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

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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
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
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

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

Mean number of drinks on typical drinking day, past 3 months

- Baseline
- 3 month FU
- 6 month FU

*BL-6MFU difference statistically significant
Self-reported alcohol use (past 3 months)

AUDIT total scores (mean)

Weekly or daily (almost daily) drinking of 6 or more drinks per occasion (%)
Self-reported alcohol use (past 3 months)

**AUDIT C scores (mean) - MALES**

Baseline | 3 month FU | 6 month FU
---|---|---
TAU | 6.3 | 6.1 | 6.0
MI/PST | 5.9 | 5.7 | 5.6

*BL-6MFU difference statistically significant

**AUDIT C scores (mean) - FEMALES**

Baseline | 3 month FU | 6 month FU
---|---|---
TAU | 4.9 | 4.8 | 4.7
MI/PST | 4.2 | 4.1 | 4.0

*BL-6MFU difference statistically significant
Biological markers for alcohol use (PEth)

**PETh scores – % positive**

- Baseline
- 3 month FU
- 6 month FU

- TAU
- MI/PST

*BL-6MFU difference not statistically significant

**PETh scores (mean)**

- Baseline
- 3 month FU
- 6 month FU

- TAU
- MI/PST

*BL-6MFU difference not statistically significant

PETh scores <8mg/ML set to zero
## Adherence Measures

### Visual Analogue Scale – VAS (mean)

- **Baseline**
- **3 month FU**
- **6 month FU**

<table>
<thead>
<tr>
<th></th>
<th>TAU</th>
<th>MI/PST</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>3 month FU</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>6 month FU</strong></td>
<td>90</td>
<td>100</td>
</tr>
</tbody>
</table>

*BL-6MFU difference statistically significant*

### Total Adherence Ratio - ACTG (mean)

- **Baseline**
- **3 month FU**
- **6 month FU**

<table>
<thead>
<tr>
<th></th>
<th>TAU</th>
<th>MI/PST</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>3 month FU</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>6 month FU</strong></td>
<td>0.9</td>
<td>0.95</td>
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</tbody>
</table>

*BL-6MFU difference not statistically significant*

### CASE Adherence Index (mean)

- **Baseline**
- **3 month FU**
- **6 month FU**

<table>
<thead>
<tr>
<th></th>
<th>TAU</th>
<th>MI/PST</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline</strong></td>
<td>13</td>
<td></td>
</tr>
<tr>
<td><strong>3 month FU</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>6 month FU</strong></td>
<td>14</td>
<td></td>
</tr>
</tbody>
</table>

*BL-6MFU difference statistically significant*

### Self-Rating Scale Item – SRSI (mean)

- **Baseline**
- **3 month FU**
- **6 month FU**

<table>
<thead>
<tr>
<th></th>
<th>TAU</th>
<th>MI/PST</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>3 month FU</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>6 month FU</strong></td>
<td>4</td>
<td>4.5</td>
</tr>
</tbody>
</table>

*BL-6MFU difference statistically significant*
Viral load (viral suppression)

Viral load (% <50 copies/ml)

Baseline 6 month FU

*BL-6MFU difference not statistically significant
Viral load (% < 50 copies) by years on ART

**TAU**

- Baseline
- 6 month FU

- 0-<4
- 4-<7
- 7-<9
- TAU (GE 9)

**MI/PST**

- Baseline
- 6 month FU

- 0-<4
- 4-<7
- 7-<9
- TAU (GE 9)
| Variable | Group | Baseline vs 3 month follow up | | | Baseline vs 6 month follow up | | | 3 months vs 6 month follow up | | |
|----------|-------|-----------------------------|---|---|-----------------------------|---|---|-----------------------------|---|
| **Primary outcome** | | Mean difference (95% CI) | p | Mean difference (95% CI) | p | Mean difference (95% CI) | p |
| 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)³ 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 – 0.0) | |
| CASE Adherence Index³ | 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)³ | 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; ³Adherence measures. *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%

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<tr>
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<th>Baseline</th>
<th>6 month follow up</th>
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<tr>
<td></td>
<td>Control</td>
<td>MI/PST</td>
</tr>
<tr>
<td>≥5 drinks on typical drinking day</td>
<td>79.5</td>
<td>84.3</td>
</tr>
<tr>
<td>Drinking ≥5 drinks on an occasion ≥ monthly</td>
<td>20.5%</td>
<td>28.6</td>
</tr>
<tr>
<td>AUDIT score ≥ 8 (risky)</td>
<td>38.4</td>
<td>45.7</td>
</tr>
<tr>
<td>PEth score ≥ 50</td>
<td>26.3</td>
<td>27.0</td>
</tr>
<tr>
<td>Adherence – VAS score (% VAS GE 98)</td>
<td>35.0</td>
<td>49.3</td>
</tr>
<tr>
<td>Viral load &lt; 50 (suppressed)</td>
<td>75.0</td>
<td>76.1</td>
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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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