Introduction
- Antiretroviral therapy can promote a longer lifespan by preventing further viral DNA integration.
- Viral Reservoirs can persist in virally suppressed HIV+ individuals and act as chronic suppliers of viral antigen for decades.
- Chronic HIV patients are often afflicted with a variety of age-related comorbidities that can manifest as cognitive sequelae.
- Frailty is a phenotypic assessment that examines different physical attributes as a generic metric for secondary anatomical etiologies.
- Frailty was defined by the Fried criteria any subject with >2 was designated as Frail and <3 was designated as Non-Frail (NF).

Aims
- In a data driven approach we assessed the relationship between brain integrity, neuropsychological performance (NP), and frailty in a well-controlled HIV+ population.

NP Methods
- Global Deficit scores (GDS) were derived from a NP battery of tests.
- Domains included executive function, psychomotor speed, and memory.

ASL Methods
- Resting Cerebral Blood Flow (rCBF): Pseudocontinuous arterial spin labeling time (1.5 seconds labeling time, 1.2 seconds post-labeling delay) was used to measure perfusion of arterial blood into cortical and subcortical brain tissue. Acquired images have a resolution of 3.4x3.4x5.0 mm.
- Voxel-wise analysis was performed between subjects labeled as Frail vs NF

Results
- The voxel-wise results for the CBF analysis are shown in Figure 1 with 8 clusters that were significantly different between Frail and NF.
- Mann-Whitney tests of the median revealed significantly lower FA for white matter connecting the four regions between frail and NF HIV+ individuals (p=0.03).
- Across the entire cohort a negative association was seen for Average FA and performance in the executive domain (p=0.02; r=-0.25) and GDS (p=0.01; r=-0.2731).
- A linear model incorporating FA and CBF significantly predicted GDS outcome (p=0.009) but only CBF significantly improved the model (p=0.034).

Summary
- We conclude that HIV+ frail individuals have reductions in CBF and decreased structural connections between those regions that were directly connected.
- Both lower CBF and reduced FA in these ROIs predicted poorer cognitive performance suggesting a possible etiology to the behavioral changes associated with the frailty index.
- CBF was the stronger predictor within the model suggesting white matter integrity may be a secondary degenerative process.
- This multi-modality approach suggests that the frailty index is capable at identifying secondary pathologies that reflects accentuated functional and structural damage in HIV+ individuals.