The Direct Economic Burden of Gout in an Elderly Canadian Population

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ABSTRACT. ***Objective.*** To estimate the direct healthcare cost and resource use from the public payer perspective between patients with incident gout and matched gout-free patients in Ontario.

Methods. Patients with incident gout aged ≥ 66 with uninterrupted Ontario Health Insurance Plan (OHIP) coverage in the 1-year baseline period were included in the study. Patients with gout were indexed at first gout diagnosis or prescription over the study period April 1, 2008, to March 31, 2014. Gout-free patients with no gout diagnosis within history were matched (up to 5:1) to each patient with gout. Linked medical records were analyzed until end of study, death, or OHIP ineligibility. Bang and Tsiatis adjusted healthcare costs and resource use were compared using bootstrap p-values and 95% CI.

Results. A total of 29,894 patients with gout and 148,231 gout-free patients were included in the study. Patients were 56% male, had a median Adjusted Clinical Group healthcare resource use band of moderate morbidity, and had a median age of 75–79 years. Baseline comorbidities were similar between groups except for renal disease. Analyzing 5-year total healthcare costs, patients with gout ($44,297) incurred a significantly higher average healthcare cost compared to gout-free patients ($33,965), for an incremental cost of $10,332 (95% CI $9617–$11,039; $p < 0.01$). Similar trends were observed in all individual healthcare component cost and use metrics.

Conclusion. Following onset of gout, patients in Ontario incur significantly greater healthcare costs and resource use compared to matched gout-free patients. Alternative gout management strategies should be investigated to reduce the incremental burden of gout borne by the Ontario healthcare system. (J Rheumatol First Release November 1 2016; doi:10.3899/jrheum.160300)

Key Indexing Terms:
AGING GOUT EPIDEMIOLOGY HEALTHCARE COSTS
CASE-CONTROL STUDIES RETROSPECTIVE STUDIES

Gout is the most common form of inflammatory joint disease and is associated with hyperuricemia, which leads to the deposition of monosodium urate crystals in joints[1]. The disease often presents itself initially with painful acute attacks, and with inadequate management can evolve into chronic tophaceous gout and joint deformity[1]. Prior studies have demonstrated that as serum uric acid (SUA) levels increase, patients face an increased risk of gout attacks[2,3]. Moreover, patients with gout tend to have a high comorbidity burden at disease onset, particularly metabolic, cardiovascular, and renal complications[4,5,6], and this burden continues to grow following the development of gout[7].

The reported prevalence of gout ranges from 100 to 10,000 per 100,000 people and appears to be increasing in developed countries[8]. Disease incidence is also highly variable, with previously reported 6-year estimates ranging from 180 to 3600 per 100,000 population[8]. Both the incidence and prevalence of gout have been observed to increase with age and to be higher in males[8,9]. In Canada, gout is commonly managed in the primary care setting and is predominantly treated with urate-lowering therapies such as allopurinol[10]. However, both in Canada and other countries, gout management is often considered suboptimal[11,12,13].

Beyond its painful and debilitating effect on patients, gout carries a substantial economic cost. A recent systematic review of US studies found incremental annual direct costs of US$2171, US$6335, and US$11,174 among employed, elderly, and treatment-refractory gout patient populations, respectively[14]. Direct costs were reported to be associated with increases in SUA level, gout attack frequency, or presence of tophi. Additionally, indirect costs, such as work-time loss, were estimated at up to US$4341 per year[14]. In a previous study of incident gout in elderly patients in the

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Sponsorship and article processing charges for this study were provided by AstraZeneca Canada. A. Fischer, M. Cloutier, J. Goodfield, and R. Borrelli are employees of IMS Health Brogan. IMS Health Brogan is a consulting company that has received research grants from AstraZeneca Canada. A. Dziarmaga and D. Marvin are employees of AstraZeneca Canada.

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Accepted for publication September 13, 2016.

Canadian province of Nova Scotia, the average cost differential between gout patients and non-gout patients was reported at Can$134 per month and Can$8020 per case over 5 years[10].

With the exception of the study conducted by Hanly, *et al* in Nova Scotia[10], limited research has been conducted on the cost burden of gout in Canada. This study evaluates an elderly, incident gout population in Ontario, Canada's largest province, to quantify the incremental healthcare use and direct costs of gout.

MATERIALS AND METHODS

We conducted a 5-year retrospective case-control study of the direct healthcare resource use and costs of an elderly, incident gout population in Ontario from the public payer perspective (Appendix 1). In Ontario, medical services, including outpatient and inpatient procedures, are paid for by the Ontario Health Insurance Plan (OHIP) and governed by the Canada Health Act[15]. Eligible populations can have home care and out-of-hospital prescriptions paid for under OHIP. For this study, we used administrative medical records kept by the Institute for Clinical Evaluative Sciences (ICES), which includes records from over 95% of Ontario residents. ICES information includes information on patient demographics, healthcare plan enrollment, healthcare use, and associated cost[16]. These records were linked by encrypted OHIP health card numbers for analysis. Our study received ethics approval from the Chesapeake Institutional Review Board (ethics registration number Pro00011776), and the research ethics plan was approved by ICES. All patient records were de-identified, anonymized, and summarized in 30-day increments prior to analysis.

Patient cohort selection. Patients with incident gout age 66 or older were identified based on the observation of either 2 gout diagnoses [ICD-9 274 or ICD-10 M10 (International Classification of Diseases)] or a gout diagnosis with a gout-treating prescription during the index period of April 1, 2008, to March 31, 2014. Gout-treating prescriptions included in the study were allopurinol, colchicine, febuxostat, probenecid, and sulfinpyrazone. Importantly, colchicine, a gout medication typically prescribed for the management of gout flares, is not reimbursed by the Ontario Drug Benefit (ODB) program and therefore was not well observed in our study. The index date was defined as the first diagnosis or first prescription for gout within the index period. To be considered incident, a patient had no record of gout diagnosis or medication prior to the index date in all available history. Because ODB coverage typically starts at the age of 65, a minimum of 1 year of prescription history was available to establish incidence.

Each patient with gout was matched with up to 5 non-gout patients based on index year, health region, age, sex, and Adjusted Clinical Group simplified morbidity category known as a healthcare resource utilization band (RUB). The RUB is a scale measuring 1 year of outpatient, inpatient, and prescription healthcare resource use ranging from 0 to 5, where 0 indicates a non-user of healthcare and 5 indicates a very high healthcare user[17]. Patients with gout were matched on their RUB prior to a gout diagnosis to calculate the incremental cost and healthcare use between equally sick gout and non-gout patients. Index year, health region, age, and sex were matched to control for access to new treatments and healthcare services, and similar patient characteristics. Non-gout patients did not have a gout diagnosis within available history. Patients with uninterrupted OHIP coverage in the 1-year baseline period were included in the study and followed from index date up to the minimum of the following: end of study, death, or OHIP ineligibility.

Statistical analysis. Baseline profiling was performed on the following variables: patient age, sex, health region, RUB, Charlson Comorbidity Index (CCI), and comorbidities (including ulcer, rheumatoid arthritis, renal disease, obesity, myocardial infarction, metabolic syndrome, hypertension, dyslipidemia, diabetes, depression, chronic obstructive pulmonary disease, chronic heart failure, cardiovascular disease, and asthma) using OHIP and hospital diagnosis codes. Categorical variables were expressed in terms of counts and proportions while continuous variables are expressed in terms of means and SD. Comparison between gout and non-gout patient comorbidity profile was conducted using p values obtained from McNemar's test for categorical variables and Wilcoxon signed-rank tests for continuous variables. Standardized differences were also reported to adjust for the effect of size on case-control comparisons[18]. A threshold of 20% has been proposed to indicate a difference[19].

The burden of gout was calculated for up to 5 years over the index period for both healthcare costs and resource use. Outpatient visits were analyzed per claim; if a patient saw 2 general practitioners (GP) on the same day, and each GP submitted an OHIP claim, then 2 visits would be recorded for that patient. The same approach was used for hospitalization visits, where visits were recorded at the episode level. While gout-specific visits were analyzed for healthcare use, gout-specific costs could not be split. The Bang and Tsiatis estimator was used to adjust for asymmetry in followup duration[20]. The burden of gout was quantified using averages and SD for both groups, and comparison of means across groups was performed using CI and p values obtained using 1000 bootstrap samples[21]. The analysis of healthcare touch points was conducted over the whole 5-year followup period and for each 1-year period of the 5-year followup, to understand the evolution of the variables of interest.

All costs were expressed in Can$ 2014 by using the Bank of Canada's consumer price index[22]. The data analysis for this study was generated using SAS software version 9.3 (SAS Institute Inc.).

RESULTS

Patients with gout and baseline statistics. A total of 29,894 gout and 148,231 matched non-gout patients were included in this study. An average exact matching ratio of 1:4.96 gout to non-gout was achieved, with 3231 patients with gout matching to fewer than 5 controls, and 2 patients with gout not included in the study owing to lack of matches. The average followup time was similar between the gout and non-gout cohorts: 1084 days and 1077 days, respectively. The median gout age range was 75-79 years, with males composing 56% of patients with gout and a medium RUB of 3 (moderate morbidity). Overall, a 1699 per 100,000 population 6-year gout incidence rate was estimated.

Baseline comorbidities, in which patients received a diagnosis within the past year, were assessed between the 2 groups (Table 1). All baseline comorbidities were significantly different ($p < 0.01$); however, only renal disease prevalence met the difference threshold when using standardized difference to account for sample size. The most prevalent baseline diseases in the gout cohort were renal disease (15%), cardiovascular disease (5%), and chronic heart failure (3%). The baseline CCI was statistically different at baseline, but did not meet the standardized difference threshold.

Healthcare use. Over the 5-year followup, patients with gout had a total of 2,120,512 outpatient visits and 126,604 inpatient visits, with 80% of patients with gout receiving a gout diagnosis from a GP or family medicine physician (GP/FM), 9% from a rheumatologist (RH), and 3% from a hospital visit. Adjusted for followup, patients with gout compared to non-gout patients incurred 21.9 more outpatient visits (95% CI 20.8–22.9; $p < 0.01$; 101.7 vs 79.8, respec-

Table 1. Baseline characteristics for patients who received a diagnosis in the prior year for gout, and for non-gout patients. Data are percentages, except where indicated.

Characteristic	Gout, n = 29,894	Non-gout, n = 148,231	SD
Asthma	1	0	1
Cardiovascular disease	5	6	5
Chronic heart failure	3	2	9
COPD	2	2	1
Depression	2	3	5
Diabetes	3	2	5
Dyslipidemia	3	2	6
Hypertension	2	3	5
Metabolic syndrome	0	0	0
Myocardial infarction	1	1	3
Obesity	1	0	5
Renal disease	15	4	37
Rheumatoid disorders	1	0	3
Ulcer	2	1	2
CCI (average SD)	0.3 (1)	0.3 (1)	2

SD: standard difference; COPD: chronic obstructive pulmonary disease; CCI: Charlson Comorbidity Index.

tively) and 1.9 more inpatient visits (95% CI 1.8–2.0; $p < 0.01$; 5.9 vs 4.0, respectively). The largest incremental number of inpatient and outpatient visits occurred within the first year of gout diagnosis, with incremental inpatient and outpatient visit count at an average of 9.2 visits (95% CI 8.9–9.5; $p < 0.01$) and 0.8 visits (95% CI 0.8–0.8; $p < 0.01$), respectively. However, the incremental visit count decreased to an average of 2.4 outpatient visits (95% CI 1.9–2.8; $p < 0.01$) and 0.2 inpatient visits (95% CI 0.2–0.2; $p < 0.01$) in the fifth year (Figure 1).

Outpatient visits were categorized into 4 groups: GP/FM, RH, internal medicine (IM), and other. Over the 5-year followup, gout and non-gout patients averaged 51.2 vs 41.1 GP/FM visits, 0.8 vs 0.4 RH visits, 13.5 vs 8.6 IM visits, and 36.3 vs 29.7 other physician visits, respectively. This translates to an average incremental 5-year visit count of 10.1 GP/FM visits (95% CI 9.5–10.6; $p < 0.01$), 0.4 RH visits (95% CI 0.4–0.4; $p < 0.01$), 4.9 IM visits (95% CI 4.6–5.1; $p < 0.01$), and 6.6 other physician visits (95% CI 6.1–7.1; $p < 0.01$) for patients with gout compared to non-gout patients. The average 5-year visit count by specialty at which gout was treated was analyzed. On average, patients with gout visited for gout treatment a GP/FM 2.5 times (95% CI 2.5–2.5; $p < 0.01$), an RH 0.3 times (95% CI 0.3–0.3; $p < 0.01$), an IM 0.3 times (95% CI 0.3–0.3; $p < 0.01$), and other physicians 0.1 times (95% CI 0.1–0.1; $p < 0.01$). Over time, the gout-specific inpatient visits decreased from an average of 2.2 visits in the first year (95% CI 2.1–2.2; $p < 0.01$) to 0.2 visits in the fifth year (95% CI 0.2–0.2; $p < 0.01$).

Healthcare costs. The total 5-year medical expenditures, including those incurred from overnight inpatient visits, emergency department visits, same-day surgery, outpatient physician visits, reimbursed prescriptions, and home care were statistically significant and greater ($44,297) for gout patients than non-gout patients ($33,965), with an incremental difference of $10,332 (95% CI $9617–$11,039; $p < 0.01$). Moreover, the individual cost components were also found to be statistically significant ($p < 0.01$) and greater for patients with gout compared to non-gout patients (Table 2). Overnight inpatient, outpatient, and home care costs were the greatest contributor to the total cost difference and accounted for about 61%, 17%, and 10%, respectively. Emergency department, same-day surgery, and prescriptions combined accounted for about 12% of the total cost difference.

When analyzed in their individual components, 5-year average prescription costs were higher in patients with gout compared to non-gout patients for all categories: gout-treating prescriptions [$121 vs $0, incurring an incre-

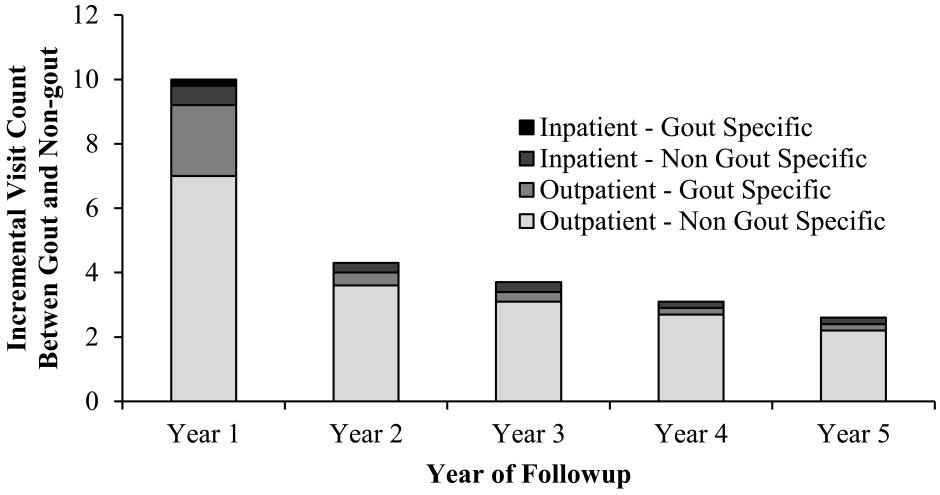

Figure 1. Differential in visit count between patients with gout and non-gout patients.

Table 2. Differential in incurred costs between patients with gout and non-gout patients. P value is < 0.01 except where indicated.

Average Cost (95% CI)	Year 1	Year 2	Year 3	Year 4	Year 5	Total
Total	$4480 ($4172–$4778)	$1853 ($1618–$2096)	$1633 ($1373–$1937)	$1358 ($1091–$1647)	$1010 ($720–$1308)	$10,332 ($9617–$11,039)
Inpatient	$3262 ($3029–$3504)	$1172 ($990–$1358)	$1037 ($829–$1250)	$821 ($612–$1044)	$634 ($429–$868)	$6927 ($6402–$7440)
Outpatient	$683 ($649–$726)	$325 ($291–$361)	$281 ($241–$325)	$263 ($217–$302)	$218 ($163–$273)	$1771 ($1661–$1899)
Home care	$333 ($278–$389)	$199 ($147–$249)	$193 ($131–$255)	$174 ($110–$240)	$118 ($44–$187)	$1017 ($804–$1218)
Gout-treating prescriptions	$27 ($27–$28)	$24 ($23–$24)	$24 ($23–$24)	$24 ($23–$25)	$23 ($22–$24)	$121 ($119–$124)
NSAID prescriptions	$6 ($5–$8)	$1 ($0–$2) p = 0.22	$0 (–$1 to $1) p = 0.73	–$1 (–$2 to $1) p = 0.43	$0 (–$2 to $2) p = 0.94	$6 ($1–$11) p < 0.05
Corticosteroid prescriptions	$2 ($2–$2)	$1 ($1–$1)	$1 ($1–$1)	$1 ($1–$1)	$1 ($1–$2)	$6 ($5–$8)
Other prescriptions	$165 ($126–$204)	$131 ($95–$170)	$96 ($46–$154)	$76 ($26–$128)	$16 (–$41 to $74) p = 0.57	$484 ($317–$658)

NSAID: nonsteroidal antiinflammatory drugs.

mental $121 (95% CI $119–$124); p < 0.01], nonsteroidal antiinflammatory drugs [NSAID; $112 vs $106, incurring an incremental $6 (95% CI $1– $11); p < 0.05], corticosteroids [$20 vs $14, incurring an incremental $6 (95% CI $5–$8); p < 0.01], and other prescriptions [$8132 vs $7649, incurring an incremental $484 (95% CI $317–$658); p < 0.01]. Over the 5-year followup period, only 60% of patients with gout received a gout-treating prescription, with the majority of prescriptions attributed to allopurinol.

Similar to visit count, the largest annual incremental difference between patients with gout and those without was incurred in the first year of gout diagnosis. Patients with gout, compared to non-gout patients, incurred an overall incremental cost of $4480 in their first year of followup (95% CI $4172–$4778; p < 0.01; $12,837 vs $8358, respectively), while in the fifth year they incurred an overall incremental cost of $1010 (95% CI $720–$1308; p < 0.01; $6651 vs $5642, respectively), with a year-over-year decrease. Costs for outpatient visits, inpatient visits, home care, and prescriptions were higher and statistically significant in both the first year and fifth year for patients with gout compared to non-gout patients (p < 0.01). However, specific costs incurred for same-day surgery, NSAID prescriptions, and other prescriptions were only statistically significant and higher for patients with gout compared to non-gout patients in the first year.

DISCUSSION

Gout, one of the most common forms of arthritis in elderly patients, characteristically manifests as extremely painful acute attacks, often prompting the patient to seek immediate medical help[12]. Because of the disease's debilitating attacks, and the increasing rate at which inpatient and outpatient clinics are treating gout, the healthcare system incurs significant costs[14].

The purpose of our study was to quantify the incremental direct costs and healthcare resources used for the first 5 years of a gout diagnosis as compared to matched, equally sick, non-gout controls in an elderly (> 65 years) gout population in Ontario.

Similarly to another study of incident gout in the elderly (≥ 65 years) conducted by Hanly, *et al*, we found a near-even split between the sexes, albeit a slightly higher proportion in males (56%) and a similar median age group[10]. While the nearly even male/female split reported in our study and by Hanly contrast with the commonly reported male:female ratio of 3–4:1, previous research supports the observation that gout often develops later in women than in men, because the prevalence of certain risk factors for gout, such as renal disease, hyperuricemia-associated hypertension, and diuretics, is different for women[10,23,24]. Interestingly, the median baseline RUB for the gout and non-gout cohort is 3, a level at which a patient typically starts to be hospitalized[25]. This high baseline resource use is expected in the gout population, given the high healthcare use of the elderly population and typically high comorbidity burden of patients with gout[26].

The 6-year incidence of gout in Ontario was estimated to be 1700 per 100,000 population, which aligns with literature estimates of 180 to 3600 per 100,000 population[8]. A 4400 per 100,000 population 5-year incidence of gout was reported in a similar elderly Canadian population in Hanly's study[10]. We did, however, expect to find a lower incidence rate than Hanly because that study required a single gout diagnosis for selection, whereas our study required a second confirmatory gout diagnosis or medication[10]. When Hanly, *et al* validated their gout definition, they found that it had a 49% positive predictive value (PPV), indicating some potential for overestimation of gout incidence[10]. A study evaluating the PPV of 2 gout diagnoses recorded in administrative data yielded a PPV of 61%[27]. In our study, we found that a majority (80%) of the patients with gout had 2 or more gout diagnoses.

Overall, we found that patients with gout incurred significantly higher costs and visit counts in all healthcare touch points compared to the non-gout cohort, with the largest cost differential incurred during the first year after diagnosis. We also found that the difference in costs and visit count decreased over time, indicating either gout or other comor-

bidities were requiring fewer medical visits. This finding does align with other studies in which a similar decrease in overall costs and visit counts by year from gout incidence was reported[2,10].

When compared to other burden-of-illness studies, our average annual incremental cost (Can$2066) was in line, albeit slightly higher, with the 2014 inflation-adjusted Can$1872 average annual incremental cost found in Hanly[10,22]. However, Hanly did not match on baseline resource use, which we would expect to reduce our study's incremental difference[10]. When compared to burden-of-illness studies in prevalent gout populations, we found that our study showed the same overall trends[14,26]. However, the average annual incremental burden of illness reported was higher in all prevalent studies, ranging between US$2171 and $11,174, likely a result of differences in gout populations, study designs, and healthcare systems and databases (Canadian vs US[14,26]). This consistency demonstrates that regardless of the population, gout causes a significantly increased burden on healthcare systems.

The number of gout-specific healthcare visits was highest in the first year after diagnosis with the average annual visit rate decreasing thereafter. The explanation for this trend may be more-adept management of gout over the disease course as appropriate medication and lifestyle strategies are implemented.

Interestingly, only 60% of patients with gout received a gout prescription and only 8% of patients with gout were ever diagnosed by a rheumatologist. While it is possible that non-gout patients with 2 erroneous gout diagnoses were included in the study, a more likely explanation is suboptimal treatment and poor adherence to guidelines[28,29,30] for what is a curable disease in the majority of patients[13]. This raises the question of whether alternative strategies or treatments are warranted to reduce the burden of gout on both patients and the healthcare system.

Several limitations exist within our study. First, no validation study on the definition used to identify patients with gout has been evaluated within the studied datasets. While other studies provide some confidence in the expected predictive value of our definition[2,3,10], the conclusions of those studies may not be directly applicable to our studied databases.

Moreover, it would be preferable to have access to laboratory data to confirm the diagnosis of the patients with gout included in the study, using intracellular urate crystals from an inflamed joint[31]. However, even if accessible, synovial fluid may only be ordered for 5%-25% of the patients[27,29]. It has been noted that rheumatologists do not necessarily rely on synovial fluid laboratory results to make a diagnosis, and this reliance is even less likely among the GP/FM who commonly manage gout[10].

Second, colchicine, a gout medication, is not reimbursed by ODB, and therefore was poorly observed in our study. This could have had an effect on identifying patients with gout and evaluating prescription costs. While it is possible that some patients with gout could have been excluded from the study because they did not meet the study definition of gout, this is unlikely because allopurinol composed the majority of gout-treating prescriptions, and is the most commonly used urate-lowering drug[25]. Therefore, a patient with gout who received colchicine would likely still be identified for our study by a gout-treating prescription for allopurinol. We acknowledge that incremental costs could be affected by not including colchicine.

Third, accurately adjusting the costs and healthcare resources for asymmetric followup was a challenge because censoring was reported quarterly while death was reported daily. The method used to adjust for loss to followup and death requires censoring and death dates to adjust the average cost per period[20]. Because censoring was reported quarterly, it is possible that costs were underadjusted and healthcare resources used for a short period until the censoring was updated. However, the effect of this limitation is likely minimal.

Fourth, similarly to other studies, we matched the patients with gout and the non-gout patients on baseline confounders to compare outcomes from similar patients at baseline[10,26]. However, we did find that renal disease was higher in patients with gout than in the non-gout patients. Moreover, there could be baseline factors that were not matched at baseline that could act as confounders. Therefore, we acknowledge that part of the incremental healthcare use and costs may be due to factors other than gout.

Fifth, our study was not designed to assess the healthcare burden of gout severity, or to assess indirect costs such as work-time loss, to the patient or society. To assess the burden by severity, we would require access to SUA test results to further segment the patients with gout at baseline. Similarly, to assess the indirect costs of gout we would need access to patient-reported outcomes and short-term and longterm disability insurance claims. It should be noted that several studies have examined the indirect costs of gout, estimating the costs as high as US$4341 per year[14,32,33,34].

Sixth, owing to confidentiality constraints, we were able to identify only whether a visit was related to gout. Ideally we would like to identify the diagnosis at each visit, so we could further identify what diagnostic categories are causing the decrease in incremental visits.

Overall, our study has shown that elderly patients with incident gout in Ontario incur higher resource use and costs compared to matched, equally sick, non-gout patients. Moreover, our study has shown that this increased resource burden is felt across all healthcare touch points. Future studies should examine the incremental cost of gout by alternative strategies or treatments to assess approaches to reduce the significant burden of gout on the patients and the healthcare system.

REFERENCES

1. Neogi T. Clinical practice. Gout. N Engl J Med 2011;364:443-52.
2. Wu EQ, Patel PA, Mody RR, Yu AP, Cahill KE, Tang J, et al. Frequency, risk, and cost of gout-related episodes among the elderly: does serum uric acid level matter? J Rheumatol 2009;36:1032-40.
3. Halpern R, Fuldeore MJ, Mody RR, Patel PA, Mikuls TR. The effect of serum urate on gout flares and their associated costs: an administrative claims analysis. J Clin Rheumatol 2009;15:3-7.
4. Richette P, Clerson P, Périssin L, Flipo RM, Bardin T. Revisiting comorbidities in gout: a cluster analysis. Ann Rheum Dis 2015;74:142-7.
5. Primatesta P, Plana E, Rothenbacher D. Gout treatment and comorbidities: a retrospective cohort study in a large US managed care population. BMC Musculoskelet Disord 2011;12:103.
6. Annemans L, Spaepen E, Gaskin M, Bonnemaire M, Malier V, Gilbert T, et al. Gout in the UK and Germany: prevalence, comorbidities and management in general practice 2000–2005. Ann Rheum Dis 2008;67:960-6.
7. Kuo CF, Grainge MJ, Mallen C, Zhang W, Doherty M. Comorbidities in patients with gout prior to and following diagnosis: case-control study. Ann Rheum Dis 2016;75:210-7.
8. Kuo CF, Grainge MJ, Zhang W, Doherty M. Global epidemiology of gout: prevalence, incidence and risk factors. Nat Rev Rheumatol 2015;11:649-62.
9. Wijnands JM, Viechtbauer W, Thevissen K, Arts IC, Dagnelie PC, Stehouwer CD, et al. Determinants of the prevalence of gout in the general population: a systematic review and meta-regression. Eur J Epidemiol 2015;30:19-33.
10. Hanly JG, Skedgel C, Sketris I, Cooke C, Linehan T, Thompson K, et al. Gout in the elderly — a population health study. J Rheumatol 2009;36:822-30.
11. Black E, Sketris I, Skedgel C, MacLean E, Hanly JG. Adherence to guidelines and the screening tool of older persons' potentially inappropriate prescriptions criteria for colchicine dosing for gout treatment in beneficiaries of the Nova Scotia Seniors' Pharmacare Program. Clin Ther 2015;37:661-7.
12. Kuo CF, Grainge MJ, Mallen C, Zhang W, Doherty M. Rising burden of gout in the UK but continuing suboptimal management: a nationwide population study. Ann Rheum Dis 2015;74:661-7.
13. Doherty M, Jansen TL, Nuki G, Pascual E, Perez-Ruiz F, Punzi L, et al. Gout: why is this curable disease so seldom cured? Ann Rheum Dis 2012;71:1765-70.
14. Rai SK, Burns LC, De Vera MA, Haji A, Giustini D, Choi HK. The economic burden of gout: a systematic review. Semin Arthritis Rheum 2015;45:75-80.
15. Madore O. The Canada Health Act: overview and options: Library of Parliament. Ottawa: Parliamentary Information and Research Service; 2005.
16. Chan B, Schultz S. Supply and utilization of general practitioner and family physician services in Ontario: an Institute for Clinical Evaluative Sciences (ICES) integrative report. Toronto: Institute for Clinical Evaluative Sciences; 2005.
17. Aguado A, Guinó E, Mukherjee B, Sicras A, Serrat J, Acedo M, et al. Variability in prescription drug expenditures explained by adjusted clinical groups (ACG) case-mix: a cross-sectional study of patient electronic records in primary care. BMC Health Serv Res 2008;8:53.
18. Austin PC. Using the standardized difference to compare the prevalence of a binary variable between two groups in observational research. Commun Stat Simul Comput 2009;38:1228-34.
19. Cohen J. Statistical power analysis for the behavioral sciences. 2nd ed. Hillsdale, NJ: Lawrence Earlbaum Associates; 1988.
20. Bang H, Tsiatis AA. Estimating medical costs with censored data. Biometrika 2000;87:329-43.
21. Efron B, Tibshirani RJ. An introduction to the bootstrap. Boca Raton, FL: CRC press; 1994.
22. Bank of Canada Inflation Calculator 2015 [Internet. Accessed September 14, 2016.] Available from: www.bankofcanada.ca/rates/related/inflation-calculator/
23. Hak AE, Curhan GC, Grodstein F, Choi HK. Menopause, postmenopausal hormone use and risk of incident gout. Ann Rheum Dis 2010;69:1305-9.
24. Harrold LR, Yood RA, Mikuls TR, Andrade SE, Davis J, Fuller J, et al. Sex differences in gout epidemiology: evaluation and treatment. Ann Rheum Dis 2006;65:1368-72.
25. Fransoo R, Martens P, The Need to Know Team, Prior H, Burchill C, Koseva I, et al. Who is in our hospitals … and why? Winnipeg, MB: Manitoba Centre for Health Policy; 2013.
26. Wu EQ, Patel PA, Yu AP, Mody RR, Cahill KE, Tang J, et al. Disease-related and all-cause health care costs of elderly patients with gout. J Manag Care Pharm 2008;14:164-75.
27. Singh JA. Veterans Affairs databases are accurate for gout-related health care utilization: a validation study. Arthritis Res Ther 2013;15:R224.
28. Singh JA, Hodges JS, Toscano JP, Asch SM. Quality of care for gout in the US needs improvement. Arthritis Rheum 2007;57:822-9.
29. Petersel D, Schlesinger N. Treatment of acute gout in hospitalized patients. J Rheumatol 2007;34:1566-8.
30. Pascual E, Sivera F. Why is gout so poorly managed? Ann Rheum Dis 2007;66:1269-70.
31. Harrold LR, Saag KG, Yood RA, Mikuls TR, Andrade SE, Fouayzi H, et al. Validity of gout diagnoses in administrative data. Arthritis Rheum 2007;57:103-8.
32. Kleinman NL, Brook RA, Patel PA, Melkonian AK, Brizee TJ, Smeeding JE, et al. The impact of gout on work absence and productivity. Value Health 2007;10:231-7.
33. Lynch W, Chan W, Kleinman N, Andrews LM, Yadao AM. Economic burden of gouty arthritis attacks for employees with frequent and infrequent attacks. Popul Health Manag 2013; 16:138-45.
34. Brook RA, Kleinman NL, Patel PA, Melkonian AK, Brizee TJ, Smeeding JE, et al. The economic burden of gout on an employed population. Curr Med Res Opin 2006;22:1381-9.
35. Ardal S. The health analyst's toolkit. Toronto: Ontario Ministry of Health and Long-Term Care; 2006.
36. Juurlink DN. Canadian Institute for Health Information discharge abstract database: a validation study. Toronto: Institute for Clinical Evaluative Sciences; 2006.

APPENDIX 1. Databases used to estimate the healthcare use and direct costs associated with an elderly incident gout population[16,35,36].

Database	Description	Use in Current Study
Canadian Institute for Health Information–Discharge Abstract Database	Demographic, administrative, and clinical data for hospital discharges (inpatient acute, chronic, and rehabilitation) and day procedures	Gout diagnosis for patient selection No. hospital stays and associated costs
Home Care Database (HCD) Resident	Demographic, administrative, and some clinical and service data for everyone receiving services from Community Care Access Centres in Ontario	No. home care services received and associated costs
National Ambulatory Care Reporting System	Administrative, clinical, financial, and demographic data for ambulatory care visits	Gout diagnosis for patient selection No. emergency department visits and associated costs
Ontario Drug Benefit (ODB) Program	Drugs for those over 65 years, on social assistance, and residents of longterm care	Gout medication for patient selection No. claims for select medications and associated costs
Ontario Health Insurance Program (OHIP)	Claims data for physician and other health professional insured services in Ontario, covering about 95% of the population	Gout diagnosis for patient selection No. primary and secondary care visits and associated costs
Ontario Registered Persons Database	Personal and demographic data for all current and previous registrants of OHIP	Patient profiling Patient eligibility and censoring