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REVIEW

New Findings on Risk Factors for Postherpetic Neuralgia From 2014 to 2024: A Systematic Review and Meta-Analysis

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Background: Postherpetic neuralgia (PHN) is a significant public health issue that severely impacts patients' quality of life. This systematic review is the first to conduct a meta-analysis of newly identified risk factors for PHN over the past decade, evaluating the temporal changes in these risk factors to assist clinicians in predicting the occurrence of PHN.

Methods: Cohort and case-control studies on PHN risk factors were retrieved from PubMed, Web of Science, Embase and Cochrane Library (January 1, 2014–March 26, 2024). Study quality was assessed using the Agency for Healthcare Research and Quality (AHRQ) or the Newcastle-Ottawa Scale (NOS). Pooled odds ratios (ORs) with 95% confidence intervals (CIs) were calculated to assess risk factor effects.

Results: Seventeen studies involving 124,078 participants were included, identifying 81 potential risk factors. Eleven factors were meta-analyzed, and significant risk factors among these included age (age 60–69 (OR=2.05, 95% CI=[1.92,2.19], P<0.00001, I^2=0%, age over 70 (OR=3.08, 95% CI=[2.89,3.29], P<0.00001, I^2=0%)), severe rash (OR=2.69, 95% CI=[1.23,1.88], P=0.01, I^2=0%), acute pain severity (OR=2.01, 95% CI=[1.28,3.15], P=0.002, I^2=21%), anxiety/depression (OR=1.30, 95% CI=[1.21,1.41], P<0.00001, I^2=0%), diabetes mellitus (OR=1.46, 95% CI=[1.40,1.53], P<0.00001, I^2=28%), malignancy (OR=1.56, 95% CI=[1.23,1.99], P=0.0002, I^2=25%), chronic obstructive pulmonary disease(COPD) (OR=1.88, 95% CI=[1.79,1.98], P< 0.00001, I^2=0%), hypertension (OR=1.22, 95% CI=[1.12,1.32], P<0.00001, I^2=2%) and peptic ulcer (OR=3.71, 95% CI=[2.31,5.96], P<0.00001, I^2=0%). Female sex (OR=0.69, 95% CI=[0.47,1.01], P= 0.06, I^2=15%) and inflammatory factors (OR=1.01, 95% CI=[0.98,1.04], P=0.45, I^2=30%) were not statistically significant.

Conclusion: COPD, hypertension, anxiety/depression, malignancy and peptic ulcers may represent newly identified PHN risk factors. Given the limitations of the research, the results should be interpreted with caution. Future research should focus on these factors to enhance clinical prediction and prevention strategies.

Trial Registration: This study is registered in the PROSPERO database (No. CRD42024543589).

Keywords: postherpetic neuralgia, risk factors, meta-analysis

Introduction

Postherpetic neuralgia (PHN), a common complication of herpes zoster (HZ), is characterized by chronic pain persisting or developing 3 months after the initial rash or HZ diagnosis.[1,2] The incidence of HZ is approximately 30%, with PHN occurring in about 12.5% of cases.[3] Patients often describe PHN as burning, pricking, or otherworldly pain, which can persist for months or years, leading to psychiatric symptoms like depression and anxiety. Current treatments, including both pharmacological and non-pharmacological approaches, are often limited in efficacy and accompanied by significant adverse effects.[4] On the pharmaceutical front, pregabalin and gabapentin are the only FDA-approved first-line oral treatments for PHN, dizziness, and

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edema. On the non-pharmaceutical side, interventions such as nerve root injection and spinal cord electrical stimulation are widely used but suffer associated with significant limitations including suboptimal efficacy, complications, and high expense.[5]

PHN imposes a substantial health economic burden globally, including in Italy,[6] Sweden,[7] China,[8] Spain,[9] and the U.S.[10] Early prediction of PHN is crucial for implementing timely clinical interventions. A previous review summarized risk factors for PHN from 1950 to 2014 (such as old age, severe rashes, etc).[11] However, given the dynamic nature of medical research and changes in population health over the past decade, an updated analysis is warranted. Therefore, the purpose of this study is to conduct a meta-analysis of literature from 2014 to 2024 to identify recent and emerging risk factors for PHN. We aim to provide clinicians with a contemporary evidence base to improve early prediction, facilitate timely intervention, and ultimately reduce the incidence and burden of PHN.

Methods

Protocol And registration

This evidence-based study was registered in the International Prospective Systematic Evaluation Registry (PROSPERO) database (No. CRD24024543589) and conducted following PRISMA guidelines (Supplementary Table 1).[12]

Search Strategy

We searched PubMed, Web of Science, Embase and Cochrane Library for case-control and retrospective studies on PHN risk factors published between January 1, 2014, and March 26, 2024. MeSH terms, index terms, and keywords were used, with detailed search strategies provided in Tables 1–4.

Inclusion Criteria

Studies meeting the following criteria were included:

1. Population: Adults.
2. Study types: Cohort or case-control studies.
3. Study focus: Patients with PHN, defined as pain persisting >90 days post-rash.[13]
4. Content: Analysis of PHN risk factors.
5. Data: Original studies with extractable or calculable (odds ratio) ORs and 95% confidence intervals (CIs).
6. Language: English.
7. Publication status: Published literature.

Table 1 Search Strategy for PubMed Database

Search	Query	Results	Date
#8	#5 AND #6 Filters: from 2014–2024	406	26 Mar 2024
#7	#5 AND #6	746	26 Mar 2024
#6	#3 OR #4	3,202,141	26 Mar 2024
#5	#1 OR #2	4,798	26 Mar 2024
#4	((((“risk ratio”[Title/Abstract]) OR (“relative risk”[Title/Abstract])) OR (“risk”[Title/Abstract])) OR (“Factor, Risk”[Title/Abstract])) OR (“Risk Factor”[Title/Abstract])	2,886,475	26 Mar 2024
#3	Search: “Risk factors”[MeSH Terms] Sort by: Most Recent	979,216	26 Mar 2024
#2	(((((“Postherpetic neuralgia”[Title/Abstract]) OR (“post-herpetic neuralgia”[Title/Abstract])) OR (“postherpetic pain”[Title/Abstract])) OR (“post herpetic pain”[Title/Abstract])) OR (“post herpetic pain”[Title/Abstract])) OR (“PHN”[Title/Abstract])	4,589	26 Mar 2024
#1	“Neuralgia, Postherpetic”[Mesh] “neuralgia, postherpetic”[MeSH Terms]	1,419	26 Mar 2024

Table 2 Search Strategy for Web of Science Database

Search	Query	Results	Date
#3	#2 AND #1	1,050	26 Mar 2024
#2	TS=(Risk factor OR risk ratio OR relative risk OR risk OR Factor, Risk OR Risk Factor)	3,580,293	26 Mar 2024
#1	TS=(Postherpetic neuralgia OR PHN OR neuralgia, postherpetic OR post-herpeticneuralgia OR postherpetic pain OR post herpetic pain OR post herpetic pain)	6,410	26 Mar 2024

Table 3 Search Strategy for Embase Database

Search	Query	Results	Date
#8	#3 AND #6 AND [01–01-2014]/sd NOT [26–03-2024]/sd AND [2014–2024]/py	753	26 Mar 2024
#7	#3 AND #6	1,344	26 Mar 2024
#6	#4 OR #5	4,535,969	26 Mar 2024
#5	"risk ratio":ab,ti OR "relative risk":ab,ti OR "risk":ab,ti OR "factor, risk":ab,ti OR "risk"	4,151,991	26 Mar 2024
#4	"risk factor"/exp	1,410,417	26 Mar 2024
#3	#1 OR #2	8,526	26 Mar 2024
#2	"phn":ab,ti OR 'neuralgia, postherpetic'ab,ti OR "post-herpetic neuralgia":ab,ti OR 'postherpetic pain':ab,ti OR "post herpetic pain":ab,ti	4,383	26 Mar 2024
#1	"postherpetic neuralgia"/exp	6,688	26 Mar 2024

Table 4 Search Strategy for Cochrane Library

Search	Query	Results	Date
#1	MeSH descriptor. [Neuralgia, Postherpetic] explode all trees	378	26 Mar 2024
#2	(PHN)ab,t;kw OR (neuralgia, postherpetic);ab.kw OR (postherpetic neuralgia);ab,ti,kw OR (postherpetic pain);ab,i,kw oR (post herpetic pain);ab.t,khw oR (postherpetic pain):ab,ti,kw OR (Postherpetic Neuralgia):ab,ti,kw	1,407	26 Mar 2024
#3	#1 OR #2	1,407	26 Mar 2024
#4	(risk ratio): ab.ti.kw OR (relative risk):ab,ti,kw OR (nisk): ab,t.kw OR (Factor, Risk):ab.ti.kw OR (Risk Factor):ab.ti.kw	300,790	26 Mar 2024
#5	#3 AND #4	157	26 Mar 2024

Exclusion Criteria

Studies were excluded if they:

1. Lacked relevant data or analysis of risk factors.
2. Were not available in full text.
3. Were non-journal articles (eg, dissertations, conference papers).

Article Selection

A two-step screening process was employed to identify relevant studies. First, three reviewers (Yiwen Wan, Xinglai Su, and Xiang Pan) independently assessed titles and abstracts, categorizing studies as "potentially relevant" or "not

relevant". In the second stage, the same reviewers evaluated the full texts of "potentially relevant" studies, classifying them as "relevant" or "irrelevant". Disagreements were resolved by a fourth reviewer (Bing Liang).

Data Extraction and Quality Assessment

Two reviewers independently extracted data, including author, publication year, study design, sample size, risk factors and OR (95% CI). Consistency tests were performed to ensure accuracy. Study quality was assessed using the Newcastle-Ottawa Scale (NOS), which evaluates selection, comparability, and outcomes.[14] Scores of 0–4, 5–6, and 7–9 indicated low, moderate, and high quality, respectively. Discrepancies were resolved through discussion with a third reviewer.

Strength of Evidence

Evidence levels were categorized as:[15,16] (in Table 5)

1. Strong: ≥3 studies, with ≥2 high-quality homogeneous studies or a synthesis of multiple high-quality studies.
2. Moderate: One high-quality study plus one or more moderate/low-quality studies with significant combined results.
3. Limited: One high-quality study or combined results from moderate/low-quality studies.
4. Very Limited: No significant pooled results or heterogeneous findings unrelated to quality.

Statistical Analysis

Meta-analysis were conducted for risk factors assessed in ≥2 studies. ORs and 95% CIs were pooled to estimate PHN risk. Heterogeneity was assessed using Cochrane Q and I^2 statistics (25%, 50% and 75% indicating low, medium, and

Table 5 Risk Factors' Pooled Analysis and Level of Evidence

Risk Factors	Number of Included Studies	Pooled Effects OR [95% CI]	P value	I^2	Level of Evidence
Female	3	0.93[0.38,2.24]	0.87	93%	Strong
Age 50–59 years	2	1.34[0.43,4.18]	0.62	12%	Moderate
Age 60–69 years	2	2.05[1.92,2.19]	<0.00001	0%	Moderate
Age >70 years	3	3.08[2.89,3.29]	<0.00001	0%	Strong
Severe rash	3	1.44[0.46,4.45]	0.53	73%	Strong
Acute pain severity	3	1.47[0.88,2.48]	0.14	65%	Strong
Anxiety and Depression	2	1.30[1.21,1.41]	<0.00001	0%	Moderate
Inflammation factor	2	1.01[0.98,1.03]	0.61	48%	Moderate
Diabetes mellitus	5	1.57[1.36,1.81]	<0.00001	69%	Strong
Malignancy	3	1.56[1.23,1.99]	0.0002	25%	Strong
Chronic obstructive pulmonary disease	2	1.88[1.79,1.98]	<0.00001	0%	Moderate
Hypertension	3	1.22[1.12,1.32]	<0.00001	2%	Strong
Peptic ulcer	2	3.71[2.31,5.96]	<0.00001	0%	Moderate

high heterogeneity, respectively).[15,17] Fixed-effects models were used for I^2<50%, and random-effects models for I^2≥50%. Sensitivity analysis were performed for high heterogeneity.[18] Statistical analysis were conducted using RevMan 5.3, with P<0.05 considered significant.

Result

Study Selection

A total of 1,860 studies were identified from 74 electronic databases. After removing 559 duplicates, 1,301 studies remained. Screening of titles and abstracts excluded 1,016 studies, including reviews, dissertations, conference papers, and non-adult studies. 41 studies were excluded due to unavailability of full texts. After screening the full texts of the 244 remaining articles, we excluded the 227 studies for the following reasons: (1) no OR reported (n=30), (2) outcomes unrelated to PHN or its risk factors (n=157), (3) unsuitable study type (n=27), (4) ineligible study population (n=7), (5) inability to combine 99% confidence intervals (n=1), (6) duplicate literature (n=2), and (7) non-English publications (n=3). Finally, 17 English-language studies were included. The selection process is summarized in the PRISMA flowchart (Figure 1).

Study Characteristics and Quality Assessment

The risk factors of PHN were extracted and summarized one by one, and a total of 81 risk domains were collected (Supplementary Table 2). Studies with the same or similar risk factors were pooled for analysis. The basic characteristics and quality evaluation of the included studies are summarized in Supplementary Table 3.[2,19–34] A total of 17 studies were

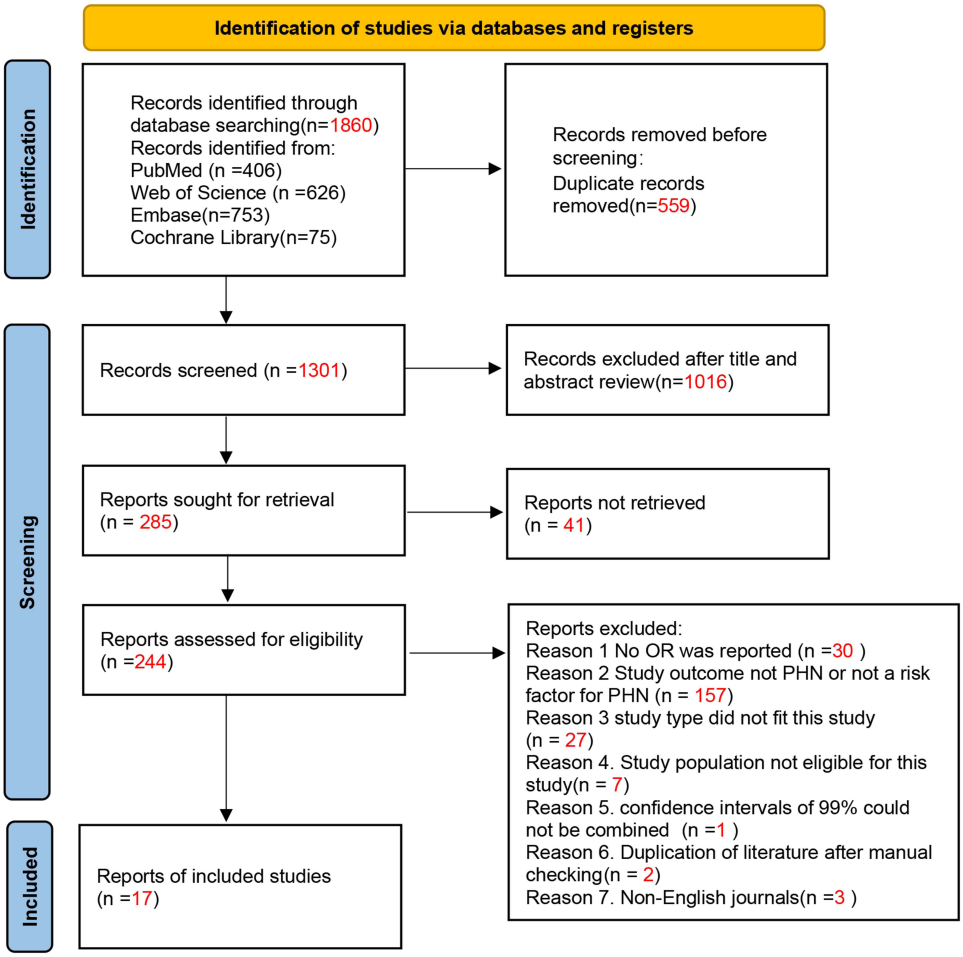

Figure 1 Flowchart of the search process for the articles.

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included in this research, including 12 cohort studies and 5 case-control studies, with a total sample size of 124,078 (15,255 in the PHN group and 108,823 in the control group). 10 studies were rated as high quality, 6 as moderate quality, and 1 as low quality, with an overall mean score of 7.18. The overall quality of the studies was positive.

Female

Three studies examined female gender as a PHN risk factor.[19,22,28] The pooled analysis showed no significant association between the two (OR=0.93, 95% CI=[0.38,2.24], P =0.87, I^2=93%) (Figure 2A). Due to high heterogeneity, sensitivity analysis excluding the Muñoz-Quiles et al study reduced I^2 to 15% (OR=0.69, 95% CI=[0.47,1.01], P= 0.06, I^2=15%),[28] but the result remained non-significant (Supplementary Figure 1A).

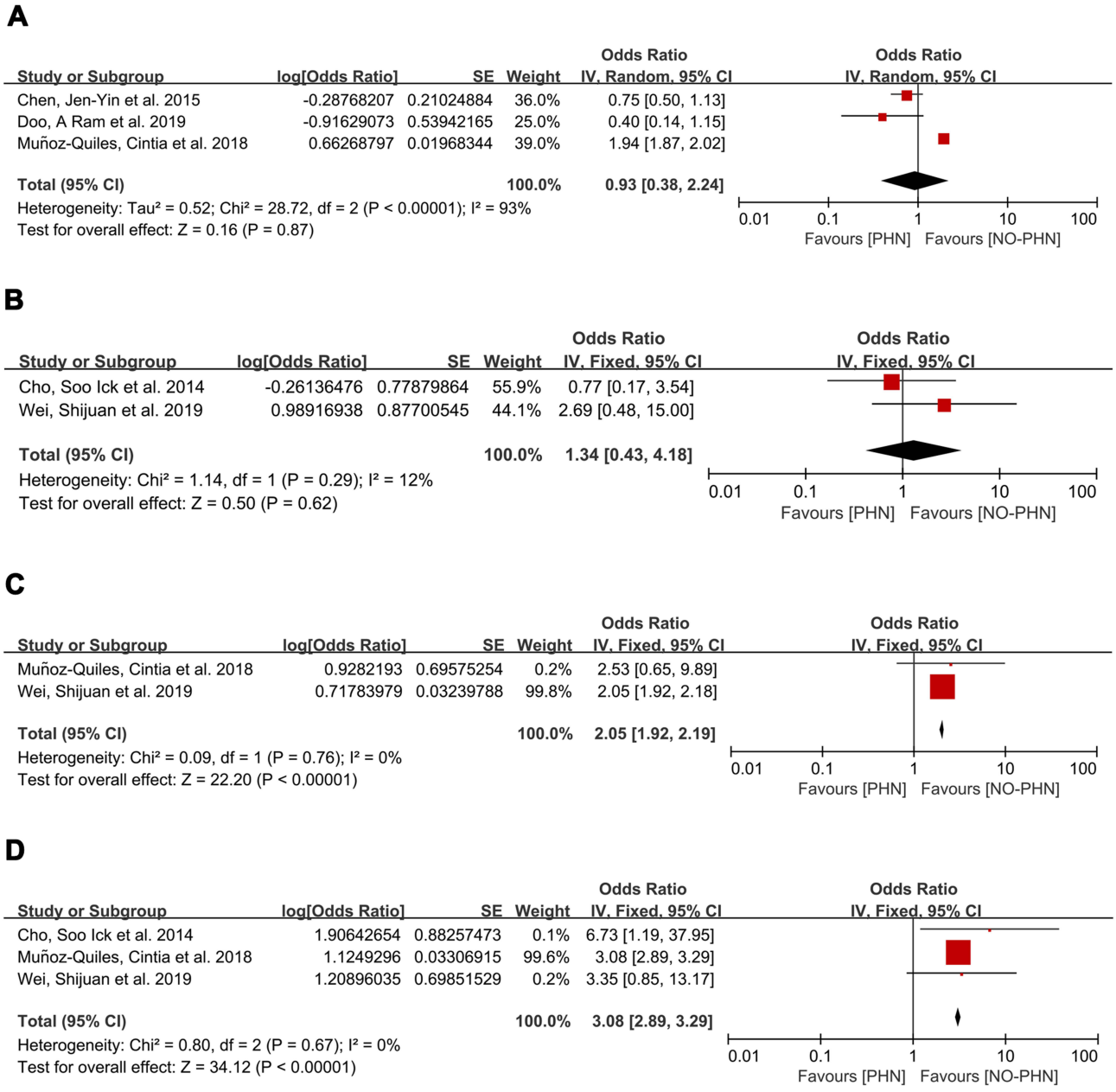

Figure 2 Meta-analysis of risk factors for PHN (**A**) female, (**B**) age 50–59 years, (**C**) age 60–69 years, (**D**) age >70 years.

Age

Three studies assessed age as a PHN risk factor, with subgroups for 50–59,[21,31] 60–69,[28,31] and ≥70 years.[21,28,31] No association was found for 50–59 years (OR=1.34, 95% CI=[0.43,4.18], P=0.62, I^2=12%) (Figure 2B). However, significant associations were observed for 60–69 years (OR=2.05, 95% CI=[1.92, 2.19], P<0.00001, I^2=0%) and ≥70 years (OR=3.08, 95% CI=[2.89,3.29], P<0.00001, I^2=0%) (Figure 2C and D).

Severe Rash

Three studies assessed severe rash as a PHN risk factor.[21,32] Initial analysis showed a non-significant association (OR=1.44, 95% CI=[0.46,4.45], P=0.53, I^2=73%) with high heterogeneity (Figure 3A). After excluding studies with high heterogeneity (Fujiwara and Aki et al),[2] heterogeneity decreased to 0% (OR=2.69, 95% CI=[1.23, 5.85], P=0.01, I^2=0%), suggesting that severe rash may be a PHN risk factor (Supplementary Figure 1B).

Acute Pain Severity

Three studies evaluated acute pain severity as a PHN risk factor.[23,33,34] Acute pain intensity was defined as a maximum visual analogue scale (VAS) score of ≥3 or a numerical rating scale (NRS) score of ≥4 within 30 days after the onset of the rash. All extracted VAS data were in the range of 0–10 points. A association was found (OR=1.47, 95% CI=[0.88,2.48], P=0.14, I^2=65%) (Figure 3B). A sensitivity analysis excluding the study by Chen et al,[33] reduced heterogeneity to 21% (OR=2.01, 95% CI=[1.28,3.15], P=0.002, I^2=21%) (Supplementary Figure 1C).

Anxiety and Depression

Two cohort studies assessed anxiety and depression using VAS scores.[2,27] Fixed-effects meta-analysis showed a significant association with PHN risk (OR= 1.30, 95% CI=[1.21,1.41], P<0.00001, I^2=0%) (Figure 3C).

Inflammation Factor

One cohort study and one case-control study evaluated inflammatory factors.[24,30] The fixed-effects meta-analysis showed no significant association with PHN (OR=1.01, 95% CI=[0.98,1.03], P=0.61, I^2=48%) (Figure 3D). A sensitivity analysis excluding Gu et al yielded similar results (OR=1.01, 95% CI=[0.98,1.04], P=0.45, I^2=30%) (Supplementary Figure1D).[24]

Diabetes Mellitus

Five studies (three cohort and two case-control) assessed diabetes as a PHN risk factor.[19,20,27,28,33] A random-effects meta-analysis showed a significant association (OR=1.57, 95% CI=[1.36,1.81], P<0.00001, I^2=69%)(Figure 4A). Sensitivity analysis excluding the study by Morena et al reduced heterogeneity to 28% (OR= 1.46, 95% CI=[1.40,1.53], P<0.00001, I^2=28%),[27] and the association remained statistically significant (Supplementary Figure 1E).

Malignancy

Three studies (two cohort and one case-control) evaluated malignancy as a PHN risk factor.[19,20,27] A fixed-effects meta-analysis showed a significant association (OR= 1.56, 95% CI=[1.23,1.99], P=0.0002, I^2=25%) (Figure 4B), indicating a higher risk of PHN in patients with malignancies.

Chronic Obstructive Pulmonary Disease (COPD)

Two cohort studies assessed COPD as a PHN risk factor.[27,28] A fixed-effects meta-analysis showed a significant association (OR=1.88, 95% CI=[1.79,1.98], P< 0.00001, I^2 = 0%) (Figure 4C), confirming COPD as a PHN risk factor.

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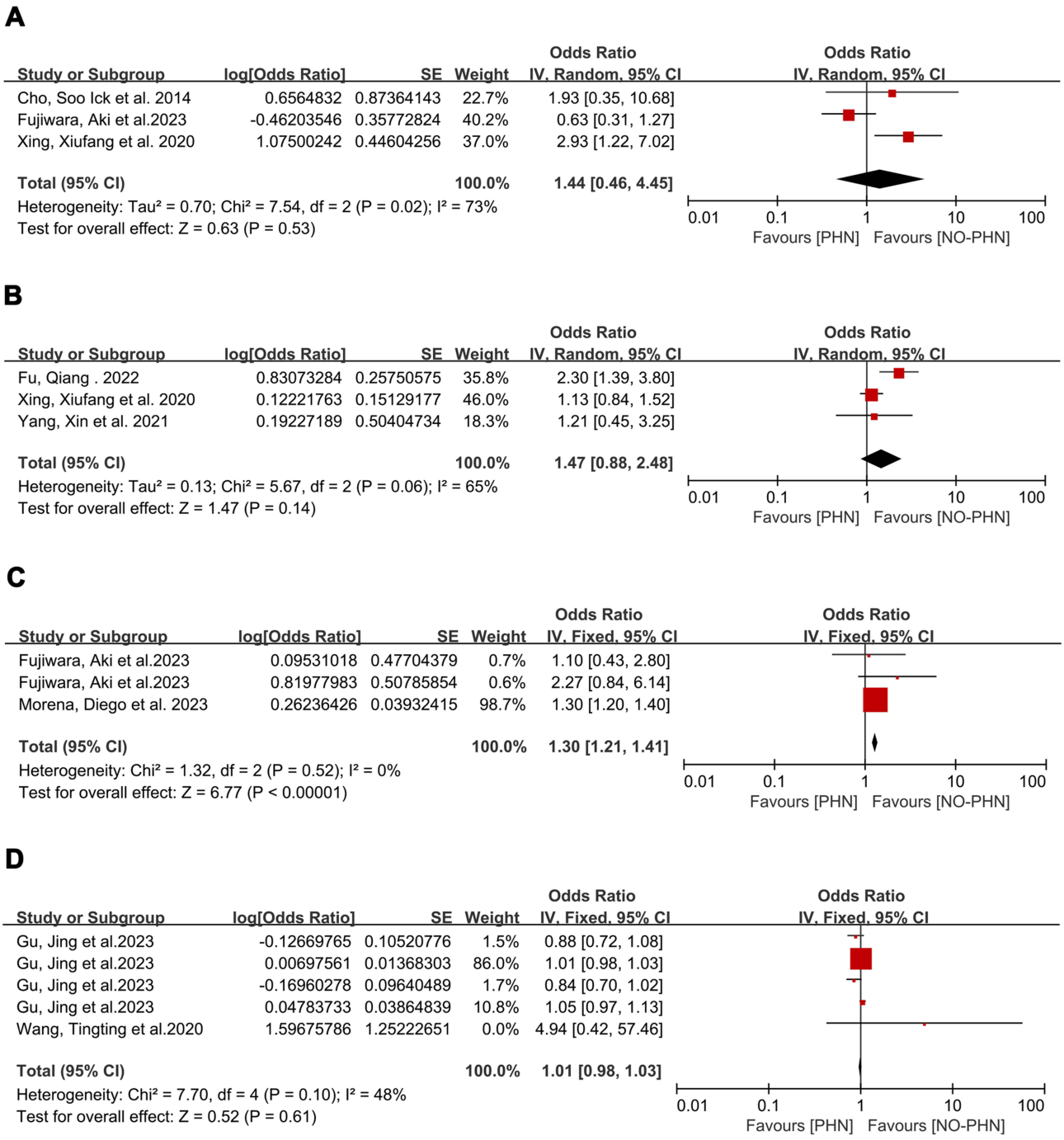


Figure 3 Meta-analysis of risk factors for PHN (**A**) Severe rash, (**B**) Acute pain severity, (**C**) Anxiety and Depression, (**D**) Inflammation factor.

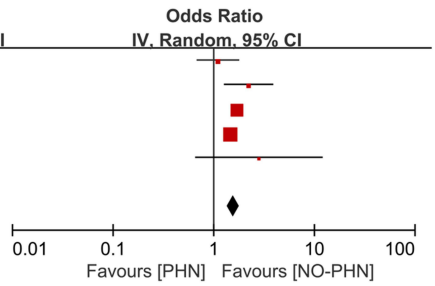
Hypertension

Three studies (two cohort and one case-control) evaluated hypertension as a PHN risk factor.[19,20,27] A fixed-effects meta-analysis showed a significant association (OR= 1.22, 95% CI=[1.12, 1.32], P<0.00001, I^2=2%) (Figure 4D), indicating a higher risk of PHN in hypertensive patients.

A

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
Chen, Jen-Yin et al. 2015	0.09531018	0.24925789	7.2%	1.10 [0.67, 1.79]
Chen, Jen-Yin et al. 2019	0.7975072	0.28823082	5.6%	2.22 [1.26, 3.91]
Morena, Diego et al. 2023	0.53062825	0.0465106	40.2%	1.70 [1.55, 1.86]
Muñoz-Quiles, Cintia et al. 2018	0.37843644	0.02265191	46.0%	1.46 [1.40, 1.53]
Xing, Xiufang et al. 2020	1.03318448	0.74443532	0.9%	2.81 [0.65, 12.09]
Total (95% CI)			**100.0%**	**1.57 [1.36, 1.81]**

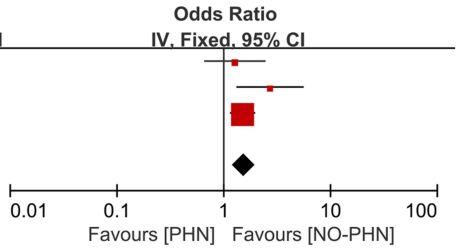
Heterogeneity: Tau² = 0.01; Chi² = 12.76, df = 4 (P = 0.01); I² = 69%
Test for overall effect: Z = 6.17 (P < 0.00001)



B

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Fixed, 95% CI
Chen, Jen-Yin et al. 2015	0.2390169	0.33746126	13.0%	1.27 [0.66, 2.46]
Chen, Jen-Yin et al. 2019	0.99694864	0.37014086	10.8%	2.71 [1.31, 5.60]
Morena, Diego et al. 2023	0.40546511	0.13942442	76.2%	1.50 [1.14, 1.97]
Total (95% CI)			**100.0%**	**1.56 [1.23, 1.99]**

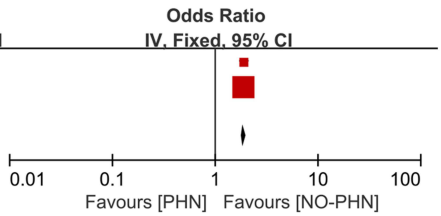
Heterogeneity: Chi² = 2.68, df = 2 (P = 0.26); I² = 25%
Test for overall effect: Z = 3.68 (P = 0.0002)



C

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Fixed, 95% CI
Morena, Diego et al. 2023	0.64185389	0.05390538	23.5%	1.90 [1.71, 2.11]
Muñoz-Quiles, Cintia et al. 2018	0.63127178	0.0298865	76.5%	1.88 [1.77, 1.99]
Total (95% CI)			**100.0%**	**1.88 [1.79, 1.98]**

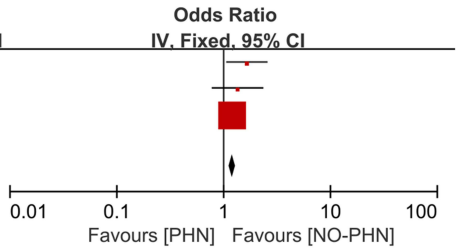
Heterogeneity: Chi² = 0.03, df = 1 (P = 0.86); I² = 0%
Test for overall effect: Z = 24.25 (P < 0.00001)



D

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Fixed, 95% CI
Chen, Jen-Yin et al. 2015	0.50077529	0.22691849	3.3%	1.65 [1.06, 2.57]
Chen, Jen-Yin et al. 2019	0.30010459	0.28350799	2.1%	1.35 [0.77, 2.35]
Morena, Diego et al. 2023	0.18232156	0.04261584	94.5%	1.20 [1.10, 1.30]
Total (95% CI)			**100.0%**	**1.22 [1.12, 1.32]**

Heterogeneity: Chi² = 2.04, df = 2 (P = 0.36); I² = 2%
Test for overall effect: Z = 4.72 (P < 0.00001)



E

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Fixed, 95% CI
Chen, Jen-Yin et al. 2015	1.36353737	0.32676884	54.9%	3.91 [2.06, 7.42]
Morena, Diego et al. 2023	1.24415459	0.36063606	45.1%	3.47 [1.71, 7.04]
Total (95% CI)			**100.0%**	**3.71 [2.31, 5.96]**

Heterogeneity: Chi² = 0.06, df = 1 (P = 0.81); I² = 0%
Test for overall effect: Z = 5.41 (P < 0.00001)

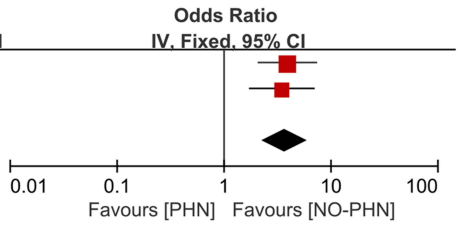


Figure 4 Meta-analysis of risk factors for PHN (**A**) Diabetes mellitus, (**B**) Malignancy, (**C**) COPD, (**D**) Hypertension, (**E**) Peptic ulcer.

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Peptic Ulcer

Two studies (one cohort and one case-control) assessed peptic ulcer as a PHN risk factor.[19,27] A fixed-effects meta-analysis showed a significant association (OR=3.71, 95% CI=[2.31,5.96], $P<0.00001$, $I^2=0\%$) (Figure 4E), confirming peptic ulcer as a PHN risk factor.

Other Risk Factors

Additional factors such as Vitamin D status,[20] myelin basic protein,[34] glucocorticoid use,[33] and genotype[23] were mentioned in individual studies. However, due to limited evidence from single studies, these factors were not included in the summary analysis.

Discussion

Summary of Evidence

This systematic review analyzed 17 studies (12 cohort and 5 case-control) published from 2014 to 2024 to identify risk factors for PHN. Consistent with previous studies, age over 60 was strongly associated with PHN, while the evidence for female gender as a risk factor remained inconclusive. Clinical features of acute HZ, including severe pain, severe rash, and high VAS scores, were linked to an increased PHN risk. Inflammatory factors showed no significant association. Diabetes mellitus was confirmed as a PHN risk factor, which was consistent with previous research findings. New evidence suggests that psychological conditions (such as anxiety and depression), COPD, hypertension, malignancy, and peptic ulcer may also contribute to PHN risk factors, though further investigation is warranted.

Interpreting New Findings

PHN arises from complex pathophysiological mechanisms, with acute HZ infection causing peripheral and central nervous system damage. The persistent pain associated with PHN may result from sustained varicella-zoster virus (VZV) levels or increased neuronal excitability due to nerve injury.[35]

Psychological Conditions and PHN

Depression and anxiety are associated with reduced immune function, which may create favorable conditions for VZV infection. These psychological conditions often triggered by the severe pain, fever, and other symptoms of HZ patients, which in turn contribute to the development of PHN, creating a complex feedback loop. Depression increases nociception by lowering pain thresholds through neurobiological changes,[36] and brain regions involved in mood regulation also modulate pain.[37] Neuropathic pain (NP) further exacerbates depressive symptoms, mental distress, and reduced quality of life.[38]

Malignancy and PHN

Malignant tumors dramatically impair immune function, thereby elevating HZ risk both before and after treatments like surgery, chemotherapy and radiation. The tumor microenvironment in malignancies, such as lung adenocarcinoma, shows reduced immune cell abundance, predisposing patients to infections like HZ.[39,40] Acute HZ infection further depletes immune cells in affected skin tissues, leading to persistent neuralgia and PHN.[41] Retrospective studies indicate a higher incidence of gastrointestinal, respiratory and hematologic malignancies in PHN patients, which suggests that there is a link between HZ, PHN, and cancer development.[42]

COPD and PHN

Chronic respiratory diseases, particularly COPD, are significant risk factors for HZ.[43] A study conducted in Taiwan (China), confirmed that COPD patients are more susceptible to HZ compared to the control group. The exact mechanisms underlying the association between COPD and VZV reactivation are not yet fully understood. However, chronic inflammation and immune dysregulation associated with COPD may contribute to the reactivation of VZV,[41] which could be a primary factor leading to the development of PHN in COPD patients.

Hypertension and PHN

Hypertension elevates angiotensin II levels,[44] which modulate pain through receptors in the central and peripheral nervous systems.[45–47] Angiotensin II receptor antagonists, such as EMA401, have demonstrated efficacy in alleviating neuropathic pain in clinical trials. Maintaining normal blood pressure may help reduce pain perception in PHN patients, suggesting a potential therapeutic approach.[48,49]

Peptic Ulcer and PHN

Peptic ulcer is a known risk factor for HZ,[50] and is also linked to PHN.[51] H. pylori infection and ulcerative drugs (eg, NSAIDs and steroids) lead to T-cell dysfunction, nutritional deficiencies, and chronic inflammation, which may impair immunity and delay neurological recovery. These factors increase susceptibility to VZV infection and exacerbate neuropathic pain, contributing to the development of PHN.[19]

Strengthens and Limitations

This study is a systematic review and meta-analysis of risk factor follow-up for PHN to identify novel risk factors for PHN. This review summarizes the results of 17 studies from the last decade that are of moderate or above moderate quality. However, this systematic review and meta-analysis has some limitations. First, we only included studies in English, which may have potential publication bias and language bias. Therefore, future studies should include more languages. Second, the definition of the duration of PHN varies from 3 to 6 months in clinical observation and its risk factors have also changed, and there is no consensus. Third, most of the included studies has a small number of subjects, and therefore there may be bias in the results.

Conclusion

In summary, this meta-analysis (2014–2024) identified five significant new risk factors for PHN: psychological conditions (such as anxiety and depression), COPD, hypertension, malignancy and peptic ulcer. Notably, these newly highlighted risk factors in this analysis, offering valuable insights for PHN prevention and early diagnosis. However, the study's limitations, including the restricted number of included studies, hinder a comprehensive meta-analysis of other potential factors. We recommend future multi-center, large-scale studies focus on these newly identified risks to strengthen evidence and guide clinical practice. A cautious and rigorous research approach will further clarify PHN's risk profile and improve patient outcomes.

Abbreviation

HZ, Herpes zoster; PHN, Postherpetic neuralgia, AHRQ, Agency for Healthcare Research and Quality; NOS, Newcastle-Ottawa Scale; ORs, Odds ratios; CI, Confidence interval; PROSPERO, Prospective Systematic Evaluation Registry; VAS, Visual analogue scale.

Data Sharing Statement

The datasets used and analyzed during the current study are available from the corresponding author (Mi Li, E-mail Address: limi@smmu.edu.cn) on reasonable request.

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Disclosure

The authors declare no competing interests in this work.

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