Unhealthy alcohol use among Persons with HIV: A modifiable barrier to optimal management of HIV and its comorbidities

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Disclosures

Dr. Chander currently receives funding from NIAAA, NIDA and NCI

Dr. Chander is a member of the Health and Human Services (HHS) Panel on Adult and Adolescent Antiretroviral Treatment Guidelines for HIV
Objectives

• Describe the role of unhealthy alcohol use in HIV disease treatment outcomes

• Describe approaches to screening for unhealthy alcohol use in HIV clinical settings

• Describe alcohol treatment strategies that can be integrated into HIV clinical care
Overview

• Unhealthy alcohol use and the HIV care continuum
• Unhealthy alcohol use and other comorbidities among PWH
• Provider barriers and facilitators to alcohol identification and treatment of unhealthy alcohol use in HIV care setting
• Screening and interventions for unhealthy alcohol use among PWH
When do you personally screen for alcohol use in your practice?

• At initial clinical visit only
• At annual visits
• At every visit
How often do you ask your patients about alcohol use when they have viral rebound?

- Almost always
- Often
- Sometimes
- Seldom
- Never
How often do you prescribe medications for alcohol use disorder (MAUD) when diagnose an individual with AUD (no history of withdrawal) in your clinic?

- Almost always
- Often
- Sometimes
- Seldom
- Never
Clinical Case


• PMH: Alcohol use disorder, 1 pint of Vodka 4 days per week, weekend injection cocaine; HCV; Tobacco

• Labs: CD4 138 cells/mm3, VL 44,000 Genotypes all WT

• Subsequent Course post 2011: Detoxification x2, continued alcohol use; 4 months later, 28 day residential program
Spectrum of unhealthy alcohol use

At-Risk Alcohol Use:
- Men < 65 years old: >4 drinks/occasion; >14 drinks/week
- Women and Men >65 years old: >3 drinks/occasion; >7 drinks/week

Unhealthy Alcohol Use: HIV – 27%

Saitz NEJM 2005; Crane AIDS Behav 2017
Unhealthy alcohol use

HIV CARE CONTINUUM

- DIAGNOSED WITH HIV
- LINKED TO CARE
- ENGAGED OR RETAINED IN CARE
- PRESCRIBED ANTIRETROVIRAL THERAPY
- ACHIEVED VIRAL SUPPRESSION

The series of steps a person with HIV takes from initial diagnosis through their successful treatment with HIV medication.

Images from UW National HIV Curriculum https://www.hiv.uw.edu/go/basic-primary-care/retention-care/core-concept/all
Alcohol and HIV acquisition and transmission

- Alive Cohort

- Prospective study of 1525 people with injection drug use, 28% women

- 34% consumed >21 drinks per week; 13% consumed >50 drinks per week

- 21-140 drinks per week increased risk of HIV (HR: 1.83: 1.07-3.12)

A prospective study of alcohol consumption and HIV acquisition among injection drug users.
Howe, Chanelle; Cole, Stephen; Ostrow, David; Mehta, Shruti; Kirk, Gregory. AIDS. 25(2):221-228, January 14, 2011
Alcohol and HIV risk in the BCHD STI Clinic

- 671 STI attendees tested for GC and underwent ACASI querying substance use and sexual risk behavior

- 21% reported sex while under the influence of alcohol

- 30% of women reported heavy episodic (binge) drinking compared to 42% of men

- Women with HED engaged in anal sex at twice the rate of women without HED and 3X the rate of women who abstained

- Multiple sex partners 2x greater among women with HED

- Gonorrhea 5x higher among women with HED compared to those with no alcohol use

Does alcohol use have a causal effect on HIV incidence and disease progression? A review of the literature and a modeling strategy for quantifying the effect

Jürgen Rehm1,2,3,A,5,6, Charlotte Probst1,4*, Kevin D. Shield1,7 and Paul A. Shuper1,6

Acute Alcohol Consumption Directly Increases HIV Transmission Risk: A Randomized Controlled Experiment

Shuper, Paul A. PhD4,1; Joharchi, Narges MSc1; Monti, Peter M. PhD2; Loutfy, Mona MD, FRCPC, MPH5,1,11; Rehm, Jürgen PhD4,*,4,7,11,‖ Author Information ‡

doi: 10.1097/QAI.0000000000001549
Unhealthy alcohol use and HIV Care continuum

Sample: VACS N=33,224

HIV care metrics assessed in year following AUDIT-C:
- Engaged in care - by CD4 or HIV viral load test
- Treatment with ART – at least one filled prescription
- Viral suppression - <500 copies/mL based on first lab after AUDIT-C

*Adjusted for race, ethnicity, gender, fiscal year of AUDIT-C screening, age, and any mental health and non-alcohol substance use disorders
## Alcohol use, Antiretroviral therapy, adherence and viral suppression

<table>
<thead>
<tr>
<th>Category</th>
<th>ART†</th>
<th>Adherence‡</th>
<th>Virological Suppression‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug use - Alcohol</td>
<td>1.0 (Reference)</td>
<td>1.0 (Reference)</td>
<td>1.0 (Reference)</td>
</tr>
<tr>
<td>Drug use + Moderate alcohol</td>
<td>1.14 (0.95–1.37)</td>
<td>0.77 (0.62–0.98)</td>
<td>1.00 (0.84–1.20)</td>
</tr>
<tr>
<td>Drug use + Hazardous alcohol</td>
<td>0.57 (0.42–0.77)</td>
<td>0.36 (0.25–0.53)</td>
<td>0.72 (0.52–0.99)</td>
</tr>
<tr>
<td>Drug use - Alcohol</td>
<td>0.54 (0.43–0.68)</td>
<td>0.50 (0.37–0.68)</td>
<td>0.60 (0.46–0.78)</td>
</tr>
<tr>
<td>Drug use + Moderate alcohol</td>
<td>0.68 (0.54–0.88)</td>
<td>0.40 (0.30–0.54)</td>
<td>0.64 (0.50–0.82)</td>
</tr>
<tr>
<td>Drug use + Hazardous alcohol</td>
<td>0.40 (0.29–0.57)</td>
<td>0.32 (0.20–0.51)</td>
<td>0.50 (0.32–0.76)</td>
</tr>
</tbody>
</table>

*Adjusted for age, sex, race, CD4 nadir, and time enrolled (days).
†Sample includes individuals either on antiretroviral therapy or with a CD4 cell count ≤350.
‡Adjusted for age, sex, race, CD4 nadir, and years on ART (days).
Meta-Analysis of Studies of Alcohol use and Adherence

Alcohol Use and Antiretroviral Adherence: Review and Meta-Analysis.
Hendershot, Christian; Stoner, Susan; Pantalone, David; Simoni, Jane

DOI: 10.1097/QAI.0b013e3181b18b6e

Forest plot indicating the effect size contributed by each study, using the most extreme comparison per study. Drinking intensity: 0 = global (eg, any use vs. none); 1 = moderate drinking (that did not exceed the NIAAA definition of at-risk drinking or constitute an alcohol use disorder) vs. nonuse; 2 = problem drinking (that met the NIAAA definition for at-risk drinking or criteria for an alcohol use disorder) vs. nonproblem use/nonuse.
Retention in care

- CFAR Network of Integrated Clinical Systems (CNICS)
  - Collaborative network of 8 CFAR HIV clinical sites (Hopkins, UAB, UCSF, UW, UNC, Fenway, UCSD, Case)
  - Independent NIH R24 funding

- Diverse Cohort
  - Racially and geographically diverse
    - 38% AA; 12% Hispanic/Latinx Ethnicity
  - sex and age representative clinical cohort
    - 19% female

- Clinical, socio-behavioral and specimen data systematically captured
- Comprehensive patient self-reported outcomes 9694 PLWH across 7 sites, 23,225 observations June 2011-2014
- Institute of Medicine (IOM) retention: 2 visits within 1 year at least 90 days apart
- Alcohol use was measured with AUDIT-C, generating drinking category (never, moderate, heavy); Drug use via ASSIST
- 82% male, 46% white, 35% black, and 14% Hispanic/Latino. 37% of participants reported never drinking, 38% moderate, and 25% heavy, and 89% of the patients were retained (IOM retention measure).
Unhealthy alcohol use and retention in care

**TABLE 2. Association Between Alcohol and Retention***

<table>
<thead>
<tr>
<th>Drinking Category</th>
<th>IOM Retention Measure</th>
<th>Visit Adherence Measure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td>Never</td>
<td>Ref</td>
<td>Ref</td>
</tr>
<tr>
<td>Moderate</td>
<td>0.93 (0.83 to 1.03)</td>
<td>0.97 (0.91 to 1.04)</td>
</tr>
<tr>
<td>Heavy†</td>
<td>0.78 (0.69 to 0.88)‡</td>
<td></td>
</tr>
</tbody>
</table>

Binge frequency category

<table>
<thead>
<tr>
<th>Drinking category</th>
<th>IOM Retention Measure</th>
<th>Visit Adherence Measure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td>Never</td>
<td>Ref</td>
<td>Ref</td>
</tr>
<tr>
<td>Monthly/less than monthly</td>
<td>0.89 (0.80 to 0.99)§</td>
<td>0.98 (0.93 to 1.03)</td>
</tr>
<tr>
<td>Daily/weekly</td>
<td>0.90 (0.74 to 1.10)</td>
<td>0.90 (0.82 to 0.98)§</td>
</tr>
</tbody>
</table>

Current drug use

<table>
<thead>
<tr>
<th>Drinking category</th>
<th>IOM Retention Measure</th>
<th>Visit Adherence Measure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td>Yes (vs. no)</td>
<td>0.88 (0.77 to 1.00)</td>
<td>0.74 (0.69 to 0.79)‡</td>
</tr>
</tbody>
</table>

Panic symptoms

<table>
<thead>
<tr>
<th>Drinking category</th>
<th>IOM Retention Measure</th>
<th>Visit Adherence Measure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td>None</td>
<td>Ref</td>
<td>Ref</td>
</tr>
<tr>
<td>Some</td>
<td>0.94 (0.83 to 1.08)</td>
<td>0.96 (0.91 to 1.02)</td>
</tr>
<tr>
<td>Panic disorder</td>
<td>0.92 (0.80 to 1.07)</td>
<td>0.85 (0.80 to 0.90)‡</td>
</tr>
</tbody>
</table>

Depression screen

<table>
<thead>
<tr>
<th>Drinking category</th>
<th>IOM Retention Measure</th>
<th>Visit Adherence Measure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td>Positive (vs. negative)</td>
<td>1.15 (1.02 to 1.30)§</td>
<td>0.92 (0.88 to 0.97)§</td>
</tr>
</tbody>
</table>

*Four different models were fit for each retention measure and drinking exposure type reported. Each model was adjusted for age, race, sex/sexual risk factor, CD4 category, viral load category, enrollment date, site, intravenous drug use as HIV risk factor.

†Heavy = AUDIT-C >3 for women or >4 for men.
‡P < 0.0001.
§P < 0.05.

PWH with heavy alcohol use 22% less likely to be retained in care; individuals with binge/heavy episodic drinking 10% less likely to be retained in care (IOM definition)
Any alcohol use: (OR: 1.63 (1.39-1.91) and alcohol consumption in sexual contexts OR: 1.98 (1.63-2.39) associated with condomless sex
Unhealthy alcohol use, comorbidities and other health outcomes among PWH
• Veterans Aging Cohort Study

• N=3565; 701 HIV/HCV; 1410 HIV; 296 HCV; 1158 neither HIV/HCV

• Outcome: Advanced hepatic fibrosis defined as Fib-4 >3.25

• Exposure: (1) Alcohol related diagnosis: ICD-9 diagnosis for alcohol dependence/abuse recorded between 12 months before and 6 months after enrollment; (2) unhealthy alcohol use: AUDIT-C score ≥4 or consumption of ≥6 drinks on any 1 occasion in the past year; and (3) moderate alcohol use defined as an AUDIT-C score <4

Odds of Advanced Hepatic Fibrosis for alcohol use category and by HIV and HCV Status
Overall and liver related mortality by self-reported and provider documented alcohol use among PLWH

- Prospective Cohort Study 1855 PLWH in Baltimore, MD 2000-2013
- Alcohol use ascertained by self-report and provider documentation of heavy/hazardous use
- Cox proportional hazard models, competing risks
- 81% African American, 34% IDU Risk Factor, 20% MSM; 37% female, 44% HCV+
- Provider documentation Heavy drinking 19%, Past heavy 16%
- 304 deaths, 43 deaths/1000 py
- Lowest among moderate drinkers with no history of heavy drinking (reference group)
- None, moderate, hazardous drinkers with provider documented heavy drinking had nearly twice the mortality of moderate without any heavy drinking
Liver related mortality among PWH

Canan C, Lau B, McCaul ME, Keruly J, Moore RD, Chander G. Effect of Alcohol Consumption on All-Cause and Liver-Related Mortality among HIV-infected individuals. HIV Medicine
Alcohol and Mortality among U.S. Veterans with and without HIV

- Veterans Aging Cohort Study
- 18,145 PLWH; 42,228 without HIV
- Alcohol Use Measures by AUDIT-C, total drinks per month and heavy episodic drinking

Main Result:
- HIV+: AUDIT-C score ≥4 (hazard ratio [HR] 1.25, 95% CI 1.09-1.44) and ≥30 drinks per month (HR, 1.30, 95% CI 1.14-1.50) were associated with increased risk of mortality
- HIV-: AUDIT-C score ≥5 (HR, 1.19, 95% CI 1.07-1.32) and ≥70 drinks per month (HR 1.13, 95% CI 1.00-1.28) were associated with increased risk

Other alcohol related comorbidities among PWH

- Alcohol use and depression and other mental health disorder including trauma, anxiety
- Alcohol and other substance use (methamphetamine, cocaine, marijuana, etc)
- Alcohol use and tobacco
- Alcohol use and diabetes, hypertension, CVD
- Alcohol use and cognition
- Alcohol use and cancer
Overview

• Unhealthy alcohol use and the HIV care continuum
• Unhealthy alcohol use and other comorbidities among PWH
• Provider barriers and facilitators to alcohol identification and treatment of unhealthy alcohol use in HIV care setting
• Screening and interventions for unhealthy alcohol use among PWH
Integration of evidence-based alcohol treatment into clinical settings

- Among PWH, unhealthy alcohol use and **alcohol use disorders (AUD)** are associated with lower utilization of medical treatment, poorer medication adherence and HIV transmission risk behaviors, liver disease progression and mortality.

- Implementation of **evidence-based alcohol treatment strategies** in this population is critically needed.

- Most people in need of alcohol treatment do not access subspecialty services (SAMHSA)
  - Not ready to stop, cannot afford, negative impact on job, unsure of where to go, stigma

- Given potential barriers to accessing traditional alcohol treatment services, integration of alcohol reduction strategies into HIV care and other clinical settings may increase treatment access and improve HIV outcomes
  - **Teachable moment**: Over time about half of people with heavy alcohol use quit without formal treatment and 65% attribute this to physical health problem
Barriers to integrating alcohol reduction interventions in HIV clinical settings

• Provider level
  - Lack of time
  - Lack of knowledge
  - Lack of confidence

• Patient level
  - Reluctance to disclose alcohol use to providers

• System level
  - Clinic flow
  - Ancillary support
HIV primary care providers—Screening, knowledge, attitudes and behaviors related to alcohol interventions

A: Alcohol Screening Practices: In new patients how often do you:

- Ask whether they drink alcohol?
- Ask how much they drink on a drinking day?
- Ask how frequently they drink?
- Use a formal screening tool such as the CAGE or AUDIT?

Never/Rarely  | Sometimes  | Usually  | Always
---|---|---|---
B: Alcohol Counseling Practices

In patients who drink, but do not have alcohol problems, how often do you advise safe drinking limits?

In hazardous drinkers, how often do you advise them to abstain?

In hazardous drinkers, how often do you advise them to cut-down?

- Never/Rarely
- Sometimes
- Usually
- Always

C: Alcohol Treatment Practices: In alcohol dependent patients, how often do you:

- Advise them to abstain?
- Advise them to cut-down?
- Refer them for treatment?
- Treat them yourself without specialty consultation or referral?

- Never/Rarely
- Sometimes
- Usually
- Always
Provider Barriers to the Use of Alcohol Pharmacotherapy

- Inadequate research on medication efficacy
- Insufficient training on use of pharmacotherapy
- Worries of offending patients
- Lack of insurance coverage for medications

Legend:
- Not a barrier
- Minor barrier
- Moderate barrier
- Major/Very major barrier
Management of Alcohol Use in HIV clinical settings

- None/Never exceeds limit
- At-risk/Hazardous
- Mild AUD
- Moderate AUD
- Severe AUD

- Screen annually
- Brief Intervention: Pharmacotherapy; Behavioral Treatment, Alcohol Treatment Program, Psychiatric Care

Approach to Screening for Alcohol Use

• Who should we screen?
  - All individuals presenting to care
  - Screen at baseline, and if negative, repeat at least annually, if positive, at every visit
  - New viremia, viral rebound
  - Transaminitis
  - High blood sugar
  - Trauma, accidents
  - Depression
  - Tobacco

• What should we use?
  - Alcohol: National Institute on Alcohol Abuse and Alcoholism recommends single question
    - How often in the last year have you had 4 or more drinks (women) or 5 or more drinks (men);¹
    - if ≥1, follow-up with quantity/frequency questions;
    - Alcohol Use Disorders Test-Consumption (AUDIT-C) Clarify that alcohol includes beer, wine, liquor

AUDIT-C (Alcohol Use Disorders Identification Test-Consumption)

**Question 1:** How often do you have a drink containing alcohol?
- (0) Never
- (1) Monthly or less
- (2) 2 to 4 times a month
- (3) 2 to 3 times a week
- (4) 4 or more times a week

**Question 2:** How many drinks containing alcohol do you have on a typical day when you are drinking?
- (0) 1 or 2
- (1) 3 or 4
- (2) 5 or 6
- (3) 7, 8, or 9
- (4) 10 or more

**Question 3:** How often do you have 4 or more (women) 5 or more (men) drinks on one occasion?
- (0) Never
- (1) Less than monthly
- (2) Monthly
- (3) Weekly
- (4) Daily or almost daily

**A positive test is >3 in women, >4 in men**
How do we measure drinking?
A standard drink

1 ½ ounces of hard liquor, 80 proof vodka, rum, whiskey
5 ounce glass of wine, 12% alcohol, red or white
12 ounce can/bottle of beer, 5% alcohol
Standard drink conversion
Challenges to provider administered assessment

- Lower sensitivity in identifying unhealthy alcohol use in clinical settings
  - Non Verbatim Screening
  - Inferences or assumptions about responses,
  - Staff introduced and adapted screening questions to enhance patient comfort.
  - Patient reluctance to disclose
- Overcoming challenges
  - Screening questionnaires, self-administered
- Computer delivered screening
  - standardized, validated screening instruments
  - proactive and universal screening at medical visits ensures that all patients assessed without regard to provider expectations of use
  - computerized assessments shown to increase likelihood of disclosure of drug use
Management of Alcohol Use in HIV clinical settings

- None/Never exceeds limit
- At-risk/Hazardous
- Mild AUD
- Moderate AUD
- Severe AUD

Screen annually

Brief Intervention
Pharmacotherapy; Behavioral Treatment, Alcohol Treatment Program, Psychiatric Care

Brief alcohol intervention

- Recommended by the USPTF for persons with unhealthy alcohol use
- Generally consists of 4 or fewer sessions, and is often 1
  - typically lasted 5 – 15 minutes;
  - included normative feedback and advice to cut-down or stop drinking;
  - in the context of recommended limits and health context
  - provided patients with written material to reinforce the intervention.
- Can consist of components of motivational interviewing, addressing ambivalence, and elements of CBT with goal settings and coping strategies
- Evidence suggests that follow-up visits further enhance outcomes
- 2018 review of BI for unhealthy alcohol use demonstrated reduced number of drinks per week among persons receiving BI versus control, with 14% more participants drinking below limits
- BI not generally effective in persons with alcohol use disorder
Brief alcohol intervention

- **Ask**: Screen for alcohol use in all patients
- **Assess**: Assess for risk/consequences
  - Family history, legal, medical or social consequences, alcohol dependence
- **Advise**: Provide feedback on drinking and medical, social, or behavioral consequences; make recommendation for cutting down/ quitting
Brief Intervention for women with HIV

- Aim: To compare the efficacy of brief intervention to treatment as usual for HIV+ women with unhealthy alcohol use

- Overview: Randomized trial in urban HIV clinic, n=148

- Women with HIV included if exceeded NIAAA weekly or daily limits; few exclusions

- Brief intervention: 20 minute face-to-face sessions, one month apart; tailored to women in Baltimore
  - First session included: 1) patient health assessment and feedback; 2) goal setting and contracting 3) drinking diary and homework
  - Second session: drinking diary cards, drinking agreement and take home exercises, barriers and facilitators to change
  - Content tailored for HIV-positive women
  - Follow-up telephone booster calls

- Assessments: 3, 6 and 12 months

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control (N=74)</th>
<th>Intervention (N=74)</th>
</tr>
</thead>
<tbody>
<tr>
<td>African American</td>
<td>81.1%</td>
<td>90.5%</td>
</tr>
<tr>
<td>Income</td>
<td>$8,189 (7239)</td>
<td>$8,497 (7166)</td>
</tr>
<tr>
<td>Undetectable HIV1-RNA (&lt;50 copies)</td>
<td>41.9%</td>
<td>40.3%</td>
</tr>
<tr>
<td>CD4 count (cells/mm) (Mean, SD)</td>
<td>393 (237)</td>
<td>398 (269)</td>
</tr>
<tr>
<td>Total number of drinking days (90day) (Mean, SD)</td>
<td>30.45 (27.57)</td>
<td>34.03 (29.47)</td>
</tr>
<tr>
<td>Total number binge drinking days (90day) (Mean, SD)</td>
<td>26.71 (28.55)</td>
<td>24.91 (26.99)</td>
</tr>
<tr>
<td># of Drinks per episode (Mean, SD)</td>
<td>9.55 (6.42)</td>
<td>9.69 (9.13)</td>
</tr>
<tr>
<td>Illegal drug in past 6 mos</td>
<td>29.7%</td>
<td>27.0%</td>
</tr>
<tr>
<td>On ART</td>
<td>67.6%</td>
<td>73.0%</td>
</tr>
<tr>
<td>HCV</td>
<td>59.5%</td>
<td>51.4%</td>
</tr>
</tbody>
</table>

Chander, Hutton et al JAIDS 2015
RCT results

90-day drinking frequency decreased among intervention group compared to control, with women in the intervention condition significantly less likely to have a drinking day (OR: 0.42 (95% CI: 0.23-0.75) (p=0.005) Chander et al. JAIDS 2015
Alcohol Outcomes:
Intervention effect on drinking frequency

- 90-day drinking frequency decreased among intervention group compared to control, with women in the intervention condition significantly less likely to have a drinking day (OR: 0.42 (95% CI: 0.23-0.75) (p=0.005)

- 90-day frequency of binge use of alcohol decreased in intervention compared to control group among women binge drinking between the 10th-95th percentile range

- 90-day quantity of drinks per drinking/day, and HIV and alcohol biomarkers not significant
### Other outcomes: HIV viral suppression <50 copies

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>41.9%</td>
<td>40.3%</td>
</tr>
<tr>
<td>3 months</td>
<td>43.9%</td>
<td>59.3%</td>
</tr>
<tr>
<td>6 months</td>
<td>46.8%</td>
<td>50%</td>
</tr>
<tr>
<td>12 months</td>
<td>42.2%</td>
<td>49.2%</td>
</tr>
</tbody>
</table>
Intervention effect on condomless vaginal sex

- Adjusting for baseline # days of condomless sex:
  - intervention group showed a 61.4% reduction in the odds of having condomless vaginal sex compared with the usual care group (AOR=0.386 with 95% CI (0.156, 0.952), P=0.041)

- Analysis restricted to sexually active:
  - the intervention showed 60.3% reduction in the odds of having condomless vaginal sex on a day. The association was marginally significant (AOR= 0.397 with 95% CI (0.153, 1.028), P=0.055), likely as a result of reduced power.
Project ReACH
Reducing Alcohol related Comorbidities in HIV treatment

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Effect Size [95% Confidence Interval]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average number of drinks per week</td>
<td></td>
</tr>
<tr>
<td>3 months</td>
<td>-4.02 [-8.18, 0.14]</td>
</tr>
<tr>
<td>6 months</td>
<td>-8.72 [-12.69, -4.76]</td>
</tr>
<tr>
<td>12 months</td>
<td>-5.98 [-9.77, -2.19]</td>
</tr>
<tr>
<td>Number of heavy drinking days (&gt;5 drinks per day/month)</td>
<td></td>
</tr>
<tr>
<td>3 months</td>
<td>0.84 [0.61, 1.14]</td>
</tr>
<tr>
<td>6 months</td>
<td>0.55 [0.38, 0.79]</td>
</tr>
<tr>
<td>12 months</td>
<td>0.50 [0.33, 0.78]</td>
</tr>
</tbody>
</table>

### Setting: FQHC in Boston
### Intervention:
- 60 minute session with personalized feedback
- 2 brief phone sessions
- Follow-up booster sessions 10-20 minute at 3, 6 months

Kahler J Consul Clin Psych 2018
Health Call--Reducing heavy drinking in HIV primary care: a randomized trial of brief intervention, with and without technological enhancement

258 Randomized to three arms
-Education, MI, MI+ HealthCall
Outcome=Mean drinks per drinking day
Management of Alcohol Use in HIV clinical settings

When BI doesn’t work, then what?

- Evidence suggests that BI may not reduce drinking in patients with more serious drinking problems.
- As in management of other health problems, medications may offer the next level of intervention.
- Managing the care of patients who take alcohol medications is similar to other disease management strategies.
- Models from depression and smoking and opioid use disorder
Rationale for Pharmacotherapy

- Alcohol use disorders are a chronic condition
- Medications can target neurotransmitters involved in the reinforcing and anxiolytic effects of alcohol use
- Beneficial in combination with non-pharmacologic therapy, including counseling and other behavioral therapies
- Can reduce relapse and help maintain abstinence
Alcohol Reward Pathway
<table>
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<tr>
<th>Medication</th>
<th>Dosage</th>
<th>Pharmacologic Target</th>
<th>Possible Use in Alcohol Use Disorder Patients with Alcoholic Liver Disease?</th>
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<td><strong>FDA-Approved Medications for Alcohol Use Disorder</strong></td>
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<tr>
<td>Acamprosate</td>
<td>666 mg TID</td>
<td>Possibly NMDA receptor agonist</td>
<td>Yes (no hepatic metabolism)</td>
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<tr>
<td>Disulfiram</td>
<td>250-500 mg QD</td>
<td>Inhibition of acetaldehyde dehydrogenase</td>
<td>No (hepatic metabolism; cases of liver toxicity have been reported)</td>
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<td>Naltrexone* PO or IM</td>
<td>PO: 50 mg QD</td>
<td>Mu opiate receptor antagonist</td>
<td>With caution (perceptions of liver toxicity limit use in advanced alcoholic liver disease)</td>
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<td>IM: 380 mg monthly</td>
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<td><strong>Not FDA-Approved Medications Tested for Alcohol Use Disorder</strong></td>
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<tr>
<td>Baclofen</td>
<td>10 mg TID; 80 mg QD max</td>
<td>GABA&lt;sub&gt;6&lt;/sub&gt; receptor agonist</td>
<td>Yes (minimal hepatic metabolism)</td>
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<td>Baclofen has been formally tested in clinical studies with alcohol use disorder patients with liver cirrhosis</td>
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<td>Gabapentin</td>
<td>900-1800 mg QD</td>
<td>Unclear: modulates GABA transmission</td>
<td>Yes (no hepatic metabolism)</td>
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<td>Ondansetron</td>
<td>1-16 μg/kg BID</td>
<td>5HT&lt;sub&gt;3&lt;/sub&gt; antagonist</td>
<td>Yes, but with caution because liver toxicity has been reported, albeit relationship to ondansetron administration is not determined</td>
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<td>Topiramate</td>
<td>300 mg QD</td>
<td>Anticonvulsant multiple targets: −glutamate/+GABA</td>
<td>Yes (partial hepatic metabolism mostly by glucoronidation)</td>
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<td>In patients with hepatic encephalopathy, use with caution: topiramate-related cognitive side-effects may confound the clinical course and treatment of hepatic encephalopathy</td>
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<td>Varenicline</td>
<td>2 mg QD</td>
<td>Nicotinic acetylcholine receptor partial agonist</td>
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Naltrexone for alcohol use disorder

Naltrexone (100 mg/d oral)

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<th>Low</th>
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Naltrexone (50 mg/d oral)

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Jonas JAMA 2014;
Extended-release Naltrexone Improves Viral Suppression Among Incarcerated Persons Living with HIV and Alcohol use Disorders Transitioning to the Community: Results From a Double-Blind, Placebo-Controlled Trial

Springer, Sandra A. MD; Di Paola, Angela M; Barbour, Russell PhD; Azar, Marwan M. MD; Altice, Frederick L. MD

Author Information

JAIDS Journal of Acquired Immune Deficiency Syndromes: September 1, 2018 - Volume 79 - Issue 1 - p 92-100

ALCOHOLISM

Hepatic Safety and Antiretroviral Effectiveness in HIV-Infected Patients Receiving Naltrexone

Jeanette M. Tetrault, Janet P. Tate, Kathleen A. McGinnis, Joseph L. Goulet, Lynn E. Sullivan, Kendall Bryant, Amy C. Justice, David A. Fiellin. For the Veterans Aging Cohort Study Team


Original Paper | Published: 02 August 2018

Efficacy of Extended-Release Naltrexone on HIV-Related and Drinking Outcomes Among HIV-Positive Patients: A Randomized-Controlled Trial

E. Jennifer Edelman, Brent A. Moore, Stephen R. Holt, Nathan Hansen, Tassos C. Kyriakides, Michael Virata, Sheldon T. Brown, Amy C. Justice, Kendall J. Bryant, David A. Fiellin, Lynn E. Fiellin
Prescribing Naltrexone

- Main contraindication: opiates
- Main side effects: nausea, dizziness
- Monitor LFTs post medication initiation
- No known drug interactions with antiretroviral therapy

Naltrexone 12.5 mg/d --> 25 mg/d --> 50 mg/d (100 mg) or 380 mg IM per month
Acamprosate

- Glutamate and GABA transmitter systems; increases duration of abstinence among alcohol-dependent individuals
- Moderate efficacy in European trials, but not replicated in U.S. studies
- Meta-analysis; 24 RCTs, 6915 patients
- Outcomes (Acamprosate vs. Placebo)
  - Reduced risk of any drinking:
    - RR: 0.86 (95% CI: 0.81-0.91)
  - Increased cumulative abstinence duration

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<th>Duration, wk</th>
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<th>Treatment Group</th>
<th>Control Group</th>
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</table>
Prescribing Acamprosate

• Main contraindication: renal insufficiency

• Main side effect: diarrhea

• No known drug interactions with antiretroviral therapy

Acamprosate 666 mg tid
Integrating alcohol treatment into HIV clinical settings

- None/Never exceeds limit
- At-risk/Hazardous
- Mild AUD
- Moderate AUD
- Severe AUD

- Screen annually
- Brief Intervention
- Pharmacotherapy; Behavioral Treatment, Alcohol Treatment Program, Psychiatric Care

Computer-Delivered Screening and Intervention

• Screening
  - standardized, validated screening instruments
  - proactive and universal screening at medical visits ensures that all patients assessed without regard to provider expectations of use computerized assessments shown to increase likelihood of disclosure of drug use
  - computerized assessments can quickly and reliably evaluate for other health-related concerns, such as mental health and sexual risk screening, and can generate an algorithm for determining needed intervention

• Computer delivered intervention
  - can reach large numbers of patients in clinic or online
  - perfectly replicable
  - offer greater anonymity
  - can be individually tailored to patient preferences and characteristics
• We evaluated a **computer-delivered brief motivational interviewing-style counseling intervention (CBI)** targeted to people with HIV with unhealthy alcohol use.
Computer-Delivered Interventions

Computerized Brief Intervention (CBI) Component:

- A tested software platform; content added included: alcohol, HIV, coping strategies
- Tablet administered CBT in MI style

- Intervention incorporated
  • Personalized feedback
  • Discussion of pros/cons of drinking
  • Goal setting to reduce or stop using alcohol

- 2-session brief (12-15 mins) intervention delivered at clinic visits
- Triage on severity and APT use, so 5 potential sessions that might be viewed
- Each session is menu-driven, branching on patient response
- Avatar is engaging, interactive, and provides occasional comic relief
- High marks on Patient Satisfaction Questionnaire on usability, information quality, avatar likeability (4.1 out of 5)
Study Inclusion

Patients receiving routine HIV clinical care at two academic medical centers as part of CNICS who were:

- ≥18 years
- English speaking
- Not pregnant

Audio Computer-Assisted Structured Interview was integrated into routine care. Eligible patients drank at unhealthy/hazardous levels defined by:

- AUDIT-C score ≥3 for women and ≥4 for men;

- Eligible PRO from January 15, 2013 – October 13, 2014 (to allow ≥9 months of follow-up for every visit).
Baseline and follow up procedures

- All patients meeting inclusion criteria were eligible for intervention; invitation was limited by the availability of clinic staff.
- No incentives were offered for study participation and consent occurred during the medical care visit.
- Intervention consisted of two (2) 20-minute motivational interviews delivered via touch-screen computer by Peedy the Parrot, a 3-D animated character.
- Intervention took place at baseline and approximately 2-4 months (coinciding with a regular clinic visit).
If PROs yearly AUDIT score is:
>3 women/>4 men

Unhealthy Alcohol Use

MINI DSM IV

Unhealthy, Not Dependent

Visit 1: Peedy Prime

Unhealthy, Not Dependent

Visit 1: Peedy Prime

Dependent

Visit 1: Peedy Pharma

At next routine visit:
PROs AUDIT-C

No Longer Unhealthy Use
AUDIT-C: < =3; <=4
Visit 2: Peedy Prize!

Unhealthy NOT Prescribed AP
AUDIT-C: > 3; >4
Visit 2: Peedy Problem NOT Prescribed Pharma

Unhealthy, Was Prescribed AP
AUDIT-C: > 3; >4
Visit 2: Peedy Problem, Was Prescribed Pharma
Enrollment Results

- PRO screening on AUDIT-C at clinic visits ~q 6 months
- 538 eligible patients were approached - June 2013-August 2015
  - If PRO AUDIT-C of ≥3 women; ≥4 men; MINI assessed dependence for triage to “Peedy Pharma”
  - Enrollment period= one year
- 226 enrolled (42%)

In multiple choice survey of 110 people who refused most common reason was “lack of interest in changing”

Patients were not: treatment seeking or provided incentives
Outcomes

• Outcome was change in drinks/week from baseline to 4-12 months of follow-up
  1. Invited to participate (n=537)
  2. Enrolled (n=226)
  3. Saw CBI (n=176)

Reference group was in-person PRO where there was not an approach (N=276)

1. Exposure Change in drinks/week

- Invited to participate: -3.9 (95% CI: -6.1, -1.8)
- Enrollment in intervention: -9.1 (95% CI: -14.5, -3.6)
- Completed ≥1 intervention session: -11.7 (95% CI: -18.8, -4.6)

Conclusion: Clinically meaningful reductions in drinking
Who Chose to Participate?

- Compared with refused/postponed, enrolled reported significantly:
  - Higher number of drinks per week (15 v. 12)
  - Greater number of abuse/dependence symptoms of AUD on the MINI
  - Greater number of panic and depressive symptoms
    - Lab testing showed: enrolled had a higher proportion of detectable VL
    - But no differences in sociodemographic or drug use characteristics

CBI implementation reached those most in need of care
Conclusions

1. CBI adapted and modified achieved high acceptability to clinic patients

2. **Non treatment** seeking patients with unhealthy alcohol use provided no incentives will nonetheless enroll and view a CBI

3. Patients most likely to enroll are those most in need of care

4. CBI produced **significantly meaningful reductions** in alcohol use
Stepped Care for alcohol use disorder

- Randomized trial across VA clinics comparing a stepped care model to treatment as usual for the treatment of AUD among PWH

- Stepped Care: Addiction medicine clinician provided medication management with alcohol pharmacotherapy; after 4 weeks, if no improvement, stepped up to MET; after 12 weeks if continued heavy drinking referred to specialty services

- 128 individuals were randomized; at the end of 24 weeks, more individuals in the integrated alcohol treatment (stepped care) received pharmacotherapy; at 52 weeks, stepped care resulted in reduced alcohol use (heavy drinking days, days abstinent and drinks per drinking day) and improved viral suppression

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Integrated stepped alcohol treatment for patients with HIV and alcohol use disorder: a randomised controlled trial

E Jennifer Edelman, Stephen A Maisto, Nathan B Hansen, Christopher J Cutler, James Dziura, Yanhong Deng, Lynn E Fiellin, Patrick G O’Connor, Roger Bedimo, Cynthia L Gibert, Vincent C Marconi, David Rimland, Maria C Rodriguez-Barradas, Michael S Simberkoff, Janet P Tate, Amy C Justice, Kendall J Bryant, David A Fiellin
NIAAA Treatment Navigator

https://alcoholtreatment.niaaa.nih.gov/
Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV

• Substance use disorders (SUDs) are prevalent among people with HIV and contribute to poor health outcomes; therefore, screening for SUDs should be a routine part of clinical care (AII).
• The most commonly used substances among people with HIV include alcohol, benzodiazepines, cannabinoids, club drugs, opioids, stimulants (cocaine and methamphetamines), and tobacco.
• Health care providers should be nonjudgmental when addressing substance use with their patients (AIII).
• Persons with HIV and SUDs should be screened for additional mental health disorders (AII).
• Persons with HIV and SUDs should be offered evidenced-based pharmacotherapy (e.g., opioid agonist therapy, tobacco cessation treatment, alcohol use disorder treatment; see Table 13) as part of comprehensive HIV care in HIV clinical settings (AI).
• Ongoing substance use is not a contraindication to antiretroviral therapy (ART) (AI). Persons who use substances can achieve and maintain viral suppression with ART.
• Substance use may increase the likelihood of risk-taking behaviors (e.g., risky sexual behaviors), the potential for drug-drug interactions, and the risk or severity of substance-associated toxicities (e.g., increased hepatotoxicity or an increased risk of overdose).
• Selection of ART regimens for individuals who practice unhealthy substance and alcohol use should take potential adherence barriers, comorbidities which could impact care (e.g., advanced liver disease from alcohol or hepatitis viruses), potential drug-drug interactions, and possible adverse events associated with the medications into account (AII).
• ART regimens with once-daily dosing of single-tablet regimens, high barriers to resistance, low hepatotoxicity, and low potential for drug-drug interactions are preferred (AIII).

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion
Clinical Case (continued)

• After 28 day residential treatment the patient returned to the office. He initiated FTC/TDF/Norvir/Atazanavir

• Offered Naltrexone for relapse prevention which he declined

• Continued to attend mutual support groups, and engage actively with a sponsor

• Has maintained an undetectable viral load (now on Biktarvy), received HCV treatment, quit tobacco

• Has missed 0 appointment in ten years

• Works as a janitor at a daycare
Summary

- Unhealthy alcohol use can interrupt steps in the HIV Care Continuum and complicate comorbidities and their management among persons with HIV.

- Given the impact of alcohol use on HIV infection and comorbidities and US goals of HIV treatment as prevention, it is critical to initiate ART among persons with unhealthy alcohol use.

- Universal screening with standardized tools can improve identification of unhealthy alcohol use.

- Evidence-based alcohol reduction interventions can be implemented in primary care/HIV settings and may improve HIV outcomes.
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