

A. SPECIFIC AIMS

HIV infects over 50,000 new people each year in the US.¹ An important reason why HIV transmission persists is not because of a dearth of effective interventions, but because effective interventions may not be implemented.²⁻¹⁰ It is difficult for decision makers to prioritize which interventions and/or portfolios of interventions deliver the most benefit and/or value, and to tailor prioritizations for particular patient groups (e.g. elderly, high comorbidity, Hepatitis C) and settings (e.g. patients entering care).⁷ For example, while alcohol plays a central role in new infections and alcohol interventions may lower HIV transmission risk, many other types of interventions may also lower HIV transmission risk. To address this problem, our proposal integrates comparative effectiveness research (which compares the effectiveness of different interventions) and operations research modeling (which compares alternative portfolios of interventions, rather than comparing single interventions in isolation), to help identify those portfolios that have the greatest health effect and/or greatest value (e.g. “bang for the buck”). A “portfolio” is defined as one or more interventions or sequences of interventions applicable to a patient or patient group.

We place particular emphasis on alcohol because it is a common modifiable risk factor for HIV transmission and progression, primarily through pathways of unsafe sex and reduced viral load suppression on combined antiretroviral therapy (ART)¹¹⁻¹³ for transmission, and reduced ART adherence for progression. Because unhealthy alcohol use¹⁴ often occurs together with multi-substance use (MSU) and depression, and acts on similar pathways, our proposal considers portfolios that address these intertwined, multimorbid conditions simultaneously or in a sequenced, prioritized progression (e.g. “stepped” interventions). We also consider intervention designs that can be further “tailored” based on individual patient characteristics (e.g. age, comorbidity burden, newly entering care).

We will implement this operations research model within an interactive web-based laboratory that aims to improve research methods by encouraging greater “cross-talk” between modeling, observational data analysis, and trial design; and aims to increase stakeholder-relevance and patient-relevance (e.g. identifying patient groups that may particularly benefit from interventions). We will work collaboratively and iteratively with stakeholders regionally (New York City Department of Health and Mental Hygiene [DOHMH]) and nationally (Center for Disease Control and Prevention [CDC]) and the Veterans Administration [VA] to assure research is accessible for decision makers and translatable to real decisions. Accordingly, our Specific Aims (COMpAAAS-Operations Modeling) synergize with the other consortia proposals (COMpAAAS-Observation and COMpAAAS-Intervention):

Specific Aim 1. Synthesize data from published literature and VACS to inform alternative intervention portfolios for HIV+ patients with unhealthy alcohol use and/or MSU and/or depression

1.1 Effects of unhealthy alcohol use, MSU, and depression on HIV transmission in the published literature can be summarized and incorporated into design of intervention portfolios

1.2 Sequences of unhealthy alcohol use, MSU, and depression observed in VACS will suggest restrictions on design of intervention portfolios [e.g. always do intervention A before intervention B]

1.3 Combinations of unhealthy alcohol use, MSU, and depression observed in VACS will suggest restrictions on design of intervention portfolios [e.g. only do intervention A if you also do intervention B]

Specific Aim 2. Develop operations research model to compare effectiveness of alternative intervention portfolios for HIV+ persons with unhealthy alcohol use and/or MSU and/or depression

2.1 Stepped interventions (e.g. sequenced in order of intensity) compared to non-stepped interventions (e.g. individual or simultaneous) are (A) more effective and (B) deliver favorable value

2.2 Tailored interventions (e.g. based on individual patient characteristics) compared to non-tailored interventions are (A) more effective and (B) deliver favorable value

2.3 Stepped and tailored interventions remain more favorable than non-stepped or non-tailored interventions regardless of whether effectiveness is defined based on HIV transmission or progression

Specific Aim 3. Develop web-based interactive laboratory to facilitate design of interventions for HIV+ persons with unhealthy alcohol use and/or MSU and/or depression. We hypothesize web-based lab can

3.1 Improve research methods by facilitating cross-talk and development between modeling, data, and trials

3.2 Improve stakeholder-relevance by making results accessible, tailored, and incorporating feedback

3.3 Improve patient-relevance by making results accessible, tailored, and incorporating feedback

Stepped interventions=Prioritized sequence of interventions with monitoring (First A, then B, then C; stop if patient responds); **Portfolios**=One or more interventions or sequences of interventions applicable to a particular patient or patient group; **Operations research**=Mathematical modeling to optimize health outcomes given resource restrictions, can compare portfolios of interventions; **Comparative effectiveness research**=Compares benefit of alternative treatment strategies (A versus B); **Tailoring**=Individualizing analyses or results based on particular patient characteristics or stakeholder requirements; **MSU**=Multi-substance use (cocaine or opiates or tobacco, based on VACS preliminary results); **COMpAAAS**=Consortium to improve Outcomes in HIV/AIDS, Alcohol, Aging, and MSU; **Unhealthy alcohol use**=At-risk and/or abuse and/or dependence (Saitz definition); **ART**=Antiretroviral therapy (combination); **USPSTF**=United States Preventive Services Task Force; **DOHMH**=New York City Department of Health and Mental Hygiene; **CDC**=Centers for Disease Control and Prevention; **VACS**=Veterans Aging Cohort Study; **Unsafe sex**=>1 partner and/or no condom (sometimes non-primary partner); **IDU**=Injection drug use; **MSM**=Men who have sex with men; **EMR**=Electronic Medical Record; **TORCH**=The Operations Research Collaboration for Health