

Management of Gout in the United States: A Claims-based Analysis

N. Lawrence Edwards,¹ Naomi Schlesinger,² Sanders Clark,³ Theresa Arndt,³ and Peter E. Lipsky⁴

Objective. Gout is the most common inflammatory arthritis in the United States. Although numerous guidelines exist for the management of gout, they are not routinely implemented. This study evaluated the real-world practice patterns in gout patients using large administrative claims databases.

Methods. An analysis of patients diagnosed with gout from October 2015 to November 2018 was carried out using the Symphony Integrated Dataverse and Truven Marketscan administrative claims databases. Patients were identified as having gout if they were more than 18 years of age and had 2 or more primary gout diagnoses on different days, separated by 3 or more months. Patients were further identified as having either acute gout or advanced forms of gout including chronic nontophaceous, tophaceous, and uncontrolled gout. Percent and frequency of serum urate testing, rheumatology specialist visits, prescriptions for urate lowering therapies (ULTs), and emergency room (ER) visits for gout flares were evaluated.

Results. We identified 1 162 747 gout patients. Gout patients were seen most frequently by internists and family medicine practitioners. Neither urate testing nor prescriptions for ULTs were uniform. Patients with acute gout were infrequently seen by rheumatologists, whereas rheumatologist care progressively increased in patients with advanced gout. The frequency of serum urate testing and prescriptions for ULTs significantly increased, whereas the frequency of ER visits decreased in gout patients seen by a rheumatologist.

Conclusion. Measurement of serum urate and prescriptions for ULTs are not consistent in gout patients. Rheumatologist care increases the frequency of urate measurement and ULT prescriptions and may also improve outcomes for gout patients.

INTRODUCTION

Gout is a common inflammatory arthropathy characterized by hyperuricemia and recurrent arthritis flares caused by monosodium urate (MSU) crystal deposition. Despite available urate lowering therapies (ULTs), many patients progress to advanced gout, which is characterized by the development of tophi, chronic arthritis, and other manifestations resulting from persistent urate deposition (1). Although numerous evidence-based guidelines exist for the management of gout, most information indicates that these guidelines are not routinely implemented. However, there is little information on the frequency of their implementation in real-world experience, especially in patients with advanced gout.

Evidence-based guidelines published by rheumatology societies recommend monitoring of serum urate and treatment with ULTs to lower levels of serum urate and reduce the burden of advanced gout. The American College of Rheumatology (ACR), European League Against Rheumatism (EULAR), and 3e (Evidence, Expertise, Exchange) Initiative all recommend routine serum urate measurements with a ULT treat-to-target approach aimed at lowering serum urate levels to below the saturation threshold at which MSU crystals form in the joints (2–5). The American College of Physicians (ACP), which primarily represents the primary care point of view, recently published guidelines that differ substantially from those of numerous international rheumatology societies. The ACP guidelines promote a “treat-to-avoid-symptoms” manage-

This work was supported by an unrestricted grant from Horizon Therapeutics.

¹N. Lawrence Edwards, MD: University of Florida, Gainesville, Florida; ²Naomi Schlesinger, MD: Rutgers Robert Wood Johnson Medical School, New Brunswick, New Jersey; ³Sanders Clark, BS, Theresa Arndt, BS: HVH Precision Analytics, LLC; Wayne, Pennsylvania; ⁴Peter E. Lipsky, MD: RILITE Research Institute, Charlottesville, Virginia.

Dr. Edwards is a consultant for Horizon Therapeutics, Takeda, Shanton Pharma, and Selecta Biosciences. Dr. Schlesinger serves on advisory boards or is a consultant to Novartis, Horizon Therapeutics, Selecta Biosciences,

Olatec Therapeutics, IFM Therapeutics, and Mallinckrodt Pharmaceuticals; Dr. Schlesinger also holds research grants from Pfizer and Amgen. Mr. Clark and Mrs. Arndt are paid employees of HVH Precision Analytics, LLC. Dr. Lipsky is a consultant for Horizon Therapeutics. No other disclosures relevant to this article were reported.

Address correspondence to Peter E. Lipsky, MD, RILITE Research Institute, 250 W Main Street, Suite 300, Charlottesville, VA 22902. E-mail: peterlipsky@comcast.net.

Submitted for publication January 23, 2020; accepted in revised form January 27, 2020.

SIGNIFICANCE & INNOVATIONS

- Many patients with gout are not being cared for according to American College of Rheumatology (ACR), European League Against Rheumatism (EULAR), and 3e (Evidence, Expertise, Exchange) Initiative guidelines established by the rheumatology community.
- Even in patients diagnosed with advanced forms of gout, serum urate testing, rheumatology consults, and urate-lowering therapy prescriptions are lower than expected.
- Patients seen by a rheumatologist at least once had a significantly increased adherence to ACR/EULAR/e3 clinical guidelines, including serum urate testing and urate-lowering therapy recommendations.
- Moreover, patients seen by a rheumatologist at least once had a significantly decreased frequency of emergency room visits for gout flares.

ment model but offer no clear recommendations for serum urate monitoring, ULT implementation, or how to avoid symptoms in advanced gout patients (6,7).

Given this discordance between rheumatologist and primary care physician guidelines, it is expected that there is a wide range of management approaches in the community. Several studies have suggested that gout patients in the United States are poorly managed and that suboptimal treatment of gout is common in clinical practice, with few patients undergoing regular serum urate testing (8) and low ULT utilization (9–12). A survey-based study in the United States estimated ULT usage at only 33%, with more than two-thirds of gout patients having serum urate levels above target levels and less than half of those treated with ULT reaching target serum urate levels (11). Although these data are informative, the surveys relied on patient self-reporting of gout diagnosis and treatment. A more objective assessment of patient management is needed to better approximate real-world clinical management of gout.

Analysis of large administrative claims data sets has emerged as a useful objective measure of real-world clinical practices in several rheumatologic diseases (13,14). Several studies have used administrative claims data to study gout management in Europe and Canada (15), but none have looked at practice patterns in the United States. In addition, most large-scale studies of gout patients have grouped patients under a single disease entity and have not taken into account the potential significant differences in managing patients with acute gout compared with more advanced stages of the disease.

The objective of this study was to use administrative claims data to identify subjects diagnosed with acute and advanced gout in the United States and to evaluate the frequency of serum urate testing and ULT treatment in these different populations. Furthermore, we sought to determine whether involvement of a rheumatologist compared with other providers affected gout

management trends. Finally, we evaluated the effect of serum urate testing, ULT, and rheumatologist management on emergency room (ER) visits related to gout.

PATIENTS AND METHODS

Data. This study used data from the Symphony Integrated Dataverse and Truven MarketScan databases, which are administrative claims databases of patients across the United States. The Truven database was used for analysis of ER visits. All other analyses were performed with data from Symphony. Both databases include medical, pharmaceutical, and procedure claims. Use of medical services was recorded in the databases with date of service, provider type, national provider identifier submitting claim, associated diagnoses, and performed procedures. Both databases are compliant with the Health Insurance Portability and Accountability Act. Because the data are commercially available and deidentified, institutional review board approval was not required. Analyses were conducted between April and June 2019.

Study design. Administrative claims data, including diagnosis, laboratory testing, and drug prescriptions, were evaluated over a 3-year identification period from October 1, 2015, to November 30, 2018. Patients more than 18 years old were included if they had at least two medical claims for a gout diagnosis on different days, separated by at least 3 months; requiring two separate gout diagnoses helped to minimize misdiagnoses. The index date was defined as the date of first gout diagnosis. Patients with gout were further stratified into one of four gout categories: 1) acute, 2) nontophaceous chronic, 3) tophaceous chronic, or 4) uncontrolled gout. Each patient was included only in one of the four categories. Patients categorized as acute gout had no claims for chronic gout. Patients categorized as nontophaceous chronic gout had no claims for tophaceous gout. “Uncontrolled gout” was defined as any patient with three gout codes (acute or chronic) as the primary diagnosis and three serum urate tests within the same calendar year. “Uncontrolled gout” was an operational term designed to identify gout patients who had frequent encounters with the health care system for urate testing to determine whether other aspects of gout care were different. Patients categorized as nontophaceous chronic, tophaceous chronic, or uncontrolled were considered to have advanced gout. Because patients were seen by multiple providers, gout coding may have differed at different encounters. Despite that, patient classification was based on the criteria listed above. Inclusion and exclusion criteria are summarized in Supplementary Table 1. Diagnoses were based on International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10) codes. This coding classification differs from the recommended nomenclature scheme proposed by a recent international consensus statement regarding labels and definitions for disease elements of gout (16). The ICD-10 codes were used in this study because of their applicability to the administrative claims

databases employed. Laboratory tests were based on Current Procedural Terminology (CPT) codes.

Patient characteristics and comorbidities. Demographic and comorbidity variables were collected for each patient at index date as well as for the entire database sample population. Age was assessed continuously and by groups including 18 to 34, 35 to 44, 45 to 54, 55 to 65, and more than 65 years. The number of years of database history for each patient was also collected. Comorbid conditions at or before index date included hypertension (ICD-10: I10), chronic kidney disease (ICD-10: N18.*, I12.*), congestive heart failure (ICD-10: I52.*, I53.*, I54.*), and hyperlipidemia (ICD-10: E78.2, E78.5). Patients were also assessed for primary versus secondary causes for gout diagnosis by identifying the number of patients in each category with at least one diagnosis code for idiopathic, secondary, or unspecified gout etiology.

Frequency of serum urate testing. The number of serum urate tests (CPT: 84550, 84560) per patient was calculated over each patient's full history in the database. To account for variable time in the database, the number of serum urate tests was normalized by the number of months in the database for each patient (resulting in tests/month). The normalized tests per month were scaled up to per year, and the mean serum urate tests per year per patient was calculated for each of the four gout categories.

Frequency of rheumatology visits. The number of rheumatology specialist visits per patient was calculated over each patient's full history in the database. A rheumatology visit was defined as any claim from a rheumatology specialist. Multiple rheumatology claims on a single day counted as only a single visit. To account for variable time in the database, the number of visits was normalized by the number of months in the database for each patient (resulting in visits/month). The normalized visits per month were scaled up to per year, and the mean rheumatology visits per year per patient was calculated for each of the four gout categories.

Frequency of ULT prescriptions. Claims for filled ULT prescriptions were recorded as National Drug Code (NDC) claims in the database. The total count of ULT prescriptions was calculated per patient as the number of NDC claims for allopurinol, febuxostat, probenecid, or lesinurad. The mean number of prescriptions was calculated for each of the four gout categories. The mean number of days with active ULT prescription was also assessed. This was measured by the total number of days of active ULT prescriptions per patient as the sum of days supplied from all NDC claims for allopurinol, febuxostat, probenecid, or lesinurad. The total days was normalized by length of time in the database per patients (resulting in days with active prescription/month). The normalized active days with ULT prescription per month was scaled up to years, and the mean was calculated for each of the four gout categories.

Clinical management with or without rheumatology visit. Patients were stratified based on whether they had at least one rheumatology specialist claim in their database history or no rheumatology claims. The percentage of patients with serum urate tests and ULT prescriptions was calculated and compared between groups. The frequency of serum urate tests (mean tests/year) and the number of ULT prescriptions (mean prescriptions/year) were also calculated as described above and compared between groups. The number of ER visits was also compared between the two groups.

ER presentations with or without rheumatology visit. Patients were stratified based on whether they had at least one rheumatology specialist claim in their database history or no rheumatology claims. The percentage of patients with at least one documented ER presentation with gout being the primary diagnosis was calculated and compared between groups. The mean number of ER visits per patient over the 3-year study period was also calculated and compared between groups.

Statistical analysis. Formal comparisons were performed between 1) patients with acute gout and each advanced gout category as well as 2) between patients in each category with and without at least one rheumatology visit. All statistical analyses for measurements of the percentage of patients were carried out with a two-proportion z-test. For statistical analysis of annual frequency measurements, a one-sided Welch *t*-test was used. Values of $P < 0.05$ were considered statistically significant.

RESULTS

Gout categories and etiologies. We identified 987 127 acute gout patients and 175 620 advanced gout patients. Of the 175 620 advanced gout patients, 122 162 were categorized as nontophaceous chronic, 27 769 as tophaceous chronic, and 25 689 as uncontrolled gout. The most common etiology for acute gout patients was unspecified, whereas idiopathic and secondary causes of gout were less common. For all categories of advanced gout, codes for both idiopathic and unspecified gout were found in the majority of patient claims histories. The large majority (more than 75%) of patients in all categories had at least 1 year of claims data before and following the date of their first gout diagnosis. These results are summarized in Table 1.

Patient characteristics. Table 2 summarizes the demographic and clinical characteristics for the patient populations. The mean age was more than 60 years with a strong male predominance for all gout categories. Supplementary Figure 1 depicts the distribution of patient ages within each gout category relative to the US census population estimates. The average years of claims history in the database was more than 5 years for all categories, and more than 93% of patients in each category had prescription

Table 1. Patient sample sizes, gout etiologies, and years of claims history in Symphony Integrated Dataverse database

Gout Category	Patient Counts	>1 Idiopathic Gout Code ^a	>1 Secondary Gout Code ^b	>1 Unspecified Gout Code ^c	>1 Year of Pre- and Postgout Claims History
Acute gout	987 127	196 364 (19.9%)	20 679 (2.1%)	834 968 (84.6%)	751 722 (76.1%)
Nontophaceous chronic gout	122 162	75 295 (61.6%)	11 265 (9.2%)	71 197 (58.3%)	96 137 (78.7%)
Tophaceous chronic gout	27 769	17 762 (64.0%)	4075 (14.7%)	20 171 (72.6%)	21 522 (77.5%)
Uncontrolled gout	25 689	14 885 (57.9%)	2716 (10.6%)	22 248 (86.6%)	18 829 (82.8%)

Abbreviation: ICD-10, International Classification of Diseases, Tenth Edition.

^aIdiopathic gout diagnosis codes include ICD-10: M10.0* and M1A.0*.

^bSecondary gout diagnosis codes include ICD-10: M10.1*, M10.2*, M10.3*, M10.4*, M1A.1*, M1A.2*, M1A.3*, and M1A.4*.

^cUnspecified gout diagnosis codes include M10.9* and M1A.9*.

drug claims data available. There was little difference in comorbidities between gout categories, with hypertension and hyperlipidemia being the most common. The most common physician specialties coding for the gout diagnosis were internal medicine, family medicine, emergency medicine, nephrology, and rheumatology (Figure 1). Acute gout was most commonly diagnosed by internal medicine or family medicine physicians. Rheumatologists were far more likely to code for tophaceous chronic or uncontrolled gout than other gout categories.

Patient management. The percentage of patients in each category with claims for serum urate testing, rheumatology specialist visits, and prescriptions for ULTs, as well as the annual frequency of these claims are shown in Table 3. As expected, these claims were least common and infrequent in patients with acute gout. However, even in patients diagnosed with chronic or uncontrolled gout, the frequencies of serum urate testing, rheumatology consults, and ULT prescriptions were inconsistent. Serum urate testing was definitional for uncontrolled gout patients but was performed in less than 70% of patients with the diagnosis of chronic gout. For acute gout, serum urate testing was performed in less than 60% of patients. Serum urate testing was performed approximately once a year for patients with tophaceous chronic gout and less than once per year for those with acute or nontophaceous chronic gout. Patients with acute gout were infrequently seen by rheumatologists. The likelihood of encountering a rheumatologist progressively increased in subjects with advanced gout. However, nontophaceous chronic gout patients were less likely to be seen by a rheumatologist

than patients with tophaceous or uncontrolled gout. Overall, less than 60% of patients with advanced gout received care by a rheumatologist, whereas less than 30% of patients with nontophaceous chronic gout were seen by a rheumatologist. For patients with acute gout, less than 15% had a documented rheumatologist visit. With regard to ULTs, less than 80% of advanced gout patients received ULT and for less than 50% of the year. The percentage of patients on ULT and the frequency of ULT prescriptions were somewhat lower for the acute gout population.

Comparison of patient management with and without a rheumatologist visit. Significant differences in gout management were observed between patients who had visited a rheumatology specialist compared with those who had not. Again, serum urate testing was definitional for uncontrolled gout, but for acute and chronic gout, a significantly greater percentage of patients received serum urate testing if they had seen a rheumatologist at least once during the study period. For all categories of acute and advanced gout, the percentage of patients and annual frequency of ULT prescriptions were also significantly higher for patients who had received care by a rheumatologist compared with those who had never visited a rheumatologist. These results are summarized in Table 4.

Comparison of ER visits in gout patients with and without a rheumatologist visit. To determine the effect of rheumatology specialist care on health outcomes, we evaluated the frequency of ER visits for patients with gout, with or

Table 2. Patient characteristics for each gout category in Symphony Integrated Dataverse population

Characteristic	Acute Gout (n = 987 127)	Nontophaceous Chronic Gout (n = 122 162)	Tophaceous Chronic Gout (n = 27 769)	Uncontrolled Gout (n = 25 689)
Mean age (range)	63.5 (18-80)	63.6 (18-80)	63.5 (18-80)	60.3 (18-80)
Male (%)	73.9%	74.8%	77.5%	75.5%
Female (%)	26.1%	25.2%	22.5%	24.5%
Mean years in Database (range)	5.6 (0.25-6.2)	5.7 (0.33-6.2)	5.6 (0.33-6.2)	5.6 (0.2-6.2)
Prescription data available (%)	93.8%	94.9%	94.3%	95.0%
Comorbidities				
Hypertension (%)	81.8%	81.7%	78.4%	77.8%
Hyperlipidemia (%)	65.2%	64.9%	57.3%	61.7%
Chronic kidney disease (%)	32.9%	34.1%	41.5%	40.3%
Congestive heart failure (%)	12.6%	12.4%	16.8%	16.4%

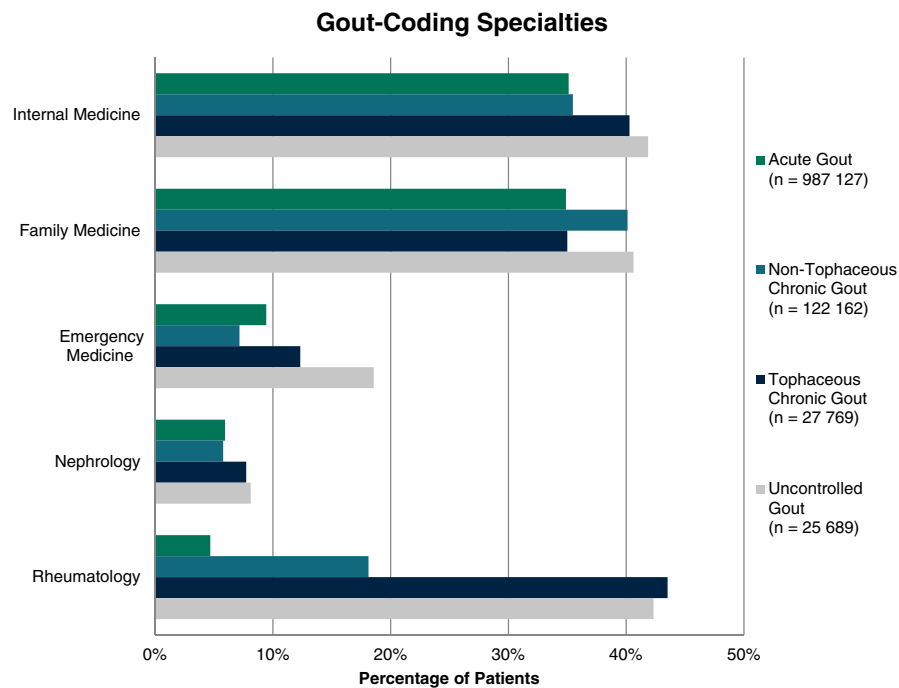


Figure 1. Distribution of percentage of gout categories diagnosed by each of the top five most common medical specialties to diagnoses gout in this study.

without a history of a rheumatologist visit. To accomplish this, we applied the same patient inclusion criteria to the Truven database, which also includes data on adjudicated claims for ER visits. We identified 284 877 total gout patients in Truven. The median age was 59.2 years, and 79.0% were male. Of the 230 698 subjects coded as acute gout, 10.7% were seen by a rheumatologist, whereas 26.9% of the 32 942 patients coded as nontophaceous chronic, 47.2% of the 7723 coded as tophaceous chronic, and 43.5% of the 13 514 coded as

uncontrolled gout were seen by a rheumatologist. In each gout category, the frequency of ER visits was significantly ($P < 0.001$) reduced in patients who had been seen by a rheumatologist (Table 5). The mean number of ER visits per patient was also significantly reduced in all categories of gout patients who had been seen by a rheumatologist. If the frequencies of rheumatologist-associated gout patient ER visits were applied to all gout patients, there would have been 3088 fewer ER visits in this cohort of 284 877 gout patients.

Table 3. Percentages and annual frequencies of uric acid testing, rheumatology visits, and serum urate-lowering therapies

Percentage of Patients with Gout Management Parameters ^a				
Population	N	Serum Urate Testing (% of patients) ^b	Rheumatology Visits (% of patients) ^b	ULTs (% of patients) ^b
Acute gout	987 127	55.22%	14.35%	64.07%
Nontophaceous chronic gout	122 162	62.8% ($P < 0.001$)	27.7% ($P < 0.001$)	76.8% ($P < 0.001$)
Tophaceous chronic gout	27 769	67.7% ($P < 0.001$)	56.1% ($P < 0.001$)	77.8% ($P < 0.001$)
Uncontrolled gout	25 689	100% ($P < 0.001$) ^c	52.4% ($P < 0.001$)	78.6% ($P < 0.001$)
Annual Frequency of Gout Management Parameters ^a				
Population	Mean Urate Tests per Year	Mean Rheumatology Visits per Year	Mean ULT Prescriptions per Patient	Mean Days with Active ULT Prescription per Year
Acute gout	0.57	0.50	4.40	115.96
Nontophaceous chronic gout	0.69 ($P < 0.001$)	1.53 ($P < 0.001$)	5.5 ($P < 0.001$)	159.9 ($P < 0.001$)
Tophaceous chronic gout	1.09 ($P < 0.001$)	3.59 ($P < 0.001$)	6.2 ($P < 0.001$)	159.8 ($P < 0.001$)
Uncontrolled gout	3.15 ($P < 0.001$)	3.54 ($P < 0.001$)	7.0 ($P < 0.001$)	162.5 ($P < 0.001$)

Abbreviation: ULT, urate-lowering therapy.

^aAnalysis performed on data from Symphony Integrated Dataverse population.

^b P values reported reflect comparisons to urate testing, rheumatology visits, and serum urate-lowering therapies in acute gout.

^cDefinitional.

Table 4. Comparison of patient management with or without history of rheumatology visit

Percentage of Patients with Gout Management Parameters ^a						
Population	Serum Urate Testing			ULT		
	With Rheumatology Visit(s)	No Rheumatology Visit(s)	P Value	With Rheumatology Visit(s)	No Rheumatology Visit(s)	P Value
Acute gout	62.5% (n = 141 664)	54.0% (n = 845 463)	<0.001	74.5% (n = 141 664)	62.3% (n = 845 463)	<0.001
Nontophaceous chronic gout	68.9% (n = 33 894)	60.4% (n = 88 268)	<0.001	82.6% (n = 33 894)	74.5% (n = 88 268)	<0.001
Tophaceous chronic gout	73.0% (n = 15 565)	60.9% (n = 12 204)	<0.001	83.4% (n = 15 565)	70.6% (n = 12 204)	<0.001
Uncontrolled gout	100% ^b (n = 13 468)	100% ^b (n = 12 221)	...	82.9% (n = 13 468)	73.8% (n = 12 221)	<0.001
Annual Frequency of Gout Management Parameters ^a						
Population	Mean Serum Urate Tests per Year			Mean ULT Prescriptions per Patient		
	With Rheumatology Visit(s)	No Rheumatology Visit(s)	P Value	With Rheumatology Visit(s)	No Rheumatology Visit(s)	P Value
Acute gout	0.68	0.55	<0.001	5.66	4.27	<0.001
Nontophaceous chronic gout	0.93	0.59	<0.001	6.70	5.10	<0.001
Tophaceous chronic gout	1.35	0.75	<0.001	7.20	4.97	<0.001
Uncontrolled gout	3.17 ^b	3.1 ^b	0.06	8.25	5.77	<0.001

Abbreviation: ULT, urate-lowering therapy.

^aAnalysis performed on data from Symphony Integrated Dataverse population.

^bDefinitional.

DISCUSSION

Over a 3-year study period, we identified nearly 1 million gout patients in the United States, with more than 175000 having an advanced form of the disease. A large majority of patients in the Symphony population had several years of longitudinal data in their treatment history. We found that many patients with gout were not being cared for according to the guidelines promulgated by the rheumatology community. Even in patients diagnosed with advanced forms of gout, serum urate testing, rheumatology consults, and ULT prescriptions were inconsistent. However, patients seen by a rheumatologist at least once had a significantly increased

adherence to ACR/EULAR/e3 clinical guidelines and a significantly decreased frequency of ER visits for gout flares. Strategies for appropriate and timely referral to a rheumatologist would seem to be important for improving the outcomes of patients with gout.

Our findings imply that many gout patients are not receiving the management recommended in the majority of published gout management guidelines to prevent irreversible consequences of advanced disease. Specifically, serum urate testing was carried out in only 60% to 70% of patients with chronic gout with a mean number of tests per year far below the ACR recommendation for measurements every 6 months once target serum urate levels are achieved (2). Patients categorized as having uncontrolled gout had

Table 5. Comparison of emergency room visits in patients with or without rheumatology visit

Emergency Room Visits ^a						
Population	Percentage of Patients with ER Visits			Mean ER Visits per Patient		
	With Rheumatology Visit(s)	No Rheumatology Visit(s)	P Value	With Rheumatology Visit(s)	No Rheumatology Visit(s)	P Value
Acute gout	5.6% (n = 24 638)	6.6% (n = 206 060)	<0.001	1.47 (n = 24 638)	1.53 (n = 206 060)	<0.001
Nontophaceous chronic gout	5.5% (n = 8863)	6.6% (n = 24 079)	<0.001	1.95 (n = 8863)	2.39 (n = 24 079)	<0.001
Tophaceous chronic gout	10.3% (n = 3648)	14.7% (n = 4075)	<0.001	2.78 (n = 3648)	2.89 (n = 4075)	<0.001
Uncontrolled gout	12.3% (n = 5886)	19.0% (n = 7628)	<0.001	2.06 (n = 5886)	2.56 (n = 7628)	<0.001

Abbreviation: ER, emergency room.

^aAnalysis performed on data from Truven MarketScan population.

higher mean serum urate tests per year by definition. However, less than 80% of all advanced gout patients, including the uncontrolled category, received prescriptions for ULT, with prescriptions covering only 50% of the year. Importantly, there was a significant increase in the frequency of both serum urate testing and ULT prescriptions in all categories of acute and advanced gout when a patient had a history of at least one rheumatology specialist visit.

There is disagreement between rheumatology and primary care physician societies with regard to gout management (6). Recently, the ACP presented a clinical practice guideline for the management of gout that differs substantially from all others developed by American and international rheumatologists (7). Specifically, the ACP guidelines do not offer clear recommendations for ULT, serum urate target levels, or routine serum urate monitoring. Our results appear to support the conclusion that primary care providers' approach to gout is more in line with the ACP guidelines than those of rheumatologists, whereas rheumatologists' practice is more in line with the sub-specialty guidelines. Although cause and effect cannot be established, the data suggest that involvement of a rheumatologist results in a reduction in ER visits, implying that more frequent monitoring and better ULT management may have a positive impact on gout patients' ER utilization, a surrogate for better health outcome.

Strengths of our study include the large number of patients and use of administrative claims. Therefore, every instance of gout diagnosis was based on a claim confirmed by a medical provider, and ULT usage was based on filled prescriptions. Moreover, rather than treating gout as a single disease entity, we have been able to evaluate the different treatment practices in acute versus more advanced forms of gout. Using this approach, we identified significant differences in management patterns and inclusion of a rheumatologist in the management team. It is notable that the frequencies of comorbidities were not different based on the coding for acute versus chronic gout. This could relate to the difficulty of determining whether to code an acute flare as acute gout even if it occurred in a subject with longstanding gout. Consistent with this is the finding that the mean length of follow-up in the database did not differ in those coded with acute versus advanced gout. Importantly, these findings are consistent with reports that many comorbidities associate with hyperuricemia and not gout per se (17–19).

Although several large administrative claims or medical records studies of gout management have been reported in Canada, Europe, and Taiwan (15,20–22), data on United States populations are more limited. Prior large-scale studies of gout patients in the United States have relied mostly on patient self-reported gout diagnosis and ULT prescriptions, which may inflate prevalence while also underestimating ULT administration (9). However, administrative claims data in other countries have reported similar trends to those found in this study. For example, one study in Germany and the United Kingdom demonstrated that just over half of patients had received ULT treatment and only 9% to 14% of patients with gout received at least one serum urate test in the

several years following diagnosis (15). ULT prescription rates were even lower in Canadian (20) and Taiwanese populations (21).

Patients in our study had demographic characteristics and comorbidities similar to those previously reported (23,24). However, we found somewhat higher rates of serum urate testing and ULT therapy compared with previous survey-based studies of gout patient medical management (9). Compared with survey-based data of providers, we also found much higher levels of ULT treatment and larger differences between rheumatology specialists compared with nonspecialists. For example, a quantitative US survey that assessed primary care provider and rheumatologist adherence to the ACR guidelines found that 53.7% of primary care providers and 35.3% of rheumatologists were poorly adherent, whereas only 36.4% and 35.2%, respectively, prescribed the recommended initial ULT dose (25).

Limitations of our study include the fact that our results were based on administrative claims and do not incorporate the full patient clinical history as well as the fact that specific gout diagnoses could not be verified with chart review. Therefore, confidence in patient gout diagnosis and categorization is less than if there were clinical confirmation based on accepted classification criteria or MSU crystal identification. Similarly, we were not able to assess the serum urate values measured to determine whether or not patients were hyperuricemic or at target levels. For ULT prescription data, because unfilled prescriptions were not counted, it is possible that we underestimated the true frequency at which providers are recommending ULT therapy for gout patients.

Recent studies have estimated that overall prevalence of gout among adults in the United States exceeds 9 million people (9). Our study identified more than 1 million patients with a gout diagnosis, indicating that the administrative claims databases may not be capturing all patients. Truven, and to a lesser extent Symphony, do not capture all Medicare and Medicaid enrollees (26). Furthermore, neither data set would capture uninsured patients or those primarily receiving care at the Veterans Health Administration. Despite the issues, there is a major discrepancy between the number of subjects we identified and the number anticipated from the most recent prevalence estimate of 3.9% of adults derived from National Health and Nutrition Examination Survey data (9). Part of this could relate to the inflation of prevalence owing to the reliance on self-reporting in the aforementioned study. On the other hand, gout may be underdiagnosed in our study. Moreover, subjects with only a small number of flares may not enter the health care system. The important issue is whether the gout patients identified in our study were representative. The demographics suggest that they are typical of other cohorts of gout patients (23,27). However, it is possible that the frequencies of serum urate measurement, ULT prescriptions, and rheumatologist involvement were inflated in our study because we identified the subset of gout patients involved in the organized health care system. Future studies will be necessary to explore this issue more fully.

Together, this study provides data on real-world management of acute and advanced gout and highlights the need for increased

gout clinical management awareness and education. We found that many patients are not being managed according to ACR/EULAR guidelines and that patients seen by rheumatology specialists are more likely to receive recommended care, which may impact patient outcomes, such as frequency of ER visits. Given that most patients with acute gout are not seen by a rheumatologist and less than half of those with advanced gout encounter a rheumatologist, follow-up studies to evaluate the effect of health outcomes related to these differences will be informative. More frequent referral to rheumatologists and closer adherence to guidelines may improve outcomes for gout patients.

ACKNOWLEDGMENTS

The authors would like to thank Dr. Jeremy Paige for providing medical direction for this project and assistance in preparing the manuscript.

AUTHOR CONTRIBUTIONS

All authors reviewed and revised the manuscript and approved of its submission.

Study conception and design. Edwards, Schlesinger, Lipsky.

Acquisition of data. Clark, Arndt.

Analysis and interpretation of data. Clark, Arndt, Lipsky.

REFERENCES

- Keenan RT. Limitations of the current standards of care for treating gout and crystal deposition in the primary care setting: a review. *Clin Ther* 2017;39:430–41.
- Khanna D, FitzGerald JD, Khanna PP, Bae S, Singh M, Neogi T, et al. 2012 American College of Rheumatology guidelines for management of gout. Part I: systematic nonpharmacologic and pharmacologic therapeutic approaches to hyperuricemia. *Arthritis Care Res (Hoboken)* 2012;64:1431–46.
- Khanna D, Khanna PP, FitzGerald JD, Singh MK, Bae S, Neogi T, et al. 2012 American College of Rheumatology guidelines for management of gout. Part II: therapy and anti-inflammatory prophylaxis of acute gouty arthritis. *Arthritis Care Res (Hoboken)* 2012;64:1447–61.
- Sivera F, Andrés M, Carmona L, Kydd AS, Moi J, Seth R, et al. Multinational evidence-based recommendations for the diagnosis and management of gout: integrating systematic literature review and expert opinion of a broad panel of rheumatologists in the 3e Initiative. *Ann Rheum Dis* 2014;73:328–35.
- Zhang W, Doherty M, Bardin T, Pascual E, Barskova V, Conaghan P, et al. EULAR evidence based recommendations for gout. Part II: Management. Report of a task force of the EULAR Standing Committee for International Clinical Studies Including Therapeutics (ESCI-SIT). *Ann Rheum Dis* 2006;65:1312–24.
- Dalbeth N, Bardin T, Doherty M, Lioté F, Richette P, Saag KG, et al. Discordant American College of Physicians and international rheumatology guidelines for gout management: consensus statement of the Gout, Hyperuricemia and Crystal-Associated Disease Network (G-CAN). *Nat Rev Rheumatol* 2017;13:561–8.
- Qaseem A, Harris RP, Forcica MA, Clinical Guidelines Committee of the American College of Physicians. Management of Acute and Recurrent Gout: a clinical practice guideline from the American College of Physicians. *Ann Intern Med* 2017;166:58–68.
- Doghramji PP, Fermer S, Wood R, Morlock R, Baumgartner S. Management of gout in the real world: current practice versus guideline recommendations. *Postgrad Med* 2016;128:106–14.
- Chen-Xu M, Yokose C, Rai SK, Pillinger MH, Choi HK. Contemporary prevalence of gout and hyperuricemia in the United States and decadal trends: the National Health and Nutrition Examination Survey, 2007–2016. *Arthritis Rheumatol* 2019;71:991–9.
- De Vera MA, Marcotte G, Rai S, Galo JS, Bhole V. Medication adherence in gout: a systematic review. *Arthritis Care Res (Hoboken)* 2014;66:1551–9.
- Juraschek SP, Kovell LC, Miller ER III, Gelber AC. Gout, urate-lowering therapy, and uric acid levels among adults in the United States. *Arthritis Care Res (Hoboken)* 2015;67:588–92.
- Yin R, Li L, Zhang G, Cui Y, Zhang L, Zhang Q, et al. Rate of adherence to urate-lowering therapy among patients with gout: a systematic review and meta-analysis. *BMJ Open* 2018;8:e017542.
- Desai SP, Yazdany J. Quality measurement and improvement in rheumatology: rheumatoid arthritis as a case study. *Arthritis Rheum* 2011;63:3649–60.
- Schmajuk G, Trivedi A, Solomon D, Yelin E, Trupin L, Chakravarty E, et al. Receipt of disease-modifying antirheumatic drugs among patients with rheumatoid arthritis in Medicare managed care plans. *JAMA* 2011;305:480–6.
- Annemans L, Spaepen E, Gaskin M, Bonnemaire M, Malier V, Gilbert T, et al. Gout in the UK and Germany: prevalence, comorbidities and management in general practice 2000–2005. *Ann Rheum Dis* 2008;67:960–6.
- Bursill D, Taylor WJ, Terkeltaub R, Kuwabara M, Merriman TR, Grainger R, et al. Gout, Hyperuricemia, and Crystal-Associated Disease Network Consensus Statement regarding labels and definitions for disease elements in gout. *Arthritis Care Res (Hoboken)* 2019;71:427–34.
- Lv Q, Meng XF, He FF, Chen S, Su H, Xiong J, et al. High serum uric acid and increased risk of type 2 diabetes: a systemic review and meta-analysis of prospective cohort studies. *PLoS One* 2013;8:e56864.
- Grayson PC, Kim SY, LaValley M, Choi HK. Hyperuricemia and incident hypertension: a systematic review and meta-analysis. *Arthritis Care Res (Hoboken)* 2011;63:102–10.
- Borghesi C, Rosei EA, Bardin T, Dawson J, Dominiczak A, Kielstein JT, et al. Serum uric acid and the risk of cardiovascular and renal disease. *J Hypertens* 2015;33:1729–41; discussion 1741.
- Rai SK, Aviña-Zubieta JA, McCormick N, De Vera MA, Shojania K, Sayre EC, et al. The rising prevalence and incidence of gout in British Columbia, Canada: population-based trends from 2000 to 2012. *Semin Arthritis Rheum* 2017;46:451–6.
- Kuo CF, Grainge MJ, See LC, Yu KH, Luo SF, Zhang W, et al. Epidemiology and management of gout in Taiwan: a nationwide population study. *Arthritis Res Ther* 2015;17:13.
- Kuo CF, Grainge MJ, Mallen C, Zhang W, Doherty M. Rising burden of gout in the UK but continuing suboptimal management: a nationwide population study. *Ann Rheum Dis* 2015;74:661–7.
- Kuo CF, Grainge MJ, Zhang W, Doherty M. Global epidemiology of gout: prevalence, incidence and risk factors. *Nat Rev Rheumatol* 2015;11:649–62.
- Stamp LK, Chapman PT. Gout and its comorbidities: implications for therapy. *Rheumatology (Oxford)* 2013;52:34–44.
- Oderda GM, Shiozawa A, Walsh M, Hess K, Brixner DI, Feehan M, et al. Physician adherence to ACR gout treatment guidelines: perception versus practice. *Postgrad Med* 2014;126:257–67.
- Kulaylat AS, Schaefer EW, Messaris E, Hollenbeak CS. Truven Health Analytics MarketScan Databases for Clinical Research in Colon and Rectal Surgery. *Clin Colon Rectal Surg* 2019;32:54–60.
- Zhu Y, Pandya BJ, Choi HK. Prevalence of gout and hyperuricemia in the US general population: the National Health and Nutrition Examination Survey 2007–2008. *Arthritis Rheum* 2011;63:3136–41.