BMJ Open

Global epidemiological profile in nasopharyngeal carcinoma: a prediction study

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To cite: Zhang Y, Gu S, Deng H, *et al*. Global epidemiological profile in nasopharyngeal carcinoma: a prediction study. *BMJ Open* 2024;**14**:e091087. doi:10.1136/bmjopen-2024-091087

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (https://doi.org/10.1136/bmjopen-2024-091087).

Received 11 July 2024
Accepted 08 November 2024

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ABSTRACT

Objectives This study delineates the global nasopharyngeal carcinoma's (NPC) incidence and mortality across 185 countries in 2020 and projects the disease's burden by 2040.

Design A prediction study.

Setting Countries within the 20 world regions.

Participants Global NPC population.

Primary and secondary outcome measures The estimated counts of NPC cases and deaths were retrieved from the GLOBOCAN 2020 database. Age-standardised incidence rates (ASIR) and age-standardised death rates (ASDR) were computed. Projections for NPC by 2040 were derived from global population forecasts.

Results In the year 2020, East Asia emerged as the epicentre of both NPC incidences and mortalities, encompassing 49.39% (65 866 of the total 133 354 cases) and 45.56% (36 453 of the total 80 008 deaths), respectively, with China's contribution being the most substantial (46.82% of cases and 43.50% of deaths). The disparity between genders was notable, as the ASIR and ASDR for males were approximately triple those observed in females. The incidence exhibited regional diversity, with South-Eastern Asia and East Asia recording the highest ASIR for males and females (7.7 and 2.5, and 3.9 and 1.5 per 100 000 person-years, respectively). Similarly, South-Eastern Asia also reported the highest ASDR for both genders (5.4 and 1.5 per 100 000 person-years, respectively). Projections for 2040 anticipate a rise in annual cases and deaths to 179 476 (indicating a 34.58% increase from 2020) and 113 851 (reflecting a 42.29% increase), respectively. Further analysis revealed a correlation between the Human Development Index and disease burden.

Conclusions NPC, primarily impacting East Asia and predominantly affecting men, is poised for a significant increase in incidence and mortality by 2040, especially in Asia.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The initial research on the incidence and mortality of nasopharyngeal carcinoma (NPC) across 185 nations in 2020.
⇒ Anticipating the health burden of NPC through to 2040.
⇒ Certain nations exhibit restricted data availability.
⇒ Unspecified influence of adjustable risk factors.
⇒ The projection did not consider recent variations and disparities among countries.

INTRODUCTION

Nasopharyngeal carcinoma (NPC), a type of epithelial cancer originating from the nasopharyngeal mucosa, ranks among the most common head and neck cancers,[1] displaying pronounced geographical variability. Despite originating from similar cellular or tissue lineages, NPC markedly diverges from other head and neck epithelial tumours, being relatively rare in comparison and showing a highly uneven geographical distribution.[2 3] Over recent decades, there has been a global decline in NPC incidence rates.[4 5] It is noteworthy that populations from high-incidence regions maintain elevated rates even after relocating to non-endemic areas, though the rates for second-generation immigrants tend to decrease. This suggests that lifestyle and environmental changes might play roles, pointing to the interplay of genetic, ethnic and environmental factors in NPC development.[6]

NPC is largely preventable, given its association with numerous modifiable risk factors. Primary causes include Epstein-Barr virus (EBV) infection, smoking, consumption of salted fish and other preserved foods and occupational exposure to wood dust.[7 8] EBV infection, in particular, is considered a significant risk factor, with a dose-response relationship between EBV antibody levels and NPC risk, attributing about 85% of NPC cases to EBV infection. Smoking increases the risk of NPC by 60% compared with non-smokers, and the relative risk of NPC for those consuming salted Chinese-style fish weekly ranges from 1.1 to 4, escalating to 1.8 to 20 for daily consumption.[9–11]

The Human Development Index (HDI) serves as a useful tool for comparing global cancer incidence and mortality rates, offering insights into the health and mortality profiles of nations.[12] Indeed, the index correlates

with the incidence and mortality rates of various diseases, making it an effective index for gauging specific disease conditions across different countries. Comprising three fundamental dimensions—life expectancy at birth, adult literacy rate and per capita GDP (gross domestic product)—the HDI helps in accurately understanding the distribution of cancer and its risk factors.[13]

Given the close association between NPC and its modifiable risk factors, and due to changing epidemiological characteristics driven by trends in incidence and mortality rates, understanding the current epidemiological features of international variations in NPC incidence and mortality is crucial. This enables public health policymakers to make evidence-based decisions for primary prevention and optimise resource allocation to alleviate the global burden of NPC. With the global population's growth and ageing, forecasting the future burden of NPC is vital for better planning cancer control strategies.[14] Therefore, based on[15] GLOBOCAN 2020 estimates, our study investigates the geographical variations in NPC incidence and mortality rates worldwide and across nations, projecting the future NPC burden up to 2040 based on population forecasts.[8]

METHODS

Data sources

The number of new cases and deaths from NPC (classified under ICD-10 (ICD International Classification of Diseases (coding system)) as C11)[16 17] were extracted from the[15] GLOBOCAN 2020 database, encompassing data from 185 countries or territories, segmented by gender and in 5-year age intervals (0–4, 5–9, 80–84, 85 and older).[18 19] Corresponding population data for the year 2020 were retrieved from the United Nations website. The population forecasts used in this study were based on future fertility rates. The data sources and methods employed to compile the global cancer estimates for 2020 have been detailed elsewhere.[8] In brief, GLOBOCAN's country estimates are contingent on the availability of recorded high-quality national and subnational incidence data (from population-based cancer registries) and national mortality data (from vital registration systems).[20 21]

Methods for estimating age-standardised rates in the Global Cancer Programme

The methods of estimation are country-specific, and the quality of the estimation depends on the quality and on the amount of information available for each country. In theory, there are as many methods as countries, and because of the variety and complexity of these methods, an overall quality score for the incidence and mortality estimates combined is almost impossible to establish.[22 23] However, an alphanumeric scoring system that independently describes the availability of incidence and mortality data has been established at the country level. The combined score is presented together with the estimates for each country with the aim of providing a broad indication of the robustness of the estimation.[24–26]

The Human Development Index

The HDI serves as a composite metric that assesses three fundamental dimensions: life expectancy, education level and access to resources necessary for a decent living. Significant advancements have been observed across all groups and regions in terms of HDI indicators, with countries classified as having low and medium human development experiencing the most rapid progress.[27 28] This has led to a reduction in global inequalities. However, national averages often conceal the vast disparities in human experiences. Significant gaps persist within and between nations of the global North and South, and income inequality within many countries and between them continues to widen.[29 30] According to the HDI, countries are categorised into four tiers: very high human development (HDI≥0.80), high human development (0.80>HDI>0.710), medium human development (0.710≥HDI≥0.535) and low human development (HDI<0.535), reflecting a spectrum of progress and challenges in global development.[31]

Statistical analysis

Our analysis presented estimated new cases and deaths in both tabular and graphical formats, employing the direct standardisation method to calculate two summary measures: the age-standardised incidence rates (ASIR) and age-standardised death rates (ASDR) per 100 000 person-years based on the 1966 Segi-Doll world standard population, along with the cumulative risk of being diagnosed with or dying from NPC before the age of 75, assuming no other causes of death.[13 32] We projected future global cases and deaths of NPC based on the United Nations' four-tier HDI, which assesses the cancer burden across varying levels of development (low, medium, high and very high HDI). Projections for China were based on population forecasts and scenarios of annual increases (+1%, +2%, +3%, +4%), stability (0%) or decreases (−1%, −2%, −3%, −4%) from the baseline year of 2020.[15] The projection calculations applied specific age ratios (and the aforementioned scenarios of change) to the corresponding projected population data estimated by the United Nations Development Programme. Results were listed by country and aggregated within the 20 world regions defined by the United Nations and by HDI categories for the year 2020. Data management and analysis were conducted using R software (V.4.0.2; R Foundation for Statistical Computing), with global maps of NPC incidence and mortality rates by country generated using R software (V.4.0.2; R Foundation for Statistical Computing).[33]

Patient and public involvement

No patient is involved.

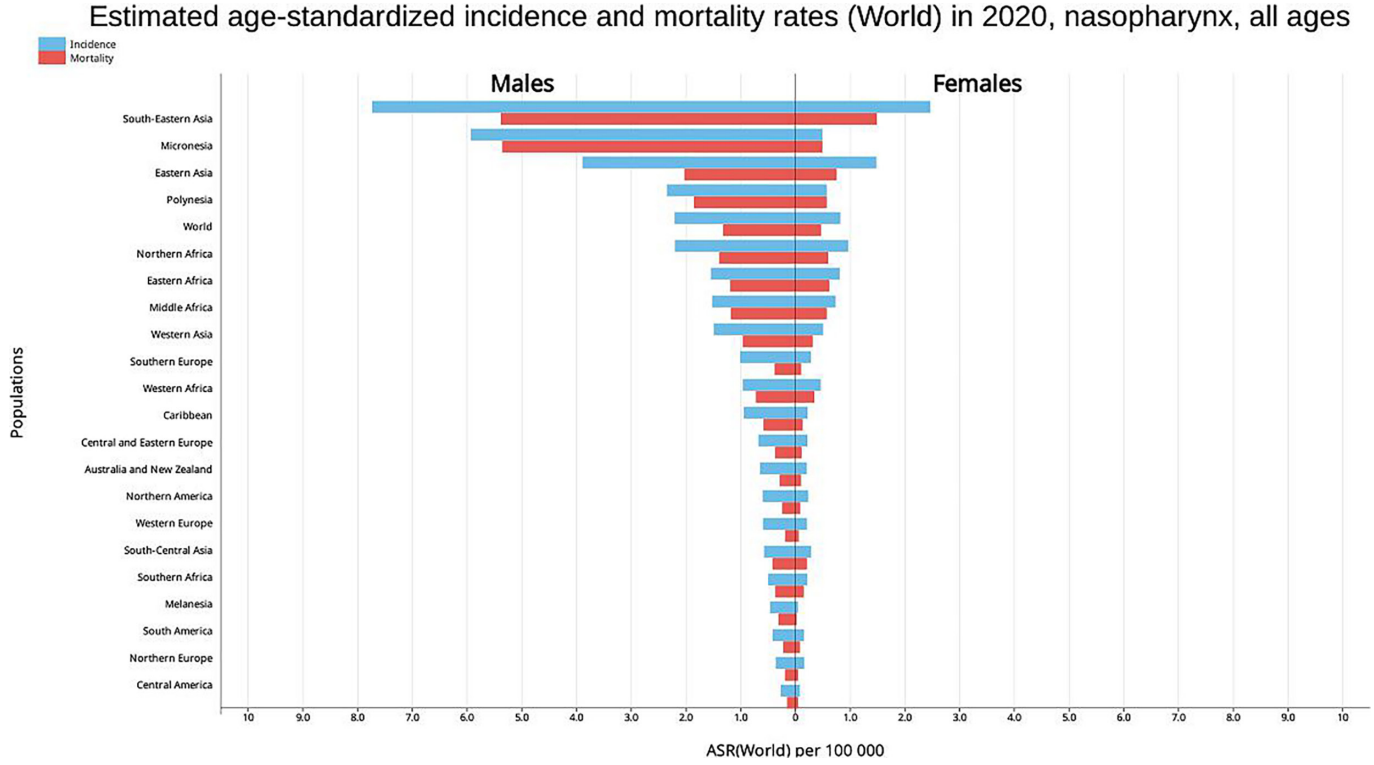

Figure 1 Global burden of disease for ASIR and ASDR in nasopharyngeal carcinoma in 2020, by region and gender. ASDR, age-standardised death rate; ASIR, age-standardised incidence rate; ASR, age-standardized rate.

RESULTS

Global burden of NPC incidence and mortality rates

In 2020, the global estimate for NPC diagnoses was 133 354 individuals, equating to an ASIR of 1.5 cases per 100 000 person-years. The incidence was higher in males (96 371 cases) compared with females (36 983 cases), with

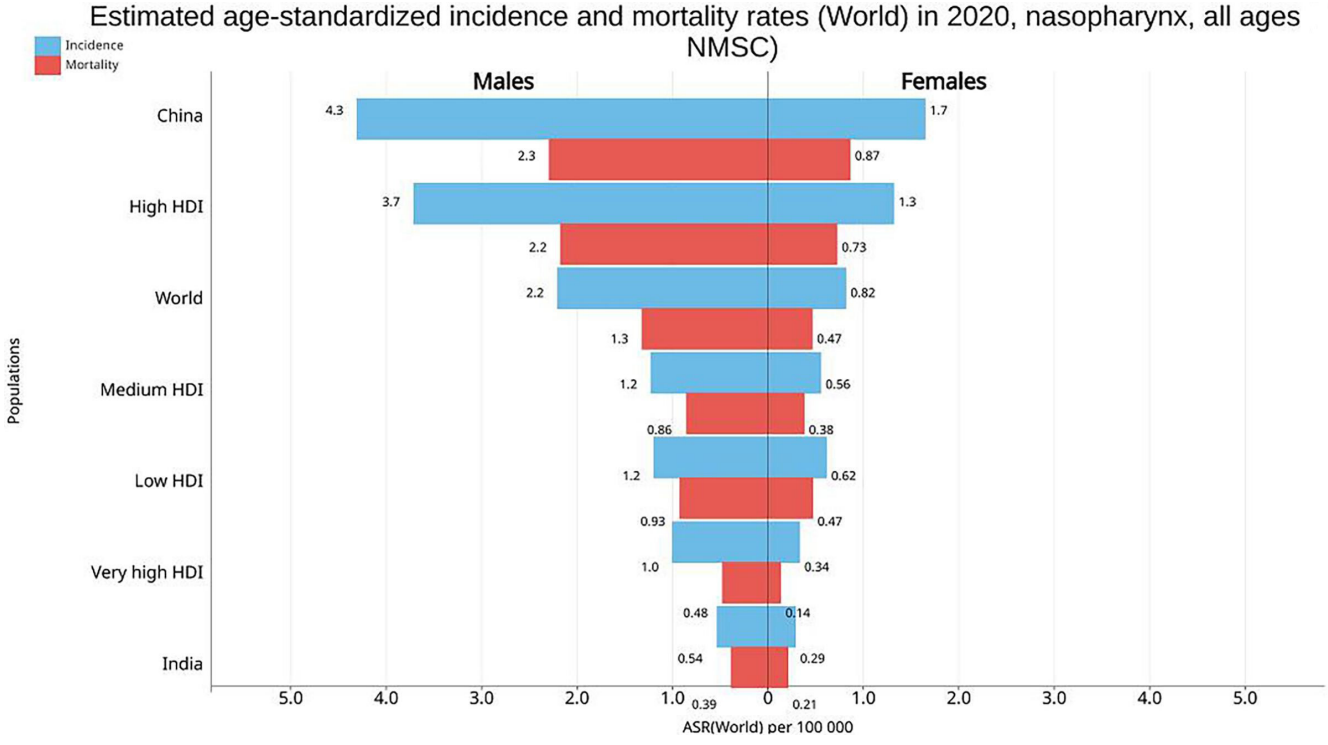

Figure 2 Global burden of disease for ASIR and ASDR in nasopharyngeal carcinoma in 2020, by HDI region and gender. ASDR, age-standardised death rate; ASIR, age-standardised incidence rates; ASR: age-standardized rateHDI; Human Development Index.

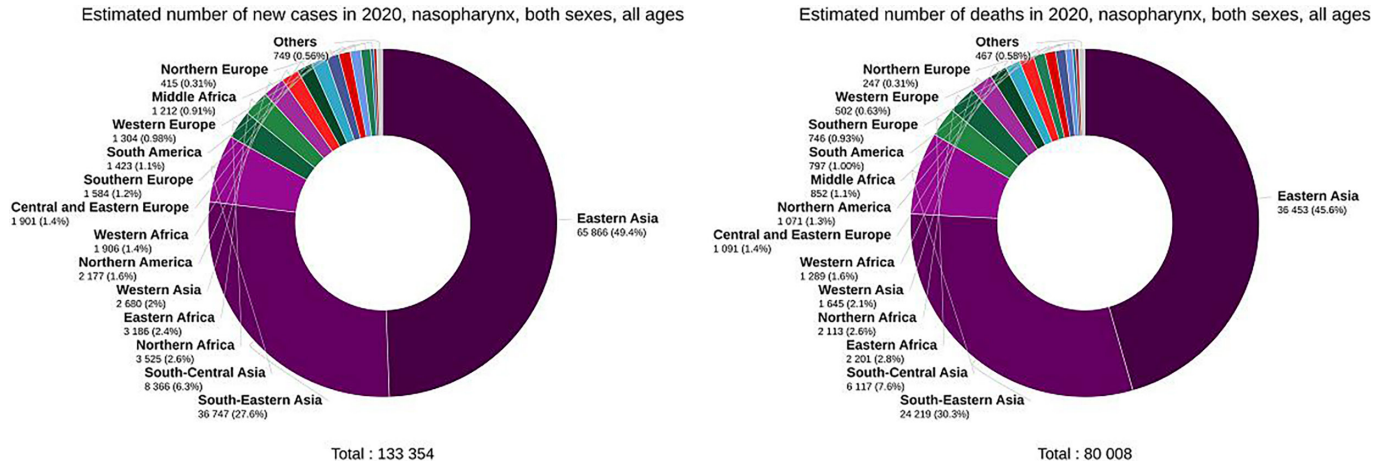

Figure 3 Global NPC disease burden pie chart for 2020 by Human Development Index region. (A) Incidence number (B) death number.

the male ASIR approximately three times that of females (2.2 vs 0.8 cases per 100 000 person-years, respectively). The global death toll from NPC was estimated at 80 008, corresponding to an ASDR of 0.9 cases per 100 000 person-years. The mortality rate was also higher in males, with 58 094 deaths compared with 21 914 in females and corresponding ASDRs of 1.3 and 0.5 cases per 100 000 person-years, respectively (online supplemental table S1; figure 1).

Nasopharyngeal carcinoma incidence and mortality rates stratified by human development level

When categorised based on the HDI, a significant majority of NPC cases and deaths are observed in countries with high HDI. These nations account for 37.32% of the world's population (2 909 468 000 out of 7 794 799 000) and bear a substantial burden of the disease, comprising 69.85% of new global cases (93 153 out of 133 354) and 68.55% of the total deaths (54 850 out of 80 008; online supplemental table S2, figure S2). The ASIR and ASDR are notably the highest in high HDI countries, recorded at 2.5 and 1.4 cases per 100 000 person-years, respectively. Interestingly, countries with very high HDI exhibit the lowest ASIRs and ASDRs. In contrast, low HDI countries show ASIRs and ASDRs that are comparable to those seen in countries with a medium level of human development (online supplemental table S2; figure 2).

Global distribution of NPC cases and mortality rates across different regions

In terms of NPC cases and deaths, Eastern Asia leads globally, accounting for approximately 49.39% of all NPC cases (65 866 out of 133 354) and 45.56% of deaths (36 453 out of 80 008). South-Eastern Asia follows, representing 27.55% of total cases (36 747 out of 133 354) and 30.15% of deaths (24 219 out of 80 008), with South Central Asia comprising 6.27% of cases (8366 out of 133 354) and 7.64% of deaths (6117 out of 80 008). A consistent trend across all regions indicates a higher incidence of NPC in males compared with females (online supplemental table S1, S2; figure 3).

There is a significant variation in NPC incidence rates worldwide, with a 29-fold difference in men and a striking 63-fold difference in women. The regions with the highest ASIR in men are South-Eastern Asia (7.7), Eastern Asia (3.9) and Micronesia/Polynesia (3.9), while the lowest is observed in Central America (0.3). For women, the highest ASIR is recorded in South-Eastern Asia (2.5), followed by Eastern Asia (1.5) and Northern Africa (1.0), with the lowest in Melanesia (less than 0.1; online supplemental table S1, S2; figure 3).

Similarly, the regional disparities in NPC mortality rates are substantial, with a 36-fold variation in men and 75-fold in women. The highest ASDR in men are found in South-Eastern Asia (5.4), followed by Micronesia/Polynesia (3.4) and Eastern Asia (2.0), with the lowest in Central America (0.2). In women, South-Eastern Asia again has the highest ASDR (1.5), followed by Eastern Asia (0.8) and Eastern Africa (0.6), with the lowest in Melanesia (below 0.1). Notably, there are significant gender disparities in NPC rates, with ASIRs and ASDRs being consistently higher in men than in women across all regions. The ratios of male-to-female ASIR and ASDR vary widely, from 1.9 in both categories in Eastern Africa to as high as 11.5 and 15.5 in Melanesia, respectively (online supplemental table S2; figure 3).

National variations in NPC prevalence and mortality rates

When analysing NPC at the national level, China stands as the predominant contributor globally. It accounts for 46.82% of NPC cases (62 444 out of 133 354) and 43.50% of NPC deaths (34 810 out of 80 008). As indicated in online supplemental table S1, China's population constitutes 18.56% of the global total (1 447 470 000 out of 7 794 799 000), and the country exhibits higher incidence and mortality rates (ASIR and ASDR at 3.0 and 1.6 per 100 000 person-years, respectively), positioning China at the forefront of NPC incidence and mortality worldwide

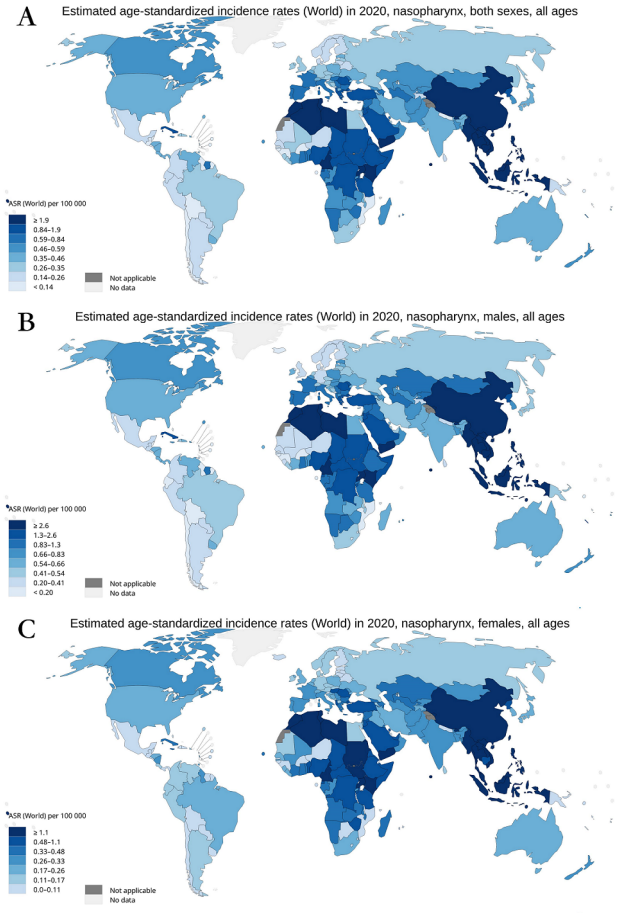

Figure 4 Heatmap of the global burden of disease for ASIR by nasopharyngeal carcinoma in 2020 by country and sex (A) both sex (B) male (C) female. ASIR, age-standardised incidence rate; ASR: age-standardized rate.

(online supplemental table S3, S4; figure 4; online supplemental figure S1).

Regarding incidence rates, Brunei Darussalam records the highest ASIR per 100 000 person-years at 13.4, followed by the Maldives and Indonesia with an ASIR of 10.7 for men. For women, Brunei Darussalam again leads with an ASIR of 6.4, with the Maldives (3.3) and Malaysia (3.1) trailing (online supplemental table S3, S4; figure 4; online supplemental figure S1).

These rates, however, exhibit remarkable regional disparities. Within the high-risk region of South-Eastern Asia, male ASIRs range from 3.3 in Thailand to 13.4 in Brunei Darussalam and female ASIRs vary from 1.1 in Cambodia to 6.4 in Brunei Darussalam. In terms of mortality rates, Brunei Darussalam tops the list again with the highest ASDR for men at 8.0 and for women at 3.4. Following Brunei are the Maldives and Indonesia for men, each with an ASDR of 7.7, and for women, Timor-Leste (2.3) and the Lao People's Democratic Republic (2.2). Within South-Eastern Asia, the ASDR per 100 000 person-years for men ranges from 2.0 in Thailand to 8.0 in Brunei Darussalam (a high-to-low ASDR ratio of 4.0), and for women, from 0.7 in Thailand to 3.4 in Brunei Darussalam (a high-to-low ASDR ratio of 4.9; online supplemental table S3, S4; figure 4; online supplemental figure S1).

The relationship between ASDR, ASIR and HDI levels across countries globally

Our analysis also extends to the comparison between ASDR and ASIR among countries categorised by their HDI. Regarding incidence rates, it was observed that countries with a higher HDI generally exhibit a higher ASIR compared with those with lower HDI levels. A similar pattern emerges for ASDR across different HDI categories. Notably, European countries with a high HDI level tend to have the lowest ASDR and ASIR, while Asian countries record higher values in both metrics. This consistency in the pattern between ASDR and ASIR across HDI levels highlights significant regional disparities in the burden of NPC disease (online supplemental table S5, figure S2).

Projected global trends in NPC incidence and mortality rates by 2040

Assuming a stable global incidence rate from 2020, it is projected that by 2040, the world will witness an increase of approximately 34.58% in new NPC cases, rising from 133 354 cases in 2020 to an estimated 179 476 cases, an increment of 46 122 cases. Furthermore, if the incidence rate escalates annually by 2% starting from 2020, the total number of annual NPC cases by 2040 could more than double. It is important to note that to ensure the number of NPC cases in 2040 (119 710 cases) remains below the count in 2020 (133 354 cases), a yearly decline of 2% in mortality rates is required (online supplemental table S6, figure S3).

In terms of mortality, assuming the 2020 death rate remains constant, the number of deaths due to NPC is estimated to rise by about 42.29% (an increase of 33 843 deaths from 80 008 in 2020 to 113 851 in 2040). To achieve a reduction in NPC deaths in 2040 compared with the estimated numbers in 2020, a consistent annual decrease of 2% in mortality rates is essential (online supplemental table S6).

When classified by HDI categories, it is estimated that countries with a high HDI will experience the largest absolute increase in both NPC cases and deaths. By 2040, these countries could see an annual case increase of 26.7% (24 874 out of 93 153 cases) and a 40.15% rise in deaths (22 024 out of 54 850 deaths), assuming the incidence and mortality rates of 2020 persist. This reflects the already high incidence rates in high HDI countries, coupled with their large and growing populations. However, countries with a low HDI are predicted to have the highest relative increases in both incidence and mortality rates, at 90.54% (an increase from 5722 to 10 903 cases) and 95.29% (an increase from 3996 to 7804 deaths, respectively; online supplemental table S6, figure S4).

DISCUSSION

In 2020, the world reported approximately 133 354 new cases of NPC, with 80 008 resulting in death. The Eastern

Asia region, particularly China, contributed significantly to this burden, leading to both NPC cases and deaths. Globally, the incidence and mortality rates of NPC were significantly higher in males than in females, with the highest rates of both incidence and mortality found in males and females from South-Eastern Asia and Eastern Asia. Over the next two decades, due to population growth and ageing alone, the global number of NPC cases and deaths is expected to increase by more than 35%, with the annual cases and deaths in countries with a low HDI nearly doubling by 2040.

The changing epidemiological profile and the disparities in NPC burden across different regions and genders can largely be attributed to variations in the prevalence of risk factors for NPC, as well as improvements in diagnostic and treatment technologies.[17 34 35] Historical studies indicate that the incidence and mortality rates of NPC have significantly declined over the past few decades in most European, North American, Eastern Asian and South-Eastern Asian countries.[36 37] The decreasing trends in NPC incidence in Europe and North America may be linked to reduced smoking rates, while the decline in Eastern and South-Eastern Asia might be attributed to decreased consumption of salted fish and preserved foods, with mortality rates also benefiting from advances in diagnostic and radiation therapy techniques.[38]

The relatively high incidence rates of NPC in Eastern and South-Eastern Asian countries are largely associated with high rates of EBV infection.[39 40] Furthermore, it is estimated that China has 316 million adult smokers, making up nearly one-third of the country's smoking population and accounting for 40% of the world's tobacco consumption. Thus, the considerable burden of NPC in China can be partly attributed to its extensive tobacco consumption and production.[41 42] The consumption of salt-preserved foods, which is relatively high in most Eastern Asian, South-Eastern Asian and North African countries, may also contribute to the significant international differences in NPC burden. Currently, screening programmes for the EB virus are available in some high-risk areas, but screening in healthy populations is still necessary to avoid missed diagnoses. Individuals with a family history of cancer need to be vigilant. Research shows that NPC often occurs in clusters within families. It is important to focus on screening high-risk populations and to implement measures that improve the diagnosis and treatment of NPC. Additionally, patients diagnosed with NPC should actively cooperate with their doctor's treatment plan. They should also focus on adjusting their diet and lifestyle, maintaining a positive mindset and working together to combat the disease. The higher incidence of NPC in males across all regions can be attributed to several factors: increased smoking rates, exposure to secondhand smoke, higher rates of alcoholism and more frequent occupational exposure to carcinogens such as pesticides, coal tar and engine oil. Furthermore, the decrease in NPC incidence among women may be related to the protective effects of endogenous oestrogen (4344). Research indicates that smoking can trigger the activation of the EBV, making smoking control—particularly reducing exposure to secondhand smoke—crucial for preventing NPC. Simultaneously, decision-makers in various regions should enhance the prevention and intervention of risk factors for NPC, improve health education and develop targeted prevention and treatment measures based on gender and regional differences in incidence to reduce the overall disease burden of NPC. These efforts aim to ultimately reduce the disease burden of NPC.

Our findings suggest that, solely due to population growth and ageing, the global number of NPC cases and deaths is projected to rise to 179 476 and 113 851, respectively, by 2040. A yearly decrease of 2% in both incidence and mortality rates is necessary to halt the increase in NPC burden by 2040.[43–45] Notably, our study indicates that to reduce the future burden of NPC in countries with middle to low HDI, even greater reductions in incidence and mortality rates are required. Given these changes, reallocating resources for primary prevention programmes in specific regions and countries to reduce levels of EBV infection, smoking, consumption of salted fish and other preserved foods and occupational exposure to NPC carcinogens, along with providing more early detection methods (such as NPC screening) and healthcare services for high-risk populations identified by our research, is crucial for reducing the global burden of NPC.[46] Currently, society is experiencing rapid socioeconomic development alongside an accelerating trend of population ageing. To reduce the burden of NPC, it is necessary to strengthen prevention and control efforts, conduct health education on its causes and risk factors and enhance public awareness of NPC and its prevention.

In our study, we also explored the differences in ASDR and ASIR among countries categorised by their HDI. We discovered that countries with a higher HDI generally exhibit a greater burden of NPC disease, with Asian countries of high HDI facing the highest burden. This finding suggests that in the Asian context, the burden of NPC is not strongly correlated with economic development or the level of healthcare but is more significantly influenced by demographic and cultural factors.[47]

To our knowledge, this research is the first to provide a comprehensive overview of the current epidemiological landscape of NPC incidence and mortality rates globally, based on the[15] GLOBOCAN 2020 data set, which is highly relevant for cancer control and clinical practice. The numbers and rates of NPC reported in this study are estimated from the best available data provided by population-based cancer registries, which have been reviewed for completeness, coverage and accuracy.

However, several limitations are inherent in our study. First, although our findings are based on the highest quality data currently available, caution is needed when interpreting the results for countries with limited cancer registry coverage and those where national estimates were obtained using substitute data. Second, our projections for NPC's future burden by 2040 did not account

for recent changes in NPC incidence and mortality rates, nor did they consider the heterogeneity in trends across countries. Given the global decline in NPC rates over recent decades, our projections may overestimate the future burden of NPC and thus, should be interpreted with caution. Lastly, our study could not differentiate the necessary changes in modifiable risk factors and their consequent impact on predicted NPC incidence and mortality rates. This indicates a need for further research to clarify the impact of changes in exposure to modifiable risk factors on the burden of NPC.

CONCLUSION

NPC presents a significant global public health challenge, notably in East Asia with China as the leading contributor. High incidence and mortality rates in men, particularly in South-Eastern and Eastern Asia, underscore the disease's impact. By 2040, NPC cases and deaths are expected to rise by over 35%, predominantly in lower HDI countries. Research indicates that NPC primarily relates to factors like EB virus infection, genetics and environmental factors. Furthermore, unhealthy lifestyles, such as excessive smoking, eating pickled foods and exposure to air pollution, can also trigger this disease (PMID: 35414057) The ongoing high prevalence of EBV infection and smoking in specific areas demands immediate attention to these modifiable risk factors. The elevated NPC incidence in higher HDI countries, especially in Asia, underscores the urgent need for effective primary prevention strategies and prioritising resources for NPC prevention and treatment in high-risk populations. This calls for targeted interventions to address the NPC burden efficiently.

Acknowledgements I would like to express my gratitude to my coworkers of enrolled studies.

Contributors YZ and SG contribute to the conception or design of the work. HD and ZS contribute to the acquisition, analysis or interpretation of data for the work. All authors draft the work and revise it critically for important intellectual content and contribute to final approval of the version to be published. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. HD is responsible for the overall content (as guarantor).

Funding This study was supported by Ningbo Top Medical and Health Research Program (No. 2023030514), Ningbo Clinical Research Center for Otolaryngology Head and Neck Disease (No. 2022L005).

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available in a public, open access repository.

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REFERENCES

1 Editors from The Medical Letter. Toripalimab (Loqtorzi) for Nasopharyngeal Carcinoma. *Med Lett Drugs Ther* 2024;66:e16–7.
2 Bossi P, Chan AT, Licitra L, *et al*. Nasopharyngeal carcinoma: ESMO-EURACAN Clinical Practice Guidelines for diagnosis, treatment and follow-up†. *Ann Oncol* 2021;32:452–65.
3 Bossi P, Gurizzan C, Chan A. Immunotherapy for Nasopharyngeal Carcinoma: The Earlier the Better. *JAMA* 2023;330:1954–5.
4 Cantù G. Nasopharyngeal carcinoma. A "different" head and neck tumour. Part B: treatment, prognostic factors, and outcomes. *Acta Otorhinolaryngol Ital* 2023;43:155–69.
5 Chang ET, Ye W, Ernberg I, *et al*. A novel causal model for nasopharyngeal carcinoma. *Cancer Causes Control* 2022;33:1013–8.
6 Albasri AM. Nasopharyngeal carcinoma metastasis to the breast. *Saudi Med J* 2020;41:1130–4.
7 De Felice F, Marchetti C, Serpone M, *et al*. Upper-neck irradiation versus standard whole-neck irradiation in nasopharyngeal carcinoma: A systematic review and meta-analysis. *Tumori* 2023;109:529–36.
8 Ding R-B, Chen P, Rajendran BK, *et al*. Molecular landscape and subtype-specific therapeutic response of nasopharyngeal carcinoma revealed by integrative pharmacogenomics. *Nat Commun* 2021;12:3046.
9 Chen YP, Chan ATC, Le QT, *et al*. Nasopharyngeal carcinoma. *Lancet* 2019;394:64–80.
10 Chen ZH, Zheng WH, Wu CF, *et al*. Thyroid dysfunction in Chinese nasopharyngeal carcinoma after anti-PD-1 therapy and its association with treatment response. *BMC Med* 2023;21:18.
11 Chua ML, Sun Y, Supiot S. Advances in nasopharyngeal carcinoma-"West meets East. *Br J Radiol* 2019;92:20199004.
12 Arnold M, Morgan E, Rumgay H, *et al*. Current and future burden of breast cancer: Global statistics for 2020 and 2040. *The Breast* 2022;66:15–23.
13 Bray F, Parkin DM, African Cancer Registry Network. Cancer in sub-Saharan Africa in 2020: a review of current estimates of the national burden, data gaps, and future needs. *Lancet Oncol* 2022;23:719–28.
14 Huang H, Yao Y, Deng X, *et al*. Immunotherapy for nasopharyngeal carcinoma. *Curr status and prospects (Rev) Int J Oncol* 2023;63.
15 Cabasag CJ, Fagan PJ, Ferlay J, *et al*. Ovarian cancer today and tomorrow: A global assessment by world region and Human Development Index using GLOBOCAN 2020. *Int J Cancer* 2022;151:1535–41.
16 Juarez-Vignon Whaley JJ, Afkhami M, Onyshchenko M, *et al*. Recurrent/Metastatic Nasopharyngeal Carcinoma Treatment from Present to Future: Where Are We and Where Are We Heading? *Curr Treat Options Oncol* 2023;24:1138–66.
17 Juarez-Vignon Whaley JJ, Afkhami M, Sampath S, *et al*. Early Stage and Locally Advanced Nasopharyngeal Carcinoma Treatment from Present to Future: Where Are We and Where Are We Going? *Curr Treat Options Oncol* 2023;24:845–66.
18 Erren TC, Reiter RJ. Defining chronodisruption. *J Pineal Res* 2009;46:245–7.
19 Ferlay J, Colombet M, Soerjomataram I, *et al*. Estimating the global cancer incidence and mortality in 2018: GLOBOCAN sources and methods. *Intl Journal of Cancer* 2019;144:1941–53.
20 Ferlay J, Colombet M, Soerjomataram I, *et al*. Cancer statistics for the year 2020: An overview. *Intl Journal of Cancer* 2021;149:778–89.

21 Ferlay J, Shin HR, Bray F, *et al*. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *Intl Journal of Cancer* 2010;127:2893–917.
22 Goetze OT, Al-Batran SE, Chevallay M, *et al*. Multimodal treatment in locally advanced gastric cancer. *Updates Surg* 2018;70:173–9.
23 Hirabayashi M, Georges D, Clifford GM, *et al*. Estimating the Global Burden of Epstein-Barr Virus-Associated Gastric Cancer: A Systematic Review and Meta-Analysis. *Clin Gastroenterol Hepatol* 2023;21:922–30.
24 Ferlay J, Soerjomataram I, Dikshit R, *et al*. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *Int J Cancer* 2015;136:E359–86.
25 Gandaglia G, Leni R, Bray F, *et al*. Epidemiology and Prevention of Prostate Cancer. *Eur Urol Oncol* 2021;4:877–92.
26 Ghoncheh M, Pournamdar Z, Salehiniya H. Incidence and Mortality and Epidemiology of Breast Cancer in the World. *Asian Pac J Cancer Prev* 2016;17:43–6.
27 Fuentefria R do N, Silveira RC, Procianoy RS. Motor development of preterm infants assessed by the Alberta Infant Motor Scale: systematic review article. *J Pediatr (Rio J)* 2017;93:328–42.
28 García-Tizón Larroca S, Amor Valera F, Ayuso Herrera E, *et al*. Human Development Index of the maternal country of origin and its relationship with maternal near miss: A systematic review of the literature. *BMC Pregnancy Childbirth* 2020;20:224.
29 Hu QD, Zhang Q, Chen W, *et al*. Human development index is associated with mortality-to-incidence ratios of gastrointestinal cancers. *World J Gastroenterol* 2013;19:5261–70.
30 Javanmard E, Niyyati M, Ghasemi E, *et al*. Impacts of human development index and climate conditions on prevalence of Blastocystis: A systematic review and meta-analysis. *Acta Trop* 2018;185:193–203.
31 Freire RCJ, Pieruccini-Faria F, Montero-Odasso M. Are Human Development Index dimensions associated with gait performance in older adults? A systematic review. *Exp Gerontol* 2018;102:59–68.
32 Bray F, Ferlay J, Soerjomataram I, *et al*. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2018;68:394–424.
33 Cao W, Chen HD, Yu YW, *et al*. Changing profiles of cancer burden worldwide and in China: a secondary analysis of the global cancer statistics 2020. *Chin Med J* 2021;134:783–91.
34 Lee VH, Lam KO, Chang AT, *et al*. Management of Nasopharyngeal Carcinoma: Is Adjuvant Therapy Needed? *JOP* 2018;14:594–602.
35 Li J, Zhu C, Zhang Y, *et al*. Incidence and Risk Factors for Radiotherapy-Induced Oral Mucositis Among Patients With Nasopharyngeal Carcinoma: A Meta-Analysis. *Asian Nurs Res (Korean Soc Nurs Sci)* 2023;17:70–82.
36 Limkin EJ, Blanchard P. Does East meet West? Towards a unified vision of the management of Nasopharyngeal carcinoma. *Br J Radiol* 2019;92:20190068.
37 Lin Y, Qiu T, Lan Y, *et al*. MultiModal Optical Imaging and Combined Phototherapy of Nasopharyngeal CarcinomaBased on a Nanoplatform. *Int J Nanomed* 2022;17:2435–46.
38 Lam WKJ, Chan JYK. Recent advances in the management of nasopharyngeal carcinoma. *F1000Res* 2018;7:1829.
39 Mui AWL, Lee AWM, Lee VHF, *et al*. Prognostic and therapeutic evaluation of nasopharyngeal carcinoma by dynamic contrast-enhanced (DCE). In: *diffusion-weighted (DW) magnetic resonance imaging (MRI) and magnetic resonance spectroscopy (MRS). Magn Reson Imaging*. . 2021: 83. 50–6.
40 Nazeer F, Poulose JV, Kainickal CT. Induction chemotherapy in nasopharyngeal carcinoma- A systematic review of phase III clinical trials. *Cancer Treat Res Commun* 2022;32.
41 Tang L-L, Chen Y-P, Chen C-B, *et al*. The Chinese Society of Clinical Oncology (CSCO) clinical guidelines for the diagnosis and treatment of nasopharyngeal carcinoma. *Cancer Commun (Lond)* 2021;41:1195–227.
42 Tang Y, He X. Long non-coding RNAs in nasopharyngeal carcinoma: biological functions and clinical applications. *Mol Cell Biochem* 2021;476:3537–50.
43 Xie C, Vardhanabhuti V. PET/CT: Nasopharyngeal Cancers. *PET Clin* 2022;17:285–96.
44 Yang GD, Wang ZC, Chen QY, *et al*. p53, latent membrane protein 1, bcl-2, and prognosis in nasopharyngeal carcinoma: a meta-analysis. *Histol Histopathol* 2019;34:103–10.
45 Zhang SQ, Pan SM, Liang SX, *et al*. Research status and prospects of biomarkers for nasopharyngeal carcinoma in the era of high-throughput omics (Review). *Int J Oncol* 2021;58.
46 Zhang Y, Pang C, Zhang C, *et al*. HILPDA-mediated lipidomic remodelling promotes radiotherapy resistance in nasopharyngeal carcinoma by accelerating mitophagy. *Cell Mol Life Sci* 2023;80:242.
47 Zhang Y, Sun Y, Ma J. Induction gemcitabine and cisplatin in locoregionally advanced nasopharyngeal carcinoma. *Cancer Commun* 2019;39:1–4.