



NORTHWEST AIDS EDUCATION AND TRAINING CENTER

Mental Health and HIV

Christine Yuodelis-Flores M.D.
Associate Professor
UW Psychiatry and Behavioral Sciences
Director of Psychiatry, Madison Clinic
Harborview Medical Center

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Outline

- Prevalence of mental disorders in HIV+
- Screening Tools
- Mental Illness, Addiction and Adherence
- Psychopharmacology
- P450 Drug interactions w/ ARVs

No Disclosures

Prevalence of HIV in mentally ill

- Prevalence rates of HIV in mentally ill inpatients & outpatients are reported to be between 3% and 23% (0.4-0.6% in general U.S. pop)*
- ↑ Behavioral risk factors and increased victimization of mentally ill → ↑ risk of infection

Prevalence of mental illness in HIV infected individuals

- **48%** screened positive for psychiatric illness according to National HIV Costs and Service Utilization Study (1,2)
- **Depression: 36%** prevalence in HIV+ [**5-fold** increase in prevalence compared to general U.S. pop] (2)
- **PTSD: 20%** prevalence (3)
- **Generalized Anxiety Disorder: 16%** [**8-fold** increase] (2)
- **Substance Use Disorders: 40%** reported using an illicit drug other than marijuana
- **Drug Dependence: 12%** screened positive during the previous 12 months [**4-6-fold** increase] (1).

1. Bing EG et al 2001

2. HIV Cost and Services Utilization Study. Fact sheet. Agency for Health Care Policy and Research, Rockville, MD. Available at <http://www.ahrq.gov/data/hcsus.htm>

3. Vranceanu AM et al. AIDS Patient Care STDS. 2008 Apr;22(4):313-21.

Screening tools for mental illness in the primary care setting

- **PHQ-9**
- **GAD-7**
- **Primary Care PTSD Screen (PC-PTSD) (1)**
 - In your life, have you ever had any experience that was so frightening, horrible, or upsetting that, in the past month, you:
 - Have had nightmares about it or thought about it when you did not want to?

YES / NO
 - Tried hard not to think about it or went out of your way to avoid situations that reminded you of it?

YES / NO
 - Were constantly on guard, watchful, or easily startled?

YES / NO
 - Felt numb or detached from others, activities, or your surroundings?

YES / NO
 - Current research suggests that the results of the PC-PTSD should be considered "positive" if a patient answers "yes" to any three items

Screening tools for addiction in the primary care setting

A Single-Question Screening Test for Drug Use in Primary Care (1)

- “How many times in the past year have you used an illegal drug or used a prescription medication for nonmedical reasons?”
- 100% sensitive and 73.5% specific for the detection of a drug use disorder.

CAGE-AID: C (cut down) G (guilty)
 A (annoyed) E (eye-opener)

AUDIT

DAST

Adherence and HIV

- Adherence is lowered by
 - Depression and Mental Illness
 - Cognitive impairment (HAND & HAD)
 - Substance use disorders (including alcohol)
- Treatment of mental illness or SUD improves adherence

ARV pharmacology: CYP 450 enzymes

- Protease Inhibitors & NNRTIs
 - Ritonavir
 - Potent inhibitor of 3A4 / 2D6 / 2C9 / 2C19 isoenzymes
 - Increases glucuronidation
 - Amprenavir, Indinavir, Nelfinavir - inhibits 3A4
 - Nevirapine, Efavirenz – inducer of 3A4

Psychopharmacology in HIV: Antidepressants

- SSRIs
 - **Fluoxetine** (Prozac) & **Paroxetine** (Paxil) are **potent inhibitors** of CYP2D6 and thus may increase plasma levels of PIs
 - Competitive inhibition with Ritonavir and can increase each other's plasma levels
 - **Sertraline** (Zoloft), **citalopram** (Celexa), & **escitalopram** (Lexapro) – little effect on PI metabolism
 - **Fluvoxamine** (Luvox): potent inhibitor of 1A2 →
↑ plasma levels of PIs?

Psychopharmacology in HIV: Antidepressants

- SNRIs (venlafaxine & duloxetine) –2D6
 - Metabolism may be inhibited by ritonavir?
- Bupropion: 2B6 metabolism
 - NNRTIs (efavirenz) & PIs (ritonavir, indinavir & saquinavir) induce CYP2B6 →
 - ↓ plasma levels of bupropion
 - PI combination of Lopinavir + Ritonavir induces CYP2B6 & UDP-GT →decreases plasma level of bupropion

Psychopharmacology in HIV: Antidepressants

- TCAs- 3A4 and 2D6 substrates → ↑ plasma levels w/ potent inhibitors (ritonavir)
- Trazodone - 3A4 & 2D6
 - Ritonavir / lopinavir / darunivir / indinavir → ↑ plasma level of trazodone
- Mirtazapine
 - Metabolism inhibited by ritonavir?

Mood stabilizers and HIV

- **Lithium** – renal clearance. Caution w/ tenofovir.
- **Divalproex sodium (Depakote)** - inhibits glucuronidation
↑ zidovudine levels
- **Carbamazepine** - potent inducer of 3A4 →
↓ plasma levels of some PIs
 - Ritonavir potent inhibitor of CYP3A4 → ↑ carbamazepine
 - Efavirenz is inducer → ↓ level of both E&C
- **Lamotrigine**-glucuronidation
 - Lopinavir and ritonavir induce glucuronidation →
↓ lamotrigine plasma levels

Antipsychotics and HIV

- Antipsychotics: **atypical** and **neuroleptics**
- PIs and especially Ritonavir inhibits 3A4 metabolism of **clozapine**, **pimozide**, **chlorpromazine**, **haloperidol**, **risperidone**
→ (↑ levels)
- **Metabolic syndrome w/ atypicals**
- **Tardive Dyskinesia w/ neuroleptics**

Drugs of abuse and ARVs

- **Methadone** – 3A4
 - Efavirenz, nevirapine, nelfinavir, ritonavir and lopinavir-ritonavir induces 3A4 → opiate withdrawal
 - Methadone increases zidovudine levels
 - QT prolongation: be careful when combining methadone w/ antipsychotics, antidepressants and **Ritonavir**.
- **Amphetamines & MDMA** - ↑ levels w/ ritonavir
- **Cocaine** - PIs & NNRTIs may increase plasma levels norcocaine

Anxiety disorders and HIV

- **Antidepressants: SSRIs, SNRIs, TCAs, mirtazapine, trazodone & nefazodone**
- **Buspirone**
- **Gabapentin**
- **Prazosin & clonidine**
- **Beta-blockers**
- **Benzodiazepines**
- **Antipsychotics**

Anxiety disorders and HIV

- Benzodiazepines & sedative-hypnotics
 - **Alprazolam, diazepam, midazolam, triazolam & zolpidem**: 3A4 substrates (**PIs, Ritonavir & NNRTIs** → ↑levels)
 - **Oxazepam, lorazepam, temazepam**: metabolized by **glucuronidation** (ritonavir & nelfinavir increases plasma clearance)
 - **Clonazepam**: 3A4 → ?

Efavirenz

- CNS side effects
 - Depression
 - Suicidal behavior
 - Nervousness
 - Euphoria / mania
 - Insomnia / nightmares
 - Psychosis

Resources for ARV Drug Interactions

- <http://www.madisonclinic.org>
- <http://www.hivinsite.ucsf.edu>
- <http://www.hiv-druginteractions.org>