HHS Public Access

Author manuscript

Ann Intern Med. Author manuscript; available in PMC 2017 December 07.

Published in final edited form as:

Ann Intern Med. 2013 December 03; 159(11): 739–745. doi: 10.7326/0003-4819-159-11-201312030-00006.

Examination of Links Between Herpes Zoster Incidence and Childhood Varicella Vaccination

Craig M. Hales, MD, MPH, **Rafael Harpaz, MD, MPH**, **M. Riduan Joesoef, MD, PhD**, and **Stephanie R. Bialek, MD, MPH**

National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia

Abstract

Background—Introduction of a universal varicella vaccine program for U.S. children in 1996 sparked concern that less-frequent exposure to varicella would decrease external boosting of immunity to varicella zoster virus and thereby increase incidence of herpes zoster (HZ).

Objective—To determine whether the varicella vaccination program has influenced trends in HZ incidence in the U.S. population older than 65 years.

Design—Retrospective study of Medicare claims.

Setting—Medicare, 1992 through 2010.

Participants—2 848 765 beneficiaries older than 65 years.

Measurements—Annual HZ incidence from 1992 through 2010; rate ratios (RRs) for HZ incidence by age, sex, and race or ethnicity; and state-level varicella vaccination coverage.

Results—281 317 incident cases of HZ occurred. Age- and sex-standardized HZ incidence increased 39% from 10.0 per 1000 person-years in 1992 to 13.9 per 1000 person-years in 2010

Requests for Single Reprints: Craig M. Hales, MD, MPH, Division of Viral Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, 1600 Clifton Road NE, Mail Stop A-34, Atlanta, GA 30333; chales@cdc.gov.

Current Author Addresses: Drs. Hales, Harpaz, Joesoef, and Bialek: Division of Viral Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, 1600 Clifton Road NE, Mail Stop A-34, Atlanta, GA 30333.

Disclaimer: The findings and conclusions in this article are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Potential Conflicts of Interest: None disclosed. Forms can be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M13-1026.

Reproducible Research Statement: *Study protocol:* Not available. *Statistical code:* Available from Dr. Hales (chales@cdc.gov). *Data set:* Not available.

Current author addresses and author contributions are available at www.annals.org.

Author Contributions: Conception and design: C.M. Hales, R. Harpaz, R. Joesoef, S.R. Bialek.
Analysis and interpretation of the data: C.M. Hales, R. Harpaz, R. Joesoef, S.R. Bialek.
Drafting of the article: C.M. Hales, R. Harpaz.
Critical revision of the article for important intellectual content: C.M. Hales, R. Harpaz, R. Joesoef, S.R. Bialek.
Final approval of the article: C.M. Hales, R. Harpaz, R. Joesoef, S.R. Bialek.
Statistical expertise: C.M. Hales, R. Harpaz.
Administrative, technical, or logistic support: R. Joesoef.
Collection and assembly of data: C.M. Hales, R. Joesoef.

with no evidence of a statistically significant change in the rate of increase after introduction of the varicella vaccination program. Before introduction of this program, HZ incidence was higher in women (RR, 1.21 [95% CI, 1.19 to 1.24]) than men and was lower in black persons (RR, 0.51 [CI, 0.48 to 0.53]) and Hispanic persons (RR, 0.76 [CI, 0.72 to 0.81]) than white persons. In a model adjusted for sex, age, and calendar year from 1997 to 2010, HZ incidence did not vary by state varicella vaccination coverage (RR, 0.9998 [CI, 0.9993 to 1.0003]).

Limitation—Uncertain level and consistency of health-seeking behavior and access and uncertain accuracy of disease coding.

Conclusion—Age-specific HZ incidence increased in the U.S. population older than 65 years even before implementation of the childhood varicella vaccination program. Introduction and widespread use of the vaccine did not seem to affect this increase. This information is reassuring for countries considering universal varicella vaccination.

Primary Funding Source—None.

Primary varicella zoster virus (VZV) infection causes varicella, a contagious rash illness that is usually mild in children but can lead to such complications as pneumonia; encephalitis; and, rarely, death (1). Infants, adolescents, adults, immunocompromised persons, and pregnant women are more susceptible to varicella complications. The congenital varicella syndrome is a feared complication of varicella, as well. Reactivation of VZV causes herpes zoster (HZ), a painful vesicular eruption occurring unilaterally in 1 or more closely overlapping dermatomes. Virtually all adults in the United States have latent VZV infection (2), and reactivation causes an estimated 1 million cases of HZ each year (3).

Although HZ can lead to serious ocular and neurologic complications (4), the most common complication is postherpetic neuralgia. Approximately 12% to 24% of older adults with HZ have persistent pain 90 days or more after onset of rash. This chronic pain can lead to substantial distress and functional limitations, with detrimental effects on quality of life (5).

In 1996, the U.S. Advisory Committee on Immunization Practices first recommended routine varicella vaccination for children aged 12 to 18 months (6). Vaccination of healthy children is routinely recommended in several countries, including Canada, Australia, Germany, and South Korea; however, some European countries reserve vaccination for susceptible adolescents or adults in whom risk for severe disease is higher or have no routine recommendation because of doubts about the importance of the disease burden and about the cost-effectiveness of the vaccine (7).

Hope-Simpson (8) hypothesized that exposure to varicella would decrease risk for HZ through boosting VZV-specific immunity. Subsequent studies (9–11) have shown decreased risk for HZ in adults who live with children or have known varicella contacts; other studies (12, 13) have not shown this effect. Mathematical models that incorporate external boosting have predicted that introduction of a universal varicella vaccine program for children would lead to adults being exposed to children with varicella less frequently and increase HZ incidence in adults (9, 14). The U.K. Health Protection Agency has raised concerns that adding the varicella vaccine to their childhood immunization program would lead to an increase in HZ in adults (15).

In the United States, several studies spanning 1945 to 2006 have reported increased HZ incidence (3, 16–19). Temporal increases in HZ incidence have also been reported in countries without a varicella vaccination program (20). However, no studies have shown an increase in HZ incidence after varicella vaccination compared with an adequate baseline before introduction of the vaccine. In 2006, the U.S. Advisory Committee on Immunization Practices recommended HZ vaccination for adults aged 60 years or older to prevent HZ and its sequelae (21). However, as of 2010, only 14.4% of adults aged 60 years or older have received the vaccine (22).

We used Medicare claims data from 1992 through 2010 to evaluate trends in HZ incidence in the U.S. population older than 65 years and determine any influence of the varicella vaccination program on these trends. We also examined the influence of age, sex, and race or ethnicity on HZ incidence.

Methods

Study Population

We obtained health care claims data on a 5% random sample of Medicare beneficiaries maintained in the Centers for Medicare & Medicaid Services Chronic Conditions Data Warehouse (23). The study population comprised U.S. residents in the 5% random sample who were older than 65 years and had more than 1 calendar year of continuous enrollment in Medicare fee-for-service Parts A and B between 1991 and 2010. The data included claims generated in outpatient, inpatient, skilled nursing facility, and home health settings. Self-reported race and ethnicity data come from U.S. Social Security Administration records. Mutually exclusive categories included white (non-Hispanic); black (non-Hispanic); Hispanic; Asian, Asian American, or Pacific Islander; American Indian or Alaska Native; or other (24).

Definition and Calculation of HZ Incidence

We defined incident HZ in a given year as the first occurrence of an International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), code (any position) for HZ (053.xx) in any health care setting with no HZ code during the previous calendar year. Claims with a code for postherpetic neuralgia (053.12 or 053.13) were excluded. We calculated incidence as the number of incident cases of HZ divided by the total person-years. Because we required 1 calendar year of enrollment without HZ before defining an incident case, the calculation of HZ incidence included beneficiaries beginning at age 66 years. We standardized HZ incidence by age and sex using the 2000 U.S. standard population (25, 26).

Analysis of HZ Incidence in an Immunocompetent Subgroup

Herpes zoster is more common in immunocompromised persons (21, 27). To exclude the possibility that changes in HZ incidence were due to changes in the prevalence of immunosuppression, we performed a separate analysis restricted to a selected cohort of beneficiaries who were least likely to be immunocompromised. This analysis excluded beneficiaries with an ICD-9-CM code indicating any potentially immunocompromising

condition or any condition that could potentially be managed with immunosuppressive treatments or corticosteroids (Appendix Table, available at www.annals.org) (19). Our definition was artificial but ensured that beneficiaries remaining in this analysis were not immunocompromised. We standardized HZ incidence in this population by age and sex using the 2000 U.S. standard population (25, 26).

Assessing the Effect of Health-Seeking Behavior or Medicare on Temporal Increases in HZ Incidence

Because cases of HZ identified through administrative data are medically attended, changes in HZ incidence can be due to changes relating to the Medicare program or to health-seeking behavior. To control for such changes, we compared trends in incidence of HZ with those of 10 preselected conditions, which, like HZ, are common and acute and typically managed in outpatient settings (19). We identified first instances of HZ and the selected conditions as the first occurrence of the corresponding ICD-9-CM codes in outpatient settings in the primary or secondary positions, with no code for the condition in the previous 4 calendar years. We derived annual incidence standardized by age and sex from the 2000 U.S. standard population and calculated ratios of HZ incidence to the incidence of each selected condition.

Analysis of HZ Incidence Trends

We used Poisson regression analysis to compare HZ trends during 3 periods of varicella vaccination program implementation: preimplementation (1992 to 1995), early implementation (1996 to 1999), and full implementation (2000 to 2010). The model included age group, sex, calendar year, indicator variables for implementation period, and interactions between calendar year and the indicator variables. We used generalized estimating equations (GEEs) to account for correlated data within states. The parameter estimates for the interaction terms allow us to compare the annual rate of increase in HZ incidence during early and full implementation periods with the rate of increase during the preimplementation period (28), adjusting for age and sex.

Assessing Potential Risk Factors for HZ and Influence of State-Level Varicella Vaccination Coverage on HZ Incidence

To evaluate risk factors for HZ, we calculated adjusted RRs for age, sex, and race or ethnicity using Poisson regression analysis with GEEs to account for correlated data within states. We limited this analysis to the period before introduction of the universal varicella vaccination program (1992 to 1996) to exclude any possibility of bias due to implementation of the program.

We examined the effect of state varicella vaccination coverage on HZ incidence during the period after implementation of the varicella vaccination program (1997 to 2010). We obtained rates of annual 1-dose varicella vaccination coverage for children aged 19 to 35 months for each of the 50 states and the District of Columbia from the National Immunization Survey (19, 29). We calculated the RR of state vaccine coverage (expressed as a percentage) for HZ incidence, adjusted for age, sex, and calendar year by using Poisson regression with GEEs to account for statistical dependence of measurements within states. To evaluate whether increasing varicella vaccination coverage had a delayed effect on HZ

incidence, which previous models (9) suggested, we replaced concurrent vaccination coverage with coverage lagged by 10 years and ran the same model.

The Centers for Disease Control and Prevention Human Subjects Coordinator determined that this study did not require review for human subjects protections because the data did not contain personal identifiers and were not originally collected specifically for this study. We used SAS, version 9.3 (SAS Institute, Cary, North Carolina), for all data management and statistical analyses. Poisson regression analyses with GEEs were performed using PROC GENMOD in SAS software.

Role of the Funding Source

No external funding was obtained for this study.

Results

The study included 2 845 353 Medicare beneficiaries from 1992 through 2010, contributing a total of 22 508 343 person-years with a median of 7 years per beneficiary (Table 1). Age and sex distributions were similar to the entire Medicare population but with fewer beneficiaries in western states and fewer Hispanic and Asian beneficiaries (data not shown). The mean age was 76.1 years in 1992 and 77.1 years in 2010.

A total of 281 317 incident cases of HZ occurred. Crude HZ incidence increased 40% from 10.2 per 1000 person-years in 1992 to 14.3 per 1000 persons in 2010; age- and sex-standardized HZ incidence increased 39% from 10.0 per 1000 person-years in 1992 to 13.9 per 1000 person-years in 2010 (Figure). Mean age at the time of HZ diagnosis remained stable at 76.9 years in 1992 and 77.9 years in 2010. The exponentiated parameter estimate for the interaction between calendar year and the indicator variable for the early varicella vaccine implementation period was 1.002 (95% CI, 0.984 to 1.020), indicating that the annual rate of increase in HZ incidence during this period (1996 to 1999) was 0.2% higher than that during the preimplementation period (1992 to 1995) but was not statistically significant. Similarly, the exponentiated parameter estimate for the interaction between calendar year and the indicator variable for full implementation period (2000 to 2010) was 1.008 (CI, 0.994 to 1.023).

Increases occurred among all age groups (Figure), racial or ethnic groups, and census divisions (data not shown) and both sexes; they remained apparent even in the selected 30% of beneficiaries without a potentially immunocompromising condition (Appendix Figure 1, available at www.annals.org). In addition, increases in HZ incidence were greater than those seen in 9 out of 10 analogous conditions that we investigated (Appendix Figure 2, available at www.annals.org). Table 2 shows data on the incidence of HZ among Medicare beneficiaries in 2010 to highlight the incidence of HZ in key subgroups.

We evaluated HZ incidence by sex, age group, and race or ethnicity (Table 3) before introduction of the universal varicella vaccination program (1992 to 1996). The RR for women was 1.21 (CI, 1.19 to 1.24) and increased for each 5-year age group up to the 80- to

84-year group. Compared with white persons, black persons (RR, 0.51 [CI, 0.48 to 0.53]) and Hispanic persons (RR, 0.76 [CI, 0.72 to 0.81]) had lower HZ incidence.

In the GEE model adjusted for sex, age, and calendar year, HZ incidence did not vary by state varicella vaccination coverage (RR, 0.9998 [CI, 0.9993 to 1.0003]). Varicella vaccination coverage lagged by 10 years was also not significant (RR, 1.0010 [CI, 0.9997 to 1.0022]). Incidence trends of HZ in states with consistently high varicella vaccination coverage from 1997 through 2010 (mean coverage, 82%) compared with states with low varicella vaccination coverage (mean coverage, 64%) overlapped with no pattern emerging (data not shown).

Discussion

Varicella exposure has been postulated to boost VZV-specific immunity and reduce the risk for VZV reactivation. Concern has been expressed that routine childhood varicella vaccination, introduced in the United States in 1996, could thereby lead to an increase in HZ incidence by reducing opportunities for exposure to varicella. Our findings suggest that, although HZ incidence has increased in elderly persons, routine varicella vaccination has not influenced this increase.

First, the rise in HZ incidence clearly predates 1996 and HZ incidence did not accelerate after implementation of the varicella vaccination program, when varicella vaccination coverage reached 90% and varicella incidence decreased by 90% (30, 31). Second, state varicella vaccination coverage had no effect on HZ incidence concurrently or 10 years later. Finally, the mean age at the time of HZ diagnosis did not decrease during the study, which might occur if external boosting helped to maintain protection. Thus, although HZ incidence has increased in the elderly population, we did not find evidence to suggest that this increase has been influenced by the varicella vaccination program in the United States. This finding confirms the results of other studies before and after introduction of the varicella vaccine (19, 32–34).

The lack of evidence for an effect of the varicella vaccination program on HZ incidence might be explained in several ways. First, although some studies suggest that exposure to varicella protects against HZ (9–11), other findings contradict this (12, 13). Because latent VZV can reactivate subclinically and boost immunity (35–37), compensatory boosting might occur among persons who are not periodically exposed to varicella (8). Alternatively, external boosting might require a degree of varicella exposure that is uncommon among elderly persons, particularly because this population has less-frequent exposure to children than do younger adults (38).

Age- and sex-standardized HZ incidence among elderly persons increased 39% from 10.0 per 1000 person-years to 13.9 per 1000 person-years during the 19-year study. On the basis of our observed values, we calculate that 14% of men and 20% of women who reach age 65 years will have HZ during their remaining lifetime (39). The observed increase is robust, occurring among all age, sex, and race or ethnicity subgroups and all geographic regions. It does not seem to be an artifact of changing prevalence of immunocompromising conditions,

because increases in age- and sex-standardized HZ incidence are seen even after restricting the analysis to a selected cohort of immunocompetent persons. Furthermore, increases in HZ incidence persisted when it was compared with 9 of 10 other acute outpatient conditions, suggesting that these increases were not due to underlying changes in health-seeking behavior or in the Medicare program over time.

Increases in HZ incidence in the elderly population have been reported in several studies in countries with and without varicella vaccination programs (3, 16, 17, 19, 20, 40, 41); however, other studies have not shown an increase (32, 33). We have no explanation for the trend and expect that it awaits a better understanding of why a substantial minority of persons have HZ during their lifetime, whereas most do not. In particular, chronic diseases prevalent among elderly persons do not explain most cases of HZ (42).

Data from the large, generalizable Medicare population provide an opportunity to more precisely characterize the well-recognized effect of age on HZ incidence. Although the association between HZ incidence and age seems to plateau after age 80 years, the risk for postherpetic neuralgia, hospitalization, and other complications continues to increase with age. We also provide precise data to confirm that older women are at greater risk for HZ than older men; most studies report increased HZ incidence among women in most age cohorts, including children, although the reason remains unknown (3, 17, 18, 20, 41, 43–47). Finally, we provide data that black and Hispanic persons are at lower risk for HZ than white persons. A few reports are available on the reduced risk for HZ among black persons (43, 45, 48), although data about HZ incidence in Hispanic persons are lacking (13). The RR for American Indians or Alaska Natives should be interpreted with caution because health services provided by the Indian Health Service were not fully captured in the Medicare data (49).

We followed elderly Medicare beneficiaries who are at high risk for HZ for a long period spanning the licensure of varicella vaccination. In 2006, the U.S. Advisory Committee on Immunization Practices recommended the HZ vaccine for adults aged 60 years or older for prevention of HZ and its sequelae (21). Uptake of the HZ vaccine has been slow, with only 1.9% coverage in adults aged 60 years or older in 2007 (50), increasing to 14.4% in 2010 (22).

Although we do not expect that such low coverage would substantially affect HZ incidence on a population level, these data provide a baseline for monitoring effects of the HZ vaccine program as coverage increases. A previous study of HZ incidence in all ages from 1993 to 2006 using MarketScan (Truven Health Analytics, Ann Arbor, Michigan), a database of health care claims from commercial insurers, had limitations in evaluating trends in adults aged 65 years or older because the size of the study population in this age group changed substantially over the observation period, allowing opportunities for unmeasured confounding (19). MarketScan did not incorporate Medicare data until 1996 and even then contained health care claims for only the selected subset of Medicare beneficiaries with managed care. The Centers for Medicare & Medicaid Services Chronic Conditions Data Warehouse used in this study contains claims for a stable and more representative population of beneficiaries in traditional fee-for-service Medicare during the study period.

The use of administrative data has limitations. The accuracy of findings from studies based on health care claims depends on high and consistent levels of health-seeking behavior and access and on accurate disease coding. These criteria are probably met for most cases of HZ because it is painful and the study population had Medicare Parts A and B coverage for health care costs; however, mild cases may not come to medical attention, resulting in an underestimate of true incidence of HZ. In a population-based survey of 141 adults aged 60 years or older who had had HZ, 95% sought medical attention (50).

Differences in health-seeking behavior or access may explain a portion of the variation in risk by sex or race or ethnicity. We could not directly assess the accuracy of HZ claims in our data through record reviews. However, previous studies of HZ have shown good concordance between coding and actual health care visits, with positive predictive values ranging from 85% to 100% (12, 18, 51). Furthermore, estimates from self-reports and health care settings of HZ incidence have been similar to ours, providing reassurance about the sensitivity of HZ coding (17).

Our study was also limited by the data available for analysis. Although more than one half of cases of HZ in the United States occur in persons younger than 65 years and therefore were missed by our Medicare analysis, HZ tends to be much more severe in older adults; thus, the Medicare population is of particular importance (3). We showed that HZ incidence was not affected by state-level variation in varicella vaccination coverage controlled for sex and age but were not able to consider other factors that vary across states and might affect HZ incidence, such as age at parenthood, family size, or living with young children.

Age-specific HZ incidence has been increasing in the U.S. population older than 65 years even before implementation of the childhood varicella vaccination program. Introduction and widespread use of this vaccine did not seem to affect this increase. This information is reassuring for countries considering universal varicella vaccination.

Our findings have several implications. First, in the absence of explanations for increasing HZ incidence, properly monitoring the effect of the HZ vaccination program or projecting future HZ incidence will be difficult. Furthermore, HZ poses a substantial burden of disease in the elderly population; continued increases in HZ incidence would be worrisome and need to be understood. Fortunately, an effective vaccine is now available that can help prevent this disabling disease.

Acknowledgments

The authors thank Carla Winston, PhD; Barbara Bardenheier, PhD, MS; Chad Heilig, PhD; John Zhang, PhD; and Ronald Henry for their valuable technical assistance.

References

1. Atkinson, W.Wolfe, S., Hamborsky, J., editors. Epidemiology and Prevention of Vaccine-Preventable Diseases. 12. Washington, DC: Public Health Foundation; 2012.
2. Kilgore PE, Kruszon-Moran D, Seward JF, Jumaan A, Van Loon FP, Forghani B, et al. Varicella in Americans from NHANES III: implications for control through routine immunization. J Med Virol. 2003; 70(Suppl 1):S111–8. [PubMed: 12627498]

3. Yawn BP, Saddier P, Wollan PC, St Sauver JL, Kurland MJ, Sy LS. A population-based study of the incidence and complication rates of herpes zoster before zoster vaccine introduction. Mayo Clin Proc. 2007; 82:1341–9. [PubMed: 17976353]
4. Gilden DH, Kleinschmidt-DeMasters BK, LaGuardia JJ, Mahalingam R, Cohrs RJ. Neurologic complications of the reactivation of varicella-zoster virus. N Engl J Med. 2000; 342:635–45. [PubMed: 10699164]
5. Drolet M, Brisson M, Schmader KE, Levin MJ, Johnson R, Oxman MN, et al. The impact of herpes zoster and postherpetic neuralgia on health-related quality of life: a prospective study. CMAJ. 2010; 182:1731–6. [PubMed: 20921251]
6. Marin M, Güris D, Chaves SS, Schmid S, Seward JF. Advisory Committee on Immunization Practices, Centers for Disease Control and Prevention (CDC). Prevention of varicella: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep. 2007; 56(RR-4):1–40.
7. Sadzot-Delvaux C, Rentier B, Wutzler P, Asano Y, Suga S, Yoshikawa T, et al. Varicella vaccination in Japan, South Korea, and Europe. J Infect Dis. 2008; 197(Suppl 2):S185–90. [PubMed: 18419395]
8. Hope-Simpson RE. The nature of herpes zoster: a long-term study and a new hypothesis. Proc R Soc Med. 1965; 58:9–20. [PubMed: 14267505]
9. Brisson M, Gay NJ, Edmunds WJ, Andrews NJ. Exposure to varicella boosts immunity to herpes-zoster: implications for mass vaccination against chickenpox. Vaccine. 2002; 20:2500–7. [PubMed: 12057605]
10. Gershon AA, LaRussa P, Steinberg S, Mervish N, Lo SH, Meier P. The protective effect of immunologic boosting against zoster: an analysis in leukemic children who were vaccinated against chickenpox. J Infect Dis. 1996; 173:450–3. [PubMed: 8568309]
11. Thomas SL, Wheeler JG, Hall AJ. Contacts with varicella or with children and protection against herpes zoster in adults: a case-control study. Lancet. 2002; 360:678–82. [PubMed: 12241874]
12. Donahue JG, Kieke BA, Gargiullo PM, Jumaan AO, Berger NR, McCauley JS, et al. Herpes zoster and exposure to the varicella zoster virus in an era of varicella vaccination. Am J Public Health. 2010; 100:1116–22. [PubMed: 20075320]
13. Chaves SS, Santibanez TA, Gargiullo P, Guris D. Chickenpox exposure and herpes zoster disease incidence in older adults in the U.S. Public Health Rep. 2007; 122:155–9. [PubMed: 17357357]
14. Garnett GP, Grenfell BT. The epidemiology of varicella-zoster virus infections: the influence of varicella on the prevalence of herpes zoster. Epidemiol Infect. 1992; 108:513–28. [PubMed: 1318219]
15. U.K. Health Protection Agency. [on 1 July 2013] Latest HPA modelling reveals chickenpox vaccination would lead to more shingles among elderly despite introduction of shingles vaccination [press release]. Sep 17. 2008 Accessed at www.hpa.org.uk/NewsCentre/NationalPressReleases/2008PressReleases/080917chickenpox/
16. Ragozzino MW, Melton LJ 3rd, Kurland LT, Chu CP, Perry HO. Population-based study of herpes zoster and its sequelae. Medicine (Baltimore). 1982; 61:310–6. [PubMed: 6981045]
17. Jumaan, AO., Seward, JF., Wooten, K., Singelton, J. Varicella and herpes zoster surveillance in the US, 1970–1994 [Abstract]. Programs and Abstracts of the 41st Annual Meeting of the Infectious Diseases Society of America; San Diego, California. 9–12 October 2003; Alexandria, VA: Infectious Diseases Soc America; 2003. p. 899Abstract 899
18. Mullooly JP, Riedlinger K, Chun C, Weinmann S, Houston H. Incidence of herpes zoster, 1997–2002. Epidemiol Infect. 2005; 133:245–53. [PubMed: 15816149]
19. Leung J, Harpaz R, Molinari NA, Jumaan A, Zhou F. Herpes zoster incidence among insured persons in the United States, 1993–2006: evaluation of impact of varicella vaccination. Clin Infect Dis. 2011; 52:332–40. [PubMed: 21217180]
20. Russell ML, Schopflocher DP, Svenson L, Virani SN. Secular trends in the epidemiology of shingles in Alberta. Epidemiol Infect. 2007; 135:908–13. [PubMed: 17291380]
21. Harpaz R, Ortega-Sanchez IR, Seward JF. Advisory Committee on Immunization Practices (ACIP) Centers for Disease Control and Prevention (CDC). Prevention of herpes zoster: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep. 2008; 57(RR-5):1–30.

22. Centers for Disease Control and Prevention (CDC). Adult vaccination coverage—United States, 2010. MMWR Morb Mortal Wkly Rep. 2012; 61:66–72. [PubMed: 22298302]
23. ResDac. [on 1 July 2013] Accessed at www.resdac.org
24. Agency for Healthcare Research and Quality. [on 24 January 2012] Creation of New Race-Ethnicity Codes and Socioeconomic Status (SES) Indicators for Medicare Beneficiaries. 2008. Accessed at www.ahrq.gov/qual/medicareindicators/medicareindicators2.htm
25. Day, JC. Population projections of the United States by age, sex, race, and Hispanic origin: 1995 to 2050. Washington, DC: Government Printing Office; 1996.
26. Klein RJ, Schoenborn CA. Age adjustment using the 2000 projected U.S. population. Healthy People 2010 Stat Notes. 2001:1–10.
27. Gnann JW Jr, Whitley RJ. Clinical practice. Herpes zoster. N Engl J Med. 2002; 347:340–6. [PubMed: 12151472]
28. Kleinbaum, D., Kupper, L., Muller, K., Nizam, A. Applied Regression Analysis and Multivariable Methods. Washington, DC: Duxbury Pr; 1998.
29. Centers for Disease Control and Prevention. [on 1 July 2013] U.S. Vaccination Coverage Reported via National Immunization Survey. 2013. Accessed at www.cdc.gov/vaccines/stats-surv/nis/
30. Guris D, Jumaan AO, Mascola L, Watson BM, Zhang JX, Chaves SS, et al. Changing varicella epidemiology in active surveillance sites—United States, 1995–2005. J Infect Dis. 2008; 197(Suppl 2):S71–5. [PubMed: 18419413]
31. Adams DA, Gallagher KM, Jajosky RA, Kriseman J, Sharp P, Anderson WJ, et al. Division of Notifiable Diseases and Healthcare Information, Office of Surveillance, Epidemiology, and Laboratory Services, CDC. Summary of notifiable diseases—United States, 2011. MMWR Morb Mortal Wkly Rep. 2013; 60:1–117. [PubMed: 23820934]
32. Tanuseputro P, Zagorski B, Chan KJ, Kwong JC. Population-based incidence of herpes zoster after introduction of a publicly funded varicella vaccination program. Vaccine. 2011; 29:8580–4. [PubMed: 21939721]
33. Jumaan AO, Yu O, Jackson LA, Bohlke K, Galil K, Seward JF. Incidence of herpes zoster, before and after varicella-vaccination-associated decreases in the incidence of varicella, 1992–2002. J Infect Dis. 2005; 191:2002–7. [PubMed: 15897984]
34. Chao DY, Chien YZ, Yeh YP, Hsu PS, Lian IB. The incidence of varicella and herpes zoster in Taiwan during a period of increasing varicella vaccine coverage, 2000–2008. Epidemiol Infect. 2012; 140:1131–40. [PubMed: 21906410]
35. Mehta SK, Cohrs RJ, Forghani B, Zerbe G, Gilden DH, Pierson DL. Stress-induced subclinical reactivation of varicella zoster virus in astronauts. J Med Virol. 2004; 72:174–9. [PubMed: 14635028]
36. Ljungman P, Lönnqvist B, Gahrton G, Ringdén O, Sundqvist VA, Wahren B. Clinical and subclinical reactivations of varicella-zoster virus in immunocompromised patients. J Infect Dis. 1986; 153:840–7. [PubMed: 3009635]
37. Luby JP, Ramirez-Ronda C, Rinner S, Hull A, Vergne-Marini P. A longitudinal study of varicella-zoster virus infections in renal transplant recipients. J Infect Dis. 1977; 135:659–63. [PubMed: 192807]
38. Mossong J, Hens N, Jit M, Beutels P, Auranen K, Mikolajczyk R, et al. Social contacts and mixing patterns relevant to the spread of infectious diseases. PLoS Med. 2008; 5:e74. [PubMed: 18366252]
39. Beiser A, D'Agostino RB Sr, Seshadri S, Sullivan LM, Wolf PA. Computing estimates of incidence, including lifetime risk: Alzheimer's disease in the Framingham Study. The Practical Incidence Estimators (PIE) macro. Stat Med. 2000; 19:1495–522. [PubMed: 10844714]
40. Fleming DM, Bartelds A, Chapman RS, Cross KW. The consistency of shingles and its significance for health monitoring. Eur J Epidemiol. 2004; 19:1113–8. [PubMed: 15678791]
41. Pérez-Farinós N, Ordobás M, García-Fernández C, García-Comas L, Cañellas S, Rodero I, et al. Varicella and herpes zoster in Madrid, based on the Sentinel General Practitioner Network: 1997–2004. BMC Infect Dis. 2007; 7:59. [PubMed: 17570859]
42. Joesoef RM, Harpaz R, Leung J, Bialek SR. Chronic medical conditions as risk factors for herpes zoster. Mayo Clin Proc. 2012; 87:961–7. [PubMed: 23036671]

43. Thomas SL, Hall AJ. What does epidemiology tell us about risk factors for herpes zoster? Lancet Infect Dis. 2004; 4:26–33. [PubMed: 14720565]
44. Opstelten W, Van Essen GA, Schellevis F, Verheij TJ, Moons KG. Gender as an independent risk factor for herpes zoster: a population-based prospective study. Ann Epidemiol. 2006; 16:692–5. [PubMed: 16516488]
45. Tseng HF, Smith N, Harpaz R, Bialek SR, Sy LS, Jacobsen SJ. Herpes zoster vaccine in older adults and the risk of subsequent herpes zoster disease. JAMA. 2011; 305:160–6. [PubMed: 21224457]
46. Insinga RP, Itzler RF, Pellissier JM, Saddier P, Nikas AA. The incidence of herpes zoster in a United States administrative database. J Gen Intern Med. 2005; 20:748–53. [PubMed: 16050886]
47. Fleming DM, Cross KW, Cobb WA, Chapman RS. Gender difference in the incidence of shingles. Epidemiol Infect. 2004; 132:1–5. [PubMed: 14979582]
48. Schmader K, George LK, Burchett BM, Pieper CF. Racial and psychosocial risk factors for herpes zoster in the elderly. J Infect Dis. 1998; 178(Suppl 1):S67–70. [PubMed: 9852978]
49. Centers for Medicare & Medicaid Services (CMS), HHS. Medicare program; revisions to payment policies and five-year review of and adjustments to the relative value units under the physician fee schedule for calendar year 2002. Final rule with comment period. Fed Regist. 2001; 66:55245–503. [PubMed: 11760761]
50. Lu PJ, Euler GL, Jumaan AO, Harpaz R. Herpes zoster vaccination among adults aged 60 years or older in the United States, 2007: uptake of the first new vaccine to target seniors. Vaccine. 2009; 27:882–7. [PubMed: 19071175]
51. Yawn BP, Wollan P, St Sauver J. Comparing shingles incidence and complication rates from medical record review and administrative database estimates: how close are they? Am J Epidemiol. 2011; 174:1054–61. [PubMed: 21920944]

Context

The incidence of herpes zoster (HZ) in older adults is increasing. This could be due to routine childhood varicella vaccination, which prevents adults from experiencing a natural boost in varicella-specific immunity through exposure to children with chickenpox.

Contribution

Information from a Medicare database showed that the age-specific increase in HZ incidence began before the introduction of routine childhood varicella vaccination and does not vary by state vaccination coverage in models adjusted for sex, age, and calendar year.

Implication

The age-specific increase in HZ incidence in older adults is currently unexplained and argues for wider use of HZ vaccination in this population.

—The Editors

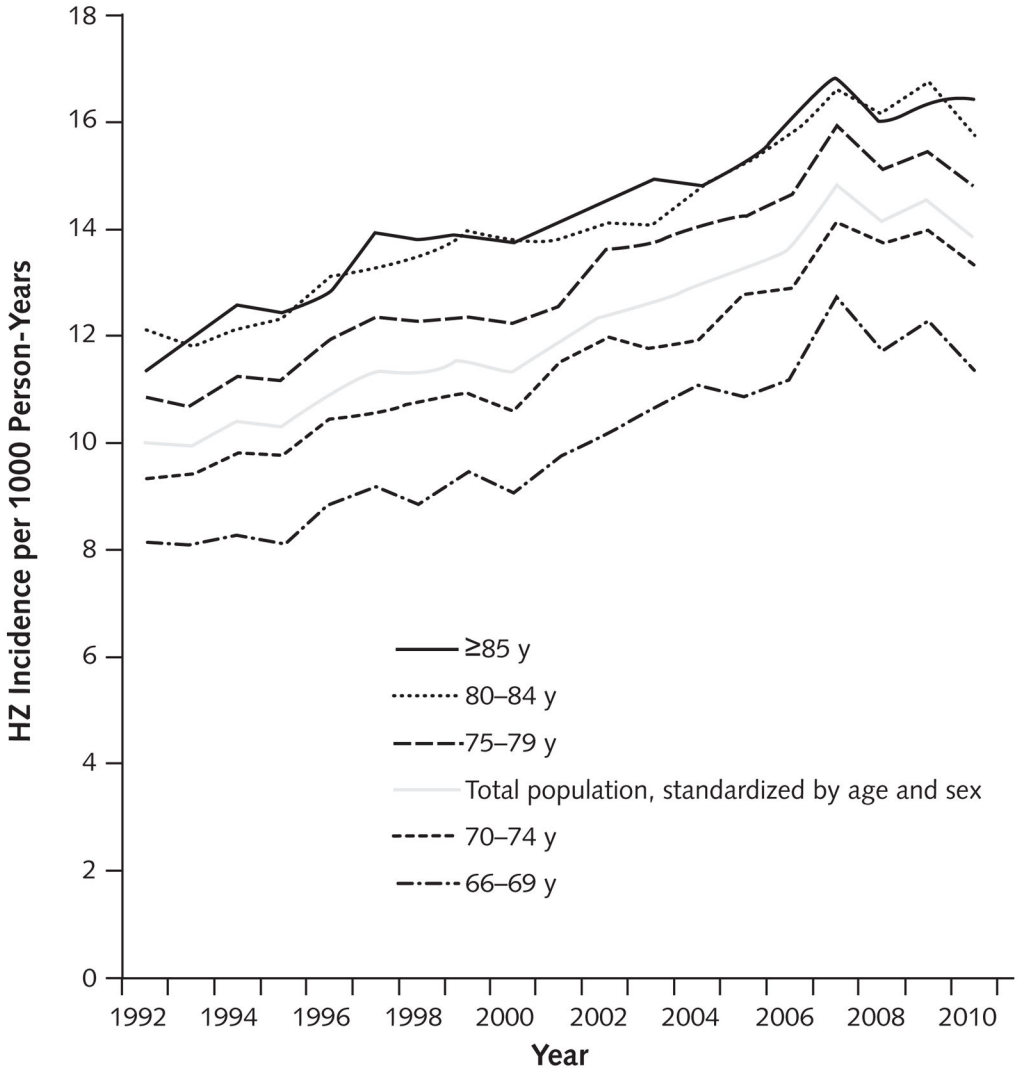
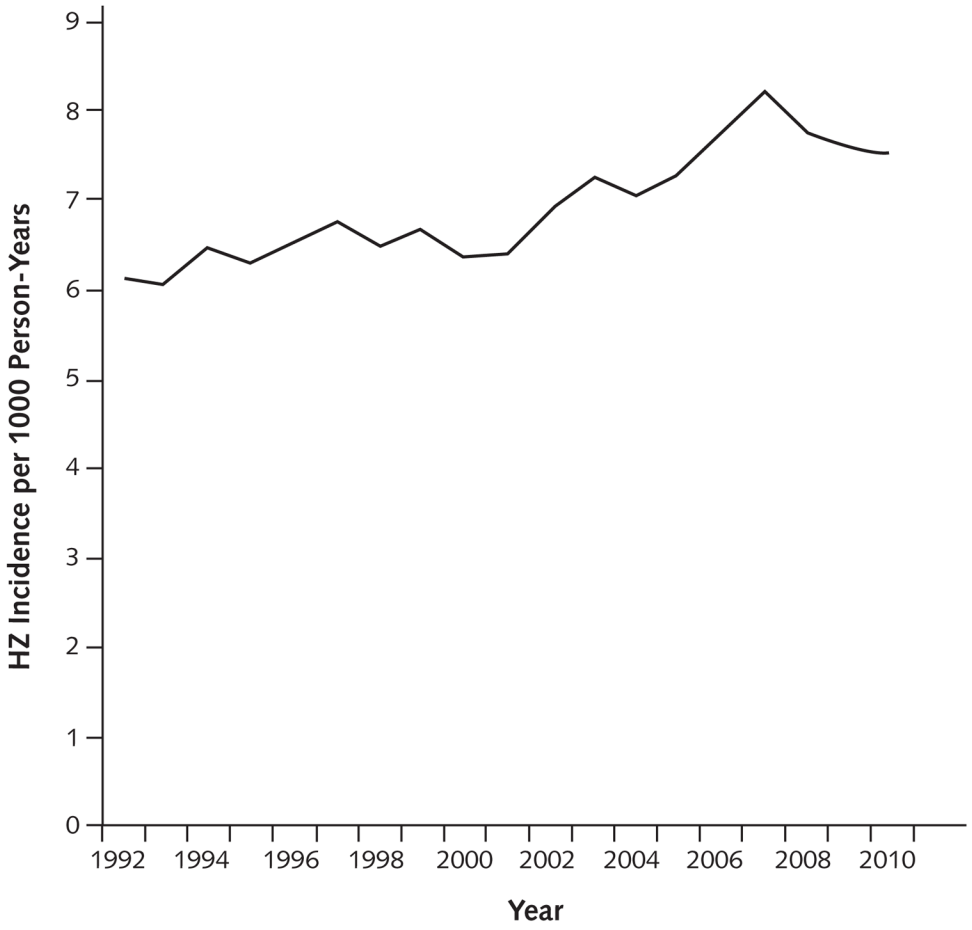


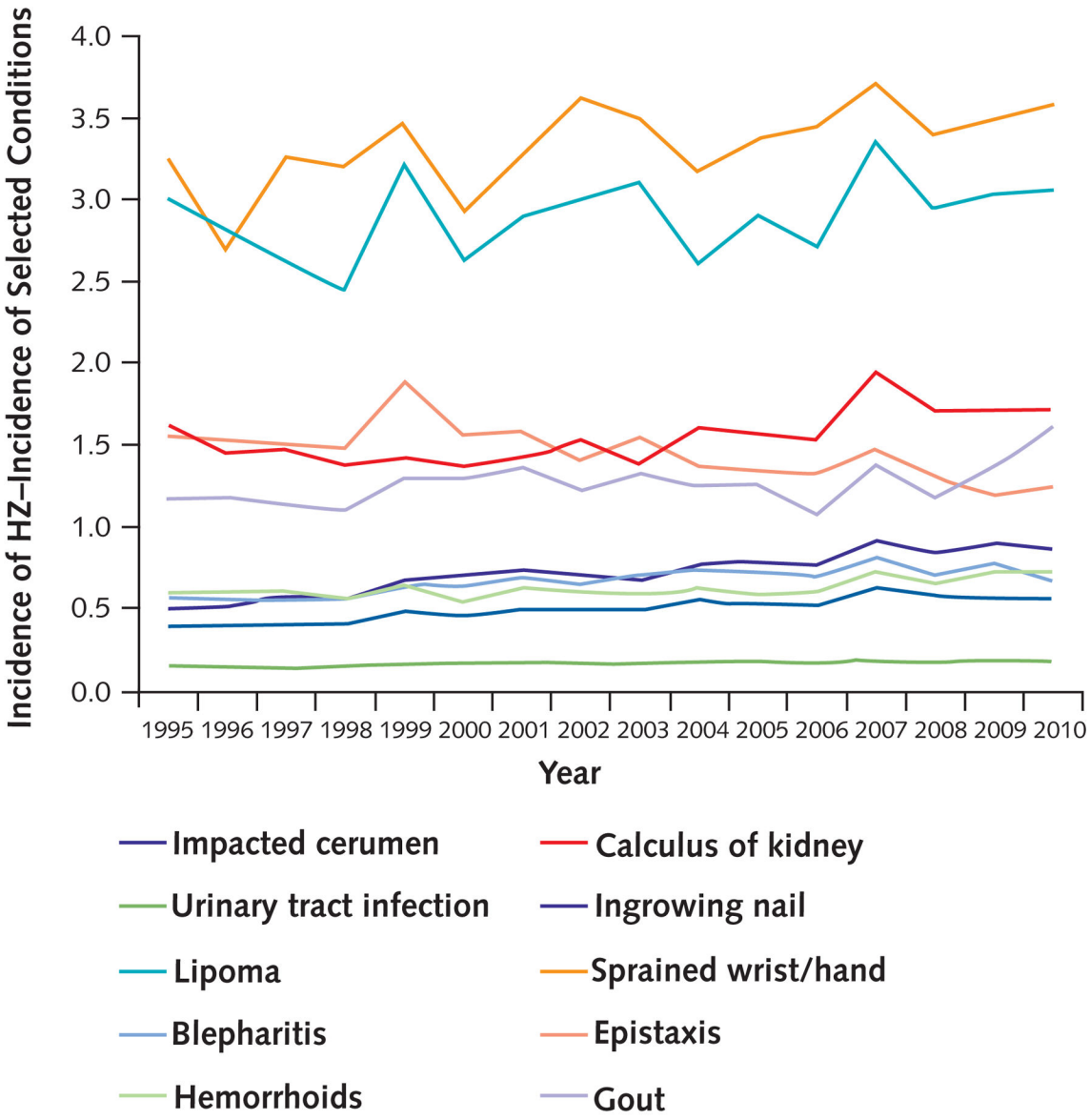
Figure 1. HZ incidence among Medicare beneficiaries older than 65 years, by age group, 1992–2010

HZ = herpes zoster.



Appendix Figure 1. Age- and sex-standardized HZ incidence among immunocompetent Medicare beneficiaries older than 65 years, 1992–2010

This immunocompetent subpopulation excluded beneficiaries with any International Classification of Diseases, Ninth Revision, Clinical Modification, code indicating a potentially immunocompromising condition or a condition that may be managed with immunosuppressive treatment (see Appendix Table for the list of codes). HZ = herpes zoster.



Appendix Figure 2. Age- and sex-standardized ratios of HZ incidence to the incidence of 10 selected conditions, 1995–2010

The 10 conditions and associated International Classification of Diseases, Ninth Revision, Clinical Modification, codes were impacted cerumen (380.4), calculus of kidney and ureter (592.x), urinary tract infection (599.0), ingrowing nail (703.0), lipoma (214.x), sprains and strains of wrist and hand (842.xx), inflammation of eyelids (373.xx), epistaxis (784.7), hemorrhoids (455.x), and gout (274.0, 274.9). HZ = herpes zoster.

Table 1

Demographic Characteristics of Medicare Beneficiaries (Selected Years)

Variable	1995	2000	2005	2010
Person-years	1 231 976	1 128 712	1 235 751	1 135 298
Sex, *n (%)*				
Men	483 817 (39.3)	441 526 (39.1)	501 394 (40.6)	470 528 (41.4)
Women	748 158 (60.7)	687 186 (60.9)	734 356 (59.4)	664 770 (58.6)
Age group, *n (%)*				
66–69 y *	226 133 (18.4)	178 631 (15.8)	214 373 (17.3)	208 882 (18.4)
70–74 y	358 162 (29.1)	306 463 (27.2)	313 114 (25.3)	287 926 (25.4)
75–79 y	279 392 (22.7)	274 404 (24.3)	283 874 (23.0)	234 389 (20.6)
80–84 y	195 768 (15.9)	191 992 (17.0)	222 579 (18.0)	195 137 (17.2)
≥85 y	172 521 (14.0)	177 223 (15.7)	201 811 (16.3)	208 964 (18.4)
Race/ethnicity, *n (%)*				
White (non-Hispanic)	1 099 459 (89.2)	1 002 902 (88.9)	1 087 942 (88.0)	993 568 (87.5)
Black (non-Hispanic)	94 718 (7.7)	84 891 (7.5)	95 728 (7.7)	83 773 (7.4)
Hispanic	15 605 (1.3)	16 483 (1.5)	18 727 (1.5)	18 038 (1.6)
Asian, Asian American, or Pacific Islander	8587 (0.7)	11 693 (1.0)	16 218 (1.3)	19 112 (1.7)
American Indian or Alaska Native	2919 (0.2)	3712 (0.3)	4407 (0.4)	4500 (0.4)
Other	6012 (0.5)	6629 (0.6)	11 322 (0.9)	15 304 (1.3)
Unknown	4676 (0.4)	2403 (0.2)	1408 (0.1)	1006 (0.1)

* Because we required 1 calendar year of enrollment without herpes zoster before defining an incident case, the calculation of herpes zoster incidence included beneficiaries beginning at age 66 y.

Table 2

Crude HZ Incidence Among Medicare Beneficiaries, by Sex, Age Group, and Race/Ethnicity, 2010

Variable	Events, *n*	Person-Years of Exposure	HZ Incidence per 1000 Person-Years (95% CI)*
Sex			
Men	5625	470 528	12.0 (11.6–12.3)
Women	10 550	664 770	15.9 (15.6–16.2)
Age group			
66–69 y	2366	208 882	11.3 (10.9–11.8)
70–74 y	3835	287 926	13.3 (12.9–13.7)
75–79 y	3463	234 389	14.8 (14.3–15.3)
80–84 y	3074	195 137	15.8 (15.2–16.3)
≥ 85 y	3437	208 964	16.4 (15.9–17.0)
Race/ethnicity			
White (non-Hispanic)	14 675	993 568	14.8 (14.5–15.0)
Black (non-Hispanic)	692	83 772	8.3 (7.7–8.9)
Hispanic	238	18 038	13.2 (11.6–15.0)
Asian, Asian American, or Pacific Islander	279	19 110	14.6 (13.0–16.4)
American Indian or Alaska Native	74	4500	16.4 (13.1–20.6)
Other	204	15 304	13.3 (11.6–15.3)
Unknown	13	1006	12.9 (7.6–22.0)
Total	16 175	1 135 298	14.2 (14.0–14.5)

HZ = herpes zoster.

*CIs calculated using the Wilson score method.

Table 3

Risk for HZ Among U.S. Medicare Recipients Older Than 65 Years, 1992–1996

Variable	Unadjusted RR (95% CI)	Adjusted RR (95% CI)
Sex		
Men	1.00 (reference)	1.00 (reference)
Women	1.24 (1.22–1.26)	1.21 (1.19–1.24)
Age group		
66–69 y	1.00 (reference)	1.00 (reference)
70–74 y	1.18 (1.14–1.21)	1.17 (1.13–1.21)
75–79 y	1.35 (1.31–1.39)	1.33 (1.29–1.37)
80–84 y	1.49 (1.44–1.54)	1.45 (1.40–1.50)
≥85 y	1.48 (1.44–1.52)	1.42 (1.38–1.46)
Race/ethnicity		
White (non-Hispanic)	1.00 (reference)	1.00 (reference)
Black (non-Hispanic)	0.51 (0.48–0.54)	0.51 (0.48–0.53)
Hispanic	0.73 (0.69–0.77)	0.76 (0.72–0.81)
Asian, Asian American, or Pacific Islander	0.90 (0.75–1.08)	0.92 (0.76–1.12)
American Indian or Alaska Native	0.61 (0.44–0.85)	0.60 (0.43–0.84)
Other	0.97 (0.84–1.11)	0.96 (0.84–1.11)
Unknown	1.09 (0.98–1.20)	0.96 (0.86–1.07)

HZ = herpes zoster; RR = rate ratio.

Appendix Table

ICD-9-CM Codes Indicating a Potentially Immunocompromising Condition or a Condition That May Be Managed With Immunosuppressive Treatments or Corticosteroids

ICD-9-CM Code	Description
010.xx	Primary tuberculous infection
011.xx	Pulmonary tuberculosis
012.xx	Other respiratory tuberculosis
013.xx	Tuberculosis of meninges and central nervous system
014.xx	Tuberculosis of intestines, peritoneum, and mesenteric glands
015.xx	Tuberculosis of bones and joints
016.xx	Tuberculosis of genitourinary system
017.xx	Tuberculosis of other organs
018.xx	Miliary tuberculosis
023.x	Brucellosis
030.x	Brucellosis
042	Leprosy
056.71	Arthritis due to rubella
075	Infectious mononucleosis
079.53	HIV, type 2 (HIV-2)
083.x	Other rickettsioses
088.81	Lyme disease
099.3	Reiter disease
115.xx	Histoplasmosis
117.3	Aspergillosis
123.x	Other cestode infection
124	Trichinosis
130.x	Toxoplasmosis
133.x	Acariasis
135	Sarcoidosis
136.1	Behçet syndrome
136.5	Sarcosporidiosis
140.x	Malignant neoplasm of lip
141.x	Malignant neoplasm of tongue
142.x	Malignant neoplasm of major salivary glands
143.x	Malignant neoplasm of gum
144.x	Malignant neoplasm of floor of mouth
145.x	Malignant neoplasm of other and unspecified parts of mouth
146.x	Malignant neoplasm of oropharynx
147.x	Malignant neoplasm of nasopharynx
148.x	Malignant neoplasm of hypopharynx

ICD-9-CM Code	Description
149.x	Malignant neoplasm of other and ill-defined sites within the lip, oral cavity, and pharynx
150.x	Malignant neoplasm of esophagus
151.x	Malignant neoplasm of stomach
152.x	Malignant neoplasm of small intestine, including duodenum
153.x	Malignant neoplasm of colon
154.x	Malignant neoplasm of rectum, rectosigmoid junction, and anus
155.x	Malignant neoplasm of liver and intrahepatic bile ducts
156.x	Malignant neoplasm of gallbladder and extrahepatic bile ducts
157.x	Malignant neoplasm of pancreas
158.x	Malignant neoplasm of retroperitoneum and peritoneum
159.x	Malignant neoplasm of other and ill-defined sites within the digestive organs and peritoneum
160.x	Malignant neoplasm of nasal cavities, middle ear, and accessory sinuses
161.x	Malignant neoplasm of larynx
162.x	Malignant neoplasm of trachea, bronchus, and lung
163.x	Malignant neoplasm of pleura
164.x	Malignant neoplasm of thymus, heart, and mediastinum
165.x	Malignant neoplasm of other and ill-defined sites within the respiratory system and intrathoracic organs
170.x	Malignant neoplasm of bone and articular cartilage
171.x	Malignant neoplasm of connective and other soft tissue
172.x	Malignant melanoma of skin
174.x	Malignant neoplasm of female breast
175.x	Malignant neoplasm of male breast
176.x	Kaposi sarcoma
179	Malignant neoplasm of uterus, part unspecified
180.x	Malignant neoplasm of cervix uteri
181	Malignant neoplasm of placenta
182.x	Malignant neoplasm of body of uterus
183.x	Malignant neoplasm of ovary and other uterine adnexa
184.x	Malignant neoplasm of other and unspecified female genital organs
185	Malignant neoplasm of prostate
186.x	Malignant neoplasm of testis
187.x	Malignant neoplasm of penis and other male genital organs
188.x	Malignant neoplasm of bladder
189.x	Malignant neoplasm of kidney and other and unspecified urinary organs
190.x	Malignant neoplasm of eye
191.x	Malignant neoplasm of brain
192.x	Malignant neoplasm of other and unspecified parts of nervous system
193	Malignant neoplasm of thyroid gland
194.x	Malignant neoplasm of other endocrine glands and related structures

ICD-9-CM Code	Description
195.x	Malignant neoplasm of other and ill-defined sites
196.x	Secondary and unspecified malignant neoplasm of lymph nodes
197.x	Secondary malignant neoplasm of respiratory and digestive systems
198.xx	Secondary malignant neoplasm of other specified sites
199.x	Malignant neoplasm without specification of site
200.xx	Lymphosarcoma and reticulosarcoma and other specified malignant tumors of lymphatic tissue
201.xx	Hodgkin disease
202.xx	Other malignant neoplasms of lymphoid and histiocytic tissue
203.xx	Multiple myeloma and immunoproliferative neoplasms
204.xx	Lymphoid leukemia
205.xx	Myeloid leukemia
206.xx	Monocytic leukemia
207.xx	Other specified leukemia
208.xx	Leukemia of unspecified cell type
209.xx	Neuroendocrine tumors
212.6	Benign neoplasm of thymus
228.xx	Hemangioma and lymphangioma, any site
235.x	Neoplasm of uncertain behavior of digestive and respiratory systems
236.xx	Neoplasm of uncertain behavior of genitourinary organs
237.xx	Neoplasm of uncertain behavior of endocrine glands and nervous system
238.xx	Neoplasm of uncertain behavior of other and unspecified sites and tissues
239.xx	Neoplasms of unspecified nature
242.xx	Thyrotoxicosis with or without goiter
245.x	Thyroiditis
250.xx	Diabetes mellitus
251.1	Other specified hypoglycemia
252.1	Other disorders of pancreatic internal secretion
255.0	Cushing syndrome
255.1x	Hyperaldosteronism
255.2	Adrenogenital disorders
255.4x	Corticoadrenal insufficiency
256.3x	Other ovarian failure
258.1	Other combinations of endocrine dysfunction
258.8	Other specified polyglandular dysfunction
258.9	Polyglandular dysfunction, unspecified
265.2	Pellagra
273.x	Disorders of plasma protein metabolism
274.xx	Gout
275.4x	Disorders of calcium metabolism

ICD-9-CM Code	Description
277.00	Cystic fibrosis without mention of meconium ileus
277.01	Cystic fibrosis with meconium ileus
277.3x	Amyloidosis
277.86	Other specified disorders of metabolism, peroxisomal disorders
277.89	Other specified disorders of metabolism
279.xx	Disorders involving the immune mechanism
283.xx	Acquired hemolytic anemias
284.xx	Aplastic anemia and other bone marrow failure syndromes
286.5	Hemorrhagic disorder due to intrinsic circulating anticoagulants, antibodies or inhibitors
286.6	Defibrination syndrome
287.0	Allergic purpura
287.3x	Primary thrombocytopenia
287.4x	Secondary thrombocytopenia
288.xx	Diseases of white blood cells
289.4	Hypersplenism
289.50	Disease of spleen, unspecified
289.51	Chronic congestive splenomegaly
289.52	Splenic sequestration
289.59	Other diseases of spleen, other
289.81	Primary hypercoagulable state
289.82	Secondary hypercoagulable state
289.89	Other specified diseases of blood and blood-forming organs
289.9	Unspecified diseases of blood and blood-forming organs
291.xx	Alcohol-induced mental disorders
303.xx	Alcohol dependence syndrome
333.5	Other choreas
334.0	Friedreich ataxia
334.8	Other spinocerebellar diseases
337.0x	Idiopathic peripheral autonomic neuropathy
337.2x	Reflex sympathetic dystrophy
340	Multiple sclerosis
341.xx	Other demyelinating diseases of central nervous system
345.6x	Infantile spasms
346.2x	Variants of migraine, not elsewhere classified
348.2	Benign intracranial hypertension
348.5	Cerebral edema
351.0	Bell palsy
351.8	Other facial nerve disorders
351.9	Facial nerve disorder, unspecified

ICD-9-CM Code	Description
354.x	Mononeuritis of upper limb and mononeuritis multiplex
357.xx	Inflammatory and toxic neuropathy
358.xx	Myoneural disorders
359.6	Symptomatic inflammatory myopathy in diseases classified elsewhere
359.8x	Other myopathies
360.11	Sympathetic uveitis
362.18	Retinal vasculitis
362.50	Macular degeneration (senile), unspecified
362.52	Nonexudative senile macular degeneration
363.0x	Focal chorioretinitis and focal retinochoroiditis
363.1x	Disseminated chorioretinitis and disseminated retinochoroiditis
363.2x	Other and unspecified forms of chorioretinitis and retinochoroiditis
364.0x	Acute and subacute iridocyclitis
364.1x	Chronic iridocyclitis
364.2x	Certain types of iridocyclitis
364.3	Unspecified iridocyclitis
364.4x	Vascular disorders of iris and ciliary body
370.xx	Keratitis
372.05	Acute atopic conjunctivitis
372.14	Other chronic allergic conjunctivitis
377.3x	Optic neuritis
379.0x	Scleritis and episcleritis
381.xx	Nonsuppurative otitis media and Eustachian tube disorders
386.0x	Ménière disease
386.3x	Labyrinthitis
391.x	Rheumatic fever with heart involvement
392.0	Rheumatic chorea with heart involvement
392.9	Rheumatic chorea without mention of heart involvement
411.xx	Other acute and subacute forms of ischemic heart disease
420.xx	Acute pericarditis
422.xx	Acute myocarditis
425.5	Alcoholic cardiomyopathy
429.4	Functional disturbances following cardiac surgery
446.xx	Polyarteritis nodosa and allied conditions
464.4	Croup
471.x	Nasal polyps
477.x	Allergic rhinitis
478.8	Upper respiratory tract hypersensitivity reaction, site unspecified
491.21	Obstructive chronic bronchitis with (acute) exacerbation

ICD-9-CM Code	Description
493.xx	Asthma
495.x	Extrinsic allergic alveolitis
503	Pneumoconiosis due to other inorganic dust
507.x	Pneumonitis due to solids and liquids
516.x	Other alveolar and parietoalveolar pneumonopathy
518.3	Pulmonary eosinophilia
528.2	Oral aphthae
528.9	Other and unspecified diseases of the oral soft tissues
530.1x	Esophagitis
535.3x	Alcoholic gastritis
555.x	Regional enteritis
556.x	Ulcerative colitis
570	Acute and subacute necrosis of liver
571.0	Alcoholic fatty liver
571.1	Acute alcoholic hepatitis
571.2	Alcoholic cirrhosis of liver
571.3	Alcoholic liver damage, unspecified
571.4x	Chronic hepatitis
571.5	Cirrhosis of liver without mention of alcohol
571.6	Biliary cirrhosis
576.1	Cholangitis
579.0	Celiac disease
579.1	Tropical sprue
579.8	Other specified intestinal malabsorption
580.xx	Acute glomerulonephritis
581.xx	Nephrotic syndrome
583.xx	Nephritis and nephropathy, not specified as acute or chronic
585.x	Chronic kidney disease
586	Renal failure, unspecified
592.x	Calculus of kidney and ureter
683	Acute lymphadenitis
690.xx	Erythematosquamous dermatosis
691.x	Atopic dermatitis and related conditions
692.xx	Contact dermatitis and other eczema
694.xx	Bullous dermatoses
695.xx	Erythematous conditions
696.x	Psoriasis and similar disorders
697.x	Lichen
698.2	Lichen

ICD-9-CM Code	Description
698.3	Lichenification and lichen simplex chronicus
701.x	Other hypertrophic and atrophic conditions of skin
704.01	Alopecia areata
706.1	Other acne
706.2	Sebaceous cyst
708.x	Urticaria
710.x	Diffuse diseases of connective tissue
711.5x	Arthropathy associated with other viral diseases
712.xx	Crystal arthropathies
713.6	Arthropathy associated with hypersensitivity reaction
714.xx	Rheumatoid arthritis and other inflammatory polyarthropathies
715.2x	Osteoarthrosis, localized, secondary
716.1x	Traumatic arthropathy
720.xx	Ankylosing spondylitis and other inflammatory spondylopathies
721.xx	Spondylosis and allied disorders
722.xx	Intervertebral disc disorders
723.x	Other disorders of cervical region
724.xx	Other and unspecified disorders of back
725	Polymyalgia rheumatica
726.xx	Peripheral enthesopathies and allied syndromes
727.xx	Other disorders of synovium, tendon, and bursa
728.89	Other disorders of muscle, ligament, and fascia, other
733.99	Disorder of bone and cartilage, unspecified, other
746.1	Tricuspid atresia and stenosis, congenital
756.5x	Osteodystrophies
759.5	Tuberous sclerosis
795.71	Nonspecific serologic evidence of HIV
802.6	Fracture of orbital floor (blow-out), closed
802.7	Fracture of orbital floor (blow-out), open
848.5	Other and ill-defined sprains and strains of pelvis
919.4	Insect bite, nonvenomous, without mention of infection
993.0	Barotrauma, otitic
993.3	Caisson disease
995.0	Other anaphylactic reaction
995.1	Angioneurotic edema
995.2x	Other and unspecified adverse effect of drug, medicinal and biological substance
995.3	Allergy, unspecified
996.8x	Complications of transplanted organ
999.5	Other serum reaction

ICD-9-CM Code	Description
E905.x	Venomous animals and plants as the cause of poisoning and toxic reactions
E933.1	Antineoplastic and immunosuppressive drugs
V08	Asymptomatic HIV infection status
V42.xx	Organ or tissue replaced by transplant
V58.0	Radiotherapy
V58.11	Encounter for antineoplastic chemotherapy
V58.12	Encounter for antineoplastic immunotherapy
V58.65	Long-term (current) use of steroids

ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification.