Responsible Opioid Prescribing Does Not Negate Compassionate Pain Management

Laura B. Gardner, MD, MPH, PhD, FACPM

No conflicts

Why is this important?

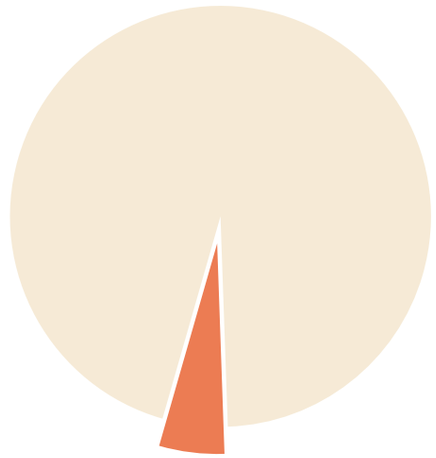
Opioid Epidemic in Numbers

259,000,000

Prescriptions in one year (2012)

2,200,000

People addicted to opioids globally



5%

of world population accounts for

21,103

Deaths from prescription opioids (2014)

10,574

Deaths from heroin overdose (2014)

80%

of the world's use of opioids

Setting the Scene

The Opium Poppy

- When the poppy loses its petals, the bulb is ready to be cut
- The liquid leaking out of the bulb is opium gum
- The gum is boiled and strained, resulting in blocks of morphine

Opium Through the Ages

3rd Century BC.

- First reference to opium was by Theophrastus
- The opium poppy was first cultivated in Mesopotamia (Southwest Asia)
- Opium contains over 20 distinct alkaloids.
- It is derived from the juice of the poppy
- The Greek word ‘opos’ means juice

17th Century

- Friedrich Serturner, isolated a component of opium that he named morphine
- The Greek god of dreams is named Morpheus
- Morphine is the analgesic component of opium

18th Century

- Opium was used to control dysentery, analgesia, sedation (“baby-doping”) and cough suppression
- Traded as a form of currency

19th Century

- Use of morphine increased dramatically after the development of the hollow needle and hypodermic syringe in the mid-1800s.

Opium Wars

- In the 1800's, British merchants began trading contraband opium for more valuable Chinese products (tea, silk, etc.)
- Commissioner Lin, a Chinese diplomat, sent a letter to Queen Victoria asking her to stop the trade
- Request ignored › Opium Wars start

Recent History

- Controlled Substances Act of 1970
  — Regulates prescribing and dispensing of psychoactive drugs
  — Resulted in significant changes in the epidemiology of opioid addiction.

- Brand-name oxycodone developed by Purdue in 1996. Advertised as “low abuse potential” because it is time-release

- Follow-up to nonfatal OD in 2000’s: 91% continued to be prescribed an opioid; usually the same prescriber.

- ACOEM 2014: Quality evidence fails to demonstrate superiority of opioids to other medications and treatments. Risk for serious harm from opioids is dose-dependent.

Now

- Opioid prescribing and high-dose prescribing continued to decrease through 2017.
- Overall, data suggest that some prescribing practices continued to improve in 2017, and sustained efforts are needed to help providers continue to adopt and maintain safe prescribing practices.
- In 2017, 17.4% of the U.S. population received one or more opioid prescriptions.

Terminology

Terminology

- Narcotics
  Imprecise term linked to narcosis (sleep)

- Opiates
  Drugs derived from opium (may be natural or semi-synthetic)

- Opioids
  Any drug that binds to the opioid receptors in the CNS and antagonized by naloxone (may be natural, semi-synthetic or synthetic)

Terminology

- Tolerance
  — Develops quickly to the pain-relieving effects
  — With frequent use, the receptors “adapt” and no longer react, leading to loss of drug effectiveness
  — Need increasing amounts to achieve the same amount of pain relief.

- Dependence
  — Drug is needed to prevent withdrawal symptoms, which include nausea, muscle spasms, anxiety, fever, diarrhea and total body pain (“flu-like” feeling).

- Addiction
  —When the user seeks the drug mainly or only for the “high” and less so for pain relief or to avoid withdrawal symptoms.

Opioid Classification

- Pure Agonists
  — Natural (morphine, codeine, endogenous endorphins)
  — Semi-synthetic (heroin, hydromorphone, oxycodone, oxymorphone, pholcodeine)
  — Synthetic (methadone, meperidine, propoxyphene, dextropropoxyphene, fentanyl, tramadol, dextromethorphan, loperamide)

- Partial Agonist (pentazocine)

- Agonist-Antagonist (buprenorphine, nalbuphine, butorphanol)

- Pure Antagonist (naloxone, naltrexone, nalorphine)

Therapeutic Indications for Opioids

Therapeutic Indications for Opioids

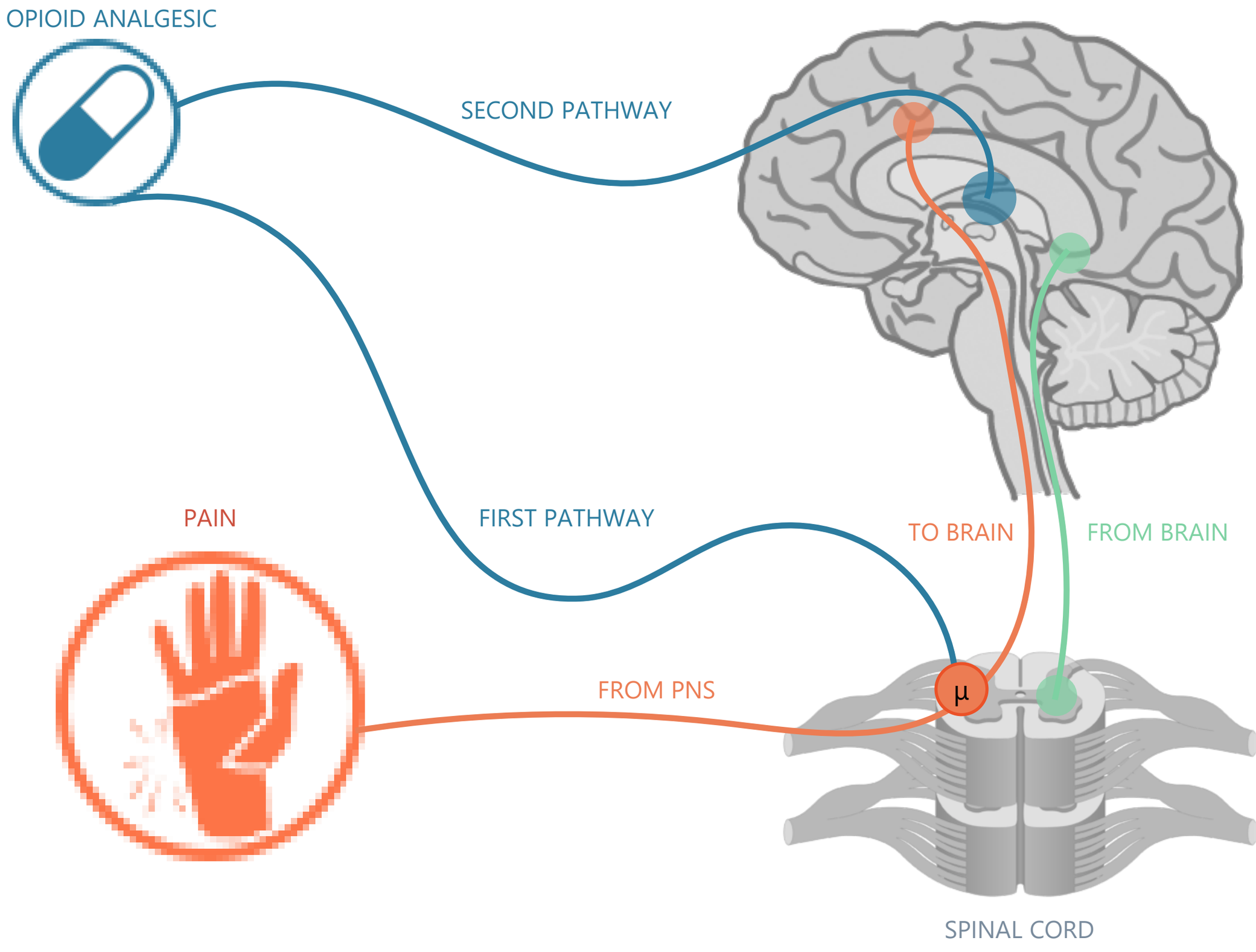
- Analgesia
- Sedation
- Acute pulmonary edema
- Epidurals
- Cough suppression
- Treatment of diarrhea
- End-of-life pain such as with advanced cancer, palliative care
- Acute, short-term post-surgical pain (+/-)
- Opioid use disorder (OUD)

How Opioids Work and Feel

Brain Chemistry

- The primary target for opioids are the Mu receptors.
- Mu receptors are distributed throughout the thalamus, cerebral cortex, visual cortex, basal ganglia, brain stem and spinal cord.
- When opioids bind to endorphin receptors in the pain pathway it leads to analgesia. When they bind to receptors in the reward pathway dopamine is relesased which produces euphoria.
- The number of Mu receptors varies among individuals and is genetically determined.
- The more Mu receptors, the greater the pain tolerance.
- Mice lack Mu receptors; they are more sensitive to pain and less likely to become dependent.

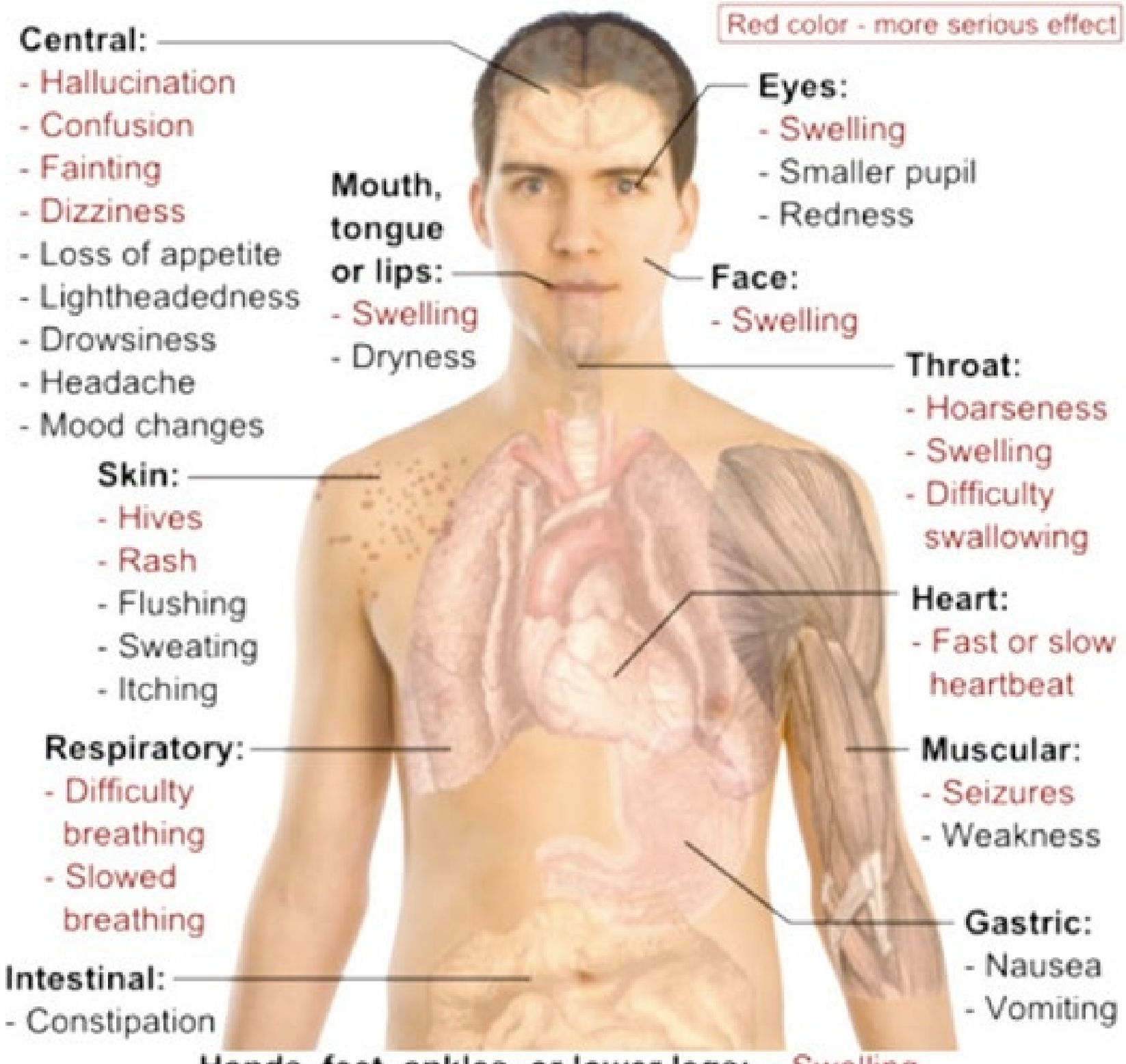
Location of Action



Effects

- Effects include analgesia, euphoria, sedation, decreased agitation and anxiety (often associated with pain), and increased sense of well-being.
- Can also produce dysphoria and hallucinations, immune effects, difficulty concentrating, apathy, constipation, itch, sleep disruption and death.
- Opioids cross the blood-brain barrier, the placental barrier and are secreted in breast milk.
- Dependent pregnant mothers will give birth to dependent babies who will experience withdrawal if not tapered by a physician. Babies also may be born with respiratory depression, which can lead to death.

Effects


Red color - more serious effect
Central:
- Hallucination
- Confusion
- Fainting
- Dizziness
- Loss of appetite
- Lightheadedness
- Drowsiness
- Headache
- Mood changes
Mouth, tongue or lips:
- Swelling
- Dryness
Eyes:
- Swelling
- Smaller pupil
- Redness
Face:
- Swelling
Throat:
- Hoarseness
- Swelling
- Difficulty swallowing
Skin:
- Hives
- Rash
- Flushing
- Sweating
- Itching
Heart:
- Fast or slow heartbeat
Respiratory:
- Difficulty breathing
- Slowed breathing
Muscular:
- Seizures
- Weakness
Intestinal:
- Constipation
Gastric:
- Nausea
- Vomiting
Hands, feet, ankles, or lower legs: - Swelling

Pin point pupils

The Opioid Experience

- First time may cause nausea/vomiting
  — Effect decreases with time
  — Longer-term side effect is constipation.

- One-to-two minute rush
  — Euphoria (in persons with pain or addiction)
  — Dysphoria (in persons without pain or addiction)
  — Relief of tension
  — Binding to endorphin receptors in pain pathway (thalamus, brain stem, spinal cord) produces analgesia.

- Four-to-five hour high
  — Warmth, drowsiness
  — Apathy, indifference to surroundings
  — Binding to receptors in reward pathway produces release of dopamine and a good feeling.

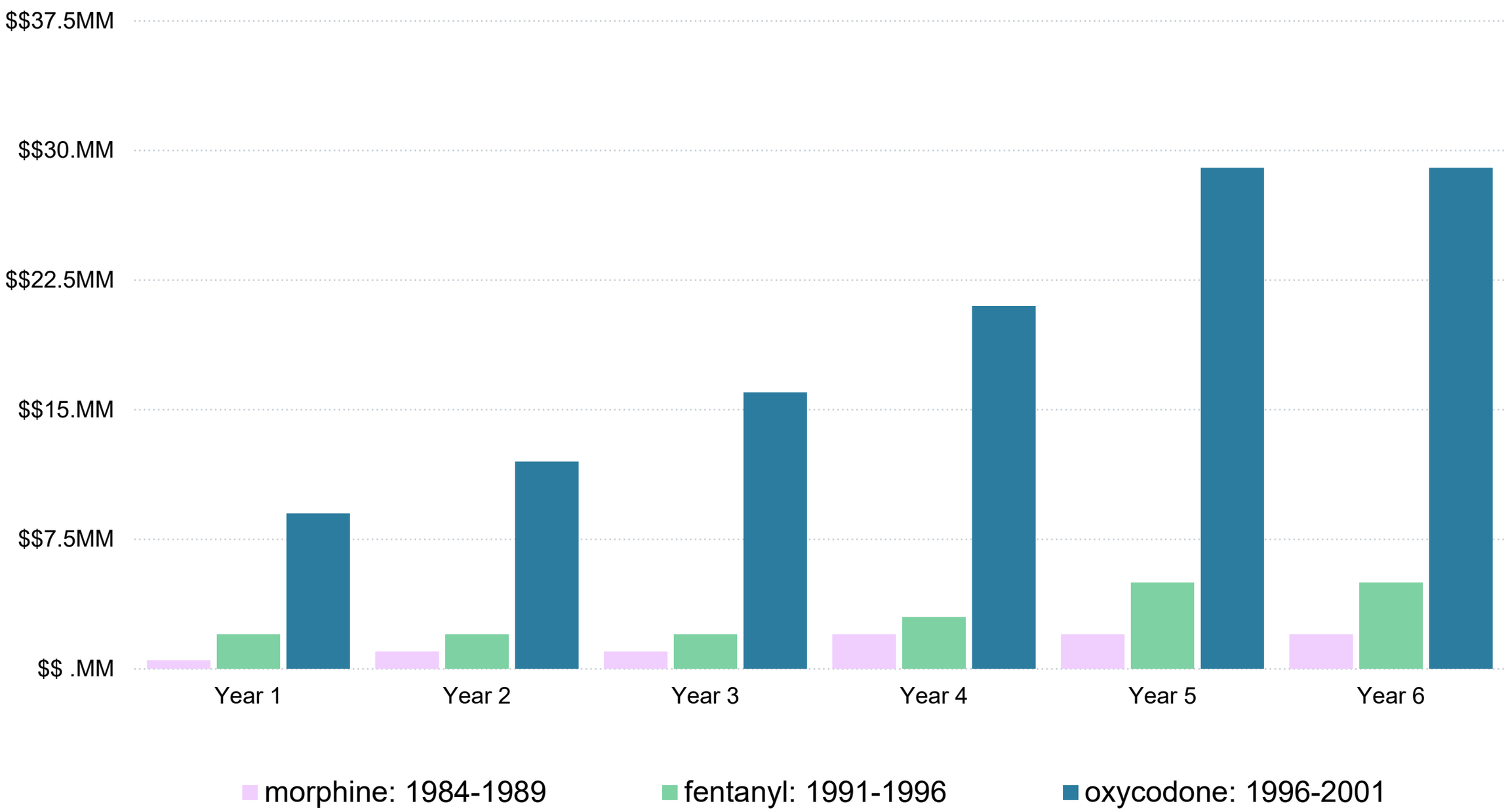
How Opioids Feel

Factors Influencing Prescription of Opioids

Factors Influencing Prescription of Opioids

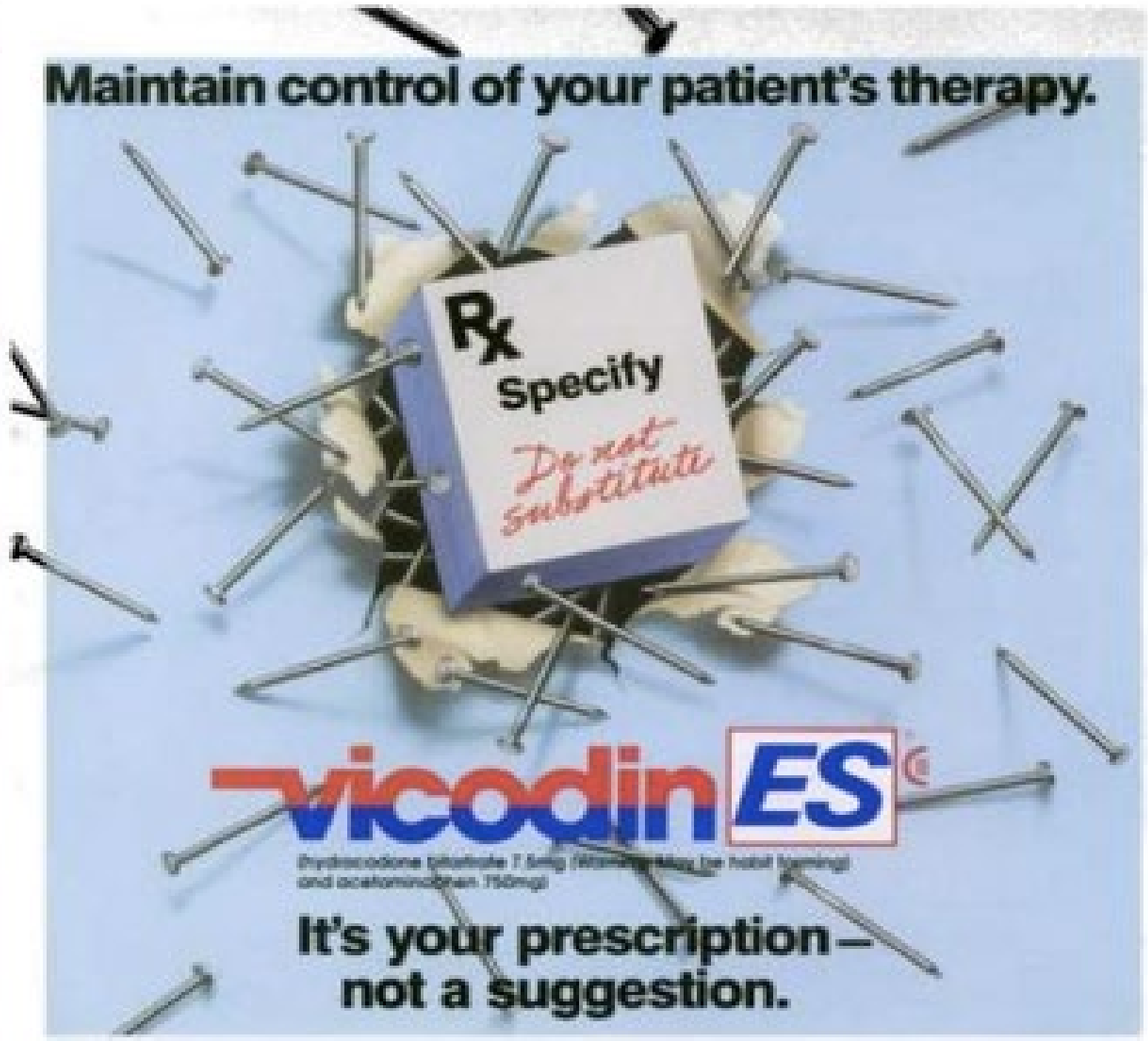
- Pain as “the fifth vital sign”
- Historically, a dearth of good evidence as to benefits vs. harms
- Ease of prescribing compared to multidisciplinary biopsychosocial treatment
- Newer brand names captured market share by claiming to have lower abuse potential
- Pharmaceutical industry promotion

Promotional Spending for Three Opioid Analgesics in First 6 Years of Sales

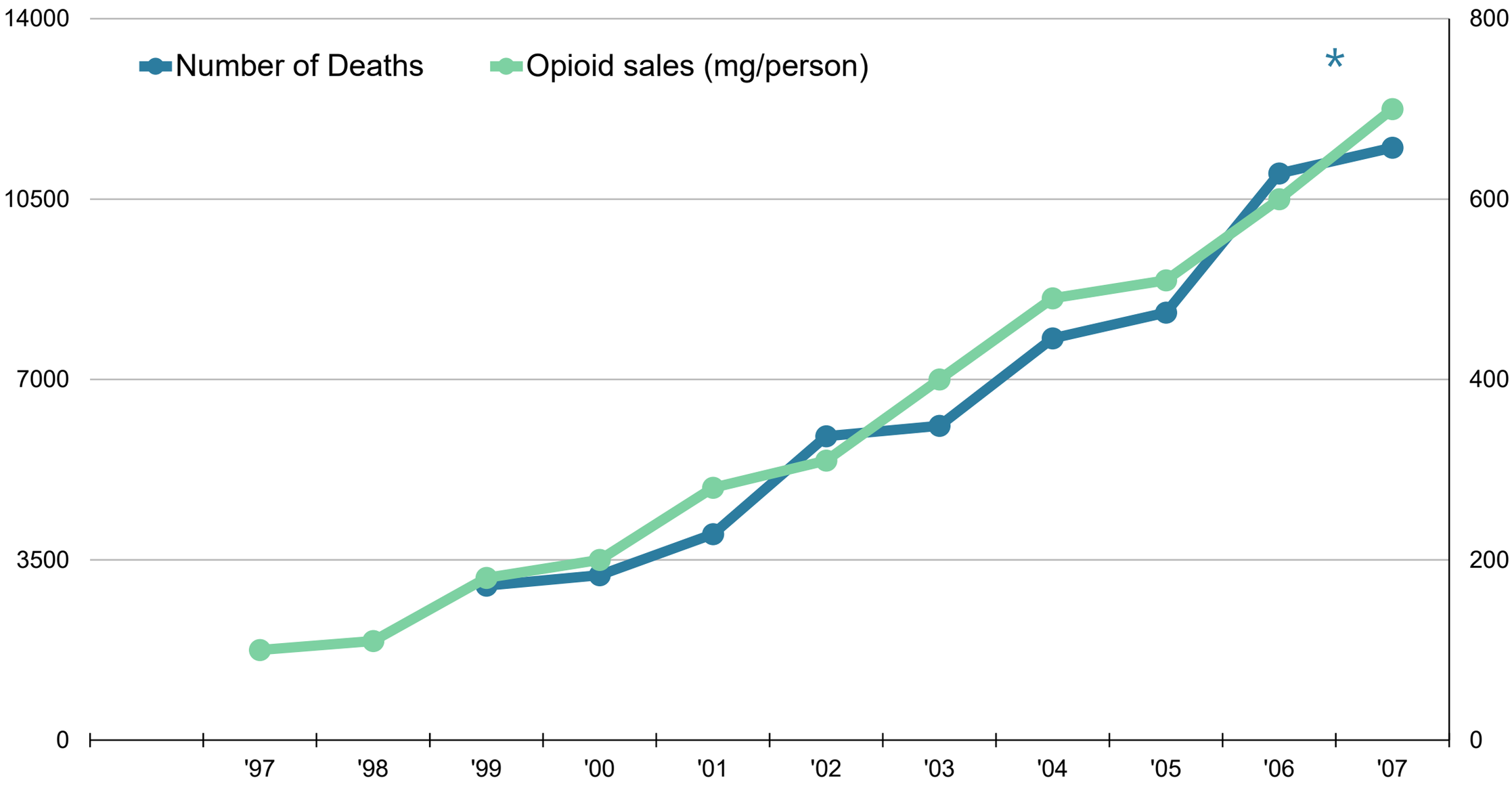


Source: United States General Accounting Office: Dec. 2003, “OxyContin Abuse and Diversion and Efforts to Address the Problem.”

FDA permits drug manufacturers to advertise opioids as safe and effective for chronic pain

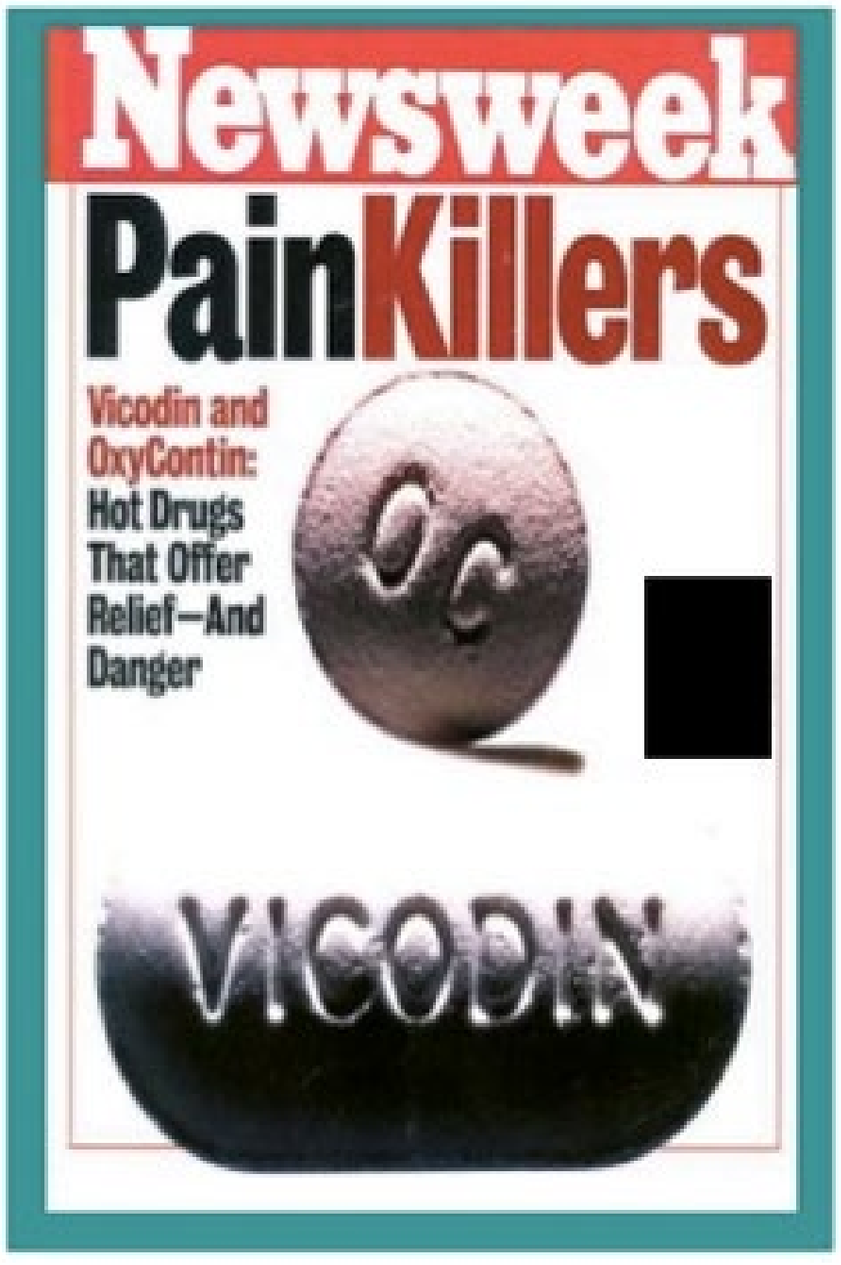


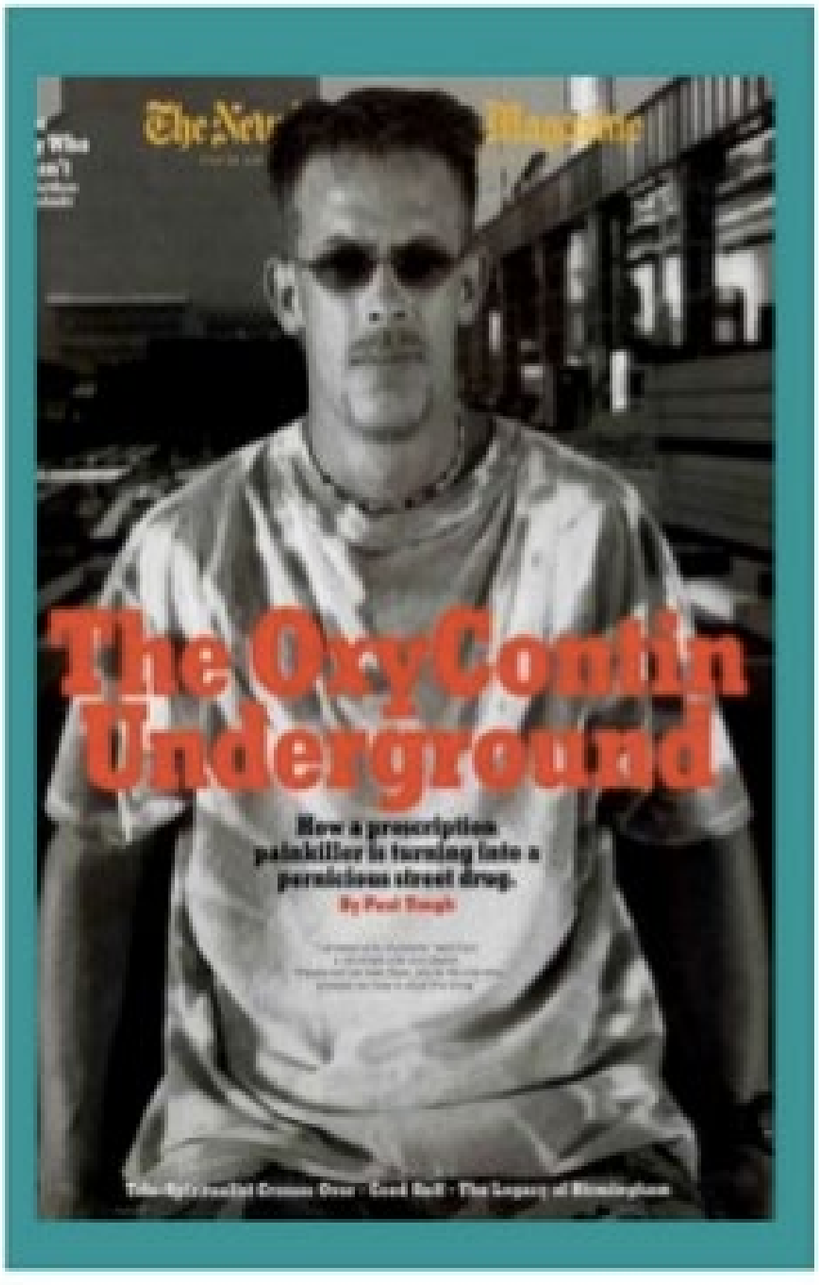
Unintentional overdose deaths involving opioid analgesics parallel per capita sales of opioid analgesics in morphine equivalents by year, U.S., 1997-2007



Source: National Vital Statistics System, multiple cause of death dataset, and DEA ARCOS
* 2007 opioid sales figure is preliminary.

Epidemic


Newsweek
PainKillers
Vicodin and OxyContin: Hot Drugs That Offer Relief—And Danger
VICODIN


The OxyContin Underground
How a prescription painkiller is turning into a pernicious street drug.

Economic Implications of Opioid Abuse

Economic Implications of Opioid Abuse

- Opium accounted for 53% of Afghanistan's GDP in 2007.
- Afghanistan supplied 87% of the world's opium in the years 2007-2011.
- High costs to health care and legal systems (nearly $500 billion annually).
- Cost factor for SA opioid is 3X; for LA opioid, 9X
- Opioids account for 40% of the medical cost in older claims.

Opioid Prescription Guidelines

Opioid Prescription Guidelines

- Introduction to guidelines
- Centers for Disease Control (CDC) guidelines
- Backlash to CDC guidelines
- Montana Prescription Drug Registry

Opioid Prescription Guidelines

- Guidelines can help to determine when to initiate or continue opioids for chronic pain.
- Decision must consider non-pharmacologic therapy, non-opioid pharmacologic therapy and opioid therapy.
- Non-pharmacologic therapy might include: cognitive behavioral therapy (CBT), mindfulness, walking, yoga, proper nutrition and adequate sleep.
- Non-opioid pharmacologic therapy might include acetaminophen, ibuprofen, anti-depressants, anti-convulsants such as pregabalin or gabapentin.
- Providers should approach chronic pain patients using a BioPsychoSocial perspective. The BioPsychoSocial approach is an interdisciplinary model that looks at the interconnection of biological factors (genetic, immune, hereditary, biochemical, medical comorbidities, etc.), psychological factors (mood, personality, behavior, etc.) and social factors (work history, cultural, familial, socioeconomic, spiritual, etc.).

CDC Guidelines

- The CDC's clinical evidence review found insufficient evidence to determine long-term benefits of opioid therapy for chronic pain and found an increased risk for serious harms related to long-term opioid therapy that appears to be dose-dependent.

- The CDC guideline states that when starting opioid therapy for chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release/long-acting (ER/LA) opioids. There is a higher risk of overdose with the ER/LA formulations.

- Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently.

- The CDC evidence review found that many nonpharmacologic therapies, including physical therapy, weight loss for knee osteoarthritis, psychological therapies such as CBT, and certain interventional procedures can ameliorate chronic pain.

- Exercise therapy also can help reduce pain and improve function in low back pain and can improve global well-being and physical function in fibromyalgia.

- Multimodal therapies and multidisciplinary biopsychosocial rehabilitation-combining approaches (e.g., psychological therapies with exercise) can reduce long-term pain and disability compared with usual care and compared with exercise alone.

Backlash to CDC Guidelines

- It is feared that policies that would limit opioid prescriptions for the purpose of saving lives would cause people to turn to heroin or fentanyl.
- Patients on stable doses of opioids may feel that the benefits of treatment outweigh the risks and may be resistant to the idea of weaning.
- Non-pharmacologic physical and psychological treatments such as exercise and CBT are not always or fully covered by insurance, and access and cost can be barriers for patients.
- Patient cost also can be a barrier to weaning because insurance coverage of buprenorphine for opioid use disorder is often limited.
- The *CDC Guideline for Prescribing Opioids for Chronic Pain* is not intended for patients who are in active cancer treatment, palliative care, or end-of-life care.

The Montana Prescription Drug Registry

The Montana Prescription Drug Registry

- The Montana Prescription Drug Registry (MPDR) was authorized by the Montana Legislature in 2011 (§37-7-15 Montana Code Annotated [MCA]) and became functional in November 2012 as an online tool.

- The MPDR provides a list of controlled substance prescriptions to health care providers to improve patient care and safety. The program may also be used to identify potential misuse, abuse and/or diversion of controlled substances.

- The MPDR's online service offers prescribers and pharmacists the ability to search their patient's medical history for controlled substance prescriptions, Schedules II - V.

- Providers can review their patients' prescription use patterns and confirm their history of controlled substances. The information in the MPDR can assist providers in optimizing patient treatment plans and, potentially, deterring diversion of controlled substances.

The Montana Prescription Drug Registry

- **Where does the MPDR's prescription information come from?** All pharmacies holding an active Montana license, with the exception of Wholesale Drug Distributors, are required to report to the MPDR within 8 days of the date the prescription was dispensed (§37-7-1503 MCA).

- **What data are stored in the MPDR?** Pharmacies submit the detailed information they are required by law to collect for all controlled substance prescriptions they dispense. This includes information that identifies the patient and the prescriber, the pharmacy, the drug name, strength and dosage, refill information, and how the patient paid for their prescription.

- **Who administers the MPDR?** The Montana Board of Pharmacy is responsible for the operation and maintenance of the MPDR (§37-7-1502 MCA). The Board of Pharmacy is administratively attached to the Department of Labor and Industry.

Putting Guidelines Into Practice

Putting Guidelines into Practice

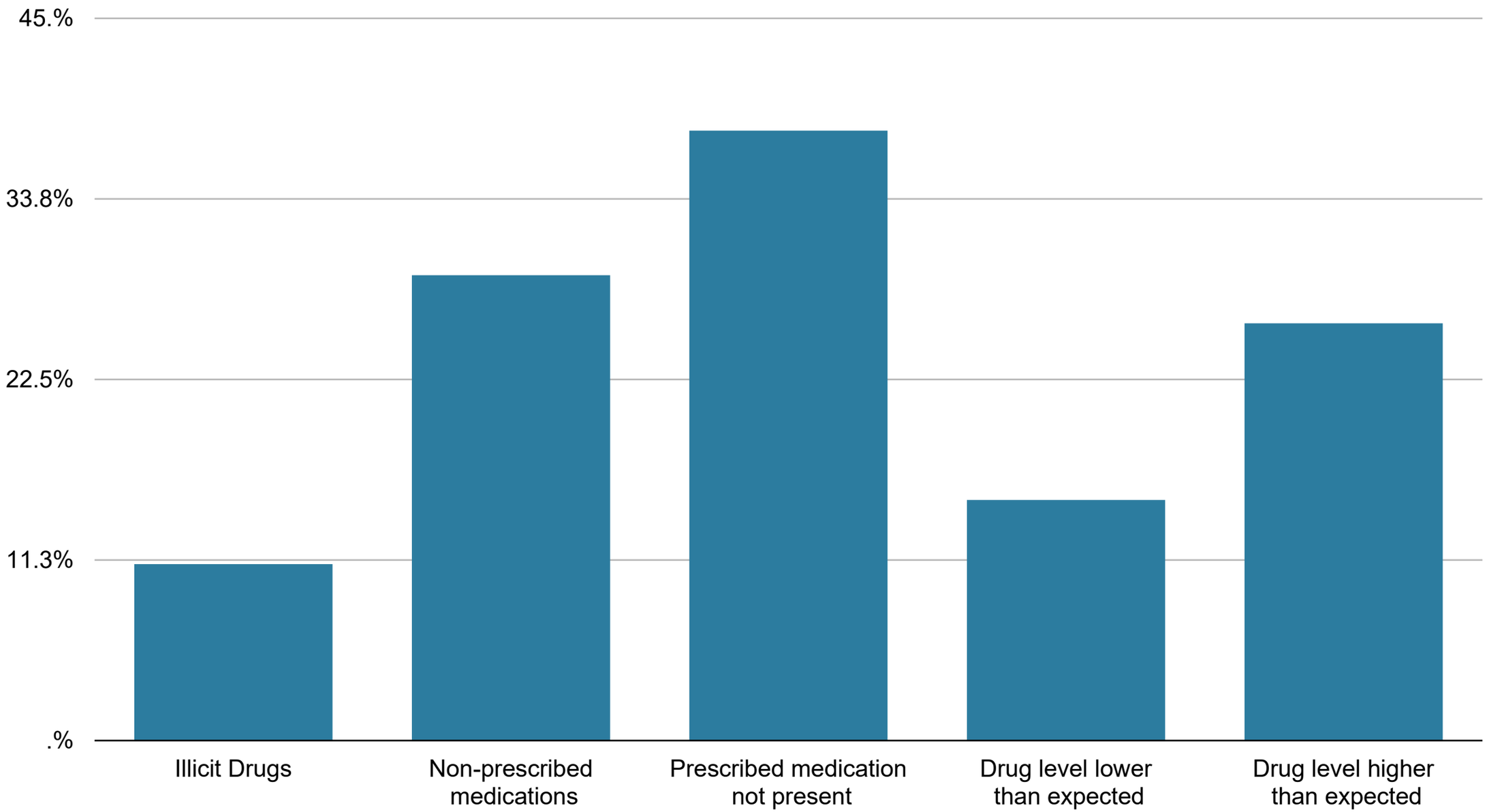
- Physicians should discuss risks and benefits of opioid therapy with patients in a collaborative and sharing manner.

- Before starting any opioids physician and patient should create a “pain contract” and establish mutually agreed-upon treatment goals with respect to function as well as opioid dose reduction goals. Clinicians seeing new patients already receiving opioids should establish a pain contract for any continued opioid therapy.

- The pain contract helps to clarify expectations regarding how opioids will be pre-scribed and monitored, as well as situations in which opioids will be discontinued or doses tapered (e.g., if treatment goals are not met, or adverse events occur).

- Physicians should review Prescription Drug Monitoring Program data and consider if urine drug testing is warranted.

Urine Tox Results in Chronic Pain Patients on Opioid Therapy



Overall test results (n=938,420)

Source: Couto JE, Goldfarb NI, Leider HL, Romney MC, Sharma S. High rates of inappropriate drug use in the chronic pain population. Popul Health Manag. 2009;12(4):185-190.

Putting Guidelines into Practice

- Surgery candidates should undergo “pre-hab”.
  1) expectations of surgery outcome and anticipated pain should be discussed and kept realistic
  2) transition from opioids to non-opioid medications
  3) cardiovascular exercise program with core strengthening and resistance training
  4) smoking cessation
  5) alcohol cessation
  6) psychotherapy to treat mood issues and maladaptive pain behavior.

- Clinicians should continue opioid therapy only if there is clinically meaningful improvement in pain and ***function*** that outweighs risks to patient safety.

- Medication-Assisted Therapy (MAT) plus counseling and other non-pharmacologic treatments should be used for weaning patients who are dependent or addicted and not receiving benefits that exceed harms. Weaning must be extremely gradual to be effective long-term.

Three Patient Journeys

Three Patient Journeys

Knee Surgery

Patients with acute, short-term post-surgical or post-procedural pain

Back Pain

Patients with chronic pain who are on a stable regimen that is not escalating

Generalized Pain

Patients with decreasing relief from opioids, escalating doses or side effects

Three Patient Journeys

Knee Surgery

Patients with acute, short-term post-surgical or post-procedural pain

First,
Do No Harm

Three Patient Journeys

Back Pain

Patients with chronic pain who are on a stable regimen that is not escalating

Appropriate Dosage, Not Zero

Three Patient Journeys

Generalized Pain

Patients with decreasing relief from opioids, escalating doses or intolerance of side effects

Assess Benefits Against Harms

Thank you!

Responsible Opioid Prescribing Does Not Negate Compassionate Pain Management

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ARCHIVED SLIDES

Mode of Action

- μ-receptor (Endorphins)
  → Analgesia Euphoria
- κ-receptor (Dynorphines)
  → Analgesia Sedation
- δ-receptor (Enkephalins)
  → Analgesia Dysphoria