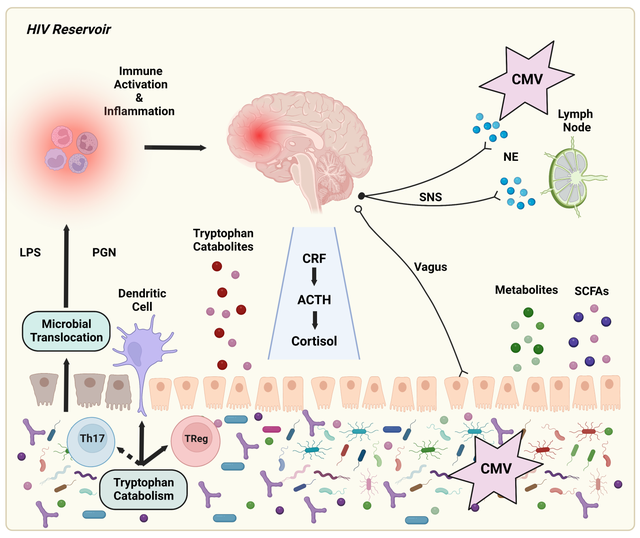
Inside Out: Inflammation in Acute HIV Predicts Persistent Depressive Symptoms Despite Antiretroviral Therapy

Jennifer V. Chavez, MPH[1], Jacob Bolzenius, PhD[2], Kyu Cho, MS[2], Julie Mannarino, BA[2], Carlo Sacdalan, MD[3,4], Phillip Chan, MBChB, PhD[5], Shelli Farhadian, MD, PhD[5], Lydie Trautmann, PhD[6,7], Lishomwa C. Ndhlovu, MD, PhD[8], Somporn Tipsuk, RN[3], Trevor A. Crowell, MD, PhD[6,7], Duanghathai Suttichom, RN[3], Donn J. Colby, MD, MPH[6,7], Nittaya Phanuphak, MD, PhD[8], Eugene Kroon, MD[3], Sandhya Vasan, MD[6,7], Somachai Sriplienchan, MD, MPH[3], Serena Spudich, MD[5], Robert Paul, PhD[2] & Adam W. Carrico, PhD[1] for the **RV254/SEARCH010 Study Team**

1. Florida International University, Miami, FL, USA
2. Missouri Institute of Mental Health, University of Missouri, St. Louis, St. Louis, MO, USA
3. SEARCH Research Foundation, Bangkok, Thailand
4. Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand
5. Yale Center for Brain and Mind Health, Yale University School of Medicine, New Haven, CT, USA
6. U.S. Military HIV Research Program, Walter Reed Army Institute of Research, Silver Spring, MD, USA
7. Henry M. Jackson Foundation for the Advancement of Military Medicine Inc., Bethesda, MD, USA
8. Institute of HIV Research and Innovation, Bangkok, Thailand

INTRODUCTION

- Depression is 2 to 3 times more prevalent among people living with HIV (PLWH) and is associated with greater risk of all-cause mortality, faster clinical HIV progression and elevated viral load.
- The time period of acute HIV acquisition (AHA) is a setpoint for several HIV clinical indicators, including viral load and chronic immune activation. Persistent inflammation has been associated with alterations in mood and cognition in PLWH.
- In recent years, the use of amphetamine-type stimulants with amyl nitrites and ED medications to enhance sexual pleasure has been on the rise among sexual minority men (SMM) around the globe, including in Southeast Asia where it is referred to as "hi-fun". Hi-fun has been associated with psychological distress among people without HIV.
- It is important to understand how pathophysiologic alterations stemming from AHA represent a setpoint for trajectories of neuropsychiatric outcomes during suppressive antiretroviral therapy (ART).



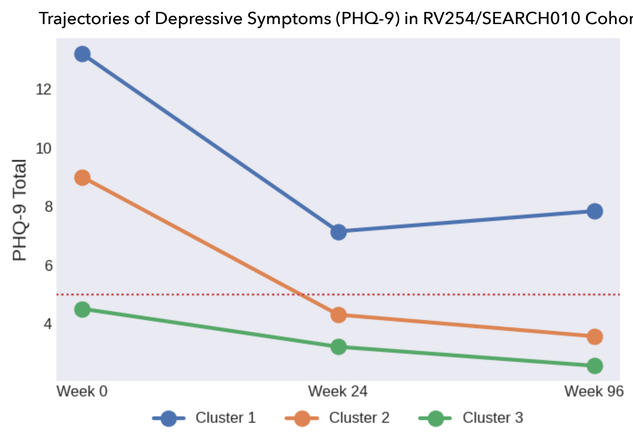
(Carrico et al., 2023)

METHODS

- RV254/SEARCH010 is an AHA cohort in Bangkok, Thailand – participants undergo extensive clinical phenotyping, including self-reported depressive symptom severity during the AHA visit and following ART initiation. Data was collected between 2009 and 2020.
- Hierarchal density-based spatial clustering with uniform manifold approximation and projection identified 3 distinct depressive symptom trajectories over 96 weeks.
- ANOVA and chi-square tests were used to examine associations of demographic, clinical, behavioral and inflammatory correlates of high persistent (versus low persistent) symptom trajectories. Logistic regressions were used to estimate odds ratios for these clusters. Alpha was set at 0.05.

RESULTS

- N=443
  - Cluster 1 (High Persistent Depressive Symptoms): n= 258, 58%
  - Cluster 3 (Low Persistent Depressive Symptoms): n= 185, 42%
- Demographic Information
  - Mean age: 27.78 (SD: 7.80)
  - >50% had a bachelor's degree or higher
  - 98% were sexual minority men
- HIV Clinical Information
  - Days from Exposure to ART: 21.38 (SD: 9.30)
  - CD4/CD8 Ratio: 0.78 (0.48)



	Cluster 1 – High Persistent Depressive Symptoms (n=258, 58%)	Cluster 3 – Low Persistent Depressive Symptoms (n=185, 42%)	P_{adj}-value
	n (%)	n (%)	
Chemsex Substance Use			
Erectile Dysfunction Medication Use	21 (10.6%)	5 (4.0%)	0.030
Amyl Nitrite Use	37 (18.6%)	11 (8.7%)	0.047
Methamphetamine Use	44 (22.1%)	17 (13.5%)	0.126
Immune Markers			
Plasma Viral Load	5.99 (1.05)	5.67 (1.23)	0.028
sTNF-αRII	3.80 (2.50)	2.83 (1.81)	0.030

DISCUSSION

- Approximately 50% of participants enrolled into the RV254/SEARCH010 cohort exhibited high persistent elevation in depressive symptoms from acute HIV through 96 weeks of suppressive ART.
- Plasma viral load, inflammation and amyl nitrite use during acute HIV were key determinants of high persistent (versus low persistent) depressive symptoms despite suppressive ART.
- Interventions to address sexualized drug use could have important implications for reducing depressive symptoms among SMM with HIV.

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Greater **systemic inflammation** and higher plasma **viral load** at acute HIV visit are associated with **high, persistent depressive symptoms** over 96 weeks of suppressive ART.

FIU Robert Stempel College of Public Health & Social Work
Florida International University

UMSL University of Missouri–St. Louis

WRAIR Walter Reed Army Institute of Research
Military HIV Research Program

INHCC International NeuroHIV Cure Consortium

iCARUS a bio-behavioral laboratory