Supplementary Material

Quality of Life Impact of an Adjuvanted Recombinant Zoster Vaccine in Adults Aged 50 Years and Older

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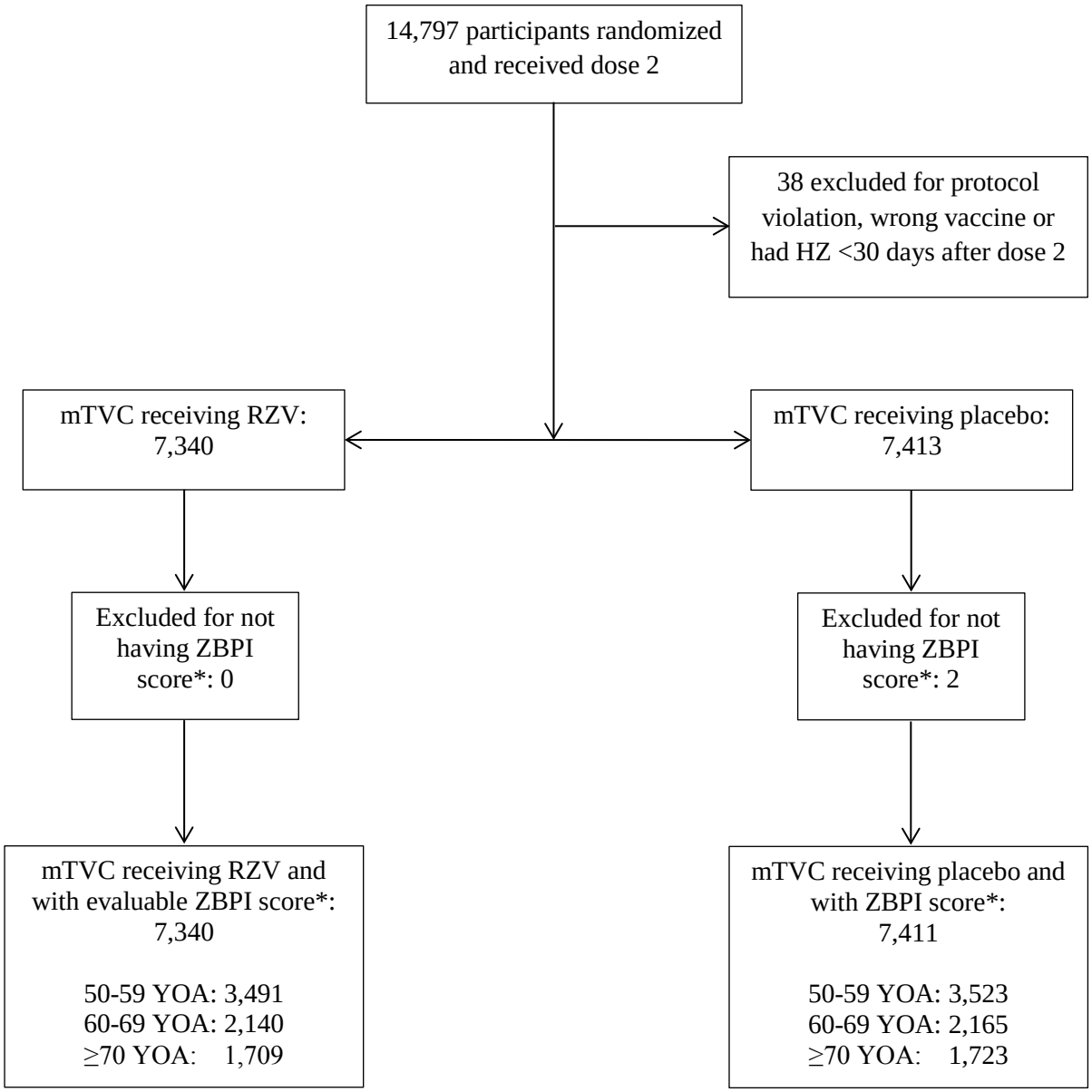
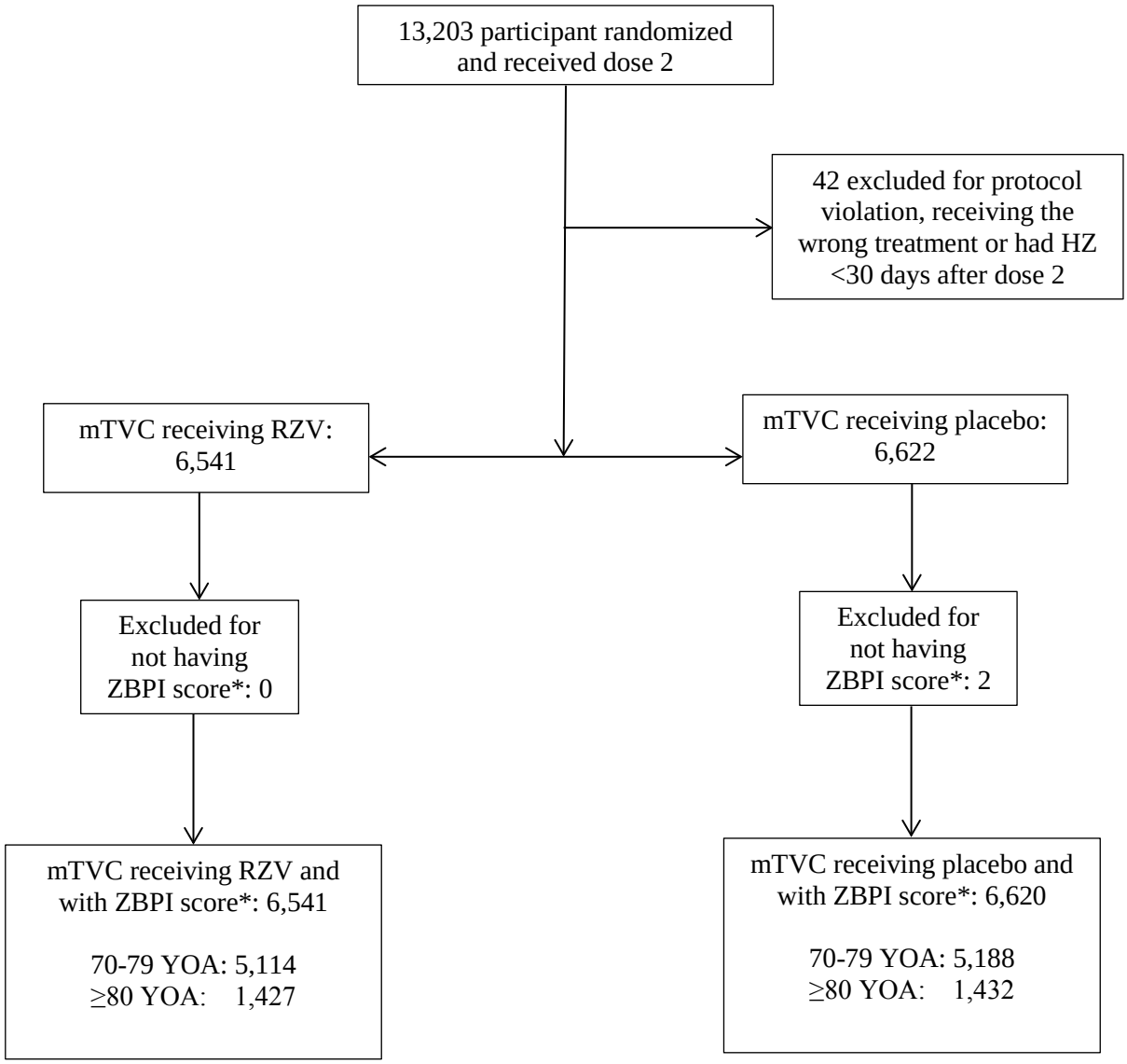
All core writing team members and named authors reviewed and approved the final submitted version of the paper. All group contributors had the opportunity to review a draft of the paper.

Figure S1. Flowchart for the ZOE-50 study



*: Participants who did not develop HZ were assigned a ZBPI score of 0. HZ: herpes zoster; mTVC: modified total vaccinated cohort; RZV: Adjuvanted Recombinant Zoster Vaccine; YOA: years of age; ZBPI: Zoster Brief Pain Inventory.

Figure S2. A. Flowchart for the ZOE-70 study



*: Participants who did not develop HZ were assigned a ZBPI score of 0. HZ: herpes zoster; mTVC: modified total vaccinated cohort; RZV: Adjuvanted Recombinant Zoster Vaccine; YOA: years of age; ZBPI: Zoster Brief Pain Inventory;

Figure S2. B. Pooled ZOE-70 analysis

*: Participants who did not develop HZ were assigned a ZBPI score of 0. HZ: herpes zoster; mTVC: modified total vaccinated cohort; RZV: Adjuvanted Recombinant Zoster Vaccine; YOA: years of age; ZBPI: Zoster Brief Pain Inventory.

Table S1. Demographics of mTVC confirmed HZ cases

	ZOE-50 study		Pooled ZOE-70 analysis	
	RZV	**Placebo**	**RZV**	**Placebo**
N:	9	254	25	284
Age (YOA)				
Mean	61.9	62.9	76.2	75.8
Range	50-75	50-87	70-86	70-92
Gender – n (%)				
Female	5 (55.6)	168 (66.1)	15 (60.0)	161 (56.7)
Male	4 (44.4)	86 (33.9)	10 (40.0)	133 (43.3)
Region – n (%)				
Australasia	3 (33.3)	76 (29.9)	4 (16.0)	81 (28.5)
Europe	3 (33.3)	105 (41.3)	12 (48.0)	120 (42.3)
Latin America	1 (11.1)	27 (10.6)	3 (12.0)	24 (8.5)
North America	2 (22.2)	46 (18.1)	6 (24.0)	59 (20.8)
Ancestry – n (%)				
African - American	0	3 (1.2)	0	1 (0.4)
East Asian	1 (11.1)	54 (21.3)	2 (8.0)	49 (17.3)
Japanese	2 (22.2)	12 (4.7)	2 (8.0)	29 (10.2)
South-East Asian	0	1 (0.4)	0	1 (0.4)
White Arabic	0	1 (0.4)	0	0
White Caucasian	5 (55.6)	165 (65.0)	20 (80.0)	190 (66.9)
Other	1 (11.1)	18 (7.1)	1 (4.0)	14 (4.9)

mTVC: modified total vaccinated cohort; N: Number of confirmed HZ cases; n: number of HZ cases in the category concerned; RZV: Adjuvanted Recombinant Zoster Vaccine; YOA: years of age

Assessment of quality of life (QoL) by means of the SF-36 instrument

The 36-Item Short Form Survey (SF-36) is another standardized questionnaire with well-established psychometric properties. It assesses the following dimensions: physical functioning, role limitations due to physical problems, role limitations due to emotional problems, bodily pain, general health perceptions, vitality, social function and mental health. Each dimension is scored on a scale from 0 to 100 with 100 signifying optimal functioning. Summary scores for the physical component score (PCS) and the mental component score (MCS) were also calculated [1].

The comparisons of the SF-36 QoL measures between the RZV and placebo groups showed in both analyses a trend towards higher QoL scores in the RZV groups than in the placebo groups. Very few of the multiple comparisons identified statistically significant differences, however. For illustration, the values observed at Week 1 with the highest completion rate are shown in Table S2.

Table S2. Summary data for SF-36: estimated LS means assessed at Week 1

	ZOE-50			Pooled ZOE-70		
Domain	**RZV**	**Placebo**	**95%CI of difference**	**RZV**	**Placebo**	**95%CI of difference**
Physical functioning	70.7	71.0	-16.0;15.2	61.9	65.6	-14.3;6.86
Physical role	72.3	61.8	-8.4;29.6	64.9	57.5	-4.8;19.5
Bodily pain	62.2	49.0	-4.4;30.8	55.8	49.8	-5.4;17.5
General health	63.9	63.4	-14.3;15.4	56.5	61.1	-13.3;3.9
Vitality	54.5	53.6	-15.2;17.0	54.7	53.4	-8.6;11.2
Social functioning	76.9	68.5	-9.4;26.2	71.4	68.2	-8.3;14.6
Role emotional	88.3	71.9	-1.0;33.8	80.2	67.4	1.0;24.5
Mental health	66.7	67.8	-15.4;13.2	65.4	67.6	-11.3;6.9
PCS	46.9	45.2	-4.0;7.3	43.7	44.2	-3.9;3.1
MCS	49.1	46.0	-4.4;10.6	48.0	45.7	-2.5;7.0

CI: confidence interval; LS: least squares; MCS: mental component score; PCS: physical component score; RZV: Adjuvanted Recombinant Zoster Vaccine; SF-36: 36-Item Short Form Survey (Scores 0 - 100, with 100 signifying optimal functioning).
LS means and corresponding CIs were taken from the repeated-measures mixed-effects model with gender and geographical region as factors and age at baseline as a covariate.

ZOE-70 Analysis

The mean delay between the date of rash onset and the first HZ evaluation was 4.6 days (range 0-33). Completion rates for the Zoster Brief Pain Inventory (ZBPI) questionnaire were approximately 15% on Day 0, >60% from Day 3 onwards and ≥80% from Day 6 onwards. For the EQ-5D and SF-36 instruments during an ongoing HZ episode, the completion rates were approximately 52% on Day 0 and ≥83% at all time points thereafter.

The estimated overall VE in reducing the ZBPI burden of illness and burden of interference were 90.5% and 88.2%, respectively (Table S3).

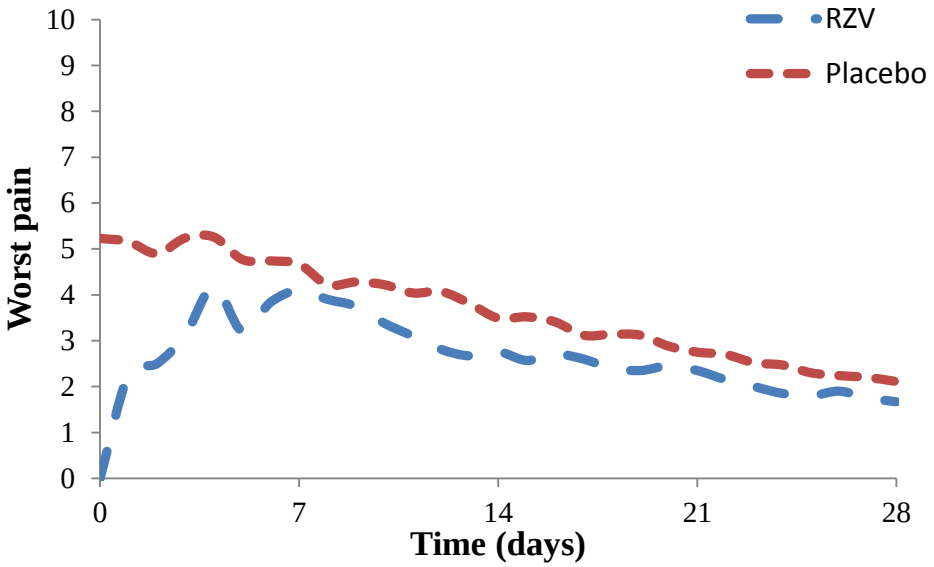
Table S3: HZ ZBPI burden of illness scores and burden of interference scores

	Age group (YOA)	RZV				Placebo				VE (95%CI for VE)
		n	m	ZBPI severity	ZBPI burden	n	m	ZBPI severity	ZBPI burden	
Burden of Illness	70-79	17	5,114	0.376	0.099	168	5,188	6.409	1.696	94.2 (91.2;97.2)
	≥80	6	1,427	1.526	0.430	53	1,432	7.109	2.023	78.8 (73.6;84.0)
	Total	23	6,541	0.627	0.168	221	6,620	6.560	1.763	90.5 (88.7;92.3)
Burden of interference	70-79	17	5,114	0.220	0.058	168	5,188	4.298	1.138	94.9 (91.0;98.8)
	≥80	6	1,427	1.690	0.476	53	1,432	5.496	1.564	69.6 (65.2;74.0)
	Total	23	6,541	0.541	0.145	221	6,620	4.557	1.225	88.2 (86.3;90.1)

CI: confidence interval; HZ: herpes zoster; n: number of subjects with follow-up; m: number of subjects with a confirmed zoster episode; RZV: Adjuvanted Recombinant Zoster Vaccine; VE: vaccine efficacy; YOA: years of age; ZBPI: Zoster Brief Pain Inventory.

Figure S3 presents the mean ZBPI 'worst-pain' scores per day during the first 28 days. The mean 'worst-pain' scores were at all times lower in the RZV group than in the placebo group.

Figure S3: Mean ZBPI 'worst-pain' scores per day during the first 28 days after rash onset



RZV: Adjuvanted Recombinant Zoster Vaccine; ZBPI: Zoster Brief Pain Inventory.

A severe ZBPI 'worst-pain' score (i.e., ≥7) was reported by 42.9% in the RZV group and 66.8% in the placebo group (VE 35.9%, 95%CI 3.5% to 63.7%, Table S4). The corresponding proportions reporting severe ZBPI 'average pain' were 23.8 and 41.8%, respectively (VE 43.1%, 95%CI -10.8% to 75.0%). The median time to resolution of clinically significant pain (i.e., ZBPI 'worst pain' ≥3) was 14 days in the RZV group and 22 days in the placebo group (p = .635).

Table S4: Distribution of maximal ZBPI 'worst-pain' and ZBPI 'average-pain' scores over the duration of the entire HZ episode

	'Worst-pain'			'Average-pain'		
	RZV (N = 21)	**Placebo (N = 208)**	**p-value**	**RZV (N = 21)**	**Placebo (N = 208)**	**p-value**
ZBPI scale	**n (%)**	**n (%)**		**n (%)**	**n (%)**	
≥ 3	17 (81.0)	188 (90.4)				
0	1 (4.8)	14 (6.7)	.085	1 (4.8)	15 (7.2)	.125
1	1 (4.8)	2 (1.0)		2 (9.5)	8 (3.8)	
2	2 (9.5)	4 (1.9)		2 (9.5)	16 (7.7)	
3	1 (4.8)	19 (9.1)		3 (14.3)	15 (7.2)	
4	3 (14.3)	12 (5.8)		2 (9.5)	16 (7.7)	
5	2 (9.5)	11 (5.3)		2 (9.5)	21 (10.1)	
6	2 (9.5)	7 (3.4)		4 (19.0)	30 (14.4)	
7	0	17 (8.2)		3 (14.3)	35 (16.8)	
8	3 (14.3)	42 (20.2)		1 (4.8)	24 (11.5)	
9	5 (23.8)	31 (14.9)		0	14 (6.7)	
10	1 (4.8)	49 (23.6)		1 (4.8)	14 (6.7)	
Mean	5.8	6.9		4.6	5.5	
SD	3.06	3.05		2.60	2.81	

HZ: herpes zoster; mTVC: modified total vaccinated cohort; N = number of HZ cases in each group; n = number of HZ cases in each category; SD: standard deviation; ZBPI: Zoster Brief Pain Inventory.
Includes only subjects in the mTVC HZ evaluable subgroup, i.e., confirmed HZ cases with a ZBPI questionnaire completed during the first 14 days after HZ onset

Table S5 presents the utility loss of the HZ patients in the placebo groups over the first 28 days after rash onset, assessed using the EQ-5D instrument. The estimated utility loss was highest on Day 0 and decreased over time in all age groups as the patients recovered from HZ but a negative impact of HZ on QoL remained until the end of Week 4.

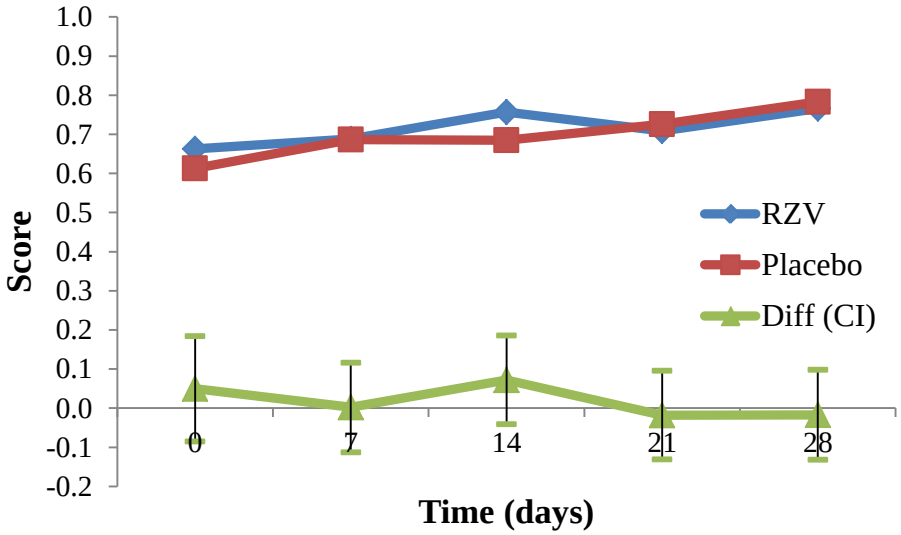
Table S5: Estimated placebo-group EQ-5D scores for utility loss by age group and time point during the acute HZ period

Age Group (YOA)	Time point	LS means estimate	Estimated utility loss	95% CI
70-79	Pre-HZ	0.844		
	Day 0	0.633	0.211	(0.162, 0.259)
	Week 1	0.700	0.144	(0.095, 0.193)
	Week 2	0.687	0.157	(0.105, 0.208)
	Week 3	0.749	0.095	(0.043, 0.148)
	Week 4	0.800	0.044	(-0.009, 0.097)
≥80	Pre-HZ	0.770		
	Day 0	0.556	0.214	(0.125, 0.303)
	Week 1	0.636	0.135	(0.048, 0.222)
	Week 2	0.677	0.093	(0.001, 0.185)
	Week 3	0.657	0.113	(0.018, 0.208)
	Week 4	0.734	0.036	(-0.059, 0.132)

CI: confidence interval; EQ-5D: EuroQol-5 Dimension; HZ: herpes zoster; LS: least squares; YOA: years of age
Note: An EQ-5D value of 1 represents the best possible health state.

The estimated differences over time in mean EQ-5D utility scores between the RZV and placebo groups are presented in Figure S4.

Figure S4: Mean EQ-5D utility scores during the first 28 days after rash onset



CI: confidence interval; Diff: difference; EQ-5D: EuroQol-5 Dimension; RZV: Adjuvanted Recombinant Zoster Vaccine.

References

[1] Ware JE Jr. SF-36 health survey update. *Spine (Phila Pa 1976)*.2000;25:3130–3139.