

Spatial Distribution of Head and Neck Cancer in Chiang Mai, Thailand

Walaithip Bunyatisai¹, Somvilai Chakrabandhu², Patumrat Sripan^{3,4}, Apinut Rankantha⁵, Sukon Prasitwattanaseree⁵, Imjai Chitapanarux^{2,3,6*}

Abstract

Background: The incidence of Head and neck (HN) cancers in Thailand is rising and survival rates not improving. Variations of its incidence among geographical areas may due to various contributing factors. **Methods:** We focused on data from 25 districts within Chiang Mai province, Thailand. The temporal change was described separately into two periods, 2007-2012 and 2013-2018. The OpenBUGS and the Quantum Geographic Information System were utilized to determine the geographical patterns in the incidence of HN cancer and focus on oropharynx. **Results:** The number of new cases of HN cancer was 1,186, of which 835 cases (70%) were male. Among those patients 548 diagnosed in 2007-2012 and 638 diagnose in 2013-2018. High risk patterns of both overall HN and oropharyngeal cancer incidences were found in the central and southern areas of the province in 2007-2013. However, the geographical patterns of the incidence of oropharyngeal cancer showed the changed pattern, with high RR in central and northern areas in more recent period. Over two periods, the RR of the cancers incidence decrease. The RR of oropharyngeal increased in Fang district and it remained high in Mueang district. **Conclusion:** This study have highlighted specific areas with a high risk of head and neck cancer and oropharyngeal cancer incidences in Chiang Mai province, along with the spatial inequalities in their distributions, with cluster formation. These results may be helpful in guiding any strategy put in place to respond to the high risk incidence of the cancers in specific areas.

Keywords: Head and neck cancers- Besag- York- Mollié- Chiang Mai- spatial analysis- Thailand

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Introduction

Head and neck (HN) cancers are defined as a group of malignant neoplasms occurring in the upper aerodigestive tract and tissues within the head and neck regions such as the oral cavity, pharynx, and larynx (Vatanasapt et al., 2011). Globally, HN cancers accounted for 686,000 and 834,860 new cases (the tenth most common cancer) and 376,000 and 431,131 deaths (the sixth most common cause of cancer mortality) in 2012 and 2018 (Ferlay et al., 2015; Bray et al., 2018), respectively, with the highest incidence having been observed in South and Southeast Asia (Mehanna et al., 2010; Gupta et al., 2016).

The HN cancer incidence in Thailand is rising with mean annual age-standardized incidence rates (ASRs per 100,000) of 14.2 for males and 9.7 for females in 2007–2009 compared to 15.7 for males and 10.7 for females in 2010–2012 (Tangjaturonrasme et al., 2018). The incidence of tumors at certain sites has also been found

to be increasing: oral cancer in females in the northeastern region with a national ASR of 1.93 and nasopharyngeal cancer in men with an ASR of 2.62 (Imsamran et al., 2018).

Chiang Mai province is the second largest in Thailand and its geography comprises a plain surrounded by high mountains where pollution tends to concentrate. In addition, it also has a border with other countries and has a diverse population, including hill tribes. Chiang Mai has a high number of cancer patients, including HN cancer, with ASRs for lip, tongue, mouth, tonsil, and other oropharyngeal, hypopharyngeal, and laryngeal cancers of 0.1, 1.5, 1.5, 1.0, 0.4, 0.9, and 1.5 for males and 0.2, 0.7, 0.6, 0.1, 0.1, 0.1, and 0.2 for females, respectively (Imsamran et al., 2018).

Previous research has shown that many risk factors are related to cancer incidence, such as sex (Simard et al., 2014), age (Marur and Forastiere, 2010; Kansy et al., 2014), ethnicity (Parasher et al., 2014), alcohol consumption and tobacco use (Hashibe et al., 2007,

¹Data Science Research Center, Department of Statistics, Faculty of Science, Chiang Mai University, Chiang Mai, Thailand.

²Division of Radiation Oncology, Department of Radiology, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand.

³Northern Thai Research Group of Radiation Oncology (NTRG-RO), Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand.

⁴Research Institute for Health Sciences, Chiang Mai University, Chiang Mai, Thailand. ⁵Department of Statistics, Faculty of Science, Chiang Mai University, Chiang Mai, Thailand. ⁶Chiang Mai Cancer Registry, Maharaj Nakorn Chiang Mai Hospital, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand. *For Correspondence: imjai@hotmail.com

2009; Kumar et al., 2015), human papillomavirus (HPV) infection (for oropharyngeal cancer) (McDonald et al., 2014), betel quid (especially in Asian countries) (Chen et al., 2008, Liao et al., 2014), poor nutrition (Chuang et al., 2011), oral health (Divaris et al., 2010), and education level (Jabbour et al., 2018). In addition, environmental or occupational exposure to formaldehyde, wood and nickel dust, asbestos and synthetic fibers, smoke, and chemicals (Sturgis et al., 2004; Shaw and Beasley, 2016) could be involved in the pathogenesis of HN cancer (Kashigar et al., 2013; Trivedi et al., 2013; Choudhury and Ghosh, 2015; van Deudekom et al., 2017). The relative prevalence of these risk factors may contribute to the variations in the observed distribution of HN cancer in different areas (Tangjaturonrasme et al., 2018) and the ways in which these inequities have manifested in geographical patterns of incidence are not yet thoroughly understood. Awareness about the current epidemiological situation and heterogeneous epidemiological patterns of HN cancer could be especially useful for health programs, cancer control planning, and the training of specialized personnel in accordance with the size of the problem and distribution of the disease. Therefore, the aim of the present study was to determine the geographical patterns in the incidence of head and neck cancer in Chiang Mai province and focus on oropharynx because specific risk factors i.e HPV infection and younger age are expected.

Material and Methods

The study area

This is a retrospective observational study. We focused on data from 25 districts within Chiang Mai province, Thailand (Figure 1). The median adult population size of the districts was 50,540 (range 8,825–97,461), of which the numbers of males and females were 25,061 (range 4,559–90,909) and 25,479 (range 4,266–106,552), respectively.

Data collection

Incidence data from 2007–2018 were obtained from the Chiang Mai Cancer Registry Maharaj Nakorn Chiang Mai, Faculty of Medicine, Chiang Mai University, Thailand. Data were encoded using International Classification of Diseases version 10 (ICD-10), consisting of the oral cavity (C01-C06), tonsil (C09), other oropharyngeal (C10), laryngeal (C32), and hypopharyngeal (C13) cancers (Edge et al., 2010). The population census database from the Official Statistics Registration Systems, Department of Provincial Administration, Thailand was used as the denominator for calculating age-standardized incidence rates for the study area.

In this study, the observed number of events was the number of incidences diagnosed with HN cancer (oral cavity, oropharyngeal, laryngeal, or hypopharyngeal). For spatial analysis, we focused on oropharyngeal cancer because of the risk factor disparity in the 25 districts within Chiang Mai province area. The temporal change was also described separately into two periods, 2007-2012 and 2013-2018. For each period, the expected number of incidences in each district was calculated by taking the

age specific incidence rate of each HN cancer type and multiplying by the population at the midpoint of the study period for each district broken down into the same strata (the observed number of HN and oropharyngeal cancer incidences in each district are given in Table 1). The population data were likewise drawn from the Official Statistics Registration Systems, Department of Provincial Administration, Thailand.

Statistical analyses

In the spatial analysis of each period, the observed number of incidences of each type of cancer Y_i ($i=1, \dots, 81$) are assumed to follow an independent Poisson distribution, $Y_i \sim \text{Poisson}(\theta_i E_i)$, with θ_i is the unknown relative risk (RR) in each district, and E_i the expected number of cases (Jones and Swerdlow, 1998; Lawson, 2013). The RR is rate ratio of incidence rate in district i compared to the rate in Chiang Mai. The Besag-York-Mollie (BYM) model (Besag et al., 1991) used to estimate the RR of HN and oropharyngeal cancer incidences includes both spatial heterogeneity (typically represented using the aggregated neighbors of each district) and uncorrelated spatial heterogeneity as follows (Riebler et al., 2016):

$$\log(\theta_i) = \alpha + u_i + v_i,$$

where α is the intercept, and u_i and v_i are the correlated and uncorrelated heterogeneity components, respectively. u_i are assumed to apply the spatial correlation since the RR estimation in each i is dependent on the neighboring areas. The spatial structure is defined based on the adjacent neighbors of each district and is assumed to follow a Gaussian intrinsic autoregression. The v_i are assumed to follow a normal distribution with zero mean (Lawson et al., 2003; Lawson, 2013) for a more in-depth explanation of this component). This model was used to explore the RR spatial distribution for HN and oropharyngeal cancer incidence among the districts in each periods. Furthermore, the deviance information criterion (DIC) for the model fitting results was calculated overall (the results are not shown) (Spiegelhalter et al., 2002).

Parameter estimation and disease mapping

Posterior estimates of the parameters were obtained by simulating from the joint posterior by means of a Markov-chain Monte Carlo algorithm using the OpenBUGS 3.2.3 implementation in R syntax (BUGS; R version 3.4.1), presented by Gerber and Furrer (Gerber and Furrer, 2015). The number of burn-in iterations on two parallel chains starting from overdispersed values was simulated and convergence was checked using the Brooks-Gelman-Rubin diagnostic: the coefficient of the between-chains and within-chain variances for each model parameter tends toward 1 when convergence is achieved (the results are not shown) (Brooks and Gelman, 1998).

In each period, we estimated the RR of the incidences of HN and oropharyngeal cancer for each district and its 95% credible interval (CrI) with the intercept of the two random effects (spatial heterogeneity and uncorrelated spatial heterogeneity). The map of the risk patterns of HN and oropharyngeal cancer incidence for the 25

districts in Chiang Mai province, Thailand was created using the Quantum Geographic Information System program version 2.8.1 (QGIS). The map used in this study was a publicly available shape-file dataset derived from the United Nations Office for the Coordination of Humanitarian Affairs - Regional Office for Asia and the Pacific (Thai district boundaries).

Patient and public involvement

No patients were involved in developing the research question, outcome measures and overall design of the study. Due to patient anonymity, we are unable to disseminate the results of the research directly to study participants.

Ethics approval and consent to participate

This study used secondary anonymous data and was approved by the Research Ethics Committee, Faculty of Medicine, Chiang Mai University.

Results

Characteristics

During 2007–2018, the number of new cases of HN cancer in adults in Chiang Mai, Thailand was 1,186 (72% of the population-based cancer incidence in Chiang Mai), of which 835 cases (70%) were male. Among those patients 548 diagnosed in 2007–2012 and 638 diagnose in 2013–2018. The median age at HN and oropharyngeal cancers diagnosis were 62 years old (IQR: 53–75) and 61 years old (IQR: 50–74.25), retrospectively in the former period and were 61 years old (IQR: 53–71) and 59 years

old (IQR: 51–71.25), retrospectively in the later period.

Spatial analysis between 2007–2012 and 2013–2018

The results of RR pattern of HN cancer between two periods are shown in Figure 2(a) and 2(b). In 2007–2012, the RR of HN cancer incidence ranged from 0.592–1.804. The highest RR was found in Doi Tao district [RR = 1.804; 95% CrI = 1.621–2.001] and the lowest RR was found in Mae Ai district [RR = 0.592; 95% CrI = 0.532–0.657]. While the RR ranged from 0.665–1.468 in 2013–2018 with the highest incidence in Doi Lo district [RR = 1.468; 95% CrI = 1.325–1.621] and the lowest incidence in Mae Ai district [RR = 0.665; 95% CrI = 0.600–0.735]. Both RR pattern of HN cancer were high in the central and southern areas of Chiang Mai. However, the RR of HN cancer incidence remarkably decreased in Doi Tao district, Mae Wang district and Hot district as compared to the earlier period.

The results of spatial analysis of oropharyngeal cancer incidence between the two periods showed that the RR of oropharyngeal cancer incidence in 2007–2012 ranged from 0.623–1.723 while the RR ranged from 0.588–1.035 in 2013–2018 (Figure 3(a) and 3(b)). The high risk pattern was found in the central and southern areas of Chiang Mai in 2007–2012, with the highest incidence in Doi Lo district [RR = 1.723; 95% CrI = 1.387–2.118] and the lowest incidence in Chai Prakan and Mae On district [RR = 0.623; 95% CrI = 0.501–0.766; RR = 0.623; 95% CrI = 0.502–0.766]. While, the high risk pattern was found in the central and northern areas of Chiang Mai in 2013–2018 with the highest incidence in Mueang district [RR = 1.035; 95% CrI = 0.834–1.037] and the lowest incidence in



Figure 1. The 25 Districts within Chiang Mai province, Thailand. [Source: United Nations Office for the Coordination of Humanitarian Affairs - Regional Office for Asia and the Pacific].

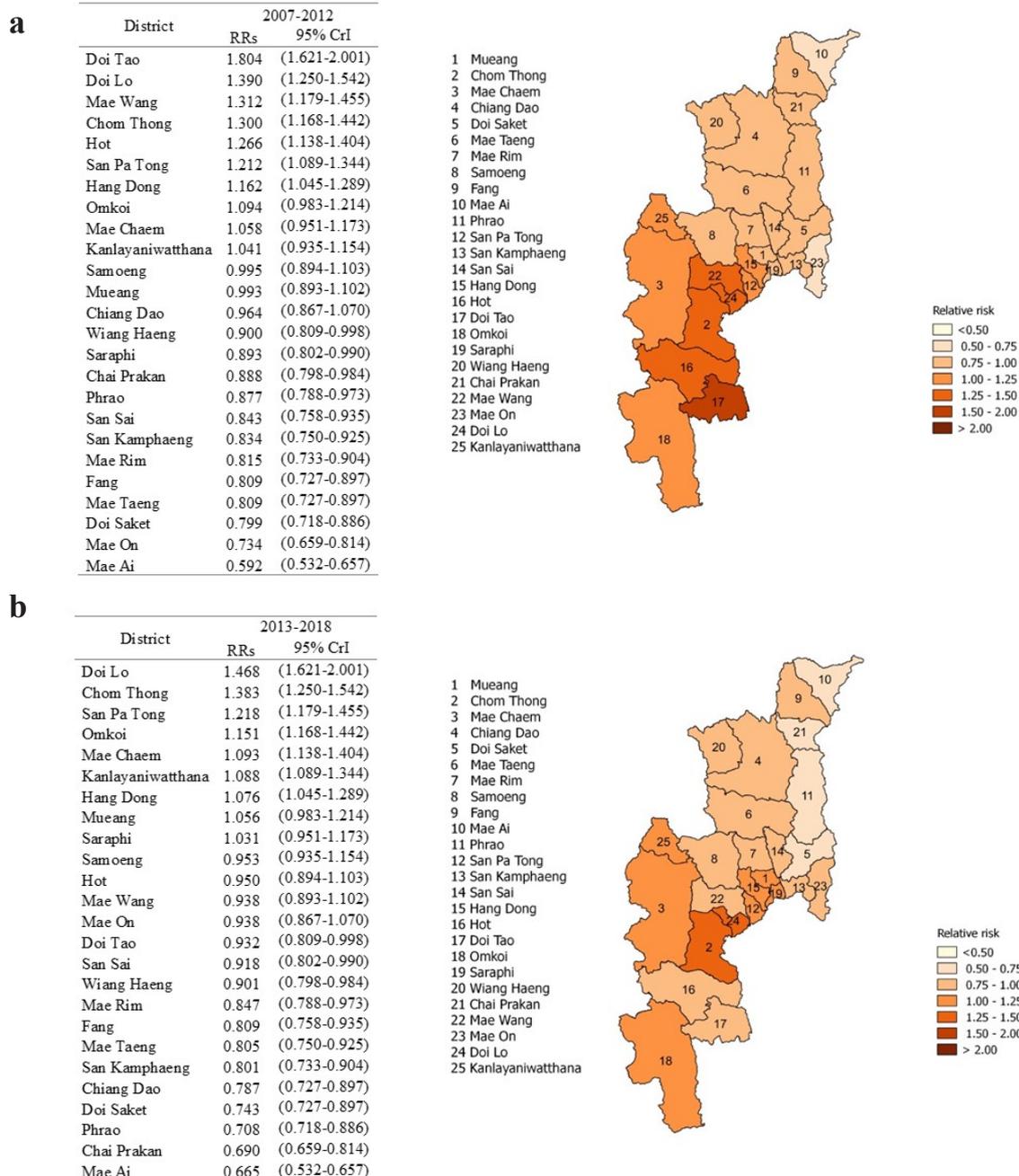


Figure 2. (a), Relative risk pattern of HN cancer incidence in Chiang Mai province, Thailand during 2007- 2012; (b), Relative risk pattern of HN cancer incidence in Chiang Mai province, Thailand during 2013- 2018

Omkoï district [RR = 0.588; 95% CrI = 0.474–0.589]. However, the RR of oropharyngeal cancer incidence remarkably decreased in Doi Lo district, Doi Tao district, Chom Thong district, Mae Wang district, Omkoï district, and San Pa Thong district. In contrast, the RR of Fang district have increased noticeably and remained high in Mueang district.

Discussion

The results of this study have highlighted specific areas with a high risk of HN and oropharyngeal cancer incidences in Chiang Mai province, along with the spatial inequalities in their distributions, with cluster formation. The analysis of geographic patterns of the incidence of

these cancers could be useful to formulate new strategies to improve screening and mitigate cancer incidence.

As several study has shown that smoking and alcohol use (Hashibe et al., 2007, 2009; Kumar et al., 2015) were risk factors of HN cancer. High risk patterns of both overall HN (both 2 periods) and oropharyngeal cancer (in 2007-2012) incidences were found in the central and southern areas of the province. This finding could be associated with a high prevalence of smoking, as was highlighted in a previous study which linked the RR of lung cancer mortality with the prevalence of smoking (Lopez-Abente et al., 2006). In our previous study on the risk pattern of lung cancer mortality in Northern Thailand (Rankantha et al., 2018), RR was high in the central and southern areas of Chiang Mai province, which conforms

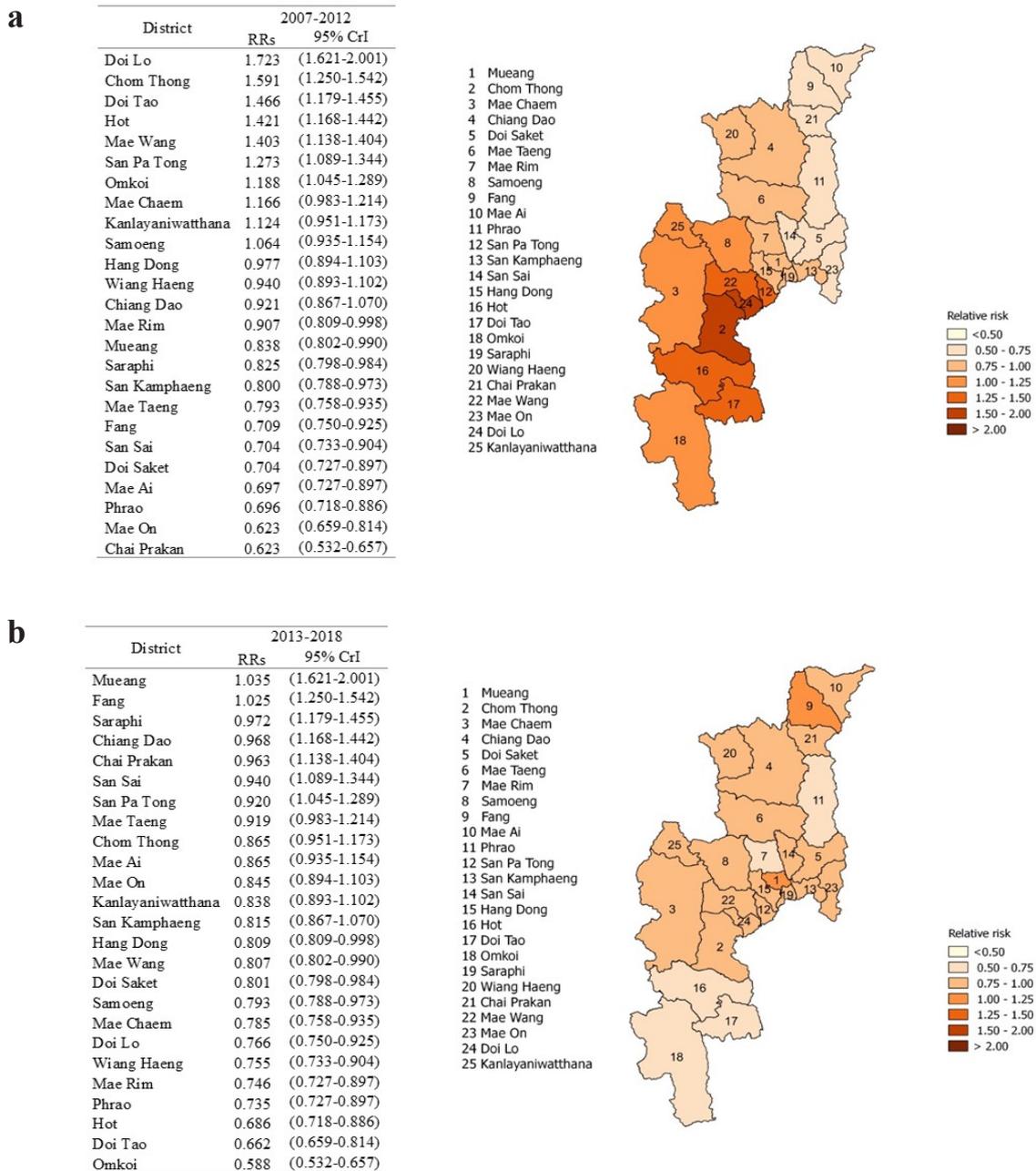


Figure 3. (a), Relative risk pattern of oropharyngeal cancer incidence in Chiang Mai province, Thailand during 2007- 2012; (b), Relative risk pattern of oropharyngeal cancer incidence in Chiang Mai province, Thailand during 2013- 2018

to the RR of HN cancer in this study. Interestingly, Doi Lo district had the highest RR of lung cancer mortality and HN cancer, which is in keeping with the cancerization theory involving squamous cell carcinoma in the oral cavity and oropharyngeal and laryngeal areas along with lung, esophageal, vulval, cervical, colon, breast, bladder, and skin cancers (Steinbeck, 2001). However, we cannot investigate the association of these factors and HN cancer incidence because the individual data of smoking and alcohol use were not recorded in cancer registry database. Moreover, in district level, the prevalence of smoking and alcohol use in Chiang Mai have not been reported in public.

The high RR of HN cancer incidence in the city center (Mueang district) and some of the surrounding districts

less than 58 kilometers from Mueang district (Doi Lo, Chom Thong, San Pa Tong, and Hang Dong) comprising the high income area of province might be related to the high consumption of cigarettes and alcohol (de Silva et al., 2011). Moreover, the supertertiary hospital in the city center (Mueang district) may attract patients to move their residents to be close by.

Most of the population in Doi Tao, Omko, Galyani Vadhana, and Mae Chaem districts are hill tribe members in Northern Thailand, as well as a group of rural Thai, indulge in betel chewing, smoking, and drinking, which are all related to oral cancer (Simarak et al., 1977; Reichart et al., 1988). In addition, hill tribe members have a low standard of living and live in mountainous areas. As a result, it is difficult for them to access government services

Table 1. The Observed and Expected HN Cancer Incidence in Chiang Mai Province, Thailand between 2007–2012 and 2013–2018.

District	2007-2012				2013-2018			
	HN Cancer		Oropharyngeal Cancer		HN Cancer		Oropharyngeal Cancer	
	O	E	O	E	O	E	O	E
Mueang	87	84	15	17	110	97	26	19
Chom Thong	34	25	10	5	44	28	7	5
Chiang Dao	21	19	6	4	19	23	7	5
Chai Prakan	12	13	0	3	9	15	4	3
Doi Tao	23	10	4	2	10	11	2	2
Doi Lo	17	11	6	2	22	12	1	2
Doi Saket	20	26	3	5	20	31	4	6
Fang	26	30	5	6	31	35	9	7
Phrao	18	20	2	4	15	22	1	4
Mae Chaem	15	17	2	3	20	17	3	4
Mae Taeng	20	27	4	6	25	31	8	6
Mae Rim	20	28	6	6	27	33	3	7
Mae Wang	18	11	5	2	7	13	2	3
Mae Ai	10	19	3	4	15	23	4	5
Mae On	5	8	0	2	11	9	2	2
Wiang Haeng	3	3	1	1	5	4	0	1
Samoeng	7	8	2	2	8	9	1	2
San Kamphaeng	25	30	6	6	27	36	5	7
San Sai	33	39	4	8	49	50	12	10
San Pa Tong	42	34	9	7	48	37	9	7
Saraphi	27	31	5	6	40	36	9	7
Hang Dong	36	28	5	6	40	34	5	7
Omkoï	10	12	2	2	19	14	1	3
Hot	18	14	5	3	13	16	2	3
Galyani Vadhana	1	2	1	0	4	3	1	1

O, Observed number; E, Expected number

in almost every aspect, such as education, profession/economy, healthcare, social, culture, natural resources, and the environment, and thus their social development has been delayed (Sairorkham et al., 2018).

It has been found that HPV is emerging as a primary cause of cervical cancer as well as for some HN cancers, especially oropharyngeal (McDonald et al., 2014). In the present study, high risk patterns of oropharyngeal cancer incidence were found in Chiang Mai province, which conforms to a study on the risk pattern of cervical cancer in northern Thai women using spatial analysis (Thongsak et al., 2016). The authors found that the risk pattern of cervical cancer was high in northern Chiang Mai, especially in the Mae Ai, Fang, Chai Prakan, Chiang Dao, and Wiang Haeng districts. This might offer an explanation for the high risk of developing oropharyngeal cancer in Chiang Dao district.

In our study, oropharyngeal cancer patients had a median age of over 54 years of age (the cutoff age for younger individuals). Hence, the most influential factor for oropharyngeal cancer in this area might not be associated with HPV, as Ang et al. found that HPV-related oropharyngeal cancer occurred in younger individuals

with a median age of 54 years old (Ang et al., 2010). Moreover, in Chiang Mai province, the geographic risk pattern of oropharyngeal cancer incidence was similar to HN cancer and thus was probably influenced by smoking and alcohol use rather than being linked to the HPV virus. This finding could be confirmed by the prevalence of HPV in oropharyngeal cancer patients in this area, but a limitation in our study is the lack of HPV test data because of the cost (\$80 per test). Fortunately, voluntary HPV testing of oropharyngeal cancer patients began in 2018, which will allow us to address this limitation in the future.

In addition, the RR of HN and oropharyngeal cancer for the period from 2007 to 2012 significant declined compared to the RR the later period (2013 – 2018). This was probably related to the reducing in smoking and tobacco use in Thailand (World Health Organization). The incidences of both cancers decreased in the majority of district, especially Doi Tao district, Mae Wang district and Hot district. Whereas, high incidences of HN cancer in Doi Lo, Chom Thong remained in both periods, and incidence of oropharyngeal cancer increased in Fang and remained high in Mueang district.

For the period from 2008 to 2012, the geographical

patterns of the incidence of the HN cancer and oropharyngeal cancer showed the similar pattern, the higher risk in the central and southern areas of Chiang Mai. Unlike the result of the period from 2013 to 2018, the geographical patterns of the incidence of the HN cancer and oropharyngeal cancer showed the changed pattern.

Our study is the first study reported the geographical pattern of HN cancer, which is ranked amidst of the common leading cancers in Thailand based on data of more than 2,000 cases from the Chiang Mai Cancer Registry. Spatial and temporal change were used highlighted specific areas with a high risk of HN cancer and oropharyngeal cancer incidences in Chiang Mai province, along with the spatial inequalities in their distributions, with cluster formation. There were some limitations in our study. As the results of a retrospective study, we cannot include some factors associating the incidence of HN cancer, e.g. smoking and alcohol consumption. However, our study provides a starting point for estimating the geographical pattern of the risk of HN cancer and for determining associations between it and spatial factors for further studies aimed at preventing this form of cancer and promoting the health of the local population.

In conclusions, this study have highlighted specific areas with a high risk of HN cancer and oropharyngeal cancer incidences in Chiang Mai province, along with the spatial inequalities in their distributions, with cluster formation. The relative risk was estimated by using the classic and fully Bayesian models taking into account spatial correlations of adjacent regions. In 2007 – 2012, the results showed that the geographic risk pattern of oropharyngeal cancer incidence was similar to HN cancer and thus was probably influenced by smoking and alcohol use rather than being linked to the human papillomavirus virus. Unlike the result of the period from 2013 to 2018, the geographical patterns of the incidence of the HN cancer and oropharyngeal cancer showed the changed pattern. The analysis of geographic patterns of the incidence of these cancers could be useful to formulate new strategies to improve screening and mitigate cancer incidence.

Author Contribution Statement

WB contributed in literature search, data collection, performed the data analyses and the writing of the manuscript. IC contributed in study design, data collection and reviewing the manuscript. SP, SC contributed in study design and reviewing the manuscript. AR and PS contributed in literature search and reviewing the manuscript.

All authors contributed to critical revisions of the manuscript and approved the final submitted version.

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Ethics approval

This study was approved by The Research Ethics Committee, Faculty of Medicine, Chiang Mai University.

Conflicts of interest

None to declare.

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