.0	95.4	[94.1, 96.6]
65-74		73.6	86.2	[84.0, 88.3]	83.3	94.1	[92.6, 95.5]
75-84		48.0	72.1	[68.6, 75.5]	58.1	80.9	[77.9, 83.9]
85-99		19.7	52.7	[43.8, 62.2]	20.2	49.0	[40.8, 57.8]
standardized*	1	92.4	95.8	[95.1, 96.5]	94.9	97.6	[97.1, 98.0]
standardized*	5	68.1	81.4	[79.8, 82.9]	77.0	88.9	[87.8, 89.9]

*Age-standardization using ICCS weights.

Table 2: Observed and relative survival estimates with 95% confidence intervals (95% CI) by calendar period and age for prostate cancer cases pooled from eleven Swiss cantons.

Age-standardized OS for the 1st year after diagnosis was slightly reduced compared with the survival expected for the general population which generated a RS of 95.8% (95% CI: 95.1, 96.5) in 1995-1999 and 97.6% (95% CI: 97.1, 98.0) in 2005-2009. Whether or not survival improved over time depended on age at diagnosis. Age-specific RS for the 1st year after diagnosis increased slightly over time for ages <85 years but remained unchanged for cases diagnosed at 85-99 years old. More substantial increases in RS for the 5th year after diagnosis were seen in younger age-groups (age <85 years) but again without improvement for the cases in the oldest age-group: age 85-99 years RS 52.7% (95% CI: 43.8, 62.2) in 1995-1999 and 49.0% (95% CI: 40.8, 57.8) in 2005-2009.

Table 3 shows trends in one- and five-year age-specific as well as age-standardized RS after a prostate cancer diagnosis in seven successive three-year periods of follow-up. There were small but consistent improvements of one-year RS for cases aged <85 years from 93.6% (95% CI: 91.9, 95.0) in 1989-1991 to 98.9% (95% CI: 98.4, 99.4) in 2007-2009, with an AAPC of 0.3 and a significant linear time trend. The five-year RS of patients <85 years statistically significantly improved from 68.8% (95% CI: 65.1, 72.4) in 1989-1991 to 92.0% (95% CI: 90.7, 93.3) in 2007-2009, with an AAPC of 1.6 and significant linear time trend. Similar observations were made for age-standardized RS estimates. In contrast, there was no statistically significant improvement in one- or five-year RS for cases 85-99 years of age at diagnosis as reflected by the lack of a linear time trends. For example, five-year RS was 49.6% (95% CI: 32.2, 70.2) in 1989-1991 and 43.2% (95% CI: 33.5, 53.9) in 2007-2009. However, the AAPC for the oldest-old age-group may be less informative since it is derived only from the first and last calendar-periods making it sensitive to the larger fluctuation seen in RS estimates for this age-group.

Discussion

These results show that prostate cancer survival in Switzerland has improved considerably over the last 20 years. However, this improvement was confined to men younger than 85 years of age.

Based on a EUROCARE-4 analysis (5-year relative survival for period analysis 2000-2002; including data from 23 European countries/regions) age-standardized 5-year relative survival for prostate cancer was 77.5%, with Switzerland (including four Swiss cancer registries) being at the upper end of survival rates (87.3%), whereas relative survival was as low as 58.4% in the Czech Republic [13] and 47.7% in Denmark [14]. When comparing relative survival rates between 1990-1994 and 1995-1999, an increase in relative survival was observed in most European countries, with particularly strong increases of more than 20% in Poland and Malta, and of 14.2% in Switzerland [14]. Some of the changes seen in mortality rates and

relative survival of prostate cancer patients in Europe are the result of PSA screening, leading to earlier diagnosis, lead-time bias, and over-diagnosis, (i.e. more frequent diagnosis of low-stage and also low-risk tumors) [15]. In some countries, such as England, the effect has also been reported to be at least in part due to improved and sometimes more aggressive treatment [14, 15].

In the US, the routine use of PSA screening started at the end of the 1980s, followed by an increase in the incidence rate of prostate cancer between 1989 and 1992 [16]. By 2001, 75% of American men age 50 years old or older reported having at least once one PSA test [17]. In the US, the use of PSA testing to detect prostate cancer in an early phase has shifted the spectrum of the diagnosed cancers, such that the introduction of PSA testing lead primarily to an increase in the diagnosis of localized tumors (http://seer.cancer.gov/publications/prostate/grade.pdf). It has, thus, been argued by many that prostate cancer diagnosed in the pre-PSA era is not the same disease as prostate cancer diagnosed after widespread introduction of PSA screening [18, 19].

It is interesting to note in our analysis that we did not observe an improvement of relative survival in men older than 85 years of age despite an improvement in men 75-84 years old. Analyses restricted to the age groups 85 years and older are rarely published. In an analysis of European data there was no improvement in 5-year relative survival among men older than 75 years of age, in Geneva (the only Swiss cancer registry included in analysis) whereas improvements were seen in all other European cancer registries [15]. The Swiss Urological Association does not recommend PSA screening for men with a life expectancy of less than 10 years and generally for men 75 years of age and older [20]. Also, the Swiss Medical Board does not support the PSA testing for screening men without symptoms (http://www.samw.ch/de/Aktuell/News.html Medienmitteilung 21.11.2012). A possibly smaller lead-time bias underlying the lack of improvement in survival in the oldest men is suggested by the 2007 Swiss Health Survey, where 29.2% of men age 70-79 years had had a prostate cancer screening examination (digital rectal examination and/or PSA) during the previous year; among men 80+ years old, a slightly smaller fraction of 22.2% had had a prostate cancer screening exam during the last year [21]. However, uptake rates of PSA screening in Switzerland are not available.

Several factors could not be taken into account in our analysis (e.g. stage at diagnosis, treatment, socioeconomic status), which have been shown to have a strong

Table 3. Trends in relative survival of prostate cancer cases pooled from eleven Swiss cantons for successive three-year calendar periods of follow-up between 1989 and 2009.

		Calendar period of death or censoring								
		1989/1991	1992/1994	1995/1997	1998/2000	2001/2003	2004/2006	2007/2009		
Age in years	Years since diagnosis	Relative Survival % [95% CI]	Relative Survival % [95% CI]	Relative Survival % [95% CI]	Relative Survival % [95% CI]	Relative Survival % [95% CI]	Relative Survival % [95% CI]	Relative Survival % [95% CI]	AAPC**	Linear trend p-value*
35-84	1	93.6	94.3	96.1	96.2	98.0	98.4	98.9	0.3	< 0.001
		[91.9, 95.0]	[92.9, 95.6]	[95.0, 97.1]	[95.2, 97.0]	[97.3, 98.6]	[97.7, 98.9]	[98.4, 99.4]		
85-99		69.7	80.6	78.4	77.5	75.5	84.1	80.2	0.7	0.091
		[60.6, 77.9]	[72.6, 87.5]	[71.6, 84.4]	[71.0, 83.4]	[68.9, 81.4]	[77.6, 89.7]	[74.0, 85.7]		
standardized***		92.6	94.1	95.6	95.6	96.8	97.6	97.8	0.3	< 0.001
		[90.9, 94.0]	[92.6, 95.3]	[94.6, 96.5]	[94.7, 96.4]	[96.0, 97.4]	[96.9, 98.2]	[97.1, 98.3]		
35-84	5	68.8	66.4	74.6	79.9	86.3	90.4	92.0	1.6	< 0.001
		[65.1, 72.4]	[63.4, 69.5]	[71.9, 77.3]	[77.6, 82.1]	[84.5, 88.1]	[88.9, 91.9]	[90.7, 93.3]		
85-99		49.6	53.2	47.2	55.4	42.8	54.9	43.2	–0.6	0.828
		[32.2, 70.2]	[37.8, 70.5]	[34.6, 61.5]	[43.8, 67.9]	[33.3, 53.3]	[43.3, 67.5]	[33.5, 53.9]		
standardized***		67.2	66.1	72.6	79.9	84.7	88.7	88.9	1.5	< 0.001
		[63.1, 71.0]	[62.7, 69.3]	[69.6, 75.3]	[77.6, 82.0]	[82.9, 86.3]	[87.1, 90.2]	[87.4, 90.1]		

* p-Value of Wald test for calendar period in a Poisson regression model of excess mortality.
** Average annual percentage change. *** Age-standardization using ICCS weights.

impact on prostate cancer mortality and survival in an analysis of the Geneva Cancer Registry [22]. In their analysis, Rapiti and colleagues reported strong differences in access to care and treatment of prostate cancer between socioeconomic groups. Men in the Geneva study with low socioeconomic status tended to receive curatively intended treatment such as surgery or radiotherapy less frequently than men with higher socioeconomic status [22]. This is a surprising observation in a country with federally mandated basic health insurance. In an analysis of Surveillance, Epidemiology and End Results data for the United States relative 5-year survival rates were lowest for distant stage tumors. However, studies on how survival rates change over time by stage of disease are currently missing.

This analysis was a first step towards understanding the development of trends in prostate cancer survival in Switzerland. Further studies, especially in Switzerland, examining survival by stage of the disease are needed since improvements in prostate cancer treatments will primarily affect survival of advanced stage tumors. Only then it will be possible to interpret the results correctly and to take adequate public health actions.

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* For additional information on prostate cancer in Switzerland please see NICER website http://nicer.org/default.aspx?NavigationID=42

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