







## Could the telescoping effect and comorbidity with substance use disorders account for sex differences in the processes and therapeutic outcomes? A latent-class moderation analysis

Daniel Dacosta-Sánchez<sup>a,c,\*</sup> , Cinta Mancheño-Velasco<sup>b,c</sup> , Marta Narváez-Camargo<sup>b,c</sup> ,  
Óscar M. Lozano<sup>b,c</sup> 

<sup>a</sup> Department of Psychology and Anthropology, Area of Personality, Evaluation, and Psychological Treatment, Faculty of Education and Psychology, University of Extremadura, Badajoz, Spain

<sup>b</sup> Department of Clinical and Experimental Psychology, University of Huelva, Huelva, Spain

<sup>c</sup> Research Center on Natural Resources, Health and the Environment, University of Huelva, Huelva, Spain

### ARTICLE INFO

#### Keywords:

Telescoping effect  
Comorbidity  
Sex-focused evaluation approaches  
Substance use disorder  
Sources of inequality  
Cluster B

### ABSTRACT

**Background:** Sex differences in substance use disorder (SUD) treatment outcomes remain unclear; protocols focused on male prevalence may overlook female-specific needs. This study tested interactions among sex, the telescoping effect, and comorbid profiles in outcomes.

**Methods:** Retrospective multisite electronic health record study (N = 4818) of patients with co-occurring disorders. Interaction regressions and latent class analysis tested sex moderation of links between years of substance use (telescoping) and outcomes within SUD and co-occurring diagnostic groups.

**Results:** Slower progression from substance use onset to diagnosis was associated with lower readmission likelihood at 3 years in males than females; similar patterns appeared at 18 and 24 months for alcohol dependence and at 18 months for co-occurring mood disorders. Six comorbid classes were identified (feature-based labels): behavioral dysregulation (Class 1), anxious distress (Class 2), adolescence–cannabis (Class 3), emotional–interpersonal dysregulation (Class 4), affective–alcohol (Class 5), and reality distortion (Class 6). Only Classes 2 and 4 showed the telescoping effect. Latent-class moderation revealed males in Classes 1 and 3 had higher readmission over 3 years, whereas females in Class 4 had lower adherence to scheduled appointments and higher predicted readmissions across all follow-ups. Females in Class 6 showed better appointment adherence than males.

**Conclusions:** Telescoping and sex differences may contribute to higher readmission in females, particularly with alcohol dependence and mood or personality disorders. Males with impulse-control or childhood disorders may require more post-treatment care. Sex-specific interventions and moderation/latent class approaches may improve targeting.

### 1. Introduction

Despite considerable research into the treatment of substance use disorders (SUDs), the impact of sex differences on therapeutic outcomes is still unclear in the evidence-based literature (Amati et al., 2018; Greenfield et al., 2007; Logan et al., 2020; McHugh et al., 2018). This may be because SUD treatments are often male-focused, reflecting the higher prevalence of substance use and SUDs, such as alcohol use

disorders, among males (Agabio et al., 2017; Goh et al., 2024; Holzhauer et al., 2020; Verplaetse et al., 2021). The absence of significant differences in therapeutic outcomes between males and females complicates the development of sex-specific interventions (Agabio et al., 2017). In particular, females may follow treatment protocols that are less focused on their biological (e.g., hormones), clinical and/or sociocultural characteristics (Goh et al., 2024; Greenfield and Grella, 2009), highlighting the need for sex/gender-focused evaluation approaches (Greaves et al.,

\* Correspondence to: Department of Psychology and Anthropology, Area of Personality, Evaluation, and Psychological Treatment, Faculty of Education and Psychology, University of Extremadura, Avda. de Elvas s/n, Badajoz 06006, Spain.

E-mail addresses: [daniels@unex.es](mailto:daniels@unex.es) (D. Dacosta-Sánchez), [cinta.mancheno@dpces.uhu.es](mailto:cinta.mancheno@dpces.uhu.es) (C. Mancheño-Velasco), [marta.narvaez@dpces.uhu.es](mailto:marta.narvaez@dpces.uhu.es) (M. Narváez-Camargo), [oscar.lozano@dpsi.uhu.es](mailto:oscar.lozano@dpsi.uhu.es) (Ó.M. Lozano).

<https://doi.org/10.1016/j.drugalcdep.2026.113062>

Received 23 May 2025; Received in revised form 31 December 2025; Accepted 21 January 2026

Available online 30 January 2026

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2020).

To achieve that, researchers emphasize the need to identify those biological and sociocultural factors that are the source of inequalities and interact with sex (Fonseca et al., 2021; Greenfield et al., 2007; McHugh et al., 2018); however, few studies have explored whether this interaction explains therapeutic outcomes (Guerrero et al., 2014; Yeom, 2015). In addition, researchers emphasize the need to identify specific male and female subgroups, as this approach may facilitate the detection of differences in therapeutic outcomes, thereby contributing to the design and development of sex/gender-specific interventions (Greaves et al., 2020; Greenfield et al., 2007).

Among the factors that can interact with sex and have shown a strong predictive capacity for therapeutic processes and outcomes is the comorbidity of SUD with other mental disorders (Fernández-Artamendi et al., 2024; Fonseca et al., 2021; Mancheño-Velasco et al., 2024). The mechanisms contributing to this condition can be diverse (Becona, 2018; Fernández-Artamendi et al., 2024), and their prevalence typically differs by sex, highlighting a source of inequality in the identification of subgroups. Notably, females often present higher rates of affective, anxiety, and personality disorders such as borderline or dependent personality disorders (De Cos, 2014; Peltier et al., 2021), whereas males frequently present higher rates of psychotic (Díaz-Fernández et al., 2023; Laia et al., 2011; Volkow and Blanco, 2023), narcissistic, and antisocial personality disorders (De Cos, 2014). Moreover, although the prevalence of seeking treatment for substance use disorders is generally lower among females, they are more vulnerable to psychiatric disorders and may have higher rates of co-occurring disorders (Díaz-Fernández et al., 2023; Hernández-Ávila et al., 2004).

In this context, it is crucial to understand how mental disorders may exacerbate substance use and accelerate treatment seeking or SUD development (Fernández-Artamendi et al., 2024; Towers et al., 2023; Volkow and Blanco, 2023). For example, anxiety and mood disorders (Crum et al., 2022; Kushner et al., 2011; Sartor et al., 2007) predict faster progression to alcohol use disorders. Regarding that, literature suggests that females with problematic alcohol use progress more rapidly from initial use to dependence diagnosis or treatment seeking than males due to their biological (e.g., metabolization) or sociocultural (e.g., social stigma) characteristics, as well as worse medical consequences of substance use (Towers et al., 2023). This accelerated progression of females vs. males from initial use to treatment seeking or SUD diagnosis, possibly characterized by biopsychosocial mechanisms, is known as the “telescoping effect” (Keyes et al., 2010; Khan et al., 2013; Volkow and Blanco, 2023) and, like co-occurring disorder, represents another potential source of inequality in subgroup identification.

The growing, though not entirely consistent, body of evidence supporting the existence of the telescoping effect highlights the need to investigate its potential interaction. For instance, it has been suggested that the presence or absence of this effect may depend on the specific type of SUD involved (McHugh et al., 2018). However, although the telescoping effect is observed in treatment-seeking females, it does not appear to be a consistent predictor of their therapeutic processes and outcomes compared with males (Diehl et al., 2007). The factors underlying this phenomenon, such as co-occurring disorder, substance metabolism, and hormonal and sociocultural factors, are still under investigation (Agabio et al., 2017; Greenfield et al., 2010; Towers et al., 2023). Considering this evidence, it is crucial to investigate the interaction between sex and co-occurring disorders, which may influence treatment outcomes. It is also important to gain an understanding of the interaction between the telescoping effect, sex, and co-occurring disorders, as this could lead to more tailored and effective interventions that address the specific needs of different patient subgroups. However, to the best of our knowledge, no studies have addressed this issue for treatment outcomes. Furthermore, the marked imbalance in the proportion of treated males and females (approximately 75–80 % vs. 20–25 %) European Monitoring Centre for Drugs and Drug Addiction, (2024)) may introduce an androcentric bias in the statistical analyses.

This imbalance can compromise statistical power and, in some cases, lead to Type II errors – thereby masking potential outcome differences. These limitations support the use of moderation or latent class analysis to clarify possible variations (Little, 2013).

Therefore, considering the above, the following objectives are proposed:

General Objective 1: To explore the presence of the telescoping effect between males and females for each type of substance used and for each comorbid mental disorder.

Specific Objective 1: To analyze whether sex moderates the relationship between the telescoping effect and therapeutic processes and outcomes for each type of substance and mental disorder.

General Objective 2: To identify profiles of comorbid mental disorders.

Specific Objective 2: To examine the moderating role of sex in the relationship between these profiles and patients' therapeutic processes and outcomes.

## 2. Method

### 2.1. Design

This multisite retrospective study (January 2, 2015 - June 15, 2023) included three follow-ups at 18 months, 24 months, and  $\geq 3$  years (up to 4.6 years) posttreatment initiation, tracking appointment adherence, treatment duration, discharge outcomes, and readmissions.

### 2.2. Participants

Of 5120 individuals with co-occurring mental health and substance use disorders, 38 were excluded due to death during treatment, 72 were referred to non-ambulatory care, 33 were released from prison without clinical follow-up, and 159 presented missing data on appointment adherence ( $n = 76$ ) or years of use ( $n = 83$ )—both missing completely at random (MCAR) and affecting less than 2 % of the initial records, which justified listwise deletion (Rubin, 1976). The final study sample therefore included 4818 individuals (27.1 % female), drawn from a population of 32,979 individuals receiving outpatient treatment (18.6 % female) in one of the 120 centers of the Public Addiction Assistance Network in Andalusia (Spain) between January 2, 2015, and January 2, 2020. Treatment outcome distribution in the sample is reported in [Supplementary Table S1](#). All analyses were conducted at the patient level. Only the first treatment admission recorded between January 2, 2015 and January 2, 2020 was included for each individual. Subsequent treatment episodes were considered as outcome data (e.g., readmission), not as repeated observations. Co-occurring disorder occurred in 21.2 % of females and 13.1 % of males in this population. The mean age of the sample at admission was 36.9 years for males ( $SD = 12.8$ ) and 40.8 years for females ( $SD = 12.9$ ). In terms of education, 19.1 % had not completed primary school (19.5 % male, 18.0 % female), 35.6 % had completed primary education (37.7 % male, 30.1 % female), 21.3 % had finished secondary school (21.8 % male, 19.9 % female), and 21.1 % had completed high school or higher (18.5 % male, 28.1 % female). In terms of employment status, 32.9 % were employed (35.0 % male, 27.5 % female), 43.4 % were unemployed (41.6 % male, 48.0 % female), and 6.0 % were studying (6.6 % male, 4.6 % female).

All disorders were diagnosed according to the International Classification of Disease-10 (ICD-10) criteria (World Health Organization, 1994):

Substance use disorders by sex were as follows: alcohol dependence (F10) in 55.7 % of males and 56.4 % of females; opioid dependence (F11) in 6.9 % of males and 7.6 % of females; cannabis dependence (F12) in 40.8 % of males and 26.8 % of females; hypnotic/sedative dependence (F13) in 5.2 % of males and 15.0 % of females; and cocaine dependence (F14) in 42.7 % of males and 25.3 % of females.

Comorbid mental disorders included psychotic disorders (F20–F29)

in 12.7 % of males and 4.2 % of females; mood disorders (F30–F39) in 19.6 % of males and 30.4 % of females; anxiety disorders (F40–F49) in 37.5 % of males and 49.7 % of females; and impulse-control disorders (F63) in 15.0 % of males and 2.2 % of females. In addition, Cluster A personality disorders (F21, F60.0, F60.1) were diagnosed in 4.2 % of the males, 2.7 % of the females; Cluster B personality disorders (F60.2, F60.3, F60.4, F60.81) were diagnosed in 7.3 % of the males, 14.6 % of the females; Cluster C personality disorders (F60.5, F60.6, F60.7) were diagnosed in 4.3 % of the males, 3.4 % of the females; and childhood/adolescent disorders (F90–F98) were diagnosed in 10.6 % of the males, 2.5 % of the females.

### 2.3. Measures

This study analyses data from patients' electronic health records (EHRs) in the Andalusian Plan on Drugs' Information System (SIPASDA), a centralized database for addiction centres in Andalusia, Spain. The database adheres to the EMCDDA's Treatment Demand Indicator Standard Protocol 3.0 (European Monitoring Centre for Drugs and Drug Addiction., 2012), including treatment admission data, sociodemographic, consumption indicators, previous treatments, diagnoses, and clinical follow-up. Sex and process and therapeutic outcome variables were defined as follows:

- Sex: collected based on sex assigned at birth.
- Telescoping effect: Measured as years of substance use, defined as the time elapsed between onset of use of the primary substance (the substance motivating treatment) and first admission to treatment for that substance, which serves as the diagnostic reference point in the registry (Greenfield et al., 2010; Towers et al., 2023).
- Retention: Time in treatment (months) from initiation to therapeutic discharge or **premature treatment discontinuation**.
- Appointment adherence: Because the number of scheduled appointments varied across patients, adherence was operationalized as a proportion of attended appointments relative to those scheduled, ensuring comparability across individuals. (e.g., attending 2 of 3 scheduled appointments corresponds to an adherence of 0.66).
- Discharge outcome: Achieving therapeutic goals or dropping out against clinical advice.
- Posttreatment outcome: Any readmission within 18 months, 24 months, or  $\geq 3$  years, indicating return to substance use. The results were also quantitatively defined for patients with a follow-up of  $\geq 3$  years.

### 2.4. Procedure

The patients' EHRs contain information from psychologists,

physicians, and nursing staff. SIPASDA employs the TDI Standard Protocol 3.0 (European Monitoring Centre for Drugs and Drug Addiction, 2012) for initial patient data, integrated with follow-up information in EHRs. This system, fully integrated by 2014, tracks clinical data, including diagnoses and return to substance use, ensuring comprehensive and confidential patient records through anonymization.

The database, accessed by request to the Andalusian Department of Equality and Social Policies, was provided in an anonymized format for research purposes.

### 2.5. Ethics approval

The data storage and encoding comply with Spain's General Health Law of 1986, Law 41/2002 on patient rights, and the European Organic Law 3/2018 on data protection. The research adhered to the Declaration of Helsinki and received ethical approval from the Andalusian Ministry of Health's Research Ethics Committee (Cod. 0661-N-22).

### 2.6. Statistical analysis

Univariate analyses described the participants' sociodemographic and diagnostic characteristics. Due to unequal sample sizes and lack of normality, the Mann–Whitney *U* test was used to examine sex differences in years of substance use before SUD diagnosis in the general sample and by comorbid mental disorders and SUD type. The association between categorical variables was analyzed using the chi-square test. Following recommendations to focus on sex interactions with specific characteristics and subgroup identification (Feingold et al., 2024; Fonseca et al., 2021; Greenfield et al., 2007, 2010; McHugh et al., 2018), a two-phase analysis was conducted. Phase one used regressions with interaction terms to assess whether sex moderated the relationship between years of substance use and therapeutic outcomes, with significant interactions analysed via simple slopes. Phase two identified six latent classes based on comorbid disorders, controlling for years of substance use until SUD diagnosis. As a sensitivity analysis, we examined measurement invariance across sex using a multigroup LCA, comparing a configural model with a model constraining item-response logits to be equal across sex. The constrained model showed significantly worse fit (Satorra–Bentler scaled  $\Delta\chi^2(48) = 541.2, p < .001$ ), using the Satorra–Bentler scaled difference test (Satorra and Bentler, 2001, 2010); therefore, sex-based equality constraints were not imposed. Model fit was evaluated via the BIC, AIC, and SABIC, with stability assessed via cross-validation, kappa coefficients, and scree plots. Local independence was assessed using  $\chi^2$  bivariate residuals (Collins and Lanza, 2009; Oberski, 2016). To ensure model stability and replicability, all latent class analyses were conducted with 500 random starts and 100 final stage optimizations, consistently applied across all class enumeration

**Table 1**  
Relationship between years of use and sex in total sample and according to diagnoses.

	Males Mdn (IQR)	Females Mdn (IQR)	M vs F (n)	Mann-Whitney U	p-value
<b>Total sample</b>	17.0 (20.0)	18.0 (21.0)	3514 vs 1304	2289998.5	.979
<b>Diagnoses of comorbid mental disorders</b>					
F20–29. Psychotic	15.0 (17.0)	11.0 (18.0)	445 vs 55	10622.5	.110
F30–39. Mood	22.0 (21.5)	21.0 (21.8)	689 vs 396	124626.5	.018
F40–49. Anxiety	20.0 (21.0)	18.0 (21.0)	1316 vs 648	597725.0	< .001
Cluster A	15.0 (18.0)	18.0 (19.0)	149 vs 35	2548.5	.835
Cluster B	12.0 (16.0)	9.50 (18.3)	257 vs 190	22595.5	.177
Cluster C	19.0 (21.0)	17.0 (20.8)	152 vs 44	2829.5	.120
F63. Impulse-control disorders	14.0 (16.0)	15.0 (12.5)	527 vs 29	7042.0	.476
F90-F98. Childhood and adolescence	8.00 (12.0)	5.00 (14.0)	371 vs 33	5719.0	.531
<b>Diagnoses of substance use disorders</b>					
F10. Alcohol	23.0 (21.0)	25.0 (17.0)	1958 vs 736	707460.5	.467
F11. Opioids	12.0 (21.0)	5.00 (12.0)	241 vs 99	8388.0	< .001
F12. Cannabis	10.0 (14.0)	9.00 (13.0)	1433 vs 350	238207.0	.145
F13. Hypnotosedatives	13.0 (17.5)	11.0 (18.0)	181 vs 196	16813.5	.382
F14. Cocaine	13.0 (13.0)	11.0 (15.3)	1499 vs 330	218116.5	< .001

Note: M: males; F: females. Years of use refers to the time from initiation of the primary drug—the substance motivating treatment—to admission.

**Table 2**

Regressions with interaction terms between sex and years of substance use, conducted within each type of substance use disorder and in the total sample.

Parameter	$\beta$	Std. Error	t / z	p-value	95 % Confidence interval	
<b>Total sample</b>						
Retention	0.02	0.04	0.52	.606	-0.05	0.09
Adherence	-0.00	0.00	-0.74	.459	-0.00	0.00
Therapeutic goal	0.00	0.01	0.06	.955	-0.01	0.01
Any readmission 18 months	0.01	0.01	1.48	.139	-0.00	0.03
Any readmission 24 months	0.01	0.01	1.52	.129	-0.00	0.02
Any readmission $\geq 3$ years	0.01	0.01	2.07	.039	0.00	0.02
Number of readmissions	0.00	0.00	1.95	.052	-0.01	-0.00
<b>F10. Alcohol use disorder</b>						
Retention	0.09	0.05	1.67	.095	-0.02	0.19
Adherence	-0.00	0.00	-1.51	.130	-0.00	0.00
Therapeutic goal	0.00	0.01	0.03	.974	-0.02	0.02
Any readmission 18 months	0.02	0.01	2.20	.028	0.00	0.04
Any readmission 24 months	0.02	0.01	2.13	.033	0.00	0.04
Any readmission $\geq 3$ years	0.02	0.01	2.40	.017	0.00	0.03
Number of readmissions	0.00	0.00	2.14	.033	0.00	0.01
<b>F11. Opioids use disorder</b>						
Retention	-0.23	0.21	-1.06	.290	-0.65	0.19
Adherence	-0.00	0.00	-0.01	.314	-0.01	0.00
Therapeutic goal	0.03	0.03	0.78	.436	-0.04	0.09
Any readmission 18 months	0.01	0.03	0.28	.776	-0.05	0.07
Any readmission 24 months	-0.02	0.03	-0.54	.591	-0.07	0.04
Any readmission $\geq 3$ years	0.01	0.02	0.50	.620	-0.03	0.06
Number of readmissions	0.01	0.01	1.40	.162	-0.01	0.03
<b>F12. Cannabis use disorder</b>						
Retention	-0.03	0.09	-0.33	.741	-0.20	0.14
Adherence	0.00	0.00	0.22	.823	-0.00	0.00
Therapeutic goal	-0.01	0.02	-0.60	.547	-0.04	0.02
Any readmission 18 months	0.00	0.02	0.08	.937	-0.04	0.04
Any readmission 24 months	-0.00	0.02	-0.21	.837	-0.04	0.03
Any readmission $\geq 3$ years	0.01	0.01	0.81	.421	-0.02	0.03
Number of readmissions	0.00	0.00	1.27	.205	-0.00	0.01
<b>F13. Hypnotosedatives use disorder</b>						
Retention	-0.04	0.15	-0.25	.797	-0.32	0.25
Adherence	0.00	0.00	0.44	.657	-0.00	0.00
Therapeutic goal	0.01	0.02	0.57	.569	-0.03	0.06
Any readmission 18 months	0.00	0.03	-0.07	.942	-0.05	0.05
Any readmission 24 months	0.01	0.02	0.39	.696	-0.04	0.06
Any readmission $\geq 3$ years	0.02	0.02	0.20	.318	-0.02	0.06
Number of readmissions	0.00	0.01	0.29	.770	-0.01	0.01
<b>F14. Cocaine use disorder</b>						
Retention	-0.17	0.10	-1.71	.087	-0.37	0.03
Adherence	-0.00	0.00	-0.75	.453	-0.00	0.00
Therapeutic goal	-0.02	0.02	-0.94	.346	-0.06	0.02
Any readmission 18 months	-0.01	0.02	-0.35	.725	-0.04	0.03
Any readmission 24 months	-0.01	0.02	-0.49	.623	-0.04	0.02
Any readmission $\geq 3$ years	0.00	0.01	0.02	.987	-0.03	0.03
Number of readmissions	0.00	0.00	0.57	.570	-0.01	0.01

**Table 3**

Regressions with interaction terms between sex and years of substance use, conducted within each comorbid diagnosis group.

Parameter	$\beta$	Std. Error	t / z	p-value	95 % Confidence interval	
<b>F20–29. Psychotic disorders</b>						
Retention	0.23	0.20	1.17	.244	-0.16	0.61
Adherence	0.00	0.00	0.66	.509	-0.00	0.01
Therapeutic goal	-0.02	0.03	-0.64	.523	-0.09	0.04
Any readmission 18 months	0.02	0.04	-0.44	.663	-0.09	0.06
Any readmission 24 months	0.01	0.03	0.24	.813	-0.06	0.07
Any readmission $\geq 3$ years	-0.00	0.03	-0.02	.985	-0.06	0.06
Number of readmissions	-0.00	0.01	-0.20	.841	-0.02	0.02
<b>F30–39. Mood disorders</b>						
Retention	0.07	0.07	0.92	.359	-0.07	0.21
Adherence	0.00	0.00	0.10	.923	-0.00	0.00
Therapeutic goal	0.00	0.01	0.01	.991	-0.02	0.02
Any readmission 18 months	0.03	0.02	2.26	.024	0.00	0.06
Any readmission 24 months	0.02	0.01	1.55	.121	-0.01	0.05
Any readmission $\geq 3$ years	0.02	0.01	1.61	.107	-0.00	0.04
Number of readmissions	0.00	0.00	0.43	.671	-0.00	0.01
<b>F40–49. Anxiety disorders</b>						
Retention	0.04	0.06	0.63	.526	-0.08	0.15
Adherence	-0.00	0.00	-0.32	.750	-0.00	0.00
Therapeutic goal	0.00	0.01	0.10	.917	-0.02	0.02
Any readmission 18 months	-0.00	0.01	-0.14	.891	-0.02	0.02
Any readmission 24 months	-0.00	0.01	-0.27	0.78	-0.02	0.02
Any readmission $\geq 3$ years	0.00	0.01	0.57	.567	-0.01	0.02
Number of readmissions	0.00	0.00	1.28	.201	-0.00	0.01
<b>Cluster A disorders</b>						
Retention	0.13	0.25	0.53	.594	-0.36	0.63
Adherence	-0.00	0.00	-1.07	.288	-0.01	0.00
Therapeutic goal	0.06	0.04	1.38	.166	-0.02	0.14
Any readmission 18 months	0.01	0.05	0.25	.799	-0.09	0.12
Any readmission 24 months	0.01	0.05	0.23	.822	-0.09	0.11
Any readmission $\geq 3$ years	-0.04	0.04	-0.92	.355	-0.12	0.04
Number of readmissions	-0.02	0.01	-1.50	.135	-0.04	0.01
<b>Cluster B disorders</b>						
Retention	0.09	0.13	0.68	.499	-0.17	0.35
Adherence	0.00	0.00	0.28	.778	-0.00	0.00
Therapeutic goal	-0.02	0.03	-0.69	.487	-0.08	0.04
Any readmission 18 months	-0.01	0.03	-0.54	.583	-0.07	0.04
Any readmission 24 months	-0.00	0.02	-0.02	.981	-0.05	0.04
Any readmission $\geq 3$ years	0.02	0.02	0.95	.343	-0.02	0.05
Number of readmissions	0.00	0.01	0.26	.791	-0.01	0.01
<b>Cluster C disorders</b>						
Retention	0.18	0.23	0.80	.426	-0.27	0.63
Adherence	-0.00	0.00	-1.34	.180	-0.01	0.00
Therapeutic goal	0.02	0.04	0.54	.590	-0.05	0.09
Any readmission 18 months	0.04	0.04	0.98	.329	-0.04	0.12
Any readmission 24 months	0.05	0.04	1.45	.148	-0.02	0.13
Any readmission $\geq 3$ years	0.02	0.03	0.71	.479	-0.04	0.08
Number of readmissions	-0.00	0.01	-0.17	.866	-0.02	0.02
<b>F63. Impulse-control disorders</b>						
Retention	-0.02	0.26	-0.06	.952	-0.53	0.50

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Table 3 (continued)

Parameter	$\beta$	Std. Error	t / z	p-value	95 % Confidence interval	
Adherence	-0.00	0.00	-0.52	.605	-0.01	0.01
Therapeutic goal	-0.03	0.05	-0.58	.561	-0.13	0.07
Any readmission 18 months	0.09	0.08	1.09	.278	-0.07	0.26
Any readmission 24 months	0.09	0.08	1.02	.307	-0.08	0.25
Any readmission $\geq 3$ years	0.07	0.05	1.37	.169	-0.03	0.16
Number of readmissions	0.01	0.01	0.53	.598	-0.02	0.04
<b>F90-F98. Childhood and adolescence disorders</b>						
Retention	-0.31	0.26	-1.20	.230	-0.81	0.20
Adherence	0.00	0.00	0.01	.989	-0.01	0.01
Therapeutic goal	-0.06	0.06	-1.04	.300	-0.18	0.06
Any readmission 18 months	-0.05	0.12	-0.43	.667	-0.28	0.18
Any readmission 24 months	-0.06	0.12	-0.49	.623	-0.29	0.17
Any readmission $\geq 3$ years	-0.04	0.06	-0.65	.514	-0.15	0.08
Number of readmissions	-0.00	0.01	-0.05	.959	-0.03	0.02

models. As an additional sensitivity analysis, replicability and minimum class size across models were reported in [Supplementary Table S2](#), complementing the fit indices. Distal outcomes were compared across classes using the BCH method ([Asparouhov and Muthén, 2014](#); [Bolck et al., 2004](#)) to account for classification uncertainty, yielding BCH-corrected class-specific means and standard errors. The resulting estimates, including 95 % confidence intervals, are presented in [Supplementary Table S3](#) and show clear differentiation between classes, providing additional descriptive support for the selected six-class solution for subsequent moderation analyses. A latent-class moderation analysis then examined sex as a moderator between each latent class and process and outcome indicators, with simple slopes calculated for significant interactions. Sex-based effect modification across significant class interactions was examined using both additive (Relative Excess Risk due to Interaction [RERI], Attributable Proportion [AP], Synergy Index [S]) and multiplicative (interaction term) scales. Results are detailed in [Supplementary Table S4](#), enhancing the causal interpretability of the findings in line with STROBE recommendations ([Knol and VanderWeele, 2012](#); [Richardson and Kaufman, 2009](#)).

To examine whether unequal follow-up affected the  $> 3$ -year readmission outcome, we repeated that analysis in the subgroup with  $> 36$  months of observation ( $n = 512$ ) using Kaplan–Meier curves and a Cox proportional-hazards model (see [Supplementary Table S5](#) and [Figure S1](#)). For the outcome “number of readmissions” (mean = 0.36; variance = 0.42; range = 0–4), we fitted an ordinary least-squares model with heteroskedasticity-consistent robust standard errors of type 3 and bootstrap resampling in the PROCESS macro version 4.2 ([Hayes, 2022](#)). The dispersion index (approximately 1.15) and the large sample size ensure that ordinary least-squares estimates converge in expectation to those from Poisson regression, preserving inferential validity ([Cameron and Trivedi, 2013](#); [Gardner et al., 1995](#)). Residual heteroscedasticity is addressed with White’s robust covariance matrix ([White, 1980](#)), and—given the absence of material over-dispersion—more complex count models offer no additional advantage ([Hilbe, 2014](#)). Finally, PROCESS macro implements linear regression only, maintaining methodological consistency across all moderation analyses in the study.

All analyses were performed via SPSS 27 using Model 1 of the PROCESS macro, version 4.2 ([Hayes, 2022](#)) and Mplus 8.7 ([Muthén and Muthén, 2021](#)).

### 3. Results

No significant differences in follow-up duration were observed between males and females across diagnostic groups, latent classes, or readmission status at 18 months, 24 months, and  $\geq 3$  years (all  $p > .27$ ). For the subgroup of 512 patients with follow-up exceeding 3 years, the Kaplan–Meier comparison by admission year was non-significant (Log-rank  $\chi^2 = 2.13$ ,  $df = 1$ ,  $p = 0.14$ ), and the Cox model likewise showed no association (overall  $\chi^2 = 3.05$ ,  $df = 4$ ,  $p = 0.55$ ; [Supplementary Table S5](#) and [Figure S1](#)). Hazard ratios for each admission year versus 2015 ranged from 0.23 to 1.09, all  $p > 0.14$ .

#### 3.1. Relationship between the telescoping effect and the therapeutic process and outcomes according to diagnoses of substance dependence and comorbid mental disorders

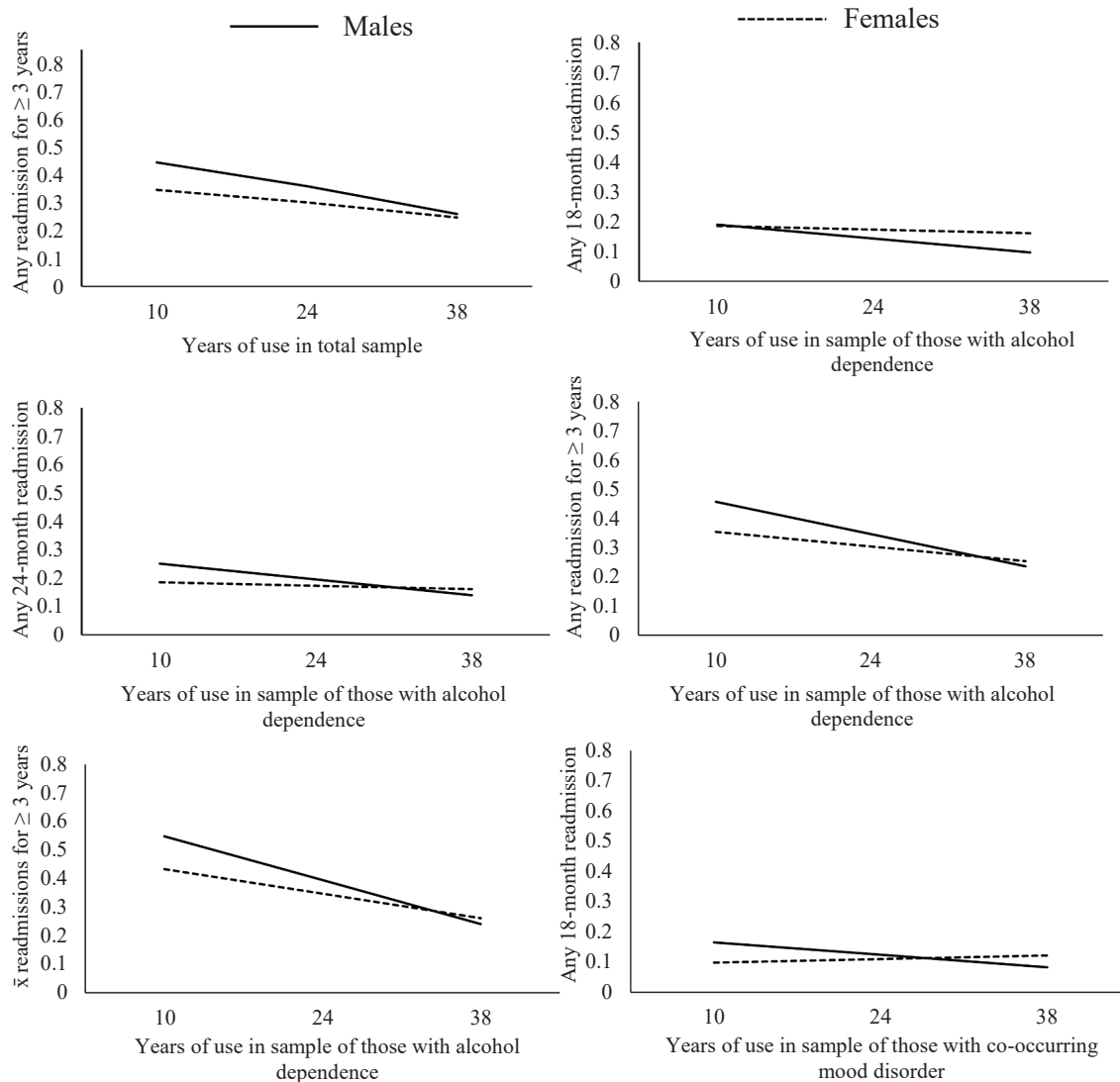
[Table 1](#) presents analyses the telescoping effect by sex across the total sample, comorbid mental disorders, and substance dependence type. No significant differences were found in the total sample ( $p = .979$ ), but a telescoping effect was observed in co-occurring mood ( $Mdn_{Females} = 21.0$ ;  $Mdn_{Males} = 22.0$ ;  $p = .018$ ) and anxiety disorders ( $Mdn_{Females} = 18.0$ ;  $Mdn_{Males} = 20.0$ ;  $p < .001$ ). On the other hand, when analyzing by type of substance dependence, a telescoping effect was observed only for opioid ( $Mdn_{Females} = 5.00$ ;  $Mdn_{Males} = 12.0$ ;  $p < .001$ ) and cocaine dependence ( $Mdn_{Females} = 11.0$ ;  $Mdn_{Males} = 13.0$ ;  $p < .001$ ).

Regressions with interaction terms for the total sample and by SUD type ([Table 2](#)) revealed a significant interaction effect between sex and years of substance use in predicting any readmission during  $\geq 3$  years of follow-up ( $\beta = 0.01$ ,  $p = .039$ ). In the sample of those with alcohol use disorder, sex moderated the relationship between years of alcohol use and any readmission for 18 months ( $\beta = 0.02$ ,  $p = .028$ ), 24 months ( $\beta = 0.02$ ,  $p = .033$ ), 3 years or more ( $\beta = 0.02$ ,  $p = .017$ ), and number of readmissions ( $\beta = 0.00$ ,  $p = .033$ ). For comorbid mental disorders ([Table 3](#)), a significant interaction was found only in the sample with co-occurring mood disorders, where sex and years of substance use predicted any readmission during 18 months of follow-up ( $\beta = 0.03$ ,  $p = .024$ ).

[Fig. 1](#) displays the simple slopes for each interaction, with the “X” axis representing years of use from onset to diagnosis and the “Y” axis representing the associated probability or number of predicted readmissions. In the total sample, the predicted effect of years of substance use on any readmission during  $\geq 3$  years of follow-up was slightly greater in males ( $\beta = -0.03$ ,  $p < .001$ ) than in females ( $\beta = -0.02$ ,  $p < .001$ ). In the sample of those with alcohol dependence, the effect of years of use on any readmission during 18 and 24 months was significant in males ( $\beta_{18months} = -0.03$ ,  $p < .001$ ;  $\beta_{24months} = -0.03$ ,  $p < .001$ ) but not in females ( $\beta_{18months} = -0.01$ ,  $p = .567$ ;  $\beta_{24months} = -0.01$ ,  $p = .454$ ). Additionally, for any readmission or the number of readmissions during  $\geq 3$  years of follow-up, years of use predicted a greater effect in males ( $\beta = -0.04$ ,  $p < .001$ ;  $\beta = -0.01$ ,  $p < .001$ ) than in females ( $\beta = -0.02$ ,  $p = .012$ ;  $\beta = -0.00$ ,  $p = .002$ ). In the sample with co-occurring mood disorders (bottom right of [Fig. 1](#)), the effect of years of use on any readmission during 18 months was significant in males ( $\beta = -0.03$ ,  $p = .004$ ) but not in females ( $\beta = 0.01$ ,  $p = .504$ ).

#### 3.2. Latent-class analysis and characterization of each class

For the latent class analysis, six models with 3–8 classes were considered. [Table 4](#) summarizes the fit statistics (BIC, AIC, SABIC), model parameters, entropy, bootstrapped likelihood ratio test, cross-validation with 75 % of the sample, and kappa coefficients. While the bootstrapped likelihood ratio test shows improved fit with more classes ( $p < .001$ ), greater stability is observed in the three-, five-, and six-class models, all with kappa coefficients of .99. The elbow plot indicates that stability in predictive gain is achieved with the six-class model (See [Supplementary Figure S2](#)). For the six-class latent model, the maximum



**Fig. 1.** Sex-specific simple slopes showing the predicted change in the probability of any readmission and in the mean number of readmissions (y-axis) across 18-, 24-, and ≥ 36-month follow-up periods, as a function of years of use. Results are presented for the total sample (top row), and for the sample of those with alcohol use disorder and the sample of those with co-occurring mood disorders (top, middle, and bottom rows, respectively).

$\chi^2$  bivariate residual observed was 2.10. No pair of indicators exceeded the 3.84 criterion. For readability, we refer to classes using numeric identifiers accompanied by brief descriptive labels reflecting the most prevalent features within each class: Class 1 (behavioral dysregulation), Class 2 (anxious distress), Class 3 (adolescence-cannabis), Class 4 (emotional-interpersonal dysregulation), Class 5 (affective-alcohol), and Class 6 (reality distortion).

After the six-class model was selected, males and females in each class were characterized by years of substance use until diagnosis, comorbid mental disorders, and substance dependence (Table 5). The behavioral dysregulation class (Class 1), which was mainly composed of patients with co-occurring impulse-control disorders, showed no telescoping effect and had higher prevalence of alcohol and cocaine use disorders, with significantly more males presenting with cocaine use disorder (59.3 % males vs. 28.6 % females,  $\chi^2 = 7.68, p = .006$ ). The anxious distress class (Class 2) exhibited a telescoping effect with females showing a significantly lower median number of years of any substance use before initiating treatment compared to males ( $Mdn_{Males} = 22.0, IQR_{Males} = 21.0; Mdn_{Females} = 20.0, IQR_{Females} = 22.0, U = 90277.5, p = .025$ ) and included mostly patients with co-occurring

anxiety disorders. This class had more females with co-occurring mood disorders (10.7 % males vs. 14.3 % females,  $\chi^2 = 5.26, p = .022$ ) and fewer females with co-occurring Cluster C (3.08 % males vs. 1.57 % females,  $\chi^2 = 3.87, p = .049$ ), impulse-control disorders (5.45 % males vs. 0.31 % females,  $\chi^2 = 31.2, p < .001$ ), and childhood and adolescence disorders (1.58 % males vs. 0.31 % females,  $\chi^2 = 5.96, p = .015$ ). Alcohol use disorder was most prevalent in Class 2, with fewer females having cannabis (28.4 % males vs. 17.9 % females,  $\chi^2 = 25.3, p < .001$ ) and cocaine use disorders (34.8 % males vs. 19.9 % females,  $\chi^2 = 45.2, p < .001$ ), but more with hypnotic dependence (5.92 % males vs. 18.3 % females,  $\chi^2 = 72.1, p < .001$ ).

The adolescence-cannabis class (Class 3) mainly included patients with co-occurring childhood and adolescence disorders, who predominantly had cannabis and cocaine use disorders, and showed no sex differences. The emotional-interpersonal dysregulation class (Class 4) was the most heterogeneous, with dependence on alcohol, cannabis, and cocaine, exhibiting a telescoping effect, with females showing a lower median number of years of any substance use before initiating treatment compared to males ( $Mdn_{Males} = 12.0, IQR_{Males} = 15.0; Mdn_{Females} = 10.0, IQR_{Females} = 15.3, U = 90277.5, p = .025$ ). Females in this class



Table 5

Characterization of males and females in each latent class by years of substance use and diagnoses.

	Class 1 Behavioral dysregulation (n = 375)		Class 2 Anxious distress (n = 1904)		Class 3 Adolescence- cannabis (n = 344)		Class 4 Emotional–interpersonal dysregulation (n = 969)		Class 5 Affective–alcohol pattern (n = 768)		Class 6 Reality distortion (n = 458)	
	Males	Females	Males	Females	Males	Females	Males	Females	Males	Females	Males	Females
Years of use Mdn (IQR)	12.5 (16.0)	15.0 (12.0)	22.0 (21.0)	20.0 (22.0)**	7.00 (11.0)	5.00 (9.50)	12.0 (15.0)	10.0 (15.3)*	23.0 (22.0)	23.0 (19.0)	15.0 (18.0)	13.0 (20.3)
<b>Diagnoses of comorbid mental disorders</b>												
F20–29. Psychotic	1.10	0.00	0.00	0.00	3.20	0.00	3.10	2.40	0.00	0.00	100	100
F30–F39. Mood	0.00	0.00	10.7	14.3*	2.22	0.00	3.85	7.82**	100	100	6.59	16.7*
F40–F49. Anxiety	0.00	0.00	93.2	94.7	4.13	6.90	14.7	13.6	0.00	0.00	5.85	4.17
Cluster A	0.00	0.00	0.00	0.00	0.00	0.00	20.7	10.9**	0.20	0.73	1.95	2.08
Cluster B	0.00	0.00	0.00	0.00	5.40	13.8	34.5	58.2**	1.42	5.47**	0.000	0.00
Cluster C	0.00	0.00	3.08	1.57*	0.00	0.00	16.3	10.9*	0.61	0.73	0.00	0.00
F63. Impulse-control disorders	100	100	5.45	0.31**	7.62	3.45	5.63	1.70**	4.25	0.00**	5.12	0.00
F90–F98. Childhood and adolescence	0.00	0.00	1.58	0.31*	100	100	4.74	0.34**	0.81	0.36	0.00	0.00
<b>Diagnoses of substance use disorders</b>												
F10. Alcohol	65.0	61.9	64.6	61.1	29.2	27.6	45.5	41.5	69.0	66.4	41.5	43.8
F11. Opioids	5.37	0.00	5.69	6.74	5.71	3.45	11.3	11.6	4.86	6.57	7.80	6.25
F12. Cannabis	39.0	28.6	28.4	17.9**	67.0	62.1	51.7	46.6	26.3	19.0*	59.8	47.9
F13. Hypnotosedatives	3.11	9.52	5.92	18.3**	5.40	3.45	6.52	12.2**	4.45	13.5**	2.93	6.25
F14. Cocaine	59.3	28.6**	34.8	19.9**	52.1	44.8	52.4	38.8**	35.8	19.0**	37.3	37.5

Note. For each latent class, the table reports the median years of use of the primary drug before diagnosis (interquartile range in parentheses) and the percentage of males and females meeting each comorbid mental- or substance-use diagnosis. Group differences were tested with the Mann-Whitney U (continuous variable) and the chi-square test (categorical variables). \* $p < .05$ ; \*\* $p < .01$ .

interrelationships between these variables and their impact on some treatment outcomes.

Nevertheless, study findings should be interpreted in the context of the Andalusian publicly funded addiction-care network captured by SIPASDA (Junta de Andalucía., 2025a, Junta de Andalucía., 2025b; Agencia de Servicios Sociales y Dependencia de Andalucía., 2023). Care is provided mainly through outpatient treatment centers with no copayment and typically combines pharmacological interventions (detoxification and anticraving medications), and opioid agonist treatment with methadone or buprenorphine) with structured cognitive-behavioral psychosocial programs (individual and group) (Junta de Andalucía, 2025b; Araque et al., 2005). Treatment length is individualized, commonly involving detoxification (approximately 1–3 weeks), an intensive outpatient phase (about 3–6 months, typically  $\geq 1$  weekly session), and maintenance follow-up that may extend beyond 12 months with less frequent visits; no fixed session quota is mandated and visit frequency is adjusted to clinical need (Araque et al., 2005).

Regarding the first objective, we found no overall telescoping effect, but it was present when comorbid mental disorders and specific SUD types were considered. Females with co-occurring mood and anxiety disorders progressed more rapidly to diagnosis of substance dependence. This trend may be influenced by factors such as substance metabolism and hormonal fluctuations that hinder craving control and accelerate SUD development (McHugh et al., 2018; Towers et al., 2023). However, the role of these variables was not directly evaluated in the present study. On the other hand, despite evidence supporting this effect (Diehl et al., 2007; Keyes et al., 2010; Piazza et al., 1989; Randall et al., 1999; Towers et al., 2023), the bivariate comparison of years of substance use did not show a telescoping effect for alcohol-use disorder, although it was observed in individuals with opioid- and cocaine-use disorders. This is surprising given the faster progression to alcohol use disorders in patients with co-occurring mood and anxiety disorders (Crum et al., 2022; Kushner et al., 2011; Piazza et al., 1989; Sartor et al., 2007). In contrast, the multivariate moderation analyses revealed that the telescoping effect significantly impacted treatment outcomes through its interaction with sex, particularly in patients with alcohol use and co-occurring mood disorders.

These findings underscore the importance of modeling interaction

effects when examining sex differences in treatment outcomes, as effects that are not evident in bivariate analyses may emerge once sex-related effect modification is taken into account. A greater number of years of substance use prior to SUD diagnosis was associated with a lower likelihood of readmission, especially in males, thereby underscoring a disadvantage for females. Tailored interventions, such as intensified contingency management and digital strategies, may be needed for females with co-occurring mood disorders and alcohol dependence (National Institute on Drug Abuse, 2024; Food and Drug Administration., 2024). Nevertheless, these findings should be interpreted cautiously, as SUD patients often present heterogeneous profiles, exhibiting multiple dependencies and comorbid mental disorders (McGrath et al., 2020). This renders arbitrary subsample extraction a less realistic approach than probabilistic latent class analysis (Bray et al., 2023).

Addressing the second objective, significant sex differences in therapeutic outcomes were found in four of the six latent classes. For the behavioral dysregulation class (Class 1) and the adolescence–cannabis class (Class 3), males had a higher associated probability of readmission, partly aligning with Davis et al. (2021). Disorders in these classes (impulse-control disorders, and childhood and adolescence disorders) are more prevalent in males (American Psychiatric Association, 2024; Jandac and Stastna, 2024; Ogundele, 2018), suggesting that males in these classes may benefit from intensified interventions to improve retention (Dacosta-Sánchez et al., 2024). In contrast, the emotional–interpersonal dysregulation class (Class 4), which include co-occurring mood and Cluster B personality disorders, and high rates of alcohol, cannabis, and cocaine dependence, had a telescoping effect and poorer outcomes for females. This class also has the highest percentage of opioid use disorders among all latent classes. Females in this class exhibited lower appointment adherence and a higher associated probability of readmission at all follow-ups. The implementation of continuous care strategies, as proposed by the Addiction Treatment Outcomes Working Group and the Recovery Management Working Group (Baxter et al., 2014; Carnevale et al., 2014), along with intensive outpatient care for co-occurring disorders (Wise, 2010), can be critical for the recovery of these females (Volkow and Blanco, 2023).

The reality distortion class (Class 6), which mainly consisted of

**Table 6**  
Regressions with interaction terms between sex and each latent class indicator.

Parameter	$\beta$	Std. Error	t / z	p-value	95 % Confidence interval	
<b>Class 1 Behavioral dysregulation</b>						
Retention	-1.55	3.40	-0.46	.649	-8.21	5.16
Adherence	-0.03	0.05	-0.54	.587	-0.12	0.07
Therapeutic goal	-0.79	0.76	-1.04	.299	-2.28	0.70
Any readmission 18 months	-1.24	1.04	-1.20	.232	-3.28	0.79
Any readmission 24 months	-1.64	1.04	-1.58	.113	-3.67	0.39
Any readmission $\geq$ 3 years	-1.19	0.57	-2.08	.038	-2.30	-0.07
Number of readmissions	-0.26	0.15	-1.81	.070	-0.55	0.02
<b>Class 2 Anxious distress</b>						
Retention	-0.99	0.98	-1.00	.316	-2.91	0.94
Adherence	0.02	0.01	1.40	.162	-0.01	0.05
Therapeutic goal	0.03	0.17	0.17	.868	-0.31	0.37
Any readmission 18 months	-0.22	0.19	-1.17	.244	-0.60	0.15
Any readmission 24 months	-0.16	0.17	-0.93	.353	-0.50	0.18
Any readmission $\geq$ 3 years	-0.02	0.14	-0.15	.880	-0.30	0.26
Number of readmissions	0.02	0.04	0.46	.643	-0.06	0.10
<b>Class 3 Adolescence-cannabis</b>						
Retention	3.30	2.95	1.12	.263	-2.48	9.08
Adherence	0.04	0.04	0.88	.379	-0.05	0.12
Therapeutic goal	0.72	0.49	1.45	.148	-0.25	1.69
Any readmission 18 months	-0.93	0.75	-1.23	.217	-2.41	0.55
Any readmission 24 months	-1.06	0.75	-1.42	.157	-2.54	0.41
Any readmission $\geq$ 3 years	-1.00	0.51	-1.96	.049	-2.00	-0.00
Number of readmissions	-0.15	0.13	-1.16	.246	-0.39	0.10
<b>Class 4 Emotional-interpersonal dysregulation</b>						
Retention	-0.79	1.18	-0.67	.504	-3.11	1.53
Adherence	-0.05	0.02	-2.83	.005	-0.08	-0.01
Therapeutic goal	-0.17	0.23	-0.77	.443	-0.62	0.27
Any readmission 18 months	0.66	0.21	3.11	.002	0.25	1.08
Any readmission 24 months	0.59	0.19	3.03	.002	0.21	0.97
Any readmission $\geq$ 3 years	0.51	0.16	3.11	.002	0.19	0.84
Number of readmissions	0.11	0.05	2.1	.035	0.01	0.21
<b>Class 5 Affective-alcohol pattern</b>						
Retention	0.42	1.25	0.34	.736	-2.03	2.88
Adherence	-0.02	0.02	-1.03	.303	-0.05	0.02
Therapeutic goal	0.16	0.22	0.71	.478	-0.28	0.59
Any readmission 18 months	-0.19	0.27	-0.69	.490	-0.72	-0.35
Any readmission 24 months	-0.10	0.24	-0.43	.667	-0.56	0.36
Any readmission $\geq$ 3 years	0.05	0.18	0.24	.808	-0.32	0.41
Number of readmissions	0.03	0.05	0.50	.614	-0.08	0.13
<b>Class 6 Reality distortion</b>						
Retention	1.51	2.34	0.64	.518	-3.08	6.10
Adherence	0.08	0.03	2.43	.015	0.02	0.15
Therapeutic goal	0.11	0.37	0.30	.764	-0.62	0.85
Any readmission 18 months	0.49	0.39	1.25	.211	-0.28	1.26
Any readmission 24 months	0.40	0.37	1.09	.275	-0.32	1.11
Any readmission $\geq$ 3 years	0.53	0.32	1.66	.096	-0.09	1.15
Number of readmissions	0.09	0.10	0.85	.394	-0.11	0.28

patients with co-occurring psychotic disorders, predicted greater appointment adherence in females but not males. While sex differences in outcomes for psychotic disorders remain inconclusive (Caton et al., 2014; Hong et al., 2023), our findings suggest that females may show better therapeutic progress, even though their readmissions do not differ from those of males.

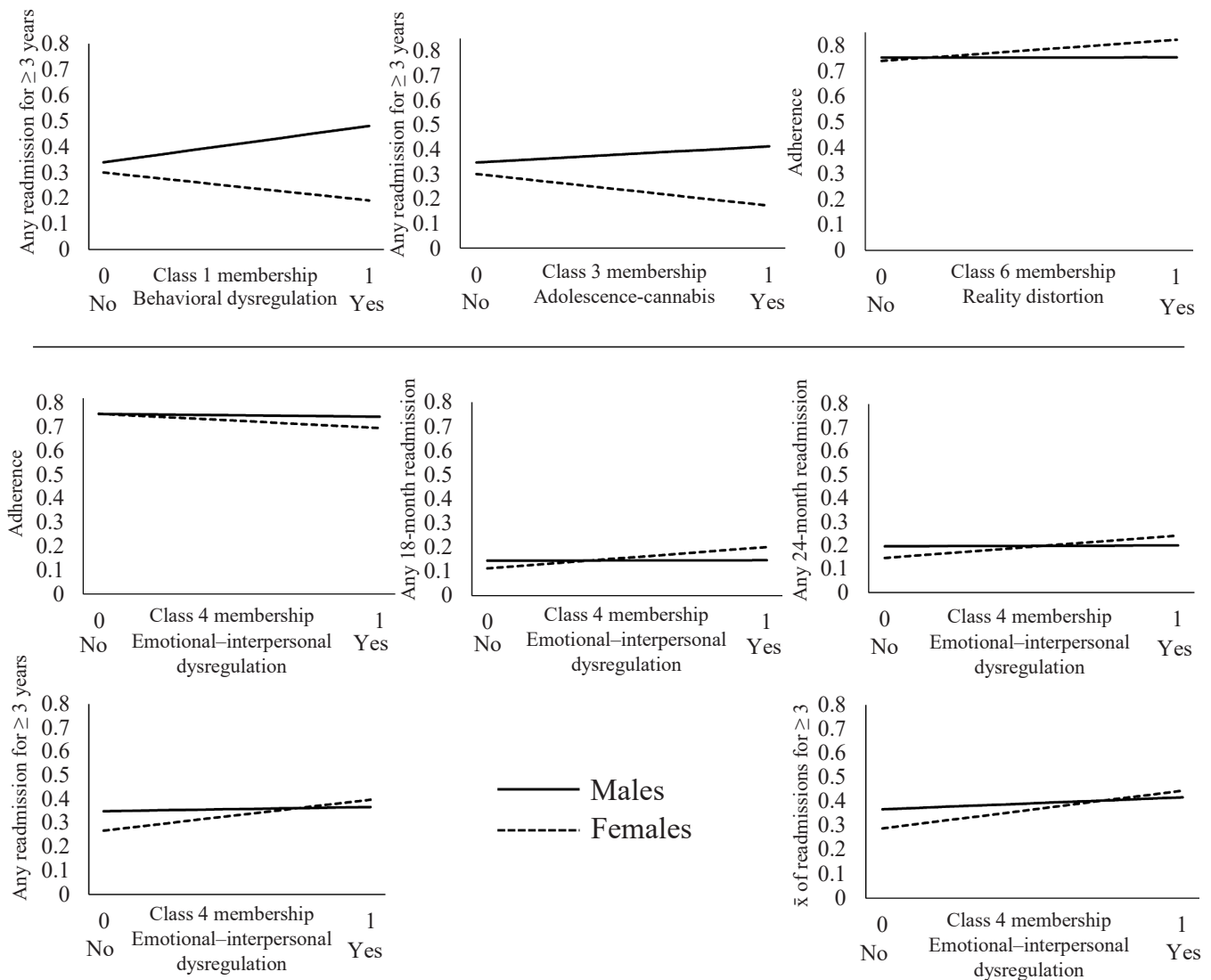
## 5. Limitations

This study has limitations regarding the generalizability of the results. While readmissions are seen as unfavorable, indicating significant return to substance use (Dacosta-Sánchez et al., 2024; Joe et al., 1999; Klimas et al., 2018), some patients may restart treatment preventively (Brandon et al., 2007), but the study lacked data to distinguish between return to substance use and prevention—an important limitation, as certain readmissions may reflect a positive development in the patient's recovery process. Additionally, EHRs often lack data on sexual minorities, complicating generalization due to potential sex misclassification. Similarly, the use of higher-order co-occurring diagnostic categories may also have overshadowed lower-order categories, increasing the risk of Type II errors (Little, 2013). In addition, although the  $\chi^2$  bivariate

residuals rule out statistically relevant local dependence, some residual clinical correlation cannot be excluded given the inherent nature of the diagnoses (Collins and Lanza, 2009; Oberski, 2016). A further limitation concerns the right-censoring of follow-up due to the administrative cutoff date, which may have resulted in unequal observation periods across subgroups (e.g., by sex or diagnosis), potentially affecting the likelihood of detecting readmissions. This decision was made to maximize statistical power and ensure subgroup representation, given the retrospective nature and long-time span of the dataset, but the possibility of informative censoring cannot be ruled out. Finally, this study is based on an administrative database from one area of Spain, which may limit the generalizability of the findings to other regions with different demographics and access to funded treatment.

## 6. Conclusions

The findings of this study have several implications for sex-focused interventions and assessment approaches. The interaction between years of substance use until SUD diagnosis and sex may explain long-term outcome differences between males and females. A slower progression toward SUD diagnosis is associated with fewer readmissions in



**Fig. 2.** Sex-specific simple slopes for the effect of latent diagnostic class membership on adherence and readmission outcomes. Upper panels correspond to classes 1, 3 and 6; lower panels to class 4. The X-axis (0 = No, 1 = Yes) indicates class membership. Y-axes present the predicted proportion of appointments attended (adherence), the probability of any readmission at 18 or 24 months or within  $\geq 3$  years, and the mean number of readmissions within  $\geq 3$  years.

both groups, but the telescoping effect negatively impacts females, leading to higher readmission rates at three or more years of follow-up, especially in patients with alcohol use disorders. Moreover, slower progression toward SUD diagnosis in patients with co-occurring mood disorder is linked to fewer readmissions at 18 months in males but not in females. The telescoping effect may explain poorer posttreatment outcomes in females, potentially owing to poorer alcohol metabolism and related consequences (Agabio et al., 2017; Becker et al., 2017; Erol and Karpyak, 2015; White, 2020), greater depressive symptoms (Kuehner, 2017), and emotional dysregulation (Albert and Newhouse, 2019). Emotional dysregulation, particularly in individuals in the emotional-interpersonal dysregulation class (Class 4), may be partly related to ovarian hormonal fluctuations in females (Garofalo et al., 2018; Newhill et al., 2021; Peters and Eisenlohr-Moul, 2019), as observed in patients with co-occurring anxiety and mood disorders.

Future research should examine factors related to emotional dysregulation in females with co-occurring Cluster B disorders and return to substance use in males with co-occurring impulse-control disorders and childhood and adolescence disorders. Research should also continue to identify groups and analyse sex's moderating role. Particularly, in the relationship between co-occurring disorders characteristics and

therapeutic outcomes, considering the therapeutic context or lower-order diagnostic categories. Given the typical male-female disproportion in SUD treatment, sex moderation and group identification are crucial for developing sex/gender-specific interventions. In response to the need for sex/gender-focused assessment approaches (Greaves et al., 2020), latent class moderation analysis is valuable for identifying variations in intervention effectiveness that might otherwise be unnoticed (Bray et al., 2023). Finally, future research should aim to distinguish between readmissions that are driven by return to substance use and those that are driven by preventive care. This distinction can be crucial for accurately assessing the effectiveness of the treatment provided.

**CRedit authorship contribution statement**

**Daniel Dacosta-Sánchez:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Investigation, Formal analysis, Conceptualization. **Marta Narváez-Camargo:** Writing – review & editing, Supervision. **Cinta Mancheño-Velasco:** Writing – review & editing, Supervision, Data curation. **Óscar M. Lozano:** Writing – review & editing, Supervision, Formal analysis.

## Funding sources

This work was supported by the grant COMPARA project, grant P20\_00735; Andalusian Research, Development and Innovation Plan; co-funded by the European Regional Development Fund [ERDF/EU] and the Junta de Andalucía, Spain. The funder had no role in the design, data collection, data analysis, and reporting of this study.

## Declaration of Competing Interest

Authors declare that they have no conflicts of interest.

## Acknowledgements

This study has been developed thanks to the transfer of data by the Department of Equality, Social Policies and Conciliation of the Junta de Andalucía.

## Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at [doi:10.1016/j.drugalcdep.2026.113062](https://doi.org/10.1016/j.drugalcdep.2026.113062).

## Data Availability

The data supporting the findings of this study are available in the figshare repository at <https://doi.org/10.6084/m9.figshare.27061447>. The data that support the findings of this study are available on request from the corresponding author.

## References

- Agabio, R., Pisanu, C., Luigi Gessa, G., Franconi, F., 2017. Sex differences in alcohol use disorder. *Curr. Med. Chem.* 24, 2661–2670. <https://doi.org/10.2174/0929867323666161202092908>.
- Agencia de Servicios Sociales y Dependencia de Andalucía, 2023. Informe Ejecutivo 2022 de la Red Pública de Atención a las Adicciones (RPAA). Junta de Andalucía. ([https://www.juntadeandalucia.es/agenciasdeserviciossocialesydependencia/images/documentacion/estatutos/Informe\\_ejecutivo2022.pdf](https://www.juntadeandalucia.es/agenciasdeserviciossocialesydependencia/images/documentacion/estatutos/Informe_ejecutivo2022.pdf))
- Albert, K.M., Newhouse, P.A., 2019. Estrogen, stress, and depression: cognitive and biological interactions. *Annu. Rev. Clin. Psychol.* 15, 399–423. <https://doi.org/10.1146/annurev-clinpsy-050718-095557>.
- Amati, F., Banks, C., Greenfield, G., Green, J., 2018. Predictors of outcomes for patients with common mental health disorders receiving psychological therapies in community settings: a systematic review. *J. Public Health (Oxf.)* 40, e375–e387.
- American Psychiatric Association, 2024. What are Disruptive, Impulse Control and Conduct Disorders? (<https://www.psychiatry.org/patients-families/disruptive-impulse-control-and-conduct-disorders/what-are-disruptive-impulse-control-and-conduct>) (accessed 22 August 2024)
- Araque, F., Arenas, F., del Valle, M., García, J., Gutiérrez, F., Luque, F., Matías-Seijo, A., Muñoz-González, P., Rodríguez-Cejas, M.A., Torres-Sánchez, A., 2005. Catálogo de servicios asistenciales de los centros de tratamiento ambulatorio de Andalucía. *Consejería para la Igualdad y Bienestar Social*. ([https://www.juntadeandalucia.es/export/drupalajda/Catalogo\\_Servicios\\_Asiestenciales.pdf](https://www.juntadeandalucia.es/export/drupalajda/Catalogo_Servicios_Asiestenciales.pdf))
- Asparouhov, T., Muthén, B., 2014. Auxiliary variables in mixture modeling: Using the BCH method in Mplus to estimate a distal outcome model and an arbitrary secondary model. *Mplus Web Notes No 21*. (<https://www.statmodel.com/examples/webnote/s/webnote21.pdf>)
- Baxter, L.E., Demitro, M., DuPont, C., DiPont, H., Fortner, N., Gitlow, S., Gold, M.S., Hansford, J., Huysman, J., Keays, B., Kelly, J.F., Kimball, W., Knepper, C.D., McDaid, C., Messinger, B., Moes, S., O'Connor, A., O'Connor, P., Philips, G., White, W.L., 2014. The New Paradigm for Recovery. Making Recovery – and Not Relapse – the Expected Outcome of Addiction Treatment. Institute for Behavior and Health, Inc. (<https://static1.squarespace.com/static/575830e0b09f958d96b6e4df/t/5759abb440261d4cd10b157d/1465494454305/IBH>)
- Becker, J.B., McClellan, M.L., Reed, B.G., 2017. Sex differences, gender and addiction. *J. Neurosci. Res.* 95, 136–147. <https://doi.org/10.1002/jnr.23963>.
- Becoña, E., 2018. Brain disease or biopsychosocial model in addiction? Remembering the Vietnam Veteran Study. *Psicothema* (30). <https://doi.org/10.7334/psicothema2017.303>.
- Bolck, A., Croon, M., Hagenaars, J.A., 2004. Estimating latent structure models with categorical variables: One-step versus three-step estimators. *Polit. Anal.* 12, 3–27. <https://doi.org/10.1093/pan/mph001>.
- Brandon, T.H., Vidrine, J.I., Litvin, E.B., 2007. Relapse and relapse prevention. *Annu. Rev. Clin. Psychol.* 3, 257–284. <https://doi.org/10.1146/annurev.clinpsy.3.022806.091455>.
- Bray, B.C., Layland, E.K., Stull, S.W., Vasilenko, S.A., Lanza, S.T., 2023. Estimating the effects of a complex, multidimensional moderator: An example of latent class moderation to examine differential intervention effects of substance use services. *Prev. Sci.* 24, 493–504. <https://doi.org/10.1007/s11121-022-01448-3>.
- Cameron, A.C., Trivedi, P.K., 2013. *Regression Analysis of Count Data*. second ed. Cambridge University Press, Cambridge, United Kingdom.
- Carnevale, J.T., Cottler, L.B., Demitro, M., Deitchman, A.N., Derendorf, H., DuPont, H., Ford, W.E., Gitlow, S., Gold, M.S., Holmes, E., Knepper, C.D., McDaid, C., McLellan, A.T., O'Brien, C.P., Thompson, K.W., 2014. Creating a new standard for addiction treatment outcomes. Institute for Behavior and Health, Inc. (<https://www.chestnut.org/resources/7d929242-77e2-4159-a202-6dbba594cbcc/IBH>)
- Caton, C.L., Xie, H., Drake, R.E., McHugo, G., 2014. Gender differences in psychotic disorders with concurrent substance use. *J. Dual Diagn.* 10, 177–186. <https://doi.org/10.1080/15504263.2014.961882>.
- Collins, L.M., Lanza, S.T., 2009. *With applications in the social, behavioral, and health sciences*. John. In: *Latent class and latent transition analysis*. Wiley Sons.
- Crum, R.M., Green, K.M., Amin-Esmaili, M., Susukida, R., Mojtabei, R., Storr, C.L., Riehm, K.E., Young, A.S., Reboussin, B.A., 2022. The role of mood disorders in the progression of and recovery from alcohol and drug use problems: A latent transition analysis. *Drug Alcohol Depend.* 238, 109566. <https://doi.org/10.1016/j.drugalcdep.2022.109566>.
- Dacosta-Sánchez, D., Fernández-Calderón, F., Díaz-Batanero, C., Mancheño-Velasco, C., Lozano, Ó.M., 2024. Modeling the therapeutic process of patients with cocaine use disorders: A guide for predicting readmission. *Eur. Addict. Res.* 30, 80–93. <https://doi.org/10.1159/000535689>.
- Davis, J.P., Eddie, D., Prindle, J., Dworkin, E.R., Christie, N.C., Saba, S., DiGuseppi, G.T., Clapp, J.D., Kelly, J.F., 2021. Sex differences in factors predicting post-treatment opioid use. *Addiction* 116, 2116–2126.
- De Cos, E.G., 2014. Gender differences in personality disorders. In: *Psychopathology in Women: Incorporating Gender Perspective into Descriptive Psychopathology*. Springer Int. Publ. Cham, pp. 679–686. [https://doi.org/10.1007/978-3-319-05870-2\\_30](https://doi.org/10.1007/978-3-319-05870-2_30).
- Díaz-Fernández, S., Fernández-Miranda, J.J., Pascual-Pastor, F., López-Muñoz, F., 2023. Gender and addiction and other mental disorders comorbidity: Sociodemographic, clinical, and treatment differences. *Arch. Women's. Ment. Health* 26, 639–650. <https://doi.org/10.1007/s00737-023-01353-w>.
- Diehl, A., Croissant, B., Batra, A., Mundle, G., Nakovics, H., Mann, K., 2007. Alcoholism in women: Is it different in onset and outcome compared to men? *Eur. Arch. Psychiatry Clin. Neurosci.* 257, 344–351. <https://doi.org/10.1007/s00406-007-0737-z>.
- Erol, A., Karpyak, V.M., 2015. Sex and gender-related differences in alcohol use and its consequences: Contemporary knowledge and future research considerations. *Drug Alcohol Depend.* 156, 1–13. <https://doi.org/10.1016/j.drugalcdep.2015.08.023>.
- European Monitoring Centre for Drugs and Drug Addiction, 2012. *Treatment Demand Indicator (TDI) Standard Protocol 3.0: Guidelines for Reporting Data on People Entering Drug Treatment in European Countries*. Publ. Off. Eur. Union. ([https://www.emcdda.europa.eu/system/files/publications/675/EMCDDA-TDI-Protocol-3.0\\_392671.pdf](https://www.emcdda.europa.eu/system/files/publications/675/EMCDDA-TDI-Protocol-3.0_392671.pdf))
- European Monitoring Centre for Drugs and Drug Addiction, 2024. *European Drug Report 2024: Trends and Developments*. Publ. Off. Eur. Union. ([https://www.emcdda.europa.eu/publications/european-drug-report/2024\\_en](https://www.emcdda.europa.eu/publications/european-drug-report/2024_en))
- Feingold, D., Tzur Bitan, D., Ferri, M., Hoch, E., 2024. Predictors of effective therapy among individuals with cannabis use disorder: A review of the literature. *Eur. Arch. Psychiatry Clin. Neurosci.* 275, 341–353. <https://doi.org/10.1007/s00406-024-01781-4>.
- Fernández-Artamendi, S., Flórez-Menéndez, G., Cortés-Tomás, M.T., Pascual-Pastor, F.S., 2024. Dual pathology? Reviewing the conceptualization of comorbidity in addictions. *Adicciones* 36, 3–10. <https://doi.org/10.20882/adicciones.2053>.
- Fonseca, F., Robles-Martínez, M., Tirado-Muñoz, J., Alías-Ferri, M., Mestre-Pintó, J.I., Coratu, A.M., Torrens, M., 2021. A gender perspective of addictive disorders. *Curr. Addict. Rep.* 8, 89–99. <https://doi.org/10.1007/s40429-021-00357-9>.
- Food and Drug Administration, 2024. FDA permits marketing of mobile medical application for substance use disorder. (<https://www.fda.gov/news-events/press-announcements/fda-permits-marketing-mobile-medical-application-s-substance-use-disorder>)
- Gardner, W., Mulvey, E.P., Shaw, E.C., 1995. Regression analyses of counts and rates: Poisson, over-dispersed Poisson, and negative binomial models. *Psychol. Bull.* 118, 392–404. <https://doi.org/10.1037/0033-2909.118.3.392>.
- Garofalo, C., Velotti, P., Callea, A., Popolo, R., Salvatore, G., Cavallo, F., Dimaggio, G., 2018. Emotion dysregulation, impulsivity and personality disorder traits: A community sample study. *Psychiatry Res* 266, 186–192. <https://doi.org/10.1016/j.psychres.2018.05.067>.
- Goh, C.M.J., Asharani, P.V., Abdin, E., Shahwan, S., Zhang, Y., Sambasivam, R., Vaingankar, J.A., Ma, S., Chong, S.A., Subramaniam, M., 2024. Gender differences in alcohol use: a nationwide study in a multiethnic population. *Int. J. Ment. Health Addict.* 22, 1161–1175. <https://doi.org/10.1007/s11469-022-00921-y>.
- Greaves, L., Poole, N., Brabete, A.C., Hemsing, N., Stinson, J., Wolfson, L., 2020. Integrating sex and gender informed evidence into your practices: ten key questions on sex, gender & substance use. *Cent. Excell. Women's Health*.
- Greenfield, S.F., Grella, C.E., 2009. Alcohol & drug abuse: what is "women-focused" treatment for substance use disorders? *Psychiatr. Serv.* 60, 880–882. <https://doi.org/10.1176/ps.2009.60.7.880>.
- Greenfield, S.F., Brooks, A.J., Gordon, S.M., Green, C.A., Kropp, F., McHugh, R.K., Lincoln, M., Hien, D., Miele, G.M., 2007. Substance abuse treatment entry, retention, and outcome in women: a review of the literature. *Drug Alcohol Depend.* 86, 1–21. <https://doi.org/10.1016/j.drugalcdep.2006.05.012>.

- Greenfield, S.F., Back, S.E., Lawson, K., Brady, K.T., 2010. Substance abuse in women. *Psychiatr. Clin. North Am.* 33, 339–355. <https://doi.org/10.1016/j.psc.2010.01.004>.
- Guerrero, E.G., Marsh, J.C., Cao, D., Shin, H.C., Andrews, C., 2014. Gender disparities in utilization and outcome of comprehensive substance abuse treatment among racial/ethnic groups. *J. Subst. Abuse Treat.* 46, 584–591. <https://doi.org/10.1016/j.jsat.2013.12.008>.
- Hayes, A.F., 2022. *Introduction to mediation, moderation, and conditional process analysis: a regression-based approach*. Third ed. Guilford Press, New York.
- Hernández-Ávila, C.A., Rounsaville, B.J., Kranzler, H.R., 2004. Opioid-, cannabis- and alcohol-dependent women show more rapid progression to substance abuse treatment. *Drug Alcohol Depend.* 74, 265–272. <https://doi.org/10.1016/j.drugalcdep.2004.02.001>.
- Hilbe, J.M., 2014. *Cambridge, United Kingdom. Modeling Count Data*. Cambridge University Press.
- Holzhauser, C.G., Cucciare, M., Epstein, E.E., 2020. Sex and gender effects in recovery from alcohol use disorder. *Alcohol Res. Curr. Rev.* 40, 1–19. <https://doi.org/10.35946/arcr.v40.3.03>.
- Hong, S.I., Bennett, D., Rosenheck, R.A., 2023. Gender differences in outcomes of early intervention services for first episode psychosis. *Early Interv. Psychiatry* 17, 715–723. <https://doi.org/10.1111/eip.13367>.
- Jandac, T., Stastna, L., 2024. Analysis of the relationship between psychiatric and addiction-related disorders in patients of an outpatient addiction treatment clinic for children and adolescents. *Children* 11, 414. <https://doi.org/10.3390/children11040414>.
- Joe, G.W., Simpson, D.D., Broome, K.M., 1999. Retention and patient engagement models for different treatment modalities in DATOS. *Drug Alcohol Depend.* 57, 113–125. [https://doi.org/10.1016/S0376-8716\(99\)00088-5](https://doi.org/10.1016/S0376-8716(99)00088-5).
- Junta de Andalucía, 2025a. Sistema de Información del Plan Andaluz sobre Drogas y Adicciones (SIPASDA). Consejería de Salud y Consumo, Sevilla. (<https://www.junta.deandalucia.es/organismos/saludyconsumo/areas/adicciones/informacion/paginas/sistema-informacion.html>) (accessed 11 July 2025).
- Junta de Andalucía, 2025b. Centros de Tratamiento Ambulatorios (CTA). Sevilla: Consejería de Salud y Consumo. (<https://www.juntadeandalucia.es/organismos/saludyconsumo/areas/adicciones/atencion/paginas/centros-tratamiento-ambulatorios.html>) (accessed 11 July 2025).
- Keyes, K.M., Martins, S.S., Blanco, C., Hasin, D.S., 2010. Telescoping and gender differences in alcohol dependence: new evidence from two national surveys. *Am. J. Psychiatry* 167, 969–976. <https://doi.org/10.1176/appi.ajp.2009.09081161>.
- Khan, S.S., Secades-Villa, R., Okuda, M., Wang, S., Pérez-Fuentes, G., Kerridge, B.T., Blanco, C., 2013. Gender differences in cannabis use disorders: results from the National Epidemiologic Survey of Alcohol and Related Conditions. *Drug Alcohol Depend.* 130, 101–108. <https://doi.org/10.1016/j.drugalcdep.2012.10.015>.
- Klimas, J., Fairgrieve, C., Tobin, H., Field, C.A., O’Gorman, C.S., Glynn, L.G., Keenan, E., Saunders, J., Bury, G., Dunne, C., Cullen, W., 2018. Psychosocial interventions to reduce alcohol consumption in concurrent problem alcohol and illicit drug users. *Cochrane Database Syst. Rev.* 12, CD009269. <https://doi.org/10.1002/14651858.CD009269.pub4>.
- Knol, M.J., VanderWeele, T.J., 2012. Recommendations for presenting analyses of effect modification and interaction. *Int. J. Epidemiol.* 41, 514–520. <https://doi.org/10.1093/ije/dyr218>.
- Kuehner, C., 2017. Why is depression more common among women than among men? *Lancet Psychiatry* 4, 146–158. [https://doi.org/10.1016/S2215-0366\(16\)30263-2](https://doi.org/10.1016/S2215-0366(16)30263-2).
- Kushner, M.G., Maurer, E., Menary, K., Thuras, P., 2011. Vulnerability to the rapid (“telescoped”) development of alcohol dependence in individuals with anxiety disorder. *J. Stud. Alcohol Drugs* 72, 1019–1027. <https://doi.org/10.15288/jsad.2011.72.1019>.
- Laia, M., Carlos, R., Cristina, L.O., Miguel, C., 2011. Epidemiological and diagnostic axis I gender differences in dual diagnosis patients. *Adicciones* 23, 165–172.
- Little, T.D., 2013. *The Oxford handbook of quantitative methods, 1. : Foundations*. Oxford University Press (Ed.).
- Logan, T.K., Cole, J., Walker, R., 2020. Examining recovery program participants by gender: program completion, relapse, and multidimensional status 12 months after program entry. *J. Drug Issues* 50, 436–454. <https://doi.org/10.1177/0022042620923985>.
- Mancheño-Velasco, C., Narváez-Camargo, M., Lozano-Rojas, Ó.M., Sanchez-García, M., 2024. Readmission and dropout in outpatient centers: an analysis of real-world data in patients with dual-diagnosis. *Int. J. Ment. Health Addict.* 1–21. <https://doi.org/10.1007/s11469-024-01360-7>.
- McGrath, J.J., Lim, C.C.W., Plana-Ripoll, O., Holtz, Y., Agerbo, E., Momen, N.C., Mortensen, P.B., Pedersen, C.B., Abdulmalik, J., Aguilar-Gaxiola, S., Al-Hamzawi, A., Alonso, J., Bromet, E.J., Bruffaerts, R., Bunting, B., de Almeida, J.M.C., de Girolamo, G., de Vries, Y.A., Florescu, S., de Jonge, P., 2020. Comorbidity within mental disorders: a comprehensive analysis based on 145990 survey respondents from 27 countries. *Epidemiol. Psychiatr. Sci.* 29, e153. <https://doi.org/10.1017/S2045796020000633>.
- McHugh, R.K., Votaw, V.R., Sugarman, D.E., Greenfield, S.F., 2018. Sex and gender differences in substance use disorders. *Clin. Psychol. Rev.* 66, 12–23. <https://doi.org/10.1016/j.cpr.2017.10.012>.
- Muthén, L.K., Muthén, B.O., 2021. *Mplus User’s Guide* (8.7 ed.). Muthén & Muthén.
- National Institute on Drug Abuse, 2024. Common comorbidities with substance use disorders research report. (<https://nida.nih.gov/publications/research-reports/common-comorbidities-substance-use-disorders/references>) (accessed 22 August 2024).
- Newhill, C.E., Yuan, Y., Wojtalik, J., Eack, S., 2021. A transdiagnostic comparison of emotion dysregulation in schizophrenia and cluster B personality disorders. *J. Soc. Soc. Work Res.* 12, 155–175. <https://doi.org/10.1086/713820>.
- Oberski, D.L., 2016. Beyond the number of classes: separating substantive from non-substantive dependence in latent class analysis. *Adv. Data Anal. Cl.* 10, 171–182. <https://doi.org/10.1007/s11634-015-0211-0>.
- Ogundele, M.O., 2018. Behavioural and emotional disorders in childhood: a brief overview for paediatricians. *World J. Clin. Pediatr.* 7, 9–27. [10.54092/wjcp.v7.i1.9](https://doi.org/10.54092/wjcp.v7.i1.9).
- Peltier, M.R., Sofuoglu, M., Petrakis, I.L., Stefanovics, E., Rosenheck, R.A., 2021. Sex differences in opioid use disorder prevalence and multimorbidity nationally in the Veterans Health Administration. *J. Dual Diagn.* 17, 124–134. <https://doi.org/10.1080/15504263.2021.1904162>.
- Peters, J.R., Eisenlohr-Moul, T.A., 2019. Ovarian hormones as a source of fluctuating biological vulnerability in borderline personality disorder. *Curr. Psychiatry Rep.* 21, 1–8. <https://doi.org/10.1007/s11920-019-1096-y>.
- Piazza, N.J., Vrbka, J.L., Yeager, R.D., 1989. Telescoping of alcoholism in women alcoholics. *Int. J. Addict.* 24, 19–28. <https://doi.org/10.3109/10826088909047272>.
- Randall, C.L., Roberts, J.S., Del Boca, F.K., Carroll, K.M., Connors, G.J., Mattson, M.E., 1999. Telescoping of landmark events associated with drinking: a gender comparison. *J. Stud. Alcohol* 60, 252–260. <https://doi.org/10.15288/jsa.1999.60.252>.
- Richardson, D.B., Kaufman, J.S., 2009. Estimation of the relative excess risk due to interaction and associated confidence intervals. *Am. J. Epidemiol.* 169, 756–760. <https://doi.org/10.1093/aje/kwn411>.
- Rubin, D.B., 1976. Inference and missing data. *Biometrika* 63, 581–592. <https://doi.org/10.1093/biomet/63.3.581>.
- Sartor, C.E., Lynskey, M.T., Heath, A.C., Jacob, T., True, W., 2007. The role of childhood risk factors in initiation of alcohol use and progression to alcohol dependence. *Addiction* 102, 216–225. <https://doi.org/10.1111/j.1360-0443.2006.01661.x>.
- Satorra, A., Bentler, P.M., 2001. A scaled difference chi-square test statistic for moment structure analysis. *Psychometrika* 66, 507–514. <https://doi.org/10.1007/BF02296192>.
- Satorra, A., Bentler, P.M., 2010. Ensuring positiveness of the scaled difference chi-square test statistic. *Psychometrika* 75, 243–248. <https://doi.org/10.1007/s11336-009-9135-y>.
- Towers, E.B., Williams, I.L., Qillawala, E.I., Rissman, E.F., Lynch, W.J., 2023. Sex/gender differences in the time-course for the development of substance use disorder: a focus on the telescoping effect. *Pharmacol. Rev.* 75, 217–249. <https://doi.org/10.1124/pharmrev.121.000361>.
- Verplaetse, T.L., Cosgrove, K.P., Tanabe, J., McKee, S.A., 2021. Sex/gender differences in brain function and structure in alcohol use: A narrative review of neuroimaging findings over the last 10 years. *J. Neurosci. Res.* 99, 309–323. <https://doi.org/10.1002/jnr.24625>.
- Volkow, N.D., Blanco, C., 2023. Substance use disorders: a comprehensive update of classification, epidemiology, neurobiology, clinical aspects, treatment and prevention. *World Psychiatry* 22, 203–229. <https://doi.org/10.1002/wps.21073>.
- White, A.M., 2020. Gender differences in the epidemiology of alcohol use and related harms in the United States. *Alcohol Res. Curr. Rev.* 40. <https://doi.org/10.35946/arcr.v40.2.01>.
- White, H., 1980. A heteroskedasticity-consistent covariance matrix estimator and a direct test for heteroskedasticity. *Econometrica* 48, 817–838. <https://doi.org/10.2307/1912934>.
- Wise, E.A., 2010. Evidence-based effectiveness of a private practice intensive outpatient program with dual diagnosis patients. *J. Dual Diagn.* 6, 25–45. <https://doi.org/10.1080/15504260903498862>.
- World Health Organization, 1994. *International statistical classification of diseases and related health problems, 10th ed.*. World Health Organization.
- Yeom, H.S., 2015. Utilization of substance abuse treatment: gender differences among participants in an aftercare program. *Soc. Work Public Health* 30, 578–591. <https://doi.org/10.1080/19371918.2015.1084773>.