Pain and Opioid Use Disorders: The Present and Future of Risk Assessment and Mitigation

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Colorado Pain Society
Conflict of interest

- MDC has no conflict of interest related to the topic of this presentation
An expert is a person who has made all the mistakes that can be made in a very narrow field.

Neils Bohr
Introduction

Pain and opioid misuse, abuse and use disorder

Risk Assessment, Monitoring and Mitigation-the present

Risk Assessment, Monitoring and Mitigation-the future

Conclusions
Persistent Pain

- Anxiety
- Depression
- Substance Misuse, Abuse
- Secondary medical problems
- Functional Disabilities
- Cognitive Distortions
- Sleep disturbance
Untreated or mismanaged pain can lead to adverse effects such as delays in healing, changes in the central nervous system (neuroplasticity), chronic stress, depression, suicide and opioid addiction.

McCaffery & Pasero 1999
Fishbain 1999
Mendell & Sahenk 2003
Cheatle 2011
Chronic pain: In the US, an estimated 100 (30%) million adults deal with chronic pain, and chronic pain's prevalence on the rise worldwide.

The annual cost of chronic pain in the United States is estimated to be $560 to over $600 billion including the cost of healthcare ($261-300 billion) and lost productivity ($297-336 billion).

Disablement from chronic pain affects sufferers, their families, and their workplaces.

Pain is part of the human condition

Protection from and relief of pain and suffering are a fundamental feature ... as well as a cardinal underpinning of the art and science of healing.
Cancer vs Diabetes vs Heart vs Pain

Prevalence in Millions

http://www.newswise.com/articles/inadequate-pain-research-funding-hampers-effort-to-find-safer-and-more-effective-treatments
The Cost to America in $ Billions

- Heart Disease: 175
- Pain: 700
The 2011 IOM report on pain outlined the following principles:

- Effective pain management is a “moral imperative”
- Pain should be considered a disease with distinct pathology
- There is a need for interdisciplinary treatment approaches
- There is a serious problem of diversion and abuse of opioid drugs
Pain and Prescription Opioid Abuse
Opioid Focused Model

Pain Management=opioids

➢ Developed for numerous reasons:
  – Unidimensional and unimodal approach to pain treatment.
  – Focus of the pharmaceutical industry
  – Use of the opioid model from end-of-life and cancer populations generalized to those with pain of non-cancer origin.

U. S. Prescription Opioid Sales, Deaths, Treatment (1999-2010)

Is the Opioid Crisis Uniquely a US Problem?
Proportion of general practice patients prescribed benzodiazepines, Z drugs, opioids, GABAergic drugs, or any of these drugs, 2000 to 2015.

Source: Clinical Practice Research Datalink

Deborah Cohen BMJ 2017;358:bmj.j4249
Comparison of fatal poisonings by prescription opioids

Margareeta Häkkinen*, Terhi Launiainen, Erkki Vuori, Ilkka Ojanperä

University of Helsinki, Hjelt Institute, Department of Forensic Medicine, PO Box 40 (Kytösuontie 31), FI-00014 Helsinki, Finland
3% – 62% of CPPs on opioid therapy exhibit problematic opioid-taking behaviors.

Martell et al., 2007; Chabal et al., 1997; Fishbain, 1996; Katz & Fanciullo 2002; Michna et al, 2007; Ballantyne & Laforge 2007.

Reported prevalence rate of substance dependence in CPPs ranges from 1%< – 40%

Fishbain et al., 1992; Reid et al., 2002; Katz & Fanciullo 2002; Ives et al., 2006; Fishbain et al, 2008.
Definitions of misuse, abuse and addiction are inconsistent across studies and behaviors evaluated vary in seriousness.

Poorly standardized methods to detect these outcomes.

Data from efficacy trials underestimate risks.
Prevalence of OUD in CNCP

- Boscarino employed the DSM-5 criteria for diagnosing OUD in a large cohort of patients with CNCP receiving opioid therapy. Results revealed that the prevalence of lifetime OUD was 34.9% and that 21.7% of this population met criteria for moderate OUD and 13.2% for severe OUD.¹

- In a more recent study-- again using the more sensitive DSM-5 criteria-- it was discovered that in a cohort of patients with CNCP receiving long-term opioid therapy, 41.3% met criteria for a lifetime prevalence of any OUD.

Opioid Abuse in Chronic Pain — Misconceptions and Mitigation Strategies

Nora D. Volkow, M.D., and A. Thomas McLellan, Ph.D.

Chronic pain not caused by cancer is among the most prevalent and debilitating medical conditions but also among the most controversial and complex to manage. The urgency of patients’ needs, the demonstrated effectiveness of opioid analgesics for the management of acute pain, and the limited therapeutic alternatives for chronic pain have combined to produce an overreliance on opioid medications in the United States, with associated alarming increases in diversion, overdose, and addiction. Given the lack of clinical consensus and research-supported guidance, physicians understandably have questions about whether, when, and how to prescribe opioid analgesics for chronic pain without increasing public health risks. Here, we draw on recent research to address common misconceptions regarding the abuse-related risks of opioid analgesics and highlight strategies to minimize those risks.

“Addiction occurs in only a small percentage of persons who are exposed to opioids — even among those with preexisting vulnerabilities”
OPIOIDS & SUBSTANCE USE DISORDERS SECTION

Original Research Article
Low Risk of Producing an Opioid Use Disorder in Primary Care by Prescribing Opioids to Prescreened Patients with Chronic Noncancer Pain

Martin D. Cheatle, PhD,* Rollin M. Gallagher, MD,†‡ and Charles P. O’Brien, MD, PhD* Setting. Private community-based internal medicine and family medicine clinics.

- Design: Longitudinal, prospective, descriptive design with repeated measures of 180 patients initiating opioid therapy for CNMP in PCP
- Measures: Standardized measures of patient status (pain, functional impairment, psychiatric disorders, family history) and treatments provided, urine drug monitoring, and medical chart audits (presence of aberrant drug-related behaviors)
- Results: Less than 5% of our study population revealed any evidence of substance use disorder.
### Prevalence of SUD in patients with chronic pain

<table>
<thead>
<tr>
<th>Setting</th>
<th>Rate</th>
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</thead>
<tbody>
<tr>
<td>Primary care clinics</td>
<td>3%-26%</td>
</tr>
<tr>
<td>Pain clinics</td>
<td>2%-14%</td>
</tr>
</tbody>
</table>

- Rates of carefully diagnosed SUD in primary care are approximately 8%.
- Rates of misuse, abuse, and addiction-related aberrant behaviors range from 15% to 26%.
Pendulum of Policies in Opioid Rx

Opioids are good

Opioids are bad
> 80 % of Americans Believe Using “Prescription Pain Killers” Can Result in Addiction

Do you think that taking prescription painkillers for long-term, chronic pain could result in addiction?

- Yes: 82%
- No: 9%
- Not sure: 10%

Source: A Research!America poll of U.S. adults conducted in partnership with Zogby Analytics in March 2013.
Opioids DO NOT Create Addiction

Biology/Genes → DRUG → Addiction

Environment → Brain Mechanisms → Addiction

Biology/Genes → Environment

DRUG

Brain Mechanisms

Addiction
Vulnerability to Opioid Use Disorder

Individuals respond differently to opioid exposure

Addictive Disease after opioid exposure

No addictive disease with exposure

No addictive disease due to lack of exposure

Slide courtesy of Lynn Webster, MD
The Issue of Pain and Addiction is complex!!

- Pain Disorders
- Addiction Disorders
- Combined Effect
- Psychiatric Disorders
- Drugs
Treatment Dichotomy
Spot the Addict
Risk Assessment, Monitoring and Mitigation

The Present
Risk Assessment and Monitoring in Opioid Therapy

- Clinical Interview
- Risk Screening Tools
- UDS
- Prescription Drug Monitoring programs
# Mental Health Screening Tools

<table>
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<tr>
<th>Tool</th>
<th># of Items</th>
<th>Time to Complete</th>
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<tbody>
<tr>
<td>Beck Depression Inventory II (Beck et al, 1996)</td>
<td>const 21</td>
<td>5 - 10 minutes</td>
</tr>
<tr>
<td>Beck Depression Inventory – Fast Screen for Medical Patients (Beck et al, 2000)</td>
<td>const 7</td>
<td>&lt; 5 minutes</td>
</tr>
<tr>
<td>Profile of Mood States II: Full (Beck et al, 2000)</td>
<td>const 65</td>
<td>10 - 15 minutes</td>
</tr>
<tr>
<td>Short (McNair et al, 1971)</td>
<td>const 35</td>
<td>5 - 10 minutes</td>
</tr>
<tr>
<td>Zung Self-Rating Depression Scale (Zung 1965)</td>
<td>const 20</td>
<td>10 minutes</td>
</tr>
<tr>
<td>Center for Epidemiologic Studies Depression Scale: Full</td>
<td>const 20</td>
<td>5 - 10 minutes</td>
</tr>
<tr>
<td>Short (Radloff, 1977)</td>
<td>const 10</td>
<td>5 minutes</td>
</tr>
<tr>
<td>Patient Health Questionnaire: PHQ-9</td>
<td>const 9</td>
<td>5 minutes</td>
</tr>
<tr>
<td>PHQ-4 (Kroenke et al 19990)</td>
<td>const 4</td>
<td>&lt; 5 minutes</td>
</tr>
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</table>
## Risk Assessment Tools: Examples

<table>
<thead>
<tr>
<th>Tool</th>
<th># of items</th>
<th>Administered</th>
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</thead>
<tbody>
<tr>
<td><strong>Patients considered for long-term opioid therapy:</strong></td>
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<td></td>
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<tr>
<td>ORT Opioid Risk Tool</td>
<td>5</td>
<td>By patient</td>
</tr>
<tr>
<td>SOAPP® Screener &amp; Opioid Assessment for Patients w/ Pain</td>
<td>24, 14, &amp; 5</td>
<td>By patient</td>
</tr>
<tr>
<td>DIRE Diagnosis, Intractability, Risk, &amp; Efficacy Score</td>
<td>7</td>
<td>By clinician</td>
</tr>
<tr>
<td><strong>Characterize misuse once opioid treatments begins:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PMQ Pain Medication Questionnaire</td>
<td>26</td>
<td>By patient</td>
</tr>
<tr>
<td>COMM Current Opioid Misuse Measure</td>
<td>17</td>
<td>By patient</td>
</tr>
<tr>
<td>PDUQ Prescription Drug Use Questionnaire</td>
<td>40</td>
<td>By clinician</td>
</tr>
<tr>
<td><strong>Not specific to pain populations:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CAGE-AID Cut Down, Annoyed, Guilty, Eye-Opener Tool, Adjusted to Include Drugs</td>
<td>4</td>
<td>By clinician</td>
</tr>
<tr>
<td>RAFFT Relax, Alone, Friends, Family, Trouble</td>
<td>5</td>
<td>By patient</td>
</tr>
<tr>
<td>DAST Drug Abuse Screening Test</td>
<td>28</td>
<td>By patient</td>
</tr>
<tr>
<td>SBIRT Screening, Brief Intervention, &amp; Referral to Treatment</td>
<td>Varies</td>
<td>By clinician</td>
</tr>
</tbody>
</table>
Urine Drug Monitoring

- Assess only the presence of a particular drug and/or metabolite in a specific concentration at a specific moment in time
- A positive result does not diagnose
  - Drug addiction
  - Physical dependence
  - Impairment
- Absence of Rx opioid may reflect diversion, but also hoarding
Prescription drug monitoring programs

- Available now in many states
- Studies show that use of PDMPs can identify cases of diversion and doctor shopping
  - Recent study found decreased inappropriate drug prescribing with use of a centralized prescribing system in Canada
  - Effects on clinical outcomes (e.g., overdose) and optimal strategies for using PDMP not known
- Use variable and generally suboptimal
- PDMPs vary in who can access, information not available across states

\(^a\)Dormuth et al. CMAJ 2012
Risk Mitigation

National VA Effort
Reduced Risky Prescriptions

High-dose opioids: ↓16%
Very high-dose opioids: ↓24%
Opioids+sedatives: ↓21%

Lin et al, PAIN, Jan. 2017

Guidelines
Risk Mitigation Strategies

- Clinician Education (eg REMS)
- Abuse Deterrent Opioid Formulations
- Opioid Prescribing Guidelines
- Dosage Limitations
Educational strategies

- No data available on impact of training and educational strategies on clinical outcomes

- REMS plan approved by FDA July 2012
  - Primarily for schedule II, long-acting or extended release opioids
  - *Voluntary* prescriber continuing education (not required for DEA licensure); financial support by manufacturers mandatory
  - No evidence yet available on impact on clinical outcomes
Education
Methods: An expert panel developed a novel methodology for characterizing USMLE questions based on pain core competencies and topical and public health relevance.

Results:

- 1,506 questions were reviewed, with 28.7% (432) identified as including the word “pain.”
- Of these, 232 questions (15.4% of the 1,506 USMLE questions reviewed) were assessed as being fully or partially related to pain, rather than just mentioning pain but not testing knowledge of its mechanisms and their implications for treatment.
- The large majority of questions related to pain (88%) focused on assessment rather than safe and effective pain management, or the context of pain.
Opioid-deterrent formulations have recently been approved by FDA or undergoing FDA approval process

- Designed to be tamper-resistant or co-formulated with medications that reverse opioid effects or produce noxious side effects when tampered with

- Effectiveness for reducing misuse/substance abuse and improving clinical outcomes yet to be established

- Likely to be primarily effective in patients who crush or inject opioids

- One study found patients placed on a new tamper-resistant formulation of long-acting oxycodone frequently switched to an alternative opioid or heroin

Opioid Prescribing Guidelines

- APS/AAPM
- Canadian guideline for safe and effective use of opioids for chronic non-cancer pain
- Federation of State Medical Boards
- Individual state guidelines
- CDC Guidelines for Prescribing Opioids for Chronic Pain- United States, 2016
Dose escalations

- No theoretical ceiling with opioids
  - But, little evidence to guide prescribing at higher doses
  - Additional risks (hyperlgesia, endocrine), unclear benefit, and can be a marker for abuse, addiction, or diversion
  - Higher doses may be associated with higher risk

- APS/AAPM and Canadian panels defined >200 mg/day of morphine (or equivalent) as “higher dose”; recent CDC guidelines recommend 50-90 mg MEDD
Dose-response relationship for opioids and overdose

- 3 large observational studies on opioid dose and risk of overdose or death

  - Cohort study (n=9940, 51 opioid overdoses, 6 fatal)
    - Risk of opioid overdose (vs. 1 to <20 mg/day)
      - >=100 mg/d: HR 8.9 (4.0-20)
      - 50-<100 mg/d: HR 3.7 (1.5-9.5)
      - 20-<50 mg/d: HR 1.4 (0.57-3.6)
  - Case-control study (VA, 750 cases)
    - Risk of opioid overdose-related death (vs. 1 to <20 mg/day)
      - >=100 mg/d: HR 7.2 (4.8-11)
      - 50-<100 mg/d: HR 4.6 (3.2-6.7)
      - 20-<50 mg/d: HR 1.9 (1.3-2.7)
  - Nested case-control study (Ontario, 498 cases)
    - Risk of opioid-related mortality (vs. 1 to <20 mg/day)
      - >=200 mg/d: OR 2.9 (1.8-4.6)
      - 100-199 mg/d: OR 2.0 (1.3-3.2)
      - 50-99 mg/d: OR 1.9 (1.3-2.8)
      - 20-49 mg/d: OR 1.3 (0.94-1.8)

Risk Assessment
The Future
There is evidence indicating that risk for opioid addiction (OUD) has substantial genetic origins (Kreek et al, 2005)

➢ Tsuang et al (1998) showed that 54% of the liability for OUD was due to genetic variance; 38% of the liability was explained by genetic variance *specific to opioids.*

➢ Karkowski et al (2000) studied > 800 female-female twin pairs for drug abuse phenotypes. Heritability of OUD in a univariate model was 52%.

➢ Kendler et al (2003) studied ~ 1200 male-male twin pairs for substance abuse phenotypes, reporting that OUD genetic liability was 48%.

*These three twin studies are consistent with an OUD model in which half the risk is genetic*
Although some diseases, such as sickle cell anemia and cystic fibrosis, are single gene disorders, vulnerability to addiction undoubtedly has a more complex genetic basis.

Complex diseases may be polygenic (being caused by many genes), but are generally considered to be oligogenic (when only a few genes play a significant role).

The human genome contains approximately 25–40,000 genes encoded in 3.2 billion nucleotides of DNA (Lander et al 2001; Venter et al).
Human Genetics of Opioid Use Disorder

- There have several candidate genes studied in human opioid use disorders- [OPRM1- rs1799971 (A118G, Asn40Asp), CYP2D6].
- Results from studies to date have been mixed due to:
  - small sample sizes (~100-500 for control and experimental groups)
  - mixed ethnic groups
  - only one sequence variant genotyped
  - variation in case definition
  - lack of matched control cohort


Clinical and Genetic Characteristics of Opioid Addiction in Chronic Pain

Martin D. Cheatle, PhD
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Wade Berrettini, MD, PhD

University of Pennsylvania
Dennis Turk, PhD

University of Washington
Lynn Webster, MD

PRA Clinical Research
Mohammed Issa, MD
Robert Jamison, PhD

Harvard University

Grant 1RO1DA032776-01 from the National Institute on Drug Abuse, National Institutes of Health
Specific Aims

- **Specific Aim 1:** Collect phenotypic measures and blood samples of 1200 patients, with a history of CNCP who have undergone treatment for addiction to prescription opioids and 1200 patients with CNCP who are receiving COT (for longer than six months), but who have not displayed any aberrant behaviors suggestive of opioid addiction.

- **Specific Aim 2:** Conduct genetic analysis of samples from all 2400 subjects.

- **Specific Aim 3:** Perform comprehensive statistical analyses of the phenotypic and genotypic results utilizing logistic regression to examine potential markers of OUD in the study group.

- **Specific Aim 4:** Reassess over 12 months subjects’ psychiatric symptoms and the emergence of aberrant behaviors suggestive of addiction in the 1200 patients in the control group to ensure phenotypic stability.
Inclusion/Exclusion Criteria

- **Inclusion Criteria:**
  - European/American descent, defined as four out of four grandparents of European origin.
  - CNCP defined as musculoskeletal or neuropathic of nonmalignant origin persisting greater than 6 months
  - Age 18 years old and up
  - For non-addictive control population no history of addiction except nicotine defined as no evidence of ADRB in medical record review and 3 consecutive (monthly) appropriate urine drug screens (presence of prescribed opioid and absence of non prescribed opioid or illicit drug).
  - For case group, patient satisfies DSM-IV criteria for OA and requiring substance abuse treatment.

- **Exclusion Criteria:**
  - Malignant pain
  - Gynecologic, abdominal, visceral, dental, trigeminal neuralgia, post-stroke syndrome, migraines
  - Neuropathic pain due to metabolic disease
  - Co-morbid CNS disease such as dementia, AIDS, psychosis, bipolar disorder, any condition interfering with informed consent
## Assessments

<table>
<thead>
<tr>
<th>Field Staff (Nurse and field RA)</th>
<th>Baseline</th>
<th>6 Month *</th>
<th>12 Month*</th>
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<td>Eligibility Criteria 1-5</td>
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<td>Blood draw</td>
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<tr>
<td>Chart Review</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Urine drug screen (via chart review)</td>
<td>X</td>
<td>X</td>
<td>X</td>
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</table>

## Phone Assessments

<table>
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<th>Demographics</th>
<th>Baseline</th>
<th>6 Month *</th>
<th>12 Month*</th>
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<tbody>
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<td>MINI (to include lifetime sections for alcohol and drug dependence)</td>
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<tr>
<td>Coping Strategies Questionnaire</td>
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<tr>
<td>DSM checklist for substance abuse or dependence</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>PHQ- 4</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>DSM checklist for alcohol/drug use</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Brief Pain Inventory</td>
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<tr>
<td>Duke Social Support</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Treatment Services Review</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Fagerstrom Nicotine Tolerance Scale</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>FHAM-Family History Assessment Module</td>
<td>X</td>
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<tr>
<td>Beliefs about medication questionnaire</td>
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<tr>
<td>Opioid Risk Tool</td>
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<tr>
<td>Current Opioid Misuse Measure</td>
<td></td>
<td>X</td>
<td>X</td>
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</tbody>
</table>
Study Subjects

CNCP Rx opioids

No h/o SUD

No OUD n=1073

OUD n=512

n=512

n=1073
Coping Strategies Questionnaire

* p < 0.001
Brief Research Reports

The Association Between Catastrophizing and Craving in Patients with Chronic Pain Prescribed Opioid Therapy: A Preliminary Analysis

Pain-related catastrophizing as a risk factor for suicidal ideation in chronic pain

Robert R. Edwards a,*, Michael T. Smith a, Ian Kudel b, Jennifer Haythornthwaite a

a Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, 600 N. Wolfe Street, Meyer 1-108, Baltimore, MD 21287, USA
b Health Services Research and Development, Cincinnati VA Medical Center, USA

Received 16 January 2006; received in revised form 13 June 2006; accepted 6 July 2006
## Psychosocial Variables

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<th>Step</th>
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<th>Number In</th>
<th>Score Chi-Square</th>
<th>Wald Chi-Square</th>
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ROCE curves for design/demographic model and best model

Demog: AUC=0.70
Best: AUC=0.79
Predicting Opioid Use Disorder
### Dichotomous Data

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<th>N_Ctrl</th>
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<th>ChisqDF</th>
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<td>312</td>
<td>50.00</td>
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<td>Smoking</td>
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Cheatle, M; Compton P; Lynch, K; Dhingra L. in preparation for publication
## Continuous Data

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Cheatle, M; Compton P; Lynch, K; Dhingra L. in preparation for publication
### Summary of Stepwise Selection

<table>
<thead>
<tr>
<th>Step</th>
<th>Entered</th>
<th>Removed</th>
<th>DF</th>
<th>Number</th>
<th>Score</th>
<th>Pr &gt; ChiSq</th>
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</thead>
<tbody>
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<td>1</td>
<td><strong>smoking</strong></td>
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</table>

Cheatle, M; Compton P; Lynch, K; Dhingra L. in preparation for publication
ROC curves for demographic model and best model

Demog: AUC=0.88
Best: AUC=0.93
Evaluated the independent association of tobacco use and OUD in a cohort of 582 patients with CNMP and no h/o OUD (controls) and 218 patients with CNMP who developed an OUD after initiating Rx opioids (cases).

Approximately 80% of the cases reported tobacco use the past 7 days as compared to 22% of the controls.

Controlling for all known other risk factors for SUD (psychiatric co-morbidities, pain intensity, sociodemographics, etc) current tobacco use was strongly associated with OUD [OR 14.1, 95% CI 9.6-20.9, p < 0.0001]
**Opioid Risk Tool (ORT)**

<table>
<thead>
<tr>
<th>Mark each box that applies</th>
<th>Female</th>
<th>Male</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. Family hx of substance abuse</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol</td>
<td>☐ 1</td>
<td>☐ 1</td>
</tr>
<tr>
<td>Illegal Drugs</td>
<td>☐ 2</td>
<td>☐ 2</td>
</tr>
<tr>
<td>Prescription drugs</td>
<td>☐ 4</td>
<td>☐ 4</td>
</tr>
<tr>
<td><strong>2. Personal hx of substance abuse</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol</td>
<td>☐ 3</td>
<td>☐ 3</td>
</tr>
<tr>
<td>Illegal Drugs</td>
<td>☐ 4</td>
<td>☐ 4</td>
</tr>
<tr>
<td>Prescription drugs</td>
<td>☐ 5</td>
<td>☐ 5</td>
</tr>
<tr>
<td><strong>3. Age (mark box if 16-45)</strong></td>
<td>☐ 1</td>
<td>☐ 1</td>
</tr>
<tr>
<td><strong>4. Hx of preadolescent sexual abuse</strong></td>
<td>☐ 3</td>
<td>☐ 3</td>
</tr>
<tr>
<td><strong>5. Psychologic disease</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ADD, OCD, bipolar, schizophrenia</td>
<td>☐ 2</td>
<td>☐ 2</td>
</tr>
<tr>
<td>Depression</td>
<td>☐ 1</td>
<td>☐ 1</td>
</tr>
</tbody>
</table>

**Scoring totals:**

- **Scoring (Risk)**
  - 0-3 Low Risk
  - 4-7 Moderate Risk
  - ≥ 8 High Risk
Development of the Revised Opioid Risk Tool to Predict Opioid Use Disorder in Patients with Chronic Nonmalignant Pain

Martin D. Cheatle, * Peggy A. Compton, † Lara Dhingra, ‡ § Thomas E. Wasser, ¶ and Charles P. O’Brien *

- The discriminant predictive validity of the ORT was evaluated in a cohort of patients with CNMP on LTOT that displayed no evidence of developing an OUD and a sample of patients with CNMP that developed an OUD after commencing opioid therapy.

- A revised unweighted ORT (ORT-OUD) removing the history of preadolescent sexual abuse item was notably superior in predicting the development of OUD in patients with CNMP on LTOT.
Multivariate logistic regression: Classification of patients with OUD versus without OUD as predicted by ORT total score with weighted and unweighted items

<table>
<thead>
<tr>
<th>Variable</th>
<th>Beta</th>
<th>p-value</th>
<th>OR</th>
<th>95% Lower Bound</th>
<th>95% Upper Bound</th>
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</thead>
<tbody>
<tr>
<td>ORT Total Score (Weighted 10-items)</td>
<td>0.485</td>
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<td>1.624</td>
<td>1.539</td>
<td>1.715</td>
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<tr>
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<td>0.500</td>
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<td>1.648</td>
<td>1.559</td>
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<tr>
<td>ORT Total Score (Unweighted)</td>
<td>1.127</td>
<td>&lt;0.001</td>
<td>3.085</td>
<td>2.725</td>
<td>3.493</td>
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</table>
Opioid Risk Tool – OUD (ORT-OUD)

This tool should be administered to patients upon an initial visit prior to beginning or continuing opioid therapy for pain management. A score of 2 or lower indicates low risk for future opioid use disorder; a score of $\geq 3$ indicates high risk for opioid use disorder.

<table>
<thead>
<tr>
<th>Mark each box that applies</th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family history of substance abuse</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Illegal drugs</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Rx drugs</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Personal history of substance abuse</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Illegal drugs</td>
<td>1</td>
<td>0</td>
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<tr>
<td>Rx drugs</td>
<td>1</td>
<td>0</td>
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<tr>
<td>Age between 16-45 years</td>
<td>1</td>
<td>0</td>
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<tr>
<td>Psychological disease</td>
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<td>ADD, OCD, bipolar, schizophrenia</td>
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<td>0</td>
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<tr>
<td>Depression</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Scoring totals</td>
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</tbody>
</table>

Conclusions

- Pain is complex
- Opioids can be efficacious for some patients with chronic pain
- There is a serious crisis of opioid abuse, diversion and fatal overdoses
- More evidence needed to understand optimal risk assessment, opioid selection, dosing, monitoring and risk mitigation
- Assessing risk of abuse in patients receiving chronic opioid therapy is a dynamic, ongoing process
- Discovering genetic markers for OUD requires further investigation but phenotypic data may lead to a more specific risk assessment tool
Clinical implications

- **No opioid is “safe”**
  - More selective and cautious prescribing appears indicated while awaiting better evidence, focus on patient safety
  - Need to assess risk as standard practice
  - Routine integration of risk mitigation strategies matched with level of assessed risk
  - Need for ready availability and use of effective non-opioid treatments for chronic pain, including those addressing psychosocial factors
  - Be cognizant of the silent epidemic of suicide in this vulnerable patient population
Opioid Epidemic and the Pain Epidemic
Acknowledgements

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  - Sebastian Pena, BA

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  - Dennis C. Turk, PhD
  - Dana Divens
  - Ann Bradshaw

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  - Lara Dhingra, PhD

- Harvard University, Boston
  - Mohammed Issa, MD
  - Robert Jamison, PhD
THANK YOU!!!