Trends in Stomach Cancer Survival in Switzerland

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Introduction

Worldwide, stomach cancer represents the fourth most common neoplasm (9.7% and 5.8% in men and women, respectively), with the highest risk of occurrence in Asia, South America and southwestern Europe, and the second most common cause of death from all malignant tumours (11.0% and 8.2% in men and women, respectively) [1].

In Switzerland, each year approximately 800 new cases are diagnosed, and there are about 500 deaths from stomach cancer (reference period: 2006-2010) [2]. The rate of occurrence is almost twice as high in men as in women and increases with age. Screening for gastric cancer is routine only in Japan and Korea, where the incidence is especially high.

Since the second half of the previous century, incidence and mortality of gastric carcinoma have declined dramatically worldwide [3]. A recent report confirmed these trends also in Switzerland, particularly in men and for persons over 70 years old [4]. This is probably due to changes in dietary patterns, better food cooling and preservation techniques (e.g. refrigerator) and reduction of *Helicobacter pylori* infection, which together with cigarette smoking, atrophic gastritis and some inherited genetic mutations represent important risk factors. Fruit and vegetables are believed to be protective against gastric cancer, and excess intake of salt increases the risk of gastric cancer [5].

Similar to other cancer types, the prognosis of stomach cancer depends on the extent of disease at the time of diagnosis. Since it is often diagnosed at a late stage, it is one of the most difficult cancers to cure and has one of the lowest survival rates worldwide [6]. Surgical resection is the only treatment modality that is potentially curative. Recently, studies suggested that there may be benefit from some adjuvant chemotherapy treatments or neo-adjuvant treatments for inoperable locally advanced disease that may be reassessed for surgery [7].

One of the main objectives of Swiss cancer registries is to survey trends in cancer survival to provide comprehensive data for cancer control. The aim of this study was to assess population-based observed and relative survival of persons diagnosed with stomach cancer in Switzerland from 1980 to 2010.

Methods

This study is based on the National Core Dataset (NCD) managed by the foundation National Institute for Cancer Epidemiology and Registration (NICER) for the purpose of national cancer monitoring in Switzerland. Sixteen of 26 Swiss cantons currently transmit cancer data annually to the NCD. Cancer cases from 13 cantons were pooled for this report: Basel-Stadt and Basel-Landschaft (BS/BL), Fribourg (FR), Geneva (GE), Grisons and Glarus (GR/GL), Lucerne (LU), St. Gallen, Appenzell Outer-Rhodes and Appenzell Inner-Rhodes (SG/AR/AI), Ticino (TI), Valais (VS) and Zurich (ZH). The cantons of Neuchâtel, Jura and Vaud could not be included, because they do not provide information on survival to the NCD.

Cancer registries recorded all incident cancer cases diagnosed in their resident population and assessed cases' survival by active or passive follow-up as of 31 December 2010. 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 the cancer. We included malignant stomach cancer diagnoses from 1980 to 2010 at ages 20 to 99 years based on the International Classification of Diseases for Oncology (ICD-O, 3rd edition; [8]): topography codes C16.0-C16.9 and all morphologies except lymphoma/leukaemia codes 9590-9989. For the cantons BS and BL the latest available year

| Cantons	Diagnosis period	Number of cases			Person-years	% of pooled person-years
		Men	Women	Both		
GE	1980-2010	861	613	1474	4181	13.6
SG/AR/AI	1980-2010	1216	862	2078	5219	16.9
BS/BL	1981-2008	1007	727	1734	5328	17.3
ZH	1980-2010	2589	1716	4305	8799	28.6
VS	1989-2010	596	352	948	2710	8.8
TI	1996-2010	513	400	913	2428	7.9
GR/GL	1989-2010	487	297	784	1914	6.2
FR	2006-2010	80	43	123	192	0.6
LU	2010	25	5	30	35	0.1
Total		7374	5015	12389	30806	100.0

Table1: Contribution of stomach cancer cases to the national pooled dataset by 13 Swiss cantons.

of diagnosis was 2008. Stomach cancer cases that were preceded by a primary cancer of a different topography were included [9]. In 11 persons with >1 malignant stomach cancer diagnoses, the first occurring diagnosis was selected. We excluded all cases diagnosed at death or with a death certificate as the only source of information (N = 726; 5.4%). Recent active follow-up was lacking for N = 82 (9%) cases in BS/BL, N = 43 (13%) in GR/GL, N = 72 (7%) in VS and N = 640 (14%) for ZH. The vital status of these cases was set lost to follow-up using the date of last contact. A total of 12,389 cases were included in the survival analysis (92% of those eligible). Completeness of case ascertainment for stomach cancer could be assessed in the cantons GE, GR/GL, SG/AR/AI, TI and VS and was found to be higher than the international standard of at least 90% within a single year after the date of diagnosis [10].

Observed (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. Time intervals were: 0.1, 0.3, 0.6, 1.0, 1.5, 2.0, 2.5, 3.0, 4.0, 5.0 and 6.0 years. 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 cantonal pool [11]. Expected cancer survival was estimated using the Ederer II method applied to all-cause mortality tables for the cantons combined [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 1.3.7) [14] written for the Stata Statistical Software [15]. Complete survival analysis was used for the comparison in Table 2. Period survival analysis was used for the analysis of time trends in Table 3 [16]. In brief, complete analysis describes the survival of cases defined by dates of diagnosis, and period analysis defines cases by follow-up dates. RS estimates were age-standardized using weights specific for stomach cancer from

Figure 1: Age- and sex-specific one- and five-year relative survival curves, with 95% confidence intervals for two calendar periods (1991-2000 and 2001-2010) of cancer diagnosis. Stomach cancer cases were pooled from 13 Swiss cantons.

Survival with stomach cancer by age, sex and period
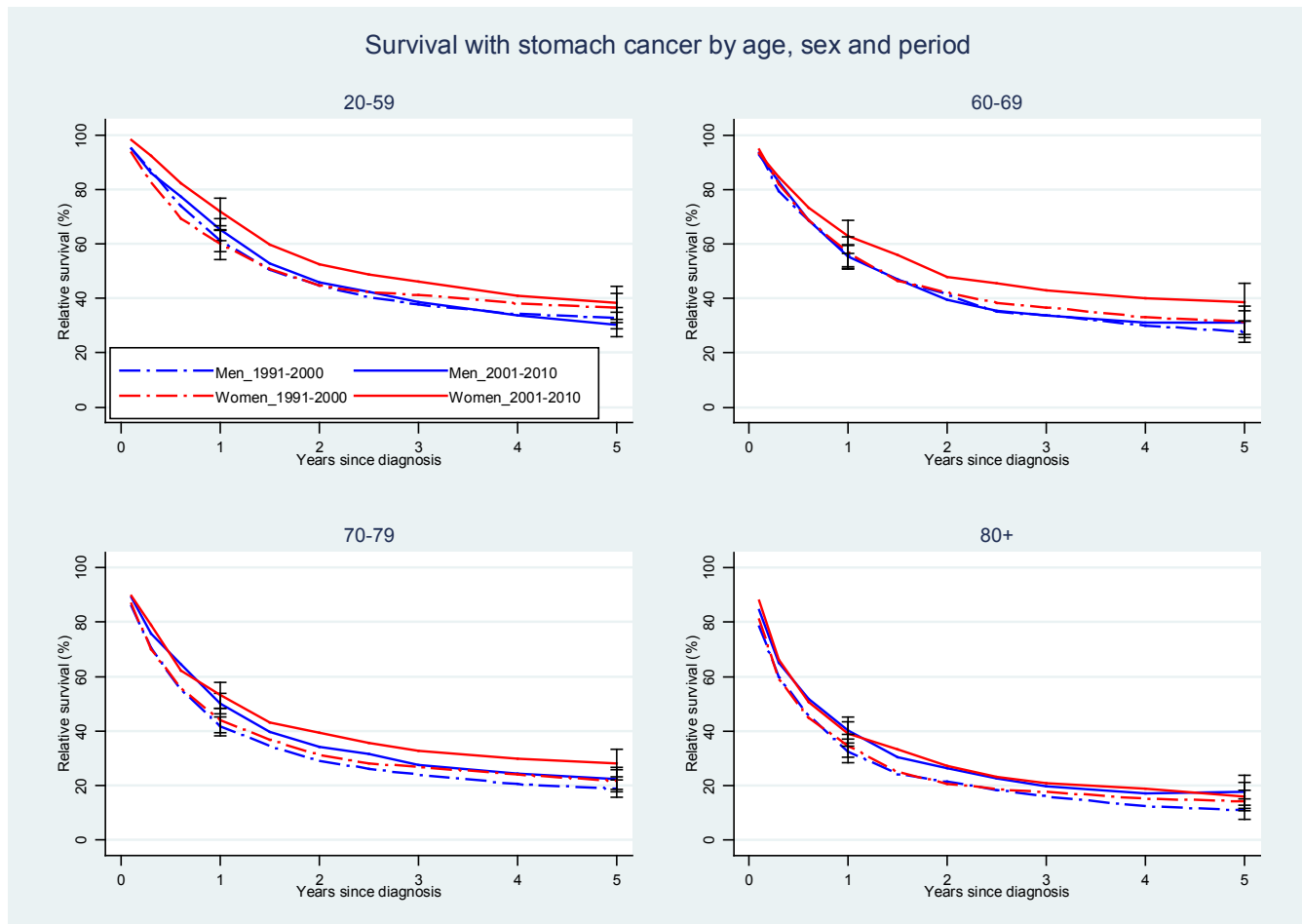
Age in years	Years since diagnosis	Observed survival %			Relative survival[1] %								
		Men	Women	Both	Men	95% CI[3] LL	UL	Women	95% CI[3] LL	UL	Both	95% CI[3] LL	UL
Calendar period of diagnosis 1991 - 2000													
20 - 59	1	60.9	59.7	60.5	61.2	57.1	65.1	59.9	54.3	65.1	60.7	57.4	63.9
60 - 69	1	54.9	56.5	55.4	55.8	51.7	59.7	57.0	50.8	62.7	56.1	52.7	59.3
70 - 79	1	39.9	42.8	41.0	41.8	38.2	45.3	43.9	39.3	48.3	42.5	39.7	45.3
80+	1	28.7	31.3	30.1	32.6	28.3	37.0	34.7	30.7	38.9	33.8	30.8	36.8
20 - 59	5	31.8	35.9	33.2	32.7	28.8	36.7	36.5	31.1	41.8	34.0	30.8	37.2
60 - 69	5	25.1	29.9	26.6	27.7	24.0	31.6	31.4	25.7	37.2	28.6	25.5	31.8
70 - 79	5	14.4	18.6	16.1	18.8	15.7	22.1	21.6	17.7	25.7	19.7	17.3	22.3
80+	5	5.6	8.2	7.0	10.9	7.5	15.1	14.2	10.7	18.3	12.9	10.3	15.8
stand.[2]	1	48.3	49.7	48.9	49.8	47.8	51.8	50.7	48.0	53.3	50.1	48.5	51.7
stand.[2]	5	21.0	25.1	22.5	24.0	22.2	26.0	27.4	24.9	30.0	25.2	23.7	26.7
Calendar period of diagnosis: 2001 - 2010													
20 - 59	1	65.2	72.1	67.7	65.4	61.3	69.3	72.2	66.9	76.8	67.9	64.6	70.9
60 - 69	1	54.8	62.4	57.2	55.6	51.3	59.6	62.9	56.4	68.6	57.7	54.2	61.1
70 - 79	1	48.7	52.2	50.1	50.4	46.5	54.2	53.2	48.3	57.8	51.4	48.4	54.4
80+	1	36.2	36.0	36.1	40.5	35.8	45.2	39.5	35.0	44.1	40.0	36.7	43.3
20 - 59	5	29.7	38.0	32.7	30.4	26.1	34.8	38.4	32.4	44.4	33.3	29.8	36.9
60 - 69	5	28.9	37.4	31.5	31.1	26.9	35.5	38.9	32.0	45.9	33.4	29.7	37.0
70 - 79	5	18.5	24.7	20.9	22.7	18.8	26.8	27.9	22.9	33.0	24.6	21.5	27.8
80+	5	9.3	9.8	9.6	17.6	12.6	23.6	16.1	11.6	21.3	16.9	13.4	20.7
stand.[2]	1	53.3	58.3	55.0	54.7	52.6	56.7	59.3	56.5	61.9	56.2	54.5	57.8
stand.[2]	5	23.2	29.7	25.5	26.4	24.2	28.7	32.2	29.1	35.2	28.3	26.6	30.1

[1] Survival analysis using the complete approach
[2] Age-standardized using ICSS weights
[3] CI: confidence limit; LL: lower limit; UL: upper limit

the International Cancer Survival Standards (ICSS) [17]. Standard weights for age groups were: 0.29 (20-59 years), 0.27 (60-69), 0.29 (70-79) and 0.15 (80-99). Ninety-five per cent confidence intervals (95% CI) were estimated using Greenwood's method [18] 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 [17].

To test for linear time trends of 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 as numeric covariate. The p-value for inclusion of calendar period as an explanatory variable, based on the Wald test, indicated the significance of a linear trend. The significance of a linear trend independent of age was tested by additionally adjusting the Poisson model for age. Annual percentage change (APC) was estimated as $APC = 100((RS_{last} / RS_{first})^{1/\Delta t}-1)$, with Δt as the difference between last and first calendar year.

Table 2: Observed and relative survival estimates after malignant stomach cancer diagnosis, with 95% confidence intervals by calendar period, age at diagnosis, years since diagnosis and sex. Data pooled from 13 Swiss cantons.

Results

This report includes more than 7,300 men and 5,000 women diagnosed with stomach cancer from 1980 to 2010 (Tab. 1). The national coverage of the NCD with respect to information on survival increased gradually over time. In 1980, 30% of the Swiss population was covered and increased to 56% in 2010. The median age in the study population was 70 years in men and 75 years in women. Table 2 and Fig. 1 compare survival by age, sex and time after diagnosis in two calendar periods of 10 years duration. The age-standardized one- and five-year relative survival in 1991-2000 for men was 49.8% and 24.0%, respectively. These values increased slightly to 54.7% and 26.4% in 2001-2010, respectively. For women, the one- and five-year

relative survival was only marginally higher: 50.7% and 27.4% for the earlier time period and improving moderately to 59.3% and 32.2% for the more recent period.

As with many cancers, survival for stomach cancer was highest in men and women below 60 years of age, even after taking account of the higher background mortality in older people, i.e. relative survival. The proportion surviving one or five years after having been diagnosed at age 80 or older was approximately one-half of the proportion of survivors in those diagnosed at below 60 years of age (Tab. 2).

Table 3 shows temporal trends in relative survival in finer detail. One- and five-year relative survival was estimated for five consecutive calendar periods of five-year duration. Small improvements were seen for one- and five-year survival in men and women, independently of whether diagnosed above or below age 70. Statistical significance was reached only for one-year survival trends. The outcome was similar if persons diagnosed at age 80 or more were compared with persons diagnosed at a younger age (not shown). The age-standardized one-year survival in men improved from 42.3% (95% CI 39.5-45.2) in the first

time period to 54.9% (95% CI 52.0-57.4) in the last. In women one-year survival improved from 44.6% (95% CI 40.7-48.5) to 60.6% (95% CI 56.8-64.2), respectively. The age-standardized survival five-years after diagnosis improved in men from 16.5% (95% CI 14.1-19.1) to 26.0% (95% CI 23.2-28.9) and in women from 23.2% (95% CI 19.5-27.0) to 33.5% (95% CI 29.6-37.5).

Discussion

Although the prognosis for stomach cancer remains poor, our findings show that survival probabilities in Switzerland have gradually improved in the last two decades. The age-standardized five-year RS for gastric cancer in Switzerland for 2001-2010 of 26% (95% CI 24-29) for men, 32% (95% CI 29-35) for women, and 28% (95% CI 27-30) for both sexes combined is in the same range as findings in other countries based on comparable calendar periods. Examples are the Nordic countries Finland (23% and 28% for men and women, respectively), Norway (24% and 26%) and Sweden (23% and 27%) [19].

Table 3: Trends in relative survival of stomach cancer cases pooled from 13 Swiss cantons for successive five-year calendar periods of follow-up.

Age in years	Years since diagnosis	Calendar period of death or censoring					APC[2]	Linear trend p-value[3]
		1986/1990	1991/1995	1996/2000	2001/2005	2006/2010		
		Relative survival[1] %	Relative survival[1] %	Relative survival[1] %	Relative survival[1] %	Relative survival[1] %		
Men								
20-69	1	50.4	54.5	61.5	57.9	61.0	0.8	<0.001
70+		31.3	32.0	36.7	40.6	46.3	1.6	<0.001
20-69	5	21.2	29.3	31.0	30.2	30.8	1.6	0.594
70+		10.4	11.8	15.6	16.9	19.8	2.7	0.279
stand.[4]	1	42.3	45.1	50.9	50.8	54.9	1.1	<0.001
	5	16.5	21.8	24.5	24.7	26.0	1.9	0.474
Women								
20-69	1	53.4	56.3	57.5	62.4	73.1	1.3	<0.001
70+		29.8	34.0	35.6	42.7	42.8	1.5	<0.001
20-69	5	27.3	30.0	33.7	37.1	40.6	1.7	0.095
70+		14.8	15.2	14.4	19.6	22.0	1.7	0.672
stand.[4]	1	44.6	47.4	49.0	54.8	60.6	1.3	<0.001
	5	23.2	24.1	26.1	29.6	33.5	1.5	0.302

[1] Survival analysis using the period approach

[2] Annual percentage change

[3] p-value of Wald test for calendar period in a Poisson regression model of excess mortality

[4] Age standardized using ICSS weights

In Germany, 30% and 31% have been reported [20]. The EUROCARE-4 study included data from 22 European countries and published a survival of 25% for both sexes combined [21]. Prognosis of stomach cancer seems to be slightly better in Italy, where RS was 34% for both sexes combined [22]. Compared with Switzerland survival seems to be worse in the UK (18% for both sexes combined) [23] or in Denmark (15% and 16% for men and women, respectively) [19].

Variations in survival are generally difficult to interpret. This report on gastric cancer survival in Switzerland is limited, because survival was only analyzed with respect to differences in sex, age and calendar period of diagnosis. Other important factors, such as earlier diagnoses at lower stages and/or improvements in surgical techniques, adjuvant and neo-adjuvant treatments, have often been proposed as explanations for differences in survival. Further possible explanations of survival differences are accessibility to specialized facilities, degree of multidisciplinary treatment planning, under-treatment and co-morbidities. In general, population-based studies on data collected by cancer registries are instrumental in understanding variations in survival, since they avoid the selection bias of hospital-based and/or specialized centre-based studies. On the other hand, population-based studies are often limited in data quality and completeness. There are only few population-based studies that investigated gastric cancer survival [24-27]. They showed that variations in survival can be explained in part by differences in tumour characteristics, such as the progression stage, subsite of occurrence and histological type, or by characteristics of the patient, such as social class. Specifically, persons with a tumour located at the gastric cardia [24], diffuse type histology [24] and low socioeconomic status [27] tended to have lower survival rates. Since surgical resection is currently the only curative treatment for stomach cancer, heterogeneity in surgical practices could represent relevant factors. It has been reported that the proportion of patients who received surgical resection correlated positively with 5-year relative survival [25]. These study outcomes suggest that improvements in diagnosis and treatment facilities could be beneficial in areas with lower survival.

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

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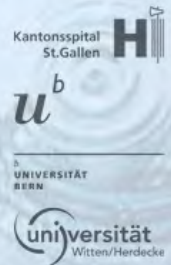
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Vorträge

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