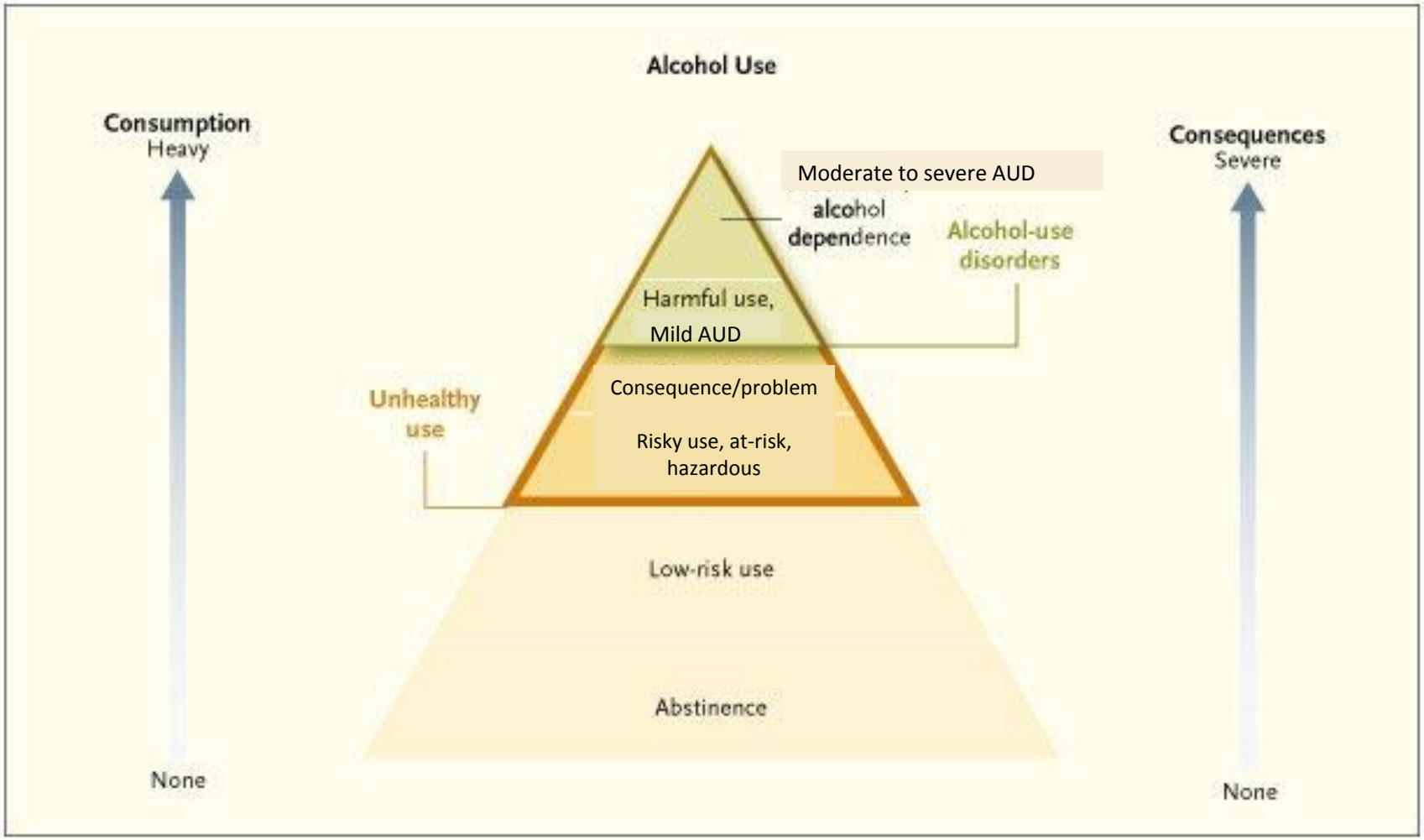
Risks, Consequences, and Addressing Unhealthy Alcohol Use in People with HIV Infection

Richard Saitz MD MPH FACP DFASAM
Professor and Chair, Community Health Sciences

Support: U01AA020784, U24AA020778, U24AA020779

Consortiums for HIV/AIDS and Alcohol Research Translation (CHAART)
National Institute on Alcohol Abuse and Alcoholism National Institutes of Health, Bethesda, MD

Unhealthy Use



The NEW ENGLAND JOURNAL of MEDICINE

URBAN ARCH 2016

Saitz R. New Engl J Med 2005;352:596.

This is substance abuse

ISAJE International Society of Addiction Journal Editors

National Addiction Centre
4 Windsor Walk
London
SE5 8AF, UK

ADDICTION TERMINOLOGY STATEMENT

The International Society of Addiction Journal Editors recommends against the use of terminology that can stigmatize people who use alcohol, drugs, other addictive substances or who have an addictive behavior.

Rationale: Terms that stigmatize can affect the perception and behavior of patients/clients, their loved ones, the general public, scientists, and clinicians (Broyles et al., 2014; Kelly, Dow & Westerhoff, 2010; Kelly, Wakeman & Saitz, 2015). For example, Kelly and Westerhoff (2010) found that the terms used to refer to individuals with substance-related conditions affected clinician perceptions. Clinicians who read a clinical vignette about "abuse" and an "abuser" agreed more with notions of personal culpability and an approach that involved punishment than did those who read an identical vignette that replaced "abuse" and "abuser" with "substance use disorder" and "person with a substance use disorder."

ISAJE is aware that terminology in the addiction field varies across cultures and countries and over time. It is thus not possible to give globally relevant recommendations about the use or non-use of specific terms. "Abuse" and "abuser" or equivalent words in other languages should, however, in general be avoided, unless there is particular scientific justification (an example of scientific justification of the use of "abuse" is when referring to a person who meets criteria for a Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, alcohol abuse; that person would be said to have "alcohol abuse"). Another example of stigmatizing language is describing people as "dirty" (or "clean") because of a urinalysis that finds the presence (or absence) of a drug (Kelly, Wakeman & Saitz, 2015). Instead, the test results and clinical condition should be described.

The above was approved by the International Society of Addiction Journal Editors at its 2015 annual meeting (Budapest, Hungary, August 31-September 2, 2015).

References

Prevalence in US PLWH

- Unhealthy use 19%-22% of PLWH receiving care
  - Higher estimates in single clinical samples (31-42%)
- Alcohol use disorder 16%
- Similar to general US population
- High risk of both HIV and unhealthy alcohol use
  - MSM
  - racial/ethnic minorities
  - persons who inject drugs
  - sex workers
  - persons of low socioeconomic status

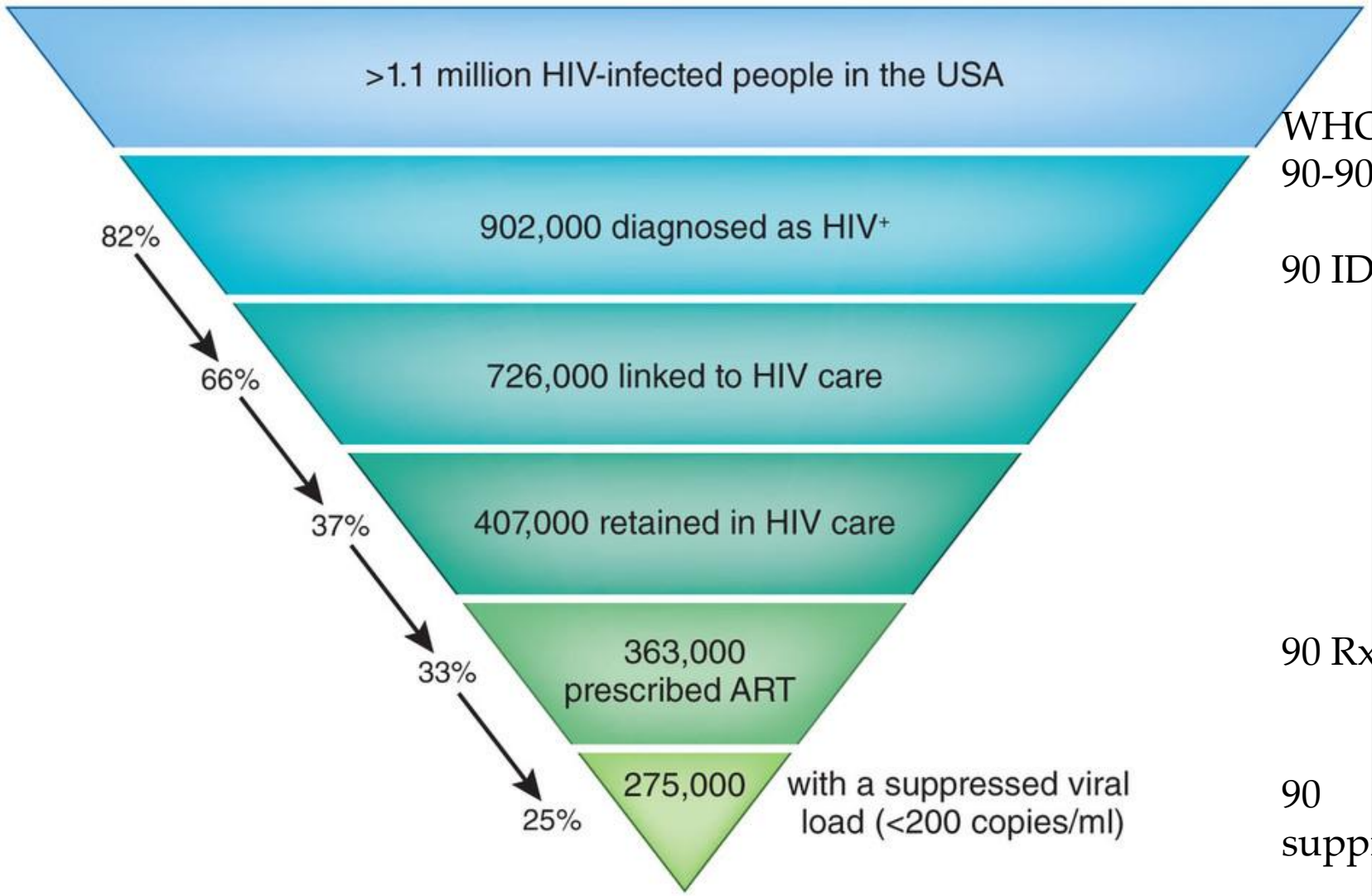
Bing et al. Arch Gen Psych 2001;58:721
McGinnis et al. Alcohol Clin Exp Res 2013;37:435
Surah et al. Int J STD AIDS 2013;24:517
Samet et al AIDS Res Hum Retro 2004;20:151

Risk for transmission

- Alcohol use associated with incident HIV
- Alcohol associated with sex risk behaviors
- Meta-analysis of RCTs of alcohol vs. placebo or no alcohol
  - Stronger intentions to engage in unprotected sex
  - Weaker sexual communication and negotiation skills
  - Higher levels of sexual arousal

Scott-Sheldon et al. AIDS Behav 2016;20:S19
Maisto & Simons AIDS Behav 2016;20:S158

HIV Treatment Cascade



WHO 2020
90-90-90

90 ID'd

90 Rx'd

90 suppressed

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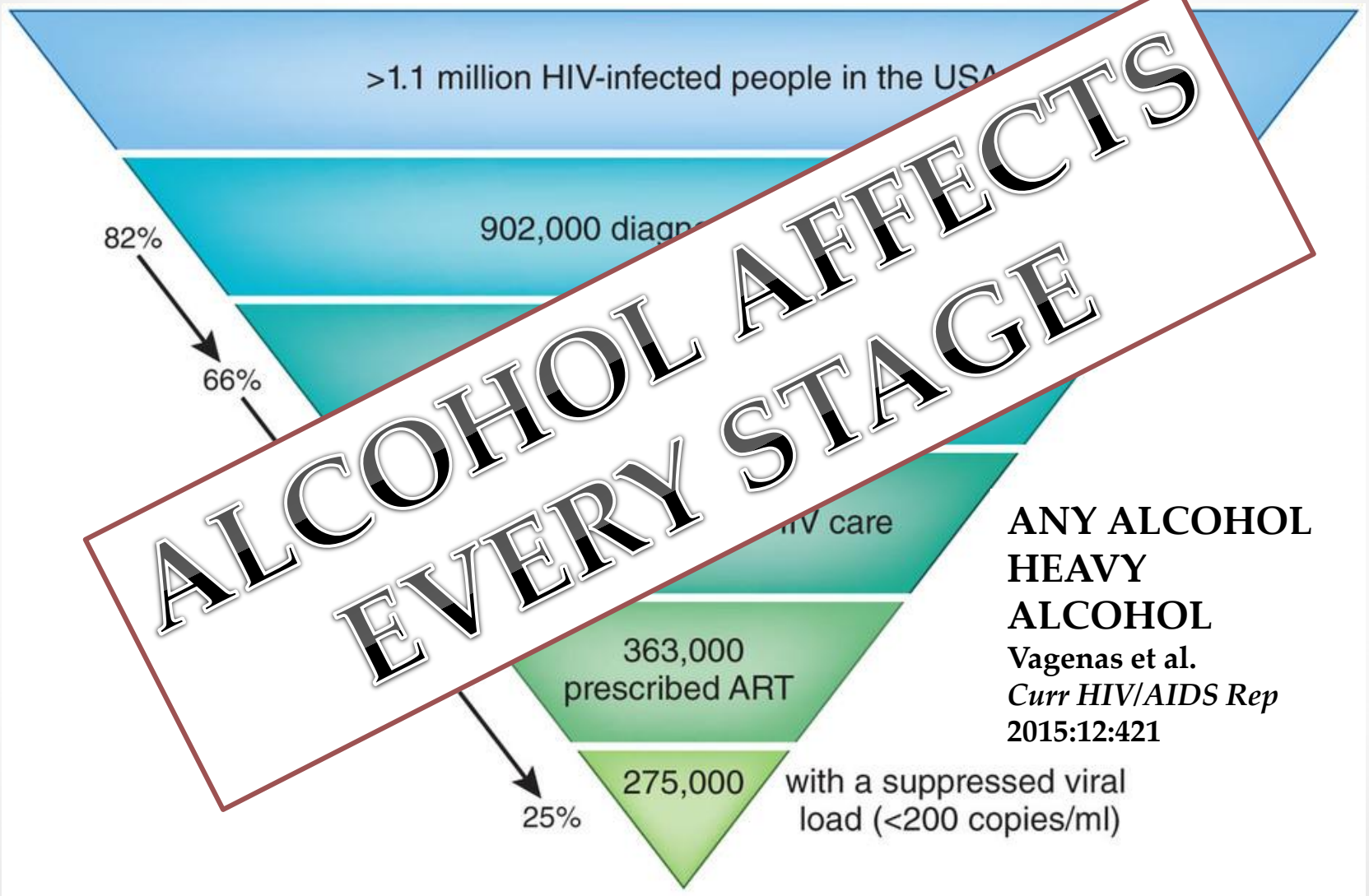
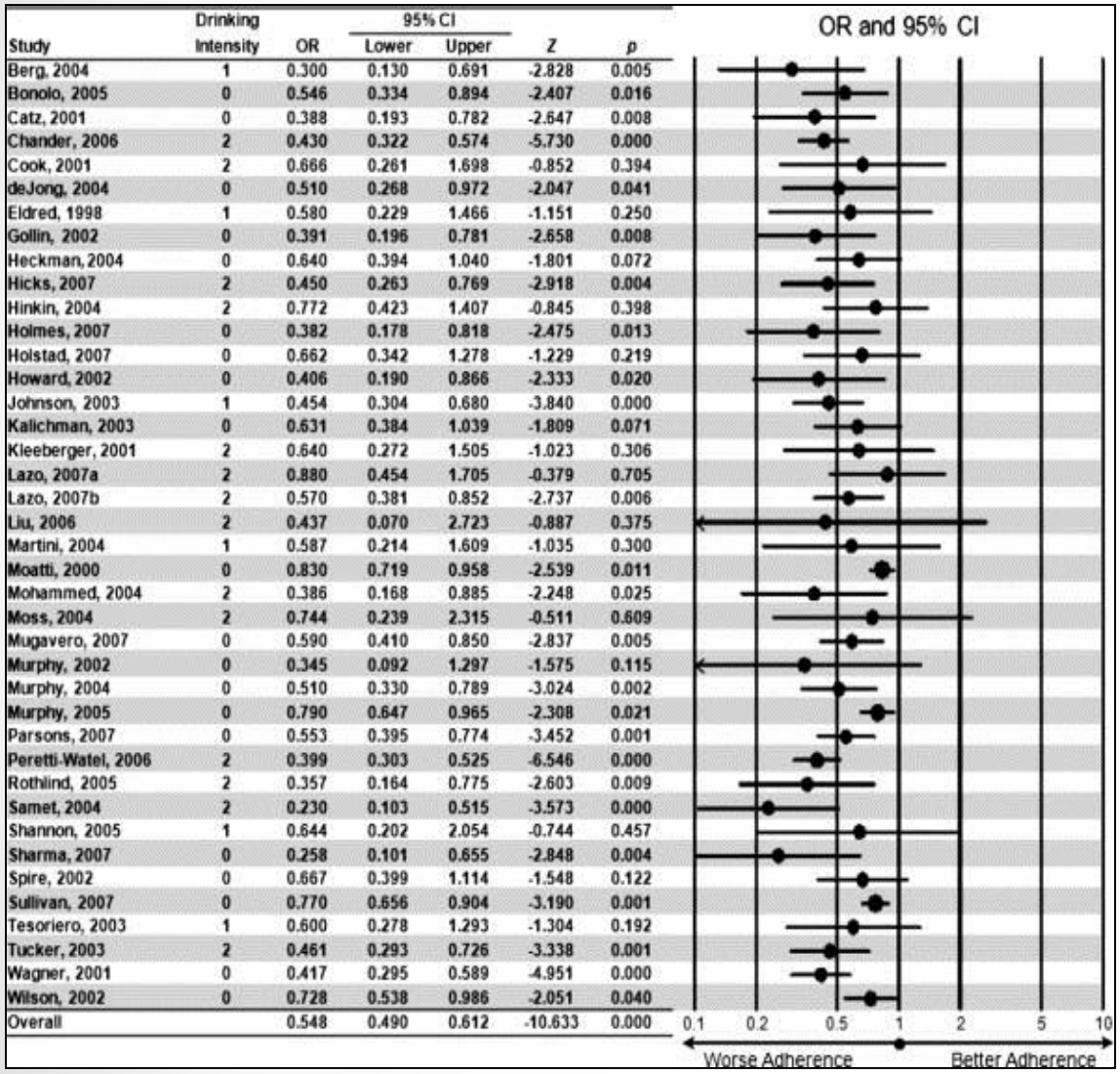
Fauci et al. Nature Immunol 2013;14:1104

HIV Treatment Cascade



Alcohol and ART Adherence



Study	Drinking Intensity	OR	95% CI Lower	95% CI Upper	Z	p
Berg, 2004	1	0.300	0.130	0.691	-2.828	0.005
Bonolo, 2005	0	0.546	0.334	0.894	-2.407	0.016
Catz, 2001	0	0.388	0.193	0.782	-2.647	0.008
Chander, 2006	2	0.430	0.322	0.574	-5.730	0.000
Cook, 2001	2	0.666	0.261	1.698	-0.852	0.394
deJong, 2004	0	0.510	0.268	0.972	-2.047	0.041
Eldred, 1998	1	0.580	0.229	1.466	-1.151	0.250
Gollin, 2002	0	0.391	0.196	0.781	-2.658	0.008
Heckman, 2004	0	0.640	0.394	1.040	-1.801	0.072
Hicks, 2007	2	0.450	0.263	0.769	-2.918	0.004
Hinkin, 2004	2	0.772	0.423	1.407	-0.845	0.398
Holmes, 2007	0	0.382	0.178	0.818	-2.475	0.013
Holstad, 2007	0	0.662	0.342	1.278	-1.229	0.219
Howard, 2002	0	0.406	0.190	0.866	-2.333	0.020
Johnson, 2003	1	0.454	0.304	0.680	-3.840	0.000
Kalichman, 2003	0	0.631	0.384	1.039	-1.809	0.071
Kleeberger, 2001	2	0.640	0.272	1.505	-1.023	0.306
Lazo, 2007a	2	0.880	0.454	1.705	-0.379	0.705
Lazo, 2007b	2	0.570	0.381	0.852	-2.737	0.006
Liu, 2006	2	0.437	0.070	2.723	-0.887	0.375
Martini, 2004	1	0.587	0.214	1.609	-1.035	0.300
Moatti, 2000	0	0.830	0.719	0.958	-2.539	0.011
Mohammed, 2004	2	0.386	0.168	0.885	-2.248	0.025
Moss, 2004	2	0.744	0.239	2.315	-0.511	0.609
Mugavero, 2007	0	0.590	0.410	0.850	-2.837	0.005
Murphy, 2002	0	0.345	0.092	1.297	-1.575	0.115
Murphy, 2004	0	0.510	0.330	0.789	-3.024	0.002
Murphy, 2005	0	0.790	0.647	0.965	-2.308	0.021
Parsons, 2007	0	0.553	0.395	0.774	-3.452	0.001
Peretti-Watel, 2006	2	0.399	0.303	0.525	-6.546	0.000
Rothlind, 2005	2	0.357	0.164	0.775	-2.603	0.009
Samet, 2004	2	0.230	0.103	0.515	-3.573	0.000
Shannon, 2005	1	0.644	0.202	2.054	-0.744	0.457
Sharma, 2007	0	0.258	0.101	0.655	-2.848	0.004
Spire, 2002	0	0.667	0.399	1.114	-1.548	0.122
Sullivan, 2007	0	0.770	0.656	0.904	-3.190	0.001
Tesoriero, 2003	1	0.600	0.278	1.293	-1.304	0.192
Tucker, 2003	2	0.461	0.293	0.726	-3.338	0.001
Wagner, 2001	0	0.417	0.295	0.589	-4.951	0.000
Wilson, 2002	0	0.728	0.538	0.986	-2.051	0.040
Overall		0.548	0.490	0.612	-10.633	0.000

Alcohol Use and ART Adherence Meta-Analysis*

- 40 studies and over 25,000 participants
- Those with unhealthy use were less likely to be adherent than lower risk drinkers and abstainers (OR 0.5)

*Hendershot, Stoner, Pantalone, Simoni. *J AIDS*. 2009. 52:180-202.

Adherence

- Intoxication and complex dosing
- Beliefs about medication interactions

HIV disease progression

HVL, CD4, AIDS

- Any effect and mechanism are debated
  - Via non-adherence
  - Via immune activation (microbial translocation, disruption of gut microbiome, systemic inflammation, T cell proliferative defects
  - SIV in macaques: studies (experimental) largely support an effect though most recent did not (Molina et al 2014)
  - Human observational studies mixed though bulk of evidence: no effect (on or off ART)
- Most likely small or no direct effect on disease progression in humans

Hahn & Samet. *Curr HIV/AIDS Rep* 2010;7: 226
Samet Saitz et al. *J AIDS* 2007;46:194 n=595 effect on CD4 among those not on ART
Deiss et al. *Alcohol Clin Exp Res* 2016;40:529 n=752, on HAART, effect on HVL

Conen et al. *J AIDS* 2013;64:472 n=5067 Swiss cohort on and off ART—null
4 others null (Ghebremichael et al., 2009; Cook et al., 2008; Chander et al., 2006b; Kowalski et al., 2012)

Alcohol and HIV comorbidities

Emily C. Williams, PhD, MPH, Judith A. Hahn, PhD, MA, Richard Saitz, MD, MPH, Kendall Bryant, PhD, Marlene C. Lira, BA, Jeffrey H. Samet.

Alcohol Use and Human Immunodeficiency Virus (HIV) Infection: Current Knowledge, Implications, and Future Directions

Under review

HIV Comorbidity

- High priority for NIH, Office of AIDS Research
- HIV and alcohol direct effects, immune senescence, inflammation, and hypercoagulability
- ?Premature aging
  - Illnesses assoc w/alcohol use seen in older adults *without* HIV infection now occurring in younger PLWH despite HVL suppression

Bryant et al. *Alcohol Res Health* 2010;33: 167
Justice & Falutz. *Curr Opin HIV AIDS* 2014;9: 291

Alcohol and HIV comorbidities

- Hepatitis C
- Tuberculosis
- Cardiovascular disease
- Cancer
- Neurological
- Metabolic
- Falls and injury
- Other substance use
- Mental health
- Mortality

Hepatitis C

- 25-30% co-infection
- HIV and heavy drinking affect progression
  - Heavy drinking increases HCV RNA, which in turn is assoc w/Rx outcomes
- Drinking (?any) affects efficacy of treatment
- Effects of low level alcohol on progression and treatment efficacy (particularly new treatments) not clear
- Abstinence thought safest

Platt *Lancet Infect Dis* 2016
Sulkowski *JID* 2013;207 Suppl 1:S26

Tuberculosis

- Increased risk of infection; leading cause of death in PLWH worldwide
- Any alcohol 3x risk active TB (immune effects, adherence)
- INH contraindicated in heavy drinking

Volkmann et al. *J Tuberc Res* 2016;4:18-22
Rehm J et al. *BMC Public Health* 2009;9:450

Cardiovascular disease

- Risk increased in HIV infection (?inflammation)
  - Not mitigated by ART or viral suppression
- Further increased 37-78% by any/heavy drinking
  - Coronary heart disease
    - ?"moderate" drinking benefits
      - Carrieri et al. BMJ Open 2012;2
      - Stockwell et al. J Stud Alcohol Drug 2016;77:185
  - Cardiomyopathy

Freiberg et al. *JAMA Intern Med 2013;*173:614
Freiberg et al. *JAIDS* 2010;53: 247-253
Kelso et al. *Am J Drug Alcohol Abuse* 2015;41:479

Cancer

- Higher rates of non-AIDS defining among PLWH
  - Direct effects, inflammation, co-infections, other risks (e.g. smoking)
  - ?alcohol
    - Liver, head & neck
    - Increased liver cancer risk accounted for by alcohol and HCV
    - Increased non-Hodgkins lymphoma seen in PLWH *not* accounted for by alcohol/HCV

Smith et al. *Lancet* 2014;384:241
McGinnis et al. *J Clin Oncol* 2006;24:5005

Neurological

- HIV-associated neurocognitive disorders (HAND)
  - Role of alcohol not clear (mixed findings) though heavy use known to affect cognition (memory, decision making)
- Neuropathy associated with HIV, ART and alcohol
  - Not well-studied
- Pain associated with HIV and heavy drinking
  - Needs study

Attonito et al. *Front Public Health* 2014;2:105
Green et al. *Am J Psychiatry* 2004;161: 249
Rothlind et al. *J Int Neuropsychol Soc* 2005;11:70
Merlin *Top Antivir Med* 2015;23:120
Merlin et al. *J Pain Symptom Manag* 2012;43:638
Merlin et al. *JAIDS* 2012;61:164
Tsui JI et al. *Drug Alcohol Depend* 2014;144:87

Metabolic

- Weight gain with ART
- Metabolic changes that increase risk for CVD and diabetes (e.g. dyslipidemia)(ART and inflammation)
- Lipodystrophy
  - Cheng Saitz et al. *Alcohol* 2009;43: 65-71.
- Role of alcohol not well studied; possible U-shape
  - Oxidative stress on bone, adipose>>dyslipidemia (Molina et al. 2014; *Curr HIV Res* 12: 265)

Paula et al. *AIDS Res Ther* 2013;10:1
Samaras et al. *Diabetes Care* 2007;30: 113-119

Falls and injury

- Up to 30% each year
- Fractures are 40-60% more common in PLWH
- Falls are the most common cause of non-fatal injury
- Alcohol use is a potent risk factor for falls and fractures
- Association between alcohol use and falls and injury among PLWH under-studied
- Little is known regarding fall prevention in younger populations (e.g. PLWH)

Erlandson et al. *JAIDS* 2012; 61: 484
Sharma et al. *JAIDS* 2015;70:54
Stevens et al. *Injury Prev* 2006;12:290
Cherpitel et al. *Addiction* 110: 1724

Other substance use

- 42% smoke (46-84% in some samples)(c/w 19% US)
  - bacterial pneumonia, COPD), CHD, decreased bone mineral density, mixed evidence re: HIV disease progression, associated with alcohol use
- Alcohol and smoking: additive inflammatory effects>>pneumonia, CHD
- Other drug use not uncommon, injection risk factor
  - Cascade
  - Neurological
  - Co-infections: e.g. up to 82% who inject have HCV
  - Alcohol increases overdose risk (greater effect of lower dose in HIV)

Cooperman *Curr Addict Rep* 2016;3:19
Braithwaite *AIDS Behav* 2016;20: 566
Armah *Clin Infect Dis* 2012;55:126
Green et al. *Drug Alcohol Depend* 2010;110: 208-220
Platt & Terrault *Lancet Infect Dis* 2016
Hauser & Knapp *Internat Rev Neurobiol* 2014;118:231
McGinnis KA et al. *AIDS Behav* 2016;20:504

Mental health

- Depression, trauma, stress, anxiety common in PLWH
  - Common co-occurrence with heavy alcohol use; effects on cascade and outcomes; interaction with alcohol not well described
- Heavy drinking associated with depressive symptoms

Chander et al. *Drugs* 2006;66:769
Sullivan et al. *Drug Alcohol Depend* 2011;117:158
Sullivan Saitz et al. *Addiction* 2008;103:1461

Mortality

- J shaped curve for mortality
  - Are J shaped curves real?
- Risk among PLWH may be higher at lower levels of alcohol (e.g. >1drink a day vs >2drinks a day)
  - Greater BAC for same amount of drinking
  - Less alcohol to "feel a buzz"

Wandeler et al. *JAIDS* 2016;71:302
Stockwell et al. J Stud Alcohol Drug 2016;77:185
Justice et al. *Drug Alcohol Depend* 2016;161:95
McCance-Katz et al. *JAIDS* 2012;60:282
McGinnis KA et al. *AIDS Behav* 2016;20:504

Interventions

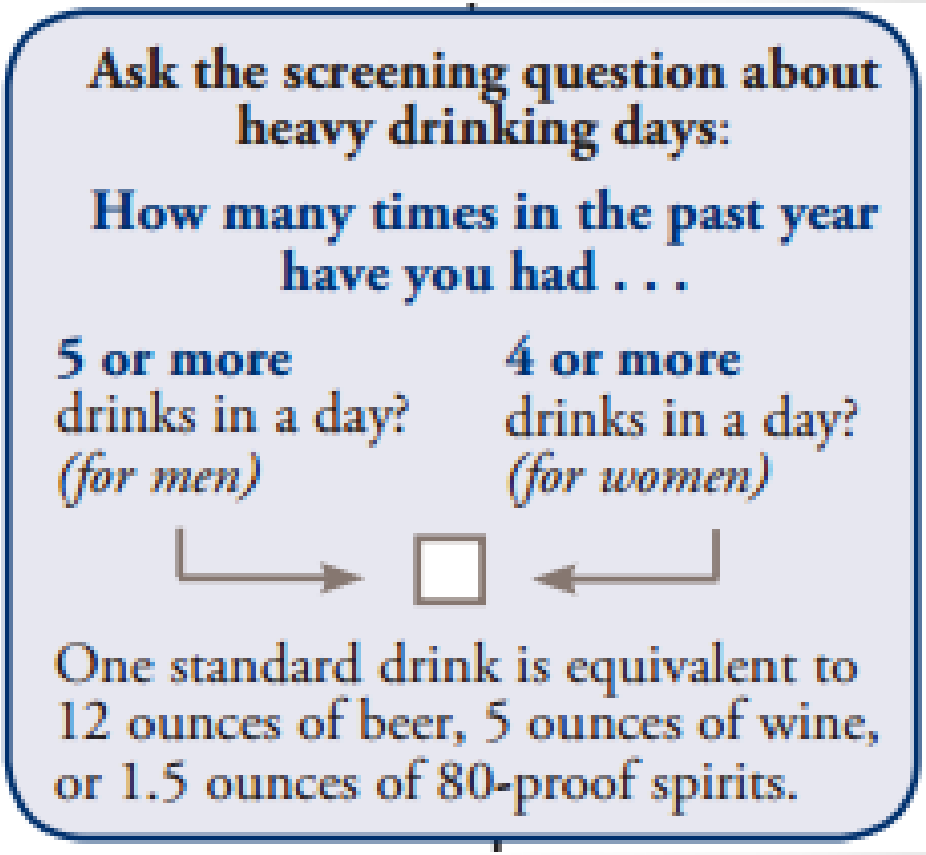
To increase adherence/reduce viral load
To reduce alcohol use and consequences

Screening

AUDIT-C

Question #1: How often did you have a drink containing alcohol in the past year?	
• Never	(0 points)
• Monthly or less	(1 point)
• Two to four times a month	(2 points)
• Two to three times per week	(3 points)
• Four or more times a week	(4 points)
Question #2: How many drinks did you have on a typical day when you were drinking in the past year?	
• 1 or 2	(0 points)
• 3 or 4	(1 point)
• 5 or 6	(2 points)
• 7 to 9	(3 points)
• 10 or more	(4 points)
Question #3: How often did you have six or more drinks on one occasion in the past year?	
• Never	(0 points)
• Less than monthly	(1 point)
• Monthly	(2 points)
• Weekly	(3 points)
• Daily or almost daily	(4 points)

The AUDIT-C is scored on a scale of 0-12 (scores of 0 reflect no alcohol use). In men, a score of 4 or more is considered positive; in women, a score of 3 or more is considered positive.



McGinnis Justice Kraemer Bryant Saitz Fiellin Alc Clin Exp Res 2013;37:435

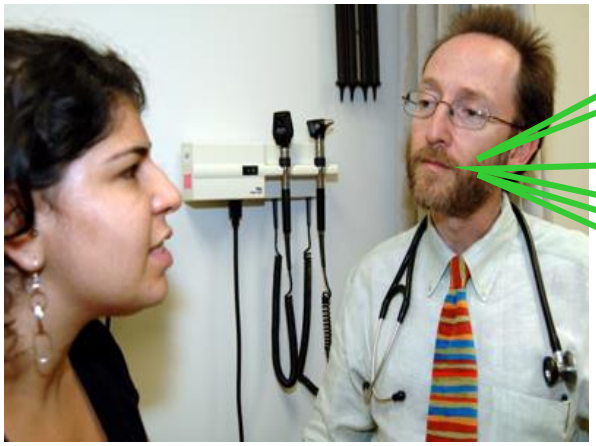
Saitz R. Screening for unhealthy use of alcohol and other drugs. UpToDate 2016.

- ≥3 women, ≥4men

NIAAA. Clinicians Guide, 2007.
Smith PC, Saitz R et al J Gen Intern Med 2009 24:783-8.
Saitz R et al. J Studies Alcohol Drugs. 2014;75(1):153-157.
McNeely J et al. J Gen Intern Med. 2015 Dec;30(12):1757-64

Brief Intervention:

*Feedback w/-permission
*Advice
*Goal-setting
*Follow-up



"You are drinking more than is safe for your health."

"My best medical advice is that you cut down or quit."

"What do you think? Are you willing to consider making changes?"

*assessment of severity and readiness
*non-confrontational, motivational interviewing-consistent/adaptations

NIAAA. Clinicians Guide to Helping Patients Who Drink Too Much, 2007.

Interventions to reduce HIV risk or alcohol use reductions to reduce HIV transmission

AIDS Behav (2016) 20:484–503
DOI 10.1007/s10461-015-1233-5

SUBSTANTIVE REVIEW

HIV-Alcohol Risk Reduction Interventions in Sub-Saharan Africa: A Systematic Review of the Literature and Recommendations for a Way Forward

Maria A. Carrasco[1] · Marissa B. Esser[1] · Alicia Sparks[1] · Michelle R. Kaufman[1]

screened, 19 met the inclusion criteria for this review. A discussion of methodological challenges, research gaps, and recommendations for future interventions is included. Relatively few interventions were found, and evidence is mixed about the efficacy of HIV-alcohol risk reduction interventions. There is a need to further integrate HIV-alcohol risk reduction components into HIV prevention programming and to document results from such integration. Additionally, research on larger scale, multi-level interventions is needed to identify effective HIV-alcohol risk reduction strategies.

ann. behav. med. (2008) 36:270–279
DOI 10.1007/s12160-008-9067-2

ORIGINAL ARTICLE

Randomized Trial of a Community-based Alcohol-related HIV Risk-reduction Intervention for Men and Women in Cape Town South Africa

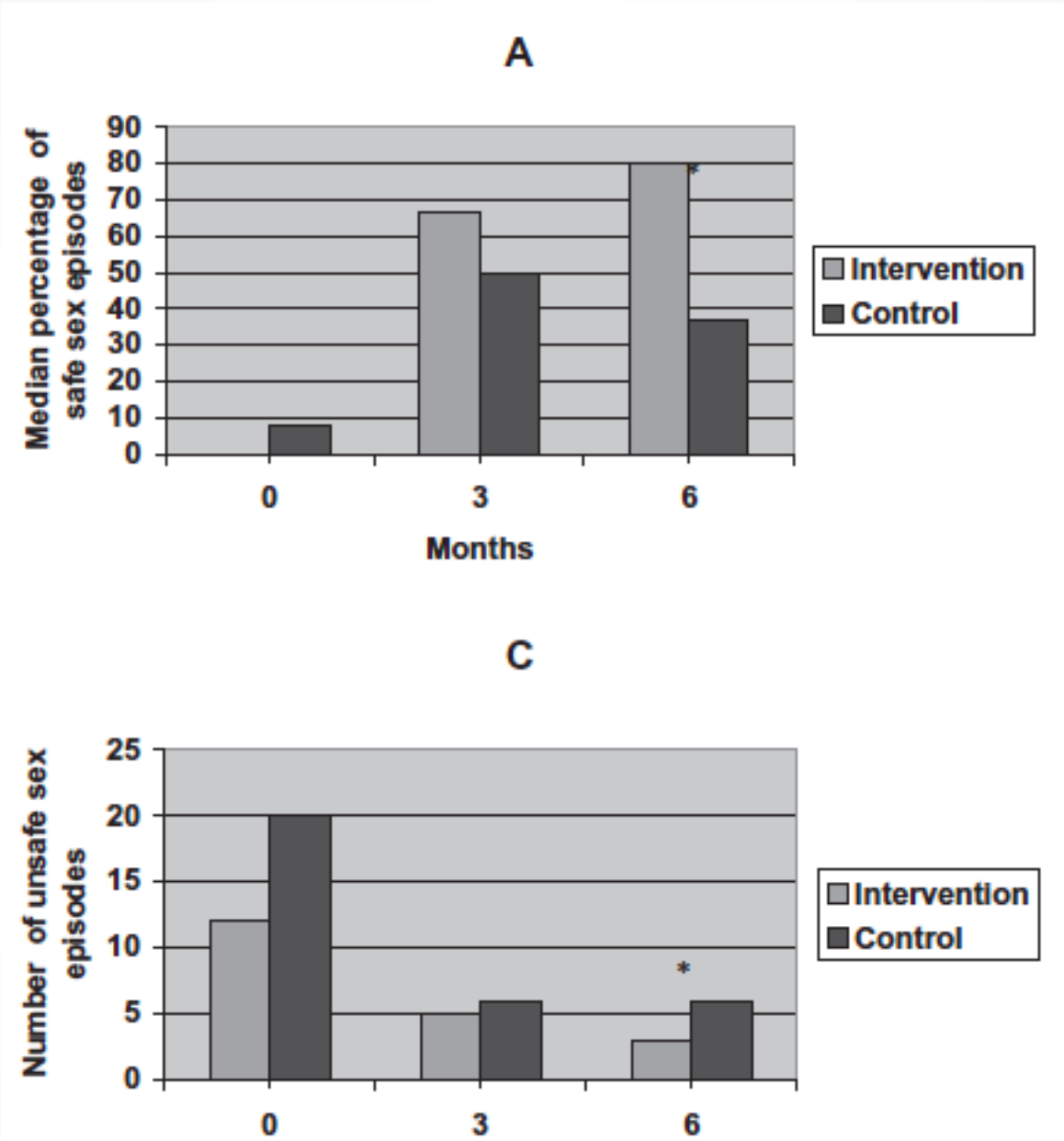
Seth C. Kalichman, Ph.D. • Leickness C. Simbayi, D.Phil. •
Redwaan Vermaak, M.A. • Demetria Cain, M.P.H. •
Gino Smith, B.A. • Jacqueline Mthebu, M.A. •
Sean Jooste, M.A.

(a) 3-h theorybased behavioral HIV–alcohol risk-reduction intervention that focused on skills training for sexual negotiation and condom use
(b) 1-h HIV–alcohol information/education control group.

Participants were followed up for 3 and 6 months post-intervention with 89% retention.

Significantly less unprotected intercourse, alcohol use before sex, numbers of sex partners, partners met at drinking establishments and greater condom use

Lighter drinkers demonstrated significantly more intervention gains than heavier drinkers



Alcohol and/or heroin dependence. Two personalized sexual behavior counseling sessions plus three telephone booster sessions. Samet et al. Addiction, 2008;103, 1474

Addiction. 2015 Jan;110(1):80-90. doi: 10.1111/add.12716. Epub 2014 Oct 16.

HERMITAGE--a randomized controlled trial to reduce sexually transmitted infections and HIV risk behaviors among HIV-infected Russian drinkers.

Samet JH, Raj A, Cheng DM, Blokhina E, Bridden C, Chaisson CE, Walley AY, Palfai TP, Quinn EK, Zvartau E, Lioznov D, Krupitsky E.

Intervention stressing disclosure of HIV serostatus and condom use, adapted for a Russian clinical setting with two individual sessions and three small group sessions

HIV risk reduction intervention does not appear to reduce sexually transmitted infections and HIV risk behaviors

in Russian HIV-infected heavy drinkers compared with attention controls

A reanalysis of a behavioral intervention to prevent incident HIV infections: Including indirect effects in modeling outcomes of Project EXPLORE. Eaton et al. AIDS Care 2013;25:805

intervention treatment condition including the counseling (HIV pre- and post- test counseling) provided in the control arm plus counseling in the form of ten behavioral counseling sessions addressing factors associated with risk taking among MSM

effect of intervention on HIV infection through unprotected anal sex to be statistically significant up through 12 months post-intervention, OR=.83

Interventions to improve adherence, HVL suppression

Samet JH and Walley AY. (2010) Interventions targeting HIV-infected risky drinkers: drops in the bottle. Alcohol Res Health 33: 267-279

Interventions to improve adherence, HVL suppression

Nurse-led multi-component intervention that included 4 visits over 3 months: **no effect on alcohol use or ART adherence** (Samet et al., 2005 Antivir Ther 10: 83)

Eight 1-hour individual sessions of motivational interviewing and cognitive behavioral skills over 3 months; **positive intervention effects on self-reported medication adherence and markers of disease progression** at 3 months, but not sustained (Parsons et al., 2007 AIDS 46: 443)

Alcohol interventions among PLWH

Papas, et al 2011 Addiction 106: 2156

Culturally adapted 6-session CBT vs assessment-only (n=102) at a Kenyan outpatient HIV clinic

Reduction in % drinking days and # of drinking days and greater abstinence (30-90 days)

Alcohol interventions among PLWH

Hasin et al 2013 Addiction 108: 1230

258 heavy drinkers, HIV primary care

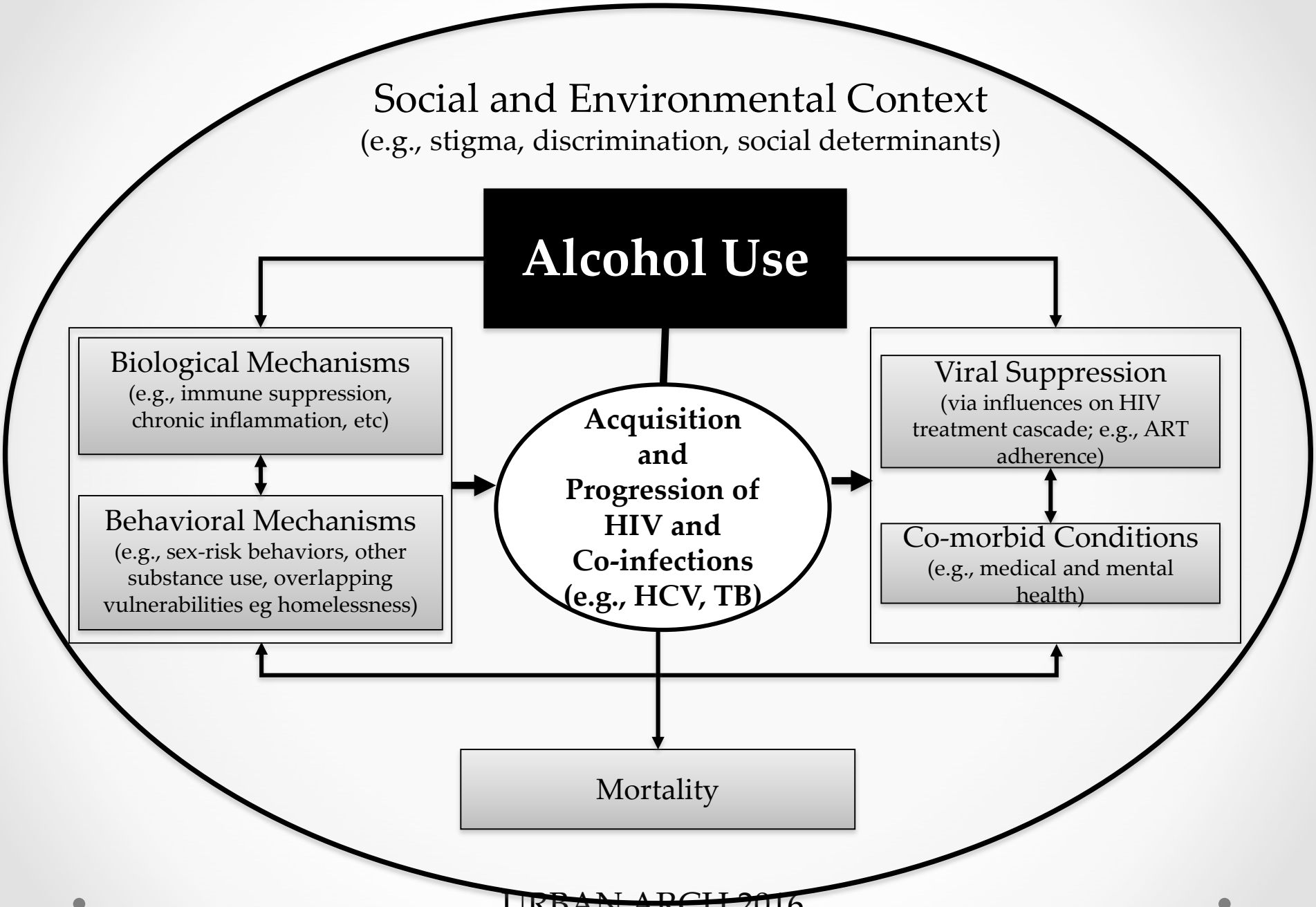
Control: educational materials and advice repeated at 30- and 60-days

MI: single 20-25 minute session of counselor-delivered MI with two 15-minute boosters at 30- and 60-days;

MI+: daily IVR calls with "HealthCall"--personalized feedback

Fewer drinking days for both interventions

MI+: fewer drinking days relative to MI among participants meeting criteria for alcohol dependence


Social and Environmental Context
(e.g., stigma, discrimination, social determinants)
Alcohol Use
Biological Mechanisms
(e.g., immune suppression, chronic inflammation, etc)
Behavioral Mechanisms
(e.g., sex-risk behaviors, other substance use, overlapping vulnerabilities eg homelessness)
Acquisition and Progression of HIV and Co-infections (e.g., HCV, TB)
Viral Suppression
(via influences on HIV treatment cascade; e.g., ART adherence)
Co-morbid Conditions
(e.g., medical and mental health)
Mortality

Thank you!

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