



Evolving Principles of Multimodal Pain Management – 2025 Fall Update

David R. Neff, DO

Associate Clinical Professor, MSUCOM

Former Chief Medical Director, Michigan Medicaid (Retired)

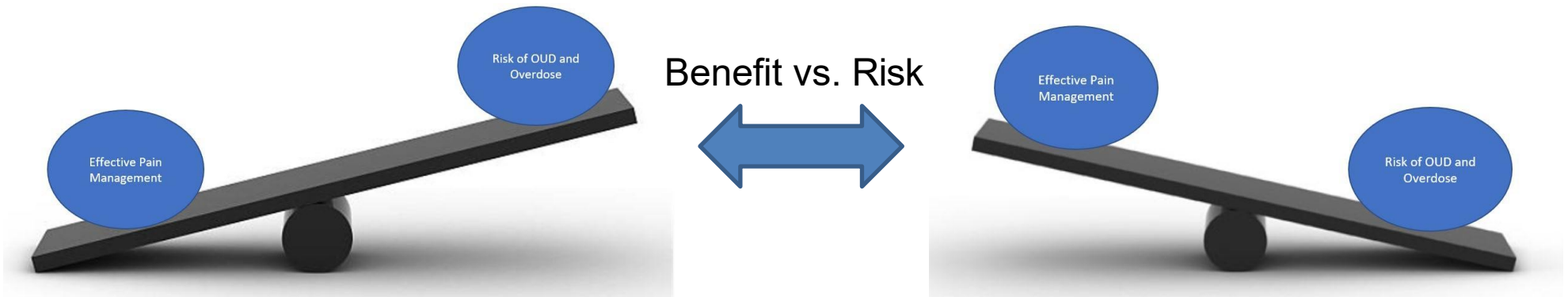
Former Medical Strategy Leader, Merck Global Medical Affairs (Retired)

Founding Member, MOA Safe Opioid Task Force Member,

Founding Member, Michigan Health Society Safe Opioid Collaborative

Consultant -Translational Research, Health Outcomes and Policy

Goal: Enable Providers to Balance Effective Pain Management When Using Opioids in the Background of Polysubstance Misuse As the 4th Wave of the Overdose Epidemic



Counterfeit Oxycodone Tablet Containing Fentanyl



Primary Objectives

At the conclusion of this talk, attendees will understand:

1. The role polysubstance misuse as the “4th Wave of the Overdose Epidemic”
2. Recently updated definitions for pain
3. Principles of assessment and treatment for acute and chronic pain - using a multimodal approach
4. New non-opioid prescription medication and future non-opioid drug targets

Conflicts: None



Understanding Opioid and Polysubstance Misuse

Understanding Opioids

Opioids

Opioids are a class of drugs—both natural and synthetic—that are primarily used for pain relief. They work by binding to opioid receptors in the brain, spinal cord, and other parts of the body, effectively blocking pain signals and producing a calming or euphoric effect.

Types of Opioids

Opioids are categorized into three main types:

1. Natural opioids (opiates) – Derived directly from the opium poppy plant.
 - Examples: Morphine, Codeine, Opium
2. Semi-synthetic opioids – Chemically modified from natural opioids.
 - Examples: Oxycodone, Hydrocodone, Heroin, Hydromorphone
3. Synthetic opioids – Fully man-made in laboratories.
 - Examples: Fentanyl, Methadone, Tramadol
4. Nitazines – A whole new subclass of newly derived synthetic opioids

Understanding Opioids

Medical Uses of Opioids

Opioids are prescribed for a variety of medical conditions, including:

- Post-surgical pain
- Cancer-related pain
- Severe injury or trauma
- Chronic pain conditions
- Palliative care
- Severe coughing
- Chronic diarrhea

Understanding Opioids

Risks and Side Effects

While effective, opioids carry significant risks:

Short-term side effects:

- Drowsiness
- Nausea
- Constipation
- Slowed breathing
- Confusion

Long-term effects:

- Hormonal imbalance
- Sleep disorders
- Depression
- Dependence

Serious risks:

- Tolerance: Needing higher doses for the same effect
- Dependence: Experiencing withdrawal symptoms when stopping
- Opioid Use Disorder (OUD): Inability to stop despite negative consequences
- Overdose: Can lead to respiratory failure and death

The Use of Opioids Goes Back Least 6 Millenium

Ancient Beginnings

- ~3400 BCE: Sumerians referred to the opium poppy as the "joy plant," indicating early psychoactive use ¹.
- ~1300 BCE: Minoan Crete featured opium in religious rituals, evidenced by statues and artifacts ¹.
- **Ancient Egypt:** Opium was used medicinally, including for calming infants, as noted in burial texts ¹.
- **Greek & Roman Eras:** Figures like Hippocrates and Galen prescribed opium for pain and sleep. It appeared in literature, coins, and art ¹.

Medieval and Islamic World

- **Persia:** Opium was part of sacred mixtures like *haoma*. Avicenna (Ibn Sina) classified it as both a painkiller and anesthetic, warning of its addictive potential ¹.
- **Islamic Golden Age:** Scholars translated global medical knowledge, including opium's uses, into Arabic at Baghdad's House of Wisdom ¹.

The Use of Opioids Goes Back Least 6 Millenium



Rise of Global Trade

- **Silk Road & Sea Routes:** Opium traveled from East to West via land and maritime trade routes. Marco Polo documented opium caravans in Central Asia ¹.
- **Crusades:** European exposure to opium increased through contact with the Middle East. It was used to treat plague symptoms during the Black Death ¹.

GB Colonial Exploitation and the Opium Wars

- **18th–19th Centuries:** Western powers, especially **Britain**, exported opium grown in **India** to **China** to balance trade deficits caused by demand for Chinese goods like tea and silk ².
- **British East India Company:** Established a monopoly on opium cultivation in Bengal. Licensed private traders smuggled opium into China despite imperial bans ².
- **Opium Wars (1839–42, 1856–60):** China's attempts to suppress the trade led to military conflicts with Britain, resulting in treaties that favored Western powers and opened Chinese ports ².

[Opium History: The Evolution From Healing Herb To Global Drug Crisis](#)

The Use of Opioids Goes Back Least 6 Millenium

1861–1865: U.S. Civil War

Morphine was widely used to treat battlefield injuries, leading to widespread addiction among soldiers. This phenomenon became known as 'soldier's disease'.

1914: Harrison Narcotics Tax Act

The U.S. passed legislation regulating and taxing the production and distribution of opiates and coca products, marking the beginning of federal drug control.

1970: Controlled Substances Act

The U.S. established a legal framework for regulating drugs, categorizing opioids and other substances into schedules based on medical use and abuse potential.

1990–2000

Rise in prescription opioid use in the United States, driven by aggressive marketing and overprescribing, marking the beginning of the modern opioid epidemic.

Late 20th Century: Rise of Synthetic Opioids

Pharmaceutical companies developed synthetic opioids like fentanyl and methadone, increasing the potency and availability of opioid medications.

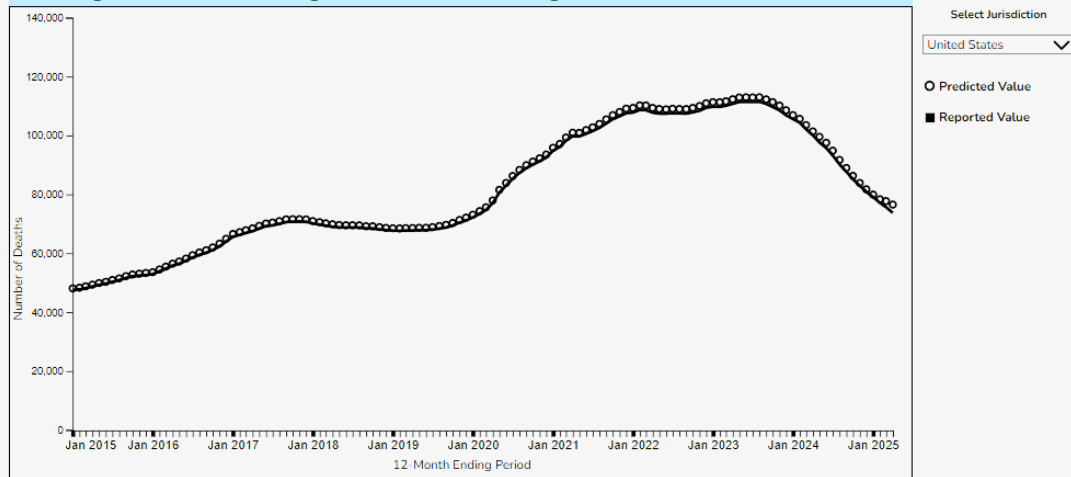
[Opium History: The Evolution From Healing Herb To Global Drug Crisis](#)

The Good News!

12 Month-ending Provisional Number and Percent Change of Drug Overdose Deaths

Based on data available for analysis on: September 7, 2025

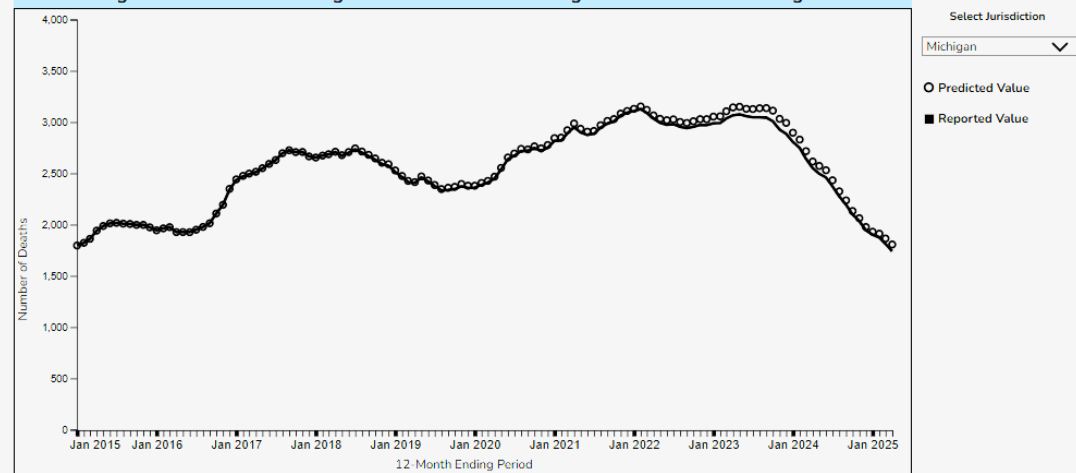
Figure 1a. 12 Month-ending Provisional Counts of Drug Overdose Deaths: United States



12 Month-ending Provisional Number and Percent Change of Drug Overdose Deaths

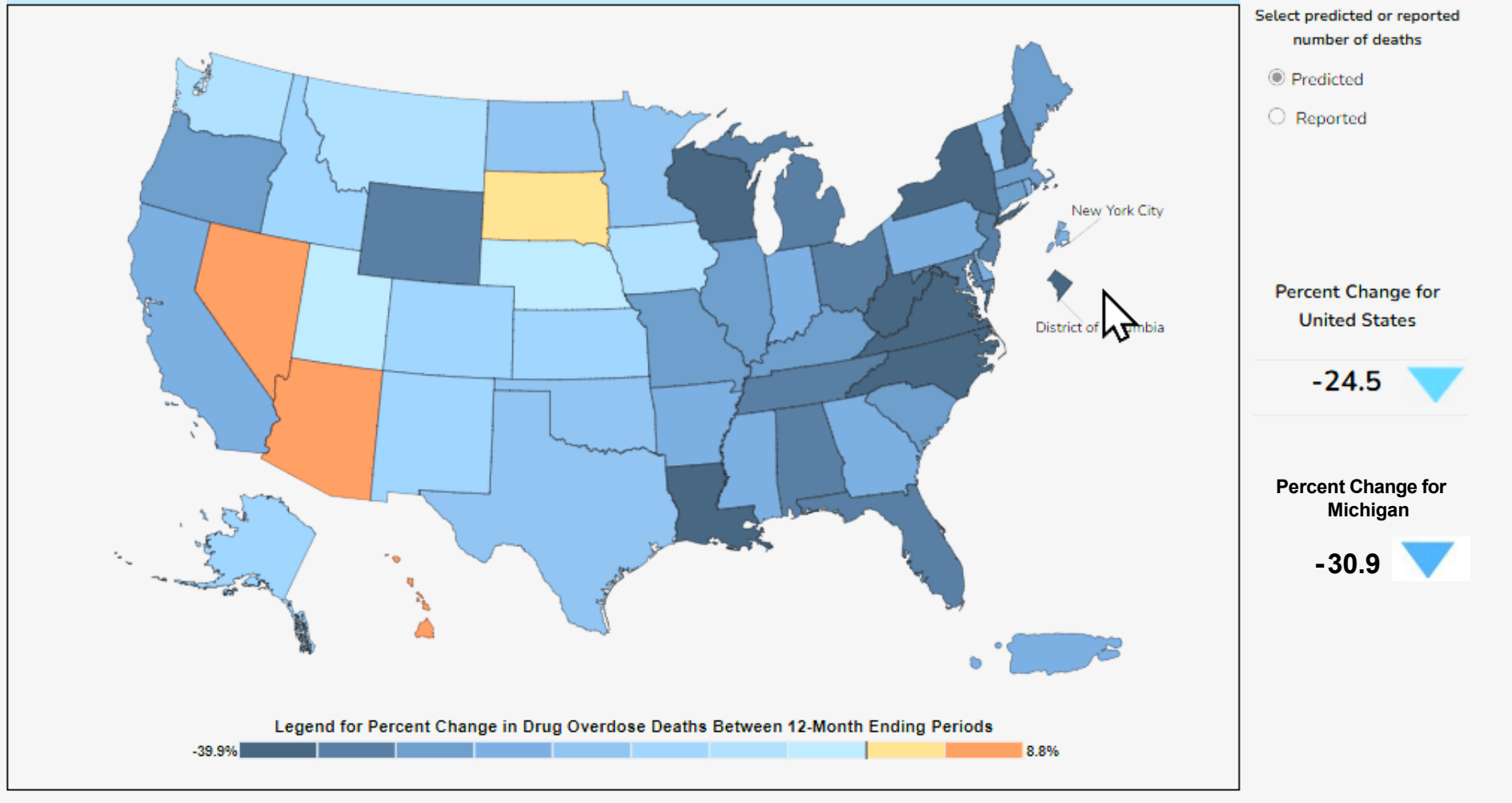
Based on data available for analysis on: September 7, 2025

Figure 1a. 12 Month-ending Provisional Counts of Drug Overdose Deaths: Michigan



The Good News!

Figure 1b. Percent Change in Predicted 12 Month-ending Count of Drug Overdose Deaths, by Jurisdiction: April 2024 to April 2025



The Bad News!

We Are in the 4th Wave of the Modern Overdose Epidemic

1. First Wave (1990s–2010): Prescription Opioids

- Began with the increased prescribing of opioids for pain management, especially non-cancer-related chronic pain.
- Drugs like OxyContin (oxycodone) and Vicodin (hydrocodone) were marketed as safe and non-addictive.
- Resulted in a sharp rise in opioid use disorder and overdose deaths involving natural and semi-synthetic opioids ³.

2. Second Wave (2010–2013): Heroin

- As regulations tightened on prescription opioids, many dependent users turned to heroin, a cheaper and more accessible alternative.
- Heroin-related overdose deaths quadrupled between 2002 and 2013 ³.
- The heroin market expanded to meet demand, especially in urban areas ².

3. Third Wave (2013–Present): Synthetic Opioids

- Marked by a surge in deaths involving illicitly manufactured fentanyl (IMFs) and its analogs.
- Fentanyl is 50–100 times more potent than morphine, often mixed with other drugs or pressed into counterfeit pills ¹.
- Overdose deaths from synthetic opioids have surpassed those from heroin and prescription opioids ².

4. Fourth Wave (2019–Present): Polysubstance Use

- Characterized by combined use of opioids with stimulants like methamphetamine or cocaine.
- This wave is geographically widespread, affecting both urban and rural communities equally ³.
- Exacerbated by the COVID-19 pandemic, which disrupted treatment access and increased isolation ³.

[Global, regional, and national burden of opioid use disorder from 1990 to 2021: a statistical analysis of incidence, mortality, and disability-adjusted life years | BMC Public Health | Full Text](#)

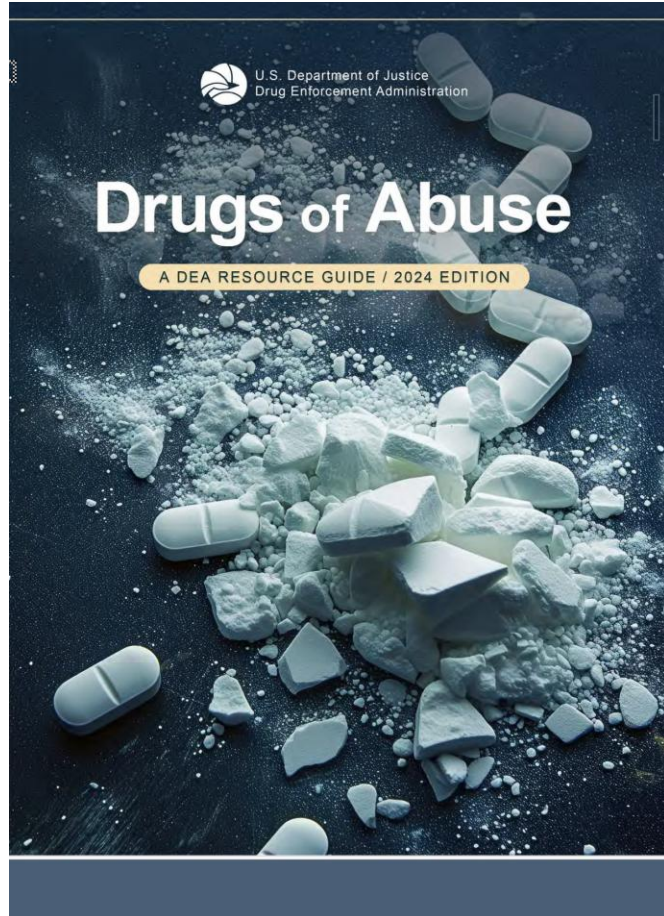
What Kind of Substances are Involved (Intentional or Unintentional) in Polysubstance Use Disorder (PUD)?

Polysubstance misuse often involves a combination of **stimulants, depressants, and other psychoactive substances**, which can lead to unpredictable and dangerous effects. Some of the most commonly misused substances include:

- **Opioids – Illicitly Manufactured Fentanyl (IMF) and Nitazines**, Prescription opioids (fentanyl, oxycodone, hydrocodone, hydromorphone), heroin, and kratom (can be reversed)
- **α 2-adrenergic agonists** – Xylazine and Medetomidine (cannot be reversed)
- **Stimulants** – Methamphetamine, cocaine, prescription amphetamines (such as Adderall), and MDMA (ecstasy) and nicotine.
- **Depressants** – Alcohol, Benzodiazepines (Xanax, Valium), barbiturates, certain muscle relaxants (Soma)
- **Cannabinoids** – marijuana and synthetic cannabinoids ("spice" or "K2"), and synthetic cathinones ("bath salts").
- **Hallucinogens** – Ketamine (NDMA Receptor Antagonist), Nitrous Oxide (huffing), LSD, psilocybin mushrooms, and PCP.

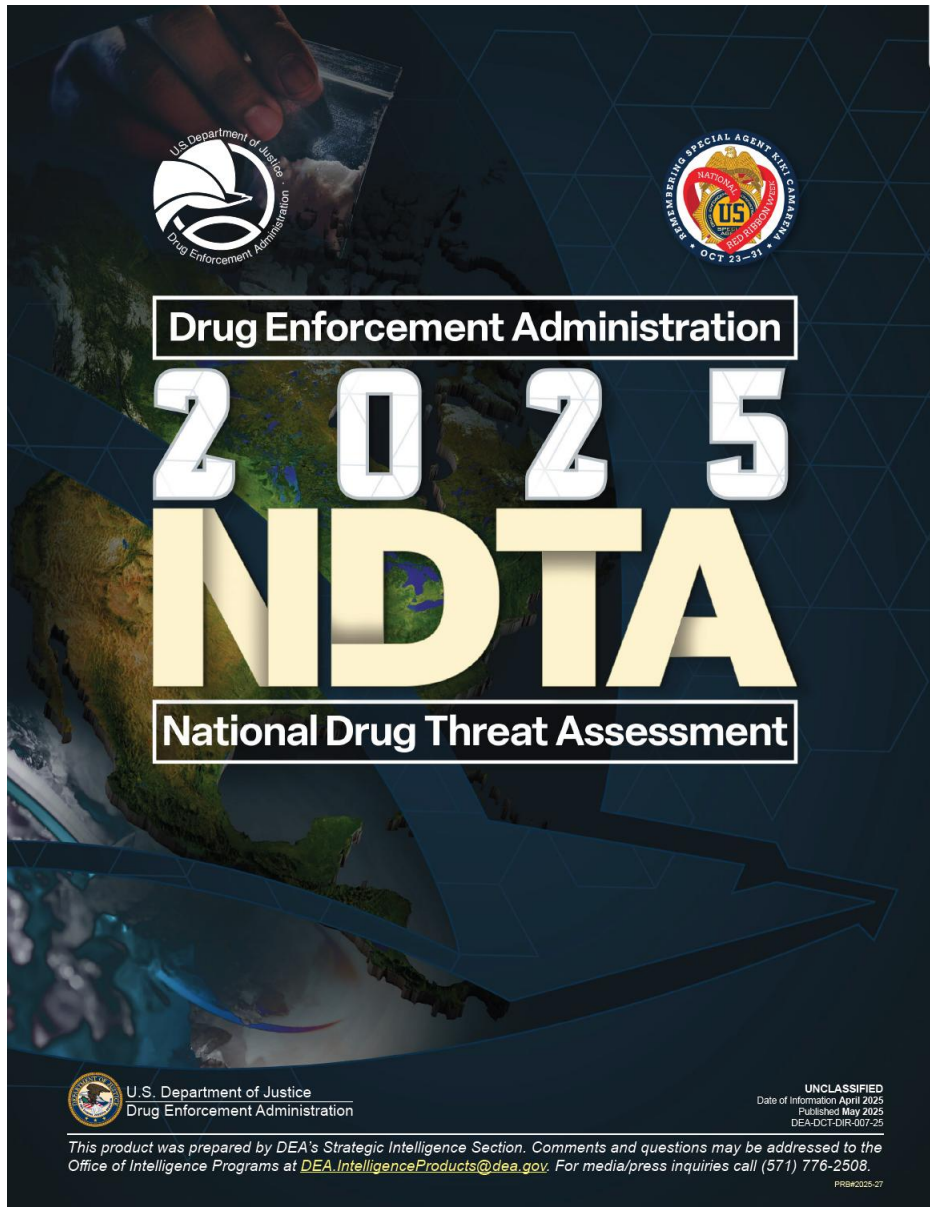
Mixing these substances can **increase the risk of overdose**, as their effects may amplify or mask each other, leading to dangerous consequences.

DEA: Multiple Drugs of Abuse on the Street



URL - [Drugs of Abuse: A DEA Resource Guide, 2024 Edition](#) (accessed 4/14/2025)

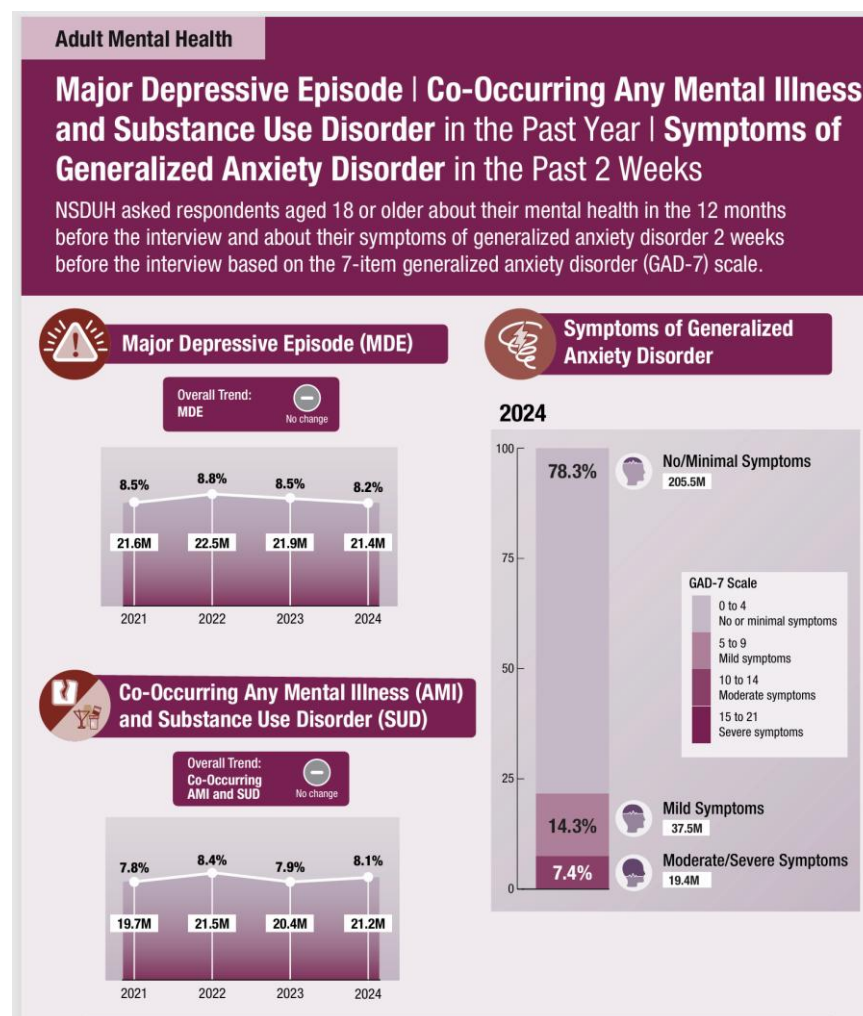
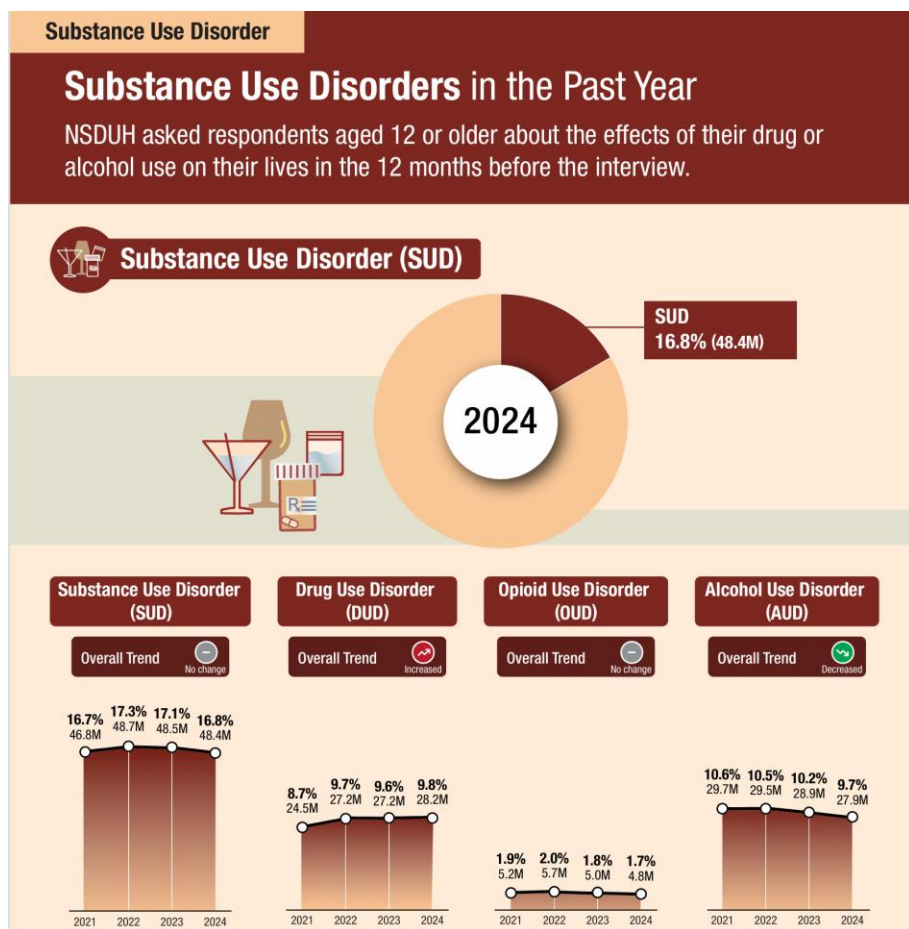
The DEA 2025 Drug Threat Assessment



- Drug overdose deaths decreased by more than 20% in 2024. October 2024 was the eleventh consecutive month in which CDC reported a reduction in drug related deaths.
- More than 80,000 Americans still dying from drug poisonings and overdose deaths, the synthetic drug and polysubstance threat remains grave.
- DEA laboratories are reporting a downward trend in fentanyl purity. This should not be mistaken for street-level fentanyl being any less dangerous. While purity levels are decreasing, the mixing of fentanyl with animal tranquilizers and other synthetic opioids is on the rise, which results in people not knowing the exact composition of what they are consuming or selling.
- The mixing of illicit substances, known as drug cocktails, is becoming more common. One in four submissions of cocaine and one in eight submissions of methamphetamine also included fentanyl. This is another indication that the drug landscape is as dangerous as ever.
- Veterinary tranquilizer xylazine remains the top adulterant found in fentanyl powder; however, a more powerful veterinary anesthetic, medetomidine, has emerged in the fentanyl supply – a dangerous development in the fight against fentanyl.
- More than four million youth and young adults (ages 12-20) reported vaping marijuana that is 100 times stronger in the past year.

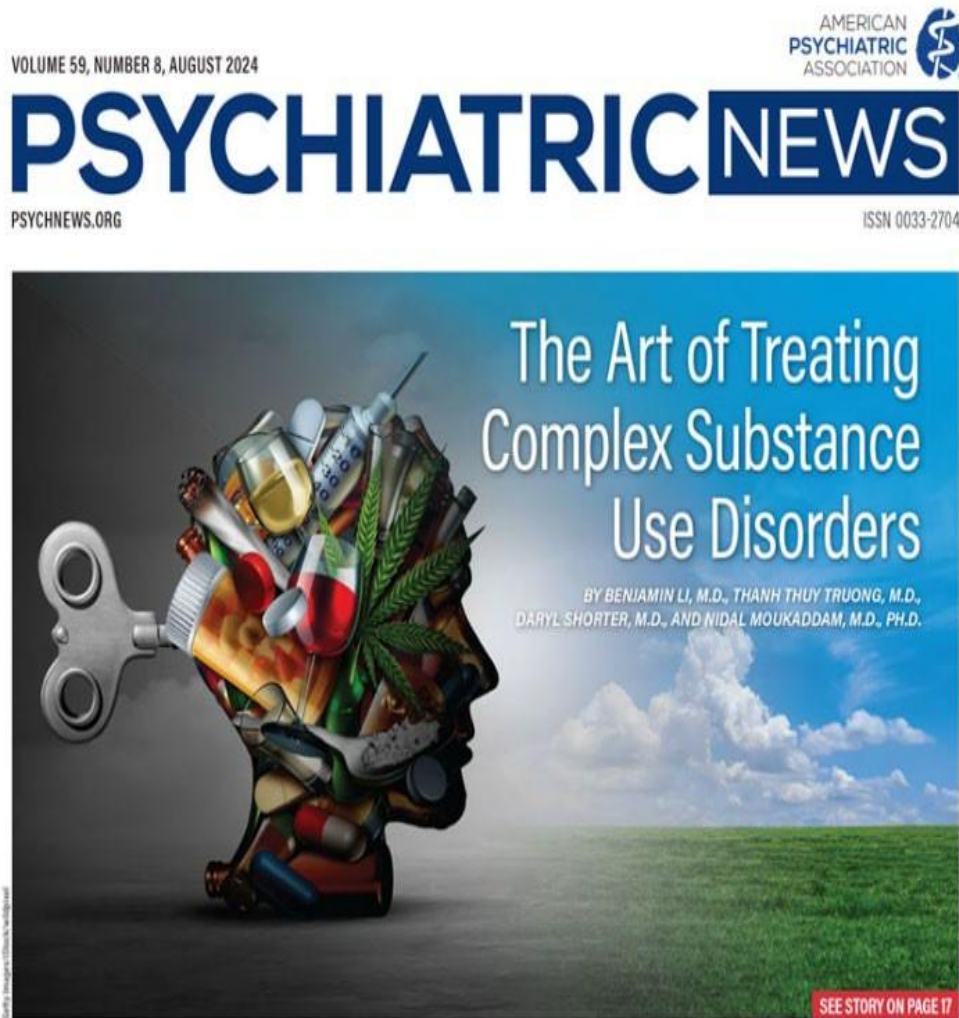
[National Drug Threat Assessment](#) (Released 5-13-25 Accessed 10-25-2025)

2025 Report on the 2024 National Survey on Drug Use and Health (NSDUH)



URL: [NSDUH National Releases | CBHSQ Data](#) and [2024 Companion Infographic Report: Results from the 2021 to 2024 National Surveys on Drug Use and Health](#)

Polysubstance Substance Use Disorder (PUD)



- The use of more than one drug, also known as polysubstance use, is common. This occurs when two or more are taken together or within a short time period, either intentionally or unintentionally.
- Whether intentional or not, mixing drugs is never safe because the effects from combining drugs may be stronger and more unpredictable than one drug alone, and even deadly.
- Polysubstance-related overdoses can lead to permanent anoxic-hypoxic brain injury or death
 - approximately 1 fatal overdose per 15 non-fatal in the U.S.

URL: [Special Report: The Art of Treating Complex Substance Use Disorders | Psychiatric News](#) Accessed 4/14/2025

Impact of OUD

Health Impact

- Opioid Use Disorder (OUD) has become a major public health crisis, especially since the 1990s ¹ ².
- In 2021, there were:
 - 1.94 million new cases of OUD
 - 99,555 deaths
 - 11.2 million disability-adjusted life years (DALYs) lost globally ¹.
- High-income regions, especially North America, bear the heaviest burden, with the U.S. showing the highest rates of prevalence, incidence, and mortality ².
- Young adults (20–39 years) are the most affected demographic, though rates among women are rising rapidly ².

Economic Impact

- OUD leads to lost productivity, increased healthcare costs, and criminal justice expenses.
- In the U.S. alone, the economic cost of the opioid crisis has been estimated in the hundreds of billions of dollars annually, factoring in healthcare, law enforcement, and lost labor ³.
- Countries with higher socio-demographic indices (SDIs) often have both greater burdens and greater potential to reduce them through policy and healthcare infrastructure ¹.

[Opium History: The Evolution From Healing Herb To Global Drug Crisis](#)

Impact of OUD

Social Impact

- Families and communities face **emotional trauma**, **neglect**, and **intergenerational cycles of addiction**.
- Opioid misuse is linked to **crime**, **homelessness**, and **child welfare issues**.
- The crisis has disproportionately affected **marginalized populations**, exacerbating social inequalities ³.

Trends Over Time

- 1990s–2000s: Surge in **prescription opioid misuse**, especially in North America.
- 2010s: Shift to **heroin** as prescriptions became harder to obtain.
- Mid-2010s to present: Rise in **synthetic opioids** like **fentanyl**, driving overdose deaths ³.
- **COVID-19 pandemic** worsened the crisis due to isolation, economic stress, and disrupted healthcare access ².

[Opium History: The Evolution From Healing Herb To Global Drug Crisis](#)



Understanding Pain

2020 Revised Definition of Pain

Pain
An unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage.
Notes
• Pain is always a personal experience that is influenced to varying degrees by biological, psychological, and social factors.
• Pain and nociception are different phenomena. Pain cannot be inferred solely from activity in sensory neurons.
• Through their life experiences, individuals learn the concept of pain.
• A person's report of an experience as pain should be respected.
• Although pain usually serves an adaptive role, it may have adverse effects on function and social and psychological well-being.
• Verbal description is only one of several behaviors to express pain; inability to communicate does not negate the possibility that a human or a nonhuman animal experiences pain.

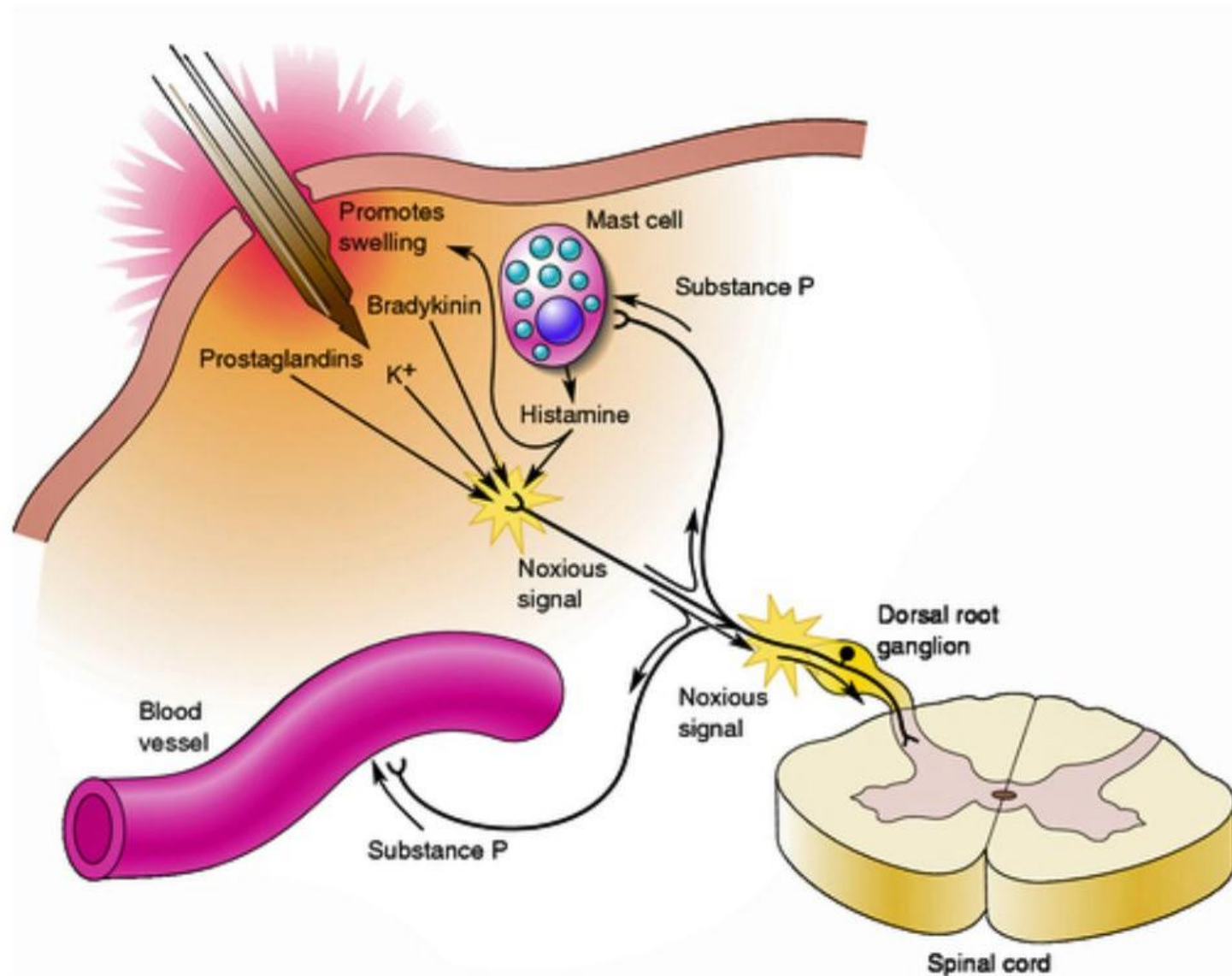
1. Declaration of Montréal. International Association for the Study of Pain. Available at: <https://www.iasp-pain.org/DeclarationofMontreal> (Accessed on 5/18/2024). From: Raja SN, Carr DB, Cohen M, et al. The revised International Association for the Study of Pain definition of pain: concepts, challenges, and compromises. PAIN 2020; 161:1976. DOI: [10.1097/j.pain.0000000000001939](https://doi.org/10.1097/j.pain.0000000000001939). Copyright © 2020 International Association for the Study of Pain.

Pain Terms and Definitions

- **Nociceptive pain:** Pain that arises from actual or threatened damage to non-neural tissue and is due to the activation of nociceptors.
- **Central sensitization:** Increased responsiveness of nociceptive neurons in the central nervous system to their normal or subthreshold afferent input.
- **Neuropathic pain:** Pain caused by a lesion or disease of the somatosensory nervous system.
- **Allodynia:** Pain due to a stimulus that does not normally provoke pain.
- **Hyperalgesia:** Increased pain from a stimulus that normally provokes pain.
- **Nociplastic pain:** Pain that arises from altered nociception despite no clear evidence of
 - actual or threatened tissue damage causing the activation of peripheral nociceptors
 - disease or lesion of the somatosensory system causing the pain.

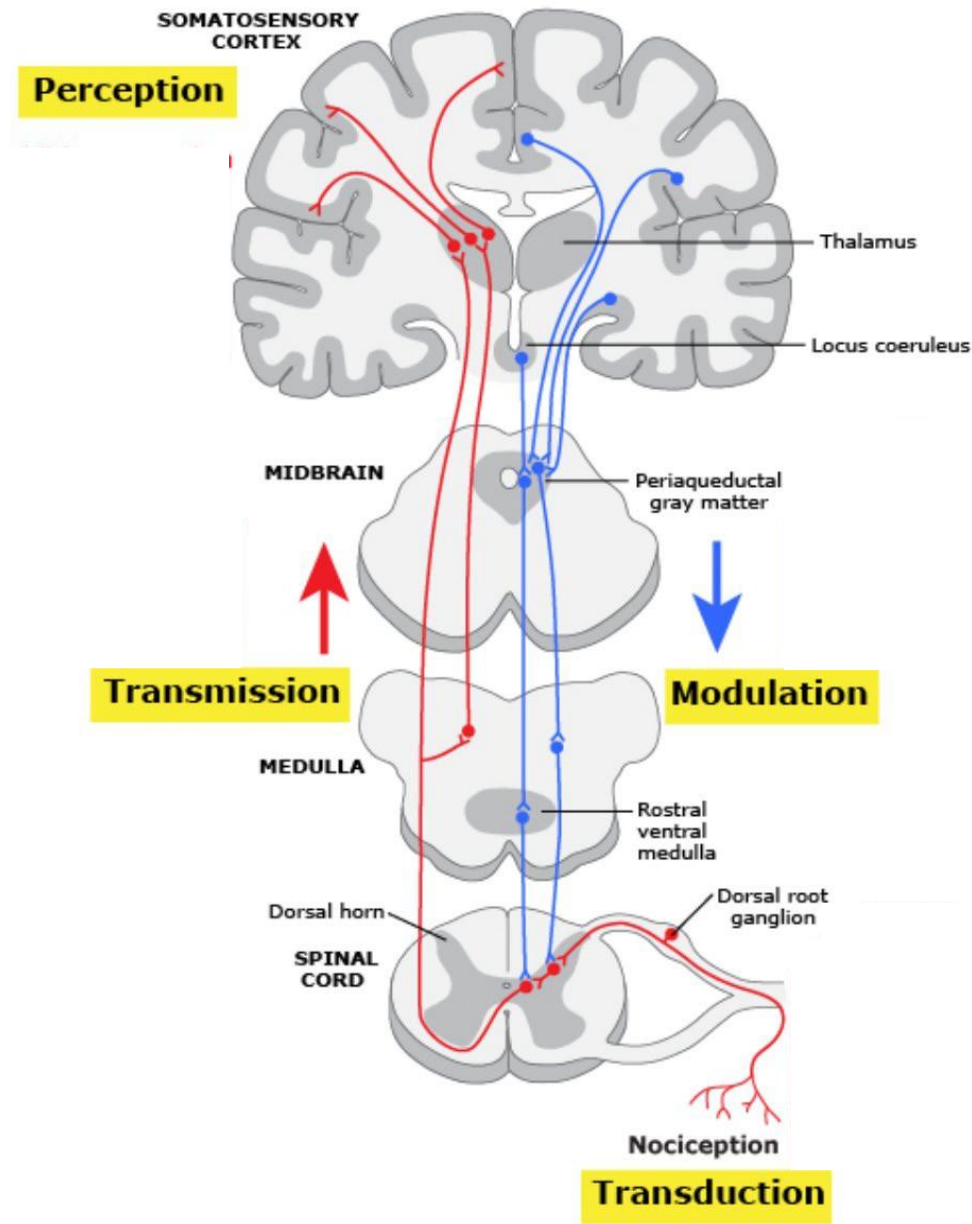
IASP Terminology. International Association for the Study of Pain. Available at: <https://www.iasp-pain.org/Education/Content.aspx?ItemNumber=1698> (Accessed on December 1, 2019).

Pain Signaling Pathways – Inflammatory Responses Mediated by Pain Receptors



URL - [Approach to the management of chronic non-cancer pain in adults – UpToDate](#) and [Pharmacologic management of chronic non-cancer pain in adults – UpToDate](#) (Accessed 4/14/2025)

Pain Signaling Pathways



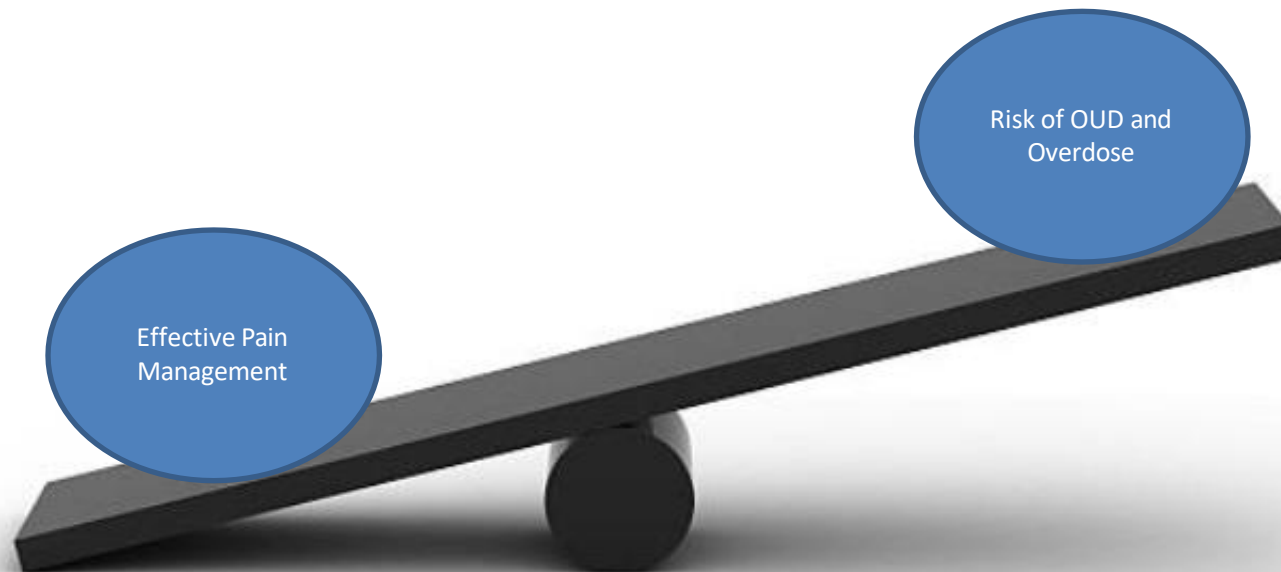
GOAL FOR ADEQUATE PAIN CONTROL

The goal for pain control should not be zero pain, but rather a tolerable level of pain that allows physical and emotional function. Often this means balancing analgesia with achieving functional goals, while avoiding preventable complications.

PRINCIPLES

1. Create an individualized plan for pain management based on the expected degree of pain and patient factors that may affect the plan
2. Offer multimodal analgesia, adding opioids only as necessary
3. Provide patient education
4. Adjust the pain management plan based on adequacy of pain relief and the occurrence of adverse events

When The Need for Effective Pain Management Using an Opioid May Outweigh Risk



1. Acute pain (duration <1 month)
2. Subacute pain (duration of 1-3 months)
3. Chronic pain (duration of >3 months) - “most days” or “every day”
 - High-impact chronic pain is based on responses of “frequently limits life or work activities”
 - Intractable pain

The Updated 2022 CDC Clinic Practice Guideline for Prescribing Opioids

Summary

This Guidelines is

- **A clinical tool to improve communication between clinicians and patients and empower them to make informed, person-centered decisions related to pain care together**
- **Intended for primary care clinicians and other clinicians providing pain care for outpatients aged ≥18 years old with:**
 - acute pain (duration <1 month);
 - subacute pain (duration of 1-3 months); or
 - chronic pain (duration of >3 months)
- **Intended to be flexible to enable person-centered decision-making, taking into account an individual's expected health outcomes and well-being.**

This clinical practice guideline is not

- **A replacement for clinical judgment or individualized, person-centered care**
- **Intended to be applied as inflexible standards of care across patients, and/or patient populations by healthcare professionals, health systems, pharmacies, third-party payers, or governmental jurisdictions or to lead to the rapid tapering or discontinuation of opioids for patients**
- **A law, regulation, and/or policy that dictates clinical practice or a substitute for FDA-approved labeling**
- **Applicable to the following types of pain treatment:**
 - sickle cell disease-related pain
 - cancer pain
 - palliative care
 - end-of-life care

URL - [CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022](#) (Accessed 4/14/2025)

URL - [Prescribing Opioids for Pain — The New CDC Clinical Practice Guideline | NEJM](#) (Accessed 4/14/2025)

CDC Clinic Practice Guideline for Prescribing Opioids – United States, 2022

Summary

1. For all patients with acute, subacute, or chronic pain – go low and go slow

- Initiate the lowest dose to achieve expected results
- For opioid naïve patients, start with immediate-release opioids instead of extended-release/long-acting (ER/LA) opioids
- Use extreme caution when prescribing opioids, benzodiazepines and other sedating substances concurrently
 - consider whether benefits outweigh risks
 - Taper cautiously to a less risky dose or discontinue
- Check the state prescription drug monitoring program (PDMP) also known as the Michigan Automated Prescription Service (MAPS), to determine whether the patient is receiving opioid dosages or combinations that put the patient at high risk for overdose
 - When initiating therapy
 - Periodically when continuing
- Consider toxicology testing to assess for prescribed medications as well as other prescribed and non-prescribed controlled substances
- Offer naloxone and other overdose mitigation strategies when risk factors for opioid overdose are present

2. For acute pain, consider initiating opioid therapy only if benefits are anticipated to outweigh risks to the patient

- Nonopioid therapies are effective for many common types of acute pain
- Prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids

CDC Clinic Practice Guideline for Prescribing Opioids – United States, 2022

Summary

3. For subacute and chronic pain, consider initiating opioid therapy only if expected benefits for pain and function are anticipated to outweigh risks to the patient

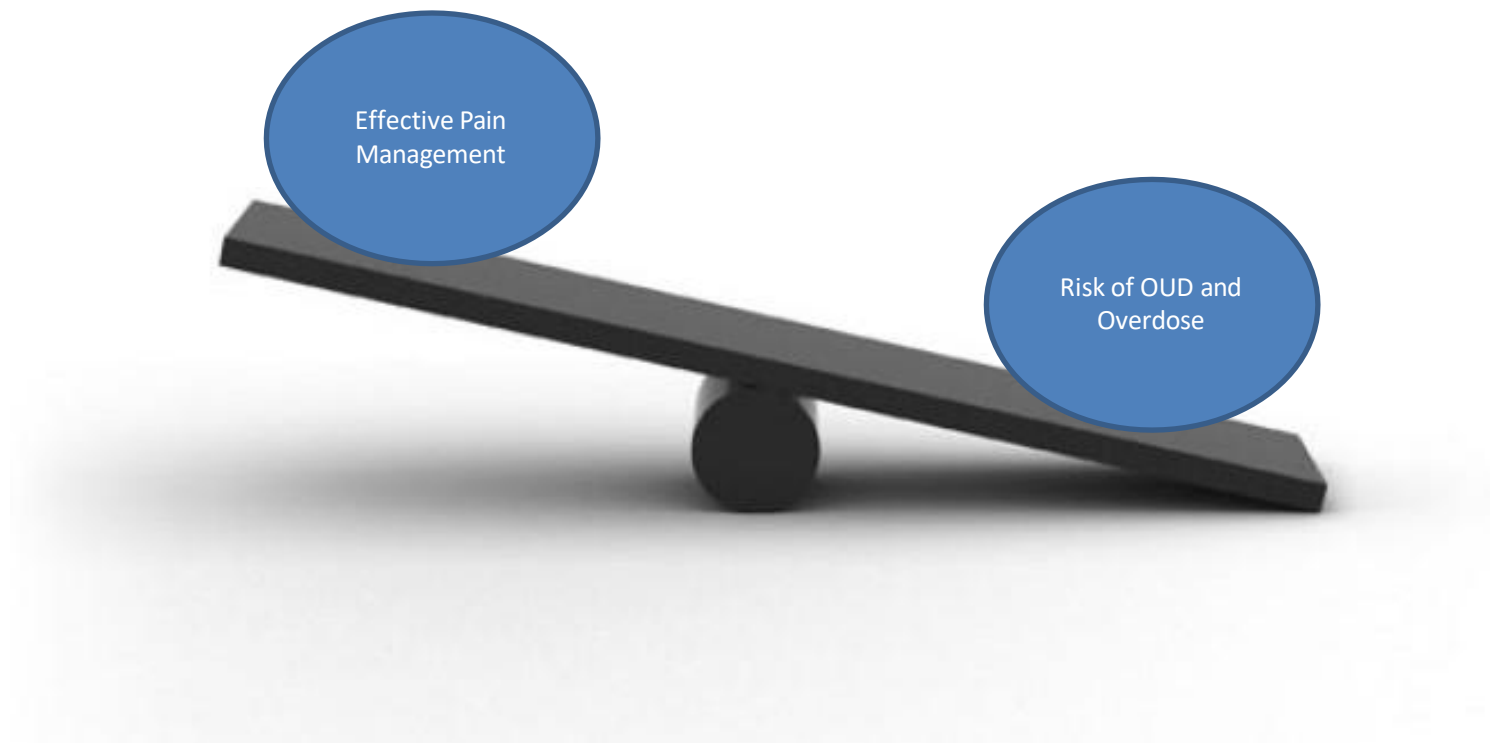
- Work with patients to establish treatment goals for pain and function
- Nonopioid therapies are preferred
- Discuss the known risks and realistic benefits of opioid therapy
- Consider how opioid therapy will be discontinued when benefits do not outweigh risks
- If opioids are continued
 - use caution when prescribing opioids at any dosage
 - avoid increasing dosage above levels likely to yield diminishing returns in benefits relative to risks to patients
 - re-evaluate benefits and risks after starting opioid therapy or when escalating dose
 - Initially at 1 to 4 weeks
 - Then every 3 months (or more frequently as indicated)

4. Carefully weigh benefits and risks for patients already receiving higher opioid dosages

- Do not abruptly discontinue opioid therapy unless there are indications of a life-threatening issue, such as warning signs of impending overdose (e.g., confusion, sedation, or slurred speech)
- Exercise care when reducing or continuing opioid dosage
- Work closely with patients to optimize other therapies
- Gradually taper to lower dosages if risks outweigh benefits of continued opioid therapy
- Taper and discontinue opioids if warranted based on the individual clinical circumstances of the patient
- Consider transitioning to buprenorphine if opioids cannot be sufficiently tapered or discontinued

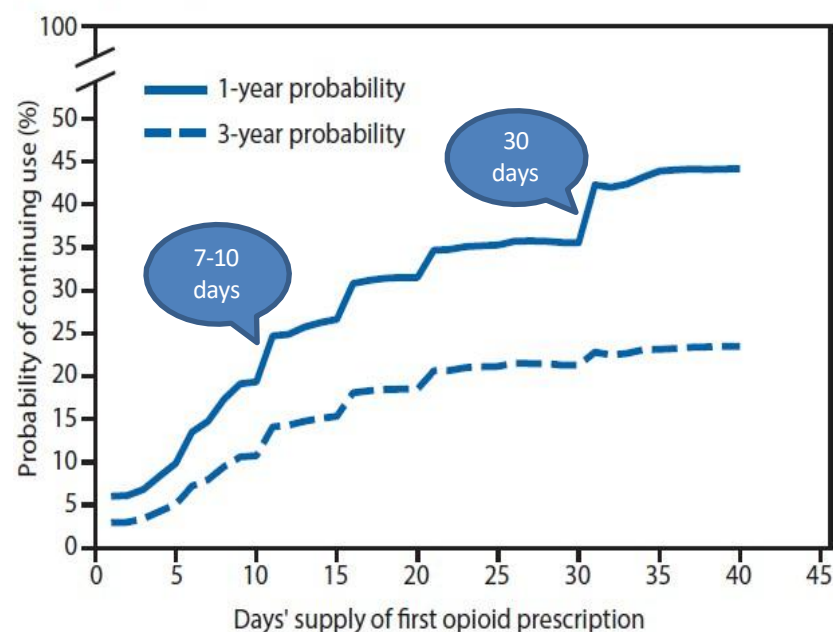
5. Offer Medications for Opioid Use Disorder (MOUD) to patients without pain and exhibiting opioid use disorder (OUD)

When Risk Begins to Outweigh Benefit



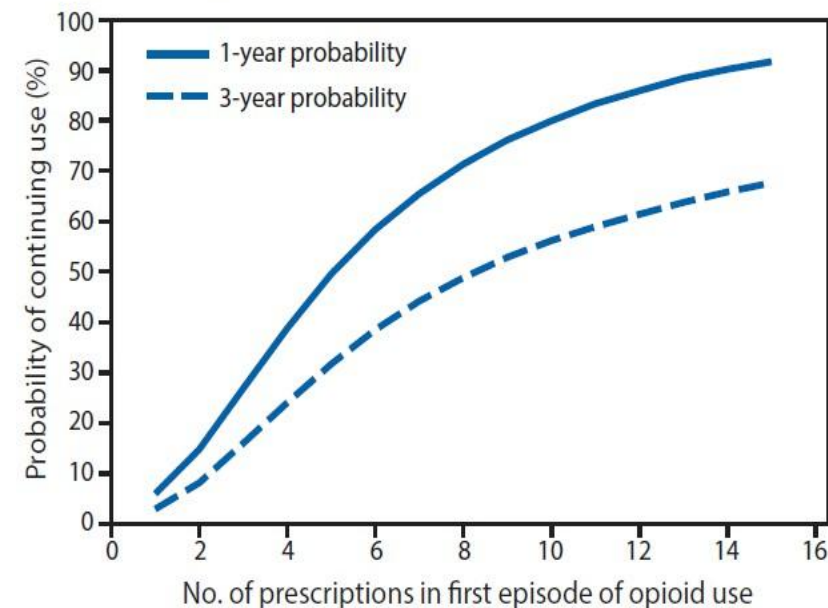
The Downside to Using Opioids Beyond 7-10 Days For Acute Pain: The Risk for Continued Opioid Use Goes Up with Days Supply and Number of Prescriptions in the First Episode of Care

FIGURE 1. One- and 3-year probabilities of continued opioid use among opioid-naïve patients, by number of days' supply* of the first opioid prescription — United States, 2006–2015



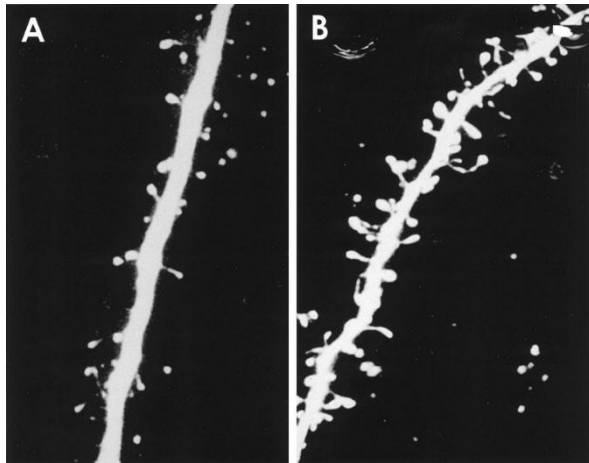
* Days' supply of the first prescription is expressed in days (1–40) in 1-day increments. If a patient had multiple prescriptions on the first day, the prescription with the longest days' supply was considered the first prescription.

FIGURE 2. One- and 3-year probabilities of continued opioid use among opioid-naïve patients, by number of prescriptions* in the first episode of opioid use — United States, 2006–2015



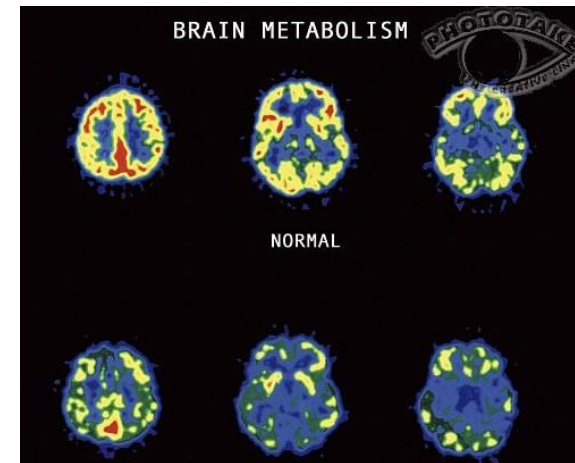
* Number of prescriptions is expressed as 1–15, in increments of one prescription.

Long-Term Opioid Exposure Can Lead to Neurodegenerative and Neurocognitive Disorders



Loss of Neural
Dendrites
(Prolonged Drug Exposure)

Normal
Dendrites



Loss of Brain Function Including the Frontal Lobe

Biological and Social Consequences of Ongoing Tolerance, Dependence and Addictive Behavior

- Prolonged exposure leading to downregulated epigenetic control of nerve cell structure and function (decreased neurotransmitters, receptors and structural proteins)
- The brain can no longer synthesize these molecules and requires exogenous source of these molecules until cells can resume synthesizing them
- Loss of self control and executive function, ie, judgement
- Inability to calculate risk versus benefit
- Possible severe, uncontrollable drug seeking to satisfy craving and avert withdrawal symptoms when opioids are rapidly discontinued
- Potential Loss of Family, Job and Shelter Leading to Possible Petty Theft, Larger Crimes, Arrest and Incarceration
- Possible Accidental overdose, cardiorespiratory arrest, anoxic-hypoxic brain injury and death

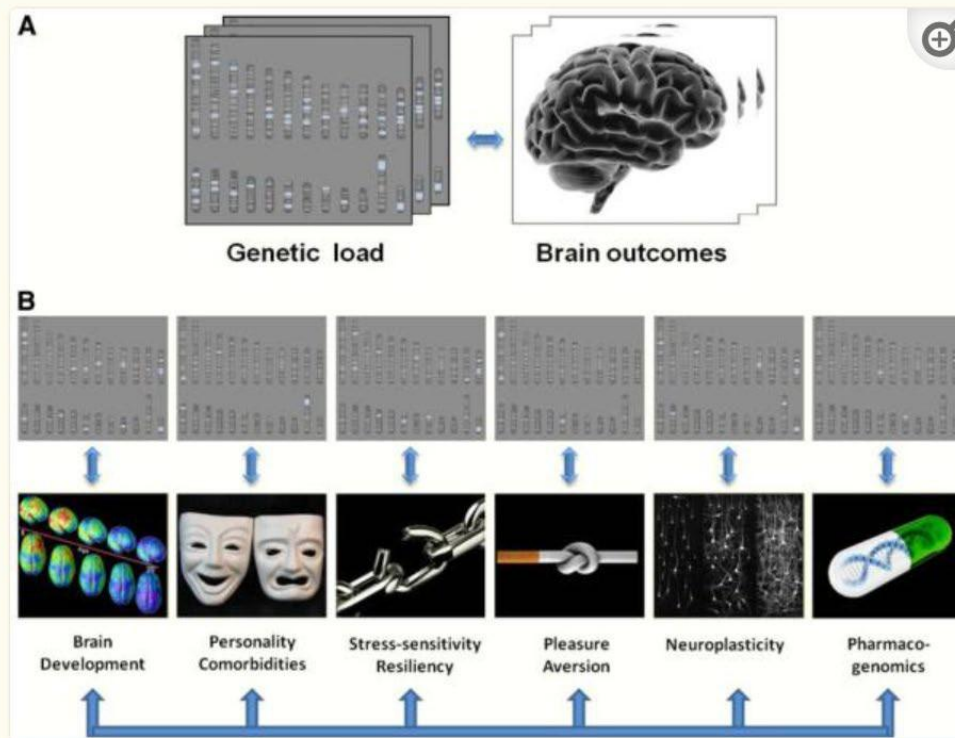
NOTE: A person's health is determined by their genes and the environment they live in. Epigenetics is the study of functional, and sometimes inherited, changes in the regulation of gene activity and expression that are not dependent on gene sequence.

Epigenetic Effects of Psychoactive Substances – Prolonged Exposure Can Lead to Genetic Changes in Brain Cell Function and Behavior

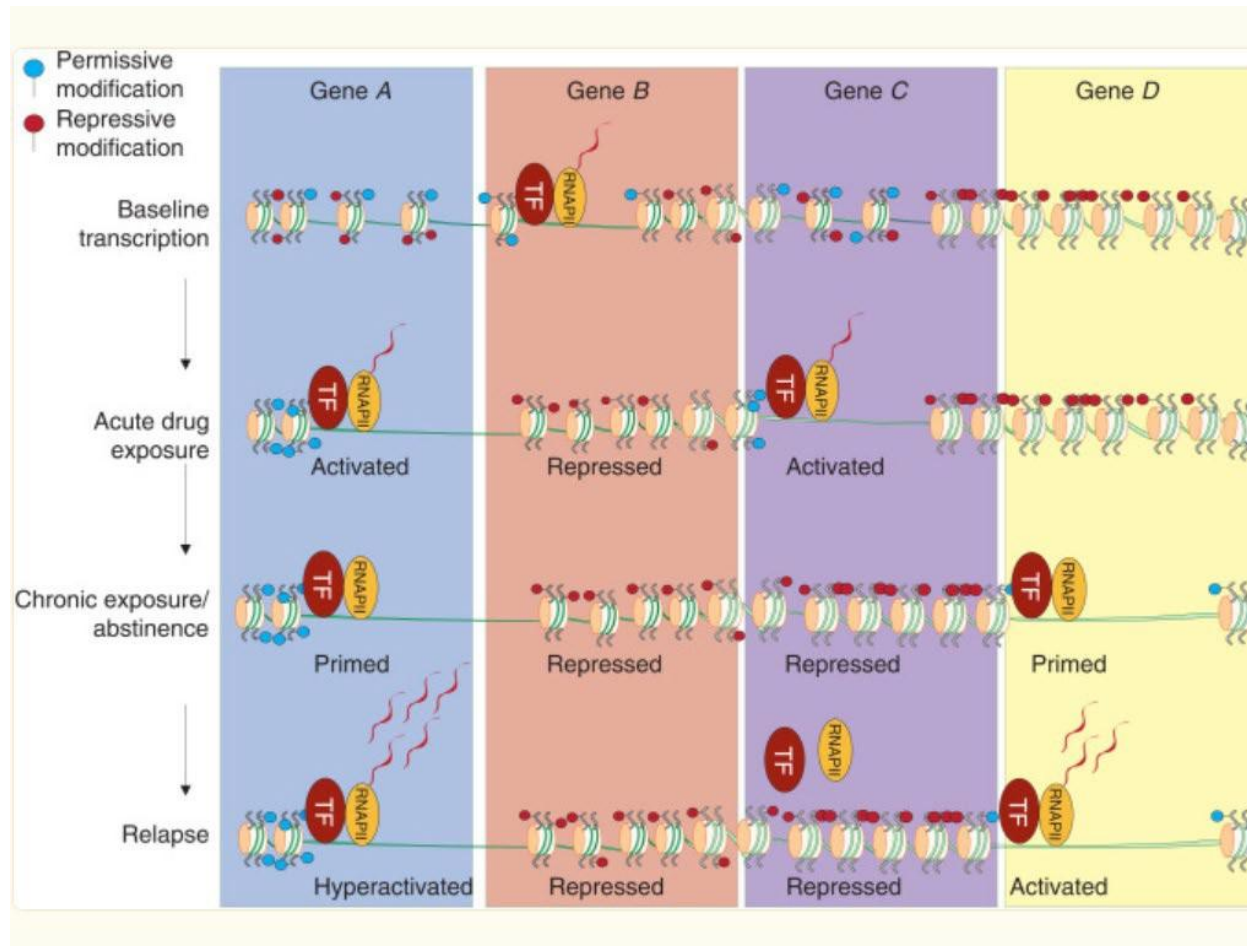
At least 3 different epigenetic mechanisms in chromatin have been identified: 1) DNA methylation, 2) histone modification, and 3) non-coding RNA (ncRNA)-associated gene silencing.

Substances that Demonstrate Epigenetic Effects

1. **Opioids**
2. **Benzodiazepines**
3. Amphetamines
4. Cocaine
5. **Methamphetamine**
6. Antipsychotics
7. Antidepressants
8. Cannabinoids
9. Kratom
10. Nicotine
11. Nitrous Oxide
12. Ketamine
13. Others



Epigenetic Effects of Psychoactive Substances – Prolonged Exposure Can Lead to Genetic and Subsequent Behavior Changes



Key: Transcription Factor (TF), RNA Polymerase II Transcription Complex (RNAPII)

- **Key Issue: Sudden Discontinuation of Psychoactive Substances May Lead to Both Acute and Chronic Withdrawal Symptoms And Deleterious Complications**
- **It Takes Time for Cellular Machinery to Start Back Up**
- **Solution: Go slow when tapering or use Medication Assisted Therapies (MAT) when available**

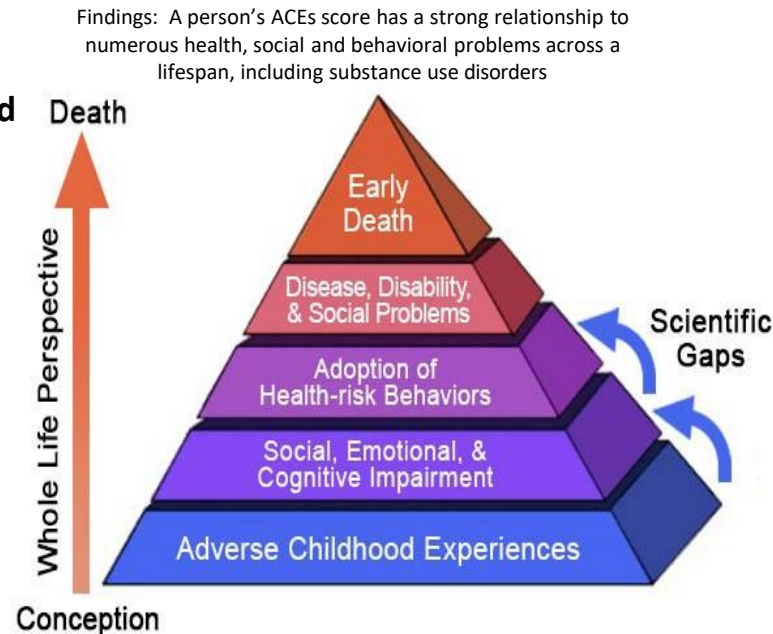
URL - [Epigenetics of Drug Addiction - PMC \(nih.gov\)](https://pubmed.ncbi.nlm.nih.gov/31111111/) (Accessed 9/9/2023)

Substance Misuse Can Promulgate From Generation to Generation with the Cyclical Nature of Post-traumatic Stress Triggers and Adverse Childhood Events (ACE's) That Lead to Aberrant Behaviors

Landmark study of 17,000 participants from 1995-1997 by the Centers for Disease Control in partnership with Kaiser Permanente

Aberrant Adult Behaviors Increase Risk for ACE's

- **Substance misuse within household**
- Physical abuse
- Sexual abuse
- Emotional abuse
- Physical neglect
- Emotional neglect
- Intimate partner violence
- Mother treated violently
- Household mental illness
- Parental separation or divorce
- Incarcerated household member



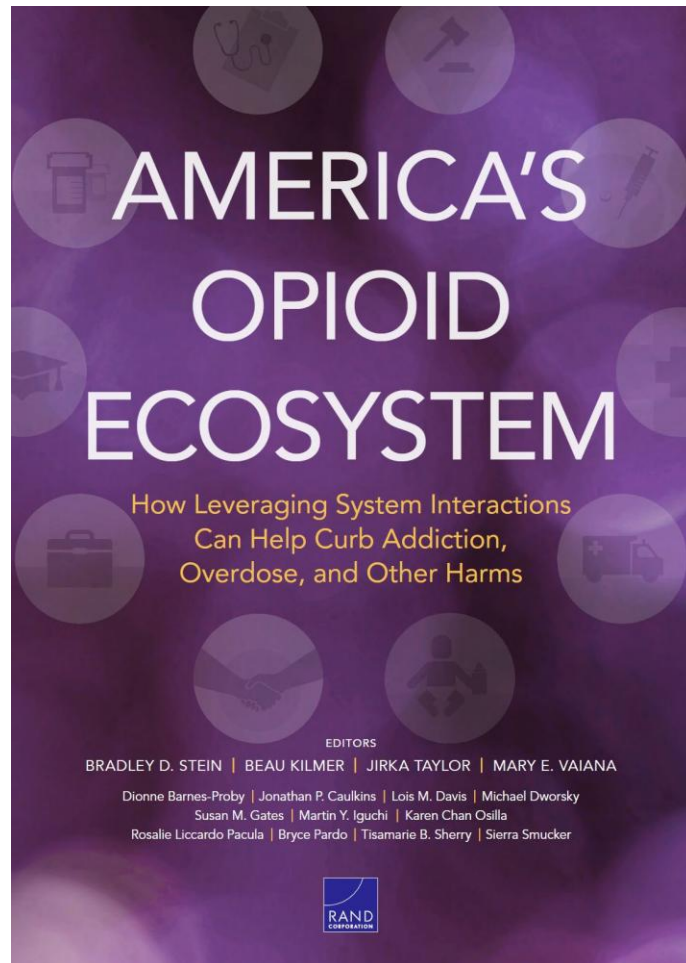
ACE's Increase Risk for Aberrant Adult Behaviors

- **Substance Misuse**
- Alcoholism and alcohol abuse
- Early Smoking/Chronic obstructive pulmonary disease (COPD)/Lung Cancer
- Ischemic heart disease (IHD)
- Diabetes/Obesity
- Liver disease
- Depression
- Health-related quality of life
- Risk for intimate partner violence
- Multiple sexual partners/STD's
- Suicide attempts
- Unintended pregnancies/fetal death

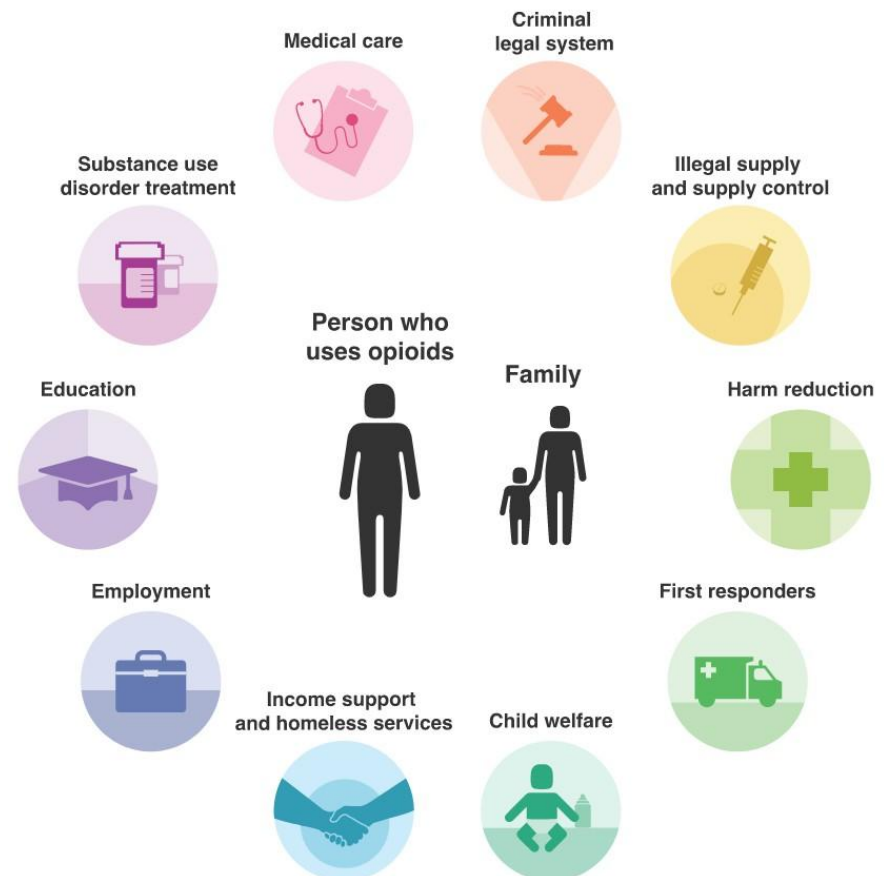
Key Principles of Pain Evaluation and Management

Work Within an Opioid Ecosystem Approach

How Leveraging System Interactions Can Help Curb Addiction, Overdose, and Other Harms



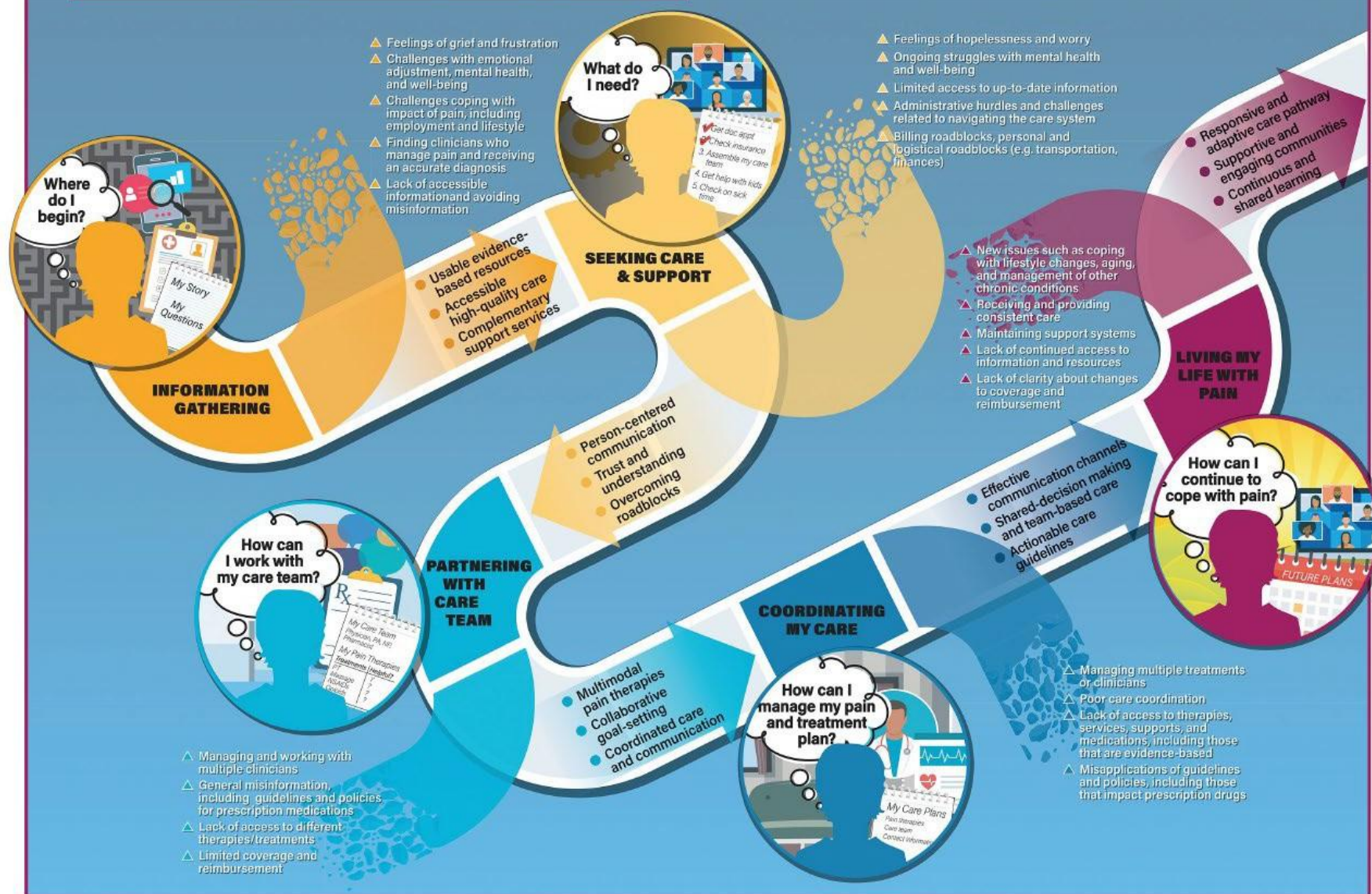
The Opioid Ecosystem



Be the Guide On the Patient's Journey to Adequate Care

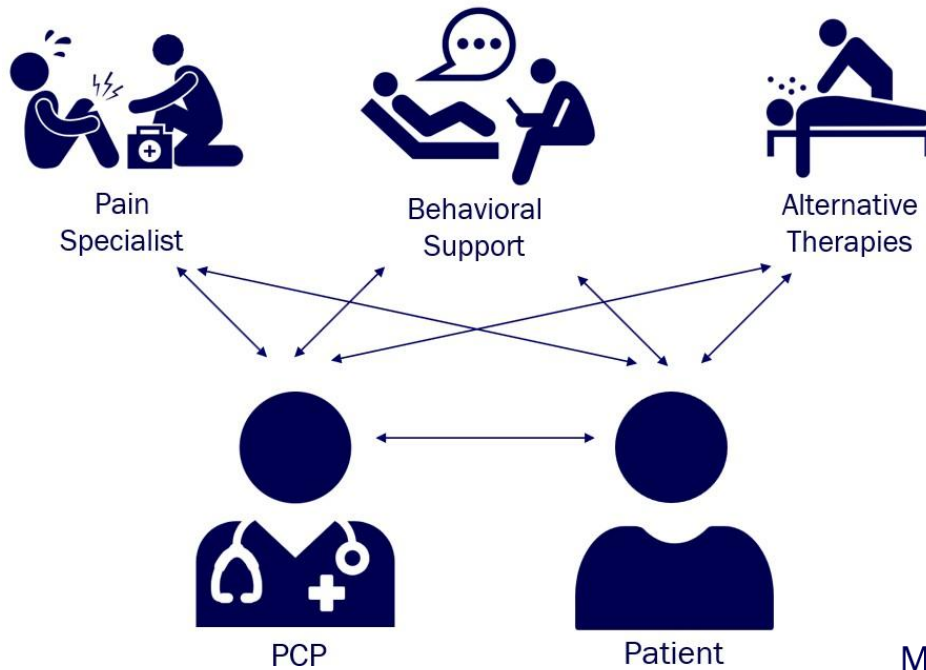
THE CHRONIC PAIN JOURNEY Opportunities for Action

This journey map visually describes the experiences of persons living with chronic, non-cancer pain and identifies key stages of the journey that have critical touchpoints with the health system. Each stage of the journey illustrates the patients' roles and responsibilities, challenges that deviate from the path to good pain management, and opportunities for action to support those with chronic pain. This map is available in an interactive version, which provides more insight into the chronic pain journey and links to tools and resources.



Coordinate Care With a Multimodality Treatment Plan

Coordinated Care



Medications

+

Behavioral Health Approaches

+

Restorative Therapies

+

Complementary and Integrative Health

+

Interventional Approaches

=

Effective
Multimodal
Treatment

Don't Ignore or Abandon Inherited "Legacy" Pain Patients Already on Opioids

Inherited Patients Taking Opioids for Chronic Pain — Considerations for Primary Care

Phillip O. Coffin, M.D., and Antje M. Barreveld, M.D.

Steps in Caring for Patients with Chronic Pain Who Have Received Long-Term Opioid Therapy from a Previous Clinician.

- 1. Review the case with the former clinician if possible.** Try to develop a treatment plan that slowly adjusts to your style of management while avoiding a radical divergence from the previous plan of care.
- 2. Consider providing a therapeutic bridge for the patient until a plan of care is determined, given the risks associated with stopping opioid therapy.** Abruptly tapering or stopping opioid therapy can be dangerous for multiple reasons. Opioids may be crucial for the patient's condition (e.g., sickle-cell disease), and the patient may be at risk for other harms when opioids are tapered or discontinued (see figure).
- 3. Develop a patient-centered care plan.** If a taper is needed, empower the patient to make decisions, including which medications to taper first and how fast. Successful tapers may take years.
- 4. Assess the patient for opioid use disorder and start discussing medication options right away.** Patients may find it challenging to accept an opioid use disorder diagnosis; give them time.
- 5. Document opioid stewardship and the rationale for the treatment plan.** Investigations into opioid prescribing are often based on insufficient documentation.

Identify and Treat the Pain Source (Starting with a Good History)

History and Physical

- Identify possible pain etiology
- Identify comorbidities that may affect treatment options
- Examine for allodynia and/or sensory changes in painful body part
- For patients who use opioids or patients with risk factors for opioid misuse or use disorder:
 - Check PDMP (aka, MAPS)
 - Screen for opioid risk

PDMP: prescription drug monitoring programs; ORT: Opioid Risk Tool; SOAPP: Screener and Opioid Assessment for Patients with Pain; COMM: Current Opioid Misuse Screen

URL - [Approach to the management of chronic non-cancer pain in adults – UpToDate](#) and [Pharmacologic management of chronic non-cancer pain in adults – UpToDate](#) (Accessed 4/14/2025)

Identify and Treat the Pain Source (Starting with a Good History)

Body diagram
• Useful for all patients
• For patients with multisite pain, screen for chronic widespread pain disorders with Widespread Pain Index and Symptom Severity Score
Pain history
OLD CARTS
• O nsset ("When did your pain start?")
• L ocation ("Where does it hurt?")
• D uration ("How long does your pain last?")
• C haracter ("How does your pain feel?", ie, aching, burning, shooting, tingling)
• A lleviating/ A ggravating ("What makes your pain better/worse?") and A ttribution ("What do you think is the cause?")
• R adiation ("Does this pain spread anywhere else?")
• T emporal pattern ("Does your pain vary over the course of a day?")
• S ymptoms associated ("How does your pain impact your physical function, your mood, your sleep?")

URL - [Approach to the management of chronic non-cancer pain in adults – UpToDate](#) and [Pharmacologic management of chronic non-cancer pain in adults – UpToDate](#) (Accessed 4/14/2025)

Identify and Treat the Pain Source (Starting with a Good History)

Patient Instructions: Please fill out both sides of this questionnaire as completely as possible.

1. HISTORY OF THE PAIN

YES
► **Do you believe the pain is due to:**

- ☐ a car accident
 - date: ____/____/____
 - time: ____:____ a.m. / p.m.
- ☐ a work-related injury
 - date: ____/____/____
 - time: ____:____ a.m. / p.m.
- ☐ physical trauma (examples: a fall, a fight, sports injury, etc.)

YES

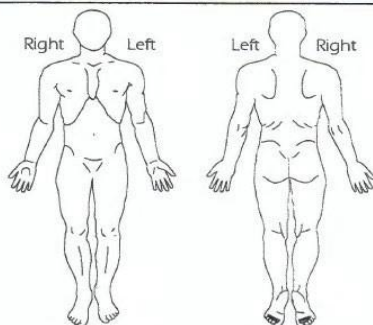
- type: _____
- date: ____/____/____
- time: ____:____ a.m. / p.m.
- other: _____
- date: ____/____/____
- time: ____:____ a.m. / p.m.
- ☐ unknown cause
- **How long have you had this pain?**
- ☐ hours — how many? _____

YES

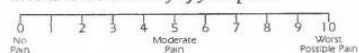
- ☐ days — how many? _____
- ☐ weeks — how many? _____
- ☐ months — how many? _____
- **Did the pain appear:**
- ☐ suddenly
- ☐ gradually
- **Right now, is the pain:**
- ☐ better
- ☐ worse
- ☐ unchanged

2. LOCATION AND INTENSITY OF PAIN

- **The most intense pain is located:** _____
- **On the diagrams to the right:**
 - mark an X or a series of X's where you feel pain.
 - shade the areas where you have numbness.
 - use arrows to point to where the pain radiates or travels to.
- **Has the pain changed in its location?**



- **On the scale below, mark an X where it best describes the intensity of your pain:**



3. DESCRIPTION OF THE PAIN

YES
► **Is the pain:**

- ☐ continuous (no relief)
- ☐ intermittent (periods of relief)
 - amount of time **pain** usually lasts: _____
 - amount of time **relief** usually lasts: _____
- ☐ other: _____

YES

► **Would you describe the pain as:**

- ☐ sharp, stabbing
- ☐ dull, aching
- ☐ throbbing
- ☐ burning like a hot poker
- ☐ steady, persistent
- ☐ waxing and waning
- ☐ feeling like a tight band
- ☐ easy to pinpoint
- ☐ difficult to pinpoint
- ☐ other: _____

YES

► **Does pain occur:**

- ☐ upon awakening
- ☐ in the morning
- ☐ in the afternoon
- ☐ in the evening
- ☐ 2-3 hours after falling asleep
- ☐ any time day or night
- ☐ only on weekends
- ☐ only at work
- ☐ only at home
- ☐ other: _____

4. DO YOU ALSO HAVE:

YES

- ☐ runny, bloodshot eyes
- ☐ blurred or double vision
- ☐ nasal congestion/runny nose
- ☐ high blood pressure
- ☐ muscle weakness
- ☐ numbness in arms or hands
- ☐ numbness in legs or feet
- ☐ felt a "sudden snap"
- ☐ felt a "tearing" sensation
- ☐ muscle aches and pains
- ☐ joint pains
- ☐ morning joint stiffness
- ☐ fever
- ☐ abdominal pain

YES

- ☐ nausea or vomiting
- ☐ diarrhea
- ☐ constipation
- ☐ bloody stools
- ☐ frequent or burning urination
- ☐ sudden loss of urine
- ☐ inability to urinate
- ☐ bloody urine
- ☐ weight gain or loss
- ☐ depression
- other: _____
- **Female patients only:**
- ☐ vaginal discharge
- ☐ heavy menstrual bleeding

YES

- ☐ bleeding between periods
- ☐ pelvic infection
- ☐ ovarian cysts
- ☐ uterine fibroids
- ☐ painful intercourse
- ☐ hot flashes
- other: _____
- **Male patients only:**
- ☐ prostate trouble
- ☐ restricted or painful urination
- ☐ interrupted sleep to urinate
- ☐ swollen or painful testicles
- ☐ penis discharge
- other: _____

5. PREVIOUS MEDICAL WORKUP INCLUDES:

YES

- ☐ seeing other doctors
- name(s): _____
- _____
- _____
- ☐ skull x-rays

YES

- ☐ neck x-rays
- ☐ lumbar and pelvis x-rays
- ☐ EEG/brain wave study
- ☐ CT scan
- ☐ brain scan

YES

- ☐ MRI
- ☐ Evoked potentials
- ☐ EMG
- ☐ blood work
- other: _____

6. DOES ANY BLOOD RELATIVE HAVE A HISTORY OF:

YES

- ☐ arthritis
- ☐ diabetes
- ☐ aortic aneurysm
- ☐ cerebral aneurysm
- ☐ migraines
- ☐ high blood pressure

YES

- ☐ stroke
- ☐ brain tumor
- ☐ spinal cord tumor
- ☐ poor leg circulation
- ☐ disk problems
- ☐ spinal stenosis

YES

- ☐ multiple sclerosis (MS)
- ☐ muscular dystrophy
- ☐ arteriovenous malformation
- ☐ Lou Gehrig's disease
- ☐ other neurological disease: _____

7. IS THE PAIN MADE WORSE OR BETTER BY:

FEELS WORSE

FEELS BETTER

- ☐ inactivity or sleep
- ☐ mild activity
- ☐ exercising or stretching
- ☐ heavy work
- ☐ climbing stairs
- ☐ walking
- ☐ standing
- ☐ sitting
- ☐ car riding
- ☐ straining at stool
- ☐ reclining or lying down
- ☐ lying on a firm bed or on the floor
- ☐ lying on one side
- ☐ getting up from bed
- ☐ bending forward

FEELS WORSE

FEELS BETTER

- ☐ lifting _____ lbs.
- ☐ carrying _____ lbs.
- ☐ stooping
- ☐ twisting
- ☐ reaching overhead
- ☐ coughing/sneezing
- ☐ sudden movement
- ☐ other movement: _____
- ☐ touching a certain point: _____
- ☐ sexual intercourse
- ☐ drinking alcohol
- ☐ emotional tension
- ☐ fatigue
- ☐ changes in weather

FEELS WORSE

FEELS BETTER

- ☐ menstrual periods
- ☐ massage
- ☐ heat
- ☐ trying to forget about it
- ☐ spinal manipulation
- ☐ spinal injections (blocks)
- ☐ physical therapy
- ☐ surgery
- other: _____
- other: _____
- Medications:**
- _____
- _____
- _____
- _____
- _____
- _____
- _____
- _____

Visual Pain Scales

A

Visual analog scale
Place a mark on the line below to indicate how bad your pain feels.

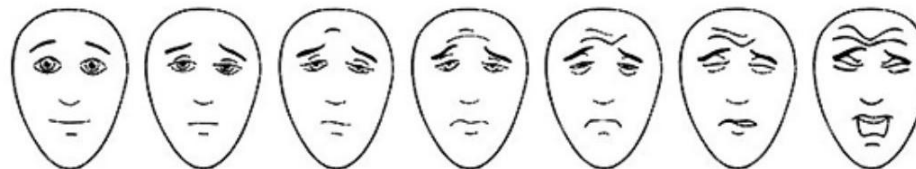
No pain  Worst pain imaginable

B

Numeric rating scale
What does your pain feel like?

0 1 2 3 4 5 6 7 8 9 10

None Mild Moderate Very bad Unbearable



Schematic representation of the faces pain scale, rated from 0 to 6 left to right.

URL - [Approach to the management of chronic non-cancer pain in adults – UpToDate](#) and [Pharmacologic management of chronic non-cancer pain in adults – UpToDate](#) (Accessed 4/14/2025)

Assess Mood and Risk for Sleep Apnea

Mood assessment				
PHQ-4				
Over the past 2 weeks, have you been bothered by these problems?	Not at all	Several days	More days than not	Nearly every day
• Feeling nervous, anxious, or on edge	0	1	2	3
• Not being able to stop or control worrying	0	1	2	3
• Feeling down, depressed, or hopeless	0	1	2	3
• Little interest or pleasure in doing things	0	1	2	3
• Scoring: Add total score • For score >5, screen for anxiety, depression, and post-traumatic stress, with GAD-7, PHQ-9, and PTSD-5				
Sleep assessment				
Sleep initiation and maintenance				
• Does pain interfere with falling asleep?				
• Does pain interfere with staying asleep?				
Screen for obstructive sleep apnea (OSA) – STOP-Bang^[2,3]				
Yes	No	Snore – Do you snore loudly (loud enough to be heard through closed doors, or your bed partner elbows you for snoring at night)?		
Yes	No	Tired – Do you often feel tired, fatigued, or sleepy during the day?		
Yes	No	Observed – Has anyone observed you stop breathing or choking/gasping during sleep?		
Yes	No	Pressure – Do you have or are you being treated for high blood pressure?		
Yes	No	Body mass index >35 kg/m ² ?		
Yes	No	Age older than 50 years?		
Yes	No	Neck size large (male: ≥17 inches, female: ≥16 inches)?		
Yes	No	Gender = male?		
• Scoring: Low risk of OSA: Yes to 0 to 2 questions • Intermediate risk of OSA: Yes to 3 to 4 questions • High risk of OSA: Yes to ≥5 questions				

1. Reproduced from: Kroenke K, Spitzer RL, Williams JB, Löwe B. An ultra-brief screening scale for anxiety and depression: The PHQ-4. *Psychosomatics* 2009; 50:613. Table used with the permission of Elsevier Inc. All rights reserved.

2. Chung F, Subramanyam R, Liao P, et al. High STOP-Bang score indicates a high probability of obstructive sleep apnoea. *Br J Anaesth* 2012; 108:768.

Assess for Opioid Use Disorder (DSM-5 Criteria)

A problematic pattern of opioid use leading to clinically significant impairment or distress, as manifested by at least 2 of the following, occurring within a 12-month period:

1. Opioids are often taken in larger amounts or over a longer period than was intended.
2. There is a persistent desire or unsuccessful efforts to cut down or control opioid use.
3. A great deal of time is spent in activities necessary to obtain, use, or recover from the effects of opioids.
4. Craving, or a strong desire or urge to use opioids.
5. Recurrent opioid use resulting in a failure to fulfill major role obligations at work, school, or home.
6. Continued opioid use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of opioids.
7. Important social, occupational, or recreational activities are given up or reduced because of opioid use.
8. Recurrent opioid use in situations in which it is physically hazardous.
9. Continued opioid use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance.
10. Tolerance, as defined by either of the following:
 - a. A need for markedly increased amounts of opioids to achieve intoxication or desired effect, or
 - b. Markedly diminished effect with continued use of the same amount of an opioid.

Note: This criterion is not considered to be met for those taking opioids solely under appropriate medical supervision.
11. Withdrawal, as manifested by either of the following:
 - a. The characteristic opioid withdrawal syndrome, or
 - b. Opioids (or a closely related) substance is taken to relieve or avoid withdrawal symptoms.

Note: This criterion is not considered to be met for those taking opioids solely under appropriate medical supervision.

Mild: Presence of 2-3 symptoms

Moderate: Presence of 4-5 symptoms

Severe: Presence of 6 or more symptoms

Assess for Psychiatric Co-morbidities

Assessing **psychiatric comorbidities** in individuals with **opioid use disorder (OUD)** is essential for effective diagnosis, treatment planning, and long-term recovery. Here's a structured approach based on clinical best practices ¹ ² ³:

1. Comprehensive Screening

- Begin with **broad screening tools** to identify potential mental health symptoms.
- Common tools include:
 - **Mental Health Screening Form III**
 - **Patient Health Questionnaire (PHQ-9)**
 - **Columbia-Suicide Severity Rating Scale**
 - **Drug Use Disorder Identification Test (DUDIT)**

These help flag issues like depression, anxiety, suicidal ideation, and substance misuse ¹.

2. Structured Clinical Interviews

- Use validated diagnostic interviews such as:
 - **Structured Clinical Interview for DSM-V (SCID-5)**
 - **Psychiatric Research Interview for Substance and Mental Disorders (PRISM)**
- These tools help differentiate between **primary psychiatric disorders** and **substance-induced conditions** ².

3. Differential Diagnosis

- Carefully distinguish between:
 - **Substance-induced symptoms** (e.g., opioid withdrawal causing anxiety or depression)
 - **Independent psychiatric disorders** (e.g., major depressive disorder, bipolar disorder)
- Reassess after **detoxification or stabilization**, as symptoms may evolve ¹.

Assess for Psychiatric Co-morbidities

4. Functional and Historical Assessment

- Evaluate:
 - Psychiatric history (including family history)
 - Substance use timeline
 - Periods of abstinence and relapse
 - Impact on functioning (work, relationships, legal issues)
- Include assessments of sleep, sexual function, and suicidality, which are often affected ².

5. Common Psychiatric Comorbidities in OUD

- Major depressive disorder (most prevalent)
- Generalized anxiety disorder
- Bipolar disorder
- Schizophrenia
- Antisocial personality disorder

Assess for Signs of Withdrawal (Using COWS)

PATIENT NAME:	DATE OF ASSESSMENT:
PATIENT DATE OF BIRTH:	MEDICAL RECORD NUMBER:

Clinical Opioid Withdrawal Score (COWS)

For each item, write in the number that best describes the patient's signs or symptom. Rate only the apparent relationship to opiate withdrawal. For example: If heart rate is increased because the patient was jogging just prior to assessment, the increased pulse rate would not add to the score.

Enter scores at time zero, 30 minutes after first dose, 2 hours after first dose, etc.	Time:	Time:	Time:	Time:
Resting Pulse Rate: Record beats per minute after patient is sitting or lying down for one minute • 0 - pulse rate 80 or below • 1 - pulse rate 81–100 • 2 - pulse rate 101–120 • 4 - pulse rate greater than 120				
Sweating: Over past ½ hour not accounted for by room temperature or activity • 0 - no chills or flushing • 1 - subjective chills or flushing • 2 - flushed or observable moistness on face • 3 - beads of sweat on brow or face • 4 - sweat streaming off face				
Restlessness: Observation during assessment • 0 - able to sit still • 1 - reports difficulty sitting still, but is able to do so • 3 - frequent shifting or extraneous movement of legs/arms • 5 - unable to sit still for more than a few seconds				
Pupil size • 0 - pupils pinned or normal size for light • 1 - pupils possibly larger than normal for light • 2 - pupils moderately dilated • 5 - pupils dilated that only rim of the iris is visible				
Bone or joint aches: If patient was having pain previously, only the additional component attributed to opiate withdrawal is scored • 0 - not present • 1 - mild/diffuse discomfort • 2 - patient reports severe diffuse aching of joints/muscles • 4 - patient is rubbing joints or muscles and is unable to sit still because of discomfort				
Runny nose or tearing: Not accounted for by cold symptoms or allergy • 0 - none present • 1 - nasal stuffiness or unusually moist eyes • 2 - nose running or tearing • 4 - nose constantly running or tears streaming down cheeks				
GI upset: Over last ½ hour • 0 - no GI symptoms • 1 - stomach cramps • 2 - nausea or loose stool • 3 - vomiting or diarrhea • 5 - multiple episodes of diarrhea or vomiting				
Tremor: Observation of outstretched hands • 0 - no tremor • 1 - tremor can be felt, but not observed • 2 - slight tremor observable • 4 - gross tremor or muscle twitching				
Yawning: Observation during assessment • 0 - no yawning • 1 - yawning once or twice during assessment • 2 - yawning three or more times during assessment • 4 - yawning several times/minute				
Anxiety or irritability • 0 - none • 1 - patient reports increasing irritability or anxiousness • 2 - patient obviously irritable or anxious • 4 - patient so irritable or anxious that participation in the assessment is difficult				
Gooseflesh skin • 0 - skin is smooth • 3 - piloerection of skin can be felt or hairs standing up on arms • 5 - prominent piloerection				
5—12 = mild; 13—24 = moderate; 25—36 = moderately severe; > 36 = severe withdrawal				
TOTAL				
OBSERVER INITIALS				

Assess Risk for Overdose (RIOSORD)

Risk Index for Overdose or Serious Opioid-Induced Respiratory Depression (RIOSORD)		
Question	Points for Positive Response	Actual Response
In the past 6 mo, has the patient had a health care visit (outpatient, inpatient, or emergency department) involving any of the following health conditions		
Substance use disorder (abuse or dependence), including alcohol, amphetamines, antidepressants, cannabis, cocaine, hallucinogens, opioids, and sedatives	25	
Bipolar disorder or schizophrenia	10	
Stroke or other cerebrovascular disease	9	
Kidney disease with clinically significant renal impairment	8	
Heart failure	7	
Nonmalignant pancreatic disease (e.g., acute or chronic pancreatitis)	7	
Chronic pulmonary disease (e.g., emphysema, chronic bronchitis, asthma, pneumoconiosis, asbestosis)	5	
Recurrent headache (e.g., migraine)	5	
Does the patient use any of the following substances?		
Fentanyl	13	
Morphine	11	
Methadone	10	
Hydromorphone	7	
Does the patient use an extended-release or long-acting formulation of any prescription opioid?	5	
Prescription benzodiazepine (e.g., diazepam, alprazolam)	9	
Prescription antidepressant (e.g., fluoxetine, citalopram, venlafaxine, amitriptyline)	8	
Is the patient's current maximum prescribed daily morphine- equivalent dose ≥ 100 mg for all opioids used on a regular basis?	7	
Total possible score	146	

Risk Classes and Predicted Probability of Serious Opioid-Induced Respiratory Depression during the Next 6 Months.			
Risk Class	RIOSORD Score	Average Predicted Probability (Percent)	Actual Observed Incidence (Percent)
1	<5	1.9	2.1
2	5–7	4.8	5.4
3	8–9	6.8	6.3
4	10–17	15.1	14.2
5	18–25	29.8	32.2
6	26–41	55.1	58.8
7	≥ 42	83.4	82.4

Adapted from: Zedler B, Xie L, Wang L et al. Development of a Risk Index for Serious Prescription Opioid-Induced Respiratory Depression or Overdose in Veterans' Health Administration Patients. Pain Medicine. Jun 2015. 16;1566-1579.

Confirm Appropriateness for Prescribing Opioids (DIRE Score)

Name: _____ DOB ____/____/____

DIRE Score: Patient Selection for Chronic Opioid Analgesia

For each factor, rate the patient's score from 1-3 based on the explanations in the right-hand column

SCORE	FACTOR	EXPLANATION
	DIAGNOSIS	1 = Benign chronic condition with minimal objective findings or no definite medical diagnosis. Examples: fibromyalgia, migraine headaches, non-specific back pain. 2 = Slowly progressive condition concordant with moderate pain, or fixed condition with moderate objective findings. Examples: failed back surgery syndrome, back pain with moderate degenerative changes, neuropathic pain. 3 = Advanced condition concordant with severe pain with objective findings. Examples: severe ischemic vascular disease, advanced neuropathy, severe spinal stenosis.
	INTRACTABILITY	1 = Few therapies have been tried and the patient takes a passive role in his/her pain management process. 2 = Most customary treatments have been tried but the patient is not fully engaged in the pain management process, or barriers prevent (insurance, transportation, medical illness). 3 = Patient fully engaged in a spectrum of appropriate treatments but with inadequate response.

RISK (R = Total of P+C+R+S below)

	Psychological	1 = Serious personality dysfunction or mental illness interfering with care. Example: personality disorder, severe affective disorder, significant personality issues. 2 = Personality or mental health interferes moderately. Example: depression or anxiety disorder. 3 = Good communication with clinic. No significant personality dysfunction or mental illness.
	Chemical Health	1 = Active or very recent use of illicit drugs, excessive alcohol, or prescription drug abuse. 2 = Chemical coper (uses medications to cope with stress) or history of chemical dependence (CD) in remission. 3 = No CD history. Not drug-focused or chemically reliant.
	Reliability	1 = History of numerous problems: medication misuse, missed appointments, rarely follows through. 2 = Occasional difficulties with compliance, but generally reliable. 3 = Highly reliable patient with meds, appointments & treatment.
	Social Support	1 = Life in chaos. Little family support and few close relationships. Loss of most normal life roles. 2 = Reduction in some relationships and life roles. 3 = Supportive family/close relationships. Involved in work or school and no social isolation.
	EFFICACY SCORE	1 = Poor function or minimal pain relief despite moderate to high doses. 2 = Moderate benefit with function improved in several ways (or insufficient info - hasn't tried opioid yet or very low doses or too short of a trial). 3 = Good improvement in pain and function and quality of life with stable doses over time.

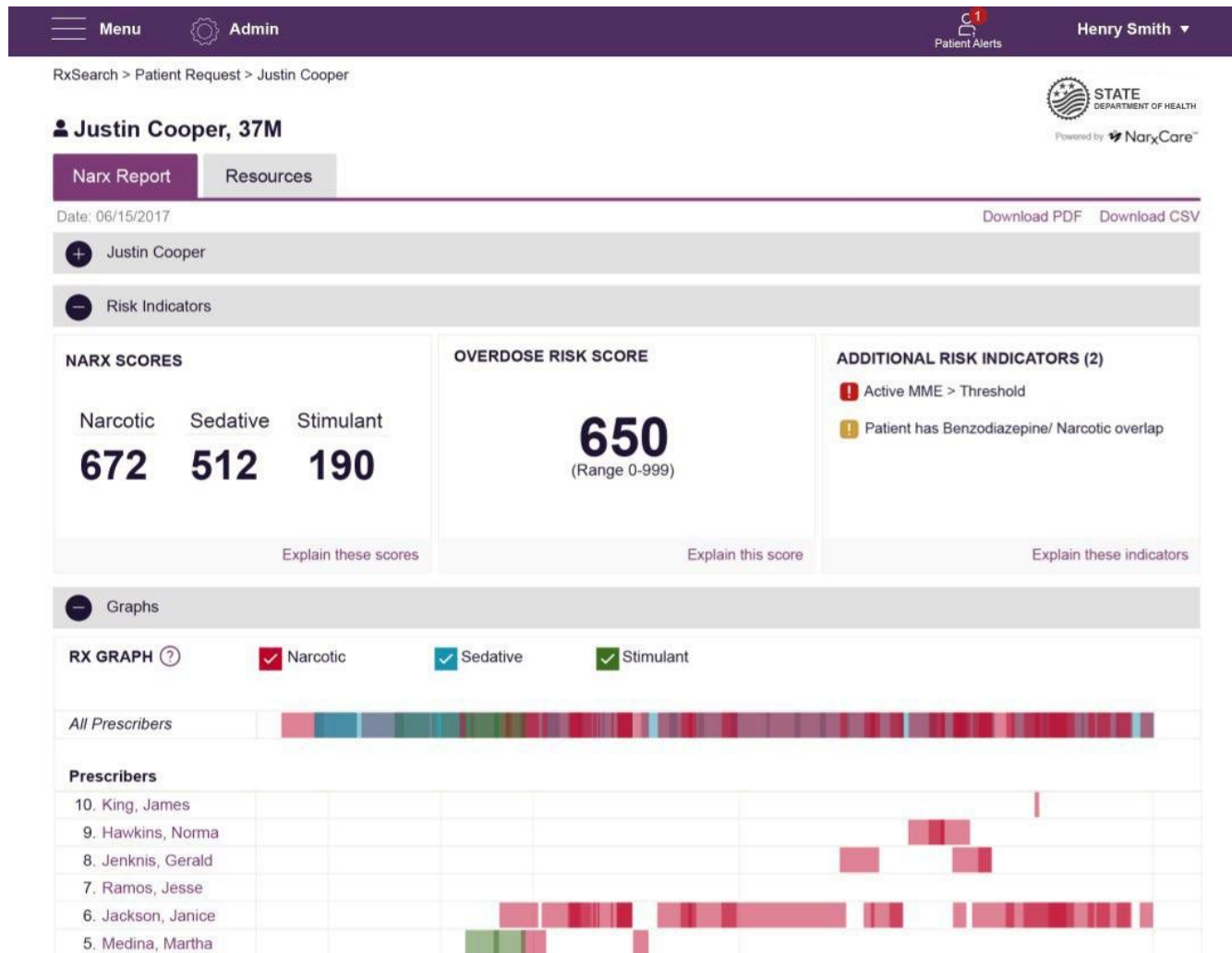
Score 7-13: Not a suitable candidate for long-term opioid analgesia

Score 14-21: May be a good candidate for long-term opioid analgesia

_____ Total score= D + I + R + E

URL - [doi:10.1016/j.jpain.2006.03.001](https://doi.org/10.1016/j.jpain.2006.03.001) (Accessed 4/14/2025)

Check the Michigan Automated Prescription Service (MAPS) to Assess for Potential Misuse, Abuse, Diversion, or Overdose Risk



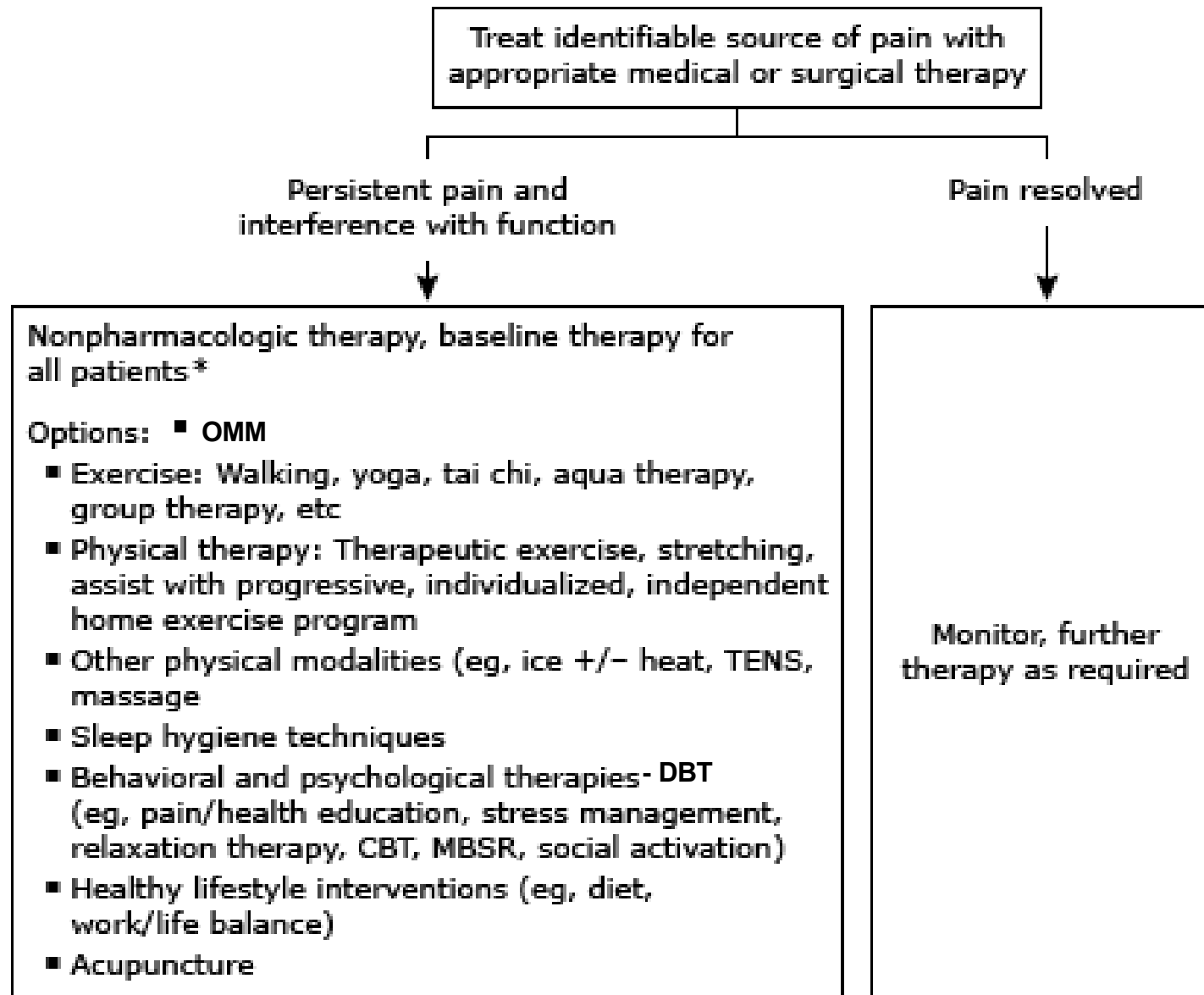
Check for Anticipated and Unanticipated Medications and Other Substances

- If you don't check, you will have no idea.
 - Qualitative - in Office
 - Test either positive or negative
 - Immunoassay
 - Quantitative (in Lab)
 - Test measures concentration of drug
- GC/MS or LC/MS

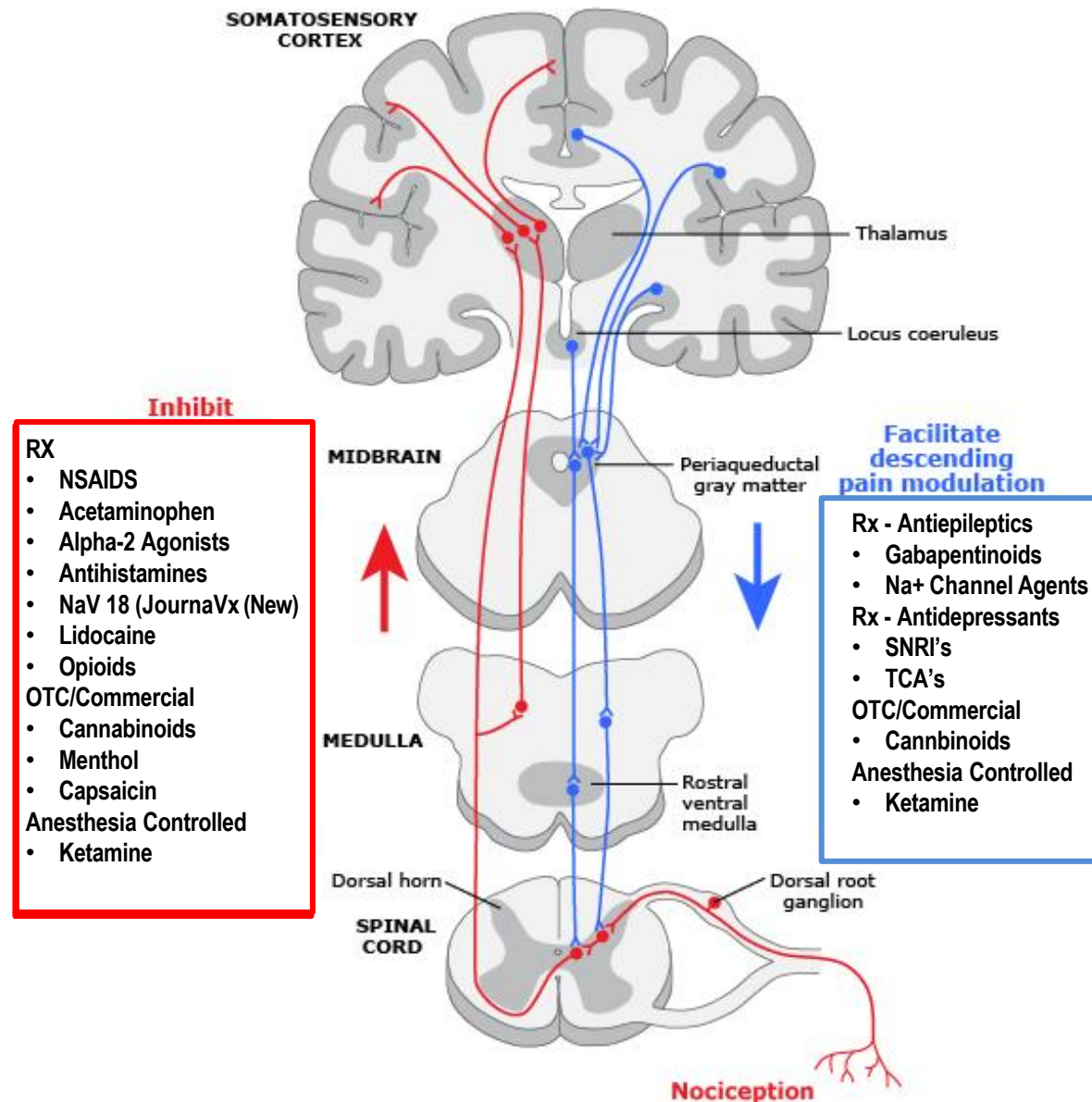
Can check for all psychoactive substances prescribed and unprescribed

 - Matrix - Urine, Saliva, Blood, Hair, Exhaled Air (breathalyzer), etc.
- A white plastic cup with a blue lid. The label reads "CLIA Waived Drug Test Cup" and "Authorized Personnel Only Remove Label for Results". There is a red hand icon on the label.
- A small, rectangular, blue and white test strip with a white cap, used for oral fluid testing.
- A white plastic container holding a test strip. The strip has multiple colored lines (green, yellow, red, blue, orange, purple, pink, brown, black) and a white cap. Below the container is a small white plastic cup.
- A black handheld breathalyzer device with a digital display showing "0.020". It has buttons for "START" and "MODE" and the "BACtrack" logo at the bottom.

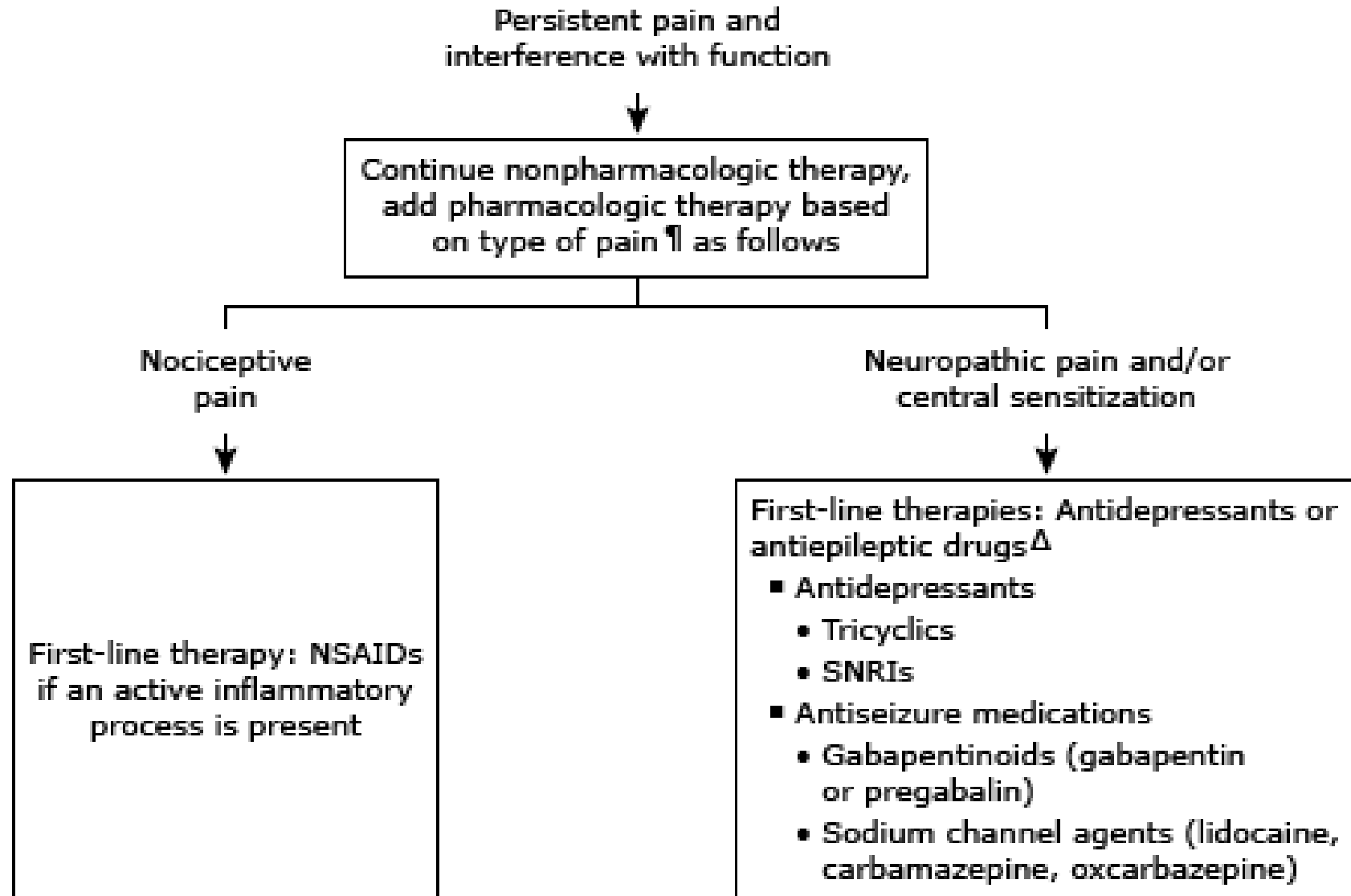
Multimodal Approaches to Pain Management



Pharmacological Approaches to Pain Management



Pharmacological Approaches to Pain Management



Pharmacological Approaches to Pain Management



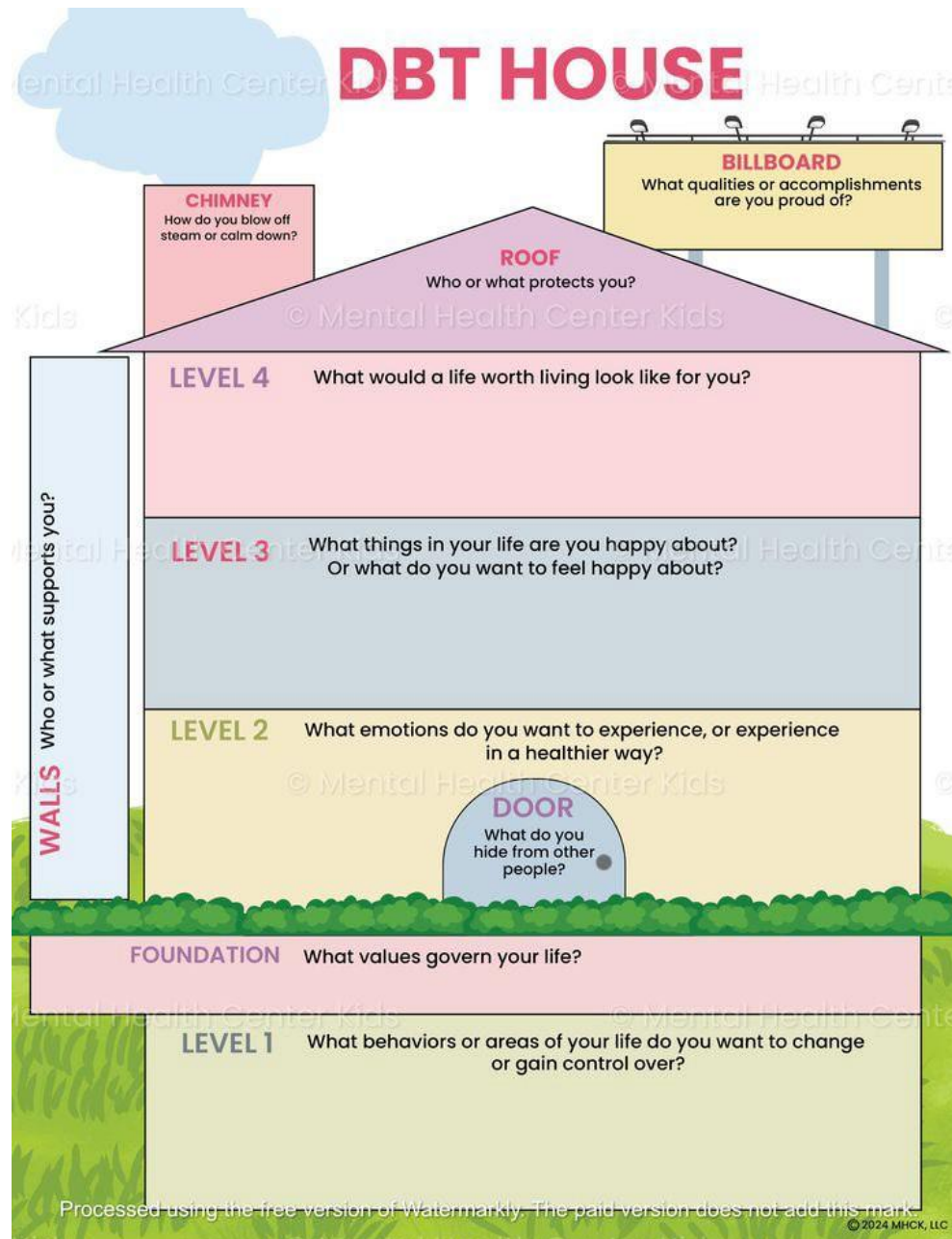
Second- and third-line therapies:

- Acetaminophen
- Topical agents (NSAIDs, lidocaine, capsaicin)
- Opioids **ONLY** when other multimodal therapy is insufficient and:
 - Pain is moderate to severe
 - Function and quality of life are improved
 - Benefits outweigh risks of opioid therapy
- Referral for interventional therapy or neuromodulation

Start the Journey and Utilize Dialectical Behavioral Therapy (DBT) at Routine Visits



Help the Patient Build Their DBT House



Example of a Multi-Modal Chronic Pain Management Plan

Name	
DOB	

Visit		Visit 1	Visit 2	Visit 3	Visit 4	Visit 5
Date						

Disease/Conditions Causing Pain

1						
2						
3						
4						
5						
6						

Pain Levels

Worst Pain Level:						
Current Pain Level:						
Achievable Pain Level:						

Pain Management Goals

1						
2						
3						
4						
5						
6						

Pain Medication

1						
2						
3						
4						
5						
6						

Name	
DOB	

Visit		Visit 1	Visit 2	Visit 3	Visit 4	Visit 5
Date						

Specialty Consultation

1	General Surgery					
2	Orthopedic Surgery					
3	Interventional Pain Medicine					
4	Physical Medicine & Rehabilitation					
5	Manual Medicine (OMM/PT/Chiropractic)					
6	Neurology					
7	Sleep Medicine					
8	Accupuncture					
9	Hypnosis/Biofeedback					
10	Other: _____					

Self Care

1	Ice/Heat Therapy					
2	Exercise					
3	Substance Management					
	Caffeine					
	NicotineTobacco					
	Marijuana					
	Vaping					
	Kratom					
	Other: _____					
3	Nutrition					
4	Weight Management					
5	Sleep Hygiene					

Obtain Meaningful Informed Consent (Sample)

Controlled Medication Management Agreement and Informed Consent

Patient Name: _____

DOB: ____/____/____

Provider: _____

Facility: _____

Date: ____/____/____

#	Controlled Medication	Dose	Quantity	Directions	New Start	Refill	Switch
1							
2							
3							
4							
5							
6							
7							
8							

The terms "I", "my" and "you" in this document refer to the patient. Where the patient is under age 18, or an adult for whom a guardian is signing the Agreement, the terms "I", "my" and "you" refer to the patient and to his or her parent or guardian.

This document lists commitments I will make before beginning one or more of these medications or continue them, if already being taken. I have received and have read the following patient education:

- ☐ Opioids (*Opioid Medication for Chronic Pain fact sheet*)
- ☐ Stimulants (*Stimulant Medicine for ADHD fact sheet*)
- ☐ Benzodiazepines, Sedatives, Hypnotics and Sleeping Pills (*Sedatives and Sleeping Pills: Understanding the Risks fact sheets*)
- ☐ Gabapentin (*Gabapentin fact sheet*)
- ☐ Others (*Describe*) _____

1. I will work with my provider(s) in a collaborative manner to develop a balanced treatment plan that considers both benefits and risks to any given treatment.
2. I have discussed the medication(s) and had the chance to ask questions about the medications being prescribed with my provider(s).
 - a. all my questions have been answered in a way I understand.
3. I will engage in all activities to continue my ongoing therapy
4. I acknowledge that I might develop tolerance, dependence, addiction or other serious and potentially life-threatening conditions when taken improperly, either individually or in combination with other controlled medications or addictive substances.
5. I will refrain from taking actions that could endanger myself or the public.
6. I understand that insurers and regulatory authorities have the right to review my records when taking controlled substances
 - a. I understand that my medical and insurance claims records may be reviewed by an independent review team to evaluate my ongoing opioid and controlled substance usage.
 - b. the Michigan Department of Licensing and Regulatory Affairs (LARA) maintains and makes available a database of my controlled drug prescriptions to all medical providers providing my care.

7. I acknowledge that unwillingness or inability to work collaboratively with my provider(s) and adhere to this agreement may result in discharge from the provider's care
 - a. Any action on my part that may be threatening to safety of your provider(s) and their staff may be subject to subsequent action
8. I acknowledge that my provider and I have reviewed this document.
9. I acknowledge the potential benefits and risks of controlled substances prescribed by my provider along with the responsibility of properly managing my medication as stated above.
10. For OPIOID USE ONLY, I understand that there are inherent risks for using opioids that are associated with increasing doses and when used in combination with other drugs. Naloxone, also known as Narcan, is an antidote that can reverse overdose of opioids by blocking their sedating effects that may slow down breathing and lead to cardiopulmonary arrest. Narcan can be helpful to reverse over sedation and may be lifesaving when too much opioid is taken by myself or others. I acknowledge that Naloxone has been offered by prescription from my provider and is also available by request at participating pharmacies under standing orders of the Chief Medical Executive for the State of Michigan. Additional information regarding Naloxone and its proper use can be found at <https://www.michigan.gov/opioids/0,9238,7-377-480835--00.html>.

My signature confirms that I have had an opportunity to ask questions about this agreement, and that I understand and agree to all the statements above. I have been given a copy of this Agreement and agree to keep the copy for my future reference.

Patient or Legal Guardian:

X _____

Date: _____

(*Patients aged 12 to 17 may sign in addition to the parent or guardian)

Patient (aged 12-17)

X _____

Date: _____

Provider:

X _____

Date: _____

Document the Need for Chronic Pain Management and Palliative Care

Chronic Pain Management & Palliative Care Certification Form

Patient Information

Patient Name:		Telephone #:	
Date of Birth:		Fax #:	
Address:		Cellphone #:	
City, STATE, Zip:		Email:	

Primary Diagnoses (relating to persistent intractable pain)

Certification Criteria

	Palliative Care Criteria
☐ YES ☐ NO	The underlying disease is protracted with an unpredictable outcome and/or is incurable
☐ YES ☐ NO	Pain is persistent and intractable despite using non-opioid therapies that have been maximized and reached maximal therapeutic benefit
☐ YES ☐ NO	Symptomatic pain treatment has a good probability to improve functionality and existing quality of life
☐ YES ☐ NO	Anticipated benefit exceeds potential risk for overdose and/or diversion
☐ YES ☐ NO	Pain management is a component of all aspects of palliative care including management of other treatable conditions and symptoms

Certification

I have performed a comprehensive and detailed examination for _____ and have developed a collaborative palliative care plan.

I have determined that this person has intractable pain and satisfied the criteria for Palliative Care Status. Support documentation is included in the patient's medical record with this certification.

I, hereby, certify this pain management and palliative care plan is medically necessary. This plan will be recertified annually or sooner if there is substantive change beforehand.

PROVIDER

Signature of Provider: _____ Date: ____/____/____

Provider Name Printed: _____

PATIENT

By signing below, and I hereby agree to all terms and conditions set forth under this certification document and accompanying treatment agreement.

Signature of Patient: _____ Date: ____/____/____

Patient Name Printed: _____

Implement a Taper Plan (with or without buprenorphine) Whenever Practicable

Name: _____ DOB ____/____/____

Opioid and/or Benzodiazepine Tapering Plan Agreement

The purpose of this document is to develop a specific tapering plan with a timeline for discontinuation or reaching a taper "target dose".

We will work with you to develop a plan that is safe, effective and will minimize any symptoms that may be associated with tapering. Enclosed is a sample of a tapering schedule that can be used to help keep everyone apprised.

Taper Schedule

Visit	Date	Medication	Taper Frequency (# weeks)	Single Dose	Dose Frequency	Total Daily Dose	Total Dose/Day	Quantities Needed
1								
2								
3								
4								
5								
6								
7								
8								
9								
10								
11								
12								
13								
14								
15								

We will allow for gradual dose reductions and will reassess regularly and adjust accordingly.

Sign and Date below:

Patient or Patient's Representative (required):

Date: _____

Mature Minor Patient:

Date: _____

Physician Signature or Provider:

Date: _____

Provide Tools to Reverse Opioid Overdose Using Narcan or Opvee With Proper Stocking and Training at the Overdose Site



- Narcan (naloxone) and Opvee (nalmefene) are both opioid overdose reversal medications, but they have key differences in duration, potency, and availability.
 - Narcan is more widely available and works well for most opioid overdoses.
- Opvee may be more effective for high-potency synthetic opioids but can cause longer-lasting withdrawal symptoms.
 - Opvee is not generic and is more expensive

Feature	Narcan (Naloxone)	Opvee (Nalmefene)
Mechanism	Blocks opioid receptors	Blocks opioid receptors
Onset of Action	3–17 minutes	2.5–5 minutes
Duration	1.3–2.7 hours	Up to 11 hours
Potency	Effective for most opioid overdoses	More effective for synthetic opioids like fentanyl
Availability	Over-the-counter	Prescription-only
Withdrawal Risk	Short-lived withdrawal symptoms	Prolonged withdrawal symptoms

Orient Patients to Dispose of Expired or Unused Medications to Avoid Pilfering and Accidental Overdose





Advances in Pain Management to Reduce Opioid Risk

Leverage Advances in Perioperative Anesthesia and Interventional Pain Management

- **Local Intraoperative Techniques Before Wound Closure – Combination Injections**
 - Ropivacaine – longest acting local anesthetic to reduce pain that lasts for 3-5 days post- op
 - Ketolorac (aka Toradol) – to reduce inflammation
 - Epinephrine – to reduce inflammation- induced edema
- **Pain Management Tools – Spinal Stimulators and Pain Pumps**
- **Interventional Pain Management – Facet and Epidural Blocks**
 - Facet and Epidural Blocks
 - Ropivacaine or Bupivacaine
 - Steroids



Consider Using Buprenorphine for Pain Management as Well As Opioid Use Disorder

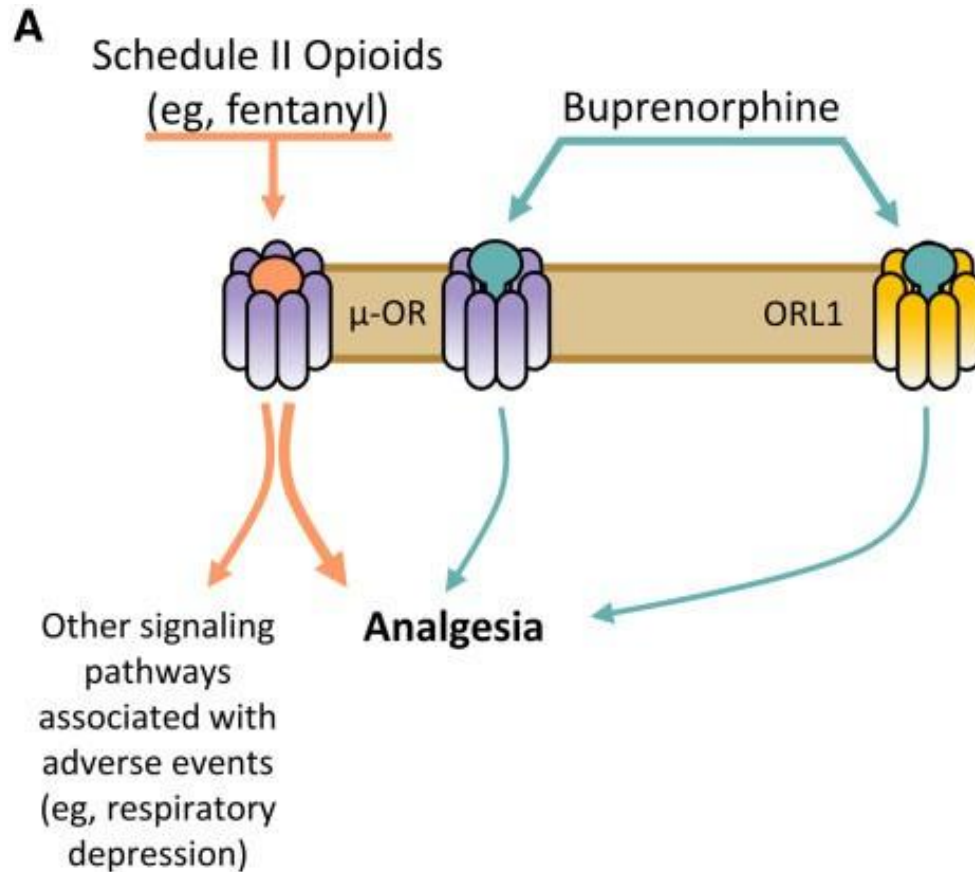
- **Effective analgesia – limits tolerance and dependence**
- **Relative ceiling on respiratory depression**
 - Fatal overdose limited but possible with other non-opioid respiratory depressants
- **Less dysphoria, sedation, constipation**
- **Limited tolerance**
- **Limited abuse potential and withdrawal**
- **Reduced endocrinopathies**
- **Convenient dosing schedule**

- **It's better than the rest.**

Dalal S, Chitneni A, Berger AA, et al. Buprenorphine for Chronic Pain: A Safer Alternative to Traditional Opioids. *Health Psychology Research*. 2021;9(1).

[healthpsychologyresearch_2021_9_1_27241.pdf](https://doi.org/10.1037/1930-9217.9.1.27241)

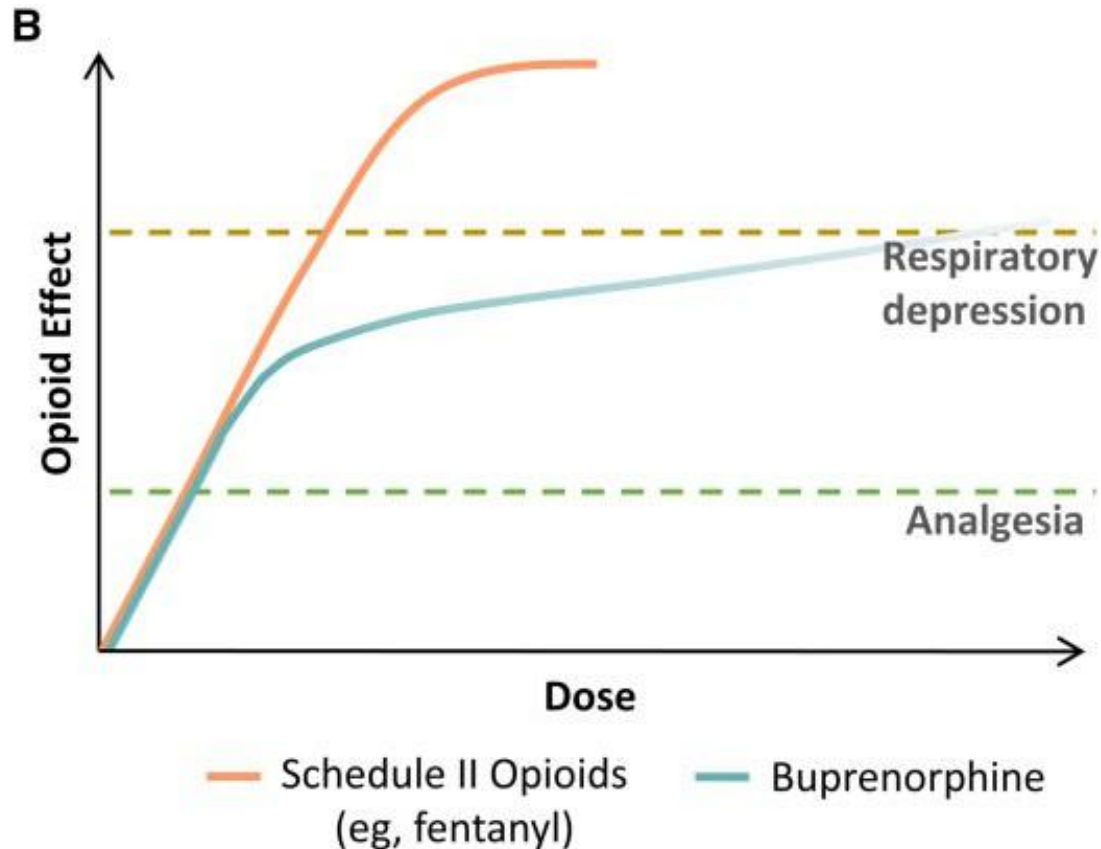
Pharmacology – Efficacy



- **Acts on the mu-opioid receptor, like other opioids**
- **Also acts on the opioid receptor-like 1 (ORL1) receptor**
- **Produces equally-efficacious analgesia**

(Raffa 2014)

Pharmacology – Side Effects



- **Antagonist at the kappa- and delta-opioid receptors**
- **Limited respiratory depression; overdose on buprenorphine alone is not fatal in adults**

Caution: Synergistic depression with benzodiazepines, z-drugs, alcohol, muscle relaxants, gabapentinoids, TCAs

When to consider JournaVx (suzetrigine) for Acute Pain

HOW JOURNAVX WORKS



A first-in-class nonopioid, JOURNAVX is a sodium channel blocker highly selective for $\text{Na}_v1.8$ ^{1,2}

By inhibiting $\text{Na}_v1.8$, JOURNAVX blocks sodium ions from entering pain-sensing neurons, disrupting the initiation and propagation of action potentials and **reducing pain signal transmission** from the PNS to the CNS^{1,2}



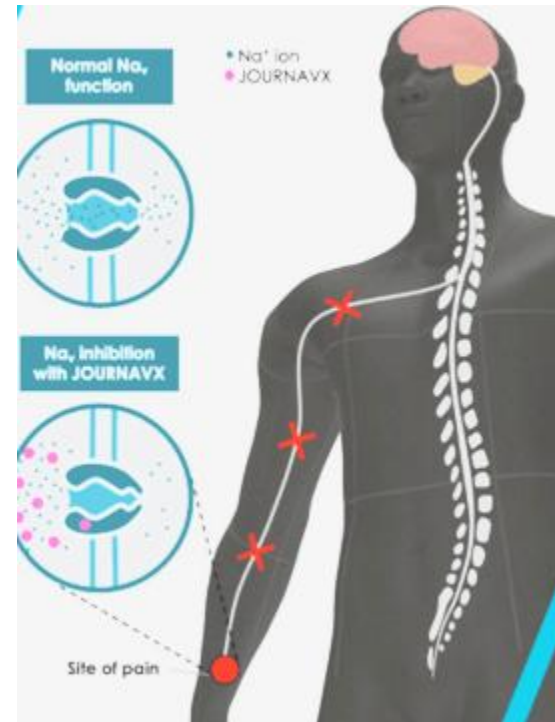
Because JOURNAVX is a **highly selective** inhibitor of $\text{Na}_v1.8$ ($\geq 31,000\times$ more selective of $\text{Na}_v1.8$ than all other Na_v subtypes as measured *in vitro*), it inhibits pain signal transmission to the spinal cord and brain^{1,2}



JOURNAVX **does not interact with μ receptors**, which are associated with addiction.^{2,8} **There is no evidence that JOURNAVX has addictive potential** based on available data, including the MOA, preclinical data, and clinical adverse event data²



JOURNAVX is **not a controlled substance**⁹

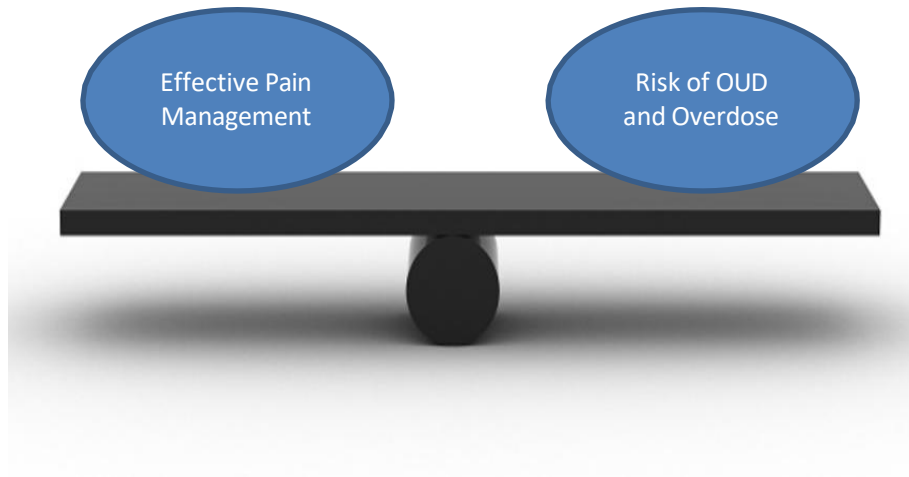


- First non-opioid pain medication in >25 years
- Stops pain in peripheral tissues at the source
- Dosing -- start with 2 tablets one day 1, then take 1 tablet daily days 2-14

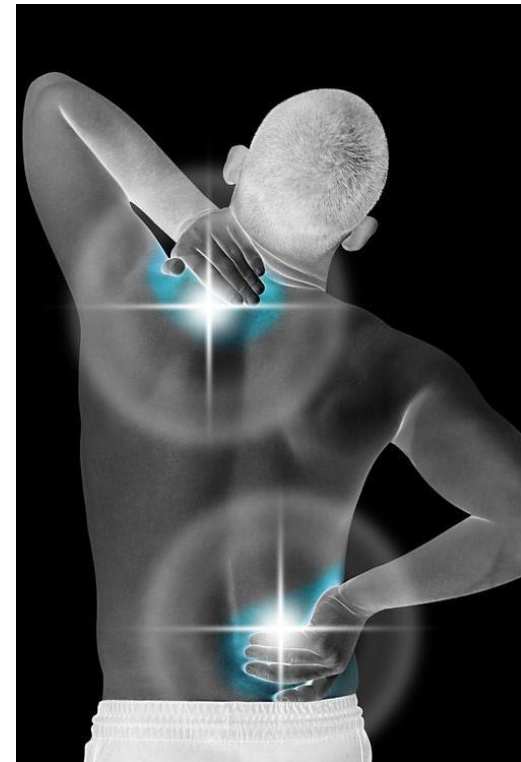
Receptor Subtypes and Inflammatory Targets Being Studied for Non-Opioid Drug Development

Drug Targets/Mechanism of Action	Examples
Nav1.7, Nav1.8 inhibitors	tetrodotoxin, saxitoxin, synthetic acyl sulfonamides
Cav2.2 inhibitors	ziconotide, CNCB-2, physalin F
TRPV1 agonist	capsaicin, resiniferatoxin
NOS inhibitors	cindunistat
mPGES-1 inhibitors	AF3485, MF63 (35)
IL-6 inhibitors	tocilizumab, sarilumab
κ -opioid agonist	butanorphanol, TRK-820, CR845 (42)
δ -opioid agonist	SNC-80, BU-48 (47)
Biased μ -opioid agonist	oliceridine (TRV130)
NMDA antagonist	ketamine
CB1, CB2 agonists	dronabinol, nabilone, APD371
FAAH inhibitors	BIA 10-2474
Anti-NGF antibodies	tanezumab

Achieving the Primary Goal: Providers Can Balance Effective Pain Management When Using Opioids While Mitigating Overdose Risk, Diversion, Misuse and Abuse



**Powerful tools can both be beneficial or harmful to individuals and society.
They must be used responsibly!**



Primary Objectives

At the conclusion of this talk, the anticipation that attendees better understand:

1. The role polysubstance misuse as the “4th Wave of the Overdose Epidemic”
2. Recently updated definitions for pain
3. Principles of assessment and treatment for acute and chronic pain - using a multimodal approach
4. New non-opioid prescription medication and future non-opioid drug targets



THANK YOU!

**Evolving Principles of Multimodal
Pain Management – 2025 Fall
Update**

Contact: drneffdo@hotmail.com