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Global burden of HPV-attributable squamous cell carcinoma of the anus in 2020, according to sex and HIV status: a worldwide analysis

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Abstract

Squamous cell carcinoma of the anus (SCCA) is caused by HPV, and is elevated in persons living with HIV (PLWHIV). We aimed to estimate sex- and HIV-stratified SCCA burden at a country, regional and global level. Using anal cancer incidence estimates from 185 countries available through GLOBOCAN 2020, and region/country-specific proportions of SCCA versus non-SCCA from the Cancer Incidence in Five Continents (CI5) Volume XI database, we estimated country- and sex-specific SCCA incidence. Proportions of SCCA diagnosed in PLWHIV, and attributable to HIV, were calculated using estimates of HIV prevalence (UNAIDS 2019) and relative risk applied to SCCA incidence. Of 30 416 SCCA estimated globally in 2020, two-thirds occurred in women (19 792) and one-third among men (10 624). 53% of male SCCA and 65% of female SCCA occurred in countries with a very high Human Development Index (HDI). 21% of the global male

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AUTHOR CONTRIBUTIONS

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CONFLICT OF INTEREST

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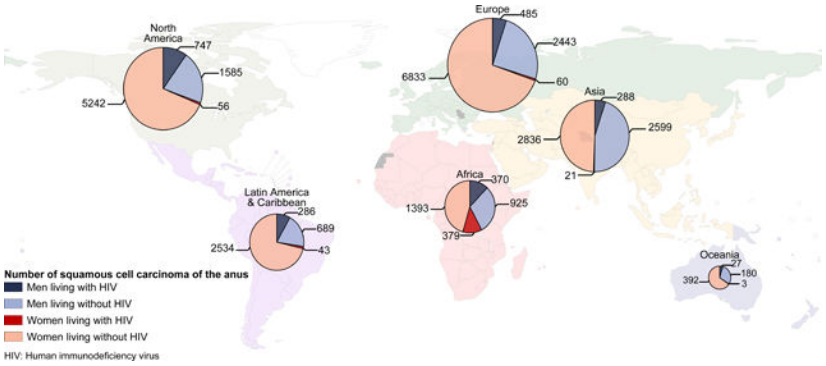
DISCLAIMER

Where authors are identified as personnel of the International Agency for Research on Cancer or WHO, the authors alone are responsible for the views expressed in this article and they do not necessarily represent the decisions, policy or views of the International Agency for Research on Cancer or WHO. The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the National Institute of Health.

SCCA burden occurred in PLWHIV (n=2203), largely concentrated in North America, Europe, and Africa. While, only 3% of global female SCCA burden (n=561) occurred in PLWHIV, mainly in Africa. The global age-standardized incidence rate of HIV-negative SCCA was higher in women (0.55 cases per 100,000) than men (0.28), whereas HIV-positive SCCA was higher in men (0.07) than women (0.02). HIV prevalence reached >40% in 22 countries for male SCCA and in 10 countries for female SCCA, mostly in Africa. Understanding global SCCA burden by HIV status can inform SCCA prevention programs (through HPV vaccination, screening, and HIV control) and help raise awareness to combat the disease.

Graphical Abstract



Keywords

anal cancer; human papillomavirus; HIV; squamous cell carcinoma of the anus; global burden

1 INTRODUCTION

Squamous cell carcinoma of the anus (SCCA) is the most common subtype of anal cancer, and is considered 100% associated with human papillomavirus (HPV) infection.[1] Studies from high- and middle-income countries have reported a 2–6% annual increase in SCCA incidence in the last few decades.[2–7]

HIV co-infection enhances the carcinogenicity of HPV, putting persons living with HIV (PLWHIV) at heightened SCCA risk.[8] Among PLWHIV, SCCA risk is particularly high in men who have sex with men (MSM), but is also elevated in men who have sex with women (MSW) and women.[9,10] In the era of highly active antiretroviral therapy, the global HIV burden rose to an estimated 38 million PLWHIV in 2019.[11] The majority of the HIV burden in high-income countries is concentrated among MSM; whereas, in low- and middle-income countries (particularly in eastern and southern Africa), HIV is endemic and disproportionately affects MSW and women.[11] Given that HIV and HPV share common sexual transmission routes, the contribution of HIV to SCCA burden can thus be expected to vary substantially by sex and world region, although it has yet to be quantified.

In 2018, the World Health Organization (WHO) launched a global call to eliminate cervical cancer as a public health problem, underpinned by prophylactic HPV vaccination, which

is expected also to have an important impact on the future anal cancer burden. As of June 2020, 107 of 194 WHO member countries have introduced HPV vaccination, with one-third of programs are currently gender-neutral.[12] However, given the prolonged time between initial HPV infection to the development of SCCA, combined with suboptimal global HPV vaccination coverage (especially in males), the impact of vaccination on anal cancer prevention will not be seen for many decades.

In the meantime, several professional organizations in high-income countries (e.g., European AIDS Clinical Society, New York State) advise SCCA early detection programs for PLWHIV, in recognition of their elevated risk.[13] These approaches include using digital anorectal examination to detect early-stage SCCA and improve treatment outcomes, or using diagnostic high-resolution anoscopy to detect and treat precancerous lesions to reduce anal cancer incidence. To date, however, an absence of international consensus and evidence-based recommendations, combined with the scarcity of appropriately trained personnel, has limited the implementation of early detection programs in PLWHIV, even in high-resource settings.

A better understanding of the global burden of SCCA according to HIV status could thus have important implications for raising awareness, mobilizing resources and informing the design of appropriate anal cancer prevention initiatives. To this end, our aim was to use global databases of cancer incidence (GLOBOCAN 2020 and CI5 Vol. XI, as compiled by the International Agency for Research on Cancer (IARC/WHO), HIV prevalence (UNAIDS 2019), and estimates of relative risk of SCCA in PLWHIV, to describe the SCCA incidence and burden in 185 countries, by sex and HIV status.

2 METHODS

2.1 Data sources

2.1.1 Country-specific estimates of SCCA and HIV prevalence—Age and gender-specific population denominators, number of anal cancer cases (International Classification of Diseases tenth edition [ICD-10] code C21), and anal cancer incidence rates (cases per 100 000 person years) were extracted for 185 individual countries/territories estimated in the GLOBOCAN database for the year 2020 via the Global Cancer Observatory (GCO) (https://gco.iarc.fr). Detailed GLOBOCAN methods are described elsewhere.[14] Given the rarity of anal cancer in persons aged <15 years (only 12 cases reported in GLOBOCAN 2020), we estimated the outcomes for persons aged 15 years or older.

Proportions of SCCA cases were calculated as described previously.[1] In brief, data on microscopically verified anal cancer were extracted from CI5 XI database of cancer registries, complemented with data submitted by population-based cancer registries for the estimation of the GLOBOCAN 2020 database, and supplemented by updated data from the African Cancer Registry Network (AFCRN) for the sub-Saharan African region. These were partitioned by sex and by age group (15–59 years and 60 years and older) for 60 countries that recorded a sufficient number of informative cases (at least 4 microscopically verified SCCA cases per sex and at least 8 cases per sex in the broader anal cancer

category C21).[15] When country-specific data were not available, or insufficient, we applied an average proportion at the sub-regional level.

Numbers of SCCA were estimated by applying these proportions to the estimated number of cases of anal cancer in GLOBOCAN, by country, sex and age group. Age-standardized incidence rates (ASIRs) for SCCA overall (i.e., persons aged 15 years and older) and for two age groups (15–59 years and 60 years and older), were calculated using the world standard population as proposed by Segi and modified by Doll and expressed as cases per 100 000 person-years.[16] The details can be found in the supplementary methods (pp 3–9, including Tables S1–S2).

HIV prevalence estimates for men and women aged 15 years or older in 2019 were acquired from UNAIDS for 176 of the 185 GLOBOCAN countries/territories. Age-specific denominators (population size) and numerators (number of PLWHIV) were provided by UNAIDS to produce HIV prevalence estimates for the age groups 15–59, and ≥60 years. For the remaining GLOBOCAN countries/territories, estimates were derived with similarly aggregated age-specific HIV prevalence for 2019 published by the Institute for Health Metrics and Evaluation (IHME) (http://ghdx.healthdata.org/gbd-results-tool).

2.1.2 Relative risks (RRs) for HIV and SCCA—

RRs for SCCA incidence among PLWHIV versus SCCA incidence in persons without HIV were derived separately for MSM, MSW and women, and by age (15–59 years and >60 years). SCCA incidence among MSM, MSW and women LWHIV came from a large population-based study in North America, the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD).[17] Population size of PLWHIV for similar groups was obtained from the USA Centers for Disease Control and Prevention's National HIV surveillance system.[18] SCCA incidence among men and women without HIV were derived from SCCA incidence in the general U.S. population (the National Program of Cancer Registries and Surveillance Epidemiology and End Results (SEER) Database),[19] after an adjustment to remove cases estimated to occur in PLWHIV from SCCA cases in the general population (detail reported in supplementary methods, pp 10–12).

2.2 Procedures and statistical analysis

For each of the 185 countries included in the GLOBOCAN 2020 database, by sex and age group (15–59 and ≥60 years), we estimated: (a) the fraction of SCCA diagnosed among PLWHIV (or HIV prevalence in SCCA), and (b) the fraction of SCCA attributable to HIV (or population-attributable fraction [PAF]), according to the following formulae:

$$HIV\ prevalence\ in\ SCCA = \frac{HIV\ prevalence \times RR}{(1 - HIV\ prevalence) + (HIV\ prevalence\ \times RR)} \quad \text{(a)}$$

$$PAF = \frac{HIV\ prevalence\ \times (RR - 1)}{1 + HIV\ prevalence\ \times (RR - 1)} \quad \text{(b)}$$

For women, we applied the same age-specific RRs in all countries. For men, however, we applied age-specific RRs in three categories according to the relative burden of HIV infection among men in the given country (as a surrogate for the concentration of the HIV epidemic in MSM): 1) >70% of HIV burden among men, RR for MSM only; (2) 50–70%, RR for all men, and (3) <50%, RR for MSW only. Country-specific RR assignments and detailed methods are available in the supplementary methods (pp 3–11, including Tables S1–S3). Finally, proportions of SCCA cases living with HIV and PAFs were validated by comparing our estimates against observed data, where available (Table S4).

For each country, by sex and age group, we calculated the number of new SCCA cases that were: (a) diagnosed among PLWHIV, and (b) attributable to HIV, on multiplying these two respective fractions by the number of SCCA cases estimated in GLOBOCAN. Finally, proportions of SCCA diagnosed in PLWHIV were applied to ASIRs to calculate ASIRs of SCCA diagnosed in a) the absence and b) presence of HIV.

In order to address the potential overestimation of HIV-attributable SCCA burden among males in countries with a high concentration of HIV epidemic among MSM (due to HIV and anal HPV sharing a common sexual transmission route), we also performed a sensitivity analysis applying RRs for MSW living with HIV (given the relatively low prevalence of high-risk anal HPV in this risk group)[20] to all countries.

Country-specific estimates were aggregated worldwide and according to UN geographic (sub)regions. Countries were also grouped by the Human Development Index (HDI) into four tiers (low, medium, high, and very high HDI).[21] All statistical analyses were conducted in Matlab (version 2020b) and world maps were created using R (version 3.6.4).

3 RESULTS

In 2020, an estimated 30 416 SCCA cases were diagnosed globally, of which one-third were among men (10 624) and two-thirds among women (19 792). 50% of male SCCA, and 62% of female SCCA, were concentrated in Europe and North America alone (Table). Indeed, the majority of the global SCCA burden occurred in more developed regions of the world, with 53% of all SCCA in men and 65% of all SCCA in women occurring in countries of very high HDI.

Global ASIRs of SCCA were 0.35 per 100 000 for men and 0.57 for women (Table). ASIRs were highest in North America (1.18 for men, and 2.32 for women) and lowest in Asia (0.16 and 0.14). In Europe, Latin America & the Caribbean, North America, and Oceania, ASIRs in women were nearly double those in men. In contrast, there were few differences in sex-specific ASIRs in Asia and Africa. Country- and sex-specific ASIRs of SCCA are shown in three categories, projected onto the world map, presented in Figure 1. Age-specific incidence rates of SCCA among men and women are presented by world region in Figure S1 and S2.

Worldwide in 2020, an estimated 20.7% (2203 of 10 624) of all new SCCA cases in men and 2.8% (561 of 19 792) of all new SCCA cases in women occurred among PLWHIV (Figure 2, Table S5), with 29% and 27% of the global SCCA cases occurring among PWLHIV

in North America and Africa, respectively. However, the global distribution of SCCA in PWLHIV varied significantly by sex. For men, 34% occurred in North America (mainly [97%] in the USA), 22% in Europe (majority [47%] in Western Europe), and 17% in Africa ([mainly [97%] in sub-Saharan Africa). Whereas, SCCA in PWLHIV among women was concentrated heavily in Africa (68%), mainly in sub-Saharan Africa. Very high HDI countries contributed 58% (1277 of 2203) of the global SCCA burden among men living with HIV, versus 20% (114 of 561) of the global SCCA burden among women living with HIV.

The proportion of SCCA cases living with HIV for men ranged from 36.0% in sub-Saharan Africa, 33.0% in the USA, 30.1% in Caribbean & Central America, down to 4.1% in Northern African. Among women, this proportion was 24.6% in sub-Saharan Africa, but ≤2% in other sub-regions (Figure 2). The range in proportions based on 95% CIs in RRs are presented in Table S5. Country- and sex-specific SCCA living with HIV are shown in six categories, projected onto the world map, in Figures 3A and 3B. Proportions were consistently higher in men than in women. The proportions were particularly high in Southern Africa where 78.9% of male SCCA and 63.2% of female SCCA occurred among PLWHIV. Of the 50 countries with the highest proportion of cases living with HIV, the majority (21 for men and 38 for women) were in sub-Saharan Africa.

Figure 4 describes ASIRs for SCCA, by sex and by HIV status. Global ASIRs for HIV-negative SCCA were 0.55 cases per 100 000 person-years for women and 0.28 for men. ASIRs for HIV-positive SCCA were 0.02 for women and 0.07 for men. The ASIR for male HIV-positive SCCA was nearly 3 fold greater in North America (0.41) compared to other regions (≤0.14), whereas for female HIV-positive SCCA, it was higher in Africa (0.11) than other regions (≤0.03). ASIRs for male HIV-negative SCCA were highest in Oceania (0.85), North America (0.78) and Europe (0.53), as were ASIRs for female HIV-negative SCCA (1.85, 2.28 and 1.26 respectively). SCCA incidence by HIV status for 60 countries with ASIRs (and proportions of SCCA:non-SCCA) derived from population-based cancer registries are presented in Figure 5.

Worldwide, an estimated 20.4% (2165 cases) of all SCCA cases among men and 2.5% (489 cases) among women were estimated to be directly attributable to HIV, and patterns of HIV-attributable SCCA by sex and worldwide region and countries (Table S6 and Figures S3 to S5) were similar to those of SCCA occurring among PLWHIV (see above). Sensitivity analysis showed that the lower estimate of attributable fraction of HIV to SCCA among men was 12.9% (1375 cases) when RRs for MSW were considered for all countries (detailed results shown by region in Table S6).

4 DISCUSSION

An estimated 30 000 SCCA were diagnosed globally in 2020, slightly higher than the previous estimate of 29 000 in 2018.[1] Women contributed two-thirds of the global SCCA burden, and the majority of SCCA cases, in both men and women, occurred in highest-resource countries. The present study is however the first to comprehensively describe the global SCCA burden according to sex and HIV status, revealing important variations.

Globally, 21% of SCCA among men and 3% among women were diagnosed among PLWHIV, of which the majority were directly attributable to HIV. However, the global distribution of SCCA in PLWHIV varied greatly by sex. For men, the burden of SCCA in PLWLHIV was mainly in very high HDI countries in North America and Europe, whereas for women, it was concentrated in Africa. These patterns are expected to be driven by a combination of differences in underlying HIV endemicity, in predominant routes of HIV transmission in different world regions, and by the extent to which these transmission routes are correlated with anal HPV exposure (see below).

The majority of worldwide SCCA occurs in women in the absence of HIV, and the incidence rates of female HIV-negative SCCA were highest in North America, Oceania, and Europe, likely representing increased exposure to anal HPV infection, the necessary cause of anal cancer. It is hypothesized that the sexual revolution that started during the 1960s-1980s in high-income countries may have contributed to the increased anal HPV exposure among contemporary birth cohorts.[2] Consistent with this hypothesis, a study from the USA reported that the rise in incidence among women was restricted to SCCA,[22] whereas non-HPV-associated anal cancer (e.g., adenocarcinoma) incidence declined or plateaued.[22] Among women ≥60 years in the USA and western Europe in the present study, SCCA incidence reached rates of 7 or above per 100 000, nearing those of cervical cancer incidence.[4,23]

Multiple lines of evidence suggest that anal HPV exposure in females may occur via the cervix/external genital region. These include studies reporting associations between anal sexual intercourse and anal HPV that are either non-significant or less significant than number of sexual partners per se,[24–28] studies showing that a majority of women with anal cancer report no history of anal sexual intercourse,[29] and a study reporting a link between front-to-back wiping and anal HPV infection.[30] Furthermore, longitudinal studies in both HIV-negative women and women living with HIV have shown that anal HPV incidence is higher among women with previous cervical HPV infection of the same type.[31,32] It is therefore unclear why female SCCA burden in the absence of HIV was relatively low in sub-Saharan Africa (and Latin America), where the population prevalence of cervical HPV infection is known to be very high. One can speculate that differences in sexual practices or possibly under-reporting of SCCA in sub-Saharan Africa may be drivers; future research is needed to understand the contribution of cervical HPV to the national variations in SCCA incidence observed here.

Among men, SCCA incidence not attributable to HIV is expected to be at least partly driven by exposure to HPV through anal sexual intercourse,[29,33] as MSM without HIV are known to be at higher SCCA risk than MSW without HIV.[9] However, anal HPV infection has also been reported among MSW without HIV, i.e., in the absence of both anal intercourse and HIV infection.[20,34,35] Due simply to their large relative population size, MSW without HIV can still contribute a substantial proportion of the male anal cancer burden at the population level[29] It thus remains unknown to what extent same-sex HPV transmission may have contributed to regional and country-level differences in male SCCA incidence not attributable to HIV.

The concentration of SCCA burden in men living with HIV in very high HDI countries in North America and Europe is likely to be a function of the greater contribution of same-sex sexual transmission to male HIV and HPV infections in these regions. Invariably, MSM living with HIV have highest SCCA risks due to the combination of increased acquisition of anal HPV and greater HPV persistence due to HIV-related immunosuppression.[36–38] The rising population size and aging of PLWHIV due to improved longevity from cART use[39] and the increasing contribution of same-sex sexual transmission to HIV means that SCCA cases living with and attributable to HIV may continue to rise.[40]

Similar to prior work for cervical cancer,[41] we present two measures of the burden of HIV-associated SCCA—SCCA diagnosed among PLWHIV (i.e., HIV prevalence among SCCA) and that attributable to HIV (i.e., PAF). The burden of HIV-attributable SCCA represents cases that could be theoretically avoided by HIV prevention. Earlier diagnosis of HIV and timelier initiation of cART could contribute to reducing the HIV attributable SCCA burden, given cART use is likely to reduce the risk of anal HPV infection and SCCA among PLWHIV.[37] Given that HIV and HPV share a common sexual transmission route, there is a potential for unmeasured confounding in our calculation of PAFs, particularly in settings where the concentration of HIV epidemic among MSM is greatest. Nevertheless, without any possibility of controlling this interaction, our estimates provide the best current approximation of the SCCA burden that would not exist in the absence of HIV, and we also provide a lower bound of male PAFs by applying RRs for MSW to all males.

Estimates of SCCA patients living with HIV are unaffected by the above methodological issue and, furthermore, can be validated against empirically observed evidence (as we compared our findings against available data from Belgium, Botswana, France, Mozambique, Rwanda, South Africa, West Africa, United States, and Puerto Rico [Table S4]). For example, our estimates of a 1% and 25% HIV prevalence in female and male SCCA in France are consistent with the 5% and 33% reported in a case series of 225 women and 137 men with SCCA, respectively,[42] and estimates of 2% and 26% HIV prevalence in female and male SCCA in Puerto Rico can be compared with 2% and 28% observed in a registry data analysis of 525 women and 197 men with SCCA, respectively.[6] This measure can be used to understand the extent to which the burden of disease falls on PLWHIV, irrespective of causality, and is relevant for informing the design and evaluating the potential impact of SCCA prevention strategies and for guiding resource allocation for SCCA prevention, notably screening. Of note, our national estimates for men in Australia were lower (14% vs 46%) compared to a study by Hillman and colleagues conducted in Sydney, where the Australian MSM community is known to concentrate (but estimates for women were comparable).[43]

Emerging data indicate that screening and treatment of anal precancer may reduce SCCA incidence among PLWHIV[44,45] with current priorities to determine the benefit to harm ratios and cost-effectiveness of different screening algorithms.[46,47] Indeed, the country- and region-specific concentration of SCCA among PLWHIV that we observe offers an opportunity to build screening infrastructure and capacity, alongside the necessary workforce trained to perform SCCA screening, diagnostic procedures, and treatment.

A few additional limitations need to be considered. Firstly, SCCA incidence estimates are limited by the availability of population-based cancer registry data, especially in low-income countries. Thus, given the rarity of anal cancer in some registries, the estimates propagated to the regional level (e.g., Africa and Asia) may be subjected to uncertainty. For example, the recorded data from which estimates of SCCA proportions in anal cancer were derived were available for 60 countries only. Correcting this proportion is, however, essential in order to exclude adenocarcinomas of the anus and the potentially larger number of misclassified adenocarcinomas derived from the lower rectum, neither of which are HPV-attributable. Country-specific HIV prevalence estimates may also be imperfect, particularly in countries with insufficient surveillance information. Of note, because of these uncertainties, and given the rarity of anal cancer below age 60 years in many countries (Supplement Figure S2), although we derived our overall estimates using age-stratified (15–59 and ≥60 years) component measures, we do not show findings stratified by age. Finally, given the lack of valid data on sexual identity at the population level, it was not possible to directly characterize the contribution of same-sex sexual vs heterosexual contact to the male SCCA burden. We did, however, apply different relative risks for MSM and MSW living with HIV in different countries according to an objective measure of the concentration of the HIV epidemic in MSM.

Finally, this study provides the first estimates of worldwide SCCA incidence, burden, and cases living with and attributable to HIV. Our findings seek to raise awareness, guide policies and programs for HIV and SCCA prevention, and should serve as a baseline in monitoring longer-term progress. To achieve long-term direct and indirect (herd immunity) protection from HPV vaccination, it is crucial to administer the HPV vaccines before sexual debut and establish optimal vaccination coverage.[20] Unfortunately, over one-third of the male and one-fifth of the female worldwide SCCA burden in 2020 occurred in countries where HPV vaccination programs are yet to be introduced, while one-fifth of the global male SCCA burden occurred in countries with female-only HPV vaccination programs. In many high-resource countries where most global SCCA burden occurred, suboptimal HPV vaccination coverage[12] combined with high vaccine hesitancy remain key barriers to SCCA prevention.[48–50] Also, MSM, who are expected to contribute greatly to the worldwide male SCCA burden may not derive any benefit from female-only HPV vaccination programs due to a lack of herd immunity, thus increasing the importance of targeted HPV vaccination of MSM and screening. PLWHIV represents an important risk group that is being prioritized for SCCA screening. Presently however, SCCA screening is limited to high-income settings with available resources in a few high-income countries. Our study shows that the contribution of HIV to the burden of SCCA is substantial but varies greatly by world region and country. Our findings may thus serve as a pivotal framework to guide the introduction and implementation of targeted SCCA screening programs for PLWHIV.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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DATA AVAILABILITY STATEMENT

Only publicly available data were used in this study, and data sources and handling of these data are described in the Materials and Methods and in the Supplementary Tables S1–S3. Further information is available from the corresponding author upon request.

Abbreviations:

AFCRN	African Cancer Registry Network
ASIR	age-standardized SCCA incidence rates
HDI	human development index
HIV	human immunodeficiency virus
HPV	human papillomavirus
HSIL	high-grade squamous intraepithelial lesions
IARC	International Agency for Research on Cancer
ICD	International Classification of Diseases
IHME	Institute for Health Metrics and Evaluation
MSM	men who have sex with men
MSW	men who have sex with women
NA-ACCORD	North American AIDS Cohort Collaboration on Research and Design
PLWHIV	persons living with HIV
SCCA	squamous cell carcinoma of the anus
SIR	standardized incidence ratio

WHO World Health Organization

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What's new?

Squamous cell carcinoma of the anus (SCCA) is the most commonly-diagnosed anal cancer subtype for which human papillomavirus (HPV) infection is considered a necessary cause and HIV is a major risk factor. The present study describes for the first time SCCA incidence, burden, and contribution of HIV among men and women at the country, region and global level. These data can help raise awareness, inform recommendations for SCCA prevention, and help mobilize screening resources.

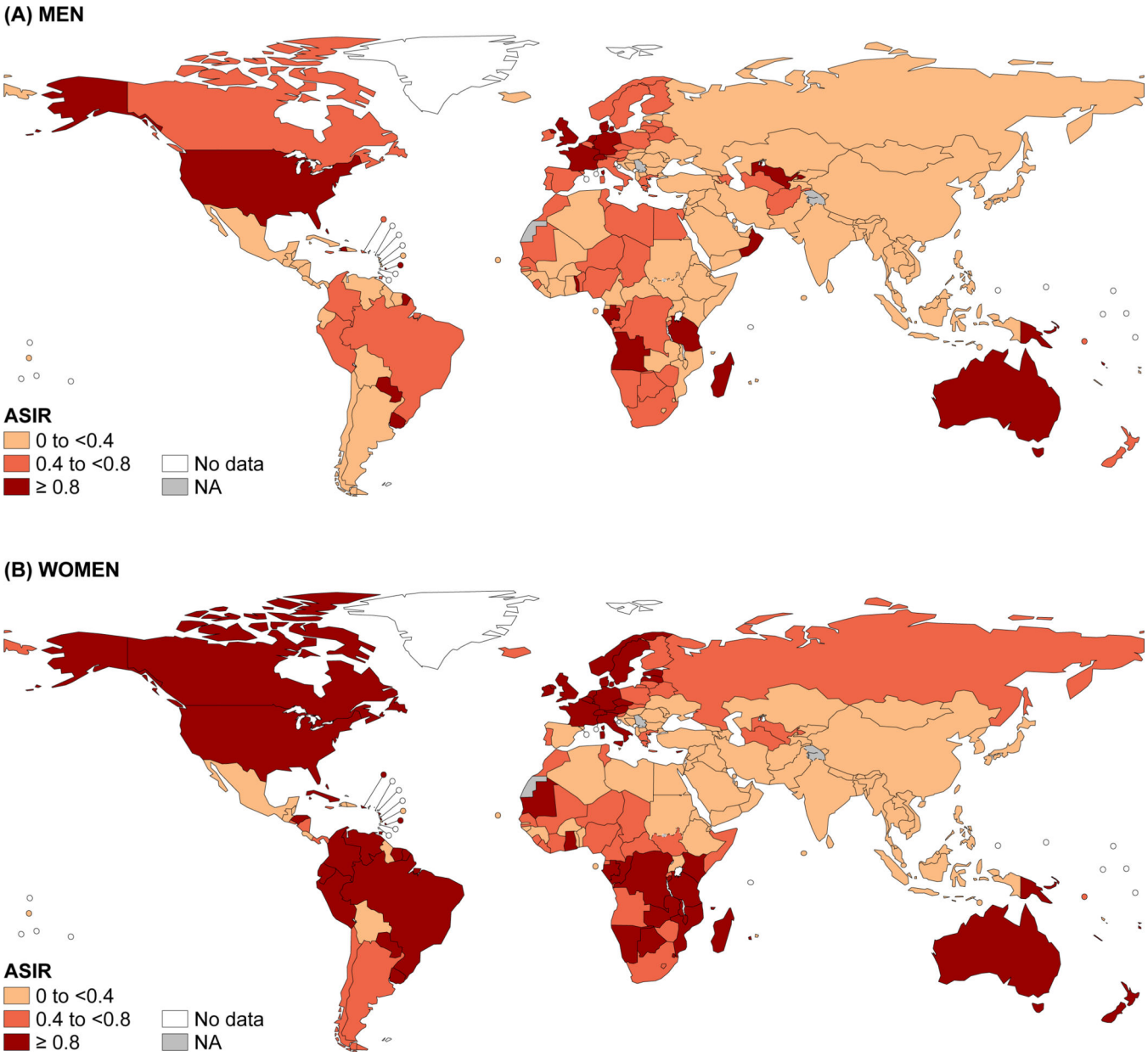

FIGURE 1.

Geographic distribution of world age-standardized incidence (per 100 000) of squamous cell carcinoma of the anus among men (A) and women (B), aged 15 years or older. ASIR, age-standardized incidence rate; NA, not available. The designations used and the presentation of the material in this Article do not imply the expression of any opinion whatsoever on the part WHO and the IARC about the legal status of any country, territory, city, or area, or of its authorities, or concerning the delimitation of its frontiers or boundaries

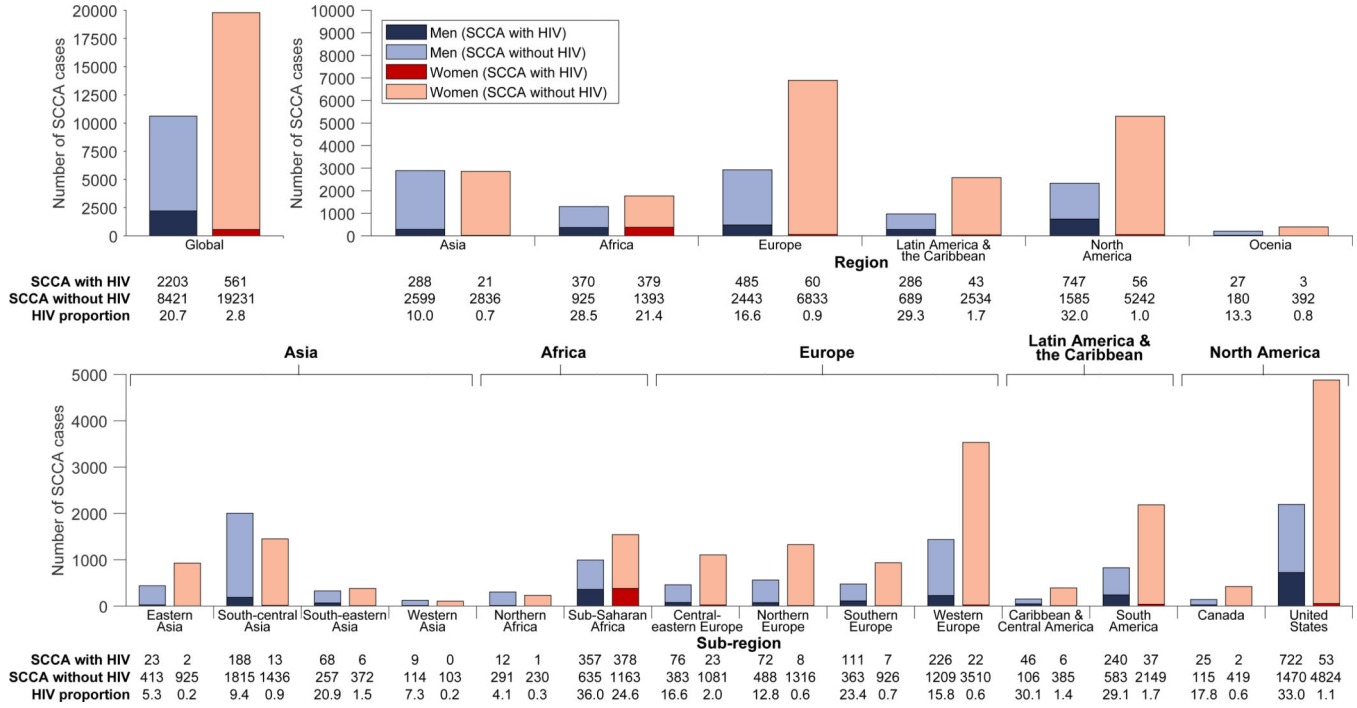

FIGURE 2.

Estimated proportions of new squamous cell carcinoma of the anus in persons living with HIV in 2020, worldwide and by United Nations region and sub-region. HIV, human immunodeficiency virus; SCCA, squamous cell carcinoma of the anus

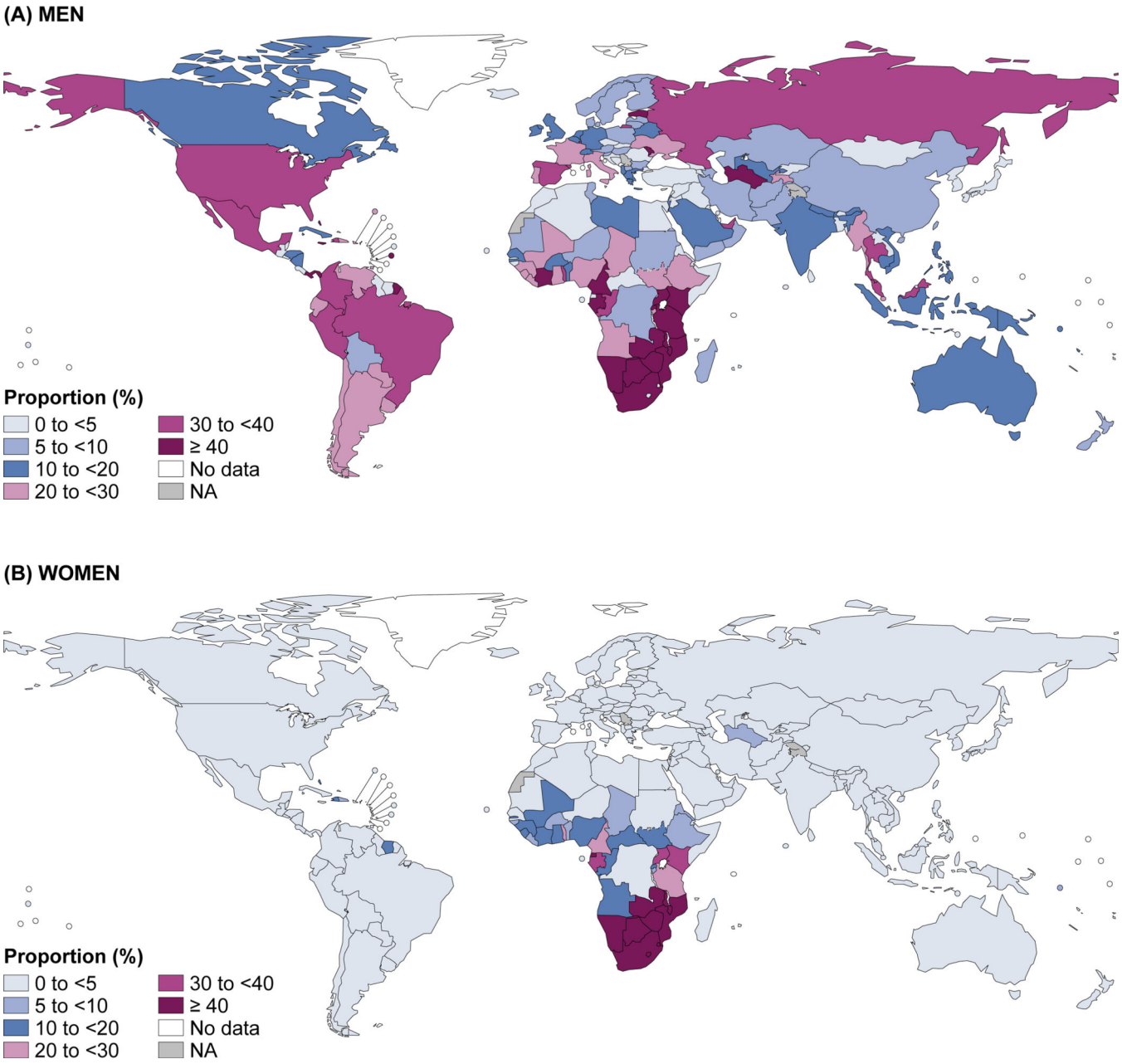

FIGURE 3.

Geographic distribution of worldwide estimation of proportion of squamous cell carcinoma of the anus in patients living with HIV in 2020. Proportions of SCCA in persons living with HIV for men (A) and for women (B). NA, not available. The designations used and the presentation of the material in this Article do not imply the expression of any opinion whatsoever on the part WHO and the IARC about the legal status of any country, territory, city, or area, or of its authorities, or concerning the delimitation of its frontiers or boundaries

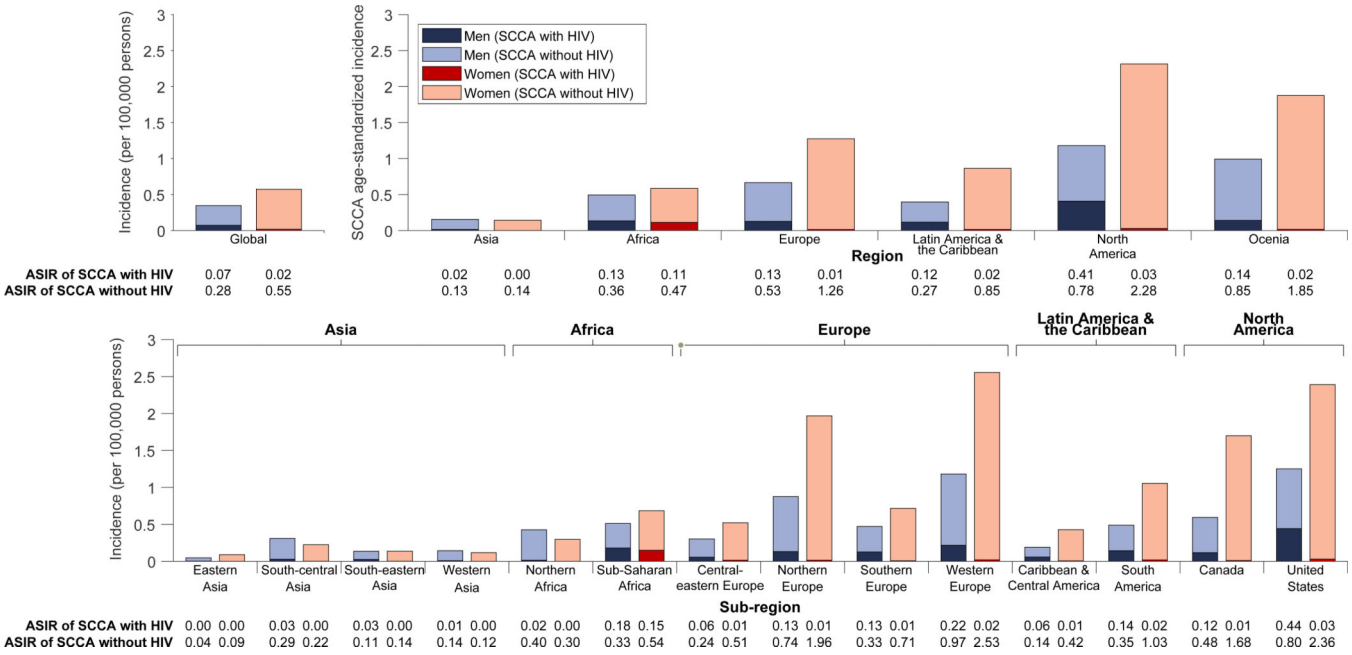

FIGURE 4.

Age-standardized incidence (per 100 000) of squamous cell carcinoma of the anus with and without HIV in 2020, worldwide and by United Nations region and sub-region.

ASIR, age-standardized incidence rate; SCCA, squamous cell carcinoma of the anus

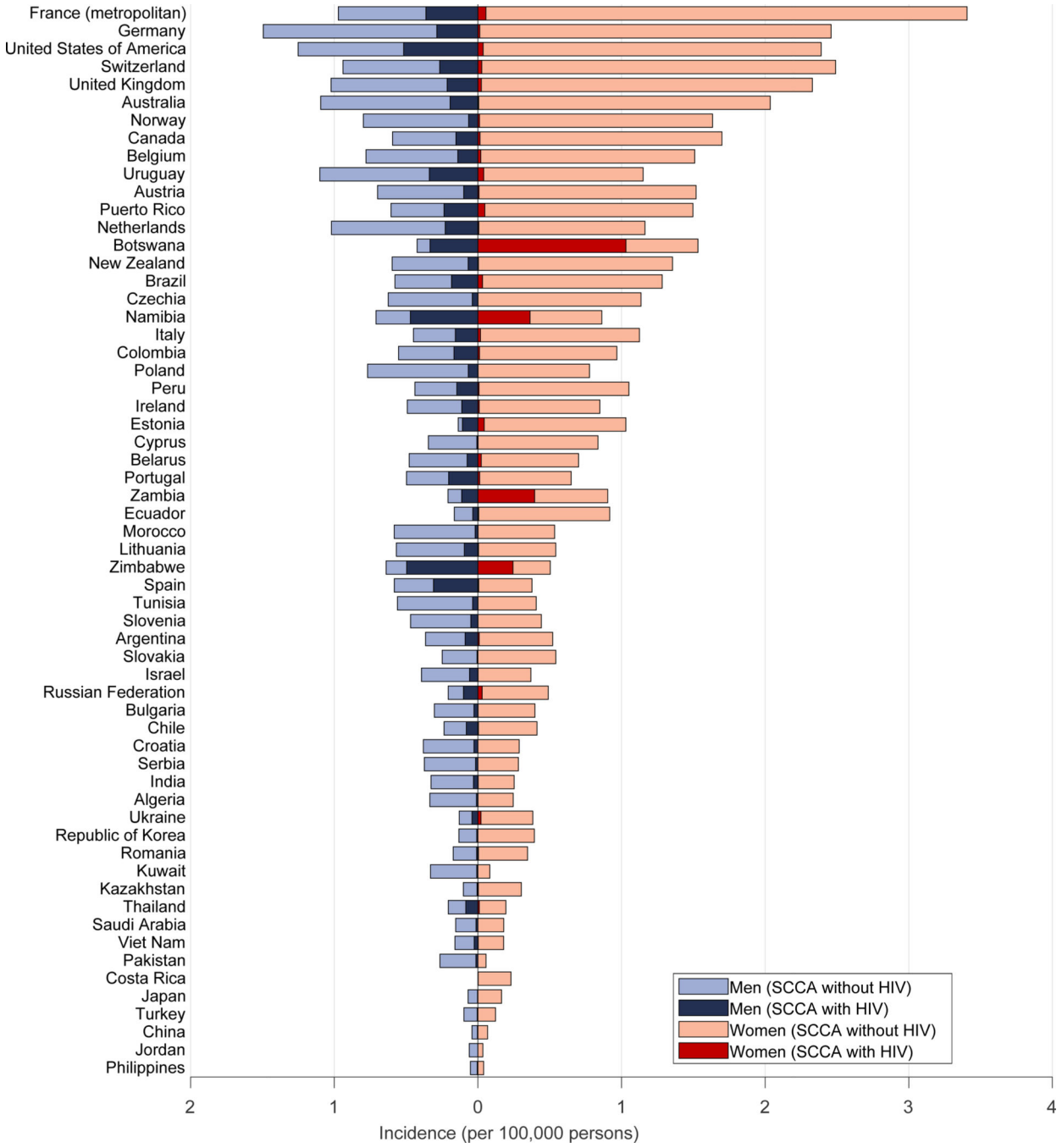

FIGURE 5.

Age-standardized incidence (per 100 000) of squamous cell carcinoma of the anus with and without HIV in 2020 among men and women in countries with available registry data. Incidence rates are arranged in decreasing order of overall SCCA incidence among men and women. ASIR, age-standardized incidence rate; SCCA, squamous cell carcinoma of the anus

Table:

Squamous cell carcinoma in men and women in 2020 worldwide, by UN (sub)region, and by HDI level

	Male				Female			
	Total male population (millions)	**Number of SCCA cases**	**Proportion of global SCCA cases (%)**	**ASIR (per 100 000) men**	**Total female population (millions)**	**Number of SCCA cases**	**Proportion of global SCCA cases (%)**	**ASIR (per 100 000) women**
Global	2895	10 624	100	0.35	2893	19 792	100	0.57
Asia	1794	2887	27.2	0.16	1736	2857	14.4	0.14
Eastern Asia	692	436	4.1	0.05	678	927	4.7	0.09
South-central Asia	748	2003	18.9	0.31	711	1449	7.3	0.22
South-eastern Asia	248	325	3.1	0.14	253	378	1.9	0.14
Western Asia	106	123	1.2	0.14	94	103	0.5	0.12
Africa	395	1295	12.2	0.49	404	1772	9.0	0.59
Northern Africa	82	303	2.9	0.43	83	231	1.2	0.30
Sub-Saharan Africa	313	992	9.3	0.51	321	1541	7.8	0.68
Eastern Africa	127	328	3.1	0.48	132	684	3.5	0.76
Middle Africa	49	173	1.6	0.62	50	253	1.3	0.83
Southern Africa	23	81	0.8	0.43	24	181	0.9	0.75
Western Africa	114	410	3.9	0.52	114	423	2.1	0.53
Europe	300	2928	27.6	0.66	328	6893	34.8	1.28
Central-eastern Europe	112	459	4.3	0.30	131	1104	5.6	0.52
Northern Europe	43	560	5.3	0.88	45	1324	6.7	1.97
Southern Europe	64	474	4.5	0.47	68	933	4.7	0.72
Western Europe	81	1435	13.5	1.18	85	3532	17.8	2.56
Latin America and the Caribbean	241	975	9.2	0.40	255	2577	13.0	0.86
Caribbean and Central America	79	152	1.4	0.19	84	391	2.0	0.43
South America	162	823	7.7	0.49	171	2186	11.0	1.05
North America	148	2332	22.0	1.18	154	5298	26.8	2.32
Oceania	16	207	1.9	0.99	16	395	2.0	1.88

	Male				Female			
	Total male population (millions)	**Number of SCCA cases**	**Proportion of global SCCA cases (%)**	**ASIR (per 100 000) men**	**Total female population (millions)**	**Number of SCCA cases**	**Proportion of global SCCA cases (%)**	**ASIR (per 100 000) women**
HDI Level								
Very high	563	5605	52.8	0.71	586	12 926	65.3	1.40
High	1007	1622	15.3	0.14	1007	3448	17.4	0.26
Medium	1023	2431	22.9	0.28	992	2164	10.9	0.24
Low	303	966	9.1	0.54	308	1254	6.3	0.60

ASIR=age-standardized incidence rate. HDI=human development index. SCCA=squamous cell carcinoma of the anus.