

Family History Density of Substance Use: Influence on Participant Substance Use Onset and Duration

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Background

- Substance use disorders (SUDs) devastate both individuals and families and are major public health challenges.
- In 2022, 1/6 Americans aged 12+ had a past-year SUD.¹
- 1/3 American adults experience a SUD in their lifetime.²
- SUDs contribute to an annual economic burden exceeding \$400 billion.³
- Family history (FH) is a key predictor of SUDs, with individuals with relatives who have experienced addiction being 2-8 times more likely to develop the disorder.^{4,5}
- Most research focuses on immediate family and male participants, often neglecting broader familial patterns, social influences, and comorbid conditions.

Introduction

We address previous shortcomings by examining how the cumulative impact of family history, quantified as **weighted family history density (WFHD)**, influences:

- Primary outcomes:** Age at first use and duration of use.
 - Secondary outcomes:** Substance use escalation, familial substance preference concordance, and sex-stratified inheritance patterns.
- Objective:** To determine how WFHD influences the trajectory of substance use—encompassing onset, duration, and escalation—while uncovering sex-specific inheritance patterns and substance preference concordance between affected family members and participants. By addressing key familial influences, this research aims to inform strategies that mitigate the profound and lasting effects of SUDs on both individuals and families.

Figure 1: Equation for Total Weighted Family History Density (WFHD)

$$\text{TOTAL WFHD} = (\sum 1^{\text{ST}} \text{DEGREE RELATIVES WITH SUP} \times 0.5) + (\sum 2^{\text{ND}} \text{DEGREE RELATIVES WITH SUP} \times 0.25)$$

SUP = Substance Use Problems (Including both Drug and Alcohol Use Problems)
 1st degree relatives = Biological parents and siblings
 2nd degree relatives = Biological grandparents, aunts, and uncles
 Values range from 0 to 18.25

Methods

Study Design: Cross-sectional analysis using NESARC-III cohort data (2012-2013)

Participants: A nationally representative random sample of 36,309 U.S. noninstitutionalized civilians aged 18+

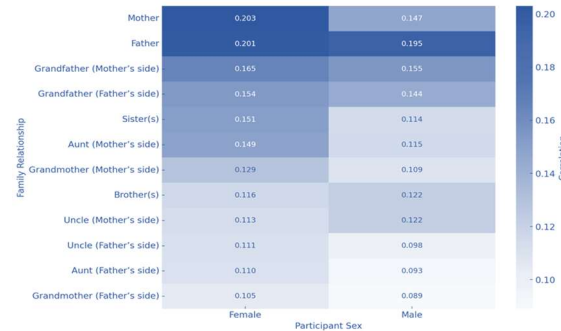
WFHD Calculation: Based on substance use problems (SUPs) in first- and second-degree relatives (Fig. 1).

- Descriptive Analysis:** Chi-Square and ANOVA tests to compare WFHD groups.
- Regression Analysis:** Linear regression models (unadjusted and adjusted) examined relationships between WFHD, age at onset, and duration of substance use. Logistic regression analyzed whether WFHD of drug or alcohol use problems predicted substance preference in participants.
- Correlation Analysis:** Correlations between family members' SUP and participants' SUD types
- Sex Differences:** Participant SUDs were stratified by sex to explore male vs female familial transmission patterns.

Tables 1 & 2: Impact of WFHD on Age at Onset and Duration of Use

Table 1. Effect of WFHD on Substance Use Onset and Duration: Unadjusted and Adjusted Models				Table 2. Effect of WFHD on Substance Use Onset and Duration: Odds Ratios and Model Fit Statistics				
Variable	Unadjusted Models ^{a,4,7}		Adjusted Models ^{a,4,8}		Outcome	Model	OR (95% CI)	R ²
	β (SE)	[95% CI]	β (SE)	[95% CI]				
All SUP on Age at Onset					Age at Onset: Before Age 18	Unadjusted ^b	1.22 (1.18-1.26)**	0.02
WFHD - All SUP	-0.54 (0.02)	[0.50, -0.59]****	-0.53 (0.02)	[-0.57, -0.49]****	Age at Onset: Before Age 18	Adjusted ^b	1.26 (1.22-1.30)**	0.07
DUP on Age at Onset					Duration: > % of Current Age	Unadjusted ^b	1.18 (1.15-1.21)**	0.27
WFHD - DUP	-0.68 (0.04)	[0.75, -0.61]****	-0.61 (0.04)	[-0.68, -0.54]****	Duration: > % of Current Age	Adjusted ^b	1.21 (1.18-1.23)**	0.30
AUP on Age at Onset					Duration: > 5 years	Unadjusted ^b	1.22 (1.18-1.26)**	0.27
WFHD - AUP	-0.82 (0.03)	[0.89, -0.76]****	-0.84 (0.03)	[-0.91, -0.78]****	Duration: > 5 years	Adjusted ^b	1.26 (1.22-1.30)**	0.30
All SUP on Duration					Duration: > 10 years	Unadjusted ^b	1.18 (1.15-1.21)**	0.39
WFHD - All SUP	0.48 (0.03)	[0.42, 0.54]****	0.55 (0.03)	[0.48, 0.61]****	Duration: > 10 years	Adjusted ^b	1.21 (1.18-1.23)**	0.41
DUP on Duration								
WFHD - DUP	0.52 (0.05)	[0.42, 0.63]****	0.59 (0.05)	[0.49, 0.70]****				
AUP on Duration								
WFHD - AUP	0.79 (0.05)	[0.69, 0.89]****	0.90 (0.05)	[0.80, 1.00]****				

Figure 2: Correlations Between Substance Preferences in Family Members and Male vs. Female Participants



Results

Age at Onset: Each unit increase in WFHD was associated with a 0.53-year earlier onset [$\beta = -0.53$, SE = 0.02] (Table 1).

Duration: Each unit increase in WFHD was associated with a 0.55-year longer duration ($\beta = 0.55$, SE = 0.03) of use (Table 1). WFHD significantly predicted use before age 18 and duration over half one's age, 5 years, and 10 years (Table 2).

Escalation: Kaplan-Meier analysis shows higher WFHD leads to faster escalation to peak alcohol use (Fig. 3).

Substance Preference: Significant concordance in substance preference (drugs vs. alcohol) between family and participants (Table 3).

Sex Differences in Inheritance Patterns: Males correlated most with paternal use, while females showed similar correlations with both parents, with a slightly stronger influence of maternal use (Fig. 2).

Figure 3: Kaplan-Meier Probability of Peak Alcohol Use by WFHD

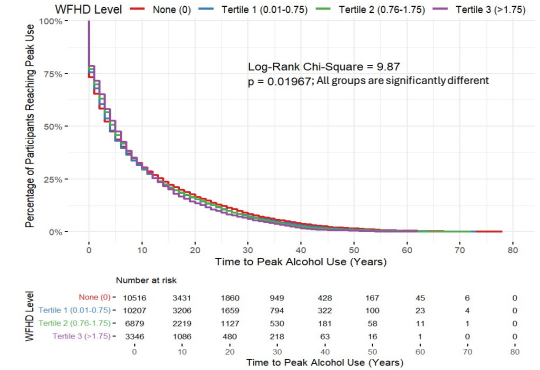


Table 3: Association Between Specific WFHD of Substance Use Problems and Corresponding Participant Outcomes

WFHD Predictor	Participant SUD Outcome	Odds Ratio (95% CI)	Std. Error	p Value
AUP	AUD	1.568 (1.530, 1.607)	0.013	< .001***
DUP	AUD	1.395 (1.360, 1.430)	0.013	< .001***
DUP	DUD	1.418 (1.383, 1.455)	0.013	< .001***
AUP	DUD	1.564 (1.526, 1.603)	0.013	< .001***

Note: CI = Confidence Interval; FHD = Family History Density; AUD = Alcohol Use Disorder; DUD = Drug Use Disorder; AUP = Alcohol Use Problem; DUP = Drug Use Problem. Significance codes: *** p < .001. Estimates are based on logistic regression models, with each unit increase in FHD reflecting changes in the odds of developing the specified SUD.

Conclusion

- Higher WFHD is linked to earlier initiation, longer duration, and a faster progression to peak substance use, even after accounting for confounding factors.
- WFHD of alcohol use problems increased risk for both alcohol and drug use disorders (AUDs, DUDs), with a slightly higher risk for AUDs. Drug-related WFHD had stronger links to DUDs.
- Sex differences:**
 - Males: Stronger correlations with paternal use.
 - Females: Stronger correlations with maternal use.
- Conclusion:** Incorporating family history is vital for prevention/intervention.
- Future research:** Longitudinal studies should explore causal mechanisms and other risk factor interactions.

References

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