2021 ACOI Annual Convention
And Scientific Sessions
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Pharmacotherapy for Opioid Use Disorder

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Disclosures

- I have nothing to disclose

Objectives

1. Describe the rationale for employing medication assisted treatment in the primary care setting
2. Outline the scope of the opioid epidemic
3. Recognize the importance of widespread access to naloxone for opioid reversal

The opioid epidemic in the U.S.

- >2.5 million persons estimated to meet criteria for opioid abuse or dependence
- 11.5 million adults misuse prescription opioids
- 116 individuals die each day from opioid related overdoses- projected to increase to 224 by 2025

The opioid epidemic in the U.S.

- 30% increase in opioid-related overdose from 7/16 to 9/17
- Economic cost >500 billion a year

- American Society of Addiction medication. Opioid addiction:2016 facts and figures- https://www.asam.org/docs/default-source/advocacy/opioid-addiction-disease-facts-figures.pdf

The opioid epidemic

- Among the more than 70,200 drug overdose deaths estimated in 2017, the sharpest increase occurred among deaths related to fentanyl and fentanyl analogs (other synthetic narcotics) with more than 28,400 overdose deaths. Source: CDC WONDER

- https://www.cdc.gov/drugoverdose/opioids/fentanyl.
- https://www.cdc.gov/drugoverdose/data/fentanyl.html

WORDS MATTER: LANGUAGE CHOICE CAN REDUCE STIGMA

"If you want to care for something, you call it a flower; if you want to kill something, you call it a weed." —Don Coyhis

Commonly Used Term	Preferred Term
Addiction	Substance use disorder (SUD) [from the *DSM-5*®]
Drug-seeking, aberrant/problematic behavior	Using medication not as prescribed
Addict	Person with substance use disorder (SUD)
Clean/dirty urine	Positive/negative urine drug screen

SOURCES: SAMHSHA Resource: https://www.samhsa.gov/capt/sites/default/files/resources/sud-stigma-tool.pdf
Scholten W. Public Health. 2017;153:147-153. DOI: 10.1016/j.puhe.2017.08.021

Definition Pain

Pain – physical suffering or discomfort caused by illness or injury

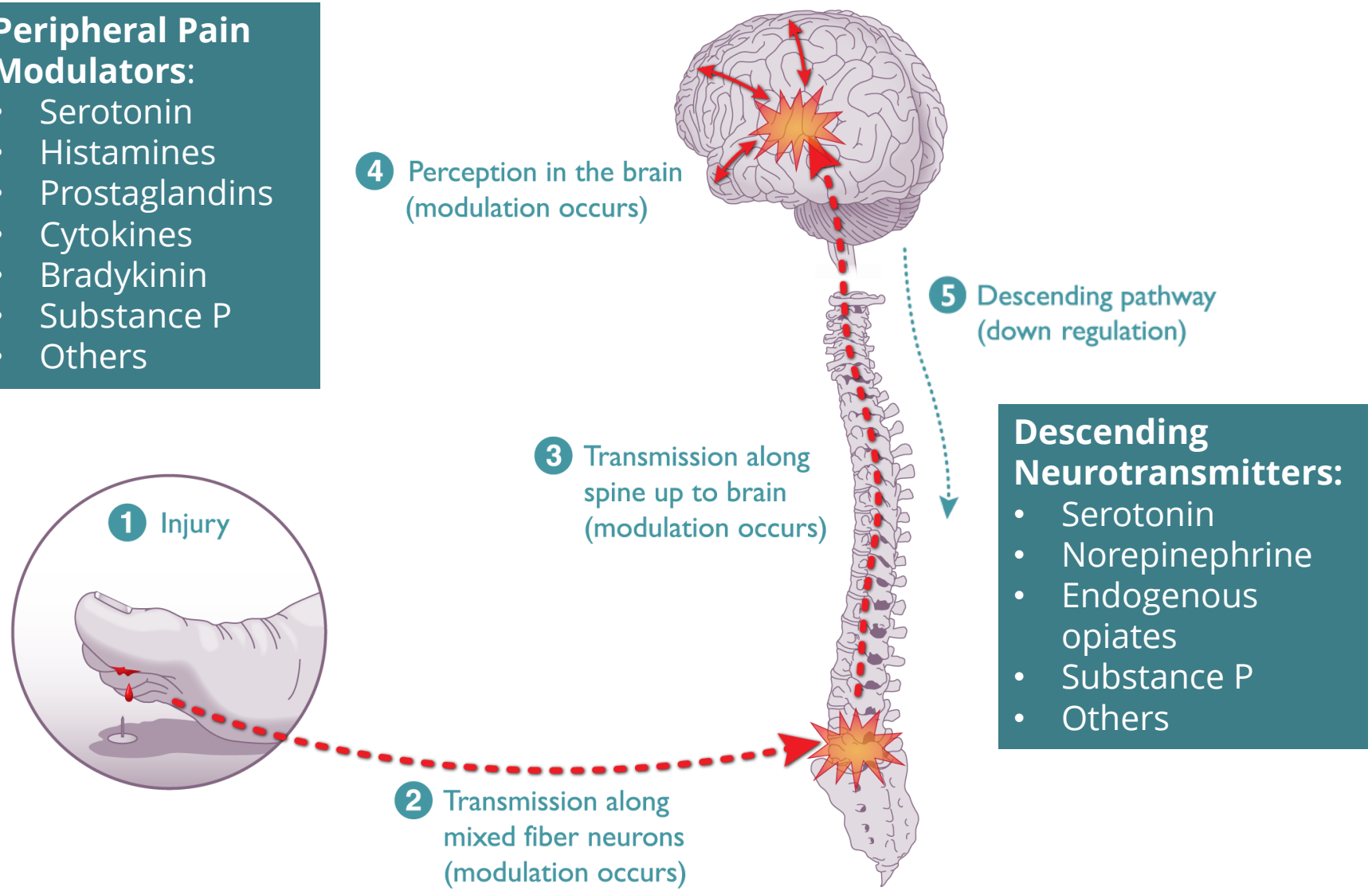
Cancer pain – pain related to cancer/tumor burden

Chronic pain/non-cancer pain –Any painful condition that persists for ≥ 3 months, or past the time of normal tissue healing, that is not associated with a cancer diagnosis

Busse JW, Schandelmaier S, et al. Opioids for chronic non-cancer pain: a protocol for a systematic review of randomized controlled trials. Systematic Reviews 2013, 2:66

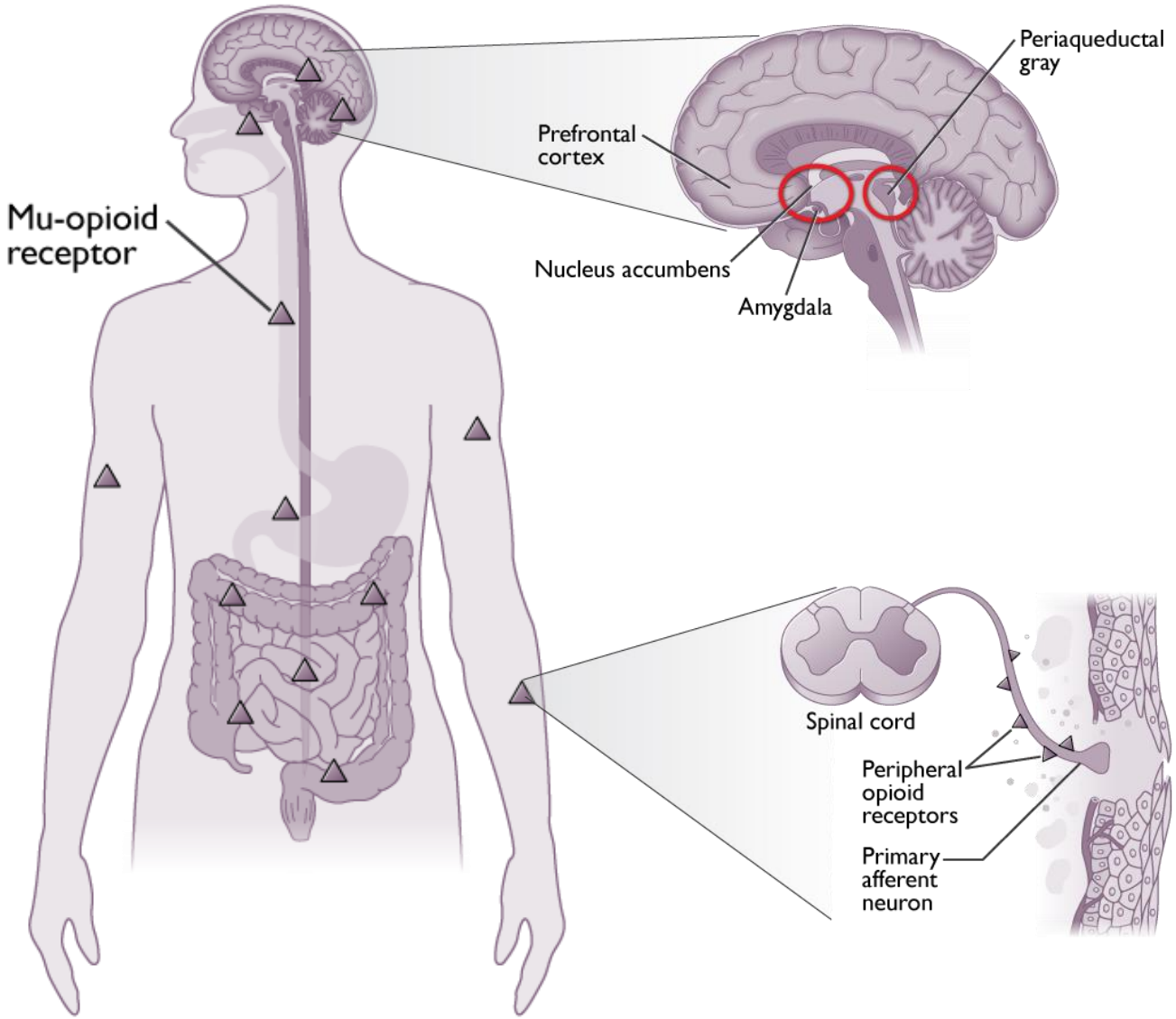
THE NEUROMECHANISMS OF PAIN

Peripheral Pain Modulators:
- Serotonin
- Histamines
- Prostaglandins
- Cytokines
- Bradykinin
- Substance P
- Others



Descending Neurotransmitters:
- Serotonin
- Norepinephrine
- Endogenous opiates
- Substance P
- Others

OPIOID RECEPTOR LOCATIONS



Pain types

- Nociceptive
- Nociplastic
- Neuropathic
- Mixed Nociceptive/Neuropathic

Evaluation pain- History/Exam/Work-up

- Good history include treatment hx
- Exam
  - Look for signs illicit drug use
- Imaging
- Labs
- Opioid risk tool
- DOCUMENT

Assessment pain

- Pain assessment tool
  - PAINAD
  - 0-10 scale
- Opioid misuse risk assessment tool
  - Examples
    - ORT-OUD-Opioid risk tool
    - SOAPP – Screener and opioid assessment for patients with pain

PAIN ASSESSMENT

DESCRIPTION OF PAIN

Location

Intensity

Quality

Onset/
duration

Variations/
patterns/rhythms

WHAT RELIEVES THE PAIN?

WHAT CAUSES OR INCREASES THE PAIN?

EFFECTS OF PAIN ON PHYSICAL, EMOTIONAL, AND PSYCHOSOCIAL FUNCTION

PATIENT'S CURRENT LEVEL OF PAIN AND FUNCTION

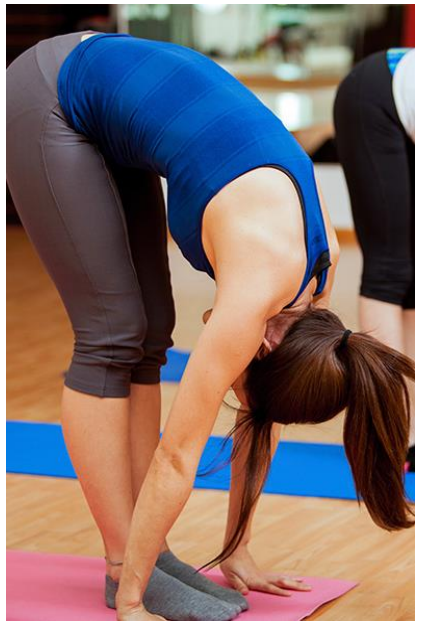
SOURCES: Heapy A, Kerns RD. Psychological and behavioral assessment. In: Raj's Practical Management of Pain. 4th ed. 2008:279-295; Zacharoff KL, et al. Managing Chronic Pain with Opioids in Primary Care. 2nd ed. Newton, MA: Inflexion, Inc.;2010.

PAST MEDICAL AND TREATMENT HISTORY

NONPHARMACOLOGIC STRATEGIES AND EFFECTIVENESS

PHARMACOLOGIC STRATEGIES AND EFFECTIVENESS

RELEVANT ILLNESSES



PAST AND CURRENT OPIOID USE

- Query your state's Prescription Drug Monitoring Program (**PDMP)** to confirm patient report
- Contact past providers and obtain prior medical records
- For opioids currently prescribed, note the opioid, dose, regimen, and duration
- Determine whether the patient is **opioid-tolerant**

GENERAL EFFECTIVENESS OF CURRENT PRESCRIPTIONS

OBTAIN A COMPLETE SOCIAL AND PSYCHOLOGICAL HISTORY

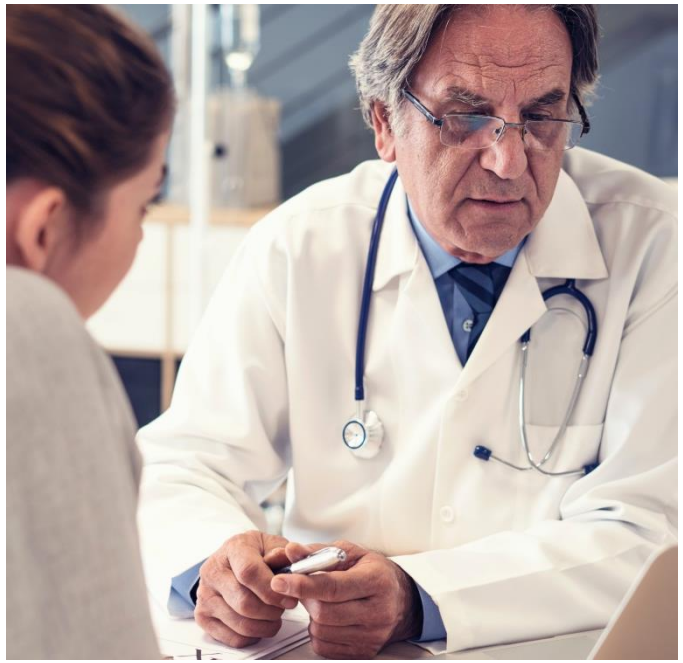
SOCIAL HISTORY

Employment, cultural background, social network, relationship history, legal history, and other behavioral patterns

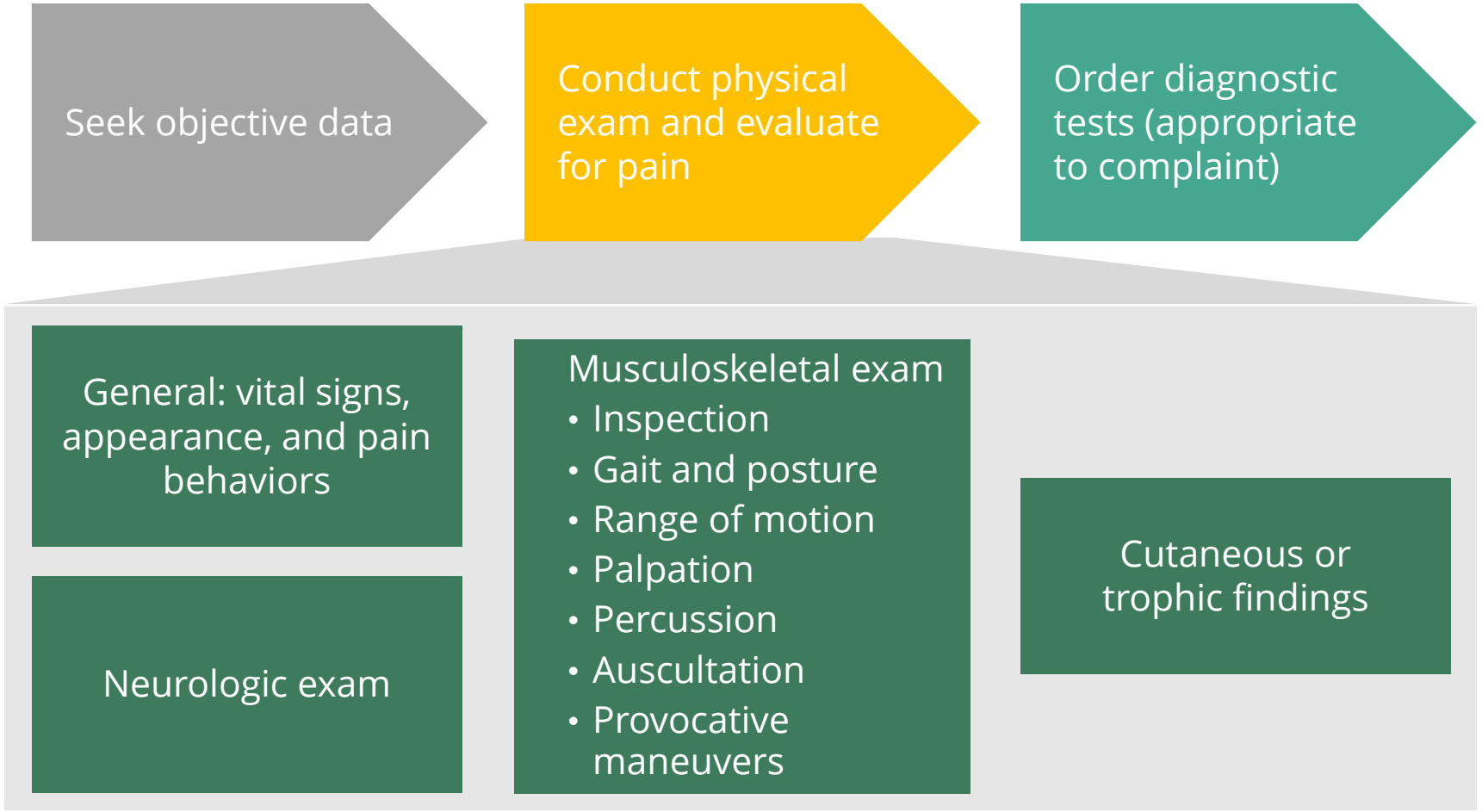
PSYCHOLOGICAL HISTORY

Screen for:

- Mental health diagnoses, depression, anxiety, PTSD, current treatments
- Alcohol, tobacco, and recreational drug use
- History of adverse childhood experiences
- Family history of substance use disorder and psychiatric disorders



PHYSICAL EXAM AND ASSESSMENT



SOURCES: Lalani I, Argoff CE. History and Physical Examination of the Pain Patient. In: Raj's Practical Management of Pain. 4th ed. 2008:177-188; Chou R, et al. J Pain. 2009;10:113-130.

PAIN ASSESSMENT TOOL BOX

http://core-rems.org/opioid-education/tools/

Pain Assessment Tools

BPI or 5 A's

Functional Assessment

SF-36, PPS, Geriatric Assessment

Pain intensity, Enjoyment of life, General activity

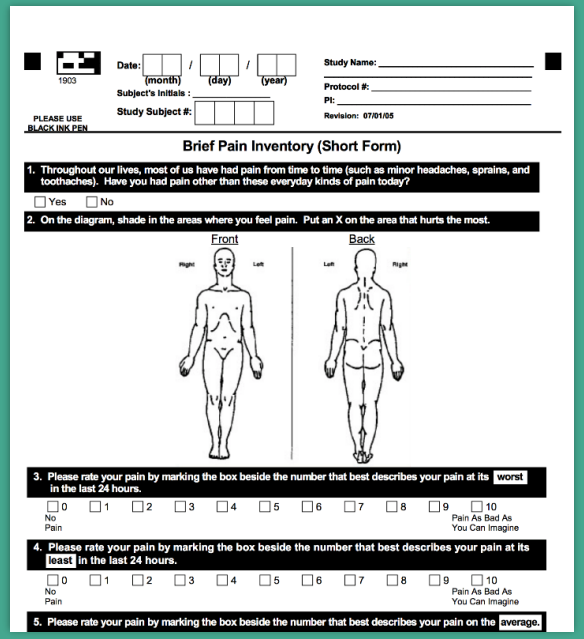
PEG

Childhood Trauma Questionnaire

ACE

Assessment in Advanced Dementia

PAINAD



1903

Date: (month) / (day) / (year)

Subject's Initials: _____

Study Subject #:

Study Name: _____

Protocol #: _____

PI: _____

Revision: 07/01/05

PLEASE USE BLACK INK PEN

Brief Pain Inventory (Short Form)

1. Throughout our lives, most of us have had pain from time to time (such as minor headaches, sprains, and toothaches). Have you had pain other than these everyday kinds of pain today?

☐ Yes ☐ No

2. On the diagram, shade in the areas where you feel pain. Put an X on the area that hurts the most.

Front Back

3. Please rate your pain by marking the box beside the number that best describes your pain at its worst in the last 24 hours.

☐0 ☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7 ☐8 ☐9 ☐10

No Pain — Pain As Bad As You Can Imagine

4. Please rate your pain by marking the box beside the number that best describes your pain at its least in the last 24 hours.

☐0 ☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7 ☐8 ☐9 ☐10

No Pain — Pain As Bad As You Can Imagine

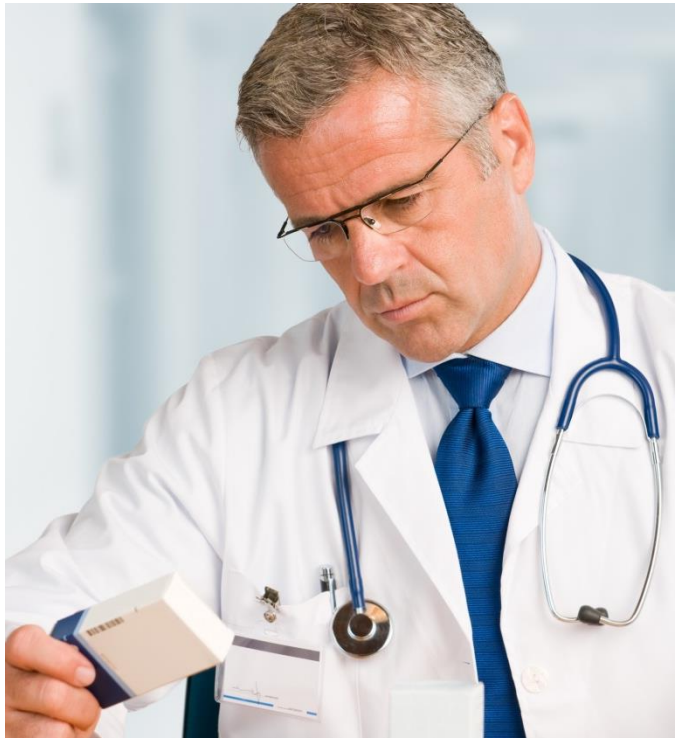
5. Please rate your pain by marking the box beside the number that best describes your pain on the average.

Brief Pain Inventory

Psychological Measurement Tools (PHQ-9, GAD-7, etc.)

CONSIDER AN OPIOID ONLY WHEN:

- Potential benefits are likely to outweigh risks
- Patient has failed to adequately respond to non-opioid and nonpharmacological interventions
- Patient has neuropathic or nociceptive pain that is moderate to severe



SOURCES: Chou R, et al. J Pain. 2009;10:113-130. Department of Veterans Affairs, Department of Defense. VA/DoD Clinical Practice Guideline for Management of Opioid Therapy for Chronic Pain. 2010.

INITIATING OPIOIDS

- Begin with IR
- Prescribe the lowest effective dosage
- Use caution at any dosage, but particularly when:
  - Increasing dosage to ≥ 50 morphine milligram equivalents (MME)/day
  - Carefully justify a decision to titrate dosage to ≥ 90 MME/day
- Always include dosing instructions, including daily maximum
- Be aware of interindividual variability of response
- Co-prescribe naloxone (if indicated)
- Co-prescribe bowel regimen
- Re-evaluate risks/benefits within 1 – 4 weeks (could be as soon as 3 – 5 days) of initiation or dose escalation
- Re-evaluate risks/benefits every 3 months; if benefits do not outweigh harms, optimize other therapies and work to taper and discontinue

There are differences in benefit, risk and expected outcomes for patients with chronic pain and cancer pain, as well as for hospice and palliative care patients.

OPIOID MISUSE RISK ASSESSMENT TOOLS

http://core-rems.org/opioid-education/tools/

TOOLS FOR PATIENTS CONSIDERED FOR OPIOID THERAPY
ORT-OUD Opioid Risk Tool
SOAPP® Screener and Opioid Assessment for Patients with Pain
DIRE Diagnosis, Intractability, Risk, and Efficacy score

TOOLS FOR SUBSTANCE USE DISORDER
CAGE-AID Cut down, Annoyed, Guilty, Eye-Opener tool, Adapted to Include Drugs
RAFFT Relax, Alone, Friends, Family, Trouble
DAST Drug Abuse Screening Test
CTQ Childhood Trauma Questionnaire
ACEs Adverse Childhood Experiences

Also for patients with chronic pain:

- Get a baseline UDT
- Check the PDMP

A CLOSER LOOK AT THE ORT-OUD

Opioid Risk Tool – OUD (ORT-OUD)

This tool should be administered to patients upon an initial visit prior to beginning or continuing opioid therapy for pain management. A score of 2 or lower indicates low risk for future opioid use disorder; a score of >/= 3 indicates high risk for opioid use disorder.

Mark each box that applies	YES	NO
Family history of substance abuse		
Alcohol	1	0
Illegal drugs	1	0
Rx drugs	1	0
Personal history of substance abuse		
Alcohol	1	0
Illegal drugs	1	0
Rx drugs	1	0
Age between 16-45 years	1	0
Psychological disease		
ADD, OCD, bipolar, schizophrenia	1	0
Depression	1	0
Scoring totals		

SOURCE: Cheatle, M., et al. JPain 2019; Jan 26.

Scoring:

- **≤ 2: low risk**
- **≥ 3: high risk**

Treatment pain

- Multi-modal
  - Non-pharmacologic
  - Topicals
  - Interventional
  - Cognitive-Behavioral
  - Physical modalities
  - OMM

Substance Use Disorder

- Opioid use disorder- usually name type of opioid
- Heroin use disorder- 2/3 people that use heroin reported to have additionally used prescription opioids

- Cicero, TJ. The changing face of heroin use in the US- a retrospective analysis of the past 50 years. JAMA Psychiatry 2014

DSM-V – Opioid Use Disorder (OUD)- over a 12 month period

1. Tolerance
2. Withdrawal
- Loss of control
3. using larger amounts and/or for longer periods
4. Inability to cut down or control use
5. Increased time spent obtaining, using or recovering
6. Craving/compulsion

Symptoms Opioid Use Disorder

- Additional symptoms
  - Giving up or reducing other activities because of opioid use
  - Using opioids even when it is physically unsafe
  - Continued use opioids despite despite physical or psychological problem
  - Impaired social function

Opioid Use Disorder

What is the risk for my patient?

- Risk of opioid use disorder in patients on chronic opioid therapy (COT) for chronic non-cancer pain (CNCP) is up to 26%
- Risk is always highest with past history of substance use disorder (SUD) or psychiatric comorbidity

Reference: Kaye, AD. Pain Physician 2017 Feb: 20(2S):S93-S109.
https://www.ncbi.nlm.nih.gov/pubmed/?term=Prescription+Opioid+Abuse+in+Chronic+Pain%3A+An+Updated+Review+of+Opioid+Abuse+Predictors+and+Strategies+to+Curb+Opioid+Abuse%3A+Part+1.

Who is Most Vulnerable

Low hedonic tone
Psychiatric illness
Genetic predisposition to substance abuse
Probability of long term opioid use increases in first 5-30 days of treatment

OUD- areas of brain

The periaqueductal gray, which sub-serves opioid analgesia.

The nucleus accumbens (part of the limbic system) which sub-serves reward or euphoria.

The locus coeruleus, which is the main noradrenergic center in the CNS and is involved in physical dependence and withdrawal

Prefrontal cortex: decision making, reasoning, judgment (shown for reference)

Vulnerable individuals- euphoria, relief anxiety via opioid interaction in the nucleus accumbens

OUD

Opioids taken regularly

- development of physical dependence
- opioid withdrawal syndrome when opioids are reduced or stopped abruptly.

hyperadrenergic signs and symptoms of opioid withdrawal are the result of unopposed noradrenergic output from the locus coeruleus, previously in homeostasis with exogenous opioid intake.

Clonidine works for withdrawal because it inactivates the locus coeruleus.

ORT-OUD

ORT: Opioid Risk Tool

Patient Name _____

OPIOID RISK TOOL

		Mark each box that applies	Item Score If Female	Item Score If Male
1. Family History of Substance Abuse	Alcohol	☐	1	3
	Illegal Drugs	☐	2	3
	Prescription Drugs	☐	4	4
2. Personal History of Substance Abuse	Alcohol	☐	3	3
	Illegal Drugs	☐	4	4
	Prescription Drugs	☐	5	5
3. Age (Mark box if 16 – 45)		☐	1	1
4. History of Preadolescent Sexual Abuse		☐	3	0
5. Psychological Disease	Attention Deficit Disorder, Obsessive Compulsive Disorder, Bipolar, Schizophrenia	☐	2	2
	Depression	☐	1	1
			TOTAL _____	_____

Total Score Risk Category
Low Risk 0 – 3
Moderate Risk 4 – 7
High Risk ≥ 8

Examples opioid misuse/abuse

-taking opioids for unintended use/prescribed use

i.e. for sleep

for new pain/HA

dose escalation

-forging prescription

Obtaining opioids from more than one source, illegal source

Treatment OUD

When you first suspect/concerned that there is an OUD, that's when you refer if you don't feel qualified to handle that.

- More important to individualize a treatment plan than an established 'best practice'.

- Medication treatment with methadone, buprenorphine, and naltrexone is evidence based. Relapse rates are in the 90% range over time in those patients with an OUD who decline pharmacotherapy.

Treatment OUD

- Medication options for addiction treatment (MAT)
  - Methadone (Schedule II)
  - Buprenorphine (Schedule III)
  - Naltrexone (not a controlled substance)
- Supplementary psychosocial and recovery support services
  - Housing, childcare, support groups, employment services
- Temporal considerations
  - Frequency of administration (daily versus long-acting formulations)
  - Length of treatment
    - No recommended time period for treatment
    - Patients who discontinue and resume risk overdose and death

Considerations for medication choice

- Setting (methadone can only be dispensed in OTPs)
- Regulations governing prescribers (e.g. waiver for buprenorphine prescribing)
- Induction time (6-10 days of withdrawal before starting naltrexone)
- Patient access and preferences

Treatment OUD

- **Methadone** for the treatment of OUD can only be accessed in Federally Regulated Opioid Treatment Programs (OTPs). Methadone may NOT be prescribed by a HCP for treatment of OUD.

- •A training course and then obtaining a WAIVER(X DEA number) is required to prescribe approved **buprenorphine** formulations for the treatment of OUD. There are regulations on number of patients a HCP can treat at any one time.

- •**Naltrexone** is not a controlled medication. Does not require any special waiver to prescribe. It is approved for both alcohol and opioid use disorders.

•"Detoxification" regimens treat the withdrawal syndrome, not the OUD. After "detoxification", relapse is the rule.

Treatment OUD

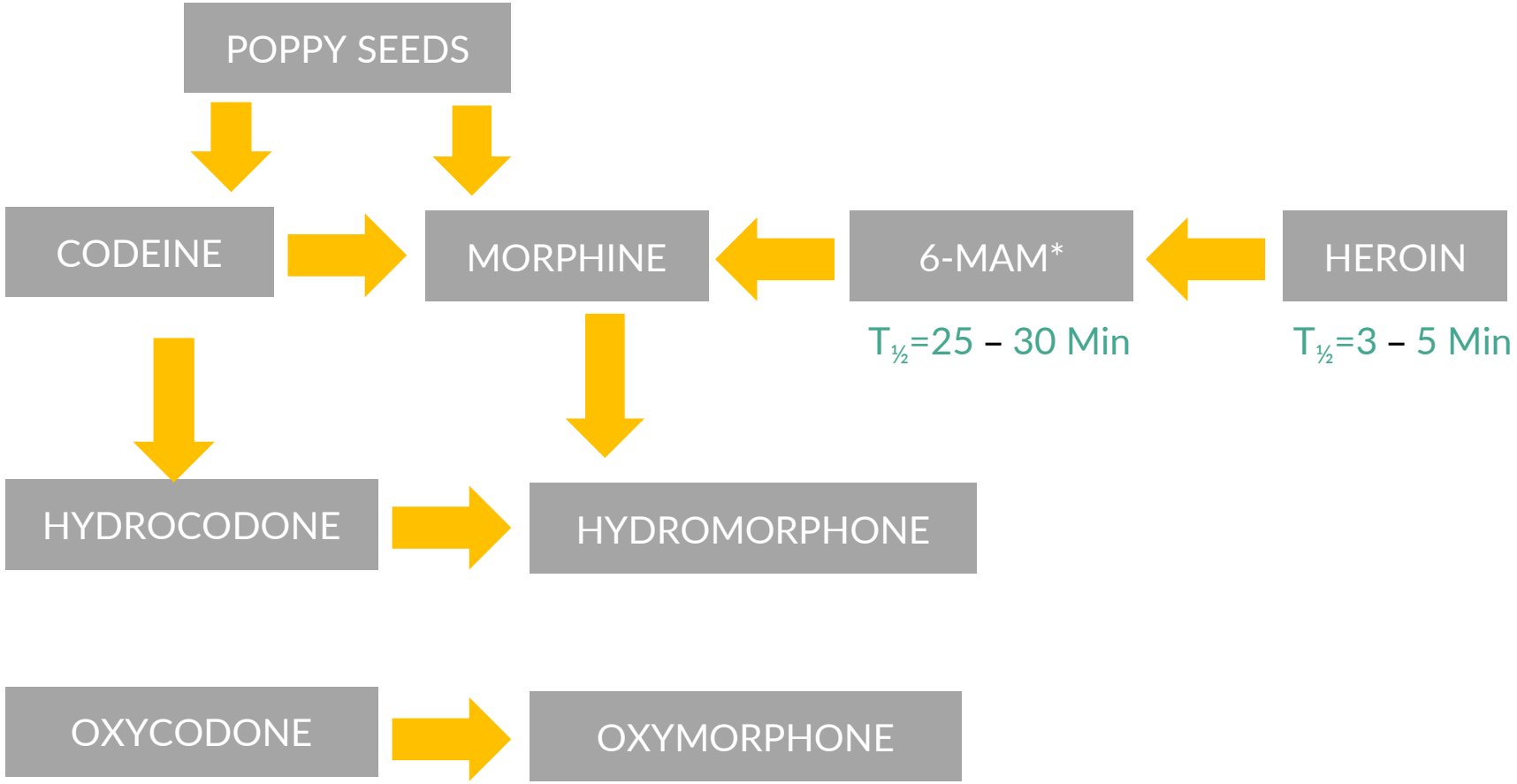
Follow CDC guidelines
methadone and buprenorphine maintained patients
-4x/day dosing
-PRN IR full opioid agonists to control pain.

Remember that oxycodone metabolizes to oxymorphone; morphine to hydromorphone, and codeine metabolizes to morphine.

Difficult to monitor with Urine drug testing

Urine drug testing

EXAMPLES OF OPIOID METABOLISM



*6-MAM=6-Monoacetylmorphine

Treating pain in patient with OUD

- Untreated pain can cause relapse-need to treat pain and OUD
- Specialist- multidisciplinary pain team
- Avoid other psychotropic medication
- Buprenorphine pain and OUD
- Use opioids that do not metabolize to other meds
- Recovery program
- Continue use all tools
- family

Medication assisted treatment (MAT)

Medication with counseling and behavioral therapies
Reduced rates of relapse
Fewer overdoses
Improved retention in treatment
Improved social functioning.

Barriers to MAT

- Only about 10% of patients with OUD receive MAT
- Lack of available prescribers and support for prescribers-limited psychiatrists
- Limits on dosages
- Authorization and reauthorization
- Minimal counseling coverage
- “fail first” criteria
- Workforce attitudes

Safety and effectiveness of MAT

- Reduces opioid-related deaths
- Keep people in treatment longer
- Help opioid-dependent pregnant women have better outcomes

MAT in primary care - obtaining the waiver

- DATA 2000 waiver
- Treat opioid addiction with Subutex and Suboxone
- 8 hours of approved training in opioid addiction
- http://www.buprenorphine.samhsa.gov.

Why become FDA-waived physician for MAT

- Improved public health
- Develop continuum of care
- Expanding currently available treatment options and increasing the overall availability of treatment.

Comprehensive addiction and recovery act

NP and PA can qualify to prescribe buprenorphine
High buprenorphine noncompliance – higher risk of relapse
Long acting buprenorphine – monthly dose developed.
Weekly subcutaneous deposit
Buprenorphine deposit

Buprenorphine

- If you use for pain- don't need a waiver
- If you use for OUD, need a waiver
- Partial mu-agonist with "plateau effect" for resp depression
- Good efficacy and safety
- FDA- approved products for pain
  - Butrans- 7 day transdermal patch
  - Belbuca – buccal mucosal film- BID

Opioid overdose

Naloxone
-opioid antagonist administered intranasally or parenterally
-Reverses acute opioid-induced respiratory depression
-may precipitate withdrawal
Safety and effectiveness

naloxone

- Displaces opioid from receptor site
- Make a plan with patient/caregiver
- Some states require co-prescribing with opioids
- Check if pharmacy dispenses

NALOXONE

What it is:

- An opioid antagonist administered intranasally (most common) or parenterally
- Reverses acute opioid-induced respiratory depression but will also reverse analgesia; may precipitate acute opioid withdrawal

What to do:

- Discuss an overdose plan with patients
- Consider offering a naloxone prescription to all patients prescribed opioids; some states *require* co-prescribing
- Involve and train family, friends, partners, and/or caregivers in the proper administration of naloxone
- Check to see if pharmacy dispenses it
- Check expiration dates and replace expired naloxone
- In the event of known or suspected overdose **call 911** and administer naloxone

Suboxone

- Combination of Naloxone and Buprenorphine
- Article on potential for buprenorphine overdose: https://bmjopen.bmj.com/content/5/5/e007629

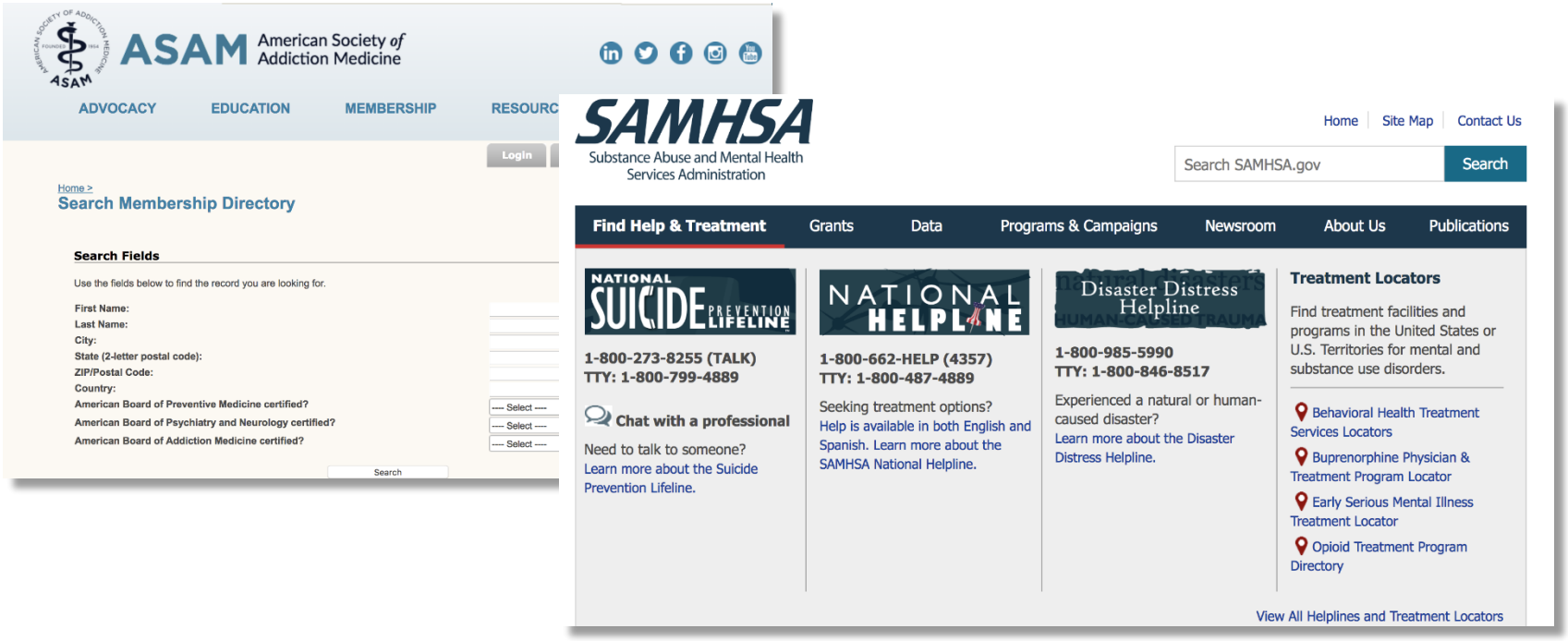
Abuse-deterrent formulation opioids

- •The FDA defines abuse-deterrent as: "those properties shown to meaningfully *deter* abuse, even if they do not fully *prevent* abuse."
- Mixed evidence on prevention misuse
- expensive

REFERRALS AND TREATMENT CENTERS

ASAM, SAMHSA, and AAAP are all helpful referral resources.

ASAM resources: https://www.asam.org/resources/resource-links
SAMHSA locator: https://findtreatment.samhsa.gov/locator
AAAP locator: https://www.aaap.org/patients/find-a-specialist/



Role of the Physician…

- To Cure Sometimes
- To Relieve Often
- To Comfort Always

Anonymous

The Death of Ivan Ilych - Tolstoy

- What tormented Ivan Ilych most was the deception, the lie . . . That he was not dying but was simply ill, and that he only need keep quiet and undergo treatment and then something very good would result.