

Syracuse University
Department of Psychology

HIV Prevention and the Alcohol Behavioral Research Agenda

National Institute on Alcohol Abuse and
Alcoholism (NIAAA)

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Sarah E. Woolf-King, PhD, MPH

Assistant Professor



*Extension of alcohol challenge
studies to investigate
mechanisms underlying the
association between
alcohol consumption &
ART adherence*

Agenda

- I. Background
- II. Review of literature on alcohol use & ART adherence
- III. Mechanisms underlying the alcohol-ART adherence association
- IV. Extending alcohol challenge studies to investigate mechanisms underlying alcohol & ART adherence

I. Background

I. Alcohol use among PLWH

- PLWH consume alcohol frequently and heavily
 - 66% of PLWH report using alcohol in the previous year (Blair et al., 2014)
 - About 30% of PLWH report binge drinking in the last 30 days (Kelly et al., 2016)
 - ~16-20% of PLWH report drinking at hazardous levels or at-risk (Kelly et al., 2016; Justice et al., 2006)
- At-risk alcohol consumption affects nearly every stage of the HIV care continuum (Vagenas et al., 2015)
 - Association with adherence perhaps most important

I. Importance of ART adherence

- Taking medications as prescribed (i.e., being *adherent*) is the single most important patient-related factor in HIV treatment success (Volberding & Deeks, 2010).
- Decades of research on ART adherence has identified multiple correlates related to (Ammassari et al., 2002):
 - the patient (age, substance use, mental health, self-efficacy)
 - the treatment (time on ART, dosing frequency)
 - the disease (time since diagnosis)
 - the patient-provider relationship (trust)
- Where does alcohol fit in?

I. Correlates of ART adherence

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ATKINSON AND PETROZZINO

TABLE 8. RANK ORDERED EFFECTS OF SPECIFIC DETERMINANTS OF TREATMENT NONADHERENCE

<i>Predictor of nonadherence</i>	<i>Pooled OR (95% CI)</i>	<i>Reference studies</i>
Poor medication self-management, low Tx self-efficacy	2.4 (2.0–3.0)	(24, 28, 42, 53)
High pill burden (more vs. less than 10 pills daily)	2.0 (1.4–3.0)	(40, 47, 52)
Frequent or severe medication side effects	1.9 (1.4–2.7)	(24, 40)
Anxiety or depression	1.6 (1.3–1.9)	(24, 27, 28, 40, 50)
Alcohol or substance abuse	1.6 (1.4–1.8)	(28, 49, 50, 51)
Twice vs. once daily dosing	1.4 (1.0–1.7)	(46, 51)
Use of more medication classes (>3 vs. ≤3)	1.3 (1.1–1.6)	(24, 50)

OR, odds ratio; CI, confidence interval; Tx, treatment.

2009 meta-analysis of 23 studies in which correlates of nonadherence were rank ordered by magnitude of association (Atkinson & Petrozzino, 2009)

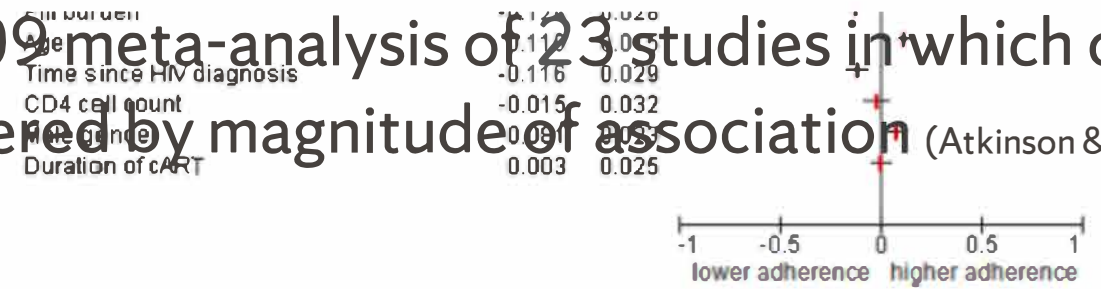


Figure 2 Predictors/correlates of adherence to anti-retroviral therapy (ART).

Why is alcohol use correlated with ART adherence?

II. Review of literature on alcohol use & ART adherence

II. Alcohol & ART adherence

What do we already know?

- **Three systematic reviews** (Grodnenky et al., 2012; Vagenas et al., 2015; Azar et al. 2010); **one narrative review** (Thomas & Lungu, 2018); **one meta-analysis** (Hendershot & George, 2009)
- Drinkers are less likely to be adherent compared to abstainers or those who drink relatively less
- Magnitude of the association depends on a number of factors
 - More extreme for problem drinkers
 - Quantity vs. frequency
 - Percent adherence criterion used

II. Alcohol & ART adherence: Issues in literature

Although the association of alcohol use and nonadherence is replicable and reliable, it remains difficult to speak to the causal nature of this association. The majority of studies included in this review were cross-sectional reports that evaluated global associations using retrospective measures of drinking and adherence. In a substantial proportion of studies there was little or no overlap among the alcohol use and adherence assessment intervals. These limitations restrict the ability to infer causal effects and leave open the possibility that these associations could be attributable to other variables. If alcohol use is embedded in a broader context of problematic

How much has the literature changed in 10 years?

II. Alcohol & ART adherence: Issues in literature

- We updated these reviews with an interest in identifying mechanisms of action
- 159 quantitative and 26 qualitative peer reviewed publications
- Little overlap in timeframes assessed, with global association studies still dominant
 - global (n = 153) → event-level (n= 6) → experimental (n = 0)

Very few studies established temporal ordering and/or examined mechanisms of action. No study used an experimental design to establish a casual process

II. Alcohol & ART adherence: Event-level data

- Event-level studies can examine temporal overlap
- Six event-level studies published in the last 5 years
 - Kalichman et al., 2013; Kalichman et al., 2013; Pellowski et al., 2016; Pellowski et al., 2016; Schensul et al., 2017; Sileo et al., 2016
- PLWH are more likely to miss ART medication on drinking days, and days following drinking days
 - e.g., Drinking any amount of alcohol, drinking more alcohol than one normally consumes, and drinking at moderate to high-risk levels increases odds of nonadherence that same day or evening by 1-4 fold (Sileo et al., 2016)

II. Alcohol & ART adherence: next steps

- Event-level studies still do not establish a causal process
- And most are atheoretical and/or do not test hypotheses about mechanisms of action
- To address this gap in the literature:
 1. we need theory-informed hypotheses about underlying mechanisms, and
 2. experimental designs to test these hypotheses



III. Possible mechanisms underlying the alcohol-ART adherence association

III. Mechanisms: types of nonadherence

- Two categories of nonadherence
- Intentional nonadherence

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S. Clifford et al. / Journal of Psychosomatic Research 64 (2008) 41–46

Table 2

Examples of patients' self-reported reasons for nonadherence classified as unintentional and intentional

Unintentional reasons

I was away from home and forgot to take my medicines with me.
I was tired and I forgot.
I went out for the evening and forgot to take the medicines with me.
I was in a hurry and I forgot.

Intentional reasons

I was worried about side effects so I reduced the dose.
I miss doses because I feel I am taking too many.
I do not take water tablets when going out of the house.
I miss the evening dose as it keeps me awake.

- Categories may overlap & different mechanisms may govern each

III. Mechanisms: Alcohol and intentional nonadherence

- About 25%-50% of people who are on ART and drink alcohol report **Interactive toxicity beliefs** intentional nonadherence when drinking (Kalichman et al., 2009; Sankar et al., 2007; Kalichman et al., 2013)
- “Beliefs that mixing medications with alcohol results in a toxic blend” (Kalichman et al., 2013)
- People who endorse ITBs: **Why?**
 - are significantly more likely to report poor adherence
 - report significantly more days with concurrent alcohol use and missed medications (Kalichman et al., 2013)
- How can these beliefs be investigated in an experimental drinking situation?
- And what type of questions could we answer by examining these beliefs in an alcohol challenge study?

III. Mechanisms: Alcohol and unintentional nonadherence

- Cognitive impairment associated with acute intoxication
 - 25-50% of PLWH who drink and are on ART report *intentional* nonadherence
 - Alcohol myopia
- Attentional bias to proximal, salient cues of drinking event in conflict with distal, less salient cues of taking meds (Morris & Albery, 2001; Steele & Josephs, 1990)
 - Then a substantial proportion of HIV+ drinkers are unintentionally nonadherent

Why?

- Exacerbation of cognitive processes known to impact adherence
 - “Forgetting”
 - Or more specifically, not remembering to remember (Zogg et al., 2012)

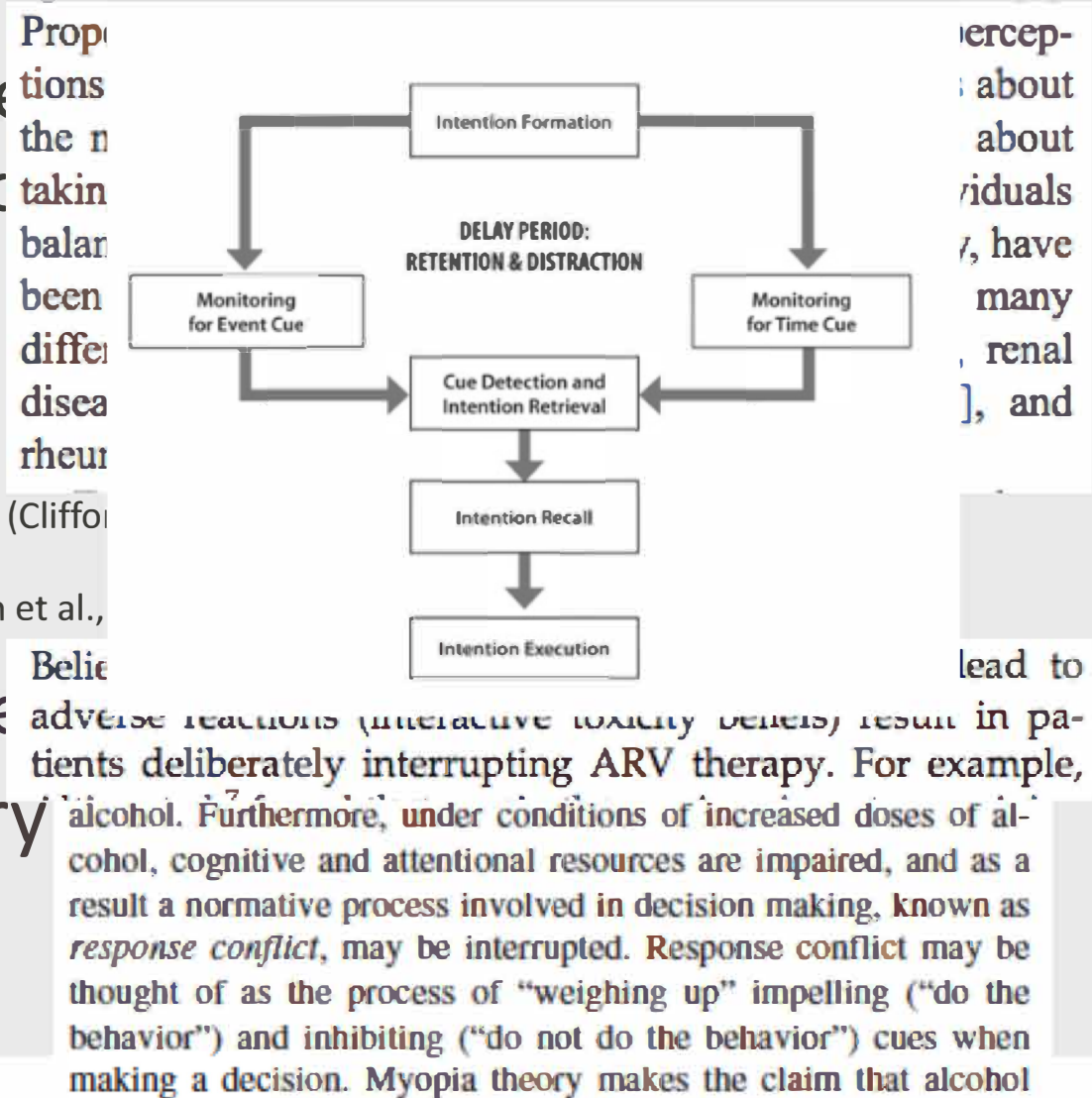
III. Mechanisms: Alcohol and unintentional nonadherence

- Prospective memory (PM) is “one’s ability to remember to do something at a later time” (Zogg et al., 2012, p.48) or the “process of repeatedly remembering to perform an action in the future” (habitual PM) (Vedhara et al., 2004)
 - Associated with medication adherence among PLWH (Woodset al., 2008)
 - PLWH report more frequent PM failures compared to HIV-uninfected persons, especially on self-cued daily tasks (Woods et al., 2007).
- How might the cognitive processes associated with PM be impacted by acute intoxication among PLWH?
- How might this be examined in an experimental drinking situation?

IV. Extending alcohol challenge studies to investigate mechanisms underlying alcohol & ART adherence

IV. Theory

- Integrate theories of medication adherence with theories of alcohol intoxication to generate hypotheses about underlying pathways
- Example intentional nonadherence:
 - Necessity-concerns framework (Clifford)
 - interactive toxicity beliefs (Kalichman et al., 2007)
- Example unintentional nonadherence:
 - Theories of prospective memory myopia (Steele & Josephs, 1990; Moss & Albery, 2009)



IV. Testing proposed mechanisms in the lab

- The effect of alcohol use on intentional ART nonadherence.
- **What questions could be asked?**
 - When PLWH are instructed to consume alcohol, to what extent and at what level of intoxication are ITBs triggered?
 - Are there person-level differences in the strength of the effect of interactive toxicity beliefs on adherence behavior?
- **How could we answer these questions?**
 - We have all the tools to design such an experiment (psychometrically sound measure of ITBs, balanced placebo design)
 - Need an analog for medication adherence behavior

IV. Approximating adherence behavior in the lab

- If we can come up with ways to approximate sexual encounters in the lab, we can come up with ways to approximate medication-taking as well.
 - Experimental vignettes? (e.g., George et al., 2009)
 - Interactive role-plays? (e.g., Maisto et al., 2012)
 - Other ideas?

IV. Testing proposed mechanisms in the lab

- The effect of alcohol use on unintentional ART nonadherence.
- **What questions could be asked?**
 - How are cognitive mechanisms of unintentional nonadherence (e.g., PM) affected by acute intoxication among PLWH?
 - What person- and situation-level variables moderate these effects?
- **How could we answer these questions?**
 - Use existing tasks that target cognitive processes relevant to unintentional nonadherence & examine under conditions of acute alcohol intoxication

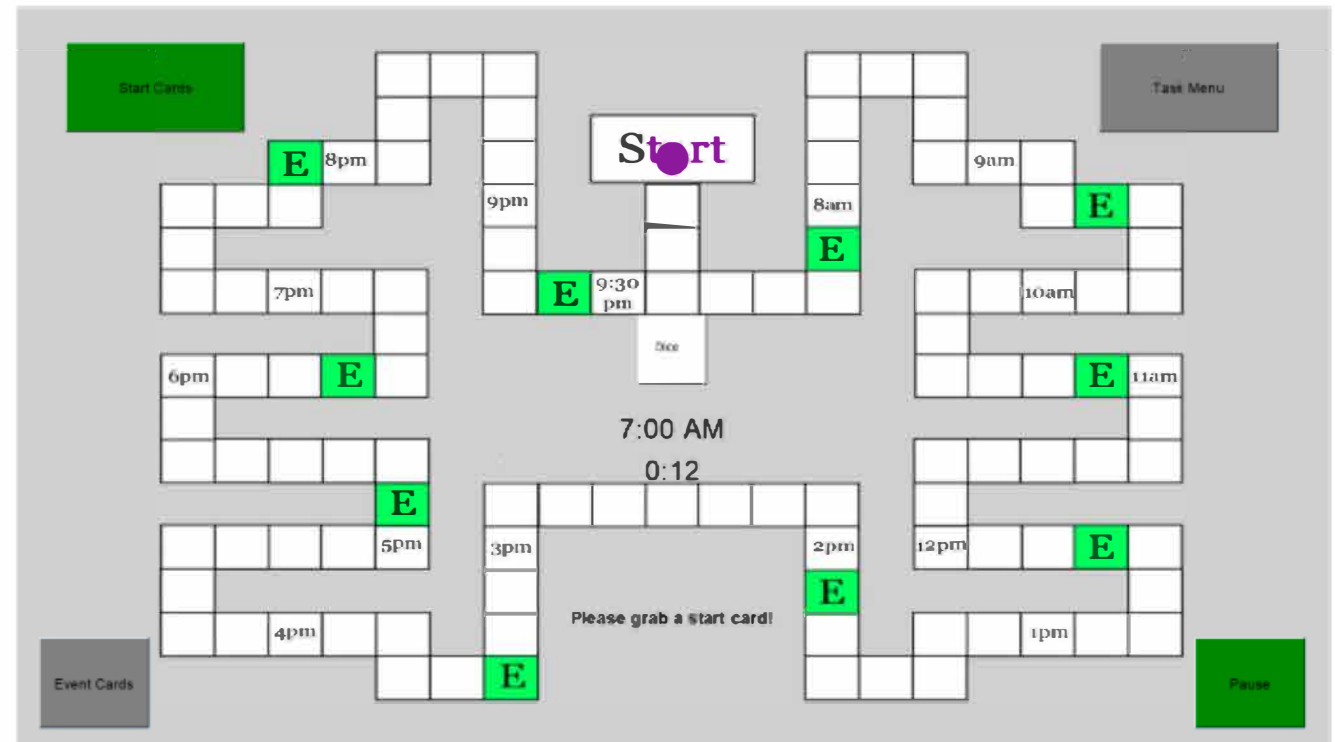
IV. An Example: The Virtual Week

- In a recent review of PM tasks, the Virtual Week (VW) (Rendell & Henry, 2009) was identified as reliable and valid (Zogg et al., 2012)
- Asks participants to complete time and event-based PM tasks that are described as activities of daily living in a simulated day (ecologically valid)
- VW has been used in alcohol administration studies with healthy adults
- We are currently adapting the VW for PLWH

IV. An Example: The Virtual Week

- Each lap around the game board is a virtual “day”
- Participants complete “time based” and “event based” tasks
- We are adapting tasks & instructions
- Assessing feasibility, acceptability, and time to complete

Welcome to the virtual week task! We are going to ask you to play a game where you make choices and move through a pretend day. First, we will go through some instructions on how to play!



IV. Extending experimental studies outside the lab

- While “experimental studies are designed to investigate whether a phenomena can occur under highly controlled conditions, not whether the phenomena does occur in every day life” (Hendershot & George, 2007).
- Basic behavioral experiments should complement and inform non-experimental studies, ultimately enhancing intervention development
- Studies that combine experiments in the lab, with intensive longitudinal data collected outside the lab, may offer the best of both worlds (and be more attractive to reviewers)

Conclusions

- The assumption that alcohol use has a causal effect on medication adherence is prevalent in this literature
- In order to establish causality, identify mechanistic pathways, and inform intervention development, we need:
 - Theory-informed hypotheses about causal mechanisms
 - Tested via experimental studies
 - Paired with intensive longitudinal data collected outside the lab

Thank you!

Alan Sheinfil, MS

Jackie Foley, MS

Dezarie Moskal, MS

Jeremy Ramos, BA

Madison Firkey, BA

Stephen Maisto, PhD

Kendall Bryant, PhD

Bob Freeman, PhD

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Questions?



Psychology
and **HEALTH** Lab