CSAM **California Society of Addiction Medicine**
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A specialty society of physicians founded in 1973. Since 1989, a State Chapter of the American Society of Addiction Medicine

28 March 2022

Austin Weaver, Manager
California Department of Justice
CURES Program
P.O. Box 160447
Sacramento, CA 95816

Tel. (916) 210-3171

RE: ***Appriss NarxCare/Bamboo Health PMP Clearinghouse*** **Implementation in California**

Dear Mr. Weaver:

The California Department of Justice (DOJ) recently awarded Bamboo Health the contract for prescription data collection services for the Controlled Substance Utilization Review and Evaluation System (CURES). Effective Wednesday, February 9, 2022, all reporting must go through **Bamboo Health's PMP Clearinghouse**. It is our understanding that **Appriss's NarxCare Prescription Data Monitoring Program** (PDMP) product has simply renamed Appriss NarxCare as a part of the Bamboo package (Appriss + PatientPing).

I am writing as the President of the California Society of Addiction Medicine (CSAM), in order to collect important information about use of **Appriss' NarxCare/Bamboo Health products,** in particular, components of NarxCare/Bamboo Health that generate **Overdose Risk Scores** or **Opioid Use Disorder (OUD) Risk Scores.** It is important to note at the outset that our medical society strongly support PDMP's--like CURES in California. But, we require additional information from the California Department of Justice (CaDOJ) to understand whether the shared datasets and operational algorithms are research-evaluated and evidence-based or merely proprietary.

It appears that NarxCare is a product with opaque algorithms, some of which are Artificial Intelligence (AI) forms of Machine Learning (ML) that are both proprietary and partially opaque to query. It also appears that this product, that can have such major impact on prescribing practices and access to opioid analgesic medications for pain patients, has been neither reviewed nor approved by the FDA or medical university researchers.

We will begin by drawing your attention to the attached October 2021 article by a *New York Times* and *Wired* contributor, Maia Szalavitz, *The Pain Was Unbearable. So Why Did Doctors Turn Her Away*? [Copy Attached] In this work of investigative journalism, she describes NarxCare as a proprietary product utilizing diverse datasets and opaque Machine Learning (ML) technologies. NarxCare produces a composite **Overdose Risk Score** that has powerful implications for pharmacist dispensing practices and physician care of complex pain patients:

> In the past few years, through a series of acquisitions and government contracts, a single company called Appriss has come to dominate the management of these state prescription databases. While the registries themselves are somewhat balkanized—each one governed by its own quirks, requirements, and parameters—Appriss has helped to make them interoperable, merging them into something like a seamless, national prescription drug registry. It has also gone well beyond merely collecting and retrieving records, developing machine-learning algorithms to generate "data insights" and indicating that it taps into huge reservoirs of data outside state drug registries to arrive at them.
>
> NarxCare—the system that inspired Kathryn's gynecologist to part ways with her—is Appriss' flagship product for doctors, pharmacies, and hospitals: an "analytics tool and care management platform" that purports to instantly and automatically identify a patient's risk of misusing opioids.
>
> On the most basic level, when a doctor queries NarxCare about someone like Kathryn, the software mines state registries for red flags indicating that she has engaged in "drug shopping" behavior: It notes the number of pharmacies a patient has visited, the distances she's traveled to receive health care, and the combinations of prescriptions she receives.

> Beyond that, things get a little mysterious. NarxCare also offers states access to a complex machine-learning product that automatically assigns each patient a unique, comprehensive Overdose Risk Score. Only Appriss knows exactly how this score is derived, but according to the company's promotional material, its predictive model not only draws from state drug registry data, but "may include medical claims data, electronic health records, EMS data, and criminal justice data." At least eight states, including Texas, Florida, Ohio, and Michigan—where Kathryn lives—have signed up to incorporate this algorithm into their monitoring programs.

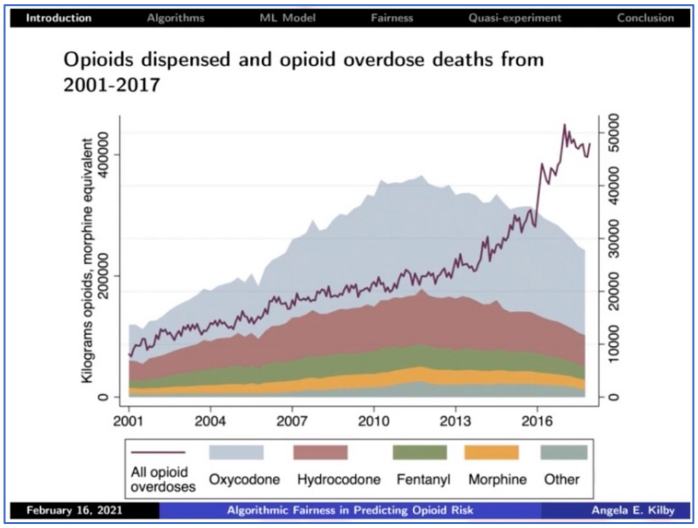
Apriss has said that the Overdose Risk Score is a screening tool that may call for deeper physician evaluation. However, it is a commonplace fact that screening tools and "guidelines" very often end up being utilized as if they were diagnostic instruments or dose ceiling regulations (for example dosage "red lines" in opioid analgesic prescribing). It is not entirely clear whether corporate marketing is focusing on identifying overdoses *per se* or more generally, opioid use disorders (OUD's). Certainly, focusing on overdoses has more public relations appeal.

Ms. Szalavitz identified a troubling discrepancy between Appriss' marketing materials and a direct response to her query:

> Later, in an emailed response to specific questions about its data sources, the company made a startling claim: In apparent contradiction to its own marketing material, Appriss said that NarxCare's predictive risk algorithm makes no use of any data outside of state prescription drug registries. "The Overdose Risk Score was originally developed to allow for ingestion of additional data sources beyond the PDMP," a spokesperson for the company said, "but no states have chosen to do so. All scores contained within NarxCare are based solely on data from the prescription drug monitoring program."

It is possible that a single Overdose Risk Score may be grossly oversimplifying our present ability to know who is truly at greatest risk when receiving opioid prescriptions, particularly in complex and terminal chronic pain patients.

Prof. Angela Kilby is a researcher at Northeastern University who has done work on ML algorithms and their relative value in predicting opioid use disorders. In the main, her findings do not find usable predictive value in such algorithms; indeed, she finds some counterintuitive patterns. She offers the graphic below that shows a major disconnect in 2012 between opioid prescribing volumes and overdose deaths in the USA.



At the same time that opioid prescriptions were forced downward in 2012, the rise in opioid overdose deaths became significantly steeper. This is counterintuitive, but must be considered. It is possible that the DOJ nationally has aimed at the wrong targets.

Surely California has contributed state data to this national rollup. Can California DOJ generate a similar graphic to display California opioid prescribing volumes against California overdose deaths, with a stratification of involved opioid compounds? It is important to understand whether very substantial shifts in prescribing/dispensing patterns in California have had the desired effects or have instead furthered access to illicit sources of imported or diverted opioids (see pp. 9-11).

Title 11 Law permits CURES access for eligible regulatory and law enforcement officials. CSAM notes that CURES is already monitoring dispensed MME's (Morphine Mg. Equivalents). In this context, it is important to point out that no international standard definition of opioid dependence relies on any "red line" daily dose amount as a criterion for an Opioid Use Disorder (OUD). This is because genetic variances in metabolic rates can vary by up to 17-fold. In this new era of Bamboo Health oversight, CSAM is concerned lest pharmacies decline legitimate fills or refills because of opaque Bamboo Health algorithms. CSAM decries any use of **Opioid Overdose Risk** or **Opioid Use Disorder (OUD) Risk** scores that have proprietary algorithms and have not been thoroughly researched for validity. Any risk score

must be transparent, the algorithms available, machine learning models must be described; and, all risk scores must be validated by research before implementation. CSAM supports the need for FDA review of NarxCare risk scores.

This brings us to our present **seven questions for California DOJ and CURES PDMP**. It is, perhaps, important to reiterate that our medical society is a strong supporter of PDMP's, but of course the practice of medicine and prescribing practices must remain evidence-based…hence, some of our exploratory questions.

We would be most grateful for a response <u>in writing</u> to the following seven domains of questions:

1. **Implementation of NarxCare/Bamboo:** What procedures were followed in awarding a patient prescription data monitoring contract to NarxCare/Bamboo? What evaluation procedures were followed by DOJ in assessing the validity of the proprietary algorithms? Has the corporate entity shared the underlying algorithms and AI/ML models that contribute to the Overdose Risk Score?
2. **Overdose Risk Score & Opioid Rx Doses:** How does NarxCare/Bamboo utilize dose ranges of opioid prescriptions in developing a final Overdose Risk Score? In particular, does the algorithm consider daily doses that are over 90 mg-equivalents of morphine as a higher risk category or a kind of red line? Is there a red line in the program?
3. **Implementation & Evaluation in CURES**: Please provide information about what CURES data will be shared and what CURES data will be withheld. And, has DOJ/CURES implemented any kind of patient outcomes assessments for patients receiving high-risk scores? If so, please describe the methodology for ongoing evaluations, if any. Will California's implementation include Overdose Risk Scores or an Opioid Use Disorder Risk score? Will CURES be able track pharmacy refusals to fill opioid prescriptions?
4. **Sharing of DOJ Criminal Justice System (CJS) Datasets**: Does California DOJ share any other CJS datasets with entities such as NarxCare or Bamboo that access prescription datasets? More specifically, are any criminal justice datasets to be accessed by NarxCare/Bamboo? And, are medical diagnoses captured from insurance or other health systems datasets by NarxCare/Bamboo?
5. **Research Evidence-Base for Validity of Overdose Risk Score**: Has CaDOJ/CURES obtained any publications of research that supports the efficacy of NarxCare/Bamboo's predictive score? We must note that opioid prescriptions are rather rare in a general prescription population; and, lethal overdoses with prescribed medications are that much more rare, thus making this kind of research quite difficult; and, good research requires huge datasets that include data on causes of overdose emergency care or death.
6. **FDA Evaluation**: Has DOJ consulted with the FDA about the validity and efficacy of this relatively novel and proprietary software? CSAM recommends that DOJ/CURES request an FDA Evaluation of metrics and outcomes.
7. **Graphic Display of CA Opioid Rx Volumes vs OD Deaths**: Please see the discussion adjacent to the national graphic included in the prior page. We request multiple years of California data that will allow production of a similar graphic for California.

Karen A. Miotto, MD,
President, California Society of Addiction Medicine
Associate Professor, Psychiatry and Biobehavioral Sciences, UCLA

Attachment:

Szalavitz, Maia (2021-Oct); *The Pain Was Unbearable. So Why Did Doctors Turn Her Away?,* Wired Magazine, https://www.wired.com/story/opioid-drug-addiction-algorithm-chronic-pain/

CC:

1. Richard Pan, MD Chair of California Senate Health Committee
2. Jim Wood, Chair of Assembly Health Committee
3. Toni G. Atkins (D), President Pro Tempore, California Senate
4. Eloise Reyes (D), Majority Leader, California State Assembly
5. Rob Bonta, Esq., Attorney General, State of California
6. William F. Haning, III, MD, President, American Society of Addiction Medicine (ASAM)
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8. Amol Soin, MD, President, American Society of Interventional Pain Physicians
9. Ripu Arora, MD, Board President, California Society of Interventional Pain Physicians
10. Richard Dang, PharmD, APh, BCACP, President, California Pharmacists Association
11. Jim Scott, PharmD, APh, M.Ed., AAHIVP, FCCP, President, Calif. Society of Health-System Pharmacists
12. Anthony D. Romero, Executive Director, American Civil Liberties Union (ACLU)
13. Carlos Marquez III, Executive Director, ACLU California Action
14. Rick Callender, President, California NAACP
15. Derek Hodel, President of the Board, Drug Policy Alliance (DPA)
16. Kassandra Frederique, Executive Director, Drug Policy Alliance (DPA)
17. Ethan Nadelman, Past President, Drug Policy Alliance (DPA)
18. Maia Szalavitz, Investigative Reporter, New York Times
19. Sarah Kliff, Investigative Health Reporter, New York Times
20. Melody Petersen, Health Reporter, Los Angeles Times
21. Cathie Anderson, Health Reporter, Sacramento Bee

References & Attachment (#1):

1. Szalavitz, Maia (2021); **The Pain Was Unbearable. So Why Did Doctors Turn Her Away?** Wired Magazine. https://www.wired.com/story/opioid-drug-addiction-algorithm-chronic-pain/ [Copy Attached]

2. Oliva, Jennifer, **Dosing Discrimination: Regulating PDMP Risk Scores** (January 18, 2021). 110 California Law Review __ (pre-publication, forthcoming 2022), Available at SSRN: https://ssrn.com/abstract=3768774 or http://dx.doi.org/10.2139/ssrn.3768774

   Abstract: Imagine the following scenario. You are a thirty-year-old Army veteran. While in the service, you were the victim of a horrific sexual assault and diagnosed with post-traumatic stress disorder (PTSD). Your military health care provider (HCP) prescribes a low dose sedative "PRN" (take as needed) to mitigate your PTSD symptoms.

   Several years later, you are diagnosed with a painful and debilitating inflammatory bowel disorder (IBD), which significantly diminishes your daily functioning without treatment. Your military HCP prescribes you hydrocodone, which allows you to manage your IBD symptoms. As your condition deteriorates, you decide to retire from the military and seek treatment at a civilian clinic.

   At first, your new HCP continues your prescription drug treatment regimen. A few months later, however, that HCP informs you that (1) she is under U.S. Drug Enforcement Administration (DEA) investigation due to her state prescription drug monitoring program (PDMP) data, (2) you have been flagged by the PDMP as at risk for opioid misuse, and (3) she has no choice but to discontinue your medication. You try to no avail to find another HCP before you lapse into opioid withdrawal and are riddled with severe IBD symptoms. Within a week of your medication discontinuation, you are bedridden, unable to work or take care of your family, severely depressed, and experiencing suicidal ideation. This article exposes and critiques the laws and policies that collude to coerce this scenario and identifies and examines a regulatory oversight framework that can mitigate such needless pain and suffering.

   The American drug overdose crisis and generous funding by U.S. law enforcement agencies have provoked forty-nine states to implement PDMP surveillance programs. PDMP platforms rely on proprietary, predictive algorithmic tools designed and manufactured by a private company to determine a patient's risk for drug misuse. Law enforcement conducts dragnet sweeps of PDMP data to target providers that the platform characterizes as "overprescribers" and patients that it deems as high risk of drug diversion, misuse, and overdose. Research demonstrates that PDMP risk scoring coerces clinicians to force taper, discontinue, and even abandon vulnerable patients without regard for the catastrophic collateral consequences that attend to those treatment decisions.

   The proxies that PDMPs utilize to generate patient risk scores are likely to produce artificially inflated risk scores for vulnerable patients. PDMPs, therefore, have the potential to exacerbate discrimination against vulnerable patients with stigmatized medical conditions by generating flawed, short-cut assessment tools that incentivize providers to deny these individuals indicated treatment. The Federal Food and Drug Administration (FDA) is authorized to regulate PDMP software platforms as medical devices and the agency has recently issued guidance that provides a robust framework for such oversight. This Article contends that FDA is obligated to exercise its regulatory authority over PDMP risk scoring software to ensure that such predictive diagnostic tools are safe and effective for patients.

3. Kilby, Angela E.; **YouTube Presentation** (20 min.): Kilby, Angela (2021-May-05); **Algorithmic Fairness** in Predicting Opioid Use Disorder Using Machine Learning. https://www.youtube.com/watch?v=O3Mjw-agzww&ab_channel=TheConferenceonFairness%2CAccountability%2CandTransparency%28FAT%2a%29

4. Kilby, Angela E.; **Algorithmic Fairness in Predicting Opioid Use Disorder using Machine Learning**, Chapter in FAccT '21: Proceedings of the 2021 ACM Conference on Fairness, Accountability, and Transparency, March 2021 Pages 272, https://doi.org/10.1145/3442188.3445891, Online:01 March 2021.

   Abstract: There has been recent interest by payers, health care systems, and researchers in the development of machine learning and artificial intelligence models that predict an individual's probability of developing opioid use disorder. The scores generated by these algorithms can be used by physicians to tailor the prescribing of opioids for the treatment of pain, reducing or foregoing prescribing to individuals deemed to be at high risk, or increasing prescribing for patients deemed to be at low risk. This paper constructs a machine learning algorithm to predict opioid use disorder risk using commercially available claims data similar to those utilized in the development of proprietary opioid use disorder prediction algorithms. We study risk scores generated by the machine learning model in a setting with quasi-experimental variation in the likelihood that doctors prescribe opioids, generated by changes in the legal structure for monitoring physician prescribing.

   We find that machine-predicted risk scores do not appear to correlate at all with the individual-specific heterogeneous treatment effect of receiving opioids. The paper identifies a new source of algorithmic unfairness in machine learning applications for health care and precision medicine, arising from the researcher's choice of objective function. While precision medicine should guide physician treatment decisions based on the heterogeneous causal impact of a course of treatment for an individual, allocating treatments to individuals receiving the most benefit and recommending caution for those most likely to experience harmful side effects, ML models in health care are often trained on proxies like individual baseline risk, and are not necessarily informative in deciding who would most benefit, or be harmed, by a course of treatment.

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CDPH (2021); *Synthetic Opioid-Related Overdose Deaths Increased at an Unpredictable Pace in 2020*; California Overdose Surveillance Dashboard, California Opioid Overdose Snapshot- 2018-Q1 through 2021-Q2, https://www.cdph.ca.gov/Programs/CCDPHP/sapb/CDPH%20Document%20Library/2020-Overdose-Mortality-Data-Brief_ADA.pdf

Coffin, P.O. and Barreveld, A.M.(2022-02-17), *Inherited Patients Taking Opioids for Chronic Pain—Considerations for Primary Care*, NEJM, https://www.nejm.org/doi/full/10.1056/NEJMp2115244

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Hoffman, Jan (2022-02-10); *The Agency Threw Out Previous Recommended Limits on Doses but Encouraged 'Nonopioid Therapies,'* NYT, https://www.nytimes.com/2022/02/10/health/cdc-opioid-pain-guidelines.html

Kilby, Angela E. (2021-Jan); *Algorithmic Fairness in Predicting Opioid Use Disorder using Machine Learning;* FAccT '21: Proceedings of the 2021 ACM Conference on Fairness, Accountability, and Transparency, https://dl.acm.org/doi/10.1145/3442188.3445891

National Academies of Sciences, Engineering, and Medicine. 2019. *Pain Management for People with Serious Illness in the Context of the Opioid Use Disorder Epidemic: Proceedings of a Workshop*. Washington, DC: The National Academies Press. https://doi.org/10.17226/25435, https://www.nap.edu/catalog/25435/pain-management-for-people-with-serious-illness-in-the-context-of-the-opioid-use-disorder-epidemic.

National Academies of Sciences, Engineering, and Medicine. 2017. *Pain Management and the Opioid Epidemic: Balancing Societal and Individual Benefits and Risks of Prescription Opioid Use*. Washington, DC: The National Academies Press. https://doi.org/10.17226/24781. https://www.nap.edu/catalog/24781/pain-management-and-the-opioid-epidemic-balancing-societal-and-individual.

Oliva, Jennifer (pre-publication 2021-01-18); *Dosing Discrimination: Regulating PDMP Risk Scores*; 110 California Law Review, Available at SSRN" https://ssrn.com/abstracts=3768774 or http://dx.doi.org/10.2139/ssrn.3768774.

Park, JN (2022); *Polysubstance Overdose Deaths in the Fentanyl Era-A Latent Class Analysis*, J Addict Med; https://journals.lww.com/journaladdictionmedicine/Abstract/2022/02000/Polysubstance_Overdose_Deaths_in_the_Fentanyl_Era_.12.aspx.

Shover, Chelsea L. et al. (2020-11-01), *Steep increases in fentanyl-related mortality west of the Mississippi River*: *Recent evidence from county and state surveillance*, Drug and Alcohol Dependence, https://www.sciencedirect.com/science/article/pii/S0376871620304798?via%3Dihub

Szalavitz, Maia (2021-Oct); *The Pain Was Unbearable. So Why Did Doctors Turn Her Away?,* Wired Magazine, https://www.wired.com/story/opioid-drug-addiction-algorithm-chronic-pain/

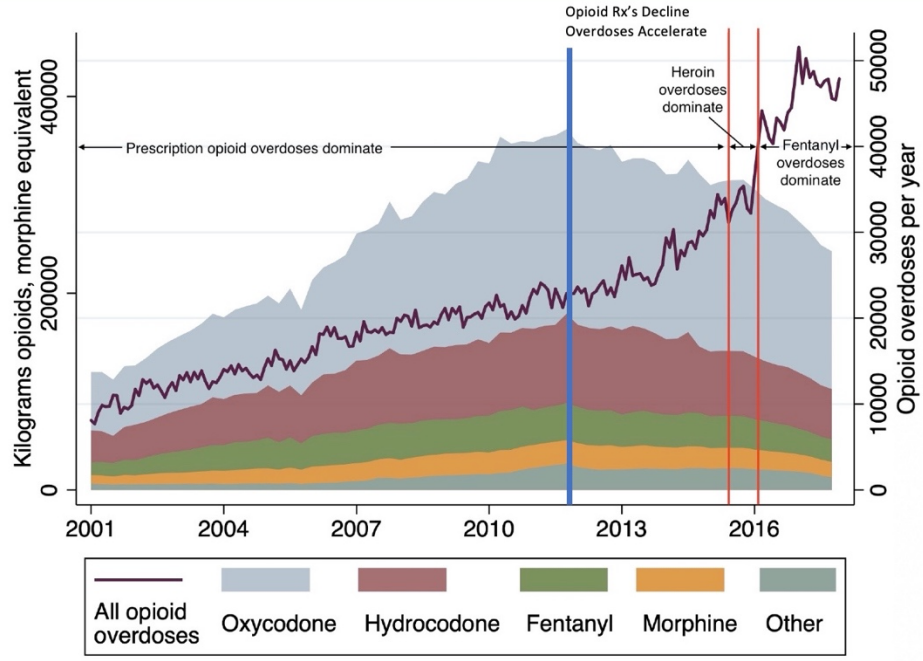
Weiner, Scott G. et al. (2022-01-28); *Factors Associated with Opioid Overdose After an Initial Opioid Prescription*, JAMA Network Open; https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2788462

The following graphic is from Prof. Kilby's chapter (p.27), referenced above. We have edited it to include a vertical blue line (with comment) to delineate the sustained decline in opioid prescriptions from 2012.

This graph is instructive. It shows a **four-phase picture** that does not supports efficacy of opioid Rx strictures in reducing annual opioid overdose deaths. What is suggested is a criminal justice enforcement-related crossover effect from prescription opioid deaths to street opioid deaths and a steeper death curve.

1. **2001--2012**: **Opioid Marketing.** Opioid prescription volumes increase gradually; and, overdose deaths closely follow this increase—except for oxycodone Rx's which greatly exceed the Rx growth curve for all of the other opioids. This was an era of heavy *Purdue Pharma* marketing of Oxycodone.
2. **2012--Mid-2015**: **Prescription Enforcement.** All opioid prescriptions are in decline, including oxycodone, but overdoses now rise steeply even as opioid prescriptions decline. However, prescription opioid overdoses remain dominant. This is the phase in which multiple efforts to reduce reliance on opioid analgesics has had an effect on prescribing practices—but not on overdose deaths, that rise ever more steeply.
3. **Mid-2015—Early 2016: Shift to Street Drugs**. There is a shift from pharmaceutical dominance to street drug dominance in deaths, related to a new predominance of **heroin** overdoses. The death curve steepens more than before.
4. **Early 2016—2017: Fentanyl Dominance**. Fentanyl overdoses dominate. Even as opioid prescriptions continue in a steep decline. Opioid overdose deaths have doubled since about 2014.

Opioids Dispensed via Pharmacies, Hospitals, Practitioners, etc., Overlayed with Opioid Overdoses, from 2001-2017



Notes: Opioid dispensing data is compiled from the DEA's ARCOS reporting system, and depicts total kilograms of opioids dispensed in morphine equivalents, and the proportion of that total accounted for by oxycodone, hydrocodone, etc. Each opioid is converted to morphine equivalents using a conversion factor, morphine milligram equivalents, or MME (Centers for Disease Control, 2018). Opioid overdose deaths are from CDC's NCHS Vital Statistics mortality data. Opioid overdose deaths are deaths with underlying cause of death code of X40-X44, X60-X64, X85, or Y10-Y14 (indicating a drug overdose), and multiple causes of death codes of T40.0-T40.4 or T40.6 (indicating opioids or heroin specifically were listed). "Prescription opioid overdoses dominate" from 2001 to mid-2015, when T40.2 – semisynthetic opioids, including drugs such as oxycodone, hydrocodone, hydromorphone, and oxymorphone – was the most frequently mentioned drug on a death certificate. "Heroin overdoses dominate" from mid-2015 to early 2016 when heroin (T40.1) was most frequently mentioned, and "fentanyl overdoses dominate" when T40.4 – synthetic opioid analgesics other than methadone, including drugs such as fentanyl and tramadol – is most frequently listed. Note that many overdoses are poly-drug overdoses and therefore include more than one T-code.

5. Johnson, Sydney (2022-02-01); **Are the City's overdose treatments working? It's impossible to tell**, San Francisco Examiner. https://www.sfexaminer.com/findings/are-s-f-s-overdose-interventions-working/

Extract: There were 50 fewer overdose deaths linked to opioids, cocaine or methamphetamine in 2021 compared with 2020, when overdose deaths reached an all-time high of 700, according to data from the San Francisco Department of Public Health. The past year marked the first decline in overdose deaths since 2018.

But other recent city data show overdose reversals are climbing, while substance use treatment admissions have been on the decline for years. The simultaneous trends point to a complicated picture of limited treatment options during the pandemic, a deadlier drug supply that requires fast-acting reversals, and a growing number of individuals treated each year with addiction medications outside publicly funded programs.

6. Weiner, Scott G., et al. (2022-01-28); **Factors Associated with Opioid Overdose After an Initial Opioid Prescription**, JAMA Network Open. https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2788462

Abstract:

Importance: The opioid epidemic continues to be a public health crisis in the US. Objective: To assess the patient factors and early time-varying prescription-related factors associated with opioid-related fatal or nonfatal overdose.

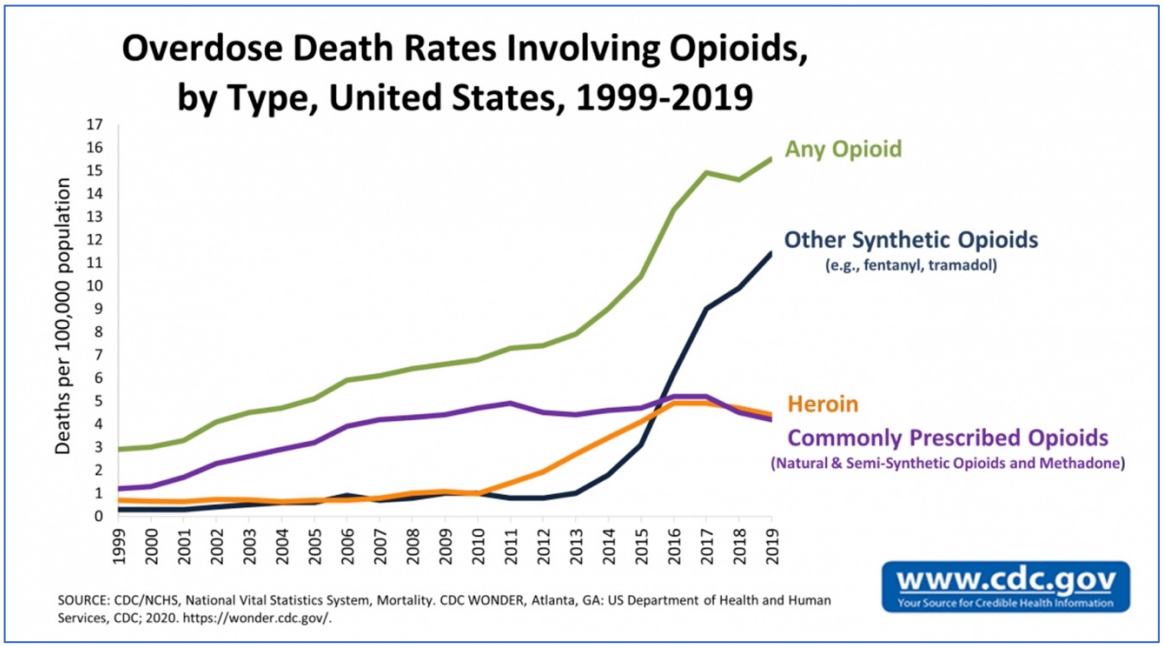
Design, Setting, and Participants: This cohort study evaluated opioid-naive adult patients in Oregon using data from the Oregon Comprehensive Opioid Risk Registry, which links all payer claims data to other health data sets in the state of Oregon. The observational, population-based sample filled a first (index) opioid prescription in 2015 and was followed up until December 31, 2018. Data analyses were performed from March 1, 2020, to June 15, 2021. Exposures: Overdose after the index opioid prescription.

Main Outcomes and Measures: The outcome was an overdose event. The sample was followed up to identify fatal or nonfatal opioid overdoses. Patient and prescription characteristics were identified. Prescription characteristics in the first 6 months after the index prescription were modeled as cumulative, time-dependent measures that were updated monthly through the sixth month of follow-up. A time-dependent Cox proportional hazards regression model was used to assess patient and prescription characteristics that were associated with an increased risk for overdose events.

Results: The cohort comprised **236921 patients** (133 839 women [56.5%]), of whom 667 (0.3%) experienced opioid overdose. Risk of overdose was highest among individuals 75 years or older (adjusted hazard ratio [aHR], 3.22; 95% CI, 1.94-5.36) compared with those aged 35 to 44 years; men (aHR, 1.29; 95% CI, 1.10-1.51); those who were dually eligible for Medicaid and Medicare Advantage (aHR, 4.37; 95% CI, 3.09-6.18), had Medicaid (aHR, 3.77; 95% CI, 2.97-4.80), or had Medicare Advantage (aHR, 2.18; 95% CI, 1.44-3.31) compared with those with commercial insurance; those with comorbid substance use disorder (aHR, 2.74; 95% CI, 2.15-3.50), with depression (aHR, 1.26; 95% CI, 1.03-1.55), or with 1 to 2 comorbidities (aHR, 1.32; 95% CI, 1.08-1.62) or 3 or more comorbidities (aHR, 1.90; 95% CI, 1.42-2.53) compared with none. Patients were at an increased overdose risk if they filled oxycodone (aHR, 1.70; 95% CI, 1.04-2.77) or tramadol (aHR, 2.80; 95% CI, 1.34-5.84) compared with codeine; used benzodiazepines (aHR, 1.06; 95% CI, 1.01-1.11); used concurrent opioids and benzodiazepines (aHR, 2.11; 95% CI, 1.70-2.62); or filled opioids from 3 or more pharmacies over 6 months (aHR, 1.38; 95% CI, 1.09-1.75).

Conclusions and Relevance: This cohort study used a comprehensive data set to identify patient and prescription-related risk factors that were associated with opioid overdose. These findings may guide opioid counseling and monitoring, the development of clinical decision-making tools, and opioid prevention and treatment resources for individuals who are at greatest risk for opioid overdose.

7. CDC: Overdose Death Rates Involving Opioids by Type, United States, 1999-2019



8. California CDPH (Feb 2021): Synthetic Opioid-Related Overdose Deaths Increased at an Unpredictable Pace in 2020.

CSAM Note: There is a large and growing illicit fentanyl supply that originates internationally (primarily from China and Mexico). The chart below shows a dramatic uptick in synthetic opioid overdoses in California from 2019. However, CDPH data does not discriminate between prescribed and trafficked fentanyl analogues. However, coroner's overdose cases could query CURES to see if the victim had a recent fentanyl prescription. Sorting prescribed from illegal sources is technically possible in the deceased.

Substance and Addiction Prevention Branch - Overdose Prevention Initiative

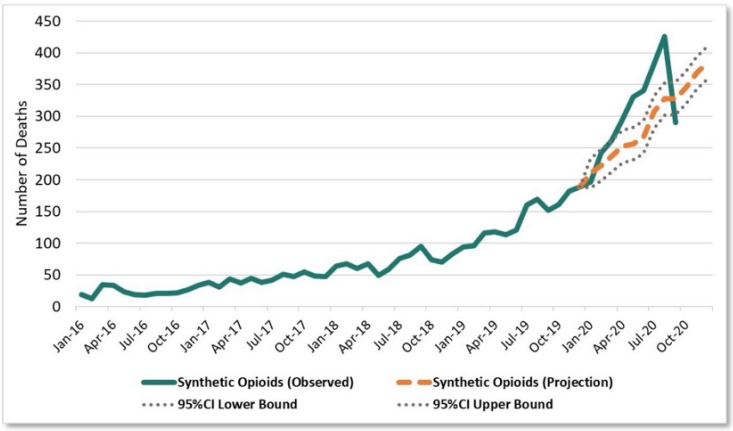
"Synthetic Opioid-Related Overdose Deaths Increased at an Unpredictable Pace in 2020"

Key Points

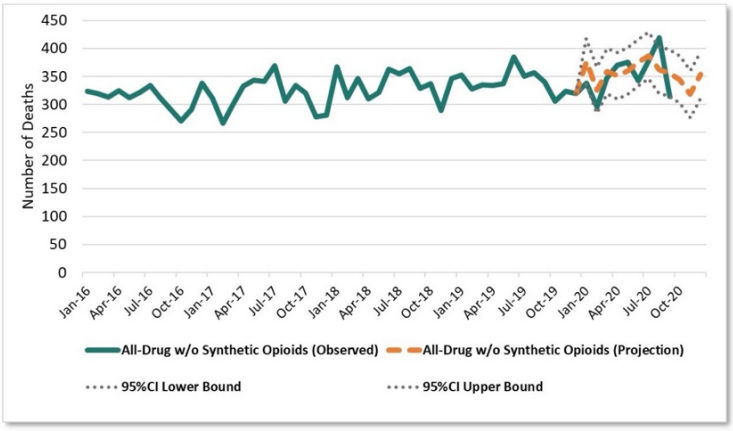
- Synthetic opioid-related overdose deaths are increasing.
- All-drug-related overdose deaths, excluding synthetic opioids, increased in 2020 at a predictable pace.
- Naloxone (Narcan), the antidote to opioid overdoses, is one of our best tools to prevent fentanyl deaths.
- Together, we can destigmatize substance use disorder by providing services in a culture of respect and safety.

Notes: CI = confidence interval; overdoses classified by the ICD-10 codes X40-X44; includes accidental deaths only; synthetic opioids excludes methadone and includes fentanyl and fentanyl analogs

Number of Preliminary Observed and Projected Synthetic Opioid-Related Overdose Deaths in California, 2016 – 2020



Number of Preliminary Observed and Projected All-Drug-Related Overdose Deaths, Excluding Synthetic Opioids, in California, 2016 – 2020



February 2021

www.cdph.ca.gov/sapb

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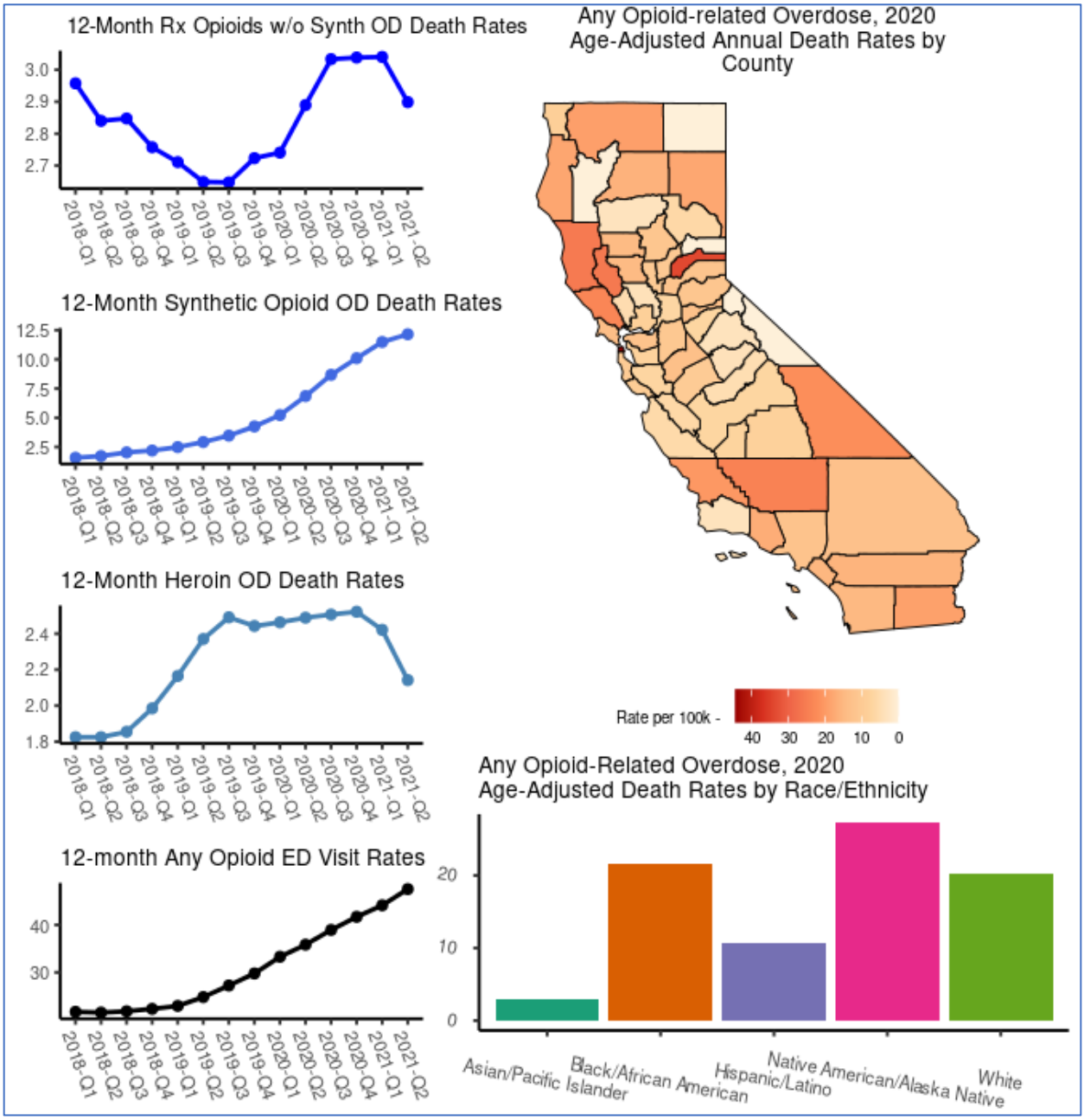
9. CDPH: California Opioid Overdose Snapshot: 2018-Q1 through 2021-Q2

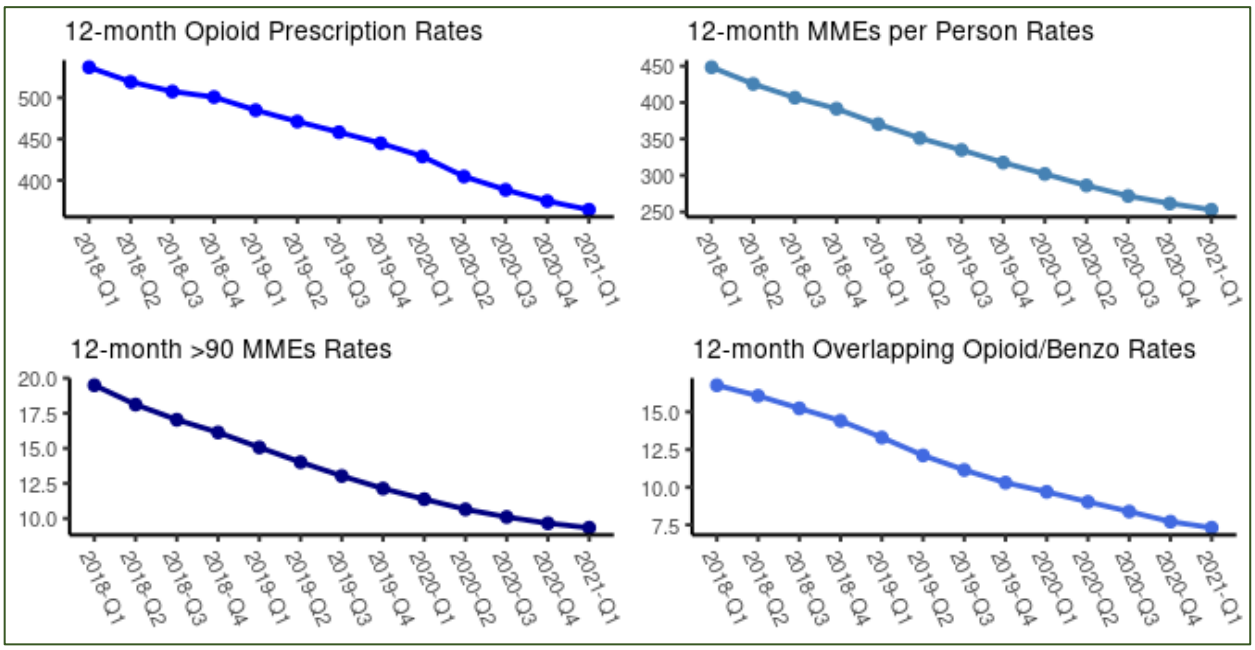
https://skylab.cdph.ca.gov/ODdash/ Downloaded 2/9/2022

California experienced 5,502 opioid-related overdose deaths in 2020, the most recent calendar year of data available. The annual crude mortality rate for 2020 was 13.87 per 100k residents. This represents a **126% increase from 2018**. The following charts present 12-month moving averages for selected opioid indicators (prescription-, heroin-, and synthetic opioid-related overdose deaths, and ED visits related to any opioid) and include trend data for 2021*. The map displays the annual county level age-adjusted rates for any opioid-related overdose deaths. Synthetic overdose deaths may be largely represented by fentanyl.



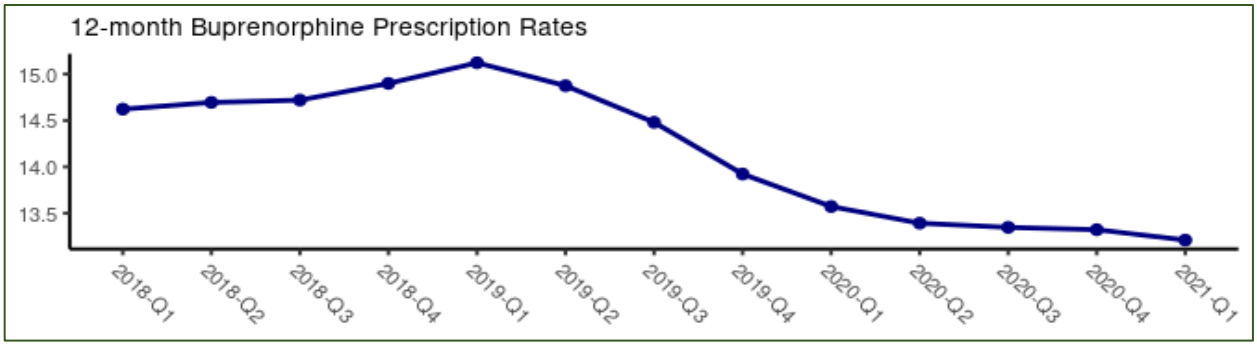
Prescribing:

There were 14,867,426 prescriptions for opioids (excluding buprenorphine) in **California in 2020**. The annual crude opioid prescribing rate for 2020 was 374.87 per 1,000 residents. This represents **a 25% decrease in prescribing from 2018.** The following charts present 12-month moving averages for crude opioid prescribing rates, the crude rate of MMEs (morphine milligram equivalents) per person, the crude high dosage rate (greater than 90 Daily MMEs in the quarter), and the crude opioid/benzodiazepine overlap rate from 2018 to 2020.



Treatment:

Buprenorphine prescriptions in the state are used to gauge the expansion of medication-assisted treatment (MAT). The annual crude buprenorphine prescribing rate for **2020** was 13.32 per 1,000 residents. This represents a **11% decrease in buprenorphine prescribing from 2018**.



The Agency Threw Out Previous Recommended Limits on Doses but Encouraged "Nonopioid Therapies" Wherever Possible.

Assorted pills and prescription drugs, including opioids, being disposed of as part of a Prescription Drug Take Back Day in Los Angeles.
Credit...Patrick T. Fallon/Agence France-Presse — Getty Images

By Jan Hoffman
The New York Times
https://www.nytimes.com/2022/02/10/health/cdc-opioid-pain-guidelines.html

Feb. 10, 2022

The federal government on Thursday proposed new guidelines for prescribing opioid painkillers that remove its previous recommended ceilings on doses for chronic pain patients and instead encourage doctors to use their best judgment.

But the overall thrust of the recommendations was that doctors should first turn to "nonopioid therapies" for both chronic and acute pain, including prescription medications like gabapentin and over-the-counter ones like ibuprofen, as well as physical therapy, massage and acupuncture.

Though still in draft form, the 12 recommendations, issued by the Centers for Disease Control and Prevention, are the first comprehensive revisions of the agency's opioid prescribing guidelines since 2016. They walk a fine line between embracing the need for doctors to prescribe opioids to alleviate some cases of severe pain while guarding against exposing patients to the well-documented perils of opioids.

Dr. Samer Narouze, president of the American Society of Regional Anesthesia and Pain Medicine, an association of clinicians, praised the tone, level of detail and focus of the project. "It's a total change in the culture from the 2016 guidelines," he said, characterizing the earlier edition as ordering doctors to "just cut down on opioids — period."

By contrast, the new proposal "has a much more caring voice than a policing one, and it's left room to preserve the physician-patient relationship," added Dr. Narouze, chairman of the Center for Pain Medicine at Western Reserve Hospital in Cuyahoga Falls, OH.

The 229-page document warns of addiction, depressed breathing, altered mental status and other dangers associated with opioids, but it also notes that the drugs serve an important medical purpose, especially for easing the immediate agony from traumatic injuries such as burns and crushed bones. In those instances when opioids seem the way to go, the recommendations said, doctors should start with the lowest effective dose and prescribe immediate-release pills rather than long-acting ones.

The recommendations are now open on the Federal Register for public comment for 60 days. The agency will review the comments and most likely issue a final version by the end of 2022. Like the 2016 guidelines, they are suggested practices and not mandatory.

"We are welcoming comments from patients who are living with pain every day and from their caregivers and providers," said Christopher Jones, a co-author of the draft and acting director of the National Center for Injury Prevention and Control, the arm of the C.D.C. that released the new guidelines.

Kate Nicholson, executive director of the National Pain Advocacy Center, a patient organization that says it does not take funding from the pharmaceutical industry, found much to admire in the new guidelines. "We went from one side of the pendulum, with overly liberal prescribing of opioids, and that did harm, to just looking at gross drops in prescribing without looking at individual needs. And that did harm," said Ms. Nicholson, whose input was sought during the development of the draft. "This is closer to a Goldilocks solution where chronic pain is not a monolith."

The guidelines do not apply to patients suffering pain from cancer or sickle cell, or are in end-of-life or palliative care. Ms. Nicholson said, however, that relying on such disease categories — which insurance companies seize upon to make reimbursement rulings — "doesn't tell us enough about who actually has severe pain."

The 2016 guidelines generated anger and fear in many chronic pain patients, many of whom rely on doses far higher than the recommended ceiling of 90 morphine milligram equivalents [MME] daily. Hundreds of pain medicine specialists protested as well.

Though the dosing ceilings were merely a recommendation, dozens of states codified them. Fearing criminal and civil penalties, many doctors misapplied them as rigid standards, tapering chronic pain patients too abruptly and even tossing some from their practices.

Studies show that the number of opioid prescriptions overall has been dropping since 2012, and the decline escalated after the 2016 guidelines came out.

The new proposed recommendations step back from the notion of one-size dosing fits all and instead builds in "flexibility to recognize that pain care needs to be individualized," Dr. Jones said.

But the recommendations make it abundantly clear that doctors should regularly reassess the benefits and risks of opioids.

"The evidence around the long-term benefits of opioids continues to remain very limited," Dr. Jones said.

In another indication that the C.D.C. sees these new guidelines as a course-correction to the earlier ones, the agency now suggests that when patients test positive for illicit substances, doctors should offer counseling, treatment and, when necessary, careful tapering. Because doctors had interpreted the 2016 dosing limits narrowly, some had worked up one-strike policies and were summarily ejecting such patients.

Dr. Jones said that such results should instead be considered one piece of diagnostic information among many. An unduly high level of opioids could indicate the patient still has untreated pain or even a substance use disorder. "If you instead retain the patient and have those conversations, there's now an opportunity to improve the patient's life," he said.

Drawing from a mountain of research that accumulated in recent years, the proposed guidelines also offer extensive recommendations for the treatment of acute pain — short-term pain that can come with an injury like a broken bone or the aftermath of surgery. They advise against prescribing opioids, except for traumatic injuries, such as burns and auto accidents.

In granular detail, they compare the relief provided by opioids to that offered by alternatives such as exercise and acupuncture and other drugs. And they give fine-tuned recommendations for discrete areas of pain, such as lower back, knees and neck.

The guidelines, for example, note that opioids should not be used for episodic migraines. They endorse, among other treatments, heat therapy and weight loss for knee osteoarthritis, and, for neck pain, suggest options like yoga, tai chi, qiqong, massage and acupuncture.

Dr. Marie Hanna, an associate professor of anesthesia and critical care at Johns Hopkins University School of Medicine, said she was particularly enthusiastic about the depth and breadth of research that the guidelines provide in support of nonopioid treatments, including manual manipulation, laser therapy and exercise.

"This is what we've been talking about for years, but no one was listening. Now we have the evidence to show that these treatments are effective. I'm very optimistic," added Dr. Hanna, a member of the American Academy of Pain Medicine, an organization of pain researchers and providers across several disciplines.

The recommendations also say that many studies show that, over time, pain alleviation from opioids usually plateaus and then wanes, requiring ever higher doses.

"We never wanted to pretend that opioids aren't really important tools," said Dr. Jeanmarie Perrone, a professor of emergency medicine at the Perelman School of Medicine at the University of Pennsylvania, who served on an advisory panel for the prescribing guidelines. "But after you've got that cast on, we're going to wean you off those opioids. One long-bone fracture doesn't mean six weeks of opioid prescriptions."

Jan Hoffman writes about behavioral health and health law. Her wide-ranging subjects include opioids, tribes, reproductive rights, adolescent mental health and vaccine hesitancy. @JanHoffmanNYT

A version of this article appears in print on Feb. 11, 2022, Section A, Page 20 of the New York edition with the headline: Proposed Opioid Guidelines By C.D.C. Walk a Fine Line.

Reference [Added by CSAM]:

The Federal Register, Proposed 2022 CDC Clinical Practice Guideline for Prescribing Opioids, A Notice by the Centers for Disease Control and Prevention on 02/10/2022

https://www.federalregister.gov/documents/2022/02/10/2022-02802/proposed-2022-cdc-clinical-practice-guideline-for-prescribing-opioids