

## Variation in survival after diagnosis of breast cancer in Switzerland

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Received 14 March 2005; revised 24 June 2005; accepted 2 August 2005

**Background:** Survival after diagnosis of cancer is a key criterion for cancer control. Major survival differences between time periods and countries have been reported by the EURO CARE studies. We investigated whether similar differences by period and region existed in Switzerland.

**Methods:** Survival of 11 376 cases of primary invasive female breast cancer diagnosed between 1988 and 1997 and registered in seven Swiss cancer registries covering a population of 3.5 million was analysed.

**Results:** Comparing the two periods 1988–1992 and 1993–1997, age-standardized 5 year relative survival improved globally from 77% to 81%. Furthermore, multivariate analysis adjusting for age, tumour size and nodal involvement identified regional survival differences. Survival was lowest in the rural parts of German-speaking eastern Switzerland and highest in urbanised regions of the Latin- and German-speaking northwestern parts of the country.

**Conclusions:** This study confirms that survival differences are present even in a small and affluent, but culturally diverse, country like Switzerland, raising the issue of heterogeneity in access to care and quality of treatment.

**Key words:** breast cancer, cancer registry, population-based, survival differences, Switzerland

### Introduction

Breast cancer is the most frequent malignancy among women in Switzerland and in developed countries. In Europe breast cancer accounted for 13% of all newly diagnosed cases and 8% of all cancer deaths in both sexes combined in 2004 [1]. Prognosis is usually better than for other major cancers, and an improvement in survival in recent decades has been reported [2–4]. This improvement has been variously ascribed to earlier diagnosis, including widespread use of mammography or mass screening campaigns, and to increasing use of effective adjuvant therapy [5–8]. Optimal locoregional control by both surgery and radiotherapy as well as adjuvant systemic therapy have had a major impact on outcome [9,10].

Survival after diagnosis of cancer is one of the major outcome measurements and key criteria for assessing quality of cancer control related to both the preventive (early detection) and the therapeutic level. Using data from cancer registries allows population-based comparisons.

EURO CARE studies have been a milestone in population-based research on survival after cancer diagnosis in Europe. Major differences have been found in different countries and time periods within Europe [5,11,12]. Data from two Swiss areas, Basel and Geneva, were included in these studies. The survival rates estimated in these two regions were favourable compared with most other European regions. However, these two Swiss registries cover highly urbanised populations and therefore are not representative of the Swiss population overall.

There are marked cultural and geographical differences within Switzerland. In addition, organisation and provision of health care remains the responsibility of the cantons to a major extent and thus varies between them. This is also reflected in the cantonal differences of per capita health care expenditure. Earlier analyses have shown clear differences in incidence (Association of Swiss Cancer Registries: [www.asrt.ch](http://www.asrt.ch)) and mortality for many cancers between the various regions of Switzerland [13]. Furthermore, a previous exploratory analysis of breast cancer in two Swiss German-speaking cantons suggested the existence of survival differences [14]. In the present study we extended the investigation to other regions of the country by including data from patients diagnosed between 1988 and 1997 in seven population-based cancer registries.

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## Materials and methods

Seven of the nine population-based Swiss cancer registries covering a population of ~3.5 million inhabitants (48% of the Swiss population) were involved. The cancer registries in Basel ( $N = 2722$ ), Geneva ( $N = 2619$ ), Graubünden–Glarus ( $N = 930$ ), St Gall–Appenzell ( $N = 2155$ ), Valais ( $N = 1200$ ), Zürich ( $N = 1124$ ) and Ticino ( $N = 626$ ) provided a total of 11 376 registered cases of primary breast cancer followed for at least 5 years after diagnosis. Cases diagnosed between 1988 or 1989 and 1997 were included in Basel, Geneva, St Gall–Appenzell, Graubünden–Glarus and Valais, between 1993 and 1997 in Zürich, and between 1996 and 1998 in Ticino. The largest Swiss tumour registry in Zürich provided survival information for a random sample of 33% of all breast cancer patients diagnosed between 1993 and 1997. Tests for representativeness of this sample with regard to age distribution and nodal status confirmed the validity of the Zürich sample. All registries used active follow-up on life status.

The data were merged into a central database after a number of quality controls for validity and accuracy. These quality controls included routine plausibility checks on diagnosis, morphology, topography, age, sex, dates and checks on completeness, as well as controls on compatibility of the variables used for staging. All participating registries contribute their data to the International Agency of Research on Cancer (IARC) and fulfil their quality controls. In cases with multiple tumours, only the first diagnosed malignant tumour was included. Bilateral synchronous breast cancers were counted as a single tumour. Cases known from their death certificate only (DCO) and cases detected at autopsy were excluded.

Six of the seven registries have collected information on stages since 1993, all but one of those by active collection of information through mailing of questionnaires to the treating physicians or consultation of patient records. All used UICC rules (fourth or fifth edition). Stage data were grouped into five EUROCCARE categories: stage 1 = T1, N0, M0; stage 2 = T2–3, N0, M0; stage 3 = T1–3, N1, M0; stage 4 = T4, any N, M0; stage 5 = any T, any N, M1; stage 6 = unspecified stage. Data on the number of lymph nodes examined were available since 1995 from all registries. The accuracy of such information was checked by local staff and, in addition, a standard procedure for checking validity and concordance was conducted centrally for all data.

The Zürich registry was unable to provide data on metastatic status at diagnosis. For this reason, Cox modelling analyses for inter-cantonal comparisons of survival were adjusted for age (continuous), tumour size (three categories: T0–1, T2–4, unknown), nodal involvement (three categories: N0, N1, unknown) and number of nodes examined (five categories: zero, 1–4, 5–9, 10–14, 15+), but not for complete stage including metastatic status. However, we used the EUROCCARE five-category staging to compare frequencies of stage distribution by age across all registries except Zürich.

Since information about the specific cause of death was not available for all registries, the effects of mortality from competing causes were taken into account by computing relative survival rates, a net survival measure representing survival in the absence of other causes of death. This is the preferred method for analysing the survival of cancer patients in population-based studies. This survival probability is calculated using general mortality tables related to each study period and each canton (one table per year and per canton) provided by the Swiss Federal Statistical Office.

Age-standardised relative survival rates were calculated taking the age distribution of the EUROCCARE-2 Study breast cancer population as the reference [12]. The confidence intervals (CIs) were calculated on the basis of likelihood ratio statistics.

In all participating registry regions there was at least one specialised radiotherapy service unit in operation in the mid-1990s. Oncology services were available in all regions except Valais, where the unit came into operation only after the period of this study. The nearest available hospital-based oncology service was about 100–150 km distant in Lausanne. However, there were three free practising oncologists available in the canton of Valais

during the study period. The centres in some of the more rural cantons (Graubünden–Glarus, St Gall–Appenzell, Valais, Ticino) are widespread, and it may take longer to reach a centre, even if available, than in urban regions (Geneva, Basel, Zürich).

## Results

The proportion of pathologically verified cases of breast cancer was  $\geq 97\%$  in all registries. The proportion of cases eliminated as DCO was  $< 2\%$  in all registries, and the same was true for cases diagnosed at autopsy. The proportion of cases lost to follow-up during the two periods of observation was generally low (3.6% and 2.2% in all registries together) except in Geneva (7.3% and 5.3%) and Graubünden–Glarus (6.7% and 3.5%). These differences were not statistically significant. The proportion of patients who died within the first month was  $\sim 1\%$  overall, ranging from 0.6% in Basel to 2.5% in St Gall–Appenzell.

Age at diagnosis was not equally distributed between the registries ( $P < 0.01$  for the whole period). During the first period (1988–1992) the differences were statistically significant for the youngest (15–44 years) and oldest ( $\geq 65$  years) age groups only, but not for women aged 45–64 years. During the second period (1993–1997/8), the differences were statistically significant for all age groups ( $P < 0.05$ ) except for 15–44 years. The cantons of St Gall–Appenzell (28%), Graubünden–Glarus (24%), Ticino (24%) and Basel (23%) had the highest proportions of cases aged  $> 75$  years (Table 1).

Information on nodal involvement was available for all registries. In the second period, the proportion of cases with unknown status was 10.5% overall, with some differences by age: 4% for 15–44 years, 5% for 45–54 and 55–64 years, 7% for 64–74 years and 28% for  $\geq 75$  years. The proportion of cases with unknown status was  $\leq 10\%$  in patients aged  $< 65$  years in all registries, and in all but Zürich and Ticino in the age group 65–74 years. Geographical differences exist for the distribution of nodal status at diagnosis (Table 2). They vary by age. For instance, during the second period (1993–1997) the proportion of nodes positive ranged from 37% (Ticino) to 54% (St Gall–Appenzell) for age 15–44 years, from 34% (Ticino) to 48% (St Gall–Appenzell) for age 45–54 years, from 41% (Geneva) to 56% (St Gall–Appenzell) for age 55–64 years, from 38%

**Table 1.** Age distribution (%) (Period 2: 1993–1997/8)

Age	Basel	St Gall	Geneva	GR–GL	Valais	Zürich	Ticino	Total
15–44	10.0	11.7	11.8	14.7	13.4	10.9	12.6	11.7
45–54	21.1	20.6	24.7	20.1	26.9	24.6	20.3	22.7
55–64	22.5	19.1	25.3	18.2	23.3	23.3	22.2	22.4
65–74	23.2	21.2	18.8	22.8	17.9	20.7	20.9	20.8
75–99	23.2	27.5	19.5	24.2	18.5	20.6	24.0	22.4
Total	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
<i>N</i>	1397	1114	1391	571	725	1124	626	6948

GR–GL, Graubünden–Glarus.

**Table 2.** Distribution of lymph node status (%), all ages (period 2: 1993–1997/8)

Node status	Basel	St Gall	Geneva	GR–GL	Valais	Zürich	Ticino	Total
Positive	39.3	46.1	40.8	43.6	43.4	39.1	34.3	41.0
Negative	53.0	43.4	52.9	44.3	44.8	47.8	46.5	48.4
Unknown	7.7	10.5	6.3	12.1	11.7	13.1	19.2	10.5
Total	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
N	1397	1114	1391	571	725	1124	626	6948

GR–GL, Graubunden–Glarus.

(Zürich) to 50% (St Gall–Appenzell) for age 65–74 years and from 24% (Ticino) to 37% (Valais) for age  $\geq 75$  years.

Based on the most recent period of observation (1997–1998), the number of lymph nodes examined is heterogeneous. In German-speaking Switzerland, surgeons usually practise larger surgical sampling than in the western part: in Basel, St Gall–Appenzell, Zürich and Graubunden–Glarus, more than 15 lymph nodes are sampled in at least 40% of cases compared with 36% in Geneva, 23% in Ticino and 22% in Valais ( $P < 0.01$ ). Overall, 39% of cases had more than 15 lymph nodes sampled, 27% between 10 and 14, 13% between five and nine, and 5% between five and zero. Information is missing for 19% of cases.

Table 3 shows the geographical distribution of T stage for all age groups combined, and Table 4 shows the stage distribution according to EUROCORE stage. Overall, stages were not equally distributed between the registries during the period 1993–1997 ( $P < 0.05$ ). For instance, Valais (12.4%) and Basel (8.4%) had more frequent stage 4 than Graubunden–Glarus (5.6%) and St Gall–Appenzell (5.8%) ( $P < 0.01$ ). This heterogeneity was also observed in age-specific figures. For example, in the age groups 55–64 years and 65–74 years, stage 1 was less frequent in St Gall–Appenzell (19%, 18%), Valais (27%, 25%) and Graubunden–Glarus (31%, 25%) than in Basel (37%, 29%), Ticino (37%, 28%) and Geneva (40%, 39%) ( $P < 0.01$ ), possibly reflecting differences in screening activities. In the age group  $\geq 75$  years, stages 2, 4 and 5 differed statistically significantly between the six registries.

Table 5 shows 1 year and 5 year age-specific and age-standardised relative survival for cases diagnosed between 1993 and 1997. Age-specific observed (data not shown) and relative survival tended to be better in Ticino, Basel and Geneva than in Graubunden–Glarus and St Gall–Appenzell, with survival in Valais and Zürich being intermediate. The difference between maximum and minimum relative survival increased with age from 2.4% (15–44 years) to 10.7% ( $\geq 75$  years) for 1 year survival, and from 9.5% (15–44 years) to 16.8% ( $\geq 75$  years) for 5 year survival.

Table 6 shows that age-standardised relative 5 year survival improved between the two periods in all cantons providing data for both periods (statistically significant for all five registries together). Table 7 shows the annual relative risk of death in relation to Zürich (reference category) after adjustment of

**Table 3.** Distribution of T stage (%), all ages (period 2: 1993–1997/8)

T, pT	Basel	St Gall	Geneva	GR–GL	Valais	Zürich	Ticino	Total
0	–	–	0.4	–	–	–	–	0.1
1	40.2	32.5	49.7	47.6	44.0	41.5	49.7	43.0
2	41.4	44.0	32.9	36.4	33.9	40.3	32.4	38.0
3	5.2	6.7	4.7	3.7	4.3	4.7	2.6	4.8
4	10.0	8.8	9.2	9.3	15.6	9.4	9.6	10.0
X	2.9	0.2	2.9	3.0	2.2	0.8	2.1	2.0
Empty	0.2	7.8	0.1	0.0	0.0	3.2	3.7	2.2
Total	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
N	1397	1114	1391	571	725	1124	626	6948

GR–GL, Graubunden–Glarus.

**Table 4.** Distribution of EUROCORE stage (%) (period 2: 1993–1997/8)

EUROCORE	Basel	St Gall	Geneva	GR–GL	Valais	Zürich	Ticino	Total
Stage 0	0.0	0.0	0.3	0.0	0.0	–	0.0	0.1
Stage 1	28.3	19.7	34.7	27.8	27.0	–	31.2	28.3
Stage 2	21.5	19.7	16.0	15.1	14.5	–	13.7	17.5
Stage 3	31.1	34.6	31.8	35.0	33.1	–	27.2	32.2
Stage 4	8.4	5.8	6.6	5.6	12.4	–	7.3	7.6
Stage 5	4.5	8.2	5.9	7.7	6.1	–	6.1	6.2
Unknown	6.0	11.9	4.7	8.8	6.9	–	14.5	8.1
Total	100.0	100.0	100.0	100.0	100.0	–	100.0	100.0
N	1397	1114	1391	571	725	–	626	5824

GR–GL, Graubunden–Glarus.

age, tumour size, nodal status and number of nodes sampled. The annual risk of death is higher for St Gall–Appenzell ( $P < 0.05$ ) and Graubunden–Glarus (not significant) and lower for Basel, Geneva and Valais ( $P < 0.05$ ). Ticino and Zürich have similar risks.

Relative 5 year survival by EUROCORE stage and registry area (except Zürich) is presented in Table 8. There were moderate differences between registries for stage 1 (range 94–99%), stage 2 (84–92%) and stage 3 (79–85%) cancers, respectively. Survival ranged from 31% (Graubunden–Glarus) to 72% (Ticino) for stage 4 (pT4 without known metastasis) and from 14% (St Gall–Appenzell) to 30% (Geneva) for stage 5 (distant metastasis). There was also a suggestion of a difference of survival for unknown stages (ranging from 56% in Geneva to 82% in Ticino).

Figure 1 shows observed and relative survival of all cases and ages combined, by canton, for the period 1993–1997. Relative survival discrepancies between cantons were larger for cases with positive lymph nodes than for cases with negative ones (Figure 2). Relative 5 year survival in St Gall–Appenzell and Graubunden–Glarus was poorer than in Ticino, Geneva and Basel for cases with both negative and positive lymph nodes. In Zürich and Valais, relative survival was close to the intercantonal mean.

**Table 5.** Age-standardised and age-specific relative survival for cases diagnosed in the period 1993–1997/8

Age at diagnosis (years)	15–44	45–54	55–64	65–74	75–99	ASR <sup>a</sup>
<b>1 year survival</b>						
Ticino	1.00	1.00	1.00	0.97	0.92	0.98
Basel	0.98	0.99	0.97	0.98	0.95	0.97
Geneva	1.00	0.98	0.98	0.99	0.87	0.96
Zürich	0.98	0.97	0.98	0.93	0.92	0.96
Graubunden–Glarus	1.00	0.96	0.98	0.92	0.90	0.95
St Gall–Appenzell	0.98	0.98	0.97	0.94	0.85	0.94
Valais	1.00	0.98	0.95	0.90	0.89	0.94
<b>5 year survival</b>						
Ticino	0.91	0.90	0.83	0.82	0.75	0.84
Basel	0.84	0.89	0.84	0.85	0.76	0.83
Geneva	0.88	0.90	0.87	0.86	0.64	0.83
Zürich	0.84	0.87	0.81	0.76	0.76	0.80
Valais	0.82	0.87	0.80	0.76	0.76	0.80
Graubunden–Glarus	0.83	0.78	0.77	0.79	0.71	0.77
St Gall–Appenzell	0.83	0.81	0.78	0.77	0.63	0.76

<sup>a</sup>Standardised to the age distribution of the EURO-CARE-2 study breast cancer population [12].

## Discussion

We identified differences in breast cancer survival by period and region (cantons) in 11 376 cases diagnosed between 1988 and 1997 in Switzerland, a small and affluent, but culturally diverse, country. Overall survival of patients diagnosed with breast cancer improved over time. The proportion of patients surviving at least 5 years was 69% for those diagnosed between 1988 and 1992 (relative survival 77%), and 73% for those diagnosed between 1993 and 1997 (relative survival 81%). Age-standardised relative survival was lower in rural regions of eastern Switzerland than in more urbanised western and northern regions. These differences became minor in the second time period for node-negative and low-stage cases, but remained present in node-positive and advanced-stage tumours. This confirms a previous exploratory study demonstrating less favourable survival rates for St Gall–Appenzell compared with Basel [14].

Our observation is in line with previous data from Europe [2–4] and with data from other countries, i.e. Italy, where major cultural differences also exist [4]. A difference in survival was observed between the south and other parts of the country for many tumours, including breast cancer. Additional analyses of time trends by region also showed that there was less improvement in survival in southern parts of the country. In the EURO-CARE study, lower survival rates had been found in Denmark than in Sweden, which are neighbouring Nordic countries. Jensen et al. [15] compared survival of breast cancer patients from Aarhus in Denmark and Malmö in southern Sweden in a population-based historical follow-up study of patients diagnosed between 1983 and 1989. Even after adjustment for several possible explanatory factors (age, tumour size, intensity of lymph

**Table 6.** Age-standardised<sup>a</sup> relative survival for two different periods of diagnosis

Relative survival	1 year		5 year		10 year
Period of diagnosis	1988–1992	1993–1997	1988–1992	1993–1997	1988–1992
Ticino		0.98		0.84	
Basel	0.97	0.97	0.80	0.83	0.69
Geneva	0.96	0.96	0.80	0.83	0.68
Zürich		0.96		0.80	
Valais	0.93	0.94	0.74	0.80	0.67
Graubunden–Glarus	0.96	0.95	0.74	0.77	0.56
St Gall–Appenzell	0.93	0.94	0.72	0.76	0.60
All excluding TI and ZH	0.95	0.96	0.77	0.81	0.66

<sup>a</sup>Standardised to the age distribution of the EURO-CARE-2 study breast cancer population [12].

**Table 7.** Annual relative risk of death for each canton compared with Zürich (period 2: 1993–1997/8)

Registries	Unadjusted RR (95% CI)	Adjusted <sup>a</sup> RR (95% CI)
Zürich ( <i>N</i> = 1125)	1	1
Basel ( <i>N</i> = 1397)	0.95 (0.83–1.08)	0.78 (0.66–0.92)
St Gall–Appenzell ( <i>N</i> = 1114)	1.32 (1.14–1.52)	1.18 (1.02–1.38)
Geneva ( <i>N</i> = 1391)	0.81 (0.71–0.93)	0.65 (0.55–0.76)
Glarus ( <i>N</i> = 82)	1.30 (0.89–1.91)	1.09 (0.74–1.61)
Graubunden ( <i>N</i> = 489)	1.18 (0.97–1.42)	1.15 (0.94–1.40)
Ticino ( <i>N</i> = 626)	0.89 (0.75–1.06)	0.97 (0.81–1.16)
Valais ( <i>N</i> = 725)	0.97 (0.81–1.15)	0.73 (0.60–0.88)

<sup>a</sup>Adjusted on age, nodal status, tumour size and number of nodes sampled.

node examination, regional and distant spread), as well as use of mammography screening, a clear difference in breast cancer survival between these two areas persisted. Differences in health care and treatment modalities may explain some of these remaining differences in two otherwise quite comparable areas. In a later comparison between Danish and Swedish patient cohorts diagnosed between 1996 and 1997 the between-country difference tended to disappear [16]. Survival of breast cancer patients in populations from 99 health authority regions in England was compared in a study based on cancer registry data [17]. Even after taking socio-economic differences between the regions into account, a statistically significant variation in breast cancer survival between health authorities in England remained. No tumour-specific prognostic factors were taken into account in this study. Differences in survival by district (health boards) were also investigated in patients from Scotland diagnosed in 1987, and the authors found statistically significantly different survival (based on disease-specific deaths) in some districts even after adjustment for clinical factors such as tumour stage [18].

Many factors may influence survival, including socio-economic status, degree of urbanisation, cultural differences,

**Table 8.** Five year relative survival by EUROCARE stage (period 2: 1993–1997/8)

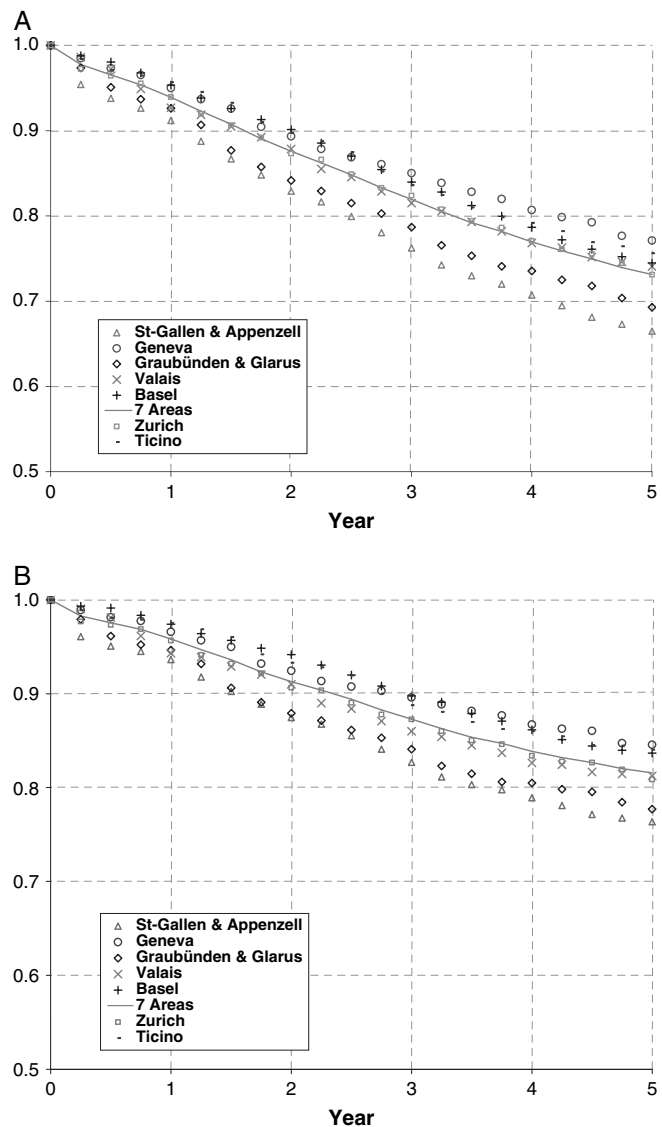
Stage	St Gall	Geneva	GR–GL	Valais	Basel	Ticino
1	0.98	0.99	0.97	0.94	0.97	0.98
2	0.89	0.91	0.84	0.90	0.91	0.92
3	0.79	0.85	0.79	0.84	0.80	0.81
4	0.38	0.52	0.31	0.69	0.71	0.72
5	0.14	0.30	0.24	0.27	0.25	0.24
Unknown	0.66	0.56	0.69	0.59	0.69	0.82

GR–GL, Graubunden–Glarus.

patient behaviour, physicians' attitudes, treatment, and health care system [19–22]. While the available data do not allow identification of specific reasons for the observed survival differences, the observed tendency of a lower proportion of early-stage cases in regions with less favourable survival rates implicates differences in secondary prevention across cantons as one potential source.

Populations from various cultural backgrounds as well as from urban and rural regions are included in this study. Zürich and Basel are highly urbanised mainly German-speaking areas, St Gall–Appenzell and Graubunden–Glarus are rural and German-speaking (in Graubunden a large part of the population is bicultural, Rumantsch and German, and a minority are Italian-speaking). Geneva is highly urbanised and French-speaking, Ticino is partly urban with an Italian background and Valais is rural with a mixed cultural background, but is predominantly French-speaking. These cultural differences are known to have an influence on the attitude to health problems in the population as well as in health care professionals (e.g. towards early detection) [23]. There were no mammography screening programmes during the study period. However, spontaneous screening regularly increased and official programmes started in 1998 in the French-speaking part of Switzerland, whereas no such programmes have been instituted so far in the German part. The prevalence of women ever having undergone a mammography differs substantially between the Latin- and German-speaking parts of Switzerland [23]. These differences in behaviour could also explain why breast cancer incidence is higher in the western cantons than in the eastern cantons of Switzerland: age-standardised incidence (European) between 85 per 100 000 in St Gall–Appenzell and 127 per 100 000 in Geneva in the period 1993–1997. Trends in mortality (European standardised rates) over the past 20 years are also clearly different in these two cantons: from 29 to 27 per 100 000 in St Gall–Appenzell, and from 40 per 100 000 to 24 per 100 000 in Geneva.

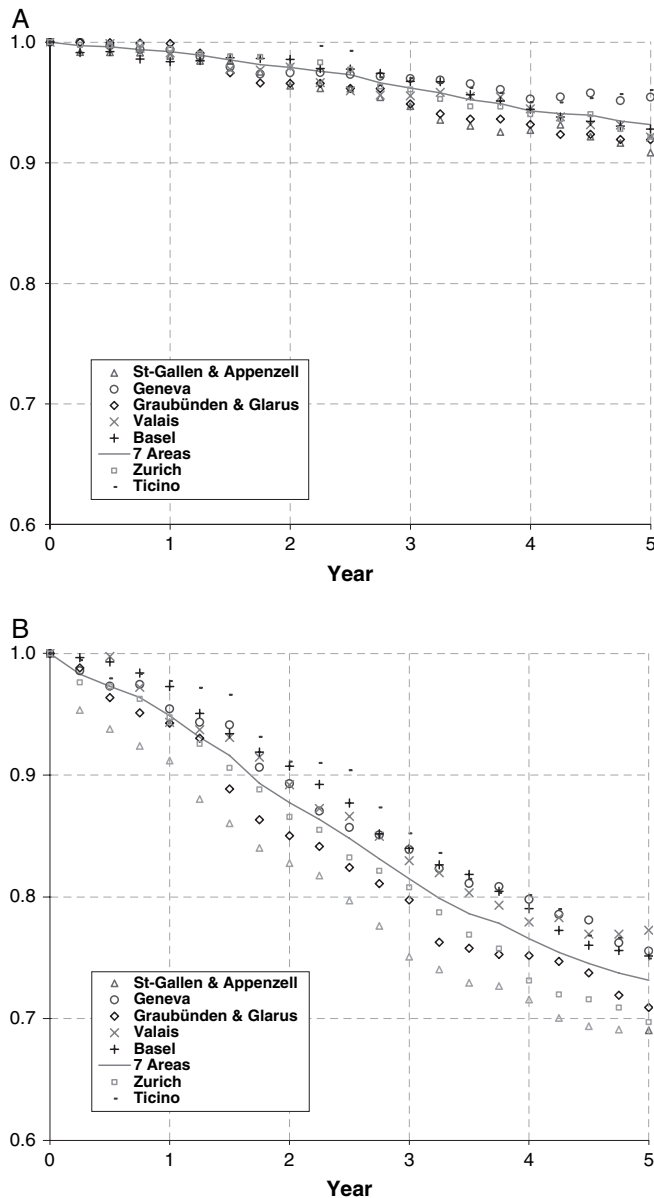
The strength of this study is its population-based case ascertainment through cancer registries, minimising the potential for selection bias as observed for hospital-based survival data and for clinical studies. The results of our study are representative of the whole population. Methodological biases and possible confounders affecting population-based survival comparisons have been discussed in depth elsewhere [11,12,24], and some of these factors are briefly mentioned below.

**Figure 1.** (A) Observed survival and (B) relative survival of breast cancer, all ages (period 2: 1993–1997/8).

Incomplete registration or coding mistakes, which can bias the survival estimates due to patient selection, is not a likely source of bias in this study. Incidence data of all participating registries have been approved by the IARC. The proportion of cases known through death certificate only is <2%, and the proportion of microscopically verified cases is  $\geq 97\%$  in all registries. In addition, cases known to registries through death certificates only (DCO) were excluded from the analysis.

Another source of bias is incomplete follow-up. All registries routinely used active follow-up, and specific central checking for follow-up has been carried out for this study. Relative survival in Geneva may have been slightly overestimated because of the migration bias described elsewhere [25], but is not likely to explain the size of the observed survival differences.

As survival continuously improved with time in all cantons, there could be an earlier or faster 'downstaging' in some cantons. Although proportions of cases with negative lymph nodes at diagnosis did not differ much during the two periods



**Figure 2.** Relative survival of breast cancer for cases with (A) negative and (B) positive lymph nodes (period 2: 1993–1997/8).

(49% compared with 48%, overall), frequency of early stage did, especially for registries with poor staging during the first period. For instance, frequency of stage 1 (all ages combined) changed from 9% to 20% in St Gall–Appenzell and from 14% to 27% in Valais, but only from 32% to 35% in Geneva and from 24% to 28% in Basel, and was unchanged in Graubünden–Glarus (28%). During the same period the proportion of unknown stage decreased from 57% to 12% in St Gall–Appenzell and from 6% to 5% in Geneva, and was unchanged in Basel (6%). Therefore the simple hypothesis of a true and rapid downstaging cannot be confirmed; we only observe a higher quality of casenotes with a better systematic staging.

Another possible explanation is the quality of staging assessment (e.g. metastasis status was not available in Zürich). Unfortunately, the group of cantons with large sampling (Basel, St Gall–Appenzell, Zürich and Graubünden–Glarus) have oppo-

site results in survival with Basel and Zürich different from St Gall–Appenzell and Graubünden–Glarus. In addition, Cox modelling clearly showed that, even after adjustment for tumour size, nodal involvement and number of nodes sampled, the differences still persisted.

As mentioned above, many factors may influence survival including differences in patient behaviour due to different cultural background or socioeconomic status, differences in physicians' attitudes, treatments and access to health care. The intercantonal differences in survival could be related to a combination of such factors. The respective contributions of these factors cannot currently be measured by data routinely collected by all registries in Switzerland, but is the focus of ongoing participation by Switzerland in the EURO CARE 4 and CONCORD projects. (<http://www.eurocare.it/> and <http://www.lshtm.ac.uk/ncdeu/cancersurvival/concord/index.htm>).

In conclusion, we found a global improvement of survival after diagnosis of breast cancer over a relatively short time period. We also found differences in survival in different regions of Switzerland, with a more favourable outcome in urbanised regions and the western part than in the more rural regions of the eastern part.

## Acknowledgements

We are grateful to Med. Pract. Nicole Doswald, Doctoral Student, Cancer Registry Zürich, and Dr. med. C. Quinto, Institute for Social and Preventive Medicine, Basel, for his help in collecting data on the health care institutions.

## References

- Boyle P, Ferlay J. Cancer incidence and mortality in Europe 2004. *Ann Oncol* 2005; 16: 481–488.
- Sant M, Allemani C, Capocaccia R et al. Stage at diagnosis is a key explanation of differences in breast cancer survival across Europe. *Int J Cancer* 2003; 106: 416–422.
- Levi F, Lucchini F, Negri E, La Vecchia C. The decline in cancer mortality in the European Union, 1988–1996. *Eur J Cancer* 2000; 36: 1965–1968.
- Survival of cancer patients in Italy in the nineties: figures from the cancer registries. *Epidemiol Prev* 2001; 25: S1–S375.
- Sant M, Capocaccia R, Verdecchia A et al. Survival of women with breast cancer in Europe: variation with age, year of diagnosis and country. The EURO CARE Working Group. *Int J Cancer* 1998; 77: 679–683.
- Coleman MP, Babb P, Damiacki P et al. Cancer Survival Trends in England and Wales, 1971–1995: Deprivation and NHS Region. London: Stationery Office 1999.
- Sant M, Allemani C, Berrino F. Breast carcinoma survival in Europe and the United States. *Cancer* 2004; 100: 715–722.
- Jones AL. Reduction in mortality from breast cancer, screening and increased use of adjuvants are responsible, adjuvants more so. *BMJ* 2005; 330: 205–206.
- Overgaard M. Radiotherapy as part of a multidisciplinary treatment strategy in early breast cancer. *Eur J Cancer* 2001; 37 (Suppl 7): S33–43.
- Kingsmore DB, Ssemwogerere A, Hole DJ et al. Increased mortality from breast cancer and inadequate axillary treatment. *Breast* 2003; 12: 36–41.

11. Berrino F, Sant M, Verdecchia A et al. Survival of Cancer Patients in Europe. The EURO CARE Study. IARC Scientific Publication 132. Lyon: International Agency for Research on Cancer 1995.
12. Berrino F, Capocaccia R, Estève J et al. Survival of Cancer Patients in Europe. The EURO CARE-2 Study. IARC Scientific Publication 151. Lyon: International Agency for Research on Cancer 1999.
13. Schüler G, Bopp M. Atlas der Krebsmortalität in der Schweiz 1970–1990. Basel: Birkhäuser Verlag 1997.
14. Fisch T, Torhorst J, Perret E et al. Results from two cancer registries in Switzerland (Basel and St Gall-Appenzell). *Bull Suisse Cancer* 2002; 2200: 15–17.
15. Jensen AR, Garne JP, Storm HH et al. Does stage at diagnosis explain the difference in survival after breast cancer in Denmark and Sweden? *Acta Oncol* 2004; 43: 719–726.
16. Jensen AR, Garne JP, Storm HH et al. Stage and survival in breast cancer patients in screened and non-screened Danish and Swedish populations. *Acta Oncol* 2003; 42: 701–709.
17. Mullee MA, De Stavola B, Romanengo M et al. Geographical variation in breast cancer survival rates for women diagnosed in England between 1992 and 1994. *Br J Cancer* 2004; 90: 2153–2156.
18. Twelves CJ, Thomson CS, Dewar JA et al. Variation of survival in women with breast cancer: Helath board remains a factor at 10 years. *Br J Cancer* 2001; 85: 637–640.
19. Rosso S, Faggiano F, Zanetti R, Costa G. Social class and cancer survival in Turin, Italy. *J Epidemiol Community Health* 1997; 51: 30–34.
20. Coleman MP. Opinion: why the variation in breast cancer survival in Europe? *Breast Cancer Res* 1999; 1: 22–26.
21. Schrijvers CTM, Mackenbach JP, Lutz JM et al. Deprivation and survival from breast cancer. *Br J Cancer* 1995; 71: 738–743.
22. Bouchardy C, Rapiti E, Fioretta G. et al. Undertreatment strongly decreases prognosis of breast cancer in elderly women. *J Clin Oncol* 2003; 21: 3580–3587.
23. Keller B, Zemp Stutz E, Tibblin M et al. Screening mammographies in Switzerland: what makes female and male physicians prescribe them? *Swiss Med Wkly* 2001; 131: 311–319.
24. Berrino F. The EURO CARE-3 study: strengths, limitations and perspectives of population based, comparative survival studies. *Ann Oncol* 2003; 14 (Suppl 5): 9–13.
25. Raymond L, Fischer B, Fioretta G, Bouchardy C. Migration bias in cancer survival rates. *J Epidemiol Biostat* 1996; 1: 167–173.