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# **HIV and drug abuse: relationship and treatment challenges**

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No conflict of interest to declare

# Introduction

- There is a **close relationship** between the Human Immunodeficiency Virus (**HIV**) and **substance use**
- About **half (50%)** of the persons living with HIV/AIDS report **current or past histories of drug or alcohol disorders**
- Substance use is associated with:
  - Non-adherence
  - Immunosuppression
  - Increased sexual risk behaviours
  - Increased burdens on health care systems
- HIV seropositive drug users have **higher** age matched **morbidity and mortality**

Durvasula, R., & Miller, T. R. (2014). Substance Abuse Treatment in Persons with HIV/AIDS: Challenges in Managing Triple Diagnosis. *Behavioral Medicine, 40*(2), 43-52

# Introduction

## Bidirectional Relationship

**HIV**



**Substance Use**

# Substance use → HIV

- Substance use may be a **direct or indirect vector in the transmission of HIV** through various risk behaviours, whether during intoxication or to obtain drugs
  - Sharing of contaminated injection equipment
  - Prostitution (crack)
  - Risky sexual behaviour (secondary to disinhibition, poor affect regulation, increased sexual arousal...)

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# HIV → Substance use

- Chronic disease, no known cure
- May not have such a negative burden nowadays, but still remains one of the most feared diseases
- Misinformation
- Stigma
- Important impact on relationships and social life

Wardell, J. D., Shuper, P. A., Rourke, S. B., & Hendershot, C. S. (2018). Stigma, Coping, and Alcohol Use Severity Among People Living With HIV: A Prospective Analysis of Bidirectional and Mediated Associations. *Annals of Behavioral Medicine*, 52(9), 762-772

# HIV → Substance use

- **Self-medication hypothesis** – Maladaptive coping
- Association between HIV stigma and the use of general **maladaptive coping** strategies such as avoidance and denial
- The pattern of maladaptive coping increases the risk of substance use
- Presence of **psychopathology** may contribute

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# HIV and Substance use

- Decreased quality of life, **worse prognosis**
- **Lower prescription of highly active antiretroviral therapies (HAART)** and frequent non-adherence
- **Increase risk of other diseases** such as **Hepatitis C** (observed in 60-90% of HIV infected drug users; co-infection accelerates HCV infection leading to cirrhosis) or tuberculosis
- Decreased health care utilization, and **poorer immunologic and virologic outcomes**

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# Objectives and Methods

- To understand the impact of substance use (alcohol, opioids, stimulants and cannabis) on the clinical course of HIV infected patients
- To identify possible drug interactions between antiretroviral therapies (ART) and the drugs used to treat the referred substance use disorders
- Literature review conducted using multiple literature databases: PubMed, Google Scholar, PsychINFO, ScienceDirect
- Employed keywords and various combinations of search terms as: substance use, substance abuse, drug use, drug abuse, alcohol use, opioid use, cocaine use, stimulants use, cannabis use, HIV, AIDS, treatment and treatment interactions.

# Substance use impact

**Alcohol use disorder is 2-4 times more prevalent in HIV patients**

## **Worsens comorbid diseases**

Role in HIV infection  
**development**

Biologically

- Liver damage → Cirrhosis → immunosuppression with reduction of CD4 cells → poorer innate immune system response to HIV → increased risk of infection
- Direct action on immunity (decreased inflammatory response; altered cytokine production) → increased susceptibility to infections such as HIV

Behaviourally

- Disinhibition effect – sexual risk behaviours

Role in **aggravating** HIV infection

Biologically

- Disease progression (viral replication increase, reduction of CD4 cells)
- If liver damage → less pharmacologic options

Behaviourally

- Non-adherence (increase in drug resistance)

Shuper, P. A., Neuman, M., Kanteres, F., Baliunas, D., Joharchi, N., & Rehm, J. (2010). Causal Considerations on Alcohol and HIV/AIDS -- A Systematic Review. *Alcohol and Alcoholism*, 45(2), 159-166

Pandrea, I., Happel, K. I., Amedee, A. M., Bagby, G. J., & Nelson, S. (2010). Alcohol's role in HIV transmission and disease progression. *Alcohol research & health : the journal of the National Institute on Alcohol Abuse and Alcoholism*, 33(3), 203-18

# Substance use impact

<b>Opioids</b>	Injected heroin is one of the greater risk factors for HIV infection
	Apparent progression of the disease (unknown mechanism; immunosuppressive effect, lymphocyte apoptosis, increased HIV replication...)
<b>Cocaine</b>	Prevalence of cocaine use in HIV patients is 25%
	<ul style="list-style-type: none"> <li>• Decreases immune responses: inhibits macrophages and neutrophils functions, suppresses cytokine production</li> <li>• Enhances replication of HIV</li> </ul>
<b>Other Stimulants</b>	<ul style="list-style-type: none"> <li>• Methamphetamines activate the sympathetic nervous system leading to an increase in norepinephrine → increased HIV replication</li> <li>• Immune disruption (unknown exact mechanisms)</li> </ul>
<b>Cannabis</b>	<ul style="list-style-type: none"> <li>• Apparently not associated with disease progression or non-adherence. Eventual benefits?</li> </ul>

Edelman, E. J., Cheng, D. M., Krupitsky, E. M., Briden, C., Quinn, E., Walley, A. Y., ... Samet, J. H. (2014). Heroin Use and HIV Disease Progression: Results from a Pilot Study of a Russian Cohort. *AIDS and Behavior*, 19(6), 1089–1097

Cook, J. A., Burke-Miller, J. K., Cohen, M. H., Cook, R. L., Vlahov, D., Wilson, T. E., ... Grey, D. D. (2008). Crack cocaine, disease progression, and mortality in a multicenter cohort of HIV-1 positive women. *Aids*, 22(11), 1355–1363

Carrico, A. W., Flentje, A., Kober, K., Lee, S., Hunt, P., Riley, E. D., . . . Aouizerat, B. E. (2018). Recent stimulant use and leukocyte gene expression in methamphetamine users with treated HIV infection. *Brain, Behavior, and Immunity*, 71, 108-115

Debeck, K., Kerr, T., Li, K., Fischer, B., Buxton, J., Montaner, J., & Wood, E. (2009). Smoking of crack cocaine as a risk factor for HIV infection among people who use injection drugs. *Canadian Medical Association Journal*, 181(9), 585-589

Tyagi, M., Weber, J., Bukrinsky, M., & Simon, G. L. (2015). The effects of cocaine on HIV transcription. *Journal of NeuroVirology*, 22(3), 261-274

Molina, P. E., Amedee, A., Lecapitaine, N. J., Zabaleta, J., Mohan, M., Winsauer, P., & Stouwe, C. V. (2011). Cannabinoid Neuroimmune Modulation of SIV Disease. *Journal of Neuroimmune Pharmacology*, 6(4), 516–527

# Drug interactions

## Methadone (Met)

Pure opioid  $\mu$ -receptor agonist

Half-life 24-36h

Metabolism via CYP 450

- ↓ injection and HIV transmission
- ↑ retention in HIV care
- ↑ effectiveness of ART

Nucleoside reverse transcriptase inhibitors (NRTIs)

- Scarcely affect Met (exception: abacavir ↑ clearance of methadone)
- Met affects NRTIs → ↑ zidovudine levels by 40%, ↓ stavudine 23%

Non-nucleoside reverse transcriptase inhibitors (NNRTIs)

- Efavirenz & Nevirapine ↓ Met in 57% and 46%; Delavirdine ↑ Met by 10%
- Met scarcely affects NNRTIs

Protease inhibitors

- Darunavir ↓ Met by 24%; Lopinavir-ritonavir ↓ Met by 26-36%; Tipranavir ↓ Met by 50%; Saquinavir ↓ Met by 20-32%
- Met ↓ indinavir by 16-28%

Integrase inhibitors and entry inhibitors

- Not studied

Altice, F. L., Kamarulzaman, A., Soriano, V. V., Schechter, M., & Friedland, G. H. (2010). Treatment of medical, psychiatric, and substance-use comorbidities in people infected with HIV who use drugs. *The Lancet*, 376(9738), 367–387

Bruce, R. D., Kresina, T. F., & Mccance-Katz, E. F. (2010). Medication-assisted treatment and HIV/AIDS: aspects in treating HIV-infected drug users. *Aids*, 24(3), 331–340.

# Drug interactions

<b>Buprenorphine (Bup)</b>  Partial opioid $\mu$ -receptor agonist and partial k-receptor antagonist  Half-life 24-36h	<ul style="list-style-type: none"> <li>• ↓ injection and HIV transmission</li> <li>• ↑ retention in HIV care</li> <li>• ↑ effectiveness of ART, and retention on ART after</li> </ul>	
	NRTIs	<ul style="list-style-type: none"> <li>• Scarcely affect Bup</li> </ul>
		<ul style="list-style-type: none"> <li>• No known interactions with Bup and NRTIs</li> </ul>
	NNRTIs	<ul style="list-style-type: none"> <li>• Efavirenz ↓ Bup by 50 %</li> </ul>
		<ul style="list-style-type: none"> <li>• Bup scarcely affects NNRTIs</li> </ul>
	Protease inhibitors	<ul style="list-style-type: none"> <li>• Scarcely affect Bup (exception: atazanavir-ritonavir ↑ Bup)</li> </ul>
<ul style="list-style-type: none"> <li>• Bup affects NRTIs → ↓ Tipranavir by 19-25%</li> </ul>		
INSTIs and entry inhibitors	<ul style="list-style-type: none"> <li>• Not studied</li> </ul>	
<b>Naltrexone</b>  Opioid $\mu$ -receptor antagonist	<ul style="list-style-type: none"> <li>• Retention in treatment lower than Met or Bup</li> <li>• No major interactions with ART</li> </ul>	

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# Drug interactions

<b>Acamprosate</b> Structural analogue of GABA	<ul style="list-style-type: none"><li>• Not studied in HIV patients</li><li>• Potential interactions with didanosine (both ↑); emtricitabine (both ↑); stavudine (both ↑); zidovudine (bothe ↑)</li></ul>
<b>Disulfiram</b> Inhibits acetaldehyde dehydrogenase	<ul style="list-style-type: none"><li>• Not studied in HIV patients</li><li>• Oral solutions of lopinavir, ritonavir and tipranavir may contain alcohol</li><li>• Atazanavir may inhibit disulfiram metabolism</li><li>• Disulfiram may ↑ abacavir concentration (no adjust needed)</li></ul>

Altice, F. L., Kamarulzaman, A., Soriano, V. V., Schechter, M., & Friedland, G. H. (2010). Treatment of medical, psychiatric, and substance-use comorbidities in people infected with HIV who use drugs. *The Lancet*, 376(9738), 367–387

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<https://www.hiv-druginteractions.org>

# Conclusions

- Close and bidirectional relationship
- Better understanding of this interaction is imperative (knowledge about the true impact of substances of abuse in HIV infection progression)
- Treatment of substance use disorders in this population leads to better prognosis
- Pharmacotherapies approved for substance use disorders seem fairly safe in this population when it comes to drug interactions
- Caution with NNRTIs, specially Efavirenz and Nevirapine, as well as combinations with Ritonavir

Thank you for your attention