Exploring latent adherence profiles among South African people living with HIV using group-based trajectory modelling

Campbell McDuling[1], Lauren Jennings[2], Christopher Ferraris[3], Paul D'Avanzo[3], Robert H Remien[3], Catherine Orrell[2], Francesca Little[1]

[1] Department of Statistics, University of Cape Town, South Africa.

[2] Centre for Adherence and Therapeutics, Desmond Tutu Health Foundation, South Africa.

[3] HIV Center for Clinical and Behavioral Studies, Psychiatric Institute, Columbia University, New York, USA.

Highlights

Adherence to ART in South Africa is a heterogenous experience. Advanced statistical methods were applied in a secondary analysis to detangle this heterogeneity via electronic adherence monitoring data observed in a prospective cohort adherence study. Subgroups of the cohort were seen to show different adherence behaviours over time. These subgroups were not distinguised along univariate analysis of measured risk factors. These results emphasize the complex relationship between adherence outcomes and psychosocial characteristics. These methods show potential for applications in the emerging field of precision public health.

A. Introduction

Adherence behaviour is crucial to understanding the persistent HIV/AIDS epidemic in South Africa. **Electronic adherence monitoring** (EAM) devices provide a relatively inexpensive and reliable proxy for adherence to antiretroviral treatment (ART). Finite Mixture Models can be applied to this longitudinal data to **identify differing patterns of adherence** behaviour. Associations between latent behavioural group membership and viral outcomes can then be investigated, as can between-group differences on postulated risk factors for non-adherence.

B. Data Description

Data was obtained from a recent prospective observational study (ADD-ART). A cohort of 238 virally-suppressed, PLWH in the Western Cape were provided with a Wisepill device and followed for 24 months.

Daily EAM data from Wisepill devices, and monthly viral loads were obtained. The daily non-adherence indicators were summarised into monthly counts. At baseline, comprehensive psychosocial and demographic data was recorded - including known psychometric scales for assessing: HIV stigma; Substance Abuse and Mental Illness; Medication-Specific Social Support; Patient-Clinic Relationship; Psychological Distress.

C. Methods

Group-Based Trajectory Modelling (GBTM), a longitudinal FMM method with simplifying assumptions, was applied to the first 12 monthly counts - accounting for a time-at-risk offset. A cubic polynomial was chosen as the form for the underlying log-linear longitudinal zero-inflated Poisson models. The number of latent groups was determined through leave-one-out cross-validation error (CVE), BIC, and group-membership numbers. Group-membership was assigned to each participant through the highest posterior mixture probability. The longitudinal model fit was investigated by comparing the observed and predicted mean trajectories for each group.

Kaplan-Meier curves and a log-rank test were used to compare the time to viral non-suppression (viral load > 50 copies/ml) between the groups.

Global between-group differences along known psychological risk-factors for non-adherence were assessed using Kruskal-Wallis test statistics and visualised with boxplots.

D. Results

For the five groups, membership numbers were as follows:
{41, 42, , 46, 47, 62}

The model with six groups minimized the CVE and BIC, and provided a reasonable longitudinal fit in all five subgroups. Groups 1 and 4 started with the poorest adherence, with the former remaining stable and poor, and the latter deteriorating rapidly. Group 2 exhibited reasonable initial adherence which deteriorated over the twelve visits. Groups 3 and 5 exhibited stable good adherence. The number of individuals assigned to each group was relatively balanced and the observed mean adherence levels closely followed the fitted mean adherence.

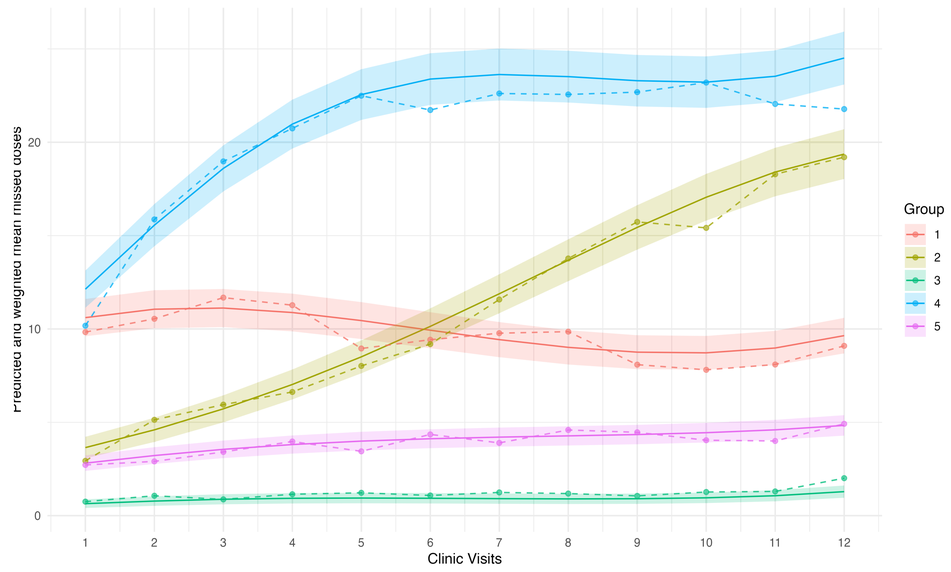

Figure 1: Predicted (solid) adherence trajectories closely follow the observed means (dashed)

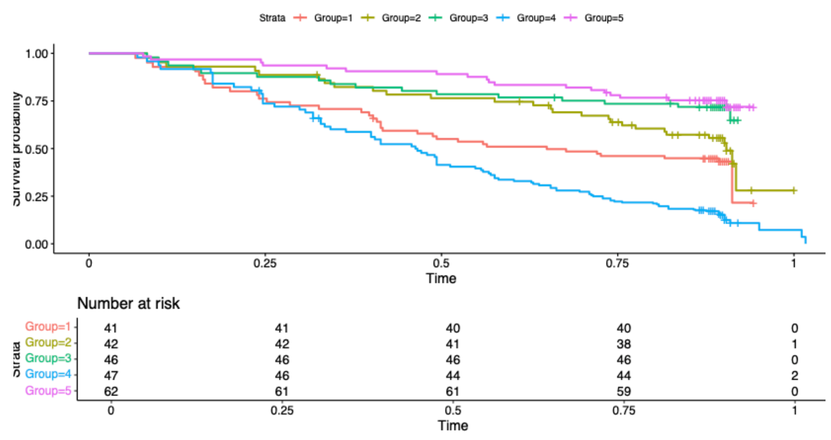

Figure 2: Kaplan-Meier Curves suggest differing experiences in time to viral non-suppression, with survival Pr of the least adherent groups (2, 3, 4) deteriorating most rapidly

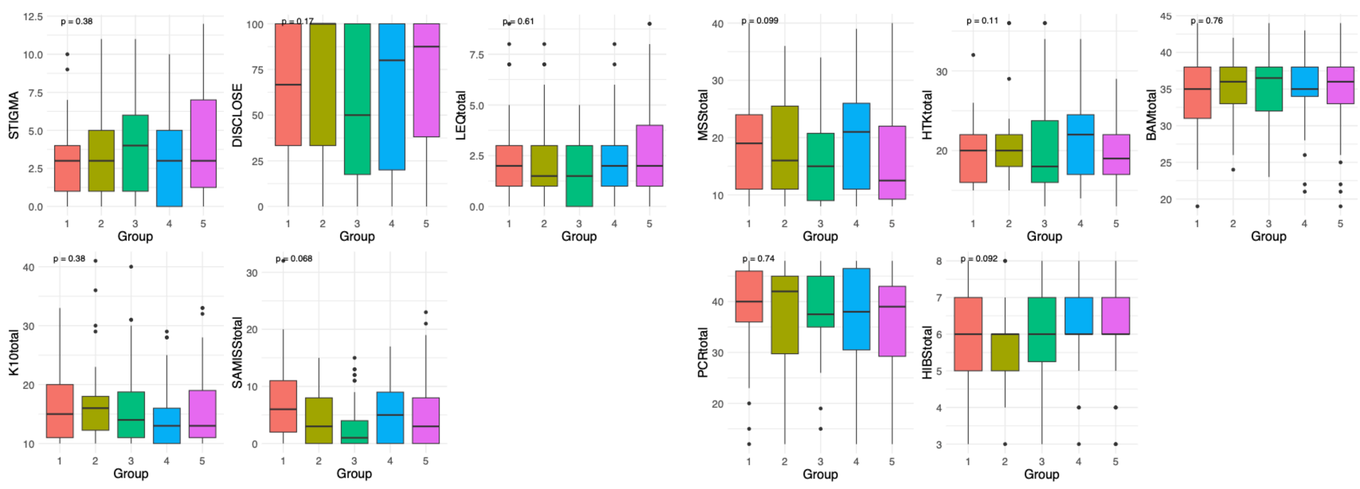

Figure 3: Little evidence to suggest significant differences between groups along any of Stigma, Disclosure, Life Events, Kessler Psychological Distress, Substance Abuse and Mental Illness

Figure 3: Little evidence to suggest significant differences between groups along any of Medication Social Support, HIV Treatment Knowledge, Beliefs About Medication, Patient-Clinic Relationship

F. Discussion & Conclusion

A FMM approach can provide more granular insights into heterogenous ART-adherence patterns, identifying different trends over time that may directly affect viral outcomes. In this application, five adherence trajectories were identified and group-membership had a differentiated effect on time-to-viral-breakthrough. Group-membership was not strongly associated, independently, with any measured psychosocial outcomes. The methods used here show potential for applications in precision public health in terms a of categorising adherence heterogeneity unique to subgroups of the broader population. The methods could be improved by accounting for random effects through Growth Mixture Models and more complex longitudinal functional forms, and by integrating the survival submodel in the latent-class determination through joint modelling.

References
- Nagin, D. (2005). Group-based modeling of development. Harvard University Press.
- Nielsen, J., Rosenthal, J., Sun, Y., Day, D., Bevc, I., & Duchesne, T. (2014). Group-based Criminal Trajectory Analysis Using Cross-validation Criteria. Communications in Statistics: Theory and Methods, 43. DOI: 10.1080/03610926.2012.719986.