

The Comparative Study Of Nasopharyngeal Carcinoma Incidence and Mortality In Malaysia and Thailand: A Systematic Review
(Kajian Perbandingan Insiden dan Kematian Karsinoma Nasofaring Di Malaysia dan Thailand: Kajian Sistematik)

Nur Andriana Sufea Hanan¹, Rosminah Mohamed¹, Nur Syahmina Rasudin²

¹Health Economic, Faculty of Health Sciences, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia

²Biomedicine, Faculty of Health Sciences, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia

*Corresponding author: syahmina@usm.my

Abstract

Nasopharyngeal Carcinoma (NPC) is characterized by a distinct geographical distribution and is particularly prevalent in East and Southeast Asia. For further studies and better planning in the future, it is vital to have knowledge about the ecological parameters, including incidence, mortality and so on. The objective of this study is to analyze the trend of incidence and mortality of nasopharyngeal carcinoma (NPC) cases over time in Malaysia and Thailand and to offer a comprehensive understanding of the epidemiological patterns of NPC in Malaysia and Thailand, considering both the unique characteristics and shared features of the disease in these two nations. A systematic review was conducted. We searched the literature databases of PubMed, MOH, IntechOpen, SpringerLink and UI Scholars Hub for empirical studies examining the prevalence of NPC cases in Malaysia and Thailand between 2010 and 2022, which were restricted to studies written in English. Nine studies were included, which are three retrospective studies, two ecological studies, three descriptive studies and one narrative review study. The studies show that the inconsistent pattern of NPC cases from 2012 to 2022 suggests that the incidence of NPC fluctuated in both countries throughout this time. Furthermore, it was discovered that Thailand's mortality trend was erratic, exhibiting both rises and falls. Nonetheless, it was found that Malaysia's mortality rate was steadily rising. This is aligned with the increase in mortality rates, particularly in the Southeast Asian region and how the Human Development Index (HDI) is involved in these studies.

Keywords: *Nasopharyngeal Carcinoma; prevalence and incidence; mortality rate; Malaysia and Thailand; Human Development Index*

Abstrak

Kanser Nasofarinks adalah kanser yang sering terjadi dalam kalangan orang Asia berbanding bukan Asia. Penting untuk mempunyai pengetahuan tentang parameter ekologi, termasuk insiden, kematian dan sebagainya sebagai kajian lanjut dan perancangan yang lebih baik pada masa hadapan. Objektif kajian ini adalah untuk menganalisis trend insiden dan mortaliti kes kanser Nasofarinks (NPC) dari semasa ke semasa di Malaysia dan Thailand serta menawarkan pemahaman yang menyeluruh tentang corak epidemiologi NPC di Malaysia dan Thailand, dengan mengambil kira kedua-dua ciri unik dan ciri-ciri penyakit yang dikongsi di kedua-dua negara ini. Ulasan sistematik telah dijalankan. Pangkalan data literatur PubMed, MOH, IntechOpen, SpringerLink dan UI Scholars Hub digunakan untuk kajian empirikal yang mengkaji kelaziman kes NPC di Malaysia dan Thailand antara 2010 dan 2022, yang terhad kepada kajian yang ditulis dalam bahasa Inggeris. Sembilan kajian telah disertakan, iaitu tiga kajian retrospektif, dua kajian ekologi, tiga kajian deskriptif, dan satu kajian ulasan naratif. Kajian menunjukkan bahawa corak kes NPC yang tidak konsisten dari 2012 hingga 2022 menunjukkan bahawa kejadian NPC berubah-ubah di kedua-dua negara sepanjang masa ini. Tambahan pula, didapati bahawa trend kematian di Thailand adalah tidak menentu, menunjukkan kenaikan dan penurunan. Namun begitu, didapati kadar kematian Malaysia semakin meningkat. Ini sejajar dengan peningkatan kadar kematian, khususnya di rantau Asia Tenggara, dan bagaimana Indeks Pembangunan Manusia (HDI) terlibat dalam kajian ini.

Kata kunci: *Kanser Nasofarinks; Prevalens dan insiden; kadar kematian; Malaysia dan Thailand; Indeks Pembangunan Manusia*

INTRODUCTION

Nasopharyngeal carcinoma (NPC), previously known as lymphoepithelioma, is an undifferentiated form of squamous cell carcinoma arising from the epithelium of the nasopharynx. It is the most common malignancy of the nasopharynx (Shah & Nagalli 2023). Its striking racial and geographic variation uniquely characterizes NPC (Argirion et al. 2020). NPC is more prevalent among Asian nations because the genetic structure of the demographics involved also plays a vital role (Okekpa et al. 2019; Almomani, Zulfiqar & Nagalli 2020). There were 50,831 NPC-related deaths (35,753 male and 15,075 female) and 86,691 instances of NPC (60,896 male and 25,795 female) were reported globally in 2012 (Okekpa et al. 2019). The majority of the predicted 129,079 new cases of NPC and 72,987 deaths that are related to 2018 will be geographically restricted to Southeast Asia and they are likely to demonstrate an annual increase (Lee et al. 2019). Males were found to dominate in the incidence of NPC cases. This scenario can be explained by biological or gender disparities in the prevalence of NPC with certain risk factors, such as smoking and hazardous occupational exposure (Abdul Hamid 2021). In many NPC-endemic regions, most cases in areas with a high disease incidence are related to Epstein-Barr virus (EBV) infection. Conversely, in EBV-endemic areas, the association between EBV and WHO type 2 and 3 tumors is definitive. In contrast with EBV non-endemic areas, WHO type 1 tumors would present (Sinha & Gajra 2021).

According to the Malaysia National Cancer Registry Report 2011-2016, NPC is the fifth most prevalent cancer overall and the fifth most common disease in men. Notably, men are 2.5–3 times more likely than women to develop NPC. Males made up 73.1% of NPC in Malaysia between 2011 and 2016, while females made up 26.9% (Nasopharyngeal Carcinoma Society of Malaysia 2019). The Malaysian National Cancer Registry Report 2012–2016 revealed that an average of 900–1,000 cases of NPC were reported each year in 2007–2011 (Ahmad et al. 2021). Moreover, in Malaysia, NPC cases are mostly diagnosed at stages 3 and 4 (63% for males and 60% for females) (Ho, Su & Yuwana 2022). NPC is most common among Chinese (49%), followed by Sabahan and Sarawakians (28%) and Malay (22%). Bidayuh (48.4%) has a high incidence of NPC in Sarawak (Guidelines Development Group 2016). Between 1996 and 1998, the Bidayuh, who are Indigenous to the Malaysian state of Sarawak, had the highest prevalence of NPC of any population-based registry worldwide (Devi et al. 2004). Based on the total annual number of reported NPC cases in Pahang, there was an increasing trend from 2012

until 2014 and then a slightly decreasing trend from 2015 to 2017 (Ahmad et al. 2021). In Malaysia, 40- to 60-year-olds are the most prevalent age range at presentations (Koay 2020). However, on the other hand, it can also occur in younger age groups and the youngest NPC case discovered was in a 6-year-old (Guidelines Development Group 2016).

Rapid socioeconomic development in Southeast Asia over the last few decades has resulted in a reduction in communicable diseases but an increase in cancer-related mortality (Argirion et al. 2020). Thailand, located in Southeast Asia, is an endemic country for NPC. Despite being the most prevalent radiosensitive malignancy, nasopharyngeal carcinoma (NPC) remains a significant health issue in Thailand. (Argirion et al. 2020; Kasemsiri, Thongrong & Suwanrungruang 2015). In 2011, almost 1500 new cases of NPC were diagnosed across the country. The majority of the patients (63%) were men. In both genders, the most significant incidence occurred between the ages of 55 and 70. The most prevalent illness extent at diagnosis was “regional”; however, these results are not uniform between provinces because many local registries did not give staging information (Tangjaturonrasme, Vatanasapt, & Bychkov 2018). The age-standardized incidence rate (ASIR) in men decreased from 3.4 (per 100,000) in 1996 to 3.1 in 2002 and then to 2.8 in 2011 (Tangjaturonrasme, Vatanasapt, & Bychkov 2018). Thailand has a higher incidence than the rest of the globe, but it is substantially lower than in surrounding endemic Southeast Asia due to dietary differences. Similarly, the mortality rate of nasopharyngeal cancer in Thailand (1.3 per 100,000 population) lies between the global (0.7) and Southeast Asian (2.5) mortality rates. The Thai population has a higher incidence of NPC than any other head and neck cancer, such as laryngeal and thyroid cancer (Tangjaturonrasme, Vatanasapt, & Bychkov 2018).

Despite Malaysia and Thailand being included in Southeast Asia, both countries were in different sections of the Human Development Index (HDI). A long and healthy life, knowledge and a reasonable standard of living are three important aspects of human development that the Human Development Index (HDI) measures in summary form. The geometric mean of the normalized indices for each of the three dimensions is known as the HDI. There is a strong, positive relationship between the overall global cancer incidence burden and the HDI for both sexes (Fidler, Bray & Soerjomataram 2017). This study aims to provide information regarding the trend of incidence and mortality of NPC cases over time in the two countries despite differences and similarities between the countries and also how the differences in HDI will affect the incidence and mortality of NPC.

MATERIALS AND METHODS

Search strategy

Sources for this systematic review are from PubMed, MOH, IntechOpen, SpringerLink and UI Scholars Hub. They were searched using a combination of the medical subheadings (MeSH) and key terms “Nasopharyngeal carcinoma, Head and neck cancer, or NPC cases” and “Asia, Prevalence of NPC, Malaysia and Thailand”. The searches were restricted to studies written in English (peer-reviewed articles, working papers, conference papers and reports) published from 2010 until 2022. We also carried out additional literature searches by appraising reference lists of the studies identified.

Inclusion and exclusion criteria

Studies were screened based on the inclusion and exclusion criteria. All patients in Malaysia and Thailand diagnosed with NPC were eligible and included in this study. Selected papers or studies must be publications related to the NPC cases; the paper must address the association of lifestyle, diet, socioeconomic and sociodemographics. Studies that did not address NPC cases in Malaysia and Thailand were excluded.

Data extraction

All data extracted from the selected articles, such as details of the trends and incidence of NPC cases, study design, data sources and key findings on the prevalence of NPC cases in Malaysia and Thailand, were considered for this review. The differences in the prevalence of NPC cases between the two countries were compared based on the reviewed articles. The differences in the variables between the two countries were also compared.

Risk of bias (quality) assessment

An adapted version of the ROBINS-1 tool was used to examine the risk of bias in the selected articles. This tool has been used in previous systematic reviews of NPC (Sterne et al. 2016). The ROBINS-1 identifies the risk of bias in each study by using the seven bias domains. A study was rated as having a critical risk of bias if the study was judged to be at critical risk of bias in at least one domain, rated as serious risk of bias if the study is judged to be at serious risk of bias in at least one domain, but not at critical risk of bias in any domain, rated as moderate risk of bias if the study is judged to be at low or moderate risk of bias for all domains and lastly rated as low risk of bias if the study is judged to be at low

risk of bias for all domains. ROBINS-I tool is used for assessing the risk of bias in the non-randomized study. For the literature review, the AMSTAR 2 tool would be most suitable to assess the overall risk of bias. This risk of bias tool only focuses on study selection, data extraction and publication bias (Lu et al. 2020).

The research methodology is illustrated in Figure 1.

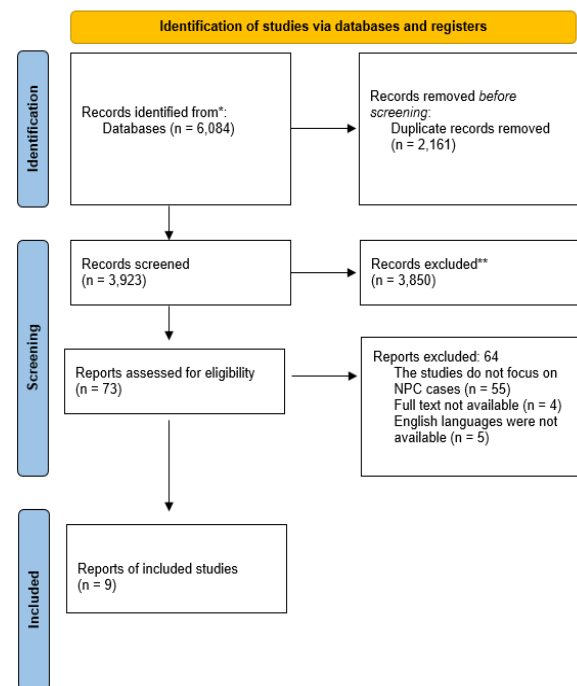


Figure 1 PRISMA flow chart of study selection

RESULTS

Study characteristics

Referring to Table 1, we identified a total of 6,084 citations from bibliographic databases. After the removal of duplicates, a total of 3,923 unique citations were screened by title and abstract and 73 full texts were sourced. 64 studies of these full texts were excluded for the following reasons: The studies did not focus on the NPC cases (55 studies); the full text of the article is not available (four studies) and the English language was not available in the article (five studies). Nine studies met the eligibility and the final inclusion criteria. Figure 1 provides details of the process of study identification. The nine included studies and data were conducted and collected in Malaysia, Thailand, the Asian region and Southeast Asia. A range of NPC cases were studied, such as the association between NPC and HDI (three studies), mortality (six studies) and risk factors (four studies)

Table 1 Study characteristic details

Study ID	Study design	Study period	Location	Participants
Ahmad et al. (2021)	A retrospective study	2012-2017	Malaysia	143 NPC cases
Mahdavifar et al. (2016)	Ecologic study	In the year of 2012	Asian region	ASR data of all Asian countries for the year 2012 were obtained from the global cancer project
Argirion et al. (2020)	A retrospective study	1990-2014	Chiang Mai, Khon Kaen, Lampang and Songkhla (Thailand)	2577 cases
Song et al. (2022)	Descriptive epidemiological studies	2019	Global	All data that were assessed from The Global Burden of Diseases, Injuries and Risk Factors Study (GBD) 2019.
Ng et al. (2024)	A retrospective data collection	2010-2020	Malaysia	892 NPC cases
Othaya Kumar & S.M.N. Mydin (2019)	A narrative review	2018	Geographic variations	All data were taken from GLOBOCAN 2018.
Lao & Le (2020)	Descriptive epidemiological study	2018	Southeast Asia	GLOBOCAN project and Human Development Reports database.
Dee et al. (2024)	Descriptive epidemiological study	2022	Southeast Asia	The number of new NPC (C11) cases and deaths were collected from the International Agency for Research on Cancer GLOBOCAN 2022
Bray et al. (2024)	Descriptive study	2022	Global	All the data and number of cases from the International Agency for Research on Cancer (IARC)

Prevalence and Incidence of NPC in Malaysia and Thailand

NPC showed a distinct racial and geographical distribution with 109,221 cases, the highest in Asia (Othaya Kumar & S.M.N. Mydin 2019), particularly in Southeast Asia, where the prevalence rate is 15-50 cases per 100,000 people (Mahdavifar et al. 2016). Men are more likely to develop NPC, with prevalence proportions often two to three times higher in men and male-to-female ratio proportions in developing localities (Mohammed et al. 2017).

In 2012, Asian countries documented a total of 68,272 NPC cases, with 48,492 cases (2/71%) diagnosed in men and 19,780 cases (97/28%) diagnosed in women (Lee et al. 2019). According to these numbers, the gender (male/female) ratio is 45:2. In Southeast Asia, Malaysia has the highest age-standardized incidence rate (ASIR) of NPC with 7.2 per 100,000 people compared to Thailand with only 2.1 per 100,000 people. There are 2,030 cases in Malaysia which 1,487 cases (10.6 per

100,000 people) were from men and 543 cases (3.9 per 100,000 people) were from women. Meanwhile, in Thailand, there are 1,867 cases which 1,328 cases (3.2 per 100,000 people) were from men and 539 cases (1.2 per 100,000 people) were from women (Mahdavifar et al. 2016).

In 2018, based on the estimated incidence and mortality rate country-specific (Asia), Malaysia and Thailand were not included in the five countries that have the highest number of incidence of NPC cases, but ranked seventh and sixth and based on world estimated ASIR, Malaysia is ranked fifth with 6.3 per 100,000 (Othaya Kumar & S.M.N. Mydin 2019). According to Lao and Le's (2020) study (Table 2), it shows that Malaysia was included in the five countries with the highest standardized incidence rate of nasopharyngeal cancer and it ranked at number fourth with ASIR 6.3 per 100,000 people (Male; 9.5 per 100,000, Female; 3.0 per 100,000), while Thailand is ranked second last, with 2.2 per 100,000 people (Male; 3.3 per 100,000, Female; 1.2 per 100,000). For the number of cases, Malaysia is ranked fifth with 2089 cases and Thailand is ranked

fourth with 2200 cases (Table 2) (Lao & Le 2020). Studies done by Lao and Le in 2020 showed that Malaysia had higher ASIR cases than Thailand but Thailand surpassed Malaysia for the number of cases in 2018 (Table 2) (Lao & Le 2020).

The number of NPC cases and ASIR in Malaysia in the year 2019 was higher than the number of NPC cases in Thailand. In Malaysia, there were 1,846 NPC cases, of which the ASIR was 6.1 per 100,000. Meanwhile, in Thailand, there were 1,539 NPC cases, of which the ASIR was 1.6 per 100,000 (Song et al. 2022).

According to World Cancer Research Fund International, there were more than 120,434 new cases of nasopharyngeal cancer in 2022. In year 2022, Thailand had a higher number of cases (2,350 cases) than Malaysia (2,144 cases). However, Malaysia had a higher ASIR than Thailand with 5.9 per 100,000 (male: 8.9 per 100,000 people, female: 2.8 per 100,000 people), respectively (Dee et al. 2024; Bray et al. 2024).

Based on a study done in 2020, between 1990 and 2014, a total of 2577 cases were diagnosed in Chiang Mai, Khon Kaen, Lampang and Songkhla, Thailand. Across all registries, cases were found primarily male (Argirion et al. 2020). Non-keratinizing NPC accounted for 66-79% of cases in Chiang Mai, Khon Kaen and Lampang, with no significant differences in gender distribution within each registry. Interestingly, in Songkhla, the keratinizing subtype, which accounts for around 60% of all reported NPCs, was determined to be the predominant case type. From 2012 to 2017, 143 new cases of NPC were recorded in Pahang, Malaysia. Undifferentiated carcinomas have monopolized the distribution of NPC patients in Pahang with 68% of the cases (Ahmad et al. 2021). In Pahang, the ASIRs for males and females were 2.4 and 0.9 per 100,000, respectively. In comparison to other regions of the country, NPC was less prevalent in this area, according to data from the Malaysia National Cancer Registry Report 2012–2016. In terms of NPC incidence, Pahang was ranked tenth compared to the other state in Malaysia during that time. In Sarawak, Malaysia, the Bidayuh Indigenous have a high incidence rate of NPC (Linton et al. 2021). According to Ng et al. (2024), a total of 892 patients from 2010 to 2020 were reported in Sarawak with males outnumbered females 3-to-1. The largest patient groups included the Iban (34%) and Bidayuh (21%), with the Chinese making up 19% and the Malay 15%. Among these, the Bidayuh exhibited the highest incidence rate, reporting 81 cases per 100,000 individuals. The primary histological type among the 892 cases was undifferentiated carcinoma, which accounted for 73%.

The Number of Mortality of NPC in Malaysia and Thailand

In a study done in 2016, the male/female mortality ratio was 52:2, with a total of 29,032 (63/71%) males and 11,498 (36/28%) females among the 40,530 people in Asia who died of NPC in 2012 (Mahdavifar et al. 2016). In this study, it stated that Thailand has 1,114 cases of NPC mortality and it ranked fifth and Malaysia was ranked eighth as the number of mortality cases is 698. However, among the Southeast Asia countries, Thailand was ranked third and Malaysia was ranked sixth. Meanwhile, for the age-standardized mortality rate (ASMR) for NPC, Malaysia's rank was higher than Thailand's. Malaysia ranked fourth with 2.5 per 100,000 people and Thailand ranked eighth with 1.3 per 100,000 people (Table 2) (Mahdavifar et al. 2016).

Nasopharyngeal cancer was responsible for 22,231 fatalities and 34,681 new cases overall in Southeast Asian nations in 2018 (Lao & Le 2020). According to a study done by Othaya Kumar and S.M.N. Mydin (2019); Lao and Le (2020), it stated that Thailand has a higher number of mortality cases than Malaysia. Malaysia and Thailand were both included in the five countries with the highest numbers of mortality cases, with Malaysia ranked fifth with 1,187 cases and Thailand ranked fourth with 1,421 cases. For the ASMR, Malaysia was ranked fifth with 3.7 per 100 000 and Thailand at eleventh with 1.4 per 100 000 (Lao & Le 2020).

In 2019, Malaysia had a higher number of mortality cases and mortality rate than Thailand, with 1,380 cases in Malaysia with ASMR (4.8 per 100,000 people) and 1,176 cases in Thailand with ASMR (1.2 per 100,000 people) (Song et al. 2022). However, the results were quite different in 2022, with Thailand having a higher number of mortality cases but a lower mortality rate than Malaysia. Thailand had 1,506 mortality cases with an ASMR of 1.3 per 100,000 people and for Malaysia, there were 1,496 mortality cases with an ASMR of 4.2 per 100,000 people (Dee et al. 2024; Bray et al. 2024).

Risk of bias (quality) assessment

Based on the ROBINS-1 tool, six of the studies have a moderate to high risk of bias; the studies have several potential areas for bias, particularly related to selection bias, confounding bias and also information bias. Other than that, based on the AMSTAR 2 tool, one of the studies has a high risk of bias. The risk of bias involved in this study was selection bias, confounding and publication. Two studies in this research have a moderate risk of bias. Confounding, inconsistent measurements and selective reporting are some of the areas where bias may be introduced.

Table 2 Nasopharyngeal Cancer Estimated Incidence and Mortality Rate Country Specific (Asia) in 2012, 2018, 2019 and 2022

2012													
Countries	Incidence					Mortality							
	Cases	Rank	ASR	Rank	ASR	Rank	Cases	Rank	ASR	Rank	ASR	Rank	ASR
			(Both sexes)		(Male)				(Female)		(Male)		(Female)
Mahdavifar et al. 2016)	Thailand	4	2.1	8	3.2	8	1114	3	1.3	8	0.7	6	1.9
	Malaysia	3	7.2	1	10.6	1	698	6	2.5	4	1.2	4	3.9
2018													
Countries	Incidence					Mortality							
	Cases	Rank	ASR	Rank	ASR	Rank	Cases	Rank	ASR	Rank	ASR	Rank	ASR
			(Both sexes)		(Male)				(Female)		(Male)		(Female)
Othaya Kumar & S.M.N. Mydin 2019; Lao & Le 2020	Thailand	4	2.2	10	3.3	10	1,421	4	1.4	11	2.2	11	0.7
	Malaysia	5	6.3	4	9.5	4	1,187	5	3.7	5	5.7	5	1.7

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...cont.

2019														
Countries	Incidence					Mortality								
	Cases	Rank	ASR	Rank	ASR	Rank	ASR	Rank	ASR	Rank	ASR	Rank	ASR	Rank
						(Both sexes)	(Male)	(Female)	(Both sexes)	(Male)	(Female)	(Both sexes)	(Male)	(Female)
Song et al. 2022	Thailand	1,539	-	-	-	-	-	-	1,176	-	1.2	-	-	-
	Malaysia	1,846	-	6.1	-	-	-	-	1,380	-	4.8	-	-	-
	2022													
Countries	Incidence					Mortality								
	Cases	Rank	ASR	Rank	ASR	Rank	ASR	Rank	ASR	Rank	ASR	Rank	ASR	Rank
						(Both sexes)	(Male)	(Female)	(Both sexes)	(Male)	(Female)	(Both sexes)	(Male)	(Female)
Dee et al. 2024; Bray et al. 2024	Thailand	2,350	-	2.2	-	3.3	-	1.2	-	1,506	-	1.3	-	0.67
	Malaysia	2,144	-	5.9	-	8.9	-	2.8	-	1,496	-	4.2	-	1.8

DISCUSSION

The findings from the study showed that both countries which are Malaysia and Thailand had higher incidences of NPC in certain years. In addition, the trend of the cases incidence for both countries was not consistent. Apart from that, the trend of number mortality in Thailand was also not consistent but it is different for Malaysia because the number of mortalities showed an increased trend. Even so, Thailand still has a higher mortality than Malaysia except for the year 2019. The socio-economic development of the nations affected the distribution trends of cancer as well. The incidence of cancer is also significantly influenced by culture and regional norms. Since these are deeply embedded in the way of life of the populace, they are frequently challenging to address (Singh et al. 2023)

Additionally, both nations show a relatively high standard of living compared to other countries in Southeast Asia. The incidence of nasopharyngeal cancer in humans is higher in medium-developed countries than in high- and very-developed nations (Lao & Le 2020). This is due to an environment with a high relative risk of carcinogenic risk factors, less funding for the healthcare and public health sectors and disparities in population incomes, educational attainment and health services. The high mortality was more prevalent in these locations because of a lack of health services and the fact that the majority of cases were diagnosed at an advanced stage (Lao & Le 2020). This means the higher the level of HDI, the lesser the mortality (United Nations Development Programme 2024). In 2012, Malaysia was included in the high human development countries meanwhile Thailand was in medium human development countries, but in 2018, Malaysia became a very highly developed nation; and Thailand move to become a highly developed nation (Mahdavifar et al. 2016; Lao & Le 2020). According to a study done by Fidler, Bray and Soerjomataram (2017), the cancer incidence burden is greater in higher Human Development Index countries. Despite that, a greater proportion of the global mortality burden is observed in less developed countries. On top of that, a nation's cancer profile changes as it progresses socially, economically and behaviorally. Declines in cancers linked to infections are counterbalanced by rises in cancers linked to industrialization.

Offering NPC screening services is one of the screening and early detection initiatives in the National Cancer Control Blueprint 2008-2010, given the high disease burden of NPC in Malaysia and the potential importance of screening for malignant conditions. Therefore, the Disease Control Division of the Ministry of Health Malaysia

has requested a Health Technology Assessment (HTA) to examine the feasibility of implementing a screening program for the early detection of NPC. Furthermore, Malaysia also examined the treatment and management of cancer from a comprehensive perspective that includes research, traditional and complementary medicine, palliative care, screening, early detection, diagnosis, therapy, rehabilitation and primary prevention (Mohd Yusof 2011).

Next, this cancer is more common among males than females and this can be confirmed by many of the other studies. The higher incidence of NPC cases among males may reflect different lifestyles, such as exposure to smoking, as well as genetic considerations (Park et al. 2022). This gender disparity in NPC prevalence suggests the need for targeted interventions and public health initiatives aimed at addressing specific risk factors and promoting early detection and prevention strategies among males. Furthermore, understanding the underlying mechanisms contributing to the higher incidence of NPC in males can help in the development of tailored treatment approaches and personalized care for affected individuals (Sinha & Gajra 2021).

In addition, Malaysia exhibits higher age-standardized rates (ASR) for both incidence and mortality compared to Thailand. The source of each nation's population structure, the standard population used for age-standardization and the age group intervals could all affect the value of age-standardized rates (Hong et al. 2021).

It is important to remember that NPC is common in Thailand and Malaysia due to various factors such as geographic diversity, epidemiological patterns, as well as non-environmental risk factors like sex, ethnicity and family history. Additionally, factors such as smoking, consumption of salted fish (especially during childhood), nitrosamine in certain traditional food items used in southern China and the use of traditional herbal medicines in the Asian population are believed to be the main reasons for NPC (Mahdavifar et al. 2016). Southeast Asia, a region with rice as a staple food, embraces salted fish as a traditional fermented food, meeting dietary needs for sodium and protein. Several case-control studies have found a significant association between consuming salted fish and the occurrence of NPC. Recent studies have suggested that the consumption of salted fish may contribute to the development of NPC (Okeke et al. 2019).

A study in Thailand showed that non-keratinizing NPC accounted for most of the NPC cases across four states which are Chiang Mai, Khon Kaen and Lampang, except for Songkhla. Due to the high prevalence of smoking in the area, Songkhla, which is in southern Thailand, was the only registry to show a higher frequency of keratinizing NPC as

opposed to non-keratinizing NPC (Argirion et al. 2020). The study was done by Ahmad et al. (2021) and Ng et al., (2024) report that undifferentiated carcinoma NPC accounted for most of the cases in the study in Pahang and Sarawak, Malaysia. Undifferentiated carcinoma is subclassified under non-keratinizing NPC (Peterson & Nelson 2013). In endemic regions such as Southeast Asia, WHO type III (non-keratinizing) NPC was responsible for over 97% of cases however WHO type I (keratinizing) NPC was more prevalent in Western nations (Su et al. 2023).

STUDY LIMITATION

The included studies were limited to those published in English. Not many studies have been done that only focus on the prevalence of NPC cases, especially in Malaysia and Thailand. Therefore, we may have a problem identifying the prevalence of NPC cases in the respective countries.

CONCLUSION

An important finding from this systematic review is the incidence and mortality of nasopharyngeal carcinoma (NPC) in Malaysia and Thailand, which was thoroughly investigated. The analysis revealed that the trend of NPC cases from 2012 to 2022 was not consistent, indicating that the incidence of NPC varied over these years in both countries. Additionally, the trend for the number of mortalities was found to be fluctuating, showing both increases and decreases for Thailand. However, for Malaysia, the trend of mortality was observed to be consistently increasing.

These findings underscore the importance of early detection, immediate administration of treatment and rapid intervention in reducing the number of NPC cases globally. The variations in trends observed in both countries emphasize the need for continuous monitoring and adaptation of healthcare strategies to effectively address NPC and its associated mortalities. This information is crucial for healthcare professionals and policymakers in developing targeted interventions and improving outcomes for individuals affected by NPC.

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REFERENCES

Ahmad, A., Yassin, W. M., Rahman, N. A. A., Leman, W. I., Rosla, L., Paul, M., Syed

- Yusof, S. N. E., Mohamed@Awang, K., Abdullah, K., & Kaderi, M. A. 2021. The Incidence of Nasopharyngeal Carcinoma in Pahang State of Malaysia from 2012 to 2017. *The Malaysian Journal of Medical Sciences: MJMS* 28 (1): 66–74. <https://doi.org/10.21315/mjms2021.28.1.9>
- Abdul Hamid, G. 2021. *Epidemiology and Outcomes of Nasopharyngeal Carcinoma. In Pharynx - Diagnosis and Treatment*, edited by Xiaoying Zhou and Zhe Zhang, 248. 10.5772/intechopen.91522
- Ahmad, A., Mustapa Kamal Basha, M. A., Mohd. Yassin, W., A. Rahman, N. A., Leman, W. I., Rosla, L., Syed Yusof, S. N. E., Paul, M., Mohamed Awang, K., Abdullah, K., & Kaderi, Mohd. A. 2022. Identification of Risk Factors Associated with Nasopharyngeal Carcinoma (NPC) in the Pahang State of Malaysia Hospitals. *Makara Journal of Health Research* 26 (1): 14–21. <https://doi.org/10.7454/msk.v26i1.1306>.
- Argirion, I., Zarins, K., Suwanrungruang, K., Pongnikorn, D., Chitapanarux, I., Sriplung, H., Vatanasapt, P., & Rozek, L. 2020. Subtype Specific Nasopharyngeal Carcinoma Incidence and Survival Trends: Differences between Endemic and Non-Endemic Populations. *Asian Pacific Journal of Cancer Prevention* 21 (11): 3291–3299. <https://doi.org/10.31557/apjcp.2020.21.11.3291>.
- Almomani, M. H., Zulfikar, H., & Nagalli, S. 2020. *Nasopharyngeal Carcinoma (NPC, Lymphoepithelioma)*. PubMed. Treasure Island (FL): StatPearls Publishing. 2020. <https://www.ncbi.nlm.nih.gov/books/NBK558922/>.
- Bray, F., Laversanne, M., Sung, H., Ferlay, J., Siegel, R. L., Soerjomataram, I., & Jemal, A. 2024. Global Cancer Statistics 2022: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA: A Cancer Journal for Clinicians* 74 (3): 229–263. <https://doi.org/10.3322/caac.21834>.
- Guidelines Development Group. 2016. Management of Nasopharyngeal Carcinoma 2016 (pp 1-40). Malaysia Health Technology Assessment Section (MaHTAS).
- Dee, E. C., Eala, M. A., Feliciano, E. J. G., Jacomina, L. E., Chua, M. L. K., Mejia, M. B., & Lee, N. Y. 2024. Nasopharynx Cancer in Southeast Asia: An Analysis of 2022 Incidence and Mortality. *International Journal of Radiation Oncology*Biophysics* 120 (2): e746–e747. <https://doi.org/10.1016/j.ijrobp.2024.07.1640>.
- Devi, B. C. R., Pisani, P., Tang, T. S., & Parkin, D. M. 2004. High Incidence of Nasopharyngeal Carcinoma in Native People of Sarawak, Borneo Island. *Cancer Epidemiology, Biomarkers & Prevention* 13 (3): 482–486. <https://doi.org/10.1158/1055-9965.482.13.3>.
- Fachiroh, J., Sangrajang, S., Johansson, M., Renard, H., Gaborieau, V., Chabrier, A., Chindavijak, S., Brennan, P., & McKay, J. D. 2012. Tobacco Consumption and Genetic Susceptibility to Nasopharyngeal Carcinoma

- (NPC) in Thailand. *Cancer Causes & Control* 23 (12): 1995–2002. <https://doi.org/10.1007/s10552-012-0077-9>.
- Fidler, M. M., Bray, F., & Soerjomataram, I. 2017. The Global Cancer Burden and Human Development: A Review. *Scandinavian Journal of Public Health* 46 (1): 27–36. <https://doi.org/10.1177/1403494817715400>.
- Ho, J. Y. and Ting, S. H., & Podin, Y. 2022. Nasopharyngeal cancer in Malaysia: Perceived severity, susceptibility and barriers in risk messages. *Human Behavior, Development and Society* 23 (2): 94-104. ISSN 2651-1762.
- Hong, D., Lee, S., Choi, Y.-J., Moon, S., Jang, Y.-Y., Cho, Y.-M., Lee, H., Min, S., Park, H., Hahn, S., Choi, J.-Y., Shin, A., & Kang, D. 2021. The Age-Standardized Incidence, Mortality and Case Fatality Rates of COVID-19 in 79 Countries: A Cross-Sectional Comparison and Their Correlations with Associated Factors. *Epidemiology and Health* 43: e2021061. <https://doi.org/10.4178/epih.e2021061>.
- Koay, C. E. 2020. Understanding Nasopharyngeal Cancer (NPC). Understanding Nasopharyngeal Cancer (NPC). <https://www.sunwaymedical.com/en/blogpost/understanding-nasopharyngeal-cancer-npc> [6 July 2023].
- Kasemsiri, P., Thongrong, C., & Suwanrungruang, K. 2015. Long-Term Survival Outcome of Treatment for Nasopharyngeal Carcinoma in Srinagarind Hospital, Thailand: 10-Year Retrospective Analysis. (*Srinagarind Medical Journal*) 30 (2): 80–86.
- Lao, T. D., & Le, T. A. huyen. 2020. Epidemiology, Incidence and Mortality of Nasopharynx Cancer in Southeast Asia: An Update Report. *DOAJ (DOAJ: Directory of Open Access Journals)* 7 (2): 86–90.
- Linton, R., Daker, M., Khoo, A., Choo, D., Viljoen, M., & Neilsen, P. 2021. Nasopharyngeal Carcinoma among the Bidayuh of Sarawak, Malaysia: History and Risk Factors (Review). *Oncology Letters* 22 (1): 514. <https://doi.org/10.3892/ol.2021.12775>.
- Lee, H. M., Okuda, K. S., González, F. E., & Patel, V. 2019. Current Perspectives on Nasopharyngeal Carcinoma. *Advances in Experimental Medicine and Biology*, 11–34. https://doi.org/10.1007/978-3-030-22254-3_2.
- Lu, C., Lu, T., Ge, L., Yang, N., Yan, P., & Yang, K. 2020. Use of AMSTAR-2 in the Methodological Assessment of Systematic Reviews: Protocol for a Methodological Study. *Annals of Translational Medicine* 8 (10): 652. <https://doi.org/10.21037/atm-20-392a>.
- Mahdaviifar, N., Ghoncheh, M., Mohammadian-Hafshejani, A., Khosravi, B., & Salehiniya, H. 2016. Epidemiology and Inequality in the Incidence and Mortality of Nasopharynx Cancer in Asia. *Osong Public Health and Research Perspectives* 7 (6): 360–72. <https://doi.org/10.1016/j.phrp.2016.11.002>.
- Mohammed, M. A., Ghani, M. K. A., Hamed, R. I., & Ibrahim, D. A. 2017. Analysis of an Electronic Methods for Nasopharyngeal Carcinoma: Prevalence, Diagnosis, Challenges and Technologies. *Journal of Computational Science* 21 (July): 241–54. <https://doi.org/10.1016/j.jocs.2017.04.006>.
- Mohd. Yusof, Mohd. A. 2011. Nasopharyngeal carcinoma screening. Health technology assessment report. <http://www.moh.gov.my> [10 July 2023].
- Ng, B. H. K., Hoe, K. C., Lim, Y. N., Wong, C. Y., Voon, P. J., & Tang, I. P. 2024. Nasopharyngeal Carcinoma in Sarawak: A 10-Year Review and Update. *European Archives of Oto-Rhino-Laryngology* 281: 6493–6498. <https://doi.org/10.1007/s00405-024-08955-9>.
- Nasopharyngeal Carcinoma Society Malaysia. 2019. Overview of NPC. [Npcresearch.org](https://npcresearch.org/overview.html). 2019. <https://npcresearch.org/overview.html> [10 July 2023].
- Othaya Kumar, K. M., & S.M.N. Mydin, R. B. 2019. Nasopharyngeal Cancer: Geographic Variation and Risk Factors. In *Malaysian Journal of Medicine and Health Sciences* 15 (SUPP9): 116–121.
- Okekpa, S. I., Mydin, R. B. S. M. N., Mangantig, E., Azmi, N. S. A., Zahari, S. N. S., Kaur, G., & Musa, Y. 2019. Nasopharyngeal Carcinoma (NPC) Risk Factors: A Systematic Review and Meta-Analysis of the Association with Lifestyle, Diets, Socioeconomic and Sociodemographic in Asian Region. *Asian Pacific Journal of Cancer Prevention: APJCP* 20 (11): 3505–3514. <https://doi.org/10.31557/APJCP.2019.20.11.3505>.
- Peterson, B. R., & Nelson, B. L. 2013. Nonkeratinizing Undifferentiated Nasopharyngeal Carcinoma. *Head and Neck Pathology* 7 (1): 73–75. <https://doi.org/10.1007/s12105-012-0401-4>.
- Shah, A. B., & Nagalli, S. 2023. Nasopharyngeal Carcinoma. PubMed. Treasure Island (FL): StatPearls Publishing. 2023. <https://www.ncbi.nlm.nih.gov/books/NBK554588>.
- Sterne, J. A., Hernán, M. A., Reeves, B. C., Savović, J., Berkman, N. D., Viswanathan, M., Henry, D., Altman, D. G., Ansari, M. T., Boutron, I., Carpenter, J. R., Chan, A.-W., Churchill, R., Deeks, J. J., Hróbjartsson, A., Kirkham, J., Jüni, P., Loke, Y. K., Pigott, T. D., & Ramsay, C. R. 2016. ROBINS-I: A Tool for Assessing Risk of Bias in Non-Randomised Studies of Interventions. *BMJ* 355 (355): i4919. <https://doi.org/10.1136/bmj.i4919>.
- Su, Z. Y., Yan Siak, P., Leong, C.-O., & Cheah, S.-C. 2023. The Role of Epstein–Barr Virus in Nasopharyngeal Carcinoma. *Frontiers Microbiology* 14 (February). <https://doi.org/10.3389/fmicb.2023.1116143>.
- Sinha, S., & Gajra, A. 2021. Nasopharyngeal Cancer. PubMed. Treasure Island (FL): StatPearls Publishing. 2021. <https://www.ncbi.nlm.nih.gov/books/NBK459256/>.
- Song, Y., Cheng, W., Li, H., & Liu, X. 2022. The Global, Regional, National Burden of Nasopharyngeal Cancer and Its Attributable Risk Factors (1990–2019) and Predictions to 2035. *Cancer Medicine* 11 (22): 4310–20. <https://doi.org/10.1002/cam4.4783>.

- Singh, M., Senthil Rajappa, Uehara, R., Schachterle, S. E., & Sajita Setia. 2023. Cancer Incidence and Mortality Trends in Asia Based on Regions and Human Development Index Levels: An Analyses from GLOBOCAN 2020. *Current Medical Research and Opinion* 39 (8): 1127–1137. <https://doi.org/10.1080/03007995.2023.2231761>.
- Tangjaturonrasme, N., Vatanasapt, P., & Bychkov, A. 2018. Epidemiology of Head and Neck Cancer in Thailand. *Asia-Pacific Journal of Clinical Oncology* 14 (1): 16–22. <https://doi.org/10.1111/ajco.12757>.
- United Nations Development Programme (UNDP). 2024. Human Development Report 2023-24. [Hdr.undp.org. https://hdr.undp.org/content/human-development-report-2023-24](https://hdr.undp.org/content/human-development-report-2023-24) [1 August 2023]