STUDY

Annual Direct and Indirect Health Care Costs of Chronic Idiopathic Urticaria

A Cost Analysis of 50 Nonimmunosuppressed Patients

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Objective: To estimate annual direct and indirect health care costs in patients with chronic idiopathic urticaria (CIU) managed with conventional therapies.

Design: A cost analysis consisting of a survey-guided and retrospective medical record review of direct and indirect health care costs from a societal perspective in patients with CIU.

Setting: The Johns Hopkins University allergy and dermatology ambulatory clinics.

Participants: Fifty adults with active CIU were recruited in sequential order. Individuals who were taking corticosteroids or other immunosuppressants in the month before enrollment were excluded from the study.

Main Outcome Measures: We estimated direct health care costs, which included laboratory, medication, outpatient visit, and emergency department and hospital visit costs. We also estimated indirect costs, which included earnings lost owing to travel to outpatient visits and absences from work owing to CIU-related illness.

Results: Patients with CIU consumed a mean (SD) of $2047 ($1483) annually. Because CIU is primarily an outpatient disease, medication costs alone accounted for 62.5% ($1280) of the total annual cost. Indirect costs accounted for 15.7% ($322) of the total costs.

Conclusions: High medication costs, followed by total indirect costs, result in the largest economic burden among patients with CIU. High medication costs may place low-income patients at risk for suboptimal treatment and increased burden due to poorly controlled disease. Our estimated total health care costs for CIU are comparable to those of other skin diseases such as vitiligo and bullous disease.


C H R O N I C U R T I C A R I A, D E F I N E D as urticaria that is present longer than 6 weeks, is estimated to occur in 0.1% of the population.\(^1\) Approximately 60% of chronic urticaria is termed ordinary and is not of physical or vasculitic origin. Chronic idiopathic urticaria (CIU) accounts for approximately two-thirds of ordinary urticarias.\(^2\) The diagnosis of CIU is supported clinically (and most importantly) by a thorough patient history because extensive diagnostic testing often does not reveal a cause.\(^3\)

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Data on disease duration in chronic urticaria are limited and varied. In a retrospective cohort study, one group reported that the disease had cleared in 29% of the patients studied after 5 years.\(^7\) In a prospective study, Toubi et al\(^7\) reported that the disease had cleared in 84% of patients after 5 years. The mean duration of chronic urticaria has been reported to be 4 years but ranges from 0 to 40 years.\(^6\)

Approximately 40% of patients with CIU have associated angioedema, which often requires emergency department (ED) visits and more aggressive therapy.\(^7\) Numerous unanticipated health care visits can contribute significantly to disease burden and reduced health-related quality of life.\(^8\) In addition to medical costs, patients with chronic urticaria miss time from work and leisure secondary to visits to the clinic or ED. In a quality-of-life analysis in patients with chronic urticaria, O'Donnell et al\(^9\) reported that 56% of working patients had missed at least 1 day of work (mean work loss, 6.4 days) because of their urticaria.

Indirect health care costs have not previously been reported in patients with CIU.

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Our main objective was to estimate annual direct and indirect health care costs from a societal perspective in patients with CIU who have not been treated with immunosuppressive therapies.10

**METHODS**

Between December 1, 2004, and May 31, 2006, 50 adults with active CIU diagnosed by an allergist or dermatologist were recruited in sequential order from The Johns Hopkins University allergy and dermatology clinics. Patients who had been taking systemic corticosteroids or other immunosuppressants in the month before enrollment were excluded because the primary study goal for this population was measurement of serum basophil histamine-releasing levels. We excluded patients diagnosed as having another skin disease, such as urticarial vasculitis, atopic dermatitis, or physical urticaria, and those who had urticaria that was caused by chronic infection or long-term medication use.

After informed consent was obtained per a protocol approved by The Johns Hopkins Hospital institutional review board, participants completed a survey capturing health care utilization and disease severity. Additional patient demographic characteristics, medication use, and frequency of outpatient and ED/hospital visits for the year prior to the survey date were obtained by medical record review. Disease severity was graded as mild, moderate, or severe by a single physician allergist (S.S.S.) on the basis of the number, duration, and intensity of disease flares, as well as medication requirements.

The 4 direct health care costs estimated were laboratory, medication, outpatient visit, and ED/hospital costs. Initial laboratory workup costs were estimated across the 34 patients who were new patients during the study period. Laboratory costs were calculated according to the 2005 Medicare reimbursement costs for Maryland for the Current Procedural Terminology codes assigned to the following panel of tests: a complete blood cell count with white blood cell count differential and determination of the erythrocyte sedimentation rate and the thyroid-stimulating hormone level.11 The annual medication cost was calculated by means of the dose and duration of the medication (trade or generic as documented) multiplied by the average wholesale price listed in the 2005 Red Book.12 The outpatient visit cost was calculated by means of the Medicare reimbursement rate in Baltimore for both facility and nonfacility costs associated with the evaluation and management code for each visit in the study period.13 The ED/hospital visit cost was estimated by calculating the number of visits related to CIU illness times a single cost multiplier that was based on Medicare reimbursement for a level 3 ED visit. Separate laboratory test charges were not included in the cost of ED visits.

The 2 indirect costs estimated were earnings lost because of travel to outpatient visits and absences from work because of CIU-related illness. The median hourly wage was calculated from weekly earnings according to education level and sex, as reported by the Bureau of Labor Statistics at the US Department of Labor in April 2006.14 A 40-hour work week and an 8-hour workday were assumed. Earnings lost because of travel to outpatient visits were calculated from the appropriate median hourly wage multiplied by round-trip travel time, determined by using MapQuest and each patient’s city, state, and zip code.15 Earnings lost owing to CIU-related absences from work were calculated from the appropriate median daily wage multiplied by the number of days absent.

Total health care costs for each patient were calculated as the sum of the 4 direct costs and the 2 indirect costs. Descriptive and nonparametric data analyses were performed with Stata statistical software (version 8.0; StataCorp, College Station, Texas). The Wilcoxon rank sum test was used to compare health care costs by sex and between age groups, and the Kruskal-Wallis test was used to compare health care costs between severity groups. P < .05 was considered statistically significant. Data are reported as mean (SD) unless otherwise indicated.

**RESULTS**

**PATIENT DEMOGRAPHICS**

The patient population was 74% (37 of 50) women and had a mean age of 43.3 (14.9) (range, 18-71) years. Sixty-eight percent (34 patients) were white. This patient population was highly educated; 90% (45 patients) had some college education. Clinically, 38% (19 patients) were classified as having mild disease; 42% (21 patients), moderate disease; and 20% (10 patients), severe disease. Angioedema was present in 42% (21 patients).
percent (24 patients) reported the duration of their CIU as being greater than or equal to 4 years.

DIRECT COSTS

Table 1 gives the distribution of outpatient visits and ED/hospital visits, and Table 2 provides the average direct costs of the 4 health care components of interest. The number of annual outpatient visits ranged from 0 to 5 visits per year, with the majority of patients (52% [26 of 50]) reporting only 1 visit. The mean number of outpatient visits per year was 1.6 (1.1); the mean annual cost for outpatient visits was $280 ($207). In addition, 30% (15 of 50 patients) had at least 1 ED/hospital visit, with 16% (8 of 50 patients) having 2 or more. Only 1 patient had a CIU-related hospitalization, which was included in the cost analysis with the ED visits. The mean annual cost of ED and hospital visits was $148 ($281). The average initial laboratory workup, $17 ($12), represented 0.8% of the total annual cost. Overall, 92% of patients (46 of 50) were taking at least 1 medication for their CIU; a mean of 2.5 (1.4) different medications were used by patients within the preceding year. Most patients (72% [36 of 50]) were taking a nonselecting H1 antihistamine during the study period. The distribution of other medications used is given in the following tabulation:

<table>
<thead>
<tr>
<th>Type of Medication</th>
<th>No. (%) of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonselecting H1 antihistamine&lt;sup&gt;a&lt;/sup&gt;</td>
<td>36 (72)</td>
</tr>
<tr>
<td>Sedating antihistamine&lt;sup&gt;b&lt;/sup&gt;</td>
<td>23 (46)</td>
</tr>
<tr>
<td>Corticosteroid taper&lt;sup&gt;c&lt;/sup&gt;</td>
<td>14 (28)</td>
</tr>
<tr>
<td>Doxepin hydrochloride</td>
<td>11 (22)</td>
</tr>
<tr>
<td>Epinephrine hydrochloride autoinjector</td>
<td>8 (16)</td>
</tr>
<tr>
<td>H1 histamine, blocker</td>
<td>8 (16)</td>
</tr>
<tr>
<td>Antiinflammatory</td>
<td>1 (14)</td>
</tr>
</tbody>
</table>

<sup>a</sup>Indicates cetirizine hydrochloride, fexofenadine hydrochloride, and loratadine.

<sup>b</sup>Indicates diphenhydramine hydrochloride and hydroxyzine hydrochloride.

<sup>c</sup>Indicates a short course of the drug with sequential reduction of the dose over a few weeks.

Of the 4 direct cost components, the mean annual cost of medication ($1280 [$1274]) resulted in the highest economic burden (62.5%).

INDIRECT COSTS

Table 1 gives the distribution of the number of days patients were absent from work or school; Table 2 provides the mean annual earnings lost to patients because of absences from work or school secondary to their CIU; 26% (13 of 50) had 3 or more absences. The mean number of workdays or school days lost per year was 1.5 (1.8) (range, 0-7) days. The mean annual earnings lost to patients because of round-trip travel time and missed work was $70 ($68), while the mean annual earnings lost to patients secondary to work absences was $252 ($316).

TOTAL COST ANALYSIS

Among all patients, the total mean annual direct and indirect health care cost was $2047 ($1483). The mean total indirect costs accounted for 15.7% ($322) of the total health care cost. The Figure is a visual representation of the cost components.

COMPARISON OF COSTS

By Sex

The data in Table 3 indicate that women had a trend toward higher mean annual direct and indirect health care costs than men across all cost components, but this trend was only statistically significant for the mean total cost ($2314 for women vs $1287 for men; P = .04). We found no statistically significant difference in disease severity between men and women (mean severity, 1.7 vs 1.9, respectively; P = .33). The mean total annual health care cost for women with CIU was $1027 per year higher that that for men (or almost twice the cost for men) and was primarily generated by medication costs and lost wages because of absences from work.

By Disease Severity

The data in Table 4 indicate that the total mean annual health care costs between severity groups were not statistically significantly different. However, there was a stepwise increase in total cost from mild to moderate to severe disease. Statistically significant differences were detected between the severity groups in outpatient visit costs (P = .004), ED/hospital costs (P = .05), and wages lost because of absences from work (P = .05) but not in medication costs (P = .63).

By Age Group

There was no statistically significant difference in mean total annual direct and indirect costs by age group (patients aged <41 vs those ≥41 years; data not shown).
This burden-of-illness study of 50 patients with CIU finds that such patients consume an annual mean of $2047. Medication costs were the largest cost component, accounting for 62.5% of the mean total annual health care costs. High medication costs were secondary to the use of nonsedating antihistamines active at the H1 receptor, which are the mainstay of treatment for CIU. Insurance carriers may not cover the high cost of these medications, which may place uninsured or low-income patients at risk for increased out-of-pocket expenses, suboptimal treatment, and increased burden due to poorly controlled disease.

The second largest component consisted of indirect costs, which accounted for 15.7% ($322) of the total health care costs and were greater than the average cost of outpatient and ED/hospital visits. Most of the patients studied (38%) missed 1 or more days of work or school secondary to their illness, which is consistent with previously published data.9 However, we have likely underestimated the indirect costs to patients because we were unable to account for time spent in the outpatient visit or other costs accrued to the patient and the patient’s family (eg, childcare costs and wages lost by the person accompanying the patient).

Women with CIU had a statistically significantly higher mean total annual health care cost than did men. This is consistent with previous studies investigating sex differences in the utilization of health care services.16 This difference in costs was due in part to the strong trend toward women having higher medication costs.

The external validity of this study may be somewhat limited because the health care costs represent costs experienced by the patients in the study. However, the study participants were not selected on the basis of disease severity, and the results are generalizable to the broader population of CIU patients. This study also does not account for the costs of lost productivity due to CIU, which may be substantial. Additionally, the study did not assess the impact of CIU on quality of life, which is an important consideration for patients with chronic disease.

### Table 3. Mean Annual Direct and Indirect Costs in Dollars by Sex

<table>
<thead>
<tr>
<th>Variable</th>
<th>Costs, $</th>
<th></th>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Direct costs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medication</td>
<td>Mean (SD)</td>
<td>708 (656)</td>
<td>680 (138-1026)</td>
<td>1481 (1381)</td>
<td>1102 (379-2269)</td>
<td>.08</td>
</tr>
<tr>
<td>Outpatient visits</td>
<td>Mean (SD)</td>
<td>202 (125)</td>
<td>234 (90-314)</td>
<td>307 (224)</td>
<td>314 (90-405)</td>
<td>.16</td>
</tr>
<tr>
<td>ED/hospital visits</td>
<td>Mean (SD)</td>
<td>146 (302)</td>
<td>0 (0-0)</td>
<td>148 (278)</td>
<td>0 (0-226)</td>
<td>.68</td>
</tr>
<tr>
<td>Laboratory</td>
<td>Mean (SD)</td>
<td>17 (12)</td>
<td>25 (0-25)</td>
<td>17 (12)</td>
<td>25 (0-25)</td>
<td>.91</td>
</tr>
<tr>
<td>Indirect costs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wages lost because of travel to outpatient visits</td>
<td>Mean (SD)</td>
<td>55 (53)</td>
<td>47 (8-81)</td>
<td>75 (72)</td>
<td>49 (26-112)</td>
<td>.43</td>
</tr>
<tr>
<td>Wages lost because of absences from work</td>
<td>Mean (SD)</td>
<td>159 (232)</td>
<td>0 (0-291)</td>
<td>285 (338)</td>
<td>197 (0-395)</td>
<td>.16</td>
</tr>
<tr>
<td>Total direct and indirect costs</td>
<td>Mean (SD)</td>
<td>1287 (828)</td>
<td>1164 (953-2084)</td>
<td>2314 (1576)</td>
<td>1840 (1166-3460)</td>
<td>.04</td>
</tr>
</tbody>
</table>

Abbreviations: ED, emergency department; IQR, interquartile range.

### Table 4. Mean Annual Direct and Indirect Costs in Dollars by Severity of Chronic Idiopathic Urticaria

<table>
<thead>
<tr>
<th>Severity Group</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n=19)</td>
<td>(n=21)</td>
<td>(n=10)</td>
</tr>
<tr>
<td>Direct costs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medication</td>
<td>Mean (SD)</td>
<td>970 (903)</td>
<td>1455 (1424)</td>
</tr>
<tr>
<td>Outpatient visits</td>
<td>Mean (SD)</td>
<td>263 (129)</td>
<td>143 (90-314)</td>
</tr>
<tr>
<td>ED/hospital visits</td>
<td>Mean (SD)</td>
<td>36 (113)</td>
<td>0 (0-0)</td>
</tr>
<tr>
<td>Laboratory costs</td>
<td>Mean (SD)</td>
<td>21 (9)</td>
<td>15 (12)</td>
</tr>
<tr>
<td>Indirect costs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wages lost because of travel to outpatient visits</td>
<td>Mean (SD)</td>
<td>71 (77)</td>
<td>50 (44)</td>
</tr>
<tr>
<td>Wages lost because of absences from work</td>
<td>Mean (SD)</td>
<td>142 (271)</td>
<td>294 (325)</td>
</tr>
<tr>
<td>Total direct and indirect costs</td>
<td>Mean (SD)</td>
<td>1503 (989)</td>
<td>2132 (1595)</td>
</tr>
</tbody>
</table>

Abbreviations: ED, emergency department; IQR, interquartile range.
experienced by the patient population seen at only 1 tertiary referral clinic and may not accurately represent or estimate the health care costs of patients with CIU at large. We may have underestimated the laboratory, medication, and other itemized annual health care costs for patients with CIU because we had a selection bias of non-immunosuppressed patients. Future work is necessary to capture the costs of patients with CIU who take immunosuppressive medications.

Furthermore, we accounted for the costs of a particular initial laboratory workup for CIU, which represents the smallest percentage of total costs. We acknowledge that there may be variation among providers in the initial laboratory tests ordered, although recommendations have been made to limit the initial laboratory tests to a white blood cell count differential and determination of the erythrocyte sedimentation rate. In addition, radiographic costs were not itemized because these tests were rarely ordered in this patient population.

Despite these limitations, this cost analysis is useful as a source of rigorous cost accounting and as the basis for future pharmacoeconomic studies because it underscores the effect of the cost of medications in a predominantly outpatient disease. In contrast to other chronic diseases with high hospitalization costs, CIU may receive insufficient national coverage and grant support for basic research that could lead to the creation of newer, more cost-effective drugs. When more drugs are on the market, more options are created, which ultimately may result in lower drug costs for patients. Our cost analysis may also serve as a model for cost-accounting studies for other dermatological conditions.

This study highlights the fact that CIU is burdensome in terms of both direct medical costs and indirect costs to society. Based on a CIU prevalence of 0.04% among the US population, we estimate that the mean total indirect and direct costs are $244 million per year, which is comparable to the total costs for vitiligo and bullous dermatoses with high hospitalization costs, CIU may receive insufficient national coverage and grant support for basic research that could lead to the creation of newer, more cost-effective drugs. When more drugs are on the market, more options are created, which ultimately may result in lower drug costs for patients. Our cost analysis may also serve as a model for cost-accounting studies for other dermatological conditions.

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Author Contributions: Drs DeLong and Chen had full access to the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study design and concept: DeLong and Chen. Acquisition of data: DeLong, Saini, and Beck. Analysis and interpretation of data: DeLong, Culler, Beck, and Chen. Drafting of the manuscript: DeLong and Culler. Critical revision of the manuscript for important intellectual content: DeLong, Culler, Saini, Beck, and Chen. Statistical analysis: DeLong and Culler. Obtained funding: Chen. Administrative, technical, and material support: Beck. Study supervision: Saini, Beck, and Chen.

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