

M-032

Markov Mixed Effects Modeling of Adherence using MEMS® Dosing Records from Partner's PrEP Ancillary Adherence Substudy

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Objectives: Adherence is a major factor in the effectiveness of pre-exposure prophylaxis (PrEP). Modeling adherence can help identify covariates influencing adherence which may be useful for adherence interventions. Here, we develop a Markov mixed effects model to discern covariates influencing adherence.

Methods: Medication Event Monitoring Systems (MEMS®) data from 1147 individuals from Partners PrEP ancillary adherence sub-study was used for model building[1]. Multiple openings on the same day were considered as only one dose taking event. One coin and, first, second and third order Markov models were fit to the data using NONMEM 7.2 and the Laplacian estimation method. Model selection criteria included NONMEM objective function value (OFV), Akaike information criterion (AIC), visual predictive checks and posterior predictive checks using longest drug holiday (LDH)[2] or non-therapeutic time (NTT)[2]. Covariates were included based on forward addition ($\alpha=0.05$) and backward elimination ($\alpha=0.001$) tests.

Results: Markov models satisfied model diagnostics better than the one coin model. A third order Markov model gave the lowest OFV and AIC but the simpler first order model was used for covariate model building as no additional benefit on LDH and NTT prediction was observed for higher order models. Final parameters were listed in table 1. Women had better adherence while younger age, weekend dosing and no sex as well as sex with an outside partner had negative impact on adherence. Arms of trial, heavy alcohol use and polygamy were also tested, but were not significant.

Conclusions: A first order Markov model was developed to describe the adherence using MEMS®. Our findings suggest adherence interventions should consider the role of gender, age and nature of sexual relationship.

References:

[1] Haberer, J.E., et al., PLoS Med, 2013. 10(9): p. e1001511

[2] Girard, P. et al., Stat Med, 1998. 17(20): p. 2313-33g

Table 1: Final parameter estimates with relative standard errors (RSE)

| Parameter | Estimate | RSE(%) |
|---|-----------------|---------------|
| P_{01} (Positively correlated with adherence) | 0.7 | 1.8 |
| P_{10} (Negatively correlated with adherence) | 0.067 | 5.5 |
| Effect of no sex on P_{01} | -0.14 | 20.8 |
| Effect of sex with partner other than study partner on P_{10} | 0.4 | 14.14 |
| Effect of sex with partner other than study partner on P_{01} | -0.13 | 36.9 |
| Effect of no sex on P_{10} | 0.18 | 19.94 |
| Effect of female gender on P_{10} | -0.6 | 12.18 |
| Effect of youth (age: 19-28) on P_{10} | 0.51 | 18.73 |
| Effect of sex with other partner and study partner on P_{01} | 0.056 | 43.61 |
| Effect of weekend on P_{01} | -0.036 | 24.45 |
| Effect of weekend on P_{10} | 0.063 | 28.75 |