Prevalence and Characteristics of Chronic Cough in Adults Identified by Administrative Data

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INTRODUCTION

Chronic cough (CC) is defined as a cough that lasts more than 8 weeks.1-4 Estimates of CC prevalence range from 2.5% to 12%, varying by study design and type of data collection (eg, survey, patient report, or physician diagnosis).1,3,5,6 Systematic approaches to the assessment7 and management of CC are highlighted in guidelines developed by professional organizations.3,4, 8-12 Studies report the substantial clinical and healthcare burden of CC.13-15 However, real-world studies of CC based on administrative health care data are challenged by the lack of specific ICD-9 or ICD-10 diagnostic codes to identify CC. To address this limitation, we identified a subgroup of CC patients seen by specialists using an internal Kaiser Permanente Southern California (KPSC)-specific CC encounter code. Burden of disease was greater in these specialist-diagnosed CC patients compared with a matched noncough cohort.16

The present study sought to determine the overall prevalence of CC at KPSC. To accomplish this objective, we needed to identify CC patients other than those who were specialist diagnosed. We used a combination of cough-related keywords or concepts in clinical notes extracted by natural language processing (NLP), ICD-9 or ICD-10 cough diagnosis codes, and dispensed antitussive medications to identify an event-diagnosed CC cohort with CC of more than 8 weeks using a prespecified algorithm. The combination of specialist-diagnosed and event-diagnosed CC patients was used to determine CC prevalence. The burden of CC was determined in the entire cohort and compared between specialist-diagnosed CC and event-diagnosed CC during the baseline and follow-up years. Given the chronicity of CC, its persistence was determined in the follow-up year.

METHODS

Study Design

This observational study used the KPSC Research Data Warehouse to capture administrative pharmacy and healthcare resource utilization (HCRU) data from 4.6 million enrollees across the Southern California region whose demographics are comparable to residents in the region.17,18 Details of HCRU data capture capabilities at KPSC have been reported.17 The study was approved with waiver of written consent by the KPSC Institutional Review Board.

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Keywords: administrative data, chronic cough, burden, healthcare resource utilization, natural language processing, specialist care
Cohort Identification

Using administrative pharmacy and HCRU data, we identified hierarchically patients aged 18 to 85 years with CC in 2013 to 2016 as specialist-diagnosed CC and event-diagnosed CC (Figure 1). Patients in both groups were required 1) to have continuous health plan enrollment (no enrollment gap of >45 days) and pharmacy benefit in the 12-month period prior to and the 12-month period after the CC index date (see the definition of index date below) and 2) no angiotensin-converting enzyme inhibitor (ACE-I) use in the year prior to and at the index date because up to 20% of ACE-I users experience cough. For both specialist-diagnosed and event-diagnosed CC patients, the baseline period was the 12 months prior to and including the index date, and the follow-up year was the 12-month period after the index date.

Specialist-diagnosed CC

A specialist-diagnosed CC group was identified using a KPSC-specific CC encounter code (#529563) during a clinic visit to a pulmonologist, allergist, otolaryngologist, or gastroenterologist as reported previously (Figure 1). ICD-9 and ICD-10 codes are not specific enough to identify CC; therefore, only the internal CC encounter code was used. The index date for the specialist-diagnosed CC cohort was the earliest date of the specialist visit with the CC-specific encounter code. A manual chart review based on a random sample of 200 specialist-diagnosed CC patients revealed that 90.5% had evidence of CC of more than 8 weeks.

Event-diagnosed CC

An event-diagnosed CC group was identified based on any 3 of the following clinical events that occurred within 120 days: 1) mentioning of cough or related keywords or concepts in qualified clinical notes extracted by NLP (Table 1); 2) physician diagnosis of cough (ICD-9: 786.2 or ICD-10: R05); the patients who were coded with the internal CC-specific encounter code were also coded with either 786.2 (ICD-9) or R05 (ICD-10) for the same encounter; and 3) dispensed antitussive medication.

The first and the last of the 3 events were required to be at least 56 days (8 wk) apart, and any 2 of the 3 events were required to be at least 21 days (3 wk) apart. If more than 3 events during the study period were found, the first 3 qualifying events were used. The third event was defined as the index event for the event-diagnosed CC cohort.

The process of information extraction from clinical notes through NLP is described in Table 1. Cough-related keywords were based on the list in the Merck/Regenstrief Institute collaboration study, ontologies in the Unified Medical Language System, and possible linguistic variations and misspelling or mistyping (Table 1). An internal validation of the NLP algorithm based on a sample of 200 clinical notes revealed a positive predictive value of 96.7% and sensitivity of 96.7%. Of the 5,219,820 NLP-identified cough events, 5,210,284 (99.82%) were for cough only, 5939 were for cough and expectorant use (0.11%), and 3597 (0.07%) were for expectorant use only.

Patient Characteristics

Measures on median household income and highest education level at the census block group-level were derived from geocoded addresses of KPSC health plan enrollees. All patient characteristics were captured electronically. Smoking status was the last measure at or before index date. All comorbidities were defined by ICD-9 and ICD-10 codes as described previously. The Charlson Comorbidity Index classified prognostic comorbidities. Obesity was defined as a body mass index of ≥30 kg/m². We determined the frequency of potential CC complications based on the occurrence of sleep disturbance, stress incontinence, costochondritis, vomiting, and subconjunctival hemorrhage determined by ICD-9 and ICD-10 codes. Respiratory-specific events as causes of emergency department (ED) visits and hospitalizations have been reported previously. The current Medi-Span Generic Product Identifier at 14 characters level granularity identified relevant studied dispensed medications. Persistence of CC was defined for the specialist-diagnosed CC patients if they had a repeated CC-specific encounter code in the follow-up year in 1 of the 4 specialist departments described above. For event-diagnosed CC patients, persistence of CC required at least 3 individual events in the follow-up year that met the event-diagnosed CC definition.

Statistical Analyses

Patient demographic characteristics, comorbidities, HCRU, and dispensed medications were determined in the baseline and follow-up years. Comparisons between specialist-diagnosed and event-diagnosed groups were performed using the χ² test or Fisher’s exact test for categorical variables and the Kruskal–Wallis test for continuous variables.

The prevalence of CC was calculated by using the formula (N/D) × 100, where D is the number of health plan enrollees between 18 and 85 years of age with at least 1 clinic visit at a KPSC facility without taking ACE-I who were continuously enrolled with pharmacy benefits for at least 120 days in the year of interest, and N is the number of CC patients in D who met the definition of CC. The requirement of 120 days ensures a minimum length of insurance and benefit coverage for chronic cough or its individual events to be recorded. The annual prevalence of CC was estimated using the same definition mentioned
Figure 1. Administrative logistics for patient identification, and number of patients identified with administrative databases. Administrative algorithm for patient identification of adult chronic cough (CC) cohort. *Refer to Table 1 for list of keywords. **No more than one event per patient per day. ACE = angiotensin-converting enzyme; KPSC = Kaiser Permanente Southern California.
above, and the calculation of D for each calendar year was
data based on the year of CC index date. The overall and annual
prevalence rates were stratified by age, sex, and race/ethnicity
using the same definitions described above within each
stratum. To estimate 95% confidence intervals for prevalence,
the normal approximation method was applied:

\[ \hat{p} \pm z_{\alpha/2} \sqrt{\frac{\hat{p}(1-\hat{p})}{n}} \]

where \( \hat{p} \) is the estimated prevalence, \( z \) is the
value from the standard normal distribution for 95%
confidence level, and \( n \) is the number of people included in
the denominator.

All analyses were conducted using SAS (version 9.4 for
Unix; SAS Institute, Cary, NC). Statistical significance was
set at \( p < 0.001 \) to account for the large sample size and was
2-sided.

**RESULTS**

**CC Cohort**

We identified 50,163 unique patients with CC. A total of
11,290 patients (22.5%) met the definition of specialist-
diagnosed CC, and 38,873 (77.5%) were event–diagnosed
CC (Figure 1). Roughly half of specialist–diagnosed CC
cases also met the definition for event diagnosis, indicating
the cohort would be 10.8% smaller without the specialist-
diagnosed definition.

**Demographics**

The CC patients were 57.4±16.5 years of age, with length
of enrollment of 18.6±12.5 years and median household
income of $75,486±31,811. The majority of the patients
were female (67.6%) and from non–White ethnicities
(56.7%) (Table 2). Among CC patients, 36.5% had Medicare
insurance, and 5.9% were current smokers.

**Comorbidities**

Respiratory comorbidities reached the following
frequencies for more common conditions: asthma (31.2%),
chronic sinusitis (28.1%), allergic rhinitis (27.3%), pneu-
omonias (23.1%), chronic rhinitis (18.8%), chronic obstructive
pulmonary disease (COPD) (14.1%), and upper airway
cough syndrome (postnasal drip) (12.1%). Common non-
respiratory comorbidities among the CC patients included
hypertension (41.3%), gastroesophageal reflux disease
(GERD) (32.5%), obesity (27.4%), depression (22.4%), and

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**Table 1. Cough related keywords, encounter types, department specialties, clinical note types used to identify cough events, and natural language processing**

<table>
<thead>
<tr>
<th>Category</th>
<th>Specifics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identifying cough events from clinical notes</td>
<td>Notes containing the concept of cough during the study period among patients 18-85 years of age. Notes not used when cough was historical, negated, resolved, nonpatient self, not referred to actual event or without affirmation, and in which angiotensin-converting enzyme inhibitors (ACE-I) were mentioned.</td>
</tr>
<tr>
<td>Cough-related keywords</td>
<td>Based on the list in the Merck/Regenstrief Institute collaboration study,20 ontologies in the Unified Medical Language System,21 and possible linguistic variations and misspelling or misspelling. The compiled keywords included cough, coughed, coughing, coughs, expectorate, expectorated, expectorates, expectorating, expectoration.</td>
</tr>
<tr>
<td>Notes extraction</td>
<td>Specific types of clinical notes with the cough-related keywords for certain medical encounters that occurred at certain departments during the study period were extracted from the Kaiser Permanente Southern California electronic medical record system.</td>
</tr>
<tr>
<td>Encounter type</td>
<td>Office visit, urgent care, telephone visit, email, phone, message, video visit, emergency department visit, long term care, home health care, hospice care, skilled nursing facility care</td>
</tr>
<tr>
<td>Department type</td>
<td>Allergy, Asthma and Immunology, Continuing Care, Family Practice, Gastroenterology, Geriatric Medicine, Home Health Care, Infectious Diseases, Internal Medicine, Obstetrics, Gynecology, Occupational Medicine, Otolaryngology, Pulmonary Diseases, Respiratory Therapy, Sleep Clinic, Speech Therapy, Urgent Care, Urology, Emergency Medicine, Pediatric Allergy, General Practice, Immunology, Primary Care, Pediatric Ambulatory Care, Medical Ambulatory Care, Pediatric Urgent Care, Continuing Care, Residential Care, Skilled Nursing Facility, Ambulatory Care Unit, Addiction Medicine, Adolescent Medicine, Employee Health, Hospice Care, Occupational Therapy, Preventive Medicine, Urology, Emergency Medicine</td>
</tr>
<tr>
<td>Type of clinical notes</td>
<td>Progress notes, emergency department provider notes, history and physical notes, consult notes, telephone encounter notes</td>
</tr>
<tr>
<td>Pre-processing of notes</td>
<td>Clinical notes were preprocessed through sentence separation and tokenization (ie, segmenting text into linguistic units such as words and punctuations). The sentence boundary detection algorithm in Natural Language Toolkit2 and an additional customized sentence boundary detection algorithm were used to separate sentences. For example, the special symbol “¶” in the clinical notes indicated the end of sentences. In addition, potential detected misspelled words/terms were corrected, including misspellings such as “cough worse at night” and “cough was mild.”</td>
</tr>
<tr>
<td>NLP algorithm development</td>
<td>A computerized NLP algorithm was developed through an iterative process in which the developed algorithm was refined to match with the results of the reference standards derived through chart review and adjudication of 200 notes at a time. A total of 1,600 clinical notes was randomly selected from the entire set of cleaned notes and split into eight subsets, each containing 200 notes that were sequentially reviewed by trained abstractors and adjudicated by clinical experts.</td>
</tr>
</tbody>
</table>

NLP = natural language processing.
Table 2. Baseline year demographic characteristics and comorbidities of entire chronic cough cohort and subgroups

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Entire CC cohort (N = 50,163)</th>
<th>Specialist-diagnosed CC (n = 11,290)</th>
<th>Event-diagnosed CC (n = 38,873)</th>
<th>p value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>57.4 (16.5)(^b)</td>
<td>60.9 (14.3)</td>
<td>56.4 (16.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Female sex</td>
<td>33,919 (67.6)</td>
<td>7535 (67.7)</td>
<td>26,384 (67.9)</td>
<td>0.024</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>White</td>
<td>21,723 (43.3)</td>
<td>5693 (50.4)</td>
<td>16,030 (41.2)</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>15,665 (31.2)</td>
<td>2809 (24.9)</td>
<td>12,856 (33.1)</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>5918 (11.8)</td>
<td>1045 (9.3)</td>
<td>4873 (12.5)</td>
<td></td>
</tr>
<tr>
<td>Asian/Pacific Islanders</td>
<td>5595 (11.2)</td>
<td>1482 (13.1)</td>
<td>4113 (10.6)</td>
<td></td>
</tr>
<tr>
<td>Others/multiple/unknown</td>
<td>1262 (2.5)</td>
<td>261 (2.3)</td>
<td>1001 (2.6)</td>
<td></td>
</tr>
<tr>
<td>Median household income ($)(^c)</td>
<td>75,486 (31,811)</td>
<td>73,275 (32,597)</td>
<td>76,042 (31,586)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Highest education ≤ grade 12 (%)(^d)</td>
<td>18.9 (14.4)</td>
<td>20.5 (16.8)</td>
<td>18.5 (13.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Years of health plan enrollment</td>
<td>18.6 (12.5)</td>
<td>19.1 (13.1)</td>
<td>18.5 (12.4)</td>
<td>0.042</td>
</tr>
<tr>
<td>Insurances</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Commercial</td>
<td>28,060 (55.9)</td>
<td>5849 (51.8)</td>
<td>22,211 (57.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Medicare</td>
<td>18,442 (36.8)</td>
<td>4740 (42.0)</td>
<td>13,702 (35.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Private pay</td>
<td>12,909 (25.7)</td>
<td>3290 (29.1)</td>
<td>9619 (24.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Medi-Cal</td>
<td>3674 (7.3)</td>
<td>485 (4.4)</td>
<td>3179 (8.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Smoking status(^e)</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Never</td>
<td>30,786 (61.4)</td>
<td>7338 (65.0)</td>
<td>23,448 (60.3)</td>
<td></td>
</tr>
<tr>
<td>Quit</td>
<td>15,901 (31.7)</td>
<td>3591 (31.8)</td>
<td>12,310 (31.7)</td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>2948 (5.9)</td>
<td>261 (2.3)</td>
<td>2687 (6.9)</td>
<td></td>
</tr>
<tr>
<td>Passive</td>
<td>417 (0.8)</td>
<td>92 (0.8)</td>
<td>325 (0.8)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>111 (0.2)</td>
<td>8 (0.1)</td>
<td>103 (0.3)</td>
<td></td>
</tr>
<tr>
<td>Comorbidities</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Charlson comorbidity index</td>
<td>1.8 (2.0)</td>
<td>1.7 (1.9)</td>
<td>1.8 (2.1)</td>
<td>0.04</td>
</tr>
<tr>
<td>Respiratory disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asthma</td>
<td>15,635 (31.2)</td>
<td>3525 (31.2)</td>
<td>12,110 (31.2)</td>
<td>0.888</td>
</tr>
<tr>
<td>Chronic sinusitis</td>
<td>14,097 (28.1)</td>
<td>2753 (24.4)</td>
<td>11,344 (29.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Allergic rhinitis</td>
<td>13,675 (27.3)</td>
<td>3689 (32.7)</td>
<td>9966 (25.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pneumonias</td>
<td>11,607 (23.1)</td>
<td>2048 (18.1)</td>
<td>9559 (24.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Chronic rhinitis</td>
<td>9449 (18.8)</td>
<td>3557 (31.5)</td>
<td>5892 (15.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>COPD</td>
<td>7094 (14.1)</td>
<td>1440 (12.8)</td>
<td>5654 (14.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Upper airway cough syndrome</td>
<td>6057 (12.1)</td>
<td>2306 (20.4)</td>
<td>3751 (9.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Obstructive sleep apnea</td>
<td>3921 (7.8)</td>
<td>981 (8.7)</td>
<td>2940 (7.6)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

(continued on following page)
Table 2. Baseline year demographic characteristics and comorbidities of entire chronic cough cohort and subgroups (continued)

<table>
<thead>
<tr>
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<th>Event-diagnosed CC (n = 38,873)</th>
<th>p value a</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bronchiectasis</td>
<td>1802 (3.6)</td>
<td>620 (5.5)</td>
<td>1182 (3.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pulmonary fibrosis</td>
<td>1687 (3.4)</td>
<td>540 (4.8)</td>
<td>1147 (3.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hemoptysis</td>
<td>1494 (3.0)</td>
<td>370 (3.3)</td>
<td>1124 (2.9)</td>
<td>0.034</td>
</tr>
<tr>
<td>Nasal polyp disease</td>
<td>436 (0.9)</td>
<td>92 (0.8)</td>
<td>344 (0.9)</td>
<td>0.48</td>
</tr>
<tr>
<td>Nonrespiratory disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>20,717 (41.3)</td>
<td>4734 (41.9)</td>
<td>15,983 (41.1)</td>
<td>0.12</td>
</tr>
<tr>
<td>Gastroesophageal reflux disease</td>
<td>16,325 (32.5)</td>
<td>4,977 (44.1)</td>
<td>11,348 (29.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Obesity</td>
<td>13,736 (27.4)</td>
<td>2749 (24.3)</td>
<td>10,987 (28.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Depression</td>
<td>11,238 (22.4)</td>
<td>2291 (20.3)</td>
<td>8947 (23.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Anxiety</td>
<td>10,770 (21.5)</td>
<td>2008 (17.8)</td>
<td>8762 (22.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Atrial fibrillation/flutter</td>
<td>2705 (5.4)</td>
<td>541 (4.8)</td>
<td>2164 (5.6)</td>
<td>0.001</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>4021 (8.0)</td>
<td>846 (7.5)</td>
<td>3175 (8.2)</td>
<td>0.02</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>2594 (5.2)</td>
<td>432 (3.8)</td>
<td>2162 (5.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Potential cough complications</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any complication (any one below)</td>
<td>10,594 (21.1)</td>
<td>2191 (19.4)</td>
<td>8403 (21.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sleep disturbance</td>
<td>5631 (11.2)</td>
<td>1210 (10.7)</td>
<td>4421 (11.4)</td>
<td>0.052</td>
</tr>
<tr>
<td>Stress incontinence</td>
<td>3398 (6.8)</td>
<td>687 (6.1)</td>
<td>2711 (7.0)</td>
<td>0.001</td>
</tr>
<tr>
<td>Costochondritis</td>
<td>1157 (2.3)</td>
<td>210 (1.9)</td>
<td>947 (2.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Subconjunctival hemorrhage</td>
<td>631 (1.3)</td>
<td>150 (1.3)</td>
<td>481 (1.2)</td>
<td>0.44</td>
</tr>
<tr>
<td>Vomiting</td>
<td>673 (1.3)</td>
<td>104 (0.9)</td>
<td>569 (1.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Rib fracture</td>
<td>254 (0.5)</td>
<td>55 (0.5)</td>
<td>199 (0.5)</td>
<td>0.74</td>
</tr>
</tbody>
</table>

COPD = chronic obstructive pulmonary disease; pneumonias = pneumonias, influenza, and acute lower respiratory tract infection.

a Comparisons were made between specialist-diagnosed and event-diagnosed subgroups; p values determined by χ² test or Fisher's exact test for categorical variables and Kruskal-Wallis test for continuous variables.

b Data presented as n (%) and mean (SD).

c Median household income and education by geocoding.

d Smoking based on the last measure prior to the index date.
anxiety (21.5%). Any potential cough complication was observed in 21.1% of the CC patients (Table 2).

CC Prevalence

The annual prevalence of CC was generally consistent from 2013 to 2016 (0.92% in 2013, 0.87% in 2014, 0.97% in 2015, and 1.04 in 2016) (Table 3), with event-diagnosed CC annual prevalence being about 4-fold higher than specialist-diagnosed CC. The relative annual prevalence of CC among female patients was about 40% higher than among male patients during the study period. CC annual prevalence increased by age, with those 65 to 85 years of age exhibiting the highest prevalence, reaching 2.2% in 2016. Blacks had the highest prevalence of CC, followed in decreasing order by Whites, Asian/Pacific Islanders, and Hispanics (Table 3).

Characteristics of CC Patients in Baseline Year

Compared with event-diagnosed CC patients, specialist-diagnosed CC patients were older, had lower median household incomes, and were less likely to have commercial health insurance. The CC patient group also exhibited a substantially lower frequency of minority ethnicity, high-school graduates, and current smokers. Additionally, specialist-diagnosed CC patients had a higher frequency of chronic and allergic rhinitis, upper airway cough syndrome, and GERD and a lower frequency of pneumonia, COPD, obesity, depression, anxiety, cardiac conditions, and any potential cough complication compared with event-diagnosed CC patients (Table 2).

Compared with event-diagnosed CC patients, specialist-diagnosed CC patients had significantly 1) a lower frequency of all-cause and respiratory-associated ED visits and hospitalizations; 2) a higher frequency of visits to different relevant specialty departments; 3) more laboratory testing, including chest and sinus imaging, pulmonary function testing, allergy radioallergosorbent tests, laryngoscopy, esophageal endoscopy, and nasal/sinus endoscopy; 4) a higher frequency of dispensed intranasal rhinitis medications, short-acting β2-agonists (SABA), asthma controller medication (inhaled corticosteroids, inhaled corticosteroids/long-acting β2-agonist [LABA], and leukotriene modifiers), proton pump inhibitors, and H2-blockers; and 5) a lower frequency of dispensed COPD medications (SABA/short-acting muscarinic antagonist and LABA/long-acting muscarinic antagonist), potential respiratory antibiotics, narcotics, antitussives including codeine, and anti-anxiety medications (anxiolytics) (Table 4).

Characteristics of CC Cohort in Follow-up Year

Persistence of CC

Persistence of CC in the follow-up year was observed in 17.9% of the CC cohort. Compared with event-diagnosed CC patients (11.3%), specialist-diagnosed CC patients (40.6%) exhibited a significantly higher prevalence of persistent CC in the follow-up year (Table 5).

Healthcare Resource Utilization

Patient Visits

The frequency of ED visits and hospitalization from all-cause or respiratory causes appeared similar in the follow-up year compared with the baseline year. Consistent with the baseline year, the event-diagnosed subgroup exhibited a significantly higher frequency of ED visits and hospitalization for all-cause or respiratory causes compared with the specialist-diagnosed subgroup (Table 5). Compared with the event-diagnosed subgroup, the specialist-diagnosed subgroup continued to have significantly higher frequency of visits to multiple specialist departments (Table 5).

Laboratory Tests

Laboratory testing for the entire CC cohort was frequent in the follow-up year but generally less than during the baseline year (Tables 4 and 5). Most tests remained significantly higher in the specialist-diagnosed compared with event-diagnosed cohort including pulmonary function tests, advanced chest and sinus imaging, allergy radioallergosorbent test tests, laryngoscopy, esophageal endoscopy, barium swallow and upper gastrointestinal testing, nasal/sinus endoscopy, and bronchoscopy (Table 5).

Dispensed Medication

Specialist-diagnosed CC patients were dispensed controller asthma medication and intranasal rhinitis medications significantly more frequently than event-diagnosed CC patients (Table 5). COPD medications (SABA/short-acting muscarinic antagonist and LABA/long-acting muscarinic antagonist) and H-1 were dispensed significantly more frequently in event-diagnosed CC patients compared with specialist-diagnosed patients (Table 5).

Gastrointestinal medication was generally dispensed at a similar frequency during the follow-up year (Table 5) compared with the baseline year (Table 5); however, proton pump inhibitors were dispensed significantly more frequently in the specialist-diagnosed CC subgroup (41.3%) compared with the event-diagnosed subgroup (28.9%) (Table 5).

Potential respiratory antibiotics and oral corticosteroids were dispensed less frequently during the follow-up year (Table 5) compared with the baseline year (Table 4) and more frequently in the event-diagnosed compared with specialist-diagnosed CC patients (Table 5).

Antitussives were dispensed less frequently in the follow-up year (Table 5) than during the baseline year (Table 4). Similar to the findings during the baseline year, event-diagnosed CC patients were dispensed antitussives including codeine
at follow-up significantly more frequently (44.6%) compared with specialist-diagnosed CC patients (39.1%). Psychotherapeutic medications (antidepressants, anxiolytics, and the neuromodulators gabapentin, pregabalin, and triptans) were dispensed during the follow-up year (Table 5) at frequencies similar to those in the baseline year (Table 4), and anxiolytics were dispensed significantly more frequently in the event-diagnosed compared with specialist-diagnosed CC subgroups (Table 5).

**DISCUSSION**

Given the lack of a standard ICD diagnosis code to identify patients with CC, we demonstrated that CC patients could be identified using electronic medical records. During the period 2013 to 2016, the prevalence of CC in the entire CC cohort was approximately 1%. Notably, this prevalence estimate is dependent on participants actively engaging the healthcare system to satisfy CC definitions. This approach may better reflect the perspective of a payer or healthcare system because CC is a chronic condition with a long duration and because CC patients may not be continuously visiting healthcare providers for diagnosis or management of CC. The prevalence of CC as measured with electronic medical records in this study was lower than published CC prevalence estimates, which have ranged from 2.5% to 12%. These estimates vary by study design and on whether determined by survey, patient report, or physician diagnosis, none of which used administrative coding or information extracted from clinical notes through NLP as in the present study. The CC prevalence reported in the present study is lower than the 2.5% CC prevalence reported in a large Korean National Health and Nutrition Examination Survey study of 11,928 adults aged over 40 years. The present CC prevalence estimated by administrative data may underestimate the prevalence of CC for the following reasons: 1) patients with long-standing refractory CC may not seek visits due to failure of prior care and thereby may not be captured; 2) to increase the specificity of CC in the event-diagnosed subgroup, we used a more conservative definition that included 3 cough events to increase specificity of diagnosis; and 3) we excluded patients dispensed ACE-I in the prior year given the high frequency of cough with this class of medication. We may have overestimated CC prevalence by only including patients with at least 1 clinic-based healthcare visit.

CC prevalence was about 30% higher in female patients than in male patients, was 5-fold higher in patients 65 to 85 years of age compared with those 18 to 44 years, and differed by ethnicity. The higher prevalence of CC in female patients and in elderly patients is consistent with findings of other studies with different designs. A lower tolerance to cough triggers such as capsaicin has been demonstrated in female patients; this may, in part, explain their higher prevalence of CC. The increase in comorbidities such as...

### Table 3. Annual prevalence of entire chronic cough cohort and by type of CC diagnosis, age, sex, and ethnicity, stratified by diagnosis year

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Annual prevalence (% and 95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2013 (95% CI)</td>
</tr>
<tr>
<td>CC cohort</td>
<td></td>
</tr>
<tr>
<td>Entire cohort</td>
<td>0.92 (0.91-0.93)</td>
</tr>
<tr>
<td>Event-diagnosed cohort</td>
<td>0.81 (0.80-0.83)</td>
</tr>
<tr>
<td>Specialist-diagnosed cohort</td>
<td>0.19 (0.18-0.20)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>1.07 (1.05-1.09)</td>
</tr>
<tr>
<td>Male</td>
<td>0.72 (0.70-0.73)</td>
</tr>
<tr>
<td>Age, y</td>
<td></td>
</tr>
<tr>
<td>18-44</td>
<td>0.42 (0.40-0.43)</td>
</tr>
<tr>
<td>45-64</td>
<td>1.02 (1.00-1.05)</td>
</tr>
<tr>
<td>65-85</td>
<td>2.07 (2.02, 2.11)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>1.31 (1.25-1.36)</td>
</tr>
<tr>
<td>White</td>
<td>1.06 (1.04-1.08)</td>
</tr>
<tr>
<td>Asian/Pacific Islanders</td>
<td>0.95 (0.90-0.99)</td>
</tr>
<tr>
<td>Hispanics</td>
<td>0.72 (0.71-0.74)</td>
</tr>
<tr>
<td>Multiple/others/unknown</td>
<td>0.51 (0.47-0.56)</td>
</tr>
</tbody>
</table>

**CC** = chronic cough.  
* The 95% confidence intervals were based on the binomial confidence interval using normal approximation.
Table 4. Baseline year health resource utilization and dispensed medications of the entire chronic cough cohort and subgroups

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Entire CC cohort (N = 50,163)</th>
<th>Specialist-diagnosed CC (n = 11,290)</th>
<th>Event-diagnosed CC (n = 38,873)</th>
<th>p value&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause patient visits</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Outpatient</td>
<td>50,102 (99.9)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>11,290 (100)</td>
<td>38,812 (99.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>≥ 1 emergency department (ED)</td>
<td>18,138 (36.2)</td>
<td>3222 (28.5)</td>
<td>14,916 (38.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>≥ 1 Hospitalization</td>
<td>6990 (13.9)</td>
<td>1103 (9.8)</td>
<td>5887 (15.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Respiratory cause patient visits&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Outpatient</td>
<td>39,631 (79.0)</td>
<td>9477 (83.9)</td>
<td>30,154 (77.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>≥ 1 ED</td>
<td>8858 (17.7)</td>
<td>1463 (13.0)</td>
<td>7395 (19.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>≥ 1 Hospitalization</td>
<td>4334 (8.6)</td>
<td>630 (5.6)</td>
<td>3704 (9.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Specialist visits</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmonologist</td>
<td>14,434 (28.8)</td>
<td>7442 (65.9)</td>
<td>6992 (18.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Otolaryngology</td>
<td>8913 (17.8)</td>
<td>3036 (26.9)</td>
<td>5877 (15.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Allergist</td>
<td>7800 (15.5)</td>
<td>3707 (32.6)</td>
<td>4093 (10.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Gastroenterology</td>
<td>7664 (15.3)</td>
<td>2008 (17.8)</td>
<td>5656 (14.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Urology</td>
<td>3982 (7.9)</td>
<td>933 (8.3)</td>
<td>3049 (7.8)</td>
<td>0.15</td>
</tr>
<tr>
<td>Speech therapy</td>
<td>638 (1.3)</td>
<td>127 (1.1)</td>
<td>511 (1.3)</td>
<td>0.11</td>
</tr>
<tr>
<td>≥ 1 different specialty department</td>
<td>29,708 (59.2)</td>
<td>11,290 (100)</td>
<td>18,418 (47.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>≥ 2 different specialty departments</td>
<td>10,465 (20.9)</td>
<td>4459 (39.5)</td>
<td>6006 (15.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>≥ 3 different specialty departments</td>
<td>2714 (5.4)</td>
<td>1238 (11.0)</td>
<td>1476 (3.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>≥ 4 different specialty departments</td>
<td>502 (1.0)</td>
<td>246 (2.2)</td>
<td>256 (0.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Laboratory tests (&gt;1%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete blood count</td>
<td>38,189 (76.1)</td>
<td>8729 (77.3)</td>
<td>29,460 (75.8)</td>
<td>0.001</td>
</tr>
<tr>
<td>Chest x-ray</td>
<td>33,167 (66.1)</td>
<td>9062 (80.3)</td>
<td>24,105 (62.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pulmonary function tests</td>
<td>13,225 (26.4)</td>
<td>5428 (48.1)</td>
<td>7797 (20.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Advanced chest imaging</td>
<td>8434 (16.8)</td>
<td>2399 (21.2)</td>
<td>6035 (15.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Allergy RAST testing</td>
<td>6433 (12.8)</td>
<td>3154 (27.9)</td>
<td>3279 (8.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Laryngoscopy</td>
<td>3646 (7.3)</td>
<td>1661 (14.7)</td>
<td>1985 (5.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sinus imaging</td>
<td>3418 (6.8)</td>
<td>1191 (10.5)</td>
<td>2227 (5.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Esophageal endoscopy</td>
<td>3113 (6.2)</td>
<td>835 (7.4)</td>
<td>2276 (5.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Barium swallow or upper GI</td>
<td>1225 (2.4)</td>
<td>311 (2.8)</td>
<td>914 (2.4)</td>
<td>0.015</td>
</tr>
<tr>
<td>Nasal/sinus endoscopy</td>
<td>1097 (2.2)</td>
<td>348 (3.1)</td>
<td>749 (1.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Bronchoscopy</td>
<td>887 (1.8)</td>
<td>226 (2.0)</td>
<td>661 (1.7)</td>
<td>0.032</td>
</tr>
<tr>
<td>Respiratory medication (oral or inhaled)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SABA singly</td>
<td>24,161 (48.2)</td>
<td>5698 (50.5)</td>
<td>18,463 (47.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Nasal corticosteroids</td>
<td>23,047 (45.9)</td>
<td>6215 (55.0)</td>
<td>16,832 (43.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ICS/LABA</td>
<td>10,153 (20.2)</td>
<td>3025 (26.8)</td>
<td>7128 (18.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ICS monotherapy</td>
<td>9603 (19.1)</td>
<td>2687 (23.8)</td>
<td>6916 (17.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Leukotriene modifiers</td>
<td>6204 (12.4)</td>
<td>2106 (18.7)</td>
<td>4096 (10.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SABA and SAMA combination</td>
<td>3654 (7.3)</td>
<td>741 (6.6)</td>
<td>2913 (7.5)</td>
<td>0.001</td>
</tr>
<tr>
<td>Nasal antihistamines</td>
<td>2812 (5.6)</td>
<td>1136 (10.1)</td>
<td>1676 (4.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>H1 antihistamines</td>
<td>2524 (5.0)</td>
<td>457 (4.0)</td>
<td>2067 (5.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LABA/LAMA</td>
<td>2298 (4.6)</td>
<td>444 (3.9)</td>
<td>1854 (4.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Nasal SAMA</td>
<td>2,18 (4.2)</td>
<td>898 (9.0)</td>
<td>1220 (3.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LAMA monotherapy</td>
<td>548 (1.1)</td>
<td>151 (1.3)</td>
<td>397 (1.0)</td>
<td>0.004</td>
</tr>
<tr>
<td>Gastrointestinal (oral)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proton pump inhibitors</td>
<td>16,654 (33.2)</td>
<td>5084 (45.0)</td>
<td>11,570 (29.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>H2 blockers</td>
<td>6881 (13.7)</td>
<td>1793 (15.9)</td>
<td>5086 (13.1)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

(continued on following page)
COPD and more frequent use of healthcare resources in elderly patients may be responsible in part for their higher prevalence of CC compared with younger patients. The prevalence of CC by ethnicity was explored in a meta-analysis, which reported higher prevalences in the US and Europe than in Asia or Africa, yet no ethnic difference in the cough reflex was noted between White, Indian, and Chinese subjects. Differences in environmental exposures, comorbidities such as obesity and asthma (which are higher in Blacks), and of HCRU may be factors associated with ethnic differences in CC.

Most prior studies relied on patient reporting of CC events and use based on local or national surveys or questionnaires, with the limitation of accurate recall. The present study, comorbidity and HCRU were captured based on recorded patient encounters and dispensed medications. Several comorbidities in the present study were similar in frequency to the chronic rhinosinusitis (40%), asthma (36%), and GERD (24%) reported in a cross-sectional study among all public service employees of two middle-sized towns in central Finland (n = 13,980) diagnosed with daily CC. In comparison, lower prevalences for GERD (16%), asthma (14%), and Upper airway cough syndrome (7%) were reported in the Copenhagen General Population CC epidemiology study and for asthma (24%) in a cross-sectional postal UK survey of CC patients with a mean age of 65 years. Results are not directly comparable due to different study populations, designs, and methods.

In the present CC cohort, ED visits and hospitalizations for all causes and respiratory causes were frequent, appeared consistent during the baseline and follow-up years, and were significantly less in specialist-diagnosed CC patients than in event-diagnosed CC patients. The lower frequency of acute care in specialist-diagnosed CC patients may in part be due to a higher frequency of the following occurrences noted among specialist-diagnosed patients during both the baseline and follow-up years: 1) visits to specialists, including asthma specialists, whose care has been shown to reduce acute care visits, 2) dispensing of relevant medications for the treatment of respiratory conditions (asthma and rhinitis controllers) and GERD (proton pump inhibitors) by these specialists, and 3) laboratory investigations (chest imaging, pulmonary function testing, laryngoscopy, and allergy testing) for the cause of CC. Another possible reason for differences in HCRU between event-diagnosed and specialist-diagnosed CC patients in the baseline year but not in the outcome year was that patients presenting to acute care settings were included in the criteria to identify the event-diagnosed group during the baseline year.

The burden of CC is also evident in its persistence in the follow-up year. CC persisted in 17.9% of the CC cohort,
Table 5. Follow-up year healthcare resource utilization and dispensed medications of the entire chronic cough cohort and subgroups

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Entire CC cohort (N = 50,163)</th>
<th>Specialist-diagnosed CC (n = 11,290)</th>
<th>Event-diagnosed CC (n = 38,873)</th>
<th>p value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persistence of CC</td>
<td>8970 (17.9)</td>
<td>4586 (40.6)</td>
<td>4384 (11.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>All-cause patient visits</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Outpatient visits</td>
<td>49,453 (98.6)</td>
<td>11,159 (98.8)</td>
<td>38,294 (98.5)</td>
<td>0.009</td>
</tr>
<tr>
<td>≥ 1 emergency department (ED)</td>
<td>16,933 (33.8)</td>
<td>3183 (28.2)</td>
<td>13,750 (35.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>≥ 1 Hospitalization</td>
<td>7261 (14.5)</td>
<td>1344 (11.9)</td>
<td>5917 (15.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Respiratory cause patient visits†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Outpatient visits</td>
<td>32,602 (65)</td>
<td>8014 (71.0)</td>
<td>24,588 (63.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>≥ 1 ED</td>
<td>8629 (17.2)</td>
<td>1583 (14.0)</td>
<td>7046 (18.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>≥ 1 Hospitalization</td>
<td>4575 (9.1)</td>
<td>862 (7.6)</td>
<td>3713 (9.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Specialist visits</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmonologist</td>
<td>12,477 (24.9)</td>
<td>5558 (49.2)</td>
<td>6919 (17.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Otolaryngology</td>
<td>8540 (17.0)</td>
<td>2728 (24.2)</td>
<td>5812 (15.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Gastroenterology</td>
<td>7899 (15.7)</td>
<td>2303 (20.4)</td>
<td>5596 (14.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Allergist</td>
<td>6106 (12.2)</td>
<td>2368 (21.0)</td>
<td>3738 (9.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Urology</td>
<td>4070 (8.1)</td>
<td>976 (8.6)</td>
<td>3094 (8.0)</td>
<td>0.019</td>
</tr>
<tr>
<td>Speech Therapy</td>
<td>685 (1.4)</td>
<td>209 (1.9)</td>
<td>476 (1.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>≥1 specialty department</td>
<td>26,769 (53.4)</td>
<td>8580 (76.0)</td>
<td>18,189 (46.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>≥2 different specialty departments</td>
<td>9745 (19.4)</td>
<td>3932 (34.8)</td>
<td>5813 (15.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>≥3 different specialty departments</td>
<td>2665 (5.3)</td>
<td>1315 (11.6)</td>
<td>1350 (3.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>≥ 4 different specialty departments</td>
<td>523 (1.0)</td>
<td>282 (2.5)</td>
<td>241 (0.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Laboratory tests (&gt; 1%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete blood count</td>
<td>35,277 (70.3)</td>
<td>7822 (69.3)</td>
<td>27,455 (70.6)</td>
<td>0.006</td>
</tr>
<tr>
<td>Chest x-ray</td>
<td>21,018 (41.9)</td>
<td>4553 (40.3)</td>
<td>16,465 (42.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pulmonary function tests</td>
<td>10,795 (21.5)</td>
<td>4796 (42.5)</td>
<td>5999 (15.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Advanced chest imaging</td>
<td>7816 (15.6)</td>
<td>2693 (23.9)</td>
<td>5123 (13.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Allergy RAST testing</td>
<td>3902 (7.8)</td>
<td>1601 (14.2)</td>
<td>2301 (5.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Laryngoscopy</td>
<td>3113 (6.2)</td>
<td>1272 (11.3)</td>
<td>1841 (4.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sinus imaging</td>
<td>3162 (6.3)</td>
<td>1293 (11.5)</td>
<td>1869 (4.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Esophageal endoscopy</td>
<td>3339 (6.7)</td>
<td>1013 (9.0)</td>
<td>2326 (6.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Barium swallow or upper GI</td>
<td>1350 (2.7)</td>
<td>499 (4.4)</td>
<td>851 (2.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Nasal/sinus endoscopy</td>
<td>1186 (2.4)</td>
<td>381 (3.4)</td>
<td>805 (2.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Bronchoscopy</td>
<td>990 (2.0)</td>
<td>465 (4.1)</td>
<td>525 (1.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Respiratory medication (oral or inhaled)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SABA singly</td>
<td>16,507 (32.9)</td>
<td>3605 (31.9)</td>
<td>12,902 (33.2)</td>
<td>0.012</td>
</tr>
<tr>
<td>Nasal corticosteroids</td>
<td>16,202 (32.3)</td>
<td>4327 (38.3)</td>
<td>11,875 (30.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ICS/LABA</td>
<td>10,058 (20.1)</td>
<td>2802 (24.8)</td>
<td>7256 (18.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ICS monotherapy</td>
<td>6494 (12.9)</td>
<td>1719 (15.2)</td>
<td>4775 (12.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Leukotriene modifiers</td>
<td>6430 (12.8)</td>
<td>2046 (18.1)</td>
<td>4384 (11.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Nasal antihistamines</td>
<td>3104 (6.2)</td>
<td>1277 (11.3)</td>
<td>1827 (4.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SABA and SAMA combination</td>
<td>3081 (6.1)</td>
<td>535 (4.7)</td>
<td>2546 (6.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LABA/LAMA</td>
<td>2609 (5.2)</td>
<td>487 (4.3)</td>
<td>2122 (5.5)</td>
<td>&lt;0.001</td>
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<tr>
<td>H1 antihistamines</td>
<td>2352 (4.7)</td>
<td>388 (3.4)</td>
<td>1964 (5.1)</td>
<td>&lt;0.001</td>
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<tr>
<td>Nasal SAMA</td>
<td>1937 (3.9)</td>
<td>888 (7.9)</td>
<td>1049 (2.7)</td>
<td>&lt;0.001</td>
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<tr>
<td>LAMA monotherapy</td>
<td>587 (1.2)</td>
<td>157 (1.4)</td>
<td>430 (1.1)</td>
<td>0.013</td>
</tr>
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</table>

* (continued on following page)
which was higher in the specialist-diagnosed CC patients (40.6%) compared with the event-diagnosed CC subgroup (11.3%). The frequency of CC cough persistence in the specialist-diagnosed CC cohort is similar to what is seen in specialist cough clinics. A small, prospective, observational study noted that CC persisted in 46% of 68 CC patients at a 5-year follow-up. More long-term follow-up studies of CC patients are needed to better understand its natural history, particularly studying its clinical burden and economic cost. Cross-sectional surveys of CC patients have documented a decrease in quality of life experienced by these patients. Specifically, CC worsens the quality of life of patients with asthma or COPD compared with those without CC.

There is an absence of approved FDA or European Medicines Agency treatments specific for refractory or idiopathic CC. Presently treatments for CC rely on nonspecific cough suppressants, including narcotic and nonnarcotic antitussives, and neuromodulators such as the anticonvulsant gabapentin and amitriptyline, owing to some efficacy in reducing neuronal hypersensitivity.

Table 5. Follow-up year healthcare resource utilization and dispensed medications of the entire chronic cough cohort and subgroups (continued)

| Characteristic | Entire CC cohort (N = 50,163) | Specialist-diagnosed CC (n = 11,290) | Event-diagnosed CC (n = 38,873) | p value*
<table>
<thead>
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</tr>
</thead>
<tbody>
<tr>
<td>Narcotics, antitussive, psychotherapeutics (oral)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Narcotics, including codeine</td>
<td>28,199 (56.2)</td>
<td>5726 (50.7)</td>
<td>22,473 (57.8)</td>
<td>&lt;0.001</td>
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<tr>
<td>Antitussives, including codeine</td>
<td>21,762 (43.4)</td>
<td>4420 (39.1)</td>
<td>17,342 (44.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Narcotics, no codeine</td>
<td>18,764 (37.4)</td>
<td>3818 (33.8)</td>
<td>14,946 (38.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Codeine</td>
<td>17,145 (34.2)</td>
<td>3309 (29.3)</td>
<td>13,836 (35.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>13,786 (27.5)</td>
<td>3015 (26.7)</td>
<td>10,771 (27.7)</td>
<td>0.036</td>
</tr>
<tr>
<td>Antitussives, no codeine</td>
<td>9464 (18.9)</td>
<td>2206 (19.5)</td>
<td>7258 (18.7)</td>
<td>0.038</td>
</tr>
<tr>
<td>Anxietyotics</td>
<td>8846 (17.6)</td>
<td>1715 (15.2)</td>
<td>7131 (18.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Neumodulators</td>
<td>7665 (15.3)</td>
<td>1660 (14.7)</td>
<td>6005 (15.4)</td>
<td>0.053</td>
</tr>
</tbody>
</table>

Abbreviations: SABA = short-acting β2-agonist, SAMA = short-acting muscarinic antagonist, LABA = long-acting β2-agonist, LAMA = long-acting muscarinic antagonist, ICS = inhaled corticosteroid, GI = gastrointestinal.

* Comparisons were made between specialist-diagnosed and event-diagnosed subgroups; p values determined by γ2 test or Fisher’s exact test for categorical variables and Kruskal-Wallis test for continuous variables.

The cough hypersensitivity syndrome was proposed by the European Respiratory Society Task Force as a major trigger for CC, which was characterized by “troublesome coughing often triggered by low levels of thermal, mechanical, or chemical exposure.” Coughing is manifested by the cough hypersensitivity syndrome by typically innocuous factors such as laughing, talking, deep breathing, exercise, temperature changes, and aerosol exposure. Chronic activation of sensory nerves in the upper and lower airways act to initiate the cough process, which, being hypersensitized, leads to the symptoms of the pathologic cough. Medications that target the specific upper and lower respiratory tract sensory nerve receptors to suppress the hypersensitivity in CC are being studied, one of which, an antagonist to the P2X purinoceptor 3 receptor, is in Phase III trials.
This study has some limitations. The absence of patient-reported outcomes and the study’s retrospective design are limiting factors that do not allow capturing of patient-reported outcomes. The consequences of varying coding expertise of physicians are not known. The present characteristics of the CC patients identified by administrative data in the large Southern California Permanente Medical Group managed care system may not be generalizable to populations identified by other methods and different medical care organizations. The full medication burden of the CC patients could not be determined because several upper respiratory, GERD, and antitussive medications are nonprescription and cannot be captured administratively. Moreover, patient use of and adherence to CC medications was not determined.

The study has several strengths, including the use of the comprehensive electronic KPSC research database, which permitted accurate capture of complete patient encounters, laboratory testing, and dispensed medications. In addition, the process of information extraction from clinical notes through NLP helped identify patients with CC, demonstrating the usefulness of the technique in a large managed care organization with comprehensive electronic medical records. The present study is one of few studies that have used clinical notes extracted by NLP to identify and characterize CC patients.

In summary, the present study demonstrates that CC patients can be identified with administrative data techniques including clinical notes, diagnosis codes, and antitussive medications. The study documented an overall 1% prevalence of CC, which was considerably higher in female patients and in elderly patients and varied by ethnicity. Comorbidities such as asthma, chronic sinusitis, allergic and chronic rhinitis, COPD, and GERD were frequently associated with CC. The burden of CC was supported by frequent laboratory testing, HCRU, dispensed medications including narcotic antitussives, and a 17.9% persistence into the follow-up year.

The present administrative data study accurately identified a CC cohort, overcoming the challenges posed by the absence of specific ICD9/10 codes for CC. The CC cohort had considerable laboratory testing, HCRU, and medications documenting the substantial burden of the condition. The methods used to identify CC patients in the present study should help foster more intensive study of CC to better understand its clinical and economic burden. This is particularly important given the promising new treatments for CC in Phase III study.19

Disclosure Statement
Dr Robert S. Zeiger reports a grant from Merck and Co. Inc. to Kaiser Permanente Southern California (KPSC) during the conduct of the study; additional grants to KPSC from NIH, Aerocine, ALK Pharma, Genentech, GlaxoSmithKline, MedImmune/AstraZeneca, and TEVA, personal fees from AAAAI as Deputy Editor of JACI: In Practice, ACAAI (manuscript), AstraZeneca, DBV Technologies, Genentech, Novartis, GlaxoSmithKline, Regeneron Pharmaceuticals, outside the submitted work. Michael Schatz, MD, reports grants to KPSC from Merck and Co. Inc, NIH, ALK Pharma, and TEVA and persons fees from the AAAAI as Editor-in-Chief of JACI: In Practice.

Acknowledgements
Jessica P. Weaver, MPH is employed by Merck Sharpe & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA; Vishal Bali, PhD, is employed by Merck Sharpe & Dohme Corp.; a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA; Jonathan Schellhout, PhD, is employed by Merck Sharpe & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA; Wansu Chen, MS, PhD, reports a research grant to KPSC from Merck and Co, Inc. Merck Sharpe & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA; USA funded a research grant to the Southern California Permanente Medical Group (SCPMG) Research and Evaluation Department to perform the study. SCPMG investigators developed the protocol, performed the analyses, and wrote the manuscript. The sponsor participated in the study discussions and provided comments to the protocol, data analysis, and manuscript.

Authors’ Contributions
Robert S Zeiger made major contributions to the conception, design, statistical analysis, execution of the study, and interpretation of the findings; drafted the manuscript and revised it critically for important intellectual content; gave final approval of the version to be published; Fagen Xie, Benjamin D Hong, Wansu Chen made substantial contributions to the design of the study as well as interpretation of the findings; data capture and analysis; revised the manuscript critically for important intellectual content; and gave final approval of the version to be published. Michael Schatz, Jessica P Weaver, Vishal Bali, Jonathan Schellhout made substantial contributions to the design of the study as well as interpretation of the findings; revised the manuscript critically for important intellectual content; and gave final approval of the version to be published.

How to Cite this Article

References