OPIOID RESEARCH UPDATE
NCATS PERSPECTIVE

Michael G. Kurilla, M.D., Ph.D.

Director, Division of Clinical Innovation

NCATS

June 22, 2018
Adapted from: See how deadly street opioids like ‘elephant tranquilizer’ have become by Dan Keating and Samuel Granados The Washington Post, Oct. 25, 2017
NUMBER AND AGE-ADJUSTED RATES OF DRUG OVERDOSE DEATHS BY STATE, US 2016

The number of deaths per 100,000 total population.

<table>
<thead>
<tr>
<th>No.</th>
<th>Cause</th>
<th>Number of deaths:</th>
<th>Deaths per 100,000 population:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Heart Disease</td>
<td>635,260</td>
<td>165.5</td>
</tr>
<tr>
<td>2</td>
<td>Cancer</td>
<td>598,038</td>
<td>155.8</td>
</tr>
<tr>
<td>3</td>
<td>Accidents</td>
<td>161,374</td>
<td>47.4</td>
</tr>
<tr>
<td>4</td>
<td>Respiratory Disease</td>
<td>154,596</td>
<td>40.6</td>
</tr>
<tr>
<td>5</td>
<td>Cerebrovascular Disease</td>
<td>142,142</td>
<td>37.3</td>
</tr>
</tbody>
</table>

Data Brief 293: Mortality in the United States, 2016
Published December 2017
In April 2018, NIH launched the HEAL (Helping to End Addiction Long-term) Initiative, an aggressive, trans-agency effort to speed scientific solutions to stem the national opioid public health crisis.

https://www.nih.gov/heal-initiative
Announcement of Research Plan

Helping to End Addiction Over the Long-term
The Research Plan for the NIH HEAL Initiative

**Opportunities**

**Components**

**Improving Treatments for Opioid Misuse and Addiction**

<table>
<thead>
<tr>
<th>Opportunities</th>
<th>Components</th>
</tr>
</thead>
<tbody>
<tr>
<td>New treatments for addiction</td>
<td>Identify new targets, develop new medications/immunotherapies; reformulate existing medicines</td>
</tr>
<tr>
<td></td>
<td>Improve overdose reversal medicines</td>
</tr>
<tr>
<td></td>
<td>Develop new therapies for opioid-induced respiratory depression</td>
</tr>
</tbody>
</table>

**Optimization of effective treatments for addiction**

<table>
<thead>
<tr>
<th>Opportunities</th>
<th>Components</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enhance NIDA Clinical Trials Network for opioid research</td>
<td></td>
</tr>
<tr>
<td>Establish Justice Community Opioid Intervention Network</td>
<td></td>
</tr>
<tr>
<td>Initiate HEALing Communities Study</td>
<td></td>
</tr>
</tbody>
</table>

**NOWS**

<table>
<thead>
<tr>
<th>Opportunities</th>
<th>Components</th>
</tr>
</thead>
<tbody>
<tr>
<td>Expand ACT NOW pilot study; use results to conduct clinical trials to determine best practices for clinical care of NOWS</td>
<td></td>
</tr>
</tbody>
</table>

**Enhancing Pain Management**

<table>
<thead>
<tr>
<th>Opportunities</th>
<th>Components</th>
</tr>
</thead>
<tbody>
<tr>
<td>Better understanding of chronic pain</td>
<td>Establish Acute to Chronic Pain Signatures program</td>
</tr>
<tr>
<td>New nonaddictive pain treatments</td>
<td>Identify new targets for pain treatment</td>
</tr>
<tr>
<td></td>
<td>Engineer preclinical testing platforms to profile potential nonaddictive treatments</td>
</tr>
<tr>
<td>Public–private HEAL Partnership to speed movement of nonaddictive treatments through clinical pipeline</td>
<td>Enhance data and asset sharing</td>
</tr>
<tr>
<td></td>
<td>Validate biomarkers to inform neurotherapeutic and pain clinical research</td>
</tr>
<tr>
<td></td>
<td>Establish clinical trials network to support and accelerate trials of nonaddictive pain therapies</td>
</tr>
</tbody>
</table>

Table. Research Plan for the NIH HEAL Initiative

Abbreviations: HEAL, Helping to End Addiction Long-term; NIDA, National Institute on Drug Abuse; NIH, National Institutes of Health; NOWS, neonatal opioid withdrawal syndrome.
CTSA Hubs

*FY2017
CTSA 3D Model
KEY AREAS IN TRANSLATIONAL SCIENCE

- **Education**
  - School children
  - Patient/Clinician
  - Novel Methods/App Development

- **Big Data**
  - EHR-Research Integration
  - Genomics
  - Predictive Modeling
  - AI

- **Innovative Trials**
  - Adaptive Design
  - Wearables
  - MHealth

- **Dissemination Tools**
  - Early adoption
  - Real-time tracking
  - Impact

- **CTSA Program**
The Opioids Crisis: A view from NIDA

Carlos Blanco, M.D., Ph.D.
Director, Division of Epidemiology, Services and Prevention
National Institute on Drug Abuse

NIH
Develop a Learning Health Care System

➢ Using **Clinical Practice** to **Generate Meaningful Research Questions**

➢ Ensuring that **Research Findings are Applied to Practice**

**6. Develop a Learning Health Care System**
Overdose Deaths Continue to Increase

Source: Data Brief 294. NCHS, National Vital Statistics System, Mortality
Estimate of Total U.S. Drug Deaths in 2016

Fentanyl-Related Deaths Surpassed Heroin or Rx Opioids in 2016

Graphs from NY Times Article based on CDC MMWR Report 2017
Outbreak of HIV Linked to IDU of Oxymorphone in Indiana, 2015

HIV Infections in a Community of 4200

- Injection Drug Use: 162
- No Injection Drug Use: 108
- Not Interviewed to Determine Status: 4
- All reported injecting tablets of oxymorphone as drug of choice: 17% (23)
- 84.4% co-infected with Hepatitis C: 114
- 53% HIV- (121), 47% HIV+ (109)
- 230 tested, 61.7% located, 4.6% not located
- 247 located, 128 not located
- 373 contacts
- Reported average of 9 syringe-sharing partners, sex partners, or other social contacts at risk for HIV infection

Social contacts regarded as at high risk for HIV:
- 74 syringe-sharing or sex partners
- 57.8% HIV-, 42.2% HIV+
- 54 not located

Centers for Disease Control and Prevention
Morbidity and Mortality Weekly Report
April 24, 2015
Increasing **Prenatal Exposure**

Admissions for Newborn Withdrawal Syndromes (Number per 1000 Admissions)

Heroin “Market” Has Changed: Heroin Price Has Been Lower in Recent Years

"Retail" Price Per Pure Gram

Increasing reports of fentanyl laced-heroin and prescription pills

Other synthetic opioids emerging i.e., Carfentanil
Opioid Prescriptions 1991-2011

Opioid morphine milligram equivalents (MME) dispensed fell by over 15% from 2010-2015

IMS’s Source Prescription Audit (SPA) & Vector One®: National (VONA)

IMS Health, U.S. Outpatient Retail Setting
NIH OPIOID RESEARCH INITIATIVE
Using Research to End the Opioid Crisis

PREVENTION
OUD

PAIN MANAGEMENT
Safe, more effective strategies

OPIOID ADDICTION
TREATMENT
New and innovative medications and technologies

OVERDOSE REVERSAL
Interventions to reduce mortality and link to treatment
1. Inadequate **Pain Treatment** as a Driver

- **91.8 million adults** used prescription opioids (37.8% of the U.S. adult population)
- **11.5 million adults** misused prescription opioids (4.7% of the U.S. adult population)
- **1.9 million adults** had prescription opioid use disorders (0.8% of the U.S. adult population)

**Reasons for Use:***

- 66.3% to relieve physical pain
- 11.2% to relax or relieve tension
- 10.8% to experiment
- 7.0% to get high or feel good
- 4.6% to help with sleep
- 4.0% to help with emotions or feelings
- 2.4% to increase/decrease effects of other drugs
- 2.2% hooked or have to misuse
- 0.9% other reason
- 0.6% other reason

2. Direct Overdose Intervention

• **Naloxone Distribution** for opioid overdose victims. The potential for direct intervention to save lives.

  ```markdown
  ➢ Note the April 3, 2014 FDA approval of the naloxone auto-injector (called “Evzio”)```

• **Naloxone Nasal Spray Development**

  Needle-free, unit-dose, ready-to-use opioid overdose antidote.

  ```markdown
  ➢ Adapt Pharma NARCAN nasal spray APPROVED BY FDA, November 18, 2015.```

  *Science = Solutions*
3. Medication Diversion: Prevention/brief interventions

- People misusing analgesics **Directly & Indirectly** obtain them by prescription

Source where pain relievers obtained for most recent misuse

- Prescription 36%
- Friend/Relative 54%
- Other 1%
- Their Prescription 87%
- Their Friend/Relative 10%
- Other 3%

4. OUD Cascade of Care

Medication Assisted Treatment (MAT)

Opioid Effect

- Full Agonist (Methadone: Daily Dosing)
- Partial Agonist (Buprenorphine: 3-4X week)
- Antagonist (Naltrexone: ER 1 month)

Log Dose

**DECREASES:**
- Opioid use
- Opioid-related overdose deaths
- Criminal activity
- Infectious disease transmission

**INCREASES**
- Social functioning
- Retention in treatment

**But MAT is highly underutilized!**
**Relapse rates are very high!**

OUD Cascade of Care in USA

Current estimates
Treatment gap
90% goal

Williams AR, Nunes E, Olfson M. Health Affairs Blog, 2017.
Helping to End Addiction Over the Long-term
The Research Plan for the NIH HEAL Initiative

Extraordinary focus by all segments of society is required to respond to the nation’s opioid crisis. Now is the time to channel the efforts of the scientific community to deliver effective—and sustainable—solutions to this formidable public health challenge. Recognizing this opportunity, Congress added $500 million to the base appropriation of the National Institutes of Health (NIH), starting in fiscal year 2018.¹ The NIH will invest these much-needed resources to support science that advances national priorities for addiction and pain research² with a bold new trans-NIH initiative called Helping to End Addiction Long-term (HEAL).³ In this Viewpoint, we outline the initial components of this cross-cutting, interdisciplinary program.

More than 25 million US adults are affected by daily pain.⁴ More than 2 million individuals in the United States have an opioid use disorder (OUD), most starting with opioid analgesics prescribed to them or procured from diverted medications, but once addicted, often shift-

<table>
<thead>
<tr>
<th>Table. Research Plan for the NIH HEAL Initiative</th>
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<tr>
<td>Enhancing Pain Management</td>
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<tr>
<td>Better understanding of chronic pain</td>
</tr>
</tbody>
</table>
Develop a Learning Health Care System

- Using *Clinical Practice* to *Generate Meaningful Research Questions*
- Ensuring that *Research Findings are Applied to Practice*
Epidemiological Perspectives on the Opioid Epidemic

Mark Olfson, M.D., M.P.H.
Columbia University
New York State Psychiatric Institute
Overview

Trends in opioid-related mortality and morbidity

Risks and course of nonfatal opioid overdose

Identifying gaps in opioid use disorder treatment

Opportunities for reducing risk
<table>
<thead>
<tr>
<th>Cause</th>
<th>2000</th>
<th>2005</th>
<th>2010</th>
<th>2015</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opioid Overdose</td>
<td>6.2</td>
<td>10.1</td>
<td>12.3</td>
<td>16.3</td>
</tr>
<tr>
<td>Suicide</td>
<td>10.4</td>
<td>10.9</td>
<td>12.1</td>
<td>13.3</td>
</tr>
<tr>
<td>Heart Disease</td>
<td>257.6</td>
<td>216.8</td>
<td>179.1</td>
<td>167.0</td>
</tr>
<tr>
<td>Stroke</td>
<td>186.8</td>
<td>148.2</td>
<td>113.6</td>
<td>98.8</td>
</tr>
<tr>
<td>Cancer</td>
<td>199.6</td>
<td>185.1</td>
<td>172.8</td>
<td>161.2</td>
</tr>
<tr>
<td>COPD</td>
<td>44.2</td>
<td>43.9</td>
<td>42.2</td>
<td>40.5</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>23.7</td>
<td>21.0</td>
<td>15.1</td>
<td>15.1</td>
</tr>
<tr>
<td>AIDS/HIV</td>
<td>5.2</td>
<td>4.2</td>
<td>2.6</td>
<td>2.0</td>
</tr>
</tbody>
</table>

CDC, 2017. (100,000 population-year)
Increasing involvement of synthetic opioids in opioid overdose deaths

Jones CM et al. JAMA 2018; Data from National Vital Statistics System multiple cause of death file. Synthetic opioids are thought to be primarily illicit fentanyl and fentanyl congeners.
Opioid-related hospitalizations & Emergency Department Visits

From AHRQ HCUP.
National trends in opioid use disorder

From National Survey on Drug Use and Health, 2016 (Persons ≥ 12 years of age)
Prescription Opioid Use Disorder Among Adults with Prescription Opioid Use

<table>
<thead>
<tr>
<th>Prescription OUD (%) (n=19,000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>18-29 y</td>
</tr>
<tr>
<td>30-49 y</td>
</tr>
<tr>
<td>50+ y</td>
</tr>
<tr>
<td>Cannabis use disorder</td>
</tr>
<tr>
<td>Suicidal ideation</td>
</tr>
<tr>
<td>Alcohol use disorder, past year</td>
</tr>
<tr>
<td>Nicotine dependence, past month</td>
</tr>
<tr>
<td>Major depressive episode. past year</td>
</tr>
</tbody>
</table>

Han B et al *Ann Int Med* 2017 (2015 NSDUH, 37.8% of adult population uses prescription opioids in past year).
Risks and Course
Following Nonfatal Opioid Overdose
### Risk of Repeat Opioid Overdose in First Year

#### Demographic Characteristics

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Rate per 1,000 Person-Years</th>
<th>Adjusted HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>75,556</td>
<td>295</td>
<td>- -</td>
</tr>
<tr>
<td>18-34, y</td>
<td>22,399</td>
<td>284</td>
<td>1.00</td>
</tr>
<tr>
<td>35-44, y</td>
<td>21,411</td>
<td>283</td>
<td>1.06 (1.01-1.11)</td>
</tr>
<tr>
<td>45-64, y</td>
<td>31,746</td>
<td>310</td>
<td>1.14 (1.10-1.19)</td>
</tr>
<tr>
<td>Male</td>
<td>30,866</td>
<td>316</td>
<td>1.09 (1.06-1.13)</td>
</tr>
<tr>
<td>Female</td>
<td>44,690</td>
<td>281</td>
<td>1.00</td>
</tr>
<tr>
<td>White</td>
<td>52,388</td>
<td>308</td>
<td>1.00</td>
</tr>
<tr>
<td>Black</td>
<td>13,030</td>
<td>266</td>
<td>0.88 (0.84-0.92)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>5,822</td>
<td>245</td>
<td>0.80 (0.75-0.86)</td>
</tr>
</tbody>
</table>

Olfson et al., Drug and Alcohol Depend (In Press). Adjusted for age, sex, race/ethnicity & region.
## Risk of Repeat Opioid Overdose in First Year
### Clinical Characteristics

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Rate per 1,000 Person-Years</th>
<th>Adjusted HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ment health dx</td>
<td>35,526</td>
<td>327</td>
<td>1.22 (1.18-1.27)</td>
</tr>
<tr>
<td>Sub use dx</td>
<td>29,011</td>
<td>364</td>
<td>1.38 (1.34, 1.43)</td>
</tr>
<tr>
<td>Opioid use dx</td>
<td>11,998</td>
<td>403</td>
<td>1.47 (1.40-1.53)</td>
</tr>
<tr>
<td>Opioid rx</td>
<td>48,999</td>
<td>305</td>
<td>1.13 (1.09-1.17)</td>
</tr>
<tr>
<td>Benzo rx</td>
<td>36,952</td>
<td>328</td>
<td>1.25 (1.20-1.29)</td>
</tr>
<tr>
<td>Heroin OD</td>
<td>9,389</td>
<td>342</td>
<td>1.22 (1.16-1.27)</td>
</tr>
</tbody>
</table>

Olfson et al., Drug and Alcohol Depend (In Press). Adjusted for age, sex, race/ethnicity & region. Diagnoses and prescriptions in 90 days before initial nonfatal opioid overdose.
Cumulative probability of all cause mortality during the 365 days after a nonfatal opioid overdose by sex

Log-rank test $\chi^2=150.65$, $p<0.0001$  Olfson et al JAMA Psych (In Press)
## Risk of Fatal Opioid Overdose in First Year Following Nonfatal Overdose: Clinical Characteristics

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Rate per 1,000 Person-Years</th>
<th>Adjusted HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ment health dx</td>
<td>35,799</td>
<td>1296</td>
<td>1.22 (1.06-1.41)</td>
</tr>
<tr>
<td>Sub use dx</td>
<td>29,254</td>
<td>1344</td>
<td>1.30 (1.12, 1.50)</td>
</tr>
<tr>
<td>Opioid rx</td>
<td>49,383</td>
<td>1223</td>
<td>1.13 (0.96-1.33)</td>
</tr>
<tr>
<td>Benzo rx</td>
<td>37,257</td>
<td>1532</td>
<td>1.71 (1.46-1.99)</td>
</tr>
<tr>
<td>Heroin OD</td>
<td>15,093</td>
<td>1399</td>
<td>1.57 (1.30-1.89)</td>
</tr>
<tr>
<td>Near fatal OD</td>
<td>5,360</td>
<td>2276</td>
<td>1.86 (1.50-2.31)</td>
</tr>
</tbody>
</table>

Olfson et al., Drug & Alcohol Depend (In Press). Adjusted for age, sex, race/ethnicity & region. Diagnoses and prescriptions in past 90 days. Near fatal OD denotes use of ventilator in ED.
Prescription of Opioids, Benzodiazepines, and Both Medications Within 30 Days of Opioid-Related Death by Clinical Diagnosis of Chronic Pain Conditions

Olfson et al. *Am J Psych* 2017; Deaths with chronic pain dx (n=8,050), Deaths without chronic pain dx (n=5,039)
<table>
<thead>
<tr>
<th>Group</th>
<th>Deaths O/E</th>
<th>Rate per 10,000 person-years</th>
<th>SMR Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug use</td>
<td>1300/10</td>
<td>194.8</td>
<td>132.1 (125.6-140.0)</td>
</tr>
<tr>
<td>Circulatory</td>
<td>689/56</td>
<td>103.2</td>
<td>12.4 (11.5-13.4)</td>
</tr>
<tr>
<td>Respiratory</td>
<td>321/10</td>
<td>48.1</td>
<td>31.5 (28.2-35.1)</td>
</tr>
<tr>
<td>Suicide</td>
<td>215/8</td>
<td>32.2</td>
<td>25.9 (22.6-29.6)</td>
</tr>
<tr>
<td>HIV</td>
<td>179/4</td>
<td>26.8</td>
<td>45.9 (39.5-53.0)</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>101/6</td>
<td>6.5</td>
<td>15.5 (12.7-18.8)</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>63/6</td>
<td>9.4</td>
<td>10.0 (7.7-12.7)</td>
</tr>
<tr>
<td>Viral hepatitis</td>
<td>49/2</td>
<td>7.3</td>
<td>30.6 (22.9-40.2)</td>
</tr>
<tr>
<td>Homicide</td>
<td>24/4</td>
<td>3.6</td>
<td>5.7 (3.7-8.4)</td>
</tr>
</tbody>
</table>

Olfson et al., *JAMA Psychiatry* 2018. (Cohort N=76,325) Adjusted for age, sex, race/ethnicity & region. SMR denotes standardized mortality rate.
Suicide rates (100,000 person-years) of adult Medicaid beneficiaries in 12 months following non-fatal opioid overdose and self-harm

Identifying and Addressing Gaps in Treatment
Opioid Use Disorder Cascade of Care

Williams AR et al (In Review)
## Populations and Interventions

<table>
<thead>
<tr>
<th>Populations</th>
<th>Settings</th>
<th>Examples of Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>General population</strong></td>
<td>Social media</td>
<td>PSAs, education, drug take-backs</td>
</tr>
<tr>
<td></td>
<td>schools, primary care</td>
<td></td>
</tr>
<tr>
<td><strong>At Risk</strong></td>
<td>Pain clinics, medical</td>
<td>Frequent clinical assessments</td>
</tr>
<tr>
<td>90+ mg MEQ/day</td>
<td>offices, schools</td>
<td>Non-opioid pain management</td>
</tr>
<tr>
<td>Prior SUD treatment</td>
<td></td>
<td>Random urine screens</td>
</tr>
<tr>
<td>Risky substance use</td>
<td></td>
<td>Refill limits, PDMP, SBIRT,</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Acute Risk</strong></td>
<td>Emergency departments</td>
<td>Naloxone, supportive measures</td>
</tr>
<tr>
<td>Overdose</td>
<td>Hospitals</td>
<td>Overdose prevention training</td>
</tr>
<tr>
<td>Entering SUD treatment</td>
<td>Substance use treatment</td>
<td>Supervised MAT induction</td>
</tr>
<tr>
<td>Criminal justice involvement</td>
<td>facilities</td>
<td>Warm handoffs for ongoing treatment</td>
</tr>
</tbody>
</table>

After Williams et al (In Review)
All cause mortality in and out of methadone and buprenorphine treatment: meta-analysis of cohort studies

<table>
<thead>
<tr>
<th></th>
<th>In treatment (95% CI)</th>
<th>Out of Treatment (95% CI)</th>
<th>Out to In Rate Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methadone</td>
<td>11.3 (8.4-15.2)</td>
<td>36.1 (24.5-53.3)</td>
<td>3.20 (2.65-3.86)</td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>4.3 (2.1-8.9)</td>
<td>9.5 (3.9-23.4)</td>
<td>2.20 (1.34-3.61)</td>
</tr>
</tbody>
</table>

Sordo et al *BMJ* 2017 Methadone results based on 16 studies, median f/u: 1.3-15.8 years, buprenorphine results based on 3 studies, median f/u: 1.1-4.5 years; total n=122,885. Mortality risks were highest in first four weeks of treatment than later and also were higher in first four weeks following treatment cessation.
Closing Thoughts

Increasing opioid-related morbidity and mortality driven recently by rising intoxication with synthetic opioids.

Adults with nonfatal opioid overdoses are at high continuing risk for fatal and repeat nonfatal overdoses.

They are also at high risk of death from a wide range of causes including suicide – need to integrate substance use, mental health, and medical care in their management.

Pervasive gaps in prevention and treatment: a critical need to develop an organized cascade of care for opioid use disorder.
A Team Effort!

Carlos Blanco, MD, PhD (NIDA)
Stephen Crystal, PhD (Rutgers)
Christine Mauro, PhD (CUMC)
Ramin Mojtabai, MD, PhD (Johns Hopkins)
Colleen Barry, PhD (Johns Hopkins)
Shang-Min Liu, MS (CUMC)
Arthur Robin Williams, MD (CUMC)
Melanie Wall, PhD (CUMC)
Shuai Wang, PhD (CUMC)
Opioid Initiatives: Research and Educational Activities

Frances R. Levin, MD
Kennedy-Leavy Professor of Psychiatry at CUMC
Chief, Division on Substance Use Disorders

Department of Psychiatry
Columbia University Medical Center/
New York State Psychiatric Institute
Email: FRL2@cumc.columbia.edu
Telephone: 646.774.6137
What Treatments Are Effective?

Medication Addiction Treatment (MAT): The use of a medication to help promote recovery

FDA-approved medications: agonist (methadone), partial agonist (buprenorphine), long-acting injectable antagonist (naltrexone)

Medications: platform to support recovery

MAT improves health, infectious disease transmission risk, criminal activity

Maintenance on MAT reduces relapse, overdose and mortality
Most Individuals With Opioid Use Disorders Go Without Treatment

- Likely only ~20% Opioid Use Disorder patients receive treatment in a given year
- Less than a third in treatment receiving MAT
- Treatment often is not quality care
  - Many patients detoxified to medication-free programs
  - Under-dosing common with methadone and buprenorphine
    - Under-dosing less likely to do well in treatment
  - Stein et al (2016) found only 53 days for average Office Based Opioid Treatment episode
  - Majority patients drop out of Medication Addiction Treatment within 3-6 months
OUD Cascade of Care

Williams AR, Nunes EV, Bisaga A, Levin FR, Olfson M. Development of a Cascade of Care for Responding to the Opioid Epidemic. Am J Addict; under review, 2018
Barriers to MAT

- Medicaid coverage limitations
- Medicaid Prior Authorization (PA) restrictions
- Commercial insurance coverage
- Provider capacity
- Accessibility and finding a provider
- Lack of behavioral health resources

**Opportunity**: What implementation research can we conduct to improve this?
Selected Research Conducted Over the Past 25 Years

PRECLINICAL STUDIES


HUMAN LABORATORY STUDIES

HUMAN BEHAVIORAL LABORATORY STUDIES (CONTINUED)

- Abuse liability of oxycodone as a function of pain and drug use history. Comer SD, Sullivan MA, Vosburg SK, Kowalczyk WJ, Houser J. Drug Alcohol Depend. 2010

- The reinforcing and subjective effects of intravenous and intranasal buprenorphine in heroin users. Jones JD, Madera G, Comer SD. Pharmacol Biochem Behav. 2014


- Impact of co-administration of oxycodone and smoked cannabis on analgesia and abuse liability. Cooper ZD, Bedi G, Ramesh D, Balter R, Comer SD, Haney M. Neuropsychopharmacology. 2018

IMAGING STUDIES/ PREVALENCE STUDIES/ REVIEWS:

- Methadone Maintenance 40 years later: thousands of lives saved but still controversial. Kleber HD. JAMA Nov 300(1): 2303-2305


**CLINICAL STUDIES**

CLINICAL STUDIES (Continued)

- Long-Acting Injectable Naltrexone Induction: A Randomized Trial of Outpatient Opioid Detoxification with Naltrexone Versus Buprenorphine.

- Long-term follow-up study of community-based patients receiving XR-NTX for opioid use disorders.

- Sociodemographic and Substance Use Disorder Determinants of HIV Sexual Risk Behavior in Men and Women in Outpatient Drug Treatment in the NIDA National Drug Abuse Treatment Clinical Trials Network.
  Kidd JD, Tross S, Pavlicova M, Hu MC, Campbell ANC, Nunes EV. *Subst Use Misuse*. 2017

- Comparative effectiveness of extended-release naltrexone versus buprenorphine-naloxone for opioid relapse prevention (X:BOT): a multicentre, open-label, randomised controlled trial.

- Outpatient transition to extended-release injectable naltrexone for patients with opioid use disorder: a phase 3 randomized trial.
Sublingual buprenorphine/naloxone produces a dose-related reduction in heroin self-administration and subjective effects.
Sustained-release NALTREXONE antagonizes the reinforcing and subjective effects of heroin for up to a month.

Main Findings:

- Depression can be identified and treated with antidepressant medication among patients with opioid use disorder.
- Depression diagnosed by clinical history to distinguish independent depressive disorder from substance related effects.
- High placebo response in many trials, likely due to improvement in mood when medication treatment (e.g. methadone) improves opioid use.
Extended Release Injection Naltrexone (XR-NTX) for Treatment of Opioid Use Disorder (Comer et al., Arch Gen Psychiatry 2006; Krupitsky, Nunes et al., Lancet 2011; Lee, Friedman, Kinlock, Nunes et al., NEJM 2016; Lee, Nunes et al., Lancet 2018)

Main Findings:

- XR-NTX improves retention in treatment and reduces relapse, compared to placebo or usual community treatment.
- XR-NTX produces outcome close to sublingual buprenorphine.
- Relapse rate is high (~50% by 6 months).
- Barriers to effectiveness of XR-NTX:
  - Induction hurdle
  - Dropout (medication discontinuation)
## The Role of Science in Addressing the Opioid Crisis - Volkow and Collins, NEJM 2017

### Overdose Prevention and Reversal

<table>
<thead>
<tr>
<th>Short-Term Strategies</th>
<th>Intermediate Strategies</th>
<th>Long-Term Strategies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comer</td>
<td>Stronger opioid antagonist formulations</td>
<td></td>
</tr>
<tr>
<td>Comer, Jones</td>
<td>Novel medications (e.g., 5-HT1A agonists, amphotericin)</td>
<td></td>
</tr>
<tr>
<td>Coricida, Inc. Naqvi, Mariani</td>
<td>Phrenic-nerve stimulation devices</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Technologies to detect overdose and alert help or autoinject naloxone</td>
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</tr>
</tbody>
</table>

### Treatment of Opioid-Use Disorders

<table>
<thead>
<tr>
<th>Short-Term Strategies</th>
<th>Intermediate Strategies</th>
<th>Long-Term Strategies</th>
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</thead>
<tbody>
<tr>
<td>Comer, Nunes, Bisaga</td>
<td>New formulations of existing medications</td>
<td></td>
</tr>
<tr>
<td>Comer, Levin, Mariani</td>
<td>Repurposing approved therapies (e.g., buprenorphine)</td>
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<tr>
<td>Kleber</td>
<td>Novel medications targeting neurobiology (e.g., losartan)</td>
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<tr>
<td>Comer</td>
<td>Vaccines and monoclonal antibodies</td>
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<tr>
<td>Martinez</td>
<td>Brain stimulation technologies</td>
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</tbody>
</table>

### Treatment of Chronic Pain

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<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Comer</td>
<td>Opioid formulations with abuse-deterrent properties</td>
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<tr>
<td></td>
<td>MOR-biased agonists</td>
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</tr>
<tr>
<td>Martinez, Haney, Cooper, Nunes, Levin</td>
<td>Cannabinoids</td>
<td></td>
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<tr>
<td></td>
<td>Novel or repurposed medications targeting pathophysiology (e.g., sodium-channel blockers)</td>
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<tr>
<td>Comer</td>
<td>Monoclonal antibodies</td>
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<tr>
<td>Martinez, Nunes, Levin, Blewin</td>
<td>Brain stimulation technologies</td>
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<td>Gene therapies</td>
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<td>Progenitor cell therapies</td>
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<td>Luo</td>
<td>Precision medicine</td>
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<td></td>
<td>Biomarkers</td>
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</tr>
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Faculty Research

Adam Bisaga, M.D.:

- **Focus on Improving Induction Onto Naltrexone**
  
  - "A Strategy to Improve Success of Treatment Discontinuation in Buprenorphine Responders" R21
  
  - "Buprenorphine as an adjunct to outpatient induction onto vivitrol “ Pilot Study

Sandra Comer, Ph.D.:

- **1) Focus on Understanding Abuse Liability of Opioid Medications and Medications that Might Reduce Self-administration**
  
- **2) Focus on improving naloxone usage in community settings**
  
  - "Medication Development for Opioid and Alcohol Abuse: Laboratory Studies in Humans,” R01
  
  - "A Randomized, Double-Blind, Placebo-Active-Controlled, Crossover Study to Evaluate the Abuse Potential of Oxymorphone Compared to Other Mu Opioid Agonists in Physically Dependent Opioid Users w/Moderate-Severe Opioid Use Disorder” FDABAA-17-00123N
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Faculty Research

**Sandra Comer, Ph.D.**

- Shared Pharmacotherapeutic Strategies for Cannabinoid & Opioid Use Disorders: Project 3 PI; U54
- Risk and Benefits of Overdose Education and Naloxone Prescribing to Heroin Users; R01; Jermaine Jones-Co PI
- “Vaccines for Prescription Opioid and Heroin Abuse” U01
- “A Phase 3 Study to Evaluate the Safety, Tolerability and Efficacy of Naltrexone for Use in Conjunction with Buprenorphine in Adults with Opioid Use Disorder” – Alkermes
- “Study to Access Subjective Opioid Effects of CAMS2038 in Adults w/Opioid Use Disorder” – Braeburn

**Elias Dakwar, MD:**

- **Improving Naltrexone Induction with Ketamine**
  - Glutamergic Modulation to Facilitate Naltrexone Initiation: A Randomized, Controlled Trial, R01
Faculty Research

Frances Levin, MD:

- **Supporting Clinical trials, Behavioral Laboratory Research, Pilot Studies, and Educational Initiatives via NIH-funded Center**
  - Shared Pharmacotherapeutic Strategies for Cannabinoid & Opioid Use Disorders: Center PI; U54
  - Adjunctive Lorcaserin Treatment for Opioid Use Disorder, CoI with Chinazo Cunningham PI); “Does medical cannabis reduce opioid analgesics in HIV+ and HIV adults with pain?”

Edward Nunes, MD:

- **Developing Methods to Improve Implementation of Evidence-based Treatments in Community Settings**
  - NIDA Clinical Trials Network: Greater New York Node: 3UG1

Arthur Robin Williams, MD:

- **Assessing How Well Evidence-Based Interventions are Implemented Nationally**
  - “Improving the treatment cascade of MAT initiation and retention for opioid use disorder,” K23
CTN NY Node New Studies: Effectiveness and Implementation

- Addressing the naltrexone induction hurdle with a 5-day rapid initiation protocol
  - Bisaga and Nunes, Lead Investigators, CTN multisite

- Lofexidine to improve induction and adherence to buprenorphine and XR-NTX
  - Nunes, Lead Investigator, CTN multisite

- Buprenorphine treatment among Native Americans
  - Aimee Campbell, Pamela Venner (New Mexico), Lead Investigators

- Gender tailored treatment for opioid use disorder
  - Aimee Campbell, Lead Investigator, Leslie Marino, Project Director

- Influence of Organizational Context on Implementation and Sustainability of the Nurse Care Manager Model in Primary Care Clinics (ancillary study to CTN0074)
  - Aimee Campbell, PhD; Lead Investigator
CTN NY Node New Studies: Effectiveness and Implementation

- Buprenorphine initiation in Emergency Departments
  - Ryan McCormack, John Rotrosen NYU, Lead Investigators
- Tablet based screening for opioid use disorder in medical settings
  - Jennifer McNeely, NYU, Lead Investigator
- Others
  - Buprenorphine, XR-naltrexone in criminal justice settings (Josh Lee, NYU)
  - Screening and treatment for mood disorders among patients with opioid use disorder
Partnership With Industry

“Automatic Phrenic Nerve Stimulation to Rescue Opioid Induced Respiratory Depression” SBIR R43 Coridea, Inc.

- Consultants: Nasir Naqvi, M.D.; Ph.D.; John Mariani, M.D.

“2 Year Phase II development completion and testing: A game-based intervention for Opioid Use Disorder.” PEAR Therapeutics

- Co-Investigators: Edward Nunes, M.D.; Aimee Campbell, Ph.D.
Faculty Research: Pending

Arthur Robin Williams, MD:
- "Medical Marijuana Program Participation and Changes in Controlled Substance Use." R21- JIT

Sandy Comer, PhD
- Phase Ia/Ib Clinical Trials of Multivalent Opioid Vaccine Components, UG3/UH3

Edward Nunes MD/ Adam Bisaga, MD
- Evaluation of safety and pharmacokinetics of naltrexone implant, UH3/UG3

Edward Nunes MD
- "Comprehensive CBT via reSET for a Hub and Spoke MAT System of Care” SAMHSA Opioid STR grant (R21/R33); Multiple PI model with Dr. Kawasaki, MD/Penn State Univ College of Medicine.

Caroline Arout, MD
- The effects of repeated cannabis administration on experimental pain and abuse liability in humans” K08

Ziva Cooper, PhD/ Caroline Arout, PhD
- Impact of vaporized cannabis with varying cannabidiol and THC ratios on opioid abuse-liability and analgesia; R21

Jermaine Jones, PhD
- Functional Genetics, Epigenetics, and Non-coding RMDAs in Substance Abuse (R21)- JIT
PCSS provides evidence-based training and resources to give healthcare providers the skills and knowledge they need to treat patients with OUD. Join the dedicated health professionals who are making a difference in millions of lives.

PI: Kathryn Cates-Wessel (CEO of AAAP)
Frances R. Levin (Medical Director)
Columbia Faculty: Drs. Adam Bisaga (Mentoring Chair), Aimee Campbell (Implementation Chair)
The goal of this project is to provide technical assistance and necessary support to State Targeted Response (STR) grantees to ensure the provision of evidence-based prevention, treatment and recovery support programs/services across all states and territories that received STR grants.

PI: Kathryn Cates-Wessel, CEO AAAP

Medical Director: Frances R. Levin, MD; Subaward RFMH and Columbia; Drs. Campbell, Nunes, Bisaga, and other Division on Substance Use Disorders faculty working on this grant
Opportunities: Working with the CTSA

New RFA: Collaborative Innovation Award. Clinical and Translational Science Award (CTSA) Program (U01 Clinical Trial Optional)

- Partnership of CTSA and Clinical Trials Network
- To provide the opportunity to explore many translational science barriers:
  - recruiting and retaining difficult to reach populations
  - harnessing technology to simultaneously deliver effective care and facilitate the conduct of research
  - integrating research and testing models for OUDS within busy clinical settings, (such as primary care, emergency departments, and neo-natal units)
Opportunities and Challenges

What are the opportunities and challenges?

- **Impacting opioid overdose epidemic**
  - Promoting and evaluating prevention efforts via PMPs or medical student/resident/faculty training

- **Fentanyl and Fentanyl Analogue implicated in majority of synthetic opioid overdoses. Multiple Naloxone dosing required to override overdoses with potent opioids**
  - Devices to reduce overdose- external and internal
  - New medications or medication strategies to combat opioid overdoses
Opportunities and Challenges

- **Poor uptake of MAT in traditional medical settings**
  - Large scale evaluation/comparative effectiveness of implementation strategies for integrating addiction medications into diverse treatment settings (primary care, community mental health, emergency rooms)
  - Identification of organizational characteristics that fit best with certain MAT service delivery models (e.g., Nurse Clinical Manager, telepsychiatry and hub/spoke, integrated behavioral health, etc.)

- **Even when physicians trained to prescribe buprenorphine, majority prescribe medications to few or no patients.**
  - Develop new interventions to improve physician prescribing (hands-on supervision; models described above)
Opportunities and Challenges

- Little uptake of XR-naltrexone, Vivitrol, in the treatment community. Difficulties in inducting individuals onto XR-naltrexone
  - Develop novel induction methods, use of ancillary medications

- Individuals taking potent opioids such as fentanyl (often unknowingly), leading to less blockade with XR-naltrexone and greater difficulty inducting patients onto buprenorphine
  - May need higher doses/increased frequency of XR-naltrexone; more potent antagonists
  - May need to alter how we induct individuals onto buprenorphine

- Many factors leading physicians to no longer prescribe opioids for chronic pain. Patients are being “dumped” or told that their pain medication doses have to be reduced to much lower dosing regimens
  - How to best do this. Are there medications/devices that can be used to help reduce or be taken off high dose opioids?
Opportunities and Challenges

- **Management of Acute and Chronic Pain**
  - Approaches to help reduce opioid dose in pain patients evaluated in the hospital
  - Investigation of barriers to non-opioid therapy in patients with pain (e.g., insurance issues, limited physician time to explain alternative therapies, patient acceptance, etc.)
  - Investigations of when opioid treatment is warranted (e.g., emergency room or surgical settings) and how opioid treatment should be managed

- **Chronic pain occurs in over 30% of Americans**
  - Are there novel non-opioid pharmacologic or device-based interventions that might be helpful?
Conclusions

The Opioid Overdose Epidemic is a Major Public Health Crisis that is Unlikely to Abate in the Near Future

As a result of greater exposure to opioids, many individuals have developed an OUD.

This has Led to the Need for Prevention, Treatment, and Recovery Interventions

The Division on SUDs is a Center of Excellence for Research, Clinical Interventions, and Training

There are many challenges and opportunities to pursue to address this critical problem

There are many potential clinical research and training collaborative efforts that are possible
Thank You

NI DA

Edward Nunes, M.D.

Sandy Comer, Ph.D.

Aimee Campbell, Ph.D

John Mariani, M.D.

Adam Bisaga, M.D.

Elias Dakwar, M.D.

Arthur Robin Williams, M.D.

Herbert D. Kleber, M.D.
Strategies for Combatting NYC’s Opioid Overdose Epidemic

June 22, 2018

Mary T. Bassett, MD, MPH
Commissioner
New York City Department of Health and Mental Hygiene
Overview

- NYC’s current drug overdose epidemic
- NYC Department of Health’s harm-reduction response to the opioid crisis
- Strategies for clinicians to mitigate this crisis
THE HEALTH IMPACT OF NYC’S OPIOID EPIDEMIC
Every 7 hours, someone dies of a drug overdose in New York City
Nearly all Drug Overdoses in NYC involve Opioids

Opioids include heroin, fentanyl, prescription painkillers

- 72% involve heroin or fentanyl
- 4/5 involve any opioid
- Nearly 3/4 involve heroin or fentanyl

Source: New York City Office of the Chief Medical Examiner & New York City Department of Health and Mental Hygiene 2000-2016*
*Data for 2015 and 2016 are provisional and subject to change (Published June 13, 2017)
The NYC Drug Overdose Epidemic

Number of unintentional drug poisoning deaths

Fentanyl enters the NYC Market

Source: New York City Office of the Chief Medical Examiner & New York City Department of Health and Mental Hygiene 2000-2017*
*Data for 2017 are provisional and subject to change
Drug Overdose Death Rates by Borough

Rate of drug overdose death, by borough of residence, 2016

<table>
<thead>
<tr>
<th>Borough</th>
<th>Rate per 100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bronx</td>
<td>28.1</td>
</tr>
<tr>
<td>Brooklyn</td>
<td>15.8</td>
</tr>
<tr>
<td>Manhattan</td>
<td>16.3</td>
</tr>
<tr>
<td>Queens</td>
<td>13.7</td>
</tr>
<tr>
<td>Staten Island</td>
<td>31.8</td>
</tr>
</tbody>
</table>

Source: New York City Office of the Chief Medical Examiner & New York City Department of Health and Mental Hygiene, 2016*
*Data for 2016 are provisional and subject to change. (Published June 13, 2017)
The NYC Overdose Epidemic

Number of confirmed overdose deaths by borough of residence**, January – December, 2017, compared to 2016 total

<table>
<thead>
<tr>
<th>Borough</th>
<th>2016 Total</th>
<th>2017 Q1 – Q4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bronx</td>
<td>342</td>
<td></td>
</tr>
<tr>
<td>Brooklyn</td>
<td>350</td>
<td></td>
</tr>
<tr>
<td>Manhattan</td>
<td>216</td>
<td></td>
</tr>
<tr>
<td>Queens</td>
<td>255</td>
<td></td>
</tr>
<tr>
<td>Staten Island</td>
<td>99</td>
<td></td>
</tr>
</tbody>
</table>

Bronx and Staten Island neighborhoods have high rates of overdose death

January 1, 2017 – December 31, 2017

Rate of Unintentional Drug Poisoning (Overdose) Death, Per 100,000 Residents
January 1, 2016 – December 31, 2017
Unintentional Overdose Deaths by Borough of Residence, 2017*
Total Deaths = 1,262*

Source: Bureau of Vital Statistics/Office of the Chief Medical Examiner, New York City. Data for 2017 is provisional and subject to change. Analysis by Health Department's Bureau of Alcohol and Drug Use Prevention, Care and Treatment.
NYC’S RESPONSE TO THE OVERDOSE CRISIS
NYC’s Public Health Approach to Opioids

1. Track what is happening

2. Prevent or reduce risky use

3. Prevent complications of opioid misuse

4. Strengthen care continuum: treatment, harm reduction, recovery supports

5. Work with multiple sectors
DOHMH HealingNYC Interventions

- $38M investment announced by the Mayor in March 2017, with additional $22M announced in March 2018 for new initiatives

- Naloxone to family and friends of person who uses drugs

- Expand access to effective medications for addiction treatment

- Use media to destigmatize treatment, promote naloxone use
Shifting the Narrative via Media

PREVENT OVERDOSE DEATHS

SAVE A LIFE CARRY NALOXONE

You can save a life with naloxone.

And emergency medicine that prevents overdose death from prescription painkillers and heroin.

Available without prescription.

To find a pharmacy that provides naloxone without prescription, call 311 or visit ny.gov/health/naloxone.

If you need help, support, or referral to treatment, call 800-NYC-Well.

I saved my neighbor's life.

“I took a different way home from work one night and found my neighbor on the ground. He was blue and not breathing. I gave him naloxone, which I always carry, and in 2 minutes he was breathing again. As we waited for the ambulance, it hit me that if I hadn't come home this way, his family would be getting a very different phone call that night.”

—Evelyn, Manhattan

NALOXONE is an emergency medicine that prevents overdose death from prescription painkillers and heroin.

I am living proof that buprenorphine treatment works.

My first addiction cost me my job and family. Then I was prescribed buprenorphine. It transformed my career. Now, I am working on my relationship with my former patient to stay on a new, more constructive path.

—Joseph

Open addiction treatment with buprenorphine and naloxone is available in New York City.

If you or someone you know needs help, call 800-NYC-WELL or visit ny.gov/health/addictiontreatment for more information.
Expanding of Buprenorphine Access

Purple star = Adolescent treatment program
Red star = Nurse care manager program site
Syringe Exchange Program (SEP) Sites Concentrated in Neighborhoods with High Rates of Overdose Deaths

Syringe Exchange Program
Storefront Sites
New York City –
as of April 9, 2018
Relay: NYC Nonfatal Overdose Response System

- Target population: individuals in emergency department (ED) after non-fatal overdose

- Deploy Wellness Advocates 24/7 to targeted EDs

- Provide naloxone, risk reduction messages, and connection to other services
  - follow up for up to 90 days

- Active in 5 hospitals; target is 15 hospitals by June 2020
Overdose Prevention Centers

- **Four** Overdose Prevention Centers (OPCs) could avert up to 130 overdose deaths a year.

- OPCs would also increase entry into drug treatment, reduce the spread of HIV and Hepatitis C, and reduce healthcare costs.

- Research shows areas with these programs have a decrease in drug crimes, including drug solicitations, public injection, and drug sales.
STRATEGIES FOR CLINICIANS TO MITIGATE THIS CRISIS
What Can Clinicians Do? NYC needs you!

1. Screen for non-medical prescription drug use; screening for other substance use
   - Advise that opioids are risky – anyone can develop a substance use disorder

2. Prescribe opioids judiciously
   - Avoid when possible
   - Shortest course, lowest dose

---

<table>
<thead>
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<tbody>
<tr>
<td>Preventing Misuse of Prescription Opioid Drugs</td>
</tr>
<tr>
<td>• Physicians and staff can play a major role in reducing risks associated with opioid analgesics, particularly fatal drug overdoses.</td>
</tr>
<tr>
<td>• For acute pain</td>
</tr>
<tr>
<td>• If opioids are prescribed, prescribe only short-acting agents.</td>
</tr>
<tr>
<td>• A 3-day supply is usually sufficient.</td>
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<table>
<thead>
<tr>
<th>Sometimes the medicine becomes the problem</th>
</tr>
</thead>
<tbody>
<tr>
<td>- For chronic nonmucous pain</td>
</tr>
<tr>
<td>- Avoid prescribing opioids unless other approaches to analgesics have been demonstrated to be ineffective.</td>
</tr>
<tr>
<td>- Avoid unnecessary prescription of opioids in patients taking benzodiazepines because of the risk of fatal respiratory depression.</td>
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</tbody>
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<thead>
<tr>
<th>TRENDS IN OPIOID ANALYSIS USE AND CONSEQUENCES, NEW YORK CITY, 2004-2010</th>
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<td>Emergency Department Visits for Opioid Prescription Drugs</td>
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<table>
<thead>
<tr>
<th>OPIOD PAINKILLERS such as</th>
<th>Pain relief?</th>
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<tbody>
<tr>
<td>Tylenol® (acetaminophen), OxyContin® (oxycodone-acetaminophen)?</td>
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<th>Pain relief?</th>
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<td>Sometimes the medicine becomes the problem</td>
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<td>- For chronic nonmucous pain</td>
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What Can Clinicians Do?  
NYC needs you!

3. Offer treatment for substance use disorder
   • Consider pharmacotherapy in specialty or primary care

4. Assist your patients in obtaining naloxone:
   • By prescription
   • At participating NYC pharmacy without prescription
     — Health Commissioner standing order
     — Available at >960 pharmacies
   • At registered opioid overdose prevention programs
Thanks!