Characterizing Healthcare Utilization, Direct Costs, and Comorbidities Associated with Interstitial Cystitis: A Retrospective Claims Analysis

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Abstract

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Introduction

Interstitial Cystitis (IC) is a debilitating condition that affects up to five percent of the United States (US) population.[1] The condition is characterized by bladder pain, urinary urgency and frequency, and in some patients, bladder lesions called Hunner's Lesions (HL). Patients with HL experience a clinical course distinctly different from patients without HL.[2] Prior research describing the burden of IC is outdated and lacks HL-level detail. This study aims to characterize healthcare utilization, direct costs, and comorbidities associated with IC, and among IC patients, elucidate differences between those with and without HL.

Methods

A retrospective analysis was conducted using healthcare claims from the Truven Health MarketScan® Research Databases. Adults with an incident IC diagnosis between 2009 and 2014 were identified and matched to non-IC patients on age, gender, and geographic region. Healthcare utilization, direct costs, and comorbidities during the first 12 months after diagnosis were compared between the two groups, as well as between IC subgroups with and without HL.

Results

IC patients (n=24,836) were predominantly (92%) female, with a mean age of 49.0 (SD = 15.3) years. IC patients utilized significantly more healthcare resources across all categories compared to non-IC patients. On average, having IC was associated with $6,798 higher total healthcare costs than not having IC (95% CI: $6,253, $7,343), with outpatient costs contributing to 71% of the difference, after adjusting for baseline age, gender, region, insurance type, plan type, and CCI. The odds of developing IC-related comorbidities were 2.61 times greater in IC patients compared to non-IC patients (95% CI: 2.52, 2.70), adjusting for baseline age, sex, region, and CCI. Among IC patients, the HL subgroup (n=292) utilized more healthcare resources, and having HL was associated with $6,486

higher total healthcare costs compared to not having HL (95% CI: $3,497, $9,475) after adjusting for baseline age, gender, region, insurance type, and plan type.

Conclusion

Our findings suggest that patients with IC have significantly higher healthcare utilization, costs, and comorbidities compared to non-IC patients. This economic burden is further amplified in those with HL.

INTRODUCTION

Interstitial Cystitis (IC) is a chronic, debilitating condition that is characterized by persistent bladder pain, urinary urgency, frequent urination, and nocturia. Though known to predominantly occur in females, the etiology and pathophysiology of IC remain unclear, making the condition both challenging to diagnose and treat.[3,4] Without clear diagnostic standards, it is common for IC patients to go undiagnosed for as long as five years.[5] Consequently, estimates of IC prevalence vary between 0.2 to 4.6 percent of the United States (US) population, with some suggesting that it could be much higher.[6-8] Additionally, approximately 10 to 56 percent of IC patients also experience painful lesions on the bladder wall, known as Hunner's Lesions (HL).[9,10] While the presence of HL has been traditionally classified as a subtype of IC, recent research suggest HL may represent its own distinct condition.[2] Not only do IC patients with HL differ from those without HL demographically, but they also respond differently to existing treatments.[11,12]

In general, IC is treated with a variety of pharmacologic and medical interventions, most of which are off-label and all of which provide temporary, suboptimal relief. The only FDA-approved treatments for IC are pentosan polysulfate sodium (Elmiron®) and dimethyl sulfoxide (RIMSO-50®). However, given conflicting evidence regarding the effectiveness of these treatments, current guidelines do not make any recommendations for using one agent over another to treat IC patients without HL.[11] In contrast, guidelines recommend fulguration, a surgical procedure that removes affected tissue, to treat those with HL.[11] Although fulguration is the best available approach to treating HL, it does not provide permanent relief.[13]

Without lasting treatment options, patients with IC experience a reduced quality of life and are expected to be a significant economic burden to society. To date, three claims-based analyses have been published on the economic burden of IC in the US. In 2006, Wu et al published a retrospective claims-based analysis to describe the healthcare utilization, costs,

and comorbidities associated with IC using data from 1999-2002. He found IC patients to spend, on average, $6,614 on direct costs during the first year after diagnosis, which was $3,756 more than non-IC patients.[14] In 2008, Clemens et al found IC patients to incur an average cost of $7,100, which was $4,106 more than non-IC patients from 1998-2003 data in a managed care population.[15] In the same year, Stanford et al found IC patients to spend on average, $9,186 in direct costs using 2000-2005 data, but did not compare these findings to a control group.[16]

Current literature falls short in fully capturing the extent of the economic burden of IC. Claims-based studies published to date are based on outdated data. Furthermore, no studies have specifically examined patients with HL, whose burden of illness is expected to differ significantly from patients without HL. The primary objective of this study is to describe and compare healthcare utilization, direct costs, and comorbidities for patients with IC and those without IC during the first-year after diagnosis. The secondary objective is to describe and compare HRU, direct costs, and comorbidities for IC patients with HL and without HL during the first-year after diagnosis.

METHODS

Data Source

Data were obtained from Truven Health MarketScan® Research Commercial and Medicare Supplemental Claims Databases. The databases are large, nationally-representative databases that contain Health Insurance Portability and Accountability Act (HIPAA) compliant, de-identified, patient-level, paid and adjudicated claims information for over 143 million unique patients in the US.[17,18] The Commercial Claims database includes private-sector claims data from approximately 100 payers and contains more than 500 million claim records.[17,18] The Medicare Supplemental Claims database contains claims data on Medicare recipients who subscribe to Medicare supplemental coverage through privately insured fee-

for-service (FFS) or capitated health plans.[17,18] Claims from the 2009-2014 annual summary enrollment, inpatient admissions, inpatient services, outpatient services, and outpatient prescription claims files were analyzed for this study. This study did not meet the federal definition of "human subjects research," and was therefore exempt from Institutional Review Board (IRB) review by the University of Washington Human Subjects Division.

Cohort Identification

IC Patients

IC patients were required to be age 18 and older; have an incident diagnosis of IC; be continuously enrolled 12 months pre- and post- index diagnosis date; and free of bladder-related cancers. An IC diagnosis was defined as having at least one ICD-9 code of 595.1 ("Chronic Interstitial Cystitis") in the inpatient or outpatient claims files. Patients' first ICD-9 code of 595.1 was considered their index diagnosis. To ensure their index diagnosis was reflective of an *incident* IC diagnosis, patients were excluded if they had any evidence of IC treatment 12 months prior to the date of their index diagnosis. Evidence of IC treatment included claims for pentosan polysulfate sodium (Elmiron®) or fulguration, but not dimethyl sulfoxide (RIMSO-50®) given that the agent is a provider-administered drug that is not identifiable from claims data. Patients were further excluded if they were younger than 18 years of age; did not have 12 months of continuous enrolled pre- and post- index date; or had any bladder-related cancers (Figure 2). The 12 months prior to the index diagnosis date formed the pre-index or baseline period. The 12 months after the index diagnosis date formed the post-index or follow-up period.

Non-IC patients

Four non-IC patients were randomly selected to match each IC patient on the basis of age, gender, and geographic region. Non-IC patients were required to not have an IC diagnosis or any evidence of IC treatment. Non-IC patients were also excluded if they were younger

than 18 years of age; did not have 12 months of continuous enrolled pre- and post- the index diagnosis date of their matched case; or had any bladder-related cancers.

HL and Non-HL Subgroups

IC patients were further stratified into HL and non-HL subgroups. Because ICD-9 codes do not distinguish between IC with HL and without HL, fulguration was used as proxy to identify IC patients with HL. To be considered an IC patient with HL, IC patients were required to have at least one claim with a CPT code for fulguration (Table 11) in the post-index period.

Assessment of Healthcare Resource Utilization, Costs, and Comorbidities

Post-index healthcare resource utilization, costs, and comorbidities were determined by identifying claims that occurred within 365 days of the index date. For healthcare resource utilization and costs, claims were categorized into the following service categories: inpatient admissions, outpatient visits, emergency department (ED) visits, and outpatient prescriptions. To further examine differences in prescription utilization and costs, the outpatient prescriptions category was further subdivided into opioid analgesics, sedative/hypnotics, and muscle skeletal relaxants.

The frequency of inpatient admissions during the post-index period was determined by counting unique admission dates for each patient in an inpatient services file. The frequency of outpatient visits during the post-index period was determined by counting unique service dates for each patient in an outpatient file. The frequency of ED visits was determined by counting unique service dates categorized as "Emergency Department Visits" during the post-index period in both inpatient and outpatient files. The frequency of prescription days'

supply fills (new or refill) was determined by counting the days supply fills for each patient during the post-index period in the drug file. To report the frequency of prescription days' supply fills by therapeutic category, the days' supply fills for each therapeutic category were counted for each patient during the post-index period in the drug file. The unadjusted mean frequency and 95% confidence intervals of each service category were reported. Additionally, unadjusted proportions and the number of patients with at least one inpatient admission, ED visit, opioid analgesic, sedative/hypnotic, or skeletal muscle relaxant prescription claim were reported. Adjusted healthcare utilization ratios and 95% confidence intervals were also reported for each service category

Likewise, costs associated with inpatient admissions, outpatient visits, ED visits, and prescriptions filled (total and by therapeutic category) were determined by summing costs for each patient in each service category during the post-index period. Costs associated with inpatient admissions, outpatient visits, and prescriptions filled were also summed to report a total healthcare cost. Costs were calculated from three perspectives: 1) *total*, which included payer and patient; 2) *payer*; and 3) *patient*, which include copay, deductible and coinsurance. For each cost perspective, unadjusted mean costs and 95% confidence intervals were reported for each service category. Adjusted incremental costs and 95% confidence intervals were also reported for each service category from the total cost perspective.

Total and incident IC-related comorbidities were reported. IC-related comorbidities refer to comorbidities that have previously been found to be associated with IC, and include anxiety, depression, insomnia, vulvodynia, chronic fatigue syndrome, sicca syndrome, irritable bowel syndrome, migraines, and fibromyalgia.[12] Total IC-related comorbidities included patients that had a claim associated with a specific IC-related comorbidity at any time during the

pre- or post-index periods. To be considered to have an incident IC-related comorbidity, patients were required to not have a claim associated with a specific IC-related comorbidity during the pre-index period but to have such a claim during the post-index period. The unadjusted proportions and number of patients with total and incident IC-related comorbidities was reported for all IC-related conditions as well as for each condition separately. The adjusted proportions and number of patients with incident IC-related comorbidities were also reported for all IC-related conditions as well as for each condition separately.

Baseline Comorbidity

To adjust for potential differences in baseline comorbidity that could affect healthcare utilization and cost during the post-index period, the Deyo-Charlson Comorbidity Index (CCI) Score was calculated for each patient using inpatient and outpatient claims data 365 days prior to their index date. The CCI score assigns weights to comorbidities such as liver disease, diabetes, AIDS, and cancer, which are then added together to create a summary indicator of baseline health status.[19] A higher CCI score indicates more baseline risk.

Statistical Analyses

Univariate analyses were conducted to estimate means and counts for continuous variables, as well as proportions and counts for categorical variables. Bivariate analyses were performed to compare utilization, costs, and IC-related comorbidities between IC patients and non-IC patients, as well as between HL and non-HL patients. Unadjusted mean counts of healthcare utilization and mean costs were compared using a two-sided, two-sample t-test of means assuming unequal variances. Unadjusted proportions of healthcare utilization and IC-related comorbidities were compared using a two-sided, two-sample t-test of proportions assuming unequal variances. For all tests, statistical significance was established at a level of $\alpha=0.05$.

Multivariable analyses were conducted to adjust for potential confounding of healthcare utilization, costs, and comorbidities.

For healthcare utilization, negative binomial regression models were used to model inpatient admission, outpatient visit, and ED visit counts. A linear regression was used to model prescription days' supply. Logistic regression models were used to model proportions with at least one inpatient admission or ED visit. Models estimating healthcare utilization adjusted for baseline age, gender, geographic region, insurance type (Commercial vs. Medicare Supplemental), insurance plan type, and CCI score.

Cost data are historically heavily right-skewed, with the majority of patients having few to no costs.[20] To overcome the violation of the normality assumption required for linear regression, cost data are often log-transformed. However, doing so creates issues with interpreting log costs given that the outcome is interpreted as a geometric mean rather than an arithmetic mean. One alternative to log-transforming costs is to use a Generalized Linear Model (GLM) with a 'log' link and 'gamma' family. The 'log' link and 'gamma' family characterizes how the dependent variable and linear combination of independent variables are related and avoids the issue of interpreting log costs. However, the disadvantage of this method is that it requires the a priori specification of a best-fit link and family. Misspecification of the link and family can result in biased estimates and incorrect inference. To overcome these issues, an extended GLM can be used to fit and allow for flexible links and families.[21] Using the 'pglm' STATA command, the extended GLM computes the best fit link and family to adjust for potential confounders. Incremental costs can then be attained with the 'pglmpredict' STATA command which predicts incremental costs using recycled predictions. The model estimating incremental costs of IC used an extended GLM to adjust for baseline age, gender, geographic region, insurance type (Commercial vs. Medicare

Supplemental), insurance plan type, and CCI score. While baseline costs is traditionally a covariate in cost models, this model did not adjust for baseline costs for several reasons. First, given that IC is often diagnosed years after its manifestation, costs incurred during the 12 months prior to IC diagnosis were thought to reflect untreated IC rather than true baseline costs. In fact, the data confirmed this expectation, showing a distribution of baseline costs for IC patients that was much higher and overlapped minimally with the distribution of baseline costs for non-IC patients (Table 1). Recycled predictions were used to model incremental costs (of IC versus no IC) among IC patients only. The model estimating incremental costs of HL also used an extended GLM to adjust for baseline age, gender, geographic region, insurance type (Commercial vs. Medicare Supplemental), and insurance plan type. Like the model estimating incremental costs of IC, this model also did not adjust for baseline costs. Additionally, this model did not adjust for CCI. While it would have been ideal to also adjust for CCI, including CCI created model convergence issues. Nevertheless, given that the distribution of CCI between HL and non-HL patients was similar in our sample, we did not expect our estimate to be biased due to confounding by comorbidities.

To model incident IC-related comorbidities, logistic regression models, adjusting for baseline age, gender, region, and CCI score.

All multivariable analyses used robust standard errors and assumed a significance level of α=0.05. Analyses were conducted using SAS version 9.3 (SAS Institute, Inc, Cary, NC) and STATA 13-IC version 13.1 (StataCorp, College Station, TX).

RESULTS

Study Population

From a total of 97,335,275 patients in the 2009 through 2014 Truven Health MarketScan® Research Databases, 112,006 patients were identified as having an incident diagnosis of IC followed by at least 12 months of enrollment in the years 2009 through 2014. As shown in Figure 2, 19,186 patients were excluded for having evidence of IC treatment during the 12 months pre-index date; 8,222 for having bladder-related cancers; 59,233 for not having continuous enrollment 12 months pre- and post- index date; and 323 for being less than 18 years of age. After applying all exclusion criteria, a total of 24,836 IC patients were identified and matched to a total of 99,344 non-IC patients on the basis of age, gender, and region.

As shown in Table 1, IC patients and non-IC patients were mostly female (n=113,965, 92%), in the age range of 41 to 60 years old (n=59,555; 48%), and from the Southern region of the US (n=53,375; 43%). The majority of IC patients and non-IC patients had Commercial health coverage (n=101,571; 82%) and subscribed to a FFS plan (n=73,595; 59%). IC patients and non-IC patients were similar across all baseline characteristics with the exception of CCI score, with IC patients having greater proportion of CCI scores greater than one when compared to non-IC patients (30% vs 21%, respectively).

Of the IC patients, a total of 292 (1.2%) patients were identified as having HL. Non-HL and HL patients were similar in age (mean age 49.0 (SD = 15.3) vs 50.8 (SD = 16.2), respectively) and in proportion of CCI score greater than or equal to one (30% vs 33%, respectively). Compared to non-HL patients, HL patients had a lesser proportion of females (88% vs 92%, respectively).

Healthcare Utilization

IC patients utilized more healthcare across all service categories when compared to non-IC patients (Table 2). Of note, IC patients had twice as many outpatient and ED visits as did non-IC patients. On average, IC patients had 22.5 (SD=20.0) outpatient visits in the first 12 months after diagnosis, whereas non-IC patients had 11.0 (SD=13.6) ($p<0.001$). Similarly, IC patients had an average of 0.45 (SD=1.5) ED visits in the first 12 months after diagnosis, whereas non-IC patients had 0.19 (SD=0.7) ($p<0.001$). Furthermore, IC patients filled a prescription days' supply of 1,079 (SD=1,071) compared to non-IC patients who filled 657 (SD=857) ($p<0.001$). Among the IC patients, HL patients utilized significantly more healthcare across all service categories compared to the non-HL patients (Table 2). The proportion of HL patients having at least one inpatient admission was twice that of non-HL patients (20% vs 11%, respectively; $p<0.001$).

After adjusting for baseline characteristics, IC patients were found to utilize significantly more healthcare across all service categories when compared to non-IC patients (Table 8). IC patients had outpatient visits 2.01 times as often and ED visits 2.25 times as often as non-IC patients ($p<0.001$). Additionally, after adjusting for baseline characteristics, IC patients filled 367 more prescription days' supply than non-IC patients ($p<0.001$). Among IC patients, adjusted healthcare utilization was significantly higher in HL patients compared to non-HL patients across all service categories except prescription days' supply. HL patients had a 1.93 times higher odds of having at least one inpatient admission compared to non-HL patients ($p<0.001$).

Prescription Utilization

IC patients utilized significantly more opioid analgesics, sedatives/hypnotics, and muscle skeletal relaxants compared to non-IC patients (Table 3). Nearly half (46%) of all IC

patients utilized opioid analgesics, whereas only 25% of non-IC patients did (p<0.001). Among IC patients, nearly three in four (72%) of patients with HL utilized opioid analgesics compared to 46% of patients without HL (p<0.001).

Direct Cost

From the total cost perspective, that is, the combined perspective of the payer and patient, IC patients had significantly higher unadjusted mean healthcare costs across all service categories (Table 5). IC patients incurred more than double the total healthcare costs compared to non-IC patients ($14,824 (SD=$26,440) vs $6,984 (SD=$20,359) , respectively; p<0.001). Of the difference in total healthcare costs, outpatient visits accounted for the greatest portion with IC patients spending three times the amount as non-IC patients ($9,160(SD=$15,639) vs $3,878 (SD=$11,632), respectively; p<0.001). After outpatient visits, prescription costs accounted for the next greatest difference in total healthcare costs, with IC patients spending twice the amount as non-IC patients ($2,939 (SD=$6,432) vs $1,442 (SD=$3,936), respectively; p<0.001). HL patients had significantly higher unadjusted mean costs in the total, inpatient admissions, and outpatient visits service categories. On average, HL patients spent nearly 50% more total costs compared to non-HL patients ($21,371 (SD=$21,590) vs $14,746 (SD=$26,483), respectively; p<.0001). Of the difference in total healthcare costs, outpatient visits accounted for the greatest portion with IC patients spending $13,625 (SD=$12,593) and non-IC patients spending $9,106 (SD=$15,665) (p<0.001).

After adjusting for baseline characteristics, having IC was associated with significantly higher costs than not having IC across all service categories (Table 9). Having IC was associated with $6,798 more in total healthcare costs than not having IC (95% CI: $6,253, $7,343). Outpatient visits still accounted for the greatest portion (71%) of this difference, with having IC associated with $4,827 more on outpatient visits (95% CI: $4,539, $5,115).

Prescriptions still accounted for the second greatest portion (19%) of the total healthcare cost difference, with having IC associated with $1,324 more on prescriptions than not having IC (95% CI: $1,240, $1,408). After adjusting for baseline characteristics, having HL was associated with significantly more total and outpatient visit costs compared to not having HL. Having HL was associated with $6,486 more in total costs than not having HL patients (95% CI: $3,497, $9,475). Again, outpatient visits accounted for the greatest portion of this difference, with having HL associated with $4,754 more on outpatient visits than not having HL (95% CI: $2,829, $6,679). Inpatient admissions accounted for the second greatest portion of the total difference, with having HL associated with $1,448 more than not having HL, although this difference was not statistically significant (95% CI: $-3,319, $6,215).

Incident IC-Related Comorbidities

As shown in Table 6, the proportion of IC patients who developed IC-related comorbidities was significantly greater than the proportion of non-IC patients across all IC-related comorbidities. The proportion of IC patients who developed any IC-related comorbidity was more than twice the proportion of non-IC patients (24% vs 11%, respectively; $p<0.001$). The most common IC-related comorbidity developed was anxiety (9% vs 4%, respectively; $p<0.001$), followed by fibromyalgia (6% vs 2%, respectively; $p<0.001$) and depression (5% vs 2%, respectively; $p<0.001$). The proportion of HL patients who developed IC-related comorbidities was not significantly different from non-HL patients across all IC-related comorbidities. The proportion of HL patients who developed any IC-related comorbidity was similar to non-HL patients (23% vs 24%, respectively; $p=0.516$).

After adjusting for baseline characteristics, the odds of developing IC-related comorbidities was significantly greater among IC patients than non-IC patients across all IC-related comorbidities. IC patients had 2.61 times higher odds of developing an IC-related

comorbidity (95% CI: 2.52, 2.70, p<0.001). IC patients had more than three times higher odds of developing vulvodynia (OR=25.69, 95% CI: 17.88, 36.93, p<0.001), IBS (OR=4.80, 95% CI: 4.34, 5.30, p<0.001), sicca syndrome (OR=3.43, 95% CI: 2.56, 4.60, p<0.001), and fibromyalgia (OR=3.11, 95% CI: 2.90, 3.34, p<0.001) than non-IC. After adjusting for baseline characteristics, the odds of developing IC-related comorbidities were not found to be significantly different between HL and non-HL patients across all IC-related comorbidities (Table 10).

DISCUSSION

This study characterized and compared healthcare resource utilization, costs, and IC-related comorbidities between IC and non-IC patients, and among IC patients, between those with and without HL. Similar to previously published claims studies, this study found IC patients to utilize significantly more healthcare resources, incur more costs, and develop more IC-related comorbidities than non-IC patients in the first 12 months after diagnosis. However, this study found the burden of IC to be higher than what has been previously described.

In terms of healthcare resource utilization, this study found IC patients to have on average, 0.15 inpatient admissions during the first 12 months after diagnosis, which was similar to Clemens et al, who found an average of 0.17 inpatient admissions. In contrast, this study found IC patients to have on average, 22.5 outpatient visits during the first 12 months after diagnosis, which was higher than the 14.1 outpatient visits found in Clemens.[15] The difference in outpatient visits could be due to the fact that Clemens estimated healthcare resource utilization in one managed care population, which could have had different practice patterns than the population of our study, which was composed of patients from a variety of health plan types.

With respect to costs, this study found the unadjusted mean total cost of IC to be $14,824, which after adjusting for baseline characteristics, was $6,798 greater than the cost of not having IC. This study also found that the difference in total healthcare cost between having and not having IC was primarily being driven by differences in outpatient visits costs, which accounted for 71% of the difference in total healthcare costs. In 2006, Wu et al found IC patients to spend, on average, $6,614 on direct costs during the first year after diagnosis, which was $3,756 more than non-IC patients.[14] Additionally, they found that outpatient visits accounted for 51% of the difference in total healthcare costs between IC and non-IC patients. One reason that this study may have found absolute value costs that were higher than Wu is that Wu only included payer costs, whereas this study included payer and patient costs. Another reason for this difference is that Wu only examined the costs that incurred over 48 weeks after index diagnosis, whereas this study examined costs that incurred over 52 weeks after index diagnosis, but this would not have contributed largely to this difference. The unadjusted mean total cost of IC found in this study was also higher than the $9,186 that Stanford et al found IC patients to spend during the first year after diagnosis, of which 56% were due to outpatient visits.[16] A potential reason for this difference is that Stanford's analysis was based on data from all managed care plans, which could collectively have lower costs than this study, which was based on data from a variety of health plan types.

Lastly, similar to this study, Wu et al found higher risks associated with certain comorbidities.[14] They found relative risks for IBS, depression, and anxiety to be 4.9, 2.8, and 4.4, respectively. In contrast to the incident IC-related comorbidities used in this study, Wu based these estimates on prevalent comorbidities. Furthermore, their estimates were not adjusted for potential confounders.

In addition, this study found that among IC patients, those with HL had a higher utilization of healthcare resources across all service categories except for prescription days' supply filled when compared to non-HL patients. Since no differences were found between HL and non-HL patients in terms of incident IC-related comorbidities, the higher healthcare resource utilization in HL patients could be related to HL patients requiring a more-intensive treatment of IC. The biggest difference in healthcare resource utilization was due first to outpatient visits. One of the reasons why HL patients could have had more outpatient visits is because they were identified using fulguration as a proxy, and fulguration itself, is primarily an outpatient procedure. Another explanation for the increased number of outpatient visits seen with HL patients is that perhaps this population has more severe symptoms and thus requires more intensive treatment. The latter explanation is also supported by the finding that HL patients were 63% more likely to used opioid analgesics than non-HL patients.

This study has several limitations. As with other claims analyses, this study is subject to potential coding error, which could lead to misclassification of both exposure and outcomes variables. Relying on ICD-9 codes to identify IC diagnosis could lead to misclassification of those who really do have IC if the ICD-9 code for IC was billed for the purposes of differential diagnosis. Additionally, as with other claims analyses, this study is subject to healthy-worker bias, as it inherently requires that patients and their dependents are healthy enough to work and receive health insurance. This bias would cause healthcare utilization, costs, and comorbidities to be higher than what was observed in this study. Furthermore, given that the Truven Health MarketScan® Research Databases have greater representation by the Southern region of the US, findings of this study could be skewed to reflect demographics or practice patterns from that region. Next, this study used fulguration as a proxy for patients with HL, which could lead to misclassification of the

exposure given that patients with HL may not have received fulguration within the first year after diagnosis. As a result, some patients with HL could have been misclassified as patients without HL, leading to an attenuation of the difference between HL and non-HL patients. Using fulguration as a proxy for HL patients could also lead to an overestimate of resource utilization and costs since fulguration, the procedure, is associated with office visits and costs. And lastly, since IC is typically diagnosed late, the costs in the first 12 months after diagnosis may not reflect the true, initial burden of the disease.

This study's strengths include a large sample size, as well as being the first study to characterize and compare differences between IC patients with and without HL. Also, it is the first study to our knowledge that uses an extended GLM to estimate and compare adjusted incremental costs of IC. Additionally, it is the first study to capture costs from both the payer and patient perspective, as well as reflect costs of a variety of health plan types. This study is also the first study to provide adjusted healthcare resource utilization and incident comorbidities.

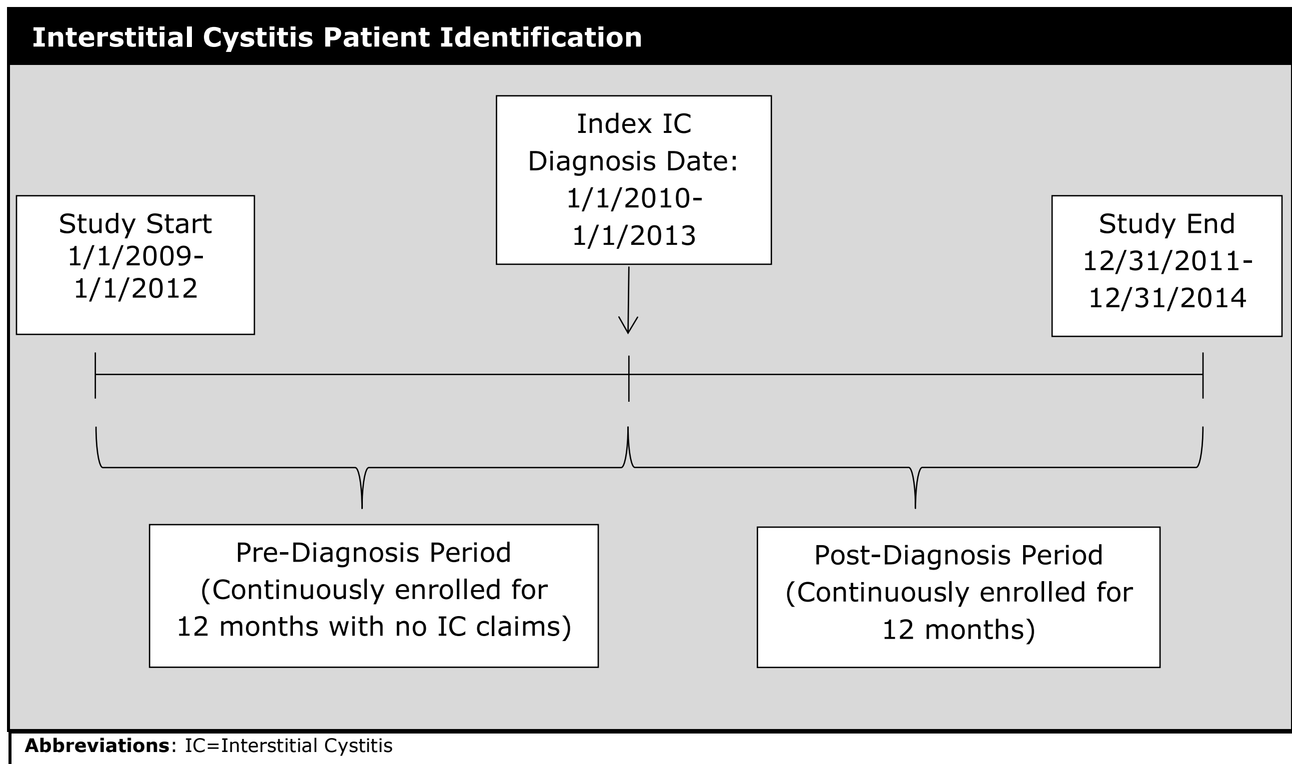
Future work is warranted to better understand whether the increase in resource utilization and costs in HL patients is due to the subgroup inherently requiring more intensive healthcare, or rather, due to the fulguration procedure itself. This could be conducted by subtracting the resource utilization and cost associated with the fulguration procedure from the total resource utilization and cost associated, and determining whether or not there was still a difference between HL patients and non-HL patients. Furthermore, increasing the follow-up time would allow for more HL patients to received fulguration and thus allow for a more accurate classification of HL patients. Additionally, it would allow for the analysis of whether or not increased utilization and costs change after the fulguration procedure. Another reason it would be interesting to increase follow-up time would be to examine the

long-term burden of IC. Since IC is not well-controlled by traditional pharmacologic agents, patients may resort to more invasive and expensive interventions in the long run.

CONCLUSIONS

The results of this study estimate total unadjusted and adjusted mean utilization and costs of inpatient admissions, outpatient visits, ED visits, and prescriptions for patients with newly diagnosed IC in a claims database. In general, the frequency and costs of these services increased with IC diagnosis, which were even higher in the presence of HL.

Figure 1: Schematic Representation of Study Design



Abbreviations: IC=Interstitial Cystitis

Figure 2: Flowchart of Cohort Identification

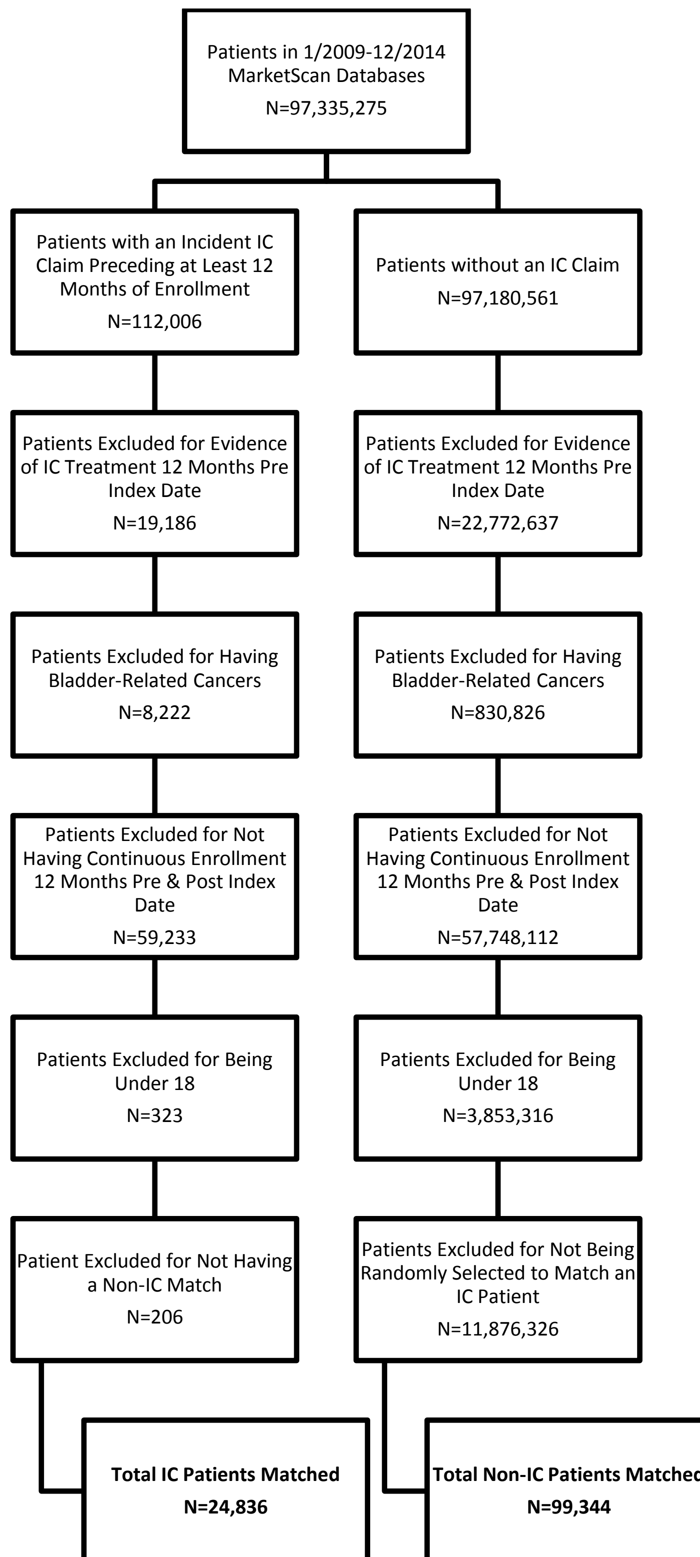


Table 1. Baseline Demographics.

	Overall Cohort (n=124,180)	IC (n=24,836)	Non-IC (n=99,344)	HL Subgroup (n=292)	Non-HL Subgroup (n=24,544)
MATCHED CHARACTERISTICS					
Age, mean(sd)	49.0 (15.3)	49.0 (15.3)	49.0 (15.3)	50.8 (16.2)	49.0 (16.2)
Age Group, n(%)					
<31	14,805 (12)	2,961 (12)	11,844 (12)	34 (12)	2,927 (12)
31-40	23,210 (19)	4,642 (19)	18,568 (19)	38 (13)	4,604 (19)
41-50	28,815 (23)	5,763 (23)	23,052 (23)	83 (28)	5,680 (23)
51-60	30.740 (25)	6,148 (25)	24,592 (25)	58 (20)	6,090 (25)
61-70	15,060 (12)	3,012 (12)	12,048 (12)	39 (13)	2,973 (12)
71-80	8,000 (6)	1,600 (6)	6,400 (6)	25 (9)	1,575 (6)
≥81	3,550 (3)	710 (3)	2,840 (3)	15 (5)	695 (3)
Female, n(%)	113,965 (92)	22,793 (92)	91,172 (92)	256 (88)	22,537 (92)
Region, n(%)					
North East	14,670 (12)	2,934 (12)	11,736 (12)	45 (15)	2,889 (12)
North Central	29,080 (23)	5,816 (23)	23,264 (23)	58 (20)	5,758 (23)
South	53,375 (43)	10,675 (43)	42,700 (43)	129 (44)	10,546 (43)
West	26,485 (21)	5,297 (21)	21,188 (21)	59 (20)	5,238 (21)
Unknown	570 (0)	114 (0)	456 (0)	1 (0)	113 (0)
NON-MATCHED CHARACTERISTICS					
Insurance Type, n(%)					
Commercial	101,571 (82)	20,423 (82)	81,148 (82)	225 (77)	20,198 (82)
Medicare Supplemental	21,039 (17)	4,413 (18)	16,626 (17)	67 (23)	4,346 (18)
Unknown	1570 (1)	0 (0)	1570 (1)	0 (0)	0 (0)
Plan Type*, n(%)					
Comprehensive	13,357 (11)	2,837 (11)	10,520 (11)	41 (15)	2,837 (11)
HMO	18,766 (15)	3,274 (13)	15,492 (16)	164 (14)	3,274 (13)
FFS	73,595 (59)	15,354 (62)	58,241 (59)	30 (56)	15,354 (62)
CDHP & HDHP	14,932 (12)	2,986 (12)	11,946 (12)	292 (10)	2,986 (12)
Unknown	3,530 (3)	385 (2)	3,145 (3)	12 (4)	385 (2)
Charlson Comorbidity Index**, n(%)					
0	95,696 (77)	17,507 (70)	78,189 (79)	195 (67)	17,312 (71)
1	19,027 (15)	4,850 (20)	14,177 (14)	58 (20)	4,792 (20)
2	6,722 (5)	1,770 (7)	4,952 (5)	24 (8)	1,746 (7)
3+	2,735 (2)	709 (3)	2,026 (2)	15 (5)	694 (3)
Baseline Costs, median (IQR)	$17,780 ($6,164, $44,634)	$35,830 ($17,047, $74,787)	$14,300 ($4,934, $36,833)	$49,512 ($26,819, $92,363)	$35,612 ($16,938, $74,417)

Abbreviations: HL=Hunner's Lesions; SD=standard deviation; HMO=health maintenance organization; IQR=interquartile range; FFS=fee for service; CDHP=consumer driven health plan; HDHP=high deductible health plan
*HMO includes Exclusive Provider Organization, HMO, and Fee-For-Service with Capitation; FFS includes Point of Service and Preferred Provider Organization Benefit Design
**The Deyo method was used to ascertain scores
1. Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. J Clin Epidemiol 1992;45:613–619.

Table 2. Health Resource Utilization

	IC (n=24,836)	Non-IC (n=99,344)	P-Value	HL Subgroup (n=292)	Non-HL Subgroup (n=24,544)	P-Value
≥ 1 Inpatient Admission, n(%)	2,810 (11)	7,491 (8)	<0.001	59 (20)	2,751 (11)	<0.001
Inpatient Admissions, mean(95% CI)	0.15 (0.14, .16)	0.09 (0.09, 0.09)	<0.001	0.25 (0.18, 0.31)	0.15 (0.14, 0.16)	0.004
Outpatient Visits, mean(95% CI)	22.5 (22.3, 22.8)	11.0 (10.9, 11.1)	<0.001	28.3 (26.0, 30.6)	22.4 (22.2, 22.7)	<0.001
≥ 1 ED Visits, n(%)	5,780 (23)	12,560 (13)	<0.001	89 (30)	5,691 (23)	0.004
ED Visits, mean(95% CI)	0.45 (0.44, 0.47)	0.19 (0.18, 0.19)	<0.001	0.60 (0.46, 0.73)	0.45 (0.43, 0.47)	0.043
Prescription Days' Supply, mean(95% CI)	1,079.0 (1065.7, 1092.3)	657.4 (652.1, 662.7)	<0.001	1,237.5 (1107.0, 1368.0)	1,077.1 (1063.7, 1090.5)	0.017

Abbreviations: ED=Emergency Room; CI=Confidence Interval; HL=Hunner's Lesions

Table 3. Prescription Utilization - By Therapeutic Class.

	IC (n=24,836)	Non-IC (n=99,344)	P-Value	HL Subgroup (n=292)	Non-HL Subgroup (n=24,544)	P-Value
Pentosan Polysulfate Sodium (Elmiron®)						
Percent Use, n(%)	3,942 (16)	--	--	91 (31)	3,851 (16)	<0.001
Prescription Days' Supply, mean(95% CI)	124.4 (--)	--	--	135 (112.4, 156.7)	124.1 (120.6, 127.6)	0.346
Opioid Analgesics						
Percent Use, n(%)	11,379 (46)	24,704 (25)	<0.001	211 (72)	11,168 (46)	<0.001
Prescription Days' Supply, mean(95% CI)	93.4 (90.1, 96.6)	51.9 (50.4, 53.4)	<0.001	71.8 (53.2, 90.5)	93.8 (90.4, 97.1)	0.024
Sedatives/Hypnotics						
Percent Use, n(%)	5,311 (21)	7,523 (8)	<0.001	83 (28)	5,228 (21)	0.003
Prescription Days' Supply, mean(95% CI)	165.5 (161.4, 169.6)	143 (139.5, 146.4)	<0.001	155.9 (122.0, 189.9)	165.6 (161.5, 169.8)	0.574
Muscle Skeletal Relaxants						
Percent Use, n(%)	4,681 (19)	8,996 (9)	<0.001	52 (18)	4,629 (19)	0.648
Prescription Days' Supply, mean(95% CI)	90.4 (87.0, 93.8)	66.4 (64.3, 68.5)	<0.001	107.9 (67.2, 148.6)	90.2 (86.7, 93.6)	0.387

Abbreviations: CI=Confidence Interval; HL=Hunner's Lesions

Table 4. Prescription Total Costs - By Therapeutic Class.

	IC (n=24,836)	Non-IC (n=99,344)	P-Value	HL Subgroup (n=292)	Non-HL Subgroup (n=24,544)	P-Value
Pentosan Polysulfate Sodium (Elmiron®), mean(95% CI)	$1,491 (--)	--	--	$1,689 ($1,369, $2,009)	$1,486 ($1,440, $1,533)	0.216
Opioid Analgesics, mean(95% CI)	$431 ($341, $521)	$168 ($148, $187)	<0.001	$200 ($98, $301)	$435 ($344, $527)	<0.001
Sedatives/Hypnotics, mean(95% CI)	$231 ($218, $245)	$217 ($207, $228)	0.126	$130 ($73, $187)	$233 ($219, $246)	<0.001
Muscle Skeletal Relaxants, mean(95% CI)	$111 ($100, $121)	$75 ($69, $81)	<0.001	$107 ($52, $162)	$111 ($100, $121)	0.888

Abbreviations: CI=Confidence Interval; HL=Hunner's Lesions

Table 5. Total, Payer, and Patient Costs

	IC (n=24,836)	Non-IC (n=99,344)	P-Value	HL Subgroup (n=292)	Non-HL Subgroup (n=24,544)	P-Value
Total						
Total, mean(95% CI)	$14,824 ($14,495, $15,153)	$6,984 ($6,857, $7,110)	<0.001	$21,371 ($18,884, $23,858)	$14,746 ($14,415, $15,078)	<0.001
Inpatient Admissions, mean(95% CI)	$2,705 ($2,507, $2902)	$1,658 ($1,579, $1,738)	<0.001	$4,303 ($2,903, $5,703)	$2,685 ($2,486, $2,885)	0.025
Outpatient Visits, mean(95% CI)	$9,160 ($8,965, $9,354)	$3,878 ($3,806, $3,951)	<0.001	$13,625 ($12,175, $15,076)	$9,106 ($8,910, $9,302)	<0.001
ED Visits, mean(95% CI)	$846 ($803, $888)	$335 ($324, 346)	<0.001	$1,132 ($771, $1,493)	$842 ($800, $884)	0.118
Prescriptions Filled, mean(95% CI)	$2,939 ($2,859, $3,019)	$1,442 ($1,418, $1,466)	<0.001	$3,430 ($2830, $4029)	$2,933 ($2,853, $3,014)	0.107
Payer						
	IC (n=24,836)	**Non-IC** (n=99,344)	**P-Value**	**HL Subgroup** (n=292)	**Non-HL Subgroup** (n=24,544)	**P-Value**
Total, mean(95% CI)	$13,135 ($12,815, $13,456)	$6,115 ($5,992, $6,238)	<0.001	$19,111 ($16,684, $21,539)	$13,064 ($12,741, $13,387)	<0.001
Inpatient Admissions, mean(95% CI)	$2,612 ($2,416, $2,808)	$1,588 ($1,510, $1,667)	<0.001	$4,148 ($2,767, $5,529)	$2,593 ($2,396, $2,791)	0.029
Outpatient Visits, mean(95% CI)	$8,073 ($7,885, $8,260)	$3,351 ($3,281, $3,421)	<0.001	$12,127 ($10,731, $13,522)	$8,024 ($7,835, $8,214)	<0.001
ED Visits, mean(95% CI)	$764 ($724, $804)	$291 ($281, $302)	<0.001	$1,040 ($693, $1,386)	$761 ($720, 801)	0.116
Prescriptions Filled, mean(95% CI)	$2,453 ($2,376, $2,529)	$1,176 ($1,153, $1,199)	<0.001	$2,837 ($2,266, $3,408)	$2,448 ($2,371, $2,525)	0.186
Patient						
	IC (n=24,836)	**Non-IC** (n=99,344)	**P-Value**	**HL Subgroup** (n=292)	**Non-HL Subgroup** (n=24,544)	**P-Value**
Total, mean(95% CI)	$1,691 ($1,669, $1,712)	$870 ($861, $880)	<0.001	$2,260 ($2,045, $2,474)	$1,684 ($1,663, $1,706)	<0.001
Inpatient Admissions, mean(95% CI)	$93 ($87, $98)	$71 ($67, $75)	<0.001	$155 ($58, $251)	$92 ($86, $98)	0.202
Outpatient Visits, mean(95% CI)	$1,089 ($1,071, $1,106)	$528 ($521, $535)	<0.001	$1,499 ($1,338, $1,660)	$1,084 ($1,067, $1,101)	<0.001
ED Visits, mean(95% CI)	$82 ($78, $85)	$44 ($43, $45)	<0.001	$92 ($58, $126)	$82 ($78, $85)	0.548
Prescriptions Filled, mean(95% CI)	$509 ($502, $517)	$271 ($269, $274)	<0.001	$606 ($542, $670)	$508 ($501, $515)	0.003

Abbreviations: ED=Emergency Room; CI=Confidence Interval; HL=Hunner's Lesions

Table 6. Incident IC-Related Comorbidities.

	IC (n=24,836)	Non-IC (n=99,344)	P-Value	HL Subgroup (n=292)	Non-HL Subgroup (n=24,544)	P-Value
Any IC-Related Comorbidity, n(%)	6,008 (24.19)	10,650 (10.72)	<0.001	66 (22.60)	5,942 (24.21)	0.516
Anxiety, n(%)	1,882 (8.96)	3,675 (3.97)	<0.001	17 (7.05)	1,865 (8.98)	0.298
Chronic Fatigue Syndrome, n(%)	209 (0.85)	287 (0.29)	<0.001	3 (0.36)	206 (0.85)	0.723
Depression, n(%)	1,181 (5.23)	2,240 (2.36)	<0.001	19 (7.17)	1,162 (5.21)	0.154
Fibromyalgia, n(%)	1,433 (6.43)	2,030 (2.11)	<0.001	14 (5.24)	1,419 (6.44)	0.428
Insomnia, n(%)	804 (3.4)	1,493 (1.53)	<0.001	7 (2.53)	797 (3.41)	0.422
Irritable Bowel Syndrome, n(%)	843 (3.61)	751 (0.76)	<0.001	13 (4.71)	830 (3.59)	0.323
Migraine Headaches, n(%)	956 (4.22)	1,729 (1.8)	<0.001	6 (2.26)	950 (4.24)	0.110
Sicca Syndrome, n(%)	85 (0.34)	95 (0.1)	<0.001	1 (0.34)	84 (0.34)	0.994
Vulvodynia, n(%)	212 (0.86)	34 (0.03)	<0.001	2 (0.69)	210 (0.86)	0.749

Abbreviations: HL=Hunner's Lesions

Table 7. Total IC-Related Comorbidities.

	IC (n=24,836)	Non-IC (n=99,344)	P-Value	HL Subgroup (n=292)	Non-HL Subgroup (n=24,544)	P-Value
Any IC-Related Comorbidity, n(%)	11,936 (48.06)	22,329 (22.48)	<0.001	129 (44.18)	11,808 (48.11)	0.181
Anxiety, n(%)	5,758 (23.18)	10,343 (10.41)	<0.001	68 (23.29)	5,690 (23.18)	0.966
Chronic Fatigue Syndrome, n(%)	486 (1.96)	603 (0.61)	<0.001	7 (2.4)	479 (1.95)	0.585
Depression, n(%)	3,485 (14.03)	6,596 (6.64)	<0.001	46 (15.75)	3,439 (14.01)	0.394
Fibromyalgia, n(%)	3,991 (16.07)	5,047 (5.08)	<0.001	39 (13.36)	3,952 (16.1)	0.204
Insomnia, n(%)	2,001 (8.06)	3,336 (3.36)	<0.001	22 (7.53)	1,979 (8.06)	0.741
Irritable Bowel Syndrome, n(%)	2,363 (9.51)	1,897 (1.91)	<0.001	29 (9.93)	2,334 (9.51)	0.807
Migraine Headaches, n(%)	3,151 (12.69)	4,824 (4.86)	<0.001	32 (10.96)	3,119 (12.71)	0.372
Sicca Syndrome, n(%)	279 (1.12)	276 (0.28)	<0.001	1 (0.34)	278 (1.13)	0.203
Vulvodynia, n(%)	395 (1.59)	67 (0.07)	<0.001	3 (1.03)	392 (1.6)	0.439

Abbreviations: HL=Hunner's Lesions

Table 8. Health Resource Utilization

Unadjusted	IC vs Non-IC	P-Value	HL vs Non-HL	P-Value
≥ 1 Inpatient Admission, OR (95% CI)	1.56 (1.49, 1.64)	<0.001	2.01 (1.50, 2.68)	<0.001
Inpatient Admissions, IRR (95% CI)	1.66 (1.58, 1.74)	<0.001	1.64 (1.26, 2.13)	<0.001
Outpatient Visits, IRR (95% CI)	2.04 (2.02, 2.07)	<0.001	1.26 (1.16, 1.37)	<0.001
≥ 1 ED Visits, OR(95% CI)	2.10 (2.02, 2.17)	<0.001	1.45 (1.13, 1.87)	0.004
ED Visits, IRR (95% CI)	2.43 (2.32, 2.54)	<0.001	1.32 (1.04, 1.66)	0.020
Prescription Days' Supply, RD (95% CI)	422 (409, 434)	<0.001	160 (37, 284)	0.011
Adjusted*				
	IC vs Non-IC	**P-Value**	**HL vs Non-HL**	**P-Value**
≥ 1 Inpatient Admission, OR (95% CI)	1.45 (1.38, 1.52)	<0.001	1.93 (1.45, 2.59)	<0.001
Inpatient Admissions, IRR (95% CI)	1.54 (1.46, 1.61)	<0.001	1.57 (1.20, 2.05)	0.001
Outpatient Visits, IRR (95% CI)	2.01 (1.98, 2.03)	<0.001	1.27 (1.17, 1.38)	<0.001
≥ 1 ED Visits, OR(95% CI)	1.98 (1.91, 2.05)	<0.001	1.45 (1.13, 1.87)	0.004
ED Visits, IRR (95% CI)	2.25 (2.15, 2.35)	<0.001	1.32 (1.04, 1.67)	0.022
Prescription Days' Supply, RD (95% CI)	367 (356,377)	<0.001	109 (-3, 220)	0.056

Abbreviations: ED=Emergency Room; CI=Confidence Interval; HL=Hunner's Lesions; IRR=Incidence Rate Ratio; OR=Odds Ratio; RD=Risk Difference
*Adjusted for baseline age, gender, region, insurance type, plan type, and CCI

Table 9. Incremental Total Costs.

Unadjusted		
	IC vs Non-IC (n=24,836)	**HL vs Non-HL** (n=24,544)
Total, mean(95% CI)	$7,840‡ ($7,488, $8,193)	$6,624‡ ($4,116, $9,133)
Inpatient Admissions, mean(95% CI)	$1,046‡ ($833, $1,259)	$1,617† ($203, $3,031)
Outpatient Visits, mean(95% CI)	$5,281‡ ($5,074, $5,489)	$4,519‡ ($3,055, $5,982)
ED Visits, mean(95% CI)	$510‡ ($467, $554)	$290 (-$74, $654)
Prescriptions Filled, mean(95% CI)	$1,497‡ ($1,413, $1,580)	$496 (-$108, $1,101)
Adjusted*		
	IC vs Non-IC (n=24,836)	**HL vs Non-HL** (n=24,544)
Total, mean(95% CI)	$6,798 ($6,253, $7,343)	$6,486 ($3,497, $9,475)
Inpatient Admissions, mean(95% CI)	$783 ($440, $1,126)	$1,448 ($-3,319, $6,215)
Outpatient Visits, mean(95% CI)	$4,827 ($4,539, $5,115)	$4,754 ($2,829, $6,679)
ED Visits, mean(95% CI)	$487 ($113, $861)	$279 ($-658, $1,216)
Prescriptions Filled, mean(95% CI)	$1,324 ($1,240, $1,408)	$351 ($-151, $853)

Abbreviations: ED=Emergency Room; CI=Confidence Interval; HL=Hunner's Lesions
*IC vs Non-IC models adjusted for baseline age, gender, region, insurance type, plan type, and CCI
*HL vs Non-HL models adjusted for baseline age, gender, region, insurance type, and plan type
†Significant with a p-value ≤0.05
‡Significant with a p-value ≤0.001

Table 10. Incident IC-Related Comorbidities Ratios.

Unadjusted				
	IC vs Non-IC	**P-Value**	**HL vs Non-HL**	**P-Value**
Any IC-Related Comorbidity, OR (95% CI)	2.66 (2.56, 2.75)	<0.001	0.91 (0.69, 1.20)	0.525
Anxiety, OR (95% CI)	2.38 (2.25, 2.52)	<0.001	0.77 (0.47, 1.26)	0.300
Chronic Fatigue Syndrome, OR (95% CI)	2.95 (2.47, 3.53)	<0.001	1.23 (0.39, 3.87)	0.723
Depression, OR (95% CI)	2.29 (2.13, 2.46)	<0.001	1.41 (0.88, 2.25)	0.156
Fibromyalgia, OR (95% CI)	3.19 (2.98, 3.42)	<0.001	0.80 (0.47, 1.38)	0.429
Insomnia, OR (95% CI)	2.26 (2.07, 2.47)	<0.001	0.74 (0.35, 1.56)	0.424
Irritable Bowel Syndrome, OR (95% CI)	4.86 (4.40, 5.36)	<0.001	1.33 (0.76, 2.32)	0.325
Migraine Headaches, OR (95% CI)	2.41 (2.22, 2.61)	<0.001	0.52 (0.23, 1.17)	0.116
Sicca Syndrome, OR (95% CI)	3.61 (2.69, 4.84)	<0.001	0.99 (0.14, 7.15)	0.994
Vulvodynia, OR (95% CI)	25.31 (17.62, 36.36)	<0.001	0.80 (0.20, 3.22)	0.750
Adjusted*				
	IC vs Non-IC	**P-Value**	**HL vs Non-HL**	**P-Value**
Any IC-Related Comorbidity, OR (95% CI)	2.61 (2.52, 2.70)	<0.001	0.95 (0.72, 1.25)	0.708
Anxiety, OR (95% CI)	2.35 (2.22, 2.49)	<0.001	0.80 (0.49, 1.32)	0.389
Chronic Fatigue Syndrome, OR (95% CI)	2.85 (2.38, 3.41)	<0.001	1.24 (0.39, 3.93)	0.710
Depression, OR (95% CI)	2.22 (2.07, 2.39)	<0.001	1.47 (0.92, 2.35)	0.109
Fibromyalgia, OR (95% CI)	3.11 (2.90, 3.34)	<0.001	0.82 (0.48, 1.42)	0.484
Insomnia, OR (95% CI)	2.22 (2.03, 2.42)	<0.001	0.74 (0.35, 1.58)	0.441
Irritable Bowel Syndrome, OR (95% CI)	4.80 (4.34, 5.30)	<0.001	1.36 (0.77, 2.39)	0.287
Migraine Headaches, OR (95% CI)	2.39 (2.20, 2.59)	<0.001	0.55 (0.25, 1.25)	0.155
Sicca Syndrome, OR (95% CI)	3.43 (2.56, 4.60)	<0.001	0.97 (0.13, 7.08)	0.976
Vulvodynia, OR (95% CI)	25.69 (17.88, 36.93)	<0.001	0.85 (0.21, 3.42)	0.816

Abbreviations: CI=Confidence Interval; HL=Hunner's Lesions; OR=Odds Ratio
*Adjusted for baseline age, sex, region, and CCI

Figure 3. Histogram of Total Baseline Healthcare Cost.

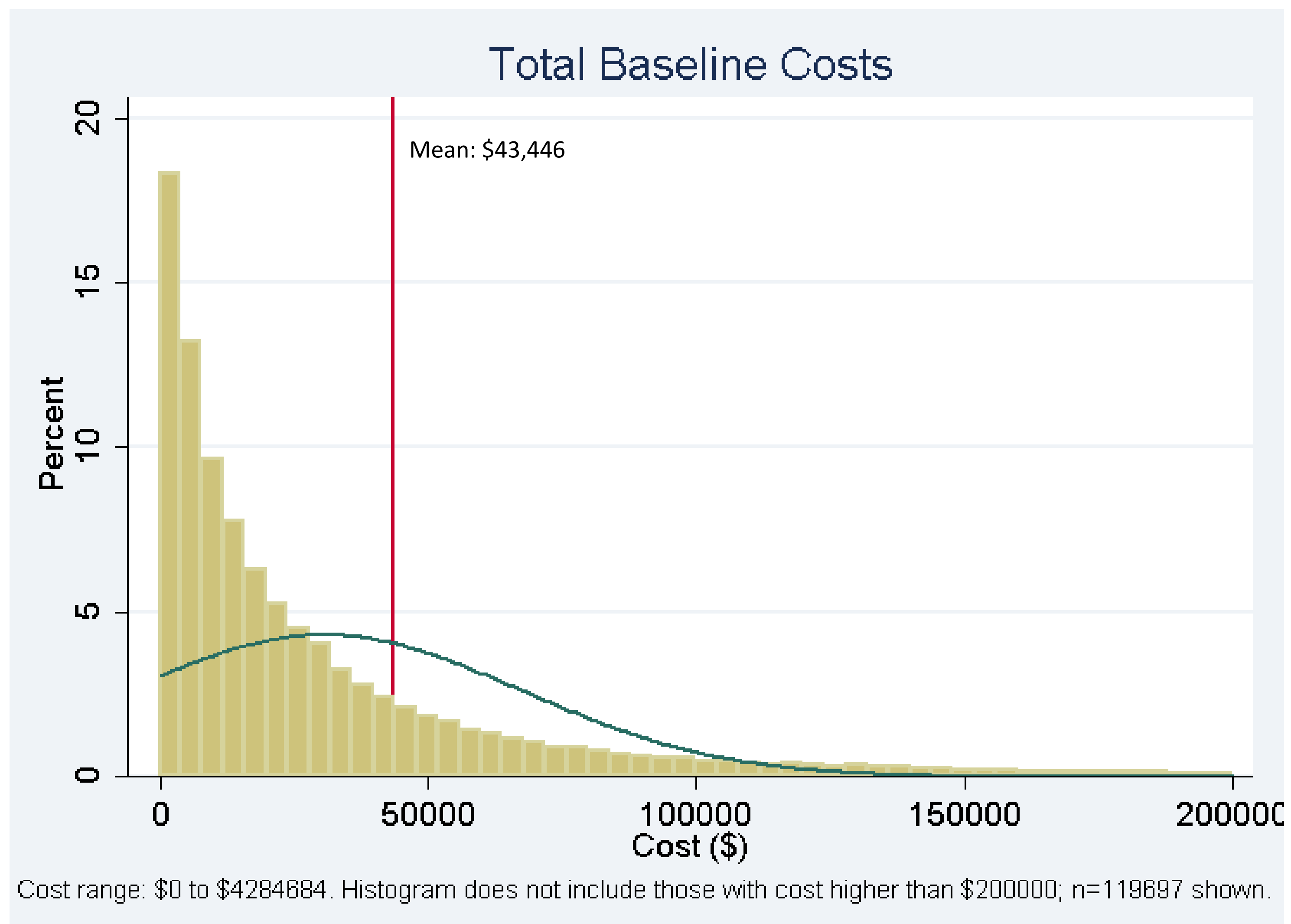


Figure 4. Histogram of Total Post-Index Healthcare Cost.

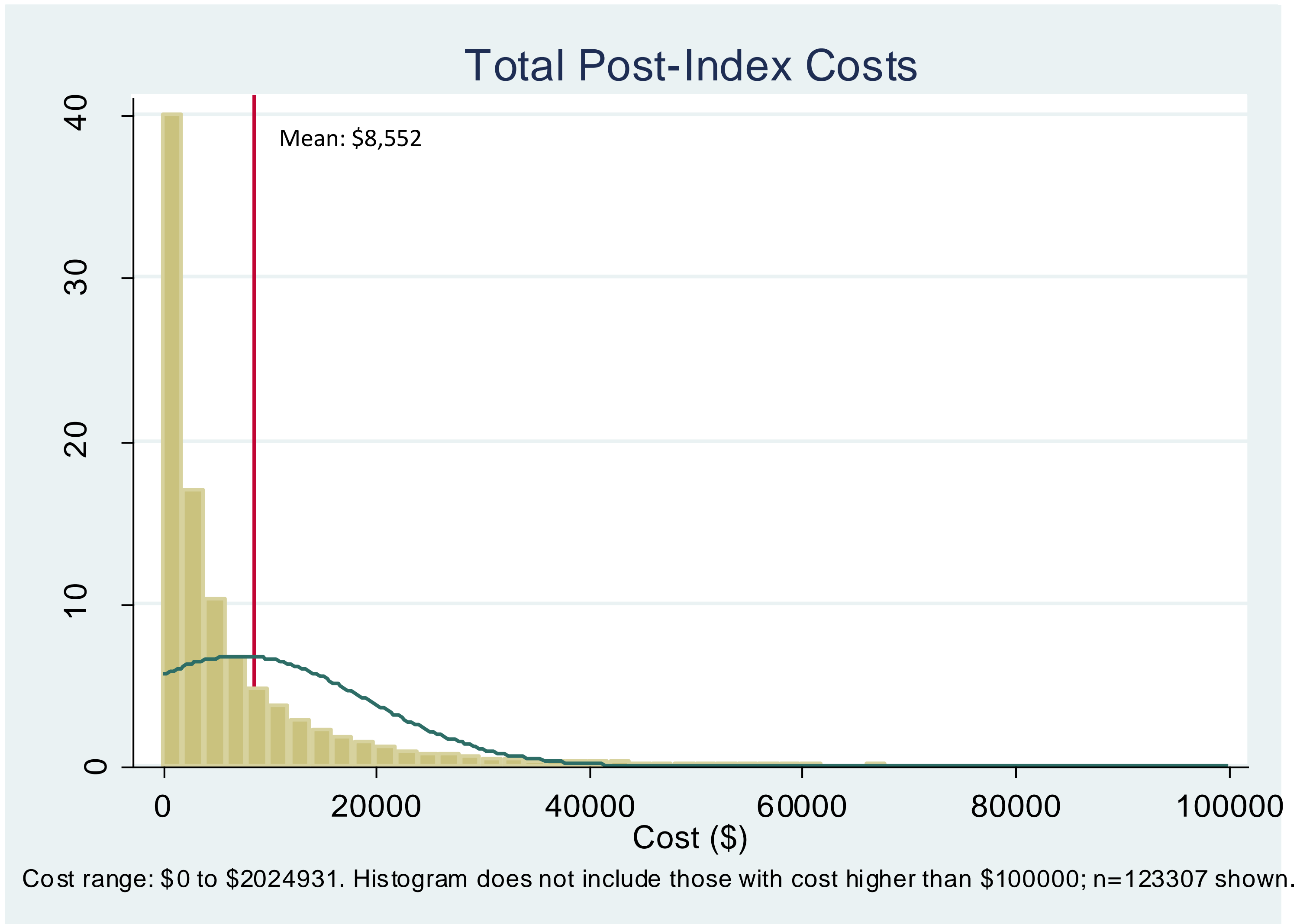


Table 11. ICD-9, CPT, and NDC Codes

Condition	Codes
Interstitial Cystitis	ICD-9 595.1
Fulguration	CPT 52214, 52224
Charlson Comorbidity Index*	
Myocardial Infarction	ICD-9 410, 412
Congestive Heart Failure	ICD-9 428
Peripheral Vascular Disease	ICD-9 441, 443.9, 785.4, V424
Cardiovascular Disease	ICD-9 430, 431, 432, 433, 434, 435, 436, 437, 438
Chronic Obstructive Pulmonary Disease	ICD-9 490, 491, 493, 494, 495, 496, 500, 510, 502, 503, 504, 505, 506.4
Dementia	ICD-9 290
Rheumatic Disease	ICD-9 725, 710.0, 710.1, 710.4, 714.0, 714.1, 714.2
Peptic Ulcer Disease	ICD-9 531,532,533,534
Liver disease	ICD-9 571.2, 571.4, 571.5, 571.6
Liver Disease, complicated	ICD-9 572.2, 456.0, 456.1, 456.20, 456.21
Diabetes, no complications	ICD-9 250.00, 250.01, 250.02, 250.03, 250.07
Diabetes, complications	ICD-9 250.04, 250.05, 250.06
Paralysis	ICD-9 342, 244.1
Renal Disease	ICD-9 582, 583, 585, 586, 588
Cancer	ICD-9 148-195, 200-208
Metastatic Cancer	ICD-9 196, 197, 198
AIDS	ICD-9 042, 043, 044
Comorbidities	
Anxiety	ICD-9 300.00, 300.01, 300.02
Depression	ICD-9 311
Migraine Headache	ICD-9 346
Fibromyalgia	ICD-9 729.1
Irritable Bowel Syndrome	ICD-9 564.1
Vulvodynia	ICD-9 625.7
Chronic Fatigue Syndrome	ICD-9 780.71
Sicca Syndrome	ICD-9 710.2
Insomnia	ICD-9 780.52
Exclusion Codes	
Pentosan Polysulfate Sodium (Elmiron®)	NDC 00062980001, 00575760001, 17314930001, 50458009801, 54569512300, 54569512301, 54868452500, 54868452501, 54868452502, 54868452503, 68115088800
Bladder Neoplasm	ICD-9 188.0–188.9
Carcinoma In Situ of Bladder	ICD-9 233.7
Malignant Neoplasm, Bladder Neck	ICD-9 188.5
Malignant Neoplasm, Prostate	ICD-9 185
Malignant Neoplasm, Urethra	ICD-9 189.3
Malignant Neoplasm, Uterus, Ovaries, Fallopian Tubes, Adnexa, & Unspecified Ovary Related	ICD-9 179.*, 180.*, 180.1, 180.8, 180.9, 182, 182.1, 182.8, 180.0, 183.2–183.5, 183.8, 183.9
Radiation Cystitis	ICD-9 595.82
Secondary Malignant Neoplasm, Genital Organs	ICD-9 198.82
Secondary Urinary Organ Neoplasm	ICD-9 198.1
Spinal Cord Injury	ICD-9 952.00–952.09, 952.10–952.19, 952.2, 952.3, 952.8–952.10
Tuberculous Cystitis	ICD-9 16.10
Unspecified Bladder Neoplasm	ICD-9 239.4
Unspecified Neoplasm, Genital Organs	ICD-9
Urethral Diverticulum	ICD-9 599.20
Urethral Stricture	ICD-9 598.0, 598.01, 598.1, 598.2, 598.8, 598.9
Vaginal Cancer	ICD-9 184.00

Abbreviations: AIDS = acquired immunodeficiency syndrome
*Charlson Comorbidity Score is calculated using the Deyo adaptation[1]
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