Moving into the Post-opioid Chronic Pain Treatment Era – Opportunities and Challenges

William C. Becker, MD
Core Investigator, PRIME Center of Innovation
VA Connecticut Healthcare System
Associate Professor, Yale School of Medicine

The PRIME Center

Pain Research, Informatics, Multimorbidities, and Education

Enhancing Pain Care for Veterans

Disclosure

I have no conflicts of interest related to the content of this presentation.

The PRIME Center

Pain Research, Informatics, Multimorbidities, and Education

Enhancing Pain Care for Veterans

Outline

Background:

- Chronic pain: pathophysiology and epidemiology
- Opioids' role in chronic pain

Intervention development:

- Management strategies for when harm outweighs benefit
- Novel use of buprenorphine
- Testing/implementing non-pharmacologic approaches

Case presentation

Mr. M is 66-year-old white man with chronic low back pain who presents for evaluation.

CC: "*I'm in a rut*."

PMHx: lumbar spondylosis, PTSD

Pertinent data:

–Morphine SA 60 mg TID, oxycodone IR 10 mg q6 hours;

–Opioid therapy started 2004 at 30 mg MEDD→240 mg MEDD

–Sedentary but intermittent high intensity activity

ROS: Daily moderate-severe back pain interfering with ADLs, nightmares, snoring, erectile dysfunction

Problem list

- Poorly controlled chronic pain
- Opioid tolerance
- Poorly controlled PTSD
- Sleep-disordered breathing
- Erectile dysfunction

- **Sub-optimal treatment of chronic pain**
- **Elevated risk of overdose death**
- **Mismatch between needs and healthcare resources**

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- **Opioids' role in chronic pain**

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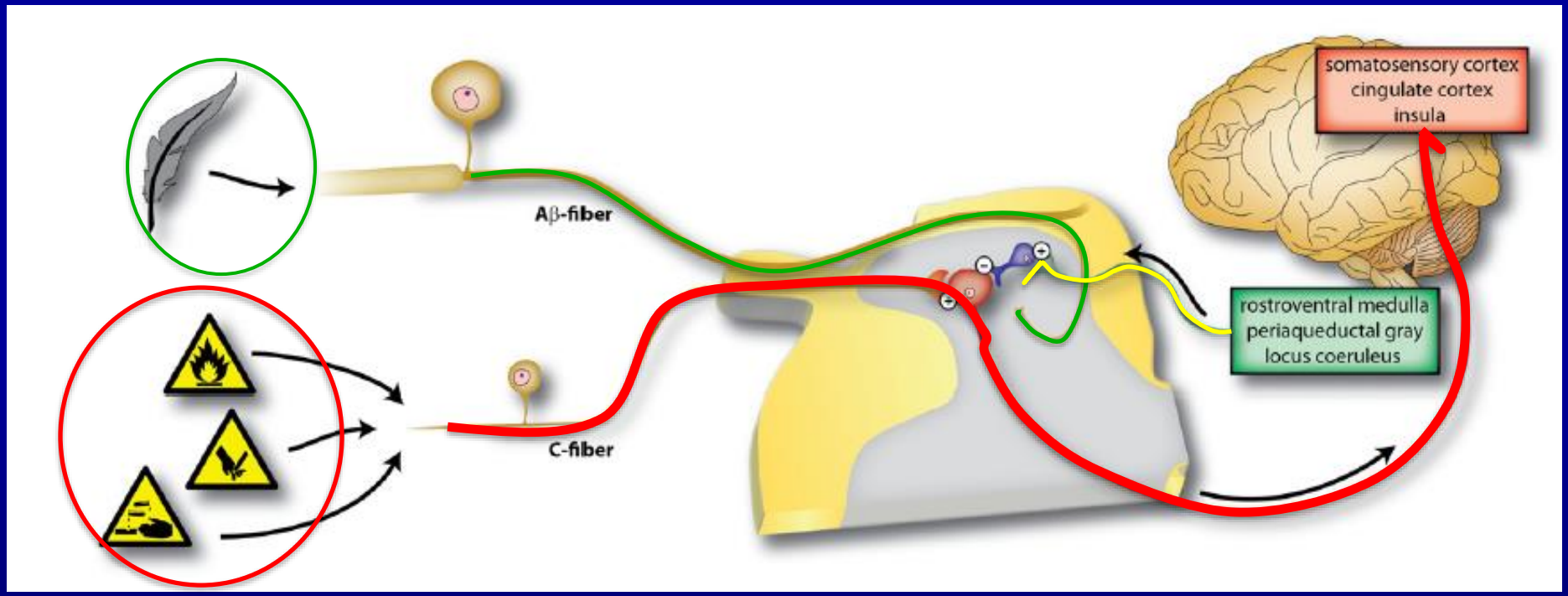
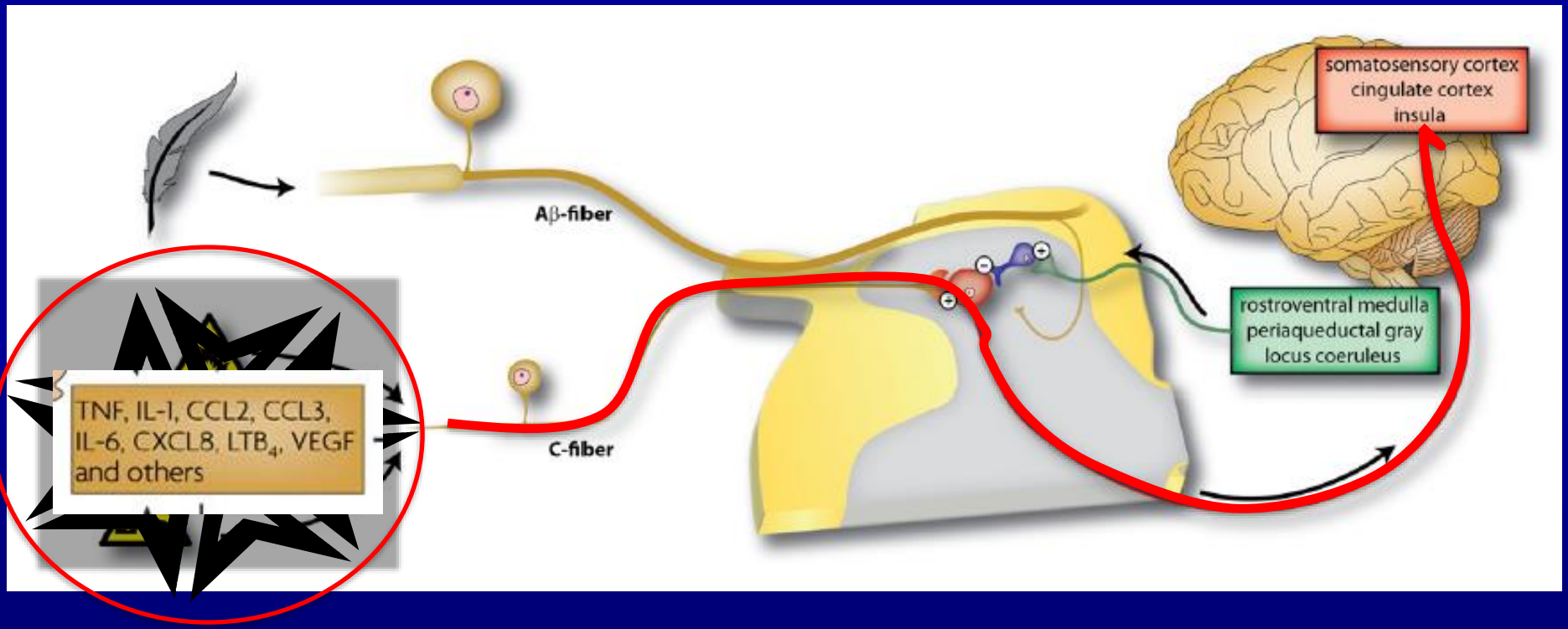
Acute pain



von Hehn CA et al. Neuron 2012

Chronic inflammatory pain



Adapted from von Hehn CA et al. Neuron 2012

Chronic pain: neuronal plasticity and central sensitization

Neuronal plasticity

Peripheral nerve injury → recruitment of macrophages and glial cells → dysregulated nerve regeneration of both AB and c-fibers

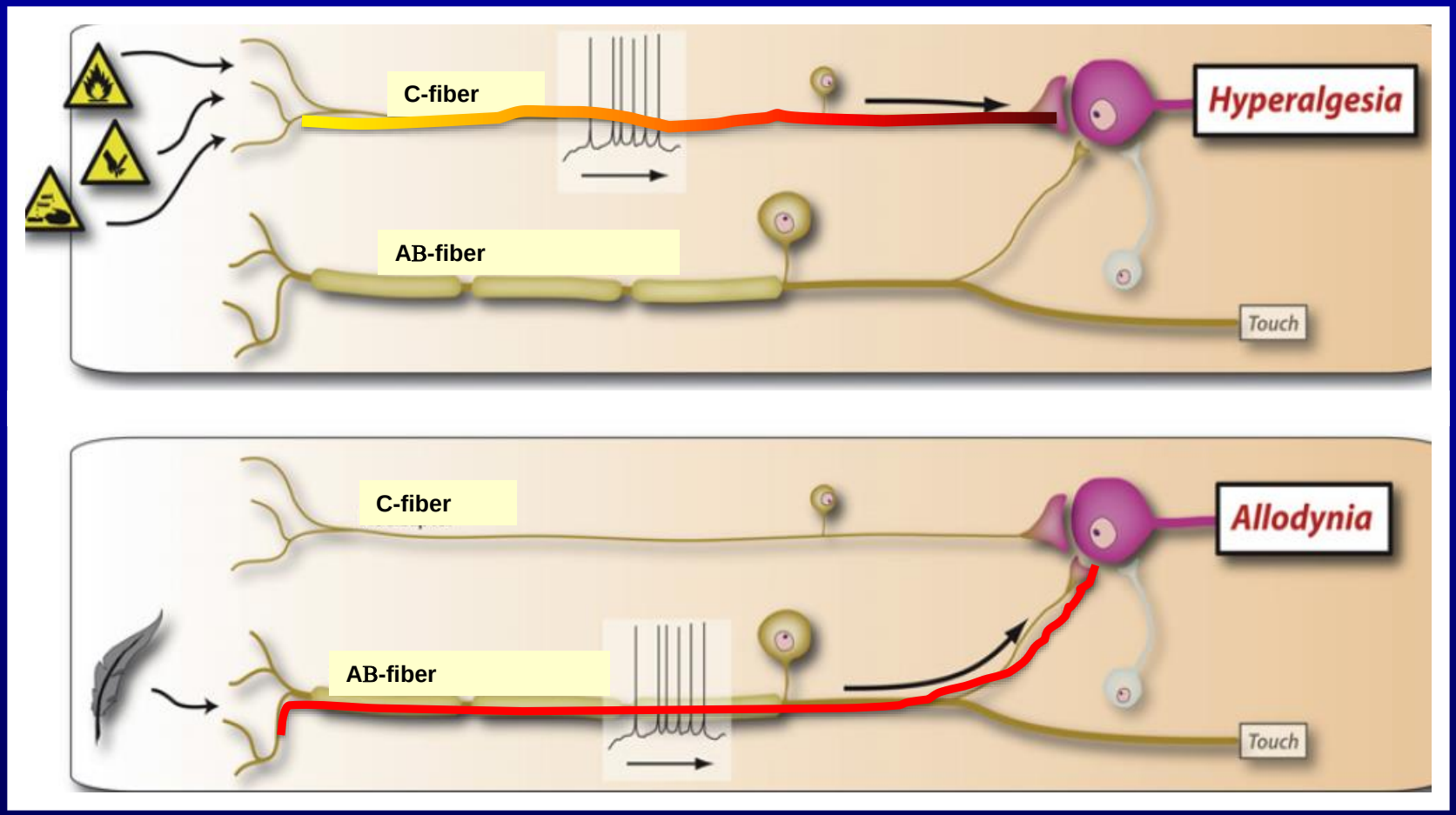
Central sensitization

Excess of AB and c-fibers in dorsal horn → compensatory changes to NMDA receptors →

lowered pain thresholds

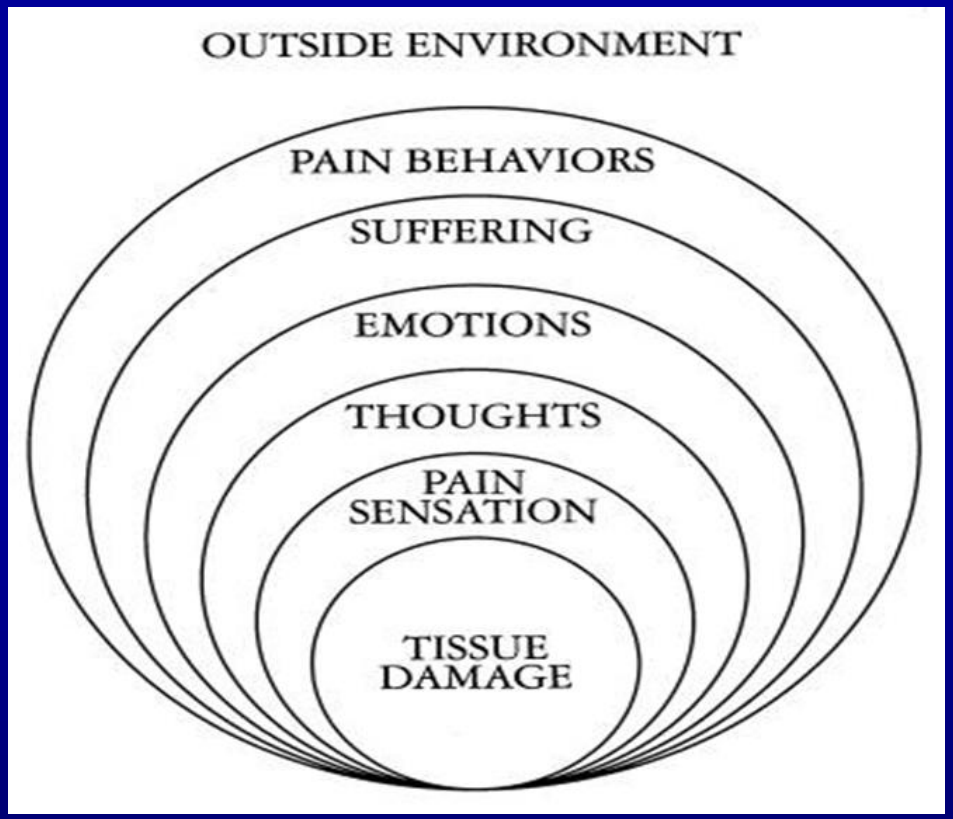
Woolf CJ. Pain 2011

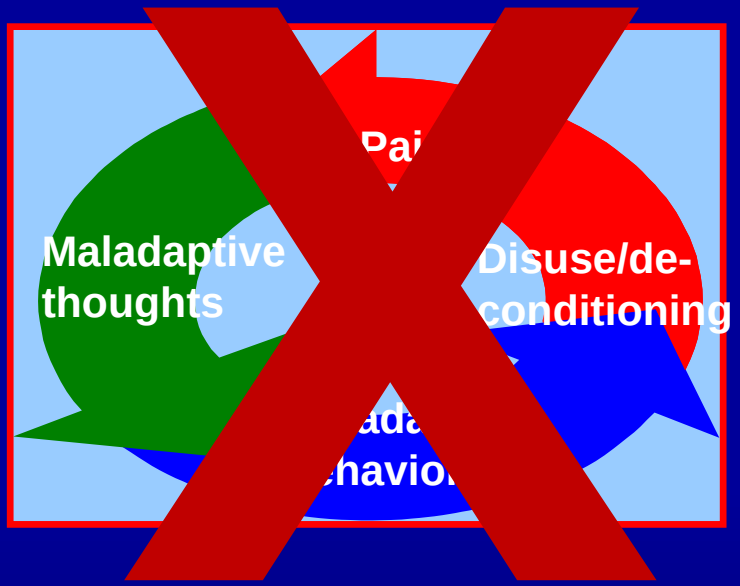
Chronic pain: hyperalgesia and allodynia

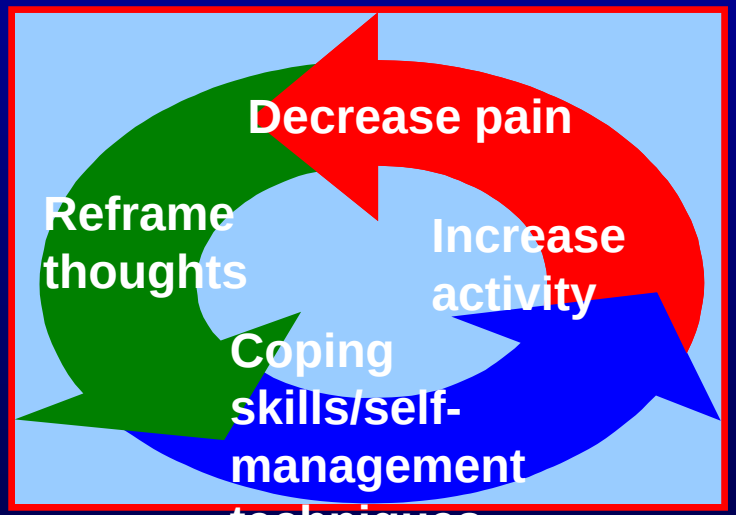


Woolf CJ. Pain 2011

Complexity of chronic pain







Deardorff, WW. APA 2008.

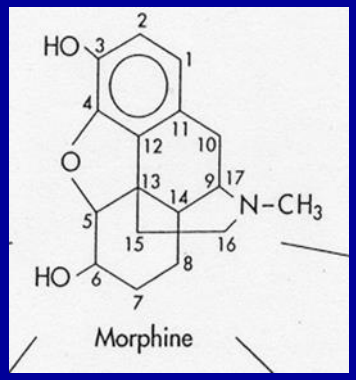
Becker, WC; Heapy AA et al. JGIM 2017.

Chronic pain epidemiology

- In 2016: 20.4% of U.S. adults had chronic pain; 8.0% had high-impact chronic pain
- Both more prevalent among adults:
  - living in poverty
  - with less than a high school education
  - with public health insurance.
- **Among veterans: 29.1%; 10.3%**
- Prevalence increasing

Dahlhamer et al. MMWR 2018.

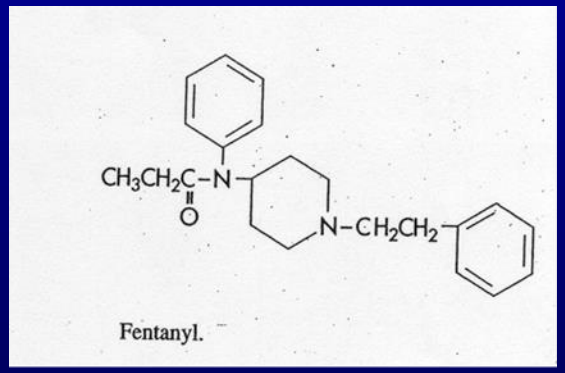
Opioid analgesics (opiates + opioids)



Morphine

Opiates

- Naturally present in opium from seedpod of *Papaver somniferum*
- Morphine, codeine



Fentanyl.

Opioids

- Manufactured
- Semi-synthetics: hydrocodone, hydromorphone, oxycodone
- Synthetics: fentanyl, methadone
- Illicitly-manufactured synthetics: fentanyl analogues

Morphine equivalent dose

- Method of standardizing potency across various opioid compounds

- Based on equianalgesic tables from dose ranging studies

- Example:

  20 mg oxycodone TID

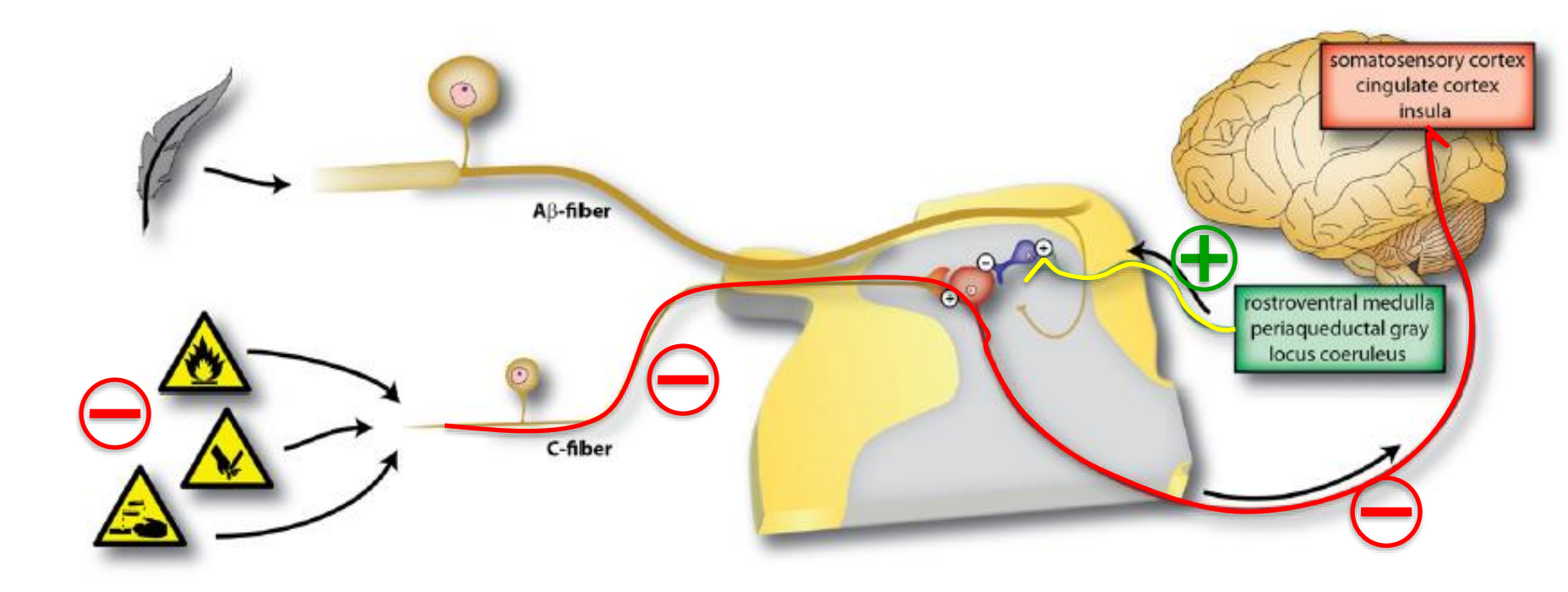
  =

  90 mg morphine

  equivalent daily dose

Equianalgesic dose (MG)	Opioid (oral)
30	Morphine
7.5	Hydromorphone
20	Oxycodone
30	Hydrocodone

Activation of mu receptors



Sequelae of long-term opioids

Tolerance → higher doses required to achieve same analgesic effect over time

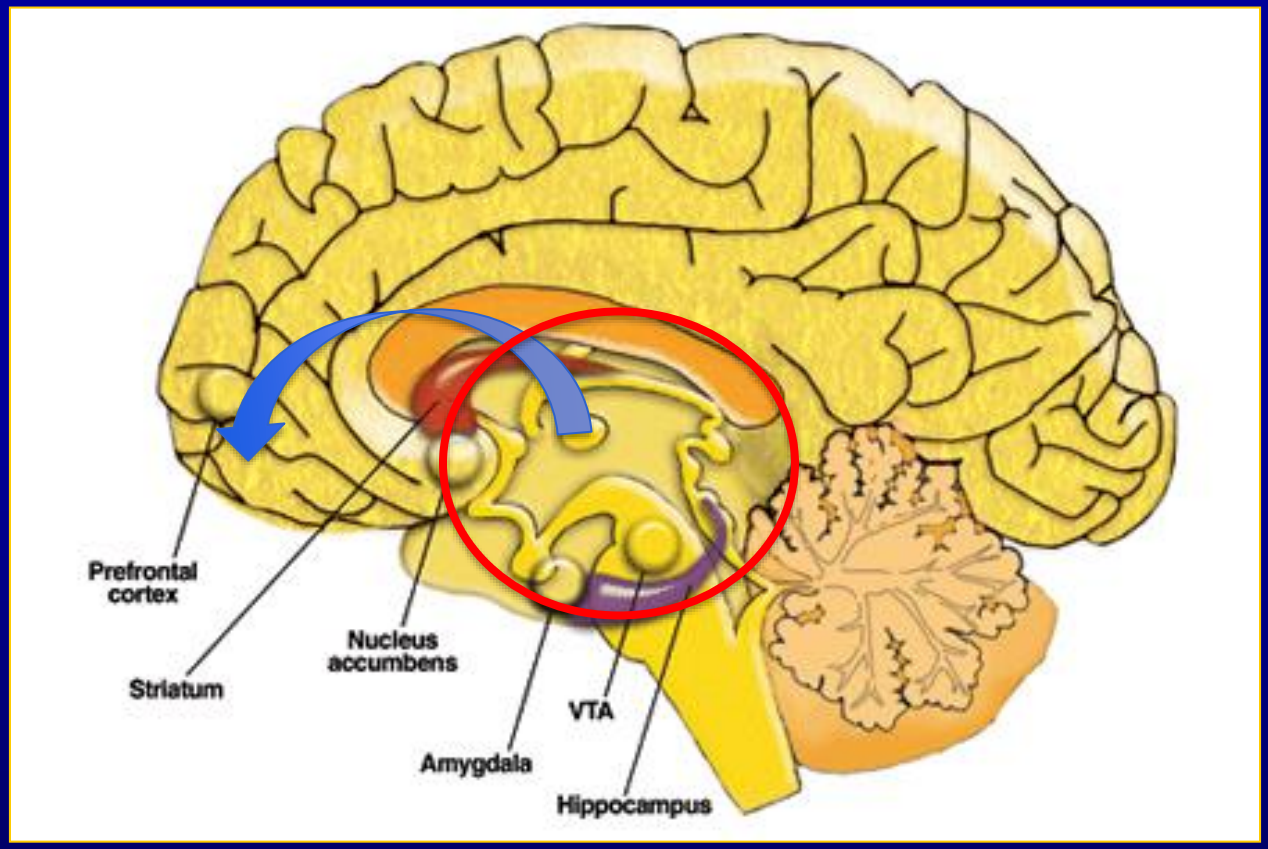
- High prevalence
- Also develops to some of the toxic effects

Withdrawal → characteristic symptoms upon abrupt cessation or lowering of opioid dose

Opioid-induced hyperalgesia → paradoxical worsening of pain with higher doses

- Prevalence unknown
- Correlation with total opioid exposure (dose x time)

Mu receptors and reward pathways



Opioid use disorder (DSM-5)

Physiologic sequelae

- Tolerance
- Withdrawal
- Opioid craving

Loss of control

- Greater amounts of use or longer period of use than intended
- Persistent desire but unsuccessful efforts to cut down
- Inordinate amount of time obtaining, using, or recovering

Adverse consequences

Summary of 5 criteria:

- Important social, occupational or recreational activities given up or reduced due to opioid use or recurrent opioid use despite physical or psychological problems caused or worsened by use

Other important toxicities

- Constipation
- Itching
- Nausea/vomiting
- Hypogonadism
- Opioid-induced hyperalgesia
- Sedation
- Impaired cognition
- Falls/motor vehicle accidents
- Blunted respiratory drive
- ***Non-fatal and fatal overdose***

Direct association between prescribed dose and overdose

Dose* (mg/day)	HR (95% CI)
1-<20	1.00 (REF)
20-<50	1.9 (1.3-2.7)
50-<100	4.6 (3.2-6.7)
≥100	7.2 (4.9-10.7)

*morphine equivalent

Bohnert et al. JAMA 2011

Long-term opioid therapy's questionable efficacy

- Martell BA, O'Connor PG, Kerns RD, Becker WC et al. *Ann Intern Med*, 2007: No RCTs longer than 16 weeks; non-significant pooled effect size in trials where opioids were compared to placebo or non-opioids.

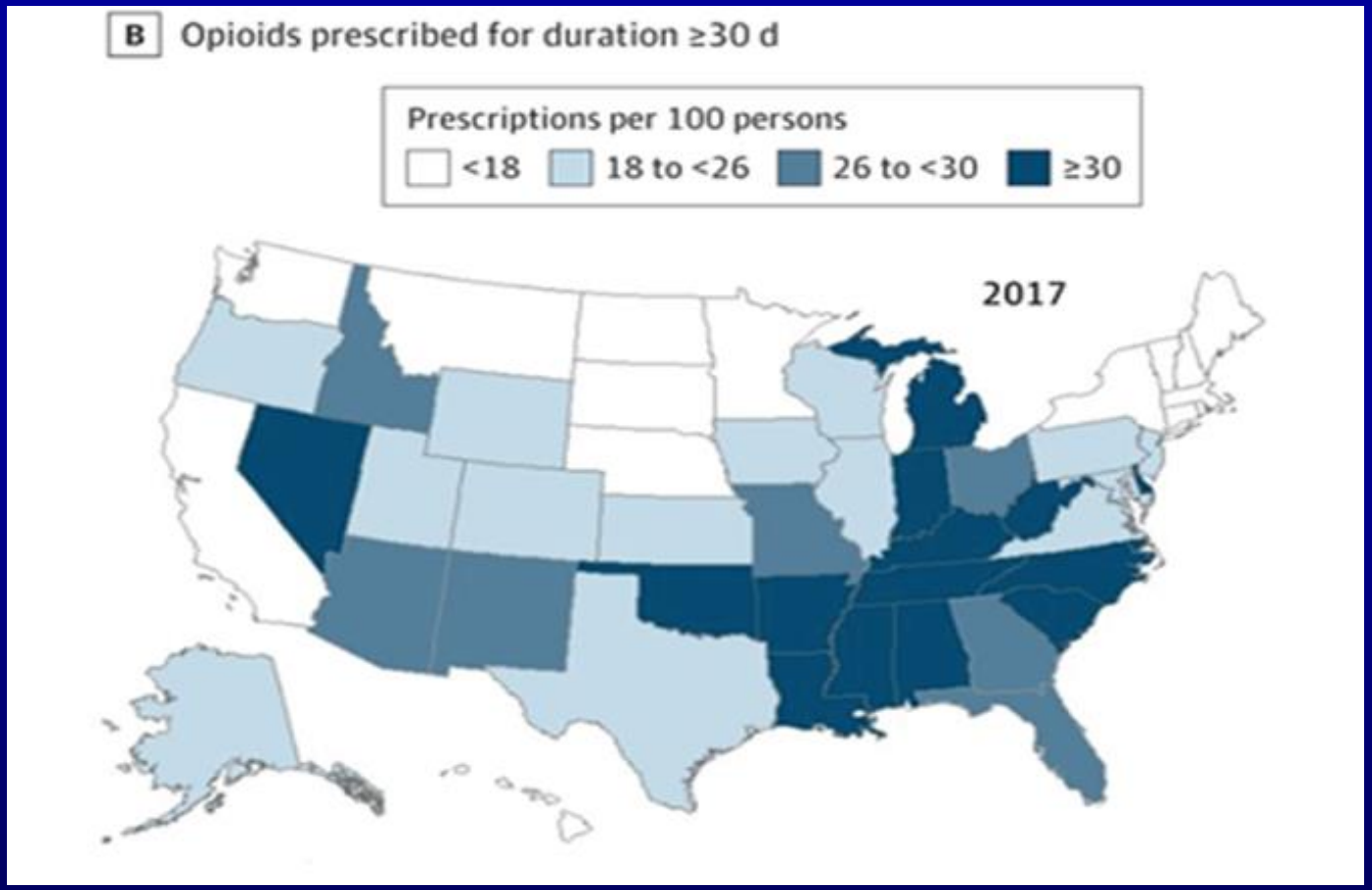
- Chou et al. *Ann Intern Med,* 2015: Benefit modest or absent; harms mounting.

- Krebs et al. *JAMA*, 2018: Opioid group – significantly worse pain intensity; no better in terms of functional interference; significantly more side effects.

Opioids for chronic pain: important limitations

- Central sensitization may not be responsive to opioids
- Chronic pain has prominent psychological component; unclear role for opioids
- Long term therapy induces tolerance, necessitating higher doses
- Higher doses chronically → increased risk of opioid-induced hyperalgesia
- Higher doses → increased risk of toxicity, both acute and chronic
- Little evidence that opioids improve outcomes in chronic pain

Nearly 40% increase in rate ≥ 30-day prescriptions: 2006-2017



Schieber LZ et al. JAMA Network Open 2019

VHA doing better

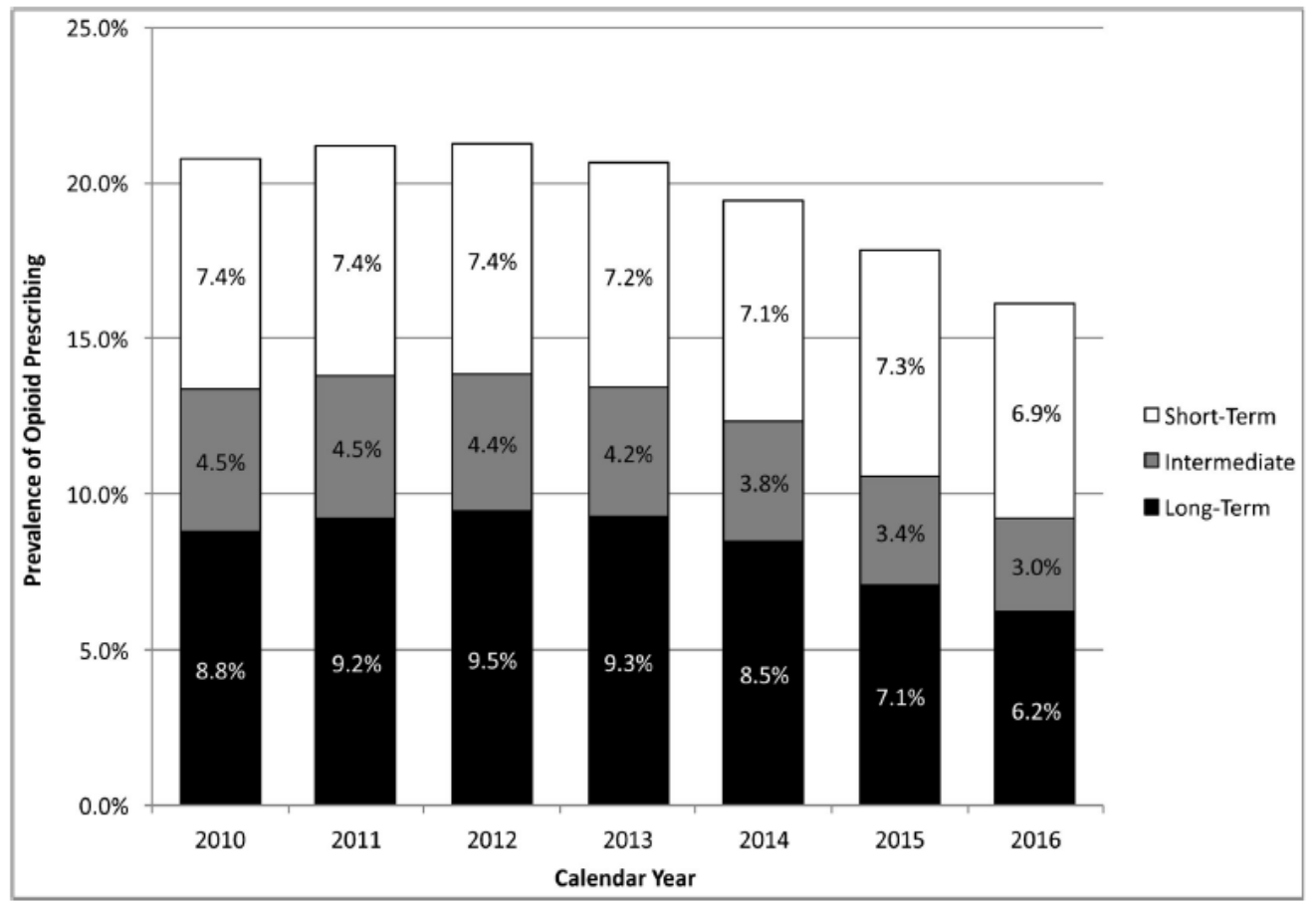


Figure 1 The changing prevalence of opioid prescribing in the VA healthcare system.

Hadlandsmyth, K et al. JGIM 2018.

How did we get here?

- **Public health campaigns against pain**

- **Aggressive & sometimes deceptive marketing**
  - Extrapolation from cancer/acute pain data
  - Purdue pharma officials found guilty of misbranding; fined $600 million
- **Clinical inertia**

Special Communication

CDC Guideline for Prescribing Opioids for Chronic Pain—United States, 2016

Deborah Dowell, MD, MPH; Tamara M. Haegerich, PhD; Roger Chou, MD

VA/DoD CLINICAL PRACTICE GUIDELINE FOR OPIOID THERAPY FOR CHRONIC PAIN

Department of Veterans Affairs

Department of Defense

- If benefits do not outweigh harms of continued opioid therapy, *optimize other therapies* and *work with patients* to taper to lower dosages or discontinue opioids.

- Non-pharmacologic therapy and non-opioid pharmacologic therapy *are preferred* for chronic pain.

Outline

Background:

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- Opioids' role in chronic pain

Intervention development:

- **Management strategies for when harm outweighs benefit**
- **Novel use of buprenorphine**
- **Testing/implementing non-pharmacologic approaches**

Problem list

Poorly controlled chronic pain with pervasive pain-related functional interference → BENEFIT is absent

Poorly controlled PTSD

Sleep-disordered breathing

Erectile dysfunction

Elevated risk of overdose death (240 mg MEDD)

→ HARM/RISK are prohibitive

Mismatch between needs and healthcare resources

- Needs:
  - Optimized pain care, including opioid tapering/discontinuation
  - Optimized mental health care
  - Optimized medical disease management

- Resources:
  - Brief, infrequent primary care visits
  - Fragmented specialty care visits

Opioid Reassessment Clinic (ORC)

- Integrated pain team, embedded in primary care
- Multidisciplinary: Psychiatry, Health Psychology, Internal Medicine, Nurse Case Management
- Longitudinal co-management
- Addictions expertise, buprenorphine-certified prescribers

Dorflinger LA, Ruser C, Sellinger J, Edens EL, Kerns RD, Becker WC. Pain Medicine. 2015

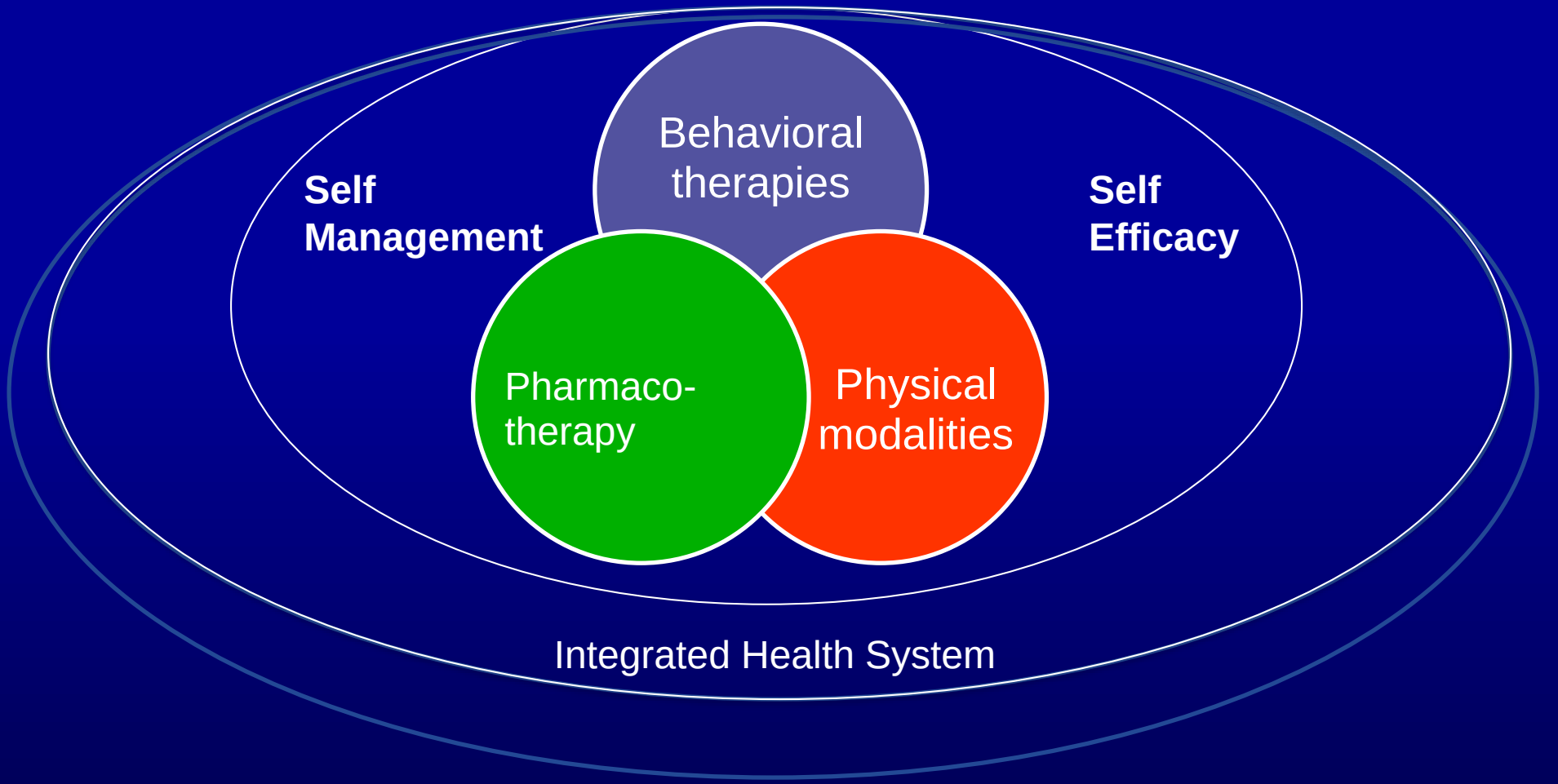
ORC approach

- Biopsychosocial, patient-centered pain assessment eliciting functional goals
- Assessment of harm/benefit of current opioid regimen
- Multi-modal treatment planning designed to help the patient achieve functional goals
- Modifying the opioid regimen to help meet functional goals

We can support you to feel better overall if you're willing to work with us.

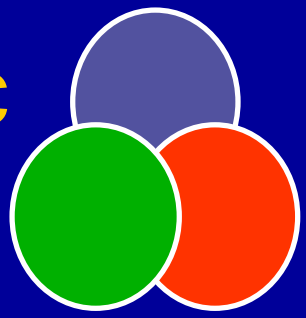
Becker WC et al. ASCP. 2016

Evidence-based high value chronic pain care



AP Wright, WC Becker, GD Schiff - JAMA IM, 2016

Evidence-based non-pharmacologic treatments for chronic pain



Active physical modalities

- Structured exercise
- Physical therapy
- Yoga
- Tai Chi
- Aqua-therapy

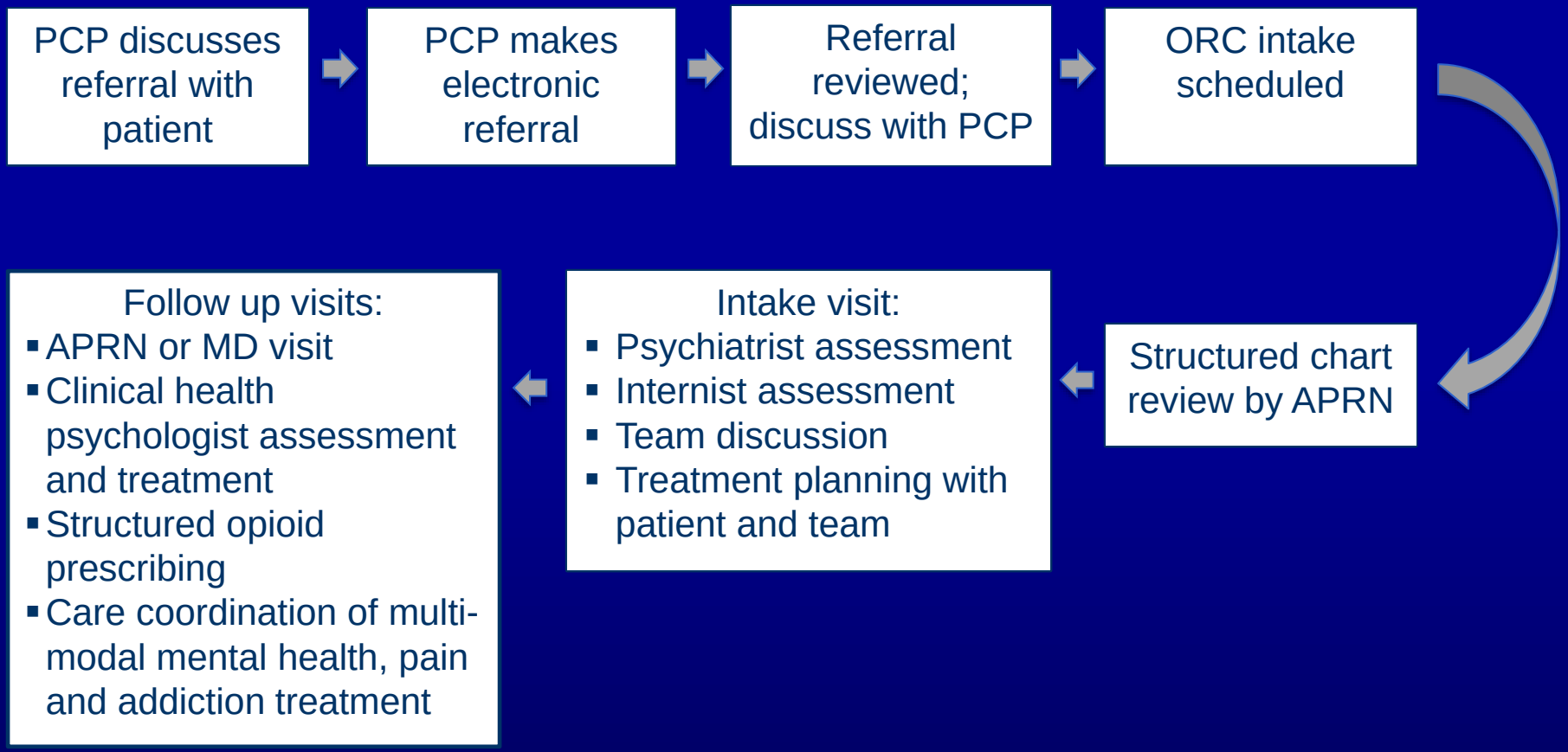
Behavioral treatments

- Cognitive behavioral therapy
- Mindfulness based stress reduction

Passive techniques

- Chiropractic
- Acupuncture
- Massage
- TENS

Opioid Reassessment Clinic flow



Dorflinger LA, Ruser C, Sellinger J, Edens EL, Kerns RD, Becker WC. Pain Medicine. 2015

CONDUIT

Specialty Care | Telehealth

Primary Care

Hospital | Emergency Department

Veteran Engagement Core (mPI: Frank)

Implementation Core (mPI: Midboe)

Quantitative/Cost Core (mPI: Zeliadt)

Coordinating Center (Corresponding PI: Becker)

Implementation Sites

- VISN 1
- VISN 7
- VISN 19
- VISN 20
- VISN 22
- VISN 23

CONDUIT; PII 19-321. PI: Becker, WC

Annals of Internal Medicine

REVIEW

Patient Outcomes in Dose Reduction or Discontinuation of Long-Term Opioid Therapy

A Systematic Review

Joseph W. Frank, MD, MPH; Travis I. Lovejoy, PhD, MPH; William C. Becker, MD; Benjamin J. Morasco, PhD; Christopher J. Koenig, PhD; Lilian Hoffecker, PhD, MLS; Hannah R. Dischinger, BS; Steven K. Dobscha, MD; and Erin E. Krebs, MD, MPH

- 67 studies (3 good quality, 13 fair, 51 poor)
- Very low quality evidence across many different programs/protocols
- Pain, function & quality of life may improve with voluntary opioid tapering supported by multidisciplinary team
- Important gaps:
  - Few studies in primary care
  - Few studies of adverse effects of tapering

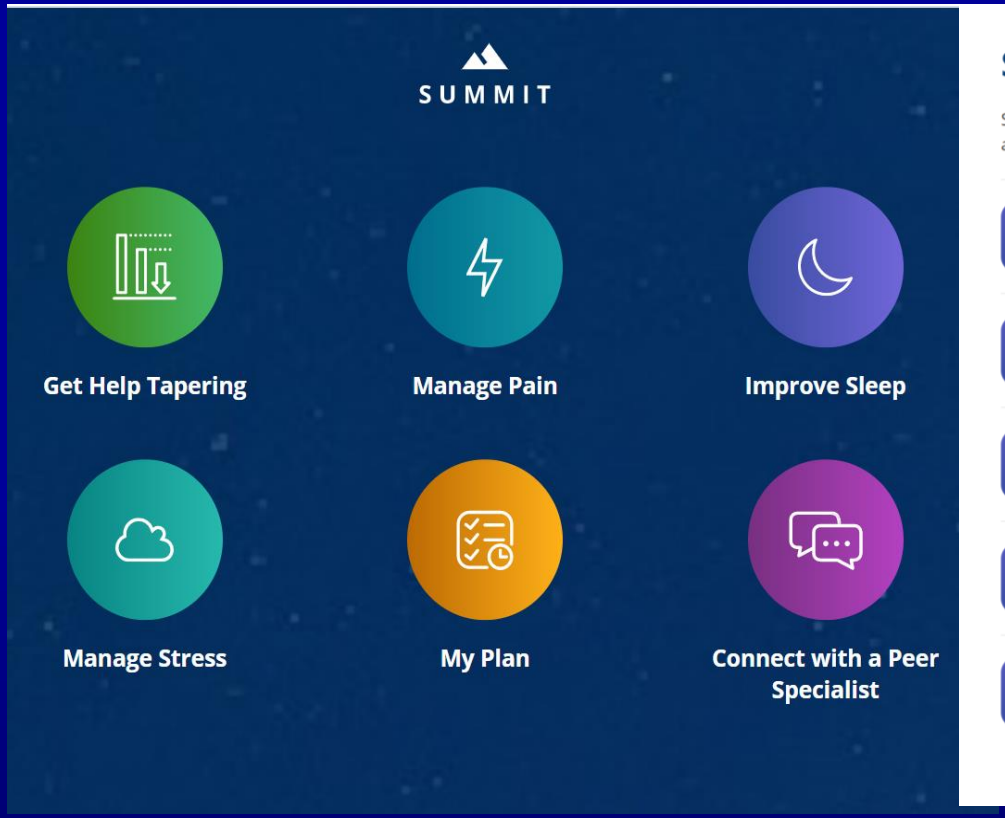
Frank JW et al. Ann Intern Med 2017

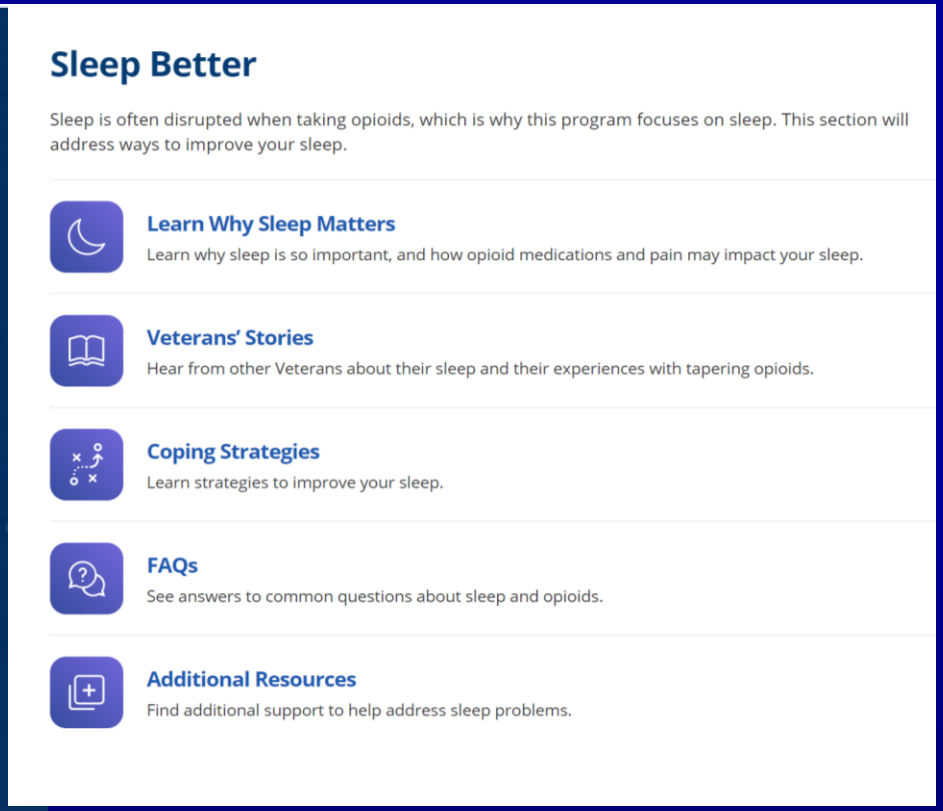
Tapering pearls

- Lead with empathy
- Express concern
- Acknowledge shared responsibility
- Highlight tangible potential benefits
- Highlight other patients' success
- Partnership/reassurance
- Celebrate micro-successes
- Offer choice whenever possible

Becker WC et al. ASCP. 2016

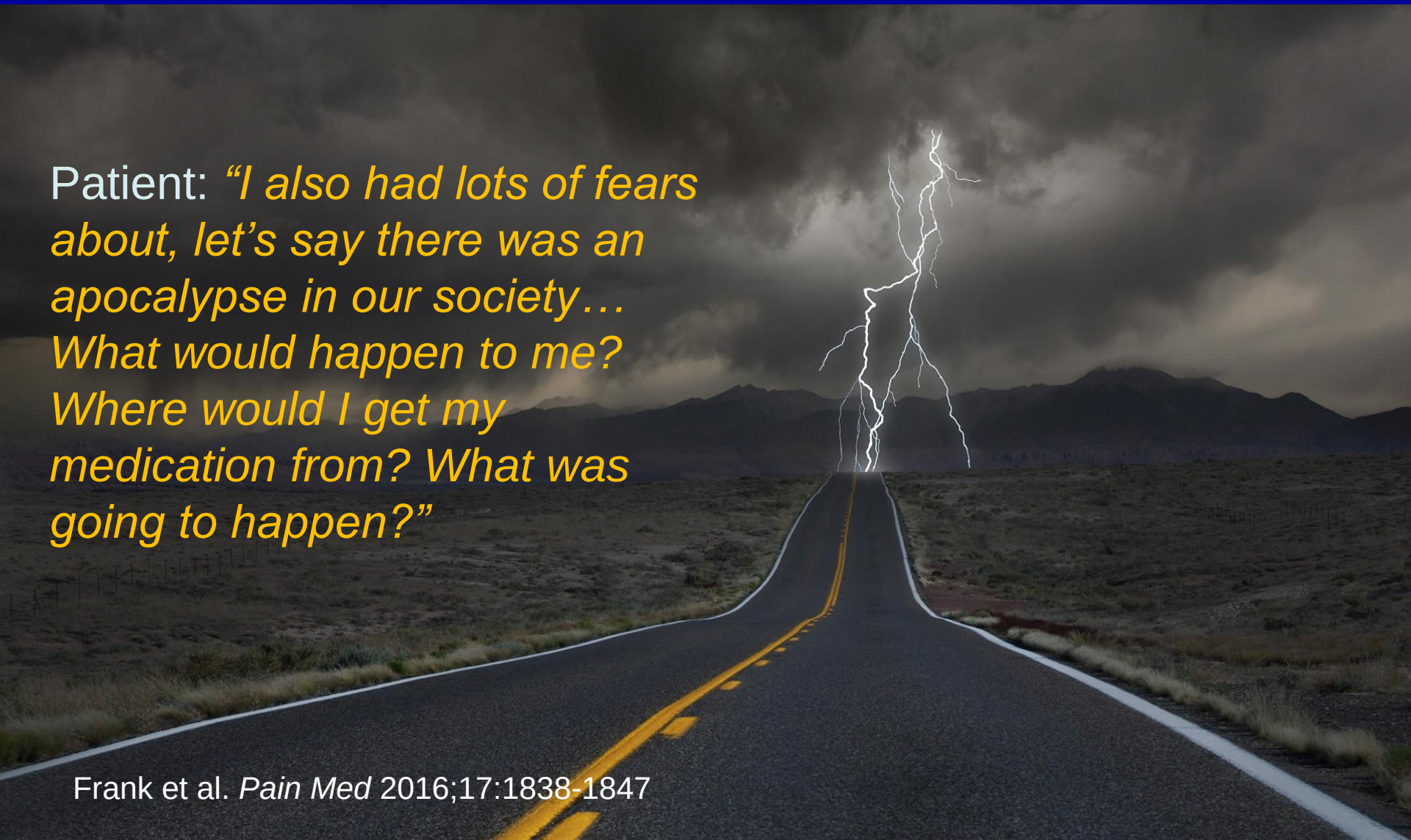
SUMMIT





HSR&D IIR 12-228. PI: Becker, WC

Neuro-adaptation and fear of tapering



Patient: *"I also had lots of fears about, let's say there was an apocalypse in our society… What would happen to me? Where would I get my medication from? What was going to happen?"*

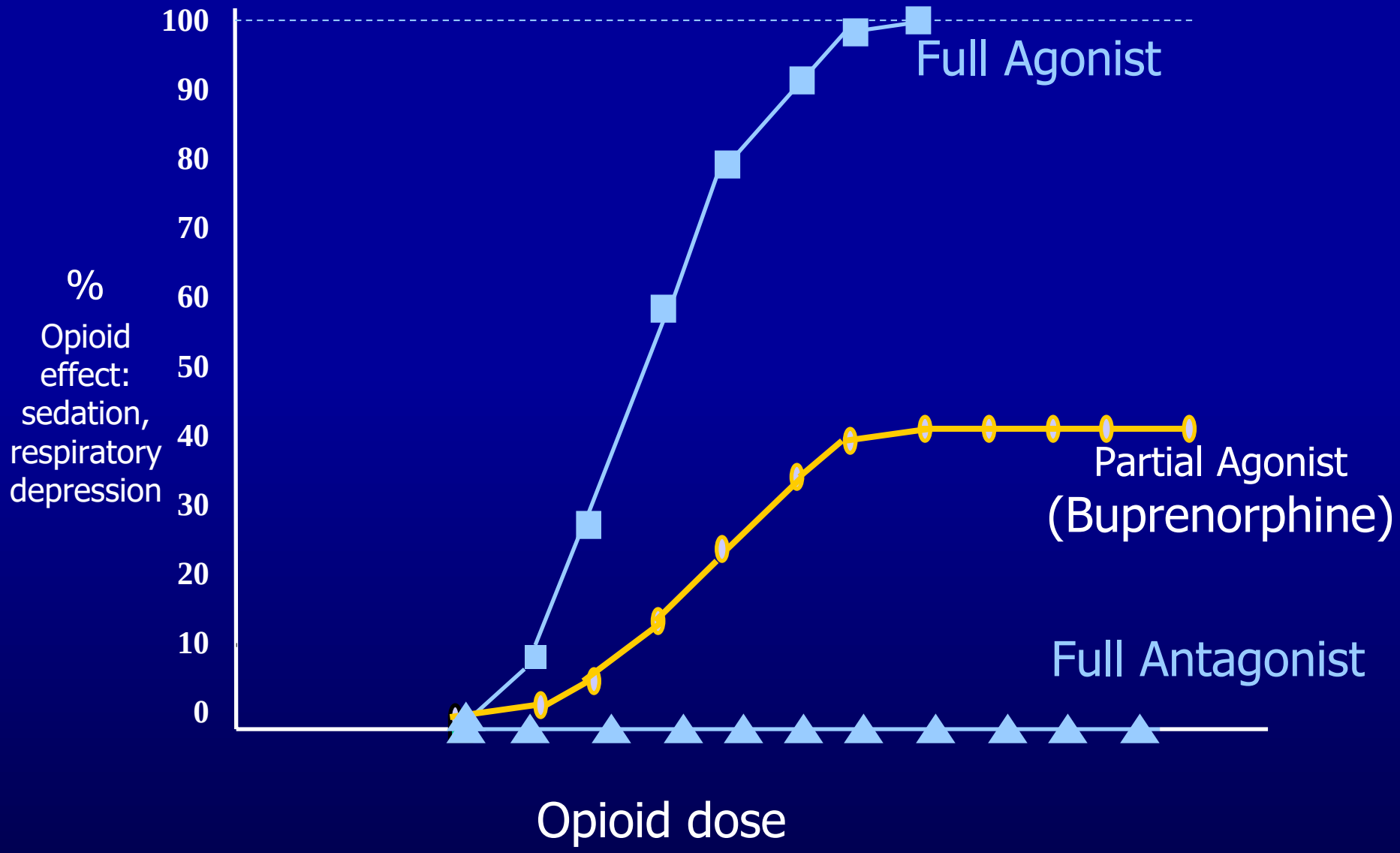
Frank et al. *Pain Med* 2016;17:1838-1847

Rationale for buprenorphine

- Potential for quicker taper off
- Addresses neuro-adaptation
- Observational data suggest chronic pain efficacy
- Multiple studies in the opioid use disorder literature demonstrate improved functioning
- Caveat: req[illegible] tot[illegible] continuation of other opioids and induction [illegible] val symptoms

Becker WC et al. JSAT. 2015

Buprenorphine: a partial μ agonist



Starting buprenorphine: overlapping approach

- Starting with very low dose bup, increase in stepwise fashion over 4-5 days
- Once bup at therapeutic dose, stop full-agonist opioids; can decrease full-agonists on last day of bup/nx up titration

Day	Buprenorphine/naloxone (buprenorphine component listed)	Morphine SA
1	0.5mg BID or 1 mg x 1	90 mg TID
2	1mg BID	90 mg TID
3	1mg TID	90 mg TID
4	2mg TID	90 mg in AM
5	4mg TID	none
5 and onward	Adjust dose to symptoms	none

Becker WC; Edens EL, Frank JW, Ann Int Med 2020

ORC study

Among patients on high-dose, full agonist opioids:

- Assessment and engagement with care team
- If no opioid use disorder:
  - "We now know more about safety problems related to opioids and we are concerned about your health and safety. We recognize that we prescribed you these medications so now we want to help you be safer while still managing your pain."
  - Constrained choice: slow taper (e.g. 10% decrease every 2-4 weeks) vs. quick taper off and switch to buprenorphine

Oldfield BJ, Edens EL, Edmond SN, Cervone D, Becker WC et al. Pain Medicine, 2018

ORC study results

Measure	Intervention (N = 66)	Control (N = 39)	*P* Value
Opted for slow taper, No. (%)	24 (37)	1 (3)	<0.01
Opted for partial agonist, No. (%)	41 (62)	1 (2)	<0.01

Oldfield BJ, Edens EL, Edmond SN, Cervone D, Becker WC et al. Pain Medicine, 2018

ORC study results

Changes in morphine equivalent daily dose among patients engaging in the ORC compared to those who did not

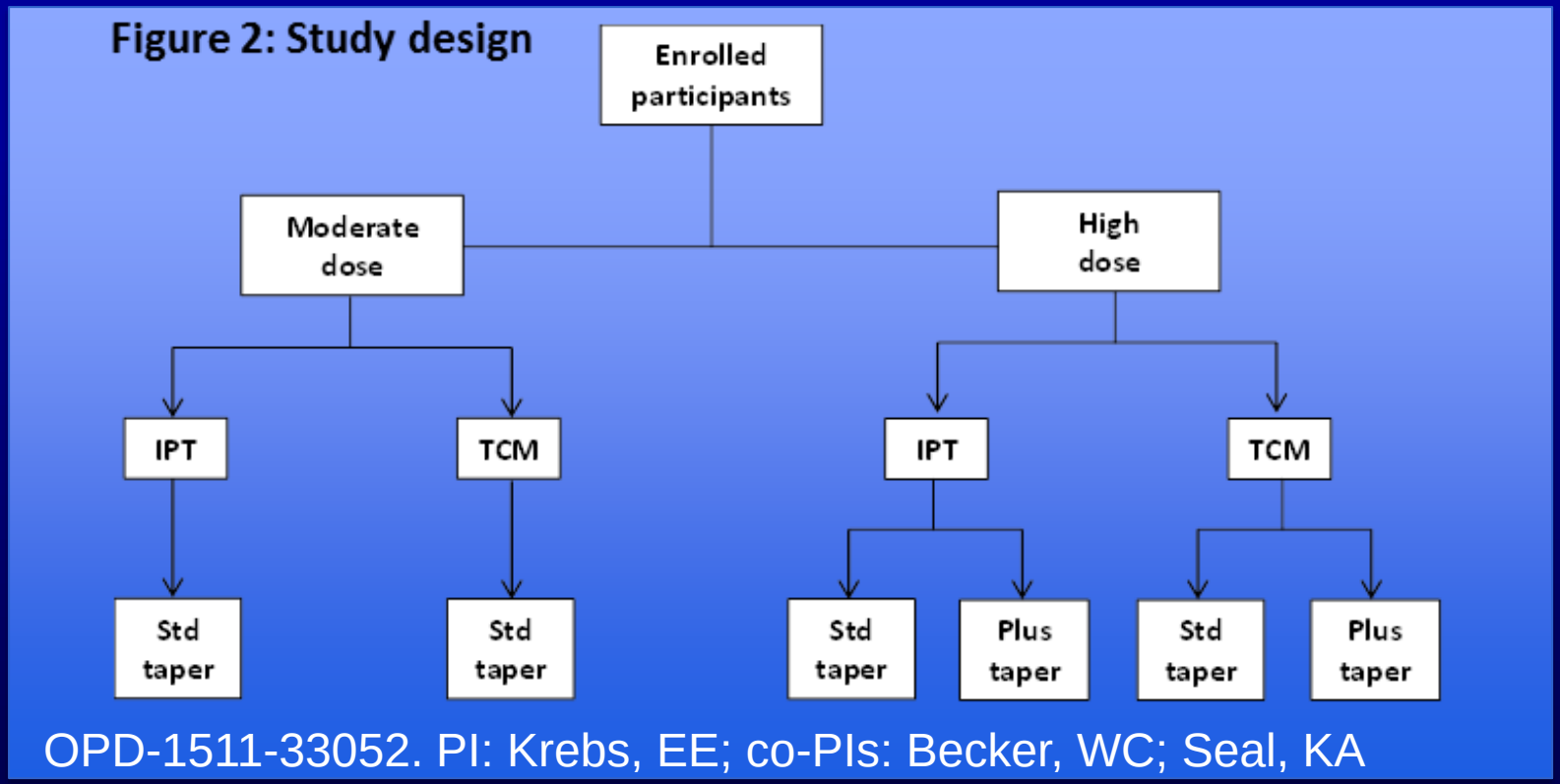
Characteristic	Intervention (N = 66)	Control (N = 39)	*P* Value
MEDD at referral, median (IQR), mg	85 (35–180)	60 (30–156)	<0.01
MEDD at reengagement with PCP, median (IQR), mg, No. (%), mg	25 (0–80)	53 (30–165)	
Benzodiazepine co-prescription at referral, No. (%)	20 (30)	11 (28)	0.44
Benzodiazepine co-prescription at reengagement, No. (%)	19 (29)	11 (28)	
Cannabinoids on urine drug test at referral, No. (%)	10 (15)	5 (13)	1.0
Cannabinoids on urine drug test at reengagement, No. (%)	10 (15)	4 (11)	

IQR = interquartile range; MEDD = morphine equivalent daily dose; ORC = Opioid Reassessment Clinic; PCP = primary care provider.

Oldfield BJ, Edens EL, Edmond SN, Cervone D, Becker WC et al. Pain Medicine, 2018

Veterans' Pain Care Organizational Improvement Comparative Effectiveness (VOICE) Study

- RCT of integrated pain team (IPT) vs. pharmacist-led telecare collaborative management (TCM)
- Patients on high-dose therapy: standard vs. "plus" taper

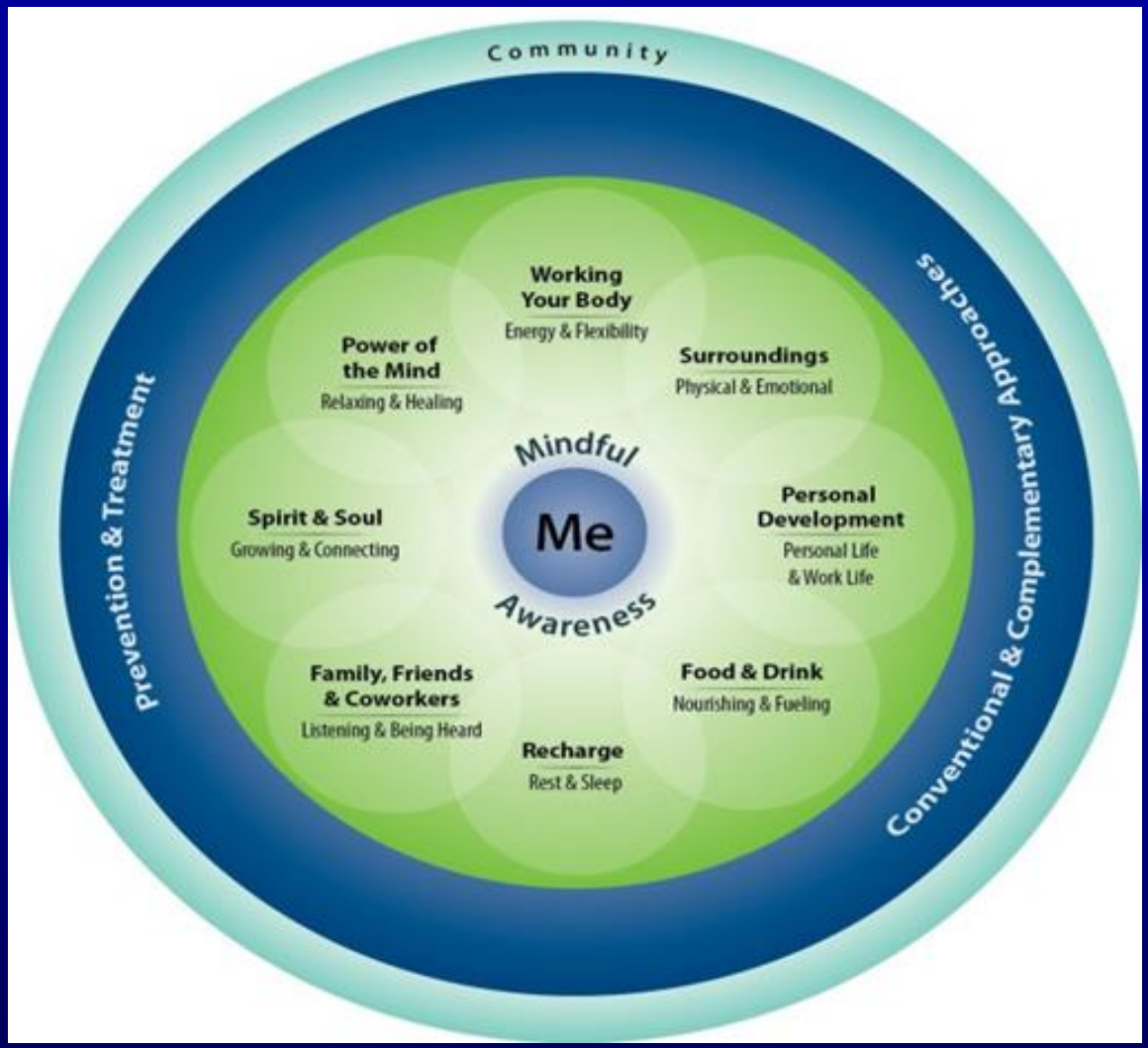


OPD-1511-33052. PI: Krebs, EE; co-PIs: Becker, WC; Seal, KA

Veterans' Voices

The “Post-Opioid” Era

VA's Whole Health Model



- Personal Health Inventory
- Personal Health Planning
- Whole Health Coaching
- Emphasis on non-pharm treatments

- Multi-site pragmatic trial of ~750 veterans with moderate to severe chronic pain

- Compare two approaches on primary outcome pain functional interference:

  (1) Whole Health Team vs.

  (2) Primary Care Group Education

1 UH3 AT009765-01. NICCH. PIs: Becker, WC; Seal, KA

Summary

- Opioid-centric chronic pain management has largely failed: harm > benefit
- CDC/VA/DoD Guidelines chart the course for change
- Promising interventions:
  - Collaborative multi-disciplinary management
  - Technology assists
  - Switch to buprenorphine
  - Non-pharm and self-management based approaches

Thank you

- **Veterans**
- Collaborators
- Funders

Questions