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MAJOR ARTICLE

Cost of Herpes Zoster in Patients With Selected Immune-Compromised Conditions in the United States

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Background. This retrospective study investigates the healthcare costs of herpes zoster (HZ) in patients with selected immune-compromised (IC) conditions in the United States (US).

Methods. Patients with incident HZ diagnosis (index date) were selected from nationwide administrative claims databases from 2005 to 2009. Baseline IC groups, analyzed separately, included adults aged 18–64 years with the following: human immunodeficiency virus infection (HIV), solid organ transplant (SOT), bone marrow or stem cell transplant (BMSCT), or cancer; and older adults (aged ≥65 years) with cancer. Herpes zoster patients (n = 2020, n = 1053, n = 286, n = 13 178, and n = 9089, respectively) were 1-to-1 matched to controls without HZ (with randomly selected index date) in the same baseline group. The healthcare resource utilization and costs (2014 US dollars) during the first 2 postindex quarters were compared between matched cohorts with continuous enrollment during the quarter.

Results. Herpes zoster patients generally had greater use of inpatient, emergency room and outpatient services, and pain medications than matched controls ($P < .05$). The incremental costs of HZ during the first postindex quarter were $3056, $2649, $13 332, $2549, and $3108 for HIV, SOT, BMSCT, cancer in adults aged 18–64 years, and cancer in older adults, respectively (each $P < .05$). The incremental costs of HZ during the second quarter were only significant for adults aged 18–64 years with cancer ($1748, $P < .05$). The national incremental costs of HZ were projected to be $298 million annually across the 5 IC groups.

Conclusions. The healthcare cost associated with HZ among patients with studied IC conditions was sizable and occurred mainly during the first 90 days after diagnosis.

Keywords. cost; herpes zoster; immune-compromised; United States.

Herpes zoster (HZ) is a painful illness, caused by the reactivation of latent varicella-zoster virus infection [1]. The manifestations include an acute, painful vesicular rash, often with complications, such as postherpetic neuralgia [2–4]. Herpes zoster can be unusually severe or fatal in immune-compromised (IC) patients [5]. More than 1 million people are diagnosed with HZ each year in the United States (US) [6]. The incidence of HZ has increased from 10/1000 person-years in 1992 to 13.9/1000 person-years in 2010 in the US population older than 65 years [7]. Herpes zoster imposes a significant economic burden in direct healthcare costs in the US [8, 9], and HZ-related complications result in substantial indirect societal costs by altering quality of life and productivity [2, 10, 11].

Even though patients with IC conditions are a small proportion of all patients with HZ, the age-specific incidence of HZ is 2 to 10 times higher among patients with conditions, such as cancer, transplantation, and human immunodeficiency virus (HIV) infection, than in the general population [12]. Moreover, the healthcare costs associated with HZ are higher among patients with IC conditions than among immune-competent patients [8, 9, 13, 14]. Thus, the increased incidence and the associated higher costs of HZ in IC patients have a disproportionate impact on the overall burden of HZ. A thorough understanding of these healthcare costs associated with HZ in IC patients would inform the cost effectiveness of HZ prevention among these patients. Because limited data have been published about specific IC conditions, the objective of this study was to estimate the costs and healthcare utilization associated with HZ in patients with 5 important IC conditions.

METHODS

Data Sources

This study used administrative medical and pharmacy claims between January 1, 2005 and December 31, 2009 from the Truven Health MarketScan Commercial and Medicare Supplemental Insurance databases. The databases cover (1) commercially insured working adults and their dependents (approximately 30 million) from more than 100 large employer-sponsored health plans and (2) Medicare-eligible retirees with Medicare supplemental insurance (approximately 3

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million). The databases contain information on enrollment status, health plan type, demographic characteristics, region of residence, and healthcare use and reimbursements.

Sample Selection

Because the charges and reimbursement for Medicare enrollees (aged ≥65 years) are known to differ greatly from younger commercially insured people, these populations were analyzed separately. Patients were selected if they had a diagnosis of HZ (*International Classification of Diseases Clinical Modification-9* [ICD-9-CM] codes listed in Supplementary Appendix Figure 1) between January 1, 2005 and December 31, 2009. The date of the first HZ diagnosis defined the index date. Newly diagnosed cases were identified in patients with continuous enrollment for at least 6 months before the index date to exclude a previous HZ diagnosis. Patients with commercial insurance were excluded if they were <18 or ≥65 years old at the index date, and those with Medicare were excluded if they were <65 years old. A cohort of individuals without HZ was obtained with a randomly selected index date, using the same sample selection criteria applied to the HZ cohort.

The diagnosis codes in the medical claims (Supplementary Appendix Table 1) during the 6-month preindex period were examined to identify the following 5 IC groups: HIV infection, solid organ transplant (SOT), bone marrow or stem cell transplant (BMSCT), and cancer (excluding skin cancer) in adults aged 18–64 years (ie, commercial insurance population); and cancer in adults aged ≥65 years (ie, Medicare population), where the other 3 conditions were not examined in this population due to the small sample size. Patients with cancer were required to have cancer diagnoses on multiple dates. A patient could have multiple conditions and contribute to multiple disease groups.

Study Measures

Demographic characteristics including age, gender, geographic region, metropolitan area, and insurance type were identified at the index date. The Charlson Comorbidity Index (CCI) adapted to predict healthcare costs were estimated based on medical claims during the 6-month preindex period [15]. In addition, we identified comorbid conditions that have been associated with the risk of HZ [16], including cancer, HIV infection, SOT, BMSCT, rheumatoid arthritis, inflammatory bowel disease, systemic lupus erythematosus, multiple sclerosis, psoriasis, and diabetes. We also examined the use of chemotherapies or other immunosuppressants, except for HIV-infected patients, as documented in pharmacy claims and procedure codes in medical claims during the preindex period (Supplementary Appendix Table 1).

Healthcare resource utilization was classified by type of service, ie, all-cause hospitalizations, emergency room (ER) visits, outpatient services, and outpatient pharmacy prescriptions for antiherpes medications (acyclovir, valacyclovir, and famciclovir) and pain medications (Supplementary Appendix Table 1). Healthcare costs were evaluated by combining patient and insurance paid amounts in all medical and pharmacy claims. Costs were adjusted to 2014 US Dollars (USD) using the Consumer Price Index [17].

Statistical Analysis

For each IC condition, patients with HZ were 1-to-1 matched to patients without HZ, based on propensity score. The logistic regression determined the propensity score of having HZ versus no HZ, adjusting for patient characteristics including demographics, occurrence of each comorbid condition (excluding the IC condition analyzed), CCI, medications usage (chemotherapies and other immunosuppressants), occurrence of hospitalization, and healthcare costs during the 6-month preindex period. For cancer patients, the HZ and non-HZ patients were directly matched on hematologic cancer versus other types of cancer, in addition to the propensity score matching.

The patient characteristics during the 6-month preindex period were compared between the HZ cohort and non-HZ cohorts, before and after the matching, respectively. The quarterly healthcare resource utilization and costs during the 2 quarters after the index date were compared between the matched pairs who had continuous enrollment during the quarter. The rationale for using the first 2 quarters post-HZ diagnosis was empirical based on the fact that in the study population, more than 97% of all the HZ claims occurred during the first 180 days (95% during the first quarter).

The differences in the mean quarterly costs between the matched cohorts defined the incremental quarterly costs of HZ for each IC condition. The statistical significance of the incremental costs was assessed by the unadjusted generalized linear model with a log link and gamma distribution, which allows adjustments for the skewedness in distribution of costs [18]. Differences in patient characteristics and healthcare resource utilization were assessed using Student's t test for continuous variables and χ^2 test for categorical variables. The comparison in healthcare resource utilization and costs was also conducted during the quarter before the index date to determine whether cost differences preceded the index date.

National Projections of Healthcare Cost Associated With Herpes Zoster

To make national projections of healthcare costs associated with HZ, we first identified the proportion of adults in the studied databases with diagnoses of HIV infection, SOT, BMSCT, and cancer by age group during the year 2009. Second, we applied the same percentages to the US population in 2009 to estimate the number of adults in the US with any of the selected IC conditions. Third, by using age-specific incidence of HZ from a study of similar design and data sources [12], we estimated the number of HZ cases in selected IC groups during 2009 in the US. Finally, to obtain annual national estimates of healthcare cost of HZ in each IC condition, we multiplied the

incremental cost of an HZ case by the projected number of HZ cases with the IC condition in the US.

RESULTS

In the commercially insured population aged 18–64 years, the study sample consisted of 25 079 HIV, 13 324 SOT, 1428 BMSCT, and 264 409 cancer patients. The HZ cohort represented 8% (n = 2 020), 8% (n = 1053), 20% (n = 286), and 5% (n = 13 178) of these 4 IC conditions. In the Medicare population aged ≥65 years, the study sample consisted of 134 577 cancer patients, from which the HZ cohort represented 7% (n = 9089). Details of sample selection are presented in Supplementary Appendix Figure 1.

Several patient characteristics, such as age, gender, comorbid condition, use of chemotherapy, and other immunosuppressant medications, and hospitalization and healthcare cost during the preindex period were different between the HZ and non-HZ cohorts before matching (Supplementary Appendix Table 2). The matching strategy was successful in each IC group, because over 95% of HZ patients could be matched to 1 non-HZ patient, and the matched cohorts were balanced with no statistically significant differences for any of the characteristics (Table 1).

Detailed healthcare utilization by type of service, quarter, and IC condition is presented in Appendix tables (Supplementary Appendix Tables 3–7). Statistically significant differences in healthcare use between matched HZ and non-HZ cohorts were observed during the first postindex quarter across all the IC conditions (Table 2). For example, 6.3%, 9.6%, 19.6%, 5.5%, and 4.7% more patients with HZ had at least 1 hospitalization in the first postindex quarter than non-HZ patients within HIV, SOT, BMSCT, cancer aged 18–64 years, and cancer aged ≥65 years groups, respectively (each group, $P < .05$). Patients with HZ also had on average more hospitalizations (range, 0.06–0.27), longer inpatient stay (range, 0.32–1.97 days), more ER visits (range, 0.14–0.21), more outpatient visits (range: 2.0–2.55, with the exception of BMSCT patients), and more pain medication usage, including opioids, than non-HZ patients within each IC group (each group, $P < .05$). Differences between cohorts in the second quarter were much smaller and mostly occurred in cancer patients (Supplementary Appendix Tables 3–7).

Incremental costs of HZ by quarter and IC condition are summarized in Table 3. During the first postindex quarter, patients with HZ had higher healthcare costs than their matched controls with the same IC condition. In particular, a patient with HZ had additional average costs (ie, incremental costs of HZ) of $3056, $2649, $13 332, $2549, and $3108 than matched non-HZ patients with HIV, SOT, BMSCT, cancer aged 18–64 years, and cancer aged ≥65 years (each group, $P < .05$). No significant differences in costs between HZ and non-HZ cohorts were observed during the second quarter for IC groups, except in cancer patients aged 18–64 years, where the incremental costs of HZ were $1748 (Table 3, $P < .05$).

We estimated national projections of the costs associated with HZ (Table 4), using the statistically significant incremental costs of HZ (ie, the incremental costs of HZ in the first quarter for all the IC groups, and those in the second quarter for cancer patients aged 18–64 years). Annual national projections of HZ cases in the selected IC populations in adults aged 18–64 years consisted of approximately 47 000 HZ cases (7276 in HIV, 8610 in SOT, 560 in BMSCT, and 30 466 cases in cancer patients) and approximately $183 million in HZ-associated healthcare cost. In cancer patients aged ≥65 years, the study projected approximately 37 000 HZ cases and more than $114 million in HZ-associated healthcare costs.

DISCUSSION

We analyzed administrative medical and pharmacy claims from commercial and Medicare supplemental insurance databases to assess healthcare utilization and costs associated with HZ in 5 selected IC populations. Within each IC population, HZ diagnosis was associated with higher inpatient and outpatient healthcare utilization, including number and duration of hospitalizations, outpatient visits, and pain medication prescriptions. The incremental healthcare costs of HZ, relative to no HZ, were significant in the first quarter after HZ diagnosis, and were approximately $3000 in HIV, SOT, or cancer populations and $13 000 in BMSCT population. The higher cost of HZ in the BMSCT may be due to increased hospitalization (Supplementary Appendix Table 5). Except for cancer patients aged 18–64 years, the costs in the second quarter after HZ diagnosis were not significantly different between patients with and without HZ. We did not see a significantly higher total healthcare cost in HZ patients compared with the matched controls in the quarter before diagnosis (Supplementary Appendix Table 3–7), but we did not separately evaluate the month before diagnosis, in which higher costs have been noted in previous studies [8]. Assuming the utilization and costs captured in the current analysis can be generalized to approximate the healthcare cost of HZ in the total US population, we estimated a total cost of $298 million dollars in healthcare costs of HZ for the IC conditions included.

Two published analyses have evaluated the incremental cost in IC populations, but without analysis of each IC population individually. Based on a US claims database in years 2000 and 2001, Insinga et al [8] estimated the healthcare costs directly attributable to acute/subacute HZ in the period from 21 days before to 90 days after the diagnosis. The HZ-attributable costs were estimated to be $674 in 2005 USD or $817 in 2014 USD among IC patients, including those who had cancer, HIV, SOT, or other potentially IC conditions or therapies; but they were $373 in 2005 USD or $452 in 2014 USD among patients without IC conditions. White et al [9] used 1998–2003 data and reported that the incremental costs of HZ, relative to matched controls, were $1745 and $983 in 2008 USD ($1919 and $1081 in 2014 USD) among patients with and without IC conditions, respectively.

Table 1. Characteristics of Patients With Herpes Zoster (HZ) and Matched Non-HZ Controls by Selected Immune-Compromised Condition[a]

Demographic and Clinical Characteristics	Age 18–64 y (Commercially insured Patients)								Age ≥65 y (Medicare Patients)	
	HIV		SOT		BMSCT		Cancer		Cancer	
	HZ	Non-HZ	HZ	Non-HZ	HZ	Non-HZ	HZ	Non-HZ	HZ	Non-HZ
Number of patients	1927	1927	1053	1053	281	281	13 137	13 137	9 088	9088
Propensity score: mean (SD)	0.09 (0.06)	0.09 (0.06)	0.09 (0.03)	0.09 (0.03)	0.21 (0.06)	0.21 (0.06)	0.07 (0.05)	0.07 (0.05)	0.08 (0.04)	0.08 (0.04)
Age: mean (SD)	43.5 (9.1)	43.7 (9.3)	50.7 (9.7)	50.4 (10.0)	49.3 (12.1)	50.1 (11.6)	54.2 (8.4)	54.3 (8.3)	75.6 (6.6)	75.6 (6.6)
Male (%)	78.1	80.3	56.5	55.9	56.6	55.5	33.3	32.8	50.5	50.5
Region of residence (%)										
Northeast	12.5	13.1	11.6	12.1	11.4	12.8	11.0	10.2	13.1	12.5
Midwest	14.8	16.6	28.0	27.6	32.7	28.8	24.6	24.8	26.8	27.0
South	57.7	55.1	45.0	45.6	44.8	46.6	48.6	49.0	36.7	37.3
West	14.8	14.8	14.8	14.5	10.7	11.7	15.6	15.6	23.2	22.9
Unknown	0.2	0.4	0.6	0.2	0.4	0.0	0.3	0.4	0.2	0.4
Metropolitan area (%)	93.8	93.8	82.9	84.9	81.9	80.8	82.8	81.9	82.6	82.4
Charlson Comorbidity Index: mean (SD)	6.9 (1.5)	7.0 (1.7)	3.1 (2.6)	3.2 (2.6)	5.7 (2.9)	5.9 (3.0)	4.4 (2.8)	4.4 (2.8)	4.5 (2.6)	4.5 (2.6)
Comorbid conditions (%)										
Cancer	5.4	5.7	8.6	8.8	91.8	91.5	—	—	—	—
Hematologic cancer	2.59	2.59	2.47	1.42	90.75	90.04	22.6	22.6	20.7	20.7
HIV	—	—	0.2	0.1	0.4	0.7	0.8	0.8	0	0
SOT	0.1	0.1	—	—	1.8	3.2	0.7	0.7	0.2	0.3
BMSCT	0	0	0.5	0.1	—	—	2	1.7	0.2	0.2
Rheumatoid arthritis	0.6	0.9	1	1	0.7	1.1	2.2	1.9	1.8	1.8
Inflammatory bowel disease	0.9	0.8	2.1	1.5	0.4	0.7	0.9	0.9	0.8	0.7
Systemic lupus erythematosus	0.2	0.4	1.9	1.3	0	0	1.1	0.8	0.2	0.2
Multiple sclerosis	0.1	0.1	0	0	0	0	0.4	0.4	0.1	0.1
Psoriasis	0.6	0.6	0.1	0.1	0.4	0	0.7	0.7	0.8	0.9
Diabetes	7.7	8.5	36.9	38.7	11	12.1	13.5	13.9	18.1	18.1
Use of chemotherapies (%)	—	—	4.4	3.9	44.5	45.6	24.3	23.8	21.7	21.7
Use of other immunosuppressants (%)	—	—	70.3	68.6	42.4	46.6	24.3	23.6	25.9	25.9
Any inpatient stay (%)	12.6	12.9	28.4	30.1	50.5	53	19.4	19.1	20.5	20.1
Total healthcare costs (2014 $): mean	$13 692	$13 508	$41 080	$45 769	$115 831	$122 850	$30 718	$29 905	$18 700	$18 301
SE	$725	$854	$3233	$2939	$8773	$8282	$532	$375	$339	$375

Abbreviations: BMSCT, bone marrow transplant or stem cell transplant; CCI, Charlson Comorbidity Index; HIV, human immunodeficiency virus infection; SD, standard deviation; SE, standard error; SOT, solid organ transplant.

[a] Differences between HZ and non-HZ cohorts were assessed by the Student's *t* test for continuous variables and χ^2 for categorical variables. No statistically significant difference ($P < .05$) was identified. (Supplementary Appendix Table 2 contains patient characteristics by selected immune-compromised conditions and HZ status before matching.)

Table 2. Differences Between Herpes Zoster (HZ) Cases and Matched Non-HZ Controls in Healthcare Resource Utilization During the First Quarter After Diagnosis by Selected Immune-Compromised Conditions

	Age 18–64 y (Commercially Insured Patients)				Age ≥65 y (Medicare Patients)
First Quarter After Index Date[a]	HIV	SOT	BMSCT	Cancer	Cancer
Number of matched pairs (HZ and non-HZ patients)	1524	836	204	10 538	7225
Hospitalizations (HZ vs non-HZ patients)					
Patients with at least 1 hospitalization, absolute % difference	+6.3%	+9.6%	+19.6%	+5.5%	+4.7%
Patients with at least 1 hospitalization ≥3 d, absolute % difference	+4.9%	+7.7%	+14.7%	+4.6%	+3.8%
Number of hospitalizations, mean difference	+0.08	+0.14	+0.27	+0.09	+0.06
Number of hospitalizations ≥3 d, mean difference	+0.07	+0.11	+0.23	+0.08	+0.04
Number of inpatient days, mean difference	+0.55	+0.83	+1.97	+0.52	+0.32
ER visits (HZ vs non-HZ patients)					
Number of ER visits, mean difference	+0.32	+0.21	+0.21	+0.14	+0.17
Outpatient visits (HZ vs non-HZ patients)					
Number of outpatient visits, mean difference	+2.21	+2.55	−0.92[c]	+2.00	+2.35
Pain medication[b] (HZ vs non-HZ patients)					
Patients with at least 1 pain prescription, absolute % difference	+27.6%	+25.7%	+17.2%	+18.9%	+27.0%
Number of pain prescriptions, mean difference	+0.79	+0.99	+0.89	+0.72	+1.11
Patients with at least 1 opioid prescription, absolute % difference	+25.1%	+21.8%	+15.2%	+16.8%	+24.1%
Number of opioid prescriptions, mean difference	+0.50	+0.57	+0.37[c]	+0.41	+0.60
Antiherpes medication (acyclovir, valacyclovir, famciclovir)					
Patients with at least 1 antiherpes prescription, absolute % difference	+54.2%	+57.8%	+60.3%	+56.0%	+65.2%
Number of antiherpes prescriptions, mean difference	+0.80	+0.89	+1.19	+0.80	+0.89

Abbreviations: BMSCT, bone marrow transplant or stem cell transplant; ER, emergency room; HIV, human immunodeficiency virus infection; NSAIDs, nonsteroidal anti-inflammatory drugs; SOT, solid organ transplant.

[a] Index date was set at the first HZ diagnosis for HZ cohort, and it was randomly selected for non-HZ cohort.

[b] Treatments for pain include the following: opioids, other analgesic medications, NSAIDs, anticonvulsants, lidoderm, other topical anesthetic, serotonin-norepinephrine reuptake inhibitors, and tricyclic antidepressants.

[c] All differences are statistically significant at $P < .05$, except those with symbol of [-] (ie, mean difference of number of outpatient visits in BMSCT group and mean difference of number of opioid prescriptions in BMSCT group). (Note: Analysis included matched pairs [HZ and non-HZ patients] with full enrollment in the quarter.) (Supplementary Appendix Tables 3–7 contain more detailed use of healthcare resources by selected immune-compromised conditions and herpes zoster status.)

Table 3. Differences Between Herpes Zoster (HZ) Cases and Matched Non-HZ Controls in Direct Medical Cost During the First and Second Quarter After Index Date by Selected Immune-Compromised Conditions

	Age 18–64 y (Commercially Insured Patients)								Age ≥65 y (Medicare Patients)	
	HIV		SOT		BMSCT		Cancer		Cancer	
Direct Medical Cost by Quarter	HZ	Non-HZ	HZ	Non-HZ	HZ	Non-HZ	HZ	Non-HZ	HZ	Non-HZ
First quarter after index date[a]										
Number of patients[b]	1524	1524	836	836	204	204	10 538	10 538	7225	7225
Total costs[c]										
Mean	$9431	$6375	$18 278	$15 630	$50 312	$36 980	$15 739	$13 191	$11 579	$8471
(SE)	($735)	($443)	($1469)	($1141)	($9346)	($4292)	($424)	($338)	($1706)	($303)
Difference in mean	$3056[d]		$2649[d]		$13332[d]		$2549[d]		$3108[d]	
Second quarter after index date[a]										
Number of patients[b]	1022	1022	578	578	126	126	7369	7369	4974	4974
Total costs[c]										
Mean	$6355	$5889	$15072	$15 588	$25 721	$32 985	$11 671	$9923	$7451	$7068
(SE)	($592)	($489)	($1775)	($1719)	($6937)	($9574)	($417)	($316)	($290)	($313)
Difference in mean	$466		−$517		−$7264		$1748[a]		$383	

Abbreviations: BMSCT, bone marrow transplant or stem cell transplant; HIV, human immunodeficiency virus infection; SE, standard error; SOT, solid organ transplant; USD, US Dollars.

[a] Index date was set at the first HZ diagnosis for HZ cohort, and it was randomly selected for non-HZ cohort.

[b] Analysis included matched pairs (HZ and non-HZ patients) with full enrollment in the quarter.

[c] Costs are in 2014 USD.

[d] Cost differences were statistically significant at $P < .05$ based on generalized linear model estimations.

Table 4. National Projections of Direct Medical Cost Attributed to Herpes Zoster (HZ) in Selected Immune-Compromised[a] Populations and Age Groups in United States in 2009[b]

Population	% of MarketScan 2009 Database With the Condition[c]	Projected Number of Patients With Condition in US	Annual Incidence of HZ/1000 PY[d]	Annual Projected Number of HZ Cases in US	Cost of an HZ Case[e,f]	Annual Costs of HZ in US[f]
HIV and age 18–64	0.23%	417 071	17.4	7276	$3056	$22 236 002
SOT and age 18–64	0.12%	200 479	42.9	8610	$2649	$22 808 224
BMSCT and age 18–64	0.02%	33 637	16.7	560	$13 332	$7 472 114
Cancer and age 18–64	1.69%	2 859 500	10.7	30 466	$4297	$130 911 416
Cancer and age ≥65	6.91%	2 612 012	14.1	36 926	$3108	$114 766 041

Abbreviations: BMSCT, bone marrow transplant or stem cell transplant; HIV, human immunodeficiency virus infection; PY, person-years; SOT, solid organ transplant; US, United States.

[a] Immune-compromised disease in this study included immune-compromised diseases or those conditions requiring immune-modulating treatments.

[b] 2009 US population with age 18–64 years old: 181 129; with age 65+ years old: 37 787 (Source: US Census Bureau, Current Population Survey, Annual Social and Economic Supplement, 2009).

[c] The denominators were individuals with full year enrollment in 2009 MarketScan database who were in the corresponding age group.

[d] The incidence rate was estimated based on the HZ incidence rate by age group (18–49, 50–59, 60–64, and 65+) previously published [12], weighted by age distribution in our study sample.

[e] Healthcare costs derived from current study. They represent the incremental costs imposed by HZ in patients with selected immune-compromised disease. Statistically significant incremental costs were observed only during the first quarter after HZ diagnosis, except for adults 18–64 years with cancer diagnosis enrolled in an employer-based commercial insurance.

[f] Costs are in 2014 US dollars.

These previous studies considered IC patients as a group, whereas IC conditions differ considerably in severity, duration of illness, extent of immune compromise, and duration and type of therapy. All of these factors will influence incremental costs of HZ. For example, in the first quarter after diagnosis, the incremental costs of HZ for 4 IC conditions was $2549 to $3108, and for the BMSCT patients aged 18–64 years the cost was approximately 5 times greater. The cost of HZ in this study was higher than those noted in prior studies (but lower than in a study in SOT patients, see Palmer et al in paragraph below), which could be due to methodological differences including different care and related costs in the periods studied. We did not measure the cost of HZ in people who did not have IC conditions.

Few studies have estimated the costs of HZ in specific IC conditions. Palmer et al [19] analyzed a claims database for SOT recipients who were commercially or Medicare insured from January 1999 to January 2007. They reported the adjusted costs directly attributable to HZ to be $5353 in 2007 USD or $6112 in 2014 USD during the first quarter after diagnosis, more than twice the cost noted in our study. Different study design and populations may explain the different estimates between the 2 studies. For example, we did not include the Medicare population in our analysis of SOT patients, so the HZ patients with SOT in our study were on average 51 years old, but the sample had an average age of 57 years in the study by Palmer et al [19].

This study has several limitations. The subjects had commercial insurance or Medicare supplements, so uninsured people or people on Medicaid, incarcerated people, and veterans were underrepresented. Diagnoses were derived from administrative billing records, which are subject to miscoding or undercoding and are not validated against medical charts. Moreover, our data source did not capture (1) the individuals developing HZ who did not seek healthcare or (2) uncompensated costs. Propensity score matching was used to balance the patient characteristics of HZ and non-HZ cohorts. However, unmeasured confounding may still exist to bias the results. Information such as severity of the HZ or the severity of IC conditions is not explicitly available in the claims data. In addition, we could not identify whether the end of continuous enrollment in the claims data was due to death or change of insurance coverage. Older patients were excluded in the analyses on HIV and transplantation populations; however, the number of such patients is likely to be small, and an association between age and the costs of HZ was not observed among IC patients in a previous study [9, 19, 20].

CONCLUSIONS

In conclusion, patients with the studied IC conditions had significantly higher healthcare utilization and cost when developing HZ than their comparable matches without HZ. The higher cost was observed only in the first quarter after the diagnosis of HZ except for cancer patients aged 18–64 years, who also had increased costs in the second quarter. Current HZ vaccine, which is licensed for individuals aged ≥50 years and recommended for individuals aged ≥60 years, is contraindicated in patients with some IC conditions. Therefore, its efficacy and safety in adults with these IC groups have not been adequately studied. New HZ vaccines under development, which could be used in IC populations [20, 21], may provide an opportunity for HZ prevention and decreased HZ-related healthcare cost in IC patients.

Supplementary Data

Supplementary material is available online at Open Forum Infectious Diseases online (http://OpenForumInfectiousDiseases.oxfordjournals.org/).

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