Integrated Treatment for Veterans with Chronic Pain and Hazardous Opioid Use

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HSR&D Cyberseminar
Spotlight on Pain Management

3 March 2020

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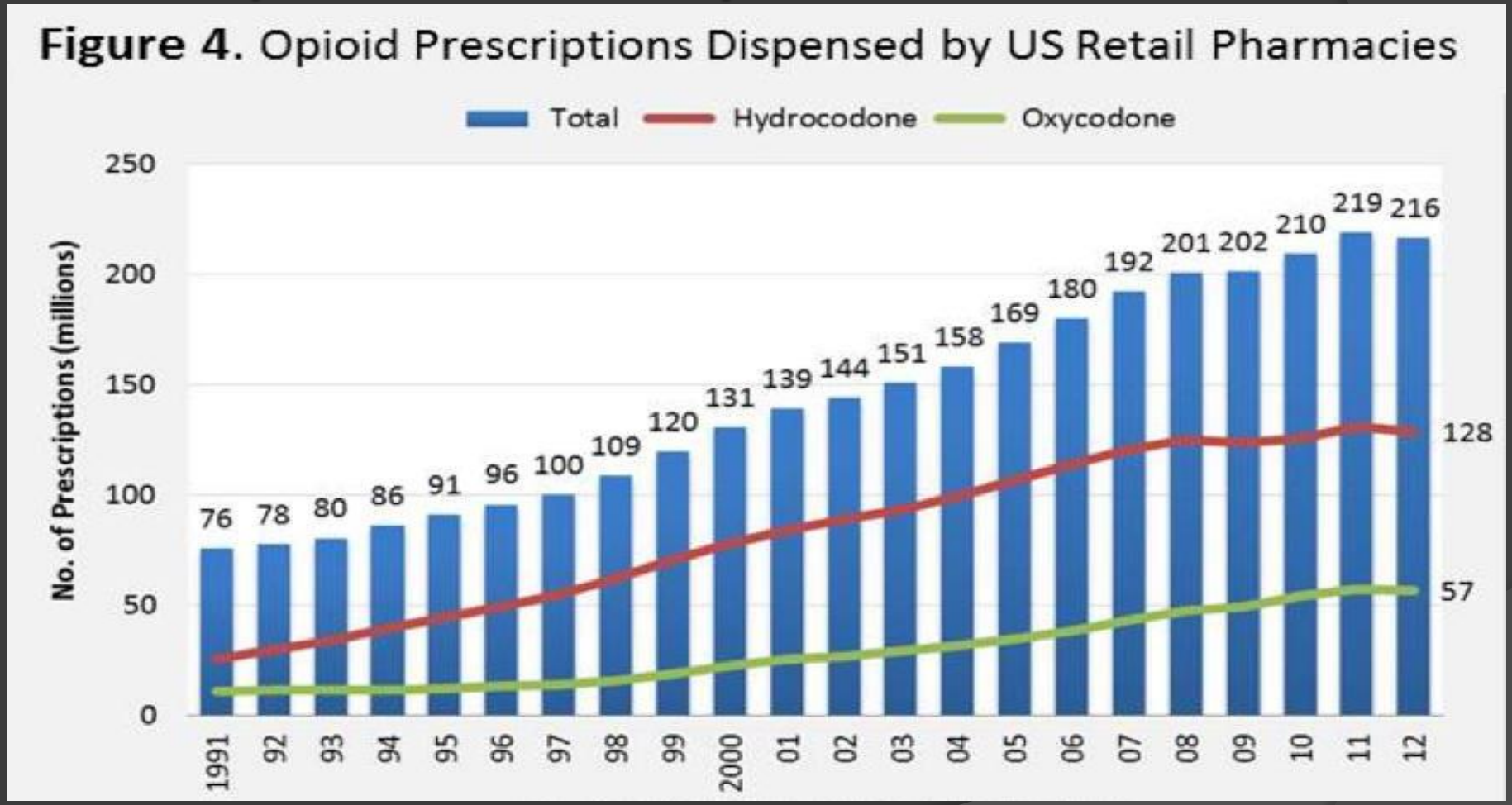
Overview

- History and context of opioid prescribing
- Scope of problematic opioid use in chronic pain
- An integrated behavioral treatment
  - Pilot results
  - Ongoing trial

History of Opioid Prescription

- Prior to mid 1980's, restricted for surgery, recovery from severe injury, or end of life.
  - Porter and Jick (1980, *New England Journal of Medicine)* – letter to the editor
  - Portenoy & Foley (1986; *Pain*) - case series
    - 38 patients on opioids followed for > 7 yrs
    - 24 patients reported "adequate pain relief"
    - No systematic dose increase over the years
    - 2 patients (both with a h/o substance abuse) had problems

Net Result 1:
Explosion of Opioid Use



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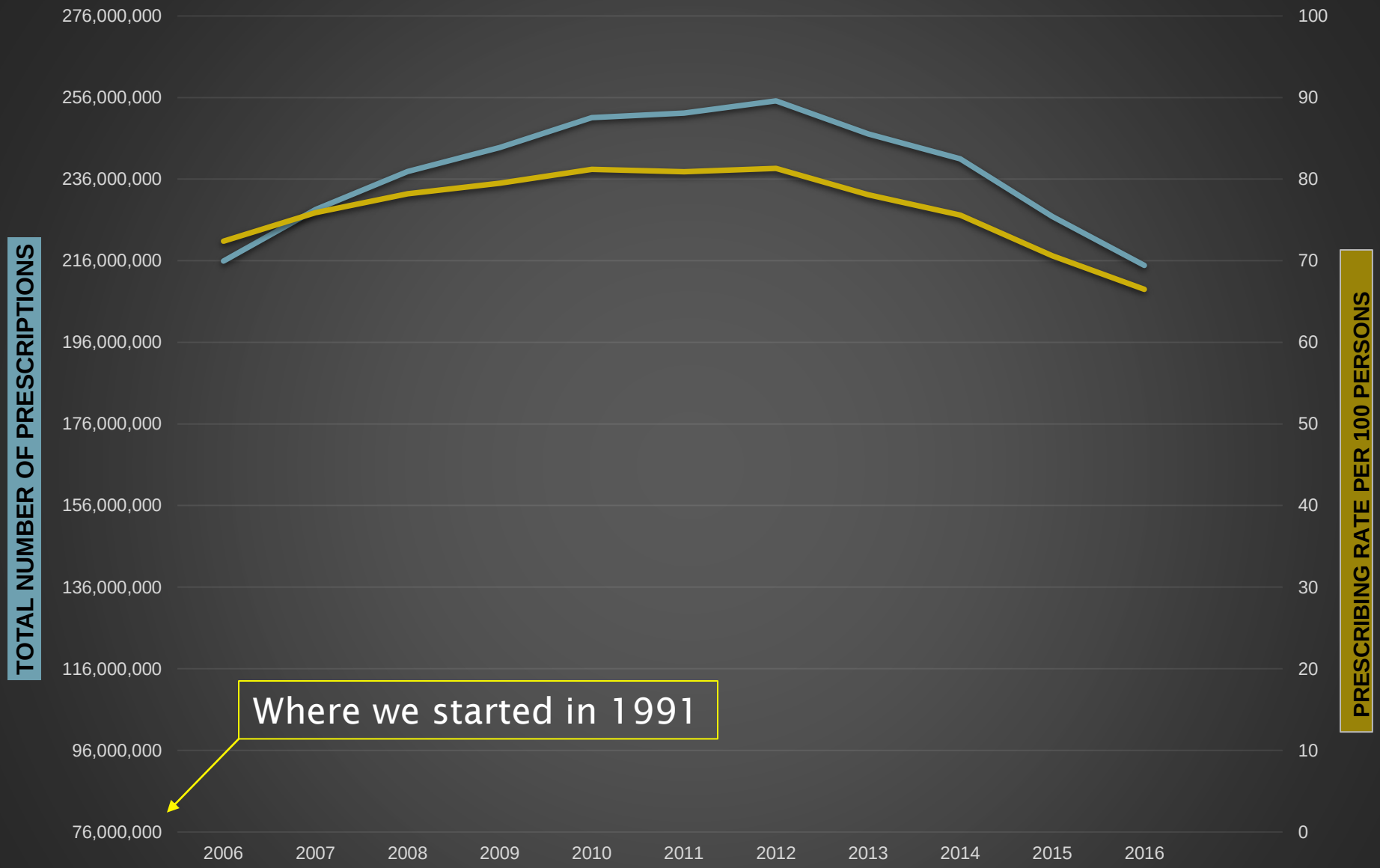
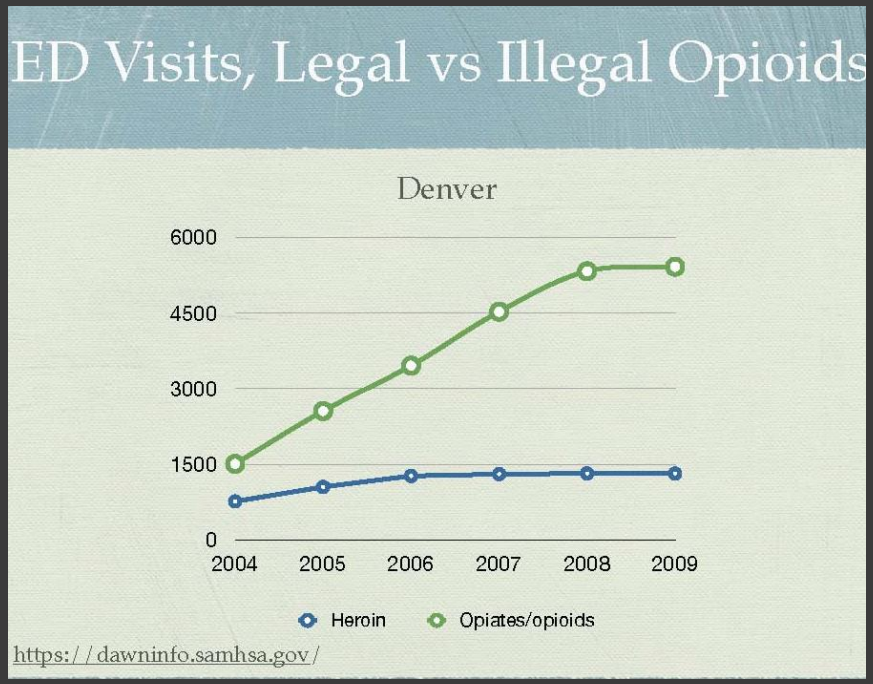
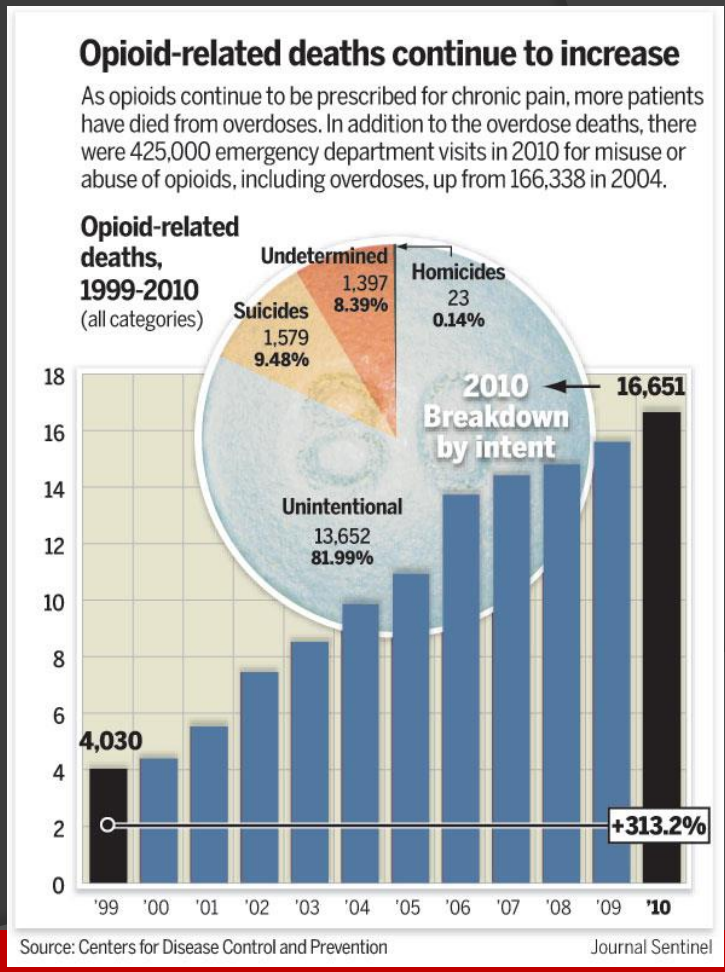
From: Volkow, 29 April 2014 Presentation to Congress. IMS Health, National Prescription Audit, Years 1997 2013. www.drugabuse.gov/about nida/legislative activities/testimony to congress/2015/prescription opioid heroin abuse



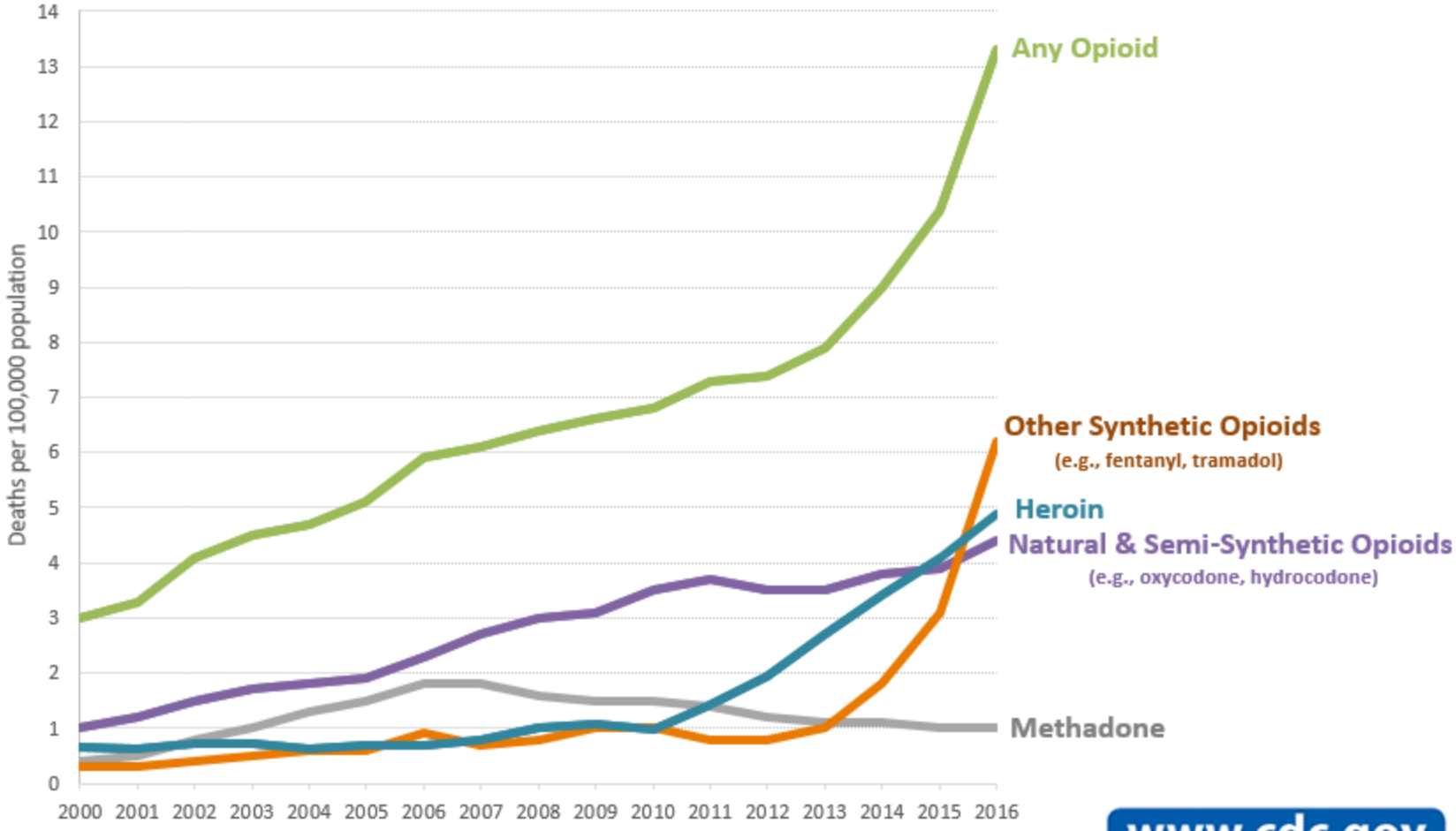
CDC, 2017; from: https://www.cdc.gov/drugoverdose/maps/rxrate-maps.html

Net Result 2:
Explosion of Opioid-Related Problems





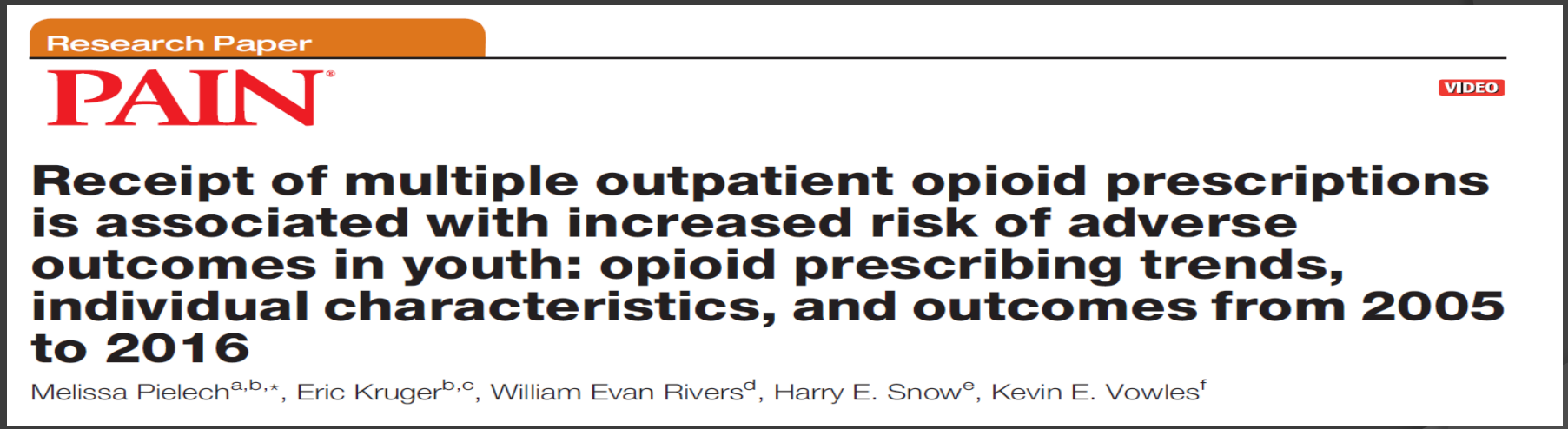
Overdose Deaths Involving Opioids, by Type of Opioid, United States, 2000-2016



SOURCE: CDC/NCHS, National Vital Statistics System, Mortality. CDC WONDER, Atlanta, GA: US Department of Health and Human Ser vices, CDC; 2017. https://wonder.cdc.gov/.

www.cdc.gov
Your Source for Credible Health Information

Brief sidenote – What about kids?



Research Paper

PAIN

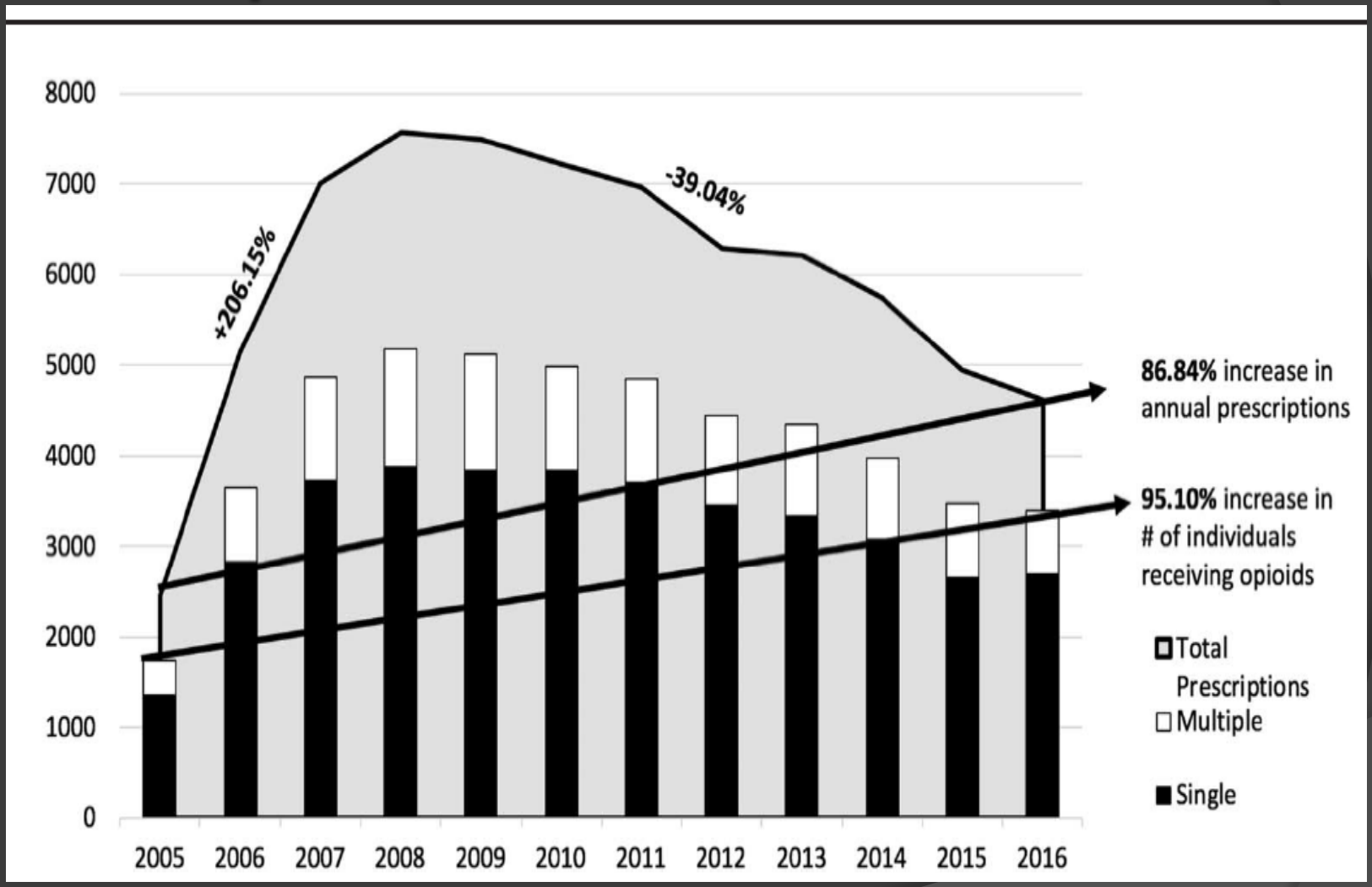
VIDEO

Receipt of multiple outpatient opioid prescriptions is associated with increased risk of adverse outcomes in youth: opioid prescribing trends, individual characteristics, and outcomes from 2005 to 2016

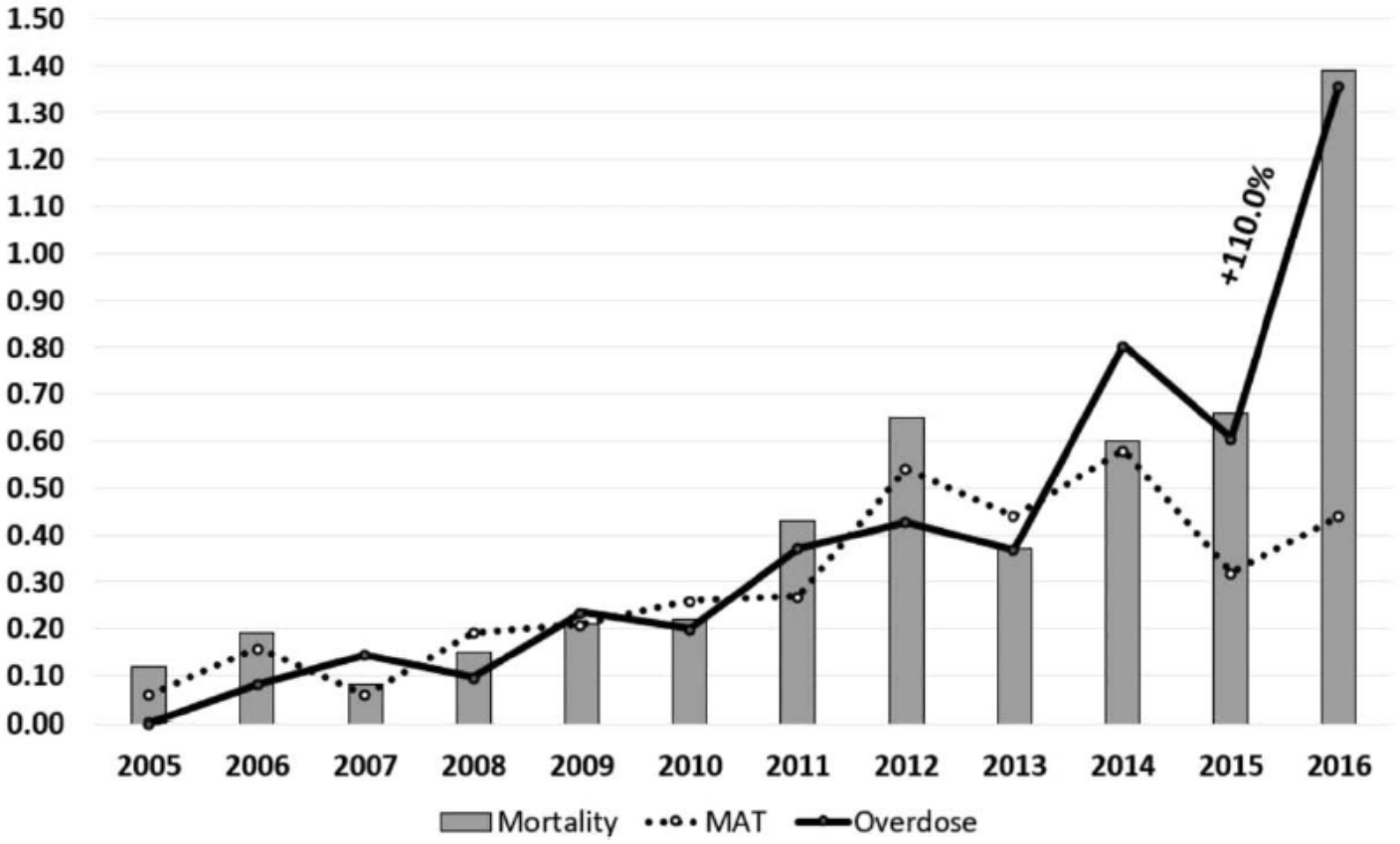
Melissa Pielech[a,b,*], Eric Kruger[b,c], William Evan Rivers[d], Harry E. Snow[e], Kevin E. Vowles[f]

Funder: New Mexico Center for Regional Studies

Prescriptions



Morbidity and Mortality



2200% increase in cases of mortality

1400% increase in cases receiving MAT

1433% increase in incidence of overdose

Conclusions thus far:

- Rates of opioid prescriptions have increased over the past three decades.
- Increased rates of problematic opioid use and impact have tracked this increase in prescription.
- *Question: How many individuals with chronic pain are using opioids in a hazardous manner?*

Defining the scope:

- Højsted & Sjøgren (2007). "Addiction to opioids in chronic pain patients: A literature review." *Eur J Pain*
  - **0% to 50%**
- Martell et al. (2007). "Opioid treatment for chronic back pain: Prevalence, efficacy, and association with addiction. *Ann Int Med*
  - **3% to 43%**

Potential source of poor precision

Terminology — *Misuse, abuse, addiction, aberrant use, dependence, nonmedical or nontherapeutic use, physical dependence, psychological dependence, and "pseudoaddiction".*

e.g., O'Connor + 38 authors. (2013), *Pain*; Smith + 22 authors (2013), *Pain;* Webster & Fine (2010), *J Pain.*

A review of the literature

- Purpose: *Clarify/Refine current estimates regarding rates of problematic (prescribed) opioid use in chronic pain.*

- Coded for different patterns of use:
  - **Misuse**: not using as prescribed; harm neutral
  - **Addiction**: use associated with demonstrated or marked potential for harm

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Funder: Center for Health Policy; Robert Wood Johnson Foundation

Vowles, McEntee, Siyahhan Julnes, Frohe, Ney, & van der Goes. (2015). *Pain*

To increase precision in estimates:

- Estimates were weighted by:
  - Raw Sample Size
  - Log Sample Size
  - Winsorized Sample Size
  - Quality (0-8; based on Chou et al., 2009)
    - >5 quality = “High Quality”
  - Log Sample Size x Quality*

Information Flow

Search terms

<chronic pain> + <opioid (+ synonyms)> + <1+ opioid "use" terms>

Inclusion/Exclusion Criteria

- Adults
- Chronic non cancer pain
- Oral opioids
- Abstract listed 1+ of "use" terms
- Quantitative information provided regarding use

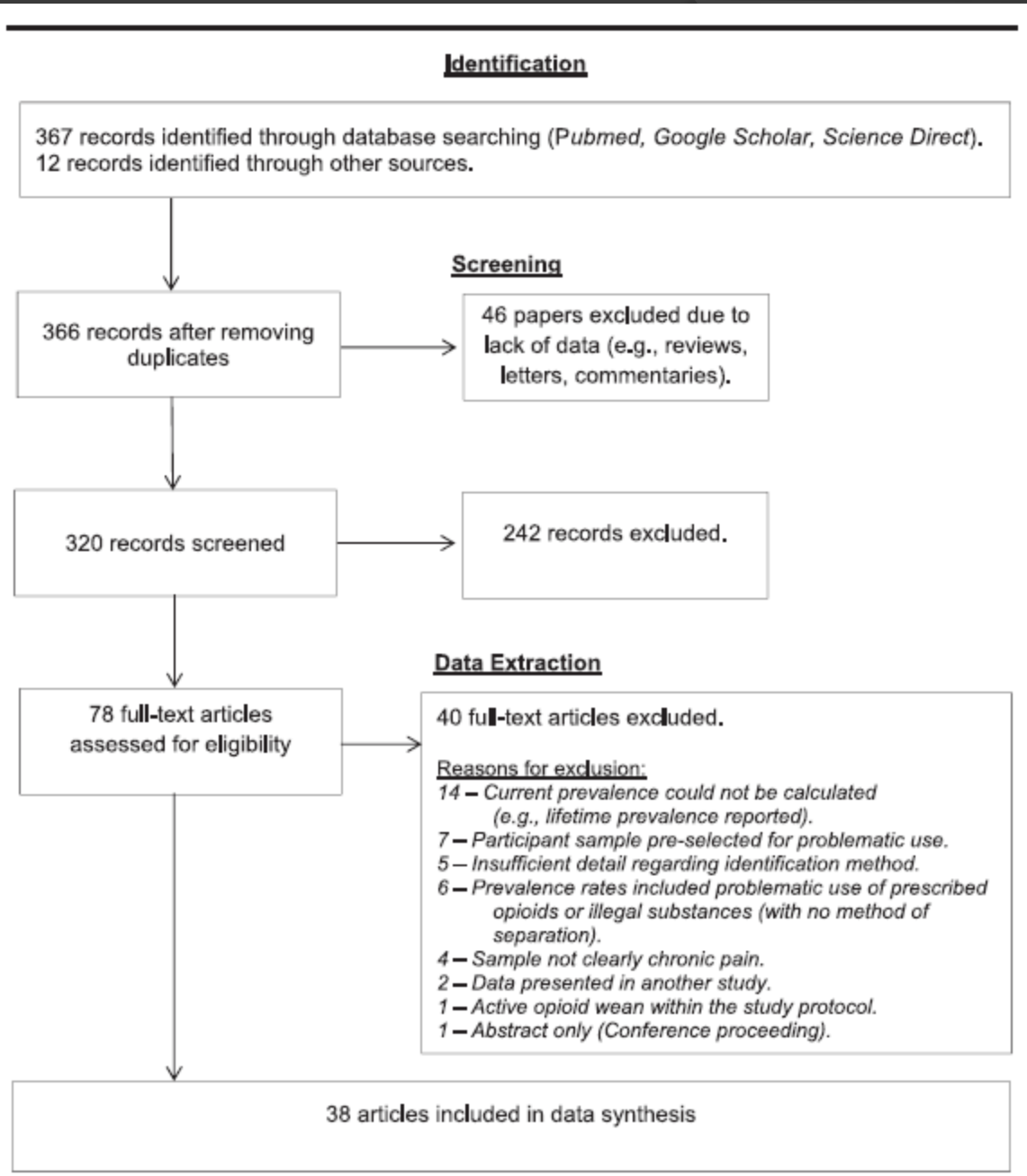

Figure 1. Flow of information thought the different phases of the review, as specified by the PRISMA statement.

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Overall results

- 29 studies reported on rates of misuse
- 12 studies reported on rates of addiction

- Many studies reported a range, therefore Minimum and Maximum rates of misuse/addiction were calculated.

Opioid Misuse Results

	Minimum		Maximum	
	Mean (SD)	95% CI	Mean (SD)	95% CI
Unweighted				
Weighted means:				
Sample Size				
Log Sample Size				
Winsorized				
Quality Rating				
Sample Size x Quality				
Quality:				
High Quality Studies				
Low Quality Studies				

Opioid Addiction Results

	Minimum		Maximum	
	Mean (SD)	95% CI	Mean (SD)	95% CI
Unweighted				
Weighted means:				
Sample Size				
Log Sample Size				
Winsorized				
Quality Rating				
Sample Size x Quality*				
Quality:				
High Quality Studies				
Low Quality Studies				

Overall conclusions

- The literature has some inconsistencies . . .
  - Raw range observed across studies:
    - Misuse: 0.08% to 81%
    - Addiction: 0.7% to 34.1%

- Some degree of convergence around:
  - Misuse: 21.7%-29.3% (95% CI: 13%-33%)
  - Addiction: 8.8%-10.7% (95% CI: 3%-16%)

Utility of opioids?

- Unclear benefit for long-term pain relief or short-term functional gains (e.g., Krebs et al., 2018)
- High side-effect profile*
- Potential for misuse/addiction*
- Additional treatment requirements
  - *with few integrated treatments for pain-related disability AND hazardous use available?*

Pragmatic issue for psychology

- Chronic pain remains prevalent.
- Hazardous substance use is either on the rise or more on our radar.
- Need to offer integrated treatments to reduce:
  - Hazardous opioid use AND pain interference

ELSEVIER

The Journal of Pain

Available online 21 November 2019

In Press, Journal Pre-proof

Original Reports

Integrated behavioral treatment for Veterans with co-morbid chronic pain and hazardous opioid use: A randomized controlled pilot trial

Kevin E. Vowles PhD [1], Katie Witkiewitz PhD [2], Karen J. Cusack PhD [3], Wesley P. Gilliam PhD [4], Karen E. Cardon MD [3], Sarah Bowen PhD [5], Karlyn A. Edwards MS [1], Mindy L. McEntee PhD [6], Robert W. Bailey PhD [7]

NCCIH: R34AT008398 (PI: Vowles)

Chronic pain and opioid use in Veterans

- Up to 68% have chronic pain[1-5]
  - Up to 66% of these are prescribed opioids for treatment of chronic pain[6]
    - ~50% of these receiving 180 mg+/day MED[6]

- Chronic pain diagnosis doubled risk of Substance Use Disorder diagnosis[7]
- Opioid prescription independent risk of AE/SAE[8]

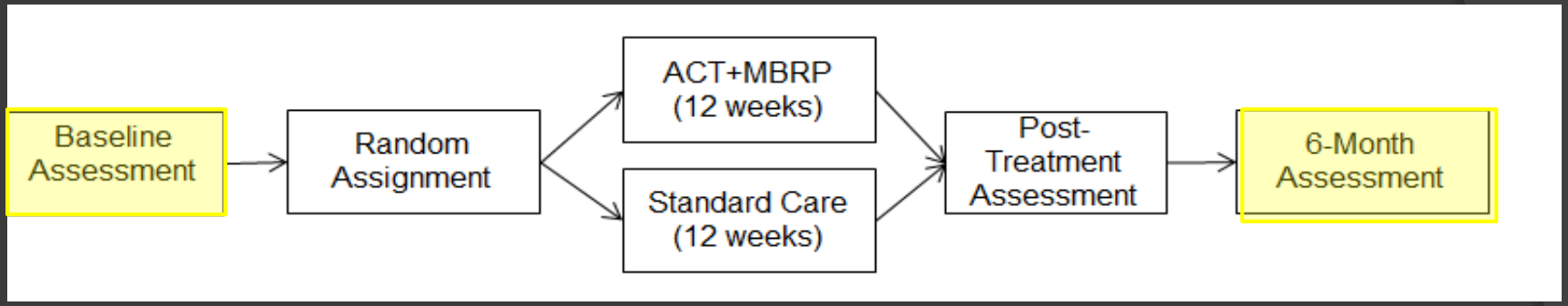
Present Study

- Sought to determine whether two behavioral interventions with empirical support for chronic pain and SUD, respectively, could be combined to treat Veterans.
  - Acceptance and Commitment Therapy (ACT)
  - Mindfulness-based Relapse Prevention (MBRP)
- Recruited Veterans with:
  - Chronic Pain
  - Evidence of Hazardous Opioid Use
    - (COMM $\geq$ 9 and/or SCID-IV diagnosis of OUD)

Treatment Condition Details

- ACT+MBRP - 12 weekly 90 minute sessions
  - ***ACT***: "Strong" empirical support for chronic pain[8]
    - Identify areas of meaningful functioning adversely impacted by pain
    - Learn methods to enhance willingness to have pain in the service of increased engagement with meaningful areas
    - Practice present focused awareness to help with identification of opportunities to engage in meaningful areas
  - ***MBRP:*** *Intended as "*Relapse prevention" add-on; promising results[9 12]
    - Decrease reactivity to substance use cues and craving
    - Cultivating of nonjudgemental and accepting attitude toward craving and automatic thought patterns.
- Standard Care
  - Received by all participants
  - Physician management through VA co-occurring disorders clinic (pain+hazardous opioid use)

Trial Design & Measure Details



COMM: *In the past 30 days:*

- how often have you used your pain medicine for symptoms other than for pain (e.g., to help you sleep, improve your mood, or relieve stress)?

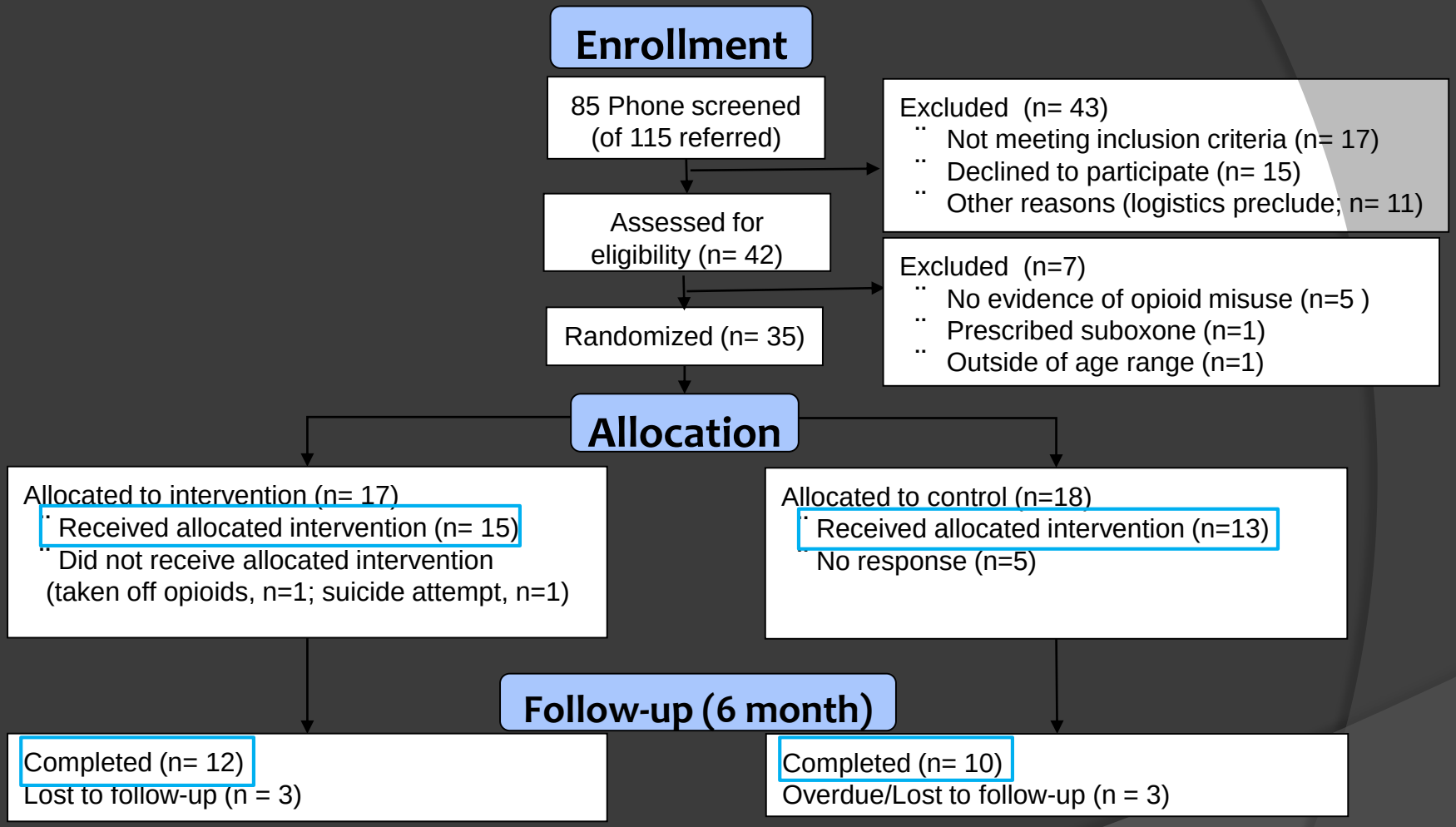
- how often have you been in an argument?

PROMIS Pain Interference (short form 8a): *In the past seven days, how much did pain interfere:*

- with your enjoyment of life?

- with your ability to concentrate?

Recruitment & Retention



Participant characteristics

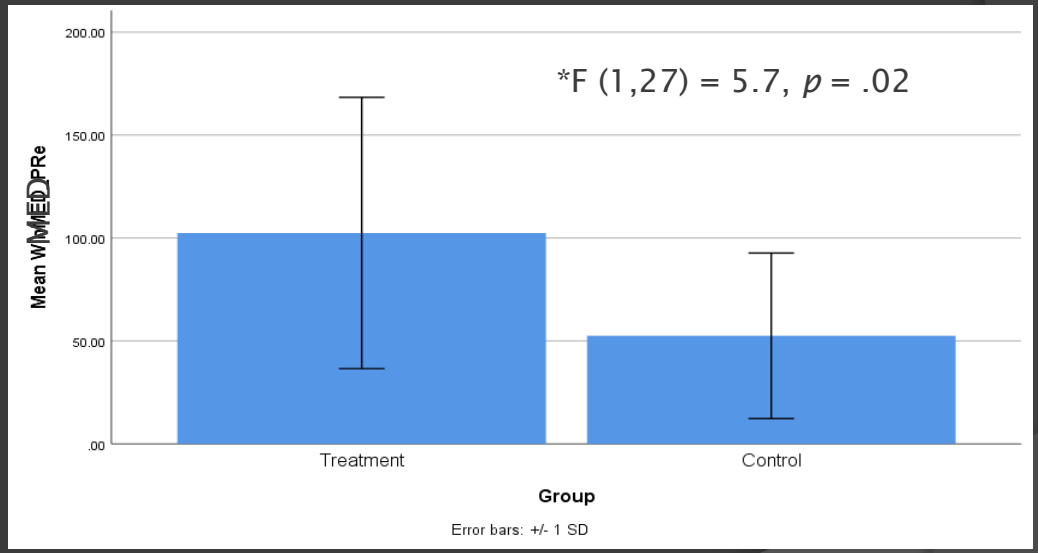
- 86% male
- Age: 51.8 yrs ± 10.1
- Ethnicity:
  - 50% Non-Hispanic white
  - 25% Latinx
  - 18% Native American
- Education: Ave 14.5 (*SD:* 2.1)
  - 11% High school
  - 54% some college
  - 14% tech/trade; 18% college
  - 4% post-grad
- Relationship Status
  - 39% married
  - 32% single
  - 29% divorced/separated
- Pain duration:
  - Ave: 17.2 yrs ± *8.7 yrs*
  - Median: 15.3 yrs (5 – 34)
- Pain Location:
  - 64% Low back,
  - 18% whole body
  - 7% Leg/hip
  - 11% Neck/upper back
- Compensation
  - 61% SS disability
  - 54% service connect
  - 4% other

Feasibility outcomes

- Randomized:
  - 41% of referrals (phone screen)
  - 83% of those formally assessed (in person screen)
- Started treatment: 80%
- Retained: 79% of those who started
  - Lost to follow-up *n* = 6 (3 per arm)
- Intervention arm details (*n* = 15 who started)
  - Session Attendance: 77%
  - 13 (87%) “completed” treatment (i.e., 75%+ attendance)

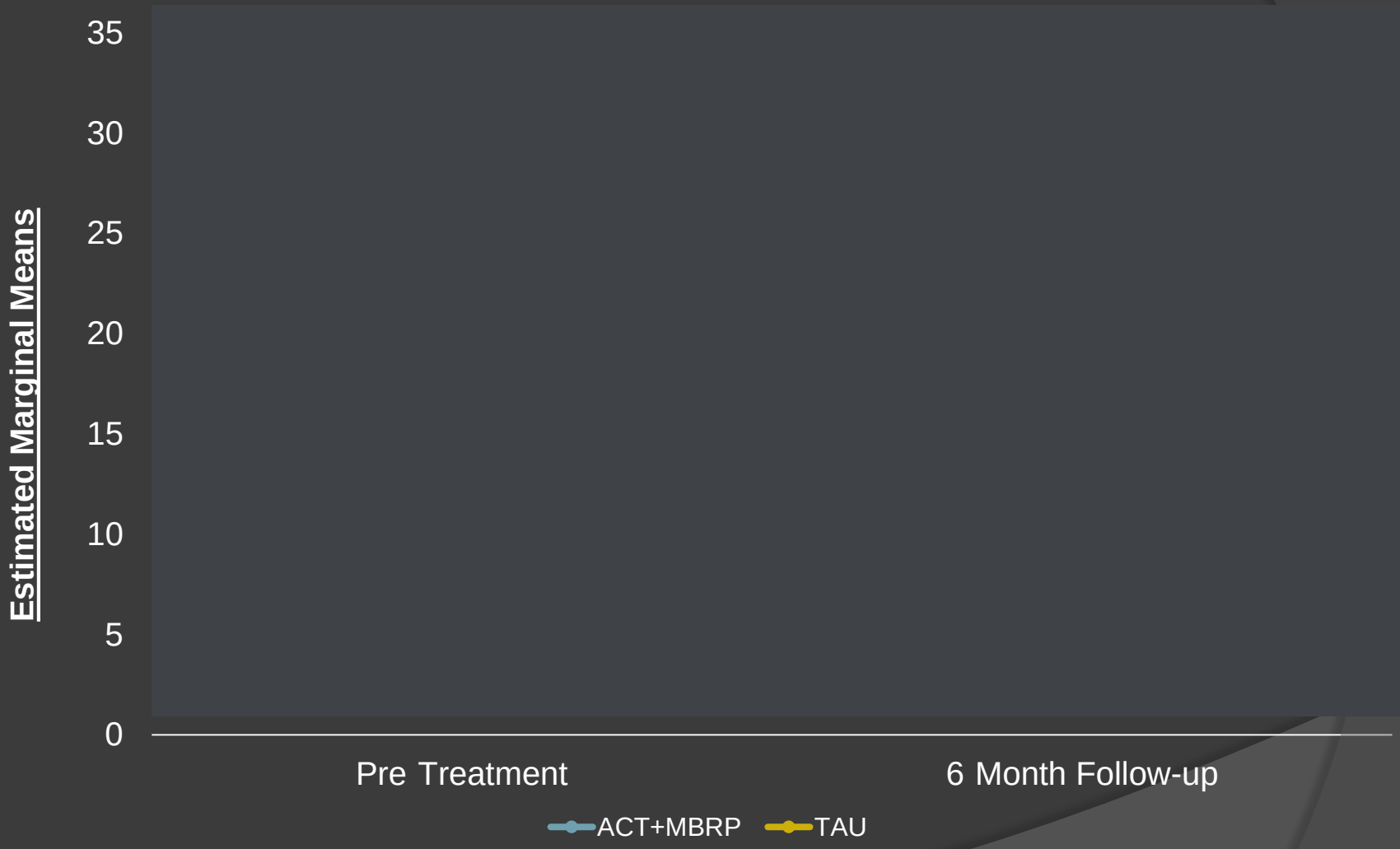
Baseline analyses

- No group differences on demographic or pain-related characteristics
- Except….
  - Opioid dose (MED)



- Proceeded with ANCOVA

Current Opioid Misuse (COMM)



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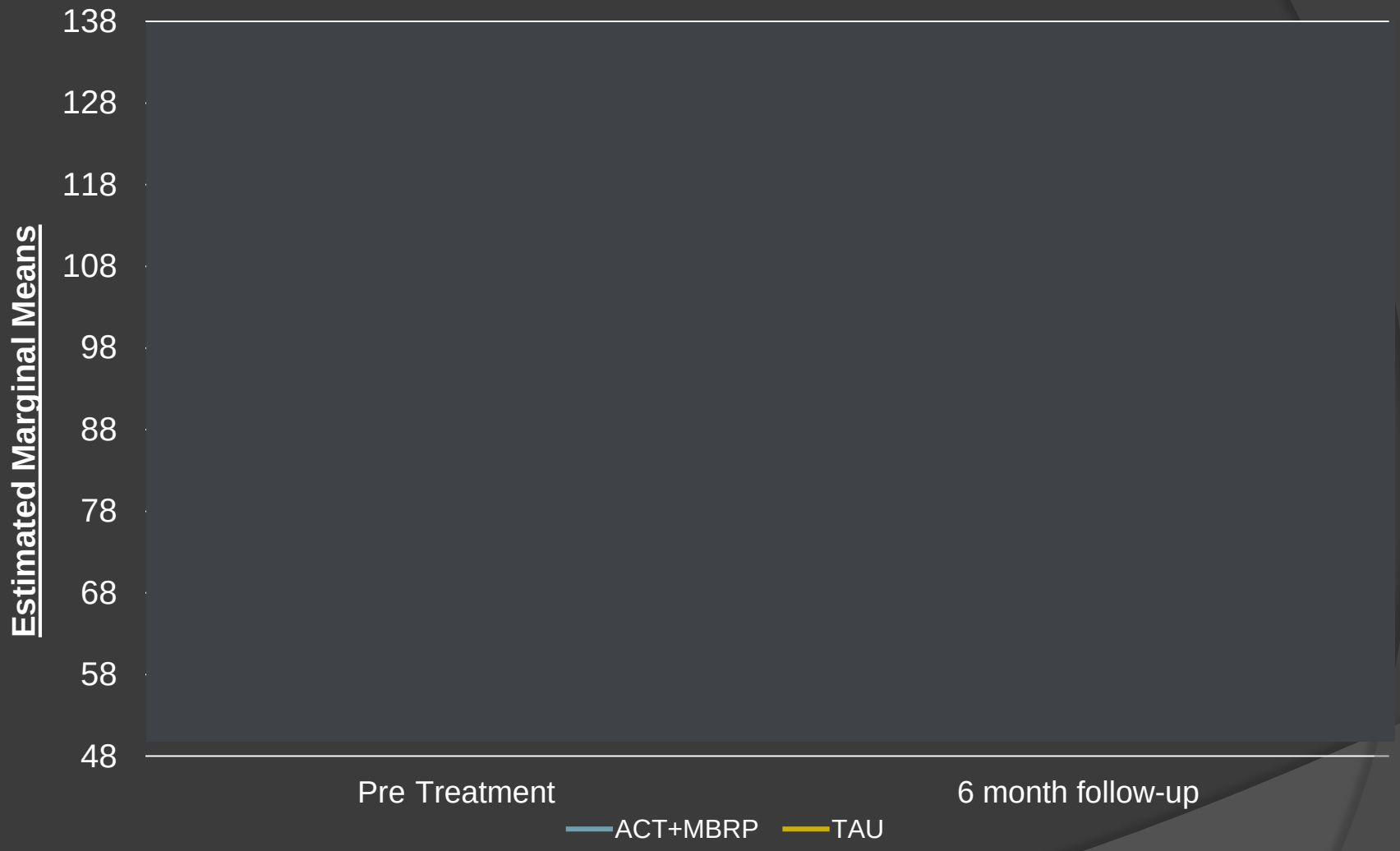
Group*Time Interaction: F = 5.7, p = .027, η_p^2 = .23

Change pre-treatment to 6 month follow-up in relation to Risk of Opioid Misuse

	Stayed "at risk"	Moved to "not at risk"	Total *n*
ACT+MBRP			12
TAU			10

Pain Interference (PROMIS 7a Short form)



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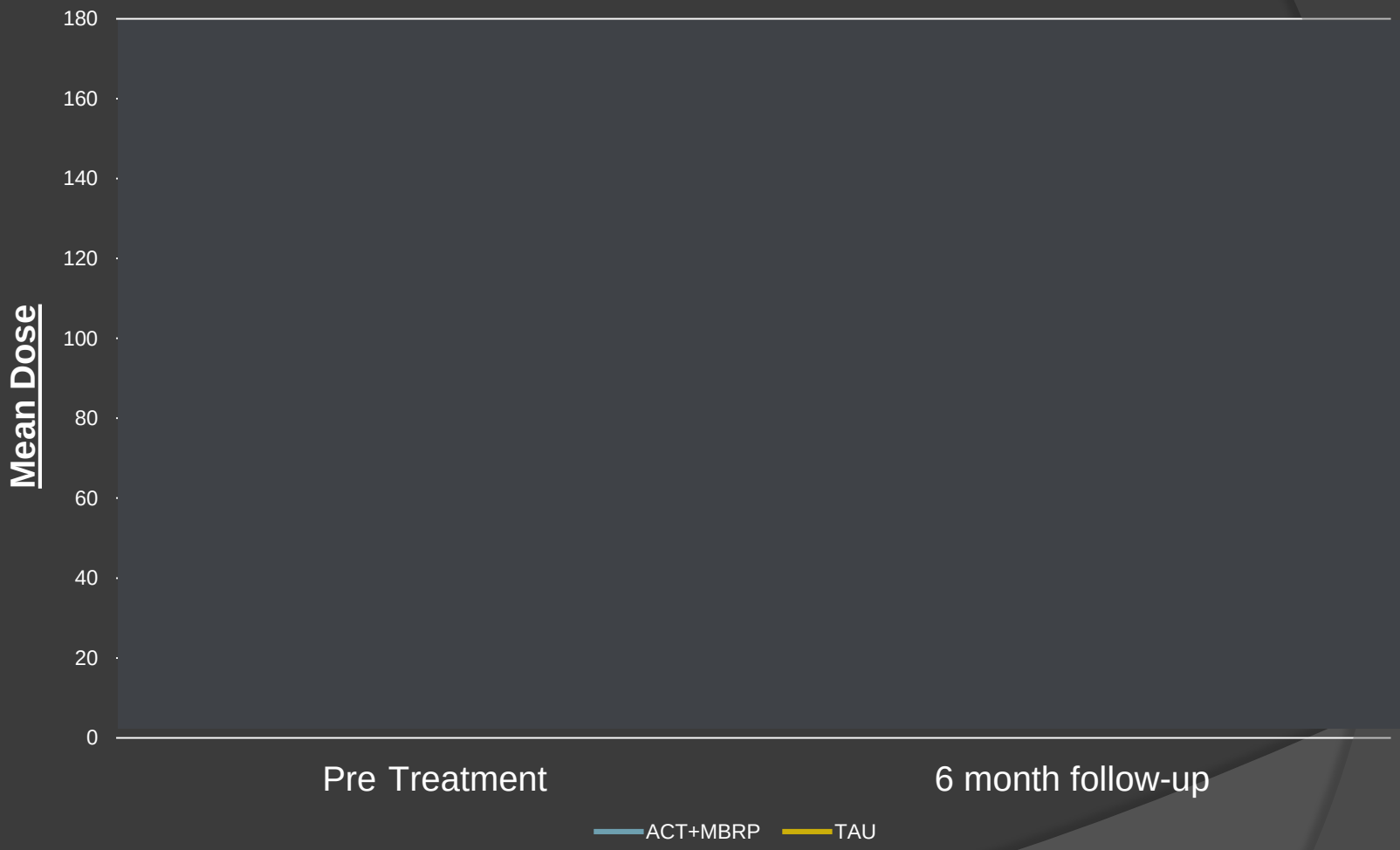
Group*Time Interaction: F = 8.7, p = .009, η_p^2 = .35

Opioid Dose



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Time: F = 8.7, p = .008, η_p^2 = .30
Group*Time Interaction: F = 0.98, p = .35

Interim Conclusions

- Treatment protocol developed; possible to recruit(?) and retain people.
- Treatment seems feasible, with reasonable outcomes.
- Opioids - Form versus function
- Preliminary given pilot nature; requires fully powered follow-up

Integrated Treatment for Veterans with Co-Occurring Chronic Pain and *Opioid Use Disorder*

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NIDA: UG3/UH3 DA051241 (Co PIs: Vowles & Witkiewtiz)

Overall Study Design and Aims

- **Design**: two arm randomized controlled trial to be conducted in two Veteran's Administration medical centers (Albuquerque and Puget Sound).

- **Changes from Pilot**:
  - Active education control (pain neurophysiology, opioids)
  - All participants stabilized on buprenorphine for Opioid Use Disorder prior to enrollment
    - Dosage independent of trial

- **Hypotheses**:
  - H1: Integrated treatment more efficacious (pain interference, substance misuse) than control
  - H2: Treatment mechanisms (pain acceptance, engagement in valued activity, opioid craving) will predict treatment response in integrated condition

Study Milestones

- UG3 Phase (2019-2020)
  - Finalize intervention materials
  - Complete agreements with sites and obtain regulatory approvals
  - Hire and train study and clinical personnel
  - Establish common data elements with other network studies
  - Complete study protocol and obtain approvals for transition to UH3
- UH3 Phase (2021-2024)
  - Recruit 160 participants and enroll in active treatment groups
  - Assess and retain participants through a 12-month follow-up
  - Analyze data and disseminate findings via presentations and publications

Study Endpoints

- Primary Endpoints
  - Significant reduction, significantly greater in ACT+MBRP group, on pain interference (PROMIS pain interference measure)
  - Significant reduction, significantly greater in ACT+MBRP group, on self-reported substance use, biochemically confirmed
- Secondary Endpoints
  - Significant reduction, significantly greater in ACT+MBRP group, on pain intensity (numeric rating scale), depression (PROMIS emotional distress – depression measure), pain-related fear (Pain Anxiety Symptoms Scale), and opioid misuse risk (Current Opioid Misuse Measure)

Conclusions

- The face of behavioral treatment is changing and requires interventions for chronic pain *and* co-morbid substance misuse
- An integrated treatment worked reasonably well in terms of feasibility of retention and effect.
  - Fully powered trial results a long way off.

Acknowledgements

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  - Karly Edwards

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  - Zachary Schmidt
  - Erik Clarke
  - Wes Gilliam
  - Sarah Bowen

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  - VA: RX-18-005

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Thanks for your attention.

Questions?

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