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Real-world effectiveness of recombinant zoster vaccine in self-identified Chinese individuals aged ≥50 years in the United States

Ana Florea D^a, Lina Sy D^a, Lei Qian D^a, Bradley Ackerson D^a, Yi Luo D^a, Jun Wu D^a, Yanjun Cheng D^a, Jennifer Ku D^a, Leticia Vega Daily D^a, Harpreet Takhar D^a, Jeannie Song D^a, Elizabeth Chmielewski-Yee D^b, O'Mareen Spence D^b, Harry Seifert D^c, Driss Oraichi D^d, and Hung Fu Tseng D^{a,e}

^aDepartment of Research and Evaluation, Kaiser Permanente Southern California, Pasadena, CA, USA; ^bDepartment of Epidemiology and Patient-Centered Outcomes, GSK, Rockville, MD, USA; ^cDepartment of Clinical Safety and Pharmacovigilance, GSK, Rockville, MD, USA; ^dDepartment of Real World Analytics, GSK, Rockville, MD, USA; ^eDepartment of Health Systems Science, Kaiser Permanente Bernard J. Tyson School of Medicine, Pasadena, CA, USA

ABSTRACT

We evaluated the vaccine effectiveness (VE) of two doses of recombinant zoster vaccine (RZV) against herpes zoster (HZ) and postherpetic neuralgia (PHN) in Chinese adults at Kaiser Permanente Southern California (KPSC). Chinese KPSC members were identified based on self-reported ethnicity or self-reported preferred spoken/written language. Those aged \geq 50 years who received two doses of RZV 4 weeks to \leq 6 months apart were matched 1:4 to RZV unvaccinated Chinese members and followed through June 2022; second doses were accrued 6/1/2018-12/31/2020. We estimated incidence and adjusted hazard ratios (aHRs) with 95% confidence intervals (CIs) comparing outcomes (HZ and PHN). Adjusted VE (%) was calculated as $(1-aHR)\times100.3978$ RZV vaccinated Chinese members were matched to 15,912 RZV unvaccinated Chinese members. The incidence per 1000 person-years (95% CI) of HZ in the vaccinated group was 1.5 (0.9–2.5) and 10.9 (9.8–12.1) in the unvaccinated group; aHR (95% CI) was 0.12 (0.07–0.21). Adjusted VE (95% CI) was 87.6% (78.9–92.7) against HZ. We identified 0 PHN cases in the vaccinated group and 19 in the unvaccinated group. Among Chinese adults aged \geq 50 years, two doses of RZV provided substantial protection against HZ and PHN supporting the real-world effectiveness of the vaccine in this population.

Introduction

Herpes zoster (HZ), or shingles, is an often-painful vesicular rash caused by the reactivation of varicella zoster virus (VZV) persisting latently in dorsal root or other sensory ganglia.^{1,2} The pain from acute HZ can be disabling, and if complicated by the development of postherpetic neuralgia (PHN), can last for months or years. The risk for HZ, and complications such as PHN, increases with age and immunosuppression.^{3,4}

In 2017, the Advisory Committee on Immunization Practices (ACIP) recommended the recombinant zoster vaccine (RZV), a two-dose subunit zoster vaccine, to be the preferred vaccine against HZ in immunocompetent adults aged \geq 50 years⁵; current ACIP guidelines also recommend RZV for immunocompromised adults aged \geq 19 years.⁶ In two large randomized clinical trials conducted among adults aged \geq 50 years and \geq 70 years, the vaccine efficacy of RZV against HZ was 97.2% and 91.3% (pooled data), respectively.^{7,8} Among adults aged \geq 50 years or \geq 65 years, real-world overall vaccine effectiveness (VE) of RZV against HZ has been reported to range from 70.1% to 85.5%, depending on the population studied.⁹⁻¹¹

China is a country with an increasingly aging population^{12,13} and a need for HZ prevention and attenuation measures. A previous study found the incidence of HZ to

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range from 2.9 to 5.8 per 1,000 person-years in Chinese adults aged \geq 50 years with at least 2.8 million cases occurring annually across China.^{14,15} As such, in 2019, the National Medical Products Administration approved RZV in China for adults aged \geq 50 years.¹⁶ Historically, clinical trials, at any phase, have lacked racial/ethnic diversity, Asian ethnicity included, in their study populations.¹⁷ However, the RZV clinical trials included Asian countries, and a post-hoc analysis of vaccine efficacy was conducted in Asian adults, which demonstrated similar efficacy as the overall study.¹⁸ Recently, a post-licensure trial in China found a vaccine efficacy against HZ of 100% in adults aged \geq 50 years. Although there are data on vaccine efficacy in Chinese adults, there are no real-world effectiveness data in Chinese adults. Therefore, this realworld evidence study will provide further information on self-identified Chinese individuals in the United States (U.S.). Kaiser Permanente Southern California (KPSC)'s diverse member population and its comprehensive health care system presented the opportunity to study a Chinese population as 11% of the members self-identified as Asian/ Pacific Islander and members can be easily followed longitudinally for health care utilization and outcomes of interest. In addition, since April 2018, RZV has been the preferred HZ vaccine for routine use and the standard of care for the prevention of HZ in adults aged \geq 50 years at KPSC.

CONTACT Ana Florea 🖾 aflorea89@gmail.com 🖃 Kaiser Permanente Southern California, 100 S Los Robles, Pasadena, CA 91101, USA.

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Therefore, we conducted a matched cohort study in adults aged \geq 50 years to evaluate the VE of RZV against HZ and PHN in older Chinese adults at KPSC.

Materials and methods

Setting

KPSC is one of the U.S.' largest not-for-profit health plans. The health plan's population includes >4.6 million members who represent 260 different ethnicities and speak more than 150 different languages. The demographic makeup of the KPSC membership closely mirrors the Southern California population.^{19,20} Compared to the racial/ethnic distribution of the U.S. population, KPSC membership is comprised of twice as many individuals of Asian/Pacific Islander descent, which encompasses members of Chinese ethnicity.

KPSC's comprehensive electronic health record (EHR) system tracks the virtual, outpatient, emergency department (ED), and hospital settings, as well as pharmacy and vaccination utilization, thus capturing data regarding demographics, services, and diagnoses. As KPSC is a pre-paid health care system, recommended vaccines such as RZV are provided to KPSC members at no charge. Vaccinations are captured in the EHR with vaccine name, dose, manufacturer, CVX code, and lot number entered at the time of vaccination. Vaccinations received outside of the health plan with appropriate documentation are also recorded in KPSC databases. Receipt of RZV was identified using CVX code 187.

Although RZV should be administered as 2 doses separated by 2–6 months, ACIP guidance followed at KPSC specifies that a second dose administered <4 weeks after the first dose should be repeated, but a second dose administered ≥4 weeks after the first dose does not need to be repeated.⁵ Furthermore, due to variation in real-world practice, the second dose may be given earlier than 2 months after the first dose. Therefore, our study refers to 2 doses of RZV given 4 weeks to 6 months apart.

This study was approved by the KPSC Institutional Review Board with waivers of informed consent.

Study design

As part of a larger, long-term effectiveness study of RZV in KPSC members,²¹ we conducted a separate observational cohort study among self-identified Chinese KPSC members (hereafter, Chinese individuals). Chinese individuals were identified based on self-reported ethnicity or self-reported preferred spoken / written language. These members were aged \geq 50 years at the index date and received two doses of RZV 4 weeks to ≤ 6 months (28–183 days, inclusive) with second dose accrual from 06/01/2018 to 12/31/2020. Individuals also had at least 1 year of continuous KPSC membership before the index date (allowing for a 31-day gap in membership). Individuals were excluded if they received an RZV dose less than 4 weeks after the first dose, had an HZ diagnosis in the 6 months prior to the index date, or if HZ occurred within 30 days of the index date. The index date was defined as the date of the second dose.

RZV vaccinated Chinese individuals were 1:4 matched to RZV unvaccinated Chinese individuals by age (50–59 years, 60–69 years, 70–79 years, and 80+ years) and sex. RZV unvaccinated Chinese individuals were assigned the same index date as their vaccinated match. Chinese individuals were followed until the end of the study period (6/30/2022), occurrence of a censoring event (receipt of an initial dose of RZV or zoster vaccine live [ZVL] among the unvaccinated group or a subsequent dose of RZV or ZVL among the vaccinated group, death, termination of KPSC membership [allowing for a 31-day gap in membership]), or occurrence of the outcome of interest, whichever came first.

The first outcome of interest was HZ, defined by International Classification of Diseases (ICD)-10 codes (B02. xx) from virtual, outpatient, ED, and hospital settings with a non-topical antiviral prescription (acyclovir, valacyclovir, famciclovir) within 7 days before or after the date of HZ diagnosis. In addition, to ensure that HZ cases were incident, we required that they did not have a non-topical (i.e., oral or parenteral) antiviral medication prescribed in the 183 days to 8 days prior to the date of HZ diagnosis.²²⁻²⁴ The second outcome of interest was PHN, defined as HZ-related pain persisting >3 months after HZ diagnosis.²⁵ HZ-related pain was defined as pain consistent with the HZ episode which was not explained by other obvious causes (e.g., rheumatoid arthritis). PHN was identified by chart review, among incident HZ events with at least 1 encounter (outpatient, ED, inpatient, and virtual settings) during the >3 to 6-month period (90-180 days) after HZ diagnosis.

Baseline patient characteristics assessed at the index date included age and sex. Covariates defined in the year prior to index date included number of virtual, outpatient, ED, and hospital encounters, and comorbidities (kidney disease, heart disease, lung disease, liver disease, and diabetes). Comorbidity status was assessed annually after index date covariate. during follow-up as а time-varying Immunocompromised status (HIV/AIDS, leukemia/lymphoma, congenital/other immunodeficiencies, asplenia/ hyposplenia, hematopoietic stem cell transplant/solid organ transplant, and receipt of immunosuppressive medications) was also included as a time-varying covariate. Other covariates included history of ZVL vaccination and HZ, continuous membership length (allowing for a 31-day gap) prior to index date, and concomitant vaccinations at the time of either the first or second RZV dose.

Statistical analysis

We described and compared the characteristics of individuals in the RZV vaccinated and RZV unvaccinated cohorts. Categorical variables were compared using χ^2 test (or Fisher's exact test, as appropriate), and continuous variables were compared using two-sample t-test (or Wilcoxon rank-sum test, as appropriate). Absolute standardized differences (ASD) were calculated to assess the balance of the distribution of covariates between the two groups. Incidence rates (IR) per 1,000 person-years of HZ and PHN for the RZV vaccinated cohort and the matched unvaccinated cohort were calculated by dividing the number of cases by the total number of personyears. The cumulative incidences of HZ and PHN were estimated by the Kaplan – Meier method. Differences between the vaccinated and unvaccinated cumulative incidence estimates were tested via the log-rank test.

Adjusted hazard ratios (aHRs) and 95% confidence intervals (CIs) comparing HZ or PHN incidence rates in the 2-dose RZV cohort and the matched unvaccinated cohort were estimated by Cox stratified proportional hazards regression models adjusting for potential confounders. Potential confounders were determined based on the ASD values (>0.1) from the bivariate analyses and scientific relevance; these included heart disease (time-varying), immunocompromised status (timevarying), number of outpatient and virtual visits, history of ZVL vaccination, and length of continuous membership. Estimates of VE (%) were calculated as (1-aHR) x 100. Since HZ cases within the first 30 days after the index date were excluded, a post-hoc sensitivity analysis excluding the 30 days after index date from follow-up was also performed; IR, HR, and VE of 2 doses of RZV in preventing HZ and PHN were assessed. Analyses were performed using SAS (version 9.4; SAS Institute, Cary, NC, USA).

Results

The study cohort consisted of 3,978 RZV vaccinated Chinese individuals and 15,912 matched unvaccinated Chinese individuals (Figure 1). Overall, 82% of individuals were aged ≥ 60 years (median, 67) and the majority were female (59.6%) (Table 1). The vaccinated and unvaccinated groups had similar characteristics (ASD ≤ 0.1) of ED visits, hospitalizations, kidney disease, lung disease, liver disease, diabetes, immunocompromised status, and history of HZ. Compared to the unvaccinated, a greater proportion of vaccinated individuals had more outpatient and virtual visits, heart disease, and ZVL vaccinations (ASD > 0.1). A greater proportion of vaccinated individuals also had longer continuous membership (at least 6 years) when compared to the unvaccinated (ASD > 0.1). Within the vaccinated group, 12.9% experienced a censoring event, while within the unvaccinated group, 45.0% experienced a censoring event. Vaccinated individuals were also followedup for a longer time versus unvaccinated individuals (mean 2.54 years [sd, 0.80] and mean 1.98 years [sd, 1.03], respectively) (ASD > 0.1).

There were 15 cases of HZ among the vaccinated group and 344 cases of HZ among the unvaccinated group, with IRs per 1,000 person-years of 1.5 (95% CI: 0.9-2.5) and 10.9 (95% CI: 9.8-12.1), respectively (Table 2); aHR (95% CI) was 0.12 (0.07–0.21). The cumulative incidence of HZ was significantly higher in the unvaccinated individuals than in the vaccinated individuals (log-rank test p < .001) (Figure 2(a)). Adjusted VE was 87.6% (95% CI: 78.9-92.7%) against HZ. There were 0 PHN cases in the vaccinated group and 19 in the unvaccinated group; IR per 1,000 person-years for the unvaccinated group was 0.6 (95% CI: 0.4-0.9). The cumulative incidence of PHN was significantly higher in the unvaccinated individuals than in the vaccinated individuals (log-rank test p = .0114) (Figure 2(b)). VE against PHN could not be estimated due to no PHN cases in the vaccinated group. The sensitivity analysis yielded similar results.

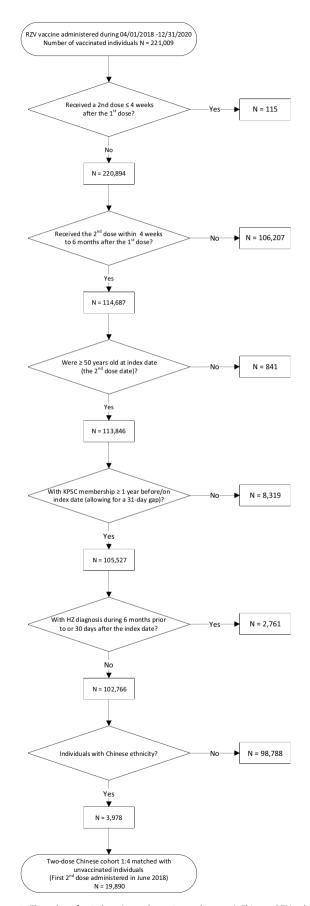


Figure 1. Flow chart for 2-dose (4 weeks to 6 months apart) Chinese RZV cohort.

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Table 1. Characteristics of 2-dose (4 weeks to 6 months apart) RZV vaccinated and unvaccinated cohort.

	Vaccinated N = 3,978	Unvaccinated N = 15,912	Total N = 19,890	Absolute	
Characteristic	. <u> </u>	N (%)		Absolute Standardized Difference	
Age at index date ^a , years, median (IQR)	68 (61, 73)	67 (61, 73)	67 (61, 73)	0.015	
Age at index date, years				N/A ^d	
50–59	719 (18.1)	2,876 (18.1)	3,595 (18.1)		
60–69	1,649 (41.5)	6,596 (41.5)	8,245 (41.5)		
70–79	1,208 (30.4)	4,832 (30.4)	6,040 (30.4)		
≥80	402 (10.1)	1,608 (10.1)	2,010 (10.1)		
Sex	402 (10.1)	1,008 (10.1)	2,010 (10.1)	N/A ^d	
		0 400 (50 6)	11.000 (50.0)	N/A	
Female	2,372 (59.6)	9,488 (59.6)	11,860 (59.6)		
Male	1,606 (40.4)	6,424 (40.4)	8,030 (40.4)		
Number of outpatient/virtual visits ^b				0.553	
0	2 (0.1)	1,663 (10.5)	1,665 (8.4)		
1–4	921 (23.2)	4,998 (31.4)	5,919 (29.8)		
5–10	1,269 (31.9)	4,035 (25.4)	5,304 (26.7)		
≥11	1,786 (44.9)	5,216 (32.8)	7,002 (35.2)		
Number of emergency department visits ^b	,,	-, - (,		0.063	
0	3,569 (89.7)	14,184 (89.1)	17,753 (89.3)		
1	325 (8.2)	1,236 (7.8)	1,561 (7.8)		
≥2					
	84 (2.1)	492 (3.1)	576 (2.9)	0.040	
Number of hospitalizations ^b	a			0.048	
0	3,410 (85.7)	13,689 (86.0)	17,099 (86.0)		
1	365 (9.2)	1,294 (8.1)	1,659 (8.3)		
≥2	203 (5.1)	929 (5.8)	1,132 (5.7)		
Baseline comorbidities ^b					
Kidney disease	337 (8.5)	1,258 (7.9)	1,595 (8.0)	0.021	
Heart disease	2,740 (68.9)	9,003 (56.6)	11,743 (59.0)	0.256	
Lung disease	378 (9.5)	1,264 (7.9)	1,642 (8.3)	0.055	
Liver disease	367 (9.2)	1,102 (6.9)	1,469 (7.4)	0.084	
Diabetes	878 (22.1)	3,386 (21.3)	4,264 (21.4)	0.019	
	070 (22.1)	3,380 (21.3)	4,204 (21.4)		
Immunocompromised status at index date	454 (2.0)	(02 (12)		0.024	
Yes	154 (3.9)	692 (4.3)	846 (4.3)		
No	3,824 (96.1)	15,220 (95.7)	19,044 (95.7)		
History of ZVL vaccination ^c				0.371	
No	2,273 (57.1)	11,106 (69.8)	13,379 (67.3)		
Yes, ≤5 years	333 (8.4)	1,865 (11.7)	2,198 (11.1)		
Yes, >5 years	1,372 (34.5)	2,941 (18.5)	4,313 (21.7)		
Concomitant vaccination ^e		, (, , , ,		N/A	
Yes	1,222 (30.7)	N/A	N/A		
No	2,756 (69.3)	15,912 (100.0)	18,668 (93.9)		
History of HZ ^c	2,750 (05.5)	13,512 (100.0)	10,000 (55.5)	0.065	
	2 407 (07 0)	14 227 (80 5)	17 724 (00 2)	0.005	
No	3,497 (87.9)	14,237 (89.5)	17,734 (89.2)		
Yes, ≤ 2 years	104 (2.6)	279 (1.8)	383 (1.9)		
Yes, >2 years	377 (9.5)	1,396 (8.8)	1,773 (8.9)		
Length of continuous membership ^c , years				0.159	
0–5	1,162 (29.2)	5,813 (36.5)	6,975 (35.1)		
6–10	693 (17.4)	2,652 (16.7)	3,345 (16.8)		
≥11	2,123 (53.4)	7,447 (46.8)	9,570 (48.1)		
Time between first and second doses, days, median (IQR)	73 (63, 103)	N/A	N/A	N/A	
Loss to follow-up	, 5 (05, 105)	1 1/ / 1	1 1/7 1	0.975	
Disenrollment	170 (10 0)	1 002 (12 5)	2 121 (12 2)	0.975	
	429 (10.8)	1,992 (12.5)	2,421 (12.2)		
Death	70 (1.8)	529 (3.3)	599 (3.0)		
Receipt of a dose of RZV or ZVL	12 (0.3)	4,640 (29.2)	4,652 (23.4)		
Average follow-up time, years, mean (sd)	2.54 (0.80)	1.98 (1.03)	2.09 (1.01)	0.602	

^aDefined as the date of the second dose of RZV.

^bDefined in the one year prior to index date.

^cDefined based on all available medical records prior to index date.

 $^{d}N/A =$ not applicable, for matching variable.

^eAmong subjects with concomitant vaccines: influenza vaccine (65%), PCV13/PPSV23 (20%), Tdap (19%), and other (7%); 66% concomitant with 1st dose only, 28% concomitant with 2nd dose only, and 6% concomitant with both 1st and 2nd dose.

^fASD > 0.1 is considered as imbalanced.

HZ, herpes zoster; IQR, interquartile range; N, sample size; N/A, not applicable; RZV, recombinant zoster vaccine; sd, standard deviation; ZVL, zoster vaccine live.

Table 2. Incidence rate, hazard ratio, and vaccine effectiveness of 2 doses (4 v	weeks to 6 months apart) of RZV in	preventing HZ and PHN.

	Vaccinated N = 3,978		Unvaccinated $N = 15,912$		Hazard Ratio (95% CI)		VE % (95% CI)	
Outcomes	Number of cases	Incidence per 1000 person-years (95% CI)	Number of cases	Incidence per 1000 person-years (95% CI)	Unadjusted	Adjusted ^a	Unadjusted	Adjusted ^a
HZ PHN	15 0	1.5 (0.9–2.5) N/A	344 19	10.9 (9.8–12.1) 0.6 (0.4–0.9)	0.14 (0.08–0.23) N/A	0.12 (0.07–0.21) N/A	86.3 (77.0–91.9) N/A	87.6 (78.9–92.7) N/A

^aAdjusted for covariates: heart disease (time-varying), immunocompromised status (time-varying), number of outpatient/virtual visits, history of ZVL vaccination, and length of continuous membership.

CI, confidence interval; HZ, herpes zoster; N, sample size; N/A, not applicable; PHN, postherpetic neuralgia; RZV, recombinant zoster vaccine; VE, vaccine effectiveness.

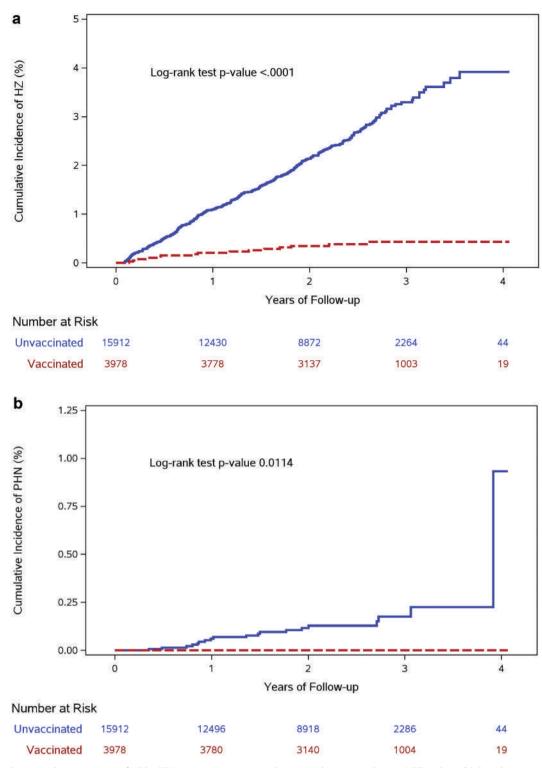


Figure 2. (a) Cumulative incidence estimates of HZ by RZV vaccination status in 2-dose (4 weeks to 6 months apart) RZV cohort. (b) Cumulative incidence estimates of PHN by RZV vaccination status in 2-dose (4 weeks to 6 months apart) RZV cohort.

Discussion

Our study sought to assess the VE of RZV in an important population subgroup. Our real-world study is the first observational study specifically looking at RZV effectiveness in Chinese individuals. Overall, we found that 2-dose RZV vaccination, with the second administered within 4 weeks to 6 months after the first dose, was effective in preventing HZ in Chinese adults aged \geq 50 years (VE 87.6% [95% CI: 78.9– 92.7%]). VE against PHN could not be assessed as there were no observed cases in the vaccinated group. However, the cumulative incidence of PHN was significantly higher in unvaccinated individuals compared to vaccinated individuals.

The general population has a lifetime risk of developing HZ of approximately 30%; this risk increases rapidly in adults

older than 50 years of age.²⁶ Two clinical trials showed high efficacy of RZV against HZ,^{7,8} with post-hoc analyses demonstrating similar efficacy in the subgroup of Asian subjects¹⁸ and across geographic regions and ethnic groups.²⁷ The vaccine was licensed for use in the U.S. and China in the general population aged \geq 50 years. Since then, one phase IV trial was conducted in China to evaluate the efficacy of RZV against HZ in adults aged ≥50 years (NCT04869982). However, few studies have been published on the VE of RZV under real-world conditions. One study was conducted among individuals aged \geq 50 years from a claims database and found an overall adjusted VE against HZ of 85.5% (95% CI: 83.5-87.3%),⁹ similar to the adjusted VE observed in our study. They also observed that VE between different race/ethnicity groups was similar with a VE in the Asian subcategory of 75.3% [95% CI: 60.2-84.7%].9 Though their observed VE in this group was lower than the VE in our study, among their >4 million person study cohort, only 3% were Asian and the median age of the vaccinated group was 72 years.⁹ In contrast, the vaccinated cohort in our study was slightly younger with a median age of 68 years. Another study conducted among individuals aged ≥50 years from Kaiser Permanente Hawaii found an overall adjusted VE of 83.5% (74.9-89.2%) with an adjusted VE in the Asian subcategory of 88.1% (95% CI: 77.5-93.7%),¹⁰ similar to our study results. Furthermore, another study conducted among Medicare recipients aged \geq 65 years found a VE against HZ of 70.1% (95% CI: 68.6-71.5%)¹¹; their vaccinated cohort was also primarily White (90.8%) with an "Other" category comprising 7.3%. Additionally, the lower VE observed in the Medicare study compared to the previous two studies discussed above may be explained by the inclusion of an older population and immunocompromised individuals. However, our current study in Chinese individuals, despite the inclusion of immunocompromised adults, demonstrated a higher VE than the Medicare study. This may be due to a possibly younger or healthier study population. As a whole, our results are in line with other overall VE results. Moreover, one recent study investigated the public health impact RZV would have on a cohort comprised of individuals aged \geq 50 years in Beijing, China.²⁸ Their analysis showed RZV vaccination reducing HZ, HZ-related complications, and healthcare resource utilization when compared to the status quo of no vaccination. Our study results provide further support for vaccinating the Chinese population with RZV.

Though our study could not estimate VE against PHN, we did observe 0 PHN cases among the 3,978 vaccinated individuals and 19 PHN cases among the 15,912 unvaccinated individuals. The previously mentioned study utilizing Medicare claims and enrollment data found a 2-dose VE against PHN of 76.0% (95% CI: 68.4–81.8%).¹¹ The study identified PHN cases through a validated automated algorithm in contrast to our study, which conducted chart reviews to identify chart-confirmed PHN cases. Harpaz previously derived from the Medicare claims-based study that the unadjusted risk of break-through HZ progressing to PHN was 2.9% in the RZV vaccinated individuals.²⁹ It is also likely that the prevention of HZ, given our observed VE, contributed to the reduction of the risk of PHN.

The study has several strengths. Our study utilized a large and stable integrated health plan population to provide real-world effectiveness information of a new vaccine in an often-understudied subpopulation.³⁰ Our study results may allow for generalizability to other populations of Chinese ethnicity in the U.S. and other countries. Additionally, our study also had a longer follow-up, which allowed for better capture of outcomes, compared to other VE studies.⁹⁻¹¹ The vaccine is also available to KPSC members at no additional cost to them, thus minimizing exposure misclassification. Lastly, KPSC's comprehensive EHR allowed for accurate capture of HZ and PHN outcomes, the latter of which involved targeted chart review of encounter notes to ascertain HZ-related pain. The EHR also enabled capture of RZV vaccinations and other covariates, including health care utilization and clinical conditions. This allowed for adjustment for differences between the vaccinated and unvaccinated individuals.

Our study also has several limitations. First, though the study adjusted for various covariates, residual confounding, from covariates not assessed, may still be present. Second, during the initial months of the vaccine accrual period when supply was limited, the RZV vaccine at KPSC was prioritized for individuals ages 60 years and older. However, this should not bias results since individuals were matched on age. Another limitation is that it is unknown if HZ vaccination leads to modified or atypical HZ presentations that are more likely to be underdiagnosed or misdiagnosed. If these cases are never diagnosed or are diagnosed as other conditions, they will not be identified through ICD-10 codes for HZ. This would lead to a potential overestimation of VE. This is less of a concern in this study, however, since the outcome of interest is defined to be medically-attended HZ diagnoses. It is also possible that there is differential misclassification of HZ due to differential health care seeking behaviors, but to address this, prior health care utilization was included as a covariate. Our cohort was also identified, in part, through self-reported spoken/written language. This allows individuals to select a preferred language that is, most likely, a language they are fluent in. They are, therefore, most likely to be members of the racial/ ethnic group that speaks the preferred language selected. This method helps capture some individuals that may otherwise be vague in their self-reported racial/ethnic group (e.g., other). Lastly, our study was not designed to measure long-term vaccine effectiveness. However, cumulative incidence curves suggest continued effectiveness of RZV against HZ with up to 4 years of follow-up, although the number of individuals with 4 years of follow-up was limited.

Our study is one of the first to assess the effectiveness of RZV in a U.S. Chinese population under real-world conditions. We found a high VE against HZ thus further supporting the recommendation for RZV vaccination in adults aged \geq 50 years. Future studies should be conducted in other Chinese populations, including in China. Furthermore, future studies with longer follow-up periods should also be considered to assess the durability of RZV vaccination.

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Disclosure statement

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ORCID

Ana Florea (D) http://orcid.org/0000-0003-0030-8737 Lina Sy (D) http://orcid.org/0000-0003-2762-9266 Lei Qian (D) http://orcid.org/0000-0001-8001-3992 Bradley Ackerson (D) http://orcid.org/0000-0002-0816-7345 Yi Luo (b) http://orcid.org/0000-0001-8990-2470 Jun Wu (b) http://orcid.org/0000-0003-3227-4818 Yanjun Cheng 🕞 http://orcid.org/0009-0003-3999-1884 Jennifer Ku (D http://orcid.org/0000-0001-9469-5875 Leticia Vega Daily D http://orcid.org/0009-0005-9675-4601 Harpreet Takhar (D) http://orcid.org/0000-0002-2734-4896 Jeannie Song (D) http://orcid.org/0009-0006-4349-5885 Elizabeth Chmielewski-Yee (D) http://orcid.org/0000-0002-3223-7964 O'Mareen Spence (D) http://orcid.org/0000-0003-1573-7809 Harry Seifert i http://orcid.org/0000-0001-8048-5885 Driss Oraichi (D) http://orcid.org/0009-0005-1921-7626 Hung Fu Tseng (D) http://orcid.org/0000-0001-6184-6534

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Author contributions

LSS, LQ, BKA, YL, OS, and HFT were involved in the study concept and design. AF, LSS, LQ, BKA, YL, JW, YC, JHK, LVD, HST, JS, ECY, HS, DO, and HFT were involved in the acquisition, analysis, or interpretation

of data. AF drafted the manuscript. LSS, LQ, BKA, YL, JW, YC, JHK, LVD, HST, JS, ECY, OS, HS, DO, and HFT critically revised the manuscript for important intellectual content. LQ, YL, JW, and YC conducted the statistical analyses. LVD, HST, and JS provided administrative, technical, or material support.

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