immunocompetent recipients ≥60 years old. Selected articles were abstracted, independently reviewed, and discrepancies adjudicated. We attempted to locate relevant unpublished work and contacted authors for additional data, where necessary. Measures of association were illustrated on a forest plot and converted to VE (1-hazard ratio or risk ratio or odds ratio).

**Results.** We screened 1,302 articles; 17 underwent full text review and 8 met inclusion criteria and were abstracted for this review. Selected studies included 1 phase III randomized controlled trial, 2 quasi experimental and 5 observational studies. One experimental and 5 observational studies estimated VE during the period from vaccination up to 4 years following vaccination; estimates across studies ranged from 33%–55%. Two quasi experimental and 3 observational studies estimated VE for 4 years following vaccination; estimates ranged from 19%–40%; the median estimate was 24% (Figure). Pooled VE was not calculated due to heterogeneity in length of follow up, age distribution of study subjects, as well as adjustment for factors such as underlying medical conditions.

**Conclusion.** Most experimental and observational studies estimated VE just above 50% during the 3 years following receipt of ZVL. Beyond 3 years, ZVL protection wanes, with most studies estimating a VE of ≤24% after 4 years. Information on overall efficacy and duration of protection from ZVL will guide policy decisions regarding its use.

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1338. Assessment of the Potential Herpes Zoster and Post Herpetic Neuralgia Case Avoidance with Vaccination in the United States
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**Background.** Herpes zoster (HZ) is a reactivation of latent varicella zoster virus in patients previously infected. Clinical characteristics of HZ include painful rash with potential complications, including post herpetic neuralgia (PHN). Care for HZ and PHN incurs significant costs and vaccination is beneficial. The aim of this study was to compare the impact on HZ and PHN case avoidance of two ZVL vaccines, an available live-attenuated zoster vaccine (zoster live vaccine [ZVL1]) vs. a candidate non-live adjuvanted HZ subunit vaccine (ZVL2), in the US population.

**Methods.** A Markov model called ZONA (ZOster ecoNomic Analyses) was developed following two age cohorts (≥60 years to represent the current ACIP recommendation and ≥65 years to represent the Medicare population) over their lifetimes beyond the year of vaccination. Demographic data were obtained from the US Census, whereas HZ incidence and the proportion of HZ individuals developing PHN were derived from published US-specific sources. Age-specific vaccine efficacy and waning rates were based on published clinical trial data. Vaccine coverage for both vaccines was assumed to be 30.6% and 34.3% in the two age cohorts, respectively, based on CDC data; compliance of the second dose of the ZVL vaccine was 69%, based on data from clinical trials and Hepatitis B second dose completion. Sensitivity analyses demonstrated robustness of the base analysis findings.

**Results.** In the US, for cohorts of 66.83 million (MO) persons aged 60+ and 47.76 million aged 65+ it was estimated that the HZ/su vaccine would reduce the number of HZ cases by 2.12M and 1.55M in the two age cohorts, respectively, compared with 0.65M and 0.45M using the ZVL. Furthermore, the HZ/su vaccine would reduce the number of PHN cases by 0.23M and 0.18M in the two age cohorts, respectively, compared with 0.10M and 0.09 using the ZVL. The number required to vaccinate to prevent one HZ case were 10 and 11, in the respective cohorts, using the HZ/su vaccine compared with 31 and 37, in the respective cohorts, using the ZVL.

**Conclusion.** Due to higher and sustained vaccine efficacy, the candidate HZ/su vaccine demonstrated superior public health impact in the US compared with the currently available ZVL.

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1339. Effectiveness of Live Zoster Vaccine in Preventing Herpes Zoster Ophthalmicus (HZO)
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**Background.** Herpes zoster ophthalmicus (HZO), caused by reactivation of varicella-zoster virus in or around the eye, can be severe and often results in care-seeking that may be less discretionary than for uncomplicated herpetic zoster (HZ). We compared the vaccine effectiveness (VE) of live zoster vaccine against HZO and VE against HZ overall.

**Methods.** Kaiser Permanente Northern California (KPNC) members enter the ongoing cohort study when age-eligible for zoster vaccine starting in 2007. Incident HZ was defined as a new diagnosis of HZ with an antiviral prescription or a positive varicella virus RNA test. Among those, an HZO case was defined as having an HZO diagnosis during an ophthalmology visit within 30 days of the initial HZ diagnosis. VE by age at vaccination and time since vaccination was estimated using Cox regression adjusted for age, race, sex and time-varying measures of healthcare use, comorbidities and average age over the time since the first vaccine was administered. Effectiveness of live zoster vaccine was calculated as a weighted average of annual VE estimates.

**Results.** During 2007–2014, ~1.3 million individuals ≥50 years of age entered the study population and 29% were vaccinated. Among 48,889 incident HZ cases, 2,858 (6%) had HZO, 87% of whom were unvaccinated (Table). For all ages combined, VE against HZO was 72% (95% CI, 64%–79%) in year 1, similar to 68% (95% CI, 65%–70%) against HZ. VE fell in years 2, 3, 4 and 5 to 47%, 45%, 42% and 27% for HZO and to 47%, 39%, 41% and 37% for HZ. For age groups 60–69 and 70–79, where we have the most data, the HZO and zoster vaccine were 49% effective against HZO for ages 50–59 years or older and small to moderate at this time. Average VE against HZO over the first 5 years following vaccination was 52% (95% CI, 42%–60%) for ages 60–69, 51% (95% CI, 39%–61%) for ages 70–79, and 39% (95% CI, 14%–57%) for ages 80+; similarly, 5-year average VE against HZ was 49%, 46%, and 44% for these 3 age groups.

**Conclusion.** VE against HZO was similar to VE against HZ regardless of age at vaccination or time since vaccination. Effectiveness of live zoster vaccine in preventing HZO was highest in year one with subsequent waning.

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1340. Immune Senescence Factors Associated with the Immuneogenicity of a Live Attenuated Zoster Vaccine (ZV) in Older Adults
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**Background.** ZV conveys protection against herpetic zoster by increasing the cell-mediated immunity (CMI) to varicella zoster virus (VZV). ZV immunogenicity and protection decrease with increasing age. We investigated effects of age and immune senescence on ZV immunogenicity.

**Methods.** 399 adults ≥50 years had VZV T-cell helper 1 (Th1) CMI measured by ex vivo VZV-stimulated IL2/IFNg ELISPOT and blood T-cell nonspecific immune senescence by flow cytometric characterization of FOXP3, CD15, IL10, TGFb, PD1, CD28 and CD3 and CD3 and CD4 expression before and after 52 weeks. ZV was given to 151 individuals at 50 weeks. Multivariate regression analysis was used to identify independent effects of age and immune senescence on ZV Th1 CMI (P < 0.025).

**Results.** IL2+ and IL2+IFNg+ Th1 memory VZV CMI peaked at 6 weeks after ZV and remained elevated at 1 year. Effectors, including VZV-specific IFNg+ Th1 and PD1+CD8+Granzyme B (Granzyme B+ PD1+CD8+) persisted at 1 year. Th1 effector cells (CTL) peaked at 1 week, but only the IFNg+ Th1 effectors remained elevated at 1 year. There was also a transient increase in blood CD8+PD1+ exhausted T cells 1
week after ZV. Independent positive effects on peak memory Th1 VZV CMI included the baseline CMI and negative effects included blood CD4+FOXP3+ % T regulatory (Treg) and CD8+PD1+ % T exhausted cells. Independent positive effects on peak effector Th1 VZV CMI included baseline CMI and negative effects included blood CD8+CD25+FOXP3+ % Treg. Age did not have an independent effect on peak CMi. Independent positive effect on persistent (1 month) memory Th1 incidence in both CMI and negative effects included age, blood CD4+FOXP3+ % Treg and CD8+PD1+ % T exhausted cells. Persistent effector Th1 CMI was negatively affected by age only.

Conclusion. ZV generated VZV-specific Th1 and CTL responses. The early increase of CD4+ and CD8+ T cells was suggested that CTL responses to the vaccine virus may be compromised by immune senescence. The negative of age on VZV Th1 CMI was fully mediated by immune senescence at peak response, but age had a negative effect on CMI persistency that was independent from the markers of immune senescence included in this study.

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1341. Humoral and Cellular Immunogenicity of Zoster Vaccine within One Year after Herpes Zoster

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Background. Herpes zoster vaccination is recommended to patients with a prior history of herpes zoster to prevent reactivation. However, the appropriate timing of vaccination is controversial. We compared immunogenicity of vaccine according to timing of vaccination after zoster illness.

Methods. In this prospective observational study, subjects were stratified into two groups by the vaccination timing since their zoster illness: 6–12 months (within-1 year group) vs. 1–5 years (after-1 year group). Blood samples were collected before and 6 weeks after vaccination. VZV-specific IgG concentrations were measured by enzyme-linked immunosorbent assay. Interferon-gamma enzyme-linked immunosorbent spot (ELISPOT) assays were performed to assess VZV-specific T-cell responses.

Results. A total of 59 patients (18 in the within-1 year group and 41 in the after-1 year group) were enrolled. Ages were not significantly different between groups. The baseline geometric mean titer (GMT) of VZV IgG was higher in the within-1 year group than in the after-1 year group (245.8 IU/mL vs. 124.9 IU/mL; P = 0.040). The geometric mean fold-rise (GMFR) of VZV IgG was lower in the within-1 year group than in the after-1 year group (1.42 vs. 2.46; P = 0.002). The GMT of spot forming cell (SFC) counts by ELISPOT at baseline and 6 weeks after vaccination were not significantly different between groups. The GMFRs of SFCs were also comparable.

Conclusion. Zoster vaccination within 1 year after zoster illness may have disadvantage in the aspect of humoral immune response (ClinicalTrials.gov number, NCT034572).

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1342. Immunogenicity and Safety of an Adjuvanted Herpes Zoster Subunit Vaccine in Older Adults Previously Vaccinated with a Live-Attenuated Herpes Zoster Vaccine: A Phase III, Group-Matched, Clinical Trial

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Background. Herpes zoster (HZ), caused by reactivation of varicella-zoster virus (VZV), typically manifests as a dermatomal rash and can lead to postherpetic neuralgia (PHN). HZ and PHN risk increase with age. Efficacy against HZ induced by a live-attenuated zoster vaccine (ZVL; Merck) declines following vaccination (21% in years 5–12 post-vaccination). To ensure protection, revaccination can be considered. Therefore, we assessed immunogenicity and safety of HZ/sa/zoster virus (VZV)-specific IgG concentrations and HZ/sa/zoster virus (VZV)-specific IgG concentrations in elderly individuals.

Methods. In this phase III, group-matched, open, multicenter study (NCT02581410), 2 parallel groups of adults ≥65 years of age (YOA) received 2 HZ/sa/zoster virus (VZV)-specific IgG concentrations and SAEs were recorded. All SAEs were recorded for 30 days post each dose with ZVL PreVac. Serious AEs (SAEs), HZ cases and potential immune-mediated events (pIMDs) will be recorded until study end. Here, we present data up to M3, as the study is still ongoing.

Results. 430 participants were vaccinated. M3 humoral immune responses in HZ PreVac were non-inferior to those in HZ NonVac and the co-primary objective was met as the UL of the 95% CI of the adjusted GMC ratio was 1.17 (Table 1). In addition, there were no apparent differences in CD4[+]/T-cell frequencies between groups (Figure 1). No clinically meaningful differences between frequencies of solicited AEs, unsolicited AEs or SAEs in the 2 groups were observed (Table 2). No SAEs considered vaccine-related by investigators, no suspected HZ cases and no pIMDs were reported up to M3.

Conclusion. HZ/sa/zoster virus (VZV)-specific IgG concentrations in adults ≥65 YOA who previously received ZVL stimulates strong immune responses and does not raise safety concerns.

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Figure 1. Descriptive statistics of the number of specific CD4[+]/T-cells (ATP cohort for immunogenicity)

Table 1. Anti-g<sub>B</sub> antibody geometric mean concentrations (GMCs) and adjusted GMC ratio (HZ/NonVac over HZ PreVac) (ATP cohort for immunogenicity)

| Timepoint | HZ-PreVac | HZ/NonVac | Adjusted GMC ratio |
|-----------|-----------|-----------|--------------------|
| N Value   | N Value   | HZ-NonVac/P | HZ-NonVac/P/PreVac |
| 204       | 0.0000    | 0.0000    | 0.0000             |
| 204       | 0.0000    | 0.0000    | 0.0000             |

Table 2. Frequencies of solicited and unsolicited AEs, SAEs and pIMDs (TVG)

| AE        | Reporting Period | HZ-PreVac | HZ/NonVac |
|-----------|------------------|-----------|-----------|
| N         | n (% [95% CI])   | N         | n (% [95% CI]) |
| Pain      | 215              | 189 (87.9 [82.8–91.9]) | 214 | 184 (86.4 [80.9–91.3]) |
| Redness   | 215              | 96 (44.7 [37.9–51.6])   | 214 | 73 (34.1 [27.8–40.1])   |
| Swelling  | 215              | 50 (23.5 [17.8–29.5])   | 214 | 37 (17.7 [12.3–23.6])   |
| Fatigue   | 215              | 50 (23.5 [17.8–29.5])   | 214 | 37 (17.7 [12.3–23.6])   |
| Headache  | 215              | 114 (53.0 [46.1–60.8])  | 214 | 111 (51.9 [45.6–58.7])  |
| Myalgia   | 215              | 49 (22.6 [17.4–29.0])   | 214 | 38 (17.7 [12.3–23.6])   |
| Nausea    | 215              | 78 (36.3 [29.8–43.1])   | 214 | 89 (41.6 [34.8–48.5])   |
| Headache  | 215              | 31 (14.3 [9.7–19.5])    | 214 | 37 (17.7 [12.3–23.6])   |
| Fever     | 215              | 30 (14.3 [9.7–19.5])    | 214 | 37 (17.7 [12.3–23.6])   |
| pIMDs     | 215              | 0 (0.0 [0.0–0.0])       | 215 | 0 (0.0 [0.0–0.0])       |

Adverse events: AE, serious AE; pIMD, potential immune-mediated disease; TVG, trial vaccinated cohort; HZ PreVac, participants 56 years of age (YOA) vaccinated with a live-attenuated zoster vaccine (ZVL) 6 (±1) years earlier; HZ NonVac, participants ≥65 YOA not previously vaccinated with ZVL, N. number of participants with a live-attenuated zoster vaccine (ZVL) 6 (±1) years before in the ZVL PreVac group and ≥65 YOA not previously vaccinated with ZVL, N. number of participants with a live-attenuated zoster vaccine (ZVL) 6 (±1) years before in the ZVL NonVac group.

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