Original Study

Economic Burden of Herpes Zoster Among Skilled Nursing Facility Residents in the United States

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A B S T R A C T

Objectives: To evaluate health care resource use and direct medical costs attributable to herpes zoster (HZ) among elderly residents of skilled nursing facilities (SNF).

Methods: This was a retrospective matched cohort study using data from 300 SNF in the United States. A total of 404 patients with HZ were matched with 1616 patients with no documented HZ or post-herpetic neuralgia using propensity scores. The study period included a 1-month pre-index period and the 90-day acute/subacute phase following the HZ index date. Health care resource utilization was captured from the long term care minimum dataset (MDS) and SNF admission-discharge records. The direct medical costs consisted of the SNF net bed revenue and hospitalization cost.

Results: Over the 4-month study period, significantly more patients were hospitalized among the HZ (20.5%) than non-HZ cohort (14.4%). Both the numbers of hospitalization episodes and hospitalization days were greater for HZ than for non-HZ patients. An average additional 0.09 hospitalization episodes and 0.55 days of hospitalization were estimated in a multivariate model for patients in the HZ compared with the non-HZ cohort. The incremental direct medical costs, which are composed of the incremental medical costs incurred in the SNF, and the incremental costs attributable to hospitalization, were estimated between $1079 and $1673 for patients with HZ.

Conclusion: In the SNF setting, the presence of HZ imposes significant health care resource utilization and direct medical costs.

Herpes zoster (HZ), caused by the reactivation of varicella-zoster virus (VZV) from a latent infection in the spinal dorsal root or cranial sensory ganglia, is usually manifested by a unilateral vesicular rash and pain.1,2 The main complications of HZ are acute and chronic neuropathic pain or postherpetic neuralgia (PHN),3,4 which can last for months, even years.3,4 Approximately 1 million Americans develop HZ each year.5 The incidence and severity of HZ, as well as the frequency and severity of its complications, increase with age.5,6 In the United States, the incidence of HZ in individuals younger than 40 years has been estimated to range from 1.1 to 1.9 cases per 1000 patient-years, after which it begins to rise, with 2.3 to 2.9 cases per 1000 patient-years among individuals aged 40 to 49 years and up to 12.0 cases per 1000 patient-years among individuals aged 80 years or older.4,7 Similar to that for HZ, the incidence and prevalence of PHN increase greatly with age.5,9 In a US study by Choo and colleagues,10 the prevalence of PHN was 14.7-fold higher (95% confidence interval [CI]: 6.8–32.0) at 30 days after HZ onset and 27.4-fold higher (95% CI: 8.8–85.4) at 60 days among individuals aged 50 years or older compared with younger patients. The results of a recent US study by Yawn and colleagues,4 where PHN was defined as zoster-associated pain persisting for at least 90 days, shows that PHN occurred in 18% of 1669 adult patients with HZ and in 33% of 246 patients aged 79 years and older. Overall, 10% of all patients with HZ experienced one or more nonpain complications such as ocular and neurological complications or skin superinfections.4

The substantial burden of illness that HZ and PHN produce in community-dwelling outpatients is well documented; HZ, and more particularly PHN, have been shown to interfere with activities of daily living, to lower health-related quality of life, and to worsen...
physical and mental health." To reflect personal burden associated with HZ, a recent study focusing on the value attributed by the community and patients to HZ prevention reported that community members "would trade substantial amounts of time or money to avoid herpes zoster, even in the least severe scenarios." Researchers have attempted to evaluate health care use and the economic burden related to HZ in various US settings. Coplan and colleagues indicated that, in 1994 among Kaiser Permanente Medical Care Program (Northern California, US) members, HZ resulted in 2.1 hospitalizations per 100,000 patient-years; this number encompassed hospitalization for HZ across all age groups. However, hospitalization was far more common among adults aged 60 years or older than in those aged 25 through 59 years. More recently, 2 US studies showed significant incremental health care use during the acute/subacute HZ period (defined as the 21 days preceding and 90 days following initial HZ diagnosis) among patients in a managed care setting. Cost estimates in these studies ranged from $431 to $605, with most of the cost burden caused by outpatient care and prescription drug costs. Interestingly, the average estimated incremental costs per patient with acute/subacute disease among individuals aged 80 years or older were more than 3 times that of individuals aged 19 years or younger. Both the aforementioned study by White and colleagues and an additional US study estimated HZ-related medical costs in the first year after HZ diagnosis compared with those for a control non-HZ population, which were propensity score matched for demographics and comorbidities. The average incremental medical costs were estimated to range from $757 to $1313 for HZ cases and from $2292 to $5742 for PHN cases.

There is empirical evidence highlighting the substantial clinical and economic burden of HZ in the US population; however, much of this research has concentrated on managed care and outpatient settings. Although the burden of HZ has proven to be high among older people, there are sparse data on burden of HZ among long-term care (LTC) cohorts. Further, because the incidence of HZ in older people from community-dwelling populations is itself often estimated, the incidence of HZ in the LTC subpopulation of older people is not known with certainty. With approximately 1.5 million elderly residents in US nursing homes, the occurrence of at least 10,500 to 16,500 HZ cases may be estimated per year using community-based studies, which report an incidence of 7 to 11 cases of HZ per 1000 elderly persons per year. It has also been suggested that residents of LTC facilities are at greater risk for developing HZ because of frailty; therefore, the number of HZ cases among residents of nursing homes may be underestimated. The objective of this study was to evaluate health care resource utilization (HCRU) and the direct medical costs of HZ for patients cared for in skilled nursing facilities (SNF).

Methods

Study Design and Patients

This was a retrospective matched cohort study of herpes zoster (HZ cohort) patients and non-HZ patients (control cohort) who received care in 1 of 300 skilled nursing facilities of a large LTC provider from 2002 to 2007. The centralized clinical and administrative data were available for these patients and the clinical and resource use data were extracted from the minimum data set (MDS). The MDS is part of the federally mandated process for clinical assessment of all residents in Medicare- or Medicaid-certified nursing homes. This process provides a comprehensive assessment of each resident's functional capabilities and helps nursing home staff identify health problems. Resident Assessment Protocols (RAs) are part of this process, and provide the foundation on which a resident's individual care plan is formulated. MDS assessment forms are completed for all residents in certified nursing homes, regardless of source of payment for the individual resident. MDS assessments are required for residents on admission to the nursing facility and then periodically, within specific guidelines and time frames.

HZ cases were first identified using the diagnosis (ICD-9) database and admission/discharge information. Subjects were included if they had a clinical diagnosis of HZ (ICD-9 diagnosis [primary or nonprimary] = 053.xx), had at least 90 days of follow-up data starting with the date of first HZ diagnosis, and had at least 180 days of baseline data before the first HZ diagnosis. This 180-day period without an HZ diagnosis was used to ensure that incident cases were analyzed and that existing cases were excluded. Patients who had no documented diagnosis of HZ and PHN were considered controls, and were required to have at least 9 months of continuous enrollment.

The date of HZ diagnosis was used as the index date for HZ cases. For control patients who had no documented diagnosis of HZ and PHN at anytime during their stay at an SNF, a random index date was assigned within the duration of the patient's SNF stay, determined after excluding the initial 180 days from admission and 90 days before discharge. Data were captured for the prodromal/acute/subacute phase of HZ, defined as the 30 days preceding (prodromal phase) and 90 days following (acute/subacute phase) the index date, for a total of 120 days, hereafter referred to as the "observation period". The baseline period encompasses the 150 days preceding the prodromal phase (see schematic).

The original sample for matching was composed of 426 HZ patients and 26,365 non-HZ patients who met inclusion criteria. A logistic-regression model was constructed to assign to each patient a propensity score defined as the predicted probability that this patient belongs to the HZ group. Predictor variables including demographics (age, gender, ethnicity), Charlson comorbidity index, total number of comorbid conditions (from MDS), and other selected characteristics (presence of specific other comorbidities such as pressure ulcers, urinary tract infections, depression, and schizophrenia; pain symptoms; resident falls/fractures; past medication history such as use of anticonvulsants, barbiturates, antipsychotics; SNF length of stay; baseline nursing labor cost; and net bed revenue) were entered into the model. Each patient in the HZ group was matched with 4 individuals in the non-HZ group who had the most similar propensity score, with the requirement that any difference between the scores of the persons in a pair did not exceed a preset limit of 0.01.

![Diagram](attachment)
The study protocol was reviewed and approved by IntegReview, an independent institutional review board located in Austin, Texas.

Outcome Measures

Hospitalization of SNF patients is captured in the discharge/admission database that records each incidence of discharging patients to hospitals and their return to the SNF. Episodes not resulting in an overnight stay at the hospital were considered as emergency room visits and were not included under direct medical costs because of their low occurrence. Both the number of hospitalization episodes and hospitalization days were analyzed. Although recorded in the MDS, because physician visits apply only to the 14 days preceding the latest entry into the MDS, the precise number of these visits within the SNF setting for the study evaluation period could not be captured and was therefore not included in the final economic evaluation.

Incremental medical costs were estimated in 2 parts. The first part estimates incremental costs incurred by patients with HZ while in the skilled nursing facility; the second part estimates the incremental cost of hospitalizations for patients with HZ. Incremental costs incurred by patients with HZ while in the skilled nursing facility were estimated from net bed revenue because reimbursements for the skilled nursing facilities were not based on the actual services provided and actual medical costs were not available. The net bed revenue, which is the monthly reimbursement received by an LTC provider for all services provided for patients based on their health status, was used as a surrogate measure for the medical costs and was adjusted to 2007 dollars using the medical consumer price index. Incremental hospitalization costs were estimated by multiplying the average costs per hospitalization (from the literature) and the difference in the number of hospitalizations between HZ and non-HZ patients. The average hospitalization costs per episode attributable to HZ for the older adult population ranged from $6815 to $13,412.20-23 Using this range, we calculated a lower and upper bond for the incremental cost of hospitalization attributable to HZ for our study population. The total direct medical costs consisted of both net bed revenue and costs attributable to hospitalization.

Statistical Analyses

Continuous variables were summarized using mean and standard deviation and sample means were compared using t tests between the HZ and control cohorts. Categorical variables were summarized using the sample size and proportions, with the comparison between cohorts based on the chi-square test.

End points such as hospital days and costs had a skewed, long tail distribution. Hence, they were analyzed using a generalized linear model,24 which accommodates more flexible mean-variance structures. With the emphasis of the study being the estimation of incremental difference between HZ and non-HZ cohorts, rather than the identification of risk factors, the final multivariate model included all clinically important baseline prognostic factors, such as age, gender, race, activities of daily living scores, pain severity at baseline, baseline costs, and an indicator variable for being hospitalized in the baseline period.

To account for the possible overdispersion and its impact on the statistical inference, a negative binomial distribution with log link was used in lieu of the Poisson distribution.25 The negative binomial distribution is a generalization of Poisson regression, which incorporates overdispersion, allowing the variance to be a quadratic function of the mean. The model’s goodness of fit was assessed via the deviance chi-square statistic. Sensitivity analyses were performed using a linear model to assess the robustness of the negative binomial results.

In the generalized linear model, the adjusted means for the HZ and control non-HZ patients were based on actual distribution of the sample population rather than the default equal weight distribution. Because a substantial number of patients were not being hospitalized, the hospitalization days were analyzed via a 2-part model: the first part was to estimate the probability of having a length of stay greater than zero for patients in the HZ and non-HZ cohorts, and the second part was to estimate the length of stay using a multivariate generalized linear model for the HZ and non-HZ patients who were hospitalized.

Results

Baseline Characteristics

Table 1 shows the characteristics at baseline from a total of 2020 patients consisting of 404 patients who later developed HZ and 1616 control non-HZ patients matched according to propensity scores. HZ patients ranged in age from 27 to 100+ years, with a mean age of 82.6 years and matched non-HZ control patients from 41 to 100+ with a mean age of 82.9 years (Table 1). Nearly all patients (91.3% and 89.9% for HZ and non-HZ patients, respectively) were 70 years or older and about three quarters (76.2% and 75.7% for HZ and non-HZ patients, respectively) were female. White patients accounted for 90.8% and 92.8% of the HZ and matched non-HZ cohort, respectively; 0.2% to 6.2% of HZ patients and 0.2% to 4.6% of non-HZ control patients were from other ethnicities. During the 150-day baseline period, 71% of the HZ patients and 69.8% of the matched controls did not report pain. The mean Charlson comorbidity index at baseline was 0.31 for the HZ population and 0.30 for the matching non-HZ population. The mean baseline score for activities of daily living was 19.3 for either cohort. At baseline, 21.3% of patients in the HZ cohort and 18.8% of patients in the non-HZ cohort had been hospitalized; the mean numbers of hospitalization days for those hospitalized were 7.95 and 8.79, respectively. There were no statistically significant differences in either the modes of locomotion or transfer, or in number of falls during the preceding 30 or 180 days between patients in the HZ and non-HZ cohorts. Patients in the matched HZ and non-HZ cohorts were similar for all demographics and baseline characteristics such as number of emergency room episodes, physician visits, or net bed revenue.

HCRU and Net Bed Revenue Associated with HZ

The proportion of patients who were hospitalized during the 4-month observation period in the HZ cohort (20.5%) was significantly higher than in the non-HZ cohort (14.4%; P <.002) (Table 2). In addition, the number of hospitalization episodes was significantly greater among HZ patients than non-HZ patients (0.28 vs. 0.19, P=.002). Among the cohort of hospitalized patients (N = 316), 72% of HZ patients and 73% of non-HZ patients had only one episode of hospitalization. The mean length of hospitalization stay for the hospitalized cohort was 8.35 days for the HZ patients and 8.74 days for non-HZ patients. For the overall study population (N = 2020), the mean length of hospitalization stay was 1.72 days and 1.26 days for the HZ and control cohorts, respectively. The number of physician visits, captured for 14 days before the last MDS update, was significantly higher among HZ than among non-HZ patients. The average net bed revenue, which does not cover the costs incurred while the patient is hospitalized, was $19,074.50 for the HZ patients and $18,474.80 for the non-HZ patients during the observation period.
US, HZ-related hospitalizations were reported in 3% of HZ patients control non-HZ cohort. In a recent population-based study in the more patients hospitalized among the HZ cohort than among the Discussion

that the direct medical costs for HZ patients were $1079 to $1673 resulting in average incremental costs of $466 for patients with HZ; $18,347 for the non-HZ patients during the observation period, adjusted mean net bed revenue was $18,813 for the HZ patients and non-HZ patients with a difference of 0.55 days (ratio: 148%). The hospitalization stay was 1.70 days for HZ patients and 1.15 days for

$1079 to $1673 for the observation period (1 month preceding through 3 months after the HZ index date) is considerably higher than previously published cost estimates in the general population. By comparison, 2 US studies estimated direct medical costs attributable to HZ at $431 and $605 during the 21 days preceding and 90 days following initial HZ

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Results from the Multivariate Model

The adjusted mean numbers of hospital episodes from the multivariate model were 0.25 and 0.16 for patients in the HZ and non-HZ cohorts, respectively, with a difference of 0.09 (Table 3). The mean incremental costs of hospitalization were estimated at $6370.15 $22,453.00 during the 4-month observation period, there were significantly more patients hospitalized among the HZ cohort than among the control non-HZ cohort. In a recent population-based study in the US, HZ-related hospitalizations were reported in 3% of HZ patients across all ages and 9% of patients aged 80 years or older. The current study, evaluating a population requiring long term care and taking into consideration all hospitalizations whether specifically HZ related or not, reported a higher proportion, 20.5%, of HZ patients requiring hospitalization compared with 14.4% in the non-HZ patients. The average number of hospitalization episodes and days were also significantly greater among the HZ than the non-HZ cohort. Interestingly, a sharp increase in the number of hospitalization episodes attributable to HZ, depending on patient age, was previously shown in the US, rising from approximately 14 hospitalizations per 100,000 patients aged 50 to 59 years to approxi-

Discussion

During the 4-month observation period, there were significantly more patients hospitalized among the HZ cohort than among the control non-HZ cohort. In a recent population-based study in the US, HZ-related hospitalizations were reported in 3% of HZ patients

Table 1
Demographics and Baseline Characteristics (During the 150-Day Baseline Period)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>HZ Cohort (n = 404)</th>
<th>Non-HZ Cohort (n = 1616)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at index (mean ± SD)</td>
<td>82.60 ± 10.31</td>
<td>82.90 ± 10.36</td>
<td>.644³</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male (%)</td>
<td>96 (23.8)</td>
<td>393 (24.3)</td>
<td>.815⁵</td>
</tr>
<tr>
<td>Female (%)</td>
<td>308 (76.2)</td>
<td>1223 (75.7)</td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White (%)</td>
<td>367 (90.8)</td>
<td>1499 (92.8)</td>
<td>.722¹</td>
</tr>
<tr>
<td>Black (%)</td>
<td>25 (6.2)</td>
<td>75 (4.6)</td>
<td></td>
</tr>
<tr>
<td>Hispanic (%)</td>
<td>7 (1.7)</td>
<td>22 (1.4)</td>
<td></td>
</tr>
<tr>
<td>Asian/Pacific (%)</td>
<td>4 (1.0)</td>
<td>17 (1.1)</td>
<td></td>
</tr>
<tr>
<td>American Indian/Alaskan (%)</td>
<td>1 (0.2)</td>
<td>3 (0.2)</td>
<td></td>
</tr>
<tr>
<td>Pain symptoms</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain free (%)</td>
<td>287 (71.0)</td>
<td>1128 (69.8)</td>
<td>.747¹</td>
</tr>
<tr>
<td>Less than daily/mild (%)</td>
<td>43 (10.6)</td>
<td>170 (10.5)</td>
<td></td>
</tr>
<tr>
<td>Less than daily/moderate (%)</td>
<td>52 (12.9)</td>
<td>208 (12.9)</td>
<td></td>
</tr>
<tr>
<td>Less than daily/excruciating (%)</td>
<td>2 (0.5)</td>
<td>20 (1.2)</td>
<td></td>
</tr>
<tr>
<td>Daily and mild (%)</td>
<td>20 (5.0)</td>
<td>90 (5.6)</td>
<td></td>
</tr>
<tr>
<td>Modes of locomotion—No tools/aid used (%)</td>
<td>153 (37.9)</td>
<td>610 (37.8)</td>
<td>.960⁴</td>
</tr>
<tr>
<td>Modes of transfer—None used (%)</td>
<td>19 (4.7)</td>
<td>96 (5.9)</td>
<td>.340⁴</td>
</tr>
<tr>
<td>Falls in past 30 days (%)</td>
<td>47 (11.6)</td>
<td>202 (12.5)</td>
<td>.640⁴</td>
</tr>
<tr>
<td>Falls in past 180 days (%)</td>
<td>115 (28.5)</td>
<td>437 (27.0)</td>
<td>.570⁴</td>
</tr>
<tr>
<td>Hospitalized</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes (%)</td>
<td>86 (21.3)</td>
<td>303 (18.8)</td>
<td>.247¹</td>
</tr>
<tr>
<td>No (%)</td>
<td>318 (78.7)</td>
<td>1313 (81.3)</td>
<td></td>
</tr>
<tr>
<td>Number of hospitalization episodes (mean ± SD)</td>
<td>0.27 ± 0.59</td>
<td>0.27 ± 0.65</td>
<td>.848⁴</td>
</tr>
<tr>
<td>Number of hospitalization days (mean ± SD)</td>
<td>1.69 ± 4.59</td>
<td>1.64 ± 5.57</td>
<td>.851¹</td>
</tr>
<tr>
<td>Number of hospitalization days for those hospitalized (mean ± SD)</td>
<td>7.95 ± 7.05</td>
<td>8.79 ± 10.19</td>
<td>.477¹</td>
</tr>
<tr>
<td>Number of ER episodes (mean ± SD)</td>
<td>0.01 ± 0.11</td>
<td>0.01 ± 0.09</td>
<td>.330⁴</td>
</tr>
<tr>
<td>Number of physician visits (mean ± SD)</td>
<td>0.61 ± 0.73 (N=350)</td>
<td>0.59 ± 0.74 (N=1366)</td>
<td>.652⁴</td>
</tr>
<tr>
<td>Activities of daily living self assessment score (mean ± SD)</td>
<td>19.30 ± 10.16</td>
<td>19.30 ± 10.00</td>
<td>.876⁴</td>
</tr>
<tr>
<td>Charlson Comorbidity Index (mean ± SD)</td>
<td>0.31 ± 0.30</td>
<td>0.30 ± 0.29</td>
<td>.441⁴</td>
</tr>
<tr>
<td>Baseline Net Bed Revenue (mean ± SD)</td>
<td>$22,763.60 ± $6370.15</td>
<td>$22,453.00 ± $6316.02</td>
<td>.378⁴</td>
</tr>
<tr>
<td>Number of long term care years before index date (mean ± SD)</td>
<td>2.87 ± 2.37</td>
<td>2.65 ± 2.38</td>
<td>.096⁴</td>
</tr>
</tbody>
</table>

Activities of daily living assessed: bed mobility, walk in the room, walk in the corridor, locomotion off unit, dressing, eating, toilet use, and personal hygiene. Pain symptoms are measured in MDS in terms of frequency and intensity. The pain measures correspond to the highest level of pain present in the past 7 days. Modes of locomotion include cane/walker/crutch, self-wheeling, wheelchairing by another person, wheeling as a primary mode of locomotion. Modes of transfer include bedfast all or most of the time, use of bed rails for bed mobility or transfer, manual lifting, mechanical lifting, transfer aid (eg, slide board, trapeze, cane/walker/crutch, wheelchair), or no assistance needed. Incidence of falls is captured under the category of “accidents” in the MDS. *n – number of patients in the cohort unless otherwise specified. ¹t test. ²Chi-square test. ³Occurring during the 14 days preceding minimum data set (MDS) form completion.
diagnosis, and during the first 90 days following HZ diagnosis, respectively.\textsuperscript{15,16} Because both studies used insurance claims from all ages, the observed disparity compared with our results may be attributable to the difference in average age between the groups studied. The frail health status of SNF residents could also contribute to the higher costs of HZ in our study, beyond that which is attributable to more advanced age alone. The most elderly age group for which costs were given in the study by Insinga and coworkers\textsuperscript{15} was over 80 years old. This group incurred incremental costs attributable to HZ of $805. In the other study, costs were not included for acute/subacute phase de...
In conclusion, this study demonstrates that the presence of HZ is associated with a substantial economic burden in SNF settings. Future research is needed to establish optimal strategies for HZ treatment,

References