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Title: Heterogeneity in head and neck Cancer incidence among black populations from Africa, the Caribbean and the USA: Analysis of Cancer registry data by the AC3

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Abstract

Background: Africa and the Caribbean are projected to have greater increases in Head and neck cancer (HNC) burden in comparison to North America and Europe. The knowledge needed to reinforce prevention in these populations is limited. We compared for the first time, incidence rates of HNC in black populations from African, the Caribbean and USA.

Methods: Annual age-standardised incidence rates (IR) and 95% confidence intervals (95%CI) per 100,000 were calculated for 2013-2015 using population-based cancer registry data for 14,911 HNC cases from the Caribbean (Barbados, Guadeloupe, Trinidad & Tobago, N=443), Africa (Kenya, Nigeria, N=772) and the United States (SEER, Florida, N=13,696). We compared rates by sub-sites and sex among countries using data from registries with high quality and completeness.

Results: In 2013-2015, compared to other countries, HNC incidence was highest among SEER states (IR: 18.2, 95%CI = 17.6 -18.8) among men, and highest in Kenya (IR: 7.5, 95%CI = 6.3-8.7) among women. Nasopharyngeal cancer IR was higher in Kenya for men (IR: 3.1, 95%CI = 2.5-3.7) and women (IR: 1.5, 95%CI = 1.0-1.9). Female oral cavity cancer was also notably higher in Kenya (IR=3.9, 95%CI = 3.0-4.9). Blacks from SEER states had higher incidence of laryngeal cancer (IR: 5.5, 95%CI = 5.2-5.8) compared to other countries and even Florida blacks (IR: 4.4, 95%CI = 3.9-5.0).

Conclusion: We found heterogeneity in IRs for HNC among these diverse black populations; notably, Kenya which had distinctively higher incidence of nasopharyngeal and female oral cavity cancer. Targeted etiological investigations are warranted considering the low consumption of tobacco and alcohol among Kenyan women. Overall, our findings suggest that behavioral and environmental factors are more important determinants of HNC than race.

Keywords: Head and neck cancer; Incidence; blacks; tobacco smoking, alcohol drinking, HPV; Caribbean; Africa; USA; Population-based cancer registry

Abbreviation

AC3: African Caribbean Cancer Consortium

CI: confidence interval

EBV: Epstein-Barr virus

HBCR: hospital-based cancer registry

HNC: head and neck cancer

HPV: human papillomavirus

ICD: International Classification of Disease

IR: incidence rate

PBCR: population based cancer registry

SEER: Surveillance, Epidemiology, and End Results

WHO: World Health Organization

Introduction

Head and neck cancer (HNC) is the 6th most common cancer in the world ¹ but the annual incidence rates (IR) vary substantially across geographical regions ²⁻⁴. Tobacco smoking and alcohol drinking are the major risk factors of oral cavity, hypopharyngeal and laryngeal cancer ⁵⁻⁷; while, the human papillomavirus (HPV) is a prominent risk factor for oropharyngeal cancer and has been linked to other HNC sites ⁸⁻¹¹. In addition, other viral factors such as Epstein-Barr virus (EBV) and HIV are associated with HNC risk notably, nasopharyngeal cancer ¹²⁻¹⁴, in areas where these viruses are more prevalent ^{10,12,15}.

Incidence rates of HNC are particularly high in North America and Europe; and they are increasing rapidly in developing countries ^{4,16}. In 2016, the age standardized incidence rates for HNC per 100,000 men and women for cancer of the oral cavity, pharynx and larynx (HNC) were 11.2 for Europe and 10.1 for North America; whereas, rates were lowest in Latin American and the Caribbean, and in Africa (7.0 and 4.8 respectively) ¹⁷. Despite lower incidence rates of HNC in the Caribbean and African populations, the mortality remains high. Most Caribbean and African countries are developing countries and are particularly vulnerable to poor cancer outcomes due to lack of access to care, late presentation and few resources for treatment ^{18,19}. Therefore, it is important to produce relevant information on the epidemiological trends to inform cancer prevention in these countries before the HNC incidence transitions to that of the developed world. Few studies have investigated HNC incidence among blacks living in various geographical regions (USA, Caribbean and Africa), who differ substantially in terms of genetics, culture and environmental exposures ²⁰⁻²². In addition, global surveillance data for most Caribbean countries are based on estimates from neighboring countries ¹⁷. Comparative analyses among populations may provide clues on risk factors which can be further investigated in aetiological studies to enhance prevention strategies in these regions.

The aim of our study was to compare for the first time, incidence rates and characteristics of HNC in black populations of Africa the Caribbean and the USA, using data from population-based cancer registries (PBCR).

Methods

African Caribbean Cancer Consortium

The African Caribbean Cancer Consortium (AC3) is a network of researchers collaborating in areas of cancer risk and outcomes among populations of African descent ²³. The AC3 is part of the Epidemiology and Genomics Research Program consortia of the National Cancer Institute (NCI), which is composed of 3 connected networks of investigators in the United States, Africa, and the Caribbean region. The AC3 has more than 120 members and is a resource for education, training, and research on cancer etiology, outcomes and various components of cancer control ²³⁻²⁵. Capacity building for cancer registration in these developing regions is a priority area for the AC3.

Study population, and data collection and quality

For the purpose of this study, we used data from cancer registries, from the Caribbean (Barbados, Grenada, Guadeloupe, Jamaica, Trinidad & Tobago), Africa (Ghana, Kenya, Nigeria) and the United States (Surveillance, Epidemiology, and End Results (SEER) program ²⁶ and Florida). Data from the SEER Registries includes cases reported to the following registries: Alaska Native Tumor Registry; Connecticut Registry; Metropolitan Detroit Cancer Surveillance System (MDCSS); Georgia Center for Cancer Statistics (Atlanta, Greater Georgia, and Rural Georgia); Greater Bay Area Cancer Registry (San Francisco-Oakland and San Jose-Monterey); Cancer Registry of Greater California; Hawaii Tumor Registry; Cancer Data Registry of Idaho; Iowa Cancer Registry; Kentucky Cancer Registry; Los Angeles County Cancer Surveillance Program; Louisiana Tumor Registry; Massachusetts Cancer Registry; New Mexico Tumor Registry; New Jersey State Cancer

Registry; New York State Cancer Registry; Seattle-Puget Sound Registry; and Utah Cancer Registry. Cases from the United States were blacks (Non-Hispanic).

Race in SEER and in Florida is obtained largely from self-report. It is very complete and seen as highly reliable, and is part of medical /pathology records. The other populations in this study are majority of African descent.

We singled out Florida because: 1) The large proportion of Afro-Caribbeans in this state make up as much as 25% of all non-Hispanic Blacks; this is unlike SEER where their proportion is largely negligible. 2) Florida is the only state analyzed that is not part of SEER, so it is a different source of data.

Table 1 outlines the data collection methods, quality control procedures and practices for each individual registry. Cases were defined using codes from the World Health Organization (WHO) International Classification of Disease (ICD-O3, and ICD-10). Cases included in this analysis were patients with solid invasive tumors of the head and neck (HNC) of any histological type and included: oral cavity, (C00.3-C00.9, C02.0-C02.3, C02.8-C02.9, C03.0, C03.1, C03.9, C04.0, C04.1, C04.8-C05.0, C06.0-C06.2, C06.8, C06.9); oropharynx, (C01.9, C02.4, C05.1, C05.2, C09.0, C09.1, C09.8, C09.9, C10.0-C10.4, C10.8, C10.9); hypopharynx, (C12.9, C13.0-13.2, C13.8, C13.9); larynx, (C32.0-C32.3, C32.8, C32.9); nasopharynx, (C11.0-C11.3, C11.8, C11.9); salivary gland, (C8.0, C8.1, C8.8, C8.9); as well as sinonasal cavity, (C30.0, C30.1, C31.0, C31.9, C31.9). Histological type was defined using ICD-O3 coding and categorized as either squamous cell carcinoma (SCC) (codes: 8050-8076, 8078, 8083, 8084, and 8094), non-SCC which includes transitional cell carcinoma (codes: 8120-8131) adenocarcinoma (codes: 8140-8149, 8160-8162, 8190-8221, 8260-8337, 8350-8551, 8570-8576, 8940-894), sarcoma (codes: 8680-8713, 8800-8921, 8990-899) and other specific carcinomas (codes: 8030-8046, 8150-8157, 8170-8180, 8230-

8255, 8340-8347, 8560-8562, 8580-867). A final category included cases with unspecified histology (codes: 8000-8005 and 8010). The sociodemographic characteristics included were sex and age (<40 years, 40–54 years, 55-64 and 65 years and older).

Data for 19,936 cases were received from the participating cancer registries and after excluding cancer sub-sites that did not fit our inclusion criteria (N =786), we identified overall 19,150 HNC malignancies (Figure 1). We excluded 25 cases due to missing information on age, sex and diagnosis date resulting in 19,125 cases included in this analysis. We used this initial sample of 19,125 to describe the characteristics of cases. We further constituted a subsample of 15,984 cases comprising only PBCRs with data between 2010 and 2015 to calculate incidence rates. All datasets were de-identified and ethics approvals for this present study was obtained from the AC3 research ethics review committee and the Fox Chase Cancer Center Institutional Review Board (protocol number: 11-875).

Statistical analysis

We described the distribution of HNC cases, for all cases, by age and histological type by sex using all available years of data from registries (hospital-based cancer registry (HBCR) and PBCRs). The proportions of cases by subsite and sex were calculated for cases diagnosed between 2010 and 2015 in countries with PBCRs. Chi-square test was used to test significant differences between proportions by geographic region (Africa, Caribbean and USA) and within geographic regions (i.e., between countries and for USA, between SEER and Florida). p-values <0.05 were considered statistically significant. The average annual sex-specific age-standardised (1960 Segi world standard) IR and 95% confidence intervals (95% CI) per 100,000 were calculated for the time periods 2010-2012 and 2013-2015 using only data from PBCRs with rigorous quality control measures (mortality-to-incidence ratio, capture-recapture etc.)²⁷ (Table 1). We compared rates by

subsites, sex and period of diagnosis among countries with registries that satisfied our quality criteria. Significant differences between rates were noted when confidence intervals did not overlap^{28,29}. Sex-and age-specific population data were used as denominators to calculate IR. We derived these population data from the American Community Survey for the USA, and national censuses from the respective countries. Statistical analysis was performed using SAS 9.4 software (SAS Institute).

Results

Description of case characteristics

This study includes a total of 19,125 HNC cases from all participating registries. Table 2 describes the characteristics of HNC cases by country. There was a higher proportion of male cases in comparison to female cases (males: 13,470 (71.2%) and females: 5,453 (28.8%) diagnosed from (1977-2017). The male:female (M:F) ratio of cases was highest for the Caribbean countries (average ratio = 3.58), intermediate for the USA (average ratio = 2.50) and lowest for the Africa countries (average ratio = 1.81). For both males and females in the Caribbean and the USA, most cases were diagnosed at ages 55 years and older, contrary to Africa where the majority of cases were diagnosed under 55 years old ($p < 0.0001$). While SCC was the most common histological type, the proportion of SCC was considerably lower among African countries when compared to the cases from the Caribbean and the USA ($p < 0.0001$). SCC proportions across all countries were greater among men except for Grenada (M: 50.0%, F: 58.3%), Jamaica (M: 97.0%, F: 96.8%) and Kenya (M: 48.7%, F: 49.2%) where proportions were similar for males and females. The proportion of non-SCC were consistently higher among women regardless of the country. Supplementary table 1 shows the frequency ranking of subsites in each country.

Of our PBCRs with high quality and uniform data, 15,984 cases were diagnosed between 2010 and 2015 from the Caribbean (Barbados, Guadeloupe, Trinidad & Tobago, N=819), Africa (Kenya,

Nigeria, N=1,469) and the United States (SEER, Florida, N=13,696). Figure 2 displays the percentage of HNC cases by subsite and sex from PBCRs between 2010 and 2015. Among all cases, tobacco/alcohol-related sub-sites pooled together, (oral cavity, laryngeal and hypopharyngeal cancers), were the most common subsites among males (59%) and females (42%). Oropharyngeal cancer (HPV-related) represented 30% of male and 17% of female HNC cases. Nasopharyngeal cancer (EBV-related) occurred among 9% of males and 8% of females.

Age-standardised incidence rates

We only considered registries with satisfactory completeness and quality assessment for the comparison of IRs. IRs for all PBCRs are presented in supplementary tables 3-4. Table 3 shows annual sex-specific age-standardized IRs and 95% CI per 100,000. Between 2013 and 2015, males had higher annual IRs for each subsite in most countries compared to females. Overall, IRs for all HNC subsites combined were highest in blacks from SEER states (IR: 18.2, 95% CI = 17.6-18.8) and Guadeloupe (IR: 17.8, 95% CI = 14.9-20.7), followed by Barbados (IR: 12.0, 95% CI = 9.2-14.7) and Kenya (IR: 12.5 95% CI = 11.0-13.9). Among women, Kenya had the highest IR for HNC (IR: 7.5, 95% CI = 6.3-8.7), followed by SEER (IR: 5.8, 95% CI = 5.5-6.1) and Florida (IR: 4.4, 95% CI = 3.9-4.9). IRs were consistently greater among the age group above 55 years old than below 55 (supplementary table 2).

Among males, Kenya had the highest IRs for oral cavity cancer (IR=3.6, 95% CI = 2.8-4.5), followed by Guadeloupe, blacks from Florida and SEER states. Among females, Kenya had the highest IR for oral cavity cancer (IR=3.9, 95% CI = 3.0-4.9) which was similar to their male counterparts.

The IR of oropharyngeal cancer among men was highest in Guadeloupe (IR=6.5, 95% CI = 4.7-8.2) and among blacks from SEER states (IR=5.1, 95% CI = 4.8-5.4), followed by Barbados and Florida.

Florida blacks had significantly lower rates than those from SEER states. Oropharyngeal cancer IR was consistently low in African countries for both sexes.

Laryngeal cancer IR for black men from SEER states was the highest (IR: 5.5, 95%CI = 5.2-5.8) and was also significantly higher among Florida males (IR: 4.4, 95%CI = 3.9-5.0). Nigeria had a significantly lower incidence for male laryngeal cancer compared to the other countries (IR: 0.6, 95%CI = 0.3-0.8).

In all countries, hypopharyngeal cancer IRs were low except for males in Guadeloupe where the IR was almost 2-fold higher than other countries (IR: 2.1, 95%CI = 1.1-3.0). Nasopharyngeal cancer IRs were consistently low among males and females except for Kenya where the IR was significantly higher than that of other countries for both males (IR: 3.1, 95%CI = 2.5-3.7) and females (IR: 1.5, 95%CI = 1.0-1.9). Incidence rates remained mostly similar between the periods 2010-2012 and 2013-2015 (supplementary tables 3-4).

We compared our data with registry data and case series from other African countries (Supplementary table 5). Kenya recorded the highest rates for nasopharyngeal cancer among men (3.2) but the rate among women was slightly lower than Uganda (1.5 vs. 1.9). Female oral cavity cancer was highest in Namibia (4.0) and Kenya (3.9). However male oral cavity cancer in Kenya (3.6) was lower than Namibia (10.2) and the islands of Seychelles (14.3) and Reunion (8.9). Seychelles also had notably higher rates for laryngeal (9.8) and pharyngeal cancer (16.3) (oropharynx, hypopharynx and unspecified pharynx) among men. Salivary gland cancer remained low across African countries. Highest rates for salivary gland cancer were recorded in Namibia (2.7) for men and in Malawi (1.7) for women.

Discussion

We compared for the first time, incidence rates of HNC from black populations of African descent from various countries using PBCRs. Also, our use of observed incidence data from certain Caribbean countries is a novel approach in HNC epidemiology.

We showed significant heterogeneity among these populations concerning characteristics of the cases and IRs. IRs were notably higher for cancer of the oral cavity in women from Kenya. Furthermore, we showed significantly lower rates for oropharyngeal and laryngeal cancer in Florida blacks compared to those from SEER states. Our study support evidence from other similar studies on cancer mortality^{30,31} which suggest that behavioral and environmental factors are the major determinants of HNC incidence rather than race.

Our findings were mostly consistent with existing risk factor data. High IRs for oropharyngeal cancer coincided with countries where HPV prevalence is high and vice-versa^{7-9,32}. Similarly, risk factor prevalence correlated well with IRs for oral cavity, larynx, hypopharynx and nasopharynx³³⁻³⁸.

However, certain IRs could not be fully explained by the prevalence of known risk factors³³. Regular tobacco smoking and hazardous alcohol drinking are very uncommon among Kenyan women^{36,37}; yet the IR for female oral cavity cancer was particularly high. Hazardous alcohol drinking refers to the quantity and pattern of alcohol consumption that places persons at risk of adverse health effects. Certain suspected oral cancer risk factors specific to Eastern Africa may however explain these high rates in women. Unlike tobacco smoking, smokeless tobacco use (snuffed or chewed) in Kenya is similar in men (4%) and women (3%)³⁹, Khat chewing is also practiced in Kenya (54% M, 20% F) and most of East Africa^{40,41}. A recent study in Kenya reported a fairly elevated prevalence of poor oral health indicators among hospital-based controls⁴².

Notably, ≥ 4 missing teeth (31%), teeth brushing with arak tree stick (28%) and oral leukoplakia (26%). Further work is warranted to identify factors attributable to this high oral cancer incidence among Kenyan women.

Concerning the laryngeal cancer disparities among blacks from SEER states and Florida, Florida has a high proportion of recent Afro-Caribbean immigrants, who tend to have a lower prevalence of tobacco use compared to US-born Blacks⁴³. Afro-Caribbean immigrants also tend to have lower rate for cancer than other residents of the USA^{44,45}.

Few African countries participated in this registry analysis. Data availability and quality needed for these grouped studies are common challenges in these low resource settings. Nevertheless, comparison with reports revealed similar IRs between what we observed for Kenya and Nigeria, and other countries in Eastern and Western Africa respectively⁴⁶⁻⁴⁹. Indeed, Eastern and Southern African countries had consistently higher IRs for cancers of the oral cavity, larynx, oropharynx and hypopharynx. Whereas, rates for Western and Central Africa were low across all subsites.

We also compared our estimates to global data. IRs for male HNC in our study was highest in SEER blacks and Guadeloupe, and were greater than the world IR¹⁷. Among females, Kenya and SEER blacks had the highest incidence, and were greater than the world IR. Furthermore, IRs for HNC calculated from the observed data for Caribbean and African countries did not coincide to estimates from the GLOBOCAN models¹⁷. Our observed registry data therefore adds new and complementary information to global estimates. Overall, the distribution by age, sex and histology of all HNC sites together were concordant with previous reports on countries around the world^{4,16}.

While our PBCRs adhere to international standards, we acknowledge that our study possesses limitations. Firstly, selection bias is probable for certain countries. The data presented for Jamaica,

Kenya and Ghana are from only one region each (Kingston/St.Andrew, Nairobi and Kumasi respectively) and may not represent entirely those countries. These are however, some of the biggest and diverse areas in these countries and could be considered as an approximation of cases from the rest of the country. In the case of Jamaica, the vast majority of all HNC cases are diagnosed in Kingston/St. Andrew due to the concentration of specialized physicians to diagnose and treat HNC in that area. Some of our cancer registries may have difficulties in capturing the entirety of cancer cases. One such example is Grenada, an island nation that has a HBCR and includes data from the single general hospital and pathology laboratory on the island ²¹. Previous work has shown inconsistent mortality data with the incidence reported by their hospital-based registry; suggesting that it cannot be considered to cover the entire Grenadian population ²². Thus, we only considered registries with satisfactory completeness and quality assessment for the comparison of IRs. IRs for all PBCRs are presented in supplementary tables 3-4. Secondly, registration practices were sometimes different between countries which could hinder our potential for future grouped studies. Therefore, we cannot exclude the possibility of misclassification of tumors. However, we combined oral cavity and oropharyngeal cancer cases to minimize this issue. Furthermore, the main finding of higher rates for Kenyan women still held when oral cavity and oropharynx were combined. Histology was unspecified for more than 30% for all African countries and two Caribbean countries (Trinidad & Tobago and Grenada). Cancers of the pharynx (not otherwise specified) were not included in our analyses and may underestimate the IR for HNC. The proportion of these cancers was small for each country; thus, the impact on our estimates are minimal. Data for HPV is not available in the cancer registries' data. Hispanic blacks were most probably underrepresented for the USA due to self-identification, and may bias our results. Florida is particularly concerned given the high proportion black Hispanics (Mostly from Cuba, Puerto Rico and the Dominican Republic). This bias is thought to be non-differential since the misclassification occurs in both cases and the

population at-risk. Thirdly, we had difficulties demonstrating significant differences with Caribbean countries because of lack of precision due partially to their inherently small populations. Finally, data were not always uniform; e.g. certain anatomical sites (larynx, salivary gland and sinonasal cavity) were not provided by all countries. We could not assess adequately temporal trends in incidence across countries due to heterogeneity in the years of available data.

On one hand, our paper highlights persistent problems faced by cancer registries in LMICs. Details on tumours in medical files are often limited and have repercussions on data quality downstream. We strongly recommend the development of more robust data capture systems in African and Caribbean countries for higher quality epidemiological research.

On the other hand, we presented new data on understudied populations using observed data from cancer registries rather than estimates based on data from neighboring countries. This is a strength as it contributes new knowledge about HNC incidence among global populations for which surveillance data have been limited^{17,50}. Our study brings further insight to these populations, and will help us learn more about HNC epidemiology among other populations of African descent.

Conclusion

We compared incidence rates of HNC among black populations of African descent from different countries for the first time. We showed heterogeneity in HNC epidemiology between-and-among regions. Kenya had considerably higher incidence for nasopharyngeal and female oral cavity cancer. In the USA, we highlighted significantly lower incidence of laryngeal cancer in blacks from Florida compared to those from SEER states. While further work is warranted on Kenya and the subgroups of US-blacks, our findings provided several clues for cancer prevention notably in Kenya where we suspect risk factors apart from tobacco and alcohol for female oral cavity cancer.

Ethics approval

All participating registries possess the necessary local regulatory authorisations to collect data from cancer patients. This present study was approved by the African Caribbean Cancer Consortium ethics committee and the Fox Chase Cancer Center Institutional Review Board (protocol number: 11-875)

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Data availability statement

The data that support the findings of this study are not available due to institutional restrictions

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Table 1: Details of cancer registries' data sources, quality control procedures and coding system.

Country (by Region)	Cancer Registry Name	Cancer Registry Type	Year Established	Cancer notifiable disease (Y/N)	Data sources (Y/N)						Completeness quality assessments (Y/N)			Coding system		
					All public and private hospitals and clinics	Medical labs	Pathology labs	Death certificates	Radiotherapy and oncology services	Follow-up for vital status	MIR	Capture-recapture	Other	ENCR	NAACR	IARC
<i>Africa</i>																
Ghana (Kumasi)	Kumasi Cancer Registry	PBCR	2012	No	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	No	No	Yes
Kenya (Nairobi)	Nairobi Cancer Registry	PBCR	2001	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes
Nigeria	Abuja Cancer Registry	PBCR	HBCR 2006 became PBCR 2009	No	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	No	No	Yes
	Adamawa Cancer Registry	PBCR	2017	No	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	No	No	Yes
	Calabar Cancer Registry	PBCR	HBCR 1979 became PBCR 2005	No	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	No	No	Yes
	Ekiti Cancer Registry	PBCR	2014	No	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	No	No	Yes
	Enugu Cancer Registry	PBCR	HBCR 1988 became PBCR 2012	No	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	No	No	Yes
	Sokoto Cancer Registry	PBCR	2013	No	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	No	No	Yes
	Uyo Cancer Registry	PBCR	HBCR 2009 became PBCR 2017	No	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	No	No	Yes
<i>Caribbean</i>																
Barbados	Barbados National Registry	PBCR	2008	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes
Grenada	Grenada General Hospital Head and Neck Cancer Data	HBCR	1991	No	Yes, but not 100% complete	Yes	Yes	No	Yes, but limited	No	No	No	No	No	No	Yes
Guadeloupe	Guadeloupe Cancer Registry	PBCR	2008	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Jamaica	Jamaica Cancer Registry	PBCR	1958	No	Yes	Yes	Yes	Yes	Yes	No	No	Yes	No	Yes	No	Yes
Trinidad and Tobago	Elizabeth Quamina Cancer Registry	PBCR	1994	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	No	Yes
<i>USA</i>																
USA	National Cancer Institute Surveillance, Epidemiology and End Results Program (SEER 21 ^a)	PBCR	1972	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No
Florida	Florida Cancer Data System (FCDS)	PBCR	1981	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No

Abbreviations: HBCR, hospital-based cancer registry; IARC, International Agency for Research on Cancer; MIR, mortality-to-incidence ratio; ENCR, European Network of Cancer registries; NAACR, North American Association of Central Cancer Registries; PBCR, population-based cancer registry

^a Data from the SEER 21 Registries includes cases reported to the following registries: Alaska Native Tumor Registry; Connecticut Registry; Metropolitan Detroit Cancer Surveillance System (MDCSS); Georgia Center for Cancer Statistics (Atlanta, Greater Georgia, and Rural Georgia); Greater Bay Area Cancer Registry (San Francisco-Oakland and San Jose-Monterey); Cancer Registry of Greater California; Hawaii Tumor Registry; Cancer Data Registry of Idaho; Iowa Cancer Registry; Kentucky Cancer Registry; Los Angeles County Cancer Surveillance Program; Louisiana Tumor Registry; Massachusetts Cancer Registry; New Mexico Tumor Registry; New Jersey State Cancer Registry; New York State Cancer Registry; Seattle-Puget Sound Registry; and Utah Cancer Registry.

Table 2: Description of characteristics of included HNC cases by country ($n = 19,125$)

	Caribbean					Africa			USA	
	Barbados	Grenada	Guadeloupe	Jamaica	Trinidad	Ghana	Kenya	Nigeria [‡]	SEER-21	Florida
Men	97 (81.5)	104 (81.3)	465 (82.2)	315 (71.6)	1082 (78.1)	58 (57.4)	1305 (66.8)	435 (59.2)	8173 (70.3)	1488 (71.7)
<i>Age</i>										
<40	4 (4.1)	4 (3.8)	7 (1.5)	9 (2.9)	42 (3.9)	12 (20.7)	337 (25.8)	152 (34.9)	281 (3.4)	65 (4.4)
40-54	28 (28.9)	29 (27.9)	119 (25.6)	64 (20.3)	267 (24.7)	17 (29.3)	402 (30.8)	142 (32.6)	1794 (21.9)	327 (22.0)
55-64	37 (38.1)	33 (31.7)	150 (32.2)	100 (31.7)	316 (29.2)	15 (25.9)	305 (23.4)	64 (14.7)	3025 (37.0)	532 (35.8)
65+	28 (28.9)	38 (36.5)	189 (40.6)	142 (45.1)	457 (42.2)	14 (24.1)	261 (20.0)	77 (17.7)	3073 (37.6)	564 (37.9)
<i>Diagnosis year</i>										
1977-2009	24 (24.7)	98 (94.2)	115 (24.7)	284 (90.2)	792 (73.2)	NA	705 (54.0)	56 (12.9)	NA	NA
2010-2012	NA	6 (5.8)	140 (30.1)	31 (9.8)	157 (14.5)	4 (6.9)	303 (23.4)	154 (35.4)	3995 (48.9)	694 (46.6)
2013-2015	73 (75.3)	NA	149 (32.0)	NA	133 (12.3)	24 (41.4)	297 (22.8)	185 (42.5)	4178 (51.1)	794 (53.4)
2016-2017	NA	NA	61 (13.1)	NA	NA	30 (51.7)	NA	40 (9.2)	NA	NA
<i>Histology</i>										
SCC	80 (82.5)	52 (50.0)	418 (89.9)	306 (97.0)	666 (61.6)	33 (56.9)	636 (48.7)	157 (36.1)	7146 (87.4)	1221 (82.1)
Non-SCC	10 (10.3)	12 (11.5)	37 (8.0)	6 (2.0)	82 (7.6)	3 (5.2)	335 (25.7)	97 (22.3)	781 (9.6)	187 (12.6)
Unspecified/Missing [†]	7 (7.2)	40 (38.5)	10 (2.1)	3 (1.0)	334 (30.9)	22 (37.9)	334 (25.5)	181 (41.6)	246 (3.0)	80 (5.4)
Women	22 (18.5)	24 (18.8)	101 (17.8)	125 (28.4)	304 (21.9)	43 (42.6)	649 (33.2)	300 (40.8)	3449 (29.7)	586 (28.3)
<i>Age</i>										
<40	2 (9.1)	2 (8.3)	8 (7.9)	8 (6.4)	38 (12.5)	9 (20.9)	198 (30.5)	116 (38.7)	228 (6.2)	49 (8.4)
40-54	5 (22.7)	2 (8.3)	24 (23.8)	19 (15.2)	88 (28.9)	18 (41.9)	193 (29.7)	79 (26.3)	873 (24.2)	156 (26.6)
55-64	5 (22.7)	8 (33.3)	23 (22.8)	21 (16.8)	67 (22)	6 (14)	119 (18.3)	55 (18.3)	1086 (32.2)	171 (29.2)
65+	10 (45.5)	12 (50)	46 (45.5)	77 (61.6)	111 (36.5)	10 (23.3)	139 (21.4)	50 (16.7)	1262 (37.4)	210 (35.8)
<i>Diagnosis year</i>										
1977-2009	6 (27.3)	22 (91.7)	25 (24.8)	116 (92.8)	216 (71.1)	NA	350 (53.9)	32 (10.7)	NA	NA
2010-2012	NA	2 (8.3)	37 (36.6)	9 (7.2)	42 (13.8)	4 (9.3)	141 (21.7)	99 (33.0)	1680 (48.7)	293 (50.0)
2013-2017	16 (72.7)	0 (0.0)	26 (25.7)	NA	46 (15.1)	26 (60.5)	158 (24.3)	132 (44.0)	1769 (51.3)	293 (50.0)
2016-2017	NA	NA	13 (12.9)	NA	NA	13 (30.2)	NA	37 (12.3)	NA	NA
<i>Histology</i>										
SCC	13 (59.1)	14 (58.3)	71 (70.3)	121 (96.8)	165 (54.3)	15 (34.9)	319 (49.2)	77 (25.7)	2433 (70.5)	371 (63.3)
Non-SCC	6 (27.3)	5 (20.8)	28 (27.7)	4 (3.2)	48 (15.8)	13 (30.2)	169 (26.0)	108 (36.0)	874 (25.3)	185 (31.6)
Unspecified/Missing [†]	3 (13.6)	5 (20.8)	2 (2.0)	0 (0.0)	91 (29.9)	15 (34.9)	161 (24.8)	115 (38.3)	142 (4.1)	80 (5.1)

[†]: ICD-O Codes for unspecified tumor type 8000, 8001, 8002, 8003, 8004, 8005, 8010

‡: Contributing registries for Nigeria were Abuja, Adamawa, Calabar, Ekiti, Enugu, Sokoto, Uyo
Trinidad: Trinidad & Tobago, NA: Not applicable, no cases provided for analysis
SEER and Florida blacks

Table 3: Age-standardised (world) IR of HNC from 2013-2015 by subsite and sex using PBCR data

	HNC	Oral cavity	Oropharynx	Oral cavity & oropharynx	Nasopharynx	Larynx	Hypopharynx	Salivary gland	Sinonasal cavity
	IR (95%CI)	IR (95%CI)	IR (95%CI)	IR (95%CI)	IR (95%CI)	IR (95%CI)	IR (95%CI)	IR (95%CI)	IR (95%CI)
Men									
<i>Caribbean</i>									
Barbados	12.0 (9.2-14.7)	1.4 (0.5-2.2)	4.2 (2.6-5.8)	5.6 (3.8-7.4)	1.5 (0.5-2.6)	2.6 (1.3-3.8)	0.6 (0.0-1.2)	0.5 (0.0-1.1)	1.2 (0.2-2.2)
Guadeloupe	17.8 (14.9-20.7)	3.2 (2.1-4.4)	6.5 (4.7-8.2)	9.7 (7.6-11.8)	0.7 (0.1-1.2)	4.0 (2.7-5.3)	2.1 (1.1-3.0)	0.9 (0.2-1.5)	0.5 (0.0-1.1)
Trinidad	5.5 (4.6-6.4)	1.2 (0.8-1.6)	0.9 (0.5-1.3)	2.1 (1.5-2.7)	0.6 (0.3-0.8)	2.2 (1.6-2.8)	0.2 (0.0-0.3)	0.5 (0.2-0.7)	NA
<i>Africa</i>									
Kenya	12.5 (11.0-13.9)	3.6 (2.8-4.5)	1.1 (0.6-1.6)	4.7 (3.8-5.7)	3.1 (2.5-3.7)	3.2 (2.4-4.1)	0.5 (0.2-0.8)	0.3 (0.1-0.4)	0.6 (0.3-0.9)
Nigeria†	3.6 (3.0-4.1)	0.6 (0.4-0.8)	0.5 (0.3-0.7)	1.1 (0.8-1.4)	1.3 (1.0-1.6)	0.6 (0.3-0.8)	0.1 (0.0-0.2)	0.3 (0.2-0.5)	0.2 (0.1-0.3)
<i>USA</i>									
Florida	14.5 (13.5-15.5)	2.6 (2.2-3.0)	4.2 (3.7-4.8)	6.8 (6.1-7.5)	0.7 (0.5-1.0)	4.4 (3.9-5.0)	1.1 (0.9-1.4)	0.9 (0.6-1.1)	0.6 (0.4-0.8)
SEER	18.2 (17.6-18.8)	2.5 (2.3-3.1)	5.1 (4.8-5.4)	7.6 (7.3-7.9)	1.0 (0.9-1.2)	5.5 (5.2-5.8)	1.1 (0.9-1.2)	1.0 (0.9-1.1)	0.7 (0.6-0.8)
Women									
<i>Caribbean</i>									
Barbados	2.3 (1.2-3.4)	0.4 (0.0-0.9)	0.2 (0.0-0.5)	0.6 (0.1-1.2)	0.3 (0.0-0.7)	0.2 (0.0-0.5)	0.3 (0.0-0.8)	0.3 (0.0-0.8)	0.5 (0.0-1.0)
Guadeloupe	2.5 (1.6-3.5)	0.8 (0.3-1.4)	0.6 (0.1-1.1)	1.4 (0.4-2.1)	0.2 (0.0-0.5)	0.3 (0.0-0.6)	0.1 (0.0-0.3)	0.3 (0.0-0.7)	0.2 (0.0-0.4)
Trinidad	1.8 (1.3-2.4)	0.8 (0.4-1.1)	0.1 (0-0.2)	0.8 (0.5-1.2)	0.4 (0.2-0.7)	0.2 (0.0-0.4)	0.1 (0.0-0.2)	0.2 (0.0-0.4)	NA
<i>Africa</i>									
Kenya	7.5 (6.3-8.7)	3.9 (3.0-4.9)	0.3 (0.1-0.6)	4.3 (3.3-5.2)	1.5 (1.0-1.9)	0.3 (0.0-0.6)	0.4 (0.1-0.7)	0.5 (0.3-0.8)	0.5 (0.2-0.8)
Nigeria†	3.1 (2.6-3.7)	0.8 (0.5-1.1)	0.1 (0.0-0.3)	0.9 (0.6-1.3)	0.9 (0.6-1.2)	0.2 (0.0-0.3)	0.1 (0.0-0.2)	0.6 (0.4-0.9)	0.4 (0.2-0.6)
<i>USA</i>									
Florida	4.4 (3.9-4.9)	1.2 (0.9-1.4)	0.9 (0.7-1.1)	2.3 (1.9-2.7)	0.4 (0.2-0.5)	0.6 (0.4-0.8)	0.2 (0.1-0.3)	0.8 (0.6-1.1)	0.4 (0.2-0.5)
SEER	5.8 (5.5-6.1)	1.3 (1.2-1.5)	1.2 (1.1-1.3)	2.5 (2.3-2.7)	0.4 (0.3-0.5)	1.1 (1.0-1.2)	0.2 (0.2-0.3)	1.0 (0.8-1.1)	0.4 (0.4-0.5)

IR: Incidence rate per 100 000 persons, and CI: Confidence intervals

14,911 Cases analysed from the Caribbean ($n=443$), Africa ($n=772$) and the USA ($n=13,969$)

†: Contributing registries for Nigeria were Abuja, Adamawa, Calabar, Ekiti, Enugu, Sokoto, Uyo

NA: Not applicable, no cases provided for analysis

Trinidad: Trinidad & Tobago

SEER and Florida blacks

Figures

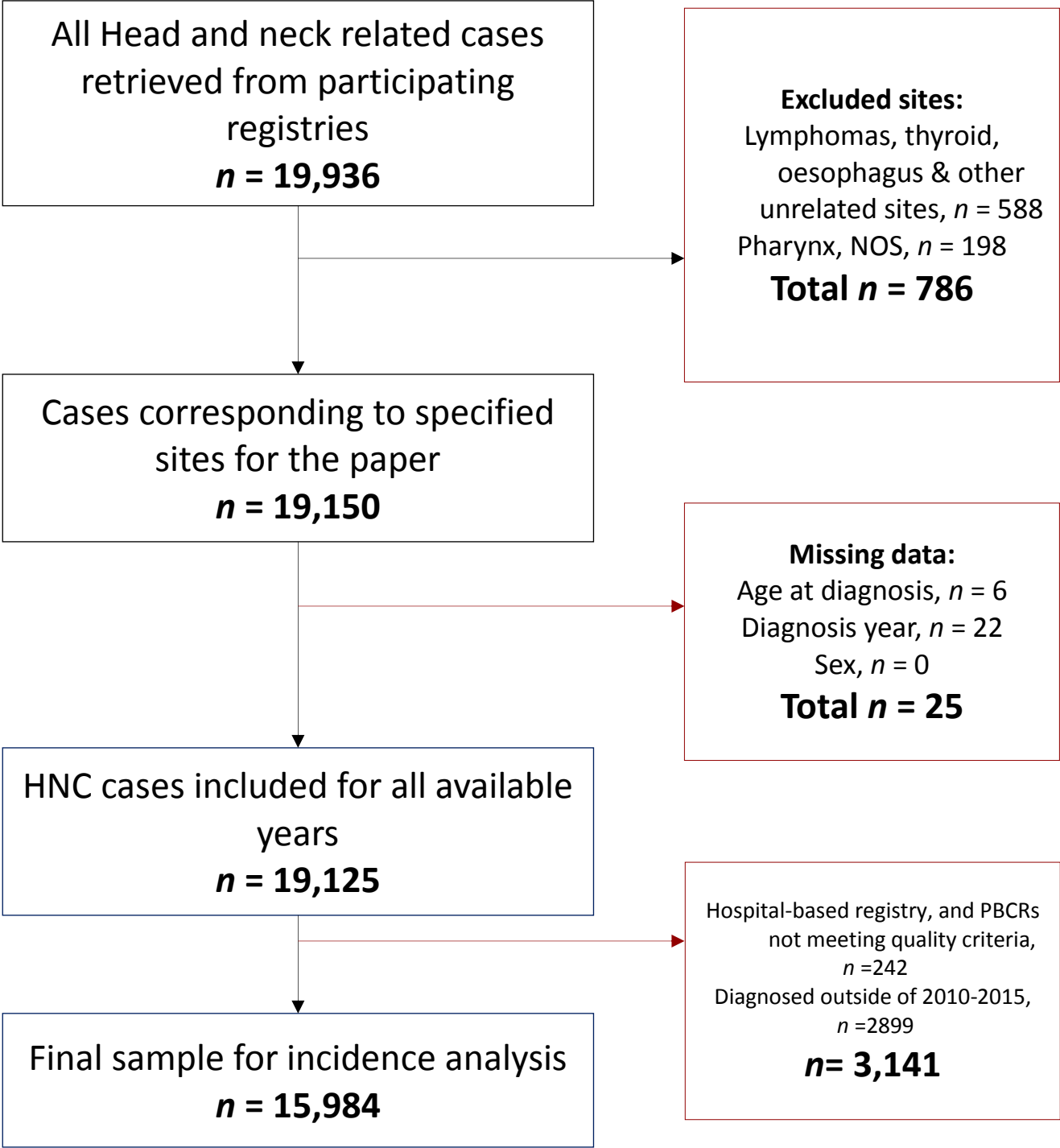


Figure 1: Flow chart of cases included for the study

NB: the frequency of missing individual characteristics are not cumulative (total ≠ 25)

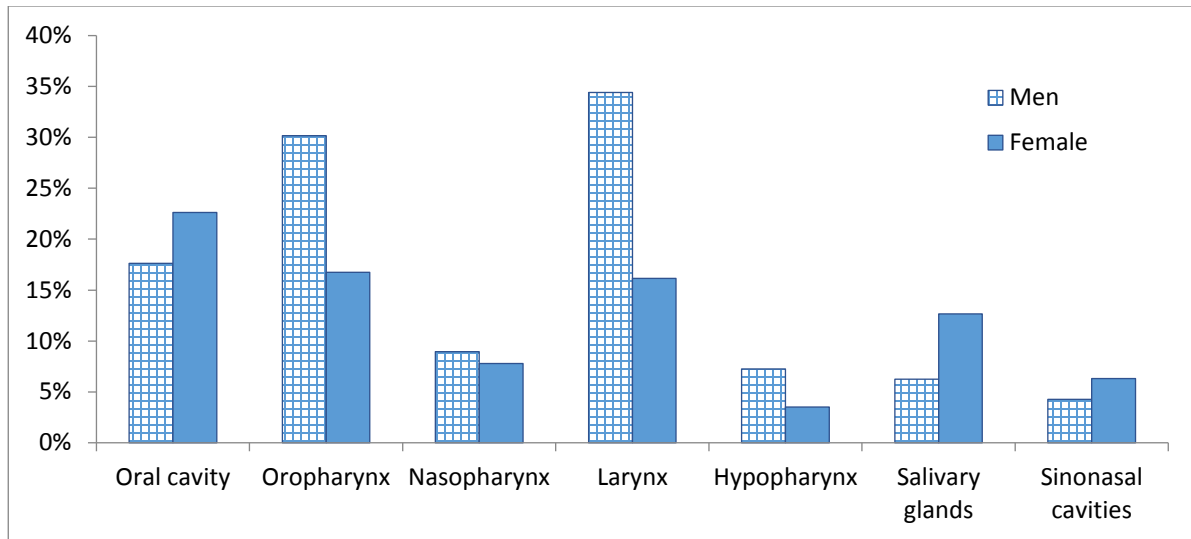


Figure 2: Percentage of HNC cases by subsite and sex from PBCRs between 2010 and 2015 (n=15,984)