Global burden of oral cancer in 2022 attributable to smokeless tobacco and areca nut consumption: a population attributable fraction analysis

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ABSTRACT

Background: Consuming products that contain smokeless tobacco (ST) and/or areca nut (AN) increases the risk of oral cancer. We aimed to estimate the burden of oral cancer attributable to ST/AN consumption globally and by type of ST/AN product in four major consuming countries.

Methods: We calculated population attributable fractions (PAFs) using prevalence of current use of ST/AN products from national surveys and corresponding risks of oral cancer from the literature. We applied PAFs to national estimates of oral cancer incidence in 2022 from the GLOBOCAN database to obtain cases attributable to ST/AN consumption. We modelled 95% uncertainty intervals (UIs) using Monte Carlo simulations.

Findings: Globally, an estimated 120 200 (95% UI, 115 300–124 300) cases of oral cancer in 2022 were attributable to ST/AN consumption, or 30·8% (29·6–31·9) of all oral cancer cases (120 200 of 389 800). Regions with the highest PAFs were Melanesia, Micronesia & Polynesia (78·6% [74·4–80·5]), South-Central Asia (57·5% [54·8–59·5]), and South-Eastern Asia (19·8% [19·0–20·6]). Lower-middle-income countries represented 90·2% (108 400 [103 400–112 200] cases) of the world total attributable cases. Products with the highest PAFs were: AN (Papua New Guinea females 83·8% [77·2–87·3], males 84·1% [78·5–87·1]; India females 29·9% [24·4–36·9], males 31·7% [26·2–38·6]); betel quid with tobacco (Bangladesh females 66·8% [64·4–68·8], males 53·5% [50·7–56·0]; India males 32·9% [30·6–35·2]); *naswar* (Pakistan males 51·9% [48·1–55·0]); *khaini* (India males 47·2% [43·2–51·0]), and *gutka* (India males 43·1% [35·7–50·6]).

Interpretation: Our findings suggest that 1 in 3 cases of oral cancer globally are attributable to ST/AN consumption and could be prevented through ST and AN control. Global cancer control efforts must incorporate further measures to reduce ST and AN consumption in populations with the largest attributable burden.

Funding: French National Cancer Institute (INCa).

Keywords: smokeless tobacco; areca nut; population attributable fraction; oral cancer; tobacco control

RESEARCH IN CONTEXT

Evidence before this study

Consuming smokeless tobacco or products containing areca nut is causally linked to numerous diseases including oral cancer. Using the terms "(smokeless tobacco OR chewing tobacco OR areca nut OR betel) AND cancer AND attributable", we searched PubMed up to 6 April 2023 and the Institute for Health Metrics and Evaluation's research articles database up to 3 September 2023 for studies quantifying the global burden of oral cancer attributable to smokeless tobacco and/or areca nut consumption. Previous global studies estimated that between 19% and 26% of oral cancer deaths were attributable to smokeless tobacco but did not assess oral cancer incidence. Furthermore, the impact of areca nut on oral cancer burden globally has thus far not been elucidated.

Added value of this study

Our estimates of oral cancer incidence attributable to smokeless tobacco and areca nut consumption provide a more complete picture of the burden of these risk factors on health care and the potential impact of primary prevention. We also reported for the first time, to our knowledge, the burden of oral cancer attributable to specific types of smokeless tobacco and areca nut product in selected countries. We showed that some specific products are responsible for between 20% and 84% of oral cancer cases among males and females in Bangladesh, India, Pakistan, and Papua New Guinea, which have the highest rates of oral cancer worldwide. Through this analysis, we uncovered higher contributions of areca nut products (with and without tobacco) to oral cancer incidence than most smokeless tobacco-only products in the four countries. These findings could also bring value to prevention and control of specific products.

Implications of all the available evidence

While there have been encouraging trends in control of tobacco smoking in many regions of the world, smokeless tobacco consumption prevalence has stalled in recent decades in many major consuming countries. Furthermore, areca nut does not fall within the framework of tobacco control and there are very few areca nut control policies worldwide. While the global proportion of oral cancers attributable to smokeless tobacco and areca nut consumption was 31%, we found that more than 95% of the burden of oral cancer attributable to smokeless tobacco and areca nut was in low- and middle-income countries. To reduce inequities in tobacco control, smokeless tobacco control must be prioritised. Furthermore, a framework on areca nut control should be developed with guidelines to incorporate areca nut prevention into cancer control programs.

INTRODUCTION

An estimated 300 million people use smokeless tobacco (ST) and 600 million people use areca nut (AN) globally, with the highest rates of use in South-Central Asia, South-East Asia, and Melanesia.[1,2] ST products are consumed without burning and can be chewed, sucked, inhaled, applied locally, or ingested. The preparation of ST products varies, being produced both commercially and non-commercially i.e. locally or home-made. ST products contain dried ground tobacco leaves and are sometimes mixed with a range of other ingredients such as slaked lime (calcium hydroxide), spices, or AN which is the seed of the fruit of the areca palm. While AN can be consumed in combination with ST, it is also often consumed alone, as betel quid without tobacco, or mixed with various condiments in commercially packaged preparations.[3] Detailed information on products containing ST and/or AN (ST/AN products) is provided in the appendix (pp 2–6).

The International Agency for Research on Cancer (IARC) Monographs program has classified ST, betel quid with tobacco, betel quid without tobacco, and AN as Group 1 carcinogens due to the strength of evidence that they cause cancer of the oral cavity.[4] In addition, the recent IARC Handbook volume 19 on oral cancer prevention concluded that cessation of use of AN products (including betel quid), with or without tobacco, reduces the risk of oral cancer.[5] The Working Group of this Handbook called for better surveillance of oral cancer risk factors such as ST, AN, tobacco smoking, and alcohol consumption, and an assessment of the burden of oral cancer attributable to consumption of ST/AN products.[5] Previous global studies estimated that oral cancers attributed to ST were the cause of 49 600 deaths and 1·4 million disability-adjusted life years (DALYs) in 2017,[6] but consumption of AN was not incorporated into their estimations. Furthermore, estimates of cancer incidence attributed to ST and AN would provide a more complete picture of the burden on health care and the potential impact of primary prevention.

Our comprehensive study aimed to estimate the number and proportion of oral cancer cases attributable to ST/AN consumption globally in 2022. To highlight the cancer burden associated with specific products, we also conducted a focused analysis by type of product in four populations that are major consumers of ST and/or AN and have reported detailed information on consumption by product type: Bangladesh, India, Pakistan, and Papua New Guinea. These four countries also have the highest rates of oral cancer incidence according to the latest global estimates for 2022.[7]

METHODS

Study design and data sources

We calculated population attributable fractions (PAFs) of oral cancer cases attributable to consumption of ST/AN using the prevalence of consumption and the associated relative risks (RRs) or odds ratios (ORs) of oral cancer.

We obtained prevalence of current consumption of ST/AN products among adults by age and sex, where available, from nationally representative surveys such as Global Adult Tobacco Survey (GATS), STEPwise approach to NCD risk factor surveillance (STEPs), Demographic Household Survey, Multiple Indicator Cluster Surveys, and national tobacco or health surveys. When multiple sources and years of data were available, we prioritised prevalence of current ST/AN use stratified by sex and selected the year closest to 2012 to allow for latency between ST/AN consumption and cancer outcome (cancer diagnosis in 2022). Measures of types of products were heterogeneous across countries because each country's questionnaire asked about locally relevant products e.g. India's GATS collected information on betel quid with tobacco, *sada*/*surti*, and *khaini*, among others; the Survey on Drug Use and Health in the United States asked about snuff and chewing tobacco; and Papua New Guinea's STEPs questionnaire only mentioned AN. Sex was collected as reported by each survey and data on race or ethnicity were not collected. In total, we obtained prevalence data from 164 countries, of which 156 reported prevalence of consumption by sex and 111 by age (appendix pp 7–11). We were unable to obtain prevalence data for 32 countries and imputed estimates using prevalence from neighbouring countries (appendix p 12).

We obtained RRs or ORs of oral cancer incidence associated with consuming ST/AN products from meta-analyses, pooled analyses, cohort and case-control studies that had been identified through the IARC Handbook vol. 19: Oral Cancer Prevention.[5] We selected RRs/ORs for each country based on the study's population and types of ST/AN products measured through discussion in focused expert meetings (OAY, PC, EG, PG, RG, SL, CM, MP, YP, KS, SW). The selected RRs and ORs are presented in the appendix (p 13).

We extracted the number of cases of cancer of the lip and oral cavity (International Classification of Diseases, 10th edition, C00-C06) in 2022 from the Global Cancer Observatory's Cancer Today (GLOBOCAN) database (https://gco.iarc.who.int/today/en). Cancer incidence estimates were obtained for 185 countries by sex and 5-year age-group (0–4, …, 85+ years).

For our focused analysis, we collected detailed prevalence of ST/AN consumption by type of product in the four countries with the highest incidence of oral cancer globally and for which prevalence data were available by product type: Bangladesh, India, Pakistan, and Papua New Guinea. Sex- and age-specific prevalence data were collected from GATS and STEPs surveys covering 13 specific products. Inhaled and drinkable ST products were excluded. More information on the product types included and sources of prevalence data and oral cancer risk estimates per product are provided in the appendix (p 14).

Statistical analysis

We calculated PAFs using a Levin-based formula by combining the sex-, age-, and country-specific prevalence (*P*) of ST and AN consumption with the RR of oral cancer, as in formula 1.

Formula 1

$$\mathrm{PAF} = \frac{P(\mathrm{RR}-1)}{P(\mathrm{RR}-1)+1}$$

While number of ST/AN-attributable oral cancer cases and PAFs are relevant for policy and allow interpretation of the absolute burden, we also provided age-standardised rates (ASRs) of cases of oral cancer attributable to ST and AN for international comparisons of the attributable burden relative to population size and age structure. We calculated ASRs using the Segi-Doll world standard population.[8] We aggregated our estimates to 18 United Nations geographical regions, six World Health Organization regions, and four World Bank income groups. For countries that we obtained prevalence data for and that national cancer estimates were not available (n=11), PAFs were aggregated in the estimates by world region. The PAFs for different product types within each country (focused analysis) should not be summed due to some cases being attributed to more than one product.

We carried out two sensitivity analyses to test the heterogeneity of the cancer risk and ST/AN prevalence data. In the first sensitivity analysis we used the RR for all smokeless tobacco use (3·94) from Siddiqi et al.'s global meta-analysis[6] for all countries to explore the change in PAF and attributable cases if assuming risk is equal across regions regardless of differences in products. In a second sensitivity analysis, we used the most recent year of ST/AN consumption data per country where more than one year of survey data was available to test whether differences in ST/AN consumption over time would affect the resulting PAFs. In this sensitivity analysis, more recent survey data were used for 67 countries (appendix pp 26–27).

Estimates of uncertainty were modelled using Monte Carlo sampling where 10 000 estimates of the prevalence of ST and AN consumption, RRs, and cancer incidence were randomly simulated based on their respective uncertainty distributions. We took the 2·5th and 97·5th percentiles from the 10 000 modelled PAF estimates to construct the 95% uncertainty intervals (UIs). All analyses and data visualisations were carried out using R (version 4.2.1).

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

RESULTS

Globally, an estimated 120 200 (95% UI, 115 300–124 300) cases of oral cancer in 2022 were attributable to consumption of ST/AN (Table 1), resulting in a PAF of 30·8% (29·6–31·9) of all oral cancer cases (120 200 of 389 800). An estimated 77·0% of attributable cases were among males (92 600 [88 000–96 500] cases) and the PAF among females was moderately lower than among males. Men also had a 4 times higher ASR of oral cancer cases attributable to ST/AN compared with women.

Between world regions, Melanesia, Micronesia & Polynesia had the highest PAF, followed by South-Central Asia and South-Eastern Asia (Figure 1, Table 1). Eastern Africa and Middle Africa also had considerable PAFs for ST/AN consumption. All European regions had PAFs less than 5%, similar to Australia and New

Zealand, South America, and Western Asia. Of the world total cases of oral cancer attributable to ST/AN, 87·8% of cases occurred in South-Central Asia (105 500 [100 500–109 300] of 120 200 cases). South-Eastern Asia and Eastern Asia had the second and third largest number of oral cancer cases attributable to ST/AN (3900 and 3300 cases, respectively). Generally, ST/AN PAFs were higher among males than females except in Southern Africa and South-Eastern Asia. The largest relative differences in PAFs between males and females were in Northern Africa, North America, Eastern Asia, and the Caribbean and Central America.

PAFs of oral cancer attributable to ST/AN among females were highest in Papua New Guinea (83·8% [77·2–87·3]), Bangladesh (60·8% [56·6–64·2]), India (51·5% [47·1–55·2]), and Myanmar (51·3% [46·7–55·1]) (Figure 2, appendix pp 15–24). Countries with the lowest PAFs were mostly in Northern and Eastern Europe and Western Asia. The highest ASR of oral cancer attributable to ST/AN in females was in Papua New Guinea (10·7 [9·9–11·1] per 100 000), followed by Bangladesh (4·3 [4·0–4·5]), India (2·6 [2·4–2·8]), and Pakistan (2·5 [2·2–2·9]) (appendix pp 15–24, 29). Female ASRs were below 2 cases per 100 000 in the remaining countries.

Among males, Papua New Guinea also had the highest PAF (84·1% [78·5–87·1]) but this was followed by Afghanistan (82·0% [78·0–84·1]), Uzbekistan (77·9% [72·8–80·9]), Tajikistan (75·1% [70·6–77·9]), and Myanmar (70·6% [66·7–73·4]) (Figure 2, appendix pp 15–24). Further countries in South-Central Asia had PAFs between 50% and 70%. The highest ASRs of oral cancer attributable to ST/AN among males were in Papua New Guinea (19·0 [17·6–19·6]), followed by India (8·8 [8·2–9·3]), Bangladesh (8·2 [7·6–8·7]), Sri Lanka (8·0 [7·3–8·5]), and Pakistan (7·8 [7·1–8·3]) (appendix pp 15–24, 29). La Réunion (France), Afghanistan, Myanmar, and Uzbekistan also had ASRs above 4 per 100 000 males, ASRs were below 4 in the remaining countries.

The group of lower-middle-income countries had the highest ST/AN PAF and ASR followed by low-income countries (Figure 3). The lower-middle-income group of countries represented the most cases of oral cancer attributable to ST/AN, with 90·2% (108 400 [103 400–112 200] cases [data not shown]) of the world total number of attributable cases. Only 3·6% of ST/AN-attributable cases were found in the high-income group of countries (4 300 [3 800–5 100] cases [data not shown]).

In our focused analysis by type of ST/AN product, consumption of betel quid with tobacco among females had the largest PAF of oral cancer cases in Bangladesh in 2022, followed by *gul* and *sada pata* (Figure 4). Although prevalence of consumption of all three products was lower among males in Bangladesh, betel quid with tobacco was also the product with the highest PAF. Of the eight ST/AN products reported in India, AN and betel quid with tobacco had the highest PAFs of oral cancer cases among females, followed by *gutka* and *khaini*, but betel quid without tobacco and AN were the most prevalent products. Among males, the products with the highest PAFs were *khaini*, *gutka*, betel quid with tobacco, and AN. In Pakistan, *naswar* had the highest PAFs among females and males despite relatively low prevalence of consumption among both sexes. AN was the sole product reported in Papua New Guinea with more than 77% of the population currently using AN, resulting in PAFs of over 83%. The PAFs for different products cannot be summed due to the potential of some oral cancer cases being attributed to more than one product.

In sensitivity analyses, the total number of oral cancer cases attributable to ST/AN consumption decreased to 97 600 (92 700–101 900) cases and a PAF of 25·0% (23·8–26·1) when we applied a global RR across all countries (appendix p 25). The drop in cases was mainly in South-Central Asia (84 200 [79 400–88 400] cases down from 105 500 [100 500–109 300]). When using the latest ST/AN consumption data rather than the survey year nearest to 2012, the total number of attributable oral cancer cases decreased to 114 400 (109 500–118 700) with a PAF of 29·3% (28·1–30·4) (appendix p 28). Most of the decrease was among women in South-Central and South-Eastern Asia, accounting for 4000 fewer cases than the main analysis. Interestingly, we found increases in attributable cases and PAFs in Eastern Europe and Eastern Asia following this sensitivity analysis compared with the main analysis.

DISCUSSION

We estimated that more than 120 000 cases of oral cancer in 2022 were attributable to ST/AN consumption, equating to 31% of the 389 000 oral cancer cases diagnosed globally in 2022. More than three quarters of attributable cases were among males. The proportion of oral cancers attributable to ST/AN was highest in Melanesia, Micronesia & Polynesia followed by South-Central Asia and South-Eastern Asia. We also found

that, generally, males had higher PAFs than females, except in Southern Africa and South-Eastern Asia. Furthermore, over 95% of cases of oral cancer attributable to ST/AN were in the low- and lower-middle-income group of countries. Our focused analysis of Bangladesh, India, Pakistan, and Papua New Guinea highlighted the substantial contributions of ST/AN products in the countries with the highest rates of oral cancer and uncovered higher PAFs among AN products with and without tobacco than most ST-only products.

Previous studies have also summarised the burden of disease attributable to ST. Siddiqi et al.[6] found that at least 2·5 million DALYs and 90 800 lives were lost due to oral, pharyngeal, and oesophageal cancers attributed to ST globally in 2017, including 49 600 oral cancer deaths (26% of all oral cancer deaths). At the national level, we generally reported higher PAFs than Siddiqi et al. with Timor-Leste (68% vs 48%) and Bangladesh (60% vs 48%) having the largest differences between our estimates. The Global Burden of Disease (GBD) study also reported that 19% of oral cancer deaths in 2019 were attributable to chewing tobacco at the global level but did not include AN products without tobacco, resulting in a PAF of only 5% for Papua New Guinea.[9] The findings from both studies differed from ours because we used alternative oral cancer risk estimates for several countries and regions and our PAFs were for oral cancer incidence rather than mortality. Our findings could be considered more representative of the true burden of oral cancer attributable to ST/AN because we used nationally representative prevalence data from 164 countries, as opposed to 127 countries collected by Siddiqi et al.[6], and our cancer estimates were based more closely on cancer registry data than the GBD's modelling approach.[9,10] Moreover, Siddiqi et al. and GBD did not specifically incorporate AN which is currently slipping under the radar of global burden estimates despite its harmful impact on societies where AN consumption is most common.

As has been well documented, ST/AN products are diverse and each product poses a different effect on cancer risk. Consuming *naswar* — a type of snuff that contains a mix of dried powdered tobacco leaves, ash, cotton, and flavourings and is most commonly used in parts of South-Central and Western Asia — is associated with an 11·8–14·5 times increased risk of oral cancer compared with those who do not use tobacco.[6,11] The magnitude of oral cancer risk associated with ST use is strongly associated with the levels of tobacco-specific nitrosamines present.[4] Specifically, levels of N'-nitrosonornicotine (NNN) and nicotine-derived nitrosamine

ketone (NNK) in *toombak* — a type of moist snuff most commonly consumed in Sudan and associated with a nearly 4 times increased risk of oral cancer[12] — were about 100 times higher than in most ST products.[13] Evidence on the risk of oral cancer associated with using Swedish *snus* is currently inconclusive, with several studies suggesting a significantly increased risk of up to 3 times among ever daily *snus* users compared with never daily users,[14] and others suggesting no statistically significant elevated risk among current users compared with non-users,[6,15] due to the considerably lower levels of NNN and NNK than other ST products.[13] The use of ST/AN products can also be region-specific within large countries such as India,[16] and sub-national estimates of attributable burden could provide valuable insights into the local impact on oral cancer.

While the Framework Convention on Tobacco Control (FCTC)'s definition of tobacco products is inclusive of ST, implementation of the FCTC has primarily emphasised cigarettes.[1] This focus on cigarettes has resulted in falling prevalence of smoking tobacco over the last 20 years but prevalence of chewing tobacco has remained stable.[1] A systematic review found ST policies in 57 countries, with the most implemented policies being mandatory use of pictorial health warnings and bans on advertisements, promotions and sponsorship, although their level of enforcement varied between settings.[17] Several countries have recently banned manufacturing and sales of ST overall (Bhutan, Singapore, and Sri Lanka) or commonly used ST products (*gutka* banned in India), as well as importing ST products (Thailand, Iran, and Niue) or use in public places (Guam, India, Myanmar, Pakistan, Nepal, and the US).[17] The authors also highlighted the importance of developing tobacco-free rather than smoke-free goals when discussing tobacco control and ensuring that ST prevention and cessation services remain a priority in high-burden countries.[17] Additionally, products containing AN without tobacco are not included under the FCTC. Guidelines on AN prevention including banning spitting in public places, prohibiting sales to minors, and putting cancer warning labels on AN product packaging, where appropriate, should be incorporated into national cancer control programs.[18] Finally, while men are the main consumers of ST/AN in most regions of the world, prevalence of ST/AN consumption among women in Southern African and South-East Asian countries is higher than among men (for example, 7% of women vs 2% of men in Botswana[19], and 5% of women vs 1% of men in Thailand.)[20] Thus, an intersectional lens must be applied to ST/AN control in order to implement gender-sensitive policies to ensure reduction of AN and smokeless and smoked tobacco in diverse cultural contexts.[21]

We consider our analysis to be the most comprehensive estimation of oral cancer burden attributable to ST/AN. Nevertheless, we were unable to obtain prevalence for 32 countries in our analysis and thus imputed from neighbouring countries. This approach might not have been reasonable due to socioeconomic disparities between neighbouring countries but oral cancer ASRs in countries missing prevalence data were generally similar to or higher than the average ASRs from their imputing countries (appendix p 12), indicating that we have taken a conservative approach. The absence of prevalence data in certain countries could be interpreted as the absence of ST/AN use, but monitoring should still be undertaken to confirm this assumption. Furthermore, the heterogeneity of the ST/AN prevalence data regarding the year, age, sex, and the level of detail on product type highlights the need to standardise data collection when possible. Most countries report overall smokeless tobacco use and do not provide a detailed breakdown by product. In order to thoroughly present the impact of specific products, we restricted our focused analysis to four populations that are major consumers of ST/AN and have reported detailed information on consumption by product type. Also, we required advice from local experts to match the most appropriate risk estimate for oral cancer with the mix of products used in each population because many of the cancer risk studies did not report the specific ST/AN products used and there were evident gaps of studies in sub-Saharan Africa and Latin America.[22] Furthermore, these observational studies might not have sufficiently adjusted for confounding by consumption of other products because our PAF of betel quid with tobacco for women in Bangladesh was higher than that for ST/AN consumption overall.

Further limitations of our study include not accounting for the potential synergistic effects of combined use of ST/AN products with other risk factors for oral cancer such as tobacco smoking or alcohol consumption.[4] Combined consumption of ST/AN, smoked tobacco, and alcohol has a multiplicative effect on oral cancer risk, with reported ORs increasing from 2·7 for ST only, 7·0 for smoked tobacco only, and 1·6 for alcohol only, to an OR of 16·2 for synergistic consumption of all three exposures compared with abstainers.[23] However, the proportion of people who chewed tobacco and also smoked in several high ST/AN prevalence countries was small; for example, in India, 6% of men and 0·5% of women in 2016-17 were dual users of both smoked tobacco and ST as opposed to 23% of men and 12% of women who only used ST.[16] Other limitations of our study include inherent uncertainties in the GLOBOCAN cancer incidence estimates which depend on

the degree of representativeness and quality of the data used as the basis of the estimation.[10] Population-based cancer registries are still limited in countries with fewer resources and where the estimated burden of oral cancer attributable to ST/AN is heaviest.[10] Increasing capacity for quality cancer registration in these regions would enable improved monitoring of oral cancer control.

In summary, more than 120 000 cases of oral cancer globally in 2022 were attributable to consumption of ST and AN. While there have been encouraging trends in the implementation of policies to control tobacco smoking in several regions of the world, progress in most countries has not extended to control of ST and AN. As a result, ST/AN consumption has not significantly decreased in recent decades in many major consuming countries. Our product-specific findings show that some specific ST/AN products are responsible for up to 84% of oral cancer cases in countries with the highest rates of oral cancer. Considering that more than 95% of oral cancers attributable to ST and AN were in low- and middle-income countries where survival from oral cancer is also the lowest,[24] primary prevention should be prioritised to tackle disparities in oral cancer globally. Finally, we must develop and reinforce control of ST and AN to reduce inequities in tobacco control.

AUTHOR CONTRIBUTIONS

BLS, STN, and IS conceived the study. HR, BLS, STN, and IS designed the study; HR, STN, JV, RS, NR, SL and IS collected the data; HR, RS, and JV verified all underlying data; HR and RS performed the analysis; HR, BLS, STN, IS interpreted the findings; HR drafted the first version of the manuscript; All authors critically reviewed the manuscript; All authors agreed with the decision to submit for publication. The corresponding author had final responsibility for the decision to submit for publication.

DATA SHARING

The ST/AN prevalence data used in this study are published in publicly available country reports. The cancer incidence data used in this study are available to the public from the Global Cancer Observatory (GLOBOCAN) https://gco.iarc.who.int/. All statistical code (R code) used to produce the results presented in this article are available to the public via GitHub at https://github.com/HRumgay/ST_AN_PAF.

DECLARATION OF INTERESTS

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TABLES AND FIGURES

Table 1. Number, population attributable fraction (PAF, %), and age-standardised rate (ASR per 100 000) of oral cancer cases in 2022 attributable to smokeless tobacco and/or areca nut consumption by sex, world region, and World Health Organization (WHO) region

	Females			Males			Both sexes		
United Nations geographical region	**Attributable cases**	**PAF (%)**	**ASR**	**Attributable cases**	**PAF (%)**	**ASR**	**Attributable cases**	**PAF (%)**	**ASR**
Africa									
Eastern Africa	220 (205–240)	11·5 (10·5–12·5)	0·2 (0·2–0·2)	460 (435–480)	17·0 (16·1–17·8)	0·4 (0·4–0·5)	680 (650–710)	14·7 (14·0–15·3)	0·3 (0·3–0·3)
Middle Africa	60 (55–70)	8·2 (7·0–9·2)	0·1 (0·1–0·2)	140 (125–155)	16·6 (14·7–18·3)	0·3 (0·3–0·4)	205 (185–220)	12·6 (11·4–13·6)	0·2 (0·2–0·3)
Northern Africa	10 (10–10)	0·6 (0·5–0·7)	0·0 (0·0–0·0)	230 (200–265)	12·2 (10·7–14·0)	0·2 (0·2–0·2)	240 (210–275)	6·7 (5·9–7·7)	0·1 (0·1–0·1)
Southern Africa	95 (85–110)	14·2 (12·5–16·3)	0·3 (0·2–0·3)	45 (40–55)	3·7 (3·2–4·4)	0·2 (0·1–0·2)	140 (125–155)	7·4 (6·8–8·3)	0·2 (0·2–0·3)
Western Africa	80 (75–85)	5·9 (5·4–6·3)	0·1 (0·1–0·1)	120 (110–135)	7·2 (6·6–8·0)	0·1 (0·1–0·1)	200 (185–215)	6·6 (6·2–7·1)	0·1 (0·1–0·1)
Americas									
North America	70 (55–100)	0·7 (0·5–1·0)	0·0 (0·0–0·0)	2 300 (1 800–3 100)	10·8 (8·4–14·6)	0·7 (0·5–0·9)	2 400 (1 800–3 200)	7·6 (5·9–10·2)	0·3 (0·3–0·5)
Caribbean and Central America	10 (10–15)	0·8 (0·6–1·1)	0·0 (0·0–0·0)	185 (165–215)	8·0 (7·1–9·2)	0·2 (0·1–0·2)	200 (175–225)	5·2 (4·6–5·9)	0·1 (0·1–0·1)
South America	130 (95–160)	2·7 (2·1–3·5)	0·0 (0·0–0·0)	345 (290–420)	3·2 (2·7–3·9)	0·1 (0·1–0·1)	475 (405–555)	3·1 (2·6–3·6)	0·1 (0·1–0·1)
Asia									
Eastern Asia	130 (115–165)	0·7 (0·6–0·9)	0·0 (0·0–0·0)	3 200 (2 800–3 700)	10·0 (8·8–11·6)	0·2 (0·2–0·3)	3 300 (3 000–3 900)	6·6 (5·9–7·6)	0·1 (0·1–0·1)
South-Eastern Asia	1 800 (1 700–1 900)	23·3 (22·0–24·7)	0·4 (0·4–0·4)	2 100 (2 000–2 200)	17·5 (16·7–18·5)	0·6 (0·6–0·6)	3 900 (3 800–4 100)	19·8 (19·0–20·6)	0·5 (0·5–0·5)
South-Central Asia	24 200 (22 500–25 500)	49·7 (46·3–52·5)	2·4 (2·3–2·6)	81 400 (76 700–85 000)	60·3 (56·8–63·0)	8·0 (7·5–8·3)	105 500 (100 500–109 300)	57·5 (54·8–59·5)	5·2 (5·0–5·4)
Western Asia	50 (45–55)	2·7 (2·4–3·0)	0·0 (0·0–0·0)	110 (100–120)	3·7 (3·3–4·1)	0·1 (0·1–0·1)	160 (145–175)	3·3 (3·0–3·6)	0·1 (0·0–0·1)
Europe									
Eastern Europe	35 (20–50)	0·5 (0·3–0·8)	0·0 (0·0–0·0)	285 (230–355)	1·7 (1·3–2·1)	0·1 (0·1–0·2)	320 (260–390)	1·4 (1·1–1·7)	0·1 (0·1–0·1)
Northern Europe	110 (80–145)	3·1 (2·3–4·2)	0·1 (0·1–0·1)	215 (160–285)	3·6 (2·7–4·8)	0·2 (0·2–0·3)	325 (265–400)	3·4 (2·8–4·3)	0·2 (0·1–0·2)
Southern Europe	145 (120–180)	3·3 (2·6–4·1)	0·1 (0·0–0·1)	235 (195–290)	3·0 (2·5–3·7)	0·1 (0·1–0·2)	385 (335–445)	3·1 (2·7–3·6)	0·1 (0·1–0·1)
Western Europe	130 (105–165)	2·2 (1·7–2·7)	0·0 (0·0–0·1)	630 (550–735)	5·8 (5·1–6·8)	0·3 (0·3–0·4)	760 (680–870)	4·5 (4·0–5·2)	0·2 (0·2–0·2)
Oceania									

Australia and New Zealand	10 (5–10)	0·8 (0·7–1·0)	0·0 (0·0–0·0)	45 (40–50)	2·1 (1·9–2·5)	0·2 (0·1–0·2)	50 (45–60)	1·7 (1·5–2·0)	0·1 (0·1–0·1)
Melanesia, Micronesia and Polynesia	370 (340–385)	78·1 (72·0–81·3)	7·2 (6·6–7·5)	610 (570–630)	78·8 (73·6–81·6)	12·6 (11·8–13·1)	980 (930–1 000)	78·6 (74·4–80·5)	9·8 (9·3–10·1)
WHO regions									
African region (AFRO)	450 (425–480)	9·5 (9·0–10·1)	0·1 (0·1–0·1)	805 (775–835)	12·3 (11·8–12·8)	0·3 (0·3–0·3)	1 300 (1 200–1 300)	11·1 (10·8–11·5)	0·2 (0·2–0·2)
Region of the Americas (PAHO)	210 (175–255)	1·3 (1·1–1·6)	0·0 (0·0–0·0)	2 800 (2 300–3 600)	8·2 (6·7–10·5)	0·4 (0·3–0·5)	3 000 (2 500–3 800)	6·0 (5·0–7·6)	0·2 (0·2–0·2)
Eastern Mediterranean region (EMRO)	2 200 (1 900–2 500)	25·9 (22·3–29·2)	0·8 (0·6–0·9)	7 800 (7 100–8 200)	52·0 (47·8–55·0)	2·4 (2·2–2·6)	10 000 (9 300–10 500)	42·5 (39·5–44·8)	1·6 (1·5–1·7)
European region (EURO)	505 (455–570)	2·3 (2·1–2·6)	0·0 (0·0–0·0)	2 400 (2 300–2 500)	5·3 (5·0–5·6)	0·3 (0·3–0·3)	2 900 (2 800–3 100)	4·3 (4·1–4·6)	0·2 (0·2–0·2)
South-East Asia region (SEARO)	23 400 (21 800–24 800)	49·2 (45·8–52·0)	2·1 (2·0–2·3)	74 800 (70 300–78 400)	57·7 (54·2–60·5)	6·9 (6·5–7·2)	98 200 (93 400–102 000)	55·4 (52·7–57·5)	4·5 (4·3–4·7)
Western Pacific region (WPRO)	825 (785–875)	3·8 (3·6–4·0)	0·0 (0·0–0·0)	4 100 (3 700–4 600)	10·5 (9·5–11·8)	0·3 (0·2–0·3)	4 900 (4 500–5 400)	8·1 (7·4–8·9)	0·2 (0·1–0·2)
World	27 600 (26 000–29 000)	22·8 (21·5–24·0)	0·6 (0·5–0·6)	92 600 (88 000–96 500)	34·4 (32·7–35·9)	2·0 (1·9–2·1)	120 200 (115 300–124 300)	30·8 (29·6–31·9)	1·3 (1·2–1·3)

Data in parentheses are 95% uncertainty intervals. ASR: Age-standardised rate per 100 000 population; PAF: Population attributable fraction.

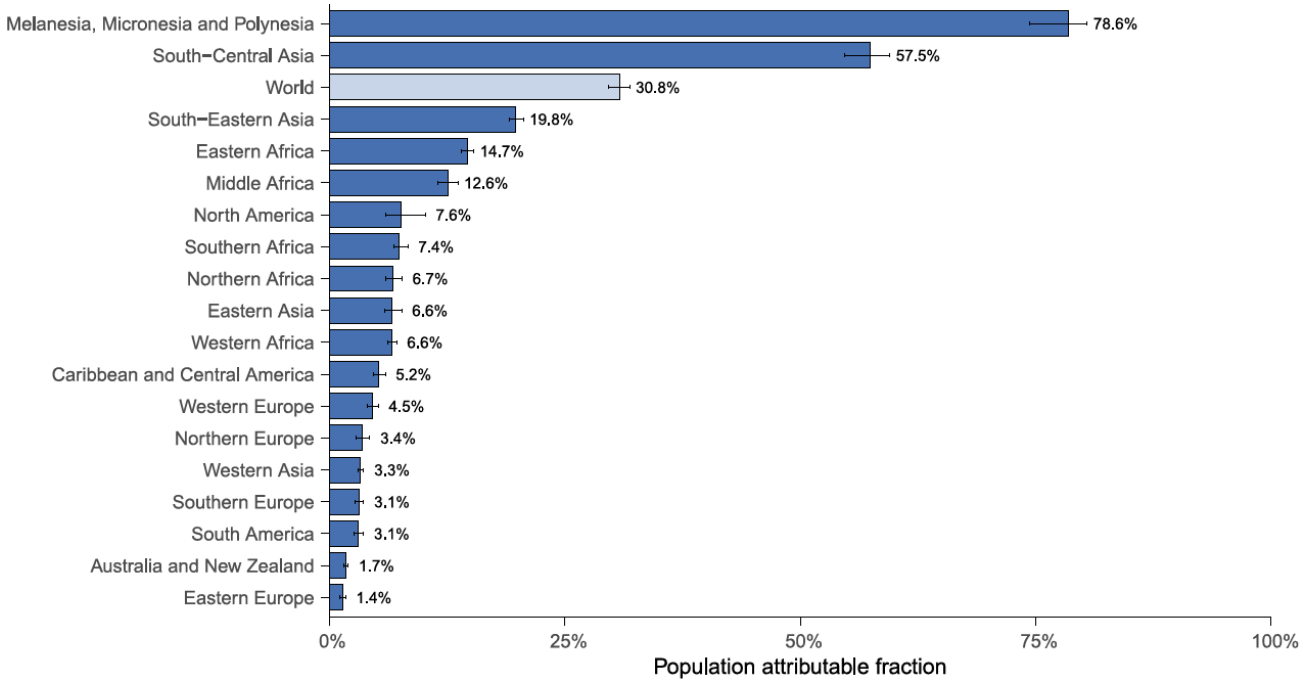


Figure 1. Population attributable fraction of oral cancer cases in 2022 attributable to smokeless tobacco and/or areca nut consumption, by world region

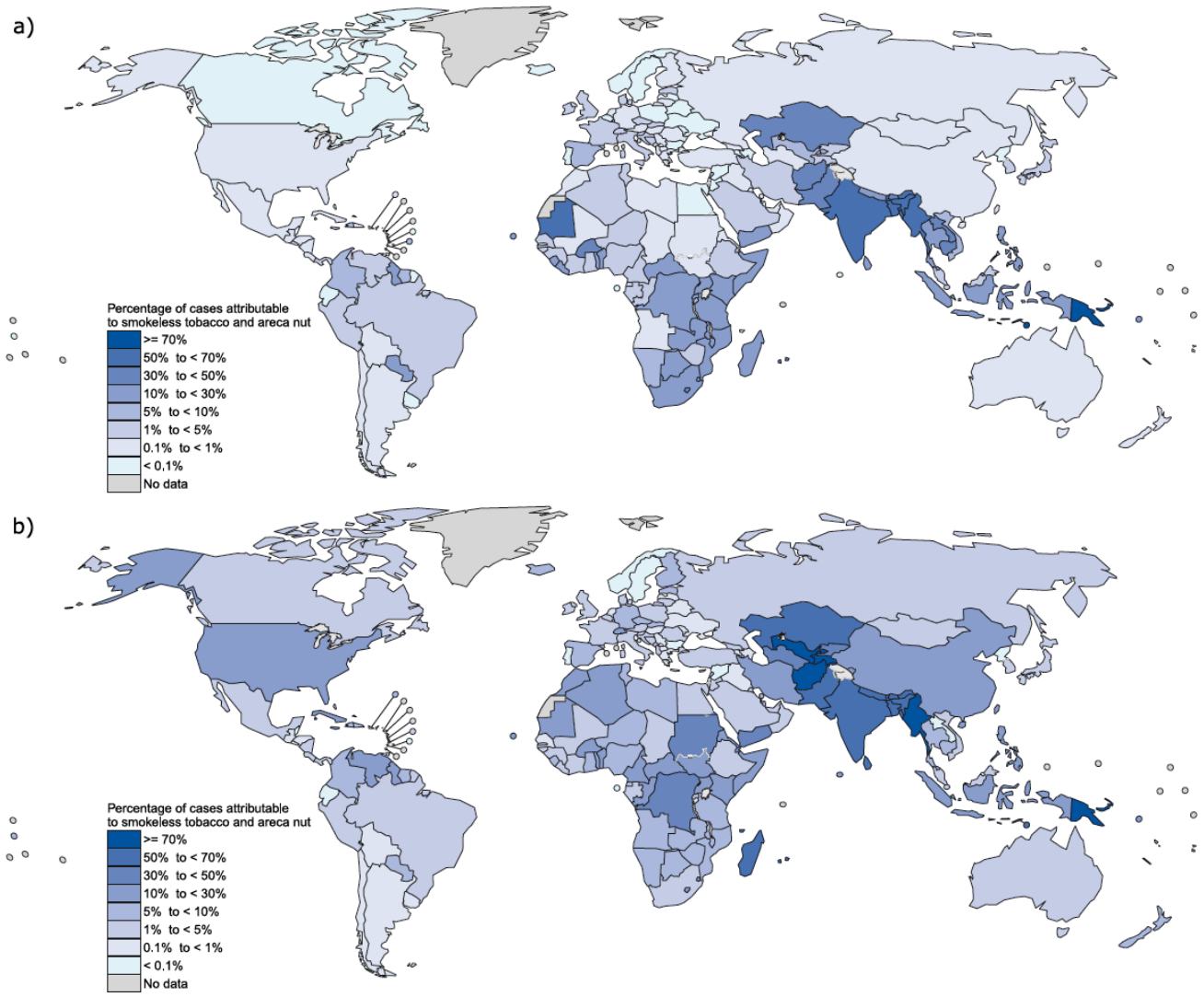


Figure 2. Population attributable fraction of oral cancer cases in 2022 attributable to smokeless tobacco and/or areca nut consumption among (a) females and (b) males, by country

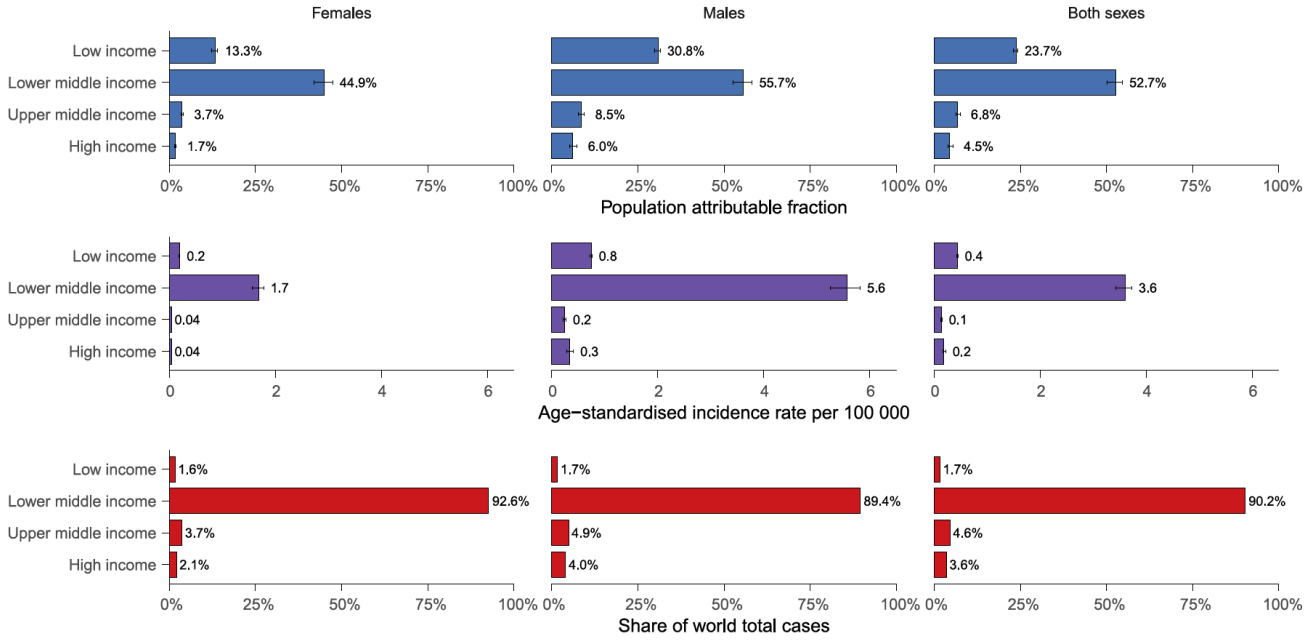
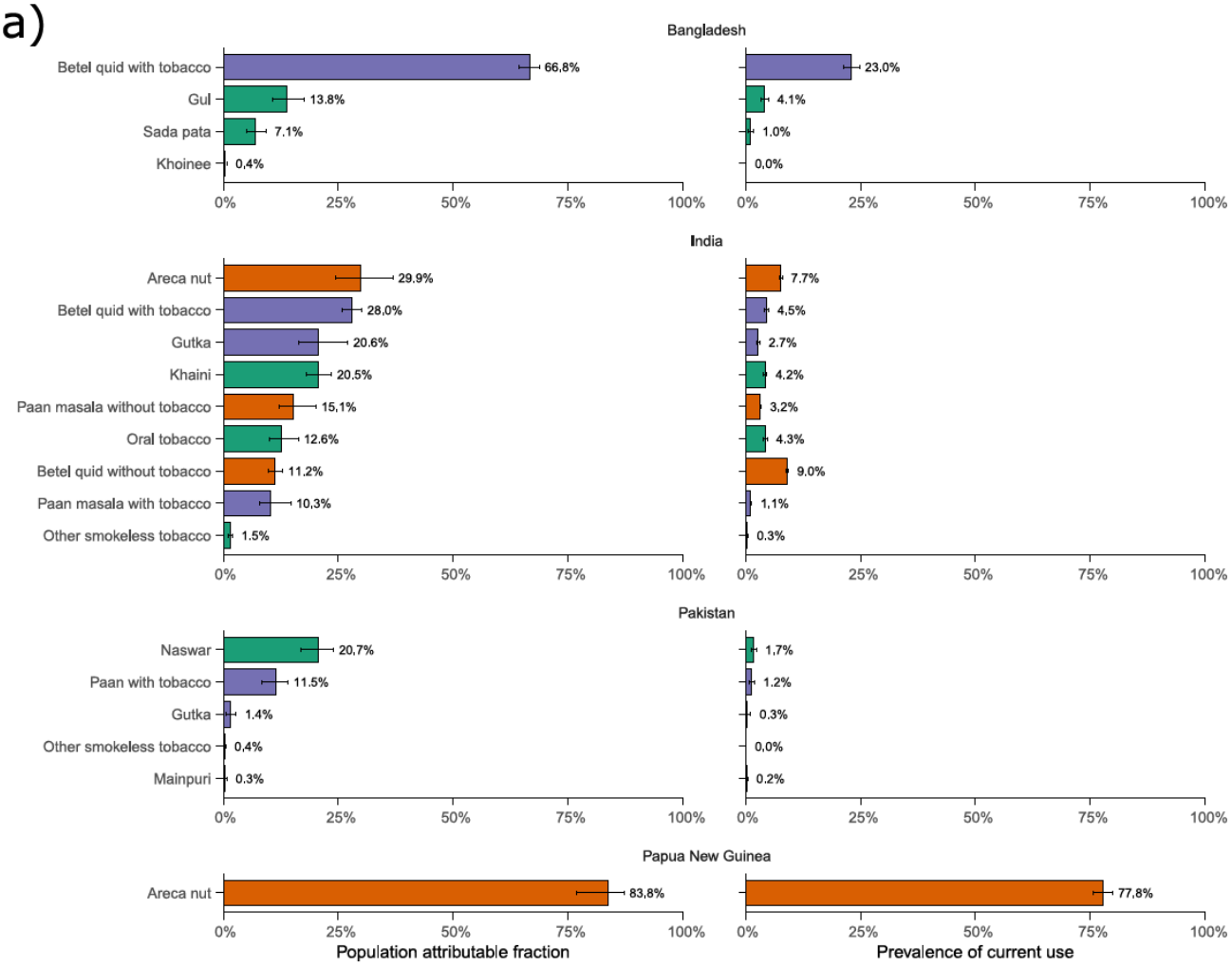


Figure 3. Population attributable fraction, age-standardised incidence rate, and share of world total oral cancer cases in 2022 attributable to smokeless tobacco and/or areca nut consumption, by sex and World Bank income group

a)


Bangladesh
Betel quid with tobacco
Gul
Sada pata
Khoinee
66.8%
13.8%
7.1%
0.4%
23.0%
4.1%
1.0%
0.0%
India
Areca nut
Betel quid with tobacco
Gutka
Khaini
Paan masala without tobacco
Oral tobacco
Betel quid without tobacco
Paan masala with tobacco
Other smokeless tobacco
29.9%
28.0%
20.6%
20.5%
15.1%
12.6%
11.2%
10.3%
1.5%
7.7%
4.5%
2.7%
4.2%
3.2%
4.3%
9.0%
1.1%
0.3%
Pakistan
Naswar
Paan with tobacco
Gutka
Other smokeless tobacco
Mainpuri
20.7%
11.5%
1.4%
0.4%
0.3%
1.7%
1.2%
0.3%
0.0%
0.2%
Papua New Guinea
Areca nut
83.8%
77.8%
0%
25%
50%
75%
100%
Population attributable fraction
Prevalence of current use

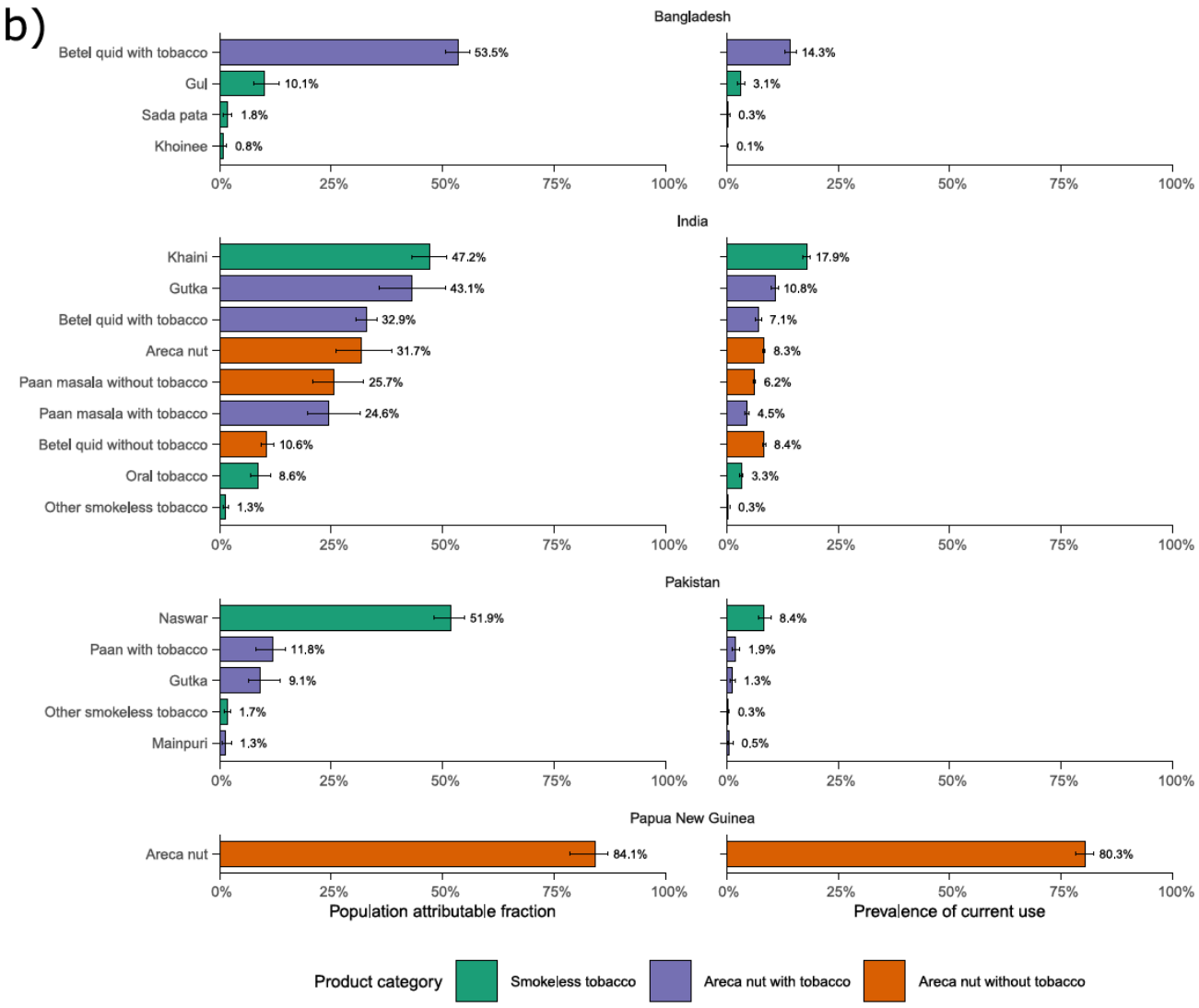


Figure 4. Population attributable fraction of oral cancer cases attributable to smokeless tobacco and/or areca nut consumption in 2022 and prevalence of current use by product type in Bangladesh, India, Pakistan, and Papua New Guinea among (a) females and (b) males