OPIOID PRESCRIBING GUIDELINES – A REVIEW

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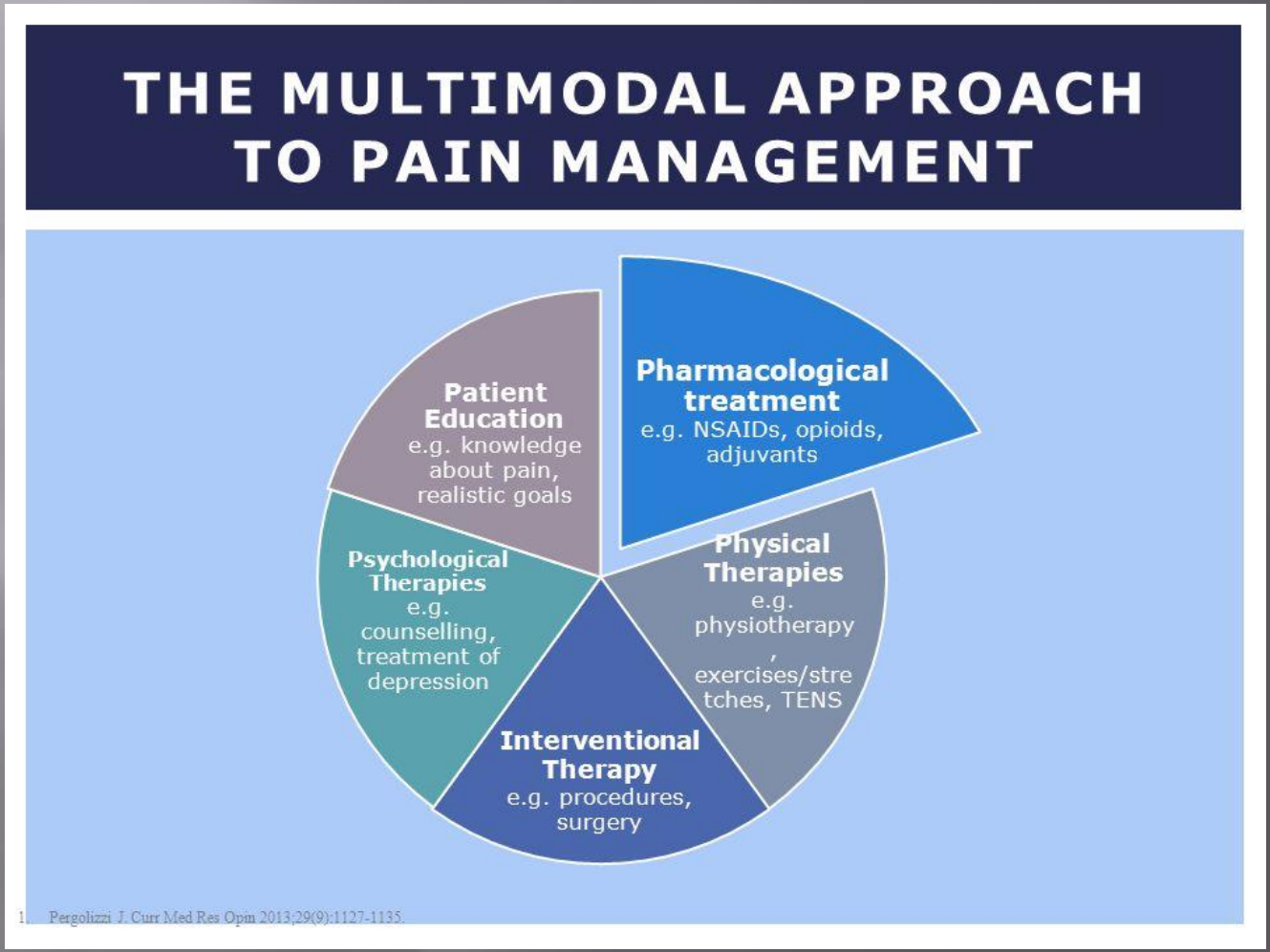
Disclosures

No Disclosures

Pain - Definition

- "An unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage"- IASP
  - Pain is always a personal experience that is influenced to varying degrees by biological, psychological, and social factors

Pain Treatment



Pharmacologic Options

- Acetaminophen
- NSAIDS
- Antidepressants
- Anticonvulsants
- Muscle Relaxants
- Topicals
- Opioids

Pharmacologic Options

- **Effect of Opioid vs Nonopioid Medications on Pain-Related Function in Patients With Chronic Back Pain or Hip or Knee Osteoarthritis Pain**

  The SPACE Randomized Clinical Trial

  Krebs, et Al, JAMA 2018

- Treatment with opioids was not superior to treatment with non opioid medications (acetaminophen, NSAIDS), for improving pain-related function over 12 months. Results do not support initiation of opioid therapy for moderate to severe chronic back pain or hip or knee osteoarthritis pain

Opioids

- Act on opioid receptors
  - Mu, Kappa, Delta
  - Mu most responsible for side effects
- Effects/Side Effects:
  - Analgesia/Euphoria
  - Sedation
  - Constipation – tolerance to this side effect does not usually develop
  - Nausea/Vomiting
  - Itching
  - Respiratory Depression
  - Physical Dependence
  - Opioid Induced Hyperalgesia

Tolerance vs Dependence vs Addiction

- Tolerance: Reduced response to a drug with repeated use.
  - Thought to be NMDA receptor mediated
    - Ketamine – NMDA receptor antagonist, may be helpful in this

Tolerance vs Dependence vs Addiction

- Physical Dependence: Adaptation to a drug that produces symptoms of withdrawal when the drug is stopped.
  - Not addiction

Tolerance vs Dependence vs Addiction

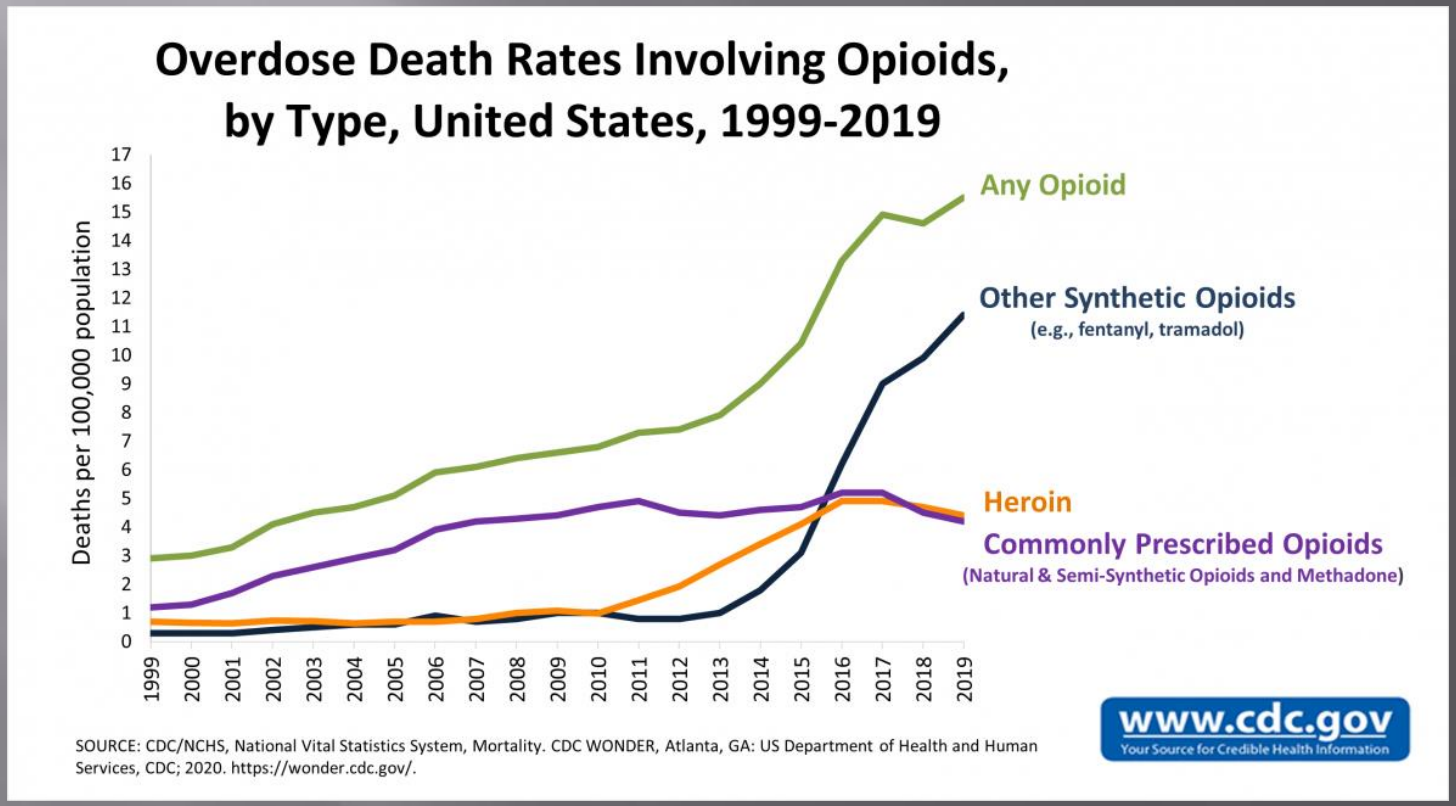
- Opioid use disorder (OUD) – A problematic pattern of opioid use that causes significant impairment or distress.
  - A diagnosis is based on specific criteria such as unsuccessful efforts to cut down or control use, or use resulting in social problems and a failure to fulfill obligations at work, school, or home, among other criteria.
  - Opioid use disorder is preferred over other terms with similar definitions, “opioid abuse or dependence” or “opioid addiction.”

-CDC

Opioids

- From CDC & ODH:
  - Drug overdose deaths and opioid-involved deaths continue to increase in the United States.
  - From 1999 to 2019, more than 840,000 people died from drug overdoses.
    - 70% involved an opioid
    - 250,000 involving prescription opioids
    - Opioids involved in 50,000 overdose deaths in 2019
  - 93,000 drug overdose deaths in 2020

Opioids


Overdose Death Rates Involving Opioids, by Type, United States, 1999-2019
Deaths per 100,000 population
0
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Any Opioid
Other Synthetic Opioids
(e.g., fentanyl, tramadol)
Heroin
Commonly Prescribed Opioids
(Natural & Semi-Synthetic Opioids and Methadone)
SOURCE: CDC/NCHS, National Vital Statistics System, Mortality. CDC WONDER, Atlanta, GA: US Department of Health and Human Services, CDC; 2020. https://wonder.cdc.gov/.
www.cdc.gov
Your Source for Credible Health Information

Opioids - Dosing

- Low Dose: 0-50 Morphine Equivalent Dose **(MED)**
- Moderate Dose: 50-90 MED
- High Dose: >90 MED
- Ohio: Pause at 80 MED
- MED > 50, Narcan?
  - Consider offering naloxone when factors that increase risk for opioid overdose, such as history of overdose/substance use disorder, opioid dosages (≥50 MME/day), or concurrent benzodiazepine
- Risk: 0-20 MED, 20-50 MED, 50-90 MED, >90 MED

Opioids - Dosing

- What does that mean?
  - Fentanyl Patch: 25 mcg = 60 mg Morphine
  - Fentanyl Patch: 50 mcg = 120 mg Morphine
  - Oxycodone: 30mg = 45mg Morphine
  - Oxycodone: 60mg = 90mg Morphine
  - Oxymorphone (Opana): 10mg = 30mg Morphine
  - Oxymorphone (Opana): 40mg = 120mg Morphine
  - Hydrocodone (Norco): 40mg = 40mg Morphine
  - Tramadol: 50mg = 5mg Morphine

Checklist for prescribing opioids for chronic pain

For primary care providers treating adults (18+) with chronic pain ≥3 months, excluding cancer, palliative, and end-of-life care

CHECKLIST

When CONSIDERING long-term opioid therapy

- ☐ Set realistic goals for pain and function based on diagnosis (eg, walk around the block).
- ☐ Check that non-opioid therapies tried and optimized.
- ☐ Discuss benefits and risks (eg, addiction, overdose) with patient.
- ☐ Evaluate risk of harm or misuse.
  - Discuss risk factors with patient.
  - Check prescription drug monitoring program (PDMP) data.
  - Check urine drug screen.
- ☐ Set criteria for stopping or continuing opioids.
- ☐ Assess baseline pain and function (eg, PEG scale).
- ☐ Schedule initial reassessment within 1–4 weeks.
- ☐ Prescribe short-acting opioids using lowest dosage on product labeling; match duration to scheduled reassessment.

If RENEWING without patient visit

- ☐ Check that return visit is scheduled ≤3 months from last visit.

When REASSESSING at return visit

Continue opioids only after confirming clinically meaningful improvements in pain and function without significant risks or harm.

- ☐ Assess pain and function (eg, PEG); compare results to baseline.
- ☐ Evaluate risk of harm or misuse:
  - Observe patient for signs of over-sedation or overdose risk.
    - If yes: Taper dose.
  - Check PDMP.
  - Check for opioid use disorder if indicated (eg, difficulty controlling use).
    - If yes: Refer for treatment.
- ☐ Check that non-opioid therapies optimized.
- ☐ Determine whether to continue, adjust, taper, or stop opioids.
- ☐ Calculate opioid dosage morphine milligram equivalent (MME).
  - If ≥50 MME/day total (≥50 mg hydrocodone; ≥33 mg oxycodone), increase frequency of follow-up; consider offering naloxone.
  - Avoid ≥90 MME/day total (≥90 mg hydrocodone; ≥60 mg oxycodone), or carefully justify; consider specialist referral.
- ☐ Schedule reassessment at regular intervals (≤3 months).

REFERENCE

EVIDENCE ABOUT OPIOID THERAPY

- *Benefits of long-term opioid therapy for chronic pain not well supported by evidence.*
- *Short-term benefits small to moderate for pain; inconsistent for function.*
- *Insufficient evidence for long-term benefits in low back pain, headache, and fibromyalgia.*

NON-OPIOID THERAPIES

Use alone or combined with opioids, as indicated:

- Non-opioid medications (eg, NSAIDs, TCAs, SNRIs, anti-convulsants).
- Physical treatments (eg, exercise therapy, weight loss).
- Behavioral treatment (eg, CBT).
- Procedures (eg, intra-articular corticosteroids).

EVALUATING RISK OF HARM OR MISUSE

Known risk factors include:

- Illegal drug use; prescription drug use for nonmedical reasons.
- History of substance use disorder or overdose.
- Mental health conditions (eg, depression, anxiety).
- Sleep-disordered breathing.
- Concurrent benzodiazepine use.

Urine drug testing: Check to confirm presence of prescribed substances and for undisclosed prescription drug or illicit substance use.

Prescription drug monitoring program (PDMP): Check for opioids or benzodiazepines from other sources.

ASSESSING PAIN & FUNCTION USING PEG SCALE

PEG score = average 3 individual question scores (30% improvement from baseline is clinically meaningful)

Q1: *What number from 0–10 best describes your **pain** in the past week?*
0="no pain", 10="worst you can imagine"

Q2: *What number from 0–10 describes how, during the past week, pain has interfered with your **enjoyment of life**?*
0="not at all", 10="complete interference"

Q3: *What number from 0–10 describes how, during the past week, pain has interfered with your **general activity**?*
0="not at all", 10="complete interference"

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

TO LEARN MORE
www.cdc.gov/drugoverdose/prescribing/guideline.html

March 2016

CDC Guidelines

- 12 recommendations grouped into three areas for consideration:
  - Determining when to initiate or continue opioids for chronic pain.
  - Opioid selection, dosage, duration, follow-up, and discontinuation.
  - Assessing risk and addressing harms of opioid use.

-CDC

CDC Guidelines

- Determining when to initiate or continue opioids for chronic pain
  - Selection of non-pharmacologic therapy, nonopioid pharmacologic therapy, opioid therapy
  - Establishment of treatment goals
  - Discussion of risks and benefits of therapy with patients

Opioids - Initiation

- **ARE THEY INDICATED?**
  - Saying No!
  - Fibromyalgia
- Have We Exhausted Other Options?
- Psych History?
- Substance Abuse History?
  - Marijuana????
- Benzodiazepine Use

Opioids - Initiation

- OSA?
- UDS - baseline
- Pain Psychology Evaluation and F/U
- Lowest Dose:
  - Tramadol, Schedule 4
    - Lower affinity for Mu receptors, SNRI as well
- Communication: PCP, ED, Specialists

CDC Guidelines

- Opioid selection, dosage, duration, follow-up, and discontinuation
  - Selection of immediate-release or extended-release and long-acting opioids
  - Dosage considerations
  - Duration of treatment
  - Considerations for follow-up and discontinuation of opioid therapy

CDC Guidelines

- Assessing risk and addressing harms of opioid use
  - Evaluation of risk factors for opioid-related harms and ways to mitigate patient risk
  - Review of prescription drug monitoring program (PDMP) data
  - Use of urine drug testing
  - Considerations for co-prescribing benzodiazepines
  - Arrangement of treatment for opioid use disorder

OARRS

- Ohio – OARRS
  - Every 90 days if patient treated with an opioid analgesic or benzo
  - Ohio Prescription Monitoring Program (PMP) Report
  - Report of your prescribing patterns compared to that of your peers
    - Must put in specialty

Opioids - Monitoring

- 4 A's of chronic opioid therapy
  - Analgesia
  - Activities of daily living
  - Adverse side effects
  - Aberrant drug-taking behaviors

Opioids - Monitoring

- Improvement in function/quality of life?
- UDS
- OARRS
- Pill Counts
- Random Pill Counts/UDS
- Re-assessment - is there pathology that warrants this?
- Can we lower this dose?
- Have we exhausted other options?

Ohio Guidelines-Acute Pain

- No more than seven days of opiates can be prescribed for adults
- No more than five days of opiates can be prescribed for minors
- The total morphine equivalent dose (MED) of a prescription for acute pain cannot exceed an average of 30 MED per day

Ohio Guidelines – Acute Pain

- Can only prescribe opiates in excess of the new limits if they provide a specific reason in the patient's medical record.
- Prescribers will be required to include a diagnosis/procedure code on every controlled substance prescription, which will be entered into OARRS.
- Does not apply to cancer, palliative care, end-of life/hospice care or medication-assisted treatment for addiction.

Ohio Guidelines- Acute Pain Exceptions to the rule

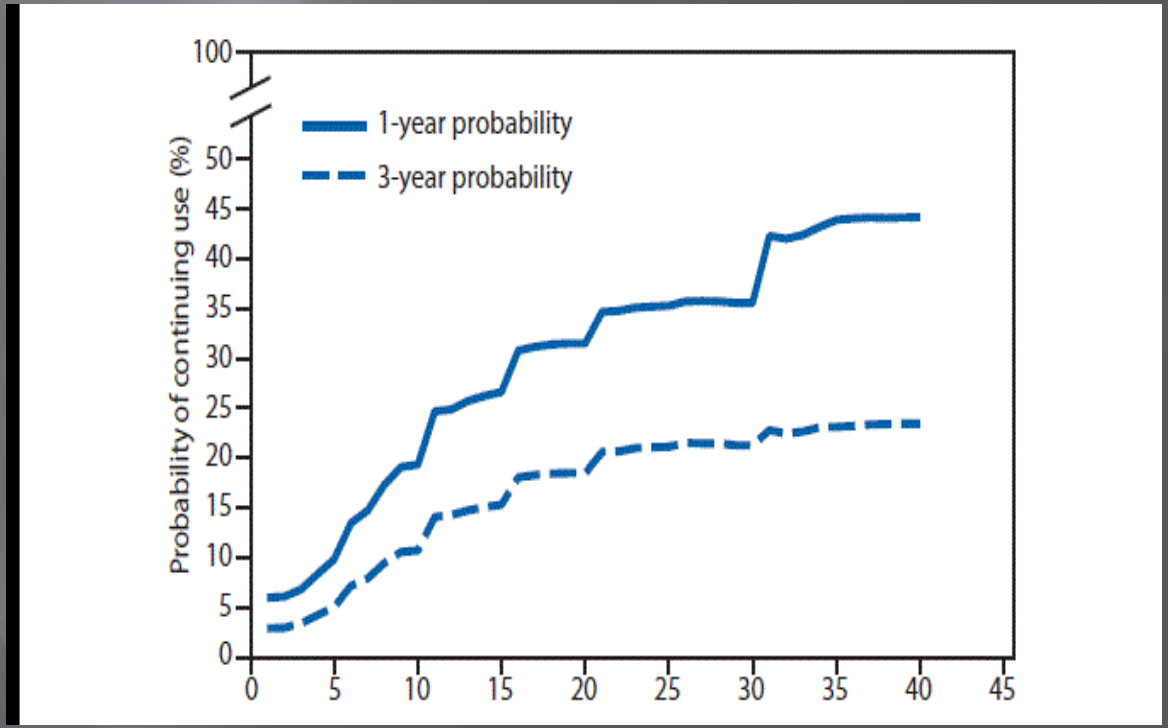
- The time limits for an acute prescription (seven days for adults and five days for minors) can be extended in a few cases.
  - Traumatic crushing of tissue
  - Amputation
  - Major orthopedic surgery
  - Severe burns
  - Pain that is expected to last longer than seven to five days

Ohio Guidelines- Acute Pain Exceptions to the rule

- The rule doesn't apply to the below situations:
  - Patients in palliative care
  - Patients diagnosed with a terminal condition or in advanced treatment (advanced cancer treatment, for example)
  - Patients in Hospice for end-of-life care
  - Patients being treated for opioid addiction with a substance approved by the FDA for opioid detoxification or management
  - Inpatient medication orders

Acute Rx → Long Term Use

- Duration of Acute Use
  - 1 day – 6% chance of still using at 1 year
  - 8 days – 13.5%
  - 31 days -29.9%



https://www.cdc.gov/mmwr/volumes/66/wr/mm6610a1.htm#F2_down

Ohio Guidelines

Physicians are required to engage in conversations with patients:

- Patient awareness of the risk of opioid misuse and addiction.

- Prior to treating or continuing to treat subacute or chronic pain with an opioid, the physician needs to first consider and document non-medication and non-opioid treatment.

- If opioid medication is appropriate, the physician should prescribe it for the least amount of days and strength to adequately address the pain.

Ohio Guidelines

- Check points, not limits:
- According to the Centers for Disease Control and Prevention, a dose of 50 MED or more per day doubles the risk of opioid overdose death. At 90 MED or more, the risk of overdose increases ten times.

Ohio Guidelines – Chronic Pain

- 50 MED
  - Re-evaluate status of underlying pain condition
  - Assess functioning
  - Look for signs of Rx misuse
  - Consider consultation with specialist
  - Obtain written informed consent
- 80 MED
  - Look for signs of Rx misuse
  - Consult with a specialist
  - Offer Rx for Naloxone
  - Obtain a written pain agreement – **80 MED or higher**
- 120 MED
  - Pain management/Hospice/Palliative care provider must be either active consultant OR the Rx Provider
  - Unless the patient was already on a dosage of 120 MED or more prior to December 23, 2018

Ohio Guidelines

- Do not apply to patients receiving medication for terminal conditions or those within a hospital or in-patient setting where they are closely monitored.

Opioids - Inheriting

- How to handle patients on opioids from previous providers?
  - Need to take into account entire clinical picture
  - Dosing? Low, medium, high?
    - Can be difficult conversation to have
    - Need to build trust and rapport
  - Pathology/Diagnosis?
    - Fibromyalgia?
  - Compliance
  - Exhausted alternative treatment options
  - Participating in treatment?
    - Smoking cessation, weight loss, PT, etc……..

Opioid Tapering

- **Consider tapering to a reduced opioid dosage or tapering and discontinuing opioid therapy when your patient:**
  - Requests dosage reduction
  - Does not have clinically meaningful improvement in pain and function (e.g., at least 30%)
  - On dosages greater or equal to 50 MME/ day without benefit.
  - Opioids are combined with benzodiazepines
  - Shows signs of substance use disorder (e.g. work or family problems related to opioid use, difficulty controlling use)
  - Experiences overdose or other serious adverse event
  - Shows early warning signs for overdose risk such as confusion, sedation, or slurred speech

- CDC

Opioid Tapering

- **Tapering plans should be individualized and should minimize symptoms of opioid withdrawal while maximizing pain treatment with nonpharmacologic therapies and nonopioid medications. In general:**
  - Consider 10% per month for pts on longer term opioids
    - *Discuss the increased risk for overdose if patients quickly return to a previously prescribed higher dose.*

- CDC

Opioid Tapering

- Make sure patients receive appropriate psychosocial support. Work with mental health providers, arrange for treatment of opioid use disorder, and offer naloxone for overdose prevention.
  - ***Watch for signs of anxiety, depression, and opioid use disorder during the taper and offer support or referral as needed.***
- Let patients know that most people have improved function without worse pain after tapering opioids. Some patients even have improved pain after a taper, even though pain might briefly get worse at first.
  - ***Tell patients "I know you can do this" or "I'll stick by you through this."***

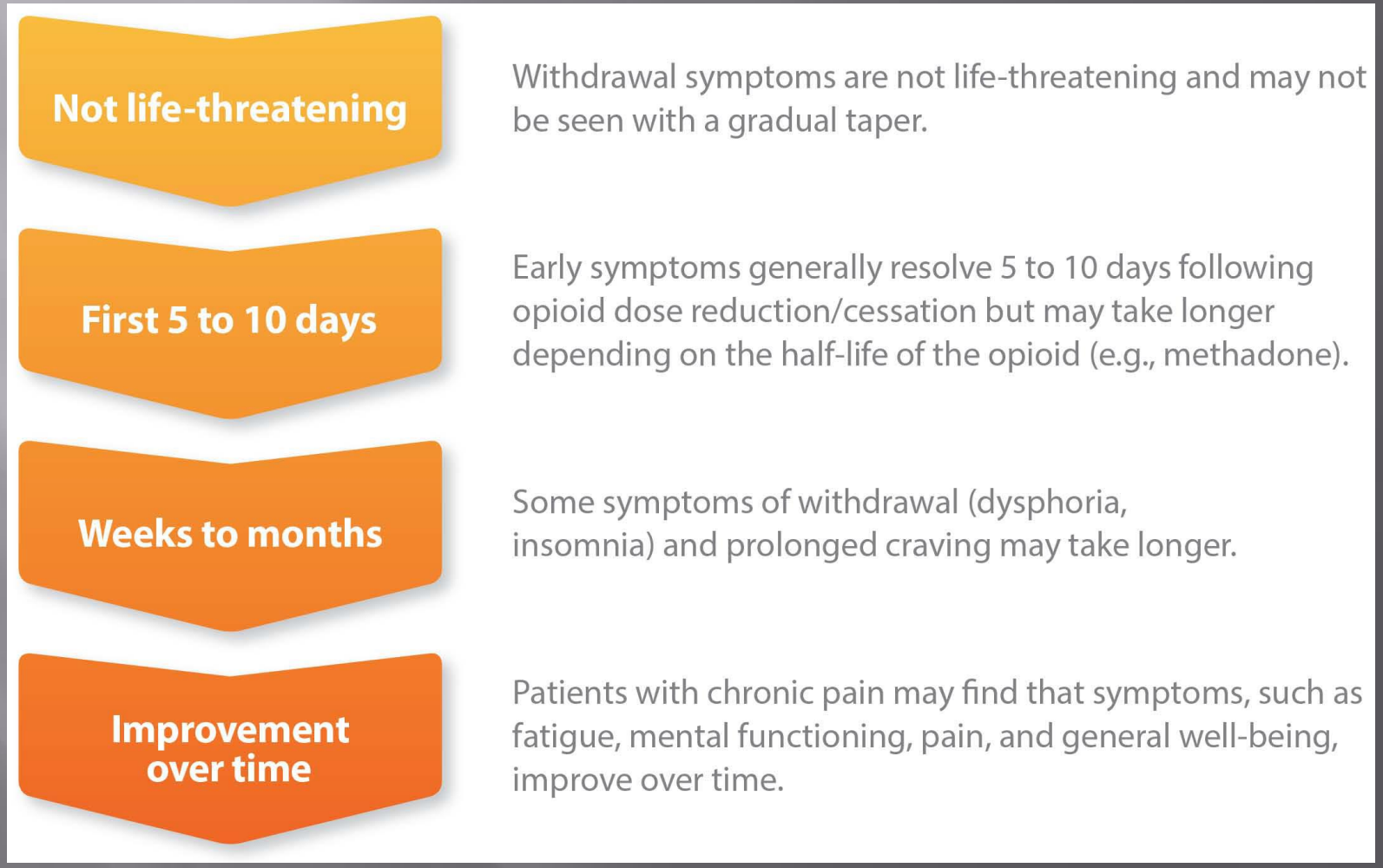
- CDC

Opioid Tapering

- Adjust the rate and duration of the taper according to the patient's response.
- Don't reverse the taper; however, the rate may be slowed or paused while monitoring and managing withdrawal symptoms.
- Once the smallest available dose is reached, the interval between doses can be extended and opioids may be stopped when taken less than once a day.

- CDC

Opioid Withdrawal



Opioid Withdrawal

- **Early Symptoms** (hours to days)
  - Anxiety/restlessness
  - Rapid short respirations
  - Runny nose, tearing eyes, sweating
  - Insomnia
  - Dilated reactive pupils

- Opioid Taper Decision Tool, US VA Clinicians Guide

Opioid Withdrawal

- **Late Symptoms** (days to weeks)
  - Runny nose, tearing eyes
  - Rapid breathing, yawning
  - Tremor, diffuse muscle spasms/aches
  - Piloerection
  - Nausea, vomiting, and diarrhea
  - Abdominal pain
  - Fever, chills

- Opioid Taper Decision Tool, US VA Clinicians Guide

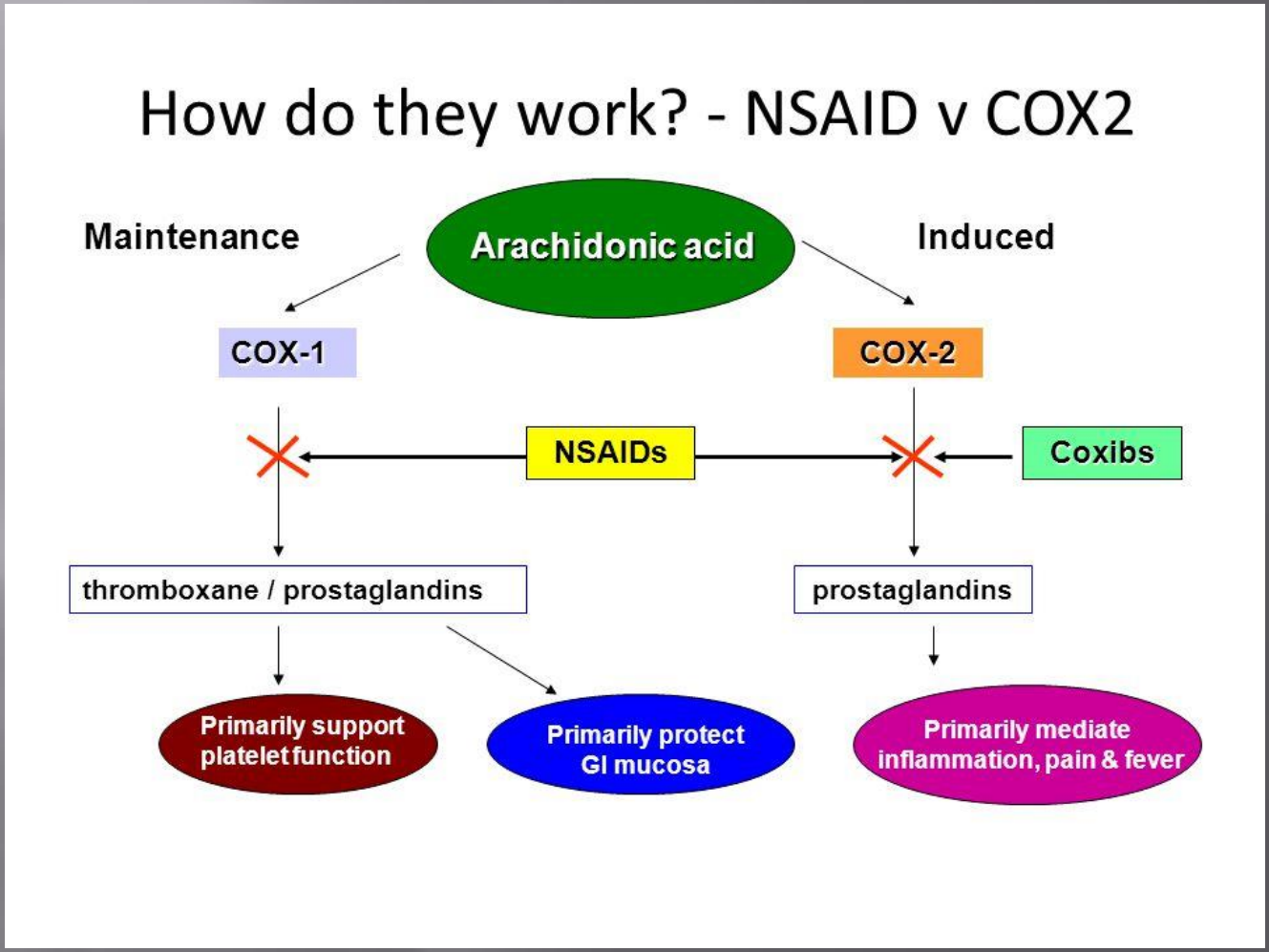
Opioid Withdrawal

Indication	Treatment Options
Autonomic symptoms (sweating, tachycardia, myoclonus)	**First line** • Clonidine 0.1 to 0.2 mg oral every 6 to 8 hours; hold dose if blood pressure <90/60 mmHg (0.1 to 0.2 mg 2 to 4 times daily is commonly used in the outpatient setting) – Recommend test dose (0.1 mg oral) with blood pressure check 1 hour post dose; obtain daily blood pressure checks; increasing dose requires additional blood pressure checks – Re-evaluate in 3 to 7 days; taper to stop; average duration 15 days **Alternatives** • Baclofen 5 mg 3 times daily may increase to 40 mg total daily dose – Re-evaluate in 3 to 7 days; average duration 15 days – May continue after acute withdrawal to help decrease cravings – Should be tapered when it is discontinued • Gabapentin start at 100 to 300 mg and titrate to 1800 to 2100 mg divided in 2 to 3 daily doses* – Can help reduce withdrawal symptoms and help with pain, anxiety, and sleep • Tizanidine 4 mg three times daily, can increase to 8 mg three times daily
Anxiety, dysphoria, lacrimation, rhinorrhea	• Hydroxyzine 25 to 50 mg three times a day as needed • Diphenhydramine 25 mg every 6 hours as needed**
Myalgias	• NSAIDs (e.g., naproxen 375 to 500 mg twice daily or ibuprofen 400 to 600 mg four times daily)*** • Acetaminophen 650 mg every 6 hours as needed • Topical medications like menthol/methylsalicylate cream, lidocaine cream/ointment
Sleep disturbance	• Trazodone 25 to 300 mg orally at bedtime
Nausea	• Prochlorperazine 5 to 10 mg every 4 hours as needed • Promethazine 25 mg orally or rectally every 6 hours as needed • Ondansetron 4 mg every 6 hours as needed
Abdominal cramping	• Dicyclomine 20 mg every 6 to 8 hours as needed
Diarrhea	• Loperamide 4 mg orally initially, then 2 mg with each loose stool, not to exceed 16 mg daily • Bismuth subsalicylate 524 mg every 0.5 to 1 hour orally, not to exceed 4192 mg/day

Acetaminophen

- Mechanism of action: exact mechanism unknown
- Maximum Dose: 4g/day
  - Consider closer to 3g/day
- Avoid with liver disease or heavy drinking
- Added to many opioids to medications to try to reduce opioid need
  - Norco 5/325, Percocet 5/325

NSAIDS


How do they work? - NSAID v COX2
Maintenance
Arachidonic acid
Induced
COX-1
COX-2
NSAIDs
Coxibs
thromboxane / prostaglandins
prostaglandins
Primarily support platelet function
Primarily protect GI mucosa
Primarily mediate inflammation, pain & fever

NSAIDS

- COX 1: Expressed in most tissues
  - "Housekeeping" enzyme, regulates normal cellular processes, gastric cyto protection, vascular homeostasis, platelet aggregation, kidney function
- COX 2: Enzyme expressed mainly in states of inflammation
  - Inhibited by glucocorticoids

NSAIDS

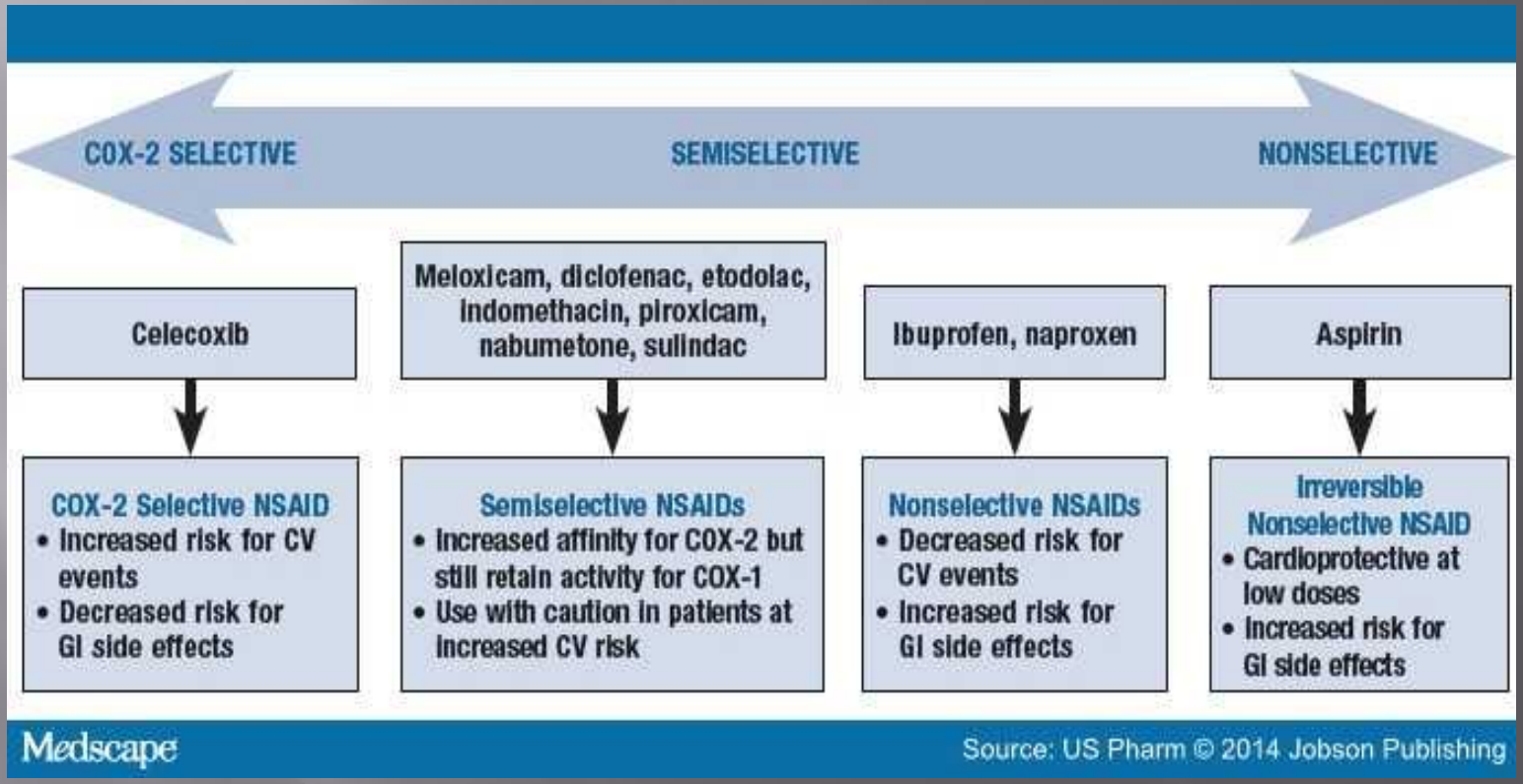
- Side Effects:
  - Interfere with platelet aggregation (non selective)
    - Caution with pts on anticoagulation
  - GI Side effects, dyspepsia, gastric ulceration
    - May be treated with PPI
  - Nephrotoxicity
  - Cardiovascular side effects
    - Interfere with protective effects of ASA
    - Prothrombotic risk – worse with COX 2 inhibitors
      - Vioxx – increased risk of heart attack and stroke – removed from market

Table 1. NSAIDs for Short-term Use (<2 weeks) for Mild to Moderate LBP

Type	Drug (Brand)	LBP-related Indication	Usual Dosage	Comments/ Side Effects
Nonselective NSAIDs				
Oxicams	Meloxicam (Mobic, generic)	OA/RA	7.5-15 mg once daily; maximum dose: 15 mg/d	
	Piroxicam (Feldene, generic)	OA/RA	20 mg once daily	
Propionic Acids	Ibuprofen (Advil, Motrin, others, generic)	Acute pain, OA/RA,	300 mg qid; maximum dose: 3,200 mg/d	*Acute pain:* 400 mg every 4-6 h as needed; *OA/RA:* 1,200-3,200 mg/d
	Keterolac (Toradol, generic)	Acute pain (short-term use <5 d)	10 mg every 4-6 h; maximum dose: 40 mg/d	
	Naproxen (Aleve, Anaprox, Naprosyn, others, generic)	Acute pain, OA/RA	250-500 mg bid; maximum dose: 1,500 mg/d	
	Oxaprozin (Daypro, generic)	OA/RA	600-1,200 mg once daily; maximum dose: 1,800 mg/d	
Naphthyl-Kanoes	Nabumetone (Relafen, generic)	OA/RA	1,000 mg/d; maximum dose: 2,000 mg/d	
Selective NSAIDs				
COX-2 Selective Inhibitors[a]	Celecoxib (Celebrex)	Acute pain, OA/RA	100-200 mg bid, depending on indication	*Use with caution in:* patients with cardiac disease, hypertension

bid, twice a day; LBP, low back pain; NSAID, nonsteroidal anti-inflammatory drug; OA, osteoarthritis; qid, four times a day; RA, rheumatoid arthritis; tid, three times a day

NSAIDS


COX-2 SELECTIVE
SEMISELECTIVE
NONSELECTIVE
Celecoxib
Meloxicam, diclofenac, etodolac, indomethacin, piroxicam, nabumetone, sulindac
Ibuprofen, naproxen
Aspirin
COX-2 Selective NSAID
• Increased risk for CV events
• Decreased risk for GI side effects
Semiselective NSAIDs
• Increased affinity for COX-2 but still retain activity for COX-1
• Use with caution in patients at increased CV risk
Nonselective NSAIDs
• Decreased risk for CV events
• Increased risk for GI side effects
Irreversible Nonselective NSAID
• Cardioprotective at low doses
• Increased risk for GI side effects
Medscape
Source: US Pharm © 2014 Jobson Publishing

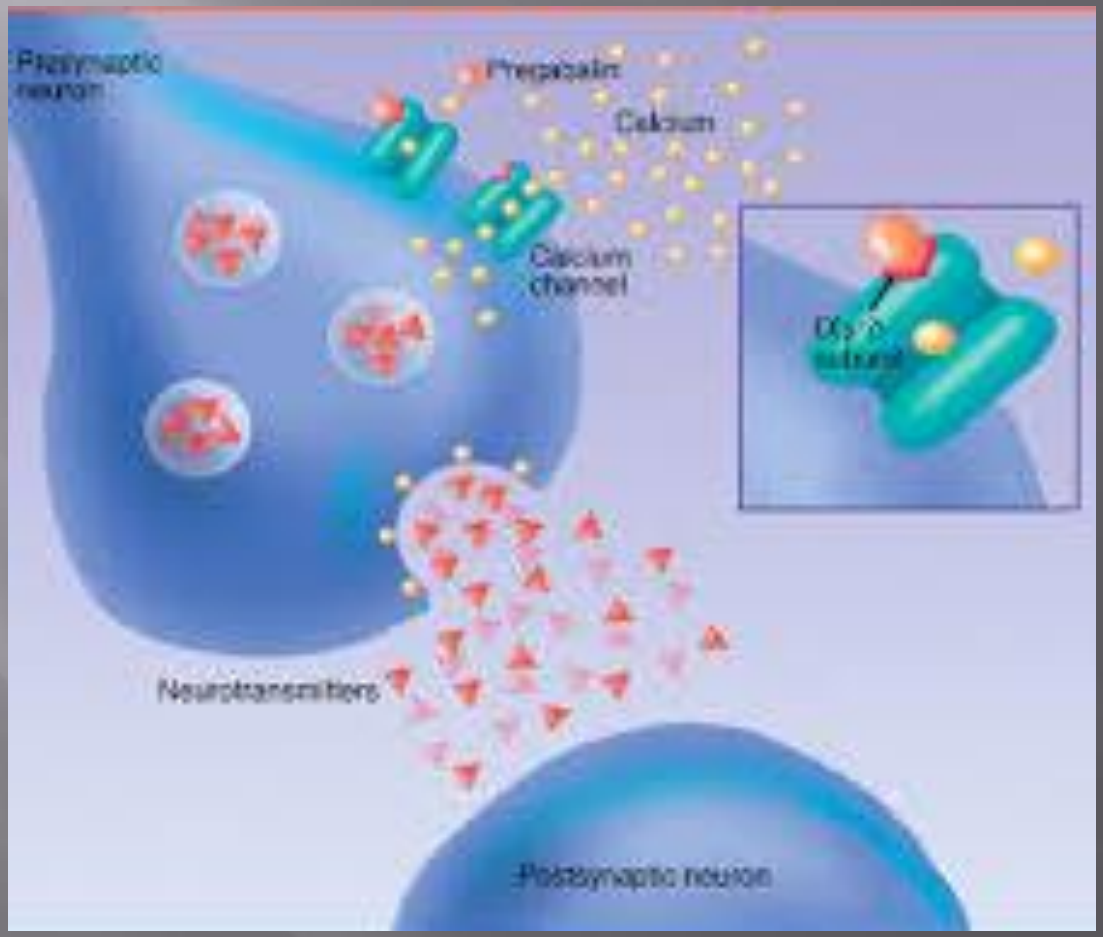
NSAIDS

NSAID Selectivity	Drugs	Notes
COX-2 Selective	Celecoxib	• Increased risk for CV events • Decreased risk for GI side effects
Semiselective	Diclofenac Etodolac Indomethacin Meloxicam Nabumetone Piroxicam Sulindac	• Increased affinity for COX-2 but still retain activity for COX-1 • Use with caution in patients at increased CV risk • Diclofenac has demonstrated the highest CV risk of any of the nonselective NSAIDs
Nonselective	Ibuprofen Naproxen	• Decreased risk for CV events • Increased risk for GI side effects • Naproxen has demonstrated the least CV risk compared to others
Irreversible Nonselective	Aspirin	• Cardioprotective at low doses • Increased risk for GI side effects

Anticonvulsants

- Pregabalin (Lyrica) and Gabapentin (Neurontin)
  - Bind to voltage gated calcium channels at the alpha 2-delta subunit and inhibit neurotransmitter release in the CNS
  - Decreased calcium channel function and release of neurotransmitters leads to reduced neuronal hyperexcitability.
  - Effective for neuropathic pain, fibromyalgia

Pregabalin/Neurontin



Pregabalin/Gabapentin

- Lyrica (Pregabalin): Dose 150-450mg/day, max 600mg/day
- Gabapentin (Neurontin): Dose 900-1800mg/day, max 3600mg/day
- Start Low and Titrate to effect

Pregabalin/Gabapentin

- Similar mechanism of action
- Gabapentin – slow and more variably absorbed, peak plasma concentration approx 3 hrs.
- Lyrica – faster onset of action, better bioavailability, peak plasma concentration approx 1 hr
  - More likely to abuse than Gabapentin

Pregabalin/Gabapentin

- Side Effects
  - Dizziness
  - Somnolence
  - Impaired Thinking
  - Weight Gain
  - LE edema
  - Blurred Vision
  - Withdrawal symptoms/seizures with abrupt D/C

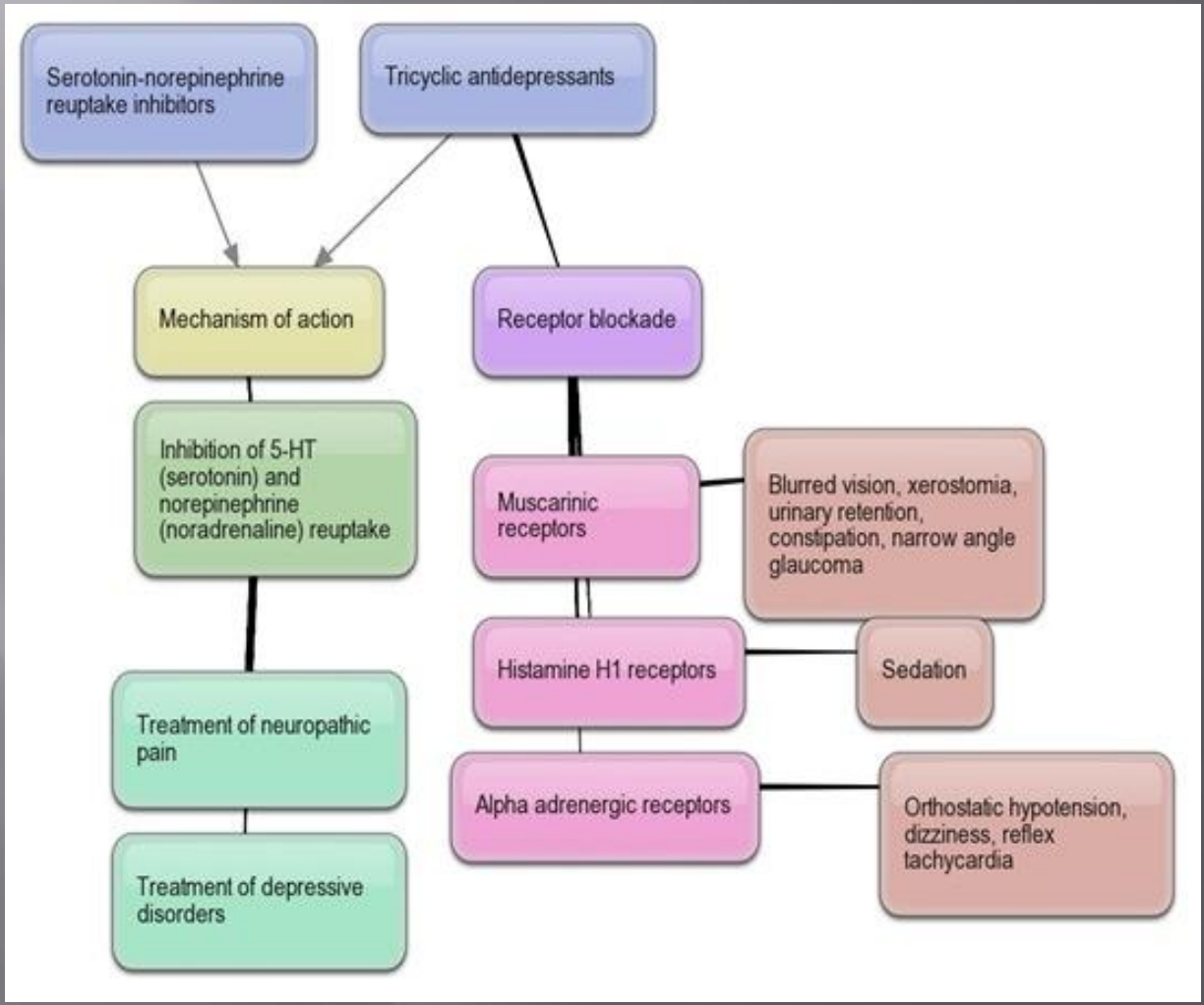
Pregabalin/Gabapentin

- Recent evidence of increased abuse
  - More available than opioids? Prescribers more willing to prescribe and less likely to check OARRS
  - Now both controlled, Lyrica schedule V
  - Lyrica may cause euphoria, higher doses
  - Both used alone at higher doses or along with other medications, frequently opioid or benzo
  - Withdrawal from abrupt cessation

Anticonvulsants

- Topiramate – multiple mechanisms of action
  - Blocks voltage gated Na channels, binds to GABA receptors (enhances activity), antagonizes glutamate receptors
- Migraine Prophylaxis
- Neuropathic pain – not as much evidence as Pregabalin/Gabapentin
- Titrate Slowly – 50mg – 400mg daily
- Side Effects: dizziness, somnolence, cognitive dysfunction, weight loss, kidney stones

Antidepressants



Antidepressants

- Tricyclic Antidepressants
  - Amitriptyline (Elavil)
  - Nortriptyline (Pamelor) – 2nd generation – less side effects
    - Start slow and titrate
    - Side effects
    - Anticholinergic: dry mouth, constipation, blurred vision
    - Antihistaminic: sedation
    - Antiadrenergic: orthostatic hypotension
    - Cardiogenic: prolonged qt interval, conduction abnormalities
    - Use with caution in elderly patients and patients with cardiac disease and conduction abnormalities

Antidepressants

- Serotonin Norepinephrine Reuptake Inhibitors (SNRI)
  - Duloxetine (Cymbalta)
  - Milnacipran (Savella)
    - Both cymbalta and milnacipran approved for fibromyalgia
  - Venlafaxine (Effexor)

Antidepressants

- SNRI
  - Side Effects
  - Nausea, Dry Mouth, Dizziness, Diaphoresis
  - Increased blood pressure
  - Headaches
  - Sexual Dysfunction

Muscle Relaxants

- Soma (Carisoprodol)
  - Converted in Liver to Meprobamate (Miltown)
    - Similar proerties to barbiturate
    - Know to result in physical and psychological dependence, problematic with substance abuse
    - Controlled substance, appears on OARRS
  - "Holy Trinity" – Opioid, Benzo, Soma

Muscle Relaxants

- Classification by proposed mechanism of action:
- CNS Depressants:
  - Antihistamine: Orphenadrine (Norflex)
  - Sedative: Soma, Metaxalone (Skelaxin), Methocarbamol (Robaxin)
  - TCA – like: Cyclobenzaprine (Flexeril)
- Central alpha 2 agonist: Tizanidine (Zanaflex)
- GABA Agonist: Baclofen, Benzo (Valium)

-Raj's Practical Management of Pain, 694

Topicals

- Topical NSAIDs – Diclofenac
- Topical Local Anesthetics – Lidocaine cream
- Compound Creams – multiple components
  - NSAIDS, local anesthetic, muscle relaxants, anticonvulsants, TCA, ketamine

Smoking Cessation

- Smoking has been identified as a modifiable risk factor for chronic pain disorders.
- Multiple clinical studies have linked smoking to a higher risk for chronic pain, and diffuse musculoskeletal pain, and smokers tend to experience greater levels of pain than nonsmokers.
- Smoking is particularly related to a high risk for back pain, which is thought to be due to higher rates of intervertebral disc degeneration among smokers.
- Smoking cessation and reduction showed to improve pain scores.

- Link Between Smoking Cessation and Back Pain, Barber et al, medscape

Marijuana

- Medical Marijuana Legal in Ohio
  - Benefits for chronic pain?
  - Less opioids?
  - Concurrent use?
  - States with medical cannabis laws had 25% lower mean annual opioid overdose mortality compared with states without medical cannabis laws.

    - JAMA 2014
  - Recent studies may question this

Case Example

- 75 yo female pmh of DM, HTN. Multiple back surgeries. Repeat MRI, no further stenosis, nothing further from surgical standpoint.
- Continued axial and radicular pain. PT and interventions with short lived benefit.
- Adjuvant medications with side effects.
- Percocet 5/325 prn, 1-2/day for years, but caused sedation and constipation
- Spinal Cord Stimulator – now opioid free

Case Example

- 45 yo female, pmh depression, fibromyalgia, osteoarthritis (shoulders/hips), OSA, chronic neck pain
  - Presented on Oxycontin 15mg BID, Norco 5/325 qid prn, MED = 65, as well as Xanax prn
  - MRI C spine significant degenerative changes and NF narrowing, X-rays with mild-mod OA
  - Multimodal approach – pain psychology, multiple non opioid trials, interventional treatment options, PT, smoking cessation, non-surgical
  - Now on Norco BID, MED = 10, goal to keep weaning
  - Lyrica 150mg BID, Prozac (failed Cymbalta) by psych
  - Pain more controlled, depression more controlled, maintains full time work

Future Treatments

- Low Dose Naltrexone
  - Opioid receptor antagonist
  - 3-5mg/day (50mg is common dose for opioid addiction treatment)
  - Proposed mechanism is centrally acting anti-inflammatory via action on microglial cells
  - Unique to low doses
  - Shown in small studies to reduce symptom severity in fibromyalgia, Crohn's disease, multiple sclerosis, and CRPS.
  - Minimal side effects, and very low abuse potential (opioid receptor antagonist)

- The use of low dose naltrexone as a novel anti inflammatory treatment for chronic pain, Younger, et al, Clin Rheumatology

Future Treatments

- Ketamine
  - NMDA Receptor Antagonist
  - Infusions have shown benefit in refractory CRPS and neuropathic pain
  - Increased duration of benefit related to higher infused doses, and longer duration of infusion
  - Variable infusion protocols

-Intravenous Ketamine Infusions for Neuropathic Pain Management: A Promising Therapy in Need of Optimization, Maher, et al, anethesia-analgesia

Treatment Options

- Conservative Measures (PT, weight loss, exercise programs, smoking cessation, chiropractic care, acupuncture, pain psychology)
- Non-opioid Medication regimen (Acetaminophen, NSAIDS, Anticonvulsants, Anti-depressants, Topicals)
  - Lyrica, Gabapentin Controlled

Treatment Options

- Interventional Therapies (Epidurals, Facet Blocks, Radiofrequency Ablation, Joint Injections, etc….)
- Surgery
- Neuromodulation (Spinal Cord stimulation, Intrathecal pump)

Questions????