DigiPrEP Statistical Analysis Plan

Official title: Feasibility and Acceptability of Digital Pills to Monitor PrEP Adherence in MSM With Substance Use

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Sociodemographics.

Descriptive statistics were calculated for selected variables.

***Digital pill system (DPS) performance and engagement metrics*.**

To analyze the performance of the DPS, the ground truth of PrEP ingestion events were defined as the pill counts obtained each month (i.e., the number of unused pills returned, subtracted from the number of pills previously dispensed). The number of DPS-recorded ingestions – which included the number of both Reader-detected and manually-reported ingestions – was compared with the aggregate pill count at each monthly timepoint; this was defined as the overall performance metric for the DPS. The Reader-detected ingestions count was used to reflect the number of times the DPS was operated correctly. Successful DPS operation was defined as ingestion of a digital pill, proper use of the wearable Reader, and confirmation of the ingestion on both the Reader and the app.

Reader-detected ingestions and manually-reported ingestions that co-occurred within 30 minutes were identified and reconciled; these events likely represented episodes in which a digital pill was ingested, and the ingestion was detected by the Reader, but the participant elected to manually record the ingestion in-app because the Reader was not correctly paired to the smartphone or was delayed in detecting the ingestion. Additionally, several ingestions were manually reported due to a known programming error in the app early in the study. As such, two participants were instructed to manually log all ingestions until an app update was made available; ingestion data for these two individuals were downloaded from their Readers at the end of the study period, and all Reader-detected ingestions were reconciled with manually-reported ingestions.

Participant engagement with the DPS was measured by calculating the total number of DPS-recorded ingestions and comparing the number of monthly DPS-recorded ingestions across each month of the study period.

TFV-DP in DBS.

We also compared drug concentrations of TFV-DP as measured in DBS at months one and three to DPS-recorded PrEP adherence. First, we identified all DBS samples that, as a result of scheduling challenges, were obtained more than five days after the conclusion of DPS-recorded ingestions, and excluded these DBS samples from analysis, as they resulted in incomplete data to compare with DPS-recorded ingestions. All other DBS samples were paired, based on their collection dates, with the corresponding average of DPS-detected ingestions during the three-week period prior to DBS collection. We dichotomized TFV-DP levels using a cutoff of ≥700 fmol/punch to indicate at least four doses of PrEP ingested per week.[1,2] Using TFV-DP in DBS <700 vs ≥700 fmol/punch as a dichotomous variable, and considering the granular continuous adherence data from the digital pill, we then calculated a point biserial correlation between TFV-DP in DBS and digital pill adherence. Finally, we analyzed the paired TFV-DP concentrations and DPS-recorded adherence data at months one and three, and calculated Pearson's correlation coefficients for each independent timepoint. Analyses were completed using SAS (version 9.4).[3]

Qualitative analyses.

Qualitative user experience interviews were transcribed and coded using applied thematic analysis.[4,5] A codebook was generated. All interviews will then double-coded by two study team members; coding was paused and evaluated every five transcripts to ensure consistency and to resolve and document any discrepancies. A kappa statistic was calculated, utilizing a cutoff of > 0.8 to ensure interrater reliability between coders. Coders reviewed aggregate coding to identify and discuss final

themes surrounding user experiences, which were reviewed by the study team as a whole. Qualitative analyses were facilitated by NVivo software.[6]

References

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Figure Captions

Figure 1. Overview of digital pill system (DPS)

The DPS includes an ingestible sensor within a gelatin capsule that over-encapsulates a medication. When ingested, it is activated by gastric fluid, broadcasting a radiofrequency signal that is acquired by a wearable Reader device and relayed to a smartphone which can display and transmit real-time adherence metrics. Image courtesy of etectRx.

Figure 2. Engagement with DPS over the 90-day study period

Engagement with the DPS was consistent over the 90-day study period. While the number of DPS-recorded ingestions decreased from month 2 to 3, this was paralleled by a decrease in PrEP adherence from month 2 to 3 (A). Individual-level engagement with the DPS was high with most participants (B). The participant who was temporarily lost to follow-up was excluded from the above graph; therefore, only 14 participants are included.

Figure 3. DPS-recorded adherence and nonadherence from sample participants

DPS adherence graphs from selected participants illustrating context around patterns of adherence and nonadherence. Identification of weekend substance use leading to nonadherence (A), but a return to PrEP adherence during the week (B); entering a new relationship with a partner who was not accepting of PrEP, resulting in long-term nonadherence (C); temporal changes, from ingesting PrEP with breakfast during the week (D), to liberalized ingestion patterns on weekends (E); and routine changes leading to nonadherence, including visiting a partner's home on weekends (F). Red X = no recorded ingestion during dosing window. Blue circle = DPS-recorded ingestion.

List of Supplemental Digital Content

Supplemental Figure 1. Study enrollment schema

Supplemental Table 1. DPS-recorded ingestion events versus pill counts, by month over study period

Supplemental Figure 2. Schematic of reconciliation surrounding manually-reported digital pill system ingestion events