

A Cohort Study of Risk Factors for Herpes Zoster in Men in Southern California

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INTRODUCTION

- Known risk factors for herpes zoster (HZ) include decline in cell mediated immunity (CMI), auto-immune, and inflammatory diseases.
- Among those without immunosuppression, risk factors for HZ remain controversial.

METHODS

Study Population and Data Sources

- Men 45 to 69 years in 2000 who were Kaiser Permanente Southern California (KPSC) members of the California Men's Health Study (CMHS).
- CMHS surveyed demographic, lifestyle factors, and medical history in 2002-2003 and 2006.
- Additional data were obtained from KPSC electronic medical record.

Case Identification and Risk Factors

- HZ cases were identified by ICD-9 code from KPSC inpatient, outpatient & emergency department files.
- Follow-up time started in 2002/2003 and ended at HZ diagnosis, end of membership, death, or June 30, 2012 (whichever came first).
- Data on disease comorbidities, healthcare utilization, demographic characteristics, lifestyle, and dietary factors were collected.

Statistical Analyses

- A Cox proportional hazards regression model was used for adjustment among covariates.
- Cumulative incidence was calculated using the Kaplan-Meier method as 1 – (Percent free) of HZ at 5 and 10 years post-baseline.

RESULTS

Cohort Characteristics

- Among 38,807 men with mean age 58.3 years (SD = 7.0), 2,166 cases of HZ were identified.
- Mean (SD) length of follow-up was 7.2 (3.1) years (Table 1).
- The overall incidence rate of HZ was 7.89 per 1,000 person-years, increasing with age from 4.39 (45-54 years) to 10.29 per 1,000 person-years (65-70 years).
- The overall cumulative risk at 5 and 10 years post-baseline was 3.2% (95% CI: 3.0, 3.4) and 7.8% (95% CI: 7.5, 8.2), respectively.

Table 1. Demographic Characteristics, Outcome of Herpes Zoster, and Herpes Zoster Vaccination Status, by Age

Characteristic	Age at CMHS Survey (years)				Total (n=38,807)	p-value
	45 to 54 (n=13,503)	55 to 59 (n=8,568)	60 to 64 (n=8,560)	65 to 69 (n=8,176)		
Length of follow-up						
Mean (SD)	7.9 (3.0)	7.2 (3.0)	6.7 (3.1)	6.8 (3.1)	7.2 (3.1)	<0.0001
Herpes Zoster n(%*)						
No	12897 (95.5)	8123 (94.8)	8012 (93.6)	7609 (93.1)	36641 (94.4)	
Yes	606 (4.5)	445 (5.2)	548 (6.4)	567 (6.9)	2166 (5.6)	<0.0001
Herpes Zoster Vaccine n(%*)						
No	11927 (88.3)	5995 (70.0)	5880 (68.7)	5726 (70.0)	29528 (76.1)	
Yes	1576 (11.7)	2573 (30.0)	2680 (31.3)	2450 (30.0)	9279 (23.9)	<0.0001
Race/Ethnicity n(%*)						
Non-Hispanic White	7626 (56.5)	5473 (63.9)	5482 (64.0)	5217 (63.8)	23798 (61.3)	
African American	1157 (8.6)	748 (8.7)	869 (10.2)	881 (10.8)	3655 (9.4)	
Asian	919 (6.8)	539 (6.3)	599 (7.0)	608 (7.4)	2665 (6.9)	
Hispanic	3154 (23.4)	1489 (17.4)	1349 (15.8)	1265 (15.5)	7257 (18.7)	
Other/Unknown	647 (4.8)	319 (3.7)	261 (3.0)	205 (2.5)	1432 (3.7)	
Body mass index (BMI) n(%*)						
<18.5	90 (0.7)	48 (0.6)	56 (0.7)	67 (0.9)	261 (0.7)	
18.5 ≤ X<25.0	3081 (23.5)	1964 (23.7)	1934 (23.4)	2031 (25.9)	9010 (24.0)	
25.0 ≤ X<30.0	6077 (46.4)	3897 (47.1)	4000 (48.4)	3717 (47.4)	17691 (47.2)	
30.0 ≤ X<35.0	2714 (20.7)	1661 (20.1)	1649 (20.0)	1510 (19.3)	7534 (20.1)	
35.0+	1147 (8.7)	702 (8.5)	624 (7.6)	510 (6.5)	2983 (8.0)	
Mean (SD)	28.3 (5.2)	28.2 (4.9)	28.0 (4.8)	27.7 (4.7)	28.1 (4.9)	
Education n(%*)						
High School or less	2469 (18.5)	1418 (16.7)	1699 (20.1)	1994 (24.7)	7580 (19.7)	
Vocational or some college	5015 (37.5)	3012 (35.4)	3014 (35.6)	2752 (34.1)	13793 (35.9)	
College or more	5894 (44.1)	4067 (47.9)	3755 (44.3)	3320 (41.2)	17036 (44.4)	
Income n(%*)						
\$0 ≤ \$39,999	2283 (17.4)	1444 (17.5)	1941 (23.8)	2802 (36.4)	8470 (22.8)	
\$40,000 ≤ \$79,999	5100 (38.9)	3102 (37.6)	3211 (39.3)	3087 (40.1)	14500 (39.0)	
\$80,000+	5718 (43.6)	3698 (44.9)	3009 (36.9)	1809 (23.5)	14234 (38.3)	

*Percentages may not sum to 100% due to missing data

**Count includes those vaccinated at any time during follow-up period

Risk Factors for Herpes Zoster

- Increasing age, Asian and Hispanic race/ethnicity, sedentary behavior, income, ≥ 3 outpatient visits in the year prior to baseline, cancer, and CMI-related disease were associated with increased risk for HZ (Table 2).
- HZ vaccination, African-American race, Parkinson's disease, and current smoking are inversely associated with risk for HZ.

Table 2. Unadjusted and Adjusted Hazards Ratios for Herpes Zoster

Parameter**		Unadjusted Hazard Ratio (95% CI)	Adjusted Hazard Ratio (95% CI)	
Smoking status *	Current vs Never	0.77 (0.66- 0.91)	0.76 (0.64- 0.91)	
	Quit vs Never	1.08 (0.99- 1.17)	1.02 (0.93- 1.12)	
Herpes Zoster Vaccination *		0.56 (0.46- 0.67)	0.47 (0.39- 0.57)	
	Age at baseline (years)	55-59 vs <55	1.26 (1.12- 1.42)	1.29 (1.14- 1.47)
	60-64 vs <55	1.64 (1.47- 1.83)	1.65 (1.46- 1.87)	
	65-69 vs <55	1.76 (1.57- 1.96)	1.67 (1.47- 1.90)	
Race/Ethnicity	African American vs White	0.71 (0.60- 0.84)	0.68 (0.57- 0.81)	
	Asian vs White	1.23 (1.06- 1.43)	1.24 (1.06- 1.46)	
	Hispanic vs White	1.15 (1.03- 1.28)	1.18 (1.05- 1.33)	
	Other/Unknown vs White	0.77 (0.59- 0.99)	0.86 (0.65- 1.13)	
Income	\$40,000-\$79,999 vs <40K	1.00 (0.90- 1.12)	1.14 (1.02- 1.29)	
	\$80,000+ vs <40K	0.86 (0.77- 0.97)	1.04 (0.91- 1.18)	
Number outpatient visits	1-2 vs 0	1.12 (0.93- 1.34)	1.13 (0.94- 1.37)	
	3-9 vs 0	1.47 (1.26- 1.71)	1.37 (1.17- 1.62)	
	10+ vs 0	2.00 (1.72- 2.34)	1.61 (1.35- 1.92)	
Any Cancer *		1.47 (1.30- 1.67)	1.27 (1.11- 1.46)	
CMI-Related Disease *†		2.67 (2.23- 3.19)	2.30 (1.90- 2.79)	
Inflammatory disease *		1.23 (1.07- 1.41)	1.08 (0.92- 1.26)	
Parkinson's Disease *		1.10 (0.74- 1.64)	0.58 (0.34- 0.99)	

*Modeled as time-varying covariate

† CMI = Cell-mediated immunity, includes HIV, leukemia, solid tumors, Hodgkin's disease, organ or tissue transplant

**Adjusted for variables in Table 2 and: Body mass index, sedentary time outside work, physical activity, any Emergency Department, any inpatient, diabetes, peripheral artery disease, neuropathy, kidney disease, multiple sclerosis, hepatitis, depression, migraine, calories per day, alcohol grams/day, fat grams/day, vegetable servings/day, fruit servings/day.

DISCUSSION

- Increased risk of HZ among Asians and Hispanics are novel findings.
 - Previous studies have lacked statistical power to evaluate Asian and Hispanic populations.
- Inflammatory diseases did not increase HZ risk in final analyses.
 - Not having females (who are at higher risk for inflammatory diseases) may have influenced our findings.
- Increased outpatient visits were associated with higher risk, identifying a high risk ambulatory group to be targeted for vaccination.
- Smoking was inversely associated with HZ. We could not identify studies showing increased risk of HZ with smoking.
 - Sensitivity analyses did not alter our findings.
 - Protective effects of smoking are known for other diseases; increased white blood cell count & systemic inflammation from smoking may suppress reactivation of latent disease.