

## A. SPECIFIC AIMS

An emerging body of work shows that unhealthy alcohol use (a spectrum including at-risk drinking and alcohol use disorder), substance use, smoking, and depression often co-occur in HIV-infected patients. In a large multisite observational study of aging and HIV, unhealthy alcohol use, substance use (in particular, marijuana, stimulants and opiates), smoking, and depression were common among those with HIV<sup>1,2</sup> and exhibited striking temporal concordance, often remitting and recurring together.<sup>3,4</sup> For example, greater alcohol use decreases the odds of smoking cessation.<sup>5,6</sup> Basic science research also supports the idea that these conditions may be mutually reinforcing.<sup>7-9</sup> All substances of abuse, including alcohol and nicotine affect the central reward pathways based in the ventral tegmental area and the nucleus accumbens.<sup>10,11</sup> and involve common genetic liability.<sup>12</sup> Epidemiological data and computer simulation suggest that unhealthy alcohol use, substance use and depression lead to new HIV infections and promote disease progression.<sup>13,14</sup> Therefore, these conditions not only “travel together” but substantially impact HIV progression and treatment.

While unhealthy alcohol use, substance use, smoking, and depression often co-occur, their screening and treatment does not. Screening and treatment strategies for these conditions are typically specified separately and enacted separately because of a multitude of factors, including distinct clinical guidelines, varying strength of evidence underlying those guidelines,<sup>15-19</sup> and distinct providers and programs for the treatment of each condition. As a result, patients who are screened for one may not be screened for another, and patients who are treated for one may not be treated for another. When multiple referrals are necessary, the requirement of additional clinic visits may lead to decreased adherence, worsening patient outcomes.

Many HIV patients in the U.S. receive care in integrated health systems (offering outpatient and inpatient care, specialty care and primary care) such as Kaiser Permanente and the Veterans Affairs Healthcare System (V.A.). Indeed, the V.A. is, the largest provider of care for HIV-infected persons in the U.S.<sup>20</sup> If integrated guidelines were developed for screening and treatment of unhealthy alcohol use, substance use, smoking and depression, integrated health systems could offer platforms for their implementation. Accordingly, this proposal aims to inform guideline development for screening and treatment of unhealthy alcohol use, substance use, smoking and depression in HIV-infected persons. We propose to develop a decision-analytic model to evaluate beneficial effects (e.g. timeliness, greater adherence) as well as potentially harmful effects (e.g. false positives) and resource implications of integrated screening and treatment. The target population is HIV-infected individuals in care at integrated health systems in regions with high HIV incidence. For Aim 1 (comparing screening strategies), the comparator is screening guidelines recommended by the United States Preventive Services Task Force. For Aim 2 (comparing treatment strategies), the comparator is treatment representative of standard care.

### **Aim 1A: Evaluate integrated screening for HIV-infected individuals newly diagnosed with unhealthy alcohol use or any of the other index conditions (smoking, substance use, depression)**

1A.1 Integrated screening increases life expectancy

1A.2 Integrated screening increases quality-adjusted life expectancy

1A.3 Integrated screening has favorable value (incremental cost-effectiveness ratio < \$100,000/QALY)

### **Aim 1B. Evaluate integrated screening for HIV-infected individuals with a history of unhealthy alcohol use or any of the other index conditions (smoking, substance use, depression)**

1B.1 Integrated screening increases life expectancy

1B.2 Integrated screening increases quality-adjusted life expectancy

1B.3 Integrated screening has favorable value (incremental cost-effectiveness ratio < \$100,000/QALY)

1B.4 Integrated screening should occur at least once yearly

### **Aim 1C. Evaluate integrated screening for HIV-infected individuals without diagnosis of unhealthy alcohol use or any of the other index conditions (smoking substance use, depression)**

1C.1 Integrated screening increases life expectancy

1C.2 Integrated screening increases quality-adjusted life expectancy

1C.3 Integrated screening has favorable value (incremental cost-effectiveness ratio < \$100,000/QALY)

### **Aim 2. Evaluate integrated treatment for HIV-infected individuals with unhealthy alcohol use and $\geq 1$ of the other index conditions (smoking, substance use, depression)**

2.1 Integrated treatment increases life expectancy

2.2 Integrated treatment increases quality-adjusted life expectancy

2.3 Integrated treatment has favorable value (incremental cost-effectiveness ratio < \$100,000/QALY)