


Incidence of head and neck cancer among first-generation immigrants and their children in Finland

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ABSTRACT

Introduction: Limited data exist regarding head and neck cancer (HNC) burden among immigrants who may have distinct characteristics, and hence different incidence rates from the general population. Variations in behavioral habits, cultural lifestyle, or diet may cause variations across different subgroups.

Methods: The whole immigrant population of Finnish residents born abroad, and their children were retrieved for the years 1970–2017. First-generation immigrants are defined as individuals born abroad, excluding their children (even if born abroad). The study comprised 0.5 million first-generation immigrants and 0.3 million children, contributing to 6 million and 5 million person-years of follow-up, respectively. Standardized incidence ratios (SIR) and excess absolute risk (EAR) per 100,000 person-years at risk were calculated to quantify the risk of HNC among immigrants relative to the general Finnish population.

Results: The overall risk of any HNC was not increased among first-generation male immigrants (SIR 1.00, 95% CI: 0.88–1.15), but significantly elevated for cancer of the pharynx (SIR 1.56, 95% CI: 1.22–1.95), and larynx (SIR 1.38, 95% CI: 1.02–1.83) and decreased for lip (SIR 0.38, 95% CI: 0.20–0.67). The increased risk of pharyngeal cancer was highest among male immigrants from Asia Pacific (SIR 4.21, 95% CI: 2.02–7.75). First-generation immigrant women had a significantly reduced risk of any HNC (SIR 0.45, 95% CI: 0.37–0.55), which remained even after stratification by site. We observed no increased risk of any HNC among the children of first-generation immigrants.

Conclusion: Healthcare professionals need to recognize the groups at higher HNC risk. Efforts to address the main etiological risk factors, such as smoking, are needed among the selected immigrant populations, that haven't yet reached similar decreasing trends, as in for example smoking, as the main population.

NOVELTY AND IMPACT

- Currently, globally, over 280 million people live outside their country of birth. Limited data exist regarding head and neck cancer (HNC) burden among immigrants who may have distinct characteristics and hence different incidence rates from the general population. Immigrant studies can provide novel data by shedding light on risk alterations and the pace of acculturation of different populations.

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Introduction

Despite the COVID-19 pandemic reshaping human flow patterns through the temporary closing of international borders in the last couple of years, growth in cross-border immigration has remained robust over the last two decades. Indeed, currently, globally, over 280 million people live outside their country of birth, which represents close to 4% of the world's population, up from 221 million in 2010 [1]. In 2021, about

440,400 Finnish residents were born abroad, representing diverse regions of origin: 14% from post-Soviet countries 11% from Estonia, 8% from Sweden, and 5% from Iraq. Foreign-born residents constituted 8% of the country's population overall (approximately 5.5 million), a relatively modest proportion when compared with other countries [2,3].

The majority of head and neck cancers (HNCs) are sporadic, attributable to known etiologic factors, such as tobacco and alcohol consumption, and are typically characterized by

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a robust correlation with chronic exposure to harmful habits [4,5]. Significant variations in cancer risk factors and prevalence across immigrant groups have been observed in several distinct countries, with some HNC types, such as nasopharyngeal cancer (NPC), being for example more common among Asian immigrants when compared with non-immigrants. The HNC burden across immigrants may differ due to variations in behavioral habits, cultural lifestyle, or diet which steer hazardous exposures, or even due to specific genetic profiles [6–11].

Besides political, humanitarian, and social perspectives, immigration also entails health implications [12]. Current overall cancer incidence rates reported for the whole population might camouflage the risk of cancer in immigrants as these populations may have distinct characteristics, and hence different incidence rates [10]. So far, no data regarding the HNC burden among immigrants in Finland have been published. Immigrant studies can provide novel data by shedding light on risk alterations and the pace of acculturation of different populations. We aim to describe the risk of HNC among immigrant groups in Finland from 1970 up to 2017 compared to the general population.

Material and methods

The study merges data from the Finnish Cancer Registry (FCR) and the Population Information System maintained by the Digital and Population Data Service Agency. Register linkage is carried out through unique personal identity numbers used in Finland. Foreign citizens are given a personal identity code upon registration into the PIN if staying in Finland legally.

Study population

The whole immigrant population is defined as all residents born abroad, and their children, 68% of whom were born in Finland. Furthermore, we defined as first-generation immigrants all individuals born abroad, except their children (born abroad or in Finland) whose group was analyzed separately. The Population Information System is a registry of all permanent Finnish residents with information on the date of birth and death, sex, birthplace, native language, address, and family linkages, allowing reliable identification of family members. Asylum seekers are not included in the registry as they do not have a permanent identification code (in Finland, by 2014, close to 11% of new arrivals were asylum seekers [13]). Follow-up for first-generation immigrants and their children begun at the date of immigration or January 1st, 1970, whichever the later, and ended either at the date of cancer diagnosis, date of death or emigration, or December 31st, 2017, whichever the latest. Subjects were excluded whenever the date of immigration was missing ($n = 5,798$, 0.7%).

Cancer data

In this study, HNCs were defined as malignancies diagnosed in the lip (ICD-O-3: C00.0–C00.9), oral cavity (C02.0–C06.9), salivary glands (C07.9–C08.9), pharynx (C01.9, C09.0–C14.8), nasal cavity and middle ear (C30.0, C30.1), paranasal sinuses (C31.0–C31.9), and larynx (C32.0–C32.9). The FCR includes all new primary cancers diagnosed in Finland since 1953 with complete follow-up data until death or emigration. However, our study included only cancers diagnosed between January 1st, 1970, and December 31st, 2017, and only the first primary cancer was taken into consideration in the analysis.

Statistical analyses

Two statistical quantities were calculated to describe the risk of HNC among first-generation immigrants and their children. Standardized incidence ratios (SIRs) were employed to quantify the risk of HNC relative to the general population. SIR is a ratio of observed to expected HNC cases in which the expected number of first cancers was calculated for the general population. The expected number of cases was calculated by multiplying the number of person-years in each age group by the corresponding average cancer incidence rates in the entire Finnish population during the follow-up period. The SIRs were stratified according to sex, geographical birth area, and age group (<35, 35–49, 50–64, 65–79, ≥80). Countries were grouped into eight geographical areas: Africa (excluding North Africa), Asia Pacific (including East and Southeast Asia, and countries in the Pacific region), Central Asia and Russia, Europe, Latin America and the Caribbean region, Middle East and North Africa, North America, and South Asia. The excess absolute risk (EAR) describes the difference in absolute risk of cancer between the immigrant population and the general population (observed cases – expected cases) per 100,000 person-years at risk (or PY). All analyses were performed using R software (The R Project for Statistical Computing) version 3.6.0 with Epi package version 2.38 and popEpi package version 0.4.7. Confidence intervals (CI) for SIRs were the exact Poisson CIs.

All analyzed results are anonymous, rendering the recognition of an individual study subject unfeasible. Moreover, for data privacy reasons, observed numbers and risk estimates are not shown, whenever less than five cancer cases were reported. Research permission for the study was granted by the Digital and Population Data Service Agency (VRK/3059/2018-2) and the National Institute for Health and Welfare in Finland (THL/1081/6.02.00/2018).

Results

The study comprised approximately 0.5 million first-generation immigrants and their 0.3 million children, contributing to 6 million and 5 million person-years of follow-up, respectively. Most first-generation immigrants (60% of men and 58% of women) were younger than 40 at the end of follow-up and nearly half were born in Europe (Table 1).

Table 1. Demographics of first-generation immigrants and their children in Finland during 1970–2017.

	Men		Women	
	Number	%	Number	%
First-generation immigrants	268,522	100	244,891	100
By country of birth				
Africa	20,375	8	14,780	6
Asia Pacific	20,423	8	31,319	13
Central Asia and Russia	37,676	14	54,335	22
Europe	128,276	48	103,907	42
Latin America and Caribbean	5267	2	4822	2
Middle East and North Africa	26,468	10	15,447	6
North America	11,681	4	9557	4
South Asia	17,679	7	10,390	4
Unknown	677	0	334	0
By age group at end of follow-up				
0–19	44,430	17	41,868	17
20–39	119,087	44	102,959	42
40–59	78,598	29	70,624	29
60–79	19,758	7	20,023	8
≥80	6639	2	9411	4
Unknown	10	0	6	0
Children of first-generation immigrants	159,929	100	152,152	100
By country of birth				
Africa	4671	3	4402	3
Asia Pacific	4924	3	4945	3
Central Asia and Russia	10,305	6	10,218	7
Europe	20,670	13	19,376	13
Latin America and Caribbean	755	0	688	0
Middle East and North Africa	6688	4	5990	4
North America	1531	1	1499	1
South Asia	2435	2	2290	2
Finland	107,950	67	102,744	68
By age group at end of follow-up				
0–19	108,774	68	103,970	68
20–39	41,542	26	39,312	26
40–59	7093	4	6444	4
60–79	2288	1	2154	1
≥80	232	0	272	0
Unknown	0	0	0	0

First-generation immigrants

The numbers of observed and expected cases and SIRs among the first-generation immigrant population stratified by site, country of birth, and age category are given in Table 2. Overall, 219 and 107 HNC cases were registered in the FCR among first-generation immigrant men and women, respectively, during the time frame of our study. In men, pharyngeal and laryngeal cases comprised 34% ($n=75$) and 22% ($n=48$) of all HNC cases. In women, the pharynx and oral cavity were the most frequently affected anatomical sites, comprising 22% ($n=24$) and 21% ($n=22$) of all HNC cases, respectively, followed by the salivary glands (20%, $n=21$).

Men

While we observed no risk difference in men for all HNC cases (SIR 1.00, 95% CI 0.88–1.15), differences were found by anatomical subsites (Table 2). Compared with the general male population, first-generation immigrant men had a significantly elevated standardized incidence of pharyngeal (SIR 1.56, 95% CI: 1.22–1.95) and laryngeal (SIR 1.38, 95% CI: 1.02–1.83) cancer corresponding to 0.9 and 0.4 excess cancers per 100,000 PY (or 26.8 and 13.3 excess cancers during the 47-year-period of our study). In contrast, we observed a significantly decreased SIR for lip cancer (SIR 0.38, 95% CI: 0.20–0.67 and EAR –0.6 per 100,000 PY). For other anatomical HNC subsites, the SIRs were not statistically significantly different between male immigrants and the general male population.

Table 2. Standardized incidence ratios (SIR) and excess burden of disease (EAR) per 100,000 PY for head and neck cancers among male and female first-generation immigrants in Finland during 1970–2017 and stratified by primary site, country of birth, and age category.

	Men						Women					
	PYRS	Obs.	Exp.	SIR	95% CI	EAR	PYRS	Obs.	Exp.	SIR	95% CI	EAR
All head and neck cancers	3,141,404	219	218	1.00	0.88–1.15	0	3,014,519	107	236.6	0.45	0.37–0.55	–4.3
By Site												
Lip	3,143,327	12	31.4	0.38	0.20–0.67	–0.6	3,015,892	<5	37.3			
Tongue	3,143,384	29	35.2	0.82	0.55–1.18	–0.2	3,015,707	20	37.3	0.54	0.33–0.83	–0.6
Salivary glands	3,143,382	16	22	0.73	0.42–1.18	–0.2	3,015,562	21	23.2	0.91	0.56–1.38	–0.1
Mouth	3,143,183	31	35.3	0.88	0.60–1.25	–0.1	3,015,710	22	38.6	0.57	0.36–0.86	–0.6
Pharynx	3,143,061	75	48.2	1.56	1.22–1.95	0.9	3,015,549	24	50.4	0.48	0.31–0.71	–0.9
Nose and sinuses	3,143,483	11	13.8	0.80	0.40–1.43	–0.1	3,015,791	10	14.8	0.67	0.32–1.24	–0.2
Larynx	3,142,913	48	34.7	1.38	1.02–1.83	0.4	3,015,842	6	38	0.16	0.06–0.34	–1.1
By country of birth												
Africa	210,002	8	11	0.73	0.31–1.43	–1.4	146,817	<5	5.1			
Asia Pacific	202,036	17	12.6	1.35	0.79–2.16	2.2	305,511	6	9.1	0.66	0.24–1.43	–1
Central Asia, Russia	478,039	48	85.2	0.56	0.42–0.75	–7.8	766,244	57	61.5	0.93	0.70–1.20	–0.6
Europe	1,660,073	112	128.3	0.87	0.71–1.05	–1	1,396,093	30	47.1	0.64	0.43–0.91	–1.2
Latin America, Caribbean	54,834	5	3.8	1.32	0.43–3.08	2.2	51,178	<5	2.6			
Middle East, North Africa	242,845	16	17.5	0.91	0.52–1.48	–0.6	129,041	<5	5.6			
North America	152,726	10	49.4	0.20	0.10–0.37	–25.8	138,600	<5	28.8			
South Asia	126,406	<5	6.94				74,667	<5	3			
By age group												
<35	1,772,185	10	303.4	0.03	0.02–0.06	–16.6	1,657,694	11	137.8	0.08	0.04–0.14	–7.6
35–49	838,945	59	148.3	0.40	0.30–0.51	–10.6	772,034	29	69	0.42	0.28–0.60	–5.2
50–64	335,904	98	59.9	1.64	1.33–2.00	11.3	347,461	34	31.2	1.09	0.76–1.52	0.8
65–79	133,857	42	23	1.83	1.32–2.47	14.2	156,841	21	12.4	1.70	1.05–2.60	5.5
≥80	60,513	10	10	1.00	0.48–1.84	0	80,491	12	6.3	1.90	0.98–3.33	7.1

Abbreviations: CI: confidence interval; EAR: excess absolute risk; Exp.: expected number; Obs.: observed number, PYR: person-years at risk; SIR: standardized incidence ratio.

Statistically significant ratios highlighted in bold.

Table 3. Standardized incidence ratios (SIR) and excess burden of disease (EAR) per 100,000 PY for head and neck cancers stratified by primary site among male and female first-generation immigrants from Central Asia and Russia, and Europe, in Finland during 1970–2017.

	Men						Women					
	PY	Obs.	Exp.	SIR	95% CI	EAR	PYRS	Obs.	Exp.	SIR	95% CI	EAR
Lip												
Central Asia and Russia	478,326	6	18.5	0.32	0.12–0.71	–2.6						
Tongue												
Central Asia and Russia							766,982	10	12.9	0.78	0.37–1.43	–0.4
Europe	1,661,190	17	18.6	0.91	0.53–1.46	–0.1	1,396,426	5	10.5	0.48	0.15–1.12	–0.4
Salivary glands												
Central Asia and Russia							766,892	11	8.2	1.35	0.67–2.41	0.4
Europe	1,661,215	7	10.2	0.68	0.28–1.41	–0.2	1,396,354	6	7.6	0.79	0.29–1.73	–0.1
Mouth												
Central Asia and Russia	478,271	9	10.7	0.84	0.39–1.60	–0.3	766,917	12	14.3	0.84	0.43–1.47	–0.3
Europe	1,661,031	19	18.3	1.04	0.63–1.62	0.000	1,396,470	6	9.8	0.61	0.23–1.34	–0.3
Pharynx (<i>p</i> =.003)												
Asia Pacific	202,088	10	3.5	2.83	1.35–5.20	3.2						
Central Asia and Russia	478,302	15	17.7	0.85	0.48–1.40	–0.6	766,875	10	10.8	0.93	0.44–1.71	–0.1
Europe	1,661,023	37	33.2	1.12	0.79–1.54	0.2	1,396,425	7	9.4	0.74	0.30–1.53	–0.2
Nose and sinuses												
Central Asia and Russia							766,985	6	4.8	1.26	0.46–2.75	0.2
Europe	1,661,212	8	7.2	1.12	0.48–2.20	0.1						
Larynx												
Central Asia and Russia	478,322	15	20.2	0.74	0.42–1.23	–1.1						
Europe	1,660,842	22	26.5	0.83	0.52–1.26	–0.3						
Middle East, North Africa	242,940	6	3.1	1.91	0.70–4.15	1.2						

Risk estimates are shown if at least five cases were observed.

Abbreviations: CI: confidence interval; EAR: excess absolute risk; Exp.: expected number; Obs.: observed number; PYR: person-years at risk; SIR: standardized incidence ratio.

Statistically significant ratios are highlighted in bold.

Among men, most HNC cases were observed among immigrants from Europe (112 cases, 51%) and Central Asia and Russia (48 cases, 22%) (Table 3). We observed a significantly decreased risk of HNC among immigrants from North America (SIR 0.20, 95% CI 0.10–0.37 and EAR –25.8 per 100,000 PY) and Central Asia and Russia (SIR 0.56, 95% CI 0.42–0.75 and EAR –7.8 per 100,000 PY). There were no statistically significant differences among immigrants from other areas compared to the general male population in Finland. However, stratification by anatomical site and country of birth revealed a significantly increased SIR of pharyngeal cancer in male immigrants from Asia Pacific (SIR 2.83, 95% CI: 1.35–5.20 and EAR 3.2 per 100,000 PY).

Elevated SIRs for HNC were observed in the age categories 65–79 (SIR 1.83, 95% CI: 1.32–2.47) and 50–64 (SIR 1.64, 95% CI: 1.33–2.00) (Table 2). After stratifying by the anatomical site (Table 4), the risk remained significantly elevated for cancer of the mouth (65–79 age category), pharynx (50–64 and 65–79), and larynx (50–64 and 65–79). Among 35–49-year-olds, the risk of oral cancer (SIR 0.22, 95% CI 0.07–0.52 and EAR –2.1 per 100,000 PY) and risk of laryngeal cancer (SIR 0.26, 95% CI: 0.12–0.49 and EAR –3 per 100,000 PY) were both significantly decreased.

Women

Compared with the general female population, first-generation immigrant women had a significantly reduced risk of any HNC (SIR 0.45, 95% CI: 0.37–0.55 and EAR –4.3 per 100,000 PY) (Table 2). After stratifying by anatomical subsite and country of origin, immigrant women did not have any significant increased risk of HNC compared to the general female population. Rather, the risk of HNC was reduced for all anatomical subsites, except for cancers of the salivary

glands and those of the nose and sinuses where no differences were observed. However, after age stratification, there was a significantly increased risk of HNC cancer among 65–79-year-old women (SIR 1.70, 95% CI: 1.05–2.60 and EAR 5.5 per 100,000 PY), and especially for pharyngeal cancer (SIR 3.45, 95% CI: 1.39–7.11 and EAR 3.2 per 100,000 PY) (Table 4).

Children of first-generation immigrants

The numbers of observed and expected cases and SIRs among the children of first-generation immigrants stratified by subsite, country of birth, and age category are given in Table 5. Overall, 28 and 22 HNCs were registered among men and women, respectively, in the FCR during 1970–2017. We observed no overall difference in the SIRs of HNC between the children of first-generation immigrants and the respective general population of Finland.

Discussion

The current study consists of the most up-to-date comprehensive assessment of HNC risk among first-generation immigrants and their children in Finland. Our findings suggest that first-generation immigrant women have, on average, a significantly reduced risk of HNC (SIR 0.45), when compared with the general female population of Finland. In contrast, among first-generation immigrant men, while the overall risk of HNC was not elevated, we observed significantly elevated SIRs in men aged 50–79 years. Additionally, we observed an increased risk of pharyngeal cancer (SIR 1.56), especially in men from Asia Pacific (SIR 2.83), when compared with the general male population of Finland. A suggestion for an

Table 4. Standardized incidence ratios (SIR) and excess burden of disease (EAR) per 100,000 PY for head and neck cancers stratified by primary site and age group (35–49, 50–64, and 65–79) among male and female first-generation immigrants in Finland during 1970–2017.

	Men						Women					
	PYRS	Obs.	Exp.	SIR	95% CI	EAR	PYRS	Obs.	Exp.	SIR	95% CI	EAR
Tongue												
35–49	839,414	13	18.53	0.70	0.37–1.20	–0.7						
50–64	336,754	10	7.49	1.33	0.64–2.45	0.7	347,768	8	6.6	1.21	0.52–2.39	0.4
65–79							157,112	6	2.4	2.48	0.91–5.39	2.3
Salivary glands												
35–49							772,266	8	8.7	0.92	0.40–1.81	–0.1
50–64	336,719	7	4.1	1.71	0.69–3.53	0.9						
Mouth												
35–49	839,390	5	22.6	0.22	0.07–0.52	–2.1	772,353	5	17.8	0.28	0.09–0.65	–1.7
50–64	336,631	13	9.1	1.43	0.76–2.44	1.2	347,800	5	8.1	0.62	0.20–1.44	–0.9
65–79	134,299	12	2.9	4.09	2.11–7.15	6.8	157,127	6	2.9	2.05	0.75–4.46	2
Pharynx												
35–49	839,358	20	36.6	0.55	0.33–0.84	–2	772,262	9	11.3	0.80	0.36–1.51	–0.3
50–64	336,599	35	15	2.34	1.63–3.25	5.9	347,729	7	5.3	1.33	0.53–2.74	0.5
65–79	134,257	15	4.9	3.06	1.71–5.05	7.5	157,078	7	2	3.45	1.39–7.11	3.2
Nose and sinuses												
35–49	839,451	6	7.4	0.81	0.30–1.75	–0.2						
Larynx												
35–49	839,353	9	34.6	0.26	0.12–0.49	–3						
50–64	336,503	26	14	1.86	1.21–2.72	3.6	347,811	5	1.8	2.84	0.92–6.62	0.9
65–79	134,227	10	6	1.66	0.80–3.06	3						

Risk estimates are shown if at least five cases were observed.

Abbreviations: CI: confidence interval; EAR: excess absolute risk; Exp.: expected number; Obs.: observed number; PYR: person-years at risk; SIR: standardized incidence ratio.

Statistically significant ratios are highlighted in bold.

Table 5. Standardized incidence ratios (SIR) and excess burden of disease (EAR) per 100,000 PY for head and neck cancers among children of first-generation immigrants in Finland during 1970–2017 and stratified by age category.

	Men						Women					
	PYRS	Obs.	Exp.	SIR	95% CI	EAR	PYRS	Obs.	Exp.	SIR	95% CI	EAR
All head and neck cancers	2,565,454	28	30.8	0.91	0.61–1.32	–0.001	2,417,910	22	29.5	0.75	0.47–1.13	–0.003
By age group												
<35	2,371,993	10	417.9	0.02	0.01–0.04	–17.2	2,237,651	7	198.2	0.04	0.01–0.07	–8.5
35–49	132,558	6	23.3	0.26	0.09–0.56	–0.3	120,051	5	10.4	0.48	0.16–1.12	–4.5
50–64	46,824	9	8.2	1.10	0.50–2.08	1.7	46,020	10	4.1	2.46	1.18–4.52	12.9
65–79	11,887	<5	2.2				117,812	<5	1.6			
≥80	2192	<5	0.40				2405	<5	0.3			

Abbreviations: CI: confidence interval; EAR: excess absolute risk; Exp.: expected number; Obs.: observed number; PYR: person-years at risk; SIR: standardized incidence ratio.

Statistically significant ratios highlighted in bold.

increased risk of laryngeal cancer was observed among men from the Middle East and North Africa, however not statistically significant.

Our results are in accordance with the high prevalence of pharyngeal and laryngeal cancers in these regions. According to the Global Cancer Observatory database (www.gco.iarc.fr), the Asia Pacific region has the highest incidence rates for pharyngeal cancer worldwide. Indeed, the vast majority of countries have incidence rates ranging from 4.5 (Japan) to 12.7 (Vietnam). For laryngeal cancer, North African and Middle Eastern countries, except Saudi Arabia (ASR 1.2) and Oman (ASR 1.6), have high incidence rates of laryngeal cancer (ASR > 3). One may thus argue that the elevated rates observed in our study for pharyngeal and laryngeal cancer among specific immigrant groups are reflective of the incidence rates of their respective native countries. Supportive of our results, in Ontario Canada, a study conducted by Noel et al. [6], reported that Chinese and South Asian ethnic groups experience higher HNC incidence [hazard ratio (HR) 1.49, 95% CI: 1.36–1.64; and 1.29, 95% CI: 1.14–1.45,

respectively] relative to non-Chinese and non-South Asian individuals, after adjustment for age, sex, rurality, deprivation, and comorbidity burden. Of note, the corresponding incidence rates for Finnish men are ASR 3.9 and ASR 1.7, for pharyngeal and laryngeal cancers, respectively.

It appears that select immigrant groups retain similar incidence rates as seen among natives of their region of origin. Cultural transmission of exogenous exposures may, at least partially, explain the increased risk among these populations. An increased risk of nasopharyngeal cancer (NPC) has been previously described among Asian and North African immigrants in Sweden [14], France [15], and Israel [9]. Although the etiology of NPC is multifactorial [16], Epstein–Barr virus (EBV), along with genetic predisposition, is regarded as playing a predominant role in the etiology of NPC through its oncogenic effect [17,18]. Regarding HPV, its association with oropharyngeal cancer is well documented, and some evidence, albeit weak, also implies a possible link with laryngeal cancer [19]. A meta-analysis revealed a prevalence of 49% (95% CI: 35–64%) of any type of HPV and 35% (95% CI: 26–

45%) of high-risk HPV in men [20]. Conversely, in the Middle East, Southeast Asia, and East Asia, reported prevalence rates of HPV do not exceed 10% [21]. The prevalence differences parallel the high incidence of pharyngeal cancer among European immigrants in our study.

Still, the most well-established risk factors for pharyngeal and laryngeal cancers remain tobacco smoking and alcohol consumption, which are the main etiological culprits of HNC in Europe. Likewise, within the Middle East, rates of smoking are high, with around 48% of men reporting current or past smoking of cigarettes or waterpipes [22]. In Algeria, a study conducted by Kariche et al. [23] described a low rate of HPV among laryngeal cancer patients, whereas tobacco and alcohol were reported for around 40% of cases. In Europe, smoking prevalence ranges from 20% to 42% in men and 15% to 34% in women [24]. In Finland, smoking prevalence among men declined from 51% to 23% between 1972 and 2017. Correspondingly, in women, it increased from 11% to 23% between 1972 and 2002, continuing with a decrease to 16% in 2017 [25]. Other environmental factors related to pharyngeal cancer to account for include betel-quid and areca-nut chewing, which are widespread in the Asia-Pacific region with prevalence rates in men up to 83% (Salomon Islands) [26]. Convincing evidence exists linking betel-quid and areca nuts chewing to oral and oropharyngeal cancer [27,28]. Additionally, diets high in nitrosamine-rich salted fish and meats, which are common in Southeast Asia, have been associated with NPC [29,30]. All in all, these lifestyle habits may contribute to the excess risk of pharyngeal and laryngeal cancers observed among immigrants from the Asia Pacific and the Middle East and North Africa regions, respectively.

Earlier research has shown that the initial difference in the incidence of cancer among immigrant groups changes over 1 or 2 generations converging to the incidence rate of the new host population [31–34]. Similarly, despite the rarity of HNC cases in this population, our study suggests that the children of first-generation immigrants experience similar HNC rates that the native population in Finland, as we observed no significant differences between these groups. This could imply that environmental factors play the most prominent role in disease onset, and the contribution of inherited genetic mutations is overall negligible. The main challenge to future immigrant studies would be to identify the exogenous factors that cause the changes cancer incidence upon migration.

A particular issue to be considered when interpreting our results relates to how representative immigrants are of the population of their respective countries of birth. The ‘healthy migrant effect’ refers to the concept of immigrants being on average healthier than the comparable population of their country of birth and host country upon arrival [35,36]. Studies have described a gradual receding of this initial health advantage leading over time to an equal or even worse health status than the native population’s [36–39] prompting some authors [40,41] to postulate that this vanishment may result from barriers to healthcare. The reduced risk of HNCs in foreign-born women in our study could

reflect a ‘healthy migrant effect’, whereby positive self-selection may have yielded a female immigrant population that is, on average, healthier than their native-born counterparts, and thus at lower risk of HNC. However, this effect was not observed among men. Smoking among male immigrants could be more prevalent than in corresponding Finnish men, and also conversely less prevalent in female immigrants when compared with their Finnish counterparts. In Finland and other Nordic countries, universal access to health care is provided to all residents. Still, it is possible that attendance to primary and preventive care is lower among immigrants which may gradually elevate cancer risk over time. For instance, decreased usage of healthcare services and lower participation rates in cervical screening was recently reported among immigrants when compared with native Finns [42,43].

Another potential fallacy relates to the salmon bias hypothesis, whereby migrants may return to their country of origin at retirement or end of life [44]. If the salmon bias hypothesis would also hold for our study, our risk estimates could be even higher. However, controversy and ambiguity still exist around the subject [45,46], and to the best of our knowledge, no convincing evidence of an existing effect on cancer incidence or mortality exists.

The foremost strength of the present study is the comprehensive and high-level population-based data from the FCR. Quality-assessment studies have demonstrated high coverage (96% of solid tumors) and accuracy of diagnosis [47]. Additionally, the long longitudinal follow-up provides us with the opportunity to assess alterations in cancer risk across immigrant generations, which may subsequently convey clues about the pace of acculturation of immigrant populations. However, inherent limitations in this study need to be addressed. The immigrant population in Finland is predominantly young, with around 60% of immigrants being younger than 40 years at the end of follow-up, which subsequently implies that late-onset cancers will not yet emerge in our study among this patient population. Thus, risk estimates could be higher with longer follow-up, since most HNCs occur in patients aged 50 or over [48]. Indeed, the increased risk of oral, pharyngeal, laryngeal cancer in the older male patient population is supportive of this conjecture. Further, while our study incorporated information on the birth country, residency duration, and age, we did not have access to other important determinants of cancer risk such as socioeconomic class and education level. Another caveat relates to multiple testing: with over 100 comparisons conducted, chance findings cannot be ruled out. Lastly, unfortunately, detailed analyses could not be performed for the children of first-generation immigrants due to the limited number of cancer cases.

Conclusions

Our results suggest that female first-generation immigrants have a reduced risk of HNC compared with the female general population. Although only female immigrants from Europe were noted to have a significantly lower occurrence

of HNC, there appeared to be a comparable incidence decrease also among immigrants from other regions, even if not statistically significant, suggestive of a 'healthy immigrant effect'. First-generation immigrant men had an overall HNC incidence rate similar to the incidence reported for the general male population of Finland. However, we observed higher risks for selected infection- and tobacco-related cancers, i.e., pharynx and larynx, especially in the 50–64 and 65–79-year age groups. This could affect diagnostics in patients presenting with symptoms and enhance early detection of the disease. Efforts to address the main etiological risk factors are needed among the selected immigrant populations, that haven't yet reached similar decreasing trends, as in for example smoking, as the main population [25,49]. Moreover, future studies on the access to and use of health services among immigrants are warranted.

Author contributions

The study was designed by Rayan Mroueh, Elli Hirvonen, Janne Pitkänieniemi, Nea Malila, Jaana Hagström, Anni Virtanen, and Antti Mäkitie. Rayan Mroueh and Elli Hirvonen performed all statistical analyses. The manuscript was devised by Rayan Mroueh, Elli Hirvonen, Janne Pitkänieniemi, Nea Malila, Jaana Hagström, Anni Virtanen, and Antti Mäkitie. All authors contributed to the revision of the manuscript and have approved the final version.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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Data availability statement

Data sharing not available due to privacy/ethical restrictions.

References

- [1] United Nations Department of Economic and Social Affairs, Population Division. International migration 2020 highlights. NY (USA): United Nations; 2020 [cited 2022 Oct 19]. Available from: <https://www.un.org/en/desa/international-migration-2020-highlights>
- [2] Statistics Finland. Persons born abroad. 2021 [cited 2022 Oct 19]. Available from: https://www.stat.fi/tup/maahanmuutto/maahanmuuttajat-vaestossa/ulkomailla-syntyneet_en.html
- [3] Pew Research Center. International migrants by country. 2019 [cited 2022 Oct 19]. Available from: <https://www.pewresearch.org/global/interactives/international-migrants-by-country/>
- [4] Hashibe M, Brennan P, Benhamou S, et al. Alcohol drinking in never users of tobacco, cigarette smoking in never drinkers, and the risk of head and neck cancer: pooled analysis in the international head and neck cancer epidemiology consortium. *J Natl Cancer Inst.* 2007;99(10):777–789.
- [5] Gandini S, Botteri E, Iodice S, et al. Tobacco smoking and cancer: a meta-analysis. *Int J Cancer.* 2008;122(1):155–164.
- [6] Noel CW, Sutradhar R, Li Q, et al. Association of immigration status and Chinese and South Asian ethnicity with incidence of head and neck cancer. *JAMA Otolaryngol Head Neck Surg.* 2020; 146(12):1125–1135.
- [7] Saraswat N, Prabhu N, Pillay R, et al. Oral cancer risk behaviours of Indian immigrants in Australia: a qualitative study. *Aust N Z J Public Health.* 2022;46(1):87–94.
- [8] Mousavi SM, Sundquist J, Hemminki K. Nasopharyngeal and hypopharyngeal carcinoma risk among immigrants in Sweden. *Int J Cancer.* 2010;127(12):2888–2892.
- [9] Rottenberg Y, Levine H, Keinan-Boker L, et al. Risk of nasopharyngeal carcinoma penetrates across immigrant generations: a migrant cohort study of 2.3 million Jewish Israeli adolescents. *Int J Cancer.* 2017;140(5):1060–1067.
- [10] Walker PF, Settgest AM, DeSilva MB. Cancer screening in refugees and immigrants: a global perspective. *Am J Trop Med Hyg.* 2022; 106(6):1600.
- [11] Gingerich MA, Smith JD, Michmerhuizen NL, et al. Comprehensive review of genetic factors contributing to head and neck squamous cell carcinoma development in low-risk, non-traditional patients. *Head Neck.* 2018;40(5):943–954.
- [12] Martinez O, Wu E, Sandfort T, et al. Evaluating the impact of immigration policies on health status among undocumented immigrants: a systematic review. *J Immigr Minor Health.* 2015; 17(3):970.
- [13] Statistics Finland. Yli puolet Suomen ulkomaalaistaustaisista muuttanut maahan perhesyistä. 2015 [cited 2022 Oct 19]. Available from: https://www.stat.fi/tup/maahanmuutto/art_2015-10-15_001.html
- [14] Mousavi SM, Hemminki K. Cancer incidence, trends, and survival among immigrants to Sweden: a population-based study. *Eur J Cancer Prev.* 2015;24(Suppl 1):S1–S63.
- [15] Bouchardy C, Parkin DM, Wanner P, et al. Cancer mortality among North African migrants in France. *Int J Epidemiol.* 1996;25(1):5–13.
- [16] El-Naggar AK, Chan JKC, Rubin Grandis J, et al. WHO classification of head and neck tumours. 4th ed. Lyon (France): International Agency for Research on Cancer; 2017.
- [17] Young LS, Dawson CW. Epstein-Barr virus and nasopharyngeal carcinoma. *Chin J Cancer.* 2014;33(12):581–590.
- [18] Tsao SW, Tsang CM, Lo KW. Epstein-Barr virus infection and nasopharyngeal carcinoma. *Phil Trans R Soc B.* 2017;372(1732): 20160270.
- [19] Hobbs CGL, Sterne JAC, Bailey M, et al. Human papillomavirus and head and neck cancer: a systematic review and meta-analysis. *Clin Otolaryngol.* 2006;31(4):259–266.
- [20] Rodríguez-Álvarez MI, Gómez-Urquiza JL, Husein-El Ahmed H, et al. Prevalence and risk factors of human papillomavirus in male patients: a systematic review and meta-analysis. *IJERPH.* 2018;15(10):2210.
- [21] Bukhari N, Joseph JP, Hussain SS, et al. Prevalence of human papilloma virus Sub genotypes following head and neck squamous cell carcinomas in Asian continent, a systematic review article. *Asian Pac J Cancer Prev.* 2019;20(11):3269–3277.
- [22] Khattab A, Javaid A, Iraqi G, et al. Smoking habits in the Middle East and North Africa: results of the BREATHE study. *Respir Med.* 2012;106(Suppl 2):S16–S24.
- [23] Kariche N, Hortal MT, Benyahia S, et al. Comparative assessment of HPV, alcohol and tobacco etiological fractions in Algerian patients with laryngeal squamous cell carcinoma. *Infect Agent Cancer.* 2018;13:8.
- [24] Gallus S, Lugo A, Liu X, et al. Who smokes in Europe? Data from 12 European countries in the TackSHS survey (2017–2018). *J Epidemiol.* 2021;31(2):151.

- [25] Vartiainen VA, Jousilahti P, Laatikainen T, et al. Contribution of smoking change to 45-year trend in prevalence of chronic bronchitis in Finland. *Scand J Public Health*. 2022;140349482211043.
- [26] Gunjal S, Pateel DGS, Yang YH, et al. An overview on betel quid and areca nut practice and control in selected Asian and South East Asian countries. *Subst Use Misuse*. 2020;55(9):1533–1544.
- [27] Guha N, Warnakulasuriya S, Vlaanderen J, et al. Betel quid chewing and the risk of oral and oropharyngeal cancers: a meta-analysis with implications for cancer control. *Int J Cancer*. 2014;135(6):1433–1443.
- [28] Sharan RN, Mehrotra R, Choudhury Y, et al. Association of betel nut with carcinogenesis: revisit with a clinical perspective. *PLOS One*. 2012;7(8):e42759.
- [29] Yu MC, Ho JH, Lai SH, et al. Cantonese-style salted fish as a cause of nasopharyngeal carcinoma: report of a case-control study in Hong Kong. *Cancer Res*. 1986;46(2):956–961.
- [30] Feng H, Zhou Y, Wang L, et al. Consumption of processed food and risk of nasopharyngeal carcinoma: a systematic review and meta-analysis. *Transl Cancer Res*. 2022;11(4):872–879.
- [31] Myrup C, Westergaard T, Schnack T, et al. Testicular cancer risk in first- and second-generation immigrants to Denmark. *J Natl Cancer Inst*. 2008;100(1):41–47.
- [32] Stirbu I, Kunst AE, Vleems FA, et al. Cancer mortality rates among first and second generation migrants in the Netherlands: convergence toward the rates of the native dutch population. *Int J Cancer*. 2006;119(11):2665–2672.
- [33] Hemminki K, Li X. Cancer risks in second-generation immigrants to Sweden. *Int J Cancer*. 2002;99(2):229–237.
- [34] Nasser K, Moulton LH. Patterns of death in the first and second generation immigrants from selected Middle Eastern countries in California. *J Immigr Minor Health*. 2011;13(2):361–370.
- [35] McDonald JT, Kennedy S. Insights into the “healthy immigrant effect”: health status and health service use of immigrants to Canada. *Soc Sci Med*. 2004;59(8):1613–1627.
- [36] Fennelly K. The “healthy migrant” effect. *Minn Med*. 2007;90(3):51–53.
- [37] Antecol H, Bedard K. Unhealthy assimilation: why do immigrants converge to American health status levels? *Demography*. 2006;43(2):337–360.
- [38] Lara M, Gamboa C, Kahramanian MI, et al. Acculturation and latino health in the United States: a review of the literature and its sociopolitical context. *Annu Rev Public Health*. 2005;26(1):367–397.
- [39] Giuntella O, Kone ZL, Ruiz I, et al. Reason for immigration and immigrants’ health. *Public Health*. 2018;158:102–109.
- [40] Starfield B, Shi L, Macinko J. Contribution of primary care to health systems and health. *Milbank Q*. 2005;83(3):457–502.
- [41] Newbold B. Health status and health care of immigrants in Canada: a longitudinal analysis. *J Health Serv Res Policy*. 2005;10(2):77–83A.
- [42] Idehen EE, Koponen P, Härkänen T, et al. Disparities in cervical screening participation: a comparison of russian, Somali and kurkish immigrants with the general finnish population. *Int J Equity Health*. 2018;17(1):56.
- [43] Mölsä M, Tiilikainen M, Punamäki RL. Usage of healthcare services and preference for mental healthcare among older Somali immigrants in Finland. *Ethn Health*. 2019;24(6):607–622.
- [44] Turra CM, Elo IT. The impact of salmon bias on the hispanic mortality advantage: new evidence from social security data. *Popul Res Policy Rev*. 2008;27(5):515–530.
- [45] Lu Y, Qin L. Healthy migrant and salmon bias hypotheses: a study of health and internal migration in China. *Soc Sci Med*. 2014;102:41–48.
- [46] Andersson G, Drefahl S. Long-distance migration and mortality in Sweden: testing the salmon bias and healthy migrant hypotheses. *Popul Space Place*. 2017;23(4):e2032.
- [47] Leinonen MK, Miettinen J, Heikkinen S, et al. Quality measures of the population-based finnish cancer registry indicate sound data quality for solid malignant tumours. *Eur J Cancer*. 2017;77:31–39.
- [48] Bajpai S, Zhang N, Lott DG. Tracking changes in age distribution of head and neck cancer in the United States from 1975 to 2016. *Clin Otolaryngol*. 2021;46(6):1205–1212.
- [49] Salama E, Niemelä S, Suvisaari J, et al. The prevalence of substance use among russian, Somali and kurkish migrants in Finland: a population-based study. *BMC Public Health*. 2018;18(1):651.