

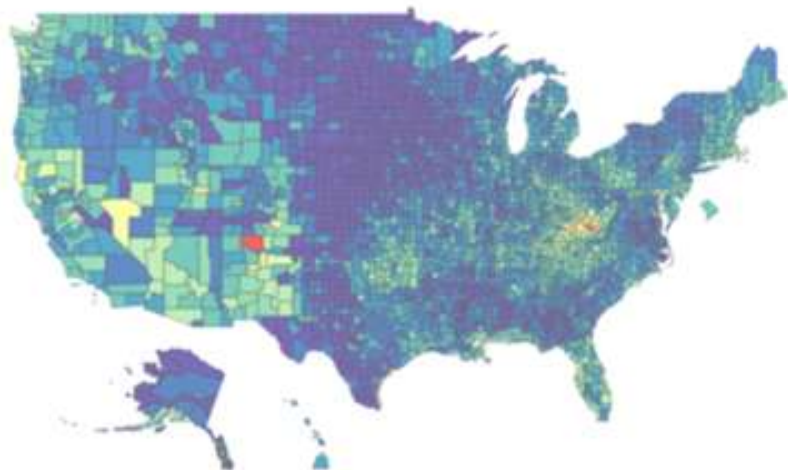
Medical research to address the opioid crisis in the United States

Iván D. Montoya, M.D., M.P.H.

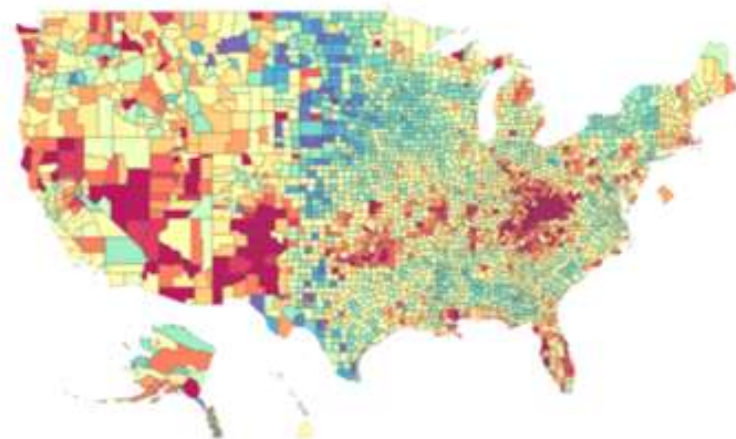
Deputy Director, Division of Therapeutics and Medical Consequences

NIDA

1999



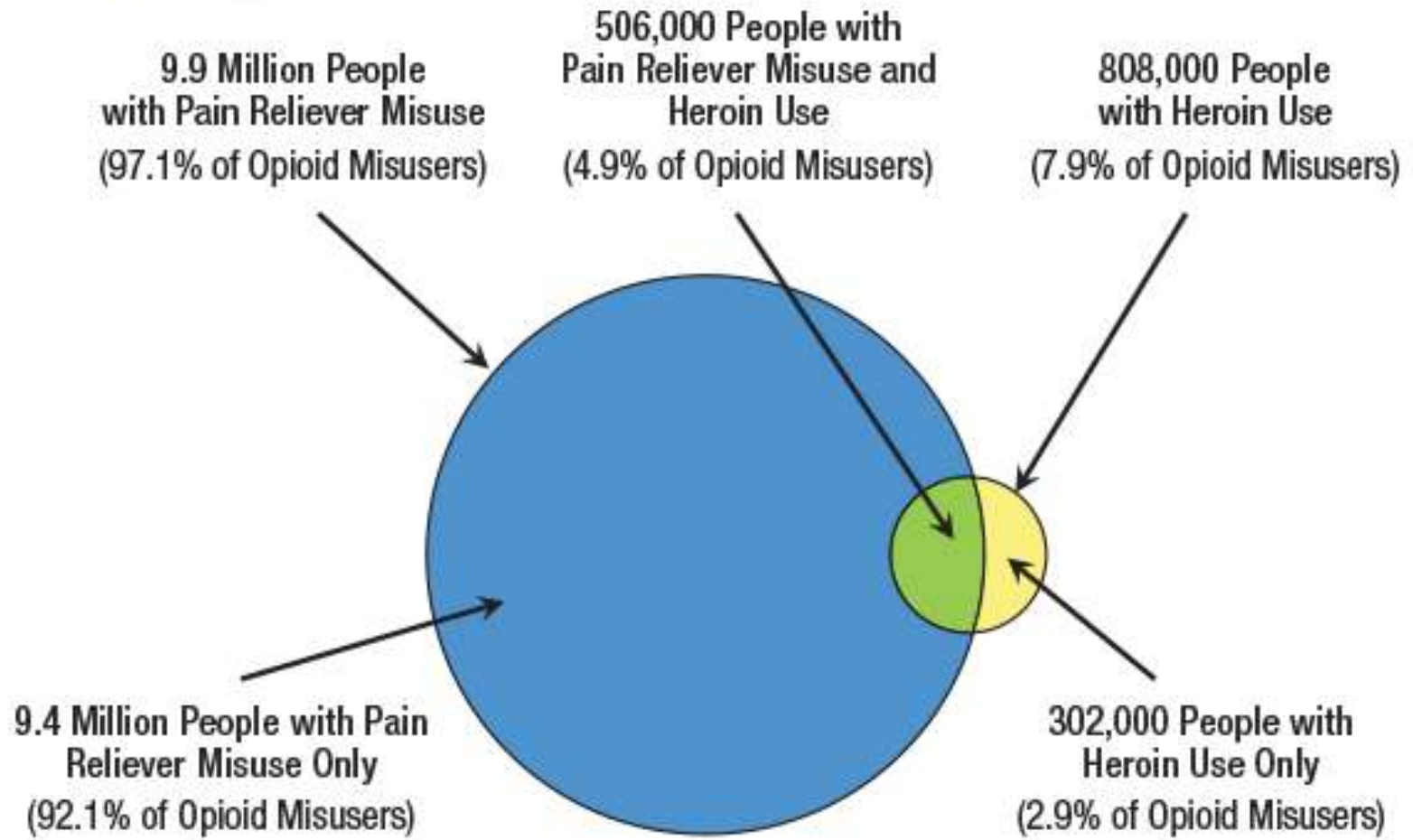
2016



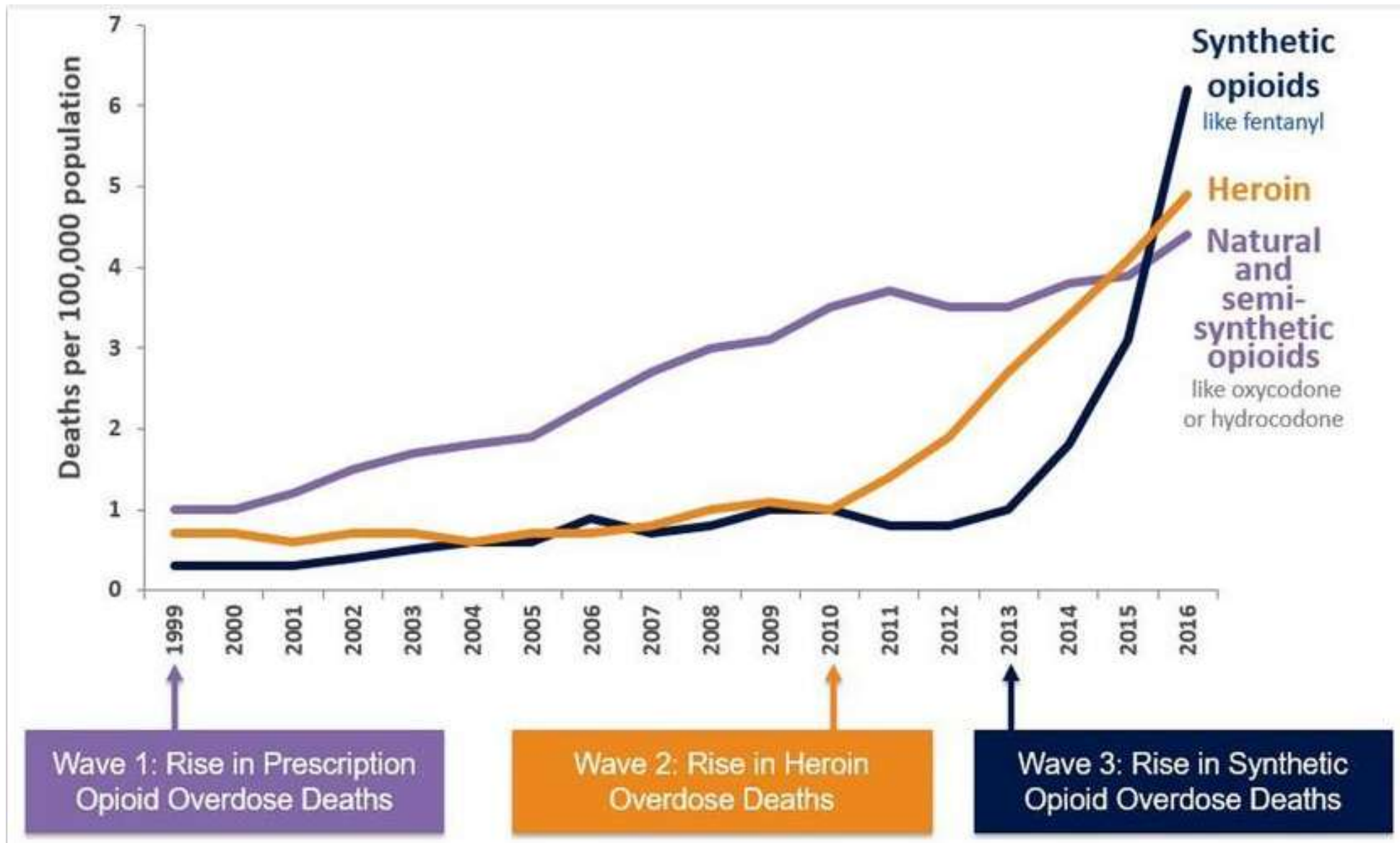
Legend for estimated age-adjusted death rate (per 100,000 population)



Past Year Opioid Misuse among People Aged 12 or Older: 2018



10.3 Million People Aged 12 or Older with Past Year Opioid Misuse



NEWS RELEASES

Thursday, September 26, 2019

NIH funds \$945 million in research to tackle the national opioid crisis through NIH HEAL Initiative

Approximately 375 awards in 41 states will accelerate scientific solutions.



To reverse the opioid crisis that continues to grip the nation, the National Institutes of Health has awarded \$945 million in total fiscal year 2019 funding for grants, contracts and cooperative agreements across 41 states through the [Helping to End Addiction Long-term Initiative](#) or [NIH HEAL Initiative](#). The trans-NIH research effort aims to improve treatments for chronic pain, curb the rates of opioid use disorder (OUD) and overdose and achieve long-term recovery from opioid addiction.

In 2016, an estimated 50 million U.S. adults suffered from chronic pain [PDF](#) and in 2018, an estimated 10.3 million people 12 years and older in the United States misused opioids, including heroin [PDF](#).

“President Trump’s approach to the opioid crisis and HHS’s strategy have both been based in the best science we have,” said HHS Secretary Alex Azar. “We have effective tools, such as medication-assisted treatment, but we still need better ways to treat opioid addiction and manage pain in an effective, personalized way. This historic investment by NIH was made possible by



- “Aggressive, trans-agency effort to speed scientific solutions to stem the national opioid public health crisis.”
- Build on extensive, well-established NIH research including:
 - Basic science of neurological pathways involved in pain and OUD
 - Clinical studies of safer and more effective treatments for pain and OUD
 - Implementation science to develop and test treatment models



With our partners, the NIH will take an “all hands on deck” approach to developing and delivering the scientific tools that will help end this crisis and prevent it from reemerging in the future.”

—Drs. Nora Volkow and Francis Collins, *New England Journal of Medicine*, 2017



NIDA HEAL Projects



- Expanding therapeutic options for Opioid Use Disorder and Overdose
- Enhancing the NIDA Clinical Trials Network
- HEALing Communities Study
- Justice Community Opioid Innovation Network (JCOIN)
- Preventing At-Risk Adolescents Transitioning into Adulthood from Developing Opioid Use Disorder
- HEALthy Brain and Child Development Study

<https://www.drugabuse.gov/drugs-abuse/opioids/nidas-role-in-nih-heal-initiative>

FDA-Approved Medications for Opioid Addiction and Overdose



- Methadone
- Buprenorphine
 - Sublingual
 - Monthly injection
 - Six month implant
- Naltrexone
 - Oral
 - Monthly
- Lofexidine
- Naloxone
 - Parenteral
 - Nasal



Close interaction with FDA

Expand therapeutic options for opioid addiction and overdose

1. New, more user-friendly formulations of existing medications
2. Longer duration, more powerful overdose treatments
3. New approaches to reverse respiratory depression
4. Immunotherapies for opioids to prevent relapse and overdose
5. New targets and approaches for treating Opioid Use Disorder (OUD)

1. New formulations of existing medications

- Long-term opioid receptor antagonists
 - 6-month naltrexone (GO Medical Pharmaceuticals/Columbia U.)
 - 3-month naltrexone implant/BICX102 (BioCorX)
 - 6-month nalmefene (Titan Pharmaceuticals)
- Long-term opioid receptor agonists
 - Weekly Oral Buprenorphine
 - Weekly R-Methadone (Lyndra Pharmaceuticals)

2. Longer duration, more powerful overdose reversal

- Intranasal Nalmefene: OPNT003 (Opiant)
- Methocinnamox: Long acting, pseudo-irreversible μ -opioid antagonist
- Nafamostat (PF614): Opioid delivery in combination with the Bio-Activated Molecular Delivery (Bio-MD™) prodrugs, for oral overdose protection
- NRS-033: Nalmefene prodrug active for >28 days

3. New approaches to reverse respiratory depression

- Almitrine: Peripheral, stimulating chemoreceptors in the carotid bodies to enhance respiration
- Ampakines (e.g., CX717): Mediators of respiratory drive through AMPA glutamatergic receptor
- Repinoptan: full agonist of 5HT1a

4. Novel Medications for OUD

- Kindolor: Peripherally acting and targets receptors, Nav 1.7 and 1.8 voltage-sensitive sodium channels, NMDA receptor and glycine site antagonist
- ITI-333: High affinity MOR partial agonist, 5-HT_{2A}, and D1 receptors antagonist
- D24M: MOR/DOR Heterodimer antagonist
- MEB-1166 or MEB-1170: Highly 'biased' MOR agonists

4. Novel Medications for OUD

- Repurposed Medications

- Guanfacine
- Suvorexant
- Duloxetine
- Ketamine
- Lorcaserin
- Gabapentin
- Dronabinol
- Cannabidiol



4. Immunotherapies

- Improve vaccine safety and efficacy by:
 - Increasing antibody titers, duration, and affinity
 - Antigen and dose sparing with novel adjuvants
 - Optimizing for target populations
 - Identifying immune correlates of protection
- Product development
 - Collaborations with experts in formulation, scale-up, GMP
- Clinical trials

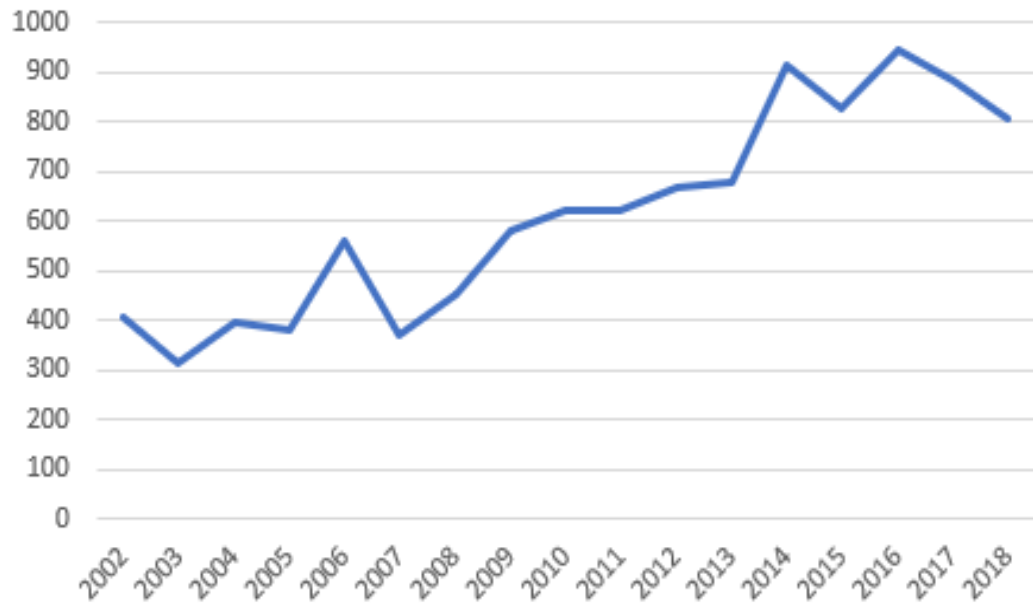
5. New Approaches

- Drugs to prevent opioid craving
 - ANS-6637 (Amygdala Pharmaceuticals): Selective ALDH2 Inhibitor that prevents pathophysiologic dopamine surge
- Safe non-addictive analgesics
 - MP1000 Arylepoxamide: Distinct from any of the traditional opioid receptors
- Protein Tyrosine Phosphatase Receptor D
 - Associated with dependence on opiates at the genetic level
- “Balanced” opioid biased agonists: PZM21

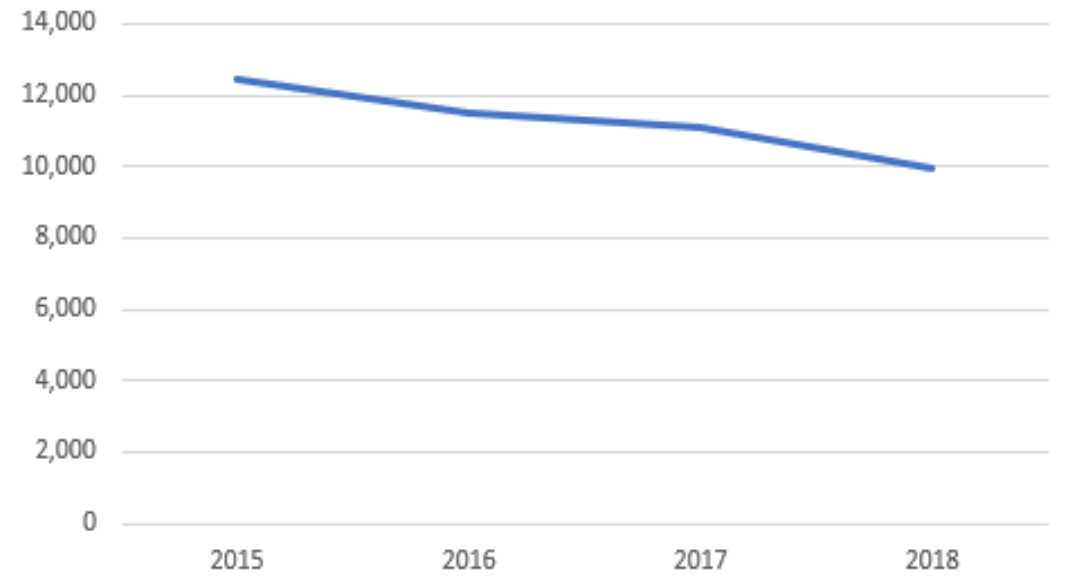


Past-Year Use

Heroin



Prescription Opioid Analgesic



Thank you

