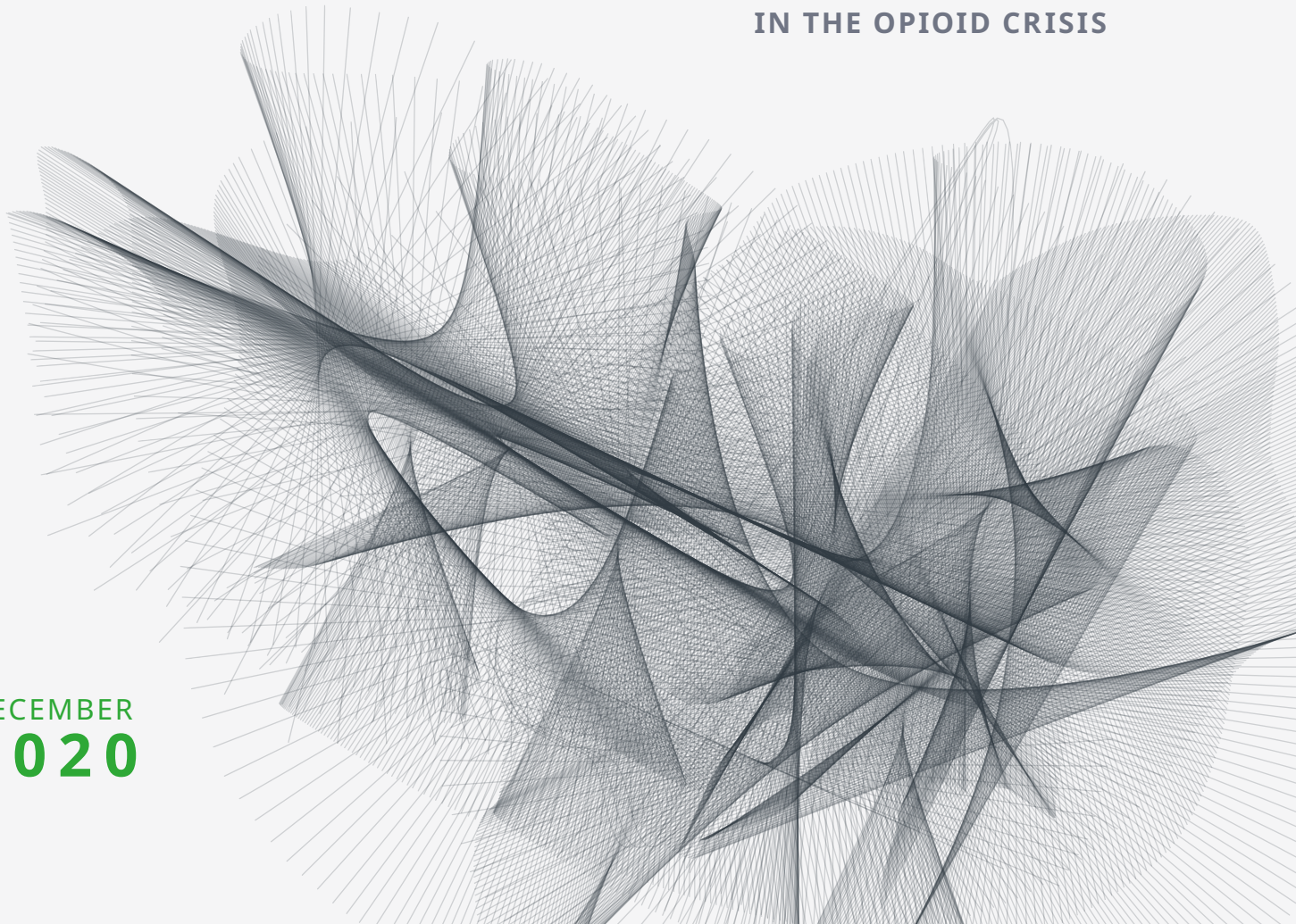




# Prescription Opioid + Trends in the United States

MEASURING AND UNDERSTANDING PROGRESS  
IN THE OPIOID CRISIS



DECEMBER  
**2020**

# Introduction

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The opioid epidemic has captivated the country for a decade, although it lost attention this year in the face of the COVID-19 pandemic. Patients with chronic pain and addiction have also been affected by disruptions to life and healthcare during COVID, when hospitals, doctors' offices, and drug treatment facilities were closed. While the human toll of the opioid epidemic is being addressed differently across the country, efforts in managing prescription opioids and in supporting medication-assisted treatment are showing measurable progress in many states.

This report provides a timely view of levels of, and trends in, opioid prescribing, how those vary by state, and how those variations illustrate progress and remaining risks. Trends show progress in reducing the highest-risk prescriptions, and reducing co-prescribing of opioids with anxiety drugs, called benzodiazepines, which are linked to a higher risk of overdose and death when taken together.

There are sometimes no other alternatives to opioids for pain management, and drugs for opioid use disorders are themselves narcotics, driving an intense research effort for alternatives, with only limited progress emerging.

The study was produced independently by the IQVIA Institute for Human Data Science as a public service,

without industry or government funding.

The contributions to this report of Bernard Gardocki, Veeru Goli, Terri Wallace, and dozens of others at IQVIA are gratefully acknowledged.

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## MURRAY AITKEN

*Executive Director*

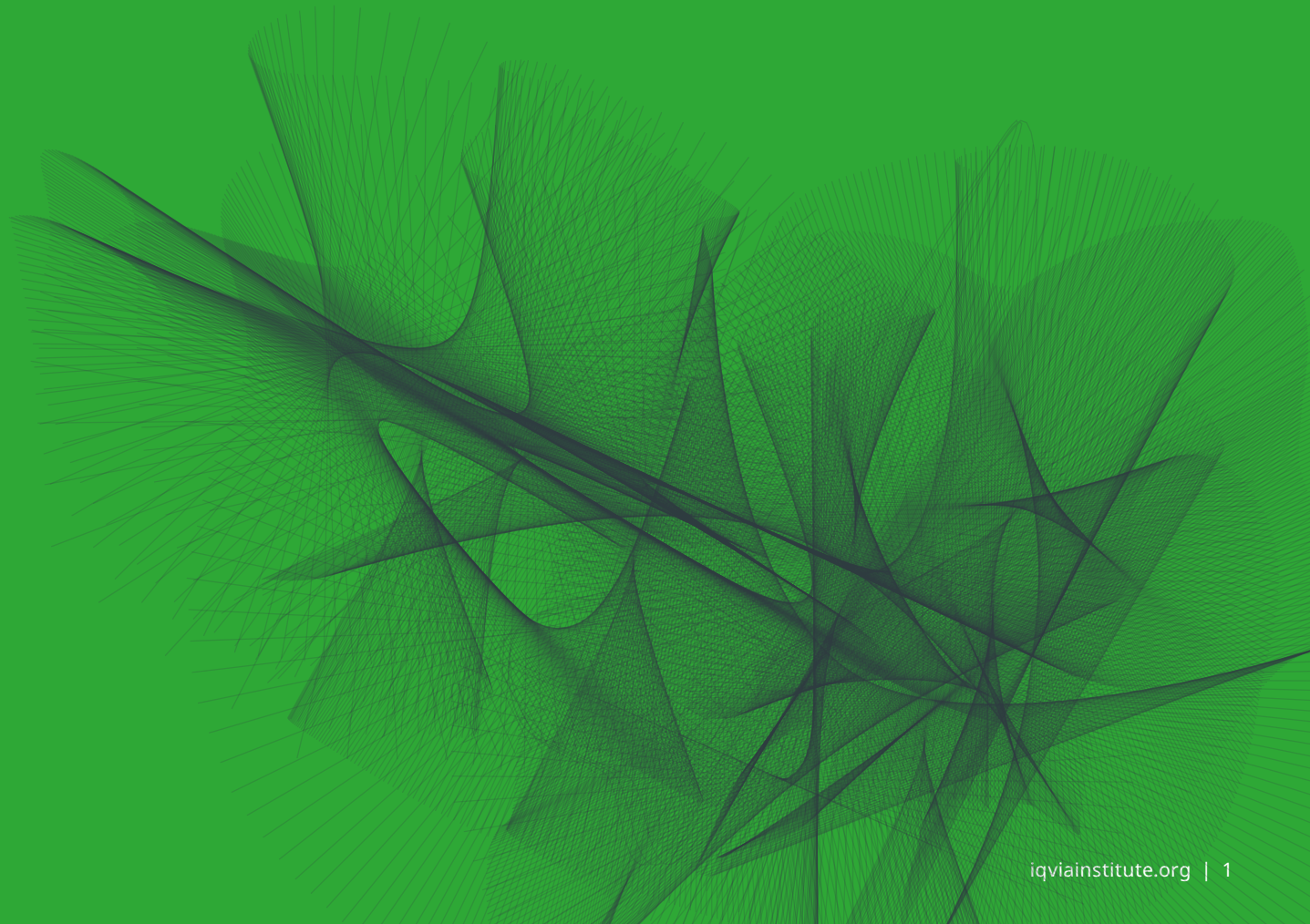
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# Overview

## LONG-TERM TRENDS

- Prescription opioid volume is expected to decline for the ninth consecutive year after peaking in 2011.
- Per capita use of prescription opioids is expected to drop back to levels of use seen in the early 2000.
- The greatest reductions in prescription opioid volume – measured in morphine milligram equivalents – have been in higher-risk segments receiving greater than 90 MMEs per day.
- Since 2011, total opioid prescriptions have declined by 40%, with declines of 51% and 63% in commercial and cash pay types, respectively.
- The number of Medicare opioid prescriptions has increased by 2% since 2011, driven by an aging population.

## COVID-19 IMPACT

- Trends in use of prescription opioids and medication-assisted treatment quickly returned to pre-pandemic levels after initial disruptions.
- Healthcare providers have prescribed longer opioid prescriptions to mitigate COVID-19 disruptions.
- Opioid prescribing declined 16% at the peak of shutdowns in late April, with significant variations across key specialties.

## STATE TRENDS

- The greatest declines in prescription opioid use are seen in states which previously had the highest per capita use.
- Cash-paying patients continue to comprise a relatively high share of total MMEs in some states, and particularly in the Southeast.
- In 2019, opioid MME per capita declined in every state compared to 2018, with the national average declining by 15%.
- States with the highest overdose deaths per capita are prioritizing MAT use, though wide variations in use remain.

## CO-PRESCRIBING

- Benzodiazepine-opioid co-prescribing carries significant risks, and continues to decline.
- Patients over 65 have the greatest use of co-prescribed opioids and benzodiazepines, and while their use is declining, it remains substantial.

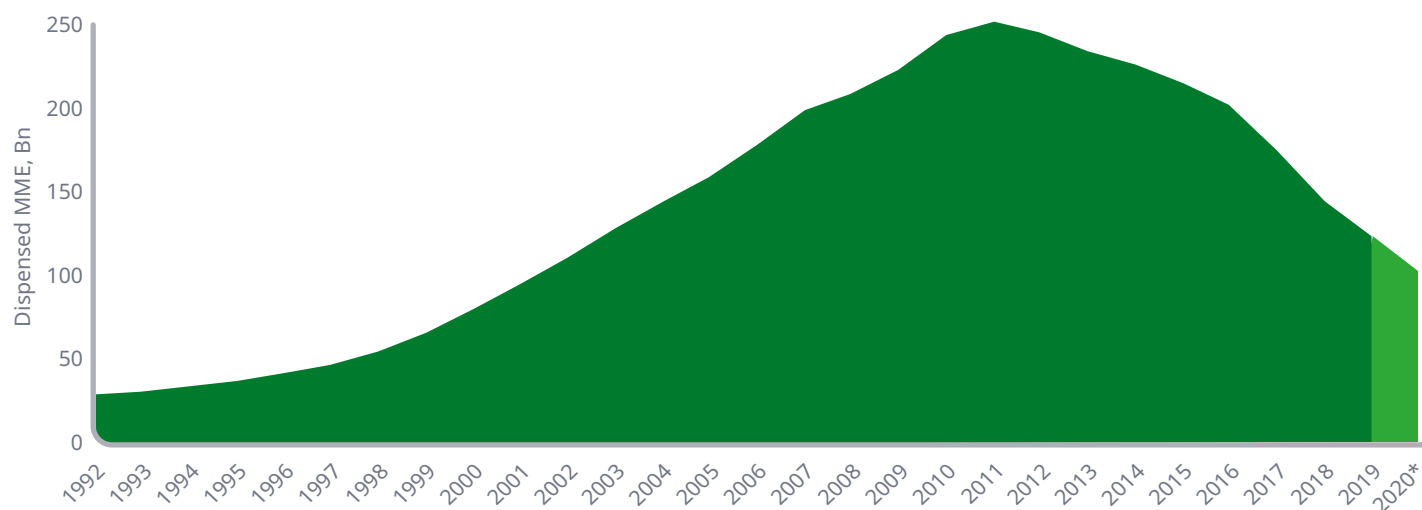
## PIPELINE

- Unmet needs in pain management and addiction are being addressed with ongoing research, including new MOAs and digital therapeutics.
- Treating underlying diseases with symptomatic pain and developing non-opioid therapies are the focus of the current pipeline.

## LONG-TERM TRENDS

# Prescription opioid use has declined to 60% of the peak volume in 2011 after another year of double-digit decline expected in 2020

Exhibit 1: Prescription Opioid Use in Morphine Milligram Equivalents (MME) Bn, 1992–2020\*



Source: IQVIA Xponent, Mar 2020; IQVIA National Prescription Audit; IQVIA Institute, Nov 2020

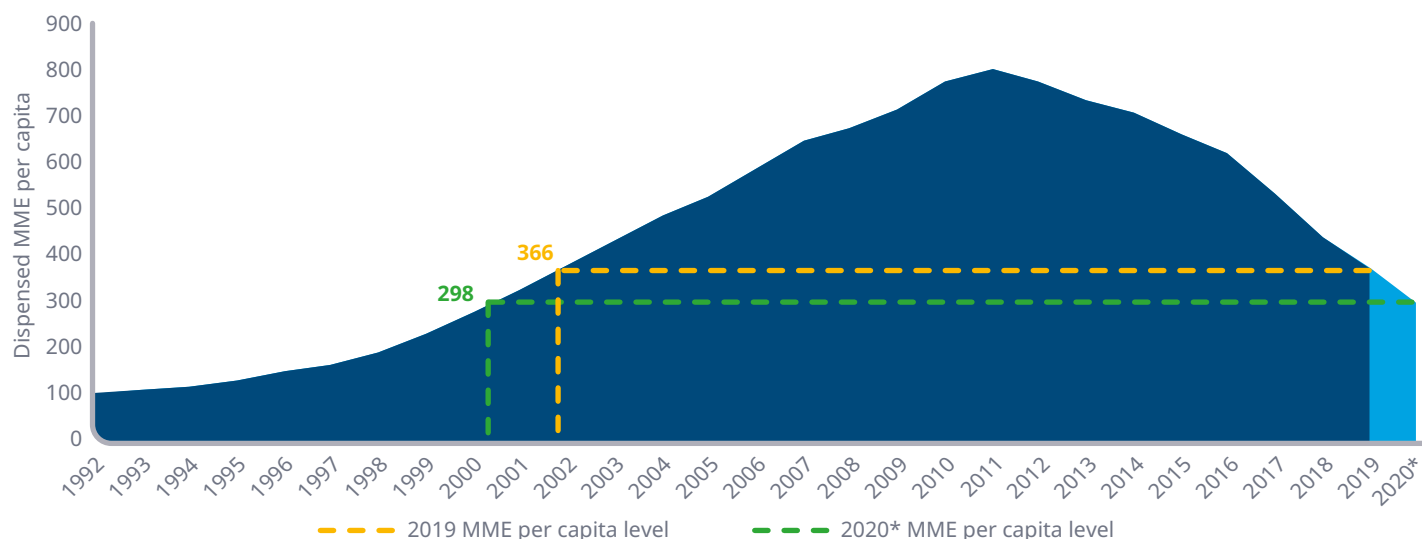
- Prescription opioid use in the United States continues to decline rapidly, with only 100 billion morphine milligram equivalents (MME) expected to be dispensed in 2020. This is a 60% decline from the 246 billion MMEs dispensed at the peak of opioid prescribing in 2011.
- Between 2019 and 2020, there is an expected 17.1% decline in MMEs, including the effects of disruptions from the COVID-19 pandemic, marking the ninth consecutive year of declines and the third year of double-digit change.
- These decreases in volume have been driven by changes in clinical usage, regulatory and reimbursement policies, and progressively more restrictive legislation enacted since 2012.
- As a result of this legislation, prescription drug monitoring programs (PDMPs) are now in place in 49 states and significantly limit prescribing of high doses of opioids, which according to the Centers for Disease Control and Prevention (CDC) carry a higher risk of dependency and overdose.<sup>1</sup>

Exhibit Notes: Historical NPA archive data for periods 1992-2005 combined with Xponent analysis for periods 2006-2020. 2020\* includes data through September, and an estimation of Q4 2020 data based on previous year trend. Analysis is based on opioid medicines for pain management and excludes those medicines used for medication-assisted opioid use dependency treatment (MAT) or overdose recovery. Opioid medicines are categorized and adjusted based on their relative intensity to morphine, called a morphine milligram equivalent (MME), see Methodology. <sup>1</sup>CDC Prescription Opioid Data. Accessed Oct 2020. Available from: <https://www.cdc.gov/drugoverdose/data/prescribing.html>

## LONG-TERM TRENDS

# Continued declines have brought normalized per capita prescription opioid use below the 2001 level

Exhibit 2: Prescription Opioid Use in Morphine Milligram Equivalents (MME) per Capita, 1992–2020\*



Source: IQVIA Xponent, Mar 2020; IQVIA National Prescription Audit; IQVIA Institute, Nov 2020

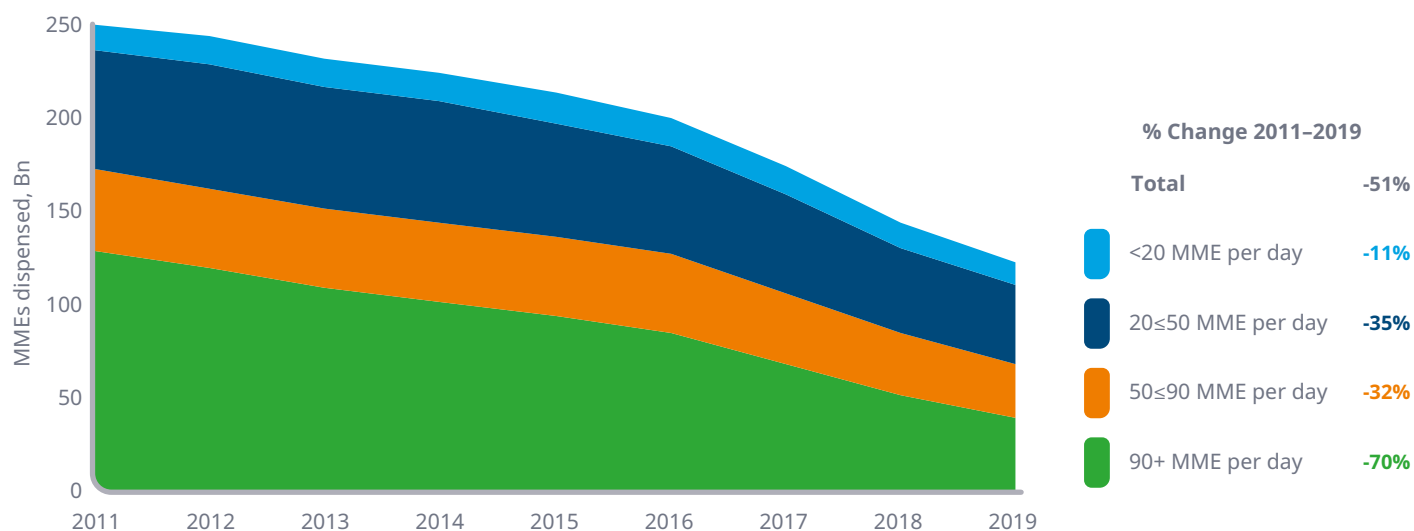
- Prescription opioid use was approximately 16 pills or 134 morphine milligram equivalents (MMEs) per adult American in 1992, and rose to a peak of 55 pills or 790 MMEs in 2011. Use has since declined by 54% to 29 pills and 366 MMEs per capita in 2019, though population growth has been 5.4% since 2011.
- In 2020, the projected decline in MME per capita is 17.1%, meaning prescription opioid use will reach mid-2000 levels. This represents a 20-year cycle, marked by 11 years of gains and nine years of reductions.
- By the end of 2020, MME per capita is expected to drop to 298, nearing the level seen in 2000, which was 270 MME per capita.
- Based on usage in the mid-1990s, it may be difficult to reduce current prescription opioid levels further, as pain medications are necessary for some patients, including cancer patients, until other non-addictive or disease-modifying treatments are available.

Exhibit Notes: Historical NPA archive data for periods 1992-2005 combined with Xponent analysis for periods 2006-2020. 2020\* includes data through September, and an estimation of Q4 2020 data based on previous year trend. Prescription data is through the retail channel. Analysis is based on opioid medicines for pain management and excludes those medicines used for medication-assisted opioid use dependency treatment (MAT) or overdose recovery. Opioid medicines are categorized and adjusted based on their relative intensity to morphine, called a morphine milligram equivalent (MME), see Methodology.

## LONG-TERM TRENDS

# The greatest reduction in prescription opioid use has been in the highest risk segment, which contain more than 90 MMEs per day

Exhibit 3: Prescription Opioid Use Segmented by Morphine Milligram Equivalents (MME) per Day, 2011–2019



Source: IQVIA Xponent, Mar 2020; IQVIA Institute, Nov 2020

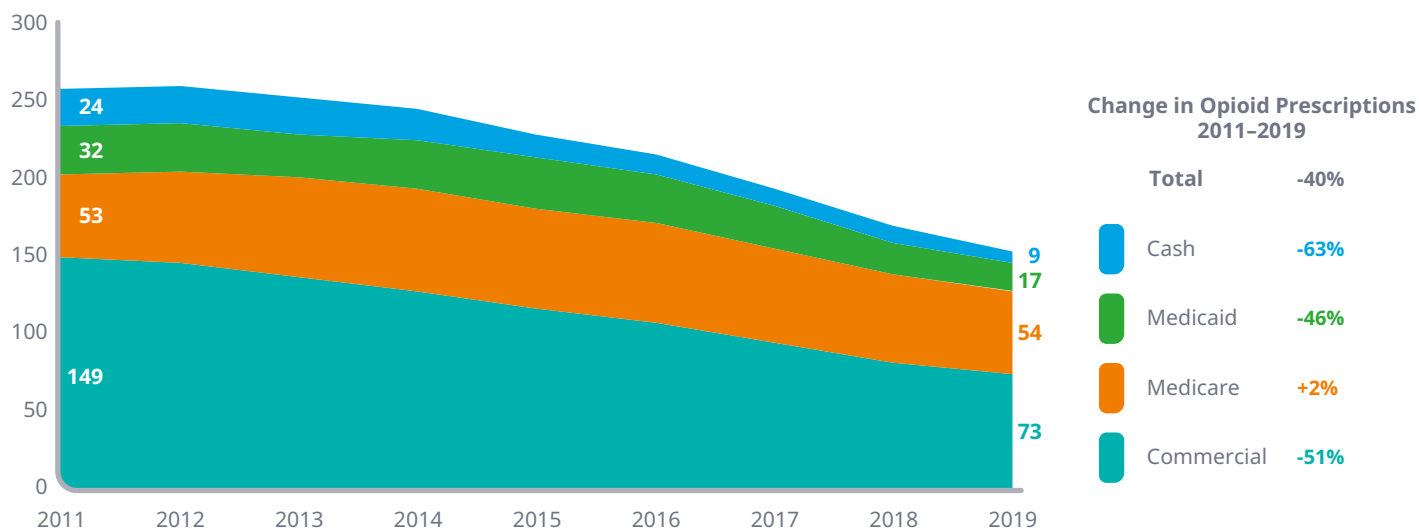
- In 2019, 120 billion morphine milligram equivalents (MMEs) were dispensed, a 51% decrease since the peak of 246 billion MMEs in 2011.
- Risks associated with prescription opioids, such as abuse and addiction, increase with opioid exposure. The greatest risks are seen in patients receiving 90 or more MMEs per day.
- The greatest reductions were in prescriptions written for 90 MME or greater per day, with a 70% reduction since 2011. The proportion of these prescriptions has also declined from 52% in 2011 to 32% in 2019.
- The least changed segment, the <20 MME per day prescriptions, declined by 11% to 12 billion in 2019, likely representing the use of opioids in acute need segments, including post-surgical use.

Exhibit Notes: Opioid medicines are categorized and adjusted based on their relative intensity to morphine, called a morphine milligram equivalent (MME), see Methodology. Medicines identified by MME potency at molecule, form and strength level, and divided by days supply at a prescription level to determine MME/day per prescription. Analysis is based on opioid medicines for pain management and excludes those medicines used for medication-assisted opioid use dependency treatment (MAT) or overdose recovery.

LONG-TERM TRENDS

## The number of Medicare opioid prescriptions has increased by 2% since 2011, while other pay types have declined

Exhibit 4: Number of Prescription Opioids Dispensed by Pay Type, Millions, 2011–2019



Source: IQVIA Xponent, Mar 2020; IQVIA Institute, Nov 2020

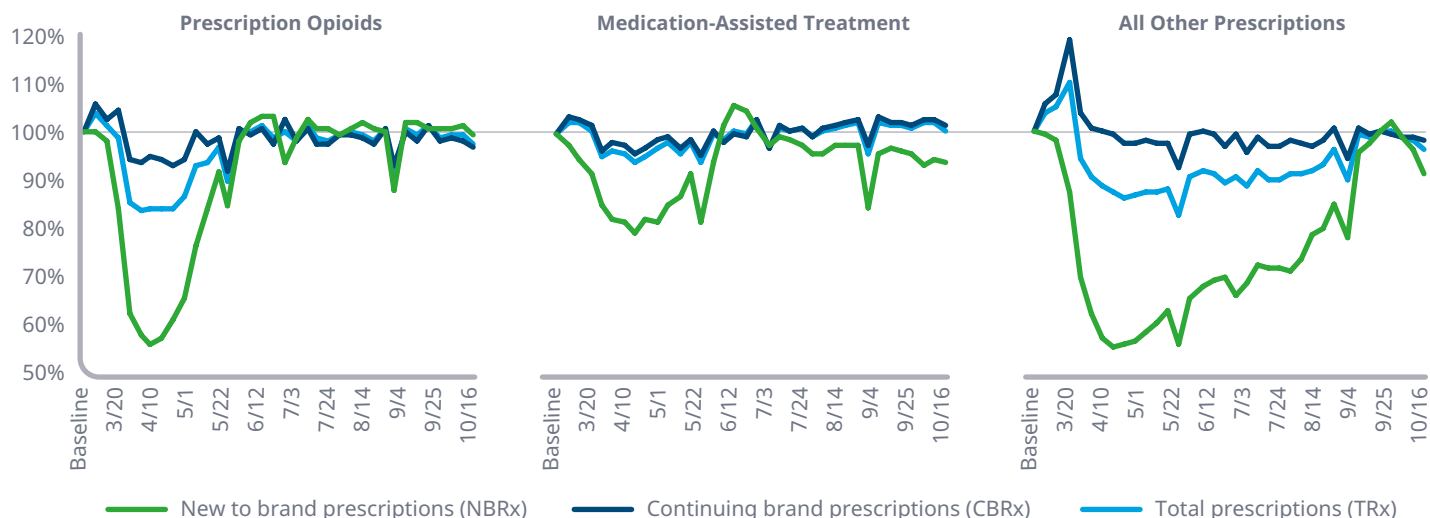
- Overall opioid prescriptions, not adjusted for MMEs, have declined by 40% since the peak of opioid prescribing in 2011, with declines seen in most pay types.
- Medicare Part D prescriptions have increased by 2% since 2011, rising from 53 million prescriptions to 54 million in 2019. The Medicare Part D share of prescriptions has increased from 21% to 35% over the same time frame, as the over 65 population has increased by 31% and seniors often require more procedures that result in opioid prescriptions, such as hip and knee surgeries.
- However, the peak number of prescriptions in Medicare occurred in 2014, when nearly 66 million prescriptions were dispensed. Comparing 2019 prescriptions to this point, there has been a 17% decline in this pay type.
- Prescriptions for commercial patients declined by 51%, suggesting enacted legislation and prescription drug monitoring programs (PDMPs) have been effective in this patient segment.
- Commercial prescriptions still comprise the largest share of prescription opioids, with 48% of the volume in 2019, down from 58% in 2011.
- Cash-paying patients decreased by a third, from 9% to 6% in 2019, suggesting some patients may have shifted insurance programs due to the Affordable Care Act.

Exhibit Notes: Analysis is based on opioid medicines for pain management and excludes those medicines used for evidence-based opioid use dependency or overdose recovery.



## During the COVID-19 pandemic, as many as 44% fewer new patients received prescription opioids while MAT was less impacted

Exhibit 5: Prescription Levels of Opioid, Medication-Assisted Treatment, and All Other Medications as a Percentage of Baseline, March–October 2020



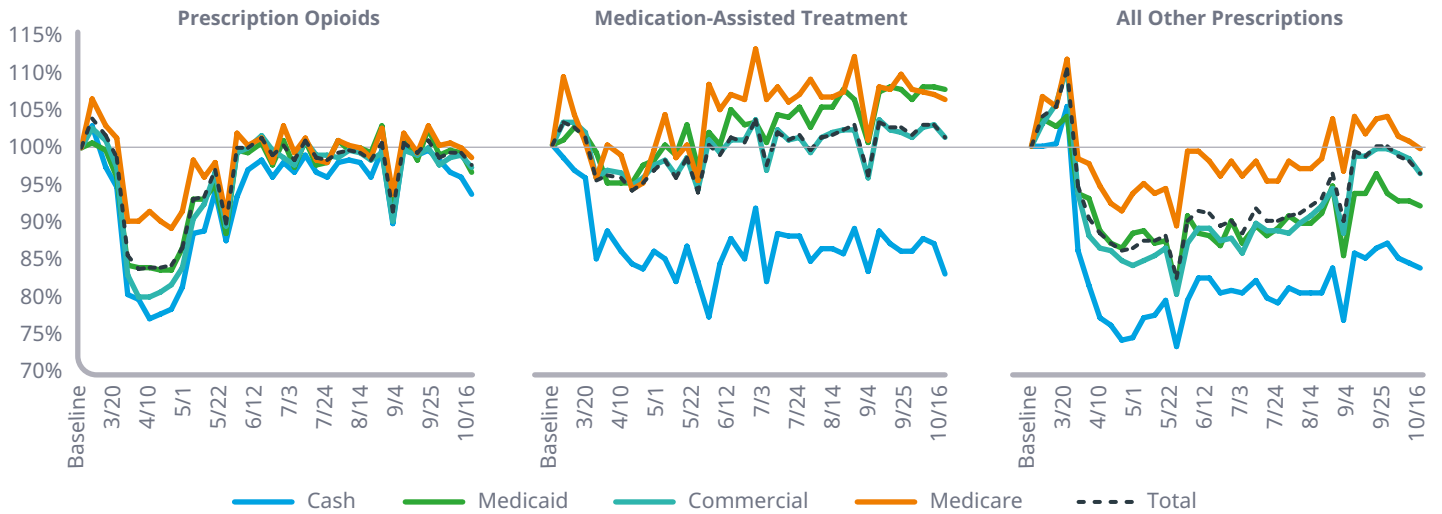
Source: IQVIA New to Brand Weekly, Nov 2020

- To understand the impact of COVID-19 on prescribing, the expected number of prescriptions, or baseline, was calculated and compared to the observed number of prescriptions. Overall, prescription opioid and medication-assisted treatment (MAT) recovered to baseline levels more quickly than the rest of the market.
- New to brand prescriptions (NBRx) represent patients who have not taken a prescription opioid in the last year. Early in the COVID-19 pandemic, there was as much as a 44% decline compared to the number of new patients expected to begin taking a prescription opioid.
- This was likely driven by providers encouraging patients to cancel non-emergency visits and surgeries as quarantines were implemented across the country, and new starts returned to baseline levels in June.
- Patients continuing on an opioid, represented by continuing brand prescriptions (CBRx), were also impacted, with CBRx prescriptions at 94% of baseline levels.
- Patients starting a new prescription regimen for MAT had as much as 22% below expected new patient starts, likely due to the closures of medical practices and drug treatment facilities.
- As seen with prescription opioids, MAT NBRx rebounded quickly in June and July as reopening across the country allowed it.
- However, MAT new start trends have begun to weaken again in September and October, a trend which, if continued, would result in a flattening in the overall number of patients receiving MAT.

Exhibit Notes: Displays weekly new, continuing, and total prescriptions. Dates represent week ending Friday. Weekly data is for retail channel only and does not include mail or long-term care facilities. Baseline level is defined as the average prescribing volume of the eight weeks prior to the pandemic, from week ending January 10, 2020, to week ending February 28, 2020.

## During the pandemic, Medicare patients were less impacted than other pay types, while the most affected were those cash

**Exhibit 6: Prescription Levels of Opioid, Medication-Assisted Treatment, and All Other Medications as a Percentage of Baseline by Pay Type, March–October 2020**



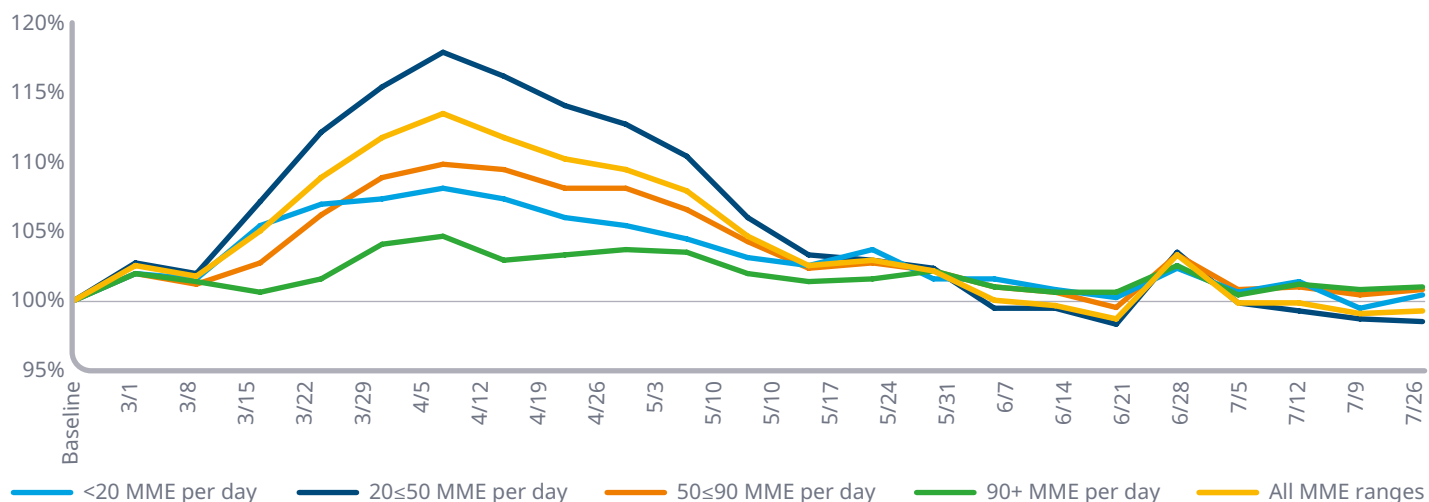
Source: IQVIA National Prescription Audit; IQVIA Institute, Nov 2020

- Each pay type for prescription opioids saw an impact during the peak of the pandemic disruption, with total prescriptions dropping to 84% of baseline prescriptions, mirroring the trend seen in the rest of the market.
- Cash-paying patients were the most affected, with only 77% of baseline prescriptions, closely followed by commercial patients with prescriptions at 80% of the expected level.
- The least impacted segment was Medicare, which saw 90% of baseline opioid prescriptions at the peak of pandemic disruption.
- Prescription opioid levels recovered across all pay types from mid-June to early July, with no appreciable differences through October 2020.
- MAT prescriptions saw less disruption, with most pay types around 94% of baseline levels, suggesting many providers and patients were able to prioritize the continuation of treatment despite office and clinic closures.
- However, the cash-paying segment of patients was disrupted. Typically, 8% of MAT prescriptions are filled by cash-paying patients, and this pay type reached a nadir of 77% in May and has yet to see a significant recovery to baseline levels.
- Given the difficult economic environment exacerbated by the pandemic and limited amount of federally-funded aid, the poor recovery in this segment may have long-standing impacts that may further delay the progress made in addressing the opioid crisis.

Exhibit Notes: Dates represent week ending Friday. Weekly data is for retail channel only and does not include mail or long-term care facilities. Baseline level is defined as the average prescribing volume of the eight weeks prior to the pandemic, from week ending January 10, 2020 to week ending February 28, 2020. Opioids include medicines for pain management and exclude those medicines used for evidence-based opioid use dependency or overdose recovery, which are classified under MAT for this analysis. All Others includes all other drug prescriptions.

## Between March and May, healthcare providers mitigated impacts from system closures by adjusting prescription quantities

Exhibit 7: Morphine Milligram Equivalents (MME) per Day per Prescription as a Percentage of Baseline, March–July 2020



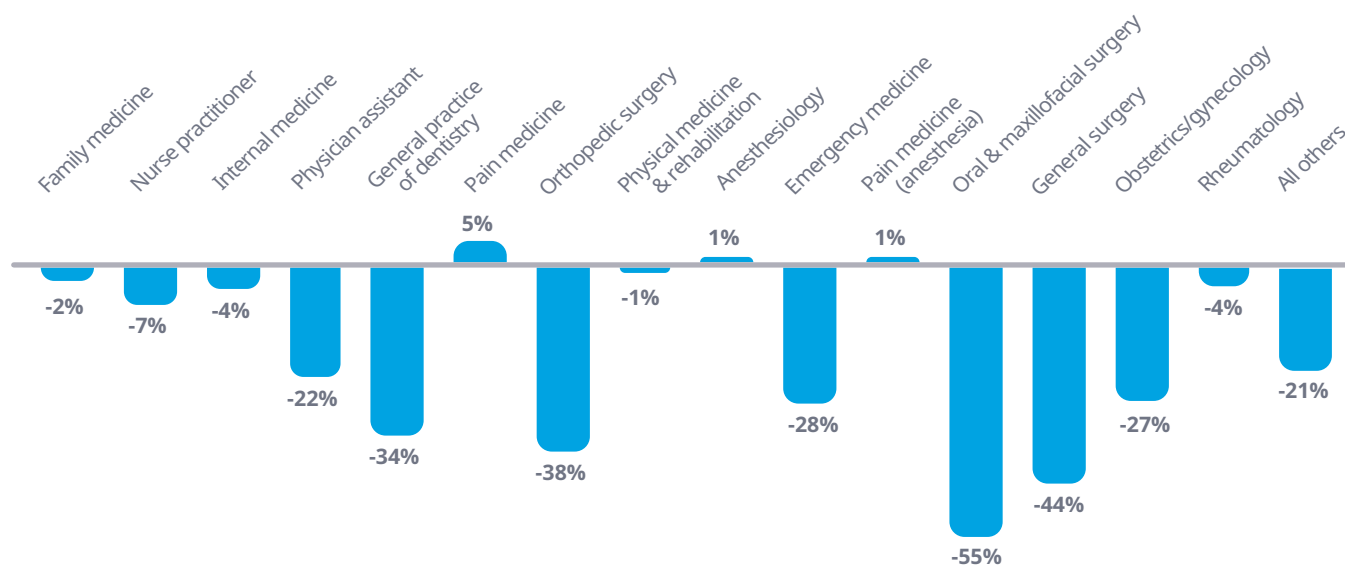
Source: IQVIA Xponent, Aug 2020; IQVIA Institute, Nov 2020

- Prior to the pandemic, the average number of MMEs per day in patient prescriptions had been relatively stable (data not shown).
- During the pandemic, fewer opioid prescriptions were dispensed; however, the number of MMEs remained relatively flat, as providers adjusted the size and duration of prescriptions to ensure patients requiring these medications had fewer gaps in care.
- This began in mid-March, prior to the peak disruption seen in late-April, ahead of system closures throughout the country.
- Notably, the alteration in prescribing was not as common in the highest risk segment, the 90 or more MMEs per day.
- Prescriptions in the 20–50 MME per day segment exceeded baseline expectations by 17% in early April, but quickly returned to baseline levels in June.
- All prescriptions followed this general trend, allowing patients to receive an appropriate amount of medication as they awaited system re-opening and were able to schedule procedures.

Exhibit Notes: Size of opioid prescriptions are measured in extended units. Dates represent week ending Sunday. Expected cumulative difference is modeled by taking the week-to-week trends of 2019 and applying them to 2020 data. Actual 2020 data is compared to expected values for each week, then added to the previous week(s) to determine cumulative differences between expected and actual values. Opioid medicines are categorized and adjusted based on their relative intensity to morphine, called a morphine milligram equivalent (MME), see Methodology. Medicines identified by MME potency at molecule, form and strength level, and divided by days supply at a prescription level to determine MME/day per prescription.

## The COVID-19 pandemic drove as much as a 55% reduction in prescriptions across the top 15 specialties dispensing opioids

Exhibit 8: Change in Opioid Prescriptions for Top 15 Specialties at Peak Pandemic Disruption Compared to Baseline



Source: IQVIA Xponent, Aug 2020; IQVIA Institute, Nov 2020

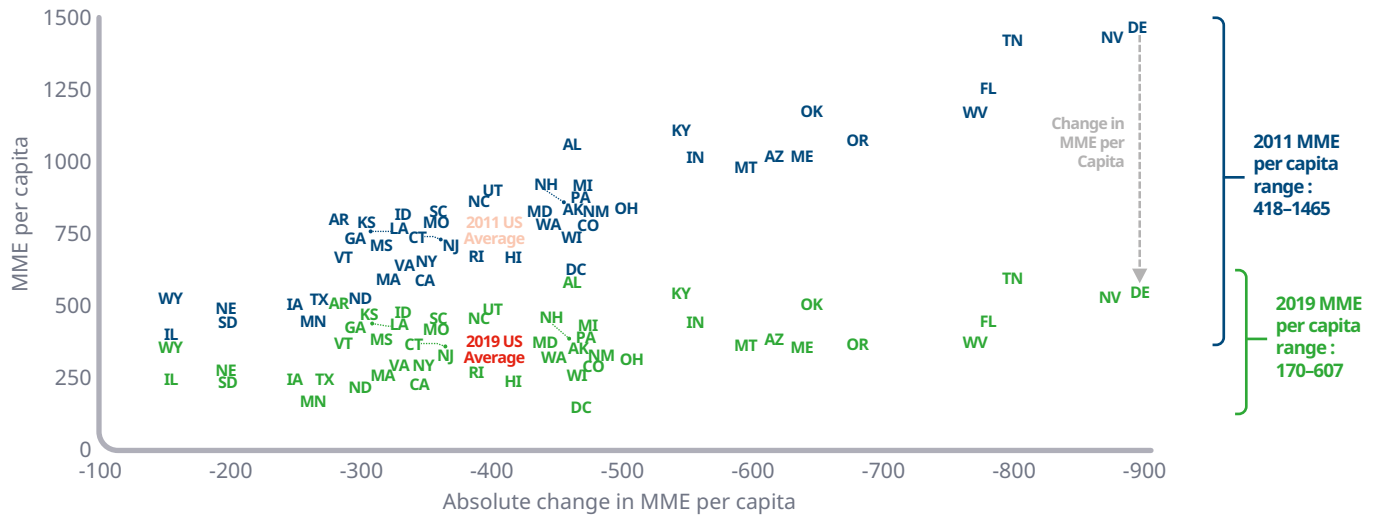
- Among the provider specialties with the most prescription opioid volume, nearly all experienced some degree of disruption to patient care during the height of health system closures, ranging from an increase of 5% to a decline of 55%.
- Half of the top 15 specialists with the highest opioid prescriptions saw declines greater than the overall total of 16%, most notably oral and maxillofacial surgery and general surgery specialists, who saw declines of 55% and 44% in opioid prescriptions, respectively.
- There were some specialties with little change who even increased their prescribing during the pandemic, such as pain specialists and anesthesiologists.
- These specialties were likely triaging patients whose care was disrupted by shutdowns but still had urgent need for pain medication and emergency procedures.
- Frontline caregivers, such as family medicine and internal medicine specialists saw only slight declines in opioid prescribing, suggesting they ensured patients requiring immediate care were able to receive it.
- Nurse practitioners and physicians’ assistants, who each support a variety of specialties, saw declines of 7% and 21%, respectively, representing the variability seen across all specialties.

Exhibit Notes: Dates represent week ending Sunday. Peak of the pandemic disruption is defined as the greatest overall market disruption of prescriptions, corresponding to week ending April 26, 2020. Baseline is defined as the average prescribing volume of the eight weeks prior to the pandemic, from week ending January 12, 2020 to week ending March 1, 2020. Top 15 specialties based on volume of prescription opioids.

STATE TRENDS

# The greatest declines in prescription opioid use are seen in states which previously had the highest per capita use

Exhibit 9: Prescription Opioid MME per Capita Absolute Change from 2011 to 2019 and MME per Capita in 2011 and 2019



Source: IQVIA Xponent, Mar 2020; US Census Bureau, Feb 2020

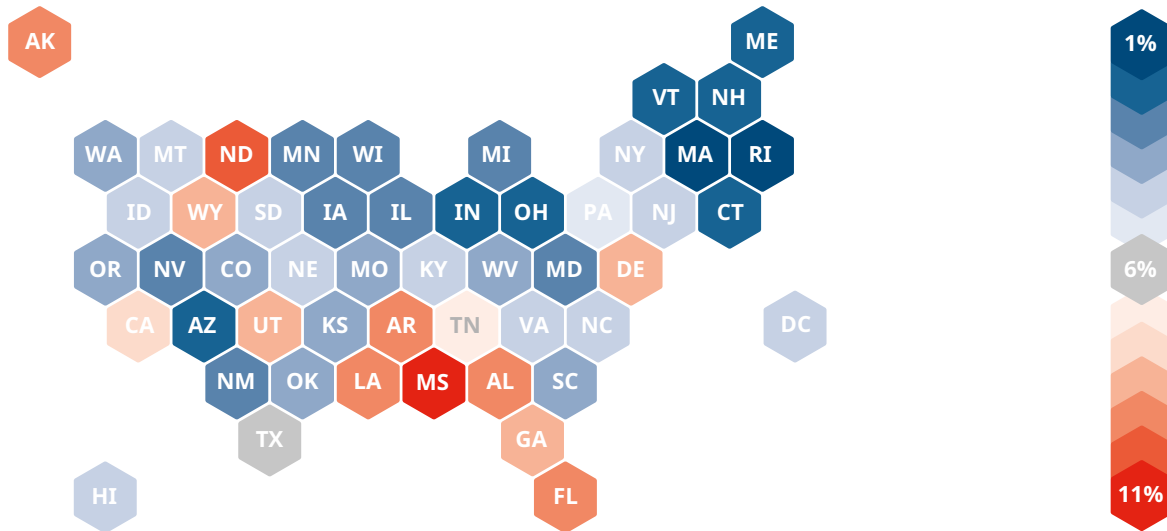
- From 2011 to 2019, the national average MME per capita declined by 54%, from 790 in 2011 to 366 in 2019, representing an average decline of 441 MMEs per state.
- The range of MME per capita in 2011 was 1,038 MME, with the highest per capita use in Delaware with 1,456, and the lowest in Illinois with 418.
- In 2019, the range in MMEs per capita is nearly three-fold narrower than 2011, as most states have begun to aggressively address opioid over-prescribing.
- The largest declines were in states that previously had the highest rates of prescription opioid use, such as Delaware, which declined by 62% to 559 MMEs per capita in 2019. Delaware is no longer the state with the highest MME per capita use.
- Other notable states with high use in 2011 include Nevada, Tennessee, Florida and West Virginia, which declined by 57%–66%.
- In 2019, Tennessee has the highest MME per capita use of any state with 607.
- Nine other states that had above average opioid use in 2011 had above average declines, including Oregon, Oklahoma, Maine, Montana, Arizona, Indiana and Kentucky.

Exhibit Notes: Opioid medicines are categorized and adjusted based on their relative intensity to morphine, called a morphine milligram equivalent (MME), see Methodology. Medicines identified by MME potency at molecule, form and strength level, and divided by days supply at a prescription level to determine MME/day per prescription. Per capita calculation is total MME volume divided by total population in millions.

## STATE TRENDS

# States in the Southeast have shares of cash-paying patients above the 6% national average, a sign of potential misuse

Exhibit 10: Share of Cash MMEs per State, 2019



Source: IQVIA Xponent, Mar 2020; IQVIA Institute, Nov 2020

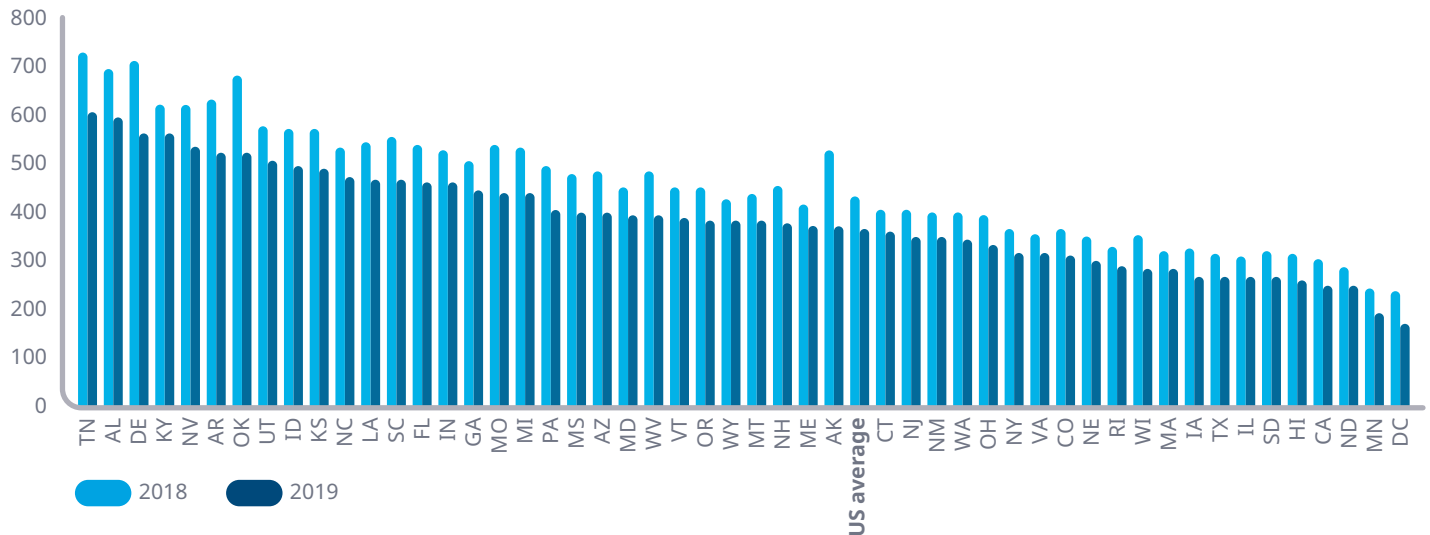
- According to the CDC, cash payments for opioid prescriptions may represent a red flag that a patient could be struggling with opioid use disorder (OUD). Cash payments may represent inconsistent or early refills of prescription opioids, or suggest a patient may be filling prescriptions from multiple providers.<sup>2</sup>
- With prescription drug monitoring programs (PDMPs), and doctors, pharmacists, and insurers closely monitoring prescription opioid use, there are fewer opportunities for patients to engage in behaviors leading to amassing large volumes of opioids.
- However, patients who pay cash for prescription opioids have more opportunities to avoid existing controls, as these prescriptions do not have oversight at an insurer level.
- In 2019, the average proportion of opioid prescriptions filled by cash-paying patients in each state was 6%, though several states across the Southeast still have a high proportion of cash-paying customers, with nearly 11% seen in Mississippi.
- Additionally, North Dakota, California, Delaware, and Alaska still have relatively high shares of cash paid opioid prescriptions, ranging from 8–10%.

Exhibit Notes: Opioid medicines are categorized and adjusted based on their relative intensity to morphine, called a morphine milligram equivalent (MME), see Methodology. Medicines identified by MME potency at molecule, form and strength level, and divided by days supply at a prescription level to determine MME/day per prescription. <sup>2</sup>[https://www.cdc.gov/drugoverdose/pdf/pharmacists\\_brochure-a.pdf](https://www.cdc.gov/drugoverdose/pdf/pharmacists_brochure-a.pdf)

STATE TRENDS

**In 2019, opioid MME per capita declined in every state compared to 2018, with the national average declining by 15%**

Exhibit 11: Morphine Milligram Equivalents (MME) per Million Population in 2018 and 2019



Source: IQVIA Xponent, Mar 2020; IQVIA Institute, Nov 2020

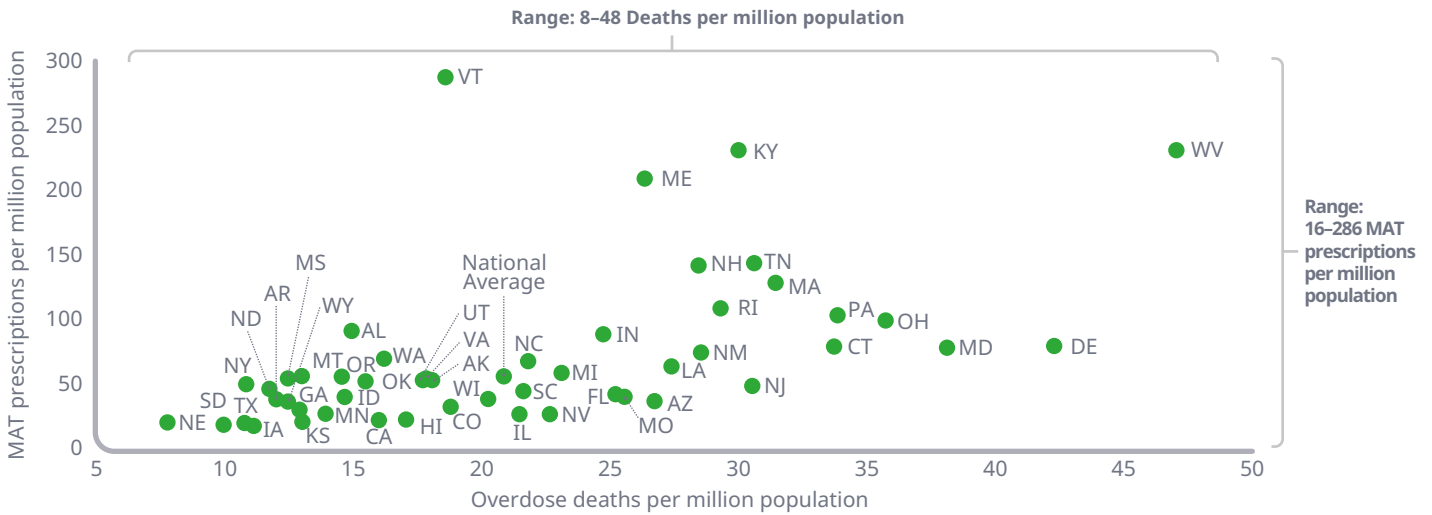
- From 2018 to 2019, the average MME per capita (per million) in the United States declined from 433 to 366, a 15% change.
- Notably, every state saw a decline in MME per capita, ranging from a 10-29% change, indicating each state has made some progress in stemming prescription opioid dispensing.
- Alaska and DC had two of the largest year-to-year differences, with declines of 29% and 28%, respectively. With these declines, Alaska shifted from the 18th highest MME per capita in 2018 to 30th in 2019. District of Columbia has the lowest MME per capita at 170.
- In 2018 and 2019, Tennessee has the highest MME per capita use, but has declined from 729 by 17% to 607.
- Of the top 10 MME per capita states in 2018, all remain in the top 10 in 2019, but all have declined by 10–23%.
- In 2019, there were 21 states that continue to fall below the national average, with declines ranging from 11–28%.
- The two states with the smallest changes, Maine and Kentucky, each declined by 10% to 374 and 559 MME per capita, respectively.

Exhibit Notes: Opioid medicines are categorized and adjusted based on their relative intensity to morphine, called a morphine milligram equivalent (MME), see Methodology. Medicines identified by MME potency at molecule, form and strength level, and divided by days supply at a prescription level to determine MME/day per prescription. Per capita calculation is total MME volume divided by total population.

STATE TRENDS

## There is a three-fold difference in MAT use in the two states with the highest overdose deaths, West Virginia and Delaware

Exhibit 12: Medication-Assisted Treatment (MAT) Use per Million Population by Overdose Deaths per Million Population by State, 2019



Source: IQVIA Xponent, Mar 2020; IQVIA Institute, Nov 2020; CDC Vital Statistics Overdose Deaths<sup>3</sup>

- In 2019, medication-assisted treatment (MAT) use is variable across the United States, with an 18-fold difference between the highest and lowest use states on a per capita basis, with an average of 54 MAT prescriptions per capita.
- Per capita opioid overdose deaths have a six-fold range, with a national average of 21 per capita.
- The disparate ranges between overdose deaths and MAT prescriptions suggest states are responding to deaths with differing strategies or priorities.
- Notably, MAT use is greatest in states with high overdose deaths per capita, suggesting at this point in the opioid crisis the hardest hit areas are actively utilizing MAT as part of their strategy to curb opioid deaths.
- As an example, West Virginia currently has the highest overdose deaths per capita at 48, and has the second-highest use of MAT, with 230 MAT prescriptions per capita.
- Delaware currently has the second highest overdose deaths per capita at 43, and is using MAT above the national average per capita at 77. Along with their significant decrease in opioid prescribing, this suggests the state is seeking multiple avenues to mitigate the crisis.
- Vermont currently has the highest MAT per capita use at 286, and their overdose deaths per capita are below the national average at 19, representing a strategy with MAT as a major component.

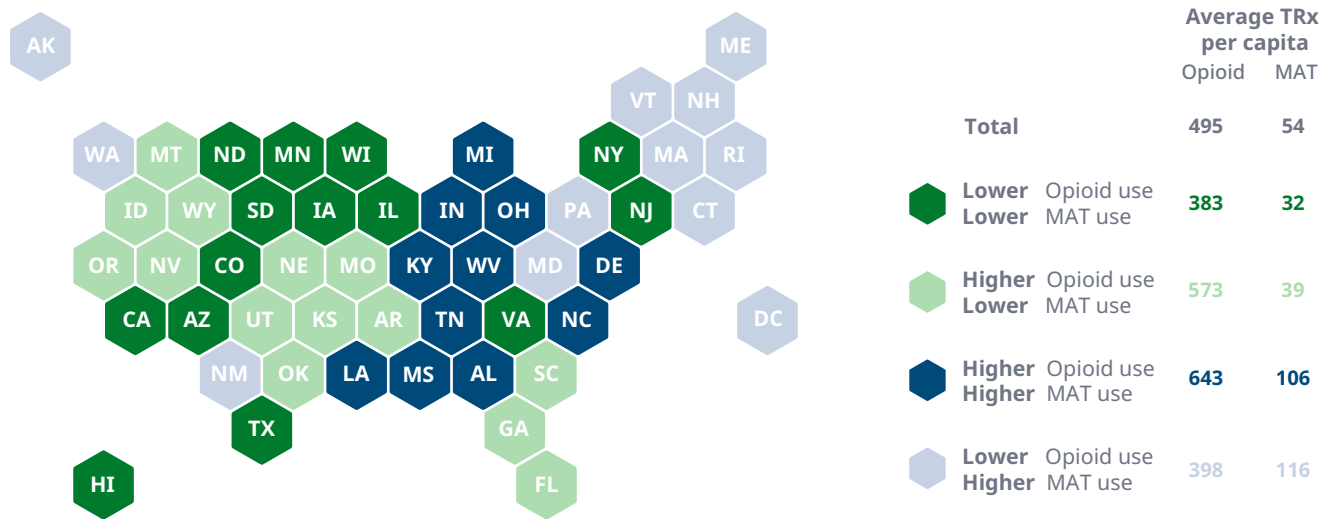
Exhibit Notes: <sup>3</sup>CDC Vital Statistics Overdose Deaths, accessed Nov 2020. Available at: <https://data.cdc.gov/NCHS/VSRR-Provisional-Drug-Overdose-Death-Counts/xkb8-kh2a>. Overdose deaths include all drug overdose deaths, including those due to illicit drug use. MAT includes medicines used for evidence-based opioid use dependency or overdose recovery.



STATE TRENDS

# There is a significant cluster of states with both opioid and MAT use above the national average

Exhibit 13: Opioid and Medication-Assisted Treatment per Capita Relative to 2019 National Average



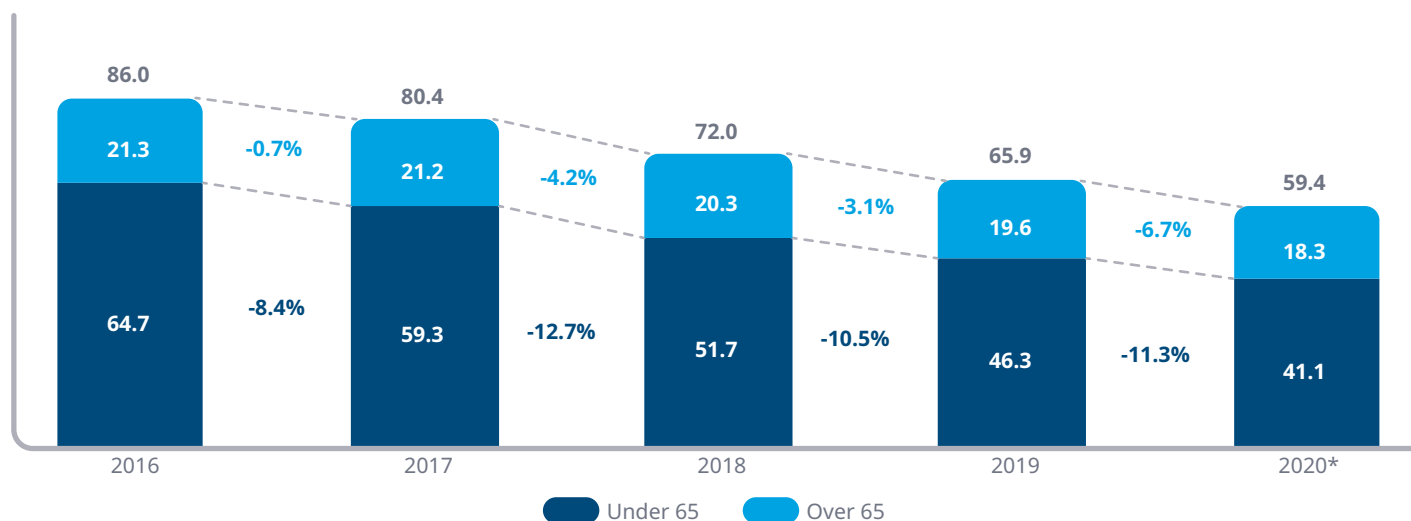
Source: IQVIA Xponent, Mar 2020; US Census Bureau, Feb 2020

- Categorizing each state by their relationship to the national averages of prescription opioid and MAT use reveals a geographic component in the trends.
- States shaded in dark green have both opioid and MAT per capita below the national average. This currently includes 14 states, mostly located in the upper Midwest and include New York and New Jersey.
- States shaded in light green have opioid per capita above the national average and MAT per capita below the average, and are found throughout the Midwest, including Arkansas, Idaho, and Wyoming.
- Dark blue states indicate high per capita use of both opioid and MAT relative to the average. This continues to include states hit hard by the opioid crisis, including Delaware, West Virginia and Tennessee.
- Light blue states have lower than average opioid per capita and higher MAT per capita compared to the average, and include all of the New England states, which have enacted new controls on opioid prescribing and support for opioid dependency in recent years.
- Compared to 2018, only Alaska and DC have moved from below the average MAT use to above average in 2019, while their opioid use remains below the national average.

Exhibit Notes: Opioids include medicines for pain management and exclude those medicines used for evidence-based opioid use dependency or overdose recovery, which are classified under MAT for this analysis. Higher denotes above the mean; lower denotes below the mean.

## Patients taking benzodiazepines, opioids, or a combination of both, have declined from 86 million to 59 million between 2016 and 2020

Exhibit 14: Patients Taking Any Benzodiazepine-Opioid, Benzodiazepine, or Opioid Therapy by Age, Millions



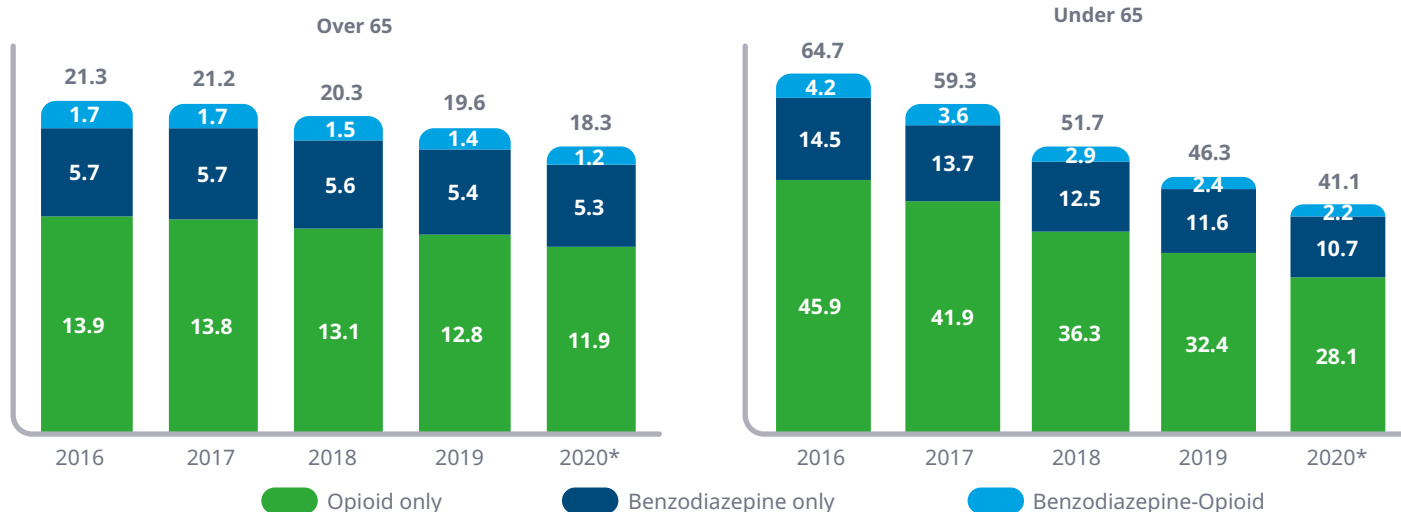
Source: IQVIA U.S. Prescription Claims (LRx), Oct 2020; IQVIA Institute, Nov 2020

- The co-prescribing of benzodiazepines and opioids has been consistently identified as increasing the risk of abuse and/or death than when these drug classes are used alone.<sup>4</sup>
- The number of unique patients taking a treatment regimen consisting of both a benzodiazepine and an opioid — defined as a patient filling a benzodiazepine prescription within one week of an opioid prescription — or a regimen consisting of a single component, has been declining over the past five years.
- The number of patients on one of these regimens has declined each year, dropping from 86 million in 2016 and expected to reach 59.4 million in 2020.
- The decline in these regimens is greater in younger patients — those under 65 years old — with the number of patients declining by 8%–11% in every year.
- As the baby boomer generation reaches 65 years old, the amount of opioids, benzodiazepines, and co-prescribing of these products in this age bracket is critical to understanding how the opioid crisis may evolve.
- In patients over 65 years old, there has been a decrease in the number of patients treated with opioid-only, benzodiazepine-only, and opioid-benzodiazepine combination regimens. There were 21.3 million patients in 2016, and an expected 18.3 million in 2020.

Exhibit Notes: 2020\* includes data through September and an estimation of Q4 2020 data based on previous year trend. Patient counts are unprojected based on claims data, representing roughly 90% of total claims, and not grossed up to a full national level. Benzodiazepine-opioid therapy includes patients with prescriptions for opioids and a benzodiazepine within seven days of each other. <sup>4</sup><https://www.drugabuse.gov/drug-topics/opioids/benzodiazepines-opioids>

## Opioid and benzodiazepine treatments have declined less in patients over 65 than in younger patients

Exhibit 15: Patients by Age Taking Benzodiazepine-Opioid, Benzodiazepine, and Opioid Regimens, Millions, 2016-2020\*



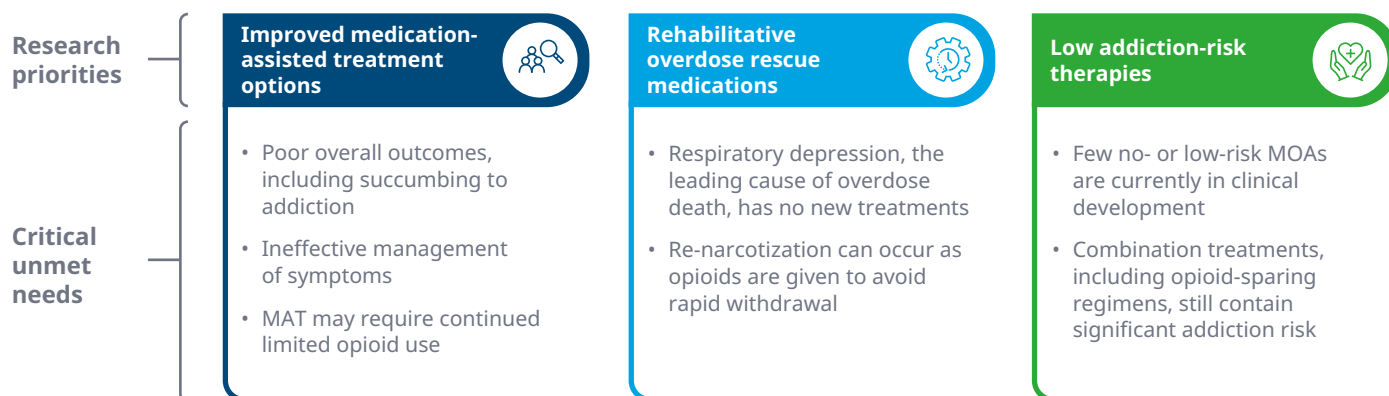
Source: IQVIA U.S. Prescription Claims (LRx), Oct 2020; IQVIA Institute, Nov 2020

- Patients over 65 are seeing declines in opioid-only, benzodiazepine-only, and benzodiazepine-opioid co-treatment regimens, though these declines are much less than those seen in patients under 65.
- In 2016, 1.7 million patients over 65 were co-prescribed these drugs, and the expected number of treated patients by year-end 2020 is 1.2 million, a decline of 30%. The decline over the same time frame for younger patients is 48%.
- Notably, in patients over 65, the greatest year-over-year decline in the number of patients on benzodiazepine-opioid combination regimens will take place between 2019 and 2020, with a projected 18.4% difference.
- In patients under 65 years old, the decline since 2016 in co-prescribing of benzodiazepines and opioids has been consistent, with double-digit year-over-year changes seen historically. In 2020, it is expected that 2.2 million will be on a combination regimen, down from 4.2 million in 2016.
- In individual component therapies, declines continue across age groups. Looking at patients over 65 taking only opioids, there was a decline of 2 million patients from 2016 to 2020, reflecting a 14% change. In younger patients the decline is 39%.
- Similarly, for benzodiazepine-only regimens, patients over 65 have experienced a 7% decline, while younger patients have seen a 26% decline.

Exhibit Notes: 2020\* includes data through September and an estimation of Q4 2020 data based on previous year trend. Patient counts are unprojected based on claims data, representing roughly 90% of total claims, and not grossed up to a full national level. Benzo-opioid therapy includes patients with prescriptions for opioids and a benzodiazepine within seven days of each other.

## Research priorities across stakeholders are centered around critical unmet needs in pain management and addiction treatment

Exhibit 16: Research Priorities with High Unmet Need in the Opioid Crisis



Source: IQVIA Institute, Nov 2020

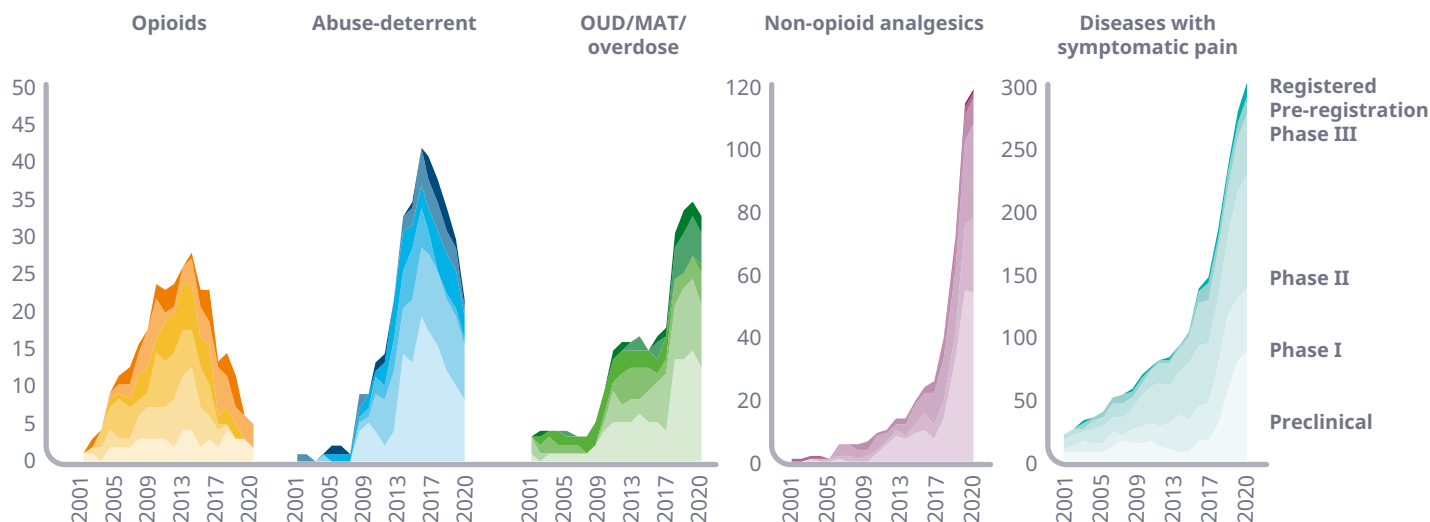
- Currently, pain management and addiction treatment have several critical unmet needs requiring additional research to help patients and providers.
- These include improved MAT options, as existing options have poor overall outcomes and adherence can be difficult as in-person visits are often required.
- Overdose rescue medications do not currently address respiratory depression, the leading cause of death in overdoses. There are currently no rescue medications with a novel respiratory mechanism of action.
- Some patients are also placed on opioid therapy following overdose rescue to decrease withdrawal symptoms, which leads to re-narcotization of patients and reduces the likelihood of recovery.
- Therapies with lower or no addiction risk are also required to treat pain disorders, as well as breakthrough pain in other diseases.
- In addition to pharmacological treatment, novel non-pharmaceutical treatment options may be required. Currently there is one FDA approved prescription digital therapeutic (PDT) available for opioid use disorder, introduced to the market in 2018.
- There are some notable treatments in development for addiction treatment, including heroin vaccines, synthetic ibogaine — a non-hallucinogenic psychedelic — and neurokinin (NK1)-targeted therapies.

Exhibit Notes: Research priorities determined through expert interviews from internal and external sources. MOAs = Mechanisms of action.

## PIPELINE

# Treating underlying diseases with symptomatic pain and developing non-opioid therapies is the focus of the current pipeline

Exhibit 17: Pipeline by Key Segments and Phases, 2001–Oct 2020



Source: IQVIA Pipeline Intelligence; IQVIA Institute, Oct 2020

- Since the peak of opioid use in 2011, there has been a decline in opioid products under investigation. In 2020, there are no products in late-stage development in the United States compared to 15 in 2011.
- Abuse-deterrent reformulations have had minimal impact, as many in development have shown little clinical differentiation and similar side effect profiles, resulting in a diminishing pipeline.
- After 2011, there were increases in opioid use disorder, MAT, and overdose rescue medications in development. However, there are currently only three products in Phase III development in the OUD/MAT/overdose pipeline, all with well-studied mechanisms of action in other disease contexts.
- In preclinical work, there are some novel mechanisms of action in development for OUD treatment, including a heroin vaccine to inoculate an individual against opioids, as well as 5HT receptor-targeted compounds, which are currently used to treat depression.
- The non-opioid analgesics pipeline, which includes compounds used to treat pain disorders and symptomatic pain but do not modify the underlying disease, has increased to 115 products, up from only 38 in 2017.
- Novel mechanisms in this area include Phase II studies of early growth response protein 1 (EGR1) inhibitors and metabotropic glutamate receptor (mGluR) agonists, as well as preclinical work in RNAi therapies.
- There is an increase in the pipeline for disease-modifying treatments for indications with symptomatic pain, including sickle cell, hemophilia, and neuropathy. Advances in these areas may prevent patients from initiating opioid treatment.

Exhibit Notes: 2020\* includes data through October 2020. Pipeline data for preclinical is a combination of 'Discovery' and 'Preclinical' flags while Phase I includes 'Phase I' and 'Clinicals' flags in the Pipeline Intelligence database. Non-opioid analgesics defined by the EphMRA ATC3 code N2B. Diseases with symptomatic pain include pain, fibromyalgia, mastalgia, neuropathy, ankylosing spondylitis, rheumatoid arthritis pericarditis, gout, hemophilia, sickle cell disease, and postsurgical adhesion.

# Notes on sources

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## **THIS REPORT IS BASED ON THE IQVIA SERVICES DETAILED BELOW**

The trends presented reflect United States' activities only.

### **IQVIA LONGITUDINAL PRESCRIPTION CLAIMS DATA**

**(LRX):** IQVIA receives nearly 4 billion prescription claims per year with history from January 2006 with coverage more than 90% for the retail channel, 60–85% for mail service, and 75–80% for long-term care. Longitudinal data derives from electronic data received from pharmacies, payers, software providers, and transactional clearinghouses. This information represents activities that take place during the prescription transaction and contains information regarding the product, provider, payer, and geography. Rx data is longitudinally linked back to an anonymous patient token and is linkable to events within the data set itself and across other patient data assets.

**IQVIA XPONENT PRESCRIPTION DATA:** Provides detailed prescriber level prescription information for the U.S. It includes dispensed drug prescription information from retail pharmacies (chain, mass merchandisers, independent, and food stores), mail service pharmacies and long-term care facilities. It covers 92% of the retail channel and up to 85% coverage in the mail and LTC channels and uses a customized and patented estimation methodology to generate accurate market estimates.

### **IQVIA NATIONAL PRESCRIPTION AUDIT (NPA):**

NPA is the industry standard source of national prescription activity for all pharmaceutical products. It measures demand for prescription drugs, including dispensed pharmaceuticals to consumers across three unique channels: retail, mail service, and long-term care pharmacies. From sample pharmacies, IQVIA collects new and refilled prescription data daily. NPA represents and captures more than 92% of all outpatient

prescription activity in the United States and covers all products, classes, and manufacturers.

### **IQVIA NATIONAL PRESCRIPTION AUDIT: NEW TO BRAND (NPA NTB):**

NPA New to Brand provides enhanced visibility into the volume of a patient's true, first-time use of a brand (or generic) versus continued therapies. IQVIA's longitudinal data allows users to analyze new therapy starts, switched to/add-on products, as well as continued therapies. In addition to reporting the new or refill information from a prescription, the therapy history for the patient is taken into account in order to categorize that prescription.

**ARK PIPELINE INTELLIGENCE™** is a drug pipeline database containing up-to-date R&D information on over 39,000 drugs and over 8,900 in active development worldwide. The database captures the full process of R&D, covering activity from discovery stage through preclinical and clinical development, to approval and launch.

# Methodology



Prescription opioid use analyses have defined the market as treatments for pain management and exclude treatments used exclusively to combat opioid use dependence, but does include medicines which are mostly used for pain treatment but have some use in opioid dependence. The Centers for Disease Control and Prevention (CDC) have defined factors to reflect the potency of different prescription opioids relative to one (1) milligram of morphine.

Separate analyses of drugs used in medication-assisted treatment and opioid use dependency are based on medicines used for that as described here.

MAT medicines: Bunavail, Buprenorphine/Naloxone, Buprenorphine (sublingual), Depade, Evzio, Naloxone, Naltrexone, Narcan, Probuphine, Revia, Sublocade, Suboxone, Subutex, Vivitrol, Zubsolv.

**Exhibit 18: Morphine Equivalency Segments and Factors**

Low Equivalency (ME factor <1)		Low Equivalency (ME factor = 1)		High Equivalency (ME factor 1.5-100+)	
Anileridine	0.25	Hydrocodone	1	Buprenorphine	10 or 75
Codeine	0.15	Morphine	1	Butorphanol	7
Dihydrocodeine	0.25	Nalbuphine	1	Fentanyl*	10-100+
Meperidine	0.10	Opium	1	Hydromorphone	4
Pentazocine	0.37			Levorphanol	11
Propoxyphene	0.06			Methadone**	4-12
Tapentadol	0.40			Oxycodone	1.5
Tramadol	0.10			Oxymorphone	3.0

Source: Centers for Disease Control and Prevention (CDC)

Exhibit Notes: \*Fentanyl is commonly referred to as having an MME of 50 or higher, but the MME factors vary based on formulation for this drug. The most commonly prescribed fentanyl formulation (transdermal patch) has an MME factor of 100. Other forms, including injectables and oral formulations (spray, buccal, sublingual, lozenges) have MME factors with scale based on strength from 10 to over 200.

\*\*Methadone MME factors vary based on the dosage with a factor of 4 for dosages up to 20mg per day, 8 if the dosage is between 21mg-40mg per day, 10 if the dosage is between 41mg - 60mg per day, and 12 if the dosage is greater than 60mg per day.

# About the authors

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**MURRAY AITKEN**  
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Murray Aitken is Executive Director, IQVIA Institute for Human Data Science, which provides policy setters and decisionmakers in the global health sector with objective insights into healthcare dynamics. He led the IMS Institute for Healthcare Informatics, now the IQVIA Institute, since its inception in January 2011. Murray previously was Senior Vice President, Healthcare Insight, leading IMS Health's thought leadership initiatives worldwide. Before that, he served as Senior Vice President, Corporate Strategy, from 2004 to 2007. Murray joined IMS Health in 2001 with responsibility for developing the company's consulting and services businesses. Prior to IMS Health, Murray had a 14-year career with McKinsey & Company, where he was a leader in the Pharmaceutical and Medical Products practice from 1997 to 2001. Murray writes and speaks regularly on the challenges facing the healthcare industry. He is editor of Health IQ, a publication focused on the value of information in advancing evidence-based healthcare, and also serves on the editorial advisory board of Pharmaceutical Executive. Murray holds a Master of Commerce degree from the University of Auckland in New Zealand, and received an M.B.A. degree with distinction from Harvard University.



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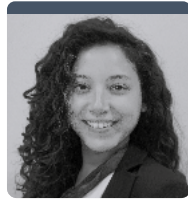
Michael Kleinrock serves as Research Director for the IQVIA Institute for Human Data Science, setting the research agenda for the Institute, leading the development of reports and projects focused on the current and future role of human data science in healthcare in the United States and globally. Kleinrock leads the research development included in Institute reports published throughout the year. The research is focused on advancing the understanding of healthcare and the complex systems and markets around the world that deliver it. Throughout his tenure at IMS Health, which began in 1999, he has held roles in customer service, marketing, product management, and in 2006 joined the Market Insights team, which is now the IQVIA Institute for Human Data Science. He holds a B.A. degree in History and Political Science from the University of Essex, Colchester, UK, and an M.A. in Journalism and Radio Production from Goldsmiths College, University of London, UK.





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Allen Campbell is the Associate Director for the IQVIA Institute, leading the IQVIA Institute's academic collaborations. He engages with researchers from universities around the world to support best practice use of IQVIA's information assets. He leads Institute research in analysis of prescription opioid data and manages collaborations with academics on the topic. Allen joined IQVIA in 1998, holding roles in sales and client service before joining the Institute in 2014. Allen holds a B.S. in Biology from Washington State University.



**ELYSE MUÑOZ, PH.D.**  
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Elyse Muñoz is a Thought Leadership Manager for the IQVIA Institute, managing aspects of IQVIA Institute research projects and conducting research and analysis within global healthcare. Elyse joined IQVIA in 2017 as an associate consultant in the Competitive Intelligence consulting group, where she developed rich clinical and commercial insights to serve million-dollar clients. She worked in major therapy areas including diabetes, cardiovascular disease and kidney dysfunction, as well as rare diseases such as hemophilia. Elyse holds a Bachelor of Science from Arizona State University in genetics, as well as a Ph.D. in genetics from Pennsylvania State University. Her research focused on understanding the genetic makeup of the parasite which causes malaria to aid in targeted drug development to help eradicate the disease.

# About the Institute

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The IQVIA Institute for Human Data Science contributes to the advancement of human health globally through timely research, insightful analysis and scientific expertise applied to granular non-identified patient-level data.

Fulfilling an essential need within healthcare, the Institute delivers objective, relevant insights and research that accelerate understanding and innovation critical to sound decision making and improved human outcomes. With access to IQVIA's institutional knowledge, advanced analytics, technology and unparalleled data the Institute works in tandem with a broad set of healthcare stakeholders to drive a research agenda focused on Human Data Science including government agencies, academic institutions, the life sciences industry and payers.

## Research Agenda

The research agenda for the Institute centers on 5 areas considered vital to contributing to the advancement of human health globally:

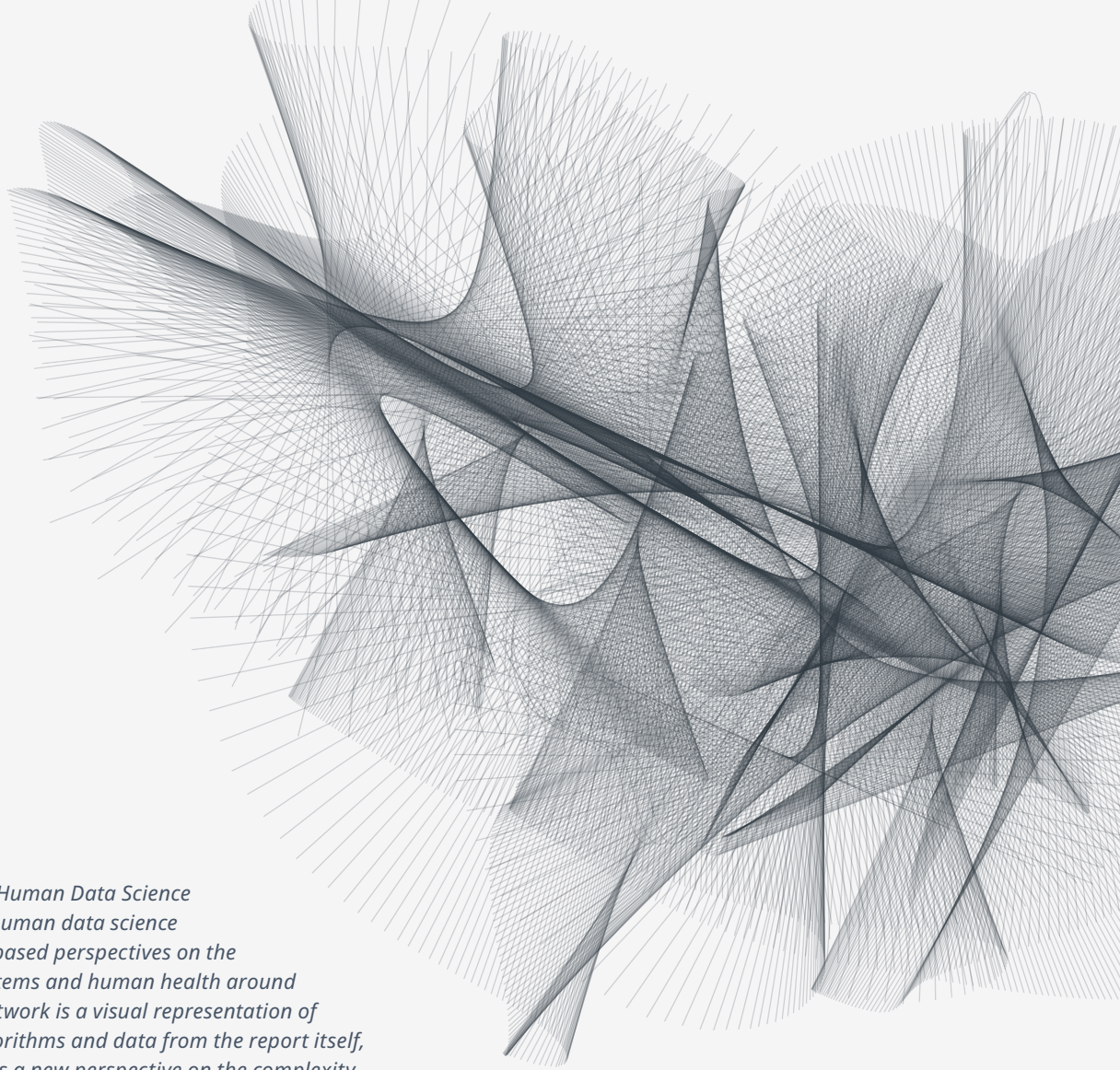
- Improving decision-making across health systems through the effective use of advanced analytics and methodologies applied to timely, relevant data.
- Addressing opportunities to improve clinical development productivity focused on innovative treatments that advance healthcare globally.
- Optimizing the performance of health systems by focusing on patient centricity, precision medicine and better understanding disease causes, treatment consequences and measures to improve quality and cost of healthcare delivered to patients.

- Understanding the future role for biopharmaceuticals in human health, market dynamics, and implications for manufacturers, public and private payers, providers, patients, pharmacists and distributors.
- Researching the role of technology in health system products, processes and delivery systems and the business and policy systems that drive innovation.

## Guiding Principles

The Institute operates from a set of guiding principles:

- Healthcare solutions of the future require fact based scientific evidence, expert analysis of information, technology, ingenuity and a focus on individuals.
- Rigorous analysis must be applied to vast amounts of timely, high quality and relevant data to provide value and move healthcare forward.
- Collaboration across all stakeholders in the public and private sectors is critical to advancing healthcare solutions.
- Insights gained from information and analysis should be made widely available to healthcare stakeholders.
- Protecting individual privacy is essential, so research will be based on the use of non-identified patient information and provider information will be aggregated.
- Information will be used responsibly to advance research, inform discourse, achieve better healthcare and improve the health of all people.



*The IQVIA Institute for Human Data Science is committed to using human data science to provide timely, fact-based perspectives on the dynamics of health systems and human health around the world. The cover artwork is a visual representation of this mission. Using algorithms and data from the report itself, the final image presents a new perspective on the complexity, beauty and mathematics of human data science and the insights within the pages.*

*The Algorithmic Art featured on this report cover is generated from IQVIA Xponent data of total opioid and medication assisted treatment prescriptions in each state, including absolute normalized per capita values in 2011 and 2019.*



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