

Cancer Stage, Treatment, and Survival Comparing HIV Clinic Enrollees and SEER.



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Background and Objectives

- Inconsistent evidence suggests that people with HIV (PWH) are diagnosed with cancer at later stages¹, are treated for cancer at lower rates², and have lower cancer survival rates^{3,4}.
- Immunosuppression related to HIV may result in more aggressive cancers and reduce treatment tolerability^{1,2}.
- Risk factors among PWH, such as smoking and viral co-infections, detrimentally affect cancer outcomes^{5,6}.
- Barriers to care are likely significant factors influencing cancer outcomes among PWH^{6,7}.
- We compared cancer outcomes among PWH enrolled in the Johns Hopkins HIV Clinical Cohort (JHHCC) and the National Cancer Institute's Surveillance, Epidemiology, and End Results Program (SEER), representing the general US population diagnosed with cancer.
- The primary goal of this analysis was to assess whether PWH who are enrolled in care are diagnosed at more advanced stages, have lower rates of initial cancer treatment, and have higher all-cause mortality than the general US population.**

- o Sub-analysis stratified by baseline CD4.

Methods

- 254 incident, first cancer cases (excluding Kaposi Sarcoma) in the JHHCC from 1997- 2014 compared to 1,888,279 incident, first cancer cases of the same cancer types in SEER from 2000-2014.
- JHHCC stage at diagnosis and initial treatment data from the Maryland Cancer Registry.
- G Computation to address covariate differences:**
 - o Equivalent to direct standardization
 - o Difference in predicted outcomes for PWH based on JHHCC covariates and what the equivalent outcome would be in SEER for those covariates.
 - o Predicted outcomes adjust for covariates using Random Forest and Random Survival Forest methods.

Three primary outcomes:

- Probability of a particular cancer stage at diagnosis: (Localized, Regional, Distant, Unstaged)
- Probability of receiving any initial cancer treatment: (any chemotherapy, radiation, or surgery).
- Restricted Mean Survival Time (RMST) to all-cause mortality over 5 years following cancer diagnosis.

Results

- Accounting for age, sex, race, year of diagnosis, and cancer type, PWH were more likely to be diagnosed at a localized stage (PD= 0.24, 95% CI= 0.18, 0.30) and at a distant stage (PD=0.36, 95% CI=0.30, 0.43). (**TABLE 1**)
- The probability of receiving any initial cancer treatment was not significantly different for PWH and the general population, at 83% and 87% respectively, even among those with low CD4. (**TABLE 2**)
- Adjusting for cancer type, age, sex, race, and year, PWH had an average survival of 32 months in the first 5 years following cancer treatment as compared to 37 months for the general population (RD= -5.4; 95% CI=-8.2, -1.4). (**TABLE 3**)
- Differences in survival were accounted for by stage and treatment among the total population but persisted among PWH with CD4≤200 (RD= -6.3; 95% CI=-15.7, -0.4). (**TABLE 3**)
- Despite wide confidence intervals, difference in 5 year RMST for each cancer type was consistent with the overall RMST difference for all cancers (**FIGURE 1**).

| JHHCC Characteristics N (%) or Median (IQR) | |
|--|--------------|
| Cancer Type | |
| NHL | 53 (21%) |
| Lung | 42 (17%) |
| Liver | 23 (9%) |
| Hogdkin | 18 (7%) |
| Prostate | 18 (7%) |
| Breast | 16 (6%) |
| Anal | 15 (6%) |
| Other | 69 (27%) |
| Age | 50 (45 – 56) |
| Male | 176 (69%) |
| Black Race | 199 (78%) |
| Diagnosis Year | |
| 1997-2000 | 15 (6%) |
| 2001-2005 | 86 (34%) |
| 2006-2010 | 103 (41%) |
| 2011-2014 | 50 (20%) |

Table 1. Difference in Cancer Stage at Diagnosis

| Stage | JHHCC Probability (95% CI) | SEER Probability (95% CI) | Probability Difference (95% CI) |
|------------------|----------------------------|---------------------------|---------------------------------|
| Localized | 0.30 (0.25, 0.36) | 0.06 (0.04, 0.09) | 0.24 (0.18, 0.30) |
| Regional | 0.21 (0.15, 0.26) | 0.83 (0.80, 0.89) | -0.63 (-0.70, -0.58) |
| Distant | 0.45 (0.39, 0.51) | 0.09 (0.05, 0.11) | 0.36 (0.30, 0.43) |
| Unstaged | 0.04 (0.02, 0.07) | 0.02 (0.003, 0.024) | 0.02 (0.0003, 0.06) |

Table 2. Difference in Probability of Receiving Initial Cancer Treatment

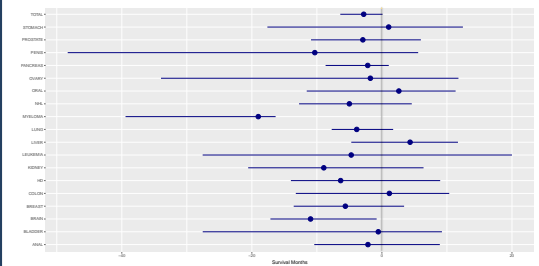
| Population | JHHCC Probability (95% CI) | SEER Probability (95% CI) | Probability Difference (95% CI) |
|-----------------------------|----------------------------|---------------------------|---------------------------------|
| All Cancers | 0.83 (0.76, 0.87) | 0.87 (0.82, 0.88) | -0.04 (-0.09, 0.02) |
| Baseline CD4 ≤200 | 0.79 (0.68, 0.88) | 0.86 (0.79, 0.92) | -0.07 (-0.18, 0.02) |
| Baseline CD4 >200 | 0.86 (0.81, 0.92) | 0.85 (0.81, 0.89) | 0.01 (-0.05, 0.08) |

Table 3. Difference in 5 Year Restricted Mean Survival Time

| Population | Model | JHHCC RMST Months (95% CI) | SEER RMST Months (95% CI) | RMST Difference Months (95% CI) |
|-----------------------------|---------------------------|----------------------------|---------------------------|---------------------------------|
| All Cancers | Model 1 | 31.9 (28.8, 35.4) | 37.3 (34.4, 39.3) | -5.4 (-8.2, -1.4) |
| | Model 1+ Stage | 31.8 (28.8, 35.3) | 35.0 (31.7, 38.1) | -3.3 (-6.8, 1.1) |
| | Model 1+ Stage+ Treatment | 32.1 (28.8, 35.4) | 35.0 (32.8, 37.8) | -2.8 (-6.4, 0.1) |
| Baseline CD4 ≤200 | Model 2 | 26.0 (19.8, 31.7) | 37.7 (33.4, 42.3) | -11.7 (-19.5, -4.7) |
| | Model 2+ Stage | 28.1 (19.9, 31.6) | 34.3 (28.6, 38.9) | -6.3 (-15.7, -0.4) |
| | Model 2+ Stage+ Treatment | 25.6 (19.9, 31.6) | 32.4 (28.8, 38.7) | -6.8 (-15.5, -0.5) |
| Baseline CD4 >200 | Model 2 | 36.2 (32.1, 40.6) | 36.0 (32.7, 39.0) | 0.1 (-3.6, 4.6) |
| | Model 2+ Stage | 35.1 (32.1, 40.6) | 34.1 (31.5, 38.4) | 1.0 (-2.3, 5.1) |
| | Model 2+ Stage+ Treatment | 36.5 (32.1, 40.6) | 35.1 (31.5, 38.5) | 1.4 (-2.4, 5.2) |

Model 1 includes cancer type, age, sex, race, and year of diagnosis. Model 2 includes cancer type, age, sex, race, year of diagnosis, and CD4 at baseline. Stage refers to SEER Summary Stage 2000 classified into localized, regional, distant, or unstaged. Treatment refers to initial cancer treatment regimen, classified into indicators for any chemotherapy, any radiation, and/or any surgery.

Figure 1. Survival Difference by Cancer Type (Model 1 + Stage + Treatment)



Discussion

- PWH present at both earlier and later stages, suggesting two possible mechanisms:
 - HIV may lead to faster progression of cancer
 - Enrollment in HIV care may result in enhanced monitoring and earlier diagnosis of cancers.
- Probability of receipt of any initial cancer treatment does not differ by HIV status in this population.
- Across all cancers, mean survival time over 5 years of follow up was 5.4 months lower in PWH accounting for cancer type and demographic characteristics.
 - o After accounting for stage, there was no survival difference in the total population,
- Among PWH with baseline CD4≤200, survival for PWH was reduced by 6 months despite accounting for cancer type, demographic covariates, stage, and treatment

References and Acknowledgements

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