**Association between poly-substance use and substance use disorder treatment noncompletion in patients** **admitted to multiple treatments between 2010-2019 in Chile**

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**Supplemental Section 1. Covariates**

**Table S1. Description of covariates**

|  |  |
| --- | --- |
| **Covariate name** | **Description** |
| Biopsychosocial compromise | A clinical appraisal from professionals in the treatment team at admission to treatment, which considers the level of withdrawal symptoms, the motive of admission, motivation to change, the severity of SUD, number of previous treatments, number of physical complaints, and characteristics of the social environment (e.g., family functioning). Is coded by the authors as mild or moderate vs. severe (Ruiz-Tagle et al., 2023). |
| Age at Admission to Treatment (First Entry) | Age of the patient at the time of admission to treatment. The value of the first available treatment is considered. |
| Birth year | In calendar years (e.g., 1995). Obtained from the registered birth date. |
| Primary substance of the initial diagnosis | Indicated by patients as the starting substance of their drug use. SISTRAT allows the presentation of up to three starting substances, which is why we kept the most vulnerable category for patients who reported more than one value ("Base paste", "Cocaine hydrochloride", "Marijuana", "Alcohol", "Other"). On the other hand, other substances, such as hallucinogens, amphetamine-type stimulants, inhalants, opiates, sedatives, hypnotics and tranquilizers, and other substances (anabolic steroids, etc.), did not exceed 3% of the responses, and were therefore classified as "Other". |
| Psychiatric comorbidity (ICD-10) | According to the ICD-10 (International Classification of Diseases 10th Edition) classification. The system allowed for submitting up to three psychiatric conditions. If, at the time of dropout or other treatment termination, patients were not diagnosed but a condition is suspected by clinical staff (though not by a specialist), then the status is coded as "under study." |
| Daily frequence of primary substance use at admission | Days of use in the last 30 days before treatment of the primary substance at admission. Patients can answer the following: Did not use, less than one day a week, one day a week or more, 2 to 3 days a week, 4 to 6 days a week and Daily. We coded as “Daily” vs. the rest of frequencies. |
| Occupational status | Coded from a single question asked whether the respondent worked at least one hour during the last week, excluding care work at home. If the respondent answered affirmatively, they were coded as “employed.” If the respondent answered negatively, their responses were categorized as follows:   * **Unemployed** for those who actively looking but unable to find work or reported being first-time job seekers. * **Inactive** or without any activity: This includes individuals studying but not working, permanently unable to work, pensioned or retired but not working, rentiers receiving income from properties or investments, those engaged in household chores, not seeking work, or other specified reasons. |
| Primary substance at admission to treatment | Identified and defined by the patient as the substance that motivates the consultation and admission, being the substance of greatest concern. |

Note. We consider the value of all covariates at the first treatment completed or not.

**Supplemental Section 2. 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 through specifying time-varying coefficients (i.e., interacting with time), (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.

We recoded several covariates to account for its interaction with time through visual inspection of Schoenfeld residuals vs. time. This transformation aims to capture the changing impact of the previous treatment outcome over different time periods. We recoded the following: Treatment outcome of the previous treatment, previous biopsychosocial compromise, previous treatment duration (<90 days), primary substance (initial diagnosis), cocaine, and Psychiatric comorbidity (confirmed comorbidity).

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. Consequently, follow-up times were stratified into the following intervals: [0,10], (10,20], (20,30], (30,50], (50,70], and (70,135] for the second stratified model.

**Table S2. Specifications of the treatment (visit) process, in Hazard Ratios (HR) and under different lagged variables scenarios**

|  |  |  |
| --- | --- | --- |
| **Term** | **HR (95% CI) lag=0** | **HR (95% CI) lag=1** |
| Treatment outcome of the previous treatment | 0.65 (0.63, 0.67) | 1.30 (1.26, 1.34) |
| Previous treatment duration (in logarithmic scaled days) | 0.85 (0.84, 0.86) | 1.48 (1.44, 1.53) |
| Previous treatment duration (<90 days) | 0.69 (0.67, 0.72) | 2.63 (2.52, 2.74) |
| Previous biopsychosocial compromise (severe) | 0.88 (0.85, 0.90) | 1.54 (1.50, 1.57) |
| Polysubstance use status of the previous treatment | 0.62 (0.61, 0.64) | 1.26 (1.22, 1.30) |
| Age at admission to treatment | 1.05 (1.05, 1.06) | 1.06 (1.06, 1.06) |
| Birth year | 1.06 (1.06, 1.06) | 1.06 (1.06, 1.06) |
| Primary substance (initial diagnosis), cocaine | 1.01 (0.95, 1.08) | 1.05 (0.98, 1.12) |
| Primary substance (initial diagnosis), alcohol | 1.01 (0.96, 1.07) | 1.04 (0.99, 1.10) |
| Primary substance (initial diagnosis), cocaine base paste | 0.98 (0.92, 1.04) | 1.05 (0.99, 1.11) |
| Primary substance (initial diagnosis), marijuana | 1.04 (0.99, 1.10) | 1.03 (0.98, 1.09) |
| Psychiatric comorbidity (confirmed comorbidity) | 1.00 (0.99, 1.02) | 0.95 (0.94, 0.97) |
| Psychiatric comorbidity (diagnosis unknown or under study) | 1.00 (0.98, 1.03) | 0.74 (0.72, 0.76) |
| Daily frequence of primary substance use at admission | 1.02 (1.01, 1.04) | 0.95 (0.94, 0.97) |
| Occupational status (inactive) | 0.99 (0.96, 1.01) | 0.96 (0.94, 0.99) |
| Occupational status (unemployed) | 1.03 (1.01, 1.05) | 0.98 (0.96, 1.00) |
| Primary substance at admission to treatment (alcohol) | 0.99 (0.93, 1.06) | 1.03 (0.96, 1.09) |
| Primary substance at admission to treatment (cocaine hydrochloride) | 1.11 (1.04, 1.19) | 1.03 (0.97, 1.10) |
| Primary substance at admission to treatment (cocaine base paste) | 1.14 (1.07, 1.22) | 1.01 (0.95, 1.08) |
| Primary substance at admission to treatment (marijuana) | 1.04 (0.96, 1.12) | 1.05 (0.98, 1.12) |

Note. 95%CI= 95% confidence intervals in parenthesis; Intensity model, in Andersen-Gill format,

lag=0: Lagged covariates were fixed to 0 for binary variables and natural logarithm of 45 days in a hypothetical previous treatment stay for the first treatment; lag=1: Lagged covariates were fixed to 1 for binary variables and natural logarithm of 90 days in a hypothetical previous treatment stay for the first treatment.

**Table S3. Descriptive characterization of inverse intensity weights**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Visit intensity model** | **Min.** | **First quartile** | **Median** | **Mean** | **Third quartile** | **Max.** |
| No time-varying coefficients, lagged covariates fixed in 0 | 0.21 | 1.00 | 1.62 | 1.83 | 2.56 | 3.79 |
| No time-varying coefficients, lagged covariates fixed in 1 | 0.13 | 0.42 | 0.68 | 0.70 | 1.00 | 1.00 |
| With time-varying coefficients, lagged covariates fixed in 0 | 0.47 | 0.67 | 1.08 | 1.33 | 1.90 | 3.03 |
| With time-varying coefficients, lagged covariates fixed in 1 | 0.10 | 0.17 | 0.55 | 0.88 | 1.36 | 3.56 |
| Stratified by follow-up intervals, lagged covariates fixed in 0 | 0.29 | 0.60 | 0.86 | 0.99 | 1.18 | 3.02 |
| Stratified by follow-up intervals, lagged covariates fixed in 1 | 0.12 | 0.12 | 0.44 | 0.60 | 0.76 | 3.07 |

All models account for inverse intensity weights, which are crucial for adjusting the likelihood of treatment visit observations in the presence of irregular admission patterns.

**Supplemental Section 3. 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.

**Table S4. Relative risk of treatment noncompletion status (dropout or spelled by misconduct) by reported polysubstance use**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Treatment setting** | **Model** | **QIC** | **RR** | **Sig** |
| Basic ambulatory |  |  |  |  |
|  | No time-varying coefficients, no weight | 19,452.9 | 1.02 (1.00, 1.05) | 0.0750 |
|  | No time-varying coefficients, no weight, NB | 19,452.9 | 1.02 (1.00, 1.05) | 0.0750 |
|  | No time-varying coefficients, lag=0 | 19,463.5 | 1.02 (0.99, 1.05) | 0.1665 |
|  | No time-varying coefficients, lag=0, NB | 19,463.5 | 1.02 (0.99, 1.05) | 0.1665 |
|  | No time-varying coefficients, lag=1 | 19,457.6 | 1.02 (1.00, 1.05) | 0.0838 |
|  | No time-varying coefficients, lag=1, NB | 19,457.6 | 1.02 (1.00, 1.05) | 0.0838 |
|  | With time-varying coefficients, no weight | 19,452.9 | 1.02 (1.00, 1.05) | 0.0750 |
|  | With time-varying coefficients, no weight, NB | 19,452.9 | 1.02 (1.00, 1.05) | 0.0750 |
|  | With time-varying coefficients, lag=0 | 19,477.3 | 1.03 (0.99, 1.06) | 0.1328 |
|  | With time-varying coefficients, lag=0, NB | 19,477.3 | 1.03 (0.99, 1.06) | 0.1328 |
|  | With time-varying coefficients, lag=1 | 19,514.7 | 1.03 (0.98, 1.07) | 0.2209 |
|  | With time-varying coefficients, lag=1, NB | 19,514.7 | 1.03 (0.98, 1.07) | 0.2209 |
|  | Stratified by follow-up intervals, no weight | 19,452.9 | 1.02 (1.00, 1.05) | 0.0750 |
|  | Stratified by follow-up intervals, no weight, NB | 19,452.9 | 1.02 (1.00, 1.05) | 0.0750 |
|  | Stratified by follow-up intervals, lag=0 | 19,465.3 | 1.04 (1.01, 1.07) | 0.0202 |
|  | Stratified by follow-up intervals, lag=0, NB | 19,465.3 | 1.04 (1.01, 1.07) | 0.0202 |
|  | Stratified by follow-up intervals, lag=1 | 19,502.8 | 1.03 (0.99, 1.07) | 0.1613 |
|  | Stratified by follow-up intervals, lag=1, NB | 19,502.8 | 1.03 (0.99, 1.07) | 0.1613 |
| General-population, intensity ambulatory |  |  |  |  |
|  | No correction | 22,259.1 | 1.04 (1.01, 1.07) | 0.0090 |
|  | No correction, NB | 22,259.1 | 1.04 (1.01, 1.07) | 0.0090 |
|  | No correction, lag=0 | 22,272.1 | 1.04 (1.01, 1.08) | 0.0112 |
|  | No correction, lag=0, NB | 22,272.1 | 1.04 (1.01, 1.08) | 0.0112 |
|  | No correction, lag=1 | 22,268.1 | 1.04 (1.01, 1.07) | 0.0127 |
|  | No correction, lag=1, NB | 22,268.1 | 1.04 (1.01, 1.07) | 0.0127 |
|  | With time-varying coefficients, no weight | 22,259.1 | 1.04 (1.01, 1.07) | 0.0090 |
|  | With time-varying coefficients, no weight, NB | 22,259.1 | 1.04 (1.01, 1.07) | 0.0090 |
|  | With time-varying coefficients, lag=0 | 22,280.5 | 1.05 (1.02, 1.09) | 0.0035 |
|  | With time-varying coefficients, lag=0, NB | 22,280.5 | 1.05 (1.02, 1.09) | 0.0035 |
|  | With time-varying coefficients, lag=1 | 22,318.8 | 1.05 (1.00, 1.09) | 0.0463 |
|  | With time-varying coefficients, lag=1, NB | 22,318.8 | 1.05 (1.00, 1.09) | 0.0463 |
|  | Stratified by follow-up intervals, no weight | 22,259.1 | 1.04 (1.01, 1.07) | 0.0090 |
|  | Stratified by follow-up intervals, no weight, NB | 22,259.1 | 1.04 (1.01, 1.07) | 0.0090 |
|  | Stratified by follow-up intervals, lag=0 | 22,265.5 | 1.02 (0.99, 1.05) | 0.1547 |
|  | Stratified by follow-up intervals, lag=0, NB | 22,265.5 | 1.02 (0.99, 1.05) | 0.1547 |
|  | Stratified by follow-up intervals, lag=1 | 22,276.1 | 1.01 (0.98, 1.05) | 0.4255 |
|  | Stratified by follow-up intervals, lag=1, NB | 22,276.1 | 1.01 (0.98, 1.05) | 0.4255 |
| General-population, residential |  |  |  |  |
|  | No correction | 9,817.2 | 0.97 (0.92, 1.02) | 0.1904 |
|  | No correction, NB | 9,817.2 | 0.97 (0.92, 1.02) | 0.1904 |
|  | No correction, lag=0 | 9,832.0 | 0.97 (0.92, 1.02) | 0.2528 |
|  | No correction, lag=0, NB | 9,832.0 | 0.97 (0.92, 1.02) | 0.2528 |
|  | No correction, lag=1 | 9,826.1 | 0.95 (0.90, 1.01) | 0.0991 |
|  | No correction, lag=1, NB | 9,826.1 | 0.95 (0.90, 1.01) | 0.0991 |
|  | With time-varying coefficients, no weight | 9,817.2 | 0.97 (0.92, 1.02) | 0.1904 |
|  | With time-varying coefficients, no weight, NB | 9,817.2 | 0.97 (0.92, 1.02) | 0.1904 |
|  | With time-varying coefficients, lag=0 | 9,828.8 | 0.98 (0.92, 1.03) | 0.4442 |
|  | With time-varying coefficients, lag=0, NB | 9,828.8 | 0.98 (0.92, 1.03) | 0.4442 |
|  | With time-varying coefficients, lag=1 | 9,865.7 | 1.00 (0.93, 1.07) | 0.9636 |
|  | With time-varying coefficients, lag=1, NB | 9,865.7 | 1.00 (0.93, 1.07) | 0.9636 |
|  | Stratified by follow-up intervals, no weight | 9,817.2 | 0.97 (0.92, 1.02) | 0.1904 |
|  | Stratified by follow-up intervals, no weight, NB | 9,817.2 | 0.97 (0.92, 1.02) | 0.1904 |
|  | Stratified by follow-up intervals, lag=0 | 9,836.6 | 0.97 (0.91, 1.04) | 0.4096 |
|  | Stratified by follow-up intervals, lag=0, NB | 9,836.6 | 0.97 (0.91, 1.04) | 0.4096 |
|  | Stratified by follow-up intervals, lag=1 | 9,883.8 | 1.01 (0.92, 1.10) | 0.9098 |
|  | Stratified by follow-up intervals, lag=1, NB | 9,883.8 | 1.01 (0.92, 1.10) | 0.9098 |
| Women-only, intensive ambulatory |  |  |  |  |
|  | No correction | 3,420.7 | 0.99 (0.92, 1.05) | 0.7075 |
|  | No correction, NB | 3,420.7 | 0.99 (0.92, 1.05) | 0.7075 |
|  | No correction, lag=0 | 3,431.1 | 0.99 (0.92, 1.07) | 0.8688 |
|  | No correction, lag=0, NB | 3,431.1 | 0.99 (0.92, 1.07) | 0.8688 |
|  | No correction, lag=1 | 3,426.7 | 0.99 (0.92, 1.06) | 0.7381 |
|  | No correction, lag=1, NB | 3,426.7 | 0.99 (0.92, 1.06) | 0.7381 |
|  | With time-varying coefficients, no weight | 3,420.7 | 0.99 (0.92, 1.05) | 0.7075 |
|  | With time-varying coefficients, no weight, NB | 3,420.7 | 0.99 (0.92, 1.05) | 0.7075 |
|  | With time-varying coefficients, lag=0 | 3,441.0 | 1.01 (0.92, 1.10) | 0.8228 |
|  | With time-varying coefficients, lag=0, NB | 3,441.0 | 1.01 (0.92, 1.10) | 0.8228 |
|  | With time-varying coefficients, lag=1 | 3,463.6 | 1.01 (0.91, 1.12) | 0.8719 |
|  | With time-varying coefficients, lag=1, NB | 3,463.6 | 1.01 (0.91, 1.12) | 0.8719 |
|  | Stratified by follow-up intervals, no weight | 3,420.7 | 0.99 (0.92, 1.05) | 0.7075 |
|  | Stratified by follow-up intervals, no weight, NB | 3,420.7 | 0.99 (0.92, 1.05) | 0.7075 |
|  | Stratified by follow-up intervals, lag=0 | 3,434.3 | 0.98 (0.91, 1.05) | 0.5343 |
|  | Stratified by follow-up intervals, lag=0, NB | 3,434.3 | 0.98 (0.91, 1.05) | 0.5343 |
|  | Stratified by follow-up intervals, lag=1 | 3,465.0 | 0.94 (0.87, 1.02) | 0.1571 |
|  | Stratified by follow-up intervals, lag=1, NB | 3,465.0 | 0.94 (0.87, 1.02) | 0.1571 |
| Women-only, residential |  |  |  |  |
|  | No correction | 4,823.9 | 1.14 (1.06, 1.23) | 0.0006 |
|  | No correction, NB | 4,823.9 | 1.14 (1.06, 1.23) | 0.0006 |
|  | No correction, lag=0 | 4,836.4 | 1.15 (1.06, 1.26) | 0.0009 |
|  | No correction, lag=0, NB | 4,836.4 | 1.15 (1.06, 1.26) | 0.0009 |
|  | No correction, lag=1 | 4,831.9 | 1.13 (1.04, 1.22) | 0.0027 |
|  | No correction, lag=1, NB | 4,831.9 | 1.13 (1.04, 1.22) | 0.0027 |
|  | With time-varying coefficients, no weight | 4,823.9 | 1.14 (1.06, 1.23) | 0.0006 |
|  | With time-varying coefficients, no weight, NB | 4,823.9 | 1.14 (1.06, 1.23) | 0.0006 |
|  | With time-varying coefficients, lag=0 | 4,837.1 | 1.11 (1.02, 1.21) | 0.0125 |
|  | With time-varying coefficients, lag=0, NB | 4,837.1 | 1.11 (1.02, 1.21) | 0.0125 |
|  | With time-varying coefficients, lag=1 | 4,857.5 | 1.13 (1.03, 1.25) | 0.0115 |
|  | With time-varying coefficients, lag=1, NB | 4,857.5 | 1.13 (1.03, 1.25) | 0.0115 |
|  | Stratified by follow-up intervals, no weight | 4,823.9 | 1.14 (1.06, 1.23) | 0.0006 |
|  | Stratified by follow-up intervals, no weight, NB | 4,823.9 | 1.14 (1.06, 1.23) | 0.0006 |
|  | Stratified by follow-up intervals, lag=0 | 4,839.3 | 1.11 (1.02, 1.20) | 0.0108 |
|  | Stratified by follow-up intervals, lag=1, NB | 4,839.3 | 1.11 (1.02, 1.20) | 0.0108 |
|  | Stratified by follow-up intervals, lag=1 | 4,870.0 | 1.09 (0.99, 1.20) | 0.0718 |
|  | Stratified by follow-up intervals, lag=1, NB | 4,870.0 | 1.09 (0.99, 1.20) | 0.0718 |

Note. NB= Negative binomial; QIC= Quasi-likelihood information criteria; 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).