



**HPTN**

HIV Prevention  
Trials Network

# **Combining Electronic Pill Records and Self-Reported Data to Identify Adherers and Non-Adherers**

## **A Latent Class Model in HPTN 069**

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# Introduction

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- HPTN 069
  - Phase II study of Maraviroc (MVC)-containing regimens for HIV PrEP in MSM and women
  - The primary objective of the study is to assess the safety and tolerability of MVC-containing regimens
  - Assessing adherence as measured by electronic drug monitoring (EDM) device and self-report is one key secondary objective

# Measuring Adherence in HPTN 069

- EDM Device
  - “Wisepill” dispenser: GSM communication chip enabled single pillbox containing the three study drugs – MVC, TDF, and FTC
  - Pillbox opening is recorded. An additional “heartbeat” signal indicates the device works properly.



# Measuring Adherence in HPTN 069

- Self-report
  - Every 8 weeks via computer-assisted self-interview (CASI) through week 48
  - Four CASI questions are relevant: over the past month,
    - Q1: “Rate your ability to take your study medications every day”
    - Q2: “Showing your best guess about how much of your study medication you took as recommended”
    - Q3: “About how much of the time did you take your study drug as recommended?”
    - Q4: “How often did you take all 3 of the prescribed tablets right around the time that you took them from the WISEPILL device?”

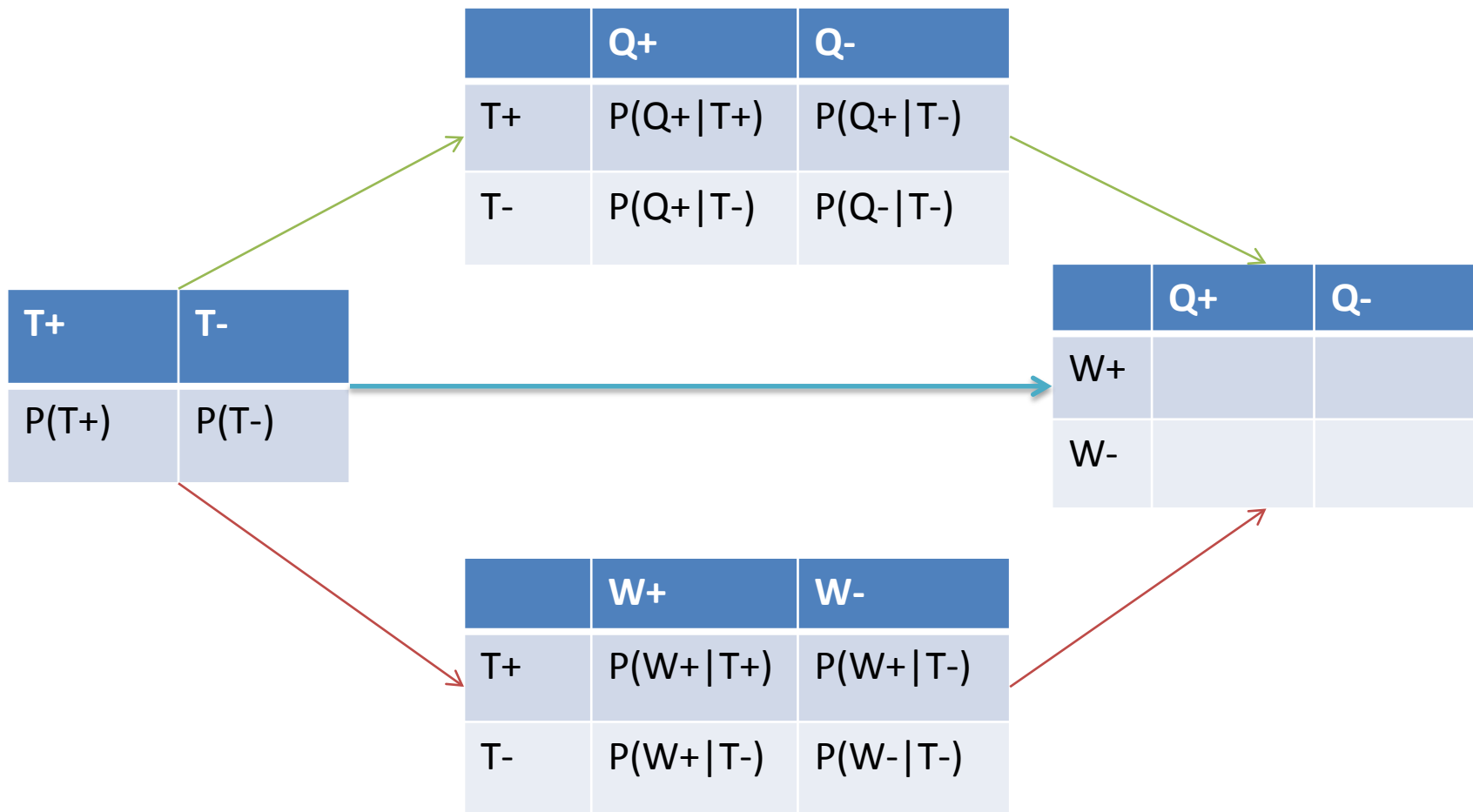
# Challenges and Opportunities

- There is no “gold standard” adherence measure
- Self-report is clearly a suboptimal measurement of adherence, although it is the most feasible method for assessing adherence after PrEP initiation
- EDM can record daily openings of the pillbox, but it suffers from a range of issues, such as SIM card compatibility
- Inclusion of self-report carries the hope of allowing for exploration of the relative correlation with EDM to “triangulate” the true adherence

# Statistical Framework

- Latent class model
  - Assume that study participants' true adherence can be classified into two latent classes:
    - T+: adherers
    - T-: non-adherers
  - Probabilities of a participant's adherence response from self-report (Q) and EDM (W) given the true latent classes are
    - $P(Q+|T+)$ ,  $P(Q-|T-)$ ,  $P(Q-|T+)$ ,  $P(Q+|T-)$
    - $P(W+|T+)$ ,  $P(W-|T-)$ ,  $P(W-|T+)$ ,  $P(W+|T-)$
    - (Q,W) are correlated

# Statistical Framework



# Statistical Framework

- Multilevel latent class model
  - Assume that true adherences follow a Dirichlet mixing distribution to accommodate correlation between self-report and Wisepill
  - With a potential to extend to multiple adherence classes, not simply yes-vs-no
  - Maximum likelihood estimation (MLE) with the Expectation-Maximization (EM) algorithm

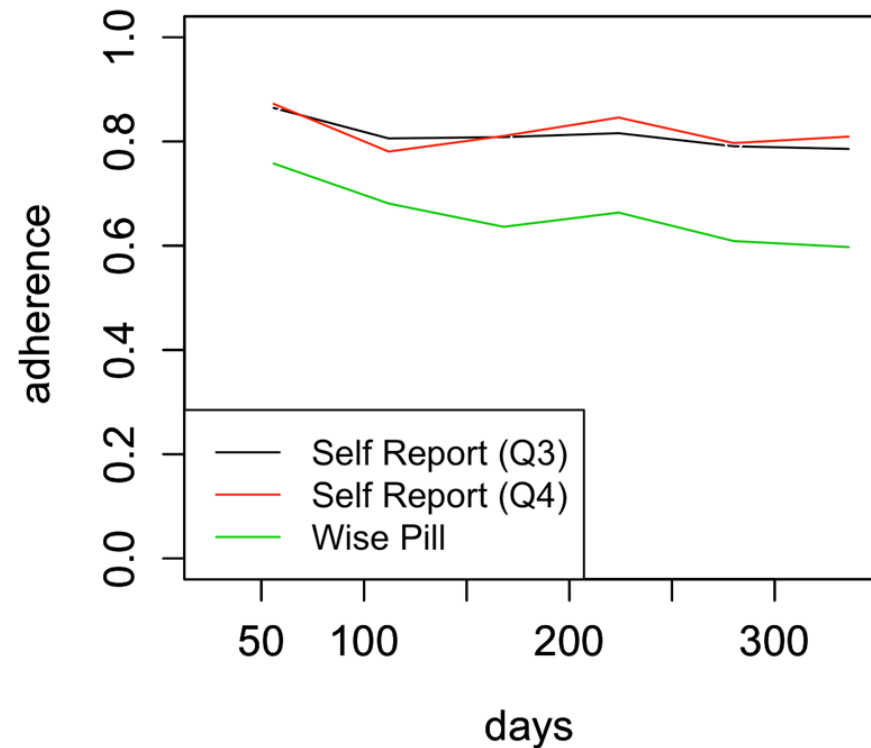


# HPTN 069 Analysis Data

- Self-report
  - Q+: more than half the time taking the drugs as recommended; Q-: otherwise
    - Q3 and Q4 are analyzed
- EDM
  - W+: device opened more than 50% of the time; W-: otherwise
    - Days receiving “heartbeat” are considered
- Only the MSM cohort is included

# Analysis Results

- Wisepill heartbeat signals received on 235 MSM participants
- Wisepill adherence response calculated in consistence with self-report's time-scale
- Wisepill adherence response tends to be lower than self-report adherence response



# Analysis Results

	Class Probability	Self-report Response Probability				EDM Response Probability	
		Q3+	Q3-	Q4+	Q4-	W+	W-
T+: Adherers	69.2%						
T-: Non-adherers	30.8%						

# Analysis Results

	Class Probability	Self-report Response Probability				EDM Response Probability	
		Q3+	Q3-	Q4+	Q4-	W+	W-
T+: Adherers	69.2%	99.5%	0.5%	97.6%	2.4%	96.2%	3.8%
T-: Non-adherers	30.8%						

# Analysis Results

	Class Probability	Self-report Response Probability				EDM Response Probability	
		Q3+	Q3-	Q4+	Q4-	W+	W-
T+: Adherers	69.2%	99.5%	0.5%	97.6%	2.4%	96.2%	3.8%
T-: Non-adherers	30.8%	81.5%	18.5%	50.5%	49.5%	13.5%	86.5%

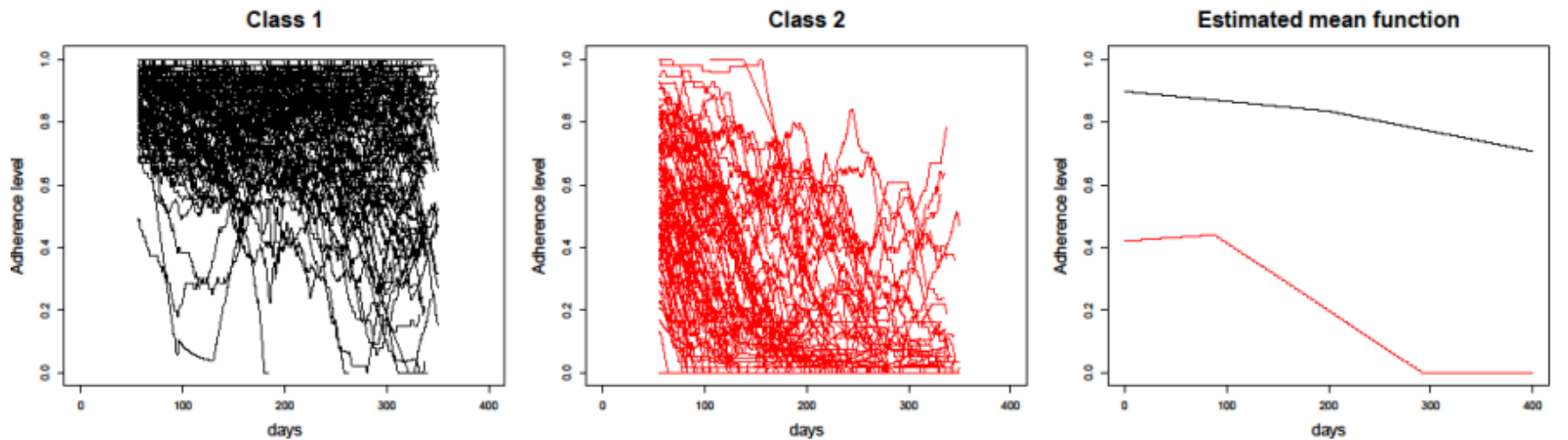
# Summary

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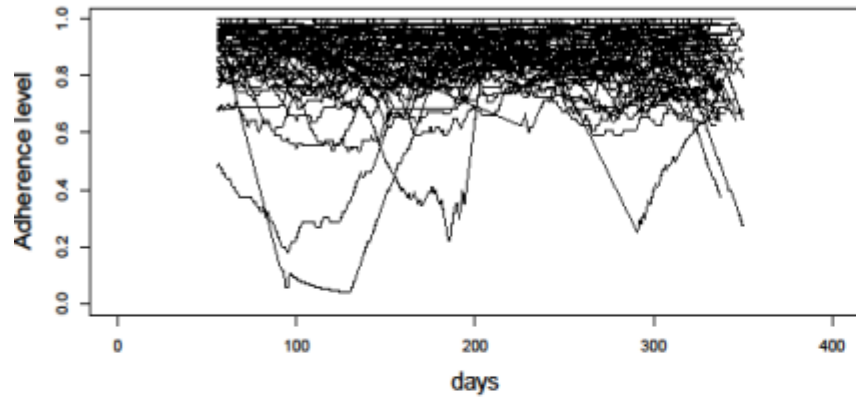
- Latent class analysis shows
  - The majority of the 069 MSM participants are likely adherers
  - Adherers very likely report their adherence consistently via self-report and EDM
  - Non-adherers might greatly over-report their adherence via self-report, but tend to report more consistently via EDM
- The proposed latent class analysis is a useful statistical tool to identify adherers and non-adherers “triangulated” by different measuring instruments

# Discussion

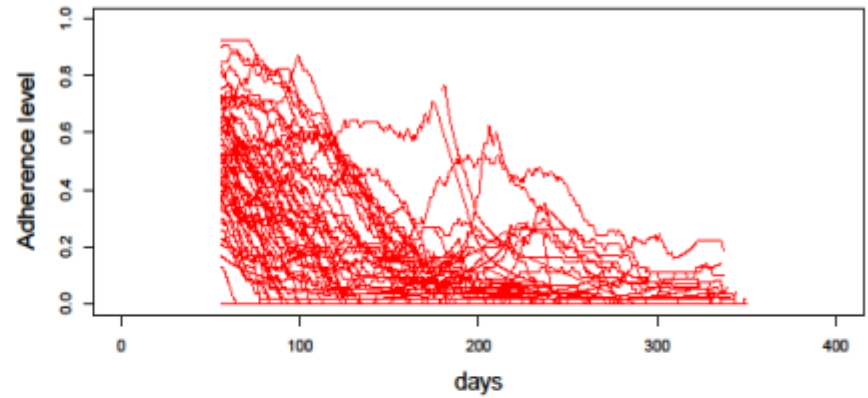
- Presented analysis is a much simplified prototype analysis
- Actual adherence can be very complex, given that
  - Adherence is very likely a function of time, affected by many factors during the course of follow-up
  - Adherence may show different patterns over time



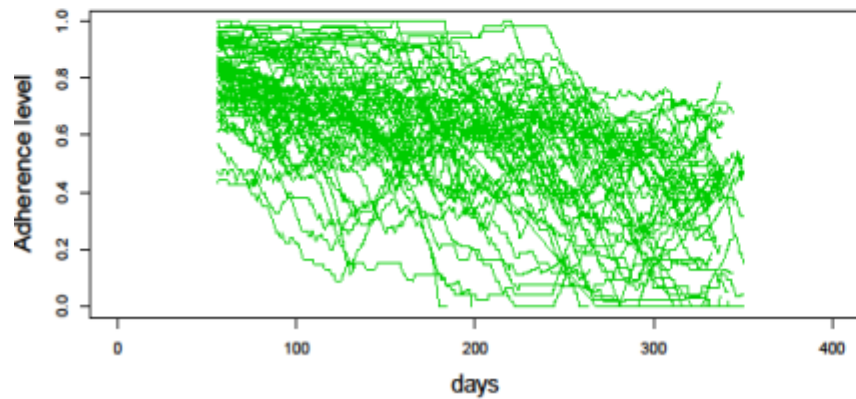
**Class 1**



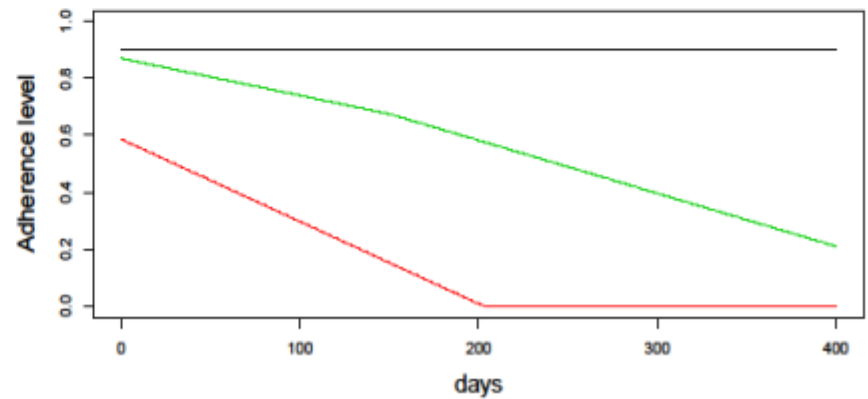
**Class 2**



**Class 3**



**Estimated mean function**





# Discussion

- Given the complexity, advanced latent class modeling needs to allow
  - Adherence as a time-varying functions
  - Classification of infinite-dimensional functions
  - Factors that may be associated with time-varying adherence
  - More importantly, the ability to include drug assay results to improve the probability estimates

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