

## RESEARCH COMMUNICATION

# No Incidence Trends and No Change in Pathological Proportions of Nasopharyngeal Carcinoma in Zhongshan in 1970-2007

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### Abstract

**Objectives:** To explore nasopharyngeal cancer (NPC) incidence and pathological data of Zhongshan, China, in 1970-2007, and to provide scientific information for prevention and control. **Methods:** From Zhongshan Cancer Registry NPC data, incident numbers, crude incidence rates, age-adjusted incidence rates, proportion of pathology and incident trends were calculated and analyzed. **Results:** The male and female NPC world age-standardized incidence rates were 27.5/10<sup>5</sup> and 11.3/10<sup>5</sup> respectively, and were relatively stable in 1970-2007 in Zhongshan. The non-keratinizing type accounted for 84.6 percent of all NPC new cases and the keratinizing type only 5.8 percent, and there was no obvious changing in pathological proportions over 38 years. **Conclusion:** NPC incidence level was high and stable in Zhongshan in 1970-2007. It suggested that its prevention and control should be enhanced.

**Keywords:** Nasopharyngeal carcinoma - incidence - pathology - trend

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### Introduction

Recent research showed that although NPC incidence and mortality rates in most countries and regions were relatively steady, the rates in some countries and regions did change obviously (Wei et al., 2010; Mei, 2010), such as NPC incidence and/or mortality rates in Hongkong (Lee et al., 2003), Singapore (Parkin et al., 1997), Taiwan (Hsu et al., 2006), Western Canada and Alaska of USA had decreased conspicuously (IARC), while its incidence rates in Singapore Malay had increased from 1968 to 1997 (Devi et al., 2004; Wang et al., 2004) NPC epidemiological trend in China had also changed recently. The results of three national death-causes sampling surveys in China showed that NPC mortality rates in the sampling areas of China had down continuously and remarkably (Xu-dong et al., 1999; Zhu, 2008). But the data from different sources showed that the NPC epidemiological trend in China was different, such as the data released by WHO on its official website revealed that NPC world age-standardized mortality rates in some Chinese areas kept stable in 1987-2000 (IARC), while the data from National Office for Cancer Prevention and Control in China showed that the NPC incidence rates in some registries of China had increased in 1988-2004, some had decreased and some kept stable (Wei et al., 2010; Mei, 2010). And the NPC epidemiological trends in Southern China where high NPC incident rates were seen were different from the trends derived from the national death-causes sampling surveys in China, such as Jia et al., (2006) reported that NPC incidence and mortality rates in Sihui of Canton in

1978-2002 and in Cangwu of Guangxi province in 1983-1997 were relatively stable, while Wei et al., (2003; 2010) covered that the NPC world age-standardized incidence and mortality rates in Zhongshan of Canton in 1970-1999 had up 21.4 percent and 44.3 percent respectively. Besides, few researches on the epidemiological characteristics of population-based NPC pathology were seen (Chinese National Office for Cancer Prevention and Control, 2004) So, for mastering correctly the epidemiological laws of NPC and its different histopathology, and to provide scientific information for its prevention and control, the population-based NPC incident and pathological data in 1970-2007 in Zhongshan were analyzed.

### Data and methods

#### Source of incidence Data

NPC incident and pathological data in Zhongshan in 1970-2007 came from Zhongshan Cancer Registry. Since 1970, Zhongshan Cancer Registry have been recorded, collated, notified and stored the incidence and mortality data of all malignant tumors of Zhongshan registered residents (the benign and borderline tumors of central nervous system and all carcinoma in situ were also registered). The registration was done through a three levels network, called Zhongshan Three Ranks Cancer Prevention and Control Network, which covered all the corners of Zhongshan, was lead by Zhongshan Cancer Research Institute, and be composed of by municipal hospitals, township health centers and community health service stations (once called village/street health station).

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**Table 1. Comparison Between the NPC Pathological Classifications of 2000 Zong and other Chinese Classifications**

Zong 2000		Other Chinese Classifications	
Keratinizing squamous cell carcinoma	Well-differentiated		Well-differentiated
	Moderately-differentiated		Moderately-differentiated
	Poorly-differentiated		Others <sup>a</sup>
Non-keratinizing carcinoma (also known as lymphoepithelial carcinoma)	Differentiated subtype		Poorly-differentiated squamous carcinoma ? Spindle cell carcinoma Pleomorphic cell carcinoma Papillary non-keratinizing carcinoma Undifferentiated
	Undifferentiated subtype		Vesicular nucleus cell carcinoma Large round cell carcinoma Poorly-differentiated squamous carcinoma? Small cell carcinoma Neuroendocrine small cell carcinoma
	Mixed subtype		
Adenocarcinoma	Traditional type	Well-differentiated Moderately-differentiated poorly-differentiated	Well-differentiated Moderately-differentiated Poorly-differentiated Others <sup>b</sup>
	Salivary gland type		Adenoid cystic carcinoma Mucinoepidermoid tumor Others <sup>c</sup>

Others a: including pleomorphic or anaplastic squamous cell carcinoma, papillary squamous cell carcinoma, adenoid squamous cell carcinoma, basal cell-like squamous cell carcinoma and clear cell squamous cell carcinoma. Others b: including adenocarcinoma with focal squamous metaplasia, adenosquamous carcinoma, papillary adenocarcinoma, intestinal-type adenocarcinoma, mucinous adenocarcinoma and signet ring cell carcinoma. Others c: including acinar cell carcinoma, and cancer in the pleomorphic adenoma, malignant basal cell adenoma, malignant myoepithelial carcinoma, epithelial - myoepithelial carcinoma and clear cell carcinoma

There were full-time or part-time registrars at each level to register all should -be-registered cancer data and to follow-up cancer prevalent patients according to the unified regulations and formats. At the very beginning, passive registration was the major method used to collect cancer data with active registration as the assisting method, but as time went by, active registration substituted gradually passive registration and became the major registering method, and until now active registration based on Hospital Information System (HIS) is the only way used to register cancer data in Zhongshan. Moreover, the staffs of Zhongshan Cancer Registry also regularly went to nearby cities such as Guangzhou, Jiangmen and Shunde to collect the incident and mortality data of cancer patients who were Zhongshan residents but seek medical help in these cities. The collected data were first collated by experienced registrars to deplete duplicate information, correct wrong items and add missing items, thereafter the data were entered into database and stored. At the end of every year the registered cancer data were also checked against the all death-causes data to see if missing notification existed.

NPC pathological diagnosing proportion in Zhongshan in 1970-2007 was 96.3 percent, imaging diagnosing proportion 3.68 percent and the proportion of Death Certificate Only (DCO) 0.03 percent. The annual (except in 1970-1972 and 1992 which ranged from 83.3 percent to 88.4 percent) and five year (except in 1970-1974 when 86.7 percent) pathological diagnosing proportions in Zhongshan during the period were all over 95 percent.

*Source of population data*

The population data of Zhongshan in 1970-2007

came from Zhongshan Statistical Bureau and Security Bureau. Gender-specific and age-specific population data of Zhongshan in 1970-1989 could be obtained, but not after 1990. Only could be got after 1990 were the total number of male and female population, so the gender-specific and age-specific proportion data in 1990-2007 in Zhongshan could only be calculated from the gender-specific and age-specific proportion of 1990 and 2000 in Zhongshan when national population census were done. 1982 Chinese standard population and 1985 world standard population were used separately when China and world age-standardized incidence rates were calculated.

*Statistical indicators and methods*

Excel software was used to set up database and to do statistical analysis. Statistical indicators include incident numbers, crude incidence rates, age-specific incidence rate, China and world age-standardized incidence rates, incident and pathological proportion and so on. The statistical methods used here were the methods recommend by the Guideline for Chinese Cancer Registration (Chinese National Office for Cancer Prevention and Control, 2004).

*Pathological diagnosing standard*

NPC pathological classifications of 1962 Boqiang Liang, 1979 the 5<sup>th</sup> Chinese NPC Prevention Collaborative Group, 1991 The Norm of Chinese Common Cancer Diagnosis and Treatment, 2000 Zong and WHO were adopted successively in China (Zong, 2001; Ming-huang and Xiang, 2003; Chinese National Office for Cancer Prevention and Control, 2009), these NPC pathological classifications were also be used in Zhongshan in 1970-

2007, so different NPC pathological names could be seen in 1970-2007 in Zhongshan. Before the proportions of different NPC pathology and its epidemiological trends in 1970-2007 in Zhongshan were analyzed, the first things should be done was to unite and link all these different pathological names or types in different classifications. Table 1 showed how this was done by the authors according to the available research results. Here to make a comparison between the classification of Zong and other previous Chinese classifications was because the former was similar to WHO's classification.

**Results**

*Incident general situation*

There were 7,608 new NPC cases in Zhongshan in 1970-2007, 5,357 of them were male and 2,251 female, and the incident sex ratio was 2.38:1. The youngest and oldest patients were 2 and 98 years old respectively, the median and the average incident age were 48 and 48.1 respectively. The male crude incidence rate, China and world age-standardized incidence rates were 24.6/10<sup>5</sup>, 22.8/10<sup>5</sup> and 27.5/10<sup>5</sup> respectively, while the female 10.39/10<sup>5</sup>, 9.46/10<sup>5</sup> and 11.28/10<sup>5</sup> respectively (Table 2).

*Incidence trend*

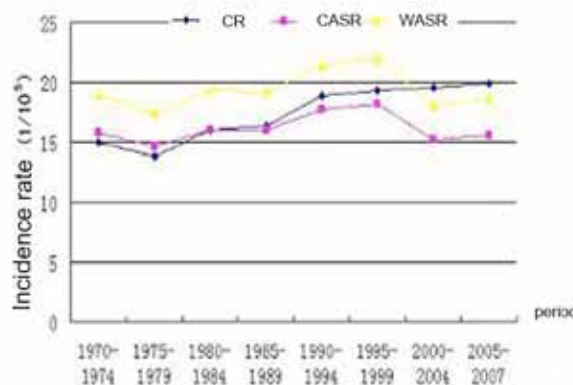
Table 2 and Figures 1 and 2 show characteristics for the 5 year NPC incidence trends in Zhongshan in 1970-2007, as follows: 1) There were no obvious ascending or descending trends for its China and world age-standardized incidence rates, its male world age-standardized incidence rates fluctuated between 25.0/10<sup>5</sup> and 31.1/10<sup>5</sup>, and the female between 10.2/10<sup>5</sup> and 13.1/10<sup>5</sup>; 2) After 1975-1979, NPC crude incidence rates in Zhongshan increased continuously; 3). In 1970-1999 there were ascending trends whether crude incidence rates, China and world age-standardized incidence rates.

*Age-specific incidence rates*

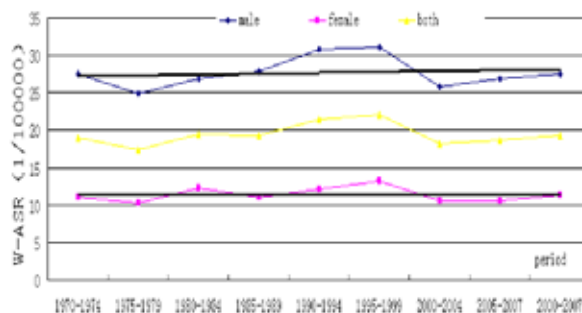
NPC incidence in Zhongshan in 1970-2007 increased rapidly from the age group of 25-29, peaked at the age group of 55-59 for male and 50-54 for female respectively, and decreased thereafter quickly especially for male.

*The proportions of different NPC pathological types*

There were 6,905 new NPC cases with explicit



**Figure 1. NPC Incidence Trends in Zhongshan in 1970-2007**



**Figure 2. NPC Gender-Specific Incidence Trend in Zhongshan in 1970-2007**

pathological diagnosis, accounted for 90.8 percent of all new NPC cases in Zhongshan in 1970-2007, 418 new NPC cases without pathological diagnosis, accounted for 5.49 percent, and 285 new NPC cases without specific pathological diagnosis, accounted for 3.75 percent. Those cases with explicit pathological diagnosis were classified into three major pathological types according to the NPC pathological classifications of Zong and WHO which were keratinizing, non-keratinizing and adenocarcinoma respectively. Among which keratinizing type accounted for 5.81 percent of all new NPC cases in Zhongshan during the period, non-keratinizing type accounted for 84.6percent, and adenocarcinoma only 0.24 percent. There were 11 new NPC cases with the pathological diagnosis of keratinizing non-keratinizing type, non-keratinizing keratinizing type and differentiated keratinizing type, and these cases were hard to be classified according the above three categories, hence were listed otherwise as

**Table 2. Nasopharyngeal Cancer Incidences at Different Time Periods in Zhongshan (N,1/10<sup>5</sup>)**

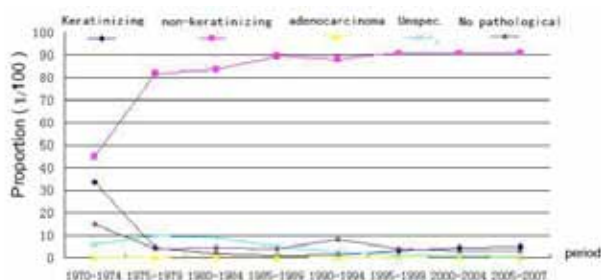
period	Male				Female				Total			
	No	C.R	C-ASR	W-ASR	No	C.R	C-ASR	W-ASR	No	C.R	C-ASR	W-ASR
1970-1974	487	21.21	22.58	27.49	206	8.87	9.40	10.99	693	15.01	15.83	19.00
1975-1979	482	19.60	21.06	24.97	204	8.20	8.46	10.24	686	13.87	14.62	17.39
1980-1984	554	21.73	22.12	26.89	264	10.29	10.19	12.25	818	15.99	16.04	19.40
1985-1989	631	23.18	22.98	27.78	255	9.46	9.16	10.95	886	16.35	15.99	19.24
1990-1994	801	26.90	25.34	30.80	313	10.69	10.07	12.11	1114	18.86	17.74	21.46
1995-1999	860	26.74	25.38	31.11	371	11.72	11.06	13.11	1231	19.29	18.23	22.07
2000-2004	941	27.58	21.55	25.84	393	11.63	8.95	10.59	1334	19.64	15.18	18.13
2005-2007	601	28.24	22.26	26.89	245	11.53	8.89	10.62	846	19.89	15.53	18.70
1970-2007	5357	24.62	22.75	27.54	2251	10.39	9.46	11.28	6708	17.52	16.03	19.30

C.R, crude incidence rate, C-ASR, China age-standardized rate, W-ASR, age-standardized rate.

**Table 3. The Proportions of Different NPC Pathological Types in Zhongshan in 1970-2007 (N,%)**

Period	Keratinizing		Non-keratinizing		Adeno-carcinoma		Unspecific.		Others		Without pathological diagnosis		Total
	No	Prop.	No	Prop.	No	Prop.	No	Prop.	No	Prop.	No	Prop.	
1970-1974	233	33.6	313	45.17	0	0	41	5.92	1	0.14	105	15.2	693
1975-1979	30	4.37	560	81.63	1	0.15	68	9.91	0	0.00	27	3.94	686
1980-1984	14	1.71	685	83.74	6	0.73	75	9.17	1	0.12	37	4.52	818
1985-1989	9	1.02	793	89.50	3	0.34	44	4.97	0	0.00	37	4.18	886
1990-1994	14	1.26	980	87.97	1	0.09	28	2.51	1	0.09	90	8.08	1114
1995-1999	39	3.17	1120	90.98	2	0.16	15	1.22	2	0.16	53	4.31	1231
2000-2004	62	4.65	1213	90.93	4	0.30	12	0.90	2	0.15	41	3.07	1334
2005-2007	41	4.85	770	91.02	1	0.12	2	0.24	4	0.47	28	3.31	846
1970-2007	442	5.81	6434	84.57	18	0.24	285	3.75	11	0.14	418	5.49	7608

No, number; Prop, proportion



**Figure 3. Proportions of Different NPC Pathological Types in Zhongshan in 1970-2007**

others (Table 3).

Except in 1970-1974 with a lower proportion, the every five years proportions of Non-keratinizing NPC were more than 80 percent of all new NPC cases in 1970-2007 in Zhongshan, and kept at about 90 percent after 1985-1989 without obvious ascending or descending trend, while the proportions of keratinizing NPC were much lower, less than 5 percent in 1970-2007 in Zhongshan except in 1970-1974 with its proportion as high as 33.62 percent (Figure 3).

## Discussion

The total NPC pathological diagnosing proportion was 96.30 percent and annual pathological diagnosing proportions were over 95 percent in Zhongshan in 1970-2007, except that its pathological diagnosing proportions ranged between 83.33 percent and 88.44 percent in 1970-1972 and 1992 (its causes maybe that in 1970-1972 Zhongshan Cancer Registry just began its cancer registration and operated not so smoothly, and also maybe associated with the lower medical, economic and culture levels in 1970s in Zhongshan, while in 1992 maybe parts of NPC pathological data might not be collected). The NPC pathological diagnosing proportion in Zhongshan in 1970-2007 was higher than those of other Chinese cancer registries in 2005-2006 (which ranged between 75.85 percent and 84.3 percent) (Chinese National Office for Cancer Prevention and Control, 1979; Curado et al., 2007), it suggested that the NPC incidence data in Zhongshan in 1970-2007 was of good quality and high credibility.

NPC incidence rates in Zhongshan had been at high level worldwide and nationwide, which was fully proved by the results of three Chinese death-causes sampling

surveys (Xu-dong et al., 1999; Zhu, 2008; Mei, 2010), while 2009 Chinese Cancer Registry Annual Report also showed that NPC incidence and mortality rates in Zhongshan were at high levels, only lower than the rates of Sihui of Canton (Chinese National Office for Cancer Prevention and Control, 2009). In addition, the male NPC incidence rates of Zhongshan in 1998-2002 ranked the first in Cancer Incidence in Five Continents Volume IX (Mei, 2010; Zong et al., 2001), higher than that of Hongkong in 1995-1999 (Lee et al., 2003).

NPC incidence trend of Zhongshan in 1970-2007 presented the following features: 1. in 1970-1999, no matter for male or female all kinds of NPC incidence rates in Zhongshan showed an increased trend, which was consistent with the previous report by Wei et al., (2003); 2. The NPC crude incidence rate of Zhongshan in 1970-2007 had an increased trend, while its China- and world-ASRs kept stable. Its cause maybe that the age-specific population proportions of Zhongshan in 2000-2007 were calculated from the population composition of Zhongshan in 2000 when China made a national population census, so the calculated proportions of NPC high-risk population in 2000-2007 in Zhongshan might be lower than the actual proportions of NPC high risk population at the same time. The stable trend of age-standardized incidence of Zhongshan in 1970-2007 was in line with the views which considered the NPC incidence worldwide was stable (Zong, 2001), and also in line with the incidence trend of Sihui of Canton and of Cangwu of Guangxi province (Wei et al., 2003; Wei-Hua et al 2006), but different from the incidence trends of Hongkong, Singapore, and Taiwan (Parkin et al., 1997; Lee et al., 2003; Mei, 2010). The fact the NPC incidence in Zhongshan in 1970-2007 was stable might also indicate that there were no obvious changing for the NPC etiological factors in Zhongshan during the period.

There were few population-based reports on NPC pathological proportions especially on the changing trends of its different pathological types before, one of the major causes might be that in different time different NPC pathological classifications had been adopted in China, but these once adopted classifications were difficult to unit and link with each other, especially the classifications of Zong and WHO with the previous Chinese classifications. Besides, it might also because the areas with population-based NPC pathological data were

very few. This article investigated the population-based NPC pathological proportions and their changing trends in Zhongshan in 1970-2007, and found that the non-keratinizing NPC accounted for 84.6 percent of all new NPC cases in Zhongshan in 1970-2007, and was the main NPC pathological type in Zhongshan, while keratinizing NPC was relatively few, accounted for about 5.73 percent, and adenocarcinoma was rare, only took up 0.22 percent. The results was basically consistent with the point which believed that in NPC high-risk areas non-keratinizing NPC dominated NPC pathology (Zong, 2001; Sun et al., 2005; Chinese National Office for Cancer Prevention and Control, 2009). But the Proportion of non-keratinizing NPC in Zhongshan was lower, its cause maybe the high proportions of NPC with unspecific pathological and no pathological diagnosis. No further studies about the subtypes of keratinizing and non-keratinizing types were carried out in this study, it was mainly because it was difficult to identify which subtypes of non-keratinizing type should poorly-differentiated squamous cell NPC belong to. Moreover, our results also showed that there was no obvious ascending or descending trends for the proportions of different NPC pathological types in 38 years in Zhongshan, and this result was similar to the result of Luo et al. (2004), only the difference between them was that the result of Luo et al was derived from the comparison between the pathological proportions of NPC diagnosed at the pathological department of Cancer Center of Sun Yat-sen University in 1999-2000 and 20 years ago, not based on population data and their data were not continuous data. In addition, our result was different from the result of Sun et al (2005), which found that there were descending trend for Type I NPC, ascending trends for type II NPC and no obvious trend for type III NPC in the male Chinese-Americans in California, Los Angeles and San Francisco.

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