



# The Epidemiology of Herpes Zoster and Postherpetic Neuralgia in China: Results from a Cross-Sectional Study

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## ABSTRACT

**Introduction:** Few studies have examined the epidemiology of herpes zoster (HZ) and postherpetic neuralgia (PHN) in China. The aim of this study was to estimate the prevalence of HZ and PHN in China, and to examine the clinical characteristics of patients identified with PHN.

**Methods:** This was a cross-sectional study conducted in 24 hospitals in seven cities in China. Prevalence of HZ and PHN was determined by physician ( $n = 100$ ) chart review of patients ( $n = 36,170$ ) aged  $\geq 40$  years seeking medical care over a 30- to 60-day period. The health history of patients identified with PHN was

obtained and included time since diagnosis of HZ or PHN, time since onset of PHN-related pain, and the methods used for diagnosing HZ and PHN.

**Results:** The prevalence rates of HZ and PHN were 7.7% [95% confidence interval (CI) 7.5–8.0] and 2.3% (95% CI 2.2–2.5), respectively. Of patients with HZ, 29.8% developed PHN. Rates of HZ and PHN increased with age and were highest in patients aged  $\geq 70$  years (10.6% and 4.1%, respectively). The majority of patients with PHN were diagnosed with HZ (80.9%) and PHN (83.8%) for  $< 1$  year, and had experienced PHN-related pain for  $< 1$  year (80.5%). Patient description and clinical examination were most commonly used to diagnose HZ and PHN.

**Conclusion:** These results provide current estimates of the prevalence of HZ and PHN in the

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general adult population in urban China. These rates are similar to previously reported rates in China and worldwide, and highlight the global nature of HZ and PHN.

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## INTRODUCTION

Herpes zoster (HZ) is caused by reactivation of the varicella-zoster virus from a latent state and is usually characterized by a unilateral, acutely painful vesicular rash that affects a single dermatome and is self-limiting, typically resolving in a few weeks [1, 2]. Postherpetic neuralgia (PHN) is a common clinical complication of HZ that presents as severe, often persistent, pain that occurs after the rash has resolved [1, 2]. The risk of developing PHN in patients with HZ varies from 5% to more than 30%, as recently reported in a systematic review of 130 studies in 26 countries [3]. The occurrence of both HZ and PHN increases with age [3, 4], and incidence rates appear to be increasing over time [3].

Most epidemiological studies have been conducted in North America and Europe, and have indicated a global incidence rate of HZ of approximately 3–5/1000 person-years [3, 5–7]. In the Asia-Pacific region, incidence of approximately 3–10/1000 person-years [8] has been reported across Australia [9], Taiwan [10–12], South Korea [13, 14], and Japan [15]. The risk of developing PHN in patients with HZ ranges from 6.2% to 52.0% in the Asia-Pacific region [8], including across Australia [9], Taiwan [10, 16], South Korea [17], Japan [18, 19], Thailand [20, 21], Singapore [22], and India [23, 24]. Few epidemiological investigations of HZ and PHN have been conducted in China. In a multistage sampling, cross-sectional study of 7149 rural and urban adults aged  $\geq 50$  years from across Guangdong province, a lifetime prevalence of HZ of 3.5% was reported [25]. Additionally, the lifetime prevalence of HZ was higher in women than in men, and increased

with age. In patients with HZ, the incidence rate of PHN, defined as pain lasting  $\geq 1$  month after the rash has healed, was 40.2%. In a separate community-based retrospective study of 49,721 rural and urban Chinese adults aged  $\geq 50$  years, the average annual incidence rate of HZ was 3.4/1000 person-years [26]. The average annual incidence rate was higher in women than in men and increased with age. Rates were higher in the urban population than in the rural population. A community-based retrospective survey in selected districts of Beijing reported an annual incidence rate of HZ of 1.9/1000 person-years, with higher rates in women (2.4/1000 person-years) than in men (1.7/1000 person-years) [27]. In a separate study of 522 patients with HZ, including some patients aged  $< 20$  years, PHN was identified in 6.9% of patients [28].

The main objective of this study was to determine the prevalence of HZ and PHN in patients seeking medical care in urban China. The secondary objective was to describe the clinical characteristics of those patients with PHN.

## METHODS

### Study Design

This cross-sectional epidemiological study was conducted between August and December 2016 at hospital sites in Tier 1 and Tier 2 cities in China. China has over 600 cities that are often categorized in different tiers based on criteria such as population size, resident average income, and development of services or infrastructure. Tier 1 cities represent the most developed areas, and Tier 5 the less developed smaller cities. This study was conducted in accordance with legal and regulatory requirements and accepted research practices described in the Good Practices for Outcomes Research issued by the International Society for Pharmacoeconomics and Outcomes Research [29, 30]. The final protocol and any amendments were reviewed and approved by the ethics committee at Chinese PLA General Hospital, Hai Dian District, Beijing. As this was a retrospective

epidemiological study, patient consent was not required.

The study consisted of two phases. In Phase 1, participating physicians reviewed the charts of patients aged  $\geq 40$  years who visited their office seeking medical care over the course of 30–60 days, and the presence or absence of HZ and/or PHN in each patient was documented. Inclusion criteria for physicians were a specialty in dermatology, neurology, and/or pain, and seeing a minimum of 200 patients aged  $\geq 40$  years over a 2-month period. In total, 100 physicians at 24 hospital sites across Tier 1 and Tier 2 cities participated. Participating hospitals were geographically dispersed across China and were all Tier 3 hospitals. The specific city locations were Guangzhou, Shenzhen, Beijing, Shanghai, Nanjing, Xi'an, and Chengdu. During Phase 1, the records of 36,170 patients were reviewed. In Phase 2, physicians conducted a chart review using paper data collection forms of those patients identified with PHN in Phase 1, to assess health history.

**Assessment of Herpes Zoster and Postherpetic Neuralgia Prevalence**

PHN was defined as pain persisting for  $\geq 1$  month following healing of the HZ rash [31]. The prevalence of HZ and PHN were determined by dividing the number of patients with each condition by the number of patients in the sample. The 95% confidence intervals (CIs) were also derived. Analysis was conducted within gender and age groups (40–50, 51–59, 60–69, and  $\geq 70$  years) for each condition.

**Clinical Characteristics of Patients with Postherpetic Neuralgia**

During Phase 2, the physician chart review of health history determined the clinical characteristics of patients with PHN identified during Phase 1. These clinical characteristics are listed in Table 1.

**Table 1** Clinical characteristics used to determine the health history of patients with postherpetic neuralgia

Characteristic	Additional information
Time since diagnosis of HZ or PHN	In years
Time since onset of pain due to PHN	In years
Specialty of the physician who diagnosed HZ or PHN	Dermatologist Neurologist Pain specialist Other
How each patient was diagnosed with HZ or PHN	By reporting physician Referred to reporting physician by another physician at the same site without diagnosis Referred to reporting physician by another physician at the same site with diagnosis Referred to reporting physician by another physician at a different site without diagnosis Referred to reporting physician by another physician at a different site with diagnosis
Method(s) used to diagnose HZ or PHN	Patient description Clinical exam Other
How the patient presented with rash and pain	Rash first followed by pain Pain first followed by rash Pain and rash at the same time Not reported

**Table 1** continued

Characteristic	Additional information
Length of time between presentation of rash and occurrence of pain, or between presentation of pain and occurrence of rash	In years
Type of previously diagnosed comorbidities	Occurring in $\geq 10\%$ of patients

*HZ* herpes zoster, *PHN* postherpetic neuralgia

### Statistical Methods

Descriptive statistics are provided, specifically counts, percentages, and sample size; 95% CIs were determined where applicable. No statistical comparisons between groups were made. All available data are reported, with no imputation strategy for missing data.

## RESULTS

### Patient Sample

The majority of the 36,170 patients who were reviewed during Phase 1 were female ( $n = 19,204$ , 53.1%). Patients were evenly split across age groups (40–50 years:  $n = 10,186$ , 28.2%; 51–59 years:  $n = 8885$ , 24.6%; 60–69 years:  $n = 8770$ , 24.2%;  $\geq 70$  years:  $n = 8329$ , 23.0%). For Phase 2, the clinical characteristics of 828 patients with PHN from seven hospital sites were assessed.

### Estimated Prevalence of Herpes Zoster

In total, 2803 patients were identified with HZ. The overall estimated prevalence of HZ was 7.7% (Table 2). Women had a slightly higher prevalence rate than men (7.9% vs. 7.6%). Prevalence rates increased with age. The lowest rate by age group was in those aged 40–50 years (5.5%) and the highest was in those aged  $\geq 70$  years (10.6%).

**Table 2** Estimated prevalence rates of herpes zoster overall, and by gender and age group

	Total number of patients	Number of patients with HZ	Prevalence (%)	95% CI
Overall	36,170	2803	7.7	7.5–8.0
Gender				
Male	16,966	1294	7.6	7.2–8.0
Female	19,204	1509	7.9	7.5–8.2
Age group, years				
40–50	10,186	562	5.5	5.1–6.0
51–59	8885	627	7.1	6.5–7.6
60–69	8770	733	8.4	7.8–8.9
$\geq 70$	8329	881	10.6	9.9–11.2

*CI* confidence interval, *HZ* herpes zoster

### Estimated Prevalence of Postherpetic Neuralgia

Of the 2803 patients with HZ, 835 (29.8%) had PHN. The overall estimated prevalence of PHN was 2.3% (Table 3). Men had a slightly higher prevalence rate than women (2.4% vs. 2.2%). Prevalence rates increased with age. The lowest rate by age group was in those aged 40–50 years (1.0%) and the highest in those aged  $\geq 70$  years (4.1%). The prevalence rate by city ranged from 1.5% in Shanghai to 3.0% in Beijing (Table 3).

### Clinical Characteristics of Patients Diagnosed with Postherpetic Neuralgia

The clinical characteristics of patients diagnosed with PHN are shown in Table 4. Of those patients who were later diagnosed with PHN, the majority were diagnosed with HZ for  $< 1$  year (80.9%), with only a small proportion having been diagnosed with HZ for  $\geq 5$  years (3.3%). Dermatologists diagnosed HZ most often (78.7%), followed by neurologists (11.9%). A substantial number of patients were referred to the reporting physician from an outside hospital with an existing diagnosis of

**Table 3** Estimated prevalence rates of postherpetic neuralgia overall, and by gender, age group and city

	Total number of patients	Number of patients with PHN	Prevalence (%)	95% CI
Overall	36,170	835	2.3	2.2–2.5
Gender				
Male	16,966	407	2.4	2.2–2.6
Female	19,204	428	2.2	2.0–2.4
Age group, years				
40–50	10,186	102	1.0	0.8–1.2
51–59	8885	179	2.0	1.7–2.3
60–69	8770	215	2.5	2.1–2.8
≥ 70	8329	339	4.1	3.7–4.5
City				
Guangzhou	8441	203	2.4	NA
Shenzhen	1402	28	2.0	
Beijing	6665	198	3.0	
Shanghai	3418	51	1.5	
Nanjing	6794	190	2.8	
Xian	5249	89	1.7	
Chengdu	4201	76	1.8	

*CI* confidence interval, *NA* not available, *PHN* postherpetic neuralgia

HZ (38.0%). Patient description and clinical exam were most commonly used to diagnose HZ, and most patients were diagnosed using a combination of both.

The majority of patients were diagnosed with PHN for < 1 year (83.8%), with a small proportion having been diagnosed with PHN for ≥ 5 years (2.7%). Similarly, most patients had PHN-related pain for < 1 year (80.5%), with only a small proportion having PHN-related pain for ≥ 5 years (4.3%). Dermatologists diagnosed PHN most often (49.5%), followed by pain specialists (28.9%) and then neurologists (18.4%). The reporting physician most commonly diagnosed PHN (46.1%), followed by referral to the reporting physician from outside the hospital with an existing diagnosis (24.6%). PHN was most commonly diagnosed by a combination of patient description and clinical examination. Similar proportions of patients

experienced a rash followed by pain (34.5%), prodromal HZ pain followed by a rash (31.6%), or rash and pain at the same time (29.5%). The mean length of time between presentation of rash and occurrence of pain, or presentation of pain and occurrence of rash, was < 1 year.

Of patients with PHN, 76.7% had comorbidities. Hypertension (35.7%), type 1 or type 2 diabetes (18.1%), osteoporosis (10.9%), and high cholesterol (10.0%) were the most common comorbidities.

## DISCUSSION

Our findings show that among patients seeking medical help at hospital sites in urban China, the estimated prevalence of HZ is 7.7% and the estimated prevalence of PHN is 2.3%. The estimated prevalence of PHN in patients with HZ

was 29.8%. HZ was slightly higher in women and PHN slightly higher in men. The prevalence of HZ and PHN increased with age, so that the highest prevalence of both occurred in patients aged  $\geq 70$  years. Most patients had HZ and PHN for  $< 1$  year. Of those with PHN, most had PHN-related pain for  $< 1$  year. Dermatologists most commonly diagnosed both HZ and PHN using a combination of patient description and clinical examination. Comorbidities were present in approximately three-quarters of patients with PHN.

The estimated overall prevalence of HZ reported here (7.7%) is higher than the lifetime prevalence of HZ reported in a 2015 cross-sectional study in Guangdong province (3.5%) [25]. However, a higher prevalence in women and increasing prevalence with increasing age was a common finding in both studies, and is in agreement with a separate study in a mixed rural and urban Chinese population [26]. The estimated prevalence of PHN in the current study was 2.3%. There have been no published surveys or previous estimates on the prevalence of PHN in China based on population. However, in the previous epidemiological study of HZ and PHN in Guangdong province, 40.2% of patients with HZ were reported as having PHN [25]. This is higher than the 29.8% of HZ patients with PHN reported here, even though the definition of PHN was the same (pain persisting for  $\geq 1$  month). This difference may be explained by the methodological differences between the two studies. For instance, in the study by Zhu et al. [25], the patient sample was older ( $\geq 50$  years vs.  $\geq 40$  years in the present study), and prevalence was based on patient recall rather than physician review of patient charts as in the current study. The study by Zhu et al. was also in a mixed rural/urban population, whereas the current study was in an urban population. A separate study identified PHN occurring in 6.9% of patients with HZ [28], which is considerably lower than that reported here. The figure reported here does agree with a recent systematic review of HZ and PHN epidemiology across the Asia-Pacific region, which reported reported between  $\leq 10\%$  and  $\geq 25\%$  of patients with HZ also had PHN [8]. However, as those authors noted, reported rates varied

**Table 4** Clinical characteristics of patients diagnosed with postherpetic neuralgia

Clinical characteristic	Patients diagnosed with PHN ( <i>n</i> = 828)
Time since HZ diagnosis, <i>n</i> (%)	
< 1 year	670 (80.9)
1 year to < 5 years	129 (15.6)
$\geq 5$ years	27 (3.3)
Specialty of physician who diagnosed HZ, <i>n</i> (%) <sup>a</sup>	
Dermatologist	192 (78.7)
Neurologist	29 (11.9)
Pain specialist	16 (6.6)
Other	6 (2.5)
How patient was diagnosed with HZ, <i>n</i> (%)	
Diagnosed by reporting physician	234 (28.3)
Referred to reporting physician from within hospital without diagnosis	32 (3.9)
Referred to reporting physician from within hospital with diagnosis already	212 (25.6)
Referred to reporting physician from an outside hospital without diagnosis	35 (4.2)
Referred to reporting physician from an outside hospital with diagnosis already	315 (38.0)
Method used for diagnosing HZ, <i>n</i> (%)	
Patient description	709 (85.6)
Clinical examination	696 (84.1)
Other	26 (3.1)
Time since PHN diagnosis, <i>n</i> (%)	
< 1 year	694 (83.8)



**Table 4** continued

Clinical characteristic	Patients diagnosed with PHN ( <i>n</i> = 828)
1 year to < 5 years	110 (13.3)
≥ 5 years	22 (2.7)
Time since onset of pain due to PHN, <i>n</i> (%) <sup>b</sup>	
< 1 year	149 (80.5)
1 year to < 5 years	28 (15.1)
≥ 5 years	8 (4.3)
Specialty of physician who diagnosed PHN, <i>n</i> (%) <sup>c</sup>	
Dermatologist	94 (49.5)
Pain specialist	55 (28.9)
Neurologist	35 (18.4)
Other	6 (3.2)
How patient was diagnosed with PHN, <i>n</i> (%)	
Diagnosed by reporting physician	382 (46.1)
Referred to reporting physician from within hospital without diagnosis	49 (5.9)
Referred to reporting physician from within hospital with diagnosis already	141 (17.0)
Referred to reporting physician from outside hospital without diagnosis	51 (6.2)
Referred to reporting physician from outside hospital with diagnosis already	204 (24.6)
Method used for diagnosing PHN, <i>n</i> (%)	
Patient description	736 (88.9)
Clinical examination	682 (82.4)
Other	13 (1.6)

**Table 4** continued

Clinical characteristic	Patients diagnosed with PHN ( <i>n</i> = 828)
How patient presented with rash and pain, <i>n</i> (%)	
Rash followed by pain	286 (34.5)
Pain followed by rash (prodromal pain of HZ)	262 (31.6)
Rash and pain at the same time	244 (29.5)
Not documented	35 (4.2)
Length of time in years between presentation of rash and occurrence of pain, mean (95% CI)	0.97 (0.83–1.10)
Length of time in years between presentation of pain and occurrence of rash, mean (95% CI)	0.73 (0.55–0.91)

The total number of patients may not sum to 828 for each characteristic because of missing data or because multiple answers could be given to a single question  
*CI* confidence interval, *HZ* herpes zoster, *PHN* post-herpetic neuralgia

<sup>a</sup> Data available for 243 patients

<sup>b</sup> Data available for 185 patients

<sup>c</sup> Data available for 190 patients

widely, and the occurrence of PHN was dependent not only on the age of the patient sample but also the definition of PHN used [8]. Methodological issues such as study design and geographic location (e.g., rural vs. urban) may also be important.

The occurrence of PHN in patients with HZ also agrees with a systematic review of global HZ and PHN epidemiology, including studies from North and South America, Europe, the Middle East, as well as the Asia-Pacific region, where rates ranged from 5% to 30% [3]. These authors also noted that reported rates were dependent on not only the ages of the patient sample and the definition of PHN used, but also the type of study.

Results from studies with similar designs to the current study have been reported globally

[32–35]. A rate of PHN at 1 month of ~ 30% was reported in patients with HZ aged  $\geq 60$  years in a study conducted by dermatologists and internists at 14 centers in Kushiro, Hokkaido, Japan [32]. In a separate study, the reported rate of PHN at 1 month was 47.6% in patients aged  $> 14$  years with HZ attending rural, urban, and semi-urban general practitioner (GP) offices in the autonomous community of Valencia, Spain [33]. A third study in the district of Pescara, Italy reported a rate of PHN at 1 month of 51.2% in patients, irrespective of age, attending GP offices and one urban hospital [34]. Finally, a study in four regions of Italy reported a rate of PHN at 1 month of 22.7% in patients aged  $> 50$  years attending GP offices [35]. Notably, although these studies were of similar, but not identical, design to the current study, there was considerable variability in the occurrence of PHN compared with the current study.

Approximately three-quarters of patients with PHN had comorbidities. The most common comorbidities were hypertension and diabetes (type 1 or type 2). This is in agreement with a recent systematic review of HZ and PHN epidemiology across the Asia-Pacific region [8], where hypertension (range 4.0–32.1%) and diabetes (2.5–20.6%) were also the most common comorbidities, although the rates in the current study were toward the upper limits of those ranges. In a hospital-based study in China [36], hypertension and diabetes were again the most common comorbidities, but rates were somewhat lower than those in the current study (22.2% and 11.7%, respectively). Differences in study design may be responsible for this discrepancy, specifically the fact that patients were seeking hospital-based medical care in the current study.

The current prevalence of HZ, and subsequently PHN, in China and across the Asia-Pacific region may be expected to be influenced by the availability of effective vaccines [25]. The Advisory Committee on Immunization Practices recommends vaccination against HZ in immunocompetent adults aged  $\geq 50$  years [37]. However, vaccination has not become routine practice in the Asia-Pacific region—in part because preventive adult healthcare, including

adult immunization, is not given high priority and also because of a paucity of epidemiological evidence [8]. The prevalence data reported in this study provide epidemiological evidence that could help inform government and policymakers when making decisions about the assessment and management of HZ and PHN [25].

This study has several limitations. The population sample consisted only of patients presenting for medical care to 24 hospitals in seven cities. The findings may not, therefore, be generalizable to the wider population, for instance those individuals with HZ and/or PHN who live in rural areas, who live in other Chinese cities, or who do not regularly present to hospitals for medical care. Cross-sectional studies also have inherent limitations, including the inability to measure incidence (only prevalence) and susceptibility to bias due to low response rates [29]. In addition, although different types of PHN exist, this study was not designed to capture these subtypes. To gain further insights into the epidemiology of HZ and PHN in China, further studies could include broader populations; for example, including individuals who live in rural or mixed rural/urban areas. The aim of this study was to estimate the prevalence of HZ and PHN in China, and to examine the clinical characteristics of patients identified with PHN. While for this purpose the data are descriptive only, we encourage other researchers to formulate hypotheses involving statistical comparisons that would advance the current research.

## CONCLUSION

This epidemiological cross-sectional study in hospital-based sites across seven different Tier 1 and Tier 2 Chinese cities reported a prevalence of HZ and PHN of 7.7% and 2.3%, respectively. Of those patients with HZ, 29.8% had PHN. Rates of HZ and PHN increased with age, and were highest in those aged  $\geq 70$  years. These results provide a current estimate of the prevalence of HZ and PHN in adults aged  $\geq 40$  years in urban China. The prevalence rates of HZ and PHN reported here are similar to previously



reported rates in China and worldwide, and further highlight the global nature of HZ and PHN.

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**Compliance with Ethics Guidelines.** This study was conducted in accordance with legal and regulatory requirements and accepted research practices described in the Good Practices for Outcomes Research issued by the International Society for Pharmacoeconomics and Outcomes Research. The final protocol and any amendments were reviewed and approved by the Ethics Committee at Chinese PLA General Hospital, Hai Dian District, Beijing. As this was a retrospective epidemiological study, patient consent was not required.

**Data Availability.** The data sets generated and analyzed during the current study are available from the corresponding author on reasonable request.

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