Maust Donovan (Orcid ID: 0000-0003-4740-2640)

Word count
Abstract: 296
Main Text: 3,071
Tables/figures: 5

Benzodiazepine Use among Medicare, Commercially-Insured, and Veteran Older Adults from 2013–2017

Running title: Trends in Benzodiazepine Use

Donovan T. Maust, MD, MS,[a,b,c] H. Myra Kim, ScD,[b,c,d] Ilse R. Wiechers, MD, MPP, MPH,[e,f,g] Rosalinda V. Ignacio, MS,[a,b] Amy S.B. Bohnert, PhD, MHS,[b,c,h] Frederic C. Blow, PhD,[a,b,c]

[a] Department of Psychiatry, University of Michigan, Ann Arbor, MI

[b] Center for Clinical Management Research, VA Ann Arbor Healthcare System, Ann Arbor, MI

[c] Institute for Healthcare Policy and Innovation, University of Michigan, Ann Arbor, MI

[d] Center for Statistical Consultation and Research, University of Michigan, Ann Arbor, MI

[e] Northeast Program Evaluation Center, Office of Mental Health and Suicide Prevention, Department of Veterans Affairs, West Haven, CT

[f] Department of Psychiatry, University of California San Francisco, San Francisco, CA

[g] Department of Psychiatry, Yale University School of Medicine, New Haven, CT

[h] Department of Anesthesiology, University of Michigan, Ann Arbor, MI

Corresponding Author:
Donovan T. Maust, MD, MS
Department of Psychiatry
2800 Plymouth Rd
NCRC 016-226W
maustd@umich.edu
(o) 734.845.3649
@dtmaust

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/jgs.16825

No related papers have been published or submitted from this study.

ABSTRACT

Background/Objectives: Benzodiazepines (BZDs) are widely prescribed to older adults. While prescribing has declined in the U.S. Department of Veterans Affairs (VA), Medicare introduced BZD coverage in 2013. It is unknown whether declines in the VA have been widespread among older adults in the U.S.

Design: Observational study in traditional fee-for-service Medicare, commercial insurance, and the VA.

Setting: United States, 2013–2017.

Participants: Adults ≥55 years in traditional Medicare (234,290,693 person-months), commercial insurance (337,827,125 person-months), and the VA (256,590,369 person-months).

Measurements: 1) Change in BZD and BZD-opioid co-prescribing modeled by Poisson regression over time; 2) standardized ratios of BZD and BZD-opioid co-prescribing, using Medicare as the reference.

Results: From April 2013 to December 2017, the monthly percent of adults ≥55 who received BZDs fell from 10.4% to 9.3% in Medicare, 6.6% to 6.5% in commercial insurance, and 5.7% to 3.0% in the VA. Monthly BZD-opioid co-prescribing over the same time fell from 4.0% to 3.0% in Medicare, 2.3% to 2.0% commercial, and 2.2% to 0.6% for the VA. Age- and sex-adjusted rates of decline for BZD and BZD-opioid co-prescribing were statistically significant for all systems. Annual BZD rate reductions were 0.98 (Medicare), 0.99 (commercial), and 0.87 (VA; $p<0.001$ for all); co-prescribing rate reductions were 0.95, 0.99, and 0.75 ($p<0.001$ for all). Using standardized ratios accounting for demographic and clinical characteristics, both prescribing and co-prescribing were lowest for the VA relative to Medicare (standardized BZD ratio 0.40,

95% confidence interval [CI] 0.39-0.40; standardized BZD-opioid co-prescribing ratio 0.35, 95% CI 0.35-0.35). Prescribing in commercial insurance was also lower (BZD 0.65, 95% CI 0.65-0.65; BZD-opioid co-prescribing 0.65, 95% CI 0.65-0.65).

Conclusion: BZD prescribing has declined much more to older adults receiving care through the VA than Medicare or commercial insurance. Other systems may learn from strategies implemented in the VA.

key words: benzodiazepine, veteran, medicare

INTRODUCTION

The link between benzodiazepine (BZD) use and fall-related injury in older adults has been known for over thirty years,[1,2] leading to their recognition as medications to avoid in older adults.[3,4] While additional evidence of potential harms has emerged, such as motor vehicle accidents[5] and impaired cognition,[6] perhaps the most concerning is increased overdose risk.[7] After opioids, BZDs are the second-most common prescription medication involved in pharmaceutical overdose mortality,[8] and they increase risk of opioid-related overdose in a dose-response fashion.[9]

Despite the potential harms associated with BZD prescribing and the availability of alternative treatment options, prevalence of use among older adults in the U.S. did not change over nearly twenty years through 2013.[10] The lack of reduction may reflect patient or physician reluctance to discontinue therapy,[11,12] lack of the resources and tools that contribute to successful reduction,[13-16] or both. This makes recent declines in BZD prescribing within the U.S. Department of Veterans Affairs system (VA)—where prevalent use among adults ≥65 fell from 9.2% to 7.3% between 2010 and 2016—notable.[17] Medicare's prescription drug coverage benefit (i.e., Part D) did not cover BZD prescriptions until 2013,[18] and prescribing since then has not been examined. It is not known whether the declines in the VA reflect broader changes nationally, or whether the declines among Veterans are unique.

This analysis had two primary goals. First, to compare the rate of change in BZD prescribing and in BZD-opioid co-prescribing to adults ≥55 over the period from 2013 to 2017 in the three parallel U.S. health care populations: traditional fee-for-service Medicare, commercial insurance (i.e., Optum, which includes both employer-sponsored insurance and Medicare

Advantage), and the VA. We used a lower age cut-off of 55 rather than 65 years given evidence of growing BZD use among middle-aged adults,[10] with use that now equals or exceeds that of adults ≥65 in the general population.[19] Second, to account for the potential that different prescribing patterns might reflect differences in patient populations (e.g., a much lower proportion of female patients in the VA), we used the final year of data (i.e., 2017) to perform cross-population comparisons of BZD prescribing and BZD-opioid co-prescribing. If BZD prescribing in the VA is lower or declines over time are limited to the VA, which is the nation's largest integrated health care system, such findings may suggest strategies that could be implemented in other settings or systems interested in reducing BZD prescribing.

METHODS

Study population. For this cohort study, we included data from three health care populations from 2013 to 2017:

- Traditional fee-for-service Medicare ("Medicare" hereafter), a national health insurance program that provides coverage to disability-eligible beneficiaries and those ≥65 years of age. Data were derived from the 20% sample, including the MedPAR, Outpatient, Carrier, Hospice, and Part D files.
- Optum Clinformatics® Data Mart Database ("commercial" hereafter), derived from a large national health insurance company in the U.S. that covers 20% of employer-sponsored insurance and also covers approximately one quarter of Medicare beneficiaries enrolled in Medicare Advantage plans (i.e., managed Medicare). All beneficiaries in this commercial population had prescription drug coverage.

- The VA, comprised of individuals who received care through the Veterans Health Administration, which serves nearly 9 million Veterans across over 150 hospitals and over 800 community-based outpatient clinics across the U.S.

In order to compare prescribing trends over time, we created a monthly rolling cohort for each of the three health care populations that included: all individuals who were ≥55 years on the first of the year; alive as of the first of each month; and resided in the 50 states or Washington, DC. For all populations, age eligibility was determined at the beginning of each year because the commercial data used in this analysis only included birth year. Because many Veterans do not obtain health care through the VA,[20] the monthly VA cohort was limited to "active" VA health care users by requiring that, in the prior 12 months, an individual had either ≥1 inpatient or outpatient health care encounter or ≥1 prescription drug claim. The monthly Medicare cohort was limited to those who had Part D prescription drug coverage but were not in Part C (i.e., managed care); all adults in the commercial and VA populations had prescription drug coverage.

Individuals who either died or had hospice use in a given month were included in that month, but then excluded from the cohort all months thereafter. In Medicare, hospice enrollment was determined using the Hospice claims file. Receipt of hospice services in Optum and VA was determined by a claim with either a hospice procedure code or a hospice revenue code.[21]

Outcomes. For each monthly cohort from January 2013 to December 2017, we determined BZD prescribing and BZD-opioid co-prescribing. BZDs were identified using American Hospital Formulary System classes 28:12.08 and 28:24.08; opioids were classes 28:08.08 and 28:08.12.

In the Medicare and commercial populations, prescription fills were identified from claims submitted by the dispensing pharmacy to the insurer (e.g., Medicare) for payment. In the VA, prescription fills were identified using the Corporate Data Warehouse, which captures pharmacy information from the electronic health record for each new prescription fill.

Information from each population included the generic medication name, fill date, and days' supply. Use each month was based on exposure to the medication(s) using the date dispensed and number of days supplied (e.g., a 30-day supply dispensed on January 20 contributed to exposure for January and February). Co-prescribing was present if there were days of medication available for both a BZD and an opioid in the same month, regardless of overlap. As a sensitivity analysis, we also used a stricter definition of co-prescribing that required ≥1 day of overlap in the BZD and opioid exposure days during the month.[7,22]

Cohort characteristics. We determined gender and age based on data at the beginning of the year; comorbidity was determined using the Elixhauser comorbidity index.[23] We also determined the presence of the following specific conditions associated with BZD prescribing: depression, anxiety, PTSD, alcohol use disorder, other substance use disorders, dementia, insomnia, and non-cancer chronic pain[24] (**Supplementary Table S1**).

Analysis, Part 1: Time Trends. To compare change in BZD prescribing over time, accounting for any changes in the age and sex distributions, we obtained monthly counts of BZD users in each population, stratified by sex-by-age subgroups ([male and female] x [55-64, 65-74, 75-84 and 85+ years]). We modeled monthly population counts of BZD users from 2013 to 2017 using a

generalized linear mixed model with Poisson distribution, with log link; the log of the monthly cohort size was the offset. The model included age groups, sex, time (incrementing by 1 for each month forward) with autoregressive correlation, and two indicators for the VA and commercial populations (with Medicare as the referent). We included a time-by-population interaction term to determine whether the monthly rate of change in prescribing risk varied between populations. Because Part D did not cover BZDs until 2013,[18] the models used data from April 2013 forward to exclude the rapid increase in BZD fills at the start of 2013 due to the coverage expansion.[25] We modeled time trends in BZD-opioid co-prescribing similarly, including the sensitivity analysis with the stricter definition of co-prescribing.

Analysis, Part 2: Cross-System Comparison. We used 2017 data to determine the overall yearly crude rate of BZD prescribing and BZD-opioid co-prescribing, as well as yearly rates by patient characteristic, within each population. The overall crude rate was calculated as the total count of persons with any BZD use in 2017 divided by the total person-years of exposure. Those who died or received hospice care in 2017 contributed a fraction of a year till death or hospice care, whichever was earlier.

To compare covariate-adjusted prescribing rates between populations, we used the 2017 Medicare population as the standard population. We first used a Poisson regression to model BZD prescribing in the 2017 Medicare population with log of person-years as the offset, adjusting for baseline characteristics in 2016. We then applied this model to the 2017 commercial and VA populations separately to obtain the expected annual count of BZD

prescribing in each population, accounting for individual covariate characteristics and exposure periods of the individuals in the respective populations.

To generate a covariate-adjusted between-system comparison of BZD prescribing, we calculated the standardized prescribing ratio in the commercial and VA populations as the ratio of expected prescribing—if the adjusted prescribing rates seen in Medicare population were applied in the commercial or VA populations—over the observed (actual) prescribing. We calculated the 95% confidence intervals using an exact method from the Poisson distribution.[26]

Analysis for BZD-opioid co-prescribing was done similarly, including the sensitivity analysis with the stricter definition of co-prescribing.

Finally, given the potential influence of 55-64-year-old disability-eligible Medicare beneficiaries on Medicare prescribing overall, we completed an additional sensitivity analysis limiting the cross-system comparison analysis outlined above to patients ≥65 years of age in the three populations.

Analyses were conducted using SAS 9.4; tests were 2-sided with α=0.05. This study was approved by the Michigan Medicine IRB; informed consent was waived.

RESULTS

Across all five years, the Medicare population included 6,292,510 individuals; commercial, 11,321,222; VA, 6,265,985. Characteristics of the three cohorts in 2013 are presented in **Table 1**. For Medicare, commercial, and VA, the mean (SD) ages were 73.2 (9.0), 68.2 (9.0), and 69.9 (9.6), respectively; the percentages female were 60.3%, 54.1% and 4.2%. 56.9% of the commercial cohort was in Medicare Advantage.

Part 1: Time Trends

In April 2013, the monthly unadjusted prevalence of BZD use in Medicare was 10.4%; by December 2017 it was 9.3%. For the same points in time, monthly commercial BZD use was 6.6% and 6.5%; for the VA, 5.7% and 3.0% (**Figure 1**; **Supplementary Tables S2-4**). In the model accounting for age and sex distribution over time, likelihood of BZD use in the Medicare population declined at a yearly rate of 0.98 (i.e., = exp[-0.002 x 12]; 95% confidence interval [CI] -0.002 to -0.002, p<0.001) (**Table 2**). There was an even smaller yearly decrease in the likelihood of BZD use in the commercial population of 0.99 (i.e., = exp[(-0.002 + 0.001) x 12]; commercial x time interaction 95% CI -0.001-0.003, p<0.001). The likelihood of BZD use in the VA declined at a much larger rate relative to Medicare, with an estimated yearly likelihood reduction of 0.87 (i.e., = exp[(-0.002 + [-0.01]) x 12]; VA x time interaction 95% CI -0.01 to -0.01, p<0.001).

In April 2013, the monthly unadjusted prevalence of BZD-opioid co-prescribing in Medicare was 4.0% and declined to 3.0% by December 2017. For the same points in time, commercial co-prescribing declined from 2.3% to 2.0%; for the VA, 2.2% to 0.6% (**Figure 2**; **Supplementary Table S2-4**). Based on the model, in the Medicare population the likelihood of BZD-opioid co-prescribing declined significantly by 0.95 per year (i.e., = exp[-0.004 x 12]; 95% CI -0.004 to -0.004, p<0.001) (**Table 2**). The annual rate of change in commercial co-prescribing was close to null at 0.99 (i.e., = exp[(-0.004 + 0.003) x 12]; commercial x time interaction 95% CI 0.003-0.003, p<0.001). As with BZD prescribing, the VA experienced significantly larger declines in BZD-opioid co-prescribing over time relative to Medicare, with an estimated annual

likelihood reduction of 0.75 (i.e., = exp[(-0.004 + [-0.02]) x 12]; VA x time interaction 95% CI -0.02 to -0.02, p<0.001). Results from the sensitivity analysis using a stricter definition of co-prescribing (i.e., requiring ≥1day of BZD-opioid overlap) were consistent in magnitude and direction (**Supplementary Table S5**).

Part 2: Cross-System Comparison

In 2017, the unadjusted yearly rate of BZD use was 17.7 per 100 person-years (PY) in Medicare, 12.6 per 100 PY in commercial, and 6.3 per 100 PY in the VA (**Table 3**). In all three populations, prescribing rates were higher for females than males and higher for those aged 55-64 than for older patients. Use increased with the burden of medical comorbidity in all three populations.

The commercial population's overall standardized BZD prescribing ratio—i.e., the observed level compared to what would have been predicted from the Medicare model—was 0.65 (95% CI 0.65-0.65). The commercial standardized ratios were lower than expected for all population strata. Among the clinical conditions of interest, they ranged from 0.66 (95% CI 0.65-0.67) for dementia to 0.91 (95% CI 0.90-0.92) for non-alcohol substance-related disorders. The overall VA standardized prescribing ratio was even lower at 0.40 (95% CI 0.39-0.40). Compared to prescribing in Medicare, the standardized ratios for clinical conditions ranged from 0.36 (95% CI 0.36-0.37) for non-alcohol substance-related disorders to 0.68 (95% CI 0.68-0.69) for those with PTSD.

In 2017, the unadjusted rate of BZD-opioid co-prescribing was 8.1 per 100 PY for Medicare, 5.5 per 100 PY for commercial, and 2.2 per 100 PY in the VA (**Table 3**). In all three

populations, the co-prescribing rate was higher for females than males and higher for those aged 55-64 than for older groups. Co-prescribing increased as the burden of medical comorbidity increased in all three populations. The overall commercial standardized co-prescribing ratio was 0.65 (95% CI 0.65-0.65). As with BZD prescribing, the co-prescribing ratios in the commercial population were lower for all population strata compared to Medicare. The VA's overall standardized co-prescribing ratio was 0.35 (95% CI 0.35-0.35). Similarly, the observed rate of VA co-prescribing was lower than Medicare for every demographic and clinical stratum.

Crude rates and standardized ratios were similar with co-prescribing that required overlap (**Supplementary Table S6**). Findings were also consistent with populations limited to those ≥65 (**Supplementary Table S7**).

DISCUSSION

This analysis of BZD prescribing in nearly 24 million U.S. adults 55 years or older finds modest reductions in prescribing among Medicare beneficiaries and commercial enrollees during 2013–2017, with lower prescribing and larger declines among the VA population. These differences are not accounted for by the different patient populations. Taking into account population differences, overall BZD prescribing in the VA in 2017 was less than half what might have been expected had Medicare prescribing practices been applied in the VA; BZD-opioid co-prescribing was about one-third what would have been expected.

The small declines in BZD prescribing to non-Veteran older adults in the U.S. have not, to our knowledge, been previously described. Analyses using the National Ambulatory Medical

Care Survey demonstrated increasing use over time among older adults through 2015,[27,28] though such estimates are based on office visits, an imperfect proxy for use. In contrast, a prevalence estimate based on the Medical Expenditure Panel Survey suggested no significant change among adults ≥65 from 1996–2013, though use among those 45–64 did grow.[10] The finding of declines in VA BZD prescribing extends results from a recent international comparison through 2016 that included the VA.[17] That analysis examined annual prevalence, which accounts for the higher 2016 prevalence (7.3%) than reported here, which are based on monthly medication possession.

Unlike BZD use, recent analyses have examined BZD-opioid co-prescribing in the U.S. and have found it to be declining. A study of commercial prescription claims from 2001–2013 found growth in BZD-opioid co-prescribing,[7] but more recent analyses through 2017 have found declines, potentially in response to the Centers for Disease Control and Prevention's 2016 Opioid Guidelines[22] and the US Food and Drug Administration's boxed warning advising against co-prescribing.[29] Declines in co-prescribing have been underway even longer in the VA, following the start of the Opioid Safety Initiative in 2013.[30]

The size of the prescribing declines in the VA—despite beginning 2013 already with lower prescribing than the other two populations—is striking. The VA is the largest integrated health care system in the U.S. and has two national initiatives focused on the safety of prescribing of psychoactive medications: the Opioid Safety Initiative and the Psychotropic Drug Safety Initiative, which both began in 2013.[30,31] Both programs include informatics tools that derive data from the electronic health record to identify high-risk patients (e.g., older Veterans prescribed a BZD; a Veteran of any age co-prescribed a BZD and opioid), allowing facility

leadership and quality improvement champions to provide feedback to the prescribing clinicians. These tools also help target educational efforts both to providers and patients alike, many of which are delivered by or with support from the VA's Academic Detailing Service.[32]

Given no reduction in BZD use among older adults through 2013[10] and the Part D BZD coverage expansion in 2013, it was surprising to find even small reductions in the non-VA populations. The declines may have been a byproduct of opioid-related prescribing guidelines, which emphasized reducing opioid-BZD co-prescribing.[33] It was also unexpected that the declines in traditional Medicare slightly exceeded those in the commercial population, which included a large proportion of Medicare Advantage enrollees. This commercial insurance group would theoretically have population health management options like utilization management (e.g., prior authorization) or programs to incentivize healthy behaviors more similar to the VA's integrated system than to traditional Medicare.[34]

A variety of interventions are effective at reducing BZD use. While they may range in complexity from brief educational approaches to multi-session psychological augmentation, even the most simple are more effective than usual care.[13,15,16] The critical element to reduce BZD prescribing may be countering clinical inertia, which may otherwise be the default prescribing approach[35,36] and would account for the years of stable use. As a large integrated health care system charged with coordinating delivery of primary care, mental health care, and prescription drugs to Veterans, the VA may be uniquely equipped to counter this clinical inertia.

This analysis has several limitations. It describes medication prescription fills but does not account for actual consumption. The measure of co-prescribing is an estimate based on the days prescribed but may not actually reflect co-consumption. Prescriptions paid for out of pocket

and misuse of another person's prescription are not captured. The Medicare population is limited to fee-for-service coverage, while the commercial population includes only a portion of Medicare Advantage. Because the analysis was completed in three separate data sources that could not be linked, it is possible that some individuals are included in more than one cohort, such as a veteran who obtained a BZD prescription from both the VA and Medicare Part D. In addition, these populations may vary in other characteristics associated with BZD prescribing that we did not adjust for, such as income.

BZD prescribing and BZD-opioid co-prescribing have declined markedly among older adults who receive care through the VA, in contrast to much smaller declines in Medicare and commercial populations. Given decades of evidence highlighting potential harms yielding minimal change in prescribing, the VA may offer lessons to apply in other health care populations to achieve meaningful reductions in BZD prescribing.

ACKNOWLEDGMENTS

Author Contributions:

Study concept and design: Maust, Kim

Acquisition, analysis, or interpretation of data: Maust, Kim, Wiechers, Ignacio, Blow, Bohnert

Drafting of the manuscript: Maust

Critical revision of the manuscript for important intellectual content: Maust, Kim, Wiechers, Ignacio, Blow, Bohnert

All authors approve this submitted version.

Conflict of Interest Disclosures: The authors have none to disclose.

Funding Source: U.S. Department of Veterans Affairs (IIR 16-210) and National Institute on Drug Abuse (R01DA045705).

Role of the Funder/Sponsor: The funding source 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.

REFERENCES

1. Tinetti ME, Speechley M, Ginter SF. Risk factors for falls among elderly persons living in the community. *N Engl J Med.* 1988;319(26):1701-1707.
2. Ray WA, Griffin MR, Downey W. Benzodiazepines of Long and Short Elimination Half-life and the Risk of Hip Fracture. *JAMA.* 1989;262(23):3303-3307.
3. Beers MH, Ouslander JG, Rollingher I, Reuben DB, Brooks J, Beck JC. Explicit criteria for determining inappropriate medication use in nursing home residents. *Arch Intern Med.* 1991;151(9):1825-1832.
4. American Geriatrics Society. Ten things physicians and patients should question. In: Choosing wisely. ABIM Foundation, 2015. http://www.choosingwisely.org/societies/american-geriatrics-society/ Accessed August 2, 2017.
5. Rapoport MJ, Lanctôt KL, Streiner DL, et al. Benzodiazepine use and driving: a meta-analysis. *The Journal of clinical psychiatry.* 2009;70(5):663-673.
6. Tannenbaum C, Paquette A, Hilmer S, Holroyd-Leduc J, Carnahan R. A systematic review of amnestic and non-amnestic mild cognitive impairment induced by anticholinergic, antihistamine, GABAergic and opioid drugs. *Drugs Aging.* 2012;29(8):639-658.
7. Sun EC, Dixit A, Humphreys K, Darnall BD, Baker LC, Mackey S. Association between concurrent use of prescription opioids and benzodiazepines and overdose: retrospective analysis. *BMJ.* 2017;356:j760.

8. Jones CM, Mack KA, Paulozzi LJ. Pharmaceutical overdose deaths, United States, 2010. *JAMA.* 2013;309(7):657-659.

9. Park TW, Saitz R, Ganoczy D, Ilgen MA, Bohnert ASB. Benzodiazepine prescribing patterns and deaths from drug overdose among US veterans receiving opioid analgesics: case-cohort study. *BMJ.* 2015;350(jun10 9):h2698-h2698.

10. Bachhuber MA, Hennessy S, Cunningham CO, Starrels JL. Increasing Benzodiazepine Prescriptions and Overdose Mortality in the United States, 1996-2013. *Am J Public Health.* 2016;106(4):686-688.

11. Cook JM, Marshall R, Masci C, Coyne JC. Physicians' Perspectives on Prescribing Benzodiazepines for Older Adults: A Qualitative Study. *J Gen Intern Med.* 2007;22(3):303-307.

12. Cook JM, Biyanova T, Masci C, Coyne JC. Older Patient Perspectives on Long-Term Anxiolytic Benzodiazepine Use and Discontinuation: A Qualitative Study. *J Gen Intern Med.* 2007;22(8):1094-1100.

13. Parr JM, Kavanagh DJ, Cahill L, Mitchell G, Young RM. Effectiveness of current treatment approaches for benzodiazepine discontinuation: a meta-analysis. *Addiction.* 2009;104(1):13-24.

14. Dollman WB, Leblanc V, Stevens L, O'connor P, Roughead EE, Gilbert AL. Achieving a sustained reduction in benzodiazepine use through implementation of an area-wide multi-strategic approach. *J Clin Pharm Ther.* 2005;30(5):425-432.

15. Tannenbaum C, Martin P, Tamblyn R, Benedetti A, Ahmed S. Reduction of Inappropriate Benzodiazepine Prescriptions Among Older Adults Through Direct Patient Education. *JAMA Intern Med.* 2014;174(6):890-898.

16. Voshaar RCO, Couvée JE, Van Balkom AJ, Mulder PG, Zitman FG. Strategies for discontinuing long-term benzodiazepine use: meta-analysis. *The British Journal of Psychiatry.* 2006;189(3):213-220.

17. Brett J, Maust DT, Bouck Z, et al. Benzodiazepine Use in Older Adults in the United States, Ontario, and Australia from 2010 to 2016. *J Am Geriatr Soc.* 2018.

18. Centers for Medicare & Medicaid Services. Transition to Part D Coverage of Benzodiazepines and Barbiturates Beginning in 2013. https://www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovContra/Downloads/BenzoandBarbituratesin2013.pdf Accessed May 6, 2016.

19. Maust DT, Lin LA, Blow FC. Benzodiazepine use and misuse among adults in the United States. *Psychiatr Serv.* 2018;70(2):97-106.

20. Congressional Research Service. The Number of Veterans That Use VA Health Care Services: A Fact Sheet. https://fas.org/sgp/crs/misc/R43579.pdf. Accessed March 30, 2020.

21. Jeffery MM, Hooten WM, Hess EP, et al. Opioid prescribing for opioid-naive patients in emergency departments and other settings: characteristics of prescriptions and association with long-term use. *Ann Emerg Med.* 2018;71(3):326-336. e319.

22. Bohnert AS, Guy GP, Losby JL. Opioid prescribing in the United States before and after the Centers for Disease Control and Prevention's 2016 opioid guideline. *Ann Intern Med.* 2018;169(6):367-375.

23. Elixhauser A, Steiner C, Harris DR, Coffey RM. Comorbidity measures for use with administrative data. *Med Care.* 1998;36(1):8-27.

24. Ilgen MA, Kleinberg F, Ignacio RV, et al. Noncancer pain conditions and risk of suicide. *JAMA Psychiatry.* 2013;70(7):692-697.

25. Maust DT, Lin LA, Goldstick JE, Haffajee RL, Brownlee R, Bohnert ASB. Association of Medicare Part D Benzodiazepine Coverage Expansion With Changes in Fall-Related Injuries and Overdoses Among Medicare Advantage Beneficiaries. *JAMA Network Open.* 2020.

26. New Mexico Department of Health, Indicator-Based Information System for Public Health. "Standardized Mortality Ratio." https://ibis.health.state.nm.us/resource/SMR_ISR.html. Accessed March 24, 2020.

27. Agarwal SD, Landon BE. Patterns in outpatient benzodiazepine prescribing in the United States. *JAMA network open.* 2019;2(1):e187399-e187399.

28. Rhee TG. Coprescribing of Benzodiazepines and Opioids in Older Adults: Rates, Correlates, and National Trends. *The Journals of Gerontology: Series A.* 2019;74(12):1910-1915.

29. Zhang VS, Olfson M, King M. Opioid and Benzodiazepine Coprescribing in the United States Before and After US Food and Drug Administration Boxed Warning. *JAMA psychiatry.* 2019;76(11):1208-1210.

30. Lin LA, Bohnert AS, Kerns RD, Clay MA, Ganoczy D, Ilgen MA. Impact of the opioid safety initiative on opioid-related prescribing in veterans. *Pain.* 2017;158(5):833-839.

31. Wiechers IR, Hermes EDA, Hoff R, Katz I. Psychotropic Drug Safety Initiative: Phase 2 Evaluation of Impact. VA Office of Mental Health Operations. West Haven, CT: Northeast Program Evaluation Center. November 2017.

32. Bounthavong M, Lau MK, Popish SJ, et al. Impact of academic detailing on benzodiazepine use among veterans with posttraumatic stress disorder. *Subst Abus.* 2019:1-9.

33. Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain—United States, 2016. *JAMA.* 2016;315(15):1624-1645.

34. Neuman P, Jacobson GA. Medicare advantage checkup. *N Engl J Med.* 2018;379(22):2163-2172.

35. Anderson K, Stowasser D, Freeman C, Scott I. Prescriber barriers and enablers to minimising potentially inappropriate medications in adults: a systematic review and thematic synthesis. *BMJ open.* 2014;4(12):e006544.

36. Jansen J, Naganathan V, Carter SM, et al. Too much medicine in older people? Deprescribing through shared decision making. *BMJ.* 2016;353:i2893.

Table 1. Characteristics of Medicare, Commercial, and VA Populations in 2013			
Characteristic[a], %	**Medicare (n=3,262,087)**	**Commercial (n=4,999,447)**	**VA (n=3,768,742)**
BZD use	18.5	12.1	9.7
Opioid use	36.0	26.5	25.5
BZD-opioid co-prescribing	9.2	5.5	4.7
Sex			
Male	39.7	45.9	95.8
Female	60.3	54.1	4.2
Age, mean (SD), y	73.2 (9.0)	68.2 (9.0)	69.9 (9.6)
55-64	14.0	38.3	34.6
65-74	45.9	36.1	34.3
75-84	27.2	23.5	21.0
85+	12.9	2.0	10.2
Clinical conditions			
Depression	3.2	2.9	4.9
Anxiety d/o	7.6	6.3	7.2
PTSD	0.3	0.2	10.2
Alcohol-related d/o	0.0	0.8	5.8
Non-alcohol substance-related d/o	0.0	0.6	3.0
Dementia	7.8	3.1	2.4
Insomnia	3.0	3.8	4.2
Chronic pain	47.2	45.8	49.6
Elixhauser score			
0	17.6	39.7	15.9
1	24.8	15.5	19.5
2	20.6	13.9	22.0
3	12.8	10.1	17.2
4+	24.3	20.8	25.3

VA: Veterans Affairs; BZD: benzodiazepine; SD: standard deviation; d/o: disorder

[a] Between-group comparisons (Chi-square tests) are statistically significant for all characteristics, which were determined based on 2013 encounters.

Figure 1. Monthly Prevalence of Benzodiazepine Use among Adults ≥55 in Medicare, Commercial, and VA Populations from 2013 to 2017. The large increases at the start of 2013 in the Medicare and commercial populations (the latter includes beneficiaries in Medicare Advantage) are artifacts of Medicare beginning coverage of BZDs in 2013.

Table 2. Trends in Monthly Likelihood of Benzodiazepine Use and Benzodiazepine-Opioid Co-Prescribing among Adults ≥55 in Medicare, Commercial, and VA Populations from 2013 to 2017

	Benzodiazepine Use[a]		Benzodiazepine-Opioid Co-Prescribing[a]	
Characteristic	**Estimate (95% CI)**	**p-value**	**Estimate (95% CI)**	**p-value**
Sex				
Female	ref		ref	
Male	-0.40 (-0.56, -0.24)	<0.001	-0.51 (-0.72, -0.30)	<0.001
Age				
55-64	ref		ref	
65-74	-0.32 (-0.55, -0.10)	0.006	-0.59 (-0.88, -0.29)	<0.001
75-84	-0.43 (-0.66, -0.20)	<0.001	-0.88 (-1.18, -0.58)	<0.001
85+	-0.51 (-0.74, -0.28)	<0.001	-1.11 (-1.40, -0.81)	<0.001
Time (months)	-0.002 (-0.002, -0.002)	<0.001	-0.004 (-0.004, -0.004)	<0.001
Commercial x time[b]	0.001 (-0.001, 0.003)	<0.001	0.003 (0.003, 0.003)	<0.001
VA x time[b]	-0.01 (-0.01, -0.01)	<0.001	-0.02 (-0.02, -0.02)	<0.001
Commercial	-0.54 (-0.73, -0.34)	<0.001	-0.70 (-0.96, -0.44)	<0.001
VA	-0.66 (-0.85, -0.46)	<0.001	-0.67 (-0.92, -0.41)	<0.001

ref: reference; VA: Veterans Affairs

[a] Results from generalized linear mixed models with Poisson distribution for the number of people using BZDs (or co-prescribed a BZD and opioid) each month from April 2013 to December 2017 to compare systems (Medicare [ref], Optum, and VA) over time, adjusting for age and gender.

[b] Estimates reflect the incremental association of time (month) with BZD use in the commercial and VA populations, relative to the association of time in Medicare. To interpret the monthly time coefficient for BZD use: the annual likelihood for BZD use in Medicare is 0.98 (i.e., exp[-0.002/month x 12 months]). The yearly likelihood for a comparison population is exp([*time* coefficient + *population* x *time* interaction coefficient]/month x 12 months). For the VA, this is exp([-0.002 + (-0.01)]/month x 12 months) = 0.87.

Figure 2. Monthly Prevalence of Benzodiazepine-Opioid Co-Prescribing among Adults ≥55 in Medicare, Commercial, and VA Populations from 2013 to 2017. The large increases at the start of 2013 in the Medicare and commercial populations (the latter includes beneficiaries in Medicare Advantage) are artifacts of Medicare beginning coverage of BZDs in 2013.

Maust Donovan (Orcid ID: 0000-0003-4740-2640)

Table 3. Annual Rates and Standardized Ratios of Benzodiazepine Use and Benzodiazepine-Opioid Co-Prescribing in Medicare, Commercial, and VA Populations in 2017

	Benzodiazepine Use					Benzodiazepine-Opioid Co-Prescribing				
	Medicare	Commercial		VA		Medicare	Commercial		VA	
Characteristics[a]	Rate[b] (per 100 person-yr)	Rate[b] (per 100 person-yr)	Standardized ratio[c] (95% CI)[d]	Rate[b] (per 100 person-yr)	Standardized ratio[c] (95% CI)[d]	Rate[b] (per 100 person-yr)	Rate[b] (Rx per 100 person-yr)	Standardized ratio[c] (95% CI)[d]	Rate[b] (per 100 person-yr)	Standardized ratio[c] (95% CI)[d]
Overall	17.7	12.6	0.65 (0.65, 0.65)	6.3	0.40 (0.39, 0.40)	8.1	5.5	0.65 (0.65, 0.65)	2.2	0.35 (0.35, 0.35)
Sex										
Male	13.2	9.1	0.63 (0.63, 0.64)	6.1	0.40 (0.40, 0.40)	6.0	4.0	0.65 (0.65, 0.65)	2.2	0.36 (0.35, 0.36)
Female	20.8	15.4	0.66 (0.66, 0.66)	9.6	0.34 (0.33, 0.34)	9.6	6.7	0.65 (0.65, 0.66)	3.5	0.28 (0.27, 0.28)
Age (years)										
55-64	29.6	13.1	0.58 (0.57, 0.58)	7.3	0.33 (0.32, 0.33)	19.0	6.2	0.55 (0.55, 0.56)	2.9	0.27 (0.26, 0.27)
65-74	15.9	12.3	0.71 (0.71, 0.71)	6.9	0.49 (0.48, 0.49)	7.0	5.4	0.74 (0.74, 0.75)	2.4	0.44 (0.44, 0.44)
75-84	16.5	12.2	0.70 (0.70, 0.71)	4.3	0.38 (0.37, 0.38)	6.8	4.9	0.73 (0.73, 0.74)	1.3	0.36 (0.35, 0.37)
≥85	18.2	12.1	0.64 (0.64, 0.65)	4.0	0.36 (0.35, 0.36)	7.2	4.7	0.67 (0.66, 0.68)	1.2	0.36 (0.35, 0.37)
Clinical conditions										
Depression	41.6	30.2	0.74 (0.73, 0.74)	15.7	0.50 (0.49, 0.50)	23.5	16.0	0.73 (0.72, 0.73)	6.0	0.38 (0.38, 0.39)
Anxiety d/o	58.7	44.7	0.77 (0.77, 0.77)	26.1	0.53 (0.53, 0.54)	32.5	21.9	0.73 (0.73, 0.73)	9.1	0.39 (0.39, 0.40)
PTSD	54.7	43.5	0.76 (0.74, 0.77)	18.0	0.68 (0.68, 0.69)	33.6	24.9	0.75 (0.73, 0.77)	6.5	0.51 (0.51, 0.52)
Alcohol-related d/o	30.1	21.5	0.79 (0.78, 0.80)	8.8	0.39 (0.38, 0.39)	17.2	11.3	0.78 (0.76, 0.80)	3.3	0.31 (0.30, 0.32)
Non-alcohol substance-related d/o	45.3	39.3	0.91 (0.90, 0.92)	10.8	0.36 (0.36, 0.37)	37.3	30.1	0.87 (0.86, 0.88)	5.0	0.27 (0.26, 0.28)
Dementia	31.5	20.6	0.66 (0.65, 0.67)	9.2	0.45 (0.48, 0.46)	13.7	8.8	0.68 (0.67, 0.69)	3.2	0.42 (0.40, 0.43)
Insomnia	45.4	33.7	0.78 (0.77, 0.78)	17.1	0.51 (0.50, 0.52)	26.0	17.3	0.74 (0.73, 0.75)	6.3	0.38 (0.37, 0.39)

Chronic pain	23.9	15.9	0.67 (0.67, 0.68)	8.3	0.43 (0.43, 0.43)	13.6	8.0	0.67 (0.66, 0.67)	3.6	0.37 (0.37, 0.37)
Elixhauser score										
0	10.7	7.0	0.59 (0.58, 0.59)	3.0	0.31 (0.30, 0.31)	3.8	2.2	0.58 (0.57, 0.58)	0.8	0.25 (0.25, 0.26)
1	17.0	10.6	0.57 (0.56, 0.57)	5.0	0.35 (0.34, 0.35)	6.8	3.6	0.53 (0.52, 0.53)	1.4	0.28 (0.28, 0.29)
2	18.7	12.5	0.62 (0.62, 0.62)	6.0	0.38 (0.38, 0.39)	8.3	4.9	0.59 (0.58, 0.60)	1.9	0.31 (0.31, 0.32)
3	20.9	14.2	0.65 (0.65, 0.66)	7.2	0.42 (0.41, 0.42)	10.1	6.1	0.64 (0.63, 0.64)	2.5	0.34 (0.34, 0.35)
4+	26.3	18.4	0.73 (0.73, 0.74)	9.8	0.49 (0.49, 0.50)	14.8	9.8	0.74 (0.74, 0.75)	4.3	0.42 (0.42, 0.43)
Prescribed opioid	27.4	23.7	0.74 (0.74, 0.74)	11.9	0.46 (0.46, 0.47)	19.5	16.4	0.68 (0.68, 0.68)	7.5	0.38 (0.38, 0.38)

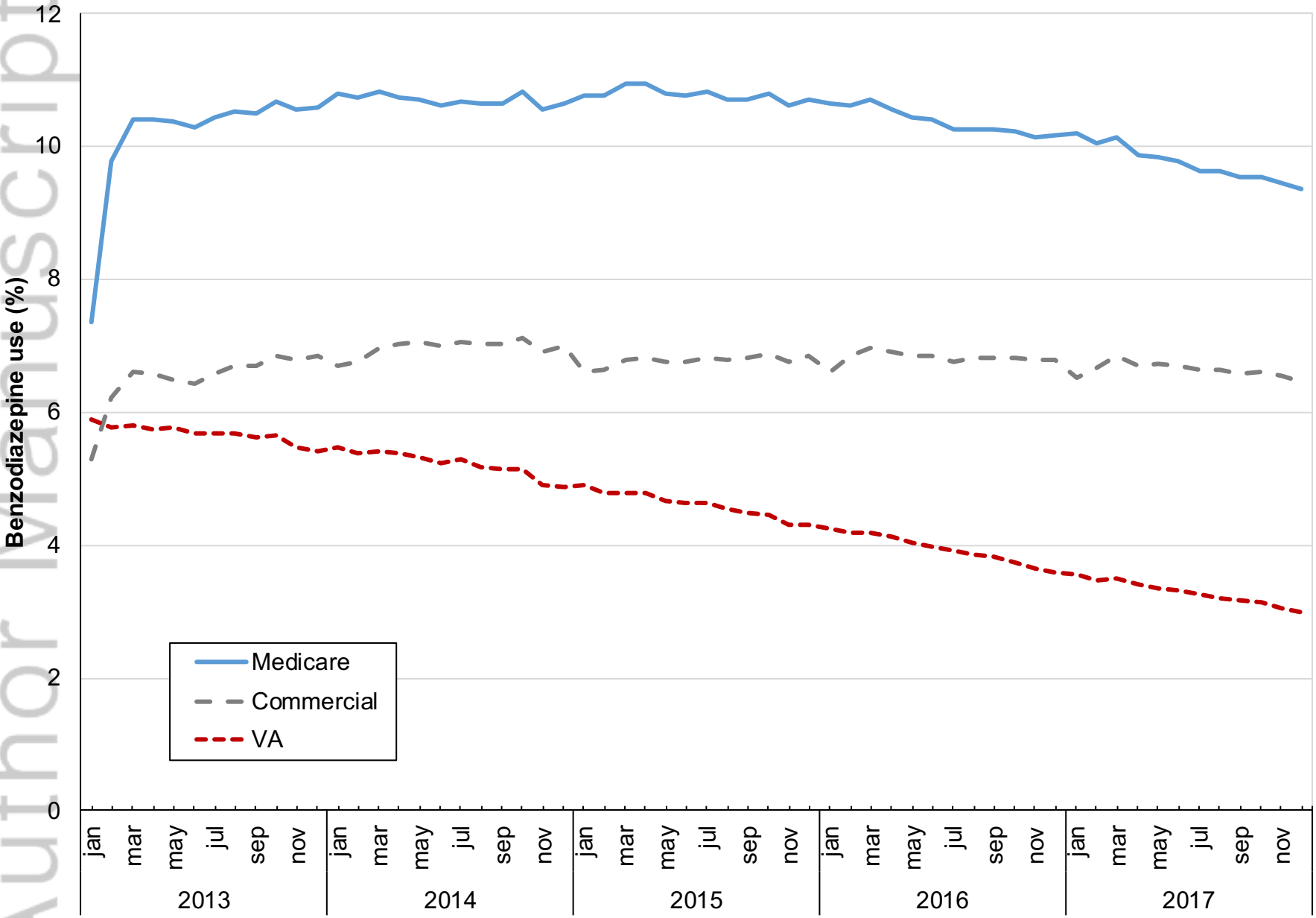
VA: Veterans Affairs; CI: confidence interval; d/o: disorder.

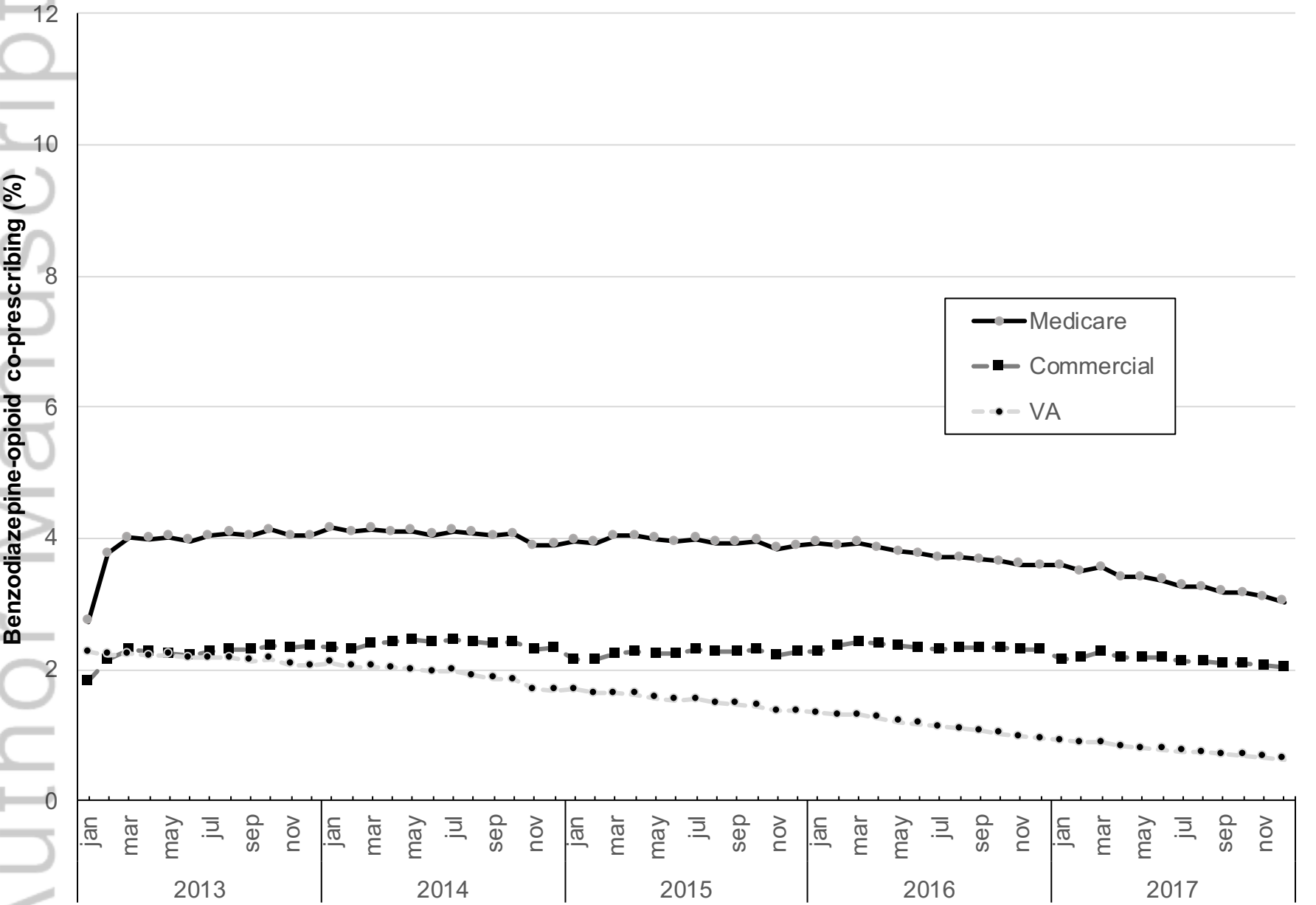
[a] Clinical characteristics determined based on 2016 encounters.

[b] 100 x number of persons with any benzodiazepine (or benzodiazepine-opioid) use in 2017 / total person-years, either overall or by stratum, where person-year is 1 if an eligible individual is alive throughout the year or a fraction (number of days to death or hospice care/365) if died or entered hospice during 2017.

[c] (observed number of persons with benzodiazepine prescription in 2017 in commercial or VA) / (expected number of persons with benzodiazepine prescription in 2017, predicted using Poisson multivariable regression model from Medicare population including all table row characteristics). For example, the rate of BZD prescribing to women in the VA is 0.34-times what would be expected if prescribing practices in the Medicare cohort were applied to female patients in the VA.

[d] 95% Confidence Interval (CI) = rate $\pm$ (1.96 x [$\sqrt{}$observed]/expected)[26]





WILEY

Color Charge Form
Journal of the American Geriatrics Society

Upload this form to your submission OR return it to:
Emily Hammond / JAGS Editorial Office
jags@jjeditorial.com

Dear Author:
If you have supplied color figures in your submission, the first color figure in print is free of cost. Any additional figures you wish to print in color will incur a fee of $500 each. Please indicate how EACH of your figures should be handled in the table below.

INSTRUCTIONS: **For EVERY figure in your paper**, an X should be provided in the appropriate row. Place an '**X**' in **column 1** for a maximum of **ONE figure.** Place an '**X**' in **column 2** if you want to pay for additional color printing. The total in this column should be entered into the Quantity field below.	**Figure No.**	**Color in PRINT (waive fee)**	**Color in PRINT (charge $500 per)***	**Color ONLINE ONLY (no charge)**	**Black/White ONLINE and PRINT**
	1	x			
	2				x
	3				
	4				
	5				
	TOTAL:				

***If you indicate ANY figures in this column, the contact information below MUST be provided.**

Please Complete & Please Print

Component(s) in Article	Charge(s)	Quantity	Estimated Charge(s) (in USD)
Color Figure Charge **Standard**	$500 per figure	0	$
			$ 0 = Total Estimated

Name: Donovan Maust
Manuscript No.: JAGS-1545-CI-Jul-20.R1
Manuscript Title: Benzodiazepine Use among Medicare, Commercially-Insured, and Veteran Older Adults from 2013–2017
Address: 2800 Plymouth Rd, Ann Arbor MI 48109
Phone Number: 734-845-3649
Fax Number: n/a
Email Address: maustd@umich.edu

Verify your agreement to pay by signing and dating below. Wiley will send an invoice to the email address you've provided:

8/21/20

Signature:_____Date:_____