Treatment options for men who are HIV+ are aimed at allowing them to live longer, healthier lives, but other factors may influence health and longevity. This is a secondary data analysis of the Multicenter AIDS Cohort Study which is an ongoing prospective cohort study of the natural and treated histories of HIV-1 infection in homosexual and bisexual men in 4 major cites in the U.S. This study aims to explore the relationship between highly active antiretroviral treatment (HAART) and the use of hard drugs, including cocaine and heroine at baseline starting treatment. This study looks at the difference in treatment response from baseline to two years on treatment by measuring viral load, CD4+ T cell count, aggregate mental quality of life(QOL) score, and aggregate physical QOL score. Outcomes are evaluated as the measurement difference between year 2 and year 0 (baseline). Data received included demographic and socioeconomic status covariates as well as the outcomes of interest. Some loss to follow-up was observed and this was discussed with the investigators, along with additional important predictors of interest other than hard drug use and these predictors were included in the analysis.

Software used for this analysis was SAS 3.6 Enterprise Edition. Data were cleaned, recoded as per investigators interests, and difference outcome variables were created for each outcome of interest: difference in viral load, difference in CD4+ T cell count, difference in aggregate mental QOL score, and difference in physical QOL score. The reference used for hard drug use those who did not report using hard drugs at baseline. Data exploration was done using PROC MEANS, PROC FREQ, and PROC UNIVARIATE. Viral load showed a left skewed distribution and the investigator determined a log 10 transformation would be best for analyzing this data. As per the investigator, viral load can be clinically interpreted on the log 10 scale and no back transformation was performed. Two outliers were observed in BMI at baseline measure for subject 113 with a BMI of 515.01 and subject 179 with a BMI of 514.25. These measures were determined by the investigator to be incorrect values and no correct values were available. These outliers were set to missing as per the investigator. A summary of the data can be viewed in Table 1.

Four analyses were performed, one for each outcome variable. Assumptions for linear models were assessed and met for each analysis. It was decided that baseline covariates would be included in each model to account for any variations among individuals who may have entered the study with larger baseline values. A correlation analysis was performed and no significant correlations were observed between hard drug use and the other covariates of interest and no further action was taken regarding correlation. The following was carried out for each analysis: a crude model of outcome difference measurement and hard drug use at baseline from year 0 to year 2 with baseline covariate, and a full model of the outcome difference measurement and hard drug use at baseline from year 0 to year 2 with baseline and additional covariates of interest (see Table 1 for additional covariates included in full models).

No model selection was performed. All additional covariates were included in full models as per investigator, as these measurements were important in the greater literature even if they were not statistically significant in the analysis. Statistical significance was evaluated at p= 0.05.

Results from the crude and full models can be viewed in Table 2. Missing data was seen at year 0 and at year 2. For those who reported using hard drugs as baseline, 27 patients were lost to follow-up at year 2 out of the 66 patients enrolled at year 0. For those who did not report using hard drugs at baseline, 182 patients were lost to follow-up at year 2 out of 649 patients enrolled at year 0. Some measurements have more missing than the number lost to follow-up and this may have been from patients declining to participate in that measurement. For example 3, subjects are missing data for baseline viral load among hard drug users and 39 subjects are missing data for baseline viral load among non-drug users (Table 1). Only complete data was included in this analysis, and this may have some effect on generalizability.

Viral Load

The crude model was overall significant (p<0.0001). In the crude model, on average, after adjusting for baseline, hard drug users have a 0.03 copies/ml (95% CI: -0.36 to 0.42) increase in the difference of log 10 viral load from year 0 to year 2 than those who did not report using hard drugs at baseline. This indicates a larger difference, or an increase in log10 viral load at year 2 compared to year 0, and could suggest some treatment mitigation by hard drug use. Hard drug use was not significantly associated with log 10 viral load difference in the crude model (p=0.88), while baseline log 10 viral was significantly associated with log 10 viral load difference (p<0.0001) as would be expected.

The full model was overall significant (p<0.0001). In the full model, on average after adjusting for baseline, additional demographic, socioeconomic status, and adherence to treatment predictors (see Table 2), hard drug users have a 0.03 copies/ml (95% CI: -0.43 to 0.36) decrease in the difference of log 10 viral load from year 0 to year 2 than those who did not report using drugs at baseline. This indicates a smaller difference, or a lower log 10 viral load at year 2 compared to year 0 in hard drug users, and this could suggest some slight improvement in log 10 viral load at year 2 on treatment when adjusting for these covariates. Hard drug use is still not significantly associated with log 10 viral load difference in the full model (p=0.86).

CD4+ T Cell Count

The crude model for CD4+ T cell count was overall statistically significant (<0.0001). In the crude model, on average, after adjusting for baseline cell count, hard drug users have a 171.95 (95%CI: -232.25 to -111.74) decrease in the difference in CD4+ T cell count from year 0 to year 2 compared to those who did not report using hard drugs at baseline. As CD4+ T cell count is expected to rise with successful treatment, this may suggest some treatment mitigation by hard drugs as cell count decreases, suggesting that cell count goes down in year 2. Hard drug use is significantly associated with CD4+ T cell count difference (p<0.0001).

The full model is also overall statistically significant (<0.0001). In the full model, on average after adjusting for baseline CD4+ T cell count, additional demographic, socioeconomic status, and adherence to treatment predictors, hard drug users have a 163.04 (95% CI: -224.62 to -101.45) lower cell count difference from year 0 to year 2 than in those who did not report using hard drugs at baseline. Hard drug use is significantly associated with CD4+ T cell count difference (p<0.0001). This suggests that after adjusting for potential confounders and covariates, possible treatment mitigation on CD4+ T cell count is still present in those using hard drugs and these patients may require a different treatment or additional substance abuse support and counseling.

Aggregate Mental QOL Score

The crude model for aggregate mental QOL score was overall statisticaly significant (p<0.0001). In the crude model, on average after adjusting for baseline aggregate mental health QOL score, hard drug users have a 0.22 (95% CI: -3.62 to 3.17) lower score difference between year 0 and year 2 compared to those who did not report using hard drugs at baseline. Hard drugs was not significantly associated with aggregate mental QOL score difference (p=0.89). This may suggest for those using hard drugs their mental health score at year 2 on treatment decreases slightly more compared to those who did not report using hard drugs at baseline. This shows the potential that treatment may have a small negative effect on mental QOL score 2 years after starting treatment in those using hard drugs. These patients may benefit from additional mental health care and support.

The full model for aggregate mental QOL score was overall statistically significant (p<0.0001). In the full model, on average after adjusting for baseline aggregate mental health QOL score, additional demographic, socioeconomic status, and adherence to treatment predictors, hard drug users have a 0.47 (95% CI: -3.97 to 3.04) lower score difference between year 0 and year 2 compared to those who did not report using hard drugs at baseline. Hard drugs was not significantly associated with aggregate mental QOL score difference (p=0.79). Although the estimates are not statistically significant, the scores have small differences in both the crude and full models, indicating that treatment may not have a large effect on aggregate mental QOL score difference from baseline to year 2. Further analysis would be needed to determine what could influence an increase in aggregate mental QOL score at year 2.

Aggregate Physical QOL Score

The crude model for aggregate metal QOL score was overall statistically significant (p<0.0001). On average after adjusting for baseline aggregate physical QOL score, hard drug users have a 3.92 (95%CI: -6.60 to -1.23) lower score difference between year 0 and year 2 compared to those who did not report hard drug use at baseline. Hard drug use is significantly associated with aggregate physical QOL score difference (p=0.004). This suggests that aggregate physical QOL score is lower in year 2 than in year 0 for those on the treatment and using hard drugs. These patients may need some extra help accomplishing daily physical tasks or a different treatment that allows them to live with a better QOL.

The full model for aggregate metal QOL score was overall statistically significant (p<0.0001). In the full model, on average, adjusting for baseline aggregate physical health QOL score, additional demographic, socioeconomic status, and adherence to treatment predictors, hard drug users have a 3.16 (95%CI: -5.92 to -0.40) lower score difference between year 0 and year 2 compared to those who did not report hard drug use at baseline. Hard drug use is significantly associated with aggregate physical QOL score difference (p=0.02). This association is consistent with the crude model, after adjusting for potential confounders as stated above, and these patients using hard drugs may need more help accomplishing daily physical tasks or an alternative treatment to help improve their quality of life in later years on treatment.

In conclusion, looking at log 10 viral load, after adjustment for baseline, additional demographic, socioeconomic status, and adherence to treatment predictors, hard drugs seems so show a negative effect on treatment from year 0 to year 2 compared to non hard drug users. For CD4+ T cell count, after adjustment for baseline, additional demographic, socioeconomic status, and adherence to treatment predictors, hard drugs has a negative effect on CD4+ T cell count difference, but this effect is unchanged by adjusting for covariates. For aggregate mental QOL score, hard drug use does not seem to have a large effect on treatment measured by aggregate mental QOL score difference, even after adjusting for baseline, additional demographic, socioeconomic status, and adherence to treatment, and for aggregate physical QOL score, hard drug use seems to show a negative effect on treatment measured by aggregate physical QOL score difference, even after adjusting for baseline, additional demographic, socioeconomic status, and adherence to treatment.

Some limitations with this study include subjects loss to follow up. The reason for which they were lost to follow-up were unknown and these reasons may or may not have been the result of hard drug use influencing treatment response. A weakness of this study is the small group of hard drug users compared to non drug users. Additional studies with a larger n of hard drug users could produce higher powered studies. A strength of this study is that adherence to treatment was measured and therefore could be adjusted for in the analysis. Overall hard drug use either seems to have little or a negative effect on treatment response and steps should be taken to help these patients live longer, healthier lives.

Reproducible Research

GitHub Path: bios6623-bbalkaran/Project1/Code/Project1.sas

Data File saved in SAS studio: /home/bridgetbalkaran0/my\_courses/BIOS\_6623 Advanced Data Analysis/Project\_1/Project 1.sas

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Table 1. Cohort Characteristics. Continuous measures presented as mean and standard deviation. Categorical measures presented as frequency and percent. | No. Missing | Hard Drug Use at Baseline | No. Missing | Non Hard Drug Use at Baseline |
| No. of Patients |  | 66 |  | 649 |
| Year 0 | 0 |  | 0 |  |
| Year 2 | 27 |  | 182 |  |
| **Clinical Measures** |  |  |  |  |
| Log 10 Viral Load Year 0, mean (sd) | 3 | 4.67 (0.84) | 39 | 4.50 (0.91) |
| Log 10 Viral Load Difference, mean (sd) | 27 | -2.70 (1.27) | 201 | -2.71 (1.23) |
| CD4+ T cell Count Year 0, mean (sd) | 0 | 335.06 (186.98) | 24 | 385.05 (211.32) |
| CD4+ T cell Count Difference, mean (sd) | 27 | 13.43 (195.73) | 201 | 182.87 (176.26) |
| Adherence to Treatment at Year 2 | 27 |  | 182 |  |
| 95% adherence or greater (%) |  | 38 (97.4) |  | 416 (89.1) |
| < 95% adherence (%) |  | 1 (2.6) |  | 51 (10.9) |
| **Ouality of Life Measures** |  |  |  |  |
| Aggregate Mental Quality of Life Score Year 0, mean (sd) | 0 | 43.36 (12.35) | 2 | 45.61 (13.36) |
| Aggregate Mental Quality of Life Score Difference, mean (sd) | 27 | 3.58 (15.07) | 189 | 2.10 (11.71) |
| Aggregate Physical Quality of Life Score Year 0, mean (sd) | 0 | 44.75 (9.58) | 2 | 50.65 (9.37) |
| Aggregate Physical Quality of Life Score Difference, mean (sd) | 27 | -3.85 (8.71) | 189 | -1.45 (8.41) |
| **Demographic and Socioecomonic Measures** |  |  |  |  |
| Age, y mean(sd) | 0 | 43.74 (9.85) | 0 | 42.44 (9.38) |
| BMI, mean (sd) | 3 | 23.54 (4.52) | 41 | 25.41 (4.58) |
| Race | 0 |  | 0 |  |
| Non-Hispanic White (%) |  | 32 (48.5) |  | 390 (60.1) |
| Other (%) |  | 34 (51.5) |  | 259 (39.9) |
| Smoking Status | 0 |  | 0 |  |
| Current Smoker (%) |  | 53 (80.3) |  | 251 (38.7) |
| Former and Non-smoker (%) |  | 13 (19.7) |  | 398 (61.3) |
| Income , USD | 0 |  |  |  |
| <10,000 (%) |  | 31 (47.0) |  | 137 (22.3) |
| 10,000 - 40,000 (%) |  | 26 (39.4) |  | 264 (42.9) |
| >40,000 (%) |  | 9 (13.6) |  | 214 (34.8) |
| Alcoholic Beverages Per Week | 0 |  | 0 |  |
| 13 or less (%) |  | 63 (95.5) |  | 605 (93.2) |
| > 13 (%) |  | 3 (4.5) |  | 44 ( 6.8) |
| Marijuana Use | 0 |  | 0 |  |
| Yes (%) |  | 24 (36.4) |  | 268 (41.3) |
| No (%) |  | 42 (63.6) |  | 381 (58.7) |
| Education | 0 |  | 0 |  |
| High School or less (%) |  | 33 (50.0) |  | 147 (22.7) |
| > High School (%) |  | 33 (50.0) |  | 502 (77.3) |

Table 2. Results of Crude and Full Models.

\*Labels are only variable names and do not indicate clinical definitions.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Predictor | Crude Model, Baseline | P-value | Full Model | P-value |
| Viral Load | Intercept | -0.52 (0.27) | 0.05 | 1.13 (0.55) | 0.04 |
| (n=457) | Hard Drug Use | 0.03 (0.20) | 0.88 | -0.03 (0.20) | 0.86 |
|  | Log 10 Viral Load Baseline | -0.49 (0.06) | <0.0001 | -0.53 (0.06) | <0.0001 |
|  | Age | -- | -- | 0.00 (0.01) | 0.96 |
|  | BMI | -- | -- | -0.02 (0.01) | 0.07 |
|  | Race | -- | -- | -0.12 (0.13) | 0.35 |
|  | Marijuana Use | -- | -- | -0.17 (0.11) | 0.12 |
|  | Heavy Alcohol Consumption\* | -- | -- | 0.13 (0.20) | 0.52 |
|  | Current Cigarette Use | -- | -- | -0.10 (0.12) | 0.41 |
|  | Income (10,000 - 40,000) | -- | -- | -0.23 (0.15) | 0.14 |
|  | Income (>40,000) | -- | -- | -0.47 (0.18) | 0.01 |
|  | Education | -- | -- | 0.00 (0.15) | 0.99 |
|  | Adherence to Treatment at Year 2 | -- | -- | -0.44 (0.17) | 0.01 |
|  |  |  |  |  |  |
| CD4+ T Cell Count | Intercept | 195.84 (17.57) | <0.0001 | 51.15 (67.58) | 0.45 |
| (n=457) | Hard Drug Use | -171.95 (30.63) | <0.0001 | -163.04 (31.34) | <0.0001 |
|  | CD4+ T Cell Count Baseline | -0.04 (0.04) | 0.38 | -0.05 (0.04) | 0.19 |
|  | Age | -- | -- | -0.61 (0.94) | 0.52 |
|  | BMI | -- | -- | 3.79 (1.92) | 0.05 |
|  | Race | -- | -- | 26.94 (19.37) | 0.17 |
|  | Marijuana Use | -- | -- | 37.22 (16.90) | 0.03 |
|  | Heavy Alcohol Consumption\* | -- | -- | -10.20 (31.65) | 0.75 |
|  | Current Cigarette Use | -- | -- | -9.68 (18.40) | 0.60 |
|  | Income (10,000 - 40,000) | -- | -- | 6.31 (23.69) | 0.79 |
|  | Income (>40,000) | -- | -- | -54.39 (27.56) | 0.05 |
|  | Education | -- | -- | 19.95 (23.43) | 0.39 |
|  | Adherence to Treatment at Year 2 | -- | -- | 61.12 (27.58) | 0.03 |
|  |  |  |  |  |  |
| Agg. Mental QOL Score | Intercept | 25.64 (1.64) | <0.0001 | 17.44 (4.02) | <0.0001 |
| (n=464) | Hard Drug Use | -0.22 (1.73) | 0.89 | -0.47 (1.77) | 0.79 |
|  | Agg. Mental QOL Score Baseline | -0.51 (0.03) | <0.0001 | -0.53 (0.03) | <0.0001 |
|  | Age | -- | -- | 0.06 (0.05) | 0.29 |
|  | BMI | -- | -- | 0.04 (0.11) | 0.71 |
|  | Race | -- | -- | -0.35 (1.11) | 0.75 |
|  | Marijuana Use | -- | -- | 1.15 (0.95) | 0.22 |
|  | Heavy Alcohol Consumption\* | -- | -- | -0.05 (1.79) | 0.97 |
|  | Current Cigarette Use | -- | -- | 1.81 (1.05) | 0.08 |
|  | Income (10,000 - 40,000) | -- | -- | 1.25 (1.34) | 0.35 |
|  | Income (>40,000) | -- | -- | 3.12 (1.57) | 0.04 |
|  | Education | -- | -- | 0.79 (1.31) | 0.54 |
|  | Adherence to Treatment at Year 2 | -- | -- | 2.31 (1.58) | 0.14 |
|  |  |  |  |  |  |
| Agg. Physical QOL Score | Intercept | 11.83 (2.17) | <0.0001 | 14.08 (3.89) | 0.0003 |
| (n=464) | Hard Drug Use | -3.92 (1.37) | 0.004 | -3.16 (1.40) | 0.02 |
|  | Agg. Mental QOL Score Baseline | -0.26 (0.04) | <0.0001 | -0.31 (0.04) | <0.0001 |
|  | Age | -- | -- | -0.10 (0.04) | 0.02 |
|  | BMI | -- | -- | 0.07 (0.09) | 0.43 |
|  | Race | -- | -- | -1.30 (0.88) | 0.14 |
|  | Marijuana Use | -- | -- | 0.38 (0.76) | 0.61 |
|  | Heavy Alcohol Consumption\* | -- | -- | -0.84 (1.41) | 0.55 |
|  | Current Cigarette Use | -- | -- | -0.75 (0.82) | 0.37 |
|  | Income (10,000 - 40,000) | -- | -- | 1.83 (1.07) | 0.09 |
|  | Income (>40,000) | -- | -- | 2.61 (1.26) | 0.04 |
|  | Education | -- | -- | 1.29 (1.03) | 0.21 |
|  | Adherence to Treatment at Year 2 | -- | -- | 1.73 (1.25) | 0.16 |