NIDA AIDS Research Program Update: High Priority Research Areas

National Advisory Council on Drug Abuse
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Redonna K. Chandler, Ph.D.
Director, AIDS Research Program & HEALing Communities Study
National Institute on Drug Abuse
NIDA’s HIV/AIDS Research Portfolio

• Addresses the intersection of drug use and HIV

• Crosses the scientific spectrum:
  • Basic research
  • Epidemiology
  • Prevention
  • Treatment
  • Implementation

• Embedded in every division and center including IRP, CTN, OTIPI

• Encompasses diverse populations and settings

• Includes feedback from key stakeholders responding to a Request for Information issued January 2019 (NOT-DA-19-015)

• Align with NIH priorities for HIV and HIV-related research
Relative Risk of HIV Acquisition Globally 2018

- Transgender people: 12x
- Gay men and other men who have sex with men: 22x
- People who inject drugs: 22x
- Sex workers: 21x

- Globally, 13M PWID of whom 1.7M are HIV+
- Globally, 10% of HIV infections are from IDU
- HIV Incidence in PWID: 1.2% in 2011; 1.4% in 2017
- PWID living with HIV (%): 11.4% in 2011; 12.5% in 2016

WHO: https://www.who.int/hiv/topics/idu/en/

Source: Volkow, IAS, 2019, UNAIDS 2018
US Opioid Epidemic has Increased Overdose Deaths and Prevalence of PWID

In 2017, 70,237 OD Deaths (9.6% higher than 2016)

Prevalence of IDU in US has increased in past 15 years
Heroin IDU in US (12 or older, past-month use)

B Coefficient: 0.1519
p Value for the trend: <0.0001

Legend for estimated age-adjusted death rate (per 100,000 population)

- 0-2
- 3-9.9
- 10-11.9
- 12-13.9
- 14-15.9
- 16-17.9
- 18-19.9
- 20-21.9
- 22-23.9
- 24-25.9
- 26-27.9
- 28-29.9
- 30+

Source: Han et al., SAMHSA (unpublished)
HIV Can Spread Rapidly Among People Who Inject Drugs

U.S. counties vulnerable to rapid spread of IDU-associated HIV

220 counties in 26 states

Kings County, WA, 27 HIV cases from IDU in 2018.

Scott County, 215 HIV cases from IDU in 2014-2015

Cabell County WV, 55 HIV cases from IDU in 2019

Lowell and Lawrence, Mass. 129 HIV cases in IDU from 2015-2018 (from 2012-2014, entire Mass had 123 IDU cases).

Philadelphia, 59 HIV cases from IDU in 2018 (60% increase from 2016)

Northern KY, 280% increase in HIV cases from IDU in 2017

Multnomah, OR, 42 HIV cases mostly IDU in 2018-2019.

Source: Van Handel et al., J Acquir Immune Defic Syndr, 2016

Estimates of HIV increases in IDU are from local newspapers (search Volkow et al., 2019)
Common Comorbidities Among PLWH and Using Drugs

- CNS Disorders (HAND, Neuropathy, Cerebrovascular Accident, Depression)
- Pulmonary Disorders (Tuberculosis, Pneumonia, Septic Emboli)
- Cardiovascular Disorders (Endocarditis, MI)
- Liver Disorders (Hepatitis B and C)
- Skin and Soft Tissue Disorders (Cellulitis, Abscess, Necrotising Fasciitis)

Source: Altice et al. Lancet 2010
Medications for Opioid Use Disorders (MOUD or MAT, OST)

Full Agonist (Methadone: Daily)
Partial Agonist (Buprenorphine: 3x/week, ER 1 month)
Antagonist (Naltrexone: ER 1 month)

DECREASES:
- Opioid use
- Opioid overdose deaths
- Criminal activity
- HIV and HCV transmission

INCREASES:
- Social functioning
- Retention in HIV treatment
- Improves HIV Outcomes

Impact of MOUD on HIV Transmission

<table>
<thead>
<tr>
<th>Study</th>
<th>Effect estimate (95% CI)</th>
<th>Effect estimate (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>North America</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Williams 1992</td>
<td>0.16 (0.02 to 1.30)</td>
<td>0.13 (0.03 to 0.50)</td>
</tr>
<tr>
<td>Metzger 1993</td>
<td>0.29 (0.09 to 0.94)</td>
<td>0.56 (0.34 to 0.92)</td>
</tr>
<tr>
<td>Chitwood 1995</td>
<td>0.67 (0.42 to 1.10)</td>
<td>0.38 (0.23 to 0.65)</td>
</tr>
<tr>
<td>Nelson 2002</td>
<td>0.17 (0.04 to 0.71)</td>
<td>0.38 (0.23 to 0.65)</td>
</tr>
<tr>
<td>Kerr 2006</td>
<td></td>
<td>0.67 (0.42 to 1.10)</td>
</tr>
<tr>
<td>Bruneau 2012 (unpublished)</td>
<td></td>
<td>0.35 (0.23 to 0.54)</td>
</tr>
<tr>
<td>Subtotal</td>
<td>0.17 (0.04 to 0.71)</td>
<td>0.38 (0.23 to 0.65)</td>
</tr>
<tr>
<td>Subtotal</td>
<td>0.40 (0.22 to 0.71)</td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>0.56 (0.34 to 0.92)</td>
<td>0.40 (0.22 to 0.71)</td>
</tr>
</tbody>
</table>

Europe
Van den Berg 2007
Judd 2012 (unpublished)
Subtotal: $i^2=17\%$, $P=0.272$

South East Asia (Thailand)
Suntharasamai 2009
Subtotal

Overall: $i^2=60\%$, $P=0.010$

MOUD reduced HIV infections by 54%

Treating Opioid Use Disorders in PLWH Improves HIV Outcomes

**Challenges:**
- Treatment and retention in MOUD
- Treatment and retention in ART

MOUD Improves uptake/retention in ART
- 69% increased recruitment to ART
- Two-fold increase in ART adherence
- 23% decrease in odds of attrition
- 45% increase in odds of plasma viral suppression (VS)

**Odds of Viral Suppression for HIV+ on MOUD**

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Location</th>
<th>N</th>
<th>Threshold copies/mL</th>
<th>OR (95% CI)</th>
<th>Weight (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abellán, 1999</td>
<td>Madrid</td>
<td>28</td>
<td>500</td>
<td>2.00 (1.41, 9.71)</td>
<td>1.25</td>
</tr>
<tr>
<td>Achmad, 2009</td>
<td>Indonesia</td>
<td>140</td>
<td>400</td>
<td>2.80 (1.35, 22.59)</td>
<td>0.72</td>
</tr>
<tr>
<td>Allie, 2011</td>
<td>USA</td>
<td>266</td>
<td>400</td>
<td>1.32 (0.67, 2.26)</td>
<td>6.12</td>
</tr>
<tr>
<td>Lucas, 2006</td>
<td>Baltimore</td>
<td>319</td>
<td>400</td>
<td>0.95 (0.55, 1.65)</td>
<td>8.12</td>
</tr>
<tr>
<td>Palapu, 2006</td>
<td>Vancouver</td>
<td>278</td>
<td>500</td>
<td>1.36 (1.07, 1.72)</td>
<td>26.52</td>
</tr>
<tr>
<td>Roux, 2009</td>
<td>France</td>
<td>153</td>
<td>500</td>
<td>2.34 (1.11, 4.93)</td>
<td>5.16</td>
</tr>
<tr>
<td>Springer, 2012</td>
<td>Connecticut</td>
<td>94</td>
<td>50</td>
<td>1.36 (0.79, 2.34)</td>
<td>4.17</td>
</tr>
<tr>
<td>Ti, 2014</td>
<td>Vancouver</td>
<td>587</td>
<td>500</td>
<td>2.14 (1.53, 3.00)</td>
<td>17.92</td>
</tr>
<tr>
<td>Weber, 2009</td>
<td>Switzerland</td>
<td>1469</td>
<td>50</td>
<td>1.15 (0.77, 1.66)</td>
<td>15.14</td>
</tr>
<tr>
<td>Westergaard, 2013</td>
<td>Baltimore</td>
<td>740</td>
<td>400</td>
<td>1.42 (0.95, 2.11)</td>
<td>14.39</td>
</tr>
<tr>
<td><strong>Overall</strong></td>
<td></td>
<td></td>
<td></td>
<td>1.45 (1.21, 1.73)</td>
<td>100.00</td>
</tr>
</tbody>
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*NOTE: Weights are from random effects analysis*

Reduced Use Associated with Viral Suppression

![Bar chart showing odds ratios for viral suppression by substance use.](https://doi.org/10.1093/cid/ciz299)
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 MOUD

Source: Montaner et al. PLoS ONE 2014
Medications for OUD are Highly Underutilized

MOUD Coverage among PWID

Source: Larney S et al. Lancet Global Health 2017
Globally Gaps in Receipt of ART for HIV+ IDUs

HIV Treatment Coverage
(UNAIDS 2014-2017, 2018 Estimates)

Provider Stigma Persists

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

ART Delayed for PWID with Advanced HIV


Source: Ferro EG et al. Open Forum Infect Dis 2017
NIDA HIV Cure Research: Eliminating HIV-1

Source: Dash et al. Nature Communications 2019
In search of a Primate model that supports HIV-1 infection

Some primate species encode a CD4 that functions as an entry receptor for an early isolate of HIV-1

Innovators:

Julio Montaner: *Seek and Treat for Optimal Outcomes and Prevention in HIV/AIDS in IDU*

Sara Sawyer: *Hunting the HIV Unicorn: Better primates Models for HIV*

Sunil Suhas Solomon: *Reaching the Hardest of the Hard-to-Reach*
Priority Area 1: Prevent new infections and transmission of HIV among people who use drugs and their sexual and/or injection partners

Primary Prevention
Preventing HIV acquisition in people using drugs and their sexual and injecting partners

- Syringe Service Programs
- Pre-(PrEP) and Post-Exposure Prophylaxis (PEP) including Long-acting PrEP
- Health Education
- Risk reduction counseling

Secondary Prevention
Prevent transmission by treating PLWH who use and misuse drugs to achieve sustained viral remission

- Linkage to testing (HIV/HCV/STI)
- Linkage to care (Immediate initiation of ART and Medications for Opioid Use Disorder)
- Recovery support and Partner services
- Retention and reengagement in care

Structural
Improving treatment systems

- Provider Stigma
- Integrated Care
Priority Area 2: Increase understanding of etiology, pathogenesis, spread, and persistence of HIV/AIDS among people who use drugs

• Assess the role of drug use in HIV infection and pathology in the central nervous system.

• Determine how drug use or substance use therapies interact with HIV and HAART to affect inflammation and immune responses.

• Elucidate mechanisms by which drug use affects HIV latency

• Use basic science findings to guide therapeutic strategies
Priority Area 3: Address comorbidities and improve health outcomes among people living with HIV who use drugs

- Identify common underlying mechanistic substrates for neurological comorbidities
- Understand interactions of drug use, HIV/AIDS, HCV, and medications used in treatment
- Elucidate mechanisms by which drug use affects clinical outcomes in HIV including progression and mortality
- Develop integrated models to address SUDs, HIV, HCV, and other comorbidities in multiple healthcare and community settings
Priority Area 4. Accelerate scientific discoveries in HIV/AIDS and substance use research.

• Enhance the pace of translational process by supporting innovation and team science.
• Leverage big data
• Training of the next generation of basic and clinical researchers
Ending the Epidemic: Supporting Science to Address Substance Use and HIV

GOAL:

- Diagnose all people with HIV as early as possible after infection
- Treat the infection rapidly and effectively to achieve sustained viral suppression
- Protect people at risk for HIV using potent and proven prevention interventions, including medication that can prevent HIV
- Respond rapidly to detect and respond to growing HIV clusters and prevent new HIV infections
- HIV HealthForce will establish elimination teams in each jurisdiction, to ensure the success of the Initiative

HHS Has Launched A New Initiative to End the HIV Epidemic in America

Source: hrsa.gov/ending the epidemic

Source: Koob and Volkow Neuropsychopharmacology Reviews 2010
Thank You and Discussion