The Impact of Alcohol and Substance Use on the Prevention and Treatment of HIV/AIDS

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Alcohol Problems among HIV-Infected Persons in USA

- HIV Cost and Services Utilization Study (n=2864)*
  - 8% current hazardous drinkers
- HIV Research Network (14 sites, n=951)†
  - 11% current hazardous drinkers
- Women’s Interagency HIV Study (WIHS, 6 sites, n=2770)‡
  - 14-24% past-year hazardous drinkers (11-year period)
- Veterans Aging Cohort Study (VACS, n=881)**
  - 36% past-year hazardous drinkers (AUDIT ≥ 8)

Alcohol Problems among HIV-Infected Persons Globally

- Cape Town, South Africa – outpatients at HIV clinic (n=465)*
  - 27% past-year hazardous drinkers (AUDIT ≥ 8)
- St. Petersburg, Russia – hospitalized patients (n=201)†
  - 47% alcohol abuse or dependence

Blood Tests to Assess Alcohol Consumption

• Carbohydrate-deficient transferrin (%CDT)
  – Typically elevated after 60g ethanol/day*

• Phosphatidylethanol (PEth)
  – Significantly correlated with ethanol use in last 7 days
  – Does not produce false positives

%CDT and Alcohol Use in HIV-Infected Persons

- HIV-LIVE (n=300)\(^1\)*
  - 36% sensitivity for “heavy” drinking
- Uganda (n=263)\(^\dagger\)
  - 16% sensitivity for those reporting alcohol use in past 30 days
- %CDT is not useful for assessing alcohol use among HIV-infected in clinical care

\(^1\) Boston HIV-LIVE [Longitudinal Interrelationships of Viruses and Ethanol]: 595 HIV-infected adults with current or past alcohol problems, 50% HCV+, 25% female
\(^*\) Ireland, Cheng, Samet, Bridden, Quinn, Saitz. *AIDS Care.* 2011;23:1483-1491.
\(^\dagger\) Hahn, Bwana, Javors, Martin, Emenyonu, Bangsberg. *AIDS Behav.* 2010;14:1265-1268.
PEth and Alcohol Use in HIV-Infected Persons

• Uganda – outpatients at HIV clinic (n=77)*
  – 88% sensitivity, 86% specificity for any alcohol consumption in prior 21 days (assessed daily)
  – PEth did not vary by age, body mass index, CD4 cell count, hepatitis B, ART use

• PEth is likely to have utility in HIV and alcohol research

* Hahn, Dobkin, Mayanja, et al. ACER. 2011. [Epub ahead of print].
IDU and HIV in USA

• In USA, injection drug use (IDU) accounted for*:
  – 8% of new HIV infections (2010)
  – 17% of people living with HIV (2010)

• In Hawaii, IDU accounted for†:
  – 8% of adult HIV/AIDS cases

Drug Use as a Risk Factor for HIV

• IDU
  – Typically heroin
  • Other drugs (e.g. cocaine, amphetamines)
  – Estimated 3 million HIV infected via IDU worldwide*
• HIV prevalence elevated among non-injecting drug users
  – IDU (past 6-month) vs. never injecting, heroin/cocaine users†
    • 13% (CI 12-15%) vs. 12% (CI 9-16%)
      – Addiction treatment center (n=2121)
    • 15% (CI 11-19%) vs. 17% (CI 12-21%)
      – Respondent-driven store-front sampling (n=448)

Global HIV Prevalence Among IDUs

Global HIV Prevalence Among IDUs

HIV Risk Behaviors in Binge Drinkers

• 2008 Behavioral Risk Factor Surveillance System Binge Drinkers
  (41,083 binge drinkers; 240,230 non-binge drinkers)

• HIV Risk Behaviors (past year)
  – IDU
  – Exchange of sex for money/drugs
  – Unprotected anal sex

• HIV risk behaviors higher among binge drinkers: 7.0% vs. 2.9% (OR 1.8, CI 1.58-2.00)

Alcohol Use and Risky Sex

- Meta-analysis (n=27 studies) found unprotected sex among HIV-infected individuals significantly associated with:
  - Alcohol consumption (OR 1.6, CI 1.4-1.9)
  - Problematic drinking (OR 1.7, CI 1.5-2.0)
  - Alcohol use in sexual contexts (OR 2.0, CI 1.6-2.4)

Alcohol Use and Vaginal HIV Detection

- HIV infected women (n=160)

<table>
<thead>
<tr>
<th>Recent Drinking (past 24 hrs.)</th>
<th>≤ 1 drink</th>
<th>≥ 2 drinks</th>
<th>p-value</th>
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<tbody>
<tr>
<td>Vaginal Detectable Virus</td>
<td>27%</td>
<td>40%</td>
<td>&lt;.05</td>
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</table>

- When stratified by ART status, recent drinking effect only observed in those on ART (n=87)

Drug Use and Sex Risk

• Crystal meth among HIV-infected MSM (n=398)*:
  – Greater sex risk- unprotected anal sex with possible serodiscordant partner - past 6 months (OR 2.6, CI 1.4-4.8)

• HIV-infected crack cocaine users, binge vs non-binge users (n=303)†
  – Greater mean # of sex partners - past 6 months (12 vs. 4)
  – More likely never use a condom - past 30 days (OR 2.5, CI 1.1-5.5)

• Sexually active, HIV-infected IDU men (n=469)‡:
  – 32% reported unprotected sex with HIV negative or status unknown main partner – past 3 months

† Harzke, Williams, Bowen. AIDS Behav. 2009;13:1106-1118.
‡ Purcell, Mizuno, Metsch, et al. J of Urban Health. 2006;83:656-668.
Depression

• **HIV-LIVE (n=400)**
  - Alcohol dependence associated with ↑ depressive symptoms (CES-D mean difference 3.49, CI 1.76-5.22)

• **VACS (n=2446; 55% HIV positive)**
  - Depression (PHQ-9 ≥ 9) associated with hazardous and binge drinking (OR 2.53, CI 1.34-4.81)
  - HIV status did not modify alcohol’s impact on depression (not an effect modifier)

• **HERS (n=871)**
  - Moderate drinking (OR 1.93, p<0.01) and heavy drinking (OR 3.94, p<0.01) associated with increased depressive symptoms (↑CES-D), regardless of ART status

Alcohol, Drug Use, and HIV

Addiction Treatment
HIV Treatment & Prevention
HCV Co-Infection
Liver Damage
HIV Disease Progression
Epidemiology
Sex Risk
Depression
Alcohol and HIV Disease Progression

- Macaques (n=16): IV alcohol vs. sucrose
  - higher viral set point (448 vs. 362 copies/mL; $p<0.05$)
  - faster disease progression (374 vs. 900 days; $p<0.05$)

Alcohol and HIV Disease Progression

- Pre-HAART (MACS): no association found*
- Post-HAART:
  - Hopkins\(^{1\dagger}\) (n=1711): alcohol associated with
    - Worse ART adherence (AOR 0.46; CI: 0.34 – 0.63)
    - Less viral suppression (AOR, 0.76; CI:0.57-0.99)
  - HIV-LIVE\(^{\ddagger}\) (n=240): Heavy alcohol use associated with lower CD4 cell count in patients NOT on ART
    - Adjusted mean decrease of 49 cells/µl compared with abstinence (p=0.03)
- Possible mechanism:
  - Immune activation, increase GI bacterial translocation, interaction with ART metabolism\(^{\S}\)

\(^{1}\) >3000 patients, 34% women, 76% African American
IDU and HIV Disease Progression

- Hopkins* (n=1,851): Heroin and cocaine use and risk of opportunistic infections (OIs)

<table>
<thead>
<tr>
<th></th>
<th>OR</th>
<th>95% CI</th>
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<tbody>
<tr>
<td>Nonuser</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Intermittent user, abstinent</td>
<td>1.4</td>
<td>1.0 - 1.9</td>
</tr>
<tr>
<td>Intermittent user, active</td>
<td>2.3</td>
<td>1.5 – 3.0</td>
</tr>
<tr>
<td>Persistent user</td>
<td>2.1</td>
<td>1.4 – 3.1</td>
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Active drug use associated with HIV disease progression

Cocaine and HIV Disease Progression

- HIV-infected drug users (n=222)
- Crack cocaine users (n=110) 2.1 times more likely to have a CD4 ≤ 200 cells/ml
  - Higher HVL
  - Of those on ART, less likely suppress HVL
  - Of those not on ART (n=53), increased RR of CD4 decline < 200 (HR 3.9, CI 1.1-14.9)

Tobacco and HIV Disease Progression

- HIV-LIVE cohort (n=462)
  - No significant association between CD4 or HVL and smoking status
  - True for the range of tobacco use compared to non-smokers

Mortality and Substance Use

- HIV-LIVE (n=595), mortality associated with*:
  - Heroin or cocaine use (HR 2.4, CI 1.1-5.3)
  - Homelessness (HR 2.9, CI 1.3-6.4)
- No association with heavy alcohol use (HR 0.6, CI 0.2-1.4)
- Johns Hopkins HIV Clinical Cohort 1997-2006, (n=1030 women)†
  - Heavy drinking associated with increased mortality (HR 1.4, CI 1.0-1.97)

IDU, HIV, and Mortality

• IDUs have the worst life expectancy among all transmission categories

• IDU life expectancy post-dx in the US (2005):
  – Male: 15.2 years (CI 14.8-15.5)
  – Female : 15.9 years (CI 15.1-16.6)

• IDU life expectancy almost half compared to those with sexual transmission risk

Alcohol Use Associated with Significant Liver Disease in HIV-Infected Persons

• Swiss HIV Cohort: Mono-infected patients (n=3365)*
  – Hazardous alcohol use (>40g/day females; >60g/day males) associated with elevated ALT levels (OR 1.83; CI 1.19-2.80)

• Johns Hopkins HIV Clinical Cohort: Mono-infected patients (n=696)†
  – Hazardous drinking (>14 drinks/wk) associated with significant liver disease – APRI\(^1\) (adjusted RRR: 3.72; 95% CI: 1.40-9.87)

\(^1\) APRI= \frac{\text{AST level / upper limit of normal}}{\text{Platelet count (10}^9/\text{L})} \text{; APRI >1.5 identifies significant liver disease}

Alcohol, Drug Use, and HIV

- Addiction Treatment
- HIV Treatment & Prevention
- HCV Co-Infection
- Liver Damage
- HIV Disease Progression
- Depression
- Epidemiology
- Sex Risk
HCV Prevalence in HIV+ IDUs

Alcohol Use among HIV/HCV-infected Persons

• HIV-LIVE (n=400)
  • Those told about HCV diagnosis were more likely to report
    – Abstinence (AOR 1.60, CI 1.13 - 2.27)
    – Not drinking unhealthy amounts (AOR 1.46, CI 1.01 - 2.11)
• Awareness of HCV diagnosis associated with greater abstinence from alcohol and less unhealthy amounts of drinking

Impact of Alcohol Use on HCV VL

- HIV/HCV co-infected persons on ART (n=44)*
  - Alcohol use (≥ 50 g/day) associated with increases in HCV RNA (>0.6 log$_{10}$ IU/mL; p=0.04)
  - HCV RNA not associated with HCV disease progression
  - However HCV RNA is related to treatment outcomes

Alcohol, Drug Use, and HIV

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- Liver Damage
- HIV Disease Progression
Presenting to Medical Care

- Entry into care in two New England clinics, 1994-1996 (n=189)†
  - 39% delayed medical care for >1 year, 32% >2 years, and 18% >5 years after diagnosis
  - IDU (p<0.001) and history of alcohol problems in men (p=0.03) associated with delay
- Entry into care in 18 states, 2000-2004 (n=3942)‡
  - 28% delayed medical care for > 3 months
  - IDU associated with delay (OR 1.4, CI 1.08-1.82)

‡ Reed, Hanson, McNaghten, et al. AIDS Patient Care STDS. 2009;23:765-773.
IDUs and HIV Treatment Engagement

• Global review of ART coverage for IDUs
  – In the five countries* with the largest IDU HIV epidemics, IDUs make up 67% of HIV cases, but only 25% of those receiving ART
  – Barriers to HIV Treatment Engagement of IDUs
    • Stigmatization of IDUs in health care settings
    • Separation of addiction and HIV care systems
    • Bans on ART in active IDUs
    • No HIV treatment of prisoners

* China, Vietnam, Russia, Ukraine, Malaysia

"The doctor said that I had to deal with one thing first, and then the other. Because I had told her straight that I used drugs. So, she said that I had to quit first and then take care of the rest. But how? ... I'm actually afraid to discuss this issue of how to combine therapy and drugs. I don't even want to ask the doctor... The doctor gave me such a look that I understood I'm kind of not entitled to ever feel good if I use drugs. So I made my conclusions. She made it clear to me that I had to deal with one thing first, then with the other."

- Elena

Alcohol and ART adherence

• Meta-Analysis of 40 studies and over 25,000 participants*
  • Risky or dependent drinkers were less adherent than non-problem drinkers or abstainers (OR 0.5, CI 0.4 -0.6)

• Study of African-Americans about beliefs of alcohol and ART (n=82)†
  – “Alcohol and ART do not mix.” (85%)
  – “I will not take my meds if I have been drinking.” (51%)

IDUs and ART Adherence

• HIV-infected persons (n=578) first prescribed ART between 1996-2000*
  • Classified as current IDU, former IDU, or non drug user
    – Current IDUs were less likely to suppress their HVL compared to non-drug users
    – Former IDUs were NOT less likely suppress HVL compared to non-drug users
• Similar findings in Swiss Cohort between 1997-2006 (n=8669)†

Efforts to Improve ART Adherence

Two RCTs to improve ART adherence among hazardous drinkers with motivational interviewing

- **ADHERE (n=151)**
  - 4 session intervention
  - No significant differences in medication adherence, CD4 count, VL, or alcohol consumption

- **Hazardous drinkers in New York City (n=143)**
  - 8 session intervention
  - Significant differences in VL, CD4 count at 3 months, but not 6 months

Interventions to Improve ART Adherence in Drug Users

• RCT of directly observed ART (DOT) in substance users (n=87):
  – Greater HVL suppression (OR 2.2, CI 1.0-4.7)
  – Estimated CD4 count improvement of 45 cells/µL (CI 5 - 85, p=0.03)

Alcohol, Drug Use, and HIV

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- Liver Damage
- Depression
- Sex Risk
- HIV Disease Progression
- Epidemiology
Behavior Change After Testing HIV Positive

• HIV Cost and Services Utilization Study (HCSUS) sample of HIV-infected persons in medical care in 1996 (n=2864)*
  – 80% of substance users quit or cut down drug use since diagnosis
  – Persons with CD4 counts <50 at some point were also more likely to quit or reduce substance use

• IDUs in the Ukraine (n=1798), after testing positive for HIV:†
  – Less unprotected sex (OR 0.6, CI 0.4-0.7)

Needle Exchange Program (NEP)

- Review of 42 studies from 1989-1999 among IDUs*
  - Decrease in HIV risk behavior
  - Decrease in HIV seroconversion

- Review of 7 international studies from 1991-2001†
  - Cost-effective
  - Feasible to implement internationally
  - Applicable to special populations

Availability of Syringe Distribution and Exchange

- Great Britain and Australia have some of the lowest HIV prevalence rates among IDUs (~2%* and ~1%†)
- Reflects early adoption of harm reduction measures (c. 1986)†
  - Needle exchange programs
  - Opioid agonist treatment

Addiction Pharmacotherapy

• Heroin*
  – Methadone
  – Buprenorphine

• Alcohol*
  – Naltrexone
  – Acamprosate
  – Disulfiram

• Cocaine = investigational†
  – Modafinil
  – GABA-ergic compounds (e.g. vigabatrin, topiramate)
  – Disulfiram
  – Vaccine (TA-CD)

Addressing Addiction in HIV Care

- HIV-infected adults (n=951) receiving care at 14 sites*
  - 71% using substances; 24% receiving substance use treatment
  - Less than half reported discussing substance use issues with HIV care provider

- Need for providers to address substance use problems

- Audio-tapes of physician-patient encounters (n=413)†

- Quality of patient-provider communication
  - Good for illicit drug users
  - Worse for those with unhealthy alcohol use (shorter visit length, fewer activating/engaging and psychosocial counseling statements)

Opioid Agonist Therapy (OAT) & HIV Outcomes

• HIV-infected Vancouver IDUs on ART, 1996-2003 (n=278)*
  – Methadone OAT associated with
    • Good adherence (OR 1.5; 95% CI 1.2-2.0)
    • HIV RNA suppression (OR 1.3, CI 1.0-1.8)
    • CD4 cell count rise (OR 1.6, CI 1.3-2.0)

• Prospective cohort of ART-naïve, HIV-infected IDUs in Vancouver, 1996-2008 (n=231)†
  – Methadone OAT associated with
    • Earlier ART initiation (RH 1.6, CI 1.2-2.3)

Integrated OAT & DOT

• RCT compared directly observed ART (DOT) to standard of care
• 12 methadone OAT clinics in the Bronx (n=77); 24-week follow-up
• DOT group at 24 weeks
  – Better adherence (86% vs. 56%, p<0.0001)
  – More likely to have undetectable viral load (OR 3.1, CI 1.1-5.4)

Buprenorphine OAT

• Advantage of buprenorphine OAT*
  – Efficacy and retention comparable to methadone
  – Milder withdrawal symptoms
  – Very low risk of overdose
  – Decreased risk of abuse and diversion with buprenorphine/naloxone (bup/nal)

• Can be delivered in the office through a collaborative nurse care-manager model†

Buprenorphine OAT

- Longitudinal analysis of HIV+ patients on bup/nal (n=166)
  - bup/nal associated with significant reductions in HIV sex and drug-related risk behaviors from baseline to 12 and 24 weeks

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<th>12 wks.</th>
<th>24 wks.</th>
<th>P value</th>
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<tbody>
<tr>
<td>IDU in past 3 months</td>
<td>37%</td>
<td>12%</td>
<td>7%</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Sex while “high”</td>
<td>64%</td>
<td>13%</td>
<td>15%</td>
<td>&lt; 0.001</td>
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</table>

Drug Interactions: ART Impacts Addiction Pharmacotherapy

- IDUs receiving ART and OAT (n=120)
  - Median methadone dose increase:
    - 20 mg/d (p<0.001) with nevirapine
    - 7.5 mg/d (p=0.004) with efavirenz
  - No significant increase required for patients on ritonavir-boosted lopinavir

Drug Interactions: Addiction Pharmacotherapy Impacts ART

- Methadone increases serum zidovudine levels by 40%, but question if clinically relevant*
  - No such interaction observed with buprenorphine

- Buprenorphine had no effect on early and newer protease inhibitors (early PIs n=30)† (newer PIs n=21)‡

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Alcohol, Drug Use, and HIV
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- Michael Holick, PhD, MPH
- Meg Sullivan, MD
- David Fiellin, MD
Acknowledgements

Special thanks to Marlene Alcorn for her assistance with this presentation.