



RESEARCH REPORT

Naloxone Products and Their Pricing in Medicaid, 2010–18

Trends for Opioid Overdose Reversal Drugs

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Executive Summary

Preliminary data suggests the number of overdose deaths in 2019 surpassed the peak number of overdose deaths that occurred in 2017, and that the COVID-19 pandemic has accelerated the number of overdoses (Ahmad et al. 2020). This underscores the urgent need for policy action to prevent these deaths. Increasing availability of naloxone, the life-saving drug used to reverse opioid overdoses, is critical and can be addressed immediately, particularly in Medicaid, which covers a large share of individuals who have opioid use disorder (Orgera and Tolbert). In this study, we examine Medicaid prescriptions for and spending on naloxone, finding dramatic increases between 2010 and 2018. This may partially owe to new naloxone formulations that offer advantages in administration; for example, needle-free naloxone nasal spray and quick-acting autoinjector naloxone work for people with nasal abnormalities (a substantial share of those with opioid use disorder). Ideally, prescribers could write different naloxone prescriptions for patients depending on each patient's circumstances. However, we find that the autoinjector formulation was not offered in any state Medicaid program in 2018, likely due to the very high prices per prescription for those formulations and the lack of generic equivalents. Here we use Medicaid State Drug Utilization Data (SDUD) for all states and the District of Columbia to examine Medicaid-covered prescriptions, net Medicaid spending on naloxone (adjusted for estimated federal rebates Medicaid programs receive from manufacturers), and net prices per prescriptions. We find the following:

- The number of Medicaid-covered naloxone prescriptions increased dramatically from 3,328 in 2010 to 236,388 in 2018, a 71-fold increase.
- Generic naloxone products (often used in a kit including a nasal spray atomizer attachment) made up 99 percent of the Medicaid naloxone prescription volume in 2010 by prescription volume but fell to 11 percent in 2018. Averaging across all generic naloxone products, rebate-adjusted prices in Medicaid started at \$17 per prescription in 2010 and increased to \$22 in 2018, a 29 percent increase, with substantial price fluctuation for certain products during the period.
- Narcan, the brand-name nasal spray formulation of naloxone, was first reimbursed in Medicaid in 2016. Narcan nasal spray captured the vast majority of the Medicaid naloxone market by 2018, when 89 percent of all Medicaid naloxone prescriptions were for Narcan. Rebate-adjusted prices for a two-pack prescription of Narcan nasal spray decreased by 23 percent between 2016 and 2018, from \$78 per prescription to \$67. Though the US Food and Drug Administration approved a generic formulation in 2018, none were available as of this writing.

- The brand-name autoinjector, Evzio, was first reimbursed in Medicaid at the end of 2014. Evzio prescriptions constituted 12 percent of all naloxone prescriptions in 2015, and 47 percent of Medicaid spending on naloxone products in that year. Rebate-adjusted prices for a two-pack prescription of Evzio varied widely across states and years and between the two National Drug Codes for Evzio products. These prices ranged from -\$34 to \$3,696 between 2014 and 2017. Negative rebate-adjusted prices owe to federal rebates for state Medicaid programs that negotiated deeply discounted prices relative to the average manufacturing price. Data show no reimbursements for the autoinjector naloxone formulation in 2018 in any state Medicaid program after the large price increases in 2017. The company that owns Evzio announced in 2018 that it would offer an authorized generic version of Evzio, but no generic formulation was available as of this writing.
- Our analysis of rebate-adjusted prices confirms previous findings that state Medicaid programs generally negotiate relatively low net prices (GAO 2014). Adjusting for estimated federal rebates reduced net Medicaid spending by 10 to 99 percent per naloxone prescription in 2017 or 2018. This had a major impact on net price trends. For example, in contrast with previous studies examining overall market prices that found the price of Narcan nasal spray did not change price over time (Gupta et al. 2016; Rosenberg et al. 2018), we find rebate-adjusted Medicaid prices fell substantially over our study period.

Opioid overdose is a national crisis, and patients' risks differ. Some overdoses require naloxone to be delivered through the fastest, most effective, and longest lasting injection routes. Some overdoses cannot be treated through nasal cavity absorption. Other overdoses can be treated effectively through slower and shorter-acting absorption into the bloodstream through the nasal cavity. Making various naloxone formulations widely available to people who need it—and at a sustainable price for the Medicaid programs on the front lines of the COVID-19 pandemic—is a critical to solving the opioid crisis. This demands immediate action, because overdoses have accelerated during the pandemic. Medicaid programs across the country are engaged in upstream and downstream policies, including prevention and treatment efforts designed to reduce the need for naloxone. However, harm reduction efforts need to be strengthened to save lives, and this includes increasing access to various life-saving naloxone products at stable, sustainable prices in Medicaid programs. Without new federal policies regulating prices and/or promoting robust price competition, including new generic competition, Medicaid enrollees' options may be limited, which could worsen the overdose crisis.

Naloxone Products and Their Pricing in Medicaid, 2010–18

According to preliminary data for 2019, the number of deaths from drug overdoses in the United States in 2019 was 4.6 percent greater than in 2018, and it exceeded the number of deaths in 2017, the previous year of peak overdose deaths (Ahmad et al. 2020). In 2018, 46,802 people died from a drug overdose attributed to opioids in the United States (Hedegaard 2020), accounting for 69.5 percent of all drug overdose deaths (Wilson 2020). Though opioid overdose has affected many communities for decades, the most recent opioid overdose epidemic started in the 1990s with prescribed opioids, shifted in 2010 to involve heroin, and in 2013 was driven by fentanyl and fentanyl analogs, which can be 10,000 times more potent than morphine (CDC 2020). Many opioid overdose deaths could be prevented if bystanders use naloxone to reverse the effects of an opioid overdose. Naloxone has been used for more than four decades by first responders and emergency department clinicians to reverse opioid overdoses and more recently by laypersons (Nadel 2016), friends and family of people at risk for opioid overdose and other bystanders. Since Medicaid covers a large share of people with opioid use disorder and at risk for opioid overdose (Orgera and Tolbert 2019), naloxone is a critical tool deployed by state Medicaid programs to address the recent opioid epidemic. A recent paper showed that states that expanded Medicaid under the Affordable Care Act dramatically increased their Medicaid-covered naloxone prescriptions in response to the crisis (Frank and Fry 2019). Medicaid-covered naloxone prescriptions were responsible for an estimated 6,692 opioid overdose reversals in 2016 (Frank and Fry 2017).

Naloxone is available in all states and the District of Columbia via a standing order prescription, under which pharmacists can dispense naloxone on request (PDAPS 2017) or without a prescription (Nebraska DHHS 2019).¹ Yet some pharmacists may be unaware of standing orders or unwilling to abide by them (FDA 2019b), particularly those serving publicly insured patients (Egan et al. 2020). Naloxone is not a controlled substance because it is unlikely to cause harm if used improperly, has no abuse potential, and has minimal clinical effects if administered to someone who has not been exposed to opioids (Lynn and Galinkin 2017; NIDA 2017). In addition, despite concerns that naloxone availability might have a “moral hazard” effect, increasing opioid misuse or overdoses, no credible evidence shows that increasing access to naloxone is associated with harm—whereas reducing access to naloxone is associated with harm (Frank et al. 2018).

Naloxone is used in four combinations of product and methods, which have been covered by some or all state Medicaid programs between 2010 and 2018: (1) a generic injectable formulation currently available as a generic in two strengths, 0.4 mg/mL (available in 1 mL or 10 mL vials) or 1 mg/mL (available in 2 mL vials), and commercially available for overdose reversal for almost 50 years; (2) Evzio, a 2 mg autoinjector formulation developed by kaléo Inc. and approved by the FDA in October 2016; (3) Narcan, a nasal spray developed by Adapt Pharma Inc. and FDA approved in November 2015; and (4) the generic injectable 1 mg/mL naloxone formulation (available in 2 mL vials), often administered with a needleless syringe and a nasal spray atomizer (a “naloxone kit”), rather than an injection. The fourth formulation combines the generic injectable product with the atomizer to create an intranasal administration route (Llyod 2014).²

Two brand-name products are no longer manufactured: The Evzio 0.4 mg autoinjector formulation, developed by kaléo Inc. and approved by the FDA in April 2014, stopped being manufactured as of February 2017. An injectable Narcan formulation, developed by Endo Pharmaceuticals Inc. and available in three strengths (0.02 mg, 0.4 mg, and 1 mg), was sold for more than 40 years but discontinued in July 2013. Adapt Pharma Inc. licensed the brand name Narcan from Endo Pharmaceuticals for its nasal spray.

New naloxone formulations are being developed (Strang et al. 2016), particularly ones that create a longer-acting naloxone to avoid repeat-dosing naloxone, which is frequently needed to fully reverse the effects of the highly potent fentanyl derivatives often involved in recent overdoses (US DHHS 2018).

The formulations have different advantages and disadvantages:

- Generic naloxone used with an atomizer is generally the least expensive option. However, research shows it delivers a much lower dose of naloxone than does Narcan nasal spray (Krieter et al. 2019; NIDA 2019). For example, research shows six administrations of generic naloxone with an atomizer are necessary to reach the naloxone blood levels achieved with one spray of Narcan (Krieter et al. 2019). This is especially problematic in the context of the more potent opioids involved in recent overdoses, as described above.
- Narcan nasal spray delivers a highly effective dose, and is a needle-free naloxone product, which eliminates the risk of contaminated needlesticks. This is an important consideration, because many people receiving this medication face higher risks of blood-borne diseases, such as HIV and hepatitis. Narcan is also ready-to-use, unlike the generic intranasal naloxone kits, which require training to assemble. However, Narcan has several limitations. The effects of

naloxone as a nasal spray are slower than those for injectable naloxone, with patients achieving at least 10 breaths per minute 17 minutes after nasal spray dosing, compared with only 8 minutes after injection (Dietze et al. 2019). Therefore, people may be more likely to need additional doses of nasal spray than additional injections. In a small study, 24 percent of patients who received naloxone through a nasal spray needed an additional “rescue dose,” compared with 9 percent of those who received naloxone through injection (Dietze et al. 2019). Lastly, Narcan may not work effectively in people with obstructive nasal pathology, which constitutes about 12 percent of populations experiencing opioid overdose (Weiner et al. 2017). In general, Narcan may not work well for people with many other nasal abnormalities (Ontario HIV Treatment Network 2018).

- Evzio is easy for laypeople to use because of its autoinjector device and because it is quicker-acting than nasal administration. It has been reported to be increasingly necessary because of the rising use of fentanyl and other high-potency synthetic opioids (Wasser 2019). Evzio is also equally effective on people who have nasal abnormalities, unlike nasal spray formulations. The most significant limitation of Evzio has been its high price.

Though community-based naloxone training and distribution programs were first to expand the naloxone use to laypeople, a growing number of naloxone prescriptions are covered by health insurance and filled at retail pharmacies. Prescriptions at retail pharmacies increased 1,170 percent between the fourth quarter of 2013 and the second quarter of 2016 (Jones et al. 2016). Retail pharmacy distribution is especially important in rural areas that may have less robust community training programs (Kerensky Walley 2017). Administration of naloxone to people experiencing overdose by people who are not medical professionals has been shown to safely and effectively prevent opioid overdose deaths (Bazazi et al. 2010). Since 1996, community-based programs have educated and trained a growing number of nonmedical laypeople in the use of naloxone for opioid overdose reversal (Mueller et al. 2015; Wheeler et al. 2015).

With the number of opioid-related overdose deaths in the US remaining high (Hedegaard 2020) and the COVID-19 pandemic further increasing overdose risks, public health agencies have prioritized improving access to and affordability of naloxone within a larger framework of prevention and treatment (Price 2017). Several reports documenting increasing naloxone costs have flagged these products’ costs as a barrier to access (Gupta et al. 2016; Luthra 2017). Another report documents the impact of the price of naloxone on localities’ budgets (Radcliffe 2017). In Baltimore, the 2017 standing order for naloxone resulted in more than 1,200 overdose reversals by laypeople, but the city ran out of funds to purchase the drug, prompting the health commissioner to call for policymakers to reduce

naloxone prices (L. Wen 2017). Concerns about increased spending on naloxone have been reported in other areas, including Washington, DC (Kodjak 2017).

Cost concerns are particularly vexing, because the raw input to naloxone products has been stable since 2011, at around \$0.01 to \$0.02 per milligram, less than one-thousandth of the product's cost (Rosenberg et al. 2018). Thus, calls to expand access to and use of naloxone have often included regulating the pricing of government-funded naloxone (Christie et al. 2017) and allowing over-the-counter purchases (McLemore and Davis 2017) to prevent deaths.

In fiscal year 2017, 46 states' Medicaid programs covered at least one naloxone formulation without prior authorization (Gifford et al. 2017).³ In 2017, 20 state Medicaid programs covered generic naloxone (used with a nasal spray atomizer, which is generally *not* covered by Medicaid⁴) without prior authorization, 42 states covered Narcan without prior authorization, and 10 covered Evzio without prior authorization (Gifford et al. 2017). The correspondence between coverage restrictions in state Medicaid programs and whether the state ever paid for these medications is loose. For example, 49 states and the District of Columbia reimbursed for generic naloxone and Narcan in 2017, and 28 states reimbursed for Evzio in 2017, including some states with coverage restrictions. Three states, Louisiana, Maryland, and Minnesota, dropped Evzio coverage for fiscal year 2018. Of them, Nevada changed Evzio to nonpreferred and may require prior authorization for Evzio going forward (Gifford et al. 2017)—and Maryland and Nevada had some of the highest numbers of Evzio prescriptions.

To date, two studies have examined naloxone pricing and have found price increases ranging from 95 percent to 3,797 percent from 2006 to 2017 (Gupta et al. 2016; Rosenberg et al. 2018). Among the few studies that have examined naloxone pricing, none have examined the price of naloxone in Medicaid. These previous studies found that increased demand for naloxone and limited competition among pharmaceutical companies led to market failures, shortages, and increases in the price of naloxone.

In this report, we assess prescriptions and prices for the full range of naloxone products in state Medicaid programs from 2010 to 2018. This analysis builds on several earlier briefs and methodological appendices (Clemans-Cope 2019; Clemans-Cope, Epstein, et al. 2019, 2020; Clemans-Cope et al. 2017; Clemans-Cope, Lynch, et al. 2019; Clemans-Cope, Winiski, et al. 2020; Lynch et al. 2019, 2020a, 2020b). We present data on Medicaid prescriptions and costs for generic naloxone, Narcan, and Evzio as reported in Medicaid State Drug Utilization Data (SDUD) for all states and DC. In assessing Medicaid costs, we adjust for estimated federal rebates Medicaid programs receive from

manufacturers, which include basic and inflationary rebates,⁵ because these rebates substantially reduce Medicaid spending on outpatient prescription drugs (MACPAC 2019a).

Data and Methods

We use Medicaid State Drug Utilization Data for all states and the District of Columbia to examine Medicaid-covered prescriptions, net Medicaid spending on naloxone (adjusted for estimated federal rebates Medicaid programs receive from manufacturers), and net prices per prescriptions. For these naloxone estimates, we compiled a list of all prescription drugs containing naloxone with a primary indication of use to reverse opioid overdose. We used the National Drug Code Directory,⁶ managed by the FDA, to identify for all substances containing naloxone hydrochloride their nonproprietary or substance name. For this analysis, we include the following drugs (which include drugs no longer on the market): Evzio autoinjector formulations, Narcan nasal spray formulations, Narcan injector formulations (no longer on the market), and generic naloxone injections (including those typically used with an atomizer spray). We exclude drugs containing buprenorphine with naloxone, because this drug combination is used primarily to treat opioid use disorder, and drugs containing naloxone and Pentazocine, which is used primarily to treat pain. We used the US National Library of Medicine DailyMed database⁷ to confirm that the primary indication of use for all included drugs is opioid-overdose reversal. We also included discontinued drugs containing naloxone in the proprietary or nonproprietary name, based on information from the FDA's *Orange Book*,⁸ archived labels from the DailyMed database, and the Wyoming Medicaid NDC to NCPCS crosswalk.⁹

For prescription and rebate-adjusted spending estimates, we report Medicaid program spending and net Medicaid spending adjusted for estimated statutory federal rebates Medicaid receives from manufacturers, which include basic and inflationary rebates. Our methodology of estimating the federally mandated **basic rebate** and **inflationary rebate** in Medicaid programs for outpatient prescription drugs is developed from previous work by Sean Dickson, who used Medicaid SDUD and other sources to estimate the federal Medicaid rebates and cap (Dickson 2019). The federal rebate adjustment methodology we use is described in detail in a separate report (Clemans-Cope, Epstein, et al. 2020).

Estimation of Federal Rebates

This analysis primarily relies on SDUD to estimate the federal Medicaid rebate. SDUD are available in aggregate by 11-digit National Drug Code (NDC), state, quarter, and utilization type (fee-for-service or managed care). As such, we compute the rebate per unit at the national level by drug and quarter and then apply the rebate to quarterly state spending by drug and by utilization type, because claims-level data are not available and this is the smallest unit of data available.

To compute both basic and inflationary federal rebates, we first estimate average manufacturer price (AMP) from data sources shown in previous research to closely approximate AMP, which differs for brand-name and generic drugs. To calculate AMP for most brand-name NDCs, we use Medicaid SDUD. To calculate AMP for most generic NDCs, we use weighted-AMP data from the Affordable Care Act Federal Upper Limits (FUL) data or National Average Drug Acquisition Cost (NADAC) data, the latter of which come from a national survey of retail pharmacies conducted for Medicaid programs (CMS 2013). For remaining NDCs without matches in FUL or NADAC data, we use Medicaid SDUD as AMP. We use average sales price (ASP) data when available, as reported by Medicare, as AMP for brand-name and generic “5i” drugs, which are inhaled, infused, instilled, implanted, or injected. When using SDUD to estimate AMP, we use the total amount spent by Medicaid and non-Medicaid entities.

We calculate the *basic federal Medicaid rebate* for brand-name and generic drugs for all quarters within our study period, 2010 to 2018. For brand-name drugs, this rebate is whichever is greater: (1) 23.1 percent of AMP or (2) estimated AMP minus a best-price estimate. We use Federal Supply Schedule (FSS) prices, published by the US Department of Veterans Affairs, to estimate best price. For generic drugs, the rebate is 13 percent of estimated AMP.

We calculate the *inflationary federal Medicaid rebate* for all study quarters for brand-name drugs. For generic drugs, we only calculate this rebate starting in 2017, when the inflationary rebate for generic drugs took effect under the Bipartisan Budget Act of 2015 (MACPAC 2018a). For each drug in each quarter, we compute the inflationary federal Medicaid rebate as the baseline AMP multiplied by an inflation rate derived from the consumer price index in the baseline quarter.¹⁰ For example, to compute the inflationary rebate for a drug in the first quarter of 2018, we compute the inflation rate using the consumer price index from the baseline quarter to the first quarter of 2018, which is multiplied by the AMP in the baseline quarter. For brand-name drugs, we define the baseline AMP as the average AMP from the first three quarters with prescription counts over five after the drug first appears in SDUD in 1993. For generic drugs, we define the baseline AMP as the AMP in the first quarter with a prescription count over five in which the drug first appears in SDUD, beginning in the

third quarter of 2014, following the Centers for Medicare & Medicaid Services regulation. This calculation results in the inflation-adjusted allowable growth from the baseline AMP.¹¹ If the current AMP is below this amount, the inflationary rebate is zero. However, if the current AMP exceeds the inflation-adjusted allowable growth, the inflationary rebate is computed as $AMP - (baseline\ AMP \times inflation\ factor)$. To calculate the total federal rebate, we add the estimated basic and inflationary rebates and cap the total rebate at the quarterly AMP, per the federal rebate cap specified in the Affordable Care Act.

Though the federal rebate, including both the basic and inflationary amounts, is capped at current AMP, the adjusted price for naloxone, accounting for estimated federal rebates, will decrease the effective price per unit Medicaid pays when the price grows above inflation. Additionally, the adjusted price can actually be *negative* for states that aggressively negotiate for prices below the national average. Negative prices can occur because the cap and the federal basic rebate are based on the current *national* average manufacturer price (where the basic rebate is the greater of either 23.1 percent of AMP or estimated AMP minus a best-price estimate), and the federal inflationary rebate is also based on national prices (both the launch and current prices). Thus, states that negotiate a lower price than the national average may be eligible for a federal rebate amount that exceeds their price, resulting in an estimated rebate-adjusted price that is actually negative.

Key Measures

For this analysis, we examine two measures:

- **Naloxone prescriptions.** These show the number of prescriptions filled and dispensed in outpatient settings, such as pharmacies, and processed as Medicaid outpatient drug claims in fee-for-service or managed-care plans through either the prescription drug or medical benefit. They are further broken down in some cases by *product type* (generic naloxone, Narcan, or Evzio) and NDC.
- **Rebate-adjusted naloxone spending.** This shows the amount spent by Medicaid amount after adjusting for the estimated manufacturer's basic and inflationary rebates for naloxone prescriptions identified in these data.

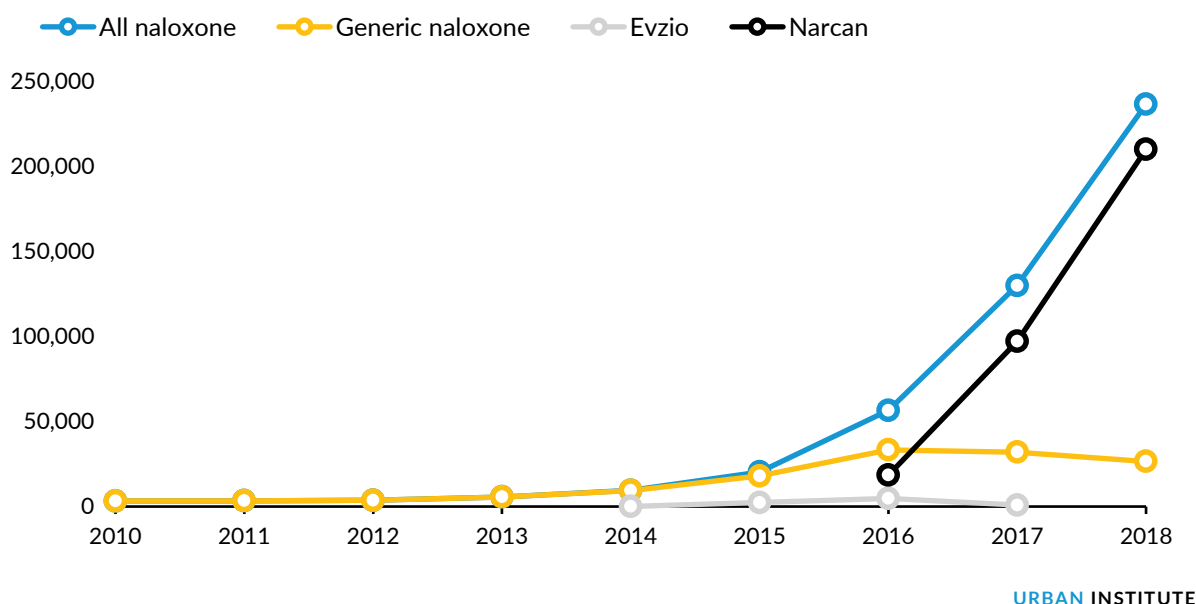
Findings

Annual Naloxone Prescriptions in Medicaid

The number of prescriptions of Medicaid-covered naloxone increased 71-fold between 2010 and 2018, from 3,328 to 236,388 (figure 1).¹² Some of this increased volume owes to Medicaid expansions occurring over that period, which included coverage for single childless adults who may be at higher risk of opioid overdose. Generic naloxone prescriptions (likely used as a naloxone kit, combining a capsule of injectable generic naloxone with a syringe and an atomizer to deliver naloxone nasally) peaked in 2016 at 33,277, and prescriptions of Evzio peaked in 2016 at 4,778. Narcan grew from 18,487 in 2016 to 97,007 in 2017 and to 209,877 in 2018. Quarterly trends highlight the rapid growth of Narcan prescriptions beginning in the second quarter of 2016 (figure A.1). The largest percent increase occurred between 2015 and 2016 (178 percent), with slower growth in the following years (table 1).

FIGURE 1

Annual Number of Naloxone Prescriptions Purchased by Medicaid, by Product Type, 2010–18



Source: Urban Institute analysis of Medicaid State Drug Utilization data from the Centers for Medicare & Medicaid Services, including some unsuppressed data (see Clemans-Cope, Epstein, et al. 2019).

Notes: Naloxone prescriptions are shown together and for the following groups: Evzio autoinjector two-pack prescriptions, including both the 0.4 mg and 2 mg formulations; Narcan nasal spray two-pack prescriptions; and all generic naloxone prescriptions, which include prescriptions of different strengths and doses. The Medicaid State Drug Utilization Data exclude prescriptions written by prescribers at some safety net providers participating in the 340B medication rebate program, such as

federally funded clinics. See the methodological appendices for more details (Clemans-Cope, Epstein, et al. 2019; Lynch, Winiski, and Clemans-Cope 2019).

TABLE 1

Growth in Annual Naloxone Prescriptions, by Product Type, 2010–18

Percent

Years	All naloxone	Generic naloxone	Narcan	Evzio
2010–11	3	3		
2011–12	6	6		
2012–13	56	56		
2013–14	68	67		
2014–15	114	90		3,635
2015–16	178	85		103
2016–17	130	-04	425	-83
2017–18	82	-17	116	-100
2010–18	7,003	697		

Source: Urban Institute analysis of Medicaid State Drug Utilization data from the Centers for Medicare & Medicaid Services, including some unsuppressed data (see methodology).

Notes: Blank cells indicate the column head does not apply. Naloxone prescriptions are shown together and for the following groups: Evzio autoinjector two-pack prescriptions, including both the 0.4 mg and 2 mg formulations; Narcan nasal spray two-pack prescriptions; and all generic naloxone prescriptions, which include prescriptions of different strengths and doses. The Medicaid State Drug Utilization Data exclude prescriptions written by prescribers at some safety net providers participating in the 340B medication rebate program, such as federally funded clinics. See the methodological appendices for more details (Clemans-Cope, Epstein, et al. 2019; Lynch, Winiski, and Clemans-Cope 2019).

Market Shares of Medicaid-Covered Prescriptions for the Most Common Naloxone Products

From 2010 to 2018, the largest market shares of naloxone in Medicaid changed dramatically from generic naloxone to Narcan nasal spray (table 2). Generic naloxone products made up 99.3 percent of the Medicaid naloxone prescription volume in 2010 and fell to 11.2 percent in 2018, whereas Narcan rose from 32.7 percent of naloxone prescriptions in 2016, when it entered the market, to 88.8 percent of such prescriptions in 2018. This shift to Narcan nasal spray happened as naloxone became more available through community- and pharmacy-based distribution by laypersons, rather than primarily from first responders and other professionals (LDI/CHERISH 2019).

The two most common generic naloxone prescriptions are the International Medication Systems (IMS) 1 mg/mL formulation in a 2 mL vial (NDC #76329-3369-01)¹³ and Hospira's 0.4 mg/mL formulation in a 1mL vial (NDC 00409-1215-01)¹⁴—constituted most of Medicaid's generic naloxone prescriptions. The overall Medicaid market share by prescription volume for the Hospira product fell from 26.4 percent in 2010 to 2.2 percent in 2018, and the market share for the IMS product fell from

5.7 percent in 2012 to 5.3 percent in 2018. There are multiple manufacturers of generic naloxone in each year studied, many with very low market shares (data not shown).

Since the FDA approved Narcan in late 2015, Medicaid-reimbursed naloxone prescriptions have increasingly shifted to Narcan (each prescription is a two pack), from 32.7 percent in 2016 to 74.7 percent in 2017 and to 88.8 percent in 2018. Evzio (each prescription is a two-pack), marketed under two NDCs,¹⁵ made up 11.6 percent of all naloxone prescriptions in 2015 and 8.5 percent of prescriptions in 2016. Such prescriptions constituted less than 1 percent of all naloxone prescriptions in Medicaid and had no Medicaid reimbursements in 2018. The Evzio 0.4 mg autoinjector formulation is no longer manufactured as of February 2017.

TABLE 2

Share of Medicaid-Covered Naloxone Prescriptions, by Product Type, National Drug Code, and Year, 2016–18

Percent

Product type/NDC	2010	2011	2012	2013	2014	2015	2016	2017	2018
All generic naloxone	99.3	99.6	99.7	99.8	99.2	88.3	58.9	24.6	11.2
Generic 0.4 mg/mL, 1 mL vial	63.6	81.8	80.3	62.9	61.1	44.0	22.9	10.7	5.0
Hospira NDC alone	26.4	49.9	60.2	50.8	49.8	34.2	14.6	5.9	2.2
Generic 0.4 mg/mL, 10 mL vial	6.9	9.5	9.5	5.3	3.5	2.5	1.0	0.5	0.3
Generic 1 mg/mL, 2 mL vial	28.8	8.3	9.9	31.6	34.6	41.8	34.9	13.4	5.9
IMS NDC alone			5.7	15.0	26.1	36.8	31.9	11.8	5.3
Narcan nasal spray 4 mg, two-pack (Adapt Pharma Inc.)							32.7	74.7	88.8
Evzio autoinjector 0.4 mg, two pack (kaléo Inc.)					0.7	11.6	8.5	0.2	
Evzio autoinjector 2 mg, two pack (by kaléo Inc.)								0.4	

Source: Urban Institute analysis of Medicaid State Drug Utilization Data from the Centers for Medicare & Medicaid Services, including some unsuppressed data (see Clemans-Cope, Epstein, et al. 2019).

Notes: NDC is National Drug Code. IMS is International Medication Systems. Blank cells indicate the column head does not apply. Injectable Narcan, packaged by Endo Pharmaceuticals Inc., is not shown because it never makes up more than 0.4 percent of annual prescriptions, and it was discontinued in July 2013. Generic IMS is NDC 76329-3369-01 (Packager: IMS); generic Hospira is NDC 00409-1215-01 (Packager: Hospira); Narcan 4mg two pack of intranasal devices is NDC 69547-0353-02 (Packager: Adapt Pharma Inc.); Evzio 0.4mg two pack of autoinjectors is NDC 60842-0030-01 (Packager: kaléo Inc.); and Evzio 2 mg two pack of autoinjectors is NDC 60842-0051-01 (Packager: kaléo Inc.). Hospira was purchased by Pfizer in 2015. International Medication Systems was purchased by Amphastar Pharmaceuticals in 2016. Adapt Pharma Inc. licensed the brand name Narcan from Endo Pharmaceuticals Inc. and used it for their branded nasal spray. Evzio 0.4 mg is no longer manufactured as of February 2017.

Annual Rebate-Adjusted Medicaid Spending on Naloxone

Adjusting for estimated federal rebates reduced net Medicaid spending substantially. For example, estimated federal rebates reduced net Medicaid spending by 10 to 99 percent per naloxone prescription in 2017 or 2018 (table 3). The inflationary rebate was particularly effective in reducing the net price of the 0.4 mg Evzio autoinjector, as it entered the market relatively low before large price increases, whereas the 2 mg Evzio autoinjector entered the market at a higher price and thus the inflationary rebate had a lesser impact on net price.

State Medicaid programs can save substantially on naloxone spending through federal rebates they receive from manufacturers. The rebate amounts per unit are calculated at the national level and then applied to state spending. In the following example, we show how the rebates are calculated and how they affect Medicaid spending. A Narcan 4 mg two pack of intranasal devices (NDC 69547-0353-02), packaged by Adapt Pharma Inc., had a national average manufacturer's price, or AMP, of \$64 in the first quarter of 2018, where AMP is estimated from Medicaid SDUD and represents the unadjusted price paid by Medicaid. First, we calculate the basic rebate as the greater of 23.1 percent of AMP, which is \$15, or AMP minus a best-price estimate from FSS data, which is \$30. Because the latter computation is greater, the basic rebate equals \$30. Second, we use the baseline AMP (\$64 from the first quarter of 2018) to compute the inflation-adjusted allowable growth, which is \$66. Because the current \$64 AMP does not exceed the allowable growth, the inflationary rebate is zero. We calculate the total rebate per unit as the sum of the basic and inflationary rebates (\$30), which reduces the national AMP by 46 percent. Applying these rebates to an example state Medicaid program in the first quarter of 2018, Indiana's Medicaid program spent \$93,424 on 1,148 two-pack prescriptions of Narcan (data not shown). This unadjusted spending comes out to \$65 per unit (31 cents higher than the national average price per unit). Because the rebate amount per unit calculated at the national level is applied to state spending, Indiana received a total rebate of \$42,861, equal to \$30 per unit (the exact value is \$29.60) for 1,148 prescriptions. This rebate reduced total state Medicaid spending by 45.9 percent, to \$50,563, and reduced the price per unit of Narcan to \$35.

TABLE 3

Unadjusted and Rebate-Adjusted Spending per Medicaid-Covered Naloxone Prescription, by Product Type and National Drug Code for Latest Year the Product Was Reimbursed by Medicaid

Product Type	Year	Unadjusted price (\$)	Rebate-adjusted price (\$)	Percent reduction
All generic naloxone	2018	29	22	26
<i>Generic .4 mg/mL, 1 mL vial</i>	<i>2018</i>	<i>13</i>	<i>3</i>	<i>75</i>
Hospira NDC alone	2018	12	6	44
<i>Generic .4 mg/mL, 10 mL vial</i>	<i>2018</i>	<i>103</i>	<i>68</i>	<i>33</i>
<i>Generic 1 mg/mL, 2 mL vial</i>	<i>2018</i>	<i>39</i>	<i>35</i>	<i>11</i>
IMS NDC alone	2018	40	36	10
Narcan nasal spray 4 mg, two pack (Adapt Pharma Inc.)	2018	125	67	46
Evzio autoinjector 0.4 mg, two pack (kaléo Inc.)	2017	4,354	27	99
Evzio autoinjector 2 mg, two pack (kaléo Inc.)	2017	4,815	3,696	23

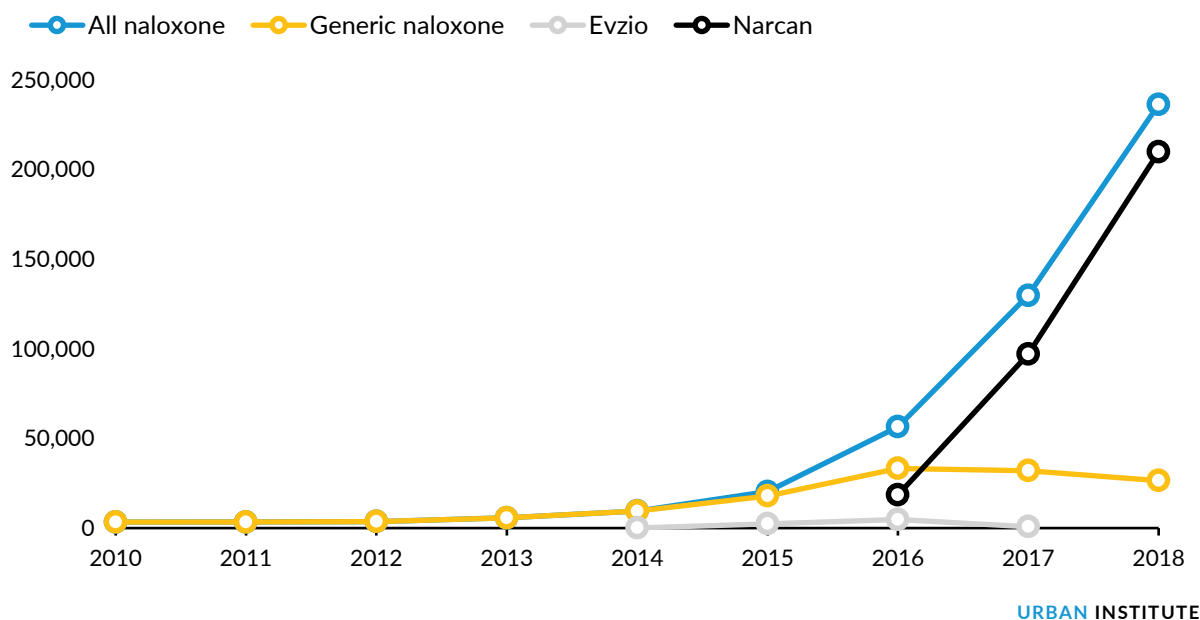
Source: Urban Institute analysis of Medicaid State Drug Utilization Data from the Centers for Medicare & Medicaid Services, including some unsuppressed data (see Clemans-Cope, Epstein, et al. 2019).

Notes: NDC is National Drug Code. IMS is International Medication Systems. Injectable Narcan, packaged by Endo Pharmaceuticals Inc., is not shown because it never makes up more than 0.4 percent of annual prescriptions, and it was discontinued in July 2013. Generic IMS is NDC 76329-3369-01 (Packager: IMS); generic Hospira is NDC 00409-1215-01 (Packager: Hospira); Narcan 4mg, two pack of intranasal devices is NDC 69547-0353-02 (Packager: Adapt Pharma Inc.); Evzio 0.4 mg, two pack of autoinjectors is NDC 60842-0030-01 (Packager: kaléo Inc.), and Evzio 2 mg, two pack of autoinjectors is NDC 60842-0051-01 (Packager: kaléo Inc.). Hospira was purchased by Pfizer in 2015. International Medication Systems was purchased by Amphastar Pharmaceuticals in 2016. Endo Pharmaceuticals Inc. discontinued Narcan in July 2013. Adapt Pharma Inc. licensed the brand name Narcan from Endo Pharmaceuticals Inc. and used it for their nasal spray. Evzio 0.4 mg is no longer manufactured as of February 2017.

Rebate-adjusted spending on Medicaid-covered prescriptions for reversals of opioid overdose increased dramatically between 2010 and 2018, most notably after 2016 (figure 2). Between 2010 and 2018, Medicaid spending on naloxone products increased 136-fold, rising from \$0.11 million to \$14.8 million. Also over this period, Medicaid spending on generic naloxone products increased 7-fold, from \$0.11 million to \$0.8 million. But the largest increases were Medicaid spending for Narcan nasal spray, which rose from \$1.4 million in 2016 to \$14 million in 2018. For the Evzio autoinjector, spending increased from \$24,000 in 2014 to \$2 million in 2017. Rebate-adjusted spending on Evzio also spiked in the first quarter of 2017 (figure A.2).

FIGURE 2

Annual Rebate-Adjusted Medicaid Spending on Naloxone Prescriptions, by Product Type, 2010–18



Source: Medicaid State Drug Utilization Data and Urban Institute analysis of Medicaid State Drug Utilization Data from the Centers for Medicare & Medicaid Services, including some unsuppressed data (see Clemans-Cope, Epstein, et al. 2019).

Notes: Adjusted-spending includes an estimate of the Medicaid Drug Rebate Program's basic and inflationary rebates. For more information about how this rebate was estimated, see our rebate methodology (Clemans-Cope, Epstein, and Winiski 2020). Naloxone prescriptions are shown together and for the following groups: Evzio autoinjector two pack prescriptions, including both the 0.4 mg and 2 mg versions; Narcan nasal spray two pack prescriptions; and all generic naloxone prescriptions, which include prescriptions of different strengths and doses. The Medicaid State Drug Utilization Data exclude prescriptions written by prescribers at some safety net providers participating in the 340B medication rebate program, such as federally funded clinics. See the methodological appendices for more details (Clemans-Cope, Epstein, et al. 2019; Lynch, Winiski, and Clemans-Cope 2019).

Rebate-Adjusted Medicaid Spending per Naloxone Prescription

Average rebate-adjusted prices across all generic naloxone products, of varying strengths and doses, increased between 2010 and 2018, with substantial price fluctuations in certain products (table 4).

Average rebate-adjusted generic naloxone products started at \$17 per prescription in 2010 and increased by 29 percent, to \$22, in 2018. The rebate-adjusted price of the generic Hospira product grew from \$6 in 2010 to \$16 in 2012 and then returned to \$6 in 2018. The rebate-adjusted price of the generic IMS product grew from \$23 in 2012 to \$36 in 2018, with modest variability over the period. The rebate-adjusted average price of .4 mg/mL 10mL vial products was highly variable between 2010 and 2018, during which the market share dropped to less than 1 percent of Medicaid naloxone prescriptions.

Rebate-adjusted prices for a Narcan prescription decreased by 23 percent, from \$78 per prescription in 2016 to \$67 in 2018. Rebate-adjusted prices for a prescription of the autoinjectable Evzio varied widely across years and between the two NDCs for Evzio products. For Evzio 0.4 mg (NDC 60842-0030-01), which was first reimbursed in Medicaid in 2016, the national average rebate-adjusted price per prescription was -\$34 in 2016. The negative rebate-adjusted price owes to a spike in the price before rebate adjustment, which resulted in a high inflationary rebate. And because of purchasing by states that negotiated lower prices than the national average, the national average rebate-adjusted spending can be negative. kaléo Inc. stopped manufacturing the Evzio 0.4 mg product in February 2017, and it was replaced with the company's more expensive 2 mg product. Evzio 2 mg was reimbursed by Medicaid only in 2017, when the national rebate-adjusted price per prescription was \$3,696, far higher than the first Evzio product. In 2018, no state Medicaid program was observed to reimburse for any Evzio product.

TABLE 4

Rebate-Adjusted Spending per Medicaid-Covered Naloxone Prescription, by Product Type, National Drug Code, and Year, 2016–18

In dollars

Product type and NDC by year	2010	2011	2012	2013	2014	2015	2016	2017	2018
All generic naloxone	17	17	28	37	27	29	28	24	22
Generic .4 mg/mL, 1 mL vial	8	10	20	19	16	16	12	10	3
Hospira NDC alone	6	12	16	15	14	14	10	9	6
Generic .4 mg/mL, 10 mL vial	38	64	87	119	105	114	181	53	68
Generic 1 mg/mL, 2 mL vial	32	32	39	57	37	37	34	34	35
IMS NDC alone			23	40	33	36	33	36	36
Narcan nasal spray 4 mg, two pack (Adapt Pharma Inc.)							78	75	67
Evzio autoinjector 0.4 mg, two pack (kaléo Inc.)					388	336	-34	27	
Evzio autoinjector 2 mg, two pack (kaléo Inc.)								3,696	

Source: Urban Institute analysis of Medicaid State Drug Utilization Data from the Centers for Medicare & Medicaid Services, including some unsuppressed data (see Clemans-Cope, Epstein, et al. 2019).

Notes: NDC is National Drug Code. IMS is International Medication Systems. Blank cells indicate the column head does not apply. Injectable Narcan, packaged by Endo Pharmaceuticals Inc., is not shown because it never makes up more than 0.4 percent of annual prescriptions, and it was discontinued in July 2013. Generic IMS is NDC 76329-3369-01 (Packager: IMS); Generic Hospira is NDC 00409-1215-01 (Packager: Hospira); Narcan 4 mg, two pack of intranasal devices is NDC 69547-0353-02 (Packager: Adapt Pharma Inc.); Evzio 0.4 mg, two pack of autoinjectors is NDC 60842-0030-01 (Packager: kaléo Inc.); and Evzio

2 mg, two pack of autoinjectors is NDC 60842-0051-01 (Packager: kaléo Inc.). Hospira was purchased by Pfizer in 2015. International Medication Systems was purchased by Amphastar Pharmaceuticals in 2016. Endo Pharmaceuticals Inc. discontinued Narcan in July 2013. Adapt Pharma Inc. licensed the brand name Narcan from Endo Pharmaceuticals Inc. and used it for their nasal spray. Evzio 0.4 mg is no longer manufactured as of February 2017.

Recent State Variation in Rebate-Adjusted Medicaid Spending per Naloxone Prescription by Product Type

In recent years, the rebate-adjusted amount states pay per naloxone prescription varied widely by type of naloxone and by state Medicaid program (figure 3 and table 4). Some states frequently had low or high rebate-adjusted spending per prescription relative to the national average from 2016 to 2018: Florida, New Jersey, New York, Ohio, and Wyoming often have low spending (hereafter called the lowest states), and Indiana, Maryland, Montana, South Dakota, and Virginia and often have high spending (hereafter called the highest states).

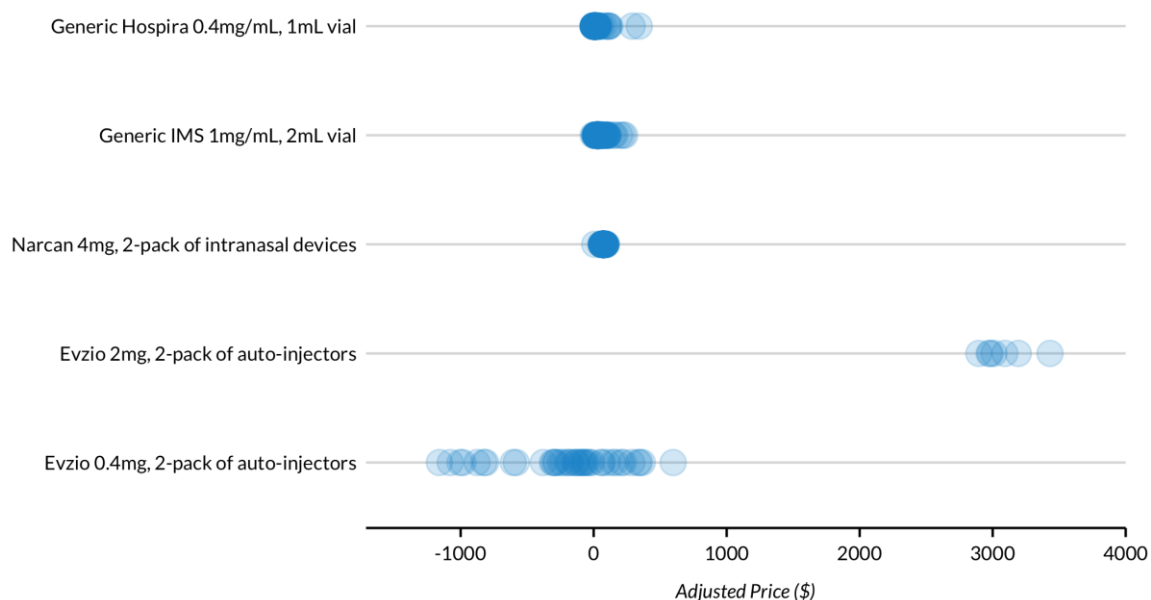
The most common generic naloxone prescriptions from 2016 through 2018, as described above, were Hospira's 0.4 mg/mL, 1 mL vial product (NDC 00409-1215-01) and the IMS 1 mg/mL, 2 mL vial product (NDC 76329-3369-01). Both showed wide variation in rebate-adjusted spending per prescription across states. For one vial of the generic Hospira product, states with lower rebate-adjusted costs per prescription generally had negative rebate-adjusted spending per prescription. Conversely, states with the highest costs often paid more than \$100, or even as much as \$350. States commonly spending the most per prescription for the Hospira product included Alaska, Oklahoma, South Dakota, and Virginia. For a vial of the generic IMS product, the lowest states' prices per prescription were generally half of the national average or less, ranging from -\$4 to \$19, whereas the highest states had prices ranging from \$100 to \$200, or higher. States commonly spending the most per prescription for the IMS product included Indiana, South Dakota, and Virginia. Because of data limitations, we cannot account for pharmacy benefit managers in our spending estimates, though some variation in net prices across states could relate to pharmacy benefit managers.¹⁶

Rebate-adjusted prices for a Narcan prescription varied across state Medicaid programs, but not as much as other naloxone products; Narcan prices generally ranged between \$50 and nearly \$100 during the study period. However, the rebate-adjusted price in New York was \$8 per prescription in 2018, 88 percent lower than the national price.

Rebate-adjusted prices for a prescription of the autoinjectable Evzio varied widely across state Medicaid programs and between the two NDCs for Evzio products. For Evzio 0.4 mg (NDC 60842-0030-01), which was first reimbursed in Medicaid in 2016, the national average rebate-adjusted price

per prescription was -\$33 in 2016 and \$13 in 2017, with the lowest three states having negative rebate-adjusted prices—some lower than -\$1,000. Manufacturing was halted for this product in February 2017, and it was replaced with the costlier product 2 mg product. Evzio 2 mg (NDC 60842-0051-01) was reimbursed by Medicaid only in 2017, when the national rebate-adjusted price per prescription was \$3,700, far higher than the first Evzio product. The lowest state prices for this second Evzio product were \$2,896 (Florida), \$2,972 (Nevada), and \$2,982 (Michigan). The highest state prices were \$3,192 (Virginia), \$3,431 (Utah), and \$6,703 (Maryland). In 2018, no state Medicaid program was observed to reimburse for any Evzio product.

FIGURE 3
Rebate-Adjusted Spending per State, by Product Type and National Drug Code, 2016–18



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Source: Urban Institute analysis of Medicaid State Drug Utilization Data from the Centers for Medicare & Medicaid Services, including some unsuppressed data (see Clemans-Cope, Epstein, et al. 2019).

Notes: IMS is International Medication Systems. Adjusted spending includes an estimate of the Medicaid Drug Rebate Program's basic and inflationary rebates. For more information about how this rebate was estimated, see our rebate methodology. Generic IMS is NDC 76329-3369-01 (Packager: IMS); purchase of atomizer device is not included. Generic Hospira is NDC 00409-1215-01 (Packager: Hospira), Narcan 4 mg two pack of intranasal devices is NDC 69547-0353-02 (Packager: Adapt Pharma Inc). Evzio 0.4 mg two pack of autoinjectors is NDC 60842-0030-01 (Packager: kaléo Inc.). Evzio 2 mg two pack of autoinjectors is NDC 60842-0051-01 (Packager: kaléo Inc.). Hospira was purchased by Pfizer in 2015. International Medication Systems was purchased by Amphastar Pharmaceuticals in 2016. Adapt Pharma Inc licensed the brand name Narcan from Endo Pharmaceuticals Inc. and used it for their branded nasal spray. Evzio 0.4 mg is no longer manufactured as of February 2017. Both Narcan and Evzio are packaged in a carton containing two doses to allow for repeat dosing during a single overdose event, if needed. Prices are shown for one prescription of Evzio (which contains two autoinjectors), one prescription of Narcan (which contains two nasal sprays), and one vial of generic naloxone. This table does not show data for Narcan NDC 63481-0358-10, which has fewer than five prescriptions per year, as well as for 25 other generic NDCs, which together made up 12.2 percent of naloxone prescriptions in 2016, 6.9 percent of naloxone prescriptions in 2017, and 3.6 percent of naloxone prescriptions in 2018.

TABLE 4

Rebate-Adjusted Spending per Prescription and Lowest and Highest Rebate-Adjusted Spending per State, by Product Type, National Drug Code, and Year, 2016–18

Product Type and NDC by Year	Rebate-Adjusted Spending per Prescription						
	National average	Lowest three states			Highest three states		
Generic Hospira product (one vial)							
2016	\$10	-\$2 (WY)	-\$0 (NM)	\$1 (NJ)	\$101 (SD)	\$115 (OK)	\$121 (AK)
2017	\$9	-\$5 (WY)	-\$2 (NE)	-\$1 (NM)	\$80 (AK)	\$113 (VA)	\$289 (OK)
2018	\$6	-\$6 (WY)	-\$3 (NM)	-\$2 (MA)	\$40 (AK)	\$59 (VA)	\$343 (OK)
Generic IMS product (one vial)							
2016	\$33	-\$4 (WY)	\$16 (NJ)	\$19 (NE)	\$97 (MT)	\$195 (SD)	\$217 (VA)
2017	\$36	\$11 (MI)	\$13 (OH)	\$18 (NJ)	\$103 (MN)	\$107 (IN)	\$233 (SD)
2018	\$36	\$6 (NJ)	\$11 (OH)	\$12 (NE)	\$113 (IN)	\$146 (SD)	\$160 (VA)
Narcan/Adapt Pharma Inc. (two pack)							
2016	\$78	\$56 (AL)	\$65 (TN)	\$66 (IA)	\$92 (MT)	\$92 (NE)	\$97 (NH)
2017	\$75	\$54 (AL)	\$55 (IA)	\$60 (SD)	\$85 (MD)	\$86 (ID)	\$90 (MO)
2018	\$67	\$8 (NY)	\$62 (IA)	\$63 (FL)	\$79 (CT)	\$81 (MO)	\$82 (IL)
Evzio/kaléo Inc. 0.4 mg NDC 60842-0030-01 (two pack)							
2016	-\$33	-\$1,160 (NJ)	-\$1,005 (OH)	-\$983 (MA)	\$334 (IN)	\$346 (CA)	\$598 (MD)
2017	\$13	-\$1,078 (NV)	-\$310 (FL)	-\$287 (NC)	\$223 (CT)	\$286 (PA)	\$365 (MD)
Evzio/kaléo Inc. 2 mg NDC 60842-0051-01 (two pack)							
2017	\$3,700	\$2,896 (FL)	\$2,972 (NV)	\$2,982 (MI)	\$3,192 (VA)	\$3,431 (UT)	\$6,703 (MD)

Source: Urban Institute analysis of Medicaid State Drug Utilization Data from the Centers for Medicare & Medicaid Services, including some unsuppressed data (see Clemans-Cope, Epstein, et al. 2019).

Notes: NDC is National Drug Code. IMS is International Medication Systems. Adjusted spending includes an estimate of the Medicaid Drug Rebate Program's basic and inflationary rebates. For more information about how this rebate was estimated, see our rebate methodology. Generic IMS is NDC 76329-3369-01 (Packager: IMS); purchase of atomizer device is not included. Generic Hospira is NDC 00409-1215-01 (Packager: Hospira). Narcan 4 mg two pack of intranasal devices is NDC 69547-0353-02 (Packager: Adapt Pharma Inc). Evzio 0.4 mg two pack of autoinjectors is NDC 60842-0030-01 (Packager: kaléo Inc.). Evzio 2 mg two pack of autoinjectors is NDC 60842-0051-01 (Packager: kaléo Inc.). Hospira was purchased by Pfizer in 2015. International Medication Systems was purchased by Amphastar Pharmaceuticals in 2016. Adapt Pharma Inc. licensed the brand name Narcan from Endo Pharmaceuticals Inc. and used it for their nasal spray. Evzio 0.4 mg is no longer manufactured as of February 2017. Both Narcan and

Evzio are packaged in a carton containing two doses to allow for repeat dosing during a single overdose event, if needed. Prices are shown for one prescription of Evzio (which contains two autoinjectors), one prescription of Narcan (which contains two nasal sprays), and one vial of generic naloxone. This table does not show data for Narcan 63481-0358-10, which has fewer than prescriptions per year, as well as 25 other generic NDCs, which together make up 12.2 percent of naloxone prescriptions in 2016, 6.9 percent of naloxone prescriptions in 2017, and 3.6 percent of naloxone prescriptions in 2018.

Discussion

Our results indicate Medicaid has rapidly increased the number of naloxone prescriptions between 2010 and 2018. We find that, after 2015, retail pharmacy sales of naloxone among those covered by Medicaid increased rapidly after 2015. We also find that Narcan nasal spray, first reimbursed in Medicaid in 2016, constituted most naloxone prescriptions in Medicaid by 2018. This likely gave the manufacturer, Adapt Pharma, significant leverage to increase future prices. One prescription of Narcan nasal spray, though more effective than generic nasal spray kits, is also about three times more expensive for Medicaid than generic naloxone, even after rebates. However, Medicaid programs generally do not cover the atomizer needed to assemble generic naloxone as a nasal spray (Seiler, Horton, and Malcarney 2014).

Our examination of price per prescription suggests trends in Medicaid differ from those of other payers. Previous research found Narcan prices fairly flat and price increases for other naloxone products ranging from 244 percent to 3,797 percent from 2006 to 2017 across all payers (Rosenberg et al. 2018). But our study focuses on rebate-adjusted Medicaid prices, finding that net Narcan prices decreased by 14 percent from 2016 to 2018 and net generic prices in Medicaid generally increased by a much smaller amount (29 percent over our study period). We find that rebate-adjusted Medicaid prices for the 0.4 mg Evzio product decreased by a substantial amount (93 percent) over our study period, but the drug was taken off the market in 2018 and replaced with the costlier 2 mg product, which did not appear to be used in any Medicaid program in 2018. Thus, except for one of the Evzio products, the results confirm other research findings that state Medicaid programs negotiate relatively low prices (GAO 2014). In contrast with previous studies that examined overall market prices and found that the price of Narcan nasal spray remained stable over time (Gupta et al. 2016; Rosenberg et al. 2018), we find that rebate-adjusted Medicaid prices fell substantially between 2010 and 2018. In addition, unlike previous studies that estimated large price increases for some .4 mg/mL and 1 mg/mL generic naloxone products, or for those products overall, our analysis shows that rebate-adjusted Medicaid prices appear to have grown far slower for these products.

This research shows that some Medicaid rebate-adjusted prices are negative because of federal rebates for state Medicaid programs that negotiated deeply discounted prices relative to the average manufacturing price. Negative effective Medicaid prices, though unexpected, have been referred to by the federal government and by pharmaceutical company in testimony (Feng et al. 2020). This appears to signal a willingness among manufacturers to incur a cost in providing the product to Medicaid. In addition, we find large variations in prices across states, including very high prices per prescription for

the autoinjector Evzio. Because these high prices were followed by the elimination of Medicaid reimbursement for Evzio in all states, high prices appear to have limited access to this formulation for Medicaid enrollees who may need it.

Despite our findings that Medicaid programs often negotiate strongly regarding postrebate pricing, failure to provide patients with competitively priced naloxone options for different formulations gives companies a strong negotiating hand and has likely led to price increases that exceed inflation before rebates are computed. In addition, failures in the regulatory process that have limited the emergence of generic versions of Narcan nasal spray and the Evzio autoinjector further limit competition. Together, these limit access to various naloxone formulations at sustainable prices for Medicaid enrollees. Most notably, pharmaceutical companies appear to have leverage to raise or lower prices so that each naloxone formulation is largely or entirely sold by a single company. No generic formulation is available for Narcan or Evzio for any payer (not just Medicaid) as of June 2020, despite the FDA's final approval for a generic version in April 2019 (FDA 2019a) and a 2018 announcement from the company that owns Evzio that said it would offer an authorized generic version of Evzio at a list price of \$178 per two-pack prescription (kaléo Inc. 2018). In addition, though the FDA indicated in 2018 that it would prioritize FDA review of generic drug applications for naloxone, the lack of generics for Narcan and Evzio make clear that more policy action is needed to get generic naloxone products to market that compete with the existing formulations. In the generics market, the dominance of a few companies may have offered leverage to keep drug prices high relative to input prices.

In 2018, the FDA also announced it would explore pathways to over-the-counter (OTC) sale of naloxone. In September 2019, the FDA reviewed efforts to encourage development of OTC naloxone products, which have not resulted in new products (FDA 2019b). Research suggests OTC status could expand retail sales by 15 percent (Murphy et al. 2019). However, this may not be the case for Medicaid enrollees, because only 42 state Medicaid programs cover OTC medications for enrollees, and requiring prescriptions for OTC coverage is a common utilization management tool across Medicaid programs (Coursolle and McCaman 2019). Thus, if naloxone was changed to OTC, rapid policy action would be needed at the state level to ensure access for Medicaid enrollees.

Conclusion

Opioid overdose is a national crisis, and patients' risks differ. Some overdoses require naloxone to be delivered through the fastest and longest-lasting injection routes. Some patients are at risk of

overdoses that cannot be treated through nasal cavity absorption. And some overdoses can be treated effectively through slower, shorter-acting, but highly effective absorption into the bloodstream through the nasal cavity. Ideally, prescribers should be able to write different naloxone prescriptions for patients depending on each patient's circumstances. In addition, the continued overdose crisis suggests access to naloxone needs to increase dramatically. Making various naloxone formulations widely available to the people who need it, and at a sustainable price for Medicaid programs on the front lines of this crisis, is a critical piece of the solution to the opioid crisis that can be addressed immediately.

Medicaid programs across the country are implementing policies focused on prevention and treatment efforts designed to reduce the need for naloxone. However, additional harm-reduction efforts, such as expanding accesses to life-saving naloxone products at stable, low prices in Medicaid, are likely needed to save lives. Without new federal policies regulating prices and/or promoting robust price competition, including for generics, Medicaid enrollees' naloxone options will remain limited, which could worsen the overdose crisis. Future studies should monitor prices of and access to new and existing naloxone products across state Medicaid programs, as well as explore the causes of the observed pricing variation and market failures.

Limitations

Our study has several limitations. First, states may have underreported prescription data in 2010, particularly as they improved reporting of prescriptions in Medicaid managed care plans to the Medicaid SDUD.¹⁷ Second, Medicaid SDUD do not include prescriptions written by prescribers at some safety net providers who participate in the 340B medication rebate program, such as federally funded clinics (MACPAC 2018b; Murrin 2016). Thus, these estimates exclude Medicaid prescriptions and spending that are part of the 340B medication rebate program. Third, several limitations apply to the estimation of federal rebates, as described in a previous report (Clemans-Cope, Epstein, et al. 2020). In addition, supplemental state rebates negotiated by nearly all state Medicaid programs or multistate coalitions (MACPAC 2019b) are not estimated because of a lack of data. Fourth, generic naloxone prescriptions are typically used with an atomizer device purchased separately. However, we do not have access to the prices of these atomizer devices in state Medicaid programs.

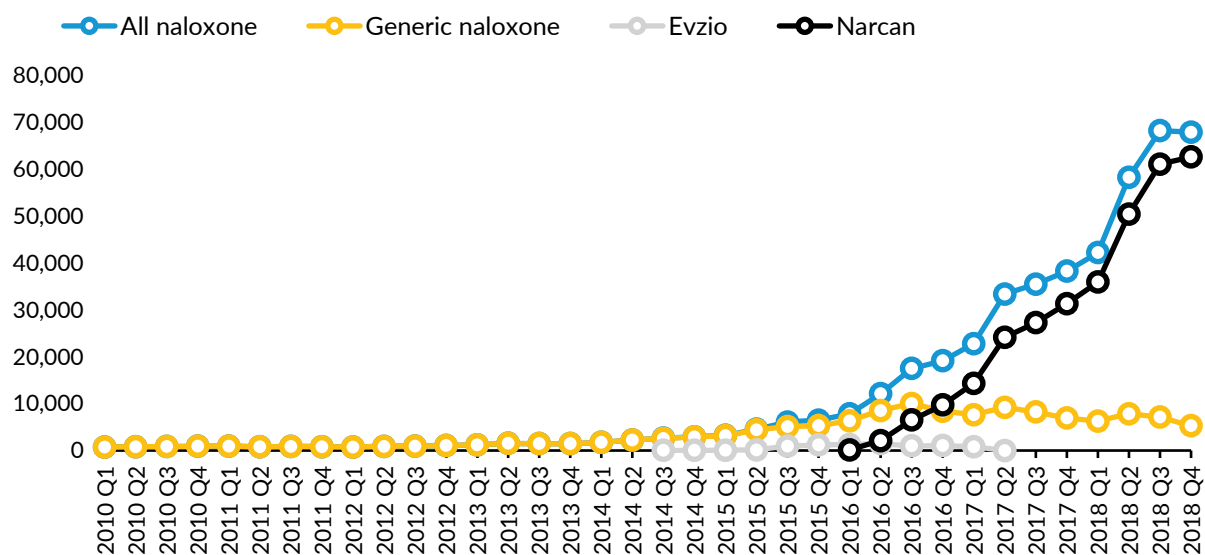
Appendix. Quarterly Prescriptions for and Rebate-Adjusted Spending on Naloxone in Medicaid, 2010–18

Prescriptions

Quarterly trends highlight the rapid growth of Narcan prescriptions beginning in the second quarter of 2016 (figure A.1). Narcan prescription growth drove overall naloxone prescription growth since quarter one of 2016, whereas generic naloxone prescriptions decreased slightly after quarter three of 2016. In the fourth quarter of 2016, the number of Narcan prescriptions exceeded the number of generic naloxone prescriptions for the first time following Narcan's entry into the market, and this divergence continued increasing through 2018.

FIGURE A.1

Quarterly Number of Naloxone Prescriptions Purchased in Medicaid, by Product Type, 2010–18



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Source: Urban Institute analysis of State Drug Utilization data from the Centers for Medicare & Medicaid Services, including some unsuppressed data (see Clemans-Cope, Epstein, et al. 2019).

Notes: Naloxone prescriptions are shown together and for the following groups: Evzio autoinjector two-pack prescriptions, including both the 0.4 mg and 2 mg versions; Narcan nasal spray two-pack prescriptions; and all generic naloxone prescriptions, which include prescriptions of different strengths and doses. The Medicaid State Drug Utilization Data exclude prescriptions written by prescribers at some safety net providers participating in the 340B medication rebate program, such as federally

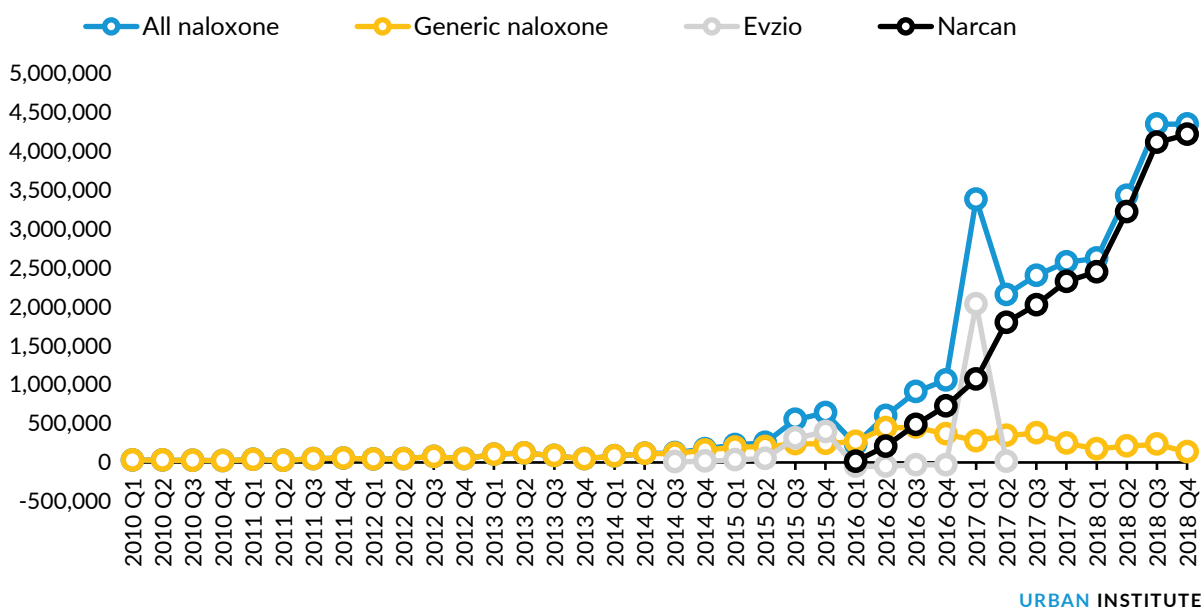
funded clinics. See the methodological appendices for more details (Clemans-Cope, Epstein, et al. 2019; Lynch, Winiski, and Clemans-Cope 2019).

Rebate-Adjusted Spending

Rebate-adjusted spending spiked significantly in the first quarter of 2017, largely because of a sharp increase in spending on Evzio (figure A.2). Rebate-adjusted spending on generic naloxone has been steadily decreasing since quarter three of 2016. Conversely, rebate-adjusted spending on Narcan has increased dramatically since the first quarter of 2016 and accounts for the overwhelming majority of all spending on naloxone prescriptions.

FIGURE A.2

Quarterly Rebate-Adjusted Medicaid Spending on Naloxone Prescriptions, by Product Type, 2010–18



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Sources: Urban Institute analysis of Medicaid State Drug Utilization Data from the Centers for Medicare & Medicaid Services, including some unsuppressed data (see Clemans-Cope, Epstein, et al. 2019).

Notes: Adjusted spending includes an estimate of the Medicaid Drug Rebate Program's basic and inflationary rebates. For more information about how this rebate was estimated, see our rebate methodology (Clemans-Cope, Epstein, Winiski 2020).

Naloxone prescriptions are shown together and for the following groups: Evzio autoinjector two-pack prescriptions, including both the 0.4 mg and 2 mg versions; Narcan nasal spray two-pack prescriptions; and all generic naloxone prescriptions, which include prescriptions of different strengths and doses. The Medicaid State Drug Utilization Data exclude prescriptions written by prescribers at some safety net providers participating in the 340B medication rebate program, such as federally funded clinics. See the methodological appendices for more details (Clemans-Cope, Epstein, et al. 2019; Lynch, Winiski, and Clemans-Cope 2019).

Notes

- ¹ Nebraska's standing order appears slated to expire August 10, 2020 (<http://dhhs.ne.gov/DOP%20document%20library/Naloxone%20Standing%20Order.pdf>), and Idaho and Oregon may not have a standing order but another arrangement that allows pharmacists to dispense naloxone without a prescription (<https://www.safeproject.us/naloxone-awareness-project/state-rules/>)
- ² Though the naloxone atomizer kits are not approved by the FDA, the FDA has stated its approval of generic naloxone distribution through pharmacy sale or community distribution programs, which presumably applies to naloxone kits (FDA 2019).
- ³ The Medicaid programs that did not cover a naloxone formulation in fiscal year 2017 without prior authorization were DC, HI, IL, ME, and TN. Only DC added this coverage for fiscal year 2018.
- ⁴ Research suggests many state Medicaid programs do not cover the atomizer needed for the naloxone kit, or impose burdensome rules for reimbursement (Seiler, Horton, and Malcarney 2014).
- ⁵ Supplemental rebates, in addition to the mandated federal rebates, are negotiated by nearly all state Medicaid programs or multistate coalitions (MACPAC 2019). However, drug-level data and/or rebate formulas are not available to estimate the size of these supplemental rebates.
- ⁶ "National Drug Code Directory," US Food and Drug Administration, accessed July 1, 2020, <https://www.fda.gov/drugs/informationondrugs/ucm142438.htm>.
- ⁷ "DailyMed," US National Library of Medicine, National Institute of Health, accessed July 1, 2020. <https://dailymed.nlm.nih.gov/dailymed/index.cfm>.
- ⁸ "Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations," US Food and Drug Administration, accessed July 1, 2020, <https://www.accessdata.fda.gov/scripts/cder/ob/>.
- ⁹ "NDC Crosswalk." Wyoming Medicaid, accessed July 1, 2020, [https://wymedicaid.acs-inc.com/bulletins/E01NDC Crosswalk 3_10_16.pdf](https://wymedicaid.acs-inc.com/bulletins/E01NDC%20Crosswalk%203_10_16.pdf).
- ¹⁰ We used the "CPI for All Urban Consumers (CPI-U)" series published by the Bureau of Labor Statistics, which can be accessed by entering the series ID "CUUR0000SA0" into the series report query page, <https://data.bls.gov/cgi-bin/srgate>.
- ¹¹ We do not account for the inflationary rebate for a new version of an existing drug (a "line extension") to be calculated using the original drug's baseline AMP. Instead we use a baseline AMP unique to each nine-digit NDC. This may underestimate the inflationary rebate for line extension drugs.
- ¹² Our estimates of the number of units of naloxone purchased by Medicaid are slightly higher than previously published estimates (Frank and Fry 2017), likely because we included naloxone products discontinued in later quarters and because data revisions tend to increase reporting of the most recent quarters.
- ¹³ 1 mg/mL, single-dose 2 ml prefilled syringe. For full information on the IMS generic naloxone product, see <https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=236349ef-2cb5-47ca-a3a5-99534c3a4996>. International Medication Systems was purchased by Amphastar Pharmaceuticals in 2016.
- ¹⁴ 0.4mg/mL, single-dose 1ml prefilled vial. For full information on the Hospira generic naloxone product, see <https://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=8535cc84-ad4a-4d67-8480-fb5a2e3406f8>. Hospira was purchased by Pfizer in 2015.
- ¹⁵ For full information on the Evzio product currently on the market, see <https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=5fbe8d17-a72f-406d-a736-48e61620f9d8>.

¹⁶ We discuss the potential limitations related to PBMs in a previous brief (Clemans-Cope, Epstein, and Winiski 2020).

¹⁷ Treatment in 2010, and less so in 2011, may be understated in some states and DC, mainly because of underreported managed-care data in these and earlier years. Medicaid managed-care organization carve-ins did not have to submit quarterly data or rebates until March 23, 2010. Wen, Hockenberry, and Pollack (2018) determined that by the end of quarter two of 2011, the 21 states using a carve-in approach to prescriptions in managed care had collected the required data and performed data verification checks; DC, which also used the carve-in approach, appeared to have incomplete managed-care data reporting in the first three quarters of 2011 data. For a detailed description of methods, see the separate methodological appendix for this study (Clemans-Cope, Epstein, et al. 2019).

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