Mental health phenotypes of well-controlled HIV in Uganda

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BACKGROUND

HIV & mental health (MH) disorders (depression, anxiety, PTSD) are among the top 10 causes of disability among PWH in Uganda. Most studies of PWH focus on MH disorders as unidimensional constructs. However, the phenotypic expression & clinical course of MH conditions among PWH in Uganda & worldwide are heterogeneous. Accordingly, there is a shift towards identifying MH phenotypes using data driven methods capable of identifying novel insights into mechanisms of divergent phenotypes among PWH. We leverage the analytic strengths of machine learning combined with inferential methods to achieve the following:

- **Aim 1**: To identify MH phenotypes among PWH in Uganda.
- **Aim 2**: To identify & characterize sociodemographic characteristics (including history of early life adversity [ELA]), HIV disease indices, & cognitive factors that correspond to specific MH phenotypes.

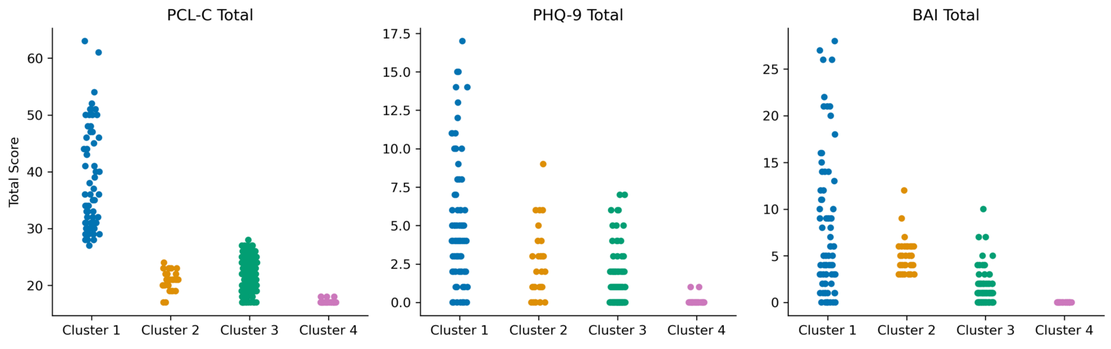
METHODS

- 277 PWH (46% female, median age=44, 93% undetectable viral load [<50copies/mL]) were enrolled in an observational community-based cohort residing in the Rakai region of Uganda.
- Participants completed the Patient Health Questionnaire (PHQ-9), Beck Anxiety Inventory (BAI), & PTSD Checklist-Civilian (PCL-C).
- Clustering pipeline consisting of: 1) dimension reduction with the UMAP algorithm (non-linear dimension reduction method); & 2) hierarchical density-based spatial clustering of applications with noise (HBDScan) to identify MH phenotypes using total symptom scores
- Inferential statistics (with false discovery rate) compared demographic & clinical factors between clusters (e.g., ELA).
- Gradient boosted multivariate regression (GBM), a form of ensemble machine learning, was used to investigate a large array of factors that could help to explain differences in MH clusters.

We identified unique mental health phenotypes among people with HIV in Uganda & identified the importance of early life adversity as an early risk determinant for unfavorable mental health among people with HIV in adulthood.

RESULTS

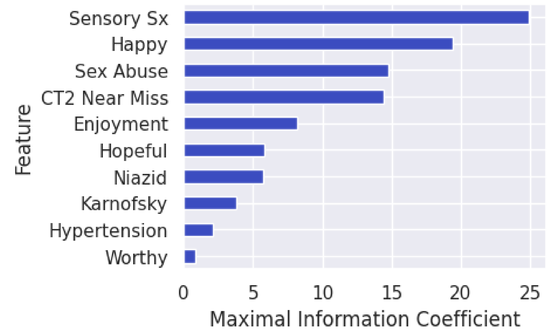
- Four MH clusters were identified. **Figure** below demonstrates the spread of scores on the 3 MH inventories across the four clusters. Cluster 1 (blue; n=76, ***PTSD phenotype***) reported clinically elevated PCL-C, with a wide distribution of BAI & PHQ-9 scores. Cluster 2 (orange; n=32, ***anxiety phenotype***) reported lower PTSD symptoms, but depressive & anxiety symptoms in the mild-moderate range. Cluster 3 (green; n=130, ***mixed anxiety/depression phenotype***) reported lower PTSD symptoms, with depressive & anxiety symptoms in the minimal-mild range. Cluster 4 (pink; n=39, ***minimal symptom phenotype***) reported very low symptoms on all measures.



- Comparisons of explanatory factors between MH phenotypes revealed a modestly higher rate of physical (14.5% vs. 5.1%; *P*=0.13) & sexual (27.6% vs. 12.8%; *P*=0.07) abuse among the PTSD phenotype (Cluster 1) vs. the minimal symptom phenotype (Cluster 4).

RESULTS

- Variables that collectively classified individuals into the PTSD phenotype (Cluster 1) vs. the normative phenotype (Cluster 4) for the GBM are in the **Figure** below. Features in rank order of relevance to classification include: **1)** endorsing sensory symptoms (e.g., tingling, burning); **2)** ratings of happiness over the past week; **3)** history of sexual abuse; **4)** near misses on Color Trails 2; **5)** ratings of life enjoyment over the past week; **6)** ratings of hopefulness over the past week; **7)** taking Niazid; **8)** Karnofsky score; **9)** hypertension; **10)** feelings of worthiness over the past week.



CONCLUSIONS

- We identified unique MH phenotypes among PWH & identified the importance of early life adversity, particularly sexual abuse, as an early risk determinant for unfavorable MH among PWH in adulthood.
- Notably, PWH in the minimal symptom MH phenotype also reported a history of sexual abuse, consistent with resilience.
- Follow-up analyses will investigate these groups to further examine mechanisms of risk vs. resilience.

ADDITIONAL KEY INFORMATION

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