Cost-Effectiveness Analysis of Herpes Zoster Vaccination in 50- to 85-Year-Old Immunocompetent Belgian Cohorts: A Comparison between No Vaccination, the Adjuvanted Subunit Vaccine, and Live-Attenuated Vaccine

Peer-reviewed author version

PIETERS, Zoe; OGUNJIMI, Benson; Beutels, Philippe & Bilcke, Joke (2022) Cost-Effectiveness Analysis of Herpes Zoster Vaccination in 50- to 85-Year-Old Immunocompetent Belgian Cohorts: A Comparison between No Vaccination, the Adjuvanted Subunit Vaccine, and Live-Attenuated Vaccine. In: PHARMACOECONOMICS, 40 (4) , p.461-476.

DOI: 10.1007/s40273-021-01099-2
Handle: http://hdl.handle.net/1942/36677

PharmacoEconomics
Supplementary material:

Cost-effectiveness analysis of Herpes Zoster vaccination in 50- to 85- year-old immunocompetent Belgian cohorts: A comparison between no vaccination, the adjuvanted subunit vaccine, and live-attenuated vaccine

Zoë Pieters, Benson Ogunjimi, Philippe Beutels, Joke Bilcke[†]

[†]Author for correspondence: Joke Bilcke, University of Antwerp, Universiteitsplein 1, 2610 Wilrijk, Belgium. Email address: joke.bilcke@uantwerpen.be. ORCHID: 0000-0001-5720-5291.

S1 Obtaining estimates for the input parameters and their uncertainty

S1.1 Hospitalisation rate

The Minimal Clinical Data (MCD) is a mandatory registration of hospitalised patient information for every hospital in Belgium. From this database, we obtained birth year, gender, hospital admission and discharge date for hospitalised patients who had a primary diagnosis of HZ in the period 2000-2007. Annual age-specific herpes zoster (HZ) hospitalisation rates were calculated by dividing the yearly number of HZ hospitalisations from the MCD by the Belgian age-specific population from the same year. The data was summarised by fitting a generalised additive model to the number of HZ hospitalisations for age_i and using the Belgian population at age_i as an offset and $g()$ is a spline [1, 2].

$$log\Big(\frac{hospitalisation_i}{population_i}\Big) = \alpha + g(age_i) \tag{1}$$

The expected HZ hospitalisation rates are shown in Fig. S1. We did not account for uncertainty in the hospitalisation rate for HZ since the MCD receives information of all hospitalisations that occur in Belgium.

We accounted for parameter uncertainty in the P(being immunocompetent |Hospitalised for HZ) using a Beta distribution due to the low sample size. The National Christian Sickness Fund (NCSF) survey inquired 153 individuals who were hospitalised for HZ about their immune status [1].

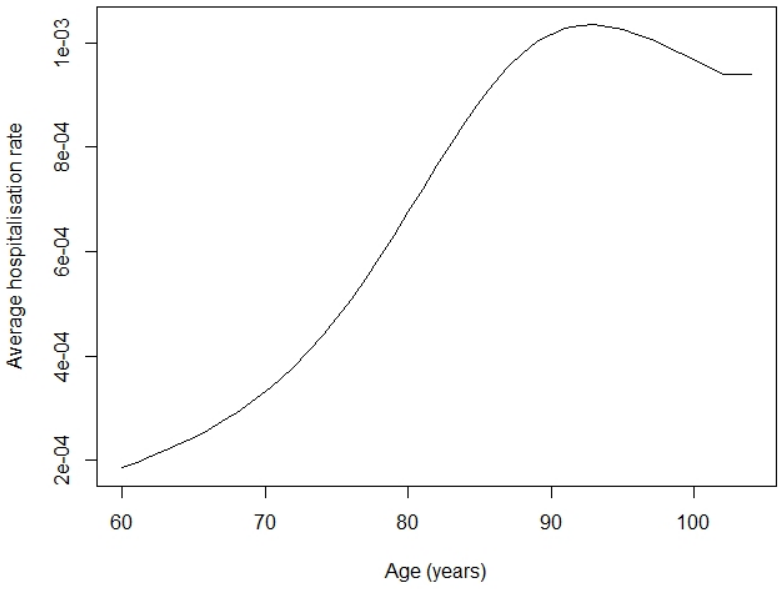


Fig. S1 Estimated average hospitalisation rates due to herpes zoster in the Belgian population

S1.2 Rate of physician consultation

The age distribution of the sentinel catchment population was lacking. Therefore the same age distribution as the complete Belgian population was assumed, such that age-specific rates could be calculated [1]. We calculated the annual rate averaged over the years 2006, 2007, and 2008. Due to no GP visits reported for ages 98-101 in the sentinel system from Sciensano and the very small population at these age groups, we assumed the same rate of physician consultation as for age 97. We accounted for parameter uncertainty in the rate of physician consultation since the sentinel system only covers 1.5% of the Belgian population. We used a Beta-distribution to characterise the uncertainty, where the number of events are the number of physician consultations and the sample size is the catchment population.

From the NCSF survey [1], we obtained information about the immune status of individuals who visited a GP at least once for HZ (denoted as P(being immunocompetent|treated ambulatory for HZ) in Table 1). Since only a total of 130 ambulatory HZ patients were surveyed, we characterised parameter uncertainty by a Beta-distribution in 4 age groups, namely $\leq$59, 60-69, 70-79, and $\geq$ 80 years of age.

S1.3 HZ mortality rate

Table S1 displays the judgement of five expert clinicians who were asked whether each of the 59 deaths would have occurred if the person would not have had HZ. The possible answers 'yes', 'no', and 'unsure' were given weight 0, 0.2, and 0.1 respectively. We summed the weights according to the possible answers (Table S1) of the five experts and multiplied them with the number of deaths in each age group. The aver-

age and standard error of the weighted deaths for each age category served as inputs for a Gamma distribution representing uncertainty in the expert opinion, with shape parameter= $mean^2/SE^2$ and rate parameter= $mean/SE^2$. Since there were no deaths observed in the age group ≤59, we did not consider the mortality rate as uncertain in this age group. The number of deaths caused by HZ from 1998-2007 is divided by the total population size for the same period for each age group.

Table S1 Expert opinion on whether deaths would have occurred if the person would not have had HZ

	Age group			
Opinion	≤59	60-74	75-89	≥90
5×Yes	0	1	4	1
4×Yes, 1×No/unsure	0	2	2	0
5× No	0	0	0	2
4×No, 1×Yes/unsure	0	0	10	5
3×Yes, 2×No	0	0	0	0
3×No, 2×Yes	0	0	0	0
3×Unsure, 2×Yes	0	0	0	0
3×Unsure, 2×No	0	1	4	3
4×Unsure, 1×No	0	0	1	1
3×Yes, 2×Unsure	0	0	0	0
3×No, 2×Unsure	0	0	5	3
2×Yes, 2×No, 1×Unsure	0	0	0	0
2×Yes, 2×Unsure, 1×No	0	0	1	0
2×No, 2×Unsure, 1×Yes	0	1	2	1
3×No, 1×Yes, 1×Unsure	0	0	6	2
3×Unsure, 1×Yes, 1×No	0	0	1	0
3×Yes, 1×No, 1×Unsure	0	0	0	0

S2 Vaccine efficacy ZVL

The vaccine efficacy of Zoster Vaccine Live (ZVL) against HZ was assessed in a randomised clinical trial, called the Shingles Prevention Study (SPS) [3]. Immunocompetent individuals who were 60 years or older at the onset of the study were included. The SPS study had a mean follow-up of 3.13 years. Two follow-up studies were performed to evaluate the waning of the vaccine efficacy over time [4, 5]. Efficacy data is available up to 11 years post-vaccination (Fig. S2). Since there is a lot of uncertainty about the vaccine efficacy at 11 years after vaccination, we only use data up to 10 years after the first vaccination. In order to estimate the duration of protection, we fitted (1) functions with an elbow shape, (2) linear functions, and (3) functions with a knee shape. The fit of the different functions to the data is shown in Fig. S3. The best fit, corresponding to the lowest AIC, is given by the one-minus-exponential function (Fig. S3, Equation 2):

$$VE_i = 1 - (e^{(log(0.3912) + 0.08057 * years_i)}) \tag{2}$$

with VE_i the vaccine efficacy of ZVL against HZ at year i since vaccination.

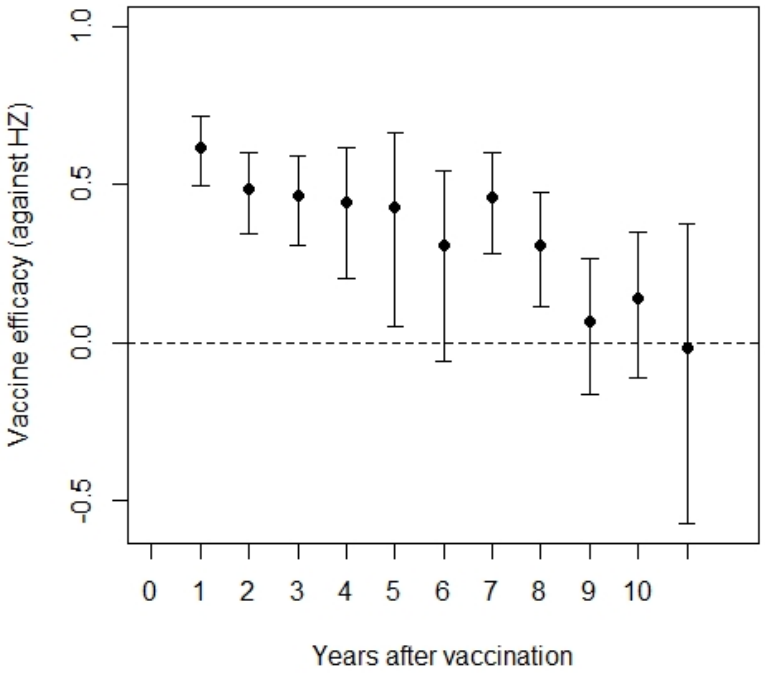


Fig. S2 Vaccine efficacy of ZVL against HZ up to 11 years post-vaccination. Bars represent 95% CI.

Equation 2 is independent of age. However, differences in the vaccine efficacy at age of vaccination were observed in the SPS study [6]. We followed the approach by De Boer *et al.* (2018) [7] to account for differences in vaccine efficacy at age of vaccination. We adjusted the vaccine efficacy at year 1 according to risk ratio per age group. The age-specific risk ratios were calculated by dividing the age-specific vaccine efficacy by the overall vaccine efficacy of the SPS trial. An additional randomised control trial was performed to evaluate the vaccine efficacy of ZVL against HZ in immunocompetent individuals between 50 and 59 years old [8]. However, the mean follow-up in this study was 1.3 years. Therefore, we extrapolated the vaccine efficacy of this age group to the mean follow-up time of the SPS trial. The age-specific risk ratios are reported in Table S2. In addition, we assumed that the waning rate is the same for all ages (Fig. S4, solid line). Since the ZVL does not provide protection after 10 years, we considered a booster after 10 years. In accordance with the literature, we assume that the booster provides the same protection as the initial dose at a given age [9]. The effect of the booster is represented by the dashed line in Fig. S4.

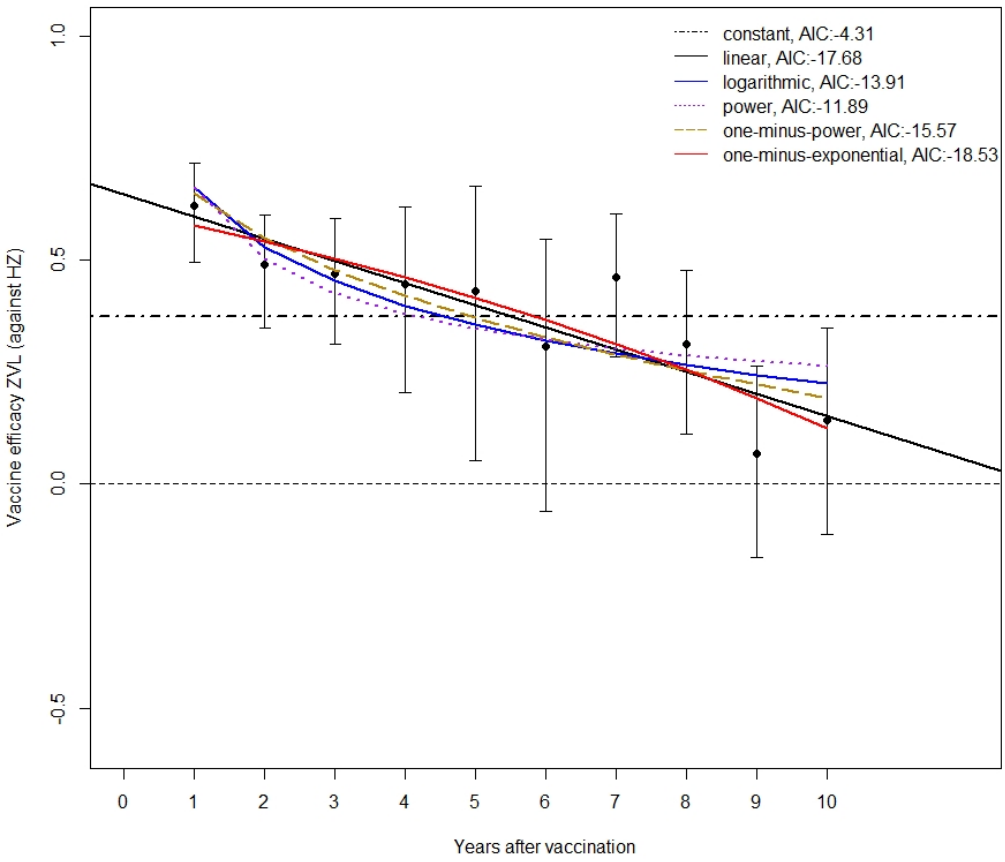


Fig. S3 Fitted functions to the vaccine efficacy of ZVL against HZ (data up to 10 years post-vaccination)

S3 Vaccine efficacy HZ/su

The vaccine efficacy of the adjuvanted HZ subunit vaccine (HZ/su; Shingrix) was obtained from two randomised control trial: ZOE-50 (average follow-up time is 3.2 years) conducted in adults who are 50 years of age or older [10] and ZOE-70 (average follow-up time is 3.7 years) conducted in adults 70 years of age or older [11]. The HZ/su vaccine is developed as a 2-dose schedule, with the second dose administered within 2 months after the first dose. We assume that everyone complied to this scheme, since observed both the ZOE-50 and ZOE-70 studies showed a high compliance for the second dose (>99% and >94.4% respectively) [10, 11].

The vaccine efficacy of the modified vaccinated cohorts for both randomised control trials (ZOE-50 and ZOE-70) are displayed in Fig. S5 [12]. The vaccine efficacy at year 1 is for both trials similar (98.4% and 97.6% respectively). However, we observe that the rate of waning during the study period is different for both trials. We assume that the ZOE-50 trial represents the waning of the 50- to 69-year-olds, this seems reasonable since only 23.3% of the individuals in the ZOE-50 trial is $\leq$70 years and we observe a different waning rate in both studies.

Table S2 Age-specific risk ratios to adjust the vaccine efficacy of ZVL against HZ according to age at vaccination.

Age group	Risk ratio
50-59 years	1.2687465
65-69 years	1.2748701
65-69 years	1.2198355
70-74 years	0.8525546
75-79 years	0.7117611
80-84 years	0.3915559
85-89 years	0.2577841

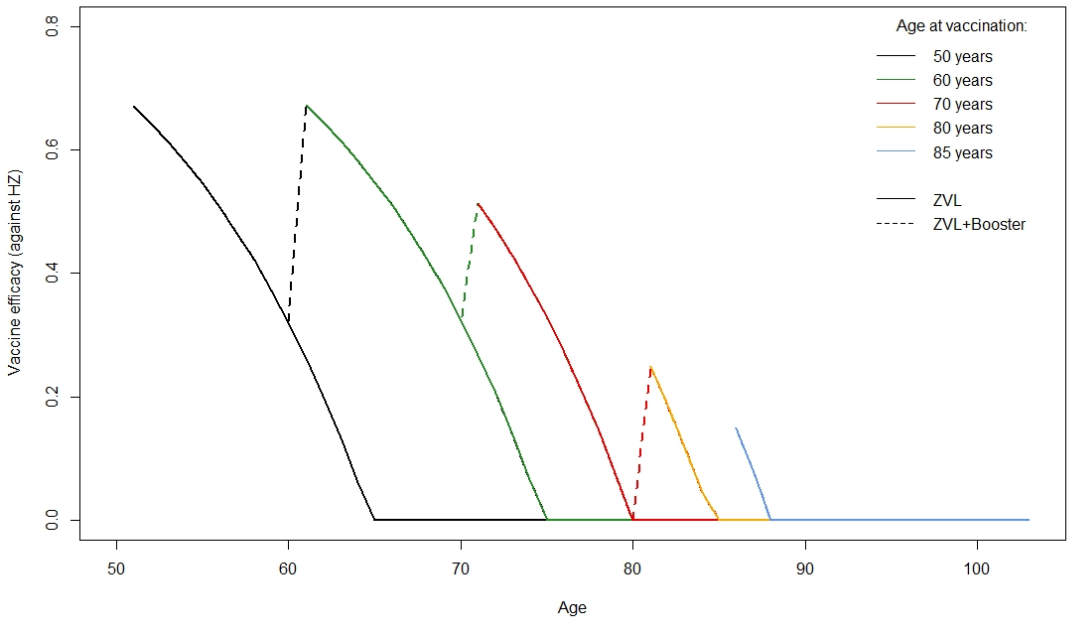


Fig. S4 The vaccine efficacy of ZVL (1 dose, solid line) or ZVL with a booster after 10 years of initial vaccination with ZVL (dashed line). After boosting, the waning of vaccine efficacy occurs at the same rate of individuals who got an initial vaccination.

We fitted (1) functions with an elbow shape, (2) linear functions, and (3) functions with a knee shape to obtain the best function representing vaccine efficacy of HZ/su. The fit of the different functions is shown in Fig. S6. Representing the vaccine efficacy in 50- to 69-year-olds can be done by any of the fitted functions as they are all very similar and provide similar AIC values. Although, the constant function provides the lowest AIC. For individuals 70 years or older, the vaccine efficacy for all fitted functions, expect the constant function, provide similar fits. We conclude that not enough data is available to estimate accurately the waning of HZ/su vaccine in both age groups.

Therefore, we will proceed by using for both age groups the functions that result in the longest and shortest duration of protection. We did not consider using the constant and power waning function since this seems to be unrealistic and not occurring naturally.

For 50- to 69-year-old individuals:

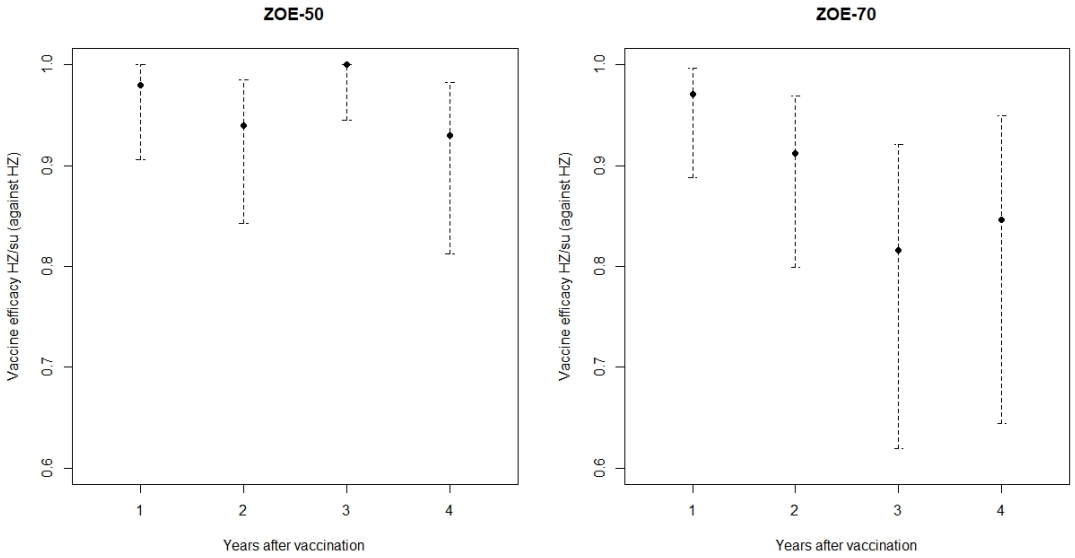


Fig. S5 The vaccine efficacy of HZ/su against HZ for the modified vaccinated cohorts during the study period over time in adults ≥50 years (ZOE-50) and ≥70 years (ZOE-70). Bars represent 95% CI.

- Longest duration of protection: Logarithmic function

$$VE_i = 0.9768 - 0.0179 * log(years_i)$$

- Shortest duration of protection: One-minus-exponential

$$VE_i = 1 - (e^{(log(0.0162) + 0.3068 * years_i)})$$

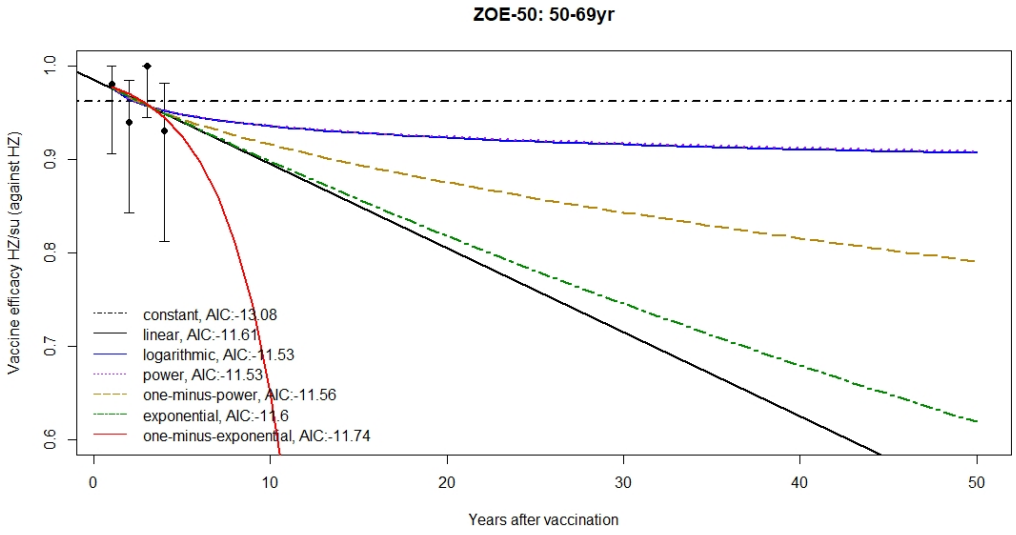
For individuals 70-years-and-older:

- Longest duration of protection: Logarithmic function

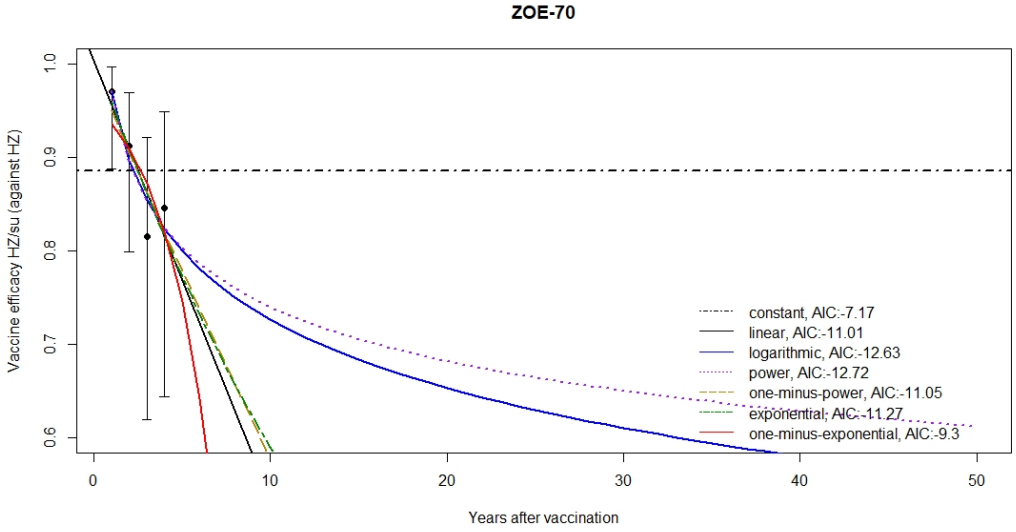
$$VE_i = 0.9702 - 0.1058 * log(years_i)$$

- Shortest duration of protection: One-minus-exponential

$$VE_i = 1 - (e^{(log(0.0456) + 0.3434 * years_i)})$$



(a)



(b)

Fig. S6 Fitted functions to the vaccine efficacy of HZ/su against HZ for the modified vaccinated cohorts during the study period over time in adults (a) 50-69 years (ZOE-50) and (b) ≥70 years (ZOE-70). Bars represent 95%CI.

S4 Input for the scenario analyses

We found that the age-specific proportion of post-herpetic neuralgia (PHN) and the distribution of severity for HZ and PHN differed quite substantially depending on the data source used. Therefore, we opted to perform a scenario analysis in which we evaluate the impact on our results when using two other data sources to inform quality-adjusted life years (QALY) lost associated with HZ and PHN (Table S3). In one scenario, we use the estimates available from Oxman *et al.* (2005) [3]. In a second scenario, we use QALYs lost and treatment cost estimates based on the severity-of-illness (SOI) score (Table 1). This approach was used and described in a previously published health eco-

nomic evaluation for vaccination with ZVL in Belgium [13]. The SOI score was derived from a prospective study conducted in East London [14, 15]. A model was fitted on this data [14, 15] to estimate the average SOI score in function of age. Subsequently, the QALY loss for an average HZ episode was estimated in function of the SOI score (Table S3).

Table S3 Model inputs for scenario analysis

Parameter	**Estimate**[a]		**Source**
Proportion of PHN			[3]
<70years	0.069		
≥70years	0.185		
Proportion of patients according to pain severity	**HZ**	**PHN**	[3][b]
<70years			
no pain	0.27	NA	
mild pain	0.41	NA	
moderate pain	0.18	0.51	
severe pain	0.14	0.49	
≥70years			
no pain	0.26	NA	
mild pain	0.32	NA	
moderate pain	0.23	0.33	
severe pain	0.14	0.67	
SOI for an average episode[c]	$e^{0.365+0.022\times Age_i+0.673\times Gender+\frac{1.453^2}{2}}$		[13]
QALYs lost for an average episode	$\frac{0.271+0.790\times SOI^{0.608}}{52}$		[13]
Cost hospitalised patient[d]	$3766.193+5.733\times SOIS_H\times\frac{0.379\times\pi}{sin(0.379\times\pi)}$		[13]
Cost ambulatory patient[d]	$e^{2.055+0.534\times log(SOIS_A+0.1}\times\frac{0.679\times\pi}{sin(0.679\times\pi)}$		[13]

Abbreviations: SOI: Severity-of-illness score; QALY: Quality-Adjusted-Life-Year; HZ: herpes zoster.
[a] We did not consider an uncertainty distribution around the estimate of the parameter.
[b] We did not have access to the raw data. Therefore, we gathered information from published health economic evaluations. [c] Gender is defined as a constant, namely 27/56, which represents the number of females in the total sample. This approach is used since we did not perform the analysis separate for sex. [d] The average SOI scores for a hospitalised patient (SOI_H) and for an ambulatory patient (SOI_A) can be found in Table 2 of Bilcke *et al.* (2012) [13].

S5 Results

The next section displays additional results, to which is referenced in the main article. More information on the results can be found in the main article.

Table S4 The number needed to vaccinate to avoid one HZ case according to the different vaccination strategies. We report the mean (median; 95%CrI) from 5,000 Monte Carlo simulations.

Vaccinated age cohort	**ZVL**	**ZVL+Booster**	**HZ/su (Optimistic)**	**HZ/su (Pessimistic)**
50	81 (80; 64-106)	36 (36; 30-43)	12 (12; 10-14)	48 (48; 38-63)
60	46 (45; 38-56)	37 (36; 31-44)	16 (16; 14-20)	46 (45; 37-58)
70	94 (92; 73-125)	80 (79; 64-104)	20 (19; 15-27)	47 (46; 37-63)
80	320 (286; 192-641)	320 (286; 192-641)	23 (21; 14-46)	34 (31; 21-68)
85	728 (651; 393-1524)	728 (651; 393-1524)	29 (26; 17-58)	33 (29; 20-66)

Table S5 Avoided health and economic burden, using the method by Bilcke *et al.* (2012) [13] to estimate HZ-related QALYs and costs, when implementing vaccination against HZ of different Belgian age cohorts throughout their lifetime. We report the mean (median; 95% CrI) from 5,000 Monte Carlo simulations, discounted at 3% (costs) and 1.5% (QALYs).

Vaccination strategy	Avoided HZ cases	Avoided hospitalisations	Avoided PHN cases	Avoided HZ deaths	Life years gained	QALYs gained	Treatment cost saved (in million €)	Intervention cost (in million €)
50 years								
ZVL	903 (905; 682-1,131)	23 (22; 15-30)	86 (86; 66-107)	0.01 (0.01; 0-0.02)	0.16 (0.15; 0.05-0.31)	89.28 (89.42; 67.89-111.33)	0.21 (0.21; 0.17-0.27)	11.86
ZVL+Booster	2,027 (2,029; 1,678-2,369)	56 (57; 43-70)	226 (226; 189-262)	0.05 (0.05; 0.02-0.1)	0.81 (0.76; 0.27-1.6)	215.04 (215.08; 178.46-250.23)	0.50 (0.50; 0.42-0.57) 19.67	
HZ/su - Logarithmic	6,005 (6,004; 5,033-6,953)	195 (195; 159-232)	847 (849; 685-998)	2.16 (2.15; 1.93-2.4)	12.98 (12.94; 11.16-15.14)	718.18 (718.96; 594.06-836.54)	1.53 (1.53; 1.33-1.74)	24.13
HZ/su - 1-minus-exponential	1,516 (1,518; 1,143-1,903)	38 (38; 25-52)	145 (145; 111-181)	0.01 (0.01; 0-0.03)	0.27 (0.25; 0.09-0.53)	150.04 (150.12; 113.75-187.71)	0.36 (0.36; 0.28-0.45)	24.13
60 years								
ZVL	1,495 (1,496; 1,207-1,788)	44 (44; 32-56)	184 (184; 149-219)	0.05 (0.05; 0.02-0.1)	0.88 (0.82; 0.29-1.74)	166.27 (166.26; 134.48-198.54)	0.43 (0.43; 0.35-0.51)	11.10
ZVL+Booster	1,864 (1,864; 1,547-2,185)	56 (57; 43-69)	245 (245; 204-285)	0.18 (0.18; 0.13-0.24)	2.19 (2.13; 1.5-3.16)	213.34 (213.3; 177.47-249.12)	0.54 (0.54; 0.45-0.62)	17.37
HZ/su - Logarithmic	4,218 (4,224; 3,456-4,936)	144 (144; 114-173)	639 (641; 510-761)	1.73 (1.72; 1.54-1.93)	10.74 (10.7; 9.16-12.59)	524.44 (526.02; 424.53-616.98)	1,27 (1.27; 1.08-1.44)	22.60

Continue on the next page

Table S5 Avoided health and economic burden, using the method by Bilcke *et al.* (2012) [13] to estimate HZ-related QALYs and costs, when implementing vaccination against HZ of different Belgian age cohorts throughout their lifetime. We report the mean (median; 95% CrI) from 5,000 Monte Carlo simulations, discounted at 3% (costs) and 1.5% (QALYs). (cont.)

Vaccination strategy	Avoided HZ cases	Avoided hospitalisations	Avoided PHN cases	Avoided HZ deaths	Life years gained	QALYs gained	Treatment cost saved (in million €)	Intervention cost (in million €)
HZ/su - 1-minus-exponential	1,500 (1,501; 1,162-1,839)	45 (45; 30-57)	174 (174; 135-213)	0.05 (0.05; 0.02-0.11)	0.94 (0.88; 0.31-1.85)	163.13 (163.24; 126.56-199.69)	0.44 (0.44; 0.34-0.52)	22.60
70 years								
ZVL	580 (580; 427-730)	19 (19; 13-25)	93 (93; 69-117)	0.15 (0.15; 0.13-0.18)	1.61 (1.6; 1.36-1.9)	72.88 (72.87; 54.13-91.29)	0.19 (0.19; 0.15-0.24)	8.77
ZVL+Booster	675 (676; 513-835)	23 (23; 17-30)	113 (113; 86-140)	0.23 (0.23; 0.19-0.26)	2.13 (2.13; 1.82-2.49)	86.48 (86.53; 66.34-106.25)	0.23 (0.23; 0.19-0.28)	12.32
HZ/su - Logarithmic	2,772 (2,786; 1,970-3,482)	107 (107; 78-135)	501 (505; 350-636)	2.1 (2.09; 1.88-2.32)	12.27 (12.25; 10.83-13.88)	380.84 (383.16; 270.48-478.64)	1.00 (1.00; 0.80-1.19)	17.84
HZ/su - 1-minus-exponential	1,154 (1,155; 850-1,453)	38 (38; 25-50)	186 (186; 137-234)	0.32 (0.32; 0.27-0.38)	3.41 (3.4; 2.9-4.01)	145.22 (145.28; 107.96-181.9)	0.39 (0.39; 0.30-0.48)	17.84
80 years								
ZVL	111 (112; 50-167)	5 (5; 3-8)	23 (24; 11-35)	0.08 (0.08; 0.07-0.1)	0.61 (0.61; 0.53-0.71)	15.78 (15.99; 7.45-23.47)	0.05 (0.05; 0.04-0.07)	5.27
ZVL+Booster	111 (112; 50-167)	5 (5; 3-8)	23 (24; 11-35)	0.08 (0.08; 0.07-0.1)	0.61 (0.61; 0.53-0.71)	15.78 (15.99; 7.45-23.47)	0.05 (0.05; 0.04-0.07)	6.32
HZ/su - Logarithmic	1,527 (1,550; 694-2,252)	70 (70; 43-98)	304 (308; 138-448)	1.94 (1.94; 1.75-2.15)	8.33 (8.31; 7.43-9.3)	228.15 (231.45; 108.49-332.6)	0.70 (0.70; 0.48-0.91)	10.72
HZ/su - 1-minus-exponential	1,032 (1,048; 469-1,522)	49 (48; 30-67)	210 (213; 96-309)	0.79 (0.78; 0.68-0.9)	5.01 (5; 4.32-5.77)	149.63 (151.72; 70.83-218)	0.48 (0.48; 0.33-0.63)	10.72
85 years								
ZVL	36 (36; 15-60)	2 (2; 1-3)	7 (7; 3-11)	0.03 (0.03; 0.03-0.04)	0.17 (0.17; 0.15-0.2)	5.44 (5.4; 2.41-8.83)	0.02 (0.02; 0.01-0.03)	3.87

Continue on the next page

Table S5 Avoided health and economic burden, using the method by Bilcke *et al.* (2012) [13] to estimate HZ-related QALYs and costs, when implementing vaccination against HZ of different Belgian age cohorts throughout their lifetime. We report the mean (median; 95% CrI) from 5,000 Monte Carlo simulations, discounted at 3% (costs) and 1.5% (QALYs). (cont.)

Vaccination strategy	**Avoided HZ cases**	**Avoided hospitalisations**	**Avoided PHN cases**	**Avoided HZ deaths**	**Life years gained**	**QALYs gained**	**Treatment cost saved (in million €)**	**Intervention cost (in million €)**
ZVL+Booster	36 (36; 15-60)	2 (2; 1-3)	7 (7; 3-11)	0.03 (0.03; 0.03-0.04)	0.17 (0.17; 0.15-0.2)	5.44 (5.4; 2.41-8.83)	0.02 (0.02; 0.01-0.03)	4.12
HZ/su - Logarithmic	909 (915; 404-1,371)	39 (39; 24-54)	173 (174; 77-260)	1.58 (1.58; 1.42-1.75)	5.07 (5.06; 4.58-5.59)	141.15 (142.15; 65.7-210.67)	0.41 (0.42; 0.28-0.55)	7.87
HZ/su - 1-minus-exponential	795 (800; 355-1,205)	33 (33; 20-45)	151 (152; 67-229)	0.75 (0.75; 0.67-0.83)	3.29 (3.28; 2.93-3.67)	120.74 (121.54; 55.68-181.36)	0.35 (0.35; 0.24-0.47)	7.87

Table S6 Avoided health and economic burden, using the proportions reported by Oxman *et al.* (2005) [3] to estimate disease severity, when implementing vaccination against HZ of different Belgian age cohorts throughout their lifetime. We report the mean (median; 95% CrI) from 5,000 Monte Carlo simulations, discounted at 3% (costs) and 1.5% (QALYs).

Vaccination strategy	Avoided HZ cases	Avoided hospitalisations	Avoided PHN cases	Avoided HZ deaths	Life years gained	QALYs gained	Treatment cost saved (in million €)	Intervention cost (in million €)
50 years								
ZVL	903 (905; 682-1,131)	23 (22; 15-30)	62 (62; 47-78)	0.01 (0.01; 0-0.02)	0.16 (0.15; 0.05-0.31)	29.24 (28.86; 18.95-41.97)	0.25 (0.25; 0.19-0.31)	11.86
ZVL+Booster	2,027 (2,029; 1,678-2,369)	56 (57; 43-70)	161 (161; 135-186)	0.05 (0.05; 0.02-0.1)	0.81 (0.76; 0.27-1.6)	77.57 (77; 56.07-102.43)	0.55 (0.55; 0.45-0.67)	19.67
HZ/su - Logarithmic	6,005 (6,004; 5,033-6,953)	195 (195; 159-232)	726 (728; 578-866)	2.16 (2.15; 1.93-2.4)	12.98 (12.94; 11.16-15.14)	379.01 (376.4; 273.13-500.24)	1.74 (1.74; 1.46-2.06)	24.13
HZ/su - 1-minus-exponential	1,516 (1,518; 1,143-1,903)	38 (38; 25-52)	105 (105; 79-131)	0.01 (0.01; 0-0.03)	0.27 (0.25; 0.09-0.53)	49.1 (48.42; 31.77-70.56)	0.42 (0.41; 0.32-0.53)	24.13
60 years								
ZVL	1,495 (1,496; 1,207-1,788)	44 (44; 32-56)	127 (127; 105-150)	0.05 (0.05; 0.02-0.1)	0.88 (0.82; 0.29-1.74)	62.35 (62.08; 44.55-82.54)	0.47 (0.47; 0.38-0.57)	11.10
ZVL+Booster	1,864 (1,864; 1,547-2,185)	56 (57; 43-69)	196 (196; 163-229)	0.18 (0.18; 0.13-0.24)	2.19 (2.13; 1.5-3.16)	99.24 (98.45; 72.41-129.51)	0.61 (0.60; 0.50-0.73)	17.37
HZ/su - Logarithmic	4,218 (4,224; 3,456-4,936)	144 (144; 114-173)	553 (555; 433-664)	1.73 (1.72; 1.54-1.93)	10.74 (10.7; 9.16-12.59)	291.31 (289.34; 207.59-388.34)	1.43 (1.43; 1.18-1.70)	22.60
HZ/su - 1-minus-exponential	1,500 (1,501; 1,162-1,839)	45 (45; 30-57)	103 (104; 80-127)	0.05 (0.05; 0.02-0.11)	0.94 (0.88; 0.31-1.85)	49.24 (48.87; 32.57-68.48)	0.47 (0.46; 0.36-0.57)	22.60
70 years								
ZVL	580 (580; 427-730)	19 (19; 13-25)	107 (107; 79-135)	0.15 (0.15; 0.13-0.18)	1.61 (1.6; 1.36-1.9)	57.49 (56.82; 38.76-80.19)	0.25 (0.25; 0.19-0.31)	8.77
ZVL+Booster	675 (676; 513-835)	23 (23; 17-30)	125 (125; 95-154)	0.23 (0.23; 0.19-0.26)	2.13 (2.13; 1.82-2.49)	67.23 (66.49; 46.54-92.56)	0.29 (0.29; 0.23-0.36)	12.32
HZ/su - Logarithmic	2,772 (2,786; 1,970-3,482)	107 (107; 78-135)	513 (515; 364-644)	2.1 (2.09; 1.88-2.32)	12.27 (12.25; 10.83-13.88)	279.45 (277.12; 184.88-387.44)	1.18 (1.18; 0.92-1.46)	17.84

Continue on the next page

Table S6 Avoided health and economic burden, using the proportions reported by Oxman *et al.* (2005) [3] to estimate disease severity, when implementing vaccination against HZ of different Belgian age cohorts throughout their lifetime. We report the mean (median; 95% CrI) from 5,000 Monte Carlo simulations, discounted at 3% (costs) and 1.5% (QALYs). (cont.)

Vaccination strategy	**Avoided HZ cases**	**Avoided hospitalisations**	**Avoided PHN cases**	**Avoided HZ deaths**	**Life years gained**	**QALYs gained**	**Treatment cost saved (in million €)**	**Intervention cost (in million €)**
HZ/su - 1-minus-exponential	1,154 (1,155; 850-1,453)	38 (38; 25-50)	213 (214; 157-269)	0.32 (0.32; 0.27-0.38)	3.41 (3.4; 2.9-4.01)	114.6 (113.27; 77.08-159.59)	0.49 (0.49; 0.37-0.63)	17.84
80 years								
ZVL	111 (112; 50-167)	5 (5; 3-8)	21 (21; 9-31)	0.08 (0.08; 0.07-0.1)	0.61 (0.61; 0.53-0.71)	11.3 (11.27; 5.12-17.92)	0.06 (0.06; 0.04-0.08)	5.27
ZVL+Booster	111 (112; 50-167)	5 (5; 3-8)	21 (21; 9-31)	0.08 (0.08; 0.07-0.1)	0.61 (0.61; 0.53-0.71)	11.3 (11.27; 5.12-17.92)	0.06 (0.06; 0.04-0.08)	6.32
HZ/su - Logarithmic	1,527 (1,550; 694-2,252)	70 (70; 43-98)	282 (287; 128-417)	1.94 (1.94; 1.75-2.15)	8.33 (8.31; 7.43-9.3)	155.53 (155.14; 71.03-242.32)	0.76 (0.76; 0.51-1.03)	10.72
HZ/su - 1-minus-exponential	1,032 (1,048; 469-1,522)	49 (48; 30-67)	191 (194; 87-281)	0.79 (0.78; 0.68-0.9)	5.01 (5; 4.32-5.77)	104.51 (104.23; 47.24-164.04)	0.54 (0.54; 0.36-0.73)	10.72
85 years								
ZVL	36 (36; 15-60)	2 (2; 1-3)	7 (7; 3-11)	0.03 (0.03; 0.03-0.04)	0.17 (0.17; 0.15-0.2)	3.68 (3.62; 1.59-6.14)	0.02 (0.02; 0.01-0.03)	3.87
ZVL+Booster	36 (36; 15-60)	2 (2; 1-3)	7 (7; 3-11)	0.03 (0.03; 0.03-0.04)	0.17 (0.17; 0.15-0.2)	3.68 (3.62; 1.59-6.14)	0.02 (0.02; 0.01-0.03)	4.12
HZ/su - Logarithmic	909 (915; 404-1,371)	39 (39; 24-54)	168 (169; 75-254)	1.58 (1.58; 1.42-1.75)	5.07 (5.06; 4.58-5.59)	92.68 (92.15; 41.73-147)	0.45 (0.44; 0.30-0.61)	7.87
HZ/su - 1-minus-exponential	795 (800; 355-1,205)	33 (33; 20-45)	147 (148; 66-223)	0.75 (0.75; 0.67-0.83)	3.29 (3.28; 2.93-3.67)	79.89 (79.31; 35.62-127.53)	0.39 (0.39; 0.26-0.53)	7.87

Table S7 ICER compared to the next best alternative, in addition to Table S6

Vaccination strategy	50 years	60 years	70 years	80 years	85 years
Comparison with HZ/su - Logarithmic					
ZVL	dominated by HZ/su	dominated by HZ/su	dominated by HZ/su	dominated by HZ/su	dominated by HZ/su
ZVL+Booster	dominated by HZ/su	dominated by HZ/su	dominated by HZ/su	dominated by HZ/su	dominated by HZ/su
HZ/su - Logathithmic	ICER HZ/su vs no vaccination: €59,069 per QALY gained	ICER HZ/su vs no vaccination: €72,740 per QALY gained	ICER HZ/su vs no vaccination: €59507 per QALY gained	ICER HZ/su vs no vaccination: €64,251 per QALY gained	ICER HZ/su vs no vaccination: €79,777 per QALY gained
Comparison with HZ/su - 1-minus-exponential					
ZVL	dominated by ZVL+Booster	dominated by ZVL+Booster	ICER ZVL vs no vaccination €146,926 per QALY gained	dominated by HZ/su	dominated by HZ/su
ZVL+Booster	ICER ZVL+Booster vs no vaccination: €248,240 per QALY gained	ICER ZVL+Booster vs ZVL €169,306 per QALY gained	dominated by HZ/su	dominated by HZ/su	dominated by HZ/su
HZ/su - 1-minus-exponential	dominated by ZVL+Booster	dominated by ZVL+Booster	ICER HZ/su vs ZVL: €150,864 per QALY gained	ICER HZ/su vs no vaccination: €97,928 per QALY gained	ICER HZ/su vs no vaccination: €93,474 per QALY gained

Table S8 Additional results for the probabilistic threshold analysis carried out for calculating the maximum vaccine price per dose (€), presented in Table 4.

		Generalised additive model				
WTP value per QALY gained	**Vaccinated age cohort**	θ_i^*	Time[a]	95% CrI	B_{retain}/B	Time[b]
Varying the price per dose (€) of HZ/su assuming a logarithmic waning						
€30,000	50	37.49	0.09	37.04-38.83	1000/1000	54.51
	60	26.90	0.22	25.29-26.59	1000/1000	57.71
	70	30.60	0.20	29.60-31.61	1000/1000	57.00
	80	31.80	0.22	30.74-33.33	1000/1000	56.54
	85	19.13	0.20	17.53-19.60	1000/1000	63.19
€35,000	50	46.46	0.26	45.46-47.06	1000/1000	64.94
	60	33.70	0.27	33.07-34.67	1000/1000	57.79
	70	38.66	0.18	38.66-40.22	1000/1000	58.95
	80	39.92	0.20	39.91-41.68	1000/1000	58.20
	85	25.41	0.21	23.81-26.06	1000/1000	58.69
€40,000	50	55.40	0.20	54.40-56.32	1000/1000	56.76
	60	40.99	0.29	40.45-41.93	1000/1000	57.47
	70	46.74	0.21	45.14-47.44	1000/1000	57.26
	80	48.03	0.20	46.25-49.62	1000/1000	56.26
	85	31.78	0.19	30.35-33.36	1000/1000	56.36
€45,000	50	64.37	0.21	63.17-65.34	1000/1000	56.03
	60	48.33	0.21	47.06-48.87	1000/1000	56.88
	70	54.84	0.21	53.56-55.99	1000/1000	56.36
	80	56.10	0.20	54.55-57.28	1000/1000	56.32
	85	38.14	0.20	37.42-40.39	1000/1000	56.25
€50,000	50	73.32	0.21	72.78-75.06	1000/1000	61.29
	60	55.60	0.23	54.60-56.62	1000/1000	61.91
	70	62.93	0.23	60.54-63.44	1000/1000	61.16
	80	64.18	0.22	60.92-65.07	1000/1000	60.51
	85	44.45	0.19	43.34-46.50	1000/1000	60.23
Varying the price per dose (€) of HZ/su assuming a 1-exponential waning						
€30,000	50	None[c]	0.1	NA-NA	1000/1000	63.49
	60	None	0.34	NA-NA	1000/1000	69.56
	70	None	0.28	NA-N	1000/1000	65.52
	80	13.24	0.28	12.40-13.96	1000/1000	77.12
	85	12.61	0.23	11.65-13.30	1000/1000	60.59
€35,000	50	None	0.28	NA-NA	1000/1000	59.83
	60	None	0.31	NA-NA	1000/1000	59.92
	70	None	0.26	NA-NA	1000/1000	63.33
	80	18.75	0.27	17.53-19.30	1000/1000	59.93
	85	17.94	0.26	16.19-18.38	1000/1000	62.91
€40,000	50	None	0.30	NA-NA	1000/1000	72.31
	60	None	0.30	NA-NA	1000/1000	74.03
	70	0.92	0.29	0.14-1.57	945/1000	70.66
	80	24.23	0.25	23.02-24.97	1000/1000	64.48
	85	23.31	0.20	21.52-23.88	1000/1000	62.76
€45,000	50	None	0.41	NA-NA	1000/1000	62.69
	60	None	0.24	NA-NA	1000/1000	62.83
	70	3.93	0.20	3.53-4.66	1000/1000	63.25
	80	29.74	0.21	28.45-31.04	1000/1000	62.50
	85	28.71	0.22	26.90-29.64	1000/1000	62.40
€50,000	50	None	0.22	NA-NA	1000/1000	62.77
	60	None	0.29	NA-NA	1000/1000	66.24
	70	6.89	0.31	6.74-7.90	1000/1000	64.78
	80	35.25	0.26	34.54-37.42	1000/1000	46.37
	85	34.12	0.16	33.18-36.61	1000/1000	46.16
Varying the price per dose (€) of Zostavax						
€30,000	50	None	0.15	NA-NA	1000/1000	121.76

Continue on the next page

Table S8 Additional results for the probabilistic threshold analysis carried out for calculating the maximum vaccine price per dose (€), presented in Table 4 (cont.)

		Generalised additive model				
WTP value per QALY gained	**Vaccinated age cohort**	θ_i^*	Time[a]	95% CrI	B_{retain}/B	Time[b]
	60	1.21	0.69	NA-NA	992/1000	182.66
	70	None	0.76	NA-NA	1000/1000	145.35
	80	None	0.41	NA-NA	1000/1000	105.60
	85	None	0.32	NA-NA	1000/1000	115.66
€35,000	50	None	0.36	NA-NA	1000/1000	116.31
	60	4.81	0.36	4.55-5.56	1000/1000	116.44
	70	None	0.34	NA-NA	1000/1000	116.46
	80	None	0.38	NA-NA	1000/1000	119.45
	85	None	0.34	NA-NA	1000/1000	114.87
€40,000	50	None	0.30	NA-NA	1000/1000	115.98
	60	8.44	0.30	8.10-913	1000/1000	114.46
	70	0.71	0.44	0.20-1.28	795/1000	114.22
	80	None	0.29	NA-NA	1000/1000	116.75
	85	None	0.41	NA-NA	1000/1000	118.59
€45,000	50	None	0.39	NA-NA	1000/1000	120.55
	60	12.07	0.35	11.44-12.50	1000/1000	115.60
	70	3.66	0.35	3.21-4.25	1000/1000	117.62
	80	None	0.50	NA-NA	1000/1000	117.59
	85	None	0.30	NA-NA	1000/1000	115.21
€50,000	50	None	0.32	NA-NA	1000/1000	114.53
	60	15.67	0.34	14.72-16.07	1000/1000	116.15
	70	6.65	0.29	6.37-7.54	1000/1000	87.63
	80	None	0.22 NA-NA		1000/1000	68.49
	85	None	0.23	NA-NA	1000/1000	70.60
Varying the price per dose (€) of Zostavax with a booster after 10 years						
€30,000	50	None	0.16	NA-NA	1000/1000	104.33
	60	None	0.48	NA-NA	1000/1000	103.44
	70	None	0.35	NA-NA	1000/1000	103.56
	80	None	0.33	NA-NA	1000/1000	110.15
	85	None	0.29	NA-NA	1000/1000	103.20
€35,000	50	None	0.34	NA-NA	1000/1000	100.62
	60	1.35	0.29	0.62-1.93	998/1000	103.88
	70	None	0.34	NA-NA	1000/1000	105.57
	80	None	0.32	NA-NA	1000/1000	102.71
	85	None	0.39	NA-NA	1000/1000	103.57
€40,000	50	None	0.33	NA-NA	1000/1000	102.71
	60	4.68	0.36	4.52-5.32	1000/1000	102.62
	70	None	0.34	NA-NA	1000/1000	103.55
	80	None	0.34	NA-NA	1000/1000	102.19
	85	None	0.34	NA-NA	1000/1000	102.11
€45,000	50	None	0.30	NA-NA	1000/1000	103.20
	60	7.94	0.32	7.73-8.70	1000/1000	90.54
	70	None	0.25	NA-NA	998/1000	82.20
	80	None	0.42	NA-NA	1000/1000	123.73
	85	None	0.43	NA-NA	1000/1000	108.39
€50,000	50	2.33	0.38	1.85-3.02	1000/1000	106.13
	60	11.27	0.34	10.87-11.74	1000/1000	101.25
	70	1.98	0.42	0.87-2.40	1000/1000	106.35
	80	None	0.35	NA-NA	1000/1000	108.81
	85	None	0.33	NA-NA	1000/1000	140.32

Notation: θ_i^* = threshold value(s), if present, for θ_i, the parameter of interest; B_{retain}= number of bootstrap samples retained to calculate the 95% credible interval (CrI).
[a] indicates the time needed to perform the generalized additive model.
[b] indicates the time needed to perform the bootstrap. [c] indicates the vaccination strategy will never become the preferred strategy over no vaccination.

S6 CHEERS checklist

CHEERS Checklist
Items to include when reporting economic evaluations of health interventions

The **ISPOR CHEERS Task Force Report**, *Consolidated Health Economic Evaluation Reporting Standards (CHEERS)—Explanation and Elaboration: A Report of the ISPOR Health Economic Evaluations Publication Guidelines Good Reporting Practices Task Force*, provides examples and further discussion of the 24-item CHEERS Checklist and the CHEERS Statement. It may be accessed via the *Value in Health* or via the ISPOR Health Economic Evaluation Publication Guidelines – CHEERS: Good Reporting Practices webpage: http://www.ispor.org/TaskForces/EconomicPubGuidelines.asp

Section/item	Item No	Recommendation	Reported on page No/ line No
Title and abstract			
Title	1	Identify the study as an economic evaluation or use more specific terms such as "cost-effectiveness analysis", and describe the interventions compared.	title
Abstract	2	Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions.	abstract
Introduction			
Background and objectives	3	Provide an explicit statement of the broader context for the study. Present the study question and its relevance for health policy or practice decisions.	intro §1-3 intro §4
Methods			
Target population and subgroups	4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	methods 2.1 line 6
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	intro §4
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	methods 2.1 last sentence
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	methods 2.1 lines 7-10 + intro §4
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	methods 2.1 lines 6-7
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	methods 2.1 last sentence
Choice of health outcomes	10	Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.	methods 2.2 qaly loss
Measurement of effectiveness	11a	*Single study-based estimates:* Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.	NA

	11b	*Synthesis-based estimates:* Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.	
Measurement and valuation of preference based outcomes	12	If applicable, describe the population and methods used to elicit preferences for outcomes.	methods 2.2 vaccine characteristics
Estimating resources and costs	13a	*Single study-based economic evaluation:* Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	NA
	13b	*Model-based economic evaluation:* Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	NA
Currency, price date, and conversion	14	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.	methods 2.2 §1
Choice of model	15	Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly recommended.	methods 2.2 second sentence
Assumptions	16	Describe all structural or other assumptions underpinning the decision-analytical model.	methods 2.1 + Fig 1
Analytical methods	17	Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.	methods 2.1
Results			
Study parameters	18	Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.	methods 2.2
Incremental costs and outcomes	19	For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.	Table 1
Characterising uncertainty	20a	*Single study-based economic evaluation:* Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact	Table 3
			NA

		of methodological assumptions (such as discount rate, study perspective).	
	20b	*Model-based economic evaluation:* Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.	Table 3 (uncertainty waning distribution) + Results 3.4
Characterising heterogeneity	21	If applicable, report differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.	NA
Discussion			
Study findings, limitations, generalisability, and current knowledge	22	Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge.	Discussion
Other			
Source of funding	23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.	see 'Funding'
Conflicts of interest	24	Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations.	see 'Conflicts of Interest'

For consistency, the CHEERS Statement checklist format is based on the format of the CONSORT statement checklist

The **ISPOR CHEERS Task Force Report** provides examples and further discussion of the 24-item CHEERS Checklist and the CHEERS Statement. It may be accessed via the *Value in Health* link or via the ISPOR Health Economic Evaluation Publication Guidelines – CHEERS: Good Reporting Practices webpage: http://www.ispor.org/TaskForces/EconomicPubGuidelines.asp

The citation for the CHEERS Task Force Report is:
Husereau D, Drummond M, Petrou S, et al. Consolidated health economic evaluation reporting standards (CHEERS)—Explanation and elaboration: A report of the ISPOR health economic evaluations publication guidelines good reporting practices task force. Value Health 2013;16:231-50.

References

1. Bilcke J, Ogunjimi B, Marais C, De Smet F, Callens M, et al. The health and economic burden of chickenpox and herpes zoster in Belgium. Epidemiology and Infection 2012; 140:2096–109. DOI: 10.1017/S0950268811002640
2. Bilcke J, Marais C, Ogunjimi B, Van Hoek AJ, Lejeune O, et al. Cost-utility of vaccination against chickenpox in children and against herpes zoster in elderly in Belgium. Tech. rep. Brussels: Belgian Health Care Knowledge Centre (KCE), 2011
3. Oxman M, Levin M, Johnson G, Schmader K, Straus S, et al. A Vaccine to Prevent Herpes Zoster and Postherpetic Neuralgia in Older Adults. New England Journal of Medicine 2005; 352:2271–84. DOI: 10.1056/NEJMoa051016
4. Schmader KE, Oxman MN, Levin MJ, Johnson G, Zhang JH, et al. Persistence of the efficacy of zoster vaccine in the shingles prevention study and the short-term persistence substudy. Clinical Infectious Diseases 2012; 55:1320–8. DOI: 10.1093/cid/cis638
5. Morrison VA, Johnson GR, Schmader KE, Levin MJ, Zhang JH, et al. Long-term persistence of zoster vaccine efficacy. Clinical Infectious Diseases 2015; 60:900–9. DOI: 10.1093/cid/ciu918
6. Vaccines and Related Biological Products Advisory Committee. FDA Clinical Briefing Document for Merck & Co., Inc. Zoster vaccine live (Oka/Merck) Zostavax. Tech. rep. FDA, 2005 :1–67
7. De Boer PT, Van Lier A, De Melker H, Van Wijck AJ, Wilschut JC, et al. Cost-effectiveness of vaccination of immunocompetent older adults against herpes zoster in the Netherlands: A comparison between the adjuvanted subunit and live-attenuated vaccines. BMC Medicine 2018; 16:1–18. DOI: 10.1186/s12916-018-1213-5
8. Schmader KE, Levin MJ, Gnann JW, McNeil SA, Vesikari T, et al. Efficacy, safety, and tolerability of herpes zoster vaccine in persons aged 50-59 years. Clinical Infectious Diseases 2012; 54:922–8. DOI: 10.1093/cid/cir970
9. Levin MJ, Schmader KE, Pang L, Williams-Diaz A, Zerbe G, et al. Cellular and humoral responses to a second dose of herpes zoster vaccine administered 10 years after the first dose among older adults. Journal of Infectious Diseases 2016; 213:14–22. DOI: 10.1093/infdis/jiv480
10. Lal H, Cunningham AL, Godeaux O, Chlibek R, Diez-Domingo J, et al. Efficacy of an adjuvanted herpes zoster subunit vaccine in older adults. New England Journal of Medicine 2015; 372:2087–96. DOI: 10.1056/NEJMoa1501184
11. Cunningham AL, Lal H, Kovac M, Chlibek R, Hwang SJ, et al. Efficacy of the herpes zoster subunit vaccine in adults 70 years of age or older. New England Journal of Medicine 2016; 375:1019–32. DOI: 10.1056/NEJMoa1603800
12. Vaccines and Related Biological Products Advisory Committee. Briefing document: Shingrix. Tech. rep. FDA, 2017. DOI: 10.7591/9781501741456-003. Available from: http://www.degruyter.com/view/books/9781501741456/9781501741456-003/9781501741456-003.xml
13. Bilcke J, Marais C, Ogunjimi B, Willem L, Hens N, et al. Cost-effectiveness of vaccination against herpes zoster in adults aged over 60 years in Belgium. Vaccine 2012; 30:675–84. DOI: 10.1016/j.vaccine.2011.10.036

14. Scott FT, Leedham-Green ME, Barrett-Muir WY, Hawrami K, Gallagher WJ, et al. A study of shingles and the development of postherpetic neuralgia in east London. Journal of Medical Virology 2003; 70:25–9. DOI: 10.1002/jmv.10316

15. Scott FT, Johnson RW, Leedham-Green M, Davies E, Edmunds WJ, et al. The burden of Herpes Zoster: A prospective population based study. Vaccine 2006; 24:1308–14. DOI: 10.1016/j.vaccine.2005.09.026