Psychiatric Comorbidity in Opioid Use Treatment Outcomes

Abstract

The Opioid Overdose Epidemic is a major challenge to the public health system in the United States; mental illnesses are common among substance abuse patients yet its association with treatment outcome has not been fully explored. With the Treatment Episode Dataset (TEDS) from 2019, this study aims to understand the relationship between psychiatric comorbidity and the incidence of treatment completion/dropout and assess whether this relationship is dependent on the race of the client using Fine-Gray models. A client's demographic factors (e.g. age, gender, race), substance use history and the type of care they received were controlled. Having psychiatric comorbidities is associated with higher incidence of treatment dropout and lower incidence of treatment completion, and this association is dependent upon the client's race. Being younger, female, African American and Hispanic is associated with worse treatment outcomes than clients not belonging to these demographic categories. Our results highlight a need to better integrate substance abuse treatments and mental health service as well as improve equity in treatment outcomes across demographic factors.

1. Introduction

1.1 Background Information

The Opioid Crisis in the United States was declared a national public health emergency in October 2017 and poses challenges to the US economy and its social welfare and criminal justice systems (HHS, 2017). In 2018, according to the US Center of Disease Control and Prevention (CDC), there were 67,367 recorded drug overdose deaths; of those deaths, 46,802 involved an opioid. There are about 130 American deaths per day from opioid overdose and opioid overdoses cost the US economy around $78 billion in 2018 (Scholl et al., 2019; National Institute on Drug Abuse, 2020). Factors that contribute to the opioid crisis include the increasing use of opioids in pain management by health care providers and the aggressive marketing of opioid analgesics as not addictive by pharmaceutical companies in the late 1990s (Hahn et al., 2011). Federal and state-level policies and guidelines have been implemented in an attempt to prevent or reduce prescription opioid misuse, abuse, diversion, and overdose (Hahn et al., 2011). To help patients overcome opioid addiction, treatment centers across the United States offer services including medical detoxification, medication-assisted treatment, mental illness treatment, counseling and post-rehabilitation planning. Typically, successful completion of treatment programs is associated with longer term abstinence, fewer relapses and other positive life outcomes (Brorson et al.,2013).

Many individuals who develop substance use disorders (SUD) are also diagnosed with mental disorders, and vice versa. Anxiety, depression and bipolar disorder and other personality disorders are commonly associated with substance abuse (National Institute on Drug Abuse, 2021). However, most studies surrounding opioid therapies were centered around evaluating the efficacy of medications in aiding treatment outcomes, and only few recent studies highlighted the role of psycho-social components (Bardy et al., 2016). This highlights a need to further explore the relationship between psychiatric comorbidity and substance abuse treatment outcomes. In addition, the effectiveness of a treatment program can vary greatly across patients depending geographic and demographic factors. For instance, African American and Hispanic population has been shown to have lower health care utilization and treatment completion rate compared to white non-Hispanic population (Stahler et al., 2018). In particular, it would be interesting to explore treatment outcomes for patients at the intersection of multiple identities since they may face additional barriers in accessing and completing treatment.

In this study, we **aim** to **first** analyze whether having psychiatric comorbidity is associated with greater likelihood of treatment dropout or completion. **Secondly**, we will investigate whether this relationship depends on the racial category of the client. We believe addressing these questions will help reveal the disparities that may exist across clients in terms of treatment outcomes and offer insights to improve equity in substance abuse treatment programs.

1.2 Data Description

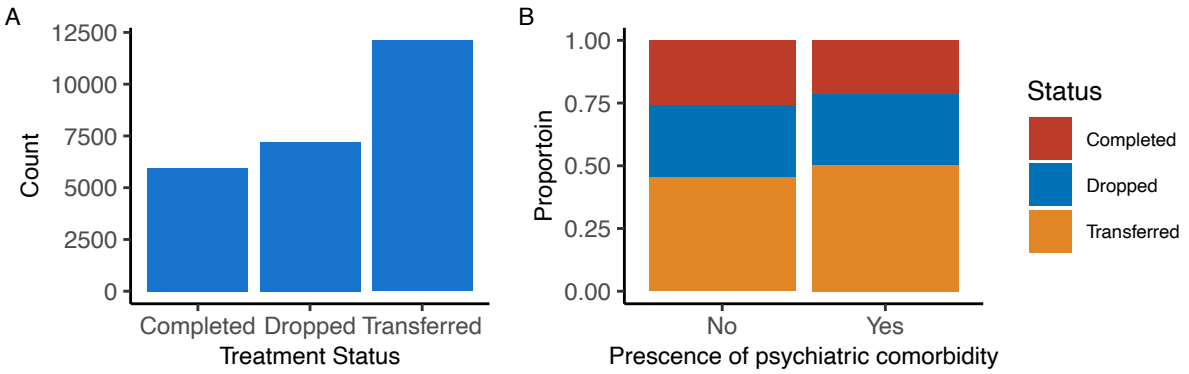
Treatment Episode Data Set (TEDS) is a publicly available dataset from the Substance Abuse and Mental Health Services Administration (SAMHSA) under the Department of Health and Human Services (HHS). The dataset is collected annually by states for the purposes of monitoring their substance use treatment systems. There are two separate systems within TEDS that each records the incidences of treatment admission and discharge in a given year (SAMHSA, 2021).

In this study, we will use the treatment episode discharge dataset from the year 2019 to conduct a cross-sectional analysis. From there, we only included the records where the client has been diagnosed with opioid dependence/abuse and opioid was their primary substance at the time of

admission. There are 324859 clients who met the inclusion criteria. Each observation in the dataset represents a client's **treatment episode** in state-licensed or certified substance use treatment centers. However, due to computational restraints, we performed the subsequent analysis on a random 10% sample of this population, resulting in a sample size was 32485. Detailed tables recording demographic characteristics of the initial cohort and the random sample are included in Appendix section B. It seems like the random sample is representative of the entire cohort.

The treatment episode dataset includes more than 70 variables and we will describe and explore the variables that are most relevant to the scope of this analysis. The variable **treatment status** records the outcome of the treatment episode, which I created using the reason for discharge. A client could either *complete* a treatment episode, *drop out* of the treatment or be *transferred* to another facility. From Figure 1 Panel A, it seems like most treatment episodes for opioid use were transferred, followed by dropped. Since completed treatment comprises the smallest proportion of all outcomes, there is a need to improve the efficacy of care delivery and investigate the contributing factors behind dropout. In Panel B, it seems like the presence of psychiatric comorbidity is correlated with higher likelihood of being transferred but lower likelihood of treatment completion.

Figure 1. The distribution of treatment outcomes and its relationship with psychiatric comorbidity

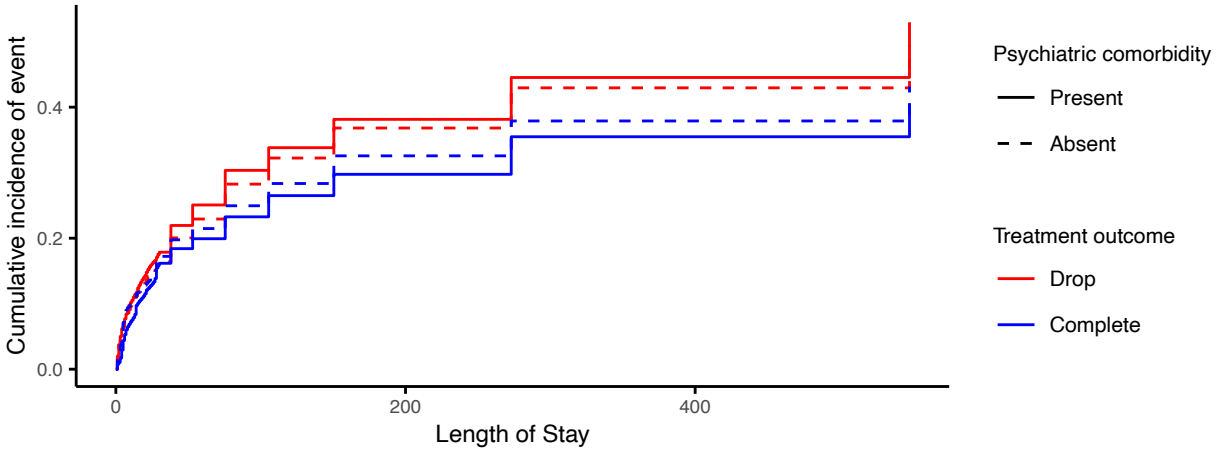


The two events of interest are treatment completion and treatment dropout. However, since clients transferred to another facility are likely still undergoing treatment of another form, this indicates the presence of censoring which need to be accounted for through survival analysis. Furthermore, if a client completes treatment, then they are no longer at risk for dropout and vice versa. This indicates treatment completion and treatment dropout are **competing risks**; they are both prevalent in the study cohort as reflected in Figure 1 Panel A. The time to event is reflected by the variable **length of stay**, which indicates how long the treatment lasted in days. If the length of stay is less than 30 days, it's encoded using the exact number of days; however, if the length of stay is greater than 30, it's encoded using an interval (i.e. greater than 60 and less than 90), suggesting that the event occurred within this window but the exact time is unknown. For technical reasons, we decided to use the mid-point of each interval to reflect a client's length of stay, and we will further address this limitation in the Discussion section.

We estimated the **cumulative incidence functions** of treatment completion and dropout, which appropriately reflect the event-specific probability of occurrence across time in the presence of competing risks (Figure 2). The commonly used Kaplan-Meier estimator would not be suitable since it views the competing risk as censoring which would overestimate the probability of event occurrence. It seems like the presence of psychiatric comorbidity is statistically significantly associated with higher incidence treatment drop out (Gray's test: p-value < 0.001) but lower incidence of

treatment completion (Gray's test: p-value < 0.001). This finding suggests that psychiatric comorbidity might be associated with differential treatment outcomes and we will further explore this relationship through modeling.

Figure 2. Cumulative incidence of treatment completion and treatment dropout, stratified by psychiatric comorbidity



There are a few variables that capture the demographics of the study population. Age at admission is recorded in 5 intervals, ranging from below 20 to above 50. Gender is recorded as male or female. Initially there are 9 different categories of race, but since some racial categories only reflects less than 1% of the study population, we recombined them into 3 main categories: White, Black/African American and Other. The Hispanic status variable reflects whether a client is of Hispanic or Latino origin. The variable veteran status reflects whether the client has served in the military. Through visualizing the incidence of treatment outcomes stratified by each of these demographic factors, it seems like disparities exist especially across racial and gender categories (Appendix section C).

There are also a few variables that are more centered around substance abuse. We have information regarding the number of prior treatment episodes a client received and the age when they first started using opioids. The type of treatment service can be broken down into 3 main categories: ambulatory, detoxification (managing acute intoxication and withdrawal), or rehabilitation (usually residential and long-term). The treatment for opioid use disorder could either be medication-assisted (including medication such as methadone) or not. A more detailed description of the values that these variables could take on is included in Appendix section A for reference.

Missingness is observed for almost all variables described above. Based on background knowledge, we assumed the data is **missing at random (MAR)**. We believe the observed missingness can be largely explained by other variables which we have data for rather than unobserved variables. Medication-assisted therapy, prior use of opioids, psychiatric comorbidity are variables with the most missingness (Appendix section B). We decided to remove observations containing missing values and perform a complete case analysis based on several reasons: 1) at most 7% of the values are missing in a single variable, 2) the sample size remains sufficiently large (n = 25273) after dropping the observations, 3) imputation, especially multiple imputation, will be extremely computationally intensive given the size of the current data. Furthermore, a mis-specified imputation model has the potential of generating biased results. However, we recognize that 7212 respondents are excluded, and we will address the associated limitations in the Discussion section.

1.3 Hypothesis

Based on the existing studies and exploratory data analysis, we **hypothesize** that clients with psychiatric comorbidity will have a higher probability of treatment dropout, but lower probability of treatment completion compared to clients without psychiatric comorbidity. Furthermore, we **hypothesize** the relationship between psychiatry comorbidity with treatment outcome will depend on the race of the client, given that we observed clients with mental illness and clients belonging to racial minorities are associated with worse treatment outcomes.

2. Methodology

2.1 Investigating psychiatry comorbidity on treatment outcome

In the presence of competing risks, the standard Cox proportional hazards model would not be adequate. Rather, there are two potential hazard functions that could be modeled. The *cause-specific hazard* represents the instantaneous rate of failing from a specific cause, given that no event of any cause has occurred; the *sub-distribution hazard* represents the instantaneous rate of failing from a specific cause, given that no event of this specific cause has occurred (i.e. the individual could have survived or already failed from a different risk). A Cox model fitted on the cause-specific hazard leads to biased estimates since it implicitly treats observations failed from competing risk as censored (Scrucca et al,, 2010; Jiang et al., 2018). Rather, the sub-distribution hazard has a corresponding relationship with the cumulative incidence function; a Fine-Gray model regressing on this hazard offers a clinically relevant interpretation of each covariate's association with the incidence of the outcome over time (Austin et al., 2017; Jiang et al., 2018). Furthermore, the Fine-Gray model is semi-parametric with an unspecified baseline hazard and each predictor will have a multiplicative influence on the sub-distribution hazard. Since treatment outcome could be influenced by a variety of factors, the assumption that it follows a specific distribution may not be appropriate. Hence, the Fine-Gray model also has advantage over other parametric models for survival analysis such as a competing-risk accelerated failure time (AFT) model (Choi et al., 2019).

Furthermore, although fitting a multinomial logistic regression model could offer insight on the relationship between psychiatric comorbidity and the odds of experiencing different outcomes, it does not consider how long each client stayed in the program. Rather, we believe performing survival analysis using the Fine-Gray model will offer a more nuanced understanding of the relationship through time (Resche-Rigon et al., 2006).

The Fine-Gray model is specified as:

$$\lambda_{r,i}(t) = \lambda_{0r}(t)\mathbf{exp}[\beta_{1,r}\text{I}(\text{Psychiatric comorbidity}_i = \text{Present}) + \sum_{k=2}^{5} \beta_{k,r}\text{I}(\text{Age}_i = \zeta) + \beta_{6,r}\text{I}(\text{Race}_i = \text{Black}) +$$

$$\beta_{7,r}\text{I}(\text{Race}_i = \text{Other}) + \beta_{8,r}\text{I}(\text{Gender}_i = \text{Female}) + \beta_{9,r}\text{I}(\text{Hispanic}_i = \text{Yes}) + \beta_{10,r}\text{I}(\text{Veteran}_i = \text{Yes}) +$$

$$\beta_{11,r}\text{I}(\text{Medication Assist}_i = \text{Yes}) + \beta_{12,r}\text{I}(\text{Prior episode}_i = \text{Yes}) + \sum_{13}^{18} \beta_{k,r}\text{I}(\text{Age of first use}_i = \omega) +$$

$$\beta_{19,r}\text{I}(\text{Service}_i = \text{Detoxification}) + \beta_{20,r}\text{I}(\text{Service}_i = \text{Rehabilitation}) + \beta_{21,r}\text{State drug overdose death rate}_i]$$

In the above notation, i represents each client in the dataset. $\lambda(t)$ denotes the sub-distribution hazard function of event r at time t, λ_0 is the baseline sub-distribution hazard function of event r at time t (unspecified). In this context, the event of interest r is either treatment completion or treatment dropout. $\zeta \in \{20-30, 30-40, 40-50, > 50\}, \omega \in \{12-14, 15-17, 18-20, 21-24, 25-29, >$

30}. Not having psychiatric comorbidity, the youngest age range (<20), white, male, non-Hispanic, non-veteran, not using Medication assisted therapy, not having prior episode, the youngest age range of first use (<11), and ambulatory care are used as the baseline for the categorical variables respectively.

In this model, the presence of psychiatric comorbidity is the variable of interest. In addition, we controlled for demographic factors including age, gender, race, Hispanic status and veteran status to account for the social determinants of health outcome. For instance, a younger client may be more impulsive in making the decision to discontinue a treatment. Furthermore, clients belonging to racial/ethnic minorities may face challenges in accessing health care resources or forming connections with provides across racial/ethnic boundaries (Mallow et al., 2020). I also controlled for veteran status since combat exposures is associated with increased incidence of mental illness (i.e. depression, PTSD) and higher rates of substance use disorders than the general population.

I controlled for the type of treatment a client received since the duration of the program and how it's offered could factor into an individual's decision to discontinue. Previous studies also suggested that medication-assisted therapy can improve treatment retention, hence it may be a confounder that needs to be controlled (Askari et al., 2020). We also accounted for the age when the client first started using the substance and their history of receiving treatment.

Lastly, the dataset included treatment episodes from all states in the United States. Since treatment outcome might be impacted by state-specific policies among other socioeconomic factors like the availability of resources, we anticipate clustering across geographical regions might exist in the dataset. Due to computational restraints, we were unable control for this effect by including an indicator variable for every state. Rather, we attempted to account for this effect through including the rate of drug overdose deaths in 2019 in each state as a continuous variable (data from CDC). We believe the rate of drug overdose deaths can help control for the severity of drug abuse problem in each state and the government's effectiveness in helping its residents to combat these issues.

2.2 Investigating interaction effect with race

In addressing how race might mediate the relationship between psychiatric comorbidity and treatment outcome, we will construct a Fine-Gray model, specified identically as above, besides including an **interaction term** between psychiatric comorbidity and race. A previous study used a similar methodology and did not find statistically significant evidence that this relationship is dependent on gender (Krawczyka et al., 2017). Extending from this study, our analysis could clarify whether this relationship would differ based on race.

In terms of diagnostics, the residuals had a locally constant mean and no obvious pattern over time, suggesting the proportional subdistribution hazards assumption is satisfied (Appendix section D).

3. Results

3.1 Investigating psychiatry comorbidity on treatment outcome

The model output for the Fine-Gray model is displayed below and the uncertainty in estimates are quantified using standard error and 95% confidence intervals. Only statistically significant terms are displayed, the full model output can be accessed in the Appendix Section E.

Table 1: Statistically significant coefficients in the Fine-Gray model (α = 0.05, 95% CI)

Term	Estimate	Standard Error	p-value	CI Lower	CI Upper
Outcome of Interest: treatment dropout					
Psychiatric comorbidity: Present	0.064	0.023	0.005	0.019	0.110
Age: 40-50	-0.274	0.104	0.008	-0.477	-0.071
Age: > 50	-0.379	0.105	<0.001	-0.585	-0.174
Race: Black	0.279	0.034	<0.001	0.212	0.346
Hispanic status: Yes	0.100	0.043	0.020	0.016	0.184
Medication use: Yes	0.128	0.024	<0.001	0.081	0.175
Prior episodes: Yes	0.071	0.027	0.009	0.018	0.124
Service: Detoxification	0.173	0.044	<0.001	0.088	0.259
Service: Rehabilitation	-0.134	0.034	<0.001	-0.201	-0.067
Drug related death %	-0.011	0.002	<0.001	-0.014	-0.008
Outcome of Interest: treatment completion					
Psychiatric comorbidity: Present	-0.088	0.027	0.001	-0.141	-0.036
Race: Black	-0.216	0.043	<0.001	-0.301	-0.131
Gender: Female	-0.087	0.028	0.002	-0.142	-0.032
Medication use: Yes	-0.471	0.031	<0.001	-0.532	-0.411
Age of first use: 12-14	-0.313	0.148	0.034	-0.603	-0.023
Service: Detoxification	1.292	0.041	<0.001	1.211	1.372
Service: Rehabilitation	0.901	0.030	<0.001	0.842	0.961
Drug related death %	0.006	0.002	0.001	0.002	0.009

Addressing our primary analysis, we observed that having psychiatric comorbidity is associated with higher incidence of treatment dropout and lower incidence of treatment completion. More specifically, holding all else constant, a client with psychiatric comorbidity is expected to have 1.05 times the subdistribution hazard of dropping out of the treatment and 0.91 times the subdistribution hazard of completing a treatment compared to a client without psychiatric comorbidity. Although the effect size of this association is modest, it still highlights that the current treatment programs need to better accommodate the special needs of this subgroup of clients.

We observed that several demographic factors (age, race, gender, Hispanic status) seem to be associated with differential treatment outcome. A client who is older than 50 is expected to have 0.68 times the subdistribution hazard of treatment dropout compared to a client who is younger than 20 at admission, holding all else constant. We also noted that the magnitude of this association is relatively large and increases with age difference. Although we didn't find statistically significant relationship between gender and treatment dropout, being female is associated with lower incidence of treatment completion. Potentially female clients are more likely to be transferred across programs and receive treatment for a longer period of time than males.

Furthermore, there seems to be a statistically significant association between treatment outcome and a client's racial identity. An African American client is expected to have 1.32 times the subdistribution hazard of treatment dropout and 0.80 times the subdistribution hazard of treatment completion compared to a white client, holding all else constant. Similarly, Hispanic clients are associated with higher incidence of treatment dropout, highlighting disparity across racial and ethnic boundaries.

Other characteristics relating to a person's substance use history are also important considerations. A client who has received previous episodes of treatment is correlated with higher incidence of attrition than a client entering the treatment program for the first time, holding all else constant. In addition, only clients belonging to the age group 12-14 at admission had a statistically significant

lower probability of treatment completion than the baseline category (<11 years old), holding all else constant. This finding highlights that early adolescence seems to be a crucial time period in mediating treatment outcomes, potentially because adolescence maybe more impulsive in decision making and easily influenced by external factors like peers. Lastly, our results suggest medication assisted treatment programs are associated with higher dropout probability and lower completion probability across clients, which doesn't align with Askari et al.'s finding (2020). The difference in efficacy might be explained by different study cohort and modeling approaches, and further research is warranted to further clarify this relationship.

3.2 Investigating interaction effect with race

Table 3: Selected coefficients in Fine-Gray model with interaction term (α = 0.05, 95% CI)

The output for the model addressing our second aim is shown below. Since the coefficients of the predictors are nearly identical to the table above, we only displayed the terms that are relevant to addressing our research question. The full model output can be accessed in the Appendix section E.

Term	Estimate	Standard Error	p-value	CI Lower	CI Upper
Outcome of Interest: treatment dropout					
Psychiatric comorbidity: Present	0.099	0.026	<0.001	0.047	0.151
Race: Black	0.365	0.044	<0.001	0.279	0.450
Psychiatric comorbidity*Black	-0.191	0.062	0.002	-0.313	-0.070
Outcome of Interest: treatment completion					
Psychiatric comorbidity: Present	-0.121	0.030	<0.001	-0.179	-0.062
Race: Black	-0.327	0.058	<0.001	-0.440	-0.215
Psychiatric comorbidity*Black	0.256	0.079	0.001	0.101	0.411

Since the interaction term between psychiatric comorbidity and race is statistically significant for both treatment dropout and completion, it supports that the relationship between psychiatric comorbidity and treatment outcome is dependent on client's racial profile.

Interestingly, among white clients, having psychiatric comorbidity is associated with 1.10 times the subdistribution hazard of treatment dropout; but among black clients, it's associated with 0.91 times the subdistribution hazard of treatment dropout compared to otherwise, holding all else constant. A similar relationship is observed for treatment completion. Psychiatric comorbidity is associated lower incidence of treatment completion among white clients, but higher incidence of treatment completion for black clients.

These results suggest that the risk factors contributing to treatment dropout is likely not homogeneous across population, and clinicians should devote more attention in understanding the specific needs of each subpopulation.

4. Discussion

4.1 Conclusions

In this study, we analyzed the association between psychiatric comorbidities and opioid treatment outcome using a national representative sample from the treatment episodes dataset (TEDS-D) in

2019. Fine-Gray models were constructed with treatment completion and dropout as the events of interest. We concluded that having psychiatric comorbidity is associated with higher incidence of treatment dropout and lower incidence of treatment completion. Our findings supported our initial hypothesis and aligned with a study suggesting psychiatric comorbidity is associated with higher odds and earlier time of treatment attrition between year 2009-2011 (Krawczyk, 2017). Our results highlight the need to better integrate mental health services with substance abuse treatment; more professional psychiatrists should be involved in designing the treatment programs for substance abuse clients and other providers should also be better equipped with mental health knowledge (Volkow, 2019).

Moreover, our model reflected differential treatment outcomes across demographic factors. African American, female and Hispanic groups are associated with worse treatment outcome, confirming our knowledge about disparities in the health care system. These demographic factors could mediate a person's access to resources and health-seeking behavior, which could all be related to treatment outcomes. These clients might benefit from additional services and support from health care providers. As the patient population in the United States become increasingly diverse, policy makers should explore innovative ways to improve healthcare outcomes for patients from all backgrounds. Furthermore, our results also highlighted that having a younger age at admission and start using substance at an earlier time in life are associated with worse treatment outcome. Since early adolescence is a critical period for behavior formation, there should be additional attention from parents and care providers on improving treatment adherence and offer preventative strategies for this age group.

Finally, we observed a statistically significant interaction effect between mental health and race. The relationship between having psychiatric comorbidity and treatment outcome can be in opposite directions depending on the client's race. Understanding how multiple identities interact pave the way in designing more individualized treatment programs. In particular, clinicians may need to provide additional support to subgroups who may face disadvantages from multiple sources. Together, our results reflect that treatment outcome can be tightly associated with many aspects of a client's identity. The insight for our study could be important for officials to design more effective and equitable treatment programs for opioid use disorder and help combat the Opioid Overdose Epidemic.

From a methodological perspective, the Treatment Episode Data Set (TEDS) has been analyzed by many researchers aiming to unpack factors behind treatment outcomes using multinomial logistic regression. However, they may have under-accounted for censoring by grouping the clients who were transferred with clients who completed the treatment. In particular, among clients receiving treatment for opioid use disorder, 48% of them were transferred (higher than the overall population rate of 25%). One study utilized a Cox proportional hazard model to study treatment attrition but may have under-accounted for competing risks (Krawczyka et al., 2017). Our modeling approach offered a more nuanced understanding of each covariate's association with treatment outcome across time and we hope this study would be helpful to researchers analyzing this dataset in the future.

4.2 Limitations and Future Directions

One limitation of the modeling approach is that in the original treatment episodes dataset, the observations are interval censored. The choice to use the mean of the interval as the survival time could have introduced bias into the survival analysis. We also had to make an assumption that clients whose length of stay was coded as "more than a year" completed treatment within two years. In the future, we would like to construct an interval censored competing risk model to capture the structure of the data more accurately. Additionally, treatment outcomes could

cluster geographically by state. Given the computational restraints, we accounted for this effect by controlling the rate of drug overdose related death in each state, but a single measure might not be sufficient to capture the heterogeneity across states. In the future, we should also consider controlling for policies regarding opioid treatment and the socioeconomic status of each state. We could explore fitting a fragility model with states as random effects.

There are several limitations associated with the dataset. Almost all variables have missing information and 7212 clients were excluded as a result. The choice to perform a complete-case analysis reduced the sample size, leading to lower power. Under the missing-at-random assumption, it could also result in biased parameter estimates. Furthermore, several key demographic factors (including income and education level) were unable to be used in the current analysis due to high percentage of missing observations.

The representativeness of the study cohort may be another limitation. Around 10 states (including California) did not collect data on psychiatric comorbidity, suggesting our analysis might have missed a substantial portion of the national population. Additionally, all facilities recorded in TEDS received public funds, so our results may not be generalizable across all opioid use treatment programs across the United States.

Currently, TEDS only measures the presence and absence of psychiatric comorbidity. However, this binary approach does not capture the varieties of psychiatric illnesses nor the different degrees of severity. For instance, clients with depression may have a very distinct set of challenges than clients with obsessive-compulsive disorder (OCD). We would like to explore additional data sources that contains more detailed information regarding each client to gain a more in-depth understanding on how different types of psychiatric comorbidity is associated with treatment outcome. More importantly, beyond solely focusing on treatment outcomes, we should also strive to understand the treatment experience of clients with mental illness more holistically. In the future, we would like to explore communal factors like social support and investigate potential stigmas that clients might face.

Our current study pointed out the interaction effect between psychiatric comorbidity and race. As a next step, we want to explore the intersectionalities between mental health and age, gender, ethnicity. In addition, the current study only uses treatment episodes in 2019, capturing a snapshot in time. Given the increasing effort from the federal government to reduce opioid overdoses as well as increasing attention from physicians to improve health care equity, it would be interesting to broaden the time scale of our analysis and observe trends across decades.

4.3 Summary

Overall, this study suggested that having psychiatric comorbidity is associated with higher incidence of treatment dropout and lower incidence of treatment completion, and this association is dependent upon the client's race. Furthermore, clients who are younger, female, black and Hispanic are generally associated with worse treatment outcomes than clients not belonging to these categories. Our finding raises the need to better integrate substance abuse treatments and mental health service and calls for improved equity in treatment outcomes across demographic factors.

Appendix

Section A: Variable descriptions (sorted in alphabetial order)

- **Age at admission** (AGE):
  - 1: Below 20 years (baseline)
  - 2: 20 - 30 years
  - 3: 30 - 40 years
  - 4: 40 - 50 years
  - 5: Above 50 years
- **Age at first use of primary substance** (FRSTUSE1)
  - 1: 11 years and under (baseline)
  - 2: 12–14 years
  - 3: 15–17 years
  - 4: 18–20 years
  - 5: 21–24 years
  - 6: 25–29 years
  - 7: 30 years and over
- **Gender** (GENDER):
  - 1: Male (baseline)
  - 2: Female
- **Hispanic status** (HISPANIC)
  - 1: Not Hispanic (baseline)
  - 2: Hispanic
- **Length of stay** (LOS)
  - 1 to 30 integers: Number of days the client stayed in the treatment
  - 31: 31 to 45 days
  - 32: 46 to 60 days
  - 33: 61 to 90 days
  - 34: 91 to 120 days
  - 35: 121 to 180 days
  - 36: 181 to 365 days
  - 37: More than 1 year (assumed to be between 1 - 2 years)
- **Medication-assisted opioid therapy** (METHUSE)
  - 1: Yes
  - 2: No (baseline)
- **Previous substance use treatment episodes** (NOPRIOR)
  - 0: No prior treatment episodes (baseline)
  - 1: One or more prior treatment episodes
- **Psychiatric comorbidity** (PSYPROB)

  - 1: Present
  - 2: Absent (baseline)

- **Race** (RACE):
  - 1: White (baseline)
  - 2: Black / African American
  - 3: Other

- **Service/treatment received at admission** (SERVICES)
  - 1: Detoxification
  - 2: Rehabilitation (baseline)
  - 3: Ambulatory

- **Treatment outcome** (STATUS)
  - 0: Transferred
  - 1: Dropped out of treatment
  - 2: Completed treatment

- **Veteran status** (VET)
  - 1: Veteran
  - 2: Not veteran (baseline)

Section B: Cohort characteristics

Table A-1: Number and percentage of missing observations

Variable	Count of missing values	Percentage of study population
Age	0	0.0
Age of first use	3684	1.1
Gender	90	0.0
Hispanic status	7447	2.3
Length of stay	0	0.0
Medication use	24127	7.4
Prior episodes	20877	6.4
Psychiatric comorbidity	24022	7.4
Race	7112	2.2
Service	0	0.0
Treatment outcome	0	0.0
Veteran status	15069	4.6

Table A-2: Baseline demographic and clinical characteristics of full population, stratified by treatment outcome

The table includes all clients who met the inclusion criteria (i.e. before random sampling).

Characteristics	Transferred (n = 122891)	Dropped (n = 71168)	Completed (n = 59368)
Age, n (%)			
<20	1000 (0.8)	1032 (1.5)	822 (1.4)
20-30	35383 (28.8)	20980 (29.5)	18329 (30.9)
30-40	48050 (39.1)	27099 (38.1)	22597 (38.1)
40-50	22825 (18.6)	11888 (16.7)	9644 (16.2)
>50	15633 (12.7)	10169 (14.3)	7976 (13.4)
Age at first use, n (%)			
<11	933 (0.8)	557 (0.8)	447 (0.8)
12-14	6025 (4.9)	3779 (5.3)	2911 (4.9)
15-17	18618 (15.2)	11158 (15.7)	8823 (14.9)
18-20	26044 (21.2)	14786 (20.8)	12589 (21.2)
21-24	23811 (19.4)	13343 (18.7)	11190 (18.8)
25-29	19784 (16.1)	12005 (16.9)	10392 (17.5)
>30	27676 (22.5)	15540 (21.8)	13016 (21.9)
Gender, n (%)			
Male	71673 (58.3)	42863 (60.2)	38936 (65.6)
Female	51218 (41.7)	28305 (39.8)	20432 (34.4)
Hispanic status, n (%)			
Not Hispanic	117951 (96.0)	63720 (89.5)	53161 (89.5)
Hispanic	4940 (4.0)	7448 (10.5)	6207 (10.5)
Medication Use, n (%)			
No	80378 (65.4)	38787 (54.5)	41884 (70.5)
Yes	42513 (34.6)	32381 (45.5)	17484 (29.5)
Prior Episode, n (%)			
0	43578 (35.5)	17239 (24.2)	15443 (26.0)
>= 1 episodes	79313 (64.5)	53929 (75.8)	43925 (74.0)
Psychiatric comorbidity, n (%)			
Absent	54325 (44.2)	33841 (47.6)	30538 (51.4)
Present	68566 (55.8)	37327 (52.4)	28830 (48.6)
Race, n (%)			
White	101505 (82.6)	53601 (75.3)	46804 (78.8)
Black	15034 (12.2)	11454 (16.1)	7570 (12.8)
Other	6352 (5.2)	6113 (8.6)	4994 (8.4)
Services, n (%)			
Rehabilitation	100076 (81.4)	50715 (71.3)	30229 (50.9)
Detoxification	10829 (8.8)	7858 (11.0)	11311 (19.1)
Ambulatory	11986 (9.8)	12595 (17.7)	17828 (30.0)
Veteran status, n (%)			
No	120796 (98.3)	69826 (98.1)	58205 (98.0)
Yes	2095 (1.7)	1342 (1.9)	1163 (2.0)

Table A-3: Baseline demographic and clinical characteristics of study cohort, stratified by treatment outcome

The table below includes the treatment episodes used in the current analysis (i.e. after random sampling).

Characteristics	Transferred (n = 12117)	Dropped (n = 7215)	Completed (n = 5941)
Age, n (%)			
<20	97 (0.8)	106 (1.5)	79 (1.3)
20-30	3520 (29.1)	2168 (30.0)	1817 (30.6)
30-40	4739 (39.1)	2752 (38.1)	2332 (39.3)
40-50	2248 (18.6)	1160 (16.1)	925 (15.6)
>50	1513 (12.5)	1029 (14.3)	788 (13.3)
Age at first use, n (%)			
<11	81 (0.7)	45 (0.6)	56 (0.9)
12-14	642 (5.3)	410 (5.7)	303 (5.1)
15-17	1785 (14.7)	1117 (15.5)	887 (14.9)
18-20	2603 (21.5)	1514 (21.0)	1247 (21.0)
21-24	2357 (19.5)	1378 (19.1)	1166 (19.6)
25-29	1976 (16.3)	1183 (16.4)	989 (16.6)
>30	2673 (22.1)	1568 (21.7)	1293 (21.8)
Gender, n (%)			
Male	7121 (58.8)	4452 (61.7)	3858 (64.9)
Female	4996 (41.2)	2763 (38.3)	2083 (35.1)
Hispanic status, n (%)			
Not Hispanic	11645 (96.1)	6472 (89.7)	5311 (89.4)
Hispanic	472 (3.9)	743 (10.3)	630 (10.6)
Medication Use, n (%)			
No	7934 (65.5)	3938 (54.6)	4222 (71.1)
Yes	4183 (34.5)	3277 (45.4)	1719 (28.9)
Prior Episode, n (%)			
0	4271 (35.2)	1719 (23.8)	1496 (25.2)
>= 1 episodes	7846 (64.8)	5496 (76.2)	4445 (74.8)
Psychiatric comorbidity, n (%)			
Absent	5452 (45.0)	3484 (48.3)	3087 (52.0)
Present	6665 (55.0)	3731 (51.7)	2854 (48.0)
Race, n (%)			
White	10055 (83.0)	5477 (75.9)	4695 (79.0)
Black	1462 (12.1)	1163 (16.1)	752 (12.7)
Other	600 (5.0)	575 (8.0)	494 (8.3)
Services, n (%)			
Rehabilitation	9897 (81.7)	5147 (71.3)	2983 (50.2)
Detoxification	1065 (8.8)	807 (11.2)	1155 (19.4)
Ambulatory	1155 (9.5)	1261 (17.5)	1803 (30.3)
Veteran status, n (%)			
No	11913 (98.3)	7069 (98.0)	5822 (98.0)
Yes	204 (1.7)	146 (2.0)	119 (2.0)

Section C: The association between demographic factors and treatment outcome

Figure A-1. Cumulative incidence of treatment dropout and treatment completion, stratified by gender

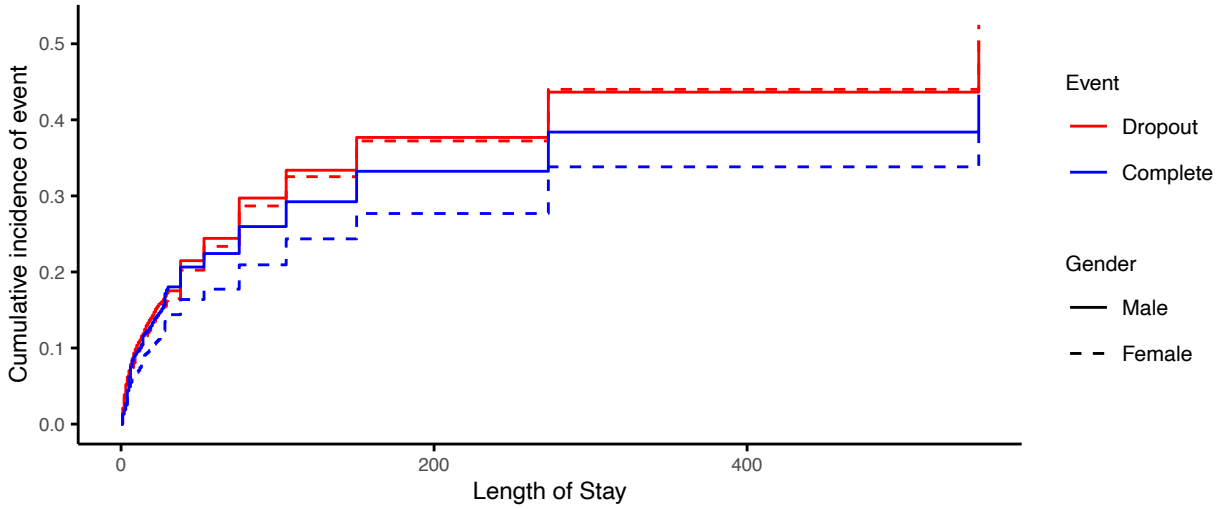


Figure A-2. Cumulative incidence of treatment dropout and treatment completion, stratified by race

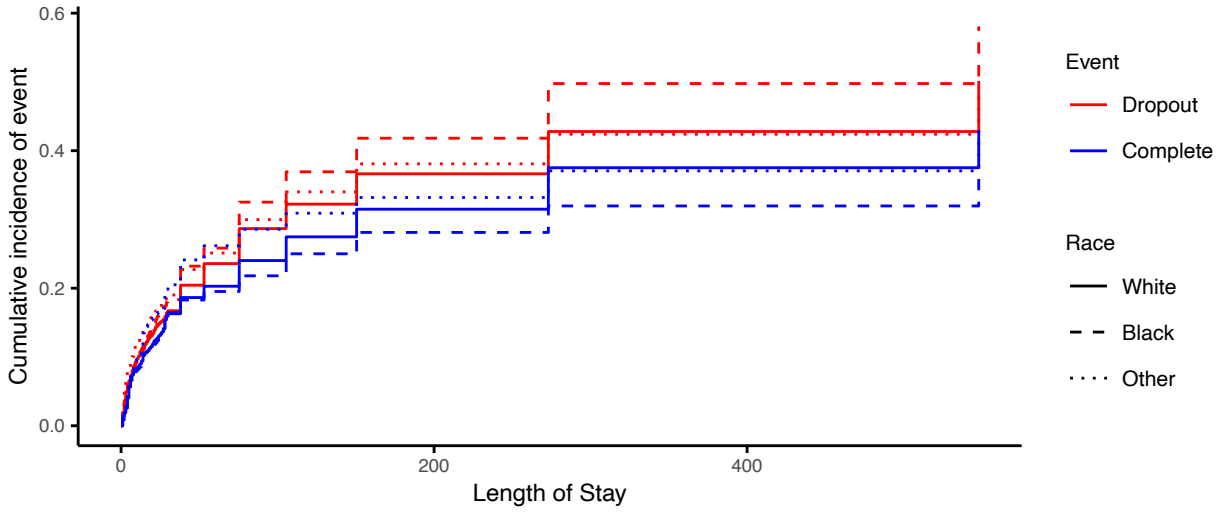


Figure A-3. Cumulative incidence of treatment dropout and treatment completion, stratified by Hispanic status

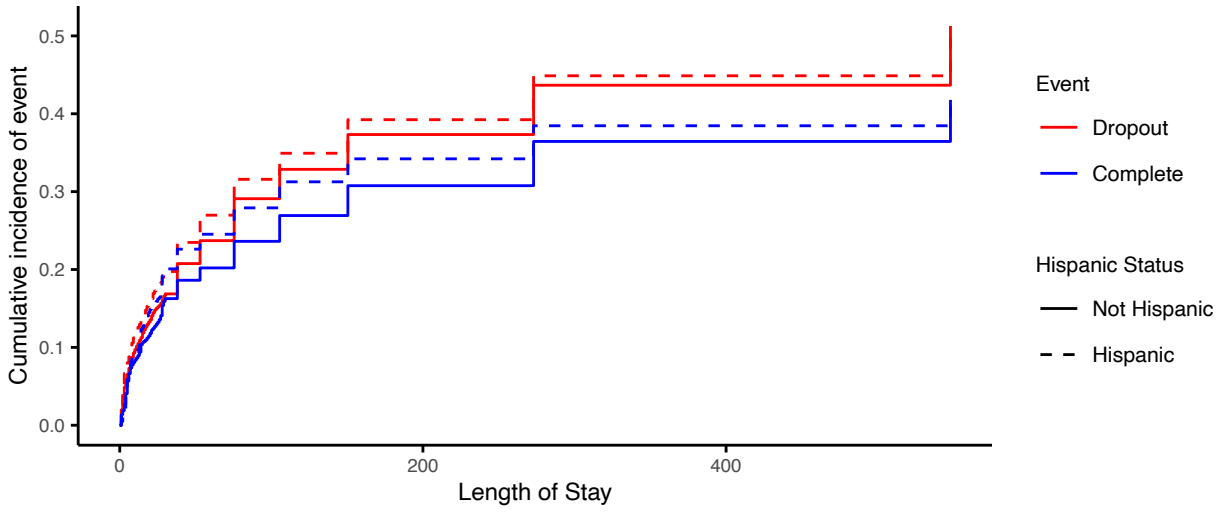
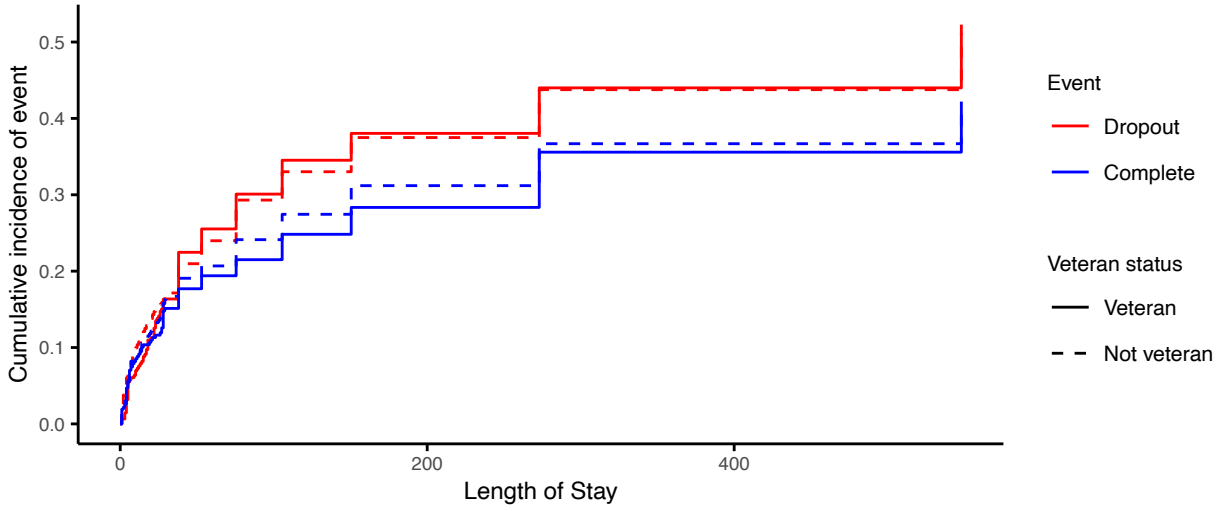


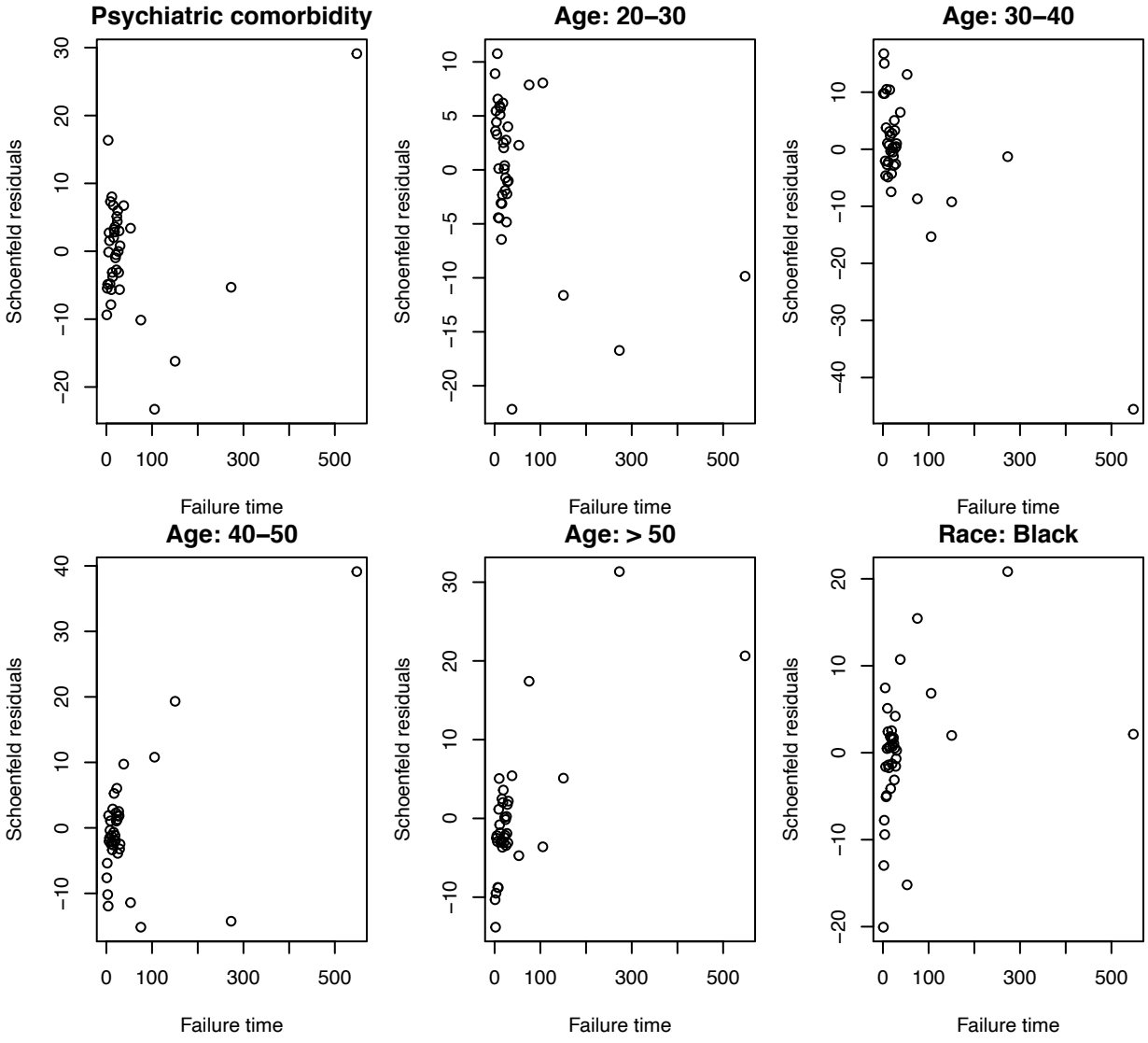
Figure A-4. Cumulative incidence of treatment dropout and treatment completion, stratified by veteran status

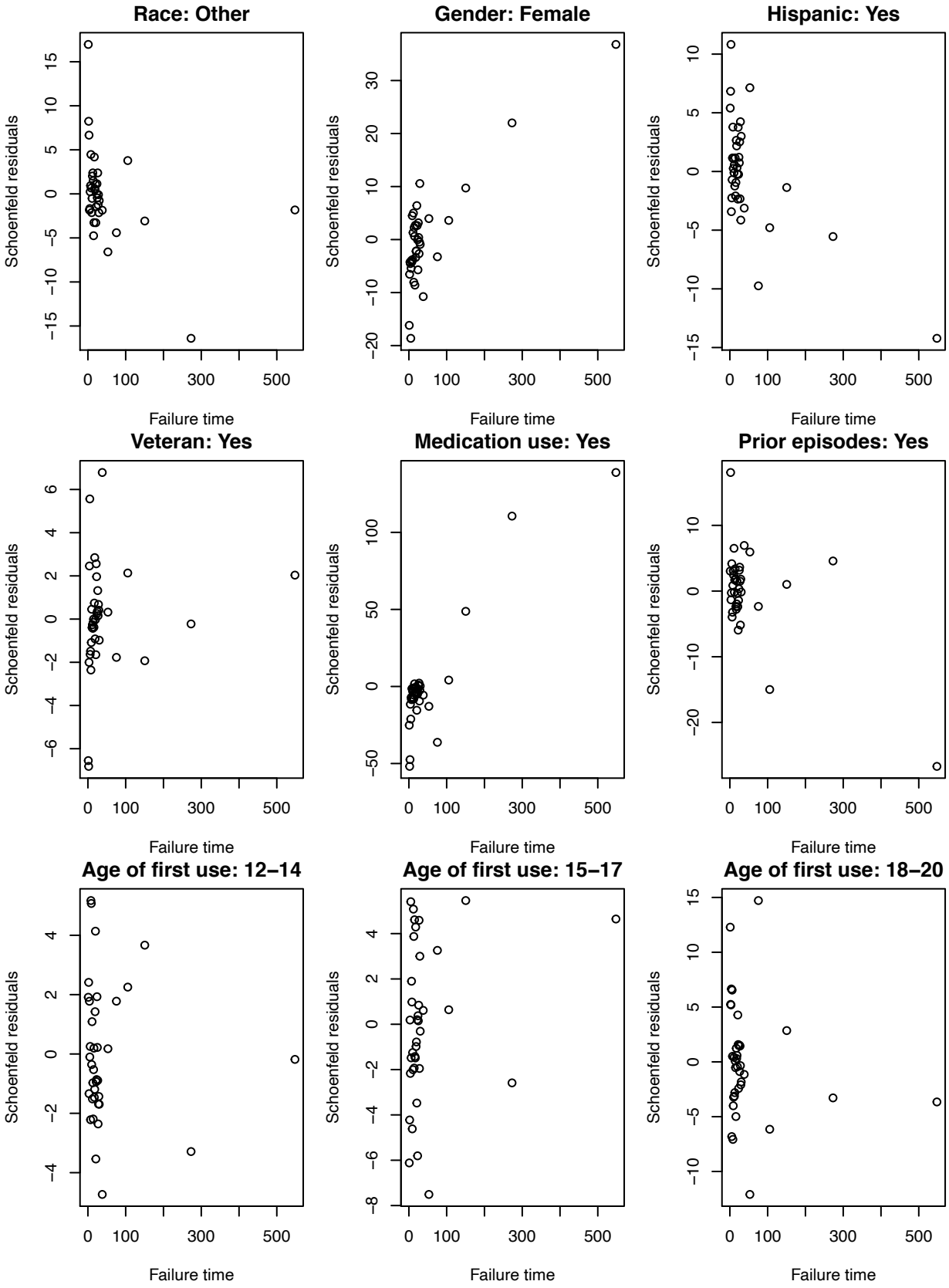


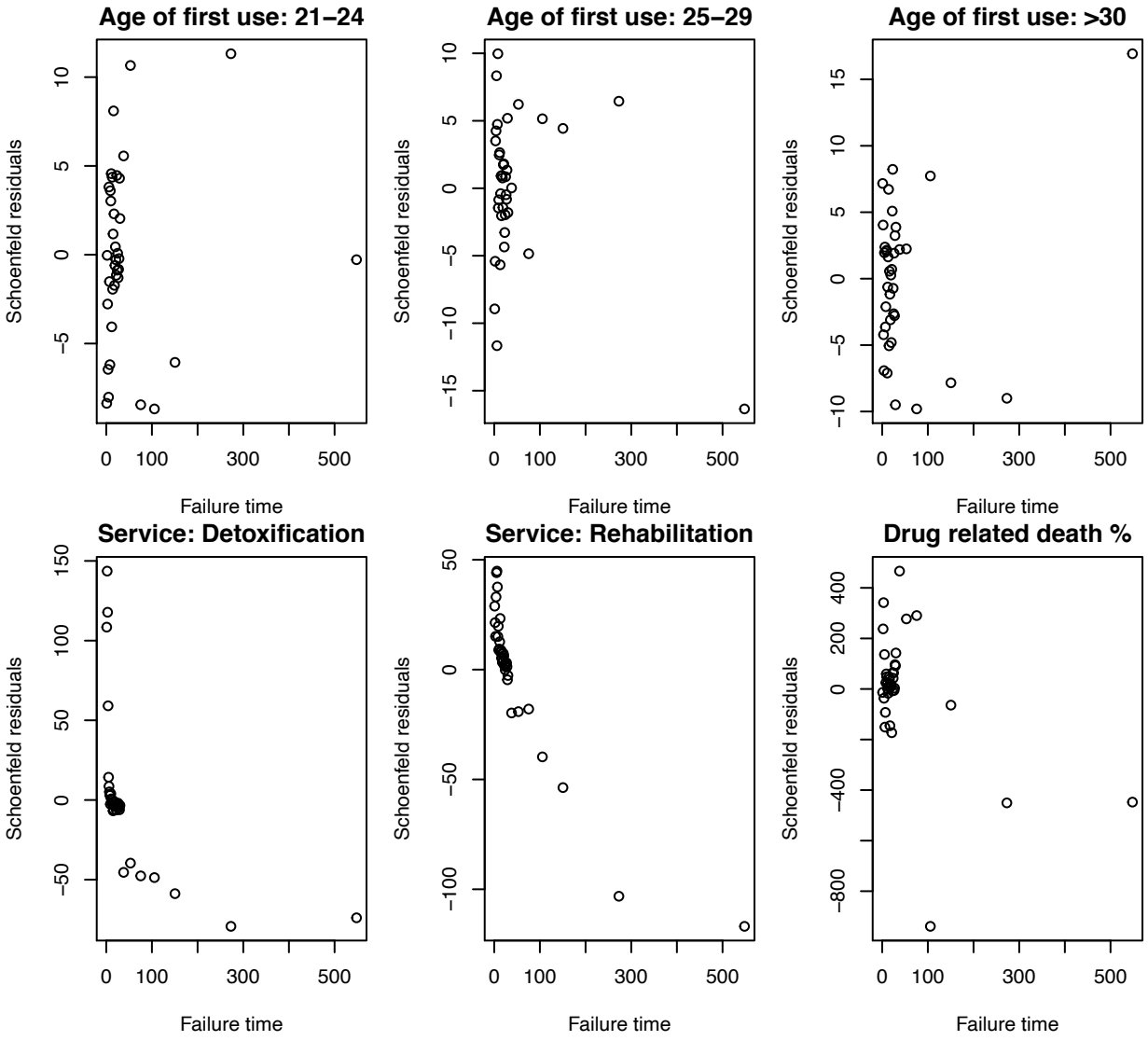
Section D: Model diagnostics

Figure A-5. Schoenfeld residuals for Fine-Gray model, outcome of interest: treatment dropout

The Schoenfeld residuals for each predictor (the difference between the observed and expected value for each failure, conditioned on all other variables) was plotted against failure time to evaluate the proportional hazards assumption on the subdistribution function. The Schoenfeld residuals seems to be randomly distributed around 0 with a locally constant mean across time, suggesting the proportional hazards assumption is satisfied. (*Due to space constraints, only one set of diagnostic plots is displayed. The diagnostic plots for the remaining models also suggest the proportional hazards assumption is satisfied).




Race: Other
Gender: Female
Hispanic: Yes
Veteran: Yes
Medication use: Yes
Prior episodes: Yes
Age of first use: 12–14
Age of first use: 15–17
Age of first use: 18–20
Schoenfeld residuals
Failure time
0
100
300
500



Section E: Full Model outputs

Table A-4: All coefficients in the Fine-Gray model with treatment dropout as the variable of interest (α = 0.05, 95% CI)

Term	Estimate	Standard Error	p-value	CI Lower	CI Upper
Psychiatric comorbidity: Present	0.064	0.023	0.005	0.019	0.110
Age: 20-30	-0.151	0.100	0.130	-0.347	0.045
Age: 30-40	-0.193	0.100	0.054	-0.390	0.003
Age: 40-50	-0.274	0.104	0.008	-0.477	-0.071
Age: $>$ 50	-0.379	0.105	$<$0.001	-0.585	-0.174
Race: Black	0.279	0.034	$<$0.001	0.212	0.346
Race: Other	0.004	0.048	0.930	-0.090	0.099
Gender: Female	-0.007	0.024	0.770	-0.054	0.040
Hispanic: Yes	0.100	0.043	0.020	0.016	0.184
Veteran: Yes	0.039	0.080	0.620	-0.117	0.195

(continued)

Term	Estimate	Standard Error	p-value	CI Lower	CI Upper
Medication use: Yes	0.128	0.024	<0.001	0.081	0.175
Prior episodes: Yes	0.071	0.027	0.009	0.018	0.124
Age of first use: 12-14	0.236	0.156	0.130	-0.070	0.542
Age of first use: 15-17	0.226	0.151	0.140	-0.070	0.523
Age of first use: 18-20	0.204	0.151	0.170	-0.091	0.499
Age of first use: 21-24	0.203	0.151	0.180	-0.093	0.498
Age of first use: 25-29	0.216	0.151	0.150	-0.080	0.512
Age of first use: >30	0.272	0.150	0.071	-0.023	0.567
Service: Detoxification	0.173	0.044	<0.001	0.088	0.259
Service: Rehabilitation	-0.134	0.034	<0.001	-0.201	-0.067
Drug related death %	-0.011	0.002	<0.001	-0.014	-0.008

Table A-5: All coefficients in the Fine-Gray model with treatment completion as the variable of interest (α = 0.05, 95% CI)

Term	Estimate	Standard Error	p-value	CI Lower	CI Upper
Psychiatric comorbidity: Present	-0.088	0.027	0.001	-0.141	-0.036
Age: 20-30	0.039	0.117	0.740	-0.189	0.268
Age: 30-40	0.040	0.117	0.730	-0.189	0.269
Age: 40-50	0.074	0.121	0.540	-0.163	0.311
Age: > 50	0.119	0.123	0.330	-0.122	0.359
Race: Black	-0.216	0.043	<0.001	-0.301	-0.131
Race: Other	0.024	0.055	0.660	-0.084	0.131
Gender: Female	-0.087	0.028	0.002	-0.142	-0.032
Hispanic: Yes	0.031	0.049	0.520	-0.064	0.126
Veteran: Yes	0.038	0.093	0.680	-0.143	0.219
Medication use: Yes	-0.471	0.031	<0.001	-0.532	-0.411
Prior episodes: Yes	0.007	0.031	0.810	-0.053	0.068
Age of first use: 12-14	-0.313	0.148	0.034	-0.603	-0.023
Age of first use: 15-17	-0.215	0.140	0.120	-0.491	0.060
Age of first use: 18-20	-0.226	0.139	0.100	-0.499	0.047
Age of first use: 21-24	-0.195	0.140	0.160	-0.469	0.079
Age of first use: 25-29	-0.198	0.140	0.160	-0.473	0.078
Age of first use: >30	-0.185	0.140	0.190	-0.460	0.089
Service: Detoxification	1.292	0.041	<0.001	1.211	1.372
Service: Rehabilitation	0.901	0.030	<0.001	0.842	0.961
Drug related death %	0.006	0.002	0.001	0.002	0.009

Table A-6: All coefficients in the Fine-Gray model with treatment dropout as the variable of interest, interaction term included (α = 0.05, 95% CI)

Term	Estimate	Standard Error	p-value	CI Lower	CI Upper
Psychiatric comorbidity: Present	0.099	0.026	<0.001	0.047	0.151
Age: 20-30	-0.149	0.100	0.140	-0.346	0.047
Age: 30-40	-0.192	0.101	0.056	-0.389	0.005
Age: 40-50	-0.272	0.104	0.009	-0.476	-0.069
Age: > 50	-0.378	0.105	<0.001	-0.584	-0.173

(continued)

Term	Estimate	Standard Error	p-value	CI Lower	CI Upper
Race: Black	0.365	0.044	<0.001	0.279	0.450
Race: Other	0.035	0.067	0.610	-0.097	0.166
Gender: Female	-0.006	0.024	0.800	-0.053	0.041
Hispanic: Yes	0.099	0.043	0.021	0.015	0.184
Veteran: Yes	0.040	0.079	0.620	-0.116	0.196
Medication use: Yes	0.128	0.024	<0.001	0.081	0.175
Prior episodes: Yes	0.071	0.027	0.008	0.018	0.124
Age of first use: 12-14	0.241	0.156	0.120	-0.064	0.547
Age of first use: 15-17	0.229	0.151	0.130	-0.067	0.526
Age of first use: 18-20	0.208	0.151	0.170	-0.088	0.503
Age of first use: 21-24	0.206	0.151	0.170	-0.090	0.502
Age of first use: 25-29	0.220	0.151	0.150	-0.076	0.516
Age of first use: >30	0.276	0.150	0.066	-0.019	0.571
Service: Detoxification	0.172	0.044	<0.001	0.086	0.257
Service: Rehabilitation	-0.131	0.034	<0.001	-0.198	-0.064
Drug related death %	-0.011	0.002	<0.001	-0.014	-0.007
Psychiatric comorbidity*Black	-0.191	0.062	0.002	-0.313	-0.070
Psychiatric comorbidity*Other race	-0.057	0.086	0.510	-0.226	0.112

Table A-7: All coefficients in the Fine-Gray model with treatment completion as the variable of interest, interaction term included (α = 0.05, 95% CI)

Term	Estimate	Standard Error	p-value	CI Lower	CI Upper
Psychiatric comorbidity: Present	-0.121	0.030	<0.001	-0.179	-0.062
Age: 20-30	0.039	0.117	0.740	-0.190	0.269
Age: 30-40	0.041	0.117	0.730	-0.189	0.271
Age: 40-50	0.074	0.121	0.540	-0.163	0.312
Age: > 50	0.121	0.123	0.330	-0.120	0.362
Race: Black	-0.327	0.058	<0.001	-0.440	-0.215
Race: Other	0.018	0.072	0.800	-0.123	0.160
Gender: Female	-0.088	0.028	0.002	-0.143	-0.033
Hispanic: Yes	0.031	0.049	0.520	-0.064	0.127
Veteran: Yes	0.040	0.092	0.670	-0.142	0.221
Medication use: Yes	-0.471	0.031	<0.001	-0.531	-0.411
Prior episodes: Yes	0.008	0.031	0.790	-0.053	0.069
Age of first use: 12-14	-0.319	0.148	0.031	-0.610	-0.028
Age of first use: 15-17	-0.219	0.141	0.120	-0.495	0.057
Age of first use: 18-20	-0.229	0.140	0.100	-0.503	0.045
Age of first use: 21-24	-0.198	0.140	0.160	-0.473	0.077
Age of first use: 25-29	-0.200	0.141	0.160	-0.476	0.076
Age of first use: >30	-0.189	0.140	0.180	-0.465	0.086
Service: Detoxification	1.292	0.041	<0.001	1.211	1.373
Service: Rehabilitation	0.900	0.030	<0.001	0.841	0.960
Drug related death %	0.005	0.002	0.002	0.002	0.009
Psychiatric comorbidity*Black	0.256	0.079	0.001	0.101	0.411
Psychiatric comorbidity*Other race	0.007	0.098	0.940	-0.185	0.199

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