Pharmaceutical Interventions for Pain

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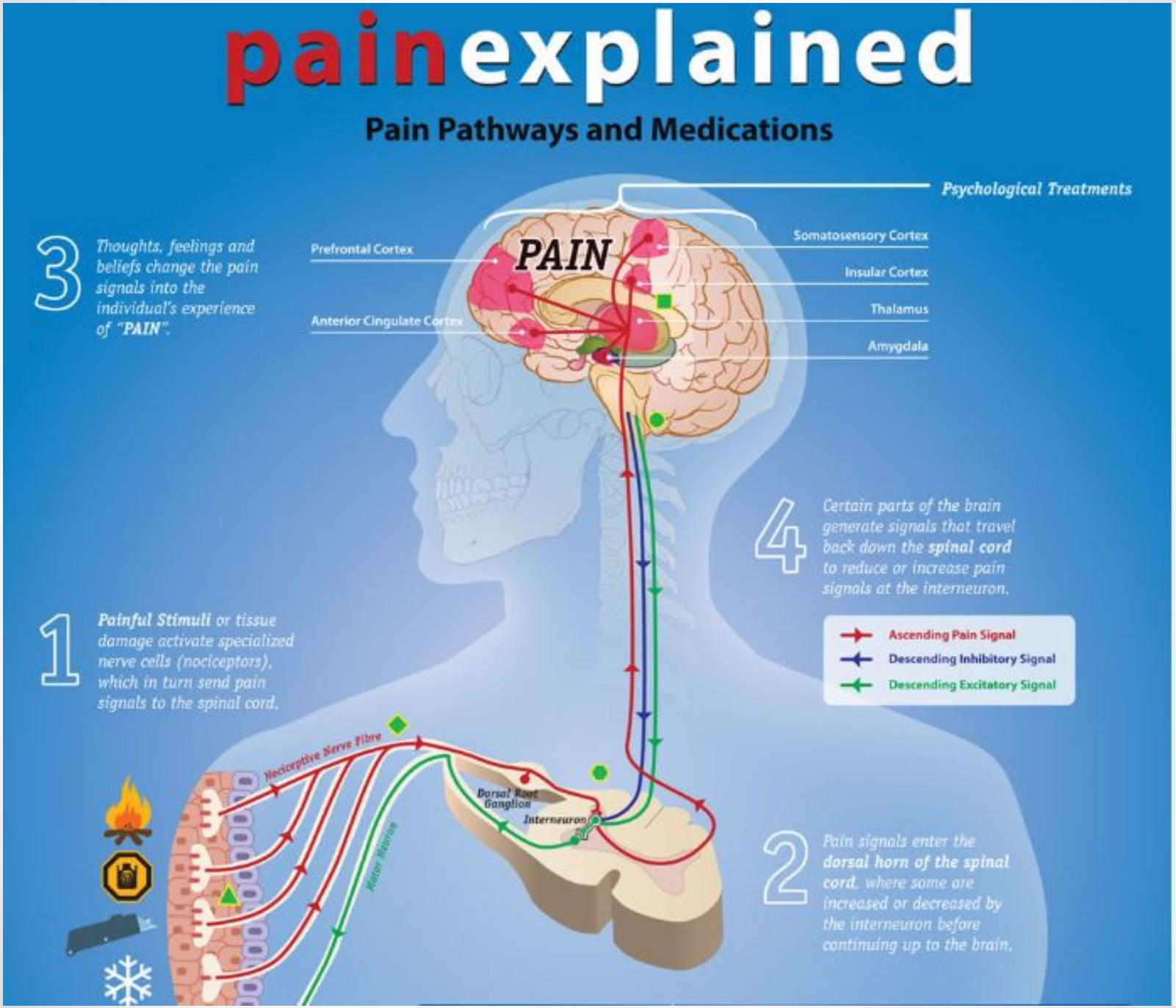
Acute vs. Chronic pain

- **Acute pain**
  - Reaction to stimulus, often very helpful
- **Chronic pain**
  - Generally considered to be pain lasting longer than 3 months
  - Pain has outlasted it's usefulness

painexplained

Pain Pathways and Medications



Catastrophizing

"The tendency to magnify the threat value of pain stimulus and to feel helpless in the context of pain, and by a relative inability to inhibit pain-related thoughts in anticipation of, during or following a painful encounter."

Quartana et al. 2009

Catastrophizing

- Patient begins having **fear** of pain, **avoidance**, **hypervigilence**
- These will reduce the threshhold at which they experience future pain.

Attention to pain

- Catastrophizing pain results in marked increase in attention to pain and pain stimuli. This distracts attention away from other tasks, resulting in decreased attention and cognitive performance.

Trauma and Pain

- Research study of 17,000 participants.
- Adverse Childhood Experiences (ACEs) can affect an individual's physical and emotional health throughout the life span.
- Trauma/traumatic experiences are far more prevalent than previously recognized.

Trauma and Pain

- Significant role of Adverse Childhood Events on multiple aspects of health, including depression, cardiovascular disease, cancer, substance use disorders and pain

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CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

R. F. Anda, MD, MS
Centers for Disease Control and Prevention

What is our goal?

- Get rid of all your pain?
- Make you forget you have pain?
- Decrease your pain and improve your function?

Complementary and Alternative Medicine

- "A broad set of health-care practices that are not part of a country's own tradition and not integrated into the dominant health-care system."

World Health Organization, 2004

Interventional Procedures

- Anesthetic Infusions
- Trigger Point Injections
- Local Neural Blockade
- Spinal Steroid Injections and Facet Injections
- Sympathetic Blockade
- Spinal Cord Stimulation

TENS

- Provides electrical impulses which confuse the pain receptors as well as pain pathway

Neurostimulation Therapy

- Delivers electrical signals to the epidural space
- Inhibits pain signals before they reach the brain and replaces them with a tingling sensation that covers the specific areas where pain is felt
- Indicated for management of chronic, intractable pain of the trunk and/or limbs, including unilateral or bilateral pain

Benefits of Neurostimulation

- An effective method of pain control for many patients when used as directed
- May reduce the need for pain medications
- Less invasive than surgical alternatives
- Reversible—can be discontinued or, if desired by the patient, surgically removed
- Systems reprogrammable without surgery
- Trial helps assess patient response
- Patient control within preprogrammed limits

Kumar K, Taylor R, Jacques L, et al. *Neurosurgery*. 2008;63:762-770.

Burchiel KJ, Anderson VC, Brown FD, et al. Prospective, multicenter study of spinal cord stimulation for relief of chronic back and extremity pain. *Spine.* 1996;21:2786-2794.

Spinal Injections

- Typical goal is to reduce inflammation around nerve
- Can be diagnostic or therapeutic

Medications

- Usually the first treatment people think of for pain
- On average medications will reduce chronic pain by no more than 30-40%
- Often do not have a corresponding improvement in physical or emotional functioning

- Wall&Melzack's Textbook of Pain Ch.42

Narcotics

- Bind to opiate receptors to block pain signals
- Receptors throughout spinal cord and brain (as well as gut)

Narcotics

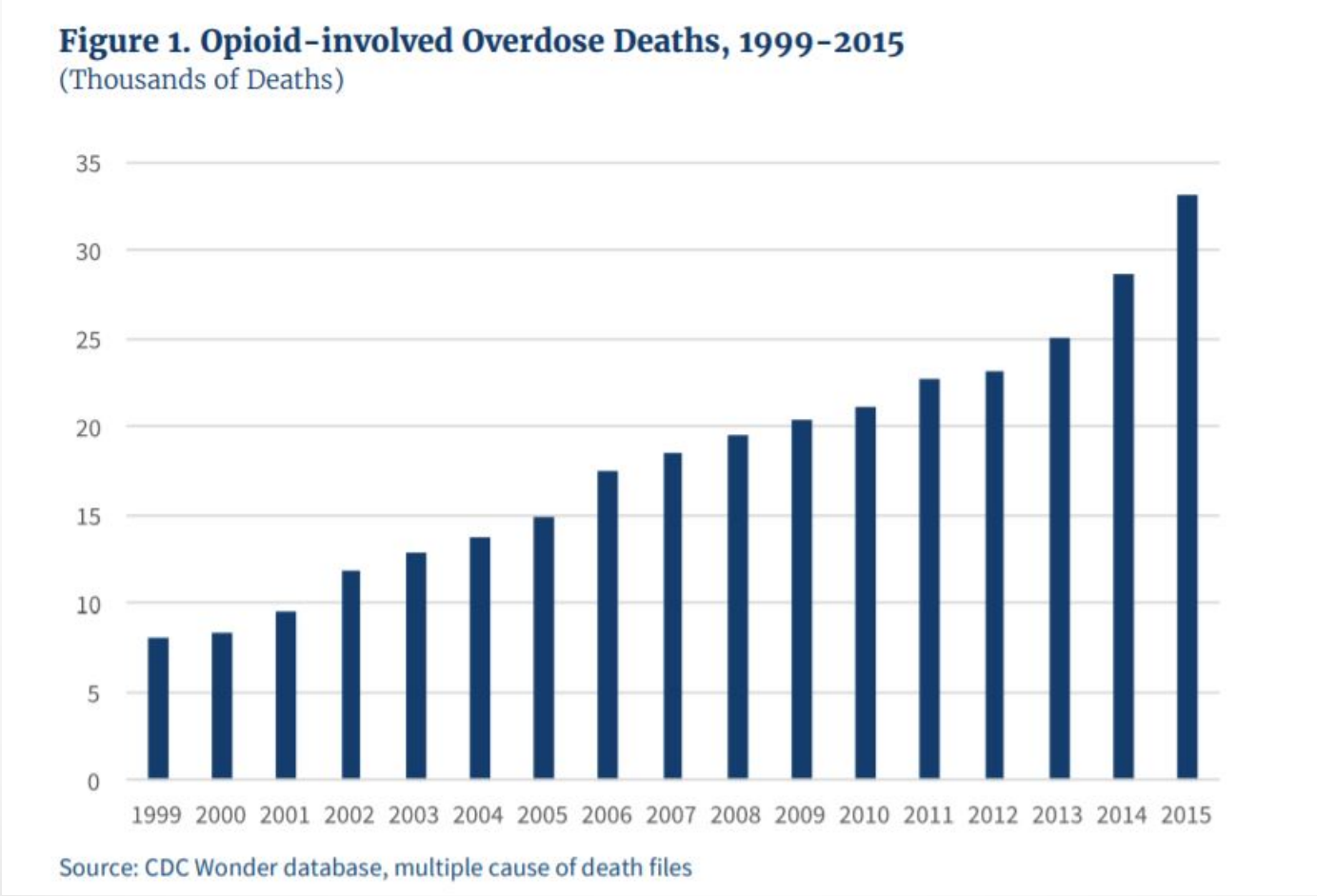
- Hydrocodone (Norco, Vicodin)
- Oxycodone (Oxycontin, Percocet)
- Hydromorphone (Dilaudid, Exalgo)
- Codiene (Tylenol #3)
- Morphine (MS Contin, MS IR)
- Fentanyl (Duragesic patch)
- Oxymorphone (Opana)
- Methadone
- Buprenorphine (Suboxone, Balbuca, Butrans)

Tramadol

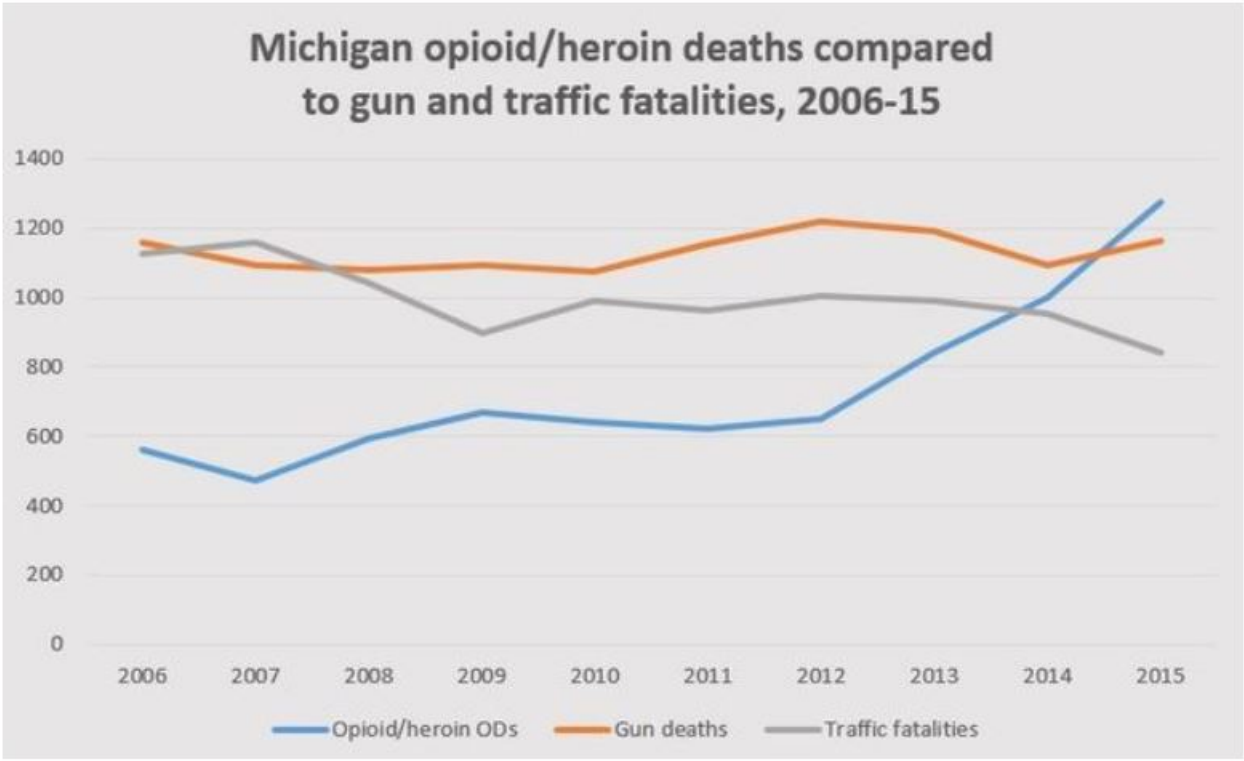
- Initially marketed as an "alternative" to opiates
- Has (mild) opiate as well as serotonin effect

Opiates The Best Medicine!

Opiates The Worst Medicine

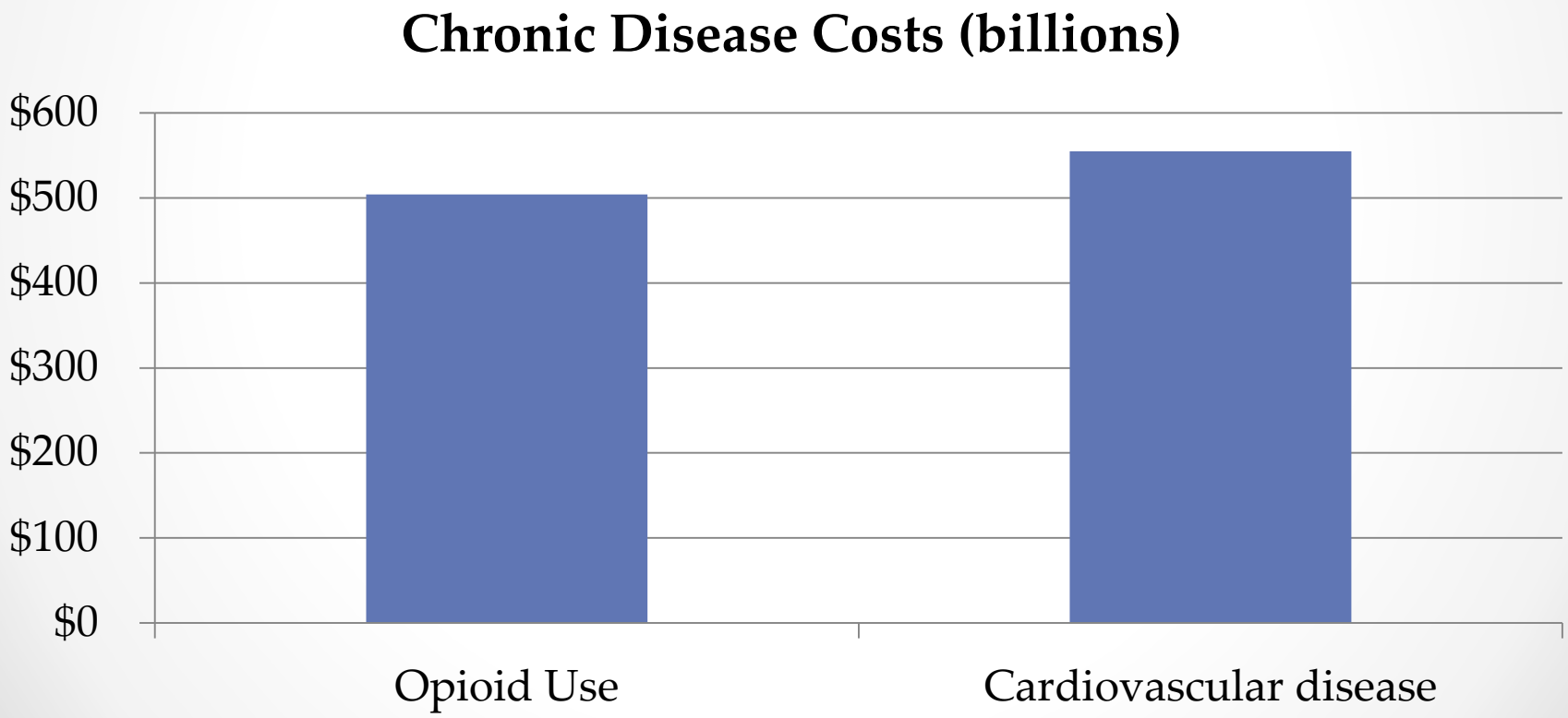


Deaths in Michigan

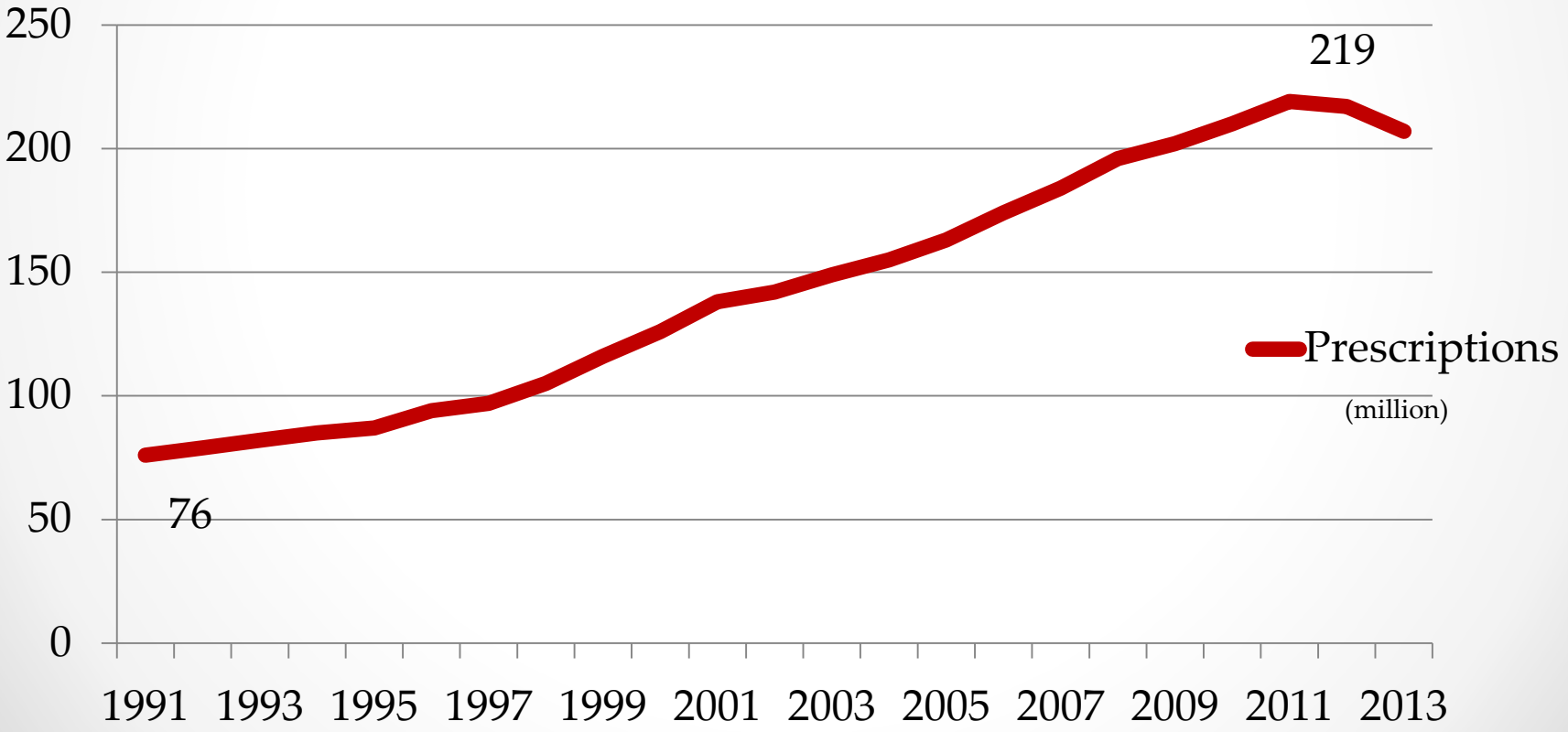


Source: Michigan Department of Health and Human Services

Cost of the Opioid Epidemic



Number of US Opioid Prescriptions



Opioid Therapy for Chronic Pain:

- 12 week studies: pain reduced 30% compared to placebo
- +/- functional improvement
- Majority of paints stop opioids: - efficacy?
- COT = less likely to return to work
- Patients with SUD or other MH disorders are more likely to receive long term COT
- >90 days COT = Long term: >1120mg ME = misuse
- "Adverse Selection": the likelihood of a patient receiving COT increases as the associated risks increases

Evidence for opiates

- 14 RCTs, 1201 patients, approximately 85/study
- Short follow-up, most less than 14 weeks
- Most compared opiate vs. placebo
- Substance abusers excluded
- Usually well defined pain causes (OA, RA)
- 13/14 showed benefit vs. placebo for pain (Analgesia)
- 7/13 showed no benefit for function (ADLs)

Membrane stabilizers

• Carbamazepine	Tegretol
• Oxcarbazepine	Trileptal
• Lamotrigine	Lamictal
• Gabapentin	Neurontin
• Pregabalin	Lyrica
• Valproic Acid	Depakote
• Topiramate	Topamax

Membrane stabilizers

- Medications which typically were originally used for seizure disorders
- Work by reducing the level of nerve impulses, therefore hopefully reducing pain
- This modulation of nerve impulses occurs both within the brain and on peripheral nerves

Membrane Stabilizers

- Carbamazepine: trigeminal neuralgia, neuropathy
- Gabapentin: neuropathy, facial pain syndromes, reflex sympathetic dystrophy, central pain, migraine prophylaxis
- Lamotrogine: trigeminal neuralgia, peripheral and central neuropathy
- Pregabalin: post herpetic neuralgia, diabetic neuropathy

Table 1

Anticonvulsants Used as Adjuvant Analgesics

	Dose Range	Dosing Interval
Gabapentin	300–3,600 mg/d	At bedtime to four times daily
Carbamazepine	100–1,600 mg/d	Twice a day to four times daily
Lamotrigine	150–500 mg/d	Twice a day
Phenytoin	100–300 mg/d	Daily
Topiramate	25–400 mg/d	Twice a day
Divalproex	150–3,000 mg/d	Three times a day
Clonazepam	1–10 mg/d	Twice a day
Oxcarbazepine	300–2,400 mg/d	Twice a day
Zonisamide	100–400 mg/d	Twice a day (daily)

Membrane stabilizers

Patients often have side effects

- Sedation
- Dizziness
- Gait disturbance
- Nausea
- Changes in cognitive function
- Changes in labs
- Rash (Lamictal)

Gabapentinoids

- Word of caution: Abuse potential
  - Euphoria
  - Potentiation of opiates

Antidepressants

- Analgesic mechanism is thought to be mediated by enhancement of inhibition in descending pain pathways
- Synthesis and release of pain promoting neurotransmitters are reduced by antidepressants
- Antidepressants may augment opiate effects within spinal cord
- Treatment of depression which often accompanies chronic pain

Antidepressants

- TCA: neuropathy, headaches, fibromyalgia, OA and RA
- SSRI: diabetic neuropathy and tension headache
- SNRI: fibromyalgia, peripheral and diabetic neuropathy
- Remeron: fibromyalgia and chronic daily headache

TCA

Drug	Starting Doses for Pain	Frequency	Maximum Dose
Amitriptyline (Elavil)	25-50mg	daily	150mg/day
Desipramine (Norpramine)	25mg	daily	150mg/day
Imipramine (Tofranil)	50mg	daily	150mg/day
Nortriptyline (Pamelor)	10-20mg	daily	160mg/day

TCA Side Effects

- Anticholinergic
- Orthostatic hypotension
- QT prolongation
- Sedation

SNRI

Drug	Starting Dose	Frequency	Maximum Dose
Duloxetine (Cymbalta)	30 mg	Daily	120mg
Milnacipran (Savella)	50 mg	Twice daily	200mg
Desvenlafaxine (Pristiq)	50 mg	Daily	50 mg*
Venlafaxine (Effexor)	37.5 – 75mg	daily	300 mg
Levomilnacipran (Fetzima)	20 mg	Daily	120 mg

SNRI Side Effects

- Nausea
- Dry mouth
- Dizziness
- Headache
- Excessive sweating
- Hypertension (venlafaxine, desvenlafaxine)
- Discontinuation symptoms (++venlafaxine)
- Tiredness
- Constipation
- Insomnia

NSAIDS

- Reduce production of COX-1 and COX-2, resulting in reduction in production of prostaglandins and other pro inflammatory molecules
- COX-1 increases platelets and protects the stomach

NSAID Side Effects

- Gastrointestinal
- Renal
- Cardiac

NSAID-Acetic Acid

Diclofenac	Volteran
Etodolac	Lodine
Indomethacin	Indocin
Ketorolac	Toradol
Nabumetone	Relafen
Sulindac	Clinoril
Tolmetin	Tolmetin

NSAID- Salicylates

Aspirin	
Diflunisal	Dolobid
Magnesium salicylate	Doan's Pills
Salsalate	Disalcid

NSAID- Propionic Acid

Fenoprofen	Nalfon
Flurbiprofen	Ansaid
Ibuprofen	Motrin
Ketoprofen	Orudis
Naproxen	Aleve, Anaprox,
Oxaprozin	Daypro

NSAID- Fenamates

Meclofenamate	Meclomen
Mefenamic Acid	Ponstel

NSAID- Oxicam

Meloxicam	Mobic
Piroxicam	Feldene

NSAID- COX2

Celecoxib	Celebrex

Acetaminophen (Tylenol)

- Pain relief and fever reduction
- Very effective for pain, patients rarely agree
- Available as an IV medication

Topicals

- Capsaicin – irritant
- Lidocaine patch or gel
- Diclofenac gel