Subsite-specific colorectal cancer trends in Switzerland (1989-2012)

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INTRODUCTION

Each year about 2'320 men and 1'820 women are newly diagnosed with colorectal cancer (CRC) in Switzerland, and about 900 men and 700 women die of CRC [1]. The lifetime risk of being diagnosed with CRC is about 6% for men, and 5% for women. The lifetime risk of dying due to CRC is about 3% for men, and 2% for women. CRC incidence ranks 2nd in women and 3rd in men, and is the 3rd most frequent cancer death in both. The slow course of development from precancerous polyp to malignant cancer provides a unique opportunity for disease prevention and early detection. Since the mid 1990s, several expert panels in the U.S. have recommended lower gastrointestinal endoscopy (in particular sigmoidoscopy and colonoscopy) for detection and removal of precancerous lesions as a primary large bowel screening method [2]. About a decade later several epidemiological studies reported diverging incidence trends for proximal and distal anatomic subsites of the large bowel, consistent with an impact of screening on the population-level, albeit less effective for proximal subsites [3,4,5,6]. Up to now, clinical randomized controlled trials as well as numerous observational studies have shown that screening sigmoidoscopy/colonoscopy with polypectomy reduces large bowel cancer incidence as well as mortality [7,8]. The aim of our study is to examine trends in CRC incidence in Switzerland with special attention to anatomic subsites.

METHODS

The analysis is based on primary malignant colon and rectal cancer (CRC) diagnoses abstracted from the Swiss National Cancer Dataset, which combines data from cantonal cancer registries for the purpose of national cancer monitoring [9].

Inclusion criteria

Data from Swiss cantons with continuous cancer registration for the entire analysis period (1989-2012) were included: Zurich (ZH), Grison (GR), St. Gallen (SG), Appenzell Ausserrhoden (AR), Appenzell Innerrhoden (AI), Vaud (VD), Valais (VS), Neuchâtel (NE), and Geneva (GE). Cases only known from a death certificate (DCO) were excluded because the date of diagnosis was unknown and in one canton there was no annual, systematic and complete matching of incident cases to the cantonal vital statistics. In the remaining cantons, DCO cases were ≤2% at all times during the analysis period.

We grouped cantons for the language spoken by the majority of the permanent resident population because it might reflect differences in health behavior and health politics [10,11]. In the cantons ZH, GR, SG, AR, and AI predominately German is spoken and in VD, VS, NE, and GE it is French. We distinguished between proximal anatomic subsites (caecum, appendix vermiformis, colon ascendens, flexura hepatica, colon transversum) and distal subsites (flexura coli sinistra, colon descendens, colon sigmoideum, recto-sigmoid junction, rectum). A third subsite was comprised of overlapping lesions of colon and colon unspecified.
Disease progression at diagnosis was divided into groups based on the UICC (Union for International Cancer Control) classification: stage I (local), stages II/III (local/regional spread and lymph node involvement), stage IV (distant metastasis), and stage information missing. Analysis was restricted to data with <20% missing stage information and included the cantons ZH, GR, VS, GE and diagnosis years 1993-2012.

Statistical analysis

Incidence rates are expressed as events per 100'000 person-years (py) of mid-year risk population. All rates, including age group-specific rates, were age-standardized with the direct method using the European standard population [12]. Annual percentage changes (APC) in incidence rates for cases pooled bi-annually to reduce variability, and points in time (change points or «joinpoints») when a linear trend significantly alters direction, were estimated with the Joinpoint Regression Program v4.0.4 [13]. In short, a heteroscedastic simple linear regression model for logarithmic transformed rates was used which assumed a linear trend

Site	Strata		1989-1992* Rate***	95% CI		2009-2012 Rate***	95% CI		Trend (pre) APC	95% CI		Change point (P value##)	Trend (post) APC	95% CI	
CRC proximal subsite	Sex	Men	13.8	12.8	14.7	13.5	12.8	14.3	0.0	-0.5	0.5	none	-	-	-
		Women	10.2	9.5	10.9	10.5	9.9	11.2	0.4	0.0	0.9	none	-	-	-
		Both	11.7	11.1	12.2	11.8	11.3	12.3	0.2	-0.1	0.5	none	-	-	-
	Age	0-49	1.42	1.19	1.68	1.68	1.45	1.95	-1.4	-4.8	2.2	2003/2004 (0.023)	6.5	-0.7	14.2
		50-64	15.9	14.2	17.6	16.9	15.5	18.5	0.5	-0.3	1.2	none	-	-	-
		65-79	59.8	55.8	64.0	57.9	54.4	61.5	0.1	-0.4	0.5	none	-	-	-
		80+	121	111	132	117	109	125	-0.2	-0.6	0.3	none	-	-	-
	Area#	Ge	11.5	10.8	12.2	11.3	10.7	12.0	0.2	-0.2	0.6	none	-	-	-
		Fr	11.9	11.1	12.8	12.4	11.7	13.1	0.2	0.0	0.5	none	-	-	-
	Stage**	I	1.19	0.95	1.47	2.04	1.79	2.32	3.1	2.0	4.1	none	-	-	-
		II/III	6.71	6.13	7.35	6.45	6.01	6.91	0.8	-0.7	2.4	2005/2006 (0.021)	-3.0	-7.1	1.2
		IV	2.78	2.41	3.20	2.64	2.36	2.95	0.5	-0.7	1.8	none	-	-	-
		Missing	1.65	1.38	1.98	0.48	0.37	0.62	-6.8	-9.4	-4.1	none	-	-	-
CRC distal subsite	Sex	Men	33.2	31.8	34.7	31.9	30.8	33.1	1.0	-0.5	2.6	2001/2002 (0.018)	-1.7	-3.4	0.1
		Women	19.7	18.7	20.7	18.1	17.2	18.9	0.6	-0.3	1.5	2001/2002 (0.006)	-1.5	-2.6	-0.4
		Both	25.2	24.4	26.0	24.3	23.6	25.0	1.0	-0.1	2.1	2001/2002 (0.005)	-1.6	-2.8	-0.3
	Age	0-49	2.55	2.24	2.89	2.77	2.48	3.09	2.9	-0.3	6.2	1997/1998 (0.010)	-0.9	-2.1	0.3
		50-64	47.1	44.2	50.1	48.0	45.5	50.7	1.4	-0.2	3.0	2001/2002 (0.016)	-1.7	-3.5	0.2
		65-79	124	118	130	120	115	125	1.2	-0.4	2.9	2001/2002 (0.028)	-1.6	-3.5	0.4
		80+	189	177	202	142	134	152	-1.2	-1.6	-0.8	none	-	-	-
	Area#	Ge	24.9	23.9	26.0	24.0	23.1	25.0	0.9	-0.4	2.1	2001/2002 (0.010)	-1.6	-3.1	-0.1
		Fr	25.6	24.3	26.9	24.6	23.5	25.7	0.9	-0.1	1.9	2003/2004 (0.007)	-2.0	-4.2	0.1
	Stage**	I	4.86	4.35	5.42	5.48	5.06	5.93	1.0	0.3	1.7	none	-	-	-
		II/III	13.0	12.1	13.8	11.3	10.7	12.0	1.7	-1.4	4.9	2001/2002 (0.011)	-3.0	-5.0	-0.9
		IV	3.77	3.33	4.27	4.92	4.53	5.34	1.4	0.8	1.9	none	-	-	-
		Missing	4.80	4.31	5.34	1.68	1.46	1.93	-6.1	-8.0	-4.2	none	-	-	-
CRC unspecified subsite	Sex	Men	1.32	1.05	1.64	0.65	0.50	0.84	-3.1	-4.7	-1.5	none	-	-	-
		Women	0.75	0.59	0.96	0.55	0.43	0.71	-1.4	-2.9	0.2	none	-	-	-
		Both	0.99	0.84	1.16	0.60	0.50	0.72	-2.2	-3.6	-0.8	none	-	-	-
	Age	0-49	0.11	0.06	0.21	0.05	0.02	0.12	-3.5	-7.5	0.7	none	-	-	-
		50-64	1.04	0.65	1.58	0.83	0.53	1.24	-1.9	-4.0	0.2	none	-	-	-
		65-79	5.05	3.93	6.40	2.34	1.69	3.15	-3.3	-4.8	-1.8	none	-	-	-
		80+	13.5	10.3	17.4	10.3	8.0	13.0	-1.0	-2.5	0.5	none	-	-	-
	Area#	Ge	0.58	0.44	0.76	0.59	0.46	0.75	0.7	-1.3	2.6	none	-	-	-
		Fr	1.54	1.25	1.87	0.61	0.47	0.80	-4.6	-6.1	-3.1	none	-	-	-
	Stage**	I	0.06	0.02	0.17	0.08	0.03	0.15	-1.6	-6.6	3.5	none	-	-	-
		II/III	0.26	0.15	0.42	0.08	0.04	0.15	-5.6	-10.0	-1.0	none	-	-	-
		IV	0.14	0.07	0.26	0.22	0.15	0.32	1.6	-2.3	5.5	none	-	-	-
		Missing	0.27	0.17	0.42	0.07	0.04	0.14	-4.7	-9.1	-0.2	none	-	-	-
CRC all subsites	Sex	Men	48.3	46.6	50.1	46.1	44.7	47.5	-0.2	-0.7	0.3	none	-	-	-
		Women	30.6	29.4	31.8	29.1	28.1	30.2	0.4	-0.3	1.1	2003/2004 (0.034)	-1.1	-2.7	0.4
		Both	37.9	36.9	38.9	36.6	35.8	37.5	0.5	-0.1	1.2	2003/2004 (0.009)	-1.4	-2.8	0.1
	Age	0-49	4.08	3.69	4.51	4.50	4.12	4.91	0.5	-0.2	1.1	none	-	-	-
		50-64	64.0	60.6	67.5	65.8	62.9	68.9	0.9	0.0	1.9	2003/2004 (0.010)	-1.7	-3.6	0.3
		65-79	189	181	196	180	174	186	0.5	-0.3	1.4	2005/2006 (0.026)	-2.3	-5.7	1.2
		80+	324	308	341	270	258	282	-0.8	-1.1	-0.4	none	-	-	-
	Area#	Ge	37.0	35.7	38.3	35.9	34.8	37.1	0.6	-0.2	1.4	2003/2004 (0.013)	-1.5	-3.2	0.2
		Fr	39.0	37.5	40.6	37.6	36.3	38.9	0.5	-0.2	1.2	2003/2004 (0.017)	-1.3	-2.8	0.3
	Stage**	I	6.11	5.54	6.73	7.60	7.11	8.13	1.4	1.1	1.7	none	-	-	-
		II/III	19.9	18.9	21.0	17.9	17.1	18.6	1.5	-1.2	4.3	2001/2002 (0.009)	-2.4	-4.2	-0.7
		IV	6.70	6.11	7.34	7.79	7.30	8.31	1.1	0.5	1.7	none	-	-	-
		Missing	6.73	6.15	7.35	2.24	1.99	2.52	-6.2	-7.9	-4.4	none	-	-	-

*: 1st time-period for Stage: 1993-1995
**: Pooled data from ZH,GR,VS,GE
***: Rates are age-standardized
#: Ge= German-speaking (pooled ZH,SG,AR,AI,GR), Fr= French-speaking (pooled VD,VS,NE,GE)
##: P value permutation test of Nullhypothesis without change point

Tab.1. Colorectal cancer (CRC) incidence rates and annual percentage changes (APC) for pooled Swiss cantons (ZH, SG, AR, AI, GR, VD, VS, NE, GE) by subsite, sex, age, and UICC stage.

between change points and continuity at the change points. To determine the location of a change point, the grid search method was applied which creates a «grid» of all possible locations for change points specified by the settings, and tests the sum square of errors (SSE) at each one to find the best possible fit [14]. A single change point was allowed in our analysis, as is recommended by the software for time series ≤12 data points, and restricted to minimally 4 data points away to either end of the time series. A significance level (α) of 0.05 was used to find the best model.

RESULTS

A total of 41'283 colorectal cancer (CRC) cases between 1989 and 2012 were distributed anatomically into 13'282 (32%) incidences at proximal colon, 27'100 (66%) at distal colon including rectum, and 901 (2%) at overlapping/unspecified sites of colon. The distribution of anatomic subsites was similar in each canton (data not shown). Almost all diagnoses were histologically verified (97%).
Table 1 presents age-standardized incidence rates at the beginning (1989-1992) and the end (2009-2012) of the analysis period, as well as incidence trends (APC) for different subsites of the large bowel, stratified by sex, age group at diagnosis, language area and UICC stage group.

Findings by sex

Age-standardized cancer incidence rates for the entire large bowel (CRC all subsites in Tab. 1) were about 50% higher in men compared with women over the whole analysis period from 1989 to 2012. During 2009-2012, the CRC incidence was 46.1 per 100'000 person-years (py) in men, and 29.1 in women, respectively (Tab. 1). Men had smaller proportions of proximal CRC as compared with women (29% vs 37%, respectively), with odds ratio 0.68 (95% confidence interval: 0.65-0.71), and subsequently higher proportions of distal CRC

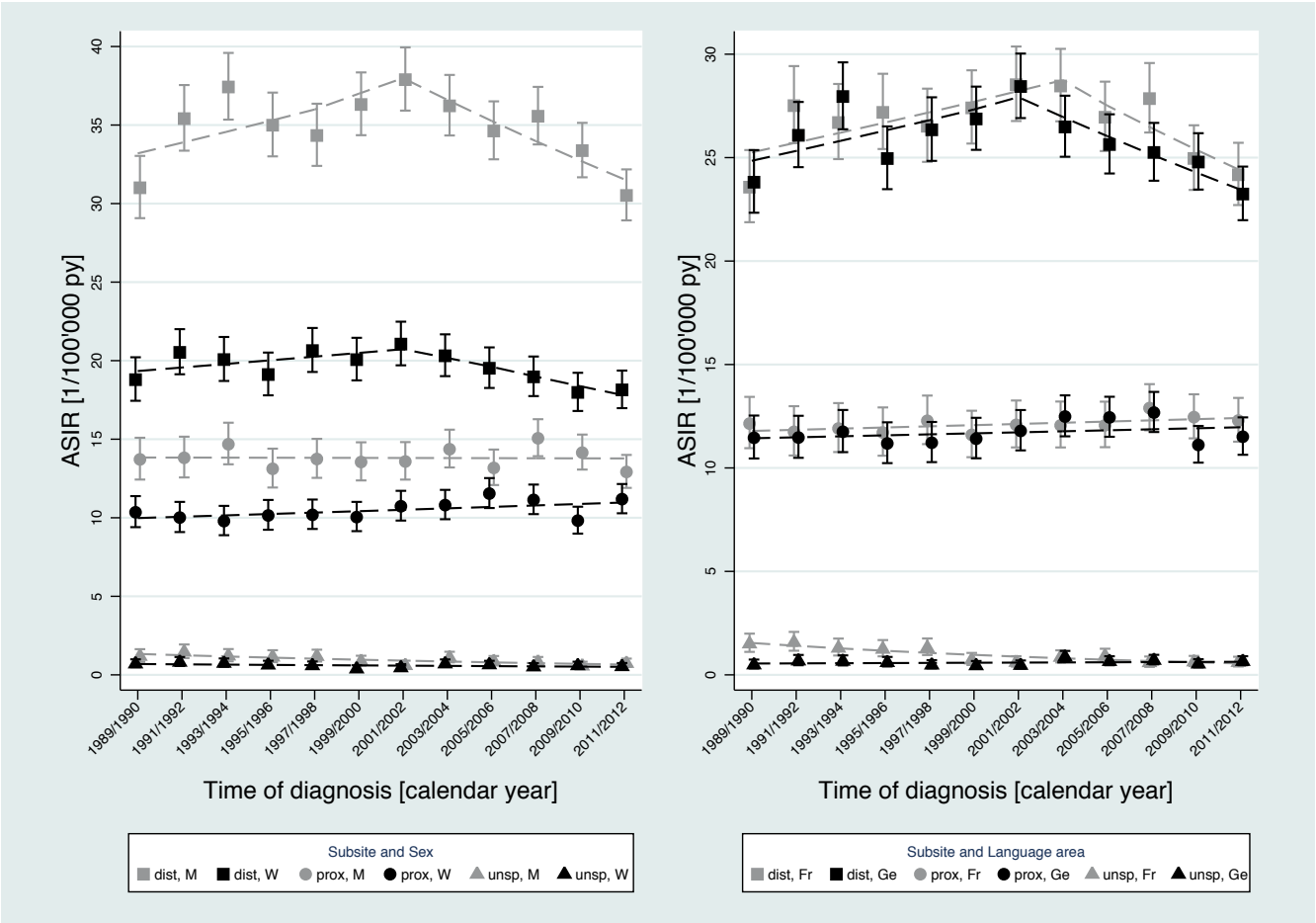

Fig. 1. Temporal trends in age-standardized cancer incidence rates (ASIR) at different colorectal subsites (dist = distal, prox = proximal, unsp = overlapping or unspecified), by sex (left panel; M = men, W = women) and language region (right panel; Fr = French-speaking, Ge = German-speaking).

(69% vs 61%), without any difference in proportion colon overlapping/unspecified (both 2%). The mean age at diagnosis was slightly lower in men as compared with women, 69.5 versus 71.5 years, respectively. Incidence rates in men and women were rather constant over time in the proximal colon, whereas a highly significant change point (P <0.01) between increasing and decreasing rates was found around 2001/2002 for distal CRC (Tab. 1 and left panel in Fig.1). The estimated annual percentage change (APC) in the rates for both sexes combined was 1.0% before the change point, and -1.6% thereafter (Tab. 1). Incidence rates for CRC with exact subsite unknown (i.e. overlapping or unspecified subsite) were small (<0.7 per 100'000 py), similar in men and women, and decreasing over time (Tab. 1, Fig. 2).

Findings by language area

CRC rates for the entire large bowel were very similar in both language regions, e.g. in the latest time-period 35.9 per 100'000 py in the German-speaking versus 37.6 in the French-speaking region, respectively (Tab. 1). Rates for CRC with exact subsite unknown were always small (≤1.5 per 100'000 py), but higher in French-speaking compared with German-speaking cantons in the years prior to 1999 (Tab. 1 and right panel in Fig. 1). There was no difference between language regions with respect to incidence trend patterns at proximal and distal anatomic subsites of CRC, with rather constant incidence rates proximally over the whole analysis period and biphasic trends distally. Statistically significant change points for distal CRC incidence rates were found between 2001 and 2004 (Tab.1 and right panel in Fig. 1). Again, incidence rates increased slightly before the change point (APC 0.9% in both language regions), and decreased afterwards (APC -1.6% and -2.0% for German- and French-speaking cantons, respectively) (Tab. 1 and right panel in Fig. 1).

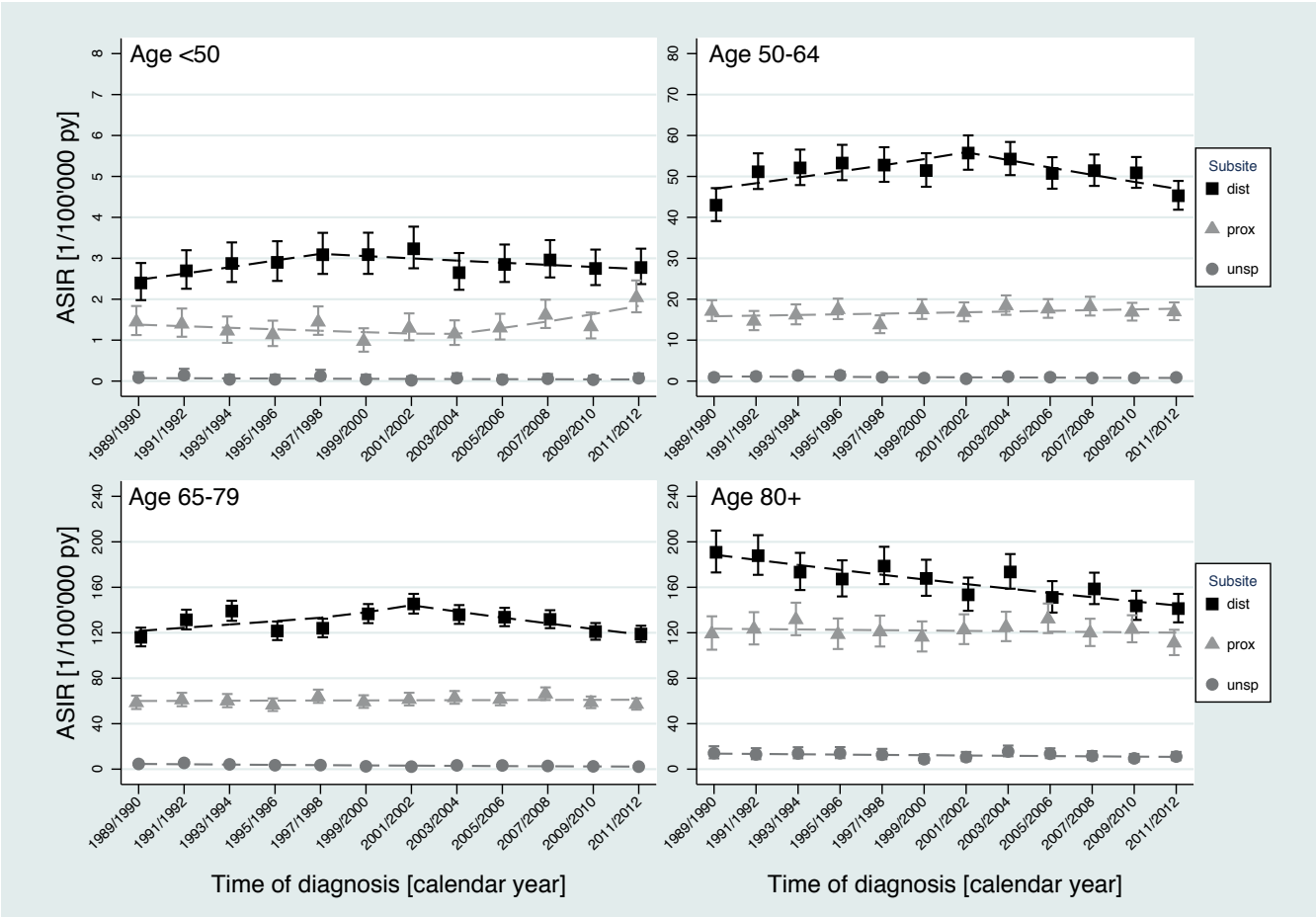

Fig. 2. Temporal trends in age-standardized cancer incidence rates (ASIR) at different colorectal subsites (dist = distal, prox = proximal, unsp = overlapping or unspecified), by age group at diagnosis. Note the differences in scale.

Findings by age

The risk of being diagnosed with CRC increased steeply with age, starting with incidence rates around 5 new cases per 100'000 py at ages below 50 and reaching levels of about 300 new cases above 80 years of age (Tab. 1, Fig. 2). The mean age at diagnosis for distal CRC (68.9 in men, 70.1 in women) was below the mean age for proximal CRC (70.9 in men, 73.4 in women). It appeared that the age-dependent risk ratio (RR) for distal as compared with proximal CRC is highest in age group 50-64 (RR 2.8 in 2009-2012) and becomes smaller at higher ages (RR 1.2 for age 80+ in 2009-2012) (Tab. 1). Again, incidence rates of proximal CRC remained almost constant over the whole analysis period in all age groups with the possible exception of those below 50 years, where a change point between decreasing to increasing rates was found around 2003/2004, albeit at very small rates (Tab. 1, Fig. 2). In contrast, age group-specific incidence trends were highly time-dependent for distal CRC, with change points between 1997/1998 and 2001/2002 in every age group below 80 years of age (Tab. 1, Fig. 2). At ages 80+, incidence rates of distal CRC have been in decline since the beginning of the analysis period with APC of -1.2% (Tab. 1, Fig. 2). They declined from 189 per 100'000 py during 1989-1992 to 143 during 2009-2012 (Tab. 1). Diagnoses without subsite of the colon specified comprised <5% of cases in every age group and rates remained constant over time (Tab. 1, Fig. 2).

Findings by UICC stage

CRC incidence trend analysis by stage was based on four instead of nine Swiss cantons and started 1993/1994 instead of 1989/1990 (see Methods). In total, 21'635 cases were available, distributed anatomically into 7'177 (33%) at proximal colon, 14'052 (65%) at distal colon and rectum, and 406 (2%) at overlapping/unspecified sites of colon, which is almost identical to the anatomic subsite distribution in the full dataset. Stage I incidences con-

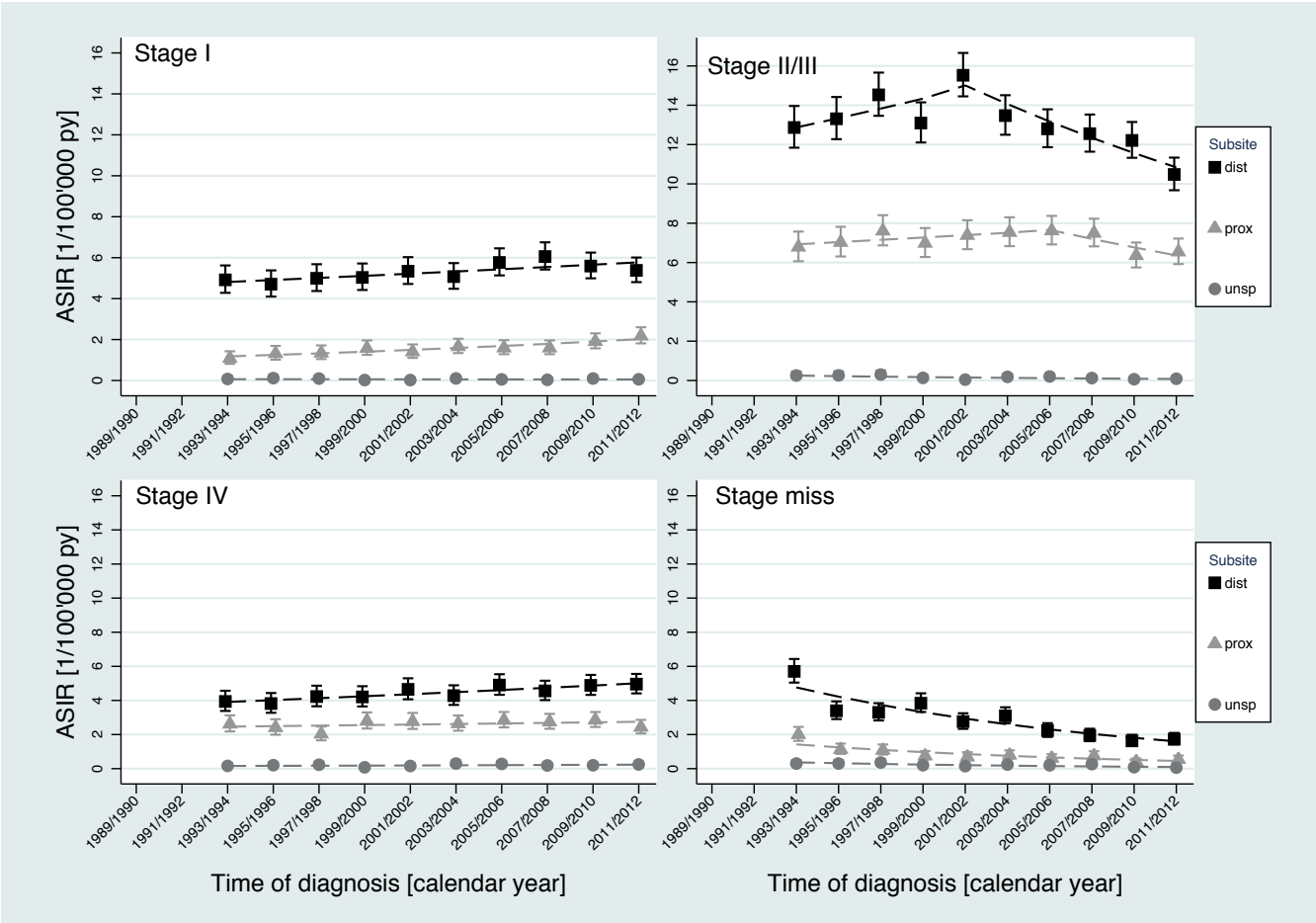

Fig. 3. Temporal trends in age-standardized cancer incidence rates (ASIR) at different colorectal subsites (dist = distal, prox = proximal, unsp = overlapping or unspecified), by UICC stage group.

tributed 18%, stage II 26%, stage III 26%, and stage IV 19% of the cases (data not shown). Stage was unknown in 11% of the cases. Rates for stage I incidences were steadily increasing at proximal and distal subsites of large bowel (Fig. 3). The APC was 3.1% for proximal colon and 1.0% for distal colon and rectum (Fig. 3), or 1.4% for the entire large bowel (Tab. 1). The corresponding incidence rate for stage I CRC (all subsites) increased from 6.11 per 100'000 py during 1993-1995 to 7.60 during 2009-2012 (Tab. 1). Steadily increasing incidence trends were also observed for distantly metastasized CRC (stage IV) with APC 0.5% for proximal colon and 1.4% for distal colon and rectum (Fig. 3), or 1.1% for all colorectal subsites (Tab. 1). Incidence rates for stage IV CRC (all subsites) increased from 6.70 per 100'000 py during 1993-1995 to 7.79 during 2009-2012 (Tab. 1). Incidence trend change points were observed for stage II/III CRC around 2005/2006 for proximal colon and somewhat earlier around 2001/2002 for distal colon plus rectum (Fig. 3). The corresponding APCs after the change points were -3.0%, for proximal and distal colon plus rectum alike (Tab. 1). The stage II/III incidence trend for the entire large bowel was negative with APC -2.4% after a change point around 2001/2002 (Tab. 1). The rates for incidences without information on stage declined steadily at each anatomic subsite of the large bowel over the whole analysis period (Tab. 1, Fig. 3).

DISCUSSION

The main findings in this report are strikingly different incidence trends on the population-level for different anatomic subsites of large bowel in Switzerland. While the risk of being diagnosed with cancer at proximal colon remained largely constant between 1989 and 2012, the risk for distal colon or rectal cancer increased from 1989 through around 2001-2004, but has decreased since then. This pattern was the same in men and in women, and was also independent of language region in Switzerland. Change points for distal CRC incidence rates were most pronounced in age groups 50-64 and 65-79, both around 2001/2002, while incidence rates for proximal CRC remained constant over the analysis period in these age groups. A change point around 2001/2002 was found for stage II/III incidence rates at distal CRC, and delayed by about 4 years also for proximal subsites, while stage I and stage IV incidences steadily increased in both anatomic subsites.

Our dataset is population-based and includes all existing diagnoses with high level of completeness. The reported cancer rates can thus be regarded as representative on the population-level. On the other hand, our dataset lacked sufficient information about risk factors or measures of prevention (e.g. previous endoscopies) on the individual level to derive conclusions about possible causes for the observed changes with any level of certainty. Potential causes underlying the observed trend pattern in this report must be able to account for its anatomical subsite specificity as well as the change in incidence trend roughly between 2000 and 2005. Likely candidates should also not depend strongly on sex or different language regions in Switzerland. In order to qualify potential causes, the time of about 10 years for a precancerous polyp to develop into malignant cancer must be considered [15].

A large range of possible risk factors for CRC have been identified. Some of these factors are modifiable while others are not. Non-modifiable risk factors include a personal or family history of colorectal cancer, chronic inflammatory bowel disease, or familial adenomatous polyposis [16]. Epidemiological studies have identified many modifiable risk factors. These include smoking and moderate-to-heavy alcohol use, obesity, physical inactivity, and dietary habits [17,18,19,20,21]. A protective role has been discussed for nonsteroidal anti-inflammatory drugs and menopausal hormones [22,23]. Furthermore, a protective effect of endoscopic examinations supplemented with polypectomy has clearly been demonstrated [8,24,6,7].

Starting 1992, a Swiss Health Survey (SHS) has been conducted every five years providing information about prevalence trends for some of the putatively involved risk factors. The fifth and latest survey took place in 2012 [25]. Summarily, only risk factors with increasing prevalence, opposing the decline in CRC risk, might safely be excluded as a main underlying factor, e.g. the increasing prevalence of obesity/overweight is unlikely involved in the negative CRC trend in adults >50 years of age.

Perhaps the most interesting hypothesis is that endoscopic examinations of the large bowel might be involved in the observed trends in CRC incidence. CRC screening in Switzerland is done opportunistically, without a national screening program. Endoscopy-based CRC screening activities are confined to regional research projects [8,26]. Screening colonoscopy became more widespread in Switzerland only during the last decade and has to be paid by the health insurance since July 2013. In 2005, lower gastrointestinal endoscopy and fecal occult blood test utilization were ascertained in the Survey of Health, Aging and Retirement in Europe (SHARE) in adults aged 50 years and older from 11 countries [27]. The Swiss age-standardized prevalence of endoscopy utilization was 19% in men and in women alike, overlapping with values from Germany, Austria and France [28]. In addition, a nationally representative Swiss survey in 2005 reported that 23% of adults aged 40-79 years have had an endoscopic large

bowel examination, without difference between German or French language regions [29]. The SHS assessed utilization of endoscopic large bowel examination in 2007 and 2012. The percentage of respondents who never had an examination stayed largely the same in 2007 and 2012 for age 40-54 (83% and 79%, respectively), but dropped from 73% to 61% for age 55-64, from 66% to 54% for age 65-74, and from 65% to 53% for age 75+, similar in men and women [25]. The SHS of 2012 reported no significant difference between German-speaking and French-speaking regions with regard to endoscopic examination of the large bowel. It is unknown whether the indication for endoscopy was screening, diagnostic, or surveillance after rectal bleeding, abdominal symptoms or other. On the other hand, a population-based case-control study from Germany showed that previous colonoscopy was associated with reduced risk of CRC regardless of the indication [6].

The prevalence proportions of lifetime use of lower gastrointestinal endoscopy in Switzerland, Germany, Austria, and France are one-half to two-third of those in the U.S. [30]. It has been suggested that higher utilization of lower gastrointestinal endoscopy in the U.S., financially covered by Medicare since 2001, contributed to declining CRC incidence rates already since the early 1990s [5,31]. Concordant with a potential role of endoscopic screening for population-based CRC rates in Switzerland, the APCs of CRC rates were least pronounced for age <50 (-0.9%), as compared with APC of -1.7% for age 50-64, -1.6% for age 65-79, and -1.2% for age 80+. Screening endoscopy is only recommended for ages 50-69. The selective decline of distal CRC could be related to serrated adenomas. They arise much more frequently in the proximal colon and are easily missed by endoscopy [32,33]. It has been shown that CRC cases diagnosed despite earlier colonoscopy occurred more frequently in the proximal colon and in persons with serrated adenomas [34]. Quality of colonoscopy seems to be crucial for the prevention of CRC especially in the proximal colon. If the more widespread use of screening colonoscopy is in fact contributing to Swiss CRC incidence trends, apparent increases in incidence due to detection of preclinical cases are to be expected, at least initially, followed by a decline in the longer run due to removal of adenomas. Manser et al. (2012) reported that while the majority, or 8 of 11 (72%), of screen-detected CRC cases were stage I, they represented the minority, or 42 of 213 (19.7%), of cases in the non-screened group. Our observation of increasing incidence rates for stage I CRC cases is thus consistent with an impact of endoscopic screening on the population-level. Earlier detection implies that fewer cases progress to higher stages which might underlie the observed decrease in stage II/III CRC incidences starting around 2001/2002. On the other hand, we found a positive trend for stage IV incidences without any indication of a change point. It is possible that increased usage of sensitive imaging techniques for diagnostic staging in recent years has resulted in upstaging from III to IV [35]. In addition, CRC incidences with stage missing often represent advanced disease, possibly because investigations to determine stage precisely may be judged less clinically relevant for patients who will only receive palliative treatment. Thus, the observed reduction in un-staged CRC incidences might have contributed to increasing rates for stage IV.

We have shown a distal to proximal shift in colorectal cancer incidences over time in Switzerland on the population-level. An attractive hypothesis for the selective decrease in distal colon cancers is cancer prevention by opportunistic lower gastrointestinal endoscopy, which might have overlooked fewer polyps in distal than in the proximal anatomic subsites. If this hypothesis can be substantiated by further studies, it lends support for the introduction of colorectal cancer screening programs in Switzerland.

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