



Early Substance Use Trajectory as a Marker of Clinical Severity Among Treatment-Seeking Patients with Substance Use Disorders in Iran

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Abstract

Background: Age at first substance use is an established developmental marker; however, age at initiation alone may not capture how rapidly substance use progresses.

Objectives: This study examined age at first use, transition time to daily use, and age at daily use in relation to clinical severity among treatment-seeking patients with substance use disorders in Iran.

Methods: This analytical cross-sectional study used baseline data from 170 adults recruited by convenience sampling from selected outpatient addiction treatment clinics in Tehran. The primary trajectory indicators were age at first substance use, age at onset of daily substance use, and the interval between these events. Early onset of daily use (≤ 22 years) was used as a secondary categorical indicator corresponding to the first quartile of the sample distribution. Outcomes included dependence severity (Leeds Dependence Questionnaire [LDQ], Substance Dependence Severity Scale [SDSS]), general health (28-item General Health Questionnaire [GHQ-28]), cigarette consumption, dose-escalation steps, treatment history, and social and behavioral indicators. Multivariable linear models were fitted using HC3 heteroskedasticity-robust standard errors.

Results: The mean age at first use was 20.60 ± 3.75 years, and the mean age at initiation of daily use was 25.21 ± 4.42 years. In robust adjusted models, a shorter transition time was associated with higher LDQ ($B = -0.316$, $P = 0.006$), higher SDSS ($B = -0.332$, $P = 0.001$), and greater dose escalation ($B = -0.153$, $P < 0.001$). An earlier age at initiation of daily use was independently associated with higher LDQ and SDSS scores, heavier cigarette smoking, greater dose escalation, and more previous residential/camp admissions.

Conclusions: An earlier transition to daily substance use, particularly a younger age at initiation of daily use, was associated with a more severe clinical profile and greater social vulnerability. These history-based indicators may complement routine assessment and risk stratification.

Keywords: Age at First Substance Use, Daily Substance Use, Substance-related Disorders, Dependence Severity, Psychological Distress, Polysubstance Use, Treatment-seeking Patients, Iran

1. Background

Substance use disorders typically develop through a developmental course rather than as a single event,

beginning with initiation and, for some individuals, progressing to repeated, regular, or daily use and dependence. Age at first substance use is an established marker of later substance-related risk (1-3). More recent

evidence also links earlier substance-use onset with persistence and problematic patterns of use (4-6). However, age at first use alone collapses potentially heterogeneous post-initiation courses: two individuals may initiate at the same age yet differ substantially in how quickly use becomes frequent or daily (7,8).

Progression after initiation therefore warrants separate attention. Classic epidemiological studies showed that the probability and speed of transition from first use to dependence vary across substances and developmental periods (9-12). Contemporary longitudinal work distinguishing first use from regular-use onset similarly indicates that these are related but non-equivalent developmental milestones. Thus, the interval from first use to daily use and the age at which daily use begins may capture clinically relevant information not represented by initiation age alone (13-15).

The mechanisms underlying early and rapid progression are likely multifactorial. Developmental reviews emphasize interactions among neurodevelopment, externalizing and internalizing symptoms, family and peer environments, socioeconomic conditions, and substance exposure itself (16). Recent neurodevelopmental evidence also cautions against assuming that brain differences observed after adolescent substance initiation are solely caused by exposure, because some may reflect pre-existing vulnerability. Accordingly, trajectory indicators are better viewed as markers of accumulated vulnerability rather than as direct causal mechanisms (17).

Substance use disorders and their associated complications represent an important public health concern in Iran (18). Recent Iranian evidence continues to document substance use among adolescents and young people, including systematic reviews and nationwide data. These findings reinforce the importance of understanding not only whether use begins early but also how quickly it progresses to sustained use (19,20).

Despite a substantial international literature on early initiation and transition to dependence, most studies have involved general-population or adolescent samples, and many have focused on a single substance. Evidence is more limited in treatment-seeking adults with established substance use disorders, in whom current severity, psychiatric distress, tobacco use, treatment history, and social vulnerability are directly relevant to clinical decision-making.

2. Objectives

The specific research gap addressed in this study is the lack of Iranian clinical evidence simultaneously examining

age at first use, transition time to daily use, and age at daily use in relation to multiple current severity indicators. This distinction is clinically important because a brief history question about when use became daily may provide information beyond age at first experimentation and may help identify patients who warrant more comprehensive assessment. Accordingly, this study examined whether age at first substance use, transition time from first use to daily use, and age at daily substance use were associated with dependence severity, psychological distress, cigarette consumption, dose escalation, previous residential treatment, secondary substance use, and social or behavioral vulnerability among treatment-seeking adults in Tehran. We hypothesized that earlier daily use and shorter transition time would show more consistent associations with clinical severity than age at first use alone.

3. Methods

3.1. Study Design and Data Source

This analytical cross-sectional study used baseline data from a broader clinical assessment of patients entering addiction treatment. This secondary analysis addressed a distinct question concerning the timing of substance-use initiation and progression to daily use in relation to current clinical severity and social vulnerability.

Baseline data were collected from patients attending selected outpatient addiction treatment clinics in Tehran, Iran, before treatment initiation.

3.2. Target Population and Study Population

The target population comprised adults with substance use disorders seeking care in outpatient addiction treatment services. The analytic population consisted of 170 patients who attended the participating clinics in Tehran, completed the baseline assessment, and had complete information on age at first substance use and age at daily substance use. In this sample, the primary substance and reason for seeking treatment were mainly opioid-related; however, many individuals also engaged in heavy, problematic use of other substances, particularly methamphetamine, alcohol, or both.

3.3. Sample Size and Sampling Method

Participants were recruited using convenience sampling. Eligible patients presenting to the participating clinics during the study period were invited to participate if they were able and willing to complete the baseline assessment. This clinic-based nonprobability sampling strategy was practical for the parent study but does not

provide a representative sample of all people with substance use disorders in Tehran or Iran.

3.4. Eligibility Criteria

Patients were eligible if they were 18 years or older, were seeking treatment for a clinically identified substance use disorder, and could provide baseline information on their substance-use history and clinical status. Patients were excluded if acute intoxication, severe withdrawal, acute psychosis, severe cognitive impairment, severe medical instability, or inability to provide informed consent prevented valid assessment.

3.5. Main Exposure Variables: Substance-Use Trajectory Indicators

The primary exposures were continuous indicators of the temporal course of substance use. Age at first substance use was the participant-reported age at first use of any psychoactive substance. Age at daily substance use was the participant-reported age when substance use became daily or near-daily, according to the original baseline item. Transition time was calculated as age at daily use minus age at first use. These historical ages were obtained retrospectively and were not independently corroborated by family informants, treatment records, or biological measures in the secondary dataset.

For secondary descriptive and group-comparison analyses, cut points were selected empirically to identify approximately the earliest or fastest quartile of the sample, rather than to define validated clinical thresholds. Early first use was defined as first use at ≤ 18 years (sample 25th percentile), rapid transition as a transition interval of ≤ 3 years (25th percentile), and early daily use as daily use beginning at ≤ 22 years (25th percentile). A combined high-risk trajectory indicated both early first use and rapid transition. To assess the robustness of the principal early-daily-use comparison, sensitivity analyses repeated key group comparisons using neighboring cut points of ≤ 21 and ≤ 23 years.

3.6. Outcome Variables and Clinical Indicators

The main clinical outcomes were substance dependence severity, psychological distress, cigarette consumption, treatment-history burden, dose escalation, and selected social or behavioral vulnerability indicators.

Substance dependence severity was assessed using the 10-item Persian Leeds Dependence Questionnaire (LDQ), scored from 0 to 30, with higher scores indicating greater psychological dependence (21, 22). In the Persian validation study, criterion-related validity with the SDSS was $r = 0.773$, construct-related validity with the GHQ was $r = 0.780$, Cronbach's alpha was 0.809, and two-week test-retest

reliability was $r = 0.963$ (16, 22). Internal consistency in the present analytic sample was high (Cronbach's $\alpha = 0.887$). For this internal-consistency calculation, one participant with an out-of-range LDQ item entry was excluded; the stored LDQ total score used in the outcome analyses was unaffected.

A second measure of dependence severity was the Substance Dependence Severity Scale (SDSS), analyzed as a continuous total score. The original clinician-administered instrument demonstrated reliability and validity for substance dependence severity (23). The Persian version showed acceptable internal consistency (Cronbach's $\alpha = 0.77$) and high test-retest reliability ($r = 0.97$) in prior validation (24). In the present sample, Cronbach's α was 0.885.

Psychological distress was assessed using the 28-item General Health Questionnaire (GHQ-28), scored on a 0 - 3 Likert scale, with higher total scores indicating greater distress (25). Persian psychometric studies have supported the reliability, construct validity, and four-domain structure of the GHQ-28 (26, 27). Internal consistency of the total GHQ-28 in the present sample was excellent (Cronbach's $\alpha = 0.932$).

Daily cigarette consumption was recorded as cigarettes smoked per day. Treatment-history indicators included previous residential treatment/camp admissions and self-treatment attempts. Main and secondary substance categories were those recorded during the baseline clinical assessment. The secondary dataset did not retain information allowing us to determine whether these categories reflected patient self-report alone or clinician adjudication; therefore, they are described only as recorded baseline clinical categories. For analysis, opioid-primary status identified patients whose recorded main substance was an opioid, and secondary methamphetamine use indicated methamphetamine recorded as a secondary substance. Any secondary substance use was defined as any recorded secondary substance. These historical substance classifications were not independently verified by toxicology in the secondary dataset. Social and behavioral indicators included injecting as the main route, a history of criminal conviction, and unstable sleeping place.

3.7. Statistical Analysis

Data were analyzed using IBM SPSS Statistics version 26, with supplementary diagnostic and robustness checks reproduced for the revision. There were no missing values in the variables used in the primary trajectory analyses, group comparisons, or main regression models; therefore, these analyses included all 170 participants and no imputation was performed. Pearson correlations were used

to examine bivariate associations between trajectory indicators and continuous clinical outcomes.

For categorical comparisons, patients with early daily use (≤ 22 years) were compared with those whose daily use began after age 22. Continuous outcomes were compared using independent-samples tests, with Welch's correction applied when equality of variances was not supported. Mean differences with 95% confidence intervals and Cohen's d were reported. Categorical outcomes were examined using chi-square tests or Fisher's exact tests when cell counts were sparse, and odds ratios with 95% confidence intervals were reported. Sensitivity analyses repeated the principal early-daily-use comparisons using ≤ 21 and ≤ 23 years as alternative cut points.

Multivariable linear regression models evaluated whether trajectory indicators were associated with LDQ, SDSS, GHQ, dose-escalation steps, and previous residential (camp) admissions after adjustment for covariates selected a priori on clinical grounds: current age, sex, education, opioid as the main substance, methamphetamine as a secondary substance, and cigarette consumption when appropriate. In the first model set, age at first use and transition time were entered simultaneously. Regression assumptions were examined using residual plots, residual-distribution checks, the Breusch-Pagan test, and variance inflation factors (VIFs). Because heteroskedasticity was detected in several models and some residual distributions showed mild departures from normality, all regression inferences were recalculated using HC3 heteroskedasticity-robust standard errors. The maximum predictor VIF was 1.93, providing no evidence of problematic multicollinearity.

A second model set used age at daily substance use as the trajectory indicator because it jointly reflects initiation timing and progression to sustained use. Model R^2 and adjusted R^2 were reported for every outcome. To explore confounding by main substance type, the main models were repeated in the opioid-primary subgroup ($n = 143$) as a sensitivity analysis. Sex-stratified models were not considered reliable because only 13 participants were women. All tests were two-sided, and $P < 0.05$ was considered statistically significant; secondary and sensitivity analyses were interpreted cautiously because of multiple testing.

3.8. Sample-Size Rationale

The largest multivariable model included eight predictors. With $n = 170$, there were approximately 21 observations per predictor, exceeding the 10 - 15 observations-per-predictor heuristic (28) and Green's thresholds for multiple regression ($N \geq 50 + 8m$ for the

overall multiple correlation and $N \geq 104 + m$ for individual predictors; with $m = 8, 114$ and 112 , respectively) (29). Nevertheless, such heuristics do not replace a formal power analysis, and potential overfitting was considered when interpreting secondary models and sparse subgroups (28).

3.9. Ethical Considerations

The original study protocol was reviewed and approved by the Ethics Committee of the University of Social Welfare and Rehabilitation Sciences (IR.USWR.REC.1395.329). Participants received an explanation of the study objectives, voluntary participation, confidentiality, and their right to withdraw. All participants provided written informed consent before assessment. The dataset used for the present secondary analysis was de-identified, and results are reported only at the group level.

4. Results

4.1. Substance-Use Trajectory Variables

Participants were predominantly male (157/170, 92.4%). Opioids were the recorded primary substance for 143 participants (84.1%), methamphetamine for 15 (8.8%), and alcohol for 12 (7.1%). The mean age at first substance use, the mean age at daily use, and the mean transition time are shown in Table 1. Using the study-specific quartile thresholds, 55 participants had early first use, 76 had rapid transition, 46 had early daily use, and 25 met the combined high-risk trajectory definition (Table 1).

4.2. Correlations Between Substance-Use Trajectory and Clinical Severity

In bivariate analyses, a younger age at first use and a younger age at daily use were associated with higher dependence severity, greater psychological distress, heavier cigarette smoking, more previous residential/camp admissions, and more dose-escalation steps. Age at daily use showed the strongest and most consistent correlations across outcomes. A shorter transition time was associated with higher LDQ and SDSS scores and more dose-escalation steps, whereas its correlation with GHQ was weaker and not statistically significant (Table 2).

4.3. Clinical Profile of Patients with Early Daily Use

Participants whose daily substance use began at age 22 years or younger had higher LDQ, SDSS, and GHQ scores, smoked more cigarettes per day, and reported more dose-escalation steps than those whose daily use began later. Mean differences were 2.95 points for LDQ, 3.52 for SDSS,

Table 1. Descriptive Characteristics of Substance-Use Trajectory Variables ^a

Variables	Definition	Values
Age at first substance use	Continuous variable	20.60 ± 3.75
Age at daily substance use	Continuous variable	25.21 ± 4.42
Transition time to daily use	Age at daily use - age at first use	4.61 ± 2.88
Early first use	First use ≤ 18 years (sample 25th percentile)	55 (32.4)
Rapid transition	Transition interval ≤ 3 years (sample 25th percentile)	76 (44.7)
Early daily use	Daily use ≤ 22 years (sample 25th percentile)	46 (27.1)
High-risk trajectory	Early first use and rapid transition	25 (14.7)

^a Values are expressed as mean ± SD or No. (%). Categorical thresholds are study-specific first-quartile cut points and are not validated clinical thresholds.

Table 2. Correlations Between Substance-Use Trajectory Indicators and Clinical Severity Outcomes ^a

Trajectory Variable	LDQ Total	SDSS Total	GHQ Total	Cigarettes/Day	Previous Camp Admissions	Dose-Escalation Steps
Age at first use	-0.327 ^b	-0.304 ^b	-0.303 ^b	-0.286 ^b	-0.223 ^c	-0.175 ^d
Age at daily use	-0.424 ^b	-0.380 ^b	-0.347 ^b	-0.297 ^b	-0.210 ^c	-0.395 ^b
Transition time to daily use	-0.225 ^c	-0.187 ^d	-0.138	-0.084	-0.032	-0.377 ^b

^a Values are Pearson correlation coefficients. Abbreviations: LDQ, Leeds Dependence Questionnaire; SDSS, Substance Dependence Severity Scale; GHQ, General Health Questionnaire.

^b $P < 0.001$.

^c $P < 0.01$.

^d $P < 0.05$.

5.93 for GHQ, 5.19 cigarettes/day, and 0.88 dose-escalation steps. Differences in previous residential/camp admissions and self-treatment attempts did not reach statistical significance (Table 3).

Early daily use was also associated with greater social and behavioral vulnerability. Secondary methamphetamine use, any secondary substance use, criminal conviction, an unstable sleeping place, and injecting as the main route were more frequent in the early-daily-use group. Opioid-primary status was also more common (93.5% vs 80.6%), but this comparison did not reach statistical significance using Fisher's exact test ($P = 0.057$) (Table 4). Using ≤ 22 years—the sample's first-quartile threshold—as the primary cutoff, sensitivity analyses were conducted using the neighboring cutoffs of ≤ 21 and ≤ 23 years. These analyses showed the same direction of association for LDQ, SDSS, GHQ, cigarettes/day, and dose escalation; for these five outcomes, all alternative-cutoff comparisons remained statistically significant (all $P \leq 0.001$), with Cohen's d values ranging from 0.66 to 0.81 for the ≤ 21-year cutoff and from 0.70 to 0.89 for the ≤ 23-year cutoff.

4.4. Multivariable Regression Analyses

After regression assumptions were examined, all multivariable models were re-estimated using HC3 robust standard errors. In models containing both age at first use and transition time, a shorter transition time remained independently associated with higher LDQ, higher SDSS, and more dose-escalation steps. Age at first use was not independently associated with LDQ, SDSS, GHQ, or dose escalation after robust adjustment; however, a younger age at first use was associated with more previous residential/camp admissions. Model R^2 values ranged from 0.414 to 0.553 (Table 5).

In the second model set, a younger age at daily use was independently associated with higher LDQ, higher SDSS, heavier cigarette smoking, more dose-escalation steps, and more previous residential/camp admissions. The adjusted association with GHQ was in the expected direction but did not reach conventional statistical significance. Model R^2 values ranged from 0.283 to 0.549 (Table 6).

Sensitivity analyses restricted to opioid-primary participants ($n = 143$) showed the same general direction of associations, although estimates were attenuated and

Table 3. Comparison of Patients with Early Versus Later Transition to Daily Substance Use ^a

Variables	Daily Use > 22 (y)	Daily Use ≤ 22 (y)	Mean Difference	P Value	Cohen's d
LDQ total	21.98 ± 4.77	24.93 ± 4.24	2.95 (1.45 to 4.46)	< 0.001	0.64
SDSS total	31.74 ± 4.31	35.26 ± 5.32	3.52 (1.77 to 5.26)	< 0.001	0.77
GHQ total	59.79 ± 9.82	65.72 ± 11.22	5.93 (2.19 to 9.66)	0.002	0.58
Cigarettes/day	14.35 ± 8.39	19.54 ± 9.44	5.19 (2.03 to 8.34)	0.002	0.60
Previous residential/camp admissions	0.94 ± 1.19	1.33 ± 1.40	0.38 (-0.08 to 0.85)	0.104	0.31
Self-treatment attempts	1.59 ± 1.82	2.22 ± 2.16	0.63 (-0.08 to 1.34)	0.083	0.33
Dose-escalation steps	3.23 ± 1.11	4.11 ± 1.37	0.88 (0.43 to 1.33)	< 0.001	0.74

^a Values are expressed as mean ± SD or 95% CI.

Table 4. Social and Behavioral Indicators by Early Daily Use Status ^a

Variables	Daily use > 22 (y)	Daily use ≤ 22 (y)	P Value	OR (95% CI)
Methamphetamine as secondary substance	22.6	47.8	0.001	3.14 (1.54 - 6.43)
Any secondary substance use	47.6	67.4	0.022	2.28 (1.12 - 4.63)
History of criminal conviction	33.9	60.9	0.001	3.04 (1.51 - 6.11)
Unstable sleeping place	12.1	37.0	< 0.001	4.26 (1.90 - 9.54)
Injecting as main route	4.8	17.4	0.023 ^b	4.14 (1.35 - 12.69)
Opioid as main substance	80.6	93.5	0.057 ^b	3.44 (0.98 - 12.03)

^a Values are expressed as percentage unless otherwise indicated.

^b Fisher exact test was used because of sparse cells.

Table 5. Multivariable Regression Models Including Age at First Use and Transition Time (HC3 Robust Standard Errors) ^a

Outcomes and Predictor	B (robust SE)	95% CI	P Value	R ² (Adj R ²)
LDQ total				
Age at first use	-0.182 (0.107)	-0.392 to 0.028	0.090	0.553 (0.531)
Transition time	-0.316 (0.114)	-0.539 to -0.092	0.006	0.553 (0.531)
SDSS total				
Age at first use	-0.221 (0.121)	-0.459 to 0.017	0.068	0.489 (0.464)
Transition time	-0.332 (0.100)	-0.528 to -0.136	0.001	0.489 (0.464)
GHQ total				
Age at first use	-0.433 (0.254)	-0.931 to 0.066	0.089	0.465 (0.438)
Transition time	-0.371 (0.264)	-0.888 to 0.146	0.160	0.465 (0.438)
Dose-escalation steps				
Age at first use	-0.034 (0.025)	-0.082 to 0.015	0.176	0.414 (0.385)
Transition time	-0.153 (0.038)	-0.227 to -0.079	< 0.001	0.414 (0.385)
Previous residential/camp admissions				
Age at first use	-0.057 (0.022)	-0.100 to -0.013	0.010	0.468 (0.442)
Transition time	-0.041 (0.029)	-0.097 to 0.016	0.159	0.468 (0.442)

^a Models were adjusted for current age, sex, education, opioid-primary status, secondary methamphetamine use, and cigarettes/day when appropriate.

several P values crossed the conventional significance threshold because of the smaller sample size. In this subgroup, age at daily use remained associated with LDQ

(P = 0.048), SDSS (P = 0.035), cigarette consumption (P < 0.001), and dose escalation (P = 0.034); its association with previous residential/camp admissions was borderline (P =

Table 6. Multivariable Models Using Age at Daily Use as the Main Trajectory Indicator (HC3 Robust Standard Errors)

Outcome	Predictor	B (robust SE)	95% CI	P value	R ² (Adj R ²)
LDQ total	Age at daily use	-0.230 (0.083)	-0.393 to -0.067	0.006	0.549 (0.529)
SDSS total	Age at daily use	-0.261 (0.091)	-0.440 to -0.082	0.004	0.487 (0.464)
GHQ total	Age at daily use	-0.411 (0.218)	-0.838 to 0.017	0.060	0.465 (0.442)
Cigarettes/day	Age at daily use	-0.684 (0.171)	-1.020 to -0.349	< 0.001	0.283 (0.256)
Dose-escalation steps	Age at daily use	-0.076 (0.025)	-0.125 to -0.028	0.002	0.363 (0.336)
Previous residential/camp admissions	Age at daily use	-0.051 (0.020)	-0.090 to -0.012	0.010	0.467 (0.444)

0.053), whereas the association with GHQ was not statistically significant ($P = 0.280$). Taken together, these findings indicate that transition time and age at daily use were more consistent severity markers than age at first use alone, while also suggesting that effect estimates depend partly on sample composition and outcome definition.

5. Discussion

The main finding was that the timing of progression to daily substance use was more consistently associated with current clinical severity than age at first use alone. In robust adjusted models, a shorter transition time was associated with higher LDQ and SDSS scores and greater dose escalation, whereas a younger age at daily use was associated with higher dependence severity, heavier cigarette smoking, greater dose escalation, and more previous residential/camp admissions. By contrast, age at first use did not independently explain LDQ, SDSS, or GHQ after HC3-robust adjustment. This pattern supports the clinical value of distinguishing initiation from subsequent progression.

These findings are broadly consistent with international evidence showing that earlier substance-use onset is associated with more persistent or problematic use (1, 3, 30-33). They also extend prior work showing that the speed of progression from first use to dependence varies across substances and developmental periods (6, 34). Recent longitudinal research that separately models first drinking initiation and regular drinking onset further supports treating these milestones as distinct developmental events rather than interchangeable measures (35, 36). Our adult treatment-seeking data suggest that the age at which use becomes daily may remain clinically informative years after initiation.

Several mechanisms could underlie these associations, but the cross-sectional data cannot distinguish among them. Early and rapid progression may reflect neurodevelopmental vulnerability, externalizing or internalizing symptoms, family or peer exposure, social disadvantage, greater drug availability, or combinations of

these factors (16, 17, 37, 38). Repeated exposure may also contribute to neuroadaptation, but recent neurodevelopmental work emphasizes that pre-existing differences can precede substance initiation and should not automatically be interpreted as consequences of use (17, 37, 39). The trajectory variables in this study should therefore be viewed as markers of accumulated vulnerability, not evidence of a causal pathway from early daily use to later severity.

The psychological-distress findings should be interpreted with greater caution. Early daily use was associated with higher GHQ scores in the unadjusted group comparison, but the adjusted association between age at daily use and GHQ did not reach conventional significance when robust standard errors were used. Psychological distress may therefore overlap with demographic, substance-use, and smoking-related factors in this clinical population. The result still supports routine mental-health assessment, but it does not establish that early daily use independently causes later psychological distress (40-42).

Early daily use was also associated with secondary methamphetamine use, polysubstance use, criminal conviction, an unstable sleeping place, and injecting. These findings align with a broader risk-clustering interpretation rather than a simple gateway model (43-48). They are particularly relevant in Iran, where opioid use remains central to treatment demand but stimulant co-use and youth substance use are important contemporary concerns (18, 49). Recent nationwide and systematic review evidence demonstrates that substance use among Iranian young people remains heterogeneous across substances and settings (19, 20), underscoring the importance of identifying developmental markers that may signal a more complex adult treatment profile.

These findings have a practical implication for intake assessment. In addition to documenting current substance use and treatment history, clinicians could ask at what age the patient first used the primary substance and at what age use of that same substance became daily. The difference between these recalled ages provides an

approximate interval from first to daily use. Earlier onset of daily use may prompt a closer assessment of dependence severity, stimulant and tobacco use, psychological symptoms, injection history, housing instability, and legal or social difficulties. A shorter transition interval may also warrant examination, but its clinical value requires further evaluation. Neither measure should be used as a diagnostic threshold or as an independent basis for determining treatment intensity.

This study has several strengths, including the simultaneous examination of three trajectory indicators, the use of validated Persian measures, adjustment for clinically relevant covariates, effect-size and confidence-interval reporting, regression-diagnostic checks, HC3 robust inference, alternative-cutoff sensitivity analyses, and an opioid-primary sensitivity analysis. Important limitations remain. The cross-sectional design precludes causal or prognostic inference. Ages at first and daily use were recalled retrospectively and were not corroborated by records or informants, creating potential recall error. Convenience sampling from outpatient clinics in Tehran may have selected patients who were more able or willing to seek treatment and limits generalizability to community populations, other regions, women, and non-opioid-primary groups. Main and secondary substance classifications were based on categories recorded during the baseline clinical assessment; the secondary dataset did not preserve whether classification reflected patient self-report alone or clinician adjudication, and historical classifications were not independently verified by toxicology. The categorical thresholds were sample-derived quartiles rather than externally validated clinical cut points. Although the largest regression model had approximately 21 observations per predictor and low VIFs, the moderate sample size, only 13 women, multiple outcomes, and several secondary models still create a risk of overfitting and unstable subgroup estimates. Finally, some outcomes were count-like and were analyzed with linear models; robust standard errors reduce sensitivity to heteroskedasticity but do not eliminate all modeling limitations.

Future research should prospectively record the timing and frequency of substance use, verify historical information where feasible, and test whether age at daily use and transition time predict treatment retention, relapse, overdose, psychiatric outcomes, and recovery. Larger multisite Iranian studies should recruit more women and participants with primary stimulant, cannabis, and alcohol disorders and should externally evaluate whether the present quartile-based thresholds generalize. International replication in treatment-seeking populations would also clarify whether the clinical

relevance of daily-use onset extends across different drug markets and treatment systems.

Overall, these findings support a distinction between when substance use begins and when it becomes sustained. In this treatment-seeking sample, transition time and age at daily use were more consistently associated with current severity than age at first use alone. Their value is therefore best understood as a low-burden addition to clinical history-taking and risk formulation, pending prospective validation.

5.1. Conclusions

Earlier progression to daily substance use was associated with greater clinical severity among treatment-seeking adults with substance use disorders in Tehran. After robust multivariable adjustment, shorter transition time and younger age at daily use showed more consistent associations with dependence severity and related clinical indicators than age at first use alone. These associations do not establish causation, and the study-specific cutoffs should not be interpreted as validated diagnostic thresholds.

Routine assessment of age at first use and age when use became daily or near-daily may nevertheless add a simple developmental dimension to clinical risk formulation. Patients with early or rapid progression may warrant closer assessment of dependence severity, polysubstance use, tobacco use, mental-health symptoms, injecting risk, and social instability. Prospective multisite studies are needed to determine whether these trajectory indicators predict future treatment and recovery outcomes.

Footnotes

AI Use Disclosure: The authors declare that no generative AI tools were used in the creation of this article.

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