SPECIFIC AIMS

Unhealthy alcohol use usually refers to at-risk drinking (according to NIAAA criteria),[1] alcohol abuse and alcohol dependence.[2,3] In the current proposal we expand this definition to include any alcohol consumption in those with liver disease including hepatitis C infection (HCV), a common comorbid condition in those with HIV. Unhealthy alcohol use has adverse effects on patients with HIV, including interfering with combined antiretroviral therapy (ART) adherence, promoting disease progression, and liver injury [4-9]. Observational data from our Veteran's Aging Cohort (VACS), a NIAAA funded cohort of HIV-infected patients (HIV+) and matched controls has helped expand the understanding of the role of alcohol in determining outcomes in HIV+.[10-28] Counseling and medications have proven efficacy in addressing unhealthy alcohol use in HIV-negative patients[29,30] but have not been thoroughly investigated in HIV+ patients where their benefit could extend to standard (CD4, viral load) and expanded prognostic biomarkers of HIV disease progression such as the VACS Index and changes in ART adherence, depressive symptoms and unprotected sex after alcohol. HIV+ patients tend to have higher levels of psychiatric comorbidity and multisubstance use (MSU) than non-HIV infected patients and these, along with liver disease, may reduce the efficacy of counseling and decrease the efficacy and safety of medications to treat unhealthy alcohol use. Engaging non-treatment seeking patients in an appropriate level of alcohol treatment is challenging. In addition, counseling and medication interventions do not uniformly decrease alcohol consumption or related harms in all patients and intervention effects tend to be modest. Two strategies to address these challenges include on-site integrated alcohol treatment in the HIV specialty clinic and stepped care. Integrated on-site alcohol treatment can address the barrier imposed by poor adherence to off-site treatment referrals. Stepped care assesses the efficacy of an intervention in a specific patient and adapts the intensity of that intervention to the patient's response. The comparative effectiveness of an integrated stepped care (ISC) approach to unhealthy alcohol use in HIV+ patients versus treatment as usual (TAU) has not been rigorously studied. In response to RFA-AA-11-003: "NIAAA Collaborative Centers for HIV/AIDS and Alcohol Outcomes Research", we propose to conduct 3 linked multi-site randomized clinical trials of ISC treatment for unhealthy alcohol use versus TAU in 642 HIV+ patients. Each clinical trial will be conducted in a unique subpopulation of patients with unhealthy alcohol use; 1) at-risk drinking, 2) alcohol abuse and dependence, or 3) those with liver disease who consume alcohol below at-risk levels and that do not meet criteria for alcohol abuse or dependence (Moderate Alcohol+Liver Disease).

The **specific aims** and **hypotheses** of the study are as follows:

Specific Aim 1: To compare the effectiveness of an ISC intervention versus TAU on alcohol consumption.
Hypothesis 1: The ISC will lead to fewer drinks per week in those with at-risk drinking and alcohol abuse and dependence, and a greater proportion reporting abstinence in the Moderate Alcohol+Liver Disease group.

Specific Aim 2: To compare the impact of an ISC intervention versus TAU on a comprehensive panel of biomarkers (including CD4 and viral load) as measured by the VACS index.
Hypothesis 2: The ISC intervention will lead to a greater proportion of patients who experience at least a 5-point decrease in the VACS Index than TAU.

Specific Aim 3 (Exploratory): To explore the impact of an ISC intervention versus TAU on ART adherence and psychosocial outcomes (e.g. depression, unprotected sex after alcohol use) and in those with multisubstance use (e.g. tobacco, marijuana, cocaine, heroin, non-medical use of prescription opioids).

Specific Aim 4 (Descriptive): To provide data for an operations research model about the actual receipt and patterns of alcohol treatment services overall, by intervention condition, and among specific patient subgroups (e.g multisubstance use, drinking category, comorbid depression).

Specific Aim 5 (Developmental): To develop web-based delivery of ancillary counseling services and allow for long-term data collection on enrolled subjects following the clinical trial.

As part of the **C**onsortium to improve **O**utcoMes in hiv/**A**ids, **A**lcohol, **A**ging, and multi-**S**ubstance use (COMpAAAS), these trials will be considered in light of findings from a parallel observational study on alcohol and MSU (see COMpAAAS Observation grant) and inform operations research (see COMpAAAS OR Model grant) to help design subsequent intervention trials.