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## Effect of chronic urticaria on US patients: analysis of the National Health and Wellness Survey

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### ABSTRACT

**Background:** Chronic idiopathic (also called spontaneous) urticaria (CIU/CSU) is the most common form of chronic urticaria and has been associated with impairment to health outcomes, although the effect has never been assessed using a nationally representative sample in the United States.

**Objectives:** To assess the burden of CIU/CSU from the patients' perspective in terms of health-related quality of life, impairment to work and nonwork activities, and health care resource use.

**Methods:** Data were obtained from the US National Health and Wellness Survey. Current use of a prescription for the treatment of chronic hives was used as a proxy for CIU/CSU. Patients with CIU/CSU in the proxy group were matched 1:4 to respondents without chronic hives using survey year, sex, age, and race. Generalized linear models were adjusted for comorbidities, smoking, body mass index, and health insurance status. Outcome measures included the Medical Outcomes Study 12-Item and 36-Item Short Form Health Surveys; self-reported depression, anxiety, and sleep difficulties; the Work Productivity and Activity Impairment questionnaire, and health care resource use.

**Results:** After matching and adjustment for covariates, those currently using a prescription for chronic hives had mental component summary scores 5.7 points lower, physical component summary scores 6.5 points lower, and health utility scores 0.11 points lower than controls, as well as higher adjusted odds of reporting depression, anxiety, and sleep difficulties. Mean adjusted work impairment was approximately double in prescription-treated chronic hives relative to controls, as was frequency of health care visits.

**Conclusion:** Chronic hives substantially affects quality of life, nonwork activities, capacity to work, and health care use, providing further evidence of a high burden of CIU/CSU across multiple health outcomes and unmet need for effective treatment.

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### Introduction

Urticaria is a disease characterized by wheals (hives), which are accompanied by an itching or burning sensation and generally resolve within 24 hours. Urticaria frequently presents with

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angioedema, which is included in some international definitions of urticaria and tends to fade more slowly and can be painful rather than itchy.<sup>1</sup> Most urticaria is acute and resolves quickly, although hives or angioedema can continue to appear and disappear during a longer period. Urticaria lasting at least 6 weeks is considered chronic.<sup>2,3</sup> Types of chronic urticaria are differentiated by the trigger (eg, sun exposure, heat, cold); if no trigger can be identified, it is termed *chronic idiopathic urticaria* (CIU), which is also known as *chronic spontaneous urticaria* (CSU; henceforth referred to as CIU/CSU).<sup>1,2</sup> Almost all cases of CIU/CSU include hives, although studies have found as many as 13% of cases experience only angioedema.<sup>3</sup>

Approximately 20% of people experience an episode of urticaria at least once in their lifetime.<sup>4</sup> The point prevalence of CIU/CSU has been estimated at approximately 0.1% in one study<sup>5</sup> but is generally

**Table 1**  
Prevalence estimate of chronic hives in US adults by sex

| Variable          | Prevalence Estimate (95% CI), % |                  |                  |
|-------------------|---------------------------------|------------------|------------------|
|                   | Overall                         | Men              | Women            |
| Ever experienced  | 0.53 (0.49–0.56)                | 0.32 (0.27–0.36) | 0.73 (0.67–0.79) |
| Ever diagnosed    | 0.40 (0.37–0.43)                | 0.21 (0.18–0.25) | 0.58 (0.53–0.63) |
| Currently treated | 0.13 (0.11–0.15)                | 0.08 (0.06–0.10) | 0.18 (0.15–0.21) |

Abbreviations: CI, confidence interval.

thought to be 0.5% to 1.0%.<sup>3</sup> The disease affects people earlier than many other chronic diseases, with peak incidence between 20 and 40 years of age.<sup>3</sup> Incidence among women is nearly twice that of men.<sup>6–8</sup> Cases of CIU/CSU can resolve spontaneously, although more severe cases tend to be more persistent. In one study, 30% of moderate and severe cases were still present after 5 years.<sup>9</sup>

The effect of CIU/CSU on the patient can be significant. A review of studies using the Dermatology Quality of Life Index revealed that chronic urticaria had an effect on health-related quality of life (HRQoL) similar in magnitude to other severe skin conditions,<sup>10</sup> as did a study comparing patients with chronic urticaria to those with psoriasis or atopic dermatitis using the

**Table 2**  
Patient characteristics in cases and controls by chronic hives after matching by age, sex, race/ethnicity, and year of survey<sup>a</sup>

| Characteristic                          | Never experienced chronic hives (n = 1,080) | Currently treated for chronic hives (n = 270) | P value |
|-----------------------------------------|---------------------------------------------|-----------------------------------------------|---------|
| Age, mean (SD), y                       | 48.6 (15.2)                                 | 48.5 (15.2)                                   | >.99    |
| Male sex                                | 284 (26.3)                                  | 71 (26.3)                                     | >.99    |
| Race/ethnicity                          |                                             |                                               | >.99    |
| White                                   | 736 (68.1)                                  | 184 (68.1)                                    |         |
| Black                                   | 132 (12.2)                                  | 33 (12.2)                                     |         |
| Hispanic                                | 84 (7.8)                                    | 21 (7.8)                                      |         |
| Asian                                   | 72 (6.7)                                    | 18 (6.7)                                      |         |
| Other                                   | 56 (5.2)                                    | 14 (5.2)                                      |         |
| Employed                                | 602 (55.7)                                  | 136 (50.4)                                    | .11     |
| Household income                        |                                             |                                               | .008    |
| Below median                            | 474 (43.9)                                  | 119 (44.1)                                    |         |
| Above median                            | 495 (45.8)                                  | 139 (51.5)                                    |         |
| Declined to answer                      | 111 (10.3)                                  | 12 (4.4)                                      |         |
| Married or living with partner          | 626 (58.0)                                  | 163 (60.4)                                    | .47     |
| Type of health insurance                |                                             |                                               | .003    |
| None                                    | 172 (15.9)                                  | 28 (10.4)                                     |         |
| Commercial                              | 700 (64.8)                                  | 165 (61.1)                                    |         |
| Medicaid                                | 42 (3.9)                                    | 19 (7.0)                                      |         |
| Military                                | 16 (1.5)                                    | 8 (3.0)                                       |         |
| Medicare                                | 134 (12.4)                                  | 48 (17.8)                                     |         |
| Not sure                                | 16 (1.5)                                    | 2 (0.7)                                       |         |
| Completed university                    | 440 (40.7)                                  | 119 (44.1)                                    | .33     |
| BMI, mean (SD) (n = 1,042 and 265)      | 28.83 (7.23)                                | 29.17 (7.42)                                  | .49     |
| Exercise, mean (SD), days in past month | 7.7 (8.9)                                   | 7.4 (8.7)                                     | .65     |
| CCI score, mean (SD)                    | 0.37 (0.83)                                 | 2.19 (5.69)                                   | <.001   |
| BMI categories                          |                                             |                                               | .29     |
| Underweight                             | 22 (2.0)                                    | 6 (2.2)                                       |         |
| Normal                                  | 353 (32.7)                                  | 77 (28.5)                                     |         |
| Overweight                              | 295 (27.3)                                  | 87 (32.2)                                     |         |
| Obese                                   | 372 (34.4)                                  | 95 (35.2)                                     |         |
| Declined to answer                      | 38 (3.5)                                    | 5 (1.9)                                       |         |
| Smoking status                          |                                             |                                               | <.001   |
| Current                                 | 204 (18.9)                                  | 81 (30.0)                                     |         |
| Former                                  | 295 (27.3)                                  | 70 (25.9)                                     |         |
| Never                                   | 581 (53.8)                                  | 119 (44.1)                                    |         |
| Alcohol use                             |                                             |                                               | .054    |
| Daily                                   | 43 (4.0)                                    | 20 (7.4)                                      |         |
| Less than daily                         | 643 (59.5)                                  | 158 (58.5)                                    |         |
| None                                    | 394 (36.5)                                  | 92 (34.1)                                     |         |

Abbreviations: BMI, body mass index; CCI, Charlson comorbidity index; SD, standard deviation.

<sup>a</sup>Data are presented as number (percentage) of patients unless otherwise indicated.

VQ-Dermato.<sup>11</sup> A study using the Nottingham Health Profile, a generic (rather than disease-specific) HRQoL measure, found that patients with CIU/CSU have health status similar to patients with coronary diseases awaiting bypass surgery.<sup>12</sup> The effect on HRQoL is attributable in part to the swelling, itching, and pain, as well as feelings of fatigue. Sleep disturbances also contribute to poor health status in CIU/CSU, with such disturbances often being the result of itching accompanying the hives.<sup>13,14</sup> Mental health can also be affected because of the unpredictability of disease flares, which create a sense of loss of control.<sup>12</sup> Patients also report emotional and social troubles, such as with home management, personal care, recreation or social interaction, and mobility.<sup>12</sup> Greater disease severity is associated with greater effect on QoL.<sup>15</sup>

Psychiatric comorbidity is also common in patients with CIU/CSU. Patients with CIU/CSU experience higher levels of stress, higher comorbidities, somatization, obsessive-compulsive disorder, depression, and anxiety,<sup>16</sup> with one-third to half of these patients thought to experience some psychiatric comorbidity, especially anxiety and depression.<sup>17</sup> Disease severity is not associated with psychiatric comorbidity, but QoL is lower in patients with CIU/CSU and psychological comorbidities.<sup>18</sup>

The economic burden of CIU/CSU has been less thoroughly studied, but the existing evidence reveals a considerable impact. The condition is associated with both regular and unanticipated health care visits, as well as costs associated with laboratory expenses.<sup>3,19</sup> Annual CIU/CSU-related economic costs were estimated at more than \$2,000 per patient per year among a sample of 50 nonimmunosuppressed outpatients in the United States.<sup>20</sup> That figure did not include impairment while at work (presenteeism), which is thought to be responsible for greater losses than work time missed in chronic illnesses.<sup>21</sup> Another study estimated annual economic cost of CIU/CSU at €2,128 (2002) per patient per year, which included losses due to presenteeism but was based on clinical trial data.<sup>22</sup>

These studies reveal a clear burden of chronic urticaria, but no study to date has reported on the effect of chronic urticaria, specifically CIU/CSU, among individuals drawn from a nationally representative survey of adults in the United States. Furthermore, few of these studies have assessed the effect of chronic urticaria or CIU/CSU on work productivity. Likewise, there is very limited information quantifying the effect of the condition on health care use. The present study was conducted to provide information about the effect of CIU/CSU on patients in the United States, specifically quantifying the burden of the illness as related to health status and HRQoL, work impairment and impairment or disruption of nonwork activities, and the use of health care resources using patients with chronic hives as a proxy.

## Methods

### Data Source

The present study is a retrospective, cross-sectional analysis of data taken from the US National Health and Wellness Survey (NHWS), a large, cross-sectional survey designed to reflect health in the general population. Potential respondents are identified through opt-in online survey panels, with stratified random sampling within the survey panel to ensure representativeness in terms of age, sex, and minority racial status. The current project incorporates data from the annual US surveys conducted in 2010 to 2012. Because sampling is conducted without regard to participation in a previous fielding of the survey, some individuals have completed the survey more than once, and for these individuals, only the most recent responses were included in the analysis. All respondents were required to be at least 18 years of age, able to read and write English, and able to provide informed consent. The

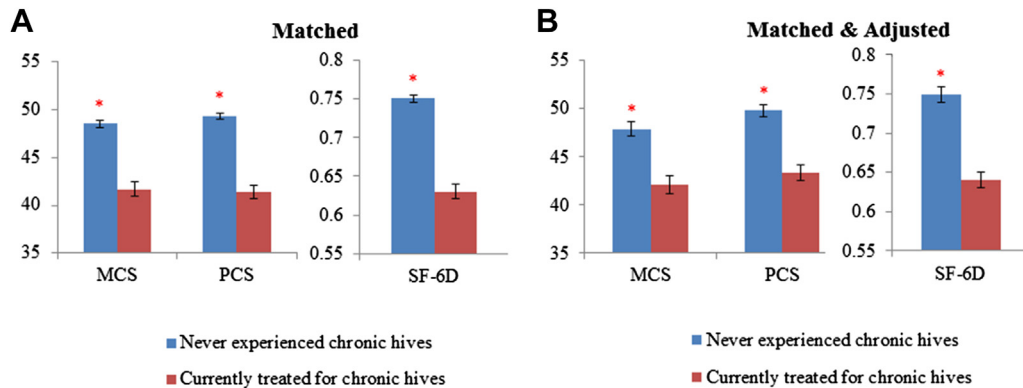


**Figure 1.** Regression analysis. A, Matched; B, matched and adjusted for comorbidities, smoking, body mass index, and health insurance status. \* $P < .001$ . Error bars indicate SEM. MCS indicates mental component summary; PCS, physical component summary; SF-6D, Short Form-6 Dimension health utility.

protocol and questionnaire for the NHWS was reviewed and approved annually by Essex Institutional Review Board (Lebanon, New Jersey).

### Measures

Items to identify respondents with CIU/CSU specifically were not included in the NHWS, but the survey did ask respondents to indicate whether they had ever experienced chronic hives (lasting  $\geq 6$  weeks). Those who indicated experiencing chronic hives were asked to indicate whether their chronic hives were diagnosed by a doctor and whether they were currently using a prescription to treat their chronic hives. Those who indicated current use of a prescription were used as the proxy for individuals with CIU/CSU (cases) because this would ensure that patients would not only be diagnosed as having chronic hives but currently be affected by the disease, as opposed to those who had been diagnosed as having chronic urticaria in the past that had since resolved. To ensure respondents with CIU/CSU were not present in the non-CIU/CSU comparison group, respondents who were not currently being treated for chronic hives but had been diagnosed as having or experienced chronic hives were excluded from analyses of burden.

HRQoL was measured using the standard recall form (4 weeks) of the Medical Outcomes Study 12-Item Short Form Health Survey version 2 (SF-12v2) for respondents surveyed in 2010 and 2011 and the Medical Outcomes Study 36-Item Short Form Health Survey version 2 (SF-36v2) for those surveyed in 2012.<sup>23,24</sup> These measures were used to calculate the mental component summary (MCS) and physical component summary (PCS) scores to summarize mental and physical health, respectively. These scores have a mean of 50 and an SD of 10 for the US population, with higher scores indicating better health. Health utility scores were also calculated from the SF-12v2 and SF-36v2 using the SF-6D algorithm, which provides a preference-based single index measure for health using general population values.<sup>25</sup>

Self-report of depression, anxiety, and sleep problems were also included as outcomes. Respondents indicating experience of depression in the prior 12 months were considered to have depression. Respondents were considered to have anxiety if they reported experiencing general anxiety disorder, panic disorder, phobia, posttraumatic stress, obsessive-compulsive disorder, social anxiety disorder, or anxiety in the prior 12 months, whereas those who indicated either insomnia or sleep difficulties in the prior 12 months were considered to have sleep difficulties.

Impairment to work and nonwork activities was measured using the general health version of the Work Productivity and Activity Impairment questionnaire, which provides percentage impairment due to health in the 7 days preceding the survey.<sup>26</sup> Metrics for employed respondents include absenteeism (the percentage of work time missed), presenteeism (the degree of impairment while at work), and overall work impairment. Activity impairment, the percentage of health-related impairment to nonwork activities, was rated by all respondents regardless of employment status.

Health care use is measured in the NHWS by the number of visits to different medical practitioners during the prior 6 months. Respondents indicate the types of practitioners seen, including a variety of traditional health care practitioners (eg, general practitioners, allergists), emergency department visits, and hospitalizations. The number of each type of visit is also included. Respondents also indicate what types of alternative health care practitioners they have visited in the prior 6 months, including herbalists, acupuncturists, chiropractors, nutritionists, and massage therapists, although the number of these visits is not included in the survey.

Other variables collected in the NHWS and considered in the analysis were demographic characteristics, including age, sex, race, marital status, medical insurance, level of household income, and employment status. General health characteristics considered in the analysis included body mass index calculated from reported height and weight, cigarette smoking, frequency of alcohol use, and days of exercise in past month. The Charlson comorbidity index

**Table 3**

Greater prevalence and adjusted odds of depression, anxiety, and sleep difficulties among respondents currently treated for chronic hives relative to matched controls<sup>a</sup>

|                    | Matched comparison              |                                                        |         | Regression estimates for those currently treated for chronic hives relative to controls |         |
|--------------------|---------------------------------|--------------------------------------------------------|---------|-----------------------------------------------------------------------------------------|---------|
|                    | Controls, No. (%)<br>(n = 1080) | Currently treated for chronic hives, No. (%) (n = 270) | P value | OR (95% CI)                                                                             | P value |
| Depression         | 216 (20.0)                      | 130 (48.1)                                             | <.001   | 3.2 (2.4–4.3)                                                                           | <.001   |
| Anxiety            | 205 (19.0)                      | 136 (50.4)                                             | <.001   | 3.4 (2.5–4.6)                                                                           | <.001   |
| Sleep difficulties | 298 (27.6)                      | 148 (54.8)                                             | <.001   | 2.6 (1.9–3.4)                                                                           | <.001   |

Abbreviations: CI, confidence interval; OR, odds ratio.

<sup>a</sup>Recall period is 12 months. Regressions were adjusted for comorbidities, smoking, body mass index, and health insurance status.

**Table 4**Elevated work and activity impairment among respondents currently treated for chronic hives relative to matched controls<sup>a</sup>

|                                           | Matched comparisons              |                                                          |                    | Regression estimates for those currently treated for chronic hives relative to controls |         |
|-------------------------------------------|----------------------------------|----------------------------------------------------------|--------------------|-----------------------------------------------------------------------------------------|---------|
|                                           | Control, mean (SD)<br>(n = 1080) | Currently treated for chronic hives, mean (SD) (n = 270) | P value            | IRR (95% CI)                                                                            | P value |
| Work impairment, %                        |                                  |                                                          |                    |                                                                                         |         |
| Absenteeism (n = 594 and 125)             | 3.4 (13.5)                       | 14.1 (25.6)                                              | <.001              | 4.0 (3.7–4.3)                                                                           | <.001   |
| Presenteeism (n = 616 and 126)            | 13.7 (22.4)                      | 35.0 (31.4)                                              | <.001 <sup>b</sup> | 2.3 (2.2–2.4)                                                                           | <.001   |
| Overall work impairment (n = 594 and 125) | 15.6 (25.1)                      | 39.4 (35.1)                                              | <.001              | 2.3 (2.2–2.4)                                                                           | <.001   |
| Activity impairment, %                    | 22.7 (28.6)                      | 47.7 (33.4)                                              | <.001 <sup>b</sup> | 1.9 (1.8–1.9)                                                                           | <.001   |

Abbreviations: CI, confidence interval; IRR, incidence rate ratio; SD, standard deviation.

<sup>a</sup>Regressions were adjusted for comorbidities, smoking, body mass index, and health insurance status.<sup>b</sup>P value adjusted for violation of homogeneity of variance assumption.

(CCI) was also included to represent the level of comorbidity among the respondents.<sup>27</sup>

### Statistical Analysis

Point prevalence of CIU/CSU among US adults was estimated using the 3 possible definitions available in the NHWS (ever experienced, diagnosed by a physician, and currently using a prescription) by applying Horvitz-Thompson weights to respondents according to sex, age (grouped as 18–34, 35–44, 55–64, 65–74, or ≥75 years), race (grouped as white, black/African American, Hispanic, or other), and educational level (bachelor's degree or greater vs no bachelor's degree) as described by the current population survey of the US Census. Race was collapsed into 2 categories (white vs nonwhite) in the 65 through 74 years and 75 years or older age groups to avoid very small sample sizes in any of the weighting categories. These were implemented in the surveyfreq procedure in SAS statistical software (SAS Institute Inc, Cary, North Carolina) to generate prevalence estimates and 95% confidence intervals.

The burden of CIU/CSU was quantified by comparing respondents currently treated with a prescription for chronic hives (cases) with similar respondents who did not report experiencing chronic hives (controls). Each case was matched to 4 controls according to year of survey, age, sex, and race (coded as Black/African American, White, Hispanic, Asian, or other). Respondent characteristics and outcomes of the cases and controls were compared using the *t* test for continuous variables and the  $\chi^2$  test for categorical ones. A series of generalized linear models were also conducted to compare cases and controls while adjusting for respondent characteristics that differed across the 2 groups. These models incorporated cigarette smoking, alcohol use, insurance status, household income, and CCI score. Logistic regression was used for binary outcomes, linear models were used for HRQoL, and Poisson models were used for all other outcomes. Regression-estimated means at the mean of the covariates are presented for

linear models, incidence rate ratios for Poisson models, and odds ratios for binary models.

### Results

A total of 270 cases currently using a prescription for chronic hives were identified. Of the remaining respondents, 809 had experienced chronic hives and were excluded from comparisons, leaving 196,384 respondents who had never experienced chronic hives from which to select controls.

The prevalence of chronic hives currently treated with a prescription was estimated at 0.13% of US adults after weighting. This number was less than half of those diagnosed as having chronic hives by a physician, which was 0.40%. A further 0.13% experienced chronic hives but had not received a diagnosis, for a total of 0.53% of the US adult population who had experienced the condition with or without receiving a diagnosis. Prevalence was lowest among young adults (18–24 years) and peaked in the 45– to 54-year age group. The condition was much more prevalent among women than men, with women at least twice as likely to report each of the 3 definitions as men (Table 1).

Sociodemographic and health characteristics of cases and controls are compared in Table 2. The distribution of type of health insurance differed across cases and controls, as did household income category, whereas alcohol use was marginally different. The CCI scores were considerably higher among those treated for chronic hives, and these respondents were also more likely to be current smokers.

Health outcomes were notably worse among those currently treated for chronic hives. The HRQoL was worse, with decrements of 6.8 points for MCS and 7.9 points for PCS scores and health utility 0.12 points lower for cases than controls (Fig 1A). Regression-adjusted HRQoL outcomes were also consistently worse among the cases, with adjusted means approximately 5 to 6 points lower on MCS and PCS scores and 0.11 points for health utilities compared with controls (Fig 1B). There was also an association between current treatment for

**Table 5**Higher numbers of health care visits among those currently treated for chronic hives relative to matched controls<sup>a</sup>

| Type of service      | Matched comparisons              |                                                          |                    | Regression estimates for those currently treated for chronic hives relative to controls |         |
|----------------------|----------------------------------|----------------------------------------------------------|--------------------|-----------------------------------------------------------------------------------------|---------|
|                      | Control, mean (SD)<br>(n = 1080) | Currently treated for chronic hives, mean (SD) (n = 270) | P value            | IRR (95% CI)                                                                            | P value |
| Physician            | 3.65 (5.34)                      | 9.37 (13.16)                                             | <.001              | 2.2 (2.0–2.3)                                                                           | <.001   |
| General practitioner | 0.97 (1.62)                      | 1.75 (2.32)                                              | <.001              | 1.7 (1.5–1.9)                                                                           | <.001   |
| Allergist            | 0.05 (0.58)                      | 0.51 (1.32)                                              | <.001              | 9.2 (6.7–12.7)                                                                          | <.001   |
| Dermatologist        | 0.09 (0.41)                      | 0.44 (1.08)                                              | <.001 <sup>b</sup> | 4.0 (3.0–5.3)                                                                           | <.001   |
| Psychotherapist      | 0.23 (1.67)                      | 0.79 (3.20)                                              | <.001 <sup>b</sup> | 2.8 (2.3–3.3)                                                                           | <.001   |
| Psychiatrist         | 0.14 (1.30)                      | 0.59 (2.12)                                              | <.001 <sup>b</sup> | 3.6 (2.8–4.5)                                                                           | <.001   |
| Emergency department | 0.21 (0.81)                      | 1.17 (6.89)                                              | .02                | 2.2 (1.8–2.7)                                                                           | <.001   |
| Hospital             | 0.12 (0.61)                      | 0.88 (4.80)                                              | .01 <sup>b</sup>   | 2.9 (2.3–3.8)                                                                           | <.001   |

Abbreviations: CI, confidence interval; IRR, incidence rate ratio; SD, standard deviation.

<sup>a</sup>Recall period for resource use is 6 months. Regressions were adjusted for comorbidities, smoking, body mass index, and health insurance status.<sup>b</sup>P value adjusted for violation of homogeneity of variance assumption.

**Table 6**Higher prevalence of health care use among those currently treated for chronic hives relative to matched controls<sup>a</sup>

| Type of service                      | Matched comparisons            |                                                        |         | Regression estimates for those currently treated for chronic hives relative to controls |                    |
|--------------------------------------|--------------------------------|--------------------------------------------------------|---------|-----------------------------------------------------------------------------------------|--------------------|
|                                      | Control, No. (%)<br>(n = 1080) | Currently treated for chronic hives, No. (%) (n = 270) | P value | OR (95% CI)                                                                             | P value            |
| Physician                            | 830 (76.9)                     | 258 (95.6)                                             | <.001   | 5.5 (2.9–10.1)                                                                          | <.001              |
| General practitioner                 | 519 (48.1)                     | 177 (65.6)                                             | <.001   | 1.9 (1.4–2.5)                                                                           | <.001              |
| Allergist                            | 23 (2.1)                       | 62 (23.0)                                              | <.001   | 11.7 (6.9–19.7)                                                                         | <.001              |
| Dermatologist                        | 73 (6.8)                       | 62 (23.0)                                              | <.001   | 3.7 (2.5–5.4)                                                                           | <.001              |
| Psychotherapist                      | 38 (3.5)                       | 32 (11.9)                                              | <.001   | 2.7 (1.6–4.6)                                                                           | <.001              |
| Psychiatrist                         | 35 (3.2)                       | 43 (15.9)                                              | <.001   | 4.4 (2.7–7.3)                                                                           | <.001              |
| Emergency department                 | 139 (12.9)                     | 71 (26.3)                                              | <.001   | 2.0 (1.4–2.8)                                                                           | <.001              |
| Hospital                             | 90 (8.3)                       | 45 (16.7)                                              | <.001   | 1.5 (1.0–2.3)                                                                           | .07                |
| Alternative health care practitioner | 150 (13.9)                     | 70 (25.9)                                              | <.001   | 1.8 (1.3–2.60)                                                                          | <.001 <sup>a</sup> |

Abbreviations: CI, confidence interval; OR, odds ratio.

<sup>a</sup>Recall period for resource use is 6 months. Regressions were adjusted for comorbidities, smoking, body mass index, and health insurance status.

chronic hives and depression, anxiety, and sleep difficulties. Approximately half of the patients reported each condition, which was approximately twice the proportion of respondents who had never experienced chronic hives. The odds of depression, anxiety, and sleep difficulties were all significantly and markedly higher among the chronic hives group after adjusting for covariates (Table 3).

Mean levels of absenteeism, presenteeism, and overall work impairment among employed patients were more than double the mean levels reported by employed controls. Impairment in nonwork activities was also doubled among the cases relative to controls (Table 4). The decrement in work and activities remained large and significant after regression adjustment. Cases had approximately double the work impairment of controls and nearly double the impairment in nonwork activities (Table 4).

Those currently treated for chronic hives also reported more health care visits than those who had never experienced chronic hives, with approximately 6 more visits to health care practitioners during the 6-month recall period, as well as more emergency department visits and hospitalizations (Table 5). The adjusted rate of traditional practitioner visits overall for cases was approximately twice that of matched controls (Table 5). A higher number of visits was noted for health care practitioners overall, as well as individual types of practitioners, including general practitioners, allergists, dermatologists, psychiatrists, and psychologists. Likewise, the mean number of emergency department visits was approximately twice as high for those currently treated for chronic hives relative to controls after taking into account covariates. The adjusted mean number of hospitalizations was 3 times that of matched controls.

Patients were more likely to make at least one visit to a physician, visit the emergency department, be hospitalized, or visit a nontraditional health care practitioner in the prior 6 months than those without chronic hives (Table 6). Modeling indicated that the adjusted odds of making at least one visit to any traditional health care professional were considerably higher among cases than controls, ranging from an odds ratio of 1.9 for general practitioners to 11.7 for allergists (Table 6). Patients also had higher adjusted odds of visiting the emergency department, although the adjusted odds of being hospitalized in the prior 6 months were not significantly higher. Patients were also more likely to look beyond conventional medicine for their health care, with higher adjusted odds of visiting at least one alternative health care practitioner.

## Discussion

The current study indicates that individuals in the United States currently treated for chronic hives have substantially worse health outcomes than those without chronic hives across a

variety of domains, including HRQoL, psychological well-being, work and daily activities, and health care use. This was true both in comparisons matching for age, race, sex, and year of survey and also after adjusting for income, smoking, alcohol use, insurance status, and comorbidities. This is the first study, to our knowledge, to estimate the humanistic and economic burden of CIU/CSU through data reported by patients diagnosed as having and treated for chronic hives in a large survey representative of US adults.

The absolute level of HRQoL among those with chronic hives was low, with mean MCS and PCS scores nearly 1 SD below the population norm of 50 points. The relative level of HRQoL was also quite poor, with differences between cases and controls exceeding the commonly accepted minimally important differences for these measures both before and after adjustment for potential confounders.<sup>24,28</sup> Consistent with previous research, this study noted a much higher prevalence of depression, anxiety, and sleep difficulties among those with chronic hives. Although patients were no less likely to be employed than other survey respondents, they missed a substantial 14% of the prior week's working hours because of health, 4 times as much as that missed by matched controls. Ratings of impairment while at work averaged 35%, and the regression-adjusted means indicated that both presenteeism and overall work impairment were approximately double than that of controls. The difference in health-related impairment to nonwork activities was of a similar magnitude.

Health care resource use was also greatly elevated among those with chronic hives, with an extra 6 health care practitioner visits per patient in a 6-month period, suggesting 12 more visits per year than matched controls, approximately double the rate of controls after adjustment for covariates.

The NHWS did not include items to specifically identify respondents with CIU/CSU, so the present analysis relied on current treatment for chronic hives as a proxy. Because CIU/CSU is the most common type of chronic urticaria, the sample is most likely primarily composed of patients with CIU/CSU, but it was not possible to confirm the diagnosis. It is less clear what proportion of those respondents to NHWS who have CIU/CSU were included in the analysis; chronic hives is neither strictly necessary nor sufficient to identify CIU/CSU, although almost all individuals with CIU/CSU experience chronic hives. As noted in the Methods section above, those who had experienced chronic hives or were diagnosed as having chronic hives but not currently receiving prescription treatment were excluded, so this analysis may reflect a more severe subgroup. Unadjusted bivariate analysis relying on self-reported experience or diagnosis of chronic hives (data not presented; available from the corresponding author) suggests that the burden does not greatly differ across these alternative proxy definitions for CIU/CSU.

There are a number of limitations that should be considered along with the results. One is the panel-based recruitment used in the NHWS. Although previous studies have found similarity between the NHWS sample and population-based health surveys on key measures, some differences exist, and these may have introduced a bias relative to the population.<sup>29,30</sup> However, because both cases and controls were drawn from the same sample, such a bias is not likely to affect the decrement between cases and controls observed here. The current study matched on key demographic variables and adjusted for measured confounders, although unmeasured differences that account for some of the observed difference in outcomes between cases and controls may be present in the data.

Likewise, differentiating the effect of the condition itself from treatments used for the condition was not possible. Some of the burden observed in this study may be due to treatments with adverse effects, such as the sedating antihistamines included in later lines of treatment in the practice parameters.<sup>2</sup> As individuals undergo treatments for non-life-threatening conditions such as CIU/CSU to improve their quality of life rather than extend their survival, the untreated disease itself is likely even more burdensome, and the negative consequences of these treatments should be considered evidence of unmet need among these patients. Unfortunately, the NHWS did not collect information on which prescriptions were being used for chronic hives, so characterizing the burden according to type of treatments used could not be done. Previous research using insurance claims indicates widespread use of nonsedating antihistamines and oral corticosteroids among those with CIU, with sedating antihistamines used by less than 10% of patients.<sup>31</sup>

In summary, this research complements the existing evidence presented in other published studies reporting substantial burden among patients with CIU/CSU drawn from a nationwide sample of nearly 200,000 US adults, with important decrements in quality of life, increased prevalence of mental health concerns, impairment in work productivity, and greatly increased use of health care. That the patients in the current study had these impairments despite current prescription treatment suggests a need for treatments beyond the current standard of care. Improved treatment of these patients would not only benefit the individuals' well-being but also potentially reduce the affect of the condition on employers, payers, and the health care system.

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