Taylor & Francis
Taylor & Francis Group

Scandinavian Journal of Rheumatology

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/irhe20

Gout in Dalarna, Sweden – a population-based study of gout occurrence and compliance to treatment guidelines

V Sigurdardottir, A Svärd, LTH Jacobsson & M Dehlin

To cite this article: V Sigurdardottir, A Svärd, LTH Jacobsson & M Dehlin (2023) Gout in Dalarna, Sweden – a population-based study of gout occurrence and compliance to treatment guidelines, Scandinavian Journal of Rheumatology, 52:5, 498-505, DOI: 10.1080/03009742.2022.2132055

To link to this article: https://doi.org/10.1080/03009742.2022.2132055

Gout in Dalarna, Sweden – a population-based study of gout occurrence and compliance to treatment guidelines

V Sigurdardottir[1,2], **A Svärd**[2], **LTH Jacobsson**[1], **M Dehlin**[1]

[1]Department of Rheumatology and Inflammation Research, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden
[2]Centre for Clinical Research Dalarna, Uppsala University, Falun, Sweden

Objective: This study aimed to describe the incidence and prevalence of gout, describe the use of allopurinol among prevalent gout cases, and determine persistence with allopurinol and degree of compliance with treat-to-target recommendations before and after the publication of Swedish national guidelines in 2016.

Method: Prospectively registered data on gout diagnoses and allopurinol prescriptions were used to calculate incidence and prevalence, and the proportion of prevalent patients on allopurinol. Gout patients starting allopurinol during 2013–2015 versus 2016–2018 were compared regarding persistence and compliance with treat-to-target principles.

Results: The incidence of gout was 221–247 per 100 000 person-years during 2014–2019, prevalence in 2018 was 2.45%. Among prevalent cases, the proportion on allopurinol ranged from 21% to 25%. Allopurinol persistence was better for individuals starting therapy during 2016–2018 compared with 2013–2015 (45% vs 39%, $p = 0.031$), as were several outcomes related to treat-to-target principles, e.g. measuring baseline serum urate (SU) (84% vs 77%, $p < 0.001$), follow-up SU (50% vs 36%, $p < 0.001$), and the proportion of patients reaching an SU level < 360 µmol/L (45% vs 30%, $p < 0.001$).

Conclusion: Incidence and prevalence were slightly higher than in previous Swedish reports. Allopurinol use among prevalent gout patients did not increase during 2014–2019. Only a minor improvement in persistence was seen, and a moderate increase in compliance with guidelines, suggesting a need for improved management and extended patient involvement to increase and optimize the use of urate lowering therapy.

An increasing incidence of gout has been reported from many parts of the world (1). Within-country geographical variations in the incidence and prevalence of gout have been reported from some countries (2–5), which could reflect variations in genetics, diet, or possibly environmental exposure.

In Sweden, register-based studies on the occurrence of gout are available from the three largest urban areas, including and surrounding Stockholm (6), Gothenburg (7), and Malmö (8). Reports on the incidence rate and prevalence of gout from areas of Sweden outside the major cities are lacking.

Gout is caused by urate crystal deposition in the setting of hyperuricaemia, which is treatable with urate-lowering therapy (ULT).

The indications for and use of ULT in gout are addressed in clinical guidelines from the European League Against Rheumatism (EULAR) (9) and the American College of Rheumatology (ACR) (10), and in the Swedish Medical Products Agency guidelines, which were published in 2016 (11); a summary of these guidelines is provided in supplementary table S1.

In brief, the Swedish guidelines are consistent with the EULAR recommendations in recommending that ULT is indicated for patients with recurrent flares, tophi, and/or renal stones, and indicated at first presentation of gout for patients with severe clinical features. Both focus on a treat-to-target-based approach to ULT, using allopurinol as a first line drug. To follow these recommendations, the clinician should practise individualized dose titration of allopurinol to achieve a serum urate (SU) goal of < 360 µmol/L (< 300 µmol/L for patients with severe gout). It is recommended to start ULT with a low dose and to increase the dose gradually until the SU target is achieved.

In Sweden, allopurinol is the most used ULT, while other available ULTs are febuxostat and probenecid. In 2021, 98% of all dispensed ULT was allopurinol (12) (supplementary figure S1).

Numerous reports from around the world have shown that ULT is underutilized in gout, and that when it is prescribed, adherence and persistence with therapy over time are poor (5, 13, 14). Adherence is a measure of

V Sigurdardottir, Centre for Clinical Research Dalarna, Box 712, 791 29 Falun, Sweden.
E-mail: valgerdur.sigurdardottir@regiondalarna.se

Accepted 30 September 2022

DOI: https://doi.org/10.1080/03009742.2022.2132055

whether the patient takes the medication as prescribed on a day-to-day basis, whereas persistence is a measure of whether the patient persists in taking the medication for the intended duration of therapy (15). Non-persistence is commonly defined in studies to occur when a gap exceeding a predefined number of days occurs in medication supply (15).

In this study, our aims were: (i) to describe the incidence rate (for 2014–2019) and prevalence (in 2018) of gout in the Swedish region of Dalarna and to compare the incidence rate to historical reports of gout incidence in other Swedish regions; (ii) to describe the proportion of prevalent cases receiving allopurinol for 2014–2019; (iii) to describe 2 year persistence on allopurinol in patients with gout initiated on allopurinol before and after the publication of treat-to-target-oriented Swedish gout treatment guidelines in 2016 (11); and (iv) to determine healthcare-provider compliance with treat-to-target principles in the management of gout with allopurinol, before and after publication of the first Swedish national guideline for gout management in 2016 (11).

Method

Study design, study population, and setting

This is a population-based study using register data from regional and national healthcare registers.

All inhabitants in the Swedish region of Dalarna (total population 285 000) over the age of 20 years with an International Classification of Diseases, 10th revision (ICD-10) or ICD-10-SE-coded gout diagnosis during the years 2000–2019 were included in the analyses of incidence rate and prevalence of gout and utilization of ULT among prevalent cases. The ICD-10-SE is an abbreviated version of the ICD-10 classification system that was used in primary care in Dalarna until 2013. Diagnostic codes used for the identification of gout patients are shown in supplementary table S2, and Anatomical Therapeutic Chemical (ATC) classification system codes used to identify ULT prescriptions are shown in supplementary table S3.

Compared to Sweden as a whole, the region of Dalarna has an older population (supplementary figure S2). The region of Dalarna is situated in the middle of Sweden, with more than 20 primary care units and four hospitals (supplementary figure S3). The region is sparsely populated, with 10.3 inhabitants per square kilometre (16). Of the total population, 83% live in smaller towns, ranging in size from 200 to 45 000 inhabitants (16).

Individuals with a gout diagnosis who were prescribed ULT with allopurinol for the first time during the years 2013–2015 and 2016–2018 were included in the analyses of persistence with ULT and compliance with treat-to-target principles of clinical guidelines (n = 1709). For this analysis, individuals with a prior prescription of allopurinol were excluded (data available from 2000).

Data sources

All data used in this study, except for information on date of death, were captured from the electronic medical health record system in the region, where all healthcare contacts are registered.

For the years 2000–2012, only data from primary care were available. From 2013 onwards, data from all healthcare levels were available (supplementary figure S4).

The electronic medical health record holds data from all visits to healthcare providers in the region, including diagnoses (according to ICD-10) and results of laboratory tests. The electronic medical health record also stores data on all electronic prescriptions, i.e. prescriptions made by a physician that are sent electronically to a pharmacy.

Information on date of death and region of residence was collected from the Swedish census register up until 31 December 2018.

Ethics and consent

The study was approved by the Ethical Review Board of Uppsala, Sweden (approval numbers 2015/435 and 2015/435/1). Individual participant consent was waived, as data were derived from administrative registers that do not require such consent according to Swedish law.

Outcomes

Incidence rate and prevalence. Incidence rate and prevalence were calculated using the date of the first ICD-10-coded gout diagnosis registered at a visit to a physician as the incident date. Incidence rate (age and sex standardized to the Swedish population in 2019 using the direct method) is reported for the years 2014–2019 and prevalence is reported for 2018.

To enable comparison to the incidence rate of gout in 2012 reported from the Western Swedish Healthcare Region (WSHCR) (7), we also calculated incidence standardized to the Swedish population in 2012 (supplementary figure S5).

Proportion of prevalent cases with ULT indication and proportion on allopurinol. For prevalent cases in 2018, we assessed the proportion of cases with an indication for ULT according to clinical guidelines. All cases with more than one healthcare contact with a gout diagnosis (interpreted as having had more than one flare of gout) were classified as having an indication for ULT. Cases with only one healthcare contact with a gout diagnosis were classified as having an indication for ULT if they

had SU > 480 μmol/L and/or renal impairment [estimated glomerular filtration rate (eGFR) < 60 mL/min], or if they were younger than 40 years at gout diagnosis. We were not able to assess the presence of tophi, renal stones, or comorbidities other than renal impairment from the available data.

For the years 2014–2018, we calculated the proportion of prevalent cases who were prescribed allopurinol at least once during the corresponding year.

Definition of baseline laboratory characteristics. SU and creatinine measurements that were performed from 90 days before to 7 days after the first allopurinol prescription date were considered as baseline values. If an individual had several measurements during this time window, the value closest in time to the date of first prescription of allopurinol was chosen as the baseline value. The rationale behind the time window was to maximize the proportion of patients with available baseline laboratory values, while treating both groups equally and still including only reasonably recent measurements. The reason for setting the cut-off to +7 days in relation to the allopurinol prescription date was that sometimes allopurinol is prescribed and a baseline SU and creatinine blood test is ordered but for practical reasons not performed until a few days later; this was the case for less than 2% of the baseline values. Sensitivity analyses using different time windows for the definition of baseline SU were performed and are presented in supplementary table S4, all producing similar results.

We estimated the baseline eGFR from the baseline creatinine values using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation (17).

Persistence with allopurinol therapy. All individuals with a first prescription of allopurinol between 5 February 2013 and 25 November 2018 were included and followed for a minimum of 730 days from the day of the first prescription or until their date of death.

The end date for inclusion of 25 November 2018 was chosen to ensure that all included individuals would have available follow-up data for a minimum of 730 days. The start date of 5 February 2013 was chosen since from that time, data from all healthcare levels, both primary and secondary care, were available.

The chosen time period was divided into two equal parts: individuals with a date of first allopurinol prescription during the first period of 1059 days, from 5 February 2013 to 31 December 2015, were assigned to the period 2013–2015; and those starting allopurinol from 1 January 2016 to 25 November 2018 were assigned to the period 2016–2018. The rationale behind this division into two periods was to enable comparison of treatment persistence and degree of compliance with treat-to-target principles by prescribers before and after publication of the Swedish national guidelines for gout management in 2016 (11).

Allopurinol prescription dates were used to define individuals as allopurinol persistent or allopurinol non-persistent.

The duration of allopurinol supply provided by each prescription was determined based on the number of iterations. Typically, prescriptions in Sweden are issued so that one iteration provides 3 months of therapy, as only 3 months of medication are reimbursed per dispensation. We assumed 80% adherence, i.e. one iteration was defined to provide a 125 day supply of allopurinol.

Non-persistence with allopurinol therapy was defined as having occurred when the duration of the previous prescription +30 days had passed without a new prescription for allopurinol being made (Figure 1).

Degree of healthcare provider compliance with treat-to-target principles during 2013–2015 and 2016–2018.

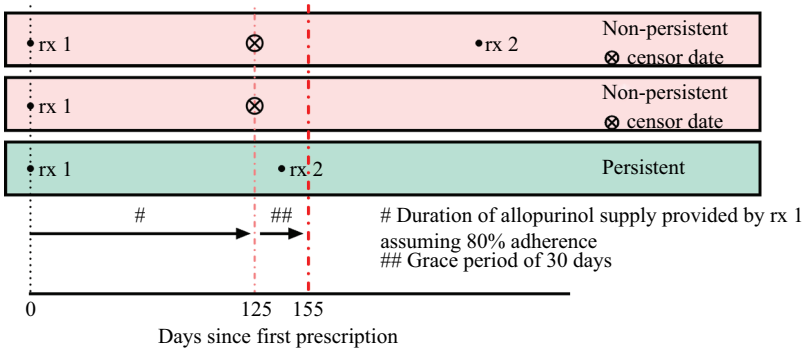


Figure 1. Schematic representation of two non-persistent individuals (represented by the top two boxes) and one persistent individual (represented by the bottom box), who all receive a first prescription of allopurinol with one iteration on day 0 (rx 1). The non-persistent individual in the uppermost box receives a second prescription (rx 2) after the end of the grace period; therefore, non-persistence is defined to have occurred at the end of the supply of allopurinol provided by the first prescription. The second non-persistent individual (middle box) receives no second allopurinol prescription and is also defined as non-persistent at the end of the supply of allopurinol from the first prescription. The third individual (bottom box) is defined as persistent until the end of follow-up (provided that subsequent allopurinol prescriptions occur within the grace period of rx 2 and so on during the whole period of follow-up).

The following outcomes were chosen based on the EULAR recommendations for management of gout (9), which are consistent with the Swedish guidelines for gout management (11): (i) the proportion of patients with a follow-up SU test within 3 months of starting allopurinol (EULAR recommendation 6); (ii) the proportion of patients achieving an SU level ≤ 360 µmol/L ever during follow-up (patients with no follow-up SU test were defined as not reaching the SU goal) (EULAR recommendation 6); (iii) the number of SU tests during follow-up (i.e. from day 8 to day 730 in relation to the initiation of allopurinol) (EULAR recommendation 6); (iv) evidence of dose titration of allopurinol over time, i.e. the mean daily dose of subsequent prescription being higher than that of the first prescription (EULAR recommendation 7) – the average prescribed daily dose was defined as the total prescribed dose in milligrams divided by days with available allopurinol (here assuming 100% adherence to reflect the daily dose intended by the prescriber); when defining exposed days/days with available allopurinol, we disregarded periods with overlapping prescriptions, i.e. if a prescription was renewed before the duration of the previous one had expired, days were not counted as exposed twice; and (v) the proportion of non-persistent patients who were subsequently prescribed febuxostat and/or probenecid (EULAR recommendation 8); this was defined as a prescription for febuxostat and/or probenecid within 2 years after non-persistence with allopurinol occurred.

In addition, we studied the proportion of patients with an SU test at or around the start of ULT (i.e. baseline SU).

Statistical analysis

Descriptive statistics were used to describe the study population, using the t-test and paired t-test to compare means as applicable for continuous measures, and the chi-squared test for between-group comparison of categorical measures. Linear regression was used to test whether there was a linear time trend in for the proportion of prevalent cases treated with allopurinol, with year as the independent variable.

Survival analyses with Kaplan–Meier curves and log-rank test were used when comparing persistence with allopurinol between patients starting allopurinol in 2013–2015 and those starting in 2016–2018. Cases were censored at death or end of follow-up, whichever occurred first.

Survival analyses, descriptive statistics, and linear regression analysis were conducted using STATA (version 16). Analyses of incidence rate and prevalence were performed in R (package 'dsr').

Results

Incidence rate and prevalence of gout

In total, 10 290 individuals with an ICD-10-coded gout diagnosis during 2000–2019 were identified. The yearly incidence rate of gout in 2014–2019 (directly standardized to the Swedish population in 2019) varied from 221 to 247 cases per 100 000 person-years (Figure 2A). The incidence rate in 2014–2019 compared with the incidence rate of gout reported from the WSHCR in 2012 is shown in supplementary figure S5.

By the end of 2018, there were 6200 alive individuals with prevalent gout residing in the region, whereas the total population older than 20 years was 222 803, corresponding to a crude prevalence of gout of 2.78% [95% confidence interval (CI) 2.71–2.85]. The standardized prevalence of gout in 2018 was 2.45% (95% CI 2.39–2.51). The prevalence of gout by age group and sex in 2018 is shown in Figure 2(B).

Proportion of prevalent cases with ULT indication and proportion on allopurinol

Among prevalent gout cases in 2018 (n = 6200), 52% had had more than one healthcare contact with a diagnosis of gout, 47% had an SU level > 480 µmol/L at or before the first gout diagnosis,

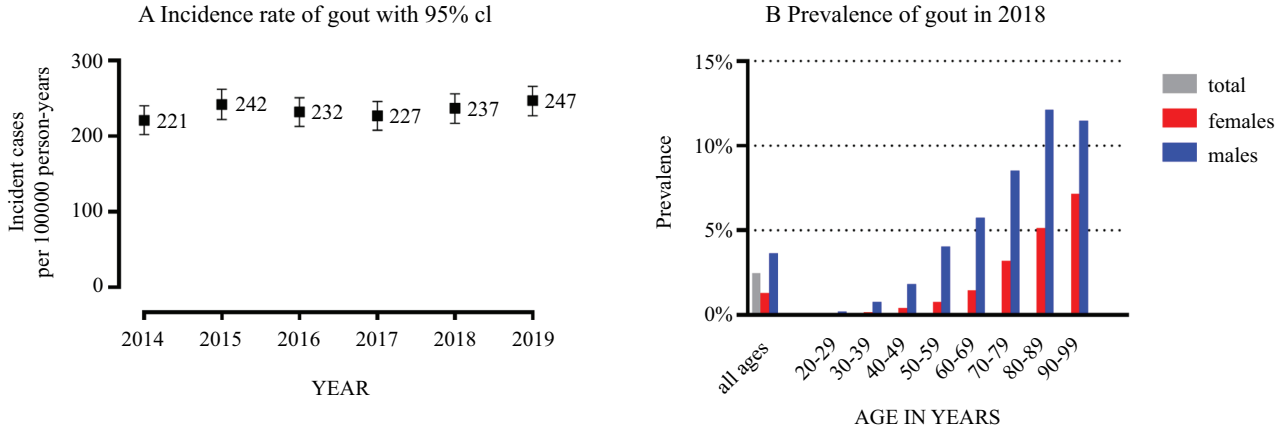
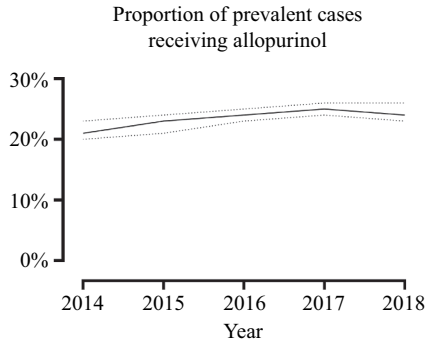


Figure 2. (A) Incidence rate of gout in 2014–2019, standardized to the Swedish population in 2019. (B) Prevalence of gout in 2018, in total and by sex and age groups.



	2014	2015	2016	2017	2018
Prevalent cases, n	5001	5334	5649	5921	6200
On allopurinol, %	21%	23%	24%	25%	24%

Figure 3. Proportion of prevalent cases receiving allopurinol per year. Dotted lines indicate the binomial 95% confidence intervals of the proportions.

7% were younger than 40 years at their first gout diagnosis, and 32% had renal impairment (eGFR < 60 mL/min). In total, 76% of the prevalent cases fulfilled one or more conditions that should lead the clinician to consider initiation of ULT.

The proportion of prevalent gout cases receiving allopurinol ranged from 21% to 25% during 2014–2018, with no significant change over time (p = 0.08) (Figure 3).

Persistence with allopurinol in patients initiated on allopurinol in 2013–2015 and 2016–2018

In total, 1709 individuals were initiated on allopurinol for the first time between February 2013 and November 2018, and were included in the analysis of persistence with allopurinol therapy and degree of compliance with treat-to-target principles.

Baseline characteristics of individuals initiated on allopurinol during the periods 2013–2015 and 2016–2018 are shown in Table 1(A).

Of those starting therapy during 2016–2018, 45% were alive and persisting with allopurinol at the end of follow-up compared with 39% of those who started therapy during 2013–2015 (log-rank p = 0.031) (Fig-Figure 4).

Compliance with treat-to-target principles

Individuals initiated on allopurinol during the period 2016–2018 were more likely to be treated with a treat-to-target approach, as reflected by a higher proportion having a baseline SU test (84% vs 77%, p < 0.001), a higher proportion having a follow-up SU test within 3 months (50% vs 36%, p < 0.001), and a higher proportion reaching an SU value ≤ 360 µmol/L ever during follow-up (45% vs

Table 1. (A) Baseline characteristics of allopurinol initiators during the period 2013–2015 and 2016–2018. (B) Outcomes related to a treat-to-target approach in those starting allopurinol for the first time, comparing patients initiating therapy in 2013–2015 and 2016–2018.

	Time period		
	2013–2015 (n = 877)	2016–2018 (n = 832)	p
(A) Baseline characteristics			
Age (years)	68 ± 14	68 ± 14	0.667
Females	253 (29)	198 (24)	0.018
Males	624 (71)	634 (76)	
Time from first gout diagnosis to allopurinol initiation (days)	629 ± 1071	714 ± 1190	0.171
SU (µmol/L)	543 ± 110	525 ± 96	0.002
Creatinine (µmol/L)	111 ± 45	106 ± 82	0.255
eGFR (mL/min)	61 ± 24	67 ± 24	< 0.001
Follow-up time (days)	692 ± 133	699 ± 120	0.278
Died during follow-up	86 (10)	73 (9)	0.463
(B) Outcomes related to treat-to-target approach			
Baseline SU test performed	677 (77)	699 (84)	< 0.001
Received no subsequent allopurinol prescription	269 (31)	208 (25)	0.009
≥ 1 follow-up SU test within 3 months after starting allopurinol	319 (36)	419 (50)	< 0.001
Number of SU tests during follow-up	1.63 ± 2.18	2.08 ± 2.40	< 0.001
Follow-up SU ≤ 360 µmol/L ever	266 (30)	378 (45)	< 0.001
Change from baseline to lowest follow-up SU (µmol/L)*	−178 (−166 to −189)	−183 (−173 to −193)	na
Dose titration of allopurinol	183 (21)	291 (35)	< 0.001
Daily dose of allopurinol prescribed during follow-up (mg)†	111 (148)	185 (177)	< 0.001
Subsequently prescribed febuxostat and/or probenecid after becoming non-persistent with allopurinol‡	12 (2)	17 (4)	0.033

Data are shown as mean ± sd or n (%), unless otherwise indicated: *mean (95% confidence interval of difference); †median (interquartile range); ‡n (% of non-persisters).
SU, serum urate; eGFR, estimated glomerular filtration rate; na, not applicable.

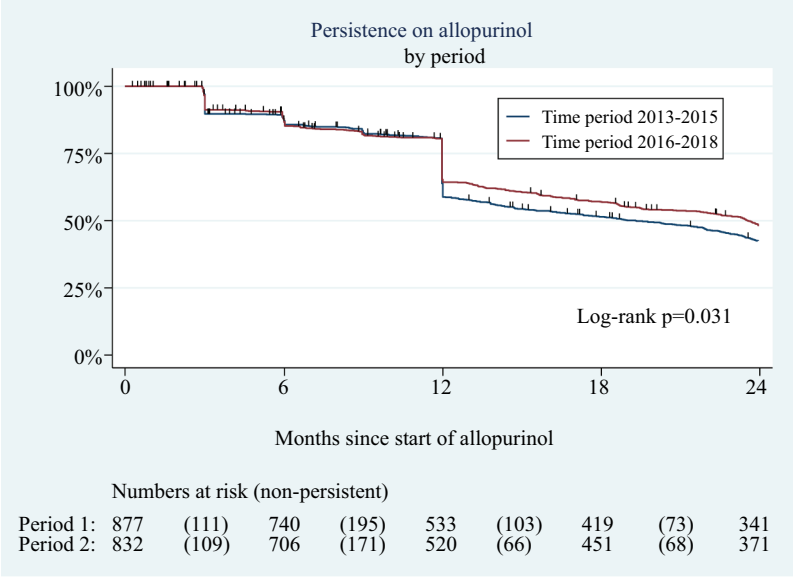


Figure 4. Kaplan–Meier curves describing the persistence on allopurinol up to 24 months after initiation. Non-persistence was defined as occurring at the time-point when a first gap in allopurinol supply of > 30 days occurred. Tick marks indicate individuals censored because of death.

30%, p < 0.001). Outcomes related to a treat-to-target approach are summarized in Table 1(B).

Discussion

In the present regional study from Sweden, we found slightly higher prevalence and incidence rates of gout than previously reported from other Swedish regions. This could be explained by temporal changes in the incidence of gout, or by different risk factor profiles of the populations examined. A slightly higher proportion of the population in Dalarna is overweight or obese (57%) compared with the total population of Sweden (52%) (18). As body mass index and other anthropometric measures, such as body weight and waist circumference, have been shown to be predictive of incident gout (19), this could be one contributory explanation for the higher incidence and prevalence of gout in the region.

Among the prevalent gout cases, we estimated 76% to have an indication for ULT, but the proportion being treated with allopurinol was only 21–25% during 2013–2018. This indicates underutilization of ULT and/or lack of persistence with ULT among prevalent cases, to an even greater degree than the proportion reported from Western Sweden, where 42% of prevalent cases received allopurinol in 2012 (7), and from the UK, where 37% of prevalent gout patients were on ULT in 2012 (5); however, our results are very similar to those reported from Taiwan (4). In a 2021 meta-analysis of ULT in gout, the pooled proportion of patients with gout who received ULT was 52% (95% CI 45–59%) (20). A plausible explanation for the proportion of ULT users among prevalent cases being comparatively low in the present study could be the long period of case ascertainment in our study, where we were able to identify and include all individuals who had received a gout diagnosis during the past two decades in the denominator.

Patient persistence with ULT at 24 months after initiation was suboptimal, although it improved slightly for those initiating therapy in 2016–2018 (45%) compared with 2013–2015 (39%) (p = 0.031). The level of persistence was low even though we used a liberal definition of persistence.

Persistence with allopurinol was higher in our study compared with reports from other settings. Scheepers et al reported persistence of 42% at 12 months in a study from the UK of patients with gout initiating allopurinol from 1987 to 2014, using a definition of non-persistence that was similar to ours (13), whereas 1 year persistence in our material was 62% (both periods combined). Persistence at 2 years in our study was also higher than that reported from Western Sweden, which was only 25% at 2 years after initiation (14).

Non-persistence with medical therapy is a problem in many chronic conditions, and not only gout. In a study from 2008, Briesacher et al reported persistence rates with medical therapy in gout and six other chronic conditions (21), finding that the proportion of patients with a medication possession ratio (MPR) > 0.8 during the first year of therapy varied between 36.8% and 72.3%; patients with gout had the lowest MPR, whereas the MPR for anti-hypertensive therapy was the highest.

Minor improvements were observed regarding the compliance of healthcare providers with treat-to-target oriented recommendations, with more patients having both baseline and follow-up SU testing performed during the period 2016–2018 compared with 2013–2015, a higher proportion of patients reaching SU ≤ 360 µmol/L, and a higher proportion of patients receiving allopurinol titration. Very few patients received a second line ULT (febuxostat and/or probenecid) within 2 years of becoming non-persistent with allopurinol.

Our results regarding treat-to-target outcomes are within the range of the findings of a 2021 meta-analysis of treat-to-target care for gout (20), where the pooled proportion of ULT users having any SU testing after starting or changing ULT was 44% (95% CI 36–52%), whereas the pooled proportion of ULT users reaching the SU goal was 34% (95% CI 28–42%). Studies reporting the proportion of patients who receive allopurinol in titrated doses based on SU are scarce; one single-centre retrospective study from the UK found that of 63 allopurinol users, 21% received dose titration based on SU (22).

Poor compliance with clinical guidelines is a widespread phenomenon seen for many clinical conditions and different healthcare settings, and thus not a problem restricted to gout (23). The implementation of clinical guidelines depends on several factors on multiple levels; on the microlevel it depends on the individual behaviour of clinicians and patients, and on the macrolevel on the organization and resources of healthcare systems (23). The publication of evidence-based clinical guidelines is thus not automatically followed by implementation in patient care. Successful implementation of clinical guidelines can be enhanced by active implementation strategies, but such strategies are rarely used in clinical reality. In a study from 2018, Doherty et al showed that the management of gout in a primary care setting, by nurses who had received training regarding gout and its management according to national and international recommendations, was efficacious and cost-effective compared with usual care (24). Key components of the nurse-led care intervention in the study were patient education on gout and shared decision making (24).

An earlier review of the effects of educational strategies to improve compliance with clinical practice guidelines in arthritis (osteoarthritis and rheumatoid arthritis) care found limited evidence for strategies of educational outreach, peer-facilitated interactive workshops, and audit and feedback. These activities resulted in only modest improvement in patterns of prescribing by clinicians (25). Employing such strategies in isolation is therefore probably unlikely to be successful in improving clinician compliance with treatment guidelines for gout. Rather, the combination of educational strategies directed towards healthcare providers with strategies aiming to promote patient engagement, as was done in the study of nurse-led gout care by Doherty et al (24), seems more likely to improve the management of gout and patient outcomes. Another potentially successful strategy to increase patient engagement could be self-managed urate measurements with at-home devices that measure SU in capillary blood samples (26), perhaps combined with e-health solutions to guide dose titration of ULT.

This study has some limitations that should be discussed. Regarding the calculations of incidence and prevalence, the case definition used was based solely on ICD-coded diagnoses of gout. This introduces the possibility of misclassification. Reassuringly, a previous validation study performed in the WSHCR found a high positive predictive value for fulfilling diagnostic criteria for gout among individuals who had received an ICD-coded diagnosis of gout (27).

A limitation of our study regarding the outcome of persistence is that our data are prescription data and not dispensation data; therefore, the data do not capture whether prescriptions were dispensed at the pharmacy, only that the prescriptions were sent electronically to the pharmacy. The prescription data in this study are, on the other hand, a good measure of healthcare provider compliance with guidelines; other studies in Sweden often use dispensation data from the prescribed drug register, which, in contrast, only has data on prescriptions that are dispensed.

Another limitation is that as prescriptions are commonly prepared with four iterations for a total duration of 12 months, we did not capture non-persistence occurring during the first year for the 57% of the study population where this was the case. This produces a (probably artificial) sharp drop in the survival curves at 1 year, as it then becomes evident that no subsequent prescription is made. In reality, persistence with therapy probably drops off gradually in the first year, with patients not dispensing their allopurinol medication at the second, third, or fourth iteration of their first prescription. Lastly, in the analysis of persistence with allopurinol, we were not able to censor patients who possibly moved out of the region during follow-up owing to incomplete data on migration on the individual level. This should not influence the results as less than 0.5% of the population in the relevant age groups move out of the region per year (16) and, in addition, differential migration patterns in the two groups seem unlikely.

Strengths of the study include the population-based design, where we were able to identify all individuals with a gout diagnosis from 2000 onwards in the region. Furthermore, we were able to capture data on all SU measurements and ULT prescriptions during a long period, enabling us to describe the real-life management of gout in the region over time.

Conclusion

We have shown that the incidence and prevalence of gout were slightly higher in our region than in other areas of Sweden. There is an underutilization of ULT by patients with gout in our region. Although management improved after the publication of national guidelines/recommendations in 2016, both utilization of and persistence with ULT remained insufficient, with only marginal improvements. To achieve greater improvements will probably require education strategies targeting both healthcare providers and patients, possibly utilizing new ways of knowledge transfer and management.

Acknowledgement

We thank Göran Rörvall for assistance with retrieving primary care data from 2000–2013.

Disclosure statement

No potential conflict of interest was reported by the authors.

Funding

The study received grants from the Ester-Åsberg Lindberg foundation; the foundation had no input in the design of the study, in the collection, analysis, or interpretation of data, or in the writing of the manuscript.

Ethics and consent

The study was approved by the Ethical Review Board of Uppsala, Sweden (approval numbers 2015/435 and 2015/435/1). Individual participant consent was waived, as data were derived from administrative registers that do not require such consent according to Swedish law.

ORCID

V Sigurdardottir http://orcid.org/0000-0002-9907-4901

A Svärd http://orcid.org/0000-0002-2470-4307

LTH Jacobsson http://orcid.org/0000-0003-4402-148X

M Dehlin http://orcid.org/0000-0001-5165-0968

References

1. Dehlin M, Jacobsson L, Roddy E. Global epidemiology of gout: prevalence, incidence, treatment patterns and risk factors. Nat Rev Rheumatol 2020;16:380–90.
2. Gardner MJ, Power C, Barker DJ, Padday R. The prevalence of gout in three English towns. Int J Epidemiol 1982;11:71–5.
3. Trifiro G, Morabito P, Cavagna L, Ferrajolo C, Pecchioli S, Simonetti M, et al. Epidemiology of gout and hyperuricaemia in Italy during the years 2005-2009: a nationwide population-based study. Ann Rheum Dis 2013;72:694–700.
4. 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.
5. 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.
6. Wandell P, Carlsson AC, Ljunggren G. Gout and its comorbidities in the total population of Stockholm. Prev Med 2015;81:387–91.
7. Dehlin M, Drivelegka P, Sigurdardottir V, Svard A, Jacobsson LTH. Incidence and prevalence of gout in Western Sweden. Arthritis Res Ther 2016;18:164.
8. Kapetanovic MC, Hameed M, Turkiewicz A, Neogi T, Saxne T, Jacobsson L, et al. Prevalence and incidence of gout in southern Sweden from the socioeconomic perspective. RMD Open 2016;2:e000326.
9. Richette P, Doherty M, Pascual E, Barskova V, Becce F, Castaneda-Sanabria J, et al. updated EULAR evidence-based recommendations for the management of gout. Ann Rheum Dis 2016;2017:29–42.
10. Fitzgerald JD, Dalbeth N, Mikuls T, Brignardello-Petersen R, Guyatt G, Abeles AM, et al. 2020 American College of Rheumatology guideline for the management of gout. Arthritis Rheumatol 2020;72:879–95.
11. Swedish Medical Products Agency. Läkemedelsbehandling av gikt - behandlingsrekommendation. [In Swedish] [cited 2022 April 25]. Available from: https://www.lakemedelsverket.se/492c55/globalassets/dokument/behandling-och-forskrivning/behandlingsrekommendationer/behandlingsrekommendation/behandlingsrekommendation-gikt.pdf.
12. The National Board of Health and Welfare. The Health and Welfare Statistical Database: pharmaceuticals (online database) [cited 2022 March 10]. Available from: https://sdb.socialstyrelsen.se/if_lak/val_eng.aspx
13. Scheepers L, Burden AM, Arts ICW, Spaetgens B, Souverein P, de Vries F, et al. Medication adherence among gout patients initiated allopurinol: a retrospective cohort study in the Clinical Practice Research Datalink (CPRD). Rheumatology (Oxford) 2018;57:1641–50.
14. Dehlin M, Ekstrom EH, Petzold M, Stromberg U, Telg G, Jacobsson LT. Factors associated with initiation and persistence of urate-lowering therapy. Arthritis Res Ther 2017;19:6.
15. Cramer JA, Roy A, Burrell A, Fairchild CJ, Fuldeore MJ, Ollendorf DA, et al. Medication compliance and persistence: terminology and definitions. Value Health 2008;11:44–7.
16. Statistics Sweden. Population statistics (online database) [cited 2022 August 15]. Available from: https://www.statistikdatabasen.scb.se/pxweb/en/ssd/START__BE__BE0101/
17. Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF 3rd, Feldman HI, et al. A new equation to estimate glomerular filtration rate. Ann Intern Med 2009;150:604–12.
18. Public Health Agency of Sweden. Folkhälsodata (online database) [cited 2022 April 25]. Available from: http://fohm-app.folkhalsomyndigheten.se/Folkhalsodata/pxweb/sv/A_Folkhalsodata/A_Folkhalsodata__B_HLV__bFyshals__bbeFyshalsvikt/hlv1bmixreg.px/.
19. Wändell P, Andreasson A, Hagström H, Kapetanovic M, Carlsson A. The use of anthropometric measures in the prediction of incident gout: results from a Swedish community-based cohort study. Scand J Rheumatol 2019;48:294–9.
20. Son CN, Stewart S, Su I, Mihov B, Gamble G, Dalbeth N. Global patterns of treat-to-serum urate target care for gout: systematic review and meta-analysis. Semin Arthritis Rheum 2021;51:677–84.
21. Briesacher BA, Andrade SE, Fouayzi H, Chan KA. Comparison of drug adherence rates among patients with seven different medical conditions. Pharmacotherapy 2008;28:437–43.
22. Lim ELPT, Ern TS. The management of gout in primary care – are we doing it right? Res Medica 2014;22:101–10.
23. Pereira VC, Silva SN, Carvalho VKS, Zanghelini F, Barreto JOM. Strategies for the implementation of clinical practice guidelines in public health: an overview of systematic reviews. Health Res Policy Syst 2022;20:13.
24. Doherty M, Jenkins W, Richardson H, Sarmanova A, Abhishek A, Ashton D, et al. Efficacy and cost-effectiveness of nurse-led care involving education and engagement of patients and a treat-to-target urate-lowering strategy versus usual care for gout: a randomised controlled trial. Lancet 2018;392:1403–12.
25. Lineker SC, Husted JA. Educational interventions for implementation of arthritis clinical practice guidelines in primary care: effects on health professional behavior. J Rheumatol 2010;37:1562–9.
26. Fabre S, Clerson P, Launay JM, Gautier JF, Vidal-Trecan T, Riveline JP, et al. Accuracy of the HumaSens(plus) point-of-care uric acid meter using capillary blood obtained by fingertip puncture. Arthritis Res Ther 2018;20:78.
27. Dehlin M, Stasinopoulou K, Jacobsson L. Validity of gout diagnosis in Swedish primary and secondary care - a validation study. BMC Musculoskelet Disord 2015;16:149.

Supplementary material

Supplemental data for this article can be accessed online at https://doi.org/10.1080/03009742.2022.2132055