

Swiss cancer prevalence and language region

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Introduction

The Foundation National Institute for Cancer Epidemiology and Registration (NICER), together with the Federal Statistical Office (FSO), makes available and continuously monitors quantitative measures of the cancer burden, whose major indicators are incidence (i.e. new diagnoses per time interval), mortality (i.e. cancer deaths per time interval), survival duration and prevalence [1]. Regular publication of prevalence estimates is a cornerstone of cancer surveillance. It quantifies cancer patients alive at a given index date, either as absolute number or as proportion of the general population. It is thus a function of previous incidence and survival rates, and general population dynamics. Its primary importance is to inform agencies charged with planning for the provision of health services for cancer patients. Prediction of future expected cancer burden is thus an important part of prevalence reporting. Prevalence estimates are often provided either for different time limits between diagnosis and index date, or without time limits (i.e. complete prevalence). The latter has rather limited application because it combines indiscriminately short- and long-term cancer survivors with very different health care needs. It is usually more informative to partition time since diagnosis and index date into survivor groups who undergo primary treatment and active follow-up and survivor groups on less intensive regimes [2]. In this regard, we provide prevalence estimates for survivors with a cancer diagnosis up to 2 years, 2 up to 5 years, and 5 up to 10 years before the index date. The first group along the clinical pathway typically requires diagnostic assessments, staging examinations, clarification of the patients treatment option and psychosocial resources, surgical interventions, neoadjuvant and adjuvant treatments of various durations, management of treatment side effects, and palliative care interventions, or end of life care. The second group along the pathway typically requires regular medical check-ups several times per year to discover and treat cancer recurrence early and deal with any problems due to past cancer treatments. Psychologically, this time is dominated by fear of recurrence. The third group along the pathway typically includes patients

with less frequent medical check-ups. Rehabilitation is important in all phases after the first treatment in order to support the patient in going back to a «new normal» life. Although patients with survival durations of 5 years or longer are often considered «cured», which is often too optimistic [3], persons who have come through a cancer experience are indelibly affected by it and reduced quality of life, or financial problems connected to employment and insurance, are common [4]. Survivors for more than ten years, which make up about 40% of the complete prevalence for all cancer sites combined [5], are not considered in the present report.

In 2014, cancer prevalence data at the national level were published by us [5], and others [6], based on incidences up to 2010, and projected for 2015. The present report will provide updated prevalence estimates based on the most recently available cancer incidences up to 2014 and extends projections for 2020, based on the future expected incidence rates, cancer survival and general population developments. The updated cancer prevalence estimates for Switzerland as a whole are available on our institutional website [www.nicer.org]. In the present report, we are distinguishing prevalence for the first time between main Swiss language regions. Variation in prevalence estimates between these regions is to be expected because of the known differences in underlying incidence rates, survival rates, and the extent of screening programs [7, 8]. Furthermore, a number of reports and publications have demonstrated that language region may serve as a proxy to capture differences in cancer risk avoidance behaviour, in the usage of preventive measures, including immunization and screening examinations, or other health care services, and in socioeconomic positions to a meaningful degree in Switzerland [9, 10, 11, 12].

Methods

Cancer diagnoses were selected from the National Cancer Dataset managed by the Foundation National Institute for Cancer Epidemiology and Registration (NICER) for

the purpose of national cancer monitoring and supporting epidemiological cancer research in Switzerland [1]. It combines about 871'000 pseudonymized cases registered by all existing 14 Swiss Cancer Registries since 1970. For the present analysis, primary malignant cancer diagnoses between 1996 and 2014 were included, restricted to the first occurring diagnosis in the patient's lifetime and analytical cancer group. Only cancer registries that covered the whole analysis period were considered. The predominantly German speaking part of Switzerland (G)

was represented by the cantons AI, AR, GL, GR, SG, and ZH. The predominantly French and Italian speaking part (F/I) was represented by the cantons GE, JU, NE, TI, VD, and VS. Thus, the G region of Switzerland was covered by about 40%, and the F/I region by about 90%. DCO cases (registration from a death certificate only) were excluded from analysis. They are infrequent in Swiss cancer registration (< 5%) for the majority of sites [13]. Completeness of case ascertainment has been recently assessed without detecting signs of overt under-

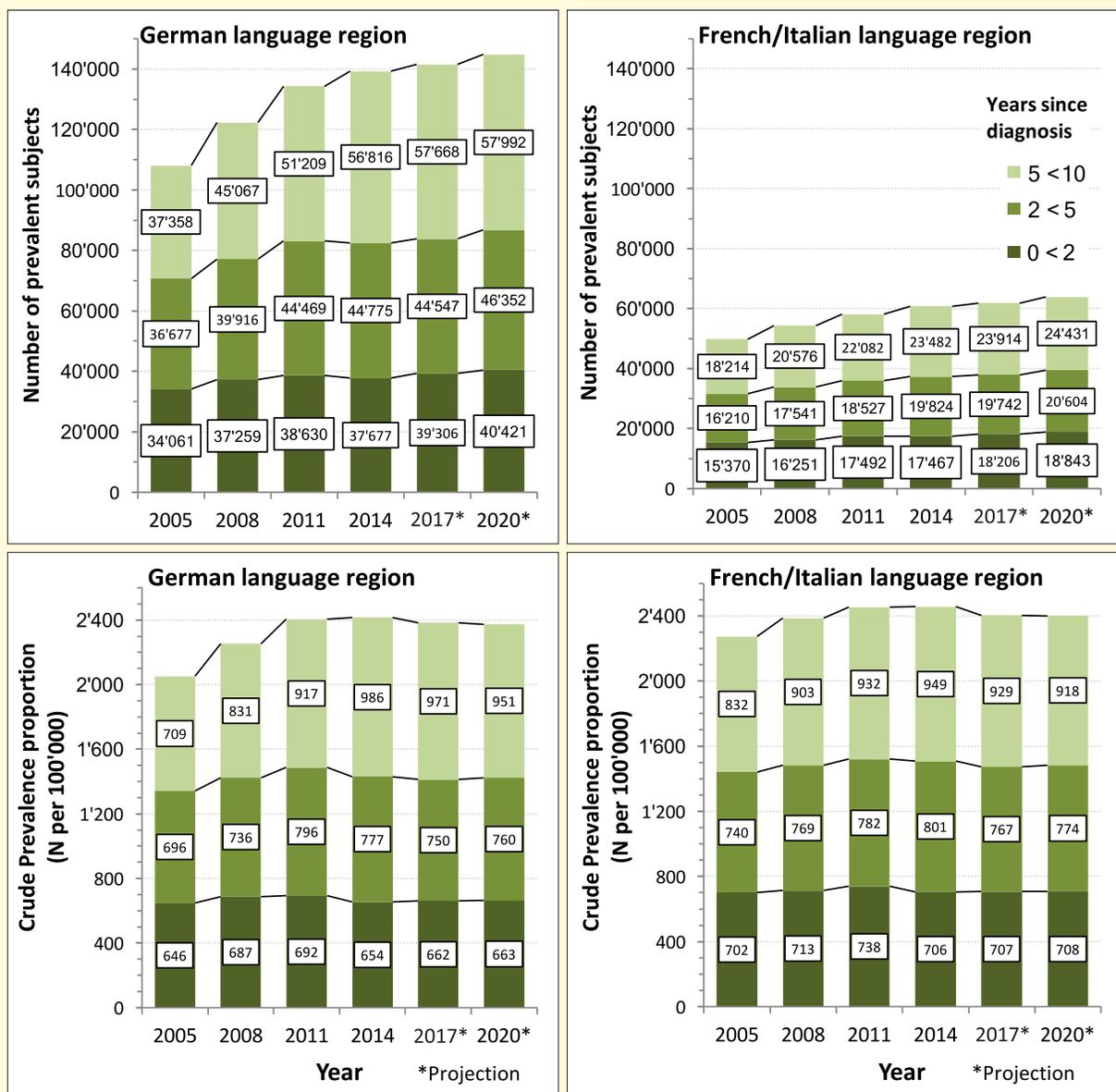


Fig. 1. Time trends of the number of prevalent subjects, and the crude proportions, for the predominantly German speaking part of Switzerland and the predominantly French/Italian speaking part. Counts refer to malignant cancer of any type, except non-melanotic skin cancer, and the 31.12. of the indicated index year.

registration [13]. For persons who are lost to follow-up, the vital status at certain index dates is unknown. The probability of each lost to follow-up patient still being alive at the index date, conditional on the length of observed survival, was estimated using cancer registry, sex and age at diagnosis as covariates [14]. We projected data observed until 2014 for six years to 2020 by estimating the future incidence and expected survival and combined both estimates to derive the expected prevalence as suggested in Pisani et al. [15]. Swiss population statistics for 1981-2015 as well as predictions for future population developments 2016-2020 («middle scenario»), stratified by canton, age and sex, were provided by the Federal Statistical Office (FSO) [16]. A detailed description of the methodological procedures involved is available at our institutional website [17].

Results

Prevalence trends for all cancer sites combined from 2005 to 2014, with projections to 2017 and 2020, are depicted in Fig. 1. The top part of Fig. 1 provides estimates of the number of cancer patients, partitioned into three groups by the time elapsed between diagnosis and 31.12. of the indicated index years. In the bottom part of Fig. 1, the numbers of prevalent patients are expressed as proportion in 100'000 of the general population at the indicated index dates. Numbers of prevalent subjects in the region where predominantly French or Italian is spoken (F/I) are smaller compared with the predominantly German speaking part (G) because it constitutes a smaller part of Switzerland. The fastest growing prevalence group between 2005 and 2014 were those with diagnoses 5 to 10 years before the index dates: 37'358 in 2005 versus 56'816 in 2014 signifies a 52% increase in region G, and 18'214 versus 23'482, or 29% increase in region F/I, respectively. According to our projections, the increasing trend is going to slow down, even increasing less than the population in general, as indicated by the slight reductions in prevalence proportions (Fig. 1, bottom panels).

In region G, the proportion of patients with a cancer diagnosis less than 10 years before 31.12.2014 amounted to 2'417 in 100'000 (i.e. 2.4%), and in the F/I region 2'456 in 100'000 (i.e. also 2.4%). There is thus no difference in crude prevalence proportions between language regions, but comparisons of prevalence proportions should only be made after adjusting for possible differences in age structure, because the risk of becoming a cancer patient is tightly connected to age. We have adjusted prevalence proportions for differences in age structure by the direct method based on the European reference population.

Table 1 provides observed prevalence estimates for 25 cancer groups in regions G and F/I for index date 31.12.2014 and projections for index date 31.12.2020. Estimates for the absolute number of prevalent cases, and the age-adjusted proportion of cases in 100'000 persons of the general population, are shown for different times between diagnosis and index dates. Ten year prevalence proportion estimates are depicted also in Fig. 2. It should be noted that we counted the first occurring cancer diagnosis per patient and cancer group as prevalent, thus a patient with multiple primary cancers from different groups contributed to several groups. For the total cancer group, only the first cancer in a patient is counted, thus the total cancer count is somewhat smaller than the summed cancer-specific counts.

In the G region, there were 139'268 patients alive in 31.12.2014 with a history of cancer going back for maximally 10 years, while there were 60'773 such cases in the F/I. This represents, after adjusting for differences in age structure, almost identical proportions of total cancer cases in the general population: 1'827.6 in 100'000 (95% confidence limits: 1'811.8, 1'843.5) in G, and 1'863.9 in 100'000 (95% confidence limits: 1'847.6, 1'880.3) in F/I, respectively. It should be noted that due to differences between the Swiss population structure and the European reference population, which is the standard for age-adjustment in Europe, the age-adjusted proportions are smaller than the crude Swiss proportions shown in Fig. 1. For index date 31.12.2020, the total number of cases is expected to increase slightly less than the projected population size, and the increase of about 5% in total cancer cases (144'765 in G, and 63'878 in F/I) translates to 6% lower age-adjusted proportions: 1'719.1 (1'440.5, 2'051.6) in 100'000 in G, and 1'741.5 (1'444.6, 2'099.5) in 100'000 in F/I, again without differences between language regions.

In both language regions, prostate and breast cancer were by far the most prevalent in 2014, followed by colorectal cancer, melanoma, cancer of the corpus uteri, and testis (Tab. 1 and Fig. 2). Similar conditions are forecasted for 2020, with a slight decrease of 5% (G) or 1% (F/I) prevalent cases of prostate cancer, and a 7% (G or F/I) increase in prevalent cases of breast cancer (Tab. 1). To identify the most conspicuous differences in prevalence proportions between language regions at index date 31.12.2014, we applied the z-Test and flagged only those cancer groups where the relative difference in proportions was greater than 10% and the P-value less than the significance level α of 0.01 after Bonferroni's correction for multiple testing (flagged cases are indicated in Tab. 1). The prevalence proportion of liver cancer was twice as high in F/I as compared with G at any diagnosis interval before the index date: e.g. 21.3

Prevalence at index date 31.12.2014										
Cancer	Ten year (0 <10)				0 < 2 year		2 < 5 year		5 < 10 year	
	Prop.*		N		Prop.*		Prop.*		Prop.*	
	G	F/I	G	F/I	G	F/I	G	F/I	G	F/I
Gallbladder	5.8	4.8	474	170	3.1	2.6	1.5	1.2	1.2	1.0
Liver	10.5	21.3	787	715	5.2	10.2	3.0	7.3	2.2	3.8
Anus	11.0	14.1	821	464	3.3	4.2	3.5	4.3	4.2	5.6
Oesophagus	13.0	13.9	1'018	455	5.7	6.8	4.2	4.2	3.1	2.8
Pancreas	14.6	14.8	1'123	496	9.4	10.0	3.4	3.3	1.8	1.5
Soft Tissue	15.9	13.1	1'108	399	4.1	4.4	5.8	4.1	6.0	4.6
Brain, CNS	20.0	15.9	1'238	417	8.5	6.8	5.4	4.1	6.1	4.9
Stomach	22.1	24.8	1'744	845	8.8	9.9	6.4	8.0	6.9	6.9
Multiple Myeloma	23.0	19.1	1'818	661	8.3	6.6	8.4	7.1	6.3	5.3
Cervix uteri	41.0	28.7	1'349	437	10.6	8.1	13.5	7.4	17.0	13.3
Bladder	41.3	48.4	3'556	1'814	13.6	16.7	14.3	14.9	13.4	16.8
Kidney	45.7	49.4	3'546	1'665	13.4	15.0	15.4	17.8	16.9	16.7
Ovary	47.9	48.5	1'794	791	15.7	16.6	16.3	15.6	15.9	16.3
Oral cavity	51.9	59.7	3'854	1'884	16.1	19.1	16.8	19.9	19.0	20.7
Leukaemia	53.0	50.7	3'767	1'557	14.4	14.6	16.0	17.6	22.6	18.5
Thyroid	55.4	71.7	3'672	2'011	14.1	20.5	18.5	24.6	22.8	26.6
Non-Hodgkin lymph.	79.0	84.9	6'003	2'786	22.9	25.9	22.7	27.5	33.3	31.5
Lung	79.1	88.3	6'046	2'937	37.2	45.1	23.6	26.1	18.3	17.1
Testis	100.0	79.7	3'116	1'018	24.5	15.4	28.5	27.2	47.0	37.1
Corpus uteri	108.1	102.6	4'446	1'876	27.2	29.2	34.8	31.8	46.1	41.5
Melanoma	189.0	180.9	14'357	5'671	51.8	44.5	64.8	59.1	72.4	77.3
Colon, Rectum	190.3	201.0	15'718	7'235	57.6	65.1	59.8	65.3	72.9	70.7
Breast#	774.2	888.0	29'982	14'881	193.7	226.8	264.4	295.2	316.1	366.1
Prostate	848.8	775.4	32'279	12'489	194.3	186.0	291.4	273.0	363.1	316.4
Total cancer***	1'827.6	1'863.9	139'268	60'773	506.4	545.2	595.4	613.6	725.8	705.0
Prevalence at index date 31.12.2020**										
Gallbladder	5.0	4.3	456	175	2.6	2.3	1.4	1.1	1.0	0.9
Anus	11.3	12.2	939	455	3.5	3.7	3.5	3.9	4.3	4.6
Liver	11.6	20.8	944	799	6.0	10.8	3.3	6.6	2.3	3.5
Oesophagus	13.8	12.5	1'208	466	6.3	6.1	4.7	3.9	2.9	2.5
Pancreas	15.7	15.0	1'344	572	10.4	10.1	3.2	3.2	2.1	1.6
Soft Tissues	16.8	13.7	1'272	459	5.2	4.6	5.8	4.2	5.8	4.8
Brain, CNS	19.3	16.1	1'277	455	8.2	7.5	6.0	3.9	5.1	4.7
Stomach	21.1	23.1	1'846	888	9.2	9.5	5.5	7.2	6.4	6.4
Multiple Myeloma	22.5	17.4	1'990	692	8.4	6.7	8.6	6.6	5.5	4.0
Bladder	38.5	44.1	3'740	1'911	13.3	14.8	12.8	15.6	12.4	13.7
Cervix uteri	42.4	26.0	1'460	424	11.1	7.4	14.0	7.0	17.4	11.6
Ovary	43.2	43.7	1'750	787	14.4	15.4	13.3	14.4	15.5	14.0
Kidney	44.3	48.6	3'818	1'853	13.5	15.7	14.9	16.5	16.0	16.4
Leukaemia	47.0	49.9	3'675	1'713	12.4	14.9	13.7	15.1	20.9	19.9
Oral cavity	50.0	53.7	4'116	1'910	15.5	17.9	16.2	18.8	18.2	17.0
Thyroid	61.6	96.8	4'342	2'946	16.0	28.6	19.0	32.1	26.6	36.1
Non-Hodgkin lymph.	74.8	87.5	6'277	3'239	21.0	25.8	22.1	29.1	31.7	32.6
Lung	78.3	84.7	6'646	3'195	38.3	43.7	23.0	25.3	17.0	15.6
Corpus uteri	98.1	95.8	4'429	1'953	24.4	28.3	30.6	29.6	43.1	37.9
Testis	103.5	75.9	3'342	1'031	24.3	16.6	30.1	25.1	49.1	34.1
Colon, Rectum	174.3	186.1	16'129	7'663	53.2	59.5	55.2	60.3	65.9	66.3
Melanoma	218.0	175.4	18'186	6'109	62.3	44.6	76.7	58.7	79.0	72.2
Prostate	698.2	648.7	30'817	12'406	177.8	173.6	240.2	218.1	280.2	257.0
Breast#	763.2	863.2	32'075	15'947	201.1	228.1	256.1	286.5	306.0	348.6
Total cancer***	1'719.1	1'741.5	144'765	63'878	491.2	522.0	556.2	566.1	671.7	653.4

*: Age-adjusted proportion per 100'000 persons

**: Projected data based on 2005-2014

***: Excluding non-melanotic skin cancer

#: Women

Tab. 1. Age-adjusted prevalence proportions (Prop.) in N per 100'000 and total age prevalence counts (N) by language region at index date 31.12.2014 and projected to index date 31.12.2020. Cancer groups are sorted ascending for 10-year prevalence in the German language region (G). Significant differences in prevalence proportion estimates for index year 2014, and larger than 10%, are depicted in bold, those larger than 20% are depicted in red.

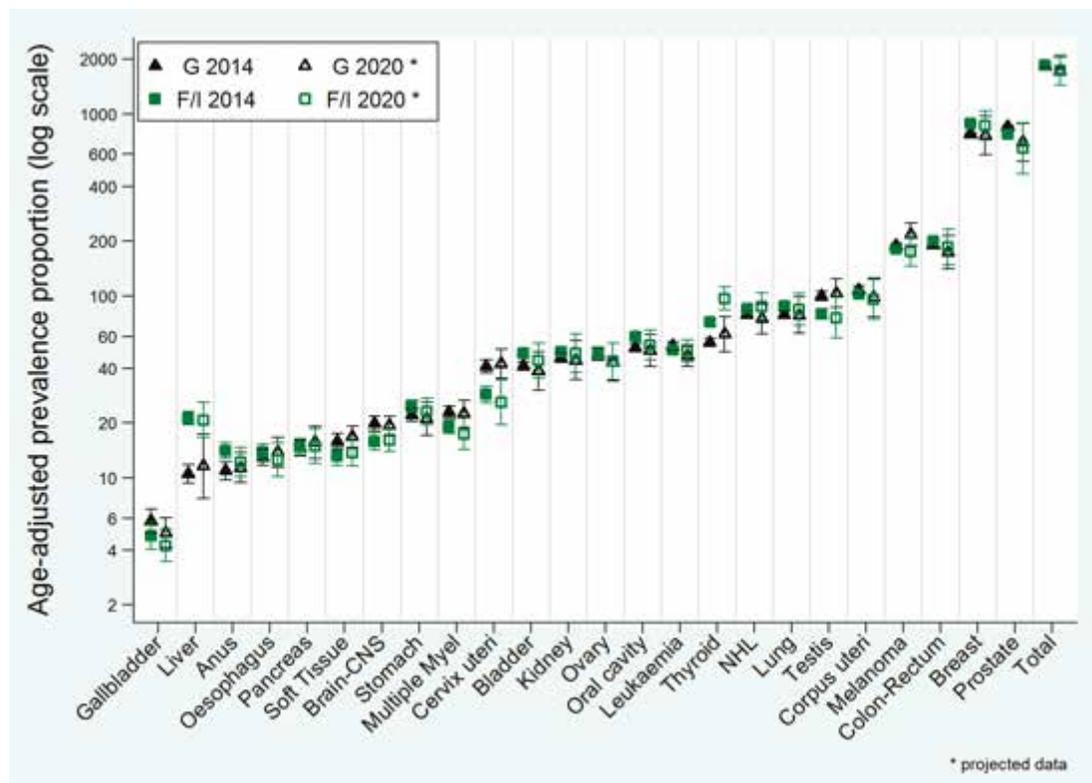


Fig. 2. Ten year age-adjusted prevalence proportions (N per 100'000) for index dates 31.12.2014 and 31.12.2020, by Swiss language region.

(19.6, 23.1) in 100'000 versus 10.5 (9.3, 11.8) in 100'000 for ten year prevalence, respectively (Tab. 1 and Fig. 2). The next largest relative difference in ten year prevalence proportions were found for cervical, thyroid and testis cancer: about 28% higher proportion in F/I for thyroid cancer, about 25% lower proportion in F/I for cervix uteri, and about 21% lower proportion in F/I for testis, as compared with region G (Tab. 1 and Fig. 2). In addition, thyroid cancer expressed a prominent increasing time trend, especially in F/I (Fig. 2). The bladder cancer prevalence proportion was about 19% higher in F/I as compared with G, breast cancer prevalence 15% higher, and lung cancer prevalence 13% higher in F/I versus G. Prostate cancer prevalence proportion were flagged only in patients where the diagnosis has occurred 5 to 10 years before 31.12.2014.

In Fig. 3, prevalence estimates, partitioned according to time since diagnosis (top to bottom panels), are plotted for different attained ages at index date, because age-adjusted figures potentially hide relevant differences at certain age groups. We restricted the presentation in this report to two medium/high incidence cancers with either poor or favorable prognosis: hepatic and lung cancer, on the one hand, breast and prostate cancer on the other hand. Readers interested in other cancer groups are encouraged to contact us for more information and the possibility to gain access to the national cancer dataset.

Proportions rise dramatically with attained age at index date, which mainly reflects the age-dependency of cancer incidence. As expected, age-specific prevalence proportions of poor prognosis cancers decrease with temporal distance between diagnosis and index date, due to short survival times (left sided panels in Fig. 3). The relative difference between language regions in age-specific liver cancer prevalence proportions seemed to remain stable in every patient group along the clinical pathway between diagnosis and index date, whereas for lung cancer survivors, the relative difference in prevalence proportions seemed to disappear with time after diagnosis. In contrast, cancers with good prognosis show an accumulation effect with larger proportions of patients having been diagnosed in the distant past as compared with the recent past (right sided panels in Fig. 3). Differences in breast cancer age-specific prevalence proportions between language regions were quite stable, whereas prostate cancer proportions diverged more with time along the patient clinical pathway, reaching about 3'500 long-term survivors per 100'000 men over 70 years of age in the general population (i.e. 3.5%) in region G. Prevalence proportions for all types of cancer combined (excluding non-melanotic skin cancer) reach very high values in the Swiss population over 70 year of age: 24.8% in region G, and 23.1% in region F/I, for ten year prevalence and index date 31.12.2014 (data not shown).

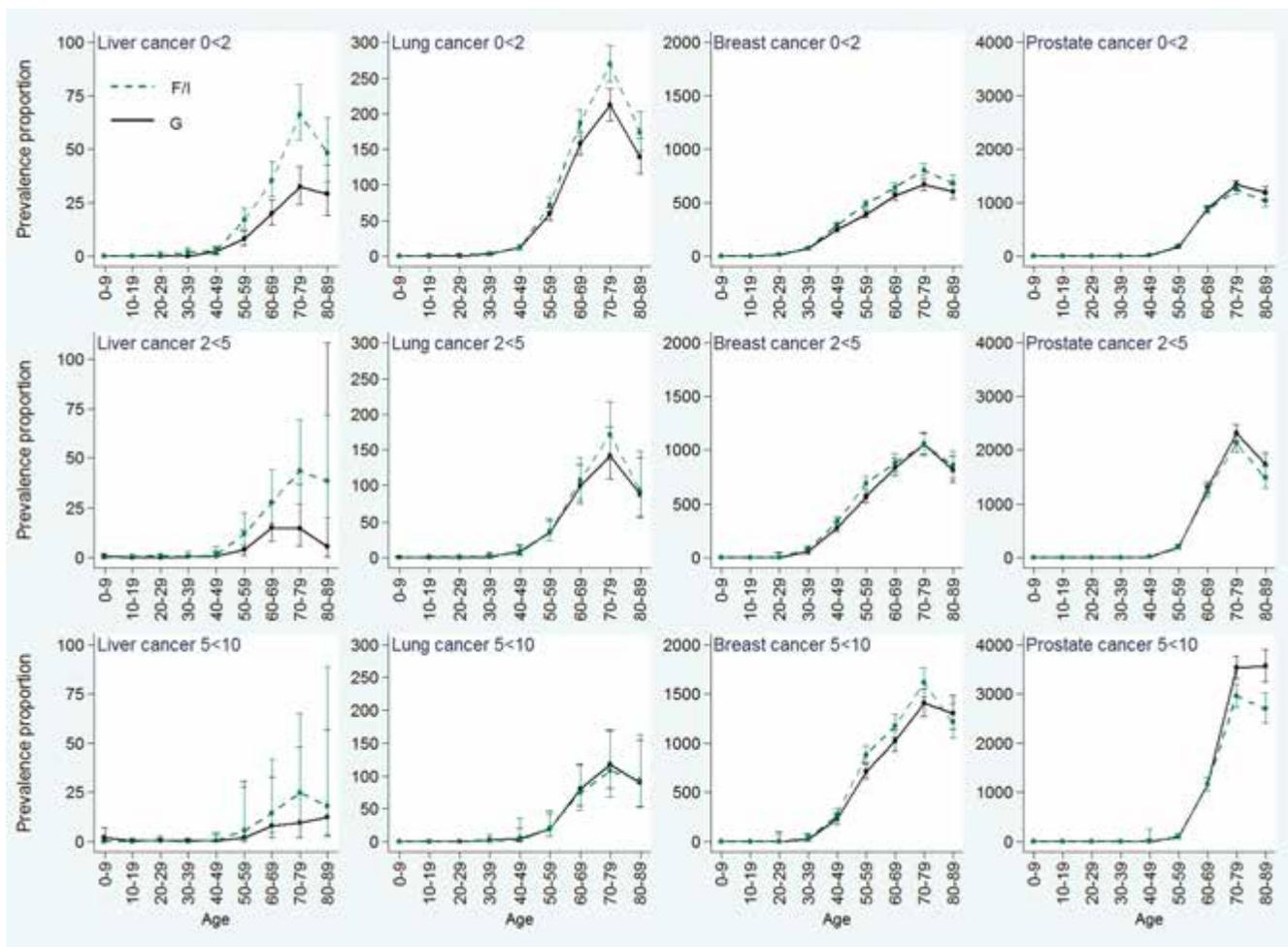


Fig. 3. Age-specific prevalence proportion estimates (N per 100'000) by Swiss language region, partitioned into 0 to < 2 years, 2 to < 5 years, and 5 to < 10 years since diagnosis. Index date 31.12.2014.

Discussion

We provided the most recent time trends and projections for the number and proportion of cancer survivors in two main language regions in Switzerland, using the time lag between diagnosis and index date as proxy for patient groups with different health care needs. The obvious value is to encourage the appropriate allocation of resources to cancer control within cantonal health systems. We expect that the consideration of sub-fractions of prevalence is helpful for this purpose, as the cancer survivors prevalent within a short time interval between diagnosis and index date may need primary treatments and active follow-up, whereas long-term survivors may require medical care regarding treatment-related late effects and second cancers.

The work updates our prevalence estimates published in 2014 and a comparison with the recent estimates can provide useful insights into the adequacy of our statistical

projection procedures [5]. We found that the most recent 10 year prevalence count of 200'041 for all cancer sites combined at index date 31.12.2014 (Fig. 1 and Tab. 1) was 6% larger as compared with the 4 year projected value for 2014 of 188'443 in the work of 2014, which is a satisfying correspondence.

The largest difference between language regions which we have found was regarding liver cancer prevalence proportions in every patient group investigated. The age-adjusted ten year prevalence proportions in the F/I region and the G region were 21.3 and 10.5 in 100'000, respectively, at index date 31.12.2014 (Tab. 1 and Fig. 2). Since prevalence is theoretically a function of incidence and survival it may be explained proximally in these terms. Based on the national cancer dataset, we calculated that liver cancer age-adjusted incidence rates during 2010-2014 for both sexes combined were almost double in the F/I region as compared with G: 10.2 (9.7, 10.7) in 100'000 versus 6.1 (5.7, 6.4)

in 100'000, respectively. Survival estimates for the corresponding diagnosis period are not yet available by language region, but only for Switzerland as a whole. The observed survival of liver cancer patients (both sexes combined) was estimated as 13.9% with respect to 5 years after diagnosis and 7.4% for 10 years [18]. Age-adjusted mortality rates for liver cancer in both sexes combined during 2010-2014 in the F/I region were 7.6 (7.2, 8.0) in 100'000, and somewhat lower in the G region: 4.9 (4.7, 5.2) in 100'000, respectively. The expression $(1 - \text{mortality/incidence ratio})$ is sometimes used as a proxy for 5 year relative survival [19], which is always somewhat larger than observed survival. The expression $(1 - \text{mortality/incidence ratio})$ amounts to 25% in F/I and 20% in G, respectively. A slightly lower relative survival in region G might indicate less favorable stage mix in the liver cancer group, which would contribute to lower prevalence in the G region. These data suggest, that higher incidence rates are the main cause for higher prevalence proportions in region F/I as compared with region G. On the ultimate level of causation, only accessible through careful epidemiological research on the patient level, the differential involvement of important risk factors for liver cancer like chronic hepatitis B or C infection, excessive alcohol consumption, and smoking may be investigated [20, 21]. Both, excessive alcohol consumption and smoking was in general more frequently reported in the F/I as compared with the G region in the public health survey in Switzerland of 2012 (SGB12) [22]. On the other hand, analysis of Swiss health insurance data in a report issued by the Federal Office of Public Health (FOPH) revealed that imaging tests such as ultrasound, computerized tomography scans and magnetic resonance imaging, which are important for liver cancer diagnosis and staging, are applied more frequently in general in the F/I region as compared with the G region [12]. It is unknown whether this remains to be the case on the level of individual liver cancer patients. If it does, it may contribute to better survival due to earlier diagnosis or improved stage determination [23]. The assessment of such factors goes beyond the goal of the present work.

Prostate cancer may serve as an example of a major prevalence cancer where age-adjusted prevalence proportions were not much different between language regions (Tab. 1 and Fig. 2). Age-adjusted incidence rates during 2010-2014 were 118.1 (115.6, 120.7) in the F/I region, not different from 119.1 (117.1, 121.2) in the G region. The observed survival of prostate cancer patients was estimated as 74.7% with respect to 5 years after diagnosis and 54.0% for 10 years [18]. Mortality rates for prostate cancer during 2010-2014 in the F/I region were 21.0 (20.0, 22.0) in 100'000, and only slightly higher in the G region 23.7 (23.1, 24.4) in 100'000, respectively. The expression $(1 - \text{mortality/incidence ratio})$ estimates the 5 year relative survival as 82% in F/I and 80% in G, respec-

tively. These data suggest, that because incidence as well as survival rates were rather similar, also the prevalence proportions in F/I and G were similar.

Limitations of the present work: regular, accurate and complete assessment of the vital status of each registered person is a prerequisite for valid prevalence statistics. Completeness of vital status follow-up as of 31.12.2014 was different between registries. Active follow-up for all cases was provided by cantons AI, AR, GE, SG, and TI. In contrast, the most recent available follow-up date was sometime before 31.6.2014 in GL and GR (17% of cases), JU and NE (6%), VD (32%), VS (35%), and ZH (20%). In these cases, the vital status at certain index dates was imputed based on assumptions that might only partially hold (see Methods). Furthermore, there was a difference in cancer registration coverage, and thus representativeness of the estimates, between language regions: coverage amounted to only 40% in the G region, as compared with 90% in the F/I region, because a large number of German speaking cantons started cancer registration after 1996. In addition, information on the disease severity, i.e. whether the cancer has spread to near or distant organs at the time of diagnosis, was not considered in the present report. This factor affects survival [24, 25] and may have contributed to prevalence differences between language regions. It is also relevant for public health policy because treatment needs are different and costs higher for patients whose cancer is more advanced at diagnosis [26]. Finally, when calculating prevalence projections for 2017 and 2020, we used the assumption that survival rates are the same as the last observed ones, i.e. that survival will not improve. Therefore, the number of projected survivors until 2020 is potentially underestimated.

Conclusions

The overall cancer prevalence was very similar in the French/Italian and German language regions for every patient group investigated. There are, however, conspicuous differences in prevalence for a few specific cancer types and patient groups, e.g. for hepatic, cervical, testicular, and thyroid cancer. While survivors up to 10 years after diagnosis represent overall 2.4% of the population, the proportion among individuals aged 70 or more is an impressive 23% - 25%, depending on language region. The elderly and long-term cancer survivors are a steadily growing population in most developed countries [27]. Thus, it becomes increasingly relevant to account for the specific health care needs of both vulnerable groups, especially when it comes to monitoring and managing persistent and late physical and psychological effects, prevention and health promotion, surveillance targeting co-morbid illnesses, and health care coordination to ensure that all long-term and wellness needs are met [28].

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