MILITARY

SCOPE of Pain

Military Safe and Competent Opioid Prescribing Education (M-SCOPE) Program

Safe and Competent Opioid Prescribing

For Providers Working with Veterans and Military Service Personnel

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BOSTON UNIVERSITY
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Continuing Medical Education

Purpose of Training

- The efficacy and safety of long-term opioids for the management of chronic pain has not been adequately studied
- Opioids are one tool for managing severe chronic pain and are indicated only when alternative treatment options are inadequate
- The purpose of this activity is to educate clinicians in the safe and competent use of opioids, when indicated
- This training is NOT a comprehensive review of the management of chronic pain

The Roadmap

Case-based Presentation

Module 1

- Scope of the problem
- Opioid pharmacology, efficacy and safety
- Changing the treatment paradigm

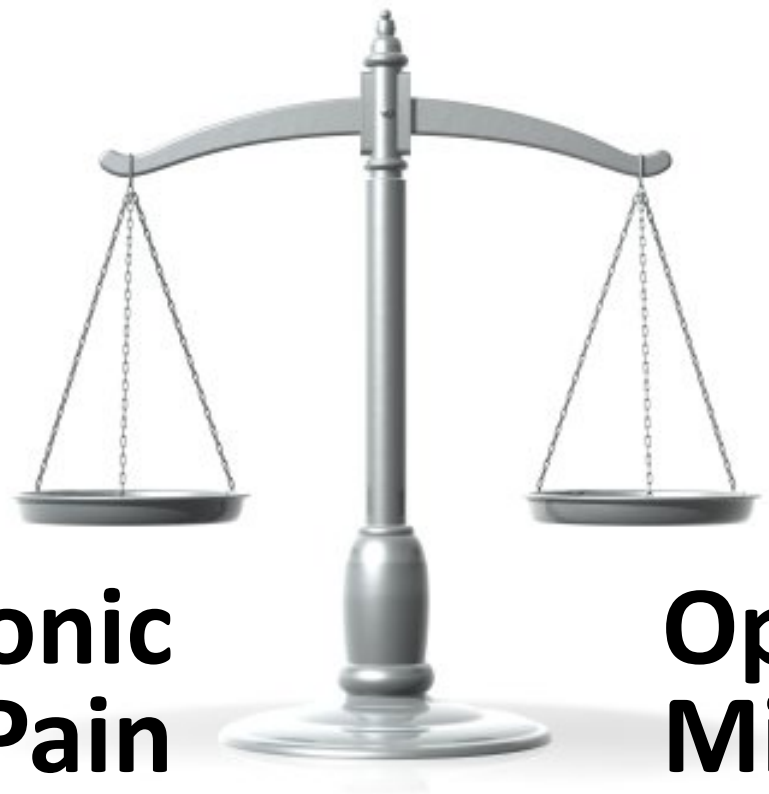
Module 2

- Partnering and educating patients
- Universal precautions in pain management
- VEMA (Validate, Educate, Motivate, Activate) Model

Module 1 Agenda

- **Scope of the Problem:** competing epidemic of chronic pain and prescription opioid misuse
- **Opioid pharmacology:** efficacy and safety
- **Changing the chronic pain treatment paradigm:** biomedical versus biopsychosocial models

Two Competing Epidemics



Chronic Pain

Opioid Misuse

(including overdose, addiction, diversion)

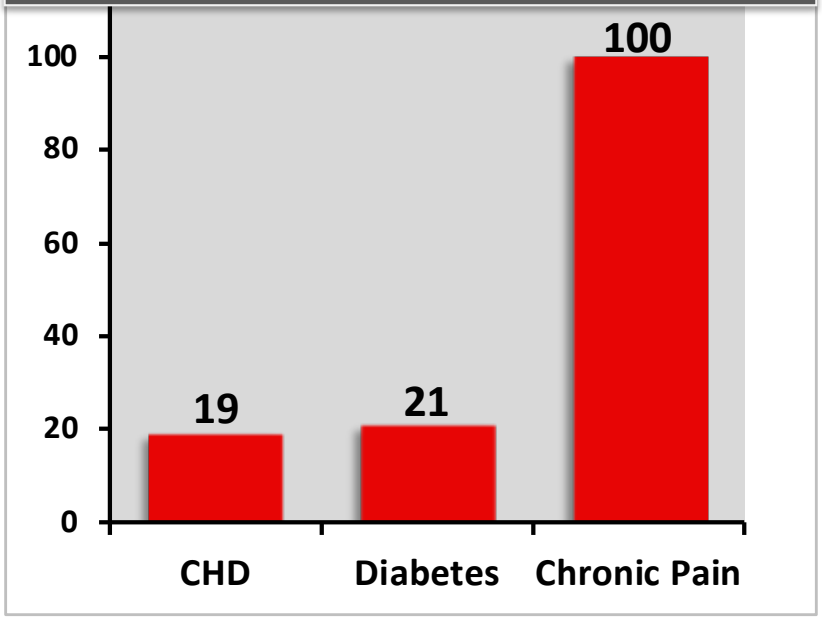
Epidemic of Chronic Pain

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

Prevalence in Millions



$600 Billion Annual Costs

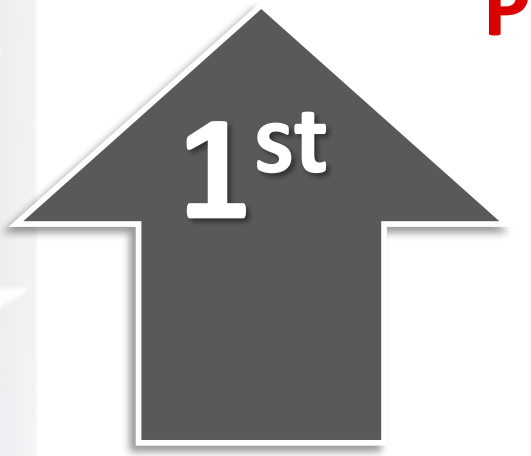
- Healthcare expenses
- Lost income
- Lost productivity

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

Chronic Pain in the Military

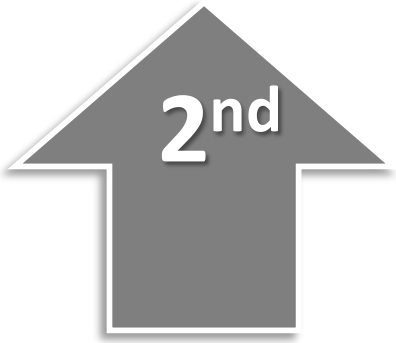
53% of military discharges are associated with chronic pain disabilities

Pain Related Disabilities



LEADING CAUSE
of Disability

- **Army**
- **Navy**
- **Marine Corps**
- **Air Force**



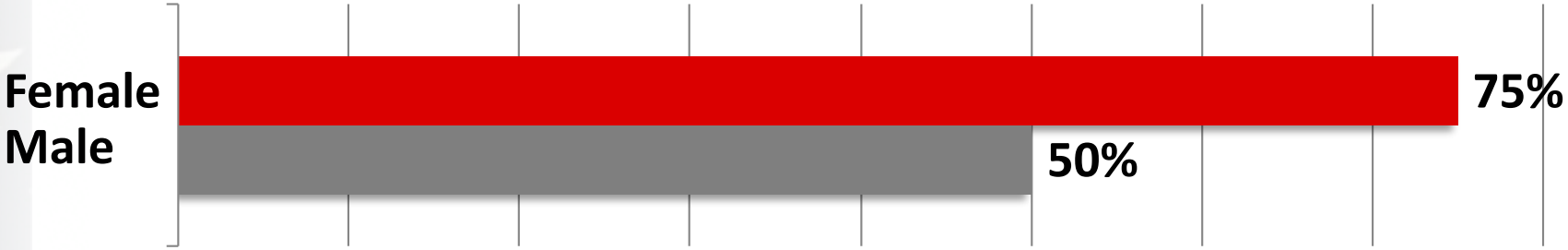
SECOND LEADING CAUSE
of Disability

- **Army**
- **Navy**
- **Marine Corps**

1. Kerns RD, et al. J Rehab Res Dev 2003;40:371–80.
2. Ruff RL, Ruff SS, Wang XF. J Rehabil Res Dev 2009;46:1071-84.
3. Amoroso PJ, and Canham ML. (1999). In BH Jones, PJ Amoroso and ML Canham (Eds.), Atlas of injuries in the US Armed Forces (pp. 4-1 - 4-73). Bethesda, MD: AMSUS.
4. Gardner JW, et al. (1999). Hospitalizations due to injury: Inpatient medical records data. In BH Jones, PJ Amoroso, and ML Canham (Eds.), Atlas of Injuries in the U.S. Armed Forces. Military Medicine (Supp), 164, 5-1 – 5-143.

Chronic Pain in Veterans

Most prevalent problem among US Veterans



Vietnam

66%- 80% of veterans with PTSD reported chronic pain[1,2]

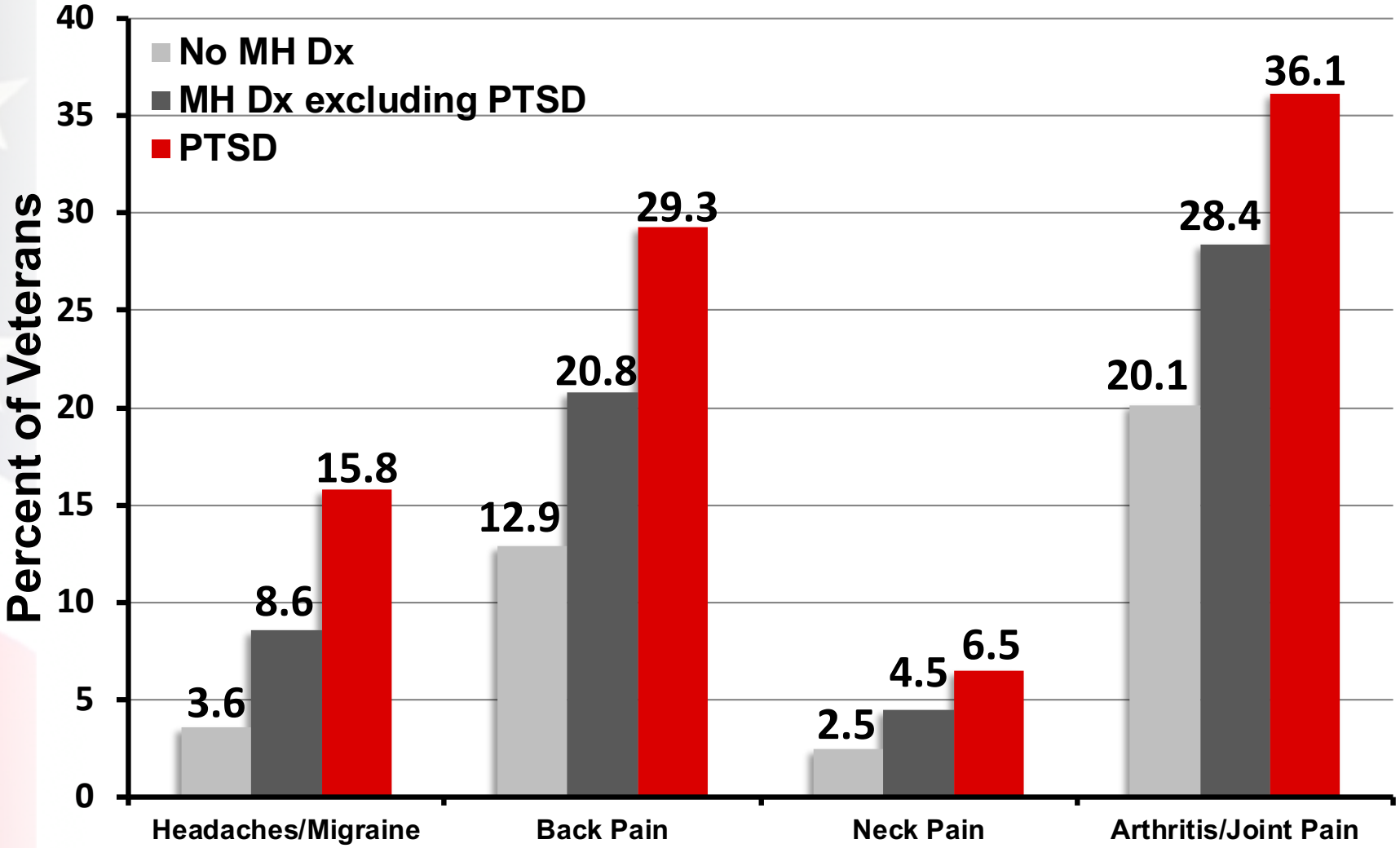
Iraq/Afghanistan

Veterans – carry heavy combat equipment/body armor and weaponry > 100 lbs

- Chronic pain more prevalent in female vets[3,4]
- >50% with PTSD have received chronic pain diagnoses[5]

1. Beckham, JC, et al. J Psychosom Res. 1997 Oct;43(4):379-89.
2. Shipherd, JC, et al. J Rehabil Res Dev. 2007;44(2):153-66.
3. Frayne, SM, et al. J Gen Intern Med. 2011 Jan;26(1):33-9.
4. Haskell, SG, et al. Pain Med. 2009 Oct;10(7):1167-73.
5. Seal KH. "PTSD in Combat Veterans: Exploring the Association with Chronic Pain and Prescription Opioid Use" American Psychological Association, Annual Meeting, Honolulu, HI, July 31- Aug 4, 2013.

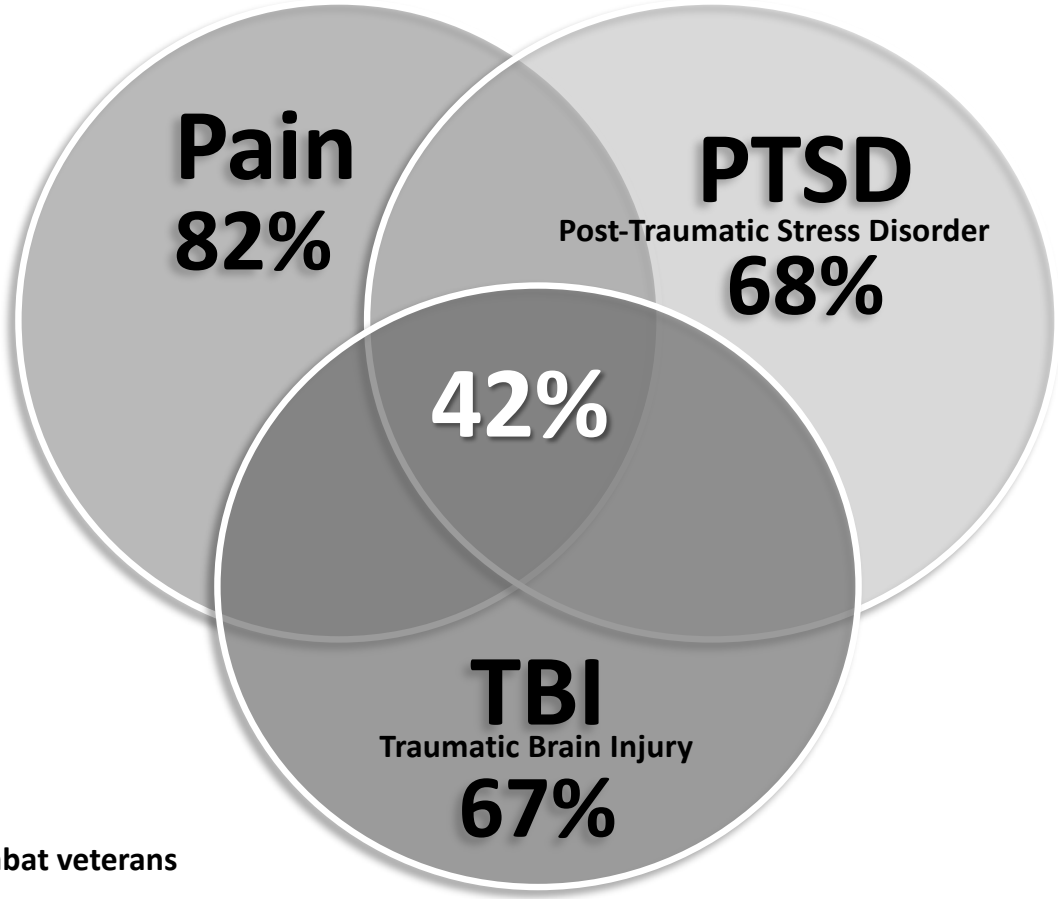
Pain and Mental Health Comorbidity in Iraq and Afghanistan Veterans



Seal KH. "PTSD in Combat Veterans: Exploring the Association with Chronic Pain and Prescription Opioid Use" American Psychological Association, Annual Meeting, Honolulu, HI, July 31- Aug 4, 2013.

"Signature Injury": Polytrauma

More veterans of Iraq and Afghanistan have survived war-related trauma than in prior wars and are living with polytrauma, e.g., overlapping TBI, PTSD and pain

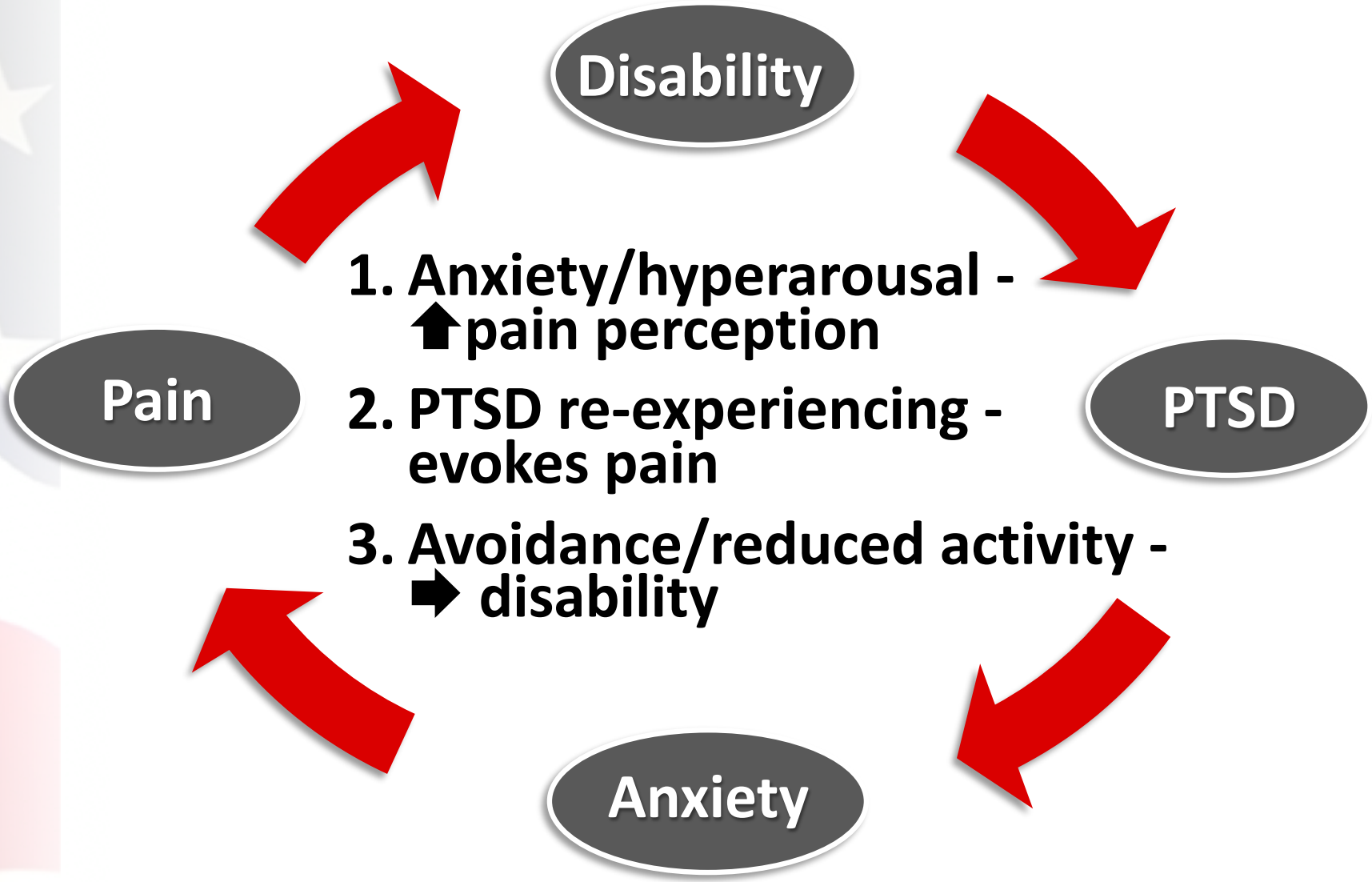


N= 340 OEF/OIF combat veterans

Lew HL, et al. J Rehabil Res Dev. 2009;46(6):697-702.

Chronic Pain and PTSD: Mutual Maintenance

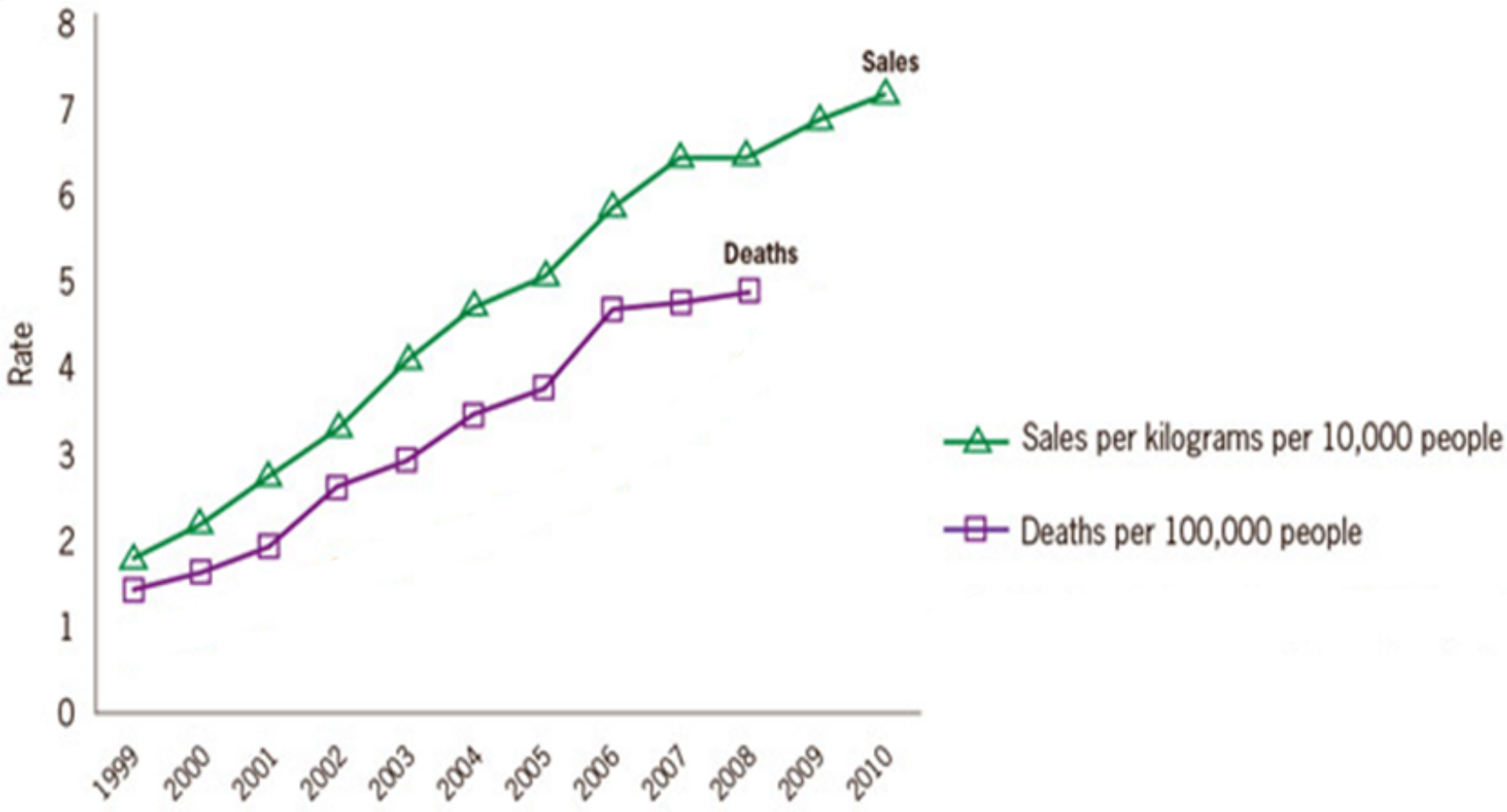
PTSD and pain can mutually reinforce and maintain each other unless cycle is interrupted



Adapted from: Sharp TJ, Harvey AG. Clin Psychol Rev. 2001 Aug;21(6):857-77.

Prescription Opioid Misuse **Epidemic**

Unintentional Overdose Deaths in U.S.

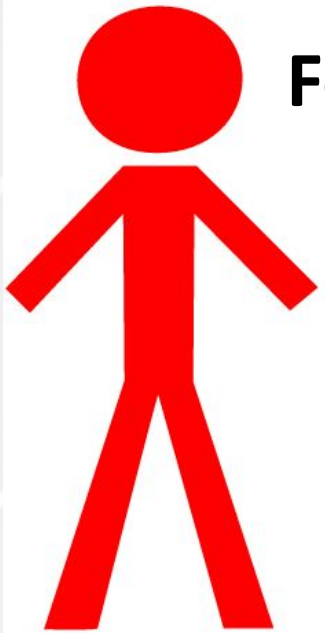


Unintentional overdose deaths

- **Parallel per capita sales of opioid analgesics**
- **Second leading cause of accidental deaths in the US[1]**

CDC: Unintentional Drug Poisoning in the United States, July 2010
National Vital Statistics System, 1999-2008; Automation of Reports and Consolidated Orders System (ARCOS) of the Drug Enforcement Administration (DEA), 1999-2010; Treatment Episode Data Set, 1999-2009.

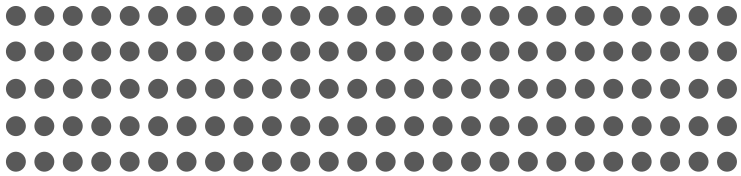
But the Problem Is Bigger…



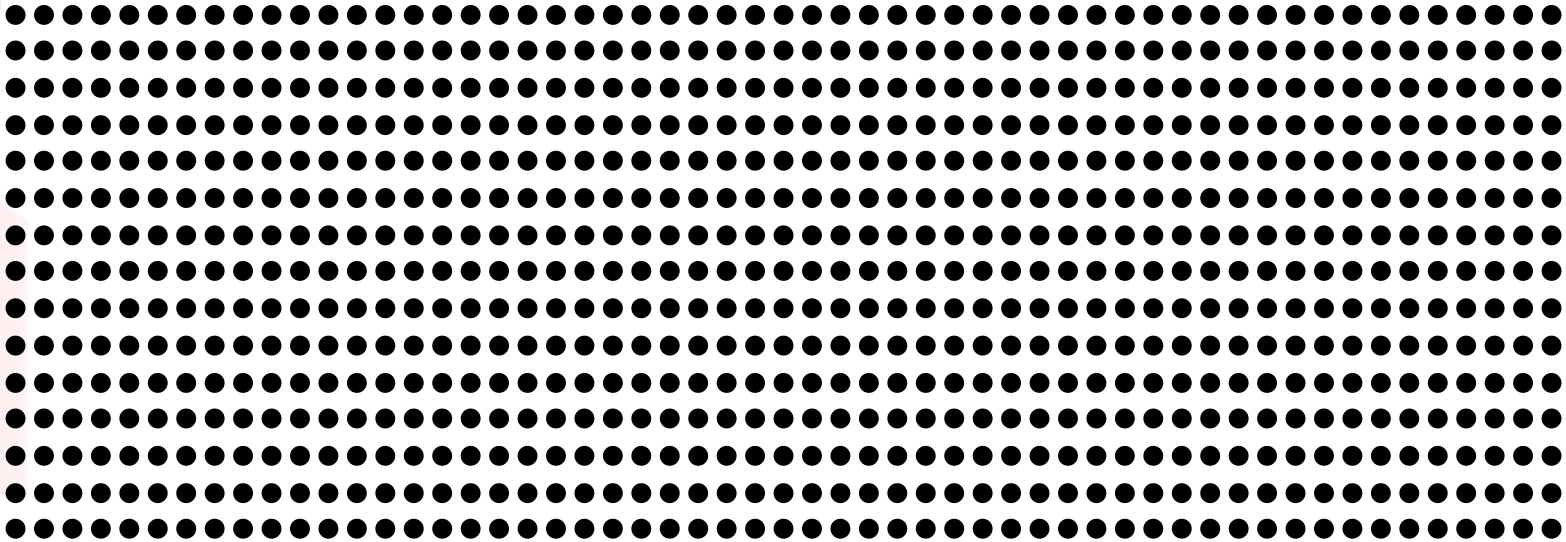
For every 1 death there is:

10 treatment admissions for abuse

32 emergency dept. visits for misuse or abuse



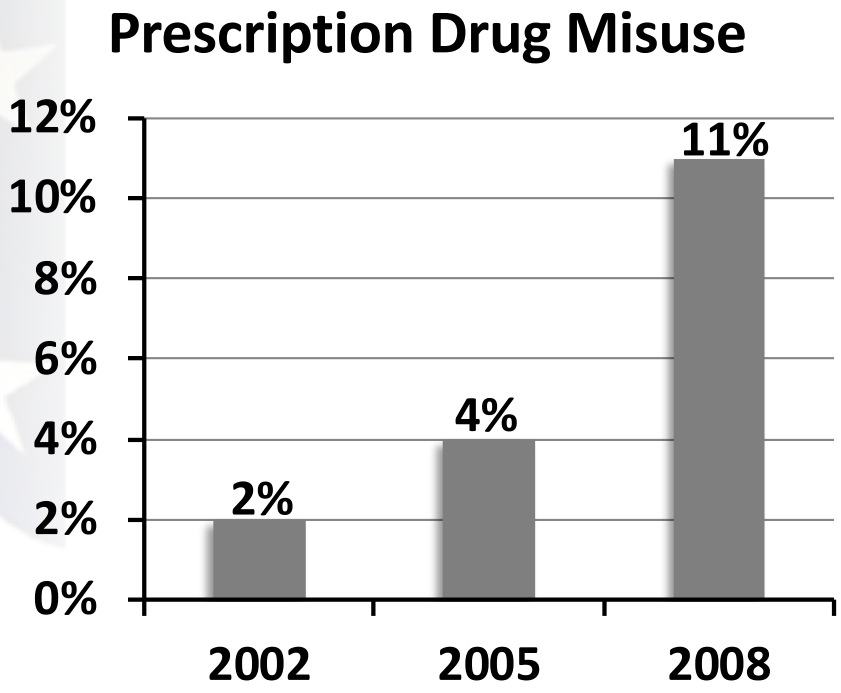
130 people who abuse or are dependent

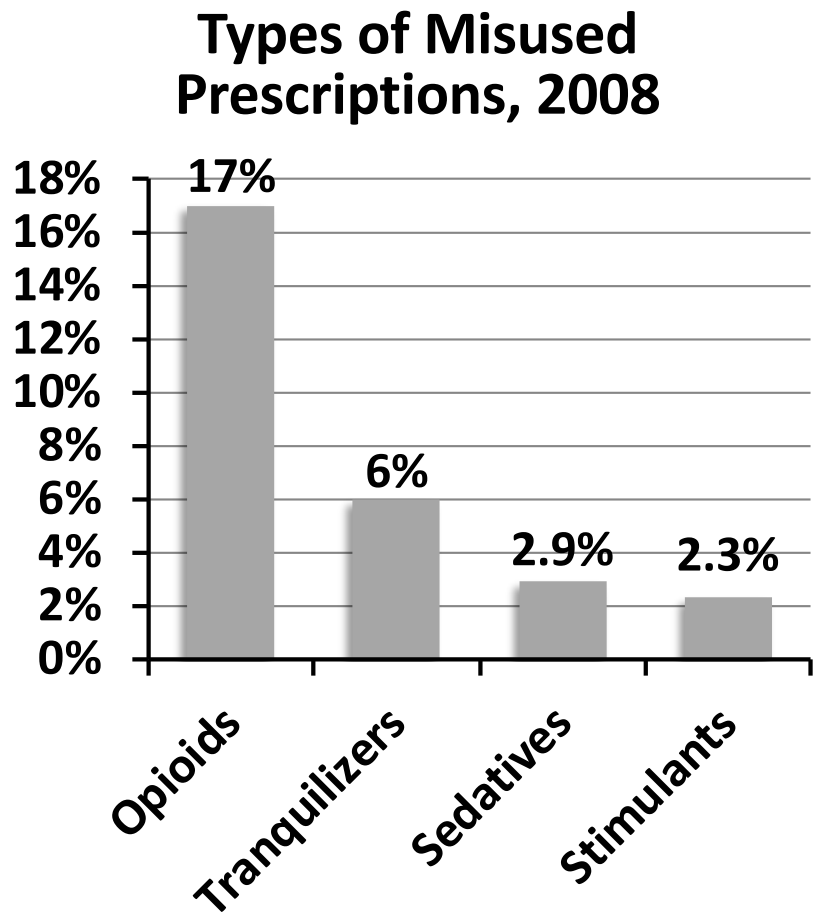


825 non-medical users

CDC. Vital Signs: Overdoses of Prescription Opioid Pain Relievers-United States, 1999-2008. MMWR 2011; 60: 1-6.

Military-Specific Prescription Drug Misuse

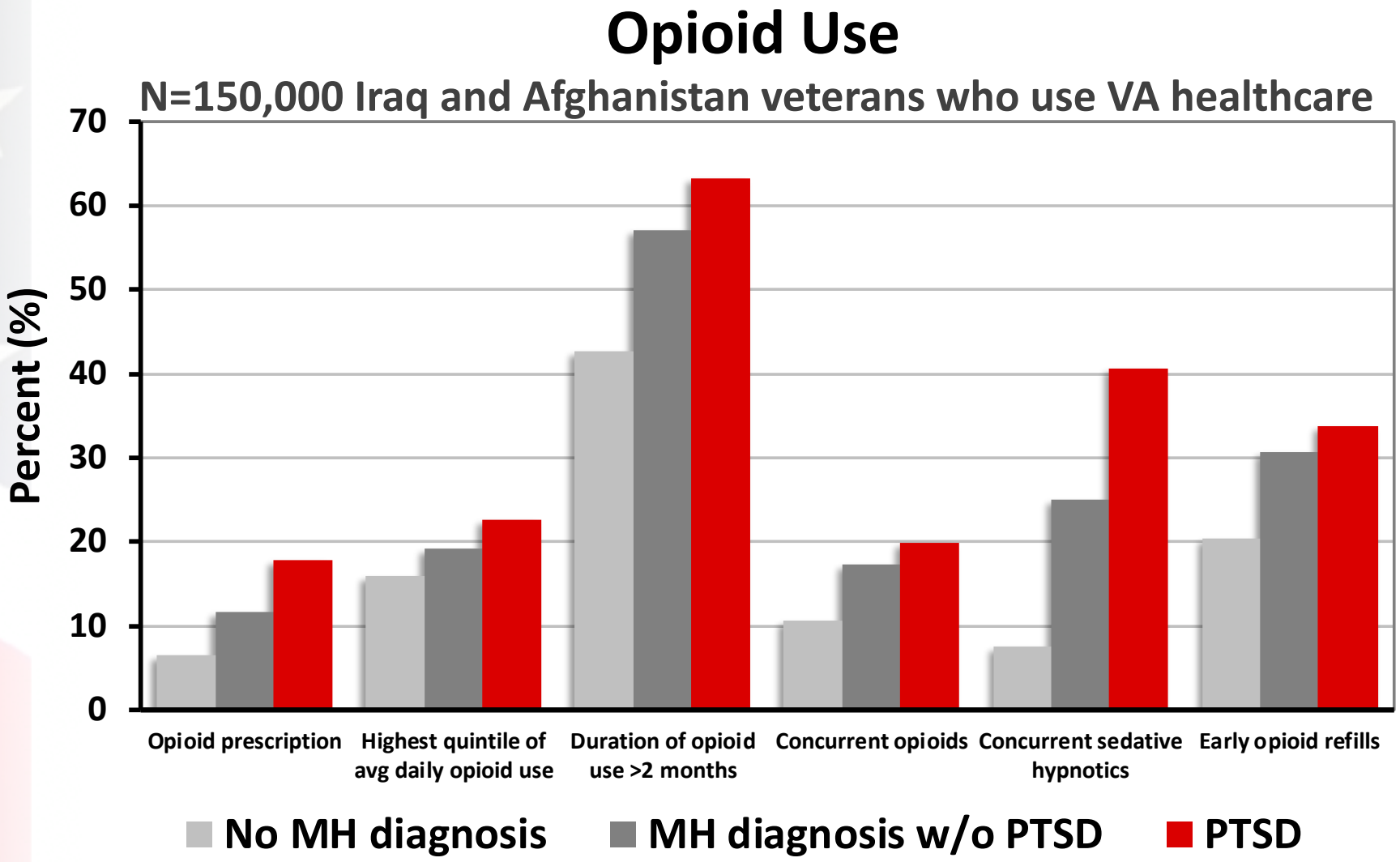




"The strongest predictor of prescription drug abuse in the military is having received a prescription for pain medication within the past month or past year."

2008 DOD Survey of Health Related Behaviors Among Active Duty Military Personnel, April 2011.

Greater Risk of Opioid Use in Iraq & Afghanistan Veterans with Mental Health Problems



Seal, KH, et al. JAMA. 2012 Mar 7;307(9):940-7.

Prescription Opioids and Adverse Outcomes in Iraq and Afghanistan Veterans

Receiving prescription opioids (vs. not) was associated with increased risk of adverse clinical outcomes

- Particularly elevated in veterans with PTSD

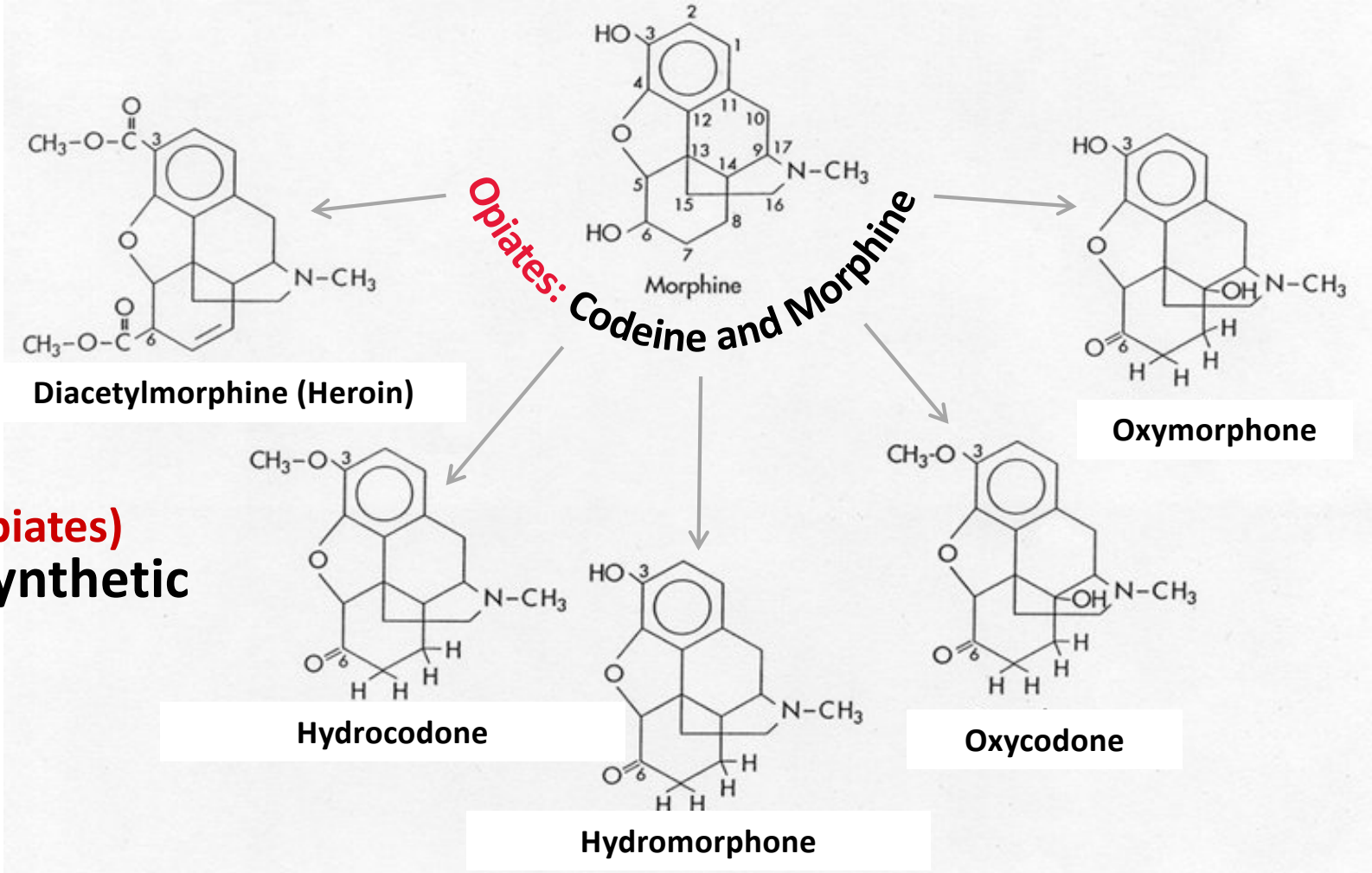
Seal, KH, et al. JAMA. 2012 Mar 7;307(9):940-7.

- Wounds or injuries
- Opioid-related accidents and overdoses
- Alcohol and non-opioid accidents and overdose
- Self-inflicted injuries
- Violence-related injuries

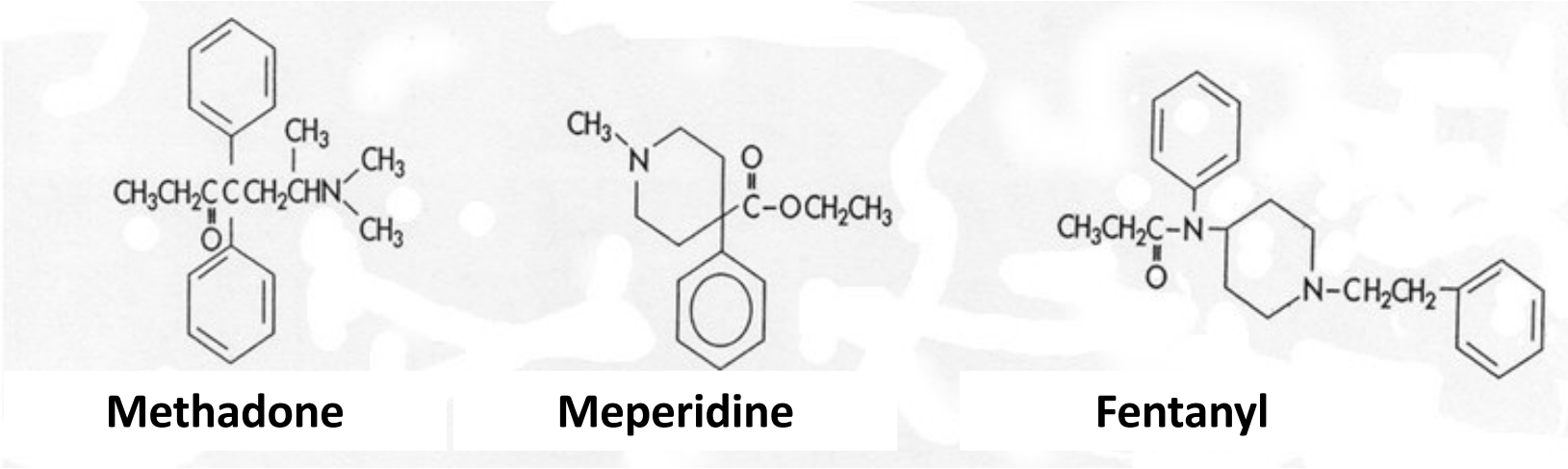
Opioid Pharmacology

Opioids Are Not All The Same

Natural (Opiates) and Semisynthetic



Synthetic



Opioids Activate Mu-Opioid Receptors

- Turn on descending inhibitory systems in the midbrain
- Prevent ascending transmission of pain signal
- Inhibit C-fiber terminals in the spinal cord
- Inhibit activation of peripheral nociceptors

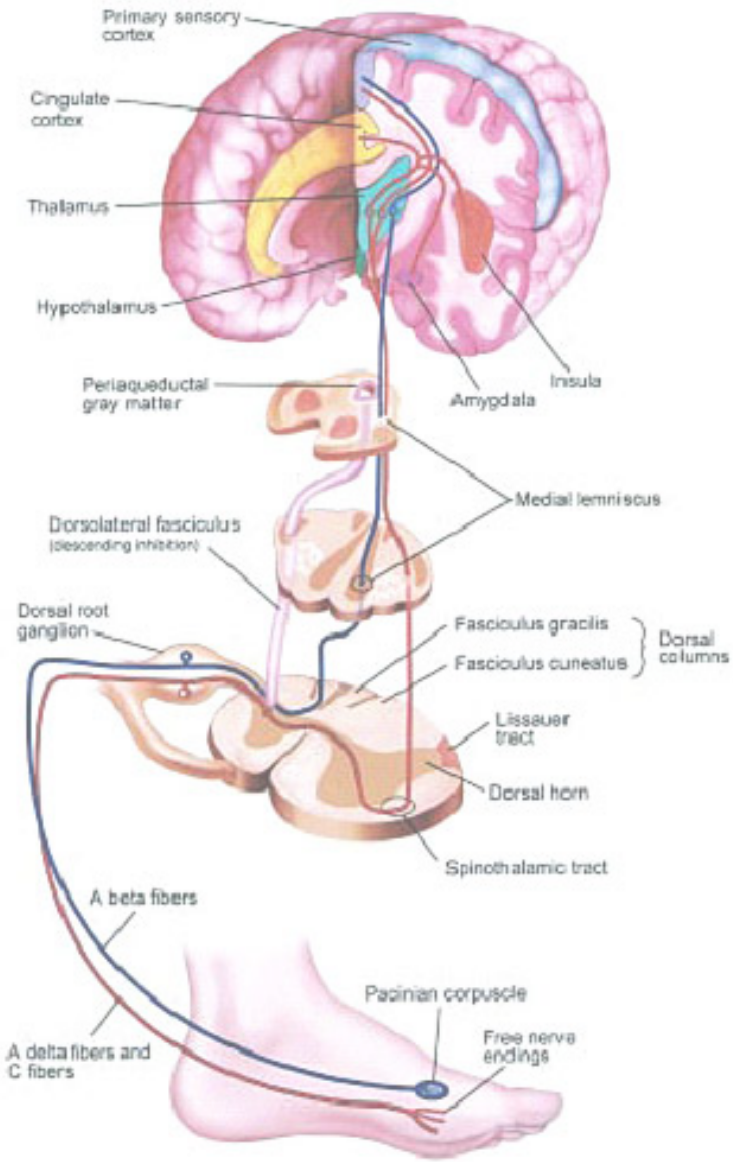


Image source: www.mayo.edu/proceedings
McCleane G, Smith HS. Med Clin North Am. 2007 Mar;91(2):177-97.

Variable Response to Opioids

- Mu-opioid receptor subtypes
- Greater than 100 polymorphisms in the human MOR gene
- Opioid metabolism differs by individual opioid and by individual patient

Smith HS. Pain Physician. 2008 Mar-Apr;11(2):237-48.
Smith HS. Mayo Clin Proc. 2009 Jul;84(7):613-24.

Opioid Efficacy for Chronic Pain

- Mostly surveys and uncontrolled case series
- RCTs of short duration with small sample sizes
- Most studies are pharma sponsored

Outcomes:

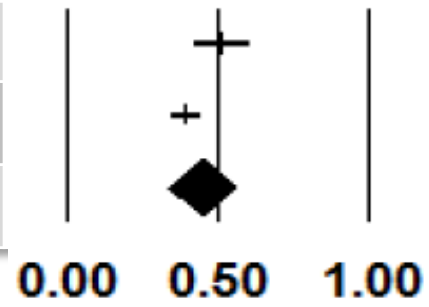
- **Better analgesia with opioids vs. placebo**
- **No difference with opioids vs. non-opioid**
- **Mixed reports on function**
- **Addiction not assessed**

Ballantyne JC, Mao J. N Engl J Med. 2003 Nov 13;349(20):1943-53.
Kelso E, et al. Pain. 2004 Dec;112(3):372-80.
Eisenberg E, McNicol ED, Carr DB. JAMA. 2005 Jun 22;293(24):3043-52.
Noble M, et al. Cochrane Database Syst Rev. 2010 Jan 20;(1):CD006605.
Furlan AD, et al. CMAJ. 2006 May 23;174(11):1589-94.
Martel B, et al. Ann Intern Med. 2007 Jan 16;146(2):116-27.
Krebs EE et al. JAMA 2018.
Meske DS et al. J Pain Res. 2018;11:923-934.

Opioid Efficacy for Chronic Pain

- Proportion of patients with at least 50% pain relief
- Oral opioids
- N = 442
- Follow-up 7.5 months (mean) to 13 months (1^2 77.3%)

Study Name	Event Rate	Lower Limit	Upper Limit	Total	Proportion
Zenz 1992	0.510	0.413	0.606	51 / 100	
Allan 2005	0.392	0.341	0.445	134 / 342	
	0.443	0.333	0.559		



44.3% of participants had at least 50% pain relief

Noble M, et al. Cochrane Database Syst Rev. 2010 Jan 20;(1):CD006605.

Contraindications to Opioid Therapy

Absolute Contraindications:

- Severe respiratory instability
- Acute psychiatric instability or active suicidality
- Diagnosed SUD not in remission & not in treatment
- True allergy to opioids or life-limiting drug-drug interactions
- QTc > 500 for methadone
- Active diversion of controlled substances

Contraindications to Opioid Therapy

Relative Contraindications:

- Receiving treatment for SUD
- Sleep apnea or COPD
- Cardiac arrhythmia (methadone)
- Risk for suicide or unstable psychiatric disorder
- Inability to manage opioid therapy responsibly
- Unwillingness or inability to comply with tx plan

Non-Opioid Analgesics are First-Line for Chronic Pain

Musculoskeletal Pain

- Acetaminophen
- Non-steroidal anti-inflammatory drugs (NSAIDs)
- Muscle relaxants
- Topical therapies
  - Capsaicin cream, menthol/ methylsalicylate cream, lidocaine ointment,
- Diclofenac gel (N/F)

Neuropathic Pain

- Antidepressants
  - Nortriptyline, venlafaxine, duloxetine (N/F)
- Anticonvulsants
  - Gabapentin, pregabalin (N/F), topiramate
- Topical therapies
  - Capsaicin cream, lidocaine patch (N/F)

N/F = non-formulary

Opioid Risks

Educating Ourselves and our Patients

Potential Side-Effects of Opioid Therapy

Nausea and vomiting	**Usually resolves in few days; antiemetics**
Sedation/ Confusion	**Decrease dose**
Constipation Most common and should be anticipated	**Senna laxatives, bowel stimulants; avoid bulking agents**
Pruritis	**Antihistamines**

Benyamin R, et al. Pain Physician. 2008 Mar;11(2 Suppl):S105-20.

Potential Adverse Effects of Chronic Opioid Therapy

- Tolerance and physical dependence
- Misuse including addiction and diversion
- CNS depression and overdose
- Respiratory depression and worsening sleep apnea
- Increased pain due to withdrawal and hyperalgesia
- Endocrine dysfunction including hypogonadism
- >50 mg (MSO4 equivalents) associated with 2x increase fracture risk

Benyamin R, et al. Pain Physician. 2008 Mar;11(2 Suppl):S105-20.
Saunders KW, et al. J Gen Intern Med. 2010 Apr;25(4):310-15.

Risks of Opioids in the Elderly

- Drug-drug interactions
- Drug-disease interactions
  - CHF, chronic liver & renal disease
  - Dementia

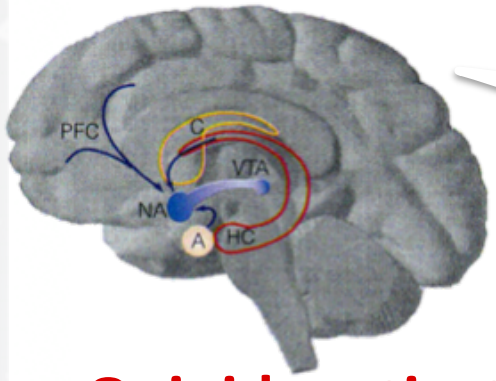
✓ **Monitor frequently**

American Geriatrics Society Panel. J Am Geriatr Soc. 2009 Aug;57(8):1331-46.

Collateral Risks of Opioids

- Young children
  - Ingestion
  - Overdose
- Adolescents
  - Experimentation leading to overdose and addiction

Opioid Addiction



Opioids activate mu-opioid receptors in midbrain causing euphoria

Dopaminergic system is very reinforcing

Most rewarding are fast onset (IR) opioids

Long-acting (ER/LA) opioids should be less rewarding if taken as prescribed

Kosten TR, George TP. Sci Pract Perspect. 2002 Jul;1(1):13-20.

Opioid Addiction

Clinical syndrome presenting as:

- Loss of Control
- Compulsive use
- Continued use despite harm
- Craving

Aberrant Medication Taking Behaviors
(pattern and severity)

Addiction is NOT the same as physical dependence

Savage SR, et al. J Pain Symptom Manage. 2003;26:655-667.

Opioid Overdose Risk Associated with Dose

	VA patients (fatal overdose)	HMO patients (any overdose)
Dose (mg/day)	Hazard Ratio (95% CI)	
<20	1.0	1.0
20-49	1.9 (1.3, 2.7)	1.4 (0.6, 3.6)
50-99	4.6 (3.2, 6.7)	3.7 (1.5, 9.5)
≥ 100	7.2 (4.9, 10.7)	8.9 (4.0, 19.7)

Dunn KM, et al. Ann Intern Med. 2010 Jan 19;152(2):85-92.
Bohnert AS, et al. JAMA. 2011 Apr 6;305(13):1315-21.

Opioid Tolerance

- Right shift of the dose-response curve
- Demonstrated in some animal models
- Not clear how common tolerance is in clinical settings

Schug SA, et al. Drug Saf. 1992 May-Jun;7(3):200-13.
Portenoy RK and Foley KM. Pain. 1986 May;25(2):171-86.
Chang G, et al. Med Clin North Am. 2007 Mar;91(2):199-211.
Joseph EK, et al. J Neurosci. 2010 Mar 31;30(13):4660-6.

Opioid-Induced Hyperalgesia

- Poorly understood paradoxical effect
- Central and peripheral sensitization anti-analgesic or hyperalgesic processes
- Increased pain sensitivity to same opioid dose
- Increased opioid dose may improve analgesia temporarily with subsequent worsening of pain
- Symptoms improve with decrease or discontinuation of opioid

Chang G, et al. Med Clin North Am. 2007 Mar;91(2):199-211.
Pain Physician. 2011 Mar-Apr;14(2):145-61.

Primary Care Challenge: Changing the Paradigm

Primary Care and Chronic Pain

THE CHALLENGE

Patients with pain can be viewed as:

- "Difficult"
- "Demanding"
- "Drug-seeking"
- "Unmotivated"
- "Not having 'real' medical problem"

The more we doubt their pain, the more patients pursue validation of their pain.

Our response is not always helpful

Case Study
John

42 year-old Iraq veteran with chronic low back pain (LBP)

- **LBP from combat injury 5 years ago**
- **Just moved to area; this is first visit with you**
- **MS Contin 60 mg TID and OC 5-10 mg q4h PRN from prior VA (per CPRS)**

- **Severe pain now because out of meds x4 days; sweaty and tremulous**
- **Requests that you fill these meds today**
- **Is impatient and irritable**

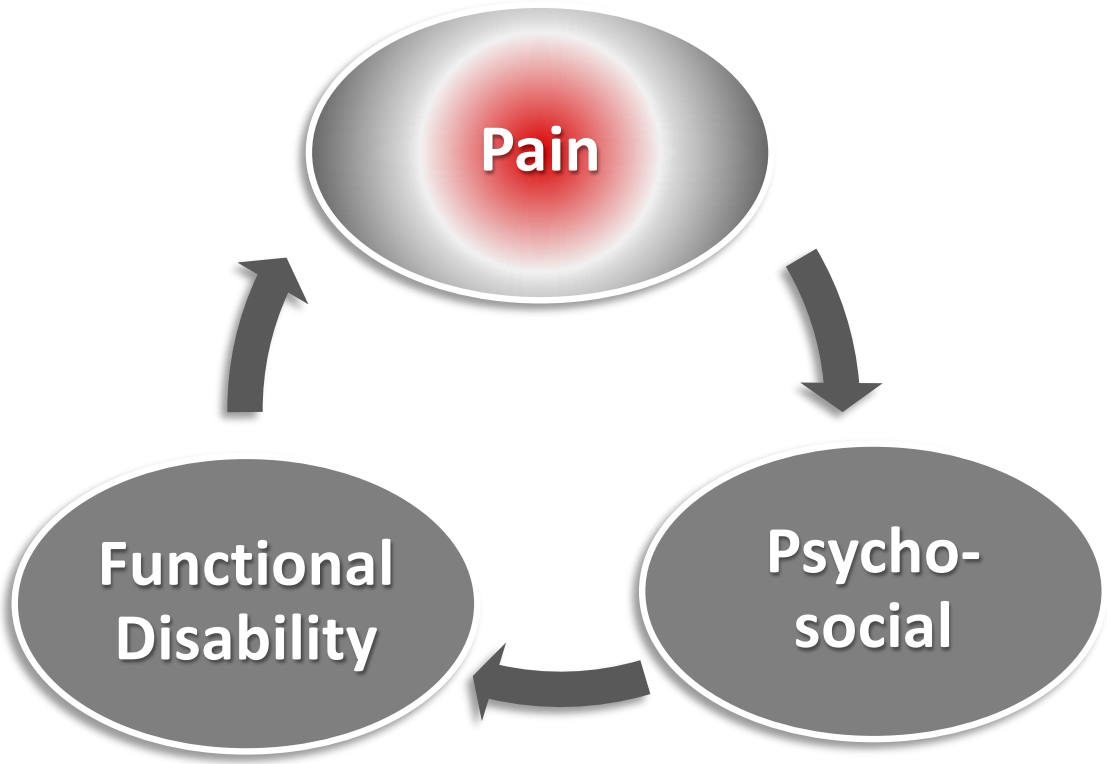
Biomedical Model of Pain

- Mind and body are separate
- Biological basis for pain symptoms
- We can fix it; “kill the pain”
- Complete pain relief is possible
- Reinforced by media, pharma, and medical education

Biopsychosocial Model of Pain

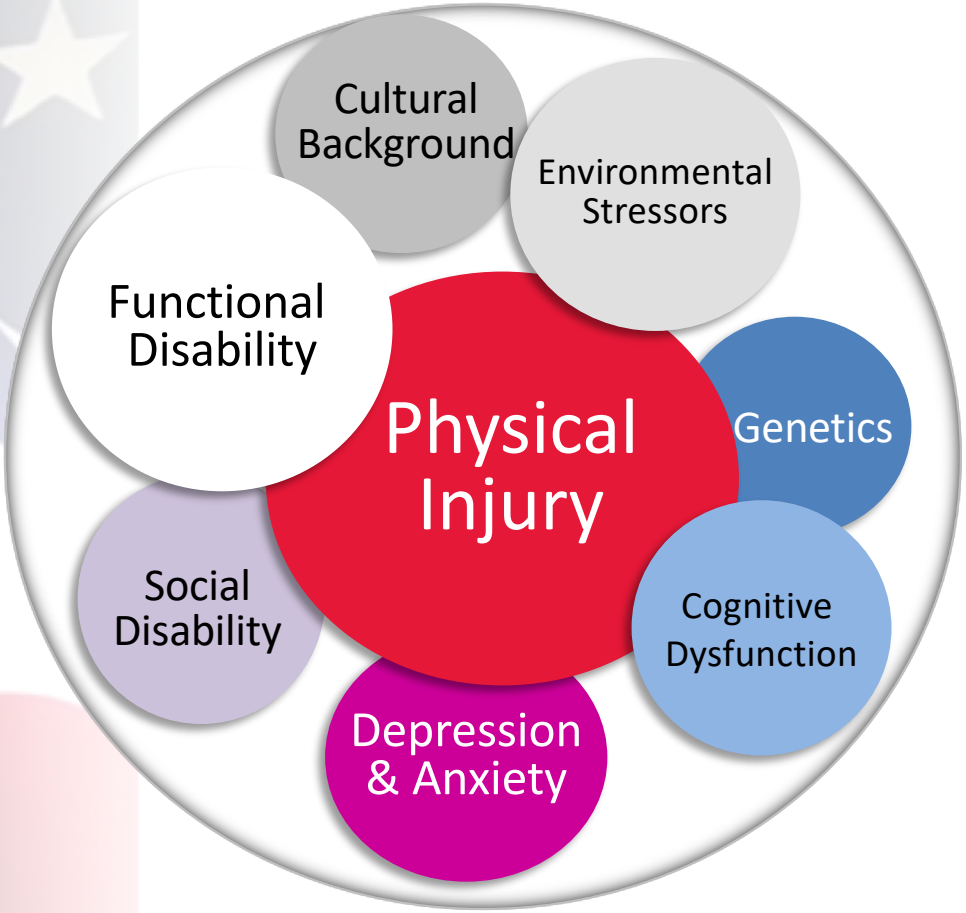
PAIN

not just a symptom -
but your patient's lived experience

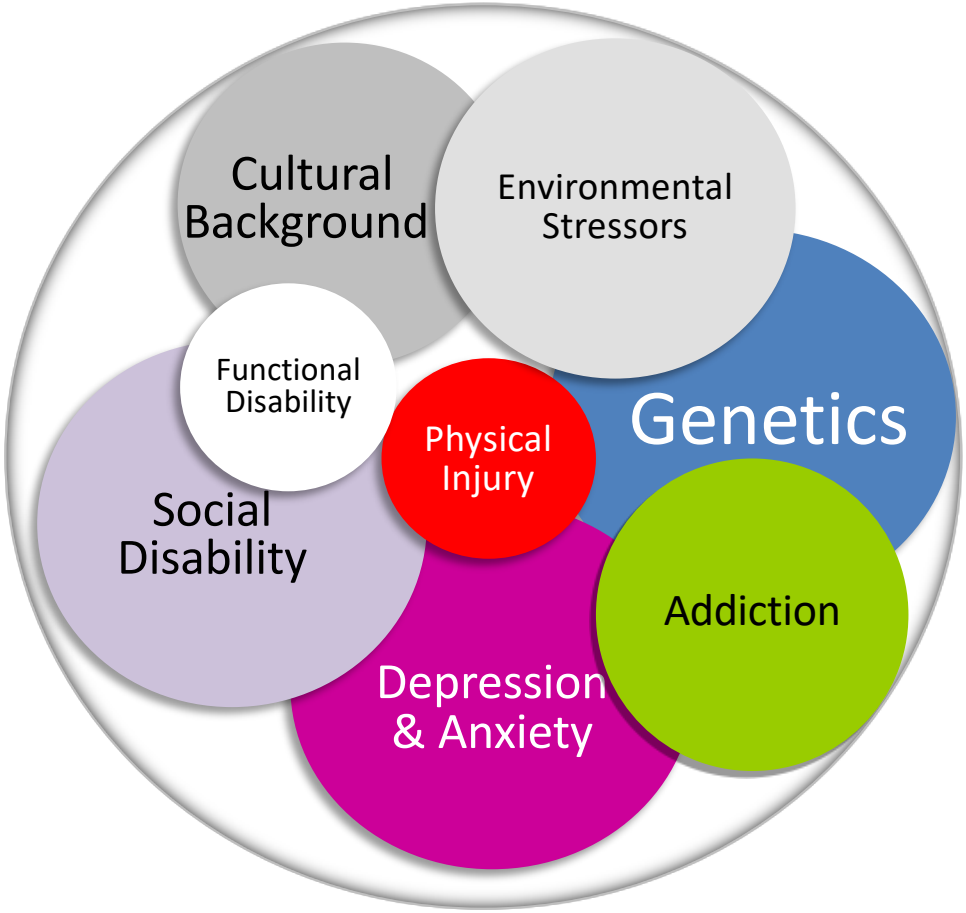


Biopsychosocial Model of Pain

Patient "A" Pain 8/10

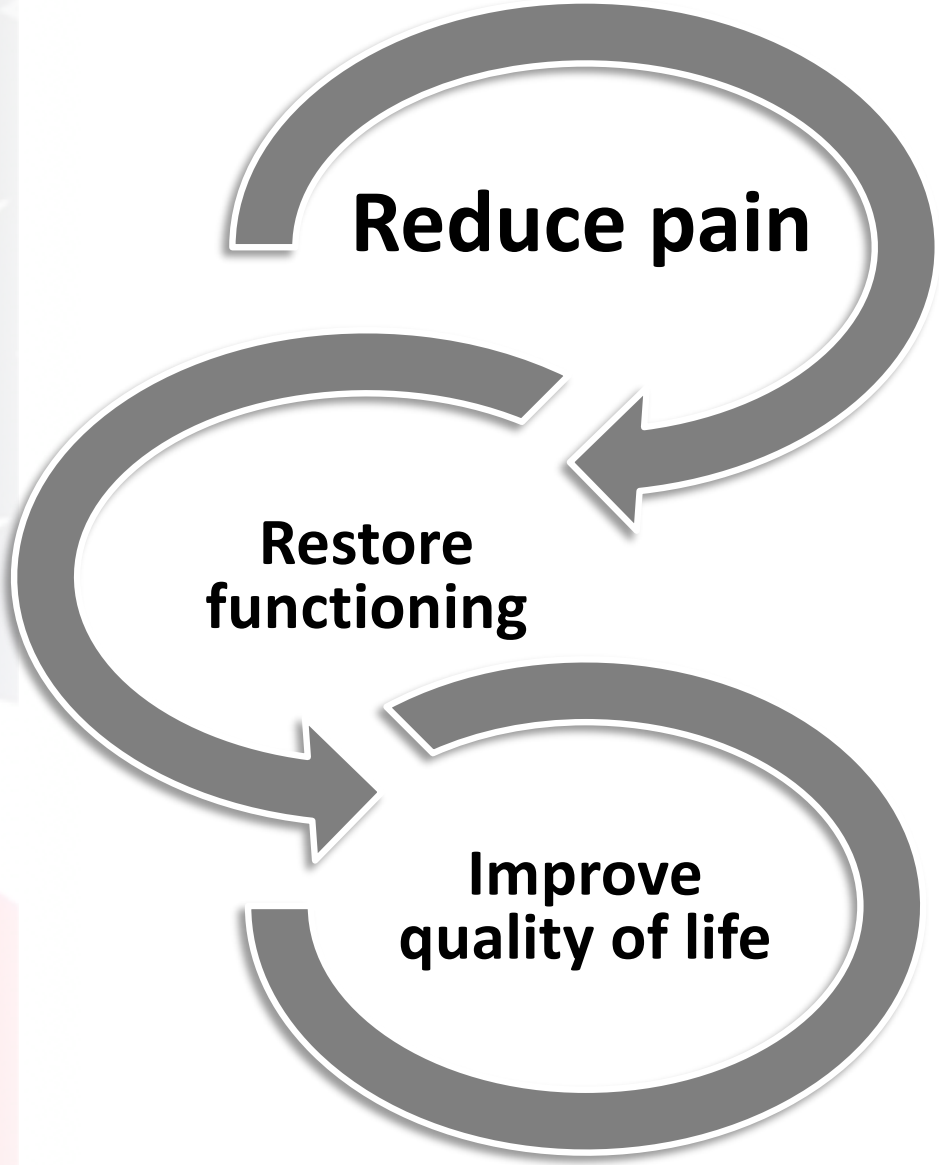


Patient "B" Pain 8/10



Gatchel RJ. Am Psychol. 2004 Nov;59(8):795-805.

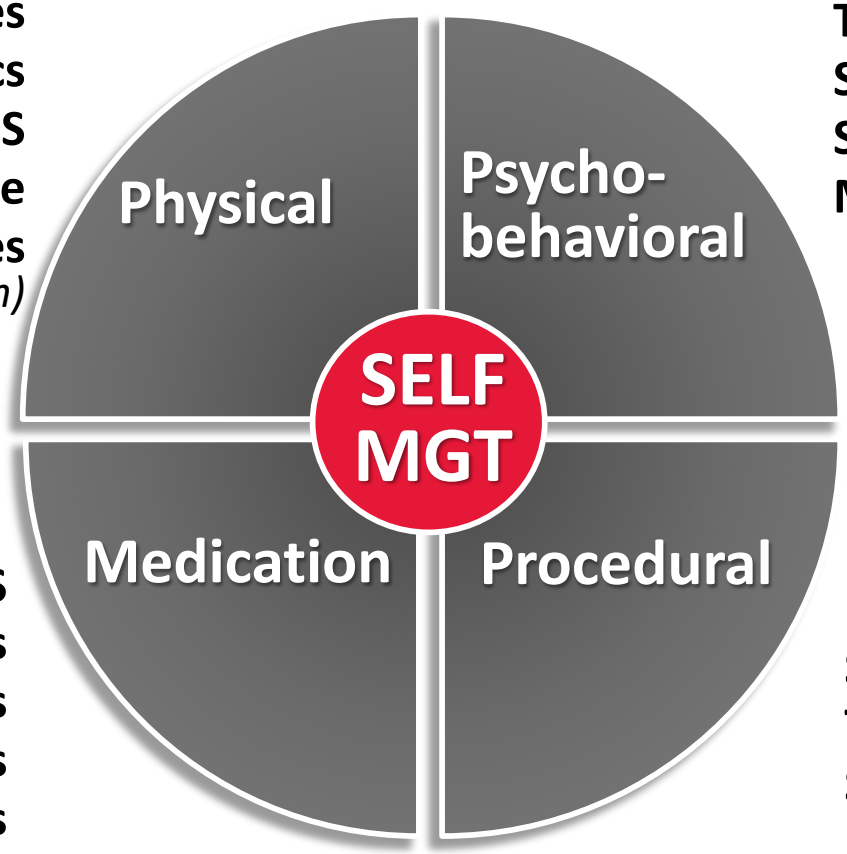
Goals of Chronic Pain Management



"A person with chronic pain is like a car with four flat tires"

Self-Management: More than Medication

Gentle exercise
Manual therapies
Orthotics
TENS
Acupuncture
Other modalities
(heat, cold, stretch)



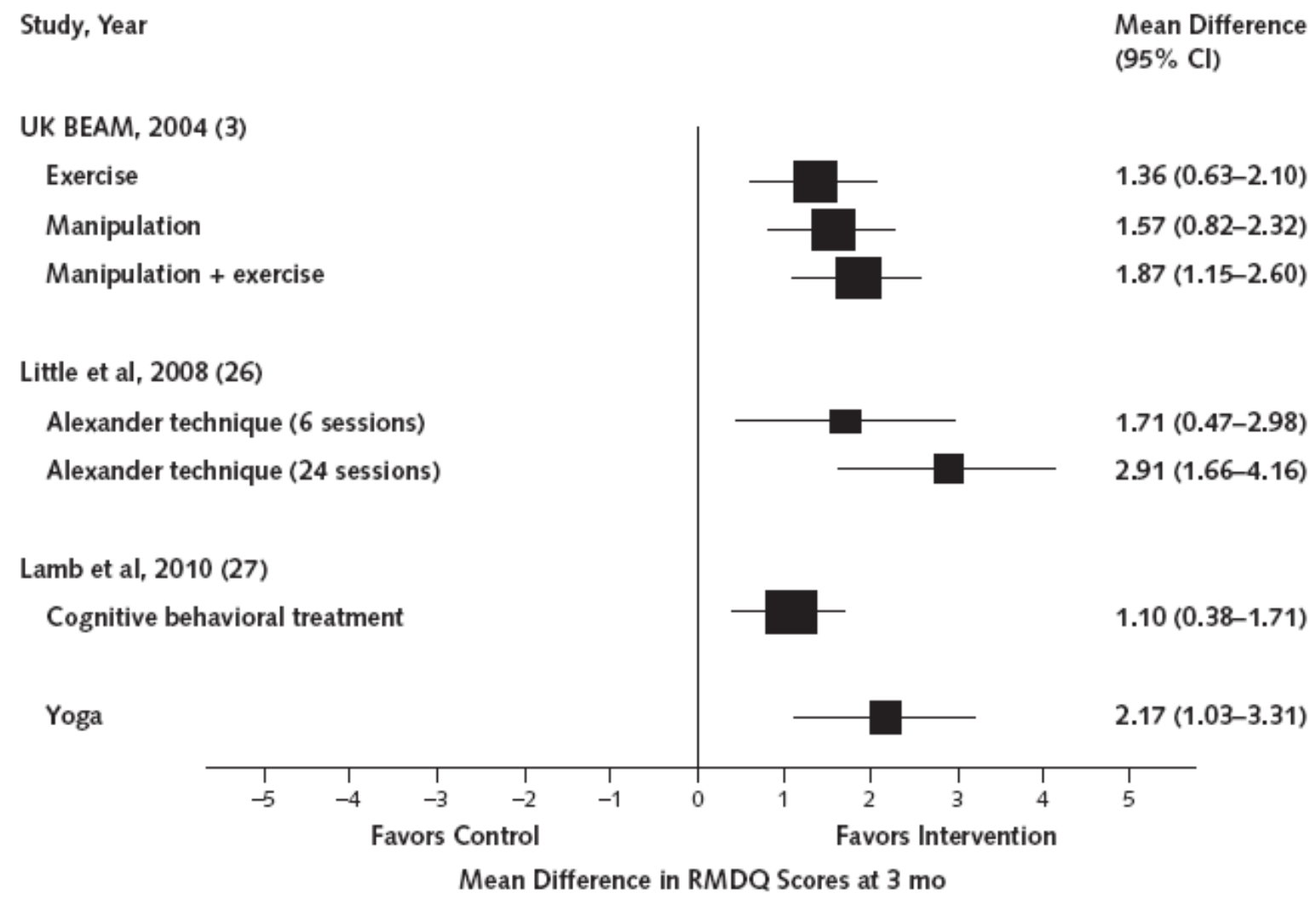
CBT
Tx mood/trauma
Substance abuse tx
Sleep Hygiene
Meditation/Relaxation

NSAIDS
Anticonvulsants
Antidepressants
Topical agents
Opioids
Others

Nerve blocks/ablation
Steroid injections
Trigger point injections
Stimulators

TENS Transcutaneous Electrical Nerve Stim
CBT Cognitive Behavioral Therapy
ACT Acceptance and Commitment Therapy

Nonpharmacologic Treatment for Chronic Pain



Tilbook HE, et al. Ann Intern Med. 2011 Nov 1;155(9):569-78.

Summary: Module 1

- Two competing epidemics: chronic pain and prescription opioid misuse
- Opioids differ and there is variability in response to different opioids
- Good quality chronic pain management should rely less on medications and more on multimodal biopsychosocial therapies and self-management

Case Study
John

42 year-old Iraq veteran with chronic low back pain (LBP)

- **John, a 42 year-old Iraq veteran with severe chronic low back pain from a combat injury on high dose opioids, is requesting refills on this first visit**

Module 1 Cliffhanger:

How will you decide whether to
continue
change
or discontinue
John's opioid therapy?