SACENDU MEETING PRETORIA 23/10/18

FLAGSHIP PROJECT:

Efficacy of an Alcohol-Focused Intervention in Improving Adherence to Antiretroviral Therapy and HIV treatment Outcomes

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Funder: South African Medical Research Council (SAMRC): SAMRC-RFA-IFSP-01-2013/AlcoholHIV
Pan African Clinical Trials Register Number: PACTR201405000815100
and Global Fund through the SAMRC Office of AIDS & TB

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Background-1

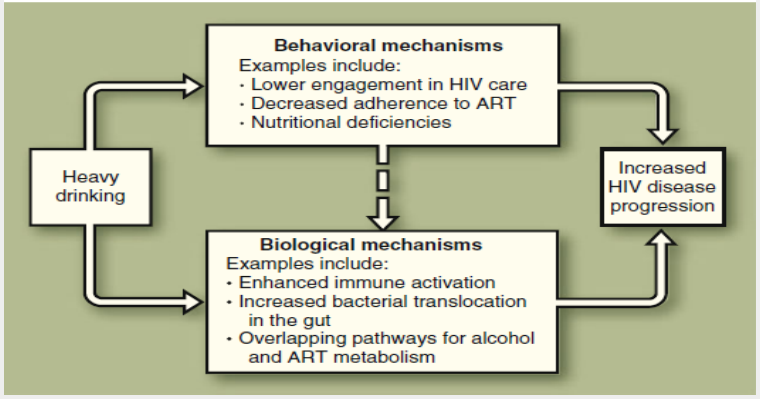
- Hazardous alcohol use directly contributes to:
  - acquisition and transmission of HIV
  - ART non-adherence, worsening of HIV disease, progression to AIDS, mortality
- South Africa has:
  - >4 million persons who are HIV positive & on ART
  - one of the highest levels of per capita alcohol consumption *per drinker* + high levels of heavy episodic drinking globally among men and women

Background-2

- For PLWHA ART is essential for improving + maintaining physical health, reducing HIV viral load
- Sub-optimal adherence to ART regimens can result in:
  - development of resistance to ART
  - poorer treatment outcomes
  - mortality
- Alcohol may impact cognitive processes necessary to maintain adequate adherence
- Beliefs that ART medications should not be taken while consuming alcohol may cause drinkers to fail to adhere to treatment

Background-3

- Hendershot et al.'s meta-analysis found that drinkers were 50%-60% as likely to be adherent as non-drinkers; & problem drinkers were only 47% as likely to be adherent as non-problem drinkers or abstainers
  - Missed ART doses occur primarily on drinking days
  - Consumption of alcohol significantly associated with time to ART treatment failure as well as subsequent survival
- At a molecular level, in vitro experiments have demonstrated that exposure to even a moderate dose of alcohol can increase HIV replication in peripheral blood mononuclear cells
  - may lead to an increase in HIV viral replication in those infected with HIV
  - may also impact CD4 cells, with research demonstrating lower CD4 counts among heavy alcohol users



Background-4

- Few RCTs have evaluated efficacy of alcohol-focused interventions in the context of HIV treatment
  - results have been equivocal
- Considerable evidence from SRs of RCTs that brief interventions (BI) are effective for reducing the volume of alcohol consumed & hazardous/harmful alcohol use among a range of patient populations, including those receiving PHC
- BIs we have chosen are based on motivational interviewing (MI) techniques and problem-solving therapy (PST) -- blended
  - Both have proven efficacy for reducing alcohol consumption and problem drinking among a range of patient populations
  - While the elements of this blended intervention are based on well-established treatment modalities of proven efficacy, they have not been implemented among PLWHA in SA

Goal

To improve knowledge on efficacy of an alcohol reduction intervention on alcohol consumption among PLWHA on ART, ART adherence and HIV treatment outcomes.

Specific objective

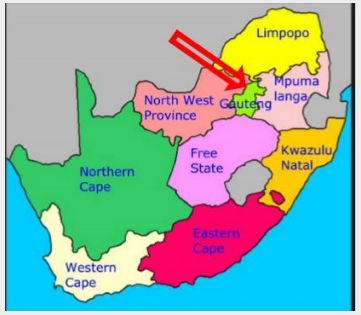
To assess *the efficacy* of blended MI-PST alcohol-focused intervention relative to TAU control group for:

- reducing the average volume of alcohol consumed (Primary Outcome)
- improving ART adherence (Secondary Outcome)
- maintaining ART adherence (Secondary Outcome)
- improving HIV treatment continuation (Secondary Outcome)
- reducing disease progression (Secondary Outcome)

Rationale

If heavy alcohol consumption is associated with disease progression *indirectly*, then reductions in alcohol consumption should be accompanied by (positive) changes in those mediators (e.g. improved ART adherence), and such changes should in turn be associated with positive changes in HIV outcomes (e.g. lower viral loads and higher CD4 counts)

MAIN TRIAL METHODS



Sites:

- District Hospitals (Pretoria West, Odi, Tshwane District, Jubillee)
- Tertiary/Regional Hospitals (Kalafong, Mamelodi)

Design:

- RCT - 2-arm comparison groups: PST/MI vs. Treatment as Usual (TAU)
- Randomisation within sites.
  - Treatment allocation done by site supervisors using pre-prepared consecutively numbered sealed, opaque envelopes, which contained the group assignment.
  - Interventionists not be blinded to which intervention the participants receive
- Repeated measures: baseline, 3-, 6-months

Participants:

Patients at ART clinics at hospitals who met eligibility criteria:

- ✓ Aged ≥ 18 years;
- ✓ AUDIT C ≥ 4 for men and ≥ 3 for women but AUDIT Total <23)
- ✓ Not on TB treatment
- ✓ HIV positive
- ✓ On ART for ≥ 3 months
- ✓ Living within the study area
- ✓ Not involved in another study

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MAIN TRIAL METHODS

Assessments:

Face-to-face interviews (structured questionnaire):

- Demographic, psycho-social, ART adherence, alcohol consumption

Biological samples:

- HIV-related outcomes (viral load – whole blood): @baseline & 6 months
- Alcohol-related outcomes (Phosphatidylethanol: Peth): 50%

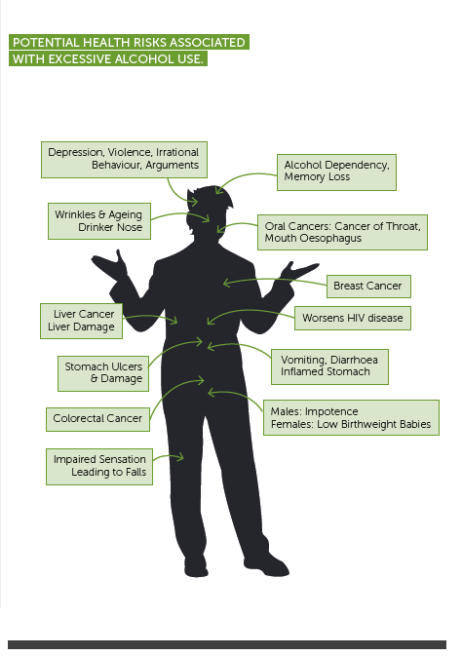
Incentives for participation

Ethical approval from SAMRC EC

- All procedures conducted in private spaces at the clinics

‘Intervention’ Groups

- Main Intervention: MI/PST Alcohol Focused Intervention
  - 4 sessions of MI-PST to reduce hazardous/harmful use of alcohol
- Treatment as Usual (TAU)
  - Standard package of care for PLWHA who are on ART and who drink at hazardous/harmful levels
  - Usually entails referral to adherence counsellor (for adherence issues) and/or clinical psychologist/social worker (for alcohol-related relational or social problems)




STEP 4:

WHAT IS LOW RISK DRINKING?

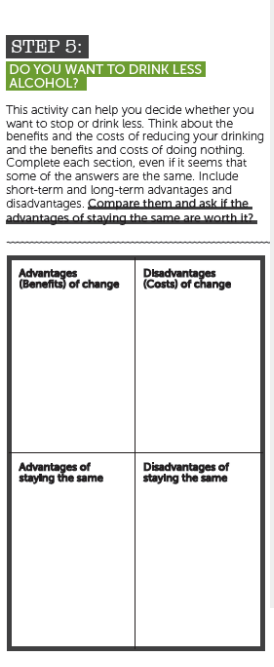
Some people can successfully reduce their drinking to low-risk limits. Others may find it hard to stay in these limits and may decide to stop drinking alcohol altogether.

HERE ARE SOME GENERAL GUIDELINES FOR LOW-RISK DRINKING:

- **Daily Limits:** No more than 4 standard drinks a day for men and 3 drinks a day for women
- **Weekly limits:** no more than 14 standard drinks a week for men and 7 standard drinks a week for women
- Keep within the daily AND weekly drinking limits
- Plan for at least two non-drinking days per week

DO NOT DRINK IF YOU ARE:

- Are driving a vehicle or using machinery and tools
- Are taking medicines that interact with alcohol
- Are doing any kind of dangerous physical activity
- Have a health condition that could be made worse by drinking
- Are pregnant or planning to be pregnant
- Are responsible for the safety of others
- Are making important decisions
- Are unable to control or


STEP 5:

DO YOU WANT TO DRINK LESS ALCOHOL?

This activity can help you decide whether you want to stop or drink less. Think about the benefits and the costs of reducing your drinking and the benefits and costs of doing nothing. Complete each section, even if it seems that some of the answers are the same. Include short-term and long-term advantages and disadvantages. Compare them and ask if the advantages of staying the same are worth it?

Advantages (Benefits) of change	Disadvantages (Costs) of change
Advantages of staying the same	Disadvantages of staying the same

Consolidated Standards of Reporting Trials (CONSORT) flow diagram showing actual participant flow

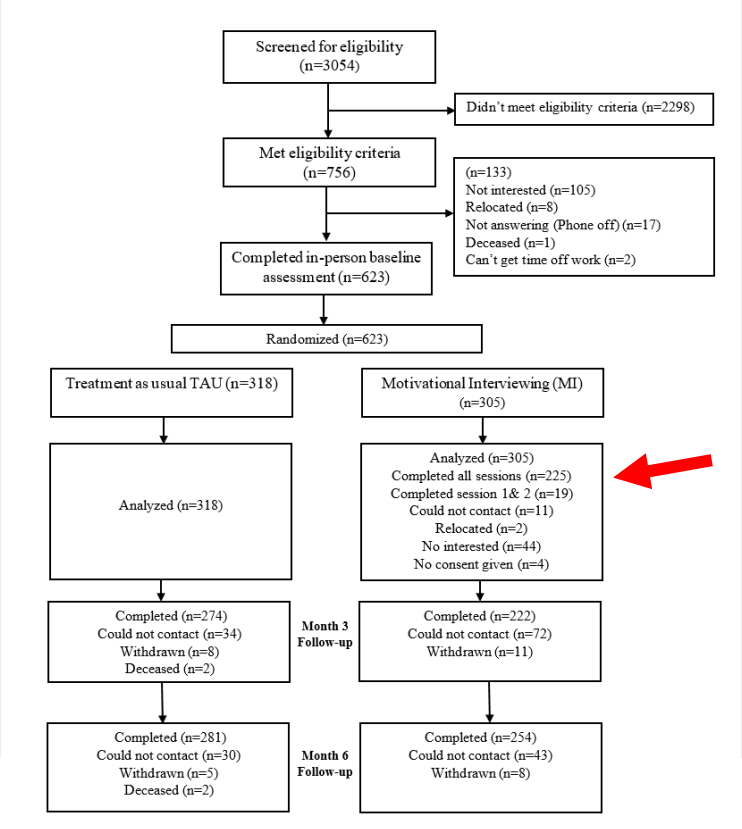
Screened

Enrollment

Allocation

Follow-Up 1

Follow-Up 2



SAMPLE DEMOGRAPHIC CHARACTERISTICS, YEARS ON ARVS, OUTCOME VARIABLES (N=623)

- Average age 41 years (TAU: 42, MI/PST: 40)*
- 58% female (TAU: 53%, MI/PST: 62%)*
- 39% high school completed
- 42% unemployed
- 52% ≤ R1600 monthly income
- Years on ARVS: 24% (0 - ≤4), 27% (4 - ≤7), 22% (7 - ≤9), 27% (>9)

* p<0.05 (comparing TAU with MI/PST

+No differences at baseline between TAU and MI/PST groups on any outcome variables

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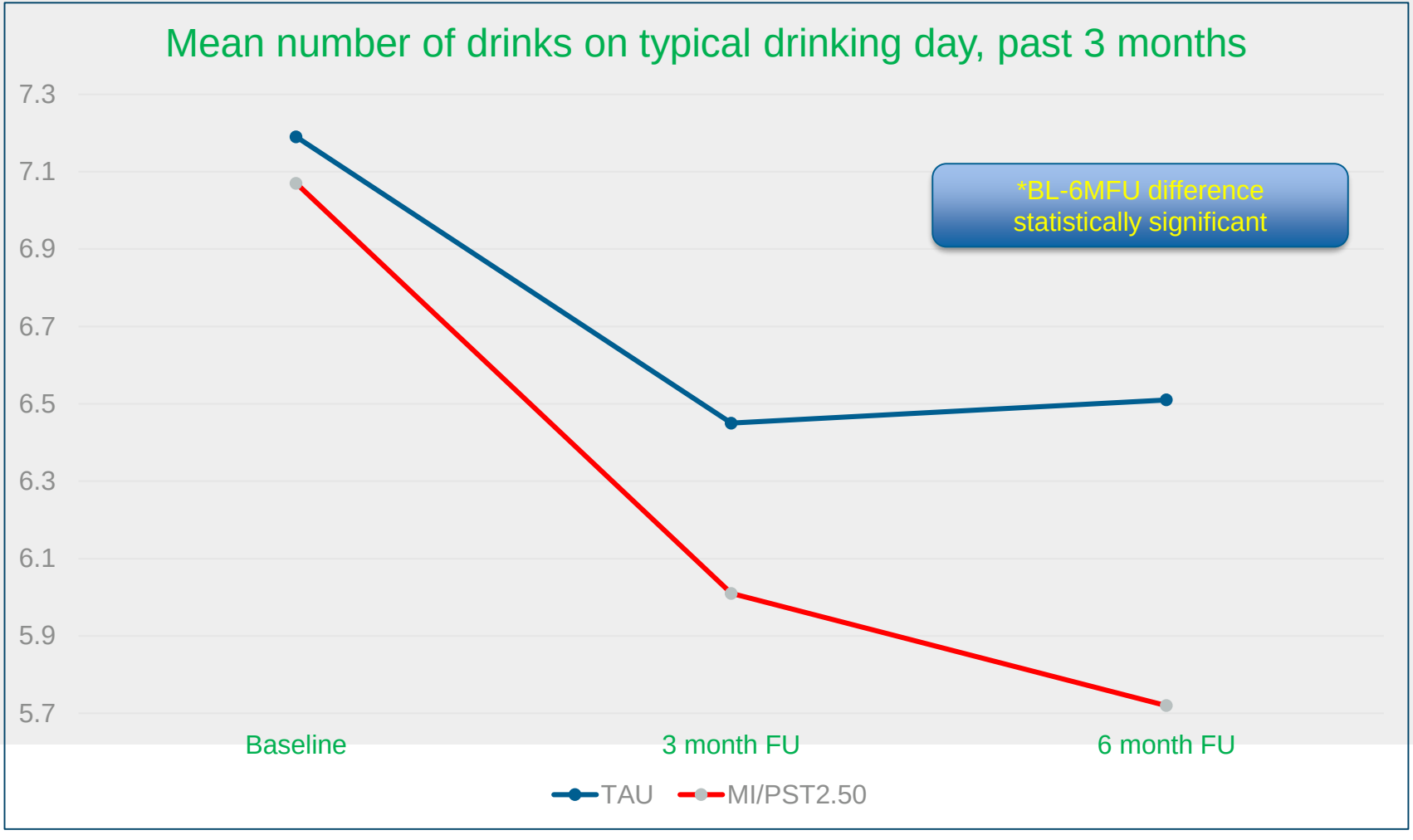
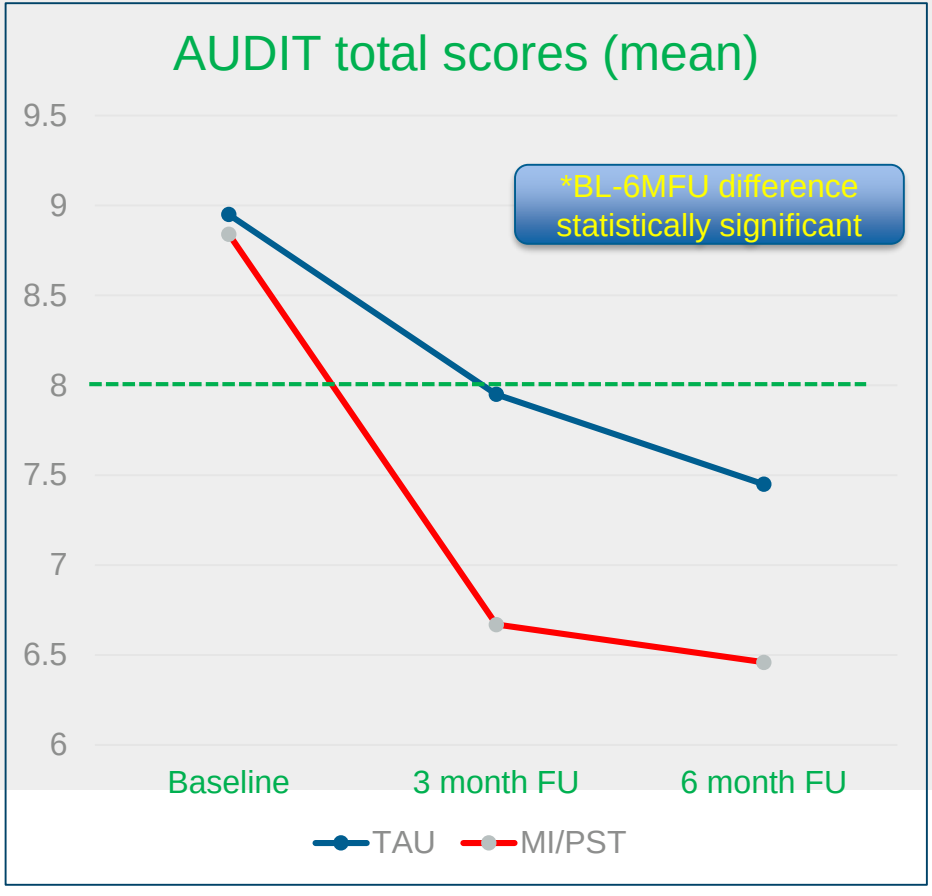
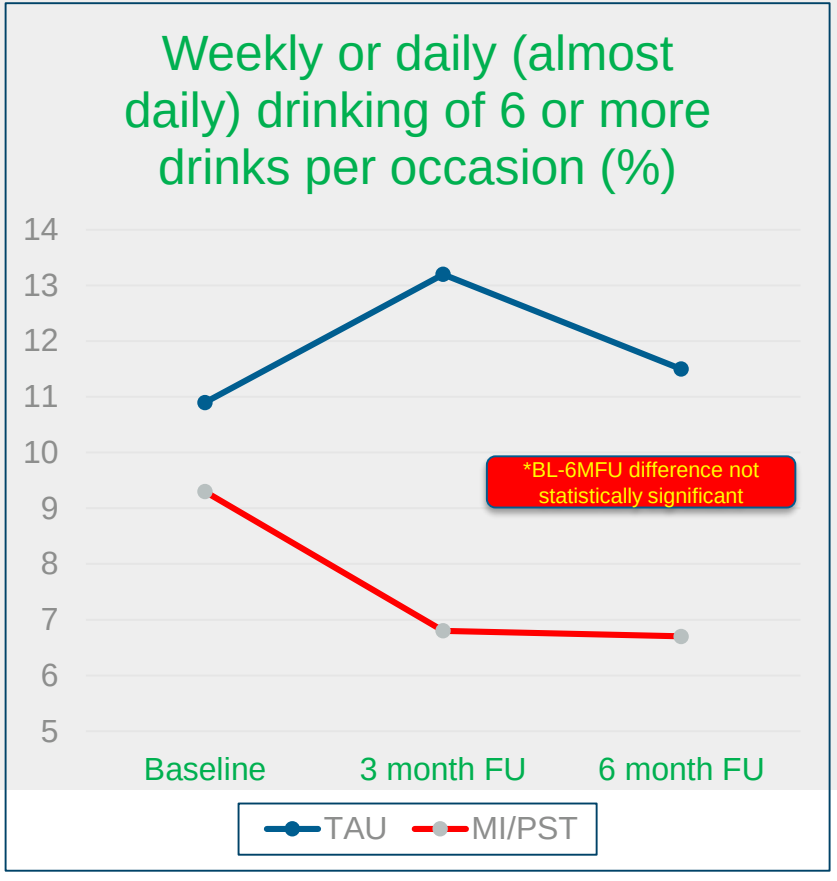
Self-reported alcohol use (past 3 months) -- AS TREATED



Self-reported alcohol use (past 3 months)





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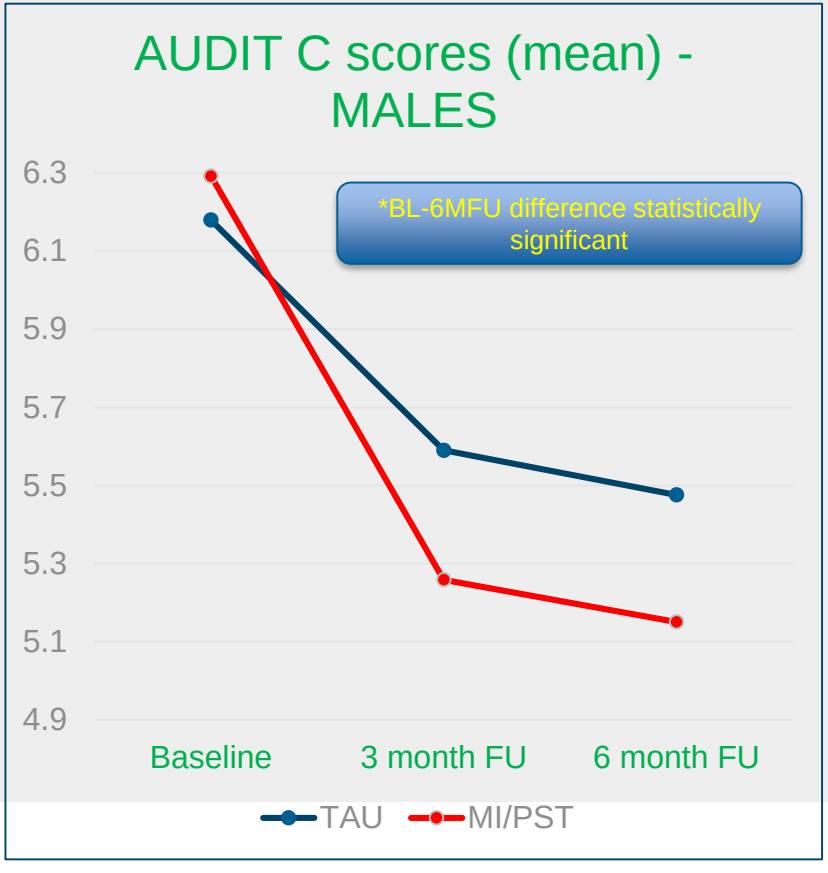
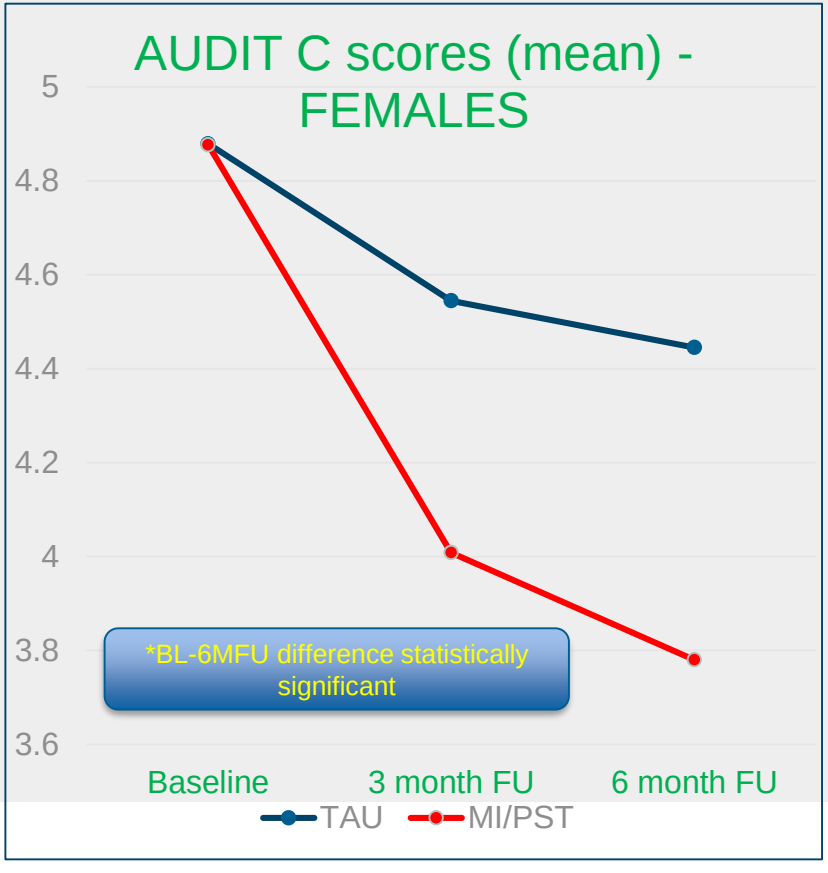
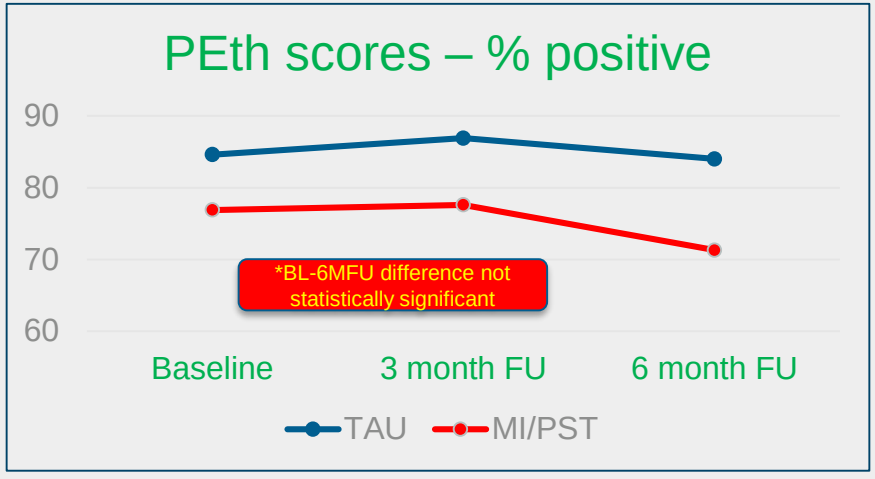
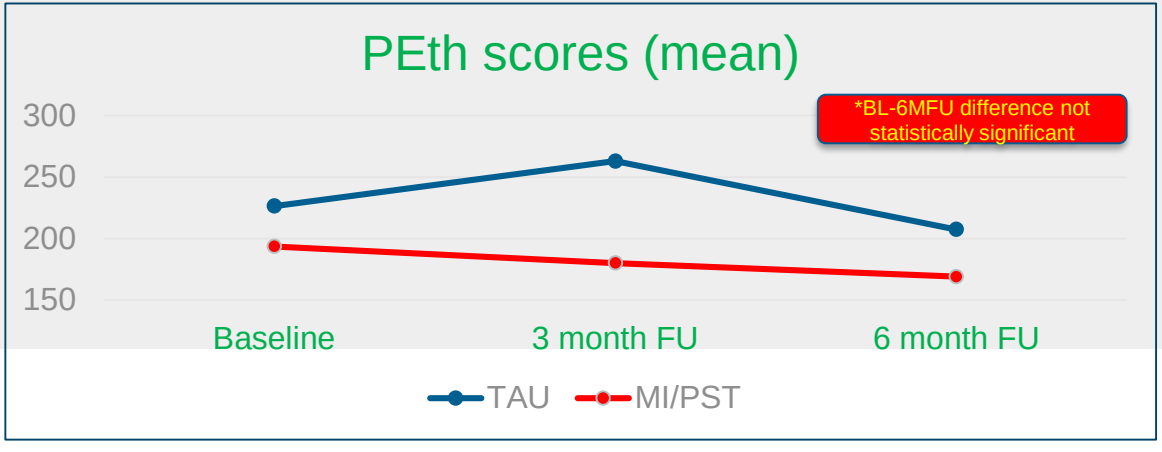




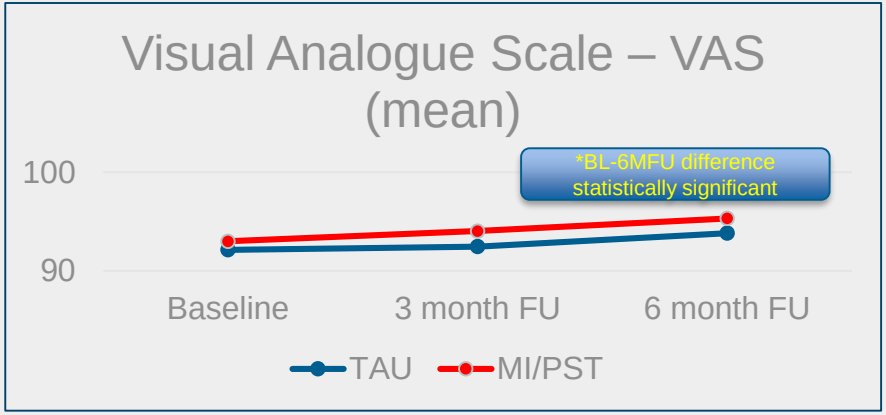
Biological markers for alcohol use (PEth)

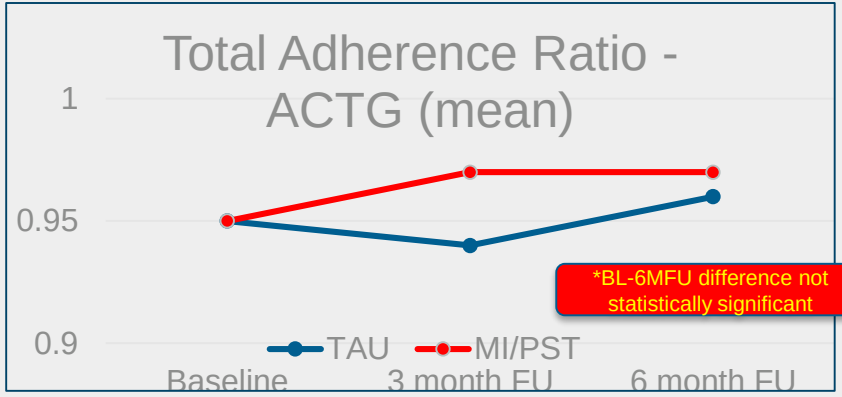


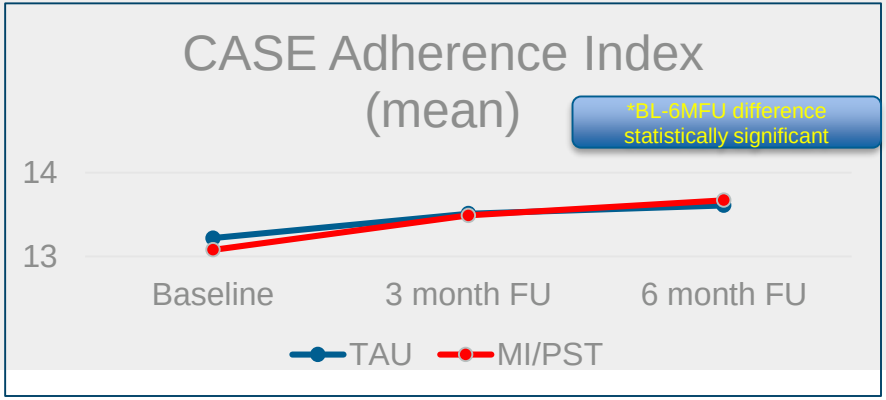
PETh scores <8mg/ML set to zero

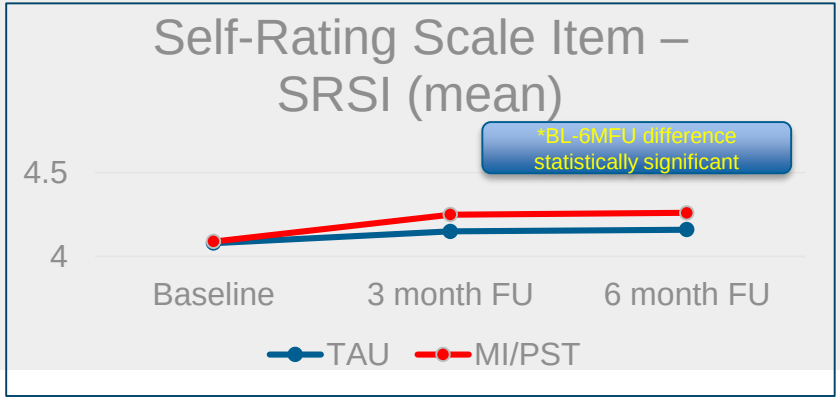


Adherence Measures

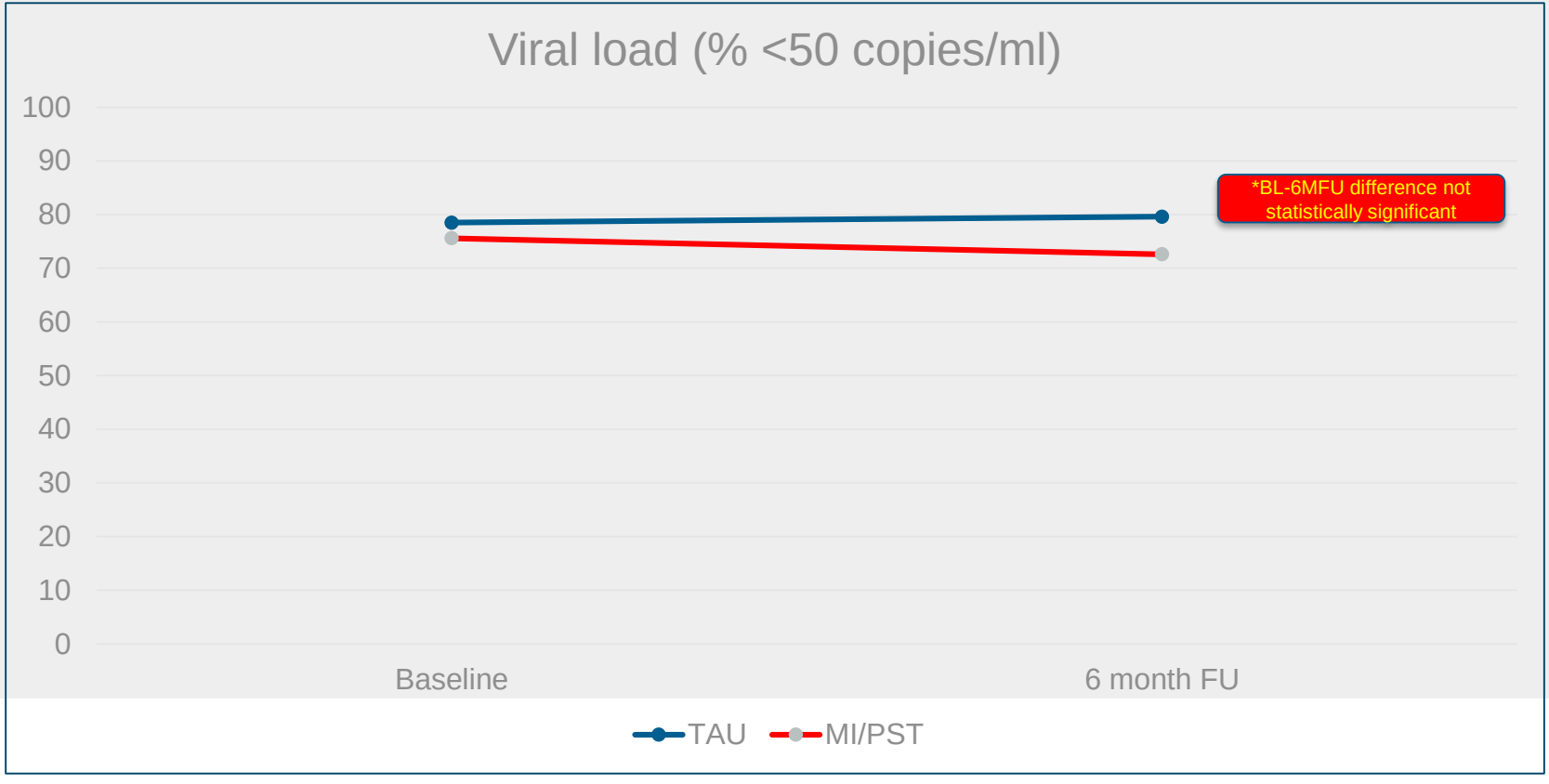




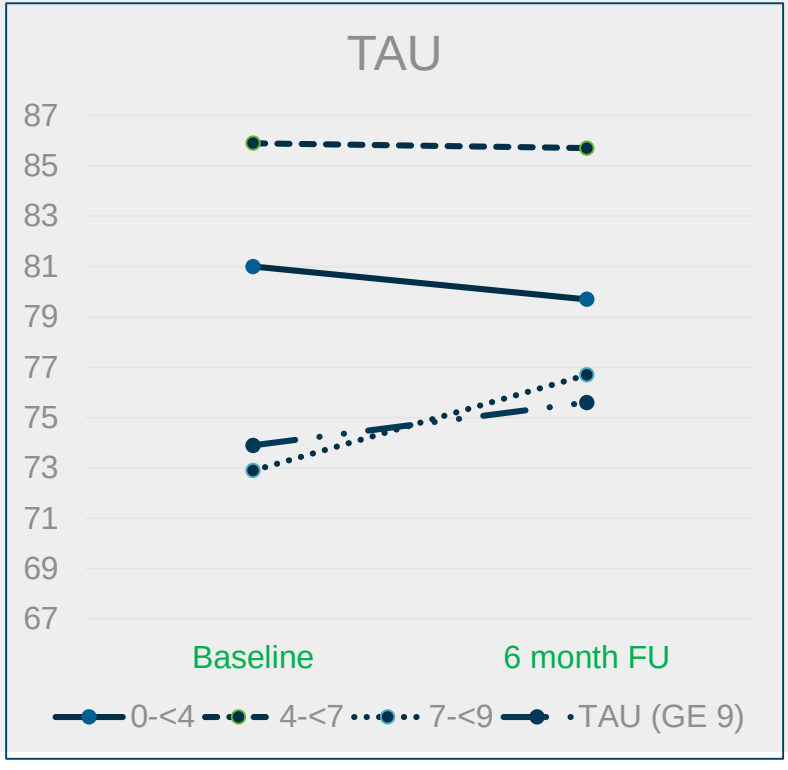




Viral load (viral suppression)



Viral load (% < 50 copies) by years on ART



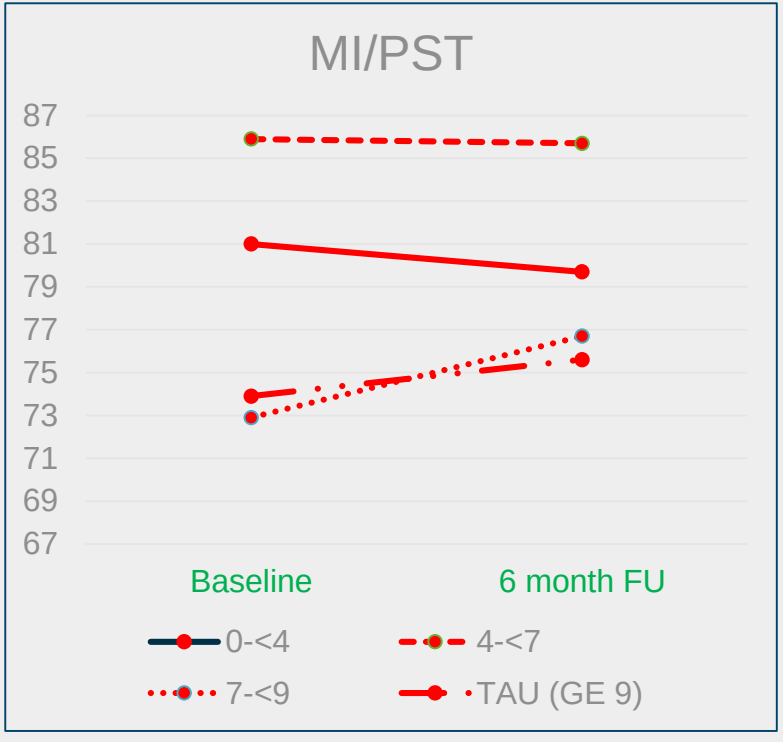


Table 3

Within group comparison of mean differences on different outcome variables at various time periods (As Treated)

Variable	Group	Baseline vs 3 month follow up		Baseline vs 6 month follow up		3 months vs 6 month follow up	
		Mean difference (95% CI)	p	Mean difference (95% CI)	p	Mean difference (95% CI)	p
Primary outcome							
Number of drinks consumed on typical drinking day past 3 months	TAU	0.61 (0.21 – 1.01)	<0.0001	0.62 (0.20 – 1.04)	<0.0001	-0.08 (-0.51 – 0.36)	0.9472
	MI/PST	1.16 (0.66 – 1.67)		1.39 (0.90 – 1.89)		0.14 (-0.41 – 0.70)	
% of weekly or (almost) daily drinking of 6 or more drinks per occasion	TAU	-1.59% (-6.56; 3.37)	0.8983	-0.80% (-5.42; 3.82)	0.6916	1.27% (-3.95; 6.49)	0.8966
	MI/PST	2.98% (-2.41; 8.36)		2.73% (-2.44; 7.90)		-1.31% (-7.10; 4.48)	
Secondary outcomes							
AUDIT total score	TAU	0.96 (0.42 – 1.50)	<0.0001	1.37 (0.83 – 1.91)	<0.0001	0.40 (-0.19 – 0.99)	0.1729
	MI/PST	2.12 (1.46 – 2.78)		2.39 (1.71 – 3.08)		0.20 (-0.50 – 0.91)	
% PEth (≥8 mg/ml)	TAU	-2.16% (-7.68; 3.36)	0.7158	1.37% (-3.71; 6.45)	0.0947	3.62% (-2.62; 9.86)	0.0453
	MI/PST	1.09% (-7.32; 9.49)		6.86% (-0.59; 14.31)		7.69% (-1.22; 16.6)	
PEth scores	TAU	-28.80 (-59.48 – 1.88)	0.2579	4.19 (-25.89 – 34.27)	0.2405	0.40 (-0.19 – 0.99)	0.0859
	MI/PST	12.37 (-13.72 – 38.45)		24.57 (-4.49 – 53.63)		0.20 (-0.50 – 0.91)	
Visual Analogue Scale (VAS)[1] M (SD)	TAU	-0.51 (-2.16 – 1.15)	0.1738	-1.60 (-3.30 – 0.10)	0.0016	-1.56 (-3.20 – 0.08)	0.0263
	MI/PST	-0.99 (-2.67 – 0.69)		-2.34 (-3.96 – -0.71)		-1.14 (-2.63 – 0.34)	
Total Adherence Ratio (ACTG)	TAU	0.01 (-0.01 – 0.03)	0.7566	-0.01 (-0.03 – 0.01)	0.1417	-0.02 (-0.04 – 0)	0.1779
	MI/PST	-0.02 (-0.03 – 0)		-0.01 (-0.03 – 0.01)		0.01 (-0.02 – 0.03)	
CASE Adherence Index[1]	TAU	-0.31 (-0.63 – 0.02)	0.0156	-0.43 (0.77 – 0.10)	0.0002	-0.13 (-0.44 – 0.18)	0.2948
	MI/PST	-0.35 (-0.77 – 0.06)		-0.60 (-1.00 – -0.20)		-0.16 (-0.60 – 0.28)	
Self-Rating Scale Item (SRSI)[1]	TAU	-0.08 (-0.19 – 0.04)	0.0170	-0.08 (-0.21 – 0.04)	0.0116	-0.03 (-0.16 – 0.10)	0.7485
	MI/PST	-0.16 (-0.31 - -0.02)		-0.19 (-0.34 - -0.03		0	
Viral load (% <50 copies/ml)	TAU			0.78% (-3.86; 5.43)	0.3102		
	MI/PST			3.02% (-2.03; 8.06)			
Additional outcomes							
AUDIT-C Score	TAU	0.44 (0.18 – 0.70)	<0.0001	0.53 (0.25 – 0.82)	<0.0001	0.07 (-0.26 – 0.39)	0.4087
	MI/PST	1.06 (0.73 – 1.40)		1.23 (0.89 – 1.57)		0.15 (-0.25 – 0.54)	

Note. TAU = treatment as usual (N=318); MI/PST = motivational interviewing/problem solving therapy (N=244); ART = antiretroviral therapy; AUDIT = Alcohol Use Disorders Identification Test; [1]Adherence measures. t-tests for continuous variables and Chi-square tests for categorical variables

ADOLESCENT GIRLS AND YOUNG WOMEN (N=115) - %

Less than Gr 12 education: 57%; Unemployed: 58%

Sometimes/often hungry: 18%

	Baseline		6 month follow up	
	Control	MI/PST	Control	MI/PST
≥5 drinks on typical drinking day	79.5	84.3	75.0	51.1
Drinking ≥5 drinks on an occasion ≥ monthly	20.5%	28.6	37.5	23.0
AUDIT score ≥ 8 (risky)	38.4	45.7	40.6	29.1
PEth score ≥ 50	26.3	27.0	29.4	26.9
Adherence – VAS score (% VAS GE 98)	35.0	49.3	32.4	46.3
Viral load < 50 (suppressed)	75.0	76.1	72.7	69.4

Discussion

- Main findings
  - Signif drop in mean # drinks/drinking day @ 6MFU after intervention
  - Signif drop in AUDIT total scores & AUDIT-6 scores@6MFU after intervention
  - Signif increase on adherence measures @6MFU after intervention on ¾ measures
  - No effect on weekly binge drinking, PEth scores or VL
  - We substantially reduced self-reported “risky/problematic” drinking in young women but not ART adherence or VL
- Compared to others
  - Samet et al. (2005), MI intervention with HIV patients on ART (Boston): no signif difference in medication adherence, CD4 count, HIV VL or alcohol consumption
  - Papas et al. (2011) among HIV+ women (Kenya) found 30 day post-tx, reductions since baseline were signif larger in CBT compared to TAU for both % of drinking days (PDD) and drinks per drinking day PDD and (DDD). More CBT than control participants reported abstinence at all follow ups
- Limitations
  - Generalisability to other sites
  - Need to do ITT analyses

PROJECT TEAM

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