HIV/AIDS and Drug Abuse: The Promise of Integrated Care

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The Crisis: National Overdose Death Rates

In 2017, there were 70,237 overdose deaths (9.6% higher than 2016)

Evolution of the Opioid Crisis

1. Over prescription of opioid medications led to misuse
2. Addiction to prescription opioids led to heroin
3. Emergence of fentanyl(s), with higher potency and greater profitability in the black market than heroin.
HIV Can Disseminate Very Rapidly among IDU

USA: new HIV cases in IDUs have decreased since 1990, to 4000 year (8-10% new HIV cases)

IDU 20% of those living with HIV

Outbreak of HIV Linked to IDU of Oxymorphone in Indiana, USA 2015

- Injection Drug Use: 80%
- No Injection Drug Use: 3%
- Not Interviewed to Determine Status: 17%

Average 9 syringe-sharing partners, sex partners,

In Scott County, a community of 4200 people there were 215 new HIV Infections in 2014-2015 attributed to IDU

220 counties in 26 states identified as vulnerable communities

Dopamine neurons in the ventral tegmental area (VTA) have smaller volumes and reduced activity with repeated exposure to morphine.

DA neuron size was decreased in postmortem human heroin addicts compared with controls.

Diminished dopamine D2 receptors in Individuals with OUD

Wang et al., Neuropsychopharmacology. 1997 Feb;16(2):174-82.
Individuals with OUD show heightened brain responses to drug cues relative to controls. These are reduced with medication assisted treatments and following prolonged abstinence.

*Moningka et al. Neuropsychopharmacology, 2018.*
Medication Assisted Treatment (MAT)

Opioid Effect vs Log Dose

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

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

INCREASES
- Social functioning
- Retention in treatment

MAT is highly underutilized!
Relapse rates are very high (50% in 6 months)

Williams AR, Nunes E, Olfson M. Health Affairs Blog, 2017

OUD Cascade of Care in USA

- OUD severe
- OUD diagnosed
- Engaged in Care
- MAT Initiation
- Retained 6+ months
- Continuous abstinence
Among IDUs Medication Assisted Treatment Improves HIV Outcomes

Methadone Maintenance Therapy Promotes Initiation Of Antiretroviral Therapy in IDU

- Adjusted Odds Ratio
  - Palepu A et al., Drug and Alc Depend 2006; 84: 188-194.

Methadone Maintenance Therapy Increases Antiretroviral Adherence and HIV Treatment Outcomes in IDU

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Graphs showing the probability of ART initiation over time for those on MMT and those not on MMT, with a log-rank p-value of 0.004.

Bar graph showing Adjusted Odds Ratios for subsequent weekly heroin use, 95% adherence, HIV-1 RNA suppression, and CD4 cell response.
Effects of OUD Medications Effects Among HIV+ IDU

ART coverage of among IDUs

On plasma viral suppression

Extended-Release Naltrexone Improves Viral Suppression Among Incarcerated PLWH & OUD

Rate of Past Year Opioid Abuse or Dependence and Rate of OA-MAT Capacity (rate per 1,000 persons aged 12 years and older)

Source: Jones CM et al., National and State Treatment Need and Capacity for Opioid Agonist Medication Assisted Treatment, AJPH 2015.
Improving Treatments for Addiction: Implementing Medication-Assisted Treatment

- Emergency department-initiated buprenorphine
  - Reduced self-reported, illicit opioid use
  - Increased engagement in addiction treatment; decreased use of inpatient addiction treatment services

Self-Reported Illicit Opioid Use in the Past 7 Days

<table>
<thead>
<tr>
<th>Days</th>
<th>Baseline</th>
<th>30 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buprenorphine</td>
<td>5.4</td>
<td>0.9</td>
</tr>
<tr>
<td>Referral</td>
<td>5.4</td>
<td>2.3</td>
</tr>
<tr>
<td>Brief Intervention</td>
<td>5.6</td>
<td>2.4</td>
</tr>
</tbody>
</table>

Infectious Clinic’s-Based Buprenorphine of Opioid-Dependent HIV+ Patients vs Tx Referral

Average Estimated Participation in Opioid Agonist Therapy (%)

- Clinic-Based BUP: 74%, P<0.001
- Referred Tx: 41%

D’Onofrio G et al., JAMA April 28, 2015.
Opioid Medication Therapy In Prison

Mortality Post Release
Survival Curve During the Year Following Release (Drug-Poisoning Mortality)

OMT resulted in a 75% reduction in mortality (85% reduction in overdoses) in the first month post release

Marsden J et al., Addiction 2017; 112:1408-1418.

Viral Load Increases Over Time After Release From Jails/Prisons

Linkage time to care as measured by first HIV RNA viral load drawn after release from prison/jail

CHALLENGES For Treating OUD HIV+ Individuals

1. Treating HIV+ Patients for their OUD with medications
2. Treating HIV+ OUD with HAART and retaining them
What is NIDA doing?

Implementation and services research
Integrated and new models of care
Health Care (i.e., STD clinics)
Criminal Justice System
Rural communities
Countries where IDU is driver of HIV epidemic

IDUs as Share of Total HIV Cases & of Patients Receiving ART, 2008

HAART as HIV Prevention: Including IDU

HIV epidemic indicators for BC

Expansion of HAART was associated with decreases in new HIV diagnoses between 1996-2012 (92% in IDU and 22% in MSM)

Facilitate expansion and adherence to HAART among IDU

- Enhanced HIV screening
- Low threshold HAART treatment facilities
- Wide availability of needle and syringe programs,
- Extensive MAT

Montaner et al., PLoS ONE 2014.
Integrated Models of Care for Individuals with Opioid Use Disorder with HIV and/or HCV

Steps Toward Care Integration

Scalable, Integrated Intervention To Engage IDU In HIV Care and MOUD (HPTN 074)

Systems navigators facilitate engagement, retention, adherence in HIV care and MAT. Psychosocial counseling, at least 2 sessions. ART at any CD4 count.

Proportion Alive & HIV RNA <40 cp/mL

All incident HIV infections among partners occurred in the SOC arm:

**Intervention:** (0 cases/215.6 p-y) (7 cases/683.6 p-y)

**IR:** 0.0/100 p-y (CI 0.00, 1.7) SOC:

**IR:** 1.0/100 p-y (CI 0.41, 2.1)
Needle and Syringe Programs Prevent HIV and HCV

Timeline of Indiana HIV Outbreak among IDUs

A. Cumulative HIV Diagnoses and Public Health Response

- Initial diagnosis
- Cluster identified
- Incident command established
- Federal support requested
- Public health emergency declared
- Syringe exchange started
- Local HIV clinic opened
- HIV testing staff and DIS deployed
- >35,000 cumulative syringes dispensed
- >77,000 cumulative syringes dispensed

B. HIV Diagnoses According to Week of Testing

What is NIDA doing?

NEW THERAPEUTICS for OUD

Long lasting medications to improve compliance
Medications not based on opioid substitution
Vaccines and other immunotherapies

SUBLOCADE™
(Buprenorphine ER),
Once-Month Injectable
FDA Approval 11.30.2017

CAM2038:
Subcutaneous ER
Buprenorphine
Weekly or monthly injection

% negative opioid urines (Weeks 5 to 24)

Heidbreder et al., CPDD 2017
Integrating Treatment at the Intersection of OUD and Infectious Disease Epidemics in Medical Settings: Call for Action After a NASEM Workshop

1) Implement screening for OUD in all relevant health care settings.

2) For patients with positive screening results, immediately prescribe effective medication for OUD and/or opioid withdrawal symptoms.

3) Develop hospital-based protocols that facilitate OUD treatment initiation and linkage to community-based treatment upon discharge.

4) Hospitals, medical schools, physician assistant schools, nursing schools, and residency programs should increase training to identify and treat OUD.

5) Increase access to addiction care and funding to states to provide effective medications to treat OUD.

Influence of IDU HIV Acquisition on CD4 Response to First ART Regimen Among Virally Suppressed Individuals

CD4 values and predicted CD4 response over time at 25th, 50th, and 75th percentiles for IDU (dashed lines) and non-IDU (solid lines) among 1,244 persons who initiated ART in JH between 2000-2015.

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Long-term Px opioids and/or benzodiazepines and mortality among HIV-infected and uninfected patients

Uninfected Patients

HIV-infected

Significant interaction between opioid receipt and HIV with mortality: HR was 1.46 in HIV+ and 1.25 in HIV-(p <0.01).

New HIV Diagnoses in the United States by Transmission Category, Race & Age, 2016-2017

- **Heterosexual Contact**: 24% (9,578)
- **Male-to-Male Sexual Contact**: 67% (26,570)
- **Injection Drug Use + Injection Drug Use**
  - Male-to-Male Sexual Contact: 6% (2,224)
  - Male-to-Female Sexual Contact: 3% (1,201)

**Age in Years**

- **13-24**
  - Total: 13,433
- **25-34**
  - Total: 8,164
- **35-44**
  - Total: 7,397
- **45-54**
  - Total: 5,735
- **55-64**
  - Total: 3,026
- **65+**
  - Total: 885

**Number of diagnoses**

- **Men Who Inject Drugs**
  - Black: 471
  - Hispanic/Latino: 259
  - White: 458

- **Gay and Bisexual Men Who Inject Drugs**
  - Black: 254
  - Hispanic/Latino: 270
  - White: 597

- **Women Who Inject Drugs**
  - Black: 338
  - Hispanic/Latina: 139
  - White: 411

*Centers for Disease Control and Prevention*
HIV+ IDUs Are Much Less Likely to Receive HAART

% Providers Who Would Defer ART
By CD4+ Count and IDU status