

Herpes zoster

Massimo Galli
Clinica delle Malattie Infettive
UNIMI

Possible European Origin of Circulating Varicella Zoster Virus Strains

Chiara Pontremoli,^{1,✉} Diego Forni,¹ Mario Clerici,^{2,3} Rachele Cagliani,¹ and Manuela Sironi¹

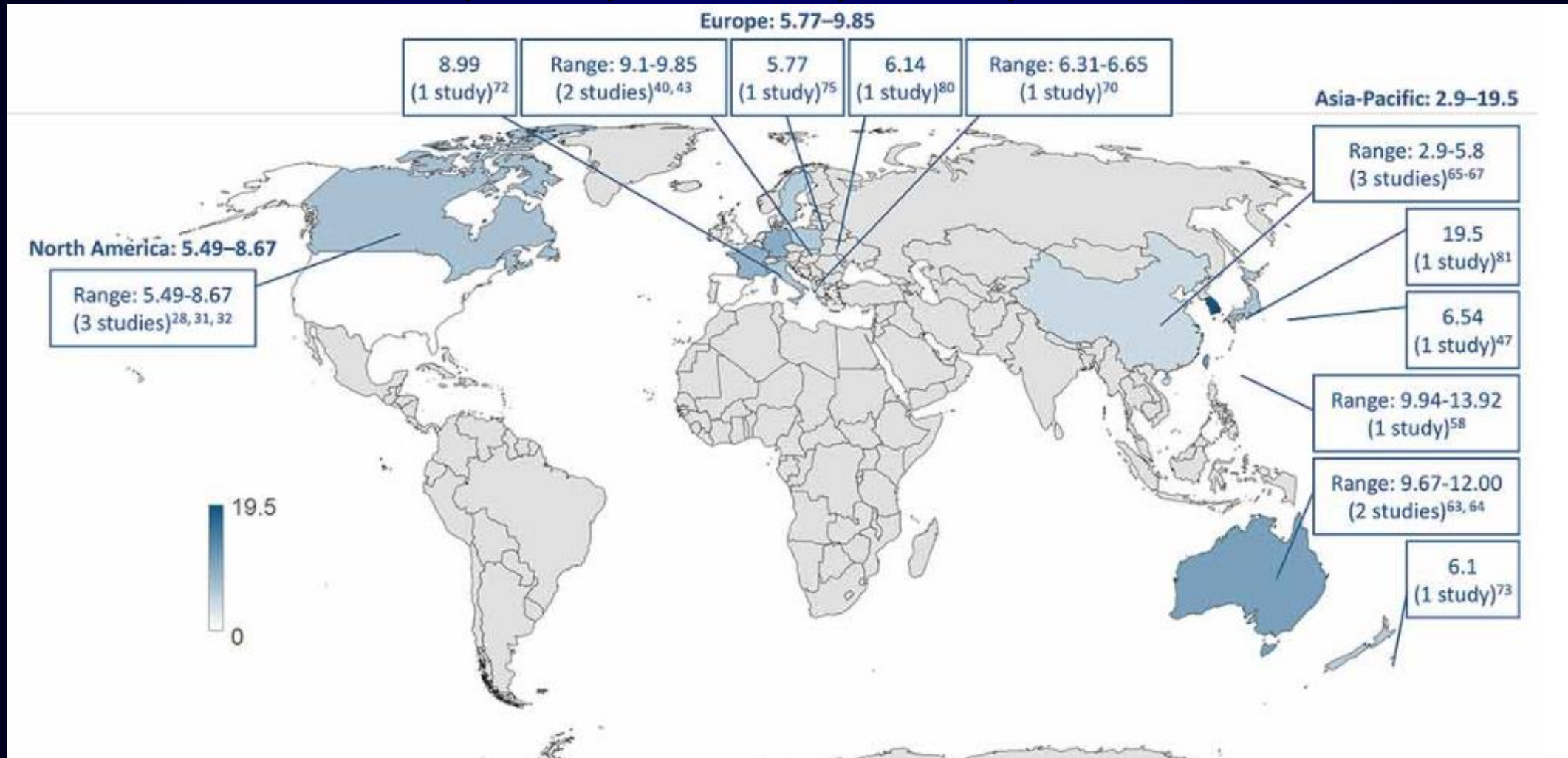
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(See the Editorial Commentary by Breuer, on pages 1213–5.)

Varicella zoster virus (VZV) is the causative agent of chickenpox and shingles. The geographic distribution of VZV clades was taken as evidence that VZV migrated out of Africa with human populations. We show that extant VZV strains most likely originated in Europe and not in Africa. Europe was also identified as the ancestral location for most internal nodes of the VZV phylogeny, including the ancestor of clade 5 strains. We also show that strains from clades 1, 2, 3, and 5 derived a major proportion of their ancestry from each of 4 ancestral populations. Conversely, viruses from other clades displayed variable levels of admixture. Some low-level admixture was also observed for clade 5 genomes, but only for non-African viruses. This pattern indicates that the clade 5 VZV strains do not represent recent introductions from Africa due to migratory fluxes. These data have also relevance for the definition and classification of VZV clades.

Keywords. varicella zoster virus; phylogeography; origin; admixture

Herpes zoster cumulative incidence in the overall population > 50 years per 1000 person years



The cumulative incidence (3.22–11.2 vs 2.44–8.0 cases per 1,000 population) and incidence rates (6.05–12.8 vs 4.30–8.5 cases per 1,000 person-years) were higher in females than males.

Herpes Zoster Vaccines

Ruth Harbecke,^{1,2} Jeffrey I. Cohen,³ and Michael N. Oxman^{1,2,4}

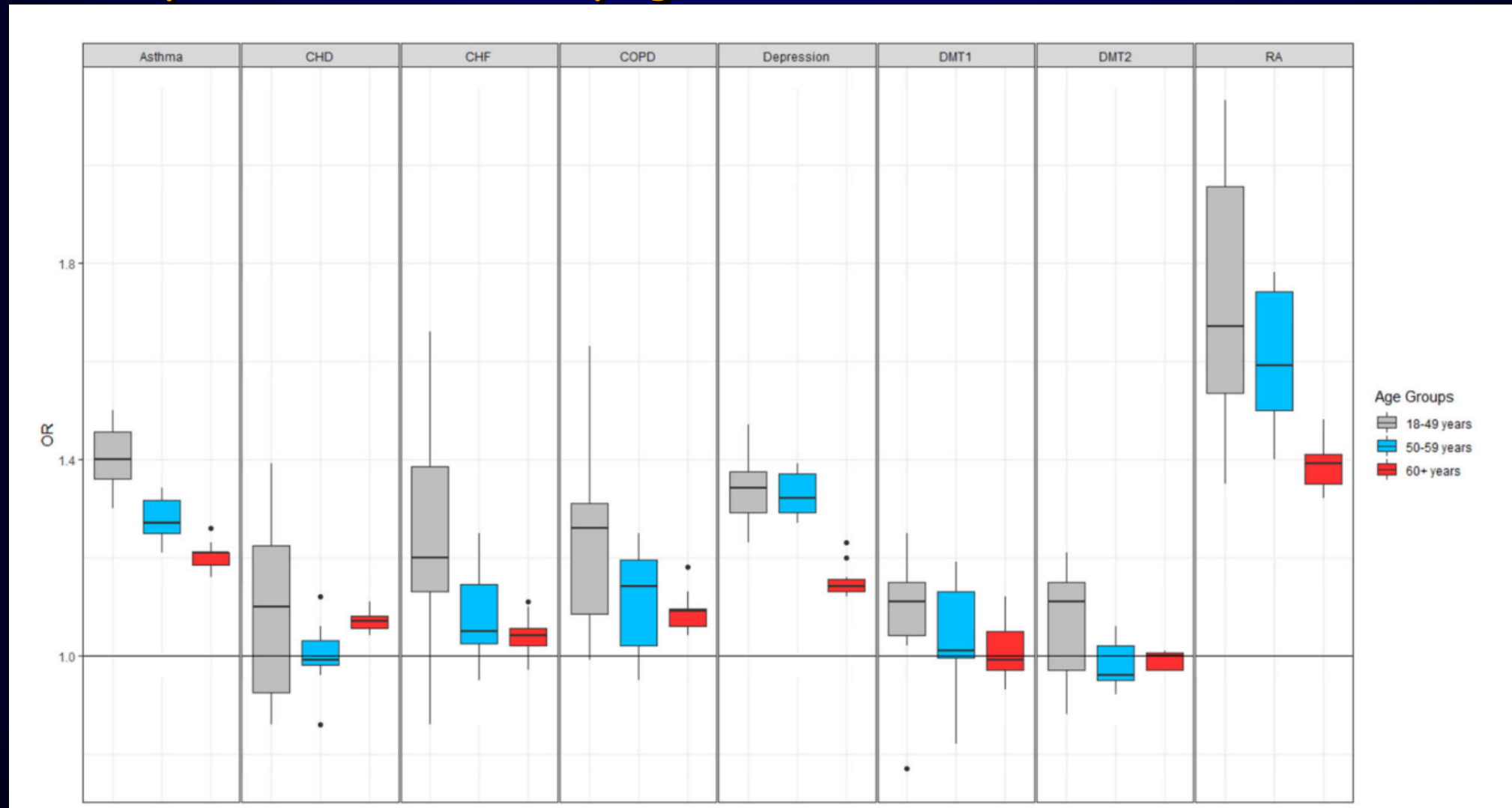
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Herpes zoster (HZ) affects approximately 1 in 3 persons in their lifetime, and the risk of HZ increases with increasing age. The most common, debilitating complication of HZ is the chronic neuropathic pain of postherpetic neuralgia (PHN). Two herpes zoster vaccines, a live-attenuated varicella-zoster virus (VZV) vaccine (zoster vaccine live [ZVL]; ZOSTAVAX [Merck]) and an adjuvanted VZV glycoprotein E (gE) subunit vaccine (recombinant zoster vaccine [RZV]; SHINGRIX [GlaxoSmithKline]) are licensed for the prevention of HZ and PHN in healthy older adults. The safety and efficacy of both vaccines has been demonstrated in clinical trials in immunocompetent adults and in selected immunocompromised persons and persons with immune-mediated diseases. Numerous real-world effectiveness studies have confirmed the safety and effectiveness of both ZVL and RZV. Recombinant zoster vaccine (RZV) is more effective for prevention of HZ than ZVL. Recombinant zoster vaccine is nonreplicating and is thus safe in immunocompromised persons. Additional zoster vaccines are in different stages of development. Wider distribution of safe and effective zoster vaccines will improve the health and well being of the rapidly growing population of older adults around the world.

Keywords. herpes zoster; zoster vaccine; live attenuated Oka varicella-zoster vaccine; recombinant zoster vaccine.

Boxplot of adjusted ORs of herpes zoster in patients with underlying conditions from 2008 to 2018.





ORIGINAL RESEARCH

Systematic Literature Review on the Incidence of Herpes Zoster in Populations at Increased Risk of Disease in the EU/EEA, Switzerland, and the UK

Alen Marijam · Nikki Vroom · Amit Bhavsar · Inga Posiuniene · Nicolas Lecrenier · Hilde Vroling

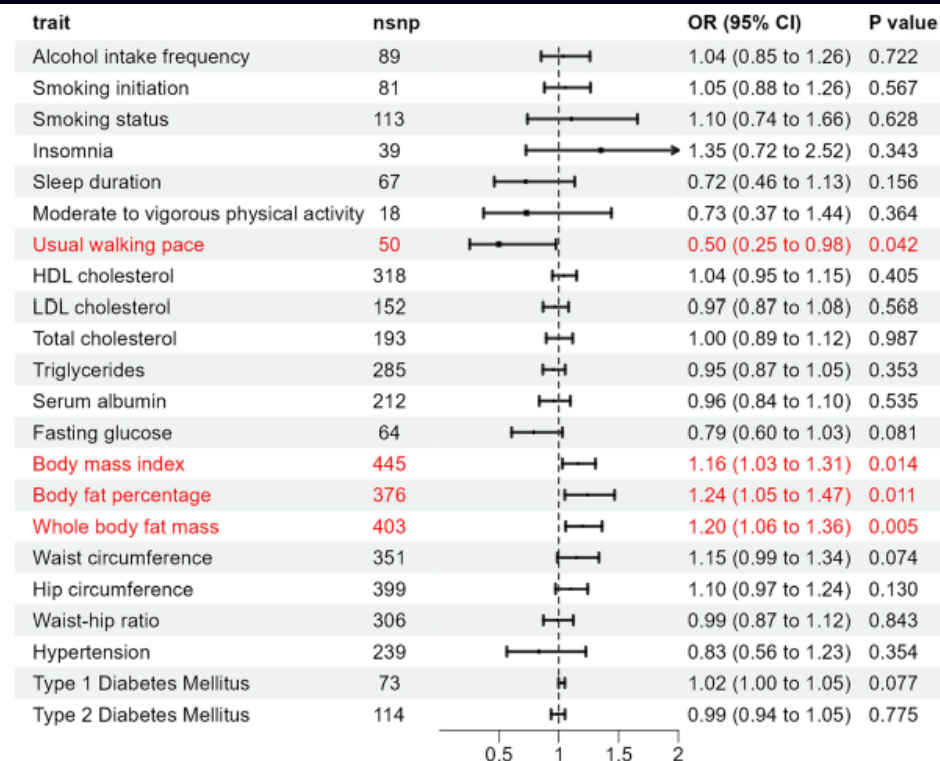
In many high-risk populations, HZ incidence was higher for older age groups, women, and some treatments.

The HZ incidence rate in Europe increased with age and varied across high-risk populations, with high rates for solid organ and stem cell transplants, cancer, and rheumatoid arthritis.

Medical condition	Incidence rates per 1000 py
Stem cell transplantation:	37.2-56.1
Solid organ transplantation:	12.1-78.8
HIV/AIDS:	11.8-13.0
IC mixed population:	11.3-15.5
Lupus:	11.0-16.5
Solid organ malignancy:	8.8 -11.0
Depression:	7.2-7.6
IBD:	7.0-10.8
MS:	5.7-6.3
Psoriasis:	5.3-6.1
Chronic respiratory diseases:	4.7-11.4
DM:	4.3-9.4
Hematologic malignancy:	2.9-32.0
Rheumatic disorders:	0.41-21.5

Causal effect of lifestyle and metabolic indicator with herpes zoster: a two-sample Mendelian randomization study

Mingsheng Huang^{1†}, Yiheng Liu^{2†}, Cheng Chen³ and Weiran Dai^{2*}



In the inverse-variance weighted (IVW) analysis, body mass index (**BMI**) (OR: 1.160, 95% CI: 1.030–1.307, $p = 0.014$), Body fat percentage (BFP) (OR: 1.241, 95% CI: 1.050–1.467, $p = 0.011$), and whole body fat mass (WBFM) (OR: 1.199, 95% CI: 1.057–1.362, $p = 0.005$) exhibited positive associations with the risk of HZ. However, **usual walking pace** (UWP) (OR: 0.498, 95% CI: 0.254–0.976, $p = 0.042$) demonstrated a significant negative correlation with HZ risk. Other factors including alcohol intake frequency, smoking initiation, smoking status, insomnia, and sleep duration did not show significant causal relationships with HZ.

REVIEW

A comprehensive, updated systematic review and meta-analysis of epidemiologic evidence on the connection between herpes zoster infection and the risk of stroke

Mohammad Heiat¹ | Mahmood Salesi² | Mohammad Hossein Peypar³  |
Ali Ramazani³ | Mahdi Abdorrashidi³ | Amin Vesal Yeganeh³

The meta-analysis consisted of 5,505,885 participants and found a statistically significant association between HZ infection and the risk of stroke (pooled RR = 1.22, 95% confidence interval [CI] 1.12-1.34). The HZO infection showed a significantly higher overall pooled RR of 1.71 (95% CI 1.06-2.75), indicating a strong connection with the risk of stroke.

Time since infection emerged as a crucial factor, with heightened stroke risk in the initial year post-HZ/HZO exposure, followed by a decline after the first year.

The effect of herpes zoster vaccination on the occurrence of deaths due to dementia in England and Wales

F. Michalik, M. Xie, M. Eytting, S. He, S. Chung, P. Geldsetzer.

medRxiv preprint doi: <https://doi.org/10.1101/2023.09.08.23295225>

- Country-wide data from death certificates in England and Wales from September 1 2004 to August 31 2022 by ICD-10 code and month of birth.
- The study population included 5,077,426 adults born between September 1 1925 and August 31 1941 who were alive at the start of the HZ vaccination program.
- Our findings indicate that HZ vaccination improved cognitive function at a fairly advanced stage of the dementia disease
- This analysis adds to the evidence base that HZ vaccination slows, or potentially even prevents, the natural history of dementia.



REVIEW

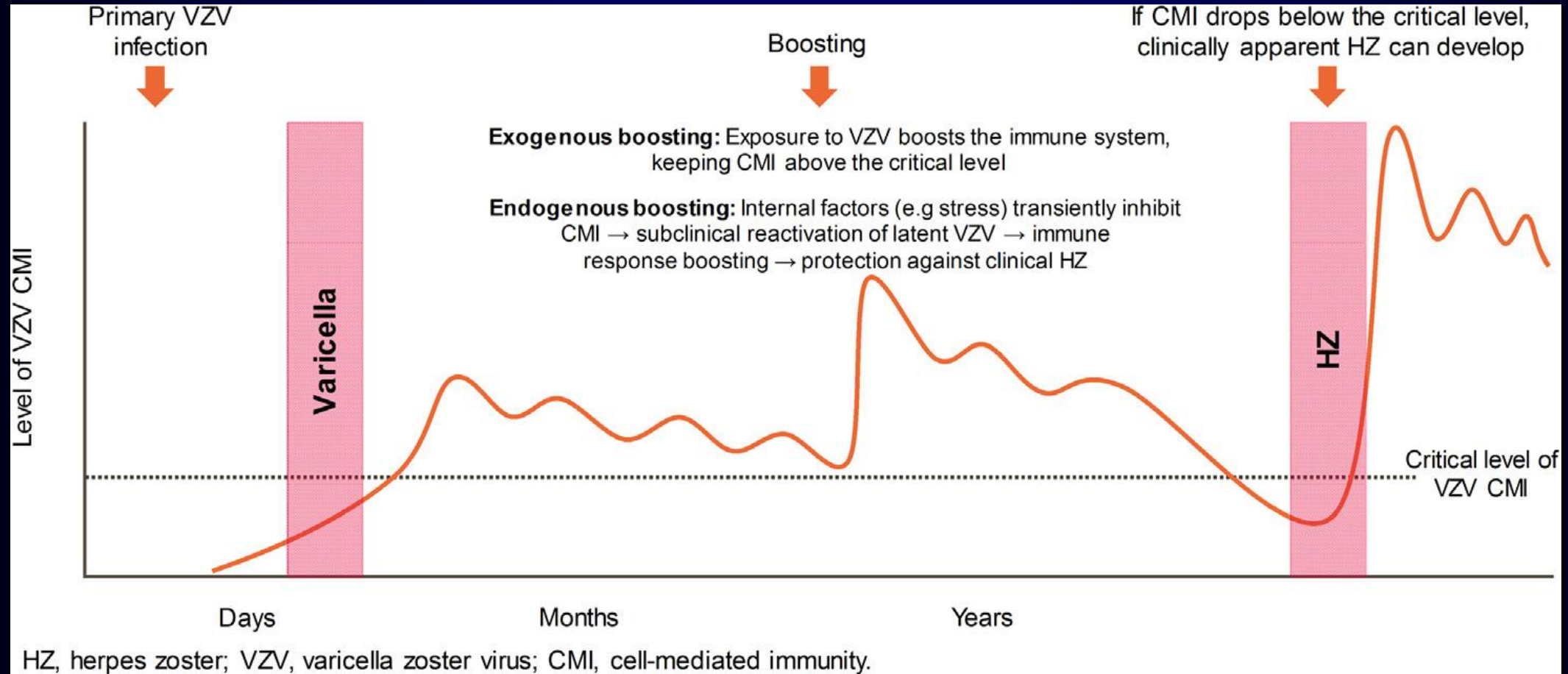
Herpes Zoster Recurrence: A Narrative Review of the Literature

Raunak Parikh · O'Mareen Spence · Nikolaos Giannelos ·

Iain Kaan

- Studies in general populations of immunocompetent or mixed populations with an initial HZ episode estimate that approximately 1.2–9.6% of individuals may experience HZ recurrence, with an incidence rate of 1.7–16.6 cases per 1000 person-years.
- HZ recurrence was reported in 0.0–18.2% of immunocompromised individuals with HZ, with an incidence rate of 17.0–55 cases per 1000 person-years.

VZV cell-mediated immunity levels over time

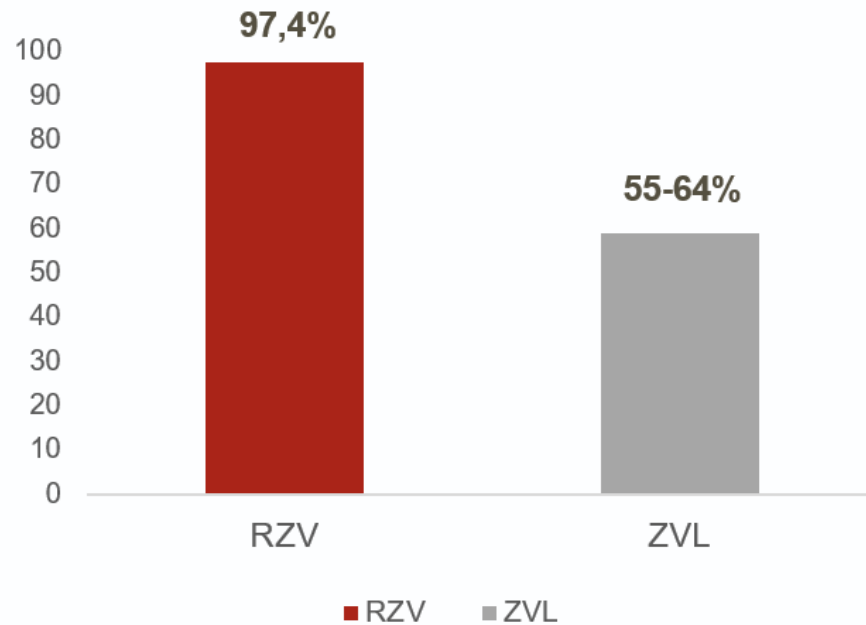


Da Oxman et al. 2009

Shingles vaccines

Efficacia nel breve periodo (0-3 anni)

Età 60-69 anni

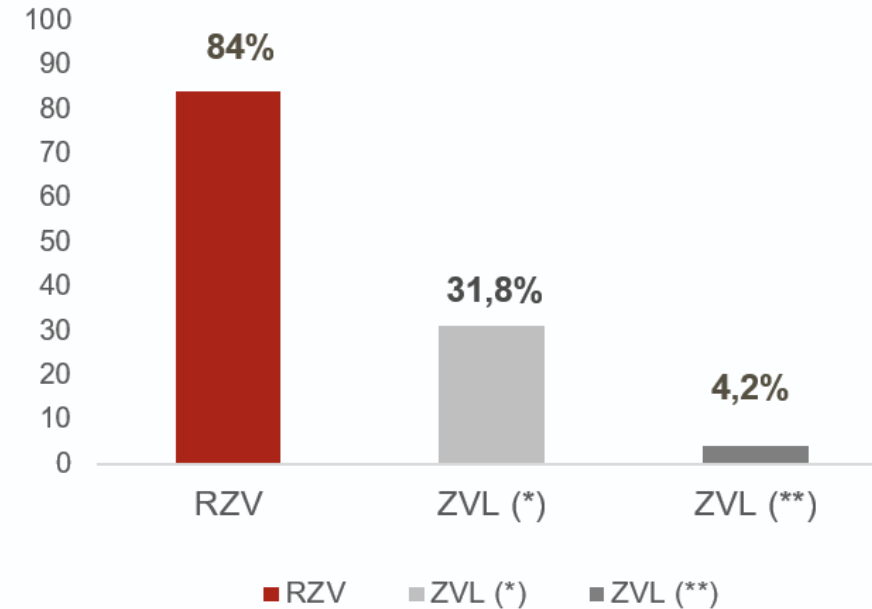


1) Shingrix. Riassunto Caratteristiche del prodotto (2020.2)

2) Zostavax. Riassunto caratteristiche del prodotto (2016)

Efficacia nel lungo periodo (7 anni)

Tutte le età in studio



SHINGRIX: Hastie A, et al. The Adjuvanted Recombinant Zoster Vaccine (RZV) Confers Long-term Protection Against Herpes Zoster. Presented at: IDWeek 2020 (virtual event). October 21-25, 2020. <https://idweek.org>. ZVL (*) Am J Epidemiol. 2018;187(1):161-169. ZVL (**) JID 2016;213 (15 June) brief report

Effectiveness of the Recombinant Zoster Vaccine in Adults Aged 50 and Older in the United States: A Claims-Based Cohort Study

Yuwei Sun,¹ Eric Kim,¹ Christina L. Kong,¹ Benjamin F. Arnold,^{1,2} Travis C. Porco,^{1,2,3} and Nisha R. Acharya^{1,2,3,4}

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- A total of 4 769 819 adults were included in this study, with 173 745 (3.6%) adults receiving 2 valid doses of the recombinant zoster vaccine.
- The incidence rate of herpes zoster was 258.8 (95% CI, 230.0–289.4) cases per 100 000 p-y in vaccinated persons compared with 893.1 (95% CI, 886.2–900.0) in unvaccinated persons.
- Recombinant zoster vaccine effectiveness was **85.5%** (95% CI, 83.5–87.3%) overall, with an effectiveness of 86.8% (95% CI, 84.6–88.7%) in individuals 50 to 79 years old compared with 80.3% (95% CI, 75.1–84.3%) in individuals aged 80 and older.
- **In patients with a history of live zoster vaccine within 5 years of study inclusion, vaccine effectiveness was 84.8% (95% CI, 75.3–90.7%).**

Recombinant Zoster Vaccine (Shingrix): Real-World Effectiveness in the First 2 Years Post-Licensure

Hector S. Izurieta,¹ Xiyuan Wu,² Richard Forshee,¹ Yun Lu,¹ Heng-Ming Sung,² Paula Ehrlich Agger,¹ Yoganand Chillarige,² Ruth Link-Gelles,³ Bradley Lufkin,² Michael Wernecke,² Thomas E. MaCurdy,^{2,4} Jeffrey Kelman,⁵ and Kathleen Dooling³

¹Center for Biologics Evaluation and Research, US Food and Drug Administration, Silver Spring, Maryland, USA; ²Acumen LLC, Burlingame, California, USA; ³Division of Viral Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia, USA; ⁴Department of Economics, Stanford University, Stanford, California, USA; and ⁵Centers for Medicare & Medicaid Services, Washington, DC, USA

- In community dwelling beneficiaries ages >65 years, we found a vaccine effectiveness of 70.1% (95% CI, 68.6–71.5) and 56.9% (95% CI, 55.0–58.8) for two and one doses, respectively.
- The two-dose vaccine effectiveness was not significantly lower for beneficiaries 80+ years, for second doses received at ≥ 180 days, or for individuals with autoimmune conditions.
- The vaccine was also effective among individuals with immunosuppressive conditions.
- Two-dose vaccine effectiveness against postherpetic neuralgia was 76.0% (95% CI, 68.4–81.8).

RESEARCH ARTICLE

 OPEN ACCESS  Check for updates

Efficacy, reactogenicity, and safety of the adjuvanted recombinant zoster vaccine for the prevention of herpes zoster in Chinese adults ≥ 50 years: A randomized, placebo-controlled trial

Diana Alexandra Echeverria Proano^{a*}, Fengcai Zhu^{b*}, Xiaodong Sun^{c*}, Jesús Zoco^a, Jyoti Soni^a, Neeraj Parmar^d, S. Omar Ali ^e, and on behalf of Zoster-076 Study Group

Of the 6138 enrolled participants, 99.2% completed the study. During a mean follow-up period of 15.2 (± 1.1) months, 31 HZ episodes were confirmed (RZV = 0; placebo = 31) for an incidence rate of 0.0 vs 8.2 per 1000 person-years and an overall VE of 100% (89.82–100). The descriptive VE was 100% (85.29–100) for 50–69-year-olds and 100% (60.90–100) for ≥ 70 -year-olds. Solicited adverse events (AEs) were more frequent in the RZV vs the placebo group (median duration: 1–3 days for both groups). Pain and fatigue were the most frequent local and general AEs (RZV: 72.1% and 43.4%; placebo: 9.2% and 5.3%).



Systematic Review

Immunogenicity of Recombinant Zoster Vaccine: A Systematic Review, Meta-Analysis, and Meta-Regression

Lorenzo Losa ^{1,†}, Ippazio Cosimo Antonazzo ^{1,2,†}, Giuseppe Di Martino ^{3,4}, Giampiero Mazzaglia ¹, Silvio Tafuri ⁵, Lorenzo Giovanni Mantovani ^{1,2,‡} and Pietro Ferrara ^{1,2,*,‡}

In a meta-analysis using a random-effects model, and subgroup and meta-regression analyses which included 37 included articles, the pooled response rate for anti-gE humoral immunity after one month from RZV-dose 2 was 95.2% (95%CI 91.9–97.2), dropping to 77.6% (95%CI 64.7–86.8) during immunosuppression. The anti-gE cell-mediated immunity-specific response reached 84.6% (95%CI 75.2–90.9).

ZOE-LTFU: Summary

- ZOE-LTFU is a long-term follow-up study of RZV pivotal phase 3 clinical trials in adults ≥ 50 years (ZOE-50/70)
- RZV VE against HZ in participants aged ≥ 50 years*
 - During ~6-year period of ZOE-LTFU was 79.77% (95% CI, 73.72–84.61)
 - RZV VE against HZ from 1-month post-dose 2 in ZOE-50/70 was 87.73% (95% CI, 84.89–90.12)
 - RZV VE against HZ at Year 11 was 82.0% (95% CI, 63.0–92.2)
- RZV VE against HZ in participants ≥ 70 years* remained high ($\geq 70\%$)^ but trended to be lower than seen in 50-69 years*
- No new concerns regarding RZV long-term safety were identified during ~6-years period of ZOE-LTFU



Differential Utility Losses in Herpes Zoster Cases Between Vaccinated and Unvaccinated Subjects: A Meta-analysis of Three Clinical Trials

Nikolaos Giannelos¹ · Bernard Francq² · Desmond Curran¹

A sensitivity analysis estimated an overall difference of 0.005 (95% confidence interval 0.001–0.009) QALYs, corresponding to 48.6% of the QALY loss value in the placebo group.

Recombinant zoster vaccine is effective in alleviating disease severity in breakthrough cases of herpes zoster.

The results may be useful in distinguishing QALY losses between vaccinated and unvaccinated cohorts in health economics studies, particularly cost-effectiveness analyses



RESEARCH PAPER



Immunogenicity and safety of an adjuvanted herpes zoster subunit candidate vaccine in adults ≥ 50 years of age with a prior history of herpes zoster: A phase III, non-randomized, open-label clinical trial

Olivier Godeaux^{a,#}, Martina Kovac^a, Daniel Shu^b, Katrijn Grunning^a, Laura Campora^a, Martine Douha^a, Thomas C. Heineman^{c,†}, and Himlal Lal^{c,‡}

^aGSK Vaccines, Wavre, Belgium; ^bGain Medical Centre, Coquitlam, BC, Canada; ^cGSK Vaccines, King of Prussia, PA, USA

ABSTRACT

This phase III, non-randomized, open-label, multi-center study (NCT01827839) evaluated the immunogenicity and safety of an adjuvanted recombinant subunit herpes zoster (HZ) vaccine (HZ/su) in adults aged ≥ 50 y with prior physician-documented history of HZ. Participants (stratified by age: 50–59, 60–69 and ≥ 70 y) received 2 doses of HZ/su 2 months apart and were followed-up for another 12 months. Anti-glycoprotein E (gE) antibodies were measured by enzyme-linked immunosorbent assay before vaccination and 1 month after the second dose (Month 3). Solicited local and general adverse events (AEs) were recorded for 7 d and unsolicited AEs for 30 d after each vaccination. Serious AEs were recorded until study end. The primary immunogenicity objective was met if the lower limit of the 95% confidence interval (CI) of the vaccine response rate (VRR), defined as a 4-fold increase in anti-gE over baseline, at Month 3 was $\geq 60\%$. 96 participants (32/age group) were enrolled. The primary immunogenicity objective was met, as the VRR at Month 3 was 90.2% (95% CI: 81.7–95.7). Geometric mean anti-gE antibody concentrations at Month 3 were similar across age groups. 77.9% and 71.6% of participants reported local and general solicited AEs, respectively. The most frequent solicited AEs were pain at injection site, fatigue, headache, myalgia and shivering. The HZ/su vaccine was immunogenic in adults aged ≥ 50 y with a physician-documented history of HZ, and no safety concerns were identified.

ARTICLE HISTORY

Received 8 September 2016
Revised 10 November 2016
Accepted 23 November 2016

KEYWORDS

herpes zoster;
immunogenicity; safety;
varicella-zoster virus; zoster
vaccine

JAMA Ophthalmology | Original Investigation JAMA Ophthalmol. 2024;142(3):249-256.

Risk of Herpes Zoster Ophthalmicus Recurrence After Recombinant Zoster Vaccination

Anushka Walia, BS; Yuwei Sun, MS; Nisha R. Acharya, MD

A total of 16408 patients were included in the matched analysis, of whom 12762 were unvaccinated (7806 [61.2%] female; mean [SD] age at diagnosis, 68.8 [10.3] years) and 3646 were vaccinated (2268 [62.2%] female; mean [SD] age at diagnosis, 67.4 [9.8] years).

Within the primary risk period of 56 days after the index date (ie, the start of follow-up for the outcome), the incidence of HZO recurrence after any RZV exposure was 37.7 per 1000 person-years compared with 26.2 per 1000 person-years in the unexposed group.

After controlling for race and ethnicity, inpatient stays, emergency department visits, concomitant vaccines, and eye care practitioner visits, the association between vaccination status and HZO exacerbation in the primary risk period had an adjusted hazard ratio for any RZV exposure of 1.64 (95% CI, 1.01-2.67; $P = .04$).

Original Investigation | Infectious Diseases

Safety of Simultaneous Vaccination With Adjuvanted Zoster Vaccine and Adjuvanted Influenza Vaccine

A Randomized Clinical Trial

- Quadrivalent adjuvanted inactivated influenza vaccine (aIIV4) and adjuvanted recombinant zoster vaccine (RZV) contain novel adjuvants.
- The proportion of patients reporting 1 or more severe reactions after simultaneous administration of RZV and aIIV4 (15 of 115 [11.5%]) was noninferior compared with simultaneous RZV and HD-IIV4 (17 of 119 [12.5%]) (absolute difference, -1.0% [95% CI, -8.9% to 7.1%]).
- There were no significant differences in the number of serious adverse events or adverse events of clinical interest between the groups.
- From a safety standpoint, this study supports the simultaneous administration of RZV and aIIV4 among older adults.

Wikivaccini

Informarsi bene non fa male

A chi è offerta gratuitamente la vaccinazione?

La vaccinazione è offerta gratuitamente a:

- **soggetti di età > 18 anni** affetti da diabete complicato, BPCO e asma severo, cardiopatie, soggetti immunodepressi o candidati a terapie immunosoppressive, soggetti con recidive o forme particolarmente gravi di Herpes Zoster
- **soggetti di età > 50 anni** affetti da diabete, BPCO, cardiopatie, soggetti destinati a terapia immunosoppressiva
- **soggetti di 65 anni di età** (nel 2024 l'offerta è estesa a partire dai nati nel 1952 fino ai nati nel 1959)



Matthias Grünewald (ca. 1480 - 1528): The Temptation of Saint Anthony. Panels of the Isenheim Altarpiece, Unterlinden Museum, Colmar.

The figure at the bottom left (enlarged in detail) of this painting, made between 1512 and 1516, shows typical lesions of secondary disseminated syphilis

Grazie per l'attenzione