Unhealthy alcohol use threatens the health of HIV-infected individuals. Varenicline, gabapentin, and topiramate decrease alcohol consumption in HIV uninfected patients and show promise to address unhealthy alcohol use in HIV-infected patients. Each of these medications, approved and used for the treatment of non alcohol-related conditions (e.g. smoking, neuropathic pain, and epilepsy), may cause adverse clinical outcomes. Varenicline may be associated with psychiatric symptoms and cardiovascular complications. Gapapentin and topiramate can cause dizziness and sedation. To date, studies have not examined the association between the use of these medications and adverse clinical outcomes or the comparative effectiveness of these medications for unhealthy alcohol use in HIV-infected patients. It is essential to conduct such studies prior to the widespread evaluation or use of these medications for unhealthy alcohol use in HIV-infected patients. Large clinical datasets, such as the NIAAA-funded Veterans Aging Cohort-Virtual Cohort (VACS-VC) with information on prescriptions, alcohol consumption, depressive symptoms, laboratory values and diagnoses provide the opportunity to investigate the safety and comparative effectiveness of these medications in HIV-infected patients and uninfected comparators. The number of VACS-VC HIV-infected individuals who have received varenicline (1235), gabapentin (10,193) and topiramate (914) presents a unique opportunity to examine safety and comparative effectiveness. The specific aims of this research are to:

Determine the incidence of adverse clinical outcomes, by HIV status, associated with the use of varenicline, gabapentin and topiramate (Aim 1),
Compare the individual effectiveness of varenicline, gabapentin and topiramate on AUDIT-C scores in HIV-infected and uninfected patients (Aim 2), and
Compare the individual effectiveness of varenicline, gabapentin and topiramate on CD4, viral load and the VACS-Index in HIV-infected patients (Aim 3).

We will conduct propensity score matched analysis (Aims 1-3) and for Aim 3 we will conduct mediation analyses to investigate the extent to which observed changes are mediated by changes in alcohol. This line of research, conducted in a large and well-characterized cohort of HIV-infected and HIV-uninfected comparators, will provide critical information that is necessary to inform implementation of these medications for unhealthy alcohol use in HIV-infected patients.