SUBSTANCEABUSE

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PROGRAM DETAILS

- **Title:** Substance Abuse
- **Dates/Term of offering:** This activity was released on May 18, 2020 and is valid for one year. Requests for credit must be made no later than May 18, 2021.
- **Joint Providership:** This activity is jointly provided by Global Education Group and Hospice and Palliative Board Review.com.

- **Target Audience:** The educational design of this activity addresses the needs of Physicians, NPs, Nurses, and health care professionals interested in learning more about hospice and palliative medicine and those who want to earn continuing education credits and/or prepare for board certification in hospice and palliative medicine.

PROGRAM DETAILS

- **Program Overview:** Clinicians and health care professionals are unaware of best practices to be utilized when performing symptom management, related to substance abuse, for patients in the palliative and hospice care setting. As such, they do not know how to adequately manage and counsel patients on interventions utilized for symptom management.
- **Faculty:** Eric Bush, MD, RPh, MBA • **Physician Accreditation Statement:**

- This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint providership of Global Education Group (Global) and Hospice and Palliative Board Review.com. Global is accredited by the ACCME to provide continuing medical education for physicians.

PROGRAM DETAILS

- **Physician Credit Designation:**
- Global Education Group designates this enduring activity for a maximum of 0.50 *AMA PRA Category 1 Credit™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.
- **Instructions to Receive Credit:** In order to receive credit for this activity, the participant must score at least a 75% on the post quiz and submit a completed evaluation and credit application form.
- **Global Contact Information:** For information about the accreditation of this program, please contact Global at 303-395-1782 or cme@globaleducationgroup.com.
- **Fee Information:** There is a fee for this educational activity.

PROGRAM DETAILS

- **System Requirements:**
- **PC:** Microsoft Windows 2000 SE or above, Flash Player Plugin (v7.0.1.9 or greater), Internet Explorer (11.0 or greater), Chrome, Firefox, Adobe Acrobat Reader*
- **MAC:** MAC OS 10.2.8, Flash Player Plugin (v7.0.1.9 or greater,), Safari, Chrome, Adobe Acrobat Readers*, Internet Explorer is not supported on the Macintoch.

  *Required to view printable (PDF) version of the lesson.
- **Disclosure of Conflicts of Interest:** Global Education Group (Global) requires instructors, planners, managers and other individuals and their spouse/life partner who are in a position to control the content of this activity to disclose any real or apparent conflict of interest they may have as related to the content of this activity. All identified conflicts of interest are thoroughly vetted by Global for fair balance, scientific objectivity of studies mentioned in the

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materials or used as the basis for content, and appropriateness of patient care recommendations.

- **Disclosure of Conflicts of Interest (continued):** The faculty reported the following financial relationships or relationships to products or devices they or their spouse/life partner have with commercial interests related to the content of this CME activity:
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- **Lindsay Borvansky:** Nothing to disclose

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- **Andrea Funk:** Nothing to disclose
- **Liddy Knight:** Nothing to disclose
- **Disclosure of Conflicts of Interest (continued):**
- **Ashley Cann:** Nothing to disclose
- **Eric Bush:** Nothing to disclose
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applicable manufacturer's product information, and comparison with recommendations of other authorities.

LEARNING OBJECTIVES

- Describe how to perform symptom management in the palliative and hospice setting.
- Describe how to counsel patients and caregivers on interventions in this setting and the applicable risk versus benefit for appropriate interventions.
- Describe how to perform discussions of US hospice regulations with patients and family.
- Describe how to counsel patients and caregivers on US hospice regulations and appropriate care for the patient and family given current regulations.
- Describe how to discuss utilization of appropriate personnel allocation in the hospice and palliative care setting.
- Describe how to counsel patients and families on appropriate personnel allocation in the hospice and palliative care setting and the benefits for patients and families undergoing this type of care.
- Describe how to perform discussions differentiating between hospice and palliative care services with patients and family.
- Describe how to counsel patients and caregivers on differentiating between hospice and palliative care services and appropriate level of care for the patient and family given current best practice.

Methadone

Methadone: Objectives

- The Drug
- Benefits
- Risks
- Dosing
- Cardiac Toxicicity

Opioid Families

Phenanthrene Derivatives:

- Morphine
- Codeine
- Hydrocodone
- Hydromorphone
- Oxycodone

Opioid Families Continued

- Phenylpiperidine Derivatives

- Meperidine
- Fentanyl
- Diphenylheptane Derivatives
- Methadone

History: Methadone

- Myth
- Executive order from Hitler due to
- Morphine shortage
- Named after him

- Reality
- Work on long line of analgesics, antipyretics
- Need for opiate substitute
- Dolor for pain; fin for end
- Opioid abstinence programs USPHS 1950
- Methadone Maintenance 1960
- Analgesic availability 1976

Methadone

- Analgesic and plasma t1/2 differ

- Onset of 15min with peak in 1 to 2 hrs
- Analgesic t1/2 of 4 to 6 hrs
- Plasma t1/2 of ~24hrs
- Clinical implications of pk properties

Methadone-Benefits

Mu agonist, synthetic opioid:

- Has two non-opiate analgesic receptor activities:
- Prevents MAO reuptake in periaqueductal gray
- Prevents N-methyl-d-aspartate (NMDA) receptors
- Lacks neuroactive metabolites

- High bioavailability (79 +/-11 hours)
- Long half life (30 +/- 16 hours)
- Highly lipophilic
- Fecal excretion-safe in ESRD
- Very inexpensive

Methadone-Risks

- Tremendous interpatient pharmacokinetic variability
- Poorly defined equianalgesic potency

- Potentially scary dosing/safety issues
- Drug interactions-?clinical relevance
- Enigma assoc with MMT

Dosing Dilemmas

- Half life (30+/- 16 Hours)
- Recommended dosing intervals (3-24 hours)
- Duration of analgesia for a single dose (4-6 hours)
- Rapid absorption-distribution

- Accumulates in tissues-initial q4hour dosing may stretch to bid

Equianalgesic Conversions

Tables typically report IV Morphine to Methadone 1:1, Oral Morphine to methadone 3:1 or 3:2

- ***Based on single dose studies***
- Not applicable to chronic dosing

Emerging Principles for Dosing Methadone Safely

- Starting with Methadone in Opioid naïve
- Start low go slow
- Back off as drug starts to accumulate
- Beware day 5

Emerging Principles for Dosing Methadone Safely

- Converting from other opioids
- Consider dose and setting
- Behaves as much more powerful opioid the higher the dose of the prior opioid---
- ??Tolerance

Emerging Principles for Dosing

- ?? NMDA receptor antagonist

Methadone Safely

- Vigilance is necessary during drug initiation, during conversion from one opioid to another, and during dose titrtion

Emerging Principles for Dosing

- *Peak respiratory depressant effects typically occur later and persist longer than its peak analgesic effects*

Interactions

Absorption, distribution, and metabolism:

- Absorption mediated by gastric pH and Pglycoprotein (Pgp) transport protein
- Metabolized principally by CYP-3A4 and CYP-2D6 enzymes
- Cimetidine ,fluoxetine increase methadone concentrations
- Carbamazepine decreases methadone concentration

Drug Interactions with Methadone

Inhibitors – Icreased methadone plasma levels (reduced calculated methadone dose by 25%)

- Amiodarone
- Cimetidine
- Ciprofloxacin
- Erythromycin
- Clarithyromycin
- Fluconazole
- Fluoxetine
- Paroxetine
- Ketoconazole

- Ritonavir

Drug interactions with Methadone

Inducers – Decreased methadone plasma levels

- (encourage use of breakthrough medication)
- Carbamazepine
- Phenobarbital
- Phenytoin
- Primidone
- Rifampin

Interactions

Avoid opioid-antagonists or partial agonists:

- Buprenorphine
- Butorphanol
- Dezocine
- Nalbuphine
- Nalorphine
- Pentazocine -displaces methadone from mureceptors

Dosage Formulations

- Tablets: 5, 10 mg; 40 mg dispersible tablets
- Oral liquid:
- 10 mg/ml oral concentrated liquid
- 5 mg/5 ml, 10 mg/5 ml oral solution
- Injectable: 10 mg/ml injectable solution
- Available as powder for compounding

Clinical Uses

- Neuropathic pain and/or mixed nociceptive pain not responding to morphine and coanalgesic
- End-stage renal failure
- True morphine allergy
- Cost

Methadone Conversion Method #1 (EPERC)

> 2000 mg	Consult Expert
> 1001 mg	20:1
801 – 1000	15:1
601 – 800	12:1
301 – 600	10:1
101 – 300	5:1
< 100	3:1

Methods of Conversion to Methadone from other Opioids

- Morley-Makin method (6 d)
- Stop and Go method (1d)
- Ripamonti method (3d)
- Manfredi-Houde method (1d)

Clinical pearls

- Methadone safe and effective when used judiciously
- Consider when failing other opioids/difficult to control pain
- QTc issues can be concern in conjunction w/other agents affect cardiac conduction(TCA’s etc.)

More Clinical Pearls

- Cheap and safe in ESRD, caution w/ESLD
- May work better for neuropathic pain but not EBM at this time
- EPERC dosing recommended(most conservative)
- Less than 300mg DOME use 1mg po Methadone equals 10mg po morphine, >600 DOME use 1:20

Just a few more Things

- Mg for mg the most potent po opiate
- Beware accumulation on day 4 and 5
- MMT dosing is once daily vs BID/TID dosing for analgesia
- Single dose studies do NOT equivocate clinical use
- Use only as prn if dire situation
- IV methadone 2x as potent as po

Case 1

- 35 yo M with chronic LBP, works in HVAC
- On Fentanyl 75mcg TD patch and oxy ir 15 to 30mg po q6h prn pain
- Sharp stabbing pain begins in L-S spine and radiates down legs, pain w/poor control limiting fxn at work
- Start methadone 5mg po tid, add pregabalin 25mg po tid as adjuvant

Case 2

- 38 yo F with cervical CA
- On Hydromorphone PCA with basal 18mg/hr
- On gabapentin as adjuvant, pain poorly controlled, primarily neuropathic
- Start methadone PCA at basal of 9mg/hr with upward titration based on symptoms

Case 3

- 57 yo F with widely metastatic breast ca
- Actively dying on Methadone 70mg po q6h atc w/worsening pain and dysphagia
- What to do?

Summary

- Works well for bone pain, neuropathic pain, pt who have failed multiple other opiates and

refractory pain, co-morbid addictions (Etoh etc), patients with ESRD, patients who cannot afford other opiates

- Be careful of pt with OSA, sedation on day 4/5, withdrawl on day 7+,drug interactions, QTc issues, ESLD

CHRONIC OPIOID THERAPY, SUBSTANCE ABUSE, DEPRESSION AND EPIDURALS

Pain

- Pain is defined by the International Association for the Study of Pain (IASP) as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage”
- Chronic pain is defined by the IASP as “pain that persists beyond normal tissue healing time,” which is assumed to be three months
- Although the term *chronic non-cancer pain* encompasses pain associated with a wide diversity of conditions, common treatment goals, regardless of the underlying cause, are pain

relief and/or improvement in physical and psychological functioning

General Pain Classification

- **Acute pain**: Short-lasting and manifesting in objective ways that can be easily described and observed. It may be clinically associated with diaphoresis and tachycardia. It can last for several days, increasing in intensity over time (subacute pain), or it can occur intermittently (episodic or intermittent pain). Usually related to a discreet event for onset: post op, post trauma, fracture, etc.

- **Chronic pain**: Long-term and typically defined if it lasts for > three months. It is more subjective and not as easily

clinically characterized as acute pain and is more psychological. This kind of pain usually affects a person's life, changing personality, their ability to function, and their overall lifestyle.

Pain as a Public Health Challenge per IOM

- **Pain is a public health problem**
- Affects at least 116 million American adults
- Reduces quality of life
- Costs society $560–$635 billion annually
- **More consistent data on pain are needed to:**
- Monitor changes in incidence and prevalence
- Document rates of treatment and under treatment

- Assess health and societal consequences
- Evaluate impact of changes in policy, payment, and care
- **A population-based strategy is needed to reduce pain and its consequences. It should:**
- Heighten national concern about pain
- Use public health strategies to foster patient self-management
- Inform public about nature of pain

IOM Underlying Pain Principles

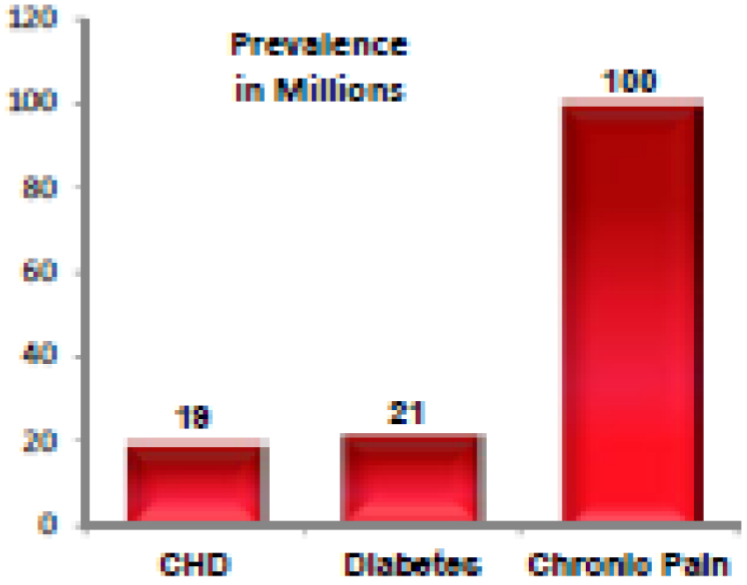
- Pain management is a moral imperative • Chronic pain can be a disease in itself
- **The value of comprehensive treatment**
- **The need for interdisciplinary approaches**

- The importance of prevention
- **Wider use of existing knowledge**
- **Recognition of the conundrum of opioids**
- Collaborative roles for patients and clinicians
- The value of a public health and community-based approach

Scope of the Problem

100 Million in U.S. with Chronic Pain

- 42% with pain lasting over one year
- 33% report pain as disabling
- 63% have seen primary care physician for help

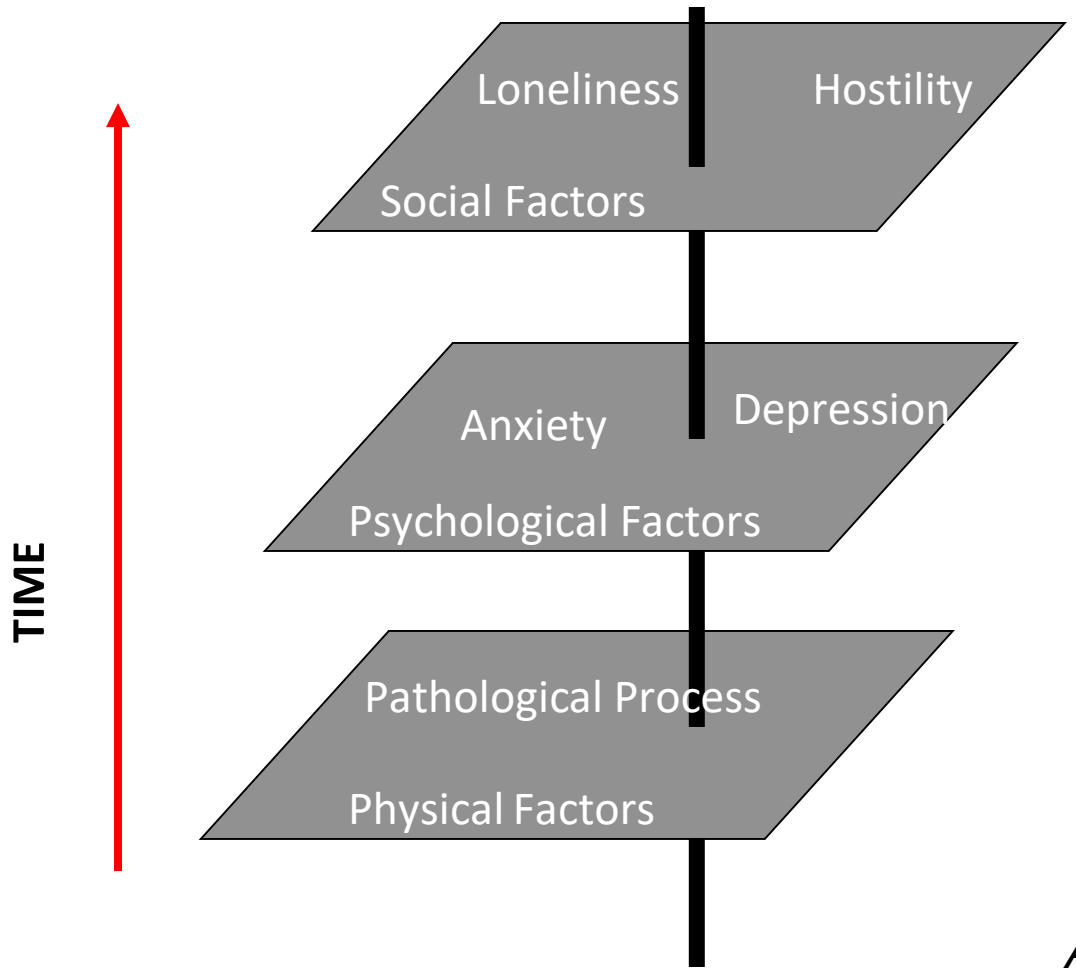


$600 Billion Annual Costs

- Healthcare expenses
- Lost income
- Lost productivity

American Academy of Pain Medicine www.painmed.org
Institute of Medicine. 2011 Relieving Pain in America. Washington DC

Dimensions of Chronic Pain



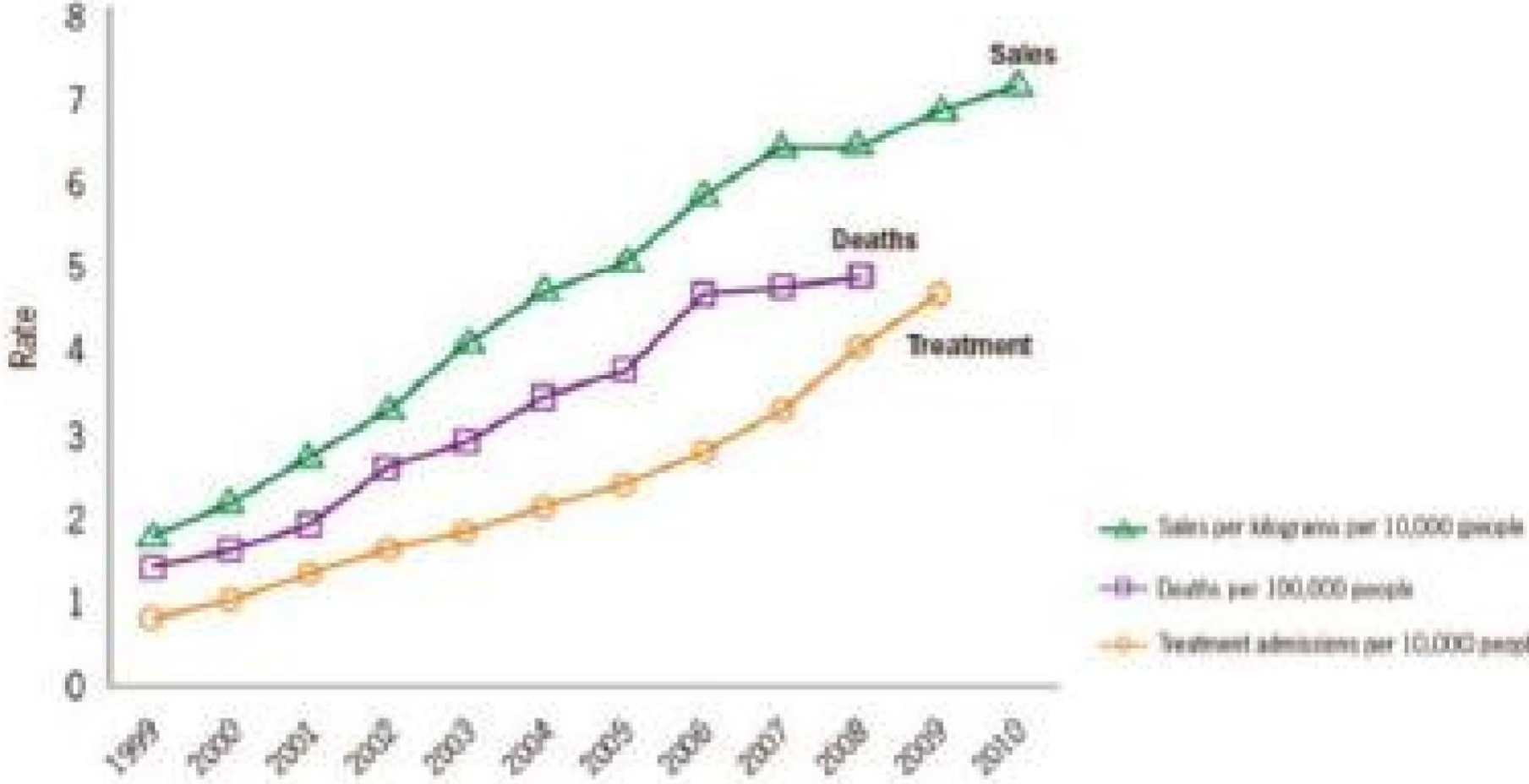
A.G. Lipman, Cancer Nursing, 2:39, 1980

Background of Opiate Use

- Opioids are drugs that exert their activity on opioid receptors. They are considered the most potent analgesics. Epidemiologic studies indicate that use of opioids for chronic non-cancer pain has increased substantially over the last two decades.
- In one large U.S. survey, the proportion of office visits for chronic musculoskeletal pain in which any opioids were prescribed doubled from 8% in 1980 to 16% in 2001.
- Use of more potent opioids (such as morphine, hydromorphone, oxycodone, and fentanyl) has also increased.

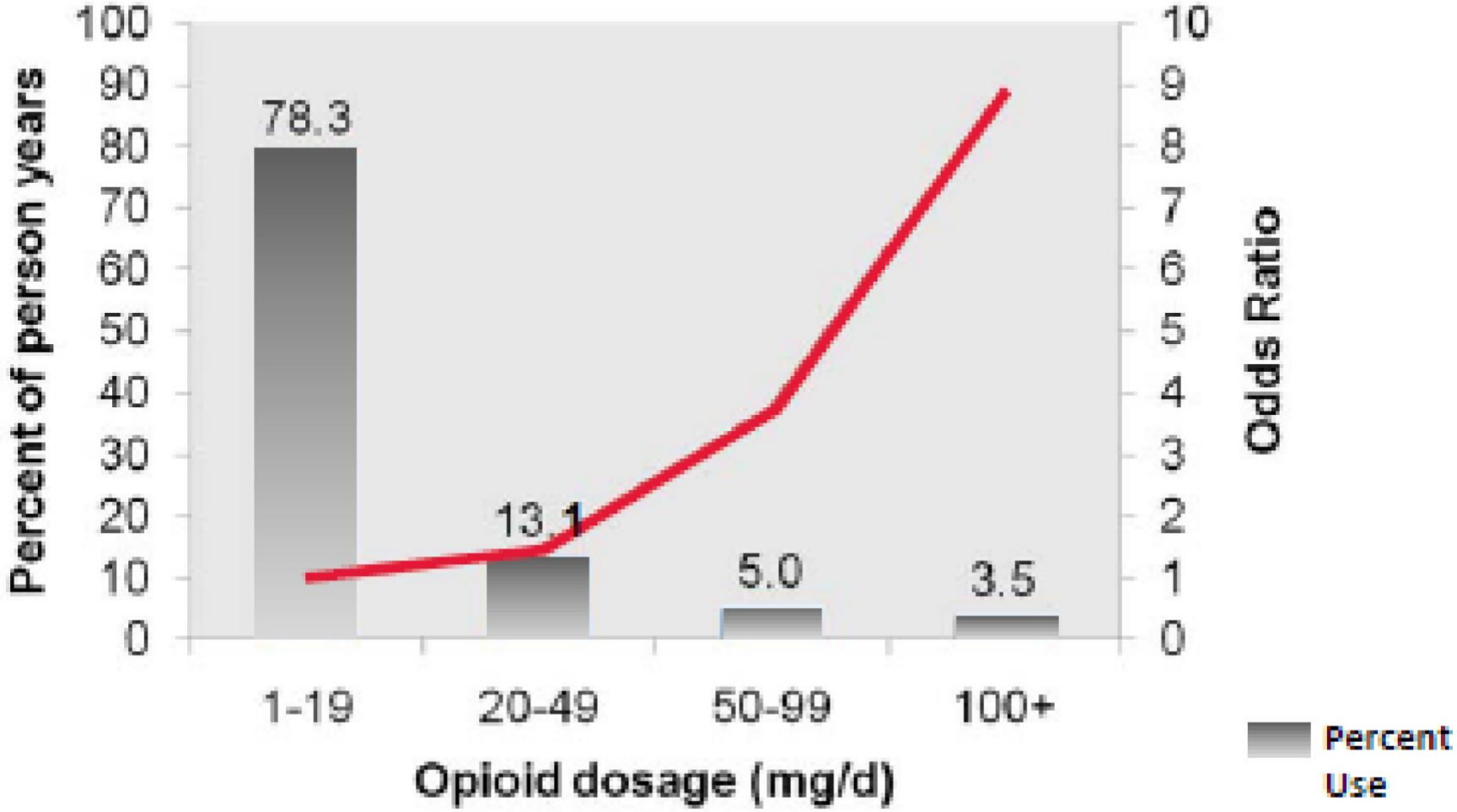
- Over the same two decades, the proportion of office visits in which prescriptions for potent opioids were given, increased from 2% to 9%.

Rates of Prescription Opioid Sales, Deaths and Substance Abuse Treatment Admissions



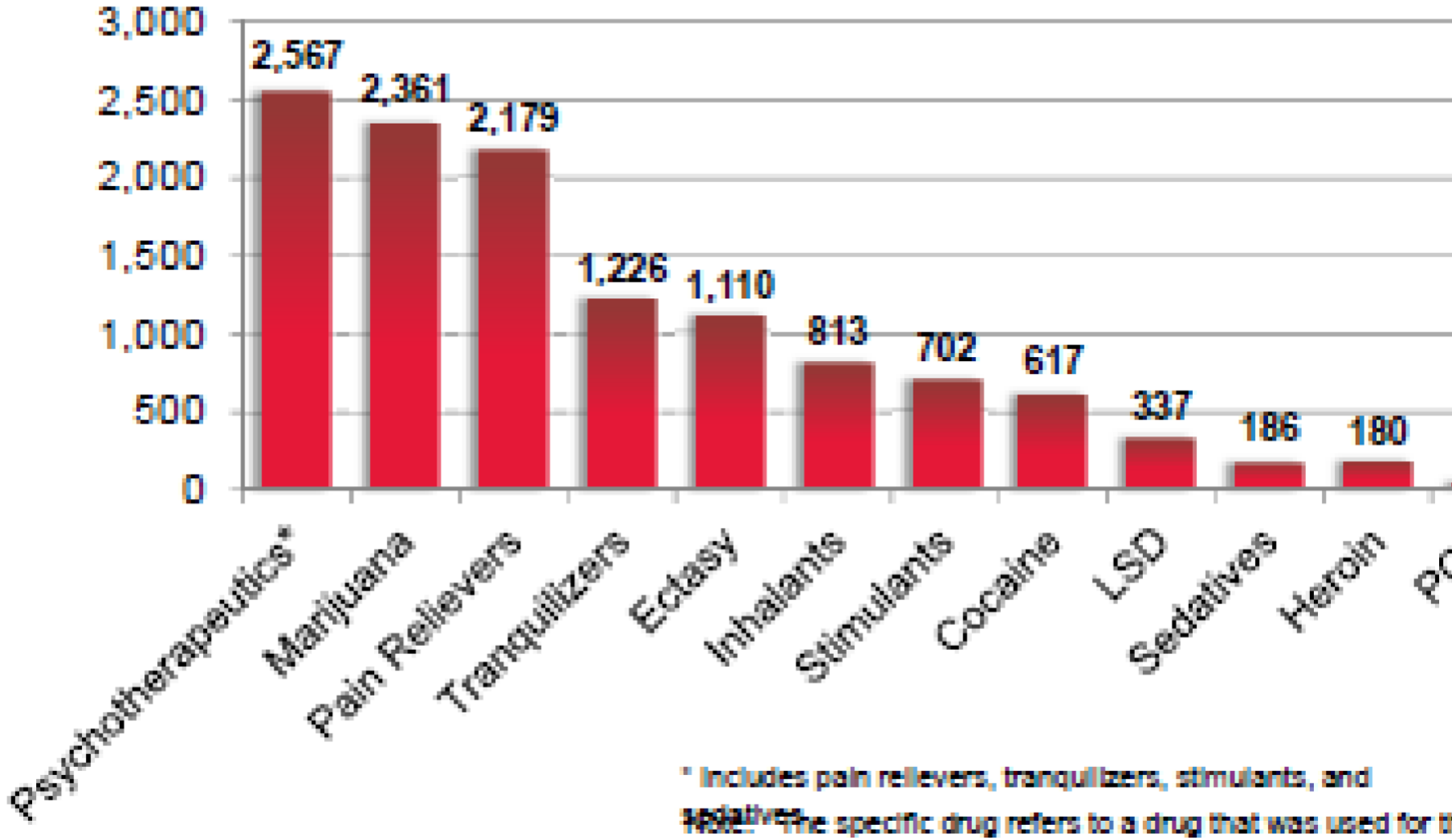
National Vital Statistics System, 1999-2006; Automation of Reports and Consolidated Orders System (ARCOS) of the Dru

Risk of Opioid Overdose



Group Health Consort Study, 1997-2005; Dunn KM, et al. Ann Intern Med. 2010 Jan 19;152(2):85-92.

New Users: Specific Illicit Drugs



* Includes pain relievers, tranquilizers, stimulants, and sedatives.

Note: The specific drug refers to a drug that was used for t

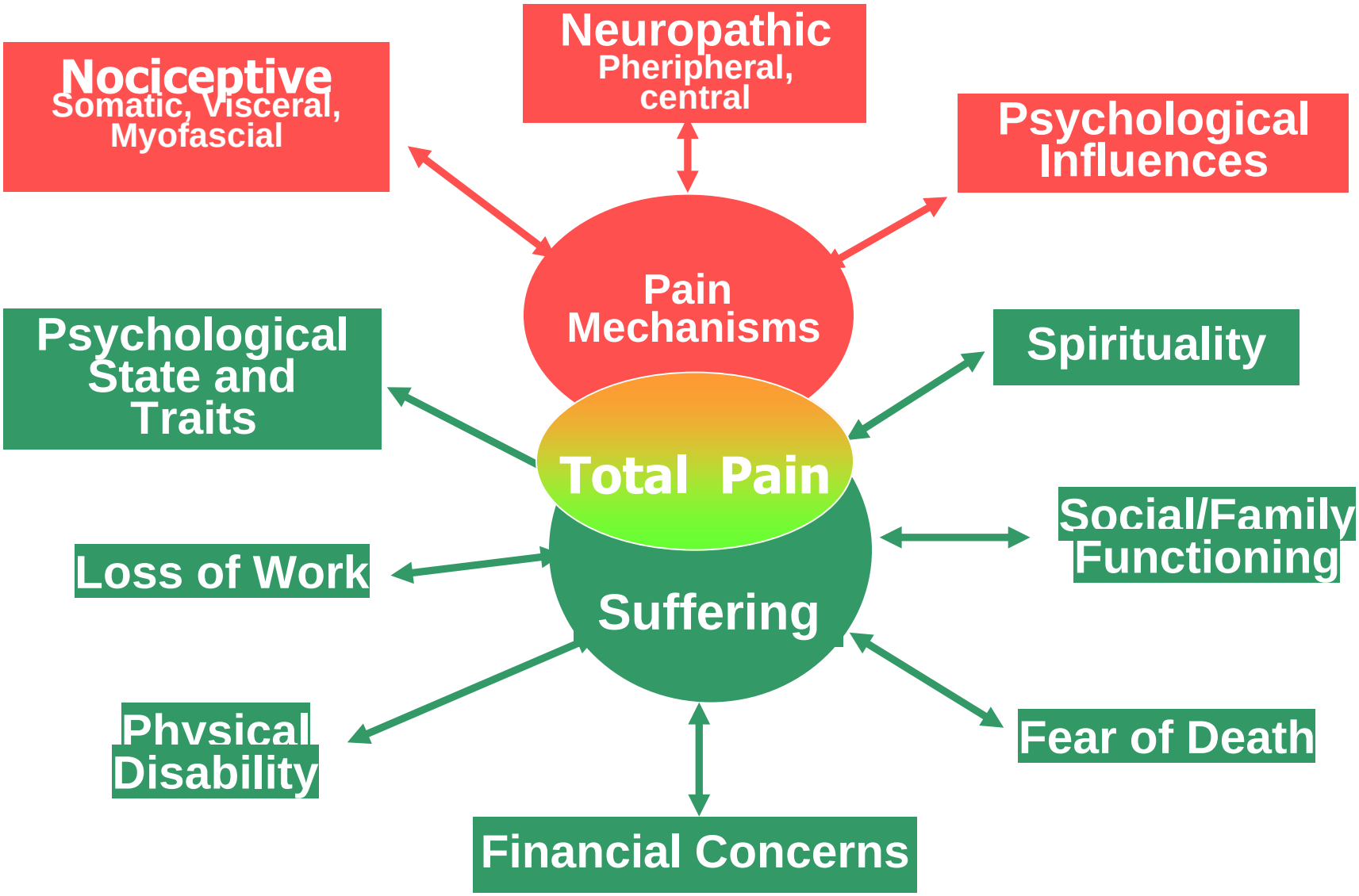
Collateral Opioid Risk

- Risks
  - Young children ingestion and overdose
  - Adolescents experimentation leading to overdose and addiction
- Mitigating risk
  - Safe storage and disposal
  - Educate family members
  - Have poison control number handy

Macro View

- Oncologic Pain: A biopsychosocial approach to pain mgmt encompassing the whole nature of suffering
- Chronic Non-Cancer Pain: Utilizing the same concepts used to manage cancer patients (chronic pain syndrome, somatoform d/o), more difficult to rationalize pain without degree of pathology noted in cancer pain
- Opioids have *NOT* been proven to restore functionality in Chronic Non-Cancer Pain (aka CNCP)

Nature of Pain


Nociceptive
Somatic, Visceral, Myofascial
Neuropathic
Pheripheral, central
Psychological Influences
Pain Mechanisms
Psychological State and Traits
Spirituality
Total Pain
Social/Family Functioning
Loss of Work
Suffering
Phvsical Disability
Fear of Death
Financial Concerns

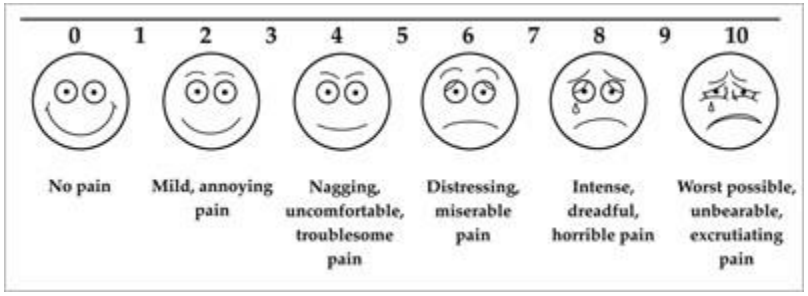
Pain Scales

- VAS
- Wong Baker Faces
- CNVI
- Functional

VAS-visual analog scale

- Validated
- Widely used
- Can over & underestimate pt pain
- Cannot differentiate between spheres of pain etiology

VAS w/Wong-Baker



Pain Assessment (Non-verbal)

CNVI Pain Scale	**w/Move**	**At rest**
• Nonverbal vocalizations:	*	*
• Facial grimaces/winces:	*	*
• Bracing:	*	*
• Restlessness:	*	*
• Rubbing:	*	*
• Vocal complaints:	*	*
• Pain score (0-12)=		

Functional Pain Scale

Functional Pain Scale-adapted from Gloth, et al:

- 0 No Pain
- 2 Tolerable (Doesn't interfere with activities)
- 4 Tolerable (Interferes with some activities)
- 6 Intolerable (Able to use phone, TV, or read)
- 8 Intolerable (Unable to use phone, TV, or read)
- 10 Intolerable (Unable to verbally communicate)

Pain Assessment: Making the Diagnosis

- Defining medical diagnosis and potential primary treatments

- Pain diagnosis is not always readily defined and may change with time
- More common pain diagnoses include: back pain, fibromyalgia, neuropathic pain, cancer-related pain
- Chronic pain itself may be considered a diagnosis that merits consideration of all available treatment options

Pain Assessment: When to Refer?

- Previous failure with opioids or other analgesics
- Significant psychosocial issues
- Conviction of a drug-related crime
- Current use of illicit drugs
- Regular contact with drug high-risk groups
- History of substance abuse

Important Definitions

- **Addiction:** A primary, chronic, neurobiologic disease, with genetic, psychosocial, and environmental factors influencing its development and manifestations. Characterized by ***aberrant behaviors*** that include one or more of the following: impaired control over drug use, compulsive use, continued use despite harm, and craving.
- **Physical Dependence:** A state of adaptation that is manifested by a drug class specific withdrawal syndrome that can be produced by abrupt cessation, rapid dose reduction, decreasing blood level of the drug, and/or administration of an antagonist.

- **Tolerance:** Tolerance is a state of adaptation in which exposure to a drug induces changes that result in a diminution of one or more of the drug's effects over time.
- **Pseudoaddiction**: A drug-seeking behavior that simulates true addiction, which occurs in patients with pain who are receiving inadequate pain medication.

Questions to Consider Before Initiating a Trial of Opioid Therapy

- What pain syndromes are appropriate for opioid analgesia?
- What patients are appropriate candidates for opioid analgesia?
- Should opioids be the first analgesic class prescribed?

- What patients are at high risk for abuse and diversion of opioids?

Alternatives to Opioid Therapy

Alternative pain management strategies:

- Adjuvant analgesics
- Nonpharmacologic modalities

- Complementary medicine

Refer complex or high-risk patients for:

- Multidisciplinary pain management

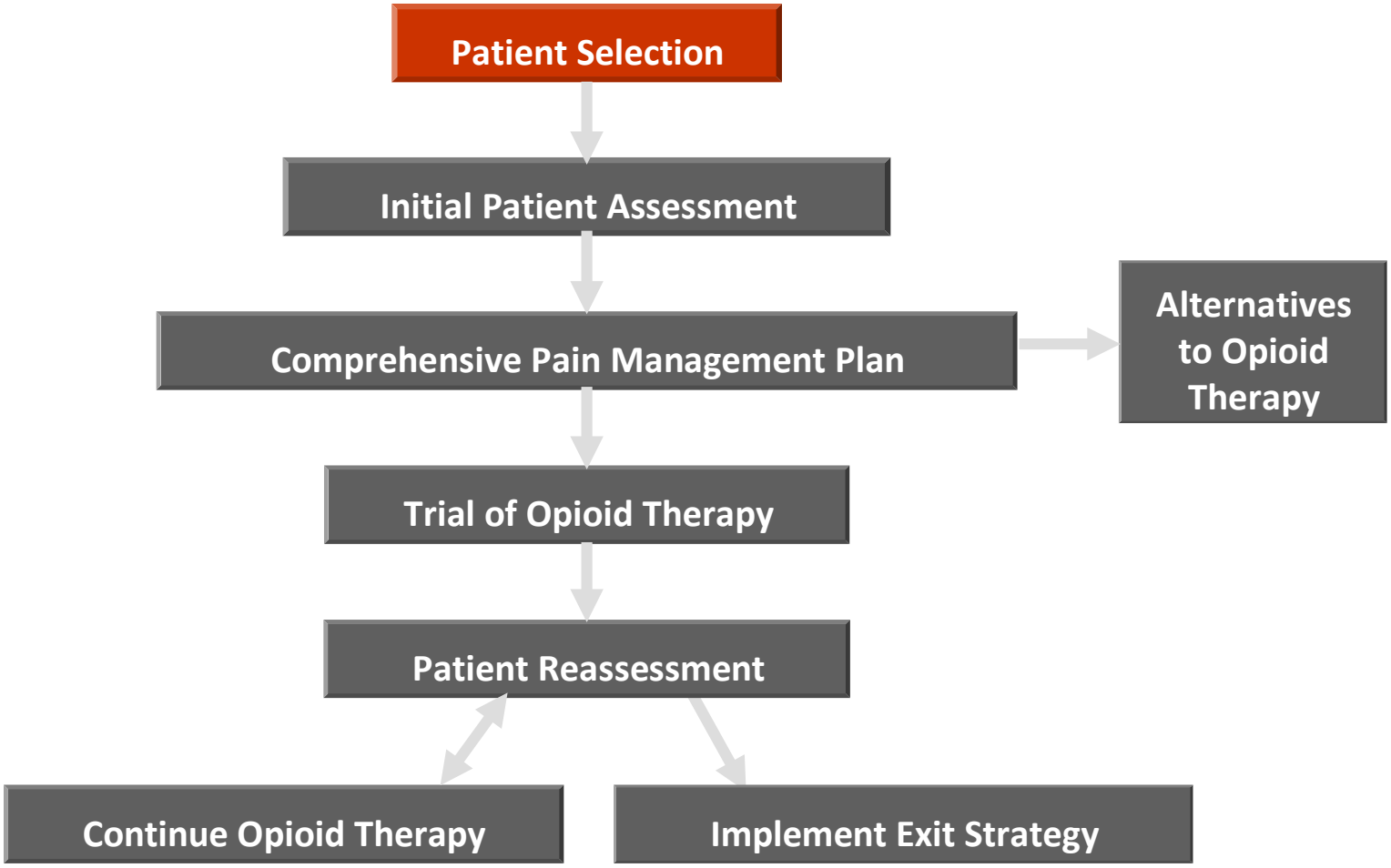
Chronic Pain Affected by Co-Morbidities

Condition	Incidence Chronic Pain Patients	References
Depression	33 - 54%	Cheatle M, Gallagher R, 2006 Dersh J, et al., 2002
Anxiety Disorders	16.5 - 50%	Knaster P, et al., 2012 Cheatle M, Gallagher R, 2006
Personality Disorders	31 - 81%	Polatin PB, et al. 1992 Fischer-Kern M, et al., 2011
PTSD	49% veterans 2% civilians	Otis, J, et al., 2010 Knaster P, et al., 2012
Substance Use Disorders	15 - 28%	Polatin PB, et al. 1992 Cheatle M, Gallagher R, 2006

Patient Selection - Who Should Be Considered for Chronic Opioid Therapy (COT)?

- Persistent pain despite reasonable trials of non-opioid analgesics and adjuvants *or*
- Severe pain requiring rapid relief *or*
- Patient characteristics contraindicate use of other analgesics

Algorithm for Opioid Treatment of Chronic Pain


Patient Selection
Initial Patient Assessment
Comprehensive Pain Management Plan
Alternatives to Opioid Therapy
Trial of Opioid Therapy
Patient Reassessment
Continue Opioid Therapy
Implement Exit Strategy

APS & AAPM Clinical Guidelines for the Use of Chronic Opioid Therapy in Chronic Non-cancer Pain

- Before initiating COT, clinicians should conduct a history, physical examination and appropriate testing, including an assessment of risk of substance abuse, misuse, or addiction (strong recommendation, low-quality evidence).
- Clinicians may consider a trial of COT as an option if CNCP is moderate or severe, pain is having an adverse impact on function or quality of life, and potential therapeutic benefits outweigh or are likely to outweigh potential harms (strong recommendation, low-quality evidence).

- A benefit-to-harm evaluation including a history, physical examination, and appropriate diagnostic testing, should be performed and documented before and on an ongoing basis during COT (strong recommendation, low-quality evidence).

Informed Consent and Opioid Management Plans

- When starting COT, informed consent should be obtained. A continuing discussion with the patient regarding COT should include goals, expectations, potential risks, and alternatives to COT (strong recommendation, low-quality evidence).

- Clinicians may consider using a written COT management plan to document patient and clinician responsibilities and expectations and assist in patient education (weak recommendation, low quality evidence).

Initiating Opioid Therapy

You've made the decision to prescribe opioid analgesics for your patient. *Now you must:*

- Consider cost, tolerability, ease of administration, compliance
- Decide whether to start a short-acting opioid analgesic or a low dose of a long-acting opioid analgesic, with or without shortacting "rescue" doses if breakthrough pain occurs

- Develop and document an Exit Strategy

Outpatient Assessment tools

- ORT
- PHQ
- SOAPP
- DAST

- ESAS-R

Opioid Risk Tool Score

		Female	Male
Family history of substance abuse			
	Alcohol	☐1	☐3
	Illegal drugs	☐2	☐3
	Prescription drugs	☐4	☐4
Personal history of substance abuse			
	Alcohol	☐3	☐3
	Illegal drugs	☐4	☐4
	Prescription drugs	☐5	☐5
Age between 16-45 years		☐1	☐1
History of preadolescent sexual abuse		☐3	☐0
Psychological disease			
	ADHD, OCD, bipolar, schizophrenia	☐2	☐2
	Depression	☐1	☐1

SCORING
0-3 Low Risk
4-7 Moderate Risk
>8 High Risk

Webster LR, Webster RM. Pain Med. 2005 Nov-Dec;6(6):432-42.

Comprehensive Pain Management Plan Components

Bio/Physical Approaches:

- Pharmacologic and/or nonpharmacologic therapies
- Physical rehabilitation
- Physical/ occupational therapy

Psychological Intervention:

- Mood disturbances
- Coping skills
- Sleep disturbance

Social Issues:

- Family/social relations
- Work issues

- Home exercise program

Depression - Common in Palliative Care, Complicates Safe, Effective Pain Management

- Prevalence 15 to 50%
- Screen - Ask are you depressed? Thoughts of harming yourself? Thoughts of harming someone else?
- Gauge - use ESAS-R other validated tools to assess
- Exacerbates pain and vice versa

- Pharmacotherapy - SSRI, SNRI, Atypical antipsychotics
- SNRI good 1st line in pt with co-morbid pain & depression
- Ego - syntonic supportive counseling important
- Screen for Axis 2 disorders and impact on care
- Co-manage with psych if complexity necessitates
- Utilize Pall Care SW for ongoing support, goals,
- Eval positive coping influences(pt social network, faith, etc)

Depression & Mental Hlth Screening Tools

- **Children (Screen for Child Anxiety Related Disorders): SCARED**
- **Depression (Patient Health Questionnaire: 9 - (PHQ-9)**

- **Generalized Anxiety Disorder (GAD):** Over the last several months, have you been continually worried or anxious about a number of events or activities in your daily life?
- **Panic:** Do you currently have times when you feel a sudden rush of intense fear or discomfort?
- **PTSD:** Over the last several months, have you been continually worried or anxious about a number of events or activities in your daily life?

Therapy for Anxiety & Depression

- Treat exacerbating factors/symptoms(pain, dyspnea, etc.)
- Supportive counseling

- Avoid benzodiazepines when possible
- Tailor pharmacotherapy to minimize drug interactions and optimize co-morbid symptom mgmt (ie; ssri vs snri vs atypical antipsychotic)
- Utilize existing social networks, faith based supports
- Optimize healthcare (SW support, psych referral, etc.)

Initiation and Titration of COT

- Clinicians and patients should regard initial treatment with opioids as a therapeutic trial to determine whether COT is appropriate (strong recommendation, low-quality evidence).
- Opioid selection, initial dosing, and titration should be individualized according to the patient's health status, previous

exposure to opioids, attainment of therapeutic goals, and predicted or observed harms (strong recommendation, lowquality evidence).

- There is insufficient evidence to recommend short acting versus long-acting opioids, or as-needed versus around-theclock dosing of opioids.

Equianalgesic Opioid Dosing

Drug	Equianalgesic Doses (mg)	
	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

*Not available in the US

Patient Reassessment Model

The "Four A's of Pain"

- Analgesia
- Activities of daily living
- Adverse effects
- Aberrant drug-taking behaviors

Important to remember two other “A’s”

- Assessment
- Action (treatment plan)

Questions to Consider In Modifying a Trial of Opioid Therapy

- When should opioid dose be raised?
- When should a different opioid be tried?
- What factors guide the choice of a second opioid?
- How reliable are urine screenings?

Deciding to Convert From a Short-acting to a Long-acting Opioid

	Short-acting Opioids	Long-acting Opioids
Advantages	Fast-acting; appropriate for acute pain, breakthrough pain	May be more appropriate for patients with a constant pain component; analgesic stability
Disadvantages	Need for repetitive dosing	Initial delayed onset of action

Rationale for Opioid Rotation

- Ineffectiveness of initial opioid
- Adverse effects/toxicity of initial opioid
- Inter-patient variability of response
- Incomplete cross-tolerance

Note: Conservative dose-conversion ratios are advised

Management of Opioid Side Effects

Side Effects	Amelioration
• Nausea and vomiting	• Switch opioids; anti-emetics
• Sedation	• Lower dose (if possible); add co-analgesics; add stimulants

• **Constipation**	• **Treat prophylactically with stool softeners, bowel stimulants; non-pharmacological measures; switch opioids**

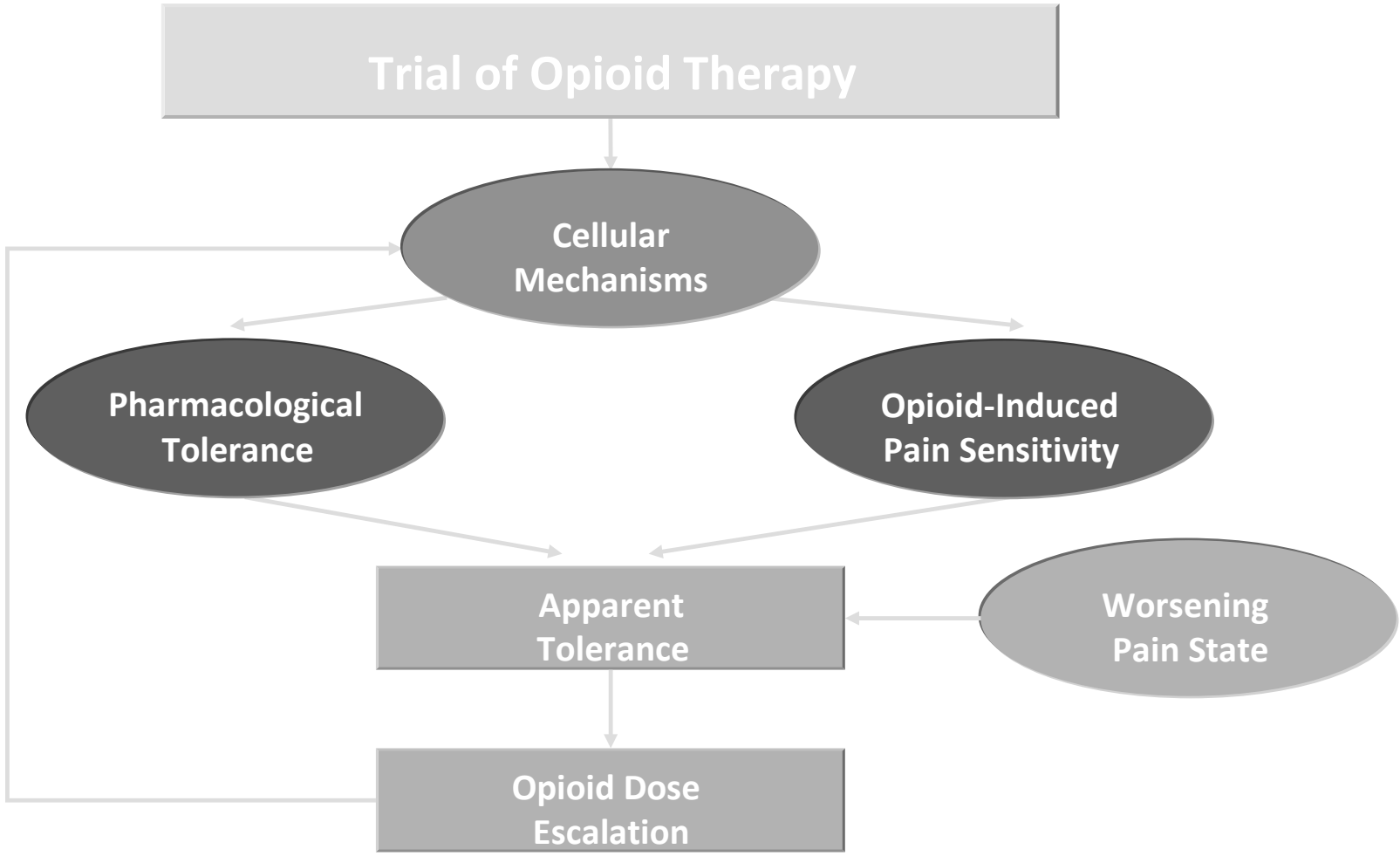
Management of Opioid Side Effects

(cont'd)

Side Effects	Amelioration
• **Itching**	• **Switch opioids; antihistamines**

• Endocrine dysfunction/ reduced libido	• Endocrine monitoring; testosterone replacement; endocrine consultation
• Edema and sweating	• Switch opioids
• Dizziness	• Antivertiginous agents (eg, scopolamine)
• Confusion	• Titrate dose; switch opioids

Development of Tolerance



Risk factors for Abuse/Misuse

- Leaving AMA
- Repeated ER admissions
- Multiple prescribers
- Mental health- self or family
- Chronic pain
- Trauma or abuse history
- Living in poverty
- High risk populations

Considerations For Patients Who May Benefit From Opioid Therapy w/prior Substance Abuse/misuse

- What are you treating? “Total pain” ?
- How long will you need to prescribe for? Is the Rx for a long term palliative trajectory, (eg; dyspnea with COPD), EOL or temporary relief of a symptom?
- What are the patients goals or concerns related to substance use disorders, personal risk or recovery?
- Can adjuvants be utilized? Is there an interdisciplinary plan for the patient’s care?

- Are the goals truly palliative?
- What is the risk vs benefit? Does the good outweigh the harms?

COWS Clinical Opiate Withdrawal Scale

Wesson & Ling, J Psychoactive Drugs. 2003 Apr-Jun;35(2):253-9.

Resting Pulse Rate: _____beats/minute *Measured after patient is sitting or lying 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	GI Upset: *over last 1/2 hour* 0 No GI symptoms 1 Stomach cramps 2 Nausea or loose stool 3 Vomiting or diarrhea 5 Multiple episodes of diarrhea or vomiting
Sweating: *over past 1/2 hour not accounted for by room temperature or patient activity.* 0 No report of chills or flushing 1 Subjective report of chills or flushing 2 Flushed or observable moistness on face 3 Beads of sweat *on* brow or face 4 Sweat streaming off face	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
Restlessness *Observation during assessment* 0 Able to sit still 1 Reports difficulty sifting still, but is able to do so 3 Frequent shifting or extraneous movements of legs/arms 5 Unable to sit still for more than a few seconds	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
Pupil size 0 Pupils pinned or normal size for room light 1 Pupils possibly larger than normal for room light 2 Pupils moderately dilated 5 Pupils so dilated that only the rim of the iris is visible	Anxiety or irritability 0 None 1 Patient reports increasing irritability or anxiousness 2 Patient obviously irritable anxious 4 Patient so irritable or anxious that participation in the assessment is difficult
Bone or Joint aches *If patient was having pain previously, only the additional component attributed to opiates 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	Gooseflesh skin 0 Skin is smooth 3 Piloerrection of skin can be felt or hairs standing up on arms 5 Prominent piloerrection
Runny nose or tearing *Not accounted for by cold symptoms or allergies* 0 Not present 1 Nasal stuffiness or unusually moist eyes 2 Nose running or tearing 4 Nose constantly running or tears streaming down cheeks	Total Score _____ The total score is the sum of all 11 items Initials of person completing Assessment:_____

Score: 5-12 mild; 13-24 moderate; 25-36 moderately severe; more than 36 = severe withdrawal

Buprenorphine

Buprenorphine and buprenorphine/naloxone (sublingual)

- Any physician with a special "X" number issued by the DEA can prescribe. The way the law is written, any doctor can prescribe buprenorphine for treating pain, however the FDA has not granted approval for buprenorphine + naloxone to be used for pain, so it would be an off-label prescription.
- However there exists other restrictions for those who want to prescribe it for opioid addiction treatment (what the FDA approved it for).
- Doctors must take an 8-hour class on addiction treatment, or already possess such credentials, and then apply for a special

DEA#. Once they obtain their # they are limited to treating only 30 patients at a time.

Methadone for Maintenance

- See other sections for reference on methadone pharmacology
- Methadone Maintenance is once daily (can only be prescribed by authorized MMT (Methadone Maintenance Therapy) prescriber/clinic/practice
- MMT dose has risen over last several decades correlating w/increased purity of heroin coming into the country
- Coordinate care with MMT prescriber when applicable
- What are goals with MMT patient? (Palliative to hospice? Terminal vs non-terminal process)

- Utilize interdisciplinary care whenever possible

Alcohol Misuse/Abuse/Dependence

- Very often co-morbid anxiety & depression (treat optimally)
- Supportive counseling
- AA & other support programs
- Pharmacologic and non-pharmacologic interventions (acamprosate, disulfiram, naltrexone, abstinence programs & psychosocial support)

Monitoring

- Clinicians should reassess patients on COT periodically and as warranted by changing circumstances. Monitoring should

include documentation of pain intensity and level of functioning, assessments of progress toward achieving therapeutic goals, presence of adverse events, and adherence to prescribed therapies (strong recommendation, low quality evidence).

- In patients on COT who are at high risk or who have engaged in aberrant drug-related behaviors, clinicians should periodically obtain urine drug screens or other information to confirm adherence to the COT plan of care (strong recommendation, low-quality evidence).

Monitoring (Continued)

In patients on COT not at high risk and not known to have engaged in aberrant drug-related behaviors, clinicians should consider periodically obtaining urine drug screens or other information to confirm adherence to the COT plan of care (weak recommendation, low-quality evidence).

High-Risk Patients

- Clinicians may consider COT for patients with CNCP and history of drug abuse, psychiatric issues, or serious aberrant drugrelated behaviors only if they are able to implement more

frequent and stringent monitoring parameters. In such situations, clinicians should strongly consider consultation with a mental health or addiction specialist (strong recommendation, low-quality evidence).

- Clinicians should evaluate patients engaging in aberrant drugrelated behaviors for appropriateness of COT or need for restructuring of therapy, referral for assistance in management, or discontinuation of COT (strong recommendation, low quality evidence).

Dose Escalations, High-Dose Opioid Therapy, Opioid Rotation, and Indications for Discontinuation of

Therapy

- When repeated dose escalations occur in patients on COT, clinicians should evaluate potential causes and reassess benefits relative to harms (strong recommendation, low-quality evidence).
- In patients who require relatively high doses of COT, clinicians should evaluate for unique opioid-related adverse effects, changes in health status, and adherence to the COT treatment plan on an ongoing basis, and consider more frequent followup visits (strong recommendation, low quality evidence).

Dose Escalations, High-Dose Opioid Therapy, Opioid Rotation, and Indications for Discontinuation of Therapy, cont.

- Clinicians should consider opioid rotation when patients on COT experience intolerable adverse effects or inadequate benefit despite dose increases (weak recommendation, lowquality evidence).
- Clinicians should taper or wean patients off of COT who engage in repeated aberrant drug-related behaviors or drug abuse/diversion, experience no progress toward meeting

therapeutic goals, or experience intolerable adverse effects (strong recommendation, low-quality evidence).

Opiate Related Adverse Effects

Clinicians should anticipate, identify, and treat common opioidassociated adverse effects (strong recommendation, moderatequality evidence).

Psychotherapeutic Interventions

As CNCP is often a complex biopsychosocial condition, clinicians who prescribe COT should routinely integrate psychotherapeutic interventions, functional restoration, interdisciplinary therapy, and other adjunctive non-opioid therapies (strong recommendation, moderate-quality evidence).

Driving & Work Safety

Clinicians should counsel patients on COT about transient or lasting cognitive impairment that may affect driving and work safety. Patients should be counseled not to drive or engage in potentially dangerous activities when impaired or if they

describe or demonstrate signs of impairment (strong recommendation, low-quality evidence).

Role of Consultation

- Patients on COT should identify a clinician who accepts primary responsibility for their overall medical care. This clinician may or may not prescribe COT, but should coordinate consultation and communication among all clinicians involved in the patient's care (strong recommendation, low-quality evidence).
- Clinicians should pursue consultation, including interdisciplinary pain management, when patients with CNCP may benefit from additional skills or resources that they

cannot provide (strong recommendation, moderate-quality evidence).

Breakthrough Pain

In patients on around-the-clock COT with breakthrough pain, clinicians may consider as-needed, opioids based upon an initial and ongoing analysis of therapeutic benefit versus risk (weak recommendation, low-quality evidence).

Opiates in Pregnancy

Clinicians should counsel women of childbearing potential about the risks and benefits of COT during pregnancy and after delivery. Clinicians should encourage minimal or no use of COT during pregnancy, unless potential benefits outweigh risks. If COT is used during pregnancy, clinicians should be prepared to anticipate and manage risks to the patient and newborn (strong recommendation, low-quality evidence).

Opioid Policies

- Clinicians should be aware of current federal and state laws, regulatory guidelines, and policy statements that govern the

medical use of COT for CNCP (strong recommendation, lowquality evidence).

- REMS: Risk Evaluation and Mitigation Strategy-The Food and Drug Administration Amendments Act of 2007 gave FDA the authority to require a Risk Evaluation and Mitigation Strategy (REMS) from manufacturers to ensure that the benefits of a drug or biological product outweigh its risks (includes Buprenorphine Transmuscosal Products for Opioid Dependence & Transmucosal Immediate-Release Fentanyl).

Regulatory Issues

- Risk of regulatory censure low if procedures are followed and documented

- Relevant regulations include:
- Federal (DEA)
- State policies
- Useful model guideline from Federation of State Medical Boards. Available at: www.fsmb.org

Summary: Ground Rules for Prescribing Opioid Analgesics

- Be safe
- Know your meds (physician know thyself)
- Carefully evaluate risk/benefit in an ongoing manner
- Know pt and co-morbidities/meds (benzos, etc.)
- If you do not feel comfortable refer pt
- Use resources CRISP, UDS, contracts
- Make this a partnership with your pt and families

Case Based Questions

- **CASE ONE:** ST is a 44 yo M with a long H/O chronic pain secondary to DDD of the L-S spine and coagulopathy with intermittent hematuria with painful passage of clots. He continues to work full-time as a welder(20+years). He is on Oxycodone Extended Release 30mg po bid and oxy ir 15mg po q4h prn for pain. He is also on Venlafaxine, pregabalin, methocarbamol and alprazolam. He has co-morbid depression and anxiety and recently began self-titrating his analgesics, he is rating is pain constantly as 7/10, and has called twice in the last several weeks for early refills. There is a h/o sexual abuse as a child and he has a personal h/o previous alcohol

"problems" but has been abstinent for the last four years (his father had a h/o EtOH abuse), he denies illicit or IVDU. Please answer the following five questions based on this scenario.

Question One (Based on Case One)

Which of the following is true:

A) He is low risk based on the ORT
B) He is moderate risk based on the ORT
C) He is high risk based on the ORT
D) It is impossible to attempt to stratify his risk
E) There is no risk in prescribing opioid therapy

ANSWER IS CHOICE C

Question Two (Based on Case One)

Which of the following is true:

A) The ORT is the best tool for opioid risk stratification

B) The SOAPP is the best tool for opioid risk stratification

C) Screening tools are never helpful for opioid risk stratification

D) No one screening tool has been proven superior to another for opioid risk stratification

ANSWER IS CHOICE D

Question Three (Based on Case One)

Which is the most correct answer:

A) A pain contract may be helpful in this case
B) UDS (urine drug screens)may be helpful in this case
C) The patient should be discharged immediately
D) He may benefit from psychiatric support
E) A, B, and D are correct
F) All the above are true

ANSWER IS CHOICE E

Question Four (Based on Case One)

Which is the most correct answer:

A) The patient has opioid dependence
B) The patient has “no reason” to have chronic painC) The patient may benefit from buprenorphine/buprenorphine+naloxone therapy
D) The patient should be allowed to continue to self-titrate his oxycodone
E) All the above are correct
F) A,B and C are correct
G) A and C are correct

ANSWER IS CHOICE G

Question Five (Based on Case One)

Which is the most correct answer:

A) The patient is not functional

B) Referral to a pain specialist is reasonable

C) Depression is often a co-morbidity with chronic pain

D) Optimizing non-narcotic adjuvant analgesics and other modalities of pain control (ie interventions,PT etc) are an important part of pain relief

E) B,C and D are true

F) All the above are trueANSWER IS CHOICE E

Case Two

PS is a 77 yo F with long h/o chronic back pain, chronic vertebral fractures, advanced COPD (felt not to be candidate for kypho/vertebroplasty by her pulmonologist), CKD stage 4, depression (failed multiple SSRI/SNRI), anxiety (on diazepam 5mg po tid prn), she ambulates with wide-based antalgic gait with utilization of a cane (at her baseline), on hydromorphone 4mg po q4h prn (the patient previously was on morphine but developed myoclonus), her pain is “manageable” with her current medications (rates 6/10), she is always compliant with her office visits and shows no signs of aberrant behaviors, she is the full-time caregiver for her husband at home (advanced dementia).

Please answer the next five questions based on her case.

Question Six (Based on Case Two)

Which is the most correct answer:

A) There is high value in doing UDS(urine drug screen) regularly on this pt

B)The patient's hydromorphone should be discontinued immediately given her COPD

C)The patient is at higher risk for sudden death given concomitant utilization of benzodiazepines

D) The patient is a good candidate for NSAID'S

ANSWER IS CHOICE C

Question Seven (Based on Case Two)

Which is the most correct answer:

A) The patient could benefit from psychiatric care
B) Optimizing functionality should be the goal for this pt
C) The patient requires referral to an addiction specialist
D) A and B true
E) All the above are true

ANSWER IS CHOICE D

Question Eight (Based on Case Two)

Which is the most correct answer:

A)Other modalities of pain management (non-narcotics, nonpharmacologic) interventions should continue to be discussed with the patient

B)The patient's anxiety and depression are likely contributing to her perception of pain

C)The patient's medications should be adjusted until her pain is a zero

D) The patient may benefit from referral to a pain specialist

E) A,B,C are true

F) A,B,D are true

G) All the above are trueANSWER IS CHOICE F

Question Nine (Based on Case Two)

Which is the most correct answer:

A) Myoclonus can be a side effect of any opiate
B) Opioid rotation may be beneficial in mitigating side effects, optimizing analgesia
C) Patients become tolerant to all opiate side effects eventually
D) Bowel regimens should only be considered once the patient is constipated
E) B, C, D are true
F) All the above are true
G) A and B are true

ANSWER IS CHOICE G

Question Ten (Based on Case Two)

Which is the most correct answer:

A) CRISP can be of value in monitoring pt meds

B) Building relationship with pt and family can be helpful in achieving goal of optimizing functionality

C) Goal for chronic opiate therapy patients should be zero pain

D) Development of opiate tolerance often signals addiction

E) Patients should be carefully evaluated prior to opiate therapy initiation

F) A, B, C are correct

G) All the above are true

H) A, B, E are correct

ANSWER IS CHOICE H

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- N Engl J Med. 2019 Jan 3;380(1):71-79

Appendix

Methadone - Pg 15: Notes

I want to call your attention to methadone. Methadone has garnered the reputation of being the opioid of choice for neuropathic pain because not only is it an opioid that works at all of the receptors, it's also a serotonin reuptake inhibitor and an NMDA blocker. So theoretically, this ought to be a good drug for neuropathic pain.

Pain Assessment: Making the Diagnosis – Pg 57: Notes

- Nociceptive, inflammatory, and neuropathic pain may result from diverse mechanisms. Some of these mechanisms are unique to one painful condition; others are present in multiple clinical syndromes, or may be expressed at different times during the natural history of a syndrome. The same symptom (eg, pain in response to light touching of the skin) may be generated by a number of mechanisms; or a single mechanism (eg, upregulation of a voltagegated sodium channel) may potentially produce different symptoms—such as spontaneous burning pain, shock-like pain, or paresthesias.

- Structural alterations in the synaptic contacts of low-threshold afferents with pain transmission neurons, or a reduction of inhibitory mechanisms due to a loss of interneurons, may represent persistent changes in the central nervous system that eventually result in a fixed state of sensitization.
- Back pain is ubiquitous and probably plagues almost everyone in all cultures and ethnic groups at some time. While it may be that precise estimates of the prevalence of neuropathic pain are not readily available, chronic neuropathic pain may be much more common than has been generally appreciated and can be expected to increase in the future. Moreover, neuropathic pain is highly prevalent in patients with cancer. Chronic widespread pain, the cardinal symptom of fibromyalgia, is common in the general population, with comparable prevalence rates of 7.3% to 12.9% across different countries.
- Effective management of chronic pain has become an increasingly critical issue in health care. Studies have shown that chronic pain is a common, persistent problem in the community, with relatively high incidence and low recovery rates.

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Pain Assessment: When to Refer? Pg58: Notes

- The effective management of pain may require a multidisciplinary approach. Previous studies have suggested that around 8% of cancer patients will require interventional techniques from an anesthesiologist with special interest in pain management to maximize pain control.

- An interesting epidemiologic study by Crook et al, compared two groups of individuals with self-reported persistent pain complaints. One group was drawn randomly from a typical family medical group practice and the other was drawn from a specialized multidisciplinary pain clinic. The two groups were similar in most demographic variables, the length of the pain history, and the most commonly reported sites of pain. However, patients from the pain clinic were more likely to have had work-related accidents, to report greater healthcare utilization, and to complain of more constant pain and greater levels of disability. Patients from the pain clinic reported greater impairment on the indices constructed to measure psychologic, social, and performance consequences of the pain experience. What most distinguished patients from the pain clinic was not medical factors alone, but reported impairment in function, and psychosocial difficulties. The implications are that patients referred to specialized pain clinics may not be representative of individuals in general who suffer persistent pain; the former likely require an interdisciplinary approach that includes attention to psychosocial and disability issues, not just medical or surgical treatments for pain.

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Alternatives to Opioid Therapy -Pg61: Notes

- Alternatives to opioids for persistent pain
- Anticonvulsants
- Tricyclic antidepressants
- Topical medications
- Adjuvant analgesics
- Acetaminophen
- Ketamine
- Interventional treatments
- Neural blockade
- Stimulatory techniques (spinal cord stimulation; peripheral nerve stimulation)
- Nonpharmacological therapies
- Biofeedback
- Relaxation therapy
- Cognitive/behavioral strategies
- Acupuncture

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Patient Selection -Who Should Be Considered for Chronic Opioid Therapy (COT)? Pg63: Notes

- Opioids are an important class of therapeutic agents used to manage chronic pain.
- Opioids are generally recommended to reduce the level of moderate to severe pain.
- Opioids should be considered if reasonable, conservative therapy has been tried and has not been found to provide adequate relief.
- Nonopioid analgesics include acetaminophen and nonsteroidal anti-inflammatory drugs (nonselective agents and selective COX-2 inhibitors).
- Adjuvants include specific medications for neuropathic pain (antidepressants, anticonvulsants, miscellaneous agents), specific medications for cancer-related pain (bisphosphonates, radioisotopes, steroids), and medications for bowel spasms.

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Algorithm for Opioid Treatment of Chronic Pain – Pg 64: Notes

- This algorithm has been created to assist in decision making about opioid therapy for chronic pain. This algorithm will be repeated throughout this module at each point at which a decision is to be made. Not only is the participant guided through patient selection and assessment, but also is shown what to consider in starting a trial of opioids, alternatives to opioid therapy, ongoing reassessment, developing an exit strategy, as well as conversion and rotation as part of the treatment strategy.
- The participant will be guided through the algorithm using highlighted text and arrows to identify decision points; then each part of the algorithm will be expanded upon in each section that follows.
- The first section to be discussed is Patient Selection.

Initiating Opioid Therapy – Pg 67: Notes

- For moderate to severe pain unresponsive to nonopioid analgesia, the WHO ladder recommends “weak” opioids such as codeine or meperidine. Meperidine, however, is more likely to be restricted to breakthrough pain; although it is fast-acting, chronic use is

contraindicated because of its conversion to the toxic metabolite normeperidine, which may cause seizures.

- For refractory severe pain, the WHO ladder recommends “strong” opioids such as morphine, oxycodone, hydromorphone, or methadone.

- Dalton JA, Youngblood R. Clinical application of the World Health Organization Analgesic Ladder. *J Intraven Nur*. 2000;23:118-124.

Comprehensive Pain Management Plan Components – Pg70: Notes

- Based on thorough assessment of a patient with chronic pain, a clinician can develop a comprehensive management plan that may or may not emphasize pharmacologic therapy among other multimodal treatment approaches.
- The best use of multimodal treatment
- When screening programs indicate the presence of disorders such as depression or anxiety
- When treating a chronically dysfunctional patient, angry patient, or one with personality disorders.
- Psychological interventions are aimed at the devastating psychological effects chronic pain can have on patients.
- Chronic pain can undermine their self-esteem and motivation and cause them to feel both helpless and hopeless.
- Psychological interventions include:
- active listening
- family therapy
- group therapy
- supportive psychotherapy
- cognitive behavioral therapy
- Most often these are provided in the context of other therapy, including pharmacologic and rehabilitative.

- Psychological intervention is an integral part of the routine management of chronic pain as it improves patients' coping skills and their ability to relax and sleep without interruption.[1]
- Support for patients with chronic pain can come from many sources, including patients' families. It is important for families to understand fully the stress and despair the patient feels.
- Social and rehabilitative issues in chronic pain focus on its social and environmental determinants. Treatment typically works with each individual and family members to change the consequences of a pain lifestyle and focus on well behavior, increased functionality, and normal socialization and activities.

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Patient Reassessment Model – Pg 76: Notes

- The "Four A's of Pain" outcome assessment provides a useful approach for the physician to appropriate follow-up for guiding optimal pain management.
- Key points include the importance of monitoring patients' pain intensity to ensure that they are receiving effective analgesia (pain relief), measuring effects on activities of daily living to document improvements in patient physical and psychosocial functioning, and closely monitoring for adverse effects (side effects) in order to minimize or counter these effects, and being vigilant for any signs of aberrant drug-taking behaviors that may precede addiction or addiction-related behaviors.

- Assessment and treatment documentation should include justification for continuing, modifying, or discontinuing opioid analgesia.

- Passik SD, Weinreb HJ. Managing chronic nonmalignant pain: overcoming obstacles to the use of opioids. *Adv Ther.* 2000;17:70-83.

Deciding to Convert From a Short-acting to a Long-acting Opioid – Page 78: Notes

- Thomsen et al note that during intervals between doses, patients treated with short-acting opioids may experience intermittent withdrawal symptoms, which may be misinterpreted as pain, or which may act to increase pain. Moreover a switch from short-acting opioids to long-acting opioids may reduce the pain-reinforcing properties of opioids, as a regularly scheduled opioid administration does not facilitate a behavior in which pain is rewarded with the administration of an opioid.
- All of these disadvantages may be exacerbated in patients whose pain is chronic and intractable.
- Although both short- and long-acting opioids have no ceiling effect, it may be more feasible to increase the dose (so as to increase the analgesia) of long-acting opioids (eg, methadone) because they tend to be less toxic than short-acting opioids (eg, morphine).
- Repeated dosing of short-acting opioids may not provide the patient with optimal relief for chronic pain. Short-acting opioids often are administered in fixed combination with an acetaminophen or

NSAID, imposing a ceiling effect on the maximum daily dose that can be administered. Long-acting agents invariably release the analgesics slowly, increase to therapeutic levels, plateau, and then decline in concentration. The long-acting opioids are better suited for moderate-to-severe pain because of their longer duration of action (typically 8 or 12 to 24 hours for oral formulations and up to 72 hours for transdermal fentanyl).

- Glajchen M. Chronic pain: treatment barriers and strategies for clinical practice. *J Am Board Fam Pract*. 2001;14:211-218.
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- McCarberg BH, Barkin RL. Long-acting opioids for chronic pain: pharmacotherapeutic opportunities to enhance compliance, quality of life, and analgesia. *Am J Ther*. 2001;8:181-186.
- Thomsen AB, Becker N, Eriksen J. Opioid rotation in chronic non-malignant pain patients. A retrospective study. *Acta Anaesthesiol Scand*. 1999;43:918923.

Rationale for Opioid Rotation – Pg 79: Notes

- In their trial of opioids for rheumatologic nonmalignant pain, Grilo et al enrolled

67 patients in whom other analgesics had failed. The opioids used were oral morphine, oral hydromorphone, oral buprenorphine, and transdermal fentanyl. The
67 patients suffered from low back pain with sciatica in 27 cases, inflammatory arthritis in 14 cases, brachial neuralgia in 6 cases, osteoarthritis in 8 cases, and miscellaneous conditions in 12 cases. The opioid rotations in most of the cases were the substitution of morphine by transdermal fentanyl or by oral hydromorphone. The principal reason for opioid rotation was failure of the first treatment. The mean of VAS improvement was 30 mm (P<.001). The authors concluded that in rheumatologic nonmalignant pain, the opioid rotation might allow the physician to bypass side effects or failure to alleviate pain in most cases.

- In their retrospective chart review, Quang-Cantagrel et al found that the first opioid prescribed was effective for 36% of patients, was stopped because of side effects in 30%, and was stopped for ineffectiveness in 34%. Of the remaining patients, the second opioid prescribed after the failure of the first was effective in 31%, the third in 40%, the fourth in 56%, and the fifth in 14%. There was one case of addiction and no cases of tolerance. The authors concluded that if it is necessary to change the opioid prescription because of intolerable side effects or ineffectiveness, the cumulative percentage of efficacy increases with each new opioid tested. Failure of one opioid cannot predict the patient's response to another.

- Grilo RM, Bertin P, Scotto di Fazano C, et al. Opioid rotation in the treatment of joint pain. A review of 67 cases. *Joint Bone Spine*. 2002;69:491-494.
- Quang-Cantagrel ND, Wallace MS, Magnuson S. Opioid substitution to improve the effectiveness of chronic noncancer pain control: a chart review. *Anesth Analg*. 2000;90:933-937.
- Simpson KH. Individual choice of opioids and formulations: strategies to achieve the optimum for the patient. *Clin Rheumatol*. 2002;21(suppl 1):S5-S8.

Management of Opioid Side Effects – Pg 80: Notes

- Side effects may include nausea, vomiting, itching, sedation, balance/ataxia (especially in older patients) and pruritus. Cognitive impairments/mental “clouding” may also occur. However, tolerance to these side effects typically occurs within a few days to weeks of therapy initiation. The most common side effect of chronic opioid therapy is constipation, which may persist, particularly if there are other predisposing causes.

- Once ruling out other causes, opioid side effects may be ameliorated by a number of approaches. For nausea, first try switching opioids and then try anti-emetics. For nausea associated with vertigo or movement, try antivertiginous agents (eg, scopolamine); for nausea associated with satiety, try metoclopramide.
- For sedation/somnolence, lower dose if possible; or add co-analgesics or psychostimulant agents. Modifications in the patient's diet and activity levels may also be beneficial.
- For constipation, treat prophylactically with stool softeners, intermittent stimulant laxatives such as docusate (at least 250 mg/d) or other osmotic laxatives and senna, and nonpharmacologic measures, or try switching opioids. Patient should be counseled to optimize fluids and fiber in diet.

- Portenoy RK. Opioid analgesics. In: Portenoy RK, Kanner RM, eds. Pain Management: Theory and Practice. Philadelphia, Pa: F.A. Davis Company;1996:248-253.

Management of Opioid Side Effects *(cont'd) – Pg 81: Notes*

- Side effects may include nausea, vomiting, itching, sedation, balance/ataxia (especially in older patients) and pruritus. Cognitive impairments/mental "clouding" may also occur.

However, tolerance to these side effects typically occurs within a few days to weeks of therapy initiation. The most common side effect of chronic opioid therapy is constipation, which may persist, particularly if there are other predisposing causes.

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Development of Tolerance – Pg82: Notes

- Opioid treatment may lead to the development of pharmacological tolerance and opioid-induced pain through similar cellular mechanisms, both of which may contribute to the clinical manifestation of apparent opioid tolerance with a demand of opioid dose escalation. Apparent opioid tolerance also may be an indication of disease progression with a resultant increase in pain intensity. Opioid dose escalation may feed back into the cellular mechanisms of pharmacological tolerance and opioid-induced pain sensitivity, further escalating the opioid demand.

- Courtesy of J. Mao, MD, PhD

Regulatory Issues – Pg101: Notes

- Growing clinical experience in the field of pain medicine has helped to clarify: (1) the misunderstanding of addiction, physical dependence and analgesic tolerance, (2) the misconception that chronic opioid therapy inevitably causes personality changes, depression, and impairment of cognitive and physical function, (3) the lack of information on the correct use of opioid analgesics with regard to titration and management of related side effects.
- The behavioral management of pain patients undergoing chronic opioid therapy is also important.
  A protocol for optimal patient management can be useful. Other issues include the patient consent form, behavioral contracting, and the consequences of noncompliance.
  - The importance of psychologic evaluation before a long-term opioid trial, to minimize future complications, is stressed. Although most patients on the opioid regimen do well, special attention must be given to patients with current addiction, a past history of addiction, or current misuse of opioid medications.
  - The federal government recognizes the validity of chronic opioid therapy.
  - Chronic opioid therapy for pain vs chronic opioid therapy for addiction are two very different circumstances that require different licensure.
  - There are no laws or regulations that consider the use of opioids for intractable pain to be an illegitimate practice.
  - The Federation of State Medical Boards' model guidelines include language on:
  - Patient evaluation
  - Development of a treatment plan
  - Obtaining of informed consent and agreement for treatment
  - Periodic review requirement
  - Consultation
  - Requirements for medical recordkeeping
  - Compliance with controlled substances laws and regulations.

- Pappagallo M, Heinberg LJ. Ethical issues in the management of chronic nonmalignant pain. *Semin Neurol*. 1997;17:203-211.
- Gilson AM, Joranson DE. U.S. policies relevant to the prescribing of opioid analgesics for the treatment of pain in patients with addictive disease. *Clin J Pain*. 2002;18(suppl 4):S91-S98.

POSTTEST/QUIZ

Please click on the link below to be taken to this activity's quiz. After successful completion, you can then fill out an evaluation and application for CME credit.

Substance Abuse