



NON COMMUNICABLE DISEASE

Lip and Oral Cavity Cancer Worldwide in 2024: A Comprehensive Ecological Study of Burden, Socio-Demographic Disparities, and Population-Level Risk Factors

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Keywords

Lip cancer • Oral cavity cancer • Ecological study • Global burden • Risk factors • Socio-demographic disparities

Summary

Background. Lip and oral cavity cancer (LOCC) remains a substantial global cancer burden with marked sex and geographical disparities. Updated global estimates integrating cancer burden, behavioral exposures, and socioeconomic context are needed to clarify current patterns and identify population-level priorities for prevention and control.

Methods. We conducted an ecological analysis of GLOBOCAN 2024 LOCC estimates (ICD-10 C00-C06) across 186 countries. Age-standardized incidence (ASIR) and mortality rates (ASMR) were examined by sex, region, and income level. Associations with age-standardized smoking and alcohol Summary Exposure Values and Human Development Index (HDI) indicators were evaluated using multivariable linear regression, with historical analyses based on 1990 and 2010 data.

Results. In 2024, an estimated 452,062 new LOCC cases (ASIR: 4.5 per 100,000) and 194,059 deaths (ASMR: 1.9) occurred glob-

ally, with higher ASIR and ASMR among males than females. In fully adjusted ecological models, smoking prevalence was positively associated with ASIR among females ($\beta=0.349$, $p=0.012$), while alcohol use was positively associated with both ASIR ($\beta=0.275$, $p=0.006$) and ASMR ($\beta=0.206$, $p=0.046$) among males. Historical analyses from 1990 and 2010 showed substantial directional concordance with contemporary associations, indicating persistent but sex-specific ecological patterns across the examined periods.

Conclusion. LOCC continues to impose a substantial and uneven global burden, with distinct sex-specific associations involving tobacco and alcohol exposure. Socioeconomic development showed no independent fully adjusted association with LOCC outcomes. These findings support context-specific prevention, sustained exposure surveillance, and stronger early detection and treatment capacity.

Introduction

Cancer remains a leading global health challenge, with head and neck malignancies comprising a heterogeneous group of tumors that affect the upper aerodigestive tract, including the oral cavity, pharynx, and larynx [1]. Among these, lip and oral cavity cancers (LOCC), defined by ICD-10 codes C00-C06, represent a distinct group of malignancies involving the lip, tongue, gingiva, floor of the mouth, palate, and other sites of the oral cavity [2, 3]. Histologically, LOCCs are predominantly squamous cell carcinomas [4, 5] and can cause substantial morbidity through impairment of essential functions, including speech, mastication, swallowing, and oral competence, as well as through significant psychosocial and aesthetic consequences [6, 7].

The etiology of LOCC is largely attributed to modifiable environmental and behavioral exposures [8]. Tobacco use - whether smoked or smokeless - remains the most significant risk factor globally [9, 10]. Excessive alcohol consumption independently increases risk and acts synergistically with tobacco, amplifying carcinogenic

effects through mechanisms such as mucosal permeability and DNA damage [10-12]. In south and southeast Asia, the habitual chewing of betel quid, containing areca nut and frequently tobacco, is a dominant and culturally ingrained practice contributing significantly to LOCC incidence [13, 14]. Other implicated factors include chronic sun exposure (particularly for lip cancer), high-risk human papillomavirus (HPV) infection, poor oral hygiene, nutritional deficiencies (notably in fruit and vegetable intake), and chronic mechanical irritation [8, 9, 15].

The interplay and prevalence of these exposures vary substantially across regions, producing marked global disparities in LOCC incidence and mortality [1, 2, 16]. Regions such as south-central Asia, Melanesia, and parts of central and eastern Europe have historically reported the highest incidence rates [17]. Shifting epidemiological landscapes - driven by demographic transitions, aging populations, evolving patterns of tobacco and alcohol consumption, and the implementation of cancer control policies - warrant continual surveillance [8, 10, 12, 13].

Despite its burden, LOCC is often underprioritized in global cancer control discourse. Thus, timely and robust epidemiological evaluations are necessary. The Global Cancer Observatory's GLOBOCAN 2024 database, curated by the International Agency for Research on Cancer (IARC), provides a standardized and comprehensive platform for global cancer estimation [1]. The present study utilizes the most recent GLOBOCAN 2024 data to provide an updated and in-depth analysis of LOCC burden across 186 countries. It aims to quantify global incidence and mortality, describe age-standardized rates across continents, World Health Organization (WHO) regions, and national income levels, and explore sex-based disparities. In addition, the study evaluates ecological correlations between LOCC burden and national-level behavioral risk factors - specifically tobacco smoking and alcohol use - and socioeconomic indicators, particularly the Human Development Index (HDI) and its core components (life expectancy, mean years of schooling, and gross national income per capita) [18-22]. Through multivariable linear regression models adjusting for potential confounders, we aim to provide a nuanced understanding of population-level determinants of LOCC incidence and mortality.

Materials and Methods

STUDY DESIGN AND DATA SOURCES

This ecological study assessed the global burden of lip and oral cavity cancer (LOCC) for the year 2024. The ecological design was selected to examine cross-country and regional variation in LOCC incidence and mortality and to evaluate population-level associations between disease burden and selected behavioral and socioeconomic factors [23].

LOCC incidence and mortality estimates for 2024 were obtained from the Global Cancer Observatory (GLOBOCAN), maintained by the International Agency for Research on Cancer (IARC), which provides standardized cancer estimates across countries [24]. In the present study, LOCC was defined according to ICD-10 codes C00-C06, encompassing malignancies of the lip, tongue, gingiva, floor of the mouth, palate, and other sites of the oral cavity. Estimates were available for males, females, and both sexes combined. For countries without population-based cancer registries, national estimates were derived using established modelling approaches incorporating incidence-to-mortality ratios, regional extrapolation, and demographic characteristics [25, 26].

RISK-FACTOR EXPOSURE DATA

Risk-factor exposure data were obtained from the Global Burden of Disease Study 2019 (GBD 2019) and its supplementary results [27]. The present study used the age-standardized Summary Exposure Values (SEVs) for the relevant risk factors. For smoking and alcohol use, point estimates were extracted for 1990, 2010, and 2019, separately for males, females, and both sexes combined. The extracted SEVs represent population-level, risk-

weighted exposure measures rather than conventional survey-based prevalence estimates. SEVs incorporate the distribution of exposure across the population and the corresponding relative risk associated with different exposure levels and are expressed on a 0-100 scale, with higher values indicating greater exposure relative to the theoretical minimum-risk level. Therefore, the smoking and alcohol variables used in the regression analyses were interpreted as SEVs rather than direct percentages of individuals reporting current smoking or alcohol use. Only reported point estimates were used in the analyses. Uncertainty intervals, percentage changes, or values derived from alternative sources were not substituted for the reported estimates. When a valid point estimate was unavailable for a specific country, sex, or year, the corresponding observation was treated as missing and was not imputed.

For the primary analyses, smoking and alcohol-use SEVs for 2019 were used. Additional historical analyses were performed using the corresponding 1990 and 2010 exposure estimates to evaluate the temporal robustness of the observed ecological associations.

HDI AND ITS COMPONENTS

Socioeconomic development was assessed using the HDI and its three core components: life expectancy at birth, mean years of schooling, and gross national income (GNI) per capita. HDI data were obtained from the United Nations Development Programme (UNDP) Human Development Reports and associated standardized time-series data [28].

For the primary analyses presented in this report, 2023 HDI values and the corresponding component indicators were used. For the additional historical analyses, HDI and its components were extracted for 1990 and 2010. This approach allowed the relationship between long-term socioeconomic development and LOCC burden to be examined across different periods.

GNI per capita was expressed in purchasing power parity-adjusted international dollars and entered into the regression models in units of 1,000 international dollars. HDI summarizes national achievement across health, education, and income dimensions, and the use of harmonized time-series data allowed consistent comparisons across the study years.

OUTCOME MEASURES

The primary outcomes were the age-standardized incidence rate (ASIR) and age-standardized mortality rate (ASMR) for LOCC, expressed per 100,000 person-years and standardized using the Segi world standard population. Crude rates and absolute numbers of incident cases and deaths were also considered. Sex-specific ASIRs and ASMRs were used to calculate male-to-female ratios, and the proportional contribution of each WHO region to the global LOCC burden was estimated.

GEOGRAPHIC AND ECONOMIC CLASSIFICATION

Analyses were conducted at global, continental (Africa, Asia, Europe, Latin America and the Caribbean,

Northern America, and Oceania), and WHO regional levels (AFRO, PAHO, SEARO, EURO, EMRO, and WPRO). Countries were also classified according to the 2024 World Bank income classification as high-income, upper-middle-income, lower-middle-income, or low-income countries.

STATISTICAL ANALYSIS

Descriptive analyses included absolute numbers, crude rates, ASIRs, ASMRs, and sex-specific ratios. Inferential analyses used multivariable linear regression to evaluate ecological associations between country-level smoking and alcohol-use exposure, HDI and its components, and LOCC outcomes (ASIR and ASMR). Regression models were estimated separately for males, females, and both sexes combined.

For analyses of smoking and alcohol use, four sequential models were specified. Model 1 was unadjusted. Model 2 adjusted for the other behavioral exposure (alcohol when smoking was the primary exposure and smoking when alcohol was the primary exposure). Model 3 adjusted for HDI. Model 4 was fully adjusted for the behavioral exposure and HDI.

For analyses of HDI and its components, Model 1 was unadjusted, Model 2 adjusted for smoking exposure, Model 3 adjusted for alcohol-use exposure, and Model 4 adjusted for both smoking and alcohol-use exposures. Regression outputs included unstandardized coefficients (B), standard errors (SE), standardized coefficients (β), and two-sided *p*-values. Statistical significance was defined as $p < 0.05$. Multicollinearity was assessed using variance inflation factors (VIF), and model assumptions, including linearity and homoscedasticity, were evaluated using residual plots.

To assess temporal robustness, additional ecological regression analyses were conducted using smoking and alcohol-use SEVs from 1990 and 2010 and HDI and its components from the corresponding years, while retaining the 2024 LOCC ASIR and ASMR as outcomes. These analyses were performed separately by sex and followed the same four-model framework. Complete-case observations were used for each model, and no missing exposure or socioeconomic values were imputed. Analyses were performed using SPSS version 26.0 (SPSS Inc., Chicago, IL, USA).

Results

GLOBAL BURDEN OF LIP AND ORAL CAVITY CANCER

In 2024, an estimated 452,062 new LOCC cases occurred globally, with an ASIR of 4.5 per 100,000. Males accounted for 70.6% of all incident cases ($n=319,240$), compared to 29.4% among females ($n=132,822$). The ASIR was 6.7 in males and 2.4 in females, yielding a male-to-female ratio of 2.79 (Tab. I).

Global LOCC mortality totaled 194,059 deaths, with 70.7% ($n=137,169$) in males and 29.3% ($n=56,890$) in females. The overall ASMR was 1.9 per 100,000, with

sex-specific rates of 2.8 (males) and 0.99 (females). The male-to-female mortality ratio was 2.83 (Tab. II).

GEOGRAPHICAL VARIATION BY CONTINENT AND WHO REGION

Marked regional disparities were observed. Among WHO regions, SEARO reported the highest LOCC burden, with ASIR of 10.4 and ASMR of 4.6, contributing the largest share of global incident cases and deaths. Other regions showed moderate burdens: EURO (ASIR 3.8; ASMR 1.4), EMRO (ASIR 2.6; ASMR 1.6), PAHO (ASIR 3.4; ASMR 0.87), and WPRO (ASIR 1.9; ASMR 0.84). AFRO reported the lowest ASIR (1.6) and ASMR (1.0).

By continent, Oceania had the highest ASIR (7.1), followed by Asia (5.3), Northern America (4.6), and Europe (4.1). In contrast, Africa (1.6) and Latin America and the Caribbean (2.4) had lower ASIRs. However, despite relatively higher incidence in Europe and North America, mortality was often lower than in Asia, reflecting regional differences in detection and treatment (Tabs. I, II).

BURDEN BY INCOME LEVEL

LOCC incidence and mortality demonstrated clear variation across national income levels, with the greatest burden observed in lower-middle-income countries, where the ASIR reached 7.7 and the ASMR was 3.6, largely reflecting the substantial contribution of South Asian populations. In contrast, high-income countries exhibited comparatively lower age-standardized rates (ASIR 3.9; ASMR 0.93), although their crude rates remained elevated, likely due to demographic aging.

A consistent male predominance was evident across all income strata, with lower-middle-income countries again showing the highest sex-specific burden, as indicated by a male ASIR of 11.7 and an ASMR of 5.4 (Tabs. I, II).

COUNTRY-SPECIFIC LOCC BURDEN

The highest number of new LOCC cases were observed in India (205,878), China (39,438), and the USA (29,547). The highest ASIRs were found in Papua New Guinea (20 per 100,000), India (13.4 per 100,000), and Bangladesh (9.4 per 100,000) (Tab. S1).

In terms of mortality, India (86,307), China (20,699), and Bangladesh (9,210) recorded the highest number of LOCC deaths. The highest ASMR were found in Papua New Guinea (12.6 per 100,000), followed by Maldives (6.7 per 100,000), and Bangladesh (5.9 per 100,000) (Tab. S1).

CORRELATION WITH SMOKING PREVALENCE

Regression analyses identified positive ecological correlations between national smoking prevalence and LOCC incidence and mortality, although the strength and statistical significance varied across sex and outcome. In the total population, smoking prevalence was positively correlated with ASIR ($\beta=0.149$, $p=0.163$) and ASMR ($\beta=0.123$, $p=0.264$) in the fully adjusted model, although

Tab. I. The ASIR of LOCC in different regions of the World in 2024.

Population Numbers		All			Males			Females		
		ASIR	Crude Rate	Numbers	ASIR	Crude Rate	Numbers	ASIR	Crude Rate	Numbers
World		452062	4.5	5.6	319240	6.7	7.8	132822	2.4	3.3
WHO regions	WHO Africa region (AFRO)	11968	1.6	0.94	7141	2.1	1.1	4827	1.2	0.76
	WHO Americas region (PAHO)	53309	3.4	5.1	35237	4.8	6.8	18072	2	3.4
	WHO East Mediterranean region (EMRO)	16767	2.6	2	10295	3.2	2.4	6472	2	1.6
	WHO Europe region (EURO)	66641	3.8	7.1	44718	5.7	9.8	21923	2.1	4.5
	WHO South-East Asia region (SEARO)	238217	10.4	11.3	180162	15.8	16.7	58055	5	5.6
	WHO Western Pacific region (WPRO)	65160	1.9	3.4	41687	2.6	4.3	23473	1.3	2.5
Continents	Africa	15364	1.6	1	9196	2.1	1.2	6168	1.2	0.81
	Latin America and the Caribbean	20187	2.4	3	13055	3.4	4	7132	1.5	2.1
	Northern America	33175	4.6	8.6	22218	6.4	11.5	10957	2.8	5.7
	Europe	62402	4.1	8.4	42065	6.3	11.7	20337	2.2	5.3
	Oceania	4721	7.1	10.2	3092	9.6	13.4	1629	4.7	7.1
	Asia	316356	5.3	6.6	229714	7.8	9.5	86642	2.7	3.7
Income levels	High income	96121	3.9	8	62079	5.4	10.3	34042	2.5	5.7
	Upper middle income	84347	2.1	3.3	55799	2.9	4.4	28548	1.3	2.2
	Lower middle income	263978	7.7	7.4	196921	11.7	10.9	67057	3.9	3.8
	Low income	6896	1.5	0.89	3986	1.9	1	2910	1.2	0.75

neither association remained statistically significant. Among males, smoking prevalence remained positively correlated with ASIR ($\beta=0.107$, $p=0.222$) and ASMR ($\beta=0.139$, $p=0.128$), but these associations were also not statistically significant after full adjustment. In contrast, among females, smoking prevalence remained significantly correlated with ASIR ($\beta=0.349$, $p=0.012$), whereas the association with ASMR was positive but not statistically significant ($\beta=0.148$, $p=0.278$). Overall, adjustment attenuated the smoking-LOCC associations, particularly for males and the total population (Tab. III).

CORRELATION WITH ALCOHOL USE PREVALENCE

Alcohol use prevalence also demonstrated a positive ecological correlation with LOCC burden, particularly among males. In the total population, alcohol use was positively correlated with both ASIR ($\beta=0.146$, $p=0.163$) and ASMR ($\beta=0.071$, $p=0.506$) in the fully adjusted model, although neither association was statistically significant. Among males, these correlations remained significant after adjustment for smoking and HDI, for both ASIR ($\beta=0.275$, $p=0.006$) and ASMR ($\beta=0.206$, $p=0.046$). In females, however, the associations were negative and non-significant for both ASIR ($\beta=-0.188$, $p=0.139$) and ASMR ($\beta=-0.179$, $p=0.153$), indicating a weaker association in this population group (Tab. IV).

Correlation with HDI and Socioeconomic Indicators
The correlation between national HDI and LOCC burden was more complex. HDI showed positive associations

with ASIR in unadjusted analyses among males ($\beta=0.239$, $p=0.002$) and in the total population ($\beta=0.195$, $p=0.013$), but these associations were attenuated after adjustment and were no longer statistically significant in the fully adjusted model (male: $\beta=0.007$, $p=0.949$; female: $\beta=-0.056$, $p=0.651$; total: $\beta=0.005$, $p=0.963$). Similarly, HDI was not significantly correlated with ASMR after full adjustment among males ($\beta=-0.198$, $p=0.075$), females ($\beta=-0.226$, $p=0.066$), or the total population ($\beta=-0.198$, $p=0.085$). Analyses of HDI components showed that life expectancy at birth and mean years of schooling were positively correlated with ASIR in unadjusted models, particularly among males, but these associations diminished after adjustment. For mortality, inverse associations were more evident for mean years of schooling and GNI per capita in the fully adjusted models, particularly among females for mean years of schooling ($\beta=-0.304$, $p=0.009$) and among males for GNI per capita ($\beta=-0.192$, $p=0.031$). However, associations with the HDI components were generally inconsistent across sex and outcomes (Tabs. V, VI).

TEMPORAL ROBUSTNESS OF ECOLOGICAL ASSOCIATIONS USING HISTORICAL EXPOSURE AND DEVELOPMENT INDICATORS

Additional analyses using historical exposure and socioeconomic data showed broadly consistent ecological patterns with those observed in Tables III-VI. For 1990, smoking remained positively associated

Tab. II. The ASMR of LOCC in Different Regions of the World in 2024.

Population Numbers		All			Males			Females		
		ASMR	Crude Rate	Numbers	ASMR	Crude Rate	Numbers	ASMR	Crude Rate	Numbers
World		194059	1.9	2.4	137169	2.8	3.4	56890	0.99	1.4
WHO regions	WHO Africa region (AFRO)	7341	1	0.58	4406	1.3	0.7	2935	0.78	0.46
	WHO Americas region (PAHO)	14762	0.87	1.4	9960	1.3	1.9	4802	0.48	0.91
	WHO East Mediterranean region (EMRO)	9729	1.6	1.2	6222	2	1.5	3507	1.1	0.87
	WHO Europe region (EURO)	24825	1.4	2.6	17313	2.2	3.8	7512	0.63	1.6
	WHO South-East Asia region (SEARO)	106251	4.6	5	78465	7	7.3	27786	2.4	2.7
	WHO Western Pacific region (WPRO)	31151	0.84	1.6	20803	1.2	2.2	10348	0.47	1.1
Continents	Africa	9159	1	0.6	5537	1.3	0.73	3622	0.75	0.48
	Latin America and the Caribbean	8718	1	1.3	6051	1.6	1.9	2667	0.52	0.79
	Northern America	6070	0.72	1.6	3929	1	2	2141	0.44	1.1
	Europe	23263	1.5	3.1	16339	2.4	4.5	6924	0.66	1.8
	Oceania	1506	2.2	3.3	978	3	4.2	528	1.5	2.3
	Asia	145392	2.4	3.1	104373	3.5	4.3	41019	1.2	1.8
Income levels	High income	26716	0.93	2.2	16833	1.4	2.8	9883	0.53	1.6
	Upper middle income	41014	0.95	1.6	28576	1.4	2.2	12438	0.5	0.98
	Lower middle income	121683	3.6	3.4	88945	5.4	4.9	32738	1.9	1.9
	Low income	4323	1	0.56	2607	1.3	0.68	1716	0.75	0.44

with LOCC incidence after full adjustment among males ($\beta=0.215$, $p=0.043$), females ($\beta=0.490$, $p=0.003$), and the total population ($\beta=0.333$, $p=0.009$), whereas associations with mortality were positive but not statistically significant. In 2010, the positive association of smoking with incidence persisted, particularly among females ($\beta=0.444$, $p=0.001$) and the total population ($\beta=0.270$, $p=0.020$), while significant positive associations with mortality were observed among males ($\beta=0.214$, $p=0.026$) and the total population ($\beta=0.237$, $p=0.045$).

Alcohol showed a similar pattern across time, with the strongest associations observed among males. In 2010, alcohol use was positively associated with both incidence ($\beta=0.306$, $p=0.002$) and mortality ($\beta=0.231$, $p=0.025$) in males after adjustment, whereas associations among females and the total population were not statistically significant. The 1990 analyses showed weaker associations, particularly after adjustment.

Associations between HDI and its components and incidence were generally attenuated after adjustment in both 1990 and 2010. In contrast, inverse associations between HDI and mortality were more evident, particularly in 2010, when fully adjusted HDI was negatively associated with mortality among males ($\beta=-0.308$, $p=0.007$), females ($\beta=-0.341$, $p=0.007$), and the total population ($\beta=-0.336$, $p=0.005$).

Overall, the historical analyses were broadly concordant with the patterns observed in Tables 3-6. Based on

the direction of the standardized β coefficients in the fully adjusted models, 60 of 72 comparisons (83.3%) were directionally concordant between the 1990/2010 analyses and the corresponding analyses presented in Tables III-VI. The greatest consistency was observed for the patterns involving smoking, alcohol use, and HDI in relation to mortality. This percentage represents a descriptive measure of directional agreement and does not imply identical effect sizes or statistical significance.

Discussion

This study provides a comprehensive ecological assessment of the global burden of LOCC in 2024 and examines population-level associations with behavioral and socioeconomic indicators. We identified 452,062 new LOCC cases and 194,059 deaths worldwide, with a pronounced male predominance in both incidence and mortality. The highest burden was observed in the WHO SEARO, where the ASIR and ASMR reached 10.4 and 4.6 per 100,000, respectively. These findings are consistent with the substantial global and regional burden of oral cancer reported in previous studies and with the established contribution of tobacco, alcohol, and other regionally prevalent exposures to LOCC risk [2, 15-7, 29-36].

The marked male predominance observed in the present study is consistent with established epidemiological

Tab. III. Examining the Correlation Between smoking prevalence and Incidence and Mortality Rates of LOCC.

Smoking prevalence Unstandardized Coefficients (SE)		Incidence			Mortality		
		Standardized Coefficients	<i>p-value</i>	Unstandardized Coefficients (SE)	Standardized Coefficients	<i>p-value</i>	Unstandardized Coefficients (SE)
Males	Model 1	0.100 (0.033)	0.223	0.003	0.030 (0.020)	0.115	0.124
	Model 2	0.048 (0.034)	0.108	0.162	0.019 (0.021)	0.072	0.375
	Model 3	0.058 (0.041)	0.125	0.162	0.042 (0.025)	0.153	0.098
	Model 4	0.050 (0.041)	0.107	0.222	0.038 (0.025)	0.139	0.128
Females	Model 1	0.063 (0.022)	0.219	0.004	-0.020 (0.013)	-0.121	0.114
	Model 2	0.089 (0.033)	0.298	0.008	0.001 (0.019)	0.007	0.947
	Model 3	0.079 (0.032)	0.264	0.014	0.013 (0.019)	0.071	0.5
	Model 4	0.107 (0.042)	0.349	0.012	0.027 (0.025)	0.148	0.278
Total	Model 1	0.103 (0.030)	0.251	≤0.001	0.007 (0.018)	0.027	0.717
	Model 2	0.063 (0.037)	0.153	0.088	0.006 (0.023)	0.025	0.789
	Model 3	0.083 (0.044)	0.193	0.061	0.037 (0.027)	0.144	0.17
	Model 4	0.064 (0.046)	0.149	0.163	0.031 (0.028)	0.123	0.264

Model 1: crude or unadjusted model. Model 2: Adjusted for alcohol use prevalence. Model 3: Adjusted for HDI. Model 4: Adjusted for HDI, and alcohol use prevalence.

Tab. IV. Examining the Correlation Between Alcohol use prevalence and Incidence and Mortality Rates of LOCC.

Alcohol use prevalence Unstandardized Coefficients (SE)		Incidence			Mortality		
		Standardized Coefficients	<i>p-value</i>	Unstandardized Coefficients (SE)	Standardized Coefficients	<i>p-value</i>	Unstandardized Coefficients (SE)
Males	Model 1	0.153(0.032)	0.338	0.001	0.037(0.020)	0.139	0.063
	Model 2	0.134(0.035)	0.296	0.001	0.029(0.021)	0.111	0.171
	Model 3	0.130(0.045)	0.284	0.004	0.059(0.028)	0.218	0.035
	Model 4	0.126(0.045)	0.275	0.006	0.056(0.028)	0.206	0.046
Females	Model 1	0.029(0.033)	0.072	0.371	-0.046(0.019)	-0.190	0.017
	Model 2	-0.060(0.046)	-0.146	0.188	-0.052(0.027)	-0.216	0.053
	Model 3	-0.003(0.047)	-0.007	0.948	-0.022(0.027)	-0.085	0.425
	Model 4	-0.081(0.054)	-0.188	0.139	-0.046(0.032)	-0.179	0.153
Total	Model 1	0.108(0.031)	0.256	0.001	0.005(0.019)	0.019	0.803
	Model 2	0.070(0.038)	0.167	0.063	0.001(0.023)	0.004	0.965
	Model 3	0.082(0.043)	0.188	0.061	0.027(0.026)	0.106	0.300
	Model 4	0.063(0.045)	0.146	0.163	0.018(0.028)	0.071	0.506

Model 1: crude or unadjusted model. Model 2: Adjusted for smoking prevalence. Model 3: Adjusted for HDI. Model 4: Adjusted for HDI, and smoking prevalence.

patterns and is likely related, at least in part, to sex differences in exposure to major behavioral risk factors. Tobacco smoking and alcohol consumption have historically been more prevalent among men in many populations, while the long latency of carcinogenesis means that contemporary cancer burden may reflect exposures accumulated over earlier decades [2, 9, 29, 30]. The historical analyses performed in this study provide additional support for this interpretation, as several associations between earlier smoking or alcohol exposure and current LOCC outcomes remained evident, although their magnitude and statistical significance varied by sex and outcome.

Our ecological regression analyses indicate that the relationship between smoking exposure and LOCC burden is sex- and outcome-specific. In the fully adjusted current models, smoking exposure remained positively associated with LOCC incidence among females ($\beta=0.349$, $p=0.012$), whereas the corresponding

associations were not statistically significant among males or in the total population. For mortality, positive but non-significant associations were observed in all three groups. Notably, the historical analyses showed a similar positive association between smoking exposure and incidence among females in both 1990 and 2010, while the total population also showed a positive association in these historical models. Smoking exposure in 2010 was additionally associated with mortality among males and the total population. The persistence of positive associations across historical periods, particularly for female incidence, suggests temporal consistency in the direction of the ecological relationship, although the variation in statistical significance indicates that the strength of the association is not uniform across time or population groups. These findings are broadly compatible with the established relationship between tobacco exposure and oral cancer reported in epidemiological studies [31, 37-41].

Tab. V. Examining the Correlation Between HDI and its components and Incidence Rates of LOCC.

HDI and components		Male			Female			Total		
		Standardized Coefficients	Unstandardized Coefficients (se)	<i>p</i> -value	Standardized Coefficients	Unstandardized Coefficients (se)	<i>p</i> -value	Standardized Coefficients	Unstandardized Coefficients (se)	<i>p</i> -value
HDI	Model 1	5.240 (1.689)	0.239	0.002	0.772 (0.757)	0.081	0.310	2.898 (1.155)	0.195	0.013
	Model 2	3.841 (1.957)	0.175	0.051	-0.953 (1.018)	-0.099	0.351	1.019 (1.518)	0.069	0.503
	Model 3	1.225 (2.160)	0.056	0.571	0.766 (1.061)	0.079	0.471	1.128 (1.480)	0.076	0.447
	Model 4	0.150 (2.328)	0.007	0.949	-0.543 (1.197)	-0.056	0.651	0.076 (1.656)	0.005	0.963
Life expectancy at birth	Model 1	0.104 (0.037)	0.217	0.006	0.023 (0.016)	0.108	0.171	0.063 (0.025)	0.195	0.013
	Model 2	0.071 (0.042)	0.148	0.096	-0.006 (0.021)	-0.028	0.787	0.025 (0.032)	0.077	0.432
	Model 3	0.035 (0.042)	0.074	0.401	0.027 (0.021)	0.128	0.198	0.034 (0.029)	0.104	0.241
	Model 4	0.016 (0.045)	0.034	0.714	0.003 (0.024)	0.016	0.886	0.016 (0.032)	0.049	0.629
Mean years of schooling	Model 1	0.225 (0.080)	0.217	0.006	0.004 (0.036)	0.010	0.903	0.105 (0.055)	0.149	0.059
	Model 2	0.150 (0.094)	0.145	0.113	-0.085 (0.046)	-0.189	0.067	-0.007 (0.071)	-0.009	0.926
	Model 3	0.005 (0.105)	0.005	0.960	-0.024 (0.049)	-0.052	0.633	-0.008 (0.072)	-0.012	0.909
	Model 4	-0.061 (0.114)	-0.059	0.596	-0.074 (0.054)	-0.162	0.168	-0.071 (0.079)	-0.102	0.371
GNI per capita	Model 1	0.021 (0.011)	0.151	0.057	0.006 (0.005)	0.103	0.194	0.014 (0.008)	0.146	0.065
	Model 2	0.014 (0.011)	0.099	0.222	-0.002 (0.006)	-0.030	0.760	0.004 (0.008)	0.046	0.594
	Model 3	0.001 (0.012)	0.004	0.964	0.006 (0.007)	0.094	0.375	0.004 (0.009)	0.039	0.658
	Model 4	-0.002 (0.012)	-0.011	0.900	-0.001 (0.007)	-0.019	0.865	0.001 (0.009)	0.005	0.952

GNI per capita based on every 1000 \$. Model 1: crude or un adjusted model. Model 2: Adjusted for smoking prevalence. Model 3: Adjusted for alcohol use prevalence. Model 4: Adjusted for alcohol use prevalence, and smoking prevalence.

Alcohol exposure demonstrated a different pattern, with the clearest associations observed among males. In the current fully adjusted analysis, alcohol exposure was positively associated with both LOCC incidence ($\beta=0.275$, $p=0.006$) and mortality ($\beta=0.206$, $p=0.046$) among males, while associations in females and the total population were not statistically significant. The 2010 historical analysis reproduced this male-specific pattern, with significant positive associations with both incidence ($\beta=0.306$, $p=0.002$) and mortality ($\beta=0.231$, $p=0.025$). Associations were weaker in the 1990 analysis and were attenuated after adjustment. The consistency of the male-specific association across the current and 2010 analyses is compatible with evidence that tobacco and alcohol jointly contribute to oral carcinogenesis and that their effects may interact biologically [10, 42-8]. However, because the present analysis is ecological and the GBD exposure measures are Summary Exposure Values rather than direct survey percentages, these findings should be

interpreted as population-level exposure associations rather than individual-level causal effects.

The socioeconomic findings were more heterogeneous. In the current analyses, HDI was positively associated with LOCC incidence in some unadjusted models, particularly among males and the total population, but these associations were largely attenuated after adjustment and were not statistically significant in the fully adjusted models. HDI was likewise not significantly associated with mortality after full adjustment. Analyses of individual HDI components showed that positive associations with incidence for life expectancy and mean years of schooling were mainly observed in unadjusted models and diminished after adjustment, whereas several inverse associations with mortality were observed for mean years of schooling and GNI per capita.

The historical analyses provide an important additional perspective on the socioeconomic findings. For both 1990 and 2010, associations between HDI and its

Tab. VI. Examining the Correlation Between HDI and its components and Mortality Rates of LOCC.

HDI and components		Male			Female			Total		
		Standard- ized Coef- ficients	Unstan- dardized Coeffi- cients (se)	<i>p-value</i>	Standard- ized Coef- ficients	Unstan- dardized Coeffi- cients (se)	<i>p-value</i>	Standard- ized Coef- ficients	Unstan- dardized Coeffi- cients (se)	<i>p-value</i>
HDI	Model 1	0.078 (1.024)	0.006	0.939	-1.287 (0.435)	-0.229	0.004	-0.643 (0.698)	-0.073	0.358
	Model 2	-0.927 (1.184)	-0.072	0.435	-1.606 (0.593)	-0.285	0.008	-1.477 (0.922)	-0.167	0.111
	Model 3	-1.734 (1.325)	-0.134	0.193	-0.990 (0.612)	-0.172	0.108	-1.237 (0.902)	-0.140	0.172
	Model 4	-2.556 (1.425)	-0.198	0.075	-1.297 (0.701)	-0.226	0.066	-1.752 (1.011)	-0.198	0.085
Life expectancy at birth	Model 1	-0.002 (0.022)	-0.008	0.921	-0.024 (0.010)	-0.199	0.012	-0.013 (0.015)	-0.067	0.398
	Model 2	-0.024 (0.025)	-0.085	0.349	-0.026 (0.012)	-0.211	0.041	-0.028 (0.019)	-0.144	0.155
	Model 3	-0.028 (0.026)	-0.100	0.272	-0.014 (0.012)	-0.114	0.242	-0.019 (0.018)	-0.100	0.273
	Model 4	-0.043 (0.028)	-0.153	0.121	-0.019 (0.014)	-0.149	0.194	-0.029 (0.020)	-0.149	0.150
Mean years of schooling	Model 1	0.005 (0.048)	0.008	0.916	-0.073 (0.020)	-0.276	≤0.001	-0.039 (0.033)	-0.094	0.237
	Model 2	-0.044 (0.056)	-0.073	0.433	-0.090 (0.027)	-0.340	≤0.001	-0.084 (0.043)	-0.201	0.054
	Model 3	-0.088 (0.064)	-0.145	0.173	-0.072 (0.028)	-0.266	0.011	-0.078 (0.044)	-0.186	0.077
	Model 4	-0.133 (0.070)	-0.218	0.059	-0.082 (0.031)	-0.304	0.009	-0.104 (0.048)	-0.251	0.032
GNI per capita	Model 1	-0.007 (0.007)	-0.080	0.312	-0.007 (0.003)	-0.199	0.011	-0.007 (0.004)	-0.117	0.140
	Model 2	-0.010 (0.007)	-0.122	0.138	-0.008 (0.004)	-0.216	0.027	-0.010 (0.005)	-0.168	0.059
	Model 3	-0.015 (0.007)	-0.179	0.043	-0.006 (0.004)	-0.147	0.156	-0.009 (0.005)	-0.165	0.069
	Model 4	-0.016 (0.007)	-0.192	0.031	-0.007 (0.004)	-0.192	0.091	-0.011 (0.005)	-0.184	0.050

GNI per capita based on every 1000 \$. Model 1: crude or unadjusted model. Model 2: Adjusted for smoking prevalence. Model 3: Adjusted for alcohol use prevalence. Model 4: Adjusted for alcohol use prevalence, and smoking prevalence.

components and incidence were generally attenuated after adjustment. In contrast, inverse associations between HDI and mortality were more consistent, particularly in 2010, when fully adjusted HDI was negatively associated with mortality among males ($\beta=-0.308$, $p=0.007$), females ($\beta=-0.341$, $p=0.007$), and the total population ($\beta=-0.336$, $p=0.005$). Similar inverse associations were also observed using 1990 HDI values. These findings are compatible with previous ecological studies showing that socioeconomic development may be associated differently with cancer incidence and mortality, potentially reflecting differences in cancer detection, stage at diagnosis, treatment availability, and health-system capacity [20, 49-53]. Nevertheless, these mechanisms remain interpretive rather than directly tested in the present study.

Taken together, the comparison of contemporary and historical analyses suggests that the principal ecological patterns are reasonably stable but not identical across

time. Smoking showed the most consistent positive relationship with incidence, particularly among females, whereas alcohol showed the clearest and most persistent association with both incidence and mortality among males. In contrast, socioeconomic indicators showed greater temporal and outcome-specific heterogeneity. Based on the direction of the standardized β coefficients in the fully adjusted models, 60 of 72 comparisons (83.3%) between the historical analyses and the corresponding current analyses were directionally concordant. This descriptive level of agreement indicates substantial consistency in the direction of associations, but it should not be interpreted as evidence of identical effect sizes or statistical significance.

The present findings should also be interpreted in light of the nature of the exposure data. GBD 2019 summarizes exposure using age-standardized SEVs, which are risk-weighted measures designed to facilitate comparisons across risks, locations, and time rather than direct

survey-based prevalence estimates [27]. Accordingly, the observed ecological associations reflect cross-national variation in modeled exposure burden and cannot be directly translated into individual-level risk estimates. This distinction is particularly relevant when interpreting the relatively strong sex-specific associations observed for smoking and alcohol.

The geographical findings further reinforce the heterogeneous epidemiology of LOCC. The particularly high burden in SEARO is consistent with the substantial contribution of smokeless tobacco and betel quid use in south and southeast Asia [13, 15, 37, 38, 54-6]. Conversely, comparatively lower incidence and mortality in some regions may partly reflect differences in cancer registration, diagnosis, access to care, and completeness of mortality ascertainment rather than genuinely lower underlying disease burden [49, 57-61]. The divergence between incidence and mortality across regions therefore likely reflects a combination of exposure patterns and differences in health-system performance.

Overall, these findings support a multifactorial and sex-specific interpretation of the global LOCC burden. The consistency of selected associations across historical periods suggests that long-term patterns of tobacco and alcohol exposure may contribute to contemporary national differences in LOCC burden, while the heterogeneous associations with HDI and its components indicate that socioeconomic development cannot be interpreted as a uniform predictor of either incidence or mortality. The findings therefore strengthen the rationale for continued tobacco and alcohol control, while also emphasizing the importance of early detection, cancer registration, treatment access, and broader health-system capacity in shaping population-level LOCC outcomes [11, 50-3].

As an ecological analysis, this study cannot establish causality or determine whether the observed national-level associations apply to individuals. In addition, LOCC has a long and variable latency period, and historical exposure patterns may therefore be more relevant to current disease burden than contemporaneous measurements alone. The use of exposure data from 1990, 2010, and 2019 provides a useful temporal perspective, but residual confounding by factors such as betel quid use, HPV infection, diet, occupational exposures, and differences in cancer detection and registration remains possible [13, 54, 62, 63]. Future longitudinal and individual-level studies integrating these determinants are needed to clarify the temporal and causal pathways underlying the observed associations.

STRENGTHS AND LIMITATIONS

A major strength of this study is its use of the most recent GLOBOCAN 2024 estimates to provide a standardized assessment of the global burden of lip and oral cavity cancer across countries, geographic regions, and sexes. The analysis combines contemporary cancer burden estimates with harmonized population-level exposure and socioeconomic indicators from the GBD study and the UNDP. In addition to evaluating contemporary associations using 2019 smoking and

alcohol exposure estimates and 2023 socioeconomic indicators, the study incorporates historical exposure and development measures from 1990 and 2010, providing an additional temporal perspective. Sex-stratified analyses and multivariable regression models further allowed examination of whether observed ecological associations differed between males, females, and the total population. The use of standardized regression coefficients, complete-case analyses, and model diagnostics including variance inflation assessment and residual examination also strengthened the analytical framework.

Several limitations should nevertheless be considered. First, the ecological design precludes individual-level inference and causal interpretation. Associations observed between country-level exposures and cancer rates may not reflect corresponding relationships at the individual level and may be influenced by within-country heterogeneity. Second, the exposure variables derived from GBD 2019 are age-standardized SEVs, which represent risk-weighted exposure distributions rather than conventional survey-based prevalence estimates. Consequently, they should not be interpreted as direct measures of the proportion of individuals exposed at a specified level. Third, temporal alignment remains an important limitation. The primary analyses relate 2019 smoking and alcohol exposure estimates and 2023 socioeconomic indicators to 2024 cancer outcomes, whereas cancer development may reflect cumulative exposures over substantially longer periods. The historical analyses using 1990 and 2010 indicators provide supportive temporal context but do not constitute longitudinal individual-level analyses or establish exposure-to-disease time sequences. Fourth, incomplete availability of some exposure and socioeconomic variables reduced the analytic sample size in selected models, and complete-case analysis may introduce selection bias when missingness is not random. Finally, residual confounding is possible because important determinants of LOCC, including smokeless tobacco and betel quid/areca nut exposure, HPV infection, dietary factors, occupational exposures, and differences in diagnostic and treatment access, could not be comprehensively incorporated into the regression models [62, 63]. These limitations warrant cautious interpretation of the observed ecological associations.

PUBLIC HEALTH IMPLICATIONS

The findings have several implications for global LOCC prevention and control. The marked geographical heterogeneity, together with the particularly high burden observed in the SEARO, supports the need for context-specific prevention strategies that address locally predominant exposures, including smokeless tobacco and betel quid/areca nut use. At the global level, continued tobacco and alcohol control, including prevention of initiation, reduction of exposure, cessation support, and effective regulatory and educational measures, remains essential given the established role of these exposures

in oral carcinogenesis and the ecological associations observed in the present study [55, 56, 64].

The sex-specific regression findings further indicate that prevention and surveillance should not necessarily be based on a uniform population-wide exposure profile. In the fully adjusted models, smoking exposure was positively associated with LOCC incidence among females, whereas alcohol exposure was positively associated with both incidence and mortality among males. These findings do not establish causality, but they provide population-level evidence that may help identify settings in which sex-specific exposure patterns and cancer burden warrant closer surveillance. The historical analyses, which showed substantial directional concordance with the contemporary models, further support the value of sustained monitoring of tobacco and alcohol exposure patterns over time.

The absence of statistically significant fully adjusted associations between HDI and LOCC incidence or mortality also has practical implications. Although selected HDI components, particularly mean years of schooling and GNI per capita, showed inverse associations with mortality in some sex groups, these ecological findings should not be interpreted as evidence of direct causal effects of socioeconomic development. Rather, they suggest that socioeconomic conditions, health-system capacity, diagnostic pathways, and treatment access may operate through complex and context-dependent mechanisms. Accordingly, improving early detection, diagnostic capacity, treatment availability, and continuity of cancer care remain important, particularly in settings where the burden of mortality is high and health-system resources are constrained [65, 66]. Prevention efforts should therefore be accompanied by strengthening oral health services and access to timely cancer diagnosis and treatment.

FUTURE RESEARCH

Future studies should validate these ecological findings through individual-level and longitudinal designs, particularly using appropriately lagged exposure measures to account for the long latency and cumulative nature of LOCC. Further research should also incorporate underrepresented determinants such as smokeless tobacco and betel quid/areca nut use, HPV infection, dietary and occupational factors, and indicators of diagnostic and treatment access.

The sex-specific patterns observed in this study, together with differences across historical and contemporary analyses, warrant further investigation of differences in exposure intensity, duration, co-exposure, and social context. Future studies should also assess whether improvements in early detection, treatment access, and health-system capacity modify the relationship between socioeconomic conditions and LOCC mortality.

Conclusion

Lip and oral cavity cancer remains a substantial global

health burden, with marked sex-based and geographical disparities and particularly high rates in the south-east Asia region. In fully adjusted ecological analyses, smoking exposure was positively associated with LOCC incidence among females, whereas alcohol exposure was positively associated with incidence and mortality among males. HDI was not significantly associated with LOCC incidence or mortality after full adjustment, although selected socioeconomic components showed inverse associations with mortality in some groups. Historical analyses from 1990 and 2010 showed substantial directional concordance with the contemporary findings, while also demonstrating variation in the magnitude and statistical significance of associations.

Overall, the findings support a multifactorial and sex-specific pattern of LOCC burden. Because of the ecological study design, the observed relationships should not be interpreted as causal effects. Sustained tobacco and alcohol control, attention to regionally relevant risk factors, and strengthening of early detection, diagnostic capacity, and access to effective treatment remain important priorities for global LOCC control.

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Ethics approval

Only publicly available, aggregated data were used. No identifiable personal information was accessed. The Shahrekord University of Medical Sciences Ethics Committee (IR.SKUMS.REC.1402.124) granted ethical approval for this study.

Consent to participate

Not applicable.

Consent for publication

Not applicable.

Ethical considerations

Only publicly available, aggregated data were used. No identifiable personal information was accessed. The Shahrekord University of Medical Sciences Ethics Committee (IR.SKUMS.REC.1402.124) granted ethical approval for this study.

Availability of data and materials

All the data generated or analysed during this study are included in this published article (and its supplementary

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Competing interests

The authors declare that they have no competing interests.

Authors' contributions

STD, AMH: Drafted the manuscript, participated in the data curation, formal analysis, and supervision. UYC, AMH: Assisted in writing - original draft, methodology, and project administration. All the authors provided final approval.

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Supplementary material

Tab. S1. The ASIR and ASMR of lip and oral cavity cancer in the countries of the world in 2024.

Population	ASIR	ASIR in males	ASIR in females	ASMR	ASMR in males	ASMR in females
Afghanistan	2.9	3.7	2.3	1.8	2.4	1.2
Albania	2.2	3.3	1.2	0.73	1.2	0.30
Algeria	0.90	1.1	0.66	0.44	0.56	0.33
Angola	3.1	5.3	1.3	2.1	3.5	0.86
Azerbaijan	0.65	1.1	0.32	0.21	0.37	0.08
Argentina	2.2	2.9	1.5	0.87	1.3	0.45
Australia	5.8	8.3	3.5	0.91	1.3	0.55
Austria	3.2	4.8	1.7	1.1	1.7	0.56
Bahamas	1.0	2.2	0.00	0.72	1.6	0.00
Bahrain	2.0	3.0	0.75	1.1	2.1	0.00
Bangladesh	9.4	11.9	6.9	5.9	7.7	4.1
Armenia	1.3	1.9	0.84	0.48	0.88	0.20
Barbados	1.4	2.6	0.28	1.0	2.1	0.20
Belgium	4.0	5.7	2.5	0.79	1.2	0.39
Bhutan	3.1	3.8	2.4	1.9	2.1	1.7
Bolivia (Plurinational State of)	0.89	1.4	0.47	0.31	0.50	0.16
Bosnia Herzegovina	2.1	3.3	1.1	0.79	1.5	0.23
Botswana	4.3	7.5	1.5	2.6	4.4	0.93
Brazil	3.9	6.1	1.9	1.6	2.7	0.64
Belize	0.00	0.00	0.00	0.00	0.00	0.00
Solomon Islands	2.7	4.4	0.96	1.2	2.0	0.32
Brunei Darussalam	0.72	0.60	0.80	0.38	0.32	0.42
Bulgaria	2.9	4.7	1.4	1.5	2.5	0.51
Myanmar	6.1	9.8	2.9	3.9	6.5	1.5
Burundi	1.5	2.0	1.1	1.1	1.4	0.72
Belarus	5.7	11.3	1.4	3.3	6.4	0.83
Cambodia	3.3	4.3	2.4	2.1	3.0	1.4
Cameroon	1.4	1.8	1.1	1.0	1.3	0.81
Canada	4.5	5.9	3.2	0.82	1.2	0.49
Cape Verde	2.8	4.4	1.6	2.2	3.2	1.6
Central African Republic	1.4	2.5	0.59	0.87	1.6	0.39
Sri Lanka	7.5	12.6	3.3	4.8	8.3	1.9
Chad	2.4	2.2	2.5	1.6	1.5	1.6
Chile	0.69	0.86	0.52	0.40	0.56	0.25
China	1.6	2.1	1.0	0.74	1.1	0.39
Colombia	1.6	1.6	1.6	0.62	0.70	0.56
Comoros	0.88	1.3	0.39	0.73	1.0	0.39
Congo, Republic of	1.0	1.8	0.33	0.62	1.1	0.18
Congo, Democratic Republic of	1.6	2.3	1.0	1.1	1.6	0.66
Costa Rica	1.5	1.8	1.3	0.57	0.79	0.36
Croatia	3.6	5.9	1.6	1.8	3.1	0.66
Cuba	3.3	4.9	1.9	1.8	3.0	0.71
Cyprus	2.5	3.4	1.7	0.69	1.1	0.31
Czechia	4.2	6.2	2.2	1.8	2.7	0.88
Benin	1.3	2.0	0.79	0.82	1.1	0.56
Denmark	4.2	5.7	2.8	1.0	1.4	0.65
Dominican Republic	1.3	1.6	1.1	0.71	1.0	0.42
Ecuador	0.90	0.80	0.98	0.50	0.51	0.48
El Salvador	1.3	1.2	1.3	0.67	0.69	0.67
Equatorial Guinea	1.4	1.9	0.91	0.98	1.3	0.68
Ethiopia	1.1	1.2	0.91	0.73	0.89	0.60
Eritrea	1.7	2.5	1.1	1.1	1.7	0.65
Estonia	4.3	7.3	1.8	1.9	3.7	0.43

Fiji	2.8	5.3	0.66	0.76	1.5	0.22
Finland	3.5	4.6	2.3	0.86	1.2	0.52
France (metropolitan)	4.8	6.8	2.9	1.0	1.5	0.53
French Guyana	0.97	2.0	0.00	0.62	1.3	0.00
French Polynesia	3.8	5.3	2.1	0.86	0.94	0.66
Djibouti	1.4	2.0	0.93	0.80	1.0	0.59
Gabon	1.2	1.7	0.72	0.90	1.2	0.57
Georgia	2.5	4.5	1.1	1.1	2.1	0.36
The Republic of the Gambia	0.28	0.00	0.51	0.21	0.00	0.38
Gaza Strip and West Bank	1.9	2.9	1.1	1.0	1.8	0.44
Germany	3.5	4.6	2.3	1.1	1.6	0.58
Ghana	1.2	2.2	0.35	0.77	1.4	0.26
Greece	3.0	4.1	2.1	0.73	1.1	0.41
France, Guadeloupe	2.5	4.5	0.88	1.0	2.3	0.00
Guam	1.6	3.2	0.00	0.00	0.00	0.00
Guatemala	0.78	0.76	0.80	0.44	0.46	0.43
Guinea	0.00	0.00	0.00	0.00	0.00	0.00
Guyana	1.7	1.4	2.0	0.74	0.86	0.65
Haiti	0.96	0.70	1.2	0.28	0.19	0.34
Honduras	0.94	1.4	0.58	0.58	0.83	0.36
Hungary	5.8	9.7	2.4	2.6	4.4	1.0
Iceland	3.9	5.2	2.5	0.40	0.54	0.25
India	13.4	20.6	6.1	5.7	8.5	2.8
Indonesia	1.5	1.8	1.3	0.92	1.2	0.68
Iran, Islamic Republic of	1.5	1.6	1.4	0.91	1.0	0.79
Iraq	0.91	1.1	0.80	0.56	0.68	0.46
Ireland	3.3	4.9	1.8	0.85	1.3	0.45
Israel	2.1	2.8	1.5	0.46	0.53	0.39
Italy	3.3	4.3	2.3	0.89	1.3	0.56
Côte d'Ivoire	0.98	1.1	0.85	0.73	0.83	0.62
Jamaica	0.95	0.77	1.1	0.40	0.46	0.37
Japan	3.6	4.7	2.5	0.71	0.95	0.47
Kazakhstan	1.7	2.4	1.1	1.0	1.5	0.61
Jordan	0.64	0.92	0.44	0.22	0.38	0.10
Kenya	2.9	2.8	2.9	1.8	1.9	1.7
Korea, Democratic People's Republic of	0.82	1.1	0.56	0.50	0.72	0.31
Korea, Republic of	1.8	2.4	1.2	0.50	0.73	0.30
Kuwait	1.4	1.7	1.1	0.73	1.1	0.34
Kyrgyzstan	2.0	2.9	1.4	1.3	1.9	0.73
Lao People's Democratic Republic	3.4	2.9	3.6	2.1	2.0	2.1
Lebanon	1.4	2.0	0.90	0.59	0.91	0.32
Lesotho	1.3	1.9	0.82	0.88	1.3	0.63
Latvia	3.9	7.2	1.5	2.5	4.6	0.97
Liberia	1.1	0.94	1.2	0.62	0.47	0.75
Libya	1.2	1.3	1.1	0.63	0.70	0.58
Lithuania	4.4	7.5	1.8	2.5	4.5	0.79
Luxembourg	1.6	2.2	1.0	0.50	0.82	0.20
Madagascar	1.4	1.6	1.1	1.0	1.3	0.77
Malawi	1.1	1.7	0.57	0.70	1.2	0.32
Malaysia	2.0	2.2	1.9	1.3	1.5	1.1
Maldives	9.4	12.2	5.5	6.7	8.5	4.4
Mali	2.3	1.7	2.8	1.6	1.3	1.9
Malta	2.8	3.2	2.5	0.79	1.3	0.34
France, Martinique	2.0	3.3	0.93	0.31	0.70	0.00
Mauritania	1.4	1.6	1.2	0.90	0.88	0.91
Mauritius	2.8	3.6	2.0	1.4	1.9	0.84
Mexico	1.0	1.0	1.1	0.49	0.62	0.37
Mongolia	1.6	2.3	1.1	0.56	0.93	0.31



Republic of Moldova	4.6	9.5	1.1	2.3	5.0	0.43
Montenegro	4.2	4.4	3.9	1.2	1.5	0.91
Morocco	1.1	1.3	0.99	0.69	0.82	0.56
Mozambique	1.3	1.7	0.94	0.93	1.3	0.64
Oman	2.2	2.7	1.3	0.96	1.4	0.42
Namibia	6.8	10.5	4.3	4.7	6.9	3.2
Nepal	5.1	7.0	3.5	3.2	4.6	2.0
The Netherlands	3.7	4.5	2.9	0.66	0.76	0.55
Curaçao	3.0	4.9	1.5	1.3	3.2	0.00
New Caledonia	3.9	5.8	2.2	0.66	1.4	0.00
Vanuatu	2.8	4.5	1.1	0.00	0.00	0.00
New Zealand	4.3	6.0	2.6	0.82	1.1	0.61
Nicaragua	1.0	1.3	0.86	0.55	0.75	0.40
Niger	2.5	3.3	2.0	1.7	2.1	1.3
Nigeria	1.6	2.0	1.2	1.1	1.3	0.87
Norway	3.9	5.1	2.8	0.65	0.84	0.48
Pakistan	5.5	7.0	4.0	3.4	4.5	2.3
Panama	1.4	1.5	1.3	0.56	0.82	0.33
Papua New Guinea	20.0	25.1	14.8	12.6	16.8	8.3
Paraguay	1.9	3.2	0.78	1.1	2.1	0.26
Peru	2.6	2.6	2.6	0.66	0.65	0.68
Philippines	1.7	2.0	1.3	1.1	1.4	0.80
Poland	4.0	6.1	2.0	2.4	3.9	1.0
Portugal	5.4	9.2	2.0	1.8	2.8	0.84
Guinea-Bissau	0.55	0.00	0.95	0.45	0.00	0.77
Timor-Leste	1.3	1.6	1.0	1.2	1.4	1.0
Puerto Rico	4.0	6.8	1.7	2.5	4.6	0.70
Qatar	2.4	2.4	1.8	1.2	1.5	0.47
France, La Réunion	4.4	7.0	2.1	1.1	1.9	0.48
Romania	5.8	10.5	1.7	2.6	4.9	0.55
Russian Federation	4.4	7.9	1.9	2.0	3.6	0.78
Rwanda	1.3	1.8	0.88	0.83	1.2	0.58
Saint Lucia	0.84	1.7	0.00	0.42	0.86	0.00
Sao Tome and Principe	0.00	0.00	0.00	0.00	0.00	0.00
Saudi Arabia	1.7	1.9	1.4	0.80	0.92	0.60
Senegal	0.85	0.58	1.1	0.56	0.43	0.69
Serbia	4.3	5.8	3.0	1.7	2.5	0.92
Sierra Leone	1.4	1.6	1.3	0.86	0.91	0.82
Singapore	1.8	2.3	1.4	0.52	0.67	0.38
Slovakia	5.4	9.4	2.0	2.8	5.1	0.84
Viet Nam	2.7	4.3	1.4	1.8	2.9	0.77
Slovenia	3.5	5.2	2.0	0.68	1.0	0.36
Somalia	2.0	2.0	1.9	1.4	1.4	1.4
South Africa	2.0	3.1	1.2	1.0	1.6	0.60
Zimbabwe	1.5	2.3	1.0	1.0	1.5	0.70
Spain	3.9	5.5	2.5	0.99	1.4	0.59
South Sudan	1.9	2.4	1.4	1.3	1.7	0.95
Sudan	2.6	3.8	1.4	1.6	2.5	0.77
Suriname	2.6	3.5	1.5	1.1	1.8	0.45
Eswatini	1.0	1.6	0.66	0.95	1.6	0.50
Sweden	3.6	4.4	2.9	0.76	1.0	0.53
Switzerland	4.2	5.5	2.9	0.98	1.3	0.63
Syrian Arab Republic	1.0	1.2	0.79	0.61	0.81	0.44
Tajikistan	1.9	2.3	1.6	1.1	1.5	0.78
Thailand	3.7	4.6	2.8	2.1	2.6	1.6
Togo	2.2	2.2	2.1	1.5	1.4	1.5
Trinidad and Tobago	1.3	1.6	0.99	0.72	1.0	0.56
United Arab Emirates	2.7	3.1	2.1	1.4	1.8	0.84



Tunisia	1.5	1.9	1.0	0.70	0.94	0.48
Türkiye	1.9	2.5	1.2	0.41	0.52	0.30
Turkmenistan	2.7	3.9	2.1	1.4	2.2	0.97
Uganda	1.8	2.5	1.3	1.3	1.9	0.87
Ukraine	4.4	8.4	1.2	2.5	4.9	0.57
North Macedonia	2.5	3.3	1.8	0.91	1.3	0.59
Egypt	1.7	2.1	1.3	0.83	1.0	0.65
United Kingdom	4.5	6.2	3.0	1.1	1.6	0.64
Tanzania, United Republic of	1.4	1.6	1.2	0.94	1.1	0.82
United States of America	4.6	6.5	2.7	0.70	0.99	0.43
Burkina Faso	2.7	1.5	3.5	1.8	1.1	2.2
Uruguay	3.0	5.0	1.2	1.3	2.1	0.56
Uzbekistan	2.0	2.6	1.5	1.1	1.6	0.74
Venezuela	1.7	2.4	1.2	0.79	1.1	0.52
Samoa	1.0	2.0	0.00	0.56	1.1	0.00
Yemen	0.90	1.0	0.80	0.55	0.67	0.45
Zambia	1.3	1.9	0.87	0.84	1.3	0.50

Tab. S2. Examining the Correlation Between smoking prevalence and Incidence and Mortality Rates of LOCC in 1990.

Smoking prevalence		Incidence			Mortality		
Sex	Model	Unstandardized Coefficients (SE)	Standardized Coefficients	<i>p-value</i>	Unstandardized Coefficients (SE)	Standardized Coefficients	<i>p-value</i>
Males	Model 1	0.110 (0.028)	0.289	≤0.001	0.028 (0.017)	0.125	0.096
	Model 2	0.084 (0.030)	0.221	0.005	0.030 (0.018)	0.134	0.104
	Model 3	0.088 (0.045)	0.208	0.052	0.049 (0.026)	0.199	0.065
	Model 4	0.091 (0.044)	0.215	0.043	0.050 (0.026)	0.202	0.060
Females	Model 1	0.057 (0.017)	0.246	0.001	-0.016 (0.010)	-0.116	0.131
	Model 2	0.092 (0.028)	0.388	0.001	0.011 (0.016)	0.082	0.491
	Model 3	0.099 (0.030)	0.391	0.001	0.026 (0.017)	0.182	0.125
	Model 4	0.127 (0.042)	0.49	0.003	0.042 (0.024)	0.28	0.080
Total	Model 1	0.104 (0.024)	0.307	≤0.001	0.006 (0.015)	0.03	0.687
	Model 2	0.099 (0.031)	0.291	0.002	0.022 (0.019)	0.108	0.258
	Model 3	0.136 (0.046)	0.36	0.004	0.054 (0.027)	0.245	0.048
	Model 4	0.126 (0.048)	0.333	0.009	0.054 (0.028)	0.244	0.057

Model 1: crude or unadjusted model. Model 2: adjusted for 1990 alcohol use prevalence. Model 3: adjusted for 1990 HDI. Model 4: adjusted for 1990 HDI and 1990 alcohol use prevalence. HDI: 1990 value. Outcome: LOCC incidence and mortality rates (2024).

Tab. S3. Examining the Correlation Between Alcohol use prevalence and Incidence and Mortality Rates of LOCC in 1990.

Alcohol use prevalence		Incidence			Mortality		
Sex	Model	Unstandardized Coefficients (SE)	Standardized Coefficients	<i>p-value</i>	Unstandardized Coefficients (SE)	Standardized Coefficients	<i>p-value</i>
Males	Model 1	0.131 (0.037)	0.257	≤0.001	0.010 (0.022)	0.033	0.663
	Model 2	0.085 (0.040)	0.167	0.033	-0.006 (0.024)	-0.022	0.792
	Model 3	0.108 (0.061)	0.202	0.080	0.033 (0.036)	0.105	0.367
	Model 4	0.112 (0.060)	0.210	0.065	0.035 (0.036)	0.112	0.329
Females	Model 1	0.031 (0.034)	0.073	0.361	-0.054 (0.020)	-0.216	0.007
	Model 2	-0.097 (0.051)	-0.223	0.060	-0.075 (0.030)	-0.294	0.014
	Model 3	0.024 (0.061)	0.052	0.698	-0.014 (0.033)	-0.053	0.680
	Model 4	-0.101 (0.073)	-0.220	0.168	-0.056 (0.041)	-0.211	0.176
Total	Model 1	0.095 (0.034)	0.205	0.006	-0.016 (0.020)	-0.059	0.432
	Model 2	0.012 (0.042)	0.025	0.782	-0.034 (0.026)	-0.126	0.188
	Model 3	0.086 (0.057)	0.176	0.133	0.018 (0.033)	0.062	0.595
	Model 4	0.045 (0.058)	0.092	0.436	0.000 (0.034)	0.000	0.997

Model 1: crude or unadjusted model. Model 2: adjusted for 1990 smoking prevalence. Model 3: adjusted for 1990 HDI. Model 4: adjusted for 1990 HDI and 1990 smoking prevalence. HDI: 1990 value. Outcome: LOCC incidence and mortality rates (2024).

Tab. S4. Examining the Correlation Between smoking prevalence and Incidence and Mortality Rates of LOCC in 2010.

Smoking prevalence		Incidence			Mortality		
Sex	Model	Unstandardized Coefficients (SE)	Standardized Coefficients	p-value	Unstandardized Coefficients (SE)	Standardized Coefficients	p-value
Males	Model 1	0.111 (0.031)	0.260	≤0.001	0.033 (0.019)	0.129	0.084
	Model 2	0.058 (0.034)	0.135	0.087	0.022 (0.021)	0.088	0.293
	Model 3	0.090 (0.042)	0.204	0.032	0.061 (0.025)	0.234	0.016
	Model 4	0.078 (0.041)	0.177	0.057	0.056 (0.025)	0.214	0.026
Females	Model 1	0.066 (0.020)	0.244	0.001	-0.017 (0.012)	-0.108	0.158
	Model 2	0.094 (0.030)	0.338	0.002	0.004 (0.018)	0.024	0.826
	Model 3	0.105 (0.030)	0.375	≤0.001	0.028 (0.018)	0.170	0.117
	Model 4	0.128 (0.039)	0.444	0.001	0.039 (0.023)	0.228	0.091
Total	Model 1	0.111 (0.028)	0.284	≤0.001	0.009 (0.017)	0.037	0.620
	Model 2	0.078 (0.036)	0.200	0.031	0.010 (0.022)	0.044	0.645
	Model 3	0.130 (0.044)	0.323	0.004	0.064 (0.027)	0.265	0.018
	Model 4	0.109 (0.046)	0.270	0.020	0.057 (0.028)	0.237	0.045

Model 1: crude or unadjusted model. Model 2: Adjusted for 2010 alcohol use prevalence. Model 3: Adjusted for 2010 HDI. Model 4: Adjusted for 2010 HDI, and 2010 alcohol use prevalence. HDI: 2010 value. Outcome: LOCC incidence and mortality rates (2024).

Tab. S5. Examining the Correlation Between Alcohol use prevalence and Incidence and Mortality Rates of LOCC in 2010.

Alcohol use prevalence		Incidence			Mortality		
Sex	Model	Unstandardized Coefficients (SE)	Sta	p-value	Unstandardized Coefficients (SE)	Standardized Coefficients	p-value
Males	Model 1	0.156 (0.032)	0.342	≤0.001	0.036 (0.020)	0.133	0.076
	Model 2	0.129 (0.036)	0.282	≤0.001	0.025 (0.022)	0.094	0.259
	Model 3	0.150 (0.046)	0.324	0.001	0.069 (0.028)	0.252	0.015
	Model 4	0.142 (0.046)	0.306	0.002	0.063 (0.028)	0.231	0.025
Females	Model 1	0.029 (0.032)	0.071	0.377	-0.045 (0.019)	-0.188	0.018
	Model 2	-0.069 (0.044)	-0.17	0.119	-0.053 (0.026)	-0.223	0.044
	Model 3	0.011 (0.046)	0.027	0.808	-0.009 (0.026)	-0.037	0.727
	Model 4	-0.072 (0.051)	-0.168	0.166	-0.038 (0.030)	-0.152	0.206
Total	Model 1	0.109 (0.031)	0.259	≤0.001	0.004 (0.019)	0.016	0.829
	Model 2	0.057 (0.039)	0.134	0.145	-0.003 (0.024)	-0.012	0.905
	Model 3	0.099 (0.043)	0.229	0.024	0.038 (0.026)	0.148	0.148
	Model 4	0.066 (0.045)	0.151	0.148	0.021 (0.027)	0.08	0.453

Model 1: crude or unadjusted model. Model 2: adjusted for 2010 smoking prevalence. Model 3: adjusted for 2010 HDI. Model 4: adjusted for 2010 HDI and 2010 smoking prevalence. HDI: 2010 value. Outcome: LOCC incidence and mortality rates (2024).

Tab. S6. Examining the Correlation Between HDI and its components and Incidence Rates of LOCC in 1990.

HDI and components	Model	Male			Female			Total		
		Standardized Coefficients	Unstandardized Coefficients (se)	p-value	Standardized Coefficients	Unstandardized Coefficients (se)	p-value	Standardized Coefficients	Unstandardized Coefficients (se)	p-value
HDI	Model 1	2.934 (1.915)	0.136	0.128	-0.156 (0.850)	-0.016	0.855	1.320 (1.312)	0.090	0.316
	Model 2	0.403 (2.292)	0.019	0.861	-2.705 (1.143)	-0.283	0.020	-2.404 (1.790)	-0.163	0.182
	Model 3	0.138 (2.472)	0.006	0.956	-0.624 (1.285)	-0.065	0.628	-0.367 (1.718)	-0.025	0.831
	Model 4	-2.588 (2.781)	-0.120	0.354	-2.157 (1.362)	-0.224	0.116	-3.014 (1.956)	-0.205	0.126
Life expectancy at birth	Model 1	0.068 (0.026)	0.207	0.009	0.010 (0.011)	0.066	0.404	0.037 (0.017)	0.168	0.034
	Model 2	0.012 (0.033)	0.037	0.716	-0.017 (0.015)	-0.117	0.261	-0.021 (0.025)	-0.094	0.398
	Model 3	0.038 (0.030)	0.117	0.207	0.011 (0.015)	0.075	0.456	0.023 (0.020)	0.104	0.260
	Model 4	-0.013 (0.036)	-0.041	0.712	-0.010 (0.017)	-0.072	0.534	-0.021 (0.025)	-0.095	0.398

Mean years of schooling	Model 1	0.220 (0.103)	0.182	0.034	0.008 (0.046)	0.014	0.869	0.105 (0.071)	0.128	0.140
	Model 2	0.092 (0.119)	0.077	0.438	-0.098 (0.060)	-0.184	0.104	-0.065 (0.090)	-0.079	0.471
	Model 3	0.090 (0.134)	0.074	0.506	-0.021 (0.066)	-0.039	0.750	0.025 (0.094)	0.030	0.792
	Model 4	-0.035 (0.146)	-0.029	0.809	-0.061 (0.070)	-0.112	0.388	-0.087 (0.101)	-0.106	0.392
GNI per capita	Model 1	0.013 (0.016)	0.069	0.400	0.004 (0.007)	0.043	0.596	0.009 (0.011)	0.070	0.391
	Model 2	-0.005 (0.016)	-0.025	0.759	-0.006 (0.008)	-0.072	0.435	-0.009 (0.011)	-0.068	0.435
	Model 3	-0.003 (0.017)	-0.015	0.859	0.003 (0.010)	0.033	0.752	0.001 (0.012)	0.005	0.958
	Model 4	-0.013 (0.017)	-0.068	0.429	-0.004 (0.010)	-0.047	0.659	-0.009 (0.012)	-0.069	0.443

Model 1: crude/unadjusted. Model 2: adjusted for 1990 smoking prevalence. Model 3: adjusted for 1990 alcohol use prevalence. Model 4: adjusted for 1990 alcohol use prevalence and 1990 smoking prevalence. HDI and its components were measured in 1990. GNI per capita was entered per 1,000 USD. Outcome: LOCC incidence and mortality rates (2024).

Tab. S7. Examining the Correlation Between HDI and its components and Mortality Rates of LOCC in 1990.

HDI and components	Model	Male			Female			Total		
		Standardized Coefficients	Unstandardized Coefficients (se)	p-value	Standardized Coefficients	Unstandardized Coefficients (se)	p-value	Standardized Coefficients	Unstandardized Coefficients (se)	p-value
HDI	Model 1	-1.400 (1.125)	-0.111	0.216	-1.680 (0.462)	-0.310	≤0.001	-1.566 (0.760)	-0.181	0.041
	Model 2	-2.815 (1.348)	-0.222	0.039	-2.355 (0.641)	-0.432	≤0.001	-3.051 (1.055)	-0.353	0.005
	Model 3	-2.248 (1.465)	-0.178	0.127	-1.513 (0.705)	-0.274	0.034	-1.914 (1.002)	-0.222	0.059
	Model 4	-3.751 (1.652)	-0.296	0.025	-2.008 (0.769)	-0.362	0.010	-3.052 (1.156)	-0.353	0.009
Life expectancy at birth	Model 1	-0.002 (0.015)	-0.010	0.895	-0.020 (0.007)	-0.231	0.003	-0.011 (0.010)	-0.085	0.282
	Model 2	-0.035 (0.020)	-0.179	0.085	-0.022 (0.009)	-0.258	0.014	-0.033 (0.015)	-0.249	0.031
	Model 3	-0.005 (0.018)	-0.027	0.780	-0.012 (0.008)	-0.135	0.169	-0.009 (0.012)	-0.068	0.466
	Model 4	-0.036 (0.022)	-0.187	0.102	-0.017 (0.010)	-0.197	0.087	-0.030 (0.015)	-0.229	0.049
Mean years of schooling	Model 1	-0.029 (0.061)	-0.042	0.629	-0.078 (0.025)	-0.259	0.002	-0.058 (0.041)	-0.121	0.160
	Model 2	-0.090 (0.071)	-0.129	0.204	-0.095 (0.034)	-0.315	0.006	-0.112 (0.054)	-0.235	0.038
	Model 3	-0.052 (0.080)	-0.074	0.518	-0.067 (0.036)	-0.218	0.068	-0.062 (0.055)	-0.130	0.263
	Model 4	-0.112 (0.088)	-0.159	0.204	-0.076 (0.040)	-0.244	0.060	-0.102 (0.060)	-0.214	0.093
GNI per capita	Model 1	-0.012 (0.009)	-0.105	0.197	-0.010 (0.004)	-0.195	0.015	-0.010 (0.006)	-0.131	0.108
	Model 2	-0.019 (0.010)	-0.167	0.049	-0.009 (0.005)	-0.187	0.046	-0.014 (0.007)	-0.184	0.043
	Model 3	-0.014 (0.010)	-0.126	0.152	-0.006 (0.006)	-0.105	0.307	-0.009 (0.007)	-0.120	0.178
	Model 4	-0.019 (0.010)	-0.167	0.061	-0.007 (0.006)	-0.137	0.200	-0.013 (0.007)	-0.163	0.078

Model 1: crude or unadjusted model. Model 2: Adjusted for 1990 smoking prevalence. Model 3: Adjusted for 1990 alcohol use prevalence. Model 4: Adjusted for 1990 alcohol use prevalence, and smoking prevalence. HDI and its components were measured in 1990. GNI per capita was entered per 1,000 USD. Outcome: LOCC incidence and mortality rates (2024).

Tab. S8. Examining the Correlation Between HDI and its components and Incidence Rates of LOCC in 2010.

HDI and components	Model	Male			Female			Total		
		Standardized Coefficients	Unstandardized Coefficients (se)	p-value	Standardized Coefficients	Unstandardized Coefficients (se)	p-value	Standardized Coefficients	Unstandardized Coefficients (se)	p-value
HDI	Model 1	4.358 (1.662)	0.204	0.010	0.361 (0.742)	0.039	0.627	2.253 (1.136)	0.156	0.049
	Model 2	1.844 (2.013)	0.086	0.361	-2.082 (1.012)	-0.223	0.041	-1.067 (1.579)	-0.074	0.500
	Model 3	-0.096 (2.112)	-0.005	0.964	0.177 (1.036)	0.019	0.865	0.170 (1.445)	0.012	0.907
	Model 4	-2.034 (2.325)	-0.095	0.383	-1.708 (1.191)	-0.181	0.154	-1.902 (1.674)	-0.132	0.258
Life expectancy at birth	Model 1	0.070 (0.030)	0.185	0.019	0.015 (0.013)	0.087	0.270	0.043 (0.020)	0.167	0.035
	Model 2	0.024 (0.035)	0.062	0.505	-0.013 (0.017)	-0.076	0.453	-0.005 (0.026)	-0.021	0.840
	Model 3	0.016 (0.033)	0.042	0.619	0.018 (0.016)	0.105	0.273	0.020 (0.022)	0.076	0.377
	Model 4	-0.010 (0.036)	-0.026	0.782	-0.007 (0.019)	-0.039	0.731	-0.007 (0.026)	-0.027	0.789
Mean years of schooling	Model 1	0.213 (0.079)	0.210	0.008	-0.000 (0.035)	-0.000	0.995	0.095 (0.054)	0.138	0.082
	Model 2	0.098 (0.095)	0.096	0.306	-0.104 (0.046)	-0.235	0.023	-0.061 (0.072)	-0.088	0.403
	Model 3	-0.033 (0.108)	-0.033	0.760	-0.032 (0.049)	-0.072	0.512	-0.034 (0.074)	-0.050	0.645
	Model 4	-0.134 (0.118)	-0.132	0.260	-0.089 (0.053)	-0.198	0.098	-0.127 (0.081)	-0.185	0.120
GNI per capita	Model 1	0.016 (0.012)	0.102	0.196	0.005 (0.005)	0.069	0.384	0.011 (0.008)	0.102	0.196
	Model 2	0.005 (0.013)	0.031	0.701	-0.005 (0.006)	-0.078	0.401	-0.003 (0.009)	-0.024	0.783
	Model 3	-0.004 (0.013)	-0.026	0.751	0.005 (0.008)	0.061	0.555	0.001 (0.009)	0.006	0.942
	Model 4	-0.007 (0.013)	-0.047	0.566	-0.006 (0.008)	-0.078	0.485	-0.005 (0.009)	-0.043	0.619

Model 1: crude or unadjusted model. Model 2: adjusted for 2010 smoking prevalence. Model 3: adjusted for 2010 alcohol use prevalence. Model 4: adjusted for 2010 alcohol use prevalence and 2010 smoking prevalence.

HDI and its components were measured in 2010. GNI per capita was entered per 1,000 USD. Outcome: LOCC incidence and mortality rates (2024).

Tab. S9. Examining the Correlation Between HDI and its components and Mortality Rates of LOCC in 2010.

HDI and components	Model	Male			Female			Total		
		Standardized Coefficients	Unstandardized Coefficients (se)	<i>p-value</i>	Standardized Coefficients	Unstandardized Coefficients (se)	<i>p-value</i>	Standardized Coefficients	Unstandardized Coefficients (se)	<i>p-value</i>
HDI	Model 1	-0.447 (1.000)	-0.036	0.655	-1.480 (0.419)	-0.270	≤0.001	-1.009 (0.679)	-0.117	0.140
	Model 2	-2.146 (1.206)	-0.171	0.077	-2.159 (0.588)	-0.395	≤0.001	-2.627 (0.952)	-0.306	0.006
	Model 3	-2.492 (1.288)	-0.198	0.055	-1.350 (0.591)	-0.242	0.024	-1.809 (0.872)	-0.210	0.040
	Model 4	-3.869 (1.412)	-0.308	0.007	-1.901 (0.696)	-0.341	0.007	-2.889 (1.015)	-0.336	0.005
Life expectancy at birth	Model 1	-0.007 (0.018)	-0.032	0.689	-0.021 (0.008)	-0.210	0.007	-0.013 (0.012)	-0.087	0.274
	Model 2	-0.035 (0.021)	-0.155	0.101	-0.023 (0.010)	-0.234	0.022	-0.032 (0.016)	-0.206	0.049
	Model 3	-0.026 (0.020)	-0.116	0.193	-0.013 (0.009)	-0.130	0.165	-0.018 (0.014)	-0.116	0.191
	Model 4	-0.045 (0.022)	-0.200	0.043	-0.018 (0.011)	-0.182	0.108	-0.032 (0.016)	-0.206	0.051
Mean years of schooling	Model 1	-0.003 (0.048)	-0.005	0.953	-0.074 (0.020)	-0.286	≤0.001	-0.045 (0.032)	-0.109	0.169
	Model 2	-0.073 (0.057)	-0.122	0.205	-0.098 (0.027)	-0.376	≤0.001	-0.109 (0.044)	-0.266	0.014
	Model 3	-0.110 (0.066)	-0.184	0.098	-0.079 (0.028)	-0.298	0.005	-0.094 (0.045)	-0.231	0.036
	Model 4	-0.173 (0.072)	-0.289	0.018	-0.091 (0.031)	-0.342	0.004	-0.133 (0.050)	-0.326	0.008
GNI per capita	Model 1	-0.010 (0.007)	-0.103	0.192	-0.008 (0.003)	-0.205	0.009	-0.008 (0.005)	-0.133	0.093
	Model 2	-0.014 (0.008)	-0.156	0.057	-0.009 (0.004)	-0.224	0.018	-0.012 (0.006)	-0.192	0.029
	Model 3	-0.017 (0.008)	-0.178	0.036	-0.007 (0.005)	-0.152	0.131	-0.011 (0.005)	-0.167	0.055
	Model 4	-0.018 (0.008)	-0.197	0.022	-0.009 (0.005)	-0.206	0.065	-0.012 (0.006)	-0.195	0.030

Model 1: crude or unadjusted model. Model 2: adjusted for 2010 smoking prevalence (sex-specific). Model 3: adjusted for 2010 alcohol use prevalence (sex-specific). Model 4: adjusted for 2010 alcohol use prevalence and smoking prevalence (sex-specific). HDI and its components were measured in 2010. GNI per capita was entered per 1,000 USD.