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Short communication

Comparing state, regional, and local variation in concurrent opioid and benzodiazepine use

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ABSTRACT

Background: Concurrent opioid and benzodiazepine use is associated with a three-fold increase in the risk of opioid-related overdose. No study has evaluated geographic variation in the concurrent use of opioids and benzodiazepines in US Medicare. We compared state, hospital-referral region (HRR), and county-level variation in concurrent opioid and benzodiazepine use among US Medicare opioid users and examined the heterogeneity in concurrent use within states.

Methods: Using 2013–2014 US Medicare Part D claims, we identified non-cancer beneficiaries who used opioids in 2014 (n = 268,678). The outcome was concurrent opioid and benzodiazepine use. We constructed logistic regression models to isolate state, HRR, and county-level variation not explained by patient characteristics, and evaluated how county and HRR quintiles are distributed within state quintiles.

Results: The adjusted probability of concurrent use ranged from 16.7%–29.6% across states, 12.1%–37.0% across HRRs, and 0%–65.2% across counties. State-level variation masks substantial county-level variation: only 18% of counties located in the lowest state quintile were in the lowest county quintile, and only 23% of counties located in the highest state quintile were in the highest county quintile. We also observed variation in concurrent use across HRRs within states, but it was not as dispersed. For example, 52% of the HRRs located in the highest state quintile were in the highest HRR quintile.

Conclusions: Large variation in concurrent use of opioids and benzodiazepines exists across the US. State variation masks substantial local variation, which beckons for polices to monitor concurrent opioid and benzodiazepine use at the county level.

1. Introduction

In 2015, prescription opioid-related overdoses resulted in over 20,000 deaths (CDC, 2018), and almost 30% of them involved the concurrent use of benzodiazepines (NIDA, 2017; Saunders et al., 2012). Benzodiazepines are central nervous system depressors, so their concurrent administration increases the risk of severe respiratory depression and subsequent death associated with opioids by two to three-fold (Dowell et al., 2016; Park et al., 2015; Sun et al., 2017).

Recent research has shown that wide geographic variation exists for concurrent opioid and benzodiazepine use (Stein et al., 2017). Specifically, Stein et al. described a 15-fold variability in the odds of concurrent opioid and benzodiazepine use among patients with an opioid use disorder across 12 states (Stein et al., 2017). However, to our knowledge, no studies have used a nationally representative sample of the US to compare state-level, regional and local variation in the concurrent use of opioids and benzodiazepines among the general population of opioid users. Because most interventions to improve opioid prescribing and use are implemented at the state-level (CDC, 2018), quantifying variation in concurrent opioid and benzodiazepine use across and within states can provide insights on the effectiveness of these policies and further orient at which geographic level future interventions should be targeted. Medicare claims data is a particularly appropriate source to study this variation because of the large and nationally-representative sample available, the homogeneous criteria for Medicare eligibility across the country, and the large prevalence of concurrent opioid and benzodiazepine use previously reported for Medicare beneficiaries (Centers for Medicare and Medicaid Services, 2016).

In this study, we compared state-level, regional, and local variation in the rate of concurrent opioid and benzodiazepine use in Medicare and examined the degree to which high-rate local and regional areas

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are clustered together within high-rate states.

2. Methods

2.1. Data source and sample selection

We used 2013–2014 claims data from a 5% random sample of US Medicare Part D beneficiaries and identified beneficiaries with no diagnosis of cancer in 2013 and 2014, who were continuously enrolled in stand-alone Part D plans in 2014, and who filled at least one prescription for an opioid (list in Supplemental Table 1) in 2014 (Sun et al., 2017). Patients who died in 2014 but were continuously enrolled in stand-alone Part D plans until death were included in the study. For the selected sample, we extracted all prescriptions for benzodiazepines (Supplemental Table 1) in 2014. Following the methods used by the US Centers for Medicare and Medicaid Services (CMS) to identify concurrent opioid and benzodiazepine use (Centers for Medicare and Medicaid Services, 2016), we calculated the number of days in 2014 when each beneficiary had an overlapping supply of opioids and benzodiazepines. We defined concurrent opioid and benzodiazepine use as having at least five days with overlapping supply of both medications in 2014. Each beneficiary was assigned to a US state, hospital-referral region (HRR), and a county using the zip code. HRRs represent regional health care markets, and are defined on the basis of the referral centers where patients are referred for neurosurgery and cardiovascular surgical procedures (The Dartmouth Institute for Health Policy and Clinical Practice, 2014). Eligible beneficiaries from Puerto Rico were not included in the analysis because there are no HRRs defined for this territory. The University of Pittsburgh Institutional Review Board approved this study as exempt.

2.2. Statistical analysis

We examined geographic variation in concurrent opioid and benzodiazepine use at three levels: states, HRRs, and counties. We constructed three logistic regression models where the outcome variable was concurrent opioid and benzodiazepine use, and predictors included beneficiary-level demographics, insurance factors and clinical characteristics (full list in Supplemental Table 1), and regional dummies –one model for states, one for HRRs, and one for counties. Using these model estimations, we calculated the adjusted probability of concurrent opioid and benzodiazepine use among opioid users for each state, HRR, and county, plugging the means of other predictors. This method enabled us to isolate geographic variation in concurrent opioid and benzodiazepine use that is not due to variation in patient demographics, insurance and clinical factors (Zhang et al., 2010).

We mapped quintiles of the adjusted probability of concurrent opioid and benzodiazepine use at the state, HRR, and county levels. All county-level analyses and maps were constructed only including counties with at least 11 opioid users in our study sample, to satisfy the minimum cell size requirement from CMS. Finally, we evaluated how HRR and county quintiles were distributed within state quintiles. Analyses were conducted with SAS 9.4 (Cary, NC) and ArcGIS Pro 1.4.0 (Redlands, CA).

3. Results

Among 268,678 Medicare Part D beneficiaries who filled at least one prescription for an opioid in 2014, 68,640 (25.6%) had at least more than five days with concurrent supply of opioids and benzodiazepines. Among concurrent users, the mean (median) number of days with overlapping supply of both medications was 134 (86).

We observed substantial geographic variation at the state, HRR, and county levels with regards to concurrent opioid and benzodiazepine use. Among opioid users, the adjusted probability of concurrent opioid and benzodiazepine use ranged from 16.7% to 29.6% across states,

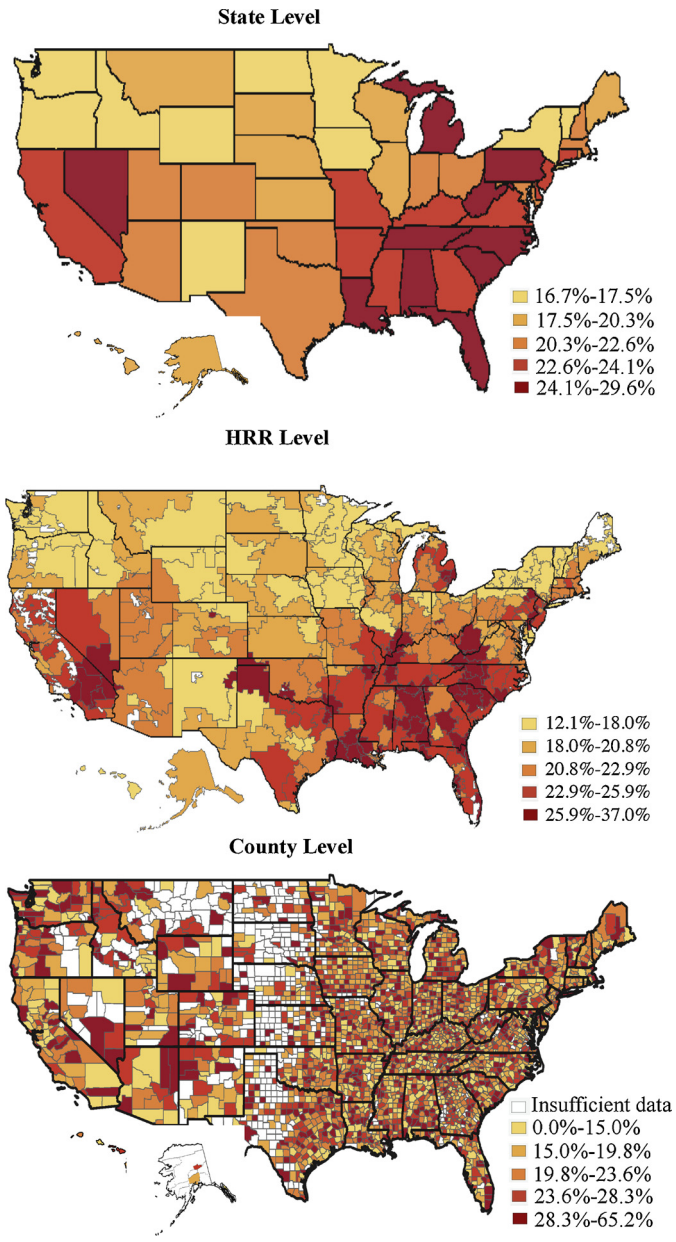

Fig. 1. Quintiles of the adjusted probability of concurrent opioid and benzodiazepine use among opioid users, at the state, hospital-referral region, and county levels.

from 12.1% to 37.0% across HRRs, and from 0% to 65.2% across counties (Supplemental Table 1). Concurrent opioid and benzodiazepine use was most prevalent in South Carolina (26.9%), Nevada (28.1%), Alabama (27.4%), Louisiana (26.7%), and North Carolina (26.1%); and less prevalent in Minnesota (13.4%), Vermont (14.0%), Wyoming (16.4%), Iowa (16.5%), and North Dakota (16.7%) (Fig. 1). Among HRRs, concurrent opioid and benzodiazepine use was highest in Spartanburg, SC (37.0%), Dearborn, MI (34.3%), Alexandria, LA (34.1%), Jackson, TN (33.4%), and Florence, SC (33.3%). Among counties, concurrent opioid and benzodiazepine use was highest in Polk, MN (65.2%), Clark, KY (64.6%), Jefferson, TN (62.7%), Oklahoma City, OK (58.2%), and Hancock, IA (58.0%).

We found that state-level variation masks county-level variation in concurrent opioid and benzodiazepine use (Fig. 2A). For example, only 18% of counties located in the lowest state quintile were in the lowest county quintile; and only 23% of counties located in the highest state quintile were in the highest county quintile. We also observed variation