

## Summary

Among those with HIV infection (HIV+) on antiretroviral therapy (ART), polypharmacy is three times more common than among those without infection and occurs 10 years earlier. Likely due to greater physiologic frailty, polypharmacy (5+ chronic medications) among those with HIV is also associated with greater mortality. Potentially inappropriate medications (PIMs) are those which likely cause more harm than benefit due to drug interactions and adverse reactions and these increase with polypharmacy. While criteria for PIMs among 65+ year olds (Aging PIMs) are established, they have not been validated among HIV+ individuals. Further, ART and alcohol use also increase PIMs. We do not know which non ART pharmacotherapies (co medications) are helpful and which are actually harmful among HIV+ who drink. Conversely, HIV and alcohol use may also be a barrier to receipt of helpful co medications. In the face of limited evidence, providers may be reluctant to treat Alcohol Use Disorder (AUD) with medications among HIV+ individuals due to safety concerns. Further, alcohol use is a relative contraindication for HCV treatment. As a result, drinkers may choose to under report alcohol use to gain access to direct acting agents (DAAs) but may experience more harm and less benefit. We draw on the rich, longitudinal clinical data in the Veterans Aging Cohort Study and enhance it with strategic additional data collection and innovative techniques to correct for systematic error in measurement and confounding by indication. We will quantify the impact of Aging, ART and Alcohol PIMs and of pharmacotherapies for AUD and HCV on patient salient outcomes (PSOs) including mortality, hospitalization, medically significant falls, bacterial pneumonia, and delirium to inform prioritization of medications and limit harm from polypharmacy among HIV+ individuals. Our study is timely and innovative. Polypharmacy is the norm, AUD is under treated, and DAAs for HCV have only recently become available. While others have quantified PIMs, we will measure their actual impact on PSOs. We will also measure the benefit from pharmacotherapy for AUD and HCV among HIV+ and uninfected individuals who drink. These studies will be instrumental in the design of eHealth interventions facilitating personalized care and simplification of co medications among HIV+ individuals (see U24s CHAMP & RIB).