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MINI REVIEW

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Impact of Herpes Zoster Vaccine on Postherpetic Neuralgia: A Comprehensive Review

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Abstract

Background: Herpes zoster (HZ), also known as shingles, is often complicated by postherpetic neuralgia (PHN), a chronic pain condition that significantly impairs quality of life. Vaccination against HZ has become a key preventive strategy to lower the risk of PHN. This review evaluates the effectiveness of HZ vaccines in reducing the incidence of PHN.
Methods and Results: In accordance with PRISMA guidelines, a systematic search was conducted across PubMed, Embase, Web of Science, and the Cochrane Library up to May 2024. Eligible studies included randomized controlled trials (RCTs), cohort studies, and observational studies that reported quantitative outcomes on the occurrence of PHN after vaccination.
The included studies encompassed diverse populations, primarily older adults. The recombinant zoster vaccine (RZV) demonstrated a substantial reduction in PHN incidence, with effectiveness approaching 60%. In contrast, the live zoster vaccine (ZVL) showed notable early protection, though its efficacy declined over time. The recombinant zoster vaccine (RZV) was associated with higher rates of mild, self-limiting adverse reactions compared with ZVL.
Conclusions: Both HZ vaccines, particularly RZV, are effective in preventing PHN and exhibit acceptable safety profiles. Broader vaccine uptake could decrease the public health burden of PHN. Long-term data on the duration of immunity and the potential role of booster doses remain areas for future investigation.(**International Journal of Biomedicine. 2025;15(4):649-652.**)

Keywords: herpes zoster • neuralgia • vaccine

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Abbreviations

HZ, herpes zoster; **PHN**, postherpetic neuralgia; **RZV**, recombinant zoster vaccine; **RCTs**, randomized controlled trials; **VZV**, varicella-zoster virus; **ZVL**, live zoster vaccine.

Introduction

Herpes zoster (HZ), also known as shingles, is caused by the reactivation of the latent varicella-zoster virus (VZV), the same virus responsible for causing chickenpox. Following primary infection, usually in childhood, VZV remains dormant within sensory ganglia and can reactivate later in life. Age-related immune decline, immunosuppression, and psychosocial stress are among the major triggers of viral reactivation, leading to the development of HZ. Clinically, HZ presents as a painful, vesicular rash in a dermatomal distribution, often preceded by prodromal symptoms such as itching, burning, or tingling sensations.[1]

The most common and burdensome complication of HZ is postherpetic neuralgia (PHN), a chronic neuropathic pain syndrome that may persist for months or years after rash resolution. PHN significantly impairs quality of life, contributing to ongoing pain, functional limitations, sleep

disturbances, and psychological distress. Beyond individual suffering, PHN imposes a considerable healthcare and economic burden due to prolonged treatment needs and increased healthcare utilization[2,3]

Because PHN is difficult to treat and often refractory to available therapies, prevention has become a major clinical priority. Vaccination against HZ has emerged as an effective strategy to reduce both the incidence and severity of HZ and, by extension, the risk of PHN. By enhancing VZV-specific immunity, vaccines aim to prevent reactivation or attenuate disease severity, thereby lowering the likelihood of PHN development.[4,5] Current recommendations target older adults, the population at greatest risk, with evidence suggesting a meaningful reduction in HZ and its complications following vaccination.[6] Nonetheless, questions remain regarding the degree of protection specifically against PHN, underscoring the need for a systematic evaluation of available evidence.

In this review, we assess the impact of HZ vaccination on the incidence of PHN. By synthesizing data across clinical trials and observational studies, we aim to clarify the effectiveness of HZ vaccines in mitigating one of the most persistent and debilitating outcomes of HZ.

Methods

We systematically searched PubMed, Embase, Web of Science, and the Cochrane Library for studies published up to May 2024, and screened reference lists of relevant articles.

Eligible studies included randomized controlled trials, cohort, case-control studies, and observational studies that assessed herpes zoster (HZ) vaccination and reported quantitative data on postherpetic neuralgia (PHN) incidence in humans. Reviews, editorials, case reports, and studies without relevant outcomes were excluded.

Search terms combined keywords and MeSH headings for "herpes zoster," "shingles," "postherpetic neuralgia," and "vaccine." Two reviewers independently screened records, extracted data, and resolved discrepancies by consensus. Extracted variables included study and participant characteristics, vaccine type and regimen, and outcomes (PHN incidence, follow-up duration, vaccine efficacy, and adverse events).

The primary outcome was the incidence of PHN after vaccination; secondary outcomes included the incidence of HZ, vaccine efficacy, and safety. The methods followed the PRISMA guidelines.

Results

Across randomized trials, cohort, and observational studies, herpes zoster (HZ) vaccination consistently reduced postherpetic neuralgia (PHN) incidence. Most studies involved adults aged ≥50 years from the United States, New Zealand, and Southeast Asia, with sample sizes up to >30,000.

The recombinant zoster vaccine (RZV) lowered PHN incidence by ~60% in older adults, with durable protection over several years. By contrast, live zoster vaccine (ZVL) showed strong early efficacy but declined markedly over time, suggesting a need for booster strategies.[6-9]

Recombinant zoster vaccine (RZV) was associated with higher rates of mild local and systemic reactions than ZVL, but serious adverse events were rare.[10-13]

Modeling studies predicted substantial public health gains: raising RZV coverage to 65% in Southeast Asia could prevent hundreds of thousands of PHN cases over 15 years, with significant healthcare cost savings.[12,13]

Subgroup analyses confirmed benefits across age groups and health statuses, with particularly strong protection in older and immunocompromised populations.[13-15]

Discussion

Herpes zoster (HZ) results from reactivation of latent varicella-zoster virus (VZV) within sensory ganglia. Following primary infection, the virus persists in neuronal cell bodies in a transcriptionally quiescent state, thereby evading immune detection.[15] Reactivation is primarily driven by immunosenescence, with age-related declines in T-cell-mediated immunity rendering older adults particularly vulnerable. Immunocompromised states such as HIV infection, organ transplantation, or long-term immunosuppressive therapy further disrupt the host–virus balance, permitting viral replication and clinical disease. In addition, stress, trauma, or neurological injury can alter the local ganglionic microenvironment via neuroendocrine and inflammatory signaling, creating conditions favorable to reactivation. Viral factors, including mutations in latency- or reactivation-associated genes, may also modulate the risk of reactivation.[15,16]

Host immune responses play a decisive role in determining disease outcomes. VZV-specific T cells are central to viral control; memory T cells maintain immune surveillance in sensory ganglia and can rapidly eliminate reactivated virus.[17] When this surveillance is compromised, viral spread along sensory nerves initiates acute HZ, characterized by a painful dermatomal rash and robust inflammatory infiltration of cytokines, chemokines, and immune cells.[15] This inflammation, while necessary for viral clearance, also contributes to neuronal injury and heightened nociceptive signaling. Persistent neuroinflammation, combined with ongoing antigenic stimulation, aberrant nociceptive processing, and neuronal sensitization, provides the basis for postherpetic neuralgia (PHN).[18]

Several risk factors predispose to PHN. Advanced age remains the strongest predictor, owing to diminished immune function, reduced regenerative capacity, and heightened neuroinflammation. Severe acute pain during HZ also strongly correlates with PHN onset, highlighting the importance of early and effective pain control.[19] Pathophysiologically, PHN is sustained by persistent inflammation, structural nerve injury (including demyelination and axonal loss), and central sensitization that amplifies pain signaling within the central nervous system.[19,20]

Management of HZ focuses on limiting viral replication and alleviating acute pain. Antivirals such as acyclovir, valacyclovir, and famciclovir, when administered early, reduce viral replication and accelerate lesion healing.[21] Pain management strategies include NSAIDs, opioids, anticonvulsants, and

topical agents such as lidocaine patches.[22] Once established, PHN requires a multimodal approach involving tricyclic antidepressants, gabapentin or pregabalin, topical capsaicin or lidocaine, and, in refractory cases, interventional procedures such as nerve blocks or spinal cord stimulation.[23] Despite these options, PHN remains challenging to treat, emphasizing the importance of preventive strategies.

Vaccination has emerged as the most effective intervention for reducing both HZ and PHN. The live attenuated vaccine (Zostavax) demonstrated efficacy in lowering disease incidence in older adults, although its protective effect wanes within a few years.[5,10,25] In contrast, the recombinant subunit vaccine (Shingrix), which contains VZV glycoprotein E and the AS01B adjuvant system, has shown superior efficacy and durability across age groups, including individuals over 70 years.[24] Shingrix induces both humoral and cell-mediated responses without viral replication, making it safer for immunocompromised populations.[5,25]

Evidence from randomized clinical trials consistently demonstrates the efficacy of vaccines. The ZOE-50 trial and related studies showed that Shingrix significantly reduces both HZ incidence and PHN risk compared to placebo, with efficacy exceeding 90% in older adults.[24] In contrast, the protective effect of Zostavax declines markedly within the first year, raising questions about the need for boosters [10,25] Both vaccines are generally safe, with adverse events limited to transient injection-site reactions and mild systemic symptoms, although live vaccines carry higher risks for immunocompromised individuals.[5,24,25]

Beyond clinical trials, real-world effectiveness studies confirm that HZ vaccination programs substantially reduce the incidence of HZ and PHN, lower healthcare utilization, and improve quality of life for older adults.[26] Population-based data further show declines in PHN rates following widespread vaccine adoption, with the greatest benefit observed in older adults and individuals with immunocompromising conditions.[7,10,14,15] Modeling and cost-effectiveness analyses suggest that the broader use of recombinant subunit vaccines could prevent a substantial proportion of PHN cases and yield significant public health benefits.[8,10]

Taken together, these findings underscore that PHN arises from a complex interplay of immune decline, neuroinflammation, and neuronal injury, which makes it difficult to manage once established. Vaccination, particularly with Shingrix, represents the most effective strategy to prevent HZ and its chronic complications. Continued efforts to expand vaccination coverage, particularly among high-risk groups, are crucial for reducing the burden of PHN at both the individual and population levels.

Challenges and Future Directions

Despite proven efficacy, herpes zoster vaccines remain underutilized due to hesitancy, cost, and limited access. Addressing these barriers through physician engagement, public education, and expanded delivery models (e.g., pharmacies, mobile clinics) will be essential to improve uptake.[27,28] Key research priorities include defining long-term immunity, optimizing booster strategies, and refining cost-effectiveness models for high-risk groups. Sustained real-world surveillance of safety and effectiveness will be crucial to maintain confidence and maximize public health impact. [10,29,30]

Limitations

Only articles written in English and with available full texts were included. Studies featuring both adult and pediatric data were considered only if they provided individual-level data specifically for pediatric patients. No meta-analysis was performed.

Conclusion

The herpes zoster vaccine, particularly RZV, represents a significant advancement in the prevention of PHN. The evidence supports its widespread use, given its effectiveness, safety profile, and potential to reduce the public health burden of HZ. Continued research and public health efforts are essential to maximize the benefits of vaccination and improve the quality of life for older adults.

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Conflicts of Interest

The authors declare that they have no competing interests.

Generative AI Disclosure

OpenAI’s ChatGPT (GPT-4, July 2025) was used for language editing and text refinement. All AI-assisted text was reviewed for accuracy and originality, and the AI is not listed as an author.

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