



Uganda Russia Boston Alcohol Network for
Alcohol Research Collaboration on HIV/AIDS

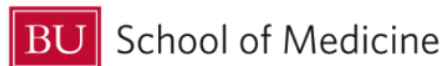


Boston Alcohol Research Collaboration on HIV (ARCH): Key Takeaways

Theresa Kim MD

URBAN ARCH 2022 Annual Meeting

May 10, 2022





Agenda



- Boston ARCH: BONE (Wave 1)
 - Alcohol and Bones
 - Substance use, Substance Use Disorders, and Complications
Alexander Walley, MD, MSc
- Boston ARCH: 4F (Wave 2)
 - Alcohol and Falls
 - Fall Prevention Intervention: Danny Shin, PhD candidate
Occupational Therapy at Boston University
 - COVID supplement



Boston ARCH (2011-2022)

Wave 1 (2011-2016)	Bone	HIV+, SUD or ever injection use	Observational cohort	Bone biomarkers supplement
Wave 2 (2016-2022)	4F study: Falls, Fractures Frailty, Functioning	BONE participant or HIV+, risky alcohol, other drug use	Observational cohort Pilot fall prevention RCT	COVID supplement



Boston ARCH: Bone



- Observational cohort (n=250)
- HIV+, past year substance dependence or any lifetime history of injection use
- Is alcohol consumption associated with change (decrease) in bone mineral density?
- Bone marker supplement
 - Serum markers of bone formation/resorption

Lifetime and recent alcohol use and bone mineral density in adults with HIV infection and substance dependence

Alicia S. Ventura, MPH^{a,b,*}, Michael R. Winter, MPH^c, Timothy C. Heeren, PhD^d, Meg M. Sullivan, MD^e, Alexander Y. Walley, MD, MSc^a, Michael F. Holick, PhD, MD^f, Gregory J. Patts, MPH^c, Seville M. Meli, MPH^b, Jeffrey H. Samet, MD, MA, MPH^{a,b}, Richard Saitz, MD, MPH^{a,b}



Abstract

- Cross-sectional
- BMD: femoral neck, total hip, lumbar spine, g/cm², T-score
- Lifetime alcohol use, recent heavy drinking
- Lifetime alcohol history no association
- **Recent alcohol was associated with low BMD**

alcohol use was associated with low BMD diagnosis ($r = -0.4$), compared to abstainers, the aOR for high risk alcohol use was 1.54



Alcohol Consumption and Bone Mineral Density in People with HIV and Substance Use Disorder: A Prospective Cohort Study

Richard Saitz , Aldina Mesic, Alicia S. Ventura, Michael R. Winter, Timothy C. Heeren, Meg M. Sullivan, Alexander Y. Walley, Gregory J. Patts, Seville M. Meli, Michael F. Holick, Theresa W. Kim, Kendall J. Bryant, and Jeffrey H. Samet 

- Past-year alcohol
 - grams/day, heavy drinking days/month, days abstinent/month, any heavy
- Annual change in BMD
 - femoral neck, total hip, spine (g/cm, >%6 change)
- **No significant associations between any measure of alcohol and annual change in any measure of BMD**

Conclusions: In this sample of PLWH and substance use disorders or ever injection drug use, we detected no association between any of the alcohol measures used in the study and changes in BMD or incident fractures.

Key Words: HIV, Alcohol, Bone Density, Osteoporosis, Fracture.





Alcohol and Bone Turnover Markers among People Living with HIV and Substance Use Disorder

Theresa W. Kim , Alicia S. Ventura, Michael R. Winter, Timothy C. Heeren, Michael F. Holick, Alexander Y. Walley, Kendall J. Bryant, and Richard Saitz

- Recent alcohol
 - average drinks/day, any ≥ 20 days/month, PEth
- Serum bone turnover markers
 - Bone formation (P1NP)
 - Bone resorption (CTx)
- All measures of alcohol associated with lower P1NP
- Change in alcohol not associated with P1NP
- No associations between alcohol and CTx

was associated with lower serum levels of bone formation markers.

Key Words: HIV, Bone Turnover Markers, Alcohol, Substance Use Disorder.



Alcohol and Bone Formation

- Among people living with HIV with a SUD or lifetime history of injection drug use:
 - No range of alcohol consumption (“moderate alcohol use”) associated with higher levels of bone formation as other studies have observed
 - Low vitamin D was not a mediator





Key Takeaways on Alcohol and Bones

- Bone mineral density (BMD)
 - **More alcohol and low BMD**
 - Alcohol and *annual change* in BMD: no association
- Bone turnover markers
 - **More alcohol and less bone formation**
 - No associations with *change in alcohol* and bone formation or resorption



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Substance use, substance use disorders,
and complications: Acute care utilization,
HIV progression, and non-fatal overdose

Alex Walley, MD, MSc
Professor of Medicine
Boston University School of Medicine





Medication for addiction treatment and acute care utilization in HIV-positive adults with substance use disorders

Boston ARCH: Do PLWH with AUD or OUD treated with MSUD report less acute care utilization than those not receiving MSUD?

- 153 participants with AUD or OUD with baseline and 6m FU
 - 88% = AUD
 - 41% = OUD
 - 31% = MSUD – buprenorphine, methadone, naltrexone
 - 36% = ED visit past 3 months
 - 25% = Hospitalization past 3 months
- MSUD not associated with ED visit (AOR 1.12, 95% CI 0.46 – 2.75) or hospitalization (AOR 1.09, 95% CI 0.39 – 3.04)
 - Homelessness associated with ED visit (AOR 2.59, 95% CI 1.21 – 5.53) and hospitalization (AOR 2.56, 95% CI 1.12 – 5.84)
 - # AUD criteria associated with hospitalization (AOR 1.27, 95% CI 1.02 – 1.59)
- *Next Steps: Address homelessness and addiction severity in HIV-positive individuals to prevent acute care utilization*



Thakrar K, Walley AY, Heeren TC, Winter WR, Ventura AS, Sullivan M, Drainoni M, Saitz R. Medication for addiction treatment and acute care utilization in HIV-positive adults with substance use disorders. *AIDS Care*. May 2019;1-5. PMC7198361



HIV-infected individuals who use alcohol and drugs and virologic suppression



Nolan S, Walley AY, Heeren TC, Patts GJ, Ventura AS, Sullivan M, Samet JH, Saitz R. HIV-infected individuals who use alcohol and drugs and virologic suppression. *AIDS Care*. 2017;29(9):1129-1136. PMC5543330

Boston ARCH: *In PLWH on antiretroviral therapy (ART) who use substances, how are substance use or substance use severity associated with lack of virologic control?*

202 participants receiving ART and with current substance use or SUD at study entry

- Substance use factors: 30d ETOH, cocaine, and MJ use, SU Severity (# of criteria)
- 75% \geq 90% 30-day ART adherence – 78% HVL suppression
- Specific substance use *not* associated with detectable HVL
- Number of drug dependence criteria remained significant (AOR= 1.23 per criterion, 95% CI: 1.04–1.46)

Optimal HIV outcomes can be achieved by individuals who use alcohol or drugs

Drug use disorder severity, not specifically substance use, were associated with lack of virologic control

Improving SUD severity may improve HIV-related outcomes



Identification of non-steroidal anti-inflammatory drug use disorder: A case report

Contents lists available at ScienceDirect
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ELSEVIER ADDICTIVE BEHAVIORS

Identification of non-steroidal anti-inflammatory drug use disorder: A case report

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HIGHLIGHTS

- We describe a rare case of non-steroidal anti-inflammatory drug (NSAID) use disorder in an HIV-infected patient.
- NSAIDs are commonly used but rarely reported as drugs with addiction potential.
- Recognition of substance use disorders in a research setting may differ from clinical assessment.

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ABSTRACT

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Commonly used for analgesic and anti-inflammatory effects, non-steroidal anti-inflammatory drugs (NSAIDs) are among the most frequently used medications in the world. In spite of their prevalence, reports of NSAID misuse and NSAID use disorder are uncommon. This case report describes a research participant who met criteria for DSM-5 moderate substance use disorder based on her use of prescribed ibuprofen as assessed by the validated Mini International Neuropsychiatric Interview (MINI). This case demonstrates that the DSM-5 criteria within the MINI can be applied to diagnose an NSAID use disorder. Addiction researchers and clinicians should consider medications generally not thought to be addictive, like NSAIDs, when evaluating patients for substance use disorder.

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1. Background

Nonsteroidal anti-inflammatory drugs (NSAIDs) are among the most commonly used medications in the United States, accounting for 60% of over-the-counter (OTC) analgesic sales and over 100 million prescriptions each year (Conaghan, 2012). In 2010, approximately 72 million people in the US used an NSAID three or more times a week for at least three consecutive months (Zhou, Boudreau, & Freedman, 2014). Studies designed specifically to measure patterns of NSAID use found that knowledge of adverse side effects was low, OTC and prescription NSAIDs were inappropriately used together and the use of quantities higher than recommended was common (Wilcox, Cryer, & Triadafilopoulos, 2005). Patterns of NSAID use have been associated with risk of adverse medical consequences such as acute interstitial nephritis and upper gastrointestinal bleeding (Castellsague et al., 2012). Despite widespread prevalence of NSAID use at the population level and frequent use above recommended doses, there are few reported cases (Etcheverrigaray, Grall-Bronnec, Blanchet, Joliet, & Victorri-Vigneau, 2014; Jang & Chang, 1999) of NSAID use disorder in the literature or national survey data. The fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) includes specific mention of NSAID use disorder in the "other (or unknown) substance use disorders" subcategory, along with drugs such as anabolic steroids and antihistamines (American Psychiatric Association, 2013). A 2013 survey of 36,309 non-institutionalized people over 18 found that only 0.05% of those surveyed met criteria for DSM-5 substance use disorder under the subcategory of "other drug use" (National Institute on Alcohol Abuse and Alcoholism, 2013). Similarly, the 2012 National Survey on Drug Use and Health found that of 68,309 individuals surveyed, only 0.3% (n = 190) reported ever using a NSAID "non-medically", the majority of whom were specifically using ibuprofen (Substance Abuse and Mental Health Services Administration, 2013).

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58-year-old woman, living with HIV met Boston ARCH enrolment criteria via NSAID dependence/Use Disorder

- no other SUD or IDU
- Met 4/11 criteria for DSM-5 moderate NSAID use disorder
 - Using more than intended, tried to stop but failed, craving, tolerance
- Experienced chronic pain, prescribed ibuprofen by her MD, one note indicating taking more than prescribed and GI upset, but no other concern from her clinicians regarding NSAID misuse
- No other substance use found
- Stopped using NSAIDs at FU visit and UD criteria->0

As ibuprofen is not commonly main substance in substance use disorders, it is reasonable to question whether the symptoms detected during the study assessment were directly caused by brain changes from using ibuprofen or whether these symptoms were motivated primarily by relieving her underlying pain.



Polypharmacy and risk of non-fatal overdose for patients with HIV infection and substance dependence

Boston ARCH cohort analyzed to determine if number and type of medications is associated with non-fatal overdose (OD) among PLWH with past-year SUD or a lifetime history of injection drug use.

- 80% prescribed sedating medication
- 50% prescribed opioids
- 51% exceeded risky drinking limits
- 37% reported lifetime non-fatal OD.
- 7% past-year non-fatal OD
- Odds of lifetime non-fatal OD higher with each additional sedating medication (OR 1.26, 95% CI 1.08, 1.46) and any opioid medication (OR 2.31; 95% CI 1.37, 3.90).
- Odds of past year non-fatal OD greater with each additional sedating medication (OR 1.18; 95% CI 1.00, 1.39, $p = 0.049$), each additional non-ARV medication (OR 1.07; 95% CI 1.00, 1.15, $p = 0.048$). Not associated with any opioid medication.





Falls and Fracture



4F Study: Falls, Fractures, Frailty, Functioning

Primary Aims:

Is alcohol (and illicit drugs and polypharmacy) associated with

1. Falls (fractures secondarily)
2. ED/hospitalization for falls and fractures

....Do frailty or poor functioning mediate associations?

Exploratory Aim:

To develop and pilot test a falls prevention intervention

Study Sample:

BONE participant or HIV+ risky alcohol and/or other drug use



Alcohol Use and Falls and Fracture: Preliminary Findings

	Fall OR (95%CI)	Number of falls IRR (95%CI)	Fracture OR (95%CI)
Alcohol ¹			
Any heavy use	1.40 (1.01, 1.95)	1.27 (0.87, 1.85)	1.36 (0.73, 2.54)
Any use	1.29 (0.94, 1.75)	1.03 (0.71, 1.49)	0.94 (0.52, 1.72)
Grams/day ²	1.04 (0.99, 1.09)	1.06 (1.01, 1.12)	1.10 (1.00, 1.20)
#Heavy days ³	1.03 (0.99, 1.07)	1.04 (0.99, 1.09)	1.07 (1.00, 1.16)

Results of separate unadjusted regression models ¹Time Line Follow Back

²per increase in 14 grams/day ³per increase in 1 heavy drinking day



Illicit Drug Use and Falls and Fracture: Preliminary Findings

	Fall OR (95%CI)	Number of falls IRR (95%CI)	Fracture OR (95%CI)
Illicit drug			
Opioid use	1.78 (1.23, 2.58)	2.02 (1.28, 3.19)	2.30 (1.06, 4.98)
Sedative use	2.22 (1.34, 3.69)	3.24 (1.93, 5.42)	2.05 (0.68, 6.17)
Cocaine/stimulant	1.06 (0.72, 1.57)	1.66 (1.04, 2.63)	1.64 (0.79, 3.43)

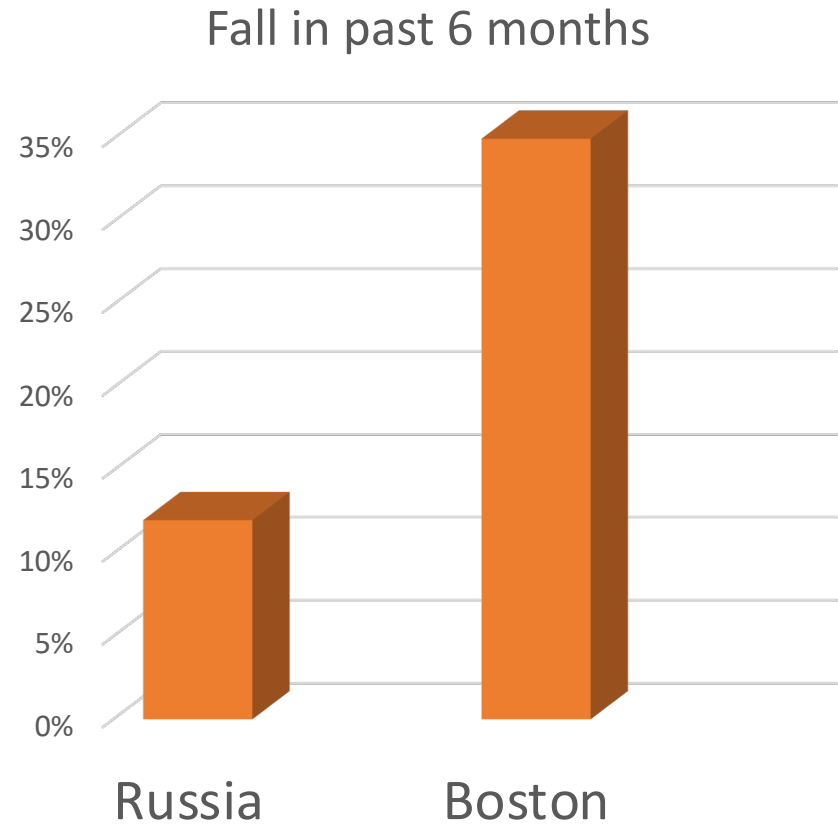
Results of separate unadjusted regression models

Addiction Severity Index



Alcohol and Falls in Russia and Boston ARCH Cohorts

- To identify whether a consumption or symptom-based measure of alcohol is associated with a fall
- AUDIT-C (consumption)
 - Higher AUDIT-C score was not associated with fall in Boston or Russia
 - Any heavy use was significantly associated with a fall in Boston¹



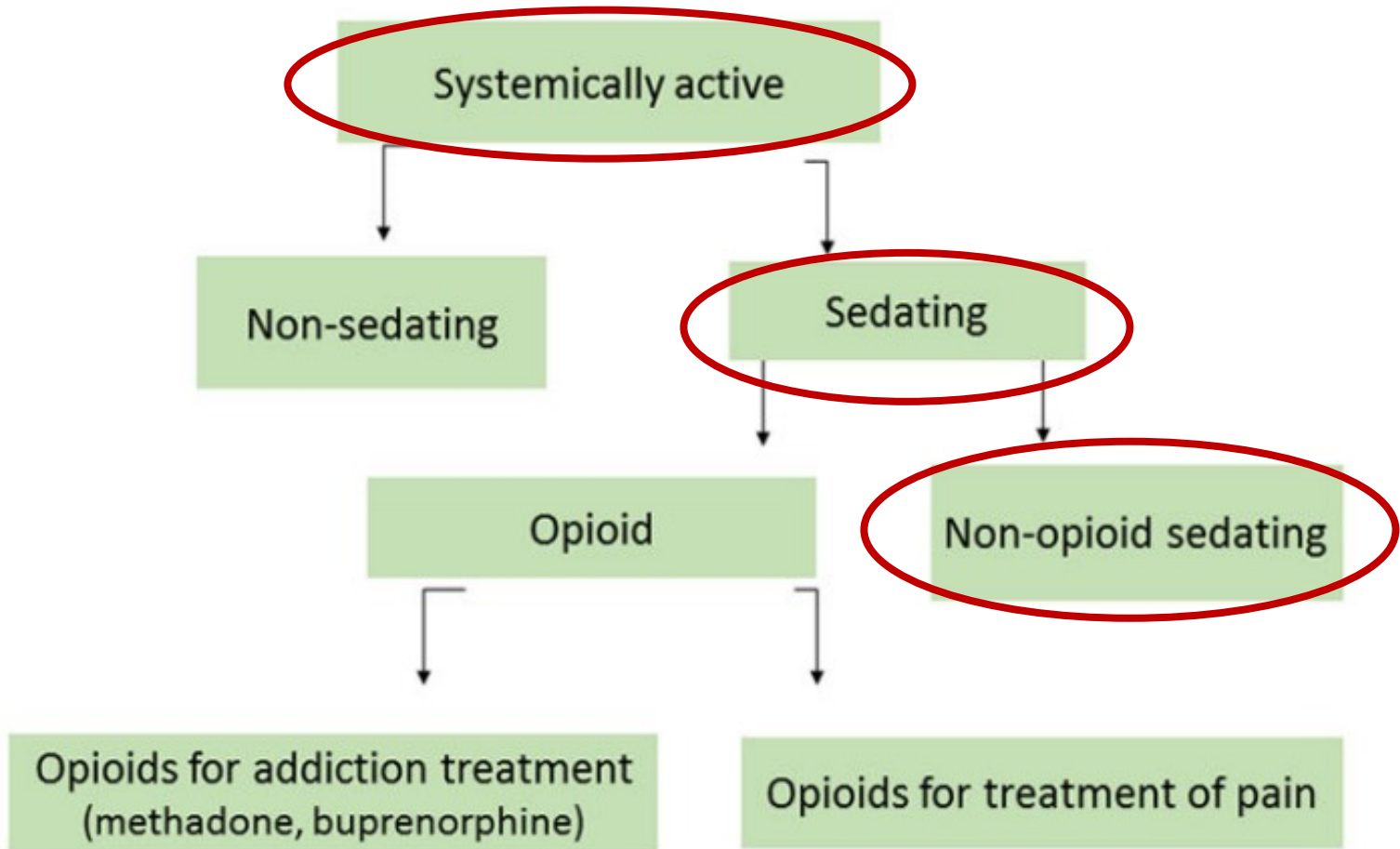
¹ Russia cohort eligibility included heavy drinking



Alcohol Use Disorder and Fall

	St. Petersburg AOR (95%CI)	Boston AOR (95%CI)
DSM-5 criteria		
Each additional criteria	1.10 (1.02, 1.18)	1.10 (1.02, 1.18)
Severity		
Moderate-severe AUD	1.74 (0.85, 3.58)	1.85 (1.10, 3.10)
Low severity AUD	Ref	1.00 (0.60, 1.66)
No AUD	0.88 (0.34, 2.32)	Ref

Polypharmacy and Falls





Key Takeaways on Fall Risk

- Alcohol, other drug (4F) (unadjusted)
 - Illicit sedative, illicit opioid → higher fall risk (opioid → fracture)
- Alcohol (Russia ARCH and 4F) and fall
 - Each additional DSM-5 criteria → higher fall risk
- Polypharmacy and fall requiring medical attention (Boston ARCH: Bone)
 - Each additional sedating medication → higher fall risk



Gaps in Understanding

- Adjusted associations
- Timing of use
- Role of frailty and physical functioning
- Potential target for interventions
 - Reducing AUD severity, number of sedative medications, any illicit opioid and/or sedative use



Boston ARCH 4F Study

Exploratory Aim: Falls Prevention Intervention



Goal: Develop and pilot test a falls prevention intervention to address identified risk factors for falls and modify the risk environment faced by PLWH at increased risk for falls

Formative research

Quantitative Analysis	Qualitative Analysis
  Dr. Simone V. Gill, PhD OTR/L Danny Shin, PhD Candidate OTR/L	  Dr. Christine Helfrich, PhD OTR/L



Boston ARCH 4F Study

Exploratory Aim: Qualitative Data



Findings from Individual Interviews

Participants' perceptions:

1. Grip strength, decreased balance are primary causes of falls
2. Falls related to substance use are differentiated from those due to balance – substance use falls aren't viewed as serious and aren't perceived as causing injury
3. Adaptive equipment not affordable, accessible
4. Structural barriers + socioeconomic challenges (e.g. resources, housing, food, ADLs, homelessness, social support, limited OT/PT)

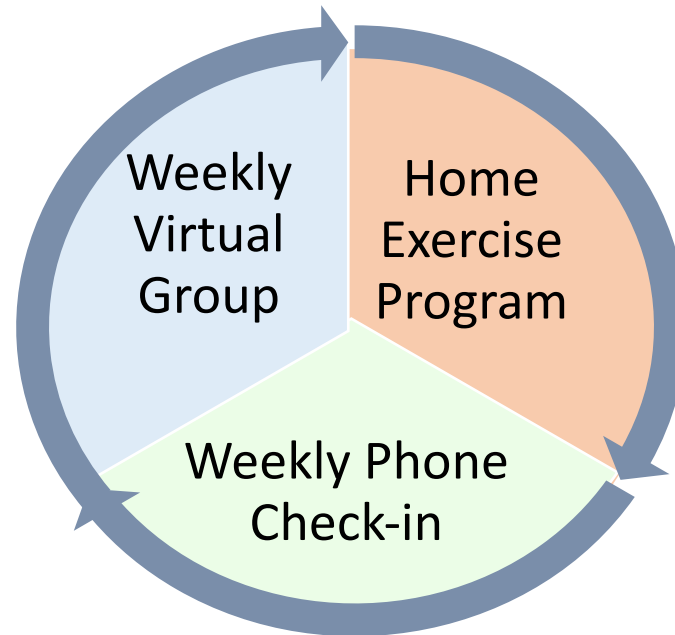


Fall Prevention Intervention Trial: Study Design

- Pilot randomized controlled trial (N=40)
- To pilot test a fall prevention intervention
 - 10-week weekly virtual group
 - Individual phone check-in
- Inclusion Criteria:
 - Any alcohol consumption in the last 30 days
 - Fall risk (CDC STEADI Fall Risk)
 - Reliable access to a phone or computer with internet connection
- Outcomes:
 - Primary: Engagement with Intervention, Satisfaction with Intervention
 - Secondary: Falls, alcohol use, physical functioning, frailty



Fall Prevention Intervention





Boston ARCH 4F Study

Exploratory Aim: Progress

First wave (n= 13)

- November 30, 2021- February 1, 2022

Second wave (n= 12)

- April 22, 2022 - ongoing

Take away points:

- Efficacious
- Complex





Boston ARCH 4F Study: COVID Supplement Aims



Objective: To assess the impact of the COVID-19 pandemic and the effects of physical (social) distancing and other mitigation strategies on outcomes:

Primary: Substance use (heavy alcohol use and/or other drug use)

Secondary: HIV medication adherence

Stressors:

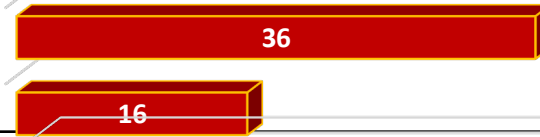
- Loneliness
- Food insecurity
- Pain interference

Pandemic Impacts Inventory Scale

% (n=96)

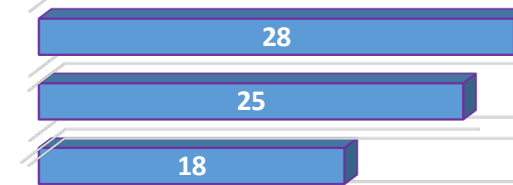
Infection history

Death of a close friend/family from COVID 36
Tested positive but no longer have it 16



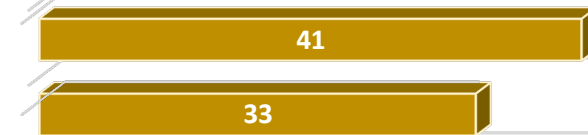
Home life

A lot of time taking care of family member 28
Increase in verbal arguments 25
Increase in physical conflict with partner 18



Economic

Unable to pay rent/utilities 41
Unable to get enough food 33



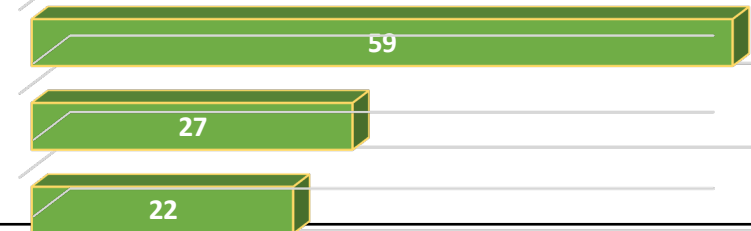
Physical health problem

Important medical procedure cancelled 27



Well-being

Increase in mental health problems 59
Increase in use of alcohol or substances 27
Unable to access mental health treatment 22



Positive effects

Less use of substances 45



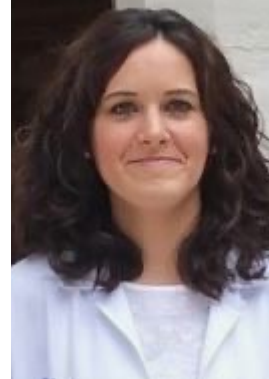


Trainee Opportunities

- Examine the impact of alcohol (and other drug, polypharmacy) use on frailty and physical functioning among PWH and substance use
- Identify associations between frailty (or poor functioning) and outcomes
 - Do relationships differ by substance use/disorder or substance type?
 - What are resiliency factors in whom frailty does not lead to falls, hospitalization, declining physical functioning?



Thanks to all of the
collaborators, trainees





Final Boston ARCH Key Takeaway

We found out how amazing Kara is – her leadership kept the 4F team on track, guided the ship through uncharted waters. Many, many thanks ❤️





QUESTIONS