Real-time electronic adherence monitoring and risk of viral rebound

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Background

- Sustained adherence to antiretroviral therapy (ART) is critical for viral suppression; yet, the risk of viral rebound associated with any given adherence interruption is poorly understood
- Real-time antiretroviral therapy adherence monitoring has been shown to be feasible in resource-limited settings and creates the opportunity to understand loss of viral suppression as it is happening
- We used real-time adherence monitoring and HIV RNA measurement during adherence interruptions to understand the characteristics of interruptions that predict viral rebound

Methods

- The Ugandan AIDS Rural Treatment Outcomes (UARTO) Study is an ongoing observational cohort study of individuals initiating ART
- Procedures include 4-monthly assessment of HIV RNA and adherence monitoring with a wireless device that transmits a cellular signal with each opening (Wisepill; Figure 1)
- If no signal is received for >48 hours, research staff visit participants' homes unannounced to ascertain the cause and collect blood for HIV RNA measurement
- For participants with prior viral suppression, we fit generalized estimating equation logistic regression models to identify predictors of rebound viremia during adherence interruptions

Figure 1. The Wisepill device



Figure 2. Identification of adherence interruptions with prior viral suppression

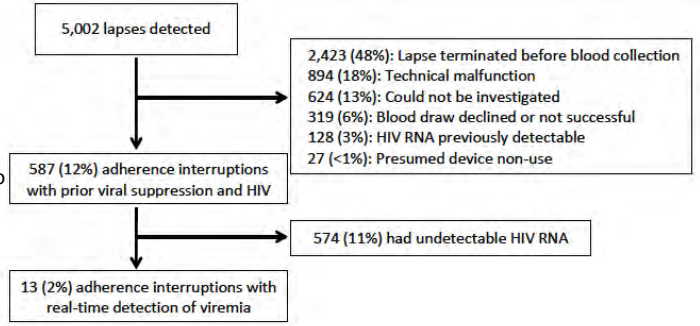
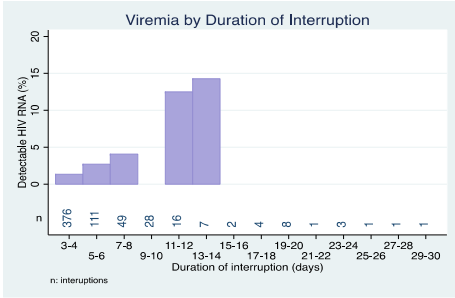


Table 1. Predictors of viral rebound during an adherence interruption

	Univariable OR (95% CI)
Duration of adherence interruption (days >48 hrs)	**1.25 (1.06-1.47; p=0.007)**
Prior duration of viral suppression (years)	0.75 (0.52-1.08; p=0.12)
30-day prior adherence (10% increments)	**0.73 (0.55-0.96; p=0.02)**
Pre-ART HIV RNA (log_{10})	1.28 (0.66-2.49; p=0.47)
Regimen– Nevirapine	(*ref*)
Efavirenz	0.41 (0.13-1.32; p=0.14)

Figure 3. Association between viral rebound and duration of adherence interruption



Results

- We monitored 479 participants between June 2011 and January 2014; median length of follow-up was 25 months (IQR 14-32)
- Cohort characteristics: 72% were women, median age was 36 years (IQR 29-43), baseline CD4 was 198 cells/mm^3 (IQR 110-295), pre-ART HIV RNA was 5.0 log_{10} copies/ml (IQR 4.5-5.5) and median duration of prior viral suppression was 13 months (IQR 3-48)
- ART involved nevirapine for 205 (43%) participants, efavirenz for 244 (52%), and other for 25 (5%)
- Overall median adherence was 86% (IQR 73-94)
- We observed a total of 5,002 lapses lasting >48 hours; median duration was 2.8 days (IQR 2-4.2)
- Participants had a median of 1 interruption per month (IQR 1-1) with a possible trend toward decreasing over time (p=0.09)
- Figure 2 shows how adherence interruptions were identified for analysis
- Of the 587 (12%) adherence interruptions with prior viral suppression, 13 (2%) revealed new viral rebound
- Predictors of viral rebound are shown in Table 1; association between viral rebound and duration of adherence interruption is shown in Figure 3
- Interruptions >14 days with no detectable viremia were considered device non-use and were excluded from the regression analysis
- HIV RNA was collected on the same day the interruption completed in 278 (47%), within 48 hours of the interruption completion in 306 (52%), and before the interruption ended in 3 (1%)
- Of the 12 available routine HIV RNA levels determined after an adherence interruption with viremia, 10 (83%) had re-suppressed

Conclusions

- Each day of adherence interruption increases risk of viral rebound
- Higher adherence prior to the lapse is protective; increased duration of prior viral suppression and use of long-half life medication (efavirenz) may also be protective
- This analysis is limited by the small number of interruptions
- Termination of nearly half of the interruption with investigation and re-suppression of most terminated interruptions are promising as proof-of-concept support for real-time adherence intervention

Acknowledgments

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