COST-EFFECTIVENESS OF ADJUVANTED RECOMBINANT ZOSTER VACCINE (RZV) FOR VACCINATING US ADULTS NOT PREVIOUSLY VACCINATED AGAINST HERPES ZOSTER

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INTRODUCTION

- Herpes Zoster (HZ) is a painful reactivation of latent varicella zoster virus, occurring predominately in older adults.
- Adjuvanted Recombinant Zoster Vaccine (RZV, Shingrix [HZ/su in abstract]) was recently approved by the Food and Drug Administration (FDA), and therefore joins only other available Zoster Vaccine Live (ZVL, Zostavax) for the prevention of HZ.
- The Advisory Committee on Immunization Practices (ACIP) for the Centers for Disease Control and Prevention (CDC) made the following recommendations[1] for RZV use:
  - Recommended for the prevention of HZ and related complications for immunocompetent adults aged ≥50 years;
  - Recommended for the prevention of HZ and related complications for immunocompetent adults who previously received ZVL;
  - Preferred over ZVL for the prevention of HZ and related complications.
- The objective of this study was to determine the cost-effectiveness of vaccination against HZ. Incremental cost-effectiveness ratios (ICERs) were calculated for RZV versus no vaccination as well as RZV versus ZVL in US adults aged ≥60 years not previously vaccinated with ZVL and US adults aged ≥50 years.

METHODS

- The ZOster ecoNomic Analysis (ZONA) model is a deterministic Markov model.
- Two, separately analyzed, hypothetical 1 million (M)-person cohorts of US adults (age stratified based on "US" census data) aged ≥50 years or ≥60 years, not previously vaccinated against HZ, were modeled for their lifetimes from the year of vaccination with annual cycle lengths.
- Three different HZ primary vaccination strategies were compared: no vaccination, vaccination with RZV, and vaccination with ZVL.
- The perspective was societal, including both direct medical costs and indirect costs.
- Model inputs included demographics, incidence and disease burden, vaccine characteristics, utilities, and vaccine costs (**Table 1**).
- Costs and quality-adjusted life-years (QALYs) were calculated over the lifetime of the cohort, both discounted 3% annually, and were used to calculate the ICERs between vaccination scenarios.
- Deterministic and probabilistic sensitivity analyses were carried out to explore the robustness of our findings considering uncertainty about model inputs for the cohort of adults aged ≥60 years.

Table 1. Key Model Inputs

Vaccine efficacy[2,3,4]	Age categories (years)	Against HZ % (LB-UB)	Against PHN % (LB-UB)
RZV (two-dose)*	Age 50-69	98.4 (95.0-100.0)	–
	Age ≥70	97.8 (94.1-100.0)	
RZV (one-dose)*	Age 50-69	90.0 (58.9-98.9)	–
	Age ≥70	69.5 (24.9-89.1)	
ZVL**	Age 50-59	69.8 (54.1-80.6)	69.8 (30.8-89.6)
	Age 60-69	63.9 (56.0-71.0)	65.7 (25.4-84.2)
	Age 70-79	40.9 (28.0-52.0)	73.4 (51.6-85.8)
	Age ≥80	18.3 (0.0-48.0)	39.5 (0.0-73.8)
Waning rate[2,3,5]			**Annual decrease % (LB-UB)**
RZV (two-dose)	1-4 years after vaccination and until age 69		1.0 (0.0-2.6)
	≥5 years after vaccination and until age 69		2.3 (0.7-4.6)
	Age ≥70		3.6 (1.4-6.6)
RZV (one-dose)#	1-4 years after vaccination		5.4 (1.0-7.4)
	≥5 years after vaccination		5.1 (3.6-6.9)
ZVL	1-4 years after vaccination		5.4 (1.0-7.4)
	≥5 years after vaccination		5.1 (3.6-6.9)
Second-dose compliance[2,3,6,7]			**% (LB-UB)**
RZV			69† (45†-89¥)
Vaccine costs per dose[8]			**$ (LB-UB)**
RZV#			140.00 (125.00-175.00)
ZVL			196.91 (117.21-212.67)
Administration cost per dose[9]			**$ (LB-UB)**
RZV and ZVL			20.00 (15.00-50.00)

–, not applicable; LB, lower bound; UB, upper bound; HZ, herpes zoster; PHN, postherpetic neuralgia; RZV, Adjuvanted Recombinant Zoster Vaccine ; $, United States dollar; ZVL, Zoster Vaccine Live.
*Initial vaccine efficacy at time 0[2,3].
**Assumed vaccine efficacy at 1.5 years[2,3].
#Assumption.
†First percentile second-dose compliance[2,3,10] – at least 2 doses of hepatitis B series[6].
‡Full series hepatitis A compliance[7].
¥Tenth percentile second-dose compliance[2,3].

RESULTS

US adults aged ≥60 years

- For 1M-person cohort, primary vaccination with RZV would reduce disease burden thereby resulting in a gain of 2,291 QALYs at a total societal cost of over $27M compared to no vaccination. This produced an ICER of $11,863 per QALY saved (**Table 2**).
- Compared to ZVL, primary vaccination of 1M-person cohort aged ≥60 years with RZV would result in a gain of 1,261 QALYs and societal cost savings of almost $96M (**Table 2**) implying that RZV would be the cost-saving option.

Table 2. Base-Case Analysis Results for 1M US Adults Aged 60 Years and Older receiving no HZ Vaccine or primary vaccination with either RZV or ZVL

Outcome	No Vaccination	RZV	ZVL	RZV vs. No Vaccination	RZV vs. ZVL
Health outcomes					
HZ cases	196,063	92,460	164,098	(103,603)	(71,638)
PHN cases	22,580	11,382	17,785	(11,197)	(6,403)
Complication cases	29,277	14,822	25,404	(14,455)	(10,582)
Ocular	10,688	5,473	9,263	(5,215)	(3,790)
Neurological	9,789	4,753	8,395	(5,037)	(3,642)
Cutaneous	4,337	2,288	3,841	(2,049)	(1,553)
Other non-pain	4,463	2,308	3,905	(2,155)	(1,597)
HZ-related deaths	45	31	43	(14)	(13)
Costs (discounted)					
Vaccination costs	$0	$304,405,178	$226,897,269	$304,405,178	$77,507,909
Direct costs due to HZ	$371,165,848	$162,208,952	$300,362,422	($208,956,896)	($138,153,470)
Indirect costs due to HZ	$96,081,531	$27,815,584	$63,215,653	($68,265,947)	($35,400,069)
Total direct costs	$371,165,848	$466,614,130	$527,259,691	$95,448,282	($60,645,562)
Total societal costs	$467,247,379	$494,429,714	$590,475,344	$27,182,335	($96,045,630)
Life-years/QALYs (discounted)					
Life-years	12,890,617	12,890,694	12,890,632	77	62
QALYs	10,119,612	10,121,903	10,120,642	2,291	1,261
Cost-effectiveness					
Incremental cost per QALY gained	–	–	–	$11,863	Cost-saving

–, not applicable; 1M.1 million; HZ, herpes zoster; PHN, postherpetic neuralgia; QALY, quality-adjusted life-year; RZV, Adjuvanted Recombinant Zoster Vaccine; US, United States; ZVL, Zoster Vaccine Live. Numbers in red are negative.

US adults aged ≥50 years

- For 1M-person cohort, vaccination with RZV would result in a gain of 1,833 QALYs at a total societal cost of over $23M compared to no vaccination. This produced an ICER of $12,617 per QALY saved (**Table 3**).
- Compared to ZVL, vaccination of 1M-person cohort aged ≥50 years with RZV would result in a gain of 1,127 QALYs and societal cost savings of almost $105M (**Table 3**), and therefore, the cost-saving option.

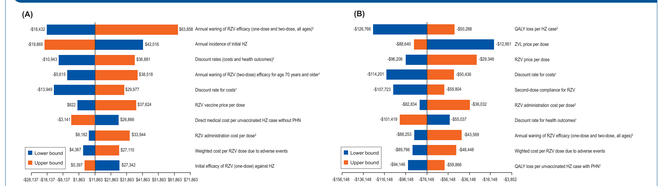
Table 3. Base-Case Analysis Results for 1M US Adults Aged 50 Years and Older receiving no HZ Vaccine or primary vaccination with either RZV or ZVL

Outcome	No Vaccination	RZV	ZVL	RZV vs. No Vaccination	RZV vs. ZVL
Health outcomes					
HZ cases	237,442	127,166	204,901	(110,276)	(77,735)
PHN cases	24,936	14,590	21,225	(10,346)	(6,635)
Complication cases	32,629	19,047	29,175	(13,582)	(10,128)
Ocular	11,936	7,010	10,679	(4,926)	(3,668)
Neurological	10,828	6,219	9,680	(4,609)	(3,460)
Cutaneous	4,837	2,875	4,334	(1,962)	(1,459)
Other non-pain	5,028	2,943	4,483	(2,085)	(1,540)
HZ-related deaths	43	33	42	(10)	(9)
Costs (discounted)					
Vaccination costs	$0	$306,818,778	$228,260,826	$306,818,778	$78,557,952
Direct costs due to HZ	$368,982,007	$181,478,746	$308,678,511	($187,503,260)	($127,199,765)
Indirect costs due to HZ	$145,783,343	$49,591,973	$105,525,962	($96,191,370)	($55,933,990)
Total direct costs	$368,982,007	$488,297,525	$536,939,337	$119,315,518	($48,641,812)
Total societal costs	$514,765,349	$537,889,497	$642,465,299	$23,124,148	($104,575,802)
Life-years/QALYs (discounted)					
Life-years	15,675,117	15,675,175	15,675,129	57	46
QALYs	12,511,295	12,513,128	12,512,001	1,833	1,127
Cost-effectiveness					
Incremental cost per QALY gained	–	–	–	$12,617	Cost-saving

–, not applicable; 1M, 1 million; HZ, herpes zoster; PHN, postherpetic neuralgia; QALY, quality-adjusted life-year; RZV, Adjuvanted Recombinant Zoster Vaccine; US, United States; ZVL, Zoster Vaccine Live. Numbers in red are negative.

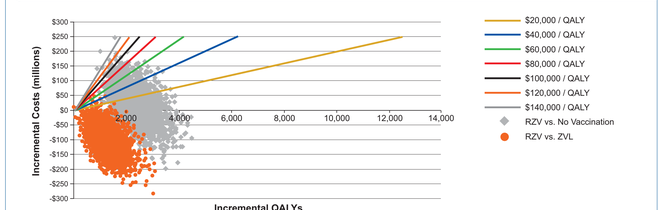
- Sensitivity analyses demonstrated the robustness of these findings across model input uncertainty for the cohort of adults aged ≥60 years (**Figures 1** & **2**).

Figure 1. One-Way Sensitivity Analysis Results for ICER of (A) RZV vs. No Vaccination (B) RZV vs. ZVL for US Adults Aged ≥60 years Not Previously Vaccinated Against HZ



ICER, incremental cost-effectiveness ratio; HZ, herpes zoster; ICER, incremental cost-effectiveness ratio; PHN, postherpetic neuralgia; QALY, quality-adjusted life-year; RZV, Adjuvanted Recombinant Zoster Vaccine; US, United States; ZVL, Zoster Vaccine Live.
Note: Top 10 inputs with large impact on ICER are displayed only.
† = Individual variation of an input that is also varied in this DSA grouped with other potentially correlated inputs. Those groups are marked by a "Δ" footnote.
‡ = Group variation of a set of potentially correlated inputs, each of which is also varied in this deterministic sensitivity analysis individually. Those inputs, when varied individually, are marked by a "‡" symbol.

Figure 2. Incremental Costs vs. Incremental QALYs from 5,000 Probabilistic Sensitivity Analysis Simulations of RZV vs. No Vaccination and RZV vs. ZVL for US Adults Aged ≥60 years Not Previously Vaccinated Against HZ



HZ, herpes zoster; QALY, quality-adjusted life-year; RZV, Adjuvanted Recombinant Zoster Vaccine; US, United States; ZVL, Zoster Vaccine Live.

CONCLUSIONS

- **In US adults aged ≥60 years who have not been previously vaccinated against HZ and US adults aged ≥50 years, RZV is cost-effective relative to no vaccination and cost-saving relative to vaccination with ZVL.**
- **Sensitivity analyses results suggest that the model results were robust to the uncertainty of input parameters.**

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