## A. SPECIFIC AIMS

The Veterans Aging Cohort Study (VACS) is the largest clinical cohort of HIV infected individuals (HIV+) in North America (n=40,594). We have collected in depth, longitudinal data on alcohol, multisubstance use (MSU), and outcomes over 8 years on 7,312 HIV+/- veterans at 8 sites (VACS 8). VACS has demonstrated that unhealthy alcohol use is common(1-5) and a major risk factor for adverse outcomes among HIV+ including depression,(6-8) risky sex,(9;10) disease progression(2;11-16), liver injury,(17;18) and mortality(19;20)—findings that have been confirmed by others.(21-30)  However, we have observed that MSU is the norm among HIV+ drinkers: overall 64% also use tobacco, opioids, or cocaine. This is true among past injection drug users (80%), those infected with hepatitis C (78%), those 50+ years (63%), women (74%), and men who have sex with men (55%). While we know that any alcohol use is often harmful among HIV+ we do not know: whether these harms are exacerbated by MSU; whether or how MSU alters response to alcohol treatment; or what changes occur, and in what order, in alcohol and MSU as individuals enter care or age. We propose to build on our prior work to create a Consortium to improve OutcoMes in hiv/Aids, Alcohol, Aging, and multi-Substance use (COMpAAAS). Our consortium mission is to build and disseminate the evidence needed to optimize health care for HIV+ harmed by alcohol, MSU, HCV, and depression through coordinated, integrated, and externally validated observation, operations research (OR) modeling, and intervention studies. Long-term (>10 year) patterns and consequences of alcohol and MSU have major implications for how we might accomplish our mission including: the comparative effectiveness, prioritization, and personalization of treatment for alcohol, MSU, and depression (COMpAAAS: OR Model Grant), identification of target conditions for combined and/or stepped alcohol interventions (COMpAAAS: Intervention Grant), and the information we should give patients regarding personal risk of adverse outcomes to motivate behavior change (this application, COMpAAAS: Observation Grant). To this end, we have developed and internationally validated the VACS Index(20) (based on age, CD4 count, HIV-1 RNA and clinical biomarkers) which is predictive of all cause mortality(31;32) and responsive to effects of antiretroviral therapy (ART),(33) changes in alcohol use, and adherence.(33) We hope to conduct a series of studies on the use of the VACS Index to quantify personal risk and motivate change in alcohol and MSU—just as the Framingham Index is used to quantify risk of cardiovascular disease and motivate change in diet and smoking. To this end we have developed a prototype VACS Calculator. Our long term goal is to quantify harm (risky sex, depression, mortality, ART adherence, and liver disease) associated with patterns of ongoing alcohol and MSU compared with curtailed alcohol and MSU to inform intervention studies, Operations Research (OR) Modeling, and patient counseling. While VACS is uniquely positioned for this goal, our alcohol funding ends September 2011. Without additional follow up, our ability to characterize long-term longitudinal patterns and consequences of alcohol and MSU within important subgroups will be limited. Further, patterns and consequences of alcohol and MSU may be influenced by the increased non medical use of prescription opioids (NMU) and changes in ART. These influences may be most pronounced among HIV+ entering care because first year mortality rates are high (60% higher than in later years). Finally, Time Line Follow Back data (TLFB) are the gold standard for alcohol research but difficult to collect. By transitioning survey collection to a Web-Based format we will be able to collect TLFB data on alcohol and MSU and begin the transformation of VACS from a clinic based cohort to an Interactive Web-Based Laboratory.

**Aim 1. Compare longitudinal patterns and consequences of alcohol and MSU in HIV+/-.**
**H1a.** Patterns of alcohol and MSU will differ by gender, age, race/ethnicity, risk group, HCV, and HIV.
**H1b.** Change in alcohol will predict simultaneous change in MSU equally in HIV+/-.
**H1c.** Alcohol use will decline less over time among HIV+ vs. HIV-, MSU vs. non MSU, and HCV+ vs. HCV-.
**H1d**. Change in alcohol and MSU will predict change in risky sex, depression and mortality in HIV+/-.
**H1e.** Change in alcohol and MSU will predict change in adherence, VACS Index, and ART in HIV+.
**H1g.** Change in alcohol will predict change in FIB 4, symptomatic cirrhosis, and liver cancer in HCV+/-.
**Aim 2. Collect TLFB in HIV+/- initiating care, to study contemporary fine grained longitudinal associations of alcohol, tobacco, opioids (heroin + NMU), and cocaine, with outcomes.**
**H2a-e.** (Reanalysis of H1a-e), opioids will be more common and have a greater impact due to NMU.
**Aim 3. (Developmental) Create an interactive Web-Based laboratory. Use it to iteratively improve interpretation of individualized risk to maximize motivation to change behavior.**
**H3a.** Patients will view, interact, and give online feedback on the VACS Index Risk Calculator.
**H3b.** Patient will prefer advice to curtail alcohol and MSU based on individual risk over generic advice.
**H3c.** Patients will be more motivated to curtail alcohol and MSU after receiving advice tailored to individual risk than generic advice.