



Effectiveness of a pharmacist-based gout care management program in a large integrated health plan: Results from a pilot study

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3 **Effectiveness of a pharmacist-based gout care management program in a large**
4 **integrated health plan: Results from a pilot study**
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Article Summary

1. Article focus: Hypotheses addressed
 - A structured, goal-directed program is effective in achieving optimal control of serum uric acid levels in patients with recurrent gout.
 - Successful management of recurrent gout can employ a leveraged approach using a pharmacist-staffed protocol with supervision by a rheumatologist.
 - Chronic gout can be managed efficiently, safely and cost-effectively using a telephone-based ‘virtual clinic’.
2. Key messages
 - A protocol based, goal directed gout management program is highly effective in achieving and maintaining serum uric acid control in patients with recurrent gout.
 - Effective urate lowering therapy can be achieved in a high percentage of gout patients using approved doses of allopurinol when dose titration is used.
 - This program appears to be a promising approach to improving gout management and may offer significant efficiency compared to current practice.
3. Strengths and Limitations

Strengths: The population we studied is representative of gout patients seen in general rheumatology practice, and therefore our results should be widely generalizable. Our program is relatively easy to implement and requires only a trained clinical pharmacist and rheumatologist to carry out.

Limitations: Although encouraging, this pilot study does not prove that our gout management program is more effective than usual care for gout because there was no control group. A study testing this hypothesis is needed. The structure of our organization, which integrates the health plan, pharmacy programs and physician care, is optimal for the use of our program. A non-integrated system might lead to barriers in setting up a similar collaboration. This may limit the applicability of the model.

Abstract

Background:

The incidence of gout has been steadily rising. While effective treatments are available, treatment is often unsuccessful because current approaches to management lack a systematic approach. To address this shortcoming we tested a protocol-based, pharmacist-staffed intervention to manage patients with recurrent gout.

Methods:

Patients in Kaiser Permanente, Northern California (KPNC) with recurrent gout were referred by their primary care physicians to a pharmacist-staffed gout management clinic supervised by a board-certified rheumatologist. The pharmacist used a protocol that employs standard gout medications to achieve and maintain a serum uric acid (sUA) level of 6.0 mg/dl or less. Results from the first 100 consecutive patients enrolled in this pilot program are reported here.

Results:

In 95 evaluable patients enrolled in our pilot program, a sUA of 6.0 mg/dl or less was achieved and maintained in 78 patients with 4 still in the program to date. Five patients declined to participate after referral, and another 13 patients did not complete the program.

Conclusions:

A structured pharmacist-staffed program can effectively and safely lower and maintain uric acid levels in a high percentage of patients with recurrent gout. This care model is simple to implement, efficient and warrants further validation in a clinical trial.

Introduction

Gout is the most common inflammatory arthritis in men (1) and results in considerable morbidity and utilization of health care resources. (2) The past 30 years have witnessed a steady increase in the prevalence of gout. (3–5) The causes of this rise in gout prevalence appear to be linked to the increasing prevalence of obesity, diabetes, chronic renal disease and hypertension. (6,7) Unlike other common rheumatic diseases, the underlying cause of gout, chronic elevation of serum uric acid (sUA), is well understood.

Current approaches for management of other common chronic conditions, such as diabetes, are based on the principle that chronic illnesses are best managed by identifying predictors of optimal outcomes, setting treatment targets, and then monitoring for success in treating to the targets. (8) In the case of gout, an appropriate treatment target has been identified by expert panels sponsored by the European League Against Rheumatism (EULAR) (9) and the American College of Rheumatology (ACR). (10) Both recommend that patients with tophaceous or recurrent gout be treated with urate-lowering therapy (ULT) to a target sUA of < 6.0 mg/dl. Unfortunately, only a minority of gout patients receives appropriate treatment, including doses of ULT sufficient to achieve this target. (11) There are several reasons for this deficiency which have been addressed by other authors. (12,13)

To address the problem of inadequate management of gout, we developed a model for gout management consisting of a ‘virtual’ clinic comprised of a clinical pharmacist under the supervision of a board-certified rheumatologist. Following a written protocol, the

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2
3 pharmacist initiates, adjusts and monitors the use of standard gout medications for
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5 patients referred by their primary care physicians for recurrent or tophaceous gout.
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7 Patients are followed by the clinic until they have 2 consecutive target sUA results at
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10 least 3 months apart, and are then discharged back to their usual care. We report here the
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12 outcomes of a pilot program by presenting the outcomes of the first 100 patients referred
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14 to the program.
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20 **Methods**

21 *Patient referral*

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24 Patients with gout whose primary care physicians practice at KPNC in Richmond, CA
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26 were eligible for referral to the gout management program. Referral was at the discretion
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28 of the primary care physician (sometimes in consultation with a rheumatologist), based
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30 on the intent to use urate-lowering therapy (ULT). The clinical pharmacist then
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32 telephoned the referred patients, introduced them to the protocol and, if they agreed to
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34 participate, entered them into the program. Patients with end stage renal disease were
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36 excluded from the program. The pharmacist, under a protocol approved by the Kaiser
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38 Permanente East Bay Pharmacy and Therapeutics Committee, was authorized to order
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40 relevant laboratory tests and initiate or change orders for the medications used to manage
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42 sUA, and for flare prophylaxis. For treatment of acute flares, medication orders were
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44 sometimes provided by the rheumatologist if outside the scope of the pharmacy protocol.
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55 *Laboratory assessment and monitoring*

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3 Baseline laboratory assessment performed on all referred patients consisted of a sUA,
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5 alanine aminotransferase (ALT), estimated glomerular filtration rate (eGFR) and
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7 complete blood count (CBC). This same panel of laboratory tests was repeated as needed
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9 to monitor progress while the patient was enrolled in the gout management clinic.
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12 13 14 15 *Treatment protocol*

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17 Figure 1 is a schematic diagram of the assessment and treatment protocol. Once entered
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19 into the program, baseline laboratory assessment was performed if not available within
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21 the prior month. If, at the time of referral, a patient was being treated for an acute flare of
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23 gout, this treatment was continued and completed. Once a baseline laboratory assessment
24
25 was available, ULT was either initiated or adjusted if the sUA was above 6.0 mg/dl. Flare
26
27 prophylaxis was used in all cases (see below). After any change in ULT, the patient was
28
29 instructed to return for laboratory assessment (sUA, ALT, CBC, eGFR) in 2 weeks, and
30
31 report any adverse drug reactions (ADRs) or gout symptoms. ADRs or gout flares were
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33 managed by the clinical pharmacist, usually in consultation with the supervising
34
35 rheumatologist. This process was continued in an iterative fashion until a target sUA of \leq
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37 6.0 mg/dl was achieved. Patients at target were asked to repeat the laboratory assessment
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39 in 3 months. At that time, patients still at target were discharged from the clinic and
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41 instructed to continue their medications and follow up with their primary care physician.
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43 Those not at target were either restarted on their ULT or it was titrated and the level re-
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45 tested in 2 weeks. Patients remained in the gout management program until they
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47 demonstrated 2 sUAs \leq 6 mg/dl at least 3 months apart.
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Pharmacological treatments

ULT was initiated with allopurinol in all patients as first-line therapy unless the patient had a known ADR or allergy to allopurinol. The starting dose for allopurinol-naïve patients was 100 mg daily (some patients were on higher doses at the time of referral). Dose titration for patients not at target sUA was done using 100 mg per day increments, or in some cases, patients on 300 mg daily were titrated to 450 mg daily. Patients already on febuxostat or probenecid were maintained on these and doses titrated as needed based on sUA. Patients who developed a significant ADR or symptoms of allergy to allopurinol were switched to either febuxostat 40 mg daily or probenecid 500 mg daily, depending on their clinical status in consultation with the rheumatologist. Dose titration was then continued with these drugs if needed.

Gout-flare prophylaxis in most instances utilized colchicine 0.6 mg daily. For patients with eGFR less than 30, the dose was reduced to 0.3 mg per day. In some patients, if recommended by the rheumatologist, a daily nonsteroidal anti-inflammatory drug (NSAID) treatment was substituted, if no contraindication prevented this.

Acute gout flares were managed by the clinical pharmacist, in consultation with the rheumatologist, using oral NSAIDs, prednisone or colchicine.

Adverse drug reactions (ADR) to medications, incident gout flares and abnormal laboratory parameters were recorded by the clinical pharmacist at each telephone encounter and reviewed by the rheumatologist for management.

Results

Patient demographics and co morbidities of the pilot sample are described in Table 1.

Table 1. Demographic and clinical characteristics of patients (N=100)

| Characteristic | Mean (range) |
|----------------------------------|--------------|
| Age, years | 61 (32-94) |
| BMI, kg/m ² | 31 (20-48) |
| | Percent |
| Male | 75% |
| Hypertension | 75% |
| Chronic kidney disease (CKD 2-4) | 29% |
| Diabetes | 29% |
| Coronary artery disease | 10% |
| Congestive heart failure | 11% |
| 2 or more co-morbidities | 46% |

Three-fourths of the patients were male. The mean age was 61 years, (range: 32 – 94 years). The mean body mass index was 31 kg/m² (range: 20 – 48 kg/m²). Common gout-associated co-morbidities were determined based on the presence of specific ICD-9 codes listed in the problem list of each patient in the electronic medical record, and verified by chart review. The majority of patients had at least one of the common co-morbidities associated with gout. Seventy-eight percent had hypertension, 29% had chronic kidney disease (CKD) stage 3 or 4, and 29% had diabetes. A smaller number had either coronary

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3 artery disease or congestive heart failure. Forty-five percent of the patients had 2 or more
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5 of these co-morbid conditions.
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10 Figure 2 is a schematic that shows the current status of the first 100 patients referred to
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12 our clinic. Five patients declined to participate when initially contacted by the
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14 pharmacist. Thus, 95 patients started the program, and at the time of this analysis, 78 had
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16 completed the program with 2 consecutive sUA measurements of < 6.0 mg/dl, and 4 were
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18 still being managed. Thirteen patients left the program prior to achieving the end point.
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20 Of these, 2 patients died while in the program. One died from complications of
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22 abdominal surgery and the other, aged 94, died at home of “natural causes”. One patient
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24 developed symptoms of an allergic reaction to allopurinol and declined further treatment.
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26 One patient lost insurance coverage, and another was incarcerated. The remaining 8
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28 patients were discharged by the program pharmacist because of a pattern of non-
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30 adherence to treatment or lab monitoring, or because they elected not to complete the
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32 program.
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41 Figure 3 shows the sUA's of each patient in the pilot gout-management study as a set of
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43 paired samples. Each pair of bars represents the baseline sUA (red bars) and final sUA
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45 (blue bars) for each patient. For those patients still in the program (i.e., those who have
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47 not yet achieved the discharge criterion of 2 consecutive sUA measurements of ≤ 6.0
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49 mg/dl), the blue bar is the most recent sUA available if the patient did not complete the
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51 program. The dotted horizontal line represents the sUA target of 6.0 mg/dl. The figure
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3 shows all the patients who entered the program, including those who are still being
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5 managed and those who did not complete the program.
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10 To provide a more detailed view of how patients responded to management by the clinic,
11 we plotted sequential sUA levels in a subset of our patients. Figure 4 shows this analysis
12 in 20 randomly selected patients entering the program. Each line represents the
13 sequential sUA measurements of a single patient for a period of 12 months. Essentially
14 all the patients in this random sample initially responded with significant reduction in
15 sUA. In many patients, this improvement was sustained, but in others, the sUA
16 subsequently rose due to discontinuation of ULT. In these patients, the pharmacist was
17 able, in most cases, to restart ULT and continue testing to assure continuing medication
18 adherence. The Figure also shows that by 12 months in the program, 16 of the 20
19 patients had achieved a target sUA and two had a normal sUA of < 6.8 mg/dl.
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36 Analysis of the 78 patients who have completed the program after achieving and
37 maintaining the targeted sUA showed that 68 (87%, 95% CI: 78% to 94%) were on
38 allopurinol at discharge. Figure 5 shows the distribution of allopurinol doses required to
39 achieve a sUA of ≤ 6.0 . The mean daily allopurinol dose required to achieve a sUA of \leq
40 6 was 311 mg. Sixty-eight percent of patients on allopurinol achieved target on 300 mg
41 per day or less. Only three patients achieved goal on the starting dose of 100 mg daily
42 and two patients required 600 mg per day. All five patients on febuxostat had achieved
43 the goal sUA level on 40 mg per day.
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3 Three patients (3%) experienced rash or other symptoms of allergy to allopurinol. None
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5 required more than discontinuation of the medication. Of these, two patients were
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7 changed to alternative ULT and one patient declined further treatment and discontinued
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9 the program. Elevation of ALT was seen at some time during treatment in 47 patients
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11 (48%), but only 7 of the patients had elevations high enough to require changing
12
13 medication. Most stabilized or returned to normal with continued treatment and
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15 monitoring. Incident acute gout flares were reported in 33 patients (34%). None resulted
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17 in discontinuation of ULT. Gastrointestinal side effects were uncommon and in no case
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19 required a change in therapy.
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27 Discussion

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32 Gout is arguably the best understood of the common inflammatory arthritic diseases;
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34 effective preventive therapy is readily available and the key outcome (sUA < 6 mg/dl in
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36 most cases) is easily measured. Why, then, is unsuccessful control of sUA so frequent? A
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38 number of factors contribute to suboptimal gout management. (11,12,14) Adherence to
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40 ULT is poor when compared to medication adherence in other chronic conditions. (15)
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42 Symptoms are typically intermittent with extended gout-free periods. Moreover, there are
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44 effective treatments for gout flares, and medications (for example, colchicine) that can
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46 reduce the incidence of flares without lowering sUA. It is not surprising therefore, that
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48 many gout patients are never started on, or discontinue ULT. Another important feature
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50 of gout management is that initiation of ULT can lead to a short-term increase in
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52 incidence of gout flares, (16) further discouraging the continuation of therapy. Better
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3 patient education could be expected to improve long-term medication adherence, but is
4 not consistently provided. (17) While diet is clearly a factor in the development of gout
5 (18), patients and physicians frequently place a disproportionate emphasis on dietary
6 restrictions. (19) Although consensus guidelines recommend treating with ULT to a
7 target sUA of 6.0 mg/dl or less, concerns about allopurinol toxicity may discourage some
8 physicians from achieving this goal. In particular, limiting doses of allopurinol in patients
9 with CKD lead to a high percentage of treatment failures (20). Finally, many clinical
10 laboratories do not correctly identify serum urate concentrations of > 6.8 mg/dl as being
11 abnormal. This leads to under-treatment and considerable confusion about diagnosis and
12 management. (21)
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29 Our pilot program was conceived as a way to re-frame the approach to gout management.
30 We hypothesized that using a structured treat-to-target approach with regular monitoring
31 and a goal-directed intervention would result in a high percentage of patients achieving a
32 target sUA. In particular, the protocol was designed to use a slow titration of ULT along
33 with flare prophylaxis and scheduled follow up calls. We also required sustained control
34 of sUA for at least 3 months as a way to promote longer term medication adherence.
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46 The results of our pilot program suggest that a structured program may be an effective
47 approach to gout management. ULT medications are highly effective, and therefore
48 almost all our patients responded with significant reductions in sUA within weeks of
49 starting the program (Figure 4). Dose titration allowed most patients to achieve a target
50 sUA of ≤ 6.0 mg/dl and to-date, all patients have been able to achieve goal using standard
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3 doses of available medications. The demographic and clinical features of the patients in
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5 our gout sample were similar to those seen in the general population of gout patients
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7 described in previous studies, (22,23) suggesting that our findings should be
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9 generalizable to gout populations outside KPNC. A nurse-staffed case management
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11 approach has been used and achieved impressive results in controlling sUA in gout
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13 patients (24). Our pilot program is also based on a structured management approach, but
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15 did not require any clinic visits. This model is highly efficient and therefore suitable for
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17 managing a large population of gout patients.
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24 We used a treat-to-target approach and did not limit doses of allopurinol specifically
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26 based on renal function. Current recommendations do not support the need to limit
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28 allopurinol doses to 100 mg daily in patients with CKD, (25–27) though a low starting
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30 dose and slow titration is recommended. (26,28) Indeed, limiting the dose of allopurinol
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32 based on the presence of chronic kidney disease has been shown to result in treatment
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34 failure in an unacceptably high percentage of patients. (17) Our data confirm this
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36 observation: only three of 68 allopurinol-treated patients (4%) completing the program
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38 achieved a sUA of ≤ 6.0 on 100 mg daily of allopurinol, and only 68% achieved target
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40 with 300 mg daily (Figure 5).
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48 Not surprisingly, we encountered many cases of medication non-adherence. Our protocol,
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50 by requiring two consecutive target sUA levels three months apart, was designed with the
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52 expectation that adherence to ULT would be inconsistent. We do not know whether our
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54 time-limited intervention will ultimately lead to long-term control of sUA in these
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3 patients, but we were able to detect medication non-adherence in the first few months and
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5 thus reinforce the importance of long-term ULT. Ideally, monitoring of sUA would
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7 continue on a regular basis, as recommended for relevant laboratory parameters in other
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9 chronic conditions.
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13 We designed our pilot to be efficient and cost-effective by leveraging physician time.
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15 The gout management program, while supervised by a rheumatologist, was staffed by a
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17 clinical pharmacist who was carefully trained in the management protocol. The
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19 pharmacist was able to manage a cohort of up to about 80 patients at a time while
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21 spending only about 6-8 hours per week. The time spent in overseeing and assisting the
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23 clinical pharmacist was never more than about 30 minutes per week for the
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25 rheumatologist once the program was in place. Moreover, our program did not require
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27 any in-person visits. This model suggests a path to improved outcomes in gout patients
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29 without generating the magnitude of increased utilization of health care resources that
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31 might otherwise be required.
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42 **Contributorship Statement**

43 Robert Goldfien

44
45 Conceived and developed protocol and program. Participated in collection and analysis of
46
47 data, and pharmacist supervision. Primary author of manuscript.
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50 Andrew Avins

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52 Consulted on project design, data capture, statistical methods and manuscript editing.
53
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55 Alice Pressman

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Oversaw data analysis and presentation. Consulted on data analysis and manuscript editing.

Alice Hwe

Oversaw development and approval of treatment protocol and supervised clinical pharmacists.

Alice Jacobson

Assisted with data collection and analysis.

Michele Ng and Goldie Yip

Worked directly with subjects to arrange data collection, adjust medications, obtain clinical information and report issues or concerns with supervising rheumatologist

Data sharing

There are no additional unpublished data from this study.

Competing Interests

None

Funding

None

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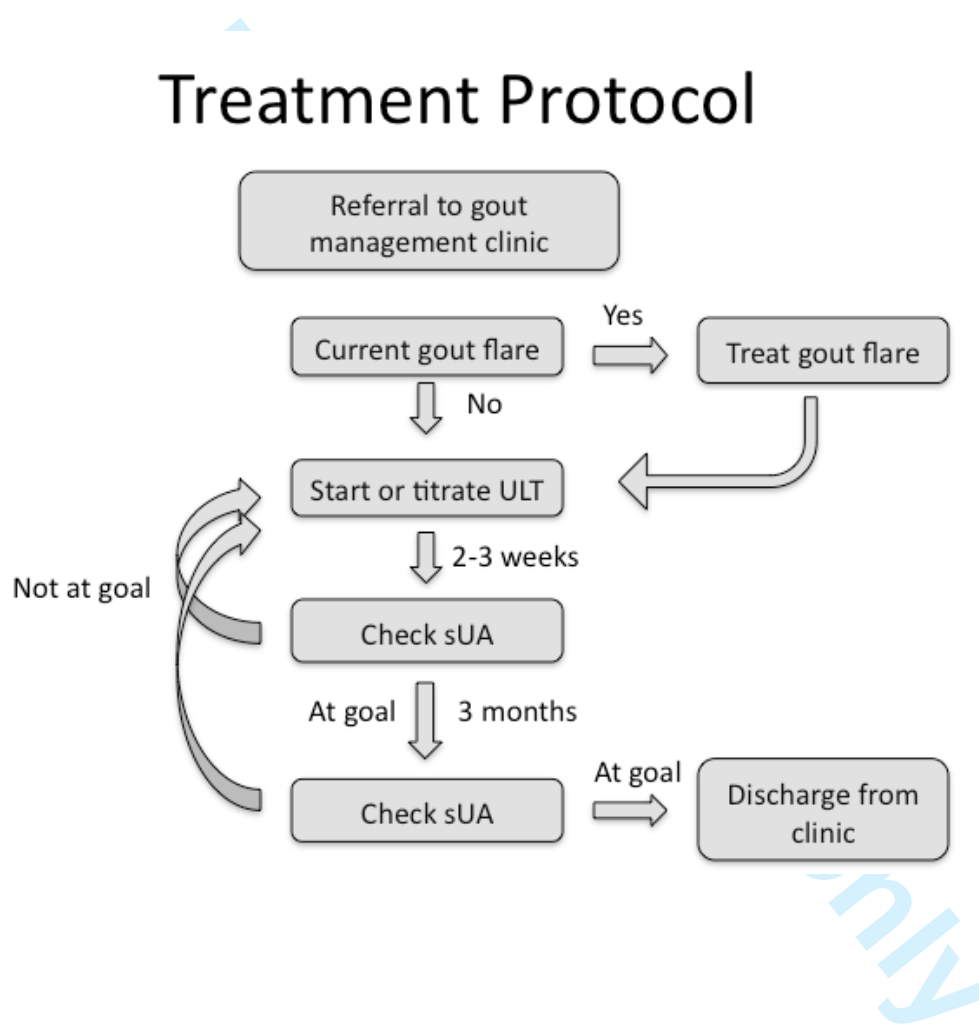
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Figures

Fig. 1 Clinic monitoring and treatment flow diagram



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Fig. 2 Current status of first 100 patients referred to program

Current Patient Status

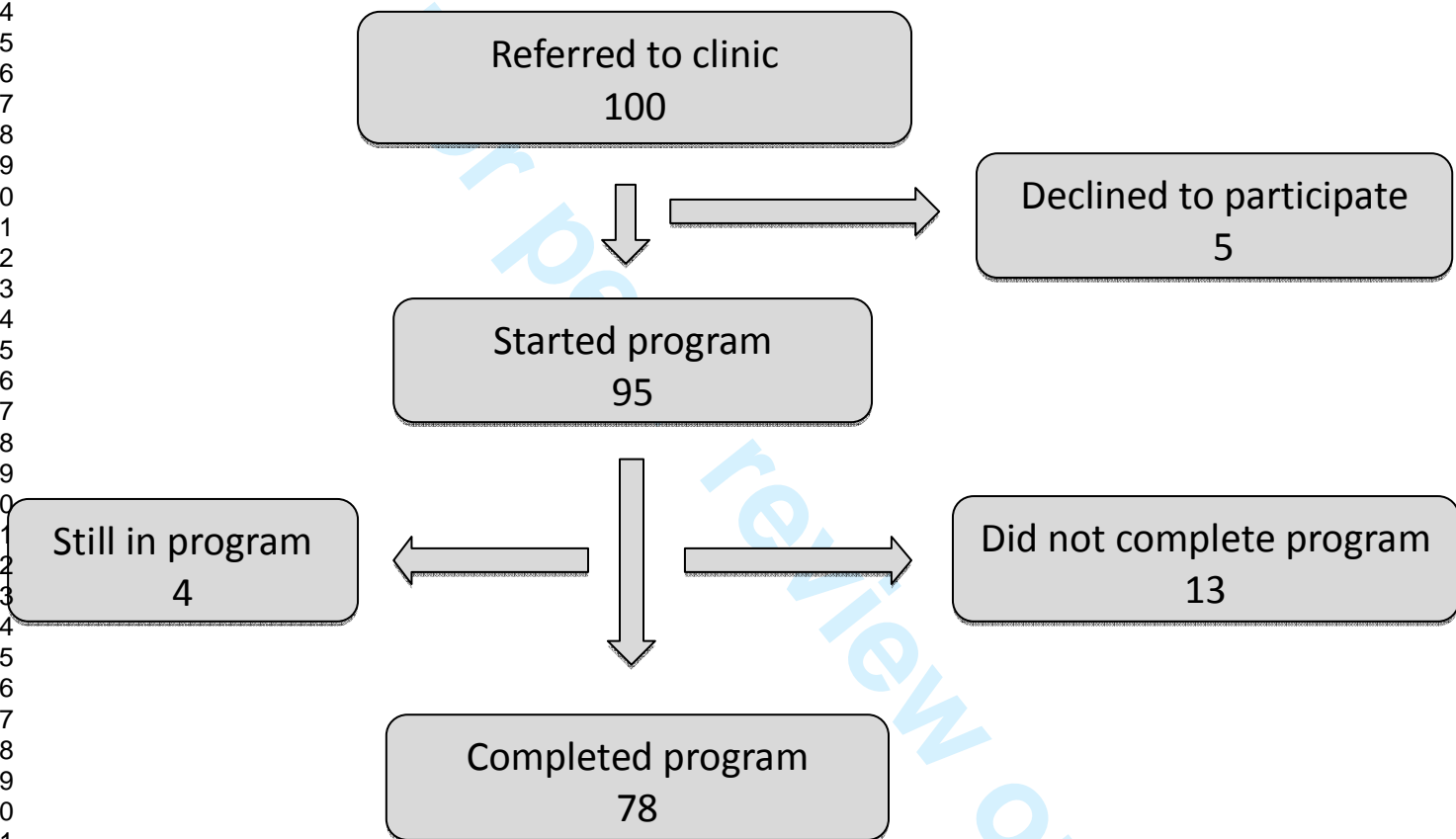


Fig. 3 Comparison of pre-treatment sUA and most recent or final sUA. Each patient is represented by a red bar (initial sUA) and a blue bar (final sUA, whether or not he/she completed the program).

sUA Pairs: First and Last

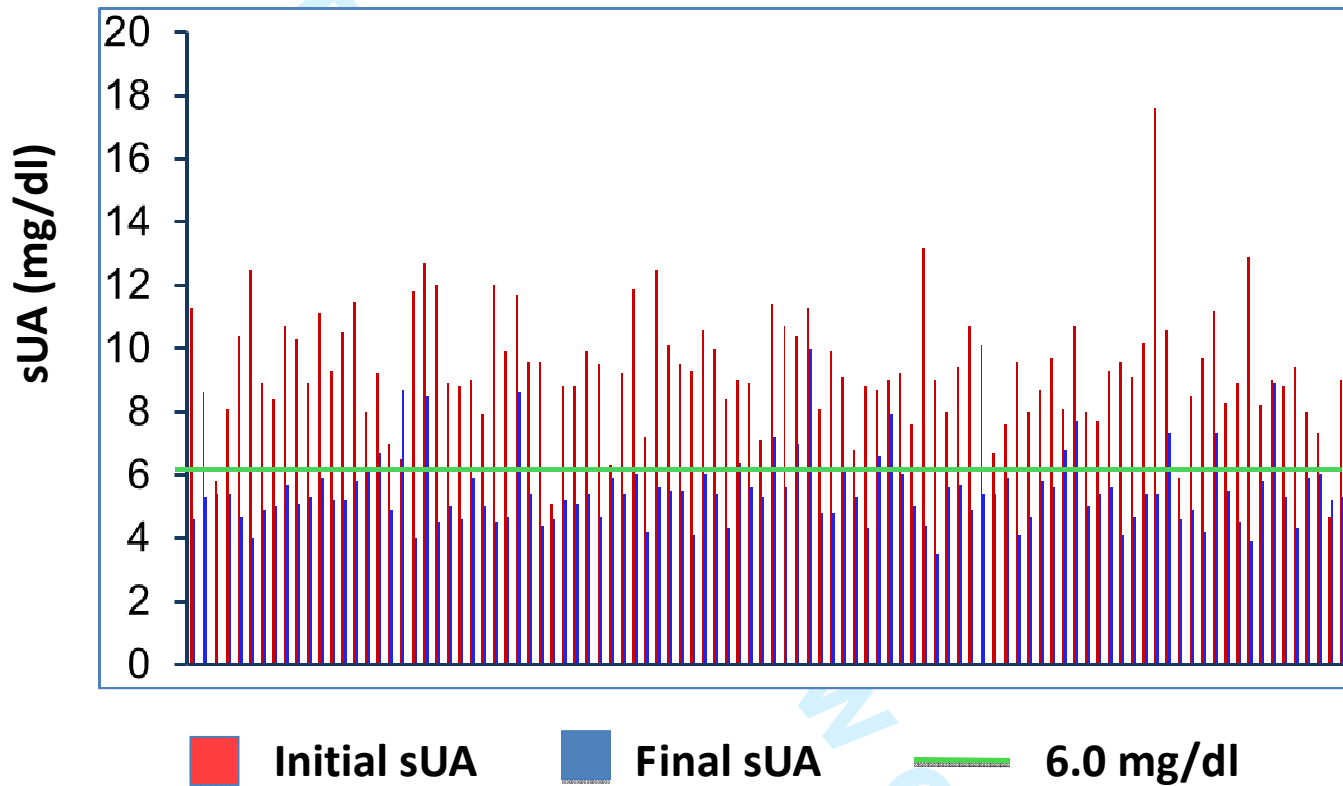
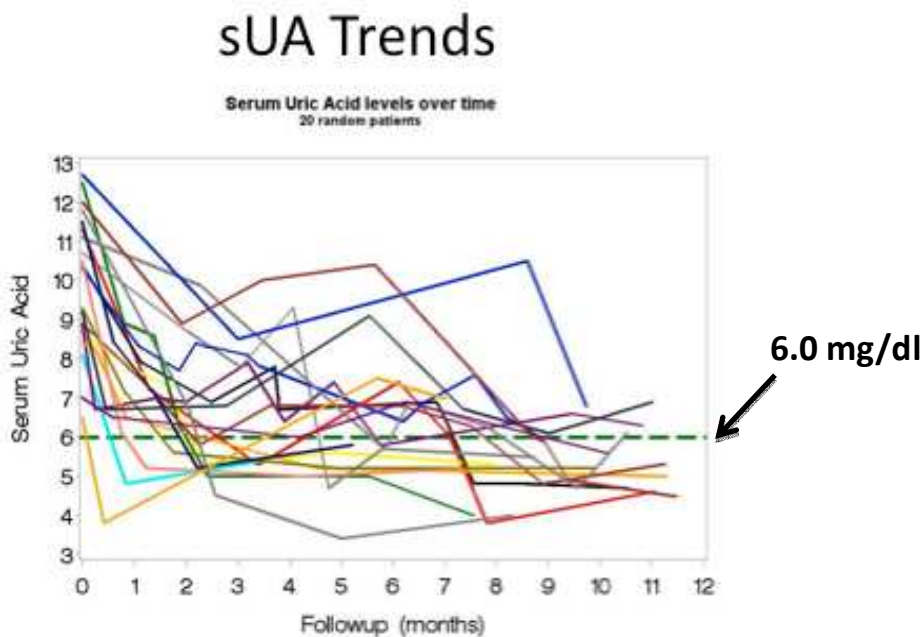


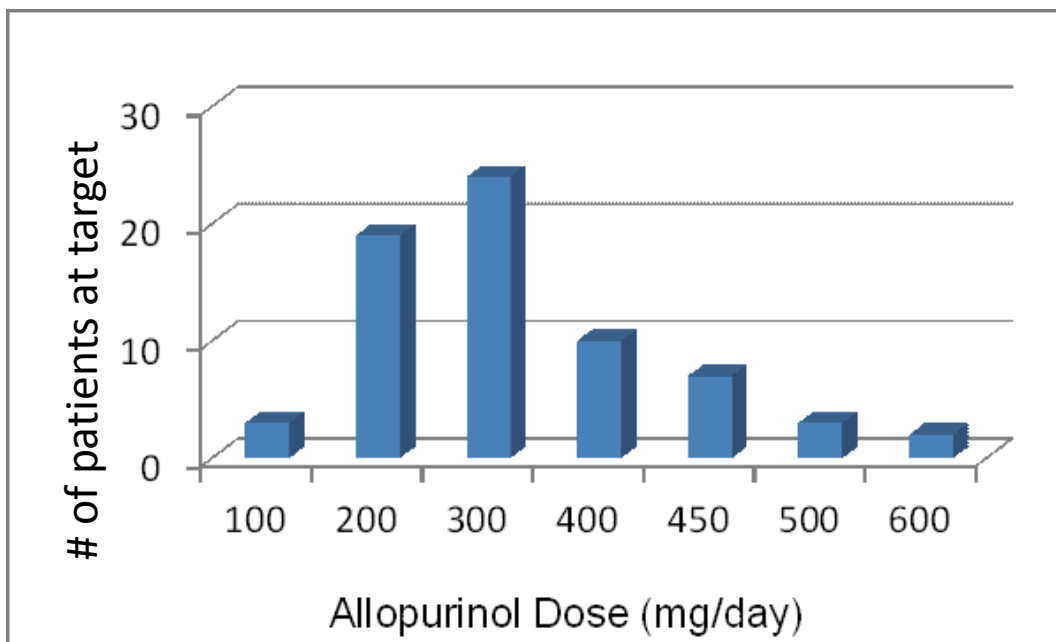
Fig. 4 sUA trend lines for 20 randomly selected patients. Each colored line represents sequential sUA levels in a single patient. Each line stops at the time of clinic discharge or is the most recent sUA if the patient had not completed or left the program.



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Fig. 5 Dose of Allopurinol required to achieve a sUA of ≤ 6.0 mg/dl



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Effectiveness of a pharmacist-based gout care management program in a large integrated health plan: Results from a pilot study

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3 **Effectiveness of a pharmacist-based gout care management program in a large**
4 **integrated health plan: Results from a pilot study**
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Abstract

Objectives:

The study objective was to determine the feasibility of using a pharmacist-staffed, protocol-based structured approach to improving the management of chronic, recurrent gout.

Setting:

The study was carried out in the outpatient clinic of a single Kaiser Permanente medical center.

This is a community based clinic.

Participants:

We report on one hundred consecutive patients between the ages of 21 and 94 (75% male) with chronic or recurrent gout, referred by their primary physicians for the purpose of management of urate lowering therapy. Patients with Stage 5 chronic kidney disease or end-stage kidney disease were excluded.

Interventions:

The program consisted of a trained clinical pharmacist and a rheumatologist. The pharmacist contacted each patient by phone, provided educational and dietary materials, and used a protocol that employs standard gout medications to achieve and maintain a serum uric acid (sUA) level of 6.0 mg/dl or less. Incident gout flares or adverse reactions to medications were managed in consultation with the rheumatologist.

Primary outcome measure:

The primary outcome measure was the achievement and maintenance of a serum uric acid of 6.0 or less for a period of at least 3 months.

Results:

In 95 evaluable patients enrolled in our pilot program, a sUA of 6.0 mg/dl or less was achieved and maintained in 78 patients with 4 still in the program to date. Five patients declined to participate after referral, and another 13 patients did not complete the program. (The majority of these were due to non-adherence.)

Conclusions:

A structured pharmacist-staffed program can effectively and safely lower and maintain uric acid

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3 levels in a high percentage of patients with recurrent gout in a primary care setting. This care
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5 model is simple to implement, efficient and warrants further validation in a clinical trial.
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19 Gout is the most common inflammatory arthritis in men (1) and results in considerable
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21 morbidity and utilization of health care resources. (2) The past 30 years have witnessed a
22
23 steady increase in the prevalence of gout. (3–5) The causes of this rise in gout prevalence
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25 appear to be linked to the increasing prevalence of obesity, diabetes, chronic renal disease
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27 and hypertension. (6,7) Unlike other common rheumatic diseases, the underlying cause of
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29 gout, chronic elevation of serum uric acid (sUA), is well understood.
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37 Current approaches for management of other common chronic conditions, such as
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39 diabetes, are based on the principle that chronic illnesses are best managed by identifying
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41 predictors of optimal outcomes, setting treatment targets, and then monitoring for success
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43 in treating to the targets. (8) In the case of gout, an appropriate treatment target has been
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45 identified by expert panels sponsored by the European League Against Rheumatism
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47 (EULAR) (9) and the American College of Rheumatology (ACR). (10) Both recommend
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49 that patients with tophaceous or recurrent gout be treated with urate-lowering therapy
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51 (ULT) to a target sUA of < 6.0 mg/dl. Unfortunately, only a minority of gout patients
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53 receives appropriate treatment, including doses of ULT sufficient to achieve this target.
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57 (11) There are several reasons for this deficiency which have been addressed by other
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3 authors. (12,13). The reasons cited have included lack of appropriate monitoring, failure
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5 to treat to target and fear of escalation of ULT in some patients, particularly patients with
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7 chronic kidney disease. Taken together, it appears that there is a great need for improved
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9 approaches to the management of gout.
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14 To address the problem of inadequate management of gout, we developed a model for
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16 gout management consisting of a 'virtual' clinic comprised of a clinical pharmacist under
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18 the supervision of a board-certified rheumatologist. Following a written protocol, the
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20 pharmacist initiates, adjusts and monitors the use of standard gout medications for
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22 patients referred by their primary care physicians for recurrent or tophaceous gout.
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26 Patients are followed by the clinic until they have 2 consecutive target sUA results at
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28 least 3 months apart, and are then discharged back to their usual care. We report here the
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30 results of a pilot program by presenting the outcomes of the first 100 patients referred to
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32 the program. Though a limited intervention, our intent was to address some of the issues
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34 identified in the literature and do it in a way that is highly leveraged and potentially
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36 suitable for a large majority of patients with chronic gout who are currently not being
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38 adequately managed.
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45 46 **Methods**

47 48 49 *Patient referral*

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51 Patients with gout whose primary care physicians practice at KPNC in Richmond, CA
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53 were eligible for referral to the gout management program. Referral was at the discretion
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3 of the primary care physician (sometimes in consultation with a rheumatologist), based
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5 on a history of recurrent or tophaceous gout and the intent to use urate-lowering therapy
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7 (ULT). Referring physicians were offered the choice of referring each patient for a
8
9 formal rheumatology consultation, or to the gout management program, supervised by the
10
11 same rheumatologist (RG). The clinical pharmacist then telephoned the referred patients,
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13 introduced them to the protocol and, if they agreed to participate, entered them into the
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15 program. Patients consenting to treatment in the program were provided written
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17 educational material including dietary guidelines at the time of program entry. Patients
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19 with end stage renal disease were excluded from the program. The pharmacist, under a
20
21 protocol approved by the Kaiser Permanente East Bay Pharmacy and Therapeutics
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23 Committee, was authorized to order relevant laboratory tests and initiate or change orders
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25 for the medications used to manage sUA, and for flare prophylaxis. For treatment of
26
27 acute flares, medication orders were sometimes provided by the rheumatologist if outside
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29 the scope of the pharmacy protocol.
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39 *Laboratory assessment and monitoring*

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41 Baseline laboratory assessment performed on all referred patients consisted of a sUA,
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43 alanine aminotransferase (ALT), estimated glomerular filtration rate (eGFR) and
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45 complete blood count (CBC). This same panel of laboratory tests was repeated as needed
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47 to monitor progress while the patient was enrolled in the gout management clinic.
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51 *Treatment protocol*

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Figure 1 is a schematic diagram of the assessment and treatment protocol. Once entered into the program, baseline laboratory assessment was performed if not available within the prior month. If, at the time of referral, a patient was being treated for an acute flare of gout, this treatment was continued and completed. Once a baseline laboratory assessment was available, ULT was either initiated or adjusted if the sUA was above 6.0 mg/dl. Flare prophylaxis was used in all cases (see below). After any change in ULT, the patient was instructed to return for laboratory assessment (sUA, ALT, CBC, eGFR) in 2 weeks, and report any adverse drug reactions (ADRs) or gout symptoms. ADRs or gout flares were managed by the clinical pharmacist, usually in consultation with the supervising rheumatologist. This process was continued in an iterative fashion until a target sUA of \leq 6.0 mg/dl was achieved. Patients at target were asked to repeat the laboratory assessment in 3 months. At that time, patients still at target were discharged from the clinic and instructed to continue their medications and follow up with their primary care physician. Those not at target were either restarted on their ULT or it was titrated and the level re-tested in 2 weeks. Patients remained in the gout management program until they demonstrated 2 sUAs \leq 6 mg/dl at least 3 months apart.

Pharmacological treatments

ULT was initiated with allopurinol in all patients as first-line therapy unless the patient had a known ADR or allergy to allopurinol. The starting dose for allopurinol-naïve patients was 100 mg daily (some patients were on higher doses at the time of referral). Dose titration for patients not at target sUA was done using 100 mg per day increments, or in some cases, although selected patients on 300 mg daily were titrated to 450 mg

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3 daily. The maximum allopurinol dose used in the program was 600 mg per day. Patients
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5 already on febuxostat or probenecid were maintained on these and doses titrated as
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7 needed based on sUA. Patients who developed a significant ADR or symptoms of
8
9 allergy to allopurinol were switched to either febuxostat 40 mg daily or probenecid 500
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11 mg daily, depending on their clinical status in consultation with the rheumatologist. Dose
12
13 titration was then continued with these drugs if needed.
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18 Gout-flare prophylaxis was used in all patients and in most instances we utilized
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20 colchicine 0.6 mg daily. For patients with eGFR less than 30, the dose was reduced to 0.3
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22 mg per day. In some patients, if recommended by the rheumatologist, a daily
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24 nonsteroidal anti-inflammatory drug (NSAID) treatment was substituted, if no
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26 contraindication prevented this.
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34 Acute gout flares were managed by the clinical pharmacist, in consultation with the
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36 rheumatologist, using oral NSAIDs, prednisone or colchicine.
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41 Adverse drug reactions (ADR) to medications, incident gout flares and abnormal
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43 laboratory parameters were recorded by the clinical pharmacist at each telephone
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45 encounter and reviewed by the rheumatologist for management.
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49 50 **Results**

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53 Patient demographics and co morbidities of the pilot sample are described in Table 1.
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Table 1. Demographic and clinical characteristics of patients (N=100)

| Characteristic | Mean (range) |
|----------------------------------|--------------|
| Age, years | 61 (32-94) |
| BMI, kg/m ² | 31 (20-48) |
| | Percent |
| Male | 75% |
| Hypertension | 75% |
| Chronic kidney disease (CKD 2-4) | 29% |
| Diabetes | 29% |
| Coronary artery disease | 10% |
| Congestive heart failure | 11% |
| 2 or more co-morbidities | 46% |

Three-fourths of the patients were male. The mean age was 61 years, (range: 32 – 94 years). The mean body mass index was 31 kg/m² (range: 20 – 48 kg/m²). Common gout-associated co-morbidities were determined based on the presence of specific ICD-9 codes listed in the problem list of each patient in the electronic medical record, and verified by chart review. The majority of patients had at least one of the common co-morbidities associated with gout. Seventy-eight percent had hypertension, and 29% had chronic kidney disease (CKD). Of these, 2 had stage 2 CKD, 22 had stage 3 CKD and 3 had stage 4 CKD. Another 29% had diabetes. A smaller number had either coronary artery disease or congestive heart failure. Forty-five percent of the patients had 2 or more of these co-morbid conditions.

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3 Figure 2 is a schematic that shows the current status of the first 100 patients referred to
4 our clinic. Five patients declined to participate when initially contacted by the
5 pharmacist. Thus, 95 patients started the program, and at the time of this analysis, 78 had
6 completed the program with 2 consecutive sUA measurements of < 6.0 mg/dl, and 4 were
7 still being managed. Thirteen patients left the program prior to achieving the end point.
8 Of these, 2 patients died while in the program. One died from complications of
9 abdominal surgery and the other, aged 94, died at home of “natural causes”. One patient
10 developed symptoms of an allergic reaction to allopurinol and declined further treatment.
11 One patient lost insurance coverage, and another was incarcerated. The remaining 8
12 patients were discharged by the program pharmacist because of a pattern of non-
13 adherence to treatment or lab monitoring, or because they elected not to complete the
14 program. The time patients spent under program management varied considerably. The
15 mean duration of participation was 47.8 weeks (range 14.9-109.6 weeks). Although our
16 program was a feasibility study and designed as a short term intervention, when we
17 examined the medical records of the 78 patients who have successfully completed the
18 program, we found that 63 of these had been tested at least one time by their regular
19 physician after clinic discharge (mean follow up time 36 weeks) and that 53 of these
20 (80%) still maintained a sUA of 6.0 or less.
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48 Figure 3 shows the sUA's of each patient in the pilot gout-management study as a set of
49 paired samples. Each pair of bars represents the baseline sUA (red bars) and final sUA
50 (blue bars) for each patient. For those patients still in the program (i.e., those who have
51 not yet achieved the discharge criterion of 2 consecutive sUA measurements of ≤ 6.0
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3 mg/dl), the blue bar is the most recent sUA available if the patient did not complete the
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5 program. The dotted horizontal line represents the sUA target of 6.0 mg/dl. The figure
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7 shows all the patients who entered the program, including those who are still being
8
9 managed and those who did not complete the program.
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15 To provide a more detailed view of how patients responded to management by the clinic,
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17 we plotted sequential sUA levels in a subset of our patients. Figure 4 shows this analysis
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19 in 20 randomly selected patients entering the program. Each line represents the
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21 sequential sUA measurements of a single patient for a period of 12 months. Essentially
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23 all the patients in this random sample initially responded with significant reduction in
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25 sUA. In many patients, this improvement was sustained, but in others, the sUA
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27 subsequently rose due to discontinuation of ULT. In these patients, the pharmacist was
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29 able, in most cases, to restart ULT and continue testing to assure continuing medication
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31 adherence. The Figure also shows that by 12 months in the program, 16 of the 20
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33 patients had achieved a target sUA and two had a normal sUA of < 6.8 mg/dl.
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41 Analysis of the 78 patients who have completed the program after achieving and
42
43 maintaining the targeted sUA showed that 68 (87%, 95% CI: 78% to 94%) were on
44
45 allopurinol at discharge. Figure 5 shows the distribution of allopurinol doses required to
46
47 achieve a sUA of ≤ 6.0 . The mean daily allopurinol dose required to achieve a sUA of \leq
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49 6 was 311 mg. Sixty-eight percent of patients on allopurinol achieved target on 300 mg
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51 per day or less. Only three patients achieved goal on the starting dose of 100 mg daily
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3 and two patients required 600 mg per day. All five patients on febuxostat had achieved
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5 the goal sUA level on 40 mg per day.
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10 Three patients (3%) experienced rash or other symptoms of allergy to allopurinol. None
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12 required more than discontinuation of the medication. Of these, two patients were
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14 changed to alternative ULT and one patient declined further treatment and discontinued
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16 the program. Elevation of ALT was seen at some time during treatment in 47 patients
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18 (48%), but only 7 of the patients had elevations high enough to require changing
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20 medication. Most stabilized or returned to normal with continued treatment and
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22 monitoring. Incident acute gout flares were reported in 33 patients (34%). None resulted
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24 in discontinuation of ULT. Gastrointestinal side effects were uncommon and in no case
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26 required a change in therapy.
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34 Discussion

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38 Gout is arguably the best understood of the common inflammatory arthritic diseases;
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40 effective preventive therapy is readily available and the key outcome (sUA < 6 mg/dl in
41
42 most cases) is easily measured. Why, then, is unsuccessful control of sUA so frequent? A
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44 number of factors contribute to suboptimal gout management. (11,12,14) Adherence to
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46 ULT is poor when compared to medication adherence in other chronic conditions. (15)
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48 Symptoms are typically intermittent with extended gout-free periods. Moreover, there are
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50 effective treatments for gout flares, and medications (for example, colchicine) that can
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52 reduce the incidence of flares without lowering sUA. It is not surprising therefore, that
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3 many gout patients are never started on, or discontinue ULT. Another important feature
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5 of gout management is that initiation of ULT can lead to a short-term increase in
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7 incidence of gout flares, (16) further discouraging the continuation of therapy. Better
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9 patient education could be expected to improve long-term medication adherence, but is
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11 not consistently provided. (17) While diet is clearly a factor in the development of gout
12
13 (18), patients and physicians frequently place a disproportionate emphasis on dietary
14
15 restrictions. (19) Although consensus guidelines recommend treating with ULT to a
16
17 target sUA of 6.0 mg/dl or less, concerns about allopurinol toxicity may discourage some
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19 physicians from achieving this goal. In particular, limiting doses of allopurinol in patients
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21 with CKD lead to a high percentage of treatment failures (20). Finally, many clinical
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23 laboratories do not correctly identify serum urate concentrations of > 6.8 mg/dl as being
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25 abnormal. This leads to under-treatment and considerable confusion about diagnosis and
26
27 management. (21)

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36 Our pilot program was conceived as a way to re-frame the approach to gout management.
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38 We hypothesized that using a structured treat-to-target approach with regular monitoring
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40 and a goal-directed intervention would result in a high percentage of patients achieving a
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42 target sUA. In particular, the protocol was designed to use a slow titration of ULT along
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44 with flare prophylaxis and scheduled follow up calls. We also required sustained control
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46 of sUA for at least 3 months as a way to promote longer term medication adherence. We
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48 realize that maintaining treatment for 3 months does not guarantee long term control of
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50 sUA. Nevertheless, of the patients for whom a follow up test was available, 80% were
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3 still at target a mean of 36.8 weeks after clinic discharge. As for any chronic condition,
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5 optimal outcomes will require some level of structured monitoring.
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10 The results of our pilot program suggest that a structured program may be an effective
11 approach to gout management. ULT medications are highly effective, and therefore
12 almost all our patients responded with significant reductions in sUA within weeks of
13 starting the program (Figure 4). Dose titration allowed most patients to achieve a target
14 sUA of ≤ 6.0 mg/dl and to-date, all patients have been able to achieve goal using standard
15 doses of available medications. The demographic and clinical features of the patients in
16 our gout sample were similar to those seen in the general population of gout patients
17 described in previous studies, (22) suggesting that our findings should be generalizable to
18 gout populations outside KPNC. A nurse-staffed case management approach has been
19 used and achieved impressive results in controlling sUA in gout patients (23). Our pilot
20 program is also based on a structured management approach, but did not require any
21 clinic visits. This model is highly efficient and therefore suitable for managing a large
22 population of gout patients, but not necessarily more effective than a case management
23 approach.
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46 There is ample evidence that therapeutic inertia contributes to inadequate results of ULT
47 (24). Our program was designed specifically to counter this problem by including
48 repeated sUA measurements and specified actions based on the results. In addition, our
49 protocol did not limit doses of allopurinol specifically based on renal function, which has
50 been one of several impediments noted in the literature to successful ULT. Current
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3 recommendations do not support the need to limit allopurinol doses to 100 mg daily in
4 patients with CKD, (25–27) though a low starting dose and slow titration is
5 recommended. (26,28) Indeed, limiting the dose of allopurinol based on the presence of
6 chronic kidney disease has been shown to result in treatment failure in an unacceptably
7 high percentage of patients. (17) Our data confirm this observation: only three of 68
8 allopurinol-treated patients (4%) completing the program achieved a sUA of ≤ 6.0 on
9 100 mg daily of allopurinol, and only 68% achieved target with 300 mg daily (Figure 5).

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22 Not surprisingly, we encountered many cases of medication non-adherence. In most
23 cases, this was detected in the course of the routine testing that comprised the protocol.
24 Typically a patient whose sUA was at or near target, had a repeat test that was no longer
25 at target. In some cases, non-adherence was discovered at the time the patient called to
26 pharmacist because of a gout flare. Our protocol, by requiring two consecutive target
27 sUA levels three months apart, was designed with the expectation that adherence to ULT
28 would be inconsistent. As noted previously, we do not know whether our time-limited
29 intervention will ultimately lead to long-term control of sUA in these patients, but we
30 were able to detect medication non-adherence in the first few months and thus reinforce
31 the importance of long-term ULT. Ideally, monitoring of sUA would continue on a
32 regular basis, as recommended for relevant laboratory parameters in other chronic
33 conditions. Despite the fact that all patients were prescribed colchicine or NSAIDs for
34 flare prophylaxis, we encountered a substantial number of gout flares during the program.
35 While some increase in flares may be expected, in our experience, many of the flares in
36 our patients occurred in connection with medication non-adherence. This tendency of
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3 gout patients to discontinue ULT accounted for the wide range of times patients had to
4 stay under management. We provided our patients with written educational material as
5 well, but could not evaluate the effectiveness of this.
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10 We designed our pilot to be efficient and cost-effective by leveraging physician time.
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12 The gout management program, while supervised by a rheumatologist, was staffed by a
13 clinical pharmacist who was carefully trained in the management protocol. The
14 pharmacist was able to manage a cohort of up to about 80 patients at a time while
15 spending only about 6-8 hours per week. The time spent in overseeing and assisting the
16 clinical pharmacist was never more than about 30 minutes per week for the
17 rheumatologist once the program was in place. Moreover, our program did not require
18 any in-person visits. This model suggests a path to improved outcomes in gout patients
19 without generating the magnitude of increased utilization of health care resources that
20 might otherwise be required. We recognize that pharmacists may not be available or
21 allowed to manage patients as was done in our protocol. Even so, a trained clinical nurse
22 could be substituted in the pharmacist's role and provide excellent care while leveraging
23 physician time.
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Contributorship Statement

Robert Goldfien

Conceived and developed protocol and program. Participated in collection and analysis of data, and pharmacist supervision. Primary author of manuscript.

Andrew Avins

Consulted on project design, data capture, statistical methods and manuscript editing.

Alice Pressman

Oversaw data analysis and presentation. Consulted on data analysis and manuscript editing.

Alice Hwe

Oversaw development and approval of treatment protocol and supervised clinical pharmacists.

Alice Jacobson

Assisted with data collection and analysis.

Michele Ng and Goldie Yip

Worked directly with subjects to arrange data collection, adjust medications, obtain clinical information and report issues or concerns with supervising rheumatologist

Data sharing

There are no additional unpublished data from this study.

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None

Competing Interests

None

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Figures

Fig. 1 Clinic monitoring and treatment flow diagram

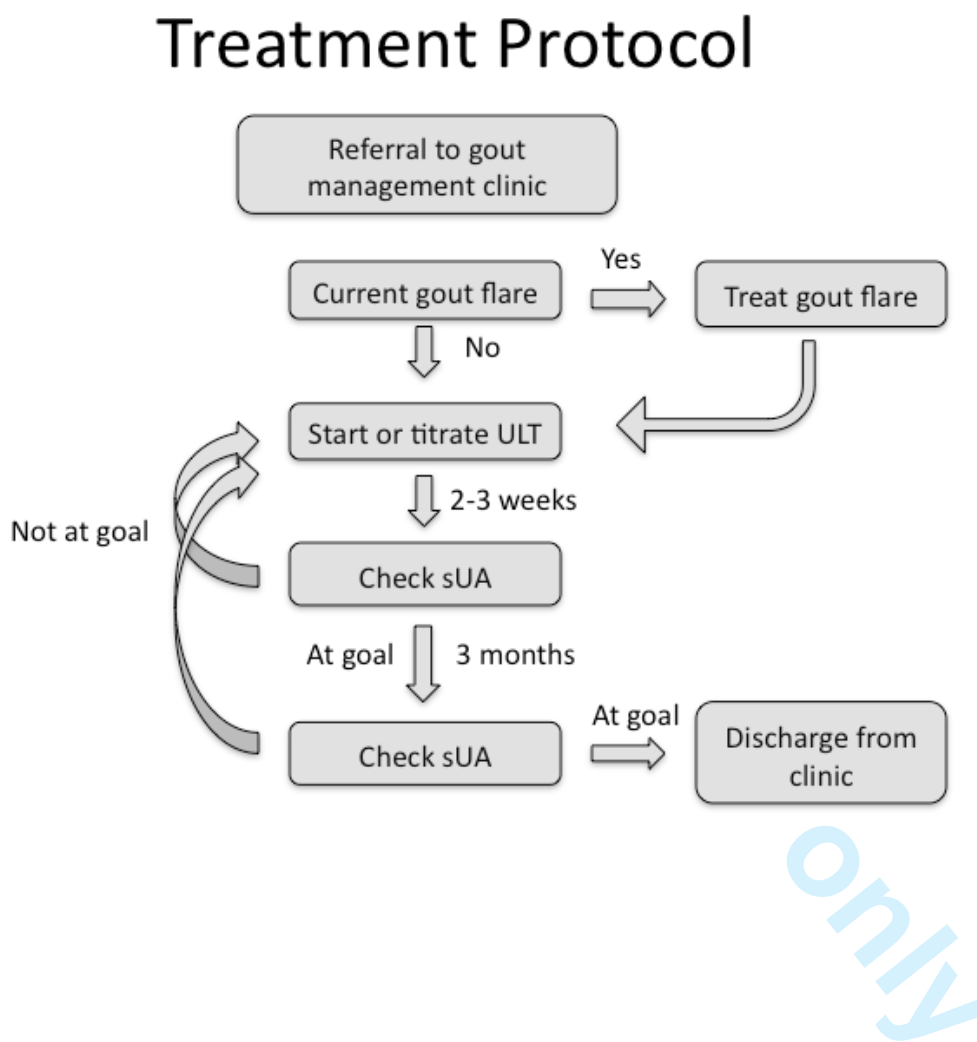
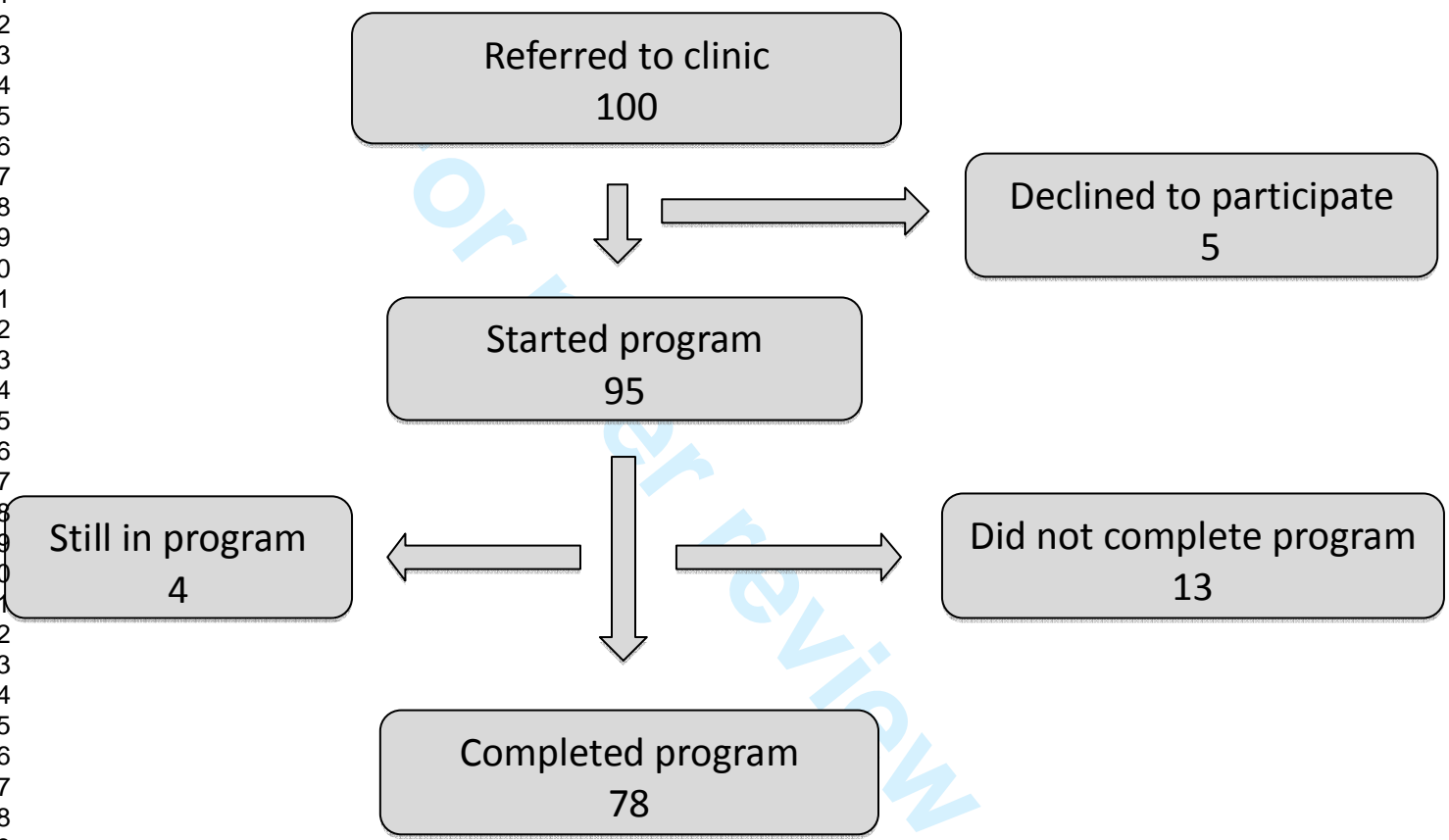


Fig. 2 Current status of first 100 patients referred to program

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Current Patient Status



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Fig. 3 Comparison of pre-treatment sUA and most recent or final sUA. Each patient is represented by a red bar (initial sUA) and a blue bar (final sUA, whether or not he/she completed the program).

sUA Pairs: First and Last

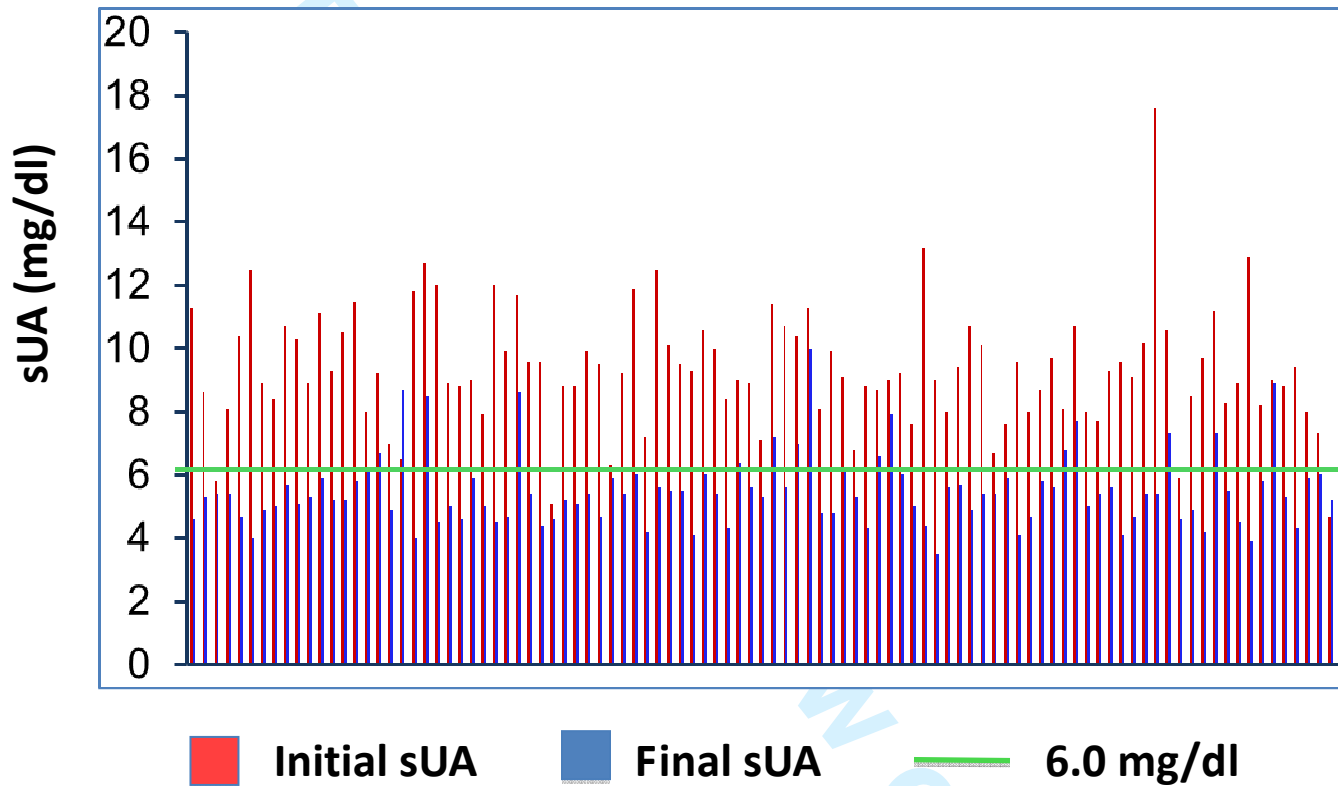
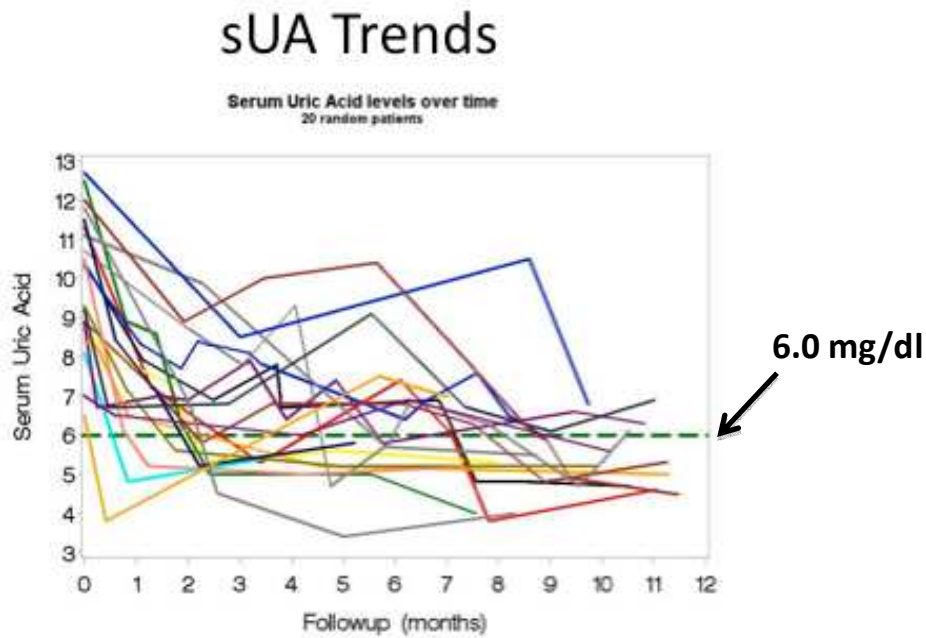
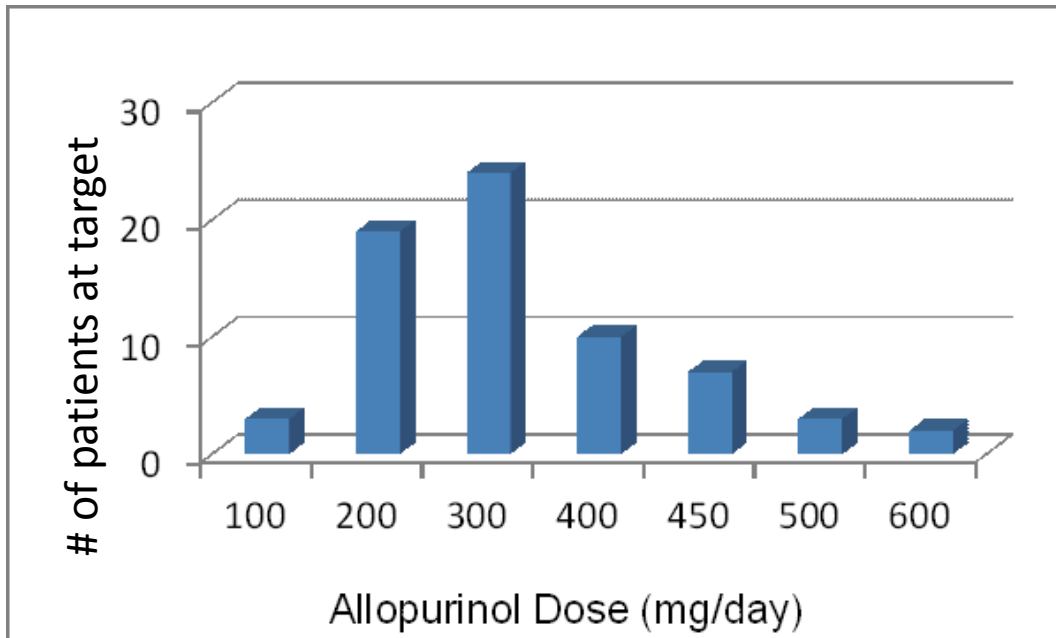


Fig. 4 sUA trend lines for 20 randomly selected patients. Each colored line represents sequential sUA levels in a single patient. Each line stops at the time of clinic discharge or is the most recent sUA if the patient had not completed or left the program.



ew only

Fig. 5 Dose of Allopurinol required to achieve a sUA of ≤ 6.0 mg/dl



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8 **Effectiveness of a pharmacist-based gout care management program in a large**
9 **integrated health plan: Results from a pilot study**
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16 Robert D Goldfien¹, Michele S Ng², Goldie Yip², Alice Hwe², Alice Jacobson³, Alice
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49 There is no additional data available
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Abstract

Background:

The incidence of gout has been steadily rising. While effective treatments are available, treatment is often unsuccessful because current approaches to management lack a systematic approach. To address this shortcoming we tested a protocol-based, pharmacist-staffed intervention to manage patients with recurrent gout.

Methods:

Patients in Kaiser Permanente, Northern California (KPNC) with recurrent gout were referred by their primary care physicians to a pharmacist-staffed gout management clinic supervised by a board-certified rheumatologist. The pharmacist used a protocol that employs standard gout medications to achieve and maintain a serum uric acid (sUA) level of 6.0 mg/dl or less. Results from the first 100 consecutive patients enrolled in this pilot program are reported here.

Results:

In 95 evaluable patients enrolled in our pilot program, a sUA of 6.0 mg/dl or less was achieved and maintained in 78 patients with 4 still in the program to date. Five patients declined to participate after referral, and another 13 patients did not complete the program. [\(The majority of these were due to non-adherence.\)](#)

Conclusions:

A structured pharmacist-staffed program can effectively and safely lower and maintain uric acid levels in a high percentage of patients with recurrent gout. This care model is simple to implement, efficient and warrants further validation in a clinical trial.

Introduction

Gout is the most common inflammatory arthritis in men (1) and results in considerable morbidity and utilization of health care resources. (2) The past 30 years have witnessed a steady increase in the prevalence of gout. (3–5) The causes of this rise in gout prevalence appear to be linked to the increasing prevalence of obesity, diabetes, chronic renal disease and hypertension. (6,7) Unlike other common rheumatic diseases, the underlying cause of gout, chronic elevation of serum uric acid (sUA), is well understood.

Current approaches for management of other common chronic conditions, such as diabetes, are based on the principle that chronic illnesses are best managed by identifying predictors of optimal outcomes, setting treatment targets, and then monitoring for success in treating to the targets. (8) In the case of gout, an appropriate treatment target has been identified by expert panels sponsored by the European League Against Rheumatism (EULAR) (9) and the American College of Rheumatology (ACR). (10) Both recommend that patients with tophaceous or recurrent gout be treated with urate-lowering therapy (ULT) to a target sUA of < 6.0 mg/dl. Unfortunately, only a minority of gout patients receives appropriate treatment, including doses of ULT sufficient to achieve this target.

(11) There are several reasons for this deficiency which have been addressed by other authors. (12,13). The reasons cited have included lack of appropriate monitoring, failure to treat to target and fear of escalation of ULT in some patients, particularly patients with chronic kidney disease. Taken together, it appears that there is a great need for improved approaches to the management of gout.

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10 To address the problem of inadequate management of gout, we developed a model for
11 gout management consisting of a 'virtual' clinic comprised of a clinical pharmacist under
12 the supervision of a board-certified rheumatologist. Following a written protocol, the
13 pharmacist initiates, adjusts and monitors the use of standard gout medications for
14 patients referred by their primary care physicians for recurrent or tophaceous gout.
15 Patients are followed by the clinic until they have 2 consecutive target sUA results at
16 least 3 months apart, and are then discharged back to their usual care. We report here the
17 outcomes results of a pilot program by presenting the outcomes of the first 100 patients
18 referred to the program. Though a limited intervention, our intent was to address some of
19 the issues identified in the literature and do it in a way that is highly leveraged and
20 potentially suitable for a large majority of patients with chronic gout who are currently
21 not being adequately managed.
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35 **Methods**

36 *Patient referral*

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39 Patients with gout whose primary care physicians practice at KPNC in Richmond, CA
40 were eligible for referral to the gout management program. Referral was at the discretion
41 of the primary care physician (sometimes in consultation with a rheumatologist), based
42 on a history of recurrent or tophaceous gout and the intent to use urate-lowering therapy
43 (ULT). Referring physicians were offered the choice of referring each patient for a
44 formal rheumatology consultation, or to the gout management program, supervised by the
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8 same rheumatologist (RG). The clinical pharmacist then telephoned the referred patients,
9 introduced them to the protocol and, if they agreed to participate, entered them into the
10 program. Patients consenting to treatment in the program were provided written
11 educational material including dietary guidelines at the time of program entry. Patients
12 with end stage renal disease were excluded from the program. The pharmacist, under a
13 protocol approved by the Kaiser Permanente East Bay Pharmacy and Therapeutics
14 Committee, was authorized to order relevant laboratory tests and initiate or change orders
15 for the medications used to manage sUA, and for flare prophylaxis. For treatment of
16 acute flares, medication orders were sometimes provided by the rheumatologist if outside
17 the scope of the pharmacy protocol.
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29 *Laboratory assessment and monitoring*

30 Baseline laboratory assessment performed on all referred patients consisted of a sUA,
31 alanine aminotransferase (ALT), estimated glomerular filtration rate (eGFR) and
32 complete blood count (CBC). This same panel of laboratory tests was repeated as needed
33 to monitor progress while the patient was enrolled in the gout management clinic.
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40 *Treatment protocol*

41 Figure 1 is a schematic diagram of the assessment and treatment protocol. Once entered
42 into the program, baseline laboratory assessment was performed if not available within
43 the prior month. If, at the time of referral, a patient was being treated for an acute flare of
44 gout, this treatment was continued and completed. Once a baseline laboratory assessment
45 was available, ULT was either initiated or adjusted if the sUA was above 6.0 mg/dl. Flare
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8 prophylaxis was used in all cases (see below). After any change in ULT, the patient was
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10 instructed to return for laboratory assessment (sUA, ALT, CBC, eGFR) in 2 weeks, and
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12 report any adverse drug reactions (ADRs) or gout symptoms. ADRs or gout flares were
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14 managed by the clinical pharmacist, usually in consultation with the supervising
15
16 rheumatologist. This process was continued in an iterative fashion until a target sUA of \leq
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18 6.0 mg/dl was achieved. Patients at target were asked to repeat the laboratory assessment
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20 in 3 months. At that time, patients still at target were discharged from the clinic and
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22 instructed to continue their medications and follow up with their primary care physician.
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24 Those not at target were either restarted on their ULT or it was titrated and the level re-
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26 tested in 2 weeks. Patients remained in the gout management program until they
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28 demonstrated 2 sUAs \leq 6 mg/dl at least 3 months apart.
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31 *Pharmacological treatments*

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33 ULT was initiated with allopurinol in all patients as first-line therapy unless the patient
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35 had a known ADR or allergy to allopurinol. The starting dose for allopurinol-naïve
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37 patients was 100 mg daily (some patients were on higher doses at the time of referral).
38
39 Dose titration for patients not at target sUA was done using 100 mg per day increments,
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41 or in some cases, although selected patients on 300 mg daily were titrated to 450 mg
42
43 daily. The maximum allopurinol dose used in the program was 600 mg per day. Patients
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45 already on febuxostat or probenecid were maintained on these and doses titrated as
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47 needed based on sUA. Patients who developed a significant ADR or symptoms of
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49 allergy to allopurinol were switched to either febuxostat 40 mg daily or probenecid 500
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8 mg daily, depending on their clinical status in consultation with the rheumatologist. Dose
9 titration was then continued with these drugs if needed.
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14 Gout-flare prophylaxis was used in all patients and in most instances we utilized
15 colchicine 0.6 mg daily. For patients with eGFR less than 30, the dose was reduced to 0.3
16 mg per day. In some patients, if recommended by the rheumatologist, a daily
17 nonsteroidal anti-inflammatory drug (NSAID) treatment was substituted, if no
18 contraindication prevented this.
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26 Acute gout flares were managed by the clinical pharmacist, in consultation with the
27 rheumatologist, using oral NSAIDs, prednisone or colchicine.
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31 Adverse drug reactions (ADR) to medications, incident gout flares and abnormal
32 laboratory parameters were recorded by the clinical pharmacist at each telephone
33 encounter and reviewed by the rheumatologist for management.
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39 Results

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42 Patient demographics and co morbidities of the pilot sample are described in Table 1.
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47 Table 1. Demographic and clinical characteristics of patients (N=100)
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| 49 Characteristic | 50 Mean (range) |
|-------------------|-----------------|
| 51 Age, years | 52 61 (32-94) |

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|----------------------------------|------------|
| BMI, kg/m ² | 31 (20-48) |
| | Percent |
| Male | 75% |
| Hypertension | 75% |
| Chronic kidney disease (CKD 2-4) | 29% |
| Diabetes | 29% |
| Coronary artery disease | 10% |
| Congestive heart failure | 11% |
| 2 or more co-morbidities | 46% |

Three-fourths of the patients were male. The mean age was 61 years, (range: 32 – 94 years). The mean body mass index was 31 kg/m² (range: 20 – 48 kg/m²). Common gout-associated co-morbidities were determined based on the presence of specific ICD-9 codes listed in the problem list of each patient in the electronic medical record, and verified by chart review. The majority of patients had at least one of the common co-morbidities associated with gout. Seventy-eight percent had hypertension, and 29% had chronic kidney disease (CKD). Of these, 2 had stage 2 CKD, 22 had stage 3 CKD and 3 had stage 4 CKD-stage 3 or 4. Another and 29% had diabetes. A smaller number had either coronary artery disease or congestive heart failure. Forty-five percent of the patients had 2 or more of these co-morbid conditions.

Figure 2 is a schematic that shows the current status of the first 100 patients referred to our clinic. Five patients declined to participate when initially contacted by the pharmacist. Thus, 95 patients started the program, and at the time of this analysis, 78 had completed the program with 2 consecutive sUA measurements of < 6.0 mg/dl, and 4 were

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8 still being managed. Thirteen patients left the program prior to achieving the end point.
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10 Of these, 2 patients died while in the program. One died from complications of
11 abdominal surgery and the other, aged 94, died at home of “natural causes”. One patient
12 developed symptoms of an allergic reaction to allopurinol and declined further treatment.
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14 One patient lost insurance coverage, and another was incarcerated. The remaining 8
15 patients were discharged by the program pharmacist because of a pattern of non-
16 adherence to treatment or lab monitoring, or because they elected not to complete the
17 program. The time patients spent under program management varied considerably. The
18 mean duration of participation was 47.8 weeks (range 14.9-109.6 weeks). Although our
19 program was a feasibility study and designed as a short term intervention, when we
20 examined the medical records of the 78 patients who have successfully completed the
21 program, we found that 63 of these had been tested at least one time by their regular
22 physician after clinic discharge (mean follow up time 36 weeks) and that 53 of these
23 (80%) still maintained a sUA of 6.0 or less.
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37 Figure 3 shows the sUA's of each patient in the pilot gout-management study as a set of
38 paired samples. Each pair of bars represents the baseline sUA (red bars) and final sUA
39 (blue bars) for each patient. For those patients still in the program (i.e., those who have
40 not yet achieved the discharge criterion of 2 consecutive sUA measurements of ≤ 6.0
41 mg/dl), the blue bar is the most recent sUA available if the patient did not complete the
42 program. The dotted horizontal line represents the sUA target of 6.0 mg/dl. The figure
43 shows all the patients who entered the program, including those who are still being
44 managed and those who did not complete the program.
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10 To provide a more detailed view of how patients responded to management by the clinic,
11 we plotted sequential sUA levels in a subset of our patients. Figure 4 shows this analysis
12 in 20 randomly selected patients entering the program. Each line represents the
13 sequential sUA measurements of a single patient for a period of 12 months. Essentially
14 all the patients in this random sample initially responded with significant reduction in
15 sUA. In many patients, this improvement was sustained, but in others, the sUA
16 subsequently rose due to discontinuation of ULT. In these patients, the pharmacist was
17 able, in most cases, to restart ULT and continue testing to assure continuing medication
18 adherence. The Figure also shows that by 12 months in the program, 16 of the 20
19 patients had achieved a target sUA and two had a normal sUA of < 6.8 mg/dl.
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31 Analysis of the 78 patients who have completed the program after achieving and
32 maintaining the targeted sUA showed that 68 (87%, 95% CI: 78% to 94%) were on
33 allopurinol at discharge. Figure 5 shows the distribution of allopurinol doses required to
34 achieve a sUA of ≤ 6.0 . The mean daily allopurinol dose required to achieve a sUA of \leq
35 6 was 311 mg. Sixty-eight percent of patients on allopurinol achieved target on 300 mg
36 per day or less. Only three patients achieved goal on the starting dose of 100 mg daily
37 and two patients required 600 mg per day. All five patients on febuxostat had achieved
38 the goal sUA level on 40 mg per day.
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49 Three patients (3%) experienced rash or other symptoms of allergy to allopurinol. None
50 required more than discontinuation of the medication. Of these, two patients were
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8 changed to alternative ULT and one patient declined further treatment and discontinued
9 the program. Elevation of ALT was seen at some time during treatment in 47 patients
10 (48%), but only 7 of the patients had elevations high enough to require changing
11 medication. Most stabilized or returned to normal with continued treatment and
12 monitoring. Incident acute gout flares were reported in 33 patients (34%). None resulted
13 in discontinuation of ULT. Gastrointestinal side effects were uncommon and in no case
14 required a change in therapy.
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24 Discussion

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27 Gout is arguably the best understood of the common inflammatory arthritic diseases;
28 effective preventive therapy is readily available and the key outcome (sUA < 6 mg/dl in
29 most cases) is easily measured. Why, then, is unsuccessful control of sUA so frequent? A
30 number of factors contribute to suboptimal gout management. (11,12,14) Adherence to
31 ULT is poor when compared to medication adherence in other chronic conditions. (15)
32 Symptoms are typically intermittent with extended gout-free periods. Moreover, there are
33 effective treatments for gout flares, and medications (for example, colchicine) that can
34 reduce the incidence of flares without lowering sUA. It is not surprising therefore, that
35 many gout patients are never started on, or discontinue ULT. Another important feature
36 of gout management is that initiation of ULT can lead to a short-term increase in
37 incidence of gout flares, (16) further discouraging the continuation of therapy. Better
38 patient education could be expected to improve long-term medication adherence, but is
39 not consistently provided. (17) While diet is clearly a factor in the development of gout
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9 (18), patients and physicians frequently place a disproportionate emphasis on dietary
10 restrictions. (19) Although consensus guidelines recommend treating with ULT to a
11 target sUA of 6.0 mg/dl or less, concerns about allopurinol toxicity may discourage some
12 physicians from achieving this goal. In particular, limiting doses of allopurinol in patients
13 with CKD lead to a high percentage of treatment failures (20). Finally, many clinical
14 laboratories do not correctly identify serum urate concentrations of > 6.8 mg/dl as being
15 abnormal. This leads to under-treatment and considerable confusion about diagnosis and
16 management. (21)
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26 Our pilot program was conceived as a way to re-frame the approach to gout management.
27 We hypothesized that using a structured treat-to-target approach with regular monitoring
28 and a goal-directed intervention would result in a high percentage of patients achieving a
29 target sUA. In particular, the protocol was designed to use a slow titration of ULT along
30 with flare prophylaxis and scheduled follow up calls. We also required sustained control
31 of sUA for at least 3 months as a way to promote longer term medication adherence. We
32 realize that maintaining treatment for 3 months does not guarantee long term control of
33 sUA. Nevertheless, of the patients for whom a follow up test was available, 80% were
34 still at target a mean of 36.8 weeks after clinic discharge. As for any chronic condition,
35 optimal outcomes will require some level of structured monitoring.
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47 The results of our pilot program suggest that a structured program may be an effective
48 approach to gout management. ULT medications are highly effective, and therefore
49 almost all our patients responded with significant reductions in sUA within weeks of
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8 starting the program (Figure 4). Dose titration allowed most patients to achieve a target
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10 sUA of ≤ 6.0 mg/dl and to-date, all patients have been able to achieve goal using standard
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12 doses of available medications. The demographic and clinical features of the patients in
13
14 our gout sample were similar to those seen in the general population of gout patients
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16 described in previous studies, (22,23) suggesting that our findings should be
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18 generalizable to gout populations outside KPNC. A nurse-staffed case management
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20 approach has been used and achieved impressive results in controlling sUA in gout
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22 patients (234). Our pilot program is also based on a structured management approach, but
23
24 did not require any clinic visits. This model is highly efficient and therefore suitable for
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26 managing a large population of gout patients, but not necessarily more effective than a
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28 case management approach.-

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31 There is ample evidence that therapeutic inertia contributes to inadequate results of ULT
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33 (24). Our program was designed specifically to counter this problem by including
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35 repeated sUA measurements and specified actions based on the results. In addition, our
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37 protocol We used a treat to target approach and did not limit doses of allopurinol
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39 specifically based on renal function, which has been one of several impediments noted in
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41 the literature to successful ULT. Current recommendations do not support the need to
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43 limit allopurinol doses to 100 mg daily in patients with CKD, (25–27) though a low
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45 starting dose and slow titration is recommended. (26,28) Indeed, limiting the dose of
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47 allopurinol based on the presence of chronic kidney disease has been shown to result in
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49 treatment failure in an unacceptably high percentage of patients. (17) Our data confirm
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51 this observation: only three of 68 allopurinol-treated patients (4%) completing the
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8 program achieved a sUA of ≤ 6.0 on 100 mg daily of allopurinol, and only 68% achieved
9 target with 300 mg daily (Figure 5).
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14 Not surprisingly, we encountered many cases of medication non-adherence. In most
15 cases, this was detected in the course of the routine testing that comprised the protocol.
16 Typically a patient whose sUA was at or near target, had a repeat test that was no longer
17 at target. In some cases, non-adherence was discovered at the time the patient called to
18 pharmacist because of a gout flare. Our protocol, by requiring two consecutive target
19 sUA levels three months apart, was designed with the expectation that adherence to ULT
20 would be inconsistent. ~~We do~~ As noted previously, we do not know whether our time-
21 limited intervention will ultimately lead to long-term control of sUA in these patients, but
22 we were able to detect medication non-adherence in the first few months and thus
23 reinforce the importance of long-term ULT. Ideally, monitoring of sUA would continue
24 on a regular basis, as recommended for relevant laboratory parameters in other chronic
25 conditions. Despite the fact that all patients were prescribed colchicine or NSAIDs for
26 flare prophylaxis, we encountered a substantial number of gout flares during the program.
27 While some increase in flares may be expected, in our experience, many of the flares in
28 our patients occurred in connection with medication non-adherence. This tendency of
29 gout patients to discontinue ULT accounted for the wide range of times patients had to
30 stay under management. We provided our patients with written educational material as
31 well, but could not evaluate the effectiveness of this.
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50 We designed our pilot to be efficient and cost-effective by leveraging physician time.
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8 The gout management program, while supervised by a rheumatologist, was staffed by a
9 clinical pharmacist who was carefully trained in the management protocol. The
10 pharmacist was able to manage a cohort of up to about 80 patients at a time while
11 spending only about 6-8 hours per week. The time spent in overseeing and assisting the
12 clinical pharmacist was never more than about 30 minutes per week for the
13 rheumatologist once the program was in place. Moreover, our program did not require
14 any in-person visits. This model suggests a path to improved outcomes in gout patients
15 without generating the magnitude of increased utilization of health care resources that
16 might otherwise be required. We recognize that pharmacists may not be available or
17 allowed to manage patients as was done in our protocol. Even so, a trained clinical nurse
18 could be substituted in the pharmacist's role and provide excellent care while leveraging
19 physician time.
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Figures

Fig. 1 Clinic monitoring and treatment flow diagram

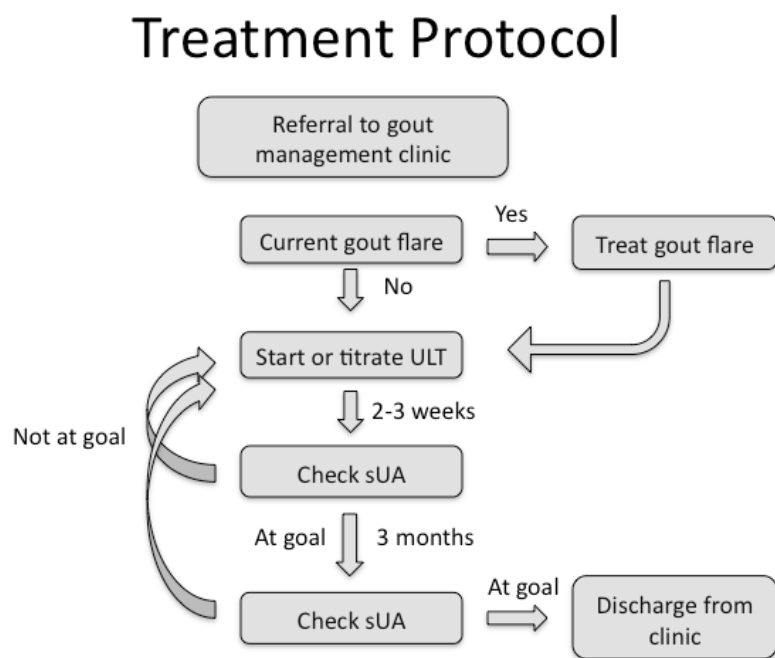
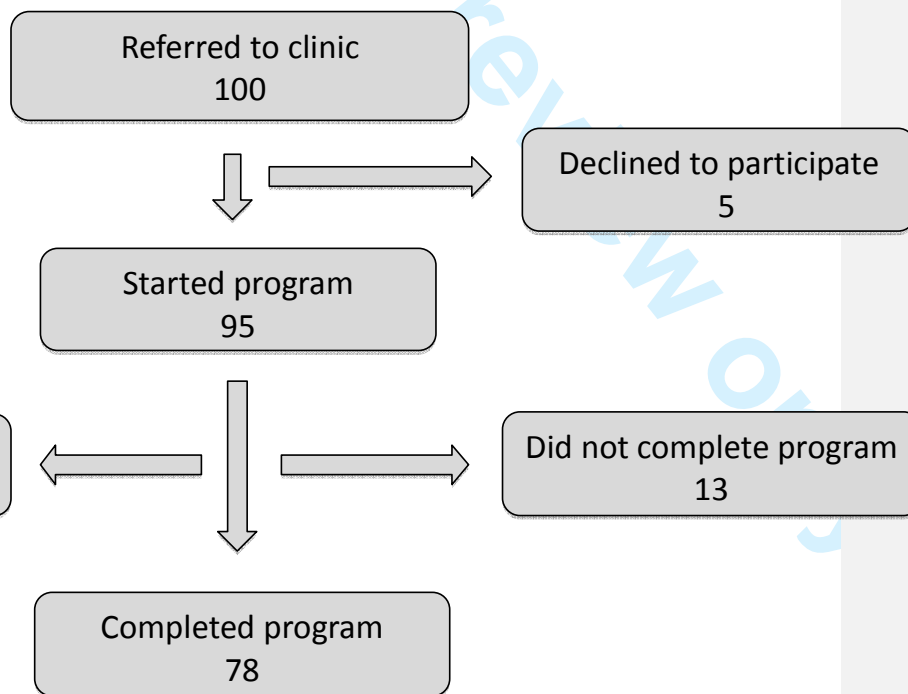


Fig. 2 Current status of first 100 patients referred to program

Current Patient Status



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Fig. 3 Comparison of pre-treatment sUA and most recent or final sUA. Each patient is represented by a red bar (initial sUA) and a blue bar (final sUA, whether or not he/she completed the program).

sUA Pairs: First and Last

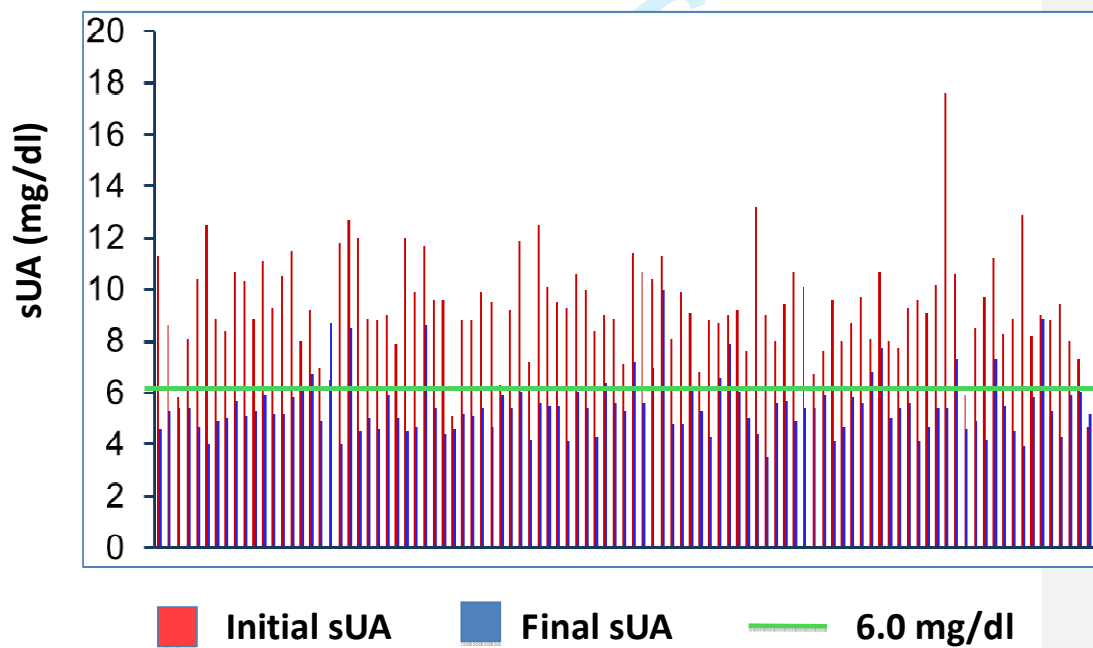
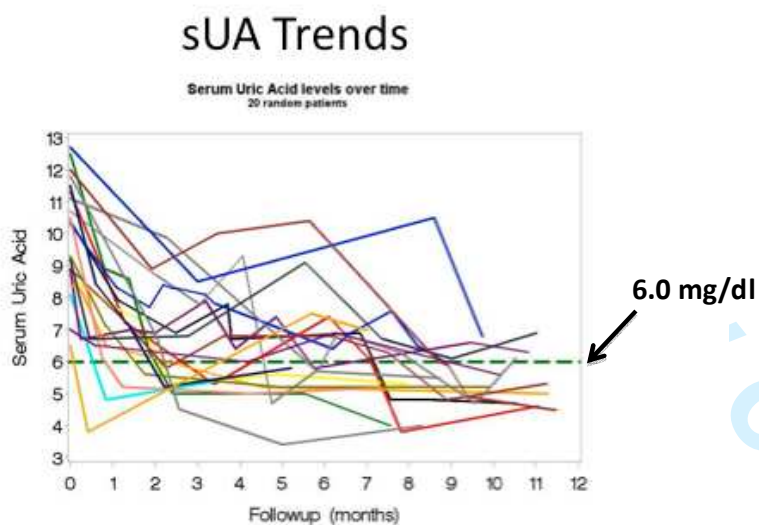


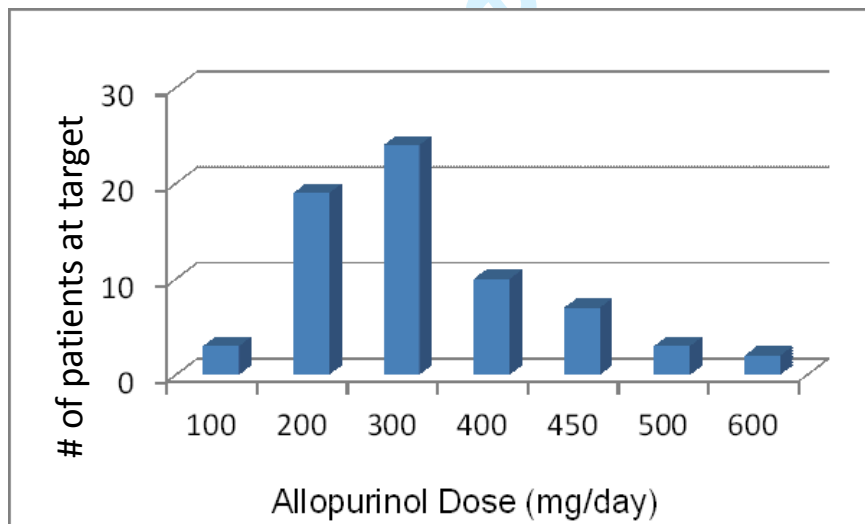
Fig. 4 sUA trend lines for 20 randomly selected patients. Each colored line represents sequential sUA levels in a single patient. Each line stops at the time of clinic discharge or is the most recent sUA if the patient had not completed or left the program.



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Fig. 5 Dose of Allopurinol required to achieve a sUA of ≤ 6.0 mg/dl





Effectiveness of a pharmacist-based gout care management program in a large integrated health plan: Results from a pilot study

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4 **integrated health plan: Results from a pilot study**
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Abstract

Objectives:

The study objective was to determine the feasibility of using a pharmacist-staffed, protocol-based structured approach to improving the management of chronic, recurrent gout.

Setting:

The study was carried out in the outpatient clinic of a single Kaiser Permanente medical center.

This is a community based clinic.

Participants:

We report on one hundred consecutive patients between the ages of 21 and 94 (75% male) with chronic or recurrent gout, referred by their primary physicians for the purpose of management of urate lowering therapy. Patients with Stage 5 chronic kidney disease or end-stage kidney disease were excluded.

Interventions:

The program consisted of a trained clinical pharmacist and a rheumatologist. The pharmacist contacted each patient by phone, provided educational and dietary materials, and used a protocol that employs standard gout medications to achieve and maintain a serum uric acid (sUA) level of 6.0 mg/dl or less. Incident gout flares or adverse reactions to medications were managed in consultation with the rheumatologist.

Primary outcome measure:

The primary outcome measure was the achievement and maintenance of a serum uric acid of 6.0 or less for a period of at least 3 months.

Results:

In 95 evaluable patients enrolled in our pilot program, a sUA of 6.0 mg/dl or less was achieved and maintained in 78 patients with 4 still in the program to date. Five patients declined to participate after referral, and another 13 patients did not complete the program. (The majority of these were due to non-adherence.)

Conclusions:

A structured pharmacist-staffed program can effectively and safely lower and maintain uric acid

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3 levels in a high percentage of patients with recurrent gout in a primary care setting. This care
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5 model is simple to implement, efficient and warrants further validation in a clinical trial.
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9 Article Summary

- 10 1. Article focus: Hypotheses addressed
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- 12
 - 13 • A structured, goal-directed program is effective in achieving optimal control of
 - 14 serum uric acid levels in patients with recurrent gout.
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 - 16 • Successful management of recurrent gout can employ a leveraged approach using
 - 17 a pharmacist-staffed protocol with supervision by a rheumatologist.
 - 18
 - 19 • Chronic gout can be managed efficiently, safely and cost-effectively using a
 - 20 telephone-based 'virtual clinic'.
 - 21
- 22 2. Key messages
- 23
- 24
 - 25 • A protocol based, goal directed gout management program is highly effective
 - 26 in achieving and maintaining serum uric acid control in patients with recurrent
 - 27 gout.
 - 28
 - 29 • Effective urate lowering therapy can be achieved in a high percentage of gout
 - 30 patients using approved doses of allopurinol when dose titration is used.
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 - 32 • This program appears to be a promising approach to improving gout
 - 33 management and may offer significant efficiency compared to current
 - 34 practice.
 - 35
- 36 3. Strengths and Limitations
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44 Strengths: The population we studied is representative of gout patients seen in general
45 rheumatology practice, and therefore our results should be widely generalizable. Our
46 program is relatively easy to implement and requires only a trained clinical pharmacist
47 and rheumatologist to carry out.
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50 Limitations: Although encouraging, this pilot study does not prove that our gout
51 management program is more effective than usual care for gout because there was no
52 control group. A study testing this hypothesis is needed. The structure of our
53 organization, which integrates the health plan, pharmacy programs and physician care, is
54 optimal for the use of our program. A non-integrated system might lead to barriers in
55 setting up a similar collaboration. This may limit the applicability of the model.
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Introduction

Gout is the most common inflammatory arthritis in men (1) and results in considerable morbidity and utilization of health care resources. (2) The past 30 years have witnessed a steady increase in the prevalence of gout. (3–5) The causes of this rise in gout prevalence appear to be linked to the increasing prevalence of obesity, diabetes, chronic renal disease and hypertension. (6,7) Unlike other common rheumatic diseases, the underlying cause of gout, chronic elevation of serum uric acid (sUA), is well understood.

Current approaches for management of other common chronic conditions, such as diabetes, are based on the principle that chronic illnesses are best managed by identifying predictors of optimal outcomes, setting treatment targets, and then monitoring for success in treating to the targets. (8) In the case of gout, an appropriate treatment target has been identified by expert panels sponsored by the European League Against Rheumatism (EULAR) (9) and the American College of Rheumatology (ACR). (10) Both recommend that patients with tophaceous or recurrent gout be treated with urate-lowering therapy (ULT) to a target sUA of < 6.0 mg/dl. Unfortunately, only a minority of gout patients receives appropriate treatment, including doses of ULT sufficient to achieve this target. (11) There are several reasons for this deficiency which have been addressed by other authors. (12,13). The reasons cited have included lack of appropriate monitoring, failure to treat to target and fear of escalation of ULT in some patients, particularly patients with chronic kidney disease. Taken together, it appears that there is a great need for improved approaches to the management of gout.

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3 To address the problem of inadequate management of gout, we developed a model for
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5 gout management consisting of a 'virtual' clinic comprised of a clinical pharmacist under
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7 the supervision of a board-certified rheumatologist. Following a written protocol, the
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9 pharmacist initiates, adjusts and monitors the use of standard gout medications for
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11 patients referred by their primary care physicians for recurrent or tophaceous gout.
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13 Patients are followed by the clinic until they have 2 consecutive target sUA results at
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15 least 3 months apart, and are then discharged back to their usual care. We report here the
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17 results of a pilot program by presenting the outcomes of the first 100 patients referred to
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19 the program. Though a limited intervention, our intent was to address some of the issues
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21 identified in the literature and do it in a way that is highly leveraged and potentially
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23 suitable for a large majority of patients with chronic gout who are currently not being
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25 adequately managed.
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34 **Methods**

35 *Patient referral*

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38 Patients with gout whose primary care physicians practice at KPNC in Richmond, CA
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40 were eligible for referral to the gout management program. Referral was at the discretion
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42 of the primary care physician (sometimes in consultation with a rheumatologist), based
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44 on a history of recurrent or tophaceous gout and the intent to use urate-lowering therapy
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46 (ULT). Referring physicians were offered the choice of referring each patient for a
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48 formal rheumatology consultation, or to the gout management program, supervised by the
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50 same rheumatologist (RG). The clinical pharmacist then telephoned the referred patients,
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3 introduced them to the protocol and, if they agreed to participate, entered them into the
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5 program. Patients consenting to treatment in the program were provided written
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7 educational material including dietary guidelines at the time of program entry. Patients
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9 with end stage renal disease were excluded from the program. The pharmacist, under a
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11 protocol approved by the Kaiser Permanente East Bay Pharmacy and Therapeutics
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13 Committee, was authorized to order relevant laboratory tests and initiate or change orders
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15 for the medications used to manage sUA, and for flare prophylaxis. For treatment of
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17 acute flares, medication orders were sometimes provided by the rheumatologist if outside
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19 the scope of the pharmacy protocol.
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27 *Laboratory assessment and monitoring*

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29 Baseline laboratory assessment performed on all referred patients consisted of a sUA,
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31 alanine aminotransferase (ALT), estimated glomerular filtration rate (eGFR) and
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33 complete blood count (CBC). This same panel of laboratory tests was repeated as needed
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35 to monitor progress while the patient was enrolled in the gout management clinic.
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41 *Treatment protocol*

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43 Figure 1 is a schematic diagram of the assessment and treatment protocol. Once entered
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45 into the program, baseline laboratory assessment was performed if not available within
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47 the prior month. If, at the time of referral, a patient was being treated for an acute flare of
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49 gout, this treatment was continued and completed. Once a baseline laboratory assessment
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51 was available, ULT was either initiated or adjusted if the sUA was above 6.0 mg/dl. Flare
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53 prophylaxis was used in all cases (see below). After any change in ULT, the patient was
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3 instructed to return for laboratory assessment (sUA, ALT, CBC, eGFR) in 2 weeks, and
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5 report any adverse drug reactions (ADRs) or gout symptoms. ADRs or gout flares were
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7 managed by the clinical pharmacist, usually in consultation with the supervising
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9 rheumatologist. This process was continued in an iterative fashion until a target sUA of \leq
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11 6.0 mg/dl was achieved. Patients at target were asked to repeat the laboratory assessment
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13 in 3 months. At that time, patients still at target were discharged from the clinic and
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15 instructed to continue their medications and follow up with their primary care physician.
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17 Those not at target were either restarted on their ULT or it was titrated and the level re-
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19 tested in 2 weeks. Patients remained in the gout management program until they
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21 demonstrated 2 sUAs \leq 6 mg/dl at least 3 months apart.
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29 *Pharmacological treatments*

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31 ULT was initiated with allopurinol in all patients as first-line therapy unless the patient
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33 had a known ADR or allergy to allopurinol. The starting dose for allopurinol-naïve
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35 patients was 100 mg daily (some patients were on higher doses at the time of referral).
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37 Dose titration for patients not at target sUA was done using 100 mg per day increments,
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39 or in some cases, although selected patients on 300 mg daily were titrated to 450 mg
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41 daily. The maximum allopurinol dose used in the program was 600 mg per day. Patients
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43 already on febuxostat or probenecid were maintained on these and doses titrated as
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45 needed based on sUA. Patients who developed a significant ADR or symptoms of
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47 allergy to allopurinol were switched to either febuxostat 40 mg daily or probenecid 500
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49 mg daily, depending on their clinical status in consultation with the rheumatologist. Dose
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51 titration was then continued with these drugs if needed.
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Gout-flare prophylaxis was used in all patients and in most instances we utilized colchicine 0.6 mg daily. For patients with eGFR less than 30, the dose was reduced to 0.3 mg per day. In some patients, if recommended by the rheumatologist, a daily nonsteroidal anti-inflammatory drug (NSAID) treatment was substituted, if no contraindication prevented this.

Acute gout flares were managed by the clinical pharmacist, in consultation with the rheumatologist, using oral NSAIDs, prednisone or colchicine.

Adverse drug reactions (ADR) to medications, incident gout flares and abnormal laboratory parameters were recorded by the clinical pharmacist at each telephone encounter and reviewed by the rheumatologist for management.

Results

Patient demographics and co morbidities of the pilot sample are described in Table 1.

Table 1. Demographic and clinical characteristics of patients (N=100)

| Characteristic | Mean (range) |
|------------------------|--------------|
| Age, years | 61 (32-94) |
| BMI, kg/m ² | 31 (20-48) |
| | Percent |
| Male | 75% |

| | |
|----------------------------------|-----|
| Hypertension | 75% |
| Chronic kidney disease (CKD 2-4) | 29% |
| Diabetes | 29% |
| Coronary artery disease | 10% |
| Congestive heart failure | 11% |
| 2 or more co-morbidities | 46% |

Three-fourths of the patients were male. The mean age was 61 years, (range: 32 – 94 years). The mean body mass index was 31 kg/m² (range: 20 – 48 kg/m²). Common gout-associated co-morbidities were determined based on the presence of specific ICD-9 codes listed in the problem list of each patient in the electronic medical record, and verified by chart review. The majority of patients had at least one of the common co-morbidities associated with gout. Seventy-eight percent had hypertension, and 29% had chronic kidney disease (CKD). Of these, 2 had stage 2 CKD, 22 had stage 3 CKD and 3 had stage 4 CKD. Another 29% had diabetes. A smaller number had either coronary artery disease or congestive heart failure. Forty-five percent of the patients had 2 or more of these co-morbid conditions.

Figure 2 is a schematic that shows the current status of the first 100 patients referred to our clinic. Five patients declined to participate when initially contacted by the pharmacist. Thus, 95 patients started the program, and at the time of this analysis, 78 had completed the program with 2 consecutive sUA measurements of < 6.0 mg/dl, and 4 were still being managed. Thirteen patients left the program prior to achieving the end point. Of these, 2 patients died while in the program. One died from complications of abdominal surgery and the other, aged 94, died at home of “natural causes”. One patient

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3 developed symptoms of an allergic reaction to allopurinol and declined further treatment.
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5 One patient lost insurance coverage, and another was incarcerated. The remaining 8
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7 patients were discharged by the program pharmacist because of a pattern of non-
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9 adherence to treatment or lab monitoring, or because they elected not to complete the
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11 program. The time patients spent under program management varied considerably. The
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13 mean duration of participation was 47.8 weeks (range 14.9-109.6 weeks). Although our
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15 program was a feasibility study and designed as a short term intervention, when we
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17 examined the medical records of the 78 patients who have successfully completed the
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19 program, we found that 63 of these had been tested at least one time by their regular
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21 physician after clinic discharge (mean follow up time 36 weeks) and that 53 of these
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23 (80%) still maintained a sUA of 6.0 or less.
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32 Figure 3 shows the sUA's of each patient in the pilot gout-management study as a set of
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34 paired samples. Each pair of bars represents the baseline sUA (red bars) and final sUA
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36 (blue bars) for each patient. For those patients still in the program (i.e., those who have
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38 not yet achieved the discharge criterion of 2 consecutive sUA measurements of ≤ 6.0
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40 mg/dl), the blue bar is the most recent sUA available if the patient did not complete the
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42 program. The dotted horizontal line represents the sUA target of 6.0 mg/dl. The figure
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44 shows all the patients who entered the program, including those who are still being
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46 managed and those who did not complete the program.
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53 To provide a more detailed view of how patients responded to management by the clinic,
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55 we plotted sequential sUA levels in a subset of our patients. Figure 4 shows this analysis
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3 in 20 randomly selected patients entering the program. Each line represents the
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5 sequential sUA measurements of a single patient for a period of 12 months. Essentially
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7 all the patients in this random sample initially responded with significant reduction in
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9 sUA. In many patients, this improvement was sustained, but in others, the sUA
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11 subsequently rose due to discontinuation of ULT. In these patients, the pharmacist was
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13 able, in most cases, to restart ULT and continue testing to assure continuing medication
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15 adherence. The Figure also shows that by 12 months in the program, 16 of the 20
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17 patients had achieved a target sUA and two had a normal sUA of < 6.8 mg/dl.
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25 Analysis of the 78 patients who have completed the program after achieving and
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27 maintaining the targeted sUA showed that 68 (87%, 95% CI: 78% to 94%) were on
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29 allopurinol at discharge. Figure 5 shows the distribution of allopurinol doses required to
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31 achieve a sUA of ≤ 6.0 . The mean daily allopurinol dose required to achieve a sUA of \leq
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33 6 was 311 mg. Sixty-eight percent of patients on allopurinol achieved target on 300 mg
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35 per day or less. Only three patients achieved goal on the starting dose of 100 mg daily
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37 and two patients required 600 mg per day. All five patients on febuxostat had achieved
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39 the goal sUA level on 40 mg per day.
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47 Three patients (3%) experienced rash or other symptoms of allergy to allopurinol. None
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49 required more than discontinuation of the medication. Of these, two patients were
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51 changed to alternative ULT and one patient declined further treatment and discontinued
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53 the program. Elevation of ALT was seen at some time during treatment in 47 patients
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55 (48%), but only 7 of the patients had elevations high enough to require changing
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3 medication. Most stabilized or returned to normal with continued treatment and
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5 monitoring. Incident acute gout flares were reported in 33 patients (34%). None resulted
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7 in discontinuation of ULT. Gastrointestinal side effects were uncommon and in no case
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9 required a change in therapy.
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12 Discussion

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15 Gout is arguably the best understood of the common inflammatory arthritic diseases;
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17 effective preventive therapy is readily available and the key outcome (sUA < 6 mg/dl in
18
19 most cases) is easily measured. Why, then, is unsuccessful control of sUA so frequent? A
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21 number of factors contribute to suboptimal gout management. (11,12,14) Adherence to
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23 ULT is poor when compared to medication adherence in other chronic conditions. (15)
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25 Symptoms are typically intermittent with extended gout-free periods. Moreover, there are
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27 effective treatments for gout flares, and medications (for example, colchicine) that can
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29 reduce the incidence of flares without lowering sUA. It is not surprising therefore, that
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31 many gout patients are never started on, or discontinue ULT. Another important feature
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33 of gout management is that initiation of ULT can lead to a short-term increase in
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35 incidence of gout flares, (16) further discouraging the continuation of therapy. Better
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37 patient education could be expected to improve long-term medication adherence, but is
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39 not consistently provided. (17) While diet is clearly a factor in the development of gout
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41 (18), patients and physicians frequently place a disproportionate emphasis on dietary
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43 restrictions. (19) Although consensus guidelines recommend treating with ULT to a
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45 target sUA of 6.0 mg/dl or less, concerns about allopurinol toxicity may discourage some
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3 physicians from achieving this goal. In particular, limiting doses of allopurinol in patients
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5 with CKD lead to a high percentage of treatment failures (20). Finally, many clinical
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7 laboratories do not correctly identify serum urate concentrations of > 6.8 mg/dl as being
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9 abnormal. This leads to under-treatment and considerable confusion about diagnosis and
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11 management. (21)
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17 Our pilot program was conceived as a way to re-frame the approach to gout management.
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19 We hypothesized that using a structured treat-to-target approach with regular monitoring
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21 and a goal-directed intervention would result in a high percentage of patients achieving a
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23 target sUA. In particular, the protocol was designed to use a slow titration of ULT along
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25 with flare prophylaxis and scheduled follow up calls. We also required sustained control
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27 of sUA for at least 3 months as a way to promote longer term medication adherence. We
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29 realize that maintaining treatment for 3 months does not guarantee long term control of
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31 sUA. Nevertheless, of the patients for whom a follow up test was available, 80% were
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33 still at target a mean of 36.8 weeks after clinic discharge. As for any chronic condition,
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35 optimal outcomes will require some level of structured monitoring.
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44 The results of our pilot program suggest that a structured program may be an effective
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46 approach to gout management. ULT medications are highly effective, and therefore
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48 almost all our patients responded with significant reductions in sUA within weeks of
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50 starting the program (Figure 4). Dose titration allowed most patients to achieve a target
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52 sUA of ≤ 6.0 mg/dl and to-date, all patients have been able to achieve goal using standard
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54 doses of available medications. The demographic and clinical features of the patients in
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3 our gout sample were similar to those seen in the general population of gout patients
4 described in previous studies, (22) suggesting that our findings should be generalizable to
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our gout sample were similar to those seen in the general population of gout patients described in previous studies, (22) suggesting that our findings should be generalizable to gout populations outside KPNC. A nurse-staffed case management approach has been used and achieved impressive results in controlling sUA in gout patients (23). Our pilot program is also based on a structured management approach, but did not require any clinic visits. This model is highly efficient and therefore suitable for managing a large population of gout patients, but not necessarily more effective than a case management approach.

There is ample evidence that therapeutic inertia contributes to inadequate results of ULT (24). Our program was designed specifically to counter this problem by including repeated sUA measurements and specified actions based on the results. In addition, our protocol did not limit doses of allopurinol specifically based on renal function, which has been one of several impediments noted in the literature to successful ULT. Current recommendations do not support the need to limit allopurinol doses to 100 mg daily in patients with CKD, (25–27) though a low starting dose and slow titration is recommended. (26,28) Indeed, limiting the dose of allopurinol based on the presence of chronic kidney disease has been shown to result in treatment failure in an unacceptably high percentage of patients. (17) Our data confirm this observation: only three of 68 allopurinol-treated patients (4%) completing the program achieved a sUA of ≤ 6.0 on 100 mg daily of allopurinol, and only 68% achieved target with 300 mg daily (Figure 5).

Not surprisingly, we encountered many cases of medication non-adherence. In most

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3 cases, this was detected in the course of the routine testing that comprised the protocol.
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5 Typically a patient whose sUA was at or near target, had a repeat test that was no longer
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7 at target. In some cases, non-adherence was discovered at the time the patient called to
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9 pharmacist because of a gout flare. Our protocol, by requiring two consecutive target
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11 sUA levels three months apart, was designed with the expectation that adherence to ULT
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13 would be inconsistent. As noted previously, we do not know whether our time-limited
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15 intervention will ultimately lead to long-term control of sUA in these patients, but we
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17 were able to detect medication non-adherence in the first few months and thus reinforce
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19 the importance of long-term ULT. Ideally, monitoring of sUA would continue on a
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21 regular basis, as recommended for relevant laboratory parameters in other chronic
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23 conditions. Despite the fact that all patients were prescribed colchicine or NSAIDs for
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25 flare prophylaxis, we encountered a substantial number of gout flares during the program.
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27 While some increase in flares may be expected, in our experience, many of the flares in
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29 our patients occurred in connection with medication non-adherence. This tendency of
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31 gout patients to discontinue ULT accounted for the wide range of times patients had to
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33 stay under management. We provided our patients with written educational material as
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35 well, but could not evaluate the effectiveness of this.
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46 We designed our pilot to be efficient and cost-effective by leveraging physician time.
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48 The gout management program, while supervised by a rheumatologist, was staffed by a
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50 clinical pharmacist who was carefully trained in the management protocol. The
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52 pharmacist was able to manage a cohort of up to about 80 patients at a time while
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54 spending only about 6-8 hours per week. The time spent in overseeing and assisting the
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3 clinical pharmacist was never more than about 30 minutes per week for the
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6 rheumatologist once the program was in place. Moreover, our program did not require
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8 any in-person visits. This model suggests a path to improved outcomes in gout patients
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10 without generating the magnitude of increased utilization of health care resources that
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12 might otherwise be required. We recognize that pharmacists may not be available or
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14 allowed to manage patients as was done in our protocol. Even so, a trained clinical nurse
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16 could be substituted in the pharmacist's role and provide excellent care while leveraging
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18 physician time.
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Contributorship Statement

Robert Goldfien

Conceived and developed protocol and program. Participated in collection and analysis of data, and pharmacist supervision. Primary author of manuscript.

Andrew Avins

Consulted on project design, data capture, statistical methods and manuscript editing.

Alice Pressman

Oversaw data analysis and presentation. Consulted on data analysis and manuscript editing.

Alice Hwe

Oversaw development and approval of treatment protocol and supervised clinical pharmacists.

Alice Jacobson

Assisted with data collection and analysis.

Michele Ng and Goldie Yip

Worked directly with subjects to arrange data collection, adjust medications, obtain clinical information and report issues or concerns with supervising rheumatologist

Data sharing

There are no additional unpublished data from this study.

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There is no additional data available.

Competing Interests

None.

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Figures

Fig. 1 Clinic monitoring and treatment flow diagram

Fig. 2 Current status of first 100 patients referred to program

Fig. 3 Comparison of pre-treatment sUA and most recent or final sUA. Each patient is represented by a red bar (initial sUA) and a blue bar (final sUA, whether or not he/she completed the program).

Fig. 4 sUA trend lines for 20 randomly selected patients. Each colored line represents sequential sUA levels in a single patient. Each line stops at the time of clinic discharge or is the most recent sUA if the patient had not completed or left the program.

Fig. 5 Dose of Allopurinol required to achieve a sUA of ≤ 6.0 mg/dl

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3 **Effectiveness of a pharmacist-based gout care management program in a large**
4 **integrated health plan: Results from a pilot study**
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52 There is no additional data available
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Abstract

Background:

The incidence of gout has been steadily rising. While effective treatments are available, treatment is often unsuccessful because current approaches to management lack a systematic approach. To address this shortcoming we tested a protocol-based, pharmacist-staffed intervention to manage patients with recurrent gout.

Methods:

Patients in Kaiser Permanente, Northern California (KPNC) with recurrent gout were referred by their primary care physicians to a pharmacist-staffed gout management clinic supervised by a board-certified rheumatologist. The pharmacist used a protocol that employs standard gout medications to achieve and maintain a serum uric acid (sUA) level of 6.0 mg/dl or less. Results from the first 100 consecutive patients enrolled in this pilot program are reported here.

Results:

In 95 evaluable patients enrolled in our pilot program, a sUA of 6.0 mg/dl or less was achieved and maintained in 78 patients with 4 still in the program to date. Five patients declined to participate after referral, and another 13 patients did not complete the program. (The majority of these were due to non-adherence.)

Conclusions:

A structured pharmacist-staffed program can effectively and safely lower and maintain uric acid levels in a high percentage of patients with recurrent gout. This care model is simple to implement, efficient and warrants further validation in a clinical trial.

Introduction

Gout is the most common inflammatory arthritis in men (1) and results in considerable morbidity and utilization of health care resources. (2) The past 30 years have witnessed a steady increase in the prevalence of gout. (3–5) The causes of this rise in gout prevalence appear to be linked to the increasing prevalence of obesity, diabetes, chronic renal disease and hypertension. (6,7) Unlike other common rheumatic diseases, the underlying cause of gout, chronic elevation of serum uric acid (sUA), is well understood.

Current approaches for management of other common chronic conditions, such as diabetes, are based on the principle that chronic illnesses are best managed by identifying predictors of optimal outcomes, setting treatment targets, and then monitoring for success in treating to the targets. (8) In the case of gout, an appropriate treatment target has been identified by expert panels sponsored by the European League Against Rheumatism (EULAR) (9) and the American College of Rheumatology (ACR). (10) Both recommend that patients with tophaceous or recurrent gout be treated with urate-lowering therapy (ULT) to a target sUA of < 6.0 mg/dl. Unfortunately, only a minority of gout patients receives appropriate treatment, including doses of ULT sufficient to achieve this target. (11) There are several reasons for this deficiency which have been addressed by other authors. (12,13). The reasons cited have included lack of appropriate monitoring, failure to treat to target and fear of escalation of ULT in some patients, particularly patients with chronic kidney disease. Taken together, it appears that there is a great need for improved approaches to the management of gout.

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6 To address the problem of inadequate management of gout, we developed a model for
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8 gout management consisting of a 'virtual' clinic comprised of a clinical pharmacist under
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10 the supervision of a board-certified rheumatologist. Following a written protocol, the
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12 pharmacist initiates, adjusts and monitors the use of standard gout medications for
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14 patients referred by their primary care physicians for recurrent or tophaceous gout.
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16 Patients are followed by the clinic until they have 2 consecutive target sUA results at
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18 least 3 months apart, and are then discharged back to their usual care. We report here the
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20 results of a pilot program by presenting the outcomes of the first 100 patients referred to
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22 the program. Though a limited intervention, our intent was to address some of the issues
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24 identified in the literature and do it in a way that is highly leveraged and potentially
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26 suitable for a large majority of patients with chronic gout who are currently not being
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28 adequately managed.
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36 **Methods**

37 *Patient referral*

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41 Patients with gout whose primary care physicians practice at KPNC in Richmond, CA
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43 were eligible for referral to the gout management program. Referral was at the discretion
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45 of the primary care physician (sometimes in consultation with a rheumatologist), based
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47 on a history of recurrent or tophaceous gout and the intent to use urate-lowering therapy
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49 (ULT). Referring physicians were offered the choice of referring each patient for a
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51 formal rheumatology consultation, or to the gout management program, supervised by the
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3 same rheumatologist (RG). The clinical pharmacist then telephoned the referred patients,
4 introduced them to the protocol and, if they agreed to participate, entered them into the
5 program. Patients consenting to treatment in the program were provided written
6 educational material including dietary guidelines at the time of program entry. Patients
7 with end stage renal disease were excluded from the program. The pharmacist, under a
8 protocol approved by the Kaiser Permanente East Bay Pharmacy and Therapeutics
9 Committee, was authorized to order relevant laboratory tests and initiate or change orders
10 for the medications used to manage sUA, and for flare prophylaxis. For treatment of
11 acute flares, medication orders were sometimes provided by the rheumatologist if outside
12 the scope of the pharmacy protocol.
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29 *Laboratory assessment and monitoring*

30 Baseline laboratory assessment performed on all referred patients consisted of a sUA,
31 alanine aminotransferase (ALT), estimated glomerular filtration rate (eGFR) and
32 complete blood count (CBC). This same panel of laboratory tests was repeated as needed
33 to monitor progress while the patient was enrolled in the gout management clinic.
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45 *Treatment protocol*

46 Figure 1 is a schematic diagram of the assessment and treatment protocol. Once entered
47 into the program, baseline laboratory assessment was performed if not available within
48 the prior month. If, at the time of referral, a patient was being treated for an acute flare of
49 gout, this treatment was continued and completed. Once a baseline laboratory assessment
50 was available, ULT was either initiated or adjusted if the sUA was above 6.0 mg/dl. Flare
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3 prophylaxis was used in all cases (see below). After any change in ULT, the patient was
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5 instructed to return for laboratory assessment (sUA, ALT, CBC, eGFR) in 2 weeks, and
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7 report any adverse drug reactions (ADRs) or gout symptoms. ADRs or gout flares were
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9 managed by the clinical pharmacist, usually in consultation with the supervising
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11 rheumatologist. This process was continued in an iterative fashion until a target sUA of \leq
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13 6.0 mg/dl was achieved. Patients at target were asked to repeat the laboratory assessment
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15 in 3 months. At that time, patients still at target were discharged from the clinic and
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17 instructed to continue their medications and follow up with their primary care physician.
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19 Those not at target were either restarted on their ULT or it was titrated and the level re-
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21 tested in 2 weeks. Patients remained in the gout management program until they
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23 demonstrated 2 sUAs \leq 6 mg/dl at least 3 months apart.
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32 *Pharmacological treatments*

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34 ULT was initiated with allopurinol in all patients as first-line therapy unless the patient
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36 had a known ADR or allergy to allopurinol. The starting dose for allopurinol-naïve
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38 patients was 100 mg daily (some patients were on higher doses at the time of referral).
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40 Dose titration for patients not at target sUA was done using 100 mg per day increments,
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42 or in some cases, although selected patients on 300 mg daily were titrated to 450 mg
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44 daily. The maximum allopurinol dose used in the program was 600 mg per day. Patients
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46 already on febuxostat or probenecid were maintained on these and doses titrated as
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48 needed based on sUA. Patients who developed a significant ADR or symptoms of
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50 allergy to allopurinol were switched to either febuxostat 40 mg daily or probenecid 500
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3 mg daily, depending on their clinical status in consultation with the rheumatologist. Dose
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5 titration was then continued with these drugs if needed.
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10 Gout-flare prophylaxis was used in all patients and in most instances we utilized
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12 colchicine 0.6 mg daily. For patients with eGFR less than 30, the dose was reduced to 0.3
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14 mg per day. In some patients, if recommended by the rheumatologist, a daily
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16 nonsteroidal anti-inflammatory drug (NSAID) treatment was substituted, if no
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18 contraindication prevented this.
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24 Acute gout flares were managed by the clinical pharmacist, in consultation with the
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26 rheumatologist, using oral NSAIDS, prednisone or colchicine.
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32 Adverse drug reactions (ADR) to medications, incident gout flares and abnormal
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34 laboratory parameters were recorded by the clinical pharmacist at each telephone
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36 encounter and reviewed by the rheumatologist for management.
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42 Results

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45 Patient demographics and co morbidities of the pilot sample are described in Table 1.
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51 Table 1. Demographic and clinical characteristics of patients (N=100)
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| 53 Characteristic | 54 Mean (range) |
|-------------------|-----------------|
| 55 Age, years | 56 61 (32-94) |

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|----------------------------------|------------|
| BMI, kg/m ² | 31 (20-48) |
| | Percent |
| Male | 75% |
| Hypertension | 75% |
| Chronic kidney disease (CKD 2-4) | 29% |
| Diabetes | 29% |
| Coronary artery disease | 10% |
| Congestive heart failure | 11% |
| 2 or more co-morbidities | 46% |

Three-fourths of the patients were male. The mean age was 61 years, (range: 32 – 94 years). The mean body mass index was 31 kg/m² (range: 20 – 48 kg/m²). Common gout-associated co-morbidities were determined based on the presence of specific ICD-9 codes listed in the problem list of each patient in the electronic medical record, and verified by chart review. The majority of patients had at least one of the common co-morbidities associated with gout. Seventy-five percent had hypertension, and 29% had chronic kidney disease (CKD). Of these, 2 had stage 2 CKD, 22 had stage 3 CKD and 3 had stage 4 CKD. Another 29% had diabetes. A smaller number had either coronary artery disease or congestive heart failure. Forty-five percent of the patients had 2 or more of these co-morbid conditions.

Figure 2 is a schematic that shows the current status of the first 100 patients referred to our clinic. Five patients declined to participate when initially contacted by the pharmacist. Thus, 95 patients started the program, and at the time of this analysis, 78 had completed the program with 2 consecutive sUA measurements of < 6.0 mg/dl, and 4 were

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3 still being managed. Thirteen patients left the program prior to achieving the end point.
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5 Of these, 2 patients died while in the program. One died from complications of
6
7 abdominal surgery and the other, aged 94, died at home of “natural causes”. One patient
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9 developed symptoms of an allergic reaction to allopurinol and declined further treatment.
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11 One patient lost insurance coverage, and another was incarcerated. The remaining 8
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13 patients were discharged by the program pharmacist because of a pattern of non-
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15 adherence to treatment or lab monitoring, or because they elected not to complete the
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17 program. The time patients spent under program management varied considerably. The
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19 mean duration of participation was 47.8 weeks (range 14.9-109.6 weeks). Although our
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21 program was a feasibility study and designed as a short term intervention, when we
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23 examined the medical records of the 78 patients who have successfully completed the
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25 program, we found that 63 of these had been tested at least one time by their regular
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27 physician after clinic discharge (mean follow up time 36 weeks) and that 53 of these
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29 (80%) still maintained a sUA of 6.0 or less.
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39 Figure 3 shows the sUA's of each patient in the pilot gout-management study as a set of
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41 paired samples. Each pair of bars represents the baseline sUA (red bars) and final sUA
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43 (blue bars) for each patient. For those patients still in the program (i.e., those who have
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45 not yet achieved the discharge criterion of 2 consecutive sUA measurements of ≤ 6.0
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47 mg/dl), the blue bar is the most recent sUA available if the patient did not complete the
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49 program. The dotted horizontal line represents the sUA target of 6.0 mg/dl. The figure
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51 shows all the patients who entered the program, including those who are still being
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53 managed and those who did not complete the program.
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6 To provide a more detailed view of how patients responded to management by the clinic,
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8 we plotted sequential sUA levels in a subset of our patients. Figure 4 shows this analysis
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10 in 20 randomly selected patients entering the program. Each line represents the
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12 sequential sUA measurements of a single patient for a period of 12 months. Essentially
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14 all the patients in this random sample initially responded with significant reduction in
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16 sUA. In many patients, this improvement was sustained, but in others, the sUA
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18 subsequently rose due to discontinuation of ULT. In these patients, the pharmacist was
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20 able, in most cases, to restart ULT and continue testing to assure continuing medication
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22 adherence. The Figure also shows that by 12 months in the program, 16 of the 20
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24 patients had achieved a target sUA and two had a normal sUA of < 6.8 mg/dl.
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32 Analysis of the 78 patients who have completed the program after achieving and
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34 maintaining the targeted sUA showed that 68 (87%, 95% CI: 78% to 94%) were on
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36 allopurinol at discharge. Figure 5 shows the distribution of allopurinol doses required to
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38 achieve a sUA of ≤ 6.0 . The mean daily allopurinol dose required to achieve a sUA of \leq
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40 6 was 311 mg. Sixty-eight percent of patients on allopurinol achieved target on 300 mg
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42 per day or less. Only three patients achieved goal on the starting dose of 100 mg daily
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44 and two patients required 600 mg per day. All five patients on febuxostat had achieved
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46 the goal sUA level on 40 mg per day.
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53 Three patients (3%) experienced rash or other symptoms of allergy to allopurinol. None
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55 required more than discontinuation of the medication. Of these, two patients were
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3 changed to alternative ULT and one patient declined further treatment and discontinued
4 the program. Elevation of ALT was seen at some time during treatment in 47 patients
5 (48%), but only 7 of the patients had elevations high enough to require changing
6 medication. Most stabilized or returned to normal with continued treatment and
7 monitoring. Incident acute gout flares were reported in 33 patients (34%). None resulted
8 in discontinuation of ULT. Gastrointestinal side effects were uncommon and in no case
9 required a change in therapy.
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20 21 22 **Discussion** 23

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27 Gout is arguably the best understood of the common inflammatory arthritic diseases;
28 effective preventive therapy is readily available and the key outcome (sUA < 6 mg/dl in
29 most cases) is easily measured. Why, then, is unsuccessful control of sUA so frequent? A
30 number of factors contribute to suboptimal gout management. (11,12,14) Adherence to
31 ULT is poor when compared to medication adherence in other chronic conditions. (15)
32 Symptoms are typically intermittent with extended gout-free periods. Moreover, there are
33 effective treatments for gout flares, and medications (for example, colchicine) that can
34 reduce the incidence of flares without lowering sUA. It is not surprising therefore, that
35 many gout patients are never started on, or discontinue ULT. Another important feature
36 of gout management is that initiation of ULT can lead to a short-term increase in
37 incidence of gout flares, (16) further discouraging the continuation of therapy. Better
38 patient education could be expected to improve long-term medication adherence, but is
39 not consistently provided. (17) While diet is clearly a factor in the development of gout
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3 (18), patients and physicians frequently place a disproportionate emphasis on dietary
4 restrictions. (19) Although consensus guidelines recommend treating with ULT to a
5 target sUA of 6.0 mg/dl or less, concerns about allopurinol toxicity may discourage some
6 physicians from achieving this goal. In particular, limiting doses of allopurinol in patients
7 with CKD lead to a high percentage of treatment failures (20). Finally, many clinical
8 laboratories do not correctly identify serum urate concentrations of > 6.8 mg/dl as being
9 abnormal. This leads to under-treatment and considerable confusion about diagnosis and
10 management. (21)
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24 Our pilot program was conceived as a way to re-frame the approach to gout management.
25 We hypothesized that using a structured treat-to-target approach with regular monitoring
26 and a goal-directed intervention would result in a high percentage of patients achieving a
27 target sUA. In particular, the protocol was designed to use a slow titration of ULT along
28 with flare prophylaxis and scheduled follow up calls. We also required sustained control
29 of sUA for at least 3 months as a way to promote longer term medication adherence. We
30 realize that maintaining treatment for 3 months does not guarantee long term control of
31 sUA. Nevertheless, of the patients for whom a follow up test was available, 80% were
32 still at target a mean of 36.8 weeks after clinic discharge. As for any chronic condition,
33 optimal outcomes will require some level of structured monitoring.
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50 The results of our pilot program suggest that a structured program may be an effective
51 approach to gout management. ULT medications are highly effective, and therefore
52 almost all our patients responded with significant reductions in sUA within weeks of
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3 starting the program (Figure 4). Dose titration allowed most patients to achieve a target
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5 sUA of ≤ 6.0 mg/dl and to-date, all patients have been able to achieve goal using standard
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7 doses of available medications. The demographic and clinical features of the patients in
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9 our gout sample were similar to those seen in the general population of gout patients
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11 described in previous studies, (22) suggesting that our findings should be generalizable to
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13 gout populations outside KPNC. A nurse-staffed case management approach has been
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15 used and achieved impressive results in controlling sUA in gout patients (23). Our pilot
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17 program is also based on a structured management approach, but did not require any
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19 clinic visits. This model is highly efficient and therefore suitable for managing a large
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21 population of gout patients, but not necessarily more effective than a case management
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23 approach.
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31 There is ample evidence that therapeutic inertia contributes to inadequate results of ULT
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33 (24). Our program was designed specifically to counter this problem by including
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35 repeated sUA measurements and specified actions based on the results. In addition, our
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37 protocol did not limit doses of allopurinol specifically based on renal function, which has
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39 been one of several impediments noted in the literature to successful ULT. Current
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41 recommendations do not support the need to limit allopurinol doses to 100 mg daily in
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43 patients with CKD, (25–27) though a low starting dose and slow titration is
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45 recommended. (26,28) Indeed, limiting the dose of allopurinol based on the presence of
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47 chronic kidney disease has been shown to result in treatment failure in an unacceptably
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49 high percentage of patients. (17) Our data confirm this observation: only three of 68
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51 allopurinol-treated patients (4%) completing the program achieved a sUA of ≤ 6.0 on
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3 100 mg daily of allopurinol, and only 68% achieved target with 300 mg daily (Figure 5).
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8 Not surprisingly, we encountered many cases of medication non-adherence. In most
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10 cases, this was detected in the course of the routine testing that comprised the protocol.
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12 Typically a patient whose sUA was at or near target, had a repeat test that was no longer
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14 at target. In some cases, non-adherence was discovered at the time the patient called to
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16 pharmacist because of a gout flare. Our protocol, by requiring two consecutive target
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18 sUA levels three months apart, was designed with the expectation that adherence to ULT
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20 would be inconsistent. As noted previously, we do not know whether our time-limited
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22 intervention will ultimately lead to long-term control of sUA in these patients, but we
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24 were able to detect medication non-adherence in the first few months and thus reinforce
25
26 the importance of long-term ULT. Ideally, monitoring of sUA would continue on a
27
28 regular basis, as recommended for relevant laboratory parameters in other chronic
29
30 conditions. Despite the fact that all patients were prescribed colchicine or NSAIDs for
31
32 flare prophylaxis, we encountered a substantial number of gout flares during the program.
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34 While some increase in flares may be expected, in our experience, many of the flares in
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36 our patients occurred in connection with medication non-adherence. This tendency of
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38 gout patients to discontinue ULT accounted for the wide range of times patients had to
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40 stay under management. We provided our patients with written educational material as
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42 well, but could not evaluate the effectiveness of this.
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53 We designed our pilot to be efficient and cost-effective by leveraging physician time.
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55 The gout management program, while supervised by a rheumatologist, was staffed by a
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3 clinical pharmacist who was carefully trained in the management protocol. The
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5 pharmacist was able to manage a cohort of up to about 80 patients at a time while
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8 spending only about 6-8 hours per week. The time spent in overseeing and assisting the
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10 clinical pharmacist was never more than about 30 minutes per week for the
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12 rheumatologist once the program was in place. Moreover, our program did not require
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14 any in-person visits. This model suggests a path to improved outcomes in gout patients
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16 without generating the magnitude of increased utilization of health care resources that
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18 might otherwise be required. We recognize that pharmacists may not be available or
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20 allowed to manage patients as was done in our protocol. Even so, a trained clinical nurse
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22 could be substituted in the pharmacist's role and provide excellent care while leveraging
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27 physician time.
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Figures

Fig. 1 Clinic monitoring and treatment flow diagram

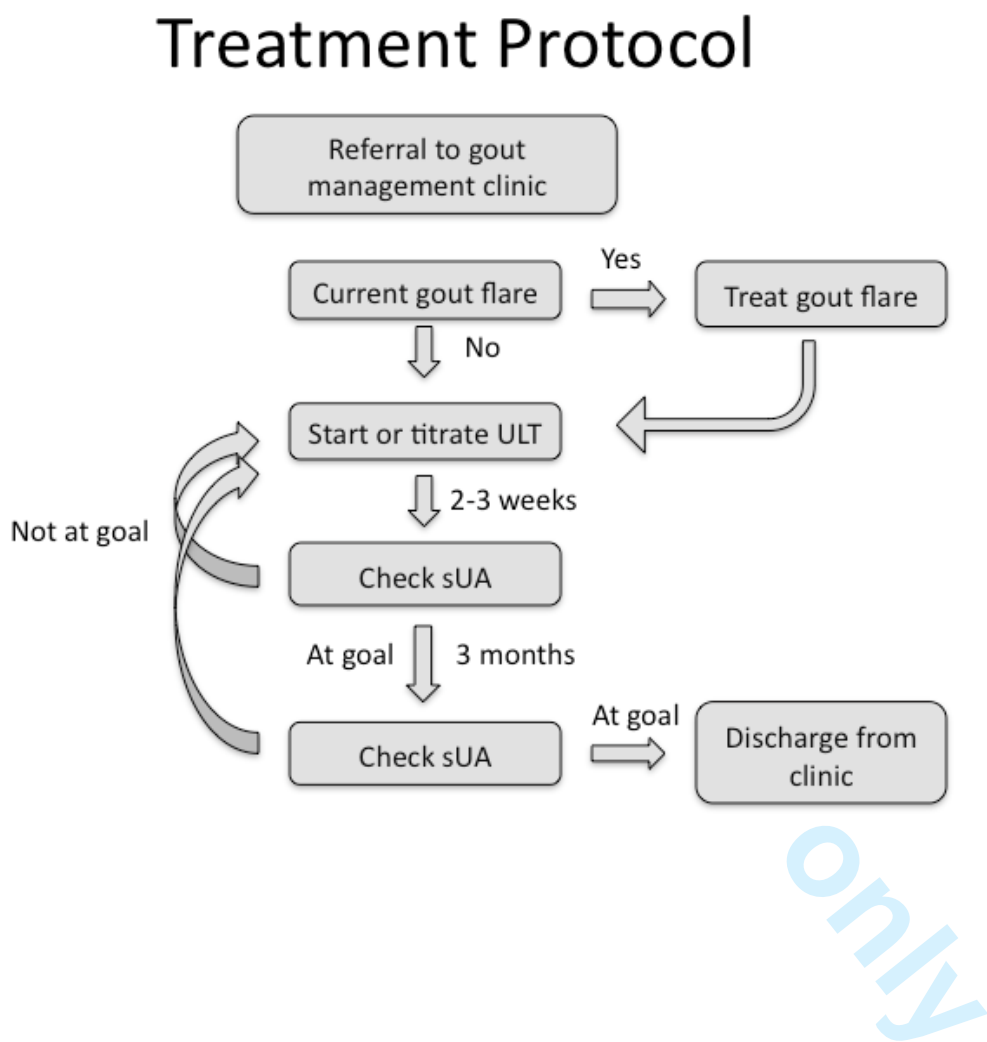
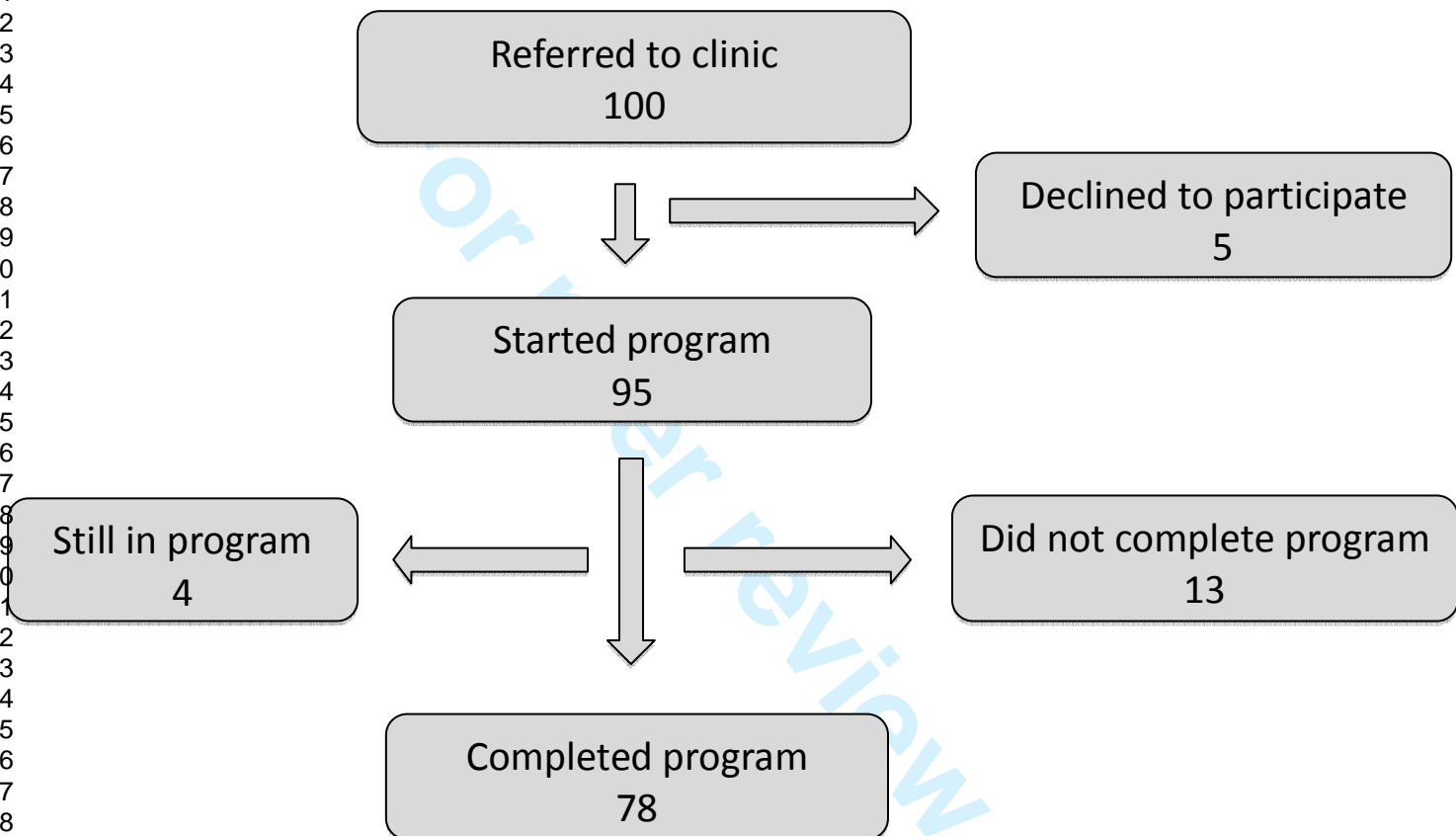


Fig. 2 Current status of first 100 patients referred to program

Current Patient Status



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Fig. 3 Comparison of pre-treatment sUA and most recent or final sUA. Each patient is represented by a red bar (initial sUA) and a blue bar (final sUA, whether or not he/she completed the program).

sUA Pairs: First and Last

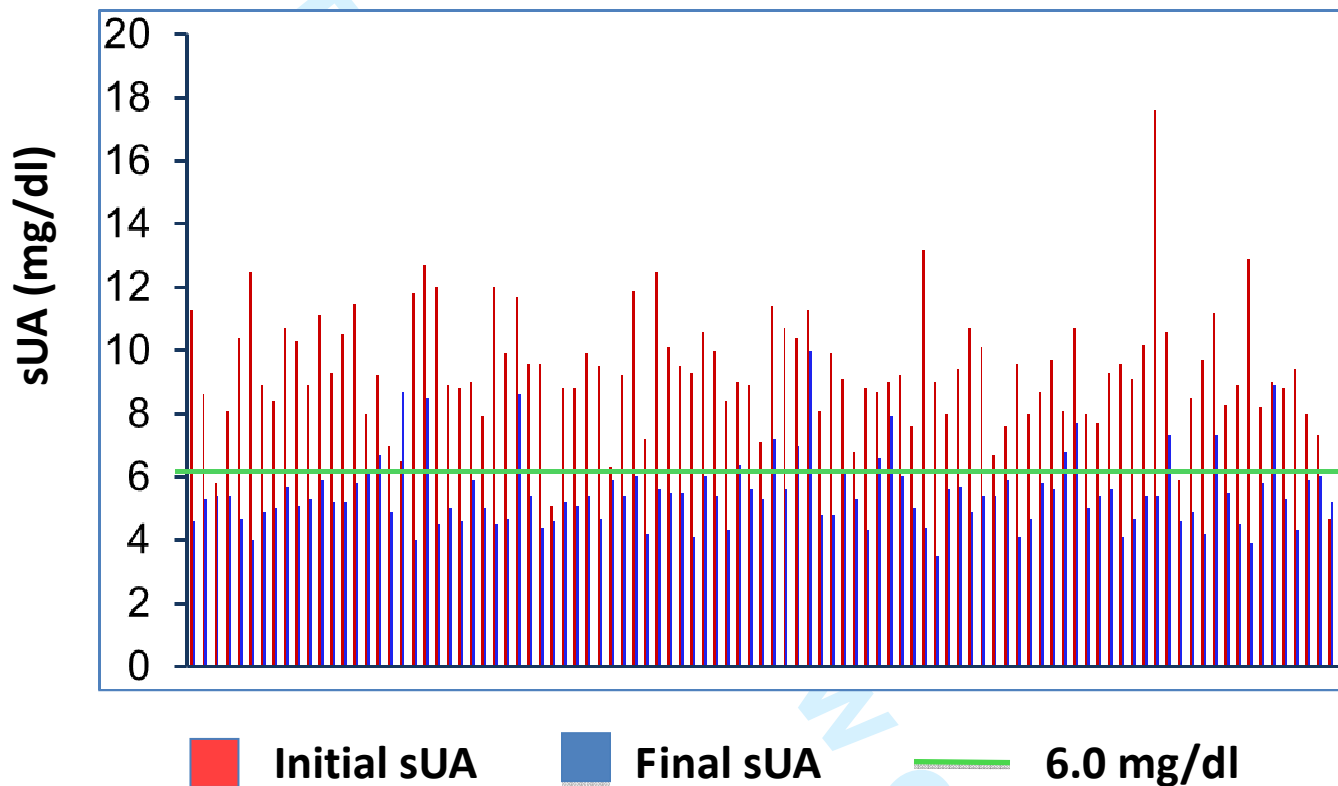
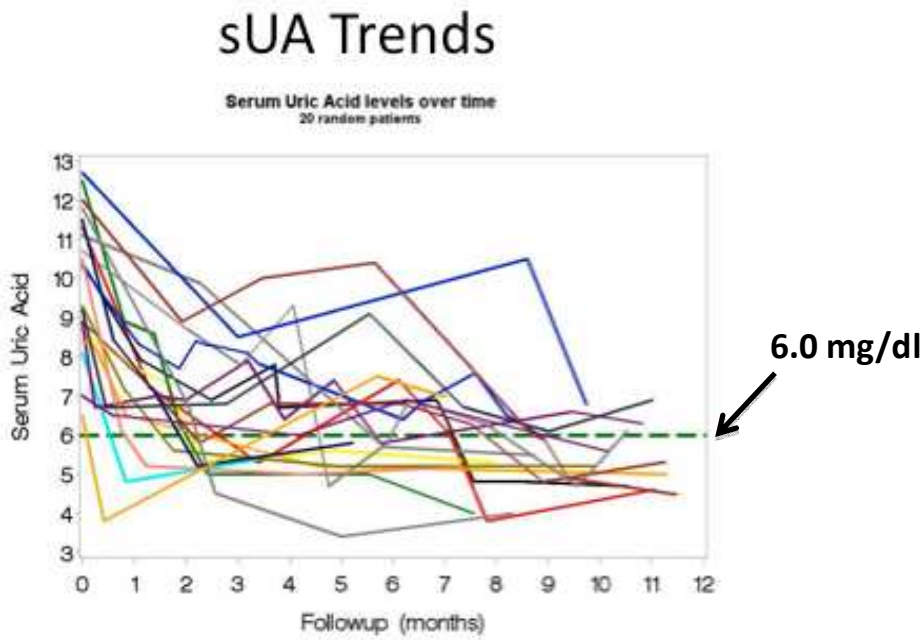
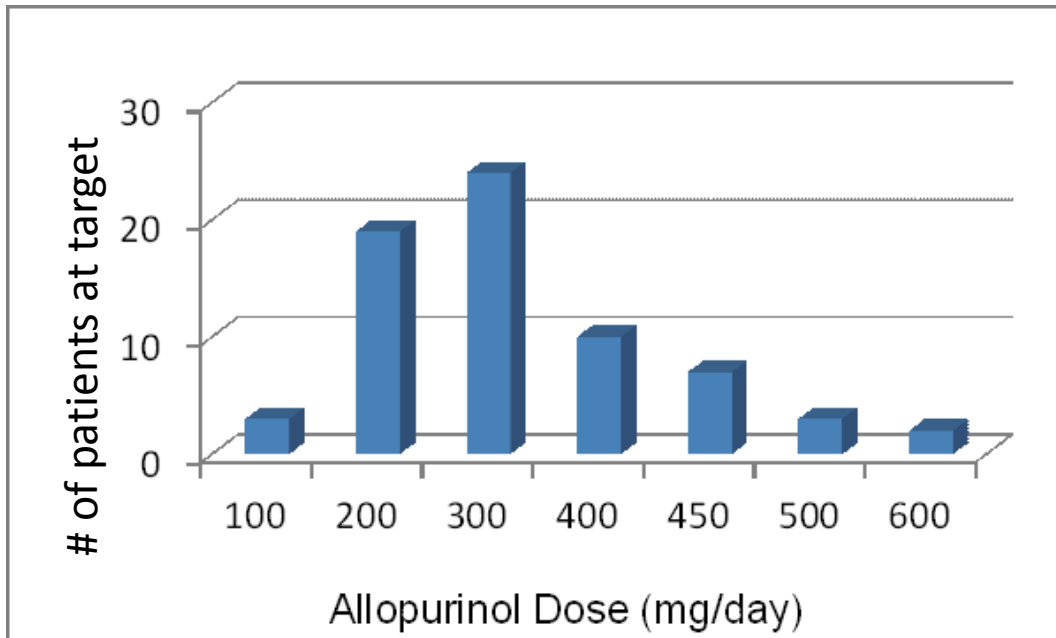


Fig. 4 sUA trend lines for 20 randomly selected patients. Each colored line represents sequential sUA levels in a single patient. Each line stops at the time of clinic discharge or is the most recent sUA if the patient had not completed or left the program.



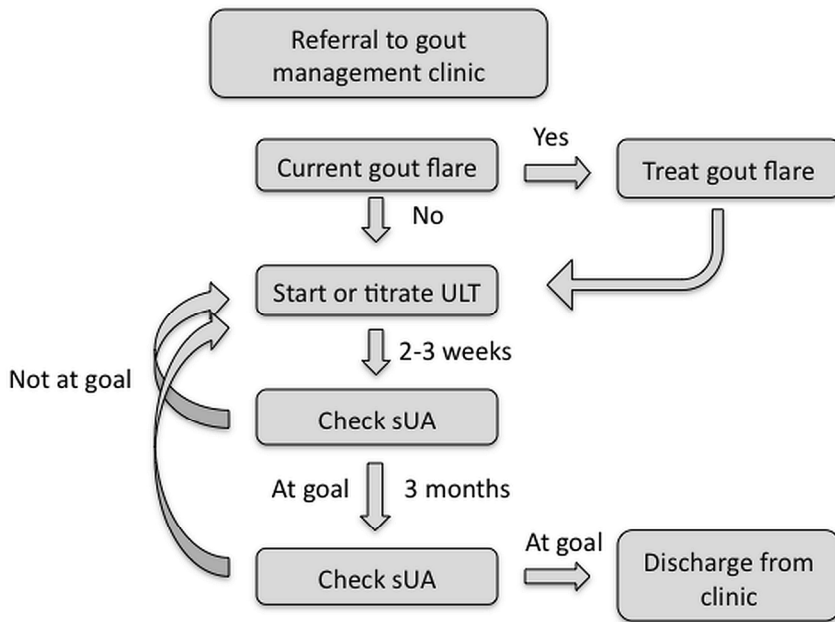
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Fig. 5 Dose of Allopurinol required to achieve a sUA of ≤ 6.0 mg/dl



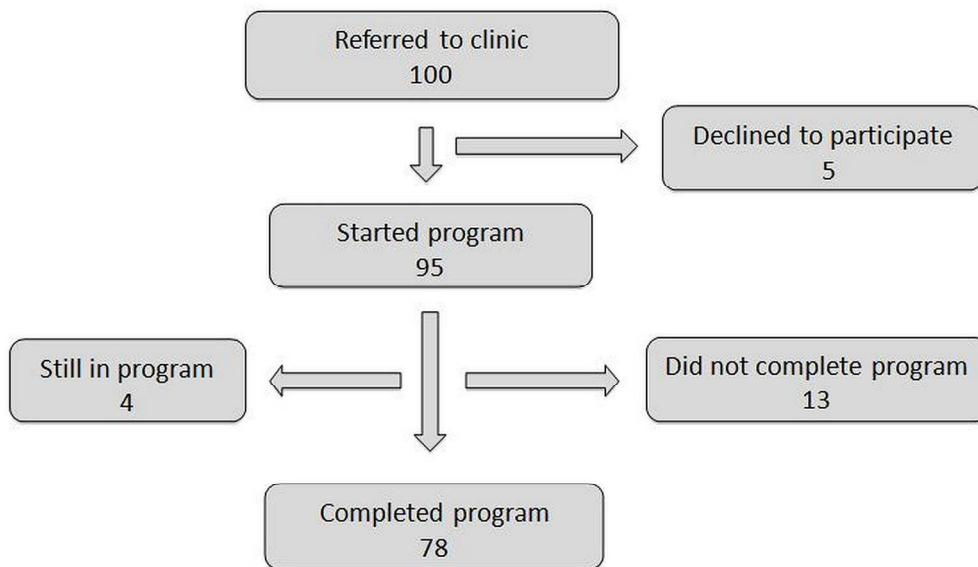
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Treatment Protocol



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Current Patient Status



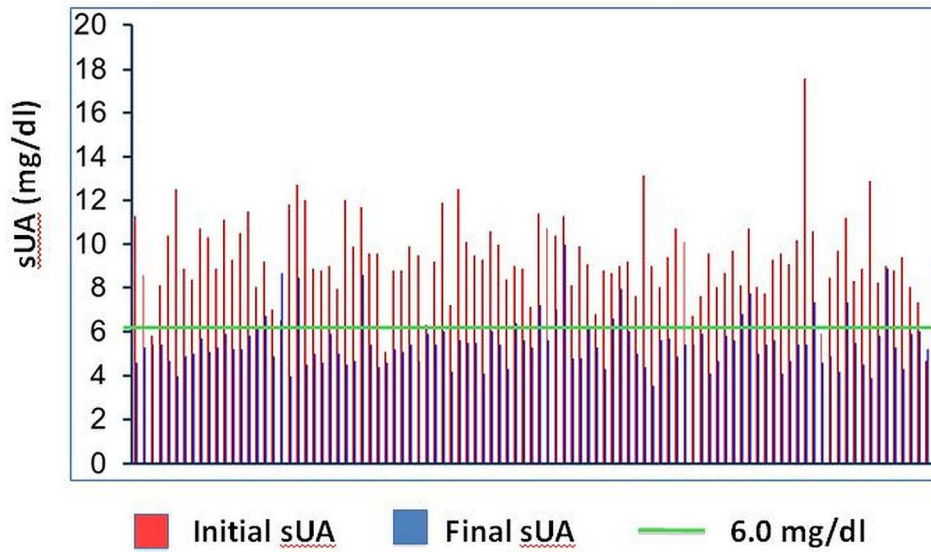
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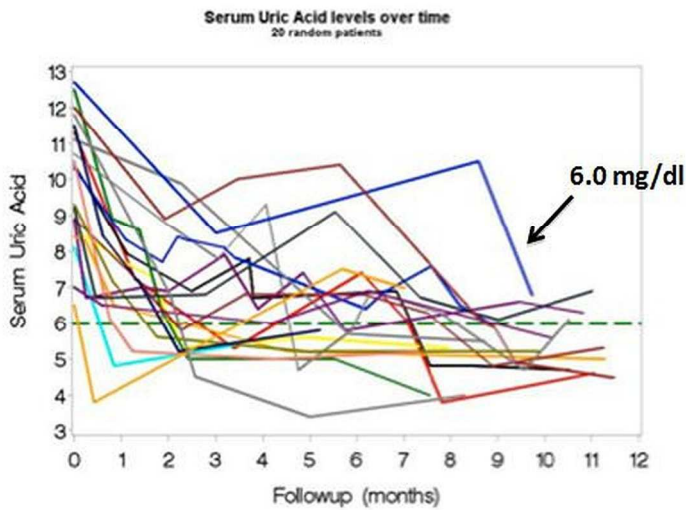
sUA Pairs: First and Last



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sUA Trends

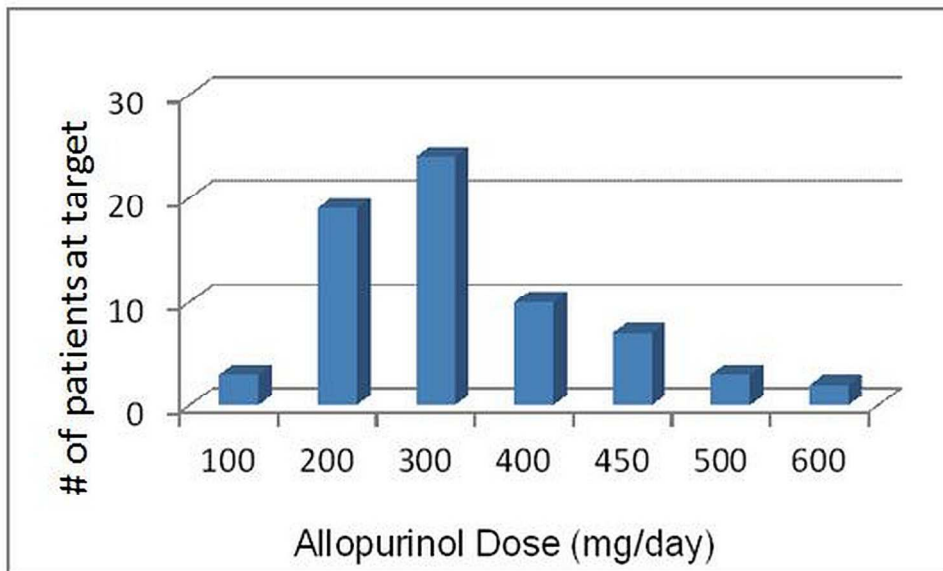


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