

Alcohol use among persons living with HIV

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Disclosures

No conflicts of interest or relationships to disclose

Outline

- Background and epidemiology
- Impacts of drinking on the HIV care cascade
- Alcohol, HIV and comorbid conditions
- Screening and treatment of alcohol problems among PLWH
- Discussion / Q&A

Background and epidemiology

Spectrum of alcohol use

DSM V Use Disorder:

Mild Moderate Severe

Nature of alcohol use

None/Never exceeds limit

At-risk

Harmful

Severe (dependent)

Chronic dependent

Recommended treatment

Screen annually

Brief intervention

Pharmacotherapy; Behavioral treatment

Definitions

- **Heavy drinking** (NIAAA): >4 drinks/day or >14 drinks/week (men); >3 drinks/day or >7 drinks/week (women)
- **Binge drinking** (NIAAA): >4 drinks (men) or >3 drinks (women) within ~2 hours, to increase BAC to 0.08%
- **At-risk/ hazardous drinking**: drinking above NIAAA limit without having incurred consequences
- **Harmful drinking / alcohol use disorder**: drinking that results in adverse health and other consequences

Guidelines

Dietary Guidelines



Persons living with HIV

?????

- A large meta-analysis of general population showed no protective effect of low level drinking¹

¹Stockwell et al, 2016; Image: CDC.gov

Background

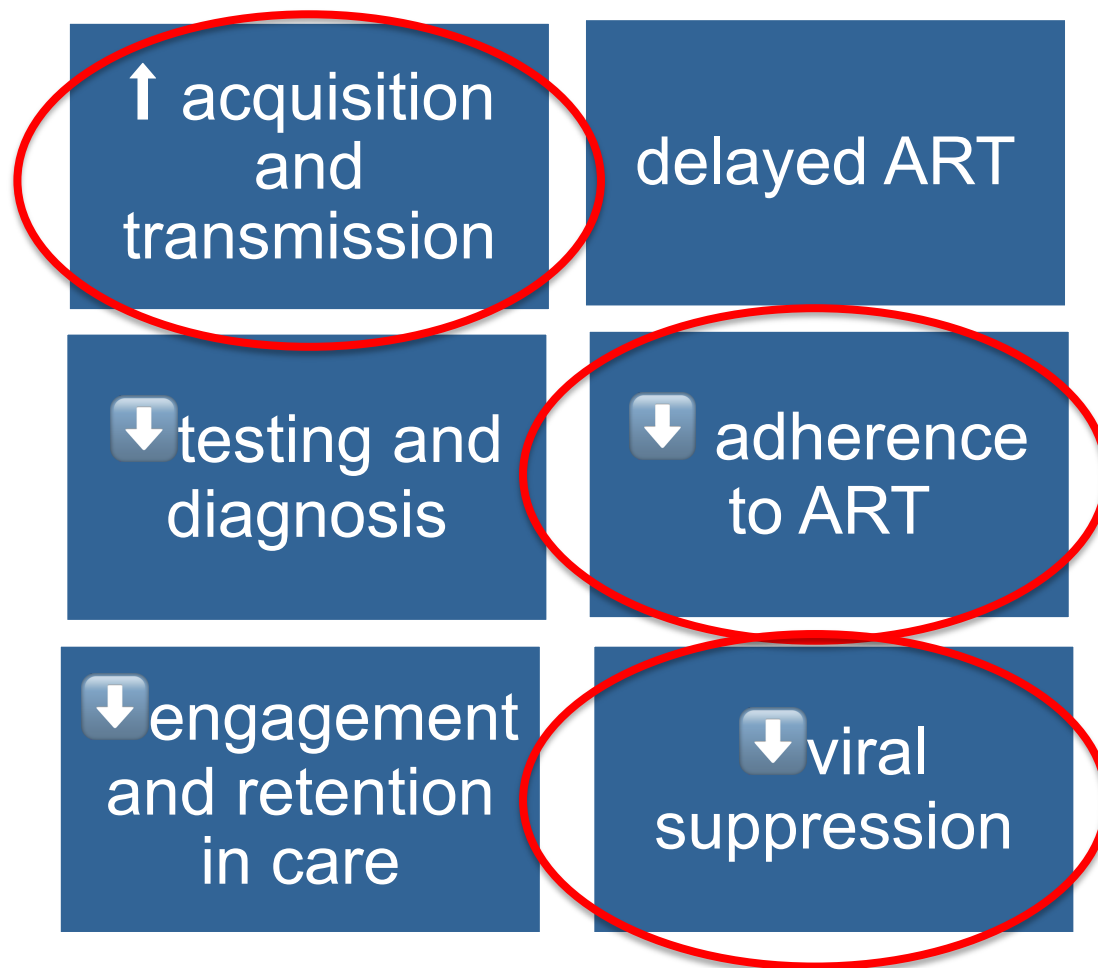
- *At same level of alcohol intake*, persons living with HIV (PLWH), compared to those who are uninfected,
 - have higher blood alcohol concentrations (BAC)
 - Are more likely to feel a "buzz"
- Among PLWH, those with unsuppressed viral load experience intoxication at lower levels of drinking than do those with suppressed viral load

Epidemiology of drinking among PLWH

- Any drinking: ~40-67%
- Unhealthy drinking: up to 27% of PLWH in care, **at least 2X that of general population**
- Binge drinking: ~34%
- Increased risk:
 - Depression** and other MH disorders (bidirectional)
 - Other substance use**, e.g., cocaine and heroin
 - Lower educational level
 - Psychosocial stressors
 - Younger age
 - Men who have sex with men
 - Sex workers

Drinking and the HIV care cascade

Alcohol and the HIV Care Cascade



Alcohol increases HIV acquisition risk

- Condomless sex¹
- Anal sex (in women: binge drinking associated with 3x rate anal sex)²
- Multiple partners
- More injection drug use

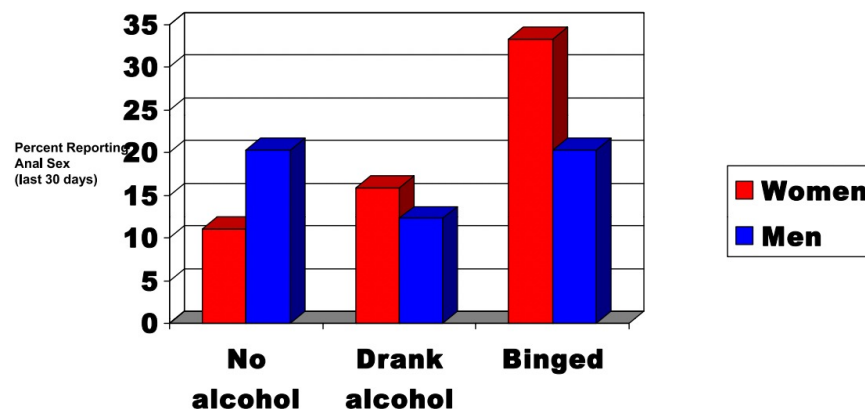


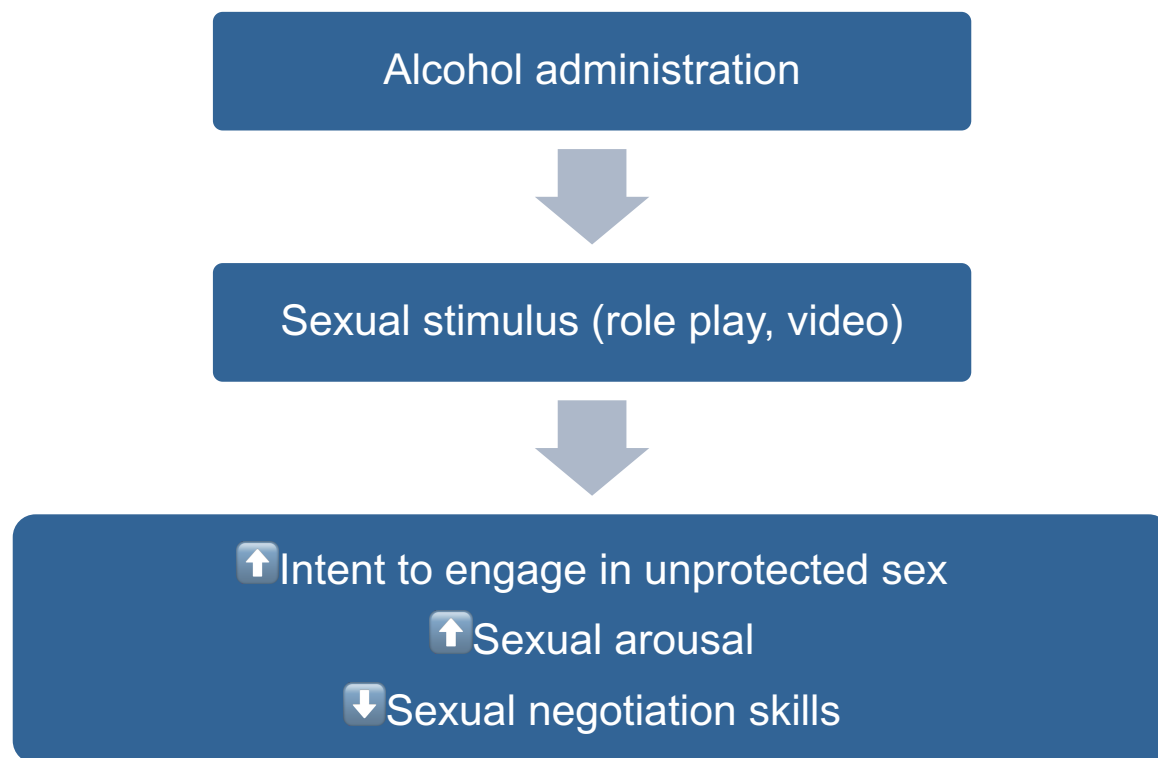
Fig. 1. Gender differences in receptive anal sex as a function of recent alcohol use.

Also: alcohol associated with decreased ART adherence-> decreased viral suppression and increased viral resistance

¹ Shuper et al, J Acquir Immune Defic Syndr. 2017 . ²Hutton et al, Alcoholism Clin Exp Res 2016

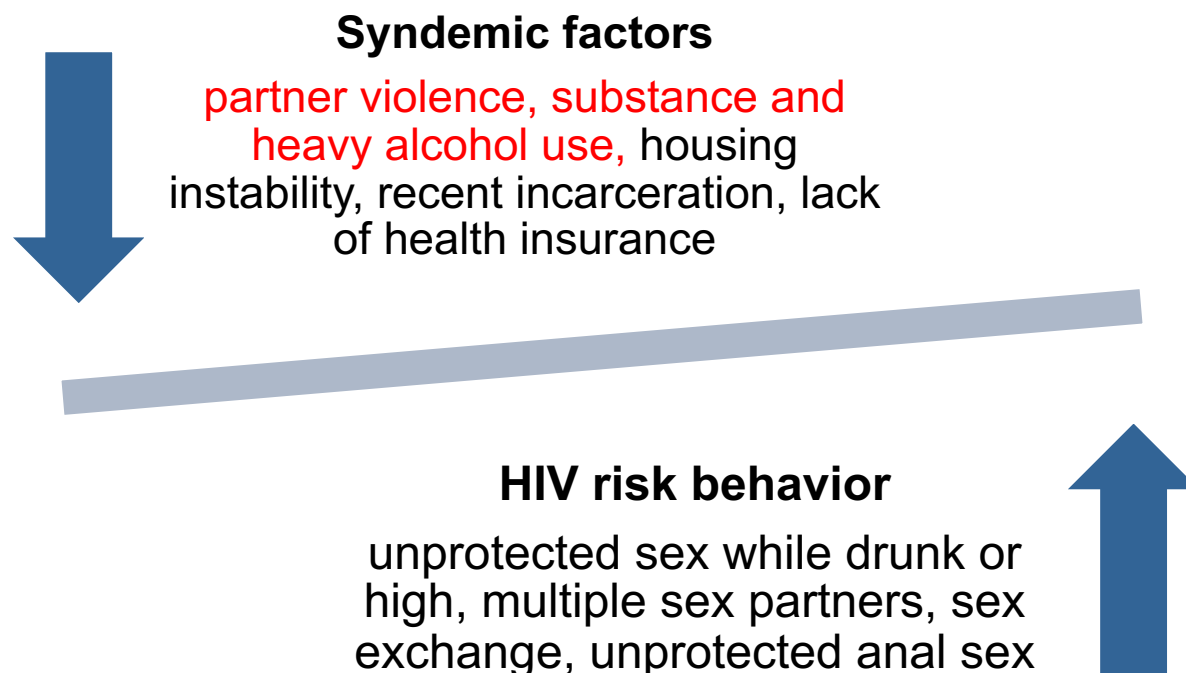
Alcohol as causal factor in HIV acquisition

- Meta-analysis of 30 studies (N=~4000) that assigned participants to alcohol vs placebo/control, involved sexual stimulus, assessed sexual decision-making



Alcohol: one of many syndemics that affect HIV acquisition risk

- ~800 uninfected women followed for 18 months

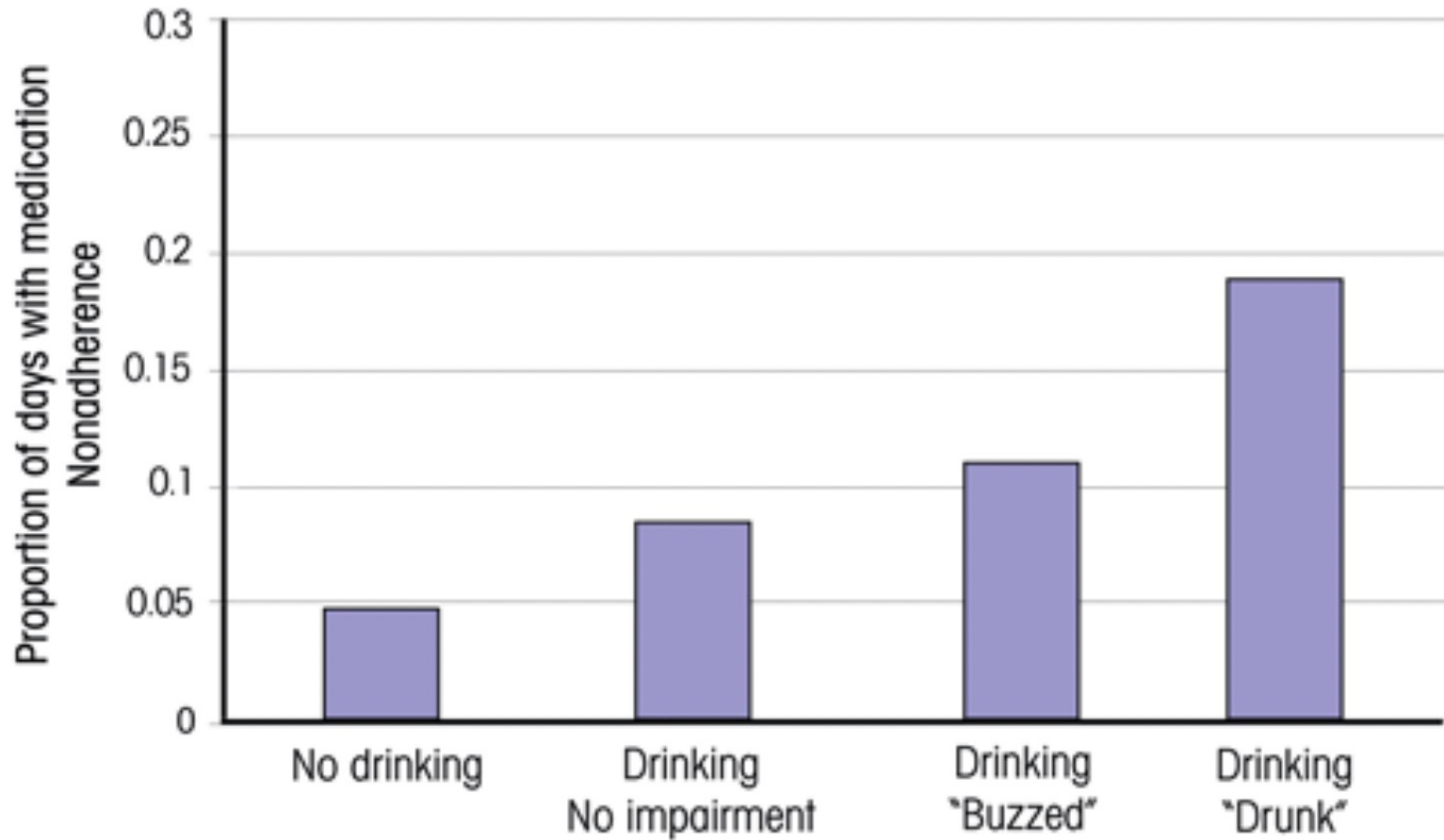


***Associated with all risk behaviors**

Multiple studies show decreased adherence to ART among those who drink

Study	Population / measures	Result
Cook et al, JGIM 2001	<ul style="list-style-type: none"> • 212, HIV+ • Problem drinking: binge, heavy, AUDIT-C >8 	<ul style="list-style-type: none"> • Problem drinkers more likely to report taking ART off schedule (45% vs 26%)
Samet et al, Alcohol Clin Exp Res. 2004	<ul style="list-style-type: none"> • 267, 81% men, HIV+ on ART, hx alcohol problems • Adherence measured by 3-day self-report • Past-month alcohol use (none, moderate, at-risk) 	<ul style="list-style-type: none"> • Abstinence vs at-risk drinking: adherence 3.6X more likely • Abstinence vs moderate drinking: adherence 3.0X more likely
Braithwaite et al, Alcohol Clin Exp Res. 2005	VA, HIV + and HIV -	<p>More missed doses with</p> <ul style="list-style-type: none"> • binge drinking > non-binge drinking > abstaining • Drinking days > post-drinking days > nondrinking days
Chander et al, JAIDS 2006	<ul style="list-style-type: none"> • >1400, HIV+, 64% men • None, moderate, hazardous use 	AOR for 2-week non-adherence was 0.46 (hazardous) and 0.78 (moderate)

Dose-response effect on adherence



Alcohol and ART adherence

- More evidence of dose –response association with adherence

Initial alcohol use risk groups ^a	N	Initial Adherence (% days) Mean (SD) ^b
Non-drinking (AUDIT-C = 0)	10,274	86.7% (20.4%)
Lower-level use (AUDIT-C = 1–3, 1–2 women)	8384	85.2% (21.1%)
Medium-level use (AUDIT-C 4–5, 3–5 women)	1557	83.4% (22.0%)
High-level use (AUDIT-C 6–7)	469	81.2% (23.0%)
Very high-level use (AUDIT-C 8–12)	591	76.8% (25.8%)

^aDefined consistent with clinically-relevant cut-points identifying increased risk of morbidity and mortality

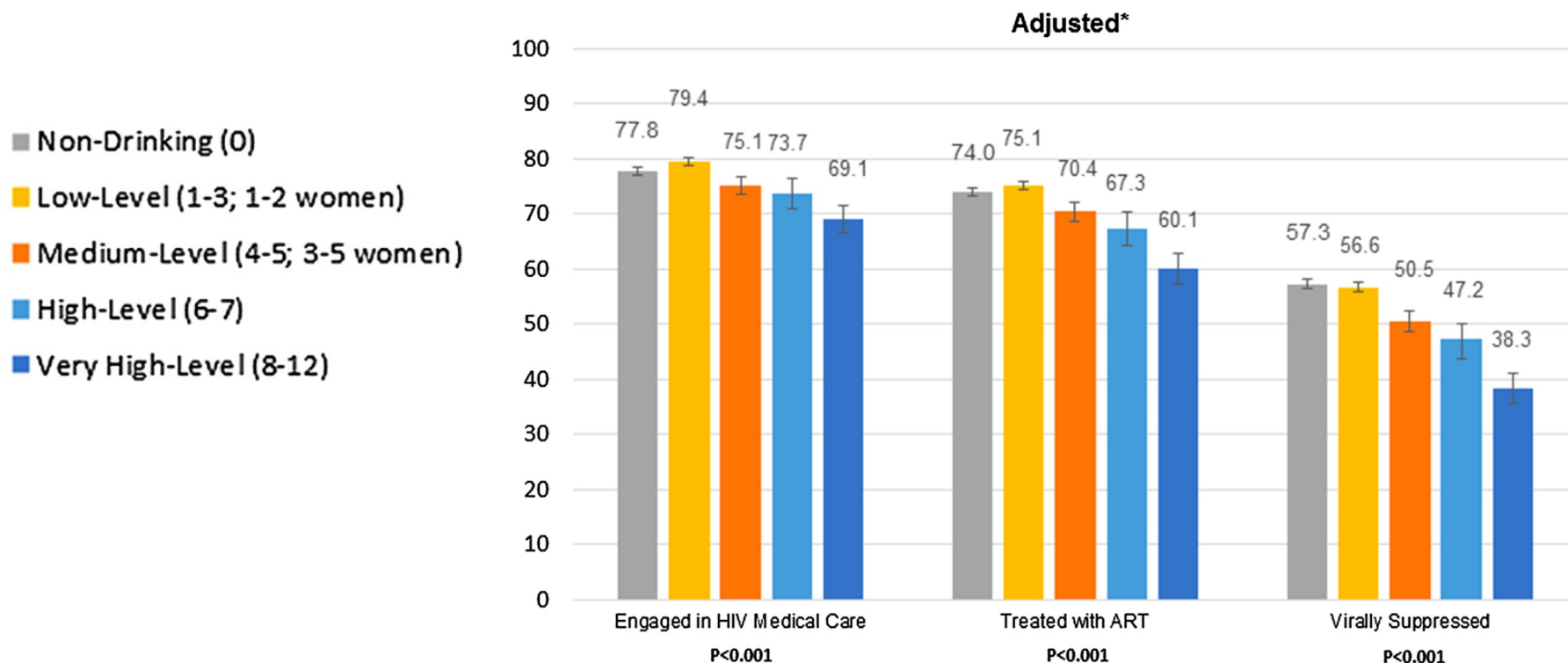
^bNon-parametric test for trend $p < 0.001$, $z = -13.92$)

Drinking and viral suppression

- Multiple studies have shown that drinking is associated with lower rates of viral suppression
- E.g., Chander et al: cohort of ~1400 PLWH in Baltimore, 1/3 with recent illicit substance use
- Those with *at-risk drinking* were 24% less likely to have viral suppression, but effect was attenuated by adherence
- Those with *alcohol + illicit substance use* were 50% less likely to have viral suppression

Longitudinal care continuum data: Veterans Aging Cohort Study

- EHR data from 2008-2014, >33,000 Veterans with HIV
- Level of drinking and HIV care continuum within one year

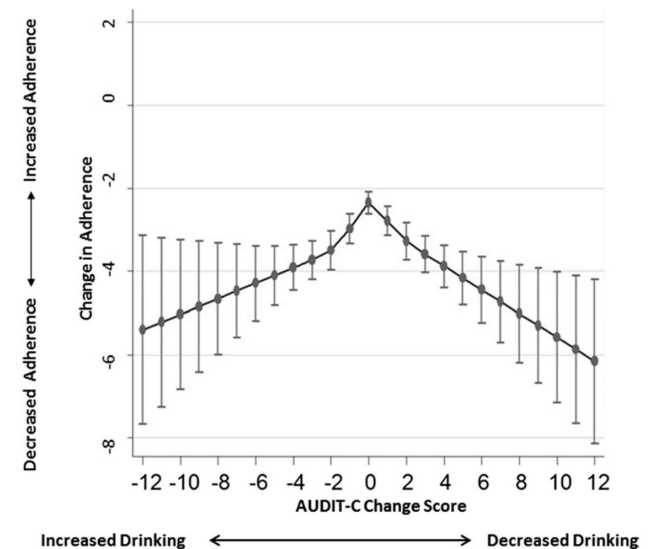


*Adjusted for race, ethnicity, gender, fiscal year of AUDIT-C screening, age, and any mental health and non-alcohol substance use disorders

Changes in drinking over time may affect adherence and HIV severity

- VA sample, >21,000 PLWH
- Adherence highest with stable drinking over time
- Similar study: stable drinking associated with greatest improvements in HIV severity
- Implications: Does unstable alcohol use reflect AUD? Is the higher of the two paired AUDIT-C values the strongest determinant of adherence, regardless of order? Is change in drinking a proxy for other life/health changes?

Mean change in percent days adherent by change in AUDIT-C score, adjusted for demographics and baseline adherence



*Adjusted for demographics and baseline adherence (Primary Model)

Mechanisms of effects

- Many potential confounders that are difficult to fully evaluate
 - Psychological processes: low health-related motivation/ self-efficacy, depression
 - Social factors: unstable housing, access to medical care
- Connections between drinking and adherence
 - Cognitive impairment/ forgetting doses
 - Concerns about alcohol interacting with medications
- Direct biological influences on viral suppression?
 - Microbial translocation in gut
 - Systemic inflammation/ immune activation
 - Viral replication: mixed results in macaques and people
 - Longer-term, larger studies needed

Summary: alcohol, adherence and viral suppression

- Any drinking is associated with decreased adherence, and there appears to be a dose-response
- At-risk/hazardous drinking associated with decreased viral suppression, but effect mediated by adherence +/- other unmeasured factors
- Combined alcohol and other substance use have greater negative effects on care cascade

Alcohol, HIV and comorbid conditions

Both HIV and alcohol use associated with biologic aging and frailty

- PLWH experience age-related comorbid conditions and organ system decline at earlier ages than similar noninfected individuals¹
- Among PLWH, lifetime alcohol use is associated with greater **biologic age and frailty**²
- Common conditions associated with alcohol use occur earlier in PLWH *in spite of viral suppression*

Alcohol worsens these comorbid conditions in PLWH

- Hypertension, coronary and cerebrovascular disease
- *Diabetes and metabolic derangements
- Viral hepatitis, tuberculosis
- Dementia/cognitive impairment
- Peripheral neuropathy
- Cardiomyopathy
- Pneumonia and chronic pulmonary disease
- Cancers
- Falls, fractures, bone disease

★ **Alcohol use** ★

May speed progression
Affects care

*may depend on "dose"

Mechanisms of comorbidity: biological factors

Immune
senescence

Precocious aging

Inflammation

Oxidative stress

Hypercoagulability

Mechanisms of comorbidity: syndemic factors

Tobacco

Stronger association with poor health outcomes among PLWH

Substance use

- ↓ Engagement with HIV treatment
- ↑ HIV consequences

Depression, anxiety, trauma

- ↓ Engagement with HIV treatment
- ↑ HIV consequences

Stigma

Chronic psychosocial stress

Disproportionate impacts on vulnerable populations

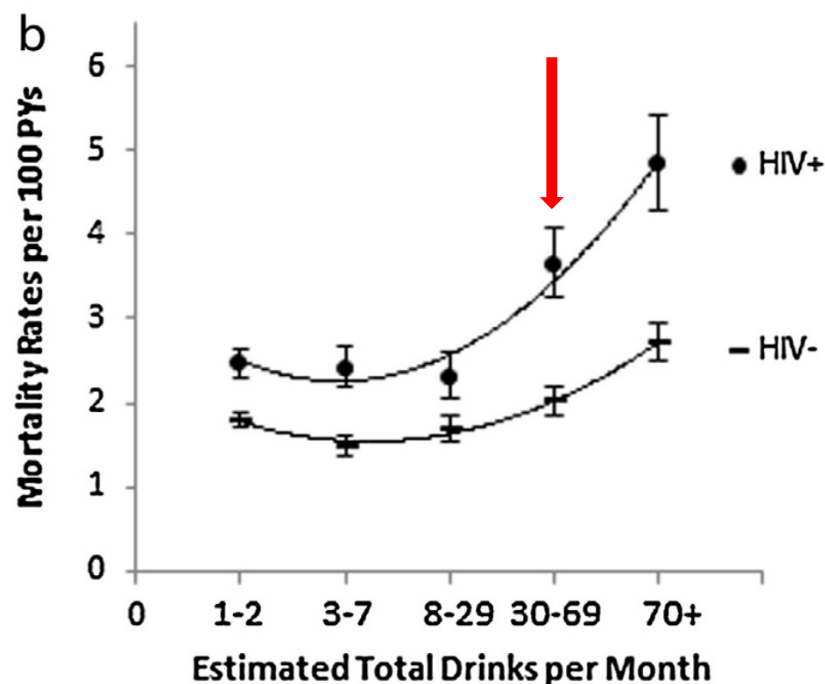
Alcohol and mortality

- Alcohol is associated with increased mortality among general population
- Among PLWH,
 - over 1 drink/day may increase mortality¹
 - HR for mortality of 1.4 for heavy compared to non-drinking²
 - Modeling study of adherence effects showed that daily hazardous drinking would decrease survival by 6.4 years³

Alcohol and mortality

Alcohol's association with mortality differs by HIV status:

- **HIV:** Increased mortality associated with AUDIT-C score ≥ 4 and ≥ 30 drinks/month
- **No HIV:** Increased mortality associated with AUDIT-C score ≥ 5 and ≥ 70 drinks/month



Mechanisms of mortality for PLWH who drink

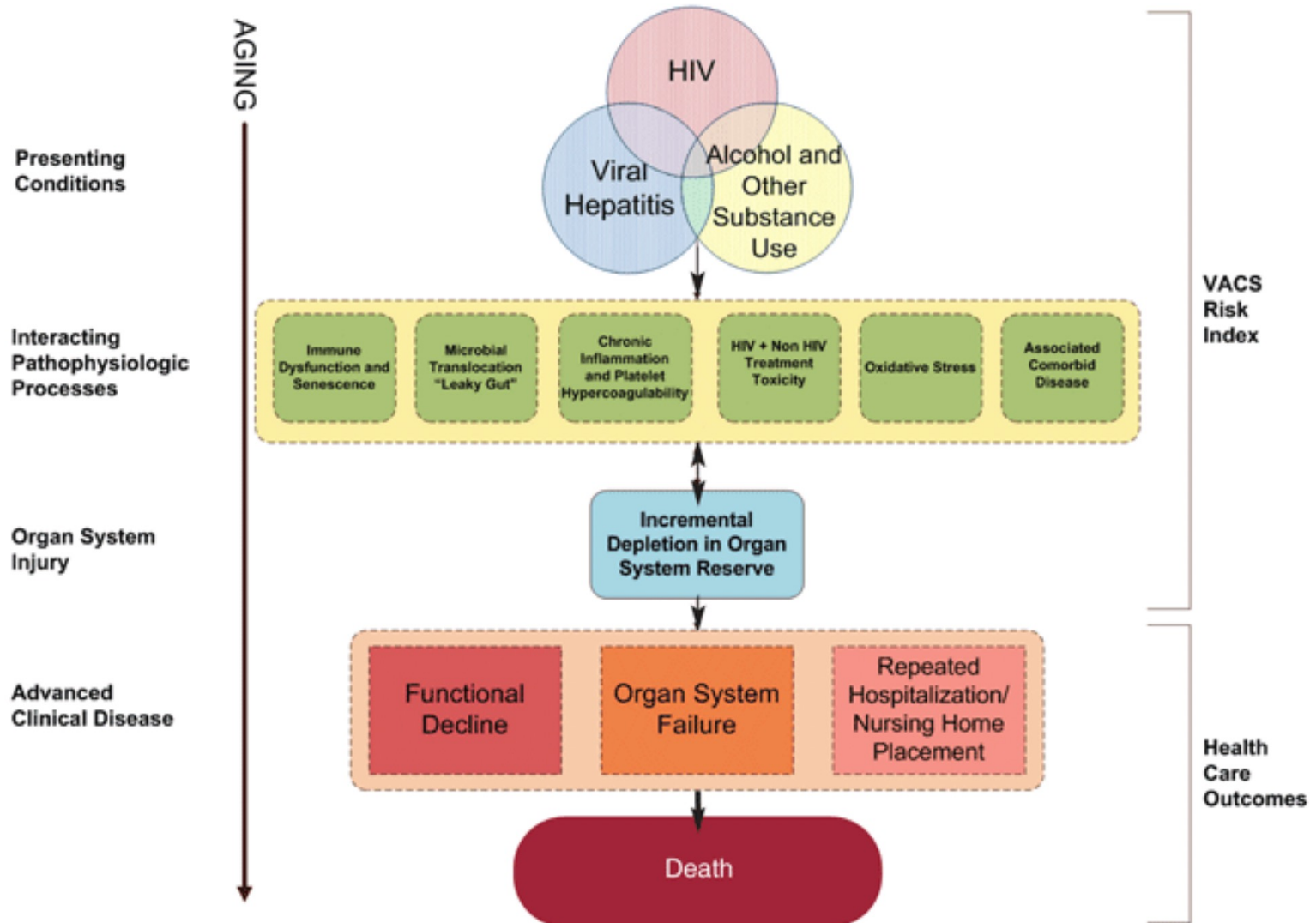
- Direct effects on HIV mortality (e.g., immunosuppression)

- Increased toxicity of ART

- Increased non-HIV, non-ART mortality

- Decreased adherence to ART

Effects of alcohol, HIV and aging



Screening and treatment of alcohol problems among PLWH

Screening and treatment

- Patients with HIV and their providers perceive alcohol problems as relatively low priority
- Providers often fail to ask about current alcohol consumption
- Providers *very often* fail to ask about *past* alcohol consumption
- Rates of treatment for alcohol are low, e.g. 13.7% of women with HIV who consumed >12 drinks/week had received any formal treatment in last 6 months
- **Large gaps in screening, treatment, knowledge and research**

Screening for alcohol use

- **Who to screen?**

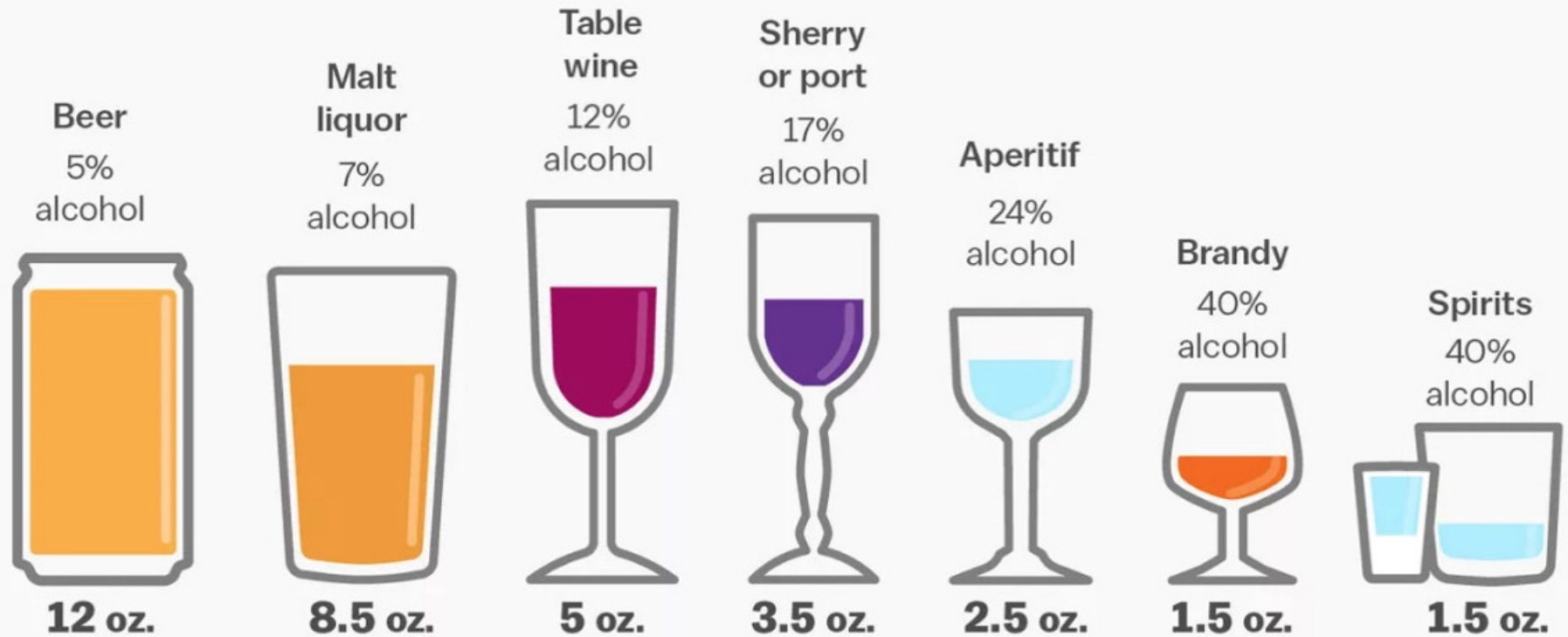
All patients presenting for care

- If negative, repeat annually
- If positive, repeat at every visit

- **Why screen?**

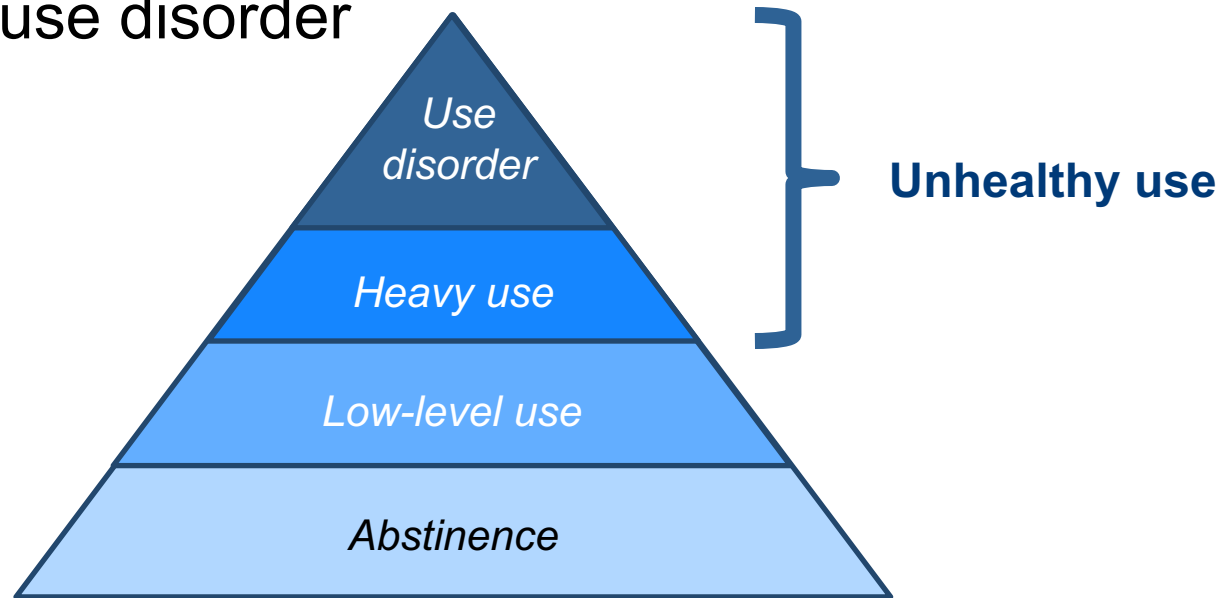
- High prevalence
- Allows for earlier diagnosis
- Provides opportunities for education
- Intervention/ treatment available

A standard “drink” is 14 grams pure alcohol



Single –item screen for unhealthy alcohol use

- How many times in the last year have you had 4 or more drinks in one day (5 or more for men)?
- 82% sensitivity, 79% specificity for unhealthy alcohol use
- Follow with questions about frequency and quantity and assess for use disorder



AUDIT-C screen for unhealthy alcohol use

- Positive screen: ≥ 3 (women/other) or ≥ 4 (men)

1. How often do you have a drink containing alcohol?

- | | |
|--|---|
| <input type="checkbox"/> Never | <input type="checkbox"/> 2-3 times a week |
| <input type="checkbox"/> Monthly or less | <input type="checkbox"/> 4 or more times a week |
| <input type="checkbox"/> 2-4 times a month | |

2. How many standard drinks containing alcohol do you have on a typical day?

- | | |
|---------------------------------|-------------------------------------|
| <input type="checkbox"/> 1 or 2 | <input type="checkbox"/> 7 to 9 |
| <input type="checkbox"/> 3 to 4 | <input type="checkbox"/> 10 or more |
| <input type="checkbox"/> 5 to 6 | |

3. How often do you have six or more drinks on one occasion?

- | | |
|--|--|
| <input type="checkbox"/> Daily or almost daily | <input type="checkbox"/> Less than monthly |
| <input type="checkbox"/> Weekly | <input type="checkbox"/> Never |
| <input type="checkbox"/> Monthly | |

Quantity, frequency and diagnosis

- HOW OFTEN and MUCH do you drink?
- How many days do you drink in a typical week?
- How many drinks do you have on a typical day?
- WHAT SIZE is your drink?
- WHAT do you drink?
- DSM-V criteria for alcohol use disorder: compulsive use, continued use despite harm, cravings, consequences (the “4 Cs”)

DSM-V criteria for substance use disorder

Clinically significant impairment and ≥ 2 criteria within 12 months:

- Alcohol taken in larger amounts than intended
- Persistent desire or unsuccessful effort to cut down
- Great deal of time spend obtaining, using, or recovering from alcohol
- Craving or urge to use
- Recurrent use resulting in failures at work, home, or school
- Continued use despite social or interpersonal issues
- Important activities given up
- Recurrent use in dangerous situations
- Recurrent use despite physical/psychological consequences
- Tolerance or withdrawal symptoms

Spectrum of alcohol use

DSM V Use Disorder:

Mild Moderate Severe

Nature of alcohol use

None/Never exceeds limit

At-risk

Harmful

Severe (dependent)

Chronic dependent

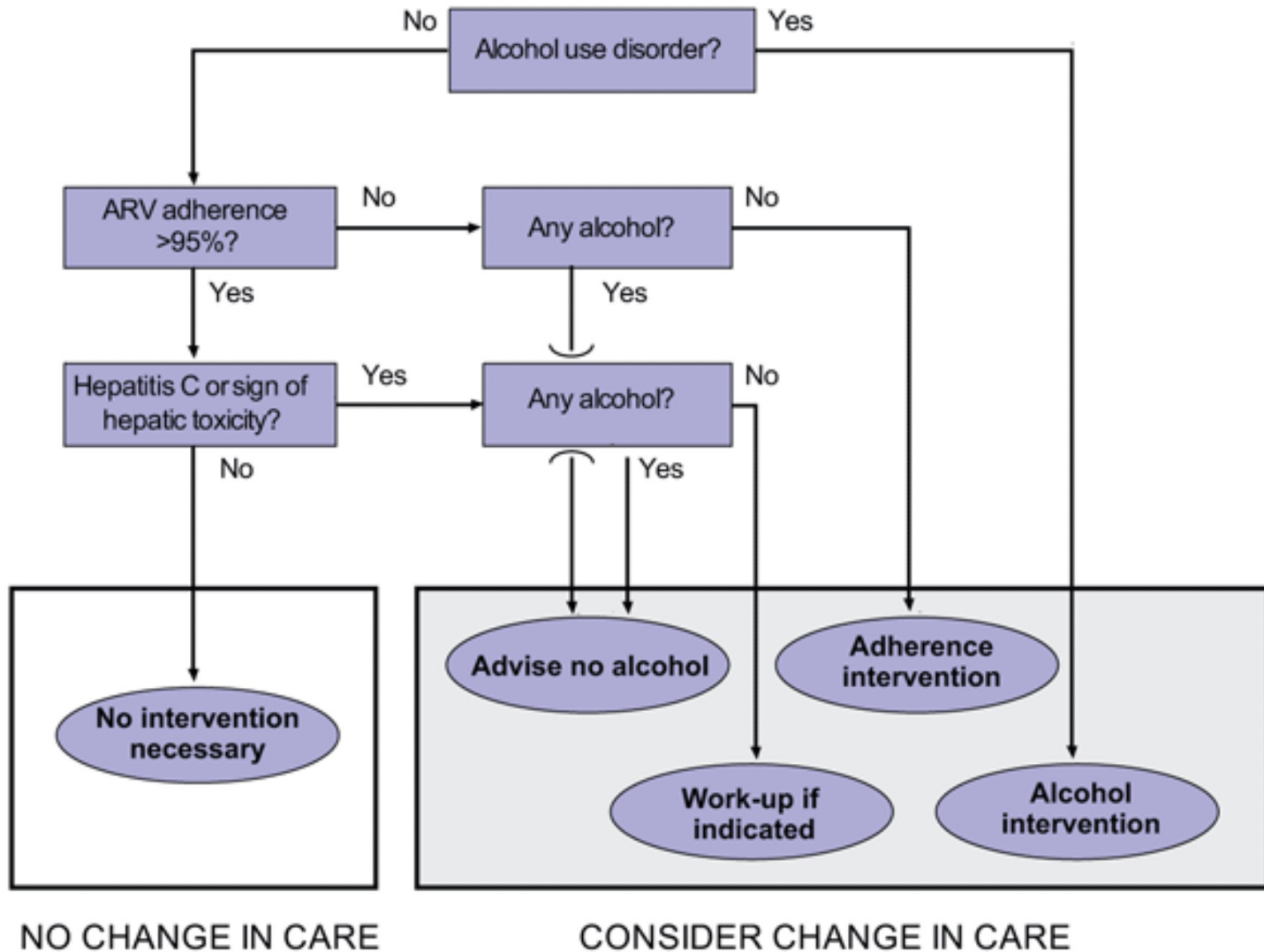
Recommended treatment

Screen annually

Brief intervention

Pharmacotherapy; Behavioral treatment

Example approach to integrating alcohol screening and tx into clinical care of PLWH



Targets of interventions

- Drinking behavior
- Adherence to ART
- Sexual risk behavior
- But, limited and mixed data to date

What is a brief intervention (BI)?

Step	Example
Raise the subject	“I see that you sometimes drink more than 5 drinks per day. Can we talk about your drinking?”
Provide feedback	“You’re drinking more than is good for your health.” “Drinking alcohol is associated with decreased adherence and progression of HIV.”
Enhance motivation	“What do you like about drinking? What do you like less?” “How important is it to you right now to cut back on your drinking or stop completely?”
Negotiate a plan	“What change would you like to make between now and your next visit?”

Medications for alcohol use disorder

- Naltrexone/Vivitrol ® (PO or IM)
- Acamprosate
- Disulfiram
- Ttopiramate (off-label)
- Gabapentin (off-label)

Behavioral treatments and HIV- mixed data

- Samet et al, Antiviral therapy 2005: 4 sessions of MI
 - No effect on ART adherence or drinking
- Parsons et al, JAIDS 2007: MI/CBT
 - Improved adherence and viral suppression
 - No effect on drinking
- Chander et al, JAIDS 2015: 2 MI sessions
 - No effect on ART adherence or viral suppression
 - 58% less likely to have drinking days (heaviest drinkers: no benefit)
 - 61% less likely to have unprotected vaginal sex
 - No effect on binge drinking, drinks per episode or HIV outcomes
- *BI may be effective, but more intensive interventions needed for those with heaviest use*
- *To impact HIV outcomes, need to reduce quantity of drinking*

Medications and HIV- limited data

- 51 PLWH, heavy drinking/ AUD and <95% ART adherence
- Randomized to XR-NTX + counseling vs placebo + counseling x 24 weeks
- No difference in >95% ART adherence (primary outcome), HIV VL or CD4 count
- XR –NTX decreased heavy drinking days

Treatment delivery

- Challenges when those with HIV, MH disorders and alcohol use must navigate multiple care delivery systems
- Good communication and shared decision-making important
- Integrated HIV clinics are well positioned to treat AUD
 - Integrated services including mental health
 - Outreach and case management
 - Prescription medication coverage

Conclusions and discussion

Conclusions

- Any and unhealthy drinking are common among PLWH
- Alcohol use impacts every level of HIV care continuum, including transmission, ART adherence and viral suppression
- Alcohol exacerbates many comorbid conditions of HIV; comorbid conditions occur earlier
- No clear “safe level” of drinking for PLWH
- Screen everyone with HIV for *past or current* drinking
- Offer range of treatments for problem drinking and AUD
- Offer psychosocial and other ART adherence supports

Discussion

- Q&A
- What has your experience been regarding PLWH who drink? What approaches have been more or less effective?

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