

Survival Trends for Kidney Cancer Patients in Switzerland

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Introduction

Kidney cancer occurs predominantly in countries with high and very high levels of socioeconomic development [1]. Concerning Switzerland, an average of about 620 men and 290 women were diagnosed with kidney cancer each year during 2008 and 2012 and caused approximately 190 deaths in men and 110 deaths in women [2]. Kidney cancer is the 8th most common cancer for men and the 14th most common cancer for women, ranking 13th and 14th of all cancer deaths in Switzerland, respectively. The age standardized incidence rates have not altered much in the past 30 years for both sexes, but the mortality rate in kidney cancer has steadily declined in Switzerland [2]. Compared to many European countries and USA, Switzerland has one of the lowest incidence and mortality rates [2, 3].

Publications about kidney cancer survival trends in European patients, based on the EURO CARE-5 dataset which includes diagnoses up to 2007, reported increased one- and five-year survival with better prognosis in Central and Southern Europe and decreasing survival in older age [4, 5, 6].

The patients' survival is influenced by tumour related prognostic factors (e.g. TNM stage, morphological features, genetic/molecular markers), patient related prognostic factors (e.g. performance status, comorbidities, health care accessibility, socioeconomic background), and treatment related prognostic factors (e.g. surgery, immunotherapy, targeted medicine) [7, 8].

We investigated kidney cancer survival trends in patients resident in Switzerland, utilizing the data of eight Swiss population-based cancer registries. The analysed cancer cases were diagnosed in the time period between 1989 and 2013 and included exclusively invasive neoplasms of the renal parenchyma (C64, ICD-10) in adult men and women.

Methods

This study is based on the National Core Dataset (NCD) managed by the National Institute for Cancer Epidemiology and Registration (NICER) for the purpose of national cancer monitoring in Switzerland. Cancer cases in 1989 to 2013 from 12 cantons were collapsed for this report: Appenzell Ausserrhoden (AR) and Appenzell Innerrhoden (AI), Basel-Landschaft (BL) and Basel-Stadt (BS), Geneva (GE), Glarus (GL), Graubünden (GR), Neuchâtel (NE), St. Gallen (SG), Ticino (TI), Valais (VS), and Zurich (ZH). The corresponding coverage of the Swiss population was 39% to 49%, depending on calendar year. The cantons Aargau, Bern, Fribourg, Jura, Lucerne, Nidwalden, Obwalden, Thurgau, Uri, Vaud, and Zug could not be included, because they either started registration after 2004 or do not provide information on patient survival to the NCD. The cantons Schwyz, Solothurn and Schaffhausen do not yet register cancer.

Cancer registries recorded all incident cancer diagnoses in their resident population and assessed cases' survival by active and/or passive follow-up until 31.12.2013. We extracted 9'137 malignant primary kidney cancer diagnoses from 1989 to 2013 (C64, ICD-10). For the cantons BL and BS the latest available year of diagnosis was 2011.

Patients with different multiple primary tumours (27%) were included [9]. We excluded 3 primary kidney cancer diagnoses because they occurred after a primary kidney cancer diagnosis in the same person. We excluded all cases diagnosed at death (N=518) or with a death certificate as the only source of information (N=114). Excluded were 257 cases because no active follow-up has been performed. Recent active follow-up was lacking for 971 cases (i.e. follow-up before July 2013) and were included based on the last available follow-up date. Age limits excluded 108

cases (107 < 15 years of age; 1 ≥100 years). A total of 8'137 cases (89%) remained for survival analysis.

Completeness of case ascertainment for kidney cancer was estimated as 90% at 3 years after the diagnosis date [10].

Because we did not assume survival up to 31.12.2013 in the absence of reported death (i.e. based on passive follow-up alone), our survival estimates will be conservative. The assumption of survival in the absence of reported death could overestimate survival because two large registries did not utilize death certificates for several diagnosis years: ZH (1980-1996) and BS/BL (1981-2001, 2008-9). Sensitivity analysis revealed that assuming survival up to 31.12.2013 in the absence of reported death would increase relative survival estimates about 4% for five-year survival, or about 8% for ten-year survival (data not shown).

Observed survival (OS) and relative survival (RS) were derived for consecutive time intervals of increasing length after diagnosis during which the hazards were assumed to remain constant. RS was calculated as the ratio of the observed survival of cancer cases and the expected survival of persons in the general population matching in age, sex, calendar year of death and canton [11]. Expected cancer

survival was estimated using the Ederer II method applied to all-cause mortality tables specific for the cantons [12]. All-cause death probabilities, transformed from age, sex- and calendar year-specific death rates, were interpolated and smoothed using the Elandt-Johnson formula [13]. RS ratios were estimated using the `strs` command (version 1.4.2) [14] written for the Stata Statistical Software [15]. Period survival analysis [16], which defines cases by follow-up dates, was applied to calendar periods 2004-2008 and 2009-2013. RS estimates were age-standardized using weights specific for kidney cancer from the International Cancer Survival Standards (ICSS) [17] using the method of Brenner et al. [18]. Ninety-five percent confidence intervals (95% CI) were estimated using the delta method to a transformation of the cumulative hazard.

To test for linear time trends of RS, the annual percentage change (APC) and its 95% CI was estimated with the Joinpoint Regression Program v4.0.4 [19].

Results

This report combines the survival experience of kidney cancer patients from 12 Swiss cantons (8 cancer registries) covering the diagnosis period 1989 to 2013 (Tab. 1).

	All combined	Swiss cantons							
		ZH	BS/BL	SG/AR/AI	GR/GL	TI	VS	NE	GE
Diagnosis period		1989 - 2013	1989 - 2011	1989 - 2013	1989 - 2013	1996 - 2013	1989 - 2013	1989 - 2013	1989 - 2013
Men (N)	5947	1959	764	846	374	537	490	294	683
Women (N)	3079	1046	383	419	197	268	263	163	340
Men, Age (median)	67.1	67.8	68.6	67.2	66.7	67.4	66.0	65.4	67.3
Women Age (median)	71.3	71.6	72.3	70.9	71.5	71.4	70.1	69.5	71.6
Men, Age (%)									
15-59	28.8	26.7	25.8	29.3	29.4	31.5	33.3	34.7	29.8
60-69	29.5	30.2	28.4	31.3	32.6	27.4	29.0	25.9	28.0
70-79	28.2	28.8	31.4	28.5	25.9	28.6	25.5	25.5	26.7
80-99	13.5	14.3	14.4	10.9	12.1	12.5	12.2	13.9	15.5
Women, Age (%)									
15-59	21.6	21.1	19.8	21.9	20.3	22.4	21.3	23.9	23.8
60-69	24.8	24.7	24.3	24.6	24.4	23.1	28.1	27.0	23.8
70-79	30.6	30.5	32.6	31.3	36.0	33.2	28.5	30.1	24.7
80-99	23.0	23.7	23.2	22.2	19.3	21.3	22.1	19.0	27.7
DCO (%)	1.6	2.8**	1.4 #	0.6	0.5	2.4	0.7	0.9	1.3
MV (%)	90.4	89.3	96.5	88.3	90.2	90.1	89.3	90.4	90.1
Unclassified malignant neoplasm (%)*	8.7	10.8	0.3	11.7	9.8	6.7	10.9	10.7	10.0

* M8000/3 - M8004/3; ** 1997-2013; # 2002-2007

DCO: Death certificate only diagnosis; MV: Microscopically verified diagnosis

Tab. 1. Comparison of kidney cancer diagnosed 1989-2013 among Swiss cantons, by sex, age at diagnosis and registration quality measures (DCO, MV, unclassified neoplasms).

Most cantons covered the entire calendar period, except BS and BL (until 2011), GL (since 1992), and TI (since 1996). A total of 9'026 patients with age at diagnosis 15 to 99 years were reported to the enclosed cancer registries. About 2/3 of the patients were men, overall and in each cancer registry. The median age at diagnosis in men was 67 years, about 4 years below the median age in women, also reflected by the smaller proportions of men older than 80 years, and the slightly larger proportions below 60 years, as compared with women. The proportions of cases where registration was based only on information from a death certificate (DCO), which were excluded from survival analysis because no diagnosis date is known, are always small and negligible (Tab. 1). About 90% of diagnoses were microscopically verified (MV) and 9% of cases lacked histological classification (Tab. 1).

The survival experiences over the last 25 years within the patient groups (observed survival, OS) and relative to persons of the general population (relative survival, RS), is shown in Tab. 2. The survival is age-standardized to correct for possible changes in the age-distribution of patients over time. In general, kidney cancer survival proportions are favourable, being 86% in the first year after diagnosis, 69% for five years after diagnosis, and still 54% for ten years

after diagnosis (most recent diagnosis period 2009-2013, both sexes combined). There were no differences in survival between men and women, at any calendar period nor time after diagnosis (Tab. 2). The temporal trend in survival proportions was significantly positive with estimated 0.7% to 1.2% annual increase (APC), depending on sex and time after diagnosis (Tab. 2). The improvement lacked statistical significance only for ten-year survival in women.

Age-standardized temporal trends may conceal heterogeneous behaviour in different age groups. Age-specific trends in RS are shown in Tab. 3 and Fig. 1. The age groups below 80 years confirmed the positive age-standardized trend (Tab. 3). There was also clear improvement in short-term RS (one year) in women over 80 years, from 46.9% in 1989-1993 to 69.1% in 2009-2013, with significant APC 1.45%, and for five-year RS, from 24.5% to 42.4%, with APC 2.2%. In men over 80 years, on the other hand, the trend was much less pronounced, with survival estimates ranging from 62.1% to 66.7% (one-year RS), or 39.9% to 43.2% (five-year RS), respectively, and APCs not significantly different from 0% (Tab. 3). Short-term RS (one year) in male and female patients below 70 years reached >90%, i.e. was almost as well as in comparable persons of the general population.

Tab. 2. Age-standardized observed (OS) and relative survival (RS) by sex, calendar period, and time after diagnosis. Cases of eight cancer registries pooled.

Sex	Period	One-year survival [%]				Five-year survival [%]				Ten-year survival [%]					
		OS	RS	LO	HI	OS	RS	LO	HI	OS	RS	LO	HI		
Men	1989-1993	72.7	75.4	72.1	78.5	45.2	54.1	50.0	58.2	29.2	42.8	38.2	47.4		
	1994-1998	72.6	75.1	71.9	78.0	48.8	57.2	53.2	61.0	33.3	46.3	41.9	50.7		
	1999-2003	76.8	79.1	76.3	81.6	54.1	62.7	59.1	66.2	35.9	49.6	45.4	53.8		
	2004-2008	80.5	82.9	80.5	85.1	57.4	66.9	63.5	70.3	38.9	54.0	49.6	58.4		
	2009-2013	84.6	86.8	84.7	88.7	59.7	68.4	65.2	71.5	40.1	55.0	50.7	59.3		
	APC [%]		0.67*					1.0*					1.07*		
Women	1989-1993	68.7	70.1	65.6	74.2	46.4	51.1	46.1	56.1	35.7	43.7	38.3	49.2		
	1994-1998	69.8	71.3	67.1	75.1	51.8	57.1	52.2	61.7	41.0	50.7	45.4	56.0		
	1999-2003	80.2	81.7	77.9	84.9	58.4	64.0	59.1	68.5	44.2	54.1	48.6	59.5		
	2004-2008	80.2	82.0	78.5	85.0	58.0	64.3	59.6	68.7	44.7	56.1	50.5	61.5		
	2009-2013	83.7	85.4	82.2	88.2	64.1	71.0	66.5	75.1	42.6	53.8	48.1	59.4		
	APC [%]		0.83*					1.24*					0.80		
Both	1989-1993	71.2	73.3	70.7	75.8	45.5	52.7	49.5	55.8	31.4	42.9	39.4	46.5		
	1994-1998	71.8	73.8	71.3	76.1	50.0	57.0	54.0	60.0	36.1	47.8	44.4	51.2		
	1999-2003	77.6	79.6	77.4	81.6	55.0	62.5	59.6	65.3	38.3	50.6	47.3	54.0		
	2004-2008	80.2	82.3	80.4	84.1	57.2	65.4	62.6	68.1	40.7	54.4	50.9	57.8		
	2009-2013	84.3	86.3	84.6	87.9	61.1	69.2	66.6	71.7	40.8	54.4	51.0	57.8		
	APC [%]		0.73*					1.10*					0.96*		

* 95% confidence interval of APC excludes 0.0%
LO, HI: 95% Confidence limits of RS; APC: Annual percentage change

Discussion

This analysis describes survival trends in adult patients after the diagnosis of kidney cancer in Switzerland between 1989 and 2013, based on data from eight Swiss population-based cancer registries.

The findings indicate that the RS steadily increased in both sexes for one-, five-, and ten-year survival, reaching 86% in the first year after diagnosis, 69% for five years after diagnosis, and still 54% for ten years after diagnosis in the most recent diagnosis period 2009-2013. The RS decreased with the patient's age and showed less convincing improvements for male patients older than 80 years in one- and five-year survival (ten-year survival not analysed).

Recent increases in five-year RS have also been reported in Germany [3], Denmark [20] and in England/Wales [21],

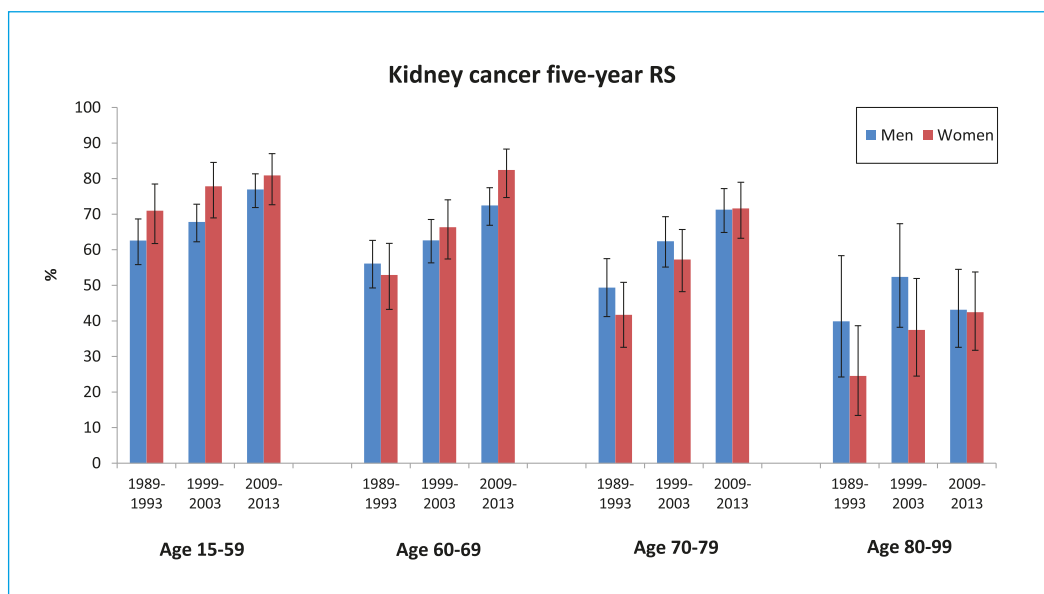
and as already mentioned for former years in other European countries [4, 5, 6]. The five-year RS of German patients living in 2011-2012 with 76% in male and 78% in female patients is higher as compared to the Swiss estimates [3]. On the other hand, the five-year RS in Danish patients younger than 70 years diagnosed with kidney cancer during 1978-2012 is 60% [20] which is lower than our result in the five-year RS. In addition, the five-year RS in England and Wales is significantly lower, being 56.5% (95% CI [56.3; 56.8]) in male and 55.7% (95% CI [55.4; 56.0]) in female patients diagnosed with kidney cancer during 2010-2011 [21]. However, the comparison of survival trends among different countries is challenging because registration practices may differ in standards and over time, as well as the distribution of prognostic factors. Additionally, methodological aspects (e.g. assumption of survival in the absence of reported death, case inclusion

Age	Period	One-year survival [%]			Five-year survival [%]			Ten-year survival [%]											
		Men		Women	Men		Women	Men		Women									
		RS	LO	HI	RS	LO	HI	RS	LO	HI	RS	LO	HI	RS	LO	HI			
15-59	1989-1993	81.7	76.1	86.1	83.5	75.5	89.1	62.6	55.8	68.7	71.0	61.7	78.5	51.1	44.0	57.9	66.5	56.8	74.7
	1994-1998	87.6	83.1	91.0	82.0	73.1	88.2	70.9	64.9	76.1	69.9	59.8	78.0	60.5	53.9	66.6	63.5	52.9	72.6
	1999-2003	83.0	78.4	86.7	90.8	83.9	94.9	67.8	62.2	72.8	77.9	69.0	84.6	59.7	53.6	65.4	68.4	58.5	76.6
	2004-2008	89.4	85.6	92.2	95.5	90.5	97.9	73.2	67.8	77.9	77.5	69.3	83.9	64.0	57.8	69.6	69.2	59.6	77.2
	2009-2013	95.2	92.5	97.1	96.3	91.0	98.5	77.0	71.9	81.4	80.9	72.6	87.0	67.2	60.9	72.9	67.9	57.8	76.2
	APC [%]	0.61*			0.65*			0.71*			0.58*			0.92*			0.20		
60-69	1989-1993	79.7	74.1	84.2	72.4	63.5	79.5	56.1	49.3	62.6	52.9	43.2	61.8	45.5	38.0	53.1	43.7	33.6	53.6
	1994-1998	79.3	73.9	83.7	74.9	67.0	81.3	57.6	50.9	63.8	60.1	51.3	68.0	45.2	38.1	52.4	53.8	44.4	62.7
	1999-2003	82.2	77.2	86.2	85.9	78.9	90.8	62.7	56.3	68.5	66.4	57.4	74.0	50.0	42.9	57.0	57.2	47.4	66.1
	2004-2008	87.3	83.2	90.5	86.2	79.3	91.0	65.9	59.8	71.4	71.8	62.8	79.2	52.9	45.6	59.9	61.7	51.3	70.9
	2009-2013	91.2	87.7	93.8	91.2	85.4	94.8	72.5	66.9	77.5	82.4	74.7	88.3	59.0	51.6	66.0	67.4	56.7	76.5
	APC [%]	0.65*			0.92*			1.12*			1.79*			1.17*			1.55*		
70-79	1989-1993	71.6	64.9	77.4	66.5	57.9	74.0	49.4	41.2	57.5	41.7	32.6	50.9	32.5	23.5	42.8	30.4	21.0	41.2
	1994-1998	69.9	63.1	75.9	67.6	60.0	74.1	55.3	46.9	63.4	54.7	46.2	62.8	39.4	30.0	49.6	47.3	37.5	57.4
	1999-2003	78.4	72.9	83.1	76.7	69.2	82.7	62.4	55.1	69.3	57.3	48.2	65.7	41.6	33.1	50.6	43.4	33.4	53.9
	2004-2008	83.5	78.7	87.4	83.1	76.4	88.2	67.6	60.6	74.2	62.1	53.0	70.4	47.4	37.4	57.8	50.9	40.3	61.5
	2009-2013	86.6	82.4	90.0	83.2	76.7	88.1	71.3	64.9	77.2	71.7	63.2	79.0	50.9	41.4	60.6	44.1	33.2	55.4
	APC [%]	0.91*			1.05*			1.47*			1.86*			1.74*			0.96		
80-99	1989-1993	62.1	49.2	73.4	46.9	35.0	58.3	39.9	24.2	58.3	24.5	13.4	38.6						
	1994-1998	49.8	38.3	60.8	51.7	40.0	62.5	25.9	14.2	41.3	27.5	16.2	41.3						
	1999-2003	64.8	54.4	74.0	63.2	51.3	73.5	52.4	38.2	67.3	37.5	24.5	51.9						
	2004-2008	65.8	56.8	73.8	60.2	51.4	68.2	59.5	45.5	73.7	39.5	28.0	51.9	nd			nd		
	2009-2013	66.7	58.3	74.2	69.1	60.2	76.7	43.2	32.6	54.5	42.4	31.8	53.7						
	APC [%]	0.61			1.45*			0.94			2.21*								

* 95% confidence interval of APC excludes 0.0%
 LO, HI: 95% confidence limits; APC: Annual percentage change; nd not determined (few observations)

Tab. 3. Age-specific relative survival (RS) of kidney cancer patients by sex, calendar period, and time after diagnosis. Cases of eight cancer registries pooled.

Fig. 1. Trend in age- and gender-specific relative survival five years after diagnosis of kidney cancer in Switzerland. The 1st, 3rd, and 5th time periods are shown. Error bars indicate the 95% confidence intervals.



criteria: ICD-10-classification C64 alone [3, 20] or combined with C65 [22] or C65, C66, C68 [21]) complicate a meaningful interpretation.

We cannot exclude that specific tumour characteristics such as histology, grade and extension at time of diagnosis are responsible for increased relative survival as already described elsewhere [1, 23]. It is also possible that most of the investigated tumours in the latter time period were detected incidentally in a localized stage and therefore relative survival rose. Unfortunately, we could not analyse the data by stage because they were mostly incomplete concerning UICC TNM stage information (range: 9-48%, average: 33% UICC TNM stage information missing; data not shown).

Other reasons for the improved relative survival to be discussed are patients' factors like e.g. co-morbidities, lifestyle, socioeconomic background, health care accessibility [4]. Also, diagnostic means and therapy could have improved in the last 25 years. All these factors can neither be verified nor neglected within our analysis because supplementary information about the patients or the treatments they received was not available in the National Core Dataset.

Age-standardized temporal trends in RS show that the one- and five-year survival increase is less convincing in the age-group older than 80 years, at least in men. Similar results were found in a study among elderly in Denmark during 1980-2012 already for patients older than 70 years [20]. The authors stated worse surgical outcomes, missing treatment guidelines for the elderly and restraining

of systematic therapy as major causes for this phenomena and appeal for interdisciplinary procedure.

The findings of this analysis have to be taken with caution with respect of generalization to whole Switzerland because the data covered only 39 to 49% of the Swiss population.

Conclusion

An encouraging steady increase in one-, five-, and ten-year relative survival of adult patients with kidney cancer can be observed in Switzerland in the last 25 years, at any age and sex, with the possible exception of men older than 80 years at diagnosis. However, further studies including stage, treatment and patient health status information are needed to clarify the underlying reasons for these findings and to guarantee further improvement of survival outcome. This will require that sufficient medical data is transmitted to the population-based cancer registries.

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- * For additional information on cancer in Switzerland, please see the NICER website at <http://nicer.org/>

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