Evolution of Opioid Tapering and Challenges

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Psychiatry and Behavioral Sciences (by courtesy)
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EMPOWER
EFFECTIVE MANAGEMENT OF PAIN AND OPIOID-FREE WAYS TO ENHANCE RELIEF

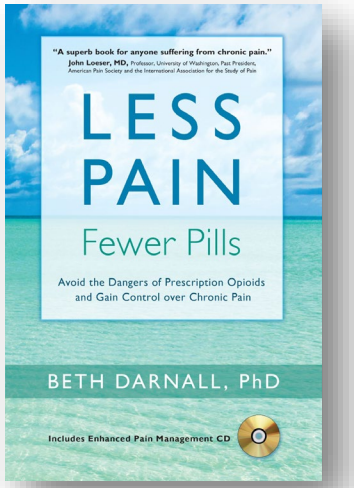
Contracts and Grants

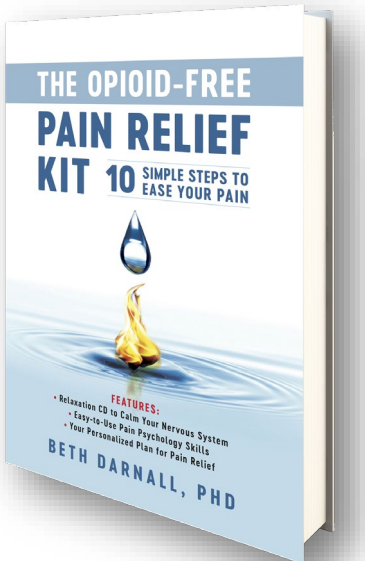
- PCORI Patient-Centered Opioid and Pain Reduction
- NIH / NCCIH: Mechanisms & Efficacy of Pain Catastrophizing Treatment

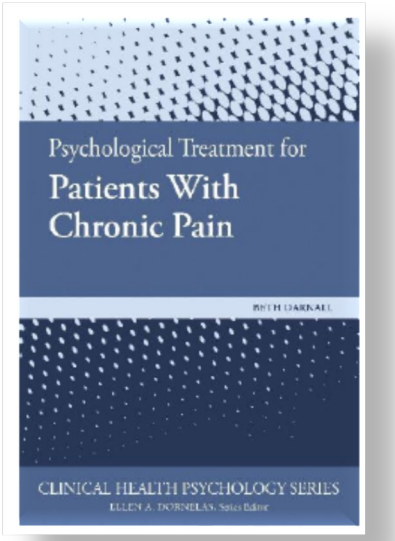
pcori
PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE

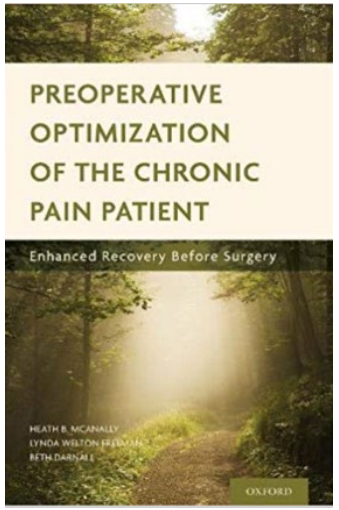
NIH National Center for Complementary and Integrative Health

Chief Science Advisor: appliedVR

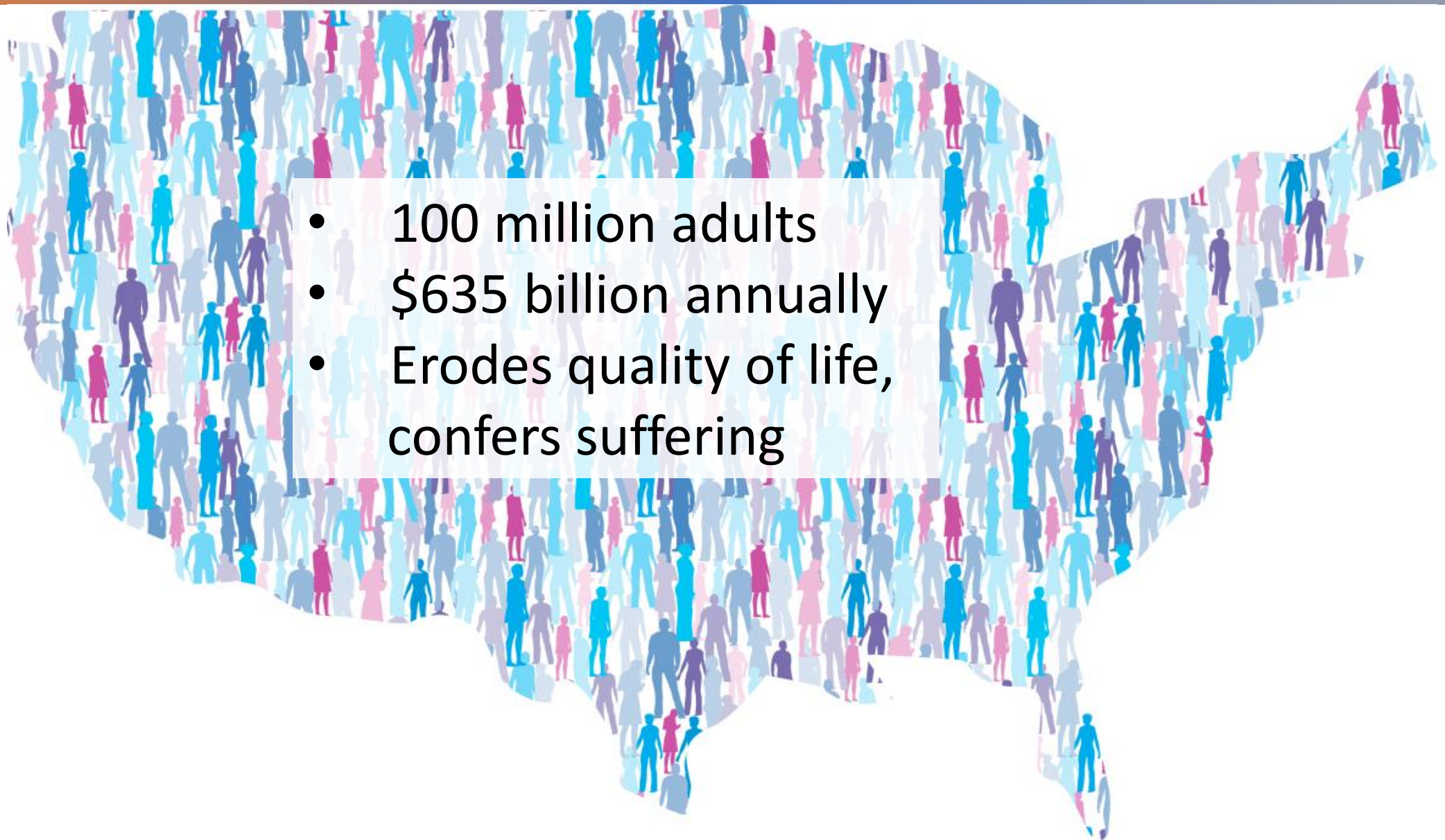








2011 IOM Report: *Relieving Pain in America*



- 100 million adults
- $635 billion annually
- Erodes quality of life, confers suffering

The biopsychosocial model of pain

EXPECTATIONS

- Analgesic (Pollo, Amanzio, et al 2001)
- Amplify pain (Benedetti, Lanotte, Lupiano, Colloca 2007)

Published in final edited form as:
Pain. 2014 January ; 155(1): 129–136. doi:10.1016/j.pain.2013.09.014.

From cue to meaning: Brain mechanisms supporting the construction of expectations of pain

Oleg V. Lobanov[1,2], **Fadel Zeidan**[2], **John G. McHaffie**[2], **Robert A. Kraft**[3], and **Robert C. Coghill**[1,2]

[1]Neuroscience Program, Wake Forest University School of Medicine, 1 Medical Center Boulevard, Winston-Salem, NC 27157-1010, USA

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DRUG EFFICACY

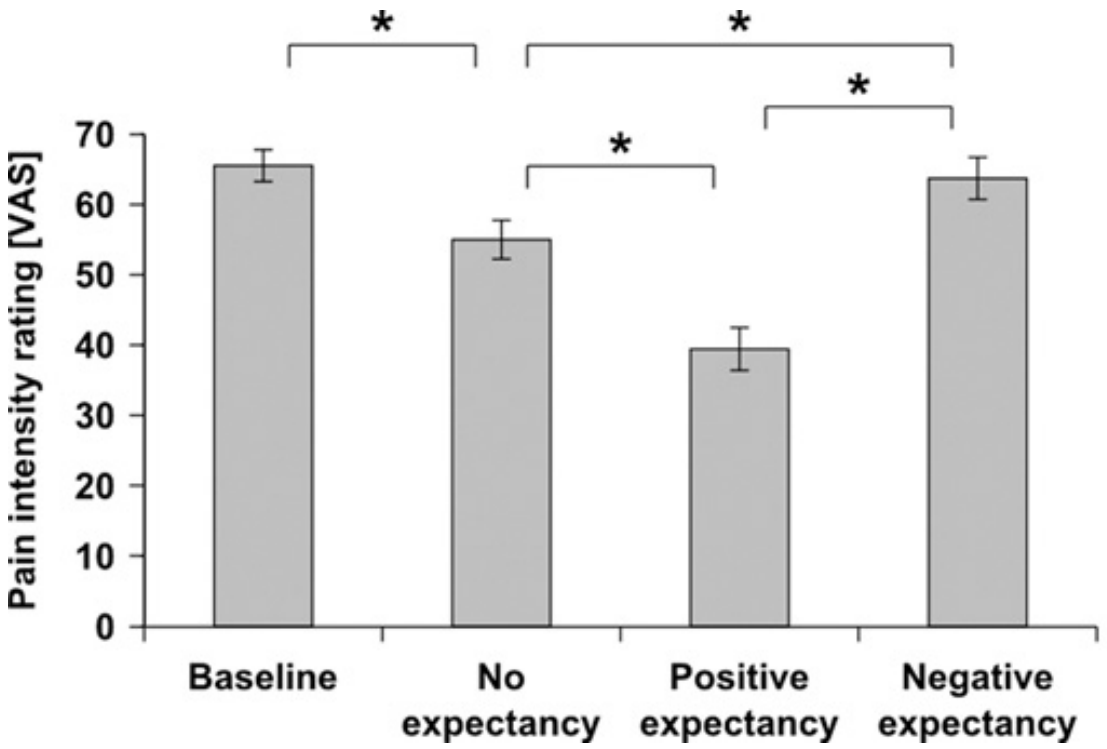
The Effect of Treatment Expectation on Drug Efficacy: Imaging the Analgesic Benefit of the Opioid Remifentanil

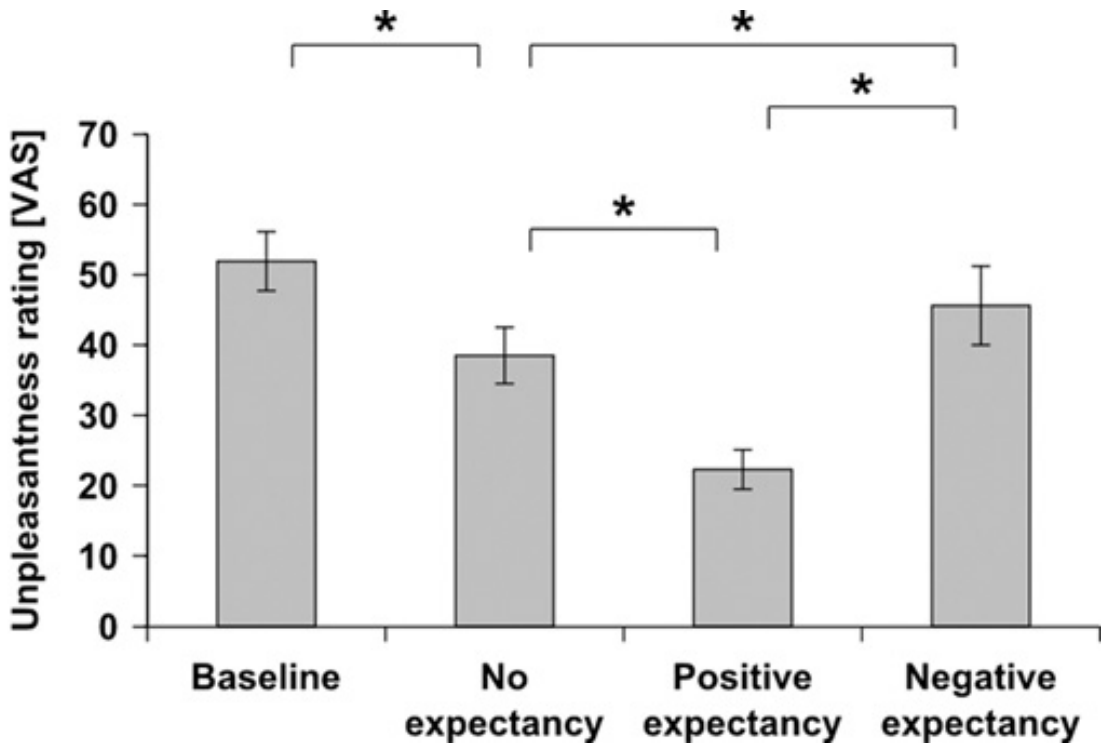
Ulrike Bingel,[1,2]* Vishvarani Wanigasekera,[1] Katja Wiech,[1] Roisin Ni Mhuircheartaigh,[1] Michael C. Lee,[3] Markus Ploner,[4] Irene Tracey[1]

Evidence from behavioral and self-reported data suggests that the patients' beliefs and expectations can shape both therapeutic and adverse effects of any given drug. We investigated how divergent expectancies alter the analgesic efficacy of a potent opioid in healthy volunteers by using brain imaging. The effect of a fixed concentration of the μ-opioid agonist remifentanil on constant heat pain was assessed under three experimental conditions using a within-subject design: with no expectation of analgesia, with expectancy of a positive analgesic effect, and with negative expectancy of analgesia (that is, expectation of hyperalgesia or exacerbation of pain). We used functional magnetic resonance imaging to record brain activity to corroborate the effects of expectations on the analgesic efficacy of the opioid and to elucidate the underlying neural mechanisms. Positive treatment expectancy substantially enhanced (doubled) the analgesic benefit of remifentanil. In contrast, negative treatment expectancy abolished remifentanil analgesia. These subjective effects were substantiated by significant changes in the neural activity in brain regions involved with the coding of pain intensity. The positive expectancy effects were associated

All received: - heat pain + IV remifentanil
- all 3 conditions in which expectations were manipulated

Psychological Modulation of Opioid Analgesia

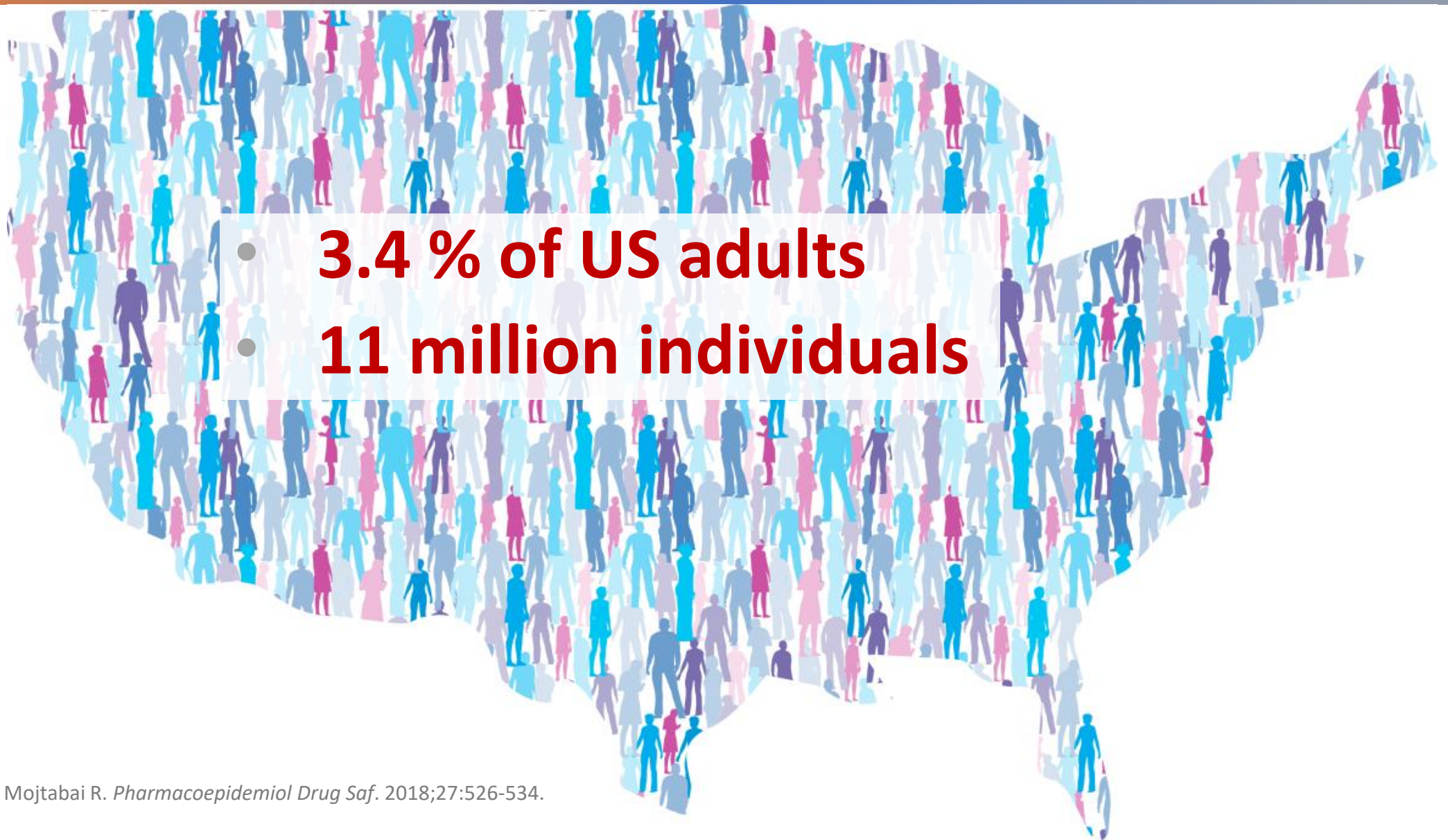




Ulrike Bingel et al., Sci Transl Med 2011;3:70ra14

Science Translational Medicine
AAAS

Long-Term Use of Daily Prescription Opioids



- **3.4 % of US adults**
- **11 million individuals**

Mojtabai R. *Pharmacoepidemiol Drug Saf*. 2018;27:526-534.

Fewer new starts is the best way to decrease opioid prescriptions

Patients taking long-term prescription opioids require careful considerations

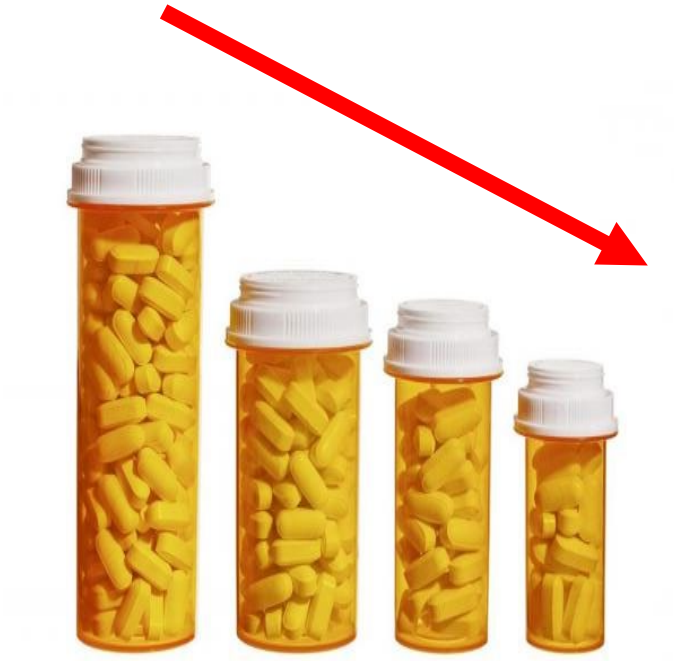
- Reducing opioid doses creates **new risks**
- Right methodology can be applied to

minimize iatrogenic risks from de-prescribing

- **Apply patient-centered principles**

Credit: Celia

- New starts
- Provided benchmarks of caution for increasing dose



Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016. MMWR Recomm Rep 2016;65(No. RR-1):1–49.

Associations between stopping prescriptions for opioids, length of opioid treatment, and overdose or suicide deaths in US veterans: observational evaluation

Elizabeth M Oliva,[1,2] Thomas Bowe[1,2] Ajay Manhapra,[3,4,5,6] Stefan Kertesz,[7,8] Jennifer M Hah,[9] Patricia Henderson,[1] Amy Robinson,[10] Meenah Paik,[1] Friedhelm Sandbrink[11,12,13] Adam J Gordon,[14,15,16] Jodie A Trafton[1,2,17]

Mortality After Discontinuation of Primary Care–Based Chronic Opioid Therapy for Pain: a Retrospective Cohort Study

Jocelyn R. James, MD[1], JoAnna M. Scott, PhD[2], Jared W. Klein, MD, MPH[1], Sara Jackson, MD, MPH[1], Christy McKinney, PhD, MPH[3], Matthew Novack, MS[3], Lisa Chew, MD, MPH[1], and Joseph O. Merrill, MD, MPH[1]

[1]Department of Medicine, Division of General Internal Medicine, Harborview Medical Center, University of Washington School of Medicine, Seattle, WA, USA; [2]University of Missouri – Kansas City School of Dentistry, Kansas City, MO, USA; [3]Tacoma Family Medicine, Multicare, Tacoma, WA, USA.

Opioid Taper Is Associated with Subsequent Termination of Care: a Retrospective Cohort Study

Hector R. Perez, MD, MS[1], Michele Buonora, MD, MS[1], Chinazo O. Cunningham, MD, MS[1], Moonseong Heo, PhD[2], and Joanna L. Starrels, MD, MS[1]

General Hospital Psychiatry 47 (2017) 29–35

Contents lists available at ScienceDirect

General Hospital Psychiatry

journal homepage: www.elsevier.com/locate/genhospsych

JAMA Network | Open™

Suicidal ideation and suicidal self-directed violence following clinician-initiated prescription opioid discontinuation among long-term opioid users

Michael I. Demidenko[a], Steven K. Dobscha[a,b], Benjamin J. Morasco[a,b], Thomas H.A. Meath[a,c], Mark A. Ilgen[d,e], Travis I. Lovejoy[a,b,f,*]

Original Investigation | Substance Use and Addiction

Association Between Opioid Dose Variability and Opioid Overdose Among Adults Prescribed Long-term Opioid Therapy

Jason M. Glanz, PhD; Ingrid A. Binswanger, MD; Susan M. Shetterly, MS; Komal J. Narwaney, PhD; Stan Xu, PhD

Growing Outcry Against Iatrogenic Opioid Reduction Risks and Harms

International Stakeholder Letter publishes

Darnall BD, Juurlink D, Kerns R, et al.

- Reuters Wire service
- >20 news outlets worldwide

Human Rights Watch

Declares the issue a “human rights violation”

- Laura Mills

HP3 Letter

Kertesz, Satel, et al.

- 300+ signatories
- 3 former U.S. Drug Czars
- AMA signs support

FDA

Clarifies labeling and cautions against abrupt discontinuation

CDC

Dowell et al. Clarification of opioid prescribing guidelines publish in *NEJM*.

HHS Guide for Clinicians on the Appropriate Dosage Reduction or Discontinuation of Long-Term Opioid Analgesics

October 2019

Avoid insisting on opioid tapering or discontinuation when opioid use may be warranted (e.g., treatment of cancer pain, pain at the end of life, or other circumstances in which benefits outweigh risks of opioid therapy). ***The CDC Guideline for Prescribing Opioids for Chronic Pain does not recommend opioid discontinuation when benefits of opioids outweigh risks.***[2,4,13]

Individualize the taper rate

The biopsychosocial model of tapering

Tapering Opioids

Patients' number one concern/fear?

Opioid Cessation and Multidimensional Outcomes After Interdisciplinary Chronic Pain Treatment

Jennifer L. Murphy, PhD, Michael E. Clark, PhD,*† and Evangelia Banou, PhD**

Clin J Pain • Volume 29, Number 2, February 2013

Outcome Variables	OP (n = 221) Mean (SD)	NOP (n = 379) Mean (SD)
Pain intensity		
Admission	7.01 (1.77)	6.91 (1.58)
Discharge	6.46 (1.74)	6.14 (1.79)

Community-Based Solutions are Needed

- Low-cost
- Low-risk
- Scalable
- Effectively reduce health risks
- Provide education and support
- Structured
- Address anxiety of patients and prescribers alike
- Promote patient trust and a good doctor-patient bond
- **Enhance patient willingness to try a gentle opioid taper**

Research Letter

ONLINE FIRST

May 2018

Patient-Centered Prescription Opioid Tapering in Community Outpatients With Chronic Pain

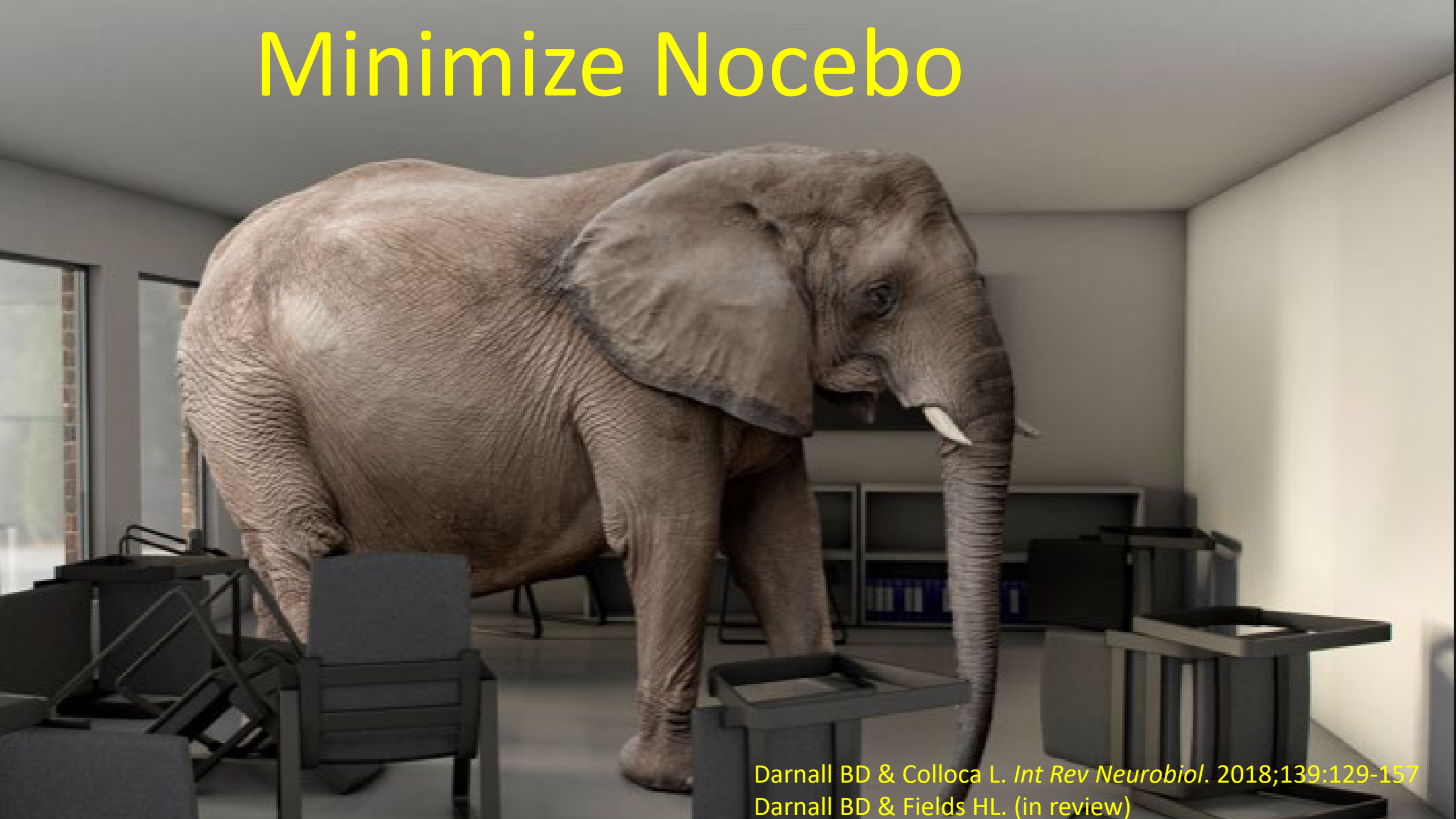
Beth D. Darnall, PhD[1]; Maisa S. Ziadni, PhD[1]; Richard L. Stieg, MD, MPH[2]; et al

» Author Affiliations | Article Information

JAMA Intern Med. Published online February 19, 2018. doi:10.1001/jamainternmed.2017.8709

The risks associated with prescription opioids are well described.[1,2] Although reducing opioid use is a national priority, existing opioid tapering models use costly interdisciplinary teams that are largely inaccessible to patients and their physicians.[3,4] Patients and physicians need solutions to successfully reduce long-term prescription opioid dosages in settings without behavioral services. We conducted a study of voluntary, patient-centered opioid tapering in outpatients with chronic pain without behavioral treatment.

Minimize Nocebo



Darnall BD & Colloca L. *Int Rev Neurobiol*. 2018;139:129-157
Darnall BD & Fields HL. (in review)

Opioid Cessation vs. Opioid Reduction

VS.

We Optimized Patient Choice and Control in Their Taper

- Participation was VOLUNTARY
- Patients could control the pace of their taper
- Patients could pause their taper
- Patients were free to drop out of the study at any time
- The taper goal was not zero unless the patient chose that goal
- The taper was NOT to a pre-defined opioid dose
- Patients partnered with their doctor to achieve their *lowest comfortable dose* over 4 months
- The taper was NOT unidirectional

- Darnall BD & Colloca L. Optimizing Placebo and Minimizing Nocebo to Reduce Pain, Catastrophizing, and Opioid Use. *Int Rev Neurobiol*. 2018;139:129-1572018;139:129-157.
- U.S. HHS Guide for Clinicians on the Appropriate Dosage Reduction or Discontinuation of Long-Term Opioid Analgesics (2019)

Study Variables

- Demographics (Gender, Age)
- Pain Treatment History (Pain Dx, Duration of Opioid Use)

- Opioid Dose (MEDD)
- Average Pain Intensity (0-10)
- Pain Catastrophizing Scale
- PROMIS Measures
- Marijuana use (Y/N)

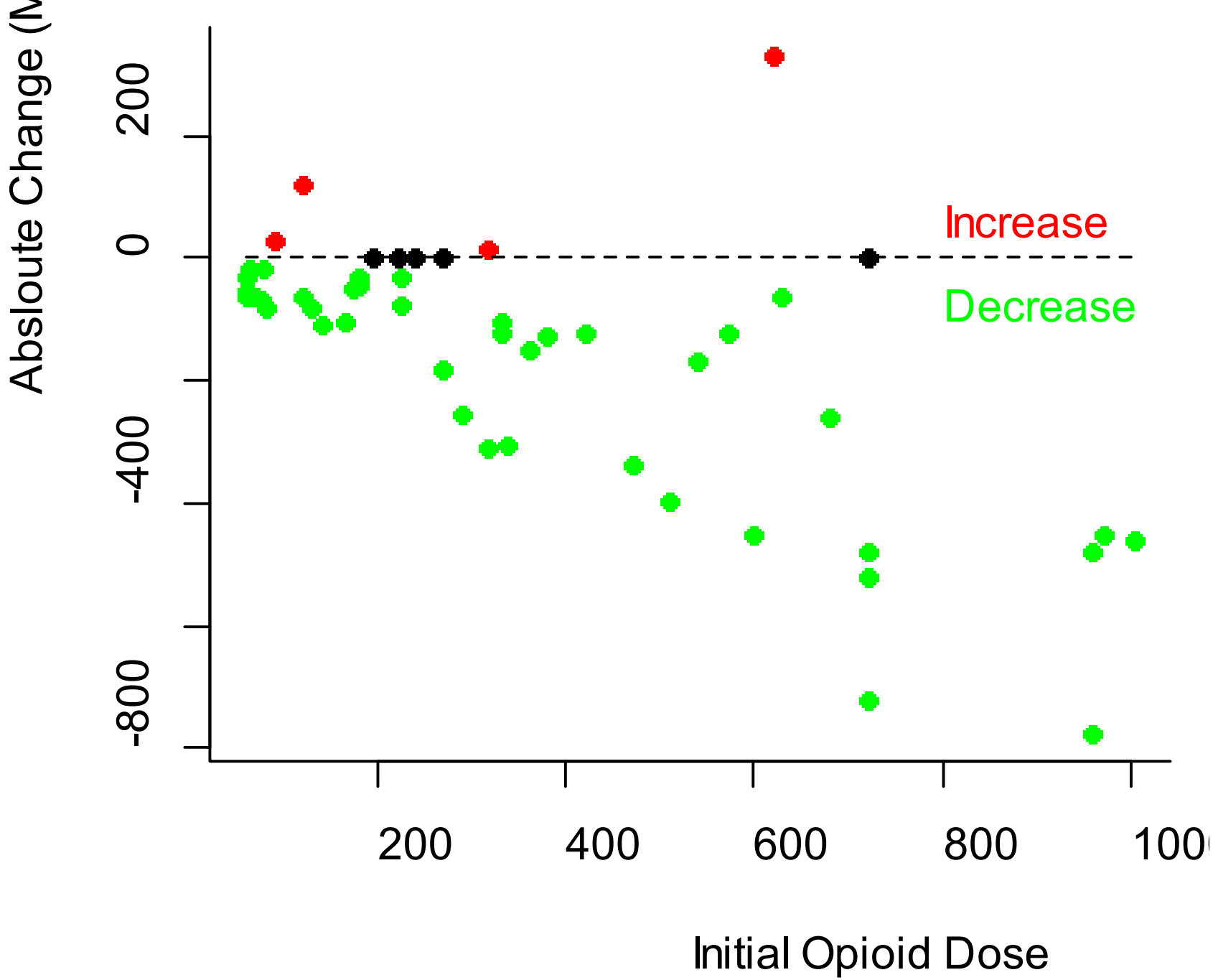
Sample Characteristics (N=51)

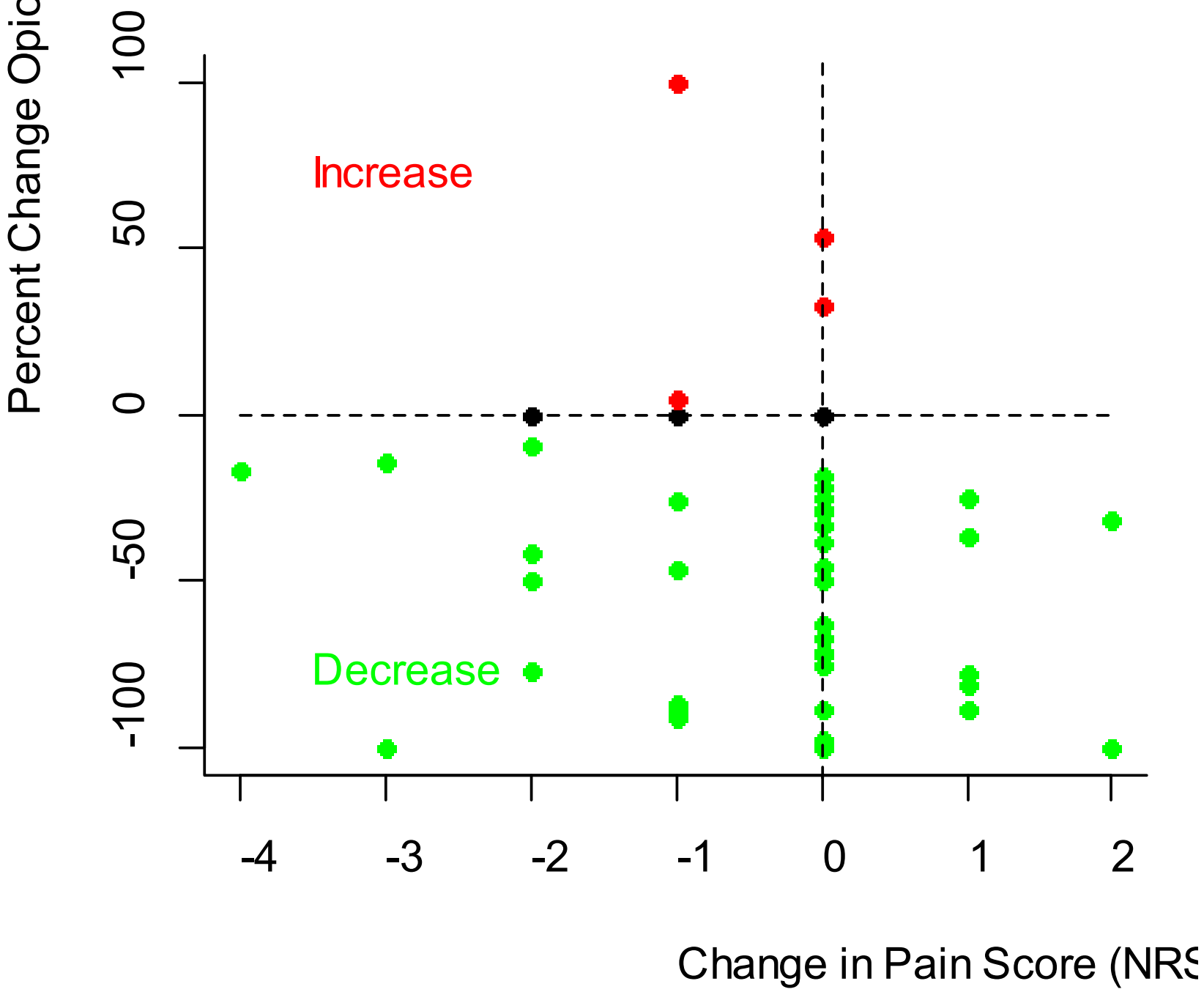
- 55% female
- 52 years of age (range = 25 – 72)
- 6 years on opioids (range = 1 – 38)
- Moderate pain intensity
- Marijuana: 37% (18)
- Opioid MEDD = 288 (60, 1005)

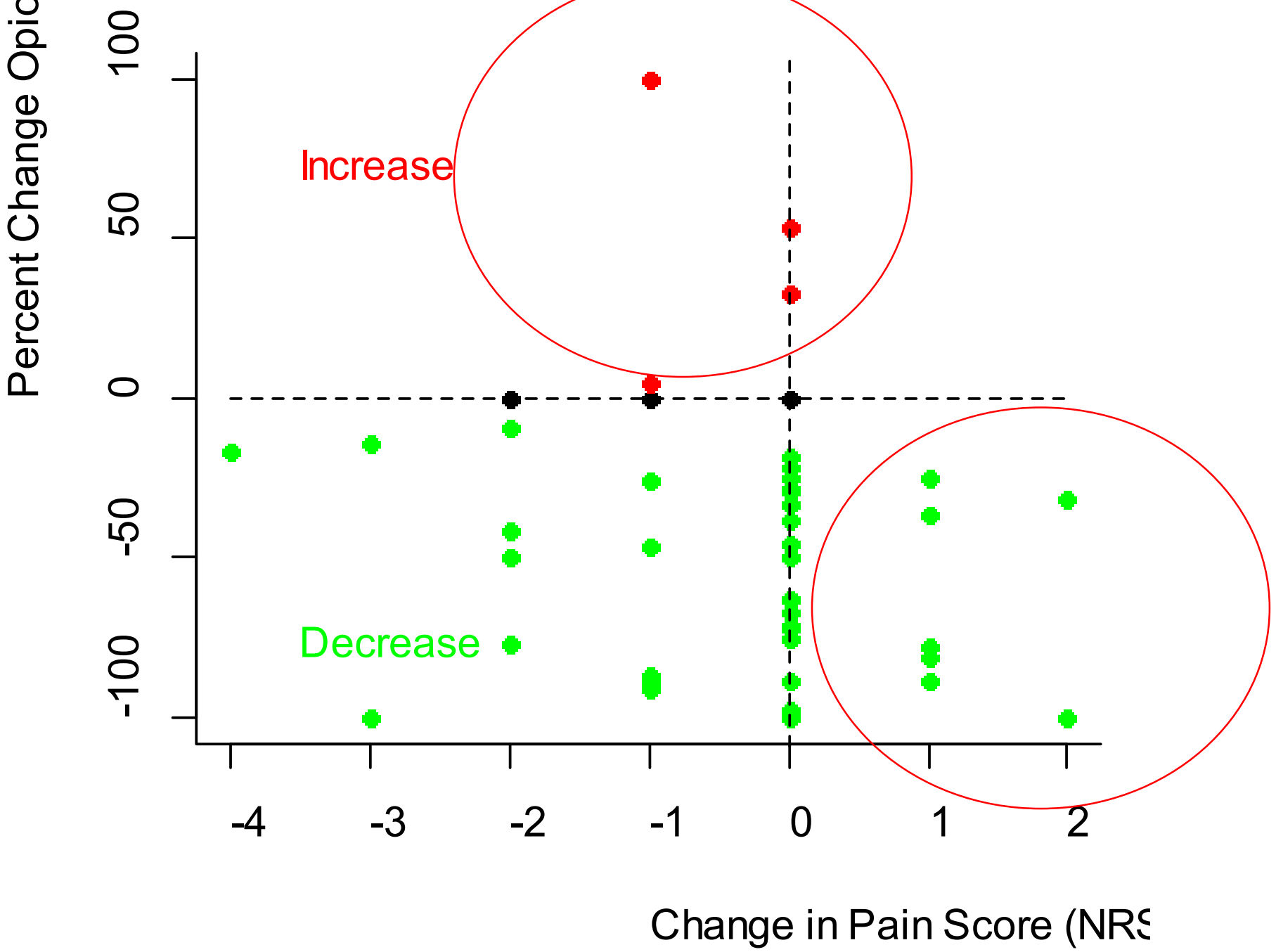
Darnall BD, Ziadni MS, Mackey IG, Kao MC, Flood P (FEB 2018; *JAMA Int Med)*

	Baseline	16 weeks	
Variable	Median (IQR)		P-val
Opioid Dose (MEDD)	288 (153, 587)	150 (54, 248)	0.002
Pain Intensity (NRS)	5.0 (3.0, 7.0)	4.5 (3.0, 7.0)	0.29
PCS (catastrophizing)	22 (10, 30)	15 (7, 23)	0.04
Fatigue	61 (54, 65)	59 (51, 65)	0.64
Anxiety	60 (53, 64)	54 (46, 62)	0.06
Depression	56 (49, 64)	55 (48, 61)	0.31
Sleep Disturbance	59 (54, 70)	56 (50, 64)	0.13
Pain Interference	63 (58, 67)	63 (57, 67)	0.44
Pain Behavior	60 (57, 63)	59 (56, 64)	0.47
Physical Function	39 (34, 41)	39 (34, 43)	0.78

Kruskal-Wallis rank sum test


Absloute Change (M
200
0
-400
-800
Increase
Decrease
200
400
600
800
100
Initial Opioid Dose


Percent Change Opic
100
50
0
-50
-100
Increase
Decrease
-4
-3
-2
-1
0
1
2
Change in Pain Score (NRS


Percent Change Opio
100
50
0
-50
-100
Increase
Decrease
-4
-3
-2
-1
0
1
2
Change in Pain Score (NRS

Comparative Effectiveness of Pain Cognitive Behavioral Therapy and Chronic Pain Self-Management Within the Context of Voluntary Opioid Reduction

Darnall BD (PI)

https://empower.stanford.edu/

EMPOWER

EFFECTIVE MANAGEMENT OF PAIN AND OPIOID-FREE WAYS TO ENHANCE RELIEF

Funded by the Patient-Centered Outcomes Research Institute®

1365 patients taking long-term opioids for chronic pain

- Stanford Pain Management Center (CA)
- Stanford Primary Care (CA)
- Kaiser Permanente (Oakland, CA)
- Intermountain Health (Utah)
- Veterans Affairs (Phoenix, AZ)
- MedNOW Clinics (Denver, CO)

CHOIR | Collaborative Health Outcomes Information Registry

EMPOWER

EFFECTIVE MANAGEMENT OF PAIN AND OPIOID-FREE WAYS TO ENHANCE RELIEF

Eligibility

- ≥ 10 MEDD daily for 3 months
- Pain for 6 months

Exclusions:

- Active suicidality
- Unable to participate in behavioral groups
- **Moderate to severe Opioid Use Disorder**

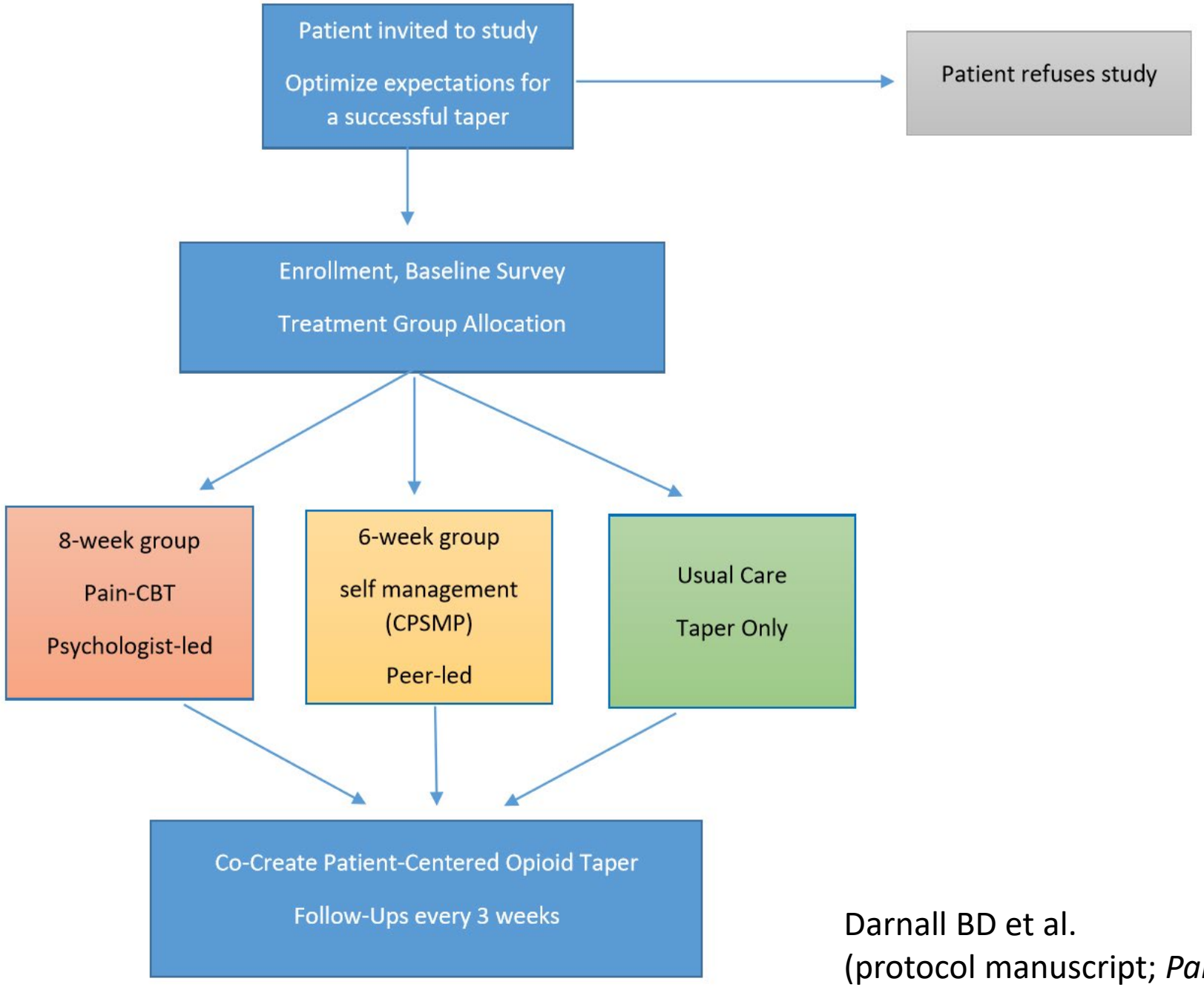
  Screening: 3 items from the TAPS + DSM-V OUD

EMPOWER

EFFECTIVE MANAGEMENT OF PAIN AND OPIOID-FREE WAYS TO ENHANCE RELIEF

We must create a caring and safe system that makes patients want to join and remain in EMPOWER

The biopsychosocial model of tapering



Darnall BD et al.
(protocol manuscript; *Pain Med.* DEC 2019)

CHOIR Collaborative Health Outcomes Information Registry

Psychosocial factors (PROMIS)

Opioids

Substance use

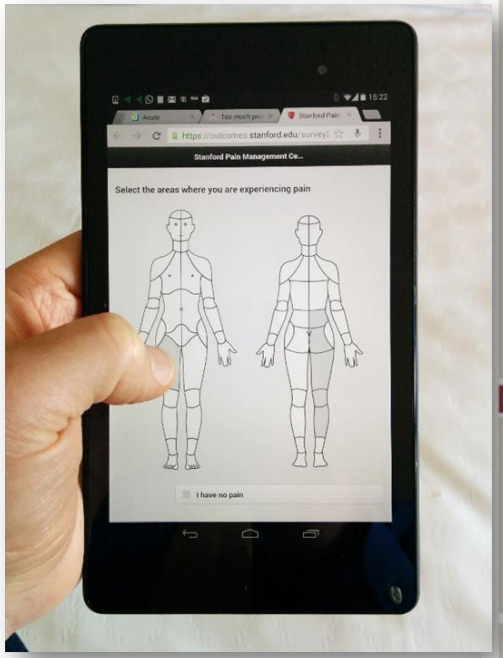
Degree of choice

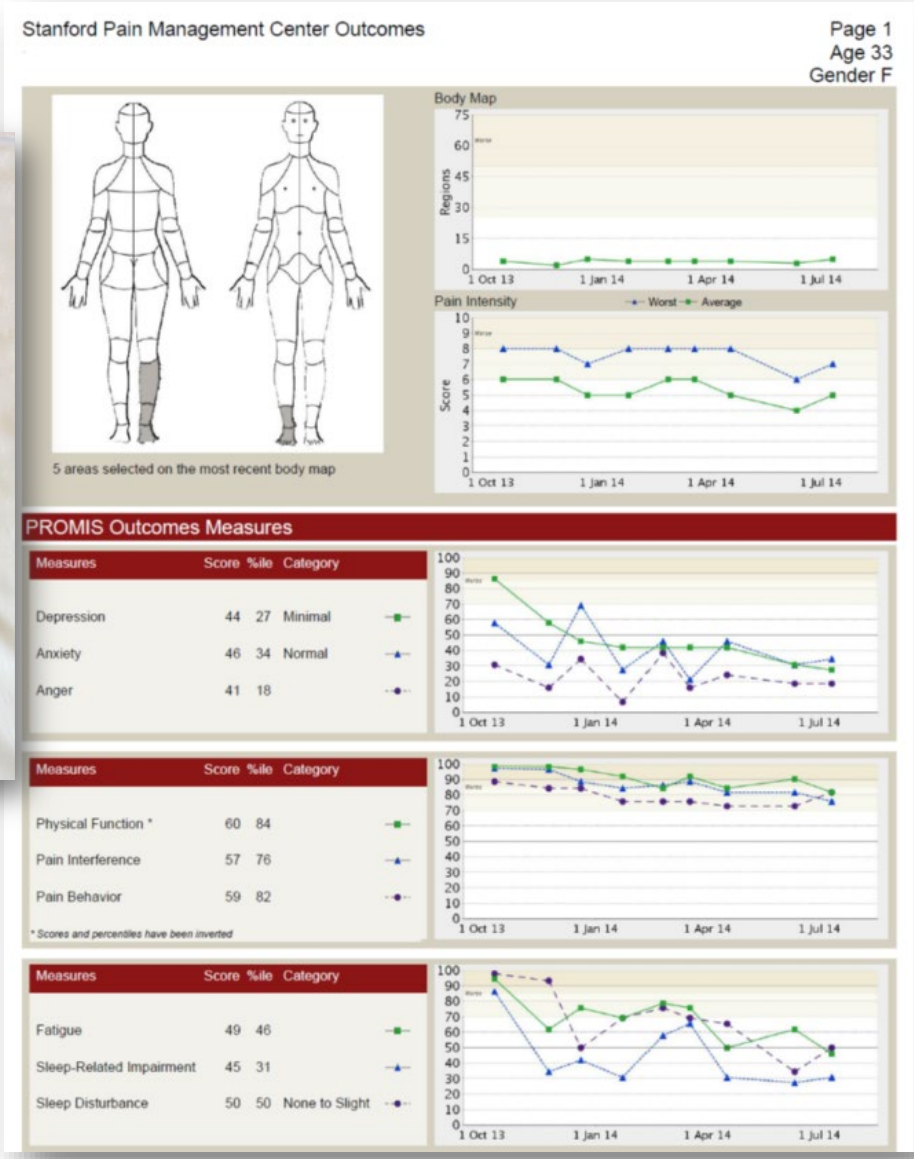
Readiness to taper

Taper beliefs

Satisfaction with clinician relationship

Comments





http://choir.stanford.edu

Google Cloud

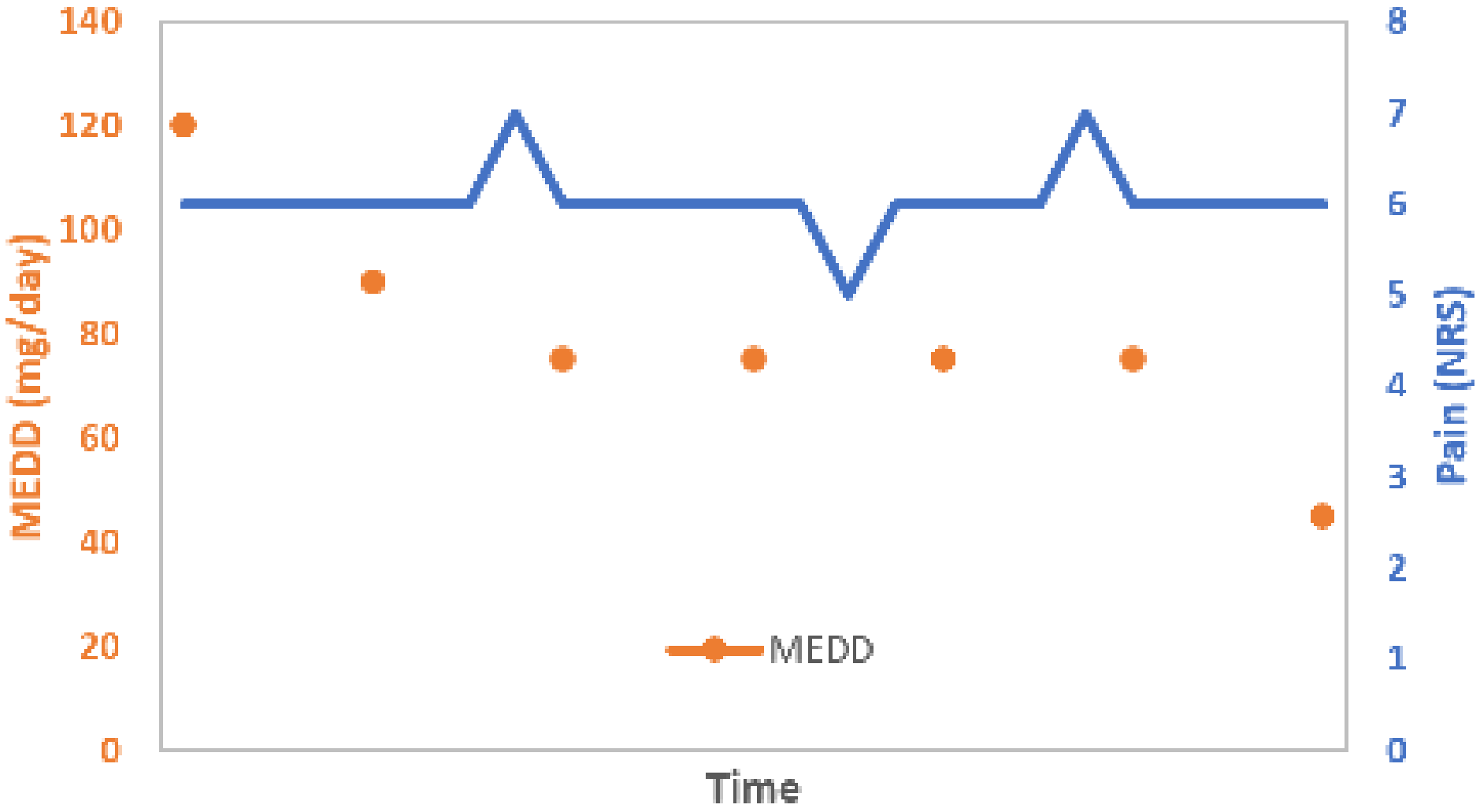
Close Monitoring of Patient Response to Opioid Reduction

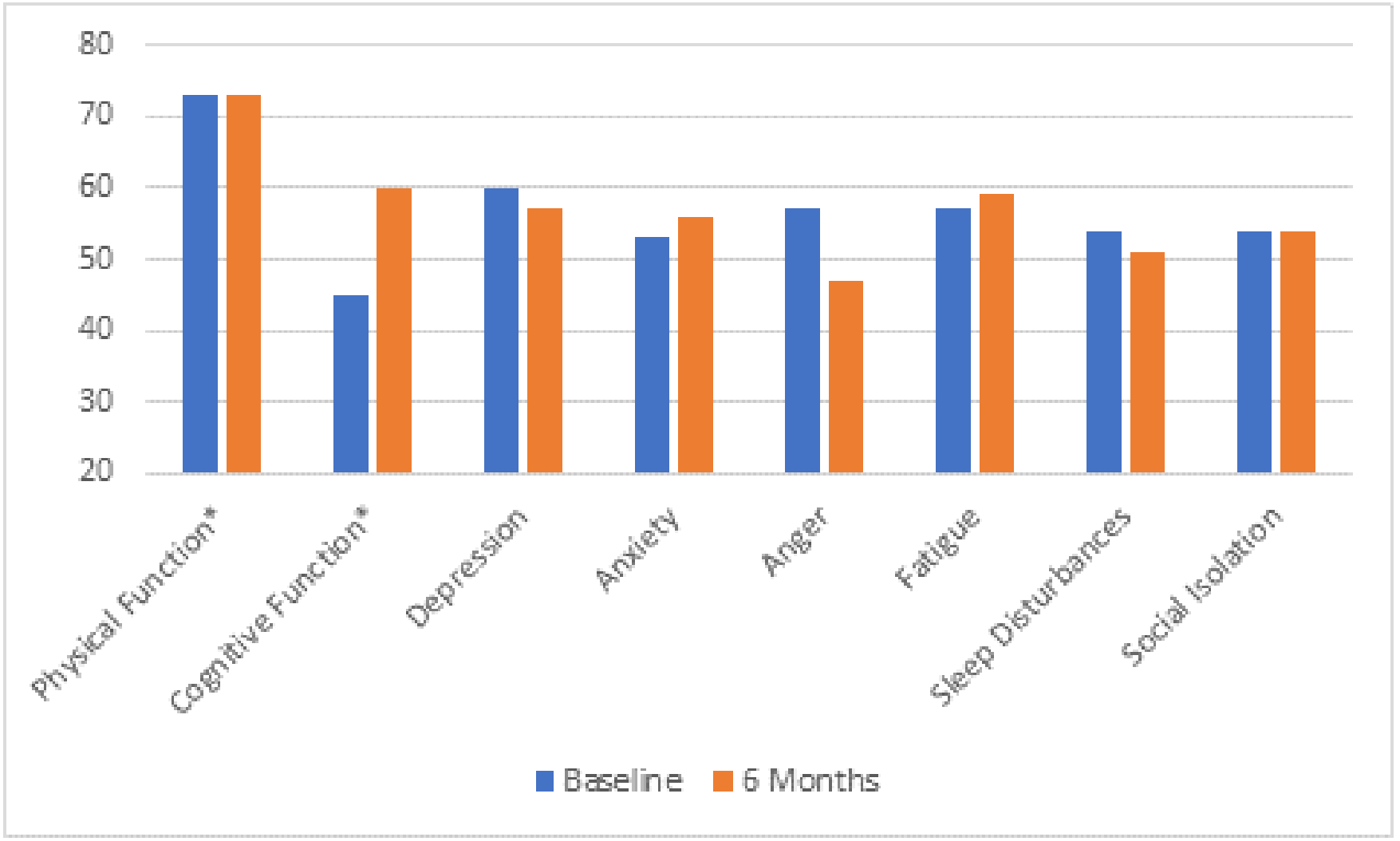
WEEKLY surveys for withdrawal symptoms, mood, comments

MONTHLY surveys for mood, suicidality, opioid dose, satisfaction, comments

- Alerts are sent to prescribers in real time
- Patients receive tailored messages

We track patients over 12 months


140
120
100
80
60
40
20
0
MEDD (mg/day)
8
7
6
5
4
3
2
1
0
Pain (NRS)
MEDD
Time


80
70
60
50
40
30
20
Physical Function*
Cognitive Function*
Depression
Anxiety
Anger
Fatigue
Sleep Disturbances
Social Isolation
Baseline
6 Months

Patient-Centered Opioid Stewardship

- Voluntary
- Enhance choice and control
- During and after taper, increase follow-up and communication
- Track closely with PROs, adjust care plan

Colleagues and Collaborators

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Lanja Sinjary
Ming-Chih Kao, PhD, MD
Jesmin Ram
Aram Mardian, MD
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