Healthcare Resource Utilization and Economic Burden of Herpes Zoster in Immunocompetent Older Adults in the United States: A Retrospective Cohort Study

Justin D. Carrico[1], Yan Wang[2], Keith A. Betts[2], Aozhou Wu[2], Shuang Wang[3], Tszshan Ma[3], Rita Campos[1], Pooja Joshi[4], Nikita Stempniewicz[1]

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Conclusions

In the 12 months following HZ diagnosis, individuals with HZ **had higher rates of all-cause HCRU** compared with those without HZ

Healthcare costs, both overall and by healthcare setting, **were also greater among those with HZ** than those without HZ; **the presence of HZ-related complications (both PHN and non-PHN) further increased this cost**

The increased HCRU and costs associated with HZ among immunocompetent adults aged ≥50 years highlight **the continued importance of HZ prevention in this population**

Background

- In the United States, approximately 1 in 3 individuals will develop herpes zoster (HZ), commonly known as shingles, over their lifetime, with incidence rising sharply after age 50 years as the latent varicella zoster virus reactivates[1,2]
- HZ and its complications are associated with a substantial economic burden in adults aged ≥50 years; however, recent US estimates are limited[3–7]
- Although HZ vaccination is recommended for all adults aged ≥50 years, uptake remains suboptimal in the US[8]

Aims

Estimate healthcare resource utilization (HCRU) and costs associated with HZ and HZ-related complications in immunocompetent US adults aged ≥50 years

Study design

Figure 1: **Study design schema**

Overview: Retrospective cohort study from the claims component of Optum's de-identified Market Clarity Data (October 2015–December 2024)

Population: Immunocompetent[e] adults aged ≥50 years without recorded HZ vaccination (Figure 1); HZ and non-HZ cohorts were matched 1:1 on index date, sex, and age

Outcomes: Incremental all-cause HCRU and costs (2024 US dollars [USD][f]) associated with HZ, compared to non-HZ controls, were estimated over 1-, 3-, and 12-month follow-up periods

Analysis:

- Multivariable regressions were used to control for differences in baseline demographic and clinical characteristics, HCRU, and costs
- Incremental costs of HZ-related complications, compared to HZ patients without complications, were estimated with linear regression models

[a]The index date for both HZ cases (date of first diagnosis of HZ, based on ICD-10-CM diagnosis code B02 in any diagnosis position on the claim) and non-HZ controls (matched to the index date of the matched HZ individual) was defined as Day 0. [b]Day –21 to Day 0 were excluded from baseline HCRU/costs due to potential HZ-related HCRU prior to diagnosis. [c]Defined as having ≥1 medical claim with a diagnosis for HZO or eye complications assessed within 30 days after index date. [d]Defined as having ≥1 medical claim in the inpatient setting with a diagnosis for HZ encephalitis or HZ meningitis assessed within 6 months after index date. [e]Immunocompetent was defined as no claim of inpatient visit or <2 claims of ambulatory visits on distinct dates with a diagnosis indicative of immunocompromising conditions during the 12-month baseline period and no medical or pharmacy claim indicative of receipt of immunocompromising medications within 120 days prior to index date.[9] [f]All costs were inflated to 2024 USD based on the Medical Care Services component of the Consumer Price Index.

Results

HZ and non-HZ cohorts were balanced on matched characteristics:

63.6% female

Age (mean, SD): 65.6 (10.5) years

N=261,154 in each cohort

The HZ cohort had...

↑ prevalence of chronic comorbidities at baseline

↑ HCRU and healthcare costs during baseline

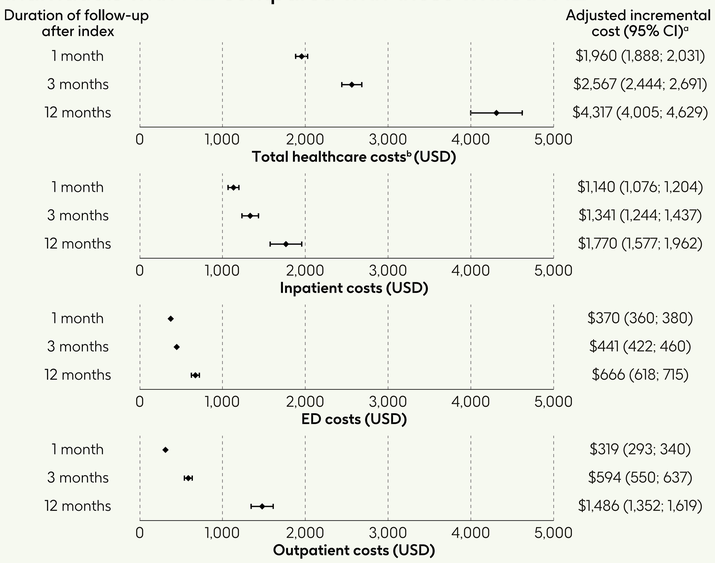
...compared with the non-HZ cohort

Note: See Supplemental Table 1 for additional demographic and clinical characteristics.

Figure 2: **All-cause HCRU was higher among individuals with HZ compared with those without HZ**

Note: All values were statistically significant based on $P<0.001$. See Supplemental Table 2 for stratification by outpatient visit type. See Supplemental Figure 1 for mean all-cause HCRU rates (PPPM) for each cohort. [a]Estimated using GLMs with a Poission distribution, log link function, and offset terms for follow-up time.

Figure 3: **All-cause healthcare costs were higher among individuals with HZ compared with those without HZ**



- Medical costs associated with HZ-related claims were also substantial in the 12 months following diagnosis among the HZ cohort (mean [SD] of $2,797 [$20,124] at 12 months post-index; Supplemental Table 3)
- Adjusted incremental all-cause healthcare costs associated with HZ increased with increasing age (see Supplemental Table 4)

Note: All values were statistically significant based on $P<0.001$. See Supplemental Table 4 for stratification by age group. See Supplemental Figure 2 for mean all-cause total healthcare costs for each cohort. [a]Estimated using linear models assuming a Gaussian distribution and an identity link function. [b]Total healthcare costs included total medical costs (sum of inpatient, ED, outpatient, and other medical costs) and pharmacy costs. Incremental all-cause pharmacy costs (95% CI) were $114 ($98; $130), $160 ($112; $209), and $320 ($160; $481) for the 1-month, 3-month, and 12-month follow-up periods, respectively.

Table 1: **Among those with HZ, presence of HZ complications further increased HZ-associated costs**

- **HZ without complications identified in claims was associated with adjusted 12-month incremental total healthcare costs of $3,405** (95% CI: 3,078; 3,731) versus non-HZ controls

	Individuals with complication, n (%) (N=261,154)	Incremental total 12-month cost due to HZ-related complication, mean (95% CI)[a]
PHN	11,814 (4.5%)	$9,908 (8,493; 11,323)
Specific non-PHN complications	40,801 (15.6%)	-
Ocular complications	21,591 (8.3%)	$2,260 (1,369; 3,152)
Neurologic complications	333 (0.1%)	$79,764 (64,220; 95,307)
Cutaneous complications	2,658 (1.0%)	$4,560 (1,694; 7,426)
Other non-PHN complications	18,868 (7.2%)	$2,782 (1,846; 3,719)

[a]Incremental costs represent the additional annual cost associated with each complication relative to HZ cases without any complications, estimated from the adjusted model. Estimates reflect the effect of each complication while holding all other baseline covariates constant at their average values.

Abbreviations

CI, confidence interval; **ED**, emergency department; **GLM**, generalized linear model; **HCRU**, healthcare resource utilization; **HZ**, herpes zoster; **HZO**, HZ ophthalmicus; **ICD-10-CM**, International Classification of Diseases, 10th Revision, Clinical Modification; **PHN**, postherpetic neuralgia; **PPPM**, per patient per month; **RZV**, recombinant zoster vaccine; **SD**, standard deviation; **US**, United States; **USD**, US dollar.

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Digital poster
Supplemental data

Narrated summary

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Supplement

Table S1. **Baseline characteristics among immunocompetent adults aged ≥50 years (1/3)**

	HZ cohort (N=261,154)	Non-HZ control cohort (N=261,154)	*P*-value
Demographics as of the index date			
Age (years), mean ± SD	65.6 ± 10.5	65.6 ± 10.5	1
Female, n (%)	166,151 (63.62%)	166,151 (63.62%)	1
Race, n (%)			<0.001
Caucasian	193,343 (74.03%)	183,905 (70.42%)	
African American	17,267 (6.61%)	25,557 (9.79%)	
Asian	7,019 (2.69%)	7,226 (2.77%)	
Other/Unknown	43,525 (16.67%)	44,466 (17.03%)	
Geographic region of residence, n (%)			<0.001
Northeast	59,179 (22.66%)	60,353 (23.11%)	
Midwest	91,409 (35.00%)	90,154 (34.52%)	
West	37,615 (14.40%)	37,788 (14.47%)	
South	63,533 (24.33%)	63,563 (24.34%)	
Other/Unknown	9,418 (3.61%)	9,296 (3.56%)	
Insurance type at index, n (%)[a]			<0.001
Commercial	106,932 (40.95%)	110,066 (42.15%)	
Medicare Advantage	111,024 (42.51%)	107,989 (41.35%)	
Medicaid	13,605 (5.21%)	14,265 (5.46%)	
More than one type	29,593 (11.33%)	28,834 (11.04%)	
Payer type at index, n (%)			<0.001
HMO	19,965 (7.64%)	20,660 (7.91%)	
POS	19,823 (7.59%)	18,442 (7.06%)	
PPO	5,413 (2.07%)	5,248 (2.01%)	
EPO	3,342 (1.28%)	3,059 (1.17%)	
Indemnity	571 (0.22%)	536 (0.21%)	
Other payer type	45,952 (17.60%)	44,241 (16.94%)	
Unknown payer type	166,088 (63.60%)	168,968 (64.70%)	

[a]Reported insurance type categories were mutually exclusive. Individuals with a combination of two or more insurance types at index were grouped into the "More than one type" category.

Abbreviations

EPO, exclusive provider organization; **HMO**, health maintenance organization; **HZ**, herpes zoster; **POS**, point of service; **PPO**, preferred provider organization; **SD**, standard deviation.

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Table S1. **Baseline characteristics among immunocompetent adults aged ≥50 years (2/3)**

	HZ cohort (N=261,154)	Non-HZ control cohort (N=261,154)	*P*-value
Calendar year at index, n (%)			
2016	9,874 (3.78%)	9,874 (3.78%)	
2017	42,387 (16.23%)	42,387 (16.23%)	
2018	46,922 (17.97%)	46,922 (17.97%)	
2019	42,216 (16.17%)	42,216 (16.17%)	1
2020	35,467 (13.58%)	35,467 (13.58%)	
2021	33,506 (12.83%)	33,506 (12.83%)	
2022	30,206 (11.57%)	30,206 (11.57%)	
2023	20,576 (7.88%)	20,576 (7.88%)	
COVID-19 period at index, n (%)			
Pre-pandemic period (October 1, 2015 to March 12, 2020)	149,437 (57.22%)	149,437 (57.22%)	
Early pandemic period (March 13, 2020 to December 10, 2020)	25,718 (9.85%)	25,718 (9.85%)	
Vaccination period (December 11, 2020 to June 14, 2021)	17,451 (6.68%)	17,451 (6.68%)	1
Delta variant predominance period (June 15, 2021 to December 1, 2021)	15,292 (5.86%)	15,292 (5.86%)	
Omicron variant predominance period (December 2, 2021 to May 11, 2023)	41,486 (15.89%)	41,486 (15.89%)	
Post-pandemic period (May 12, 2023 to December 31, 2023)	11,770 (4.51%)	11,770 (4.51%)	
Chronic comorbidities during the baseline period			
Hypertension, n (%)	148,073 (56.70%)	131,693 (50.43%)	<0.001
Diabetes mellitus, n (%)	64,209 (24.59%)	56,181 (21.51%)	<0.001
Coronary artery disease, n (%)	43,666 (16.72%)	35,052 (13.42%)	<0.001
Chronic kidney disease, n (%)	30,353 (11.62%)	25,926 (9.93%)	<0.001
Chronic obstructive pulmonary disease, n (%)	27,951 (10.70%)	21,877 (8.38%)	<0.001
Asthma, n (%)	24,086 (9.22%)	17,916 (6.86%)	<0.001
Heart failure, n (%)	19,304 (7.39%)	15,160 (5.81%)	<0.001
Myocardial infarction, n (%)	19,114 (7.32%)	15,522 (5.94%)	<0.001
Stroke, n (%)	14,662 (5.61%)	12,277 (4.70%)	<0.001
CCI during the baseline period			
CCI, mean ± SD[b]	1.05 ± 1.62	0.83 ± 1.44	<0.001

[b]CCI was defined based on criteria by Quan (2011).[1] Conditions included in CCI: AIDS/HIV, any malignancy except malignant neoplasm of skin, cerebrovascular disease, chronic obstructive pulmonary disease, congestive heart failure, dementia, diabetes with chronic complications, diabetes without chronic complications, hemiplegia or paraplegia, metastatic solid tumor, mild liver disease, moderate to severe liver disease, myocardial infarction, peptic ulcer disease, peripheral vascular disease, renal disease, and rheumatic disease.

Abbreviations

AIDS/HIV, acquired immunodeficiency syndrome/human immunodeficiency virus; **CCI**, Charlson Comorbidity Index; **COVID-19**, coronavirus disease 2019; **HZ**, herpes zoster; **SD**, standard deviation.

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Table S1. **Baseline characteristics among immunocompetent adults aged ≥50 years (3/3)**

	HZ cohort (N=261,154)	Non-HZ control cohort (N=261,154)	*P*-value
HZ-related clinical conditions during the baseline period			
Any clinical conditions potentially associated with HZ, n (%)	5,932 (2.27%)	3,852 (1.47%)	<0.001
Other interstitial pulmonary disease, n (%)	3,405 (1.30%)	2,321 (0.89%)	<0.001
Sicca syndrome, n (%)	1,584 (0.61%)	904 (0.35%)	<0.001
Sarcoidosis, n (%)	847 (0.32%)	547 (0.21%)	<0.001
Systemic sclerosis, n (%)	317 (0.12%)	189 (0.07%)	<0.001
Wegner's granulmonatosis, n (%)	51 (0.02%)	24 (0.01%)	<0.01
All-cause baseline HCRU from 365 days to 22 days (inclusive) before the index date, PPPM			
Number of inpatient admissions, mean ± SD	0.01 ± 0.06	0.01 ± 0.06	<0.01
Number of emergency department visits, mean ± SD	0.06 ± 0.21	0.04 ± 0.20	<0.01
Number of outpatient visits, mean ± SD	1.64 ± 2.45	1.30 ± 2.33	<0.01
All-cause baseline healthcare costs from 365 days to 22 days (inclusive) before the index date, PPPM, in 2024 USD			
Total costs, mean ± SD	$1,914 ± $4,549	$1,442 ± $3,736	<0.01
Total medical costs, mean ± SD	$1,569 ± $3,945	$1,159 ± $3,289	<0.01
Pharmacy costs, mean ± SD	$345 ± $1,938	$283 ± $1,528	<0.01

Abbreviations

HCRU, healthcare resource utilization; **HZ**, herpes zoster; **PPPM**, per patient per month; **SD**, standard deviation; **USD**, United States dollar.

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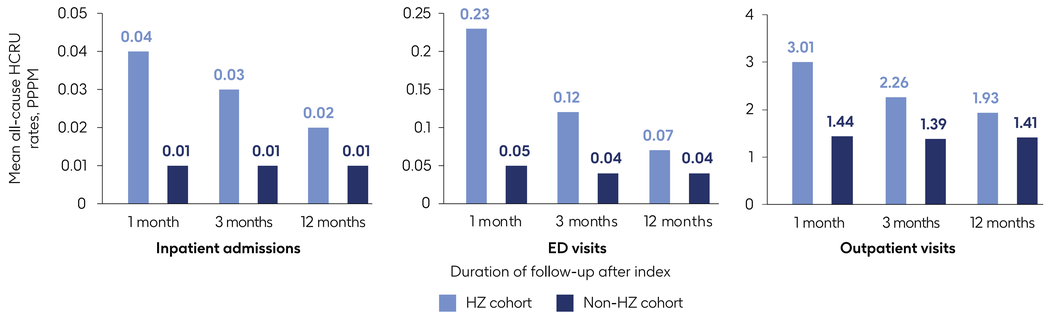
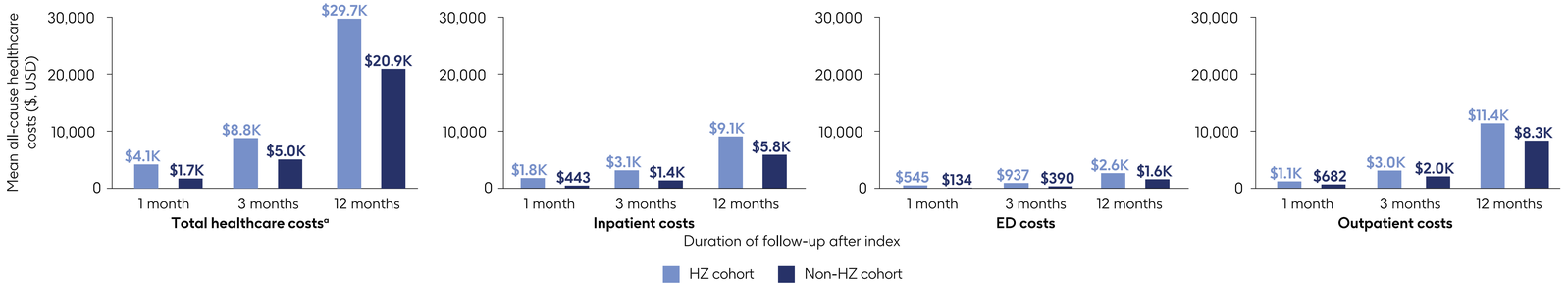
Supplemental Figure 1: **Mean all-cause HCRU rates among immunocompetent adults aged ≥50 years, HZ cohort versus non-HZ cohort**



Supplemental Figure 2: **Mean all-cause healthcare costs among immunocompetent adults aged ≥50 years, HZ cohort versus non-HZ cohort**



[a]Total healthcare costs included total medical costs (sum of inpatient, ED, outpatient, and other medical costs) and pharmacy costs.

Abbreviations

ED, emergency department; **HCRU**, healthcare resource utilization; **HZ**, herpes zoster; **K**, thousand; **PPPM**, per patient per month; **USD**, United States dollar.

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Table S2. **Adjusted rate ratios of HCRU during follow-up associated with HZ compared to non-HZ controls among immunocompetent adults aged ≥50 years, stratified by outpatient visit type**

Incremental HCRU of HZ, adjusted rate ratio (95% CI)	Immunocompetent HZ patients by outpatient visit type[a]		
	Specialist office visits	PCP office visits	Urgent care visits
1 month of follow-up	1.767*** (1.748; 1.787)	3.882*** (3.837; 3.927)	10.685*** (10.188; 11.205)
3 months of follow-up	1.466*** (1.453; 1.479)	2.199*** (2.180; 2.220)	4.603*** (4.459; 4.752)
12 months of follow-up	1.291*** (1.282; 1.300)	1.473*** (1.461; 1.484)	2.156*** (2.110; 2.204)

*$P<0.05$, **$P<0.01$, ***$P<0.001$. [a]Telehealth and other outpatient visits were also observed in the analysis but are not reported here.

Table S3. **HZ-related[a] medical costs during follow-up among immunocompetent adults aged ≥50 years with HZ**

Cumulative outcome[b]	1 month of follow-up	3 months of follow-up	12 months of follow-up
Total medical costs, mean (SD)	$2,041 ($15,647)	$2,345 ($17,239)	$2,797 ($20,124)
Inpatient costs, mean (SD)	$1,317 ($15,367)	$1,515 ($16,773)	$1,834 ($19,440)
ED costs, mean (SD)	$340 ($1,428)	$358 ($1,527)	$377 ($1,606)
Outpatient costs, mean (SD)	$365 ($2,004)	$449 ($2,445)	$558 ($3,067)
Other medical costs, mean (SD)	$19 ($300)	$23 ($420)	$28 ($502)

[a]HZ-related HCRU and costs were defined based on medical claims with a diagnosis code for HZ or HZ-related complications. [b]All costs were inflated to 2024 USD based on the Medical Care Services component of the Consumer Price Index.

Table S4. **Adjusted incremental total healthcare costs during follow-up associated with HZ compared to non-HZ controls among immunocompetent adults aged ≥50 years, stratified by age group**

Incremental total healthcare costs of HZ, adjusted cost difference (95% CI)[a]	Immunocompetent HZ patients by age subgroups[b]				
	50–59 years	60–64 years	65–69 years	70–79 years	≥80 years
1 month of follow-up	$1,235*** (1,148; 1,323)	$1,451*** (1,297; 1,606)	$1,806*** (1,608; 2,003)	$2,401*** (2,209; 2,592)	$3,850*** (3,607; 4,093)
3 months of follow-up	$1,570*** (1,381; 1,760)	$1,950*** (1,696; 2,204)	$2,429*** (2,083; 2,775)	$3,077*** (2,776; 3,377)	$5,123*** (4,726; 5,520)
12 months of follow-up	$2,942*** (2,441; 3,443)	$3,233*** (2,551; 3,915)	$4,133*** (3,273; 4,994)	$ 4,996*** (4,262; 5,729)	$7,957*** (7,051; 8,863)

*$P<0.05$, **$P<0.01$, ***$P<0.001$. [a]All costs were inflated to 2024 USD based on the Medical Care Services component of the Consumer Price Index. [b]Age stratifications included the following number of individuals in both the HZ cohort and non-HZ control cohort: age 50–59 years, N=92,493; age 60–64 years, N=45,859; age 65–69 years, N=28,968; age 70–79 years, N=56,837; age ≥80 years, N=36,997.

Abbreviations

CI, confidence interval; **ED**, emergency department; **HCRU**, healthcare resource utilization; **HZ**, herpes zoster; **PCP**, primary care physician; **SD**, standard deviation; **USD**, United States dollar.

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