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*

Wisepill device™

- 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

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?

Monitoring Adherence in Masivukeni

masivukeni
let's wake up!

- 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: ≤40 copies/mL at 4 and 12 months

Wisepill Adherent: ≥80% of prescribed device openings for a given month

$$\%\ \text{Wisepill Adherence (openings)} = \frac{\#\ \text{days device opened}}{\#\ \text{days device detected as active*}}$$

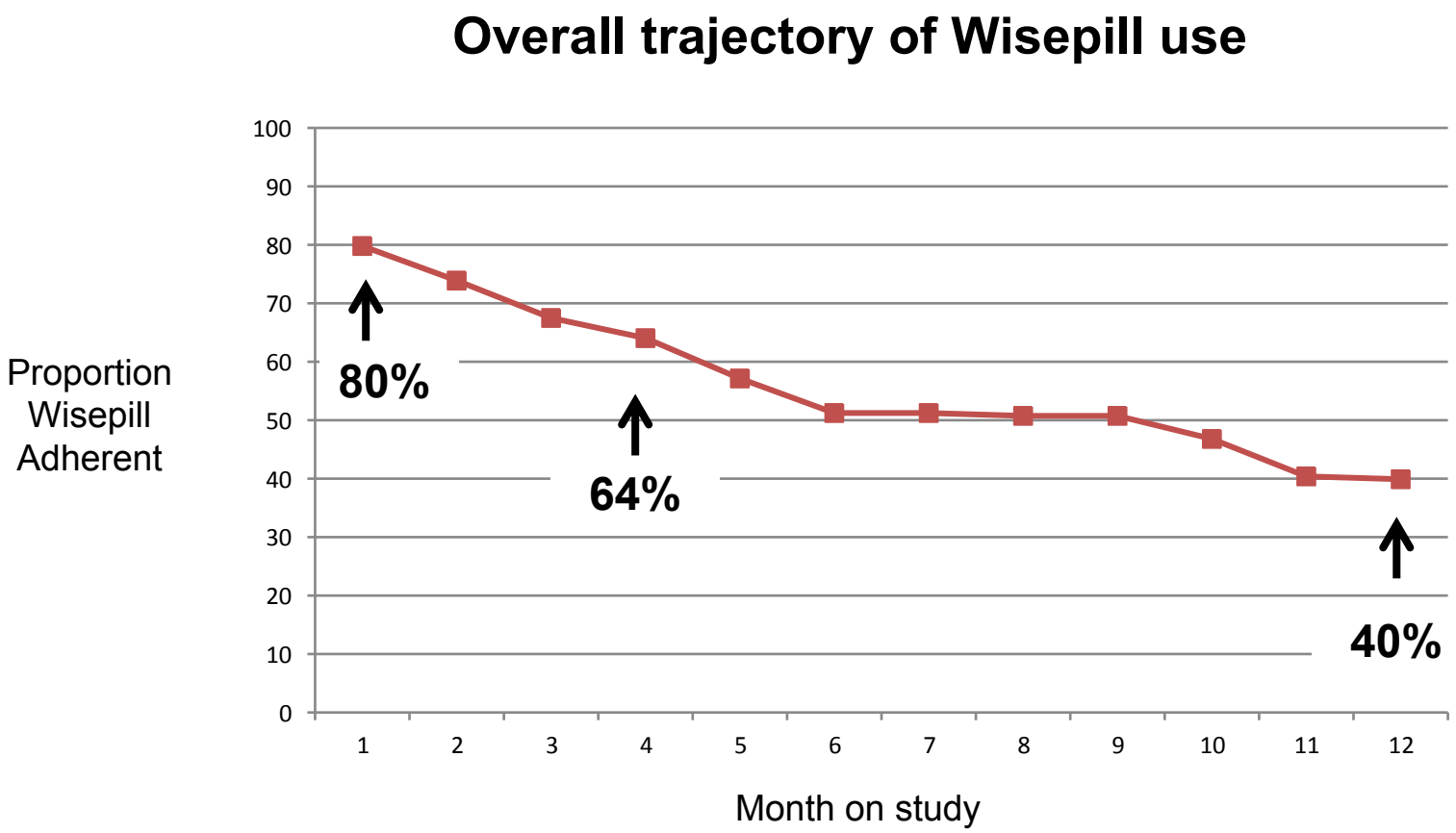
**usually 28 days - removed days device was not active (battery dead)*

Analysis sample : 203 virally suppressed participants

Data Analysis

- 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

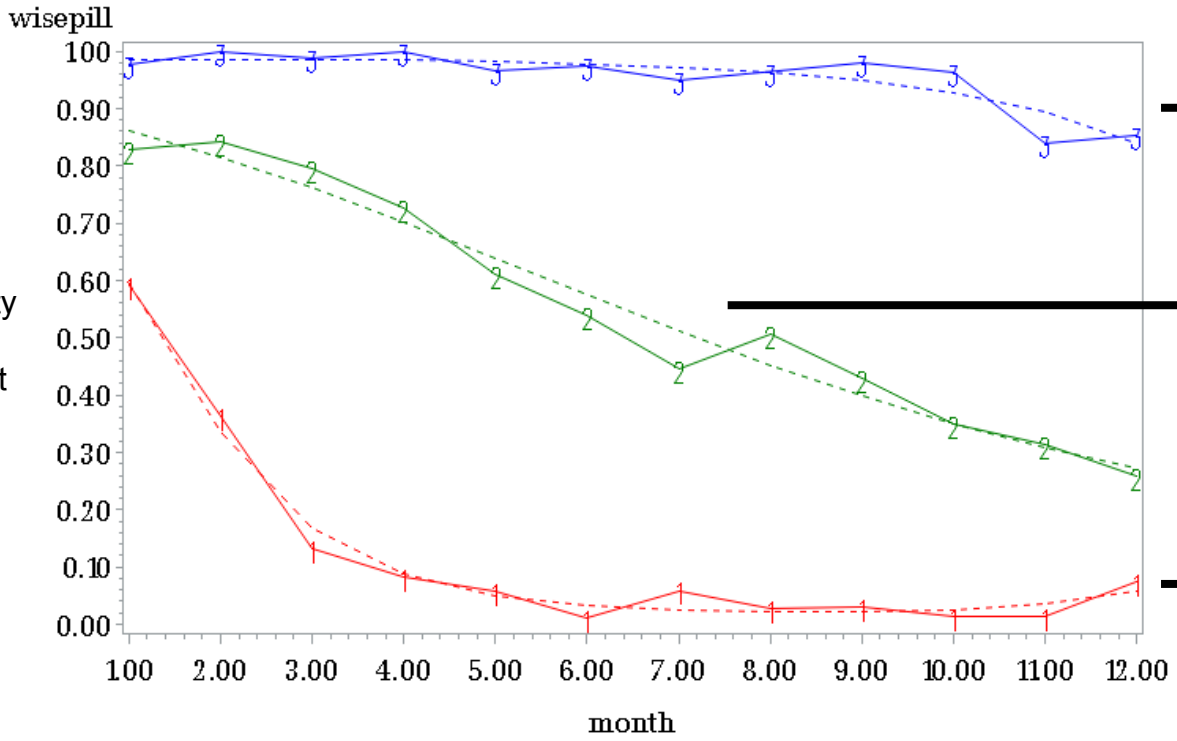
Results: Wisepill Adherence



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

Conclusions

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

Conclusions

- 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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