

## PREVENTING SHINGLES: THE OVERLOOKED BURDEN OF HERPES ZOSTER AND ITS IMPACT

Dr Goh Tze Chien Kelvin

**ABSTRACT**

**Herpes zoster is a viral infection that occurs as a result of reactivation of the dormant varicella zoster virus. Herpes zoster carries a high healthcare burden, especially in older adults aged 50 years and older and those who are immunocompromised due to underlying medical conditions or immunosuppressive therapy. Without vaccination, an approximate 27.0 percent, 4.5 percent, and 3.6 percent of adults aged 50 years and older in Singapore could develop herpes zoster, post-herpetic neuralgia (PHN), and other complications, respectively. Well known complications of herpes zoster are the painful, blistering rash and PHN; however, the lesser-known effect of herpes zoster is its association with cardiovascular implications, including stroke and myocardial infarction. Herpes zoster is a vaccine-preventable disease. Recombinant Varicella Zoster Vaccine is an effective vaccine.**

**Key words: Herpes Zoster, Shingles, Comorbidities, Complications**

SFP2025; 51(4): 18-24

**INTRODUCTION**

Herpes zoster (HZ), more widely known as shingles, is caused by the reactivation of the dormant varicella-zoster virus (VZV) in cranial nerve ganglia and dorsal root ganglia along the entire neuroaxis.<sup>1</sup> HZ mainly affects older adults aged 50 years and above, people with comorbidities, people with autoimmune diseases, and people with immunocompromised conditions (IC).<sup>2</sup> It is estimated that approximately 27.0 percent, 4.5 percent, and 3.6 percent of adults aged 50 years and older in Singapore could develop herpes zoster, post-herpetic neuralgia, and other complications, respectively, without vaccination.<sup>3</sup> The National Centre for Infectious Diseases (NCID) estimates that 30,000 people develop shingles annually in Singapore.<sup>4</sup> Despite the prevalence of HZ, vaccine uptake remains poor in Singapore likely due to the high cost. HZ not only causes a painful vesicular rash; its complications can be severe and debilitating. In 2024, *The Straits Times* correspondent Salma Khalik described her shingles experience: "For almost two weeks, I endured excruciating pain that no medicine could

alleviate."<sup>5</sup> The natural course of HZ after the acute infection may follow with chronic complications such as post-herpetic neuralgia (PHN) and herpes zoster ophthalmicus (HZO), and cardiovascular events including stroke and myocardial infarction (MI).<sup>1,6-9</sup> The risk of developing post-HZ chronic complications is high with approximately 10 percent of patients aged 50 years and older having experienced at least one non-PHN complication.<sup>10</sup>

**BURDEN OF DISEASE****Epidemiology**

The global incidence of HZ and PHN increases with age, showing an exponential rise from the age of 50 years. In Singapore, the incidence of HZ is expected to rise due to our rapidly ageing population. By 2030, 1 in 4 Singaporeans will be aged 65 years or older, up from 1 in 10 in 2010.<sup>11</sup> This increased susceptibility is greatly attributed to immunosenescence, the age-related decline in immunity.<sup>12</sup>

In Singapore, varicella (chickenpox) vaccine was introduced in 2020 under the National Children Immunisation Schedule (NAIS).<sup>11</sup> Studies have shown that the seroprevalence of varicella zoster among Singaporeans aged above 25 years old is high, at 88 percent between 1998 and 2010.<sup>12</sup> In parliament on 22 November 2023, MP Mr Muralli Pillai asked the Minister of Health for action regarding the fact that 90 percent of Singaporeans above 50 years of age are infected with the Varicella Zoster Virus and 1 in 3 would be expected to develop HZ in their lifetime.<sup>15</sup> Most of these would have been wild-type varicella strains rather than the OKA varicella strain from varicella vaccination.

**Complications and Impact**

HZ is sometimes regarded as a simple latent viral reactivation disease; however, most overlook its potential long-term implications. The most common complication is Post-Herpetic Neuralgia (PHN). The US CDC defines PHN as pain persisting for 90 days or more after the onset of the herpes zoster rash. This is a chronic neuropathic painful condition occurring in the same dermatomal distribution as the previous episode of herpes zoster. The pain is typically characterised by burning, stabbing, or electric shock-like pain, often accompanied by allodynia or hyperalgesia. This can occur in as many as 30 percent of older people with HZ.<sup>10</sup> PHN has been demonstrated to persist up to years even after the rash has resolved, which can result in a poor quality of life, impacting social, psychological, physical, and functional aspects.<sup>16</sup>

Another common and severe complication is HZO (Herpes Zoster Ophthalmicus). HZO results from the reactivation of latent varicella-zoster virus residing in the trigeminal ganglion. Upon reactivation, the virus travels

DR GOH TZE CHIEN KELVIN

Family Physician

United Primary Care Network, Singapore

along the ophthalmic branch, leading to development of a vesicular rash in the ophthalmic branch dermatome of the trigeminal nerve. HZO is associated with numerous complications, including keratitis, cornea scarring, uveitis, and glaucoma.<sup>12,17</sup> Not limited to PHN and HZO, less common complications of HZ include facial nerve palsy (Ramsey Hunt syndrome), VZV encephalitis, transverse myelitis, VZV retinitis, cerebral arteritis, and post-herpetic pruritus.<sup>1,17,18</sup>

Emerging evidence indicates a direct relationship between HZ and acute cardiovascular (CV) events such as MI and stroke.<sup>7</sup> Postulated mechanisms underlying this association include hypothesis of vasculitis, systemic inflammation, and autonomic dysfunction that are amplified by VZV reactivation.<sup>19-22</sup> VZV vasculitis may induce inflammation, thrombosis, and vascular remodelling, while autonomic dysfunction may worsen immunological status, sympathetic tone, and blood pressure. These combined effects can contribute to vasculopathy, potentially leading to stroke or MI.<sup>19-21</sup> The first week and month after an episode of HZ is when the relative risk of stroke and MI is highest, and this increased risk may persist for up to a year. The risk of stroke two weeks post-HZ is 1.80 times (1.42-2.29) and decreases to 1.27 times (1.15-1.40) at one year. The risk of MI/ACS within three months of HZ is 1.31 times (1.02-1.70) and decreases to 1.19 times (1.01-1.41) at one year (refer to **Figures I and II**).<sup>7,23-28</sup> Beyond CV complications, studies suggest that HZ may impact diabetes control,<sup>29</sup> accelerate chronic kidney disease (CKD) progression, and increase the risk of end stage renal disease.<sup>30</sup>

**LINK TO IMMUNE AGEING, COMORBIDITIES, AND IMMUNOCOMPROMISED CONDITIONS**

**Immune Ageing and Immunosenescence**

For young adults, VZV can maintain its latency as cell-mediated immunity (CMI) prevents the reactivation of VZV. However, a decline in CMI due to immunosenescence can lead to reactivation of latent VZV.<sup>2,31</sup> Due to this dependency on CMI, individuals with weakened immunity are more susceptible to developing HZ. Although HZ can also affect individuals at a younger age, this is less frequent and usually associated with less-severe disease.<sup>32</sup>

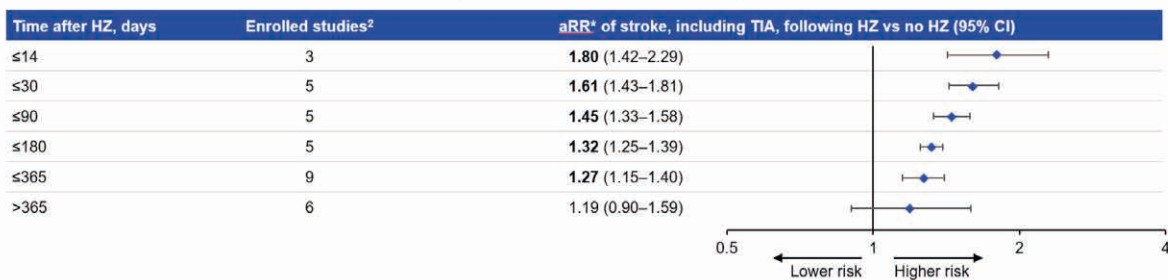
**Effect on Chronic Disease and Immunosuppressive Therapy**

In addition to immunosenescence among older adults, there is an increased risk of HZ among people with comorbid chronic conditions such as respiratory, cardiovascular, metabolic, and autoimmune disease among others.<sup>1,33-36</sup> Beyond the effects of acute infection with HZ, long-term effects include the exacerbation of their underlying chronic conditions, disrupting otherwise stable management of their comorbidities.<sup>29,30,37</sup>

Many patients with rheumatoid arthritis, systemic lupus erythematosus, and other autoimmune diseases are frequently on oral prednisolone, anti-TNF monoclonal antibodies, Interleukin 6 inhibitors, and Janus Kinase Inhibitors. These populations have a higher incidence of HZ as well as an increased risk of complications.<sup>38</sup> In these populations, VZV reactivation can cause visceral organ involvement, multi-dermatomal involvement, and disseminated zoster.<sup>38</sup> The risk factors for HZ are summarised in **Table I**.<sup>33,39,40</sup>

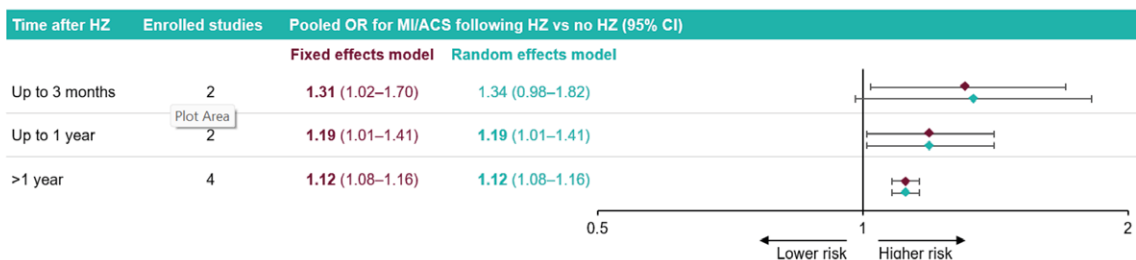
**Figure I: Risk of stroke by time since HZ; meta-analysis of data from 15 studies (1986-2020; n=1,276,021 HZ cases/N=11,119,984; all ages) (Figure adapted from Lu P et al, 2023)<sup>27</sup>**

Risk of stroke/TIA by time since HZ; meta-analysis of data from 15 studies (1986-2020; n=1,276,021 HZ cases/N=11,119,984; all ages)



**Figure II: Risk of MI or ACS by time since HZ; meta-analysis including 4 studies (1986-2010; UK, USA and Taiwan; n=188,447 HZ cases/N=731,303; all ages) Figure adapted from (27)**

Risk of MI or ACS by time since HZ; meta-analysis including four studies (1986-2010; n=188,447 HZ cases/N=731,303; all ages)



**Table I: Risk factors for HZ**

Risk Category	Factor
Non modifiable	Age (Older adults)
	Sex (female)
	Family history
Immunosuppression	HIV/AIDS
	Malignancies
	Allogenic/autologous stem cell transplant
Co-morbidities	Systemic lupus erythematosus
	Rheumatoid arthritis
	Psoriasis
	Psoriatic arthritis
	Multiple sclerosis
	Chronic obstructive pulmonary disease
	Cardiovascular conditions
	Inflammatory bowel disorder
	Chronic renal disease
	Asthma
	Diabetes
Immunosuppressive therapy or medications	Chemotherapy
	Radiotherapy
	Chronic use of corticosteroids
	Immunosuppressants (biologics, non-biologics, Janus Kinase inhibitors, biologic-immune modulators)

**ANTIVIRALS AND VACCINATION**

Antiviral drugs including acyclovir, valacyclovir, and famciclovir can be used to treat acute HZ (refer to **Table II**). For optimal treatment, these medications must be started within 72 hours of rash onset. Although antiviral treatments can effectively lower neuronal inflammation and reduce symptoms and PHN severity and duration, they remain limited in the prevention of complications like PHN.<sup>12,41</sup> Taking this limitation into consideration, proactive prevention should be taken instead of reactive management of HZ. HZ is a vaccine-preventable disease. In Singapore, the Society of Infectious Disease recommends the recombinant zoster vaccine (RZV), Shingrix, for adults aged 50 years and older and for those over 19 years old who are at increased risk due to immunodeficiency or immunosuppression.<sup>42</sup> In clinical studies (refer to **Figure III**), RZV demonstrated 97.2 percent overall vaccine efficacy and

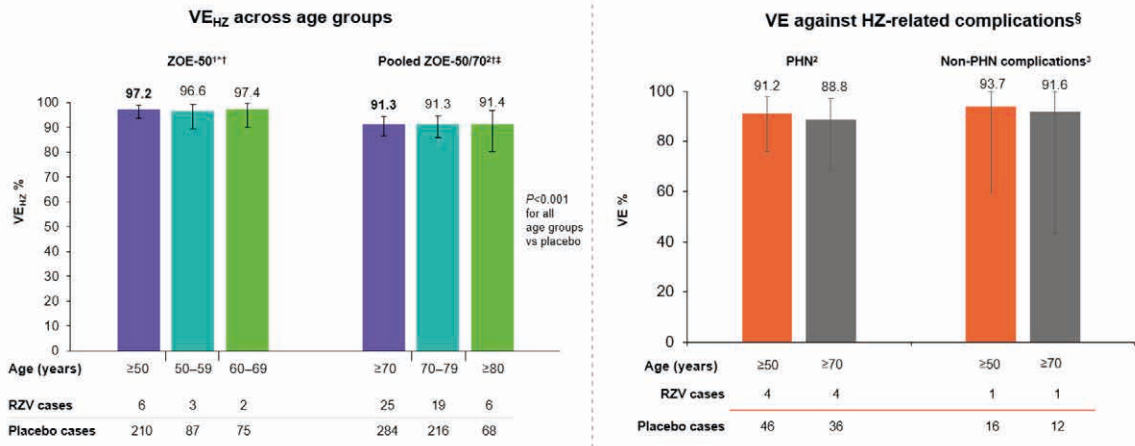
91.2 percent protection against PHN in immunocompetent adults aged 50 years old and above. Even in older adults above 70, the vaccine efficacy was 91.3 percent with 88.8 percent protection against PHN.<sup>43</sup> There is currently no recommendation for booster with evidence indicating that vaccine efficacy is sustained at 87.7 percent up to 11 years post-vaccination.<sup>44</sup> Common side effects include injection site pain, myalgia, fatigue, and injection site redness (refer to **Table III**).<sup>47</sup> Main serious adverse reactions were similar in RZV and placebo group. Recent studies have also shown that HZ vaccination is associated with lower risk of major adverse cardiovascular events, including stroke and coronary artery disease.<sup>45,46</sup>

Timely vaccination is crucial as postponing immunisation can lead to preventable morbidity and burden our already strained medical system.

**Table II: Antivirals for HZ**

Medication	Dosage	Route	Duration
<b>Acyclovir</b>	800 mg every 4 hours, 5 times daily	Oral	7-10 days
<b>Acyclovir</b>	10 mg/kg every 8 hours	Intravenous (IV)	7 days
<b>Valacyclovir</b>	1 gram 3 times daily	Oral	7 days
<b>Famciclovir</b>	500 mg every 8 hours	Oral	7 days

**Figure III: Efficacy of RZV against HZ (VE<sub>HZ</sub>) and HZ-related Complications**



**Table III: Vaccine Adverse Reactions compared to placebo**

Pooled analysis from ZOE-50 and ZOE-70

Adverse Reaction	RZV (%)	Placebo (%)
Pain	-68	-7
Redness	-28	-1.5
Swelling	-18	-1.0
Myalgia	-34	-6
Fatigue	-32	-9
Headache	-26	-8
Shivering	-16	-3
Fever	-13	-2.5
Gastro-intestinal symptoms	-11	-4

**NAIS AND OTHER RECOMMENDATIONS**

Perceived affordability may contribute to the resistance to HZ vaccine uptake. Increasing availability through public health initiatives and making funding alternatives clearer might improve this. From September 2025 (refer to **Figure IV**), all Singaporeans and Permanent Residents aged 60 years and above, and immunocompromised adults aged 18 to 59 years, can get subsidies of up to 75 percent

at CHAS GP clinics, polyclinics, and MOH-funded long-term care institutions (refer to **Figure III**). After subsidies, Singaporeans can expect to pay around \$75 to \$300 per course of RVZ vaccine (two doses) and permanent residences can expect to pay \$450 per course. From 2026, MediSave can be utilised to pay for RZV across the abovementioned settings.<sup>47</sup> This will remove out-of-pocket payments for some patients and reduce financial barriers to vaccination.

**Figure IV: Summary of RHZV recommendations to be included in the NAIS**

Summary of RHZV recommendations to be included in the NAIS  
(From September 2025)

**Annex A**

Vaccine	Recommendations	Additional information
<b>Recombinant herpes zoster vaccine (RHZV)</b>	RHZV is recommended for persons aged 18 years or older who are at increased risk of developing shingles and associated complications, as follows: <ul style="list-style-type: none"> <li>All persons aged 60 years or older;</li> <li>Persons aged 18 years or older with immunocompromising conditions</li> </ul>	<ul style="list-style-type: none"> <li>Two doses are recommended at an interval of 2-6 months.</li> <li>For persons with immunocompromising conditions, the interval can be shorter at 1-2 months if earlier protection is desired.</li> <li>For persons aged 60 years or older, all persons are recommended for RHZV regardless of medical condition.</li> <li>For persons aged 18-59 years, only those with immunocompromised conditions are recommended for RHZV.</li> <li>Detailed information on examples of immunocompromised conditions will be provided in another circular prior to the implementation date.</li> </ul>

Table IV summarises the recommendations for the recombinant herpes zoster vaccine under the National Adult Immunisation Schedule Singapore, The Handbook of Adult Vaccinations by Society of Infectious Disease Singapore, US Advisory Committee on Immunisation Practices, and Joint Committee on Vaccination and Immunisation UK.

**Table IV: Summary of Recommendations**

Issuing Body	Recommendations
Singapore National Adult Immunisation Schedule – 2025	<ul style="list-style-type: none"> <li>Adults aged 60 or older</li> <li>Aged 18 or older with immunocompromising conditions</li> </ul>
Handbook of Adult Vaccination 2023 (Society of Infectious Disease Singapore)	<ul style="list-style-type: none"> <li>Adults aged 50 years or older</li> <li>Adults 19 years of age or older at increased risk of herpes zoster due to immunodeficiency or immunosuppression caused by known disease or therapy</li> </ul>
US Advisory Committee on Immunisation Practices (ACIP), CDC 2023	<ul style="list-style-type: none"> <li>Adults aged 50 and above</li> <li>For immunocompromised adults aged 19 and above</li> </ul>
Joint Committee on Vaccination and Immunisation (JCVI) UK 2023	<ul style="list-style-type: none"> <li>National programme for adults aged 60 to 79 years</li> <li>Immunosuppressed adults aged 50 years or older</li> </ul>

**CONCLUSION**

Herpes zoster is a preventable disease. There is a growing body of evidence supporting the risk of stroke, MI, and other long-term complications. The RVZ vaccine is safe and effective. Patients above 60 years of age or above 18 with significant immunocompromising conditions should be inoculated.

**REFERENCES**

- Mueller NH, Gilden DH, Cohrs RJ, Mahalingam R, Nagel MA. Varicella zoster virus infection: clinical features, molecular pathogenesis of disease, and latency. *Neurol Clin.* 2008 Aug;26(3):675-97, viii. doi: 10.1016/j.ncl.2008.03.011. PMID: 18657721; PMCID: PMC2754837.
- Wareham DW, Breuer J. Herpes zoster. *BMJ.* 2007 Jun 9;334(7605):1211-5. doi: 10.1136/bmj.39206.571042.AE. PMID: 17556477; PMCID: PMC1889999.
- Oh H, Tan C, Williams C, Giannelos N, Ng C. Public health impact of herpes zoster vaccination on older adults in Singapore: a modeling study. *Hum Vaccin Immunother.* 2024 Dec 31;20(1):2348839. doi: 10.1080/21645515.2024.2348839. Epub 2024 May 28. PMID: 38804600; PMCID: PMC11135959.
- NCID. What is shingles and how is it prevented? [Available from: <https://www.ncid.sg/News-Events/News/Pages/What-is-shingles-and-how-is-it-prevented.aspx>.
- Khalik S. "I wanted to bang my head": How a delayed shingles diagnosis caused much suffering. 11 Dec 2024. [Available from: <https://www.straitstimes.com/singapore/i-wanted-to-bang-my-head-how-a-delayed-shingles-diagnosis-caused-much-suffering>].
- Parameswaran GI, Wattengel BA, Chua HC, et al. Increased Stroke Risk Following Herpes Zoster Infection and Protection With Zoster Vaccine. *Clin Infect Dis.* 2023 Feb 8;76(3):e1335-e1340. doi: 10.1093/cid/ciac549. PMID: 35796546.
- Curhan SG, Kawai K, Yawn B, Rexrode KM, Rimm EB, Curhan GC. Herpes Zoster and Long-Term Risk of Cardiovascular Disease. *J Am Heart Assoc.* 2022 Dec 6;11(23):e027451. doi: 10.1161/JAHA.122.027451. Epub 2022 Nov 16. PMID: 36382961; PMCID: PMC9851464.
- Forbes HJ, Bhaskaran K, Grint D, et al. Incidence of acute complications of herpes zoster among immunocompetent adults in England: a matched cohort study using routine health data. *Br*

- J Dermatol.* 2021 Jun;184(6):1077-1084. doi: 10.1111/bjd.19687. Epub 2021 Jan 4. PMID: 33216946; PMCID: PMC8607468.
- Patterson BJ, Rausch DA, Irwin DE, Liang M, Yan S, Yawn BP. Analysis of Vascular Event Risk After Herpes Zoster From 2007 to 2014 US Insurance Claims Data. *Mayo Clin Proc.* 2019 May;94(5):763-775. doi: 10.1016/j.mayocp.2018.12.025. Epub 2019 Apr 5. PMID: 30955916.
- Kawai K, Gebremeskel BG, Acosta CJ. Systematic review of incidence and complications of herpes zoster: towards a global perspective. *BMJ Open.* 2014 Jun 10;4(6):e004833. doi: 10.1136/bmjopen-2014-004833. PMID: 24916088; PMCID: PMC4067812.
- MOH. ACTION PLAN FOR SUCCESSFUL AGEING 2023. 13 Aug 2024. [Available from: <https://www.moh.gov.sg/others/resources-and-statistics/action-plan-for-successful-ageing>].
- Harpaz R, Ortega-Sanchez IR, Seward JF; Advisory Committee on Immunization Practices (ACIP) Centers for Disease Control and Prevention (CDC). Prevention of herpes zoster: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2008 Jun 6;57(RR-5):1-30; quiz CE2-4. PMID: 18528318.
- Lim DZJ, Tey HL, Salada BMA, et al. Herpes Zoster and Post-Herpetic Neuralgia-Diagnosis, Treatment, and Vaccination Strategies. *Pathogens.* 2024 Jul 17;13(7):596. doi: 10.3390/pathogens13070596. PMID: 39057822; PMCID: PMC11280284.
- Fatha N, Ang LW, Goh KT. Changing seroprevalence of varicella zoster virus infection in a tropical city state, Singapore. *Int J Infect Dis.* 2014 May;22:73-7. doi: 10.1016/j.ijid.2013.10.003. Epub 2013 Nov 21. PMID: 24269652.
- ORDER PAPER WEDNESDAY, 22 NOVEMBER 2023. [Available from: <https://www.parliament.gov.sg/docs/default-source/default-document-library/orderpa-per---22-nov-2023.pdf>].
- Pica F, Gatti A, Divizia M, et al. One-year follow-up of patients with long-lasting post-herpetic neuralgia. *BMC Infect Dis.* 2014 Nov 1;14:556. doi: 10.1186/s12879-014-0556-6. PMID: 25361823; PMCID: PMC4226872.
- Volpi A. Severe complications of herpes zoster. *Herpes.* 2007 Sep;14 Suppl 2:35-9. PMID: 17939894.
- Dworkin RH, Johnson RW, Breuer J, et al. Recommendations for the management of herpes zoster. *Clin Infect Dis.* 2007 Jan 1;44 Suppl 1:S1-26. doi: 10.1086/510206. PMID: 17143845.
- Wu PH, Chuang YS, Lin YT. Does Herpes Zoster Increase the Risk of Stroke and Myocardial Infarction? A Comprehensive Review. *J Clin Med.* 2019 Apr 22;8(4):547. doi: 10.3390/jcm8040547. PMID: 31013629; PMCID: PMC6518274.
- Yawn BP, Lindsay AC, Yousefi M, Wang C. Risk of, and risk factors for, vasculopathy associated with acute herpes zoster. *J*

- Stroke Cerebrovasc Dis. 2023 Feb;32(2):106891. doi: 10.1016/j.jstrokecerebrovasdis.2022.106891. Epub 2022 Dec 5. PMID: 36473399.
21. Nagel MA, Jones D, Wyborny A. Varicella zoster virus vasculopathy: The expanding clinical spectrum and pathogenesis. *J Neuroimmunol*. 2017 Jul 15;308:112-117. doi: 10.1016/j.jneuroim.2017.03.014. Epub 2017 Mar 18. PMID: 28335992; PMCID: PMC5489071.
  22. Yue J, Yao M. Humoral Cytokine Levels in Patients with Herpes Zoster: A Meta-Analysis. *J Pain Res*. 2024 Mar 5;17:887-902. doi: 10.2147/JPR.S449211. PMID: 38476878; PMCID: PMC10929134.
  23. Erskine N, Tran H, Levin L, et al. A systematic review and meta-analysis on herpes zoster and the risk of cardiac and cerebrovascular events. *PLoS One*. 2017 Jul 27;12(7):e0181565. doi: 10.1371/journal.pone.0181565. PMID: 28749981; PMCID: PMC5531458.
  24. Minassian C, Thomas SL, Smeeth L, Douglas I, Brauer R, Langan SM. Acute Cardiovascular Events after Herpes Zoster: A Self-Controlled Case Series Analysis in Vaccinated and Unvaccinated Older Residents of the United States. *PLoS Med*. 2015 Dec 15;12(12):e1001919. doi: 10.1371/journal.pmed.1001919. PMID: 26671338; PMCID: PMC4682931.
  25. Yang Q, George MG, Chang A, Tong X, Merritt R, Hong Y. Effect of herpes zoster vaccine and antiviral treatment on risk of ischemic stroke. *Neurology*. 2020 Aug 11;95(6):e708-e717. doi: 10.1212/WNL.00000000000010028. Epub 2020 Jul 7. PMID: 32636330; PMCID: PMC8931944.
  26. Lapi F, Marconi E, Concia E, et al. Time-varying association between herpes zoster infection and subsequent occurrence of stroke. *Public Health*. 2024 Apr;229:80-83. doi: 10.1016/j.puhe.2024.01.024. Epub 2024 Feb 26. PMID: 38412697.
  27. Lu P, Cui L, Zhang X. Stroke risk after varicella-zoster virus infection: a systematic review and meta-analysis. *J Neurovirol*. 2023 Aug;29(4):449-459. doi: 10.1007/s13365-023-01144-0. Epub 2023 May 23. PMID: 37219811.
  28. Forbes HJ, Williamson E, Benjamin L, et al. Association of herpesviruses and stroke: Systematic review and meta-analysis. *PLoS One*. 2018 Nov 21;13(11):e0206163. doi: 10.1371/journal.pone.0206163. PMID: 30462656; PMCID: PMC6248930.
  29. Muñoz-Quiles C, López-Lacort M, Ampudia-Blasco FJ, Díez-Domingo J. Risk and impact of herpes zoster on patients with diabetes: A population-based study, 2009-2014. *Hum Vaccin Immunother*. 2017 Nov 2;13(11):2606-2611. doi: 10.1080/21645515.2017.1368600. PMID: 28933622; PMCID: PMC5798425.
  30. Lin SY, Liu JH, Yeh HC, et al. Association between herpes zoster and end stage renal disease entrance in chronic kidney disease patients: a population-based cohort study. *Eur J Clin Microbiol Infect Dis*. 2014 Oct;33(10):1809-15. doi: 10.1007/s10096-014-2143-6. Epub 2014 May 17. PMID: 24838650.
  31. Arvin AM. Humoral and cellular immunity to varicella-zoster virus: an overview. *J Infect Dis*. 2008 Mar 1;197 Suppl 2:S58-60. doi: 10.1086/522123. PMID: 18419410.
  32. Johnson RW, Wasner G, Saddier P, Baron R. Herpes zoster and postherpetic neuralgia: optimizing management in the elderly patient. *Drugs Aging*. 2008;25(12):991-1006. doi: 10.2165/0002512-200825120-00002. PMID: 19021299.
  33. Marra F, Parhar K, Huang B, Vadlamudi N. Risk Factors for Herpes Zoster Infection: A Meta-Analysis. *Open Forum Infect Dis*. 2020 Jan 9;7(1):ofaa005. doi: 10.1093/ofid/ofaa005. PMID: 32010734; PMCID: PMC6984676.
  34. Joeseof RM, Harpaz R, Leung J, Bialek SR. Chronic medical conditions as risk factors for herpes zoster. *Mayo Clin Proc*. 2012 Oct;87(10):961-7. doi: 10.1016/j.mayocp.2012.05.021. PMID: 23036671; PMCID: PMC3538398.
  35. Poirrier JE, Meyers JL, Nagar SP, Patterson BJ, Glasser LI, Jabbour SA. Herpes Zoster Incidence and Burden in Adults With Type 2 Diabetes in the U.S.: A Retrospective Database Analysis. *Diabetes Care*. 2022 Nov 1;45(11):2585-2593. doi: 10.2337/dc21-2053. PMID: 36149780; PMCID: PMC9862293.
  36. Thompson-Leduc P, Ghaswalla P, Cheng WY, et al. Chronic obstructive pulmonary disease is associated with an increased risk of herpes zoster: A retrospective United States claims database analysis. *Clin Respir J*. 2022 Dec;16(12):826-834. doi: 10.1111/crj.13554. Epub 2022 Nov 22. PMID: 36415956; PMCID: PMC9716712.
  37. Giorda CB, Picariello R, Tartaglino B, et al. Hospitalisation for herpes zoster in people with and without diabetes: A 10-year-observational study. *Diabetes Res Clin Pract*. 2024 Apr;210:111603. doi: 10.1016/j.diabres.2024.111603. Epub 2024 Mar 8. PMID: 38460790.
  38. Chen SY, Suaya JA, Li Q, et al. Incidence of herpes zoster in patients with altered immune function. *Infection*. 2014 Apr;42(2):325-34. doi: 10.1007/s15010-013-0550-8. Epub 2013 Nov 10. PMID: 24214127; PMCID: PMC3968442.
  39. Marra F, Lo E, Kalashnikov V, Richardson K. Risk of Herpes Zoster in Individuals on Biologics, Disease-Modifying Antirheumatic Drugs, and/or Corticosteroids for Autoimmune Diseases: A Systematic Review and Meta-Analysis. *Open Forum Infect Dis*. 2016 Sep 28;3(4):ofw205. doi: 10.1093/ofid/ofw205. PMID: 27942537; PMCID: PMC5144657.
  40. Qian J, Heywood AE, Karki S, et al. Risk of Herpes Zoster Prior to and Following Cancer Diagnosis and Treatment: A Population-Based Prospective Cohort Study. *J Infect Dis*. 2019 Jun 5;220(1):3-11. doi: 10.1093/infdis/jiy625. PMID: 30544213.
  41. Bruxelle J, Pinchinat S. Effectiveness of antiviral treatment on acute phase of herpes zoster and development of post herpetic neuralgia: review of international publications. *Med Mal Infect*. 2012 Feb;42(2):53-8. doi: 10.1016/j.medmal.2011.11.001. Epub 2011 Dec 12. PMID: 22169279.
  42. Handbook on Adult Vaccination in Singapore 2023 Singapore: Society of Infectious Diseases Singapore; 2024.
  43. Lal H, Cunningham AL, Godeaux O, et al. Efficacy of an adjuvanted herpes zoster subunit vaccine in older adults. *N Engl J Med*. 2015 May 28;372(22):2087-96. doi: 10.1056/NEJMoa1501184. Epub 2015 Apr 28. PMID: 25916341.
  44. Strezova A, Díez Domingo J, Cunningham AL, et al. Final analysis of the ZOE-LTFU trial to 11 years post-vaccination: efficacy of the adjuvanted recombinant zoster vaccine against herpes zoster and related complications. *eClinicalMedicine*. 2025 May;83.
  45. Lee S, Lee K, Oh J, et al. Live zoster vaccination and cardiovascular outcomes: a nationwide, South Korean study. *Eur Heart J*. 2025 May 5;ehaf230. doi: 10.1093/eurheartj/ehaf230. Epub ahead of print. PMID: 40324473.
  46. Kornelius E, Lo SC, Huang CN, Wang CC, Wang YH, Yang YS. Association of herpes zoster vaccination and cardiovascular risk in patients with diabetes: long-term insights from a retrospective cohort study. *BMJ Open*. 2025 Feb 18;15(2):e090428. doi: 10.1136/bmjopen-2024-090428. PMID: 39965942; PMCID: PMC11836834.
  47. SUBSIDIES AND MEDISAVE COVERAGE FOR SHINGLES VACCINE [press release]. MOH2025.

**LEARNING POINTS**

- **Early Diagnosis of Herpes Zoster and early treatment with 72 hours of rash is key.**
  - **Herpes zoster can lead to serious complications like PHN, HZO, stroke, and MI.**
  - **Older adults above 50 years old are at risk of shingles and its complications.**
  - **Vaccination with recombinant zoster vaccine is safe and effective even for immunocompromised and elderly patients.**
-