Ann Allergy Asthma Immunol 114 (2015) 393–398

Contents lists available at ScienceDirect

Validation of an *ICD-9*–based claims algorithm for identifying patients with chronic idiopathic/spontaneous urticaria

Dasha Cherepanov, PhD [*]; Karina Raimundo, BPharm, MS [†]; Eunice Chang, PhD [*]; Marianne Eagan, MSc [*]; James L. Zazzali, PhD, MPH [†]; Paul G. Solari, MD [†]; Bruce DeCotiis, MD [‡]; Iftikhar Hussain, MD [§]; Syed Maseeh Rehman, MD [||]; Nada Shahab, MBBS, CRC [||]; Stephen A. Tilles, MD [¶]; and Michael S. Broder, MD, MSHS [*]

[*] *Partnership for Health Analytic Research, LLC, Beverly Hills, California*
[†] *Genentech Inc, South San Francisco, California*
[‡] *Ocean Allergy and Respiratory Research Center, Brick, New Jersey*
[§] *Allergy, Asthma and Immunology Center, PC, Vital Prospects Clinical Research Institute, Tulsa, Oklahoma*
[||] *Asthma & Allergy Center, Toledo, Ohio*
[¶] *ASTHMA, Inc, Clinical Research Center, Seattle, Washington*

ARTICLE INFO

Article history:
Received for publication October 25, 2014.
Received in revised form January 14, 2015.
Accepted for publication February 4, 2015.

ABSTRACT

Background: There is no specific *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*) code for chronic idiopathic urticaria or spontaneous urticaria (CIU/CSU), a skin condition characterized by hives and angioedema lasting at least 6 weeks with no known cause.
Objective: To validate an *ICD-9-CM*–based algorithm for identification of patients with CIU/CSU and thus facilitate claims-based research.
Methods: Patient records were reviewed at 4 US practices. Patients included in the study were from a random sample of those identified by their physician as having CIU/CSU or because they met the following diagnosis-based algorithm: (1) at least 2 outpatient *ICD-9-CM* diagnosis codes 708.1, 708.8, or 708.9 at least 6 weeks apart or (2) 1 outpatient diagnosis of 708.1, 708.8, or 708.9 and 1 diagnosis of 995.1 at least 6 weeks apart. Data collected included *ICD-9-CM* codes, diagnoses of urticaria and allergy-related conditions, and medication use. Sensitivity and positive predictive value were calculated. The study was approved by the Western Institutional Review Board.
Results: One hundred forty-nine patient records were reviewed (mean age 41.1 years; 73.8% were women; 69.1% were white): 115 were identified with the diagnosis-based algorithm, 90 were patients with "known CIU/CSU", and 56 were in the 2 groups. The mean duration of CIU/CSU was 2.9 to 3.1 years. The 2 cohorts most frequently had diagnoses of idiopathic urticaria, unspecified urticaria, and other specified urticaria. The diagnosis-based algorithm had a positive predictive value of 90.4% and a sensitivity of 71.1%.
Conclusion: The high positive predictive value suggests that patients identified using the algorithm are highly likely to have CIU/CSU. The 71.1% sensitivity suggests that most patients with CIU/CSU will be identified. The validation statistics support the use of the diagnosis-based algorithm in claims-based research, although future studies could refine the algorithm further.

Introduction

Chronic idiopathic urticaria or spontaneous urticaria (CIU/CSU) is a debilitating heterogeneous skin condition that affects individuals of all ages and can last for several years.[1–5] CIU/CSU also is known to significantly decrease patients' quality of life.[6–9] Often co-occurring with angioedema, CIU/CSU is characterized by daily or almost daily symptoms such as itchy hives or wheals lasting longer than 6 weeks. It is prevalent in approximately 0.08% to 0.5% of the population and predominately affects women.[1–5,10–12]

Different studies have investigated the underlying biologic mechanisms and management of CIU/CSU,[13,14] but few have

Reprints: Karina Raimundo, BParm, MS, Genentech Inc, 1 DNA Way, South San Francisco, CA 94080; E-mail: raimundo.karina@gene.com.
Disclosure: Drs Broder, Chang, and Cherepanov, and Ms Eagan are employees of the Partnership for Health Analytic Research, LLC, a health services research company paid to conduct this research. Ms Raimundo, and Drs Zazzali and Dr Solari are employees of Genentech Inc. Drs DeCotiis, Hussain, Rehman, and Tilles have received research support from Genentech.
Funding: This study was funded by Genentech.
Part of this research was presented at the 19th annual meeting of the International Society for Pharmacoeconomics and Outcomes Research; Montreal, Quebec, Canada; May 31 to June 4, 2014.

http://dx.doi.org/10.1016/j.anai.2015.02.003
1081-1206/

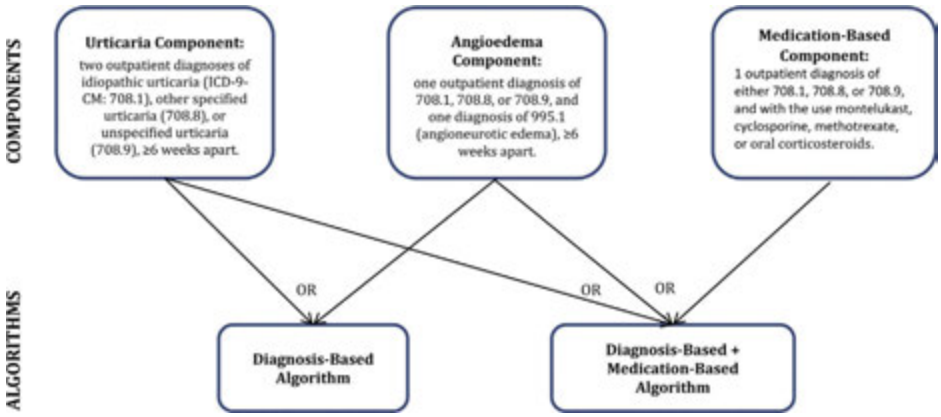

Figure 1. Algorithm construction. *ICD-9-CM, International Classification of Diseases, Ninth Revision, Clinical Modification.*

examined epidemiology, treatment patterns, or burden of illness,[8,9] which includes the effects of comorbidity, health care costs, and use. This could be because CIU/CSU is difficult to assess in the general population and a lack of an *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*) diagnosis code for CIU/CSU limits secondary data analyses. One study used health insurance claims to describe patterns of health service use in CIU/CSU.[12] These findings were consistent with prior results,[2,3,5,10,15] but the *ICD-9-CM* algorithms used to identify patients with CIU/CSU had not been validated, potentially limiting the reliability of the findings.

To enable accurate research using administrative claims, a multicenter chart review was conducted to validate and revise the previously used *ICD-9-CM*–based algorithms that could be used to identify patients with CIU/CSU. Then, the resulting algorithms were tested in an insurance claims database.

Methods

Study Design and Setting

A retrospective review of patients' medical and billing records was conducted at 4 specialized asthma and allergy centers in the United States, with a large volume of CIU/CSU, a wide variety of practice settings, and different geographic regions. The *ICD-9-CM* algorithm also was tested in an insurance claims database. The Western Institutional Review Board (www.wirb.com) approved the study (protocol 1140461).

Patient Population

Chart review included a random sample of patients who (1) met an *ICD-9-CM* code algorithm or (2) were identified by their physician as having CIU/CSU. Patients in the algorithm positive sample had 2 outpatient diagnoses of idiopathic urticaria (*ICD-9-CM* code 708.1), other specified urticaria (708.8), or unspecified urticaria (708.9), with the 2 diagnoses at least 6 weeks apart, or had 1 outpatient diagnosis of 708.1, 708.8, or 708.9 and 1 diagnosis of 995.1 (angioneurotic edema) at least 6 weeks apart. The 6-week interval was used to avoid identifying patients with acute urticaria conditions that resolved in a short period. Patients who did not have at least 1 visit to the study site from January 1, 2010 through June 1, 2013 were excluded. The goal was to achieve a relatively large sample size by including 150 eligible patients divided among the 4 centers. The algorithms were tested in a patient population selected from a Health Insurance Portability and Accountability Act compliant administrative claims database, containing data on approximately 28 million patients.

Data Collection

Study abstractors (site clinical office staff) were trained in screening charts and data entry. Data were collected using a secure, Web-based application (http://www.project-redcap.org/; supported by grant UL1TR000011 from the National Center for Advancing Translational Sciences at the National Institutes of Health). Medical and billing record data were collected from January 1, 2010 through June 1, 2013 for every patient. Medical record data included demographics (age, sex, and race or ethnicity), presence of angioedema, various urticaria conditions (physical urticaria, contact urticaria, urticaria vasculitis, and other urticaria conditions), allergy-related conditions (angioedema, asthma, allergic rhinitis, atopic dermatitis, allergic purpura, and other allergy conditions), and medication use. Billing record data included the use of *ICD-9-CM* codes 708.1 (idiopathic urticaria), 708.2 (urticaria due to cold and heat), 708.3 (dermatographic urticaria), 708.4 (vibratory urticaria), 708.5 (cholinergic urticaria), 708.8 (other specified urticaria), 708.9 (urticaria, unspecified), and 995.1 (angioneurotic edema).

Statistical Analysis

Validation statistics included positive predictive value (PPV) and sensitivity. PPV is defined as the proportion of confirmed cases ("true positives") of all patients identified by a test ("test positives").[16] Sensitivity is defined as the proportion of patients correctly identified by a test ("true positives") in a group known to have the condition ("condition positives").[16] PPV was calculated only for patients from the algorithm positive sample (the "test positives"), and sensitivity was calculated only for patients known to have CIU/CSU (the "condition positives"). Descriptive statistics summarizing the distribution of demographics, *ICD-9-CM* codes, duration of CIU/CSU, urticaria conditions, allergy-related conditions, and medication use were reported. Missing data were not imputed.

The main algorithm ("diagnosis-based algorithm") had 2 components (Fig 1). The first component ("urticaria component") identified patients with at least 2 outpatient *ICD-9-CM* diagnoses of urticaria (idiopathic, other specified, or unspecified) at least 6 weeks apart. The second component ("angioedema component") identified patients with 1 outpatient *ICD-9-CM* diagnosis of urticaria and 1 of angioedema at least 6 weeks apart. The algorithm proposed by Zazzali et al[12] had a third component that identified people with 1 outpatient *ICD-9-CM* diagnosis of urticaria and an overlapping supply of a prescription antihistamine and a second antihistamine, montelukast, cyclosporine, methotrexate, or oral corticosteroids. During initial testing for the present study using

Table 1
Patients' demographics and clinical characteristics

	Algorithm positive[a] (n = 115)	Known CIU/CSU (n = 90)	All (N = 149)
Age (y), mean (SD)	41.0 (21.7)	44.6 (17.6)	41.1 (20.8)
Age (y), n (%)			
≤11	13 (11.3)	0 (0)	13 (8.7)
12–17	12 (10.4)	8 (8.9)	16 (10.7)
18–34	19 (16.5)	21 (23.3)	28 (18.8)
35–44	15 (13.0)	12 (13.3)	20 (13.4)
45–54	25 (21.7)	21 (23.3)	30 (20.1)
55–64	15 (13.0)	18 (20.0)	23 (15.4)
≥65	16 (13.9)	10 (11.1)	19 (12.8)
Female, n (%)	86 (74.8)	66 (73.3)	110 (73.8)
Race or ethnicity, n (%)			
White	81 (70.4)	55 (61.1)	103 (69.1)
Black or African American	9 (7.8)	9 (10.0)	15 (10.1)
Other or multiple	4 (3.5)	2 (2.2)	6 (4.0)
Unknown	21 (18.3)	24 (26.7)	25 (16.8)
ICD-9-CM codes, n (%)			
708.1 Idiopathic urticaria	63 (54.8)	54 (60.0)	87 (58.4)
708.2 Cold/heat urticaria	2 (1.7)	2 (2.2)	3 (2.0)
708.3 Dermatographic urticaria	2 (1.7)	1 (1.1)	2 (1.3)
708.4 Vibratory urticaria	1 (0.9)	1 (1.1)	1 (0.7)
708.5 Cholinergic urticaria	0 (0.0)	1 (1.1)	1 (0.7)
708.8 Other specified urticaria	52 (45.2)	43 (47.8)	78 (52.3)
708.9 Urticaria, unspecified	24 (20.9)	23 (25.6)	27 (18.1)
995.1 Angioneurotic edema	17 (14.8)	13 (14.4)	24 (16.1)
CIU/CSU duration (y)[b]			
Mean (SD)	3.1 (3.2)	2.9 (3.3)	2.9 (3.0)
Median	2.5	2.3	2.2
Urticaria conditions, n (%)			
Physical urticaria	10 (8.7)	8 (8.9)	12 (8.1)
Contact urticaria	4 (3.5)	1 (1.1)	4 (2.7)
Urticaria vasculitis	0 (0.0)	0 (0.0)	0 (0.0)
Other	22 (19.1)	27 (30.0)	28 (18.8)
Allergy-related conditions, n (%)			
Angioedema	22 (19.1)	16 (17.8)	31 (20.8)
Asthma	25 (21.7)	20 (22.2)	37 (24.8)
Allergic rhinitis	62 (53.9)	51 (56.7)	87 (58.4)
Atopic dermatitis	20 (17.4)	5 (5.6)	20 (13.4)
Allergic purpura	0 (0.0)	0 (0.0)	0 (0.0)
Other allergic	31 (27.0)	19 (21.1)	41 (27.5)
Medication use, n (%)			
Any	114 (99.1)	90 (100.0)	148 (99.3)
Antihistamine	113 (98.3)	89 (98.9)	146 (98.0)
Nonsedating[c]	109 (94.8)	88 (97.8)	142 (95.3)
Other[d]	65 (56.5)	47 (52.2)	82 (55.0)
Omalizumab	15 (13.0)	12 (13.3)	17 (11.4)
Oral corticosteroids	57 (49.6)	48 (53.3)	70 (47.0)
Doxepin hydrochloride	18 (15.7)	13 (14.4)	20 (13.4)
Montelukast sodium	26 (22.6)	18 (20.0)	31 (20.8)
H_2 blockers	33 (28.7)	16 (17.8)	33 (22.1)
Dapsone	0 (0.0)	0 (0.0)	0 (0.0)
Sulfasalazine	6 (5.2)	7 (7.8)	7 (4.7)
Epinephrine auto injector	38 (33.0)	26 (28.9)	47 (31.5)
Cyclosporine	24 (20.9)	25 (27.8)	25 (16.8)
Other medications for CIU/CSU[e]	13 (11.3)	10 (11.1)	16 (10.7)

Abbreviations: CIU/CSU, chronic idiopathic urticaria/spontaneous urticaria; *ICD-9-CM*, *International Classification of Diseases, Ninth Revision, Clinical Modification*.
[a]One diagnosis of 708.1, 708.8, or 708.9 and (1) a second of the same or (2) 1 diagnosis of 995.1 at least 6 weeks from the first.
[b]Number of patients with information of the date of first CIU/CSU diagnosis varied by group (Algorithm positive, 81; known CIU/CSU, 62; all, 110).
[c]Includes cetirizine hydrochloride, desloratadine, fexofenadine hydrochloride, levocetirizine dihydrochloride, and loratadine.
[d]Includes diphenhydramine hydrochloride, chlorpheniramine maleate, brompheniramine maleate, clemastine fumarate, pheniramine maleate, and hydroxyzine hydrochloride.
[e]Includes any other oral, injectable, and topical medications listed by the abstractor as being used to treat CIU/CSU.

claims data from 2013, there was a decrease in the proportion of patients who filled a prescription for an antihistamine, from 68% in 2007 (the data used in the study by Zazzali et al[12]) to 23% in 2013, which was attributed to the increased availability of over-the-counter antihistamines. Accordingly, the medication component was excluded from the first round of validation.

In exploratory analyses, the authors examined how the initial validation statistics were affected by 4 changes to the main diagnosis-based algorithm. First, *ICD-9-CM* code 708.8 (other specified urticaria) was eliminated. Second, the gap required between *ICD-9-CM* codes was shortened from 6 to 4 weeks. Third, a new "diagnosis + medication-based algorithm" was defined by allowing the use of montelukast, cyclosporine, methotrexate, or oral corticosteroids to substitute for a confirmatory urticaria or angioedema code. Fourth, the effect of the diagnosis + medication-based algorithm was tested, which required at least 90 days of use (vs any use) of one of the listed medications.

The 2 best performing algorithms identified (main diagnosis-based and diagnosis + medication-based) and the original algorithm developed by Zazzali et al[12] underwent further validation tests in the claims database. The populations identified by each of these 3 algorithms were compared because, for the diagnosis + medication-based algorithm and the algorithm developed by Zazzali et al,[12] the chart review sample was missing an unknown number of "test positive" patients (because the algorithm used to identify patients would not have identified all modified algorithm "test positive" patients). Therefore, PPV could not be accurately estimated and further validation was conducted.

All data transformations and statistical analyses were performed using SAS 9.4 (SAS Institute, Cary, North Carolina).

Results

One hundred fifty patient records were collected, 1 of which was included based on an incorrect *ICD-9-CM* code. The final sample consisted of 149 patients: 115 in the algorithm positive sample and 90 in the known CIU/CSU sample (56 were in the 2 samples). The algorithm positive sample had a mean age of 41.0 years (SD 21.7) and the known CIU/CSU sample had a mean age of 44.6 years (SD 17.6). Women constituted 74.8% of the algorithm positive group and 73.3% of the known CIU/CSU group. White patients constituted 70.4% of the algorithm positive group and 61.1% of the known CIU/CSU group (Table 1).

The mean duration of CIU/CSU was nearly identical between the cohorts: 3.1 years (SD 3.2; median 2.5) in the algorithm positive sample vs 2.9 years (SD 3.3; median 2.3) in the known CIU/CSU group. The distribution *ICD-9-CM* codes differed somewhat between groups, with slightly fewer patients in the algorithm positive group being coded with idiopathic urticaria (54.8% vs 60.0%) and unspecified urticaria (20.9% vs 25.6%). "Other" urticaria conditions (eg, other than idiopathic, physical, or contact urticaria or urticaria vasculitis) were less common in the algorithm positive sample compared with the known CIU/CSU sample (19.1% vs 30%). Allergy-related conditions were found in similar proportions between groups, although atopic dermatitis was seen in 17.4% of the algorithm positive group compared with 5.6% of the known CIU/CSU group.

The rank ordering of the most commonly used long-term medications was similar between groups, with antihistamine and oral corticosteroids most common in the 2 groups. H_2 blockers, cyclosporine, and montelukast were the next most commonly used medications, and doxepin, omalizumab, and sulfasalazine were least commonly used (although the rank order differed somewhat between groups). Epinephrine auto-injector was prescribed in approximately one third of cases (Table 1).

Algorithm Development

In the algorithm positive sample (N = 115), there were 104 true positives, for a PPV of 90.4%. The algorithm correctly identified 64 of

Table 2
Validation statistics for CIU/CSU patient identification algorithms

	Algorithm positive sample			Known CIU/CSU sample[a]		
	True positive, n	Test positive, n	PPV, %[b]	True positive, n	Condition Positive, n	Sensitivity, %
Diagnosis-based algorithm[c]	104	115	90.4	64	90	71.1
Exploratory analysis: excluding diagnosis of other specified urticaria[d]	79	81	97.5	51	90	56.7
Exploratory analysis: gap requirement decreased from 6 to 4 wk[e]	—	—	—	69	90	76.7
Exploratory analysis: diagnosis + medication-based algorithm[f]	—	—	—	75	90	83.3
Exploratory analysis: diagnosis + 90-d medication-based algorithm[g]	—	—	—	67	90	74.4

Abbreviations: CIU/CSU, chronic idiopathic urticaria/spontaneous urticaria; PPV, positive predictive value.
[a]CIU/CSU confirmed by physician.
[b]PPV not calculable because the chart review did not encompass all patients meeting this exploratory algorithm definition.
[c]One diagnosis of 708.1, 708.8, or 708.9 and (1) a second of the same or (2) 1 diagnosis of 995.1 at least 6 weeks apart.
[d]One diagnosis of 708.1 or 708.9 and (1) a second of the same or (2) 1 diagnosis of 995.1 at least 6 weeks apart.
[e]One diagnosis of 708.1, 708.8, or 708.9 and (1) a second of the same or (2) 1 diagnosis of 995.1 at least 4 weeks apart.
[f]One diagnosis of 708.1, 708.8, or 708.9 and (1) a second of the same or (2) 1 diagnosis of 995.1 at least 6 weeks apart or (3) any use montelukast, cyclosporine, methotrexate, or oral corticosteroids.
[g]One diagnosis of 708.1, 708.8, or 708.9 and (1) a second of the same or (2) 1 diagnosis of 995.1 at least 6 weeks apart or (3) at least 90-day use of montelukast, cyclosporine, methotrexate, or oral corticosteroids.

90 patients with known CIU/CSU (64 "true positives"), resulting in a sensitivity of 71.1% (Table 2). The urticaria component alone had a PPV of 90.3% and a sensitivity of 67.8% compared with a PPV of 88.2% and a sensitivity of 8.9% for the angioedema component alone (not shown).

In exploratory analyses, the algorithms were modified and the validation statistics were recalculated. Chart review was not performed on all patients meeting each definition, but only for those meeting the main algorithm definition. Therefore, PPV could not be calculated for the exploratory algorithms that were less restrictive than the original (all but the first one). First, the elimination of the "other specified urticaria" code increased the PPV of the diagnosis-based algorithm to 97.5% but decreased sensitivity to 56.7%. Second, shortening the gap required between diagnoses codes from 6 to 4 weeks increased sensitivity to 76.7%. Third, the authors allowed any use of montelukast, cyclosporine, methotrexate, or oral corticosteroids to substitute for a confirmatory urticaria or angioedema code. This diagnosis + medication-based algorithm had a sensitivity of 83.3%. Fourth, requiring at least 90 days (rather than any) of use of 1 of the listed medications resulted in sensitivity of 74.4% (Table 2, Fig 2).

Algorithm Testing

Only the diagnosis + medication algorithm showed a significant sensitivity gain compared with the main diagnosis-based algorithm, so the modifications were eliminated from further testing. The diagnosis-based, diagnosis + medication-based, and original[12] algorithms were tested in the claims database. Of a group of patients continuously enrolled from January to December 2012, the diagnosis-based algorithm identified 6,350 patients and the diagnosis + medication-based algorithm identified 29,913 patients as having CIU/CSU, with 23,563 identified by the medication portion of the algorithm but not by the diagnosis-based portion. The original algorithm

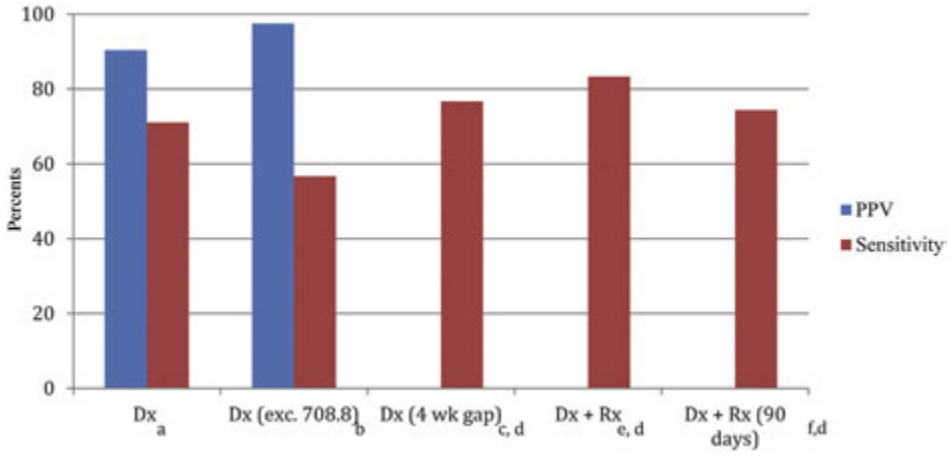

Figure 2. Positive predictive value (PPV) and sensitivity of chronic idiopathic urticaria or spontaneous urticaria (CIU/CSU) patient identification algorithms. [a]One diagnosis of 708.1, 708.8, or 708.9 and (1) a second of the same or (2) 1 diagnosis of 995.1 at least 6 weeks apart. [b]One diagnosis of 708.1 or 708.9 and (1) a second of the same or (2) 1 diagnosis of 995.1 at least 6 weeks apart. [c]One diagnosis of 708.1, 708.8, or 708.9 and (1) a second of the same or (2) 1 diagnosis of 995.1 at least 4 weeks apart. [d]PPV not calculable because the chart review did not encompass all patients meeting this exploratory algorithm definition. [e]One diagnosis of 708.1, 708.8, or 708.9 and (1) a second of the same or (2) 1 diagnosis of 995.1 at least 6 weeks apart or (3) any use montelukast, cyclosporine, methotrexate, or oral corticosteroids. [f]One diagnosis of 708.1, 708.8, or 708.9 and (1) a second of the same or (2) 1 diagnosis of 995.1 at least 6 weeks apart or (3) at least 90-day use of montelukast, cyclosporine, methotrexate, or oral corticosteroids. Dx, diagnosis-based algorithm; Rx, medication-based component.

identified 6,450 patients, 100 of whom were not identified by the main diagnosis-based algorithm.

Discussion

Despite the detrimental effects of CIU/CSU, the burden of this skin condition is not well described. One possible reason is the lack of a specific *ICD-9-CM* code for CIU/CSU, thus limiting the use of insurance claims databases to conduct research in patients with this condition. To fill this gap, the authors validated the previously used *ICD-9-CM*–based algorithms for the identification of patients with CIU/CSU to allow for a variety research using commercial insurance claims databases, including studies of treatment patterns and disease epidemiology in patients with CIU/CSU.

The authors found that a diagnosis-based algorithm requiring at least 1 urticaria code (*ICD-9-CM* code 708.1, 708.8, or 708.9) plus (1) another of the same code or (2) a diagnosis of angioedema (995.1) at least 6 weeks from the first code had a PPV of 90.4% and a sensitivity of 71.1%.

The PPV expresses how likely patients identified with a given test are to have the condition of interest. Overall, PPVs from 85% to 89% are considered acceptable, and PPVs from 70% to 75% are considered moderate.[17] A study of *ICD-9-CM* codes for 32 conditions found a median PPV of 80.7%, a mean of 77%, and a range of 23% to 100%.[18] High PPV algorithms are required in claims studies to reliably identify samples, such as in comparisons of different treatment groups. The PPV of 90% reported for the present algorithm is above the threshold considered "acceptable" and identifies a large percentage of patients who are very likely to have CIU/CSU.

Sensitivity of *ICD-9-CM* algorithms is often less important than PPV, because many claims studies are concerned with drawing a valid sample from a large population, which is feasible with low sensitivity. High sensitivity is important in the identification of the entire population (eg, to estimate disease prevalence). There are no agreed-to standards for adequate sensitivity. In a study of more than 4,000 medical records, sensitivity of *ICD-9-CM* codes for chart review-validated conditions ranged from 9% for weight loss to higher than 83% for metastatic cancer.[18] The median value was 46% and the mean was 49%, and in only 6 of 32 conditions was sensitivity above 70%. Two other studies reported the sensitivity of *ICD-9-CM* codes for multiple conditions and found similar ranges: Lee et al[19] reported a range of 2.9% to 81.2%, with only 1 of 12 higher than 70%, and Quan et al[20] reported a range of 24.6% to 87.8%, with 6 of 17 higher than 70%.

Although the initial sensitivity result of 71.1% with the main algorithm was higher than 70%, the authors attempted to improve it with various modifications. Adding a medication-based component increased sensitivity to 83.3%. However, in the claims-based portion of the study, this modified algorithm identified almost 5 times as many patients as the main one. Possibly, the revised algorithm incorrectly included many patients without CIU/CSU, and the modest increase in sensitivity came at the expense of a dramatic decrease in specificity. Perhaps, medications prescribed for something other than CIU/CSU (eg, allergy or asthma) are common in patients with a single diagnosis of urticaria. Although a decrease in specificity cannot be directly confirmed with the present study design, it can be inferred because the main algorithm failed to identify only 28.9% (100% minus sensitivity) of patients with CIU/CSU. It follows that any modification, no matter how sensitive, should not find more than 30% of cases than the main diagnosis-based algorithm.

In this chart study, 100% of patients with CIU/CSU had evidence of antihistamine use (the records did not specify whether over-the-counter or prescription), yet an examination of recent insurance claims found only 23% of patients with CIU/CSU had a claim for a prescription antihistamine. The original algorithm developed by Zazzali et al[12] included a medication component that relied on the use of antihistamines to identify patients. The original algorithm identified only 100 more patients than the 6,350 with the main diagnosis-based algorithm, likely a result of how antihistamines are obtained.

Thus, the authors propose 3 potential algorithms as virtually identical in their ability to accurately identify patients with CIU/CSU in insurance claims: the entire diagnosis-based algorithm (PPV 90.4%, sensitivity 71.1%), its urticaria component alone (2 codes of 708.1, 708.8, or 708.9 at $\geq$6 weeks apart; PPV 90.3%; sensitivity 67.8%), or the original algorithm (which adds some complexity and identifies a minimally different patient population).

Strengths and Limitations

This is the first study to directly validate an *ICD-9-CM* algorithm to identify patients with CIU/CSU. The study reports an algorithm that can be used in administrative insurance claims-based studies to identify patients who are very likely to have CIU/CSU and that the algorithm will identify most patients with the condition. Limitations include a sample of fewer than 150 patients and the potential non-representativeness of the coding practices at the 4 specialized practices. For example, if CIU/CSU is typically coded using a different combination of *ICD-9* codes at other asthma and allergy centers compared with the centers included in this study, then PPV and sensitivity values would be affected.

The authors were unable to calculate the negative predictive value and specificity because this study included only patients who met an *ICD-9* code algorithm ("test positive" patients) or were identified by their physician as having CIU/CSU ("condition positive" patients). The calculation of negative predictive value and specificity requires data on patients without CIU/CSU (ie, "test negative" patients and "condition negative" patients), which this study did not collect.

Conclusion

A relatively simple 2-part algorithm can accurately identify patients with CIU/CSU. The diagnosis-based algorithm validated in this study had 90.4% PPV and 71.1% sensitivity, suggesting that patients identified with this algorithm are highly likely to have CIU/CSU and that it will identify a reasonably large proportion of all cases. This algorithm enables researchers to explore a vast array of epidemiology and health services research topics using administrative insurance claims databases to gain knowledge about CIU/CSU.

References

[1] Grattan CE, Sabroe RA, Greaves MW. Chronic urticaria. *J Am Acad Dermatol*. 2002;46:645–657.
[2] Greaves M. Chronic urticaria. *J Allergy Clin Immunol*. 2000;105:664–672.
[3] Greaves MW. Chronic idiopathic urticaria. *Curr Opin Allergy Clin Immunol*. 2003;3:363–368.
[4] Powell RJ, Du Toit GL, Siddique N, et al. BSACI guidelines for the management of chronic urticaria and angio-oedema. *Clin Exp Allergy*. 2007;37:631–650.
[5] Toubi E, Kessel A, Avshovich N, et al. Clinical and laboratory parameters in predicting chronic urticaria duration: a prospective study of 139 patients. *Allergy*. 2004;59:869–873.
[6] Engin B, Uguz F, Yilmaz E, Ozdemir M, Mevlitoglu I. The levels of depression, anxiety and quality of life in patients with chronic idiopathic urticaria. *J Eur Acad Dermatol Venereol*. 2008;22:36–40.
[7] Grob JJ, Gaudy-Marqueste C. Urticaria and quality of life. *Clin Rev Allergy Immunol*. 2006;30:47–51.
[8] Weldon D. Quality of life in patients with urticaria and angioedema: assessing burden of disease. *Allergy Asthma Proc*. 2014;35:4–9.
[9] Weldon DR. Quality of life in patients with urticaria. *Allergy Asthma Proc*. 2006;27:96–99.
[10] Isik SR, Karakaya G, Celikel S, Demir AU, Kalyoncu AF. Association between asthma, rhinitis and NSAID hypersensitivity in chronic urticaria patients and prevalence rates. *Int Arch Allergy Immunol*. 2009;150:299–306.
[11] Maurer M, Bindslev-Jensen C, Gimenez-Arnau A, et al. Chronic idiopathic urticaria (CIU) is no longer idiopathic: time for an update. *Br J Dermatol*. 2013;168:455–456.
[12] Zazzali JL, Broder MS, Chang E, Chiu MW, Hogan DJ. Cost, utilization, and patterns of medication use associated with chronic idiopathic urticaria. *Ann Allergy Asthma Immunol*. 2012;108:98–102.

[13] Kaplan AP. Chronic urticaria: pathogenesis and treatment. *J Allergy Clin Immunol*. 2004;114:465–474. quiz 475.
[14] Kaplan AP, Joseph K, Maykut RJ, Geba GP, Zeldin RK. Treatment of chronic autoimmune urticaria with omalizumab. *J Allergy Clin Immunol*. 2008;122:569–573.
[15] Delong LK, Culler SD, Saini SS, Beck LA, Chen SC. Annual direct and indirect health care costs of chronic idiopathic urticaria: a cost analysis of 50 non-immunosuppressed patients. *Arch Dermatol*. 2008;144:35–39.
[16] Rosner B. *Fundamentals of Biostatistics*. 2nd ed. Boston, MA: Prindle, Weber, & Schmidt/Duxbury Press; 1986:54–55.
[17] Kim SY, Servi A, Polinski JM, et al. Validation of rheumatoid arthritis diagnoses in health care utilization data. *Arthritis Res Ther*. 2011;13:R32.
[18] Quan H, Li B, Saunders LD, et al. Assessing validity of ICD-9-CM and ICD-10 administrative data in recording clinical conditions in a unique dually coded database. *Health Serv Res*. 2008;43:1424–1441.
[19] Lee DS, Donovan L, Austin PC, et al. Comparison of coding of heart failure and comorbidities in administrative and clinical data for use in outcomes research. *Med Care*. 2005;43:182–188.
[20] Quan H, Parsons GA, Ghali WA. Validity of information on comorbidity derived from ICD-9-CCM administrative data. *Med Care*. 2002;40:675–685.