Assessing HIV/AIDS Treatment: Monotherapy vs. Combination Therapy Effects on Time-to-AIDS Diagnosis

Jiachen Ai[1], Peike Li[1], Hsin Ying (Angel) Tseng[1], and Yingxin Zhang[1]
[1] University of California, Los Angeles

Introduction

The HIV/AIDS epidemic remains a crucial public health issue in society, where formative research is needed to improve patient health outcomes and well-being [1]. Numerous treatments have been developed over the years to optimize patient health and increase their survival outcomes. One approach would be to combine different treatments that adapt the usages of multiple drugs or interventions simultaneously. For instance, prior research has examined the effectiveness of actively used HIV/AIDS treatment drugs of zidovudine (AZT) with the combinations of zalcitabine (ddc) or didanosine (ddl) [2]. Combination therapy thus becomes a prevalent treatment application for HIV/AIDS.

However, there have also been adherence issues with persons with HIV/AIDS receiving combination therapy [3]. Prior studies [4,5] showed they may struggle to adhere to treatment guidelines in combination therapy, leading to unsuccessful treatments. With the intent to provide to patients the most effective treatment, this study hopes to clarify whether it is necessary to adapt combination therapy using these treatment drugs. In expanding on existing research, we aim to analyze whether treatment effects on survival using monotherapy is sufficient, or if the effect of combination therapy is significant such that it should be administered. Furthermore, stigma towards persons with HIV/AIDS based on their sexual orientation has always been a prevalent cultural concern [6]. The study shall also explore sexual orientation as a potential factor along with other demographic variables in influencing the impact on treatment effects, contributing to understanding future treatment approaches for living persons with HIV/AIDS.

Methods & Materials

A. Study Population

The target population of this study is current HIV-infected persons without AIDS living in the United States. To be included in this study, participants must have HIV but have not developed AIDS. Patients with current AIDS-related conditions other than minimal Kaposi sarcoma (KS), grade 2 or worse peripheral neuropathy, and malignancy requiring systemic therapy are excluded from the study [2]. If the patient is actively taking other medications of other anti-HIV drugs,

biologic response modifiers other than recombinant erythropoietin (rEPO) and granulocyte colony-stimulating factor (G-CSF), systemic cytotoxic chemotherapy, chronic systemic corticosteroids, or any drug that affects AZT glucuronidation or clearance, then they were also excluded from the study [2]. Additional exclusion criteria included currently receiving radiotherapy other than limited local therapy to skin and acute therapy for an infection or other medical illness within the past 14 days prior to enrollment into the study.

B. Dataset

In this project we use a dataset from the AIDS Clinical Trials Group Study 175, a randomized, double-blind phase II/III trial of monotherapy versus combination therapy for people living with HIV. This is a publicly available dataset containing clinical and demographic information from patients undergoing antiretroviral therapy for HIV/AIDS. The dataset contains 2,139 observations without missing values. Main variables used for analysis are displayed in Table 1.

We can see that overall, the study sample is made up of 82% males and 18% females with the mean age of 35.2 (SD = 8.7). 71% of the participants identified as White and 29% of the participants identified as non-White. For other interested risk factors, 66% of the participants

Table 1: Base-Line Characteristics of the Patients According to the Therapy Strategy*

Characteristic	**All Patients** (N=2139)	**Monotherapy** (N=1093)	**Combination Therapy** (N=1046)
Male sex — no. (%)	1771 (82)	902 (83)	869 (83)
Age — yr	35.2 ± 8.7	35.2 ± 8.7	35.3 ± 8.7
Race or ethnic group — no. (%)			
White	1522 (71)	764 (70)	758 (72)
non-White	617 (29)	329 (30)	288 (28)
Risk factors — no. (%)†			
Homosexuality	1414 (66)	720 (66)	694 (66)
Injection-drug use	281 (13)	132 (12)	149 (14)
Length of prior antiretroviral therapy — no. (%)			
Naive	886 (41)	461 (42)	425 (41)
> 1 but ≤ 52	410 (19)	198 (18)	212 (20)
> 52	843 (39)	434 (40)	409 (39)
Karnofsky score of 100 — no. (%)	1263 (59)	629 (58)	634 (61)
Symptomatic HIV infection — no. (%)‡	370 (17)	185 (17)	185 (18)
CD4 cell count — cells/mm^3§	351 ± 119	350 ± 114	351 ± 123
CD8 cell count — cells/mm^3	987 ± 480	979 ± 489	994 ± 471

*Plus-minus values are means ± SD. Because of rounding, not all columns total 100 percent.
† Patients could have more than one risk factor. Only major risk factors are shown here.
‡ An infection was considered symptomatic if candidiasis, oral hairy leukoplakia, or herpes zoster was reported within 30 days before randomization.
§The values are the mean of two measurements made at least three days apart. Values obtained at screening, which had to be 200 to 500 cells per cubic millimeter, were excluded.

stated their sexual orientation is homosexuality and 13% have had drug usage from injection. As for prior antiretroviral therapy status, 41% of the participants reported having not received antiretroviral therapy before, 19% reported having received the therapy but not more than a year, and 39% reported receiving the therapy for more than a year. Karnosky score is a measure of functional impairment in daily activities, and 59% of participants had a score of 100, which means no impairment.

C. Statistical Methods

1. Survival Comparison

1.1 Kaplan-Meier Estimator

Kaplan-Meier (KM) survival analysis was conducted to estimate and compare the survival probabilities between two treatment groups: monotherapy and combination therapy. To conduct initial exploratory analysis, we compared the KM curves of the two treatment groups with a graph. The survival function $S(t)$ at a given time t was estimated using the Kaplan-Meier estimator:

$$\widehat{S}(t) = \prod_{t_i \leq t} (1 - \frac{d_i}{n_i})$$

where t_i represents the time of each observed event, d_i is the number of AIDS diagnosis or the number of people with clusters of differentiation 4 (CD4) cell counts drop below 50% occurring at t_i, and n_i is the number of individuals at risk just before t_i. The estimated survival curves were plotted with survival probability on the y-axis and time in days on the x-axis.

1.2 Log-Rank Test

To statistically compare the survival distributions, a log-rank test was performed. The test compares the observed number of AIDS diagnoses or the number of people with CD4 cell counts drop below 50% to the expected number under the null hypothesis of no difference in survival between treatment groups. The test statistic follows a chi-square distribution with one degree of freedom. Further stratified log rank tests were performed to test whether gender and sexual orientation are confounders to the treatment effect on survival. These tests allow us to examine the treatment effect in different gender and sexual orientation groups, detecting potential interactions. The test statistics follow a chi-square distribution with one degree of freedom.

2. Models

2.1 Variable Selection

Because we have numerous covariates of interest, we decided to use variable selection methods to identify an optimal subset of variables prior to fitting models. We applied stepwise AIC, stepwise BIC, and LASSO, each offering distinct advantages. Akaike Information Criterion (AIC) balances model fit and complexity by penalizing additional parameters. In contrast, Bayesian Information Criterion (BIC) applies a stronger penalty for model size, favoring more parsimonious models and improving interpretability. LASSO (Least Absolute Shrinkage and Selection Operator) performs variable selection by imposing an L_1-penalty, shrinking less informative coefficients to zero, thereby enhancing model sparsity and stability in high-dimensional settings.

2.2 Model Comparison

For our analysis, we used the Cox proportional hazards (PH) model and the accelerated failure time (AFT) model to analyze models with multiple covariates. The Cox PH model estimates the hazard function as $\lambda(t|\mathbf{x}_i) = \lambda_0(t)\exp(\mathbf{x}_i^T\boldsymbol{\beta})$ that assumes a constant hazard ratio across time. We will fit a Cox PH model using specified covariates on the survival time to AIDS diagnosis or when the CD4 cell count drops below 50%. Wald, Score, and Likelihood Ratio tests were also done to test for whether there is a treatment difference between monotherapy and combination therapy. Model assumptions on Cox's PH can be tested using a time-dependent covariate, $Treatment_2(t_i) = Treatment \times log(t_i)$, and evaluating its significance. Graphical diagnostics including the baseline cumulative hazard plot, Anderson plot, and Schoenfeld residuals plot were also created to visually assess deviations from proportional hazards. If the Cox's PH assumption is not satisfied, the AFT model will be fitted assuming $log(t_i) = \mathbf{x}_i^T\boldsymbol{\beta} + \sigma W_i$, where $W_i \overset{\text{iid}}{\sim} f$ and f is a specific distribution. To determine the most appropriate AFT model, we considered multiple distributional assumptions for W_i, including Exponential, Weibull, Logistic, Log-Logistic, Gaussian, and Log-Normal. To assess the log-linearity assumption of the AFT model, we examine the residuals, defined as, $\hat{\epsilon} = \dfrac{log(T_i) - \hat{\mu}_i}{\hat{\sigma}}$, where T_i is the observed survival time, $\hat{\mu}_i$ is the predicted survival time, and $\hat{\sigma}$ is the estimated scale parameter of the AFT model. A close alignment between the Kaplan-Meier curve and $S_{\text{theoretical}}(\epsilon)$ supports the validity of the AFT model.

2.3 Goodness-of-Fit

Cox-Snell residuals, defined as $r_i = -log(\hat{H}(t_i))$, are used for assessing an overall check for lack of fit of the Cox PH model as well as the fitted AFT models. If the model was correct and the estimated regression coefficients β are close to the true values of β, then the Cox-Snell residuals follow a unit exponential distribution. By plotting the Nelson-Aalen estimator, defined as $\hat{H}(r_i) = \sum_{t_j \leq t_i} \frac{\delta_j}{n_j}$, with Cox-Snell residuals, we can check whether the residuals follow an exponential(1) distribution. We expect the plot should follow a 45-degree reference line if the Cox model that we fit was appropriate.

2.4 Prediction Accuracy Diagnostics

Harrell's C-index (also known as the concordance index) introduced in Harrell et al.[7] and censoring-adjusted C-statistics proposed by Uno et al.[8], are goodness of fit measures for models which produce risk scores. They are commonly used to evaluate risk models in survival analysis, where data may be censored. We would use these metrics to evaluate our models' accuracy performance.

Results

1. Survival Comparison

1.1 Kaplan-Meier Curves

The Kaplan-Meier estimated survival curves of the two groups indicate that patients receiving combination therapy tended to have higher survival probabilities over time compared to those receiving monotherapy, as shown in Figure 1. Within approximately the first 200 days, both groups had similar survival probability, but the monotherapy group then displayed a more rapid decline in survival probability as time progressed. By the end of the study, the combination therapy group had a higher survival probability than the monotherapy group, suggesting a potential benefit of combination therapy in improving patient outcomes.

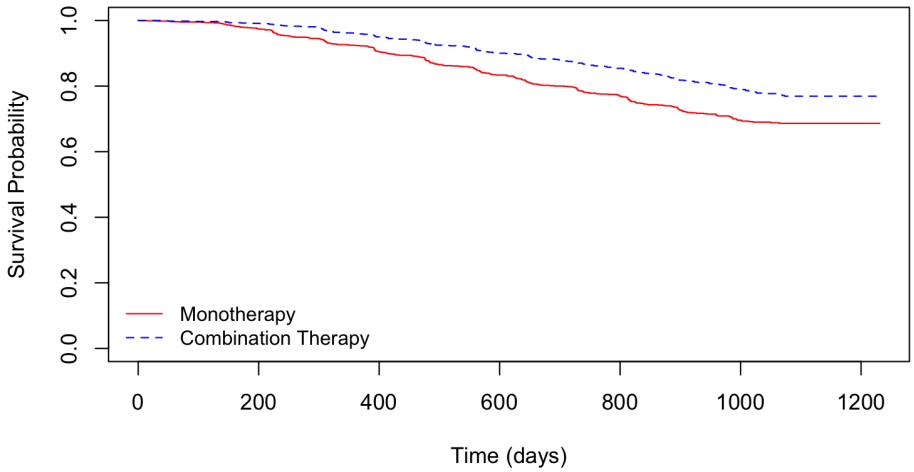

Figure 1. Estimated Survival Function for Two Treatment Groups

1.2 Log-Rank Test

Using the log-rank test, we conclude that there is a significant difference in survival between the two treatment groups ($\chi^2(1) = 22.40$, $p < 0.001$), consistent with the KM curves observations.

Because the sample's distribution was not balanced between females and males, we performed subgroup analysis on sex. The survival between treatment groups were compared for females and males, followed by a stratified log-rank test adjusting for sex. For females, there was a significant difference in survival between the treatment groups ($\chi^2(1) = 5.6$, $p = 0.02$), suggesting a survival benefit with combined therapy for females. For males, a significant survival difference was also observed between treatment groups ($\chi^2(1) = 17.3$, $p < 0.001$), meaning a larger survival benefit with combined therapy for males. When adjusting for sex using a stratified log-rank test, the survival benefit of treatment remained significant ($\chi^2(1) = 22.5$, $p < 0.001$), indicating the treatment is associated with better survival outcomes across both sexes. The test results allow us to conclude the effect of treatment is significant regardless of sex, with a potentially stronger effect in males given the larger chi-square statistic.

Similarly, when adjusting for sexual orientation using a stratified log-rank test, the effect of treatment is significant regardless of sexual orientation ($\chi^2(1) = 22.5$, $p < 0.001$), with a stronger effect in subjects with homosexual activities ($\chi^2(1) = 17.3$, $p < 0.001$) compared to subjects with no homosexual activities ($\chi^2(1) = 22.5$, $p = 0.002$). Overall, the log rank tests demonstrated a significant effect of combined therapy in survival and have no indication of potential interaction between treatment and demographic factors of sex and sexual orientation.

2. Model

2.1 Variable Selection

From the covariates potentially associated with survival, we performed variable selection among the 17 available predictors using AIC, BIC, and LASSO, which can be seen in Table 2. Methods of AIC selected 11 variables, BIC retained seven variables, and the LASSO identified 13 variables.

The exploratory regression among variables selected by all three methods indicated that homosexuality and race did not significantly impact survival time, likely due to cohort imbalance. We opted for the AIC-selected model, which balances model complexity and goodness-of-fit. The final model includes age, history of IV drug use, Karnofsky score, prior non-zidovudine antiretroviral therapy, prior zidovudine treatment in the past 30 days, prior antiretroviral therapy length, symptoms of AIDS, off-treatment between 91 and 101 weeks, CD8 cell count at baseline, CD8 cell count between 15 and 25 weeks, and treatment, the primary variable of interest.

Table 2: Variable Selection Results

Stepwise AIC	**Stepwise BIC**	**LASSO**
		Age,
Age,		Homosexual activity,
History of IV drug use,		History of IV drug use,
Karnofsky score,	Karnofsky score,	Karnofsky score,
Prior Non-ZDV antiretroviral therapy,	Prior anti-retroviral therapy days,	Prior Non-ZDV antiretroviral therapy,
Prior ZDV in the 30 days,	Symptom,	Prior ZDV in the 30 days,
Prior anti-retroviral therapy days,	Off-treatment before 96±5 weeks,	Prior anti-retroviral therapy days,
Symptom,	CD8 at baseline,	Race,
Off-treatment before 96±5 weeks,	CD8 at 20±5 weeks,	Symptom,
CD8 at baseline,	Treatment	Off-treatment before 96±5 weeks,
CD8 at 20±5 weeks,		CD8 at baseline,
Treatment		CD8 at 20±5 weeks,
		Treatment

2.2 Model Comparison

With the variable selection results, we then fitted a Cox PH model with the selected variables, along with sex and sexual orientation because they were factors of interest based on prior literature. Through the Wald test, we see a significant effect from the treatment on survival ($\chi^2(12) = 23.90$, $p = 0.02$). The Score test ($\chi^2(2) = 24.27$, $p < 0.001$) and the Likelihood Ratio test ($\chi^2(2) = 24.36$, $p < 0.001$) also showed the same results, where we failed to reject the null hypothesis and conclude that the treatment effect between monotherapy and combination therapy is significant.

For model diagnostics, we assessed the proportional hazards assumption of Cox's model using a time-dependent covariate of treatment into the model and evaluating its significance. The resulting coefficient yielded a *p*-value of 0.01, suggesting a violation of the proportional hazards assumption as shown in Figure A1 in Appendix. Graphical diagnostics further confirmed this, as illustrated in Figure 2 below. Specifically, the baseline cumulative hazard plot (Figure 1.a) showed non-parallel stratified curves, with an early crossing, suggesting non-proportionality for the model. The Anderson plot from Figure 1.b exhibited deviations from the expected straight line through the origin, with the observed curve falling predominantly below the reference, further supporting the violation of the PH assumption. Schoenfeld residuals plot for treatment (Figure 1.c) had an upward trend, indicating that the effect of the covariate changes over time. All model diagnostic findings led us to determine that the AFT model was a more suitable framework for analyzing this dataset.

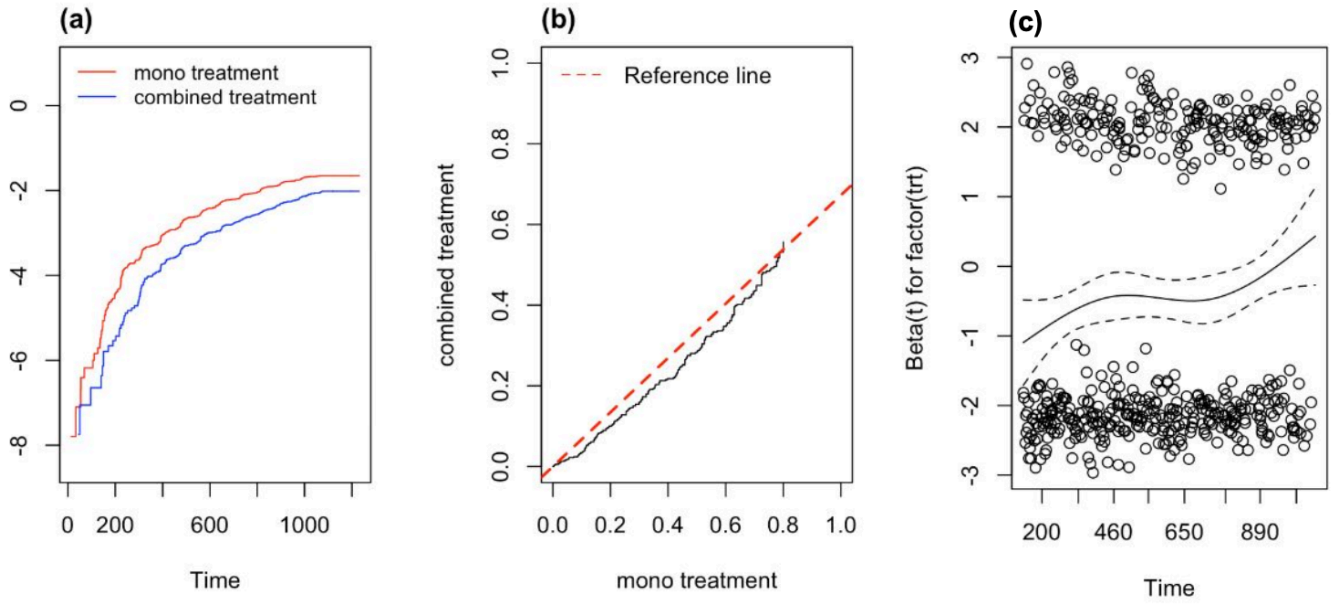

Figure 2. Graphical checking violation of PH assumption for Cox's model. (a) baseline cumulative hazard plot (b) Anderson plot (c) Schoenfeld residuals plot for treatment

2.3 Goodness of Fit

A goodness of fit assessment was also done using Cox-Snell Plot for the fitted Cox PH model. The plot in Figure 3 reveals the curve does not follow a 45-degree line. This means that the fitted Cox PH model was indeed not appropriate for representing the data, with its lack of fit.

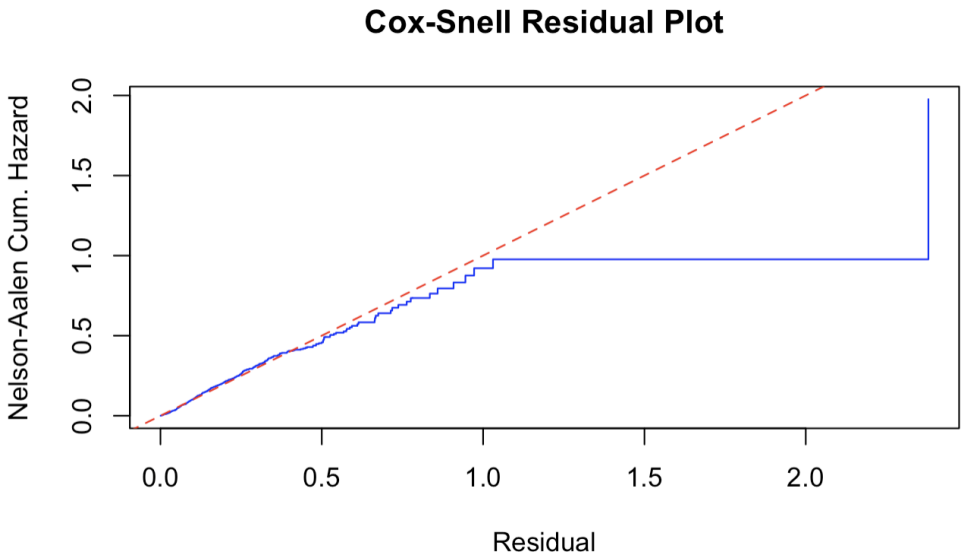

Figure 3. Cox-Snell plot for fitted Cox PH model diagnostics

3. Final Model

3.1 Goodness-of-fit of AFT Models

For determining an appropriate distribution for our AFT model, we constructed and compared Cox-Snell residual plots for exponential, Weibull, logistic, log-logistic, Gaussian, and log-normal AFT models to evaluate the goodness of fit, results are illustrated in Figure 4. In a well-fitted model, the Nelson-Aalen cumulative hazard estimate of the Cox-Snell residuals should align closely with the 45-degree reference line, indicating adherence to the unit exponential distribution. Among all models, the log-normal AFT model portrayed the best fit, particularly in the early and mid-range of survival times, where data is more reliable. While deviations appear in the tail of the distribution, these are likely due to higher variance and limited observations in later survival times, a common issue in survival analysis. To evaluate the log-linearity assumption of the log-normal AFT model, we examined residuals against the standard normal survival function (Figure 5). The residual plots show alignment with the expected pattern, suggesting that the log-normality of survival times and the linear predictor's adequacy hold.

3.2 Estimation

With our fitted log-normal AFT model, we observe that IV drug use history (TR [time ratio] = e^{β} = 1.31; 95% CI [confidence interval]: 1.09 - 1.59; $p = 0.005$), functional impairment (TR = 1.01; 95% CI: 1.01 - 1.03; $p < 0.001$), prior zidovudine treatment in the past 30 days (TR = 0.82; 95% CI: 0.70 - 0.96; $p = 0.01$), prior antiretroviral therapy treatment length (TR = 1.00; 95% CI: 1.00 - 1.00; $p = 0.046$), symptoms of AIDS (TR = 0.67; 95% CI: 0.58 - 0.78; $p < 0.001$), off-treatment

between 91 and 101 weeks (TR = 0.57; 95% CI: 0.50 - 0.64; $p < 0.001$), CD8 cell count at baseline (TR = 1.00; 95% CI: 0.99 - 1.00; $p < 0.001$), CD8 cell count between 15 and 25 weeks (TR = 1.00; 95% CI: 1.00 - 1.00; $p < 0.001$), and treatment (TR = 1.42; 95% CI: 1.26 - 1.61; $p < 0.001$) are all significant factors contributing to time to AIDS diagnosis, as shown in Table 3.

We can infer that the combination therapy group has a survival time of AIDS diagnosis that is approximately 42% longer than that of the monotherapy group, while controlling for other predictors. The patients with IV drug use history have a longer survival time of 31% than those who do not have a history of IV drug use, with other predictors constant. One unit of increase in Karnofsky score (functional impairment) will prolong patients' survival time by 1.7% adjusting by other covariates. And for one cell increase in the CD8 cell count at baseline, the expected survival time to AIDS diagnosis changes by about -0.001%, with other factors constant. Similarly, the expected survival time increases by about 0.001% when there is a one cell increase in CD8 cell count between 15 and 25 weeks, adjusting for other predictors. Additionally, symptomatic patients have approximately 33% shorter survival time compared to that of asymptomatic patients when controlling for other covariates. Patients who are off treatment between 91 and 101 weeks have approximately 43% shorter survival time than that of patients who are not off treatments, while controlling for other predictors. And for patients who have had prior zidovudine treatment in the past 30 days, their survival time to AIDS diagnosis is 18% shorter than that of patients who had not received this treatment in the past 30 days when other factors were adjusted. Finally, a one day increase in prior antiretroviral therapy length would increase the survival time by approximately 0.001% as well, with other predictors constant.

Table 3: Final LogNormal AFT model

Characteristic	Value	exp(value)	95% CI of exp(value)	P-value
Intercept	6.596	732.453	[264.916, 2025.124]	< 0.001**
Age	-0.006	0.994	[0.987, 1.000]	0.068
History of IV drug use	0.273	1.314	[1.087, 1.589]	0.005**
Karnofsky score	0.017	1.017	[1.007, 1.027]	< 0.001**
Prior Non-ZDV antiretroviral therapy	-0.272	0.762	[0.530, 1.094]	0.140
Prior ZDV in the 30 days	-0.202	0.817	[0.696, 0.959]	0.013*
Prior anti-retroviral therapy days	0.0002	1.000	[1.000, 1.000]	0.046*
Symptom	-0.401	0.670	[0.578, 0.777]	< 0.001**
Off-treatment before 96±5 weeks	-0.570	0.565	[0.499, 0.640]	< 0.001**
CD8 at baseline	-0.0004	1.000	[0.999, 1.000]	< 0.001**
CD8 at 20±5 weeks	0.0004	1.000	[1.000, 1.001]	< 0.001**
Treatment	0.353	1.423	[1.262, 1.606]	< 0.001**
log(scale)	0.043	1.044	[1.007, 1.081]	0.222

*Significant; ** extremely significant

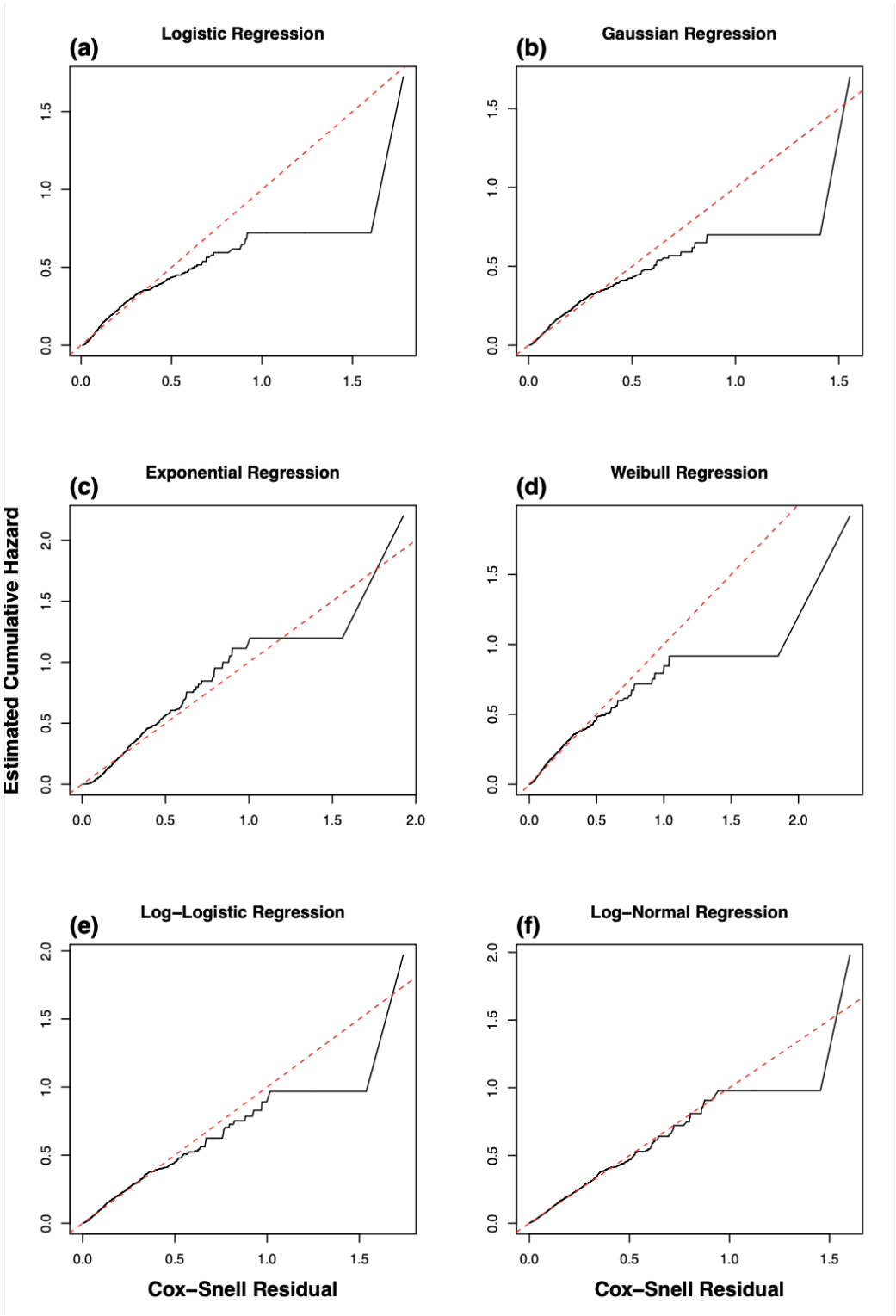

Figure 4. Cox-Snell regression plots. (a) Logistics AFT model (b) Gaussian AFT model (c) Exponential AFT model (d) Weibull AFT model (e) Log-Logistic AFT model (F) Log-Normal AFT model

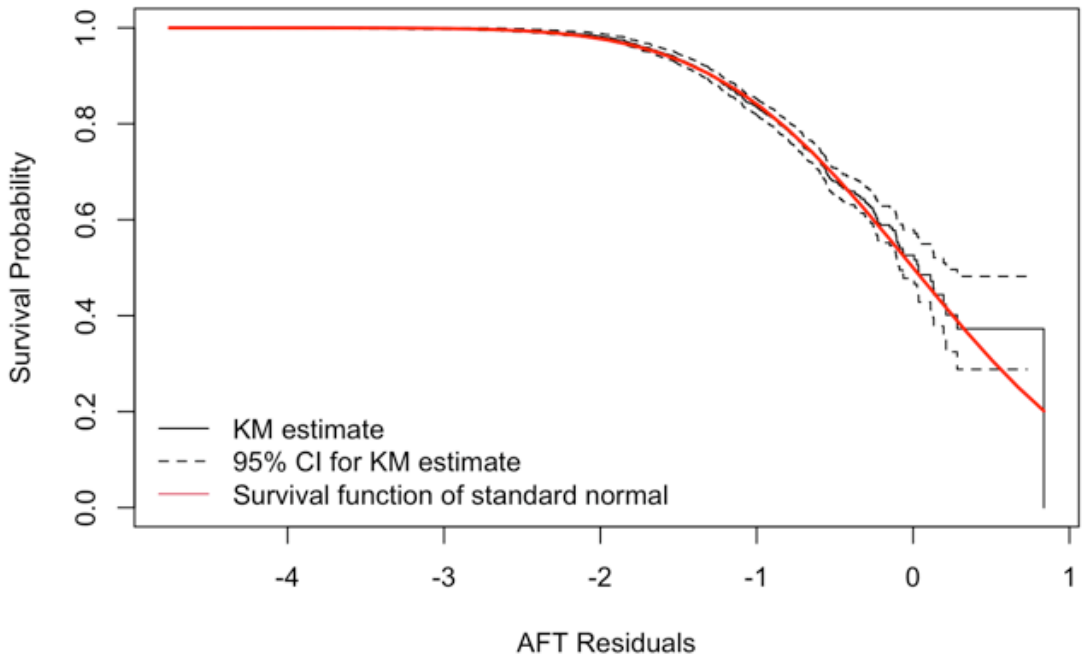

Figure 5. Residuals plot for AFT model

4. Prediction Diagnostics

We evaluated the predictive discrimination of our AFT model using Harrell's C-index and Uno's C-statistic, both of which assess a model's ability to correctly rank survival times. Higher C-statistics indicate better concordance between predicted and observed survival outcomes. Among the potential distributions, the log-normal AFT model consistently achieved the highest C-statistic, suggesting superior predictive accuracy (Table 4). This result indicates that the log-normal distribution best captures the underlying survival process, leading to more reliable risk stratification and ranking of survival probabilities.

Table 4: Prediction Accuracy Measures

Models	**Harrell's C**	**Uno's C**
Exponential	0.6758	0.6661
Weibull	0.6760	0.6662
Logistic	0.6765	0.6666
LogLogistic	0.6769	0.6671
Gussian	0.6770	0.6669
LogNormal	**0.6773**	**0.6675**

Discussion

With the overall aim of formulating effective AIDS/HIV treatments while considering patient well-being, we strive to examine whether it is necessary to assign combination therapy in comparison to monotherapy. Past research has found that patient adherence to combination therapy may be a concern, leading to ineffective therapies and unsatisfactory patient outcomes. This analysis contributes to the existing literature by re-evaluating the reactions of existing AIDS/HIV drugs of zidovudine, zalcitabine, and didanosine in the form of monotherapy and combination therapy. Our findings reveal the effects of combination therapy are indeed significant to those of monotherapy on the survival of HIV patients leading up to AIDS diagnosis.

In terms of related factors, we find that age, history of IV drug use, functional impairment, prior non-zidovudine antiretroviral therapy, prior zidovudine treatment in the past 30 days, prior antiretroviral therapy length, symptoms of AIDS, off-treatment between 91 and 101 weeks, CD8 cell count at baseline, and CD8 cell count between 15 and 25 weeks are significantly associated with time to AIDs diagnosis. While we continue to observe significant effects of the treatment when stratifying on sex and sexual orientation, it is important to consider the demographic composition of the study population when interpreting these findings. The dataset is predominantly male, which limits our study sample and results to be generalizable to the general population. It is noteworthy that prior ZDV usage within 30 days appears to be associated with shortened patient survival, which aligns with findings by Bhoopat L, et.al.[9] suggesting that extended prophylaxis (at least 60 days) is more effective in reducing HIV expression in the placenta and is associated with a lower risk of vertical transmission to neonates. Additionally, our results show that having previously used IV drugs would also enhance survival time, which is inconsistent with the existing literature and research. We believe the discrepancies observed may be attributed to the demographic makeup of our sample, leading to biased results.

Our analysis is limited as it is from an older clinical trial in the 1990s, so treatment guidelines and available drugs may have changed over time. Our analysis relies on the available patient data in the United States and Puerto Rico and over 80% of the study sample was male, which may not be widely applicable to the HIV/AIDS population in our country today. Limitations also exist on employing statistical methods. For prediction diagnostics, we were unable to apply calibration measures, such as pseudo R-squared or L-squared, due to challenges in using the *pam.survreg* function from the PAmeasure package. Specifically, the function failed to evaluate prediction performance due to the presence of binary covariates in the model. As a result, we focused on discrimination metrics, such as Harrell's C-index and Uno's C-statistic, to assess the model's predictive performance.

Future work may explore alternative calibration approaches or modifications to the existing methodology to account for categorical predictors. Another direction this analysis provides is the investigation on the interventions that can be used to promote patient adherence to combination therapies. Despite these limitations, our research provides valuable insights into optimizing HIV/AIDS treatment for different patient groups. It is crucial to ensure positive patient experience during the administering of the therapies, as it is already stressful for them to monitor the HIV/AIDS symptoms. Only by offering optimal means to encourage patient adherence can we achieve patient health and well-being simultaneously.

Acknowledgement

We would like to acknowledge the researchers from The AIDS Clinical Trials Group Study 175 in providing their data for public access. Funding organizations for the creation of the dataset involved both the AIDS Clinical Trials Group of the National Institute of Allergy and Infectious Diseases and the General Research Center units funded by the National Center for Research Resources. Additionally, we would like to thank Dr. Gang Li and Zian Zhuang for offering insights to survival analytical methods for time-to-event data.

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Appendix

I. Source Data File

https://archive.ics.uci.edu/dataset/890/aids+clinical+trials+group+study+175

II. Data set

Data dictionary with definitions of each variable:

Table A1. Data Variable Descriptions

Name	Role	Type	Description	Missing Values
pidnum	ID	Integer	Patient ID	no
cid	Target	Binary	censoring indicator (1 = failure, 0 = censoring)	no
time	Feature	Integer	time to failure or censoring	no
trt	Feature	Integer	treatment indicator (0 = ZDV only; 1 = ZDV + ddI, 2 = ZDV + Zal, 3 = ddI only)	no
age	Feature	Integer	age (yrs) at baseline	no
wtkg	Feature	Continuous	weight (kg) at baseline	no
hemo	Feature	Binary	hemophilia (0=no, 1=yes)	no
homo	Feature	Binary	homosexual activity (0=no, 1=yes)	no
drugs	Feature	Binary	history of IV drug use (0=no, 1=yes)	no
karnof	Feature	Integer	Karnofsky score (on a scale of 0-100)	no
oprior	Feature	Binary	Non-ZDV antiretroviral therapy pre-175 (0=no, 1=yes)	no
z30	Feature	Binary	ZDV in the 30 days prior to 175 (0=no, 1=yes)	no
zprior	Feature	Binary	ZDV prior to 175 (0=no, 1=yes)	no
preanti	Feature	Integer	# days pre-175 anti-retroviral therapy	no
race	Feature	Integer	race (0=White, 1=non-white)	no
gender	Feature	Binary	gender (0=F, 1=M)	no
str2	Feature	Binary	antiretroviral history (0=naive, 1=experienced)	no
strat	Feature	Integer	antiretroviral history stratification (1='Antiretroviral Naive', 2='> 1 but $\leq$ 52 weeks of prior antiretroviral therapy', 3='> 52 weeks)	no
symptom	Feature	Binary	symptomatic indicator (0=asymp, 1=symp)	no
treat	Feature	Binary	treatment indicator (0=ZDV only, 1=others)	no
offtrt	Feature	Binary	indicator of off-trt before 96+/-5 weeks (0=no, 1=yes)	no
cd40	Feature	Integer	CD4 at baseline	no
cd420	Feature	Integer	CD4 at 20+/-5 weeks	no
cd80	Feature	Integer	CD8 at baseline	no
cd820	Feature	Integer	CD8 at 20+/-5 weeks	no

III. Other Figures

Schoenfeld Residuals Test on PH Assumption

Variable	Chisq	DF	p.value
age	1.11	1	0.29
weight	0.32	1	0.57
homo	0.23	1	0.64
drugs	0.47	1	0.49
karnof	0.59	1	0.44
oprior	0.49	1	0.48
z30	0.02	1	0.89
preanti	0.63	1	0.43
race	0.00	1	0.96
gender	0.00	1	0.97
str2	0.21	1	0.65
strat	0.13	1	0.72
symptom	1.25	1	0.26
offtrt	**18.41**	**1**	**0.00**
cd80	2.12	1	0.15
cd820	0.09	1	0.76
treatment	**7.10**	**1**	**0.01**
GLOBAL	38.94	17	0.00

Figure A1. Schoenfeld Residuals Test on Cox's PH Assumption

IV. Code

The statistical analysis was conducted using R software version 4.4.3.

https://jacenai.github.io/Biostatistics/BIOS215_project.03.16.html