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

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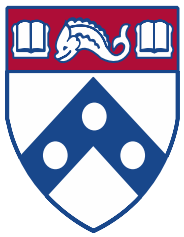


Perelman
School of Medicine
University of Pennsylvania

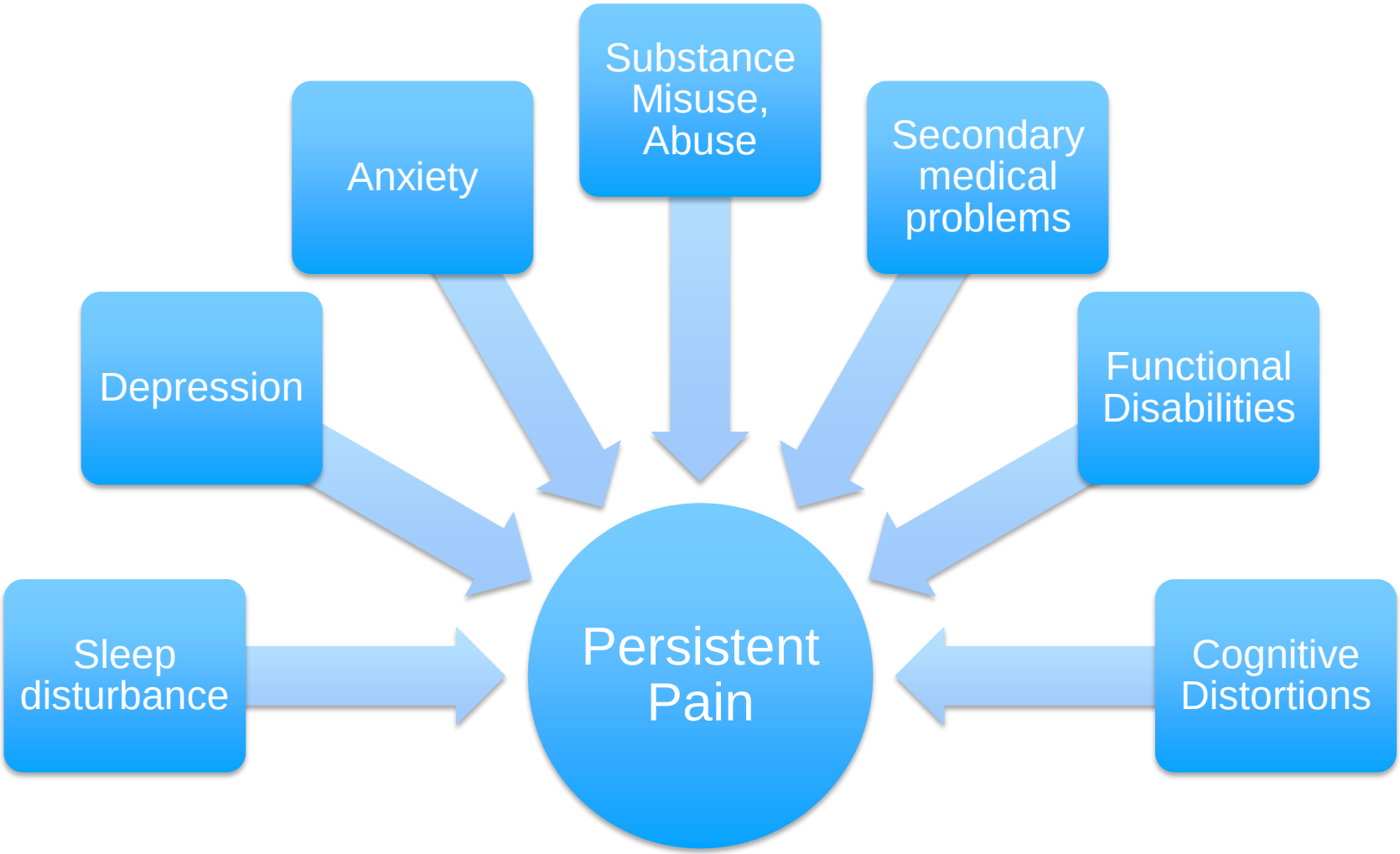
Conflict of interest

- 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


Substance Misuse, Abuse
Anxiety
Secondary medical problems
Depression
Functional Disabilities
Sleep disturbance
Persistent Pain
Cognitive Distortions

CPS-Consequences

- **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**

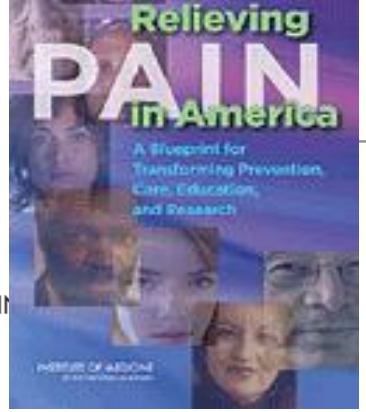
McCaffery & Pasero 1999

Fishbain 1999

Mendell & Sahenk 2003

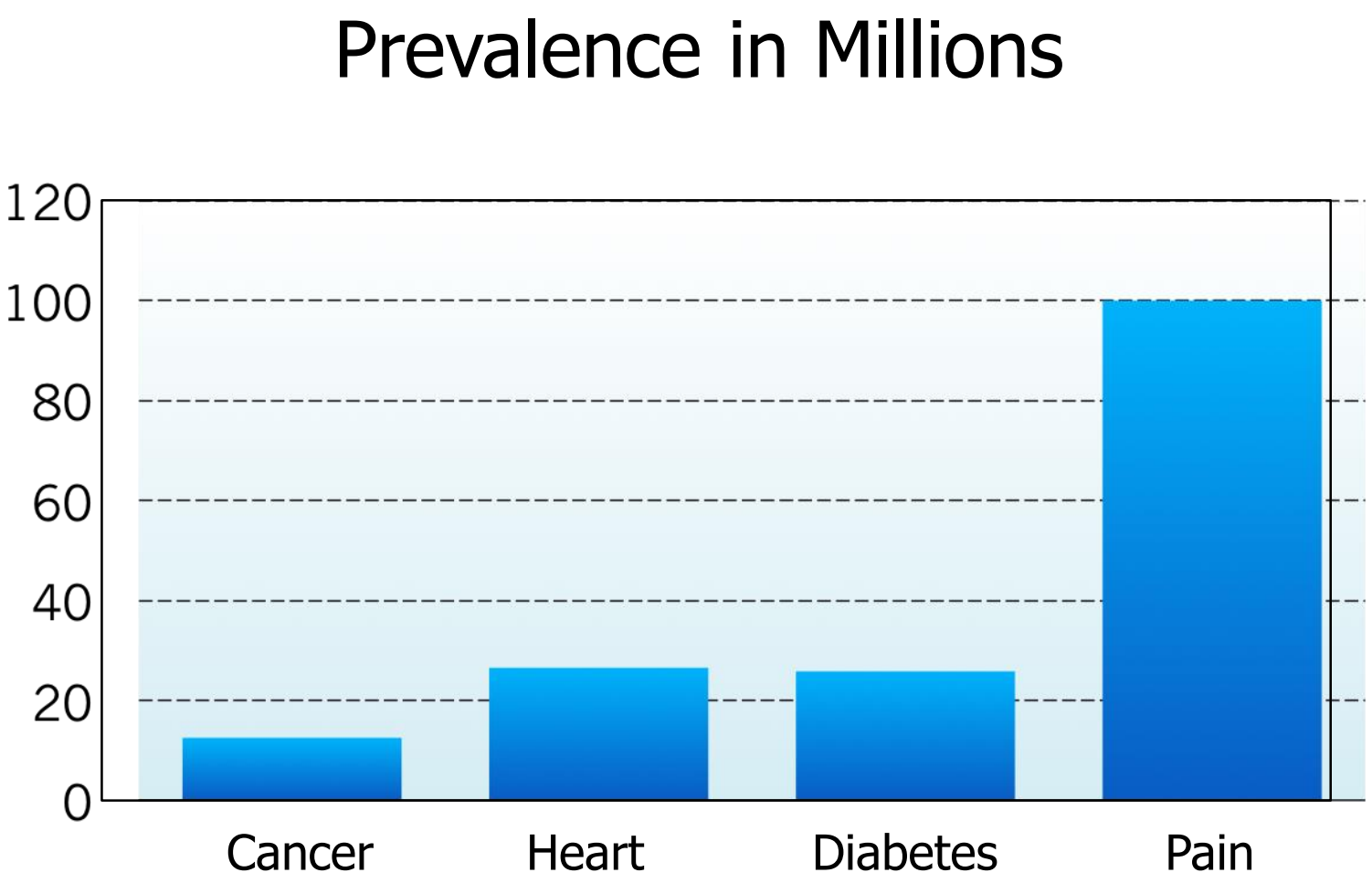
Cheatle 2011

Relieving Pain in America:
A Blueprint for Transforming Prevention, Care, Education, and Research.
Inst of Med of the National Academies. 2011

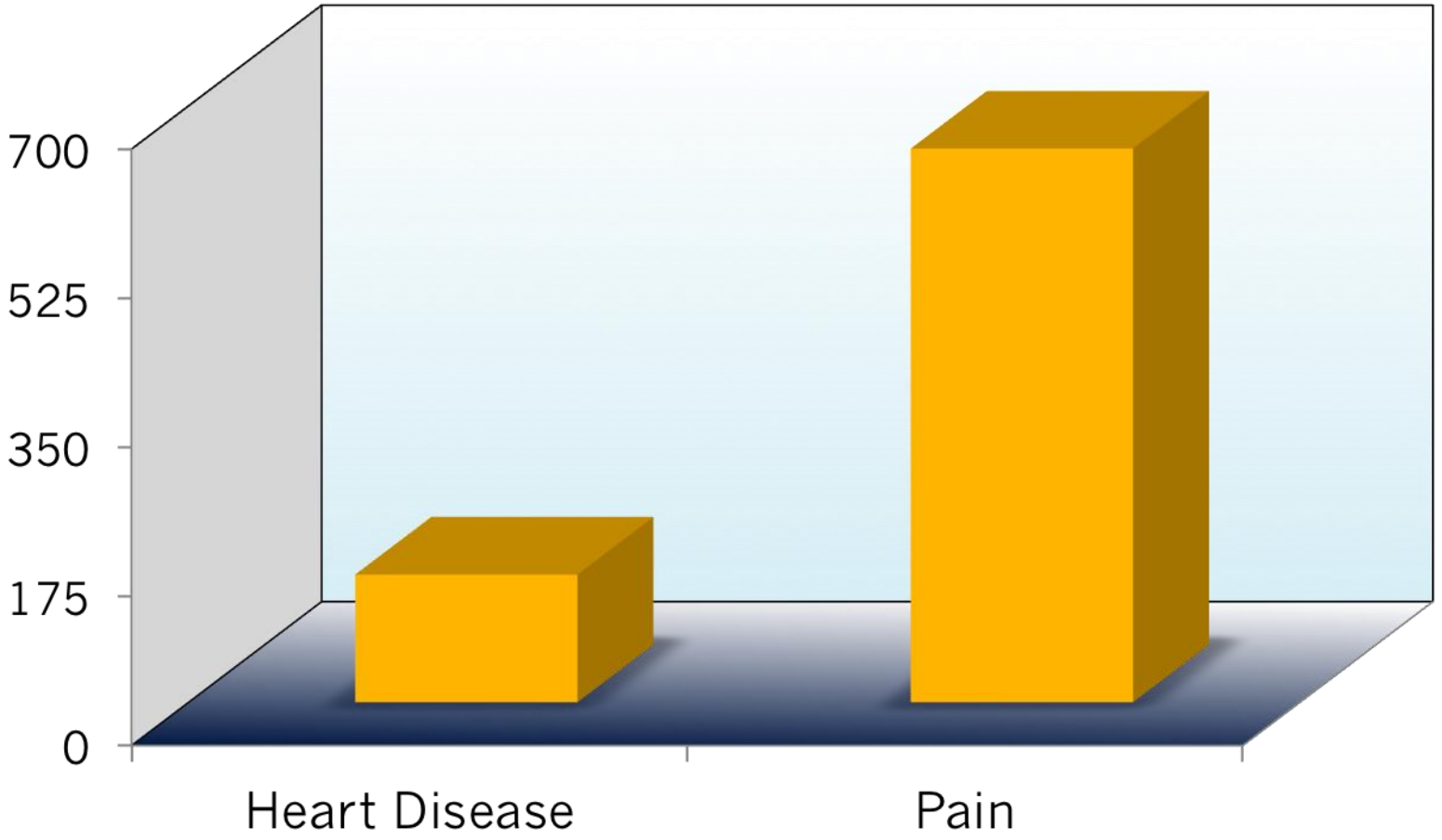


- **Chronic pain: In the US, an estimated 100 (30%) million adults deal with chronic pain, and chronic pain's prevalence on the rise worldwide.**
- **The annual cost of chronic pain in the United States is estimated to be $560 to over $600 billion including the cost of healthcare ($261-300 billion) and 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



The Cost to America in $ Billions



Relieving Pain in America:
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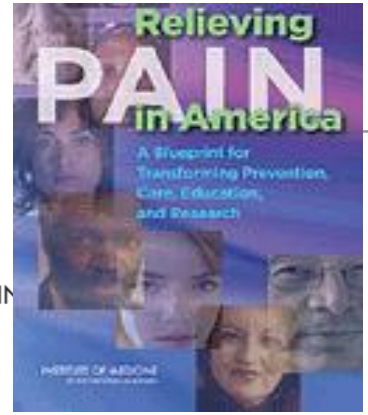
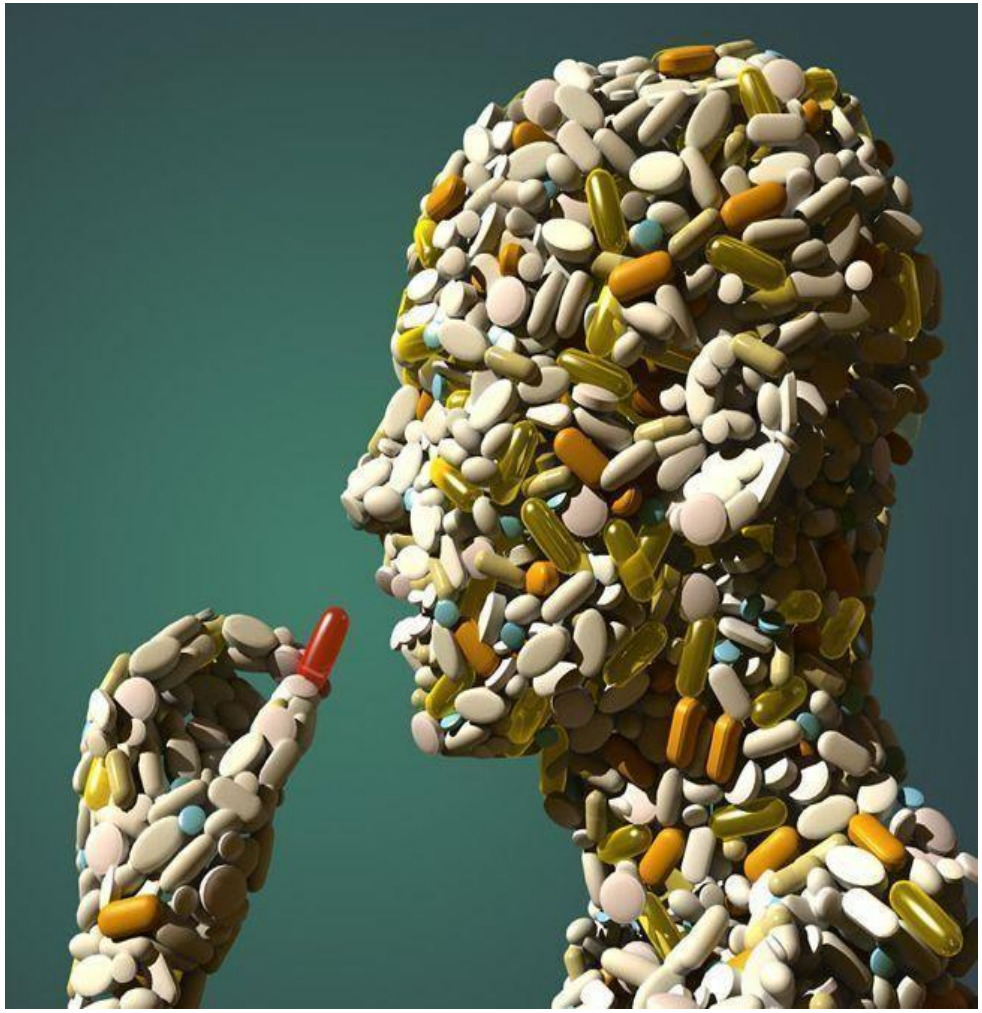


- The 2011 IOM report on pain outlined the following principles:
  - effective pain management is a "moral imperative"
  - pain should be considered a disease with distinct pathology
  - there is a need for interdisciplinary treatment approaches
  - there is a serious problem of diversion and abuse of opioid drugs

Pain and Prescription Opioid Abuse



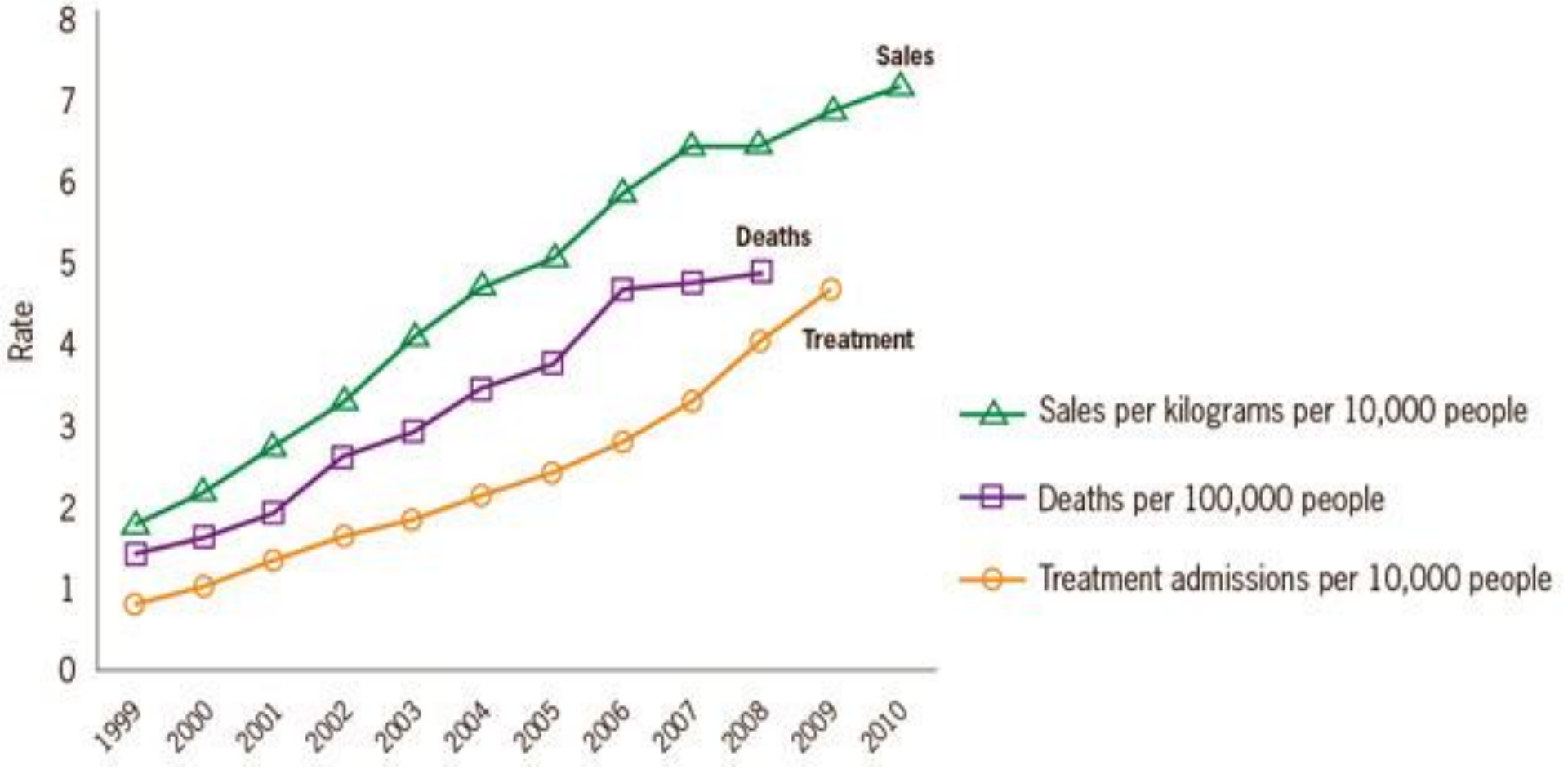
Opioid Focused Model

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.

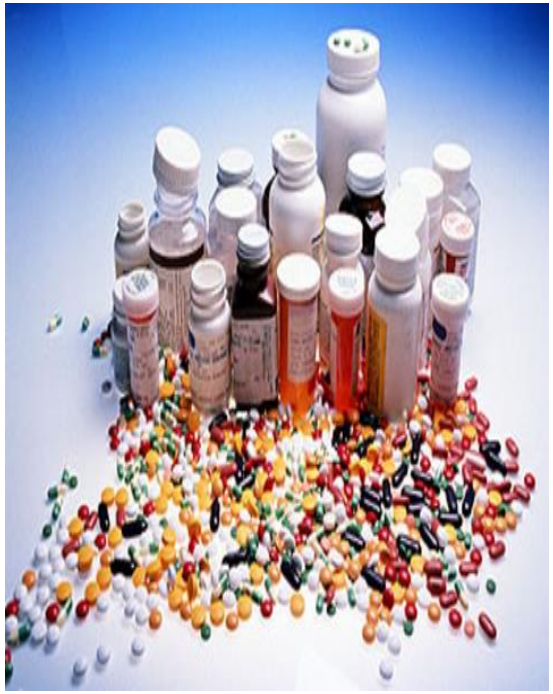
Peppin, J.F., Cheatle, M.D., Kirsh, K., McCarberg, W. The complexity model: A novel approach to improve chronic pain care. Pain Medicine, 16 (4): 653-666, 2015.

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

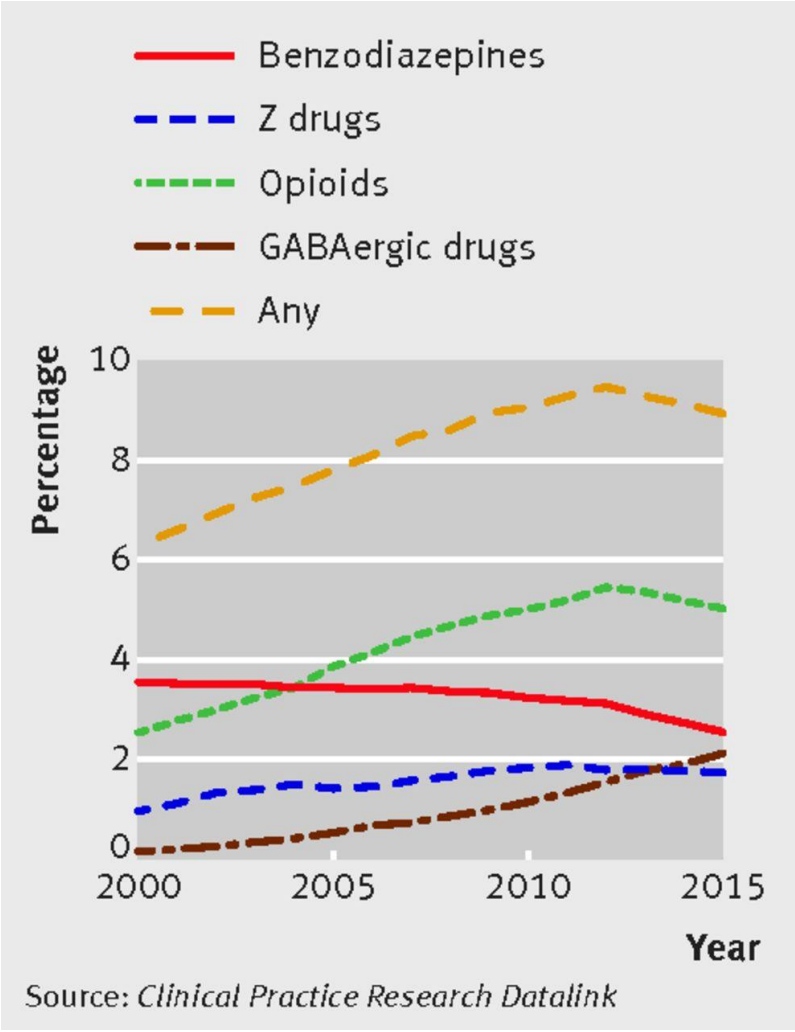


SOURCES: National Vital Statistics System, 1999-2008; Automation of Reports and Consolidated Orders System (ARCOS) of the Drug Enforcement Administration (DEA), 1999-2010; Treatment Episode Data Set, 1999-2009

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.



Deborah Cohen BMJ 2017;358:bmj.j4249

thebmj

Forensic Science International 222 (2012) 327–331

Contents lists available at SciVerse ScienceDirect

Forensic Science International

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

Comparison of fatal poisonings by prescription opioids

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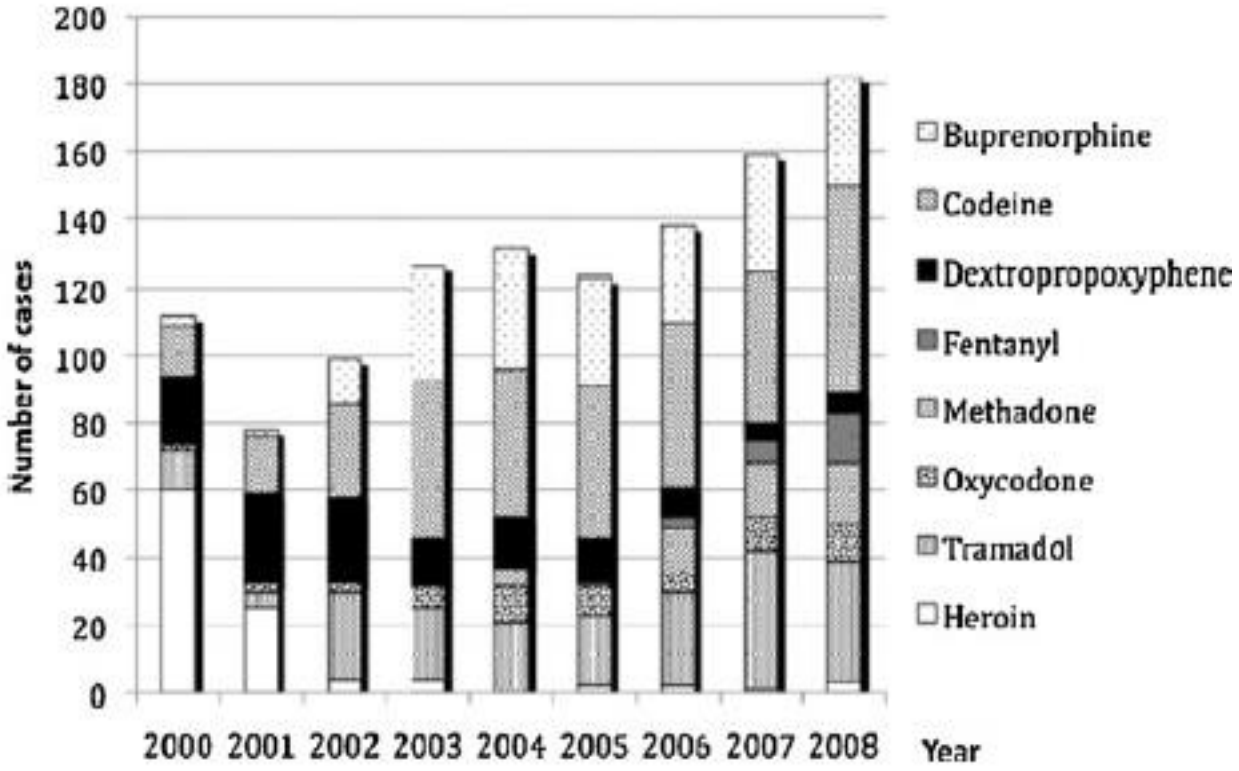
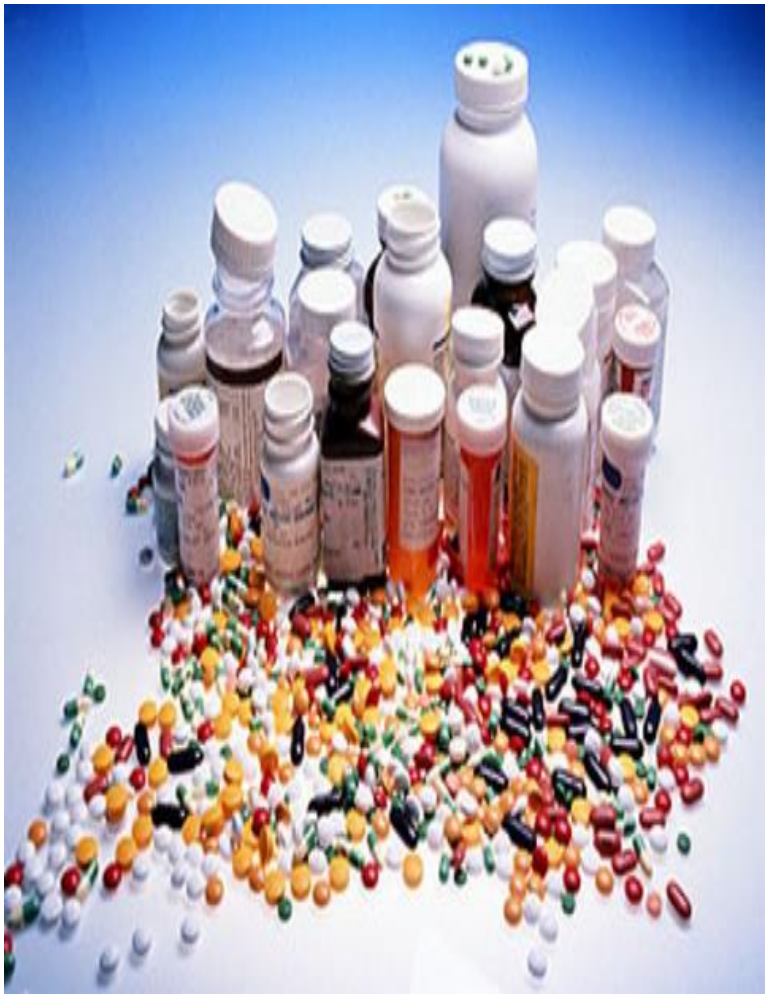




- **3% – 62% of CPPs on opioid therapy exhibit problematic opioid-taking behaviors.**

  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.

Misuse, Abuse, Addiction

- 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.**

1.Boscarino JA, Rukstalis MR, Hoffman SN, Han JJ, Erlich PM, Ross S, Gerhard GS, Stewart WF. Prevalence of prescription opioid-use disorder among chronic pain patients: comparison of the DSM-5 vs. DSM-4 diagnostic criteria. J Addict Dis 2011;30(3):185-94.; 2. Boscarino JA, Hoffman SN, Han JJ. Opioid-use disorder among patients on long-term opioid therapy: impact of final DSM-5 diagnostic criteria on prevalence and correlates. Subst Abuse Rehabil. 2015 Aug 19;6:83-91.

The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

Dan L. Longo, M.D., *Editor*

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.

From the National Institute on Drug Abuse, National Institutes of Health, Bethesda, MD (N.D.V.); and the Treatment Research Institute, Philadelphia (A.T.M.). Address reprint requests to Dr. Volkow at the National Institute on Drug Abuse, National Institutes of Health, 6001 Executive Blvd., Bethesda, MD 20892, or at nvolkow@nida.nih.gov.

N Engl J Med 2016;374:1253-63.
DOI: 10.1056/NEJMra1507771

"Addiction occurs in only a small percentage of persons who are exposed to opioids — even among those with preexisting vulnerabilities"

Pain Medicine 2018; 19: 764–773
doi: 10.1093/pm/pnx032

OXFORD

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.**

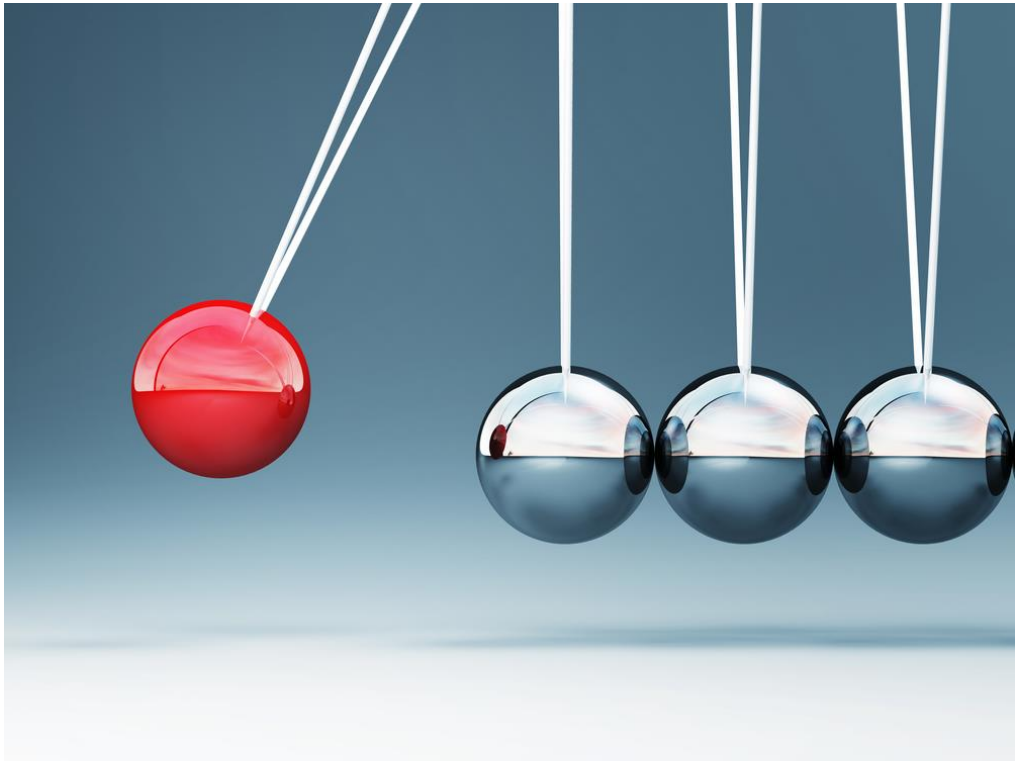
Prevalence of SUD in patients with chronic pain

Primary care clinics	**3%-26%**
Pain clinics	**2%-14%**

- 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

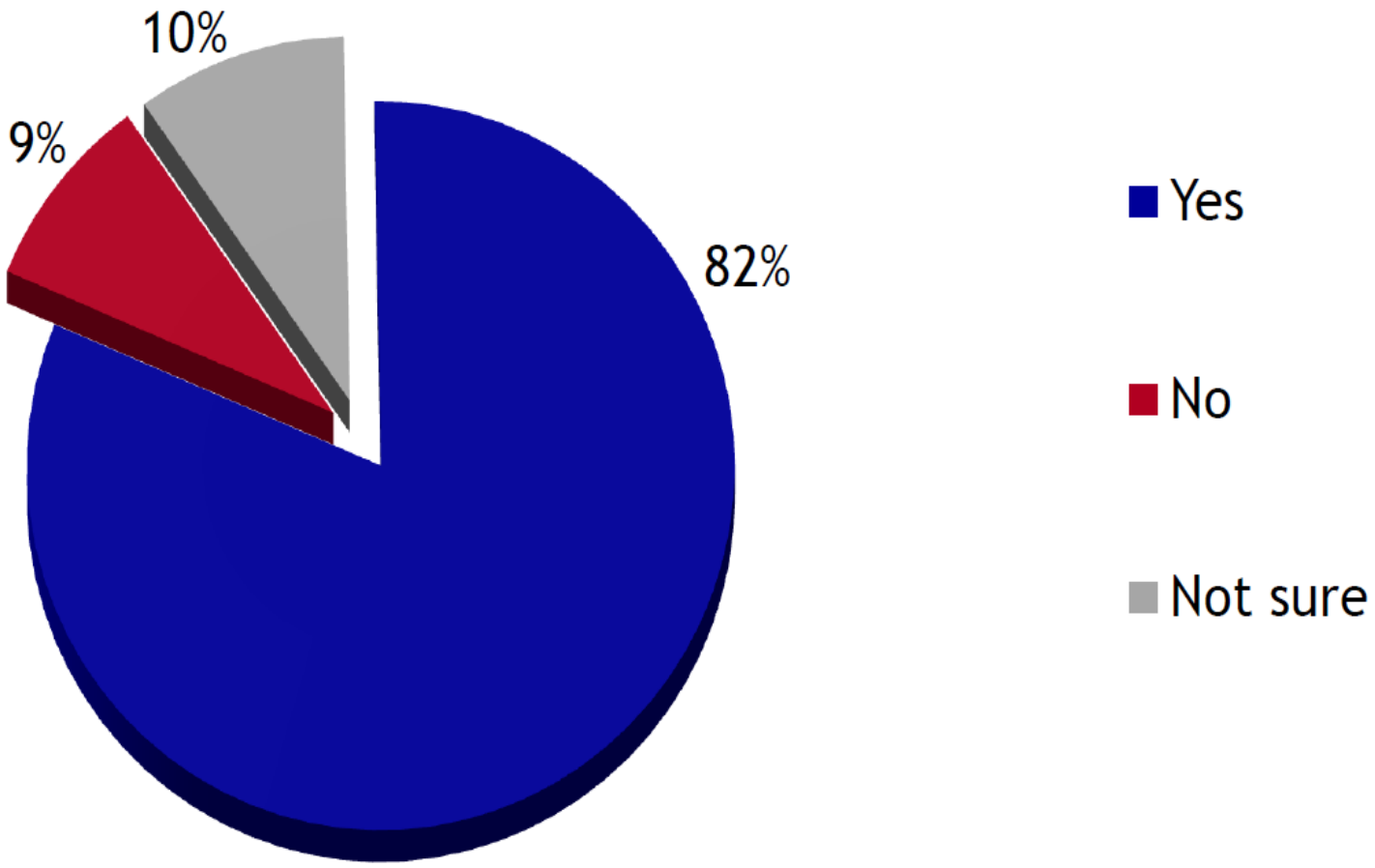
Opioids are good



Opioids are bad

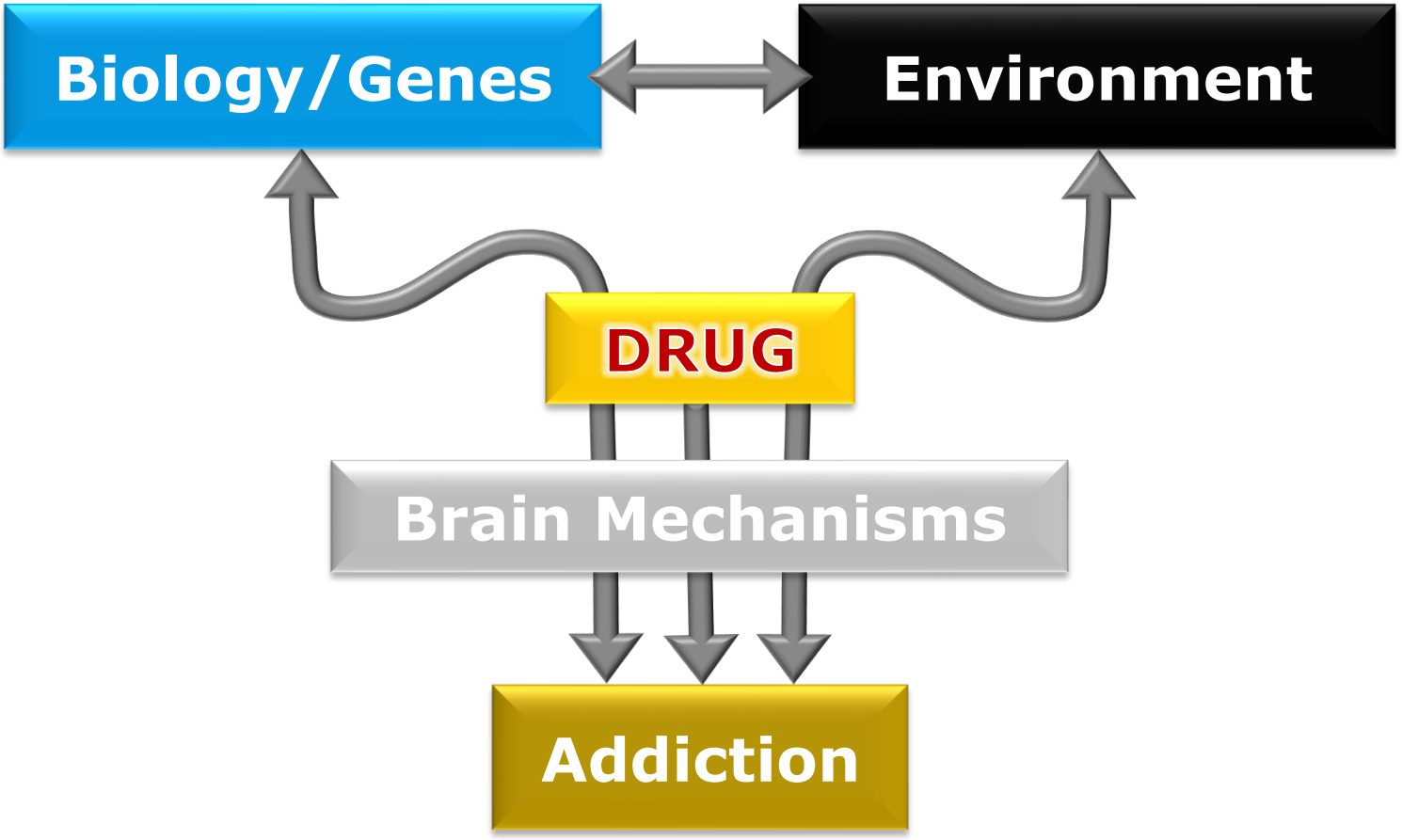
> 80 % of Americans Believe Using "Prescription Pain Killers" Can Result in Addiction

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



Source: A Research!America poll of U.S. adults conducted in partnership with Zogby Analytics in March 2013.

Opioids DO NOT Create Addiction



NIDA
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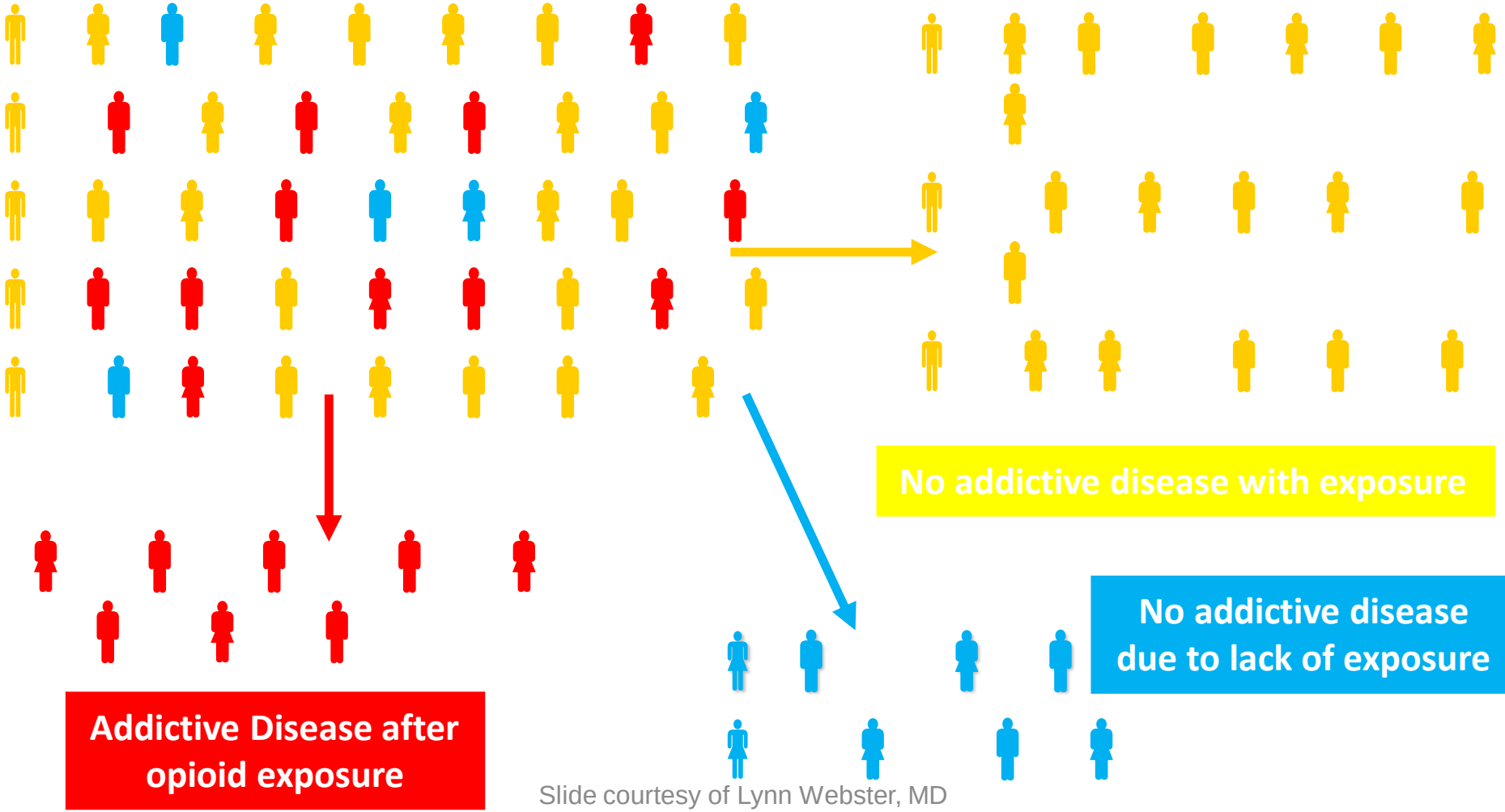
ON DRUG ABUSE

Perelman School of Medicine
University of Pennsylvania

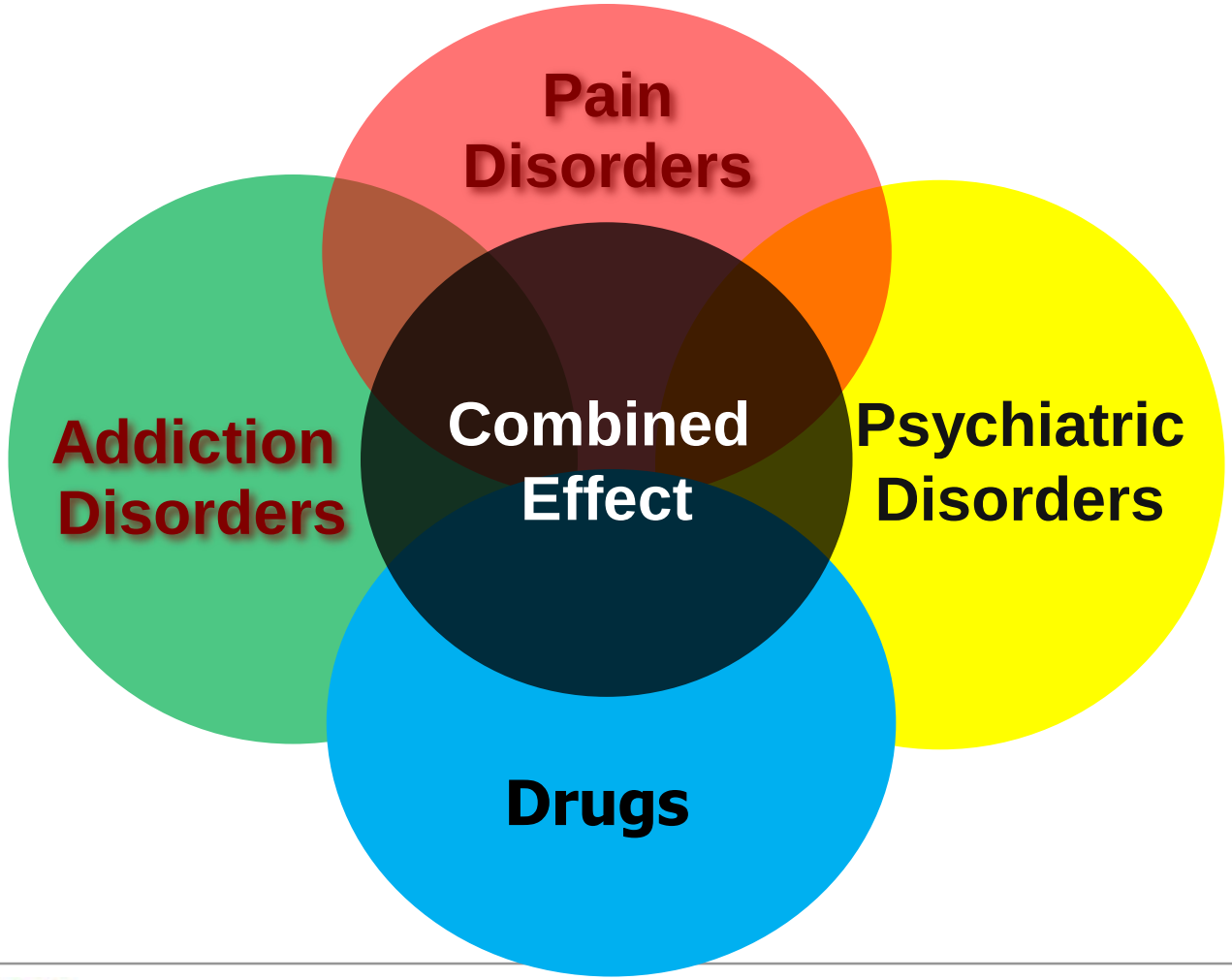
Vulnerability to Opioid Use Disorder

Individuals respond differently to opioid exposure

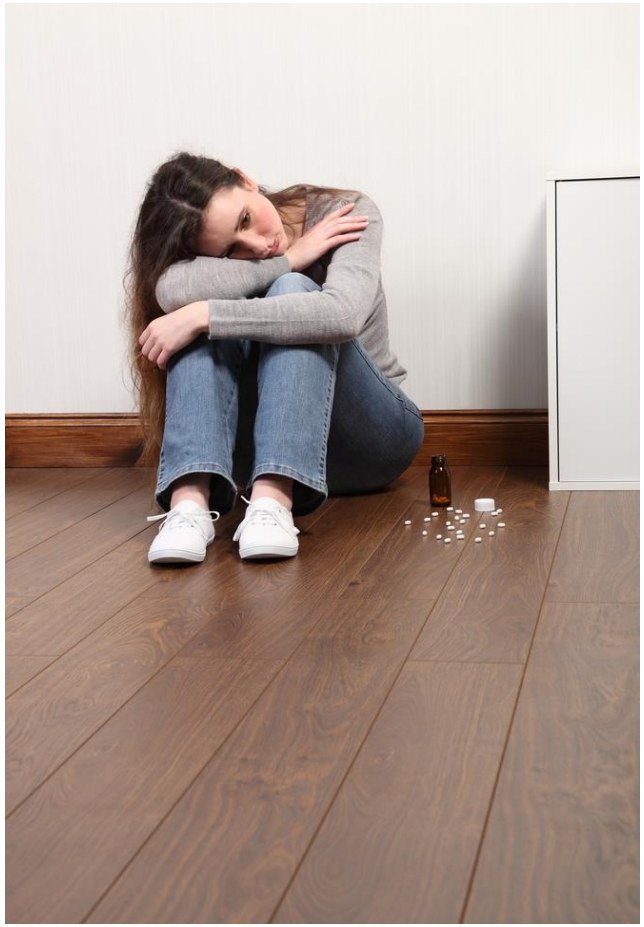


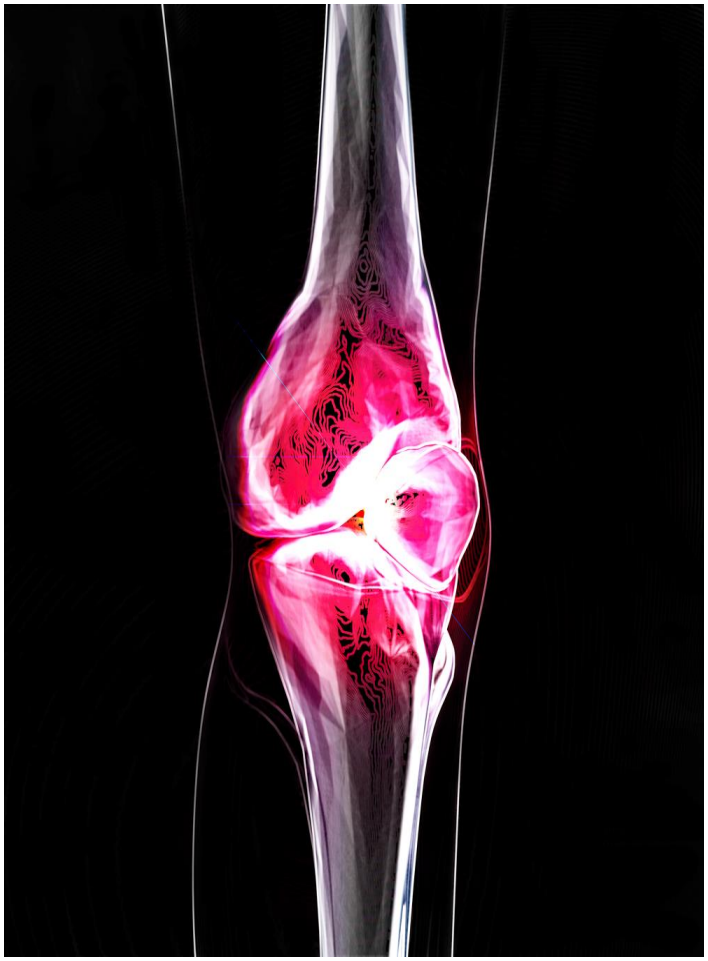
Slide courtesy of Lynn Webster, MD

The Issue of Pain and Addiction is complex!!



Treatment Dichotomy





Spot the Addict

Risk Assessment, Monitoring and Mitigation
The Present

Prescription Monitoring

Risk Assessment and Monitoring in Opioid Therapy

- Clinical Interview
- Risk Screening Tools
- UDS
- Prescription Drug Monitoring programs

Mental Health Screening Tools

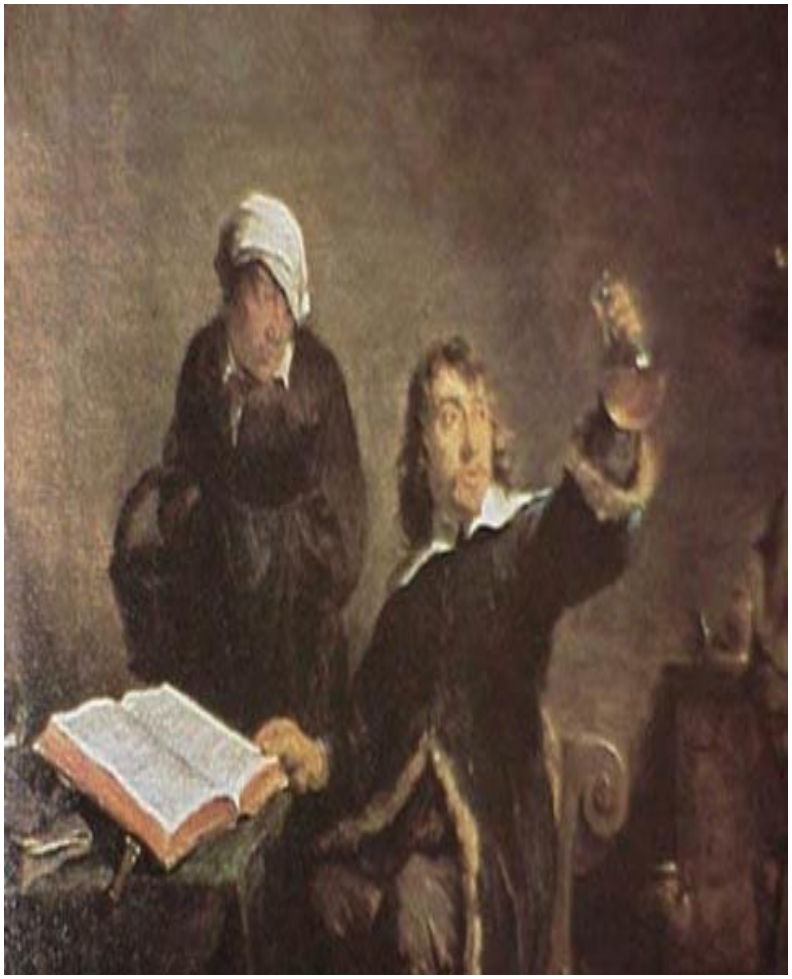
Tool	# of Items	Time to Complete
Beck Depression Inventory II (Beck et al, 1996)	21	5 - 10 minutes
Beck Depression Inventory – Fast Screen for Medical Patients (Beck et al, 2000)	7	< 5 minutes
Profile of Mood States II: Full	65	10 - 15 minutes
Short (McNair et al, 1971)	35	5 - 10 minutes
Zung Self-Rating Depression Scale (Zung 1965)	20	10 minutes
Center for Epidemiologic Studies Depression Scale: Full	20	5 - 10 minutes
Short (Radloff, 1977)	10	5 minutes
Patient Health Questionnaire: PHQ-9	9	5 minutes
PHQ-4 (Kroenke et al19990	4	< 5minutes

Risk Assessment Tools: Examples

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

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**

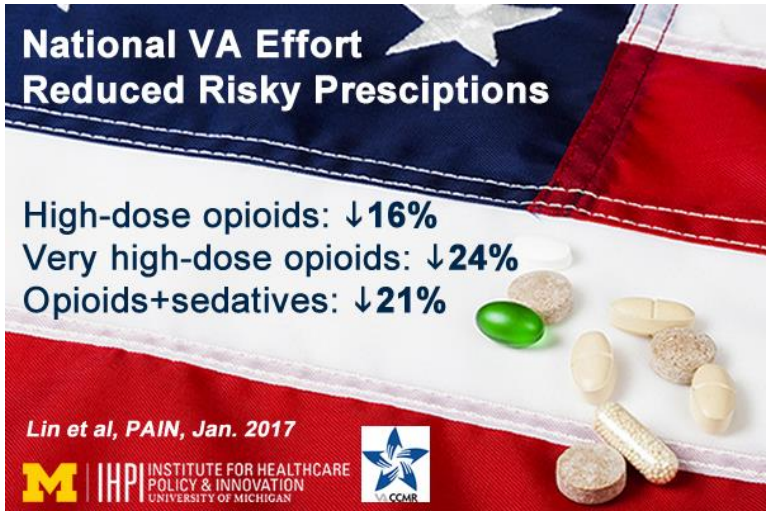


Prescription drug monitoring programs

- **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[a]
  - 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



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

Pain Medicine 2018; 19: 449–459
doi: 10.1093/pm/pnx336

OXFORD

EDUCATION & TRAINING SECTION

Special Article

Scope and Nature of Pain- and Analgesia-Related Content of the United States Medical Licensing Examination (USMLE)

Scott M. Fishman, MD,* Daniel B. Carr, MD,† Beth Hogans, MD, PhD,‡ Martin Cheatle, PhD,§ Rollin M. Gallagher, MD, MPH,§ Joanna Katzman, MD,¶ Sean Mackey, MD, PhD,‖ Rosemary Polomano, PhD, RN, FAAN,‖‖ Adrian Popescu, MD,§ James P. Rathmell, MD,** Richard W. Rosenquist, MD,†† David Tauben, MD,‡‡ Laurel Beckett, PhD,§§ Yueju Li, MS,§§ Jennifer M. Mongoven, MPH,¶¶ and Heather M. Young, PhD, RN‖‖

The Mayday Fund provided a grant to support air and train transportation expenses and two nights' lodging in a hotel near the NBME headquarters in Philadelphia for panelists and the single staff organizer (JMM). The NBME provided two meals per day for panelists during the two-day review. Some panelists resided in Philadelphia and did not require travel or lodging reimbursement. All other expenses (such as airport transfer,

- **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

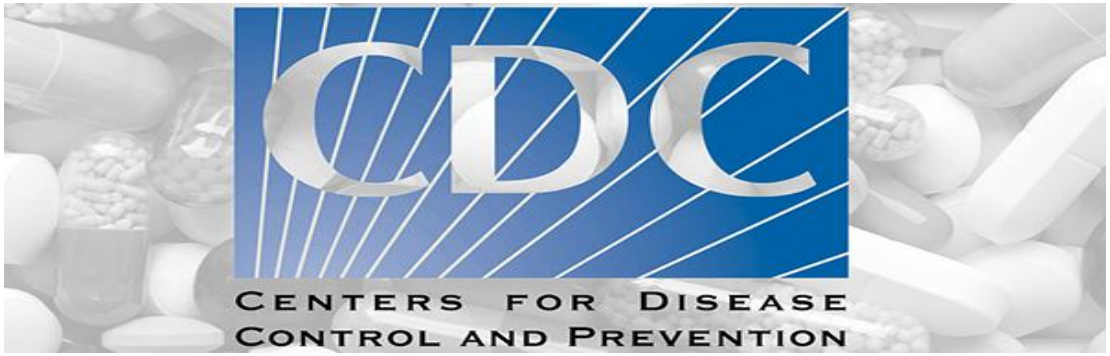
❑Opioid-deterrent formulations have recently been approved by FDA or undergoing FDA approval process

- 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 [1]

1. Cicero TJ, Ellis MS. Abuse-Deterrent Formulations and the Prescription Opioid Abuse Epidemic in the United States: Lessons Learned From OxyContin. JAMA Psychiatry. 2015 May;72(5):424-30.

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 (hyperalgesia, endocrine), unclear benefit, and can be a marker for abuse, addiction, or diversion
  - Higher doses may be associated with higher risk

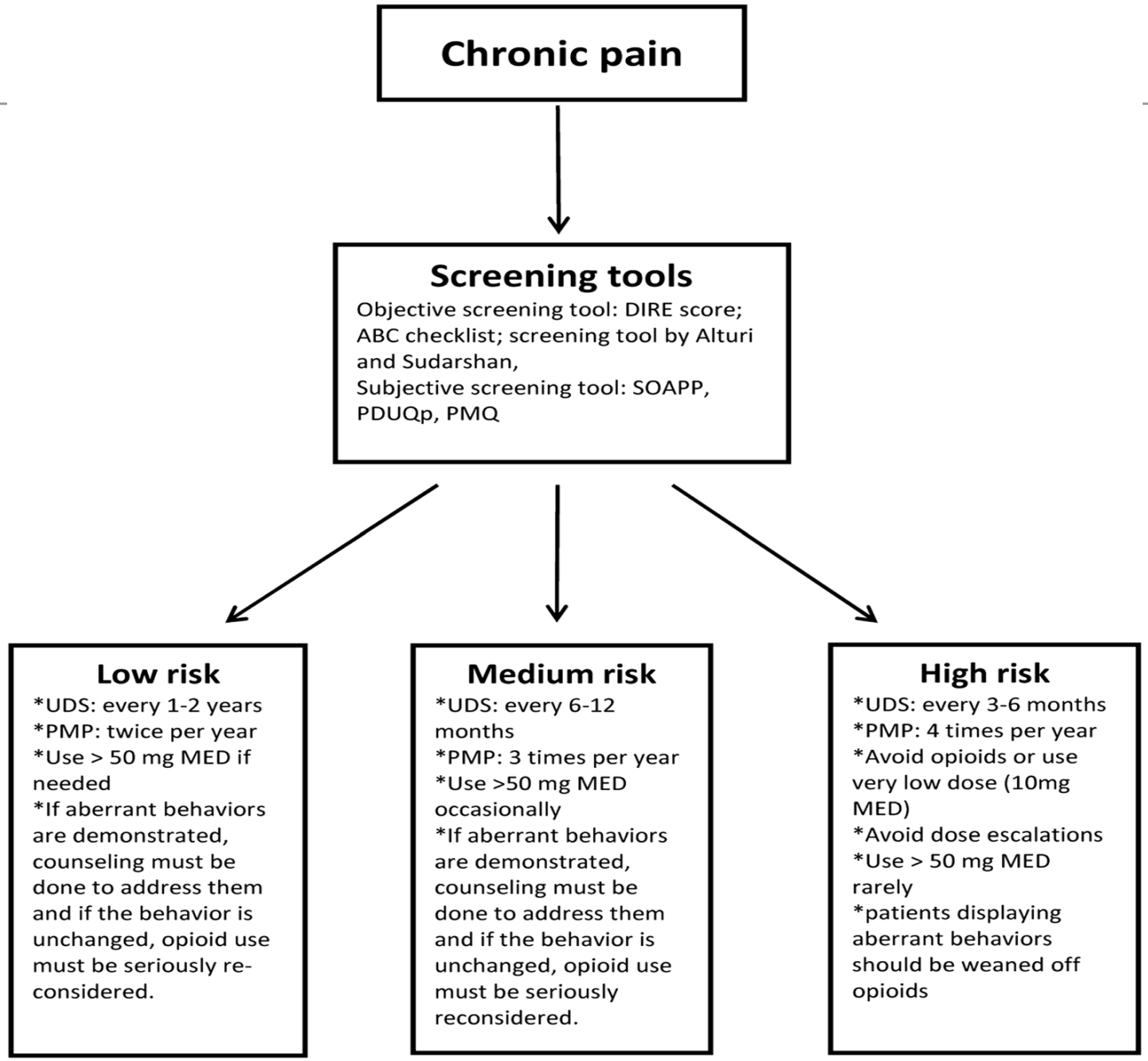
- **APS/AAPM and Canadian panels defined >200 mg/day of morphine (or equivalent) as "higher dose"; recent CDC guidelines recommend 50-90 mg MEDD**

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. 1to <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)

Dunn et al. Ann Intern Med 2010;152:85-92; Bohnert et al. JAMA 2011;305:1315-21; Gomes et al. Arch Intern Med 2011;171:686-91



Chang Y, Compton, P Addict Sci Clin Pract. 2013 Dec 16;8(1):21 (adopted from Atluri S, Akbik H, Sudarshan G, 2012):

Risk Assessment
The Future

Human Genetics of Opioid Dependence

- **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***

Human Genetics of Opioid Dependence

- 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].** [1,2]
- **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

1. Linares OA, Daly D, Stefanovski D, Boston RC. The CYP2D6 gene determines oxycodone's phenotype-specific addictive potential: Implications for addiction prevention and treatment. Med Hypotheses. 2014 Mar;82(3):390-4.

2. Schwantes-An TH, Zhang J, Chen LS, et al. Association of the OPRM1 Variant rs1799971 (A118G) with Non-Specific Liability to Substance Dependence in a Collaborative de novo Meta-Analysis of European-Ancestry Cohorts. Behav Genet. 2015 Sep 21. [Epub ahead of print]

Clinical and Genetic Characteristics of Opioid Addiction in Chronic Pain

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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.**

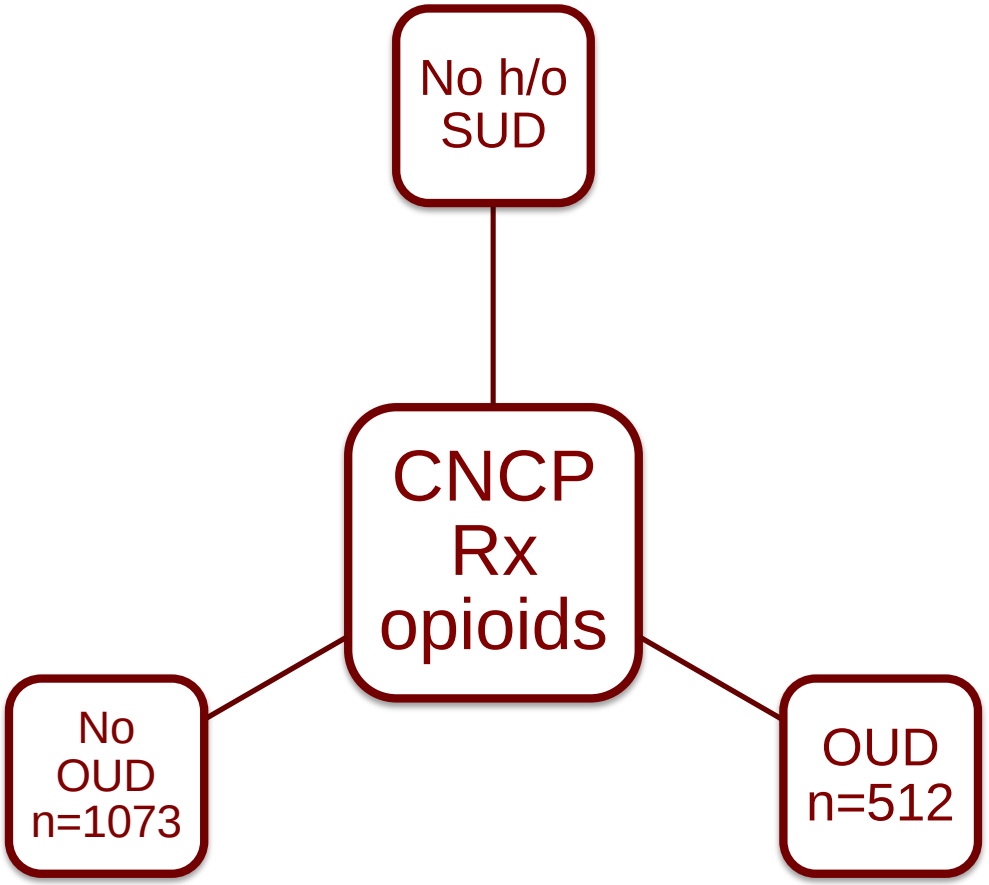
Inclusion/Exclusion Criteria

- **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**

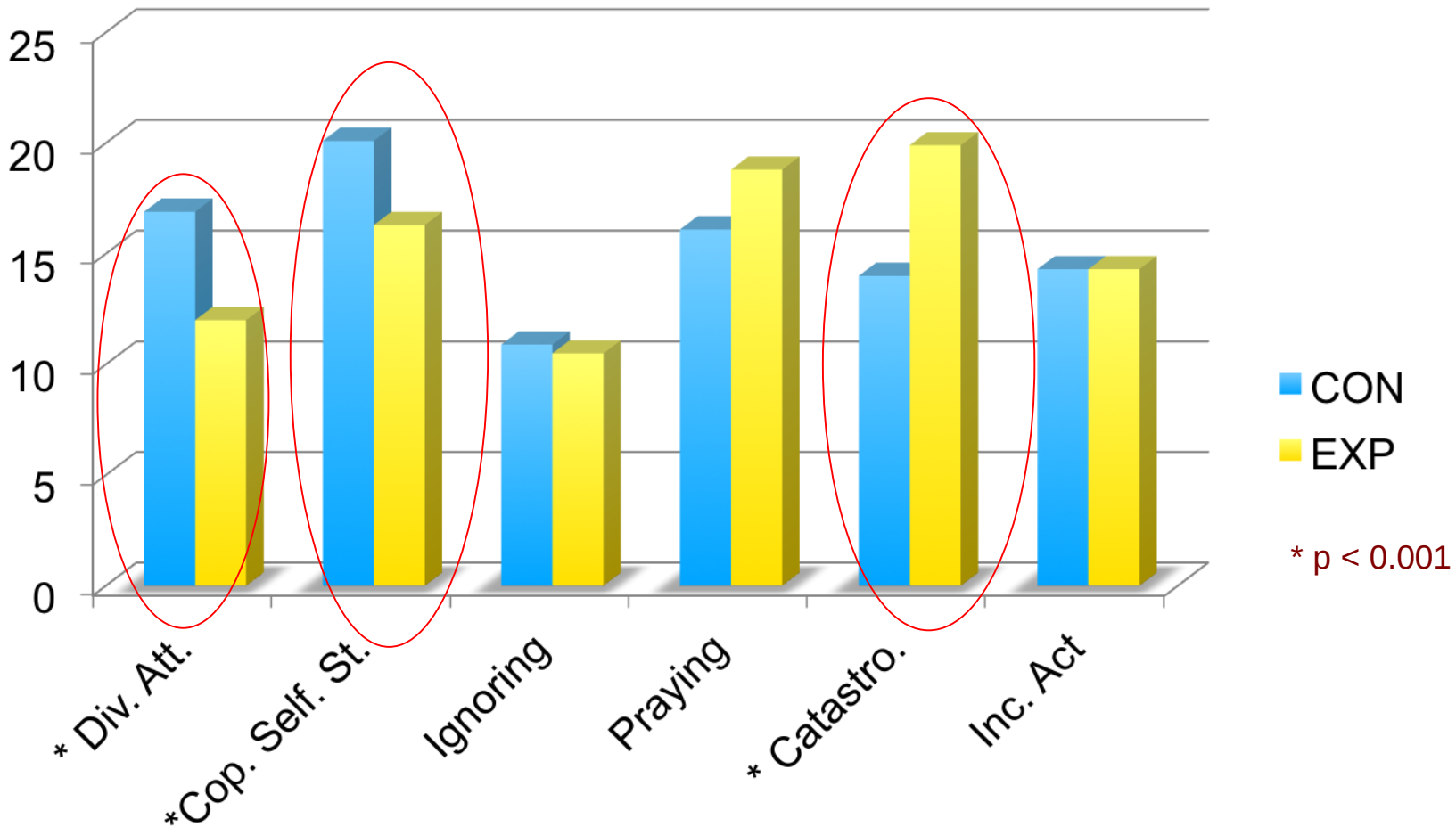
Assessments

	Baseline	6 Month *	12 Month*
Field Staff (Nurse and field RA)			
Eligibility Criteria 1-5	X		
Blood draw	X		
Chart Review	X	X	X
Urine drug screen (via chart review)	X	X	X
Phone Assessments			
Demographics	X		
MINI (to include lifetime sections for alcohol and drug dependence)	X		
Coping Strategies Questionnaire	X		
DSM checklist for substance abuse or dependence	X	X	X
PHQ- 4	X	X	X
DSM checklist for alcohol/drug use	X	X	X
Brief Pain Inventory	X	X	X
Duke Social Support	X	X	X
Treatment Services Review	X	X	X
Fagerstrom Nicotine Tolerance Scale	X	X	X
FHAM-Family History Assessment Module	X		
Beliefs about medication questionnaire	X	X	X
Opioid Risk Tool	X		
Current Opioid Misuse Measure		X	X

Study Subjects



Coping Strategies Questionnaire



Pain Medicine

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Brief Research Reports

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

PAIN

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www.elsevier.com/locate/pain

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

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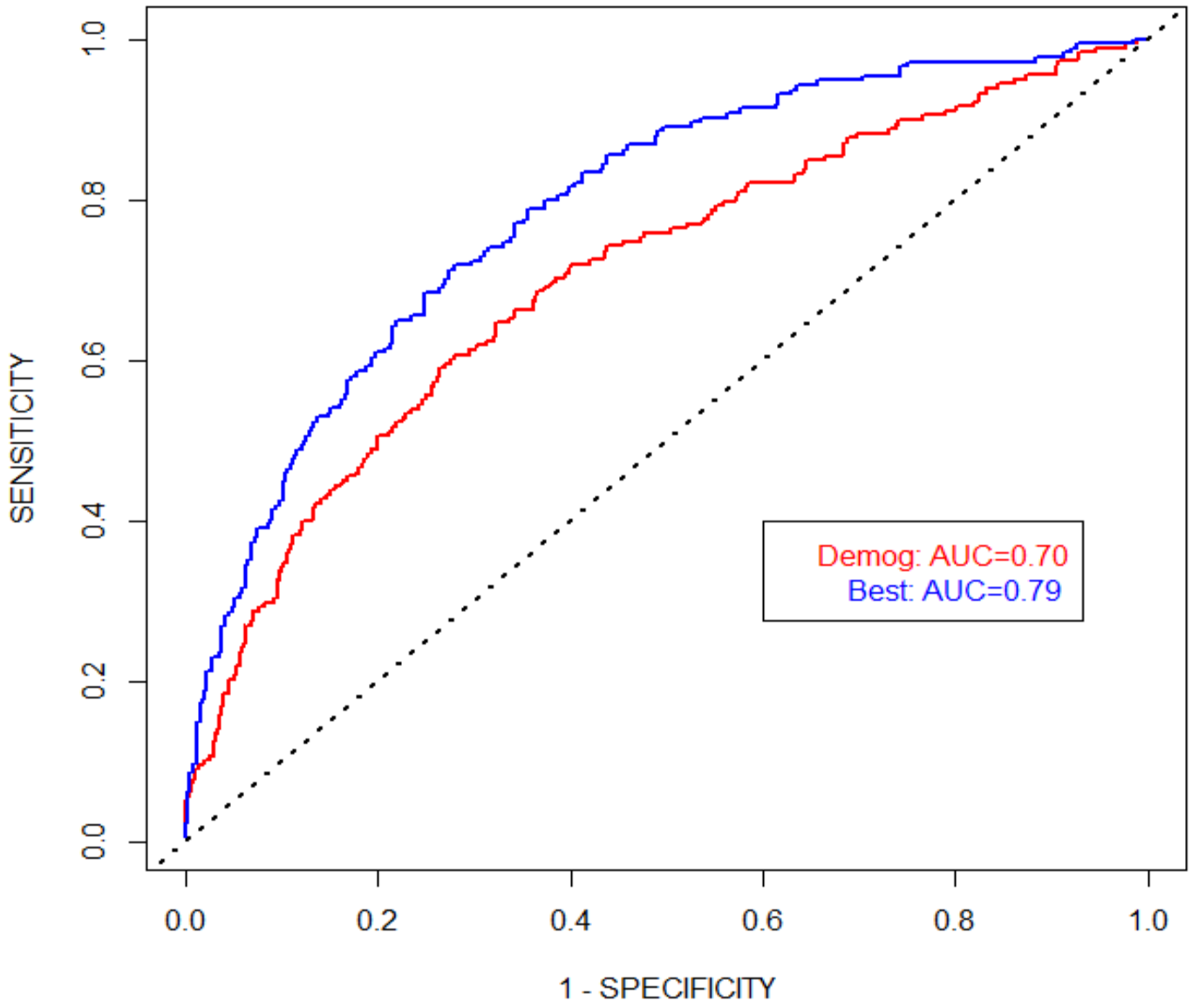
Psychosocial Variables

Summary of Stepwise Selection							
Step	Effect Entered	Effect Removed	DF	Number In	Score Chi-Square	Wald Chi-Square	Pr > ChiSq
1	Total_Cat		1	7	50.0514		<.0001
2	majdep_epi		1	8	13.2524		0.0003
3	DukeSS_SubjSupp		1	9	8.1069		0.0044

ROC curves for design/demographic model and best model



Predicting Opioid Use Disorder

Dichotomous Data

Variable	N_Ctrl	Pct_Ctrl_Yes	N_Exp	Pct_Exp_Yes	OddsRatio	ChiSq	ChisqDF	ChisqP
Male	687	34.21	312	50.00	1.92	22.47	1	0.0000
Smoking	688	21.22	313	72.52	9.80	242.21	1	0.0000
MajorDepEpisode	686	33.38	310	52.90	2.24	34.06	1	0.0000
OCD_current	683	2.64	309	16.18	7.13	61.14	1	0.0000
PTSD_current	685	3.94	310	17.10	5.03	49.95	1	0.0000
ASPD_life	686	0.29	311	16.72	68.66	112.74	1	0.0000

Cheatle, M; Compton P; Lynch, K; Dhingra L. in preparation for publication

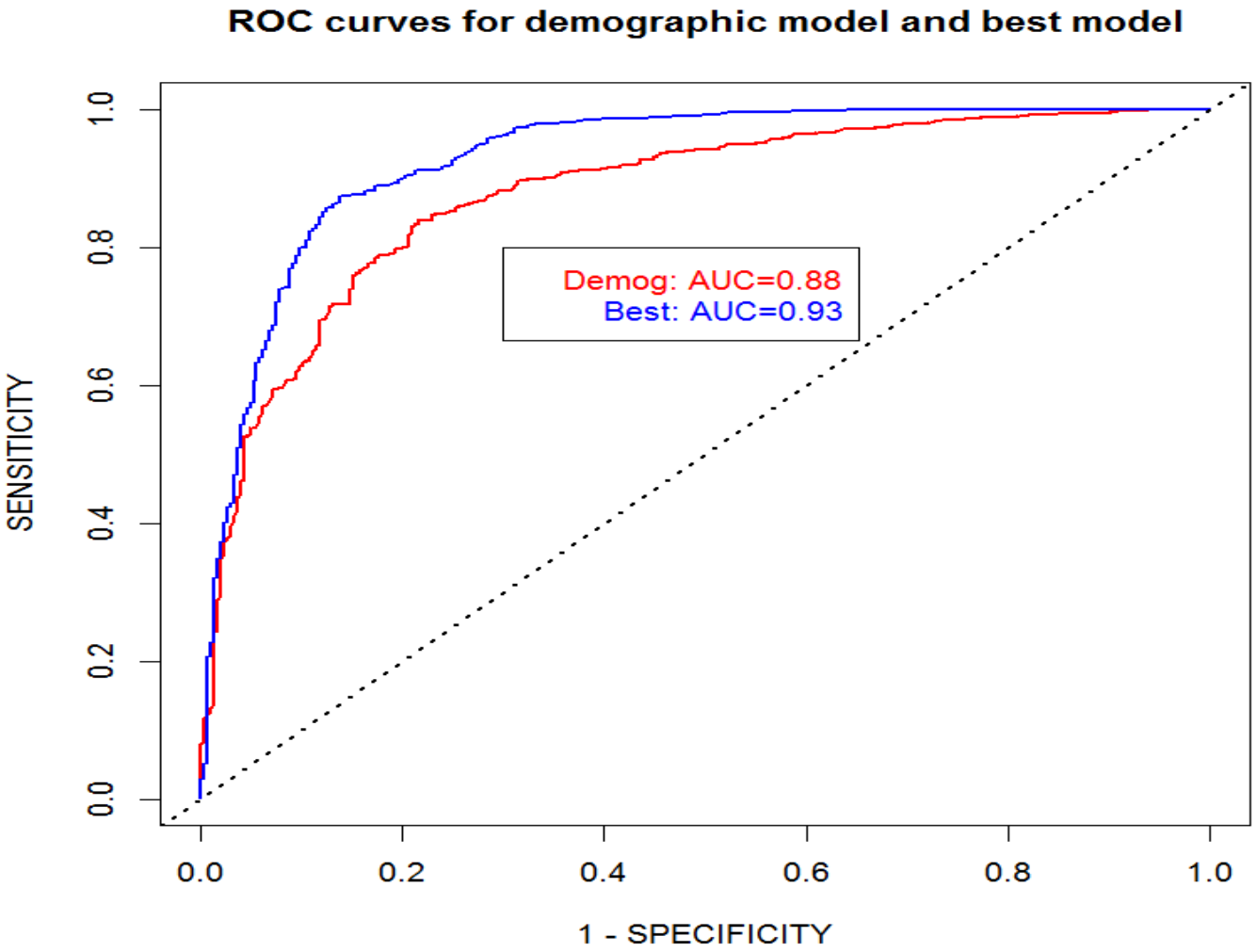
Continuous Data

Variable	Ctrl_N	Ctrl_mean	Ctrl_SDV	Exp_N	Exp_mean	Exp_SDV	Z_WIL	P2_WIL
Age	687	53.39	12.52	312	39.22	10.78	-15.21	0.0000
DukeSS_SubjSupp	680	18.01	3.23	312	16.00	3.88	-8.09	0.0000
DukeSS_InstSupp	685	8.73	2.70	312	8.29	3.26	-1.29	0.1973
BpiAvgPain	682	5.60	1.79	311	4.91	2.23	-4.51	0.0000
BpiIntScore	675	39.76	17.44	306	36.70	17.88	-2.55	0.0109
Total_Cat	678	14.11	8.16	299	18.20	7.64	7.30	0.0000
alc_fhd	685	0.12	0.25	310	0.29	0.36	8.13	0.0000
drug_fhd	683	0.02	0.11	311	0.18	0.32	11.70	0.0000

Cheatle, M; Compton P; Lynch, K; Dhingra L. in preparation for publication

Summary of Stepwise Selection							
Step	Effect Entered	Effect Removed	DF	Number In	Score Chi-Square	Wald Chi-Square	Pr > ChiSq
1	smoking		1	5	105.5530		<.0001
2	ASPD_life		1	6	24.7167		<.0001
3	BpiAvgPain		1	7	18.4828		<.0001
4	DukeSS_SubjSupp		1	8	14.7682		0.0001
5	drug_fhd		1	9	11.2285		0.0008
6	MajorDepressiveEpiso		1	10	8.7492		0.0031

Cheatle, M; Compton P; Lynch, K; Dhingra L. in preparation for publication


ROC curves for demographic model and best model
SENSITICITY
0.0
0.2
0.4
0.6
0.8
1.0
1 - SPECIFICITY
Demog: AUC=0.88
Best: AUC=0.93

Independent Association of Tobacco and Opioid Use Disorder in Patients with Chronic Nonmalignant Pain (in preparation for publication)

Martin D. Cheatle, PhD, Mary Falcone PhD, Lara Dhingra, PhD, Caryn Lerman, PhD

- 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)

Mark each box that applies	Female	Male
1. Family hx of substance abuse Alcohol Illegal Drugs Prescription drugs	☐ 1 ☐ 2 ☐ 4	☐ 1 ☐ 2 ☐ 4
2. Personal hx of substance abuse Alcohol Illegal Drugs Prescription drugs	☐ 3 ☐ 4 ☐ 5	☐ 3 ☐ 4 ☐ 5
3. Age (mark box if 16-45)	☐ 1	☐ 1
4. Hx of preadolescent sexual abuse	☐ 3	☐ 3
5. Psychologic disease ADD, OCD, bipolar, schizophrenia Depression	☐ 2 ☐ 1	☐ 2 ☐ 1
Scoring totals:		

Scoring (Risk)
0-3 Low Risk
4-7 Moderate Risk
≥ 8 High Risk

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Available online at www.jpain.org and www.sciencedirect.com

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**

Perelman School of Medicine University of Pennsylvania

Mulitvariate logistic regression: Classification of patients with OUD versus without OUD as predicted by ORT total score with weighted and unweighted items

Variable	Beta	p-value	OR	95% Lower Bound	95% Upper Bound
ORT Total Score (Weighted 10-items)	0.485	<0.001	1.624	1.539	1.715
ORT Total Score (Weighted without Sexual Abuse item 9-item)	0.500	<0.001	1.648	1.559	1.742
ORT Total Score (Unweighted)	1.127	<0.001	3.085	2.725	3.493

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 >/= 3 indicates high risk for opioid use disorder.

Mark each box that applies	YES	NO
Family history of substance abuse		
Alcohol	1	0
Illegal drugs	1	0
Rx drugs	1	0
Personal history of substance abuse		
Alcohol	1	0
Illegal drugs	1	0
Rx drugs	1	0
Age between 16-45 years	1	0
Psychological disease		
ADD, OCD, bipolar, schizophrenia	1	0
Depression	1	0
Scoring totals		

Cheatle M, Compton P, Dhingra L, Wasser T, O'Brien. Development of the Revised Opioid Risk Tool to Predict Opioid Use Disorder in Patients with Chronic Non-Malignant Pain. Journal of Pain, in press.

Conclusions

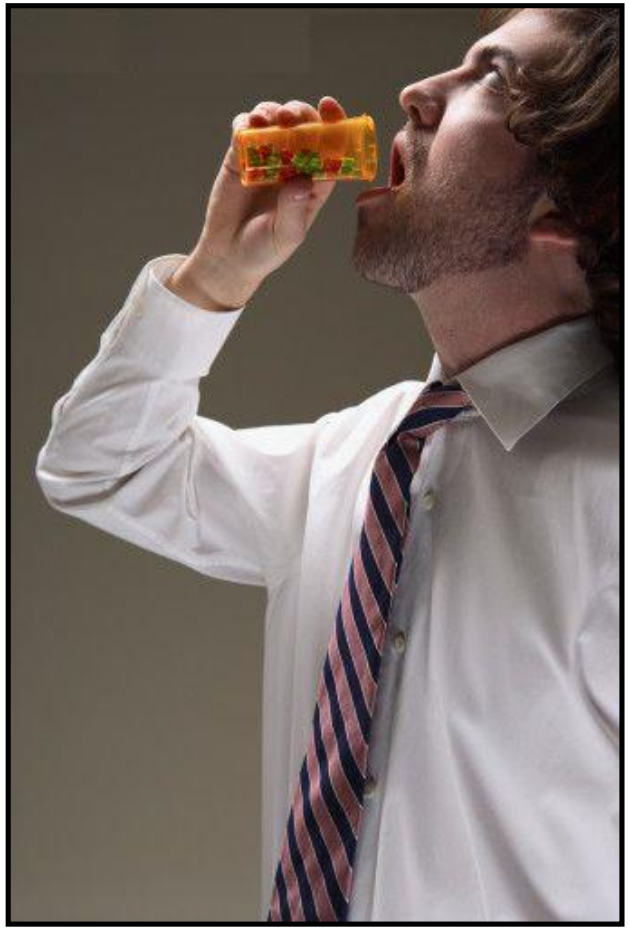
- Pain is complex
- Opioids can be efficacious for some patients with chronic pain
- There is a serious crisis of opioid abuse, diversion and fatal overdoses
- More evidence needed to understand optimal risk assessment, opioid selection, dosing, monitoring and risk mitigation
- Assessing risk of abuse 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



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