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Evidence of telescoping in females across two decades of US treatment admissions for injection drug use: 2000–2020

Nicholas L. Bormann^{a,*}, Benjamin Miskle^{b,c}, Paul Holdefer^b, Stephan Arndt^{b,d}, Alison C. Lynch^{b,f}, Andrea N. Weber^{b,e}

^a Department of Psychiatry and Psychology, Mayo Clinic, 404 W Fountain St, Albert Lea, Rochester, MN 56007, USA

^b Department of Psychiatry, University of Iowa, Iowa City, IA, USA

^c Department of Pharmacy, University of Iowa, Iowa City, IA, USA

^d Department of Biostatistics, University of Iowa, Iowa City, IA, USA

^f Department of Family Medicine, University of Iowa, Iowa City, IA, USA

^e Department of Internal Medicine, University of Iowa, Iowa City, IA, USA

HIGHLIGHTS

• Injection drug use (IDU) is associated with greater risk of infection and overdose.

• Treatment Episode Dataset-Admission 2000-2020 provided initial admission IDU cases.

• 1,458,695 (38.5 % female) cases were seen; probablistic index (PI) gave effect sizes.

• Females began their primary substance later in life (PI = 0.47, p < 0.0001).

• Females entered treatment after a shorter period of use (PI = 0.57, p < 0.0001).

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ABSTRACT

Background: People who inject drugs (PWID) have an increased risk of soft tissue infection, drug overdose and death. Females may be particularly vulnerable due to barriers to substance use disorder (SUD) treatment entry, stigma, and telescoping, or the greater severity in substance use-related comorbidity and consequences despite a shorter history of use. We set out to identify sex differences in United States injection drug use (IDU). *Methods:* The Treatment Episode Dataset-Admission (2000–2020) provided data to identify PWID undergoing

their initial SUD treatment admission. Mann-Whitney U test, chi-square, and Spearman correlations were used for ordinal variables, categorical variables, and to assess similarity of male/female trends over the 21 years, respectively. The probabilistic index (PI) and Cramer's V provided effect sizes for Mann-Whitney U tests and chisquare tests, respectively.

Results: A total of 13,612,978 records existed for cases entering their initial treatment. Mapping to a history of IDU left 1,458,695 (561,793 females). Females had a higher prevalence among PWID across all 21 years; IDU trends were essentially identical between males and females (r = 0.97). Females endorsed beginning their primary substance later in life (PI = 0.47, p < 0.0001) and entered treatment after a shorter period of substance use (PI = 0.57, p < 0.0001).

Conclusions: We saw evidence of telescoping among PWID with a SUD entering their initial episode of treatment. Interventions should be implemented prior to the transition to IDU, and this window of opportunity is shortened in females. Utilizing gender-responsive treatment options may be a way to increase treatment-seeking earlier in the disease course.

* Corresponding author.

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E-mail address: bormann.nicholas@mayo.edu (N.L. Bormann).

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1. Introduction

Worldwide, it is estimated that 15.6 million people inject drugs, 3.2 million of which are female (Degenhardt et al., 2017). The transition to injection drug use (IDU) increases the risk of overdose and long-term medical comorbidities, including hepatitis C and human immunodeficiency virus (HIV) (Mathers et al., 2013; Novak and Kral, 2011; Robertson et al., 2021). People who inject drugs (PWID) also have a significantly elevated standardized mortality ratio as compared to the general population (Mathers et al., 2013). Mixed findings exist regarding when the transition to IDU occurs, with reports indicating no difference between sexes (Doherty et al., 2000) versus females engaging in IDU use earlier than males (Evans et al., 2003; Miller et al., 2006).

Non-sterile practices such as sharing or reusing needles and not adequately cleaning the skin increase bloodborne infection risks (Robertson et al., 2021). Infection occurrence and end-organ progression has been suggested as a surrogate marker for substance use severity (Gray et al., 2018). Females appear differentially impacted, with higher odds of injection site infection and injection-related injury (Hope et al., 2008; Topp et al., 2008). Females are more likely to share needles and be injected by a sexual partner, placing them at increased risk (Magnus et al., 2013). When considering HIV-positive individuals, females, particularly those with a history of IDU, also have a greater prevalence of medical comorbidities (Weiss et al., 2010).

High risk injection practices are also associated with an increased severity of mental health symptoms (Adams et al., 2020). Among PWID, females report greater psychological distress (Topp et al., 2010) and increased prevalence of depression, past physical or emotional abuse, and affective symptoms (Mackesy-Amiti et al., 2012; Magnus et al., 2013; Wisniewski et al., 2005). Among PWID, depression severity in females has been correlated with higher risk sexual activity (Pettes et al., 2015). Increasing years of IDU has also been differentially predictive of depression in females versus males (Risser et al., 2010).

PWID commonly experience stigma. Within this population, stigma can limit healthcare engagement and has been associated with increased rates of hepatitis C infection (Williams et al., 2021). Females who use substances are particularly stigmatized, stemming partly from expected gender norms (Grella, 2008) and is increased during pregnancy (Weber et al., 2021). Treatment offerings have also been historically male-focused (Greenfield et al., 2007a; Grella, 2008). Transitioning to a gender-responsive approach, or treatment designed to meet the unique needs of women, has shown benefits in decreased substance use, improved psychological health, and greater treatment satisfaction (Greenfield et al., 2007b; Messina et al., 2010; Saxena et al., 2014). These offerings are unfortunately not widespread (Campbell et al., 2007; Grella, 2008).

Females enter treatment at lower rates than males, and when they do, females' clinical profiles are typically more severe despite a shorter history of use (referred to as telescoping) (Greenfield et al., 2010, 2007a; McHugh et al., 2018). This effect decreases the timeframe when effective interventions may be implemented to halt the progression of SUD in females. These treatment barriers subsequently place females in a vulnerable position. Female deaths by drug overdose rose significantly from 2001 to 2021. From 2020 to 2021, the age-adjusted rate for female drug overdose deaths increased by 15% to 19.6 deaths per 100,000 standard population (Spencer et al., 2022). As the prevalence of SUDs in females is increasing globally, these trends require action to reduce further preventable morbidity and mortality (GBD 2016 Alcohol and Drug Use Collaborators, 2018).

Pro et al. analyzed Treatment Episode Dataset (TEDS) discharges from 2010 to 2019 and reported a significant increase in methamphetamine IDU. Beginning in 2010, 18.7 % of cases reported IDU being the primary route of use; this increased to 27.3 % in 2019 (Pro et al., 2022). This study did not evaluate sex differences. Jones et al. evaluated TEDS admissions over the same timeframe, also assessing rates of methamphetamine IDU. They similarly reported increases, adding that males had an adjusted odds ratio of 1.13 (CI = 1.10-1.15) relative to females (Jones et al., 2023). Neither study indicated how their findings related to initial treatment episodes. We, therefore, wanted to pursue this inquiry further, broadening to IDU of any substance, and narrowing to first-time admissions. Focusing on initial treatment episodes limits bias from individuals who return to treatment multiple times and leaves unique cases, or people, remaining. As IDU has significant medical comorbidity and mortality, those individuals may be more likely to return to treatment, which may impact findings. We focused our analysis on sex differences. Based on telescoping, we hypothesized that we would see a shorter duration of drug use in females with a history of IDU as compared to males.

2. Materials and methods

2.1. Data source

Substance Abuse and Mental Health Services Administration (SAMHSA) produces annual Treatment Episode Dataset-Admissions (TEDS-A) public use files. Data for this study used the combined 2000-2020 dataset (Substance Abuse and Mental Health Services Administration, 2022). TEDS-A contains data on admissions for people aged 12 years or older. Facilities that report to SAMHSA include state-licensed or certified SUD treatment facilities that receive public funding. TEDS-A compiles data collected through the state data collection systems. 13, 612,978 records indicated that this was the client's first admission to treatment. Endorsement of a history of IDU allowed for mapping the incidence of the first episode PWID cases. We then focused on this cohort.

2.2. Measures

Staff at the treatment facility interview clients during admission and information is self-reported. The SAMHSA codebooks asks for "client's biological sex"; we therefore used this language (male, female) throughout to be consistent with the dataset. Due to confidentiality, SAMHSA recodes the client's age and age of first use for problem substances into categories. Because of low numbers, race and ethnicity were recoded as Race/Ethnicity, i.e., White (non-Hispanic), Black/African American, Latino, and Other. Treatment and substance use characteristics included referral source, service setting, and state. Referral sources from schools and employers merged with other community referrals due to low frequency. Service settings were recoded as inpatient, outpatient, and detoxification only. Some drug categories were collapsed for analysis due to low percentages (<2 %). For example, tranquilizers, barbiturates, and hypnotics became classified as Other. The number of substances was generated by including the total number of problem substances listed for each case. This variable ranged from one to three since only three can be listed. A person was coded as a PWID if they reported a history of injecting any substance.

2.3. Statistical analysis

Due to the large sample size, we focused on effect sizes. We used Mann-Whitney U tests for ordinal variables and chi-square for categorical variables for statistical tests. Spearman correlations assessed the similarity of male/female trends over the 21 years. The probabilistic index (PI or common language) measure of effect sizes accompanied the U tests. This measure shows the probability that a random male's measure is higher than a random female's measure. An index value of 0.5 indicates no difference, and the chances are 50/50. If the value is 0.6, then the probability that the male is higher is 0.6 and the female's probability is therefore 0.4. A small, medium, and large effect is considered as 0.56, 0.64, and 0.70, respectively (Acion et al., 2006). Cramer's V accompanied the chi-square tests for effect size.

We also performed two sensitivity analyses to control for the effects

of state. The first used ordinal logistic regression to predict either age or the age of first use groups from the client's sex while controlling for state. The second analysis performed a Mann-Whitney test and PI for sex and either age or the age of first use within each state's data. Thus, we could assess the consistency of the effects over all states. Model prediction error for both sensitivity analyses was estimated with the Akaine Information Criterion (AIC).

3. Results

Fig. 1 shows the percentage of PWID admitted to treatment over the period. Females have a higher prevalence of PWID throughout the 21-year span. However, the pattern is nearly identical across sexes ($r_S = 0.97$). Both sexes are steady during the first decade and then rise, peaking in 2018, and then declining. The remaining analyses focus on the 1,458,695 PWID admissions.

Tables 1 and 2 provide demographic, substance use, and treatment information for male and female PWID. Female PWID were more often White, more educated, less frequently in the labor force, and more lived independently than males. Females came to treatment referred by community organizations more than males. Compared to males, females more often used methamphetamine and less often used heroin. Females also tended to use fewer substances, were outpatients, and were less frequently treated as detoxification only.

Our hypotheses suggested that females would begin use of their primary substance later than males and go to their first treatment earlier. These hypotheses were confirmed. Fig. 2 shows the distributions of first use. Females (Mann-Whitney p < 0.0001) tended to start later with a small effect size (PI = 0.47). Fig. 3 displays females' earlier admission to their first treatment (Mann-Whitney p < 0.0001) with a moderate effect size of 0.57. For all years, women more frequently went to treatment in their 20s (see Fig. 4).

The results of the sensitivity analysis confirmed the main results. For both ordinal logistic regression models, adding state dummy variables improved the AIC in the models. However, the effect of sex was unaffected for either age at first use or age at first treatment. For the withinstate analyses, all states showed a consistent direction for the age of the first treatment, and females went to treatment earlier than males in all states. Two states were inconsistent in the age of first use, i.e., Hawaii and West Virginia, where females initiated use of the reported substances earlier than males. The rest were consistent with the main results that females initiated use of their primary substance later.



Fig. 1. Percentage of first-time substance use disorder treatment admission of people who have injected drugs displayed by sex from 2000 to 2020.

Caption: The Treatment Episode Dataset-Admission (TEDS-A) had a total of 13,612,978 records for first-time substance use disorder treatment admission cumulatively from years 2000 to 2020. Of these, 1,458,695 (561,793 females) identified a history of injection drug use. Females had a significantly greater prevalence of people who injected drugs (PWID) at each year compared to males.

Table 1

Demographic	comparisons	for	first	episode	substance	use	disorder	treatment
admissions.								

	Male	Female	p^1
N =	896902	561793	
Age (%)			< 0.001
12-14	383 (0.0)	550 (0.1)	
15-17	5654 (0.6)	6446 (1.1)	
18-20	39932 (4.5)	36479 (6.5)	
21-24	117611 (13.1)	94819 (16.9)	
25-29	183555 (20.5)	131380 (23.4)	
30-34	155020 (17.3)	102144 (18.2)	
35-39	119936 (13.4)	71644 (12.8)	
40-44	94320 (10.5)	49412 (8.8)	
45-49	75136 (8.4)	33596 (6.0)	
50-54	54065 (6.0)	20063 (3.6)	
55-64	44900 (5.0)	13793 (2.5)	
65+	6390 (0.7)	1467 (0.3)	
Race/Ethnicity (%)			< 0.001
White	631155 (70.4)	439109 (78.2)	
Black	77578 (8.6)	33550 (6.0)	
Latino	143634 (16.0)	56569 (10.1)	
Other	44535 (5.0)	32565 (5.8)	
Education (%)			< 0.001
<=8th Grade	57447 (6.6)	34878 (6.4)	
Grades 9-11	218294 (25.1)	136160 (25.1)	
High School or equivalent	436489 (50.2)	243868 (44.9)	
1-3 years college	128402 (14.8)	107303 (19.8)	
4+ years college	28457 (3.3)	20439 (3.8)	
Employment (%)			< 0.001
Full-time	121681 (14.0)	41765 (7.7)	
Part-time	51239 (5.9)	32754 (6.1)	
Unemployed	382670 (44.2)	250182 (46.2)	
Not in labor force	310483 (35.8)	216550 (40.0)	
Living Arrangement (%)			< 0.001
Independent living	480916 (60.7)	324867 (64.5)	
Dependent living	171660 (21.7)	108754 (21.6)	
Homeless	140122 (17.7)	70200 (13.9)	

 1 Ordinal variables were tested using Mann-Whitney, and categorical variables were tested with chi-square tests.

4. Discussion

This study extends previous findings of an increasing history of IDU of methamphetamine from 2010 to 2019 (Jones et al., 2023; Pro et al., 2022) by incorporating IDU of any substance, increasing the timeframe assessed, and focusing on sex differences. Our outcomes were consistent with the a priori hypotheses: (1) females begin use of their primary injected substances later than males (small effect size), and (2) females enter their first SUD treatment earlier than males (medium effect size).

4.1. Evidence of a telescoping effect

Females entering their first SUD treatment were significantly more likely than males to endorse a history of IDU each year over the twodecade period. This peaked in 2018 and began to drop, with the gap narrowing between sexes. It is of particular interest that females also reported initiating use of their primary substance later than males while entering their first treatment program at younger ages. This shortened period of substance use onset to IDU is concerning and may be reflective of an acceleration in their SUD.

These findings are consistent with previous literature that has described a telescoping effect in females. While the existence of this has been questioned in the general population (Keyes et al., 2010), when looking at individuals with a SUD, females appear to have a more rapid time course in developing physical and psychosocial consequences of substance use (Greenfield et al., 2010; Lewis et al., 2014; McHugh et al., 2018). IDU demarcates the transition to an increasingly dangerous route of use, placing individuals at an elevated risk for infectious diseases and overdose fatalities (Mathers et al., 2013; Novak and Kral, 2011; Robertson et al., 2021). Females who inject drugs may be particularly

Table 2

Substance use and treatment variables for Males and Females.

Male Devi	1
Male Female p	-
N = 896902 561793	
Referral Source (%) <	0.001
Self 462581 (52.7) 274859 (50.0)	
SUD provider 78676 (9.0) 48154 (8.8)	
Healthcare 52746 (6.0) 39097 (7.1)	
Community 68691 (7.8) 67592 (12.3)	
CJ system 214916 (24.5) 119757 (21.8)	
Service Type (%) <	0.001
Detox 262836 (29.3) 129449 (23.0)	
Residential 177613 (19.8) 116596 (20.8)	
Outpatient 456453 (50.9) 315748 (56.2)	
Primary Substance (%) <	0.001
Alcohol 57091 (6.4) 26382 (4.7)	
Cocaine 29917 (3.3) 21499 (3.8)	
Marijuana 23453 (2.6) 14270 (2.5)	
Heroin 548101 (61.1) 303111 (54.0)	
Other opiates 79810 (8.9) 66076 (11.8)	
Methamphetamine 133616 (14.9) 109892 (19.6)	
Other 24914 (2.8) 20563 (3.7)	
Age 1st Used (%) <	0.001
< 12 31599 (3.8) 16552 (3.1)	
12-14 99189 (11.9) 59537 (11.3)	
15-17 182421 (22.0) 103718 (19.7)	
18-20 188048 (22.7) 111749 (21.2)	
21-24 126016 (15.2) 89738 (17.0)	
25-29 97830 (11.8) 70440 (13.4)	
30+ 105037 (12.7) 75527 (14.3)	
Number of Substances (%) <	0.001
1 3176 (0.4) 1010 (0.2)	
2 235920 (26.3) 135461 (24.1)	
3 657806 (73.3) 425322 (75.7)	

 1 Ordinal variables were tested using Mann-Whitney, and categorical variables were tested with chi-square tests.



Fig. 2. Age of first substance use.

Caption: The Treatment Episode Dataset-Admission (TEDS-A) collects age of first use of a patient's self-reported problematic substance. Due to confidentiality concerns, Substance Abuse and Mental Health Services Administration (SAMHSA) recodes the client's age of first use into categories. A Mann-Whitney U test (W = 207073680546) has p<0.0001. The common language effect size (or probabilistic index) is 0.473, indicating a small effect size. Females initiate use of their primary substance later than males; this is most notable for ages over 21 years.

vulnerable. High rates of stigma can decrease willingness to access healthcare or harm reduction services (Muncan et al., 2020; Shirley-Beavan et al., 2020). Specifically for IDU, females have been historically excluded from studies or results were not stratified by sex, limiting the identification and development of sex-specific findings (Springer et al., 2015). The shortened window of time from initiation of substance use to IDU adds urgency to addressing the needs of this population to minimize risk of future medical comorbidity (Lewis et al., 2014).



Fig. 3. Age of first treatment.

Caption: The Treatment Episode Dataset-Admission (TEDS-A) collects age of first substance use treatment admission. Due to confidentiality concerns, Substance Abuse and Mental Health Services Administration (SAMHSA) recodes the client's age into categories. A Mann-Whitney U test (W = 287665627367) has p<0.0001. The common language effect size (or probabilistic index) is 0.571, indicating a moderate effect size for females entering treatment earlier than males. This is most notable for the age of treatment admissions for those between 18 and 29 years old.



Fig. 4. Percentage of 21–29 year olds with a history of injection drug use who have entered their first substance use disorder treatment.

Caption: A total of 1,458,695 records (561,793 females) existed for individuals with a history of injection drug use who were entering their first substance use disorder treatment from 2000 to 2020. The Y-axis displays the prevalence of those aged 21-29 (data in bins for confidentiality) among total cases per year. There was a pattern of increasing prevalence of those aged 21-29 being admitted that peaked soon after 2010 then went down. The rise and fall pattern for females and males was nearly identical (Spearman correlation = 0.99).

Our finding of higher rates of endorsed IDU by females with a SUD entering their first treatment program is in juxtaposition of the general population. Globally, most individuals endorsing past IDU are male. However, in high income populations such as our sample, this gap is narrowed (Degenhardt et al., 2017). Additionally, given that our sample was limited to initial lifetime admission, one may anticipate based on telescoping that females would have a higher prevalence of lifetime IDU in this specific sample. Females seek out medical care at higher rates than males (Bertakis et al., 2000; Thompson et al., 2016). As IDU is associated with both acute (i.e., soft tissue infections) and chronic medical comorbidities (i.e., end-organ damage), this may contribute to females with a history of IDU entering treatment earlier. Based on referral source for this data however, females and males were not referred from a healthcare provider at a meaningfully different rate (7.1 % vs 6 % of admissions, respectively). Pregnancy may be an additional differential factor. Once pregnant, females may be more motivated to

seek out treatment to limit IDU-related harms to the pregnancy. Again, based on this data, cases endorsing pregnancy were small in total number (4.8 %) and did not explain this effect.

4.2. Unique factors for females

Study trends in IDU over time were essentially identical between males and females, despite significant broad-scale changes. The past two decades have seen an unprecedented increase in drug overdose deaths, accelerated by a changing drug supply (i.e., fentanyl) (Jannetto et al., 2019). Most recently, there has been a rise in overdoses related to co-ingestion of stimulants (i.e., cocaine, methamphetamine) and opioids (Ciccarone, 2021). Additionally, the COVID-19 pandemic saw increases in substance use and an overall decrease in SUD treatment admissions (Cantor et al., 2022). The persistence of this sex difference despite these changes is of interest.

Females have unique risk factors that may predispose a transition to IDU. Female IDU is more impacted by interpersonal forces compared to male IDU, especially when occupying traditional female roles. In a population of PWID in San Francisco, females reporting IDU were younger, more likely to be injected by others, and more likely to be in an IDU partnership (Evans et al., 2003). Female IDU is also associated with interpersonal violence and decreased access to resources (Biondi et al., 2022). Gender norms and stigma effect females engaging in IDU who are in caretaker roles. Childcare responsibilities and fear of child welfare involvement are differential barriers for females not seeking substance use treatment (Scheidell et al., 2022; Shirley-Beavan et al., 2020). These highlight how traditional submissive and domestic female roles may predispose to IDU transitions more than male counterparts.

Although the gap between males and females entering treatment has been shrinking over the past 1-2 decades, females continue to have lower representation in initial treatment populations (McHugh et al., 2018). Given that females report that mental health symptoms, childcare responsibilities, and gender-based violence not only increase IDU but also impact engagement in services (Biondi et al., 2022), creating gender-specific programs that address these factors should be prioritized. For example, a harm reduction outreach service provided by trauma-informed females to safe spaces with on-site childcare, such as domestic violence shelters, may increase engagement (Milaney et al., 2022). Similarly, special substance use treatment programs that allow for on-site childcare and care provided by a trauma-informed, majority female staff may further increase the rates of female self-referral and completion of treatment. Ultimately, additional research is needed to identify causal mechanisms and evidenced-based solutions.

4.3. Adults 30 years and younger

The most notable differences between males and females occurred primarily in the third decade of life. A small effect was seen for females beginning their initial substance later than males, particularly after 21 years of age. Time from primary substance initiation to treatment had a moderate effect, especially for females between 18 and 29 years old, who entered treatment quicker after onset of use. Additionally, a pattern of increasing prevalence of younger males and females (< 30 years old) entering their initial treatment was seen, peaking in 2012 and 2013; this trend was essentially identical between sexes.

Several reasons may account for these trends. Developmentally, there are sex differences in rates of brain maturation (i.e., prefrontal cortex) that have implications for increased sensation-seeking and reward-related behavior in young males (Hammerslag and Gulley, 2016). These developmental differences may partially account for young males initiating substance use earlier in life. Regarding the peak seen in 2012-13, the data are unable to answer this question. A plausible explanation may be the Affordable Care Act in 2010, which led to an increase in Americans having health care coverage. This was particularly true with young adults who were allowed to stay on parental

insurance through the age of 26 (Levy and Botticelli, 2021). This change, followed by certain states accepting Medicaid expansion, may have made care more accessible for individuals with a SUD (McCarty et al., 2019). Whether these changes had a differential impact between sexes is unknown and warrants future research.

4.4. Limitations

This analysis does have limitations. While TEDS-A collects a significant amount of SUD admission across the US, it does not catch all. Some states do not report to TEDS-A, along with services from methadone clinics or the carceral system. Data is also self-report, which may incorporate error. We attempted to look at unique cases, or people, by only utilizing the first treatment episode. The accurateness of this is contingent on the quality of data entered at the SUD treatment sites. Attempting to utilize unique cases may show the results for less severe cases, as repeated treatment episodes were removed. This may be particularly relevant for PWID, as a greater degree of psychiatric and medical comorbidity is seen in this population. Since such individuals may repeat treatment more often, they could be overrepresented in expected caseloads. We collapsed IDU of any substance as a PWID. While unique harms may exist between substances, non-pharmaceutical grade substances are rarely exclusively one substance and IDU itself is a significant risk factor for medical harms. While this may limit generalizability to specific substances, it may be generalizable to the act of injection. There also lacked a precise measurement for substance use, such as how many years someone engaged in IDU, the frequency of substance use and the total duration of substance use. Data for age existing in bins also impairs the exactness of effect sizes across age groups.

5. Conclusions

Over the past two decades, there has been an overall increase in PWID entering their initial SUD treatment. Within this group, females consistently have a higher prevalence than males for a history of IDU. As IDU increases risks for infection, overdose, and mortality, it is concerning that this gap persists. Utilizing a national dataset and focusing on PWID, we found that females reported initial use of their selfreported problematic substance later in life, however, were entering treatment after fewer years of use. This shortened window for therapeutic intervention calls for urgency to address structural barriers and policies that may make females more vulnerable. Increases in genderresponsive services and providing treatment in a trauma-informed way may increase willingness to seek treatment and allow for earlier interventions.

Data statement

Data used is publicly available from SAMHSA and can be found at htt ps://www.datafiles.samhsa.gov/dataset/treatment-episode-data-set-ad missions-2000-2020-teds-20002020-ds0001.

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CRediT authorship contribution statement

Nicholas L. Bormann: Writing – original draft, Writing – review & editing. Benjamin Miskle: Writing – review & editing. Paul Holdefer: Writing – review & editing. Stephan Arndt: Conceptualization, Formal analysis, Visualization, Writing – review & editing. Alison C. Lynch: Writing – review & editing. Andrea N. Weber: Writing – original draft, Writing – review & editing.

Declaration of Competing Interest

No conflict declared.

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