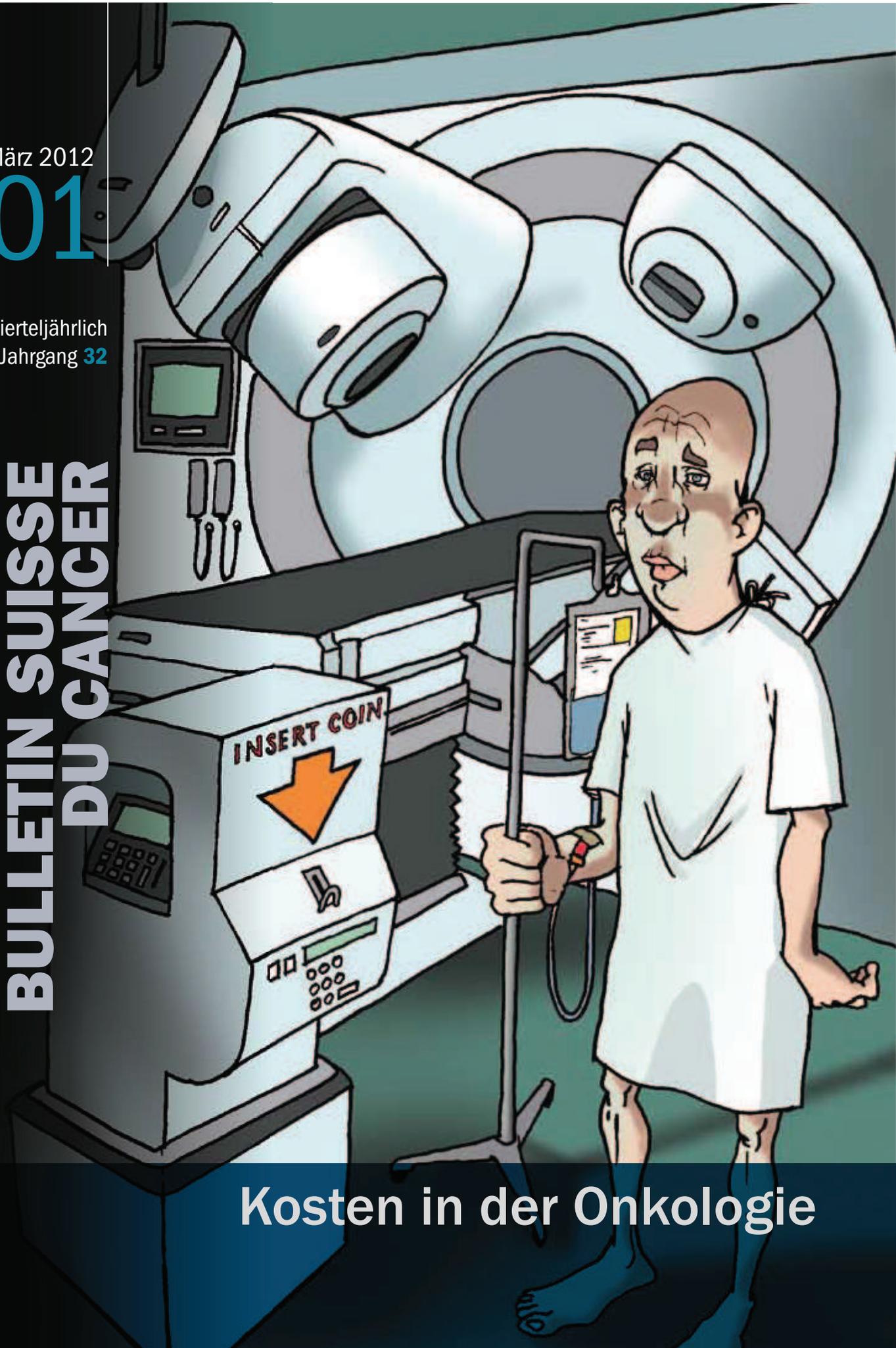


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DU CANCER**



Kosten in der Onkologie

Trends in Colorectal Cancer Survival in Switzerland

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Introduction

In Switzerland the incidence of colorectal cancer ranks third in males and second in females, with about 4000 new patients diagnosed each year (1). Incidence trends over the last decades have remained constant in both sexes, whereas mortality rates have been decreasing. Decreasing mortality is thought to be related to improved treatment during the past years as well as generalisation of colorectal cancer screening among the Swiss population. Colorectal cancer relative survival in Switzerland has been previously reported to be among the highest in Europe according to EURO-CARE, a population-based study of cancer survival in European countries (2).

One of the main objectives of Swiss cancer registries is to provide careful surveillance of trends in cancer survival in order to have comprehensive data for cancer control. The aim of the present study was to analyse relative and observed one-, five- and ten-year survival of patients diagnosed with a colorectal cancer between 1980 and 2009 in Switzerland.

Methods

Data were extracted from the anonymised national cancer dataset managed by the Foundation National Institute for

Cancer Epidemiology and Registration (NICER). Six cancer registries contributed data to this study, representing the cantons Basel (BS/BL), Fribourg (FR), Geneva (GE), Ticino (TI), Valais (VS) and Zürich (ZH). Registries recorded all incident cancer cases diagnosed in their resident population and assessed patients' survival through 31st December 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 the colorectal cancer. Completeness of case ascertainment for colorectal cancer has been determined in GE, Grison (GR), Glarus (GL), TI and VS and found to be higher than the international standard of at least 90% (3). In ZH and BS/BL, the last available follow-up date in 36% and 30% of alive patients, respectively, occurred before 31st December 2009 (see Table 1). The life-status of these patients was changed to lost-to-follow-up.

We selected patients with first primary malignant colorectal cancer (C18.0 to C20.9 in ICD-O, 3rd edition) (4), aged 15-99 years and diagnosed 1980-2009. All morphologies were included. If the colorectal cancer diagnosis was preceded by a diagnosis of non-melanotic skin cancer, the case was retained. The diagnosis of colorectal cancer was also included if it occurred within 30 days of another cancer diagnosis. We excluded all patients diagnosed at death. In total, 6.2% of the original diagnoses were excluded due to data quality considerations and 17.1% by the stated inclusion criteria.

First we derived observed survival probabilities for patients without taking cause of death into consideration. Then we calculated relative survival as the ratio of the observed probability of survival of cancer patients and persons in the general population of corresponding age, sex, calendar year of death, and geographical area (i.e. estimation of survival for colorectal cancer accounting for general population mortality) (5, 6). Expected cancer survival proportions were estimated using Hakulinen's method (7) applied to all-cause mortality tables supplied by the Swiss Federal Statistical Office. Death probabili-

Registry	Incidence period	Number of Patients	Person years	% of pooled person years	Last follow-up
GE	1980-2008	5172	27890.1	19.9	2009
ZH	1980-2009	13575	56747.2	40.5	1990-2009
BS/BL	1981-2008	6151	33668.4	24.0	2003-2009
VS	1989-2009	2425	11019.5	7.9	2009
TI	1996-2009	2613	10187.2	7.3	2009
FR	2006-2009	494	747.9	0.5	2009
Total		30430	140260.3	100.0	

Table 1: Contribution of colorectal cancer cases to the pooled dataset including patients aged 15-99 years from six cancer registries.

ties, transformed from age-, sex- and calendar year-specific death rates, were interpolated and smoothed using the Elandt-Johnson formula (8). Relative survival ratios (RSR) were estimated using the `strs` command (version 1.3.5) (9), written for the Stata Statistical Software (Stata-Corp LP, v 12.0) (10). Period analysis was used to derive more up-to-date relative survival estimates compared to those possible from traditional cohort analysis (11). In brief, period analysis describes the survival experience of patients selected by a period of follow-up dates. This is achieved by left censoring (truncation) of person-times at risk at the beginning of the specified period in addition to right censoring at its end. All 95% confidence intervals (CI) were estimated based on Greenwood's formula (12).

Results

Table 1 presents the years of inclusion, the number of colorectal cancer cases, person years contributed, and the date of last follow-up by all six cancer registries. Colorectal cancer relative survival in Switzerland improved between 1995-1999 and 2005-2009 (Table 2, Figure 1). Within each period only nominal differences by gender and between five- and ten-year relative survival were seen. The most pronounced improvement between periods was observed for shorter-term survival (one-year RSR 0.78 vs. 0.83; five-year RSR 0.57 vs. 0.62) with little change in long-term survival (ten-year RSR 0.53 vs. 0.54). Figure 2 displays trends in one-, five- and ten-year colorectal cancer relative survival 1989-2009 based on seven successive three-year periods. An increase of one-year survival was seen in the period 2001-2003 that remained consistent in all subsequent periods. However, five- and ten-year

colorectal cancer relative survival showed a more inconsistent pattern over follow-up. Five- and ten-year survival increased in the period 1995-1997, decreased 1998-2000, increased 2001-2003 and 2004-2006 then levelled off (slightly decreasing) 2007-2009. Figure 3 shows age-specific colorectal cancer relative survival for 2005-2009. Persons aged 45-54 years had the best overall colorectal cancer survival, while persons aged 75 years and older had poorer relative survival than younger persons.

Discussion

The main finding in the current study was an overall improvement in colorectal cancer relative survival in Switzerland during the last decades for both males and females. However, the increase was not seen in long-term survival or older patients. Interpreting comparisons over longer-periods are limited by the fact that the population at risk in earlier periods was smaller, because fewer cantons registered cancer cases in the earlier years. Furthermore, we did not attempt to adjust for possible changes in the prognosis relevant stage-distribution between patients diagnosed 1987±2 years and those diagnosed 1997±2 years, on which the 10-year survival estimates for follow-up periods 1997±2 years and 2007±2 years are based, respectively. Changes in stage-distribution are expected as a result of recent colorectal cancer screening activity. Thus, it is likely that 10-year survival based on diagnoses 1997±2 years underestimated true survival more strongly than those based on diagnoses 1987±2 years, because there was a larger change in screening related stage-distribution for the former compared to the latter (13).

Table 2: Cumulative relative colorectal cancer survival with 95% confidence intervals (CI) by gender and calendar period of follow-up. Includes patient aged 15-99 years, diagnosed 1980-2009 with follow-up through 2009. Cases from six cancer registries pooled.

Years since Diagnosis	Gender	Calendar Period			
		1995-1999		2005-2009	
		Relative Survival Ratio	95% CI	Relative Survival Ratio	95% CI
1	Men	0.79	[0.77, 0.81]	0.84	[0.82, 0.85]
	Women	0.76	[0.74, 0.78]	0.82	[0.80, 0.83]
	Both	0.78	[0.76, 0.79]	0.83	[0.82, 0.84]
5	Men	0.55	[0.53, 0.58]	0.62	[0.60, 0.64]
	Women	0.58	[0.56, 0.61]	0.62	[0.60, 0.64]
	Both	0.57	[0.55, 0.58]	0.62	[0.61, 0.64]
10	Men	0.51	[0.48, 0.55]	0.53	[0.50, 0.56]
	Women	0.55	[0.52, 0.58]	0.56	[0.53, 0.59]
	Both	0.53	[0.51, 0.56]	0.54	[0.52, 0.56]

Swiss survival results observed herein (62% five-year survival) are consistent with EUROCARE-4 analyses. Results from both studies indicate that Switzerland has one of the highest colorectal cancer survival probabilities in Europe; similar to those observed in highly ranked Scandinavian countries like The Netherlands (61.9%) and Sweden (60.3%). Though, caution should be used making direct comparisons between studies since the data stem from different time periods (EUROCARE-4 2000-2003, NICER 2005-2009) (14).

The increase in overall survival is consistent with the declining mortality and stable incidence rates observed over the past decades in Switzerland (1). Improvements in survival are also likely due to multiple factors. For example, increased early detection from colorectal cancer screening (e.g. blood tests or colonoscopy exams in asymptomatic patients) could have a positive effect on survival. Colorectal cancer screening is recommended internationally although to date no Swiss-wide organized screening programs exist. Other contributing factors may be increasing access to best clinical practices by the spread of the multidisciplinary case discussion approach, adoption of improved surgical techniques (e.g. total meso-rectal excision or liver metastasis resection), widespread use of chemotherapy for stage III colon cancer, or neo-adjuvant radiotherapy for rectal tumours. Finally, the influence of increased patient awareness of symptoms may have contributed as well.

Several studies within the Swiss context underscore some of these potentially contributing factors. A 2009 study in Ticino reported a down-staging trend of colorectal cancer with a decrease in patients with lymph node metastasis (15). Moreover, the study also showed that patients increasingly benefited from histological analysis of at least 12 lymph nodes. Increased node assessment improved staging quality and permitted more precise indication of adjuvant treatments. Another recent Swiss regional population-based study showed a high prescription of neo-adjuvant radiotherapy for locally advanced rectal cancers (16). While an older population-based study in Geneva reported that the use of chemotherapy for node positive colon cancer increased between 1990 and 1996 but age strongly modulated chemotherapy use (17). For example, in 1996 54% of eligible patients received chemotherapy but only 13% among those diagnosed after age 70 years. This study concluded that a strong beneficial effect of adjuvant chemotherapy on advanced stage colon cancer can be achieved in routine practice. However, chemotherapy is probably not optimally utilised in Switzerland, particularly among older patients.

Similarly to breast cancer, we observed a statistically significant lower relative survival probability for patients

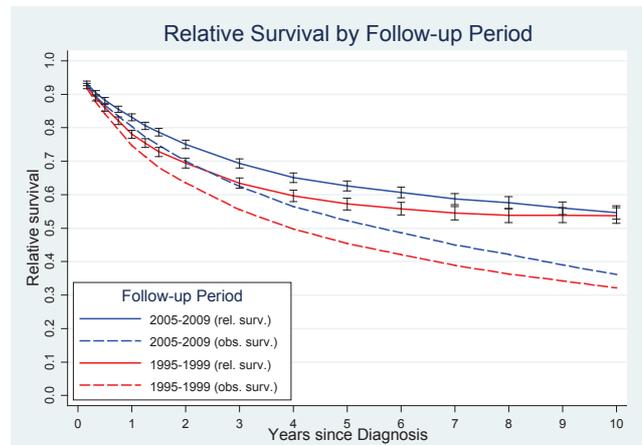


Figure 1: Colorectal cancer cumulative observed and relative survival with 95% confidence intervals in two separate calendar periods for all six registries pooled.

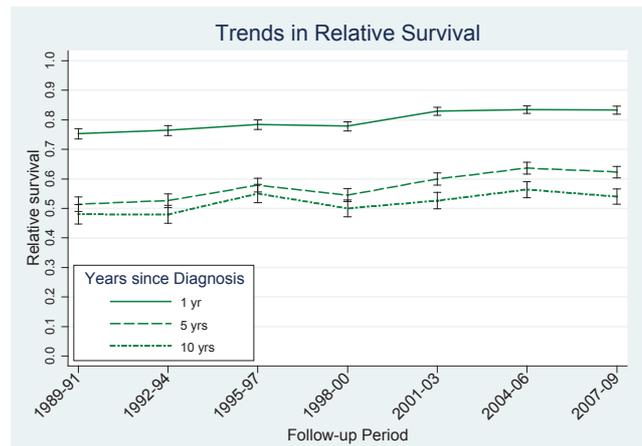


Figure 2: Trends in colorectal cancer cumulative relative survival ratios with 95% confidence intervals from 1989 to 2009 in successive three-year intervals for all six registries pooled.

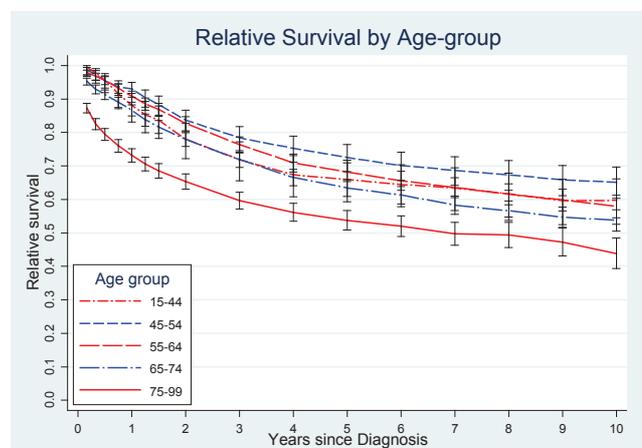


Figure 3: Age-specific colorectal cancer cumulative relative survival ratios with 95% confidence intervals in the calendar period 2005-2009 for all six registries pooled.

older than 75 years (18). The same pattern has been observed in EUROCORE-4 and other studies (2). This difference has been attributed to both the increased probability of comorbidity with age and potentially less rigorous adoption of best clinical practices in older cancer patients.

In conclusion, we observed over the study period an overall increase in colorectal cancer relative survival. Even if these population-based survival results reflect screening and treatment recommendations, there is still room for additional improvement including public health strategies for increasing screening coverage and better access to best clinical practice in particular among older patients.

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

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