

Opioid Epidemic: Best Practices in Pain Management

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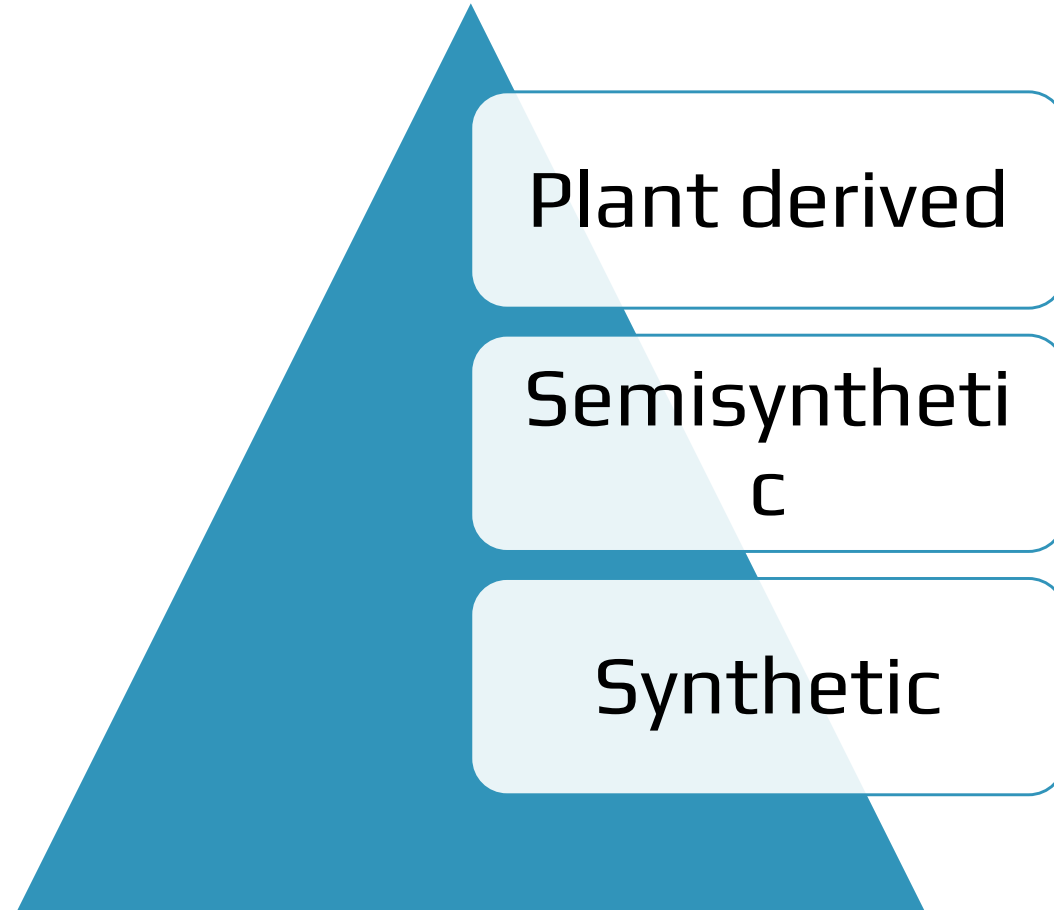
Objectives

- Describe the current state of the opioid epidemic
- Identify pharmacological and non-pharmacological approaches for pain management
- Identify best practices to alleviate opioid misuse and overdose

Opioid Abuse Facts

- In 2019, 1.6 million people had an opioid use disorder
- 1.6 million people newly misused prescription pain medications
- 10.1 million people misused prescription opioid medications
- Over 70,000 deaths occurred due to drug overdoses

What Are Opioids?



Plant Derived

- Opium
 - Extract of the poppy plant
- Morphine
 - Analgesic found in opium
 - Basis for comparing equivalent doses of opioid analgesics (MMEs)



["Opium Poppy" Images – Browse 23,340 Stock Photos, Vectors, and Video | Adobe Stock](#)



[Morphine Detox Timeline | Memphis, TN | Detox West Tennessee](#)

Semi-Synthetic

- Codeine
- Heroin
- Hydrocodone
- Hydromorphone
- Oxycodone
- Oxymorphone



[Heroin Bottle | DEA Museum](#)



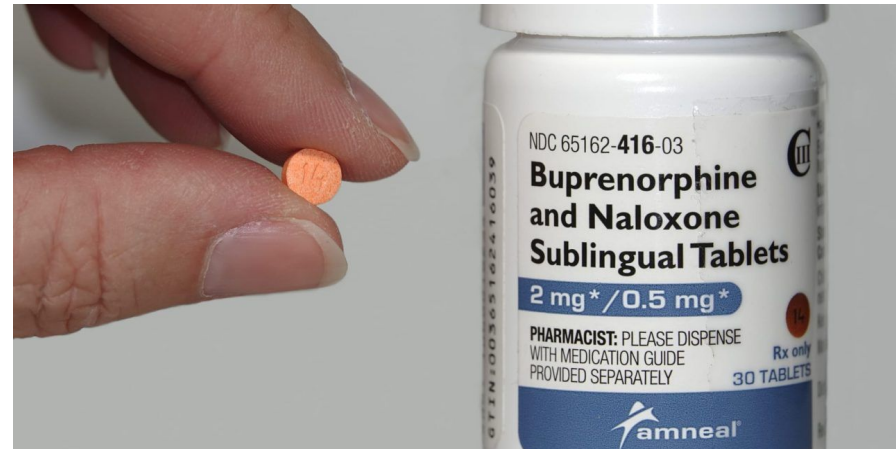
<https://www.oceanrecovery.com/addiction-blog/oxycodone-overdose/>

Synthetic

- Buprenorphine
- Fentanyl
- Meperidine
- Methadone
- Tramadol



<https://www.dea.gov/resources/facts-about-fentanyl>



<https://respiratory-therapy.com/wp-content/uploads/2024/09/buprenorphine-1280x640.jpg>

The Opioid Epidemic

The Opioid Epidemic

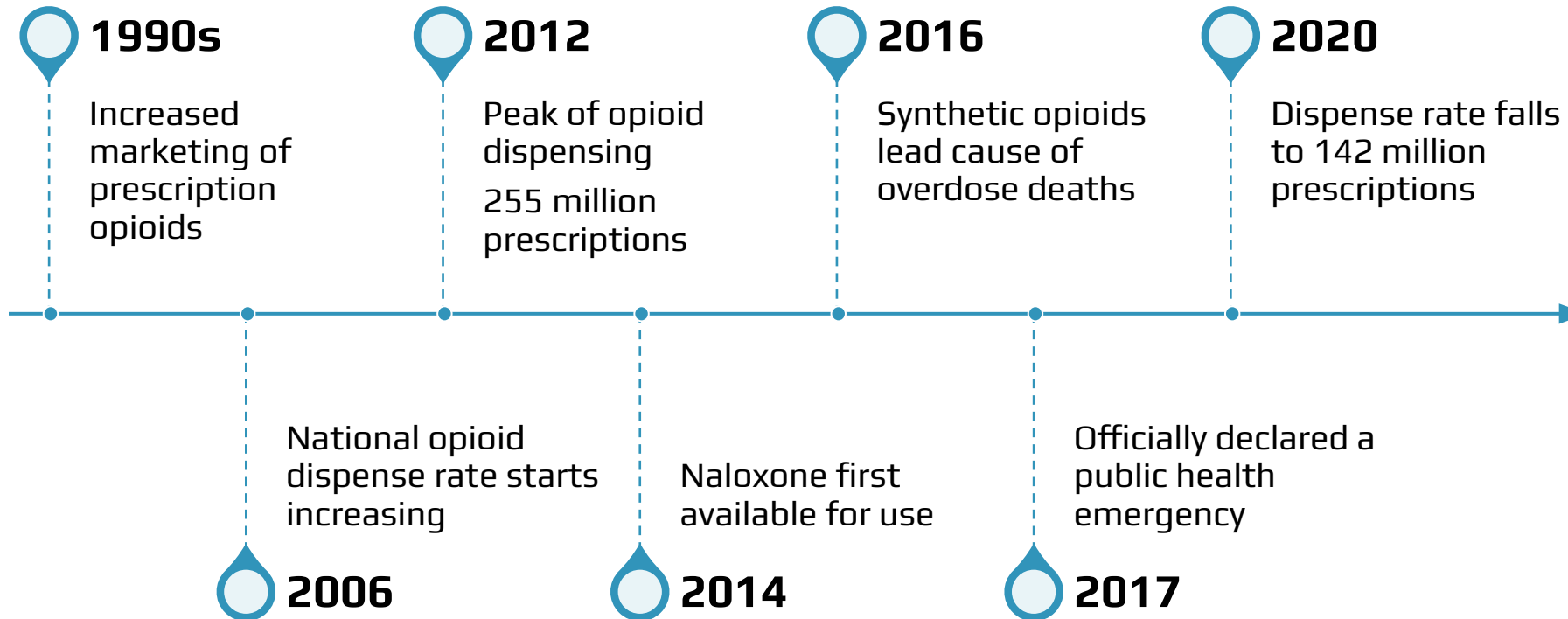
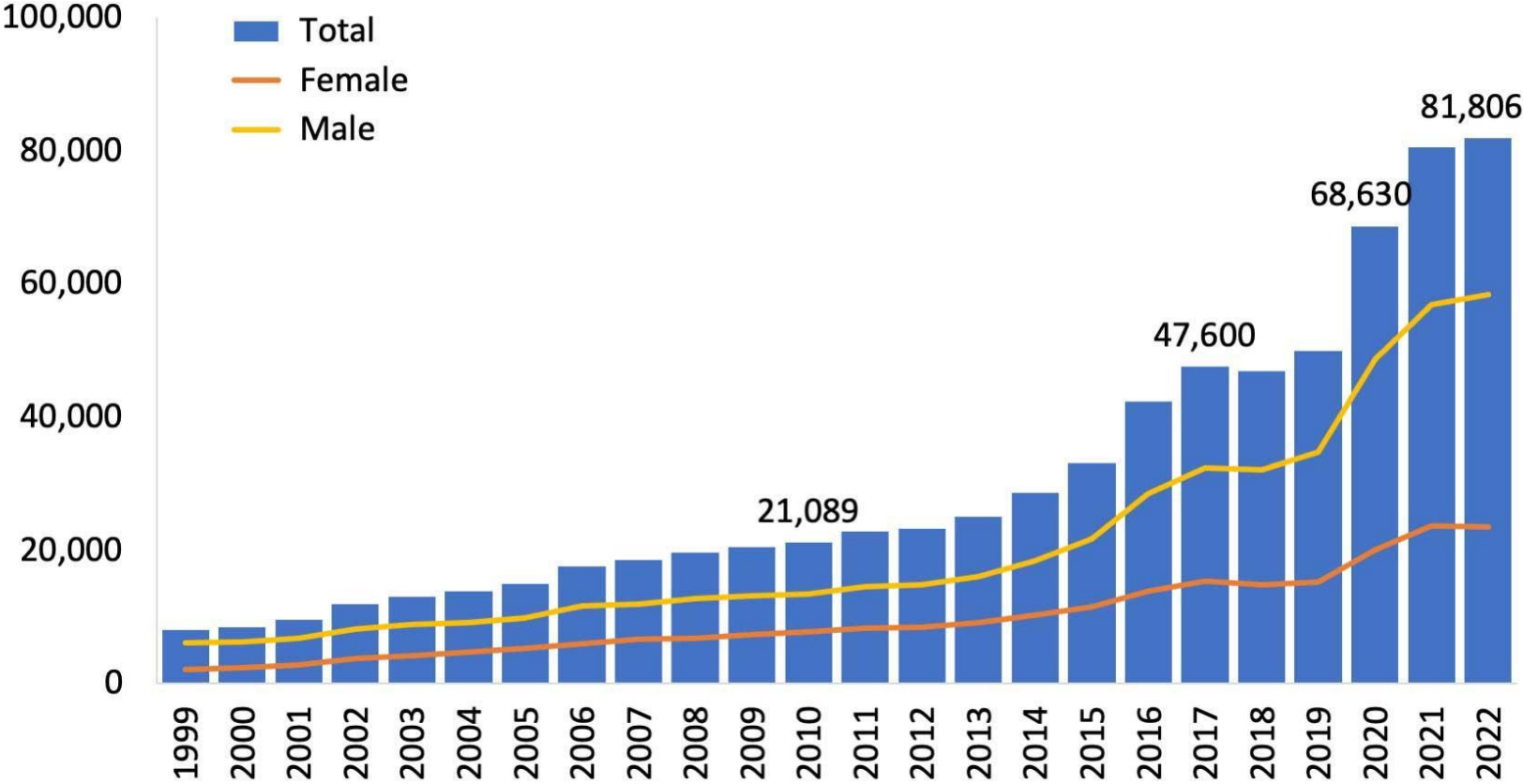
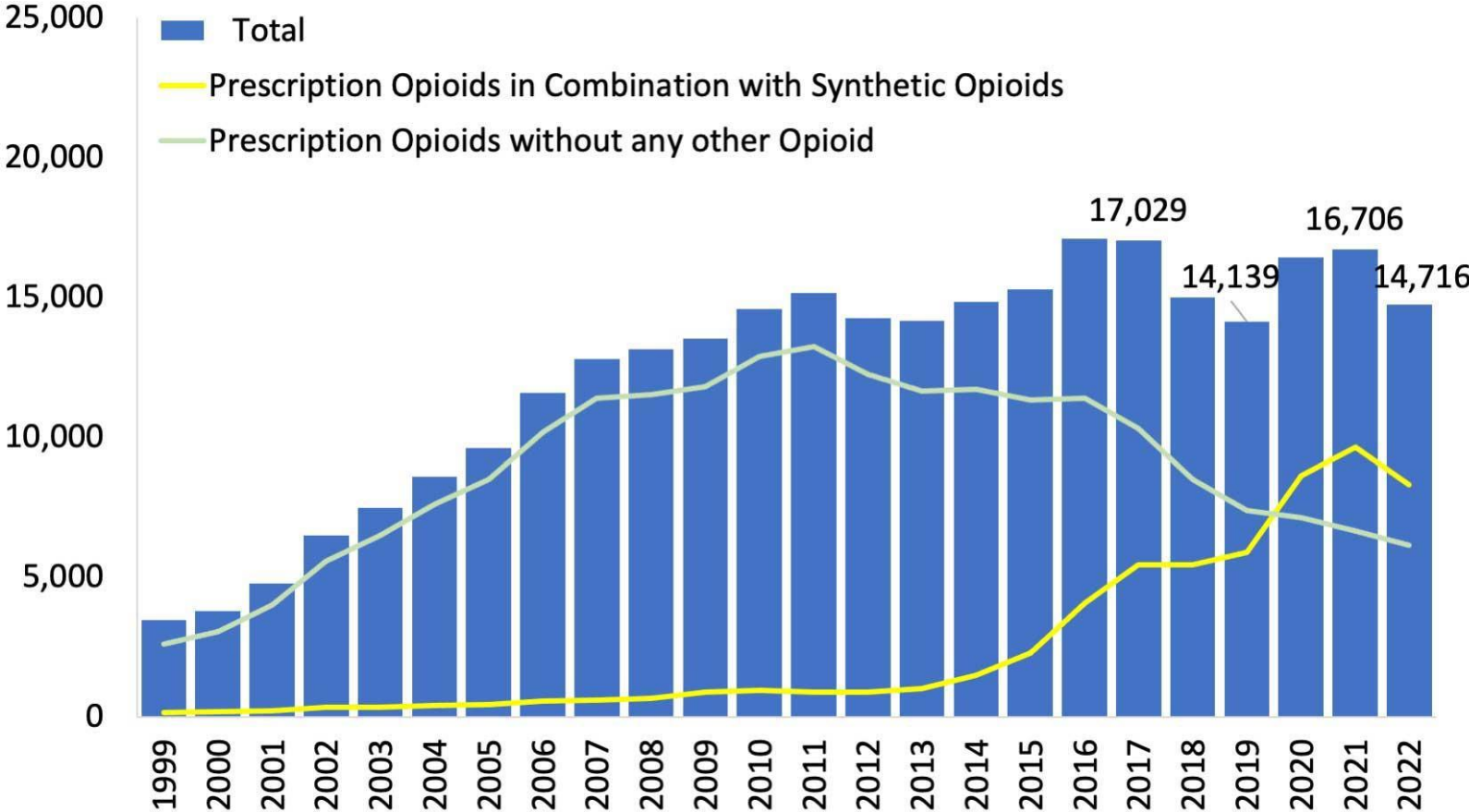


Figure 3. U.S. Overdose Deaths Involving Any Opioid* by Sex, 1999-2022



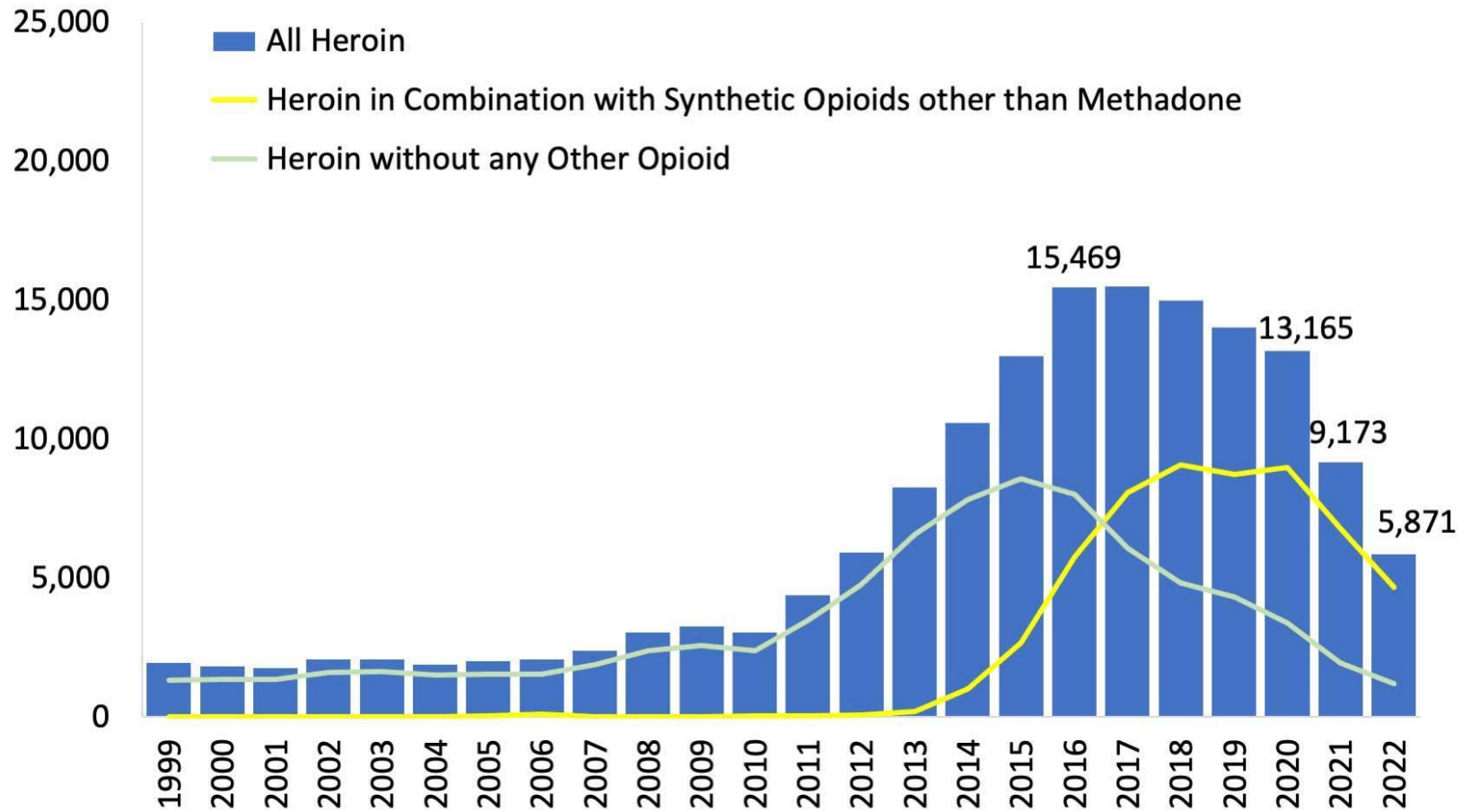
*Among deaths with drug overdose as the underlying cause, the “any opioid” subcategory was determined by the following ICD-10 multiple cause-of-death codes: natural and semi-synthetic opioids (T40.2), methadone (T40.3), other synthetic opioids (other than methadone) (T40.4), or heroin (T40.1). Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2022 on CDC WONDER Online Database, released 4/2024.

Figure 4. U.S. Overdose Deaths Involving Prescription Opioids*, 1999-2022



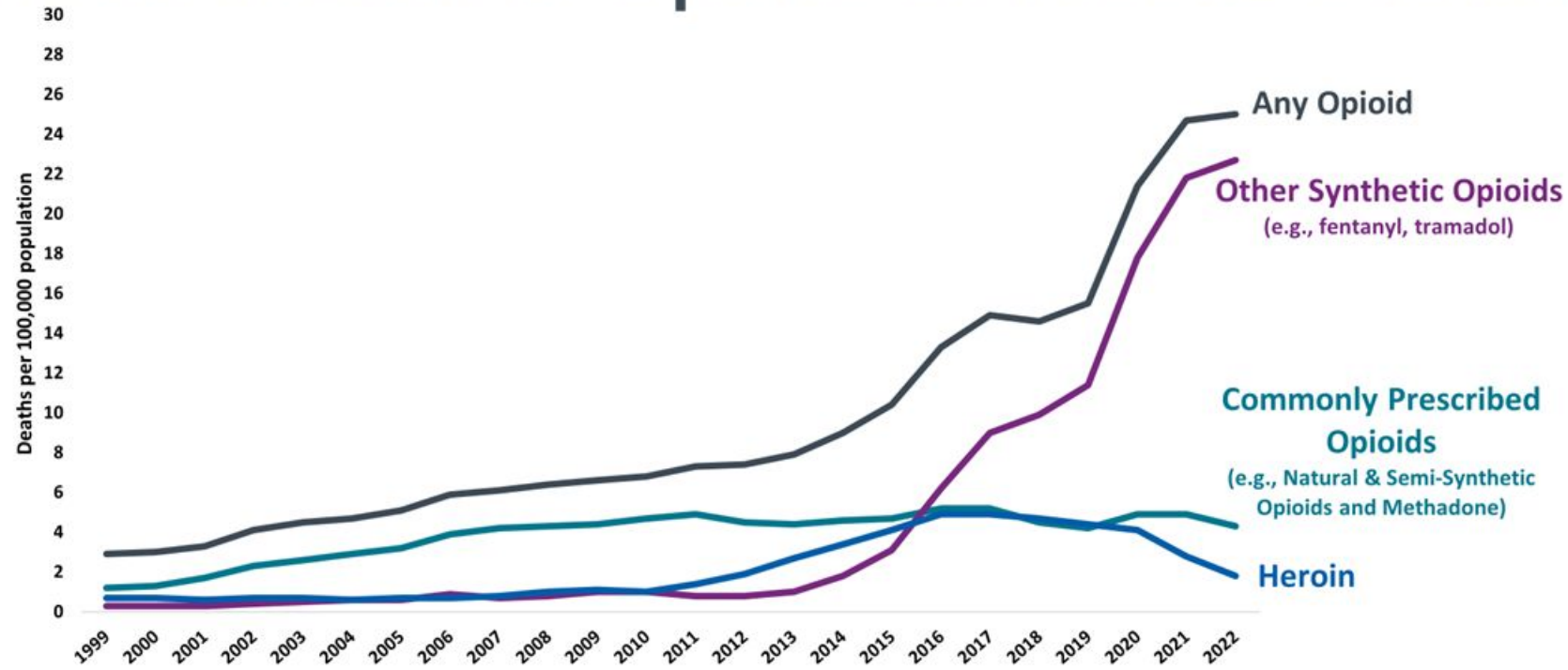
*Among deaths with drug overdose as the underlying cause, the prescription opioid subcategory was determined by the following ICD-10 multiple cause-of-death codes: natural and semi-synthetic opioids (T40.2) or methadone (T40.3). Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2022 on CDC WONDER Online Database, released 4/2024.

Figure 5. U.S. Overdose Deaths Involving Heroin*, by other Opioid Involvement, 1999-2022



*Among deaths with drug overdose as the underlying cause, the heroin category was determined by the T40.1 ICD-10 multiple cause-of-death code. Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2022 on CDC WONDER Online Database, released 4/2024.

Three Waves of Opioid Overdose Deaths



Wave 1: Rise in Prescription Opioid Overdose Deaths Started in the 1990s

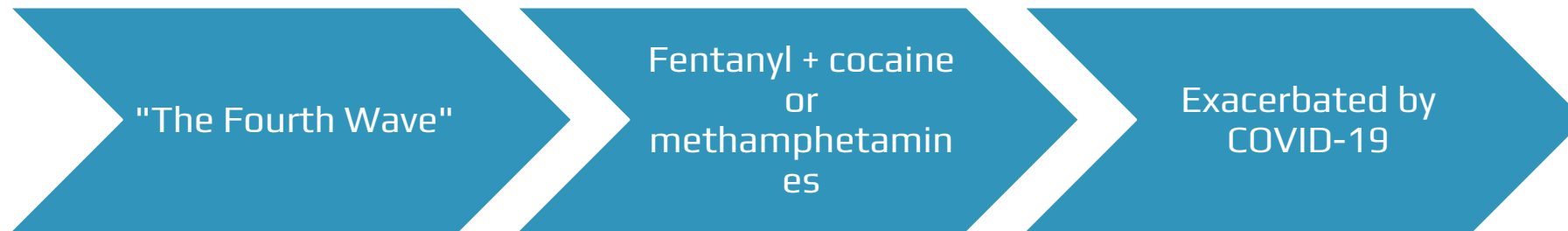
Wave 2: Rise in Heroin Overdose Deaths Started in 2010

Wave 3: Rise in Synthetic Opioid Overdose Deaths Started in 2013

SOURCE: CDC/NCHS, National Vital Statistics System, Mortality. CDC WONDER, Atlanta, GA: US Department of Health and Human Services, CDC; 2024. <https://wonder.cdc.gov/>.



The Opioid Endemic Now



Pain Management in Opioid Abuse Disorder

What is Pain?

- Unpleasant sensory response from actual tissue or potential tissue damage
- 40% of hospitalized patients complain of pain
- American Pain Society included pain as the “5th vital sign” in 1996

Prevalence of Pain

- Chronic post surgical pain affects 44%-53% of patients
- Chronic non-cancer pain affects 25% of 45-64 year-old patients and 30% of patients older than 65
- Cancer pain
 - 66% of patients with advanced or terminal disease
 - 55% of patients actively undergoing cancer treatment
 - 39% of patients in remission
- Patients with opioid use disorders
 - Chronic pain affects 55-60% of patients on methadone or buprenorphine

Managing Pain

- Recommend using non-pharmacological and pharmacological treatment
- Unrelieved pain can lead to detrimental effects in patients
 - Decreased quality of life
 - Disability
 - Increased length of stay
 - Lost work days

Meet our Patient

- 45 year old female
- CC/HPI: Presents to the hospital for LLQ abdominal pain, diarrhea, nausea and vomiting x 2 days
- PMH: heroin use (now on buprenorphine-naloxone treatment)
- Diagnosis – acute diverticulitis with microperforation and small abscesses
- Decision – admit to general medical floor for conservative treatment

Assessing Withdrawal Risk

- How much do they use
 - Dependence occurs after 2-3 weeks of daily use
- When was the last use
 - Heroin/short-acting opioids – withdrawal within 4-6 hours
 - Long-acting opioids – withdrawal within 24-36 hours
 - Fentanyl – withdrawal very unpredictable
- Are they on any medications used to treat opioid use disorders
 - Buprenorphine (+/- naloxone)
 - Methadone
 - Naltrexone

Treating Withdrawal

- Not on maintenance medications for opioid use disorder
 - Can initiate treatment inpatient if withdrawal will negatively impact patient care
- On maintenance medications for opioid use disorder
 - Inpatient – ensure medication is resumed
 - Outpatient – ensure compliance

Pain Management Principles

- Use multimodal strategy with non-opioids
- Utilize opioids
- Continue maintenance dose or equivalent of medications used for opioid use disorder
- Patients with opioid use disorder may require higher doses than others due to tolerance
- Utilize PO, if able, over IV options

Effects of Opioid Use Disorder and Pain

- Opioid-induced hyperalgesia
- Withdrawal hyperalgesia
- Increased tolerance

Acute Pain Management

- Resuming home buprenorphine or methadone will **not** control acute pain
- Patients often require more frequent administration or higher doses of opioid analgesics
- Withdrawal can precipitate worse pain symptoms

Concomitant Treatment

| Medication | Continuation inpatient | Mild pain treatment | Moderate/Severe pain treatment |
|--------------------------|------------------------|--|---|
| Buprenorphine | Yes | <ul style="list-style-type: none"> - Non-opioid medications - Increase total buprenorphine dose (max = 32 mg per day) | <ul style="list-style-type: none"> - Short acting opioid for breakthrough pain |
| Methadone | Yes | <ul style="list-style-type: none"> - Non-opioid medications - Could adjust home dose (recommend contacting methadone clinic first) | <ul style="list-style-type: none"> - No specific recommendations - Consider adding short acting opioid for breakthrough |
| Naltrexone | No | <ul style="list-style-type: none"> - non-opioid medications - Avoid opioids until off naltrexone for 3 days | <ul style="list-style-type: none"> - May use opioids, higher than normal doses will be needed to overcome blockade |
| No outpatient medication | N/A – may start new | <ul style="list-style-type: none"> - non-opioid medications | <ul style="list-style-type: none"> - Short acting opioids |

Non-Pharmacological Methods

Aromatherapy

Breathing
techniques

Hot or cold
compress

Massage
therapy

Positional
changes

Relaxation

Non-Opioid Pain Management

| Medication | Mechanism of Action | Dosing | Adverse Effects | Monitoring/Cautions |
|---------------|---|---|--|---|
| Acetaminophen | Activation of serotonergic inhibitory pathways | PO: 325-650 mg every 4-6 hours as needed OR 975-1000 mg q6 hours as needed (max 4g/day) IV: 650-1000 mg every 6 hours (max 4g/day) | PO: erythema IV: nausea, vomiting, anxiety, fatigue | <ul style="list-style-type: none"> - Hepatotoxicity - Acute generalized exanthematous pustulosis - Stevens-Johnson syndrome (SJS) - Toxic epidermal necrolysis (TEN) - May get level if suspected overdose |
| Amitriptyline | Serotonin and norepinephrine reuptake inhibitor | PO: 10-25 mg once daily – increase based on response (max 150 mg/day) | Cardiac arrhythmias, edema, syncope, nausea, constipation, confusion, dizziness, fatigue, seizures | <ul style="list-style-type: none"> - Caution in cardiovascular disease - Caution in myasthenia gravis - Caution with patients at risk for seizures |

Non-Opioid Pain Management

| Medication | Mechanism of Action | Dosing | Adverse Effects | Monitoring/Cautions |
|---------------|--|--|---|---|
| Carbamazepine | Limits influx of sodium ions across cell membranes to decrease synaptic transmission | PO: 200-400 mg per day in 2-4 divided doses up to 800 mg per day (max 1200 mg/day) | Nausea, vomiting, ataxia, dizziness, drowsiness | <ul style="list-style-type: none"> - Must test for HLA-B*1502 allele prior to initiation - BBW: anemia or agranulocytosis - BBW: TEN and SJS |
| Gabapentin | Modulates release of excitatory neurotransmitters | IR: 100-300 mg 1-3 times daily up to 1200 mg 3 times daily ER: 300 mg daily up to 3600 mg daily | Ataxia, dizziness, drowsiness, fatigue | <ul style="list-style-type: none"> - Caution in myasthenia gravis - Potential for drug dependency |
| Ibuprofen | Inhibits cyclooxygenase (COX) 1 and COX-2 enzymes □ decreased prostaglandin | PO/IV: 200-400 mg every 4-6 hours as needed OR 600-800 mg every 6-8 hours as needed (max 3200 mg daily) | Decreased hemoglobin, heartburn, dizziness | <ul style="list-style-type: none"> - Increased risk of hyperkalemia - Blurred/diminished vision |

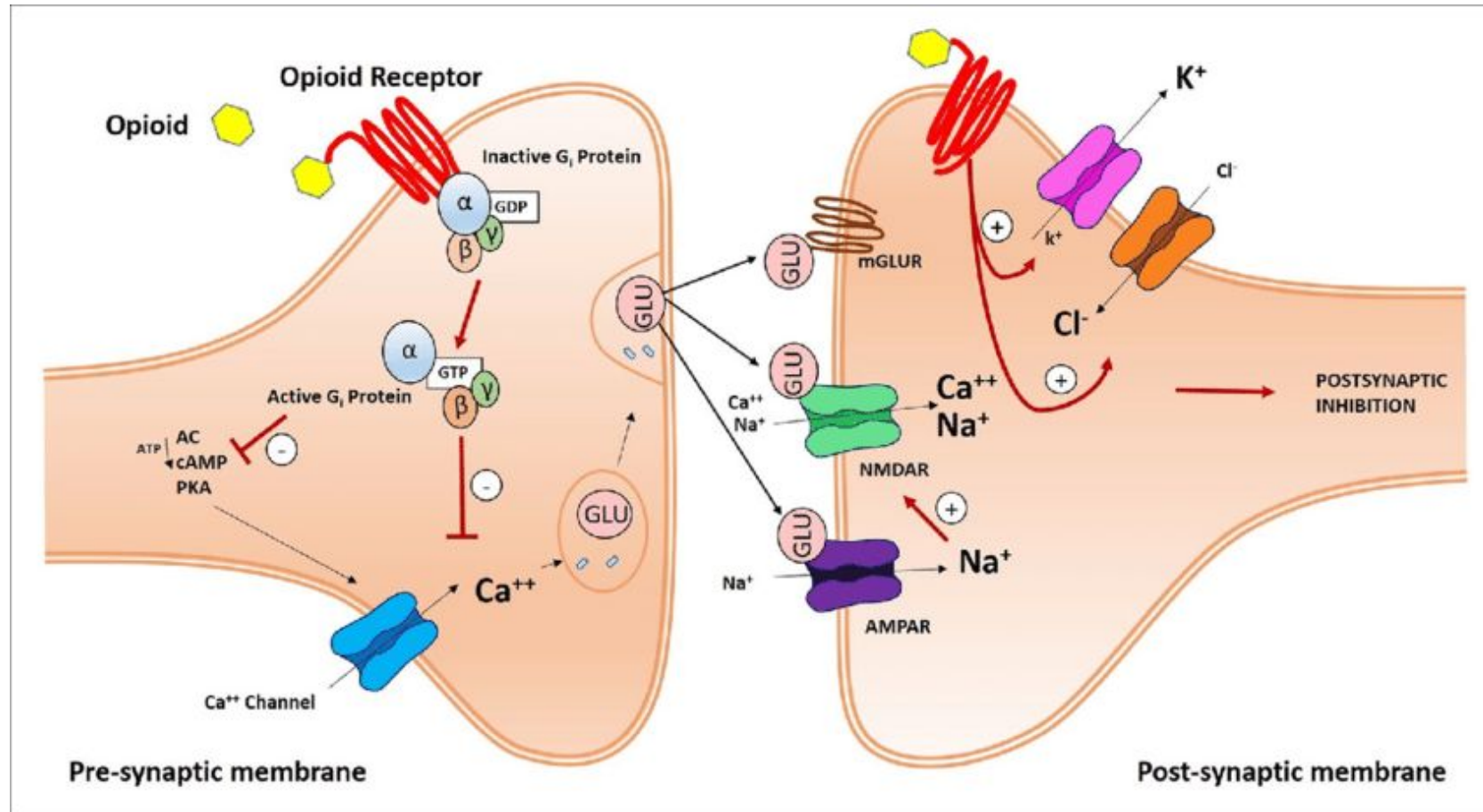
Non-Opioid Pain Management

| Medication | Mechanism of Action | Dosing | Adverse Effects | Monitoring/Cautions |
|------------|---|---|---|--|
| Ketamine | NDMA receptor antagonist that blocks glutamate | IV: 0.25-0.5 mg/kg bolus (max 35 mg), 0.05-0.25 mg/kg/hr infusion (max 1mg/kg/hr) | Hallucinations, irrational behavior, confusion, agitation | <ul style="list-style-type: none"> - May be useful in conditions that don't respond well to standard analgesics - Don't recommend using longer than 72 hours |
| Lidocaine | Blocks nerve impulses by blocking sodium channels | *Patch: apply up to 3 patches to the painful area, keep in place for 12-24 hours | Exfoliation of skin, blisters, dermatitis,, erythema | <ul style="list-style-type: none"> - Avoid application to broken/inflamed skin |
| Pregabalin | Binds to calcium channels in CNS to inhibit excitatory neurotransmitter release | PO: 50-150 mg in 2-3 divided doses up to 600 mg daily in divided doses | Peripheral edema, weight gain, xerostomia, dizziness, drowsiness, fatigue, blurred vision | <ul style="list-style-type: none"> - Controlled substance (C-V) - Angioedema - Taper off gradually to avoid withdrawal |

*several other formulations exist, only focusing on patches for this presentation

Opioids

Opioid Mechanism of Action



Opioid Receptors

Table 1. **Opioid Receptor Activity**

| Receptor | Activity |
|--------------------|--|
| Mu (μ) | Supraspinal and spinal analgesia, euphoria, miosis, sedation, constipation, respiratory depression, addiction, hormonal changes |
| Kappa (κ) | Supraspinal and spinal analgesia, diuresis, sedation, miosis, dysphoria, psychomimetic effects, respiratory depression, constipation |
| Delta (δ) | Supraspinal and spinal analgesia |

Source: References 4, 5.

Plant Derived

| Medication | Route | Dosing | Warnings/Cautions |
|------------------|------------------|--|--|
| Morphine IR | Oral (PO) | <p>Acute Pain:</p> <ul style="list-style-type: none"> - 7.5-30 mg every 4 hours as needed <p>Chronic Pain:</p> <ul style="list-style-type: none"> - 5-15 mg every 4 hours as needed or scheduled, adjust as needed to patient response | <ul style="list-style-type: none"> - Metabolite undergoes enterohepatic cycling - Possible accumulation in renal disease |
| Morphine XR | PO | <p>Acute Pain:</p> <ul style="list-style-type: none"> - Do NOT use <p>Chronic Pain:</p> <ul style="list-style-type: none"> - Dose based off IR dosing requirements | |
| Morphine sulfate | Intravenous (IV) | <p>Acute Pain:</p> <ul style="list-style-type: none"> - 1-4 mg every 1-4 hours (max 10mg per dose) <p>Chronic Pain:</p> <ul style="list-style-type: none"> - 2-5 mg every 3-4 hours as needed | |

Semi-Synthetic

| Medication | Route | Dosing Range | Other Information |
|-------------|---|--|---|
| Codeine | PO | 15-60 mg every 4 hours as needed (max dose = 360 mg/day) | <ul style="list-style-type: none"> - Therapeutic effect may be altered by patient's CYP2D6 status |
| Heroin | IV, subcutaneous, intranasal, intramuscular | Not established <small>Morphine. In: Lexi-Drugs</small> Control I Substance | <ul style="list-style-type: none"> - No medicinal use - Initially marketed by Bayer |
| Hydrocodone | PO | IR: 5-10 mg every 4-6 hours as needed ER: 20 mg daily, titrate up to achieve adequate analgesia | <ul style="list-style-type: none"> - IR product typically in combination with acetaminophen - Watch total acetaminophen usage when using IR product |

Semi-Synthetic

| Medication | Route | Dosing | Other Information |
|---------------|--------|---|---|
| Hydromorphone | PO, IV | PO: 1-4 mg every 4-6 hours as needed IV: 0.2-1 mg every 2-4 hours as needed | - Available as oral liquid as well |
| Oxycodone | PO | Acute Pain: - IR: 5 mg every 4-6 hours as needed, titrate to response - ER: do NOT use Chronic Pain: - Dosing based off total requirements and split between IR and ER formulations | - Several abuse-deterrent formulations available - One of the first prescription opioids implicated in the opioid epidemic |
| Oxymorphone | PO | Acute Pain: - IR: 5-10 mg every 4-6 hours as needed Chronic Pain - ER: 5 mg every 12 hours Titrate to effective dose | - Noted incidences of thrombocytopenic purpura - Caution in cachectic patients, increased risk of respiratory depression |

Synthetic

| Medication | Route | Dosing Range | Other Information |
|---------------|---------------------------------|---|--|
| Buprenorphine | PO, Buccal, IM, IV, transdermal | <p>Acute Pain:</p> <ul style="list-style-type: none"> - IM or slow IV: 0.3 mg every 6-8 hours as needed <p>Chronic Pain:</p> <ul style="list-style-type: none"> - Buccal: 75 mcg once daily (max 900 every 12 hours) - Patch: 5 mcg/hr every 7 days (max 20 mcg patch) | <ul style="list-style-type: none"> - Also can be used for treatment of opioid use disorder - Partial opioid receptor agonist |
| Fentanyl | IM, IV, Transdermal | <p>Acute Pain:</p> <ul style="list-style-type: none"> - IV/IM: 25-50 mcg OR 0.35-0.5 mcg/kg every 30-60 minutes <p>Chronic Pain:</p> <ul style="list-style-type: none"> - Patch: initial dosing based on current opioid use | <ul style="list-style-type: none"> - Never use patches for acute pain - Patches should only be started in opioid tolerant patients |

Synthetic

| Medication | Route | Dosing Range | Other Information |
|------------|-------|---|---|
| Methadone | PO | Chronic Pain: <ul style="list-style-type: none"> - 2.5-5 mg every 8-12 hours - Titrate to effect | <ul style="list-style-type: none"> - Also used for opioid use disorder - Extremely long half life |
| Tramadol | PO | Acute Pain: <ul style="list-style-type: none"> - IR: 50 mg every 4-6 hours as needed (max 400 mg/day) Chronic Pain <ul style="list-style-type: none"> - IR: 50-100 mg every 4-6 hours (max 400 mg/day) - ER: 100 mg daily (max 300 mg/day) | <ul style="list-style-type: none"> - Inhibits reuptake of norepinephrine and serotonin in addition to binding to opioid receptors - Therapeutic effect altered by patient's CYP2D6 status |

Morphine Milligram Equivalents

| <u>Opioid (mg, Except Where Noted)</u> | <u>Oral MME Conversion Factor ¹</u> |
|--|--|
| Buprenorphine | N/A |
| Codeine | 0.15 |
| Fentanyl, intravenous (mcg) | 0.3 |
| Hydrocodone | 1 |
| Hydromorphone | 4 |
| Meperidine | 0.1 |
| Methadone | 3 |
| Morphine, oral | 1 |
| Morphine, intravenous | 3 |
| Oxycodone | 1.5 |
| Tramadol | 0.1 |

Risks of Opioid Use

Respiratory
Depression

Aspiration

QTc
prolongation

Physical
Dependence

Constipation

Opioid
Induced
Hyperalgesia

Opioid-Induced Hyperalgesia

- Increased feelings of pain with opioid use
 - May spread beyond the initial site of pain
 - Dose dependent

- Mechanism
 - Activation of NMDA receptors on spinal cord neurons
 - Descending pain facilitation system activation from mu opioid receptor activation
 - Neuroinflammatory reaction

- Most commonly occurs in
 - Patients taking medications for opioid use disorder
 - Surgical patients who received opioids

Physical Dependence

- Physiological change occurring due to presence of a drug that when stopped produces withdrawal symptoms
- Withdrawal syndrome occurs due to administering a reversal agent, abrupt cessation, or decreasing doses quickly
- Expected after 2-10 days of regular use
- Opioid withdrawal symptoms
 - Diarrhea, sweating, increased blood pressure, increased heart rate, large pupils

Mitigating Misuse and Overdose

Mitigating Misuse

- Several opioids are formulated with abuse-deterrent properties
- More difficult to use improperly
 - Crush to dissolve and inject
 - Crush to snort
- Medications available
 - RoxyBond – coated to resist chemical extraction and make difficult to manipulate or transform for injection
 - Xtampza – capsules with microspheres that resist chewing, crushing, cutting, dissolving, melting
 - Hysingla ER – properties that make it more difficult to crush, break, or dissolve
 - OxyContin – properties that make it more difficult to crush, break, or dissolve

Prescriber Responsibility

- Nonpharmacologic and nonopioid therapy preferred for chronic pain
 - Use opioids in combination, never without
- Establish treatment goals for pain management
- Opioid treatment agreement
- Use the lowest effective dose
- Avoid concurrent benzodiazepine use

Avoiding overdose

- Use lowest effective dose
- IR formulations preferred
- Overdose risk odds in morphine milligram equivalents (MME)
 - MME < 20 mg/day – 1.3
 - MME 20-50 mg/day – 1.9
 - MME > 50 mg/day – 4.6
- Recommend increased follow up in patients receiving MME > 50 mg/day

2016 CDC Guidance

- Addresses when to initiate opioids for chronic pain; opioid dose, duration, discontinuation; and assessment of risk mitigation
- Risks and benefits should be re-assessed if increasing MME >50 mg/day, and extra caution if exceeding MME of 90 mg/day
- Review PDMP frequently – even as often as with every prescription
- Acute pain should be treated with the lowest dose and duration expected to be needed for severe pain
 - 3 days of treatment is often adequate
 - More than 7 days should rarely be needed
- Evaluate risks and benefits every 3 months, consider tapering or discontinuing if risks outweigh benefits

2016 CDC Guidance Problems

- Providers too strictly adhered to recommendations on dosing and quantity limits
- Increase concern for adverse events in chronic pain patients
 - Suicide
 - Overdose
 - Mental Health Crises
- States have implemented laws for opioid prescribing and dispensing in response to these guidance statements
- Authors have now emphasized the guidance was not meant to be absolute rules for everyone
 - No update has been issued though

Key Takeaways

- Opioid epidemic is still ongoing
 - Fentanyl is of increasing concern
 - More difficult to reverse
- Pain management is multifactorial
 - Nonpharmacologic
 - Nonopioid medications
 - Opioid medications
- Continuing maintenance medication is not a replacement for acute pain management
- Formulation changes have decreased the ability to misuse several prescription opioid medications
- Line between helping and harming is often a gray area

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