Factors influencing the effectiveness of allopurinol in achieving and sustaining target serum urate in the national Veterans Administration gout cohort

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Abstract

Objective: To assess factors associated with the ability to achieve and maintain target serum urate (SU) with allopurinol in patients with gout.

Methods: We used National VA national databases from 2002-2012. Eligible patients had ≥1 inpatient or ≥2 outpatient visits with a diagnostic code for gout, filled a new index allopurinol prescription, had at least one post-treatment SU measured, and met 12-month observability rule. Treatment successes were defined as the achievement of post-index SU <6 mg/dl (success 1) and post-index SU <6 mg/dl that was sustained (success 2).

Results: Of the 198,839 unique patients with allopurinol use, 41,153 unique patients (with 47,072 episodes) and 17,402 unique patients (with 18,323 episodes) were eligible for analyses for success 1 and success 2; 42% each achieved (success 1) or achieved and maintained post-index SU <6 mg/dl (success 2). In multivariable-adjusted models, factors associated with significantly higher odds of both outcomes were: older age, normal BMI, Deyo-Charlson index score of 0, rheumatologist as the main provider rather than non-rheumatologist, Midwest U.S. location for the healthcare facility, a lower hospital bed size, military service-connection for medical conditions of 50% or more (a measure of healthcare access priority), longer distance to the nearest VA facility, and lower pre-index SU.

Conclusion: We identified novel factors associated with maintaining SU <6 mg/dl based on a theoretical model. Several potentially modifiable factors can be targeted by individual/provider/systems interventions for improving successful achievement and maintenance of target SU in patients with gout.

Keywords: Gout; allopurinol; effectiveness; target serum urate; predictors;

Running Title: Effectiveness of Allopurinol in Gout

Introduction

Failure to achieve and maintain target serum urate (SU) is a critical shortcoming of current gout management (1-3). Less than 50% patients treated with allopurinol, an effective and inexpensive urate-lowering therapy (ULT), achieve target SU <6 mg/dl (1, 4). Maintenance of target SU is associated with lower risk of gout flares and tophi and lower healthcare costs (4-10) and is recommended by every treatment guideline (11-16).

A single Veterans Affairs (VA) center study (n=643; 253 with SU; 39%) reported that a lower medical comorbidity load was associated with higher odds of reaching the target SU <6 mg/dl (1). In claims database studies, factors associated with higher likelihood of achieving target SU <6 mg/dl were older age, female gender, higher allopurinol dose and the lack of kidney disease (n=3,363; 2,059 had SU; 61%) (19), higher allopurinol adherence (n=18,243; 4,277 with SU; 23%) (20), and female sex, older age, White race, rheumatologist care, higher allopurinol start dose and adherence (n=9,581 incident users) (21). These studies had important limitations. All studies, except two (1, 21), used prevalent user design, which tends to bias estimates and overestimate adherence. None examined factors associated with maintaining target SU, the main goal recommended by gout guidelines (11, 24, 25). Most studies examined demographic and clinical characteristics (i.e., predisposing factors), but none evaluated gout severity (i.e., need factors), or important system-level or healthcare access factors, such as region, rural location, distance to the medical center etc. (i.e., enabling factors) (1, 19-21). Therefore, significant knowledge gaps remain. No conceptual model was invoked in any of these studies. Andersen's Behavioral Model of need, enabling and predisposing factors (22, 23), offers a potential solution to improve our understanding of associated factors.

We examined the data from the VA healthcare system (26, 27), the largest integrated healthcare system in the U.S. that provides care to 6 million participants annually (27). We hypothesized that in patients with gout taking allopurinol (1) needs, enabling and predisposing factors based on Andersen's model (22, 23) would be associated with patient's ability to achieve and maintain target SU <6 mg/dl; and (2) the initial allopurinol dose and previous allopurinol use in the baseline year will also be associated independently with these outcomes.

Methods

Study Cohort and Eligibility and Data Sources

We used the VA national databases from 2002-2012 (28-30), reliable for demographics and most common diagnoses (31), and valid for specific diagnoses (32). The Institutional Review Boards (IRBs) at the University of Alabama at Birmingham (X120928002) and the Birmingham VA Medical Center (01487) approved the study. We followed the Strengthening of Reporting in Observational studies in Epidemiology (STROBE) guidelines (33).

Patients were eligible if they had ≥1 inpatient or ≥2 outpatient visits with an International Classification of Diseases-ninth version (ICD-9) code 274.x for gout, were treated with allopurinol, had a post-index SU and met the 12-month observability period, i.e. for each 12 months, there must be an ICD-9 code 274.x recorded in the system. Index allopurinol prescription was defined as no allopurinol exposure in the previous 121 days. This included a 91-day clearance period and a 30-day grace period between prescriptions, since patients often have a small stock of medication especially with the 90-day prescriptions, which is the commonest day supply at the VA. A gap of >30 days between any two allopurinol prescriptions was considered as the end of an episode and led to the beginning of another drug exposure period.

Patient demographic and comorbidity data were obtained from VA Patient Treatment File (PTF) and Outpatient Clinic (OPC) tables. Results of serum urate were obtained from each Veterans Health Information Systems and Technology Architecture (VistA) system accessed using VA Informatics and Computing Infrastructure (VINCI) (34). Medication data were obtained through the Decision Support System's (DSS) Pharmacy (National Data Extract (NDE), which contains records for all inpatient and outpatient prescriptions, including every medication fill and refill from all VA facilities, including the number of days' supply, dose, number of pills, start and end date for medication fill and refills. Provider factors were obtained from the MedSAS Outpatient provider data. Systems factors (VA location, bed size, community-based outpatient clinic [CBOC] vs. VA clinic etc.) were obtained from the VA planning systems support group office and VINCI.

Outcome

We examined two key outcomes of success: (1) Achieving target SU < 6 mg/dl: Success was defined as the SU level < 6 mg/dl post-index allopurinol prescription, i.e., during the follow-up at any time 14 days or after the index allopurinol prescription (success 1); (2) Maintaining target SU < 6 mg/dl: Success was defined as those who met the previous definition and had all subsequent (≥2) SU levels < 6 mg/dl post-index prescription during the follow-up, with at least one day gap between laboratory assessments (success 2).

Associated Factors: Covariates and potential Confounders

We examined the following factors, as they mapped to the Andersen's Model (22, 23).

Predisposing factors

Patient Factors: age (in years); sex; race/ethnicity (White; Hispanic, Black or African-American; other; and Unknown); Body mass index; and marital status, categorized as single, married, divorced, widowed and unknown;

Comorbidity: assessed using Deyo-Charlson index (35), a validated measure, consisting of 17 comorbidities, examined as summation score, categorized as 0, 1 and 2 or more comorbidities;

Enabling factors

Provider Factors: The main provider of gout care categorized by provider specialty as rheumatologists vs. other (non-rheumatologist; including primary care).

System Factors: location of the VA facility, rural vs. urban; Affiliation to a teaching hospital, yes vs. no; outpatient clinic type, Community-based outpatient clinics (CBOCs) vs. VA medical center vs. both vs. other; VA facility bed size, categorized into ≤50, 51-100, 101-200, and >200; and Region, categorized as mid-Atlantic, Midwest, Northeast, South and West;

Healthcare access Factors: Distance to nearest VA medical center as a measure of accessibility, an important predictor of outcomes (36, 37), was calculated as the straight-line miles from the centroid of patient's residential zip code to the nearest VA site, as previously. Military service

connection and means test were also included, as both were significant predictors of SU monitoring in our previous VA study (38), and measure healthcare access. Military service connection is an indicator of access to care. It ranges from 0-100% and is awarded for conditions beginning during or resulting from active military duty (39). Veterans with ≥50% service-connection do not have co-payments for medical care or prescriptions, and get priority in VA healthcare access. Means test measures household income and assets and is completed yearly by most veterans (40), categorized as: AN, most needy but not service connected; AS, most needy and service-connected; and C, not "most needy".

Medication Factors: Allopurinol start dose was calculated as unit dose*quantity divided by days' supply based on the first and last filled prescription and categorized as ≤100, 101-200, 201-300 and >300 mg/day. We also examined any previous allopurinol use in the one-year baseline.

Need factors

Disease severity Factors: Duration of gout, assessed as the time from meeting the definition (1 inpatient ICD-9 code or 2 or more outpatient ICD-9 codes) to the beginning of the index allopurinol prescription; and pre-index SU level, categorized as, <6, 6-<8, 8-<10, 10-<12 and ≥12 mg/dl.

Statistical analyses

We compared the characteristics of patients who did or did not receive a post-allopurinol SU testing as well as did or did not achieve success 1 or 2, using chi-square/comparison of proportions test or t-test as applicable. We used multivariable-adjusted logistic regression models to assess whether needs, enabling and predisposing factors were associated with the ability to achieve target SU <6 mg/dl (Model 1a) and achieve and maintain SU <6 mg/dl in gout patients taking allopurinol (Model 1b). We reported odds ratios (OR) and 95% confidence intervals (CI). We performed sensitivity analyses by: (1) replacing Deyo-Charlson individual comorbidities in the main model with a score (0, 1, ≥2; **model 2a, 2b**); (2) additionally adjusting the main model for allopurinol use in the baseline 1-year and the starting allopurinol dose (**model 3a, 3b**). We performed exploratory analyses

by additionally adjusting the main model for allopurinol variables including the start and the end dose, use in the baseline 1-year, dose escalation (normal, fast, slow, none), and medication possession ratio (MPR; **model 4a, 4b),** calculated as the medication supply actually received by the patient divided by medication supply that could have been received.

Results

Cohort Characteristics

Of the 627,693 patients with gout, 198,839 patients (310,695 episodes) had a new allopurinol prescription and at least 12 months of observability (**Figure 1**). Of these, 41,153 patients (47,072 episodes) and 17,402 patients (18,323 episodes) contributed to the analyses for achieving target SU (success 1) or maintaining target SU (success 2).

Study cohort for achieving target SU (success 1) had a mean age of 66.8 years, BMI of 33.6 kg/m^2, 99% were male and 61% White (**Table 1**). Comorbidities were common and were higher compared to patients who did not get a post-index prescription SU testing (**Table 2**). Characteristics were similar for the two study cohorts for achieving target SU (success 1; **Table 3**) or maintaining target SU (success 2; **Table 4**).

Unadjusted characteristics of patients achieving or maintaining target SU

For success 1 cohort, the mean follow-up duration was 784.8 days (~26 months; SD, 810.3 days). The mean time to achieving target SU was 273.3 days (~9 months; SD, 303 days) and mean allopurinol dose was 193.5 mg/day (SD, 104 mg/day; **Table 1**). Only 42% patients each achieved target SU (success 1: 17,284/41,153 patients; 19,535 episodes) or achieved and maintained target SU (success 2: 7,309/17,402 patients; 18,323 episodes). Unadjusted characteristics are shown in **Tables 3 and 4**. Mean (SD) pre-index SU was lower in patients reaching versus not reaching target SU during follow-up: 7.8 (2.2) vs. 8.9 (2.0) mg/dl for achieving target SU (success 1); and 8.1 (2.2) mg/dl vs. 9.2 (2.1) mg/dl for achieving and maintaining target SU (success 2).

Multivariable-adjusted correlates of achieving or maintaining target SU

Factors associated with significantly higher odds of achieving target SU <6 mg/dl (success 1) were older age, male sex, White race, rheumatologist as the main provider of gout care, a lower hospital bed size of ≤50 or 101-200 (compared to >200), Midwest location for the healthcare facility, and the presence of comorbidities (rheumatologic disease, peptic ulcer disease, diabetes with complications and severe liver disease) (**Table 3**). Medical comorbidities (heart disease, diabetes, and renal disease), pre-index SU higher than 8 mg/dl (vs. 6 to <8) and longer gout duration were significantly associated with lower odds of achieving target SU (**Table 3**).

Factors associated with significantly higher odds of maintaining target SU <6 mg/dl (success 2; *at least two SU levels at target post-index prescription*) were White race, rheumatologist as the main provider, a lower hospital bed size 101-200 (ref >200 beds) and a normal BMI (**Table 4**). Medical comorbidities (heart disease, mild liver disease, diabetes. renal disease, malignancy and malignant neoplasm without specification of site), being single, Southern U.S location for the healthcare facility (vs. Midwest) and pre-index SU higher than 8 mg/dl (vs. 6 to <8) were associated with lower odds.

In sensitivity analysis (model 2), a higher Deyo-Charlson comorbidity index score ≥2 was associated with lower likelihood of achieving (**Figure 2**) or maintaining target SU (**Figure 2**).

Analyses of effect modification including allopurinol dose and use variables, overall and in explaining racial differences in achieving or maintaining target SU

In multivariable-adjusted models adjusted additionally for previous allopurinol use and start dose, compared to start dose of ≤100 mg/day, higher allopurinol doses were associated with higher odds and allopurinol use in the baseline 1-year with lower odds, of achieving or maintaining target SU (**Appendix 1 and 2**). In exploratory analyses, normal or fast allopurinol escalation (compared to no escalation), higher allopurinol end dose and higher allopurinol medication possession ratio, were associated with higher odds of both outcomes, with higher allopurinol start dose being only borderline significant (**Appendix 3**).

Although in the main analysis African-Americans had significantly lower adjusted odds of achieving target SU (OR 0.94; 95% CI: 0.89,0.99) and similar odds of maintaining target SU (OR 1.02; 95% CI: 0.93,1.11)**,** after adjusting for the rate of allopurinol dose escalation and MPR, they had significantly higher odds of achieving target SU (OR 1.16: 95% CI: 1.09, 1.23) and maintaining target SU (OR 1.22; 95% CI: 1.11, 1.34) (**Appendix 3**). Further analyses revealed that this effect modification was due to allopurinol MPR.

Discussion

To our knowledge, no study to date has examined factors associated with maintaining target SU. Our comprehensive, national cohort study performed robust analyses that controlled for patient, provider, systems, medication and disease severity factors and advances the understanding of factors associated with target SU. Compared to non-rheumatologist, patients who saw rheumatologists (<3% patients) as the main providers for gout care were more likely to achieve target SU, and to maintain target SU. A better quality of gout care with rheumatology provider (1) and higher odds of target SU achievement with a rheumatologist provider (21) explain our finding. This may be due to the prioritization of gout management during a rheumatology visit. This finding has potential policy implications for the VA.

We recognize that a multifaceted approach with several policy initiatives is required to address this quality gap. Expanded rheumatology care teams (nurse practitioners, physician assistants, community health workers), and technology-based solutions (tele-health, e-consults and virtual health communities) may address this problem. This would require provision of more resources for the VA rheumatology workforce. Nurse- or pharmacist-led interventions are effective in improving gout care and outcomes (43-45). Maintaining target SU <6 mg/dl is associated with reduction in gout flares, resolution of gouty tophi and improvement in quality of life and function (5, 10) and is key to optimal management (11, 24, 25).

It took mean of 9 months to achieve target SU, apparently longer than might be expected based on the ACR treatment guideline with frequent ULT dose titration (11). Only 42% of the patients

maintained target SU, a key treatment goal recommended by gout guidelines (11-16). Allopurinol is well-tolerated with few adverse events, which is unlikely to explain this low rate of success. Patients prioritized lowering of SU (to target) in gout as an important patient goal (18), challenging the recent ACP's position to treat-to-symptom control and not to the SU-target . Thus, improvement in rates of target SU achievement and maintenance in gout are needed.

African-Americans had lower odds of achieving target SU in models not accounting for allopurinol adherence and gout severity factors, but higher odds of achieving or maintaining target SU, in exploratory analyses. This is a novel insight. It indicates that the lower chance of target SU achievement in African-Americans can be explained largely by lower allopurinol adherence, and to a lesser degree by worse baseline disease, lower allopurinol start dose and improper dose escalation. After accounting for these confounding factors, African-Americans with gout have a better SU outcome than Caucasians (**Appendix 3**). Addressing these modifiable factors has the potential of improving gout outcomes in African-Americans and reducing health disparities in gout.

Prior studies lacked a theoretical model and were limited due to inclusion of a select few variables or univariate analysis (1, 19-21) or single-center (1) or a regional sample (21), lacked gout disease severity variables (1, 19-21), or used a prevalent allopurinol user design (and not incident user design) (19, 20). Using the Andersen model (22, 23), we specified *a priori* that system, healthcare access and disease severity factors (i.e. *enabling and predisposing factors, not included in previous studies*) in addition to patient and provider factors (need factors) will be associated with target SU outcomes. We found higher odds of target SU achievement in males compared to females in contrast to previous studies (19, 21). Differences in setting (national vs. regional sample), population (veterans vs. US population), design (incident vs. prevalent user design (19)), control for disease severity (disease duration and SU vs. SU (21) or neither (19)) and additional covariate adjustment (system and healthcare access vs. neither (19, 21)) may explain these differences.

Our study highlights the role of comorbidities in the achievement of target SU with allopurinol. The presence of 2 or more comorbidities was independently associated with 20% lower odds of maintaining target SU <6 mg/dl compared to no comorbidities. A linear dose-gradient was seen with

increasing comorbidity load. This novel finding adds to the current knowledge. We found that heart disease, renal disease and diabetes were associated with lower odds of achieving or maintaining target SU <6 mg/dl. This confirmed previous findings from regional/single center studies controlled for selected conditions (1, 19-21), now in a national sample, controlled using the Deyo-Charlson index, a validated comorbidity index. Although polypharmacy might be associated with higher allopurinol adherence (21), negative effects of higher comorbidity or specific medications on SU levels might make it more challenging to achieve target SU in people with specific comorbidities or an overall high comorbidity load, as our study and other studies show (1, 19, 21, 41, 42). Future studies should examine whether optimization of comorbidity management can improve gout outcomes.

Geographic region was associated with odds of achieving and maintaining target SU. Compared to the Midwest, patients living in South were less likely to achieve or to achieve and maintain target SU. Differences in resources, regional economies and/or patient populations may underlie these differences. Policy makers may need to provide additional VA resources in these U.S. regions to improve gout outcomes. This finding indicates that findings from even well designed studies limited to one U.S. region (21) are likely not generalizable to the entire U.S.

We assessed allopurinol start dose and previous allopurinol exposure as potential confounders of achieving or maintaining target SU, rather than mediators, since they meet the classic definition of confounders by being associated both with the covariates and the outcome. For example, while adjusting for allopurinol MPR clearly changed the apparent relationship between race and achieving SU targets, it seems more reasonable to infer that adjusting for MPR accounted for the confounding between race and medication adherence than the mediation interpretation that the effect of race on SU adherence 'acted through' medication adherence.

Higher allopurinol start doses >100 mg/day increased the odds of achieving or maintaining target SU by 1.8-3.5 fold, slightly higher than 1.9-2.1 fold in a previous study of (21). Higher allopurinol end dose, higher allopurinol MPR and normal or fast allopurinol escalation were also associated with very high odds of achieving or maintaining target SU. This is not surprising, since allopurinol is an effective ULT. Most treatment guidelines recommend a low allopurinol starting dose of 100 mg/day,

and a gradual allopurinol dose escalation, to avoid gout flares and rare allopurinol hypersensitivity. Thus, the pros and the cons of high vs. low allopurinol start dose and fast vs. normal/slow allopurinol dose escalation must be considered and discussed with an individual patient in a shared decision-making approach. A high allopurinol MPR and higher end dose (i.e., to adequately lower SU) are non-controversial approaches in gout care.

The study findings must be interpreted considering limitations. The use of ICD-9 codes for the diagnosis of gout and other comorbidities using the VA databases is subject to misclassification bias. However, ICD-9 codes for gout in the VA had high accuracy with sensitivity of 90% and specificity of 100% (38) and VA databases are valid and reliable for several diagnoses (31, 32), although other database studies have reported lower accuracy for gout code (46). Findings from this predominantly male veteran population may not be generalizable to women and non-veterans. However, no previous studies have found gender or veteran status as confounders of these associations and the male predominant VA population made it an excellent clinical laboratory to study gout, also a male-predominant condition. As in any other U.S. healthcare system (Medicare, Medicaid etc.), care provided outside of the system could not be accounted for in these analyses and may have contributed to precision. The impact of this missingness on our results is unclear. Our findings are likely not generalizable to other healthcare systems, since systems-level factors can vary. However, identified factors can now be targeted to improve these outcomes nationally for the large VA healthcare system at a minimum.

Study strengths include the use of an integrated national VA database, a large sample size, an incident allopurinol user design, the use of a theoretical model, inclusion of several important covariates previously not included, examination of several models to test the robustness of findings and examination of factors associated with maintaining target SU, not reported previously.

In conclusion, we conducted a comprehensive national study of factors associated with achieving and maintaining target SU <6 mg/dl in patients with gout, using data from one of the largest integrated national U.S. healthcare systems. We identified key patient, comorbidity, physician, system, healthcare access, allopurinol dose/adherence and disease severity factors independently

associated with achieving and maintaining target SU <6 mg/dl. Several characteristics may be amenable to patient/physician/systems-targeted interventions to improve the chances of maintaining target SU <6 mg/dl in gout in this large national healthcare system. This, in turn, can improve gout outcomes and reduce the patient morbidity and the societal impact of gout.

Abbreviations:

SU, serum urate

VA, Veterans Affairs

OR, odds ratio

CI, confidence intervals

ICD-9, International Classification of Disease, ninth revision

STROBE, Strengthening of Reporting in Observational studies in Epidemiology

VINCI, VA Informatics and Computing Infrastructure

NDE, National Data Extract

BMI, Body mass index

Declarations:

Ethics approval and consent to participate: The study was approved by the Institutional Review Board (IRB) at the University of Alabama at Birmingham (X120928002) and the Birmingham VA Medical Center (01487). The IRBs waived the need for informed consent for this database study.

Consent for publication: No individual person's data were presented in any form in this study and therefore no consent to publish is required.

Availability of Data and material: We are ready to share the data with colleagues, after obtaining appropriate permissions from IRBs at the Birmingham VA Medical Center and the University of Alabama at Birmingham, related to their privacy and data sharing policies.

Competing Interests: JAS has received consultant fees from Crealta/Horizon, Fidia, UBM LLC, Medscape, WebMD, the National Institutes of Health and the American College of Rheumatology.

JAS owns stock options in Amarin and Viking pharmaceuticals, Inc. JAS is a member of the Veterans Affairs Rheumatology Field Advisory Committee. JAS is the editor and the Director of the UAB Cochrane Musculoskeletal Group Satellite Center on Network Meta-analysis. JAS served as a member of the American College of Rheumatology's (ACR) Annual Meeting Planning Committee (AMPC) and Quality of Care Committees, the Chair of the ACR Meet-the-Professor, Workshop and Study Group Subcommittee and the co-chair of the ACR Criteria and Response Criteria subcommittee. JAS is a member of the executive of OMERACT, an organization that develops outcome measures in rheumatology and receives arms-length funding from 36 companies. SY has no conflicts. KGS serves as a consultant for Amgen, Merck, and Radius and receives funding from Amgen and Merck.

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Authors' contributions: JAS designed the study and developed the study protocol. SY obtained the data and performed the statistical analyses. All authors reviewed analyses and provided critical feedback on the manuscript. JAS wrote the first draft of the paper. All authors made the decision to submit the final manuscript.

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Figure Legends

Figure 1. Cohort Selection Flow Chart

Legend: The flow chart shows the selection of sample for the study, based on eligibility criteria. We examined 41,153 people with gout for achievement of target serum urate (success 1) and 17,402 people with gout for achievement and maintenance of target serum urate (success 2)

Figure 2. Association of Deyo-Charlson comorbidity index score with achieving or maintaining target serum urate in multivariable-adjusted model

Legend: The figure shows the association of Deyo-Charlson comorbidity index score with the odds of achieving target serum urate (Figure 2a) and with the achieving and maintaining target serum urate (Figure 2b). Reference category is Deyo-Charlson comorbidity index score of zero (no comorbidity). Odds ratio estimates are shown as diamonds and 95% confidence intervals (CI) are shown as whiskers. Estimates with 95% CI overlapping the odds ratio of 1 (solid line) are statistically not significant. For example, compared to score of 0, a Deyo-Charlson comorbidity index score of 2 or more was significantly independently significantly associated with lower odds of achieving or maintaining target serum urate with OR (95% CI) of 0.82 (0.79, 0.86) and 0.63 (0.59, 0.68), respectively. The results are from model 2, in which the individual Deyo-Charlson individual comorbidities in the main model (model 1) were replaced with a Deyo-Charlson index score of 0, 1 or ≥2.

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Table 1. Selected Characteristics of overall sample and the study cohort

Variable	Total Sample (n=310,695 episodes) N (%) or mean (SD)	Study cohort with at least 1 post-index SU (n=47,072 episodes) N (%) or mean (SD)
Male Sex	307992 (99.1%)	46,659 (99.1%)
Race/ethnicity		
White	196,479 (63.2%)	28,572 (60.7%)
Black	65,664 (21.1%)	11,376 (24.2%)
Hispanic	11,928 (3.8%)	2,527 (5.4%)
Other	19,444 (6.3%)	2,810 (6.0%)
Unknown	17,180 (5.5%)	1,787 (3.8%)
Age, mean (SD)	67.5 (11.8)	66.8 (11.5)
Body Mass Index (kg/m2), mean (SD)	33.5 (7.5)	33.6 (7.6)
Marital Status		
Married	184,084 (59.5%)	26,687 (57.0%)
Divorced	67,217 (21.7%)	10,694 (22.8%)
Single	32,037 (1034%)	5,535 (11.8%)
Widowed	25,916 (8.4%)	3,946 (8.4%)
Deyo-Charlson comorbidity index score, mean (SD)	1.4 (1.6)	1.6 (1.7)
Main Provider Type		
Any Physician	163,131 (52.5%)	23,564 (50.1%)
Nursing	31,405 (10.1%)	3,887 (8.3%)
Physician Assistant or Nurse Practitioner	28,258 (9.1%)	3,863 (8.2%)
Other	87,901 (28.3%)	15,758 (33.5%)
Provider Specialty		
Rheumatology	8,140 (2.6%)	2,543 (5.4%)
Others	302,555 (97.4%)	44,529 (94.6%)
Veterans Integrated Service Network (VISN)		
Northeast	28,846 (9.3%)	6,685 (14.2%)
Mid-Atlantic	69,414 (22.3%)	13,620 (28.9%)
South	93,584 (30.1%)	10,612 (22.6%)
Mid-West	65,957 (21.2%)	5,045 (10.7%)
West	52,872 (17.0%)	11,106 (23.6%)
Affiliated to University Hospital (Yes)	290,131 (93.4%)	42,787 (90.9%)
Outpatient Clinic Type		
Community Based Outpatient Clinic (CBOC)	62,822 (20.2%)	8,525 (18.1%)
Veterans Affairs Medical Center (VAMC)	43,420 (14.0%)	29,107 (61.8%)
VAMC and CBOC	16,347 (5.3%)	2,193 (4.7%)
Other	43,420 (14.0%)	7,247 (15.4%)
Operating Beds, mean (SD)	162.7 (94.7)	169.6 (94.4)
Operating VAMC Bed Size		

>200	93,847 (30.2%)	15,812 (33.6%)
≤50	42,073 (13.5%)	7,471 (15.9%)
>50 to ≤100	56,082 (18.1%)	5,815 (12.4%)
>100 to ≤200	118,693 (38.2%)	17,974 (38.2%)
Distance from Closest VA Facility within Network (miles), mean (SD)	13.3 (13.9)	12.6 (15.3)
Distance from Closest VA Medical Center within Network (miles), mean (SD)	44.3 (78.6)	47.8 (124.1)
Rural location of the VA facility	162,420 (52.4%)	22,405 (47.7%)
MEANS test category		
Most needy but not service connected (AN)	104,088 (33.5%)	16,961 (36.0%)
Most needy and service-connected (AS)	123,729 (39.8%)	19,800 (42.1%)
Not "most needy" (C)	68,367 (22.0%)	8,252 (17.5%)
Other (G/N/U/X)	14,489 (4.7%)	2,055 (4.4%)
Daily Allopurinol Dose (mg/day), mean (SD)		
Start Daily Dose	206.1 (119.6)	192.7 (105.2)
End Daily Dose	215.4 (118.8)	213.4 (116.2)
Average Dose	200.8 (106.6)	193.5 (103.8)
Follow-Up Time (censored by Event)	524.3 (536.5)	273.3 (303.5)
Time to achieve target SU <6 mg/dl, mean (SD)	--	179 (102,330)
Medication Possession Ratio (MPR; censored by Event), mean (SD)	0.8 (0.2)	0.9 (0.1)

BOLD text denotes statistically significant p<0.05 between the overall sample and that with at least one post-index SU

SD, standard deviation; MPR, medication possession ratio; BMI, body mass index; VAMC, VA medical center clinic PA, physician assistant; APN, advanced practitioner nurse; CBOC, community-based outpatient clinic; VISN, veterans Integrated service network.

Table 2. Comorbidity Characteristics of overall sample and the study cohort

	Overall sample (n=310,695)	Study cohort without SU test post-index filled allopurinol prescription (n=263,623)	Study cohort with at least one SU test post-index filled allopurinol prescription (n=47,072)
Deyo-Charlson index comorbidities			
Myocardial Infarction	9,841 (3.2%)	8,063 (3.1%)	1,778 (3.8%)
Coronary heart disease	38,989 (12.5%)	32,111 (12.2%)	6,878 (14.6%)
Peripheral vascular disease	25,655 (8.3%)	21,266 (8.1%)	4,389 (9.3%)
Cerebrovascular Disease	23,948 (7.7%)	20,012 (7.6%)	3,936 (8.4%)
Dementia	1,693 (0.5%)	1,447 (0.6%)	246 (0.5%)
Chronic pulmonary disease	52,886 (17.0%)	44,339 (16.8%)	8,547 (18.2%)
Rheumatologic disease	5,052 (1.6%)	3,993 (1.5%)	1,059 (2.3%)
Peptic ulcer disease	4,780 (1.5%)	4,050 (1.5%)	730 (1.6%)
Mild liver disease	2,435 (0.8%)	2,004 (0.8%)	431 (0.9%)
Diabetes	10,8283 (34.9%)	90,891 (34.5%)	17,392 (37.0%)
Diabetes with complications	27,629 (8.9%)	22,561 (8.6%)	5,068 (10.8%)
Paraplegia	855 (0.3%)	697 (0.3%)	158 (0.3%)
Renal disease	20,556 (6.6%)	16,112 (6.1%)	4,444 (9.4%)
Malignancy	34,221 (11.0%)	28,532 (10.8%)	5,689 (12.1%)
Severe liver disease	830 (0.3%)	701 (0.3%)	129 (0.3%)
Malignant neoplasm without specification of site	1,631 (0.5%)	1,350 (0.5%)	281 (0.6%)
AIDS	912 (0.3%)	705 (0.3%)	207 (0.4%)
Cancer	34,443 (11.1%)	28,721 (10.9%)	5,722 (12.2%)
Hepatic Coma	175 (0.1%)	145 (0.1%)	30 (0.1%)
Deyo-Charlson Comorbidity index Score	1.4 (1.6)	1.3 (1.6)	1.6 (1.7)

BOLD text denotes Deyo-Charlson comorbidities that were statistically significant between the two groups with an unadjusted p-value of <0.05

Table 3. Unadjusted and Adjusted analyses of patients with gout for patients for **achievement of** target SU of < 6 mg/dl

	Achieved target SU (N=19,535 episodes)	Did not achieve target SU (N=27,537 episodes)	Achieved target SU **Unadjusted Model** OR (95% CI)	Achieved target SU **Adjusted Model** OR (95% CI)
Male Sex (REF, female)	19,321 (98.9%)	27,338 (99.3%)	**1.51 (1.24, 1.85)**	**1.63 (1.32, 2.01)**
Race				
White	12,387 (63.4%)	16,185 (58.8%)	REF	REF
Black	4,413 (22.6%)	6,963 (25.3%)	**0.84 (0.80, 0.88)**	**0.94 (0.89, 0.99)**
Hispanic	873 (4.5%)	1,654 (6.0%)	**0.70 (0.64, 0.76)**	**0.77 (0.70, 0.85)**
Other	1,097 (5.6%)	1,713 (6.2%)	**0.83 (0.76, 0.90)**	**0.80 (0.73, 0.88)**
Unknown	765 (3.9%)	1,022 (3.7%)	0.96 (0.87, 1.07)	0.94 (0.84, 1.05)
Age, mean (SD)	67.7 (11.1)	66.2 (11.7)	**1.01 (1.01, 1.01)**	**1.01 (1.01, 1.01)**
Marital status				
Married	11,267 (57.6%)	15,420 (56.0%)	REF	REF
Divorced	4,372 (22.4%)	6,322 (23.0%)	**0.95 (0.90, 0.99)**	1.02 (0.97, 1.08)
Single	2,143 (11.0%)	3,392 (12.3%)	**0.87 (0.82, 0.93)**	0.99 (0.92, 1.06)
Widowed	1,676 (8.6%)	2,270 (8.2%)	0.78 (0.58, 1.06)	0.89 (0.65, 1.22)
Unknown	77 (0.4%)	133 (0.5%)	1.02 (0.95, 1.10)	0.95 (0.88, 1.02)
Deyo-Charlson Comorbidities				
Myocardial Infarction	674 (3.5%)	1,104 (4.0%)	**0.85 (0.77, 0.94)**	0.93 (0.83, 1.04)
Coronary heart disease	2,254 (11.5%)	4,624 (16.8%)	**0.65 (0.62, 0.69)**	**0.75 (0.70, 0.80)**
Peripheral vascular disease	1,744 (8.9%)	2,645 (9.6%)	**0.93 (0.87, 0.99)**	0.95 (0.88, 1.02)
Cardiovascular Disease	1,684 (8.6%)	2,252 (8.2%)	1.07 (0.99, 1.14)	1.06 (0.99, 1.14)
Dementia	110 (0.6%)	136 (0.5%)	1.13 (0.87, 1.46)	0.96 (0.73, 1.26)
Chronic pulmonary disease	3,482 (17.8%)	5,065 (18.4%)	0.96 (0.92, 1.01)	1.04 (0.98, 1.09)
Rheumatologic disease	485 (2.5%)	574 (2.1%)	**1.21 (1.06, 1.37)**	**1.19 (1.04, 1.36)**
Peptic ulcer disease	361 (1.9%)	369 (1.3%)	**1.43 (1.23, 1.67)**	**1.33 (1.13, 1.56)**
Mild liver disease	169 (0.9%)	262 (1.0%)	0.90 (0.74, 1.10)	0.87 (0.70, 1.10)
Diabetes	6,837 (35.0%)	10,555 (38.3%)	**0.88 (0.85, 0.92)**	**0.95 (0.90, 0.99)**
Diabetes with complications	1,962 (10.0%)	3,106 (11.3%)	**0.89 (0.84, 0.95)**	**1.09 (1.01, 1.17)**
Paraplegia	80 (0.4%)	78 (0.3%)	**1.44 (1.04, 1.98)**	1.31 (0.94, 1.85)
Renal disease	1,480 (7.6%)	2,964 (10.8%)	**0.69 (0.65, 0.74)**	**0.77 (0.71, 0.83)**

Malignancy, including leukemia & lymphoma	2,548 (13.0%)	3,141 (11.4%)	**1.16 (1.09, 1.23)**	1.05 (0.98, 1.12)
Severe liver disease	65 (0.3%)	64 (0.2%)	**1.42 (0.98, 2.03)**	**1.67 (1.11, 2.51)**
Metastatic solid tumor	134 (0.7%)	147 (0.5%)	1.31 (1.03, 1.66)	1.01 (0.78, 1.31)
Acquired immunodeficiency syndrome	81 (0.4%)	126 (0.5%)	0.93 (0.70, 1.24)	1.08 (0.80, 1.46)
Provider Specialty[1]				
Rheumatology	1,125 (5.8%)	1,418 (5.2%)	REF	REF
Other	18,410(94.2%)	26,119 (94.9%)	**0.88 (0.81, 0.95)**	**0.79 (0.72, 0.86)**
Region of country				
Midwest	2,292 (11.7%)	2,757 (10%)	REF	REF
Northeast	3,047 (15.6%)	3,638 (13.2%)	1.03 (0.95, 1.11)	1.04 (0.95, 1.14)
Mid-Atlantic	5,604 (28.7%)	8,016 (29.1%)	**0.85 (0.80, 0.91)**	**0.89 (0.82, 0.96)**
South	4,066 (20.8%)	6,546 (23.8%)	**0.74 (0.69, 0.80)**	**0.81 (0.75, 0.89)**
West	4,526 (23.2%)	6,580 (23.9%)	**0.84 (0.78, 0.90)**	**0.87 (0.80, 0.95)**
Affiliated with University (REF, No)	17,644 (90.3%)	25,143 (91.3%)	**0.89 (0.84, 0.96)**	1.04 (0.95, 1.14)
VA Clinic Type				
VA Medical Center (VAMC)	11,911(61.0%)	17,196 (62.5%)	REF	REF
Community-based outpatient clinic (CBOC)	3,655 18.7%)	4,870 (17.7%)	**1.06 (1.01, 1.12)**	1.00 (0.95, 1.06)
Other	3,131 (16.0%)	4,116 (15.0%)	**1.09 (1.04, 1.16)**	1.09 (1.02, 1.15)
VAMC and CBOC	838 (4.3%)	1,355 (4.9%)	0.92 (0.84, 1.01)	0.86 (0.78, 0.95)
Operating Bed				
>200	6,213 31.8%)	9,599 (34.9%)	REF	REF
≤50	3,257 16.7%)	4,214 (15.3%)	**1.18 (1.11, 1.25)**	**1.13 (1.04, 1.22)**
51 to 100	2,492 12.8%)	3,323 (12.1%)	**1.14 (1.07, 1.22)**	1.04 (0.97, 1.12)
101 to 200	7,573 38.8%)	10,401 (37.8%)	**1.12 (1.07, 1.17)**	**1.18 (1.12, 1.24)**
Means test[2]				
Most needy but not service connected (AN)	6,836 35.0%)	10,125 (36.8%)	REF	REF
Most needy and service-connected (AS)	8,268 42.3%)	11,532 (41.9%)	**1.06 (1.02, 1.11)**	0.98 (0.85, 1.12)
Not "most needy" (C)	3,598 18.4%)	4,654 (16.9%)	**1.13 (1.07, 1.20)**	0.99 (0.93, 1.05)
Other (G/N/U/X)	832 (4.3%)	1,223 (4.4%)	**0**.99 (0.89, 1.09)	**0.90 (0.81, 0.99)**
Duration of gout, mean (SD)	2.2 (2.3)	2.1 (2.2)	1.01 (1.00, 1.02)	**0.97 (0.96, 0.98)**
Pre-index SU level, mg/dl				
<6	3,769 (21.3%)	1,513 (5.9%)	**3.02 (2.81, 3.24)**	**3.00 (2.79, 3.22)**

6 to <8	5,079 (28.7%)	6,135 (24.1%)	REF	REF
8 to <10	6,169 (34.8%)	10,831 (42.5%)	**0.69 (0.66, 0.72)**	**0.70 (0.66, 0.73)**
10 to <12	2,199 (12.4%)	5,385 (21.1%)	**0.49 (0.47, 0.53)**	**0.51 (0.48, 0.55)**
≥12	509 (2.9%)	1,637 (6.4%)	**0.38 (0.34, 0.42)**	**0.42 (0.37, 0.47)**

BOLD text denotes statistically significant odds ratios

[1]Provider Specialty: Other category includes non-physician rheumatologist, physician assistant or advanced nurse practitioner; numbers were too small to separate physician assistant or advanced nurse practitioner

[2]Means test is an assessment of socio-economic status of a veteran

SD, standard deviation; OR, odds ratio; CI, confidence interval; MPR, medication possession ratio; BMI, body mass index; VAMC, VA medical center clinic; CBOC, community-based outpatient clinic

Rheumatologic diseases includes lupus, systematic sclerosis, polymyositis, polymyalgia rheumatica, rheumatoid lung and rheumatoid arthritis

Adjusted Model: includes patient factors including age (in years), sex, race/ethnicity (White; Hispanic, Black or African-American, other, unknown), body mass index, marital status, Deyo-Charlson index medical comorbidities, physician factors including provider specialty (rheumatologists vs. non-rheumatologist), system factors including location of the VA facility (rural vs. urban), affiliation to a teaching hospital, outpatient clinic type, VA facility bed size (≤50, 51-100, 101-200, and >200) and region (mid-Atlantic, Midwest, Northeast, South and West); health care access, including distance to nearest VA medical center, %service connection, Means test, duration of gout, and pre-index serum urate (SU) level; BMI was also associated; other factors adjusted in the model that were not significant included location of the VA, %service connection and distance to the nearest VA.

Unique patients =17,284 for patients who achieved target SU and =23,869 for patients who did not achieve target SU.

C Statistic for the adjusted model was 0.66

Table 4. Unadjusted and adjusted analyses of patients with gout for **achievement and maintenance of** target SU of < 6 mg/dl

	Achieved and maintained target SU (Episodes =7,462)	Did not achieve and maintain target SU (Episodes =10,861)	Unadjusted Model OR (95% CI)	Multivariable-adjusted Model OR (95% CI)
Male Sex (Ref, Female)	7,388 (99.0%)	10,772 (99.2%)	1.17 (0.85, 1.16)	1.31 (0.94,1.82)
Race				
White	4,889 (65.5%)	6,706 (61.7%)	REF	REF
Black	1,645 (22.1%)	2,615 (24.1%)	**0.88 (0.82, 0.95)**	1.02 (0.93, 1.11)
Hispanic	314 (4.2%)	606 (5.6%)	**0.72 (0.62, 0.83)**	**0.80 (0.68, 0.94)**
Other	374 (5.0%)	637 (5.9%)	**0.80 (0.70, 0.93)**	**0.74 (0.64, 0.86)**
Unknown	240 (3.2%)	297 (2.7%)	1.09 (0.91, 1.31)	1.02 (0.84, 1.24)
Age, mean (SD)	67.9 (10.8)	66.8 (11.4)	**1.01 (1.01, 1.01)**	**1.01 (1.01, 1.01)**
Marital status				
Married	4,253 (57.0%)	6,010 (55.3%)	REF	REF
Divorced	1,702 (22.8%)	2,481 (22.8%)	0.97 (0.90, 1.05)	1.02 (0.94, 1.10)
Single	787 (10.5%)	1,382 (12.7%)	**0.79 (0.72, 0.88)**	**0.86 (0.77, 0.96)**
Widowed	696 (9.3%)	946 (8.7%)	0.86 (0.52, 1.43)	0.97 (0.86, 1.09)
Unknown	24 (0.3%)	42 (0.4%)	1.05 (0.94, 1.17)	0.96 (0.57, 1.64)
Deyo-Charlson comorbidities				
Myocardial Infarction	7,179 (96.2%)	10,367 (95.5%)	**0.81 (0.70, 0.95)**	0.98 (0.83, 1.16)
Coronary heart disease	938 (12.6%)	23,17 (21.3%)	**0.53 (0.48, 0.57)**	**0.64 (0.58, 0.70)**
Peripheral vascular disease	741 (9.9%)	1,230 (11.3%)	**0.87 (0.78, 0.96)**	0.96 (0.86, 1.07)
Cerebrovascular Disease	697 (9.3%)	1,042 (9.6%)	0.97 (0.88, 1.08)	1.01 (0.90, 1.13)
Dementia	40 (0.5%)	57 (0.5%)	0.99 (0.65, 1.49)	0.91 (0.59, 1.41)
Chronic pulmonary disease	1,376 (18.4%)	2,262 (20.8%)	**0.86 (0.80, 0.93)**	0.99 (0.91, 1.07)
Rheumatologic disease	233 (3.1%)	297 (2.7%)	1.14 (0.95, 1.36)	1.11 (0.92, 1.34)
Peptic ulcer disease	157 (2.1%)	182 (1.7%)	**1.26 (1.01, 1.57)**	1.24 (0.98, 1.56)
Mild liver disease	65 (0.9%)	138 (1.3%)	**0.67 (0.49, 0.90)**	**0.63 (0.45, 0.90)**
Diabetes	2,705 (36.3%)	4,651 (42.8%)	**0.77 (0.73, 0.82)**	**0.89 (0.82, 0.95)**
Diabetes with complications	840 (11.3%)	1,616 (14.9%)	**0.74 (0.68, 0.81)**	1.00 (0.90, 1.11)
Paraplegia	35 (0.5%)	41 (0.4%)	1.29 (0.81, 2.04)	1.38 (0.85, 2.25)
Renal disease	644 (8.6%)	1,579 (14.5%)	**0.57 (0.51, 0.62)**	**0.64 (0.58, 0.72)**
Malignancy	982 (13.2%)	1,461 (13.5%)	0.98 (0.89, 1.07)	**0.88 (0.80, 0.97)**
Severe Liver Disease	26 (0.4%)	38 (0.4%)	1.03 (0.62, 1.71)	1.41 (0.78, 2.57)

Malignant neoplasm without specification of site	53 (0.7%)	87 (0.8%)	0.88 (0.62, 1.24)	**0.66 (0.45, 0.96)**
AIDS	37 (0.5%)	59 (0.5%)	0.90 (0.60, 1.37)	0.96 (0.62, 1.49)
Provider Specialty[1]				
Rheumatology	596 (8.0%)	749 (6.9%)	REF	REF
Other	6,866 (92.0%)	10,112 (93.1%)	**0.85 (0.76, 0.95)**	**0.77 (0.68, 0.87)**
Region of country				
Midwest	803 (10.8%)	995 (9.2%)	REF	REF
Northeast	1,358 (18.2%)	1,752 (16.1%)	0.98 (0.87, 1.11)	0.87 (0.76, 1.00)
Mid-Atlantic	2,126 (28.5%)	2,100 (28.6%)	**0.87 (0.77, 0.97)**	0.96 (0.83, 1.11)
South	1,416 (19.0%)	2,427 (22.4%)	**0.73 (0.65, 0.82)**	**0.76 (0.66, 0.88)**
West	1,759 (23.6%)	2,586 (23.8%)	**0.85 (0.76, 0.96)**	0.89 (0.78, 1.03)
Affiliated with University (REF, No)	6,774 (90.8%)	9,971 (91.8%)	**0.87 (0.78, 0.97)**	0.98 (0.84, 1.13)
Outpatient Clinic Type				
VAMC	4,620 (61.9%)	6,841 (63.0%)	REF	REF
CBOC	1,335 (17.9%)	1,802 (16.6%)	1.08 (0.99, 1.17)	1.00 (0.92, 1.10)
Other	1,210 (16.2%)	1,781 (16.4%)	1.00 (0.91, 1.08)	1.01 (0.92, 1.11)
VAMC and CBOC	297 (4.0%)	437 (4.0%)	0.98 (0.84, 1.15)	0.89 (0.75, 1.05)
Operating Bed Size				
>200	1,216 (16.3%)	1,651 (15.2%)	REF	REF
≤50	930 (12.5%)	1,248 (11.5%)	**1.14 (1.04, 1.26)**	1.05 (0.93, 1.19)
51 to 100	2,830 (37.9%)	4,032 (37.1%)	**1.17 (1.06, 1.29)**	1.07 (0.95, 1.20)
101 to 200	2,486 (33.3%)	3,930 (36.2%)	**1.01 (1.03, 1.18)**	**1.17 (1.08, 1.26)**
MEANS test[2]				
Most needy but not service connected (AN)	2,685 (36.0%)	4,085 (37.6%)	REF	REF
Most needy and service-connected (AS)	3,227 (43.3%)	4,728 (43.5%)	1.04 (0.97, 1.11)	1.01 (0.81, 1.26)
Not "most needy" (C)	1,255 (16.8%)	1,621 (14.9%)	**1.16 (1.06, 1.28)**	0.99 (0.89, 1.09)
Other (G/N/U/X)	295 (4.0%)	426 (3.9%)	1.02 (0.87, 1.20)	0.95 (0.80, 1.13)
Duration of gout, mean (SD)	2.1 (2.2)	2.0 (2.1)	**1.02 (1.01, 1.04)**	0.98 (0.97, 1.00)
Pre-index SU level, mg/dl				
<6	1,237 (17.8%)	512 (5.0%)	**2.76 (2.44, 3.11)**	**2.80 (2.48, 3.17)**
6 to <8	1,816 (26.1%)	2,072 (20.1%)	REF	REF
8 to <10	2,637 (37.8%)	4,280 (41.5%)	**0.70 (0.65, 0.76)**	**0.72 (0.66, 0.78)**
10 to <12	1,010 (14.5%)	2,559 (24.8%)	**0.45 (0.41, 0.50)**	**0.49 (0.45, 0.54)**

≥12	270 (3.9%)	881 (8.6%)	**0.35 (0.30, 0.41)**	**0.44 (0.38, 0.52)**

BOLD text denotes statistically significant odds ratios

[1]Provider Specialty: Other category includes; non-rheumatologist physician, physician assistant or advanced nurse practitioner; numbers were too small to separate physician assistant or advanced nurse practitioner

[2]Means test is an assessment of socio-economic status of a veteran

SD, standard deviation; OR, odds ratio; CI, confidence interval; MPR, medication possession ratio; BMI, body mass index; VAMC, VA medical center clinic; CBOC, community-based outpatient clinic

Rheumatologic diseases includes lupus, systematic sclerosis, polymyositis, polymyalgia rheumatica, rheumatoid lung and rheumatoid arthritis;

Adjusted Model: patient factors including age (in years), sex, race/ethnicity (White; Hispanic, Black or African-American, other, unknown), body mass index, marital status; Deyo-Charlson index medical comorbidities; physician factors including provider specialty (rheumatologists vs. non-rheumatologist), system factors including location of the VA facility (rural vs. urban), affiliation to a teaching hospital, outpatient clinic type, VA facility bed size (≤50, 51-100, 101-200, and >200) and region (mid-Atlantic, Midwest, Northeast, South and West), health care access, including distance to nearest VA medical center, %service connection, means test, duration of gout, and pre-index serum urate (SU) level

Unique patients =7,309 for patients who achieved and maintained target SU and =10,389 for patients who did not.

7,309 patients (with 7,462 episodes) achieved and maintained target SU of <6 mg/dl and 10,389 patients (with 10,861 episodes) did not

C statistic for the adjusted model was 0.66

Figure 1. Cohort Selection Flow Chart

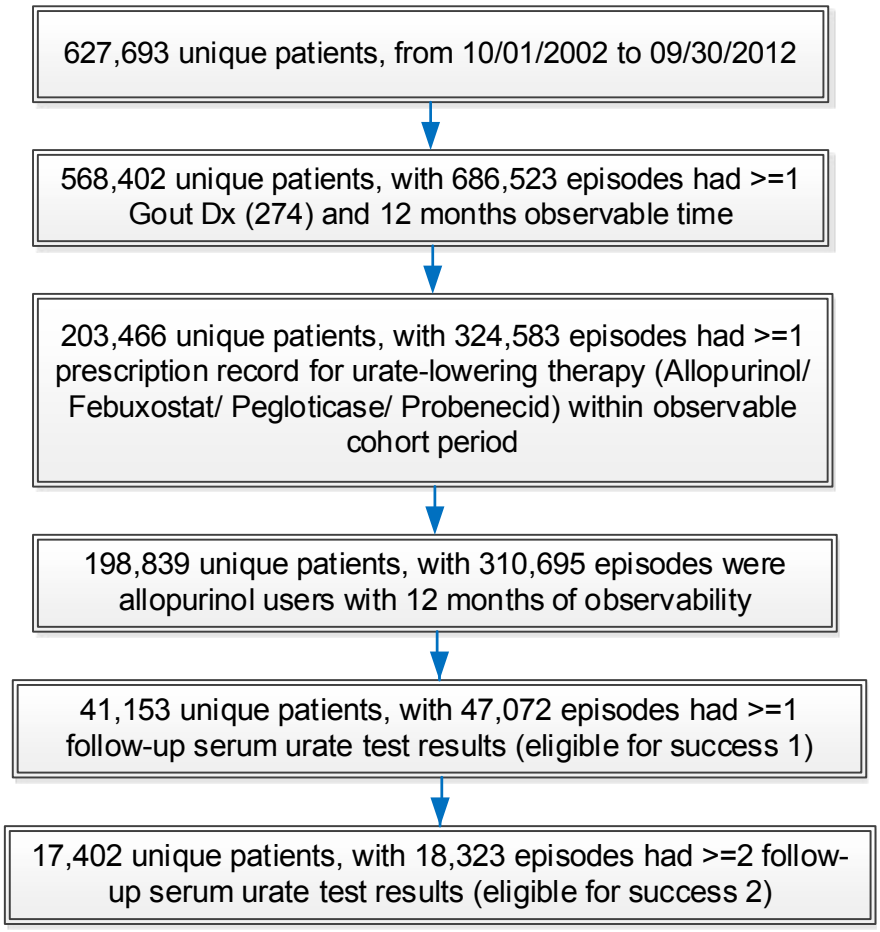
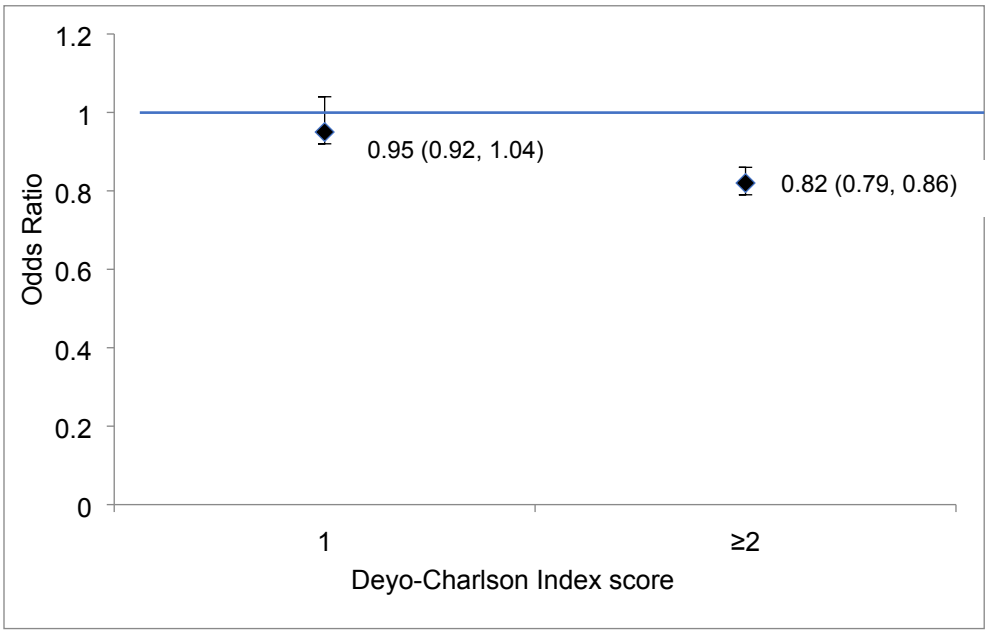


Figure 2. Association of Deyo-Charlson comorbidity index score with achieving or achieving and maintaining target serum urate of <6 mg/dl in the multivariable-adjusted model

2a. Odds Ratio of achieving target serum urate of <6 mg/dl (success 1) by Deyo-Charlson Comorbidity Index Score



2b. Odds Ratio of achieving and maintaining target serum urate of <6 mg/dl (success 2) by Deyo-Charlson Comorbidity Index Score