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

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# INTRODUCTION

Polysubstance use (PSU) refers to the concurrent or sequential use of more than one substance, unintentionally or intentionally [(Bunting et al., 2024; Quek et al., 2013)](https://www.zotero.org/google-docs/?FW5yDA). People with substance use disorders (SUD) often engage in PSU during their lifetime [(Connor et al., 2014)](https://www.zotero.org/google-docs/?MKrndu). Importantly, individuals with PSU are a high-risk population due to higher mortality rates [(Gjersing & Bretteville‐Jensen, 2018)](https://www.zotero.org/google-docs/?E9GoKQ), increased risk of relapse [(Chen et al., 2019; Hassan & Le Foll, 2019)](https://www.zotero.org/google-docs/?mpl1eZ), and reduced responsiveness to substance use treatment [(Bonfiglio et al., 2022)](https://www.zotero.org/google-docs/?7CrhNC). PSU might also be associated with risky sexual behavior [(Daskalopoulou et al., 2014; Sewell et al., 2017)](https://www.zotero.org/google-docs/?e0CnJa), violence [(Choi et al., 2022; Steele & Peralta, 2020)](https://www.zotero.org/google-docs/?JVGTq5), and psychiatric comorbidities [(Mefodeva et al., 2022)](https://www.zotero.org/google-docs/?GzOhtr). Over the last three decades, evidence has shown a significant increase in the number of patients with PSU in high-income countries from North America, Europe, and Oceania [(Bonfiglio et al., 2022)](https://www.zotero.org/google-docs/?i0Uqfr), highlighting the relevance of studying this topic. A meta-analysis of Global North studies on cocaine use found that over 70% of cocaine users concurrently consumed alcohol, and between 38% and 64% reported concurrent marijuana use [(Liu et al., 2018)](https://www.zotero.org/google-docs/?eyglEd). However, there remains a knowledge gap regarding the prevalence of PSU in the Global South.

Moreover, evidence on the long-term consequences of reporting PSU on treatment outcomes is limited and mixed. Most studies have focused on the association between completing SUD treatment and long-term benefits, such as a lower risk of readmission to treatment [(Ruiz-Tagle Maturana et al., 2023)](https://www.zotero.org/google-docs/?OBoM2l) and a lower risk of relapse [(Andersson et al., 2019)](https://www.zotero.org/google-docs/?6SGWsD). The lack of research on PSU is partly explained because most studies have focused on individual substances in isolation and have considered multiple substance use histories as an exclusion criterion for clinical studies on treatment effectiveness [(Bonfiglio et al., 2022)](https://www.zotero.org/google-docs/?6Wv5z3). Regarding treatment outcomes, some studies have found a higher likelihood of dropping out of treatment among patients reporting PSU [(Andersson et al., 2021; Levola et al., 2021)](https://www.zotero.org/google-docs/?4R33Od), while others have found no association [(Andersson et al., 2018)](https://www.zotero.org/google-docs/?d5VOUK) or even lower non-completion rates [(Basu et al., 2017)](https://www.zotero.org/google-docs/?Vc39vz). Therefore, it is crucial to determine the role of reporting PSU [(Bhondoekhan et al., 2023; Price et al., 2023)](https://www.zotero.org/google-docs/?jI6xzc) in treatment non-completion to improve treatment effectiveness and research translatability [(Crummy et al., 2020)](https://www.zotero.org/google-docs/?U6NvAI).

Moreover, the role of PSU in treatment effectiveness should be understood in the context of SUDs as a chronic condition, where many patients will transition through multiple treatments over their lifetime [(Bórquez et al., 2024; Fleury et al., 2016)](https://www.zotero.org/google-docs/?75wTDB). Patients with persistent SUD show different characteristics from those who no longer have a disorder after a single treatment or without any treatment [(Beaulieu et al., 2024a)](https://www.zotero.org/google-docs/?5rHt8j). The latter requires developing empirical strategies to account for explanations other than causal associations (e.g., confounding). This presents a methodological challenge, as studies on the relationship between PSU and treatment outcomes have overlooked these complex dynamics.

Additionally, treatments recorded in routine healthcare data are irregularly spaced but not random, as the time between treatments might be related to biopsychosocial and treatment-related factors. Hence, patients with worse outcomes in previous treatments might have different treatment intensities in the future, which may also explain treatment outcomes, such as completion or dropout [(Hansen et al., 2020; Vázquez-Real et al., 2022)](https://www.zotero.org/google-docs/?B1f6qy). Observing individuals more frequently due to their specific characteristics, practices, contexts, or treatment trajectories can lead to under- or overestimation of the association between PSU and treatment outcomes. However, limited research has considered this potential bias.

Thus, this study aimed to estimate the association between having reported PSU and SUD treatment non-completion (i.e., treatment dropouts or spelled by misconduct) across different treatment settings among adult patients admitted to multiple SUD treatment programs in Chile from 2010 to 2019, taking advantage of a large and high-quality administrative dataset that includes all treatment episodes of patients with public health insurance (~80% of the population) since its creation in 2010 up to 2022 [(Mateo Pinones et al., 2022)](https://www.zotero.org/google-docs/?p41BUx).

* 1. The Chilean context

In Chile, treatments for adults with SUD are delivered in residential, intensive ambulatory, and basic ambulatory settings. Residential programs are planned for approximately twelve months, although the duration may vary according to patients' needs. They are offered from five to seven days a week with at least five weekly interventions. Intensive ambulatory settings have a duration of six to eight months, with weekly six-hour sessions that include up to four interventions. Residential and intensive-ambulatory SUD treatment programs offer two modalities: one for the general population and another designed for women, addressing needs such as pregnancy and childcare. In contrast, basic ambulatory settings are offered only under general-population programs. Like several Latin American countries and most South American nations, Chilean treatment services receive mostly patients with alcohol use disorder, followed by those with disorders related to the use of cocaine and cocaine base paste, cannabis, and pharmaceutical products. While the proportion of patients using opioids and injecting drug use is uncommon in the Latin American context [(Ruiz-Tagle Maturana et al., 2023)](https://www.zotero.org/google-docs/?JNyup7). Importantly, PSU is frequent in the Chilean population. A study conducted in a Chilean hard-to-reach population that used cocaine base paste found that 47–66% had PSU [(Olivari et al., 2022)](https://www.zotero.org/google-docs/?aXiJSo). Moreover, the Chilean Budgetary Office study found that two out of three patients admitted to SUD treatments reported PSU, highlighting the need for further research to determine whether treatments effectively address the care priorities of patients with PSU [(DIPRES, 2017)](https://www.zotero.org/google-docs/?KdGSQz).

# MATERIAL AND METHODS

* 1. Setting and participants

The design is a retrospective cohort study, using administrative records of adult patients (+18 years old) with SUD treatments from 2010 to 2019. Censoring occurred after the date of data retrieval (November 13, 2019). Patients with only one treatment episode (i.e., one treatment record) were excluded (See Supplemental Section 1 for details). To account for variability by treatment setting, we stratified the analysis by baseline treatment: basic ambulatory (n=4,360), intensive ambulatory for the general population (n=4,998), general-population residential (n=2,178), women-specific or women-only intensive ambulatory (n=745) and residential (n=1,036). After excluding records of ongoing treatments and referrals outside the treatment network, 72,404 patients with 90,075 treatment episodes were selected. We focused on patients who received more than one treatment (18%), identifying 13,317 patients and 30,988 treatment episodes. This study was approved by the Griffith University Human Research Ethics Committee (GUHREC GU Ref. No: 2022/919).

* 1. Variables

The exposure variable was PSU at each admission, based on the presence of primary and secondary substances that met the criteria for SUD, evaluated in one or more clinical interviews [(Crummy et al., 2020; Font-Mayolas & Calvo, 2022)](https://www.zotero.org/google-docs/?SMbb56).

The outcome variable was SUD treatment outcome/non-completion (1=dropout or spelled by misconduct; 0=completed treatment). In addition, the models were adjusted for various baseline confounding variables related to substance use, demographics, and social factors.

The following covariates registered at admission to treatment were included in the model assessing the association between reported PSU and treatment non-completion status: age, birth year (to capture potential cohort effects), primary substance of the initial diagnosis (cocaine hydrochloride, cocaine base paste, marijuana, and other substances), psychiatric comorbidity (confirmed comorbidity or diagnosis unknown or under study), daily frequency of primary substance use, occupational status (inactive or unemployed), primary substance (cocaine hydrochloride, cocaine base paste, marijuana, and other substances), and biopsychosocial compromise. The biopsychosocial compromise is a holistic severity classification from clinical assessments that considers factors such as withdrawal symptoms, motivation to change, substance use patterns, social environment, and health symptoms. For further information about covariates, review Supplemental Section 2.

* 1. Missing data

Given the complex longitudinal structure of the data, a random-forest-based imputation was conducted using the *missRanger* package. The data showed 95% complete cases in the variables studied. Missingness was most pronounced for biopsychosocial compromise (1.8%) and primary substance of the initial diagnosis (1.1%), and remaining variables had minimal missing data (<1%). Three hundred trees were set with five candidate values of predictive matching (thus aiming for plausible imputations given predictor values), with a maximum of 50 iterations per chaining step. This imputation procedure may circumvent the specification of interactions or nonparametric relationships and handle collinearity between imputation variables (Hong & Lynn, 2020; Sheetal et al., 2023).

* 1. Bivariate analyses

Differences between patients reporting and not reporting PSU at baseline were quantified using standardized mean differences (SMD), which compare covariate means or proportions relative to the pooled standard deviation (values <0.2 are small, >0.8 are large). Chi-square (χ2) and chi-square standardized residuals tests were employed to compare the proportion of patients by baseline treatment setting, PSU and treatment completion. Statistical significance was set at p < .05.

Incidence rates (IR) were calculated per 1,000 person-months to explore the crude association between reporting PSU and treatment non-completion while accounting for heterogeneous follow-up times.

* 1. Model adjustment

Marginal regression models were fitted to estimate the relative risk (RR) and 95% confidence intervals of non-completing SUD treatments among patients with or without PSU at admission using generalized estimating equations (GEE), assuming a Poisson distribution with a log-link function and an independent covariance structure [(Grafféo et al., 2018)](https://www.zotero.org/google-docs/?Smflbm).

Given that data collection was based on administrative records with varying frequencies of patient admissions and follow-up periods, the irregular timing of assessments was examined and included in the analyses (See Supplemental Section 3). GEE models were weighted using inverse intensity weights (IIW) to address the irregular patterns of admission to treatment. Intensities were measured through a Cox proportional hazards model to account for the time-to-event (e.g., remaining in treatment or being readmitted) as a counting process, predicted by covariates of the previous treatment episode. For initial treatment episodes with no prior information available, lagged dichotomized categorical predictors (through *one hot encoding*) were fixed to either 0 (*lag0*) or 1 (*lag1*), and log-scaled continuous covariates of previous days in treatment were fixed to reference values of 45 or 90 days, respectively. These fixed covariate values allowed modelling of different baseline scenarios (See Supplemental Section 4 for model specification). This was implemented in the *IrregLong* package (v. 0.4.0; Pullenayegum, 2024). Heterogeneity tests were conducted to explore potential effect measure modification using ratio metrics [(Kaufman & MacLehose, 2013)](https://www.zotero.org/google-docs/?xVePCj).

* 1. Sensitivity analyses

Sensitivity analyses were conducted through a traditional GEE model without weights and compared using the Quasi-likelihood Information criterion (See Supplemental Sections 4 & 5). All analyses were performed in R v. 4.1.2 (R Core Team, Vienna).

* 1. Data and code availability

Code & markdowns are available here: bit.ly/4cE8gyf.

# RESULTS

* 1. Characteristics of the study sample

Patients underwent an average of 2.3 ± 0.68 SUD treatments (median = 2, 1st quartile= 2, 3rd quartile= 2) during 2010-2019. Several key differences were notable among the individuals who reported PSU. In terms of demographics at baseline, patients with PSU, when compared to patients who reported single substance use, tended to be younger with a higher proportion of severe biopsychosocial compromise (44% vs 29%). In addition, they had a higher proportion of marijuana (35.3% vs 20.3%) as a primary substance at the first diagnosis, and cocaine base paste (54.8% vs 37.9%) as a primary substance at admission to treatment. A higher percentage of the participants were unemployed. These differences led to adjust for covariates to estimate the relative risk of treatment non-completion between patients who reported PSU and those who did not (Table 1).

[Insert Table 1 here]

* 1. Prevalence and incidence of PSU and treatment completion

The data suggest that the strength and direction of the association between PSU and treatment completion status varied across treatment settings (Figure 1). This variability indicates that a common association [χ²(1) = 76.04, p<.001] among different baseline settings may be unreliable [Woolf test: χ²(4)= 13.74, p=.008]. Specifically, there is no evidence of an association within patients in baseline residential general-population [χ²(1)= 0.57, p=.418] and in women-only intensive ambulatory settings [χ²(1)= 2.82, p=.092]. Conversely, an association was found within patients in general-population basic ambulatory [χ²(1)= 36.39, p<.001], general-population intensive ambulatory ([χ²(1)= 45.06, p<.001], and women-only residential settings [χ²(1)= 22.46, p<.001]. From another perspective, non-completion was associated with baseline treatment setting [χ²(4)= 177.64, p<.001]. Patients in baseline basic ambulatory settings showed the highest percentages of non-completion (80% in patients with PSU and 74% in patients with single substance use) (Post-hoc χ2 residuals= 8.07, p<.001), followed by patients in general-population intensive ambulatory settings (Post-hoc χ2 res.= 3.61, p=.003). In contrast, patients in general-population (Post-hoc χ2 res.= -11.07, p<.001) and in women-only residential (Post-hoc χ2 res.= -5.05, p<.001) settings showed lower non-completion. Also, there is evidence of an association between baseline treatment setting and reporting polysubstance use [χ2(4)= 194.31, p<.001]. The greatest proportion of patients with PSU was found in residential general-population settings (84%; Post-hoc χ2 res.= 8.78, p=.028) and in women-only residential settings (82%; Post-hoc χ2 res.= 2.99, p=.028). In contrast, the lowest proportion was in basic ambulatory settings (75%; Post-hoc χ2 res.= -12.30, p<.001).

[Insert Figure 1 here]

However, a longitudinal analysis across multiple treatment episodes revealed that patients who reported PSU at admission had a lower incidence of treatment non-completion (Table 2). The incidence of at least one non-completion episode per patient followed from the first admission until the censoring date (November 2019), was lower in patients who reported PSU at admission to the first treatment (11.6 [95%CI: 11.3, 11.8] per 1,000 person-months) compared to patients who did not report PSU (13.2 [95%CI: 12.6, 13.8]). Similarly, the incidence of non-completion at the first admission was lower among patients who reported PSU at admission to the first treatment (9.9 [95%CI: 9.7 10.1]) versus patients who did not report PSU (11.3 [95%CI: 10.8, 11.9]), even though the follow-up time in patients with PSU was 18% higher than patients without PSU. When focusing longitudinally on patients who had at least one treatment in which they reported PSU, rates of at least one non-completion were lower in this group (11.6 [95%CI: 11.4,11.9]) compared to patients who did not report PSU at any time (13.9; [95%CI: 13.1, 14.8]). This trend was also observed when looking at the incidence of non-completion at the first treatment episode alone (10.0 [95%CI: 9.8,10.2] versus 11.9 [95%CI: 11.1, 12.6]), even though the follow-up time in patients reporting PSU at least one time was 20% higher compared to patients who never reported PSU.

[Insert Table 2 here]

* 1. Marginal longitudinal association between PSU at admission and treatment outcome

There was a very weak association between PSU and treatment non-completion (RRlag0 [weights with lagged covariate values fixed to 0]= 1.03 [95%CI: 1.01,1.05]; RR lag1[weights with lagged covariate values fixed to 1]= 1.02 [95%CI: 1.00, 1.04]; RR= 1.02 [95% CI: 1.01, 1.04]). However, the association between PSU and treatment non-completion varied significantly across treatment settings (Cochran's Qlag0 = 14.24, p=.007; Cochran's Qlag1 = 13.32, p=.010). According to Table 3, we found a modest association between PSU and treatment non-completion among users in general-population intensive ambulatory settings (RRlag0=1.04 [95%CI: 1.01,1.07]; RRlag1=1.04 [95%CI: 1.01, 1.08]). Also, the risk of treatment non-completion was at least 13% higher for patients reporting PSU in women-only residential settings (RRlag0=1.15 [95%CI: 1.06, 1.25]; RRlag1= 1.13 [95%CI: 1.04, 1.22]). In contrast, there was no evidence of an increased risk of treatment non-completion for patients reporting PSU in general population residential and ambulatory settings.

[Insert Table 3 here]

* 1. Sensitivity analyses

The associations between PSU and treatment non-completion were stable across models, with intervals overlapping the null associations for women-only intensive ambulatory settings and general-population residential settings. Associations without IIWs were almost equal to the main analyses in terms of direction and strength (Table 3). However, sensitivity analyses with other intensity model specifications, particularly weighting from an intensity model that stratified follow-up times in basic ambulatory settings, showed an association that maintained the same direction and magnitude of the main analyses but the confidence interval did not overlap the null (RRlag0=1.04 [95%CI: 1.01, 1.07]). In contrast, the main association weakened in general population intensive ambulatory settings, particularly in a marginal model with IIWs from an intensity model with stratified follow-up times and lagged covariates fixed to 1 (RRlag1=1.01 [95%CI: 0.98, 1.05]). In women-only residential settings, only the marginal model with IIWs from an intensity model stratified by follow-up with lagged covariates fixed at 1 had confidence intervals overlapping the null (RRlag1= 1.09 [95%CI: 0.99, 1.20]), although the association remained positive (See Supplemental Table S5).

# DISCUSSION

Our results indicate that PSU is associated with a higher risk of treatment non-completion among patients admitted to SUD treatment programs in Chile between 2010 and 2019. We focused on patients with a persistent pattern of substance use disorder rather than a transient substance use disorder. These patients are characterized by repeated treatment episodes, varying periods of abstinence, and relapses leading to the resumption of moderate or problematic substance use, as highlighted in the literature [(Beaulieu et al., 2024b)](https://www.zotero.org/google-docs/?737jJZ). Specifically, the risk was modestly higher in patients in baseline general-population intensive ambulatory (RRlag0=1.04 [95%CI: 1.01,1.07]; RRlag1=1.04 [95%CI: 1.01, 1.08]) and in women-only residential settings (RRlag0=1.15 [95%CI: 1.06, 1.25]; RRlag1= 1.13 [95%CI: 1.04, 1.22]). We did not find evidence that PSU is related to a higher risk of treatment non-completion in basic ambulatory, residential or women-only intensive ambulatory settings. Our results indicate that while PSU poses challenges, the specific context and characteristics of the treatment setting may play a critical role in determining outcomes, highlighting the need for focused interventions to diminish future negative consequences [(Manning et al., 2017)](https://www.zotero.org/google-docs/?4sQ8pL).

Sensitivity analyses supported these findings, showing stability in the associations across the different model specifications and treatment settings. The risk estimates are stable and robust. Patients with PSU in specific treatment settings face heightened risks, a challenge shared across the region where there is a need to broaden the range of services offered, ensuring a more effective response to individuals’ needs [(United Nations Office on Drugs and Crime [UNODC], 2023)](https://www.zotero.org/google-docs/?8wZ8F1). Regarding the reasons for non-completion among patients in treatment (with or without PSU), a study conducted in Latin America found that the main reasons for abandonment were “not accepting the rules of the institution,” “lack of money,” and “not feeling comfortable with the facilities” [(Gómez-Restrepo et al., 2017)](https://www.zotero.org/google-docs/?s9wBWN). Additionally, an impact evaluation of treatments led by the Budget Directorate of the Chilean Government (DIPRES) identified a lack of time to attend (in ambulatory treatments) and a perceived sense of having achieved the expected well-being before completing treatment [(DIPRES, 2017)](https://www.zotero.org/google-docs/?vCaNds) as the main reasons for non-completion. However, it remains unclear whether these reasons for not completing treatment are the same for patients with PSU as for those with single substance use.

Bivariate analyses highlight the various demographic and clinical characteristics that differentiate patients reporting PSU from those using a single substance. Patients with PSU tended to be younger and were more likely to be unemployed than single-substance users. The primary substances leading to treatment admission differed significantly, with PSU patients reporting cocaine hydrochloride and base paste as their main substances, unlike patients without PSU, who reported alcohol as their main substance. Moreover, severe biopsychosocial compromise is more prevalent among patients with PSU. Although individuals reporting PSU had a higher cumulative prevalence of dropout or administrative discharge, the incidence of these outcomes per person-month was lower than that of patients not reporting PSU. This finding is attributable to the longer observation period for the former group in the database, potentially influencing the observed association, as shown in Table 2. We suspect that the continuity of SUD treatments throughout the recovery process, as considered in our study, is often overlooked in other research, which has generally reported lower treatment responsiveness among patients with PSU [(Bonfiglio et al., 2022)](https://www.zotero.org/google-docs/?a8ImYP). These seemingly contradictory results underscore the importance of examining not only the crude incidence, but the count of these events by considering other confounding variables and adjusting for the influence of these variables in the counting process. Therefore, future studies should qualitatively explore treatment retention, baseline settings, and recovery trajectories.

Additionally, our findings suggest gender differences regarding the implications of alcohol for PSU. Women reporting PSU had greater risks of non-completion among patients in women-only residential settings. Women in residential treatments tend to have a severe substance use profile that develops rapidly. Additionally, women with severe alcohol use disorder are prone to prolonged PSU [(Stephenson et al., 2022](https://www.zotero.org/google-docs/?03yYTj)), which in turn is associated with worse treatment outcomes, regardless of the substances used. Gender roles may help explain the observed differences, as women who use substances face heightened stigmatization for failing to fulfill family roles (e.g., as mothers or daughters) and moral expectations, particularly regarding self-control and sexual propriety. This pattern has been observed in both Western countries [(MacGregor & Thom, 2020)](https://www.zotero.org/google-docs/?O0WhbU) and the Latin American context [(Mascayano et al., 2016)](https://www.zotero.org/google-docs/?ObUtSC).

Regarding secondary analyses, we observed that accounting for irregular assessment of patients with multiple treatments (i.e., different frequency of treatments and time between treatments) through inverse intensity weighting did not substantially change the associations between reporting PSU and treatment non-completion. Interestingly, some factors that we expected to be influential, such as PSU in previous treatments, specific primary substances at admission, and certain psychiatric comorbidities [(Passos & Camacho, 2000)](https://www.zotero.org/google-docs/?bVgxhW), had negligible or non-significant effects on treatment return rates. We suspect adjusting for biopsychosocial compromise and stratification by treatment setting would have captured the variability attributed to these factors and substantially attenuated these associations. Future studies should explore whether a causal conclusion can be drawn from these associations by employing other advanced causal inference methods.

This study had some limitations. First, the proportional intensity model that calculates IIWs imposes a proportional hazard assumption on assessment intensity. However, this assumption is debatable. Diagnosing proportionality in a Cox model with recurrent events can be quite challenging, and statistical tools might not account for changes in intensities due to possible changes in baseline risks for cumulative events, making interpretations of nonproportionality less straightforward [(Royston & Altman, 2013)](https://www.zotero.org/google-docs/?larcy2). Tests based on Schoenfeld residuals are insufficient because contrasting the null hypothesis for changes as a function of time may not be entirely indicative of nonproportional hazards [(Dickman, 2023)](https://www.zotero.org/google-docs/?KrLUA5). Even small violations can become apparent because of sample size [(Keele, 2010)](https://www.zotero.org/google-docs/?yavU1T). Additionally, given that the intensity model has prediction purposes (i.e., readmission), it can still be used effectively even if hazards are not proportional [(Jardillier et al., 2022)](https://www.zotero.org/google-docs/?4NmrT9). However, the association described here may lack causal interpretation, given that the recurrent event process might be associated with the right censoring mechanism. For example, patients admitted for treatment on dates closer to administrative censorship or in ongoing treatments might have different characteristics that may change the inverse of susceptibility to recurrent treatments [(Rytgaard & van der Laan, 2024)](https://www.zotero.org/google-docs/?gShfc1).

# CONCLUSION

Our study showed that PSU at admission was associated with higher treatment non-completion rates in specific settings, notably in intensive ambulatory and women-only residential programs. These findings underline the need for tailored interventions to address the unique challenges of patients with PSU, such as enhancing practices aimed at treatment retention for this population. Additionally, demographic factors such as age and birth cohort significantly influenced treatment outcomes. This study provides valuable insights for improving SUD treatment programs in Latin America, emphasizing the importance of comprehensive data collection and the development of personalized treatment strategies to enhance patient retention and completion rates.

1. **BIBLIOGRAPHY**

[Andersson, H. W., Lauvsnes, A. D. F., & Nordfjærn, T. (2021). Emerging Adults in Inpatient Substance Use Treatment: A Prospective Cohort Study of Patient Characteristics and Treatment Outcomes. European Addiction Research, 27(3), 206-215. https://doi.org/10.1159/000512156](https://www.zotero.org/google-docs/?Y23e5N)

[Andersson, H. W., Steinsbekk, A., Walderhaug, E., Otterholt, E., & Nordfjærn, T. (2018). Predictors of Dropout From Inpatient Substance Use Treatment: A Prospective Cohort Study. Substance Abuse: Research and Treatment, 12, 1178221818760551. https://doi.org/10.1177/1178221818760551](https://www.zotero.org/google-docs/?Y23e5N)

[Andersson, H. W., Wenaas, M., & Nordfjærn, T. (2019). Relapse after inpatient substance use treatment: A prospective cohort study among users of illicit substances. Addictive Behaviors, 90, 222-228. https://doi.org/10.1016/j.addbeh.2018.11.008](https://www.zotero.org/google-docs/?Y23e5N)

[Basu, D., Ghosh, A., Sarkar, S., Patra, B. N., Subodh, B. N., & Mattoo, S. K. (2017). Initial treatment dropout in patients with substance use disorders attending a tertiary care de-addiction centre in north India. Indian Journal of Medical Research, 146(Suppl 2), S77-S84. https://doi.org/10.4103/ijmr.IJMR\_1309\_15](https://www.zotero.org/google-docs/?Y23e5N)

[Beaulieu, M., Tremblay, J., & Bertrand, K. (2024a). Adjustments to Service Organization in Specialized Addiction Services and Clinical Strategies for Better Meeting the Needs of People with a Persistent Substance Use Disorder. International Journal of Mental Health and Addiction, 22(4), 2229-2246. https://doi.org/10.1007/s11469-022-00982-z](https://www.zotero.org/google-docs/?Y23e5N)

[Beaulieu, M., Tremblay, J., & Bertrand, K. (2024b). Adjustments to Service Organization in Specialized Addiction Services and Clinical Strategies for Better Meeting the Needs of People with a Persistent Substance Use Disorder. International Journal of Mental Health and Addiction, 22(4), 2229-2246. https://doi.org/10.1007/s11469-022-00982-z](https://www.zotero.org/google-docs/?Y23e5N)

[Bhondoekhan, F., Li, Y., Gaither, R., Daly, M. M., Hallowell, B. D., Chambers, L. C., Beaudoin, F. L., & Marshall, B. D. L. (2023). The impact of polysubstance use patterns on engagement of substance use disorder treatment among emergency department patients at high risk of opioid overdose. Addictive Behaviors Reports, 18, 100512. https://doi.org/10.1016/j.abrep.2023.100512](https://www.zotero.org/google-docs/?Y23e5N)

[Bonfiglio, N. S., Portoghese, I., Renati, R., Mascia, M. L., & Penna, M. P. (2022). Polysubstance Use Patterns among Outpatients Undergoing Substance Use Disorder Treatment: A Latent Class Analysis. International Journal of Environmental Research and Public Health, 19(24), 16759. https://doi.org/10.3390/ijerph192416759](https://www.zotero.org/google-docs/?Y23e5N)

[Bórquez, I., Cerdá, M., González‐Santa Cruz, A., Krawczyk, N., & Castillo‐Carniglia, Á. (2024). Longitudinal trajectories of substance use disorder treatment use: A latent class growth analysis using a national cohort in Chile. Addiction, 119(4), 753-765. https://doi.org/10.1111/add.16412](https://www.zotero.org/google-docs/?Y23e5N)

[Bunting, A. M., Shearer, R., Linden-Carmichael, A. N., Williams, A. R., Comer, S. D., Cerdá, M., & Lorvick, J. (2024). Are you thinking what I’m thinking? Defining what we mean by “polysubstance use.” The American Journal of Drug and Alcohol Abuse, 50(1), 1-7. https://doi.org/10.1080/00952990.2023.2248360](https://www.zotero.org/google-docs/?Y23e5N)

[Chen, T., Zhong, N., Du, J., Li, Z., Zhao, Y., Sun, H., Chen, Z., Jiang, H., & Zhao, M. (2019). Polydrug use patterns and their impact on relapse among heroin‐dependent patients in Shanghai, China. Addiction, 114(2), 259-267. https://doi.org/10.1111/add.14451](https://www.zotero.org/google-docs/?Y23e5N)

[Choi, H. J., Grigorian, H., Garner, A., Stuart, G. L., & Temple, Jeff. R. (2022). Polydrug Use and Dating Violence Among Emerging Adults. Journal of Interpersonal Violence, 37(5-6), 2190-2217. https://doi.org/10.1177/0886260520934427](https://www.zotero.org/google-docs/?Y23e5N)

[Connor, J. P., Gullo, M. J., White, A., & Kelly, A. B. (2014). Polysubstance use: Diagnostic challenges, patterns of use and health. Current Opinion in Psychiatry, 27(4), 269-275. https://doi.org/10.1097/YCO.0000000000000069](https://www.zotero.org/google-docs/?Y23e5N)

[Crummy, E. A., O’Neal, T. J., Baskin, B. M., & Ferguson, S. M. (2020). One Is Not Enough: Understanding and Modeling Polysubstance Use. Frontiers in Neuroscience, 14, 569. https://doi.org/10.3389/fnins.2020.00569](https://www.zotero.org/google-docs/?Y23e5N)

[Daskalopoulou, M., Rodger, A., Phillips, A. N., Sherr, L., Speakman, A., Collins, S., Elford, J., Johnson, M. A., Gilson, R., Fisher, M., Wilkins, E., Anderson, J., McDonnell, J., Edwards, S., Perry, N., O’Connell, R., Lascar, M., Jones, M., Johnson, A. M., … Lampe, F. C. (2014). Recreational drug use, polydrug use, and sexual behaviour in HIV-diagnosed men who have sex with men in the UK: Results from the cross-sectional ASTRA study. The Lancet HIV, 1(1), e22-e31. https://doi.org/10.1016/S2352-3018(14)70001-3](https://www.zotero.org/google-docs/?Y23e5N)

[Dickman, P. (2023). An introduction to flexible parametric survival models and a discussion of the proportional hazards assumption. Department of Statistics and Quantitative Methods, University of Milano-Bicocca. https://www.pauldickman.com/pdf/talk-milan-mar2023.pdf](https://www.zotero.org/google-docs/?Y23e5N)

Budget Directorate, Ministry of Finance, Government of Chile [[DIPRES]. (2017). Informe Final: Evaluación de resultados de los programas de tratamiento y rehabilitación del Servicio nacional para la prevención y rehabilitación del consumo de drogas y alcohol](https://www.zotero.org/google-docs/?Y23e5N) [*Final Report: Evaluation of the Results of Treatment and Rehabilitation Programs of the National Service for the Prevention and Rehabilitation of Drug and Alcohol Consumption*][.](https://www.zotero.org/google-docs/?Y23e5N) Retrieved from: https://justiciaysociedad.uc.cl/wp-content/uploads/2023/09/Evaluacion-SENDA\_.pdf

[Fleury, M.-J., Djouini, A., Huỳnh, C., Tremblay, J., Ferland, F., Ménard, J.-M., & Belleville, G. (2016). Remission from substance use disorders: A systematic review and meta-analysis. Drug and Alcohol Dependence, 168, 293-306. https://doi.org/10.1016/j.drugalcdep.2016.08.625](https://www.zotero.org/google-docs/?Y23e5N)

[Font-Mayolas, S., & Calvo, F. (2022). Polydrug Definition and Assessment: The State of the Art. International Journal of Environmental Research and Public Health, 19(20), 13542. https://doi.org/10.3390/ijerph192013542](https://www.zotero.org/google-docs/?Y23e5N)

[Gjersing, L., & Bretteville‐Jensen, A. L. (2018). Patterns of substance use and mortality risk in a cohort of ‘hard‐to‐reach’ polysubstance users. Addiction, 113(4), 729-739. https://doi.org/10.1111/add.14053](https://www.zotero.org/google-docs/?Y23e5N)

[Gómez-Restrepo, C., Maldonado, P., Rodríguez, N., Ruiz-Gaviria, R., Escalante, M. Á., Gómez, R. Á., De Araujo, M. R., De Oliveira, A. C. S., Rivera, J. S. C., García, J. A. G., Ferrand, M. P., & Blitchtein-Winicki, D. (2017). Quality measurers of therapeutic communities for substance dependence: An international collaborative study survey in Latin America. Substance Abuse Treatment, Prevention, and Policy, 12(1), 53. https://doi.org/10.1186/s13011-017-0129-y](https://www.zotero.org/google-docs/?Y23e5N)

[Grafféo, N., Latouche, A., Geskus, R. B., & Chevret, S. (2018). Modeling time‐varying exposure using inverse probability of treatment weights. Biometrical Journal, 60(2), 323-332. https://doi.org/10.1002/bimj.201600223](https://www.zotero.org/google-docs/?Y23e5N)

[Hansen, E. M., Mejldal, A., & Nielsen, A. S. (2020). Predictors of Readmission Following Outpatient Treatment for Alcohol Use Disorder. Alcohol and Alcoholism, 55(3), 291-298. https://doi.org/10.1093/alcalc/agaa018](https://www.zotero.org/google-docs/?Y23e5N)

[Hassan, A. N., & Le Foll, B. (2019). Polydrug use disorders in individuals with opioid use disorder. Drug and Alcohol Dependence, 198, 28-33. https://doi.org/10.1016/j.drugalcdep.2019.01.031](https://www.zotero.org/google-docs/?Y23e5N)

[Jardillier, R., Koca, D., Chatelain, F., & Guyon, L. (2022). Prognosis of lasso-like penalized Cox models with tumor profiling improves prediction over clinical data alone and benefits from bi-dimensional pre-screening. BMC Cancer, 22(1), 1045. https://doi.org/10.1186/s12885-022-10117-1](https://www.zotero.org/google-docs/?Y23e5N)

[Kaufman, J. S., & MacLehose, R. F. (2013). Which of these things is not like the others? Cancer, 119(24), 4216-4222. https://doi.org/10.1002/cncr.28359](https://www.zotero.org/google-docs/?Y23e5N)

[Keele, L. (2010). Proportionally Difficult: Testing for Nonproportional Hazards in Cox Models. Political Analysis, 18(2), 189-205. https://doi.org/10.1093/pan/mpp044](https://www.zotero.org/google-docs/?Y23e5N)

[Levola, J., Aranko, A., & Pitkänen, T. (2021). Psychosocial difficulties and treatment retention in inpatient detoxification programmes. Nordic Studies on Alcohol and Drugs, 38(5), 434-449. https://doi.org/10.1177/14550725211021263](https://www.zotero.org/google-docs/?Y23e5N)

[Liu, Y., Williamson, V. G., Setlow, B., Cottler, L. B., & Knackstedt, L. A. (2018). The importance of considering polysubstance use: Lessons from cocaine research. Drug and Alcohol Dependence, 192, 16-28. https://doi.org/10.1016/j.drugalcdep.2018.07.025](https://www.zotero.org/google-docs/?Y23e5N)

[MacGregor, S., & Thom, B. (Eds.). (2020). Risk and Substance Use: Framing Dangerous People and Dangerous Places (1.a ed.). Routledge. https://doi.org/10.4324/9781351033503](https://www.zotero.org/google-docs/?Y23e5N)

[Manning, V., Garfield, J. B., Best, D., Berends, L., Room, R., Mugavin, J., Larner, A., Lam, T., Buykx, P., Allsop, S., & Lubman, D. I. (2017). Substance use outcomes following treatment: Findings from the Australian Patient Pathways Study. Australian & New Zealand Journal of Psychiatry, 51(2), 177-189. https://doi.org/10.1177/0004867415625815](https://www.zotero.org/google-docs/?Y23e5N)

[Mascayano, F., Tapia, T., Schilling, S., Alvarado, R., Tapia, E., Lips, W., & Yang, L. H. (2016). Stigma toward mental illness in Latin America and the Caribbean: A systematic review. Revista Brasileira de Psiquiatria, 38(1), 73-85. https://doi.org/10.1590/1516-4446-2015-1652](https://www.zotero.org/google-docs/?Y23e5N)

[Mateo Pinones, M., González-Santa Cruz, A., Portilla Huidobro, R., & Castillo-Carniglia, A. (2022). Evidence-based policymaking: Lessons from the Chilean Substance Use Treatment Policy. International Journal of Drug Policy, 109, 103860. https://doi.org/10.1016/j.drugpo.2022.103860](https://www.zotero.org/google-docs/?Y23e5N)

[Mefodeva, V., Carlyle, M., Walter, Z., Chan, G., & Hides, L. (2022). Polysubstance use in young people accessing residential and day‐treatment services for substance use: Substance use profiles, psychiatric comorbidity and treatment completion. Addiction, 117(12), 3110-3120. https://doi.org/10.1111/add.16008](https://www.zotero.org/google-docs/?Y23e5N)

[Olivari, C. F., Gaete, J., Rodriguez, N., Pizarro, E., Del Villar, P., Calvo, E., & Castillo-Carniglia, A. (2022). Polydrug Use and Co-occurring Substance Use Disorders in a Respondent Driven Sampling of Cocaine Base Paste Users in Santiago, Chile. Journal of Psychoactive Drugs, 54(4), 348-357. https://doi.org/10.1080/02791072.2021.1976886](https://www.zotero.org/google-docs/?Y23e5N)

[Passos, S. R. L., & Camacho, L. A. B. (2000). Factors associated with immediate dropout of outpatient treatment for drug abuse in Rio de Janeiro. Social Psychiatry and Psychiatric Epidemiology, 35(11), 513-517. https://doi.org/10.1007/s001270050273](https://www.zotero.org/google-docs/?Y23e5N)

[Price, O., Sutherland, R., Man, N., Bruno, R., Dietze, P., Salom, C., Akhurst, J., & Peacock, A. (2023). Trends and psychosocial correlates of same day polysubstance use among people who inject drugs in Australia, 2012-2022. International Journal of Drug Policy, 104150. https://doi.org/10.1016/j.drugpo.2023.104150](https://www.zotero.org/google-docs/?Y23e5N)

Pullenayegum, E. (2024, September 05). IrregLong: Analysis of longitudinal data with irregular observation times (*Version 0.4.0*) [*Computer software*]. https://cran.r-project.org/web/packages/IrregLong/index.html

[Quek, L.-H., Chan, G. C. K., White, A., Connor, J. P., Baker, P. J., Saunders, J. B., & Kelly, A. B. (2013). Concurrent and Simultaneous Polydrug Use: Latent Class Analysis of an Australian Nationally Representative Sample of Young Adults. Frontiers in Public Health, 1. https://doi.org/10.3389/fpubh.2013.00061](https://www.zotero.org/google-docs/?Y23e5N)

[Royston, P., & Altman, D. G. (2013). External validation of a Cox prognostic model: Principles and methods. BMC Medical Research Methodology, 13(1), 33. https://doi.org/10.1186/1471-2288-13-33](https://www.zotero.org/google-docs/?Y23e5N)

[Ruiz-Tagle Maturana, J., Cruz, A. G.-S., Rocha-Jiménez, T., & Castillo-Carniglia, Á. (2023). Does substance use disorder treatment completion reduce the risk of treatment readmission in Chile? Drug and Alcohol Dependence, 248, 109907. https://doi.org/10.1016/j.drugalcdep.2023.109907](https://www.zotero.org/google-docs/?Y23e5N)

[Rytgaard, H. C. W., & van der Laan, M. J. (2024). Nonparametric efficient causal estimation of the intervention-specific expected number of recurrent events with continuous-time targeted maximum likelihood and highly adaptive lasso estimation (Versión 1). arXiv. https://doi.org/10.48550/ARXIV.2404.01736](https://www.zotero.org/google-docs/?Y23e5N)

[Sewell, J., Miltz, A., Lampe, F. C., Cambiano, V., Speakman, A., Phillips, A. N., Stuart, D., Gilson, R., Asboe, D., Nwokolo, N., Clarke, A., Collins, S., Hart, G., Elford, J., & Rodger, A. J. (2017). Poly drug use, chemsex drug use, and associations with sexual risk behaviour in HIV-negative men who have sex with men attending sexual health clinics. International Journal of Drug Policy, 43, 33-43. https://doi.org/10.1016/j.drugpo.2017.01.001](https://www.zotero.org/google-docs/?Y23e5N)

[Steele, J. L., & Peralta, R. L. (2020). Are Polydrug Users More Physically and Verbally Aggressive? An Assessment of Aggression Among Mono- Versus Polydrug Users in a University Sample. Journal of Interpersonal Violence, 35(21-22), 4444-4467. https://doi.org/10.1177/0886260517715024](https://www.zotero.org/google-docs/?Y23e5N)

[Stephenson, M., Aggen, S. H., Polak, K., Svikis, D. S., Kendler, K. S., & Edwards, A. C. (2022). Patterns and Correlates of Polysubstance Use Among Individuals With Severe Alcohol Use Disorder. Alcohol and Alcoholism, 57(5), 622-629. https://doi.org/10.1093/alcalc/agac012](https://www.zotero.org/google-docs/?Y23e5N)

[United Nations Office on Drugs and Crime [UNODC]. (2023). Treatment Services for Substance Use Disorders in Latin American Countries: Findings from the UNODC-WHO Facility Survey for Field Testing. https://www.unodc.org/documents/drug-prevention-and-treatment/UNODC\_QALAT\_mapping\_report\_ENGLISH.pdf](https://www.zotero.org/google-docs/?Y23e5N)

[Vázquez-Real, M., Talero-Barrientos, E. M., & Franco-Fernández, M. D. (2022). Sociodemographic, clinical and pharmacological factors influencing early readmission in mental health settings. Actas Espanolas De Psiquiatria, 50(6), 248-255.](https://www.zotero.org/google-docs/?Y23e5N)