**PROGRESS REPORT**

**Impact of Poly-substance use on substance use disorder treatment completion between 2010-2019 in Chile**

**Research team**

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# Project Overview

The research question and design of this project has been modified due to administrative constraints. Therefore, below is presented the current and original (discarded) project designs.

## Current project (modified from original)

* **Research question:** What are the effects of having reported polysubstance use (PSU) at admission to substance use disorder (SUD) treatments on treatment completion in Chile?
* **Specific Aims:** (1) To describe the incidence of PSU reports and treatment completion in the sample, (2) to compare the occurrence rate of treatment completion between people with reporting poly and single-substance use, and (3) to estimate the association between reporting PSU at admission and treatment completion, accounting for irregular and informative observation times.
* **Hypothesis:** Reporting PSU at admission to SUD treatment is related to lower treatment completion rates.

## Original project (discarded)

* **Research question:** What are the mediating effects of completing SUD treatment on the relationship between baseline PSU and contact with CJS in Chile in the short (six months), middle (one year), and long term (three years)?

# Progress milestones

In this section we described the main milestones achieved so far.

* **Data wrangling**

This research relies on a population-based record-linkage retrospective cohort design. The data wrangling includes managing an administrative database that contains information of patients receiving substance use treatment financed by the National Service for the Prevention and Rehabilitation of Drug and Alcohol Use (SENDA).

* *Data exploration and cleaning:* Considering all the variables available in the database, we explored the data focusing on missing data, variance, and other descriptive measures.
* *Data normalization:* We standardised variables, labelled fields, and corrected data integrity issues (e.g., typographical errors in dates, automation bias, or variations in name spelling or form). We also modified the time (in months) from the first admission for each subject and formatted to avoid overlapping between treatments.
* **Ethics application**

The study was approved by the Griffith University Human Research Ethics Committee (GUHREC GU Ref No: 2022/919).

* **Theoretical framework**

We have conducted a literature review according to the project design and the selected outcome variables. The theoretical framework progress is exposed in the next section (III). Changes to the theoretical framework will be introduced after concluding the analysis.

* **Preliminary analysis**
* *Data structure*

Patients’ entry to the retrospective cohort starts at the time they were admitted to a SUD treatment listed in the SENDAs yearly databases with information on treatments between 2010-2019. We considered patients who had ongoing treatments from 2010 until 2019. Censoring occurred after the date of data retrieving (November 13, 2019), after an outcome event occurred, or when a patient left the cohort with no other outcomes. We excluded from the sample patients with only one treatment episode. The degree of irregularity of assessment times (times in which reported PSU was measured), in this case, in admission processes, is measured through the area under the curve (AUC) and log-transformed area under the curve. To inspect the degree of visit irregularity, the entire follow-up period was divided into adjacent and equally sized timeframes, and the number of bins changed. The AUC was obtained by plotting the mean proportions of individuals with 0 visits per bin against the mean proportions of individuals with > 1 visit per bin. AUC was log-transformed for better interpretation, in which 100 is very irregular, and 0 is equivalent to a repeated measures design.

* *Measures*

The exposure variable will be PSU at admission (self-report of using more than one main substance among alcohol and illicit drugs at admission to SUD treatment, whether sequential or concurrent) (Crummy et al., 2020; Font-Mayolas & Calvo, 2022).

The outcome variable will be SUD treatment outcome/completion status (1=dropout or spelled by misconduct; 0= completed treatments).

Additionally, the models adjust for various baseline and time-varying confounding variables related to substance use, demographics, and social factors mainly to correct irregular observation times that may be related to the outcomes.

Covariates:

Covariates for weights are listed below: Treatment outcome of the previous treatment, previous biopsychosocial compromise (severe status), previous treatment duration (<90 days), previous treatment duration (in logarithmic scaled days), polysubstance use status of the previous treatment, age at admission to treatment, birth year, primary Substance (initial diagnosis; alcohol, cocaine hydrochloride, cocaine base paste, marijuana), Psychiatric comorbidity under International (diagnosis unknown or under study and with confirmed comorbidity), daily frequence of primary substance use at admission, occupational status (inactive or unemployed), and primary substance at admission to treatment (alcohol, cocaine hydrochloride, cocaine base paste, and marijuana).

Covariates for the outcome model of the association between reported substance use and treatment outcome: biopsychosocial compromise (severe status) at admission to treatment, age at admission to treatment, birth year, primary substance of the initial diagnosis (alcohol, cocaine hydrochloride, cocaine base paste, marijuana), psychiatric comorbidity (diagnosis unknown or under study and With confirmed comorbidity), daily frequence of primary substance use at admission, occupational status (inactive and unemployed), primary substance at admission to treatment (cocaine hydrochloride, cocaine base paste, marijuana, alcohol).

To account for variability by treatment setting, we stratified the analysis by setting at baseline treatment: basic ambulatory (n= 4,360) GP intensive ambulatory (n= 4,998) GP residential (n= 2,178) WO intensive ambulatory (n= 745) WO residential (n= 1,036).

* *Missing data*

Given the complex longitudinal structure of the data, we conducted random-forest-based imputation using the *missRanger* package. We will use 300 trees, using 5 candidate values of predictive matching (thus, aiming for plausible imputations given predictor values), with a maximum of 50 iterations per chaining steps. This imputation procedure may circumvent specification of interactions or nonparametric relationships and can handle collinearity between imputation variables (Hong & Lynn, 2020; Sheetal et al., 2023).

* *Model adjustment*

Models such as marginal structural models, g-computation, and targeted maximum likelihood estimation assume that observation times and gaps between them are not informative of the outcome of interest (E. M. Pullenayegum et al., 2023). The models adjust for the mentioned confounding variables. The study sample is based on a pseudo population in which the counting process (i.e., subsequent SUD treatment episodes and times between them) is static, hence, completely at random and ignorable (Carrero et al., 2023), based on generalized estimating equations and inverse probability weights given previously observed data (Cole & Hernán, 2008). We obtained these stabilized weights from a proportional intensity model in which we adjusted for baseline covariates, previous treatment outcomes, and previous polysubstance use (if any). The weights are represented through a proportional intensity model as: , where is a vector of covariates before , is a vector of regression coefficients, and the denominator is , a constant baseline hazard to stabilize weights (E. Pullenayegum, 2022). Auxiliary covariates may include confounders of the outcome model. Here, time is defined since the first individual admission in the study period (2010-2019), followed and divided by months (30.1 days). Weights were truncated at the 2.5th and 97.5th percentiles to mitigate the influence of extreme weights, aiming for a more stable and reliable analysis. Sensitivity analyses to the potential violations of proportional hazards assumption for the intensity model were tested (See Supplemental Section 1).

Supplemental Section 1. Counting process and alternative weighting schemes

To tackle potential violations of the proportional hazards assumption for outcome assessment intensity, several strategies were tested: non-proportional hazards without variable transformations, proportional hazards with time-dependent transformations (recode multiple variables interacting with different functional forms of follow-up time), and stratifying follow-up times using the 'survSplit' method. Hence, three approaches were employed: (A) no correction for intensity proportionality violations, (B) correction using time-dependent coefficients via variable transformation and interaction with time, following the method outlined by Putter et al. (2005), and (C) stratification of survival time among 30 different stratifications with better balance of. Each method considered cases where lag values of lagged variables (i.e., Treatment outcome of the previous treatment, Previous severe biopsychosocial compromise, Previous treatment duration of less than <90 days, Previous treatment duration in logarithmic scaled days, Polysubstance use status of the previous treatment) were 0 or 1 in case of missing binary values (i.e., accounting for potential missing values due to the absence of prior treatments within the study period), and ensuring a rigorous evaluation of model validity under potential assumption breaches. Continuous variables such as follow-up time and Previous treatment duration in logarithmic scaled days was fixed in 2.95 months and the natural logarithm of 90 days or 45 days if the rest of the lagged covariates were fixed in 0, respectively. Choosing the stratification involved considerations such as the distribution of events across different treatment settings and time intervals, which likely provided a good balance between granularity and statistical power, and improve model diagnostics such as the AIC (Akaike Information Criterion) and tests for proportional hazards (Keele, 2010 Consequently, follow-up times were stratified into the intervals [0,15], (15,30], (30,45], (60,75], and (75,135] for the first stratified model, and [0,10], (10,20], (20,30], (30,50], (50,70], and (70,135] for the second stratified model.

Posteriorly, we estimated the relative risk of people with PSU at admission completing treatment (Grafféo et al., 2018) using generalized estimating equations (GEE) with Poisson distributions with a log link function and assuming an independence structure. Sensitivity analyses due to differences between variance and the mean of PSU reports using Negative Binomial distributions were tested using Quasi-likelihood Information criterion for model selection (See Supplemental Section 2).

Supplemental Section 2. Model selection, alternatives accounting for overdispersion

In Poisson distribution, the variance equals the mean, implying that the theta value serves as the denominator of the squared mean and provides an indication of the degree of overdispersion present in the data. To evaluate the appropriate model for the data, a sequence of theta values ranging from 0.1 to and incrementing by 1,000. After finding an optimal value, a range of values from to incrementing by 100 were tested. Both Poisson and negative binomial models were compared using Quasi-likelihood Information criterion (QIC), a measure similar to Akaike Information Criterion for generalized estimating equations. The model that best fit the data (lowest QIC values) was selected based on this comparison. This approach highlights the methodology used to ascertain the presence of overdispersion and to determine the most suitable statistical model for handling such data deviations.

* *Data and code availability*

Preliminary code & markdowns are available here: <https://fondecytacc.github.io/nDP/index_prop_grant23_24.html>.

# Theoretical Framework

People with substance use disorder (SUD) tend to use more than one substance unintentionally and unnoticedly (e.g., due to unregulated and contaminated supplies) or intentionally [(Bunting et al., 2023; Quek et al., 2013)](https://www.zotero.org/google-docs/?46rrTq) during active use in their lifetime (Connor et al., 2014). Some reasons for intentional polysubstance use (PSU) include additive or synergistic reward, compensation for undesired effects or negative internal states, predisposition, or related to supply (e.g., due to shortages of the main substance)(Karamouzian et al., 2024). Importantly, people with PSU are a high-risk population because it is related to a higher mortality rate (Gjersing & Bretteville-Jensen, 2018), a higher risk of relapse (Chen et al., 2019; Hassan & Le Foll, 2019), less responsive to substance use treatment (Bonfiglio et al., 2022), and other detrimental features such as risky sexual behavior (Daskalopoulou et al., 2014; Sewell et al., 2017), violence (H. J. Choi et al., 2022; Steele & Peralta, 2020), and psychiatric comorbidities (Mefodeva et al., 2022). Over the last three decades, evidence has shown that the rate of people with PSU has significantly increased, at least in high-income countries from North America, Europe, and Australia (Bonfiglio et al., 2022), highlighting the relevance of studying this topic.

Despite the association between completing SUD treatment and long-term benefits, such as lower risk of readmission to treatment (Ruiz-Tagle Maturana et al., 2023), lower risk of relapse (Andersson et al., 2019), abstinence (McPherson et al., 2017), and better quality of life (N. G. Choi & DiNitto, 2020) is well known, evidence regarding the long-term consequences of reporting PSU on treatment outcomes is limited and mixed. The lack of research on PSU is partly because most studies have focused on individual substances in isolation and have considered a multiple substance use history as an exclusion criterion for clinical studies on treatment effectiveness, which raises the problem of its translatability to real health contexts (Bonfiglio et al., 2022). Regarding the treatment outcomes, some studies report a lower likelihood of treatment completion among people with PSU (Andersson et al., 2021; Levola et al., 2021), while others found no association (Andersson et al., 2018) or higher completion rates (Basu et al., 2017). In any case, it is crucial to determine the role of reporting PSU in treatment completion to improve treatment effectiveness and research translatability (Crummy et al., 2020).

However, this role must be understood in a context of patients who experience multiple and recursive treatments (Bórquez et al., 2024). Treatments are expected to change behavior relative to no treatment. Patients not benefiting from treatments often switch to other alternatives. Those facing adverse effects or resistance to change might quit, while some persevere and follow other recommendations, such as lifestyle changes that affect their prognosis. Hence, treatment outcomes such as dropout or treatment completion are linked to subsequent exposures such as a readmission(Ruiz-Tagle Maturana et al., 2023) to a posterior treatment, what is known as “feedback loop”(Hernan & Robins, 2020). Given that SUD is understood as a chronic condition, the association between reporting PSU and treatment completion on first SUD treatment alone requires accounting that some patients may be readmitted to treatment through the follow-up period (See Figure 1a). Thus, checking for group biases and adjusting for confounders is needed (Griffin et al., 2014; Hansen et al., 2020). Additionally, these treatments are irregularly spaced, nevertheless, not at random, as the time between treatments might be related to biopsychosocial and treatment-related factors (See Figure 1b). Thus, patients with worst outcomes in a previous treatment might have more or less intense frequency of treatments in the future, that may also explain treatment outcomes such as completion or dropout (Hansen et al., 2020; Vázquez-Real et al., 2022).

Additionally, the relationship between people reporting PSU and treatment completion can be affected by various factors, such as heterogeneous PSU patterns (Bhondoekhan et al., 2023; Price et al., 2023), treatment goals, patient characteristics, resource availability, and SUD severity profiles. In turn, these characteristics are highly dependent on treatment settings (Fiestas & Ponce, 2012; Reif et al., 2021; Tiet et al., 2007). In Chile, Olivari and colleagues found that women-specific treatment settings had different readmission and treatment completion than the general population. In a similar vein, Ruiz-Tagle et al. found that completion was less likely among ambulatory settings . Most research on PSU comes from the Global North, where the treatment settings are usually specialized on particular substances (Babor, 2021; Körkel, 2021). This is not the reality of other contexts, such as Latin America, due to scarce resources and a shortage of mental health workforce, in which treatment is mostly delivered in non-specialized settings. However, studying the role of PSU on treatment outcomes in Latin America is challenging due to limited local data (Lalwani et al., 2022). Furthermore, using evidence from the Global North is not straightforward, as it focuses on opioids and injecting drug use, which are epidemiologic features that are not prevalent in the Latin American context (Castaldelli-Maia et al., 2023).

Moreover, as many studies in the Global North have often overlooked high-risk populations, there are reasons to believe that is also the case in Latin America, where the prevalence of individuals with PSU is notably high (Reyes et al., 2013). A meta-analysis focusing on Global North studies on cocaine found that more than 70% of people who use cocaine have concurrent alcohol consumption. In addition, between 38% and 64% of the participants had concurrent marijuana use (Liu et al., 2018). A recent study conducted in a Chilean hard-to-reach population that used cocaine base paste found that between 47% and 66% of users had simultaneous substance use (Olivari et al., 2022). Similarly, an analysis of data from studies conducted in six Latin American countries found that 21% of the participants reported PSU (Vilugrón et al., 2022), which was more frequent among males and young adults( 18-34) from Chile, Uruguay, and Argentina. In addition, PSU is related to school dropout, unemployment, sexual and antisocial risk behaviors (Olivari et al., 2022; Santis B et al., 2007; Vilugrón et al., 2022).

Chile has a robust public treatment system that produces a large and high-quality dataset that includes all treatment episodes of people with public health insurance (~80% of the population) since its creation in 2010 (Mateo Pinones et al., 2022). Annually, nearly 15,000 individuals are admitted for treatment. Each patient identifies the primary substance that prompted them to seek treatment, as well as any additional substances that may have contributed to their decision. However, findings from the Chilean Budgetary Office study substantiate the need for further research to determine whether treatments address characteristics such as PSU behaviors effectively in a context where 2 out of 3 reported PSU (DIPRES, 2017). Understanding the PSU-treatment completion relationship could inform effective prevention and intervention strategies for people with PSU. Moreover, expanding the knowledge about patterns of social inequalities and vulnerabilities in access to health services can serve as input to raise awareness among society and decision-makers and as a guide for developing policies and actions to reduce health inequities. Thus, this study aims to address this gap by estimating the effect of having reported PSU on treatment completion among adult patients admitted to SUD treatment programs in Chile from 2010-2019.

# Preliminary analysis

The preliminary analysis is structured with a summary of covariate baseline characteristics by polysubstance use status reported at admission. Then, we formatted the database and structured it by patient id and treatment number. Also, we provide a summary of the trajectories of patients by polysubstance use status and treatment outcome. Finally, we show a glimpse of missingness patterns.

* Characteristics of the study sample at treatment admission

After excluding records of ongoing treatments and referred outside the treatment network, 72,404 patients with 90,075 treatments were selected. In the total sample, 82% had one treatment episode, while 1% had more than 3 treatment episodes. We focused on patients with more than one treatment, identifying 13,317 patients and 30,988 observations. Several key differences were notable among individuals reporting polysubstance use.

In terms of **demographics** at baseline, people with PSU, when compared to people who report single substance use had their first admission to treatment earlier in life. Also, a higher percentage of them were unemployed. Regarding of **substance use** at baseline, people with PSU when compared to people who report single substance use: were more likely to report using cocaine paste and hydrochloride cocaine instead of alcohol as the primary substance that led them to treatment. In terms of the type of initiation substance, fewer started with alcohol, while more began with marijuana. In terms of other **health** information at baseline, severe biopsychosocial compromise was more frequent among people with PSU (See Table 1).

* Treatment history

Interestingly, among patients with only one treatment, 72% reported PSU. However, when examining patients with multiple treatment episodes, between 80% and 88% reported PSU. This suggest that exposure to PSU could be overrepresented in the sample, as readmission is associated with PSU. This association is also evident when comparing the number of treatments to the proportion of non-complete treatments. Specifically, 71% of patients with only one treatment did not complete it, while 79%, 81% and 85% of the treatment episodes of patients with two, three or four and more, respectively, correspond to non-completion status. According to Figure XX, when considering a bin width of 2% of the gap between treatments, the proportion of patients with two or more admissions was 0.33, decreasing to a proportion of 0.04 when considering a bin width of 6%. An AUC of 0.21 (log-transformed= 80) suggest there is likely a counting process behind visits rather than perfectly repeated and thus regular measures. Therefore, it seems reasonable to conduct an analysis that considers irregularity in observations and an extent of informative assessment times, conditional on several covariates, including past observed outcomes, past assessment history, and baseline covariates (Lokku et al., 2020).

* Modelling of the observation process

We tested various weighting schemes for the visiting process. Therefore, to measure the association between reported PSU and dropouts, it is crucial to incorporate the visit process (See Table 2).

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Inverse intensity weights are shown in Supplemental Table 1.

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Table 1a. Characteristics of the study sample

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Variable** | **Category** | **No PSU (n=2,383)** | **PSU (n=10,934)** | **Overall (n= 13,317)** | **SMD** |
| Complete status of treatment (Dropout / Misspelled) (%) | 1 | 1833 (76.9) | 8615 (78.8) | 10448 (78.5) | 0.045 |
| Biopsychosocial compromise (Severe) (%) | 1 | 690 (29.0) | 4806 (44.0) | 5496 (41.3) | 0.315 |
| Treatment duration (binary) (<90 days) (%) | 1 | 567 (23.8) | 2702 (24.7) | 3269 (24.5) | 0.021 |
| Treatment duration (log-scaled days) (median [IQR]) |  | 5.1 [4.5, 5.6] | 5.1 [4.5, 5.7] | 5.11 [4.5, 5.7] | 0.043 |
| Age at admission to treatment (median [IQR]) |  | 37.1 [29.4, 46.2] | 31.4 [26.1, 38.1] | 32.18 [26.5, 39.6] | 0.542 |
| Birth year (median [IQR]) |  | 1976.0 [1968.0, 1984.0] | 1981.0 [1974.0, 1987.0] | 1981.0 [1973.0, 1986.0] | 0.446 |
| Primary substance (initial diagnosis): alcohol (%) | 1 | 1484 (62.3) | 5440 (49.8) | 6924 (52.0) | 0.254 |
| Primary substance (initial diagnosis): cocaine hydrochloride (%) | 1 | 108 (4.5) | 519 (4.7) | 627 (4.7) | 0.010 |
| Primary substance (initial diagnosis): cocaine base paste (%) | 1 | 251 (10.5) | 872 (8.0) | 1123 (8.4) | 0.088 |
| Primary substance (initial diagnosis): marijuana (%) | 1 | 483 (20.3) | 3865 (35.3) | 4348 (32.6) | 0.341 |
| Psychiatric comorbidity (ICD-10): In study (%) | 1 | 420 (17.6) | 2233 (20.4) | 2653 (19.9) | 0.071 |
| Psychiatric comorbidity (ICD-10): Diagnosis (%) | 1 | 986 (41.4) | 4850 (44.4) | 5836 (43.8) | 0.060 |
| Daily frequence of primary substance use at admission (%) | 1 | 1013 (42.5) | 5229 (47.8) | 6242 (46.9) | 0.107 |
| Occupational Status: Inactive (%) | 1 | 468 (19.6) | 1942 (17.8) | 2410 (18.1) | 0.048 |
| Occupational Status: Unemployed (%) | 1 | 764 (32.1) | 4507 (41.2) | 5271 (39.6) | 0.191 |
| Primary substance at admission to treatment: cocaine hydrochloride (%) | 1 | 292 (12.3) | 2078 (19.0) | 2370 (17.8) | 0.187 |
| Primary substance at admission to treatment: cocaine base paste (%) | 1 | 902 (37.9) | 5996 (54.8) | 6898 (51.8) | 0.346 |
| Primary substance at admission to treatment: marijuana (%) | 1 | 64 (2.7) | 653 (6.0) | 717 (5.4) | 0.162 |
| Primary substance at admission to treatment: alcohol (%) | 1 | 1082 (45.4) | 2062 (18.9) | 3144 (23.6) | 0.593 |
| Treatment setting (%) | Basic ambulatory | 1040 (43.6) | 3320 (30.4) | 4360 (32.7) | 0.298 |
|  | GP intensive ambulatory | 786 (33.0) | 4212 (38.5) | 4998 (37.5) |  |
|  | GP residential | 272 (11.4) | 1906 (17.4) | 2178 (16.4) |  |
|  | WO intensive ambulatory | 138 (5.8) | 607 (5.6) | 745 (5.6) |  |
|  | WO residential | 147 (6.2) | 889 (8.1) | 1036 (7.8) |  |

Note. n= frequency of patients; descriptive statistics of baseline characteristics used the median (Q2) and percentiles 25 and 75 in brackets for continuous variables. Furthermore, categorical variables are represented in frequencies and percentages (%) in parenthesis.

Figure 1a. Causal diagram as a conceptual reference

Diagrama

Descripción generada automáticamente

Note: A= Reporting PSU at admission; Y= Time to treatment completion status from admission; L0=Baseline confounders; {L1, L2, ..., Lt} = time-dependent biopsychosocial; U= Unobserved confounders; t= individual treatments from 2010)

Figure 1b. Causal diagram hypothesized as the observation process

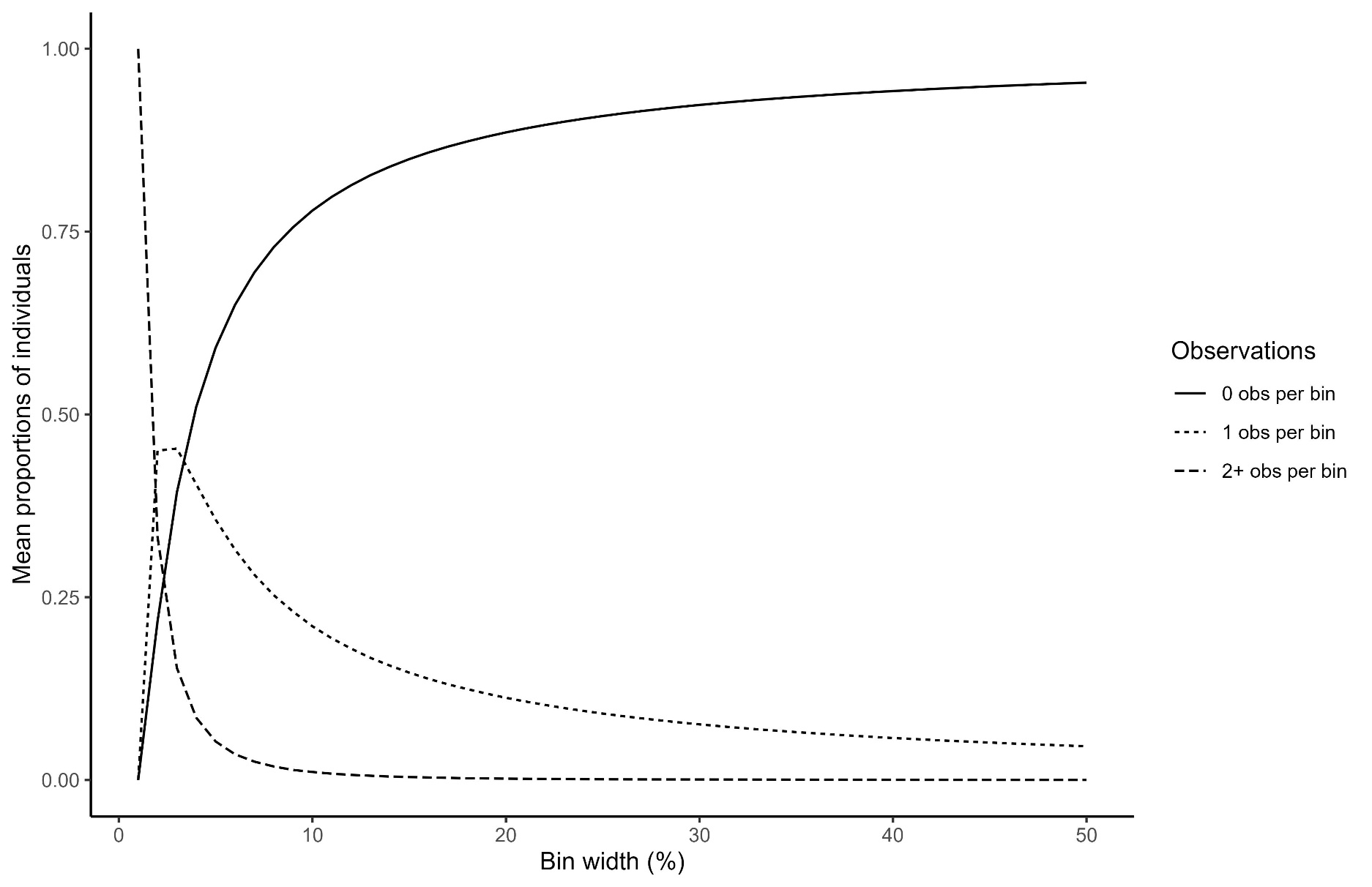
Diagrama

Descripción generada automáticamente

Note. All the backdoors of the month of assessment (admission to treatment), may pass through observed outcomes, history of evolution or baseline covariates to impact on outcomes. If we assume that is a proportional intensity model holds, we can search evidence in the data that previous variables are associated with outcomes.

Source: Pullenayegum, E. M., & Scharfstein, D. O. (2022). Randomized Trials With Repeatedly Measured Outcomes: Handling Irregular and Potentially Informative Assessment Times. Epidemiologic Reviews, 44(1), 121-137. https://doi.org/10.1093/epirev/mxac010

Figure XX. Mean proportions of patients with 0,1, and >1 admissions per bin as bin width varies from 1 to 50% of the gap between readmissions.



Note. Modified= Time in months from the first admission, and formatted to avoid overlapping between treatments, complete cases; Modified (imputation)= Time in months from the first admission, and formatted to avoid overlapping between treatments, imputed missing values; Original calendar= Formatted in calendar date, no further format.

Table 2. Specifications of the treatment (visit) process

|  |  |  |  |
| --- | --- | --- | --- |
| **Model** | **Term** | **Hazard ratio (95% CI)** | **Sig.** |
| First model | Previous dropout | 1.50 (1.43, 1.57) | <0.001 |
|  | Biopsychosocial compromise (moderate) | 1.06 (0.99, 1.13) | 0.090 |
|  | Biopsychosocial compromise (severe) | 1.57 (1.46, 1.67) | <0.001 |
|  | Less than 90 days in previous treatment | 1.71 (1.66, 1.78) | <0.001 |
|  | Reported PSU in previous treatment | 1.08 (1.04, 1.13) | <0.001 |
|  | Count of treatments | 0.97 (0.95, 1.00) | 0.030 |
| Second model |  |  |  |
|  | Previous dropout | 1.48 (1.42, 1.55) | <0.001 |
|  | Biopsychosocial compromise (moderate) | 1.05 (0.98, 1.12) | 0.180 |
|  | Biopsychosocial compromise (severe) | 1.61 (1.5, 1.71) | <0.001 |
|  | Less than 90 days in previous treatment | 1.77 (1.71, 1.82) | <0.001 |
|  | Reported PSU in previous treatment | 1.05 (1.00, 1.10) | 0.030 |
|  | Reported PSU in actual treatment | 1.22 (1.19, 1.24) | <0.001 |

Note. First model= Intensity model, restricted to cases with more than one treatment and lag values were fixed to one (excepting on moderate biopsychosocial compromise); In Andersen-Gill format, not restricted to cases with more than one treatment and lag values were fixed to one (excepting on moderate biopsychosocial compromise).

lag=0: Lagged covariates were fixed to 0 for binary variables and natural logarithm of 45 days; lag=1: Lagged covariates were fixed to 1 for binary variables and natural logarithm of 90 days

Table 3. Association between Polysubstance use at admission and Treatment completion status (dropout or spelled by misconduct) from Poisson Regression Multivariable Model with independence structure

|  |  |  |  |
| --- | --- | --- | --- |
| **Treatment setting** | **RR (95%CI)** | **Inverse intensity weighted RR (95%CI) (lag=0)** | **Inverse intensity weighted RR (95%CI) (lag=1)** |
| Basic ambulatory |  |  |  |
|  | 1.02 (1.00, 1.05) | 1.02 (0.99, 1.05) | 1.02 (1.00, 1.05) |
| General-population intensive ambulatory |  |  |  |
|  | 1.04 (1.01, 1.07) | 1.04 (1.01, 1.08) | 1.04 (1.01, 1.07) |
| General-population residential |  |  |  |
|  | 0.97 (0.92, 1.02) | 0.97 (0.92, 1.02) | 0.95 (0.90, 1.01) |
| Women-only intensive ambulatory |  |  |  |
|  | 0.99 (0.92, 1.05) | 0.99 (0.92, 1.07) | 0.99 (0.92, 1.07) |
| Women-only residential |  |  |  |
|  | 1.14 (1.06, 1.23) | 1.15 (1.06, 1.26) | 1.13 (1.04, 1.22) |

Note: RR= Relative risk; 95%CI= 95% confidence intervals in parenthesis; lag=0: Lagged covariates were fixed to 0 for binary variables and natural logarithm of 45 days; lag=1: Lagged covariates were fixed to 1 for binary variables and natural logarithm of 90 days. All models adjusted for the following covariates: biopsychosocial compromise (severe status) at admission to treatment, Age at admission to treatment, Birth year, Primary substance of the initial diagnosis (alcohol, cocaine hydrochloride, cocaine base paste, marijuana), Psychiatric comorbidity (in study and with comorbidity), Daily frequence of primary substance use at admission, Occupational status (inactive and unemployed), Primary substance at admission to treatment (Cocaine hydrochloride, cocaine base paste, marijuana, alcohol).