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Real-time electronic adherence monitoring plus follow-up improves adherence compared to standard electronic adherence monitoring

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Summary

The impact of real-time electronic monitoring on antiretroviral therapy adherence warrants further study. We conducted an analysis of cohort participants that initially involved standard electronic adherence monitoring (EAM), followed by real-time EAM plus home visits for sustained ≥48-hour adherence interruptions. Immediately after switching between the two types of EAM, mean adherence among 112 participants increased from 84% to 93% and remained elevated for six months ($p<0.001$). Real-time EAM is a promising approach for improving adherence.

Keywords

HIV; adherence; real-time electronic adherence monitoring; antiretroviral therapy

Introduction

In electronic adherence monitoring (EAM), a device records each opening with a date-and-time stamp as a proxy for medication ingestion. Standard EAM devices store this data for later transfer to a computer; wireless devices are been increasingly used and transmit this data over cellular networks in real time[1].

Recent randomized trials have generally shown improvement in adherence when real-time EAM are coupled with text message reminders[2–4]; however, it is unclear how EAM monitoring itself or other types of associated interventions influence adherence behavior.

We present an ad hoc analysis of a cohort study of adults taking ART in Uganda that initially involved a standard EAM device, followed subsequently by a real-time EAM device plus

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Conflicts of interest: None

home visits for sustained adherence interruptions. We assessed differences in overall adherence and sustained adherence interruptions between these two periods.

Methods

Participants were drawn from a observational cohort (NCT01596322)[5,6] in which ART adherence was monitored by standard EAM (medication event monitoring system [MEMS; WestRock, Switzerland]) from 2005–2011, followed by real-time EAM (Wisepill; Wisepill Technologies, South Africa) from 2011–2015. During real-time EAM, sustained (≥48-hour) interruptions triggered home visits to characterize the cause and assess HIV RNA levels ("real-time EAM plus follow-up"). Cohort enrollment occurred through 2012. Some participants were therefore monitored with both types of EAM; others were monitored only with real-time EAM.

We analyzed data from participants whose ART adherence was monitored for six months with standard EAM, and who were switched within one day to monitoring with real-time EAM plus follow-up for six additional months. We used regression modeling (linear, logistic, or Poisson) with fixed effects and robust standard errors to compare participant characteristics, weekly average adherence, and ≥48-hour adherence interruptions between the six-month periods. Next, we used least squares regression modeling to 1)project estimated standard EAM adherence per participant as if he/she had not switched to real-time EAM plus follow-up, and 2)compare projected and observed adherence during real-time EAM plus follow-up. We estimated the total difference between projected and observed adherence per participant, and tested the null hypothesis of no difference between the two variables, stratifying by tertiles of time on ART. We used generalized estimating equations to compare adherence data during real-time EAM plus follow-up for participants initiating ART versus participants who had six months of prior ART with standard EAM.

Ethical approval was received from Mbarara University of Science and Technology, the Uganda National Council for Science and Technology, Partners Healthcare, and the University of California San Francisco.

Results

One hundred twelve participants had standard EAM for six months, followed by six months of real-time EAM plus follow-up. Median age was 36 years, 68% were female, 82% were literate, and pre-ART CD4 count was 141 cells/ml (similar to the clinic from which participants were recruited)[7,8]. No change was seen in household size, household income, time to clinic, alcohol use[9], depression[10], social support[11], food insecurity[12], or ART regimen between the two monitoring periods (all $p>0.05$).

Immediately after switching from standard EAM to real-time EAM plus follow-up, mean adherence increased from 84% to 93% (Figure 1; $p<0.001$). The increase was similar for participants triggering home visits ≤30 versus >30 days after the device switch. When compared to projected average adherence with standard EAM and adjusting for time on ART, this difference persisted over six months. The mean number of ≥48-hour interruptions per six-month monitoring period decreased from 2.2 (SD 3.1) to 0.7 (SD 1.2) per participant

after switching from standard EAM to real-time EAM plus follow-up. No difference was seen in viral suppression (6% versus 7%, p=0.48).

Two hundred fifty-five participants initiated ART with real-time EAM plus follow-up. We found no difference in average adherence for the first six months of follow-up in these participants compared to the first six months of real-time EAM plus follow-up in the 112 participants who had prior experience with standard EAM (92% versus 93%; p=0.35); the mean number of ≥48-hour adherence interruptions per participant was significantly higher for those initiating ART with real-time EAM plus follow-up (1.9 [SD 2.8] versus 0.7 [SD 1.2]; p<0.001).

Discussion

Compared to standard EAM, real-time EAM plus home visits for sustained interruptions was associated with increased average adherence and fewer adherence interruptions—both of which are associated with viral suppression[13,14] and reduced immune activation[15]. No differences in common factors affecting adherence were seen between the two monitoring periods.

Adherence with real-time EAM plus follow-up was high regardless of prior experience with standard EAM, suggesting that a real-time approach may effectively promote adherence during early and chronic treatment. Sustained adherence interruptions during real-time EAM with follow-up were more frequent for those initiating ART compared to those with prior ART experience, possibly reflecting initial challenges in establishing high adherence habits[16].

Our findings strengthen growing evidence that real-time EAM with follow-up triggered by incomplete adherence is an effective intervention. One mechanism may be provision of support precisely when needed. Follow-up visits were not designed as interventions; however, participants likely perceived support from research staff. Given the resource intensity of home visits, cellular phone follow-up may be more feasible, especially if adherence challenges are frequent. Additionally, real-time monitoring itself can convey a sense of support[17]. Indeed, the similarity in increased adherence when comparing study participants who triggered home visits early versus later after the device switch suggests the change in monitoring, not the follow-up, may be responsible for the effect. The impact of anticipated follow-up, including phlebotomy for HIV RNA assessment, however, cannot be excluded.

This analysis has limitations. First, it is ad hoc and compares different adherence measurement devices; differences in technology and/or acceptability may have influenced the measurements. Second, we assume no other confounding changes occurred concomitantly with the device switch and trends in these other factors were stable throughout the observation period. Third, overall high adherence reduced the ability to show a difference in viral suppression between the monitoring periods. Additionally, we did not directly compare standard versus real-time adherence monitoring and cannot estimate relative Hawthorne effects[18].

In conclusion, this analysis provides support for the effectiveness of real-time EAM with follow-up as an ART adherence intervention.

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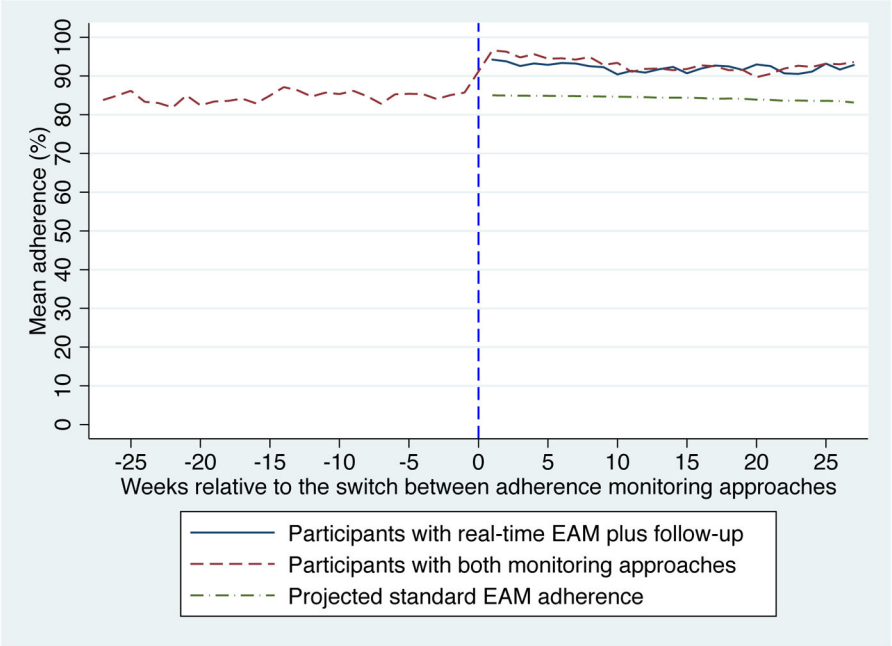

Figure 1.
Comparison of adherence during monitoring with standard EAM and real-time EAM plus follow-up.