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Long-Term Follow-up of a Randomized Controlled Trial of Allopurinol Dose Escalation to Achieve Target Serum Urate in People With Gout

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ABSTRACT. ***Objective.*** To determine the long-term use of and adherence to urate-lowering therapy (ULT), serum urate (SU) control, and self-reported flares in participants from a randomized controlled trial of allopurinol dose escalation, in order to achieve target SU concentration (< 0.36 mmol/L) in people with gout.

Methods. For surviving study participants, ULT dispensing and SU testing within the preceding 12 months was obtained by medical record review. A phone interview was conducted to determine self-reported flares and adherence.

Results. Over a mean follow-up of 6.5 (SD 2.5) years since enrollment, 60 out of 183 (33%) participants had died. Review of the 119 surviving participants showed that 98 (82%) were receiving allopurinol, 5 (4%) were receiving febuxostat, and 10 (8%) were not receiving ULT; for the remaining 6 (5.0%), ULT use could not be determined. In those receiving allopurinol, the mean dose was 28.1 (range –600 to 500) mg/day lower than at the last study visit; 49% were receiving the same dose, 18% were on a higher dose, and 33% were on a lower dose than at the last study visit. SU values were available for 86 of the 119 (72%) participants; 50 out of 86 (58%) participants had an SU concentration of < 0.36 mmol/L. Of the 89 participants who participated in the phone interview, 19 (21%) reported a gout flare in the preceding 12 months and 79 (89%) were receiving allopurinol; 71 (90%) of those receiving allopurinol reported 90% or greater adherence.

Conclusion. Most of the surviving participants in the allopurinol dose escalation study had good real-world persistence with allopurinol, remained at target SU, and had a low number of self-reported flares.

Key Indexing Terms: allopurinol, gout, follow-up studies

Urate-lowering therapy (ULT) is the cornerstone of effective long-term gout management. However, ULT use is frequently suboptimal. A large systematic review reported that ULT was prescribed to less than 50% of people with gout in primary care, and only around 30% had serum urate (SU) monitored on a regular basis.[1] Long-term persistence with ULT is also low, with only 40% of patients continuing ULT after 5 years.[2] Reasons for suboptimal use of ULT include lack of clarity in guidelines of when to initiate ULT, health professional and patient misconceptions about gout, and time constraints in primary care consultations, making education and long-term management discussions difficult.[3]

Allopurinol is the mainstay of ULT in gout because of its effectiveness, favorable safety profile, low cost, and widespread availability. Our previous allopurinol dose escalation study[4,5] showed that dose escalation of allopurinol above a creatinine clearance–based dose is safe and effective in achieving target SU, including in people with chronic kidney disease (CKD). A key part of this trial, as well as in other successful urate-lowering studies, was regular, usually monthly, contact with participants and their availability by phone or email as required. When each participant completed the allopurinol dose escalation study, a letter was sent to their primary care physician (PCP) recommending lifelong ULT and the monitoring of SU every 6 months, as per the American College of Rheumatology 2012 gout guidelines, in order to encourage target SU maintenance.[6] Herein, we report a follow-up study that aimed to determine the long-term use of and adherence to ULT, SU control, and self-reported flares in participants more than 5 years after exiting the trial.

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METHODS

Study design and participants. We undertook a follow-up study with data collected between December 2020 and March 2021 at 2 sites in Aotearoa New Zealand. The study was approved by the Southern Health and Disability Ethics Committee, Aotearoa New Zealand (20/STH/205). Participants provided written informed consent in the original study; we attained verbal informed consent for our follow-up study where possible, among all contactable participants.

All participants who had enrolled in the allopurinol dose escalation trial[4,5] were eligible, including those who did not complete the initial trial (n = 45). The only participants excluded were those who did not consent to be contacted for future studies.

The original study was a 24-month trial of people with gout receiving allopurinol,[4,5] whose SU was ≥ 0.36 mmol/L, and who were enrolled between March 2012 and March 2014. At baseline, participants were randomized to 1 of 2 groups: one that would continue their current dose of allopurinol (control) or one that would have immediate allopurinol dose escalation (intervention). For those participants randomized to the control group, allopurinol dose escalation commenced at month 12. In both groups, allopurinol was increased monthly until SU was < 0.36 mmol/L for 3 consecutive months.

Study procedures. A New Zealand–wide electronic health database—Patient Information Care System—was used to determine which participants were deceased and their date of death. All surviving participants who had previously consented to be contacted for follow-up studies were sent the written participant information. Unless participants opted out by phone, email, or postal mail within 2 to 3 weeks of the information sheet having been sent, their electronic health record (EHR) was accessed to collect the required data and they were contacted for a telephone interview.

Data from the preceding 12 months were collected from the EHR, including the most recent SU concentration, creatinine concentration, and estimated glomerular filtration rate (eGFR); the latest ULT dispensed with dose; and comorbidities.

A phone interview was conducted, after verbal consent was obtained, to confirm current ULT and dose, any reason for ULT cessation, self-reported flares (ie, number of flares requiring treatment in the preceding 1 month, 3 months, and 12 months), and comorbidities. For participants receiving allopurinol, adherence was surveyed over the preceding month using a 5-part self-reported percentage scale (100%, 90% to < 100%, 50% to < 90%, < 50%, or never); this was our modification of a single-item visual analog scale for ease of use, which was administered by telephone.[7] If < 100% adherence was reported, the Intentional Non-Adherence Scale (INAS)[8] was administered. This 22-item scale identifies reasons why people may intentionally stop taking their medication. Item responses are scored on a 5-point Likert scale, where 1 = strongly disagree, 2 = disagree, 3 = neutral, 4 = agree, and 5 = strongly agree. The EHR was taken as the gold standard when there was a conflict with the phone interview medication dose.

Study outcomes. The primary outcome measures were the number of surviving participants who continued ULT and the number who remained at the target SU concentration (< 0.36 mmol/L). Secondary outcome measures included participant survival; change from last study visit in allopurinol dose, SU concentration, and eGFR; reasons for allopurinol discontinuation; adherence; and number of gout flares. Clinical features were compared between patients receiving ULT and those not receiving ULT. Finally, associations between SU concentration, creatinine concentration, allopurinol dose, and gout flares were examined.

Statistical analysis. Participant demographic and baseline clinical characteristics were summarized descriptively using frequencies, means, medians, ranges, SDs, and IQRs as appropriate. Comparisons of demographic and clinical features between those currently prescribed ULT and those not prescribed ULT were undertaken using chi-square tests, independent *t* tests, and Mann-Whitney *U* tests. The changes from the last study visit in SU concentration, allopurinol dose, and eGFR were tested using paired *t* tests and Wilcoxon signed-rank tests. Associations between SU concentration, allopurinol dose, creatinine concentration, and gout flares were examined using Spearman correlation coefficients and Kruskal-Wallis nonparametric tests. Kaplan-Meier estimates were used to summarize participant mortality from the point of randomization in the original study. A 2-sided *P* value of < 0.05 was taken to indicate statistical significance.

Patient and public involvement. Tikanga (Māori customary practices and behaviors) was incorporated into the study methodology with the guidance of Te Komiti Whakarite (The Māori advisory committee) at Christchurch Hospital, New Zealand.

RESULTS

Over a mean follow-up of 6.5 (SD 2.5) years since enrollment, 60 out of 183 (33%) participants had died. Of the surviving participants, 4 declined to participate and 1 declined to do the telephone interview (Figure). Of the 119 eligible surviving participants, 105 had laboratory results available and 97 had dispensing results available within the preceding 12 months. A telephone interview was completed for 89 out of 118 (75%) eligible participants. The remainder of the participants (n = 29) could not be contacted because they had no available contact number (n = 18) or did not respond (n = 11). Of the 29 who did not complete the telephone interview, 23 (79%) had up-to-date dispensing data, allowing for current ULT to be determined.

Demographic details. Demographic and clinical features of the surviving participants (n = 119) were recorded and grouped based on current ULT status (Table 1). The mean age of these participants was 64 (SD 12) years, and most of the participants were male (n = 109, 92%). The most common ethnicity was New Zealand European (n = 48, 40%), followed by Pacific Islander (n = 39, 33%) and Māori (n = 23, 19%). Obesity (n = 73, 61%), cardiovascular disease (n = 49, 41%), diabetes (n = 46, 39%), hypertension (n = 86, 72%), and hyperlipidemia (n = 82, 69%) were common coexisting conditions.

Participant survival. Kaplan-Meier estimates of participant survival following randomization (Supplementary Figure S1, available with the online version of this article) revealed a 1-year mortality of 6%, 5-year mortality of 24%, and 7-year mortality of 30%.

ULT use. Of the 119 surviving participants, 98 (82%) were still receiving allopurinol, 5 (4%) were receiving febuxostat, and 10 (8%) were not receiving any ULT (Table 1); for the remaining 6 (5%), ULT use could not be determined. Compared to the last study visit, out of 98 participants, 48 (49%) were receiving the same dose of allopurinol, 18 (18%) were on a higher dose, and 32 (33%) were receiving a lower dose. The mean allopurinol dose was 391 (range 100-950) mg/day, which was 28.1 (range −600 to 500) mg/day lower than at last study visit (Table 2). The mean allopurinol dose in those with eGFR that was < 30 mL/min/1.73 m^2 was 230 (SD 39) mg/day, as compared to 473 (SD 201) mg/day in those with eGFR > 60 mL/min/1.73 m^2 (P < 0.001; Supplementary Table S1, available with the online version of this article). There were 10 conflicts in allopurinol dose between the EHR and the patient report; in these 10 participants, the mean telephone-reported allopurinol dose was 110 mg/day lower than that reported in the EHR.

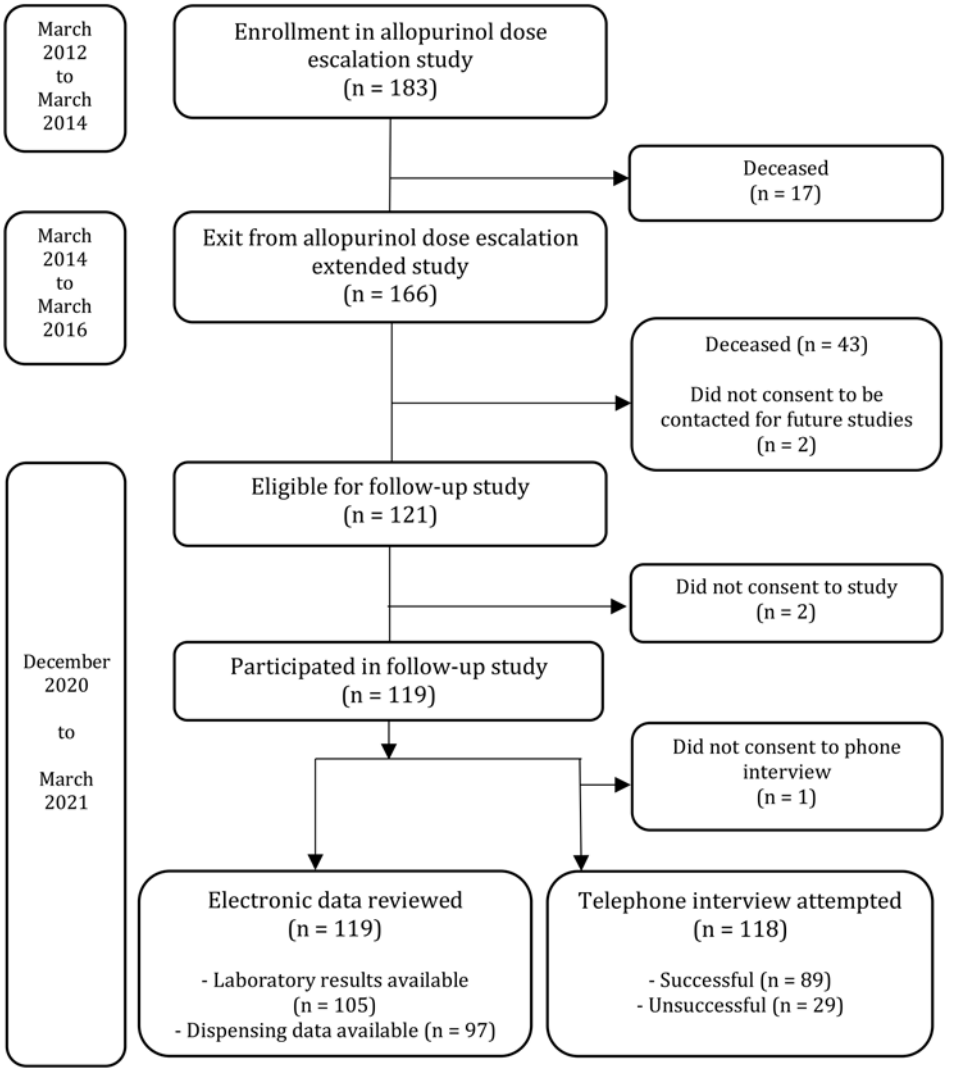

Figure. Flow diagram of participation in the study.

Of the 79 participants taking allopurinol at the time of the phone interview, 62 (79%) reported 100% adherence, 9 (11%) reported 90% to < 100% adherence, 4 (5%) reported 50% to < 90% adherence, 3 (4%) reported < 50% adherence, and 1 (1%) did not take any allopurinol over the preceding month. Reasons for allopurinol discontinuation were explored through telephone interview with 10 out of 15 of the participants who had stopped allopurinol. In total, 5 participants reported that it was "no longer needed," reporting no flares of gout in the long term; 2 stopped when they had kidney transplants; 1 changed to febuxostat, as they reported ongoing gout flares on allopurinol; 1 stopped because of a suspected adverse effect (feeling lightheaded); and 1 wanted to use Tongan traditional medicine as ULT. The INAS scores were calculated for the 17 participants who reported < 100% adherence (Table 3). Overall, the most agreed-upon reasons for intentional nonadherence were allopurinol being inconvenient to take all the time (mean score 2.9, SD 1.4), seeing if the medication is necessary (mean 2.7, SD 1.4), and the drug schedule not fitting in with participants' lifestyle (mean score 2.7, SD 1.4).

Serum urate. There were 86 out of 119 (72%) participants with an SU measurement available in the preceding year. Of those with any laboratory results available, 86 out of 105 (82%) had their SU tested. The mean SU concentration was 0.36 (SD 0.13) mmol/L, and 50 out of 86 (58%) participants with an SU measurement available were at target (< 0.36 mmol/L). The mean SU concentration was significantly lower in those receiving ULT (0.34, SD 0.12 mmol/L) compared to those not receiving ULT (0.50, SD 0.12 mmol/L; $P < 0.001$). Compared to the last study visit, the mean SU concentration was 0.02 (SD 0.12) mmol/L higher (Table 2). At follow-up, fewer participants were at target SU concentration compared to at the last study visit (50/86, 58% vs 136/183, 74%; $P = 0.007$).

The clinical characteristics of participants at target SU concentration (< 0.36 mmol/L) compared to those not at target SU concentration are shown in Table 4. Although not reaching statistical significance, the participant group at target SU concentration had, on average, a higher allopurinol dose, lower INAS score, and higher self-reported adherence. Median number of flares over the preceding 12 months were low in both groups.

Table 1. Participant demographic and clinical features.

	All Participants	Receiving ULT	Not Receiving ULT
Age, yrs, mean (SD)	64 (12)	64 (12)	61 (8)
Participants per group	119 (100)	103 (87)	10 (8)
Male participants	109 (92)	97 (94)	8 (80)
Ethnicity			
NZ European	48 (40)	43 (42)	2 (20)
Māori	23 (19)	18 (17)	4 (40)
Pacific Islander	39 (33)	36 (35)	2 (20)
Asian	6 (5)	4 (4)	2 (20)
Other	3 (3)	2 (2)	0 (0)
Coexisting conditions			
Obesity[a]	73 (61)	67 (65)	6 (60)
Kidney stones	13 (11)	13 (11)	0 (0)
CVD[b]	49 (41)	48 (47)	1 (10)
Diabetes	46 (39)	44 (43)	2 (20)
HTN	86 (72)	81 (79)	5 (50)
Hyperlipidemia	82 (69)	76 (74)	6 (60)
Kidney transplant	2 (2)	0 (0)	2 (20)
ULT			
Allopurinol	98 (82)	98 (95)	0 (0)
Febuxostat	5 (4)	5 (5)	0 (0)
Probenecid	1 (1)	1 (1)	0 (0)
Laboratory results available[c]	105 (88)	96 (93)	9 (90)
SU value available[c]	86 (72)	79 (77)	7 (70)
SU concentration, mmol/L, mean (SD)	0.36 (0.13)	0.34 (0.12)	0.50 (0.12)
At target SU concentration, < 0.36 mmol/L			
Yes	50 (42)	48 (47)	2 (20)
No	36 (30)	31 (30)	5 (50)
Unknown	33 (28)	24 (23)	3 (30)
Creatinine value available[c]	100 (84)	92 (89)	8 (80)
Creatinine concentration, μmol/L, mean (SD)	194 (258)	202 (268)	100 (27)
eGFR, mL/min/1.73 m^2, mean (SD)	55 (25)	53 (25)	70 (19)
eGFR, mL/min/1.73 m^2			
≥ 60	48 (40)	42 (41)	6 (60)
30 to < 60	34 (29)	32 (31)	2 (20)
< 30	18 (15)	18 (17)	0 (0)
Unknown	19 (16)	11 (11)	2 (20)
Phone interview complete	89 (75)	81 (79)	8 (80)

Data are in n (%) unless otherwise indicated. [a] Obesity is defined as BMI ≥ 30 (calculated as weight in kilograms divided by height in meters squared). [b] CVD is defined as ischemic heart disease, heart failure, or peripheral vascular disease. [c] Available within 12 months. CVD: cardiovascular disease; eGFR: estimated glomerular filtration rate (Modification of Diet in Renal Disease Study equation); HTN: hypertension; NZ: New Zealand; SU: serum urate; ULT: urate-lowering therapy.

There were 2 participants who were at target SU concentration who were not receiving ULT. Of these, 1 was a 57-year-old man with an SU concentration of 0.35 mmol/L who had a kidney transplant between initial study end and our follow-up. The second was a 75-year-old man who reported recent self-cessation of his allopurinol the week prior to our follow-up study, as he no longer experienced gout flares. His most recent SU concentration of 0.35 mmol/L was measured 4 months prior when he was still taking allopurinol.

Renal function. The overall mean eGFR was 55 (SD 25) mL/min/1.73 m^2. The mean eGFR was significantly lower in those receiving ULT (53, SD 25 mL/min/1.73 m^2) compared to those not receiving ULT (70, SD 19 mL/min/1.73 m^2; P = 0.008; Table 1). The mean eGFR at follow-up was 7 (SD 13) mL/min/1.73 m^2 lower than at study end (Table 2). Participants in lower eGFR groups at follow-up had a higher mean allopurinol dose reduction (Supplementary Table S2, available with the online version of this article); however, this did not meet statistical significance (P = 0.29). There was no statistically significant correlation between eGFR at the last study visit and subsequent allopurinol dose change (r = 0.12, P = 0.27).

Gout flares. Of the 89 out of 119 (75%) participants who participated in the phone interview, 8 (9.0%) reported ≥ 1 gout flare in the prior month, 10 (11%) reported a flare in the last 3 months, and 19 (21%) reported a gout flare in the preceding 12 months. In those participants who were receiving any ULT, 18 out of 81 (22%) reported a flare in the last 12 months, compared with 1 out of 8 (13%) who were not receiving ULT.

Associations between SU concentration, creatinine concentration, gout flares, and current allopurinol dose were examined

Table 2. Allopurinol dose, serum urate concentration, and eGFR compared to last study visit.

	Values
Allopurinol, n = 98	
Dose, mg/day, mean (range)	
At last study visit	419 (0 to 900)
At follow-up study	391 (100 to 950)
Change	–28.1 (–600 to 500)
Participants, n (%)	
Increase in dose	18 (18)
Same dose	48 (49)
Decrease in dose	32 (33)
Serum urate, n = 86	
Concentration, mmol/L, mean (SD)	
At last study visit	0.33 (0.07)
At follow-up study	0.36 (0.13)
Change	+0.02 (0.12)
Participants, n (%)	
Increase in concentration	45 (52)
Same concentration	3 (3.5)
Decrease in concentration	38 (44)
eGFR, n = 77	
Rate, mL/min/1.73 m^2, mean (SD)	
At last study visit	60 (24)
At follow-up study	53 (24)
Change	–7 (13)
Participants, n (%)	
Increase in rate	24 (31)
Decrease in rate	53 (69)

eGFR: estimated glomerular filtration rate.

(Supplementary Table S3, available with the online version of this article). There was a positive correlation between SU concentration and flares ($r = 0.35$, $P = 0.004$). There was a negative correlation between allopurinol dose and SU concentration ($r = –0.32$, $P = 0.003$) and between allopurinol dose and creatinine concentration ($r = –0.26$, $P = 0.009$).

DISCUSSION

We were provided with a unique opportunity to follow up participants from the allopurinol dose escalation study. The majority of participants continued to receive ULT after study exit and remained at target SU concentration. To our knowledge, this is the first study to review long-term outcomes in people with gout in the community following allopurinol dose escalation.

Our study showed that there was 82% persistence with allopurinol at a mean follow-up of 6.5 years from enrollment. This is high compared to large retrospective studies that reported persistence with allopurinol at 5 years to be around 40%.[1,9] It should be noted that our participants were already taking allopurinol prior to enrollment in the dose escalation study. In addition, the participants had regular, usually monthly, contact with the study coordinators, who were also contactable by phone or email, during the 24-month study. The rigorous focus on participants' gout may have provided more time for education and placed more emphasis on the importance of long-term management.

At follow-up, allopurinol continued to be well tolerated, and only 5 participants moved to febuxostat. In total, 15 participants had stopped allopurinol, and in those who were contactable (n = 10), only 1 reported allopurinol intolerance (ie,

Table 3. INAS statements and scores.

No.	Statement	Score[a], n = 17, Mean (SD)
1	To see if my gout is still there	2.2 (1.3)
2	To see if I can do without it	2.6 (1.4)
3	To see if I really need it	2.7 (1.4)
4	Because I am not convinced that the medicine is really right for me	1.8 (0.6)
5	Because I am not sure that the doctor chose the right medicine for me	1.8 (0.4)
6	To give my body a rest from the medicine	2.3 (1.1)
7	Because the medicine is harsh on my body	2.1 (0.9)
8	Because I don't like the medicine to accumulate in my body	1.9 (0.7)
9	Because my body is sensitive to the effects of medicine	2.1 (1.0)
10	Because I don't like the side effects	1.8 (0.4)
11	Because I don't like chemicals in my body	2.4 (1.2)
12	Because it may affect the body's own natural healing processes	2.5 (1.2)
13	Because I think I am on too high a dose	2.4 (1.1)
14	Because I think the drug might become less effective over time	2.1 (0.9)
15	Because I worry about becoming dependent on my medicine	2.5 (1.2)
16	Because I want to think of myself as a healthy person again	2.4 (1.2)
17	Because it reminds me that I have gout	2.0 (0.9)
18	Because I want to lead a normal life again	2.5 (1.3)
19	Because it is good not to have to remember	2.5 (1.2)
20	Because it is inconvenient to take all the time	2.9 (1.4)
21	Because the drug schedule doesn't fit with my lifestyle	2.7 (1.4)
22	Because I don't think the drug treatment is worth it	1.9 (0.9)

[a] INAS scoring: strongly disagree = 1, disagree = 2, neutral = 3, agree = 4, and strongly agree = 5. INAS: Intentional Non-Adherence Scale.

Table 4. Characteristics of participants at target SU concentration vs those not at target.

	SU Concentration		*P*
	< 0.36 mmol/L	≥ 0.36 mmol/L	
Participants, n = 86, n (%)	50 (58)	36 (42)	—
SU concentration, mmol/L, mean (SD)	0.27 (0.06)	0.48 (0.10)	< 0.001
Age, yrs, mean (SD)	67 (10)	60 (12)	0.005
Male participants, n (%)	45 (90)	35 (97)	0.16
eGFR, mL/min/1.73 m^2, mean (SD)	53 (23)	53 (29)	0.98
Allopurinol dose, mg/d, mean (SD)	388 (168)	335 (256)	0.28
Self-report of < 100% adherence, n (%)	3 (6)	10 (28)	0.006
INAS score, mean (SD)	2.0 (0.97)	2.3 (0.57)	0.08
Self-reported flares[a], median (IQR)	0 (0-0)	0 (0-1)	0.14

[a] Flares over the past 12 months. eGFR: estimated glomerular filtration rate; INAS: Intentional Non-Adherence Scale; SU: serum urate.

light-headedness). We note there was a mean overall reduction in allopurinol dose at follow-up by 28.1 mg/day, with 33% of participants having a dose reduction. We did not collect data on the reason for dose reduction. Therefore, we do not know if allopurinol doses were reduced because of intolerance, low SU, or other reasons. At completion of the original study, participants' PCPs were instructed to continue ULT for the long term and monitor SU every 6 months, but they were not provided with specific instructions regarding dose escalation or de-escalation. It appears that some PCPs continued with the treat-to-target approach, with 18% of participants having an increased allopurinol dose at follow-up.

Self-reported adherence to allopurinol was high, with 79% of participants reporting 100% adherence over the last month. The INAS was useful in identifying reasons for nonadherence. The most common reasons for intentional nonadherence were allopurinol being inconvenient to take, seeing if the medication is necessary, and the drug schedule not fitting in with participants' lifestyle, rather than reports of adverse effects or the medicine being harsh on participants' bodies. Most participants disagreed or strongly disagreed with each INAS statement. The scale was difficult to complete over the telephone because it had 5 response options for each statement; more honest and accurate scores may have been collected if participants had completed the written scale in their own time.

The small mean increase in SU concentration of 0.02 mmol/L at follow-up resulted in a significantly lower number of participants at target SU concentration (58%) compared to at the final study visit (74%; $P = 0.007$). This SU increase may reflect the variable real-world adherence to ULT[2] and overall mean allopurinol dose reduction in our study. In those who had laboratory results available within 12 months, the majority had their SU levels checked (82%), indicating that SU continued to be monitored regularly following study end.

Self-reported gout flares remained low, with the majority (79%) of participants having no flares over the preceding year. There is a paucity of community-based data on the prevalence of gout flares among patients receiving ULT with which to compare our data. Our flare rate was lower than that in a study by Proudman et al[10] who used the South Australian Health Omnibus Survey and showed that 40% of people with gout receiving ULT reported at least 1 flare in the preceding 12 months.

Strengths of this study included combining both electronic and telephone interview data, allowing for a high rate of successful follow-up; all except 6 participants had current ULT determined, and only 14 participants did not have laboratory results available within the preceding 12 months. Our study provided a reasonable representation of the New Zealand gout population, with about 50% Māori and Pacific Islander participants. Inequities in gout management are not unique to Māori or Pacific Islander people and are seen in most Indigenous populations; thus, our study may be relevant to international settings.

There are several limitations of this study. A large percentage (33%) of participants had died since enrollment, and their cause of death was not reviewed. The decision not to review cause of death was made because participants who had died could not have consented to be involved in our study; in addition, it respected the Tikanga (Māori customary practices and behaviors) methodology. At enrollment, the trial participants had a large burden of comorbidities, including cardiovascular disease (43%) and CKD, with 52% having a creatinine clearance rate < 60 mL/min/1.73 m^2. A further limitation of our study was that 29 participants were not contactable for the telephone survey, which may have created bias in the self-reported data.

Although persistence with allopurinol was high, there is still significant room for improvement, given that only 58% of the participants were at target SU concentration at follow-up. The INAS, which identifies reasons for intentional nonadherence, could allow for targeted interventions to improve adherence at both the individual level and the group level. For example, our highest-scoring INAS reason—allopurinol being "inconvenient to take all the time"—could be targeted through blister packing of medication or electronic medication reminders.

Despite its efficacy and safety, the allopurinol dose escalation treat-to-target SU strategy is difficult to implement outside of a clinical trial setting, as it is time and resource intensive for both the individual with gout and the healthcare system. Real-life

clinical studies of this strategy in primary care settings, where the majority of gout is managed, have not been as successful.[11] Strategies to improve the uptake and persistence of ULT and ways to implement the findings from allopurinol dose escalation, including pharmacy-led strategies, nurse-led strategies, and use of mobile technologies, are ongoing. Of particular interest is the ability to predict the dose of allopurinol required to achieve target SU, which could streamline the dose escalation process. Given that ULT is generally considered a lifelong therapy for people with gout, SU monitoring and education on the importance of medication adherence should be undertaken at regular intervals.

In summary, this follow-up study showed that most participants in the allopurinol dose escalation study had good real-world persistence with allopurinol, remained at target SU, and had a low number of self-reported flares. While treatment of gout in the community has generally been suboptimal,[3,4] these data show that people with gout can have good outcomes following allopurinol dose escalation. These findings support the allopurinol dose escalation approach, and recommendations to continue allopurinol dose escalation in the long term are appropriate and achievable.

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ONLINE SUPPLEMENT

Supplementary material accompanies the online version of this article.

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