12-month results from the real-life observational treat-to-target and tight-control therapy NOR-Gout study: achievements of the urate target levels and predictors of obtaining this target

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ABSTRACT

Objectives Gout is often not adequately treated, and we aimed to apply urate lowering treatment (ULT) combined with individual information to achieve target serum urate (sUA) in clinical practice, and to identify predictors of achievement of this sUA target.

Methods Patients with a recent gout flare and sUA >360 µmol/L (>6 mg/dL) were consecutively included in a single-centre study and managed with a treat-to-target approach combining nurse-led information about gout with ULT. All patients were assessed with tight controls at baseline, 1, 2, 3, 6, 9 and 12 months including clinical examination, information on demographics, lifestyle, self-efficacy and beliefs about medicines. The treatment target was sUA <360 µmol/L and multivariable logistic regression was used to identify predictors of target attainment with ORs and 95% CIs.

Results Of 211 patients (mean age 56.4 years, disease duration 7.8 years, 95% males), 186 completed the 12-month study. Mean sUA levels decreased from baseline mean 500 to 311 µmol/L at 12 months with 85.5% achieving the treatment target. Alcohol consumption at least weekly versus less frequently (OR 0.14; 95% CI 0.04 to 0.55) as well as beliefs in overuse of medicines (OR 0.77; 95% CI 0.62 to 0.94) decreased the chance of reaching the treatment target, while higher self-efficacy for arthritis symptoms (OR 1.49 per 10 units; 95% CI 1.09 to 2.05) increased the likelihood.

Conclusions This study shows that target sUA can be achieved with ULT in most patients. Less self-reported alcohol consumption, low beliefs in overuse of medicines and higher self-efficacy are associated with treatment success.

INTRODUCTION

Gout is a prevalent inflammatory joint disease. Long-standing hyperuricaemia leads to formation and deposition of monosodium urate crystals in joints and other tissues with inflammation causing erosions, severe pain and disability. Globally, gout entails a significant burden of disease.

To reduce disease burden, initiation of urate lowering therapy (ULT) is recommended, and should be considered shortly after diagnosis. However, despite established and clear treatment recommendations and easily available and effective medication, gout is often poorly managed, and ULT is seldom started early in the disease. The concept of ULT gout treatment is challenged and not well perceived by physicians. Physicians do not view the impact of gout nearly as severely as patients do, and the majority of patients do not reach required target levels. These practices have led to...
poor medication adherence, with as few as 10% of patients with gout adhering to their treatment. A nurse-led study from Nottingham, UK, involved patients and included lifestyle advice along with a treatment-target strategy for ULT, demonstrating that >90% of participants reduced their serum urate (sUA) to <360 μmol/L at 1 year. A subsequent new randomised controlled trial demonstrated similar effectiveness over 2 years as compared with usual general practitioner-led care.

Reasons for unsuccessful treatment of gout with ULT may be inherent to treatment traditions among physicians contributing to low adherence to coping, lifestyle changes and medication. High alcohol consumption is seen in many patients with gout, but psychological factors, such as self-efficacy and beliefs in medicines have not been studied. Further, there is a scarcity of prospective clinical practice research to examine the effectiveness of ULT in a tight control and treat-to-target strategy and to identify factors associated with the sUA outcome (the target). In this study, we applied ULT and patient information in tightly scheduled follow-up visits to estimate how often the sUA target could be reached, and examined which factors predicted achievement of the target.

METHODS

Study design and participants

NOR-Gout (Gout in Norway) is a prospective, observational single-centre study in a hospital-based rheumatology unit. Patients were eligible if having a gout flare within the last month, had increased sUA levels (>360 μmol/L), and no contraindication for ULT. No other previous gout flares were required. They were consecutively included according to the protocol (ACTRN12618001372279). All had been diagnosed with gout based on identification of monosodium urate crystals in polarised microscopy after arthrocentesis and also satisfied the American College of Rheumatology/EULAR classification criteria. Exclusion criteria were unstable medical conditions (eg, ischaemic heart disease, impaired liver function); known stage 3b or higher chronic kidney disease (estimated glomerular filtration (eGFR) rate/creatinine clearance <45 mL/ min); recent surgery or gastrointestinal bleed; and age <18 years. Study candidates were identified during an acute clinical gout flare after examination in the department. Persons indicating willingness to participate in the study were contacted by a study nurse from the outpatient clinic for prescreening, received written information, and were scheduled for a baseline rheumatology outpatient visit at Diakonhjemmet Hospital. The sponsor of the study was Diakonhjemmet Hospital.

Treatment strategy

Trained research nurses had at the baseline visit individual consultations with patients comprising:

a. Information on disease and disease process, diagnosis, causes, recommended treatments, disease control.

b. Lifestyle advocacy on exercise, weight reduction and alcohol consumption.

c. Discussion of patient expectations, advice when to get help and coping. Further, a brochure addressed advice on diet.

At every visit, drug use was recorded for non-steroidal anti-inflammatory drugs (NSAID), colchicine, prednisolone and for ULT (allopurinol, febuxostat), registering drug dosage, adverse events and symptoms of flares.

All patients not already on ULT started as recommended oral allopurinol 100 mg one time a day and escalated in 100 mg increments monthly according to sUA concentrations to a maximum of 900 mg daily. If intolerance for allopurinol, febuxostat was started at 40 mg one time a day and escalated monthly to 80 and 120 mg as needed. Probencid or lesinurad could be added if necessary, but were not used in any patients. Patients received flare prophylaxis with colchicine 0.5–1 mg daily for 3–6 months. In this treat-to-target approach, ULT was escalated to reach <360 μmol/L (or <300 μmol/L if clinical tophi were present) and the dose was maintained when the target was reached.

Visits

All patients were assessed both by a study nurse and a rheumatologist (HBH, LK) at baseline as well as after 3, 6 and 12 months. Additional fixed visits with only study nurse were at 1, 2 and 9 months, and if necessary monthly, until the treatment target was reached. Telephone contact with review of the sUA results could substitute the face-to-face visits.

Covariates

Demographics and self-reported measures
At baseline, patients reported age, gender, ethnicity, marital status, family history for gout, disease duration, highest level of education, comorbidities and working status. For comorbidities, the Self-Administered Comorbidity Questionnaire was used (range 0–36); it includes 12 medical problems, allocating 1 point per problem including presence, receiving treatment and causing a functional limitation.

Alcohol consumption was assessed with the categories ‘Daily’, ‘Weekly’, ‘Monthly’ and ‘Never’, then aggregating the categories to daily/weekly and monthly/never. Daily and previous smoking, consumption of daily glasses with sugar sweetened drinks, and the frequency of physical activity were reported by patients.

At baseline, information on number of flares ever and during the last year (before the recent flare) was collected as well as pain severity during the most recent and the strongest flare (0–10 numerical rating scales), with 0=no pain and 10=unbearable pain.

Questionnaires at visits recorded present joint pain due to gout, general pain, fatigue and patient global assessment of disease activity on 0–10 numerical rating scales.
Physical function was measured with the Health Assessment Questionnaire (HAQ) without adjustment for help or devices. Health status was assessed by the Short Form general health questionnaire.

Self-efficacy with subscales for pain (five items) and symptoms (six items) was measured with the Arthritis Self-Efficacy Scales. This instrument measures whether patients have confidence in coping with pain, function and other symptoms due to arthritis (numeric rating scales 10–100, 100=highest).

The Beliefs about Medicines Questionnaire (BMQ) explores patients’ beliefs about medicines and includes scales on perceived necessity or concerns for the patient’s own medicines (5 items each, range 5–25), and for perceived general overuse and harm of medicines (4 items each with range 4–16). Items were scored on Likert scale 1–5, 5=highest agreement, and a high scale score reflects stronger belief in the expressed concept.

Clinical assessments
Clinical assessments included weight and height for calculation of body mass index (BMI) and 44-swollen and tender joint counts. Clinical subcutaneous tophi were counted. The largest was defined as index tophus, measured in length and width in millimetres.

Laboratory assessments
Laboratory examinations included sUA (µmol/L), erythrocyte sedimentation rate mm/hour, C reactive protein mg/L, creatinine (µmol/L), eGFR (mL/min/1.73 m²), as well as hematological status at baseline and each follow-up visit.

Outcomes
The primary outcome in this study was the percentage of patients who achieved sUA concentrations<360 µmol/L at 12 months, also for patients with tophi where a more ambitious target <300 µmol/L was applied. Secondary outcomes in the study were baseline factors tested for prediction of the primary outcome at 12 months.

Statistics
Descriptive measures of baseline variables are presented using absolute and relative frequency, mean and SD. Differences between groups were explored by use of independent samples t-test and by the χ² test or Fisher’s exact. OR and their 95% CIs were calculated by logistic regression analyses. Bivariate analyses were performed first. Candidate predictor variables of sUA target attainment were selected from the baseline data, based on their potential clinical relevance. We then included these in multivariable logistic regression analyses adjusting for age, gender, race, education, disease duration, BMI, comorbidities and baseline sUA. In the full model, we also included from bivariate analyses candidate variable if p<0.10 and we stepwise removed other variables not statistically significant. The patients not completing the 12-month assessment followed the same demographic profile as the completers. P<0.05 was defined as statistically significant. We did not adjust for multiple analyses. Calculations were performed with IBM SPSS Statistics (V.25).

RESULTS
Patient characteristics
Among patients with a recent gout flare, 242 patients were identified and prescreened for inclusion into the study, and 211 met inclusion criteria. Reason for non-inclusion were not meeting the required sUA or eGFR values (n=12), unpractical schedule (n=11), withdrawal of consent (n=7) and failure to meet for the scheduled baseline visit (n=1).

Of 211 patients, 186 (88.2%) completed the visit for the primary sUA endpoint at 12 months. The number of patients meeting for other time points was 202 (month 1), 193 (month 2), 189 (month 3), 176 (month 4), 75 (month 5), 187 (month 6), 55 (month 7), 42 (month 8), 167 (month 9), 60 (month 10), 27 (month 11). Patients not completing the 12-month follow-up had shorter disease duration, were more frequently daily smokers (both p<0.01), less frequently educated at college/university, married/cohabiting, working, physically active and had fewer previous gout flares (all p<0.05).

Patient baseline characteristics are provided in table 1. Females constituted 47.7% of included patients, and in the total cohort 16.6% had a clinical tophus.

Primary outcome
From baseline to 12 months, mean (SD) sUA decreased in all patients from 500 (77) to 311 (48) µmol/L (p<0.001), and in patients not reaching the target from 517 (117) to 393 (33) µmol/L (p=0.001, data not shown).

Table 2 gives sUA levels and frequencies for achieving sUA <360 µmol/L during the 12-month period, and separately also for the subgroup of patients with tophi for achieving sUA <300 µmol/L. A total of 85.5% of all patients at the 12-month visit reached the target sUA <360 µmol/L, and 69.3% already after 3 months. The proportions reaching the target did not increase between months 6 and 12. For the subgroup of patients with clinical subcutaneous tophi (n=35), sUA continuously declined and 54.8% met the treatment target <300 µmol/L after 12 months (table 2).

Medication and secondary outcomes
All 211 patients initiated or escalated ULT. Only 14.7% of patients had ever used allopurinol and none had used febuxostat, while 78% had experience with NSAID, and about half with colchicine and prednisolone. During the course of the first year, prescription of allopurinol decreased from 95.0% to 87.6%, and increased from 3.5% to 12.4% for febuxostat (table 3). Mean doses for allopurinol remained just below 300mg and below 60mg for febuxostat.

A flare during the study was experienced by 80.6% (150/187). During the 12-month study period, the percentage of patients with at least one swollen joint
was reduced from 35.3% (65/184) to 10.8% (20/185) (p<0.001) and with tophi from 16.7% (31/186) to 11.3% (21/186) (p=0.01), and with no statistically significant differences with respect to whether the sUA target was achieved or not. Creatinine and eGFR values remained unchanged, 96 (17) to 98 (19) µmol/L and 78.0 (19) to 79 (19) mL/min/1.73 m², respectively.

Bivariate analyses examined factors leading to achieving the treatment target <360 µmol/L after 12 months (table 4). Patients achieving the treatment target had less belief that medicines were generally overused compared with those not achieving the target (p=0.04).

Variables as predictors for reaching the treatment target

Baseline variables which could predict achieving the treatment target of sUA <360 µmol/L were then analysed in bivariate and multivariable logistic regression analyses and are described in table 5. In the first model, crude baseline values are shown with OR and CIs. Then, adjustments were made for age, gender, ethnicity, education, disease duration, BMI, comorbidities and baseline sUA. The final model is also fully adjusted for these variables.

Some factors predicted achieving the sUA target after 12 months in partly adjusted analyses: alcohol consumption at least weekly/daily versus monthly/never, low physical function according to HAQ, self-efficacy for symptoms and a perception of general overuse of medicines (BMQ). In the fully adjusted logistic regression model, three factors statistically significantly predicted

| Table 1 Baseline characteristics of all patients | N | % or mean (SD) |
|---|---|---|
| Age (years) | 211 | 56.4 (13.7) |
| Male | 201/211 | 95.3% |
| Caucasian | 183/202 | 90.6% |
| Disease duration (years) | 204 | 7.8 (7.6) |
| College education | 118/206 | 57.3% |
| Married/cohabiting | 155/208 | 74.5% |
| Working | 133/208 | 63.9% |
| Body mass index (kg/m²) | 211 | 28.8 (4.5) |
| Comorbidities (SCQ sum) | 210 | 3.7 (3.2) |
| Physical activity ≥3 times weekly | 163/207 | 30.4% |
| Smoking, daily | 23/208 | 11.1% |
| Alcohol consumption | 207 | |
| Daily | 17 | 8.2% |
| Weekly | 111 | 53.6% |
| Monthly | 55 | 26.6% |
| Never | 24 | 11.6% |
| Sugar sweetened drinks consumed daily | 80/207 | 38.6% |
| Tophus present (≥1) | 35/211 | 16.6% |
| No. tophi | 211 |
| 0 | 176 | 83.4% |
| 1–5 | 30 | 14.2% |
| >5 | 5 | 2.4% |
| Allopurinol use ever | 31/211 | 14.7% |
| NSAID use ever | 160/205 | 78.0% |
| Colchicine use ever | 107/201 | 53.2% |
| Prednisolone use ever | 91/199 | 45.7% |
| Baseline sUA (µmol/L) | 211 | 500 (77) |
| ESR (mm/hour) | 199 | 14.5 (14.2) |
| Creatinine (µmol/L) | 211 | 96.3 (18.6) |
| eGFR (mL/min per 1.73 m²) | 210 | 78 (19) |
| No. flares before recent one | 208 |
| None | 16 | 7.7% |
| 1 | 25 | 12.0% |
| 2–5 | 65 | 31.3% |
| >5 | 102 | 49.0% |
| Other flare experienced last 12 months before inclusion? | 151/206 | 73.4% |
| Strongest joint pain ever (0–10) | 208 | 8.4 (1.6) |
| Joint pain last flare (0–10) | 207 | 7.5 (5.5) |
| Swollen joint present | 72/209 | 34.4% |
| Tender joint present | 110/210 | 52.4% |
achieving the treatment target after 12 months (table 5); higher alcohol consumption at least weekly and belief that medicines were overused reduced the odds for achieving this target, whereas higher self-efficacy for symptoms, as an indicator for coping, increased it.

Neither baseline sUA nor final ULT dose with allopurinol were associated with the treatment target. Also, previous flares, baseline tophi, presence of swollen joints, as well as flares during the study were unrelated to reaching the treatment target. Sensitivity analyses examined also factors which predicted achievement of the most stringent treatment target of sUA <300 µmol/L in 35 patients with tophi. In bivariate analyses, only two variables—daily working and eGFR—were statistically significantly related to this target, but in multivariate analyses none of these or any other variables predicted reaching the target.

**DISCUSSION**

In this study, we examined how many patients with gout reached the sUA target of <360 µmol/L after 1 year when they were followed frequently by a nurse and a rheumatologist with information and escalating ULT as needed. This target was reached by 85.5% of patients completing the 12-month follow-up, in almost 70% already after 3 months, and few other patients achieved the treatment target after 6 months. We further identified predictors of reaching the treatment target. More frequent alcohol consumption at least weekly as well as a belief that drugs are overused reduced odds for achieving the target, while coping with arthritis symptoms increased the odds. Identification of all these three factors as predictors for achieving the treatment target are novel findings. Our study is large and with frequent follow-up visits, showing that the promoted urate target is realistic in daily clinical practice if patients are followed by a treat-to-target strategy.

The response rate in a randomised controlled trial from Nottingham, UK, was even higher than in our study with 95% after both 1 and 2 years, when care was provided by a nurse combining ULT and education as compared with primary care.20 A recent study from the Netherlands compared two treatment strategies,28 a more ambitious approach with a target of sUA <300 mol/L as compared with a target <360 µmol/L. During follow-up, an sUA value of <360µmol/L was numerically more frequently reached in the more ambitious approach by 83% versus 74%, but differences were not statistically significant.28 In a Mexican study, the target sUA was achieved in only 50%–70% after 3–4 years in spite of regular visits,29 and response rates by 12 months among general practitioners in the UK with sUA <360 µmol/L were 45%.30

### Table 2

| Month | 0       | 1       | 2       | 3       | 6       | 9       | 12      |
|-------|---------|---------|---------|---------|---------|---------|---------|
| All patients | sUA µmol/L (mean, SD) | 500 (78) | 413 (77) | 371 (64) | 341 (61) | 327 (59) | 316 (56) | 311 (48) |
| Target <360 achieved (%) | 0/211 | 43/202 | 94/193 | 131/189 | 151/187 | 136/166 | 159/186 |
| Patients with tophi | sUA µmol/L (mean, SD) | 506 (80) | 431 (78) | 388 (70) | 334 (56) | 318 (59) | 317 (59) | 298 (52) |
| Target <300 achieved (%) | 0/35 | 1/35 | 4/33 | 8/32 | 12/31 | 12/26 | 17/31 |

### Table 3

| % (n) allopurinol | % (n) febuxostat | Mean mg dose (range) allopurinol users | Mean mg dose (range) febuxostat users | Total prescription urate lowering therapy at follow-up |
|------------------|------------------|----------------------------------------|----------------------------------------|--------------------------------------------------|
| Before Baseline  | 14.7 (31/211)    | 0                                      | 109 (100–500)                         | 14.7%                                            |
| Month 1          | 95.0 (192/202)   | 3.5 (7/202)                            | 119 (100–600)                         | 51 (40–80)                                       | 98.5%                                           |
| Month 2          | 95.3 (184/193)   | 4.7 (9/193)                            | 190 (50–700)                         | 49 (40–80)                                       | 100.0%                                          |
| Month 3          | 94.2 (178/189)   | 5.8 (11/189)                           | 236 (50–700)                         | 54 (40–80)                                       | 100.0%                                          |
| Month 6          | 90.4 (169/187)   | 8.6 (16/187)                           | 273 (100–800)                        | 52 (40–120)                                      | 99.0%                                           |
| Month 9          | 89.2 (149/167)   | 9.6 (16/167)                           | 280 (100–900)                        | 50 (40–80)                                       | 95.8%                                           |
| Month 12         | 87.6 (163/186)   | 12.4 (23/186)                          | 289 (100–900)                        | 59 (40–120)                                      | 100.0%                                          |
| Participant baseline variables by response status after 12 months | Target achieved (sUA <360 µmol/L) | Target not achieved (sUA >360 µmol/L) | P value |
|---|---|---|---|
| Age (years) | 186 | 56.8 (13.6) | 57.4 (13.5) | 53.5 (13.4) | 0.17 |
| Male | 186 | 95.2% | 94.3% | 100% | 84.6% | 0.21 |
| White | 180 | 90.6% | 91.6% | 84.6% | 0.26 |
| Disease duration (years) | 182 | 8.2 (7.) | 8.0 (7.8) | 9.4 (8.3) | 0.42 |
| Education level college | 182 | 60.4% | 61.5% | 53.8% | 0.46 |
| Married/cohabiting | 183 | 77.0% | 77.7% | 73.1% | 0.60 |
| Working versus not | 183 | 66.7% | 66.9% | 65.9% | 0.52 |
| Body mass index | 186 | 28.9 (4.6) | 28.8 (4.6) | 29.6 (4.5) | 0.41 |
| Comorbidities (SCQ sum) | 185 | 3.8 (3.3) | 3.9 (3.3) | 3.0 (3.3) | 0.18 |
| Physical activity ≥3 times weekly | 182 | 33.0% | 33.8% | 28.0% | 0.57 |
| Smoking, daily | 183 | 8.2% | 7.6% | 11.5% | 0.93 |
| Alcohol consumption (at least weekly) | 182 | 61.5% | 59.0% | 76.9% | 0.08 |
| Sugar sweetened drinks consumed daily | 182 | 37.9% | 38.5% | 34.6% | 0.71 |
| Tophus present (≥1) | 186 | 16.7% | 18.2% | 7.4% | 0.16 |
| Allopurinol ever use | 186 | 14.0% | 13.8% | 14.8% | 0.90 |
| NSAID ever use | 180 | 79.4% | 77.9% | 88.5% | 0.22 |
| Colchicine ever use | 177 | 52.5% | 53.0% | 50.0% | 0.78 |
| Prednisolone ever use | 176 | 49.4% | 49.7% | 48.0% | 0.88 |
| Baseline sUA (µmol/L) | 186 | 498 (80) | 495 (72) | 517 (117) | 0.36 |
| ESR (mm/hour) | 176 | 14 (14) | 14 (14) | 16 (14) | 0.57 |
| Creatinine (µmol/L) | 186 | 96 (18) | 96 (17) | 98 (18) | 0.55 |
| eGFR (mL/min) | 185 | 78 (18) | 78 (18) | 79 (20) | 0.69 |
| No. flares before recent one | 187 | 0.82 |
| 0–1 | 34 | 18.6% | 17.9% | 23.0% | |
| 2–5 | 53 | 29.0% | 29.3% | 26.0% | |
| >5 | 96 | 52.5% | 52.9% | 50.0% | |
| Other flare last 12 months before inclusion | 181 | 75.1% | 74.2% | 80.8% | 0.79 |
| Strongest joint pain ever (0–10) | 183 | 8.3 (1.6) | 8.4 (1.5) | 8.1 (2.0) | 0.48 |
| Joint pain last flare (0–10) | 182 | 7.1 (2.0) | 7.1 (1.9) | 7.4 (2.4) | 0.40 |
| Swollen joint present | 184 | 35.3% | 35.7% | 33.3% | 0.82 |
| Tender joint present | 184 | 53.3% | 53.5% | 51.9% | 0.87 |
| Health Assessment Questionnaire | 184 | 0.36 (0.57) | 0.33 (0.54) | 0.56 (0.71) | 0.13 |
| SF-36 physical component summary (0–100) | 182 | 38.9 (10.8) | 39.2 (10.5) | 37.1 (12.4) | 0.38 |
| SF-36 mental component summary (0–100) | 182 | 50.4 (10.1) | 50.5 (10.5) | 50.2 (7.6) | 0.89 |
| Self-efficacy pain (10–100) | 184 | 65.3 (19.2) | 65.6 (19.1) | 63.9 (20.1) | 0.68 |
| Self-efficacy symptoms (10–100) | 180 | 72.8 (17.0) | 73.7 (16.9) | 66.9 (17.2) | 0.06 |
| Beliefs about Medicines Questionnaire | | | | | |
| Necessity (5–25) | 176 | 17.0 (4.3) | 17.0 (4.3) | 16.7 (4.5) | 0.74 |
| Concern (5–25) | 175 | 13.4 (4.4) | 13.4 (4.5) | 13.3 (3.7) | 0.92 |
| Overuse (4–16) | 179 | 10.6 (2.8) | 10.4 (2.7) | 11.6 (2.7) | 0.04 |
| Harm (4–16) | 179 | 9.4 (2.4) | 9.3 (2.5) | 10.0 (2.0) | 0.18 |

eGFR, electronic glomerular filtration rate; ESR, erythrocyte sedimentation rate; NSAID, non-steroidal anti-inflammatory drug; SCQ, Self-Administered Comorbidity Questionnaire; SF-36, Short-form 36.
Many patients with gout have high alcohol intake, and alcohol intake is related to the incidence of gout and frequency of flares. Compared with men who did not drink alcohol, the multivariate relative risk of gout increased dose dependently. We found that patients consuming alcohol at least weekly at baseline had a clearly reduced chance (OR 0.14) to prospectively achieve the treatment target as compared with less frequent or no alcohol consumption. This extends knowledge on the unfavourable effect of alcohol consumption from the risk of gout flares to achieving the sUA target.

Beliefs about medicines and patients’ attitudes towards administering medications are generally a good indicator of their intentions to adhere to treatments. One cross-sectional study from Hong Kong applied the BMQ in a mix of hospital outpatients including gout, and showed that the majority of the participants had strong beliefs that medicines were necessary and beneficial, while a minority had strong beliefs that medicines, in general, were overused, harmful and causing them concern. Our study was the first to longitudinally apply the BMQ with four subscales in gout and found that higher belief in overuse of medication independently impeded achieving the treatment goal, whereas beliefs on necessity, concerns and harm of medication did not.

Table 5 Predictors of baseline variables for reaching the treatment target serum urate (sUA) <360 µmol/L

| Predictor                              | Unadjusted OR (95% CI) | Partly adjusted OR (95% CI)* | Fully adjusted model OR (95% CI)† | Fully adjusted model p value |
|----------------------------------------|------------------------|------------------------------|---------------------------------|-----------------------------|
| Age (per 10 years)                     | 1.23 (0.99 to 1.66)    | 1.06 (0.72 to 1.57)          |                                 |                             |
| Disease duration (years)               | 0.98 (0.93 to 1.03)    | 0.99 (0.94 to 1.05)          |                                 |                             |
| Education college                      | 1.37 (0.60 to 3.16)    | 1.36 (0.54 to 3.42)          |                                 |                             |
| Body mass index                        | 0.96 (0.87 to 1.05)    | 0.98 (0.89 to 1.09)          |                                 |                             |
| Comorbidities (SCQ sum)                | 1.10 (0.96 to 1.26)    | 1.09 (0.90 to 1.31)          |                                 |                             |
| Alcohol (at least weekly vs less)      | 0.43 (0.16 to 1.13)    | 0.24 (0.04 to 0.78)          | 0.14 (0.04 to 0.55)             | 0.005                       |
| Baseline sUA (µmol/L)                  | 0.997 (0.992 to 1.002) | 0.996 (0.991 to 1.001)       |                                 |                             |
| Health Assessment Questionnaire        | 0.56 (0.30 to 1.04)    | 0.47 (0.20 to 0.99)          |                                 |                             |
| Self-efficacy pain subscale (10 units) | 1.05 (0.85 to 1.30)    | 1.13 (0.88 to 1.40)          |                                 |                             |
| Self-efficacy symptoms scale (10 units)| 1.26 (0.99 to 1.61)    | 1.38 (1.04 to 1.84)          | 1.49 (1.09 to 2.05)             | 0.014                       |

Beliefs about Medicines Questionnaire

| Belief Scale                         | Unadjusted OR (95% CI) | Partly adjusted OR (95% CI)* | Fully adjusted model OR (95% CI)† | Fully adjusted model p value |
|--------------------------------------|------------------------|------------------------------|---------------------------------|-----------------------------|
| Necessity (5–25)                     | 1.02 (0.91 to 1.12)    | 1.03 (0.91 to 1.16)          |                                 |                             |
| Concern (5–25)                       | 1.00 (0.91 to 1.11)    | 1.03 (0.93 to 1.14)          |                                 |                             |
| Overuse (4–16)                       | 0.84 (0.71 to 0.99)    | 0.83 (0.70 to 0.99)          | 0.77 (0.62 to 0.94)             | 0.013                       |
| Harm (4–16)                          | 0.88 (0.74 to 1.06)    | 0.88 (0.72 to 1.07)          |                                 |                             |

*Adjusted for age, gender, race, education, disease duration, body mass index, comorbidities, and baseline sUA and all other variables in logistic regression model.
†Adjusted for age, gender, race, education, disease duration, body mass index, comorbidities and baseline sUA and all other variables remaining in model logistic regression model.
SCQ, self-administered comorbidity questionnaire.

improve adherence to ULT. Qualitative research has also shown that trust in doctor and medication effectiveness were identified as the most important factors for adherence, indicating that thorough information and personal contact with the health provider could improve medication compliance.

Self-efficacy is related to the belief that one can cope with pain, reduced function or symptoms mediated by the disease. While no study previously assessed self-efficacy in gout, one study applied qualitative research and found that a sense of control was described as an important contributor to the overall patient experienced severity of gout. These results were supported by a study in diabetes where self-efficacy was increased by monitoring self-management patterns and accordingly providing feedback. In our study, information by the nurse as well as information about the decreasing load of crystal depositions during ultrasound assessments during the tight frequency of study visits may have contributed to increased self-efficacy and improved adherence.

We found no association between baseline sUA value and meeting the sUA target. An interpretation could be that persistent treatment with frequent adjustment of ULT was continuously applied to all patients when needed, making the initial sUA level less important. Two randomised controlled trials found that baseline sUA was related to the treatment response as measured by sUA. Further, healthcare access, patient and provider factors as well as presence of comorbidities were recently
reported associated to achieving and maintaining the target sUA level. 

Limitations of our study include that patients were entered from only one centre and findings cannot necessarily be extrapolated to other clinical settings. Second, the observational nature and lack of a control group in our study does not allow causal inferences. Further limitations were exclusion of patients with chronic kidney disease stage 3b and higher, and assessment of alcohol consumption by one question only.

Our findings support that existing treatment recommendations with a focus on ULT as well as information leads to achievement of the treatment target in the majority of patient. In this large prospective follow-up study in clinical practice, we found that patient information with escalating ULT lead to meeting the treatment target in gout in the vast majority of patients (about 85%) at follow-up. This study also provided new knowledge on predictors for the treatment outcome in gout. More frequent alcohol consumption and general beliefs that drugs are overused decreased the change achieving low sUA target values, whereas self-efficacy contributed to a good treatment outcome.

Successful gout management is attainable, and more attention towards addressing these modifiable factors could increase long-term adherence to ULT and health promoting lifestyle. Further research is required to investigate modifiable factors for achieving successful gout outcomes such as target sUA.

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Contributors TU has made a substantial contributions to the conception and design of the work; the acquisition of data, some of the analysis, interpretation of data for the work; and drafted the manuscript as well as revising it critically for important intellectual content; and given a final approval of the version to be published; and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. LFK, TB, EAH, TKK, and HBH have given substantial contributions to the design of the study as well as the interpretation of data for the work; and revised the manuscript critically for important intellectual content; and given a final approval of the version to be published; and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. JS has given substantial contributions to the design of the study as well as the interpretation of data for the work as a statistician; and revised the manuscript critically for important intellectual content; and given a final approval of the version to be published; and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Patient consent for publication Not required.

Ethics approval The study was approved by the Norwegian Regional Committee for Medical and Health Research Ethics South East (reference number 2015/990) and the patients gave their written informed consent according to the Declaration of Helsinki.

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Data availability statement Data are available upon reasonable request. The data will be shared if there is a reasonable request for it.

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