Assessing CDC's Revised Guideline On Opioid Prescriptions

By Kenneth Weinstein, Nicholas Van Niel and Kate Uthe

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Kenneth Weinstein


Nicholas Van Niel


Kate Uthe

In the face of continuing public and legislative concerns over the consequences and societal costs of opioid addiction, there is an ongoing tension between regulatory approaches intended to restrict inappropriate prescribing, on the one hand, and the desire to maintain patient access for legitimate medical care, on the other.

For example, each year, the U.S. Drug Enforcement Administration sets annual production quotas for opioids and other controlled substances. In its proposal for 2024, issued in November 2023, the DEA for the eighth straight year called for cutting the supply of most Schedule II opioids. However, the proposed reductions for 2024 are smaller than in recent years for the two opioids prescribed most frequently: oxycodone and hydrocodone.[1]

In another example, in late 2022, the Centers for Disease Control and Prevention issued its most recent guideline on prescribing opioids for chronic pain, which revised its earlier guideline from 2016. Among other issues, both versions of the guideline discuss the risks of high-dose and long-duration opioid prescriptions.

In fact, our analysis of pharmacy claims and industry data shows a gradually declining trend in high-dose and long-duration prescriptions of oxycodone and hydrocodone.[2]

This guideline was influential in regard to state and federal policy, and it has been credited by some for reductions in opioid prescribing.[3] However, it was also controversial for its perceived restrictions on medical judgment and corresponding effects on patient access to treatment.

The 2016 guideline was intended as a recommendation, but it was often applied, and codified, in ways its authors had not intended. In 2019, a letter to the CDC cosigned by former White House Drug Control Policy Director Barry McCaffrey stated that within a year of publication of the 2016 document, "there was evidence of widespread misapplication of some of the Guideline recommendations."[4]

The revised CDC guideline issued in late 2022 was developed partly in response to such concerns. These concerns were shared by the authors of the 2022 guideline, whose commentary states that new laws, regulations, and policies, in some cases purportedly derived from the 2016 guideline, went beyond — and were inconsistent with — its recommendations. Such misapplication, including inflexible application of recommended dosage and duration thresholds, contributed to patient harms."[5]

With the passage of six years since the original guideline, we have now analyzed claims data over the 2011-2022 period to compare post-2016 patterns in opioid prescriptions to pre-2016 patterns.[6]

We have focused our analysis on two specific metrics that have been perceived by some as hard lines in the 2016 guidance, but which are presented differently or removed in the revision: first, the share of oxycodone and hydrocodone prescriptions that are at or above the 90 morphine milligram equivalent, or MME, level, and second, the share of oxycodone and hydrocodone prescriptions for a longer than seven-day period.

Below, we share some observations on how specific recommendations changed from 2016 to 2022 and update our analysis of the prescription data related to these recommendations.[7]

What do the CDC guidelines say about high-dosage opioid prescriptions?

The table below highlights the main differences in the language used in the 2016 and 2022 guidelines when providing summary recommendations related to dosages:

2016 guideline summary recommendation	2022 guideline summary recommendation
"When opioids are started, clinicians should prescribe the lowest effective dosage. Clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when increasing dosage to ≥50 morphine milligram equivalents (MME)/day, and should avoid increasing dosage to ≥90 MME/day or carefully justify a decision to titrate dosage to ≥90 MME/day."	"When opioids are initiated for opioid-naïve patients with acute, subacute, or chronic pain, clinicians should prescribe the lowest effective dosage. If opioids are continued for subacute or chronic pain, clinicians should use caution when prescribing opioids at any dosage, should carefully evaluate individual benefits and risks when considering increasing dosage, and should avoid increasing dosage above levels likely to yield diminishing returns in benefits relative to risks to patients."

Although the 2016 guideline's summary recommendation urged that clinicians "should use caution when prescribing opioids at any dosage," the summary recommendation then went on to cite two specific dosages: ≥50 MME/day and ≥90 MME/day.

In the context of the opioid public health epidemic and the large volume of high-stakes litigation, it was perhaps unsurprising that recommendations the CDC provided as guidance were interpreted by some legislators more strongly than intended. For example, the Arizona Opioid Epidemic Act of 2018 inscribed into law certain limitations and requirements for prescriptions over 90 MME/day.

In doing so, the Arizona legislators summarized the "carefully justify" language from the 2016 guideline as "Federal prescribing guidelines recommend doctors use ... extreme caution in prescribing above 90 MME/day."[8]

Although this is a subtle change in wording, it also is one that could be interpreted as a caution against writing prescriptions for this dosage, rather than as providing guidance on how to go about prescribing opioids at such levels when needed.

State and federal enforcement actions against individual pharmacies have also used the 90 MME cutoff as a de facto red flag on individual prescriptions. For example, a July 2023 consent decree resulting from a DEA investigation of one pharmacy prohibited the pharmacy from filling any such prescriptions.[9]

In fact, a more careful reading of the 2016 guideline makes clear that the summary recommendation was not intended as a prohibition on prescriptions above a specific threshold:

> The contextual evidence review found that although there is not a single dosage threshold below which overdose risk is eliminated, holding dosages <50 MME/day would likely reduce risk among a large proportion of patients who would experience fatal overdose at higher prescribed dosages. Experts agreed that lower dosages of opioids reduce the risk for overdose, but that a single dosage threshold for safe opioid use could not be identified.

As shown in the table above, in the 2022 guideline, the CDC avoided specific dosages in its summary recommendation. Elsewhere, the agency clarified that

> the recommendations related to opioid dosages are not intended to be used as an inflexible, rigid standard of care; rather, they are intended to be guideposts to help inform clinician-patient decision-making. Risks of opioid use, including risk for overdose and overdose death, increase continuously with dosage, and there is no single dosage threshold below which risks are eliminated.

That said, the implementation considerations and supporting rationale in the full 2022 guideline do make reference to the 50 MME and 90 MME levels that were included in the headline recommendation from 2016. In doing so, the CDC also cited some of the same evidence underlying the 2016 recommendation:

> Many patients do not experience benefit in pain or function from increasing opioid dosages to ≥50 MME/day but are exposed to progressive increases in risk as dosage increases. Therefore, before increasing total opioid dosage to ≥50 MME/day, clinicians should pause and carefully reassess evidence of individual benefits and risks. … Benefits of high-dose opioids for pain are not well established. Few trials evaluated opioid dosages of ≥90 MME/day.

What does the data show for high-dosage opioid prescriptions?

In data for noncancer patients, we observe a decreasing rate of prescriptions for ≥90 MME/day following the publication of the 2016 guideline. From 2011 until March 2016, when the 2016 guideline was issued, 26% of oxycodone prescriptions and 2% of hydrocodone prescriptions were for dosages equivalent to or higher than 90 MME/day.

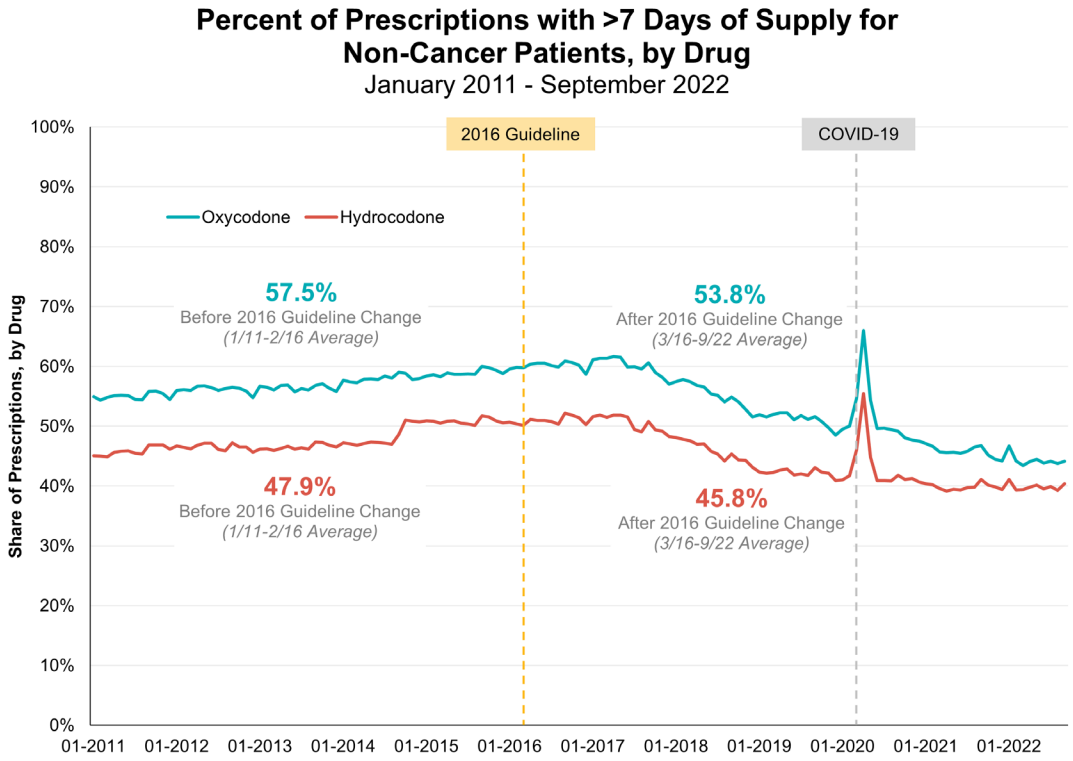
From April 2016 through September 2022, these rates dropped to 18% of oxycodone prescriptions and 1% of hydrocodone prescriptions. In other words, the rate of high-dose oxycodone prescriptions dropped by nearly a third, and the rate of high-dose hydrocodone prescriptions dropped by half.

However, Figure 1 shows that these decreases were by no means sudden reactions to the 2016 guideline. Instead, the rate of 90 MME/day prescriptions dropped gradually each year, with the largest decrease occurring in 2019.

Although such prescriptions have declined in frequency, the continued prevalence of prescriptions over 90 MME, especially for oxycodone, shows that despite the aggressive interpretation of some regulators and state legislators, many prescribers and pharmacies did not view the 2016 guideline as a hard-and-fast rule.[10]

Rather, they appear to have understood the guidance as it was intended and used more caution in making clinical judgments regarding the necessity and effectiveness of high-dose prescriptions. It is important to note that it is not possible to tell from this data whether these decreases reflect the elimination of illegitimate prescriptions or if there was impact to legitimate patient need.

Figure 1



What do the CDC guidelines say about high-volume and long-duration opioid prescriptions?

Similar to its guidance regarding dosages, in 2022, the CDC also adjusted its language around quantity and duration of opioid prescriptions. The table below highlights these differences between the 2016 and 2022 summary recommendations related to quantity:

2016 guideline summary recommendation	2022 guideline summary recommendation
"Long-term opioid use often begins with treatment of acute pain. When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids. Three days or less will often be sufficient; more than seven days will rarely be needed."	"When opioids are needed for acute pain, clinicians should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids."

Again, although the spirit of both recommendations is similar, the 2016 guideline was more specific in identifying seven days as a prescription length that would be rarely needed.

In this instance, the 2022 implementation considerations avoid reference to any specific threshold. The closest language to the 2016 guideline are statements that "[f]or many common causes of nontraumatic, nonsurgical pain, when opioids are needed, a few days or less are often sufficient" and "[i]f opioids are continued for ≥1 month, clinicians should ensure that potentially reversible causes of chronic pain are addressed and that opioid prescribing for acute pain does not unintentionally become long-term opioid therapy."

What does the data show about high-volume and long-duration opioid prescriptions?

In fact, however, our previous analysis of claims data suggested that the 2016 guideline was out of step with clinical practice at that time. From 2011 until March 2016, the data shows that 58% of oxycodone prescriptions and 48% of hydrocodone prescriptions were for more than seven days.

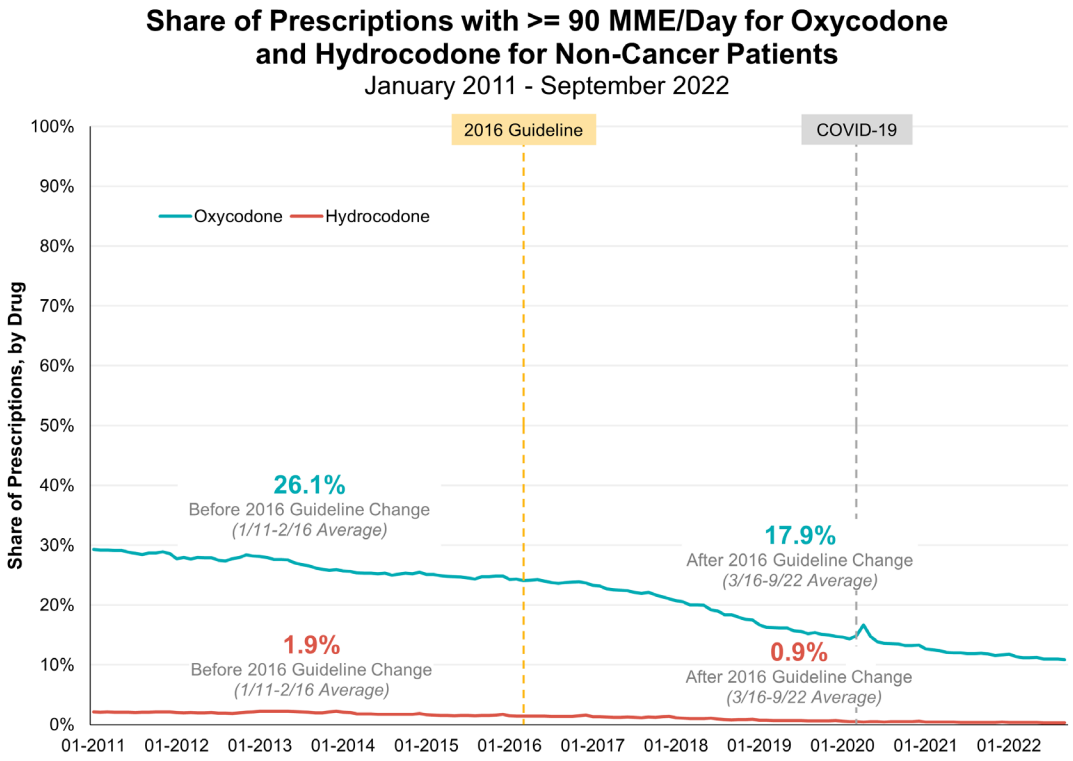
Although neither CDC document states a specific limit on dosage units per prescription, we have evaluated both days of supply and total doses per prescription in order to assess the potential impact of the 2016 guideline on present-day prescribing practices for oxycodone and hydrocodone.

Overall, as we also observed in 2016, such prescriptions continued to be quite common, even more so than for the high-dose prescriptions discussed above.

As shown in Figure 2, from April 2016 to September 2022, prescriptions for longer than seven days of supply decreased only slightly for both opioids, from 58% to 54% for oxycodone prescriptions and from 48% to 46% for hydrocodone prescriptions.[11]

There are likely many reasons for this change; one reality for many patients is that insurance design can favor longer prescription lengths as a means to avoid multiple copayments.

Figure 2



Prescriptions are written both in terms of days of supply and doses per day, which multiplied together define the actual number of pills dispensed. For that reason, we looked to see if there could have been a decrease in large prescriptions that was apparent in the total pills dispensed per prescription, but not in the days of supply.

In fact, we observed a similar decline in prescriptions for over 30 pills — from 64% to 58% for oxycodone and from 48% to 46% for hydrocodone — as in prescriptions for over seven days. Meanwhile, prescriptions for over 90 pills have remained a relatively steady, though small, share of the total, at roughly 23% for oxycodone and 11% to 26% for hydrocodone.

Conclusion

We observe gradual decreases in the relative prevalence of high-strength and long-duration opioid prescriptions after 2016, with most of the decrease occurring from 2016 to 2020.

At the same time, the CDC reports that overall, per capita opioid prescribing decreased by 35% over those years.[12] For the prescription types that constituted a decreasing share of the total, this means their absolute prevalence decreased by even more than the 35% overall rate.

This is in line with anecdotal evidence and concerns regarding patient access to such prescriptions.[13] The causes of the overall and specific decreases in opioid prescribing are numerous and difficult to disentangle, however, with the 2016 guideline one factor among many, including major litigation and regulatory changes to quotas.

It remains to be seen if any further changes in these trends can be observed following the 2022 updates to the CDC guideline. In turn, we will also need to closely monitor whether such a change, if observed, strikes an effective balance between the twin objectives of maintaining appropriate access to opioids for those with a legitimate medical need while restricting inappropriate prescribing.

Kenneth Weinstein is a managing principal, Nicholas Van Niel is a vice president and Kate Uthe is an associate at Analysis Group, Inc.

Endnotes

1 "Proposed Aggregate Production Quota 2024 (2023-24282) DEA1228," Drug Enforcement Administration, November 3, 2023, https://www.regulations.gov/document/DEA-2023-0150-0001.

2 Crystal Pike, et al., "Viewing Recent Opioid Regulations In Context," Law360, April 1, 2016, https://www.law360.com/articles/778707/viewing-recent-opioid-regulations-in-context.

3 See, for example, Tarlise Townsend, et al., "CDC Guideline For Opioid Prescribing Associated With Reduced Dispensing To Certain Patients With Chronic Pain," Health Affairs 40, no. 11 (2021): 1766-1775.

4 "Health Professionals Call on the CDC to Address Misapplication of its Guideline on Opioids for Chronic Pain through Public Clarification and Impact Evaluation," Health Professionals for Patients in Pain (HP3), March 6, 2019, https://healthprofessionalsforpatientsinpain.org/the-letter-1.

5 Deborah Dowell, et al., "Prescribing Opioids for Pain — The New CDC Clinical Practice Guideline," N Engl J Med 387, no. 22 (2022): 2011-2013. For example, the Arizona Opioid Epidemic Act inscribed into law certain limitations and requirements for prescriptions with over 90 MME per day ("The Arizona Opioid Epidemic Act: Protecting Individuals with Chronic Pain," Arizona Governor's Office, 2018, https://azgovernor.gov/sites/default/files/related-docs/chronicpainweb_0.pdf).

6 Our analysis is based on prescription claims data from January 2011 to September 2022 from the IQVIA PharMetrics Plus database. For simplicity and consistency with our 2016 analysis, we have limited the data to oxycodone and hydrocodone tablets, the two most commonly dispensed prescription opioids. Except where

otherwise noted, results exclude patients who had a diagnosis for cancer at any point in the claims period, as the guidelines and associated state laws and enforcement actions generally make an exception for such patients given their medical need for higher-strength prescriptions. In total, the data analyzed include over 40 million prescriptions for oxycodone and over 80 million prescriptions for hydrocodone.

7 All excerpts are taken from the complete guidelines: Deborah Dowell, Tamara M. Haegerich, and Roger Chou, "CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016," MMWR Recomm Rep 65, no. 1 (2016): 1-49; Deborah Dowell, et al., "CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022," MMWR Recomm Rep 71, no. 3 (2022): 1-95. For further discussion of differences between the guidelines, see Andrew Joseph, "New CDC opioid guidelines emphasize flexibility in treating pain," STAT, November 3, 2022, https://www.statnews.com/2022/11/03/new-cdc-opioid-guidelines-emphasize-flexibility-in-treating-pain/.

8 "The Arizona Opioid Epidemic Act: Protecting Individuals with Chronic Pain," Arizona Governor's Office, 2018, https://azgovernor.gov/sites/default/files/related-docs/chronicpainweb_0.pdf.

9 In reference to the consent decree for Beckman's Greene Street Pharmacy, Inc., see "Consent Decree Approved Among the United States and Cumberland, Maryland Based Pharmacy and Pharmacist Alleged to Have Illegally Dispensed Controlled Substances," US Attorney's Office, District of Maryland, July 6, 2023, https://www.justice.gov/usao-md/pr/consent-decree-approved-among-united-states-and-cumberland maryland-based-pharmacy-and. For an example of a state Board of Pharmacy action from California citing the 90 MME guidance, see In the Matter of the First Amended Accusation Against: M & S Pharmaceuticals, Inc. d/b/a OC Wellness and Specialty Pharmacy, Case No. 6979 (Board of Pharmacy, Department of Consumer Affairs, State of California 2022), https://www.pharmacy.ca.gov/enforcement/fy1920/ac196979_rph65658.

10 As a reminder that many other factors have been at play since 2016, the chart also shows a visible uptick in high-dose oxycodone prescriptions in April 2020, as prescription patterns were disrupted by the early months of the COVID-19 pandemic, and opioids were used for some patients on ventilators. This effect seems to have dissipated quickly.

11 We again note a brief spike in longer prescriptions at the outset of the COVID-19 pandemic.

12 "United States Dispensing Rate Maps," Centers for Disease Control and Prevention, last reviewed December 11, 2023, https://www.cdc.gov/drugoverdose/rxrate-maps/index.html.

13 See, for example, Vishakha Darbha, Lucy King, and Adam Westbrook, "They Live in Constant Pain, but Their Doctors Won't Help," The New York Times, August 17, 2023, video, https://www.nytimes.com/video/opinion/100000008971121/opioids-chronic-pain-patients.html.