

# **A Potentially Bidirectional Relationship Between CSF HIV and Depression**

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# Disclosures of Dr. Hammond

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# Depression in HIV

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- Major depressive disorder (MDD) is the most common psychiatric disorder during HIV disease
- Up to 45% lifetime prevalence in HIV disease
  - General population lifetime prevalence 5-17%
- Associated with poor viral control, progression of HIV, immune suppression and activation, earlier mortality

*Kessler, Arch Gen Psy 2005; Krishnan, Biol Psy 2002, Sherr, Psy Heath Med 2011; Hutton, 2004; Alvy, 2011; Evans, 2002; Ickovics, 2001; Treisman, 2004; Sherr, 2011, Blume, 2011; Raison, 2006*

# CSF Viral Escape

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- Detectable CSF HIV RNA in the presence of clinically undetectable plasma levels, or
- CSF HIV RNA concentration  $\geq 1 \log_{10}$  greater than the plasma HIV RNA concentration
- Estimated 10% prevalence
- Unknown if depression is associated with CSF viral escape

# CHARTER Study & Inclusion Criteria

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- **CNS HIV Anti-Retroviral Therapy Effects Research**
  - CHARTER Study: 6-Center longitudinal US cohort
- Participants taking ART followed semiannually between 2004 through 2009
- Free of DSM-IV major depression and CSF viral escape at study entry
- Minimum of three lumbar puncture
- Longitudinal analyses, N=223; 2,496 person-months of follow-up

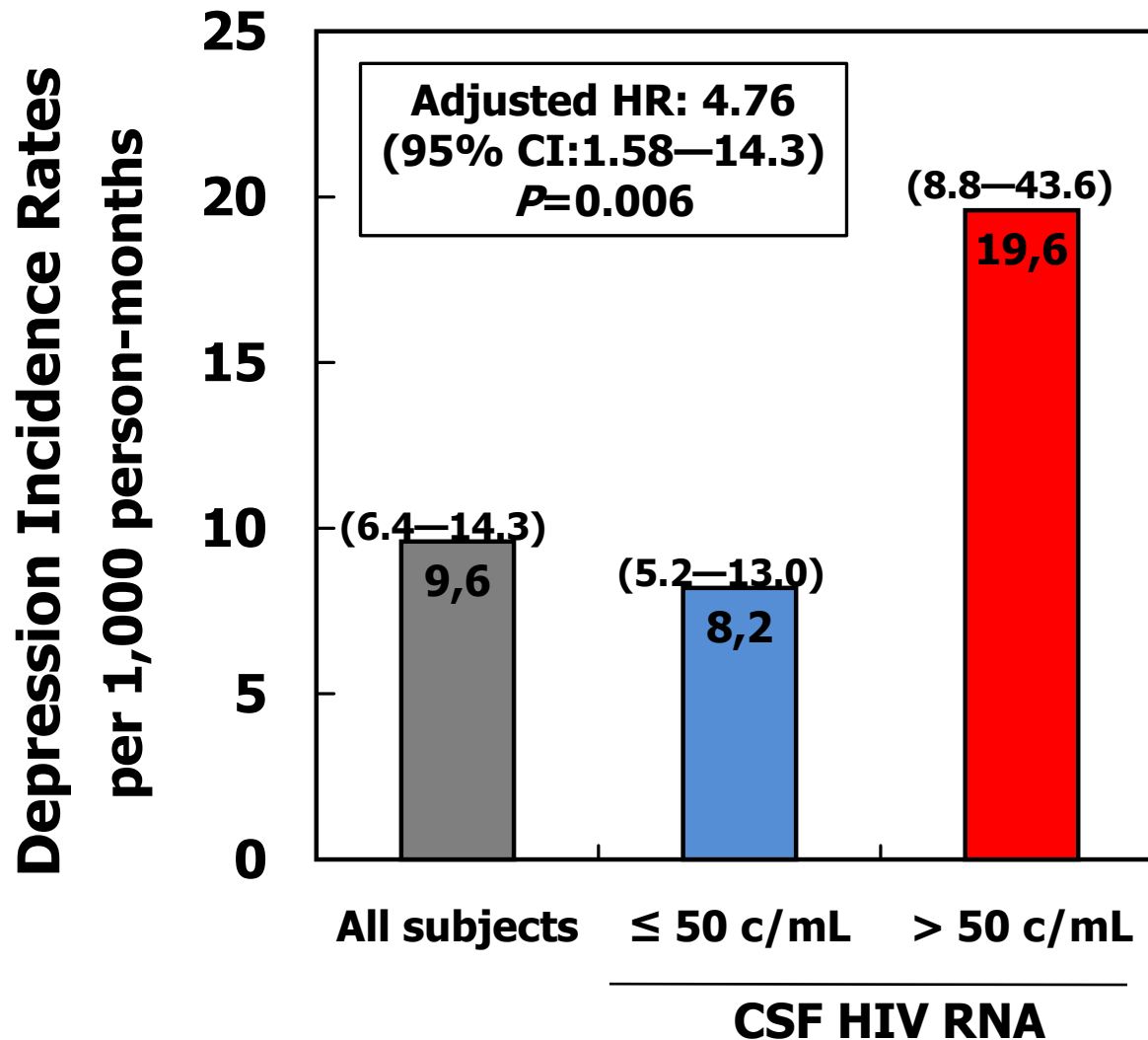
# Participant Characteristics

Characteristic	CSF HIV RNA	
	> 50 c/mL n=32 (14.4%)	≤ 50 c/mL n=191 (85.6%)
Age, mean (SD)	<b>41.1 (8.3)*</b>	<b>45.5 (7.0)</b>
Gender, number male (%)	154 (81%)	28 (88%)
Plasma HIV RNA, log <sub>10</sub> c/mL	<b>3.8 (1.1)*</b>	<b>2.1 (0.8)</b>
Current CD4+ T-cells (/mm <sup>3</sup> )	<b>370.3 (270.3)*</b>	<b>495.6 (287.7)</b>
CPE, mean (range)	<b>7.2 (5-12)*</b>	<b>7.8 (4-14)</b>
Adherence, number ≥ 95% (%)	<b>22 (69%)*</b>	<b>170 (89%)</b>
Current ART duration, months, mean (SD)	13.6 (20.0)	18.8 (21.2)
HIV disease duration, months, mean (SD)	<b>113.0 (66.1)*</b>	<b>144.0 (71.0)</b>

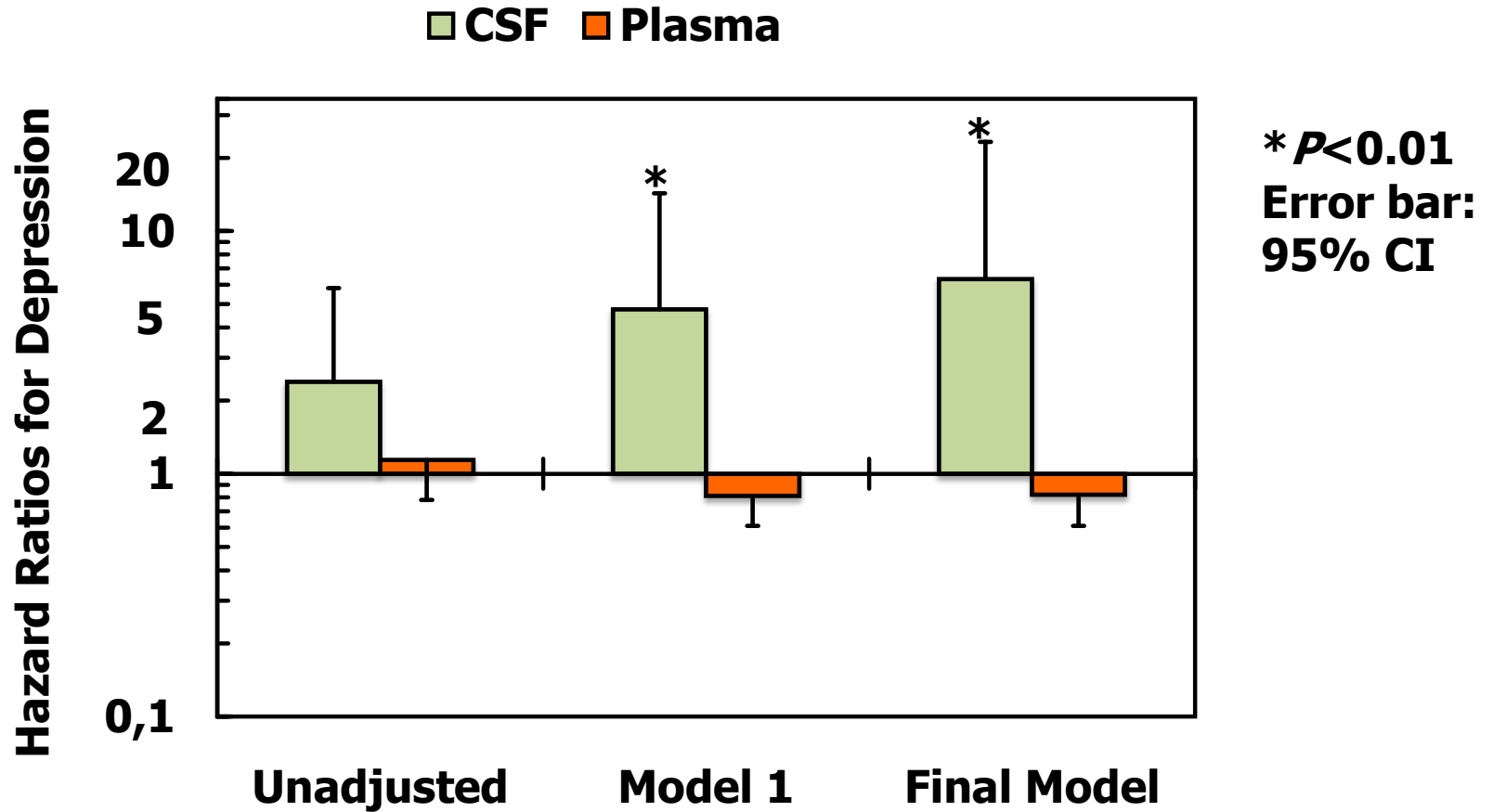
\*P<0.05; CPE:

CPE = CNS Penetration Effectiveness;  
MDD = Major Depressive Disorders;  
ART = Antiretroviral therapy

# Incidence Rates (95% CIs) for Depression by CSF HIV RNA



# Risk of New-onset Depression by HIV Compartment

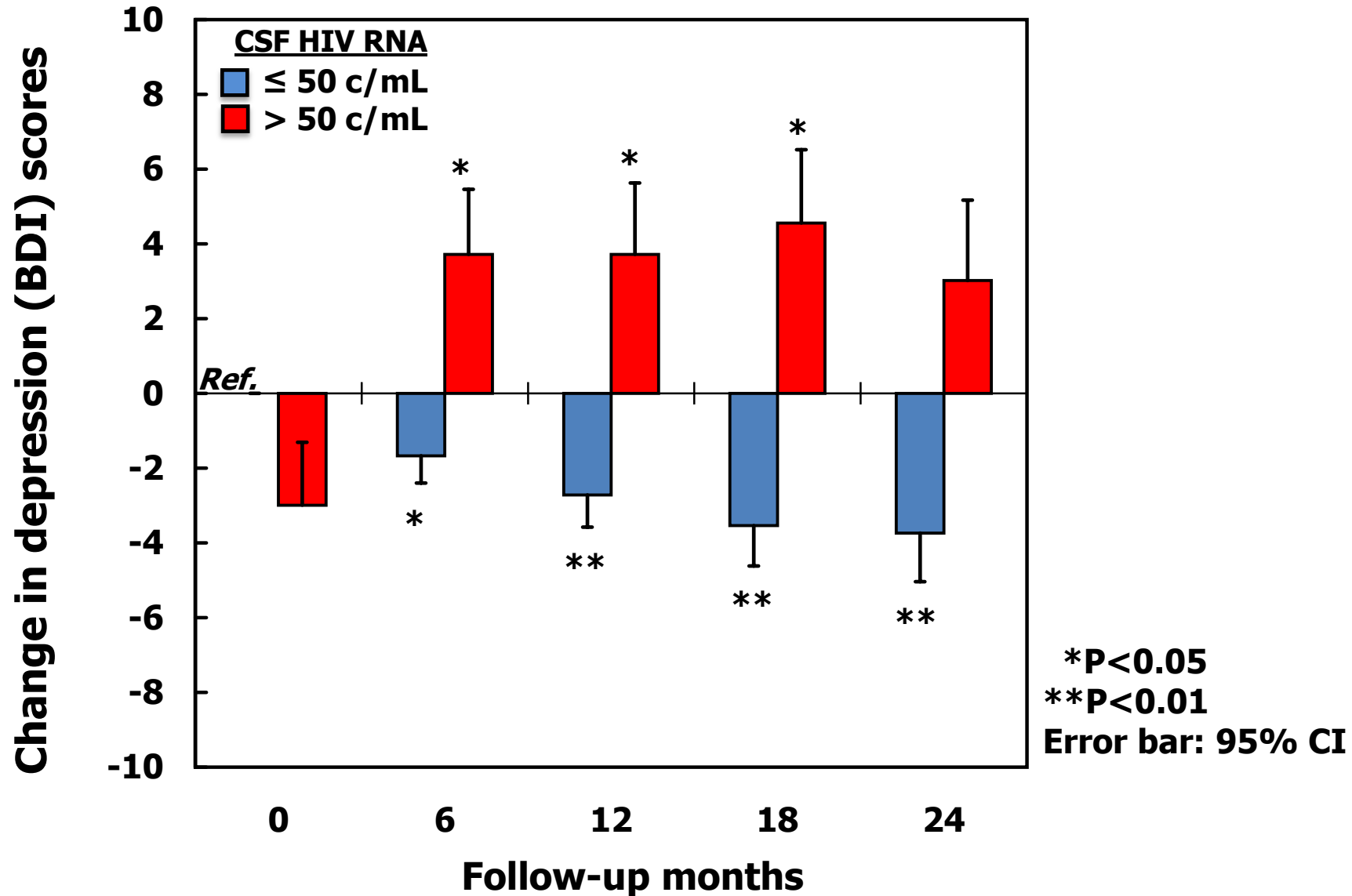


Model 1: Adjusted for Plasma/CSF HIV RNA and adherence

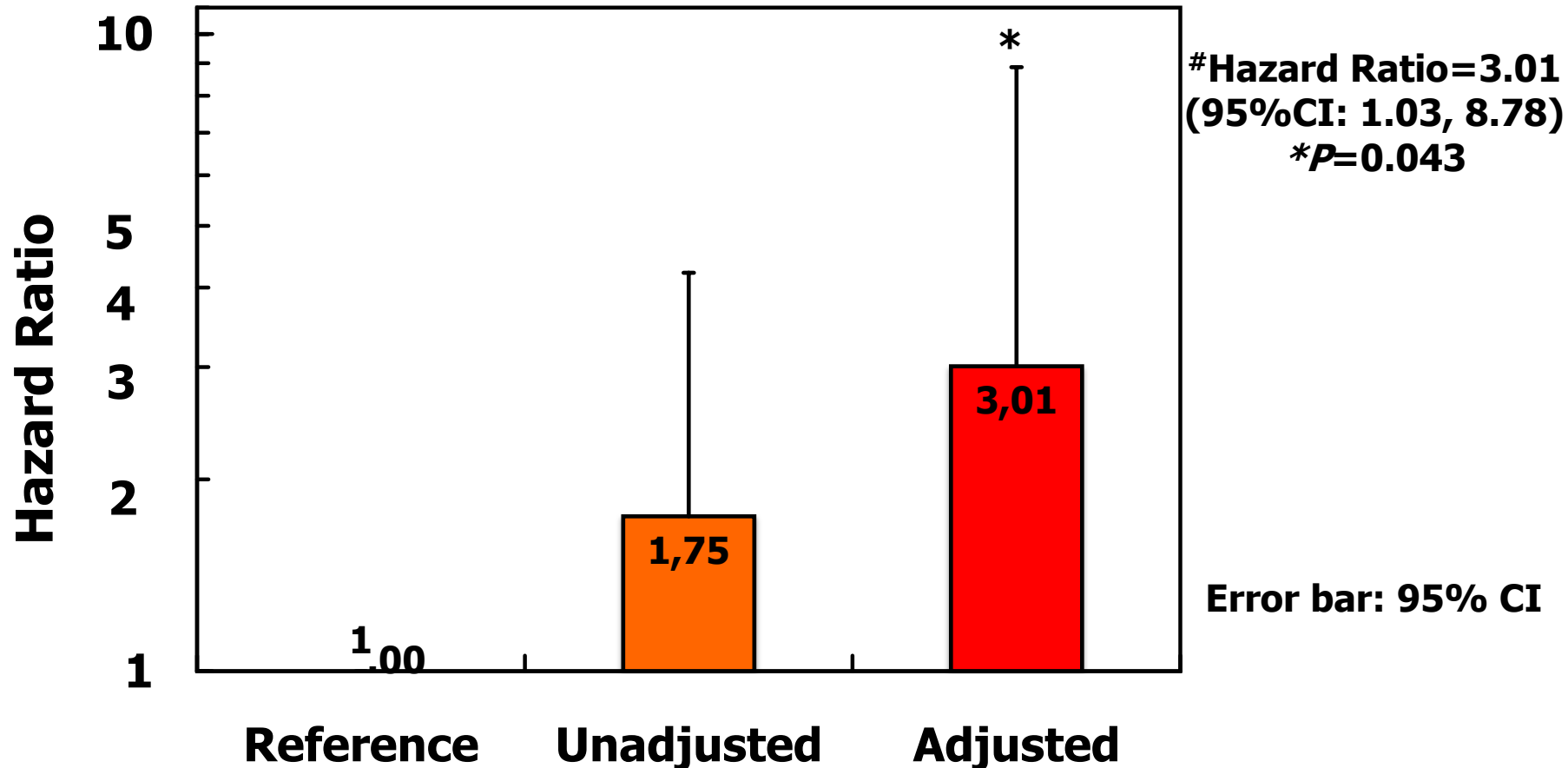
Model 2: Adjusted for Model 1 and lifetime MDD, lifetime alcohol and substance abuse, duration of ART, CPE, age, sex, race. Error bars represent 95% confidence intervals



# Trajectories of Beck Depression Inventory (BDI) Scores by CSF HIV RNA



# Association Between Depression and CSF Viral Escape



#Adjusted for CPE2.0: CNS penetration effectiveness score 2.0; adherence by AIDS Clinical Trials Group 4-Day Adherence Questionnaire; cART: combination antiretroviral therapy; lifetime alcohol and substance use disorder based on Diagnostic and Statistical Manual of Mental Disorders, IV using the Composite International Diagnostic Interview (CIDI DSM-IV); cART: combination antiretroviral therapy; SSRI: selective serotonin reuptake inhibitor

# Bidirectional Association

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CNS penetration  
CNS viral replication  
Drug toxicity  
Immune recovery  
Genetics

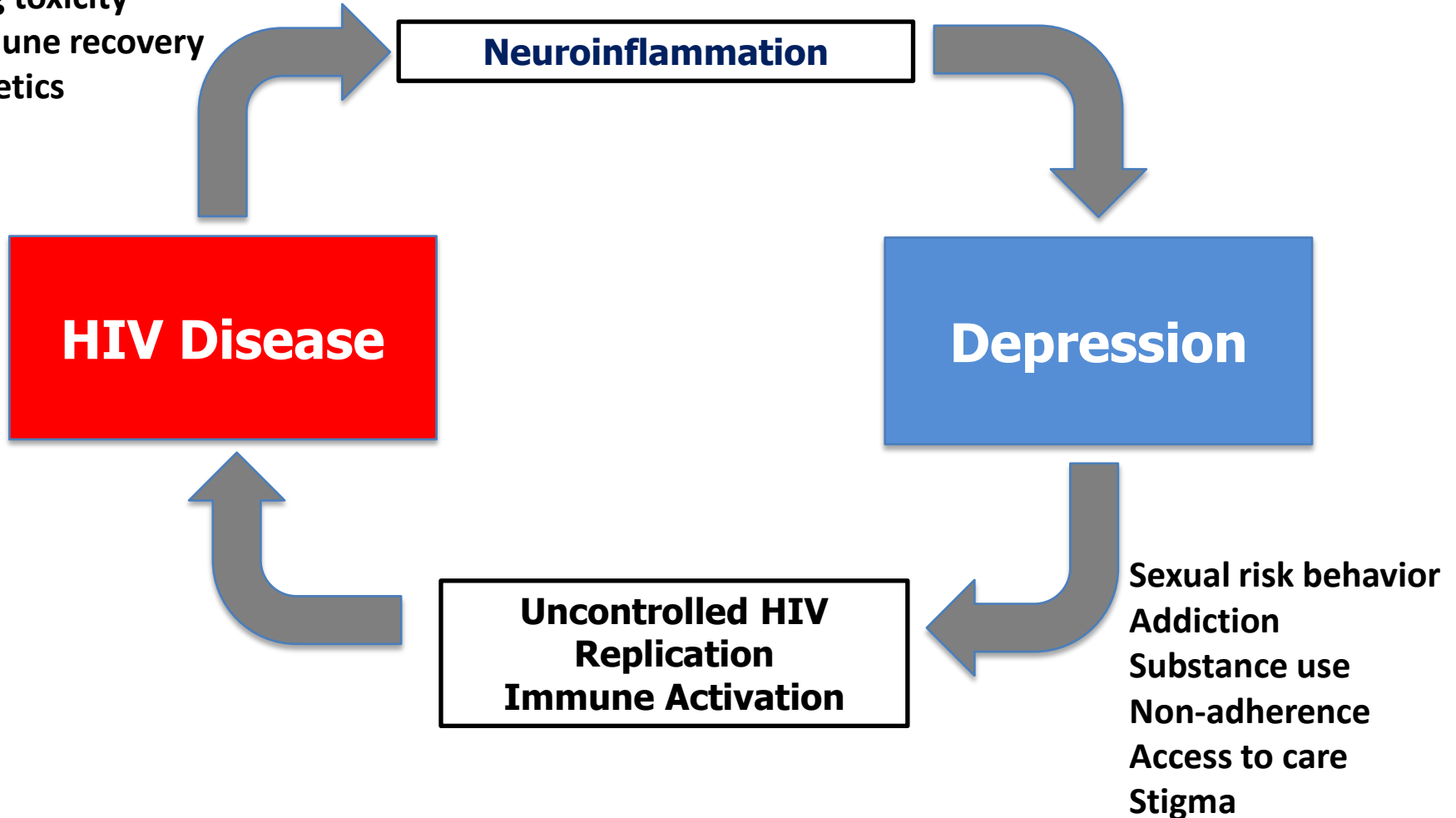
**Neuroinflammation**

**HIV Disease**

**Depression**

**Uncontrolled HIV  
Replication  
Immune Activation**

Sexual risk behavior  
Addiction  
Substance use  
Non-adherence  
Access to care  
Stigma



# Investigators

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