

Clustering of CD4+ T cell trajectories in people living with HIV

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Background

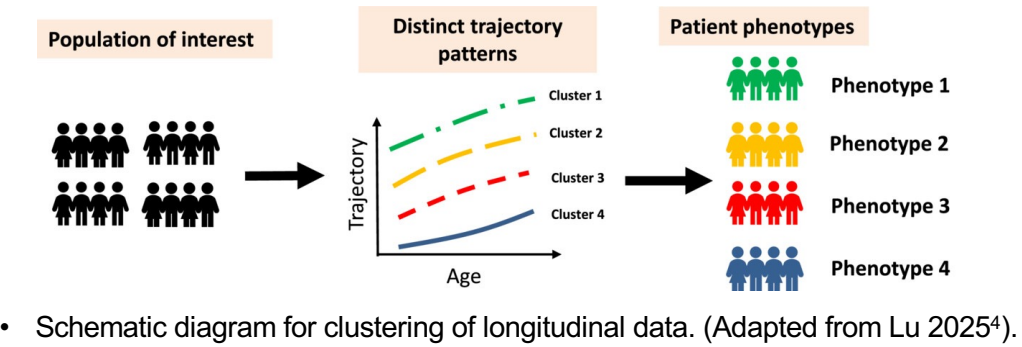
- The HIV reservoir in people living with HIV (PHIV) is the main barrier for a cure, therefore by understanding how CD4 counts recover after antiretroviral therapy (ART) could help provide insights into HIV cure strategies.
- An international sub-study of the START study found that PHIV who initiated ART with CD4 >800 cells/μL had a substantially smaller HIV reservoir on ART, compared to individuals who commenced ART at lower CD4 counts (500-799 cells/μL)¹.
- Smaller HIV reservoirs were also seen in PHIV who achieved a CD4 count >1000 cells/μL within 48 months of ART initiation².
- Clustering of longitudinal CD4 data could be used to further explore different subgroups of PHIV and identify similar or varying traits between clusters.

Aims

- Cluster participants based on similar CD4 count trajectories following ART initiation using appropriate clustering methods.
- Compare differences between any identified clusters of participant to distinguish between clusters.

Methods

- Data:** Retrospective CD4 count data from ART initiation was obtained from hospital records of 70 PHIV participants. Only the first 5 years of from ART initiation were utilised.
- Clustering:** Latent process mixed models (l-splines with 4 knots) were implemented using the *lcmm* package³ in R. To determine the best fitting model with the optimal number of clusters, the model with the lowest AIC and highest entropy values was chosen.
- Differences between clusters:** Descriptive statistics of participants' clinical and demographic data were compared between clusters.

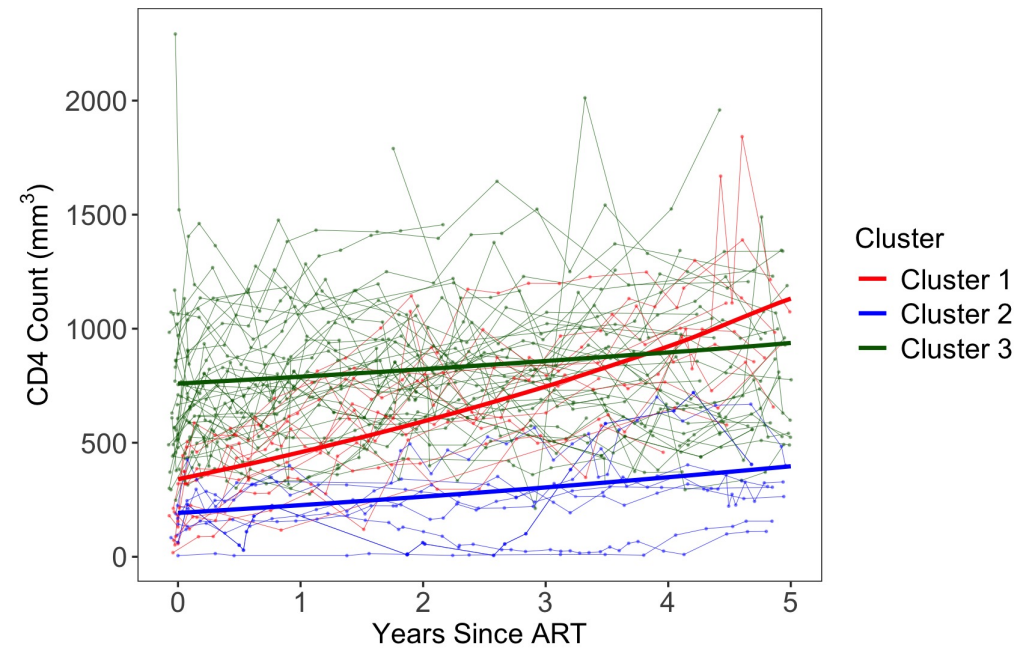


PHIV who commence ART at low CD4 counts and in chronic infection (>6 months from diagnosis), have lower CD4 recovery

Results

- Up to 4 clusters were explored, and 3 clusters were determined to be the optimal number of clusters (after 1 cluster).
- The model split participants into 3 clusters that can be described as:
 - Low to high CD4 group:** Cluster 1 starts at low CD4 counts and increases sharply to end at high CD4 counts.
 - Low CD4 group:** Cluster 2 starts and ends at lower CD4 counts.
 - High CD4 group:** Cluster 3 starts and ends at higher CD4 counts.

Clusters of CD4 trajectories of PHIV over the first 5 years since ART



Results

- Cluster 2 has higher proportion of PHIV starting ART >6 months from diagnosis.
- Cluster 3 has higher mean CD4 at initiation compared to other clusters.
- No other variables appeared to have significant differences between clusters.

	Cluster 1 (N=11)	Cluster 2 (N=9)	Cluster 3 (N=42)	p-value
Gender				
Male	9 (81.8%)	7 (77.8%)	32 (76.2%)	1
Non-male	2 (18.2%)	2 (22.2%)	10 (23.8%)	
Total HIV DNA (copies per million)				
Mean (SD)	370 (766)	113 (195)	135 (253)	0.18
CD4 at initiation (cells per mm³)				
Mean (SD)	190 (123)	128 (70.7)	691 (387)	<0.001
HIV Subtype				
AE	1 (9.1%)	0 (0%)	6 (14.3%)	0.30
B	6 (54.5%)	3 (33.3%)	22 (52.4%)	
C	1 (9.1%)	0 (0%)	6 (14.3%)	
CRF01AE	0 (0%)	1 (11.1%)	1 (2.4%)	
Unknown	3 (27.3%)	5 (55.6%)	7 (16.7%)	
Year of diagnosis				
<2006	2 (18.2%)	0 (0%)	2 (4.8%)	0.46
2006-2013	2 (18.2%)	1 (11.1%)	10 (23.8%)	
>=2014	7 (63.6%)	8 (88.9%)	30 (71.4%)	
Timing of ART from HIV diagnosis				
Less than 6 months	7 (63.6%)	2 (22.2%)	27 (64.3%)	0.08
More than 6 months	4 (36.4%)	7 (77.8%)	15 (35.7%)	

p-values are calculated through ANOVA (continuous variables) or a Fisher's Exact test (categorical variables) between each variable and clusters

Conclusions

- 3 different clusters of distinct CD4 trajectories were observed through the clustering model.
- Individuals that start ART at low CD4 counts and in chronic infection (>6 months from diagnosis) have lower CD4 recovery.
- Individuals that start ART in acute infection (<6 months from diagnosis) have better CD4 recovery.
- More longitudinal data is needed to validate findings further, and better support differences in clinical and demographic characteristics between clusters.

References

1. Rasmussen et al. (2022), *Clinical Infectious Diseases*

2. Rodríguez-Castañón et al. (2022), *AIDS Research and Human Retroviruses*

3. Proust-Lima et al. (2017), *J Stat Soft*

4. Lu Z. (2025), *Int Statistical Rev*