Evolution of Opioid Tapering and Challenges

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Contracts and Grants

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

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:


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

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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 Tracey1

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

1. Receiving powerful opioid Painkiller
2. Receiving nothing; saline
3. Receiving a substance that will worsen pain
Psychological Modulation of Opioid Analgesia

Ulrike Bingel et al., Sci Transl Med 2011;3:70ra14
• 3.4 % of US adults
• 11 million individuals

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.
• New starts
• Provided benchmarks of caution for increasing dose

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 Manhapa,3,4,5,6 Stefan Kertesz,7,8 Jennifer M Hah,9 Patricia Henderson,1 Amy Robinson,10 Meenah Paik,1 Friedhelm Sandbrink11,12,13 Adam J Gordon,14,15,16 Jodie A Trafton1,2,17

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

Hector R. Perez, MD, MS1, Michelle Buonora, MD, MS1, Chizae O. Cunningham, MD, MS2, Moonseong Heo, PhD3, and Joann L. Starrels, MD, MS1

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

Jocelyn R. James, MD1, JoAnna M. Scott, PhD2, Jared W. Klein, MD, MPH1, Sara Jackson, MD, MPH4, Christy McKinney, PhD, MPH5, Matthew Novack, MS6, Lisa Chew, MD, MPH1, and Joseph O. Mertli, MD, MPH1

*Department of Medicine, Division of General Internal Medicine, Harborview Medical Center, University of Washington School of Medicine, Seattle, WA, USA; †University of Missouri – Kansas City School of Dentistry, Kansas City, MO, USA; ‡Tacoma Family Medicine, MultiCare, Tacoma, WA, USA.

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

Michael I. Didenko2, Steven K. Dobscha2, Benjamin J. Morasco2,3, Thomas H.A. Meath4,5, Mark A. Ilgen4,5, Travis I. Lovejoy4,5,6

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

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?

Not Interested!
### 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*

<table>
<thead>
<tr>
<th>Outcome Variables</th>
<th>OP (n = 221) Mean (SD)</th>
<th>NOP (n = 379) Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain intensity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Admission</td>
<td>7.01 (1.77)</td>
<td>6.91 (1.58)</td>
</tr>
<tr>
<td>Discharge</td>
<td>6.46 (1.74)</td>
<td>6.14 (1.79)</td>
</tr>
</tbody>
</table>
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
May 2018

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

Beth D. Damall, PhD; Maia S. Ziadni, PhD; Richard L. Stieg, MD, MPH; et al


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 & Fields HL. (in review)
Opioid Cessation vs. Opioid Reduction
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

- 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)

16 Weeks
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 MEED = 288 (60, 1005)

Darnall BD, Ziadni MS, Mackey IG, Kao MC, Flood P (FEB 2018; JAMA Int Med)
<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>16 weeks</th>
<th>P-val</th>
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</thead>
<tbody>
<tr>
<td><strong>Median (IQR)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Opioid Dose (MEDD)</td>
<td>288 (153, 587)</td>
<td>150 (54, 248)</td>
<td>0.002</td>
</tr>
<tr>
<td>Pain Intensity (NRS)</td>
<td>5.0 (3.0, 7.0)</td>
<td>4.5 (3.0, 7.0)</td>
<td>0.29</td>
</tr>
<tr>
<td>PCS (catastrophizing)</td>
<td>22 (10, 30)</td>
<td>15 (7, 23)</td>
<td>0.04</td>
</tr>
<tr>
<td>Fatigue</td>
<td>61 (54, 65)</td>
<td>59 (51, 65)</td>
<td>0.64</td>
</tr>
<tr>
<td>Anxiety</td>
<td>60 (53, 64)</td>
<td>54 (46, 62)</td>
<td>0.06</td>
</tr>
<tr>
<td>Depression</td>
<td>56 (49, 64)</td>
<td>55 (48, 61)</td>
<td>0.31</td>
</tr>
<tr>
<td>Sleep Disturbance</td>
<td>59 (54, 70)</td>
<td>56 (50, 64)</td>
<td>0.13</td>
</tr>
<tr>
<td>Pain Interference</td>
<td>63 (58, 67)</td>
<td>63 (57, 67)</td>
<td>0.44</td>
</tr>
<tr>
<td>Pain Behavior</td>
<td>60 (57, 63)</td>
<td>59 (56, 64)</td>
<td>0.47</td>
</tr>
<tr>
<td>Physical Function</td>
<td>39 (34, 41)</td>
<td>39 (34, 43)</td>
<td>0.78</td>
</tr>
</tbody>
</table>

Kruskal-Wallis rank sum test
Initial Opioid Dose

Sample Graph: Absolute Change vs. Initial Opioid Dose

- Increase
- Decrease
Change in Pain Score (NRS)

Percent Change Option:

Increase

Decrease
Change in Pain Score (NRS)

Percent Change Option

Increase

Decrease
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/

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)
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
We must create a caring and safe system that makes patients want to join and remain in EMPOWER
The biopsychosocial model of tapering
Psychosocial factors (PROMIS)
Opioids
Substance use
Degree of choice
Readiness to taper
Taper beliefs
Satisfaction with clinician relationship
Comments

http://choir.stanford.edu
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
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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