Updates In Best Practice: Opioid Management

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- No conflicts of interest.

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Learning Objectives

- Defining acute pain and outlining its application to surgical care
- Summarizing the optimal use of opioids throughout the perioperative continuum
- Reviewing medications used for opioid use disorder (MOUD)

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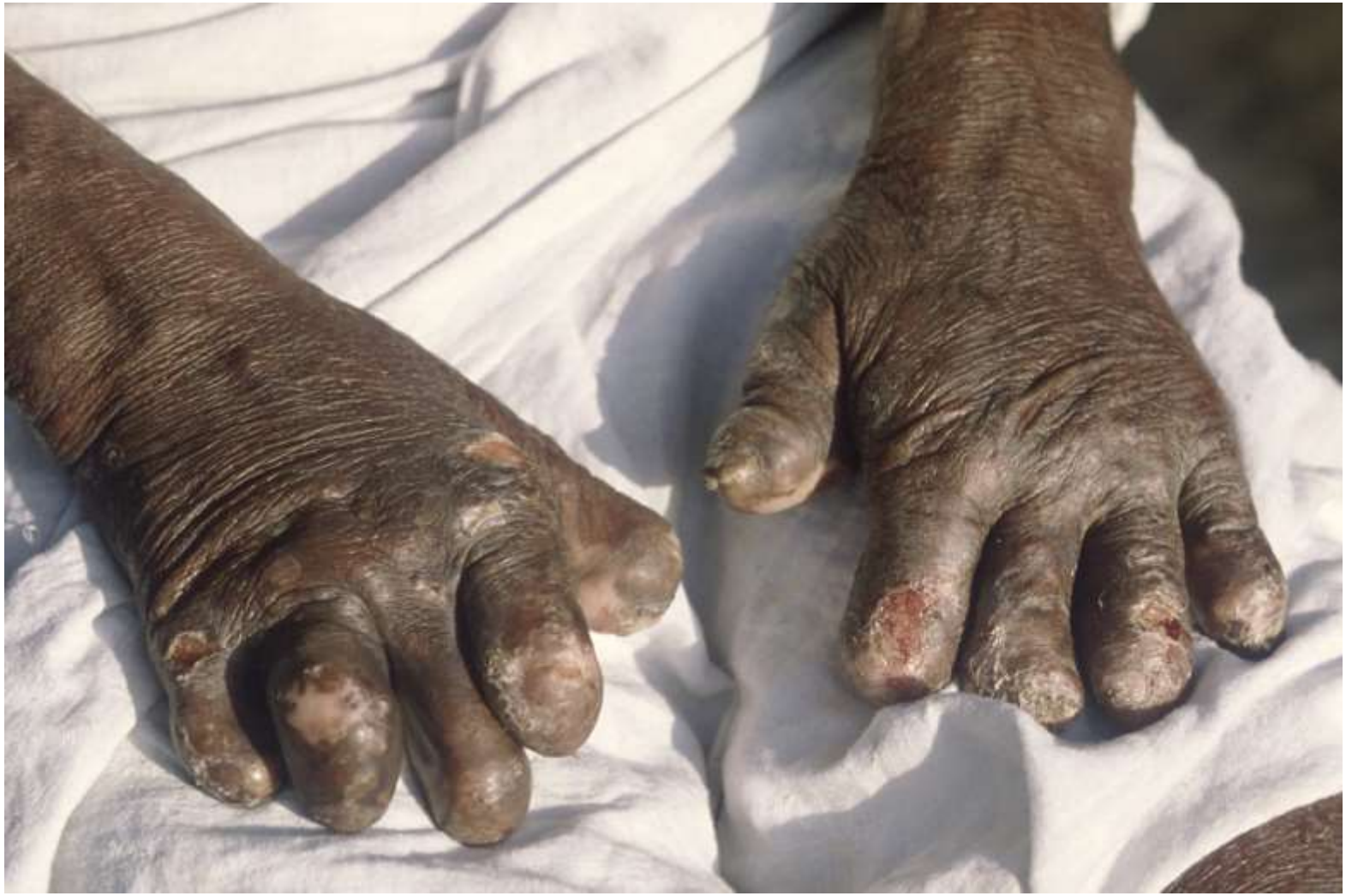
THE PAIN STARTS IN MY HUSBAND'S LOWER BACK, THEN IT TRAVELS UP HIS SPINE TO HIS NECK, THEN IT COMES OUT HIS MOUTH AND INTO MY EARS. AND THAT'S WHY I GET THESE HEADACHES.

Acute Pain

- < 3 months
- Actual tissue damage or threat of that damage, a warning/alarm; we recover; helpful
- Leprosy (Hansen's) disease – damaged sensory nerves, cannot register pain
- Monofilament testing in a diabetic, need to visually inspect for ulcers
- "Congenital Analgesia"
  - PRDM12 gene/Sodium Channelopathy
  - Too much endorphins in the Brain
  - Naloxone therapy Treatment
  - Often Die During Childhood

- A symptom of disease or injury whereas chronic pain is the disease itself



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Chronic Pain

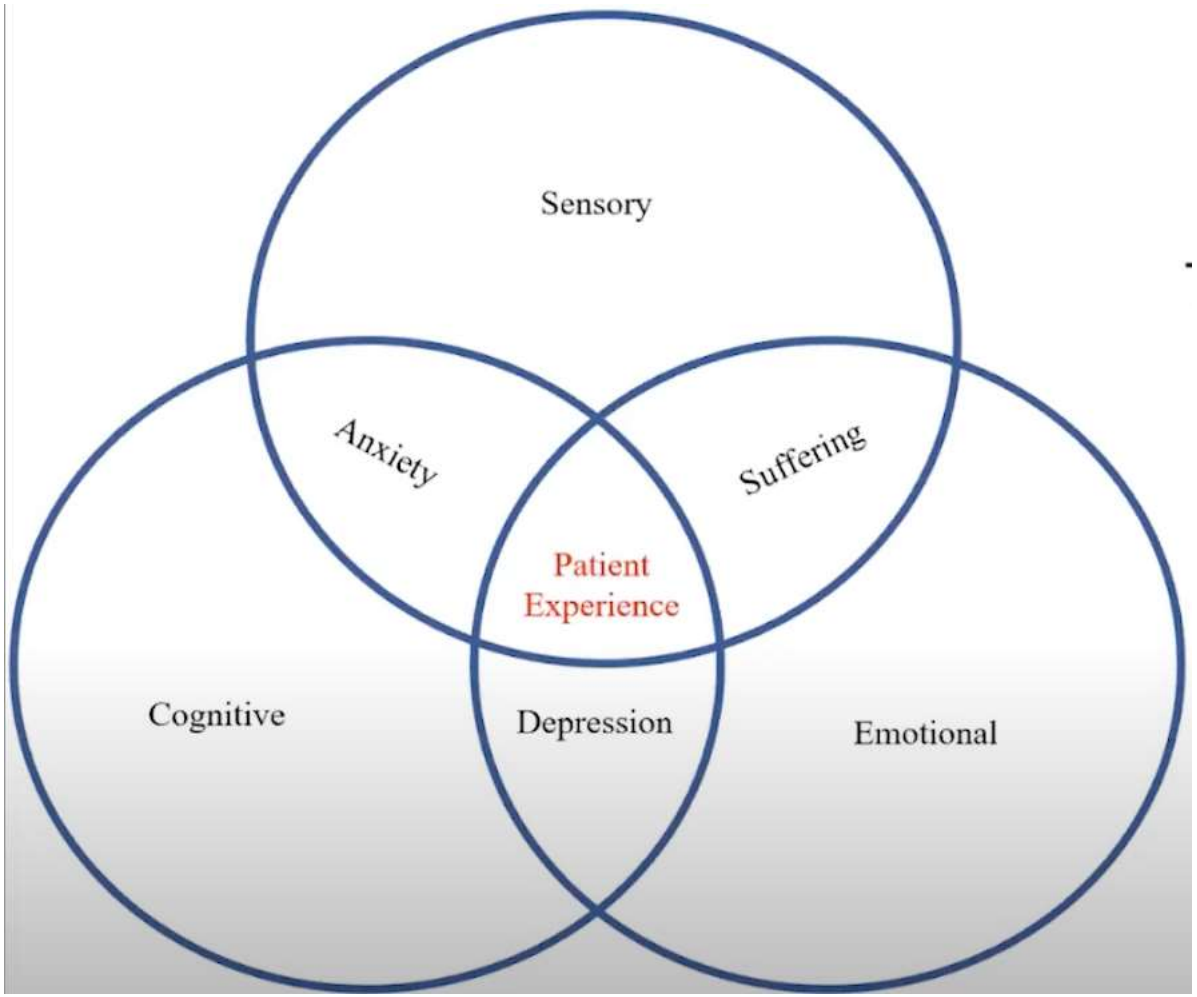
- Chronic pain: Harder to find exact source of the pain
  - We often order an MRI of the spine and may see multiple pathologies with variable pain patterns
  - We want treatment to focus on exercise, being outside, socialization, going back to work but patients stay inside, stay in a chair, start to get depressed
  - Overactivity of ascending pain signals or underactivity of descending pain pathways
- Pain > 3 months
- A disease itself

Pain

- An unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage
- With the Numeric Scale of 0-10 sensory aspect of pain can be a 3 but if depressed/anxious the emotional component can raise the manifested score to a 5/10
- Emotional components lead to suffering, more likely to get more pain medication

Cognitive Aspect of Pain

- An art to breed optimism in a patient
- Placebo affect: if you give a saline flush and advertise it up saying this will make you feel better, “You will be back together in no time”; patients will indeed feel 20 % better
- Nacebo affect: a situation where a negative outcome occurs due to a belief that the intervention will cause harm. “You had a huge back surgery it was much more extensive than I thought it would be”; patients will feel 20 % worse



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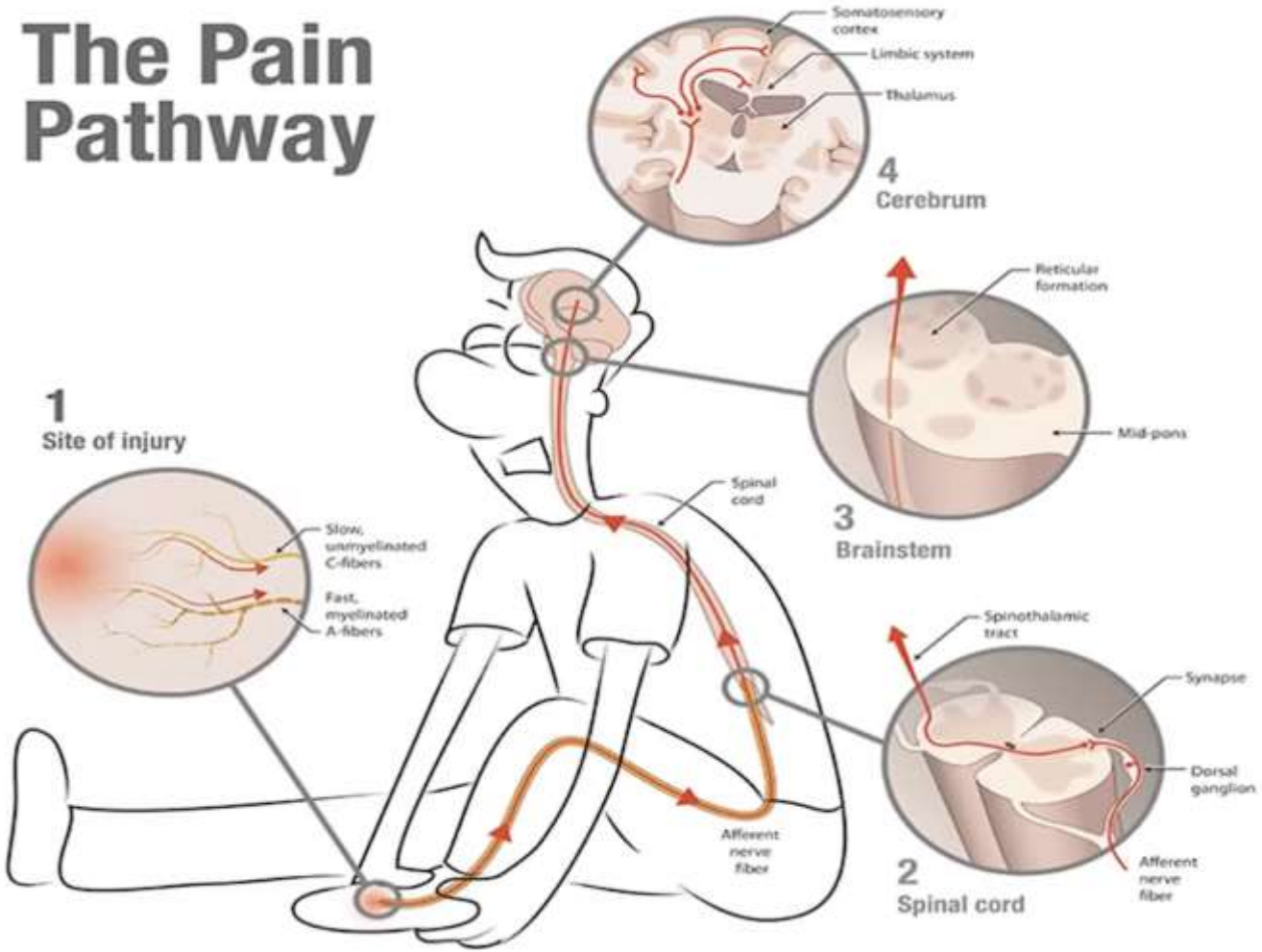
Our Brain Modulates Pain



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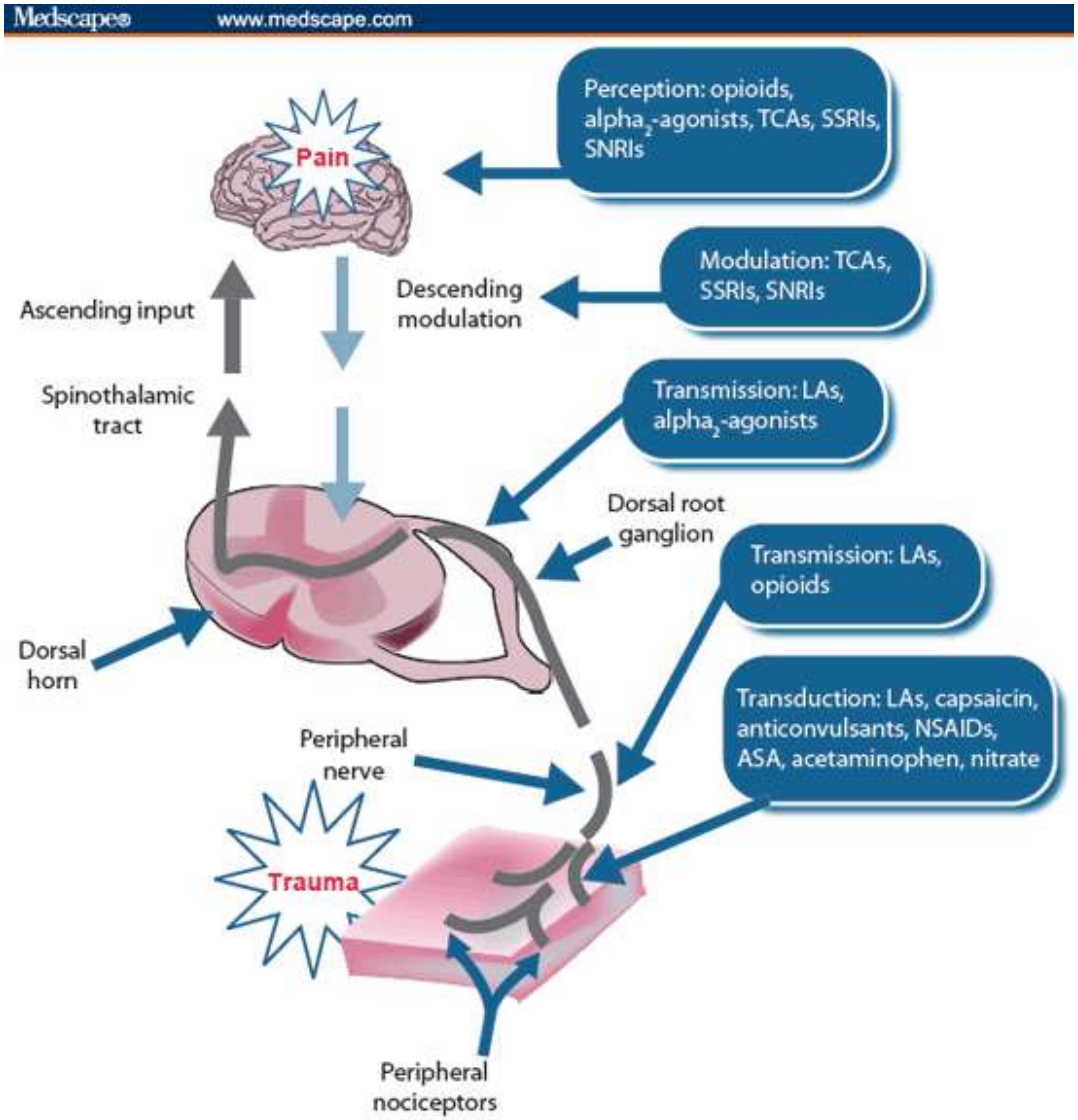
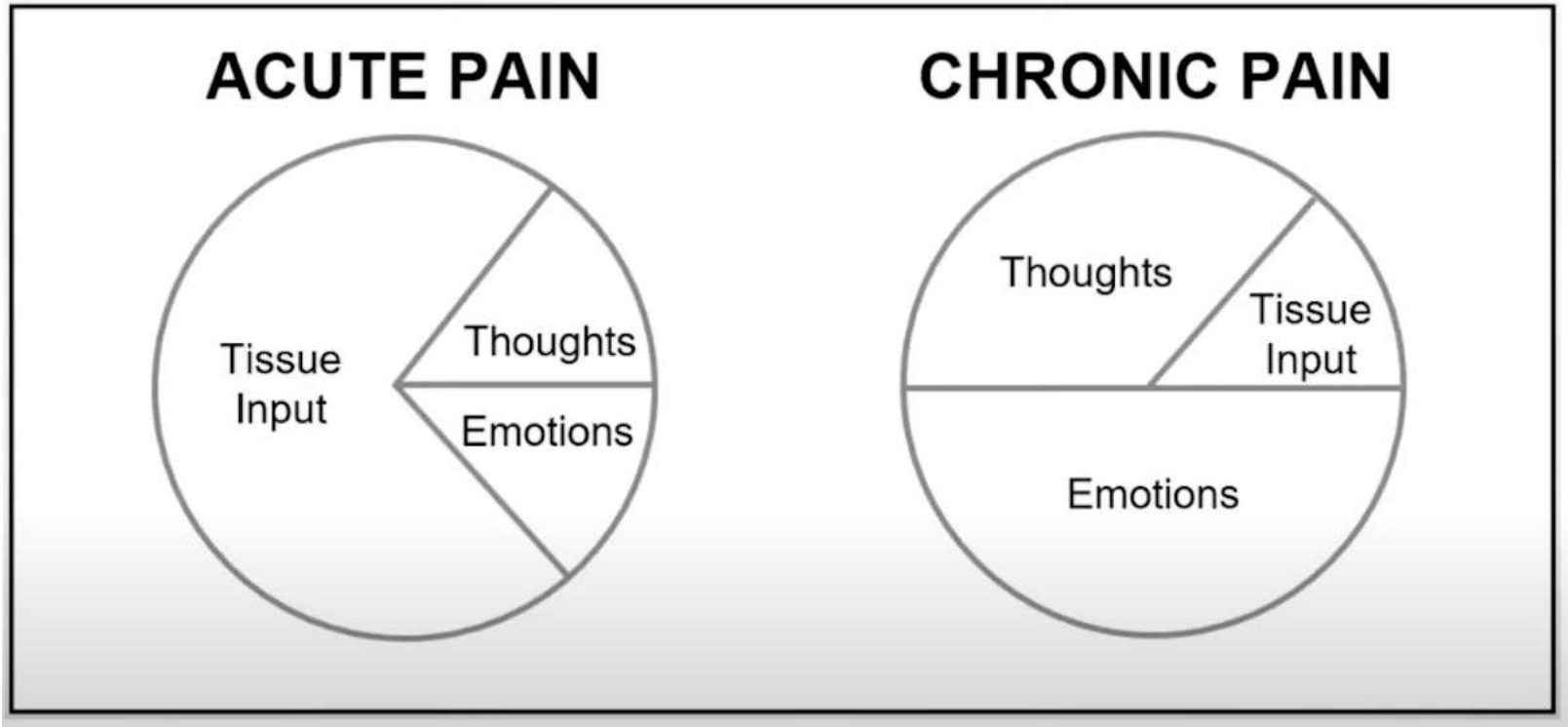
The Dress

Variable Neuroscience and Color Perception

Multimodal Analgesia





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Mechanisms of Pain

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Perioperative Pain Management

Why Treat Pain?

- Basic human right!
- ↓ pain and suffering
- ↓ complications – *next slide*
- ↓ likelihood of chronic pain development
- ↑ patient satisfaction
- ↑ speed of recovery → ↓ length of stay → ↓ cost
- ↑ productivity and quality of life

Adverse Effects of Poor Pain Control

- CVS: MI, dysrhythmias
- Resp: atelectasis, pneumonia
- GI: ileus, anastomotic failure
- Endocrine: "stress hormones"
- Hypercoagulable state: DVT, PE
- Impaired immunological state
  - Infection, cancer, wound healing
- Psychological:
  - Anxiety, Depression, Fatigue

Chronic Post-surgery/trauma Pain

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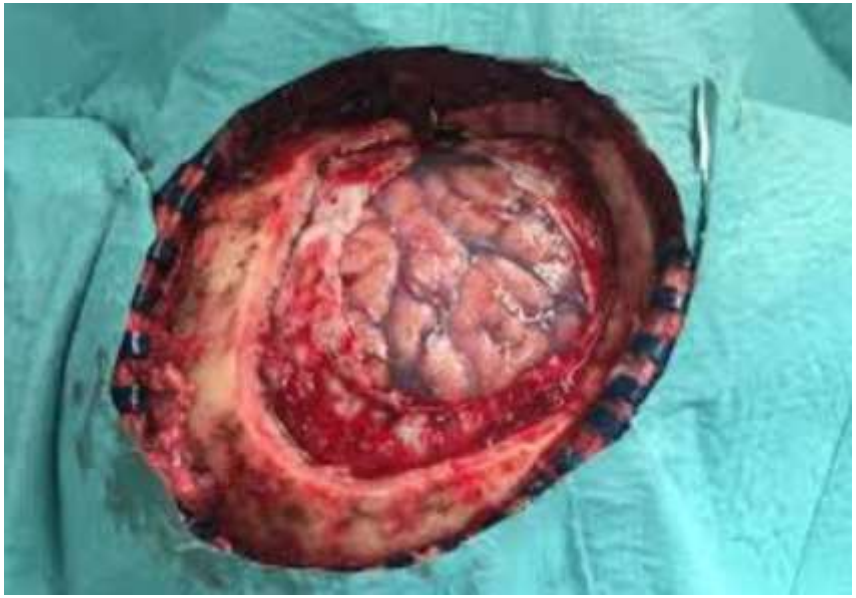
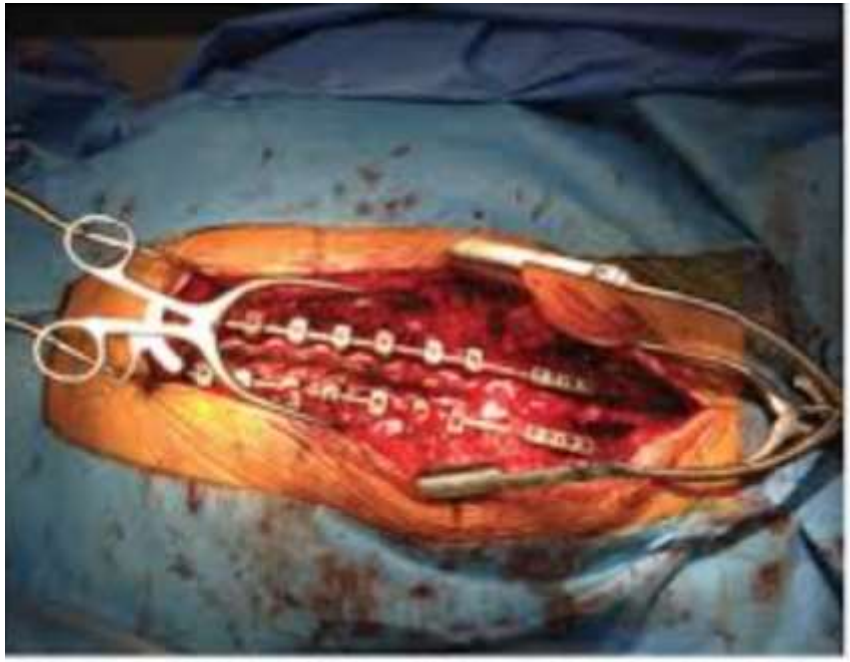
Neurosurgery

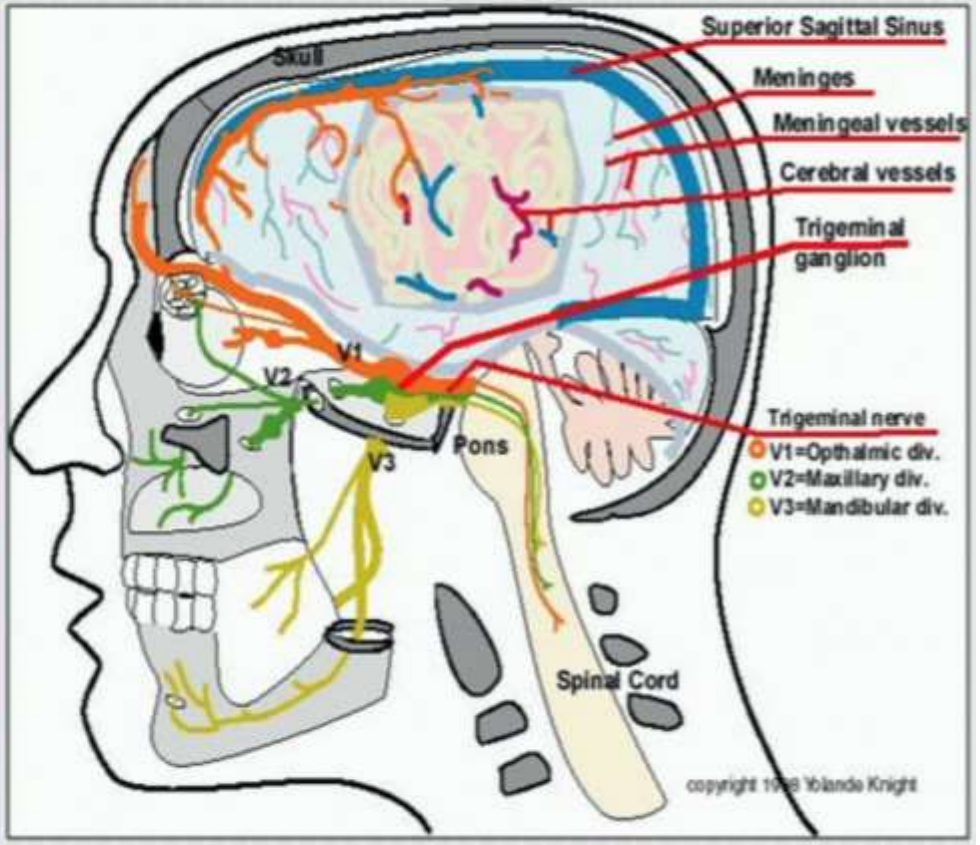




Head Pain – Sources

Dura
Dural veins and arteries
Intracranial arteries
Cranial nerves 3,5,7,9,10
C1-3 roots
Periosteum
Scalp
Scalp muscles
Scalp vessels
Sinuses
Eyes
Ears
Teeth, TMJ
Carotids, vertebrals
C-spine periosteum
Cervical muscles

Insensitive:
parenchyma
pia, arachnoid, ventricles
skull



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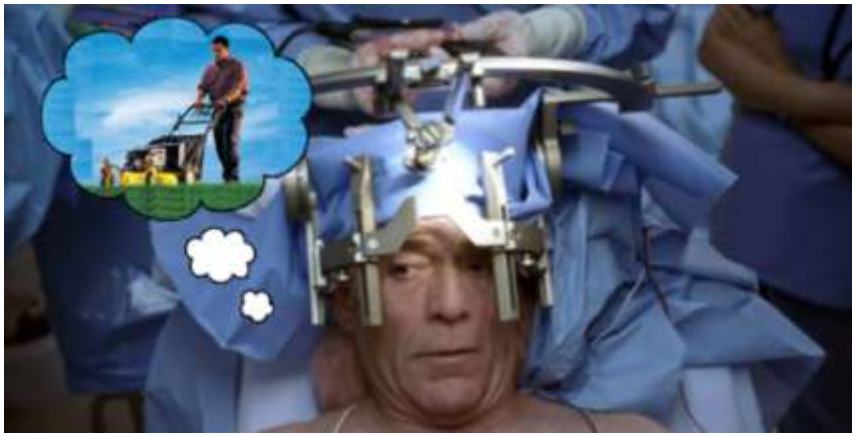
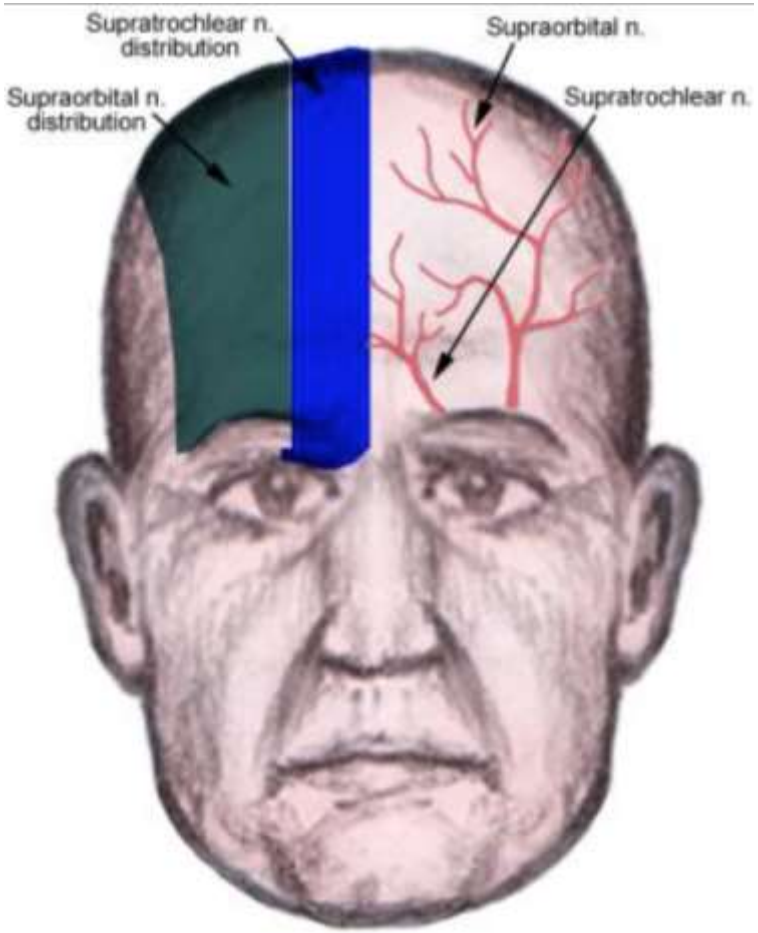
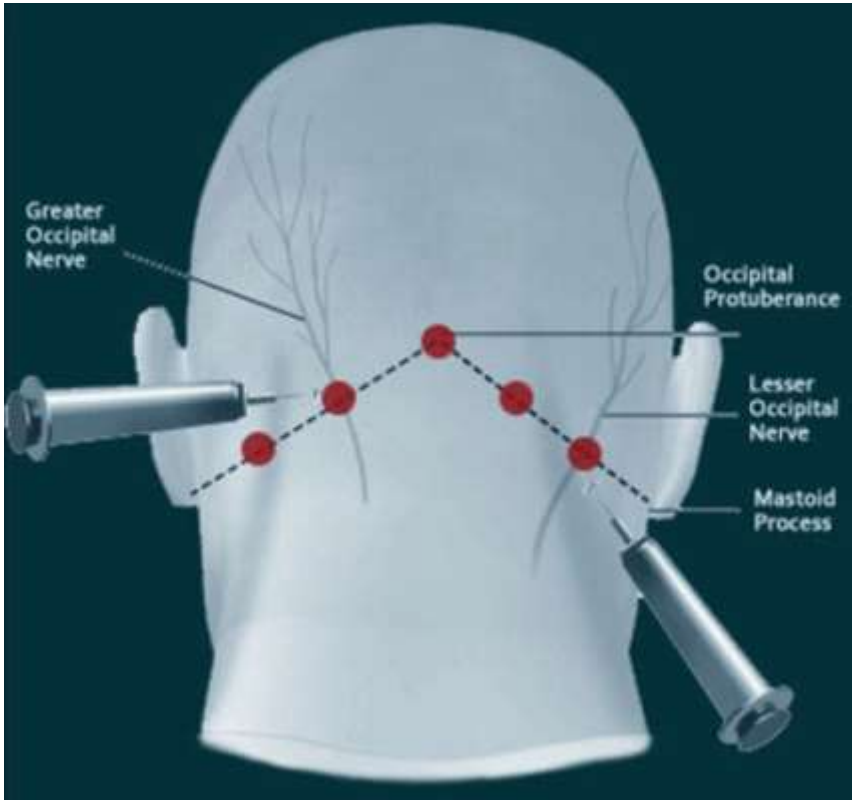
Craniotomy

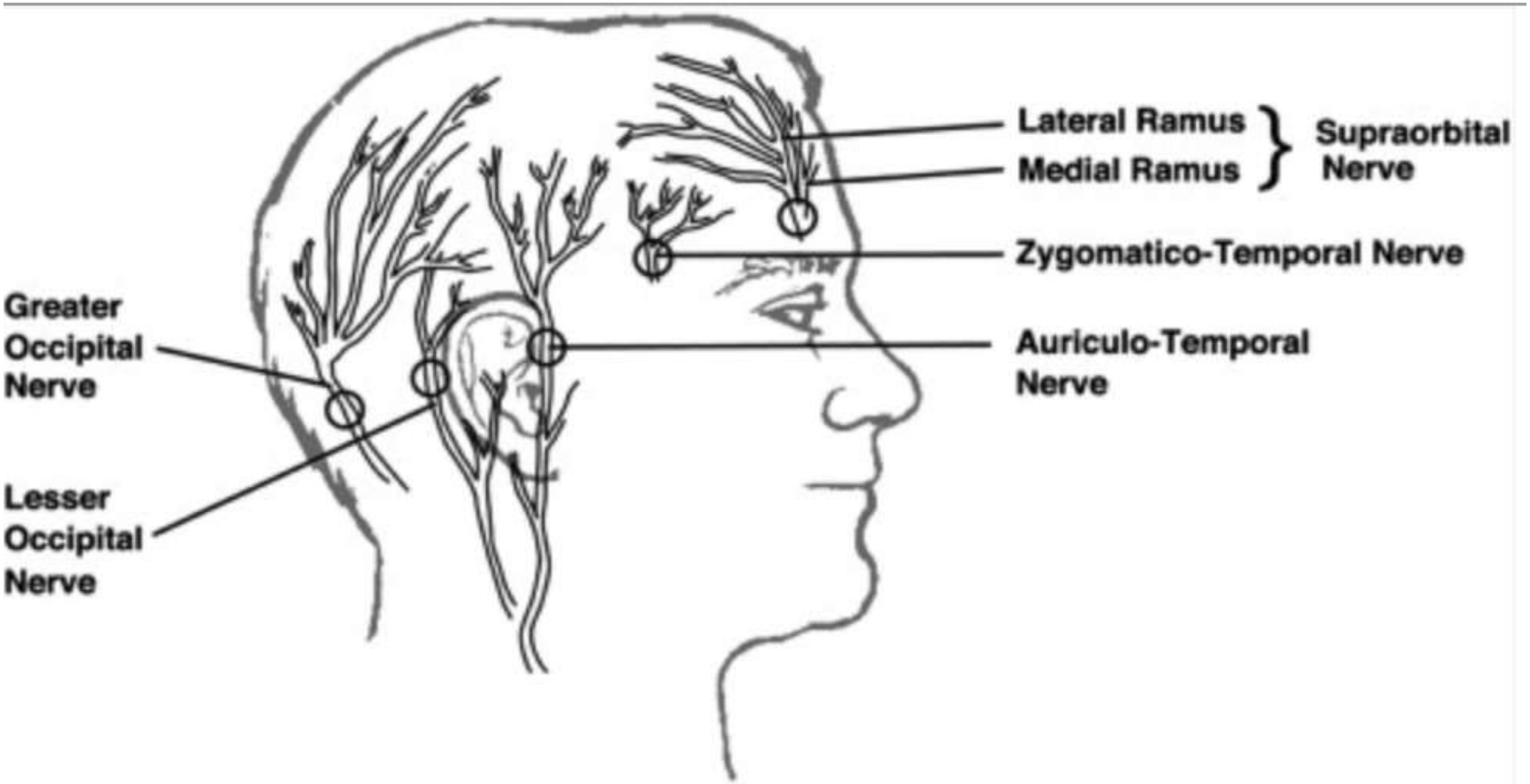


- Can even do an “Awake” Craniotomy
  - Remifentanil
  - Dexmedetomidine
  - Tylenol
- Quick On/Off
  - Do Not Want to Blunt Neuro-Exam
  - CO2/ICP response curve not altered
  - Nausea/Vomit Mitigation

Scalp Blocks







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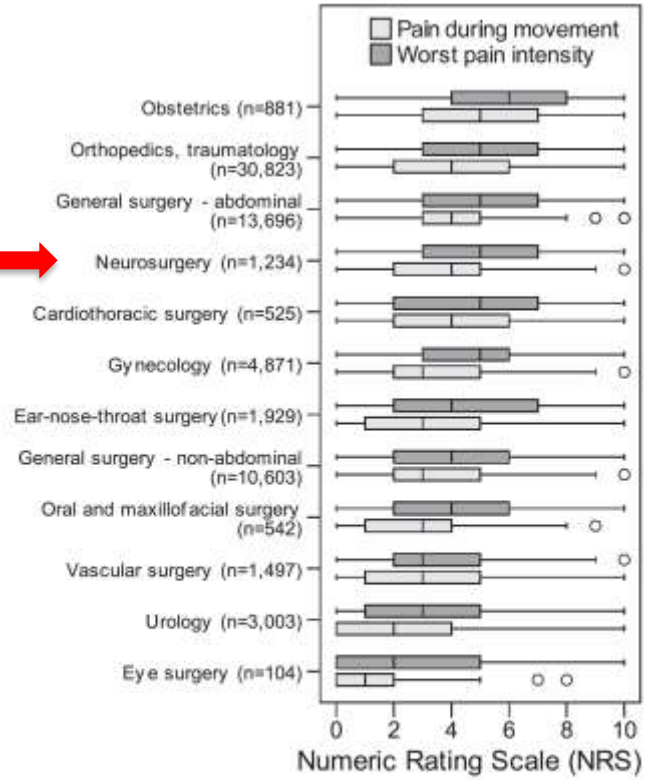
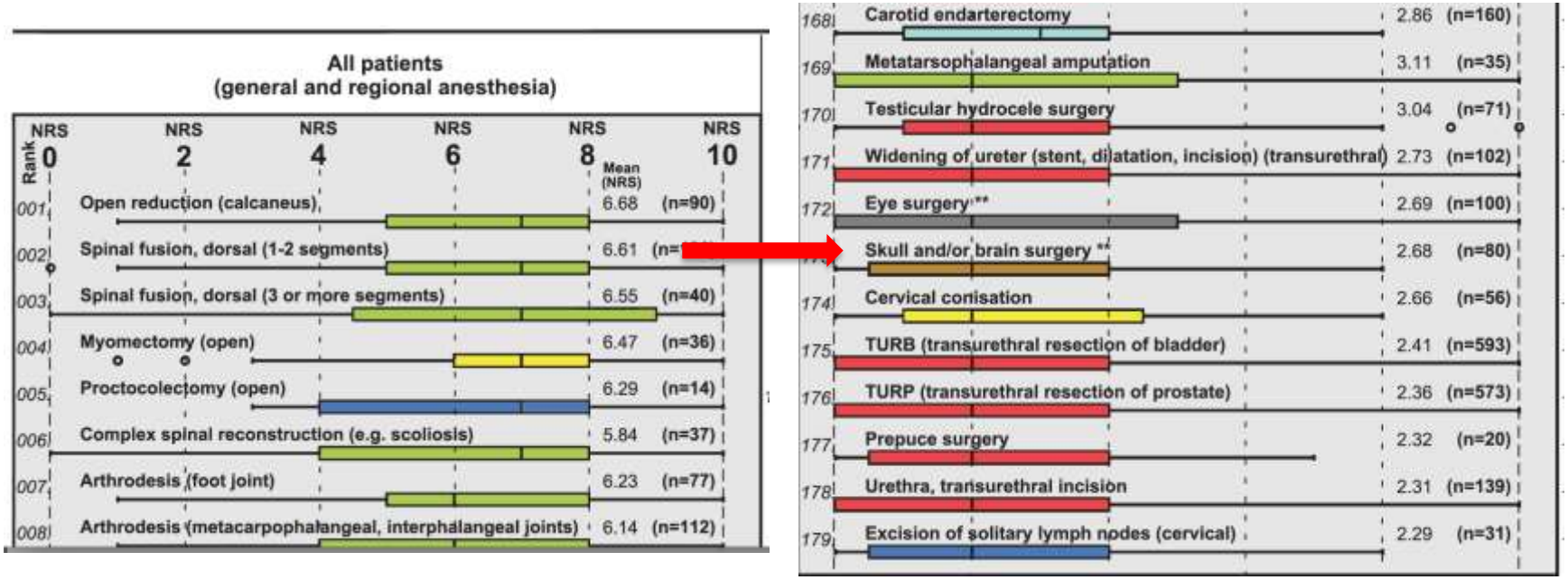


Fig. 2. Comparison of pain intensities between surgical specialties. Worst pain and pain during movement since surgery were assessed on the first postoperative day.

Anesthesiology 2013; 118:934-44


All patients
(general and regional anesthesia)
Rank
NRS 0
NRS 2
NRS 4
NRS 6
NRS 8
NRS 10
Mean (NRS)
001 Open reduction (calcaneus) 6.68 (n=90)
002 Spinal fusion, dorsal (1-2 segments) 6.61 (n=
003 Spinal fusion, dorsal (3 or more segments) 6.55 (n=40)
004 Myomectomy (open) 6.47 (n=36)
005 Proctocolectomy (open) 6.29 (n=14)
006 Complex spinal reconstruction (e.g. scoliosis) 5.84 (n=37)
007 Arthrodesis (foot joint) 6.23 (n=77)
008 Arthrodesis (metacarpophalangeal, interphalangeal joints) 6.14 (n=112)
168 Carotid endarterectomy 2.86 (n=160)
169 Metatarsophalangeal amputation 3.11 (n=35)
170 Testicular hydrocele surgery 3.04 (n=71)
171 Widening of ureter (stent, dilatation, incision) (transurethral) 2.73 (n=102)
172 Eye surgery** 2.69 (n=100)
Skull and/or brain surgery ** 2.68 (n=80)
174 Cervical conisation 2.66 (n=56)
175 TURB (transurethral resection of bladder) 2.41 (n=593)
176 TURP (transurethral resection of prostate) 2.36 (n=573)
177 Prepuce surgery 2.32 (n=20)
178 Urethra, transurethral incision 2.31 (n=139)
179 Excision of solitary lymph nodes (cervical) 2.29 (n=31)

- Common Conception → "Opioids are the most potent medications we have for treatment of pain"
  - Let's not confuse potency with efficacy
  - A lot of clinical benefit comes from a calming/relaxing affect
  - With tolerance, anxiety increases
  - Same can be seen with depression
  - In chronic use, little data to support pain reduction or augmented functionality

Triple Wave

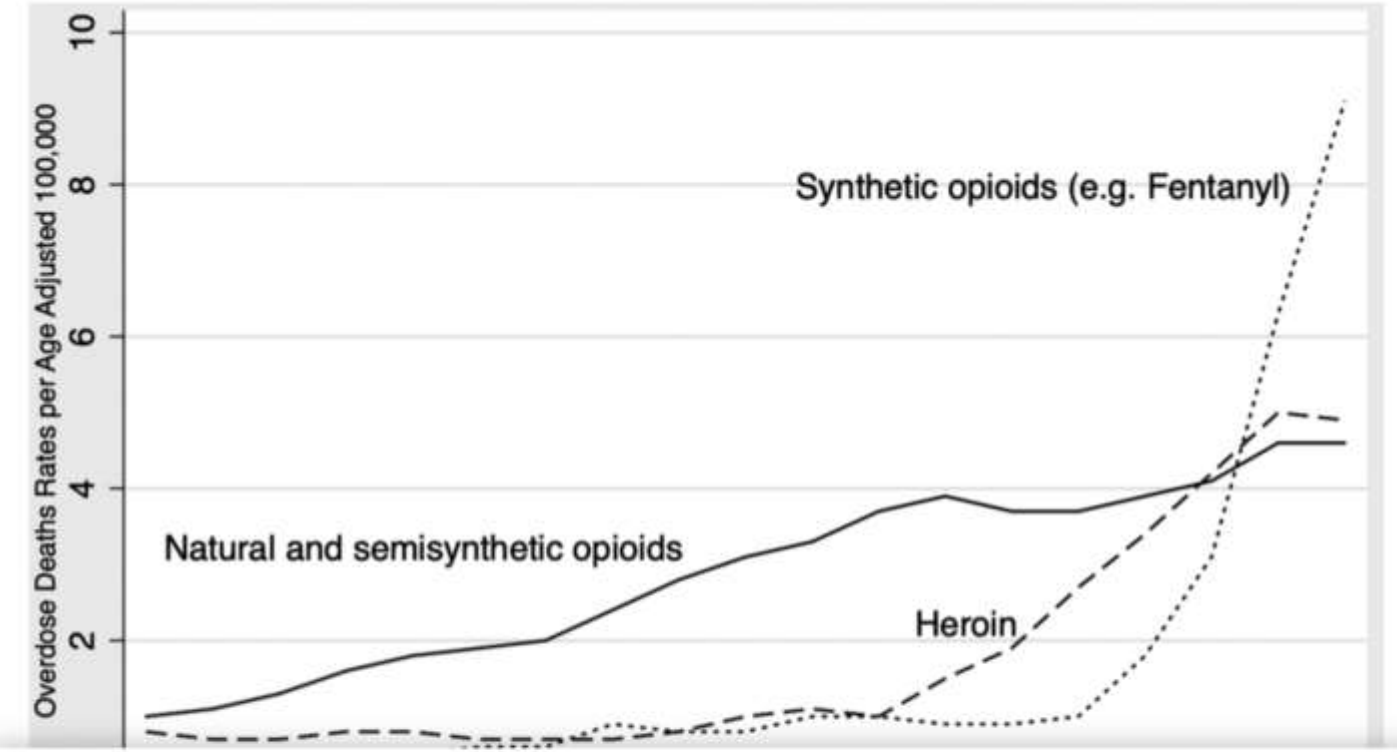


Fig. 1. Opioid Overdose Deaths by Type of Opioid.

Published in The International journal on drug policy 2019

The triple wave epidemic: Supply and demand drivers of the US opioid overdose crisis.

D. Ciccarone

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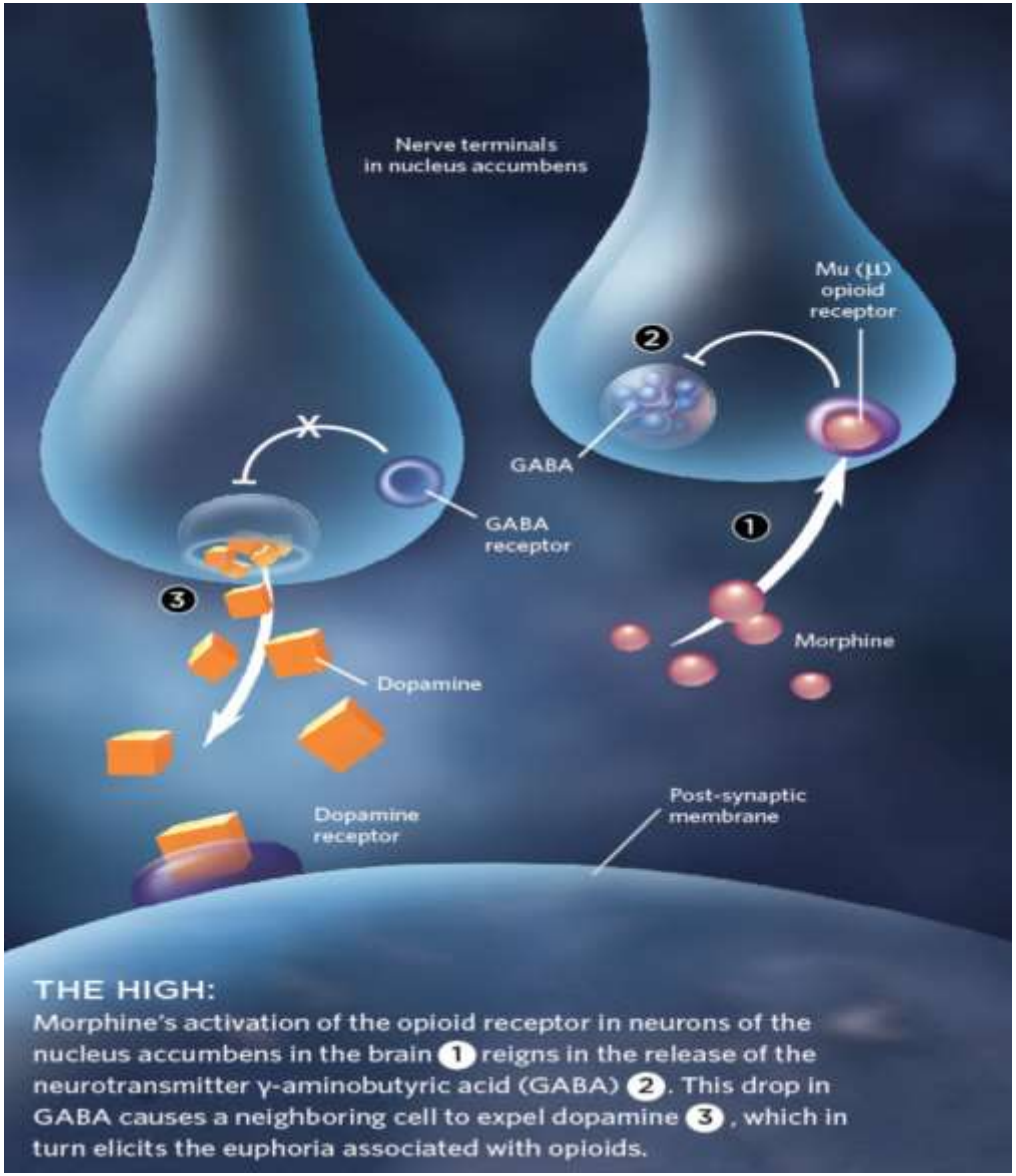

Nerve terminals
in nucleus accumbens
Mu (μ)
opioid
receptor
2
GABA
GABA
receptor
1
3
Morphine
Dopamine
Dopamine
receptor
Post-synaptic
membrane
THE HIGH:
Morphine's activation of the opioid receptor in neurons of the nucleus accumbens in the brain 1 reigns in the release of the neurotransmitter γ-aminobutyric acid (GABA) 2. This drop in GABA causes a neighboring cell to expel dopamine 3, which in turn elicits the euphoria associated with opioids.

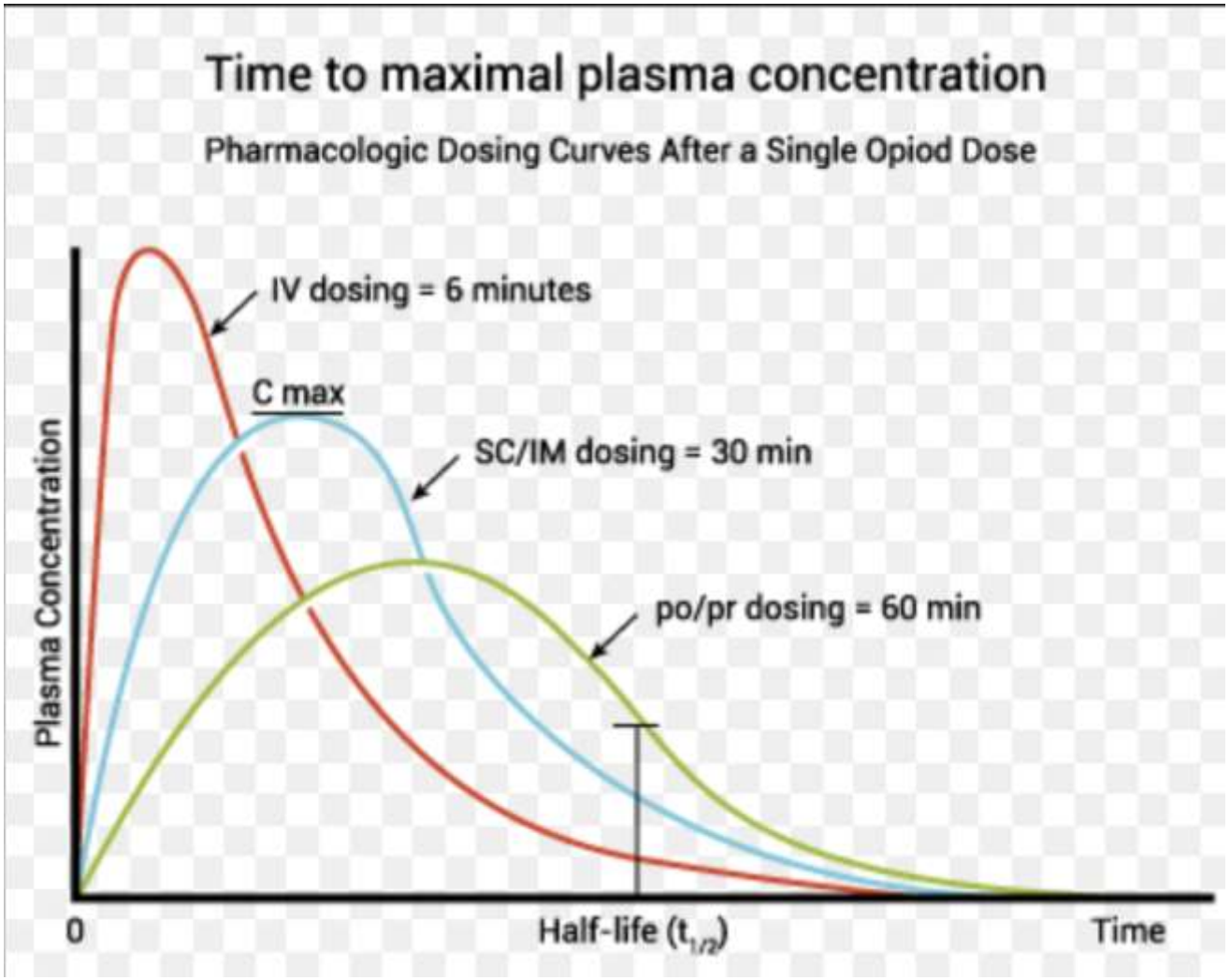
Positive Symptoms

Negative Symptoms

Equianalgesic Table

Drug	Route	Equianalgesic Dose (mg)	Strength (morphine)
Morphine	PO	30	1
Morphine	IV	10	3x morphine
Codeine	PO	300	1/10 morphine
Oxycodone	PO	20	1.5x morphine
Hydromorphone	PO	7.5	4-7x morphine
Hydromorphone	IV	1.5	20x morphine
Meperidine	PO	300	1/10 morphine
Meperidine	IV	75	1/3 morphine
Fentanyl	IV	0.1	50-100x morphine
Hydrocodone	PO	30	1x morphine
Tramadol	PO	300	1/10 morphine

Reference: “Selected opioid analgesics for pain and equianalgesic doses" table, UpToDate®, 2013.



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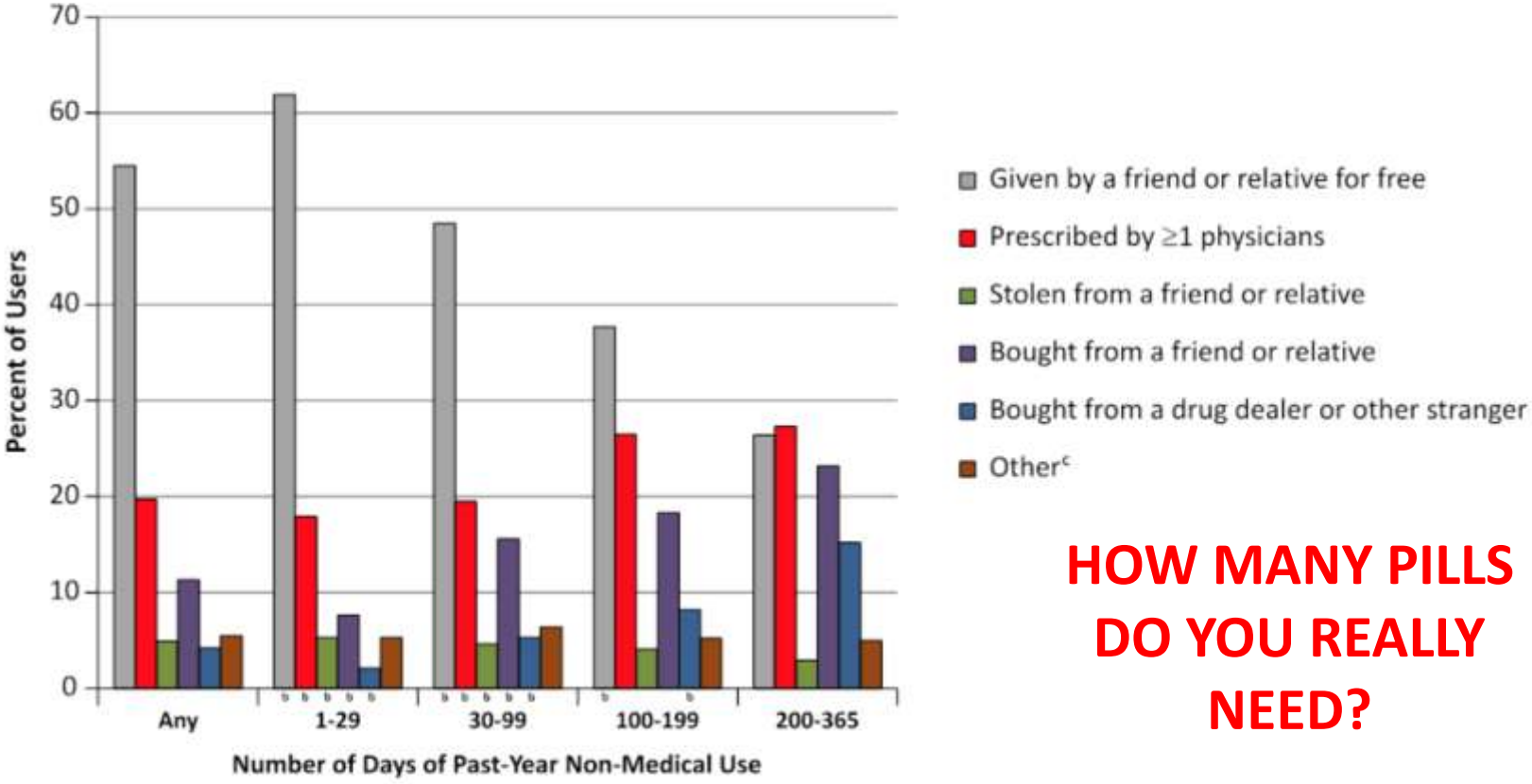
- Abuse – nonmedical use
- Misuse – medical use
- Dependence – withdrawal
- Tolerance – escalating doses
- Diversion – unauthorized re-routing
- Addiction – compulsive behavior; harmful consequences
  - Replaced by Opioid Use Disorder
- Under-treated pain
  - Historically called “Pseudo-addiction”

Opioid Side effects

- Mental Impairing (shouldn't be driving, sensitive positions, elderly)
- Tolerance
- Physical dependence
- Addiction
- Increased sensitivity to pain (hyperalgesia) -> Buprenorphine least likely, maybe methadone
- Constipation
- Nausea, vomiting, and dry mouth
- Sleepiness and dizziness/Falls and Fractures
- Depression
- Low testosterone/decreased libido
- Itching and sweating
- Doubles chance of disability (if prescribed > 7 days of opioid)
- Immune Suppression/Cancer
- Higher Risk of Cardiac events x 3

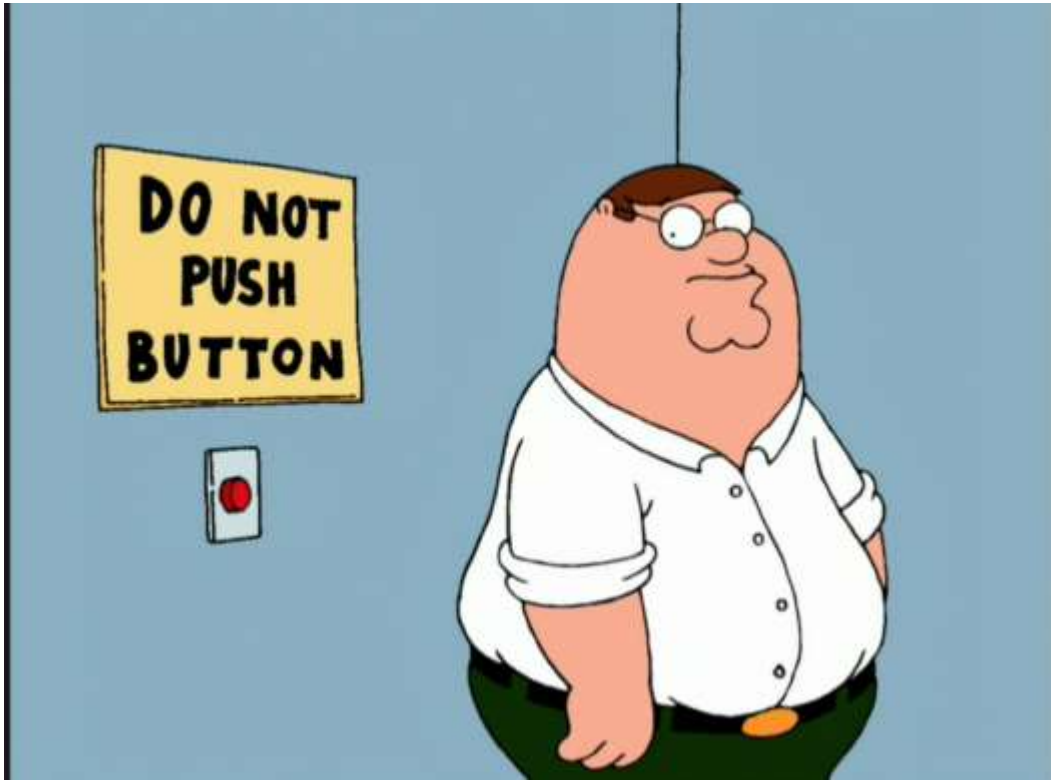
Sources of Prescription Painkillers Among Past-Year Non-Medical Users[a]



HOW MANY PILLS DO YOU REALLY NEED?

[a] Obtained from the US National Survey on Drug Use and Health, 2008 through 2011.[5]
[b] Estimate is statistically significantly different from that for highest-frequency users (200-365 days) ($P < .05$).
[c] Includes written fake prescriptions and those opioids stolen from a physician's office, clinic, hospital, or pharmacy; purchases on the Internet; and obtained some other way.

SOURCE: Jones C, Paulozzi L, Mack K. Sources of prescription opioid pain relievers by frequency of past-year nonmedical use: United States, 2008–2011. JAMA Int Med 2014; 174(5):802-803.


DO NOT
PUSH
BUTTON

2019: CDC ADVISES AGAINST MISAPPLICATION OF THE GUIDELINE

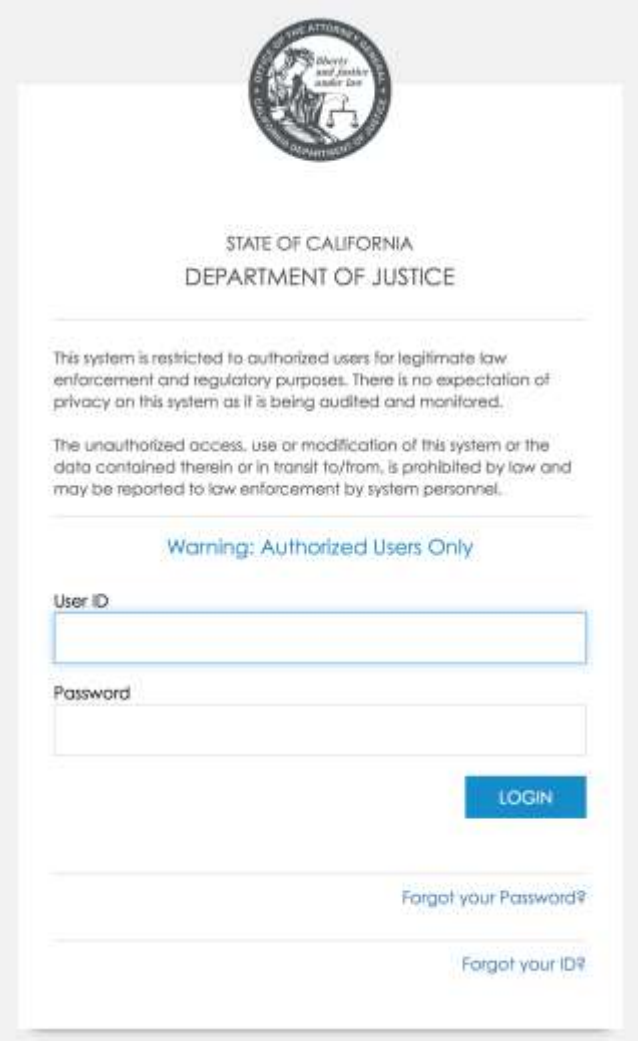
- Examples of misapplication include applying the guidelines to patients in active cancer treatment, patients with acute sickle crises, or post surgical pain
- The recommendation does not suggest abrupt discontinuation of opioids already prescribed at higher doses
- Does not apply for patients on medication-assisted treatment for opioid use disorder

2022 Updates

Changes include:

- The CDC would no longer suggest trying to limit opioid treatment for acute pain to three days.
- The agency would drop the specific recommendation that doctors avoid increasing dosage to a level equivalent to 90 milligrams of morphine per day.
- The CDC would say doctors should consider having patients undergo urine tests to see if they are using other controlled and illicit drugs, but no longer would call on having such testing done annually.
- For patients receiving higher doses of opioids, the CDC would urge doctors to not abruptly halt treatment unless there are indications of a life-threatening danger. The agency would offer suggestions about how to taper patients off the drugs.

Prescription Drug Monitoring Programs: It's the Law!



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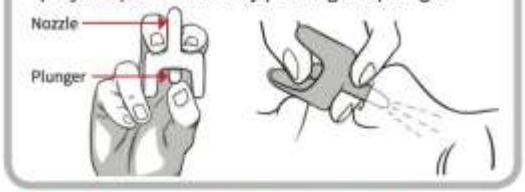
How to give naloxone:

There are 4 common naloxone products. Follow the instructions for the type you have.

Nasal spray

This nasal spray needs no assembly and can be sprayed up one nostril by pushing the plunger.



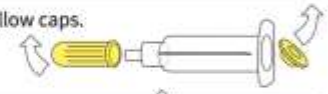
Auto-injector

The naloxone auto-injector needs no assembly and can be injected into the outer thigh, even through clothing. It contains a speaker that provides step-by-step instructions.

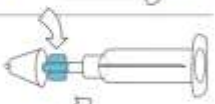
Nasal spray with assembly

This requires assembly. Follow the instructions below.

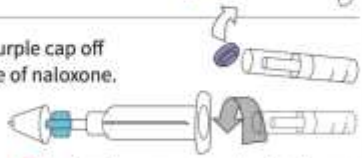
1 Take off yellow caps.



2 Screw on white cone.



3 Take purple cap off capsule of naloxone.



4 Gently screw capsule of naloxone into barrel of syringe.

5 Insert white cone into nostril; **give a short, strong push** on end of capsule to spray naloxone into nose: **ONE HALF OF THE CAPSULE INTO EACH NOSTRIL.**

Push to spray.

6 If no reaction in 3 minutes, give second dose.

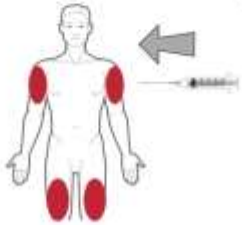
Injectable naloxone

This requires assembly. Follow the instructions below.

1 Remove cap from naloxone vial and uncover the needle.

2 Insert needle through rubber plug with vial upside down. Pull back on plunger and take up 1 ml.

3 Inject 1 ml of naloxone into an upper arm or thigh muscle.



4 If no reaction in 3 minutes, give second dose.

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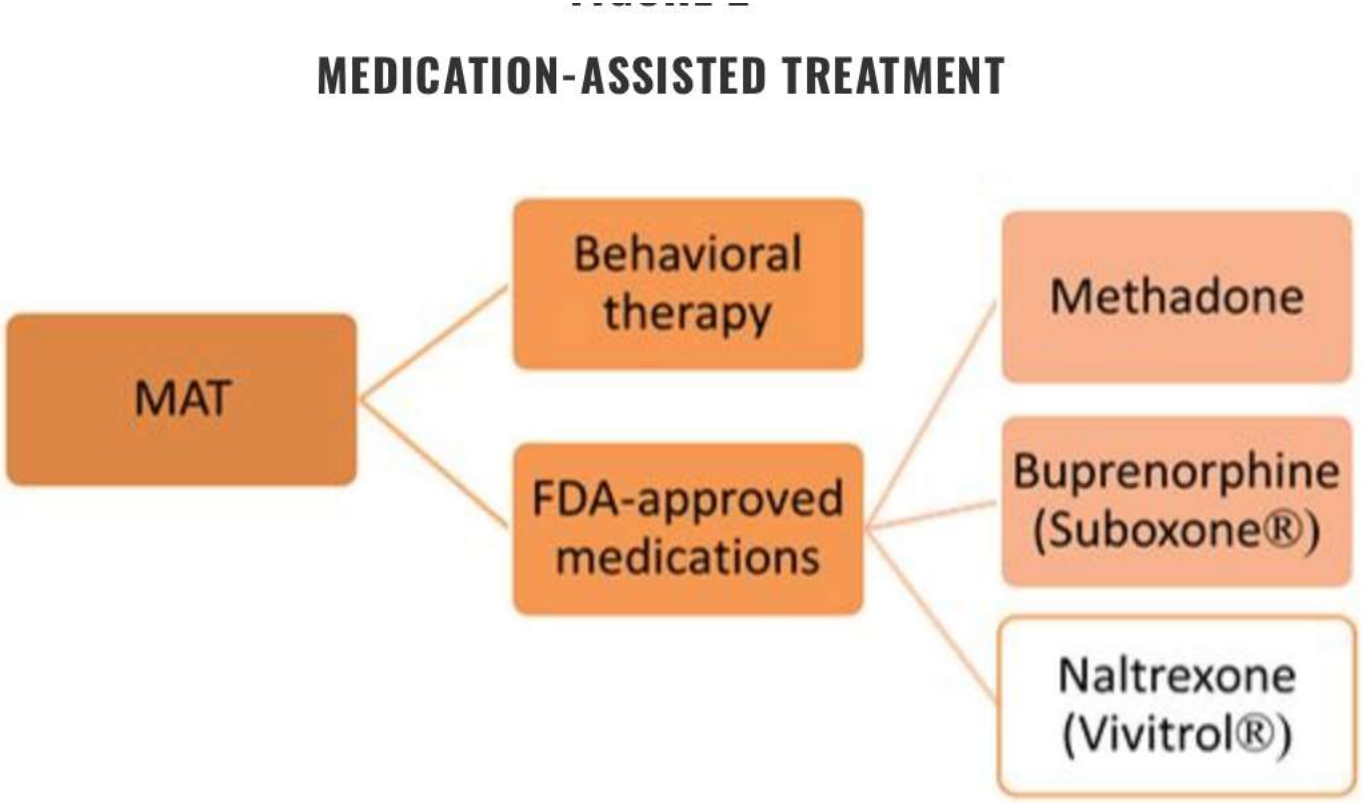
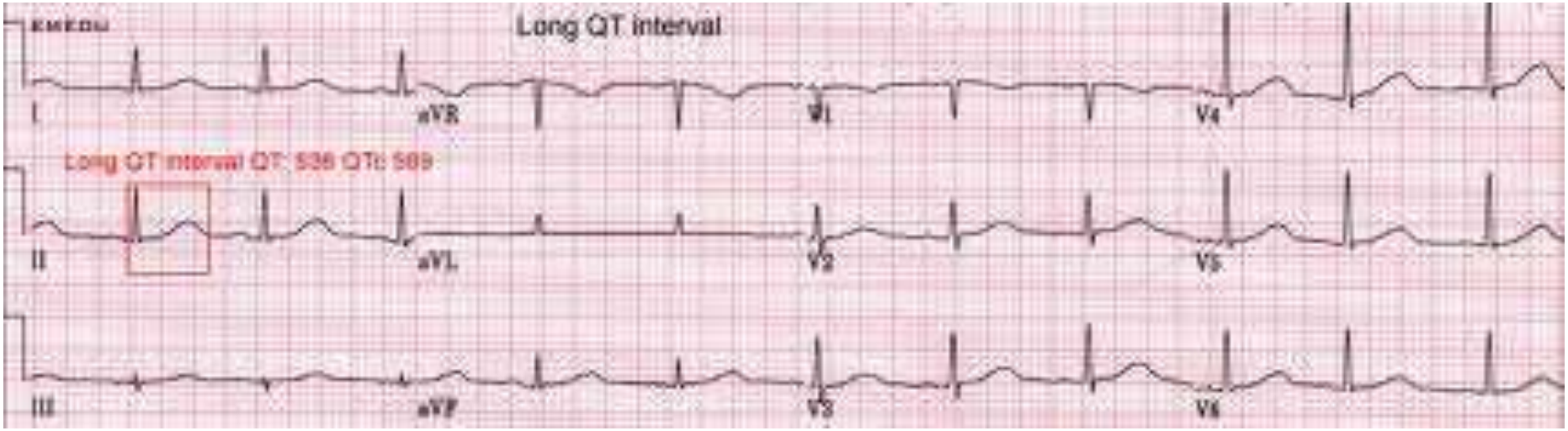
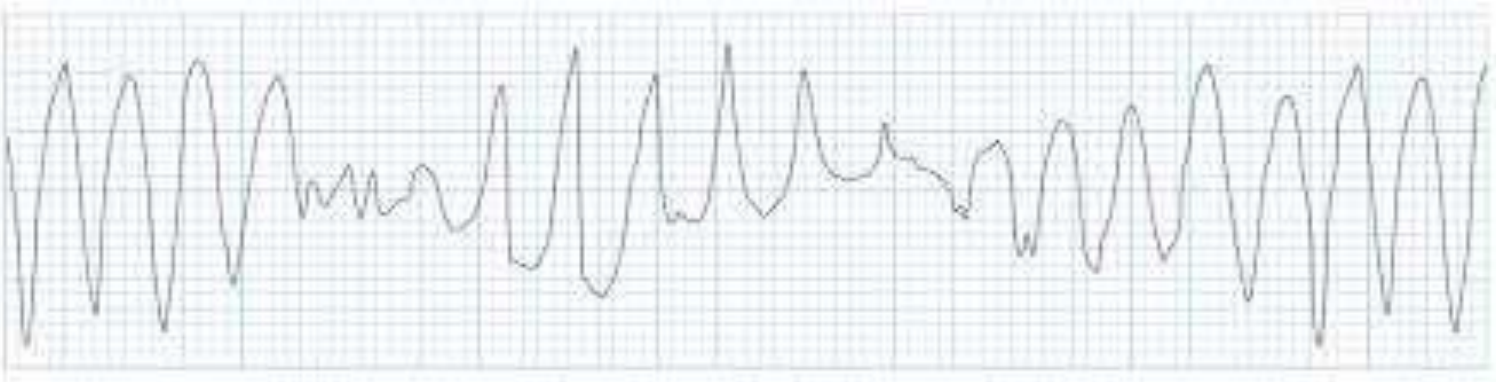
“MAT” or “MOUD”


MEDICATION-ASSISTED TREATMENT
MAT
Behavioral therapy
FDA-approved medications
Methadone
Buprenorphine (Suboxone®)
Naltrexone (Vivitrol®)

Methadone

- The usual dose for pain treatment in an opioid naïve patient can range from 2.5 to 10 mg PO every 8 hours
- The usual maintenance dose for abuse is 80 – 120 mg/day orally
- NMBA antagonist; 5HT and NE reuptake inhibitor
- Black box warning: can cause QT prolongation and serious arrhythmia (torsades de pointes)
  - Baseline EKG!


Long QT interval
I
aVR
V1
V4
Long QT interval QT: 536 QTc: 569
II
aVL
V2
V5
III
aVF
V3
V6



Opioid Conversion

Convert to daily methadone

Daily Oral Morphine Equivalents	Oral morphine: oral methadone conversion ratio
< 100 mg	3:1
100 – 300 mg	5:1
300 – 600 mg	10:1
600 – 800 mg	12:1
800 – 1000 mg	15:1
> 1000 mg	20:1

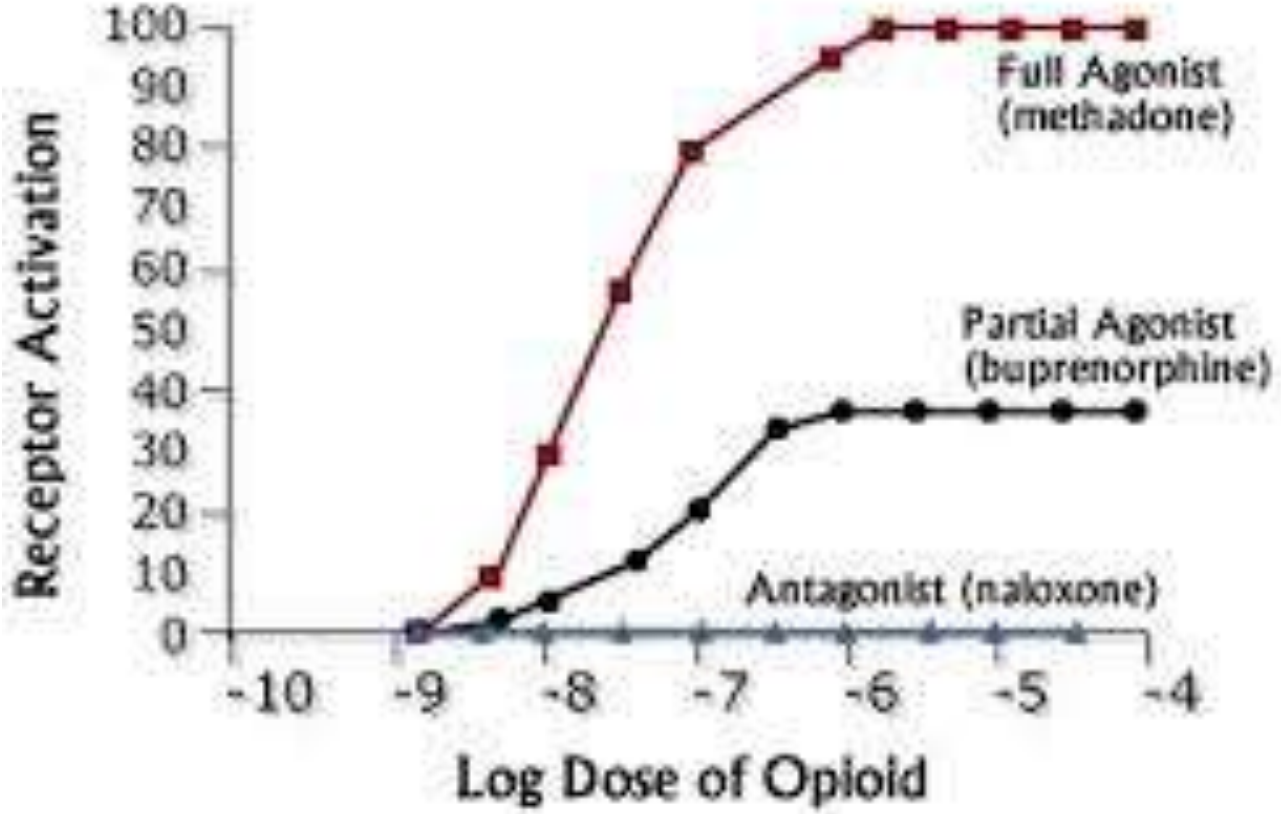
Buprenorphine

- Butrans Patch & Belbuca
- Subutex = Buprenorphine
- Suboxone = Buprenorphine + naloxone
- Used for detoxication and long term replacement therapy for opioid dependence as well as for pain management
- Buprenorphine: partial agonist at mu-opioid receptor and antagonist at k receptor. T1/2 24 to 42 hours
- Ceiling effect
- High-affinity blockade significantly limits the effect of subsequently administered opioid agonists

Management of Patients Maintained on Suboxone/Subutex

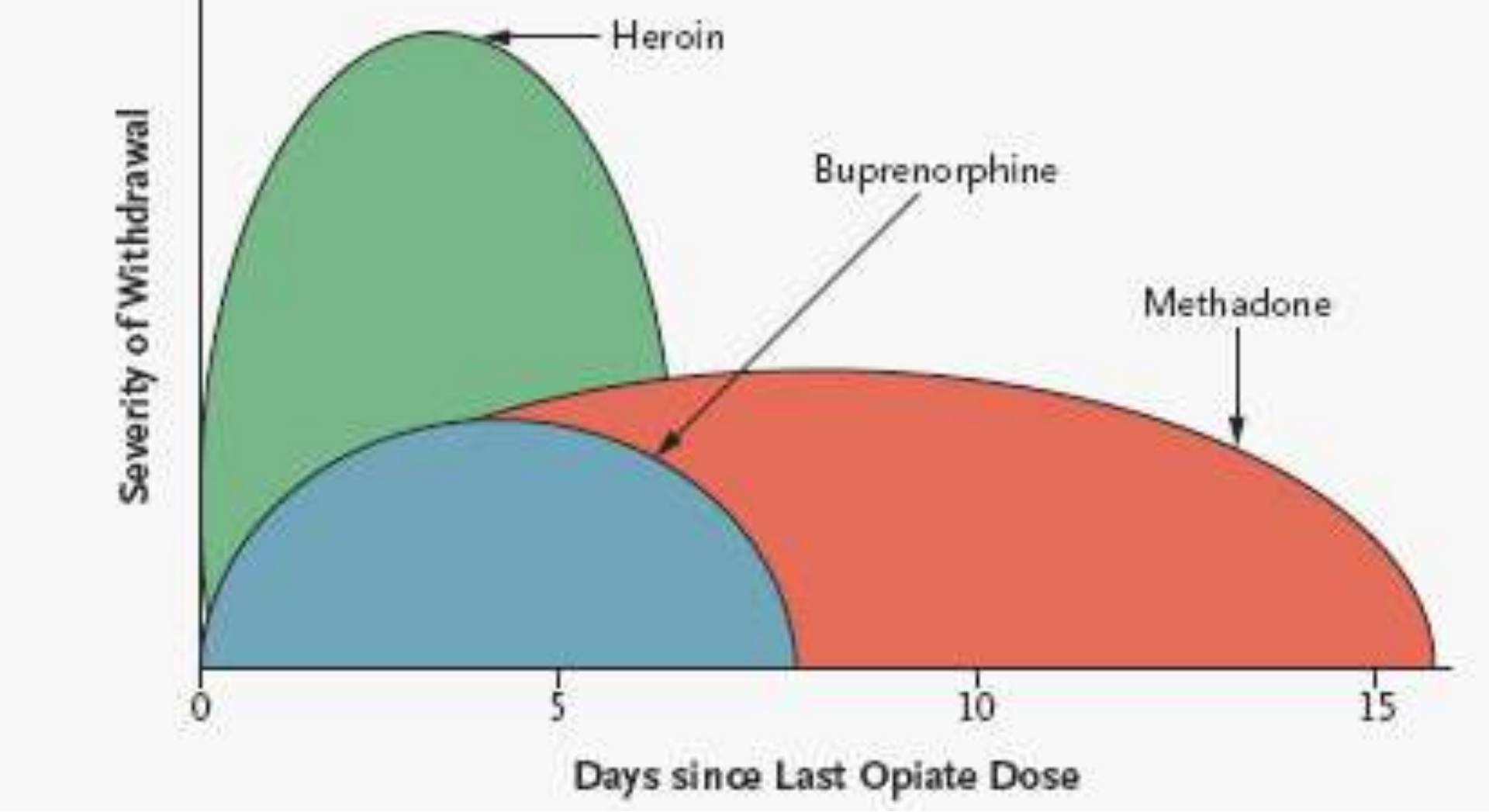
- Updated Recs: Continue the Buprenorphine perioperatively; typical maintenance doses 8-12 mg
- Can give higher dose buprenorphine
- Can still give IV drugs, in particular fentanyl and hydromorphone effective
- Consider non opioid drugs
- Consider regional techniques

Receptor Activation:
Full Agonist, Partial Agonist, Antagonist



Low Dose Naltrexone vs Naltrexone

- Low Dose Compounded medication typically PO 3 to 4.5 mg starting dose
- Reduces inflammation in nerve tissue
- Revs up endogenous opioids
- Minimal side effects
- Very helpful for nociplastic pain
- Regular Naltrexone: 50 or 100 mg PO dose for opioid or alcohol use disorder



- **Blinded abrupt d/c buprenorphine 8mg/day:**
  - **Less intense vs heroin, methadone withdrawal**
  - **Briefer duration of withdrawal sx vs methadone**

Kosten, O'Connor NEJM 2003

Urine Drug Screen

Drug	Time
Alcohol	7-12 hours
Amphetamine	48 hour
Benzodiazepine	3 days (short acting)
	30 days (long acting)
Cocaine	2-4 days
THC	3 days (single use)
	10-15 days (daily use)
	> 30 days (long term use)
Codeine	48 hours
Heroine	48 hours
Methadone	3 days
Oxycodone	2-4 days
Hydromorphone	2-4 days
PCP	8 days

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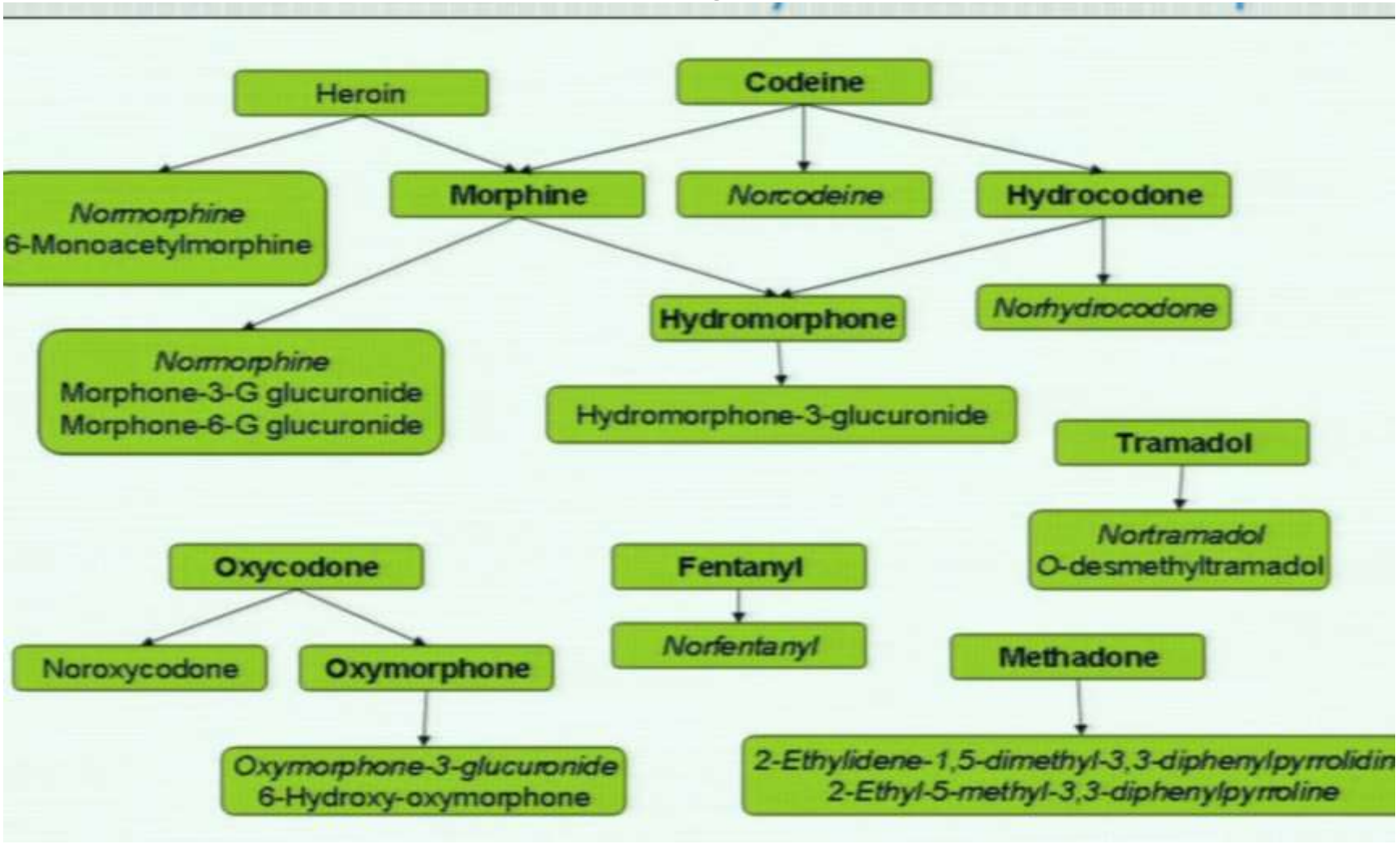
UDS Interpretation



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