Although the current state of health of the ECR is satisfactory, we should remember that the registry is a fragile organism. It could not survive if turned into an experimental playground of IT solutions, if overloaded with data items collected for whatever purpose and of unknown quality, if having no scientific output.

Disclosure statement

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

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LETTER TO THE EDITOR

Incidence and survival of head and neck squamous cell carcinoma in children and young adults in Denmark: a nationwide study from 1980 to 2014

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Introduction

Head and neck squamous cell carcinoma (HNSCC) is exceedingly rare among children and young adults. When observed, there is often association to predisposing factors such as DNA repair defects (Fanconi anemia, Bloom syndrome), prior irradiation of the head and neck among cancer survivors, oral graft versus host disease or oncogenic virus infection [1–4].

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Because of its rarity few studies have reported the incidence and survival of HNSCC among children and young adults and data from a nation-wide setting is sparse. The aims of this study were to report the incidence and survival of HNSCC based on gender, age at diagnosis and tumor location among patients aged 0–24 years in Denmark from 1980–2014.

Material and methods

Data was obtained from the Danish Cancer Registry (DCR), the Danish Pathology Data Bank (DPDB), the central population register (CPR), and the National Patient Register (NPR). The DCR contains nation-wide data on cancers diagnosed in Denmark from the year 1943 and onward. Reporting to the DCR became mandatory in 1987 [5]. The DPDB is a nation-wide database of pathology investigation performed in Denmark since 1970 (including all departments of pathology in Denmark since 1990), samples are registered according to a Danish version of the Systematized Nomenclature of Medicine (SNOMED) [6]. The CPR has provided every resident in Denmark with a unique personal identification number since 1968, making individual level linking across registries possible. Further it holds data on vital status and emigration among others. The NPR provides every contact a patient have with the health care system with a record number, to which information on the contact is linked, including diagnosis.

All patients between the age of 0 and 24 years registered with HNSCC cancer from 1980 to 2014 in the DCR or the DPDB were included in the study. Duplicates were excluded.

HNSCC was defined as registration in the DCR or the DPDB with any form of SCC located at the oral cavity, nasal cavity, sinuses, pharynx or larynx. Even though there are many morphology codes for SCC, we only found registration with M80703, M80713, M80763 and M80833 in the DPDB.

The tumor location was defined according to the WHO ICD-8 (1980–1993) and ICD-10 (1994–2014) classification from the DCR, as well as the SNOMED classification from the DPDB. For statistical analysis we categorized tumor location in four groups: Oral cavity (T52210, T54910, DC020, DC021, DC022, DC023, DC029, DC030, DC039 and DC049), nasopharyngeal (DC119), laryngeal (T24100 and DC320) and others (oropharynx and sinuses: DC051 and DC318). We categorized age at diagnosis of the first incidence of HNSCC in two groups, children aged 0–17 years and young adults aged 18–24 years.

Age at diagnosis was obtained from the DCR and the DPDB. Vital status and emigration were obtained from the CPR, information on prior diagnosis was obtained from the NPR. We did not include information on TNM classification due to missing data in the included registries.

Statistical analysis

Statistical analyses were performed in R statistics version 3.4.3(Stanford University, Stanford, CA, USA) [7]. The incidence rates were calculated as age-adjusted incidence rates (AAIRs) and crude incidence rates. The AAIRs were calculated per 100,000 using the direct method with the EpiTools package [8] and the Danish population between 0 and 24 years of age as reference and the WHO world standard population weighing [9]. The weight of the age-groups between 0 and 24 years were recalculated so the weights in total had the sum of 100. Age-specific incidences were calculated using the average population between 1980 and 2014 for the given age. The average annual percent change (AAPC) was calculated using Joinpoint trend analysis software v. 4.2.0.2, growth were assumed to be logarithmic with the formula $\ln(y) = xb$.

Survival was defined as time from diagnosis to death by any cause. Patients who were alive at the last date of follow-up were censored at this date. The date for the last follow-up was 31 December 2016. We used Cox regressions analyses to elucidate survival differences. P-values $< .05$ indicate statistical significance.

Results

We identified 32 patients diagnosed with HNSCC between the age of 0 and 24 years in the DCR and the DPDB from 1980 to 2014. Twenty-eight patients were registered in the DCR and 25 in DPDB, together 21 patients were registered in both the databases. Seven patients were therefore only registered in the DCR, whereas four patients only were registered in the DPDB. The overall median age at diagnosis was 19.5 years (range: 7–24 years), among children aged 0–17 ($n = 9$) the median age at diagnosis was 13 years (range: 7–17 years). The patients were primarily male (69%) and there was no difference in the distribution of gender between the age-groups (Table 1). The most common tumor location was the oral cavity, accounting for 43%, however, the distribution of location between age-groups differed significantly. Laryngeal carcinomas were the one that differed most between the age-groups as none were identified among children (aged 0–17 years), whereas six cases were observed among young adults (aged 18–24 years) (Table 1).

Incidence

The overall average AAIR per 100,000 was 0.052 and showed no significant change during the study period. The incidence of HNSCC among children was significantly lower compared to young adults (Table 1). HNSCC incidence increased with age from a total crude incidence rate of 0 per 100,000 among infants to 0.12 per 100,000 at the age of 24 years, with a peak of 0.28 at the age of 21 (AAPC: 76.0%, 95%CI:39.9;121.5) (Figure 1(A)).

There was no difference in the incidence rates based on gender or tumor location during the study period (Table 1).

Survival

The median follow-up from time of diagnosis was 16.6 years (range: 0.7–36.3 years). In total, nine deaths were registered, 3

Table 1. Baseline characteristics, incidence and risk of head and neck squamous cell carcinoma among patients aged 0–24 years in Denmark from 1980 to 2014, stratified on gender, tumor location and age-groups.

	Incidence						Survival		
	Cases (%)	0–17 years	18–24 years	*p*		*p*	Number of deaths	Hazard ratio (95%CI)	*p*
					Age-adjusted incidence rate				
Gender									
Male	22 (68.8)	5 (55.6)	17 (73.9)		0.034		5	Ref	
Female	10 (31.2)	4 (44.4)	6 (26.1)	.56[a]	0.018	.069[b]	4	2.22 (0.52–7.21)	.24
					Age-adjusted incidence rate				
Location									
Oral cavity	14 (43.8)	5 (55.6)	9 (39.1)		0.023		6	Ref	
Nasopharyngeal	10 (31.3)	2 (22.2)	8 (34.8)		0.014		2	0.37 (0.07–1.83)	.22
Laryngeal	6 (18.8)	0 (0)	6 (26.1)		0.0096		0	0 (0–infinity)	1
Other	2 (6.3)	2 (22.2)	0 (0)	.042[a]	0.0037		1	1.01 (0.12–8.387)	1
					Crude incidence rate				
Age at diagnosis									
0–17 years	9 (28.1)	–	–		0.02		3	Ref	
18–24 years	23 (71.9)	–	–		0.13	<.01[b]	6	0.69 (0.17–2.79)	.6

[a]*p* Value calculated with Chi square test.
[b]*p* Value calculated with *T*-test.

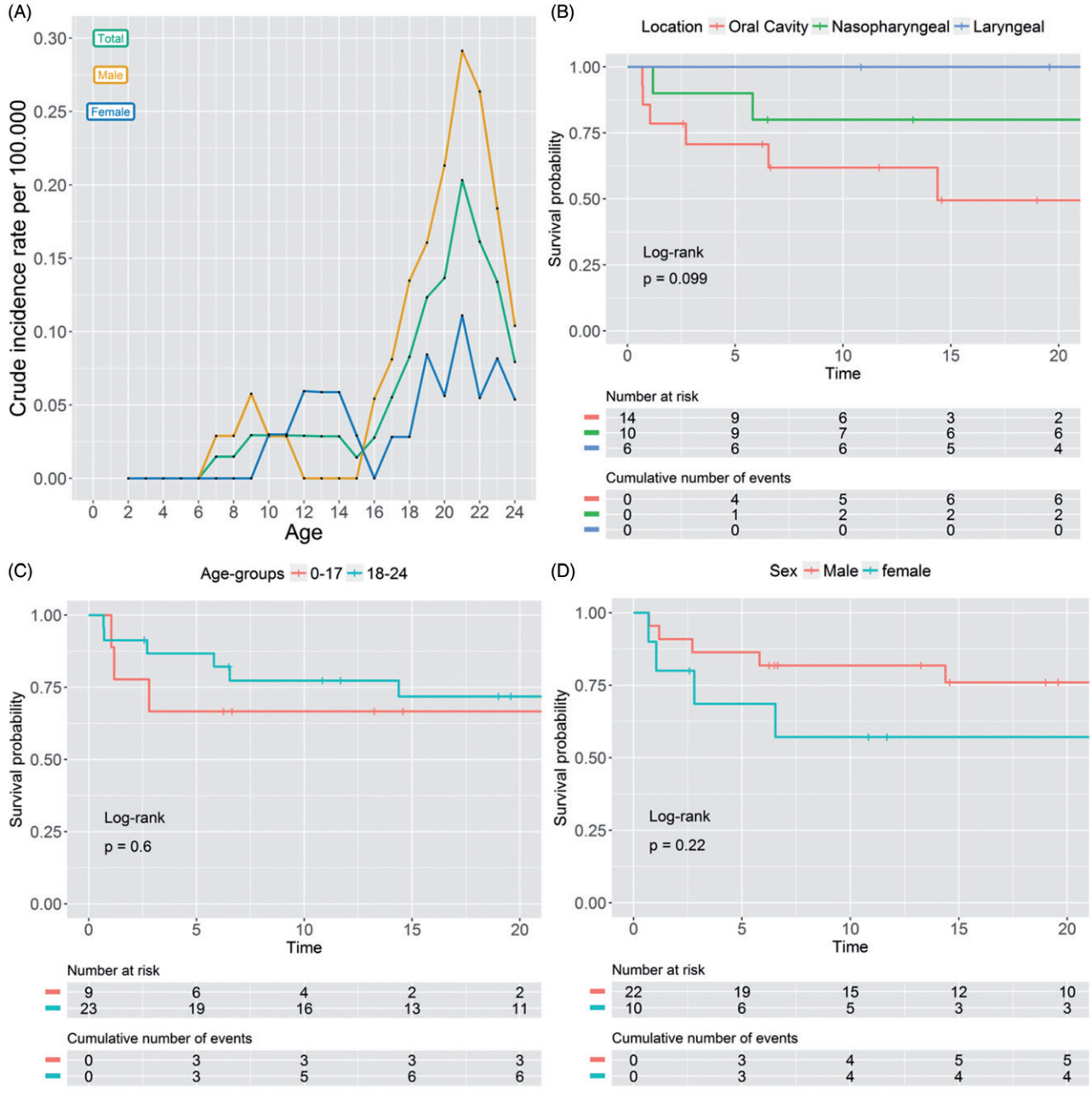

Figure 1. (A) Three-year rolling average of age-specific incidence. (B). Kaplan–Meier curve for location without the others group. (C) Kaplan–Meier curve for age-groups. (D) Kaplan–Meier curve for gender.

among children and 6 among young adults. The overall 5-year survival was 81%. For gender the 5-year survival was 86% for males and 70% for female (Figure 1(D)). For age-groups the 5-year survival was 67% for children and 87% for young adults (Figure 1(C)). The 5-year survival was highest among patients with Laryngeal cancers at 100% (Figure 1(B)) compared to 71% for oral cavity cancers (Figure 1(A)). There were no significant differences in the overall survival between genders, locations, or age-groups (Table 1) (Figure 1(B–D)).

Discussion

Similar to other reports, we found no increase in the incidence of HNSCC among children and young adults over time, however, reports of increasing incidence also exist [10–13].

The high amount of HNSCC located at the oral cavity **is** similar to other reports of HNSCC among children and young adults, however, the share of oral cavity cancers are considerably higher compared to the adult population [12,14,15]. A hypothesis for this finding is that the tongue and gingiva have a particularly high number of stem cells [14].

Almost a third of the cases were nasopharyngeal cancers, which differs from that nasopharyngeal cancers overall constitute 2.6% of head and neck cancers in Denmark[15]. In certain ethnic groups such as inhabitants of Southeast Asia or Alaskan Eskimo areas, the incidence is, however, much higher and has often been attributed to Epstein-Barr virus (EBV) infection [2,3,16]. Therefore, the etiology is often different for these patients, as EBV-genes such as Epstein-Barr virus nuclear protein (EBNA) and latent membrane protein (LMP) possibly are involved in the replication and cell growth [16]. For this reason we investigated whether the patients with nasopharyngeal cancer had residency in Greenland, where the citizens predominantly are of Eskimo ethnicity, however, this was only observed in one case.

The high survival in patients with laryngeal cancer has been demonstrated before [12]. Applicable to both pediatric and adults with laryngeal cancer is the association to better survival, if the cancer is located to the vocal chords as this often results in development of hoarseness with early diagnosis. Further the vocal cords have no lymph drainage, and the risk of metastases is therefore lower.

In an attempt to explain early onset, information on prior disease was obtained from the NPR, available from 21 patients. Of these, two had been diagnosed with Fanconis anemia. However, no relevant prior diagnosis was observed for the remaining 19 patients [4].

Four patients were only registered in the DPDB and not in the DCR, even though both registries are nationwide. As three of the patients had oral cavity tumors, this might be explained by dentists taking the biopsies who do not have the same procedure of registering to the DCR. The last patient was diagnosed with larynx cancer in 1983, which was before it was mandatory to report to the DCR.

Disclosure statement

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