

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

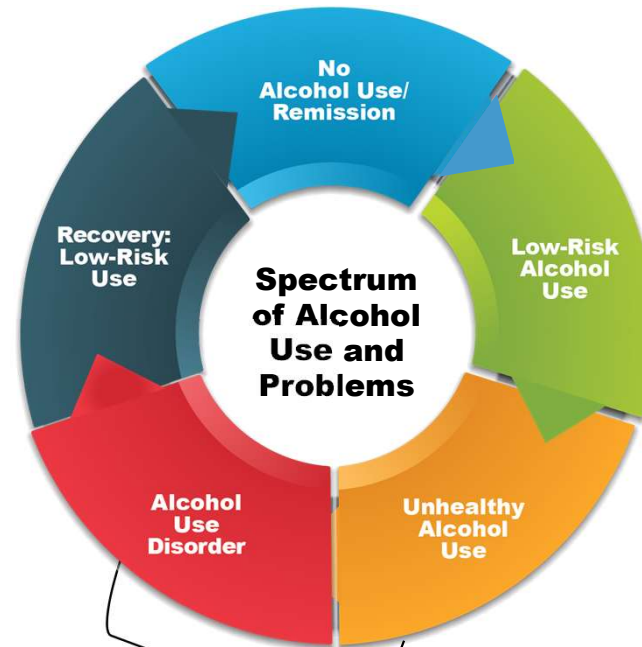
How often do you prescribe medications for alcohol use disorder (MAUD) when diagnose an individual with AUD(no history of withdrawal) in your clinic?

- Almost always
- Often
- Sometimes
- Seldom
- Never

Clinical Case

- 53 year old man diagnosed with HIV 2004. Established care in 2005 at HIV clinic co-located with substance use treatment program. Initiated Epivir/TDF/Efavirenz, with viral suppression for 2 years. Then in and out of care, prescribed PI-based regimen but did not start. Re-entered care in 2011 after 18 month lapse and repeated hospitalizations for pneumonia.
- 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 \leq 65 years old:

>4 drinks/occasion;

>14 drinks/week

Women and Men >65 years old:

>3 drinks/occasion;

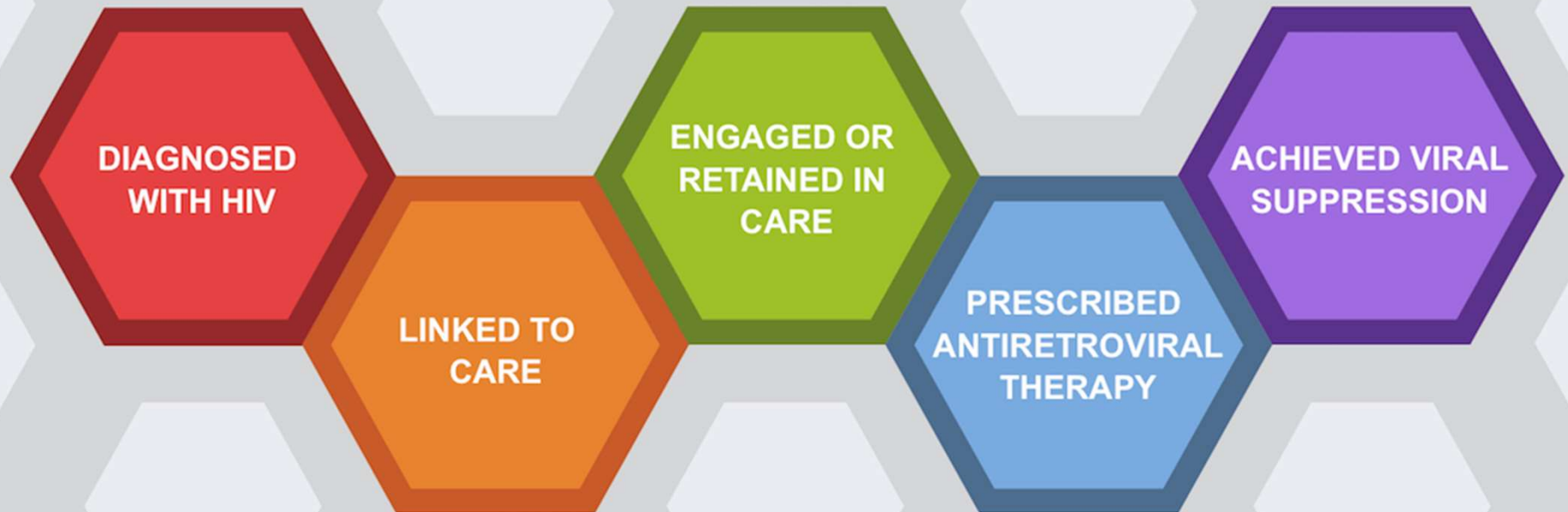
>7 drinks/week

Unhealthy Alcohol Use:
HIV – 27%

Saitz *NEJM* 2005; Crane *AIDS Behav* 2017

Unhealthy alcohol use

HIV CARE CONTINUUM

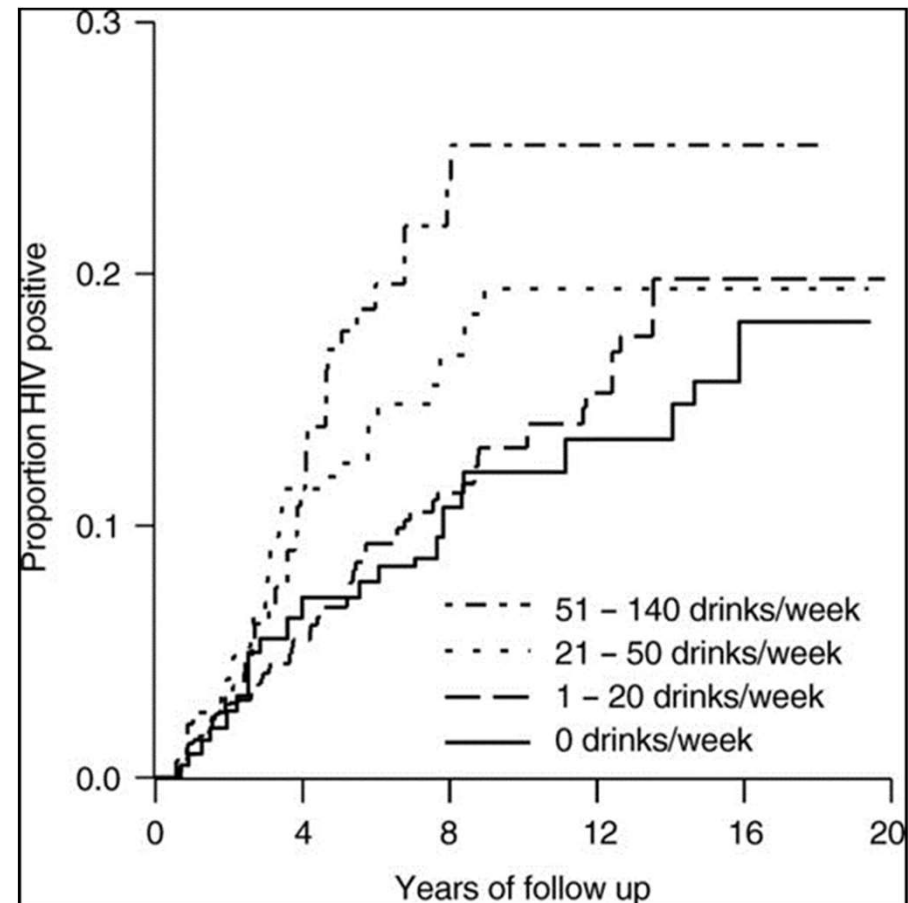


The series of steps a person with HIV takes from initial diagnosis through their successful treatment with HIV medication

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)



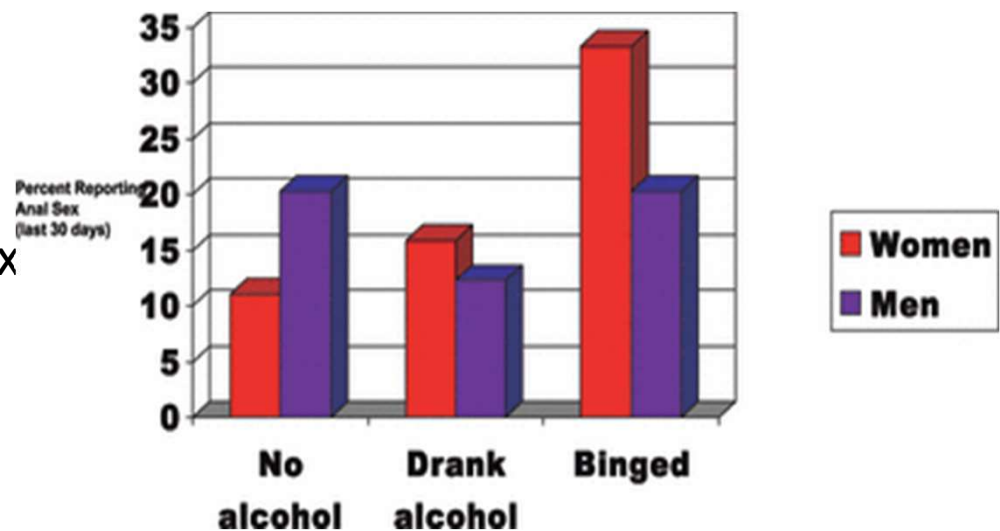
A prospective study of alcohol consumption and HIV acquisition among injection drug users.

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 Rehm^{1,2,3,4,5,6}, Charlotte Probst^{1,4*}, Kevin D. Shield^{1,7} and Paul A. Shuper^{1,6}

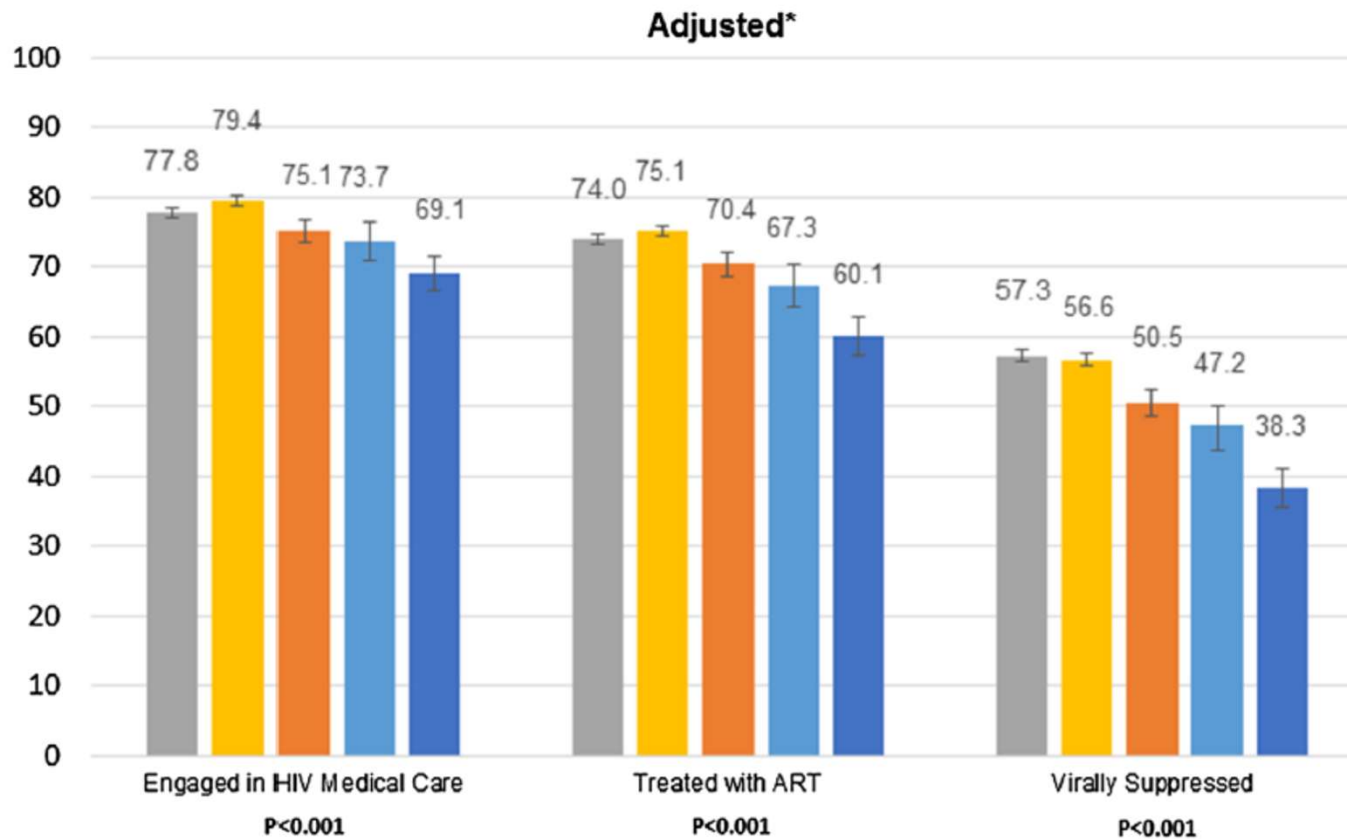
Acute Alcohol Consumption Directly Increases HIV Transmission Risk: A Randomized Controlled Experiment

Shuper, Paul A. PhD^{*,†}; Joharchi, Narges MSc^{*}; Monti, Peter M. PhD[‡]; Loutfy, Mona MD, FRCPC, MPH^{§,¶,||}; Rehm, Jürgen PhD^{*,†,#,**,††,‡‡,§§,||} [Author Information](#) 

JAIDS Journal of Acquired Immune Deficiency Syndromes: December 15, 2017 - Volume 76 - Issue 5 - p 493-500

doi: 10.1097/QAI.0000000000001549

Unhealthy alcohol use and HIV Care continuum



*Adjusted for race, ethnicity, gender, fiscal year of AUDIT-C screening, age, and any mental health and non-alcohol substance use disorders

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 - <500copies/mL based on first lab after AUDIT-C

- Non-Drinking (0)
- Low-Level (1-3; 1-2 women)
- Medium-Level (4-5; 3-5 women)
- High-Level (6-7)
- Very High-Level (8-12)

Alcohol use, Antiretroviral therapy, adherence and viral suppression

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

*Adjusted for age, sex, race, CD4 nadir, and time enrolled (days).

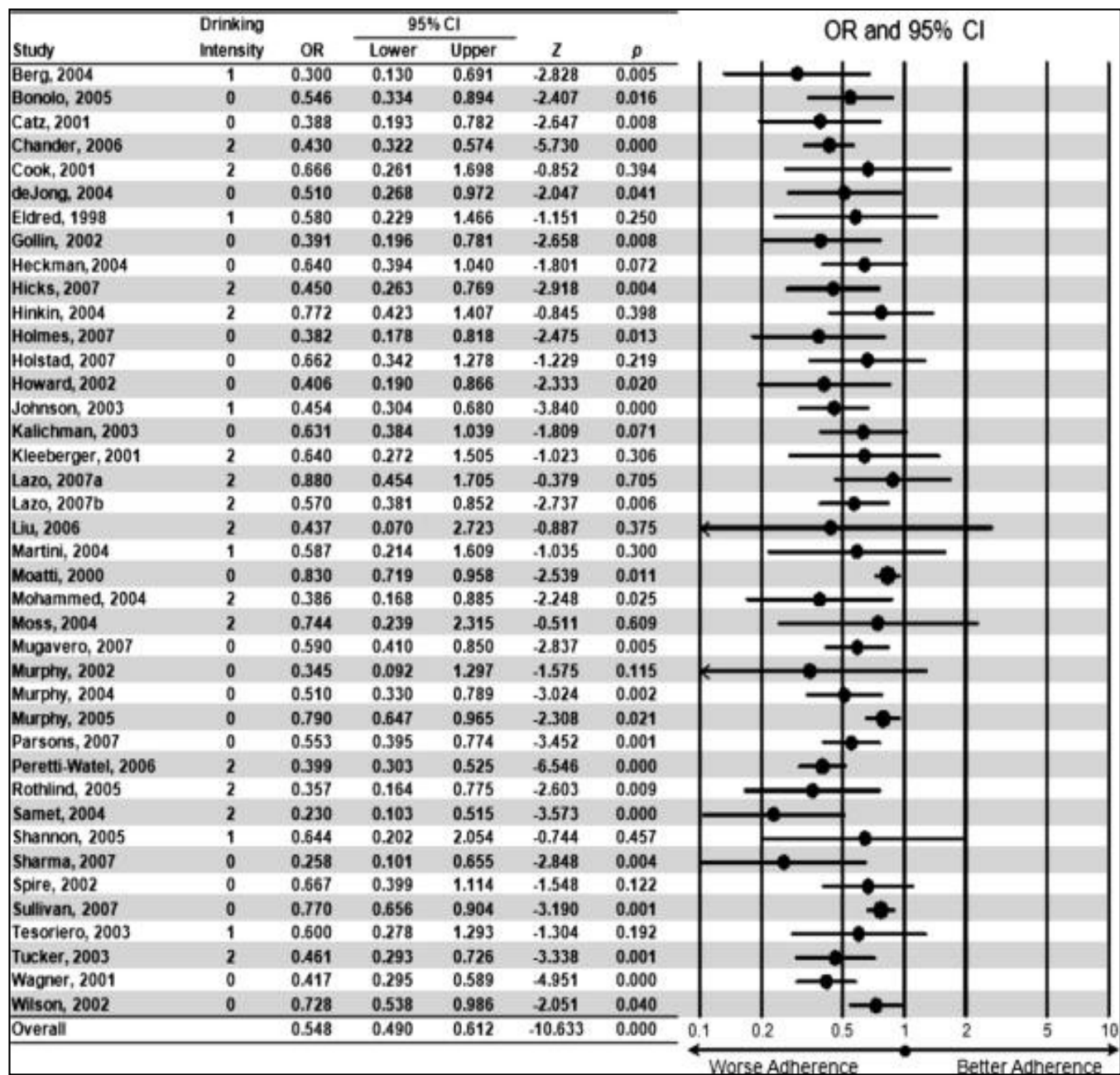
†Sample includes individuals either on antiretroviral therapy or with a CD4 cell count ≤ 350 .

‡Adjusted for age, sex, race, CD4 nadir, and years on ART (days).

Hazardous Alcohol Use: A Risk Factor for Non-Adherence and Lack of Suppression in HIV Infection

Geetanjali Chander; Bryan Lau; Richard Moore;

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

JAIDS Journal of Acquired Immune Deficiency Syndromes. 52(2):180-202, October 2009.

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*

	IOM Retention Measure		Visit Adherence Measure	
	Drinking Categories	Binge Frequency Categories	Drinking Categories	Binge Frequency Categories
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Drinking category				
Never	Ref	Ref	Ref	Ref
Moderate	0.93 (0.83 to 1.03)	—	1.01 (0.96 to 1.07)	—
Heavy†	0.78 (0.69 to 0.88)‡	—	0.97 (0.91 to 1.04)	—
Binge frequency category				
Never	Ref	Ref	Ref	Ref
Monthly/less than monthly	—	0.89 (0.80 to 0.99)§	—	0.98 (0.93 to 1.03)
Daily/weekly	—	0.90 (0.74 to 1.10)	—	0.90 (0.82 to 0.98)§
Current drug use				
Yes (vs. no)	0.88 (0.77 to 1.00)	0.87 (0.76 to 0.99)§	0.74 (0.69 to 0.79)‡	0.74 (0.70 to 0.79)‡
Panic symptoms				
None	Ref	Ref	Ref	Ref
Some	0.94 (0.83 to 1.08)	0.94 (0.82 to 1.07)	0.96 (0.91 to 1.02)	0.96 (0.91 to 1.02)
Panic disorder	0.92 (0.80 to 1.07)	0.92 (0.80 to 1.07)	0.85 (0.80 to 0.90)‡	0.85 (0.80 to 0.90)‡
Depression screen				
Positive (vs. negative)	1.15 (1.02 to 1.30)§	1.15 (1.02 to 1.30)§	0.92 (0.88 to 0.97)§	0.92 (0.88 to 0.97)§

*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.

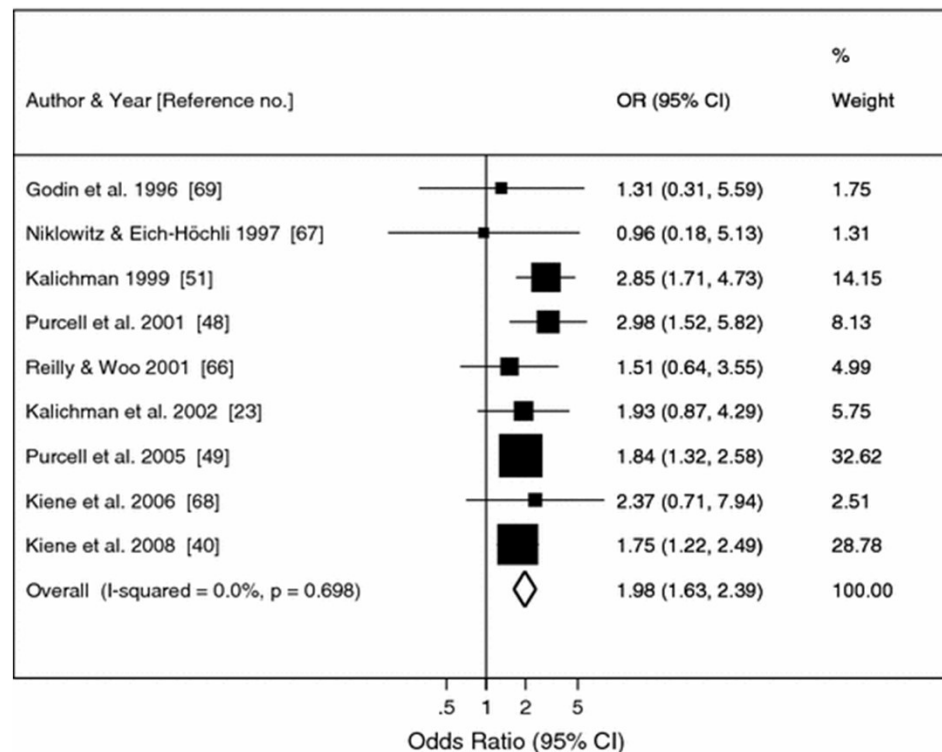
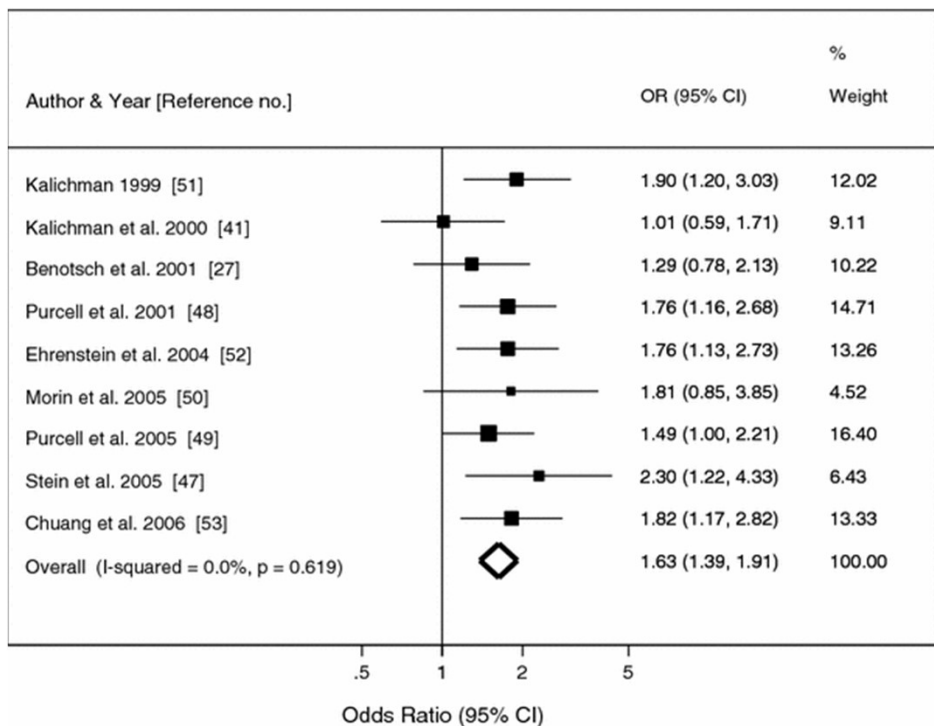
‡P < 0.0001.

§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)

Alcohol as a Correlate of Unprotected Sexual Behavior Among People Living with HIV/AIDS: Review and Meta-Analysis

Paul A. Shuper · Narges Joharchi · Hyacinth Irving · Jürgen Rehm

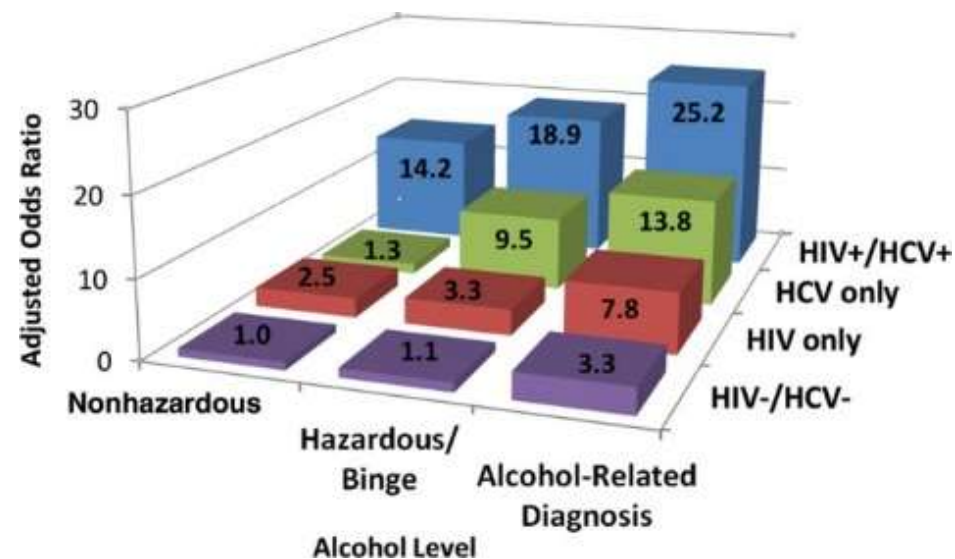


Any alcohol use: (OR: 1.63 (1.39-1.91) and alcohol consumption in sexual contexts OR: 1.98 (1.63-2.39) associated with condomless sex

Unhealthy alcohol use, comorbidities and other health outcomes among PWH

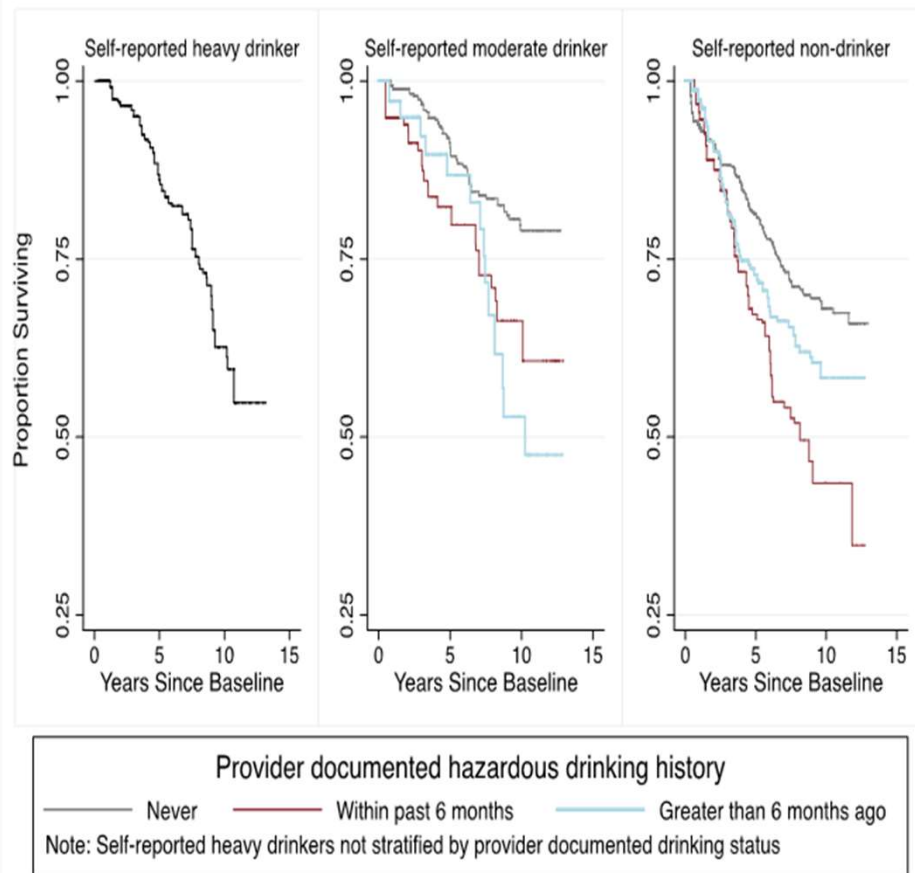


- Veterans Aging Cohort Study
- N=3565; 701 HIV/HCV; 1410 HIV; 296 HCV; 1158 neither HIV/HCV
- Outcome: Advanced hepatic Fibrosis Defined as Fib-4 >3.25
- Exposure: (1) Alcohol related diagnosis: *ICD-9* diagnosis for alcohol dependence/abuse recorded between 12 months before and 6 months after enrollment; (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

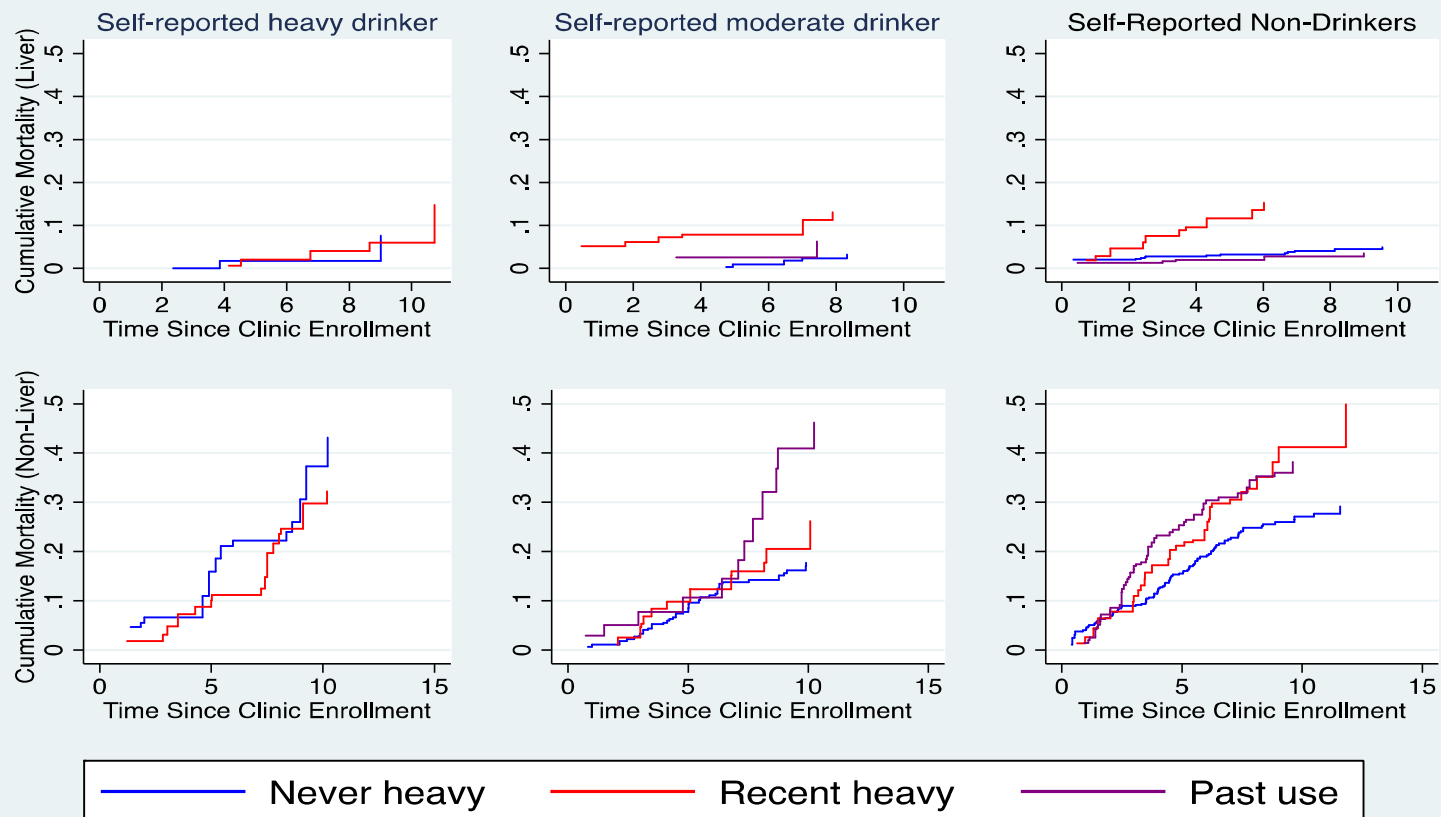
Overall and liver related mortality by self-reported and provider documented alcohol use among PLWH



- 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

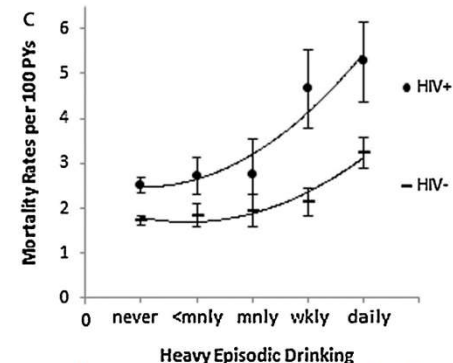
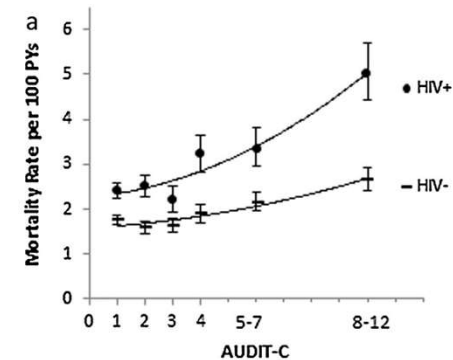
Liver related mortality among PWH

Liver-Related (top) and Non Liver-Related (bottom) Mortality



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



Justice AC, McGinnis KA, Tate JP, Braithwaite RS, Bryant KJ, Cook RL, Edelman EJ, Fiellin LE, Freiberg MS, Gordon AJ, Kraemer KL, Marshall BD, Williams EC, Fiellin DA. Risk of mortality and physiologic injury evident with lower alcohol exposure among HIV infected compared with uninfected men. *Drug Alcohol Depend.* 2016 Apr 1;161:95-103



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

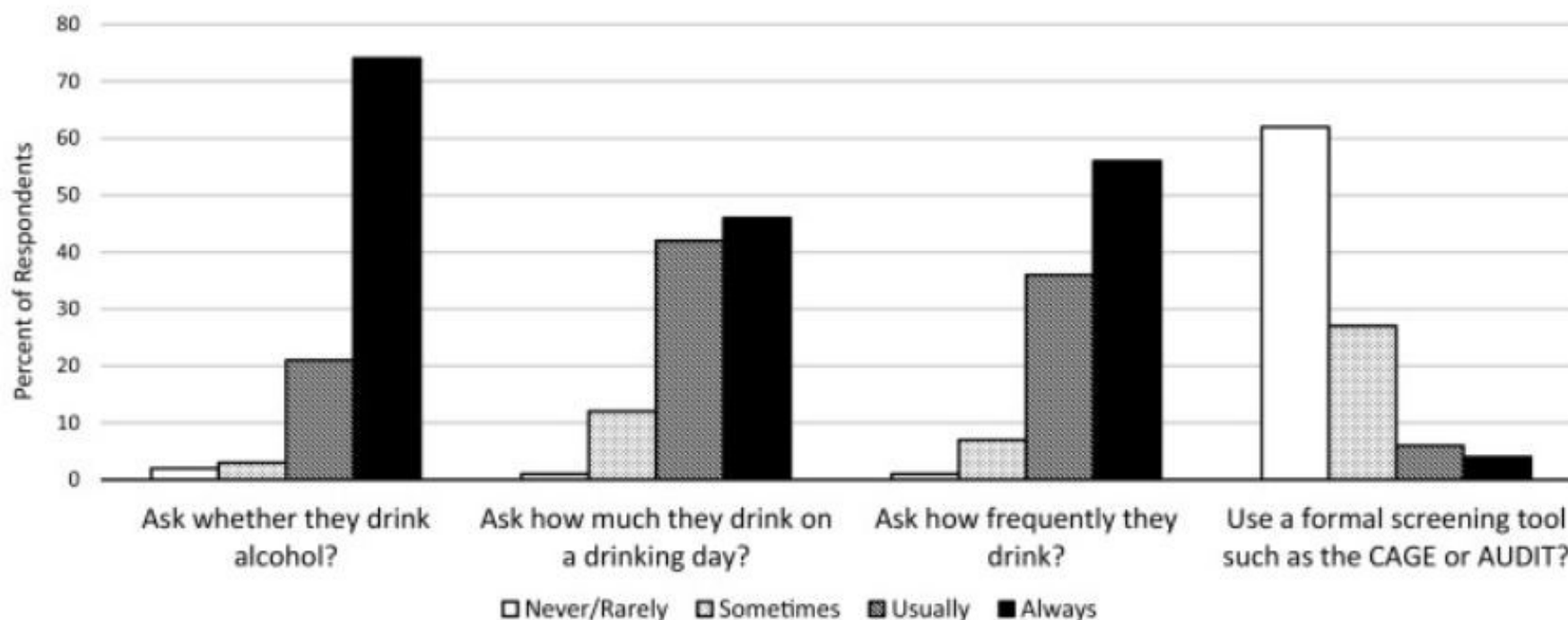


Full length article

HIV primary care providers—Screening, knowledge, attitudes and behaviors related to alcohol interventions



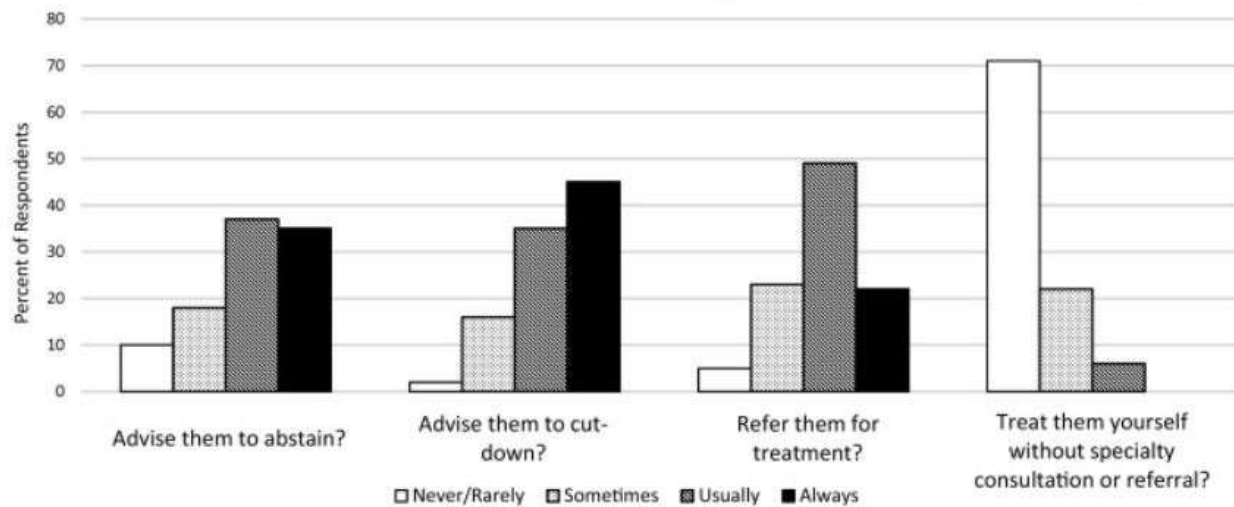
A: Alcohol Screening Practices: In new patients how often do you:



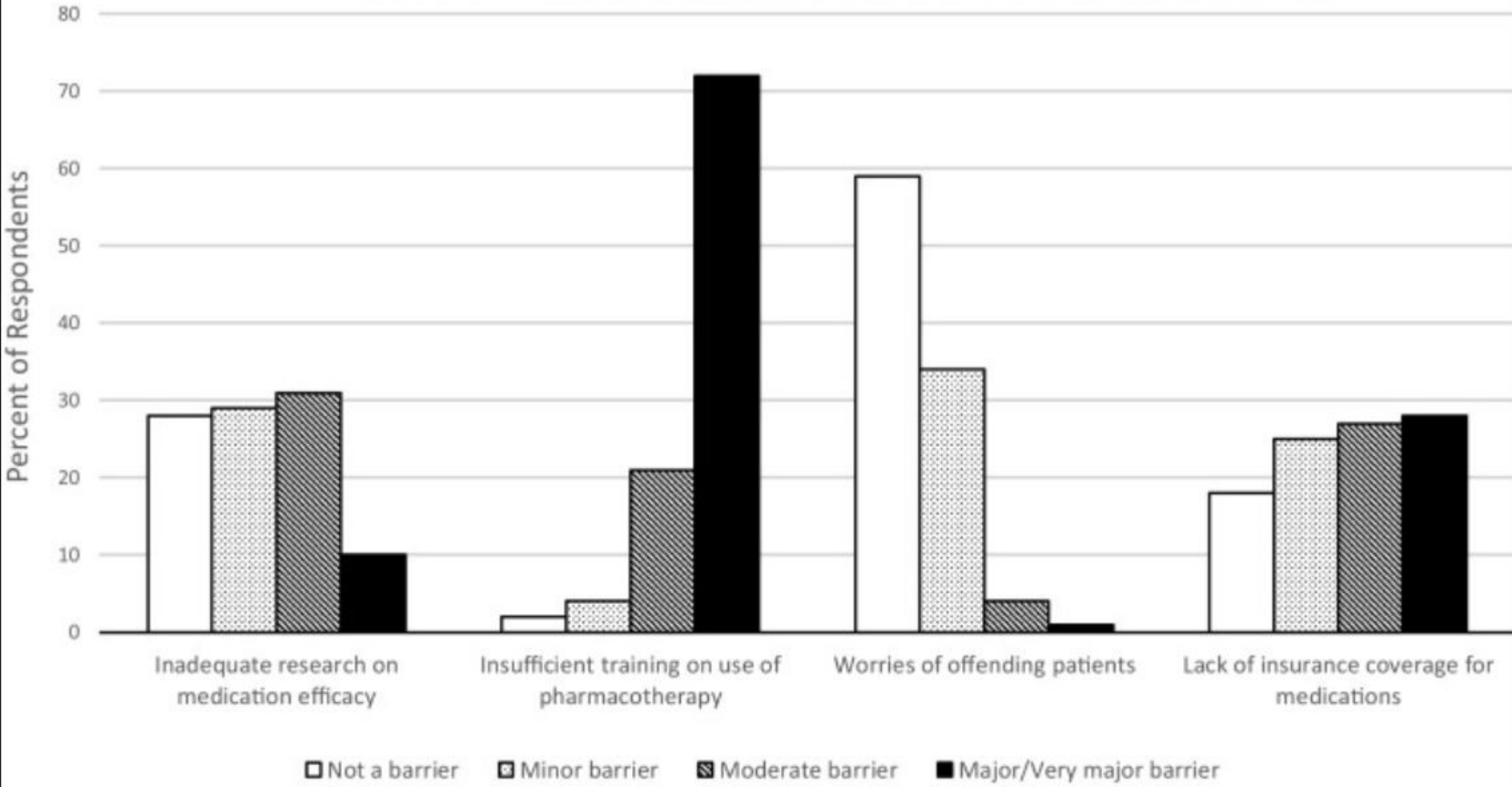
B: Alcohol Counseling Practices

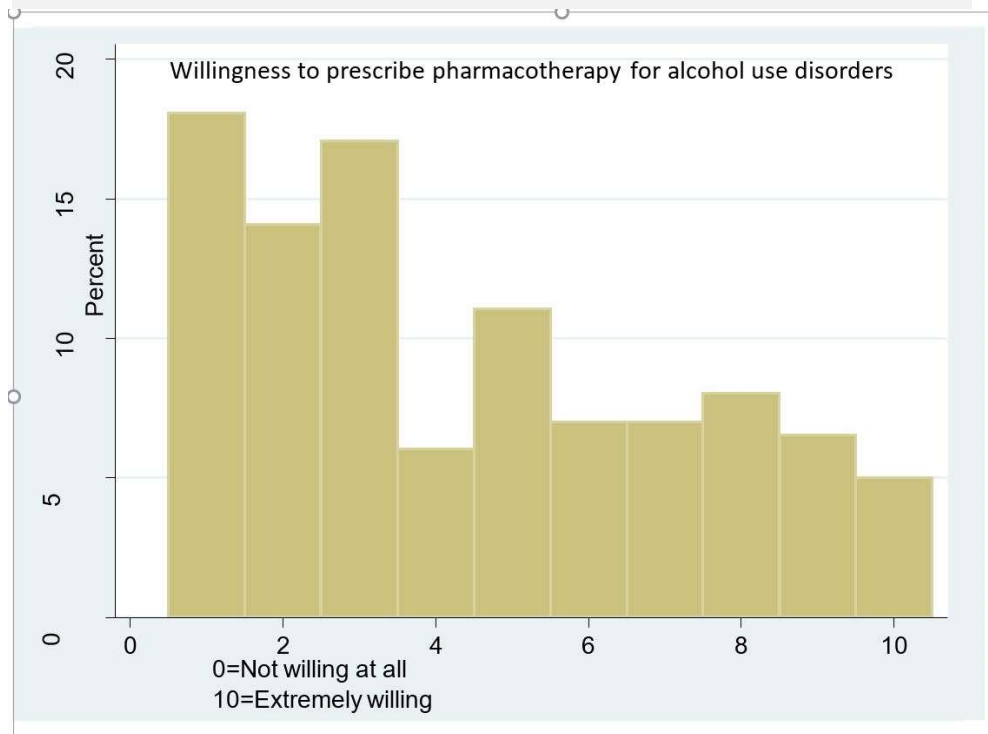
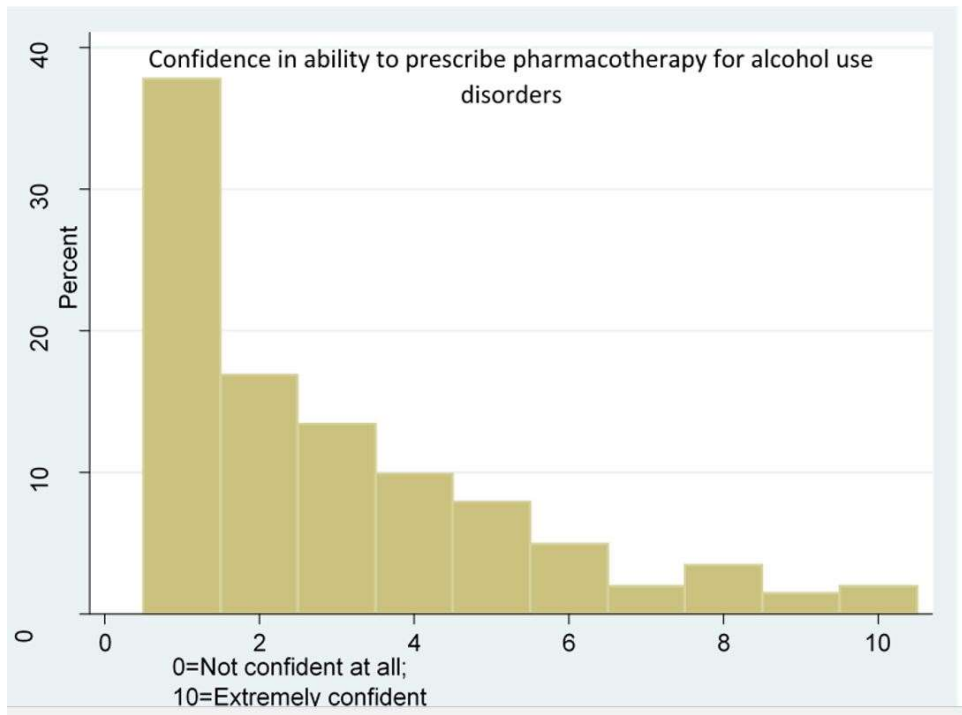


C: Alcohol Treatment Practices: In alcohol dependent patients, how often do you:

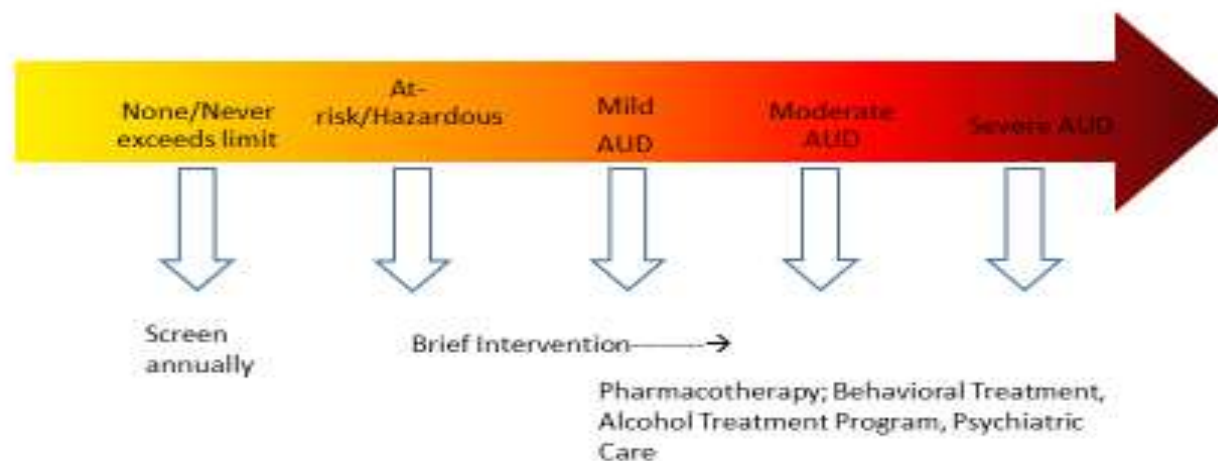


Provider Barriers to the Use of Alcohol Pharmacotherapy





Management of Alcohol Use in HIV clinical settings



Adapted from Willenbring ML, et al. *American Family Physician*. 2009. Volume 80, issue 1 and Willenbring ML. *Addiction Professional* 2008. <http://www.addictionpro.com>.

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

¹Smith PC. J Gen Intern Med. 2009 24:783-8.

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**



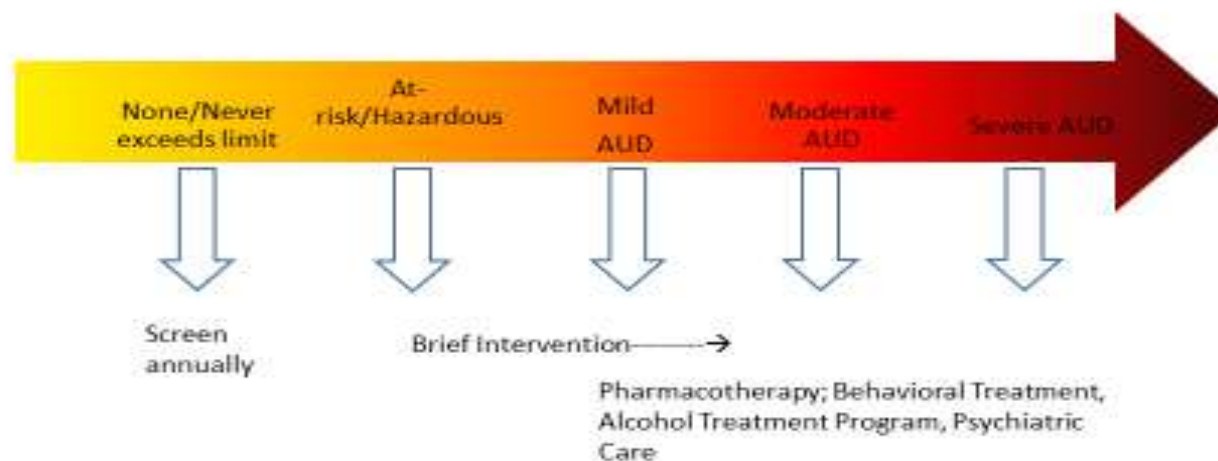
Standard drink conversion



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



Adapted from Willenbring ML, et al. *American Family Physician*. 2009. Volume 80, issue 1 and Willenbring ML. *Addiction Professional* 2008. <http://www.addictionpro.com>.

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

ACT Curriculum. Boston University.

<http://www.bu.edu/act/mdalcoholtraining/index.html>

Helping Patients Who Drink Too Much. A Clinician's Guide. NIAAA.

<http://pubs.niaaa.nih.gov/publications/practitioner/cliniciansguide2005/guide.pdf>

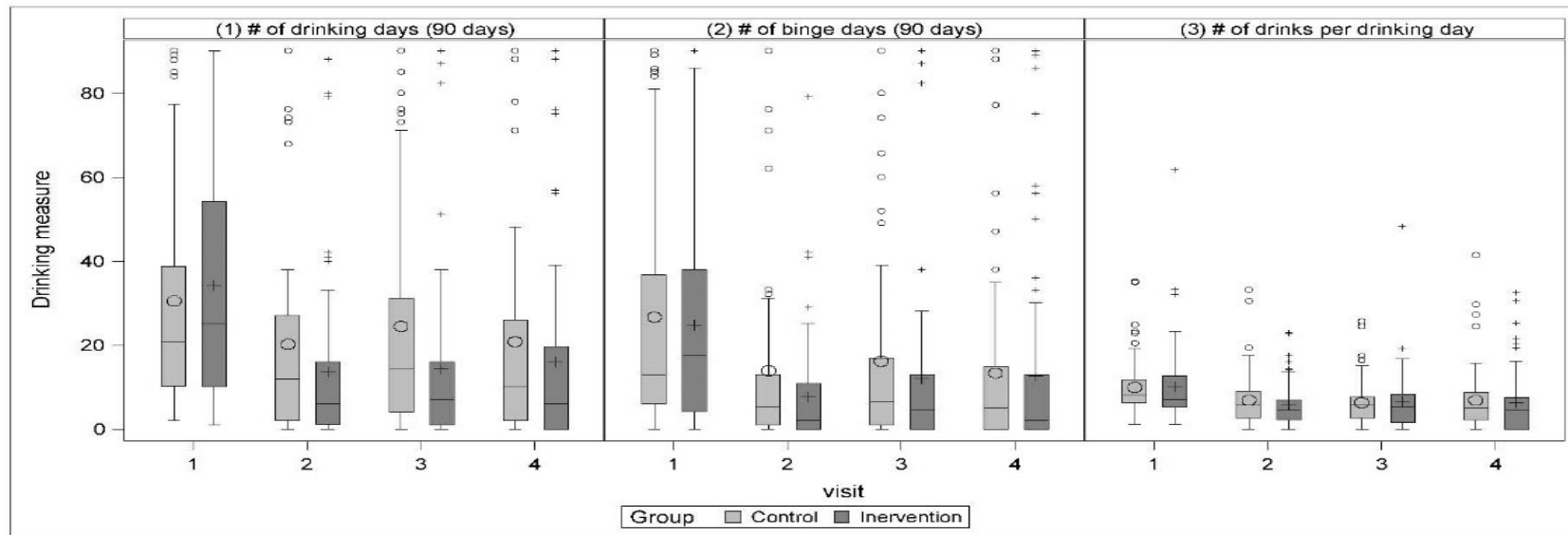


Brief Intervention for women with HIV

- **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**

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

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

	Control	Intervention
Baseline	41.9%	40.3%
3 months	43.9%	59.3%
6 months	46.8%	50%
12 months	42.2%	49.2%

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

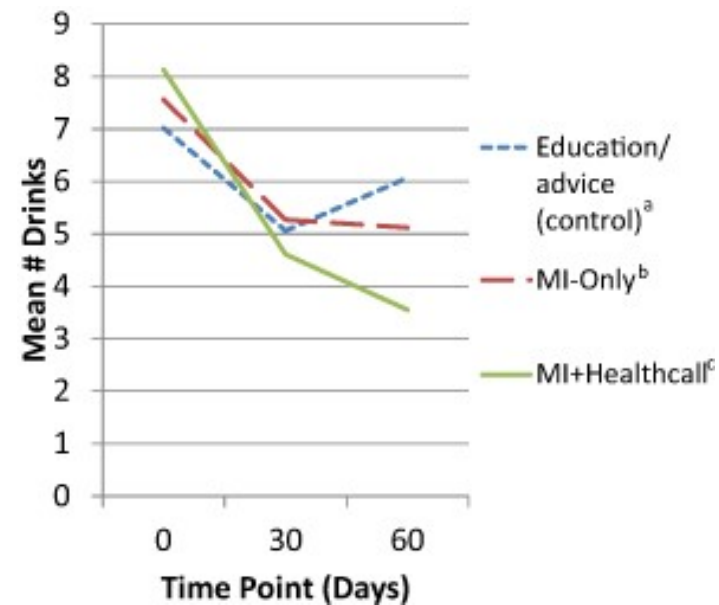
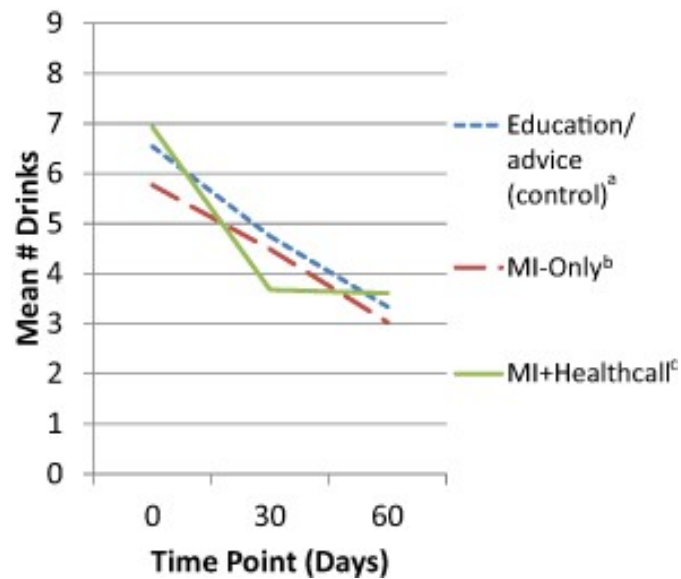
Effect of MI vs. Treatment as Usual over time	
Parameter	Effect Size [95% Confidence Interval]
<i>Average number of drinks per week</i>	
3 months	-4.02 [-8.18, 0.14]
6 months	-8.72 [-12.69, -4.76]
12 months	-5.98 [-9.77, -2.19]
<i>Number of heavy drinking days (>5 drinks per day/month)</i>	
3 months	0.84 [0.61, 1.14]
6 months	0.55 [0.38, 0.79]
12 months	0.50 [0.33, 0.78]

- **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

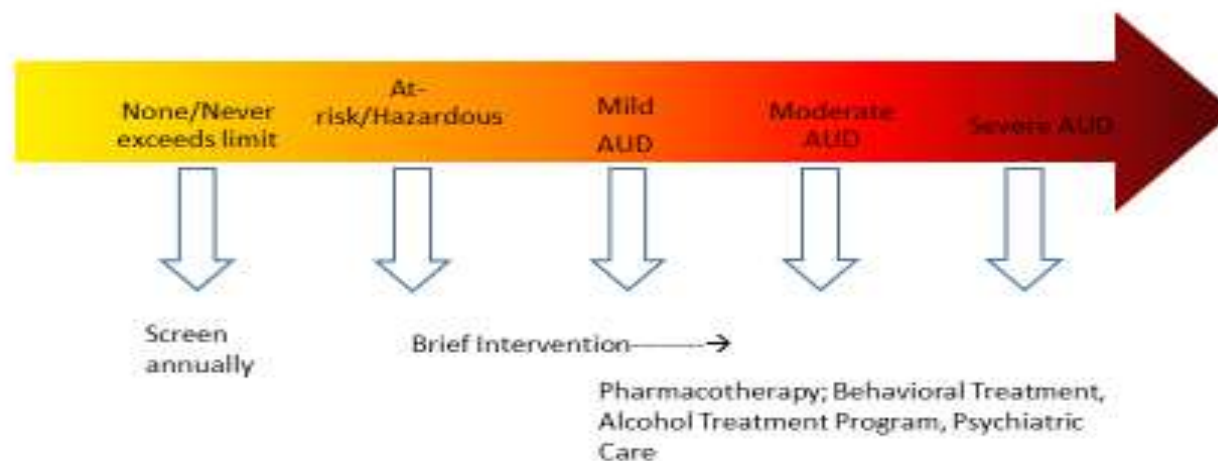


Health Call--Reducing heavy drinking in HIV primary care: a randomized trial of brief intervention, with and without technological enhancement



258 Randomized to three arms
-Education, MI, MI+ HealthCall
Outcome=Mean drinks per drinking day

Management of Alcohol Use in HIV clinical settings



Adapted from Willenbring ML, et al. *American Family Physician*. 2009. Volume 80, issue 1 and Willenbring ML. *Addiction Professional* 2008. <http://www.addictionpro.com>.

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

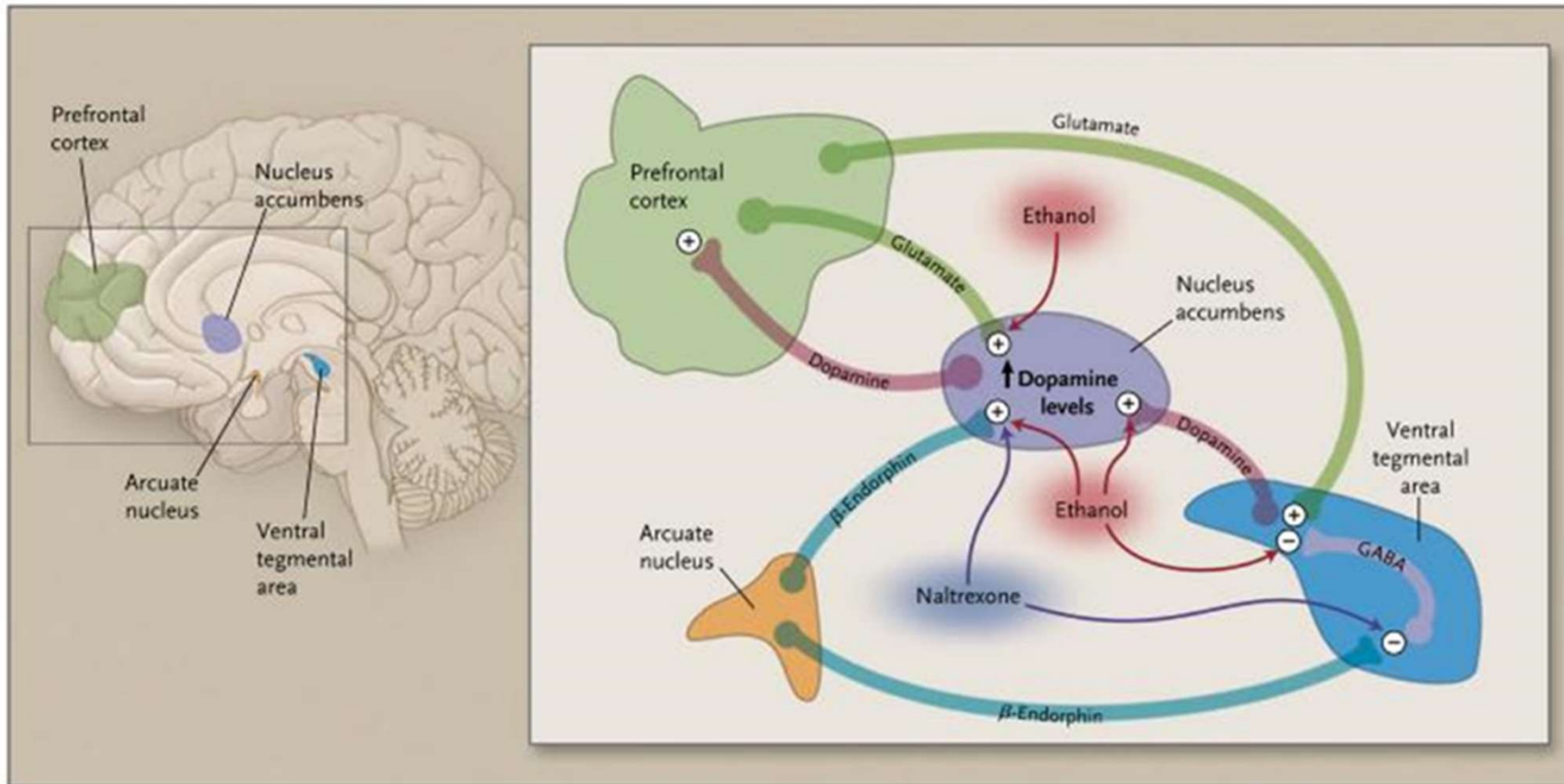


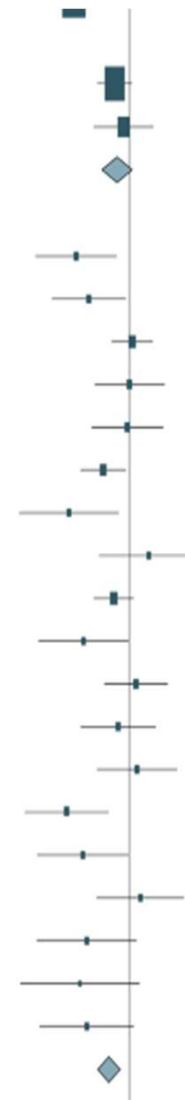
Table 6 US Food and Drug Administration (FDA)-Approved Medications and Others Tested in Alcohol Use Disorder Patients

Medication	Dosage	Pharmacologic Target	Possible Use in Alcohol Use Disorder Patients with Alcoholic Liver Disease?
FDA-Approved Medications for Alcohol Use Disorder			
Acamprosate	666 mg TID	Possibly NMDA receptor agonist	Yes (no hepatic metabolism)
Disulfiram	250-500 mg QD	Inhibition of acetaldehyde dehydrogenase	No (hepatic metabolism; cases of liver toxicity have been reported)
Naltrexone* PO or IM	PO: 50 mg QD IM: 380 mg monthly	Mu opiate receptor antagonist	With caution (perceptions of liver toxicity limit use in advanced alcoholic liver disease)
Not FDA-Approved Medications Tested for Alcohol Use Disorder			
Baclofen	10 mg TID; 80 mg QD max	GABA _B receptor agonist	Yes (minimal hepatic metabolism) Baclofen has been formally tested in clinical studies with alcohol use disorder patients with liver cirrhosis
Gabapentin	900-1800 mg QD	Unclear: modulates GABA transmission	Yes (no hepatic metabolism)
Ondansetron	1-16 µg/kg BID	5HT ₃ antagonist	Yes, but with caution because liver toxicity has been reported, albeit relationship to ondansetron administration is not determined
Topiramate	300 mg QD	Anticonvulsant multiple targets: -glutamate/+GABA	Yes (partial hepatic metabolism mostly by glucuronidation) In patients with hepatic encephalopathy, use with caution: topiramate-related cognitive side-effects may confound the clinical course and treatment of hepatic encephalopathy
Varenicline	2 mg QD	Nicotinic acetylcholine receptor partial agonist	Yes (minimal hepatic metabolism)

Leggio and Lee, Am J Med 2017

Naltrexone for alcohol use disorder

Naltrexone (100 mg/d oral)							
Anton et al, ³⁰ 2006	16	Low	207	102	226	83	-0.06 (-0.13 to 0.01)
Oslin et al, ⁵⁷ 2008	24	Med	73	47	76	44	-0.03 (-0.15 to 0.10)
Subtotal: $I^2=0.0\%$; $P=.61$							-0.05 (-0.11 to 0.01)
Naltrexone (50 mg/d oral)							
Anton et al, ⁵⁹ 1999	12	Med	26	42	38	25	-0.22 (-0.39 to -0.05)
Anton et al, ⁷² 2005	12	Med	33	48	46	34	-0.17 (-0.32 to -0.02)
Ballardin et al, ⁶⁰ 2003	24	Low	53	3	58	4	0.01 (-0.07 to 0.10)
Chick et al, ⁵⁰ 2000	12	Med	57	28	53	26	-0.00 (-0.14 to 0.14)
Gastpar et al, ⁶¹ 2002	12	Med	34	50	36	51	-0.01 (-0.16 to 0.14)
Guardia et al, ⁶² 2002	12	Med	8	93	19	82	-0.11 (-0.20 to -0.02)
Kiefer et al, ³⁹ 2003	12	Low	20	20	30	10	-0.25 (-0.45 to -0.05)
Killeen et al, ⁶³ 2004	12	Med	21	30	12	24	0.08 (-0.13 to 0.28)
Krystal et al, ⁶⁴ 2001	12	Med	183	235	105	104	-0.06 (-0.15 to 0.02)
Latt et al, ⁷⁴ 2002	12	Med	19	37	27	24	-0.19 (-0.37 to -0.01)
Mann et al, ⁴⁰ 2013	12	Med	86	83	41	44	0.03 (-0.10 to 0.16)
Monti et al, ⁷⁵ 2001	12	Med	16	48	19	45	-0.05 (-0.20 to 0.11)
Morley et al, ³⁸ 2006	12	Low	39	14	43	18	0.03 (-0.13 to 0.20)
Morris et al, ⁶⁵ 2001	12	Med	28	27	43	13	-0.26 (-0.43 to -0.09)
O'Malley et al, ⁶⁶ 1992	12	Med	24	28	34	18	-0.19 (-0.38 to -0.01)
O'Malley et al, ⁶⁷ 2007	12	Med	39	18	32	18	0.04 (-0.14 to 0.22)
O'Malley et al, ³⁶ 2008	16	Med	22	12	28	6	-0.18 (-0.38 to 0.03)
Oslin et al, ⁶⁸ 1997	12	Med	3	18	8	15	-0.20 (-0.45 to 0.04)
Volpicelli et al, ⁷⁰ 1997	12	Med	17	31	26	23	-0.18 (-0.37 to 0.02)
Subtotal: $I^2=43.7\%$; $P=.02$							-0.09 (-0.13 to -0.04)



Jonas JAMA 2014;

September 26, 2013

Blood opioid receptors → attenuates positive reinforcing effects of alcohol consumption
 Decreases heavy drinking days and relapse to heavy drinking; decreases craving
 Oral naltrexone was associated with reduction in return to drinking providing evidence for improving alcohol consumption outcomes for patients with AUD
 The NNT to prevent return to any drinking was 20 for naltrexone
 The NNT to prevent return to heavy drinking was 12 for naltrexone

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 MS[‡]; 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



 Full Access


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

First published: 28 July 2011 | <https://doi.org/10.1111/j.1530-0277.2011.01601.x> | Citations: 29

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

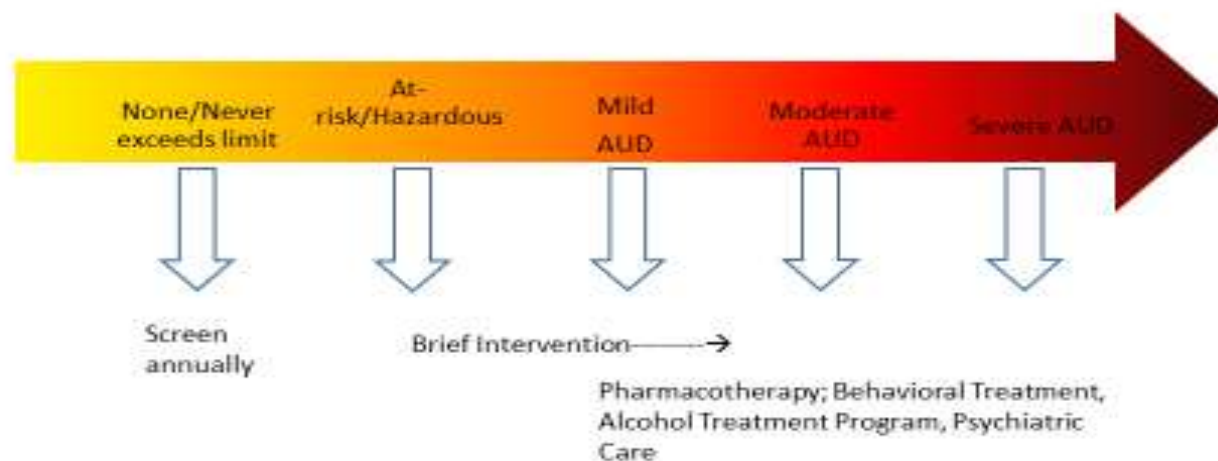
Source	Duration, wk	Risk of Bias	Treatment Group		Control Group		Risk Difference (95% CI)	Favors Treatment	Favors Control	Weight, %
			Events, No.	No Events, No.	Events, No.	No Events, No.				
Acamprosate										
Anton et al, ³⁰ 2006	16	Low	244	59	254	55	-0.02 (-0.08 to 0.04)			7.73
Baltieri et al, ⁴⁷ 2004	12	Med	15	25	21	14	-0.22 (-0.45 to -0.00)			3.21
Berger et al, ⁴⁶ 2013	12	Med	48	3	40	9	0.12 (-0.00 to 0.25)			5.61
Besson et al, ⁴⁸ 1998	51	Med	41	14	47	8	-0.11 (-0.26 to 0.04)			4.94
Chick et al, ⁴⁹ 2000	24	Med	254	35	260	32	-0.01 (-0.06 to 0.04)			8.01
Geerlings et al, ⁵¹ 1997	26	Med	96	32	116	18	-0.12 (-0.21 to -0.02)			6.66
Gual et al, ⁴⁵ 2001	26	Med	92	49	109	38	-0.09 (-0.19 to 0.02)			6.28
Kiefer et al, ³⁹ 2003	12	Low	30	10	37	3	-0.17 (-0.33 to -0.02)			4.68
Mason et al, ³⁷ 2006	24	Low	328	13	240	20	0.04 (0.00 to 0.08)			8.34
Morley et al, ³⁸ 2006	12	Low	44	11	50	11	-0.02 (-0.16 to 0.12)			5.08
Paille et al, ⁵² 1995	51	Med	294	67	157	20	-0.07 (-0.13 to -0.01)			7.74
Pelc et al, ⁵³ 1997	13	Med	74	52	53	9	-0.27 (-0.39 to -0.14)			5.72
Poldrugo et al, ⁵⁴ 1997	26	Med	63	59	84	40	-0.16 (-0.28 to -0.04)			5.78
Sass et al, ²⁸ 1996	48	Med	75	61	102	34	-0.20 (-0.31 to -0.09)			6.11
Tempesta et al, ⁵⁵ 2000	26	Med	87	77	115	51	-0.16 (-0.27 to -0.06)			6.35
Whitworth et al, ⁵⁶ 1996	52	Med	183	41	208	16	-0.11 (-0.17 to -0.05)			7.76
Subtotal: $I^2 = 80.8\%$; $P < .001$							-0.09 (-0.14 to -0.04)			100.00
Disulfiram										
Fuller et al, ³¹ 1979	52	Med	34	9	37	5	-0.09 (-0.25 to 0.07)			18.43
Fuller et al, ³² 1986	52	Med	164	38	167	32	-0.03 (-0.10 to 0.05)			81.57
Subtotal: $I^2 = 0.0\%$; $P = .48$							-0.04 (-0.11 to 0.03)			100.00
Naltrexone (100 mg/d oral)										
Anton et al, ³⁰ 2006	16	Low	241	68	254	55	-0.04 (-0.10 to 0.02)			66.19
Oslin et al, ⁵⁷ 2008	24	Med	95	25	96	24	-0.01 (-0.11 to 0.09)			25.15
Pettinati et al, ⁵⁸ 2010	14	Med	39	10	30	9	0.03 (-0.15 to 0.20)			8.66
Subtotal: $I^2 = 0.0\%$; $P = .69$							-0.03 (-0.08 to 0.02)			100.00
Naltrexone (50 mg/d oral)										
Anton et al, ⁵⁹ 1999	12	Med	36	32	42	21	-0.14 (-0.30 to 0.03)			5.46
Ballidin et al, ⁶⁰ 2003	24	Low	55	1	59	3	0.03 (-0.03 to 0.09)			12.01
Chick et al, ⁵⁰ 2000	12	Med	70	15	64	15	0.01 (-0.11 to 0.13)			7.96
Gastpar et al, ⁶¹ 2002	12	Med	41	43	45	42	-0.03 (-0.18 to 0.12)			6.21
Guardia et al, ⁶² 2002	12	Med	53	48	54	47	-0.01 (-0.15 to 0.13)			6.84
Kiefer et al, ³⁹ 2003	12	Low	26	14	37	3	-0.28 (-0.44 to -0.11)			5.35
Killeen et al, ⁶³ 2004	12	Med	30	21	21	15	0.00 (-0.21 to 0.22)			3.95
Krystal et al, ⁶⁴ 2001	12	Med	255	163	140	69	-0.06 (-0.14 to 0.02)			10.81
Morley et al, ³⁸ 2006	12	Low	44	9	50	11	0.01 (-0.13 to 0.15)			6.72

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



Adapted from Willenbring ML, et al. *American Family Physician*. 2009. Volume 80, issue 1 and Willenbring ML. *Addiction Professional* 2008. <http://www.addictionpro.com>.

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**

Study Objective

- 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**

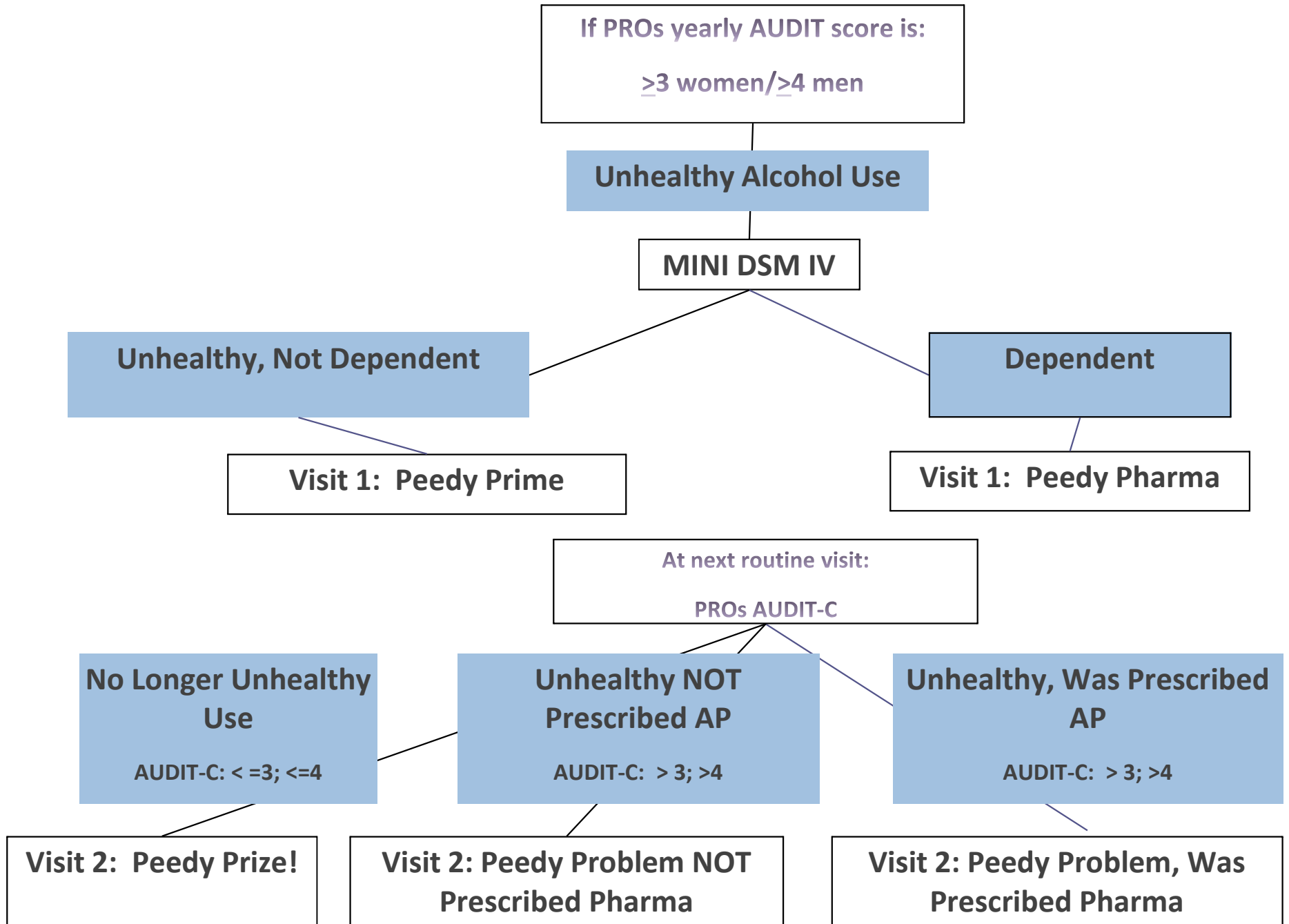
Audio Computer-Assisted Structured Interview was integrated into routine care. Eligible patients drank at unhealthy/hazardous levels defined by:

- **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).**



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

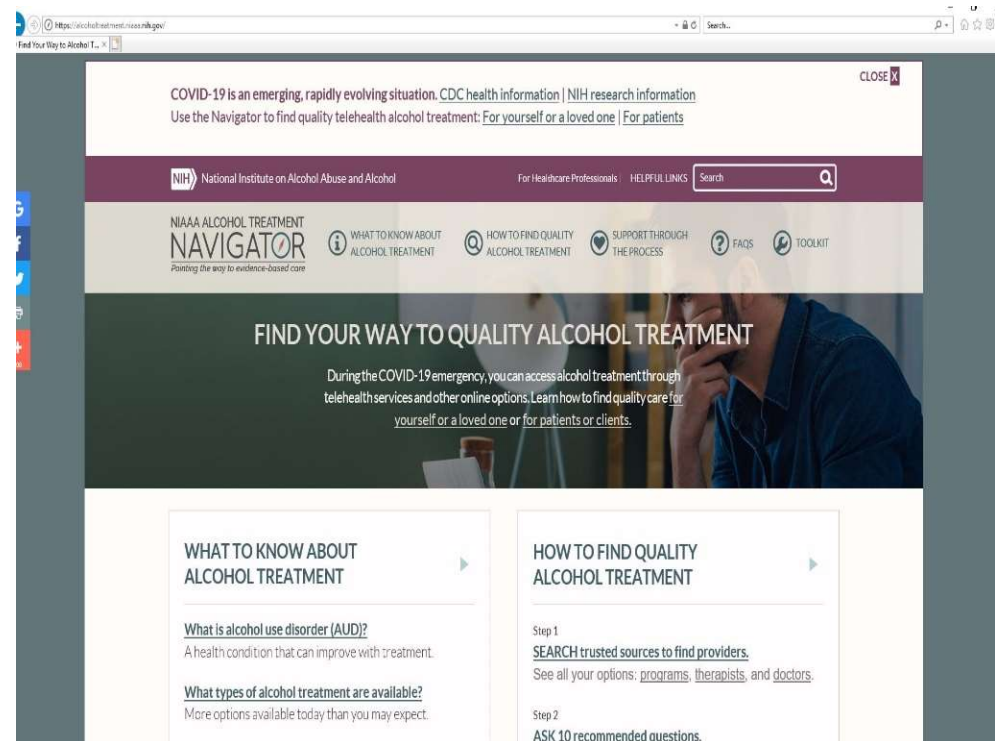
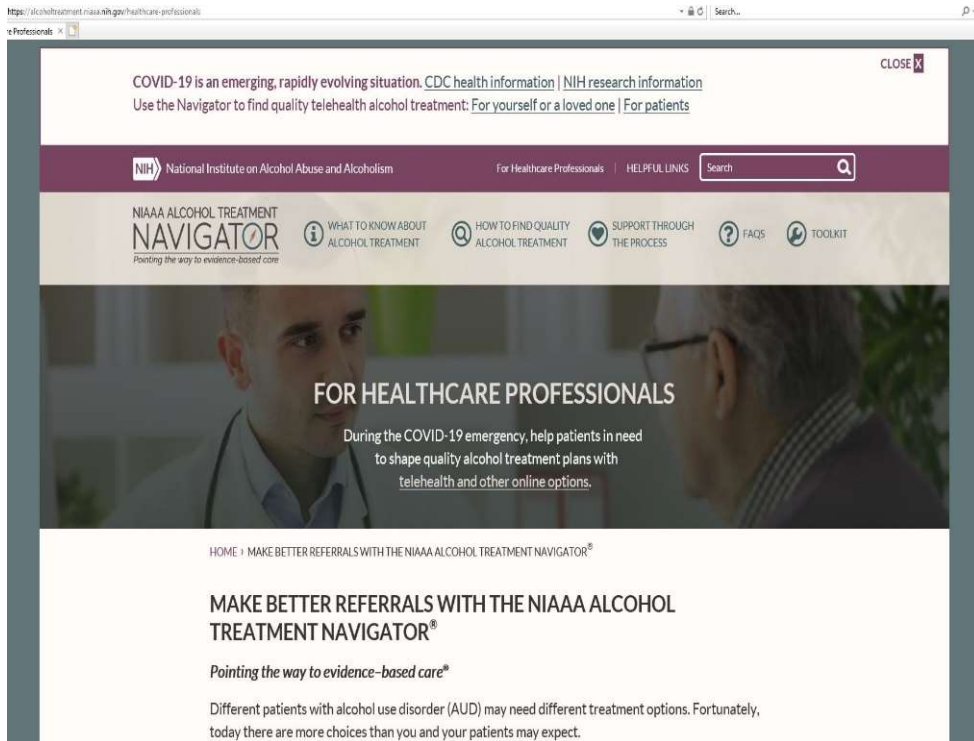
- Randomized trial across VA clinics comparing a stepped care model to treatment as usual for the treatment of AUD among PWH
- Stepped Care: Addiction medicine clinician provided medication management with alcohol pharmacotherapy; after 4 weeks, if no improvement, stepped up to MET; after 12 weeks if 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

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 Cutter, 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

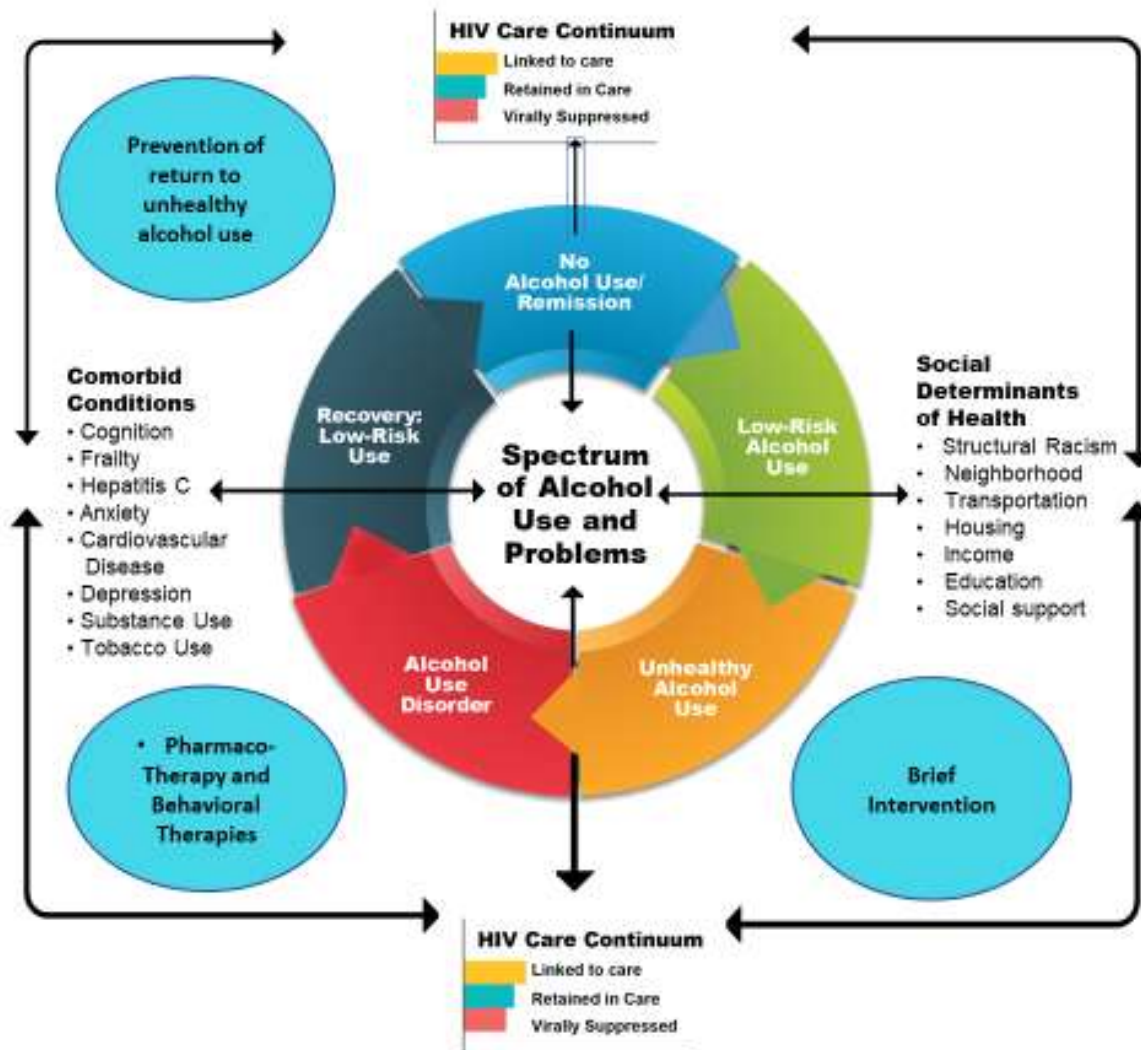
Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

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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The content in this presentation are those of the author(s) and do not necessarily represent the official views of, nor an endorsement, by HRSA, HHS, or the U.S. Government.



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