Persistence of the Efficacy of Zoster Vaccine in the Shingles Prevention Study and the Short-Term Persistence Substudy

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Background. The Shingles Prevention Study (SPS; Department of Veterans Affairs Cooperative Study 403) demonstrated that zoster vaccine was efficacious through 4 years after vaccination. The Short-Term Persistence Substudy (STPS) was initiated after the SPS to further assess the persistence of vaccine efficacy.

Methods. The STPS re-enrolled 7320 vaccine and 6950 placebo recipients from the 38 546–subject SPS population. Methods of surveillance, case determination, and follow-up were analogous to those in the SPS. Vaccine efficacy for herpes zoster (HZ) burden of illness, incidence of postherpetic neuralgia (PHN), and incidence of HZ were assessed for the STPS population, for the combined SPS and STPS populations, and for each year through year 7 after vaccination.

Results. In the STPS as compared to the SPS, vaccine efficacy for HZ burden of illness decreased from 61.1% to 50.1%, vaccine efficacy for the incidence of PHN decreased from 66.5% to 60.1%, and vaccine efficacy for the incidence of HZ decreased from 51.3% to 39.6%, although the differences were not statistically significant. Analysis of vaccine efficacy in each year after vaccination for all 3 outcomes showed a decrease in vaccine efficacy after year 1, with a further decline thereafter. Vaccine efficacy was statistically significant for the incidence of HZ and the HZ burden of illness through year 5.

Conclusions. Vaccine efficacy for each study outcome was lower in the STPS than in the SPS. There is evidence of the persistence of vaccine efficacy through year 5 after vaccination but, vaccine efficacy is uncertain beyond that point.

Herpes zoster (HZ) results from the reactivation, multiplication, and spread of varicella-zoster virus (VZV) that remains latent in sensory neurons following earlier primary VZV infection (ie, varicella or chickenpox) [1]. Department of Veterans Affairs (VA) Cooperative Study 403: The Shingles Prevention Study was a randomized, double-blind, placebo-controlled efficacy trial of live attenuated Oka/Merck HZ vaccine (zoster vaccine) in 38 546 adults ≥60 years of age. The Shingles Prevention Study demonstrated that zoster vaccine reduced the HZ burden of illness by 61.1% (95% confidence interval [CI], 51.1–69.1), the incidence of postherpetic neuralgia (PHN) by 66.5% (95% CI, 47.5–79.2), and the incidence of HZ by 51.3% (95% CI, 44.2–57.6) through 4 years of postvaccination follow-up [2–4].

After the completion of the Shingles Prevention Study, a cohort of subjects was re-enrolled into a short-term persistence substudy. The Short-Term Persistence Substudy extended the follow-up of this cohort of subjects to collect data on the persistence of zoster vaccine efficacy for the 3 end points described above during the interval between the closeout of VA Cooperative Study 403 and the completion of the final data analysis. The Short-Term Persistence Substudy also provided a cohort of the original Shingles Prevention Study vaccine recipients who could subsequently be enrolled in a long-term persistence substudy to further assess the persistence of vaccine efficacy. In addition, data on the persistence of vaccine efficacy for each year after vaccination in the Shingles Prevention Study have not been published. Therefore, the objectives of this article are to assess the persistence of vaccine efficacy for the 3 study end points in the Short-Term Persistence Substudy population, the Shingles Prevention Study population, and the combined Shingles Prevention Study and Short-Term Persistence Substudy populations and to assess the persistence of vaccine efficacy for the 3 study end points for each year through year 7 after subjects received zoster vaccine or placebo in the Shingles Prevention Study.

METHODS

Study Design and Time Line
The Shingles Prevention Study was a randomized, double-blind, placebo-controlled clinical trial initiated in November 1998 [2]. All vaccine and placebo recipients were actively followed for new cases of HZ through September 2003. There was a break in surveillance for cases of HZ of approximately 15 months between the completion of the Shingles Prevention Study surveillance in September 2003 and resumption of follow-up in the Short-Term Persistence Substudy in December 2004.

Beginning in October 2005, open-label zoster vaccine was offered without charge to Shingles Prevention Study placebo recipients. Placebo recipients enrolled in the Short-Term Persistence Substudy completed the study upon receiving zoster vaccine, since they could then no longer serve as unvaccinated controls. The Short-Term Persistence Substudy subjects who were zoster vaccine recipients in the Shingles Prevention Study continued to be followed until the initiation of the Long-Term Persistence Substudy in March 2006.

Study Population and Sites
Participation in the Short-Term Persistence Substudy was limited by funding constraints to 12 of 22 original Shingles Prevention Study sites, with preference given to sites that had high enrollment. A telephone-based consent procedure to enroll subjects into the Short-Term Persistence Substudy was approved by the VA Cooperative Studies Program, the

Cooperative Studies Program Coordinating Center's Human Rights Committee, and local institutional review boards. Inclusion and exclusion criteria were the same as in the Shingles Prevention Study except that subjects who had previously received zoster vaccine on enrollment into the Shingles Prevention Study were not excluded. With 12 participating sites, we sought to enroll 15 000–20 000 subjects.

Follow-up
Active follow-up with surveillance for new cases of HZ was the same as in the Shingles Prevention Study. As in the Shingles Prevention Study, the threshold for evaluating suspected cases of HZ was set very low, to ensure "capture" of any mild, atypical, or vaccine-modified cases of HZ.

HZ Case Determination and End Point Measurements
Methods for evaluation of suspected cases of HZ, for diagnosis and management of cases of HZ, for measurement of HZ-associated pain and discomfort, and for determination of evaluable cases were the same as those used in the Shingles Prevention Study [2–6]. The only change from the Shingles Prevention Study was to reduce the frequency of contacts after week 4 from weekly to monthly. The burden of illness for each case of HZ (ie, the HZ severity of illness score) was defined as the area under the Zoster Brief Pain Inventory worst pain and discomfort severity-by-duration curve. The HZ burden of illness was defined as the sum of all of the HZ severity of illness scores in the group (eg, placebo recipients ≥70 years of age) divided by the person-years of observation. Subjects who did not develop HZ during the period of observation were assigned an HZ severity of illness score of 0.

Statistical Methods
The definition of HZ burden of illness and methods for calculating vaccine efficacy for study outcomes have been published elsewhere [2–5, 7]. The analysis of the incidence of postherpetic neuralgia and of HZ assumed a Poisson distribution for events and used a conditional exact method for calculating rates [8–10]. Data management and statistical programming were performed using SAS software [11], with exact CIs calculated using StatXact [12]. Vaccine efficacy for HZ burden of illness, incidence of postherpetic neuralgia, and incidence of HZ were determined for the entire Short-Term Persistence Substudy period (primary analysis) and for the combined population from the Shingles Prevention Study and Short-Term Persistence Substudy (secondary analyses). Analyses were stratified by age at time of randomization in the Shingles Prevention Study into the 2 prespecified age groups: 60–69 years and ≥70 years. To calculate the vaccine efficacy for incident HZ during a specific year after vaccination and age stratum, the number of HZ cases occurring within that year

and the number of person-years of follow-up for subjects in that year were determined for each treatment group, and vaccine efficacy was estimated as 1 – [(incidence of HZ among vaccine recipients)/(incidence of HZ among placebo recipients)]. Vaccine efficacy for incidence of PHN and for HZ burden of illness were calculated similarly. The Shingles Prevention Study and Short-Term Persistence Substudy populations were pooled by adding the number of HZ cases and the number of person-years of follow-up from the 2 studies for the overall calculation and were also calculated for each year after vaccination for the by-year postvaccination analysis. Results are presented as point estimates of event outcomes and as vaccine efficacies with 95% CIs. Follow-up time for the Short-Term Persistence Substudy subjects did not include the interval between 30 September 2003 (when surveillance for new cases

of HZ ceased in the Shingles Prevention Study) and their date of enrollment in the Short-Term Persistence Substudy, since HZ cases occurring during this gap in follow-up were not reportable and could not be validated according to study criteria. However, any Shingles Prevention Study subjects reporting that they experienced HZ during this gap in follow-up were not eligible to enroll in the Short-Term Persistence Substudy.

RESULTS

Study Subjects
Among the 12 sites, 21 198 (90.5%) of all subjects enrolled in the Shingles Prevention Study were screened for enrollment in the Short-Term Persistence Study over a 9-month period, nearly all by telephone-based interview. Of those screened, 14 270 (67.3%)
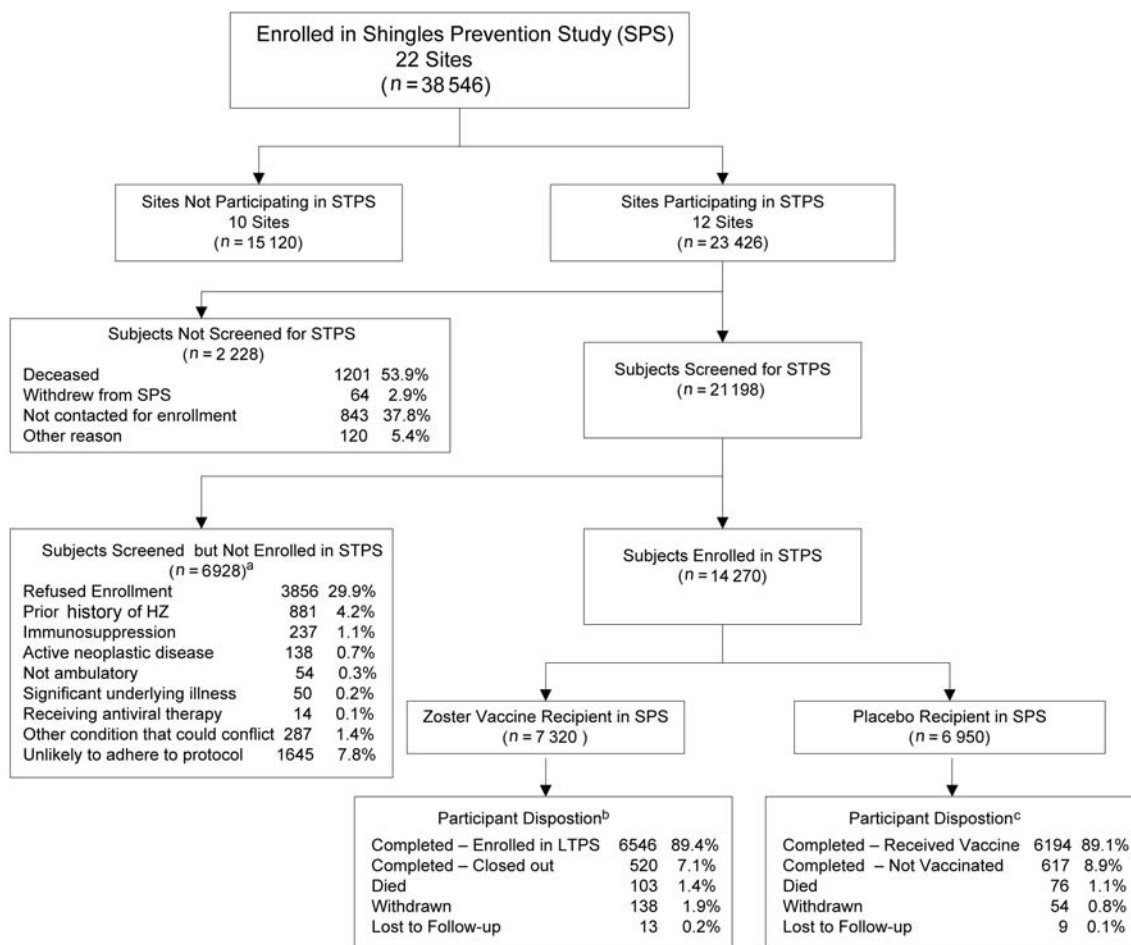
Figure 1. Participant characteristics and flow through the Short-Term Persistence Substudy (STPS). [a]Reasons are not mutually exclusive (ie, subjects may have had >1 reason for not enrolling in the STPS). [b]A total of 6546 subjects enrolled in the STPS agreed to enroll in the Long-Term Persistence Substudy (LTPS), and 520 enrolled in the STPS completed follow-up and a closeout interview but did not enroll in the LTPS. [c]A total of 6194 subjects received zoster vaccine in the STPS, at which time they completed a closeout interview, and follow-up in the STPS was terminated; and 617 were followed until they were offered but refused zoster vaccine, at which time they completed a closeout interview, and follow-up in STPS was terminated. Abbreviations: HZ, herpes zoster; SPS, Shingles Prevention Study.

(7320 vaccine recipients and 6950 placebo recipients) were enrolled in the Short-Term Persistence Substudy (Figure 1). The main reasons for subjects not enrolling were as follows: subjects declined participation (29.9%), subjects were considered unlikely to adhere to the protocol (7.8%), and subjects had a history of HZ occurring in the Shingles Prevention Study (4.2%; 3.2% of vaccine recipients and 5.1% of placebo recipients) (Figure 1). Except for history of HZ, other reasons for not enrolling in the STPS were comparable for the vaccine and placebo recipients. Subjects who enrolled in the Short-Term Persistence Substudy were younger when they enrolled into the Shingles Prevention Study than the subjects who did not enroll in the Short-Term Persistence Substudy (mean age, 68.6 years vs 70.6 years).

The mean age at time of enrollment into the Short-Term Persistence Substudy was 73.3 years for the vaccine and placebo recipients. There were no significant differences in race, sex, and general health status at the time of enrollment into the Shingles Prevention Study between the vaccine and placebo groups (data were not recorded at onset of the Short-Term Persistence Substudy).

Surveillance and Follow-up of Cases of HZ in the Short-Term Persistence Substudy

The vaccine recipients accrued more years of follow-up than the placebo recipients in the Short-Term Persistence Substudy (9967 years vs 6802 years) because of attrition among the placebo recipients due to administration of zoster vaccine to the Shingles Prevention Study placebo recipients. The mean follow-up time (±SD) was 0.98 ± 0.30 years for placebo recipients and 1.36 ± 0.29 years for the vaccine recipients. More than 96% of the zoster vaccine recipients and 98% of the placebo recipients completed closeout interviews (Figure 1).

A total of 703 rashes were evaluated during the 27 months of the Short-Term Persistence Substudy (with approximately 17 000 person-years of follow-up); 300 in the placebo group and 403 in the vaccine group. Of these rashes, 231 were clinically diagnosed by site investigators as suspected cases of HZ; 118 were in the placebo group, 113 were in the zoster vaccine group. Of the 113 subjects with suspected cases of HZ in the HZ vaccine group, 84 (74.3%) had evaluable cases of HZ. Of the 118 subjects with suspected cases of HZ in the placebo group, 95 (80.5%) had evaluable cases of HZ. HZ case determinations were made by polymerase chain reaction (PCR) assay for 168 subjects, by local virus culture for 1 subject, and by clinical events committee adjudication for 10 subjects for whom diagnostic specimens for PCR assay were not available or were inadequate. The Oka vaccine strain of VZV was not identified in any specimen.

Safety Monitoring

No serious adverse events occurred during the Short-Term Persistence Substudy that were judged possibly, probably, or definitely related to the vaccination. There was no significant difference in deaths between placebo recipients (1.12 deaths/100 person-years) and zoster vaccine recipients (1.03 deaths/100 person-years) (stratified log-rank $P = .173$).

Vaccine Efficacy for the Short-Term Persistence Substudy Population

The incidence of HZ in the zoster vaccine group was 8.4 cases/1000 person-years, compared with 14.0 cases/1000 person-years in the placebo group, and the incidence of PHN was 0.70 and 1.76 cases/1000 person-years, respectively (Table 1). Vaccine efficacy for the 3 outcome measures was 50.1% (95% CI, 14.1–71.0) for the HZ burden of illness, 60.1% (95% CI, −9.8 to 86.7) for the incidence of PHN, and 39.6% (95% CI, 18.2–55.5) for incidence of HZ (Table 2). The vaccine efficacy for the incidence of postherpetic neuralgia showed the largest treatment effect but was derived from only 19 cases of PHN, and thus the lower boundary of the 95% CI does not exclude 0.

Vaccine Efficacy in the Combined Short-Term Persistence Substudy and Shingles Prevention Study Populations

Surveillance in the Shingles Prevention Study primarily covered years 1–4 after vaccination, whereas surveillance in the Short-Term Persistence Substudy primarily covered years 5–7 after vaccination. Combining the Shingles Prevention Study and Short-Term Persistence Substudy increased the surveillance time in the zoster vaccine group by 17.1% (58 203 person-years in the Shingles Prevention Study plus 9967 person-years in the Short-Term Persistence Substudy) and by 11.8% in the placebo group (57 736 person-years in the Shingles Prevention Study plus 6802 person-years in the Short-Term Persistence Substudy). Vaccine efficacy for the combined study results for the 3 outcome measures was 58.6% (95% CI, 48.6–66.6) for the HZ burden of illness, 64.9% (95% CI, 47.4–77.0) for the incidence of PHN, and 48.7% (95% CI, 42.0–54.7) for the incidence of HZ (Table 2).

Vaccine Efficacy for Each Year After Vaccination

In the Shingles Prevention Study population, vaccine efficacy for the HZ burden of illness and vaccine efficacy for the incidence of HZ were significantly >0 for each year of follow-up through year 4 after vaccination (Table 2 and Figure 2A–C). Point estimates for vaccine efficacy for the incidence of PHN showed persistence of the vaccine effect, but these were not significant after year 2 within a given year because of the small number of cases of postherpetic neuralgia. Vaccine efficacy was greatest in the first year after vaccination for all 3 outcome measures. The vaccine efficacy for the HZ burden of illness declined from 79.2% in year 1 to 54.9% and 44.4% in years 2 and 3, respectively, but increased to 66.9% in year 4. The vaccine efficacy for the incidence of postherpetic neuralgia declined from 83.4% in year 1 to 69.8% in year 2. The

Table 1. Summary of Study Outcomes, by Year After Vaccination, in the Shingles Prevention Study (SPS) Population, the Short-Term Persistence Substudy (STPS) Population, and the Combined SPS and STPS Populations

Time Since Random-ization (Years)[a]	Zoster Vaccine (n = 19 270)						Placebo (n = 19 276)					
	Cases of HZ, No.	Subjects in Follow-up, No.	Total Follow-up Time, Person-Years	Observed Incidence of HZ, Cases/ 1000 Person-Years	Observed Incidence of PHN, Cases/ 1000 Person-Years	HZ Burden of Illness	Cases of HZ, No.	Subjects in Follow-up, No.	Total Follow-up Time, Person-Years	Observed Incidence of HZ, Cases/ 1000 Person-Years	Observed Incidence of PHN, Cases/ 1000 Person-Years	HZ Burden of Illness
Year 1	69	19 254	17 584	3.9	0.28	0.49	181	19 247	17 539	10.3	1.71	2.11
Year 2	102	19 024	18 869	5.4	0.37	0.82	198	18 948	18 731	10.6	1.23	1.84
Year 3	92	18 692	15 181	6.1	0.66	1.04	171	18 494	14 998	11.4	1.07	1.80
Year 4	49	11 689	6264	7.8	0.64	0.98	87	11 474	6158	14.1	1.62	2.42
Year 5	26	7197	3180	8.2	0.63	0.72	42	6887	2921	14.4	2.40	2.71
Year 6	48	7086	4850	9.9	0.82	1.82	47	6055	3295	14.3	1.21	2.39
Year 7[b]	13	4054	2243	5.8	0.89	1.44	11	2237	896	12.3	2.23	3.59
SPS												
Years 0–4.9	315	19 254	58 203	5.4	0.46	0.73	642	19 247	57 736	11.1	1.39	1.89
STPS												
Years 3.3–7.8	84	7320	9967	8.4	0.70	1.42	95	6950	6802	14.0	1.76	2.69
SPS + STPS Years Years 0–7.8	399	19 254	68 171	5.9	0.50	0.89	737	19 247	64 538	11.4	1.43	2.05

Abbreviations: HZ, herpes zoster; PHN, postherpetic neuralgia; SPS, Shingles Prevention Study; STPS, Short-Term Persistence Study.

[a] For the calculation of vaccine efficacy, HZ events and person-years of follow-up were pooled for SPS and STPS populations. For years 1, 2, and 3, 100% of person-years of follow-up were from SPS subjects. For year 4, 97% of person-years of follow-up were from SPS subjects, and 3% were from STPS subjects. For year 5, 16% of person-years of follow-up were from SPS subjects, and 84% were from STPS subjects. For years 6 and 7, 100% of person-years of follow-up were from STPS subjects.

[b] Year 7 includes a small number of events and person-years of follow-up from year 8 (111.5 person-years for the zoster vaccine group and 13.3 person-years of follow-up for the placebo group).

Table 2. Estimated Efficacy of Zoster Vaccine, by Year After Vaccination, in the Shingles Prevention Study (SPS) Population, the Short-Term Persistence Substudy (STPS) Population, and the Combined SPS and STPS Populations

Time Since Randomization (Years)[a]	Vaccine Efficacy for HZ BOI Point Estimate, % (95% CI)	Vaccine Efficacy for Incidence of PHN Point Estimate, % (95% CI)	Vaccine Efficacy for Incidence of HZ Point Estimate, % (95% CI)
Year 1	79.2 (66.8–86.9)	83.4 (56.7–95.0)	62.0 (49.6–71.6)
Year 2	54.9 (32.0–70.1)	69.8 (27.3–89.1)	48.9 (34.7–60.1)
Year 3	44.4 (17.6–62.5)	38.3 (−44.7 to 75.0)	46.8 (31.1–59.2)
Year 4	66.9 (37.5–82.5)	60.7 (−36.3 to 91.0)	44.6 (20.5–61.8)
Year 5	74.9 (48.6–87.7)	73.8 (−37.8 to 97.3)	43.1 (5.1–66.5)
Year 6	23.6 (−58.1 to 63.1)	32.0 (−100.0 to 87.3)	30.6 (−6.0 to 54.6)
Year 7[b]	72.5 (9.9–91.6)	60.0 (−4.5 to 97.1)	52.8 (−16.5 to 80.5)
SPS			
Years 0.0–4.9	61.1 (51.1–69.1)	66.5 (47.5–79.2)	51.3 (44.2–57.6)
STPS			
Years 3.3–7.8	50.1 (14.1–71.0)	60.1 (−9.8 to 86.7)	39.6 (18.2–55.5)
SPS + STPS			
Years 0.0–7.8	58.6 (48.6–66.6)	64.9 (47.4–77.0)	48.7 (42.0–54.7)

Abbreviations: BOI, burden of illness; CI, confidence interval; HZ, herpes zoster; PHN, postherpetic neuralgia; SPS, Shingles Prevention Study; STPS, Short-Term Persistence Study.

[a] For the calculation of vaccine efficacy, HZ events and person-years of follow-up were pooled for SPS and STPS for years 4 and 5 after vaccination. For year 4, 97% of person-years of follow-up were from SPS subjects, and 3% were from STPS subjects. For year 5, 16% of person-years of follow-up were from SPS subjects, and 84% were from STPS subjects. For years 6 and 7, 100% of person-years of follow-up were from STPS subjects.

[b] Year 7 includes a small number of person-years of follow-up from year 8 (111.5 person-years of follow-up for the zoster vaccine group and 13.3 person-years of follow-up for the placebo group).

vaccine efficacy for the incidence of HZ declined from 62.0% in year 1 to 48.9%, 46.8%, and 44.6% in years 2, 3, and 4, respectively.

Analysis of the combined Shingles Prevention Study and the Short-Term Persistence Substudy populations permitted an assessment of vaccine efficacy through 5 years after vaccination (Figure 2). Vaccine efficacy for the HZ burden of illness and for the incidence of PHN were both greater in year 5 than in year 4. However, the CIs for these 1-year interval estimates are wide, and thus the change in vaccine efficacy is not statistically significant. Vaccine efficacy on the incidence of HZ for year 5 (43.1%) was similar to that for year 4 (44.6%).
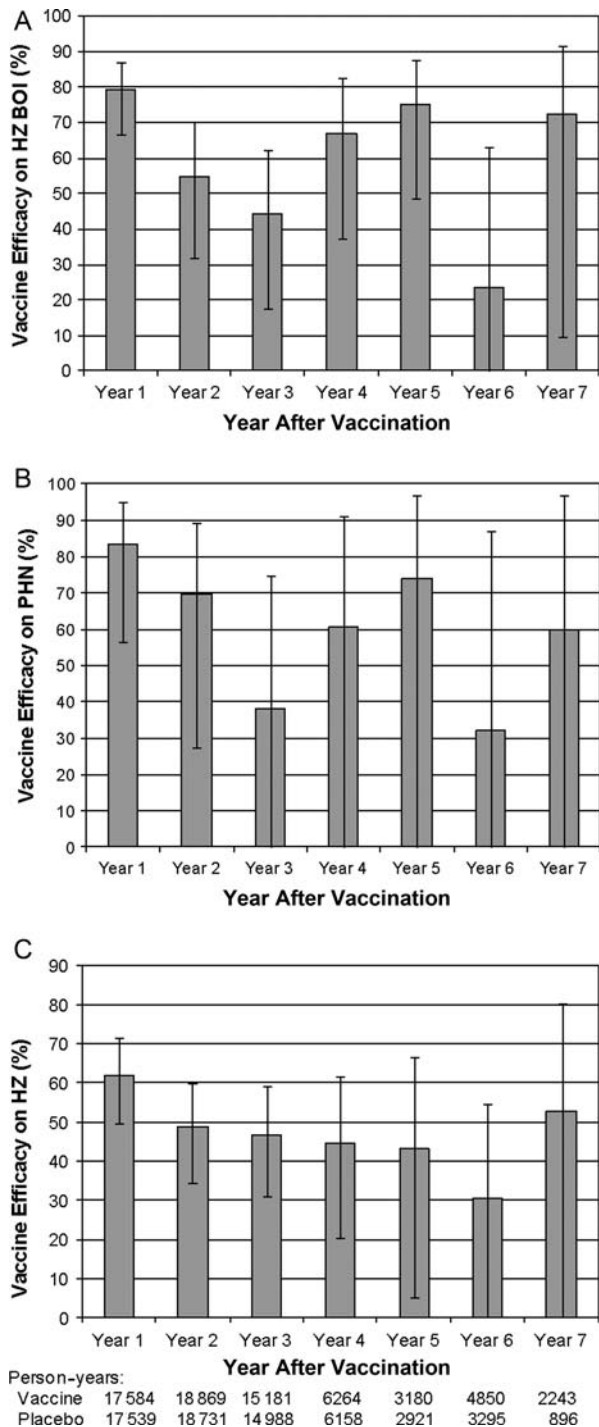
In the Short-Term Persistence Substudy population, results for year 6 show reductions in the point estimates for all 3 outcomes, but the CIs are wide. Year 6 results show a low point in vaccine efficacy for all 3 outcomes, with wide CIs (Figure 2) that are due to an increase in incidence of HZ among vaccine recipients and a decrease in the incidence of postherpetic neuralgia among placebo recipients followed in year 6 after vaccination (Figure 3).

DISCUSSION

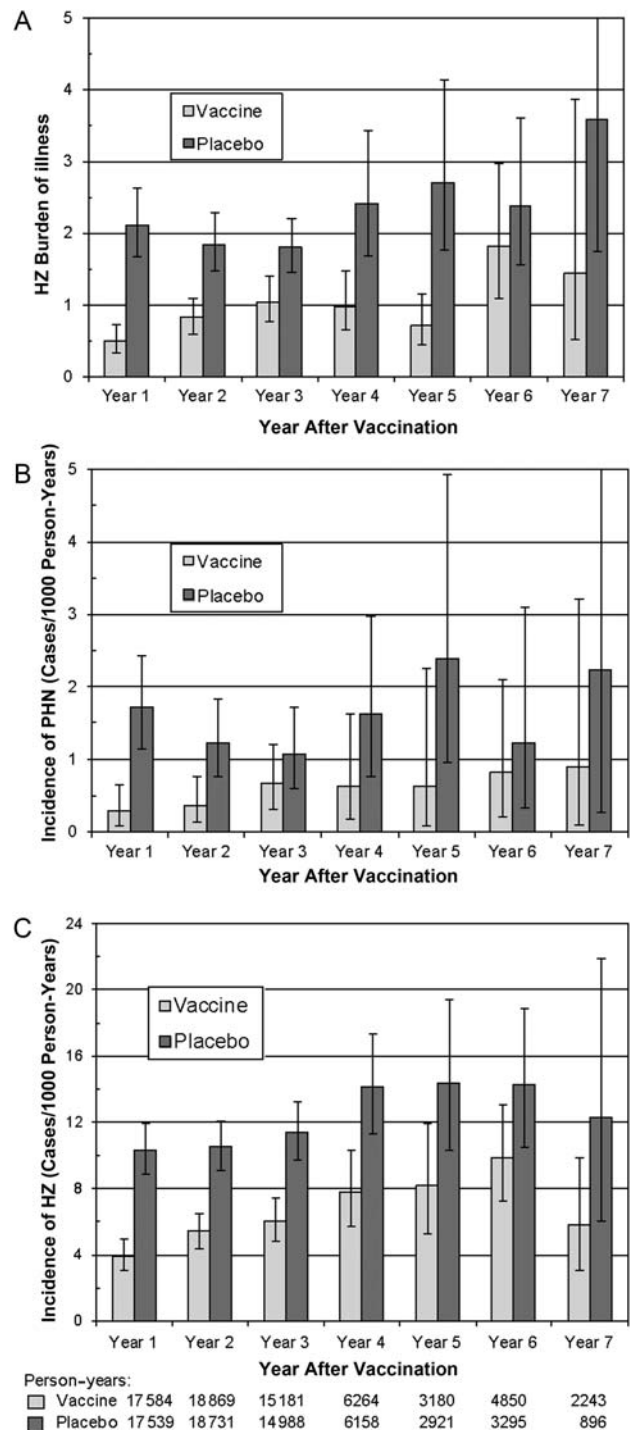Zoster vaccine reduced the HZ burden of illness by 50%, the incidence of PHN by 60%, and the incidence of HZ by nearly 40%, compared with placebo, in the Short-Term Persistence Substudy population evaluated from 3.3–7.8 years after vaccination. Compared with the Shingles Prevention Study population, vaccine efficacy in the Short-Term Persistence Substudy was 11.0 percentage points lower for the HZ burden of illness, 6.4 percentage points lower for the incidence of PHN, and 11.7 percentage points lower for the incidence of HZ. When the Shingles Prevention Study and Short-Term Persistence Substudy populations were combined, zoster vaccine reduced the HZ burden of illness by nearly 59%, the incidence of PHN by 65%, and the incidence of HZ by >48%, compared with placebo. These results suggest that the zoster vaccine continues to have benefit, albeit with a declining magnitude, beyond the median follow-up time of 3.1 years in the SPS.

When the data were analyzed for vaccine efficacy for each year from year 1 through year 7 after vaccination in the combined Shingles Prevention Study and Short-Term Persistence Substudy populations, the efficacy of zoster vaccine for the HZ burden of illness and the incidence of HZ were statistically significant for each year through the end of year 5. The point estimates for year 6 and year 7 suggested continued efficacy for the HZ burden of illness and incidence of HZ, but the results were not statistically significant, except for the HZ burden of illness in year 7. The small number of cases in the later years reduced the power to detect true differences. The efficacy of zoster vaccine for the incidence of PHN also appeared to persist, but because of the small number of cases of PHN,

Figure 2. Estimates of zoster vaccine efficacy in the combined Shingles Prevention Study and Short-Term Persistence Substudy populations. *A*, Vaccine efficacy for HZ BOI; *B*, Vaccine efficacy for incidence of PHN; *C*, Vaccine efficacy for incidence of HZ. Abbreviations: BOI, burden of illness; HZ, herpes zoster; PHN, postherpetic neuralgia. Whiskers, 95% confidence intervals.

Figure 3. Incidence and severity of herpes zoster (HZ) in the zoster vaccine and placebo groups in the combined Shingles Prevention Study and Short-Term Persistence Substudy populations. *A*, HZ BOI; *B*, Incidence of PHN; *C*, Incidence of HZ. Abbreviations: BOI, burden of illness; HZ, herpes zoster; PHN, postherpetic neuralgia. Whiskers, 95% confidence intervals.

vaccine efficacy for the incidence of PHN was not statistically significant beyond 2 years after vaccination. The analysis of change in vaccine efficacy for each year after vaccination

showed a decrease in efficacy after the first year for all 3 study outcomes, indicating that protection wanes to some degree after 1 year. The greatest decline in vaccine efficacy was

observed for the incidence of HZ (Figure 3C), which is also associated with an increase in the incidence of HZ in both the vaccine and placebo groups (Figure 3C). In the SPS, the incidence of HZ was the outcome most impacted by the increasing age, where vaccine efficacy against new cases of HZ was significantly lower for subjects aged ≥70 years, compared with subjects aged 60–69 years (37.6% vs 63.9%) [2]. The results of the Long-Term Persistence Substudy should help to determine whether the vaccine provides protection beyond the period investigated this study and thus the need for booster vaccination.

The comparable mortality rates observed among vaccine and placebo recipients in the Short-Term Persistence Substudy and the absence of vaccine-related adverse events supports the long-term safety of zoster vaccine [2, 11].

Study limitations are important to note. The selection of the Short-Term Persistence Substudy population was limited by resources, permitting the inclusion of only 12 of 22 original Shingles Prevention Study sites. In addition, a delay in approval of the Short-Term Persistence Substudy until after the Shingles Prevention Study was closed led to a gap in surveillance for HZ between the end of the Shingles Prevention Study and the initiation of the Short-Term Persistence Substudy. This interval and any events that might have occurred between studies were excluded from all analyses. However, the Short-Term Persistence Substudy successfully enrolled >14 000 subjects. Similar eligibility criteria were used to enroll subjects in the Short-Term Persistence Substudy, and, other than enrolling an older population, there were no differences in subject characteristics between the Shingles Prevention Study and the Short-Term Persistence Substudy. If censoring due to vaccination introduced a bias that increased the incidence of HZ among the remaining placebo recipients, the incidence of HZ would have been expected to be higher in year 7 than in years 5 and 6 (Figure 3) and higher during the period when most vaccinations were occurring (ie, January 2005–June 2007), but the observed rates are lower or similar for those periods relative to earlier intervals.

In conclusion, zoster vaccine continued to reduce the HZ burden of illness, the incidence of postherpetic neuralgia, and the incidence of HZ in the Short-Term Persistence Substudy population. Vaccine efficacy for each study outcome was lower in the Short-Term Persistence Substudy than in the Shingles Prevention Study. The duration of zoster vaccine efficacy is not known beyond 5 years after vaccination. The Long-Term Persistence Substudy, currently being analyzed, may provide additional data on the duration of zoster vaccine efficacy.

Notes

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