Alternative Facts:
Adherence to an Electronic Monitoring Device (Wisepill) Does Not Always Reflect Adherence to Medication

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Introduction

- Antiretroviral therapy (ART) non-adherence is a critical public health issue
  - More people on ART earlier in their disease course
  - Keeping patients engaged in care remains a challenge

- Efforts to study and improve ART adherence hampered by lack of objective measures of medication adherence
  - Annual viral loads may miss critical points for intervention
  - Need to target the right interventions to the right people at the right time
Objective Measures of Adherence

Desirable traits of an objective adherence measure

- Not subject to recall or social desirability bias
- Minimal burden
- Timely feedback
- Measures medication ingestion
- Reflects biological outcomes
Monitoring Adherence

Electronic monitoring devices (EMDs), such as Wisepill, can provide objective, real-time measurement of adherence… *but only if people use them as directed*

- Electronic pill box, holds 1 month pills
- Device openings recorded in real-time
- Data stored on device when service not available
- Batteries last up to 6 months; SMS reminders to charge batteries

**Wisepill device™**
KEY ASSUMPTION

Adherence to Wisepill device = Drug ingestion

But is this always true?
*Does Wisepill use reflect viral load?*

And is it true for everyone?
*Does Wisepill use vary across participants?*
Randomized controlled trial of a laptop based, lay-counselor delivered adherence intervention for ART initiators in Cape Town, South Africa

- 432 HIV+ adults (mean age 33, 74% female)
- Continuous Wisepill data for 12 months
- Viral load from clinic records at ~4 months and ~12 months post ART initiation
- Among participants with 12 month viral load data, >90% were virally suppressed
Data Analysis: Variable Definition

**Viral Suppression**: \( \leq 40 \text{ copies/mL} \) at 4 and 12 months

**Wisepill Adherent**: \( \geq 80\% \) of prescribed device openings for a given month

\[
\% \text{ Wisepill Adherence} = \frac{\# \text{ days device opened}}{\# \text{ days device detected as active}}
\]

*usually 28 days - removed days device was not active (battery dead)*

**Analysis sample**: 203 virally suppressed participants
Group-based trajectory modeling to examine patterns of Wisepill use among participants who were virally suppressed at both 4 and 12 months post ART initiation

- Latent variable model similar to latent class analysis (LCA)
- Identify clusters (i.e. trajectory groups) of participants with similar patterns of Wisepill adherence over time
- Considered models with 2-6 groups
- To select best fitting model: Bayesian Information Criterion (BIC), group size, and average posterior probabilities
- Proc Traj in SAS
Results: Wisepill Adherence

Overall trajectory of Wisepill use

Proportion of study participants who were Wisepill adherent (open device daily) ≥80% of the time or more, by month on study
Results: Wisepill Adherence

Sub-group trajectories of Wisepill use

- **38%** Consistent use
- **31%** Steady decreasing use
- **31%** Rapid decreasing use

Great variation in Wisepill use among virally suppressed participants
ART-initiators enrolled in an randomized controlled trial in Cape Town, South Africa

- Overall, only 40% of virally suppressed participants were Wisepill adherent at 12 months

- Wisepill use patterns were not uniform across participants
  - Only 38% had a sustained high probability of being Wisepill adherent
  - But all participants in this analysis were virally suppressed
Adherence measured by EMDs may not always reflect medication ingestion

- Potential to underestimate ART adherence because of non-adherence to the device

- **Caveat:** Great variation in how studies use Wisepill
  - From passive monitoring to active intervention
  - Influence participant adherence to device, medication, or both
Conclusions

- Importance of distinguishing between device adherence versus medication adherence/ingestion

- Need for biological measures of adherence beyond viral load that capture drug ingestion
  - Drugs levels in dried blood spots and hair samples
  - Ingestible sensors

- Consider the context
  - Study setting, study population, study design
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