

# **PTSD, Chronic Pain and Substance Use: Treatment Implications**

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# Mediators of Adverse Child Events and Non Medical Prescription Opioid Use

- ▶ Every increase of one ACE was associated with 32% higher odds of NMPO use for males and 24% for females.
- ▶ Delinquency was a strong and consistent mediator across the adolescent and young adult life course.
- ▶ Other mediators included impulsivity, risk taking, anxiety, depression, suicidality.

## DSM 5 PTSD

Criterion A: Exposure to actual or threatened death, serious injury or **sexual violation**. The exposure must result from one or more of the following scenarios, in which the individual:

- ◆ Directly experiences the traumatic event
- ◆ Witnesses the traumatic event in person
- ◆ Learns that the traumatic event occurred to a close family member or close friend (**with actual or threatened death being either violent or accidental**)
- ◆ **Experiences first-hand repeated or extreme exposure to aversive details of the traumatic event (not through media, pictures, television or movies unless work-related)**

# PTSD symptoms

First included in DSM nomenclature in 1980.

## *1. Intrusions*

- (e.g., distressing memories and thoughts, dreams, flashbacks)

## *2. Avoidance*

- (e.g., people/places/situations that are reminders of the event)

## *3. Negative alterations in cognitions and mood*

- (e.g., negative beliefs about self/others, anger, guilt, shame, detached from others)

## *4. Alterations in reactivity*

- (e.g., difficulty sleeping or concentrating, hypervigilance)

# Factors Increasing Vulnerability to PTSD

- ▶ Childhood adversity or childhood trauma
- ▶ Female gender
- ▶ Lower socioeconomic/lower education
- ▶ History of psychiatric illness/family psychiatric hx (including depression, anxiety, panic, personality disorders/traits)
- ▶ Type of trauma - severity/dose, perceived life threat, injury
- ▶ Prolonged or repeated exposure/previous trauma
- ▶ Dissociation during trauma
- ▶ Coping strategies - fatalistic/self-blaming
- ▶ Poor social support following the trauma



# How common is PTSD?

- ▶ Approximately 20% of trauma exposed individuals develop chronic PTSD.
- ▶ General Population: 6.8% – 8.3% lifetime prevalence
- ▶ Veteran populations: 13–20%
- ▶ Treatment-seeking individuals:

SUDs: 20–60% have PTSD

Veteran SUD – 41% have PTSD

PTSD: 22–43% have SUDs

- ▶ Female: Male ratio is 2:1
- ▶ More than 1 / 3 of people with PTSD fail to recover.

*Kilpatrick et al., 2013; Kessler et al., 1995, 1998, 2005  
Jakupcak et al., 2010; Petrakis et al., 2011; Greene et al., 2016*



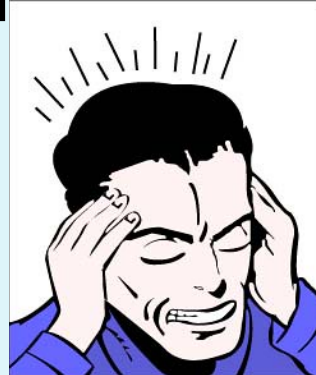
# PTSD in Primary Care



- ▶ Point prevalence of diagnosis via interviewer-rated PTSD ranges between 2% to 32.5%.
- ▶ Median rate of 12.5% in civilian and 24.5% in veteran primary care individuals.
- ▶ Lifetime prevalence via interviewer-rated diagnosis ranges from 14.5% to 44.3%.
- ▶ 20–40% of injured survivors experience PTSD or depression in the year following the injury.

# Chronic Pain and PTSD

- ▶ Rates of PTSD within the general population of chronic pain is about 9.8% (.7%–50%).
- ▶ 66% of Veterans presenting to PTSD clinic had chronic pain diagnosis.
- ▶ Those with current comorbid chronic pain and PTSD (versus those without PTSD)
  - Have shown higher subjective pain ratings
  - More significant pain-related problems and pain-related functional impairment
  - High rates of prescription opioid use for pain management, especially among women
  - Avoidance symptoms were significantly related to opioid medication use.

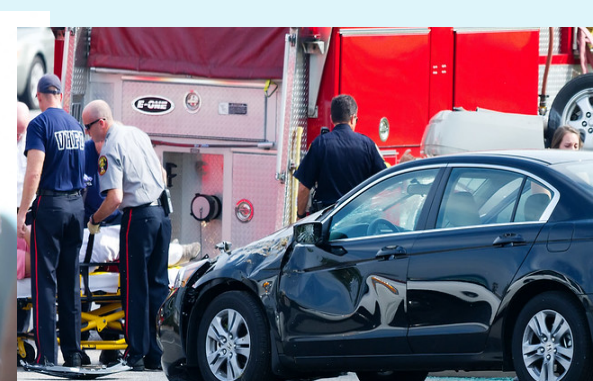


Phifer et al., Pain. 2011;152:2233–2240;  
Fishbain et. al, 2017



# Sources of chronic pain in patients with PTSD

- ▶ Combat related
- ▶ Domestic violence
- ▶ Physical and/or sexual abuse
- ▶ Traumatic Injury – car/vehicle accident, fire, work related accident, injuries from catastrophic events



# Temporal relationship of chronic pain and PTSD

- ▶ Individuals experience event that leads to chronic pain and PTSD.
  - Traumatic event with physical injury and chronic pain increases the risk for PTSD (MVA, sexual abuse/pelvic pain).
- ▶ Individuals with a history of PTSD develop chronic pain.
- ▶ Individuals with chronic pain experience a traumatic event and develop PTSD.

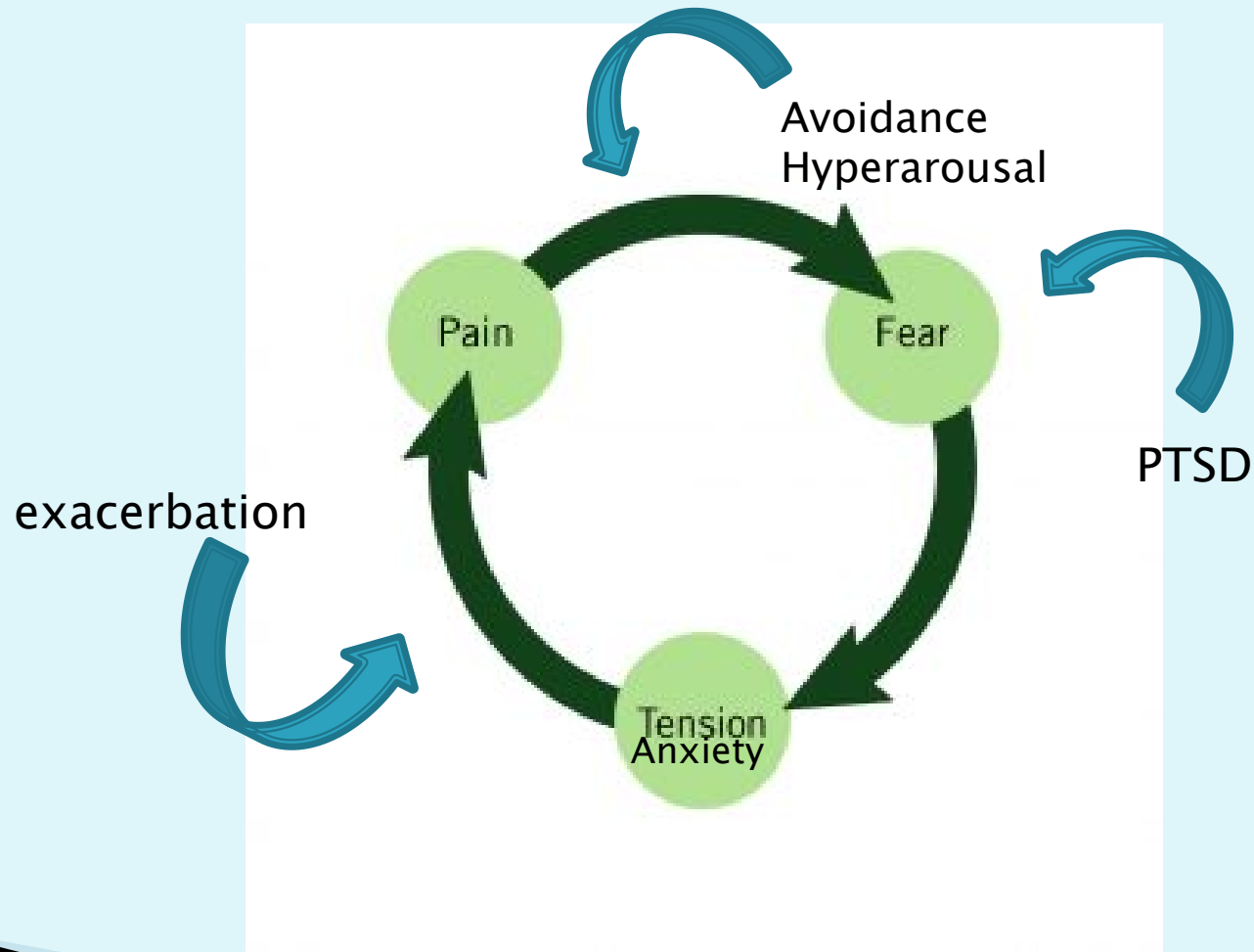
# Theories on chronic pain/PTSD association

- ▶ **Mutual maintenance model** – pain serves as a reminder of trauma, triggering arousal response thereby maintaining PTSD symptoms.
- ▶ **Shared vulnerability model** – both share elevated anxiety sensitivity (fear/arousal elicited beliefs that pain sensations have harmful consequences).
- ▶ **Fear avoidance model** – physiologic sensations of arousal are misinterpreted as being pain related and elicits fear response and reinforces avoidance.

Fishbein et al., 2017;  
Asmundson et al., 2002)



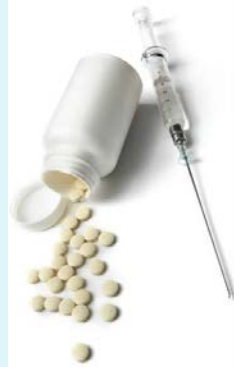
# PTSD and Pain



# Comorbid OUD and PTSD



- NESARC-III National Epidemiologic Survey on Alcohol and Related Conditions wave 3 (N = 356 **adults** with OUD)
  - ▶ 21.8 – 59.5% reported child maltreatment.
  - ▶ 17 – 34% of individuals with OUD had a past year comorbid PTSD.
  - ▶ Those with > 2 other SUD in addition to OUD were over 4 more likely to have active PTSD.

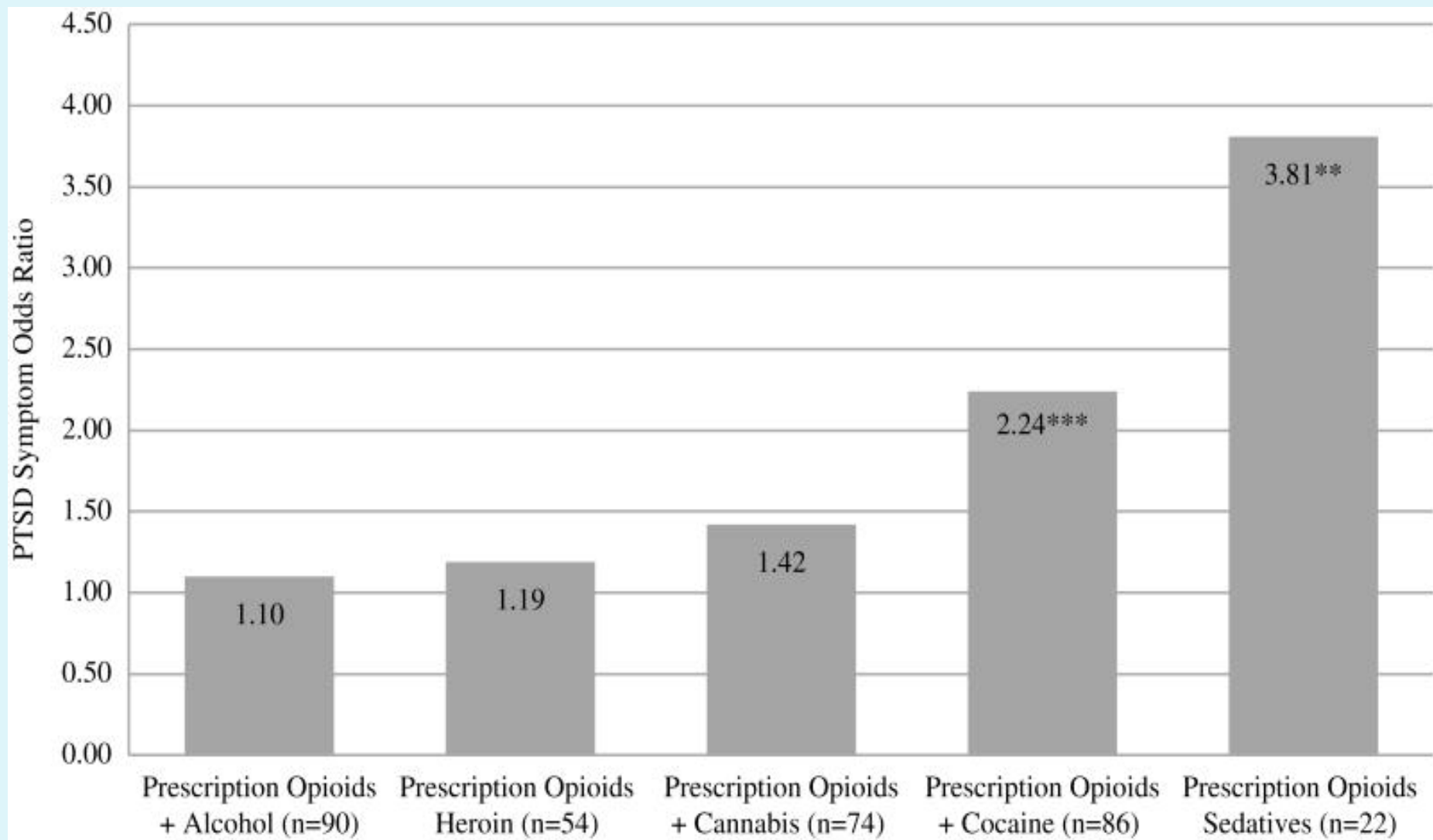


# PTSD with OUD compared to PTSD without OUD

- ▶ More likely to have other SUD (OR; 2.4), particularly sedatives and amphetamines
- ▶ More SUD hospitalizations
- ▶ Higher PTSD symptom severity, particularly in the avoidance cluster
- ▶ More depression and anxiety







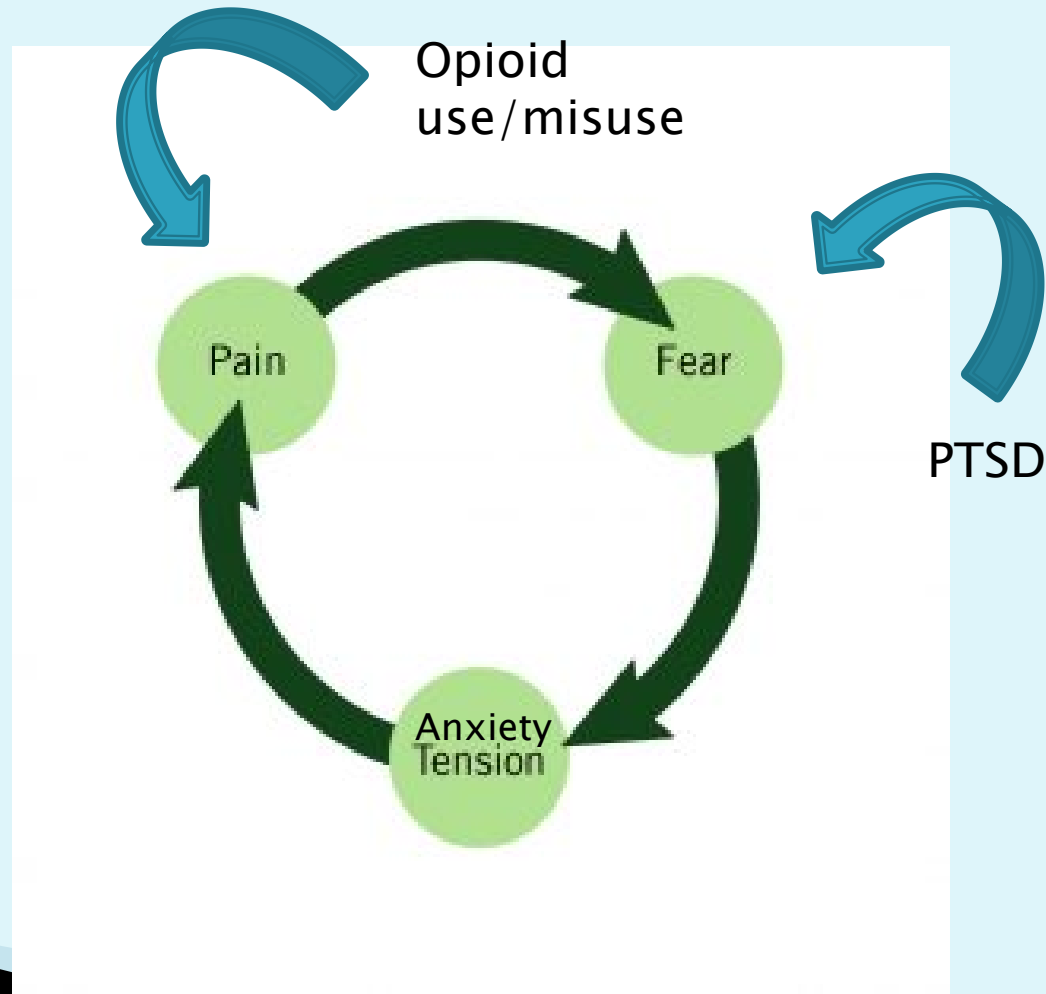
- ▶ Odds ratios for posttraumatic stress disorder (PTSD) symptom severity by prescription opioid use problem in combination with other substances ( $n = 573$ )

# PTSD and chronic opioid use

- ▶ Opioid use is common in veterans with 23% OIF/OEF/OND veterans receiving opioids and 35% in those with TBI (FY 2009–2012).
- ▶ Factors associated with chronic use included younger age, male, white race, being married, living in rural settings.
- ▶ Comorbid **PTSD**, depression and tobacco use associated with chronic opioid use.
- ▶ Back pain and increasing pain severity associated with PTSD among those with chronic opioid use.



# PTSD, Pain and OUD



# PTSD+SUD Commonly Co-Occurs and has Negative Outcomes



More severe  
clinical profile



Poorer treatment  
outcomes

Substance use  
& mental health

Physical health

Psychosocial

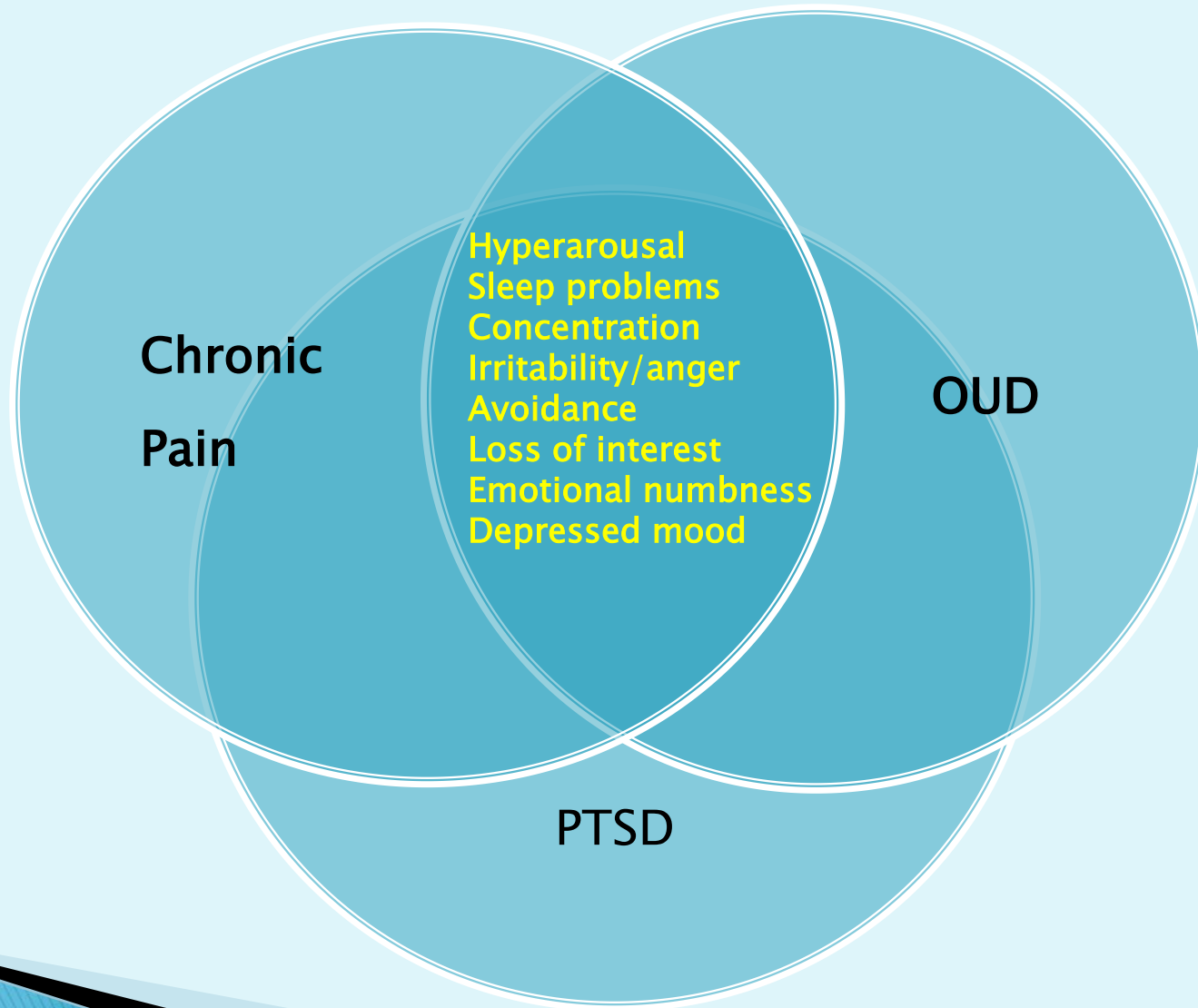
- More polysubstance use
- Earlier age onset substance use/longer durations of use
- Other mental health problems
- Poorer physical health/HIV risk behavior
- Poorer psychosocial functioning
  - Unstable living conditions
  - Legal/ Unemployment
  - Domestic violence

(Back et al., 2000; Brady et al., 2009; Killeen et al., 2015; Mills et al., 2005; Torchalla et al., 2012; Ouimette et al., 2006; van Dam et al., 2012)

# Models of PTSD/SUD Functional Associations

- ▶ **Self medication Model** – substance use to ease PTSD symptoms.
- ▶ **High Risk Model** – substance use increases risk for trauma exposure and/or affects perceptions of danger cues.
- ▶ **Susceptibility Model** – substance use interferes with natural process of recovery from PTSD (i.e. emotional processing) and substance withdrawal increases PTSD symptoms (anxiety, hyperarousal).
- ▶ **Shared vulnerability Model** – noncausal associations but rather shared risk factors (i.e. genetic, environmental) and personal characteristics.
- ▶ **Mutual Maintenance Model** – bidirectionality of PTSD/SUD mutually maintain and exacerbate the symptoms of both disorders.

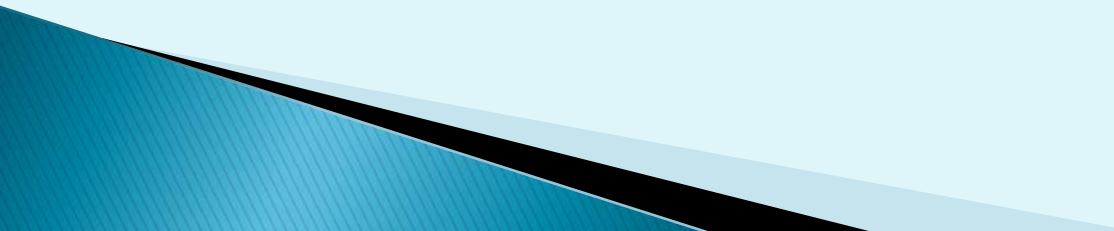
# Symptom Overlap





# Screening in Primary Care

# Trauma Screening question

- ▶ Have you ever experienced or witnessed a traumatic event such as a serious accident, natural disaster, physical or sexual abuse, rape or other stressful event?
  - ▶ Do you find that you are still affected by the event?
- 

# Screening for PTSD in Primary Care

## Primary Care PTSD Screener (PC-PTSD)

In your life, have you ever had any experience that was so frightening, horrible or upsetting that, in the past month, you:

- 1. Have had nightmares about it or thought about it when you did not want to?
- 2. Tried hard not to think about it or went out of your way to avoid situations that reminded you of it?
- 3. Were constantly on guard, watchful, or easily startled?
- 4. Felt numb or detached from others, activities, or your surroundings?
- 5. Felt guilty or unable to stop blaming yourself or others for the events(s) or any problems the event(s) may have caused?

cut off score of 4 for maximal efficiency or **3 for maximal sensitivity**

(Prins et al., 2016)

# PTSD Checklist (PCL-5) Abbreviated

In the past month, how much were you bothered by:

1. Repeated, disturbing, and unwanted memories/thoughts of the stressful experience?
2. Avoid activities and situations because they remind your of the stressful experience?
3. Having strong negative beliefs about yourself, other people or the world?
4. Feeling jumpy or easily startled?

Suggested cut-off of 10 (scale from 0 = not at all to 4 = extremely)

# Treatment

## **EMOTIONAL PAIN**

**PAIN IN THIS LIFE IS NOT  
AVOIDABLE, BUT THE PAIN  
WE CREATE AVOIDING PAIN IS  
AVOIDABLE.**

**RD LAING, MD**

**TRAUMAANDDISSOCIATION  
[WWW.DISSOCIATIVE-IDENTITY-DISORDER.NET](http://WWW.DISSOCIATIVE-IDENTITY-DISORDER.NET)**

# How do we treat comorbid PTSD/SUD?

- ▶ Sequential Model – SUD first, then PTSD
- ▶ Parallel Model – SUD and PTSD, different clinicians
- ▶ Singular Model – Treat the “primary” disorder
  - Treat only the SUD
  - Treat only the PTSD
- ▶ *Integrated Model* – SUD and PTSD together, same clinician



# Integrative Model of PTSD/SUD Treatment

Both conditions concurrently, by the same clinician.



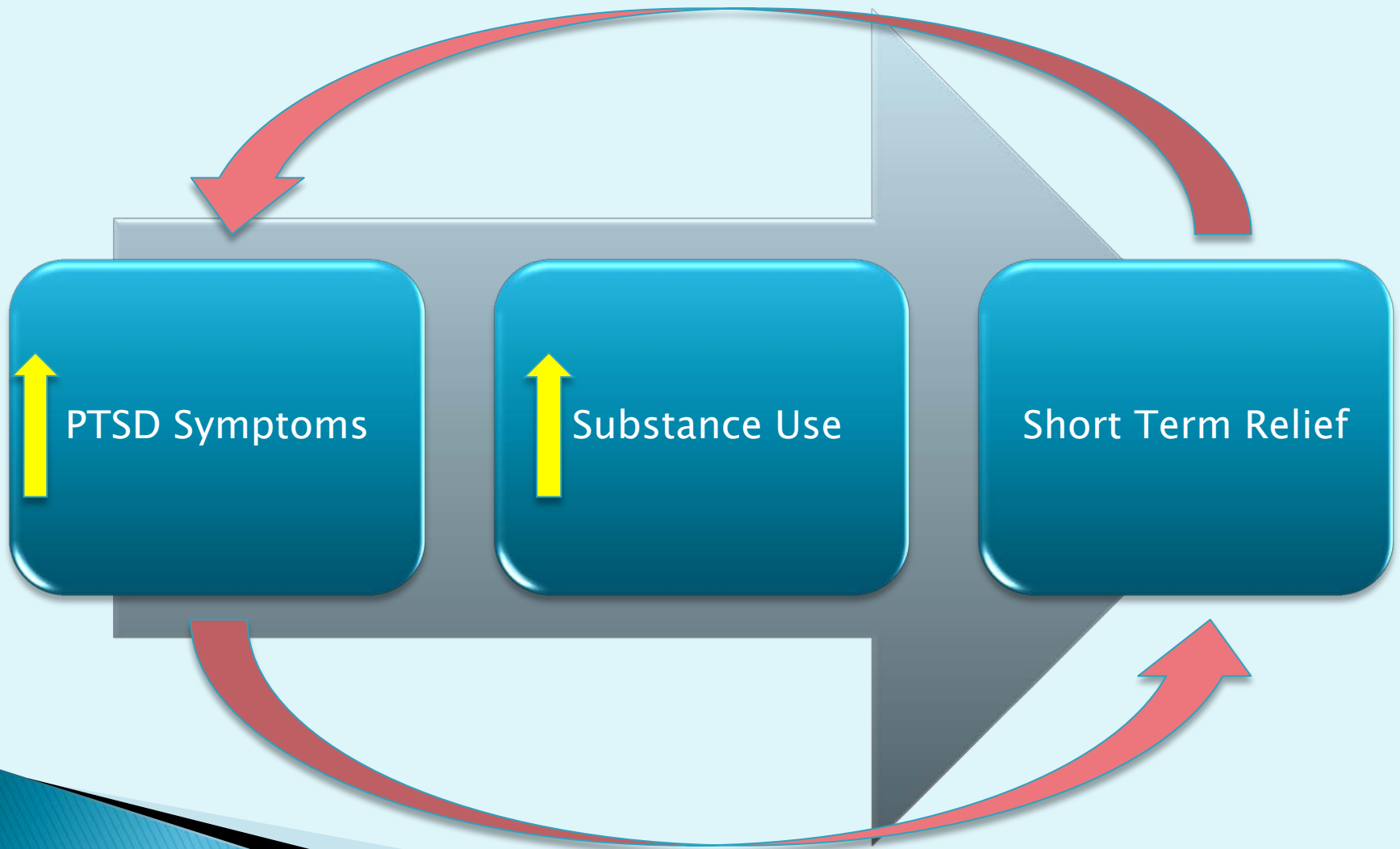
Clinic  
#1

Integrative model driven by:

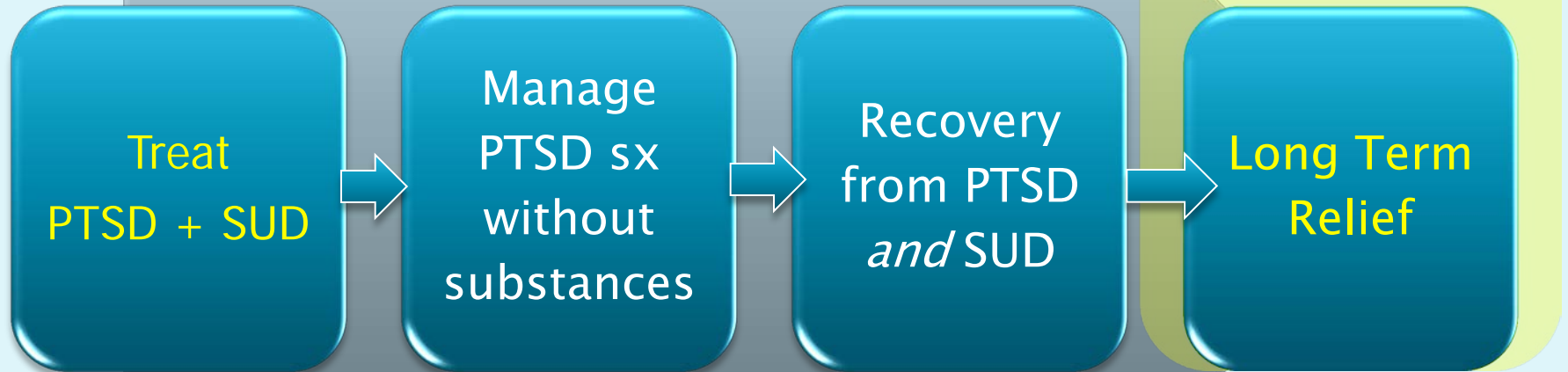
- a) Hypothesis that PTSD sx lead to substance abuse.
- b) Data showing reductions in PTSD symptom severity are more likely to lead to improvement in SUD, than the reverse.
- c) Research on patient preferences.
- d) Efficacy and effectiveness research demonstrating improved PTSD and SUD outcomes.

# Overview of PTSD – SUD Connection

Self Medication Hypothesis (Khantzian, 1985)



# Overview of PTSD - SUD Integrative Treatment



# Trauma treatment in Veterans with comorbid PTSD and OUD

- ▶ Chart review of consecutive referrals (N = 140) to Buprenorphine maintenance therapy.
- ▶ 67 or 47.9% with PTSD Dx.
- ▶ Veterans treated with buprenorphine who received concurrent PTSD treatment (N=21 (31.3%)) were more likely to remain on buprenorphine maintenance at 6 months (90.5%) compared to those who did not receive concurrent treatment (23.9%) and those without PTSD (46.6%).
- ▶ Older age and having a heroin use history (lower than use of pills) was associated with retention.

# Treatment Approaches

## ▶ Trauma Informed –

- Psychoeducational – understanding the functional relationship between OUD and PTSD (i.e. Seeking Safety, TREM)

## ▶ Trauma Focused –

- Cognitive Processing Therapy (CPT)
- Prolonged Exposure (PE)
  - Primary Care Prolonged Exposure (PC-PE)
- Integrated PE and SUD relapse prevention therapy (COPE)

## ▶ Pharmacotherapy



# SUD-PTSD Integrated Psychotherapies

Najavits (2002) - Seeking Safety Relapse prevention + education + affect management

Back, Foa, Killeen et al. (2014) - Relapse prevention + in vivo exposure + imaginal exposure. COncurrent treatment of PTSD and Substance Use Disorders with Prolonged Exposure or COPE



# Techniques Used in COPE Intervention

- Coping Skills Training - decrease SUD symptom severity , initiate and maintain abstinence or goal use reduction.
- Psychoeducation – education about common reactions, normalize symptoms, help understand avoidance & how it maintains PTSD symptoms.
- Breathing Retraining technique to decrease anxiety.
- Prolonged Exposure (PE):
  - In-Vivo Exposure
  - Imaginal Exposure



# Exposure Therapy

- ▶ A set of techniques designed to help clients approach their feared objects, situations, places, conversations, memories, and images in a safe, therapeutic manner.

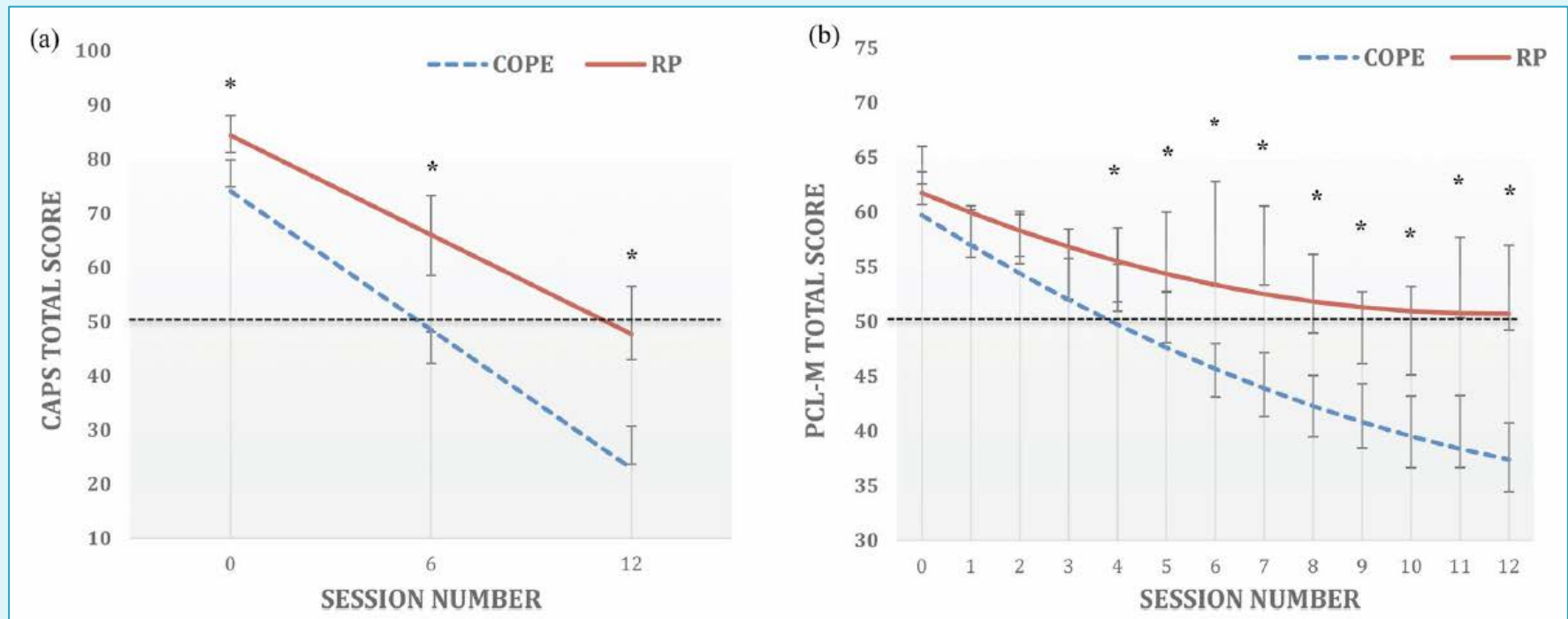


# Concurrent treatment of substance use disorders and PTSD using prolonged exposure: A randomized clinical trial in military veterans

Sudie E. Back<sup>a,b,\*</sup>, Therese Killeen<sup>a</sup>, Christal L. Badour<sup>c</sup>, Julianne C. Flanagan<sup>a</sup>, Nicholas P. Allan<sup>d</sup>, Elizabeth Santa Ana<sup>a,b</sup>, Brian Lozano<sup>a,b</sup>, Kristina J. Korte<sup>e</sup>, Edna B. Foa<sup>f</sup>, Kathleen T. Brady<sup>a,b</sup>

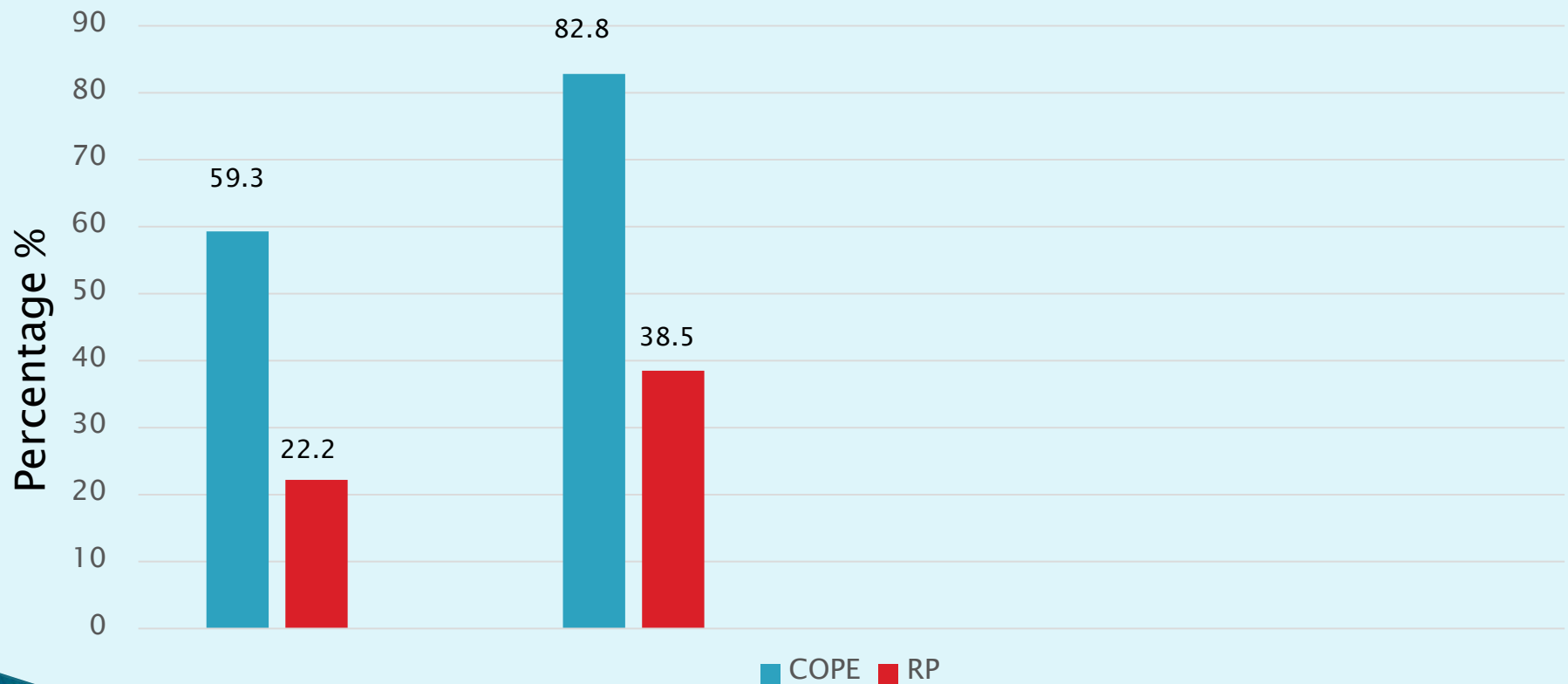
Addictive Behaviors 90 (2019) 369–377

- N=81 military veterans
- Mean age = 40
- 90.1% male, 60.5% White, 37.0% Black/African American
- 81% had military-related index trauma



- COPE had significantly lower PTSD symptoms (CAPS and PCL-M), higher rates of PTSD diagnostic remission (OR = 5.3), and lower depression (BDI) than RP at end of treatment. Treatment gains maintained during 6-month follow up.

# PTSD Diagnostic Remission: ITT and Completers



# PTSD and SUD symptom change during treatment

- Direct test of mediation models of symptom change using lagged multilevel mediation

Model 1: Does Change in PTSD mediate change in substance use?

**55.5% of the change in substance use is mediated by change in PTSD symptoms**

Model 2: Does change in substance use mediate change in PTSD symptoms?

**5.3% of the change in PTSD symptoms is mediated by change in substance use**

# Modified PE in individuals with PTSD and AUD with and without OUD

- ▶ 60 minute session length for 9–12 sessions
- ▶ Psychoeducation about the PTSD/SUD relationship
- ▶ Breathing retraining
- ▶ Imaginal and real-life exposures
- ▶ In the PTSD/AUD with OUD group treated with mPE, large reductions in PTSD symptom severity (CAPS score from BL to post tx: 87.2 – 41.4), sleep disturbances, anxiety, depression, alcohol craving similar to those without OUD.
- ▶ mPE shows efficacy in PTSD/AUD with OUD comparable to PTSD/AUD without OUD.

# Collaborative Behavioral Care Models

- ▶ Several attempts to create collaborative behavioral models in PC (VA and FQHC) for PTSD.
- ▶ Care management to enhance communication, coordination and the referral process between primary care and mental health providers through use of care managers.
- ▶ Involves education, weekly case management, initial in-person visit, regular follow-up telephone or in-person contact, telehealth psychotherapy.

Hoerster et al., 2015; Schnurr et al., 2013



# PTSD treatment in primary care

## Benefits

- ▶ Improved outreach for PTSD screening and treatment
- ▶ Less stigma
- ▶ Primary care treatment/ not mental health
- ▶ Higher motivation to receive treatment in primary care clinic
- ▶ Increased retention
- ▶ Improvement in other comorbid medical conditions

## Shortcomings

- ▶ Absence of brief therapies
- ▶ Typically more trauma informed care
- ▶ Not receiving a full dose of treatment

# Prolonged Exposure– Primary Care (PC–PE)

- ▶ Four brief trauma focused sessions delivered in four 30 minute PC appointments.
- ▶ Patients asked write a first person, detailed narrative of most distressing traumatic event.
- ▶ Narrative includes addressing accompanying personal thoughts, feelings and physical sensations.
- ▶ Record level of distress (0–100) before and after writing assignment.
- ▶ Assignment includes emotional processing questions:
  - How has this event changed how you think of yourself?
  - How has this event changed how you think of others?

# PE-PC vs Minimal Contact Control

	PE-PC N=34	MCC N=33	p value	ES
PCL Total (BL)	49.8(12.8)	52.2(14.1)		
PCL (8 weeks)	38.9	48.7	.02	-.55
PTSD Dx % (BL)	59%	67%		
PTSD Dx % (8 weeks)	37%	63%	.11	-.38
PTSD Dx % (6 months)	26%			

# Pharmacotherapy

- ▶ Best outcomes are when combined with an evidence based psychosocial therapy.
- ▶ Medications have different targets.
  - Alcohol and other drugs
  - PTSD symptoms
  - Facilitate efficacy of psychosocial therapies

# Medications that target mood and affective states

- ▶ Selective serotonin reuptake inhibitors (SSRI's)– Sertraline, Paroxetine
- ▶ Norepinephrine reuptake inhibitor (NRI's)– Desipramine
- ▶ Serotonin norepinephrine reuptake inhibitors – Venlafaxine

Brady et al. 2005; Petrakis et al, 2012;  
Hien et al., 2015

# Medications targeting adrenergic activity

- ▶ Propranolol – Beta1 adrenergic antagonist that can disrupt memory reconsolidation of fear conditioning following a trauma.
- ▶ Prazocin – alpha adrenergic antagonist – reduction in PTSD nightmares/improvement in sleep and daytime hyperarousal symptoms/– reduces alcohol use/craving

# Medications that target AUD/SUD

## Alcohol

- ▶ Naltrexone –  
opioid antagonist
- ▶ Acamprosate –  
NMDA modulator
- ▶ Disulfiram –  
acetaldehyde  
dehydrogenase  
inhibitor

## Drugs (opioids)

- ▶ Naltrexone
- ▶ Buprenorphine
  - Suboxone
  - Sublocade
  - CAM 2038
- ▶ Methadone



# Buprenorphine vs opioid therapy in managing individuals with chronic pain, OUD and PTSD

- ▶ Retrospective cohort of Veterans N=382 with OUD, chronic pain and PTSD initiated on buprenorphine vs high dose opioid therapy.
- ▶ Twice as many veterans treated with buprenorphine vs opioid therapy had improvements in PTSD symptom severity (23.7% vs 11.7%).
- ▶ Improvements maintained at 8 and 24 months.
- ▶ No differences in pain ratings.

# Buprenorphine/naloxone and PTSD

- ▶ Retrospective chart review exploring Bup/naloxone vs opioid therapy vs SSRI in VA patients screening positive for PTSD.
- ▶ Bup/naloxone patients exhibited the lowest final average PTSD score (2.47) and the largest change from baseline (−24%) compared to opioids (−16.1%) or SSRIs (−1.16%).
- ▶ The average buprenorphine dose was 23.3 mg/day, and the average length of therapy was 860 days.

(Lake et al, 2019)

# Medications that target GABA and glutamate

- ▶ Topirimate –GABA receptor agonist and a glutamate receptor antagonist
- ▶ N-acetylcystine – normalizes intracellular glutamate levels in the nucleus acumbens
  - Modest reduction in cocaine use/craving
  - Adolescent cannabis use but not adults

Blodgett et al., 2014; Johnson et al., 2014; Watts et al., 2013; Batki 2014; Gray et al., 2014; Brown et al., 2013;Back et al, 2016

# Summary

1. PTSD, chronic pain and OUDs are highly comorbid necessitating PTSD screening in both OUD and CP pts.
2. In PC, target PTSD, SUD and CP together using a collaborative care management.
3. Integrated, trauma-focused treatments (including exposure-based) lead to reduced PTSD and SUD, *not* increased use.
4. Pharmacotherapy has limited effectiveness without adjunct psychotherapy.
5. Benzodiazepines contraindicated in exposure based therapies and responsible for many overdoses when combined with opioids.

