Evolving Principles of Multimodal Pain Management: 2026 Spring Update

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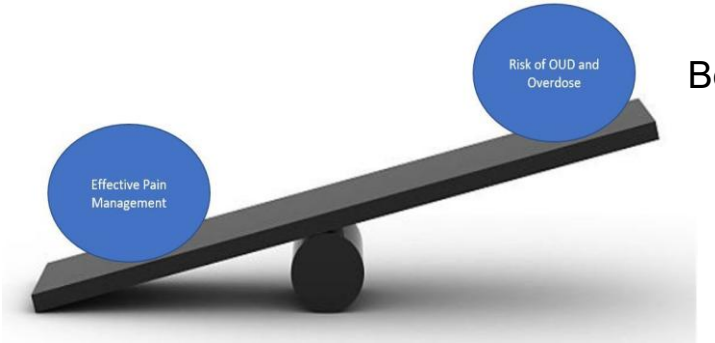
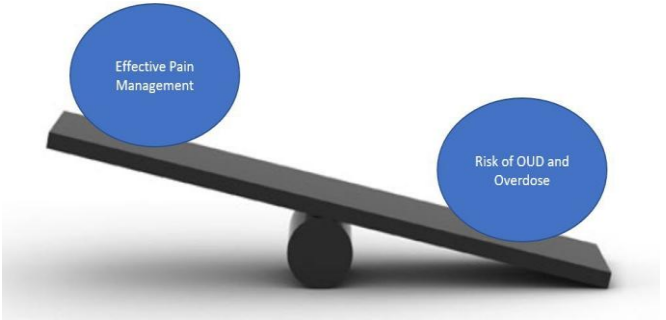
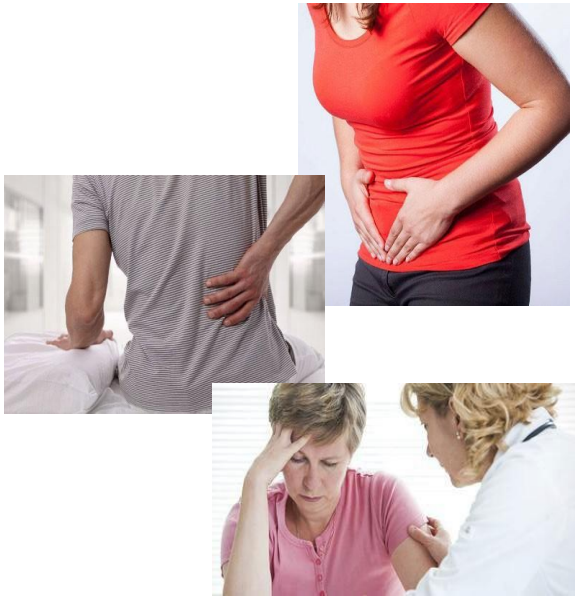
Goal: Enable Providers to Balance Effective Pain Management in the Background of Polysubstance Misuse As the 4th Wave of the Overdose Epidemic

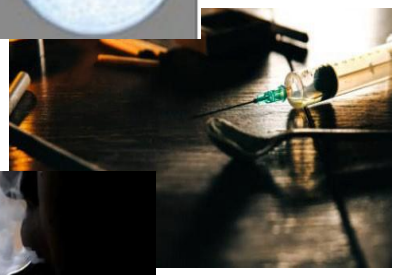


Benefit vs. Risk





Counterfeit Oxycodone Tablet Containing Fentanyl



Primary Objectives

At the conclusion of this talk, attendees will understand:

1. Recently revised definitions for pain
2. Principles of assessment and treatment for acute and chronic pain - using a multimodal approach
3. New non-opioid prescription medication and future non-opioid drug targets

Conflicts: None

2020 Revised Definitions of Pain

2020 Revised Definitions of Pain

Pain
An unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage.
Notes
• Pain is always a personal experience that is influenced to varying degrees by biological, psychological, and social factors.
• Pain and nociception are different phenomena. Pain cannot be inferred solely from activity in sensory neurons.
• Through their life experiences, individuals learn the concept of pain.
• A person's report of an experience as pain should be respected.
• Although pain usually serves an adaptive role, it may have adverse effects on function and social and psychological well-being.
• Verbal description is only one of several behaviors to express pain; inability to communicate does not negate the possibility that a human or a nonhuman animal experiences pain.

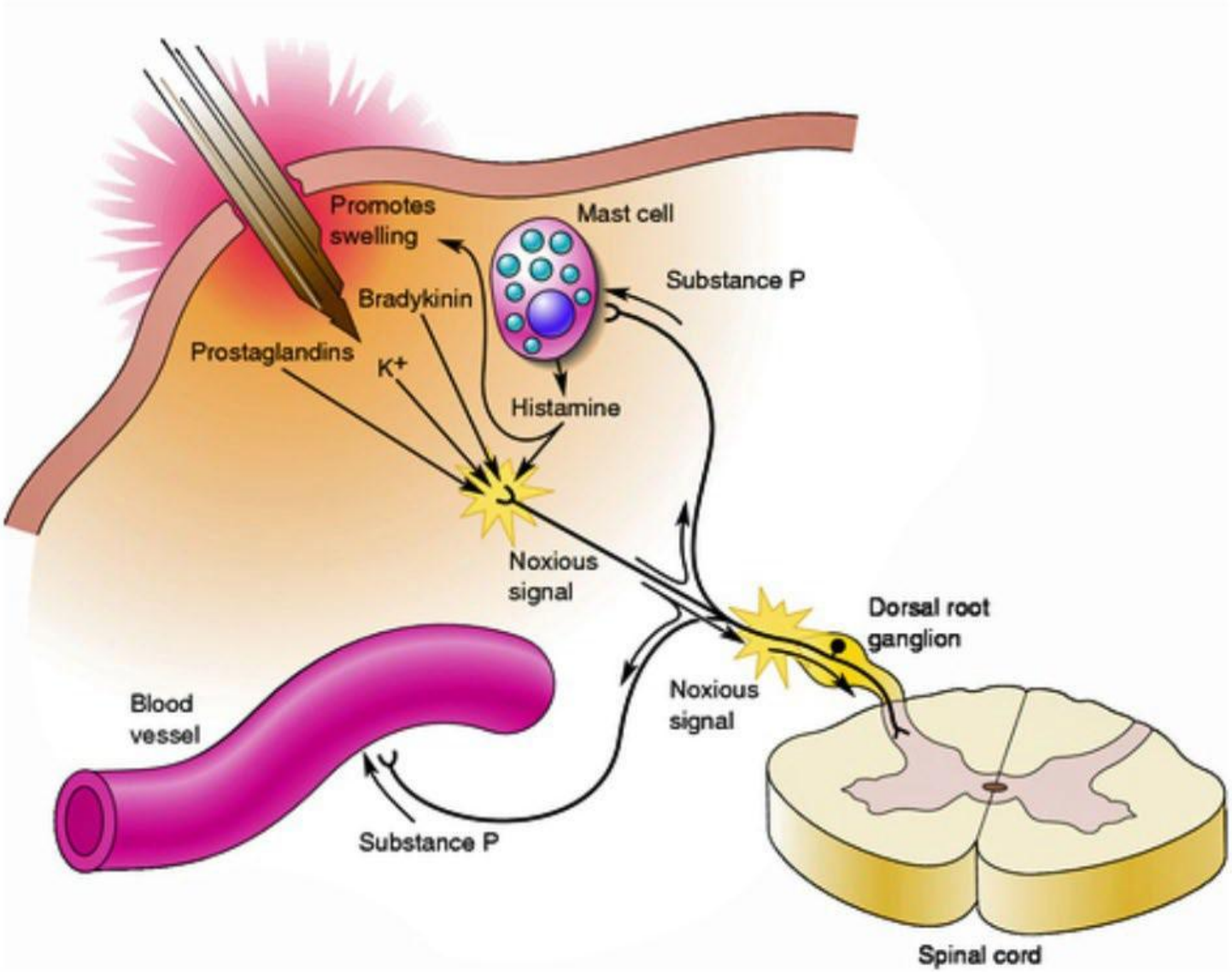
1.Declaration of Montréal. International Association for the Study of Pain. Available at: https://www.iasp-pain.org/DeclarationofMontreal (Accessed on 5/18/2024). From: Raja SN, Carr DB, Cohen M, et al. The revised International Association for the Study of Pain definition of pain: concepts, challenges, and compromises. PAIN 2020; 161:1976. DOI: 10.1097/j.pain.0000000000001939.

Pain Terms and Definitions

- **Nociceptive pain:** Pain that arises from actual or threatened damage to non-neural tissue and is due to the activation of nociceptors.
- **Central sensitization:** Increased responsiveness of nociceptive neurons in the central nervous system to their normal or subthreshold afferent input.
- **Neuropathic pain:** Pain caused by a lesion or disease of the somatosensory nervous system.
- **Allodynia:** Pain due to a stimulus that does not normally provoke pain.
- **Hyperalgesia:** Increased pain from a stimulus that normally provokes pain.
- **Nociplastic pain:** Pain that arises from altered nociception despite no clear evidence of
    - actual or threatened tissue damage causing the activation of peripheral nociceptors
    - disease or lesion of the somatosensory system causing the pain.

IASP Terminology. International Association for the Study of Pain. Available at: https://www.iasp-pain.org/Education/Content.aspx?ItemNumber=1698 (Accessed on December 1, 2019).

Pain Signaling Pathways – Inflammatory Responses Mediated by Pain Receptors



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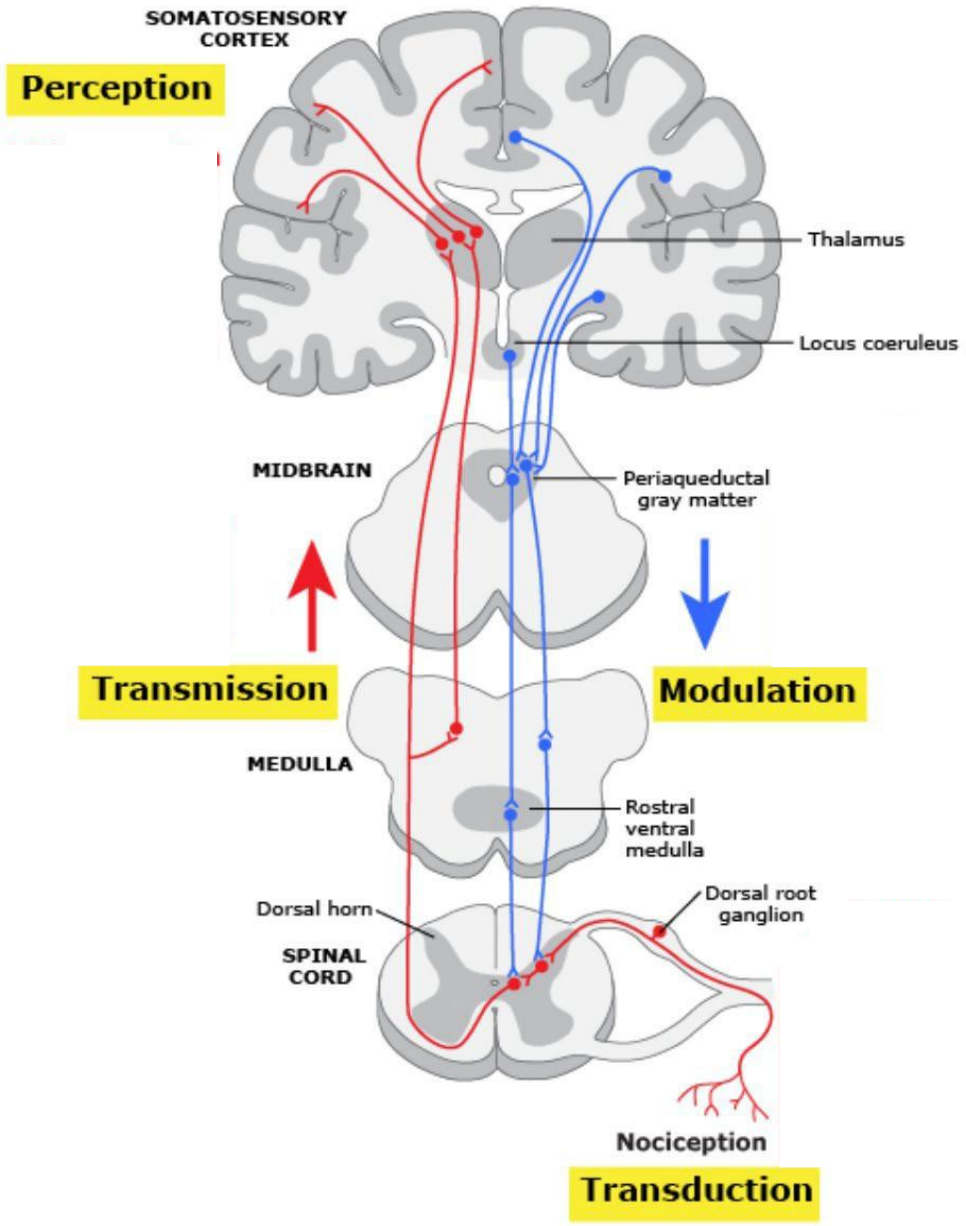
Pain Signaling Pathways



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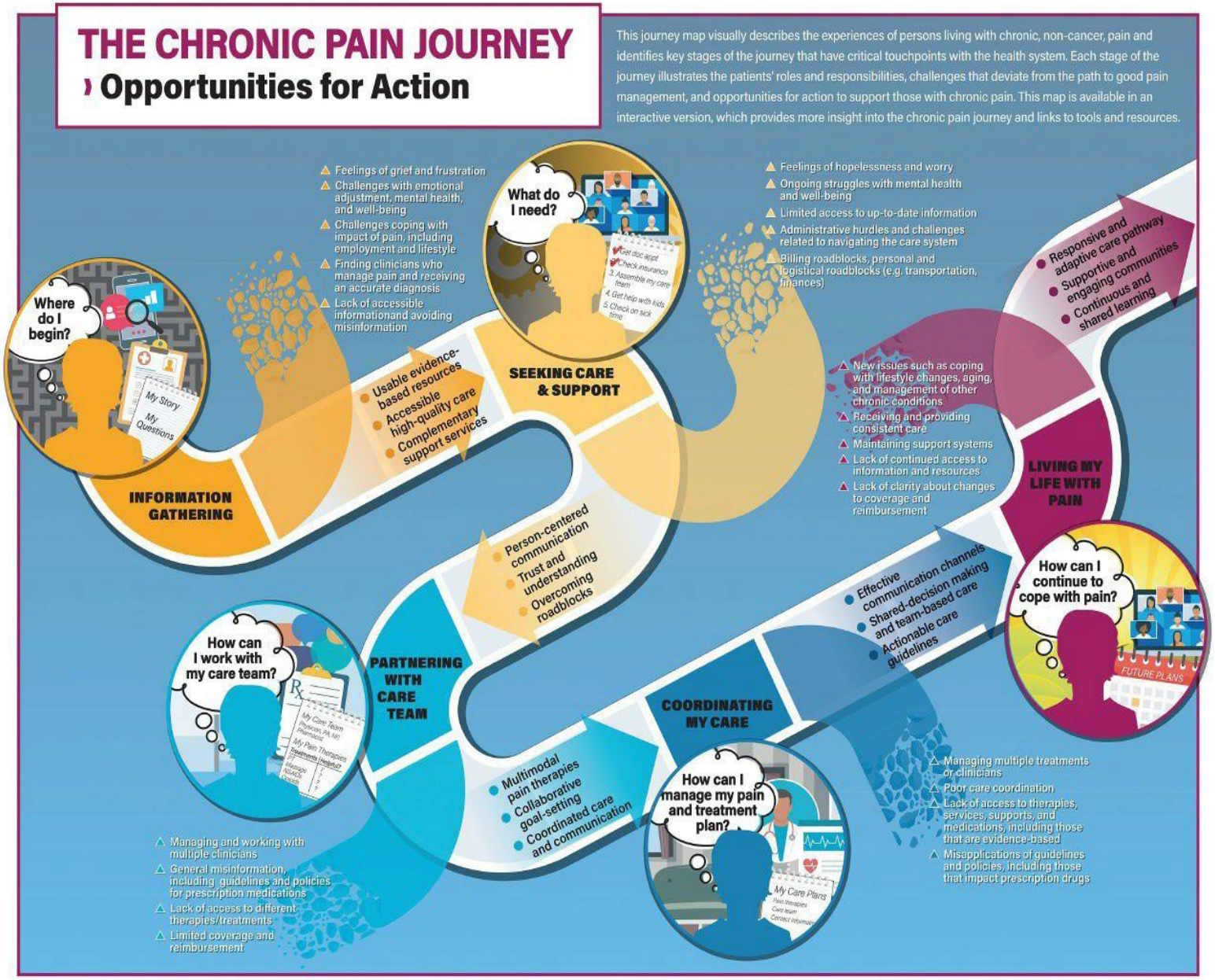
Key Principles of Pain Evaluation and Management

Be the Guide On the Patient's Journey to Adequate Care



Chronic Pain Journey Map - National Academy of Medicine (nam.edu) – Accessed 5/9/22

Identify and Treat the Pain Source (Starting with a Good History)

History and Physical
• Identify possible pain etiology
• Identify comorbidities that may affect treatment options
• Examine for allodynia and/or sensory changes in painful body part
• For patients who use opioids or patients with risk factors for opioid misuse or use disorder: • Check PDMP (aka, MAPS) • Screen for opioid risk

PDMP: prescription drug monitoring programs; ORT: Opioid Risk Tool; SOAPP: Screener and Opioid Assessment for Patients with Pain; COMM: Current Opioid Misuse Screen

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Identify and Treat the Pain Source

Body diagram
•Useful for all patients
•For patients with multisite pain, screen for chronic widespread pain disorders with Widespread Pain Index and Symptom Severity Score
Pain history
OLDCARTS
• **O**nset ("When did your pain start?")
• **L**ocation ("Where does it hurt?")
• **D**uration ("How long does your pain last?")
• **C**haracter ("How does your pain feel?", ie, aching, burning, shooting, tingling)
• **A**lleviating/**A**ggravating ("What makes your pain better/worse?") and **A**ttribution ("What do you think is the cause?")
• **R**adiation ("Does this pain spread anywhere else?")
• **T**emporal pattern ("Does your pain vary over the course of a day?")
• **S**ymptoms associated ("How does your pain impact your physical function, your mood, your sleep?")

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Identify and Treat the Pain Source (Starting with a Good History)

Patient Instructions: Please fill out both sides of this questionnaire as completely as possible.

1. HISTORY OF THE PAIN

YES

► *Do you believe the pain is due to:*

☐ a car accident
- date: ____/____/____
- time: ____:____ a.m. / p.m.

☐ a work-related injury
- date: ____/____/____
- time: ____:____ a.m. / p.m.

☐ physical trauma *(examples: a fall, a fight, sports injury, etc.)*

YES

- type :_____
- date: ____/____/____
- time: ____:____ a.m. / p.m.

☐ other: _____
- date: ____/____/____
- time: ____:____ a.m. / p.m.

☐ unknown cause

► *How long have you had this pain?*

☐ hours — how many? _____

YES

☐ days — how many? _____
☐ weeks — how many? _____
☐ months — how many? _____

► *Did the pain appear:*

☐ suddenly
☐ gradually

► *Right now, is the pain:*

☐ better
☐ worse
☐ unchanged

2. LOCATION AND INTENSITY OF PAIN

► *The most intense pain is located:*_____.

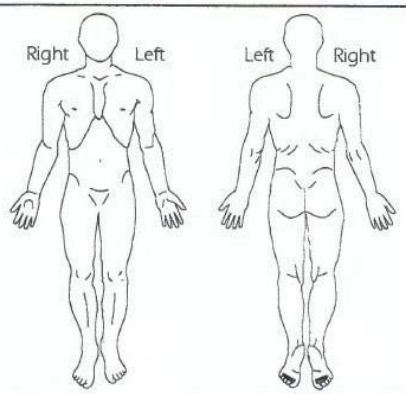
► *On the diagrams to the right:*
- mark an X or a series of X's where you feel pain.
- shade the areas where you have numbness.
- use arrows to point to where the pain radiates or travels to.

► *Has the pain changed in its location?*

_____
_____
_____

► *On the scale below, mark an X where it best describes the intensity of your pain:*

0 1 2 3 4 5 6 7 8 9 10
No Pain — Moderate Pain — Worst Possible Pain



3. DESCRIPTION OF THE PAIN

YES

► *Is the pain:*

☐ continuous *(no relief)*
☐ intermittent *(periods of relief)*
- amount of time **pain** usually lasts: _____
- amount of time **relief** usually lasts: _____

☐ other_____
_____
_____
_____

YES

► *Would you describe the pain as:*

☐ sharp, stabbing
☐ dull, aching
☐ throbbing
☐ burning like a hot poker
☐ steady, persistent
☐ waxing and waning
☐ feeling like a tight band
☐ easy to pinpoint
☐ difficult to pinpoint
☐ other_____

YES

► *Does pain occur:*

☐ upon awakening
☐ in the morning
☐ in the afternoon
☐ in the evening
☐ 2-3 hours after falling asleep
☐ any time day or night
☐ only on weekends
☐ only at work
☐ only at home
☐ other_____

→

4. DO YOU ALSO HAVE:

YES

☐ runny, bloodshot eyes
☐ blurred or double vision
☐ nasal congestion/runny nose
☐ high blood pressure
☐ muscle weakness
☐ numbness in arms or hands
☐ numbness in legs or feet
☐ felt a "sudden snap"
☐ felt a "tearing" sensation
☐ muscle aches and pains
☐ joint pains
☐ morning joint stiffness
☐ fever
☐ abdominal pain

YES

☐ nausea or vomiting
☐ diarrhea
☐ constipation
☐ bloody stools
☐ frequent or burning urination
☐ sudden loss of urine
☐ inability to urinate
☐ bloody urine
☐ weight gain or loss
☐ depression
☐ other: _____

► ***Female patients only:***

☐ vaginal discharge
☐ heavy menstrual bleeding

YES

☐ bleeding between periods
☐ pelvic infection
☐ ovarian cysts
☐ uterine fibroids
☐ painful intercourse
☐ hot flashes
☐ other: _____

► ***Male patients only:***

☐ prostate trouble
☐ restricted or painful urination
☐ interrupted sleep to urinate
☐ swollen or painful testicles
☐ penis discharge
☐ other: _____

5. PREVIOUS MEDICAL WORKUP INCLUDES:

YES

☐ seeing other doctors
name(s): _____
_____
_____

☐ skull x-rays

YES

☐ neck x-rays
☐ lumbar and pelvis x-rays
☐ EEG/brain wave study
☐ CT scan
☐ brain scan

YES

☐ MRI
☐ Evoked potentials
☐ EMG
☐ blood work
☐ other: _____

6. DOES ANY BLOOD RELATIVE HAVE A HISTORY OF:

YES

☐ arthritis
☐ diabetes
☐ aortic aneurysm
☐ cerebral aneurysm
☐ migraines
☐ high blood pressure

YES

☐ stroke
☐ brain tumor
☐ spinal cord tumor
☐ poor leg circulation
☐ disk problems
☐ spinal stenosis

YES

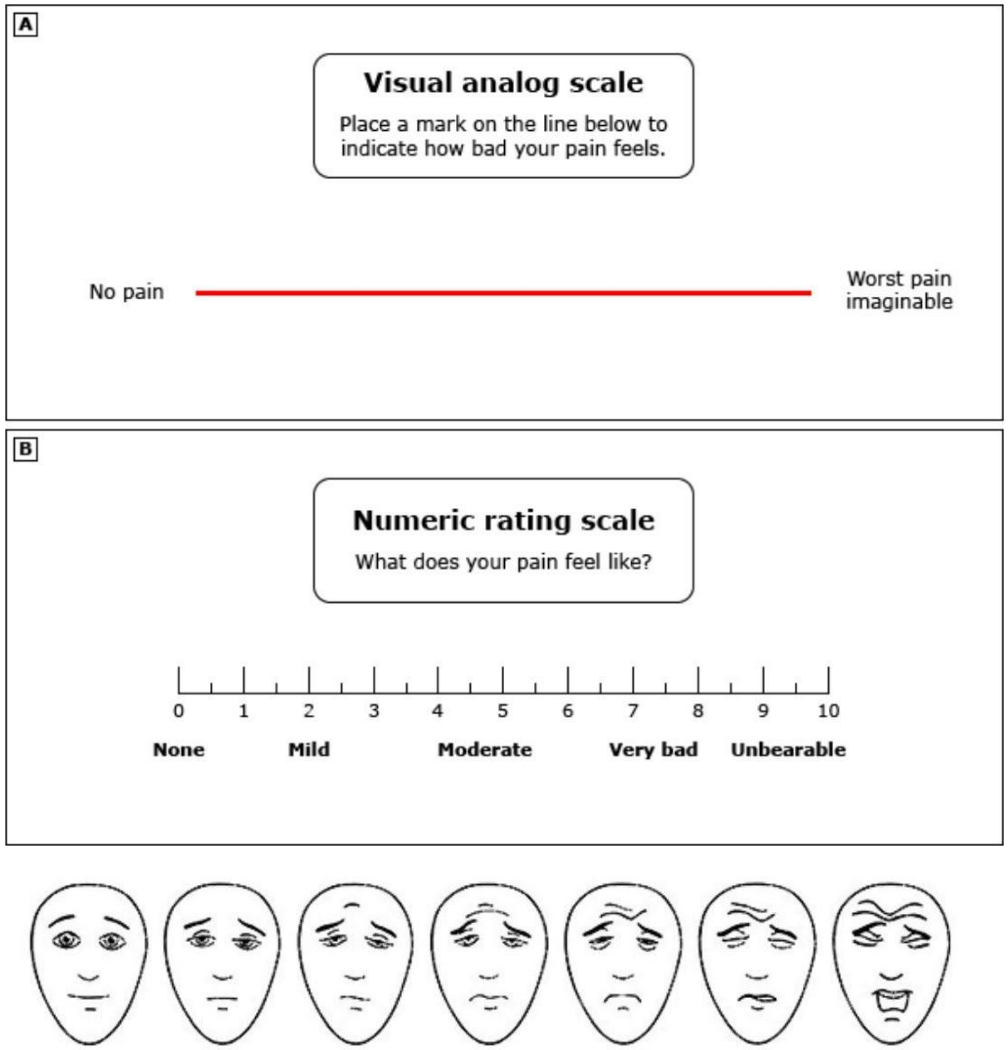
☐ multiple sclerosis (MS)
☐ muscular dystrophy
☐ arteriovenous malformation
☐ Lou Gehrig's disease
☐ other neurological disease:
_____

7. IS THE PAIN MADE WORSE OR BETTER BY:

FEELS WORSE	FEELS BETTER		FEELS WORSE	FEELS BETTER		FEELS WORSE	FEELS BETTER	
☐	☐	inactivity or sleep	☐	☐	lifting _____ lbs.	☐	☐	menstrual periods
☐	☐	mild activity	☐	☐	carrying _____ lbs.	☐	☐	massage
☐	☐	exercising or stretching	☐	☐	stooping	☐	☐	heat
☐	☐	heavy work	☐	☐	twisting	☐	☐	trying to forget about it
☐	☐	climbing stairs	☐	☐	reaching overhead	☐	☐	spinal manipulation
☐	☐	walking	☐	☐	coughing/sneezing	☐	☐	spinal injections (blocks)
☐	☐	standing	☐	☐	sudden movement	☐	☐	physical therapy
☐	☐	sitting	☐	☐	other movement:	☐	☐	surgery
☐	☐	car riding			_____	☐	☐	other:_____
☐	☐	straining at stool	☐	☐	touching a certain point:	☐	☐	other:_____
☐	☐	reclining or lying down			_____			*Medications:*
☐	☐	lying on a firm bed or on the floor	☐	☐	sexual intercourse	☐	☐	_____
			☐	☐	drinking alcohol	☐	☐	_____
☐	☐	lying on one side	☐	☐	emotional tension	☐	☐	_____
☐	☐	getting up from bed	☐	☐	fatigue	☐	☐	_____
☐	☐	bending forward	☐	☐	changes in weather	☐	☐	_____

Courtesy of David Neff, DO

Use Visual Pain Scales



Schematic representation of the faces pain scale, rated from 0 to 6 left to right.

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Assess Mood and Risk for Sleep Apnea

Mood assessment				
PHQ-4				
Over the past 2 weeks, have you been bothered by these problems?	**Not at all**	**Several days**	**More days than not**	**Nearly every day**
• Feeling nervous, anxious, or on edge	0	1	2	3
• Not being able to stop or control worrying	0	1	2	3
• Feeling down, depressed, or hopeless	0	1	2	3
• Little interest or pleasure in doing things	0	1	2	3
• **Scoring:** Add total score • **For score >5**, screen for anxiety, depression, and post-traumatic stress, with GAD-7, PHQ-9, and PTSD-5				

Sleep assessment		
Sleep initiation and maintenance		
• Does pain interfere with falling asleep?		
• Does pain interfere with staying asleep?		
Screen for obstructive sleep apnea (OSA) – STOP-Bang[2,3]		
Yes	No	**S**nore – Do you snore loudly (loud enough to be heard through closed doors, or your bed partner elbows you for snoring at night)?
Yes	No	**T**ired – Do you often feel tired, fatigued, or sleepy during the day?
Yes	No	**O**bserved – Has anyone observed you stop breathing or choking/gasping during sleep?
Yes	No	**P**ressure – Do you have or are you being treated for high blood pressure?
Yes	No	**B**ody mass index >35 kg/m^2 ?
Yes	No	**A**ge older than 50 years?
Yes	No	**N**eck size large (male: ≥17 inches, female: ≥16 inches)?
Yes	No	**G**ender = male?
• **Scoring:** Low risk of OSA: Yes to 0 to 2 questions • Intermediate risk of OSA: Yes to 3 to 4 questions • High risk of OSA: Yes to ≥5 questions		

1. *Reproduced from: Kroenke K, Spitzer RL, Williams JB, Löwe B. An ultra-brief screening scale for anxiety and depression: The PHQ-4. Psychosomatics 2009; 50:613. Table used with the permission of Elsevier Inc. All rights reserved.*
2. *Chung F, Subramanyam R, Liao P, et al. High STOP-Bang score indicates a high probability of obstructive sleep apnoea. Br J Anaesth 2012; 108:768.*

Assess for Opioid Use Disorder (DSM-5 Criteria)

A problematic pattern of opioid use leading to clinically significant impairment or distress, as manifested by at least 2 of the following, occurring within a 12-month period:

1. Opioids are often taken in larger amounts or over a longer period than was intended.
2. There is a persistent desire or unsuccessful efforts to cut down or control opioid use.
3. A great deal of time is spent in activities necessary to obtain, use, or recover from the effects of opioids.
4. Craving, or a strong desire or urge to use opioids.
5. Recurrent opioid use resulting in a failure to fulfill major role obligations at work, school, or home.
6. Continued opioid use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of opioids.
7. Important social, occupational, or recreational activities are given up or reduced because of opioid use.
8. Recurrent opioid use in situations in which it is physically hazardous.
9. Continued opioid use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance.
10. Tolerance, as defined by either of the following:
    a. A need for markedly increased amounts of opioids to achieve intoxication or desired effect, or
    b. Markedly diminished effect with continued use of the same amount of an opioid.
    Note: This criterion is not considered to be met for those taking opioids solely under appropriate medical supervision.
11. Withdrawal, as manifested by either of the following:
    a. The characteristic opioid withdrawal syndrome, or
    b. Opioids (or a closely related) substance is taken to relieve or avoid withdrawal symptoms.
    Note: This criterion is not considered to be met for those taking opioids solely under appropriate medical supervision.

Mild: Presence of 2-3 symptoms Moderate:
Presence of 4-5 symptoms Severe: Presence of 6 or more symptoms

Assess for Psychiatric Co-morbidities

Assessing **psychiatric comorbidities** in individuals with **opioid use disorder (OUD)** is essential for effective diagnosis, treatment planning, and long-term recovery. Here's a structured approach based on clinical best practices [1] [2] [3]:

🧠 1. Comprehensive Screening

- Begin with **broad screening tools** to identify potential mental health symptoms.
- Common tools include:
  - **Mental Health Screening Form III**
  - **Patient Health Questionnaire (PHQ-9)**
  - **Columbia-Suicide Severity Rating Scale**
  - **Drug Use Disorder Identification Test (DUDIT)**

These help flag issues like depression, anxiety, suicidal ideation, and substance misuse [1].

💉 2. Structured Clinical Interviews

- Use validated diagnostic interviews such as:
  - **Structured Clinical Interview for DSM-V (SCID-5)**
  - **Psychiatric Research Interview for Substance and Mental Disorders (PRISM)**
- These tools help differentiate between **primary psychiatric disorders** and **substance-induced conditions**

🧩 3. Differential Diagnosis

- Carefully distinguish between:
  - **Substance-induced symptoms** (e.g., opioid withdrawal causing anxiety or depression)
  - **Independent psychiatric disorders** (e.g., major depressive disorder, bipolar disorder)
- Reassess after **detoxification or stabilization**, as symptoms may evolve [1].

[Opioid Addiction with Psychiatric Comorbidities - Providers Clinical Support System-Medications for Opioid Use Disorders]

Assess for Psychiatric Co-morbidities

4. Functional and Historical Assessment

- Evaluate:
  - **Psychiatric history** (including family history)
  - **Substance use timeline**
  - **Periods of abstinence and relapse**
  - **Impact on functioning** (work, relationships, legal issues)
- Include assessments of **sleep, sexual function, and suicidality**, which are often affected [2].

5. Common Psychiatric Comorbidities in OUD

- Major depressive disorder (most prevalent)
- Generalized anxiety disorder
- Bipolar disorder
- Schizophrenia
- Antisocial personality disorder

[Opioid Addiction with Psychiatric Comorbidities - Providers Clinical Support System-Medications for Opioid Use Disorders]

Assess for Signs of Withdrawal (Using COWS)

PATIENT NAME:	DATE OF ASSESSMENT:
PATIENT DATE OF BIRTH:	MEDICAL RECORD NUMBER:

Clinical Opioid Withdrawal Score (COWS)

For each item, write in the number that best describes the patient's signs or symptom. Rate only the apparent relationship to opiate withdrawal. *For example: If heart rate is increased because the patient was jogging just prior to assessment, the increased pulse rate would not add to the score.*

Enter scores at time zero, 30 minutes after first dose, 2 hours after first dose, etc.	Time:	Time:	Time:	Time:
Resting Pulse Rate: *Record beats per minute after patient is sitting or lying down for one minute* • 0 - pulse rate 80 or below • 1 - pulse rate 81–100 • 2 - pulse rate 101–120 • 4 - pulse rate greater than 120				
Sweating: *Over past ½ hour not accounted for by room temperature or activity* • 0 - no chills or flushing • 1 - subjective chills or flushing • 2 - flushed or observable moistness on face • 3 - beads of sweat on brow or face • 4 - sweat streaming off face				
Restlessness: *Observation during assessment* • 0 - able to sit still • 1 - reports difficulty sitting still, but is able to do so • 3 - frequent shifting or extraneous movement of legs/arms • 5 - unable to sit still for more than a few seconds				
Pupil size • 0 - pupils pinned or normal size for light • 1 - pupils possibly larger than normal for light • 2 - pupils moderately dilated • 5 - pupils dilated that only rim of the iris is visible				
Bone or joint aches: *If patient was having pain previously, only the additional component attributed to opiate withdrawal is scored* • 0 - not present • 1 - mild/diffuse discomfort • 2 - patient reports severe diffuse aching of joints/muscles • 4 - patient is rubbing joints or muscles and is unable to sit still because of discomfort				
Runny nose or tearing: *Not accounted for by cold symptoms or allergy* • 0 - none present • 1 - nasal stuffiness or unusually moist eyes • 2 - nose running or tearing • 4 - nose constantly running or tears streaming down cheeks				
GI upset: *Over last ½ hour* • 0 - no GI symptoms • 1 - stomach cramps • 2 - nausea or loose stool • 3 - vomiting or diarrhea • 5 - multiple episodes of diarrhea or vomiting				
Tremor: *Observation of outstretched hands* • 0 - no tremor • 1 - tremor can be felt, but not observed • 2 - slight tremor observable • 4 - gross tremor or muscle twitching				
Yawning: *Observation during assessment* • 0 - no yawning • 1 - yawning once or twice during assessment • 2 - yawning three or more times during assessment • 4 - yawning several times/minute				
Anxiety or irritability • 0 - none • 1 - patient reports increasing irritability or anxiousness • 2 - patient obviously irritable or anxious • 4 - patient so irritable or anxious that participation in the assessment is difficult				
Gooseflesh skin • 0 - skin is smooth • 3 - piloerrection of skin can be felt or hairs standing up on arms • 5 - prominent piloerrection				
5—12 = mild; ***13—24 = moderate;*** ***25—36 = moderately severe;*** ***> 36 = severe withdrawal*** **TOTAL**				
OBSERVER INITIALS				

Journal of Psychoactive Drugs Volume 35 (2), April - June 2003Source: Wesson, D. R., & Ling, W. (2003). The Clinical Opiate Withdrawal Scale (COWS). *J Psychoactive Drugs*, 35(2), 253–9.

Assess Risk for Overdose (RIOSORD)

Risk Index for Overdose or Serious Opioid-Induced Respiratory Depression (RIOSORD)		
Question	**Points for Positive Response**	**Actual Response**
In the past 6 mo, has the patient had a health care visit (outpatient, inpatient, or emergency department) involving any of the following health conditions		
Substance use disorder (abuse or dependence), including alcohol, amphetamines, antidepressants, cannabis, cocaine, hallucino- gens, opioids, and sedatives	25	
Bipolar disorder or schizophrenia	10	
Stroke or other cerebrovascular disease	9	
Kidney disease with clinically significant renal impairment	8	
Heart failure	7	
Nonmalignant pancreatic disease (e.g., acute or chronic pancreatitis)	7	
Chronic pulmonary disease (e.g., emphysema, chronic bronchitis, asthma, pneumoconiosis, asbestosis)	5	
Recurrent headache (e.g., migraine)	5	
Does the patient use any of the following substances?		
Fentanyl	13	
Morphine	11	
Methadone	10	
Hydromorphone	7	
Does the patient use an extended-release or long-acting formulation of any prescription opioid?	5	
Prescription benzodiazepine (e.g., diazepam, alprazolam)	9	
Prescription antidepressant (e.g., fluoxetine, citalopram, venlafaxine, amitriptyline)	8	
Is the patient's current maximum prescribed daily morphine- equivalent dose ≥100 mg for all opioids used on a regular basis?	7	
Total possible score	**146**	

Risk Classes and Predicted Probability of Serious Opioid-Induced Respiratory Depression during the Next 6 Months.			
Risk Class	**RIOSORD Score**	**Average Predicted Probability (Percent)**	**Actual Observed Incidence (Percent)**
1	<5	1.9	2.1
2	5–7	4.8	5.4
3	8–9	6.8	6.3
4	10–17	15.1	14.2
5	18–25	29.8	32.2
6	26–41	55.1	58.8
7	≥42	83.4	82.4

Adapted from: Zedler B, Xie L, Wang L et al. Development of a Risk Index for Serious Prescription Opioid-Induced Respiratory Depression or Overdose in Veterans' Health Administration Patients. Pain Medicine. Jun 2015. 16;1566- 1579.

Confirm Appropriateness for Prescribing Opioids (DIRE Score)

Name: _____ DOB___/____/___

DIRE Score: Patient Selection for Chronic Opioid Analgesia

For each factor, rate the patient's score from 1-3 based on the explanations in the right-hand column

SCORE	FACTOR	EXPLANATION
	DIAGNOSIS	1 = Benign chronic condition with minimal objective findings or no definite medical diagnosis. Examples: fibromyalgia, migraine headaches, non-specific back pain. 2 = Slowly progressive condition concordant with moderate pain, or fixed condition with moderate objective findings. Examples: failed back surgery syndrome, back pain with moderate degenerative changes, neuropathic pain. 3 = Advanced condition concordant with severe pain with objective findings. Examples: severe ischemic vascular disease, advanced neuropathy, severe spinal stenosis.
	INTRACTABILITY	1 = Few therapies have been tried and the patient takes a passive role in his/her pain management process. 2 = Most customary treatments have been tried but the patient is not fully engaged in the pain management process, or barriers prevent (insurance, transportation, medical illness). 3 = Patient fully engaged in a spectrum of appropriate treatments but with inadequate response.
	RISK	(**R** = Total of **P+C+R+S** below)
	Psychological	1 = Serious personality dysfunction or mental illness interfering with care. Example: personality disorder, severe affective disorder, significant personality issues. 2 = Personality or mental health interferes moderately. Example: depression or anxiety disorder. 3 = Good communication with clinic. No significant personality dysfunction or mental illness.
	Chemical Health	1 = Active or very recent use of illicit drugs, excessive alcohol, or prescription drug abuse. 2 = Chemical coper (uses medications to cope with stress) or history of chemical dependence (CD) in remission. 3 = No CD history. Not drug-focused or chemically reliant.
	Reliability	1 = History of numerous problems: medication misuse, missed appointments, rarely follows through. 2 = Occasional difficulties with compliance, but generally reliable. 3 = Highly reliable patient with meds, appointments & treatment.
	Social Support	1 = Life in chaos. Little family support and few close relationships. Loss of most normal life roles. 2 = Reduction in some relationships and life roles. 3 = Supportive family/close relationships. Involved in work or school and no social isolation.
	EFFICACY SCORE	1 = Poor function or minimal pain relief despite moderate to high doses. 2 = Moderate benefit with function improved in several ways (or insufficient info - hasn't tried opioid yet or very low doses or too short of a trial). 3 = Good improvement in pain and function and quality of life with stable doses over time.

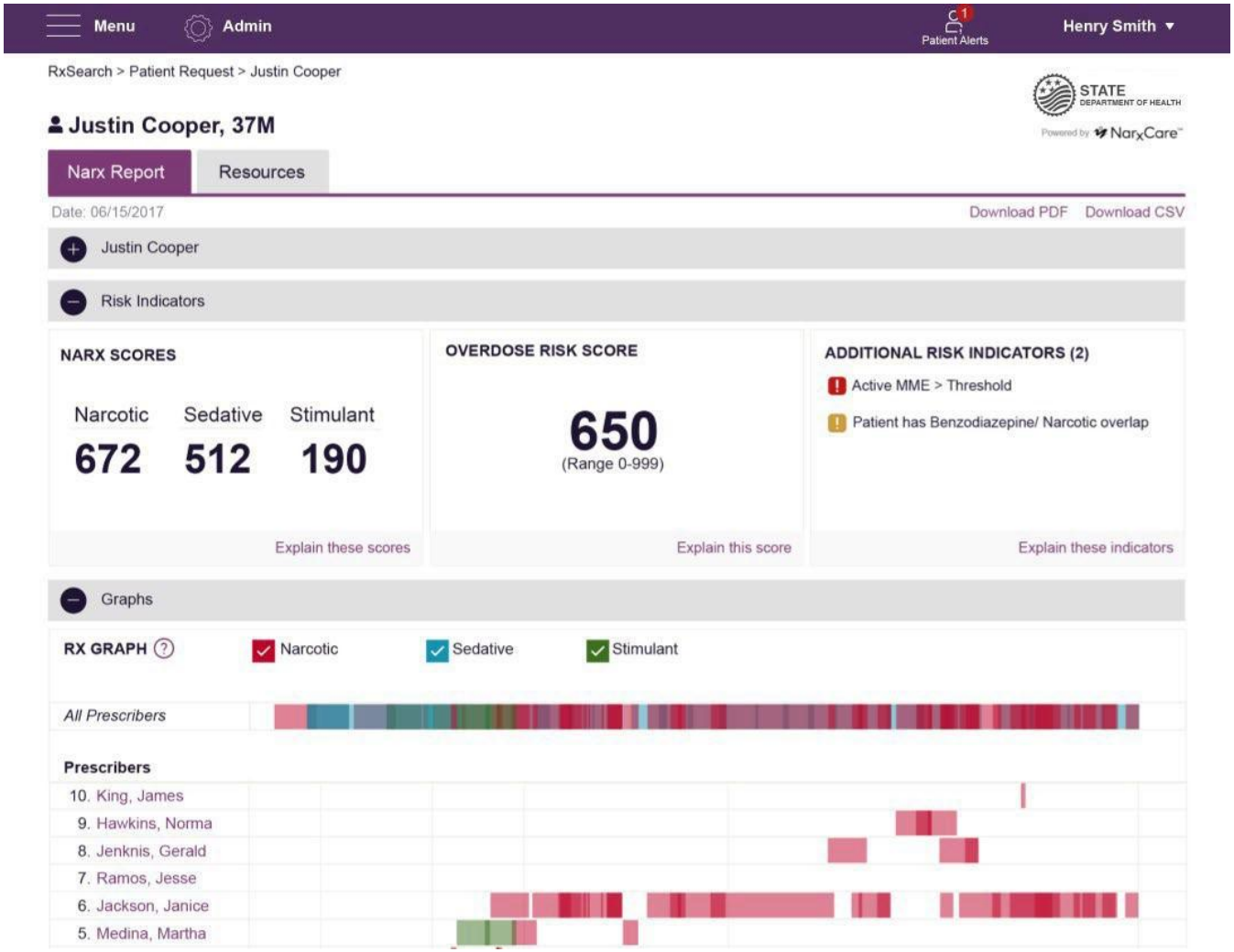
Score 7-13: Not a suitable candidate for long-term opioid analgesia

Score 14-21: May be a good candidate for long-term opioid analgesia

_____ **Total score= D + I + R + E**

URL - doi:10.1016/j.jpain.2006.03.001 (Accessed 4/14/2025)

Check the Michigan Automated Prescription Service (MAPS) to Assess for Potential Misuse, Abuse, Diversion, or Overdose Risk



https://michigan.pmpaware.net

Be Mindful of Polysubstance Substance Use Disorders (PUD)

- The use of more than one drug, also known as polysubstance use, is common. This occurs when two or more are taken together or within a short time period, either intentionally or unintentionally.
- Whether intentional or not, mixing drugs is never safe because the effects from combining drugs may be stronger and more unpredictable than one drug alone, and even deadly.
- Polysubstance-related overdoses can lead to permanent anoxic-hypoxic brain injury or death
  - approximately 1 fatal overdose per 15 non-fatal in the U.S.

URL: Special Report: The Art of Treating Complex Substance Use Disorders | Psychiatric News Accessed 4/14/2025

What Kind of Substances are Involved (Intentional or Unintentional) in Polysubstance Use Disorder (PUD)?

Polysubstance misuse often involves a combination of **stimulants, depressants, and other psychoactive substances**, which can lead to unpredictable and dangerous effects. Some of the most commonly misused substances include:

- **Opioids** – Illicitly Manufactured Fentanyls (IMF) and Designer Nitazines, Prescription opioids (fentanyl, oxycodone, hydrocodone, hydromorphone), heroin, and kratom (mitragynine, 7-hydroxygynine)
- **α2-adrenergic agonists –** Xylazine and Medetomidine
- **Stimulants** – Methamphetamine, cocaine, prescription amphetamines (such as Adderall), and MDMA (ecstasy) and nicotine.
- **Depressants** – Alcohol, Benzodiazepines (Xanax, Valium), barbiturates, certain muscle relaxants (Soma)
- **Cannabinoids** – marijuana and synthetic cannabinoids ("spice" or "K2"), and synthetic cathinones ("bath salts").
- **Hallucinogens** – Ketamine (NDMA Receptor Antagonist), Nitrous Oxide, LSD, psilocybin mushrooms, and PCP.

Mixing these substances can **increase the risk of overdose**, as their effects may amplify or mask each other, leading to dangerous consequences.

Polysubstance Overdose | Overdose Prevention | CDC

Check for Anticipated and Unanticipated Medications and Other Substances

- If you don't check, you will have no idea.
- Qualitative - in Office
  - Test either positive or negative
  - Immunoassay
- Quantitative (in Lab)
  - Test measures concentration of drug
  - GC/MS or LC/MS

  Can check for all psychoactive substances prescribed and unprescribed
  - Matrix - Urine, Saliva, Blood, Hair, Exhaled Air (breathalyzer), etc.

Courtesy of David Neff, DO

Treatment Goals for Managing Pain

GOAL FOR ADEQUATE PAIN CONTROL

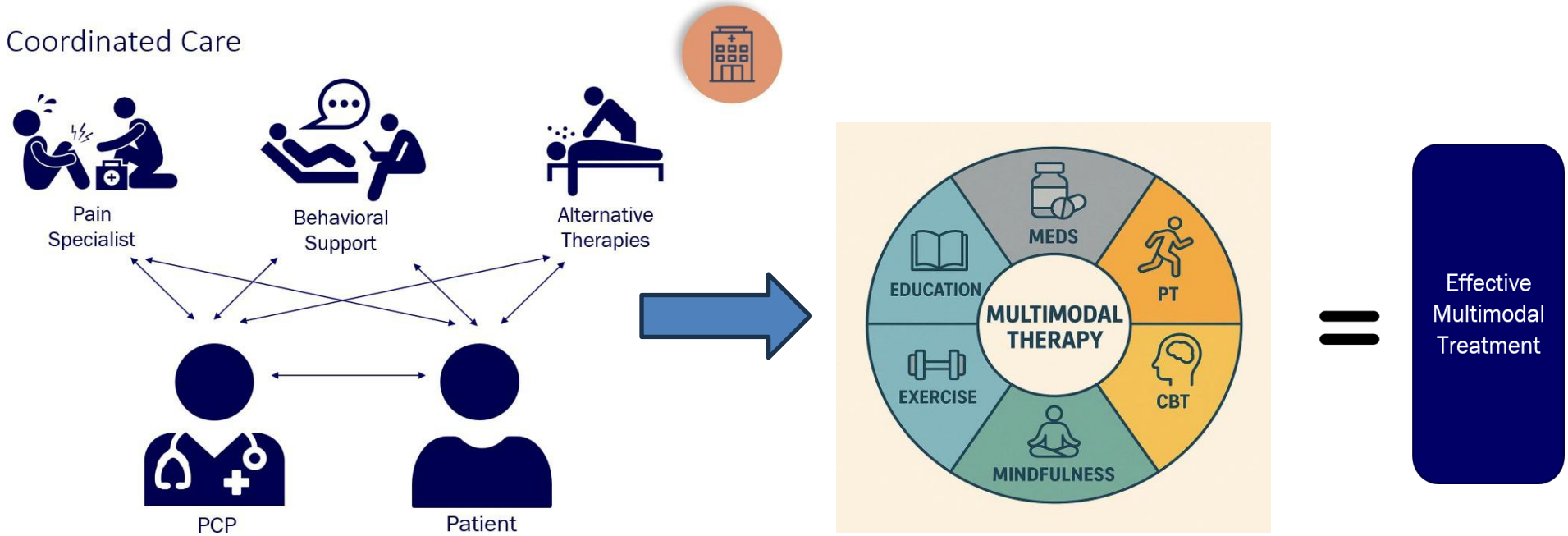
The goal for pain control should not be zero pain, but rather a tolerable level of pain that allows physical and emotional function. Often this means balancing analgesia with achieving functional goals, while avoiding preventable complications.

PRINCIPLES

1. Create an individualized plan for pain management based on the expected degree of pain and patient factors that may affect the plan
2. Offer multimodal analgesia, adding opioids only as necessary
3. Provide patient education
4. Adjust the pain management plan based on adequacy of pain relief and the occurrence of adverse events

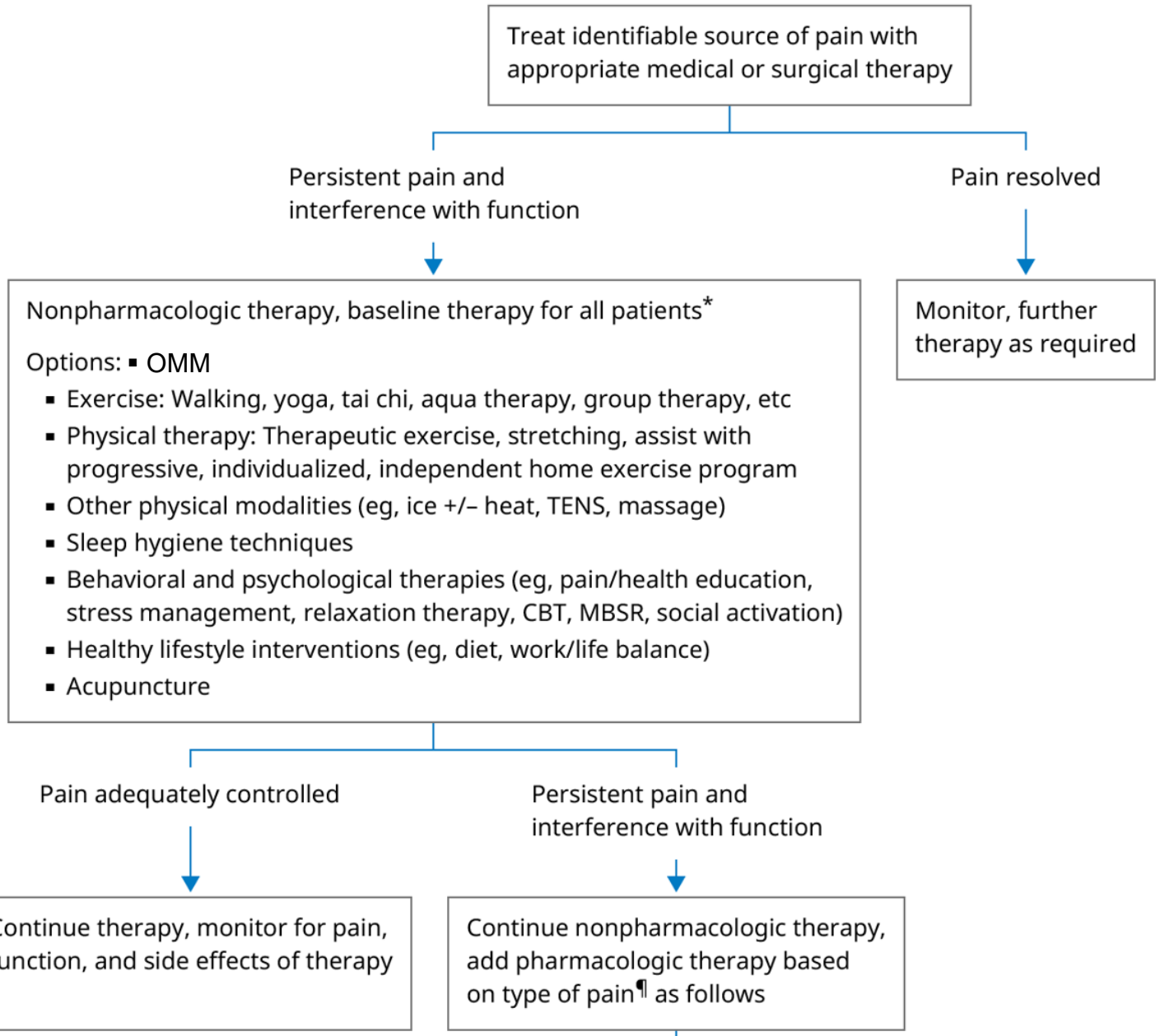
Adopted from a program developed by the University of Washington Anesthesia and Pain Medicine Department, Seattle, WA Published in UpToDate (Last Checked 4/15/2025)

Coordinate Care With a Multimodality Treatment Plan



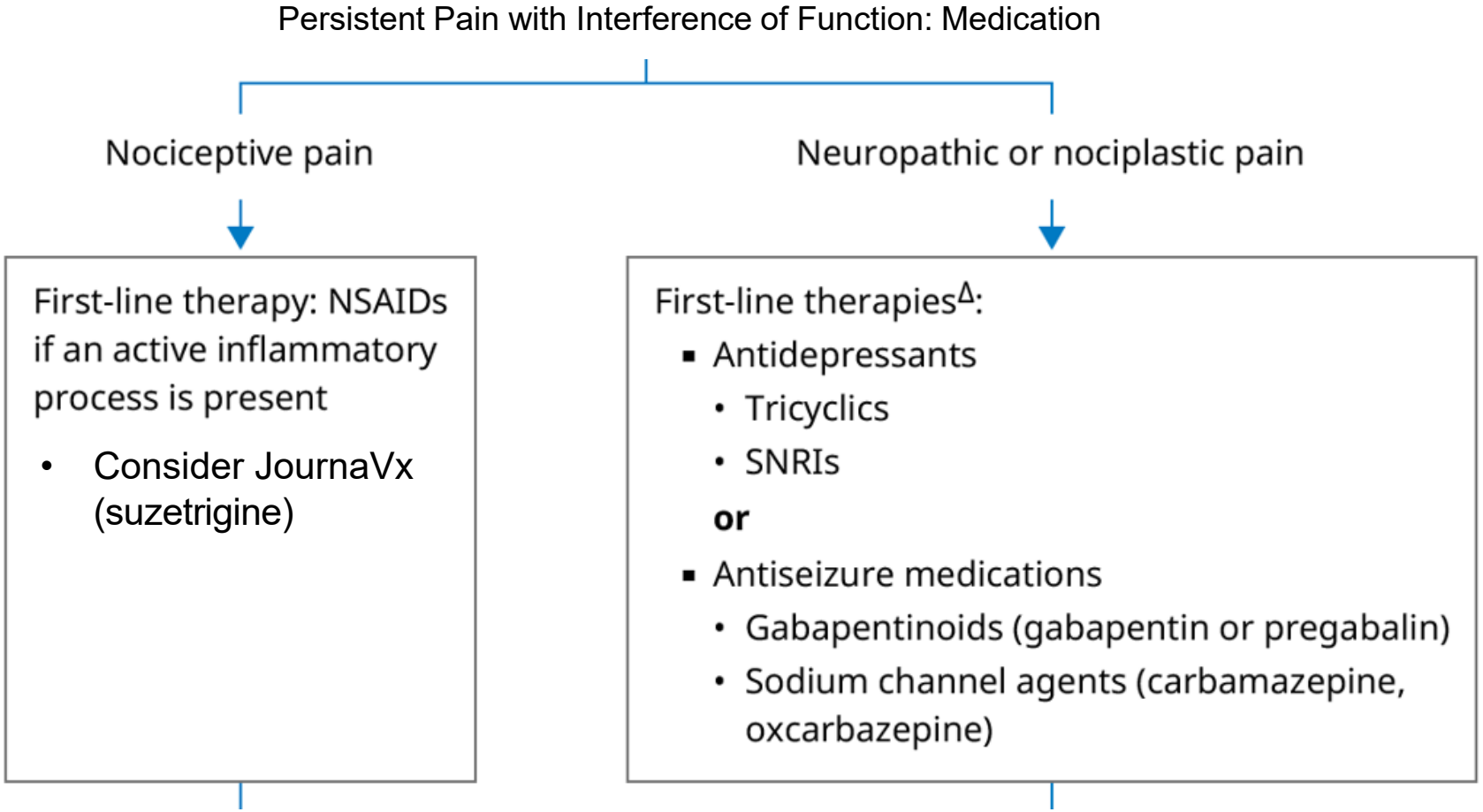
U.S. Department of Health and Human Services. Pain Management Best Practices Inter-Agency Task Force Report. 2019.

Multimodal Pain Management



URL - Approach to the management of chronic non-cancer pain in adults – UpToDate and Pharmacologic management of chronic non-cancer pain in adults – UpToDate (Accessed 10/25/2024)

Multimodal Pharmacological Approaches to Pain Management



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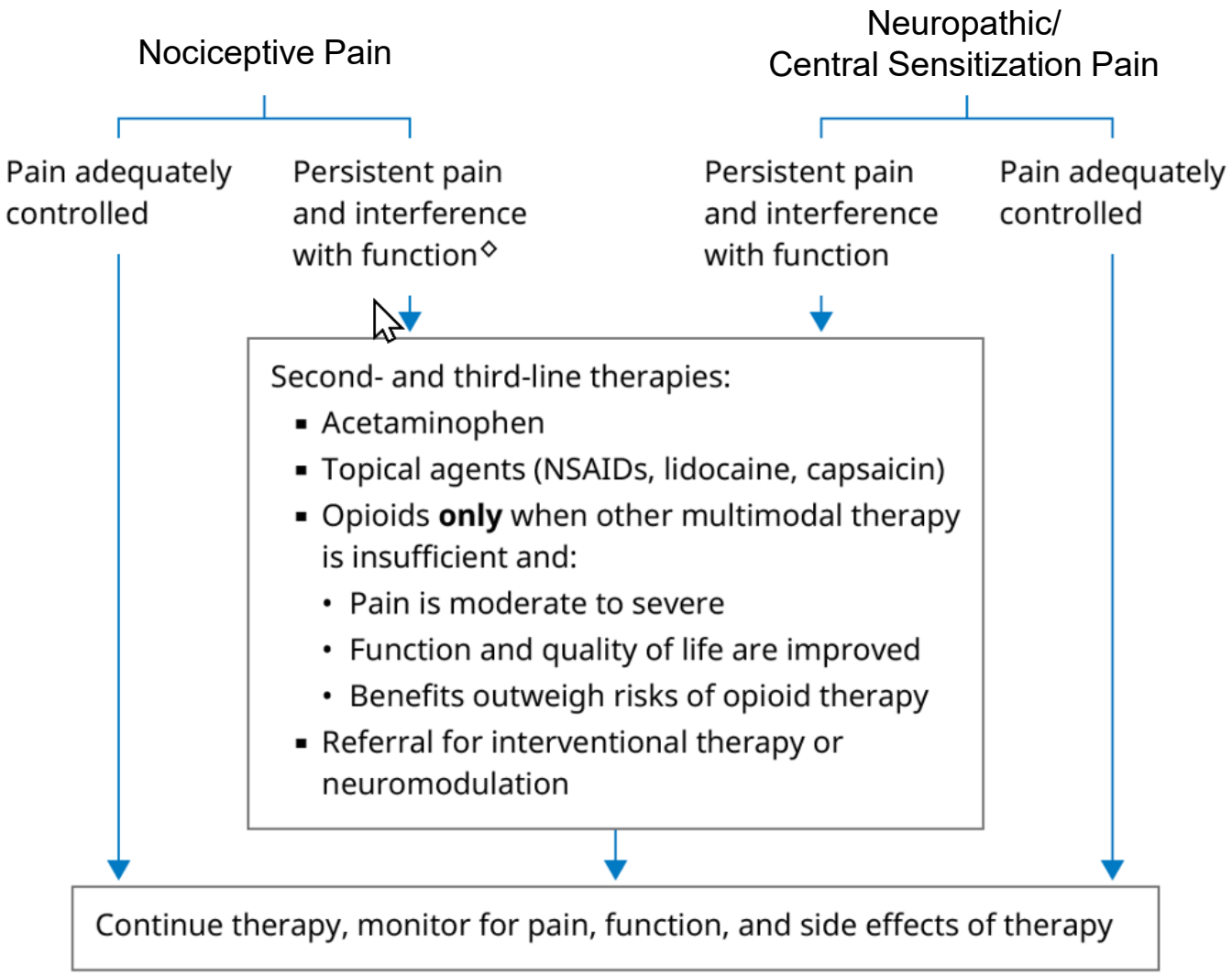
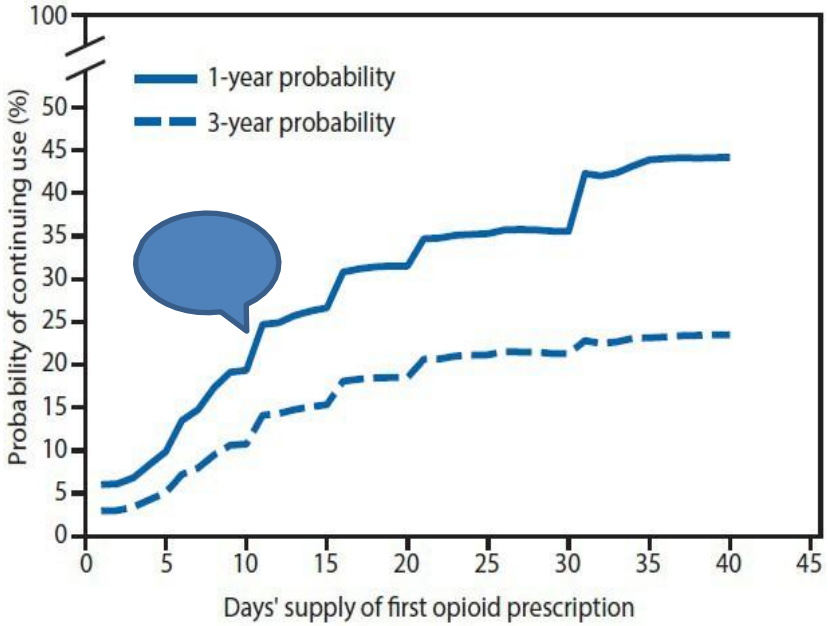
Multimodal Pharmacological Approaches to Pain Management



URL - Approach to the management of chronic non-cancer pain in adults – UpToDate and Pharmacologic management of chronic non-cancer pain in adults – UpToDate (Accessed 10/25/2024)

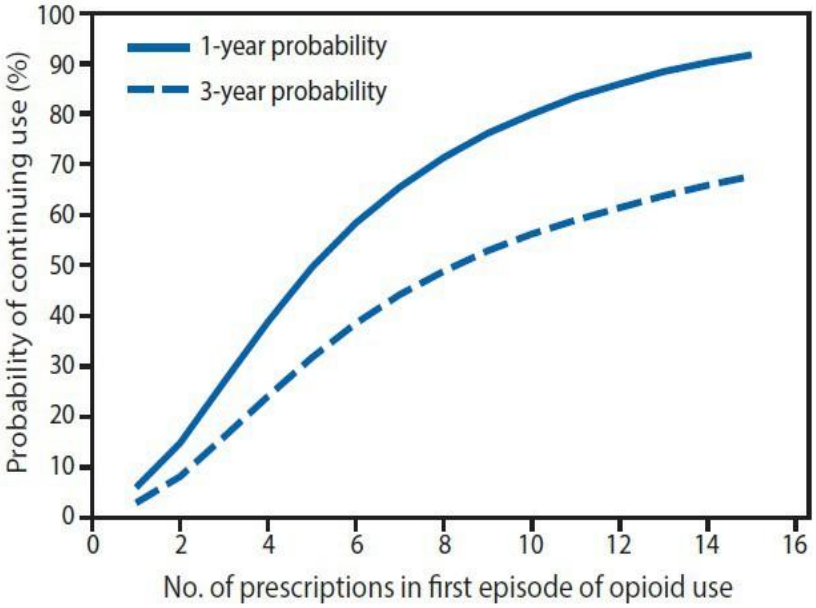
Consider The Downside to Using Opioids Beyond 7-10 Days For Acute Pain: The Risk for Continued Opioid Use Goes Up with Days Supply and Number of Prescriptions in the First Episode of Care

FIGURE 1. One- and 3-year probabilities of continued opioid use among opioid-naïve patients, by number of days' supply* of the first opioid prescription — United States, 2006–2015



* Days' supply of the first prescription is expressed in days (1–40) in 1-day increments. If a patient had multiple prescriptions on the first day, the prescription with the longest days' supply was considered the first prescription.

FIGURE 2. One- and 3-year probabilities of continued opioid use among opioid-naïve patients, by number of prescriptions* in the first episode of opioid use — United States, 2006–2015



* Number of prescriptions is expressed as 1–15, in increments of one prescription.

Don't Ignore or Abandon Inherited "Legacy" Pain Patients Already on Opioids

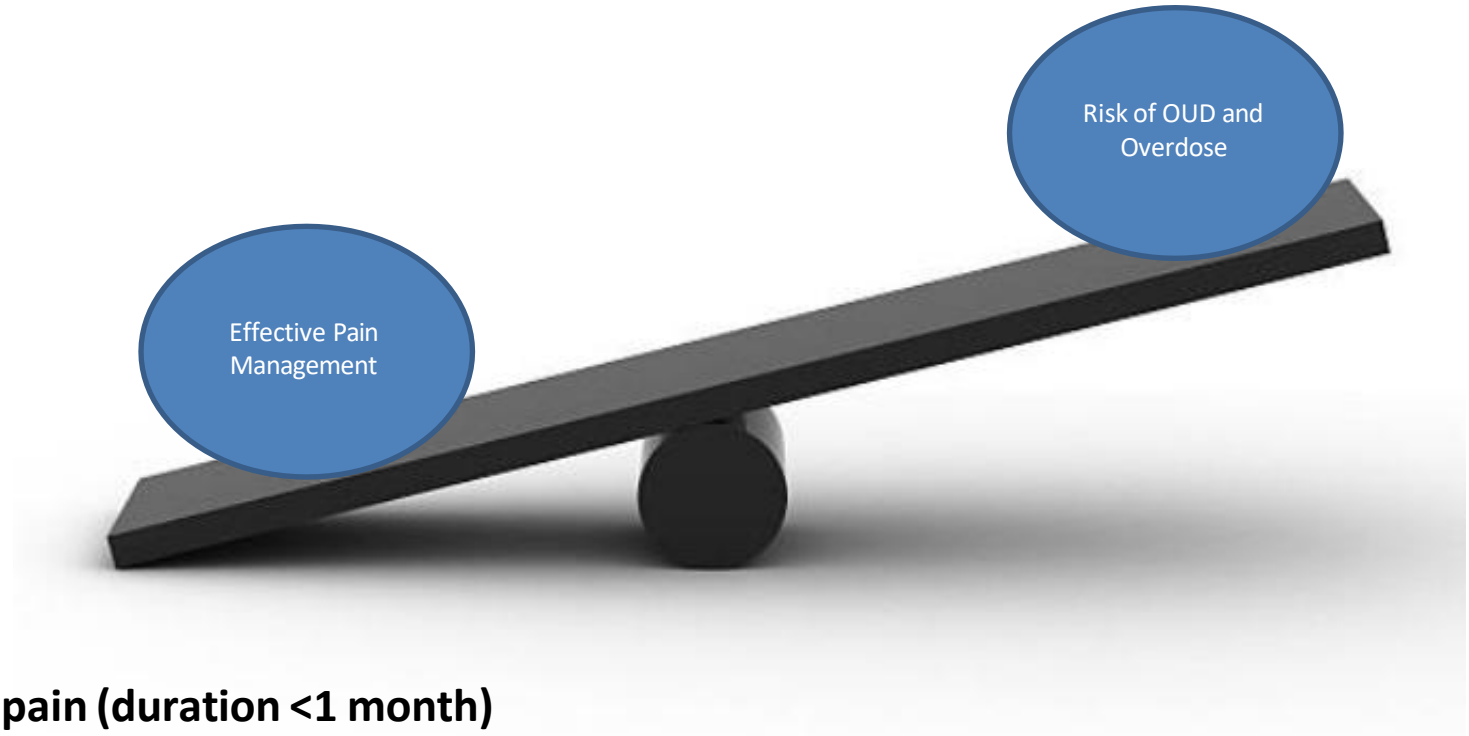
Inherited Patients Taking Opioids for Chronic Pain — Considerations for Primary Care

Phillip O. Coffin, M.D., and Antje M. Barreveld, M.D.

Steps in Caring for Patients with Chronic Pain Who Have Received Long-Term Opioid Therapy from a Previous Clinician.

1. **Review the case with the former clinician if possible.** Try to develop a treatment plan that slowly adjusts to your style of management while avoiding a radical divergence from the previous plan of care.
2. **Consider providing a therapeutic bridge for the patient until a plan of care is determined, given the risks associated with stopping opioid therapy.** Abruptly tapering or stopping opioid therapy can be dangerous for multiple reasons. Opioids may be crucial for the patient's condition (e.g., sickle-cell disease), and the patient may be at risk for other harms when opioids are tapered or discontinued (see figure).
3. **Develop a patient-centered care plan.** If a taper is needed, empower the patient to make decisions, including which medications to taper first and how fast. Successful tapers may take years.
4. **Assess the patient for opioid use disorder and start discussing medication options right away.** Patients may find it challenging to accept an opioid use disorder diagnosis; give them time.
5. **Document opioid stewardship and the rationale for the treatment plan.** Investigations into opioid prescribing are often based on insufficient documentation.

When The Need for Effective Pain Management Using an Opioid May Outweigh Risk



1. **Acute pain (duration <1 month)**
2. **Subacute pain (duration of 1-3 months)**
3. **Chronic pain (duration of >3 months) - "most days" or "every day"**
   - **High-impact chronic pain is based on responses of "frequently limits life or work activities"**
   - **Intractable pain**

The Updated 2022 CDC Clinic Practice Guideline for Prescribing Opioids

This Guideline is

- **A clinical tool to improve communication between clinicians and patients and empower them to make informed, person-centered decisions related to pain care together**
- **Intended for primary care clinicians and other clinicians providing pain care for outpatients aged ≥18 years old with:**
  - acute pain (duration <1 month);
  - subacute pain (duration of 1-3 months); or
  - chronic pain (duration of >3 months)
- **Intended to be flexible to enable person-centered decision-making, taking into account an individual's expected health outcomes and well-being.**

This guideline is not

- **A replacement for clinical judgment or individualized, person-centered care**
- **Intended to be applied as inflexible standards of care across patients, and/or patient populations by healthcare professionals, health systems, pharmacies, third-party payers, or governmental jurisdictions or to lead to the rapid tapering or discontinuation of opioids for patients**
- **A law, regulation, and/or policy that dictates clinical practice or a substitute for FDA-approved labeling**
- **Applicable to the following types of pain treatment:**
  - sickle cell disease-related pain
  - cancer pain
  - palliative care
  - end-of-life care

URL - CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022 (Accessed 4/14/2025)
URL - Prescribing Opioids for Pain — The New CDC Clinical Practice Guideline | NEJM (Accessed 4/14/2025)

The Updated 2022 CDC Clinic Practice Guideline for Prescribing Opioids

1. **For all patients with acute, subacute, or chronic pain – go low and go slow**
   - Initiate the lowest dose to achieve expected results
   - For opioid naïve patients, start with immediate-release opioids instead of extended-release/long- acting (ER/LA) opioids
   - Use extreme caution when prescribing opioids, benzodiazepines and other sedating substances concurrently
     - consider whether benefits outweigh risks
     - Taper cautiously to a less risky dose or discontinue
   - Check the state prescription drug monitoring program (PDMP) also known as the Michigan Automated Prescription Service (MAPS), to determine whether the patient is receiving opioid dosages or combinations that put the patient at high risk for overdose
     - When initiating therapy
     - Periodically when continuing
   - Consider toxicology testing to assess for prescribed medications as well as other prescribed and non-prescribed controlled substances
   - Offer naloxone and other overdose mitigation strategies when risk factors for opioid overdose are present
2. **For acute pain, consider initiating opioid therapy only if benefits are anticipated to outweigh risks to the patient**
   - Nonopioid therapies are effective for many common types of acute pain
   - Prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids

URL - CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022 (4/14/2025)

The Updated 2022 CDC Clinic Practice Guideline for Prescribing Opioids

3. **For subacute and chronic pain, consider initiating opioid therapy only if expected benefits for pain and function are anticipated to outweigh risks to the patient**
   - Work with patients to establish treatment goals for pain and function
   - Nonopioid therapies are preferred
   - Discuss the known risks and realistic benefits of opioid therapy
   - Consider how opioid therapy will be discontinued when benefits do not outweigh risks
   - If opioids are continued
     - use caution when prescribing opioids at any dosage
     - avoid increasing dosage above levels likely to yield diminishing returns in benefits relative to risks to patients
     - re-evaluate benefits and risks after starting opioid therapy or when escalating dose
     - Initially at 1 to 4 weeks
     - Then every 3 months (or more frequently as indicated)

URL - CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022 (Accessed 4/14/2025)

The Updated 2022 CDC Clinic Practice Guideline for Prescribing Opioids

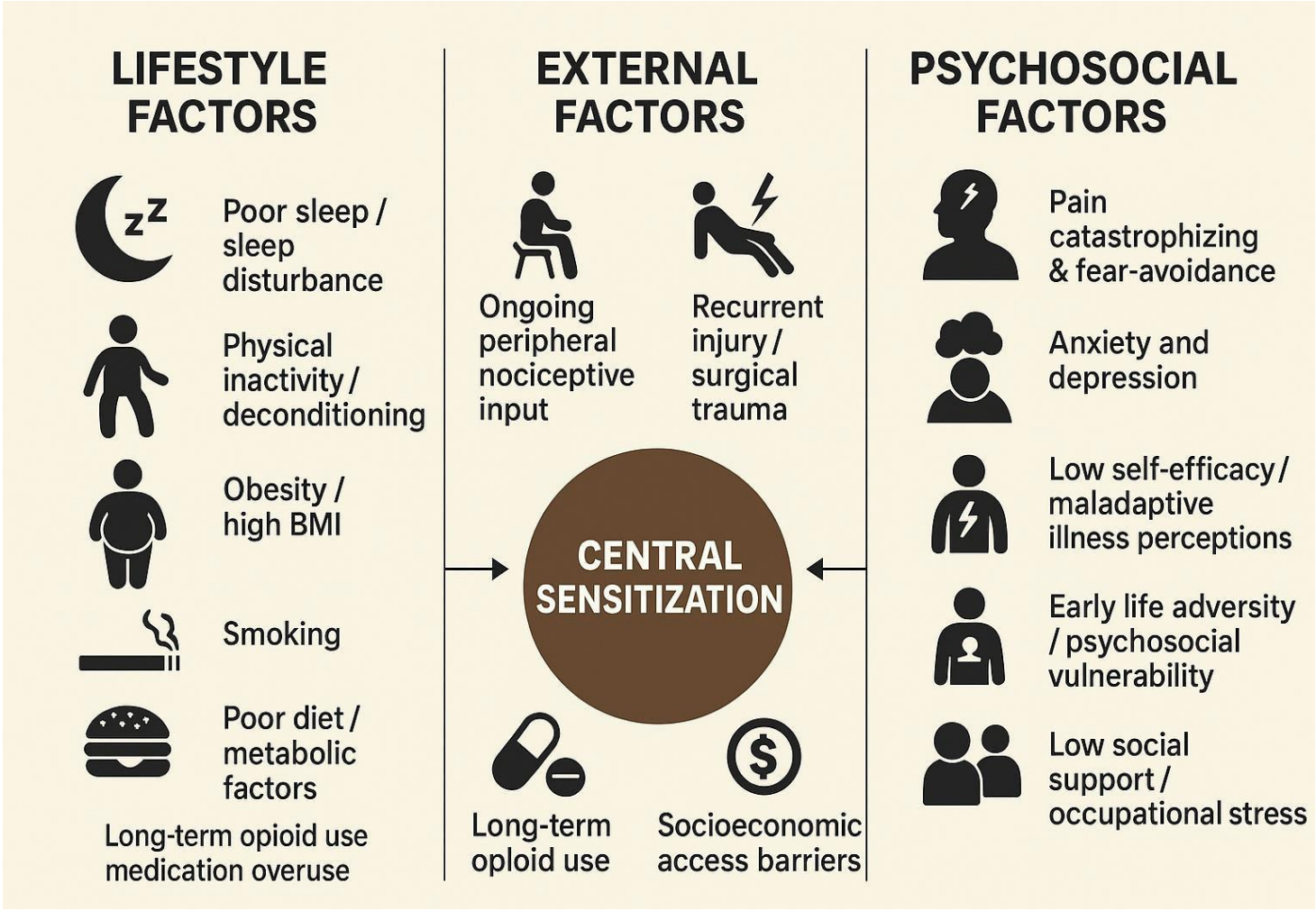
4. **Carefully weigh benefits and risks for patients already receiving higher opioid dosages**
   - Do not abruptly discontinue opioid therapy unless there are indications of a life-threatening issue, such as warning signs of impending overdose (e.g., confusion, sedation, or slurred speech)
   - Exercise care when reducing or continuing opioid dosage
   - Work closely with patients to optimize other therapies
   - Gradually taper to lower dosages if risks outweigh benefits of continued opioid therapy
   - Taper and discontinue opioids if warranted based on the individual clinical circumstances of the patient
   - Consider transitioning to buprenorphine if opioids cannot be sufficiently tapered or discontinued
5. **Offer Medications for Opioid Use Disorder (MOUD) to patients without pain and exhibiting opioid used disorder (OUD)**

URL - CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022 (Accessed 4/14/2025)

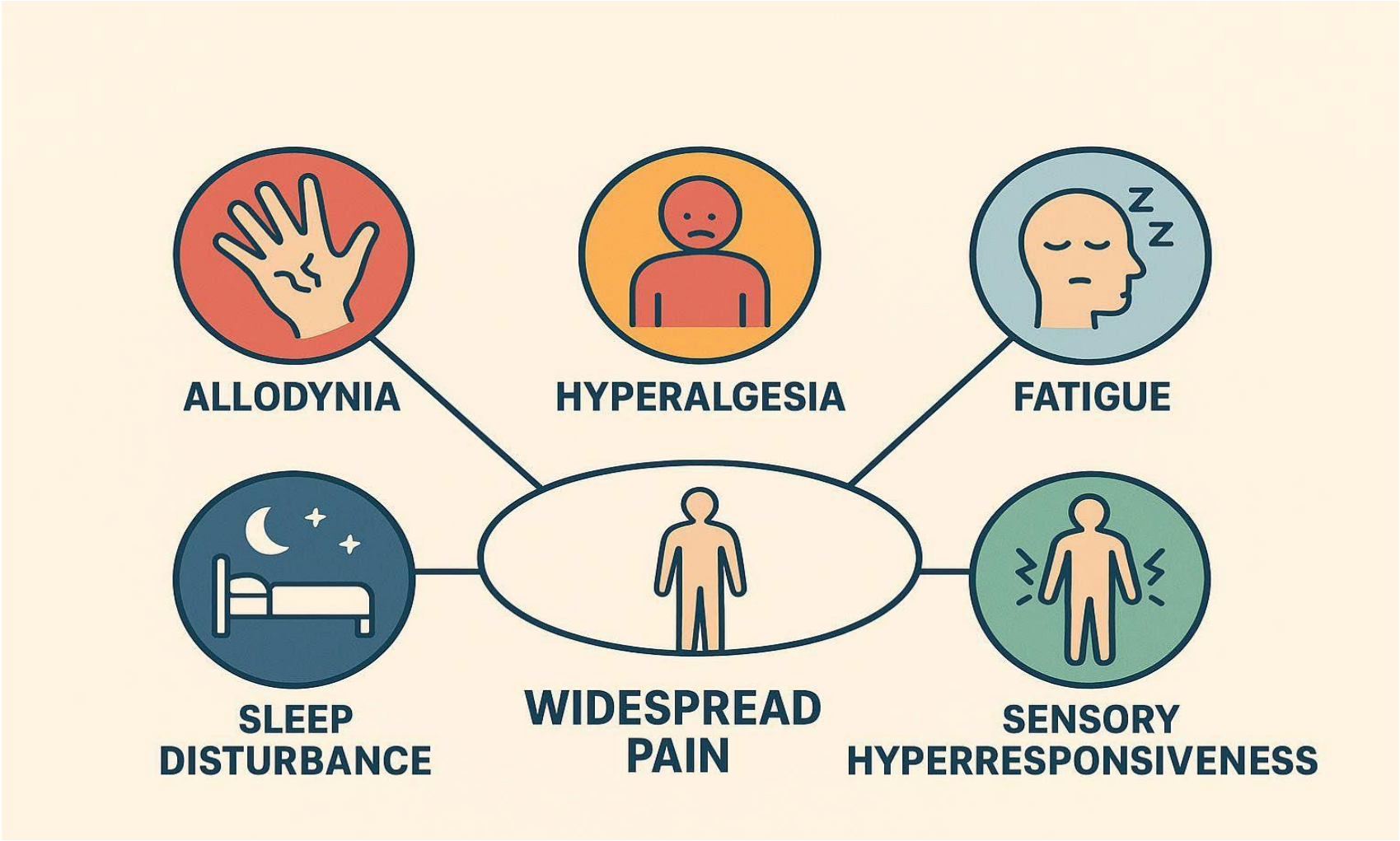
Address Central Sensitization Upfront

- CNS is hyperexcited even without sensory input.
- Pain no longer reflects tissue damage alone.
- Central sensitization can be maintained with or without continued peripheral input
- Present in up to 70% of chronic pain patients
- Common in fibromyalgia, CRPS, chronic low back pain, post-stroke pain
- Associated with poor response to purely biomedical approaches
- Requires multimodal management using an opioid sparing approach

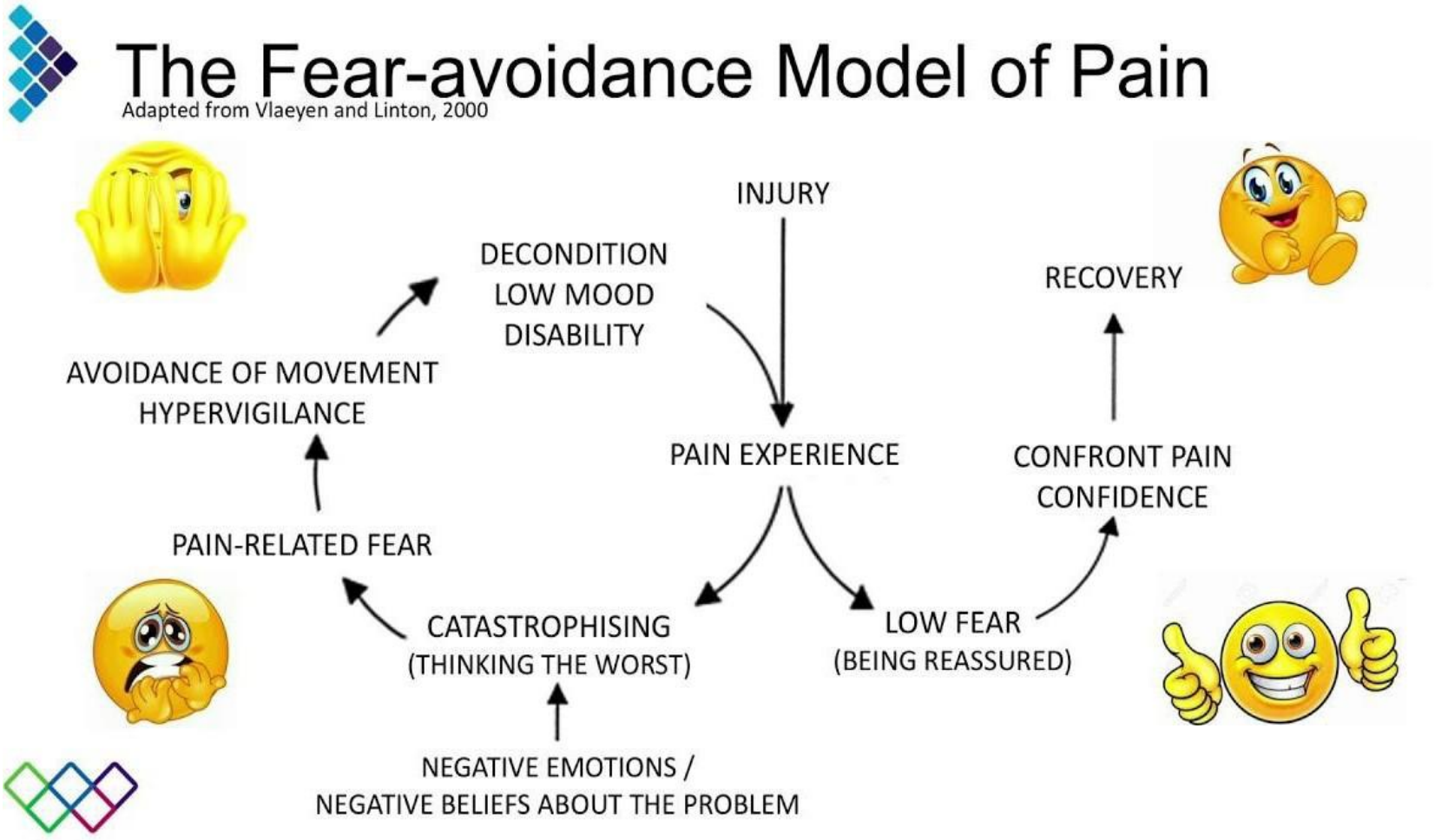
Central Sensitization – Cause and Effect



Central Sensitization – Cause and Effect



Central Sensitization – Approaches to Treating



Central Sensitization – Cause and Effect

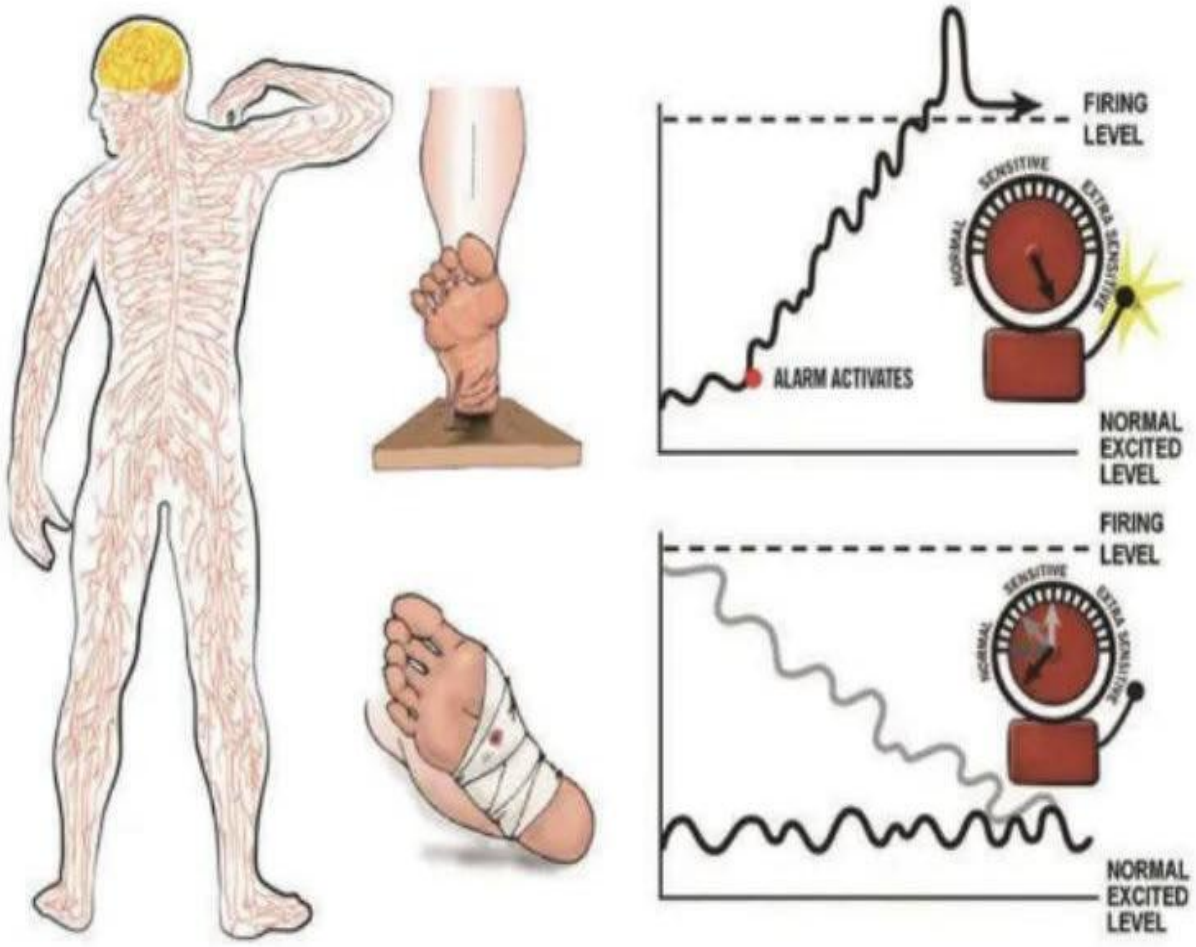
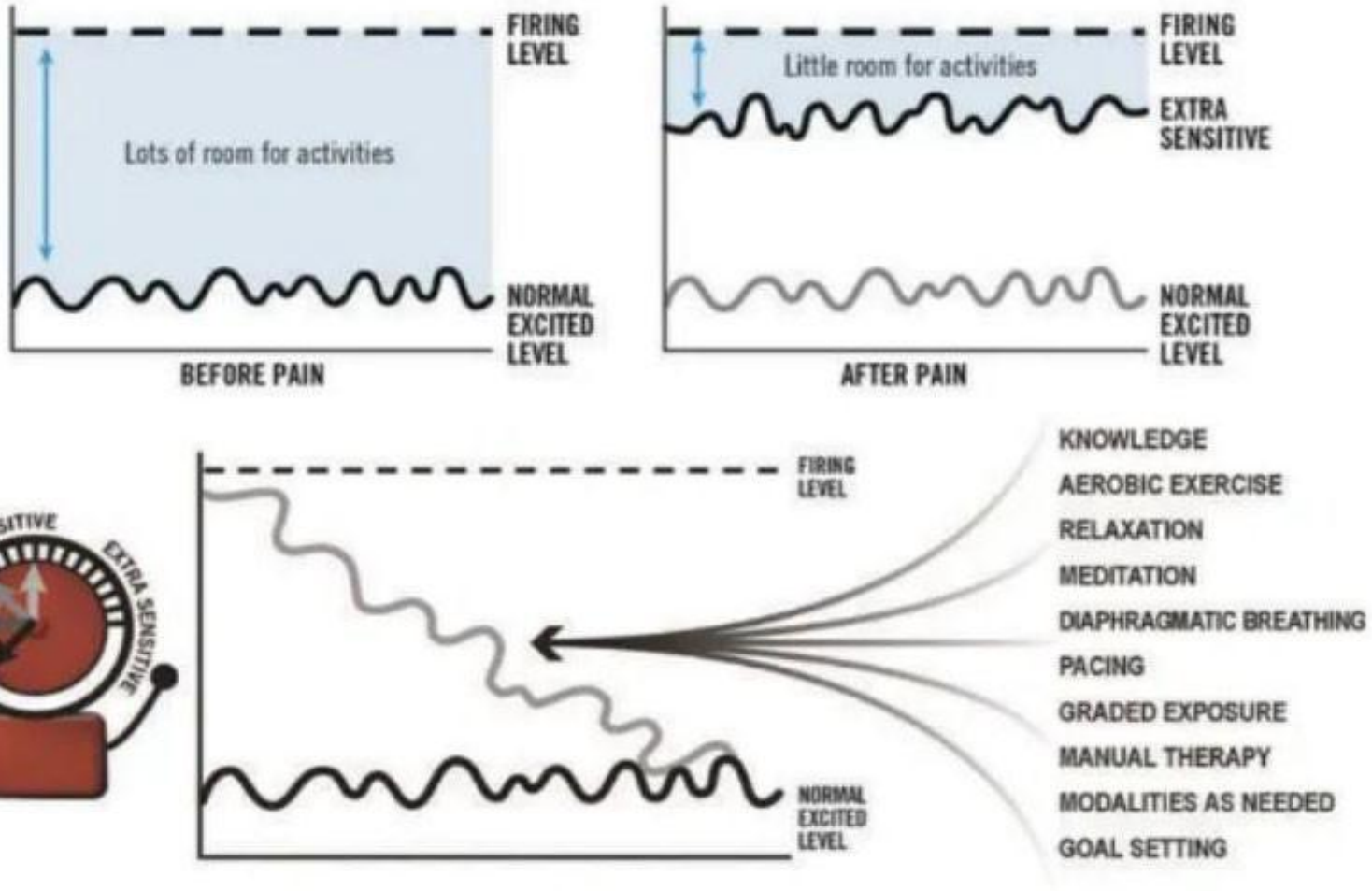


Figure 1. Metaphorical explanation of the nervous system as an alarm system during nociceptive activation (Images with permi
from Louw, 2013).

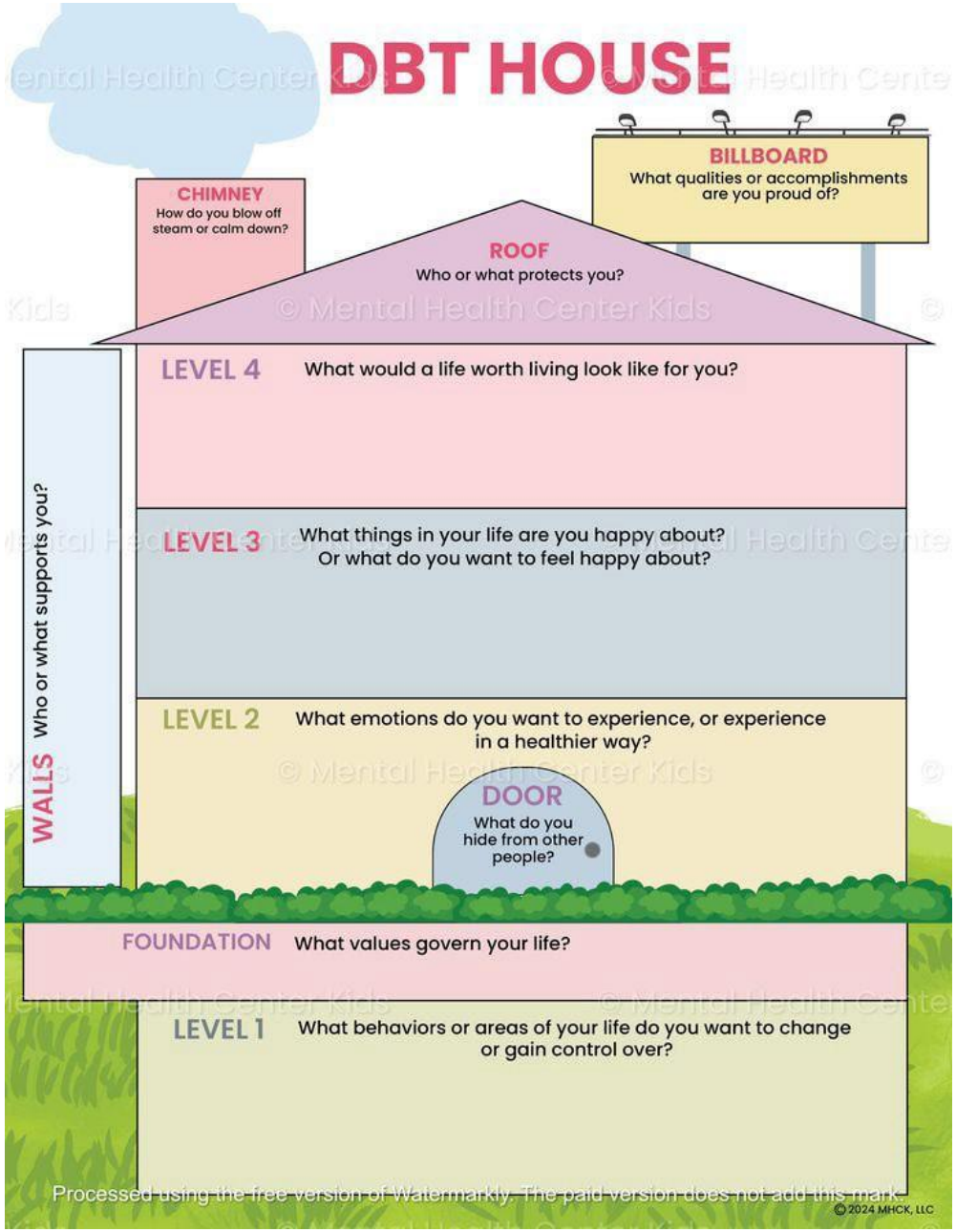
Central Sensitization – Approaches to Treating



Start the Journey and Utilize Dialectical Behavioral Therapy (DBT) at Routine Visits

[Certified Dialectical Behavior Therapy Professional (CDBT) Training | PESI US]

Help the Patient Build Their DBT House



[Certified Dialectical Behavior Therapy Professional (CDBT) Training | PESI US]

Example of a Multi-Modal Chronic Pain Management Plan

Name	
DOB	

Visit		Visit 1	Visit 2	Visit 3	Visit 4	Visit 5
Date						

Disease/Conditions Causing Pain

1						
2						
3						
4						
5						
6						

Pain Levels

Worst Pain Level:						
Current Pain Level:						
Achieveable Pain Level:						

Pain Management Goals

1						
2						
3						
4						
5						
6						

Pain Medication

1						
2						
3						
4						
5						
6						

Specialty Consultation

1	General Surgery					
2	Orthopedic Surgery					
3	Interventional Pain Medicine					
4	Physical Medicine & Rehabilitation					
5	Manual Medicine (OMM/PT/Chiropractic)					
6	Neurology					
7	Sleep Medicine					
8	Accupuncture					
9	Hypnosis/Biofeedback					
10	Other: _____					

Self Care

1	Ice/Heat Therapy					
2	Exercise					
3	Substance Management					
	Caffeine					
	NicotineTobacco					
	Marijuana					
	Vaping					
	Kratom					
	Other: _____					
3	Nutrition					
4	Weight Management					
5	Sleep Hygiene					

Courtesy of David Neff, DO

Obtain Meaningful Informed Consent (Sample)

Controlled Medication Management Agreement and Informed Consent

Patient Name: _____

DOB: ___/___/___

Provider: _____

Facility: _____

Date: ___/___/___

#	Controlled Medication	Dose	Quantity	Directions	New Start	Refill	Switch
1							
2							
3							
4							
5							
6							
7							
8							

The terms "I", "my" and "you" in this document refer to the patient. Where the patient is under age 18, or an adult for whom a guardian is signing the Agreement, the terms "I", "my" and "you" refer to the patient and to his or her parent or guardian.

This document lists commitments I will make before beginning one or more of these medications or continue them, if already being taken. I have received and have read the following patient education:

- ☐ Opioids *(Opioid Medication for Chronic Pain fact sheet)*
- ☐ Stimulants *(Stimulant Medicine for ADHD fact sheet)*
- ☐ Benzodiazepines, Sedatives, Hypnotics and Sleeping Pills *(Sedatives and Sleeping Pills: Understanding the Risks fact sheets)*
- ☐ Gabapentin (*Gabapentin fact sheet*)
- ☐ Others *(Describe)* _____

1. I will work with my provider(s) in a collaborative manner to develop a balanced treatment plan that considers both benefits and risks to any given treatment.
2. I have discussed the medication(s) and had the chance to ask questions about the medications being prescribed with my provider(s).
   a. all my questions have been answered in a way I understand.
3. I will engage in all activities to continue my ongoing therapy
4. I acknowledge that I might develop tolerance, dependence, addiction or other serious and potentially life-threatening conditions when taken improperly, either individually or in combination with other controlled medications or addictive substances.
5. I will refrain from taking actions that could endanger myself or the public.
6. I understand that insurers and regulatory authorities have the right to review my records when taking controlled substances
   a. I understand that my medical and insurance claims records may be reviewed by an independent review team to evaluate my ongoing opioid and controlled substance usage.
   b. the Michigan Department of Licensing and Regulatory Affairs (LARA) maintains and makes available a database of my controlled drug prescriptions to all medical providers providing my care.
7. I acknowledge that unwillingness or inability to work collaboratively with my provider(s) and adhere to this agreement may result in discharge from the provider's care
   a. Any action on my part that may be threating to safety of your provider(s) and their staff may be subject to subsequent action
8. I acknowledge that my provider and I have reviewed this document.
9. I acknowledge the potential benefits and risks of controlled substances prescribed by my provider along with the responsibility of properly managing my medication as stated above.
10. For OPIOID USE ONLY, I understand that there are inherent risks for using opioids that are associated with increasing doses and when used in combination with other drugs. Naloxone, also known as Narcan, is an antidote that can reverse overdose of opioids by blocking their sedating effects that may slow down breathing and lead to cardiopulmonary arrest. Narcan can be helpful to reverse over sedation and may be lifesaving when too much opioid is taken by myself or others. I acknowledge that Naloxone has been offered by prescription from my provider and is also available by request at participating pharmacies under standing orders of the Chief Medical Executive for the State of Michigan. Additional information regarding Naloxone and its proper use can be found at https: //www.michigan.gov /opioids/0,9238,7-377--480835--,00.html.

My signature confirms that I have had an opportunity to ask questions about this agreement, and that I understand and agree to all the statements above. I have been given a copy of this Agreement and agree to keep the copy for my future reference.

Patient or Legal Guardian:

X _____

Date: _____

*(*Patients aged 12 to 17 may sign in addition to the parent or guardian)*

Patient (aged 12-17)

X _____

Date: _____

Provider:

X _____

Date: _____

Document the Need for Chronic Pain Management and Palliative Care

Chronic Pain Management & Palliative Care Certification Form

Patient Information

Patient Name:		Telephone #:	
Date of Birth:		Fax #:	
Address:		Cellphone #:	
City, STATE, Zip:		Email:	

Primary Diagnoses (relating to persistent intractable pain)

Certication Criteria

	Palliative Care Criteria
☐ YES ☐ NO	The underlying disease is protracted with an unpredictable outcome and/or is uncurable
☐ YES ☐ NO	Pain is persistent and intractable despite using non-opioid therapies that have been maximized and reached maximal therapeutic benefit
☐ YES ☐ NO	Symptomatic pain treatment has a good probability to improve functionality and existing quality of life
☐ YES ☐ NO	Anticipated benefit exceeds potential risk for overdose and/or diversion
☐ YES ☐ NO	Pain management is a component of all aspects of palliative care including management of other treatable conditions and symptoms

Certification

I have performed a comprehensive and detailed examination for_____ and have developed a collaborative palliative care plan.

I have determined that this person has intractable pain and satisfied the criteria for Palliative Care Status. Support documentation is included in the patient's medical record with this certification.

I, hereby, certify this pain management and palliative care plan is medically necessary. This plan will be recertified annually or sooner if there is substantive change beforehand.

PROVIDER

Signature of Provider: _____Date: ___/___/___

Provider Name Printed:_____

PATIENT

By signing below, and I hereby agree to all terms and conditions set forth under this certification document and accompanying treatment agreement.

Signature of Patient: _____Date: ___/___/___

Patient Name Printed:_____

Courtesy of David Neff, DO

Implement a Taper Plan (with or without buprenorphine) Whenever Practicable

Name: _____ **DOB**___/____/___

Opioid and/or Benzodiazepine Tapering Plan Agreement

The purpose of this document is to develop a specific tapering plan with a timeline for discontinuation or reaching a taper "target dose".

We will work with you to develop a plan that is safe, effective and will minimize any symptoms that may be associated with tapering. Enclosed is a sample of a tapering schedule that can be used to help keep everyone apprised.

Taper Schedule

Visit	Date	Medication	Taper Frequency (# weeks)	Single Dose	Dose Frequency	Total Daily Dose	Total Dose/Day	Quantities Needed
1								
2								
3								
4								
5								
6								
7								
8								
9								
10								
11								
12								
13								
14								
15								

We will allow for gradual dose reductions and will reassess regularly and adjust accordingly.

Sign and Date below:

Patient or Patient's Representative (required):

_____ Date: _____

Mature Minor Patient:

_____ Date: _____

Physician Signature or Provider:

_____ Date: _____

Courtesy of David Neff, DO

Provide Tools to Reverse Opioid Overdose Using Narcan or Opvee With Proper Stocking and Training at the Overdose Site

- Narcan (naloxone) and Opvee (nalmefene) are both opioid overdose reversal medications, but they have key differences in duration, potency, and availability.
  - Narcan is more widely available and works well for most opioid overdoses.
- Opvee may be more effective for high-potency synthetic opioids but can cause longer-lasting withdrawal symptoms.
  - Opvee is not generic and is more expensive

Feature	Narcan (Naloxone)	Opvee (Nalmefene)
Mechanism	Blocks opioid receptors	Blocks opioid receptors
Onset of Action	3–17 minutes	2.5–5 minutes
Duration	1.3–2.7 hours	Up to 11 hours
Potency	Effective for most opioid overdoses	More effective for synthetic opioids like fentanyl
Availability	Over-the-counter	Prescription-only
Withdrawal Risk	Short-lived withdrawal symptoms	Prolonged withdrawal symptoms

Orient Patients to Dispose of Expired or Unused Medications to Avoid Pilfering and Accidental Overdose

[Safe Opioid Disposal - Remove the Risk Outreach Toolkit | FDA]
(Accessed 9/5/22)

The Michigan Osteopathic Association
Learning Center
CME as close as your keyboard
On demand CME

Advances in Pain Management to Reduce Opioid Risk

Leverage Advances in Perioperative Anesthesia and Interventional Pain Management

- **Local Intraoperative Techniques Before Wound Closure – Combination Injections**
  - Rovipicaine – longest acting local anesthetic to reduce pain that lasts for 3-5 days post- op
  - Ketolorac (aka Toradol) – to reduce inflammation
  - Epinephrine – to reduce inflammation- induced edema
- **Interventional Pain Management – Facet and Epidural Blocks**
  - Facet and Epidural Blocks
  - Rovipicaine or Buvipicaine
  - Steroids
- **Spinal Stimulators and Pain Pumps**

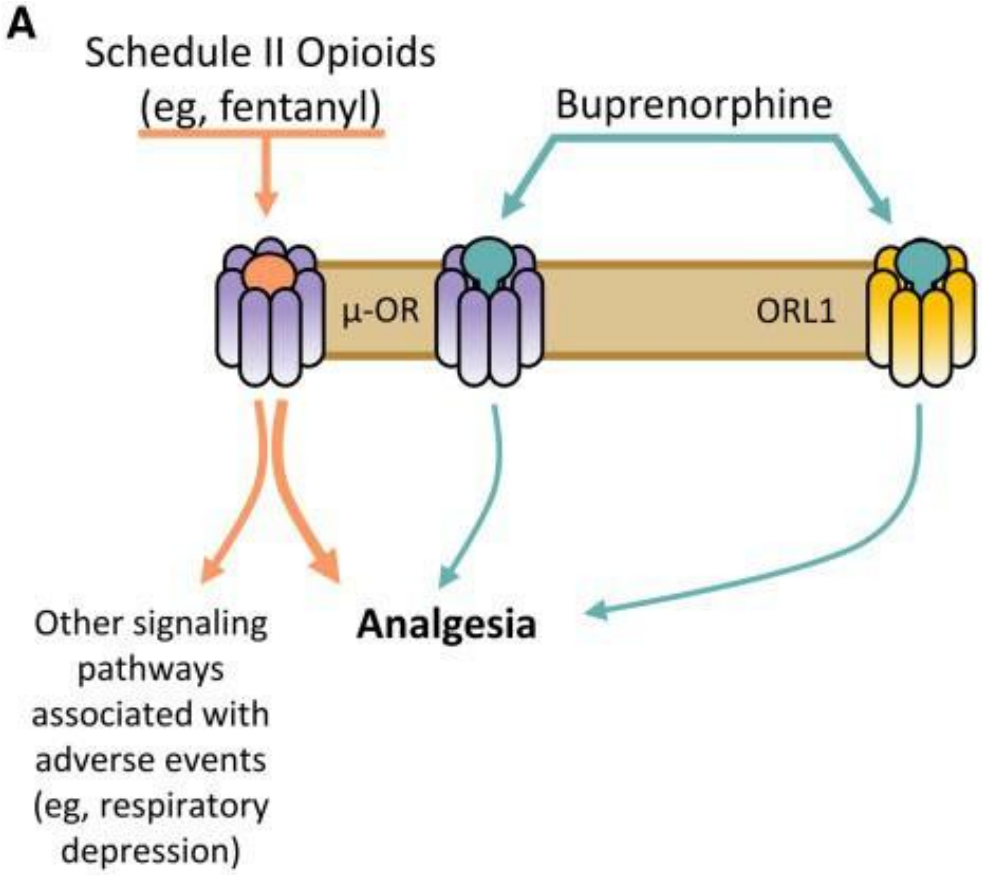
Consider Using Buprenorphine for Pain Management as Well As Opioid Use Disorder

- **Effective analgesia – limits tolerance and dependance**
- **Relative ceiling on respiratory depression**
  - Fatal overdose limited but possible with other non-opioid respiratory depressants
- **Less dysphoria, sedation, constipation**
- **Limited tolerance**
- **Limited abuse potential and withdrawal**
- **Reduced endocrinopathies**
- **Convenient dosing schedule**

- **It's better than the rest.**

Dalal S, Chitneni A, Berger AA, et al. Buprenorphine for Chronic Pain: A Safer Alternative to Traditional Opioids. *Health Psychology Research*. 2021;9(1). healthpsychologyresearch_2021_9_1_27241.pdf

Buprenorphine Pharmacology – Efficacy



Webster 2020

- **Acts on the mu-opioid receptor, like other opioids**
- **Also acts on the opioid receptor-like 1 (ORL1) receptor**
- **Produces equally-efficacious analgesia**

(Raffa 2014)

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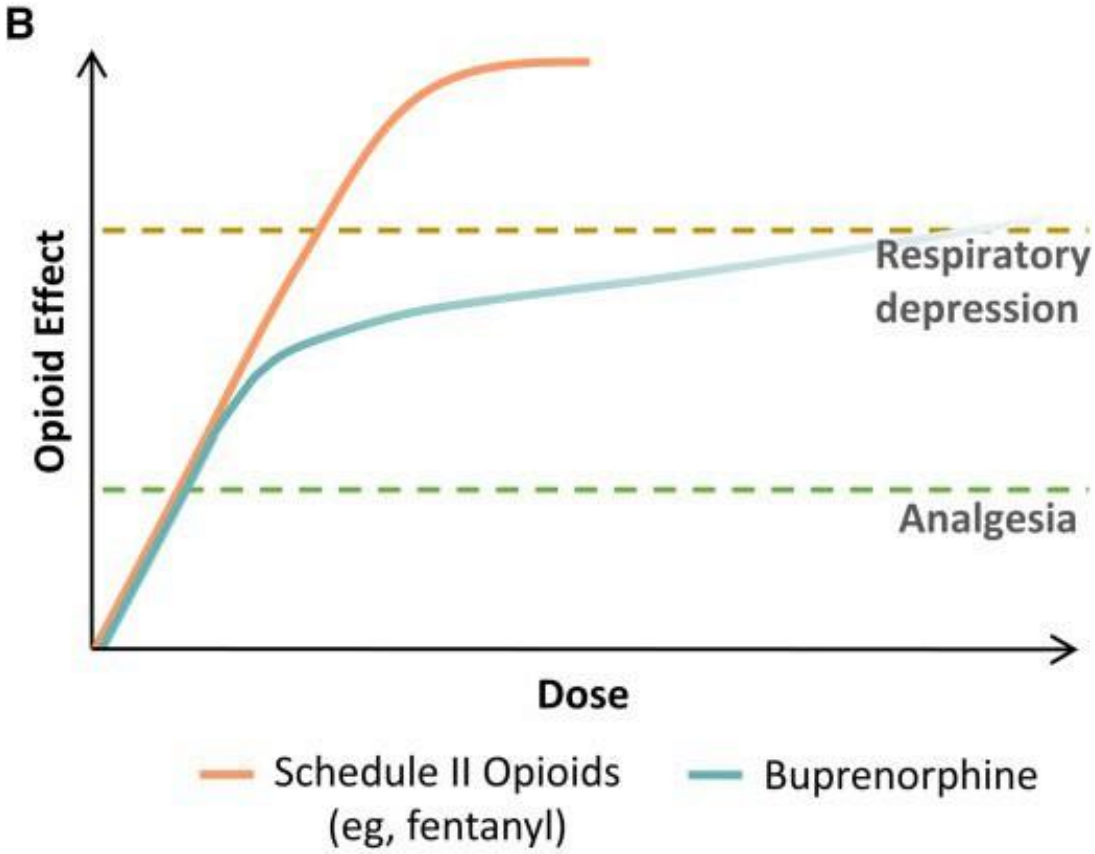
Buprenorphine Pharmacology – Side Effects



Webster 2020

- **Antagonist at the kappa- and delta-opioid receptors**
- **Limited respiratory depression; overdose on buprenorphine alone is not fatal in adults**

Caution: Synergistic depression with benzodiazepines, z-drugs, alcohol, muscle relaxants, gabapentinoids, TCAs

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When to Consider JournaVx (suzetrigine) for Acute Pain

HOW JOURNAVX WORKS

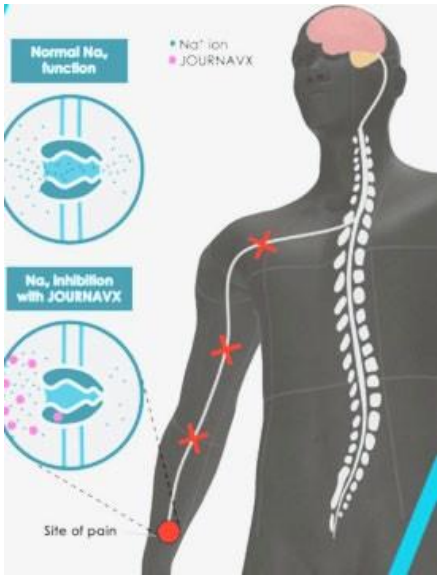
A first-in-class nonopioid, JOURNAVX is a sodium channel blocker highly selective for $Na_V1.8$[1,2]

By inhibiting $Na_V1.8$, JOURNAVX blocks sodium ions from entering pain-sensing neurons, disrupting the initiation and propagation of action potentials and **reducing pain signal transmission** from the PNS to the CNS[1,2]

Because JOURNAVX is a **highly selective** inhibitor of $Na_V1.8$ (≥31,000x more selective of $Na_V1.8$ than all other Na_V subtypes as measured *in vitro*), it inhibits pain signal transmission to the spinal cord and brain[1,2]

JOURNAVX **does not interact with μ receptors**, which are associated with addiction.[2,8] **There is no evidence that JOURNAVX has addictive potential** based on available data, including the MOA, preclinical data, and clinical adverse event data[2]

JOURNAVX is **not a controlled substance**[9]

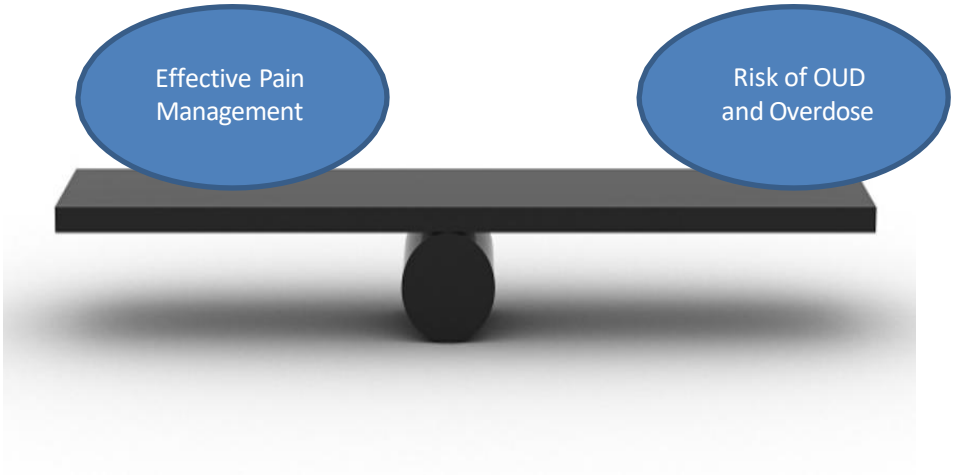


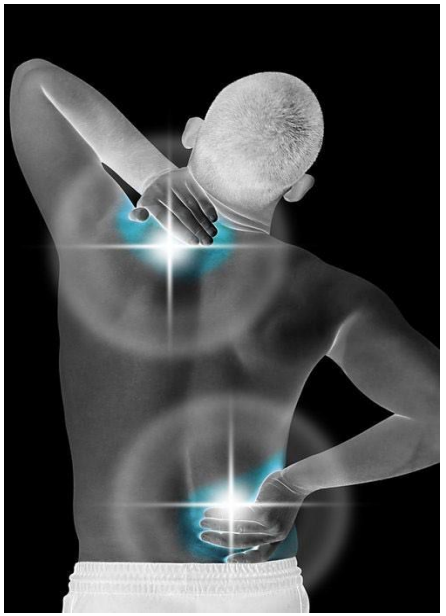
- Stops pain in peripheral tissues at the source
- Dosing -- start with 2 tablets initially, then take 1 tablet twice daily until pain has sufficiently resolved

Receptor Subtypes and Inflammatory Targets Being Studied for Non-Opioid Drug Development

Rank	Target (Abbrev)	Full Target Name	Mechanism Class
1	**Nav1.8**	Voltage-Gated Sodium Channel Subtype 1.8 (SCN10A)	Peripheral nociceptor excitability
2	**CGRP**	Calcitonin Gene-Related Peptide Pathway (ligand + receptor)	Neuropeptide signaling
3	**NGF–TrkA**	Nerve Growth Factor – Tropomyosin Receptor Kinase A	Neurotrophin signaling
4	**Nav1.7**	Voltage-Gated Sodium Channel Subtype 1.7 (SCN9A)	Pain initiation threshold channel
5	**TRPV1 / TRPA1**	Transient Receptor Potential Vanilloid 1 / Ankyrin 1	Nociceptor ion channels (thermal/chemical sensing)
6	**P2X3 / P2X7**	Purinergic Receptor P2X Ligand-Gated Ion Channels 3 and 7	ATP-mediated pain & neuroinflammation signaling
7	**Neuroinflammation targets**	Microglial / cytokine pathways (e.g., IL-1β, TNF, CSF1R)	Immune-mediated pain amplification
8	**FAAH / MAGL**	Fatty Acid Amide Hydrolase / Monoacylglycerol Lipase	Endocannabinoid degradation enzymes
9	**NMDA / mTOR**	N-Methyl-D-Aspartate Receptor / Mechanistic Target of Rapamycin	Central sensitization & plasticity pathways
10	**SCN9A gene therapies**	Gene modulation of Nav1.7 (SCN9A)	Disease-modifying / gene therapy
11	**Regenerative targets**	Neural repair / cell therapies	Structural restoration

Achieving the Primary Goal: Providers Can Balance Effective Pain Management When Using Opioids While Mitigating Overdose Risk, Diversion, Misuse and Abuse





Primary Objectives

At the conclusion of this talk, the anticipation is that attendees better understand:

1. Recently updated definitions for pain
2. Principles of assessment and treatment for acute and chronic pain - using a multimodal approach
3. New non-opioid prescription medication and future non-opioid drug targets

THANK YOU!

Evolving Principles of Multimodal Pain Management – 2026 Spring Update

Contact: neff@msu.edu