UCSD Internal Medicine Resident Research Proposal

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Title: Impact of Insurance Coverage on Outcomes in Patients with HIV-Associated Cancers

Abstract: The development of highly active antiretroviral therapy (HAART) has improved survival in persons living with HIV (PLWH). However, PLWH continue to be at significantly increased risk for malignancies, collectively known as HIV-associated cancers, and have greater overall mortality. HIV-associated cancers can be classified as AIDS-defining or non-AIDS-defining cancers. AIDS-defining cancers include Kaposi sarcomas (KS), aggressive non-Hodgkin lymphomas (NHL), and advanced cervical cancer. Non-AIDS-defining cancers refer to the other various types of infection-related and non-infection-related malignancies. Treatment options and clinical outcomes in HIV-associated cancers may to some extent be influenced by patients' insurance coverage. For instance, the AIDS Drug Assistance Program (ADAP), authorized as an extension of the Ryan White CARE Act to provide HAART and other FDA-approved medications for HIV/AIDS-related conditions, does not cover a significant number of medications used to treat KS and NHL. Antineoplastic agents used to treat non-AIDS-defining cancers are also not generally covered. This study will examine how medical coverage affects clinical outcomes in HIV-associated cancers in PLWH.

Background: Mortality among PLWH have greatly decreased with the advent of HAART. Nevertheless, PLWH continue to experience higher mortality than their age-matched, HIV-negative counterparts. A recent study examined the impact of insurance coverage on PLWH and concluded that patients with public insurance, which included Medicaid and Medicare, had increased mortality compared to those with private insurance[1]. Uninsured patients who obtained coverage after their diagnosis also fared better than those who did not[1]. One avenue to insurance coverage is through the Ryan White HIV/AIDS Program (RWHAP), first authorized by Congress in 1990 to provide primary care and support services to uninsured or underinsured patients living with HIV. In 2009, a legislative extension fashioned the ADAP, which furnishes low-income HIV patients not adequately covered by private insurance, Medicare, or Medicaid with FDA-approved medications. Even with the Affordable Care Act, over 40% of HIV patients still had RWHAP assistance, and 15% fully relied on RWHAP for HIV care[2]. Notably, uninsured patients with RWHAP assistance were far more likely to be on HAART and virally suppressed than those without RWHAP assistance[2].

The ready availability of HAART has markedly reduced the incidence of HIV-associated infections and malignancies. For instance, the Swiss HIV Cohort Study revealed that the incidences of KS and aggressive NHL have decreased by several fold in the HAART era[3]. In fact, the incidences of all cancers, including AIDS-defining and non-AIDS-defining malignancies, have decreased by 81% compared to the pre-HAART era[3]. For patients who rely solely on RWHAP for HIV care, however, many antineoplastic agents used to treat KS and NHL (e.g., pomalidomide, etoposide, rituximab) are not still covered by ADAP. Antineoplastic agents used to treat non-AIDS-defining cancers such as skin cancer, Hodgkin lymphoma, and lung cancer, are also generally not reimbursed by the program. These restrictions may affect regimen selection and lead to treatment delays in underinsured PLWH. While a large body of literature exists on the spectrum and evolution of HIV-associated cancers in the United States, studies that survey the impact of insurance coverage on outcomes in PLWH affected by these cancers are sparse[4]. This study sets out to examine the impact of medical coverage on treatment selection and clinical outcomes in PLWH diagnosed with HIV-associated cancers.

Specific Aims/Hypothesis: The aim of this study is to elucidate how insurance coverage affects outcomes in HIV-associated (both AIDS-defining and non-AIDS-defining) cancers in PLWH. We hypothesize that PLWH with private insurance have fewer and shorter treatment delays, improved access to optimal therapy, and improved survival rates compared with those with public insurance (*e.g.*, MediCal, Medicare, Ryan White) and those who are uninsured. We also anticipate impact of insurance type on the treatment regimen received due to differences in insurance coverage.

- **Specific Aim 1:** Assess whether type of insurance coverage at initial presentation with HIV-associated cancers is associated with differences in therapy received, including time to initial therapy and receipt of optimal therapy, using the relevant National Cancer Center Network Guidelines as benchmark[5-7]. Subset analyses will be performed for the most common cancers in PLWH, including but not limited to aggressive NHL, skin cancers (non-melanomatous skin cancers and melanomas), KS, Hodgkin lymphoma, lung cancer, head and neck cancers, anal cancer, liver cancer, prostate cancer, breast cancer, and kidney cancer.
- **Specific Aim 2:** Assess whether type of insurance coverage at initial presentation with HIV-associated cancers is independently associated with response. Subset analyses will be performed for the most common cancers in PLWH, including but not limited to aggressive NHL, skin cancers, KS, Hodgkin lymphoma, lung cancer, head and neck cancers, anal cancer, liver cancer, prostate cancer, breast cancer, and kidney cancer.
- **Specific Aim 3:** Assess whether type of insurance coverage at initial presentation with HIV-associated cancers is independently associated with survival. Subset analyses will be performed for the most common cancers in PLWH, including but not limited to aggressive NHL, skin cancers, KS, Hodgkin lymphoma, lung cancer, head and neck cancers, anal cancer, liver cancer, prostate cancer, breast cancer, and kidney cancer.

Methods: We will conduct a retrospective cohort study using an *existing registry* of HIV/AIDS patients with malignancies that is part of the UCSD Center for AIDS Research Clinical Investigation Core, which pulls requested data from UCSD electronic medical records on patients who have previously consented to inclusion in this research database through the already approved Owen Clinic Master Protocol (UCSD project #170462). As such, this study is expected to qualify for expedited IRB review. Using ICD codes, we will request data from the subset of HIV/AIDS patients diagnosed with malignancies from 2004 to 2019. This range reflects a period during which HAART has been available and will allow for at least 1 year of follow-up regarding response to therapy and survival. From these patients, we will request and analyze baseline information at the time of presentation with the malignancy: demographics (age, race, ethnicity), type of insurance coverage (Ryan White, MediCal, Medicare, private insurance, no insurance), CD4 count, HIV viral load, whether the patient is on HAART, disease stage, and performance status. We will also collect the following information regarding treatment used, time to initial treatment, treatment response, and survival status (primary outcome). Treatment will be assessed as "optimal" or "suboptimal" using NCCN guidelines as the benchmark. The minimum criteria for inclusion in the study are diagnosis of HIV seropositivity and any cancer between 2004 and 2019, availability of survival status at 1 year after cancer diagnosis, and access to insurance and type of insurance at time of diagnosis.

	ICD-9 Codes	**ICD-10 Codes**
HIV	042.*	B20
Cancer	140.*-209.*	C00-C96

Statistics: Descriptive statistics will be used to summarize baseline and treatment characteristics of the cohort. Comparisons of insurance coverage with patient characteristics will be made using the Pearson χ^2 test for categorical variables and the Kruskal-Wallis H test for continuous variables. Overall survival and progression-free survival will be estimated using the Kaplan-Meier method, and Cox proportional hazards model will be used to assess differences between insurance type and other baseline variables. Subset analyses will be performed for the most common types of cancers in PLWH: aggressive NHL, non-melanomatous skin cancer, KS, Hodgkin lymphoma, lung cancer, head and neck cancers, anal cancer, and liver cancer. We anticipate a sample size of at least 500 subjects based on experience with prior retrospective CFAR Network of Integrated Clinical Systems (CNICS) studies and clinical volume at UCSD. Assuming two-sided alpha of 0.05 and testing margin of 1.25, this sample size provides an overall power of 80% to find a hazard ratio of 1.6 or more.

References:

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