Trends in the cancer survival gap between elderly and middle-aged patients in Switzerland from 1996 to 2012

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Introduction

The proportion and the number of persons around and above pension age, and especially persons above 80, have increased strongly during the last decades in Switzerland as in many other countries, a trend which will continue in the future [1]. Addressing the specific problems involved in healthcare for older cancer patients is of growing concern.

The known fact that prognosis tends to worsen with age for adult cancer patients is related to a number of mechanisms. Older adults do not only have a higher risk for cancer, but also for other diseases that may affect cancer treatment, care, and recovery. Regarding the issue whether tumours diagnosed in late age are more aggressive or more often at an advanced stage, the answer is not uniform and depends on the type of cancer [2,3]. Elderly persons are less frequently screened for cancer and they receive fewer tests that help determine the stage of cancer, important for optimal treatment decisions [4,5]. In some cases, they receive milder treatments or no treatment at all [6,7], even though several studies have shown that cancer treatment can be equally beneficial for older people [8]. Elderly cancer patients are under-represented in clinical trials [9], and therefore the evidence base for safety and efficacy of therapeutic regiments in this group is weaker. Older people with cancer are less likely to have a social support system, also playing a role in survival [10].

Many epidemiological and clinical studies have shown that survival from cancer has been improving for most types of cancer over the last decades in Switzerland and world-wide [11,12]. The survival experience of elderly patients was, however, not often the focus of these studies. Extension of clinical and epidemiological studies to older cancer patients is needed to optimize prevention and treatment strategies. As a result, a number of epidemiological studies have appeared, reporting that relative survival for many forms of cancer is poorer among older patients and that they shared less in the survival improvements achieved during the last decades [13-18]. Thus, the survival gap between younger and older cancer patients has widened.

The present study compares the survival of elderly (75-94) and middle aged (60-74) cancer patients in Switzerland, with an emphasis on the question whether age-related survival gaps have changed over time.

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. For this report, we combined data from all nine cantons registering cancer from 1996 up to 2012 and providing vital status follow-up information: Zurich (ZH), St. Gallen (SG), Appenzell Ausserrhoden (AR), Appenzell Innerrhoden (AI), Geneva (GE), Graubünden (GR), Glarus (GL), Ticino (TI), and Valais (VS).

Cases included in this study were all invasive primary cancers (excluding non-melanotic skin cancer), diagnosed 1996-2012, and with age at diagnosis 60-94 (N= 273'948 diagnoses, 251'249 patients). The vital status was actively and/or passively followed-up until the end of the year 2012. We excluded diagnoses at death or with a death certificate as the only source of information (N= 5'715, 2.1%). Patients with multiple primary tumours were included (N= 37'642). Excluded were 9'049 cases (3.3%) because no active follow-up had been performed. Recent active follow-up was lacking for 16'757 cases (6.1%), i.e. the last date of follow-up was before December 2012 with vital status alive. The vital status of these cases was set «lost to follow-up» using the date of last contact. Because we did not assume survival up to 31.12.2012 in the absence of reported death, our survival estimates are conservative. Using the assumption of survival in the absence of reported death could overestimate survival due to incomplete registration of deaths. The final study included 259'184 diagnoses or 236'934 patients.

The relative survival (RS) was derived for consecutive time intervals after diagnosis, during which the mortality hazard ratios 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 after matching for age, sex, calendar year of death, and cantonal pool [19]. Expected cancer survival was estimated using the Ederer II method applied to all-cause mortality tables for the cantons combined [20]. All-cause death probabilities, transformed from age-, sex- and calendar year-specific death rates, were interpolated and smoothed using the Elandt-Johnson formula [21]. RS was estimated using the strs command (version 1.4.0) written for the Stata Statistical Software [22,23]. Period survival analysis was used, which defines cases by follow-up dates [24]. Confidence intervals at 95% (95% CI) were estimated by the delta method applied to a transformation of the cumulative hazard. Relative excess risk of death due to cancer (RER) was calculated as the ratio of the logarithm of RS in elderly divided by the logarithm of RS in middle-aged persons [15]. A value of > 1 indicates that mortality in older cancer patients is disproportionally higher than in younger cancer patients, after accounting for age specific baseline mortality.

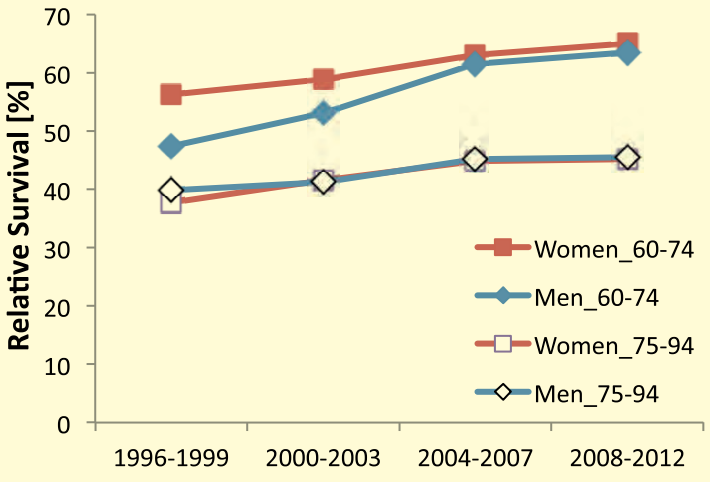

Fig. 1. Improvement of five year relative survival over time in Switzerland, for eldery (75-94) and middle-aged (60-74) men and women. All cancer sites combined, excluding non-melanotic skin cancer.

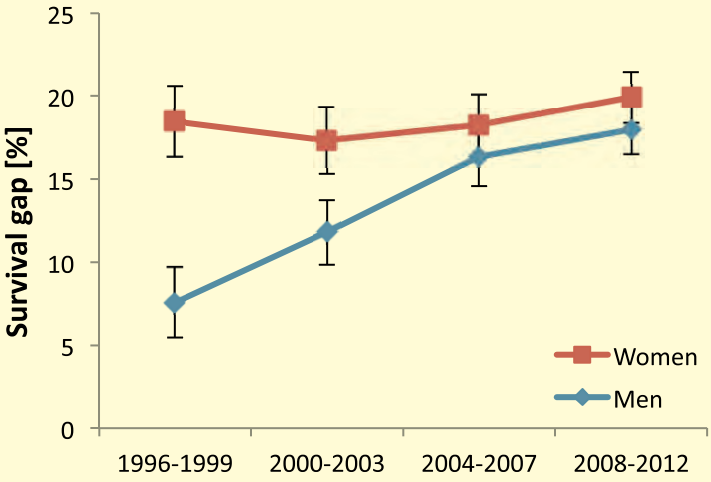

Fig. 2. Trends in the difference between five-year relative survival of elderly and middle-aged men or women in Switzerland (survival gaps). All cancer sites combined, excluding non-melanotic skin cancer.

Results

All cancers combined

Survival gap

Fig. 1 shows relative survival (RS) trends in age groups for men and women at five years after a diagnosis of cancer. There is a clear survival disadvantage of elderly (75-94) as compared to middle-aged persons (60-74). Survival in the elderly was very similar in men and women, but middle-aged women survived better than middle-aged men (Fig.1). The trend in the difference between survival of elderly and middle-aged patients (survival gap) was gender-specific (Fig. 2). The survival gap in women was larger as compared to men at all points in time, and remained stable over time, because elderly women gained similarly in RS as middle-aged women: the survival gap in women was 18.5% [95% CI 16.4%,20.6%] in the first time period (1996-1999) and 19.9% [18.4%,21.4%] in the last time period (2008-2012) (Tab. 1). The survival gap between elderly and middle-aged men was relatively small during 1996-1999: 7.6% [5.5%,9.7%], and increased steeply until 2008-2012, reaching 18.0% [16.5%,19.5%], almost the same value as in women (Tab. 1). The increasing survival gap was due to higher survival gains of middle-aged men: RS ranging from 47.4% [46.2%,48.6%] in 1996-1999 to 63.5% [62.7%,64.3%] in 2008-2012, as compared with lesser survival gains of elderly men, ranging from 39.8% [38.1%,41.6%] in 1996-1999 to just 45.5% [44.3%,46.8%] in 2008-2012 (Tab. 1).

Relative excess risk of death

Elderly women had significantly higher five-year relative excess risks of death due to cancer (RERs) as compared with men (Tab. 2). While the RER trend was only slightly increasing in women, ranging from 1.69 [1.63,1.75] in 1996-1999 to 1.85 [1.80,1.90] in 2008-2012, the trend in men was more pronounced, ranging from a small value of 1.23 [1.17,1.29] in 1996-1999 to 1.73 [1.69,1.78] in 2008-2012 (Tab. 2).

Site	Sex	Age	1996-1999 RS [95% CI]	1996-1999 Survival gap [95% CI]	2000-2003 RS [95% CI]	2000-2003 Survival gap [95% CI]	2004-2007 RS [95% CI]	2004-2007 Survival gap [95% CI]	2008-2012 RS [95% CI]	2008-2012 Survival gap [95% CI]
All cancer*	Men	60-74	47.4 [46.2,48.6]	7.6 [5.5,9.7]	53.0 [51.9,54.1]	11.8 [9.8,13.7]	61.5 [60.5,62.5]	16.4 [14.6,18.1]	63.5 [62.7,64.3]	18.0 [16.5,19.5]
		75-94	39.8 [38.1,41.6]		41.3 [39.6,42.9]		45.1 [43.6,46.6]		45.5 [44.3,46.8]	
	Women	60-74	56.2 [54.8,57.5]	18.5 [16.4,20.6]	58.9 [57.6,60.1]	17.3 [15.3,19.3]	63.0 [61.9,64.1]	18.2 [16.4,20.1]	65.1 [64.1,65.9]	19.9 [18.4,21.4]
		75-94	37.7 [36.1,39.4]		41.6 [39.9,43.2]		44.8 [43.3,46.3]		45.2 [43.9,46.4]	
All cancer#	Men	60-74	35.8 [34.5,37.1]	9.4 [7.2,11.6]	36.7 [35.5,37.9]	8.2 [6.1,10.3]	42.6 [41.4,43.7]	10.0 [8.0,12.0]	45.3 [44.3,46.3]	10.3 [8.6,11.9]
		75-94	26.4 [24.6,28.2]		28.5 [26.8,30.2]		32.5 [30.9,34.2]		35.0 [33.7,36.4]	
Prostate	Men	60-74	78.5 [76.2,80.6]	10.5 [6.3,14.7]	87.6 [85.8,89.3]	18.3 [14.6,22.0]	94.1 [92.8,95.2]	19.7 [16.5,22.9]	95.1 [94.2,96.0]	21.8 [19.1,24.5]
		75-94	68.0 [64.4,71.6]		69.3 [66.0,72.5]		74.3 [71.3,77.3]		73.3 [70.7,75.8]	
Breast	Women	60-74	78.6 [76.2,80.7]	12.9 [8.4,17.5]	84.3 [82.5,86.0]	8.6 [4.5,12.7]	88.0 [86.5,89.4]	10.6 [6.9,14.2]	88.0 [86.7,89.2]	11.9 [8.9,14.9]
		75-94	65.6 [61.6,69.5]		75.7 [71.9,79.3]		77.4 [74.0,80.7]		76.1 [73.3,78.8]	
Colon, rectum	Men	60-74	57.9 [54.4,61.3]	14.4 [8.3,20.5]	58.5 [55.2,61.6]	8.3 [2.6,13.9]	64.6 [61.8,67.3]	13.4 [8.5,18.4]	64.9 [62.4,67.2]	10.0 [5.7,14.3]
		75-94	43.5 [38.6,48.6]		50.2 [45.5,54.9]		51.2 [47.1,55.3]		54.9 [51.3,58.4]	
	Women	60-74	61.4 [57.5,65.1]	12.5 [6.6,18.4]	58.3 [54.6,61.8]	13.9 [8.6,19.3]	68.0 [64.7,71.2]	15.3 [10.3,20.3]	65.4 [62.5,68.2]	12.4 [8.0,16.7]
		75-94	48.9 [44.4,53.4]		44.4 [40.4,48.4]		52.7 [48.9,56.5]		53.0 [49.7,56.3]	
Lung	Men	60-74	12.6 [10.8,14.5]	8.2 [5.6,10.7]	13.3 [11.6,15.0]	5.4 [2.6,8.2]	14.8 [13.1,16.6]	6.5 [3.8,9.1]	17.5 [15.9,19.2]	8.7 [6.3,11.1]
		75-94	4.4 [2.8,6.5]		7.9 [5.9,10.3]		8.3 [6.5,10.5]		8.8 [7.2,10.6]	
	Women	60-74	16.5 [13.1,20.3]	8.9 [3.6,14.3]	17.0 [14.1,20.2]	5.9 [0.7,11.0]	18.4 [15.7,21.4]	9.5 [5.5,13.4]	22.9 [20.4,25.4]	10.3 [6.7,14.0]
		75-94	7.6 [4.3,12.1]		11.1 [7.5,15.7]		8.9 [6.5,11.9]		12.5 [10.0,15.4]	
Melanoma	Men	60-74	80.2 [73.6,85.9]	19.8 [6.6,33.1]	86.1 [80.0,91.2]	18.5 [5.9,31.1]	82.1 [77.2,86.3]	3.6 [-6.5,13.8]	85.0 [81.6,88.1]	2.0 [-5.2,9.3]
		75-94	60.4 [48.8,72.0]		67.6 [56.2,78.7]		78.4 [69.2,87.2]		83.0 [76.4,89.3]	
	Women	60-74	92.4 [87.0,96.5]	25.5 [13.5,37.6]	89.9 [84.3,94.1]	15.0 [3.8,26.2]	91.3 [86.7,94.8]	10.4 [0.8,20.0]	93.4 [90.3,95.9]	7.8 [0.7,14.8]
		75-94	66.9 [55.7,77.7]		74.9 [64.4,84.6]		80.9 [71.8,89.2]		85.7 [78.9,91.9]	
Corpus uteri	Women	60-74	70.6 [65.7,75.0]	14.5 [4.7,24.4]	78.1 [73.6,82.1]	19.4 [10.7,28.2]	79.2 [75.2,82.8]	16.6 [8.7,24.5]	78.5 [75.0,81.7]	17.0 [10.2,23.7]
		75-94	56.1 [47.4,64.7]		58.6 [50.9,66.2]		62.6 [55.5,69.4]		61.5 [55.6,67.3]	
Non-Hodgkin Lymphoma	Men	60-74	53.2 [46.3,59.8]	25.2 [14.6,35.9]	55.2 [49.5,60.7]	14.9 [4.4,25.3]	66.6 [60.8,71.9]	30.2 [20.9,39.6]	75.2 [70.6,79.3]	21.6 [13.7,29.5]
		75-94	28.0 [20.3,36.7]		40.4 [31.9,49.4]		36.3 [29.1,44.1]		53.6 [47.0,60.1]	
	Women	60-74	55.3 [48.7,61.6]	15.6 [5.2,26.0]	67.2 [60.9,72.9]	29.1 [19.7,38.5]	68.9 [63.4,73.9]	21.6 [12.9,30.2]	80.9 [76.6,84.6]	28.0 [21.0,34.9]
		75-94	39.7 [31.8,48.0]		38.1 [31.0,45.5]		47.3 [40.5,54.2]		52.9 [47.2,58.6]	
Oral cavity, pharynx	Men	60-74	41.4 [35.3,47.5]	-5.5 [-20.4,9.3]	39.1 [33.6,44.7]	18.6 [8.3,28.9]	40.9 [35.6,46.2]	5.8 [-5.7,17.3]	48.2 [43.9,52.4]	-4.5 [-14.7,5.7]
		75-94	46.9 [33.9,60.6]		20.6 [12.9,30.1]		35.1 [25.4,45.7]		52.7 [43.5,62.0]	
	Women	60-74	65.9 [54.2,75.8]	27.7 [9.4,46.0]	52.9 [43.7,61.4]	11.3 [-5.3,28.0]	58.7 [49.6,66.9]	1.6 [-14.6,17.8]	57.7 [51.2,63.9]	2.1 [-11.0,15.3]
		75-94	38.3 [24.5,53.5]		41.6 [28.1,55.9]		57.0 [43.4,70.5]		55.6 [44.1,66.9]	
Kidney	Men	60-74	53.1 [46.0,60.0]	18.9 [5.0,32.7]	65.3 [58.2,71.7]	14.4 [-0.6,29.3]	63.0 [56.6,68.9]	-0.7 [-13.2,11.8]	71.0 [66.0,75.7]	10.8 [1.1,20.5]
		75-94	34.2 [23.1,46.8]		50.9 [37.9,64.3]		63.7 [52.7,74.3]		60.3 [51.8,68.6]	
	Women	60-74	62.9 [53.6,71.2]	35.8 [22.2,49.4]	61.6 [52.4,69.8]	24.4 [9.9,38.9]	67.7 [58.7,75.5]	20.2 [5.5,34.8]	75.7 [68.4,81.8]	27.3 [16.1,38.4]
		75-94	27.2 [17.7,38.1]		37.2 [26.2,49.0]		47.6 [35.7,59.5]		48.5 [39.6,57.4]	
Ovary	Women	60-74	32.6 [26.9,38.4]	17.8 [9.6,26.0]	40.5 [34.9,46.0]	23.4 [15.2,31.6]	32.2 [27.2,37.3]	11.9 [4.2,19.7]	34.4 [30.0,38.9]	13.1 [6.4,19.8]
		75-94	14.8 [9.6,21.2]		17.1 [11.7,23.6]		20.3 [14.8,26.5]		21.4 [16.7,26.6]	

Tab.1. Time trends in five-year relative survival (RS) for elderly (75-94) and middle-aged (60-74), and survival difference (gap) between age-groups, by sex and cancer site.

RS: Relative survival. CI: Confidence interval

*: All sites combined, except non-melanotic skin cancer

#: All sites combined, except non-melanotic skin cancer and prostate cancer

		1996-1999	2000-2003	2004-2007	2008-2012
Site	**Sex**	**RER [95% CI]**	**RER [95% CI]**	**RER [95% CI]**	**RER [95% CI]**
All cancer*	Men	1.23 [1.17,1.29]	1.40 [1.34,1.45]	1.64 [1.58,1.69]	1.73 [1.69,1.78]
	Women	1.69 [1.63,1.75]	1.66 [1.60,1.72]	1.74 [1.68,1.80]	1.85 [1.80,1.90]
All cancer#	Men	1.30 [1.23,1.36]	1.25 [1.19,1.31]	1.31 [1.26,1.37]	1.33 [1.28,1.37]
Prostate	Men	1.59 [1.41,1.77]	2.77 [2.57,2.96]	4.85 [4.61,5.09]	6.22 [6.00,6.44]
Breast	Women	1.75 [1.56,1.93]	1.64 [1.42,1.85]	2.01 [1.80,2.22]	2.14 [1.97,2.31]
Colon, rectum	Men	1.52 [1.35,1.70]	1.28 [1.11,1.45]	1.53 [1.38,1.69]	1.39 [1.25,1.52]
	Women	1.47 [1.29,1.65]	1.51 [1.35,1.66]	1.66 [1.49,1.83]	1.49 [1.35,1.64]
Lung	Men	1.51 [1.36,1.66]	1.26 [1.13,1.39]	1.30 [1.19,1.42]	1.39 [1.30,1.49]
	Women	1.43 [1.20,1.67]	1.24 [1.04,1.43]	1.43 [1.27,1.58]	1.41 [1.28,1.53]
Melanoma	Men	2.29 [1.77,2.81]	2.62 [2.01,3.23]	1.23 [0.68,1.78]	1.15 [0.67,1.63]
	Women	5.11 [4.34,5.88]	2.71 [2.02,3.40]	2.32 [1.62,3.02]	2.27 [1.62,2.93]
Corpus uteri	Women	1.66 [1.33,1.99]	2.16 [1.83,2.49]	2.01 [1.69,2.32]	2.01 [1.74,2.27]
Non-Hodgkin Lymphoma	Men	2.02 [1.71,2.33]	1.53 [1.23,1.82]	2.49 [2.20,2.78]	2.19 [1.91,2.47]
	Women	1.56 [1.26,1.86]	2.43 [2.13,2.73]	2.01 [1.73,2.29]	3.00 [2.71,3.29]
Oral cavity, pharynx	Men	0.86 [0.44,1.27]	1.69 [1.38,1.99]	1.17 [0.86,1.49]	0.88 [0.58,1.18]
	Women	2.31 [1.75,2.87]	1.38 [0.91,1.85]	1.05 [0.54,1.56]	1.07 [0.66,1.47]
Kidney	Men	1.69 [1.31,2.08]	1.58 [1.12,2.04]	0.98 [0.54,1.41]	1.48 [1.14,1.82]
	Women	2.81 [2.39,3.24]	2.04 [1.61,2.47]	1.91 [1.44,2.37]	2.60 [2.20,3.01]
Ovary	Women	1.70 [1.44,1.96]	1.95 [1.70,2.20]	1.41 [1.18,1.64]	1.45 [1.26,1.64]

Tab. 2. Time trends in five-year relative excess risks of death (RER) for elderly (75-94) compared with middle-ages patients (60-74) by sex and cancer site.

RER: Relative excess risks of death. CI: Confidence interval

*: All sites combined, except non-melanotic skin cancer

#: All sites combined, except non-melanotic skin cancer and prostate cancer

Survival gaps and RERs for ten common cancers

Prostate cancer

The strongest increase in survival disadvantage of elderly men was seen in prostate cancer. The survival gap doubled from 10.5% [6.3,14.7] in 1996-1999 to 21.8% [19.1,24.5] in 2008-2012, due to larger survival gains of middle-aged men as compared with elderly men (Tab. 1). The RER almost quadrupled from 1.59 [1.41,1.77] in 1996-1999 to 6.22 [6.00,6.44] in 2008-2012 (Tab. 2). The trend in prostate cancer was mainly responsible for the all cancer trend observed in men. If prostate cancer is removed from the all cancer group, the survival gap in men remained stable over time: ranging from 9.4% [7.2%,11.6%] in 1996-1999 to 10.3% [8.6%,11.9%] in 2008-2012 (Tab. 1). There was also no longer an increase in relative excess risk of death over time for elderly men after removal of prostate cancer diagnoses from the all cancer group, with RERs ranging from 1.30 [1.23,1.36] in 1996-1999 to 1.33 [1.28,1.37] in 2008-2012 (Tab. 2).

Breast cancer, uterine cancer, large bowel cancer, lung cancer, non-Hodgkin lymphoma

The survival gaps in elderly versus middle-aged women remained relatively stable for breast cancer and uterine cancer (Tab. 1, Tab. 2). Due to the improving prognosis both in elderly and middle-aged women with breast cancer, the RERs for elderly women with breast cancer tended to increase over time. Survival gaps and RERs also remained stable in both sexes for cancer of the large

bowel, lung, and non-Hodgkin lymphoma. It is noteworthy that survival-gaps in non-Hodgkin lymphoma were comparably large (15-30%) and in lung cancer comparably small (5-10%) at all calendar periods and for both genders (Tab. 1).

Melanoma
In melanoma, strongly decreasing survival gaps and RERs were found. The survival gap of 19.8% [6.6%,33.1%] in 1996-1999 in men, and the large gap of 25.5% [13.5%,37.6%] in women, decayed to a mere 2.0% [-5.2%,9.3%] in men, no longer significantly different from zero, and to 7.8% [0.7%,14.8%] in women (Tab. 1). This was caused by very little improvement in the already high RS values of middle-aged patients, especially in women (90-93%), but larger survival gains over time in the elderly. Corresponding RERs of 2.29 [1.77,2.81] in men in 1996-1999 decayed to 1.15 [0.67,1.63] in 2008-2012, which was no longer significantly different from equal RS for elderly versus middle-aged men (Tab. 2). The RER in women developed from a very high value of 5.11 [4.34,5.88] in 1996-1999 to 2.27 [1.62,2.93] in 2008-2012 (Tab. 2).

Oral cavity, pharynx
For oral and pharyngeal cancers, the trend was gender-specific. While age-specific RS as well as survival gaps indicated no clear difference between elderly and middle-aged men (with an unexplained high value 2000-2003), there was a clear reduction of survival gaps, as well as the RERs, in womenbetween 1996-1999 and 2008-2012: the survival gap in women decayed from 27.7% [9.4%,46.0%] in 1996-1999 to 2.1% [-11.0%,15.3%], no longer significantly different from zero, in 2008-2012 (Tab. 1), and the RER from 2.31 [1.75,2.87] down to non-significant 1.07 [0.66,1.47] (Tab. 2). Elderly women have gained more in RS than middle-aged women over calendar periods: from 38.3% [24.5%,53.5%] in 1996-1999 to 55.6% [44.1%,66.9%] in 2008-2012 in elderly, and 65.9% [54.2%,75.8%] to 57.7% [51.2%,63.9%] in the middle-aged.

Kidney
There was a large and persistent gender-specific survival disadvantage for elderly women compared with elderly men diagnosed with renal cancer, while survival of middle-aged women was slightly better than for middle-aged men. Thus, age-related survival gaps were about twice as wide in women as compared to those of men, and also large if compared with other cancer sites (with the exception of non-Hodgkin lymphoma). The survival gap in women was 35.8% [22.2%,49.4%] in 1996-1999 and remained as high as 27.3% [16.1%,38.4%] in 2008-2012 (Tab. 1). The gap decreased slightly in men from 18.9% [5.0%,32.7%] to 10.8% [1.1%,20.5%]. Age-specific RS values, on the other hand, have clearly improved over time in men and in women (Tab. 1). Correspondingly, RERs in women were significantly larger compared with men, with minor temporal change in RER for both genders (Tab. 2).

Ovary
Age-related survival gaps also seemed to decrease in ovarian cancer, but less prominently. Survival gaps between elderly and middle-aged women decreased from 17.8% [9.6%,26.0%] in 1996-1999 to 13.1% [6.4%,19.8%] in 2008-2012 (Tab. 1), and RERs from 1.70 [1.44,1.96] to 1.45 [1.26,1.64] (Tab. 2).

Discussion

We have presented data on the differential survival of elderly (75-94) and middle-aged (60-74) cancer patients in Switzerland during 1996-2012. The survival experience of patients was expressed as relative survival (RS), which is the ratio of observed survival in cancer patients and expected survival in a group of people of similar age without cancer. This approach adjusts for the much higher comorbidity in the elderly, thus making comparisons with persons of middle age more meaningful. We have measured the survival disadvantage of the elderly using two approaches: as difference in age-specific RS (survival gap) and as relative excess risk of death due to cancer (RER). Survival gaps are intuitively easier to understand, but a ratio measure such as RER is weighted for severity of the disease, i.e. a certain survival difference will generate higher RER, if RS in the reference level is good as compared to poor reference survival. For example, the survival gap of 21.8% in prostate cancer (period 2008-2012) corresponds to RER 6.2, while the survival gap of 21.6% in non-Hodgkin lymphoma in men (period 2008-2012) corresponds to RER of 2.2, because the RS in the reference level (i.e. age 60-74) is much better in prostate cancer.

Our main finding is that survival gaps between elderly and middle-aged patients have been rather stable in Switzerland for most cancer sites since 1996. We observed, however, a prominent widening of the survival gap selectively for prostate cancer, and clearly decaying survival gaps for melanoma (in men and women) and oral cavity/pharynx (in women only).
The international studies reporting increasing RERs in elderly (70-84) women for all cancers combined, breast cancer, and uterine cancer, and increasing RERs also for prostate cancer [16,17] were based on the data collected through the EUROCARE projects which included information on patients diagnosed between 1988-1999 in 16 European countries. Our different findings for Switzerland, except for

prostate cancer, suggest that either the age-specific trends have stabilized since 1999 in Europe as a whole, or that the Swiss pattern deviates from the average pattern of the European pool. A recent study from Germany also reported stable five-year RS gaps for breast cancer between 1993 and 2004, if ages 70+ were compared with 50-69 [25]. Only in the time period 2005 – 2008, the age group 50-69 experienced a larger survival gain as compared with age group 70+, presumably because organized mammography screening for women between 50 and 69 years of age started in 2003 [25]. In Switzerland, organized mammography screening started 1999 in two Swiss cantons GE and VS, among the nine cantons contributing data to this report. It may be assumed that mammography usage and screening, either opportunistically as well as organized, was lower in Switzerland as compared with other countries over the whole study period (1996-2012), thus survival gains in middle-aged versus elderly women were more even.

Increase in prostate cancer incidence was marked in Switzerland especially for men of 50-69 years of age until 2007 [26], most likely due to opportunistic Prostate Specific Antigen (PSA)-screening. Because of the high probability of the PSA test to identify slowly growing tumours that would otherwise have remained undiagnosed during life (overdiagnosis), part of the survival gain, especially in middle-aged men, is likely the effect of increased diagnosis of potentially indolent tumours rather than real advances in survival time.

In melanoma, we have found prominent temporal improvements regarding survival gaps as well as RERs in both genders. Survival disadvantages for the elderly were most pronounced around the year 2000 in Switzerland, as reported also for numerous other countries [27]. Furthermore, the Swiss data corroborate the known survival advantage of women [28]. Age was associated with poor prognostic factors in many studies, but seemed to play also an independent prognostic risk factor [28]. The situation in Switzerland around 2010 has changed. Because gains in survival occurred almost exclusively on the part of the elderly, their survival disadvantage has almost disappeared. Also elderly men survived equally well as women. Several factors may have been involved: earlier diagnosis due to improved health behavior and practices in elderly [29], or physicians judging more elderly fit for complete diagnostics and curative treatments [30]. The role of earlier detection without true prolongation of life time seems to play a minor role in melanoma [31].

We report decreasing survival gaps for women with oral and pharyngeal cancer due to stagnation in survival in middle-aged persons and gains in survival in the elderly. A number of epidemiological studies in the United States have reported that survival rates in younger females, though younger (<35 years) than in our study, do not share the improvements observed in older women [32]. Different trends in tobacco and alcohol use, together with changing sexual mores and increasing orogenital sexual practices, fostering the transmission of human papillomavirus and potentially other sexually transmitted carcinogenic vectors have been discussed as possible causes for stagnation of survival in younger women with oral and pharyngeal cancer [33].

For the interpretation of our findings, a number of limitations should be considered. Data completeness and accuracy represent a major source of bias in the analysis of older populations. In particular the incomplete ascertainment of diagnoses at a late stage and receiving only palliative care outside the hospital may lead to a selective loss of poor prognosis patients and overestimation of survival. Age specific differences, and temporal trends, in the proportion of diagnoses without known date of diagnosis (DCO) are another source of bias affecting survival time estimation (Tab. 3). We always observed higher DCO percentages in the elderly, but the values remained ≤7% for all types of cancer and periods (Tab. 3). Thus, selection bias caused by DCO cases would have slightly underestimated actual existing survival gaps. We have also assessed whether diagnoses for the elderly were based on a lesser level of certainty, probably associated with less aggressive forms of treatment [34]; i.e. the smaller proportion of diagnoses based on microscopic (cytologic or histologic) verification (MV). The proportion was ≥95% in middle-aged patients for all cancer sites and periods, and systematically smaller in the elderly, ranging from 20%-30% difference in renal cancer to just 0%-1% in melanoma. Age-related differences in %MV decreased over time for cancer of the breast, large bowel, oral cavity/pharynx (especially in women), and ovary. It is possible that the reduction of age-related difference in %MV diagnoses from 8.3% to 0.6% between 1996-1999 and 2008-2012 for oral and pharyngeal cancer in women is related to the observed reduction in the survival gap, possibly due to more aggressive treatments. Finally, the interpretation of trends for all sites combined has to consider changes in the composition of tumour sites, as can be seen from the comparison of trends in RER for all sites with and without prostate cancer. Similarly, differences in the case mix, i.e. the proportions of diagnoses with good and bad prognosis, have to be considered as described for the example of prostate cancer.
Overall, our analysis reveals that prognosis for most types of cancer has increased over time at a similar rate for elderly and middle-aged patients. Nevertheless, survival gaps still exist and further efforts are necessary to improve earlier diagnosis and optimize cancer care, especially among the elderly.

			DCO [%]				MV [%]			
Site	**Sex**	**Age**	**1996-1999**	**2000-2003**	**2004-2007**	**2008-2012**	**1996-1999**	**2000-2003**	**2004-2007**	**2008-2012**
All cancer	Men	60-74	1.5	0.8	0.5	0.4	94.7	95.3	96.3	96.8
		75-94	4.7	4.2	2.2	2.4	84.3	83.4	84.6	86.2
	Women	60-74	1.2	1.0	0.4	0.5	96.5	96.4	97.5	97.7
		75-94	6.8	5.4	2.8	2.9	81.3	83.4	85.4	86.3
Prostate	Men	60-74	0.6	0.5	0.1	0.1	97.0	98.0	98.9	99.1
		75-94	4.0	4.6	2.7	2.8	84.7	81.7	81.3	84.5
Breast	Women	60-74	0.7	0.8	0.2	0.2	98.6	98.6	99.6	99.6
		75-94	4.1	4.5	1.7	1.7	89.5	90.4	94.5	95.8
Colon, rectum	Men	60-74	1.5	0.6	0.3	0.2	98.0	98.8	99.3	99.2
		75-94	3.0	3.3	1.0	1.4	92.7	93.5	95.2	95.8
	Women	60-74	1.1	1.1	0.1	0.3	98.2	97.9	99.3	99.0
		75-94	6.0	4.7	1.6	2.1	86.8	89.6	92.2	92.3
Lung	Men	60-74	1.9	1.1	1.2	0.9	94.5	93.9	94.9	96.1
		75-94	5.0	4.8	2.0	2.6	81.2	79.0	80.5	80.6
	Women	60-74	1.6	1.9	0.6	0.9	95.1	93.6	96.2	95.8
		75-94	7.3	5.6	2.7	3.5	78.5	73.2	79.3	78.8
Melanoma	Men	60-74	0.0	0.0	0.2	0.1	99.7	100.0	99.7	99.6
		75-94	0.8	0.0	0.5	0.3	98.8	99.3	98.6	99.4
	Women	60-74	0.0	0.3	0.0	0.0	99.7	99.7	100.0	100.0
		75-94	1.3	0.0	0.6	0.4	98.2	100.0	98.9	99.4
Corpus uteri	Women	60-74	0.5	0.0	0.0	0.3	98.7	99.7	99.7	99.5
		75-94	4.5	2.7	1.6	0.2	91.8	94.2	95.9	95.1
Non-Hodgkin Lymphoma	Men	60-74	1.9	0.5	0.0	0.0	97.6	98.6	99.1	99.5
		75-94	2.8	2.5	1.2	1.3	94.5	95.6	97.1	94.7
	Women	60-74	1.5	0.0	0.2	0.2	98.2	100.0	99.8	99.4
		75-94	3.9	1.7	1.5	1.6	94.1	95.8	96.3	95.7
Oral cavity, pharynx	Men	60-74	0.0	0.5	0.4	0.4	98.7	99.0	98.8	98.8
		75-94	2.7	1.4	0.0	1.5	94.7	96.6	98.6	98.1
	Women	60-74	0.7	0.7	0.0	0.7	99.3	98.0	99.5	98.3
		75-94	4.5	2.7	3.6	0.6	91.0	94.6	93.8	97.7
Kidney	Men	60-74	1.0	0.9	0.0	0.0	93.6	92.1	96.3	96.9
		75-94	5.7	5.5	3.0	2.8	71.5	80.1	69.6	79.8
	Women	60-74	1.7	0.6	0.6	0.4	95.5	97.4	94.2	96.0
		75-94	5.8	4.4	5.2	3.7	70.8	67.9	58.4	68.2
Ovary	Woman	60-74	1.3	0.0	0.5	0.8	98.5	98.6	97.7	97.9
		75-94	7.0	2.3	0.7	3.8	80.6	81.8	84.0	86.3

Tab. 3. Trends in proportions of diagnoses registered as DCO (death certificate only) and proportions of diagnoses based on microscopic verification (MV).

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