Sriwijaya Journal of Otorhinolaryngology e-ISSN 2987-131X
https://phlox.or.id/index.php/sjorl Vol. 3 No. 2 (2025)
Original Research Article

Spatiotemporal Trends and Attributable Risk Factors of Nasopharyngeal Carcinoma in Southeast Asia (1990–2023): An Ecological Analysis of the Global Burden of Disease Study with Projections to 2050

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ARTICLE INFO

Article history:
Received: *August 25, 2025*
Accepted: *September 30, 2025*
Published: *October 30, 2025*

Keywords:
Nasopharyngeal carcinoma
Global Burden of Disease
Southeast Asia
Epidemiology
Attributable risk

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DOI: 10.59345/sjorl.v3i2.306

ABSTRACT

Background: Nasopharyngeal carcinoma (NPC) is an Epstein–Barr virus-associated epithelial malignancy with a strikingly uneven geography concentrated in Southeast Asia and southern China. Its region-specific burden, temporal dynamics and attributable risk factors have not been synthesised in a dedicated spatiotemporal ecological analysis.

Objective: To characterise NPC burden, trends and attributable risks across Southeast Asia.

Methods: We conducted an ecological analysis of Global Burden of Disease (GBD) estimates. Age-standardised incidence (ASIR), mortality (ASMR) and disability-adjusted life-year (DALY) rates for the GBD Southeast Asia region (1990–2021, GBD 2021) and constituent ASEAN countries (to 2023, GBD 2023) were compiled; temporal trends were summarised by the estimated annual percentage change (EAPC); attributable fractions for tobacco, alcohol and occupational carcinogens were obtained from GBD comparative risk assessment; and age-standardised rates were projected toward 2050.

Results: In 2021 the Southeast Asia region recorded the highest NPC mortality of any world region (ASMR 1.60 per 100,000). Age-standardised rates declined (EAPC: incidence −0.39, mortality −0.76, DALYs −0.84% per year), yet absolute incident cases more than doubled (6,209 to 13,661; +120%). National ASIR ranged from 1.3 (Cambodia) to 14.2 (Singapore); Indonesia carried the greatest absolute burden (5,163 cases; 4,306 deaths). Incidence rose in Indonesia (EAPC +0.8), Laos (+0.7) and Viet Nam (+0.6). Alcohol-attributable burden increased most steeply (Southeast Asia EAPC +2.27), against declining tobacco- and occupational-attributable rates.

Conclusion: Southeast Asia bears the world's heaviest NPC mortality; falling age-standardised rates mask a rising absolute burden and a growing alcohol-attributable component, underscoring the need for Epstein–Barr virus-informed early detection and region-tailored prevention.

All authors have reviewed and approved the final version of the manuscript.

1. Introduction

Nasopharyngeal carcinoma (NPC) is an epithelial malignancy arising from the mucosal lining of the nasopharynx that is aetiologically distinct from other head and neck cancers and is almost universally associated with Epstein–Barr virus (EBV) infection in its endemic, non-keratinising form.[1] Unlike most solid tumours, NPC exhibits one of the most sharply demarcated geographical distributions in oncology: age-standardised incidence exceeds 3 per 100,000 in parts of East and Southeast Asia while remaining below 0.5 per 100,000 across most of Europe and the Americas.[1,2] This clustering in southern China and Southeast Asia has long implicated a convergence of viral, environmental, dietary and genetic determinants acting on a susceptible host background.[3]

The central aetiological role of EBV is now firmly established, and circulating EBV DNA and antibody signatures underpin emerging early-detection and vaccine strategies that could shift NPC from a late-presenting to a screen-detectable disease.[4] Yet EBV infection is near-ubiquitous worldwide, so viral carriage alone cannot explain the endemic geography. Population and case–control studies implicate consumption of salt-preserved fish and other nitrosamine-rich preserved foods, particularly during early childhood, as a modifiable dietary driver that interacts with family history and viral reactivation.[5] Host genetic susceptibility, especially within the

human leukocyte antigen (HLA) region on chromosome 6p21 and additional non-HLA loci, further concentrates risk in specific ancestral populations and interacts with tobacco exposure and EBV serology.[6] Tobacco smoking and heavy alcohol use are the principal behavioural risk factors captured in comparative risk assessments of NPC.[7]

Southeast Asia occupies a singular position in the global NPC landscape. Several of its populations—including the Bidayuh and other indigenous groups of Sarawak in East Malaysia and communities across the Malay Peninsula—rank among the highest-incidence groups outside southern China, and hospital-based series from Malaysia and neighbouring countries consistently report NPC among the commonest cancers in men.[3,8] Despite this, the regional burden is frequently subsumed within broader Asian or global analyses, and a dedicated, spatially and temporally resolved appraisal of NPC across Southeast Asia—linking the descriptive epidemiology to its attributable behavioural and occupational drivers—has been lacking.

The Global Burden of Disease (GBD) study offers a coherent framework to address this gap, providing internally consistent, age-standardised estimates of incidence, mortality and disability-adjusted life-years (DALYs) for NPC across 204 countries and territories, together with a comparative risk assessment that partitions burden across behavioural and occupational exposures.[9,10] Recent GBD-based analyses have mapped the global and continental patterns of NPC, documenting an overall decline in age-standardised rates alongside a rising absolute case count, persistent male predominance and shifting risk-factor contributions.[1,11,12,13,14] However, these syntheses treat Southeast Asia only as one line in a global table, without resolving the marked heterogeneity between its constituent nations or interrogating why the region carries a disproportionate mortality burden.

We therefore undertook a focused spatiotemporal ecological analysis of NPC in Southeast Asia using GBD estimates. The contribution of this work is incremental but distinct. Recent GBD analyses have described NPC at the level of Asia as a whole[11] or reported ASEAN country estimates in isolation,[15] but none has integrated, within a single framework, a nation-resolved and fully uncertainty-quantified appraisal of all eleven Southeast Asian countries, an explicit reconciliation of that national layer with the longer-run regional and global trajectory, and a decomposition of the burden by attributable risk factor. First, therefore, this study provides a consolidated Southeast Asia-specific synthesis that pairs the spatial gradient with formally reported estimated annual percentage changes (EAPC) and their confidence intervals.[15] Second, it explicitly integrates the descriptive burden with the region's attributable risk-factor profile—tobacco, alcohol and occupational carcinogens—thereby linking epidemiological trend to preventable cause.[7,16,17,18] Third, it foregrounds the persistent evidence gap for Indonesia, the most populous ASEAN nation, whose large absolute burden is poorly represented in the international literature.[19,20,21,22] Accordingly, the aim of this study was to characterise the magnitude, spatial distribution, temporal trends, attributable risk factors and projected trajectory of NPC across Southeast Asia, and to identify the priorities these patterns imply for regional cancer control.

2. Methods

2.1 Study design and data sources

We performed an ecological (population-level) analysis of NPC burden across Southeast Asia using estimates from the Global Burden of Disease study, which synthesises vital-registration, cancer-registry, verbal-autopsy and survey data within a Bayesian modelling framework to generate comparable age-standardised estimates.[9] The primary spatiotemporal analysis was conducted within a single cycle and a single geographical definition—the eleven countries of the Association of Southeast Asian Nations (ASEAN) plus Timor-Leste and their pooled aggregate—using GBD 2023 (reference period 1990–2023), the most recent release and the only source providing openly reported country-resolved NPC estimates for every Southeast Asian nation.[15] To place these national estimates in a longer-run and global context, and because the GBD comparative risk assessment for NPC was most completely reported for the preceding cycle, we additionally drew the GBD 2021 "Southeast Asia" regional trajectory (1990–2021) and the corresponding global figures.[12] The GBD 2021 region and the ASEAN grouping are not identical—the GBD region additionally includes several South-Asian and Indian-Ocean territories—and each release re-estimates its inputs; these layers are therefore reported separately and their differences are explicitly reconciled (Sections 3.2 and 4.7) rather than treated as interchangeable. Estimates were obtained from the Global Burden of Disease Results Tool of the Institute for Health Metrics and Evaluation and cross-checked against the primary GBD publications; where a downstream report contained an evident transcription error (for example, a global DALY count mis-stated as 249,019 rather than 2,490,191), the value was corrected against the primary source. No individual patient data were used and no ethical approval was required.

2.2 Case definition and geographical scope

NPC was defined per the GBD cause hierarchy (International Classification of Diseases, Tenth Revision, codes C11 and equivalents). The GBD "Southeast Asia" region was used as the regional unit, and the national layer comprised the eleven countries of mainland and maritime Southeast Asia: Brunei, Cambodia, Indonesia, Laos, Malaysia, Myanmar, the Philippines, Singapore, Thailand, Timor-Leste and Viet Nam. Three burden metrics were analysed: the age-standardised incidence rate (ASIR), the age-

standardised mortality rate (ASMR) and the age-standardised DALY rate, each standardised to the GBD global reference population, expressed per 100,000 population with 95% uncertainty intervals, and reported alongside absolute counts of incident cases, deaths and DALYs. Regional and national estimates use the same reference standard and age structure, ensuring comparability of the age-standardised rates across the analysis.

2.3 Temporal-trend analysis

Secular trends were quantified with the estimated annual percentage change (EAPC), the standard summary of the average yearly percentage change in an age-standardised rate derived from a log-linear regression of the natural logarithm of the rate on calendar year; a rate is considered to be rising if both the EAPC and the lower bound of its 95% confidence interval exceed zero, falling if both are below zero, and otherwise stable.[1,15] EAPC point estimates with their 95% confidence intervals were compiled for the ASEAN aggregate and for every country (1990–2023) and for the GBD 2021 regional series (1990–2021), and are reported for all trend estimates. Our shared analytical pipeline implements the estimator EAPC = 100 × (exp(β) − 1), where β is the slope of a linear regression of the natural logarithm of the age-standardised rate on calendar year, and reproduces the reported values where the underlying annual series is available; fully independent re-estimation of every EAPC would require the complete annual rate series from the GBD Results Tool, which we identify as the natural next step (Section 4.7). Absolute change was additionally expressed as the percentage difference in case, death and DALY counts between the baseline and most recent year, to distinguish trends in standardised risk from trends in the total number of people affected.

2.4 Attributable-risk analysis

The contribution of modifiable exposures was assessed using the GBD comparative risk assessment, which estimates the population attributable fraction—the proportion of NPC deaths and DALYs that would be averted under a theoretical minimum-risk exposure distribution—for tobacco smoking, alcohol use and occupational carcinogens (for NPC, occupational formaldehyde).[10] Global and Southeast Asian attributable rates and fractions, together with their temporal trends, were compiled from GBD risk-factor analyses.[7,16,17,18,23]

2.5 Projection to 2050

The published GBD Bayesian age–period–cohort forecast of global age-standardised rates to 2050, which incorporates the Socio-demographic Index, was reported directly as the principal forward-looking estimate.[12] To indicate the plausible ASEAN trajectory within a single cycle, we additionally derived an illustrative constant-EAPC projection, applying the GBD 2023 EAPC—together with the bounds of its 95% confidence interval—forward from 2023 to 2050 to generate an uncertainty band. This naïve extrapolation deliberately assumes an unchanged log-linear trend, ignores age–period–cohort structure and demographic change, and is therefore presented only as a scenario and not as a formal forecast; a Bayesian age–period–cohort or Nordpred model fitted to the annual series would be preferable and is proposed as future work. Analyses and visualisations were performed in Python (NumPy, pandas and Matplotlib) and the code is shared for reproducibility.

3. Results

3.1 Regional burden and temporal trends

In 2021 the Global Burden of Disease Southeast Asia region accounted for an estimated 13,661 incident NPC cases, 11,177 deaths and 376,855 DALYs, corresponding to an age-standardised incidence rate of 1.89 per 100,000, an age-standardised mortality rate of 1.60 per 100,000 and an age-standardised DALY rate of 50.77 per 100,000, as detailed in Table 1.[12] The regional mortality rate was the highest of any GBD world region and markedly exceeded the corresponding global figure of 0.87 per 100,000, even though the regional incidence rate (1.89) was lower than that of East Asia (3.41), indicating a comparatively high case-fatality profile. Between 1990 and 2021 all three age-standardised rates declined, with EAPCs of −0.39% per year for incidence, −0.76% per year for mortality and −0.84% per year for DALYs, as shown in Figure 1A.

This age-standardised decline, however, coexisted with a substantial expansion of the absolute burden. As illustrated in Figure 1B, incident cases more than doubled between 1990 and 2021 (from 6,209 to 13,661; +120%), deaths nearly doubled (from 5,608 to 11,177; +99%) and DALYs rose by 83% (from 206,433 to 376,855). This divergence—falling risk per standardised individual but rising totals—reflects population growth and ageing across the region and is the central epidemiological signature of NPC in Southeast Asia, quantified in Table 1.

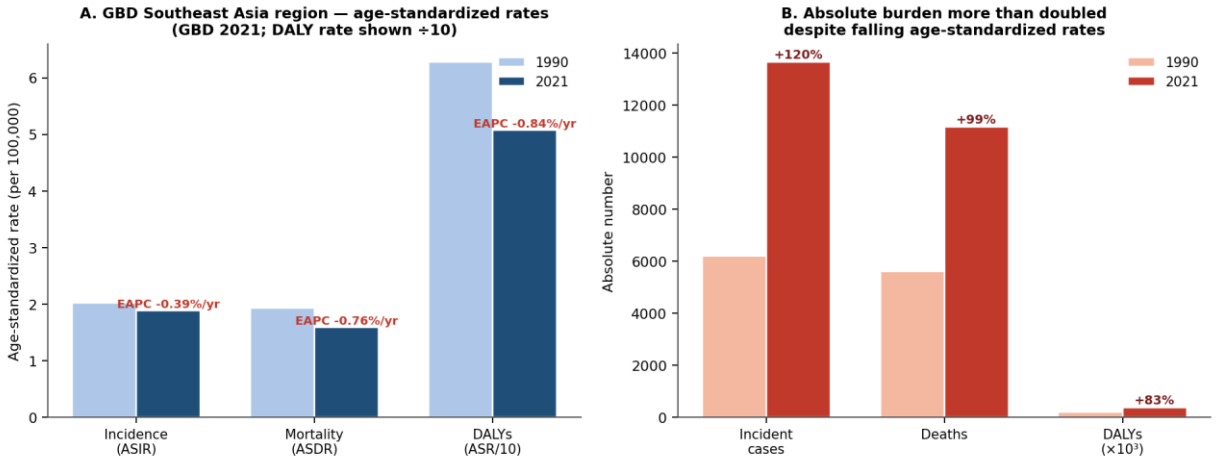

Figure 1. Nasopharyngeal carcinoma in the GBD Southeast Asia region, 1990 versus 2021. (A) Age-standardised incidence, mortality and DALY rates with estimated annual percentage change (EAPC); the DALY rate is shown divided by ten for scale. (B) Absolute incident cases, deaths and DALYs, showing that the total burden more than doubled despite falling age-standardised rates.

Table 1. Burden of nasopharyngeal carcinoma in the GBD Southeast Asia region, 1990 and 2021 (GBD 2021), with global comparison. Values are age-standardised rates per 100,000 (95% uncertainty interval) or absolute counts; the final column reports the estimated annual percentage change for rates and the percentage change for counts. ASIR, age-standardised incidence rate; ASMR, age-standardised mortality rate; DALY, disability-adjusted life-year; EAPC, estimated annual percentage change.

Indicator (Southeast Asia region)	1990	2021	EAPC / change	Global 2021
ASIR, per 100,000	2.03 (1.77–2.32)	1.89 (1.65–2.14)	−0.39 (−0.45, −0.32)	1.38 (1.22–1.58)
ASMR, per 100,000	1.94 (1.69–2.21)	1.60 (1.41–1.81)	−0.76 (−0.81, −0.70)	0.87 (0.78–0.97)
DALY rate, per 100,000	62.81 (54.84–71.85)	50.77 (44.30–57.72)	−0.84 (−0.90, −0.78)	28.91 (25.69–32.24)
Incident cases, n	6,209	13,661	+120%	118,878
Deaths, n	5,608	11,177	+99%	75,359
DALYs, n	206,433	376,855	+83%	2,490,191

3.2 National spatial distribution

The national picture was strikingly heterogeneous, as presented in Table 2 and Figure 2.[15] Age-standardised incidence spanned more than a ten-fold range, from 1.3 per 100,000 in Cambodia to 14.2 per 100,000 in Singapore—the latter being among the highest national rates worldwide and reflecting the predominance of high-risk southern-Chinese ancestry in its population. Viet Nam and Brunei followed (each 3.9 per 100,000), then Malaysia (3.2), with Thailand, Myanmar and Laos at an intermediate 2.0–2.1, and Indonesia, the Philippines and Timor-Leste at 1.6–1.7. Age-standardised mortality was highest in Viet Nam and Malaysia (each 2.6 per 100,000), as depicted in Figure 2. Singapore's incidence estimate carries a wide uncertainty interval (95% uncertainty interval 9.0–19.3, Table 2) and derives from a comparatively small population; although it is congruent with the historically high rates long recorded in the Singapore Chinese population and with global cancer statistics, its precise magnitude should be read with corresponding caution.[2]

Crucially, the ranking by age-standardised rate diverged sharply from the ranking by absolute burden, as shown in Table 2. Indonesia, despite a modest ASIR of 1.7 per 100,000, carried by far the largest absolute burden of any ASEAN country—an estimated 5,163 incident cases and 4,306 deaths in 2023—by virtue of its population size, followed by Viet Nam (4,607 cases; 3,046 deaths). Across the eleven countries the ASEAN aggregate reached 17,077 incident cases, 12,422 deaths and 435,087 DALYs, with a pooled ASIR of 2.3 and ASMR of 1.7 per 100,000. Consistent with global GBD estimates, the burden fell disproportionately on men, with an approximately two- to three-fold male excess that is directly relevant to targeting early-detection efforts.[13]

A direct comparison of the two GBD layers illustrates why they are reported separately rather than merged. Under GBD 2021, Malaysia was estimated to have the highest national age-standardised incidence in the world (approximately 6.1 per 100,000), whereas the newer GBD 2023 release revises this figure markedly downward to 3.2 per 100,000 (Table 2), with smaller revisions for other countries. Such cycle-to-cycle changes reflect updated input data and remodelling rather than genuine epidemiological shifts, and they reinforce our decision to base the national spatiotemporal analysis on a single GBD 2023 cycle while using the GBD 2021 regional and global figures only for longer-run and comparative context.[12,15]

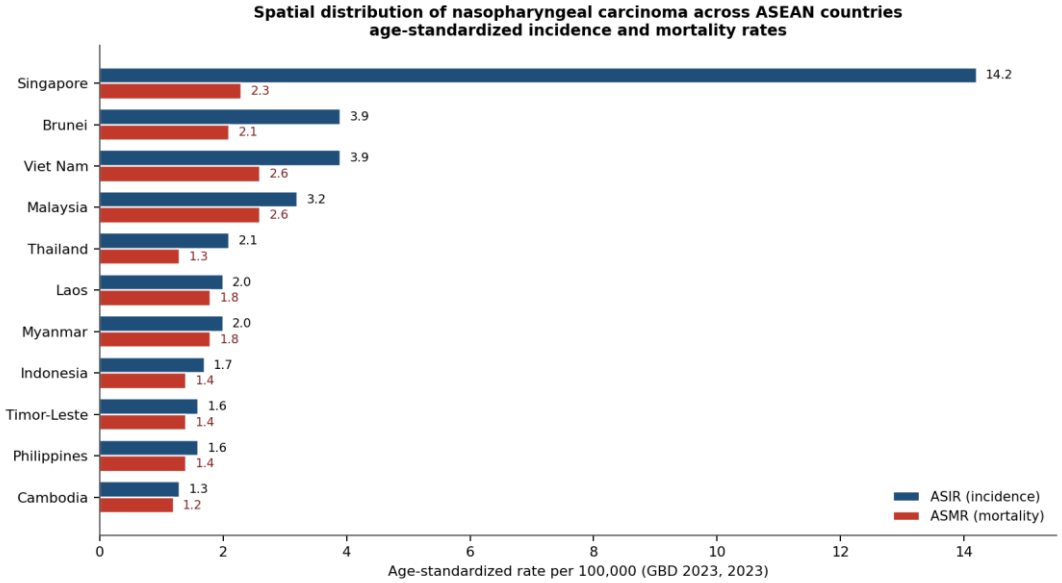

Figure 2. Spatial distribution of nasopharyngeal carcinoma across the eleven Southeast Asian countries (GBD 2023, reference year 2023): age-standardised incidence (ASIR) and mortality (ASMR) rates per 100,000, ranked by incidence. Singapore's rate greatly exceeds those of its neighbours.

Table 2. National burden and temporal trends of nasopharyngeal carcinoma across the eleven Southeast Asian countries (GBD 2023, reference year 2023), ranked by age-standardised incidence. Rates are per 100,000 with 95% uncertainty intervals (UI); EAPC (1990–2023) is shown with its 95% confidence interval (CI). ASIR, age-standardised incidence rate; ASMR, age-standardised mortality rate; DALY, disability-adjusted life-year; EAPC, estimated annual percentage change.

Country	Cases	ASIR (95% UI)	Incidence EAPC (95% CI)	ASMR (95% UI)	Mortality EAPC (95% CI)	DALY rate (95% UI)
Singapore	1,212	14.2 (9.0–19.3)	+0.2 (−0.0, 0.5)	2.3 (2.0–2.6)	−3.4 (−3.6, −3.1)	69.5 (60.8–79.3)
Viet Nam	4,607	3.9 (2.6–5.6)	+0.6 (0.4, 0.8)	2.6 (1.8–3.5)	−0.1 (−0.2, 0.1)	92.4 (63.7–125.8)
Brunei	19	3.9 (2.6–5.5)	−0.2 (−0.3, −0.2)	2.1 (1.6–2.6)	−1.1 (−1.1, −1.0)	65.3 (51.0–80.9)
Malaysia	1,094	3.2 (2.5–3.9)	−1.0 (−1.2, −0.8)	2.6 (2.1–3.1)	−1.4 (−1.6, −1.2)	79.0 (63.0–95.1)
Thailand	1,944	2.1 (1.6–2.7)	0.0 (−0.2, 0.3)	1.3 (1.1–1.6)	−0.9 (−1.1, −0.6)	45.2 (37.9–55.3)
Myanmar	1,104	2.0 (1.4–2.7)	−0.4 (−0.5, −0.2)	1.8 (1.3–2.4)	−0.5 (−0.6, −0.3)	58.3 (40.3–79.0)
Laos	125	2.0 (1.4–2.8)	+0.7 (0.5, 0.9)	1.8 (1.2–2.5)	+0.5 (0.4, 0.7)	60.9 (41.1–83.2)
Indonesia	5,163	1.7 (1.2–2.3)	+0.8 (0.6, 0.9)	1.4 (1.0–2.0)	+0.5 (0.3, 0.6)	48.9 (34.6–66.3)
Philippines	1,582	1.6 (1.3–1.9)	−0.0 (−0.2, 0.1)	1.4 (1.1–1.7)	−0.1 (−0.2, 0.1)	44.8 (35.7–53.3)
Timor-Leste	17	1.6 (1.1–2.4)	−0.1 (−0.3, 0.1)	1.4 (1.0–2.0)	−0.3 (−0.5, −0.1)	46.8 (32.2–65.2)
Cambodia	210	1.3 (0.9–1.9)	−0.7 (−0.8, −0.5)	1.2 (0.8–1.7)	−0.6 (−0.7, −0.5)	39.8 (27.1–56.1)
ASEAN total	**17,077**	**2.3 (1.7–2.9)**	**+0.4 (0.3, 0.4)**	**1.7 (1.3–2.1)**	**−0.2 (−0.2, −0.1)**	**56.8 (43.8–70.8)**

3.3 Divergent national temporal trends

Countries diverged not only in level but in direction of change, as displayed in Figure 3. Incidence was rising in Indonesia (EAPC +0.8% per year), Laos (+0.7), Viet Nam (+0.6) and, more modestly, Singapore (+0.2), while it was falling most steeply in Malaysia (−1.0), Cambodia (−0.7) and Myanmar (−0.4); Thailand and the Philippines were essentially static. Mortality trends were more uniformly downward, with the steepest decline in Singapore (EAPC −3.4% per year)—a fall in mortality against rising incidence that signals substantial improvement in survival—followed by Malaysia (−1.4), Brunei (−1.1) and Thailand (−0.9). Notably, Indonesia and Laos were the only countries in which both incidence and mortality rates rose over the study period, as shown in Figure 3, marking them as priority settings where the age-standardised burden is genuinely worsening rather than merely accumulating through demographic growth. Where the 95% confidence interval of an EAPC excludes zero (Figure 3), the trend is statistically significant: the rising incidence in Indonesia (+0.8; 95% CI 0.6 to 0.9) and Laos (+0.7; 0.5 to 0.9), and the declines in Malaysia incidence (−1.0; −1.2 to −0.8) and Singapore mortality (−3.4; −3.6 to −3.1), are all significant, whereas the incidence intervals for Thailand and the Philippines span zero and are properly regarded as stable.

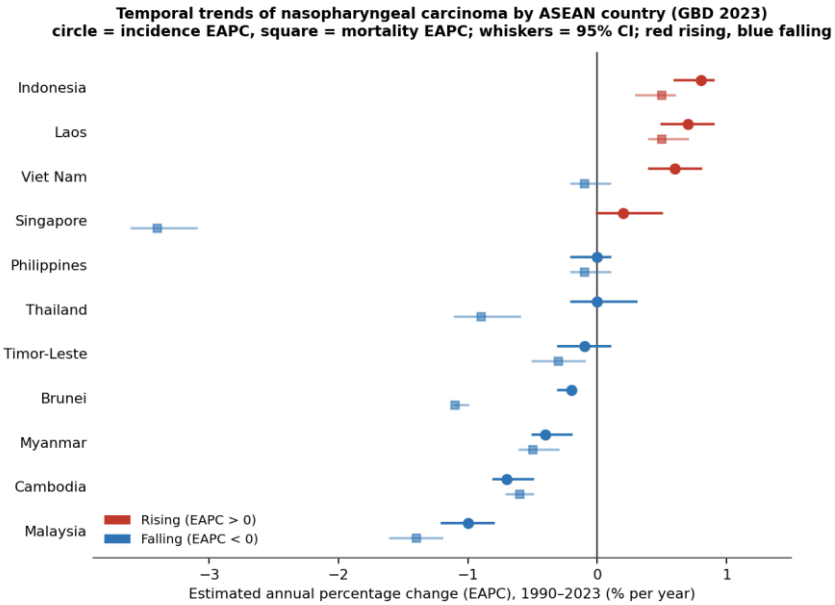

Figure 3. Temporal trends of nasopharyngeal carcinoma by Southeast Asian country (GBD 2023), shown as a forest plot of the estimated annual percentage change (EAPC): circles denote incidence and squares mortality, with whiskers giving the 95% confidence interval, 1990–2023. Red denotes a rising and blue a falling rate; a trend is statistically significant where its interval excludes zero. Indonesia and Laos show significant rising incidence and mortality, whereas Singapore shows the steepest mortality decline.

3.4 Attributable risk factors

The attributable-risk profile is summarised in Table 3 and Figure 4. Globally, tobacco smoking remained the leading modifiable contributor to NPC, accounting for approximately 21.9% of NPC DALYs in 2021, although its share had fallen from 23.5% in 1990; over the same interval the fraction attributable to alcohol use rose from 18.0% to 19.8%, as shown in Figure 4A.[7] This divergence was especially pronounced within Southeast Asia. Alcohol-attributable burden increased faster in Southeast Asia than in any other world region: among older adults the region's alcohol-attributable age-standardised rate nearly doubled, from 11.19 to 21.22 per 100,000 (EAPC +2.27% per year), even as smoking-attributable mortality declined (EAPC −1.30% per year), as depicted in Figure 4B.[7] An independent all-age analysis likewise identified Southeast Asia as showing the most pronounced increase of any region in alcohol-attributable mortality (average annual percentage change +1.76%), with Viet Nam emerging as a national hotspot (alcohol-attributable ASMR 0.78 per 100,000).[16] An important interpretive caveat applies to all of these fractions: the GBD comparative risk assessment for NPC models only behavioural and occupational exposures—tobacco, alcohol and occupational formaldehyde—and does not quantify Epstein–Barr virus infection or early-life intake of salt-preserved, nitrosamine-rich foods, the exposures generally regarded as the dominant causes of endemic NPC. The attributable fractions reported here therefore represent the modifiable behavioural and occupational component of causation rather than its entirety, and the large residual reflects viral, dietary and genetic determinants that GBD does not capture.[5,6]

Occupational exposure contributed a smaller but non-trivial burden, mediated for NPC essentially entirely by formaldehyde.[17,18] Globally, occupational formaldehyde was associated with 592 NPC deaths and 25,383 DALYs in 2021 (age-standardised DALY rate 0.30 per 100,000); within the Southeast Asia region the corresponding figures were 99 deaths and 4,301 DALYs (age-standardised DALY rate 0.55 per 100,000), with Malaysia exhibiting one of the highest national formaldehyde-attributable rates worldwide (age-standardised DALY rate 1.93 per 100,000), as summarised in Table 3.[18] In contrast to alcohol, occupational-attributable age-standardised rates were broadly declining, consistent with strengthening industrial-hygiene standards.[23]

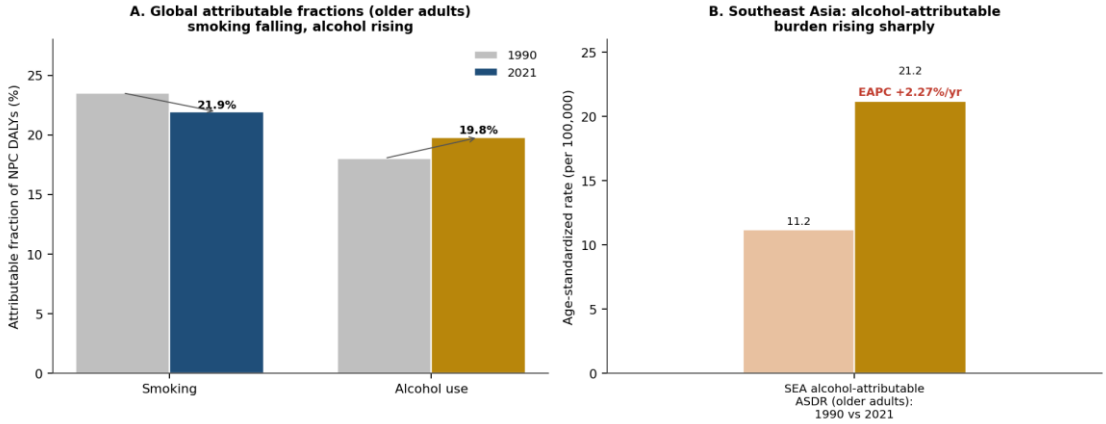

Figure 4. Attributable risk factors for nasopharyngeal carcinoma. (A) Global attributable fraction of NPC DALYs for tobacco smoking (falling) and alcohol use (rising), 1990 versus 2021. (B) Southeast Asia: alcohol-attributable age-standardised burden among older adults rose steeply between 1990 and 2021 (EAPC +2.27% per year), the fastest increase of any world region.

Table 3. Attributable risk factors for nasopharyngeal carcinoma: global and Southeast Asian burden and temporal trends (GBD 2021). ASDR, age-standardised DALY rate; ASMR, age-standardised mortality rate; EAPC, estimated annual percentage change; AAPC, average annual percentage change.

Attributable risk	Global burden, 2021	Southeast Asia	Temporal trend
Tobacco smoking	≈21.9% of NPC DALYs (from 23.5% in 1990)	Leading attributable factor; mortality declining	Smoking-attributable mortality EAPC −1.30 (SE Asia)
Alcohol use	≈19.8% of NPC DALYs (rising from 18.0%)	ASMR/ASDR rising fastest of any region; Viet Nam a national hotspot (ASMR 0.78)	Older-adult ASDR 11.19→21.22 (EAPC +2.27); all-age AAPC ASMR +1.76
Occupational formaldehyde	592 deaths; 25,383 DALYs; ASDR 0.30	99 deaths; 4,301 DALYs; ASDR 0.55; Malaysia ASDR 1.93 (among highest)	Age-standardised rates broadly declining

3.5 Projection to 2050

Published GBD forecasts indicate that the global age-standardised incidence of NPC is expected to rise modestly to about 1.53 per 100,000 by 2050 (an average annual increase of +0.43%, driven by male incidence), while global age-standardised mortality and DALY rates are projected to continue falling, to approximately 0.75 and 23.09 per 100,000 respectively, as shown in Figure 5A.[12] For the ASEAN aggregate, an illustrative single-cycle constant-EAPC projection (GBD 2023) implies that age-standardised incidence would continue to rise gradually, to approximately 2.56 per 100,000 (95% CI 2.49–2.63) by 2050, while age-standardised mortality would decline modestly, to approximately 1.61 per 100,000 (95% CI 1.57–1.65), as depicted with its uncertainty band in Figure 5B. Because this naïve projection assumes an unchanged log-linear trajectory and ignores age–period–cohort structure and demographic momentum, it is presented only as a scenario; under any realistic demographic assumption the absolute number of cases and deaths is likely to keep climbing even where standardised rates fall.

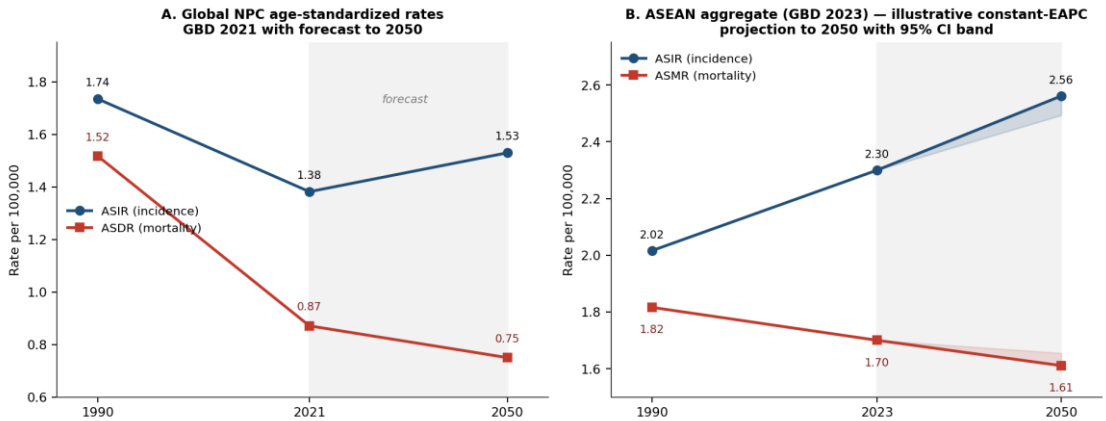

Figure 5. Projected trajectory of nasopharyngeal carcinoma age-standardised rates to 2050. (A) Global incidence and mortality with the published GBD Bayesian age–period–cohort forecast; incidence is projected to rise while mortality continues to fall. (B) ASEAN aggregate (GBD 2023, single cycle) under an illustrative constant-EAPC projection from 2023 to 2050, with the shaded band showing the 95% confidence interval derived from the EAPC; the 1990 point is back-computed from the same EAPC. Panel B is a scenario, not a formal forecast.

4. Discussion

This spatiotemporal ecological analysis yields four principal findings. First, the Global Burden of Disease Southeast Asia region carries the heaviest nasopharyngeal-carcinoma mortality of any world region, with a 2021 age-standardised mortality rate of 1.60 per 100,000, as quantified in Table 1.[12] Second, age-standardised incidence, mortality and DALY rates have all declined over three decades, yet the absolute burden has more than doubled, a divergence with major implications for health-system planning, as shown in Figure 1. Third, the region is profoundly heterogeneous: national age-standardised incidence spans a ten-fold range and, critically, the countries with the highest standardised rates (Singapore, Viet Nam) are not those with the greatest absolute burden (Indonesia, Viet Nam), as presented in Table 2 and Figure 2. Fourth, against a backdrop of falling tobacco- and occupational-attributable burden, alcohol has emerged as the fastest-rising attributable driver of NPC in Southeast Asia, as summarised in Figure 4 and Table 3.[7,16]

4.1 The paradox of falling rates and rising burden

The coexistence of declining age-standardised rates with a rising absolute count is the defining feature of NPC epidemiology in Southeast Asia and mirrors patterns reported globally and for neighbouring China.[1,24] Falling standardised rates plausibly reflect reductions in early-life exposure to salt-preserved foods with economic development, declining childhood infection intensity, improved diagnosis and, for mortality, better access to radiotherapy and chemoradiotherapy.[3,5] Yet because these relative gains are outpaced by population growth and ageing, the number of patients requiring complex, resource-intensive treatment continues to climb. For health systems across Southeast Asia—many still expanding radiotherapy capacity—the operational reality is therefore one of an expanding caseload, not a shrinking one, and cancer-control planning anchored solely to age-standardised trends risks underestimating future demand.

4.2 Aetiological interpretation of the spatial pattern

The extraordinary national heterogeneity is best understood through the interplay of ancestry, EBV and environment. Singapore's exceptional incidence, coupled with its steep mortality decline, reflects a population enriched for high-risk southern-Chinese genetic background combined with a high-income health system delivering early detection and modern chemoradiotherapy—precisely the configuration in which EBV-based screening yields its greatest returns.[4,6] The high rates in East Malaysia and among specific indigenous populations similarly point to genetic susceptibility acting together with EBV and traditional preserved-food diets.[3,6] Host HLA and non-HLA variation modulates the immune response to EBV and interacts with tobacco exposure, providing a biological substrate for the observed clustering.[6] These mechanisms explain why NPC does not distribute like other tobacco-related aerodigestive cancers and why region-tailored, ancestry-aware prevention and screening are likely to outperform generic approaches. It is relevant for the target readership that the overwhelming majority of Southeast Asian cases are the WHO type III (non-keratinising, undifferentiated) variant that is tightly Epstein–Barr virus-associated, and that regional variation in EBV strain and in HLA background is thought to underlie part of the incidence gradient; this histological and virological homogeneity is precisely what makes EBV-derived biomarkers—antibody panels and circulating plasma EBV DNA—attractive for both screening and post-treatment monitoring across the region.[4,6]

4.3 The rising alcohol-attributable burden

Perhaps the most actionable finding is the rapid growth of the alcohol-attributable component of NPC in Southeast Asia, which increased faster than in any other world region, as shown in Figure 4B and Table 3.[7,16] This trend tracks rising per-capita alcohol consumption across parts of the region and is epidemiologically important because alcohol is a directly modifiable exposure amenable to taxation, marketing restriction and screening-and-brief-intervention policies. Viet Nam, identified as a national alcohol-attributable hotspot and simultaneously exhibiting rising incidence, exemplifies a setting where alcohol-control policy could plausibly bend the NPC trajectory.[16] The concurrent decline in tobacco- and occupational-attributable burden shows that exposure-specific prevention can work, and reinforces the case for extending comparable policy attention to alcohol.[17,23]

4.4 The Indonesia evidence gap

Indonesia epitomises a broader tension between epidemiological importance and scientific visibility. With the largest absolute NPC burden in ASEAN—an estimated 5,163 incident cases and 4,306 deaths—and with both incidence and mortality rates rising, Indonesia is arguably the region's highest-priority setting, yet it remains under-represented in the international NPC literature, as reflected in Table 2.[15] The available Indonesian evidence is dominated by single-centre cohorts describing late presentation, prolonged treatment-waiting times and their impact on survival, together with early molecular and immunological characterisation of local tumours.[19,20,21,22] These studies underscore both the magnitude of the clinical problem and the feasibility of high-quality research in-country, and argue for investment in population-based cancer registration and multicentre studies to convert Indonesia's large burden into actionable local evidence.

4.5 Nasopharyngeal carcinoma in global and demographic context

Placing the region in global context sharpens these priorities. Whereas East Asia records the world's highest NPC incidence (age-standardised incidence 3.41 per 100,000), the distinction of Southeast Asia is its mortality, the highest of any world region despite a lower incidence—an excess that points to later-stage presentation and uneven access to modern radiotherapy rather than to a uniquely aggressive tumour biology.[1,12] Globally, age-standardised NPC rates have fallen since 1990 even as absolute cases have grown, and both this analysis and independent syntheses confirm that Southeast Asia follows the same direction of travel but from a higher mortality baseline.[1,11] The disease also retains a pronounced and persistent male predominance, with men bearing roughly two to three times the burden of women, together with a measurable adolescent-and-young-adult component, so that much of the burden falls on economically productive men in the third to fifth decades of life.[13,14] These demographic features amplify the economic consequences of the rising absolute caseload and reinforce the case for concentrating awareness and early-detection efforts on working-age men in endemic communities.

4.6 Implications for prevention and control

Taken together, these findings support a differentiated, region-aware control strategy. Primary prevention should prioritise the two rising or high-impact modifiable exposures—alcohol use region-wide and, where relevant, occupational formaldehyde in industrialising economies such as Malaysia—while sustaining tobacco control.[16,18] Secondary prevention through EBV-based serological and plasma-DNA screening, already validated in high-incidence Chinese populations and advancing toward vaccination, is most immediately transferable to high-rate, higher-resource settings such as Singapore and urban Malaysia, and should be piloted in high-incidence sub-populations elsewhere.[4] Tertiary gains—narrowing the incidence-to-mortality gap seen in several countries—depend on expanding radiotherapy access and shortening diagnostic and treatment delays, with plasma Epstein–Barr virus DNA kinetics offering a means to monitor treatment response and relapse—lessons emerging from Indonesian and regional cohorts.[19,25] Persistent male predominance and a measurable adolescent-and-young-adult burden further argue for targeting awareness and early-detection efforts at working-age men.[13,14]

4.7 Strengths and limitations

The strengths of this analysis include its explicit regional focus, the integration of descriptive burden with attributable-risk decomposition, the use of internally consistent GBD estimates spanning three decades, transparent trend quantification by EAPC and fully reproducible, shared analytical code. Several limitations must be emphasised. First, the analysis is ecological. To preserve internal consistency the primary national spatiotemporal analysis was confined to a single GBD 2023 cycle and a single geographical definition (ASEAN), and the earlier-cycle GBD 2021 regional and global figures are used only for longer-run and comparative context; nonetheless, the two layers derive from different releases and, as the Malaysia example shows (Section 3.2), are not strictly interchangeable, so cross-layer comparisons should be read with that caveat.[12,15] Second, GBD estimates for countries with sparse cancer-registration and vital-registration systems—which includes several ASEAN members—carry wide uncertainty and rely on statistical modelling and covariates, so national point estimates should be interpreted with appropriate caution. Third, ecological associations between regional risk-factor trends and NPC burden cannot establish individual-level causation. Fourth, the ASEAN projection is a deliberately naïve constant-EAPC extrapolation rather than a formal Bayesian forecast, and is presented only to bound the plausible trajectory. These limitations map directly onto the next analytical steps: a definitive study would extract the complete annual rate series for a single GBD cycle from the IHME Global Burden of Disease Results Tool and re-estimate every EAPC and its confidence interval de novo, apply joinpoint (segmented) regression to detect change-points that a single average EAPC can obscure, formally test the ecological association between national rates and the Socio-demographic Index, and replace the illustrative projection with a Bayesian age–period–cohort or Nordpred forecast. These constraints notwithstanding, the convergent signals—highest regional mortality, rising absolute burden, a widening alcohol-attributable component and a conspicuous Indonesian evidence gap—are robust to the specific data cycle and define a clear agenda for regional cancer control.

5. Conclusion

Southeast Asia bears the world's heaviest burden of nasopharyngeal-carcinoma mortality, and although age-standardised incidence, mortality and DALY rates have declined over three decades, this progress is masked by an absolute burden that has more than doubled since 1990. Beneath the regional aggregate lies profound national heterogeneity, with a ten-fold spread in age-standardised incidence and a decoupling of standardised risk from absolute burden that places Indonesia—large, rising and under-studied—at the centre of the regional agenda. The rapid growth of the alcohol-attributable component, unique among world regions, identifies a directly modifiable target for prevention, while the persistent incidence-to-mortality gap signals the value of expanding Epstein–Barr virus-based early detection and radiotherapy access. Region-tailored, ancestry-aware prevention, strengthened cancer registration and investment in Indonesian and wider Southeast Asian research are the priorities these patterns demand.

Declarations

Funding: No specific or external funding. **Competing interests:** None declared. **Data availability:** All estimates derive from the publicly reported Global Burden of Disease outputs of the Institute for Health Metrics and Evaluation (IHME), obtained from the GBD Results Tool (https://vizhub.healthdata.org/gbd-results) and used under the IHME Free-of-Charge Non-commercial User Agreement; the compiled dataset and analysis code (npc_sea_dataset.csv; gbd_analysis.py) are available in the supplementary files. **Author contributions:** LP conceived and designed the analysis, curated the data, performed the analysis and drafted the manuscript (guarantor); PK, MM and AN contributed to data curation, interpretation and critical revision of the manuscript. All authors approved the final version.

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