Title

Changes in Prescription Drug and Health Care Use Over 9 Years After the Large Drug Price Increase for Colchicine

Journal

JAMA Internal Medicine, 183(7)

ISSN

2168-6106

Authors

Ly, Dan P
Giuriato, Mia A
Song, Zirui

Publication Date

2023-07-01

DOI

10.1001/jamainternmed.2023.0898

Peer reviewed

Changes in Prescription Drug and Health Care Utilization Over 9 Years After the Large Drug Price Increase for Colchicine

Dan P. Ly, MD, PhD, MPP[1,2]

Mia A. Giuriato, BBA, MA[3]

Zirui Song, MD, PhD[3,4,5]

1. Division of General Internal Medicine and Health Services Research, David Geffen School of Medicine at UCLA
2. VA Greater Los Angeles Healthcare System
3. Department of Health Care Policy, Harvard Medical School
4. Department of Medicine, Massachusetts General Hospital
5. Center for Primary Care, Harvard Medical School

February 15, 2023

Words: 2999

Correspondence: Zirui Song, MD, PhD, Department of Health Care Policy, Harvard Medical School, 180A Longwood Avenue, Boston, MA 02115; Phone: 617-432-3430, Fax: 617-432-0173, e-mail: song@hcp.med.harvard.edu

Key Points

Question: What are long-term implications of large drug price increases?

Findings: After the Food and Drug Administration discontinued lower-priced colchicine in 2010, the average price per colchicine prescription increased from $11.25 to $190.49—a 16-fold rise; the out-of-pocket price increased 4.4-fold. The use of colchicine decreased by 17% in year 1 and approximately 27% over 9 years. Meanwhile, use of allopurinol increased by 32% and oral corticosteroids by 8%. Emergency department visits for gout rose by 40% and rheumatology visits for gout by 11%.

Meaning: The large and sharp increase in colchicine prices was associated with a sustained decrease in colchicine use, increased use of other medications for gout, and increased clinical encounters for gout consistent with poorer disease control.

Abstract

Importance: Prescription drug prices are a leading concern among patients and policymakers. There have been large and sharp price increases for several drugs, but the long-term implications of large drug price increases remain poorly understood.

Objective: Using a case study of the large 2010 price increase in colchicine, a common treatment for gout, we examined long-term changes in colchicine utilization, substitution to other drugs, and medical utilization associated with this price increase.

Design: Longitudinal cohort study from 2007 through 2019

Setting: Enrollees with employer-sponsored insurance in Marketscan

Participants: Individuals with a diagnosis of gout

Exposure: The Food and Drug Administration's discontinuation of lower-priced versions of colchicine from the market in 2010, which led to its sharp price increase.

Main Outcomes and Measures: Price of colchicine; utilization of colchicine, allopurinol, and oral corticosteroids; and emergency department (ED) visits and rheumatology visits for gout in year 1 and over the first decade of the policy.

Results: We examined 2,723,327 patient-year observations from 2007 to 2019 (mean age 57.0 years, 20.9% female). The average price per prescription of colchicine increased sharply from $11.25 in 2009 to $190.49 in 2011—a 16-fold increase—with the out-of-pocket price increasing 4.4-fold. At the same time, colchicine utilization declined from 35.0 to 27.3 pills per patient in year 1 and to 22.6 in 2019; in adjusted analyses, there was a 16.7% reduction in year 1 and 27.0% reduction over the decade ($p<0.001$). Meanwhile, allopurinol utilization rose by 32.0% and oral corticosteroid utilization increased by 8.3% over the decade ($p<0.001$). ED visits for gout increased by 21.5% in year 1 and by 39.8% over the decade ($p<0.001$); rheumatology visits for gout increased by 10.5% over the decade ($p<0.001$).

Conclusions and Relevance: Among individuals with gout, the large increase in colchicine prices in 2010 was associated with an immediate decrease in colchicine utilization that persisted over roughly a decade, alongside substitution toward allopurinol and oral corticosteroids, as well as increased ED and rheumatology visits for gout that suggested poorer disease control.

Abstract words: 332

Introduction

Prescription drug prices in the U.S. are a leading concern among patients and policymakers.[1-3] Large and often sharp increases in drug prices—stemming from manufacturer decisions or policies that lead to reduced competition—have been challenging for patients, employers, and insurers.[4-6] To date, the long-term implications of large price increases remain poorly understood. To address this evidence gap, we examined the case of colchicine, a common treatment for gout, which exhibited a large price increase in 2010.

Until 2010, colchicine was never formally approved for a particular clinical indication.[7] That year, the Food and Drug Administration (FDA) approved brand-name Colcrys under its Unapproved Drug Initiative after its manufacturer conducted a clinical trial. The FDA awarded Colcrys 3 years of market exclusivity and removed all non-authorized (non-Colcrys) versions of colchicine from the market in Fall 2010.[8] Early evidence suggested that the price of colchicine rose and its utilization declined in the first two years.[7-9]

However, longer-term evidence stemming from this FDA policy—prices (including patient out-of-pocket prices), utilization, and substitution to alternative medications—remains scant. Moreover, evidence on clinical implications, including emergency department (ED) and outpatient specialist encounters for gout that may represent markers for disease control, remains absent. Surveys have shown that patients cut back on medications when facing higher prices.[10-12] Moreover, in other contexts, higher drug prices have led to adverse clinical consequences and downstream health care use, including ED visits.[12,13]

In this study, we examined these longer-term outcomes using a large nationwide sample of individuals with employer-sponsored insurance from 2007 through 2019, thus spanning about

a decade after the FDA policy. We measured changes in use of colchicine as well as of other medications that can be prescribed with or in place of colchicine for patients with gout: allopurinol and oral corticosteroids. To assess implications for disease control, we examined changes in ED visits and rheumatology visits for gout.

Methods

Data and Study Population

We analyzed 2007-2019 Marketscan data, comprising a large, convenience sample of individuals with employer-sponsored coverage or employer-sponsored Medicare supplemental plans. The prescription drug claims contain detailed medication prices and utilization.[14] We included all enrollees with a diagnosis of gout—International Classification of Diseases 9th revision (ICD-9) codes beginning with 274 and ICD-10 codes beginning with M10 or M1A[15]—who had medical and prescription drug coverage across all years in which they were enrolled for 12 months.

Outcomes

We focused on three main outcomes. First, we examined the price of colchicine, defined as the paid amount per script and per pill. Transacted prices resulted from negotiations between insurers, their pharmacy benefit managers, and pharmaceutical manufacturers, similar to those used in other studies.[16,17] We also identified patient out-of-pocket price—the sum of deductible, copayment, and coinsurance. All dollar values were adjusted to 2019 dollars.

Second, we analyzed prescription drug utilization, defined as number of pills supplied per patient per year. We used medication reference data ("Redbook") within Marketscan data to identify National Drug Codes (NDCs) corresponding to medications of interest. In addition to colchicine, we focused on two types of medications that were potential substitutes for colchicine: allopurinol and oral corticosteroids (eTable 1). That is, we examined how patients and clinicians adjusted to a large price increase for an important medication, including changing their use of medications that may be imperfect substitutes.

One key hypothesis was that, when the price of a therapeutic treatment rises substantially, patients and clinicians may increase their focus on prevention, which may be a beneficial outcome. Allopurinol is considered the first-line medication for prevention of recurrent gout flares, tophi, and disease progression.[18-20] When the patient experiences a gout flare, colchicine or oral corticosteroids may be used to treat the flare. Therefore, another key hypothesis was that, when the price of a therapeutic option rises substantially, patients and clinicians may turn to alternative therapeutic medications, such as corticosteroids. Non-steroidal anti-inflammatory drugs (NSAIDs), which are available over-the-counter, can also be used for gout flares. Although our data lacked over-the-counter medications, we examined prescription NSAIDs in a secondary analysis.

Third, we examined health care services plausibly related to changes in the clinical control of gout. Given that gout attacks rarely lead to hospitalization, we focused on ED visits and rheumatology visits with a coded diagnosis of gout. ED visits, defined by Current Procedural Terminology (CPT) codes 99281-99285, generally address acute presentations of disease, during which stable, chronic diseases are usually not coded. Thus, the presence of gout diagnoses on ED claims served as a signal of poorer disease control. Similarly, we examined outpatient

rheumatology visits (defined using evaluation and management CPT codes 99201-99205 and 99211-99215) that addressed gout. While we did not expect rheumatology visits to increase in the short-term given that ED visits may better account for gout flares, we hypothesized that rheumatology visits for gout could increase over the longer-term.

Statistical Analyses

In unadjusted analyses, we first calculated the average price and out-of-pocket price for colchicine in each year, both per colchicine prescription and per colchicine pill. Next, for colchicine and its potential substitute drugs, we measured utilization as the average number of pills prescribed per patient per year. This was our preferred measure of utilization (the intensive margin), as the number of prescriptions (extensive margin) fails to account for the variation in pills prescribed per prescription. Analogously, we measured the number of ED visits and rheumatology visits for gout per patient per year.

In adjusted analyses, we calculated the difference in means in prescription drug and medical utilization between the pre-FDA removal period (2007-2010) and the post-FDA removal period (2011-2019) using an ordinary least squares model. Given that the composition of enrollment in this population with employer-sponsored insurance may change over time, we calculated these differences in outcomes adjusted for patient age, sex, Diagnostic Cost Group (DxCG) risk score, insurance type, and region. The DxCG risk score is a measure of overall health status commonly used for risk adjustment.

Given the sharp onset of the FDA policy in 2010, we complemented our main estimates with an interrupted time series (ITS) approach. This strategy modeled the changes in utilization

and medical encounters at 2010 as a trend break and separately estimated changes in the slopes of these outcomes post-policy relative to before (the coefficient of interest), adjusted for covariates. Finally, we did a falsification test of the 2010 trend break in colchicine utilization by examining 3 other immune-modulating medications—methotrexate, azathioprine, and hydroxychloroquine—by assessing their outcomes while assuming the same 2010 policy.

We adopted a conservative strategy that interpreted the FDA policy as a plan type level intervention. As a result, we clustered robust standard errors at the level of the plan type (HMO, PPO, high-deductible health plan, etc.; eTable 2). P-values were calculated using 2-sided tests. Statistical significance was defined at the $p<0.05$ level. Analyses were performed using Stata, version 16.1 (StataCorp). This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline. This study was approved by the Harvard Medical School IRB.

Results

Patient Characteristics

The sample included 2,723,327 patient-year observations with gout from 2007 through 2019. The average age was 57.0 years, and 20.9% were female. About 75% were under-65 with commercial plans, while 25% were retirees with Medicare supplemental coverage (eTable 2).

Colchicine Prices

Before the 2010 policy, average price of colchicine per prescription was approximately $11—$10.97 (95% CI, 10.95 to 10.98) in 2007 and $11.25 (11.23 to 11.28) in 2009. During the same period, out-of-pocket price was similarly stable--$7.97 (7.97 to 7.98) per prescription in 2007 and $7.37 (7.37 to 7.38) in 2009.

In 2011, immediately after removal of lower-priced versions of colchicine, average price per prescription increased to $190.49 (190.07 to 190.91)—a 15.9-fold increase—and average out-of-pocket price per prescription increased to $39.49 (39.42 to 39.56), a 4.4-fold increase. This increase was sustained through 2019 (Figure 1A). This sharp increase in overall price and out-of-pocket price after 2010 and continuously elevated prices in the decade that followed were analogous at the pill level (eFigure 1).

Prescription Drug Utilization

Colchicine use exhibited a sharp reduction shortly after the 2010 policy. In unadjusted analysis, number of colchicine pills per patient averaged 35.0 (34.6 to 35.5) in 2009 and decreased to 27.3 (26.9 to 27.6) in 2011; it further declined to 22.6 (22.2 to 23.0) in 2019 (Figure 1B). Adjusted for covariates, colchicine utilization declined by 5.9 (-6.3 to -5.5) pills per patient in year 1—a 16.7% reduction from baseline ($p<0.001$)—and by 9.6 (-9.8 to -9.3) pills per patient through 2019, a 27.0% reduction ($p<0.001$) (Table 1).

Allopurinol use increased from 106.8 (106.0 to 107.5) pills per patient in 2009 to 114.4 (113.7 to 115.1) in 2011, further rising to 153.4 (152.2 to 154.6) by 2019 (Figure 2A). Adjusted for covariates, this increase was 7.8 (6.9 to 8.7) pills per patient or 7.6% in year 1 ($p<0.001$) and

33.1 (32.6 to 33.7) pills per patient over the decade—a 32.0% increase from baseline (p<0.001) (Table 1).

Use of oral corticosteroids demonstrated a less clear change relative to baseline, with unadjusted rates of 18.0 (17.7 to 18.4) pills per patient in 2009, 19.4 (19.1 to 19.7) in 2011, and 21.9 (21.5 to 22.3) in 2019 (Figure 2B). Adjusted for covariates, we observed no significant changes in year 1 of the policy, but an average increase of 1.5 (1.3 to 1.7) pills per patient over the subsequent decade—an 8.3% increase (p<0.001) (Table 1).

Changes in slope of utilization post-policy were modest (eTable 3). Colchicine use, after dropping sharply following the FDA policy, slowed its slope of decline by 0.5 (0.2 to 0.7) tablets per patient per year or 1.4% annually over the decade (p<0.001). The slopes of allopurinol utilization and oral corticosteroid utilization similarly increased by 2.6% and 3.8%, respectively, after the policy relative to before (p<0.001). In our secondary analysis, the secular decline in prescription NSAIDs slowed after 2010 (eFigure 2 and eTable 3).

In our falsification test, methotrexate, azathioprine, and hydroxychloroquine exhibited no significant change in utilization in year 1 (0.1, 95% CI -0.2 to 0.3, p=0.47) and no change in the slope of utilization thereafter relative to pre-policy trends (0.0, 95% CI -0.1 to 0.2, p=0.45).

Medical Utilization

ED visits for gout increased from 0.11 (0.11 to 0.11) per patient in 2009 to 0.13 (0.13 to 0.14) in 2011, and further increased to 0.20 (0.19 to 0.21) in 2015. After newer colchicine competitors were introduced in 2015, ED visits for gout declined to 0.17 (0.17 to 0.18) per patient by 2019 (Figure 3A). Adjusted for covariates, ED visits for gout rose by 0.02 (0.02 to

0.03) per patient in year 1, a 21.5% increase ($p<0.001$). By 2019, ED visits for gout had risen on average by 0.05 (0.04 to 0.05) per patient, or a 39.8% increase relative to the pre-FDA policy mean ($p<0.001$) (Table 1).

Rheumatology visits for gout, adjusted for covariates, decreased by 0.02 (-0.03 to -0.01) per patient in year 1 . However, over the ensuing decade, rheumatology visits increased by 0.02 (0.02 to 0.03) visits per patient, adjusted for covariates, which amounted to a 10.5% increase relative to baseline (Figure 3B and Table 1). Neither ED nor rheumatology visit utilization demonstrated a measurable change in slope after the FDA policy (eTable 3).

Discussion

In a large nationwide dataset comprising commercial and Medicare patients with gout, this study found that FDA removal of lower-priced competitors to Colcrys in 2010 led to a sharp and substantial increase in price and patient cost-sharing for colchicine. This was associated with an immediate decrease in use of colchicine. Meanwhile, use of allopurinol and oral corticosteroids increased in patients with gout. This suggests a substitution effect and potentially greater efforts to prevent gout flares, which had become more expensive to treat. The policy was also followed by an increase in ED and rheumatology visits for gout over the ensuing decade.

To treat gout flares, patients substituted to oral corticosteroids, though the substitution was modest—averaging an 8.3% increase over the decade as compared with the 27.0% decline in colchicine use. The use of allopurinol, not a direct substitute for colchicine but used alongside colchicine for prevention of gout flares, increased substantially by 32.0%. This suggests that as gout flares became more expensive to treat, patients and clinicians may have been more

aggressive in preventing such flares by increasing allopurinol use. That is, when the price of a treatment rises, prevention may receive more attention, which is beneficial. However, on net, these prevention efforts were likely exceeded by worsened disease control, given the increased clinical visits for gout. While disease severity was difficult to assess, colchicine is typically effective for treating acute flares and for gout flare prophylaxis in the early stages of using allopurinol. Thus, its mechanism is consistent with our empirical findings.

Given the lack of a control group, our estimates are susceptible to secular trends, such as a decline in primary care visits that may explain a slowdown in prescription volume. However, prescriptions per capita have increased over this time period,[21] and prescriptions are commonly issued without a visit (electronic refills, etc.). Meanwhile, specialist visits have remained stable in the commercial population[22,23] and ED visits have also been stable over this period.[24]

Taken together, our results imply that a large price increase—especially a large out-of-pocket price increase—in medications that have few or no substitutes could have adverse economic and clinical consequences. These results demonstrate a similar pattern as findings in the literature for insulin, for which surveys suggest substantial price-related medication nonadherence.[25] In addition, although we found a fairly large decrease in colchicine utilization among patients with gout, this decrease may not have been as large as one might expect given the magnitude of the out-of-pocket price increase. This suggests that patients and insurers may largely absorb price increases in medications that lack substitutes, and for those who do lower their utilization, adverse clinical outcomes may follow.

Our findings are directionally consistent with a prior study of the 2010 FDA colchicine policy, which focused on the likelihood of initiating colchicine using data from 2009 to 2012.[9] Our use of data starting in 2007 allows a fuller sense of trends prior to the 2010 policy. Our

study, which extends to 2019, provides more time to examine changes in utilization of colchicine, substitution away from colchicine, and possible clinical implications of such utilization patterns, all of which may not be immediately apparent within 2 years of a large price increase. In addition, other research has found lower prescription drug use in response to increased patient cost-sharing.[10-13] However, this literature has generally not examined substitution patterns and possible clinical outcomes in response to large and sharp price increases in medications, which have different policy implications than changes in cost-sharing.

Although the case of colchicine may be unique given the FDA removal of generic competitors from the market, the economic basis for the subsequent price increase ultimately rests in the reduction in competition—a familiar mechanism that underlies other increases in prescription drug prices stemming from a drug's market power. Therefore, despite the rather unique policy intervention that gave rise to colchicine's price increase, our findings may nevertheless be applicable to large future increases in drug prices. Such price increases could include, for example, manufacturers' responses to the Inflation Reduction Act, which gives Medicare the ability to negotiate prices of select drugs. Because a proposal to cap drug price growth in the commercial population was not included in the legislation, reductions in Medicare drug prices might lead to compensatory increases in commercial drug prices, for which this study may offer a useful data point.

This study has several limitations. First, without a control group, our estimates were susceptible to unmeasured confounding. We relied on the sharp trend break in colchicine prices and the immediate change in colchicine utilization from pre-policy levels as the identification strategy. We also relied on pre-policy trends as the counterfactual in ITS analyses (although the trends in colchicine utilization and in ED and rheumatology visits before 2010 remain a

concern). Our falsification test supported the findings. However, in the absence of exogenous variation in colchicine prices and ideal counterfactual medications to colchicine, results were not causal. Moreover, changes in outcomes farther out from the date of the price change are plausibly more susceptible to secular effects (such as economic changes and health care system changes) and other sources of confounding.

Second, patient mix could evolve over time, as enrollees could enter and leave the sample in each year, though we required 12-month enrollment within year each. However, a sensitivity analysis of individuals with gout continuously enrolled for 5 years yielded qualitatively similar results (eFigure 3).

Third, clinical details such as gout severity and functional impairment were unobservable in claims. Similarly, the presence of a gout diagnosis on an encounter may not mean that acute gout was contributory. For example, it is possible that ED visits with gout recorded were instead focused on a different medical issue with gout recorded as a comorbidity. Fourth, over-the-counter medications (e.g., NSAIDs) were unobservable in claims, and we could not rigorously evaluate opioid use relative to the policy given the changing opioid landscape during this period. However, to the extent that over-the-counter NSAIDs or opioids were used as substitutes for colchicine, our findings of increased allopurinol and corticosteroid use would be a conservate reflection of overall substitution.

Finally, our findings may not generalize to populations outside of enrollees with employer-sponsored insurance or Medicare supplemental coverage, such as individuals with traditional Medicare or Medicaid. They also may not generalize to large price increases for medications other than colchicine, which may pertain to different clinical situations and have

different (or possibly no) substitutes that lead to different patterns of utilization and clinical implications.

Conclusions

After a 4.4-fold increase in out-of-pocket colchicine prices nationwide, patients with gout used less colchicine, used more substitute medications, and likely experienced poorer disease control over 9 years. Increasing drug prices where competition is lacking can have important implications for patients and payers in the long term.

Article Information

Funding/Support: This work was supported by the National Institutes of Health (NIH Director's Early Independence Award No. DP5-OD024564 and P01-AG032952) and the Laura and John Arnold Foundation (Grant ID: 20-04402), to Dr Song.

Role of the Funder/Sponsor: The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Disclaimer: The views expressed in this manuscript are those of the author and do not necessarily represent the views of the US Department of Veterans Affairs or the US government.

Conflicts of Interest Disclosures: Dr Ly and Ms Giuriato have no potential conflicts of interest to disclose. Dr Song reported personal fees from the Research Triangle Institute for work on Medicare risk adjustment; from Google Ventures, VBID Health LLC, and the International Foundation of Employee Benefit Plans for academic lectures outside of this work; and for providing consultation in legal cases.

Author Contributions: Ms Giuriato and Dr Song had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Data Sharing Statement: Marketscan claims data involving protected health information are not available per the data use agreement.

References

1. Deb C, Curfman G. Relentless Prescription Drug Price Increases. *JAMA*. Mar 3 2020;323(9):826-828. doi:10.1001/jama.2020.0359
2. Robinson JC. Why Is Aducanumab Priced at $56,000 per Patient? Lessons for Drug-Pricing Reform. *N Engl J Med*. Nov 25 2021;385(22):2017-2019. doi:10.1056/NEJMp2113679
3. Jazowski SA, Dusetzina SB. Recommendations for Lowering Prescription Drug Spending in Public Programs. *Ann Intern Med*. Dec 3 2019;171(11):855-856. doi:10.7326/M19-2895
4. Alpern JD, Song J, Stauffer WM. Essential Medicines in the United States--Why Access Is Diminishing. *N Engl J Med*. May 19 2016;374(20):1904-7. doi:10.1056/NEJMp1601559
5. Fralick M, Kesselheim AS. The U.S. Insulin Crisis - Rationing a Lifesaving Medication Discovered in the 1920s. *N Engl J Med*. Nov 7 2019;381(19):1793-1795. doi:10.1056/NEJMp1909402
6. Lyon J. Significant Increases in EpiPen Price. *JAMA*. Oct 11 2016;316(14):1439. doi:10.1001/jama.2016.14178
7. Kesselheim AS, Solomon DH. Incentives for drug development--the curious case of colchicine. *N Engl J Med*. Jun 3 2010;362(22):2045-7. doi:10.1056/NEJMp1003126
8. McCormick N, Wallace ZS, Yokose C, et al. Prolonged Increases in Public-Payer Spending and Prices After Unapproved Drug Initiative Approval of Colchicine. *JAMA Intern Med*. Feb 1 2021;181(2):284-287. doi:10.1001/jamainternmed.2020.5017
9. Kesselheim AS, Franklin JM, Kim SC, Seeger JD, Solomon DH. Reductions in Use of Colchicine after FDA Enforcement of Market Exclusivity in a Commercially Insured Population. *J Gen Intern Med*. Nov 2015;30(11):1633-8. doi:10.1007/s11606-015-3285-7
10. Piette JD, Heisler M, Wagner TH. Cost-related medication underuse among chronically ill adults: the treatments people forgo, how often, and who is at risk. *Am J Public Health*. Oct 2004;94(10):1782-7. doi:10.2105/ajph.94.10.1782
11. Soumerai SB, Pierre-Jacques M, Zhang F, et al. Cost-related medication nonadherence among elderly and disabled medicare beneficiaries: a national survey 1 year before the medicare drug benefit. *Arch Intern Med*. Sep 25 2006;166(17):1829-35. doi:10.1001/archinte.166.17.1829
12. Tamblyn R, Laprise R, Hanley JA, et al. Adverse events associated with prescription drug cost-sharing among poor and elderly persons. *JAMA*. Jan 24-31 2001;285(4):421-9. doi:10.1001/jama.285.4.421
13. Chandra A, Flack E, Obermeyer Z. The health costs of cost-sharing. NBER working paper no. 28439. Accessed February 10, 2023, https://www.nber.org/papers/w28439
14. IBM. IBM MarketScan Research Databases. https://www.ibm.com/products/marketscan-research-databases/databases
15. Li JW, Suh M, Brigham MD, et al. A Retrospective Cohort Study of the Effect of Gout on Mortality Among Patients with a History of Kidney Transplantation. *Ann Transplant*. Apr 14 2020;25:e920553. doi:10.12659/AOT.920553
16. Fu M, Naci H, Booth CM, et al. Real-world Use of and Spending on New Oral Targeted Cancer Drugs in the US, 2011-2018. *JAMA Intern Med*. Dec 1 2021;181(12):1596-1604. doi:10.1001/jamainternmed.2021.5983
17. Lee J, Joo H, Maskery BA, et al. Increases in Anti-infective Drug Prices, Subsequent Prescribing, and Outpatient Costs. *JAMA Netw Open*. Jun 1 2021;4(6):e2113963. doi:10.1001/jamanetworkopen.2021.13963
18. Gaffo AL. Treatment of gout flares. UpToDate. 2021. https://www.uptodate.com/contents/treatment-of-gout-flares

19. Neogi T. Clinical practice. Gout. *N Engl J Med*. Feb 3 2011;364(5):443-52. doi:10.1056/NEJMcp1001124
20. Perez-Ruiz F. Pharmacologic urate-lowering therapy and treatment of tophi in patients with gout. UpToDate. 2021. https://www.uptodate.com/contents/pharmacologic-urate-lowering-therapy-and-treatment-of-tophi-in-patients-with-gout
21. Congressional Budget Office. Prescription Drugs: Spending, Use, and Prices. Accessed February 10, 2023, https://www.cbo.gov/publication/57772
22. Ganguli I, Shi Z, Orav EJ, Rao A, Ray KN, Mehrotra A. Declining Use of Primary Care Among Commercially Insured Adults in the United States, 2008-2016. *Ann Intern Med*. Feb 18 2020;172(4):240-247. doi:10.7326/M19-1834
23. Frost A, Hargraves J. HCCI Brief: Trends in Primary Care Visits. Accessed February 10, 2023, https://healthcostinstitute.org/hcci-research/trends-in-primary-care-visits
24. Cairns C, Ashman J, Kang K. Emergency Department Visit Rates by Selected Characteristics: United States, 2018. Accessed February 10, 2023, https://www.cdc.gov/nchs/products/databriefs/db401.htm
25. Herkert D, Vijayakumar P, Luo J, et al. Cost-Related Insulin Underuse Among Patients With Diabetes. *JAMA Intern Med*. Jan 1 2019;179(1):112-114. doi:10.1001/jamainternmed.2018.5008

Table 1. Changes in Prescription Drug and Health Care Utilization

	Unadjusted Averages		Adjusted Difference in Year 1 (2011)			Average Adjusted Difference (2011-2019)		
	Pre-Policy (2007-2010)	Post-Policy (2011-2019)	Difference (95% CI)	Percent change (%)	P value	Difference (95% CI)	Percent change (%)	P value
Prescription Drugs								
Colchicine	35.4	26.0	-5.9 (-6.3 to -5.5)	-16.7	<0.001	-9.6 (-9.8 to -9.3)	-27.0	<0.001
Allopurinol	103.4	138.1	7.8 (6.9 to 8.7)	7.6	<0.001	33.1 (32.6 to 33.7)	32.0	<0.001
Oral corticosteroids	18.4	20.3	-0.3 (-0.7 to 0.0)	-1.8	0.07	1.5 (1.3 to 1.7)	8.3	<0.001
Visits for Gout								
ED visits	0.11	0.15	0.02 (0.02 to 0.03)	21.5	<0.001	0.05 (0.04 to 0.05)	39.8	<0.001
Rheumatology visits	0.21	0.24	-0.02 (-0.03 to -0.01)	-10.2	<0.001	0.02 (0.02 to 0.03)	10.5	<0.001

Note: Prescription drug and medical utilization were defined as number of pills supplied or visits per patient per year. Differences in year 1 and over the 2011-2019 period were calculated relative to the pre-policy mean levels of the outcomes. The differences were adjusted for covariates (patient age, sex, DxCG risk score, insurance type, and region), with robust standard errors clustered at the level of the plan type. The corresponding percentage changes were calculated by dividing the adjusted change by the pre-policy mean levels of the outcomes.

Figure 1: Price and Utilization of Colchicine, 2007-2019

A. Price per Colchicine Prescription

B. Utilization of Colchicine

Figure 2: Utilization of Allopurinol and Oral Corticosteroids, 2007-2019

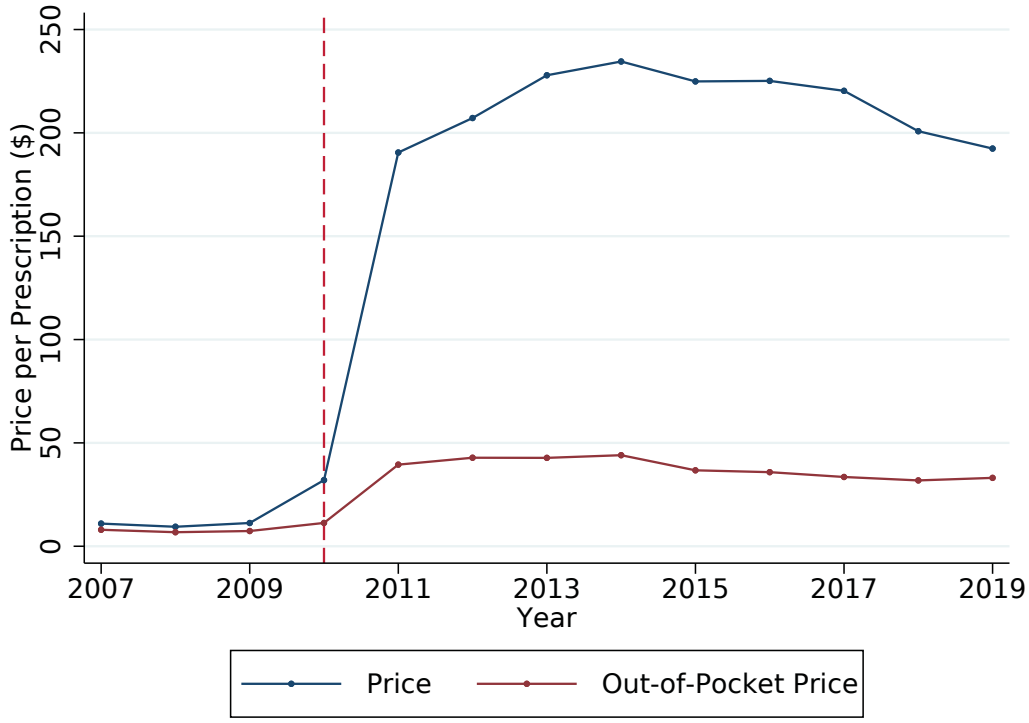
A. Allopurinol

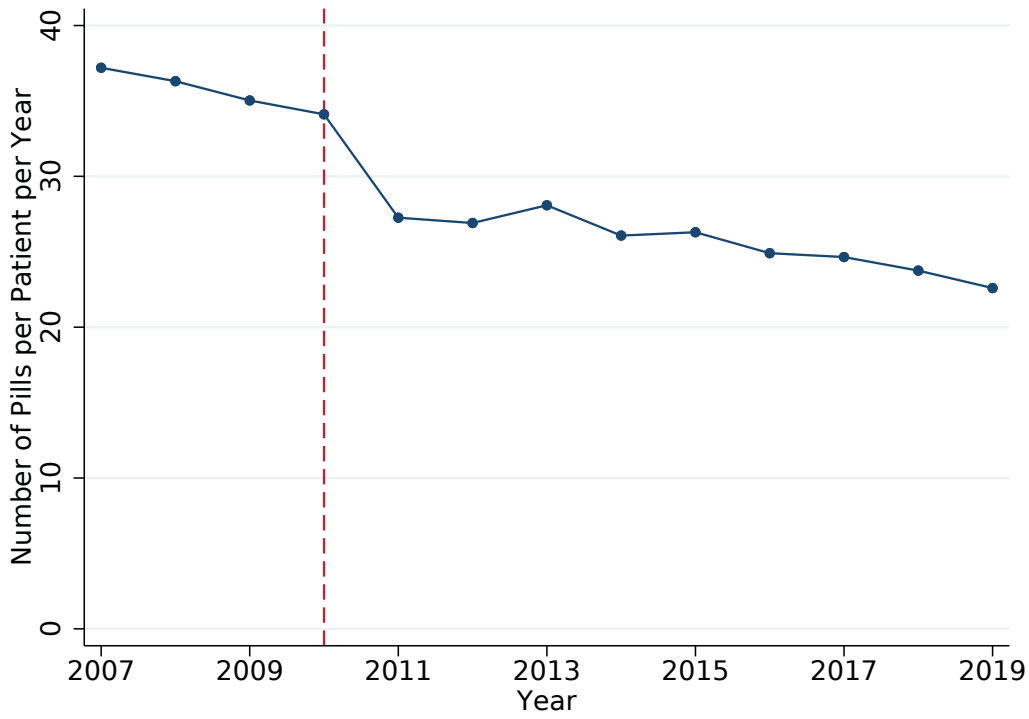
B. Oral corticosteroids

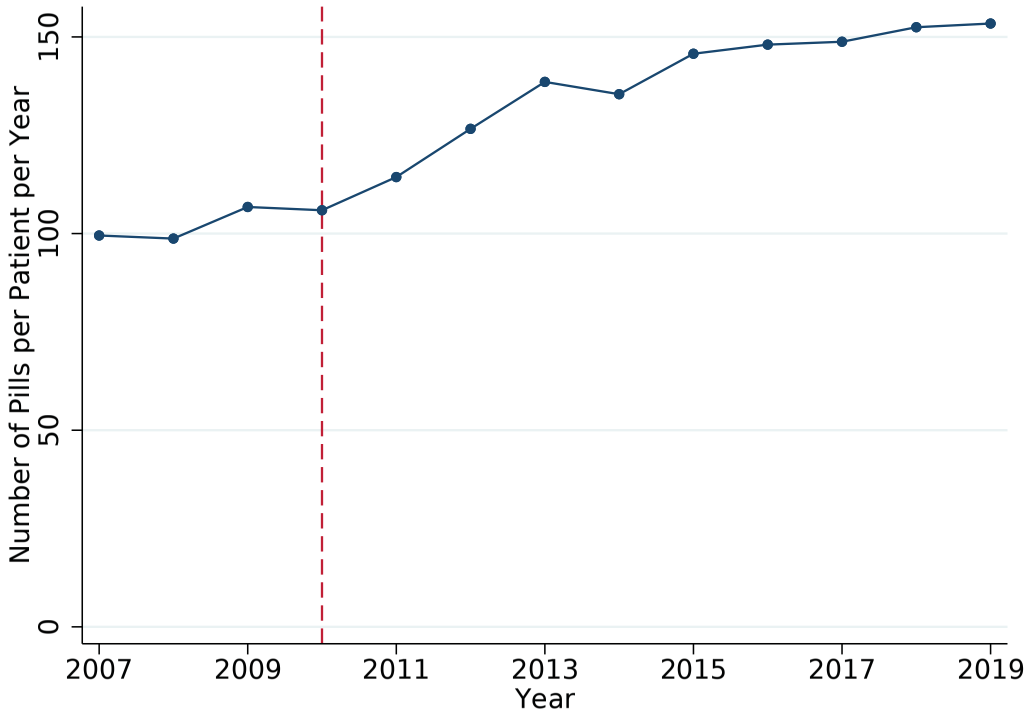
Figure 3: Emergency Department and Rheumatology Visits for Gout, 2007-2019

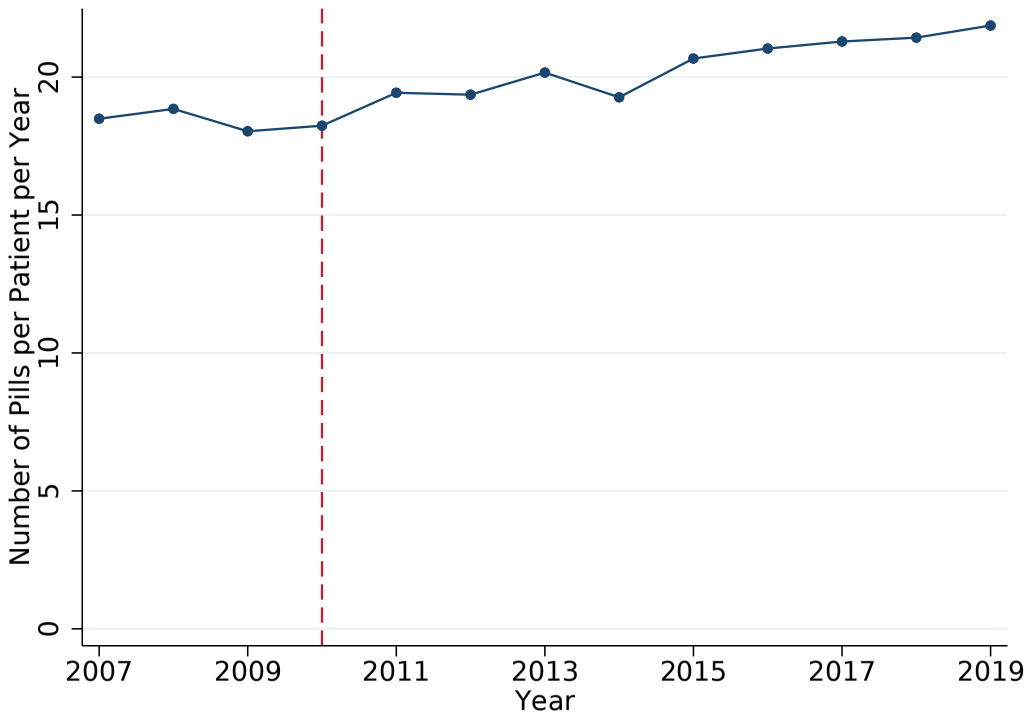
A. Emergency Department Visits

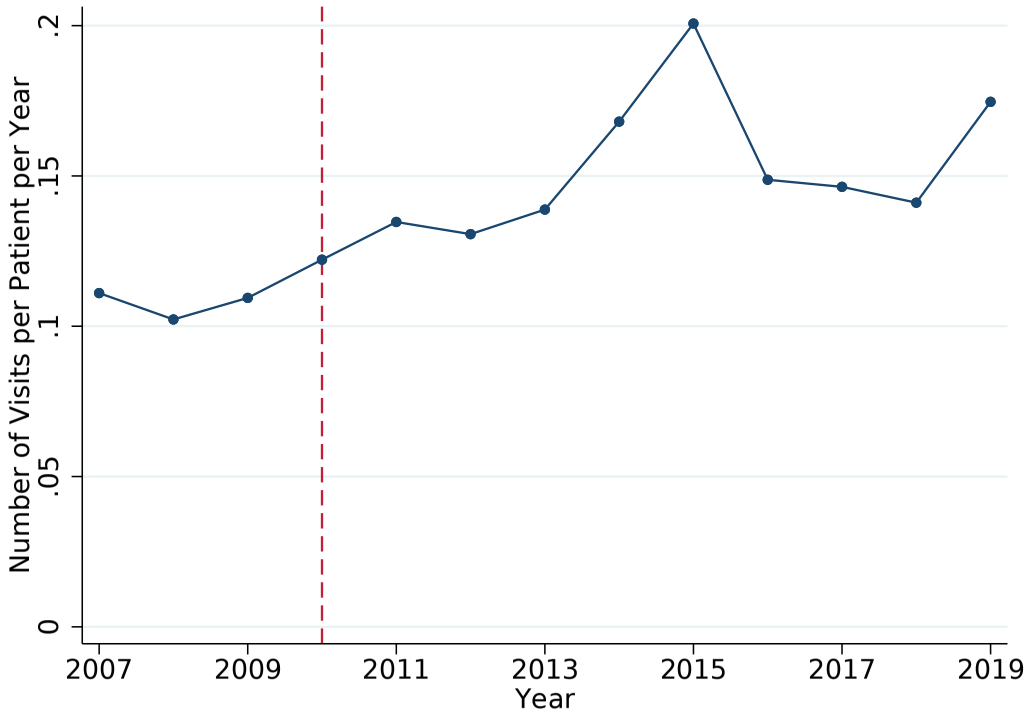
B. Rheumatology Visits

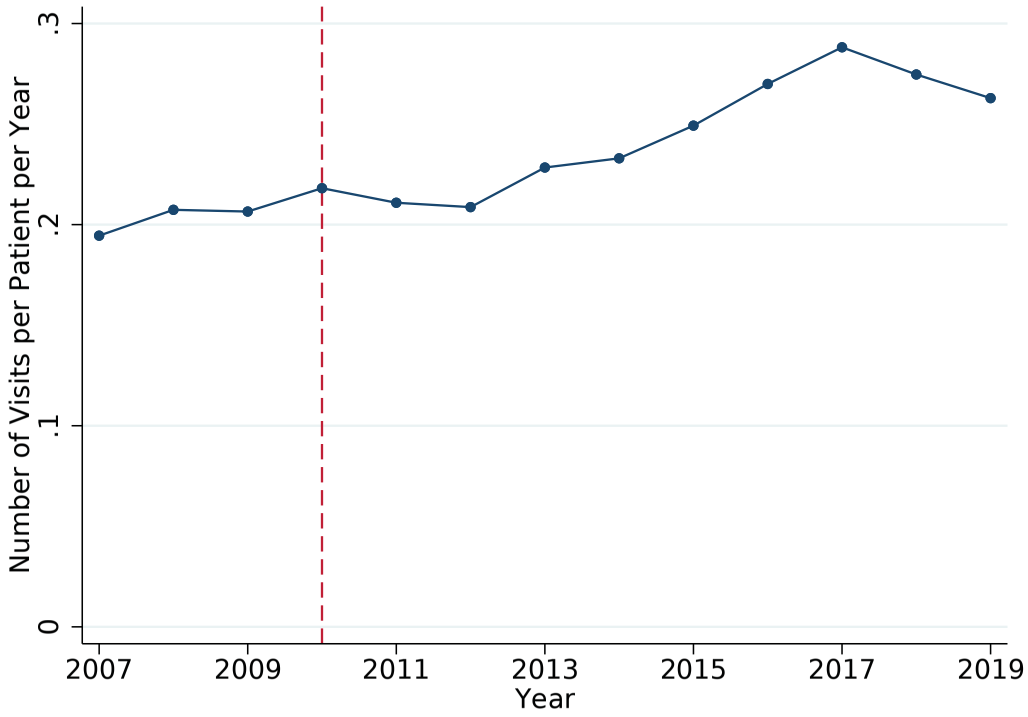

Price per Prescription ($)
0
50
100
150
200
250
2007
2009
2011
2013
2015
2017
2019
Year
Price
Out-of-Pocket Price


Number of Pills per Patient per Year
0
10
20
30
40
2007
2009
2011
2013
2015
2017
2019
Year


Number of Pills per Patient per Year
0
50
100
150
2007
2009
2011
2013
2015
2017
2019
Year


Number of Pills per Patient per Year
0
5
10
15
20
2007
2009
2011
2013
2015
2017
2019
Year


Number of Visits per Patient per Year
0
.05
.1
.15
.2
2007
2009
2011
2013
2015
2017
2019
Year


Number of Visits per Patient per Year
0
.1
.2
.3
2007
2009
2011
2013
2015
2017
2019
Year