Supporting the Art: Medication Adherence Patterns in Persons Prescribed Ingestible Sensor-enabled Oral Pre-Exposure Prophylaxis to Prevent HIV Infection

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Adherence 2022 • November 7-9 • Washington, DC
Effective Long-Term Therapy: An ART

“The art has three factors, the disease, the patient, the physician. The physician is the servant of the art. The patient must cooperate with the physician in combatting the disease.” -Hippocrates

This Art requires:

• Highly individualized series of investigations
• Understanding how each patient and their disease risk intertwine over time
• Trust and honesty between both patient and physician

A. Richey et al., JMIR Mental Health, 2022
S.H. Browne et al., Clinical Infectious Diseases, 2022
Ingestible Sensor Technology

- Evaluated IS-Truvada* within Digital Health Feedback System (DHFS)

*IS: Ingestion Sensor enabled
Evaluated

• Adherence measurement accuracy
• Persistence of use & adverse events
• Adherence as continuous variable & a priori ‘successful’ 80% adherence threshold
• Association of predictors with adherence
• Ability to capture adherence patterns
Methods

Clinical Trial
• Single arm open label intervention
• IS-Truvada® with DHFS for 12 weeks
• HIV-ve adults starting oral PrEP
• Baseline demographics
• Utox

Self-report questionnaires*
• Habitual Self-Control
• Self-efficacy beliefs
• Depression scale (PHQ-8)
• Alcohol use (AUDIT)
• Drug use (DAST-10)
• Pittsburg Sleep Quality Index (PSQI)
• HIV Risk Perception

*S.H. Browne et al., CID, 2022
Statistics

• Positive detection accuracy & adverse events as %
• Kaplan Meier Estimate for persistence-of-use.
• Primary end point: Proportion of IS Truvada prescribed doses captured by DHFS per participant and overall
• Persisting ≥ 28 days: mixed-effects logistic regression modelled associations with medication adherence.
• Adherence patterns (taking and timing) analyzed
Results: Study Enrollment & Demographics

- Mean age 37.6 yrs (18-69)
- Mostly male (90.1%), white (77.5%; 33.8% Hispanic), housed (95.8%) & employed (74.6%)
- Baseline Utox +ve 40.6%: 24.6% marijuana, 14.5% amphetamines, 11.6% methamphetamines
Results

Adverse Events
- Well tolerated
- 5.6 % device related
- Mild ≤ Grade 2
- Patch: Rash, pruritis
- Patch: 1 dermatitis – discontinuation

Detection Accuracy
- 99.3% (CI$_{95}$ 97.2%, 100%) excludes held doses, patch not worn, mobile device not functioning
- 95.4% (CI$_{95}$ 91.8%, 98.2%) all study visits
Results: Persistence of Use

- Persistence amongst 71 participants
- Week 4: 88.7% (81.7%, 96.4%)
- Week 12: 66.2% (56.1%, 78.2%)
Primary End Point

- 63 participants (88.7%) ≥28 days
- 4987 observation days (av. 79.2, range 29-105)
- Total proportion confirmed doses was 86.2% (CI_{95} 82.5%, 89.4%)
- *a priori* individual-level adherence proportion of ≥80% confirmed doses 79.4% (CI_{95} 66.7%, 87.3%).
- Consistent participant associations across adherence analyses
## Confirmed Dose Associations

<table>
<thead>
<tr>
<th>Variable</th>
<th>Single-predictor model</th>
<th>Multi-predictor model</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>P-value</td>
</tr>
<tr>
<td>Age, per year</td>
<td>1.065 (1.034, 1.098)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Female or transgender vs male</td>
<td>1.750 (0.528, 5.810)</td>
<td>0.354</td>
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<tr>
<td>Race/Ethnicity</td>
<td></td>
<td></td>
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<tr>
<td>- White, non-Hispanic</td>
<td>1 (reference)</td>
<td></td>
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<tr>
<td>- Black, non-Hispanic</td>
<td>1.949 (0.312, 12.659)</td>
<td></td>
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<tr>
<td>- Asian, non-Hispanic</td>
<td>0.807 (0.113, 5.624)</td>
<td></td>
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<tr>
<td>- Hispanic</td>
<td>0.866 (0.298, 2.480)</td>
<td></td>
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<tr>
<td>Positive screen, any drugs</td>
<td>0.478 (0.237, 0.965)</td>
<td>0.040</td>
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<tr>
<td>Number of drugs</td>
<td>0.589 (0.432, 0.801)</td>
<td>0.001</td>
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<tr>
<td>Positive methamphetamine screen</td>
<td>0.162 (0.065, 0.397)</td>
<td>&lt;0.001</td>
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<tr>
<td>Unemployed/retired/disabled</td>
<td>0.879 (0.401, 1.932)</td>
<td>0.742</td>
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<tr>
<td>Transient or homeless</td>
<td>0.431 (0.085, 2.201)</td>
<td>0.305</td>
</tr>
<tr>
<td>Global PSQI score, per point</td>
<td>0.977 (0.875, 1.091)</td>
<td>0.670</td>
</tr>
<tr>
<td>Self-efficacy, per point</td>
<td>0.921 (0.369, 2.321)</td>
<td>0.857</td>
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<tr>
<td>Habitual self-control, per point</td>
<td>1.390 (0.697, 2.811)</td>
<td>0.343</td>
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<tr>
<td>HIV risk perception (PRHS 8-item) per point</td>
<td>1.010 (0.952, 1.072)</td>
<td>0.730</td>
</tr>
<tr>
<td>PHQ-8 total, per point</td>
<td>0.950 (0.890, 1.014)</td>
<td>0.118</td>
</tr>
<tr>
<td>Depressed mood (4-level), per level</td>
<td>0.696 (0.446, 1.081)</td>
<td>0.105</td>
</tr>
<tr>
<td>Cumulative time on study (per week)</td>
<td>0.899 (0.876, 0.923)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Confidence intervals and p-values from likelihood ratio test. Confidence intervals for race/ethnicity are Bonferroni-corrected. Depressed mood from question 2 of PHQ-8.
Data Gaps

• Worse confirmed adherence associated with higher proportion of data gap days OR 0.964 (CI$_{95}$ 0.942, 0.987) per % of days with data gap, p=0.003.

• Consistent participant associations across analyses with and without data gaps.
Patterns of Adherence

Days on Study

- Dose recorded
- Dose not recorded, DOT completed
- Dose not recorded, no data gap
- Dose not recorded, data gap
- Dose not recorded, held dose
Patterns of Adherence

Individual Plots

Individual Clustering

• No confirmed dose days clustered $p=0.003$
• Data gap days clustered $p<0.001$
Dose Timing & Adherence

![Box plot showing proportion of doses taken within ±2h window for confirmed doses.](image)

- Confirmed doses:
  - Less than 80%: n=13
  - 80%: n=50

- Proportion of doses taken within ±2h window:
  - p < 0.001
Summary & Conclusion I

- Highly accurate equivalent to DOT
- Marked individual variation in adherence
- 20% below ≥80% *a priori* individual-level adherence proportion
- Predictors of adherence: age, methamphetamine use, depressive symptoms and length of treatment.
- Predictors consistent across analyses
- Data gaps surrogates for lapses in adherence
Summary & Conclusions II

- Clustering of days with no dose confirmation - rationale for real-time intervention studies
- Color coded visuals allow rapid patient identification for follow-up
- Individualized data and visuals may support honest, compassionate physician – patient discussion and guide PrEP choices over time
Acknowledgements

Digital Medicine UCSD
Sara Browne
Florin Vaida
Anya Umlauf
Constance Benson
Amanda Tucker
Bianca Ramirez

Funding
National Institute of Mental Health R01MH110057
Program Officer: Mike Stirratt

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