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Survival Analysis from 1998-2010 of a Closed Prisoner Cohort Incarcerated in the Georgia Department of Corrections

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2009

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Abstract

Survival Analysis from 1998-2010 of a Closed Prisoner Cohort Incarcerated in the Georgia Department of Corrections

By: Tristan A. Cordier

Background: The high prevalence of HIV among the population flowing in and out of correctional facilities each year has made state prisons a target for HIV interventions. The effect of comorbid mental illness in these populations is of concern, as any barriers to HIV treatment adherence and compliance can have severe health consequences in this vulnerable population.

Objective: This study aims to evaluate the interaction of HIV infection with severe mental illness and its effect on mortality in a cohort of prisoners once incarcerated in the Georgia Department of Corrections.

Methods: Survival analysis was performed using a Cox proportional hazards model to evaluate the interactive effects of HIV and severe mental health issues on a cohort of prisoners from 1998-2010. Time dependent interaction terms were introduced to maintain the proportionality assumption, causing hazard ratios to be time sensitive. Sensitivity analysis was performed to assess the stability of a final model when undiagnosed deaths attributed to HIV caused reclassification of diagnosed persons as HIV infected.

Results: A total of 22,351 inmates were followed. 792 (3.5%) were HIV positive; of these, 124 (15.7%) had a recorded psychiatric problem. HIV positive status was associated with a marked increase in mortality (β=2.12, 95% CI: 1.88, 2.37), but over time this effect became less pronounced. Mild mental illness was associated with reduced hazard (β=-0.95, 95% CI: -1.52, -0.388), though over time this effect was diminished. The interaction between HIV and mental illness was significantly protective for more severe mental illness (β=-0.82, 95% CI: -1.58,-0.07).

Discussion: The protective effects of mental health illness on mortality may be due to the benefits of more intensive case management found within prison settings for those who require mental health services. The extension of these benefits to all of the HIV infected subpopulation is warranted.

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INTRODUCTION

The "dual epidemic" (1,2) of incarceration and HIV in the United States has driven increased attention to the use of jails and prisons as sites of interventions for HIV testing and linkage to treatment. The return of HIV infected prisoners into the community has been associated with a reduction in adherence to antiretroviral therapy and, as a consequence, unsuppressed viral loads (3–5), making this issue of linkage of vital importance to public health. Incarcerated populations face numerous barriers to maintaining treatment regimens; factors such as low levels of education, unemployment, and homelessness as well as clinical issues such as alcohol and drug dependence, serious mental illness, and other chronic conditions create a web of problems that require attention at both the individual and societal level.

The effect of severe mental illness on HIV infected inmates has not been fully explored. Statistics regarding persons with severe mental illness in the general population suggest they are disproportionately vulnerable to the barriers of successful linkage to care. They are disproportionately likely to suffer from drug and alcohol abuse, unemployment and homelessness.

This study aims to characterize the relationship between HIV and severe mental illness using a cohort of state prisoners under the Georgia Department of Corrections (GDC) on June 30, 1991. A survival analysis will be used to show the interactive effect of these dual exposures on mortality as the cohort ages from 1998-2010. The years between 1991 and 1998 are excluded on the basis of high HIV mortality experienced during the years before effective combination antiretroviral therapy (ART) was available.

BACKGROUND

Corrections in the United States

In 2009, one in every 31 adults in the United States was under the criminal justice system, a statistic that includes persons in prisons, jails and under community supervision. Between 1982 and 2007 the population under criminal justice supervision increased by 5 million, from 2.2 million to 7.3 million, representing a 150% increase in the proportion of the population under some form of local, state or federal supervision. One and a half million (21%) of those supervised reside in state or federal prisons, an environment for inmates who have been sentenced to extended removal from the community (6). Georgia's rate of incarceration is particularly pronounced, with 1 in 13 adults under correctional supervision in 2009 (6). Nationwide, black men are incarcerated at six times the rate of their white counterparts (7).

The epidemic of incarceration has resulted in an increase of the number of former prisoners and parolees released into the community. In 2010, 708,677 prisoners were released into the community (8), representing a 17% increase from 2000. This growth in releases represents a significant increase in the number of men and women in the community who are vulnerable to gaps in healthcare and as a result increased rates of mortality. Incarcerated populations carry a heavy burden of disease; roughly 40% suffer from some form of chronic illness (9). They have increased risk of chronic infections such as HIV, HBV, HCV, and TB when compared to the general population and are more likely to have problems with mental illness, substance dependence or abuse, and generally reside in communities with higher rates of violent crime and homicide (10–12). The Federal government has in recent years enacted legislation that targets the

vulnerabilities of this population; trying to increase linkage to care and community reintegration (The Second Chance Act) (13), increased access to mental health services (Mental Health Parity and Addiction Equity Act) (14), and increased Medicaid eligibility (Affordable Care Act) (15).

Mortality in Correctional Populations

Mortality in incarcerated and recently released prisoner populations has been the subject of increasing review as evidence-based interventions are sought to address the health concerns of a population that is both vulnerable and stigmatized. Incarcerated cohorts followed after release have been shown susceptible to increased all-cause mortality, although whether or not this is attributable to the prison environment, issues related to selection bias, or some interactive combination of both is debatable.

Spaulding et al.(12) showed in a Georgia cohort that standardized mortality rates attributable to incarceration had no protective effect after adjusting for compassionate releases in a sensitivity analysis. Race did appear to have a protective effect, however, as black race was associated with significantly reduced rates of mortality when in prison while white men saw increased rates relative to the general population (age, sex, race, and education adjusted). Similar disparities in mortality between black and white were found in a North Carolina cohort (16), though the SMR for black race showed no direction from the null. These findings are indicative of broad health disparities associated with race and poverty; Spaulding notes that the Georgia cohort experienced reduced mortality due to homicide, transportation, accidental poisoning (overdose), and suicide while incarcerated. Incarceration may reduce the likelihood of successful self-

harm, drug use, or violence resulting in death. This is further evidenced as the cohorts in both states experienced significantly higher standardized mortality rates once released from prison.

An assessment of parolees in New York found a dose-response relationship between incarceration and decreased life expectancy in a cohort of prisoners and previously imprisoned subjects between 1988-2003 (17). The author found that the period after release was particularly sensitive to mortality, in keeping with various findings on high rates of drug overdose early after release (12,18–20), but that a return to population mortality rates was possible assuming post-incarceration survival beyond a period of time equal to roughly 2/3 the length of incarceration. It does not appear that the author was able to consider the impact of HIV mortality on the cohort, which may have had considerable impact on mortality estimates given the location and the time period. Excess death from HIV would have likely affected the cohort's life expectancy disproportionally to that of the general population due to differing prevalence rates. In the years prior to effective ART this would likely have accounted for a considerable proportion of all deaths, skewing downward estimates of life expectancy during incarceration and soon after release. However, while estimates of the effect of prison on mortality may be inflated, the core finding that there is a period after release of heightened mortality needs to be addressed.

Ineffective linkage to care of at-risk prisoners and releasees is an issue that severely impacts excess mortality attributable to chronic health problems such as HIV, liver disease, substance abuse and mental illness (12,16). This inquiry into correctional

populations will focus in particular on the case management of HIV positive and mentally ill current and former prisoners in Georgia.

HIV in Corrections: Diagnosis, Treatment, and Linking to Care

The fluid nature of entry and exit in prisons and jails has meant that 1 in 7 of the 150,000 HIV positive in U.S. pass through jails and prisons each year. In a given year, an estimated 22%–28% of HIV-infected black men pass through prisons or jails, compared to an estimated 11%–17% of HIV-infected white men (21). While this represents a substantial racial disparity, the high rate at which HIV positive persons are passing through the corrections system is a call for evidence-based interventions that will benefit not only the correctional population, but ultimately the community as a whole (21). In state and federal prisons nationwide, the prevalence in 2010 of HIV was 1.46%; although there were considerable differences between states, ranging from 0.2% in Vermont to 5.5% in New York (22). Georgia's 2010 prevalence increased 0.1% from 2008-09 estimates to 1.9%. In Georgia, it has been shown that HIV transmission is does occur in the correctional setting due to MSM contact and tattooing (23). Thus, despite mandatory testing laws at admission starting in 1988 (24), prevalence estimates do not capture the full scope of the HIV epidemic in incarcerated populations. Several states have offered testing after exposure incidents, and almost all offer testing at inmate request (25), increasing the number of cases found. Questions remain, however, of the willingness of inmates to use these services given the stigma associated with HIV risk behaviors (26).

Regardless of the correctional system's ability to diagnose all cases of HIV, it is known that the proportion of death from HIV/AIDS in prisons has decreased substantially

from its peak of 34.2% in 1995 to < 5% in 2009. Today, mortality attributable to HIV in prison is the same as of the general population (22,27), however, these figures do not adjust for compassionate releases, which might cause an underestimation of the mortality due to HIV in the prison setting. The drop in HIV mortality in prisons over the last 15 years is attributed to both improved treatment as well as reduced HIV rates overall in state and federal facilities (22).

ART in the state prison setting has been successful at reducing AIDS-related mortality (28). In 2009, the rate of AIDS-related deaths in 15-54 year olds was higher in the general population than in state prisons, though this is something of a skewed statistic, as it does not take into account compassionate releases or sentence expiration close to time of death. The notion of a "healthy prisoner effect" (12) would suggest that it is less likely that a patient with AIDS-related illness be capable of committing a crime, than a inmate with an AIDS-related illness be released. Confounding aside, the reductions in in-prison AIDS-related mortality have been substantial.

Improved HIV mortality outcomes require control of viral load, achieved with continuous adherence and compliance to ART therapies. Association with the criminal justice system has been associated with reduced odds of HIV-1 RNA suppression; studies in Canada showed an adjusted hazard ratio (AHRs) of 0.68 (95% CI: 0.51, 0.89) (29), while a study of IDU users showed further reductions in adherence: AOR 0.22 (0.09, 0.58) (30). However, once incarcerated, extended stays were associated with increased adherence. Baillargeon notes in a 2009 paper that federal disability benefits, which are often linked with Medicare and Medicaid coverage, are by law interrupted during

incarceration. Administrative hurdles in reinstating benefits can present a significant barrier to care among releases, a population that is more likely to be uneducated, mentally ill, and/or abusing drugs and alcohol. HIV positive inmates have been demonstrably at risk upon release of discontinued treatment (31).

The Texas cohort studied by Baillargeon followed after release from prison was found to have low rates of adherence, with only 30% (28.1%, 32.0%) filling a first prescription within 60 days. Factors found to be negatively associated with initial adherence were being African American and ethnicity. The factors most strongly associated with increased adherence were receiving assistance completing a Texas AIDS Drug Assistance Program application, having undetectable viral load before release, and being released on parole (4).

The national initiative EnhanceLink, which followed jailed inmates in 10 cities and evaluates HIV testing and linkage programs (32) provided insight into numerous factors that that improved linkage to care. Linkage to care within 30 days of release was associated with receipt of HIV or medication education, having a case manager meet the inmate at release, and the attainment of stable housing within 30 days (5).

Effective evidence-based programs are important to the most vulnerable prisoners for reintegration back into the community. The problem of recidivism still remains, however, as repeated incarceration present more challenges to successful adherence to HIV treatment. Often a consequence of severe mental illness (33), substance dependence or abuse, homelessness, and/or a low level of education (34,35), recidivism and subsequent re-releases in HIV positive inmates leads to multiple interruptions of

treatment, with direct effects on viral load control. Those who are repeatedly incarcerated are likely to have discontinued treatment and resumed high risk behaviors, a situation that has been associated with increased HIV transmission in the community (3), and therefore an area worth continued investigation.

Mental Health in Prisons and the Intersection with HIV Infection

The prevalence if mental illness in prison populations is estimated to be 45% for federal prisons and 56% in state institutions (33). Mental health statistics from the Bureau of Justice Statistics estimate that only one-third of those with mental health problems were receiving treatment at the time of arrest. This proportion increases during and after incarceration, although it is unclear the length of time this increase holds for post-release. The mentally ill are twice as likely to have experienced homelessness, and 74% have abused drugs, with 50% claiming dependence (33) making mental health issues even more difficult to address. Many attribute the high prevalence of severe mental illness to federal policy since the 1970s that inadequately funded mental health issues in community facilities. As a result the "criminalization of mentally ill populations" is occurring (36), leading to high rates of repeated incarceration, and an overrepresentation of the mentally ill under correctional supervision. Despite high prevalence, mental illness does not affect the incarcerated in a demographically uniform way. Women (73.1%), those of white race (62.2%), and the young (62.6%) show increased risk of morbidity (33).

In order to address the needs of mentally ill HIV positive inmates in treatment, it is necessary to address the fundamental needs of each inmate so that sustained adherence

is achievable. Springer et al. developed an adapted framework to address the needs of HIV positive inmates, using Maslow's hierarchy of needs to develop the programmatic themes around which case management can be supplemented by elements to increase the odds of successful linkage to care. Using Maslow's framework is a powerful way to understand the barriers to successful adherence; HIV treatment education may be of little use if the inmates are homeless or still drug and alcohol dependent. The programmatic priorities explored beyond HIV adapted case management and continuation of combination ART therapy are addressing drug dependence, mental health, and reducing HIV associated risk taking behaviors (37).

The development of HIV education with mental health components for the incarcerated has been discussed outside of the United States. Peng et al. discuss the potential beneficial effects of such programs for Taiwanese inmates, who also suffer high levels of psychiatric morbidity (~46%) (38), though at levels lower than the U.S.. Other factors associated with increased mental illness in the HIV positive cohorts examined were poor self-rated health status, recidivism, and trouble understanding, concentrating, or remembering. Given the literature on recidivism, mental illness and HIV, it is possible that low level of education might also be a driving fundamental problem that is manifest by repeated incarceration and failed linkage (35,39).

Research Question

Current trends in mental health prevalence and comorbid factors such as drug and alcohol dependence, low education, and a high likelihood of recidivism suggest that linkage to HIV care after release in the mentally ill has numerous barriers. Additional

structural barriers such as loss of Medicaid due to extended incarceration could present further problems to successful adherence in the community. It has been hypothesized by this author that inmates with comorbid HIV infection and severe mental illness (SMI) likely suffer higher rates of mortality when compared to HIV positive inmates with no record of mental health problems. This would be attributable to the "double burden" they face, as well as the myriad of competing health risks that affect the mentally ill disproportionately.

MATERIALS AND METHODS

GDC Data

This retrospective follow-up survival analysis tracked a cohort of all persons incarcerated in a Georgia state prison on June 30th, 1991. Data collected on each observation included lifetime incarceration history, demographic information, as well as HIV testing information and psychiatric evaluation score at intake. Cohort members with unknown mortality status as of December 31, 2006 and again on December 31, 2010 were matched with death information from the Georgia Death Registry. Records that remained unmatched in both mortality follow-ups were submitted to the National Death index (NDI). In both cases persons were matched by name, Social Security number, age, home address, and known aliases. Both the matches by the Georgia Death Registry and the NDI were assumed to be true; if date of death was recorded before the final release date, then final release was recoded to date of death.

The number of admissions and releases were often overlapping due to multiple crimes being adjudicated across a span of months or years. In such cases, overlapping time periods were collapsed as long as the inmate was continuously incarcerated (see Appendix A). Days in prison were subsequently calculated from these collapsed periods and divided by 365.25 in order to create a "continuous years in prison" variable, which accounted for lifetime incarcerations including those before the cohort was defined in 1991. Because years in prison was deemed to have a strong, unwanted effect on survival time, an attempt to dull this effect was used by dividing calculated years in prison by inmate age. The result gives an estimates percent of life spent in prison. This value may be subject to some error as year of birth was provided en lieu of specific birth dates. Age was calculated by setting all birthdates to June 30th of the year of birth, with the goal of creating a symmetric distribution for the true of birth dates of the cohort around a reasonable midpoint. In all analyses, age at the start of the study was used to determine coefficients, while percent of life in prison used age calculated at the date of censoring.

Due to the strong influence of ART therapy on mortality outcomes in HIV patients the period of analysis was restricted from January 1, 1998 to September 2, 2010, the last date at which incarceration data was observed. By 1998 it was assumed that effective ART therapies would have been available to all prisoners with a known HIV status who met treatment criteria current for its time (40). Restricting the length of follow up resulted in 1,092 (4.6%) observations being dropped due to death prior to the beginning of the study period. HIV testing dates and results were included in the data provided by the GDC. HIV testing results outside of prison were not available, however, some positive tests appear to have been recorded while an inmate was not incarcerated.

Fifty-three inmates were recorded as dying of HIV/AIDS despite no record of a positive test. Due to the lack of a definite diagnosis, these inmates were categorized as HIV negative in analyses, as the counterfactual experience – those inmates who were HIV infected but undiagnosed – could not be accounted for. The fifty-three deaths attributable to HIV were not disproportionately categorized as having refused/missing/unknown testing status. All inmates were categorized as ever HIV positive or HIV negative, those with missing or indeterminate results were coded as HIV negative for all regression analyses.

Assessment of severe mental illness was performed using the results of psychiatric screening information found in the GDC data. The psychiatric state of each inmate was recorded at admission as part of the assessment during which overall health and capabilities are examined. The psychiatric assessment is performed with the goal of understanding personality, intellectual, cognitive, behavioral, and emotional fluctuations of each inmate. The scale on which these assessments are measured is seen in Table 2**.** In analyses, inmates were placed into one of three categorical groups: S1, S2, or a combined category for S3 and S4 patients. Higher scores represent an increased need for mental health services. S2 inmates are housed with the general prison population, however S3 and S4 inmates must be held in facilities with more intensive mental health capabilities. During all regression analyses the maximum psychiatric evaluation score recorded at any incarceration was used. 3 records (0.01%) were dropped due to having a maximum psychiatric score S5 as their experience required inpatient care. No inmates in the cohort were designated S6 at any point during the study. Psychiatric categorizations were not recorded regularly at each admission. 83.2% of admissions were missing psychiatric

evaluation data; an additional 0.7% of admissions were coded as ‘0’ meaning that only 1 in 6 admissions had usable grade information prior to assessment. The missing and ‘0’ coded admissions were coded as S1 upon advice of Timothy Carr (41).

The small number of inmates whose race was not categorized as white or black (n=72, 0.3%) were removed from analysis due to the unreliable estimates caused by small sample size. Education and employment were categorized into groups based on similar log-log curves and survival experience. Education was categorized into three groups based on last known education level: participants who completed high school, those who did not complete high school, and those for whom education level not recorded. Last known employment was also categorized into three groups based on employment status at final incarceration. The first level described full-time or part-time employees and students, the second described those who had never worked or were unemployed, and the third identified those incapable of work. A dichotomous variable was also used to describe whether or not an inmate had a prior or current drug offense. Drug offenses were included in the analysis as a proxy for drug use, as no other illicit drug-related information was available without significant missing data.

All data management and analysis was performed using the Statistical Analysis System Enterprise Guide, version 4.3 (SAS Institute Inc., Cary, North Carolina) Data were stripped of identifying information prior to receipt by this researcher. Figures and tables were created using Microsoft Excel spreadsheet software.

Modeling process

A time on study Cox proportional hazards model was used to model the association between mortality and comorbid HIV infection with elevated psychiatric assessment at any incarceration. Both primary exposures HIV infection and psychiatric assessment as well as employment were shown in extended Cox regressions to violate the proportional hazards assumption, resulting in the inclusion of time dependent interaction terms of the form X*g(t) = (X*time on study) in the full model. The final hazard functions are therefore time dependent and hazard ratios were variable during the study period when compared to the referent group (HIV negative, S1 psychiatric grade).

Bivariate extended Cox models with time-covariate interaction terms were examined for all other covariates to assess the proportional hazards assumption. Due to the χ^2 distribution of these tests and the large sample size, an alpha level of 0.01 was used to avoid an inflated rate of false positives. An alpha level of 0.05 was used for all other modeling steps. Time dependent interaction terms that showed significant Wald p-values were included in the full model.

Crude Kaplan-Meier and log-log curves were generated to test the proportionality assumption for each covariate. Log-log curves were also stratified for each covariate by HIV infection and psychiatric state in order to examine any potential interactive effects with the variables of interest. Continuous covariates were categorized using univariate logit plots to assess linear trends in the odds relationship between the predictors and death. Covariates with more than two levels were assessed using Log-Rank tests with Sidak adjustments to account for the differences between levels. Log-Rank tests showed

significant differences for all covariates other than sex, which was kept in the full model-based on the assumption of systematic differences in mortality experiences in the presence of other confounders and interaction.

A model with all confounders and interaction terms was first assessed for multicollinearity. Models with multiple covariates with variable decomposition proportions (VDPs) greater than 0.50 within a condition index >10 were flagged as sufficient evidence of a multicollinearity problem. Age and sex interactions with both psychiatric assessment and HIV status were dropped during this stage.

Upon completion of inspection for multicollinearity, an assessment of interaction terms was performed. A Wald χ^2 chunk test was performed to test for the inclusion of all interaction terms; the result was significant ($P < 0.001$). Following this significant test, backward elimination was used to reduce the model based on insignificant type 3 Wald tests. Interaction terms with dummy variables for employment and psychiatric assessment were kept in the model if at least one of the dummy interactions was significant. The model at the end of this backward elimination was deemed to be the gold standard against which nearly all-possible subsets would be compared.

Confounding assessment was performed with covariates not included in any interaction terms to maintain a hierarchically well-formulated model. Due to insignificance in the gold standard model, having a drug charge was dropped from all contending subsets, resulting in 15 competing models assessed for confounding and precision.

Confounding and precision were assessed using the estimates for the interaction term between HIV status and maximum psychiatric grade. The threshold for confounding was defined to be a difference in hazard ratios exceeding 10%. Seven models did not exceed this threshold and were further examined for precision of hazard ratio estimates. Precision was examined using the ratio of the 95% confidence interval (CI), and CI widths. All CI ratios were within 0.4% of the gold standard, but CI widths showed increased differences. The final model selected dropped sex.

Due to the inclusion of time dependent interaction terms, residual analyses could not be performed on the final model. To assess goodness of fit a likelihood ratio chunk test was performed on the time dependent interaction terms, this test was significant was significant ($P < 0.001$) thus time interaction terms were kept in.

In an attempt to check whether the linear use of time on study within the interaction terms was appropriate for the time dependent interactions a residual analysis of a reduced model without the time interaction terms was performed. Non-linear residual plots for confounders with significant association with time might be indicative of a more appropriate function for time on study existing, such as log(time on study) or (time on study)^2. Time dependent variables were thus removed from the final model in order to perform non-parametric residual analyses. Cox-Snell (Score), Schoenfeld, and scaled Schoenfeld residuals showed significant correlations with HIV status, psychiatric grade S2, and employment. Visual inspection of the residual plots for each of these covariates exhibited no gross departure from the assumption of linearity, thus the linear g(t) selected in the final model was given confidence.

Deviance residuals were visually examined with a LOESS smoothing factor of 0.3. A small but noticeable departure from 0 was noticed in the smoothed analysis. This departure occurs on the left side of the **X*β** – residual estimates plot, most likely due to the higher mortality attributable to HIV death early during the study period. There were a large number of outliers outside the deviance range (-2.5, 2.5) indicating that this model was not a strong predictor of all-cause mortality. This was deemed reasonable as no clinical factors were included beyond HIV infection and psychiatric assessment.

The final model was tested for sensitivity to an expanded definition of HIV infection, using the 53 undiagnosed HIV related deaths as additional HIV positive observations. Results were then compared using a comparison of the hazard ratios for the interaction term of interest (Psychiatric grade*HIV status) as well as the CI ratio. Comparative goodness of fit was then assessed using the $\chi^{2\text{-distributed}}$ likelihood:

-2*[Likelihood(Final Model) – Likelihood(Reduced Model)].

Because both models had the same degrees of freedom, a ratio test could not be performed; however, an assessment of overall fit was performed using the crude likelihood ratio test expression.

RESULTS

Baseline Characteristics

The original cohort of Georgia inmates consisted of 23,510 persons alive and incarcerated on June 30 1991. Due to deaths and exclusions (see Figure 1), by January 1,

1998 the cohort held 22,351 current and former inmates, of which 8,062 were incarcerated. Table 1 shows selected demographic characteristics of the remaining cohort's experience until September 2, 2010. At the end of the analysis period 2,771 (12.4%) of the examined cohort had died. The sample was 94% male and 66% black and <1% Hispanic. Due to the lagged period of interest, the mean age of the cohort was 39.2 years (Standard Deviation: 8.9 years), 6.7 years higher than the study start which was only 6.5 years earlier, indicating increased mortality in younger members of the cohort during the period June 30, 1991 to January 1, 1998. By 2010, inmates had been incarcerated an average of 3.0 times (SD: 2.2) spending an average total of 10.7 years (SD: 8.9) in custody

792 inmates (3.5%) in the cohort starting on January 1, 1998 were classified as having ever tested positive for HIV infection. Of the 792, 174 (22.0%) seroconverted during the study period. Age, race, and sex adjusted survival curves in Figure 2 show significant difference in all-cause mortality between HIV positive and negative inmates (Wald Chi-Square $P < 0.001$). The high levels of mortality were particularly pronounced in inmates diagnosed before 1998. 38.2% of those infected before the analysis period died, compared to 12.6% of those diagnosed after 1998 (Wilcoxon $P <0.001$). Mean survival time for those diagnosed before 1998 was 9.9 years (Standard Deviation: 4.2 years), while those who were diagnosed after study start survived an average 12.2 years (Standard Deviation: 1.5 years).

Table 3 shows HIV prevalence across various demographic factors. Prevalence between races was significantly different. Over five percent of black inmates were infected compared to 1.0% of whites (Fisher's $P <0.001$). White inmates were more

likely to have contracted HIV after 1998, though the difference was not significant (26.9% vs. 21.4%). Females showed higher prevalence of HIV infection than males (4.8% vs. 3.5%; Fisher's $P<0.001$), but men were more likely to have documented seroconversion during the study period, as 23.1% of male infections were diagnosed after January 1, 1998, compared with 7.0% for females (Fisher's $P<0.01$).

Using the maximum lifetime grade from the GDC psychiatric assessments (see Table 2), mental illness was detected in 1,791 (8.0%) of inmates. 1,369 (71%) of these were categorized S2, while the remaining 546 (29%) were S3 or S4. Mortality was significantly lower for those graded S2 than those graded S1 (9.3% vs. 12.6%; Log-Rank $P<0.01$), however there was no significant difference in mortality between those graded S3 or S4 and S1 (13.2% vs. 12.6%; Log-Rank $P=0.189$). Table 4 describes the prevalence of each psychiatric grade in the cohort by demographic factor. Women were significantly more likely to be diagnosed S2 than men (11.8% vs. 5.8%; Fisher's $P<0.001$), however, there were no significant differences by sex for S3/S4 grading (Fisher's $P = 0.496$). S3/S4 grades were also not differentiable by race, however, white inmates were significantly more likely than their black counterparts to be diagnosed S2, but the difference was not large (5.8% vs. 6.9%; Fisher's $P < 0.01$).

A significant positive trend was found between the total number of incarcerations and the probability the prisoner received a psychiatric grade S2 or higher (Pearson Correlation Rank Scores; $P<0.0001$, see Figure 3). Further analysis revealed that HIV infected inmates were incarcerated more frequently regardless of mental status (Figure 4), though the length of incarceration for the HIV infected shorter on average (Figure 5).

Examining HIV infection psychiatric status together, the prevalence of comorbid HIV infection with psychiatric grade ≥ S2 was 0.6% in the cohort records. This translates to one in every six cases of HIV having a recorded mental health problem. Table 5 shows mean differences for various cohort characteristics by HIV and mental health problems; the mean differences show again that HIV is disproportionately affecting black inmates. White HIV+ inmates are underrepresented across all psychiatric grades, however it is worth noting that they make up only 7.6% of HIV+/S1 cases. Table 5 also suggests that there is increased comorbidity of mental health problems and HIV infection in female prisoners, however the sample of HIV positive female inmates is small making it difficult to interpret this trend.

Regression Analyses

The time on study extended Cox proportional hazards model results can be seen in Table 6. HIV and maximum lifetime psychiatric assessment grades were shown to have significant individual and interactive effects on mortality. HIV infection was the strongest driver of increased hazard (β=2.12, 95% CI: 1.88, 2.37). Psychiatric grades had varied effects, though both in the opposite direction. Grades of S2 (β=-0.95, 95% CI: -1.52, -0.39) had a significant protective effect while S3/S4 estimates showed null response (β=-0.01, 95% CI: -0.75, 0.72).

The time dependent interaction term with HIV status (HIV status*time on study) had a significant protective effect (β=-0.007, 95% CI: -0.010,-0.004), while the time dependent interaction terms for psychiatric grades were similar to the regular coefficient:

S2 saw a significant increase in hazard over time (β=0.007, 95% CI: 0.002, 0.011), while S3/S4 again showed no difference from the referent (S1).

The exposures of interest (HIV*Psychiatric grade) saw an interesting reversal. S2 did not show significant interaction with HIV (β=-0.48, 95% CI: -1.03, 0.06), while S3/S4 showed significant protective effect in HIV positive patients (β=-0.82, 95% CI: -1.58, -0.07). Psychiatric grade S2 also showed evidence of significant interaction with various levels of employment; increased hazard of mortality was seen in S2 interaction with inmates who were unemployed (β=0.45, 95% CI: 0.01, 0.89) or incapable of work (β=0.59, 95% CI: 0.08, 1.11). As expected, an increase in age saw an increase in mortality (β=0.07, 95% CI: 0.07, 0.08). Confounders of interest were race, which had an increase in hazard for white inmates (HR=1.34, 95% CI: 1.23, 1.45). Having an increased percent of life spent in prison showed a protective effect (β=-1.53, 95% CI: -1.79,-1.27).

Due to the time dependent interaction terms the Cox proportional hazards regression resulted in time dependent hazard ratios for each combination of HIV status and psychiatric grade. Hazard ratios were calculated for these combinations, with the referent set to the modeling referent (HIV-/S1). The adjusted hazard ratio attributable to HIV infection in inmates with no mental health problems on January 1, 1998 was 8.36 (95% Confidence Interval: 6.52-10.72). This ratio decreased as time progressed, by the end of the analysis period the hazard ratio attributable to HIV infection was 2.72 (95% Confidence Interval: 2.05-3.60).

This study yielded several similar results to previous analyses of all-cause mortality in retrospective follow up studies of prisoner cohorts. Increased age at study start was associated with increased hazard of mortality (β=0.073, CI =0.069, 0.076). White race was shown to increase hazard (HR: 1.34, CI: 1.23,1.45), a comparable finding to analyses by Rosen in North Carolina (16) and work by Spaulding et al. (12) on the same cohort over a different period. There was significant hazard associated with unemployment (HR: 1.24, CI: 1.04, 1.50), however this effect was dulled over time (β=-0.002, CI =-0.004, 0.000), potentially due to increased likelihood of surviving members accessing social services.

The protective effect of time served in prison, which was measured in this analysis as percentage of life spent in prison was again found in this cohort (β=-1.54, CI =-1.80, -1.27) (11,12). Crude differences between the sexes yielded no significant disparity in mortality outcomes, and confounding effects attributable to sex were not seen. It is possible that interactive effects were present in this cohort between sex and HIV or mental illness, however, due to evidence of multicollinearity, these terms were dropped from the final model prior to interaction assessment. The use of prior or current drug offenses as a proxy for confounding effects due to drug abuse did not show significant the predicted significant effects. However, this may be attributable to the weakness of the variable as a proxy for hazardous behavior, rather than evidence against the hypothesis.

Table 7 lists the respective hazard ratios and confidence intervals calculated using the final model. These hazard ratios use HIV negative and S1 (HIV-/S1) graded inmates as their referent category (hazard ratio = 1) and use mean values for employment at each

combination of HIV status and psychiatric grade for the interaction term between employment level and psychiatric grade. Figures 6-8 show the changing hazard ratios over time for HIV status-psychiatric categorization combinations and the respective 95% confidence bands. As maximum psychiatric assessment grade increases the difference in hazard ratios between HIV positive and negative inmates is less prominent, indicating a convergence of mortality experience over time in spite of HIV diagnosis. The hazard ratios for all elevated psychiatric categorizations and HIV+ subpopulations converge to a level above that of HIV-/S1 participants.

Figures 9-11 show the same hazard calculations from Table 7, but represent pairwise comparisons of HIV+ populations by psychiatric categorization. These figures describe the differences in effect modification over time of the psychiatric categorization. Over time, the significantly increased hazard initially seen in the HIV+/S1 participants is reduced to levels similar to those of HIV+/S2 and HIV+/S3 populations.

Sensitivity analysis was performed by substituting a variable for HIV that included deaths attributable to HIV without a positive test in the GDC data. The final model was used in order to assess its stability. Results of this analysis can be seen in Table 8, which provides beta estimates for the adjusted model. There was only one change in significance, which occurred in the exposure variable for (HIV status)*(S2 psychiatric categorization). In the final model the coefficient was not significant, but in the adjusted model a p-value of P=0.0446 was observed. A comparison of adjusted hazard ratios at the beginning and conclusion of the study with 95% confidence intervals can be seen in Table 9. In this assessment, the adjusted model exhibits superior precision at all intervals and HIV status / psychiatric category combinations. This superior

precision is coupled with increased hazard ratio estimates over time for HIV positive groups. A comparison of Likelihoods results in: $-2*\ln(L_F/L_R) = 142.64$, an indication of markedly better fit by the adjusted model, although this is not surprising as one would expect precision to increase with the addition of observations with a known exposure-outcome match.

DISCUSSION

Analysis of Outcomes

Results from regression analyses indicate there is evidence from the GDC cohort that recorded psychiatric problems in the prison setting had beneficial modifying effects on mortality in HIV infected participants in the first years of analysis, suggesting improved long-term survival in the cohort that is attributable to mental health status. An explanation for this effect may be that persons with comorbid HIV infection and mental illness have more extensive engagement with healthcare services. This increased engagement may increase adherence to ART, subsequently decreasing mortality. The magnitude of this protective effect is significantly larger in HIV+/S3 patients, which may be attributable to the specialized facilities these inmates go to due to their more severe mental illness.

A comparison of HIV+/S1 and HIV+/S2 participants reveals a decline in the difference in hazard seen between the two groups (see Figure 9). Six years (72 months) into the study period the HIV+/S1 participants no longer show significantly increased hazard ratios when compared to the HIV+/S2 population. The most plausible explanation

to this author for the differential survival pattern is that early in the analysis period there existed a portion of the HIV+/S1 group that exhibited lower adherence to treatment than the HIV+/S2 participants. This adherence gap drove a divergence of the survival curves for the first 6 years, after which only similarly adherent groups remain, which is revealed in the non-differential hazard. The reason for this adherence gap may be the lack of engagement or experience HIV+/S1 inmates have being 'patients' relative to their HIV+/S2 counterparts whose mental illness may have exposed them to healthcare institutions earlier in life and at a higher frequency.

It is noted that mental illness is not globally protective; regression results revealed that over time S2 patients saw a significantly increased hazard of mortality attributed to their recorded status. The increase in hazard over time may be attributable to the cumulative lifetime effect of factors unmeasured that disproportionately affect the mentally ill such as drug and alcohol abuse. Also of note is that the time dependent covariates for HIV positive status and S2 designation are equivalent in magnitude, suggesting that some of the gains made in reducing mortality due to HIV may be offset over time by other risks associated with mental illness. Figure 7 illustrates this hypothesis, as the hazard ratios for the HIV+/S2 population remain stable over time while the hazard for the HIV-/S2 population increases as the study period progresses. It therefore may be that while S2 participants experience comparatively superior outcomes when diagnosed HIV positive, that the external problems associated with mental health such as drug and alcohol abuse or homelessness are undercutting the potential gains to be made by effective case management.

Similar comparisons and conclusions between HIV+/S1 and HIV+/S3,S4 participants are difficult to make due to the small HIV+/S3,S4 sample size (n=39) leading to wider confidence limits (see Figure 10); however it should be noted that the direction and magnitude of the shift in hazard ratios for HIV+/S3,S4 is similar in size and direction to that of the HIV+/S2 population (see Figure 11), leading one to believe that a similar experience is likely. The increased magnitude of the HIV+/S3/S4 regression coefficient provides further evidence that this protective effect does exist and is attributable to the benefits of increased engagement in care attributable to the population's mental health status.

The attribution of HIV positive status to the 53 undiagnosed participants that listed HIV infection as cause of death resulted in a model that generated more precise estimates, as well as increased estimates for the hazards of HIV positive cohorts at the end of the study period. These results were not a departure from expectation. An interesting product of this analysis was the gained significance of the HIV+/S2 interaction term (Final model P=0.084, Expanded definition: P=0.045), providing further evidence of the protective effect provided by S2 categorization in those with HIV. A caveat to this analysis is the lack of a counterfactual group; there was no uncovering of undiagnosed HIV+ inmates who did not die, or who died of other causes, thus estimates are likely biased away from the null, though the magnitude of this bias is unclear.

Limitations

There are several limitations to this study that may have affected estimates. The Cox proportional hazards model used did not use repeated observations format, meaning

that the maximum psychiatric categorization at any incarceration was used, as well as the last known employment status. This could have biased estimates either way, as it is uncertain whether the evidence of a protective effect holds found in this analysis holds or whether more severe categorizations are made at incarcerations later in life.

The use of a Cox proportional hazards model also relies heavily on the proportional hazards assumption. While efforts were made to check all covariates extensively, the choices of time functions [g(t)] in the use of time dependent interaction terms was based heavily on assumptions made using a non-parametric test; due to the large number of time interactions (5 total) it is possible that in combination these are not the optimum g(t) choices.

No data about time spent outside of prison was included in the analysis, leaving a significant gap in understanding of the cohort experience. Linkage data was therefore unavailable, thus from the results obtained conclusions can only be inferred. Additionally, the number of releases was not included in the model. This may have into the additional hazard posed by release that has been supported by the literature. Also of concern was the lack of person time with HIV. Future modeling strategies may look to examine age of diagnosis or HIV positive person-time to account for exposure-related left truncation issues.

By 1998, the GDC cohort was 6.5 years older than at study start, thus to a certain extent the results may not be generalizable for younger prison cohorts. The aging of the cohort may have seen some of the frailest members die before study start, leaving in the cohort only the ‘fittest’ members. This is especially true of HIV infected prisoners, who

were shown to suffer disproportionate mortality if they were diagnosed prior to the period of analysis. Truncating the cohort experience prior to 1998, was part of an effort to control for the introduction of effective ART and the corresponding decrease in mortality; however, as seen in the model estimates and hazard ratios calculated, mortality due to HIV was still not stable. Moving forward it will be interesting to see if high levels of HIV mortality are persistent early during the study of more contemporary cohorts. This might suggest problems with early detection as well as differential engagement with healthcare services within the cohort.

Some problems in data management were encountered regarding the coding of the psychiatric assessment. As previously noted there were a large number of missing and '0' coded values, which were interpreted to be S1 due to the lack of an assessment. Reports produced by the GDC show these categorizations are not different when you look at Active lifers (42), although there are other GDC reports that report much higher S2+ (43) prevalence. The root cause of this disparity is not clear.

Public Health Implications, Future Directions and Conclusion

The aim of this study was to evaluate the interactive effects of severe mental illness and HIV infection on mortality in a cohort of prisoners currently and formerly under the Georgia Department of Corrections. Analysis of the cohort has revealed how a set of complex parameters defines the relationship between HIV, psychiatric assessments and mortality.

The hazard benefit of recorded mental health problems in this prisoner and released prisoner cohort suggests that those participants with mental health problems

show greater engagement with healthcare provision. Whether or not this is occurring uniquely within the prison setting, or extending into the community through superior linkage to care will hopefully be a topic of future study. Only five sixths of the GDC cohort's HIV infected population did not have a recorded mental illness, suggesting that the extension of these benefits could have a significant impact on the overall mortality differential between HIV positive and HIV negative prisoners.

Programmatically, it may be beneficial to assess the reasons for which HIV positive prisoners with both mild and severe mental illness may have improved outcomes. Whether it is increased responsiveness to case management, more frequent contact with healthcare professionals, or other external factors; extending the decreased hazard of mortality seen in those with comorbid HIV infection and mental illness to those similarly infected but without mental health problems should be a future topic of inquiry.

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TABLES

Table 1. Characteristics and mortality of 22,351 current and former prisoners in the custody of the Georgia Department of Corrections (GDC) on June 30,1991, surviving from January 1, 1998 to September 2,2010.

Characteristic	Total n (%)	Died n (%)	p-value
Total	22351 (100)	2771 (12.4)	
Gender			
Women	1249 (5.6)	153 (12.3)	
Men	21102 (94.4)	2618 (12.4)	Log-Rank *P*=0.847
Race			
Black	14807 (66.2)	1588 (10.7)	Log-Rank *P*<0.001
White	7544 (33.8)	1183 (15.7)	
Employment Status			
Fully or Part-time Employed/Student (referent)	8313 (37.2)	838 (10.1)	
Unemployed/Never Worked/Missing	13193 (53.0)	1735 (13.2)	Log-Rank* *P*<0.001
Incapable of Work	845 (3.8)	198 (23.4)	Log-Rank* *P*<0.001
Education			
12+ Years (referent)	8359 (37.4)	995 (11.9)	
<12 Years	13144 (58.8)	1641 (12.5)	Log-Rank* *P*<0.606
Unknown/Other	848 (3.8)	135 (15.9)	Log-Rank* *P*<0.024
Mean Age [SD] at Study Start (years)	39.2 [8.9]	46.3 [11.1]	Unpooled T-test *P*<0.001
Mean % [SD] of Life Spent in Prison	21.1 [17.0]	16.7 [13.5]	Unpooled T-test *P*<0.001
Ever Drug Charge			
No	18302 (81.9)	2354 (12.9)	Log-Rank *P*<0.001
Yes	4049 (18.1)	417 (10.3)	
HIV+ During Study			
No	21556 (96.4)	2513 (11.7)	Wilcoxon *P*<0.001
Yes	792 (3.5)	258 (32.6)	
*Mental Health Assessment***			
S1 (referent)	20436 (91.4)	2571 (12.6)	
S2	1369 (6.1)	128 (9.3)	Log-Rank* *P*<0.001
S3/S4	546 (2.4)	72 (13.2)	Log-Rank* *P*=0.159

* Sidak adjusted p-values for between group comparisons

** 3 S5 categorized observations dropped from analysis

Table 2. Description of GDC psychiatric grades assessed at admission for each incarceration, Georgia, 1998-2010.

Analysis Grouping	GDC Grade	Description
1	S1	No impairment or disorder of adaptive functioning. Requires no Scheduled mental health services
2	S2	Mental health disorder in remission or stable with minimal residual symptoms or mild impairment of adaptive functioning or mild mental retardation. S2 inmates/probationers may need periodic supportive mental health counseling and psychological/psychiatric treatment with or without psychotropic medications and may be housed in general population
3	S3	Mental health disorder and/or symptoms which seriously impair adaptive functioning. S3 inmates/probationers require placement into a Level III SLU. These inmates/probationers require continuous case management and psychological/psychiatric treatment with or without psychotropic medication.
	S4	Severe mental health disorder and/or symptoms which seriously impair adaptive functioning. S4 inmates/probationers require placement in a Level IV SLU where more intense mental health services are available. These inmates/probationers require continuous outpatient case management and psychological/psychiatric treatment with or without psychotropic medications.
Excluded (n=3)	S5	Severe mental health disorder and/or symptoms which seriously impair adaptive functioning. S5 inmates/probationers cannot be safely managed as outpatients and require Crisis Stabilization Unit (CSU) inpatient care.
Excluded (n=0)	S6	Severe mental health disorder and/or symptoms which seriously impair adaptive functioning and there is a need for psychiatric inpatient care, with or without involuntary commitment to Central State or another psychiatric hospital.

Source: Georgia Department of Corrections Inmate Research File Bible

Table 3. Characteristics of persons ever identified by GDC as HIV positive among current and former prisoners in the GDC cohort, Georgia, 1998-2010

Characteristic	Total n (%)	HIV+ n (%)	p-value
Total	22351 (100)	792 (3.5)	
Gender			
Women	1249 (5.6)	57 (4.6)	Chi-Square *P*=0.045
Men	21102 (94.4)	735 (3.5)	
Race			
Black	14807 (66.2)	714 (4.8)	Chi-Square *P*<0.001
White	7544 (33.8)	78 (1.0)	
Employment Status			
Fully or Part-time Employed/Student (referent)	8313 (37.2)	237 (2.9)	Chi-Square *P*<0.001
Unemployed/Never Worked/Missing	13193 (53.0)	482 (3.7)	
Incapable of Work	845 (3.8)	73 (8.6)	
Education			
12+ Years (referent)	8359 (37.4)	272 (3.3)	Chi-Square *P*=0.187
<12 Years	13144 (58.8)	487 (3.7)	
Unknown/Other	848 (3.8)	33 (3.9)	
Mean Age at Study Start [SD] (years)	39.9 [8.9]	37.8 [6.7]	Unpooled T-test *P*<0.001
Mean % of Life Spent in Prison [SD]	20.7 [16.2]	21.4 [15.5]	Pooled T-test *P*=0.202
Ever Drug Charge			
No	18302 (81.9)	588 (3.2)	Log-Rank *P*<0.001
Yes	4049 (18.1)	204 (5.0)	
*Mental Health Assessment**			
S1 (referent)	20436 (91.4)	668 (3.3)	Chi-Square *P*<0.001
S2	1369 (6.1)	85 (6.2)	
S3/S4	546 (2.4)	39 (7.1)	

* 3 S5 categorized observations dropped from analysis

Table 4. Characteristics of maximum psychiatric grade at any incarceration among current and former prisoners in the GDC cohort, Georgia, 1998-2010

Characteristic	Total n (%)	S2 (%)	S3/S4 (%)	p-value
Total	22351 (100)	1396 (6.1)	514 (2.4)	
Gender				
Women	1249 (5.6)	147 (11.8)	32 (2.6)	Chi-Square *P*<0.001
Men	21102 (94.4)	1222 (5.8)	514 (2.5)	
Race				
Black	14807 (66.2)	852 (5.8)	363 (2.4)	Chi-Square *P*=0.005
White	7544 (33.8)	517 (6.8)	183 (2.4)	
Employment Status				
Fully or Part-time Employed /Student (referent)	8313 (37.2)	539 (6.5)	138 (1.6)	Chi-Square *P*<0.001
Unemployed/Never Worked /Missing	13193 (53.0)	640 (4.9)	269 (2.0)	
Incapable of Work	845 (3.8)	190 (22.5)	139 (16.4)	
Education				
12+ Years (referent)	8359 (37.4)	386 (4.6)	142 (1.7)	Chi-Square *P*<0.001
<12 Years	13144 (58.8)	948 (7.2)	380 (2.9)	
Unknown/Other	848 (3.8)	35 (4.1)	24 (2.8)	
Mean Age at Study Start [SD] (years)	39.9 [8.9]	37.2 [7.3]	38.8 [8.2]	Unpooled T-test *P*<0.001
Mean % of Life Spent in Prison [SD]	20.7 [16.2]	28.4 [13.8]	30.2 [13.3]	Unpooled T-test *P*<0.001
Ever Drug Charge				
No	18302 (81.9)	982 (5.3)	430 (2.3)	Chi-Square *P*<0.001
Yes	4049 (18.1)	387 (9.6)	116 (2.9)	

*T-tests performed on binary psychiatric grade variable defined as (S1 = 0, S2,S3,S4 = 1)

Table 5. Mean characteristics of prisoner cohort stratified by HIV status and maximum psychiatric grade at any incarceration, Georgia, 1998-2010.

	HIV-			HIV+		
Characteristic	**S1**	**S2**	**S3/S4**	**S1**	**S2**	**S3/S4**
n	19768	1284	507	668	85	39
Age (SD)	39.4 (9.0)	37.3 (7.3)	38.9 (8.3)	38.1 (6.8)	36.2 (5.9)	37.1 (6.2)
% Black	65.6%	61.2%	65.5%	92.4%	77.6%	79.5%
% Male	94.8%	89.1%	94.5%	93.1%	91.8%	89.7%
% Ever drug conviction	17.1%	28.1%	21.7%	25.7%	30.6%	15.4%
% of life in prison	19.9%	28.4%	30.4%	20.2%	28.5%	27.5%

Table 6. Cox proportional hazards regression model describing the association between health, demographic, and prison related covariates on participant mortality, Georgia, 1998-2010

Variable	**Beta**	**SE**	**p-val**
HIV+	2.124	0.127	<.0001
HIV+ x Time on study[a]	-0.007	0.002	<.0001
S2 Grade	-0.953	0.288	0.001
S2 Grade x Time on study	0.007	0.002	0.004
S3/S4 Grade	-0.013	0.376	0.972
S3/S4 Grade x Time on study	0.003	0.003	0.364
HIV+ x S2 Grade	**-0.483**	**0.280**	**0.084**
HIV+ x S3/S4 Grade	**-0.825**	**0.387**	**0.033**
Age at Study Start	0.073	0.002	<.0001
Race[b]	0.289	0.040	<.0001
Ethnicity[c]	0.115	0.355	0.746
Race x Ethnicity	-1.607	0.519	0.002
Education: <12 Years	0.135	0.096	0.158
Education: Unknown	0.140	0.041	0.001
Employment1: Never worked/unemployed/unknown	0.221	0.093	0.018
Employment2: Incapable of Work	0.169	0.184	0.360
Employment1 x Time on Study	-0.002	0.001	0.023
Employment2 x Time on Study	0.001	0.002	0.502
% of Life in Prison	-1.536	0.133	<.0001
S2 Grade x Employment1	0.451	0.226	0.046
S2 Grade x Employment2	0.594	0.264	0.025
S3/S4 Grade x Employment1	0.086	0.323	0.789
S3/S4 Grade x Employment2	-0.034	0.353	0.924

[a] Time on study measured in months.

[b] 0=Black, 1=White

[c] 0=Not Hispanic, 1=Hispanic

Table 7. Adjusted hazard ratios and 95% confidence intervals across time on study (months) describing mortality by HIV status and maximum psychiatric grade at any incarceration in a cohort of prisoners in Georgia, 1998-2010

Month	HIV-/S1	HIV-/S2	HIV-/S3 or S4
0	1 (Ref.)	0.52 (0.33,0.84)	1.05 (0.59,1.85)
36	1 (Ref.)	0.66 (0.47,0.93)	1.15 (0.78,1.71)
72	1 (Ref.)	0.84 (0.66,1.06)	1.27 (0.96,1.67)
108	1 (Ref.)	1.06 (0.86,1.31)	1.40 (1.05,1.85)
144	1 (Ref.)	1.34 (1.00,1.81)	1.54 (1.02,2.31)
Month	**HIV+/S1**	**HIV+/S2**	**HIV+/S3 or S4**
0	8.37 (6.53,10.73)	2.95 (1.53,5.69)	3.78 (1.62,8.82)
36	6.41 (5.40,7.61)	2.86 (1.65,4.97)	3.19 (1.52,6.69)
72	4.91 (4.27,5.65)	2.78 (1.68,4.58)	2.69 (1.34,5.40)
108	3.76 (3.14,4.51)	2.69 (1.61,4.51)	2.27 (1.09,4.69)
144	2.88 (2.22,3.74)	2.61 (1.44,4.74)	1.91 (0.84,4.36)

Table 8. Cox proportional hazards regression model describing the association between health, demographic, and prison related covariates on prisoner mortality. Updated to include 53 previously unknown cases of HIV, Georgia, 1998-2010

Variable	Beta	SE	p-val
HIV+	2.175	0.119	<.0001
HIV+ x Time on study[a]	-0.006	0.001	<.0001
S2 Grade	-0.935	0.288	0.001
S2 Grade x Time on study	0.006	0.002	0.005
S3/S4 Grade	0.012	0.376	0.975
S3/S4 Grade x Time on study	0.002	0.003	0.392
HIV+ x S2 Grade	**-0.533**	**0.265**	**0.045***
HIV+ x S3/S4 Grade	**-0.851**	**0.367**	**0.020**
Age at Study Start	0.073	0.002	<.0001
Race[b]	0.315	0.041	<.0001
Ethnicity[c]	0.125	0.355	0.725
Race x Ethnicity	-1.625	0.519	0.002
Education: <12 Years	0.133	0.096	0.164
Education: Unknown	0.138	0.041	0.001
Employment1: Never worked/unemployed/unknown	0.220	0.093	0.018
Employment2: Incapable of Work	0.154	0.184	0.403
Employment1 x Time on Study	-0.002	0.001	0.022
Employment2 x Time on Study	0.001	0.002	0.477
% of Life in Prison	-1.526	0.133	<.0001
S2 Grade x Employment1	0.446	0.226	0.049
S2 Grade x Employment2	0.596	0.264	0.024
S3/S4 Grade x Employment1	0.076	0.323	0.813
S3/S4 Grade x Employment2	-0.034	0.353	0.924

Exposure of interest HIV status S2 psychiatric grade is significant in expanded definition model.

Table 9. Assessment of final model sensitivity to updated definition for HIV infection using HIV status-psychiatric grade-time on study combinations. Includes 53 HIV infections (Expanded Definition) not known to be positive by GDC records at date of death.

Projected Case	Final Model HR (CI 95%)	Expanded Definition HR (CI 95%)	ΔHR	CI Ratio Final Model	CI Ratio Expanded Model
HIV-, S1, t=0	1 (Ref.)	1 (Ref.)	-	-	-
HIV-, S1, t=152	1 (Ref.)	1 (Ref.)	-	-	-
HIV-, S2, t=0	0.39 (0.22, 0.68)	0.39 (0.22, 0.69)	-0.7%	3.09	3.10
HIV-, S2, t=152	1.05 (0.68, 1.62)	1.04 (0.67, 1.61)	0.1%	2.39	2.39
HIV-, S3/S4, t=0	0.99 (0.47, 2.06)	1.01 (0.48, 2.11)	-2.5%	4.37	4.36
HIV-, S3/S4, t=152	1.47 (0.78, 2.79)	1.48 (0.78, 2.8)	-0.1%	3.59	3.59
HIV+, S1, t=0	8.36 (6.52, 10.72)	8.80 (6.98, 11.11)	-5.3%	1.64	1.59
HIV+, S1, t=152	2.71 (2.05, 3.6)	3.56 (2.77, 4.58)	-31.2%	1.76	1.66
HIV+, S2, t=0	1.99 (0.94, 4.19)	2.03 (0.98, 4.19)	-1.9%	4.43	4.28
HIV+, S2, t=152	1.75 (0.87, 3.52)	2.18 (1.11, 4.27)	-24.7%	4.06	3.83
HIV+, S3/S4, t=1	3.62 (1.32, 9.93)	3.8 (1.42, 10.19)	-5.1%	7.53	7.18
HIV+, S3/S4 t=152	1.75 (0.64, 4.8)	2.24 (0.85, 5.92)	-28.0%	7.50	6.95

^t = time on study, measured in months

*LCL and UCL indicate the lower and upper bounds of the 95% confidence interval for the estimates hazard ratios.

ΔHR shows the percentage difference in the hazard ratio between the two models.

CI Ratio is the percentage difference in the confidence interval widths, a positive value indicates better precision by the updated model, whereas a negative value indicates better fit by the final model.

FIGURES

Figure 1. Exclusion criteria for analysis of GDC prisoner cohort, Georgia, 1998-2010.

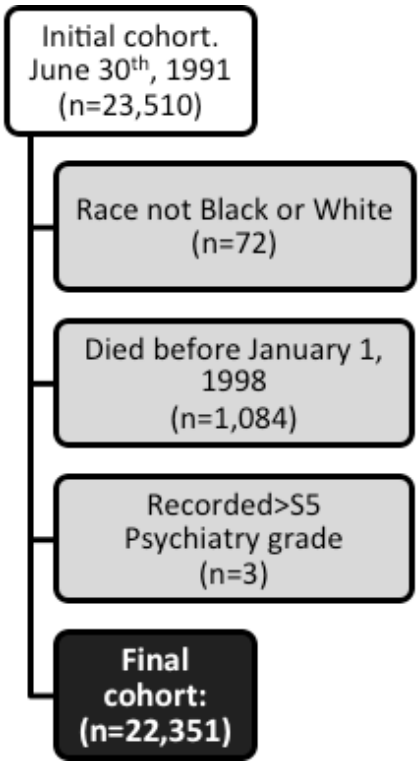


Figure 2. Adjusted all-cause mortality in the GDC cohort by HIV status, Georgia, 1998-2010. Adjusted for age, race, and sex.

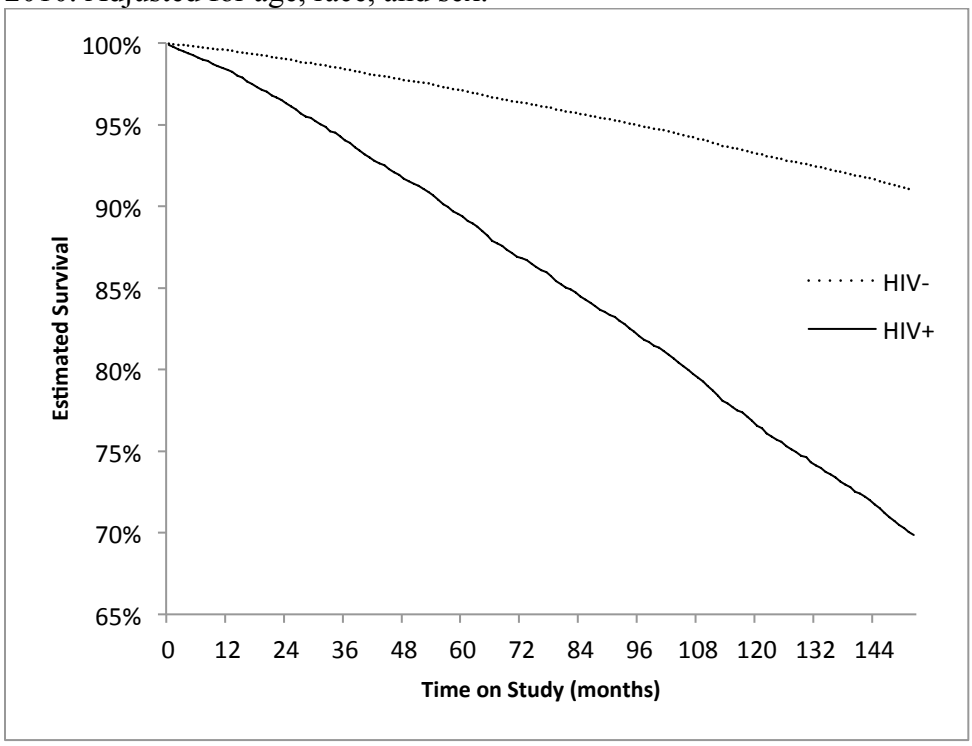


Figure 3. Proportion of prisoners receiving elevated psychiatric categorizations at final incarceration. Georgia (1998-2010)

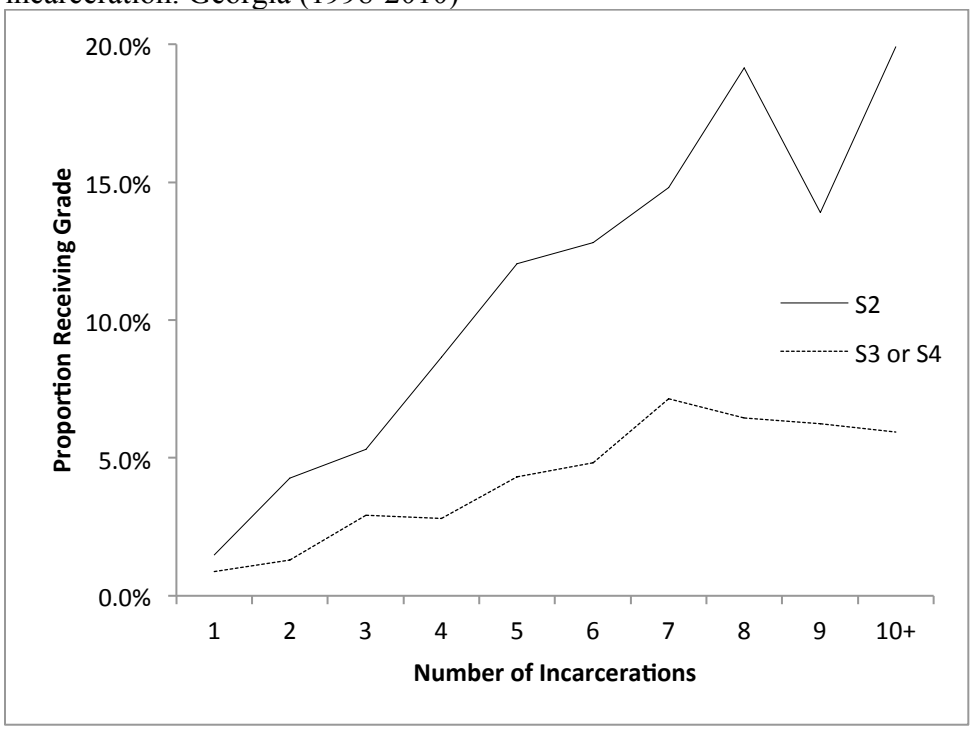


Figure 4. Average number of incarcerations in a cohort of prisoners assessed by HIV status and maximum psychiatric grade recorded, Georgia, 1998-2010. * Difference by HIV status is significant (Unpooled t-test $P < 0.05$)

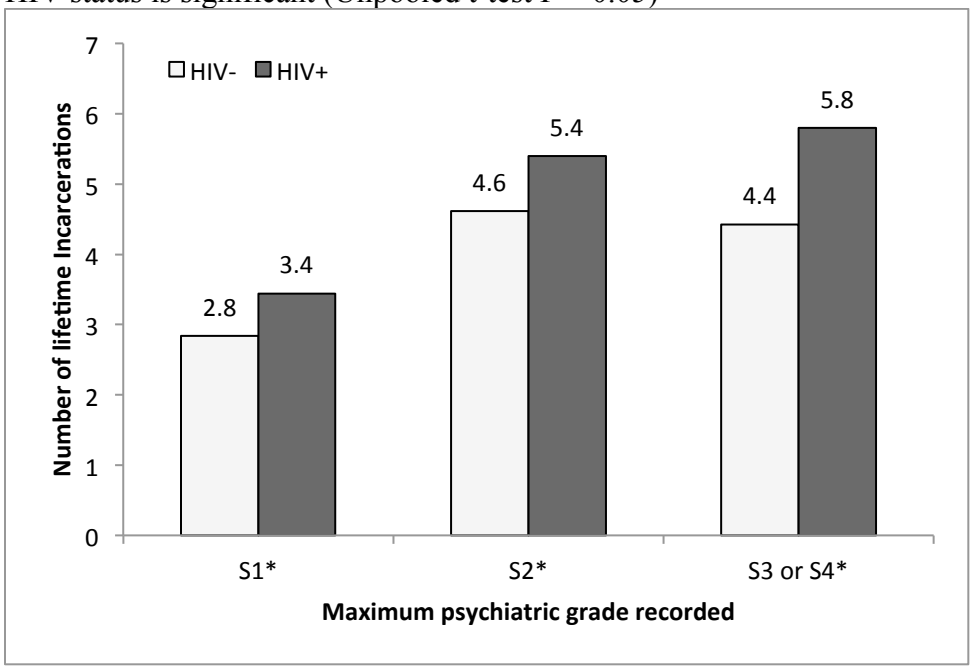
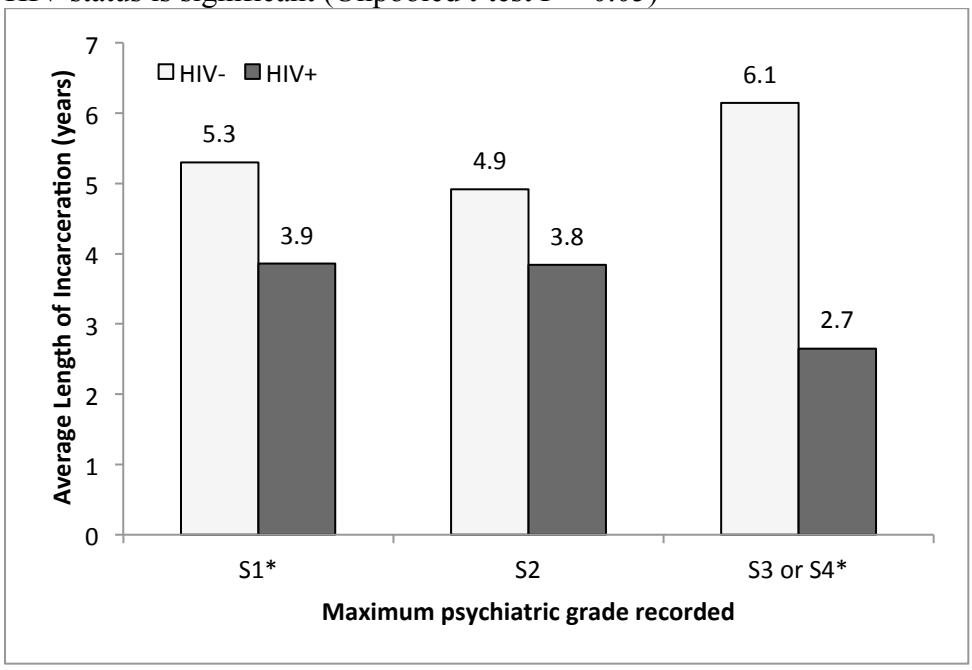


Figure 5. Average length of each incarceration in a cohort of prisoners assessed by HIV status and maximum psychiatric grade recorded, Georgia, 1998-2010. * Difference by HIV status is significant (Unpooled t-test $P < 0.05$)



Figures 6-8 Show the adjusted hazard ratios and 95% confidence bands for each psychiatric categorization by HIV status. These hazard ratios are derived from the final model using 3-year intervals to show trend starting January 1st, 1998. The referent for all hazard ratios is HIV-/S1.

Figure 6. Adjusted Hazard Ratios for S1 graded inmates, by HIV status.

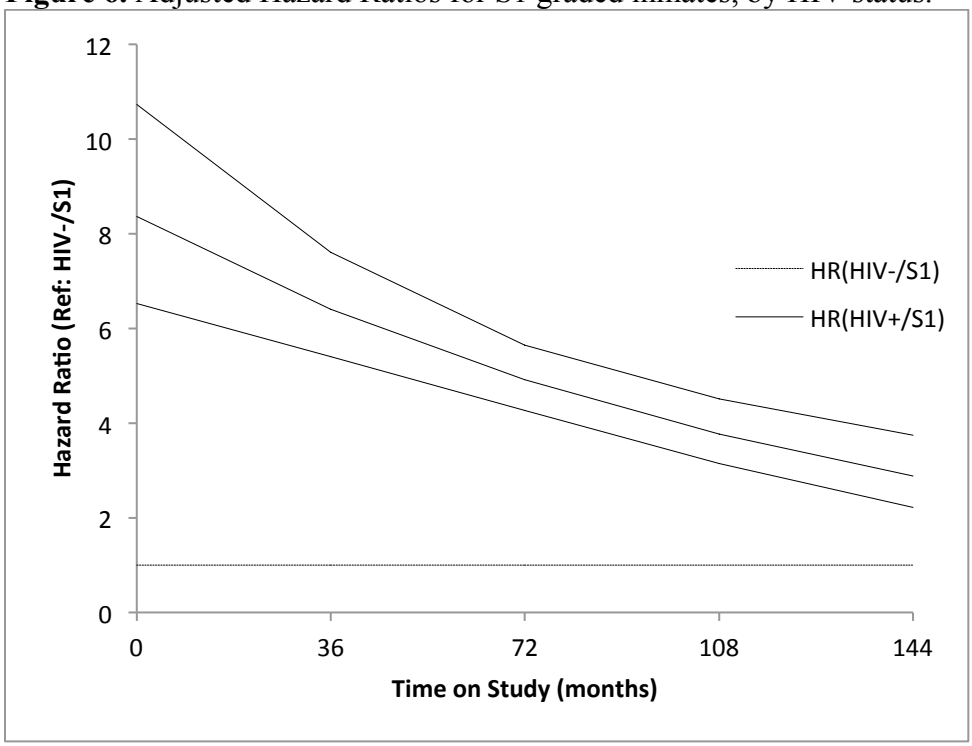


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Figure 7. Adjusted Hazard Ratios for S2 graded inmates, by HIV status.

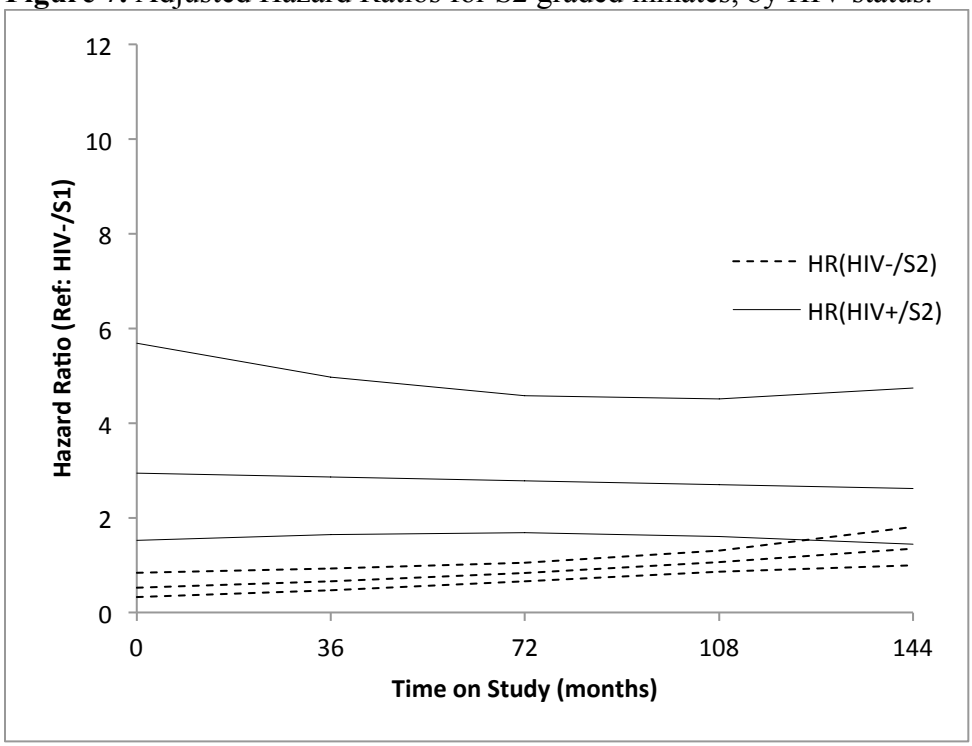
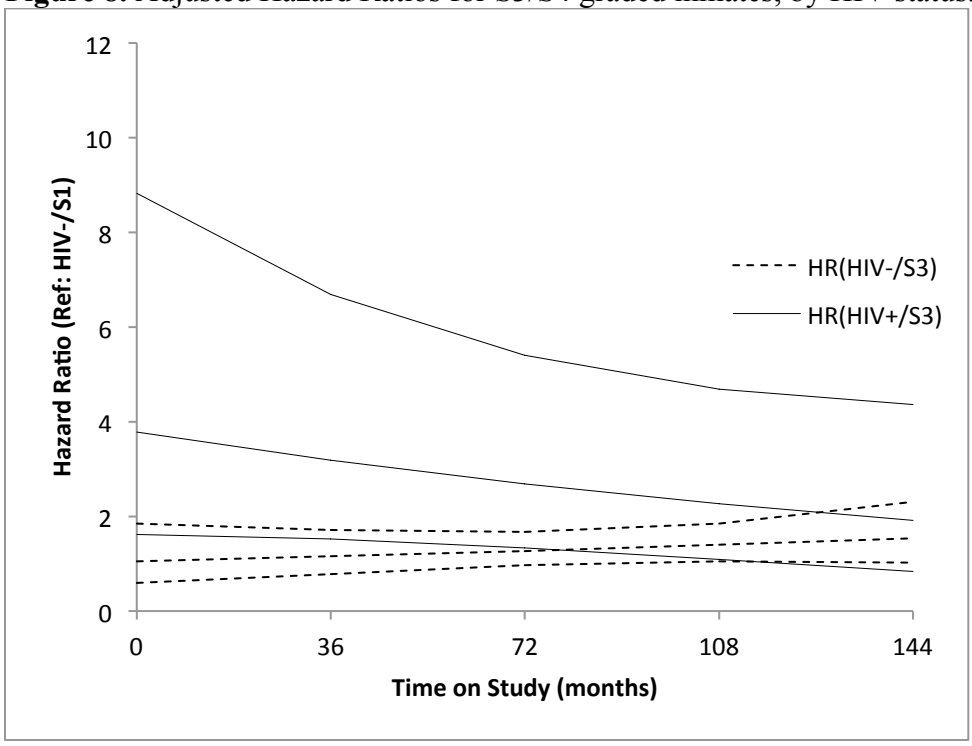


Figure 8. Adjusted Hazard Ratios for S3/S4 graded inmates, by HIV status.



Figures 9-11 Show the adjusted hazard ratios and 95% confidence bands for HIV+ by psychiatric categorization. These hazard ratios are derived from the final model using 3-year intervals to show trend starting January 1st, 1998. The referent for all hazard ratios is HIV-/S1.

Figure 9. Adjusted Hazard Ratios for HIV+/S1 and HIV+/S2 inmates.

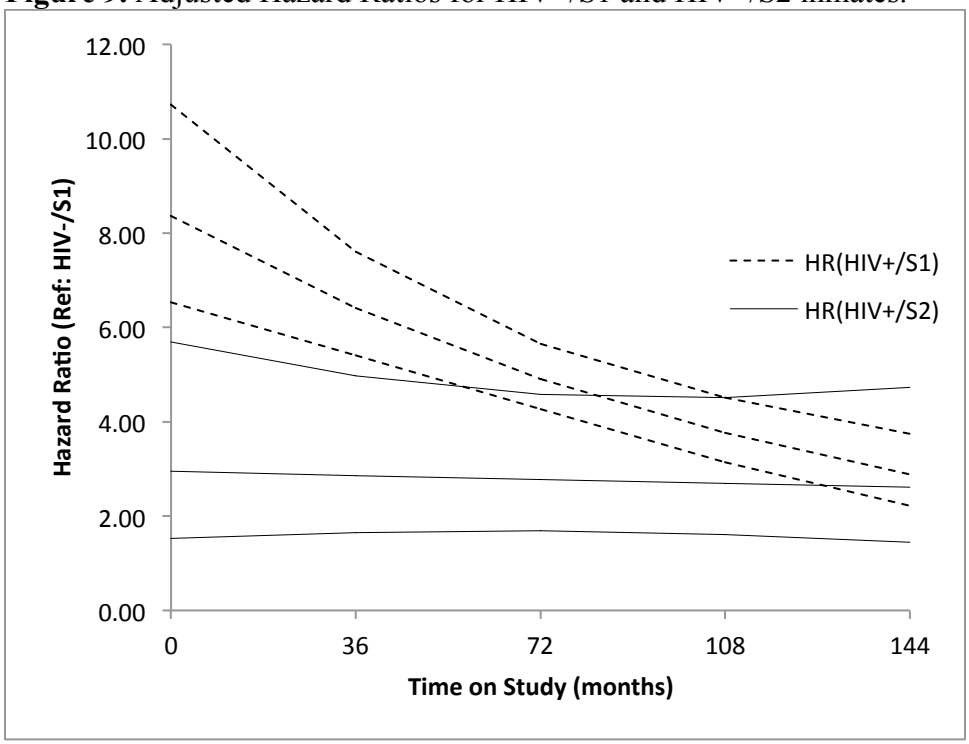


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Figure 10. Adjusted Hazard Ratios for HIV+/S1 and HIV+/S3 inmates.

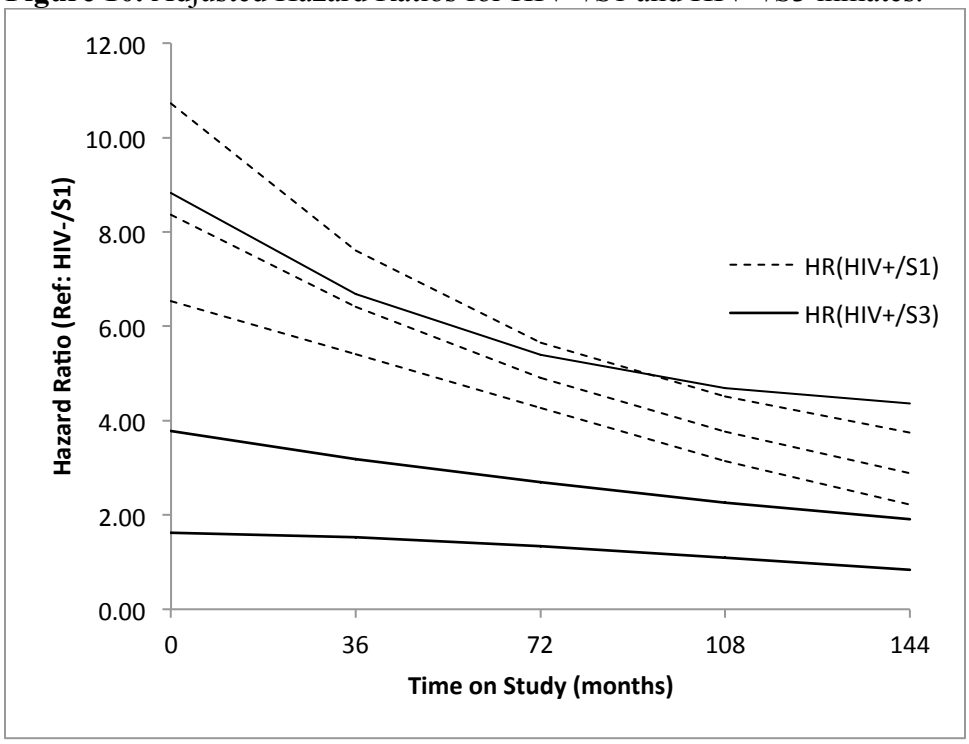
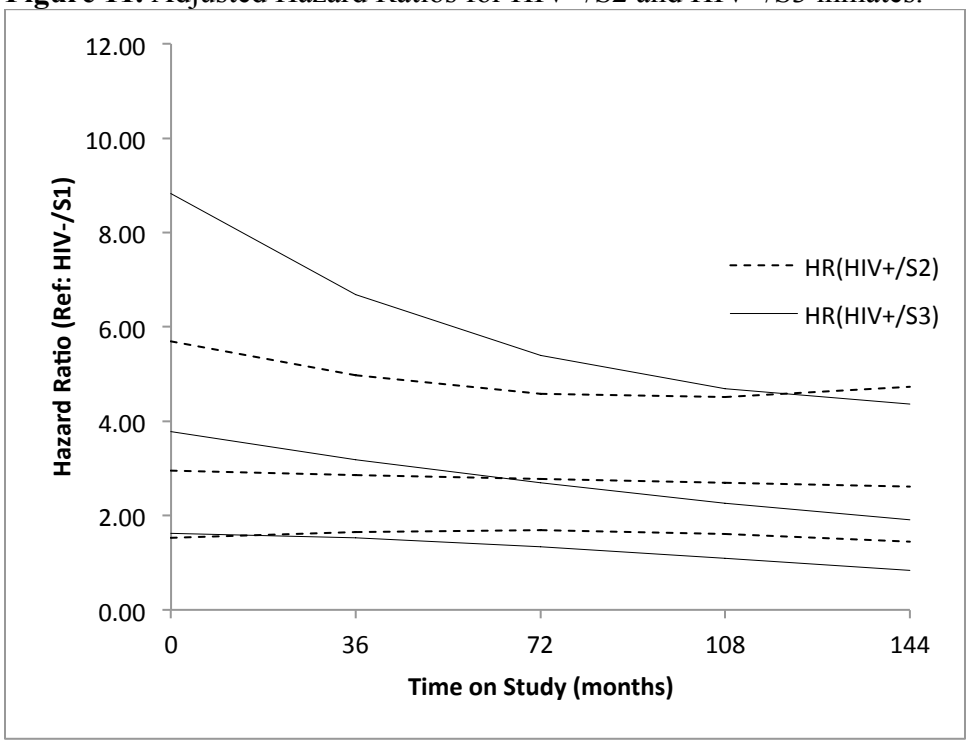
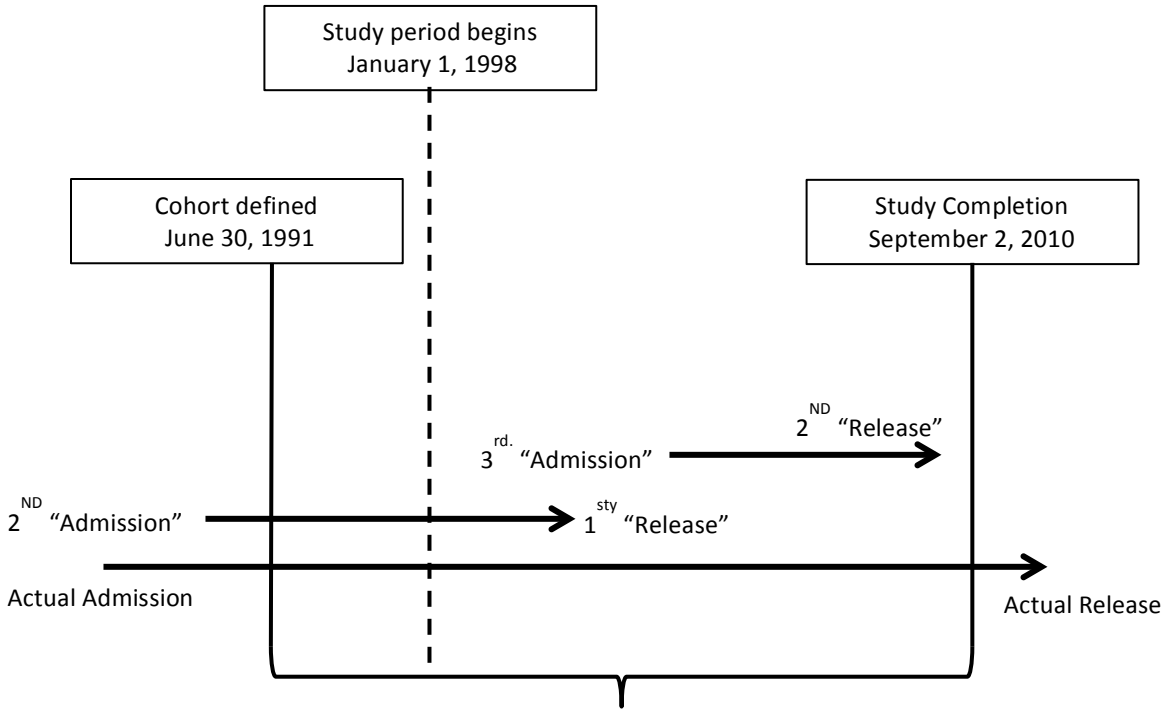


Figure 11. Adjusted Hazard Ratios for HIV+/S2 and HIV+/S3 inmates.



APPENDIX A

Figure. Visualization of simultaneous incarcerations for the same inmate; length of stay and number of prison visits were calculated using only the actual admissions and releases which entailed the prisoner entering and leaving a facility.



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APPENDIX B

SAS Code and Output

Starting Model Code:

```
proc phreg data= t.TOS_1998 covout outest=phreg1;
model TOS_STOP1*death(0)=

/*Exposure Variables */
POS HIVTime Psy2_1 Psy2xTime psy3_1 Psy3xTime PSY2xHIV PSY3xHIV

/*Confounders*/
AGE_ANAL_START sex_cd race_cd ethnicity EDU1 EDU2 EMP1 EMP2
EMP1Time EMP2Time PCT_LIFE_PRISON PLPTime prior_drug

/*psy Interaction*/
PSY2xAge PSY3xAge PSY2xSex PSY3xSex   PSY2xEMP1 PSY2xEMP2
PSY3xEMP1 PSY3xEMP2 PSY2xPLP PSY3xPLP PSY2xdrug PSY3xdrug

/*HIV Interaction*/
HIVxAge HIVxSex  HIVxEMP1 HIVxEMP2 HIVxEDU1 HIVxEDU2 HIVxPLP
HIVxdrug

/*Other Interaction*/
racexethn
;
/* Define Interaction Terms */
HIVTime = POS*TOS_STOP1;
HIVxAge = POS*AGE_ANAL_START;
HIVxSex = POS*Sex_cd;
HIVxEMP1 = POS*EMP1;
HIVxEMP2 = POS*EMP2;
HIVxEDU1 = POS*EDU1;
HIVxEDU2 = POS*EDU2;
HIVxPLP = POS*POS*PCT_LIFE_PRISON;
HIVxdrug = POS*prior_drug;
PSY2xHIV = Psy2_1*POS;
PSY3xHIV = Psy3_1*POS;
Psy2xTime= TOS_STOP1*psy2_1;
Psy3xTime= TOS_STOP1*psy3_1;
PSY2xAge = psy2_1*AGE_ANAL_START;
PSY3xAge = psy3_1*AGE_ANAL_START;
PSY2xSex = psy2_1*sex_cd;
PSY3xSex = psy3_1*sex_cd;
PSY2xEMP1 = PSY2_1*EMP1;
PSY2xEMP2 = PSY2_1*EMP2;
PSY3xEMP1 = PSY3_1*EMP1;
PSY3xEMP2 = PSY3_1*EMP2;
PSY2xPLP = PSY2_1*PCT_LIFE_PRISON;
PSY3xPLP = PSY3_1*PCT_LIFE_PRISON;
PSY2xdrug = psy2_1*prior_drug;
```

```
PSY3xdrug = psy3_1*prior_drug;
racexethn = race_cd*ethnicity;
EMP1Time=TOS_STOP1*EMP1;
EMP2Time=TOS_STOP1*EMP2;
PLPTime=TOS_STOP1*Pct_Life_Prison;
run;
```

Final Model Code:

```
proc phreg data= t.TOS_1998;
model TOS_STOP1*death(0)=

/*Exposure Variables*/
POS HIVTime Psy2_1 Psy2xTime psy3_1 Psy3xTime PSY2xHIV PSY3xHIV

/* Confounders */
AGE_ANAL_START race_cd ethnicity EDU1 EDU2 EMP1 EMP2 EMP1Time
EMP2Time PCT_LIFE_PRISON
/*PSY Interaction*/
PSY2xEMP1 PSY2xEMP2   PSY3xEMP1 PSY3xEMP2

/*Other Interaction*/
racexethn

/ risklimits=wald;

/* Define Interaction Terms */
HIVTime = POS*TOS_STOP1;
PSY2xHIV = Psy2_1*POS;
PSY3xHIV = Psy3_1*POS;
Psy2xTime= TOS_STOP1*psy2_1;
Psy3xTime= TOS_STOP1*psy3_1;
PSY2xEMP1 = PSY2_1*EMP1;
PSY2xEMP2 = PSY2_1*EMP2;
PSY3xEMP1 = PSY3_1*EMP1;
PSY3xEMP2 = PSY3_1*EMP2;
racexethn = race_cd*ethnicity;
EMP1Time=TOS_STOP1*EMP1;
EMP2Time=TOS_STOP1*EMP2;

run;
```

Final Model Output:

Summary of the Number of Event and Censored Values			
Total	Event	Censored	Percent Censored
22327	2761	19566	87.63

Model Fit Statistics		
Criterion	Without Covariates	With Covariates
-2 LOG L	54008.620	51688.522
AIC	54008.620	51734.522
SBC	54008.620	51870.759

Testing Global Null Hypothesis: BETA=0			
Test	Chi-Square	DF	Pr > ChiSq
Likelihood Ratio	2320.0981	23	<.0001
Score	2951.1657	23	<.0001
Wald	2749.4412	23	<.0001

Analysis of Maximum Likelihood Estimates								
Parameter	DF	Parameter Estimate	Standard Error	Chi-Square	Pr > ChiSq	Hazard Ratio	95% Hazard Ratio Confidence Limits	
POS	1	2.12446	0.12662	281.5149	<.0001	8.368	6.529	10.726
HIVTime	1	-0.00740	0.00151	24.0624	<.0001	0.993	0.990	0.996
psy2_1	1	-0.94159	0.28837	10.6621	0.0011	0.390	0.222	0.686
Psy2xTime	1	0.00656	0.00226	8.4159	0.0037	1.007	1.002	1.011
psy3_1	1	0.00220	0.37614	0.0000	0.9953	1.002	0.479	2.095
Psy3xTime	1	0.00265	0.00291	0.8311	0.3619	1.003	0.997	1.008
PSY2xHIV	1	-0.48840	0.28000	3.0425	0.0811	0.614	0.354	1.062
PSY3xHIV	1	-0.84786	0.38651	4.8120	0.0283	0.428	0.201	0.914
Age_Anal_Start	1	0.07250	0.00170	1814.6990	<.0001	1.075	1.072	1.079
race_cd	1	0.28775	0.04035	50.8568	<.0001	1.333	1.232	1.443
ethnicity	1	0.10987	0.35463	0.0960	0.7567	1.116	0.557	2.237
EDU1	1	0.13400	0.09583	1.9554	0.1620	1.143	0.948	1.380
EDU2	1	0.14217	0.04061	12.2551	0.0005	1.153	1.065	1.248
EMP1	1	0.21751	0.09337	5.4271	0.0198	1.243	1.035	1.493
EMP2	1	0.16557	0.18425	0.8075	0.3688	1.180	0.822	1.693
EMP1Time	1	-0.00221	0.0009730	5.1613	0.0231	0.998	0.996	1.000
EMP2Time	1	0.00126	0.00187	0.4535	0.5007	1.001	0.998	1.005
Pct_Life_Prison	1	-1.58422	0.13115	145.9029	<.0001	0.205	0.159	0.265
PSY2xEMP1	1	0.46056	0.22635	4.1401	0.0419	1.585	1.017	2.470
PSY2xEMP2	1	0.59515	0.26411	5.0781	0.0242	1.813	1.081	3.043
PSY3xEMP1	1	0.09082	0.32245	0.0793	0.7782	1.095	0.582	2.060
PSY3xEMP2	1	0.00124	0.35297	0.0000	0.9972	1.001	0.501	2.000
racexethn	1	-1.60539	0.51906	9.5661	0.0020	0.201	0.073	0.555

%COLLIN Macro, used to assess multicollinearity in PHREG:

```
OPTIONS MPRINT SYMBOLGEN;
%MACRO COLLIN(COVDSN=, PROCDR=, PARMINFO=);
%IF &PROCDR=GENMOD %THEN %DO;
DATA NEXT_1; SET &PARMINFO;
ATTRIB PARNUM FORMAT=$12.;
PARNUM=PARAMETER;
IF PARNUM = 'Prm1' THEN PARNUM = 'Prm01';
IF PARNUM = 'Prm2' THEN PARNUM = 'Prm02';
IF PARNUM = 'Prm3' THEN PARNUM = 'Prm03';
IF PARNUM = 'Prm4' THEN PARNUM = 'Prm04';
IF PARNUM = 'Prm5' THEN PARNUM = 'Prm05';
IF PARNUM = 'Prm6' THEN PARNUM = 'Prm06';
IF PARNUM = 'Prm7' THEN PARNUM = 'Prm07';
IF PARNUM = 'Prm8' THEN PARNUM = 'Prm08';
IF PARNUM = 'Prm9' THEN PARNUM = 'Prm09';
RENAME PARNUM=PARM;
RUN;
PROC SORT;
BY PARM;
RUN;
DATA NEXT_1A; SET &COVDSN;
ATTRIB PARM FORMAT=$12.;
PARM=ROWNAME;
IF PARM = 'Prm1' THEN PARM = 'Prm01';
IF PARM = 'Prm2' THEN PARM = 'Prm02';
IF PARM = 'Prm3' THEN PARM = 'Prm03';
IF PARM = 'Prm4' THEN PARM = 'Prm04';
IF PARM = 'Prm5' THEN PARM = 'Prm05';
IF PARM = 'Prm6' THEN PARM = 'Prm06';
IF PARM = 'Prm7' THEN PARM = 'Prm07';
IF PARM = 'Prm8' THEN PARM = 'Prm08';
IF PARM = 'Prm9' THEN PARM = 'Prm09';
RUN;
PROC SORT;
BY PARM;
RUN;
DATA NEXT_2(DROP=EFFECT); MERGE NEXT_1A(IN=IN1A) NEXT_1(IN=IN1);
BY
PARM; IF IN1A;
PARM=EFFECT;
RENAME PARM=_NAME_;
RUN;
%* IN SOME OUTPUT VARIANCE-COVARIANCE MATRICES, THERE WILL BE A
RECORD FOR;
%* SCALE. DELETE THIS RECORD.;
DATA NEXT_3; SET NEXT_2;
IF _NAME_='SCALE' THEN DELETE;
RUN;
```

```
%* INSERT A DUMMY RECORD FOR ESTIMATE TO SIMULATE COVARIANCE
OUTPUT
FROM LOGISTIC
%* AND PHREG.;
DATA NEXT_4;
_NAME_= 'ESTIMATE';
OUTPUT;
RUN;
DATA NEXT_5; SET NEXT_4 NEXT_3;
RUN;
proc print; run;
%END;
%ELSE %DO;

DATA NEXT_5; SET &COVDSN;
RUN;
%END;
proc print data=next_5; run;
%IF (NEXT_5 NE ) %THEN %DO;
OPTION MPRINT;
%LET __STOP=0;
PROC IML;
USE NEXT_5;
READ ALL VAR {_NAME_} INTO _VARNAME;
_NRVNAME=NROW(_VARNAME);
IF (_NRVNAME>1) THEN DO;
_VARNAM2=_VARNAME(|2:_NRVNAME, |);
NMISSING=J(NROW(_VARNAM2),1,.);
LABELS={"EIGENVAL","CONDINDX","  "};
_VARNAM2=LABELS//_VARNAM2;
FREE _VARNAME LABELS;
READ ALL VAR _NUM_ INTO VARCOV(|COLNAME=_NVNAME|);
_NRCVC=NCOL(VARCOV);
LASTVNAM=_NVNAME(|1,_NRCVC|);
IF (LASTVNAM="_LNLIKE_") THEN
VARCOV2=VARCOV(|2:_NRVNAME,1:_NRCVC-
1|);
IF (LASTVNAM^="_LNLIKE_") THEN VARCOV2=VARCOV(|2:_NRVNAME,|);
%* IF COVARIANCE MATRIX IS FROM PROC GENMOD USING THE REPEATED
MEASURES
DESIGN;
%* THEN THE LOWER DIAGONAL WILL HAVE THE CORRELATIONS AND THE
UPPER
DIAGONAL WILL HAVE;
%* THE COVARIANCES. THIS NEXT SECTION OF CODE REPLACES THE LOWER
DIAGONAL WITH THE UPPER;
%* DIAGONAL TO MAKE A SYMMETRIC COVARIANCE MATRIX. IF THE MATRIX
IS
SYMMETRICAL ALREADY;
%* THEN THE NEXT SECTION OF CODE WILL NOT AFFECT ANYTHING.;
VC2_C = NCOL(VARCOV2);
VC2_R = NROW(VARCOV2);
```

```
DO CL=1 TO VC2_C;
DO RW=1 TO VC2_R;
VARCOV2(|RW,CL|) = VARCOV2(|CL,RW|);
END;
END;
%* PRINT THE VARIANCE-COVARIANCE MATRIX FOR DIAGNOSTIC PURPOSES;
PRINT VARCOV2;
FREE VARCOV _NRCVC LASTVNAM VC2_C VC2_R CL;
COVBINV=INV(VARCOV2);
SCALE=INV(SQRT(DIAG(COVBINV)));
R=SCALE*COVBINV*SCALE;
FREE COVBINV SCALE;
CALL EIGEN(MUSQR,V,R);
FREE R;
SROOTMUS=SQRT(MUSQR);
CI=1/(SROOTMUS/MAX(SROOTMUS));
PHI=(V##2)*DIAG(MUSQR##(-1));
SUMPHI=PHI(|,+|);
PI=PHI#(SUMPHI##(-1));
FREE PHI SUMPHI SROOTMUS V;
FINAL=(MUSQR||CI||NMISSING||PI`)`;
FREE PI MUSQR CI NMISSING;
_NCFINAL=NCOL(FINAL);
_NRFINAL=NROW(FINAL);
FINAL2=J(_NRFINAL,_NCFINAL,0);
_NCFP1=_NCFINAL+1;
__VDP="VDP";
DO I=1 TO _NCFINAL;
FINAL2(|,_NCFP1-I|)=FINAL(|,I|);
X=CHAR(I,3);
Y=COMPRESS(CONCAT(__VDP,X));
IF I=1 THEN _VDPNAME=Y;
ELSE _VDPNAME=_VDPNAME||Y;
END;
FREE FINAL _NRFINAL _NCFINAL I X Y;
CREATE FINAL2 FROM FINAL2(|ROWNAME=_VARNAM2 COLNAME=_VDPNAME|);
APPEND FROM FINAL2(|ROWNAME=_VARNAM2|);
FREE _VARNAM2 _VDPNAME FINAL2;
END;
IF (_NRVNAME=1) THEN DO;
X="1";
CALL SYMPUT("__STOP",LEFT(X));
PRINT " ";
PRINT
"*********************************************************";
PRINT "YOU NEED TO SPECIFY THE COVOUT OPTION";
PRINT " IN EITHER PROC LOGISTIC OR PROC PHREG.";
PRINT " THIS PROGRAM WILL NOT CALCULATE COLLINEARITY
DIAGNOSTICS.";
PRINT
"*********************************************************";
PRINT " ";
```

```
END;
QUIT;
RUN;
%IF (&__STOP EQ 0) %THEN %DO;
PROC PRINT DATA=FINAL2 LABEL NOOBS;
ID _VARNAM2;
TITLE8 "COLLINEARITY DIAGNOSTICS FOR NONLINEAR MODELS USING";
TITLE9 "THE INFORMATION MATRIX: EIGENVALUES, CONDITION INDEXES,";
TITLE10 "AND VARIANCE DECOMPOSITION PROPORTIONS (VDP'S)";
LABEL _VARNAM2="VARIABLE";
RUN;
%END;
%END;
%ELSE %DO;
%PUT;
%PUT "*******************************************************";
%PUT "WHEN YOU INVOKE THIS MACRO, YOU HAVE TO SPECIFY THE NAME";
%PUT " OF A SAS DATA SET THAT CONTAINS THE VARIANCE-COVARIANCE";
%PUT " MATRIX FROM EITHER PROC LOGISTIC OR PROC PHREG.";
%PUT;
%PUT "YOU CAN CREATE THIS MATRIX BY INCLUDING THE FOLLOWING
OPTIONS";
%PUT " ON THE PROC STATEMENT: COVOUT AND OUTEST=SASDSN,";
%PUT " WHERE SASDSN IS THE NAME OF THE SAS DATA SET CONTAINING";
%PUT " THE VARIANCE-COVARIANCE MATRIX.";
%PUT "*******************************************************";
%PUT;
%END;
PROC DATASETS;
DELETE NEXT_1 NEXT_1A NEXT_2 NEXT_3 NEXT_4 NEXT_5;
RUN;
QUIT;
%MEND;
```

Model Diagnostics – Schoenfeld and Deviance Residuals Assessment

```
/* FINAL model after confounding assessment*/
proc phreg data= t.TOS_1998;
model TOS_STOP1*death(0)=

/*Exposure Variables*/
POS HIVTime Psy2_1 Psy2xTime psy3_1 Psy3xTime PSY2xHIV PSY3xHIV

/* Confounders */
AGE_ANAL_START race_cd ethnicity EDU1 EDU2 EMP1 EMP2 EMP1Time
EMP2Time PCT_LIFE_PRISON

/*PSY Interaction*/
PSY2xEMP1 PSY2xEMP2   PSY3xEMP1 PSY3xEMP2

/*Other Interaction*/
racexethn

/ risklimits=wald;

/* Define Interaction Terms */
HIVTime = POS*TOS_STOP1;
PSY2xHIV = Psy2_1*POS;
PSY3xHIV = Psy3_1*POS;
Psy2xTime= TOS_STOP1*psy2_1;
Psy3xTime= TOS_STOP1*psy3_1;
PSY2xEMP1 = PSY2_1*EMP1;
PSY2xEMP2 = PSY2_1*EMP2;
PSY3xEMP1 = PSY3_1*EMP1;
PSY3xEMP2 = PSY3_1*EMP2;
racexethn = race_cd*ethnicity;
EMP1Time=TOS_STOP1*EMP1;
EMP2Time=TOS_STOP1*EMP2;

/*Test Time Interaction with LR Test*/
Proportion_Test_Time_Interaction : test HIVTime, Psy2xTime,
Psy3xTime, EMP1Time, EMP2Time;
run;
```

Time interaction test is significant:

Linear Hypotheses Testing Results			
Label	Wald Chi-Square	DF	Pr > ChiSq
Proportion_Test_Time_Interaction	41.9962	5	<.0001

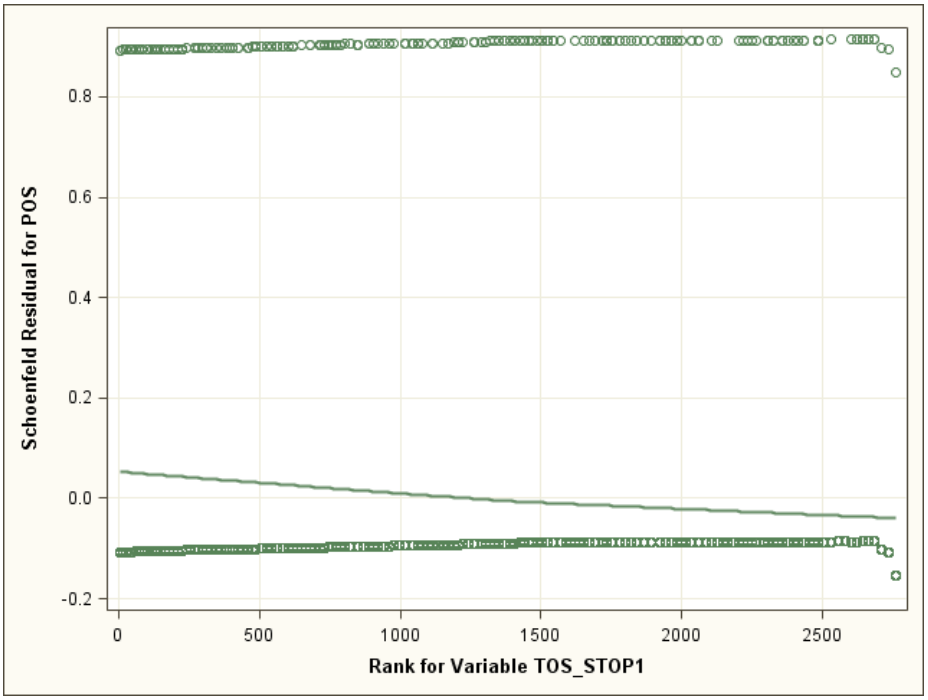
Final model reduced to exclude time dependent interaction in order to facilitate a proxy diagnostics test:

```
ods graphics on / ANTIALIASMAX=22400;
proc phreg data= t.TOS_1998 covout outest=phreg1;
model TOS_STOP1*death(0)=

/*Exposure Variables*/
POS /*HIVTime*/ Psy2_1 /*Psy2xTime*/ psy3_1 /*Psy3xTime*/
PSY2xHIV PSY3xHIV

/*Confounders*/
AGE_ANAL_START race_cd ethnicity EDU1 EDU2 EMP1 EMP2 /*EMP1Time
EMP2Time*/ PCT_LIFE_PRISON

/*psy Interaction*/
PSY2xEMP1 PSY2xEMP2 PSY3xEMP1 PSY3xEMP2

/*Other Interaction*/
racexethn

/ risklimits=wald ties=exact;

/* Define Interaction Terms */
/*HIVTime = POS*TOS_STOP1;*/
PSY2xHIV = Psy2_1*POS;
PSY3xHIV = Psy3_1*POS;
/*Psy2xTime= TOS_STOP1*psy2_1;
Psy3xTime= TOS_STOP1*psy3_1;*/
PSY2xEMP1 = PSY2_1*EMP1;
PSY2xEMP2 = PSY2_1*EMP2;
PSY3xEMP1 = PSY3_1*EMP1;
PSY3xEMP2 = PSY3_1*EMP2;
racexethn = race_cd*ethnicity;
/*EMP1Time=TOS_STOP1*EMP1;
EMP2Time=TOS_STOP1*EMP2;*/
output out=RESIDUAL_PLOTS ressch=SCH1-SCH18 wtressch=wtsch1-
wtsch18 ressco=sco1-sco18 xbeta=Xb resmart=Mart resdev=Dev
lmax=influence;

run;

DATA FAILED;
SET RESIDUAL_PLOTS;
WHERE death =1;
RUN;

PROC RANK DATA=FAILED OUT=RANKED TIES=MEAN;
VAR TOS_STOP1;
RANKS TIMERANK;
RUN;
```

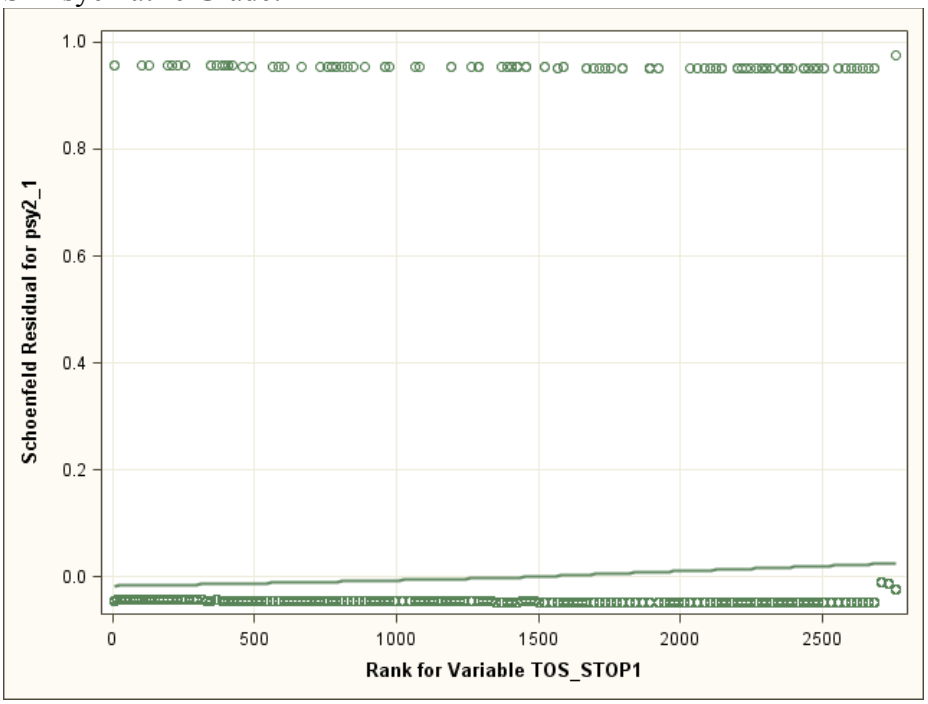
```
PROC CORR DATA=RANKED NOSIMPLE;        /* Schoenfeld Correlates */
WITH TIMERANK;
VAR SCH1-SCH18;
RUN;

/* Plot Significant Schoenfeld Correlations vs. event-ranked
deaths*/
PROC SGSCATTER DATA=RANKED;            /* POS */
PLOT SCH1*TIMERANK / LOESS GRID; title "Schoenfeld Residual Plots
for POS";
PROC SGSCATTER DATA=RANKED;            /* PSY2 */
PLOT SCH2*TIMERANK / LOESS GRID; title "Schoenfeld Residual Plots
for PSY2";
PROC SGSCATTER DATA=RANKED;            /* EMP1 */
PLOT SCH11*TIMERANK / LOESS GRID; title "Schoenfeld Residual
Plots for EMP1";
PROC SGSCATTER DATA=RANKED;            /* EMP2 */
PLOT SCH12*TIMERANK / LOESS GRID; title "Schoenfeld Residual
Plots for EMP2";
PROC SGSCATTER DATA=RANKED;            /* PSY2*EMP2*/
PLOT SCH15*TIMERANK / LOESS GRID; title "Schoenfeld Residual
Plots for PSY2xEMP2";
run;
```

Continued on next page

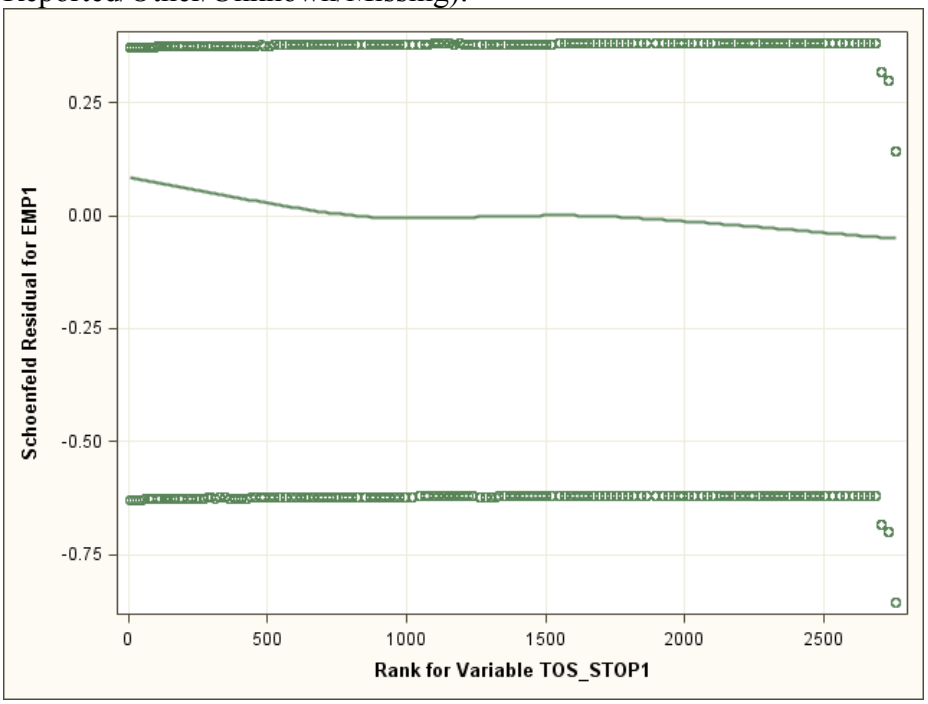
Output for Schoenfeld residuals, significant correlations shown
HIV Status:



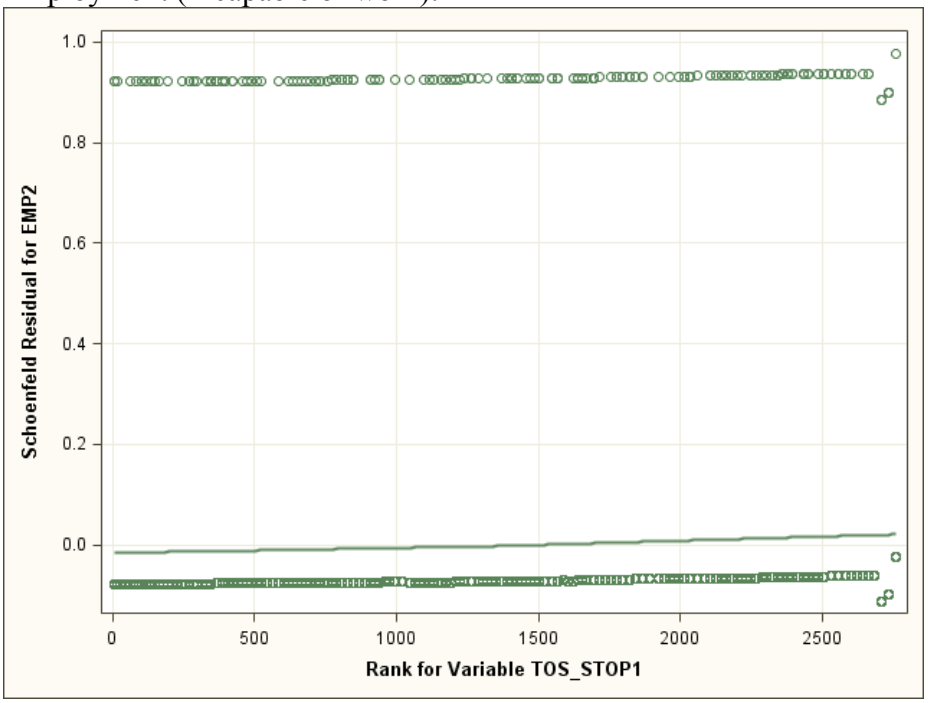
S2 Psychiatric Grade:



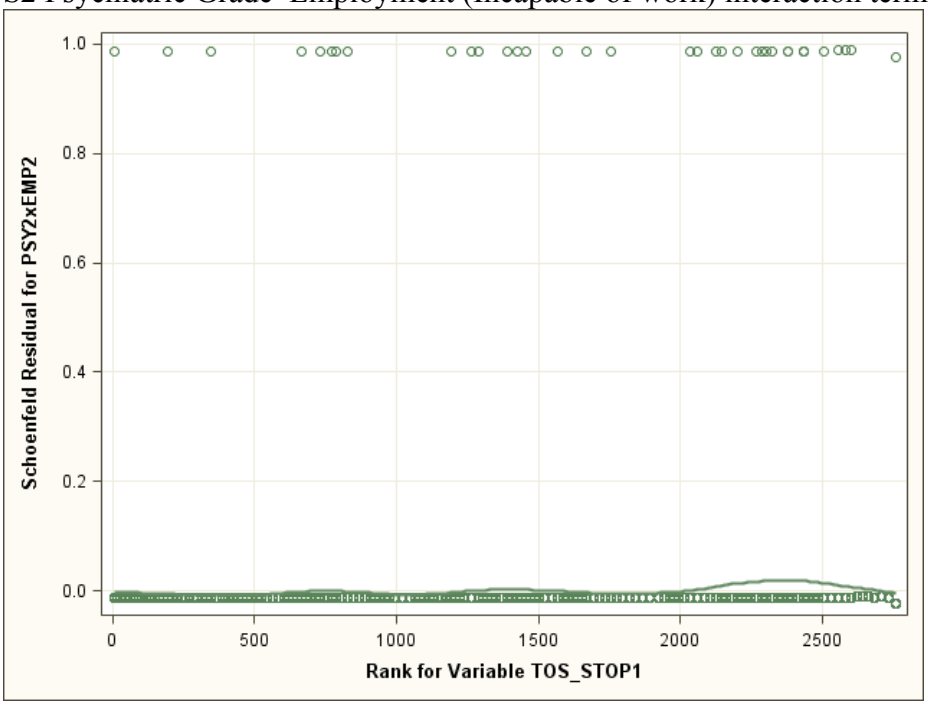
Employment (Never worked/Unemployed (for <6 and 6+ months) or Not Reported/Other/Unknown/Missing):



Employment (Incapable of work):



S2 Psychiatric Grade*Employment (Incapable of work) interaction term:

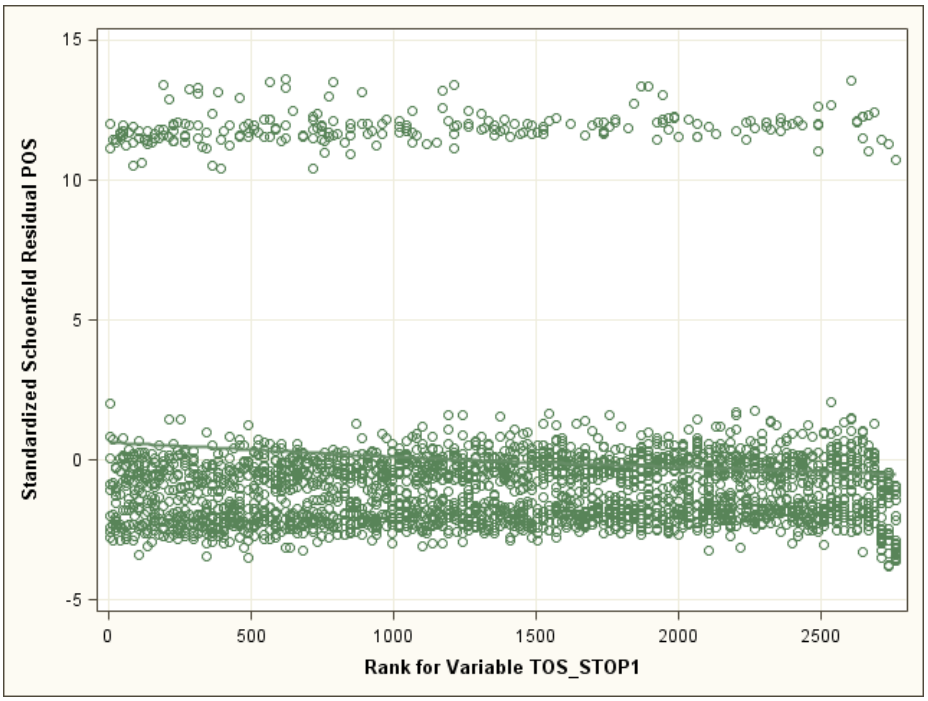


Plots of significant residuals for HIV, Employment, and S2 Psychiatric grade each show ~linear trend that would be accounted for by time dependent interaction terms (e.g. HIV status*Time on Study). These time dependent interactions are each present in the final model.

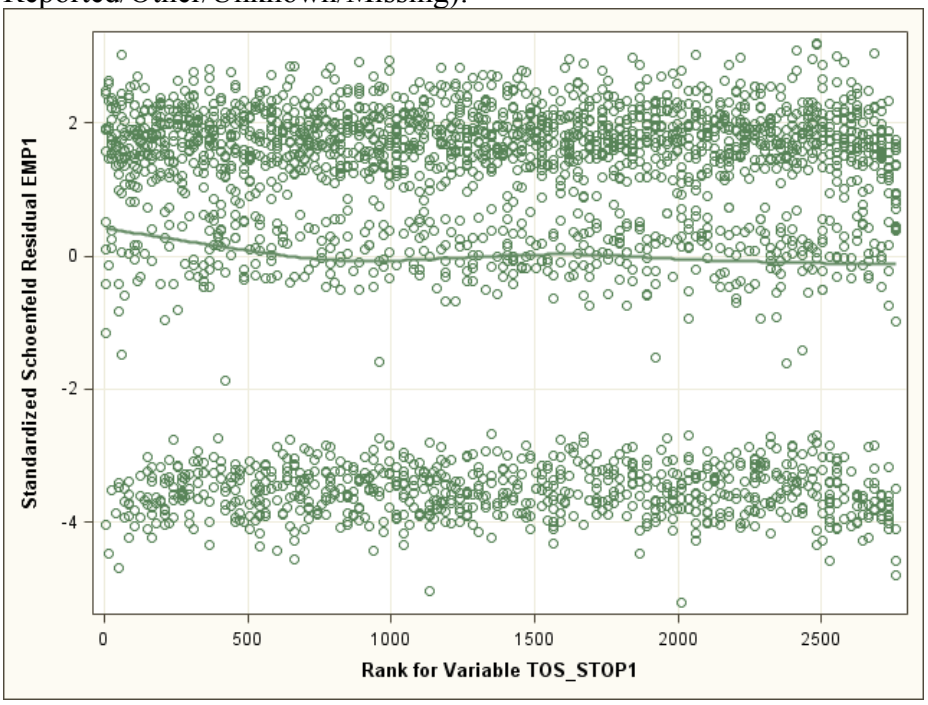
Standardized Schoenfeld Residuals:

```
PROC CORR DATA=RANKED NOSIMPLE;  /* Weighted Schoenfeld */
WITH TIMERANK;
VAR wtsch1-wtsch18;
RUN;

/* Plot Significant Weighted Schoenfeld Correlations vs. event-
ranked deaths */
PROC SGSCATTER DATA=RANKED;            /* POS */
PLOT wtsch1*timerank / LOESS GRID; title "Standardized Schoenfeld
Residual Plots for POS";
PROC SGSCATTER DATA=RANKED;            /* EMP1 */
PLOT wtsch11*timerank / LOESS GRID; title "Standardized
Schoenfeld Residual Plots for EMP1";
```

Output for weighted Schoenfeld residuals, significant correlations shown
HIV Status:

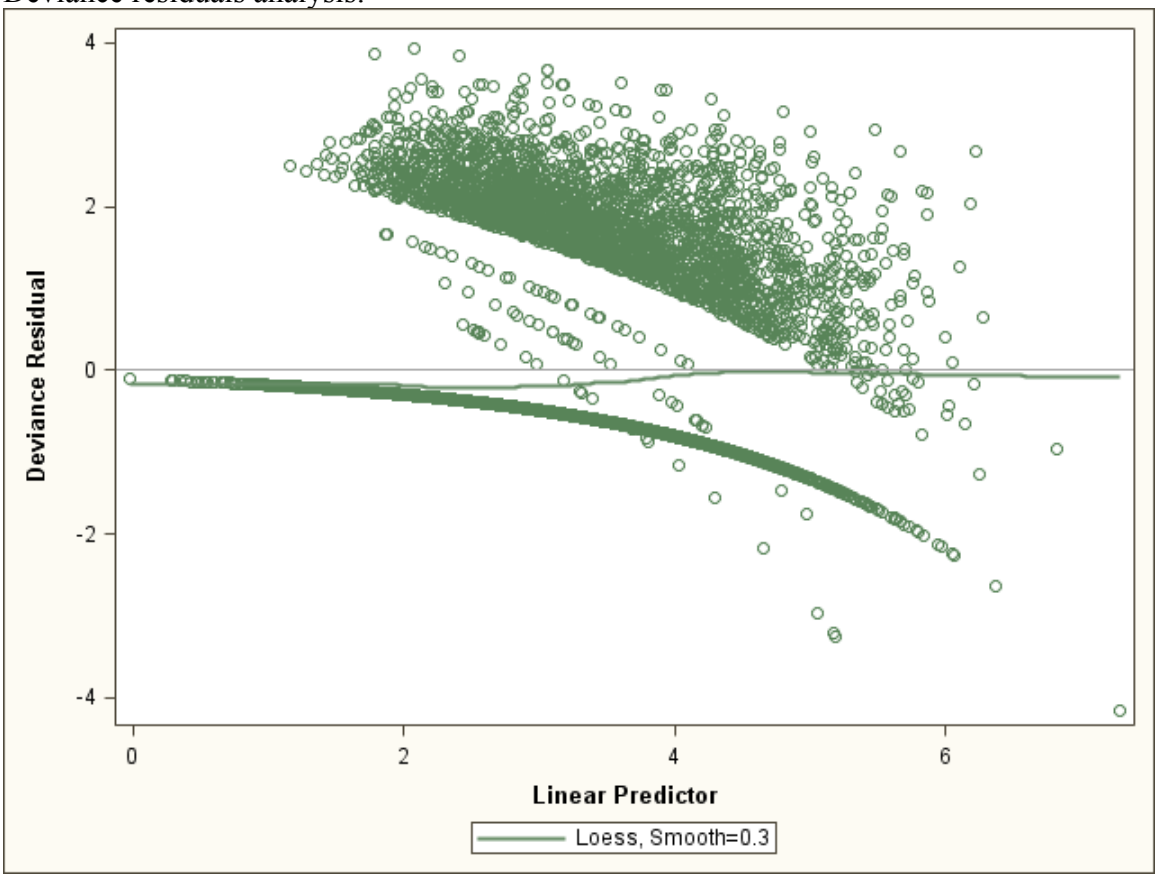


Employment (Never worked/Unemployed (for <6 and 6+ months) or Not Reported/Other/Unknown/Missing):



Plots of significant residuals for HIV and Employment each show ~linear trend that would be accounted for by time dependent interaction terms (e.g. HIV status*Time on Study). These time dependent interactions are each present in the final model.

Deviance residuals analysis:



Residual analysis of reduced model indicates that the final model with time dependent interaction terms will likely benefit from the inclusion of time dependent terms.

Sensitivity Analysis:
To assess the robustness of the final model and the potential impact of the lack of an HIV diagnosis on mortality, a sensitivity analysis was performed with an updated HIV status variable that redefined those listed as dying of HIV as HIV infected.

Final model fit statistics:

Model Fit Statistics		
Criterion	Without Covariates	With Covariates
-2 LOG L	54008.620	51704.108
AIC	54008.620	51750.108
SBC	54008.620	51886.345

Testing Global Null Hypothesis: BETA=0			
Test	Chi-Square	DF	Pr > ChiSq
Likelihood Ratio	2304.5117	23	<.0001
Score	2946.0843	23	<.0001
Wald	2742.7981	23	<.0001

Expanded Definition Model Output:

Model Fit Statistics		
Criterion	Without Covariates	With Covariates
-2 LOG L	54008.620	51561.471
AIC	54008.620	51607.471
SBC	54008.620	51743.708

Testing Global Null Hypothesis: BETA=0			
Test	Chi-Square	DF	Pr > ChiSq
Likelihood Ratio	2447.1489	23	<.0001
Score	3194.7707	23	<.0001
Wald	2911.4944	23	<.0001

$-2*\ln(L_F/L_R) = 2447.1489 - 2304.5117 =$ **142.6372**

Expanded definition model provides better fit to mortality data.