Prescription Opioid Use and Medications to Treat Opioid Use Disorder in North Carolina Medicaid: 2013–2018

November 19, 2019

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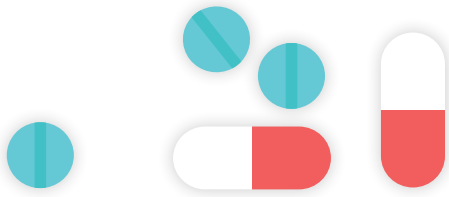
EXECUTIVE SUMMARY

The opioid epidemic has exacted enormous human, social, and financial costs affecting individuals, families, and communities throughout the United States. Here in North Carolina, more than 10,000 people have died from an opioid-related overdose since 2008.[1]

Arnold Ventures supported a study by researchers at Duke University and the University of North Carolina at Chapel Hill of prescription opioids and medications to treat opioid use disorder (OUD) in North Carolina Medicaid claims between 2013 and 2018.

This report describes the results of that study, and builds on the State's Opioid Action Plan, by profiling opioid-related medication utilization and describing populations at risk of opioid-related harms in the North Carolina Medicaid program. NC Medicaid* serves over 2 million low-income adults, children, pregnant women, elderly adults, and people with disabilities throughout the State.

To identify criteria that characterize people at risk of opioid-related harms, we reviewed the scientific literature and consulted medical experts. We then designed this study to apply those criteria to NC Medicaid claims data and investigate trends over time. We also characterized the degree to which Medicaid enrollees diagnosed with opioid use disorder (OUD) receive medications to treat OUD.[2] The North Carolina Department of Health and Human Services approved the use of NC Medicaid data for this study.



*Unless otherwise noted, this study is confined to the NC Medicaid population under age 65. Most references to Medicaid enrollees in this report refer to the under-65 population only.

KEY FINDINGS INCLUDE:

Even as more people have been served by NC Medicaid since 2013, fewer NC Medicaid enrollees overall are filling Medicaid-paid opioid prescriptions.*

- In 2013-2014, nearly 1 in 5 of all NC Medicaid enrollees (19%) filled at least 1 opioid prescription. By 2017-2018, that figure dropped to 13%.

In addition to fewer people filling opioid prescriptions, fewer people meet various criteria for opioid-related risk.

- For example, in 2017-2018, the number of NC Medicaid enrollees under age 65 exposed to particularly high doses of prescription opioids was roughly half of what it was in 2013-2014 (from 53,000 to 28,000).

Absolute declines in reported opioid-related overdoses in the NC Medicaid population have been modest.

- In 2013-2014, 1,788 NC Medicaid enrollees under age 65 had a diagnosed, claims-documented overdose, compared to 1,656 in 2017-2018.

While there are some encouraging trends to report, there is ongoing cause for concern and need for action.

- In 2017-2018, over 45,000 people in our study population had a documented diagnosis of opioid use disorder (OUD). This represents an increase of 66% since 2013-2014. This increase is likely due to a combination of an increase in the development of OUD in the population, and increased recognition and diagnosis by the clinical community.
- Moreover, there is a need to manage and support high-risk populations even if the numbers of persons remaining in certain at-risk cohorts have declined.
  - For example, while the number of Medicaid enrollees with a documented opioid overdose has declined by 7% since 2013-2014, 40% of NC Medicaid enrollees with opioid overdoses go on to fill more opioid prescriptions in the year following their overdose.
- In some cases, it is important to bear in mind the potential unintended consequences of the trends we report.
  - A sharp reduction in the number of Medicaid enrollees receiving Medicaid-paid prescription opioids from multiple providers coincides with a period in which the opioid epidemic overall (not specific to NC Medicaid) has shifted to illicit opioids like heroin and non-medical fentanyl.[3] While policies enacted by governments at all levels and greater vigilance and coordination on the part of clinicians can reduce the supply of opioids in the formal health system, it is less clear what effect this may have on persons accessing such medications outside the formal health system or illicit opioids.
  - Similarly, it is important to balance reductions in high-dose opioid exposure with the need for effective pain relief among persons who depend on prescription opioids to maintain quality of life. For example, some individuals suffering from intractable chronic pain may need ongoing access to prescription opioids, or would benefit from a slow transition from opioids to other pain management approaches, rather than rapid dosage reductions that can result from the introduction of strict limits on opioid prescriptions.

*This study evaluates Medicaid-paid opioid prescriptions. We cannot observe opioid prescriptions which were written, but never dispensed, nor can we observe prescriptions for which enrollees paid cash out of pocket instead of using their Medicaid coverage. We reiterate this by using the phrase "Medicaid-paid opioid prescriptions" in various places throughout this report, but even when it isn't specified, all references to "opioid prescriptions" refer only to prescriptions that were actually dispensed to an enrollee and paid for by NC Medicaid.

Our main finding relates to gaps in the provision of medications for treatment of OUD for the growing number of NC Medicaid enrollees with a diagnosis of OUD.

- Medications for the treatment of OUD have been consistently demonstrated in the scientific literature to reduce nonmedical opioid use, improve health and quality of life, and prevent overdose and death.[2, 4, 5, 6]
- While more Medicaid enrollees are accessing medications for treatment of OUD, there is an ongoing gap between the number of people who have OUD and the number of people who receive treatment for it.
- In 2017, among persons with a diagnosis of OUD, 41% received at least 1 instance of a medication to treat OUD.[2]
- Among adults diagnosed with OUD who started treatment in early 2017 with medication, 48% received medication for at least 6 consecutive months, the period that the scientific literature suggests could be the minimum time necessary for patients to derive substantial benefit from them.[7, 8]

Overall, there is important progress to report along with ongoing cause for concern and need for action. As the opioid epidemic evolves, it is increasingly important to devote attention to harms associated with use of heroin and other illicit substances. As awareness of OUD (stemming from prescription or illicit opioids) grows, there is a concomitant need to focus on efficient and effective methods to help people get and stay on evidence-based, long-term treatment.

INTRODUCTION

The opioid epidemic has exacted enormous human, social, and financial costs affecting individuals, families, and communities throughout the United States. Between 1999 and 2017, almost 400,000 people died from an overdose involving a prescription or illicit opioid.[3] Drug overdose is now the leading cause of accidental death in the United States, with opioids being the most common drug contributing to these deaths.[9] The scope, scale, and severity of the opioid epidemic is profound. For the last several years, the opioid epidemic has contributed to a measurable decline in overall life expectancy in the United States.[10]

Here in North Carolina, more than 10,000 state residents have died from a fatal opioid-related overdose since 2008.[1] Thousands more have been affected by the epidemic in less severe but still significant ways.

Policymakers, clinicians, and community leaders have a taken a wide range of steps to address the epidemic. To be sure, there are both successes to acknowledge and build on (e.g., progress in primary prevention) and new, complex challenges to address (e.g., the increasing availability of inexpensive and potent illicit substances, the harms from which are difficult to track and mitigate). Meanwhile, as the epidemic continues to evolve, it also continues to overwhelm medical providers, strain prevention and treatment efforts, and devastate affected families and communities.

The Opioid Action Plan

In 2017, the North Carolina Department of Health and Human Services (NCDHHS) launched a Statewide Opioid Action Plan to prioritize a range of key metrics associated with the State's ongoing opioid crisis and to guide the State's policy response. Components of the Plan included:

- Coordinating the State's infrastructure to tackle the opioid crisis
- Reducing the oversupply of prescription opioids
- Reducing the diversion of prescription drugs and the flow of illicit drugs
- Increasing community awareness and prevention
- Increasing the availability of naloxone, a medicine used to reverse opioid overdose
- Expanding treatment and recovery systems of care
- Measuring the effectiveness of these strategies based on results

In May of 2018, NCDHHS convened over 75 opioid experts from universities, government, and the private sector to identify the most urgent research priorities that, if pursued, could improve efforts to address the opioid epidemic in North Carolina. This report stemmed from that effort, with researchers and policy officials prioritizing the need to track the degree to which at-risk opioid users are receiving safe and effective treatment.

More recently, in 2019, NCDHHS released Opioid Action Plan 2.0. The State's newly updated plan incorporates feedback from partners and stakeholders, as well as actions on the ground at the community level over the last few years. Action Plan 2.0 includes practical strategies that counties, coalitions, and stakeholders can use to fight the opioid epidemic, emphasizing 3 key areas of focus: prevention, harm reduction, and connections to treatment.

With generous support from Arnold Ventures, researchers at Duke University and the University of North Carolina at Chapel Hill have compiled this report to examine trends in opioid-related utilization and outcomes within the North Carolina Medicaid population.

In any given month, NC Medicaid covers approximately 2.1 million people*, including low-income adults, children, pregnant women and women receiving postpartum care, refugees, and people with disabilities. NC Medicaid enrollees live in all of the state's 100 counties.

By profiling opioid-related trends in NC Medicaid over the last several years, this report aims to augment and build on the NCDHHS action plans to broaden understanding and catalyze further targeted actions to combat the ongoing epidemic.

The key objectives of this report are:

1. To characterize utilization of Medicaid-paid opioids in the North Carolina Medicaid population, including the characteristics of enrollees who fill opioid prescriptions
2. To understand trends over time using various evidence-informed definitions to classify risk of adverse outcomes associated with prescription opioids
3. To identify the degree to which Medicaid enrollees with documented opioid use disorder receive evidence-based medications to treat opioid use disorder

*Average monthly enrollment is 2.1 million according to the NC Medicaid Annual Report; in our analysis that relies on 2-year cohort periods, we found that a total of almost 2.5 million unique individuals were covered for any length of time during the 2017-2018 period

METHODS AND BACKGROUND

Study design

This descriptive cohort study uses claims and eligibility data from the NC Medicaid program from 2013-2018 to study opioid use and related trends. In addition to reporting on overall opioid use patterns, we reviewed the scientific literature to identify specific criteria or factors associated with adverse opioid-related health outcomes. We organized these criteria into 6 distinct (but often overlapping) categories representing different types of risk and for each, defined and characterized multiple at-risk "cohorts" (i.e., sub-groups of NC Medicaid beneficiaries meeting certain criteria).

In addition to understanding the subgroup of NC Medicaid enrollees who fill at least 1 prescription opioid in any given 2-year period and over time, this report includes the following categories:

- **CATEGORY 1:** Enrollees with high doses of prescription opioids
- **CATEGORY 2:** Enrollees with risky opioid-related medication combinations
- **CATEGORY 3:** Enrollees with substance use disorders who also filled opioid prescriptions
- **CATEGORY 4:** Enrollees who receive opioid prescriptions from multiple providers
- **CATEGORY 5:** Enrollees with a clinical diagnosis of opioid overdose
- **CATEGORY 6:** Enrollees with a clinical diagnosis of opioid use disorder

In addition to these categories and their associated cohorts, we also assess trends and characteristics of persons receiving medications for the treatment of OUD, which are well-established as effective first-line treatment for OUD.[4] Evidence indicates that, nationally, many individuals with OUD do not receive needed treatment.[4, 8] We examined whether NC Medicaid enrollees with OUD diagnoses received medications for the treatment of opioid use disorder.

To observe meaningful changes over time, we constructed each of the cohorts over three, non-overlapping 2-year time periods, as follows: 2013-2014, 2015-2016 , and 2017-2018. For each 2-year time period, we identified Medicaid enrollees under 65 who were not dual-eligible for Medicare in the overall population and in each defined cohort.

The overall under-65 population is described using each beneficiary's latest enrollment record for the end of each 2-year period, whereas each cohort is defined as of the day they entered the cohort. We also include patient demographics, including age, sex, race, and county of residence. For cohorts with definitions including a requirement that enrollees filled opioid prescriptions, we also describe characteristics of their enrollees' Medicaid-paid opioid prescriptions, including mean dosage and days' supply.

We also incorporated a set of disease comorbidities* to better characterize and understand the populations in each cohort. For example, this method allows us to compare the percentage of NC Medicaid enrollees with prescription opioids in 2017-2018 who also had a diagnosis of depression (15%) to that of the general Medicaid population (5%).

We tracked all-cause hospitalization, all-cause outpatient emergency department (ED) visits, reported unintentional opioid overdoses, and all-cause mortality in the year following the NC Medicaid enrollee's date of entry into each patient cohort. We used common ICD-9-CM and ICD-10-CM diagnosis codes to identify unintentional opioid overdoses and identified hospitalizations and ED visits using institutional and professional claims. We incorporate these outcomes not to imply that various patterns of opioid use "cause" these outcomes, but rather to better understand how the characteristics of enrollees differ between cohorts.

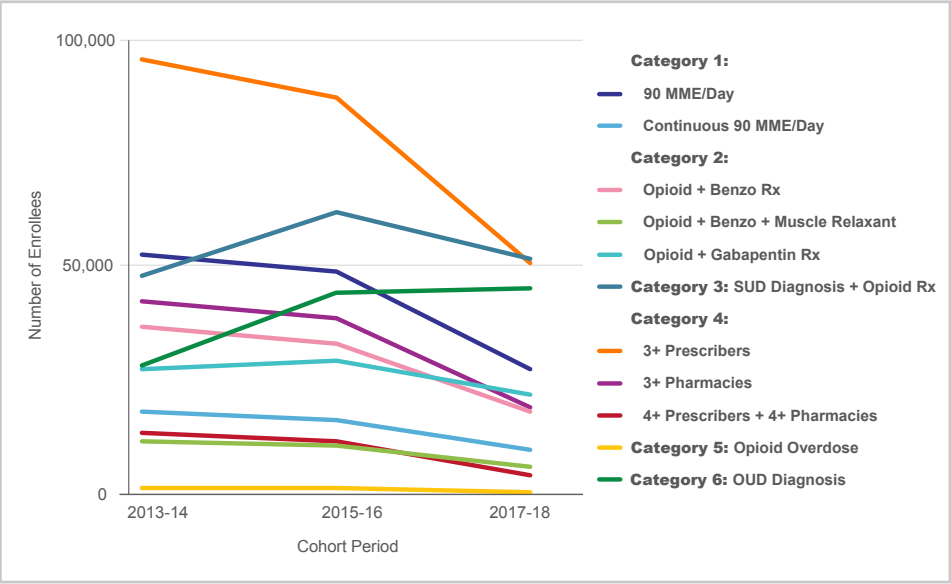
*ICD-9 codes, ICD-10 codes, and references for three comorbidities: depression, mood disorders, and pain, can be found on page A4.

Finally, for the assessment of medications to treat OUD, we identified Medicaid beneficiaries diagnosed with OUD with an expanded definition compared to the OUD cohort in Category 6. We included individuals age 14 or older who received at least 1 administrative diagnosis of OUD or an opioid-specific overdose in the claims data or used either methadone or formulations of buprenorphine used only for OUD treatment. We examined diagnosis and treatment rates by county, and characteristics of buprenorphine prescriptions, as well as characteristics of prescribers.

Background on Cohort Definitions

This section briefly reviews the scientific background and rationale for including these 6 categories of opioid-related risk and the specific patient cohorts we examined for each category.

Figure 1. NC Medicaid Enrollees in Each Cohort Category Over Time*



*The 2017-2018 numbers are subject to change due to ongoing claims adjustments

CATEGORY 1: NC MEDICAID ENROLLEES WITH HIGH DOSES OF PRESCRIPTION OPIOIDS

- People who use higher doses of opioids are at an increased risk of overdose and of developing OUD.[11] The Centers for Disease Control and Prevention (CDC) has suggested that daily dosages "close to or greater than 100 morphine milligram equivalents (MME) per day [are] associated with significant risks."[11] Accordingly, the CDC recommends initiating opioid therapy at low doses and increasing dosage, as needed. The CDC specifically recommends avoiding increasing a patient's opioid dosage to 90 MME/day or above.[11]
- Longer durations of high-dose opioid use also increase overdose and addiction risk. People who have long-term opioid use of 3 months or more are also at higher risk of having an overdose and developing OUD.[11, 12]
- Accordingly, we report on enrollees who fill opioid prescriptions with a dosage of at least 90 MME/day and, separately, enrollees who have prescriptions for 90 MME/day for at least 90 consecutive days.

CATEGORY 2: ENROLLEES WHO FILL PRESCRIPTION OPIOIDS AND OTHER MEDICINES THAT, WHEN TAKEN TOGETHER, ARE KNOWN TO INCREASE RISKS OF OPIOID-RELATED HARMS

- Opioids taken in combination with certain other medications are associated with increased risk of medication-related harms.
- Researchers have found that opioid users who also take benzodiazepines have increased likelihood of overdose and death because both medications cause depression of the central nervous system, and the medications can be additive in causing an individual to stop breathing – the ultimate cause of death in opioid overdoses.[11, 13, 14]
- Likewise, use of opioids in combination with other muscle relaxants, such as carisoprodol (Soma) and cyclobenzaprine (Flexeril), or gabapentin (Neurontin), a drug used to treat seizures and neuropathic pain, has similarly been shown to increase the likelihood of opioid-related overdose and death.[15, 16, 17, 18, 19]
- We report on NC Medicaid enrollees who fill opioid prescriptions concurrently with benzodiazepines and gabapentin, separately, for at least 30 days. Additionally, we describe the subgroup of NC Medicaid enrollees who fill opioids, benzodiazepines, and muscle relaxants concurrently for at least 30 days.

CATEGORY 3: ENROLLEES WITH SUBSTANCE USE DISORDERS AND PRESCRIPTION OPIOIDS

- Substance use disorder (SUD) is diagnosed when the recurrent use of alcohol and/or drugs (including prescription medications) causes clinically significant impairment—such as health problems, disability, and failure to meet major responsibilities at work, school, or home.[20] Evidence suggests that other SUDs are an independent risk factor for opioid-induced respiratory depression.[21, 22, 23] While the relationships between SUD, depression, and other psychiatric disorders are highly complex, comorbidities of SUDs with major depression and other psychiatric disorders are common and can complicate treatment of other disorders.[24, 25, 26]
- Accordingly, we identify subgroups of NC Medicaid enrollees with a diagnosis of SUD who fill at least 1 Medicaid-paid opioid prescription.

CATEGORY 4: ENROLLEES WHO FILL PRESCRIPTION OPIOIDS FROM MULTIPLE PROVIDERS

- Individuals who receive multiple opioid prescriptions from different prescribers and individuals who fill multiple opioid prescriptions at different pharmacies are also at higher risk of opioid overdose.[11, 27] Though visiting multiple prescribers and pharmacies can happen for innocuous reasons, such as people moving from place to place and changing provider relationships, it can also be due to more concerning reasons, such as individuals seeking access to prescription drugs to sell or give to others (diversion), or individuals circumventing opioid dosage limits by obtaining multiple prescriptions - this behavior could be symptomatic of opioid use disorder.
- Accordingly, in this study, we tracked NC Medicaid enrollees who fill prescription opioids from 3 or more prescribers, 3 or more pharmacies, and persons who receive opioids from 4 or more prescribers *and* 4 or more pharmacies, all within 6 months. The 4 or more pharmacies and 4 or more prescribers metric is the basis for a current national quality measure.[28]

CATEGORY 5: ENROLLEES WHO FILL OPIOID PRESCRIPTIONS WHO ALSO HAVE A DIAGNOSIS OF OPIOID OVERDOSE

- "Overdose" refers to the mental and physical symptoms that occur when the level of opioids in someone's body "overwhelms the brain," causes loss of consciousness, and threatens the individual's respiratory drive, sometimes resulting in death – a fatal overdose.[29] People who have experienced an opioid overdose are at a higher risk for a subsequent overdose,[30] and at a higher risk for a fatal overdose.[11, 31] A non-fatal overdose may damage the body even though the individual survives the overdose.[32]
- Accordingly, we examine NC Medicaid enrollees who were diagnosed with an unintentional opioid overdose. Individuals who had an overdose without health care system interaction could not be included in this study.

CATEGORY 6: ENROLLEES WITH A DIAGNOSIS OF OPIOID USE DISORDER

- Opioid Use Disorder (OUD) is defined as "a problematic pattern of opioid use leading to clinically significant impairment or distress."[8] People who have been diagnosed with OUD die sooner than the general population.[33] Persons with OUD who begin using injection drugs such as heroin are at risk for additional health consequences, such as HIV, hepatitis C, and endocarditis, due to infectious agents being introduced to the bloodstream by needles, especially if needles are shared between multiple injection drug users.[34]
- OUD is diagnosed when at least 2 symptoms from a list of 11 are present, with more symptoms leading to classification of moderate or severe OUD. Some of the possible symptoms include "a persistent desire or unsuccessful efforts to cut down opioid use," "craving or a strong desire to use opioids," and "continued opioid use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by opioid use."[35]
- We examined NC Medicaid enrollees with a diagnosis of OUD reported in their NC Medicaid claims.

ENROLLEES WHO RECEIVE MEDICATIONS FOR OPIOID USE DISORDER

In addition to the 6 categories above, we also described enrollees receiving medications for opioid use disorder. Here, we expanded our criteria for OUD as described above, to give a more comprehensive view of the population receiving medications to treat OUD. Treatment for OUD that includes daily medication to reduce opioid cravings and reduce the likelihood of relapse has been shown to be much more effective than OUD treatment without medication.[2]

Limitations

The study has limitations that are important to consider when interpreting its findings. First, the study population only includes NC Medicaid beneficiaries. The results, therefore, may not generalize to different people covered by different sources of insurance (or the uninsured population) in North Carolina or elsewhere. Second, the study excludes Medicaid beneficiaries who are eligible for both Medicare and Medicaid. Due to data limitations, the report is restricted to the population under age 65. Third, with currently available data, we are unable to track prescriptions that Medicaid beneficiaries obtain by paying cash (and not using their Medicaid card). Fourth, we do not have information on those with OUD who have not received a diagnosis from a health care provider, as captured in the medical claims data. This means that our estimates may undercount individuals with OUD not detected and diagnosed by a health care provider.

Finally, the prescription data used to generate this report are derived from claims data, not on observing actual consumption of prescriptions in the real world. Among other implications, this means we cannot capture so-called "diverted" prescriptions or illicit opioid use (e.g., if 1 person who fills an opioid prescription written by his or her doctor then supplies those pills to another person). It is also important to note that data for 2018 are subject to potential updates/adjustments based on claims adjustments and finalization.

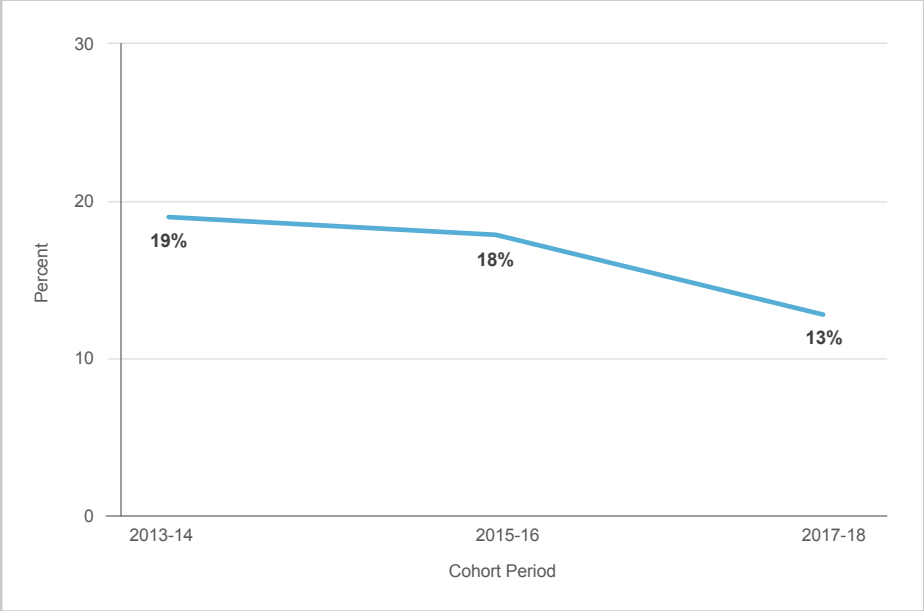
Despite these limitations, we believe and hope this report will yield helpful insight to the evolving opioid epidemic in North Carolina and catalyze or refine targeted actions to address it.

RESULTS

CHARACTERISTICS OF PERSONS WITH AT LEAST ONE OPIOID PRESCRIPTION

- While more people have been enrolled in Medicaid from 2013-2014 to 2017-2018, the number and percentage of NC Medicaid enrollees with opioid prescriptions has declined. During this time period:
  - The overall number of people in our study population has increased by 14%, from 2.1 million unique people with at least 1 enrollment month during 2013-2014 up to almost 2.5 million by 2017-2018 (see appendix).
  - In 2013-2014, nearly 416,000 enrollees in the study population filled at least 1 opioid prescription, representing nearly a fifth (19%) of all Medicaid enrollees in the study population during this time period. By 2017-2018, just about 323,000 NC Medicaid enrollees in the study population filled at least 1 opioid prescription, or 13% of the total study population.

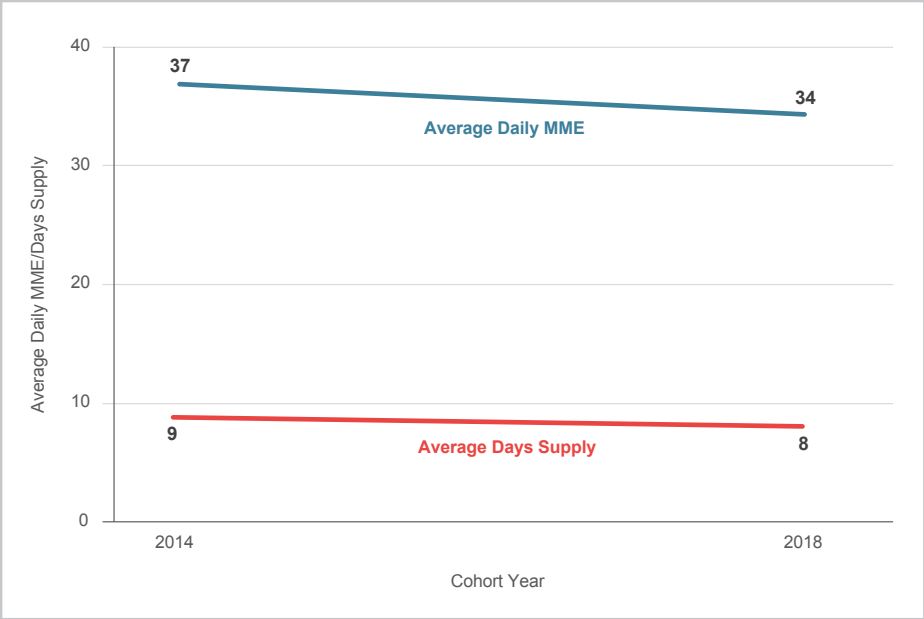
Figure 2. Percentage of NC Medicaid Enrollees with at least One Medicaid-Paid Opioid Prescription



- The population filling any opioids is older than the general Medicaid population in the study population.
  - In 2017-2018, the mean age of NC Medicaid enrollees with at least 1 opioid prescription was 32 years compared to the 20 years in the general NC Medicaid population. This difference has been consistent throughout the study period.
  - More than 3 in 5 NC Medicaid enrollees (61%) in the study population were under 20 years old in 2017-2018. Roughly 6% of the under-20 enrollees filled at least one opioid prescription in that time period. This group of approximately 90,000 enrollees under age 20 accounted for 28% of all NC Medicaid enrollees with at least 1 Medicaid-paid opioid prescription in 2017-2018.
- NC Medicaid enrollees with at least 1 opioid prescription are disproportionately female.
  - In 2017-2018, women accounted for 57% of the NC Medicaid study population and yet accounted for 69% of Medicaid enrollees with at least 1 opioid prescription. This has been consistent across the study period.
- The proportions of NC Medicaid enrollees in the study population with at least 1 opioid prescription mostly reflect the racial composition of the NC Medicaid program overall.
- Not surprisingly, the NC Medicaid enrollees filling opioid prescriptions are much more likely to have pain-related diagnoses in their claims than the general NC Medicaid population (38% versus 8% in 2017-2018).

- Perhaps less predictable, NC Medicaid enrollees with at least 1 opioid prescription are more likely to also have behavioral health conditions.
  - 15% of NC Medicaid enrollees with at least 1 opioid prescription in 2017-2018 also had a diagnosis of a mood disorder, compared to just 4.5% of the NC Medicaid study population.
  - This gap has grown since 2013-2014, when 8% of the NC Medicaid enrollees with at least 1 opioid prescription had a mood disorder, compared to 4.9% of the general Medicaid population.

Figure 3. Characteristics of Medicaid-Paid Opioid Prescriptions

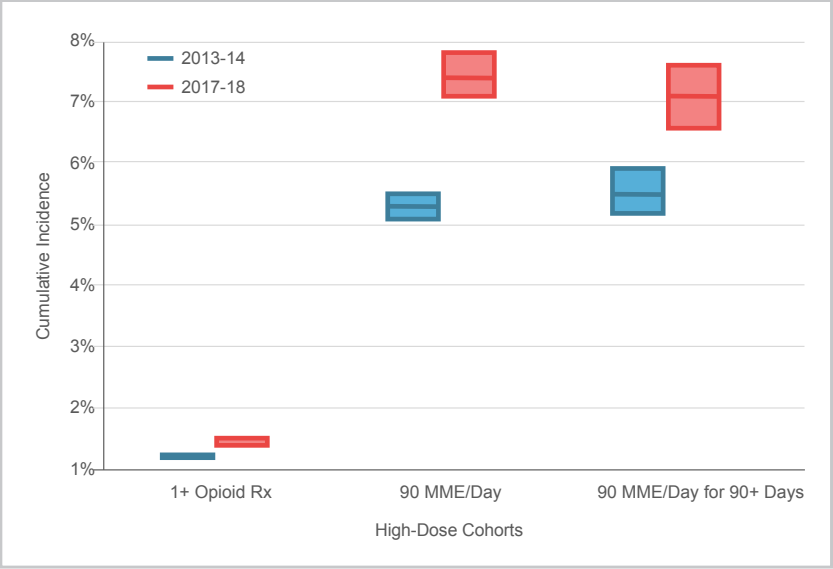


- Many NC Medicaid enrollees with at least 1 opioid prescription visit an emergency department and a substantial number become hospitalized (for any cause).
  - In 2017-2018, 54% of enrollees with opioid prescriptions had an emergency department visit, and 16% had a hospitalization (any cause).
- We also tracked trends in the composition of opioid prescriptions themselves.
  - We identified decreases in both the average daily MME and days' supply over our study period, from 37 MME/day and 9 days of supply in 2013-2014 to 34.3 MME/day and 8.1 days of supply by 2017-2018 (see Figure 3).

CATEGORY 1: ENROLLEES WITH HIGH DOSES OF PRESCRIPTION OPIOIDS

This category includes NC Medicaid enrollees in the study population who have filled at least 1 opioid prescription and who have a total opioid dose of at least 90 MME/day. We separately highlight the subset of these persons having at least 90 MME/day for at least 90 consecutive days.

Figure 4. One-Year Risk of All-Cause Mortality (with Confidence Interval) Among Medicaid Enrollees with High-Dose Opioid Prescriptions



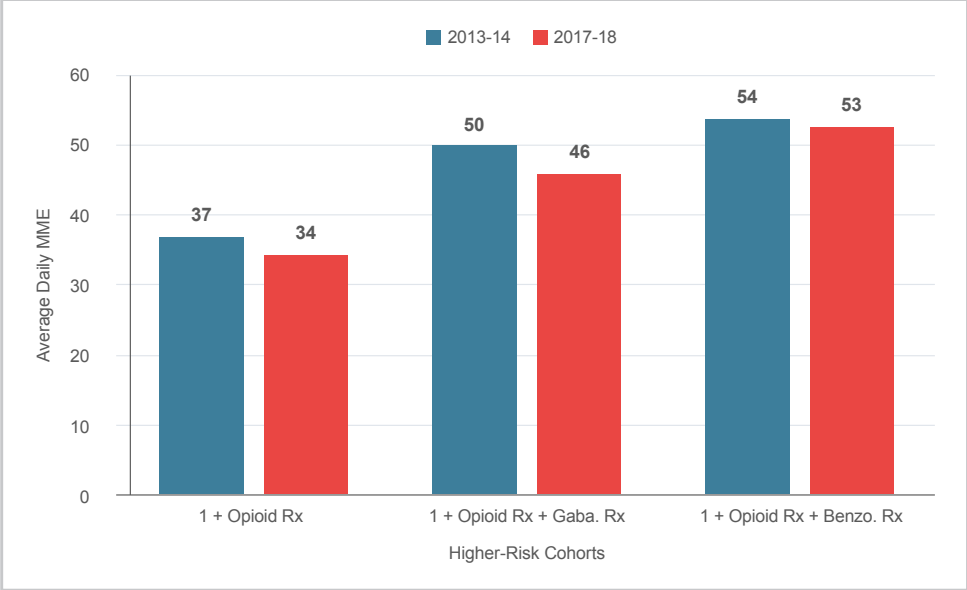
- Among NC Medicaid enrollees with at least 1 opioid prescription, the proportion with high doses of opioids is low and decreasing over time.
  - In 2017-2018, just under 28,000 NC Medicaid enrollees (9% of enrollees with at least 1 opioid prescription) were dispensed high doses of opioids, down from nearly 53,000 enrollees (13%) in 2013-14.
  - In 2017-2018, just over 10,000 enrollees (3% of NC Medicaid enrollees with at least 1 opioid) were dispensed a high dose of opioids for at least 90 days, down from just over 18,000 enrollees (4%) in 2014.
- While there is some incidence of high-dose opioid prescription claims among NC Medicaid beneficiaries under 20 years old, very little of this prescribing is chronic.
  - In 2017-2018, around 3,000 enrollees under 20 years old were dispensed high doses of opioids. This represents about 3.5% of the individuals prescribed any opioids in this age group.
  - Fewer than 50 of these younger NC Medicaid enrollees had more than 90 continuous days at these high doses.
- Half of older NC Medicaid enrollees with any receipt of high-dose opioids are on high doses chronically.
  - Over 15,000 enrollees aged 40-64 years old were dispensed high-dose opioids. This represents about 16% of all opioid users in this age group.
  - Over 50% of these roughly 15,000 NC Medicaid enrollees received 90 or more continuous days of high-dose opioids.
- Perhaps unsurprisingly, enrollees receiving high doses of opioids had higher prevalence of certain medical conditions compared to all opioid users.
  - We identified a pain diagnosis for 66% of NC Medicaid enrollees who had been dispensed a high dose of opioids. This figure was 89% for those with a high dose for at least 90 continuous days, compared to 38% in the group receiving any opioids.
  - We identified a cancer diagnosis for 12% of those who had been dispensed high-dose opioids and for 15% of those with a high dose for at least 90 days, compared to less than 3% in the group receiving any opioids.
  - In 2017-2018, diagnoses of opioid use disorder were 2 to 4 times more common in the subgroup of NC Medicaid enrollees dispensed high-dose opioids—almost 10% in the group dispensed a high dose at least once and almost 19% in those with at least 90 continuous days of high-dose opioids—compared to NC Medicaid enrollees receiving any opioids (5%).

- NC Medicaid enrollees with high doses of opioids are at greater risk of death compared to the overall population of enrollees (see Figure 4). Here, we are assessing death from any cause; these deaths are not necessarily caused by opioids, and could be caused by the disease process that underlies the opioid use, such as cancer.
  - In 2017-2018, all-cause mortality was over 5 times more common among recipients of high-dose opioids, who experienced a mortality rate of 7.4%, than in the overall opioid-receiving population (any dose), for whom the mortality rate was 1.4%.

CATEGORY 2: ENROLLEES WITH RISKY OPIOID-RELATED MEDICATION COMBINATIONS

This category includes NC Medicaid enrollees filling prescription opioids along with other medications that are known to increase risk of adverse health outcomes when used concurrently with prescription opioids.

Figure 5. Average Daily MME Among Enrollees with Risky Opioid-Related Medication Combinations

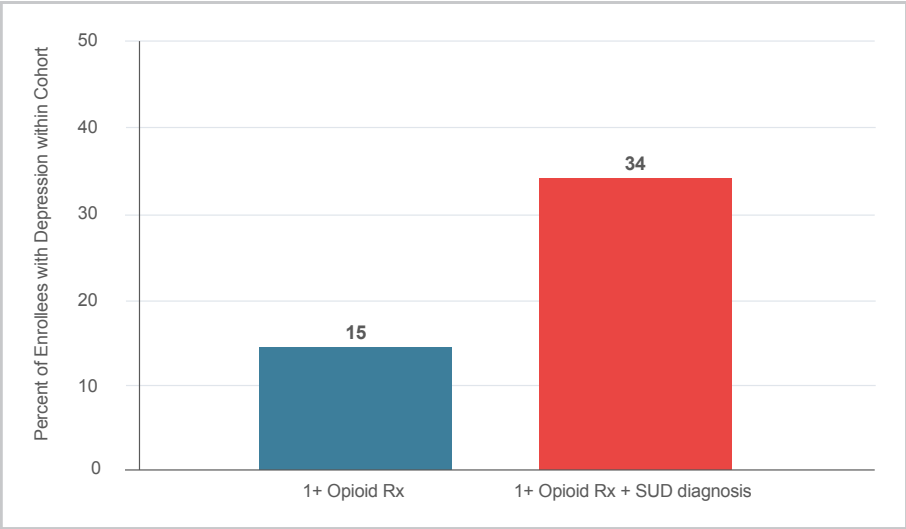


- The proportion of NC Medicaid enrollees with at least 1 opioid prescription who concurrently filled other medications that increase the risk of overdose and death slightly declined or remained stable from 2013-2014 to 2017-2018.
- Of enrollees with at least 1 opioid prescription:
  - The proportion who also concurrently used a benzodiazepine decreased slightly from 2013-2014 to 2017-2018 (from 9% to 6%).
  - The proportion who also concurrently used a benzodiazepine and a skeletal muscle relaxant decreased slightly from 2013-2014 to 2017-2018 (from 3% to 2%).
  - The proportion who also concurrently used Gabapentin remained consistent from 2013-2014 to 2017-2018 (approximately 7%).
- In 2017-2018, NC Medicaid enrollees with risky opioid-related medication combinations were disproportionately older and more likely to be classified as white compared to enrollees with any opioid prescription fills.
- Compared to the NC Medicaid population with at least 1 opioid prescription, 2 to 3 times more of the subgroup with risky opioid-related medication combinations have the behavioral health comorbidities we examined.
- Many NC Medicaid enrollees with risky opioid-related medication combinations are also at risk for other reasons. For example, compared to the population of NC Medicaid enrollees with any opioid prescriptions, the subgroup with risky opioid-related medication combinations also have higher daily opioid dosages and are more likely to receive opioid prescriptions from at least 3 prescribers or pharmacies.

CATEGORY 3: NC MEDICAID ENROLLEES WITH SUBSTANCE USE DISORDERS WHO ALSO FILL OPIOID PRESCRIPTIONS

This category includes NC Medicaid enrollees who had a diagnosis of a substance use disorder (SUD) and also filled at least 1 opioid prescription.

Figure 6. Depression Prevalence Among Enrollees in Selected Cohorts, 2017-18

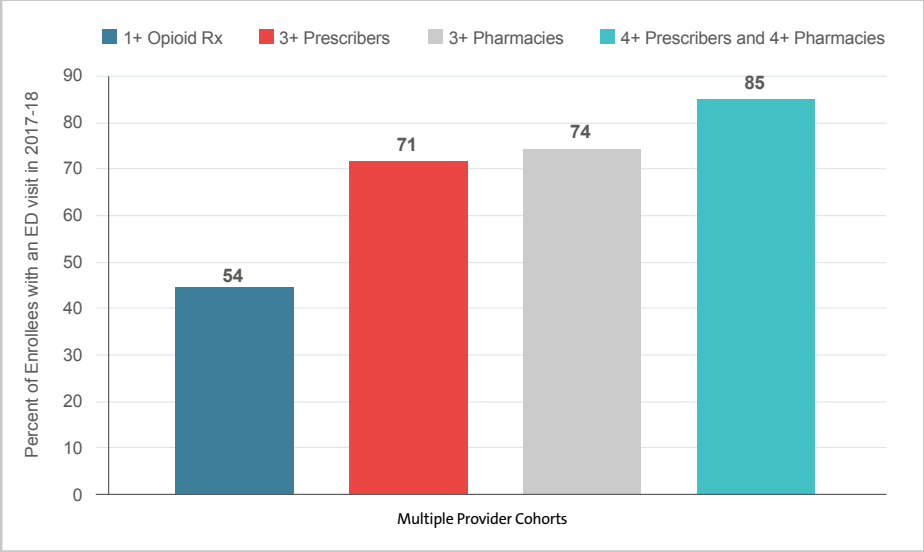


- In several ways, this subgroup differs from both the general NC Medicaid population and the NC Medicaid population with any Medicaid-paid opioid prescriptions.
  - In 2017-2018, NC Medicaid enrollees with a diagnosis of SUD and at least 1 opioid prescription were on average 20 years older than the overall NC Medicaid population (mean 41 vs 20 years).
  - NC Medicaid enrollees with a SUD diagnosis and at least 1 opioid prescription were also about 10 years older than the larger group of NC Medicaid enrollees with Medicaid-paid prescription opioids (mean 41 vs 32 years), and more likely to be white (59% vs 52%).
- The prevalence of SUD among the NC Medicaid study population with opioid prescriptions increased from 12% in 2013-2014 to 16% in 2017-2018. This may reflect the reduction and changing composition of the enrollees with any opioids over the study period.
- Enrollees who have both a SUD diagnosis and Medicaid-paid opioid prescriptions are more likely to have a comorbid behavioral health condition compared to the larger group of NC Medicaid enrollees with opioid prescriptions. For example, the prevalence of depression was two times greater among enrollees with both a SUD diagnosis and opioid prescriptions (34% vs 15%).
- A pain diagnosis was much more common among those with both a SUD diagnosis and opioid prescriptions compared to all enrollees with Medicaid-paid opioid prescriptions (61% vs 38%).
- Various poor outcomes among those with both a SUD diagnosis and opioid prescriptions were more common compared to those outcomes in all enrollees with Medicaid-paid opioid prescriptions in 2017-2018.
  - Higher incidence of unintentional opioid overdose (1.2% vs 0.3%).
  - Higher incidence of death from any cause (3.8% vs 1.4%).
  - Higher incidence of outpatient ED visits from any cause (71% vs 54%).

CATEGORY 4: NC MEDICAID ENROLLEES WHO RECEIVE OPIOIDS FROM MULTIPLE PROVIDERS

This category includes NC Medicaid enrollees receiving opioid prescriptions from multiple sources: from 3 or more prescribers, 3 or more pharmacies, or at least 4 prescribers *and* at least 4 pharmacies.

Figure 7. All-Cause Emergency Department Visit Rates Among Enrollees in Multiple Provider Cohorts, 2017-18

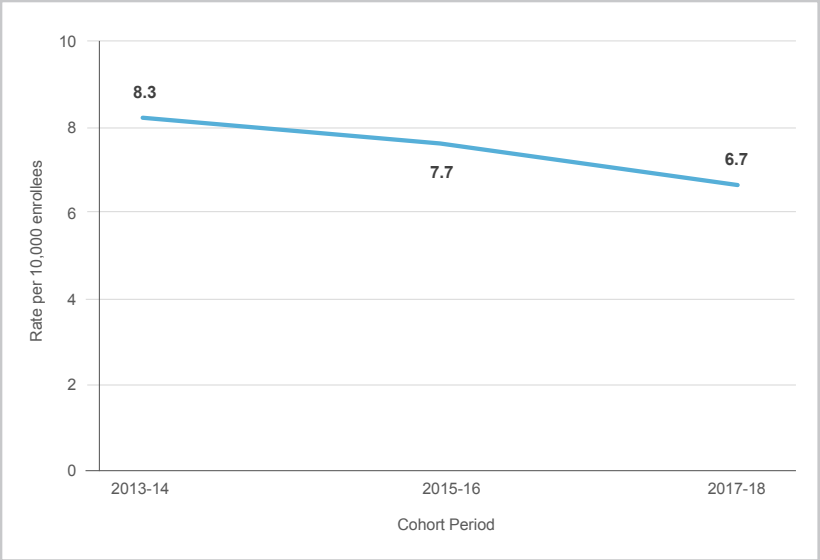


- The number of NC Medicaid enrollees receiving prescription opioids from multiple providers has dropped sharply over time. In 2017-2018:
  - Just over 51,000 NC Medicaid enrollees (16% of enrollees with any opioid prescription) received opioids from 3 or more prescribers, down from over 95,000 enrollees (23% of enrollees with any Medicaid-paid opioid prescriptions) in 2013-2014.
  - Nearly 20,000 enrollees (6% of enrollees with any opioid prescriptions) received opioids from 3 or more pharmacies, down from nearly 43,000 enrollees (10% of enrollees with any opioid prescriptions) in 2013-2014.
  - Under 4,000 NC Medicaid enrollees (1% of enrollees with any opioid prescriptions) received opioids from more than 4 or more prescribers and from 4 or more pharmacies, down from over 13,000 enrollees (3% of enrollees with opioid prescriptions) in 2013-2014.
- Medicaid enrollees who receive opioid prescriptions from multiple providers are more likely to have a diagnosis of pain or depression compared to the larger group of NC Medicaid enrollees with any Medicaid-paid opioids. For example, in 2017-2018:
  - Approximately 75% of NC Medicaid enrollees who received opioids from at least 3 different prescribers had a diagnosis of pain compared to 38% in the larger group of NC Medicaid enrollees with any opioids.
  - Similarly, 30% of NC Medicaid enrollees who receive opioids from at least 3 different prescribers have a diagnosis of depression compared to 15% in the larger group of NC Medicaid enrollees with any opioids.
- NC Medicaid enrollees with opioid prescriptions are provided by multiple prescribers or pharmacies are also 3 to 4 times more likely to have a diagnosis of opioid use disorder.
  - The incidence of opioid use disorder among NC Medicaid enrollees was 12% for those who received opioids from 3 or more prescribers, 16% for those who received opioids from 3 or more pharmacies, and 20% for those who received opioids from at least 4 prescribers and at least 4 pharmacies, compared to 5% among the enrollees with any Medicaid-paid opioids.
- NC Medicaid enrollees with opioids prescribed or dispensed by multiple providers are also more likely to have emergency room visits for any cause.
  - In the year following identification as someone receiving opioids from multiple providers, the percentage of enrollees with an emergency room visit for any cause was 71% (3 or more prescribers), 74% (3 or more pharmacies), and 85% (more than 4 prescribers and more than 4 pharmacies), compared to 54% among those with any Medicaid-paid opioids.

CATEGORY 5: ENROLLEES WITH CLINICAL DIAGNOSIS OF OPIOID OVERDOSE

This category includes NC Medicaid enrollees who had a diagnosed unintentional prescription opioid overdose.

Figure 8. Diagnosed Opioid Overdoses in NC Medicaid



- Opioid overdose diagnoses in NC Medicaid have remained relatively stable from 2013-2014 to 2017-2018.
  - There have been about 1,700 opioid overdoses in NC Medicaid in each of the time periods in this study.
- Demographic distributions in the opioid overdose population differ from the general NC Medicaid study population.
  - The average enrollee with an opioid overdose was 36 years old in 2017-2018 compared to a mean age of 20 years in the overall Medicaid population.
  - Enrollees with a diagnosis of opioid overdose are more likely to be white than the general Medicaid population (73% versus 51% in 2017-2018).
- The composition of enrollees in this cohort has changed over time, especially in relation to comorbid conditions.
  - The likelihood that enrollees with opioid overdoses had a diagnosis of schizophrenia decreased from 10% in 2013-2014 to 6% in 2017-2018.
  - Similarly, the prevalence of mood disorders has decreased in this cohort, from 50% in 2013-2014 to 36% in 2017-2018.
- Outcomes among this cohort are concerning:
  - The cumulative incidence of all-cause mortality has increased, from about 8% in 2013-2014 to 10% in 2017-2018.
  - Although we see a decline in the cumulative incidence of subsequent diagnosed unintentional synthetic overdoses (10% in 2013-2014 versus less than 4% in 2017-2018), there has been a 6-fold increase in the cumulative incidence of subsequent diagnosed unintentional heroin overdoses (from 1% in 2013-2014 to over 6% in 2017-2018).
  - There has also been a sharp increase in the cumulative incidence of endocarditis infections: from 0.5% in 2013-2014 to nearly 2% in 2017-2018.
- The cumulative incidence of individuals filling a Medicaid-paid opioid prescription after a diagnosed opioid overdose was 40% in 2017-2018.

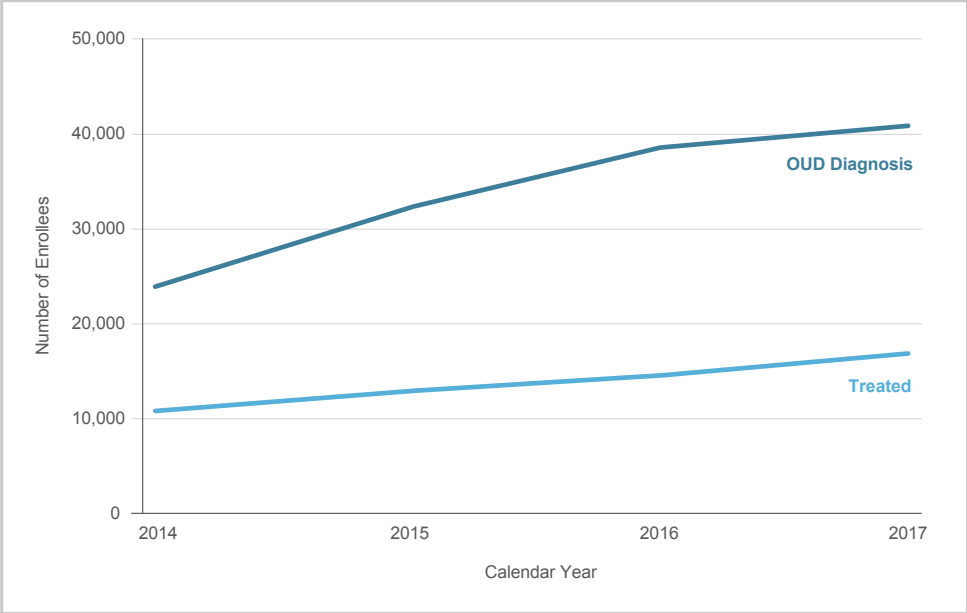
CATEGORY 6: ENROLLEES WITH A CLINICAL DIAGNOSIS OF OPIOID USE DISORDER

- This category includes enrollees who have a diagnosis of OUD reflected in their NC Medicaid claims.
  - The number of NC Medicaid enrollees with a reported diagnosis of OUD went from just over 27,000 (around 1% of the total Medicaid population) in 2013-2014 to over 45,000 (almost 2% of the Medicaid population) in 2017-2018. This represents an increase of 66% during our study period, most of which occurred between the 2013-2014 and 2015-2016 periods. This may reflect both rising underlying risk of the population and heightened awareness of opioid-related harms, as well as growing commitment of providers to document OUD.
- The demographic composition of enrollees with OUD is different than the overall study population.
  - NC Medicaid enrollees with an OUD are older (mean age of 38 versus 20), more likely to be white (73% versus 51%) and more likely to be female (68% versus 57%) compared to the overall Medicaid population.
- There is a greater comorbidity burden among enrollees with OUD.
  - In 2017-2018, compared to the general Medicaid population, enrollees with a diagnosis of OUD had a higher prevalence of mood disorders (30% versus 5%), schizophrenia (4% versus 1%), depression (29% versus 5%), and pain (46% versus 8%).
- We also examined the cumulative incidence of selected outcomes among enrollees with OUD:
  - The incidence of all-cause mortality has remained stable between 2.2 and 2.4% over the study period.
  - Although the incidence of unintentional opioid overdose has decreased over time, from 1.8% in 2013-2014 to 1.3% in 2017-2018, the incidence of unintentional heroin overdose has more than doubled from 0.6% in 2013-2014 to 1.4% in 2017-2018.
  - Similar to the rise in heroin overdose events, the incidence of endocarditis infections among this cohort has tripled from 0.4% in 2013-2014 to 1.2% in 2017-2018.

ENROLLEES WHO RECEIVE MEDICATIONS FOR OPIOID USE DISORDER

As noted above, the number of NC Medicaid enrollees with OUD diagnoses has risen steadily in recent years. In this section, we examine the degree to which persons diagnosed with OUD receive medications used to treat it.*

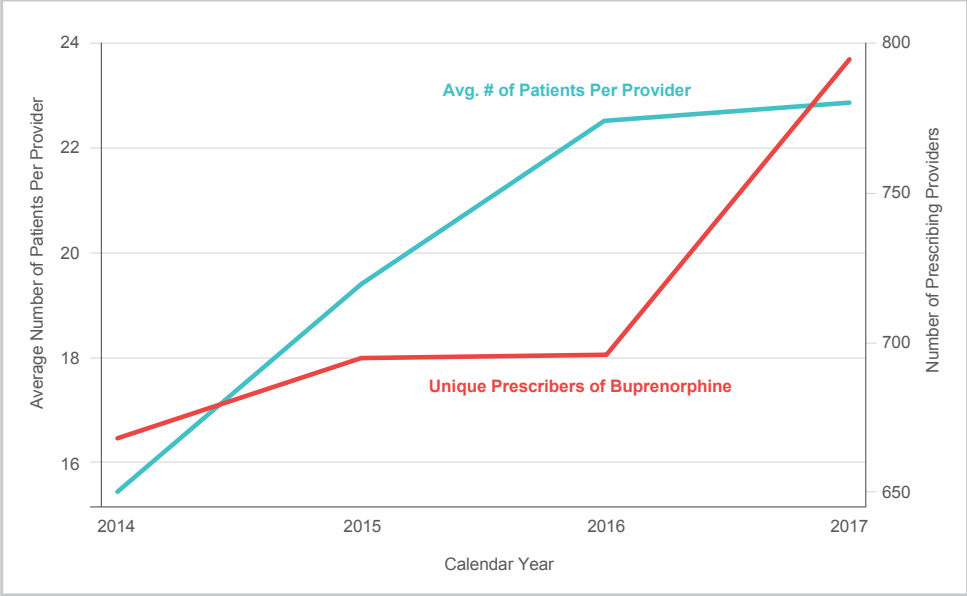
Figure 9. OUD and Treatment for OUD in NC Medicaid



- More people are receiving treatment for OUD. The number of Medicaid enrollees receiving at least 1 episode of treatment (buprenorphine, methadone, or naltrexone) for OUD increased from just under 10,800 in CY 2014 to nearly 17,000 by CY 2017.
- However, given the rising prevalence of OUD in the population, the rate of treatment is not keeping up with the increasing number of people who need it. From CY 2014 to CY 2017, the treatment rate declined from 45% to 41%.

Treatment supply (i.e., the number of providers available to prescribe medications to treat OUD) is an important factor influencing the treatment rate. We found that the number of buprenorphine prescribers in Medicaid and the average number of Medicaid enrollees receiving buprenorphine prescriptions per provider has increased in recent years.

Figure 10. Buprenorphine Prescribers and Average Number of Patients in NC Medicaid

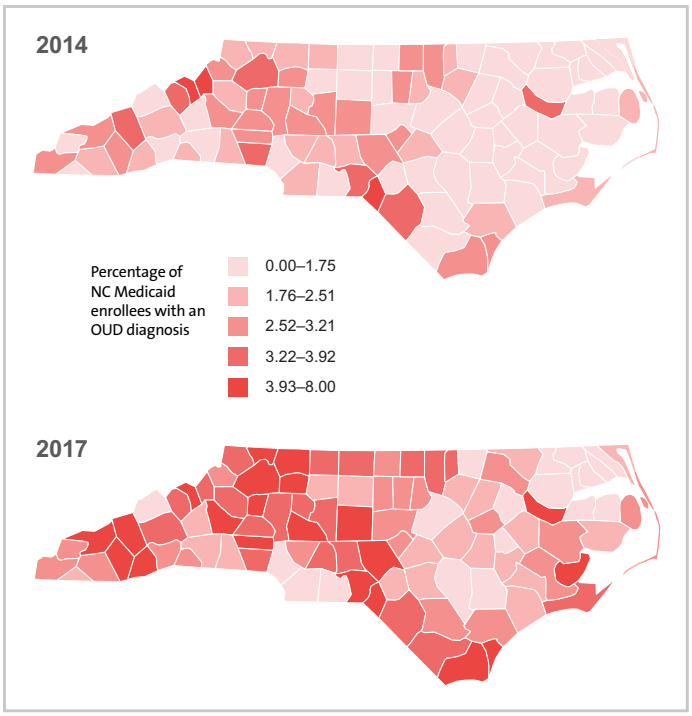


- The number of prescribers of Medicaid-paid buprenorphine increased from 668 in CY 2014 to 795 in CY 2017, with most of the increase occuring between 2016 and 2017.
- The average number of patients treated with buprenorphine per prescriber rose from 15 in CY 2014 to 23 in CY 2017, with most of the increase occurring between 2014 and 2016.

*Note that the methodology in the Enrollees Who Receive Medications for Opioid Use Disorder section differs from what was used in the previous sections. For example, a single calendar year (CY) measurement period was used (instead of the 2-year cohort definitions used in the remainder in the report).

The prevalence of OUD in Medicaid has increased in most counties from 2014 to 2017.

Figure 11. Prevalence of OUD in NC Medicaid



Medication treatment rates for OUD in Medicaid have remained fairly constant by county from 2014 to 2017.

Figure 12. Medication Treatment Rates for OUD in NC Medicaid

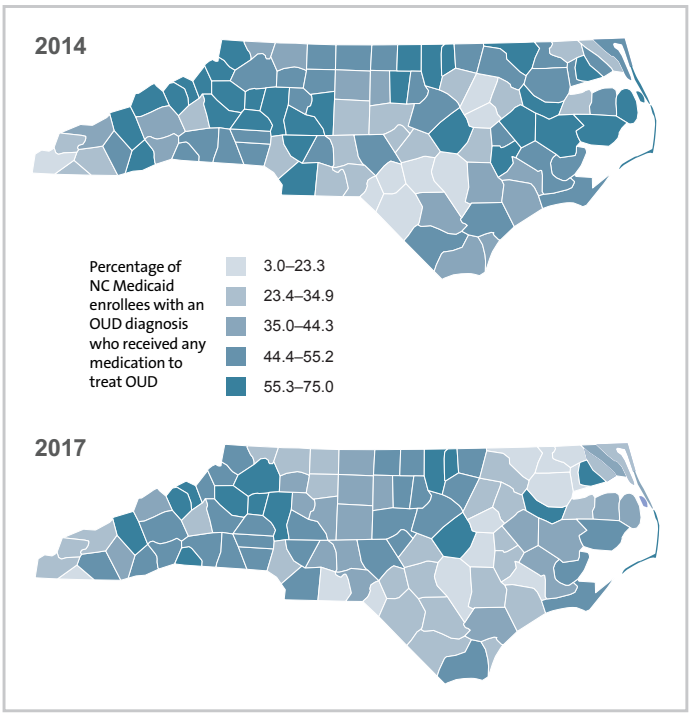
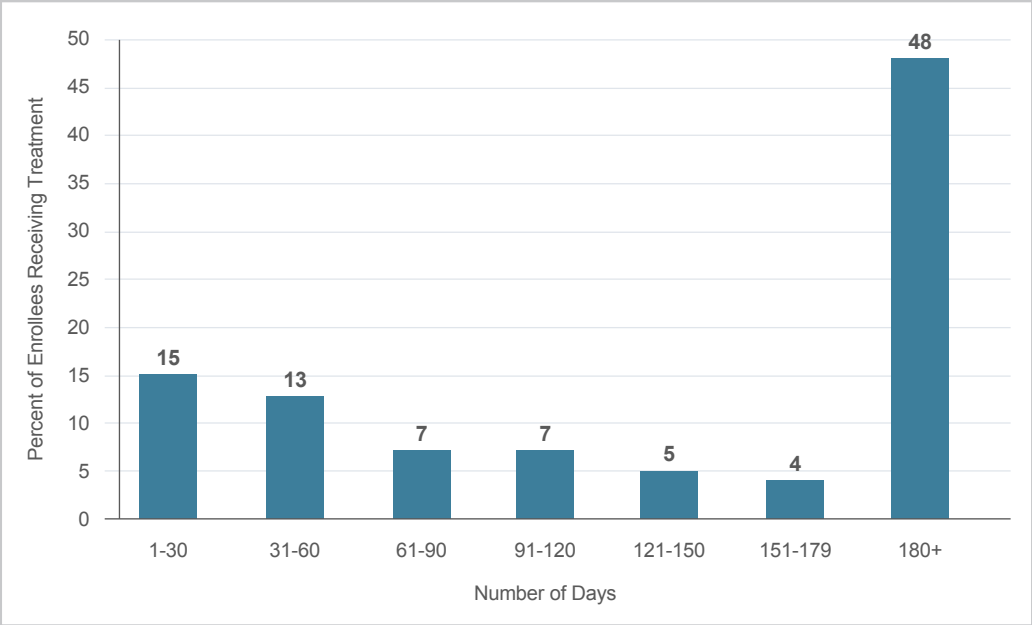


Figure 9 illustrated the gap between OUD prevalence and treatment.

Moreover, the treatment rates reported above include *any* instance of medication* used to treat OUD, even minimal treatment episodes. However, the scientific literature indicates that treatment should likely continue for 6-12 months at minimum to be beneficial, and often even longer.[3,4]

We report the distribution of treatment episodes among NC Medicaid enrollees over age 18 with a diagnosis of OUD and who initiated buprenorphine for treatment between January and June of 2017.

Figure 13. Episode Lengths for Enrollees Receiving Buprenorphine Treatment



Please note total does not add up to 100% due to rounding.

- Roughly half (48%) of such enrollees persist on buprenorphine therapy for 180 days or more, which could be considered the minimum recommended duration.
- A seventh (15%) of enrollees age 18-64 with a diagnosis of OUD who initiate buprenorphine receive treatment for 30 or fewer days.

*The treatment rates in Figure 9 and Figure 12 include any of the medications currently used for OUD treatment: buprenorphine, methadone, or naltrexone.

CONCLUSIONS

In summary, key findings from this report include:

- Fewer NC Medicaid enrollees have filled opioid prescriptions since 2013-2014.
- Fewer enrollees over time are exposed to particularly high doses of prescription opioids.
- Fewer enrollees who fill opioid prescriptions are also filling other medications that pose additional risk when taken concurrently with opioids.
- Fewer enrollees are receiving Medicaid-paid opioid prescriptions from multiple different prescribers and pharmacies than in prior years.

In several areas, there is ongoing cause for concern and action.

- Despite overall reductions in the percentage of enrollees filling opioid prescriptions, there is still a consistent number of people with SUD who fill opioid prescriptions.
- The rate of opioid-related overdose has been flat since 2013-14. Of those who experienced a documented overdose, a substantial percentage of enrollees go on to fill subsequent opioid prescriptions.
- There has been a large increase in the enrollees diagnosed with OUD. This is likely due to a combination of an increase in the development of OUD in the population and increased recognition and documentation of OUD by the clinical community.
- Our main finding is that the rate of treatment for OUD is lower than ideal and has remained low. Even though more people with OUD are being treated with evidence-based medications, those increases are not keeping up with the rising prevalence of OUD in NC Medicaid.
- Increased provision of evidence-based long-term, continuous treatment for OUD, beyond minimal exposure, is needed.

As we note and has been documented elsewhere, the opioid epidemic is evolving rapidly. In particular, it is shifting from an epidemic characterized by prescription opioids to one characterized by illicit substances. It is therefore crucial to maintain and expand ongoing monitoring and management of the increasing harms associated with heroin and other illicit substance use. Amid greater awareness and more prevalent documentation of OUD from prescription or illicit opioids, the greatest urgency is for deploying efficient and effective methods to get those who need it into evidence-based, long-term treatment.

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APPENDIX 1: TOTAL COUNTS OF MEDICAID ENROLLEES <65 YEARS OLD, NOT DUALLY-ENROLLED IN MEDICARE, IN VARIOUS OPIOID-RELATED COHORTS

			Total counts			% of all Medicaid enrollees			% of Medicaid enrollees with 1+ opioid claims			Total counts per 1,000 Medicaid enrollees			Total counts per 1,000 enrollees with 1+ opioid claims		
	Category	Cohort Description	2013-2014	2015-2016	2017-2018	2013-2014	2015-2016	2017-2018	2013-2014	2015-2016	2017-2018	2013-2014	2015-2016	2017-2018	2013-2014	2015-2016	2017-2018
All	All	All Medicaid enrollees <65 years old and not dually-enrolled in Medicare	2,160,117	2,319,536	2,457,174	100.0%	100.0%	100.0%				1,000	1,000	1,000			
	Any prescription opioids	Enrollees with at least one opioid prescription claim	415,839	411,193	322,835	19.3%	17.7%	13.1%	100.0%	100.0%	100.0%	197	177	131	1,000	1,000	1,000
At-risk cohorts	High-dose opioids	Enrollees with at least one opioid prescription for 90+ MME/day	52,748	48,638	27,820	2.4%	2.1%	1.1%	12.7%	11.8%	8.6%	25	21	11	127	118	86
		Enrollees with opioid prescriptions for 90+ MME/days for 90+ consecutive days	18,166	16,536	10,211	0.8%	0.7%	0.4%	4.4%	4.0%	3.2%	9	7	4	44	40	32
	Risky opioid-related medication combinations	Enrollees with prescription opioids overlapping with benzodiazepines	36,799	32,668	18,197	1.7%	1.4%	0.7%	8.8%	7.9%	5.6%	17	14	7	88	79	56
		Enrollees with prescription opioids overlapping with gabapentin	27,318	29,020	22,289	1.3%	1.3%	0.9%	6.6%	7.1%	6.9%	13	13	9	66	71	69
		Enrollees with prescription opioids overlapping with benzodiazepines and muscle relaxants	12,036	11,098	5,946	0.6%	0.5%	0.2%	2.9%	2.7%	1.8%	6	5	2	29	27	18
	Prescription opioids and diagnoses of substance use disorder	Enrollees with a diagnosis of a substance use disorder who also fill prescription opioids	48,434	62,172	51,640	2.2%	2.7%	2.1%	11.6%	15.1%	16.0%	23	27	21	116	151	160
	Prescription opioids from multiple providers	Enrollees with prescription opioids from 3+ different prescribers	95,268	87,189	51,189	4.4%	3.8%	2.1%	22.9%	21.2%	15.9%	45	38	21	229	212	159
		Enrollees with prescription opioids from 3+ different pharmacies	42,767	39,137	19,536	2.0%	1.7%	0.8%	10.3%	9.5%	6.1%	20	17	8	103	95	61
		Enrollees with prescription opioids from 4+ different prescribers AND 4+ different pharmacies	13,439	11,328	3,782	0.6%	0.5%	0.2%	3.2%	2.8%	1.2%	6	5	2	32	28	12
	Diagnoses of overdose	Enrollees with a diagnosis of opioid overdose	1,788	1,778	1,656	0.1%	0.1%	0.1%	0.4%	0.4%	0.5%	1	1	1	4	4	5
	Diagnoses of opioid use disorder	Enrollees with a diagnosis of opioid use disorder	27,181	44,195	45,171	1.3%	1.9%	1.8%	6.5%	10.7%	14.0%	13	19	18	65	107	140
	Any opioid-related risk category	Enrollees included in any (at least one) at-risk cohort	155,606	162,493	126,107	7.2%	7.0%	5.1%	37.4%	39.5%	39.1%	74	70	51	374	395	391

APPENDIX 2: COUNTS OF MEDICAID ENROLLEES <65 YEARS OLD WITH SELECTED DEMOGRAPHICS AND SELECTED MEDICAL COMORBIDITIES FOR EACH OPIOID-RELATED COHORT (2013-14, 2017-18)*

Demographics and selected medical comorbidities		2013-2014												
			Any opioids	Opioid-related Risk Categories and Cohorts										
				1) High doses		2) Risky combinations			3) SUD	4) Multiple providers			5) Overdose	6) OUD
		Total Medicaid enrollees < 65 years old	Enrollees with at least one opioid prescription claim	Enrollees with at least one opioid prescription for 90+ MME/day	Enrollees with opioid prescription for 90+ MME/day for 90+ consecutive days	Enrollees with prescription opioids overlapping with benzodiazepines	Enrollees with prescription opioids overlapping with gabapentin	Enrollees with prescription opioids overlapping with benzodiazepines and muscle relaxants	Enrollees with a diagnosis of a substance use disorder who also fill prescription opioids	Enrollees with prescription opioids from 3+ different prescribers	Enrollees with prescription opioids from 3+ different pharmacies	Enrollees with prescription opioids from 4+ different prescribers AND 4+ different pharmacies	Enrollees with a diagnosis of opioid overdose	Enrollees with a diagnosis of opioid use disorder
All Medicaid enrollees <65	All	2,160,117	415,839	52,748	18,166	36,799	27,318	12,036	48,434	95,268	42,767	13,439	1,788	27,181
Age	Mean	18	30	39	45	44	46	44	39	38	38	37	36	35
	0-14	1,128,181	55,525	833	25	83	50	20	211	1,398	406	61	182	386
	15-19	307,859	71,875	5,093	88	224	182	47	2,252	6,062	1,827	446	184	1,174
	20-24	150,754	48,921	4,449	396	1,080	593	245	4,385	8,920	3,789	1,249	115	3,226
	25-29	129,249	49,248	5,378	1,043	2,568	1,493	648	6,240	11,851	5,826	2,127	142	5,230
	30-34	109,458	43,376	6,075	1,930	4,410	2,605	1,385	6,420	12,819	6,528	2,299	182	4,843
	35-39	85,621	34,108	5,726	2,323	4,768	3,235	1,687	5,513	11,374	5,648	1,830	165	3,383
	40-44	65,689	27,817	5,681	2,630	5,202	3,731	1,909	5,030	10,267	4,912	1,575	172	2,517
	45-49	50,330	23,186	5,301	2,731	5,167	3,958	1,836	4,894	9,290	4,263	1,322	174	2,033
	50-54	49,580	24,479	5,995	3,155	5,629	4,667	1,923	5,850	10,063	4,426	1,280	204	2,006
	55-59	46,070	22,648	5,227	2,579	4,813	4,302	1,515	4,969	8,717	3,538	898	171	1,633
	60-64	37,326	14,656	2,990	1,266	2,855	2,502	821	2,670	4,507	1,604	352	97	750
Sex	Male	930,745	131,898	18,747	7,442	10,576	9,374	2,808	18,167	28,541	13,512	4,170	650	8,834
	Female	1,229,372	283,941	34,001	10,724	26,223	17,944	9,228	30,267	66,727	29,255	9,269	1,138	18,347
Race	African American	787,408	152,305	14,447	3,544	5,334	6,852	1,502	18,167	29,903	11,634	3,444	306	3,984
	White	1,053,408	222,506	34,033	13,197	28,718	17,710	9,643	14,369	58,100	27,682	8,921	1,334	21,114
	Other	319,301	41,028	4,268	1,425	2,747	2,756	891	30,312	7,265	3,451	1,074	148	2,083
Rural Status	Rural	963,170	215,022	28,783	10,899	21,652	15,938	7,060	24,790	51,047	22,476	6,755	937	13,893
	Suburban	514,821	102,826	13,984	4,309	9,603	6,854	3,325	13,426	24,634	11,366	3,759	474	8,241
	Urban	682,126	97,991	9,981	2,958	5,544	4,526	1,651	10,218	19,587	8,925	2,925	377	5,047
Opioid prescription characteristics	Average daily MME	--	37	95	165	54	50	57	--	39	49	48	--	--
	Average days supply	--	9	14	26	24	24	25	--	13	15	13	--	--
Selected Medical Comorbidities	Any cancer	17,590	8,362	4,536	1,868	1,942	1,400	357	1,936	5,141	2,246	823	77	490
	HIV	4,501	2,087	508	202	277	312	79	901	1,076	526	216	--	219
	Schizophrenia	21,165	4,873	1,035	354	1,190	835	362	2,536	2,343	1,089	483	178	895
	Mood Disorders	105,815	33,659	10,804	4,907	11,614	7,397	4,277	14,380	21,691	10,643	4,278	899	6,809
	Depression	115,948	32,418	10,060	4,585	10,751	6,814	3,893	12,546	19,731	9,708	3,843	822	5,970
	Pain	231,992	122,823	32,050	16,032	27,664	23,033	10,357	30,287	65,104	31,956	11,236	1,050	12,641
	Diabetes	64,001	28,177	7,673	3,630	6,374	6,981	2,215	6,562	15,013	6,271	1,981	273	2,397

Demographics and selected medical comorbidities		2017-2018												
			Any opioids	Opioid-related Risk Categories and Cohorts										
				1) High-doses		2) Risky combinations			3) SUD	4) Multiple providers			5) Overdose	6) OUD
		Total Medicaid enrollees < 65 years old	Enrollees with at least one opioid prescription claim	Enrollees with at least one opioid prescription for 90+ MME/days	Enrollees with opioid prescription for 90+ MME/days for 90+ consecutive days	Enrollees with prescription opioids overlapping with benzodiazepines	Enrollees with prescription opioids overlapping with gabapentin	Enrollees with prescription opioids overlapping with benzodiazepines and muscle relaxants	Enrollees with a diagnosis of a substance use disorder who also fill prescription opioids	Enrollees with prescription opioids from 3+ different prescribers	Enrollees with prescription opioids from 3+ different pharmacies	Enrollees with prescription opioids from 4+ different prescribers AND 4+ different pharmacies	Enrollees with a diagnosis of opioid overdose	Enrollees with a diagnosis of opioid use disorder
All Medicaid enrollees <65	All	2,457,174	322,835	27,820	10,211	18,197	22,289	5,946	51,640	51,189	19,536	3,782	1,656	45,171
Age	Mean	20	32	41	48	47	48	47	41	42	41	40	36	38
	0-14	1,164,849	34,922	434	12	35	47	13	300	678	191	31	202	671
	15-19	329,012	56,654	2,779	33	71	106	12	2,175	2,048	539	92	98	1,446
	20-24	208,624	31,404	1,665	110	204	242	52	3,555	2,738	986	213	106	3,555
	25-29	162,394	39,210	2,276	301	694	756	178	6,361	5,175	2,069	449	168	7,713
	30-34	143,163	34,491	2,505	678	1,425	1,583	428	6,675	5,919	2,606	572	162	7,975
	35-39	118,153	29,250	2,886	1,111	2,255	2,355	774	6,158	6,273	2,679	560	158	6,444
	40-44	86,565	21,419	2,585	1,201	2,362	2,635	855	4,814	5,442	2,206	439	144	4,243
	45-49	67,853	18,579	2,905	1,608	2,615	3,119	976	4,913	5,494	2,262	443	147	3,557
	50-54	59,858	19,467	3,478	1,923	2,979	3,911	981	5,885	6,450	2,384	428	160	3,600
	55-59	61,279	21,849	3,782	1,992	3,264	4,491	1,057	6,596	6,852	2,380	381	172	3,720
	60-64	55,424	15,590	2,525	1,242	2,293	3,044	620	4,208	4,120	1,234	174	139	2,247
Sex	Male	1,053,440	100,832	10,470	4,364	5,267	7,922	1,371	18,824	16,143	6,117	1,211	682	14,343
	Female	1,403,734	222,003	17,350	5,847	12,930	14,367	4,575	32,816	35,046	13,419	2,571	974	30,828
Race	African American	884,886	115,821	7,824	2,103	2,906	5,795	876	15,601	16,680	6,078	1,157	272	7,599
	White	1,246,427	168,011	17,045	7,092	13,592	13,466	4,539	30,401	28,882	11,226	2,176	1,211	33,181
	Other	325,861	39,003	2,951	1,016	1,699	3,028	531	5,638	5,627	2,232	449	173	4,391
Rural Status	Rural	1,072,739	163,292	14,928	6,008	10,759	13,569	3,398	27,365	27,093	10,069	1,841	820	24,364
	Suburban	589,903	79,474	7,212	2,461	4,529	5,269	1,618	13,133	12,987	5,080	1,007	486	11,929
	Urban	794,532	80,069	5,680	1,742	2,909	3,451	930	11,142	11,109	4,387	934	350	8,878
Opioid prescription characteristics	Average daily MME	--	34	94	161	53	46	54	--	42	44	44	--	--
	Average days supply	--	8	14	27	26	25	26	--	12	15	12	--	--
Selected Medical Comorbidities	Any cancer	14,888	9,026	3,353	1,484	1,337	1,464	244	2,484	4,183	1,608	466	61	1,025
	HIV	4,256	2,066	347	137	193	281	50	860	655	296	83	20	393
	Schizophrenia	21,128	6,375	627	212	880	865	235	3,134	1,730	678	188	101	1,859
	Mood Disorders	111,044	48,586	7,175	3,138	7,473	7,467	2,680	18,405	15,756	6,134	1,484	596	13,457
	Depression	134,206	49,500	7,026	3,015	7,209	7,186	2,530	17,418	15,107	5,928	1,414	542	12,930
	Pain	193,651	121,931	18,227	9,091	15,265	19,886	5,344	31,572	38,245	15,349	3,188	846	20,806
	Diabetes	57,365	31,716	4,769	2,288	4,032	6,340	1,428	7,943	10,487	3,721	723	246	4,743

*This analysis excludes NC Medicaid enrollees who are dually-enrolled in Medicare, and only includes prescriptions paid for by Medicaid.

APPENDIX 3: CUMULATIVE INCIDENCE OF SELECTED OUTCOMES AMONG ENROLLEES IN EACH OPIOID-RELATED RISK COHORT (2017-2018)

	2017-2018																							
	Any opioids		Opioid-related Risk Categories and Cohorts																					
			1) High doses				2) Risky combinations						3) SUD		4) Multiple providers						5) Overdose		6) OUD	
	Enrollees with at least one opioid prescription claim		Enrollees with at least one opioid prescription for 90+ MME/day		Enrollees with opioid prescriptions for 90+ MME/day for 90+ consecutive days		Enrollees with prescription opioids overlapping with benzodiazepines		Enrollees with prescription opioids overlapping with gabapentin		Enrollees with prescription opioids overlapping with benzodiazepines and muscle relaxants		Enrollees with a diagnosis of a substance use disorder who also fill prescription opioids		Enrollees with prescription opioids from 3+ different prescribers		Enrollees with prescription opioids from 3+ different pharmacies		Enrollees with prescription opioids from 4+ different prescribers AND 4+ different pharmacies		Enrollees with a diagnosis of opioid overdose		Enrollees with a diagnosis of opioid use disorder	
Selected outcomes	Incidence (%)	95% Confidence Interval	Incidence (%)	95% Confidence Interval	Incidence (%)	95% Confidence Interval	Incidence (%)	95% Confidence Interval	Incidence (%)	95% Confidence Interval	Incidence (%)	95% Confidence Interval	Incidence (%)	95% Confidence Interval	Incidence (%)	95% Confidence Interval	Incidence (%)	95% Confidence Interval	Incidence (%)	95% Confidence Interval	Incidence (%)	95% Confidence Interval	Incidence (%)	95% Confidence Interval
All-cause mortality	1.4	(1.4, 1.5)	7.4	(7.1, 7.8)	7.1	(6.6, 7.6)	4.3	(4.0, 4.6)	4	(3.7, 4.3)	2.9	(2.5, 3.4)	3.8	(3.6, 4.0)	4	(3.8, 4.2)	4.1	(3.8, 4.4)	6.3	(5.5, 7.2)	10.1	(8.6, 11.9)	2.4	(2.3, 2.6)
Unintentional opioid overdose	0.3	(0.2, 0.3)	0.7	(0.6, 0.8)	1.4	(1.1, 1.6)	1.1	(1.0, 1.3)	0.9	(0.8, 1.1)	1.5	(1.2, 1.8)	1.2	(1.1, 1.3)	0.7	(0.6, 0.7)	0.9	(0.7, 1.0)	1.1	(0.8, 1.6)	18.3	(16.5, 20.4)	1.3	(1.2, 1.5)
Unintentional synthetic opioid overdose	0	(0.0, 0.0)	0	(0.0, 0.1)	0.1	(0.0, 0.1)	0.1	(0.1, 0.2)	0.1	(0.0, 0.1)	0.1	(0.1, 0.3)	0.1	(0.1, 0.1)	0.1	(0.0, 0.1)	0	(0.0, 0.1)	0.1	(0.0, 0.3)	3.5	(2.7, 4.5)	0.1	(0.1, 0.2)
Unintentional heroin overdose	0.1	(0.1, 0.2)	0.3	(0.2, 0.4)	0.3	(0.2, 0.4)	0.2	(0.1, 0.3)	0.2	(0.2, 0.3)	0.2	(0.1, 0.3)	0.7	(0.7, 0.8)	0.2	(0.2, 0.3)	0.4	(0.3, 0.5)	0.6	(0.3, 0.9)	6.3	(5.1, 7.7)	1.4	(1.3, 1.5)
All-cause hospitalization	15.6	(15.5, 15.7)	22.3	(21.7, 22.8)	28.3	(27.4, 29.2)	25.1	(24.4, 25.7)	26.2	(25.6, 26.8)	24.5	(23.3, 25.6)	32.7	(32.3, 33.2)	26.9	(26.4, 27.3)	27.8	(27.1, 28.4)	35.6	(34.0, 37.3)	38.9	(36.3, 41.6)	29.5	(29.1, 30.0)
Endocarditis infection	0.2	(0.2, 0.3)	0.6	(0.5, 0.7)	0.8	(0.7, 1.0)	0.6	(0.5, 0.7)	0.7	(0.6, 0.8)	0.6	(0.4, 0.9)	0.8	(0.7, 0.9)	0.6	(0.5, 0.7)	0.7	(0.6, 0.8)	0.8	(0.6, 1.2)	1.8	(1.2, 2.6)	1.2	(1.1, 1.3)
Outpatient ED visit (all-cause)	54.4	(54.2, 54.6)	57.1	(56.4, 57.8)	61.6	(60.6, 62.6)	63.9	(63.1, 64.6)	64.5	(63.8, 65.1)	64.1	(62.8, 65.4)	70.5	(70.0, 70.9)	71.2	(70.8, 71.6)	73.6	(72.9, 74.3)	84.5	(83.2, 85.8)	70.8	(68.3, 73.3)	63	(62.5, 63.5)
HIV infection	0.9	(0.9, 0.9)	1.3	(1.2, 1.5)	1.6	(1.4, 1.9)	1.4	(1.2, 1.5)	1.6	(1.4, 1.8)	1.1	(0.9, 1.4)	2.1	(2.0, 2.2)	1.7	(1.6, 1.8)	2	(1.8, 2.2)	2.7	(2.2, 3.3)	1.2	(0.8, 2.0)	1.2	(1.1, 1.3)
Hepatitis C infection	0.2	(0.2, 0.2)	0.3	(0.3, 0.4)	0.5	(0.3, 0.6)	0.4	(0.3, 0.5)	0.4	(0.3, 0.5)	0.4	(0.3, 0.6)	0.7	(0.6, 0.8)	0.3	(0.3, 0.4)	0.4	(0.3, 0.5)	0.7	(0.5, 1.1)	0.7	(0.4, 1.4)	1	(0.9, 1.1)
Substance use disorder (SUD)	11.8	(11.7, 11.9)	14.6	(14.0, 15.1)	25	(24.1, 26.1)	25.4	(24.7, 26.2)	23.9	(23.2, 24.6)	24.8	(23.6, 26.1)	--		18.8	(18.4, 19.2)	23.6	(22.8, 24.3)	29.1	(27.2, 31.1)	9.4	(7.3, 12.0)	--	
Opioid use disorder (OUD)	5.2	(5.1, 5.3)	9.5	(9.0, 9.9)	18.6	(17.7, 19.5)	17.2	(16.6, 17.8)	16.1	(15.6, 16.7)	17.8	(16.8, 18.9)	--		11.5	(11.2, 11.9)	15.7	(15.1, 16.3)	20.4	(18.8, 22.0)	25.9	(23.1, 29.1)	--	

APPENDIX 4: REFERENCES & CODES FOR SELECTED COMORBIDITIES

Depression

Reference: Quan H et al. Coding Algorithms for Defining Comorbidities in ICD-9-CM and ICD-10 Administrative Data. Medical Care 2005 43(11):1130-1139

ICD-9: 296.2*, 296.3*, 296.5*, 300.4*, 309.*, 311*

ICD-10: F31.3*-F31.5*, F31.75, F31.76, F32.*, F33.*, F34.1*, F43.10, F43.11, F43.12, F43.2*, F43.8*, F43.9*, F93.0*, F94.8*

Mood disorders

Reference: HCUP CCS. Healthcare Cost and Utilization Project (HCUP). March 2017. Agency for Healthcare Research and Quality, Rockville, MD. www.hcup-us.ahrq.gov/toolssoftware/ccs/ccs.jsp.

ICD-9: 296.*, 293.83, 300.4*, 311.*

ICD-10: F30.*-F34.*, F39.*, F06.3, R45.86

Pain

Reference: Tian TY, Zlateva I, Anderson DR. J Am Med Inform Assoc 2013; 20: e275–e280.

ICD-9: 338.0*, 338.2*, 338.4*, 307.8*, 307.89, 719.41, 719.49, 719.45, 719.46, 719.47, 720.2*, 720.9*, 721.1*, 721.2*, 721.3*, 721.41, 721.42, 721.6*, 721.8*, 721.9*, 721.91, 722.*, 722.1*, 722.11, 722.2*, 722.3*, 722.31, 722.32, 722.39, 722.4*, 722.51, 722.52, 722.6*, 722.7*, 722.71, 722.73, 722.8*, 722.81, 722.82, 722.83, 722.9*, 722.91, 722.92, 722.93, 723.1*, 723.3*, 723.4*, 723.5*, 723.6*, 723.7*, 723.8*, 723.9*, 724.01, 724.02, 724.09, 724.1*, 724.2*, 724.3*, 724.4*, 724.5*, 724.6*, 724.79, 724.8*, 724.9*, 729.1*, 729.2*, 729.4*, 729.5*

ICD-10: F45.41, F45.42, G44.209, G89.0*, G89.21, G89.22, G89.28, G89.29, G89.4*, M25.50, M25.51, M25.55- M25.57, M25.78, M43.2*, M43.6*, M43.8*9, M46.1*, M46.41-M46.47, M46.9*, M47.0*, M47.02, M47.1*, M47.24-M47.28, M47.814, M47.815, M47.816, M47.817, M47.818, M47.894-M47.898, M48.04-M48.08, M48.1*, M48.9*, M50.0*, M50.1*, M50.3*, M50.8*, M50.9*, M51.04-M51.06, M51.1*, M51.24, M51.25, M51.3*, M51.4*, M51.8*, M51.9*, M53.1*, M53.2*7, M53.2*8, M53.3*, M53.8*, M53.9*, M54.*, M60.8*, M60.9*, M62.830, M67.88, M72.9*, M79.1*, M79.2*, M79.6*, M79.7*, M96.1*, M99.22-M99.29, M99.32-M99.39, M99.42-M99.49, M99.52-M99.59, M99.62-M99.69, M99.72-M99.79