Associations Between Copays, Coverage Limits for Naloxone, and Prescribing in Medicaid

John C Messinger1,2, Aaron S Kesselheim1,2,3, Seanna M Vine2, Michael A Fischer1,3 and Rachel E Barenie2,4

1Harvard Medical School, Boston, MA, USA. 2Program on Regulation, Therapeutics, and Law (PORTAL), Boston, MA, USA. 3Division of Pharmacoepidemiology and Pharmacoeconomics, Department of Medicine, Brigham and Women’s Hospital, Boston, MA, USA. 4The University of Tennessee Health Science Center, Memphis, TN, USA.

ABSTRACT

AIMS: To describe naloxone dispensing in Medicaid fee-for-service (FFS) and examine relationships between copays and coverage limits for naloxone and its dispensing rates.

METHODS: Cross-sectional study using Medicaid FFS State Drug Utilization Data to quantify the use of naloxone in 2018. The primary outcomes of this study were the proportion of naloxone prescriptions relative to all prescriptions and all opioid prescriptions dispensed in each state. We obtained drug benefit design information from the Medicaid Behavioral Health Services Database. The primary analysis examined the influence of copays (yes/no), copay amounts, and coverage limits on medication dispensing using simple linear regression, excluding states with no measurable use or less than 5% Medicaid FFS.

RESULTS: We found substantial variability across 50 states and DC in the proportion of prescriptions dispensed for Narcan and generic naloxone. We found a positive relationship between copay and copay amount and dispensing of generic naloxone. However, a sensitivity analysis including the broadest possible cohort of states failed to confirm this relationship. We found no other relationships between copays or coverage limits and dispensing of any naloxone formulation.

CONCLUSIONS: Substantial variation exists between the rates of naloxone dispensing across the US for Medicaid patients, but we did not find a meaningful relationship between plan design and dispensing. Whether drug benefit designs in Medicaid influence naloxone use requires further evaluation to avoid limiting access to this life-saving medication.

KEYWORDS: Naloxone, drug benefit design, copay, coverage limit, dispensing, Medicaid

Introduction

Thousands of people die every year from opioid-related overdoses in the US, with an estimated 72,000 deaths in 2019.1 Patients, payors, and policymakers continue to scramble to find viable approaches to reduce opioid overdose deaths, which is even more urgent during times of a global pandemic in which opioid overdoses are reportedly spiking.2 One widely-discussed approach to curtail the opioid overdose crisis would be to expand access to naloxone, the extremely effective opioid overdose reversal agent. Research has shown that an increase in distribution of naloxone has been linked with reductions in overdose mortality.2-4

Naloxone access has increased in recent years through Medicaid expansions5,6 and numerous other strategies.7 At the start of data collection for this study, all states except for Nebraska had an active standing order for naloxone, meaning that a patient or caregiver could obtain the medication without an individual prescription.8 Researchers have found that standing orders are associated with a 74% increase in naloxone dispensing for Medicaid beneficiaries.9 Another strategy is mandating co-prescribing of naloxone with opioids for patients at high-risk of overdose. Prior to 2018, 2 states (VA and VT) had laws establishing mandatory co-prescription for naloxone and 5 more states (AZ, FL, OH, RI, and WA) added such statutes during that calendar year.10 Still, rates of co-dispensing naloxone for patients at high-risk for overdose is low.11

Stigmatization of naloxone by patients and providers still hinders its prescription and dispensation.12,13 States without Medicaid expansion have been found to have lower rates of naloxone dispensation.5,6 Laws that offer different levels of prescriber and dispenser civil and criminal immunity for the consequences of naloxone distribution may also influence dispensation.14 One more factor contributing to low naloxone use might be the cost of naloxone, with average copays (out of pocket costs for patients to fill a prescription) nearing $25.15,16 Insurance coverage for naloxone can also play a key role in

*Michael A Fischer is also affiliated to the Chief of the Section of General Internal Medicine, Department of Medicine, Boston Medical Center, Boston University School of Medicine, Boston, MA 02118, USA

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ensuring patients can access this life-saving medication. High drug costs sometimes lead insurers to impose coverage limits (such as requirements for prior authorizations or restrictions on the number of prescriptions filled in a given time frame), even for crucial medicines such as naloxone. These rules can affect medication compliance and result in prescription abandonment at the pharmacy or reduce the likelihood that patients will refill their prescription.17,18

Federal law requires that state Medicaid programs provide coverage for low-income individuals, qualified pregnant women and children, and individuals receiving supplemental income from the government.19 In 2010, the Affordable Care Act created the opportunity for states to expand Medicaid to cover nearly all low-income individuals under the age of 65, and by 2018, 32 states and DC had elected to do so.20 Medicaid insurance plans are typically separated into 2 categories: fee-for-service (FFS), where the state directly pays providers for each service, and managed care organizations (MCOs), where a fee is paid to a third-party insurer for each patient covered. One study found that when compared to FFS beneficiaries, MCO beneficiaries were younger, healthier, and more likely to be female.21

To assess the impacts of drug benefit designs (measures implemented by insurance companies, such as copays and coverage limits, that dictate what drugs, in what quantities, and at what price a beneficiary has access to) for dispensing of naloxone, we evaluated the association between copays and coverage limits for different formulations of this medication and their dispensing in FFS Medicaid, which covers the majority of opioid prescriptions in the US.

Methods

Data Sources

We used the State Drug Utilization Data, which is provided on-line by the Centers for Medicare and Medicaid Services (CMS) and contains aggregated quarterly drug spending data from each state’s Medicaid program, to quantify prescription dispensing.22 The Medicaid data are organized at the level of the National Drug Code (NDC), a unique identifier of a specific active ingredient, dose, formulation, and manufacturer. For each NDC, this dataset provides the number of prescriptions reimbursed by Medicaid, which would only include prescriptions that were dispensed to patients at a pharmacy. CMS suppresses data for any cell with 1 to 10 prescriptions dispensed in that state per quarter to ensure anonymity.23 We used NDCs to identify medications that have an indication for overdose reversal and a comprehensive list of other opioid medications. Overdose reversal medications included naloxone nasal spray (Narcan, Emergent Biosolutions, Maryland, USA), generic naloxone nasal spray atomizer, and naloxone auto-injector (Evzio, Kaleo, Virginia, USA). To create a comprehensive list of opioid medications, we included NDCs with all formulations of the following: buprenorphine, codeine, dihydrocodeine, fentanyl, hydrocodone, hydromorphone, meperidine, methadone, morphine, oxycodone, oxymorphone, tapentadol, pentazocine, tramadol, and levorphanol.

We used the Medicaid Behavioral Health Services Database to extract state-level information about copay amounts and coverage limits (eg, prior authorizations) in 2018 (Table 1).24 This information was obtained through a survey of Medicaid Directors in all 50 states and the District of Columbia, conducted by Kaiser Family Foundation in partnership with Health Management Associates, which inquired about drug coverage policies in FFS Medicaid as of July 1, 2018.24 Copay amounts ranged from $0.00 to $4.00 for both Narcan and generic naloxone. Coverage limits included: prior authorizations; restrictions on dose, duration, quantity, patient age, medication formulation, dispensing setting, medical necessity/diagnosis, prescriber qualifications; and availability of additional services to manage patients’ substance use disorder. States that did not submit information about copay or coverage limits were excluded (Figure 1). This study used only aggregated medication use data and did not require Institutional Board Review approval.

Since the Medicaid Behavioral Health Services Database reported copay and coverage limits only related to state fee-for-service plans in 2018, we limited the State Drug Utilization Data to filled prescriptions in FFS Medicaid in that year as well. Eight states (AR, CO, DE, HI, NE, NH, ND, and TN) with under 5% of total filled prescriptions covered by fee-for-service Medicaid were excluded.25

Analyses

The primary outcomes were the proportion of prescriptions dispensed for each naloxone formulation relative to all prescriptions and all opioid prescriptions in fee-for-service Medicaid summed from all quarters recorded in each state’s State Drug Utilization Data in 2018. This outcome was reported as the number of naloxone prescriptions dispensed per 10000 total or opioid prescriptions dispensed for ease of interpretation. Proportions were used instead of the absolute number of dispensed prescriptions to account for the differences in size of Medicaid fee-for-service programs across states. Reliable data on the number of Medicaid fee-for-service beneficiaries per state in 2018 were not available at the time of these analyses, and so total prescriptions were used as a proxy measure. The proportion of prescriptions measure was calculated by dividing total dispensed prescriptions for each naloxone formulation in a given state by the total dispensed prescriptions of all medications in that state and total dispensed opioid prescriptions in that state, respectively.

The first analyses evaluated if exposure to either the presence of a copay (yes/no) or presence of a coverage limit (yes/no) was correlated to changes in the primary outcome of proportion of naloxone prescriptions dispensed relative to all prescriptions and opioid prescriptions. The second analysis evaluated if exposure to a greater copay amount ($0-$2.00 vs $2.01 or more for Narcan and $0-$0.99 vs $1.00 or more for generic naloxone) was correlated to the same primary outcome. This analysis
Table 1. Number of prescriptions dispensed and proportion of naloxone prescriptions dispensed in Medicaid fee-for-service, 2018.

| STATE | NUMBER OF PRESCRIPTIONS (FEE-FOR-SERVICE MEDICAID, 2018) | PROPORTION OF ALL PRESCRIPTIONS (PER 10,000 PRESCRIPTIONS) | PROPORTION OF OPIOID PRESCRIPTIONS (PER 10,000 PRESCRIPTIONS) |
|-------|---------------------------------------------------------|----------------------------------------------------------|----------------------------------------------------------|
|       | NARCAN GENERIC NALOXONE | ALL PRESCRIPTIONS | OPIOID PRESCRIPTIONS* | NARCAN GENERIC NALOXONE | NARCAN GENERIC NALOXONE |
| AK    | 594 | — | 105,937 | 130,5473 | 4.55 | — | 56.07 | — |
| AL    | 456 | 28 | 342,208 | 739,5840 | 0.62 | 0.04 | 13.33 | 0.82 |
| AR    | 337 | 20 | 248,402 | 492,7478 | 0.68 | 0.04 | 13.57 | 0.81 |
| AZ    | 91  | — | 11,160  | 93,747  | 9.71 | — | 81.54 | — |
| CA    | 12,272 | 562 | 1,154,798 | 263,39743 | 4.66 | 0.21 | 106.27 | 4.87 |
| CO    | 3,560 | 602 | 556,390 | 721,0256 | 4.94 | 0.83 | 63.98 | 10.82 |
| CT    | 9514 | 214 | 490,068 | 942,2702 | 10.10 | 0.23 | 194.14 | 4.37 |
| DC    | 225  | — | 33,410  | 901,922 | 2.49 | — | 67.35 | — |
| DE    | —   | 34 | 1,892   | 36,718  | — | 9.26 | — | 179.70 |
| FL    | 206  | — | 21,937  | 146,2366 | 1.41 | — | 93.91 | — |
| GA    | 94  | 258 | 396,106 | 721,114 | 0.13 | 0.36 | 2.37 | 6.51 |
| HI    | —   | 0  | 501     | 2498    | — | — | — | — |
| IA    | —   | —  | 11,506  | 224,712 | — | — | — | — |
| ID    | 456 | 51 | 129,393 | 230,8789 | 1.98 | 0.22 | 35.24 | 3.94 |
| IL    | 426 | — | 135,569 | 407,3245 | 1.05 | — | 31.42 | — |
| IN    | 123  | — | 43,547  | 254,0175 | 0.48 | — | 28.25 | — |
| KS    | —   | —  | 57      | 126,64  | — | — | — | — |
| KY    | 14  | — | 14,254  | 105,8200 | 0.13 | — | 9.82 | — |
| LA    | —   | —  | 7,397   | 78,2651 | — | — | — | — |
| MA    | 5276 | 214 | 344,892 | 831,1750 | 6.35 | 0.26 | 152.98 | 6.20 |
| MD    | 16,063 | 516 | 300,484 | 447,1695 | 35.92 | 1.15 | 534.57 | 17.17 |
| ME    | 735 | — | 157,401 | 195,3813 | 3.76 | — | 46.70 | — |
| MI    | 415  | — | 259,717 | 944,3200 | 0.44 | — | 15.98 | — |
| MN    | 447  | — | 61,096  | 197,9696 | 2.26 | 0.00 | 72.21 | — |
| MO    | 2668 | 933 | 514,127 | 11,956,314 | 2.23 | 0.78 | 51.89 | 18.15 |
| MS    | 26  | — | 36,521  | 969,206 | 0.27 | — | 7.12 | — |
| MT    | 751 | 39 | 373,220 | 288,307 | 2.60 | 0.14 | 20.12 | 1.04 |
| NC    | 4623 | 525 | 826,143 | 15,804,613 | 2.93 | 0.33 | 55.96 | 6.35 |
| ND    | —   | — | 20,614  | 491,151 | — | — | — | — |
| NE    | —   | 0  | 141     | 3134    | — | — | — | — |
| NH    | 15  | — | 8,320   | 74,588  | 2.01 | — | 18.03 | — |
| NJ    | 48  | — | 12,819  | 33,3948 | 1.44 | — | 37.44 | — |
| NM    | 113 | — | 10,716  | 105,071 | 10.75 | — | 105.45 | — |
| NV    | 875 | 25 | 148,273 | 201,8394 | 4.34 | 0.12 | 59.01 | 1.69 |

(Continued)
### Table 1. (Continued)

| STATE | NUMBER OF PRESCRIPTION (FEE-FOR-SERVICE MEDICAID, 2018) | PROPORTION OF ALL PRESCRIPTIONS (PER 10,000 PRESCRIPTIONS) | PROPORTION OF OPIOID PRESCRIPTIONS (PER 10,000 PRESCRIPTIONS) |
|-------|------------------------------------------------------|------------------------------------------------------------|-------------------------------------------------------------|
|       | NARCAN | GENERIC NALOXONE | ALL PRESCRIPTIONS | OPIOID PRESCRIPTIONS* | NARCAN | GENERIC NALOXONE | NARCAN | GENERIC NALOXONE |
| NY    | 903    | 63             | 96535            | 10454237             | 0.86   | 0.06             | 93.54  | 6.53             |
| OH    | 1001   | 119            | 213306           | 3735645              | 2.68   | 0.32             | 46.93  | 5.58             |
| OK    | 1640   | 230            | 336306           | 5649987              | 2.90   | 0.41             | 48.77  | 6.84             |
| OR    | 311    | —              | 60344            | 2174341              | 1.43   | —                | 51.54  | —                |
| PA    | 508    | —              | 16784            | 1546662              | 3.28   | —                | 302.67 | —                |
| RI    | 86     | —              | 3375             | 101283               | 8.49   | —                | 254.81 | —                |
| SC    | 90     | —              | 27538            | 1074640              | 0.84   | —                | 32.68  | —                |
| SD    | 31     | —              | 27408            | 599912               | 0.52   | —                | 11.31  | —                |
| TN    | 1450   | —              | 467874           | 12428527             | 1.17   | —                | 30.99  | —                |
| TX    | —      | —              | 32688            | 945619               | —      | —                | —      | —                |
| UT    | 795    | 47             | 35765            | 1098218              | 7.24   | 0.43             | 222.28 | 13.14            |
| VA    | 1208   | —              | 122391           | 1120053              | 10.79  | —                | 98.70  | —                |
| VT    | 722    | —              | 227920           | 1505149              | 4.80   | —                | 31.68  | —                |
| WA    | 603    | 13             | 87585            | 1317294              | 4.58   | 0.10             | 68.85  | 1.48             |
| WI    | 3052   | —              | 681714           | 11526773             | 2.65   | —                | 44.77  | —                |
| WV    | 2992   | 86             | 584993           | 9354884              | 3.20   | 0.09             | 51.15  | 1.47             |
| WY    | 115    | —              | 24201            | 409866               | 2.81   | —                | 47.52  | —                |

—Data suppressed by CMS.

excluded states in both analyses that had less than 5% of Medicaid prescriptions covered by FFS, reported not covering Narcan or generic naloxone under FFS Medicaid, reported drug benefit designs, and had data suppressed by CMS. In addition, copay amounts reported as ranges spanning the set cutoffs (eg, $0–$3.90) could not be categorized and were excluded from analysis (Figure 1). The analyses tested for association with a basic simple linear regression (SAS version 9.4; SAS Institute). The use of simple linear regression assumes a linear relationship between outcome and exposure, the residual variance is equal for all exposures, each observation (eg, state) is independent, and for the residual variance of each exposure, the outcome is normally distributed. To assess symmetry and distribution, we calculated the skewness and kurtosis of each outcome. Since most of our outcomes had high values for both, we reran each model as a generalized linear model with robust errors to address the nonsymmetric distribution. We also ran each model as a robust regression to address outliers (Supplemental Table 2).

To avoid excluding states with data suppressed by CMS (eg, quarters with 1–10 naloxone prescriptions dispensed for a given formulation) from analysis altogether, the analysis was repeated imputing prescription dispensings for each NDC in each quarter where data was suppressed. This included imputing additional prescription dispensing in states that were included in initial analysis when NDCs were suppressed in a given quarter. In quarters where an NDC reported 0 dispensings, the input remained 0. For each NDC in each quarter that had data suppressed due to a low number of prescriptions, ranging from 1 to 10, this analysis assumed 5 prescriptions were dispensed. Inclusion and exclusion criteria remained the same, with the only alteration being inclusion of states with data suppressed by CMS. These analyses again tested for association with a basic simple linear regression (SAS version 9.4; SAS Institute).

### Results

**Rates of Naloxone Dispensing by States**

All 50 states and the District of Columbia were included in the analysis. Overall, in 2018, 75,930 prescriptions for Narcan and 4,579 prescriptions for generic naloxone were dispensed (Table 2A). The analysis found wide variability in dispensing...
Figure 1. Analysis inclusion criteria.
rates for Narcan and generic naloxone across different states (no dispensing data for Evzio were identified, due likely in part to suppression and high medication cost).

### Rates of Naloxone Dispensing Among All Prescriptions

The proportion of Narcan prescriptions ranged from 0.13 to 36 per 10000 total prescriptions (Table 2B). The proportion of generic naloxone prescriptions ranged from 0.04 to 9.3 per 10000 total prescriptions. Narcan accounted for a greater proportion of overdose reversal medications in all states except for Delaware and Georgia when compared to generic naloxone. Maryland had the highest Narcan proportion of any state with 36 per 10000 prescriptions, which was over 3-fold higher than the next highest state, Virginia. Mississippi, Kentucky, and Georgia had the lowest Narcan proportion. Delaware had the highest generic naloxone proportion with 9.3 per 10000 prescriptions followed by Maryland with just 1.2 per 10000 prescriptions. Delaware, Maryland, and Colorado had the highest generic naloxone proportion while West Virginia, New York, and Alabama had the lowest.

### Rates of Naloxone Dispensing Among Opioid Prescriptions

Maryland had the highest proportion of Narcan prescriptions compared to all opioid prescriptions of any state with 535 per 10000 while Georgia had the lowest with 2 per 10000 (Table 2B). Missouri had the highest proportion of generic naloxone prescriptions compared to all opioid prescriptions with 18 per 10000 while Alabama had the lowest with less than 1 per 10000. For some states, the proportion of Narcan prescriptions changed relative to other states when calculated as a proportion

### Table 2. Association between copays, coverage limits, and medication dispensing.

| VARIABLES | ALL PRESCRIPTION DISPENSING | | | OPIOID PRESCRIPTION DISPENSING | | |
| --- | --- | --- | --- | --- | --- | --- |
| | COEFF (CI) | P-VALUE | R² | COEFF (CI) | P-VALUE | R² |
| **Narcan** | | | | | | |
| Copay (yes/no) | | | | | | |
| Primary (31 states + DC) | 1.8 (−3-7) | .44 | .020 | −2 (−81-77) | .96 | .0001 |
| Sensitivity (34 states + DC) | 1.5 (−3-6) | .46 | .016 | 4 (−63-71) | .91 | .0004 |
| Copay (higher/lower)* | | | | | | |
| Primary (28 states + DC) | 3.5 (−2-9) | .20 | .061 | 21 (−71-112) | .64 | .008 |
| Sensitivity (31 states + DC) | 2.9 (−2-8) | .21 | .053 | 26 (−52-104) | .54 | .015 |
| Coverage limits (yes/no) | | | | | | |
| Primary (26 states + DC) | −1.2 (−4-2) | .39 | .030 | −28 (−90-35) | .37 | .033 |
| Sensitivity (29 states + DC) | −0.6 (−3-2) | .57 | .012 | −17 (−62-28) | .45 | .020 |
| **Generic naloxone** | | | | | | |
| Copay (yes/no) | | | | | | |
| Primary (10 states) | 0.5 (0.2-0.8) | .009 | .594 | 11 (5-16) | .002 | .718 |
| Sensitivity (19 states + DC) | 0.5 (−0.4-1) | .24 | .076 | 16 (−8-40) | .17 | .100 |
| Copay (higher/lower)** | | | | | | |
| Primary (8 states) | 0.6 (0.2-1) | .017 | .641 | 12 (7-17) | .0008 | .864 |
| Sensitivity (17 states + DC) | 0.5 (−0.5-2) | .32 | .063 | 19 (−8-45) | .15 | .125 |
| Coverage limits (yes/no) | | | | | | |
| Primary (6 states) | −0.1 (−0.8-0.6) | .66 | .054 | −3 (−20-14) | .62 | .066 |
| Sensitivity (14 states + DC) | 0.4 (−2-0.9) | .48 | .038 | −14 (−50-21) | .41 | .054 |

Bold indicates correlations with P-value < .05.
*Narcan cut-off: ⩽$2.00 or >$2.00
**Generic naloxone cut-off: <$1.00 or >$1.00.
of opioid prescriptions rather than all prescriptions. Pennsylvania ranked 15th in dispensing of Narcan as a proportion of all prescriptions but second in dispensing of Narcan as a proportion of opioid prescriptions. Conversely, Vermont ranked ninth in dispensing of Narcan as a proportion of all prescriptions but thirtieth in dispensing of Narcan as a proportion of opioid prescriptions.

**Relationships of Copay to Dispensing**

The first copay analysis evaluated the association between Narcan or naloxone prescribing and existence of any copay. The analysis included 32 states for the Narcan analysis and 11 states for the generic naloxone analysis (Figures 1 and 2). In the Narcan copay cohort, 15 of 32 states had a copay requirement (Table 2). In the generic naloxone cohort, 5 out of 11 states had a copay requirement (Table 2). No relationship was found between copay requirements and dispensing of Narcan (proportion of all prescriptions, CI = −0.4–1, proportion of opioid prescriptions, CI = −8–40) and copay amount (proportion of all prescriptions, CI = −0.5–2, proportion of opioid prescriptions, CI = −8–45) (Table 2).

**Relationships of Coverage Limits to Dispensing**

The first coverage limit analyses included 27 states for the Narcan analysis and 7 states for the generic naloxone analysis (Figure 1). In the Narcan coverage limit cohort, 8 out of 27 states had a coverage limit (Table 2). In the generic naloxone cohort, 3 out of 7 states had a coverage limit (Table 2). No relationship was found between coverage limits and dispensing of Narcan or generic naloxone (Table 2).

When low levels of dispensing were imputed to states with suppressed data, the cohort for coverage limit analysis included 30 states for Narcan (9 had a coverage limit) and 15 states for generic naloxone (5 had a coverage limit). The results did not change.

**Discussion**

The analysis found that the proportion of all prescriptions and of all opioid prescriptions dispensed via Medicaid for Narcan and generic naloxone varied greatly between states in 2018. In addition, state drug benefit designs also varied in copay amounts and coverage limits for these medications. When the broadest cohort of states was analyzed, there was no meaningful relationship between copay or coverage limits and dispensing across states for Narcan or generic naloxone prescribing either as a proportion of all prescriptions or as a proportion of all opioid prescriptions.

States differed in regard to the number of opioid analgesic prescriptions dispensed under FFS Medicaid. Although limited to observational studies, some evidence suggests geographic associations between rates of opioid prescription and opioid-related mortality. Accordingly, states with greater opioid analgesic dispensing should target initiatives to increase naloxone dispensing. Findings from this study demonstrate that states varied widely in regard to the rates of naloxone prescription as a proportion of opioid analgesic prescriptions. While the rate of naloxone prescription as a proportion of patients with an opioid prescription may be a more useful metric in targeting efforts to increase naloxone dispensing, states such as Georgia with just 2.4 Narcan and 6.5 generic naloxone prescriptions per 10,000 opioid prescriptions may signal an opportunity for overdose prevention interventions. Given the inherent risk of overdose with each opioid prescription, it is highly likely that such low rates of naloxone dispensing reflect...
a deficiency in naloxone distribution. While we are not able to explain these findings by differences drug benefit design as was our initial hypothesis, we feel this is an important finding that warrants consideration of other factors that influence distribution, such as barriers at the pharmacy, physician knowledge and willingness to prescribe naloxone, and stigmatization of naloxone that may occur at any step of the process. The substantial variation found in the proportion as well as the absolute dispensing of naloxone across states has implications for public health efforts to reduce the rate of overdose death.

Notably, this proportion does not account for rates of non-prescription opioid use, which is particularly important as individuals using illicit opioids account for the greatest number of opioid overdoses and may be the least likely to obtain naloxone.

Figure 2. (A) Dispensing of Narcan and (B) generic naloxone calculated as a proportion of all prescriptions and as a proportion of opioid prescriptions for states included in primary copay analyses.
directly from the health care system. Additionally, it is hard to interpret the exact proportion of naloxone to opioid prescriptions that would represent sufficient distribution as many patients receive 1 naloxone prescription and do not have to use it while regularly filling long-term opioid prescriptions. Finally, our proportion comparing rates of naloxone dispensation to total opioid dispensation does not highlight specific types of opioid prescriptions that pose the greatest risk for overdose, which may provide a more nuanced understanding of the impact of the interplay between naloxone dispensing, opioid analgesic dispensing, and overdose outcomes.

Maryland appeared to have had the greatest success in providing naloxone or Narcan to its patients receiving opioids through Medicaid fee-for-service. Alternatively, states with data suppressed by CMS represent those with the lowest dispensing of Narcan and generic naloxone amongst FFS Medicaid beneficiaries. Further research should examine what policies and practices are contributing to the results from these states and how these policies translate to opioid overdose related outcomes. One potential point of investigation would be identifying which states mandated co-prescribing of naloxone with high-risk opioid prescriptions. Research has shown that legally mandated co-prescribing may be associated with a substantial increase in naloxone dispensing. Co-prescribing, which requires providers to prescribe naloxone for any patient receiving certain opioid prescriptions, however, does not ensure co-dispensing, when these prescriptions are actually filled and delivered to the patient. It would be interesting to investigate whether there is an association between states with mandatory co-prescribing laws and lower copays or fewer coverage limits.

Other research has found that a low copay is a strong predictor of generic use of certain classes of drugs, notably for statins. The lack of an association between copayments and Narcan use may reflect the fact that the copayments in Medicaid are much lower than the national averages. This discrepancy in co-pay amount can be explained by limits set by Medicaid on out of pocket costs for its beneficiaries, including a $4 copay limit on preferred drugs. Finding a relationship between copay and dispensing for generic naloxone in the smaller cohort was possibly due to the fact that dispensing rates for this formulation were extremely low, which led to confounding due to data suppression in many states. In all states besides Georgia, Narcan was prescribed at a higher rate than generic naloxone. One reason for this finding may be because Narcan is formulated as a preassembled nasal spray that is relatively easy to administer. In 2018, generic naloxone was only available as a nasal atomizer that required additional assembly, which is difficult or intimidating for consumers to use. Additionally, some states (such as West Virginia) cover the generic naloxone medication but do not pay for the nasal atomizer required for its administration, which represents an additional cost that could not be captured by the current analyses.

The lack of association between coverage limits and dispensing of Narcan and generic naloxone may be due to the fact that such limits would reduce total prescribing of these drugs, which may not be reflected in the primary outcome.

Data for generic naloxone were suppressed for 9 states, making up almost half of the states in the cohort for those analyses. CMS suppresses any cell in Medicaid data that contains fewer than 11 observations in order to protect the confidentiality of Medicaid beneficiaries. This is relevant for the analyses as this criterion excluded states with low dispensing, where drug benefit design including copays and coverage limits may be particularly influential in relation to dispensing rates. When adding just 5 prescriptions per suppressed cell for generic naloxone during sensitivity analyses, the significant relationship between copay and dispensing disappeared. The changes in the significance of the results after including of states with suppressed data demonstrates one of the limitations of aggregate state level data. When evaluating policies for drugs with low use rates, the need to eliminate states with data suppressed by CMS may confound analyses, which may limit the overall utility of publicly available datasets. Future studies would benefit from testing different methods to better estimate drug dispensing rates on a state-by-state level for those subject to data suppression.

These results can aid state policymakers, particularly those designing drug benefit elements for FFS Medicaid coverage, because they provide insight into the proportion of prescriptions that naloxone accounts for in each state in 2018. However, insurers must proceed with caution when dictating copay amounts; although no association was found between copay or coverage limits and naloxone dispensing, no states had a copay greater than $4.00, limiting the generalizability of these results to higher copays. The proportion of naloxone prescriptions represents an important metric in determining the efficacy of efforts to expand distribution of naloxone as a means of preventing overdose. Efforts to increase the proportion of naloxone prescriptions should be combined with other evidence-based methods of addressing overdose deaths, such as screening, brief intervention, and referral to therapy (SBIRT) programs, educational programs targeting high-risk populations, and more. This study represents a step toward generating the evidence-base for the impact of formulary design on dispensing for naloxone.

This study has several limitations. First, this study did not account for other factors that may have influenced the dependent variables, such as policies intended to increase naloxone distribution, which are known to influence the rate of naloxone prescription. One factor of particular importance is whether the FFS Medicaid program in a given state covered the nasal atomizer used for administration of generic naloxone, which influences dispensing of this medication. Second, this study could not appreciate all of the distribution of naloxone because it occurs via numerous channels outside of prescription dispensing, such as through overdose prevention programs. Similarly, the estimations of opioid analgesic use fail to capture prescription opioids acquired by Medicaid beneficiaries illicitly,
which may differ state to state. Third, the correction for population using a proportion of total prescriptions to make cross sectional comparisons between states is an imperfect proxy for the number of beneficiaries in each state Medicaid program. Fourth, the use of dispensation as our sole outcome limits the understanding of what factors may be driving our findings. For instance, we are unable to evaluate how provider prescribing practices may differ between states as only prescriptions that are filled enter our database. Finally, these findings do not account for copay exemptions\textsuperscript{13} and other individual factors, which prevents conclusions regarding individual behavior based on state-level data. Future studies assessing out-of-pocket costs on an individual basis may more accurately measure effects of copays on prescription dispensing.

Conclusions

Substantial variation exists between the rates of naloxone dispensing across the US in 2018 Medicaid data. At the state level, copays and coverage limits were not associated with dispensing of Narcan or naloxone. Further research evaluating the impact of different drug benefit designs, and the effect that making certain assumptions may have on association analyses for medications with low dispensing in Medicaid, should be explored to avoid inadvertently increasing out of pocket costs for beneficiaries and thus limiting access to life-saving medications.

Author Contributions

JCM, ASK, and REB conceived of and designed this project. JCM, SMV, and REB performed data collection and analysis. JCM, ASK, SMV, MAF, and REB aided in the interpretation of results and the production and editing of the manuscript.

Supplemental Material

Supplemental material for this article is available online.

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