# Pain Management: An Overview


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# Objectives

1. List various types of pain.
2. Describe clinical presentation of pain.
3. Discuss pharmacologic and nonpharmacologic therapies for the management of pain.

# Cases to Think Through…

1. Mark: 72 y.o. complaining of continued pain s/p knee replacement 6 weeks ago
2. Stan: 57 y.o. complaining of lower back pain
3. Maggie: 78 y.o. with pain around her mid torso
4. Lindsay: 23 y.o. complaining of abdominal pain
5. Ann: 36 y.o complaining of severe headaches

- What assessment questions do you have for the individual?
- What type of pain might the person have?
- What treatment would seem to be most appropriate?
- What considerations might impact your recommendations/counseling?

# Whole Person Pain

- Pain is multidimensional, affecting people physically, psychologically, socially and spiritually. Due to:
  - genetics, age, gender, ethnicity, socioeconomic and psychiatric factors, catastrophizing, culture, religion, previous experiences, patient perceptions & expectations


https://pami.emergency.med.jax.ufl.edu/resources/dosing-guide/

# Patient Perception

- A patient's response to prescribed pain treatment can be influenced by factors **unrelated to actual pharmacological treatments**. Influenced by:
  - Perceived effective communication between the healthcare team and the patient
  - Perceived responsiveness by the treating team
  - Perceived empathy by the treating team

https://pami.emergency.med.jax.ufl.edu/resources/dosing-guide/

# Pain Catastrophizing

## Magnification

I wonder if something more serious will happen.

I'm afraid the pain will get worse.

I remember how bad the pain was before.

## Rumination

I really want the pain to go away

I can't stop thinking about the pain.

I just want the pain to stop!

## Helplessness

I feel I can't go on

I just can't stand it anymore

It's terrible and I think it's never going to get any better

I worry all the time that it will *never* end.

https://pami.emergency.med.jax.ufl.edu/resources/dosing-guide/

# Identifying Goals and Expectations

- “What does your pain keep you from doing that you would like to do?”
- “Do you feel you can cope with your pain better if you are a little more relaxed/sleepy or would you rather be more alert? ….There is no wrong answer. ”

# Pain History Mnemonics

## OPQRST

- Onset of event
- Provocation and palliation of symptoms
- Quality
- Region and radiation
- Severity
- Timing

## SOCRATES

- Site
- Onset
- Character
- Radiation
- Associations
- Time course
- Exacerbating/Reliving factors
- Severity

## QISS TAPED

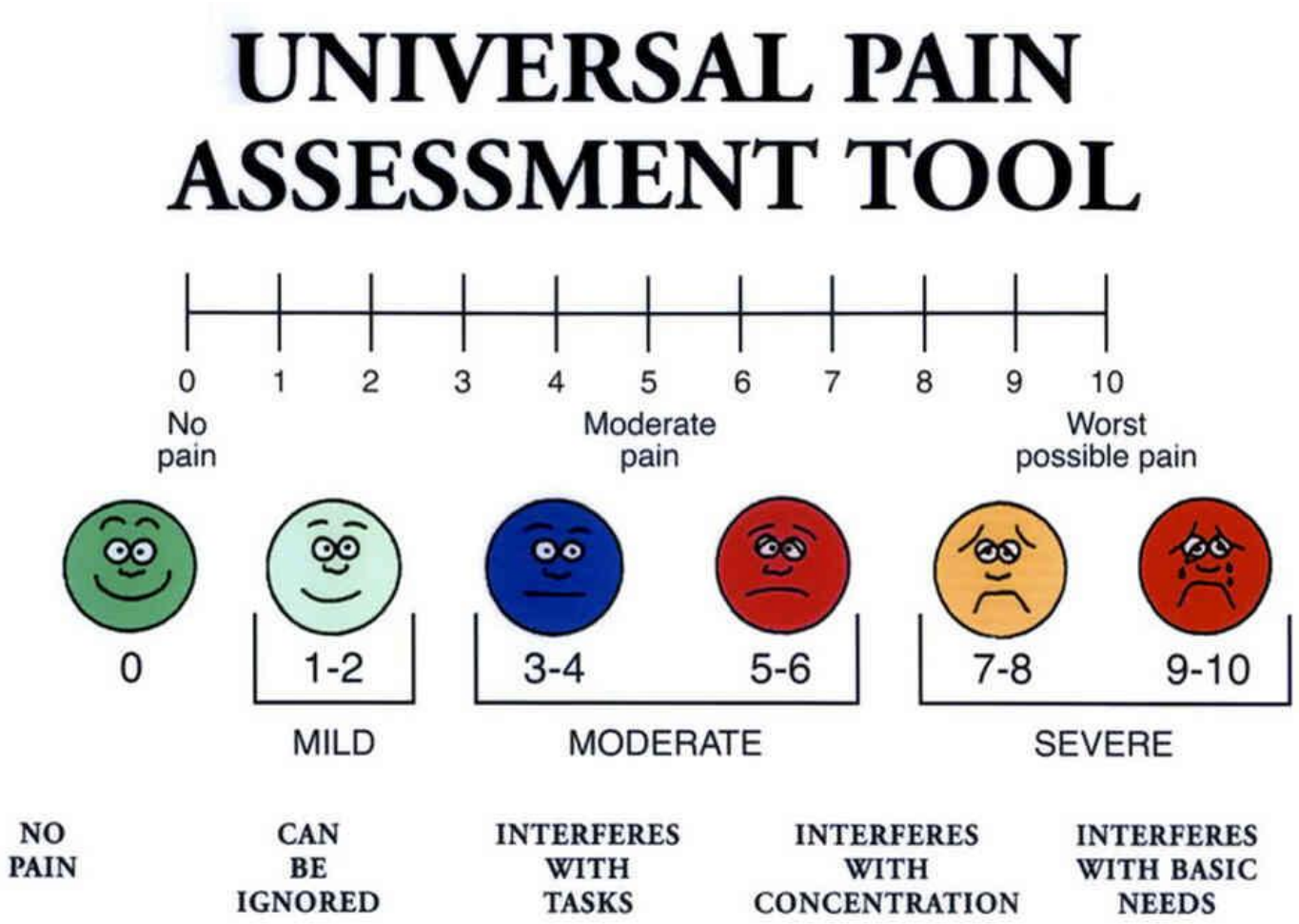
- Quality
- Impact
- Site
- Severity
- Temporal
- Aggravating and alleviating
- Past response and preferences
- Expectations and goals
- Diagnostics and physical exam

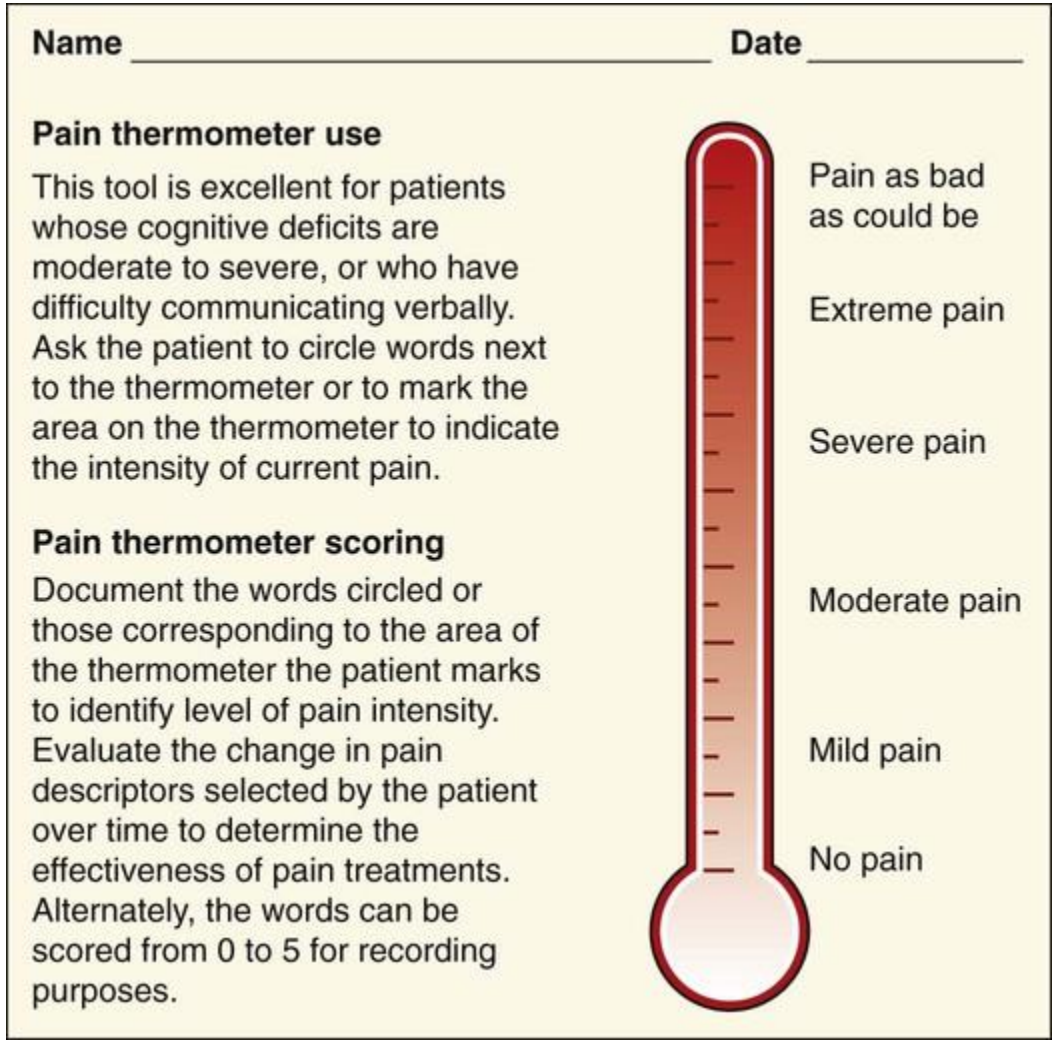
# Assessment Tool: PQRST (U)

- **P = Palliative/Provocative:** What makes it better or worse
- **Q = Quality :** burning, stabbing, gripping, aching, etc
- **R = Radiation:** Localized or not
- **S = Severity:** 0-10
- **T = Temporal:** onset, duration
- ***U = You:*** sleep, mood, ADLs, relationships, general well-being

https://pami.emergency.med.jax.ufl.edu/resources/provider-resources/pain-assessment-scales/

# Standard Unidimensional Pain Scales




https://pami.emergency.med.jax.ufl.edu/resources/provider-resources/pain-assessment-scales/

## Comparative Pain Scale

| | | |
|---|---|---|
| | 0 | No pain. Feeling perfectly normal. |
| **Minor**<br>Does not interfere with most activities. Able to adapt to pain psychologically and with medication or devices such as cushions. | 1<br>Very Mild | Very light barely noticable pain, like a mosquito bite or a poison ivy itch. Most of the time you never think about the pain. |
| | 2<br>Discomforting | Minor pain, like lightly pinching the fold of skin between the thumb and first finger with the other hand, using the fingernails. Note that people react differently to this self-test. |
| | 3<br>Tolerable | Very noticable pain, like an accidental cut, a blow to the nose causing a bloody nose, or a doctor giving you an injection. The pain is not so strong that you cannot get used to it. Eventually, most of the time you don't notice the pain. You have *adapted* to it. |
| **Moderate**<br>Interferes with many activities. Requires lifestyle changes but patient remains independent. Unable to adapt to pain. | 4<br>Distressing | Strong, deep pain, like an average toothache, the initial pain from a bee sting, or minor trauma to part of the body, such as stubbing your toe real hard. So strong you notice the pain all the time and *cannot completely adapt*. This pain level can be simulated by pinching the fold of skin between the thumb and first finger with the other hand, using the fingernails, and squeezing real hard. Note how the similated pain is initially piercing but becomes dull after that. |
| | 5<br>Very Distressing | Strong, deep, piercing pain, such as a sprained ankle when you stand on it wrong, or mild back pain. Not only do you notice the pain all the time, you are now so preoccupied with managing it that you normal lifestyle is curtailed. Temporary personality disorders are frequent. |
| | 6<br>Intense | Strong, deep, piercing pain so strong it seems to partially dominate your senses, causing you to think somewhat unclearly. At this point you begin to have trouble holding a job or maintaining normal social relationships. Comparable to a bad non-migriane headache combined with several bee stings, or a bad back pain. |
| **Severe**<br>Unable to engage in normal activities. Patient is disabled and unable to function independently. | 7<br>Very Intense | Same as 6 except the pain completely dominates your senses, causing you to think unclearly about half the time. At this point you are effectively disabled and frequently cannot live alone. Comparable to an average migraine headache. |
| | 8<br>Utterly Horrible | Pain so intense you can no longer think clearly at all, and have often undergone severe personality change if the pain has been present for a long time. Suicide is frequently contemplated and sometimes tried. Comparable to childbirth or a real bad migraine headache. |
| | 9<br>Excruciating Unbearable | Pain so intense you cannot tolerate it and demand pain killers or surgery, no matter what the side effects or risk. If this doesn't work, suicide is frequent since there is no more joy in life whatsoever. Comparable to throat cancer. |
| | 10<br>Unimaginable Unspeakable | Pain so intense you will go unconscious shortly. Most people have never experienced this level of pain. Those who have suffered a severe accident, such as a crushed hand, and lost consciousness as a result of the pain and not blood loss, have experienced level 10. |

# Pain Assessment Mnemonic (QISS TAPED)

http://projects.hsl.wisc.edu/GME/PainManagement/tables.html?panel=2 Accessed 6/1/201

| | | |
|---|---|---|
| Q | Quality | • What were your first symptoms? What words would you use to describe the pain? (achy, sharp, burning, squeezing, dull, icy, etc...)<br>• Besides sensations you consider to be "pain," are there other unusual sensations, such as numbness? |
| I | Impact | • How does the pain affect you?<br>• How does the pain impact your sleep, activity, mood, appetite (other - work, relationships, exercise, etc.)<br>• What does the pain prevent you from doing?(Depression screen) Do you feel sad or blue? Do you cry often? Is there loss of interest in life? Decreased or increased appetite?<br>• (Anxiety screen) Do you feel stressed or nervous? Have you been particularly anxious about anything? Do you startle easily? |
| S | Site | • Show me where you feel the pain. Can you put your finger/hand on it?<br>• Or show me on a body map?<br>• Does the pain move/radiate anywhere? Has the location changed over time? |
| S | Severity | • On a 0-10 scale with 0 = no pain and 10 = the worst pain imaginable, how much pain are you in right now?<br>• What is the least pain you have had in the past (24 hours, one week, month)?<br>• What is the worst pain you have had in the past (24 hours, one week, month)?<br>• How often are you in *severe* pain? (hours in a day, days a week you have pain)? |
| T | Temporal Characteristics | • When did the pain start? Was it sudden? Gradual? Was there a clear triggering event?<br>• Is the pain constant or intermittent? Does it come spontaneously or is it provoked?<br>• Is there a predictable pattern? (e.g., always worst in the morning or in the evening? Does it suddenly flare up?) |
| A | Aggravating and Alleviating Factors | • What makes the pain better?<br>• What makes the pain worse? When do you get the best relief? How much relief do you get? How long does it last? |
| P | Past Response, Preferences | • How have you managed your pain in the past? (Ask about both drug and non-drug methods<br>• What helped? What did not help? (Be specific about drug trials - how much and how long?)<br>• What medications have you tried? Was the dose increased until you had pain relief or side effects? How long did you take the drug? Are there any pain medicines that have caused you an allergic or other bad reaction?<br>• How do you feel about taking medications?<br>• Have you tried physical or occupational therapy? What was done? Was it helpful?<br>• Have you tried spinal or other injections for pain treatment? What was done? Was it helpful? |
| E | Expectations, Goals, Meaning | • What do you think is causing the pain?<br>• How may we help you? What do you think we should do to treat your pain?\What do you hope the treatment will accomplish?<br>• What do you want to do that the pain keeps you from doing?<br>• What are you most afraid of? (Uncovers specific fears, such as fear of cancer, which should be acknowledged and addressed.) |
| D | Diagnostics & Physical Exam | • Examine and inspect site (see below)<br>• Perform a systems assessment and examination as indicated<br>• Review imaging, laboratory and/or other test results as indicated |

# Adult Pain Severity Scales

Verbal, alert and oriented

| Measurement Scale | Description |
|---|---|
| **Verbal Numeric Scale (VNS)/ Numeric Rating Scale (NRS)** | Self-report scale. Eleven point scale that requires understanding of numbers, addition and subtraction. |
| **Verbal rating scale (VRS)** | Five pain levels are indicated in large print on a sheet give to the patient: no, pain, mild pain, moderate pain, severe pain, unbearable pain. |
| **Visual Analogue Scale** | A 100-mm rule with a movable cursor: "no pain" is written at he left end of the horizontal line along which the cursor is moved, and "maximal pain" at the right end. |
| **Defense and Veterans Pain Rating Scale 2.0 (DVPRS)** | Self-report scale. Eleven point scale that requires the patient to identify pain by numerical rating, color intensity, facial expression, and pain disruption. Followed by four supplemental questions evaluating the biopsychosocial impact of pain. |

Non-verbal or Cognitive Impairment

| Measurement Scale | Description |
|---|---|
| **Adult Non-Verbal Pain Scale (NVPS)** | Behavioral scale. Based on FLACC scale and contain behavioral dimensions and physiology dimensions that are graded by severity. |
| **Pain Assessment in Advanced Dementia (PAINAD) Scale** | Assesses pain in patients with dementia. Total scores range from 0 to 10 (based on a scale of 0 to 2 for five items: breathing. Vocalization, facial expression, body language, and consolability), higher score indicates more severe pain |
| **Behavioral Pain Scale (BPS)** | Behavioral scale. Three observational items (facial expression, upper limbs, and compliance with ventilation). Higher score, greater discomfort. |
| **Critical-Care Observation Tool (CPOT)** | Behavioral scale. Used for intubated and nonintubated critical care patients. Four domains (facial expressions, movements, muscle tension, and ventilator compliance. Higher score, great pain level |

https://pami.emergency.med.jax.ufl.edu/resources/provider-resources/pain-assessment-scales/

# Pediatric Pain Severity Scales

- **The Neonatal Infant Pain Scale (NIPS):** used in the Neonatal Intensive Care Unit.
- **The FLACC (Face, Legs, Activity, Cry, Consolability):** for children from birth and older including developmentally delayed patients
  - Observational scale (excluding patients who are paralyzed, have spasticity
- **The FACES-R** For children 4-18 years old
  - shows faces with numbers 0-10 that correspond to different degrees of pain.
  - The child points to the picture of the face he / she feels most like.
- **The NRS (the Numeric Rating Scale)**: For children ages 6 to adult
  - Zero (no pain) and 10 (worst imaginable)
- **The COMFORT scale:** For unconscious children on a ventilator

https://pami.emergency.med.jax.ufl.edu/resources/provider-resources/pain-assessment-scales/

# Anxiety and Depression Assessment

General Anxiety Disorder Scale

## GAD-7

| Over the last 2 weeks, how often have you been bothered by the following problems? (Use "✔" to indicate your answer) | Not at all | Several days | More than half the days | Nearly every day |
|---|---|---|---|---|
| 1. Feeling nervous, anxious or on edge | 0 | 1 | 2 | 3 |
| 2. Not being able to stop or control worrying | 0 | 1 | 2 | 3 |
| 3. Worrying too much about different things | 0 | 1 | 2 | 3 |
| 4. Trouble relaxing | 0 | 1 | 2 | 3 |
| 5. Being so restless that it is hard to sit still | 0 | 1 | 2 | 3 |
| 6. Becoming easily annoyed or irritable | 0 | 1 | 2 | 3 |
| 7. Feeling afraid as if something awful might happen | 0 | 1 | 2 | 3 |

***(For office coding: Total Score T____ = ____ + ____ + ____ )***

**PATIENT HEALTH QUESTIONNAIRE (PHQ-9)**

NAME:_____ DATE:_____

| Over the last *2 weeks*, how often have you been bothered by any of the following problems? *(use "✓" to indicate your answer)* | Not at all | Several days | More than half the days | Nearly every day |
|---|---|---|---|---|
| 1. Little interest or pleasure in doing things | 0 | 1 | 2 | 3 |
| 2. Feeling down, depressed, or hopeless | 0 | 1 | 2 | 3 |
| 3. Trouble falling or staying asleep, or sleeping too much | 0 | 1 | 2 | 3 |
| 4. Feeling tired or having little energy | 0 | 1 | 2 | 3 |
| 5. Poor appetite or overeating | 0 | 1 | 2 | 3 |
| 6. Feeling bad about yourself—or that you are a failure or have let yourself or your family down | 0 | 1 | 2 | 3 |
| 7. Trouble concentrating on things, such as reading the newspaper or watching television | 0 | 1 | 2 | 3 |
| 8. Moving or speaking so slowly that other people could have noticed. Or the opposite — being so figety or restless that you have been moving around a lot more than usual | 0 | 1 | 2 | 3 |
| 9. Thoughts that you would be better off dead, or of hurting yourself | 0 | 1 | 2 | 3 |
| add columns | | + | + | |

*(Healthcare professional: For interpretation of TOTAL, please refer to accompanying scoring card).* TOTAL:

| 10. If you checked off *any problems*, how *difficult* have these problems made it for you to do your work, take care of things at home, or get along with other people? | |
|---|---|
| | Not difficult at all _____ |
| | Somewhat difficult _____ |
| | Very difficult _____ |
| | Extremely difficult _____ |



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# Assessing Pain Management Efficacy

## SUBJECTIVE

- **Pain ratings**
- Subjective description of pain severity
  - Pain rating changes
  - Ability to achieve goals

## OBJECTIVE

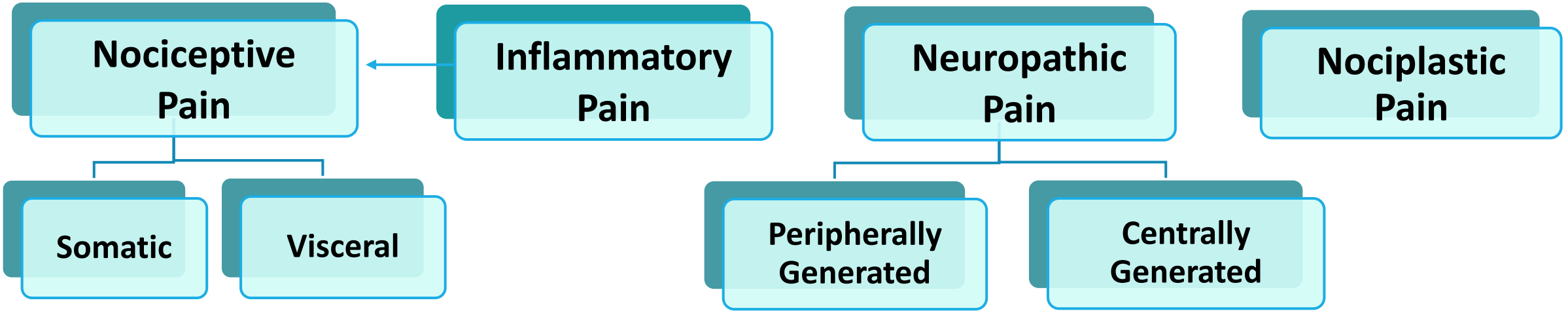
- **Functional status ratings**
- Objective assessment of improved
  - Sleep
  - Ability to perform ADLs
  - Ability to walk farther distance
  - Ability to work longer

# Pain Classifications

| | |
|---|---|
| Acute Pain | • Identified event<br>• Resolves within days-weeks<br>• Usually nociceptive |
| Chronic Pain | • Multifactorial, cause not easily identified<br>• ≥ 3 months of persistent pain<br>• Nociceptive or neuropathic |
| Acute on Chronic Pain | • Incident pain<br>• Breakthrough pain |

Dowell et al, 2016.

# Types of Pain

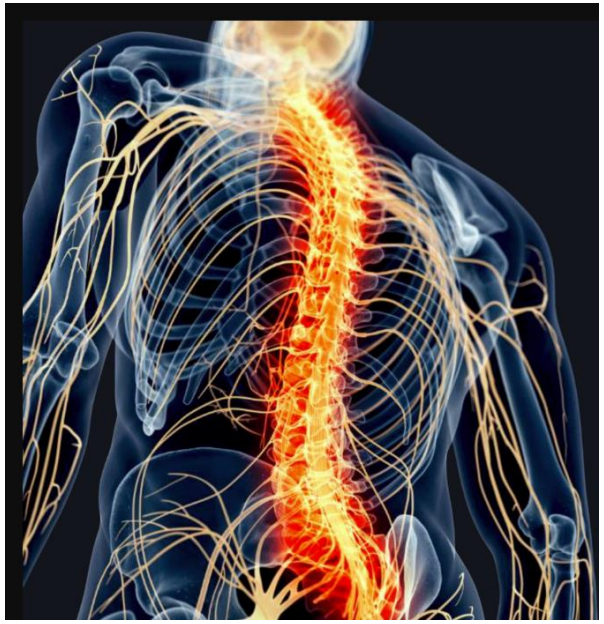



**Nociceptive Pain**
- Normal processing of stimuli
- Usually responds to non-opioid and/or opioid analgesics

**Neuropathic Pain**
- Abnormal processing of sensory input
- Treatment usually includes adjuvants

# Nociplastic Pain

## (Previously Central Sensitization)



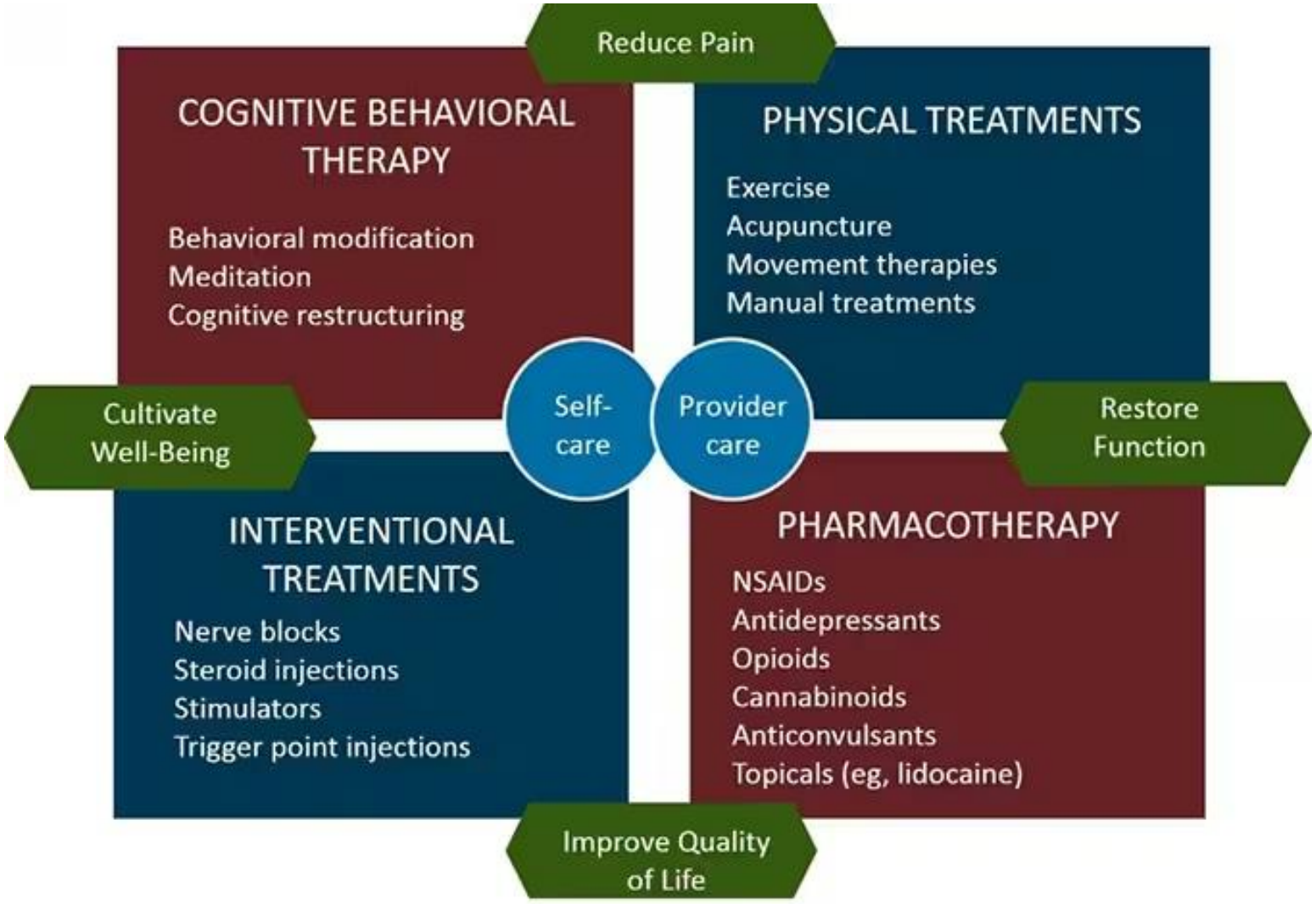
- Persistent pain that arises from altered nociception
- No clear evidence of actual or threatened tissue damage
- Causing the activation of peripheral nociceptors
- Examples:
  - Chronic primary :
    - widespread pain (e.g., fibromyalgia), headache, oro-facial pain, visceral, musculoskeletal pain
  - Complex regional pain syndrome
- Alters sleep & mood,
- Causes fatigue and inability to do ADLs

- No longer a just symptom → chronic disease

# Pain Management Goals

- Maximize the patient's health related quality of life:
  - Decrease pain intensity
  - Maintain level of functioning
  - Minimize physical deterioration
  - Improve family and social relationships
  - If possible, minimize dependency on medications
- Select the most effective agent with least side effects

# Multimodal Pain Management



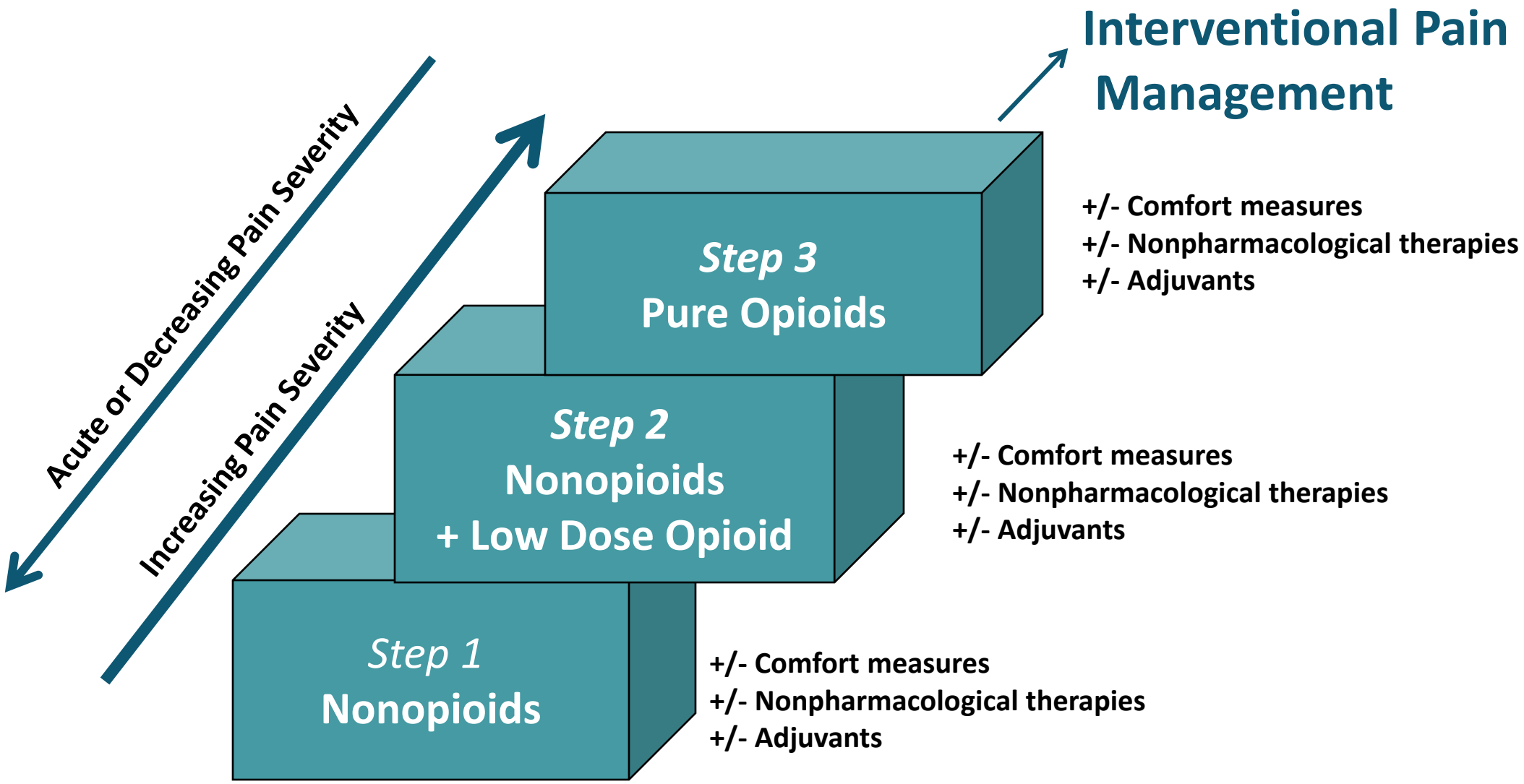

https://www.medscape.org/viewarticle/917714_3

# Pharmacogenomics

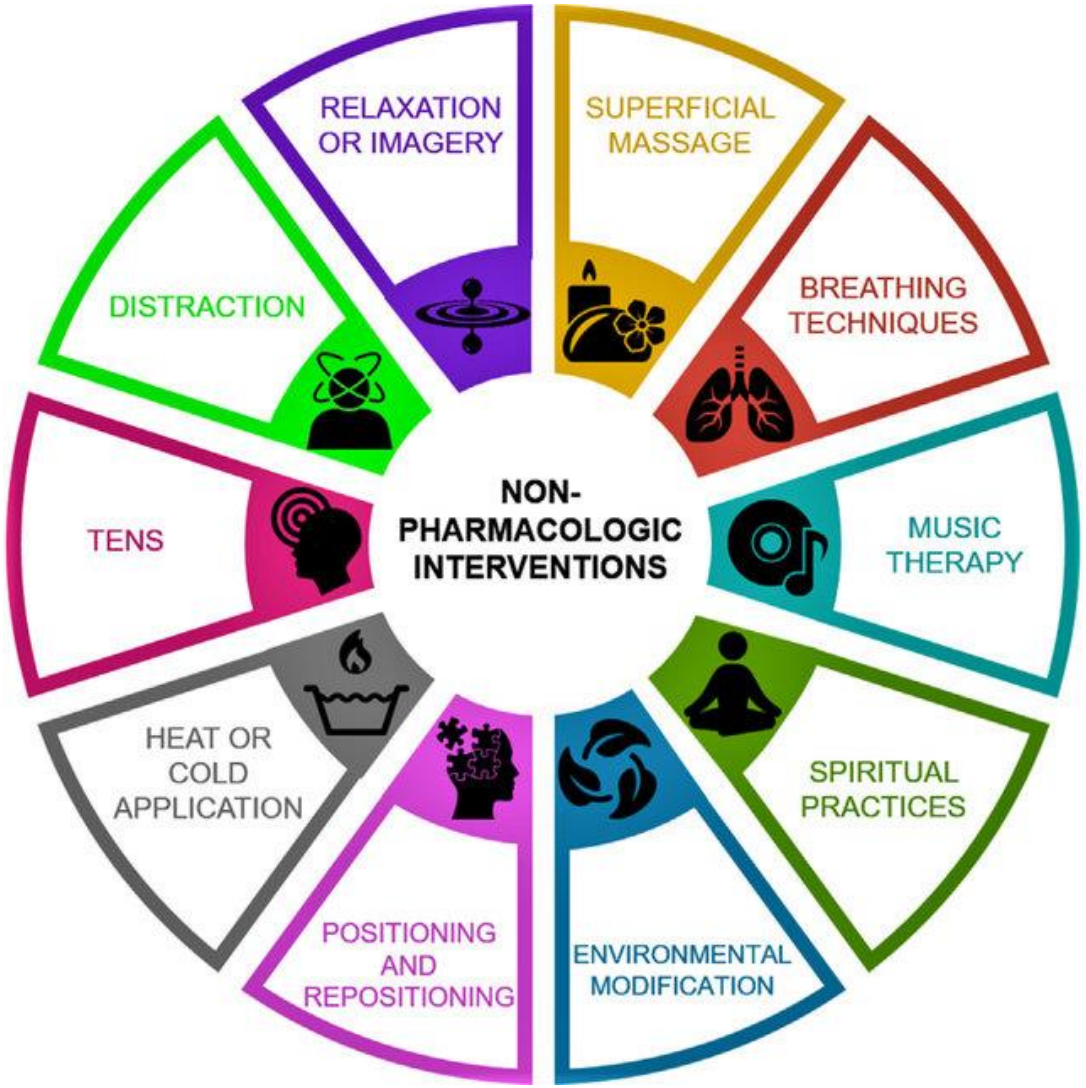
- Certain ethnic groups are known to carry genetic mutations of the liver CYP450 enzymes responsible for drug metabolism.
  - "Ultra-rapid metabolizers" of certain drugs such as codeine → morphine can result in supra-therapeutic dosing.
  - "Slow metabolizers" and do not efficiently metabolize codeine never achieve therapeutic levels.
- Caucasian and African American populations have approximately equal proportions of fast and slow metabolizers.
- 90% of certain Asian groups are fast acetylators.


analgesia
pain
medicine
medical
healthcare
surgery
patient
illness
syringe
anesthesia
people
doctor
injury
anesthetic
treatment
epidural
back
condition
paraplegia
drug
selective
medicament
inhalation
awareness
hospital
loss
procedure
injection
painless
painful
human
pharmacy
injecting
confusion
needle
composition
therapy
mask
surgical
relaxation
operating
muscle
equipment
relief
section
tablet
stethoscope
painkiller
fluid
disease
anaethesia
cure
concept
physician
drugstore
medication
pills
diagnosis
intervention
addiction
anaesthesia
spinal
ache
glove
catheter
cerebrospinal
health

# WHO Analgesic Ladder

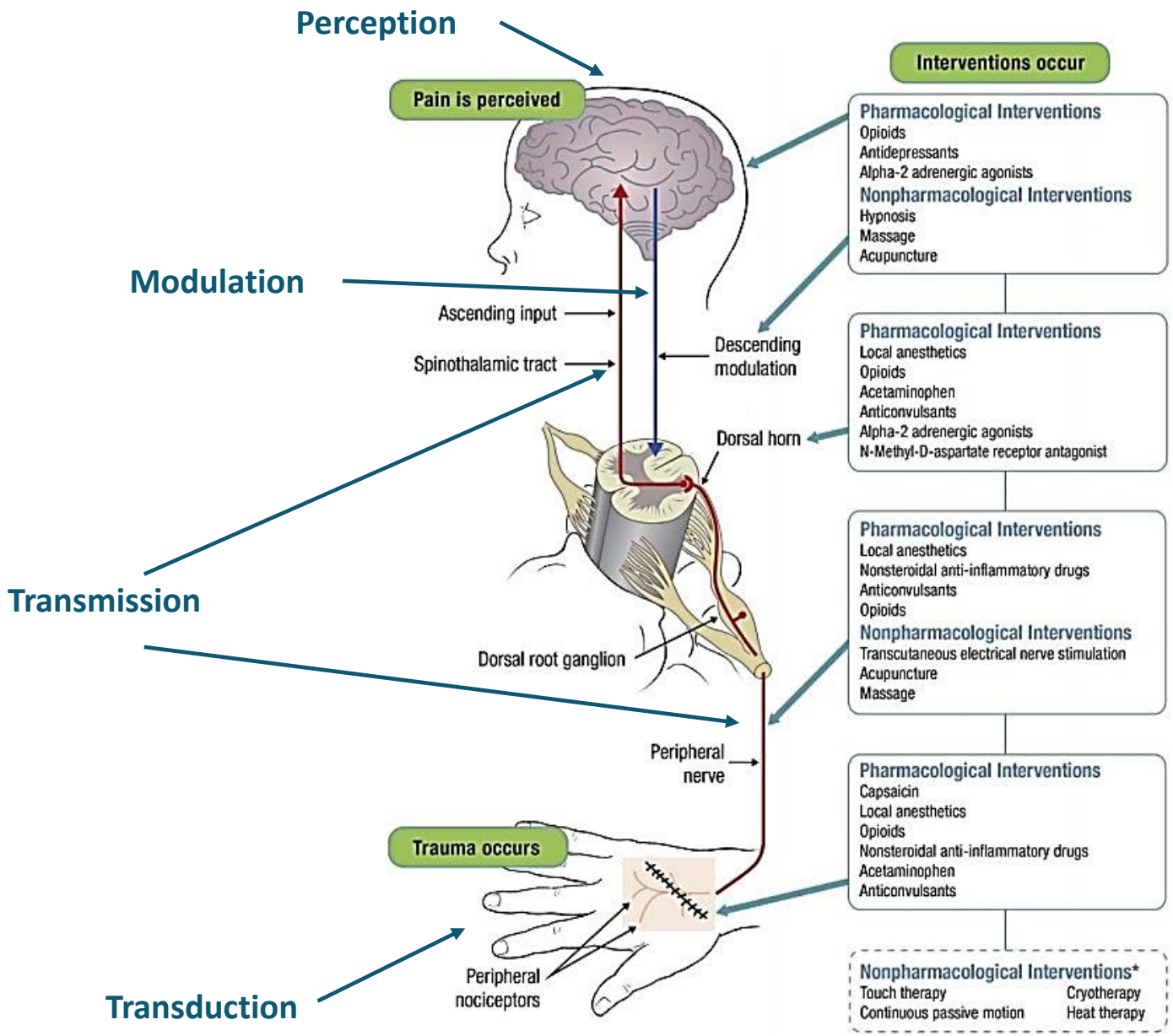


# Non-Pharmacological Therapy




| Psychosocial Interventions | Complementary and Integrative Health (CIH) Therapies | Rehabilitation Therapies | Exercise |
|---|---|---|---|
|  |  |  |  |
| • Cognitive-Behavoiral Therapy (CBT)<br>• Acceptance and Commitment Therapy (ACT)<br>• Progressive relaxation therapy<br>• Mindfulness-based Therapies<br>• Pain School<br>• Behavior groups | • Acupuncture<br>• Massage<br>• Chiropractic therapy<br>• Ice and heat therapy<br>• Meditation | • Physical therapy<br>• Occupational therapy | • Stretching<br>• Tai chi<br>• Swimming<br>• Hiking<br>• Walking<br>• Yoga<br>• Chair exercises |

# Pain Pathways



# Nonopioids

| Medications | Mechanism of Action | Indication | Side Effects | Cautions |
|---|---|---|---|---|
| Acetaminophen<br><br>Not a peripheral anti-inflammatory | Uncertain; May decrease prostaglandin production in the brain, not the periphery | Mild to moderate pain | Few side effects at therapeutic dose | Hepatotoxic at high dose. No more than 4 g/24 h or 2 g/ 24 h if consume more than 2-3 alcoholic drinks per day. Caution: many opioid combination products contain acetaminophen |
| Aspirin | **Irreversible** inhibition of both cyclooxygenase (COX) isozymes, COX-1 and COX-2 | Mild to moderate pain | GI bleed, ↓kidney function, ↓platelet aggregation, hypersensitivity reactions | Risk of Reye's syndrome in children |
| Ibuprofen, Naproxyn, Diclofenac, Ketorolac | Reversibly inhibit both COX-1 and COX-2 | Mild to moderate pain | Same as aspirin except reversible effect on platelets | Use lowest dose for shortest period of time. High dose may increase the risk of MI and stroke. Formulations of topical diclofenac are available |
| Meloxicam<br>Celecoxib | Primarily inhibits COX-2 | Mild to moderate pain | No effect on platelets; 50% less risk of GI effects unless taken in combination with aspirin; ↓kidney function | Only "selective" COX-2 inhibitor marketed. High dose increases the risk of myocardial infarction and stroke |

# Antidepressants

| Medications | Mechanism of Action | Indication | Side Effects | Cautions |
|---|---|---|---|---|
| **Tricyclics**<br>nortriptyline, desipramine, amitriptyline, | Central inhibition of norepinephrine and serotonin reuptake; also block $Na^+$ channel | Neuropathic pain | Sedative, **anticholinergic effects**; impaired balance ; cognitive impairment; postural hypotension; weight gain; cardiac toxicity (arrhythmia, tachycardia, stroke, acute myocardial infarction) | **Avoid amitriptyline in elderly.** Use small doses and titrate slowly. Check EKG for conduction abnormalities prior to prescribing Antidepressant effect manifests at higher doses, analgesic effect seen at lower doses |
| **SNRIs- dual reuptake inhibitors**<br>duloxetine, venlafaxine milnacipran | Inhibit norepinephrine and serotonin reuptake in CNS | Neuropathic pain,<br>FDA approved for fibromyalgia | GI upset, ataxia, sedation, | Relieve insomnia, depression and anxiety |

# Discontinuation syndrome:

## Abrupt discontinuation or interruption of antidepressant therapy

- Common Symptoms :
  - nausea, vomiting, diarrhea, headaches, lightheadedness, dizziness, diminished appetite, sweating, chills, tremors, paresthesias, fatigue, somnolence, and sleep disturbances (e..g, vivid dreams, insomnia).
- Less common symptoms :
  - electric shock-like sensations, cardiac arrhythmias (more common with tricyclic antidepressants), myalgias, parkinsonism, arthralgias, and balance difficulties.
  - Psychological symptoms: agitation, anxiety, akathisia, panic attacks, irritability, aggressiveness, worsening of mood, dysphoria, mood lability, hyperactivity, mania/hypomania, depersonalization, decreased concentration, slowed thinking, confusion, and memory or concentration difficulties.

# Antiepileptics

| Medications | Mechanism of Action | Indication | Side Effects | Cautions |
|---|---|---|---|---|
| gabapentin, pregabalin | Bind to $\alpha_2\delta$ subunit of the calcium channel in the dorsal horn. | Neuropathic pain; pregabalin also approved for fibromyalgia | Somnolence; mental clouding dizziness; ataxia; weight gain | Many side effects but all reversible after discontinuation. Also have antianxiety effects. No drug-drug interactions |
| carbamazepine | $Na^+$ channel blockers | Neuropathic pain; CBZ drug of choice for trigeminal neuralgia | CBZ: sedation, dizziness, nausea, unsteadiness, 2% leukopenia, thrombocytopenia. lamotrigine, Stevens Johnson syndrome (necrotizing rash) | Considered third-line agents for neuropathic pain |
| topiramate | Multiple effects | Migraine prophylaxis | Somnolence, fatique, nervousness | The rare medication used in pain management that causes weight loss |

# Gabapentin & Pregabalin Disease-Related Concerns

- Renal impairment: Use with caution in patients with renal impairment; dose adjustment required.

- Seizure disorder: The safety and efficacy of the extended release formulation has not been studied in patients with epilepsy.

# Topical Anesthetics

- **Lidocaine Patch:** [*US Boxed Warning:* Life-threatening and fatal events in infants and young children]
  - Do not apply to non-intact skin.
  - May be cut
  - Avoid exposing to external heat sources (eg, heating pad, electric blanket, heat lamp, hot tub).
  - ≤ 3 patches at once
  - 4% OTC; 5% RX (OTC usually less expensive than RX)
- **Other Topical Preparations**: multiple uses!

# Common Types of Headaches (~150 types)

- **Tension-type**
- **Migraine**
  - **Aura (classic)**
  - **No Aura (common)**
  - Ophthalmologic
  - Basilar
  - Atypical
- **Cluster**
- **Chronic Daily Headache**
- **Sinus**
- **Analgesic Rebound**
- Symptomatic
- **Medication Induced**
  - Nitrates
  - Birth control medications
  - Hormone Replacement medications
  - Stimulants
- Chronic Paroxysmal Hemicrania

# Headaches

## Tension

Pain experienced as a squeezing band around the head

## Sinus

Pain behind browbone and/or cheekbones

## Cluster

Pain localized in one eye

## Migraine

Typical signs are pain,nausea and alfered vision

# Tension-Type Headaches: Treatment

- **Occasional:**
  - Acetaminophen, NSAIDs, Aspirin
- **Chronic:**
  - Tricyclic antidepressants:
  - Other antidepressants: venlafaxine & mirtazapine
  - Anticonvulsants: topiramate
- **Alternative stress reduction therapies:**
  - Cognitive behavioral therapy
  - Biofeedback
  - Massage therapy
  - Acupuncture

# Migraine Abortive Treatment

- **Nonopioid analgesics:** NSAIDs- ibuprofen, celecoxib, diclofenac, or indomethacin; combination acetaminophen, aspirin, and caffeine,
- **Triptans:** almotriptan, eletriptan,frovatriptan, naratriptan, rizatriptan, sumatriptan, zolmitriptan
- **Ergots** such as dihydroergotamine nasal (Migranal, Trudhesa), or ergotamine tartrate (Ergomar)
- **Calcitonin gene-related peptide antagonists (gepants)** ubrogepant (Ubrelvy), rimegepant (Nurtec ODT) or intranasal zavegepant (Zavzpret)
- **Ditans**: lasmiditan (Reyvow)
- **Opioids and anti-nausea drugs** chlorpromazine, droperidol, metoclopramide, and prochlorperazine

# Migraine Preventative Treatment

- **Antihypertensives:** beta-blockers (propranolol, timolol) or calcium channel blockers (verapamil)
- **Antidepressants:** amitriptyline or nortriptyline
- **Antiepileptics:** topiramate or valproic acid
- **Calcitonin gene-related peptide (CGRP) inhibitors** : atogepant (Qulipta), eptinezumab (Vyepti), erenumab (Aimovig), fremanezumab (Ajovy), galcanezumab (Emgality), and rimegepant (Nurtec ODT -- helps treat and prevent migraines)
- **Botox**

# Cluster Headaches

- Excruciating pain striking quickly without warning
- Generally, in or around one eye, but may radiate to face, head, neck & shoulders
- Males (3-7 times ) > Females; Can be alcohol induced
- **Abortive Treatment**
  - Oxygen: 100% oxygen through a mask at least 12 liters within 15 minutes.
  - Intranasal lidocaine, triptans, octreotide, ergot alkaloids
- **Prophylactic Treatment**
  - Verapamil (drug of  choice), prednisone, lithium carbonate, nerve block, melatonin

# Sinus Headache Treatment

- OTCs: acetaminophen,NSAIDs
- Decongestants.
- Nasal steroid sprays
- Antihistamines
- Normal saline
- Moisture
- Antibiotics ?

# Medication Overuse Headache

A) Headache occurring on ≥15 days/month in a patient with a preexisting headache disorder

B) B) Regular overuse for >3 months of 1 or more drugs that can be taken for acute and/or symptomatic treatment of headache, with medication overuse defined as:

   1. 10 or more days/month for ergot derivatives, triptans, opioids, combination analgesics, and a combination of drugs from different classes that are not individually overused

   2. 15 or more days/month for nonopioid analgesics, acetaminophen, and NSAIDs (including aspirin)

C) C) Not better accounted for by another diagnosis ICHD, International Classification of Headache Disorders

ICD3 Criteria The American Headache Society Position Statement On Integrating New Migraine Treatments Into Clinical Practice American Headache Society. Headache 2019;59:1-18

# Opioid Terminology

The opium poppy was cultivated as early as 3400 BC in Mesopotamia

- **Opium**: mixture of alkaloids from the poppy seed
- **Opiates**: naturally occurring alkaloids: morphine, codeine,& thebaine
- **Opioid**: broad term including naturally occurring, semi-synthetic and synthetic opioid compounds

**X** **Narcotic**: from Greek word for stupor, originally used to describe medications for sleep, then used to describe opioids, now a legal term used to describe all illicit drugs.

- *Prescription opioids should not be called NARCOTICS*

# General Principles for Opioid Selection

**Consider the following when making recommendations for the *initiation and optimization* of opioid therapy**:

1. Develop an individualized, patient-specific treatment regimen
2. Design an adequate analgesic trial
3. Appropriately monitor response to therapy
4. Anticipate, recognize and address opioid-induced adverse effects
5. Assess risk for aberrant behavior

# Types of Opioids

- **Endogenous opioids:**

***(produced naturally in the body)***

  - **endorphins**
  - **enkephalins,**
  - **dynorphins**

- **Natural <u>opiates</u>:**

(found in the opium resin of the opium poppy)

  - Codeine
  - Morphine
  - Thebaine

- **Semi-synthetic opioids:**
  - Hydrocodone
  - Oxycodone
  - Heroin
  - Hydromorphone
  - Oxymorphone
  - Buprenorphine
- **Synthetic opioids:**
  - Meperidine
  - Fentanyl
  - Methadone

# Opioid Receptors

## Mu agonist:

- Analgesia
- Euphoria
- Respiratory depression

## Kappa agonist:

- Dysphoria
- Psychosis

## Delta agonist

- Analgesia
- Psychosis

# Opioid Chemical Classifications

| Class and Generic Name (Brand Name) |
| --- |
| **Phenanthrenes** |
| Morphine (various) |
| Codeine (various) |
| Hydrocodone (combination) |
| Hydromorphone (Dilaudid, various) |
| Oxycodone (various) |
| Oxymorphone (Numorphan, Opana) |
| Levorphanol (Levo-Dromoran) (NMDA Receptor Antagonist+Norepinephrine/Serotonin Reuptake inhibitors) |
| **Phenylpiperidine**s |
| Meperidine (Demerol, various) |
| Fentanyl (Sublimaze, Duragesic. Actiq, Onsolis, Fentora, various) |
| **Diphenylheptanes** |
| Methadone (Dolophine) (NMDA Receptor Antagonist+Norepinephrine/Serotonin Reuptake inhibitors) |

# Opioid Chemical Classifications

| Class and Generic Name (Brand Name) |
| --- |
| **Agonist-Antagonist** |
| Pentazocine (Talwin, various) |
| Butorphanol (Stadol, various) |
| Nalbuphine (Nubain, various) |
| **Partial Agonist** |
| Buprenorphine (Buprenex, Butrans, Belbuca, various) |
| **Antagonist** |
| Naloxone (Narcan, various) |
| Naltrexone (Revia, Vivitrol) |
| **Central Analgesics (Norepinephrine/Serotonin Reuptake inhibitors)** |
| Tramadol (Ultram, various) |
| Tapentadol (Nucynta) |

# Opioid Pharmacokinetics

- Absorption
- Bioavailability
- First Pass Effect
- Solubility
  - Has significant impact on bioavailabilty
  - Lipophilicity impacts onset, duration of action

| Solubility | IR OPIOID | Onset of Action | Duration of Action |
|---|---|---|---|
| Hydrophilic | Morphine | 30-40 minutes | 4 hours |
|  | Oxycodone | 30 minutes | 4 hours |
| | Oxymorphone | 30 minutes | 4-6 hours |
| | Hydromorphone | 30 minutes | 4 hours |
| | Methadone | 10-15 minutes | 4-8 hours |
| Lipophilic | Fentanyl (transmucosal) | 5-10 minutes | 1-2 hours |

Bennett D, Burton AW, Fishman S et al. Consensus panel recommendations for the assessment and management of breakthrough pain: part 2 management *P&T*. 2005; 30:354-61.

# Opioid Metabolism

| Primarily Rely on CYP450 | CYP Metabolism | Metabolite |
|---|---|---|
| Codeine | CYP-2D6 | Morphine |
| Fentanyl | CYP-3A4 | |
| Hydrocodone | CYP-2D6, 3A4 | Hydromorphone |
| Methadone | CYP-2D6, 3A4, 2C8, 2C9, 2C19, 2B6 , 1A2 | |
| Oxycodone | CYP-2D6, 3A4 | Oxymorphone, Noroxycodone |
| Tramadol | CYP-2D6 | Transmethyl-tramadol |
| **Rely on Glucuronidation** | | **Comments** |
| Hydromorphone | HM-3G | Glucuronide metabolism may affect efficacy or toxicity<br><br>No evidence that genetic polymorphism of CYPs alters metabolism to affect efficacy or toxicity |
| Morphine | M-3G, M-6G | |
| Oxymorphone | Oxymorphone -3G | |
| Tapentadol | | |

# Opioid Potency and Efficacy

- Potency
  - Intensity of analgesic effect for a given dose
- Efficacy
  - maximal effect produced by a drug
    - E.g. Oxycodone 20mg = Morphine 30mg
- Most pure agonist opioids are considered to have equal maximal efficacy
- Exception: codeine

# Equianalgesic Opioid Dosing

| | Equianalgesic Doses (mg) | |
|---|---|---|
| **Drug** | **Parenteral** | **Oral** |
| Morphine | 10 | 30 |
| Buprenorphine | 0.3 | 0.4 (sl) |
| Codeine | 100 | 200 |
| Fentanyl | 0.1 | NA |
| Hydrocodone | NA | 30 |
| Hydromorphone | 1.5 | 7.5 |
| Meperidine | 100 | 300 |
| Oxycodone | 10* | 20 |
| Oxymorphone | 1 | 10 |
| Tramadol | 100* | 120 |

** Fentanyl Transdermal: 25mcg/hr ≈ 50mg/24hr oral morphine*
***Methadone should only be prescribed by knowledgeable clinicians*

McPherson, M. (2010). Demystifying Opioid Conversion Calculations: A Guide for Effective Dosing.

# Equianalgesic Chart Limitations

1. Chart values are often estimates based on single-dose parenteral studies
2. There is considerable interpatient variability in the efficacy and safety response to opioids due to:
   - tolerance and cross tolerance, pharmacokinetic and pharmacodynamic variability,
   - use of coanalgesics and other CNS-active medications,
   - psychological variables
3. Use the same equianalgesic chart to calculate dose to minimize the risk of dose conversion errors.
4. When switching patients from one opioid to another, there is not complete cross-tolerance
5. Terminology:
   - Oral Morphine Equivalent (**OME**)=Morphine Equivalent Dose (**MED**)= Morphine Equivalent Daily Dose (**MEDD**)

# PRN and Scheduled Opioids Dosing

- **PRN opioids**
  - Use along with ATC dosing or alone
    - Breakthrough or incident pain
  - Start with **10-20%** of the scheduled ATC dose
  - May be dosed on **peak effect or duration of action**
    - Peak effect – terminal pain and dose finding
  - In general, peak effect:
    - PO= 1-2 hour
    - SC= 30 mins
    - IV= 15 mins (fentanyl= 6 mins)
- **Scheduled opioids**
  - Schedule immediate release, sustained release, or continuous infusion ATC
  - Schedule **based on duration of action**

# Evaluation of Request of Dose Escalation

- Progression of disease
- New pain source
- Increased functional activity
- Inadequate equianalgesic conversions
- Emotional distress
- Unrealistic expectations of efficacy

# Fentanyl Transdermal Conversion:

## Information From Package Insert vs. Clinical Practice

| **24hr OME (PI)** (mg/day) | **Fentanyl Patch Dose** (mcg/hr) | **Safer 24 hr OME** (mg/day |
|---|---|---|
| 60-134 | 25 | ~ MSO4 50mg/24hrs |
| 135-224 | 50 | ~ MSO4 100mg/24hrs |
| 225-314 | 75 | ~ MSO4 150mg/24hrs |
| 315-404 | 100 | ~ MSO4 200mg/24hrs |

# Buprenorphine Patch Dosing

| Daily Morphine Equivalents | Starting Buprenorphine Patch Dose |
|---|---|
| ≤ 30mg/24 hours | 5mcg/hr |
| 30-80mg/24 hours | 10mcg/hr |
| • Morphine daily doses >80mg/24 hours may not be suitable candidates | |
| • Patients should be weaned to ≤ 30mg of morphine/24 hours x 7 days | |
| • Dose titration may occur every 72 hours | |

# Centrally Acting Analgesics

## Tramadol (Ultram®) C IV

- Opioid agonist and norepinephrine and serotonin reuptake inhibitor
- Metabolism CYP3A4 and CYP2D6
- Precautions: History of seizures, concurrent serotonergic agents (serotonin syndrome), renal impairment, hepatic impairment

## Tapentadol (Nucynta) CII

- Opioid agonist and norepinephrine reuptake inhibitor
- **Metabolism:** Glucuronidation
- **Precautions:** Pulmonary function impairment, severe renal impairment, severe hepatic impairment, history of seizures

# Opioid Adverse Effects

| Common | Uncommon |
|---|---|
| Constipation (80%) | Bad Dreams/Hallucinations |
| Dry Mouth | Dysphoria/Delirium |
| Nausea (20%)/ Vomiting (15%) | Myoclonus/Seizures |
| Sedation | Urinary Retention |
| Pruritus (2 – 10%) | Respiratory Depression |

Benyamin R, Trescot AM, Datta S, et al. Opioid Complications and side effects. Pain Physician. 2008;11:S105-S120
McNicol E. Opioid side effects. Clinical updates. Pain 2007;15:1 – 6
McNicol E, Horowicz-Mehler N, Fisk RA, et al. Management of opioid side-effects in cancer related and chronic noncancer pain: a systematic review. J Pain 2003;4:231 – 256

# Opioid-Induced Neurotoxicity

- Signs:
  - Myclonus – twitching of large muscle groups
  - Delirium
  - Hallucinations/Seizures
  - Rapidly escalating dose requirement
  - Hyperalgesia/ Allodynia
- Pain “doesn’t make sense”; not consistent with recent pattern or known disease

# Treatment of Neurotoxicity

Probability of opioid induced neurotoxicity by drug:

**Morphine** > Hydromorphone > Oxycodone> Fentanyl > **Methadone**

Treatment:

- Rotate to structurally dissimilar drug
  - **Methadone** → Fentanyl → Oxycodone
- Hydration

# Managing Opioid-Related Adverse Effects

1. Dose Adjustment
    - Decrease dose
    - If analgesia not achieved with dose reduction, increase dose frequency
2. Optimization of Multimodal Therapy
    - Non-opioids, co-analgesics
    - Review nonpharmacologic options
3. Trial another opioid
4. Add medication to manage symptoms of adverse opioid effect
    - Caution of cascade effect

# Opioid Treatment Plan

**Despite best efforts, interindividual variability underscores need for balanced, flexible plan**

1. *Establish realistic treatment goals for patient and provider*
   - Anticipated pain relief: 30-50%
   - Medication/dose changes as result of unrealistic analgesia goals subject patient to increased risks
2. *Identify temporal characteristics of pain*
   - Treat constant, around the clock pain with long-acting option
   - Determine opioid requirements/tolerance prior to initiating long-acting opioid therapy
3. *Long-acting opioids can be titrated every 24 hours if sub-optimal analgesia achieved*
   - Exceptions:
     - Methadone
     - Transdermal Fentanyl
4. *Provide comprehensive pain assessment*

# Pain Management: An Overview

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