








**ORIGINAL ARTICLE**

# Persistence with urate-lowering therapy in Australia: A longitudinal analysis of allopurinol prescriptions

Matthew J. Coleshill<sup>1,2</sup>  | Richard O. Day<sup>1,2</sup>  | Karson Tam<sup>1</sup>  |  
Mahsa Kouhkamari<sup>3</sup> | Vincent Caillet<sup>3</sup> | Eindra Aung<sup>1,2</sup>  |  
Diluk R. W. Kannangara<sup>1,4</sup>  | Peter Cronin<sup>3</sup> | Anthony Rodgers<sup>5</sup>  |  
Sophie L. Stocker<sup>1,2,6</sup> 

<sup>1</sup>Department of Clinical Pharmacology & Toxicology, St Vincent's Hospital, Sydney, Australia

<sup>2</sup>St Vincent's Clinical School, University of New South Wales, Sydney, Australia

<sup>3</sup>Prospection Pty Ltd, Sydney, Australia

<sup>4</sup>Notre Dame Medical School, Sydney, Australia

<sup>5</sup>George Institute for Global Studies, University of New South Wales, Sydney, Australia

<sup>6</sup>Sydney Pharmacy School, Faculty of Medicine & Health, The University of Sydney, Sydney, Australia

**Correspondence**

Professor Richard Day MD, Department of Clinical Pharmacology, St Vincent's Hospital, Darlinghurst, NSW 2010, Australia.  
Email: [r.day@unsw.edu.au](mailto:r.day@unsw.edu.au)

**Funding information**

Lexy Davies Bequest at St Vincent's Hospital, Sydney

**Aim:** Gout is the most common form of inflammatory arthritis in men. Despite the availability of effective urate-lowering therapies (ULT), the management of gout is suboptimal due to poor persistence with ULT. This study examined national prescribing patterns of ULT to determine persistence with allopurinol in Australia.

**Methods:** A 10% sample of the Australian Pharmaceutical Benefits Scheme dispensing claims database was used to identify individuals initiated on allopurinol between April 2014 and December 2019. The number of allopurinol scripts dispensed was used to estimate persistence with allopurinol. Persistence was defined as the number of months from initiation until discontinuation (last prescription with no further scripts acquired for a period thereafter). Kaplan-Meier curves were used to examine persistence, while Cox regression analysis was used to examine the influence of gender, concomitant colchicine and age.

**Results:** The largest drop in persistence occurred immediately after initiation, with 34% of patients discontinuing allopurinol 300-mg therapy in the first month. Median persistence with allopurinol 300 mg was 5 months (95% confidence interval 4.76-5.24), with around 63% of individuals not persisting with this therapy for more than 12 months. Concomitant prescription of colchicine on the day of allopurinol initiation only occurred in 7% of allopurinol initiations. No increase in persistence was observed for those co-prescribed colchicine.

**Conclusion:** Persistence with allopurinol was poor. More effective methods targeting prescribers, patients and systems are required to promote persistence with allopurinol. Improving persistence to allopurinol is an important public health goal given the proven potential of this medication to eliminate gout.

The authors confirm that the Principal Investigator for this paper is Professor Richard Day. As this paper was a retrospective evaluation of national deidentified prescribing data, the Principal Investigator did not require direct clinical responsibility for the study subjects.

Matthew J Coleshill and Richard O Day contributed equally to this article and are considered joint first authors.

This is an open access article under the terms of the [Creative Commons Attribution-NonCommercial-NoDerivs](https://creativecommons.org/licenses/by-nc-nd/4.0/) License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2022 The Authors. *British Journal of Clinical Pharmacology* published by John Wiley & Sons Ltd on behalf of British Pharmacological Society.

## KEYWORDS

allopurinol, colchicine, gout, medication adherence, medication persistence, urate-lowering therapy

## 1 | INTRODUCTION

Gout is the most common form of inflammatory arthritis in men and has a prevalence of 1-4% globally.<sup>1</sup> In Australia, the prevalence of gout ranges from 1.6%<sup>2</sup> to 6.8%.<sup>3</sup> The incidence of gout is rising worldwide, including in both developing and, more dramatically, in developed nations.<sup>2,4,5</sup>

Treatment for acute gout flares focuses on alleviating the pain due to the intense inflammation and includes short courses of non-steroidal anti-inflammatory drugs (NSAIDs), colchicine or glucocorticosteroids.<sup>6</sup> Treatment of chronic gout centres on preventing gout flares and promoting dissolution of tophi (urate deposits, if present) with urate-lowering therapy (ULT). The goal of ULT is to eliminate gout flares by reducing serum urate (SU) concentrations to  $\leq 0.36$  mmol/L (or  $< 0.30$  mmol/L if tophi are present). These targets are below the saturation point for SU (0.42 mmol/L), making the crystallisation and deposition of urate in the form of monosodium urate in joints less likely.<sup>6</sup> Life-long treatment with ULT is recommended. Co-prescription of low dose colchicine or NSAIDs for 6 months on initiation of ULT is recommended to prevent a paradoxical increase in gout flares related to sudden ULT-induced reduction in SU.<sup>7,8</sup> Available ULTs in Australia include xanthine oxidoreductase inhibitors (allopurinol, febuxostat) and uricosuric agents (probenecid). Of these treatments, allopurinol is overwhelmingly the ULT prescribed.

Despite the availability of effective and generally tolerable preventative treatments for gout, inadequate dosage and poor rates of persistence with ULT treatment regimens are prominent barriers to successful management.<sup>9-12</sup> In the last decade substantial efforts have been made to educate prescribers about titrating doses of ULT to reach target SU concentrations, rather than selecting a dose based on, and limited by, renal function, a historical approach dictated by concerns around toxicity.<sup>13,14</sup> However, interventions to encourage dosing ULT to target SU concentrations have been very limited in their effect.

Adherence to ULT, defined as taking the medication as prescribed at least 80% of the time, was on average only 46.0% (95% confidence interval [CI] 40.8-51.2) in a recent meta-analysis. These data are consistent across the United States, the United Kingdom, Korea, Ireland, Israel and New Zealand.<sup>15</sup> In addition, persistence, defined as the length of time from initiation to discontinuation,<sup>16</sup> in three of these studies (United States and Israel) ranged from 4 to 12 months.<sup>15</sup> Similarly, a study from Canada examining persistence with ULT among older adults with diabetes over 3 years observed that 41% of patients discontinued treatment by the third year.<sup>17</sup> There is a paucity of data on persistence with ULT in Australia, therefore we examined persistence with ULT in individuals between 2014 and 2019 using national

### What is already known about this subject

- Allopurinol is effective at reducing serum urate concentrations and preventing gout flares.
- Allopurinol persistence (length of time between initiation and discontinuation of therapy) is often poor and is a common reason for failure to control gout.

### What this study adds

- Patients persisted with allopurinol 300 mg for a median of 5 months. Around 34% of patients discontinued allopurinol 300 mg within the first month. By 12 months, around 63% had discontinued allopurinol 300 mg and by 24 months 72% had discontinued treatment.
- Older age and male gender were associated with better persistence allopurinol 300 mg.
- In contrast to guidelines, prescription of colchicine on the day of initiation of allopurinol was uncommon, with approximately 7% of initiations on allopurinol co-prescribed colchicine.

dispensing records to better understand trends in gout management in Australia.

## 2 | METHODS

### 2.1 | Data source

The Australian Pharmaceutical Benefits Scheme (PBS)\* database for government-subsidised medications at point of dispensing in pharmacies was accessed for prescriptions written for individuals initiated on treatment with ULT and/or colchicine during a 69-month period (April 2014 to December 2019). A 10%, randomly selected, anonymised cohort from this database is made available by Services Australia for

\*Medicines listed on the PBS are available to all Australian citizens via Medicare. A co-payment is payable if the cost of the medicine to the PBS exceeds the co-payment. The co-payment increases annually with the cost of living index. 'Concessional' patients pay a substantially smaller co-payment than nonconcessional patients and Medicare pays the balance. Older, off-patent medicines, such as allopurinol and colchicine, cost more than the concessional but less than the regular co-payment. The bulk of ULT and colchicine prescriptions in Australia are captured on the PBS database.

approved research purposes. The daily dose prescribed for the patient is not recorded in the PBS10 sample database, only the drug tablet size and pack size (eg, allopurinol, 300-mg tablet, pack size 60) are captured. Research approval was obtained from the External Request Evaluation Committee of Medicare Australia, the government agency responsible for managing the PBS (EREC/RMS0047).

## 2.2 | Identification of patients with gout

People who were initiated on ULT (allopurinol, febuxostat), based on unique PBS item codes (**Supporting Information Table S1**), were identified as suffering with gout. Initiations were defined as individuals whose first allopurinol dispensing of any tablet size occurred between April 2014 and December 2019. Whether or not an individual initiated allopurinol during this period was validated against historical prescribing data from January 2006 to March 2014 as well as in the April 2014 to December 2019 study database, confirming no previous prescription of allopurinol.

During the period of observation, allopurinol was available in 100-mg scored tablets (in 100- and 200-tablet pack sizes) and 300-mg scored tablets (in a 60-tablet pack size). Dispensing data of febuxostat were collected, although prescription rates were very small (<2%).

Colchicine dispensing was also analysed. PBS pack size for colchicine 0.5 mg is 30 tablets. Use can be intermittent and short-term for flares, but also regular in low doses of one or two tablets daily as prophylaxis against flares. NSAIDs, although used to treat gout attacks, are widely used for other indications and are available without prescription. Similarly, prednisone is widely used to treat other inflammatory conditions, therefore the provision of NSAIDs and prednisone via the PBS was not collected.

## 2.3 | Data analysis

The longitudinal record of prescriptions of ULT and colchicine for individual patients was examined. Between April 2014 and December 2019 ULT script purchases were reported for each month. The script purchases were described according to the patient's age, sex and concessional status. Concession card holders are mainly composed of people  $\geq 65$  years of age who are no longer working but also include individuals with chronic health or social reasons for their concessional status.

Kaplan-Meier curves were used to examine overall persistence while life table analyses were used to identify proportions of patients discontinuing after the first month and at 6, 12 and 24 months. Persistence with allopurinol treatment was defined as the number of months from initiation of the drug until discontinuation (ie, apparent end of therapy with no further scripts being acquired for a period). As the daily dose prescribed for an individual was unknown, this period until discontinuation was conservatively defined as 6 months (300-mg dose) or 12 months (100-mg dose) to account for lower prescribed

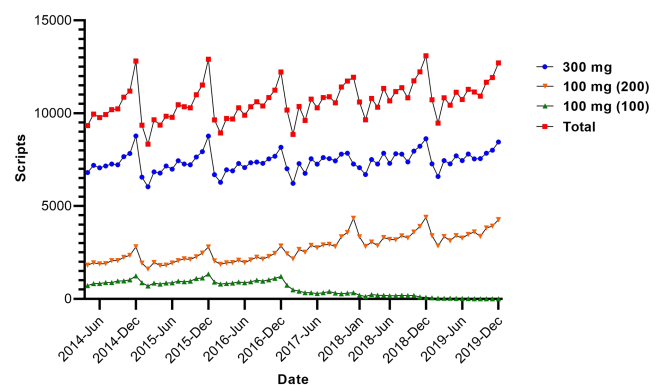
doses. An individual prescribed allopurinol 300 mg/day is expected to require a new script within 2 months. An individual prescribed allopurinol 100 mg/day is expected to require a new script within either 3 months (100-tablet pack size) or 6 months (200-tablet pack size). These common doses were based on the previous literature<sup>18–20</sup> and confirmed through estimates of averaging dosing (see **Supporting Information Figures S1 and S2**). The substantial difference in pack size between the 100-mg and 300-mg therapies makes a single definition of discontinuation problematic. As such, the two therapies were analysed separately. Given that the 300-mg therapy is the likely end-point of guideline-recommended dose escalation, we propose that persistence with the 300-mg tablet provides a relevant indicator of the quality of gout management in Australia. Cox regression analyses were used to examine the influence of gender, concomitant colchicine (initiated on the same day as allopurinol prescription) and age on persistence with allopurinol.

Data analysis was undertaken using the PharmDash software platform (Prospection Pty Ltd, Sydney, Australia) and data were analysed using IBM SPSS Statistics for Windows, version 26 (IBM Corp, Armonk, NY, USA). Results from the random 10% sample of the PBS data set reflect national dispensing data.

## 3 | RESULTS

### 3.1 | Trends in allopurinol prescribing

Allopurinol was the overwhelming choice for ULT (98.4% of total ULT prescription numbers). The monthly average number of allopurinol scripts for the 10% sample was 10 828 (95% CI 10575–11 081) (Figure 1). Most individuals who purchased a script of allopurinol were



**FIGURE 1** The monthly number of allopurinol scripts purchased between April 2014 and December 2019. The 300-mg tablet strength (blue circles), 100-mg tablet strength (100-tablet pack size, green triangles) and 100-mg tablet strength (200-tablet pack size, orange triangles) as well as all three tablet sizes combined (total, red squares) are depicted (10% representative national population sample). Safety net provisions allow patients to ‘stockpile’ medicines towards the end of each year, accounting for the rise in prescriptions over the year

male (84.9%), over the age of 60 years (72%) and concessional card holders (62.2%) (Supporting Information Table S2).

The 300-mg dose accounted for 68.3% of all allopurinol scripts purchased between April 2014 and December 2019 (mean = 7392 per month, 95% CI 7261-7523). The 100-mg dose in the 200-tablet pack size accounted for 25.1% of all scripts (mean = 2715 per month, 95% CI 2543-2887). This proportion increased over the observed period, particularly after September 2017 (Figure 1). The 100-tablet pack size of the 100-mg dose accounted for only 5.0% of scripts purchased (mean = 546 per month (95% CI 447-644), with a substantial decrease after December 2016. This pack size was discontinued in November 2018.

### 3.2 | Colchicine use and co-medication between allopurinol and colchicine

The monthly average of colchicine scripts was 4475 (95% CI 4381-4569). Colchicine's use as prophylaxis during initiation of allopurinol was very low. Only 6.7% of initiations on allopurinol 300 mg and 6.9% of initiations on allopurinol 100 mg (200-tablet pack size) were dispensed colchicine on the same day.

### 3.3 | Persistence with allopurinol 300 mg

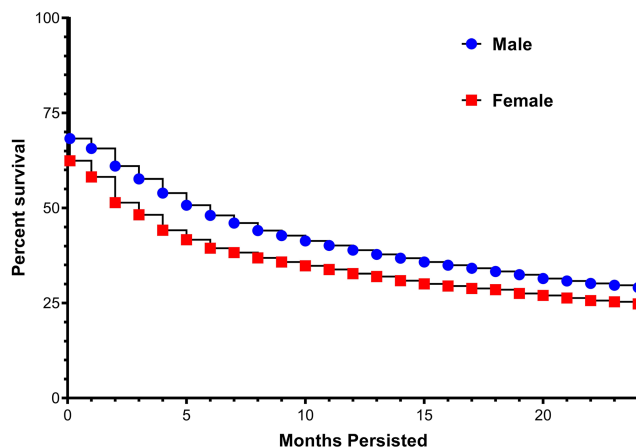
Data for a total of 22 337 individuals were included in the persistence analyses for the 300-mg therapy. If an individual had not been dispensed allopurinol 300-mg tablets for at least 6 months, they were classified as having discontinued therapy at the time the last dose was prescribed. The median number of months from initiation to discontinuation of allopurinol 300 mg was 5 months (95% CI 4.76-5.24). The largest reduction in persistence occurred in the first month, with 34% of patients discontinuing treatment

**TABLE 1** Cox regression analysis results for the HR discontinuation with allopurinol 300-mg therapy

Covariate	HR (95% CI)	P value
<b>Gender</b>	0.79 (0.76-0.82)	<.01
<b>Age</b>		
0-20	2.62 (2.12-3.19)	<.01
21-30	2.06 (1.84-2.31)	<.01
31-40	1.77 (1.63-1.92)	<.01
41-50	1.53 (1.42-1.64)	<.01
51-60	1.29 (1.21-1.38)	<.01
61-70	1.15 (1.07-1.23)	<.01
71-80	1.09 (1.02-1.17)	.011
81+	1.00 [reference]	
<b>Colchicine</b>	1.05 (0.98-1.12)	.156

Abbreviations: CI, confidence interval; HR, hazard ratio.

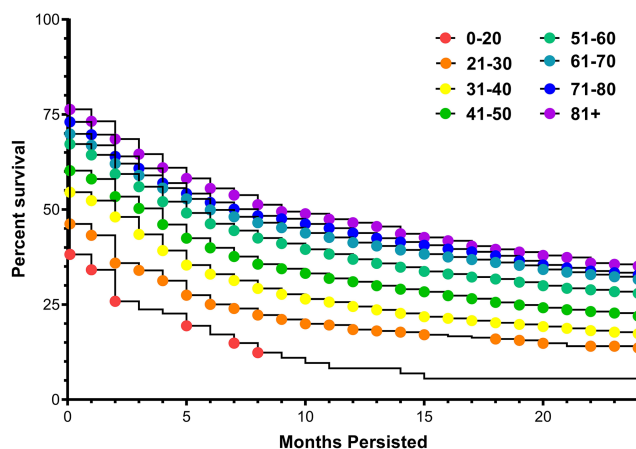
immediately. By 6 months, 54% discontinued, by 12 months 63% discontinued and by 24 months 72% had discontinued. Cox regression analysis (Table 1), using female gender, 81+ age and concomitant colchicine as references, observed that persistence with the 300-mg therapy was associated with male gender and older age (Figure 2).



Number at risk

	0	5	10	15	20
Male	18259	8497	6188	4888	3985
Female	4078	1414	1021	783	621

(A) Gender



Number at risk

	0	5	10	15	20
0-20	110	21	8	5	0
21-30	504	123	72	51	41
31-40	1714	557	355	266	212
41-50	3252	1299	892	674	527
51-60	4712	2142	1566	1235	1023
61-70	5852	2821	2136	1710	1415
71-80	4284	2041	1549	1235	997
81+	1909	907	631	495	387

(B) Age

**FIGURE 2** The persistence to allopurinol 300 mg over 24 months since initiating therapy stratified based on (A) gender and (B) age at initiation

### 3.4 | Persistence with allopurinol 100 mg

Data for a total of 35 869 individuals were included in the persistence analyses for the 100-mg therapy. If an individual had an interruption of continual allopurinol therapy for at least 12 months between scripts, they were deemed to have discontinued the allopurinol 100-mg therapy at the time the last dose was prescribed. The median time from initiation to discontinuation was 9 months (95% 8.71-9.29). The largest reduction in persistence occurred in the first month, with 34% of patients discontinuing therapy. By 6 months, 45% had discontinued, by 12 months 57% had discontinued and by 24 months 67% had discontinued. Cox regression analysis (Table 2), using female gender, 81+ age and concomitant colchicine as references, observed that persistence with the 100-mg therapy was associated with an absence of concomitant colchicine and older age (Figure 3).

Owing to the discontinuation of the 100-tablet pack size of the 100-mg dose, the assessment of persistence with this pack size was not performed.

## 4 | DISCUSSION

This study has, for the first time, provided an understanding of the prescribing and dispensing of allopurinol in Australian individuals with gout over almost 7 years in a nationally representative sample. In general, persistence with taking allopurinol was short, with a median 5 months for the 300-mg tablet size. This is consistent with previous studies indicating that persistence with allopurinol ranged from 4 to 12 months,<sup>15</sup> but is much shorter than the 42 months from a Korean study.<sup>21</sup> Our study also found that 64% of patients discontinued the 300-mg tablet size within a year, with 72% discontinuing by 2 years. A recent study conducted in Canada examining persistence with ULT over 3 years observed that 41% of patients discontinued therapy by the third year.<sup>17</sup> While these two findings differ substantially, our study examined all individuals taking ULT, as opposed to only older adults with diabetes –

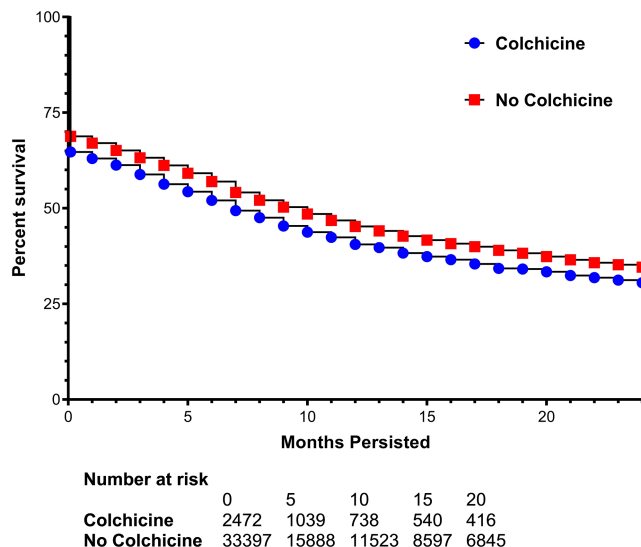
**TABLE 2** Cox regression analysis results for the HR discontinuation with allopurinol 100-mg therapy

Covariate	HR (95% CI)	P value
Gender	0.99 (0.96-1.02)	.496
<b>Age</b>		
0-20	2.30 (1.88-2.82)	<.01
21-30	2.38 (2.17-2.62)	<.01
31-40	2.16 (2.02-2.30)	<.01
41-50	1.95 (1.85-2.06)	<.01
51-60	1.70 (1.62-1.79)	<.01
61-70	1.43 (1.36-1.50)	<.01
71-80	1.18 (1.13-1.24)	<.01
81+	1.00 [reference]	
<b>Colchicine</b>	0.92 (0.88-0.97)	<.01

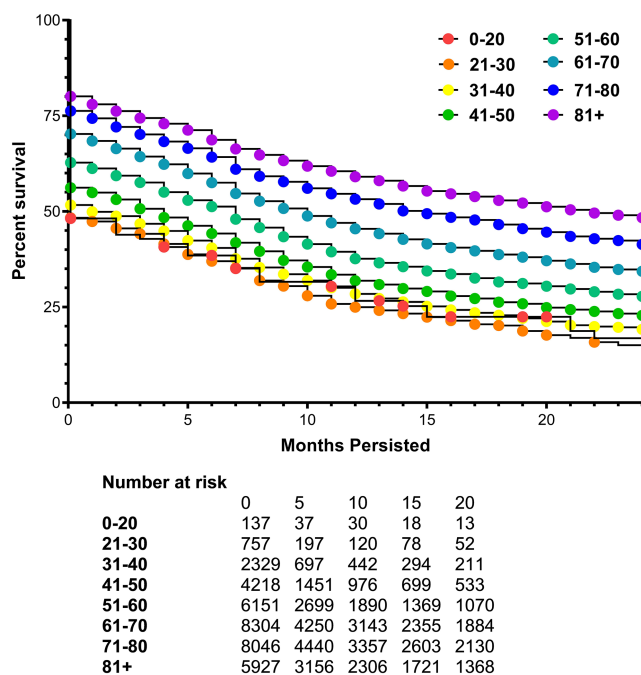
Abbreviations: CI, confidence interval; HR, hazard ratio.

two factors associated with improved adherence to ULT.<sup>15</sup> Irrespective of dose, a third of individuals in the present study did not fill their second script of allopurinol 300 mg. This steep decline in persistence highlights that a large proportion of gout patients who are prescribed allopurinol are not receiving consistent long-term treatment.

Data based on medical records have revealed that the most common reasons for ULT discontinuation were poor health literacy, followed by perceived lack of effectiveness and adverse events.<sup>21</sup> Poor health literacy



(A) Colchicine



(B) Age

**FIGURE 3** The persistence to allopurinol 100 mg over 24 months since initiating therapy stratified based on (A) presence of concomitant colchicine and (B) age at initiation

is increasingly recognised as a public health problem worldwide,<sup>22</sup> and approximately half of patients with gout were reported to have insufficient health literacy.<sup>23</sup> Poor health literacy is likely to lead to poor ULT persistence. For example, misunderstanding the difference between the acute treatment for gout flares (eg, colchicine) and prophylactic ULT to prevent future gout flares (eg, allopurinol) will impact persistence with ULT. There is some evidence that many individuals (50-72%) who stop ULT recommence ULT at a later time.<sup>10,17,24</sup> The asymptomatic nature of gout between gout flares is a contributing factor to the discontinuation of allopurinol. We can assume that gout patients who have not experienced a gout flare for some time may consider ULT unnecessary and therefore decide to stop taking allopurinol. Comprehensive national initiatives which improve the health literacy of people with gout are required to improve persistence to allopurinol.

Consistent with previous studies on gout<sup>15</sup> and the wider medication adherence and persistence literature,<sup>25</sup> older individuals were more likely to persist with allopurinol. While health literacy tends to decline with age,<sup>26</sup> research has observed that several other age-related factors, such as the presence of comorbidities, particularly hypertension and diabetes, is associated with greater adherence to ULT.<sup>15</sup> One explanation for this relationship is familiarity with managing chronic conditions,<sup>27</sup> which may counteract declining health literacy with age in gout. Qualitative studies have reported a perception of gout as a disease of old age as well as hesitancy to take lifelong ULT in younger individuals.<sup>28,29</sup> These factors may contribute to lower persistence with allopurinol in younger adults. This finding is important to consider when designing interventions to improve persistence with allopurinol.

Guidelines recommend co-prescription of anti-inflammatory therapy for the first 6 months of ULT to manage precipitated gout flares.<sup>6</sup> Colchicine, NSAIDs or corticosteroids may be used but guidelines recommend colchicine because of its better safety profile. Persistence with allopurinol in these individuals who initiated colchicine on the day of allopurinol initiation was not better than in those receiving allopurinol alone. This is an unexpected finding as experiencing gout flares when initiating allopurinol is likely discouraging for individuals and therefore thought to contribute to poor persistence to allopurinol. Confounding factors are likely, such as access to colchicine from a prescription prior to commencement of allopurinol, but this is an important observation that demands further investigation using more controlled research designs.

The major indication for colchicine therapy is gout, with other accepted indications being familial Mediterranean fever and acute and chronic pericarditis. While this means that colchicine prescriptions are most likely to indicate someone is affected by gout, flares are also managed with NSAIDs or glucocorticosteroids, which were not evaluated in our study as they are commonly indicated for other conditions.

In addition to patient-related factors, prescribers' knowledge of gout and its management may also impact persistence with allopurinol. Australian primary care physicians report a lack of familiarity with current guidelines,<sup>20</sup> which may account for the high rates of initiation on the 300-mg therapy as well as the low rates of co-prescribed colchicine on initiation of allopurinol therapy. By not providing guideline-recommended care in this manner, patients may be more at risk of

experiencing precipitated gout flares and discontinuing therapy.<sup>24</sup> Common misconceptions around allopurinol, such as stopping allopurinol during a gout flare,<sup>30</sup> may have contributed to the low rates of persistence observed in the present study.

The findings from this study highlight the need for improvements in gout education and management in Australia. To date, a range of interventions have been examined internationally with promising results.<sup>31</sup> In particular, a Community Pharmacy Gout Management Service has proven successful in improving outcomes for people with gout in New Zealand.<sup>32</sup> While barriers exist in Australia to community pharmacists providing such gout management services,<sup>33</sup> they are still well placed as a primary care service to support gout management in urban, regional and remote Australia.

The data analysed in this study represent 10% of the Medicare-eligible Australian population and all their reimbursed dispensations over almost 7 years. As such, this study represents the largest assessment of persistence with allopurinol in Australia to date, with high generalisability to wider gout management in Australia. However, there is currently no specific code to identify patients with gout in PBS data. Therefore, we relied on the PBS item codes for allopurinol to identify patients with probable gout diagnosis within the dataset. While the most common indication for allopurinol is gout, other indications exist for acute uric acid nephropathy and tumour lysis syndrome. As the PBS does not provide medicines supplied to public hospital inpatients, where these other indications are likely dealt with, the impact on the present study is minimal. Furthermore, PBS data does not include information on prescribed dose. As such, the present data could not be used to calculate other medication adherence metrics such as proportion of days covered.

In conclusion, persistence with allopurinol is remarkably poor, particularly in younger individuals who are more at risk of long-term damage from untreated gout. Overall, around a third of patients discontinued the allopurinol 300-mg therapy within 1 month, with nearly two-thirds stopping treatment after 12 months. Furthermore, colchicine as prophylaxis during initiation of allopurinol, although recommended, is seldom co-prescribed at initiation of ULT. Persistently elevated serum urate concentrations and repeated gout flares can lead to permanent joint destruction and disfiguring deposits of tophi, all of which reduce quality of life.<sup>34</sup> More effective, likely novel and multimodal methods of education of prescribers and patients are required to promote appropriate dose rates of, and persistence with, allopurinol. Improving persistence with allopurinol is an important public health goal given the effectiveness of this medicine and its potential to eliminate gout.

## ACKNOWLEDGEMENTS

This work was funded by the Lexy Davies Bequest at St Vincent's Hospital, Sydney. The funding body had no input in the design of the study, collection, analysis and interpretation of the data, and writing of the manuscript. Open access publishing facilitated by University of New South Wales, as part of the Wiley - University of New South Wales agreement via the Council of Australian University Librarians.



## COMPETING INTERESTS

R.O.D., M.J.C., K.T., M.K., E.A., A.R. and S.L.S. declare no conflicts of interest. P.C. is founder and Chief Executive of Prospecion Pty Ltd, the software used in the analyses in this work. M.K. and V.C. are employees of Prospecion Pty Ltd. P.C., M.K. and V.C. acknowledge receipt of fees paid to Prospecion Pty Ltd from R.O.D.'s Lexy Davies Bequest funding to update Prospecion's PharmDash platform with relevant PBS data for the purposes of the study.

## CONTRIBUTORS

M.J.C., R.O.D., D.R.W.K. and S.L.S. designed the research. M.J.C., R.O.D., K.T., M.K., V.C., P.C. and S.L.S. performed the research. M.J.C., R.O.D., K.T., M.K., V.C., P.C. and S.L.S. analysed the data. All authors contributed to the development of the manuscript.

## DATA AVAILABILITY STATEMENT

Research data are not shared.

## ORCID

Matthew J. Coleshill  <https://orcid.org/0000-0003-1906-1893>

Richard O. Day  <https://orcid.org/0000-0002-6045-6937>

Karson Tam  <https://orcid.org/0000-0003-1055-5897>

Eindra Aung  <https://orcid.org/0000-0001-7297-5593>

Diluk R. W. Kannangara  <https://orcid.org/0000-0003-1463-7320>

Anthony Rodgers  <https://orcid.org/0000-0003-1282-1896>

Sophie L. Stocker  <https://orcid.org/0000-0002-2114-587X>

## REFERENCES

- Smith E, Hoy D, Cross M, et al. The global burden of gout: estimates from the Global Burden of Disease 2010 study. *Ann Rheum Dis*. 2014; 73(8):1470-1476. doi:10.1136/annrheumdis-2013-204647
- Robinson PC, Kempe S, Tebbutt I, Roberts L. Epidemiology of inpatient gout in Australia and New Zealand: temporal trends, comorbidities and gout flare site. *Int J Rheum Dis*. 2017;20(6):779-784. doi:10.1111/1756-185X.12941
- Pisaniello HL, Lester S, Gonzalez-Chica D, et al. Gout prevalence and predictors of urate-lowering therapy use: results from a population-based study. *Arthritis Res Ther*. 2018;20(1):143. doi:10.1186/s13075-018-1633-9
- González-Chica DA, Vanlint S, Hoon E, Stocks N. Epidemiology of arthritis, chronic back pain, gout, osteoporosis, spondyloarthropathies and rheumatoid arthritis among 1.5 million patients in Australian general practice: NPS MedicineWise MedicinesInsight dataset. *BMC Musculoskelet Disord*. 2018;19(1):20. doi:10.1186/s12891-018-1941-x
- Kuo C-F, Grainge MJ, Zhang W, Doherty M. Global epidemiology of gout: prevalence, incidence and risk factors. *Nat Rev Rheumatol*. 2015; 11(11):649-662. doi:10.1038/nrrheum.2015.91
- Richette P, Doherty M, Pascual E, et al. 2016 updated EULAR evidence-based recommendations for the management of gout. *Ann Rheum Dis*. 2017;76(1):29-42. doi:10.1136/annrheumdis-2016-209707
- Borstad GC, Bryant LR, Abel MP, Scroggie DA, Harris MD, Alloway JA. Colchicine for prophylaxis of acute flares when initiating allopurinol for chronic gouty arthritis. *J Rheumatol*. 2004;31(12):2429-2432.
- FitzGerald JD, Dalbeth N, Mikuls T, et al. 2020 American College of Rheumatology Guideline for the Management of Gout. *Arthritis Rheumatol*. 2020;72(6):879-895. doi:10.1002/art.41247
- Graham GG, Kannangara DR, Stocker SL, et al. Understanding the dose-response relationship of allopurinol: predicting the optimal dosage. *Br J Clin Pharmacol*. 2013;76(6):932-938. doi:10.1111/bcp.12126
- Harrold LR, Andrade SE, Briesacher BA, et al. Adherence with urate-lowering therapies for the treatment of gout. *Arthritis Res Ther*. 2009; 11(2):R46. doi:10.1186/ar2659
- Zandman-Goddard G, Amital H, Shamrayevsky N, Raz R, Shalev V, Chodick G. Rates of adherence and persistence with allopurinol therapy among gout patients in Israel. *Rheumatology (Oxford)*. 2013;52(6): 1126-1131. doi:10.1093/rheumatology/kes431
- Dehlin M, Ekström EH, Petzold M, Strömberg U, Telg G, Jacobsson LT. Factors associated with initiation and persistence of urate-lowering therapy. *Arthritis Res Ther*. 2017;19(1):6. doi:10.1186/s13075-016-1211-y
- Peterson G. Gout: a very old disease with some new approaches. *Aust Pharm*. 2013;32(3):37-40.
- Hande K, Noone R, Stone W. Severe allopurinol toxicity. Description and guidelines for prevention in patients with renal insufficiency. *Am J Med*. 1984;76(1):47-56. doi:10.1016/0002-9343(84)90743-5
- Scheepers LE, van Onna M, Stehouwer CD, Singh JA, Arts IC, Boonen A. Medication adherence among patients with gout: a systematic review and meta-analysis. *Semin Arthritis Rheum*. 2018;47(5): 689-702.
- de Geest S, Zullig LL, Dunbar-Jacob J, et al. ESPACOMP medication adherence reporting guideline (EMERGE). *Ann Intern Med*. 2018; 169(1):30-35. doi:10.7326/M18-0543
- Weisman A, Tomlinson GA, Lipscombe LL, Perkins BA, Hawker GA. Allopurinol adherence, persistence and patterns of use in individuals with diabetes and gout: A retrospective, population-based cohort analysis. *Semin Arthritis Rheum*. 2021;51(6):1162-1169. doi:10.1016/j.semarthrit.2021.09.003
- Chung Y, Lu C, Graham G, Mant A, Day R. Utilization of allopurinol in the Australian community. *Intern Med J*. 2008;38(6a):388-395. doi:10.1111/j.1445-5994.2008.01641.x
- Cottrell E, Crabtree V, Edwards JJ, Roddy E. Improvement in the management of gout is vital and overdue: an audit from a UK primary care medical practice. *BMC Fam Pract*. 2013;14(1):1-11. doi:10.1186/1471-2296-14-170
- Vaccher S, Kannangara DR, Baysari MT, et al. Barriers to care in gout: from prescriber to patient. *J Rheumatol*. 2016;43(1):144-149. doi:10.3899/jrheum.150607
- Kim A, Kim Y, Kim G-T, Ahn E, So MW, Lee S-G. Comparison of persistence rates between allopurinol and febuxostat as first-line urate-lowering therapy in patients with gout: an 8-year retrospective cohort study. *Clin Rheumatol*. 2020;39:3769-3776.
- Lindquist LA, Go L, Fleisher J, Jain N, Friesema E, Baker DW. Relationship of health literacy to intentional and unintentional non-adherence of hospital discharge medications. *J Gen Intern Med*. 2012; 27(2):173-178. doi:10.1007/s11606-011-1886-3
- van Onna M, Hinsenvelde E, de Vries H, Boonen A. Health literacy in patients dealing with gout: a qualitative study. *Clin Rheumatol*. 2015; 34(9):1599-1603. doi:10.1007/s10067-014-2838-1
- Sarawate CA, Brewer KK, Yang W, et al. Gout medication treatment patterns and adherence to standards of care from a managed care perspective. *Mayo Clin Proc*. 2006;81(7):925-934. doi:10.4065/81.7.925
- Gast A, Mathes T. Medication adherence influencing factors—an (updated) overview of systematic reviews. *Syst Rev*. 2019;8(1):1-17. doi:10.1186/s13643-019-1014-8
- Baker DW, Gazmararian JA, Sudano J, Patterson M. The association between age and health literacy among elderly persons. *J Gerontol B Psychol Sci Soc Sci*. 2000;55(6):S368-S374. doi:10.1093/geronb/55.6.S368
- McGowan B, Bennett K, Silke C, Whelan B. Adherence and persistence to urate-lowering therapies in the Irish setting. *Clin Rheumatol*. 2016;35(3):715-721. doi:10.1007/s10067-014-2823-8

28. Chandratre P, Mallen CD, Roddy E, Liddle J, Richardson J. "You want to get on with the rest of your life": a qualitative study of health-related quality of life in gout. *Clin Rheumatol*. 2016;35(5):1197-1205. doi:[10.1007/s10067-015-3039-2](https://doi.org/10.1007/s10067-015-3039-2)
29. Spencer K, Carr A, Doherty M. Patient and provider barriers to effective management of gout in general practice: a qualitative study. *Ann Rheum Dis*. 2012;71(9):1490-1495. doi:[10.1136/annrheumdis-2011-200801](https://doi.org/10.1136/annrheumdis-2011-200801)
30. Robinson PC, Stamp LK. The management of gout: much has changed. *Aust Fam Physician*. 2016;45(5):299-302.
31. Ramsubeik K, Ramrattan LA, Kaeley GS, Singh JA. Effectiveness of healthcare educational and behavioral interventions to improve gout outcomes: a systematic review and meta-analysis. *Ther Adv Musculoskelet Dis*. 2018;10(12):235-252. doi:[10.1177/1759720X18807117](https://doi.org/10.1177/1759720X18807117)
32. Lawrence A, Scott S, Saparelli F, et al. Facilitating equitable prevention and management of gout for Māori in Northland, New Zealand, through a collaborative primary care approach. *J Prim Health Care*. 2019;11(2):117-127. doi:[10.1071/HC18082](https://doi.org/10.1071/HC18082)
33. Counsell AB, Nguyen AD, Baysari MT, Kannagara DR, McLachlan AJ, Day RO. Exploring current and potential roles of Australian community pharmacists in gout management: a qualitative study. *BMC Fam Pract*. 2018;19(1):1-7. doi:[10.1186/s12875-018-0744-3](https://doi.org/10.1186/s12875-018-0744-3)
34. Khanna PP, Nuki G, Bardin T, et al. Tophi and frequent gout flares are associated with impairments to quality of life, productivity, and increased healthcare resource use: results from a cross-sectional survey. *Health Qual Life Outcomes*. 2012;10(1):117. doi:[10.1186/1477-7525-10-117](https://doi.org/10.1186/1477-7525-10-117)

#### SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

**How to cite this article:** Coleshill MJ, Day RO, Tam K, et al. Persistence with urate-lowering therapy in Australia: A longitudinal analysis of allopurinol prescriptions. *Br J Clin Pharmacol*. 2022;88(11):4894-4901. doi:[10.1111/bcp.15435](https://doi.org/10.1111/bcp.15435)