



Application of Systems Science in Opioid Misuse

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All pictures of articles are hyperlinked to their full text.

Credit: All credits go to lab members, students, and colleagues.

Disclaimer: This presentation does not represent the views of any institutions. Opinions expressed are my own.

Conflict of interest: None

Systems Science

- An **interdisciplinary** field that studies complex systems and their behavior.
- It seeks to understand **the behavior** of these systems by examining their components, interactions, and feedback mechanisms.
- It helps identify potential **leverage points** for effective interventions and policies.

Health Research Policy and Systems

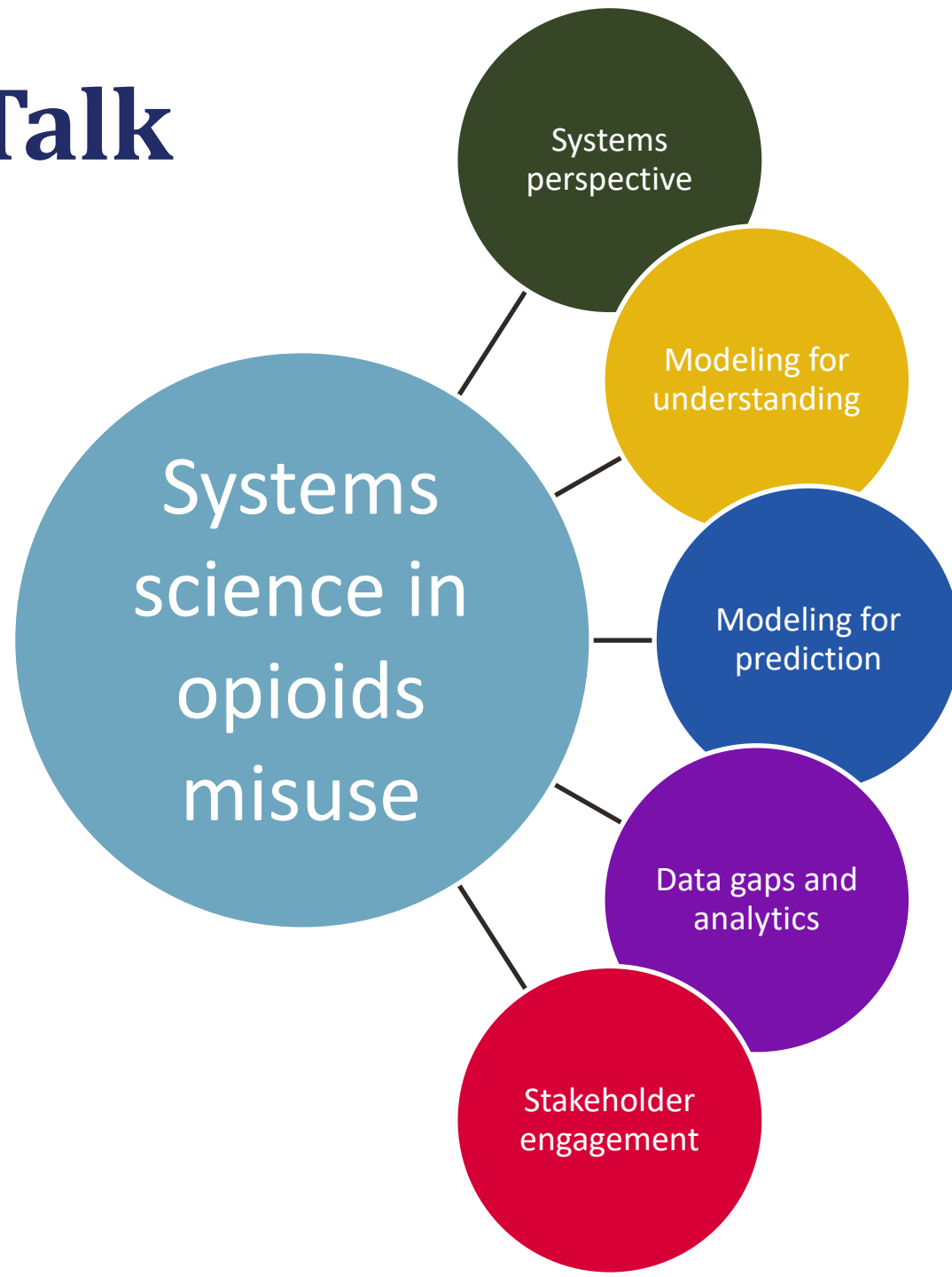
Commentary | [Open Access](#) | [Published: 08 August 2020](#)

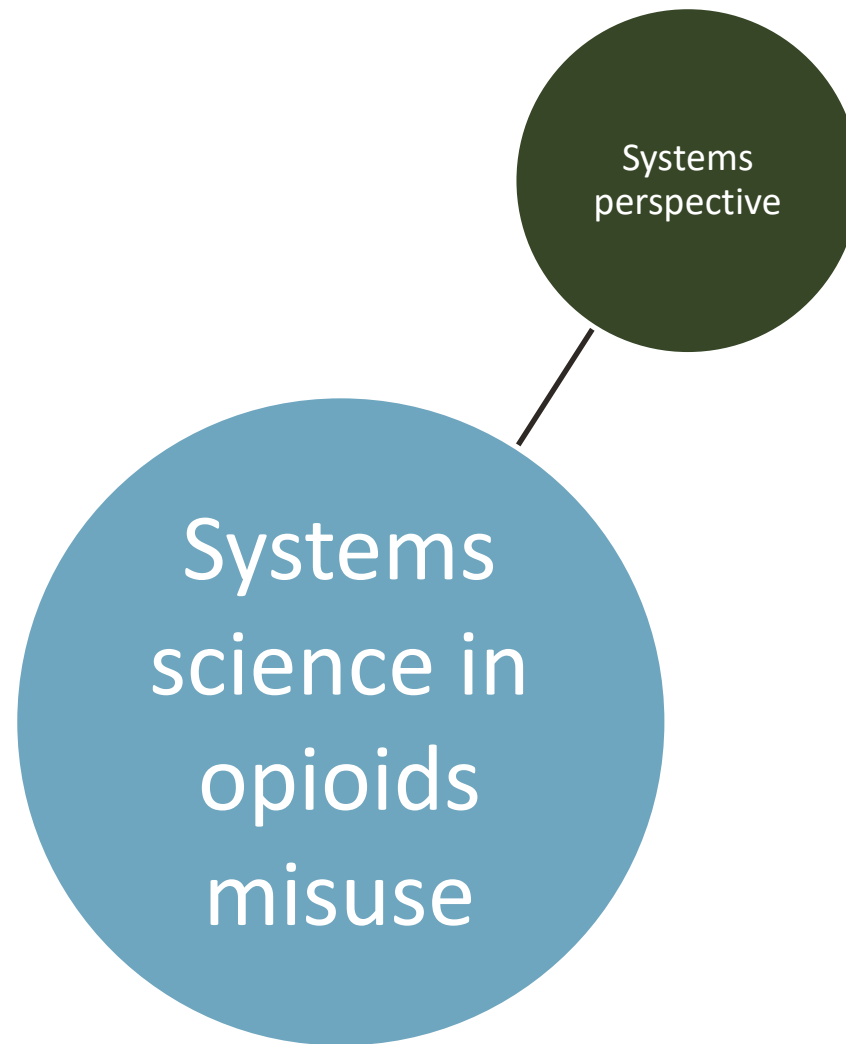
The opioid crisis: need for systems science research

[Mohammad S. Jalali](#) , [Michael Botticelli](#), [Rachael C. Hwang](#), [Howard K. Koh](#) & [R. Kathryn McHugh](#)

[Health Research Policy and Systems](#) **18**, Article number: 88 (2020) | [Cite this article](#)

In This Talk





Holistic view of various interconnected components

Systems thinking

- The opioid crisis is a complex and multifaceted problem
 - involves multiple factors and stakeholders
 - requires a **systems perspective** to understand and address it
- A systems perspective recognizes the interconnectedness and interdependence of these factors and stakeholders, and their impact on each other and the larger system.

Health Research Policy and Systems

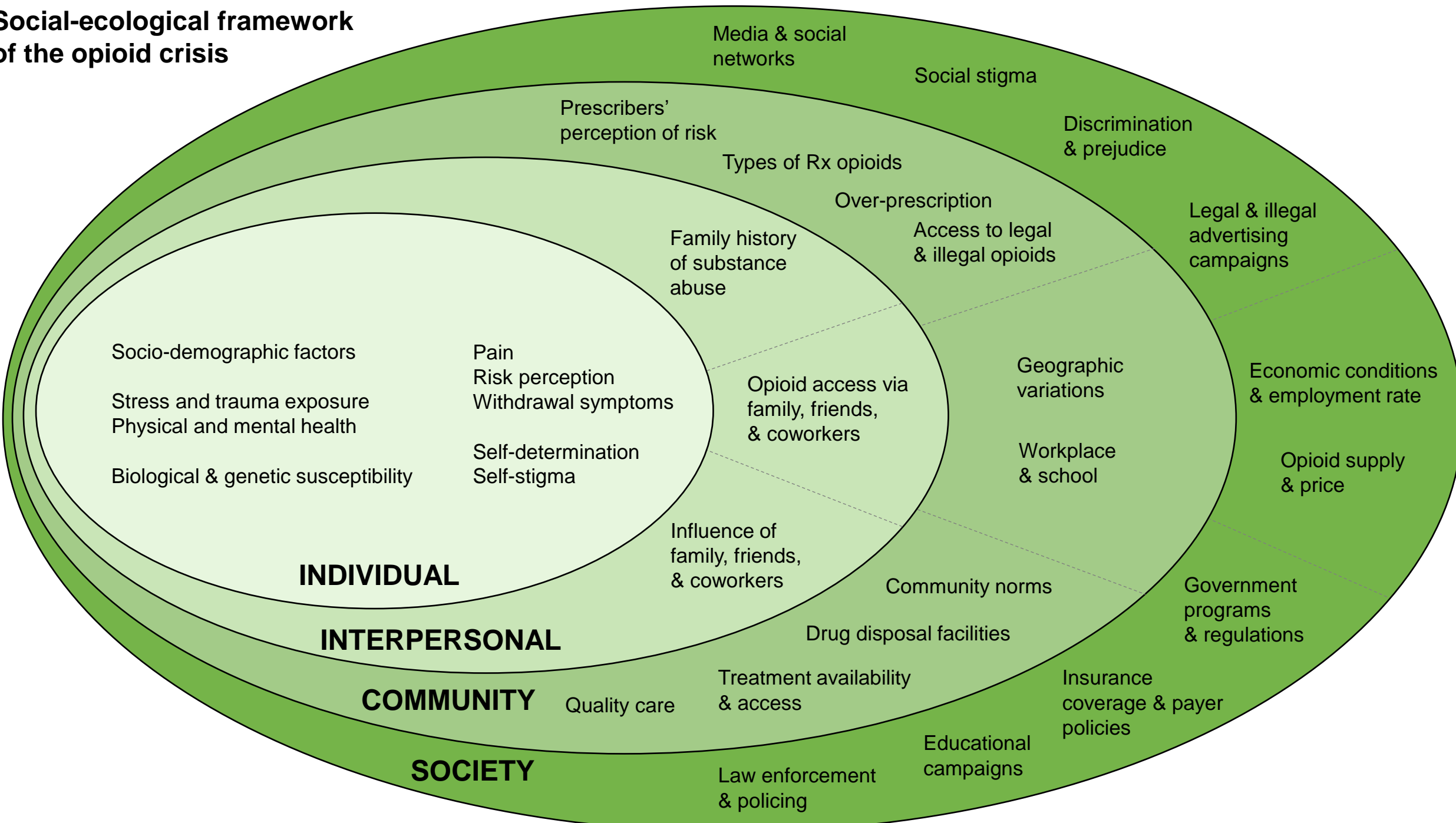
Commentary | [Open Access](#) | [Published: 06 August 2020](#)

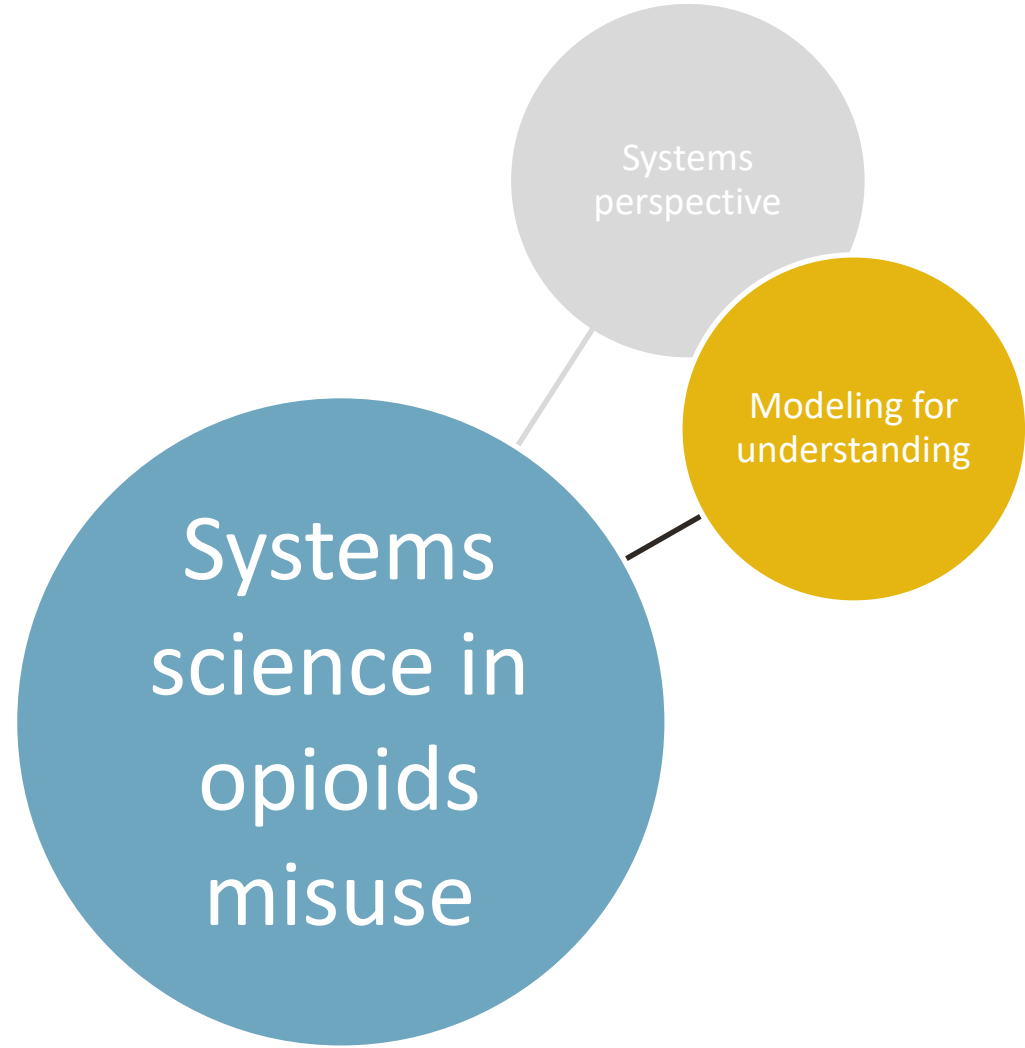
The opioid crisis: a contextual, social-ecological framework

[Mohammad S. Jalali](#) , [Michael Botticelli](#), [Rachael C. Hwang](#), [Howard K. Koh](#) & [R. Kathryn McHugh](#)

Health Research Policy and Systems **18**, Article number: 87 (2020) | [Cite this article](#)

Social-ecological framework of the opioid crisis



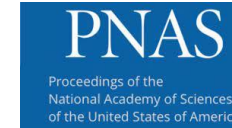


- Key dynamics
- The status quo
- Counterfactuals





Simulation Modeling

Through a collaboration with FDA, we developed SOURCE, a population-based simulation model.

The model addresses strategic “what if” questions and goals.



Modeling the evolution of the US opioid crisis for national policy development

Tse Yang Lim , Erin J. Stringfellow, Celia A. Stafford,  +10, and Mohammad S. Jalali   [Authors Info & Affiliations](#)

Edited by Andrea Bertozzi, University of California, Los Angeles, CA; received August 26, 2021; accepted March 16, 2022

May 31, 2022 | 119 (23) e2115714119 | <https://doi.org/10.1073/pnas.2115714119>

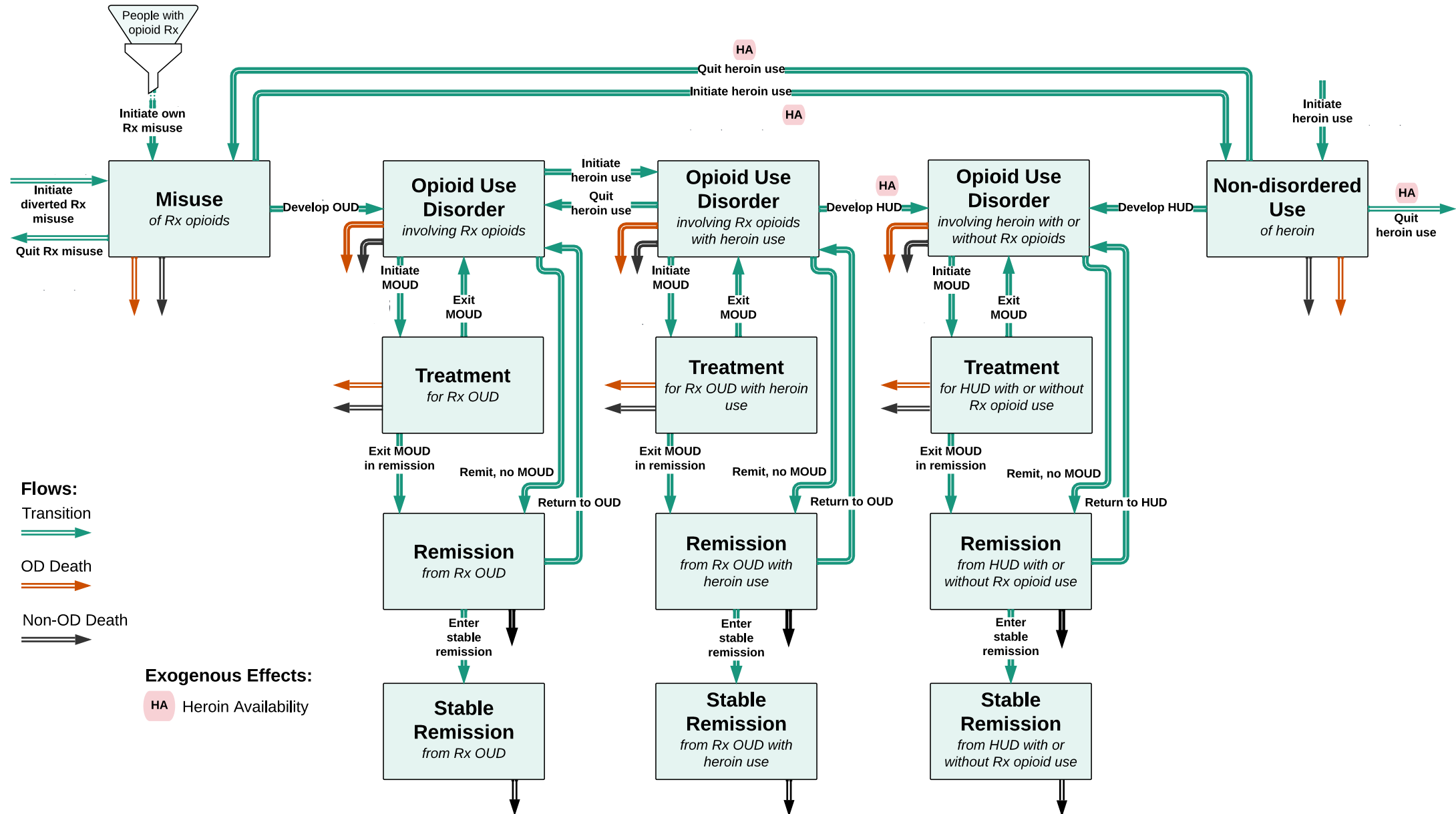


Reducing opioid use disorder and overdose deaths in the United States: A dynamic modeling analysis

ERIN J. STRINGFELLOW , TSE YANG LIM , KEITH HUMPHREYS , CATHERINE DIGENNARO , CELIA STAFFORD , ELIZABETH BEAULIEU , JACK HOMER , WAYNE WAKELAND , BENJAMIN BEARNOT , [...] MOHAMMAD S. JALALI   +6 authors [Authors Info & Affiliations](#)

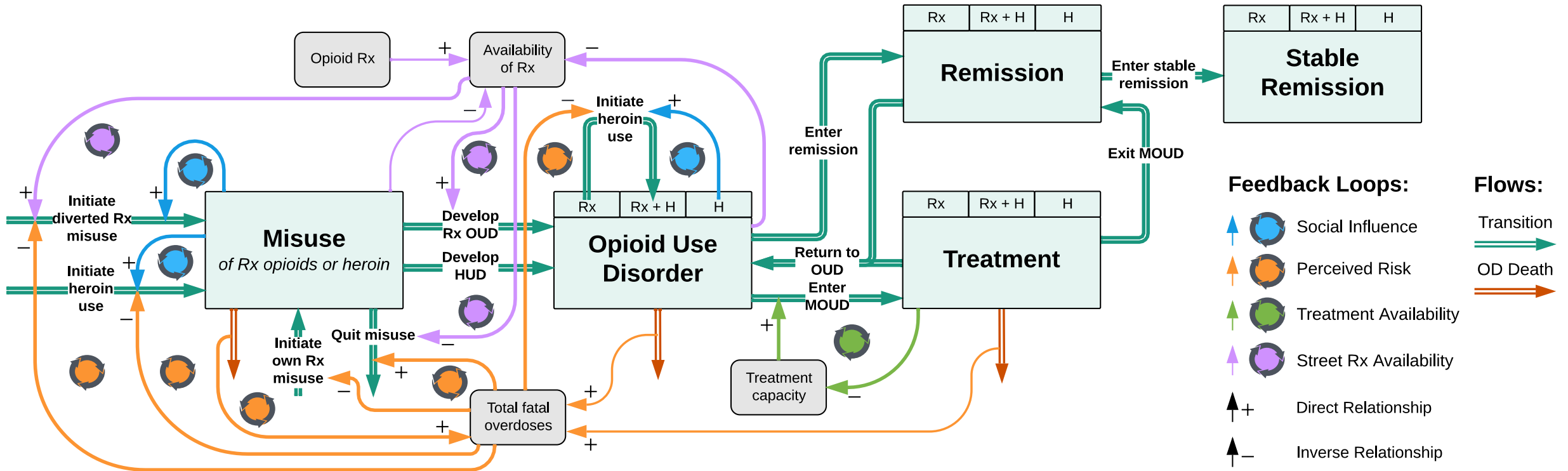
SCIENCE ADVANCES • 24 Jun 2022 • Vol 8, Issue 25 • DOI: 10.1126/sciadv.abm8147

Essential to capture the flows of individuals across various states

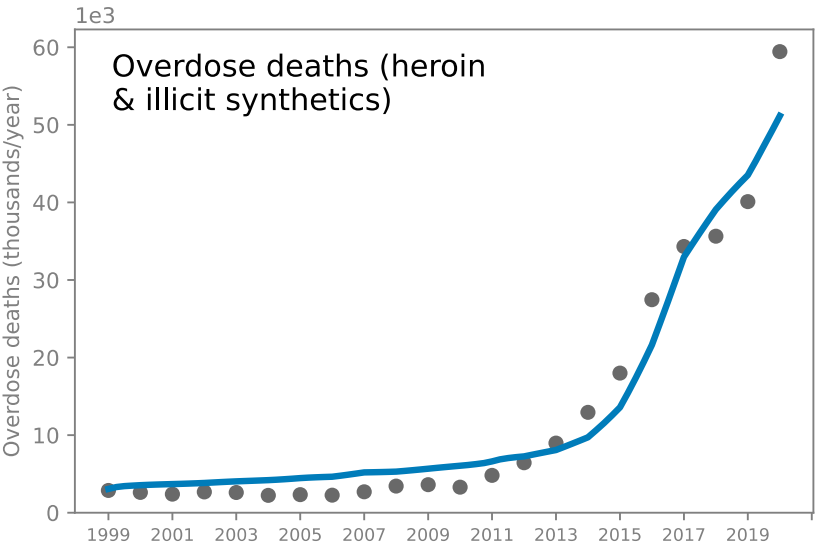
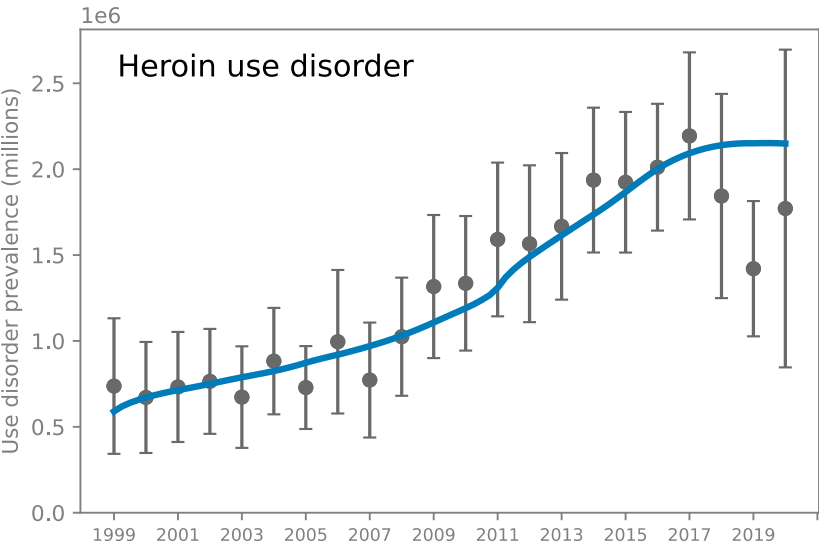
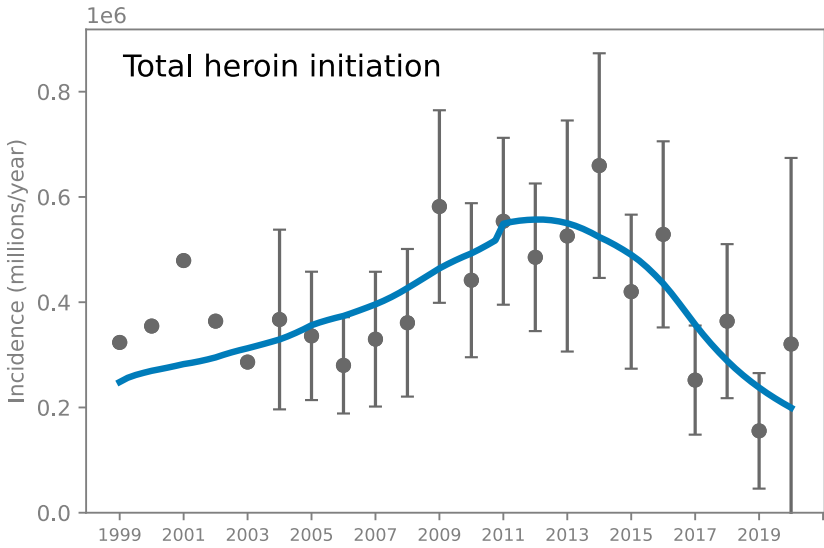
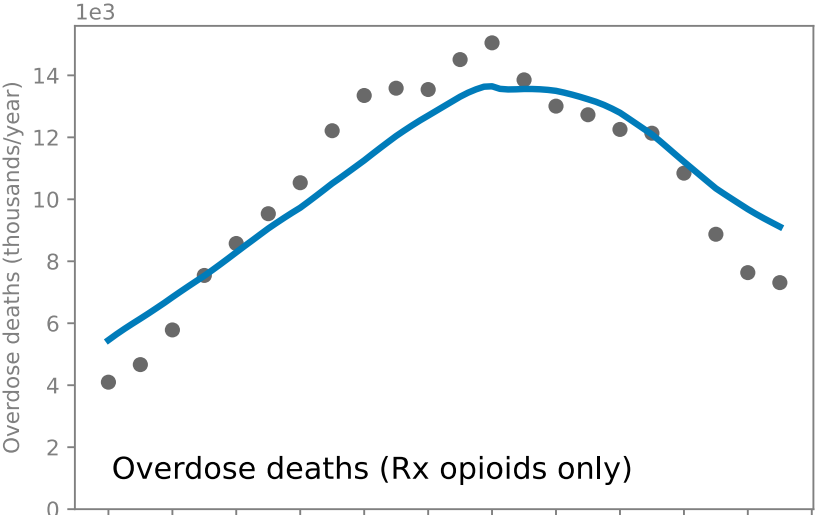
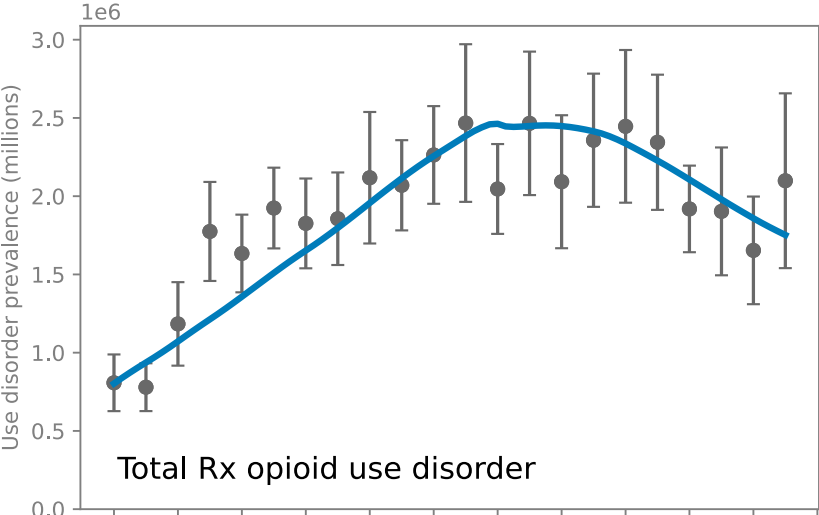
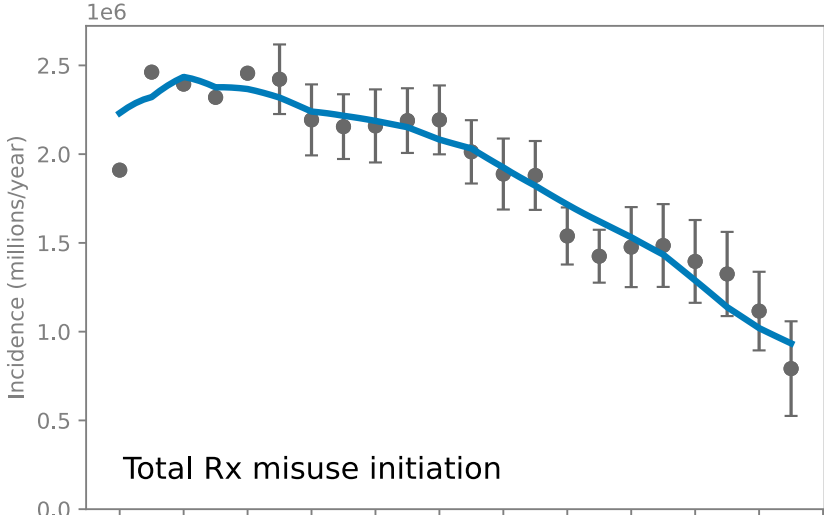


But going beyond the flows:

Including feedback loops, better representing the real world



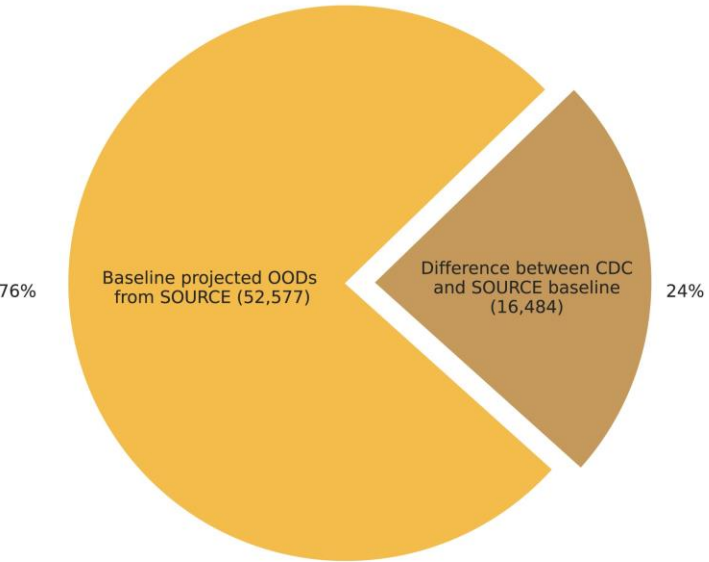
SOURCE replicates 15 longitudinal datasets at once; six shown here



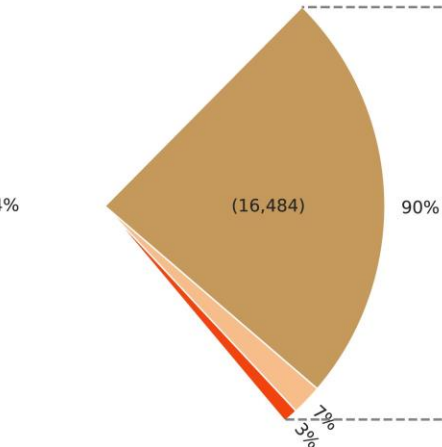
Complex estimations: Was the unprecedented **rise** in opioid overdose deaths (OODs) in 2020 **only** because of **COVID-19**?

SOURCE: 43% of the excess OODs due to continued increases in **fentanyl**s

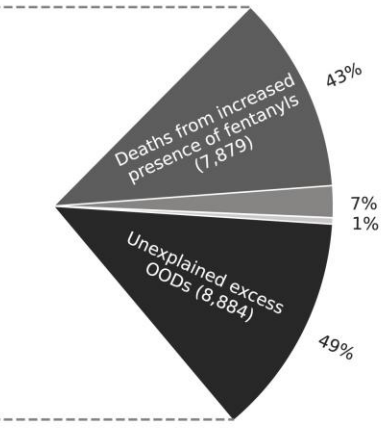
A CDC reported OODs in 2020: 69,061



B Potential excess OODs: 16,484+1,209+583



C Distribution of potential excess OODs



- Lives saved from increased buprenorphine providers [89], increased naloxone distribution [1,057], and decreased opioid prescribing [63], total = 1,209
- Lives saved from additional increased buprenorphine receipt (583)
- Deaths from decreased MMT / XR-NTX receipt (1,265)
- Deaths from interaction of increased fentanyl and decreased MMT / XR-NTX receipt (249)

CDC: Centers for Disease Control and Prevention
OODs: Opioid Overdose Deaths



Enumerating contributions of fentanyl and other factors to the unprecedented 2020 rise in opioid overdose deaths: model-based analysis

Erin J Stringfellow, Tse Yang Lim, Catherine DiGennaro, Zeynep Hasgul, Mohammad S Jalali ✉ Author Notes

PNAS Nexus, Volume 2, Issue 4, April 2023, pgad064, <https://doi.org/10.1093/pnasnexus/pgad064>

Overdose death hazard; competing influences of fentanyl & naloxone

Overdose death hazard among people who use illicit opioids has shifted noticeably due to two competing influences:



Fentanyl: Starting around 2013, highly potent synthetic opioids like fentanyl have been increasingly present in the illicit drug supply.

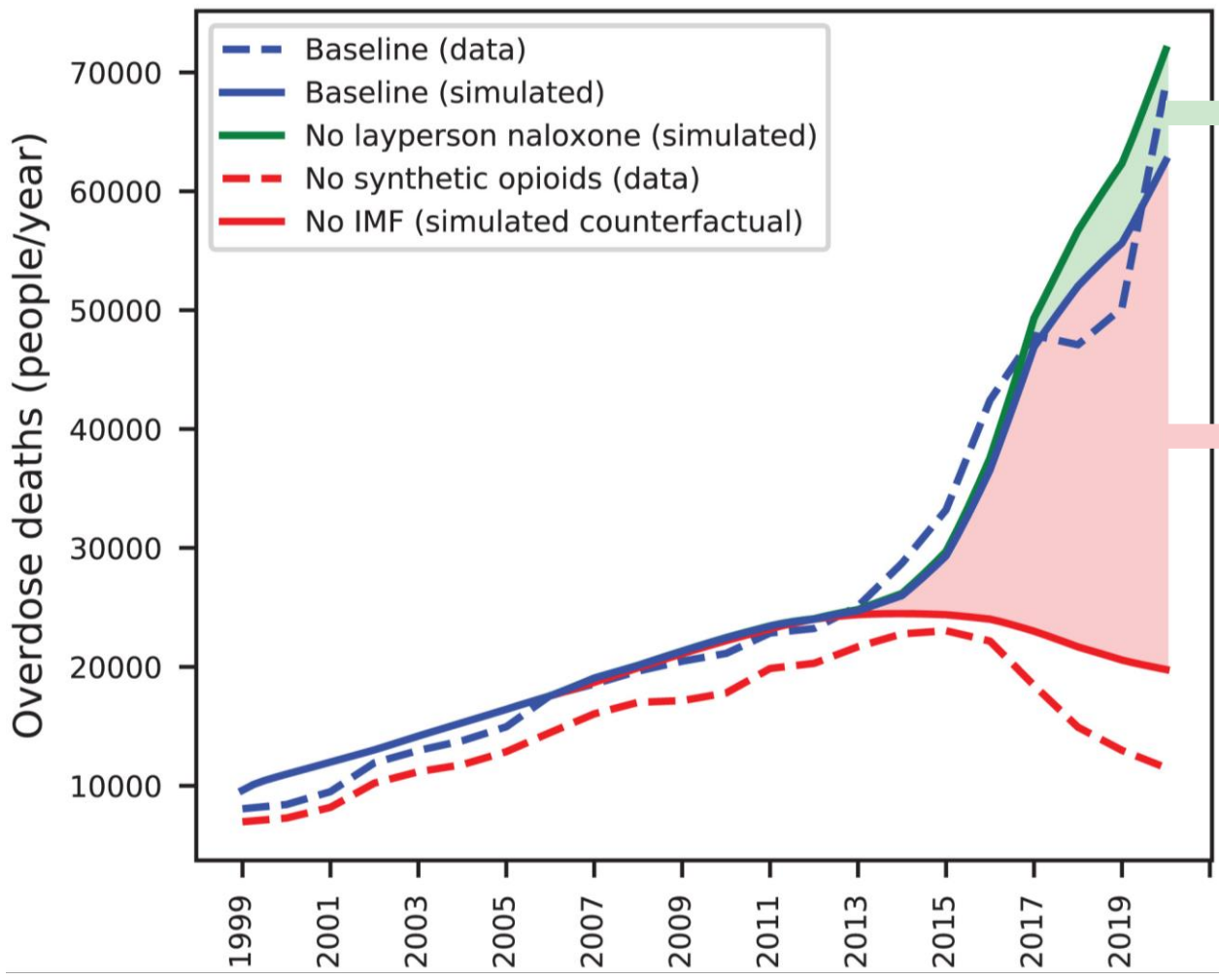


Naloxone: Over roughly the same period, there have been numerous efforts to increase access to the lifesaving overdose reversal drug naloxone.

Counterfactuals

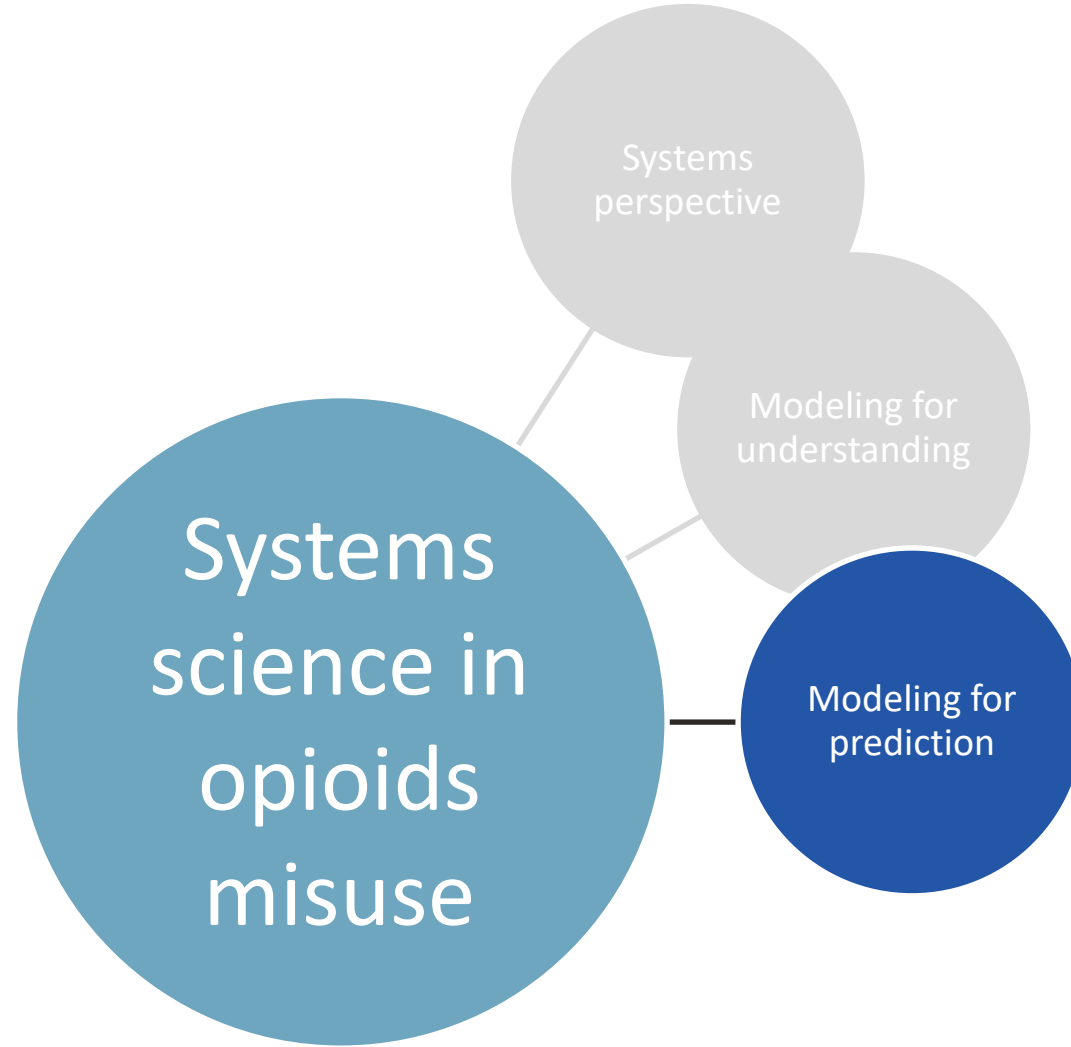
What if there were **no naloxone**?

What if there were **no illicitly manufactured fentanyl**?



About **20,000 lives** saved due to layperson naloxone

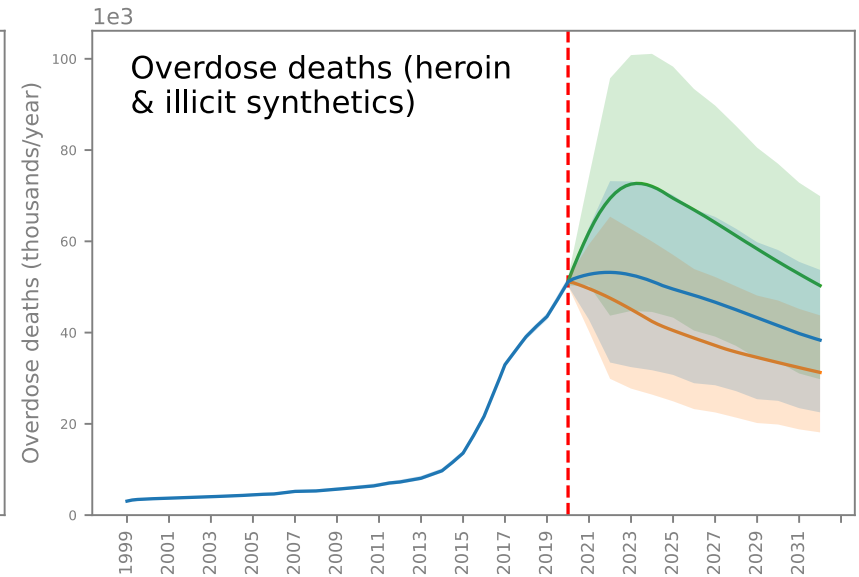
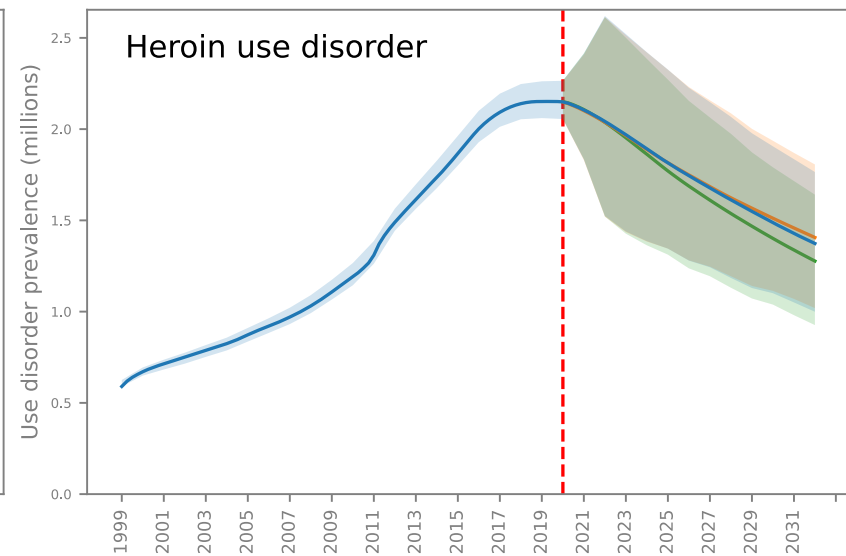
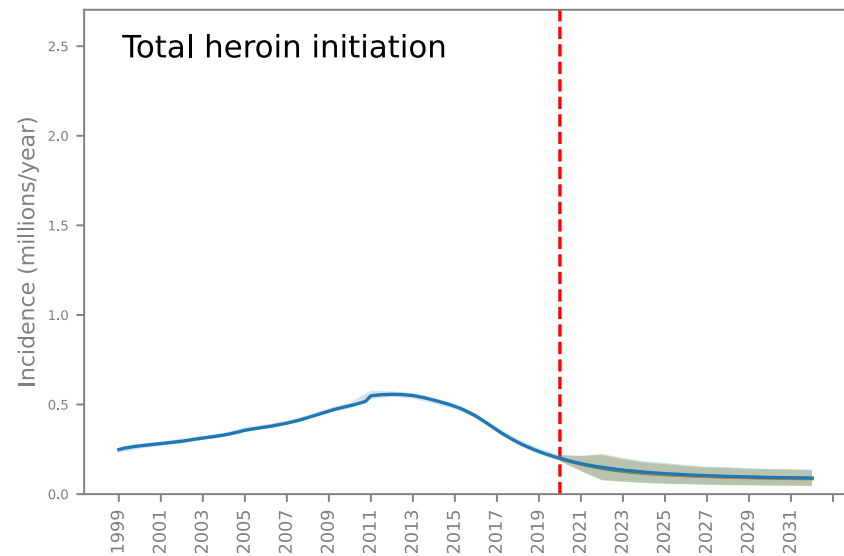
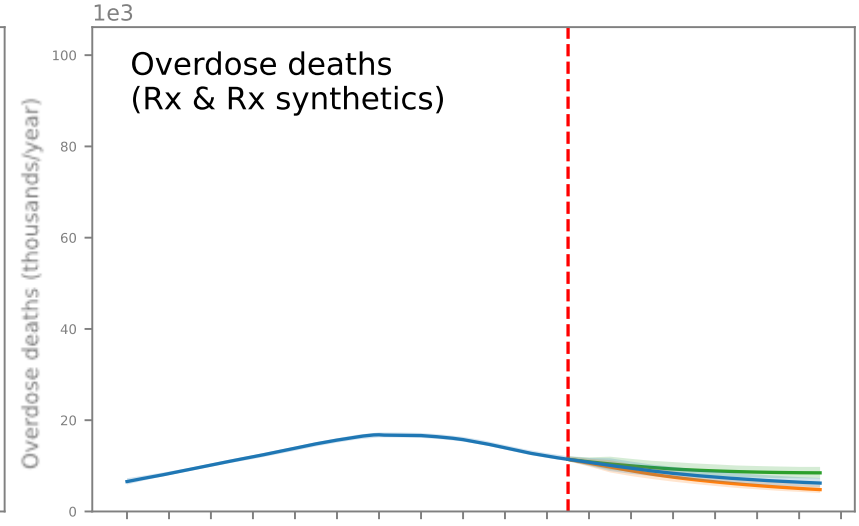
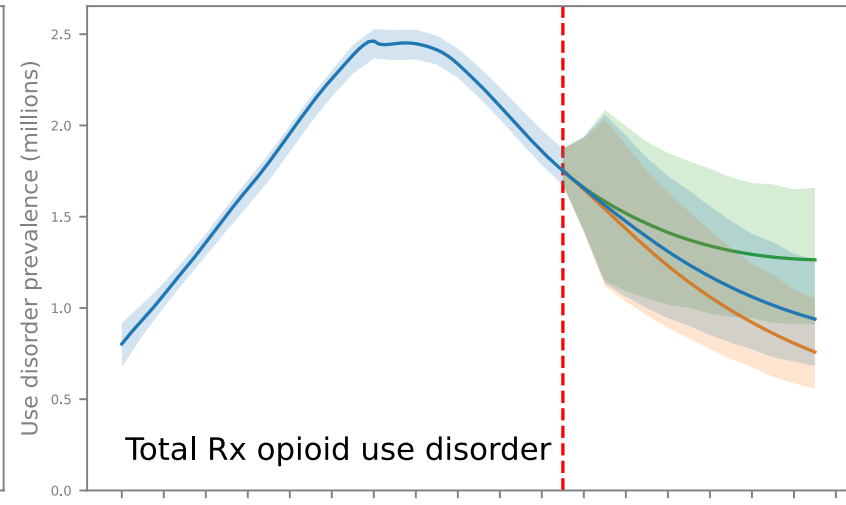
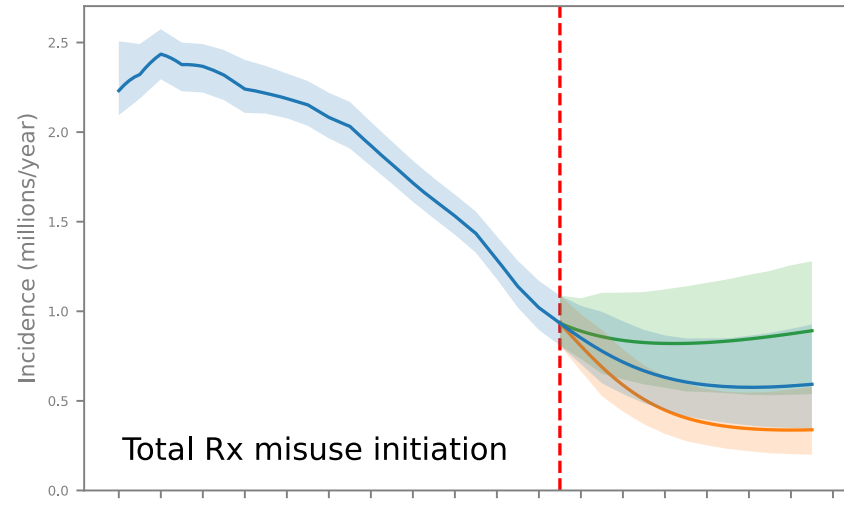
About **59,000 lives** would have been saved in the absence of illicitly manufactured fentanyl



- Projection of future trends
- Intervention analysis and comparison
- Cost-effectiveness analysis

Projecting various outcomes over the next decade

Over the next decade, total deaths range from **543,000** to **842,000**



— Exogenous Trends Continue (ETC) — Optimistic Scenario — Pessimistic Scenario - - - Projection start time

Strategy analysis

Strategies Simulated in SOURCE

(Changed by 20% in desired direction)

Goal and *Intervention Strategy*

A) Opioid Misuse and OUD Prevention

Interventions targeting people at risk for misuse

- (1) ↓ Diverted Rx Init
- (2) ↓ Heroin Init
- (3) ↓ Own Rx Init

Interventions targeting systems, including health care

- (4) ↓ People with Rx
 - (5) ↓ Developing OUD
-

B) Buprenorphine Treatment Capacity

Interventions to increase buprenorphine prescribing

- (6) ↑ Bup Providers
 - (7) ↑ Bup Prov Capacity
-

C) Recovery Supports

Interventions to support sustained improvements in functioning

- (8) ↓ Return to OUD
 - (9) ↑ Peer Recovery
-

D) Overdose Harm Reduction

Interventions to reduce risk of overdose

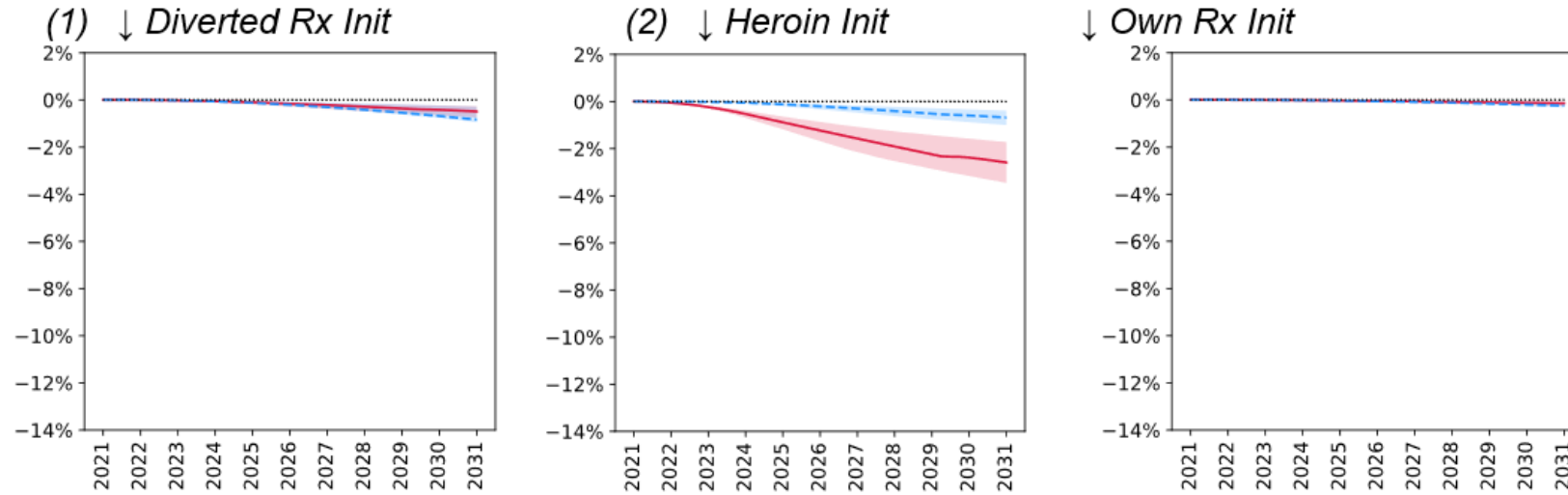
- (10) ↓ Fent OD Risk)

Interventions to reduce death from overdose

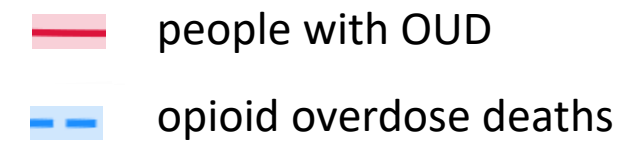
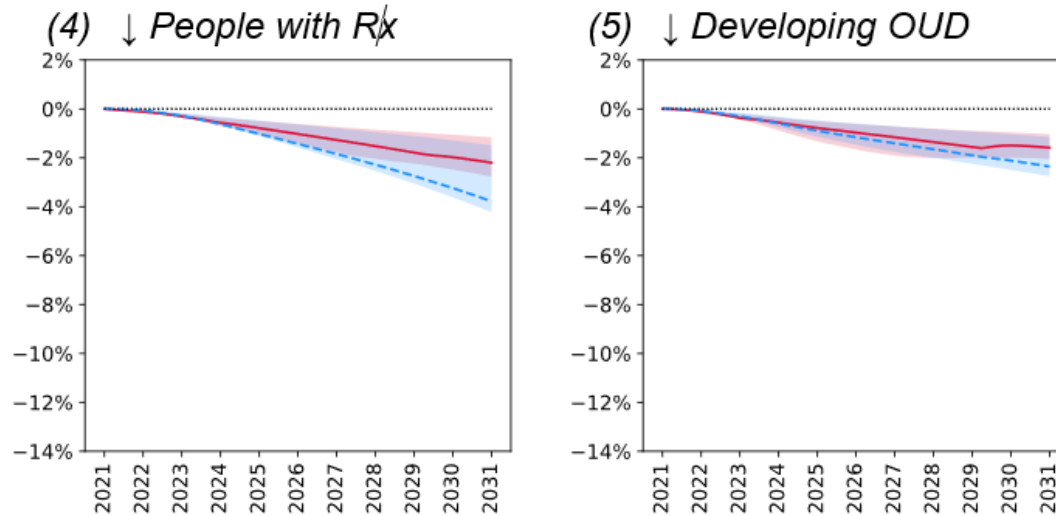
- (11) ↑ Naloxone (Nx) Kits
-

Misuse and OUD Prevention

Interventions targeting people at risk for misuse

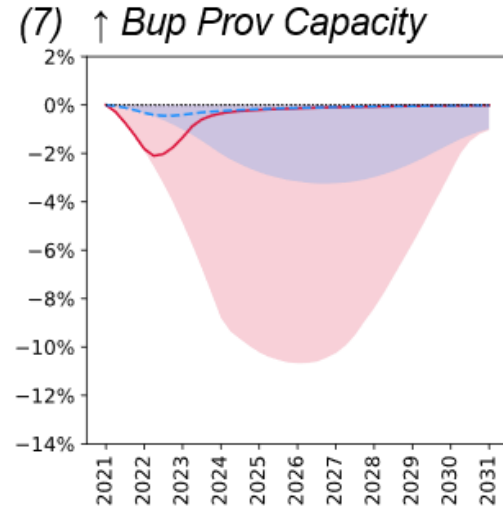
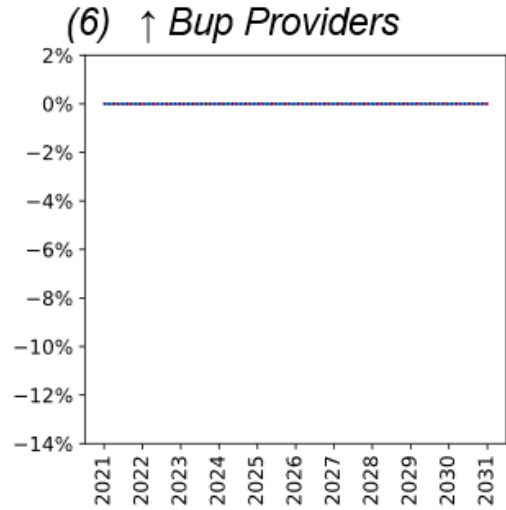


Interventions targeting systems, including health care



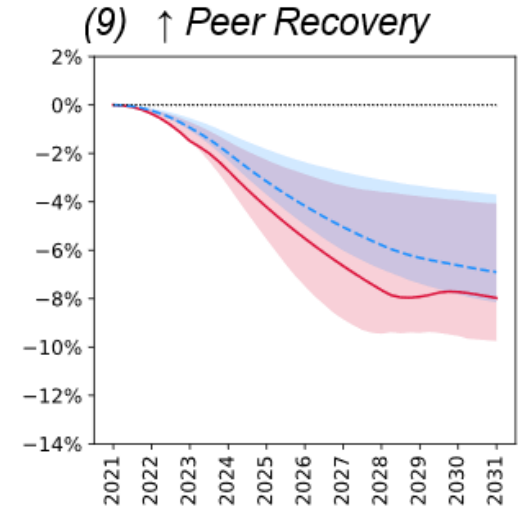
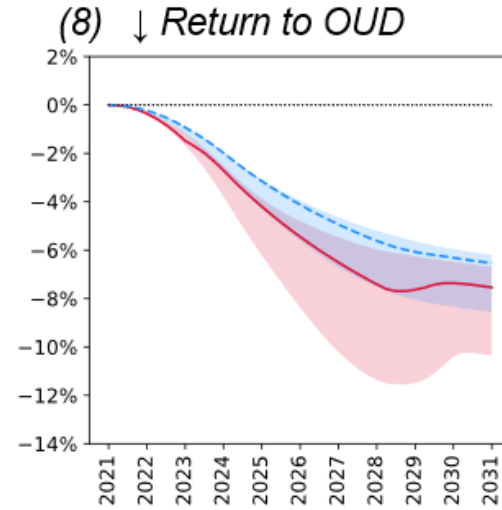
Buprenorphine Treatment Capacity

Interventions to increase buprenorphine prescribing



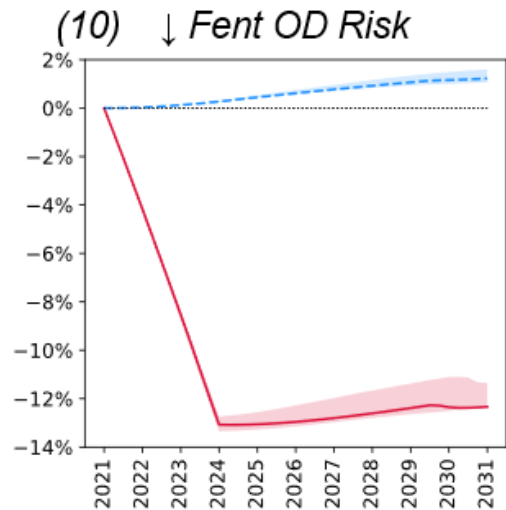
Recovery Supports

Interventions to support sustained improvements in functioning

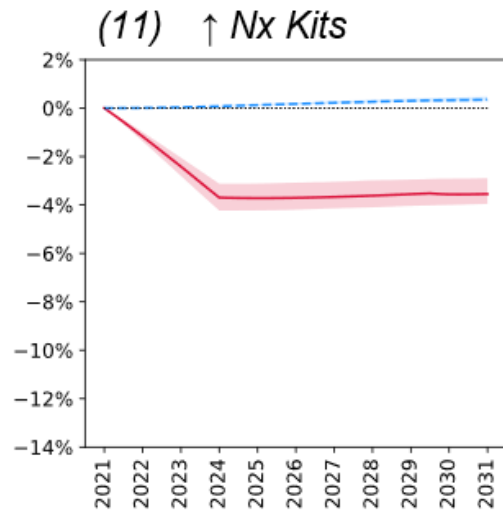


Overdose Harm Reduction

Interventions to reduce risk of overdose

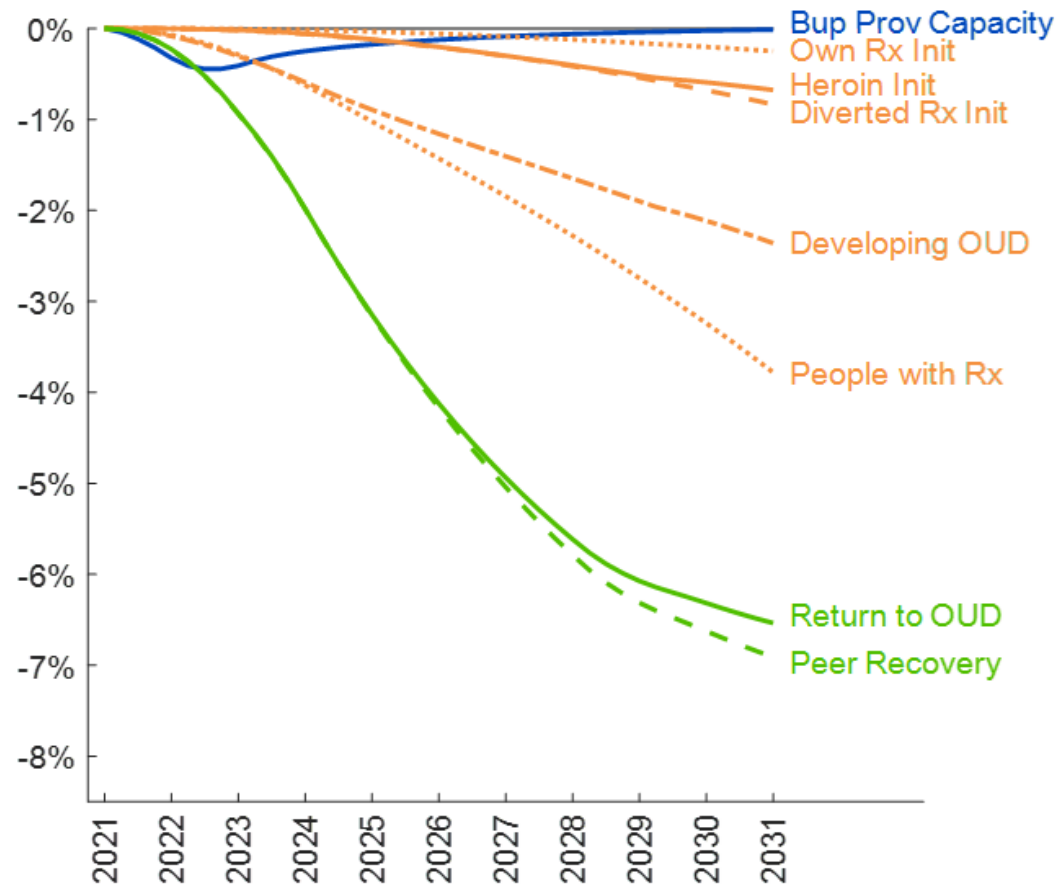


Interventions to reduce death from overdose

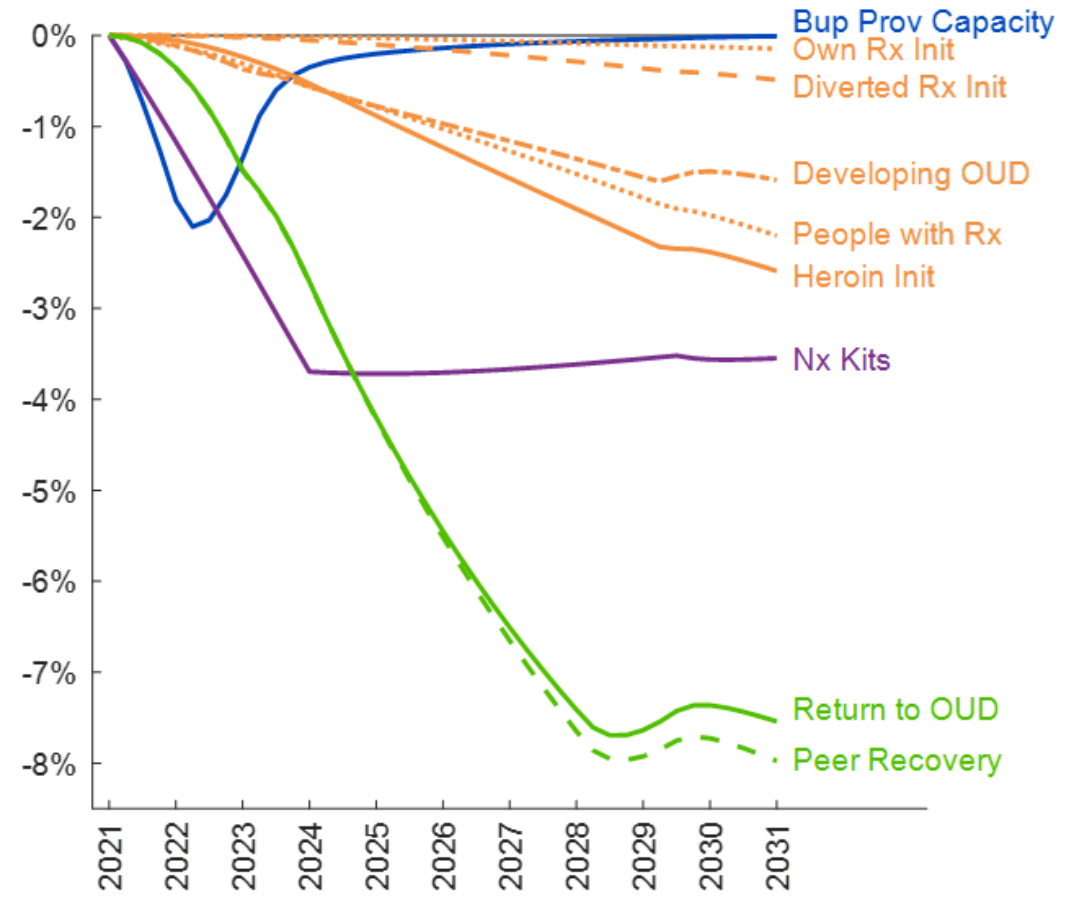


— people with OUD
- - - opioid overdose deaths

Change in prevalence of OUD



Change in opioid overdose deaths



Diving deeper...

From discussing ongoing policy questions

HEALTH AFFAIRS FOREFRONT

RELATED TOPICS:
PHARMACEUTICALS | ACCESS TO CARE | SYSTEMS OF CARE | SUBSTANCE USE DISORDER | REGULATION
| PRESCRIPTION DRUGS | NONSUBSTANCE RELATED ADDICTIONS

Removing The X-Waiver Is One Small Step Toward Increasing Treatment Of Opioid Use Disorder, But Great Leaps Are Needed

[Erin J. Stringfellow](#), [Keith Humphreys](#), [Mohammad S. Jalali](#)

APRIL 22, 2021

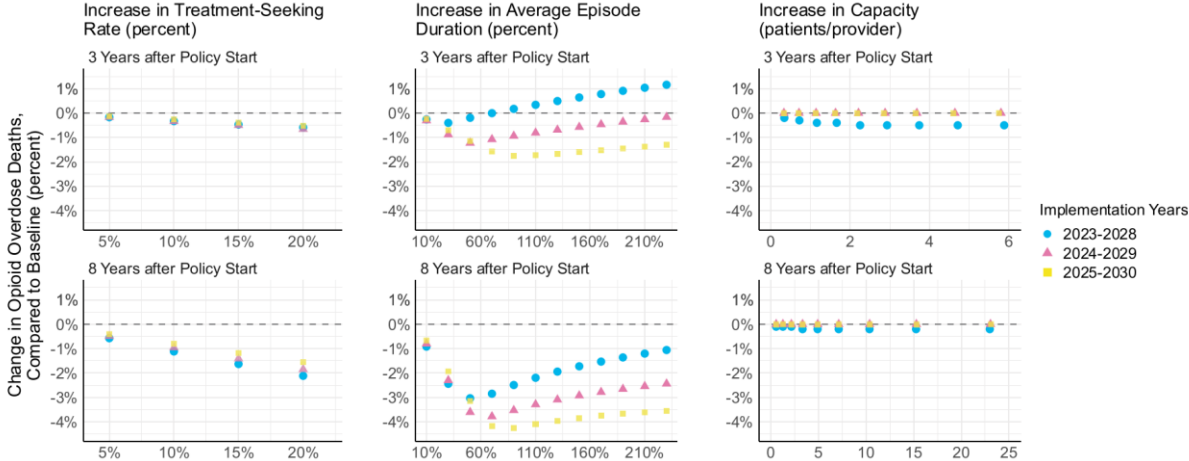
10.1377/forefront.20210419.311749

To informing implementation of policy solutions

JOURNAL OF **Addiction Medicine** The Official Journal of the American Society of Addiction Medicine

Long-Term Effects of Increasing Buprenorphine Treatment Seeking, Duration, and Capacity on Opioid Overdose Fatalities: A Model-Based Analysis

Stringfellow, Erin J. PhD; Lim, Tse Yang PhD; DiGennaro, Catherine BA; Zhang, Ziyuan; Paramasivam, Pritika; Bearnot, Benjamin MD; Humphreys, Keith PhD; Jalali, Mohammad S. PhD

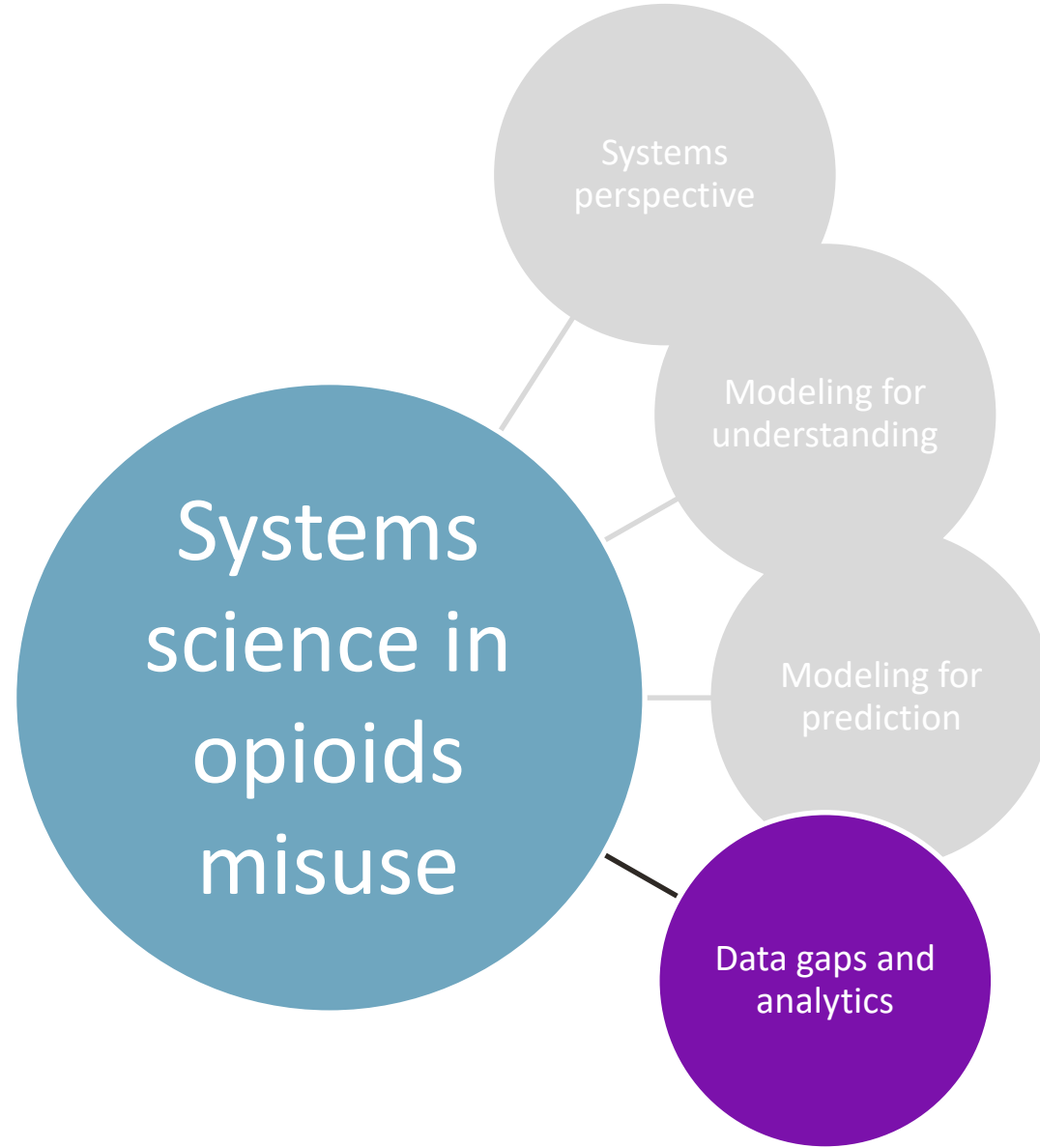


If policymakers only target 2 policies to reduce OODs, they should be to increase capacity and duration, enacted quickly and aggressively.



Stay tuned for SOURCE-based cost-effectiveness analysis of buprenorphine interventions...

forthcoming in ***JAMA Health Forum***



- Identifying incomplete data on the components of the system
- Empowering data science and machine learning methods

Data Gaps

A systems perspective can highlight areas where data is lacking or incomplete

Examples:

- Underreporting of opioid-related overdoses
- Lack of standardized data collection
- Insufficient data on the social and economic determinants of the crisis
- Lack of longitudinal data on many factors



American Journal of Preventive Medicine

Volume 60, Issue 2, February 2021, Pages e95-e105



Research Methods

Data Needs in Opioid Systems Modeling: Challenges and Future Directions

Mohammad S. Jalali PhD, MSc^{1,2} ✉, Emily Ewing MPP³, Calvin B. Bannister MS³, Lukas Glos MA³, Sara Eggers PhD³, Tse Yang Lim MS^{2,3}, Erin Stringfellow PhD, MSW¹, Celia A. Stafford MPH^{1,4}, Rosalie Liccardo Pacula PhD^{5,6,7}, Hawre Jalal MD, PhD⁸, Reza Kazemi-Tabriz PhD³

Data Analytics

- Data science and machine learning have been increasingly used in the opioid crisis to help identify patterns and trends in data and predict outcomes of interest (e.g., overdoses).
- By using a systems thinking approach, data science methods can better account for multiple factors influencing opioid misuse.



Identifying key risk factors for premature discontinuation of opioid use disorder treatment in the United States: A predictive modeling study

Celia Stafford ^{a, 1} ✉, Wesley J. Marrero ^{a, b, 2} ✉, Rebecca B. Naumann ^{c, 3} ✉, Kristen Hassmiller Lich ^{d, 4} ✉, Sarah Wakeman ^{e, 5} ✉, Mohammad S. Jalali ^{a, f, 6} ✉

Research Letter

November 9, 2022

JAMA Psychiatry

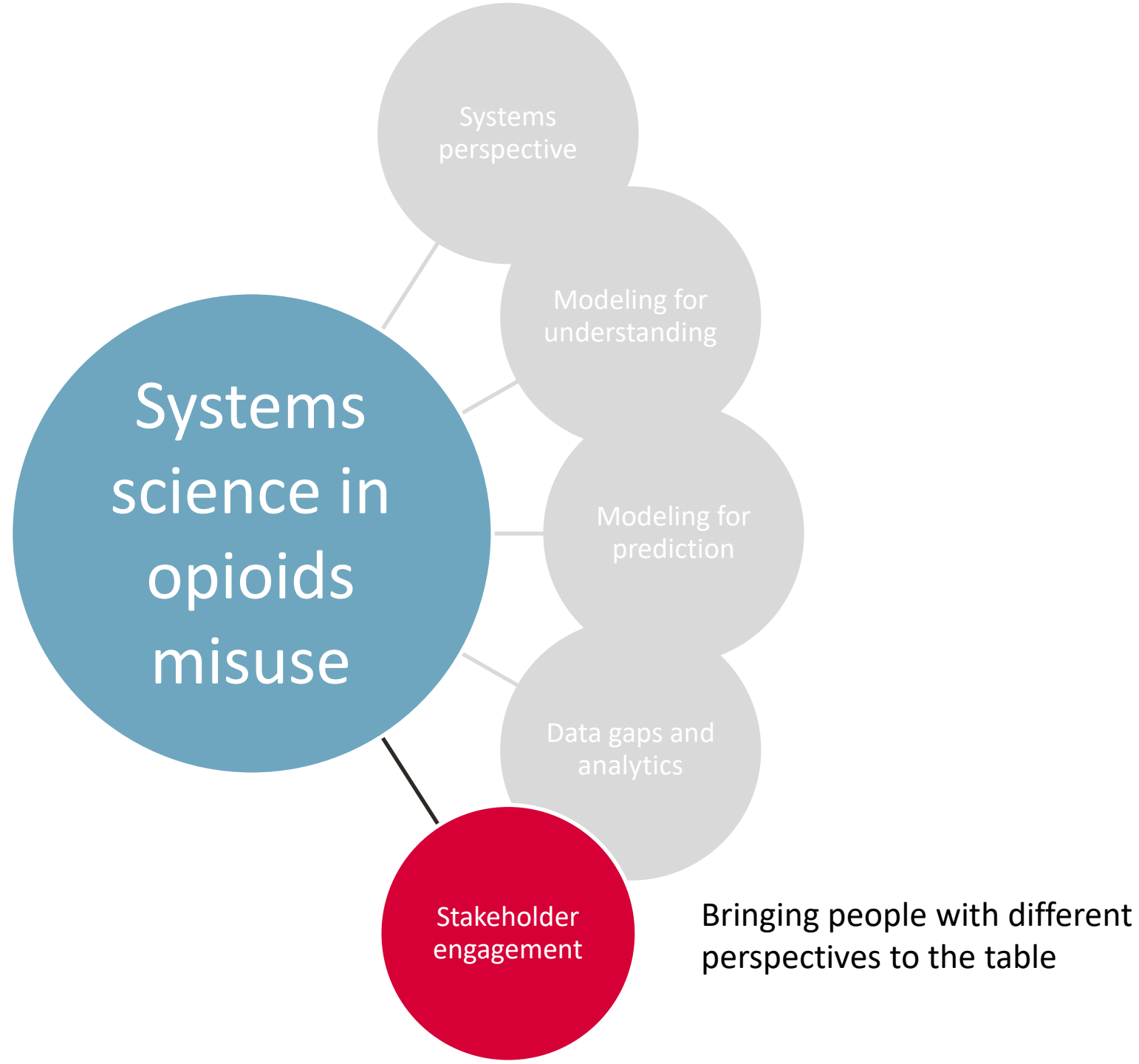
Racial and Ethnic Disparities in Buprenorphine Treatment Duration in the US

Huiru Dong, PhD¹; Erin J. Stringfellow, PhD¹; W. Alton Russell, PhD²; et al

The New York Times

Medication Treatment for Addiction Is Shorter for Black and Hispanic Patients, Study Finds

The analysis of 15 years of prescription data showed that the racial disparities are widening.



Stakeholder Engagement

- Providing a **common language** and **framework** for stakeholders to understand the complex issues
- Facilitating a **shared understanding** of the complex and interconnected factors that contribute to the opioid crisis,
- Facilitating **collaborative** problem-solving and decision-making processes, taking into account the perspectives and interests of all stakeholders

- **Engage communities in building and using the models**

Not Only for Opioids...

- **Our work does not limit to opioids;** alcohol, stimulants, polysubstance
- **Systems science can similarly help with psychedelics**
 - Provide a framework for understanding the complex interactions between the biological, psychological, social, and environmental factors that influence the effects of psychedelic substances
 - Develop effective interventions and policies for
 - safe and responsible use of psychedelics
 - prevention of potential harms
 - Analyze potential unintended consequences



@msjalali

All articles shown today are publicly available:

mj-lab.mgh.harvard.edu

Acknowledgment: Several studies reported in this presentation were supported by research grants from the U.S. FDA. See each article for the respective grant number.