

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

Sara H. Browne MD MPH

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)



5 Social Support Network 6 4 Secure Server **Provider Web Portal** 3 Patient Mobile Application **Digital Medicines**

Adhesive Patch

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

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





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 \leq Grade 2
- Patch: Rash, pruritis
- Patch: 1 dermatitis discontinuation

Detection Accuracy

- 99.3% (CI₉₅ 97.2%, 100%) excludes held doses, patch not worn, mobile device not functioning
- 95.4% (CI₉₅ 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%) \geq 28 days
- 4987 observation days (av. 79.2, range 29-105)
- Total proportion confirmed doses was 86.2% (CI₉₅ 82.5%, 89.4%)
- *a priori* individual-level adherence proportion of ≥80% confirmed doses 79.4% (CI₉₅ 66.7%, 87.3%).
- Consistent participant associations across adherence analyses

Confirmed Dose Associations



	Single-predictor model		Multi-predictor model	
Variable	OR (95% CI)	P-value	OR (95% CI)	P-value
Age, per year	1.065 (1.034, 1.098)	< 0.001	1.060 (1.033, 1.091)	< 0.001
Female or transgender vs male	1.750 (0.528, 5.810)	0.354		
Race/Ethnicity		0.704		
- White, non-Hispanic	1 (reference)			
- Black, non-Hispanic	1.949 (0.312, 12.659)			
- Asian, non-Hispanic	0.807 (0.113, 5.624)			
- Hispanic	0.866 (0.298, 2.480)			
Positive screen, any drugs	0.478 (0.237, 0.965)	0.040		
Number of drugs	0.589 (0.432, 0.801)	0.001		
Positive methamphetamine screen	0.162 (0.065, 0.397)	< 0.001	0.198 (0.087, 0.444)	< 0.001
Unemployed/retired/disabled	0.879 (0.401, 1.932)	0.742		
Transient or homeless	0.431 (0.085, 2.201)	0.305		
Global PSQI score, per point	0.977 (0.875, 1.091)	0.670		
Self-efficacy, per point	0.921 (0.369, 2.321)	0.857		
Habitual self-control, per point	1.390 (0.697, 2.811)	0.343		
HIV risk perception (PRHS 8-item)	1.010 (0.952, 1.072)	0.730		
per point				
PHQ-8 total, per point	0.950 (0.890, 1.014)	0.118		
Depressed mood (4-level), per level	0.696 (0.446, 1.081)	0.105	0.710 (0.489, 1.028)	0.069
Cumulative time on study (per week)	0.899 (0.876, 0.923)	<0.001	0 903 (0 878 0 929)	< 0.001

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 (CI₉₅ 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

1	••••••	••••••						
3					•••			
4			••••••••••••••••••••)	••			
6	**********							
8	•••••••							
9 10)				
11	•••••••••••••••••••••				•			
12								
14	***************************************	**********************						
16	*************************	***************						
17								
19	•••••••••••••••							
20			•••••••••••••••					
22	***************************************							
23								
25								
27	*******************************							
28				• • • • • • • • • • • • • • • • • • •				
30	•••••••••••••••							
32								
33								
35	***************************************							
36 37								
38	****************							
39 40								
41	***************************************	****************						
43	***************************************							
44 45								
46			***************					
47	••••••••••••••••••••••							
49								
51								
52 53		••••••••••••••••••••••			Dose recorded			
54	***************************************		***************		 Dose recorded Dose net recorded DOT complete 			
56					Dose not recorded, DOT complete			
57	***************************************				 Dose not recorded, no data gap 			
59					 Dose not recorded, data gap 			
60 61					Dose not recorded, held dose			
62	*******************							
63								
		10	00	00	100			
	0 20	40	60	80	100			
			-					
Days on Study								



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





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

#ADHERENCE2022 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 Questions: shbrowne@health.ucsd.edu