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## Drug Use and Dependence in Cocaine Dependent Subjects, Community-Based Individuals, and Their Siblings

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### Abstract

**Background**—The purpose of this study was to examine substance use and dependence among cocaine dependent subjects and their siblings compared to individuals recruited from the same neighborhood and their siblings in order to better understand family and neighborhood contributions to the development of dependence.

**Methods**—Cocaine dependent subjects were recruited through treatment centers. Community-based subjects were matched to cocaine dependent index cases on age, ethnicity, gender, and zip code. One full sibling for each case and community-based subject participated.

**Results**—Cocaine dependent subjects were significantly more likely than community-based subjects to use all substances studied and were 2 to 10 times more likely to be dependent on alcohol and other illicit drugs. Dependence only on cocaine was uncommon (<10%). The siblings of cocaine dependent subjects had higher rates of substance use and were 1.3 to 3 times more likely to have a diagnosis of substance dependence compared siblings of community-based subjects. However, when analyses focused only on those who ever used a specific substance, the siblings of cocaine dependent cases were at a similar or modestly elevated risk (1.5 times) of developing dependence.

**Conclusions**—Cocaine dependence is characterized by polysubstance use and dependence. In addition, the prevalence of substance dependence in the community subjects was higher than reported for the general population, indicating that cocaine dependent cases live in high-risk communities with elevated prevalence of substance dependence. A potential intervention to decrease the family clustering of dependence is to reduce the initiation of drug use in at risk relatives.

## 1. Introduction

### 1.1 Familial contributions to use and dependence

Multiple factors contribute to the development of substance dependence, including genetic and environmental characteristics, and one of the most important risk factors is a family history of dependence. Numerous studies of alcohol, opiate, and polysubstance dependence have assessed the clustering of dependence in families. Consistently, relatives of alcohol and drug dependent individuals are more likely to develop substance use disorders than relatives of non-dependent subjects (Bierut et al., 1998; Merikangas et al., 1998; Nurnberger et al., 2004; Rhee et al., 2003). Similarly, twin and adoption studies demonstrate that a vulnerability to

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dependence on multiple substances is transmitted between biologic relatives and is related to genetic factors (Kendler et al., 2003; Tsuang et al., 1998).

In addition to family and genetic factors that contribute to dependence, epidemiological studies have identified numerous personal characteristics that are associated with alcohol, nicotine, and drug dependence. In general, lower educational attainment and decreased income are seen in individuals with substance dependence (Stinson et al., 2005). Community factors are also important and a clustering of drug use and dependence is seen in neighborhoods (Hawkins et al., 2002). Substance dependence is thus a complex disorder that includes important contributions of biologic background (such as genetic predispositions), individual environmental risk factors (educational attainment and income), and community-based exposures. The division of these characteristics into “genetic” and “environmental” factors is at times arbitrary because both genes and environment can contribute to a specific trait such as school success and socioeconomic status.

## 1.2 Development of dependence – A transition of use to dependence

In the study of factors that contribute to the development of substance dependence, it is also important to remember that dependence on alcohol, nicotine, and other drugs is a multi-step sequence that begins with access to a substance, initial use, and then the transition to dependence. The most commonly used substances (i.e., alcohol and nicotine) are essentially obtainable by everyone. Most of the U.S. population has used alcohol and many have tried smoking (Substance Abuse and Mental Health Services Administration, 2006). Thus, differences in the population prevalence and prevalence among users are minimal. However, this is not the case in the study of illicit drug dependence. Illicit drugs have restricted availability, and access has changed over time and across communities. Yet, most epidemiologic, family, and twin studies of substance misuse present the prevalence rates of dependence within the total population rather than among the population of people who have used the substance (Hasin et al., 2005; Kendler et al., 2003; Stinson et al., 2005).

Though the overall prevalence of drug dependence is important in determining the impact of drug use disorders and treatment needs in a population, these rates can be misleading when studying of the etiology of the development of dependence. For example, in the National Comorbidity Survey (NCS), 4.4% of the sample met DSM-III-R criteria for marijuana dependence whereas only 2.7% were cocaine dependent (Wagner and Anthony, 2002). Thus, one may argue that marijuana dependence is a more severe problem than cocaine dependence because it affects a greater percentage of the population. These numbers, however, do not reflect the proportion of users who become dependent. The picture is much different when the prevalence of dependence among only individuals who have used the specific substance is examined. In the NCS sample, the prevalence of marijuana dependence among users (8.9%) is much lower compared the prevalence of cocaine dependence among users (16.5%) (Wagner and Anthony, 2002). Focusing the analysis on subjects who have used the substance reveals that cocaine dependence may be viewed as a more addictive drug and a more severe problem among users because a greater number of cocaine users than marijuana users progress to dependence.

Both overall prevalence and prevalence conditional upon use are helpful and relevant measures. The purpose in assessing the prevalence of dependence in users, which this paper defines as “conditional dependence,” is to better understand potential differences in the familial risk of developing dependence that are not related to use. For example, if men have higher rates of drug dependence than women, is this because men are more likely to develop dependence or because more men use drugs than women do? It is important to make this distinction when trying to understand the development of dependence, especially in the study of genetic and environmental factors that contribute to dependence. In addition, it allows a better planning of

prevention and treatment strategies that can be tailored to populations at risk, and perhaps even tailored for specific drugs. In the NCS sample described above, it appears that cocaine is more addictive than marijuana because proportionately more users progressed to dependence. Other studies also suggest that cocaine may be the most addictive substance among the common drugs (i.e., alcohol, marijuana, opiates) (Ridenour et al., 2003; Ridenour et al., 2005). Thus, an increase of cocaine use in the population will lead to a greater change in drug dependent individuals than will an increase in marijuana use, and may be a more severe public health problem.

### 1.3 Purpose

The purpose of this study is to examine the rates of substance use, dependence, and conditional dependence in a cocaine dependent treatment population and their siblings, and in a matched community-based group and their siblings. This is a unique study design that allows the examination of both genetic risks and shared family environment through the sibling design. The community-based subjects are matched to cases on age, gender, and zip code, which are important components that allow a “matching” of the many unmeasured community characteristics that influence the development of alcohol, nicotine, and drug dependence. With this design, an improved understanding of the genetic and environmental risks related to dependence can be determined. Importantly, this is the first family study to focus on cocaine dependence. The research questions addressed are:

1. What are the rates of other substance use and dependence in cocaine dependent subjects and how do they compare with individuals recruited from their neighborhoods? The comparison between cocaine dependent cases and community-based subjects provides a better control of underlying community based factors that may contribute to the development of other substance use and dependence, and it allows a more precise estimation of other substance use and dependence that is associated with cocaine dependence.
2. Do the rates of substance use and dependence differ for siblings of cocaine dependent individuals compared to siblings of community-based individuals? This analysis of siblings of cocaine dependent cases and community-based comparison subjects provides an analysis of the clustering of substance use and dependence that is related to family members of a cocaine dependent person as opposed to general community characteristics that contribute to substance use and dependence.
3. If there are differences in the lifetime prevalence of dependence, is it primarily a function of different rates of drug use? This study of conditional dependence can help dissect if differences of the development of substance dependence are based on increased drug experimentation or to higher vulnerability to the development of dependence once a substance has been used.

## 2. Methods

### 2.1 Sample

Data presented are from the Family Study of Cocaine Dependence, a project designed to assess neighborhood and family factors associated with cocaine dependence. This study was reviewed by the Washington University IRB, and all subjects provided informed consent.

Cocaine dependent subjects were recruited from publicly and privately funded inpatient and outpatient chemical dependency treatment centers in the St. Louis region. Eligibility requirements included DSM-IV cocaine dependence, being at least 18 years of age, speaking fluent English, and having a full sibling within five years of their age who was willing to participate. Of the eligible cocaine dependent subjects, 55.1% participated. Non-participation

for cocaine dependent subjects was most often due to inability to locate a subject or sibling after initial contact (57.2%), siblings being unable to or unwilling participate (26.4%), subject refusal (5.9%) and other miscellaneous reasons (10.6%). Eligible individuals provided contact information for their siblings who were sent letters describing the study and then called and screened for eligibility. Siblings were eligible if they were at least 18 years old, spoke fluent English, and had the same biological parents as the cocaine dependent proband. Of the seven hundred eligible siblings, 541 (77.3%) participated, 100 (14.3%) refused, 48 (6.8%) were disqualified due to inappropriate behavior, the proband refusing to participate, or repeatedly missing appointments, and 11 (1.6%) could not be contacted after initial agreement to participate.

Community-based comparison subjects were recruited through driver's license records from the Missouri Family Registry maintained by Washington University in St. Louis for research purposes. Community-based comparison participants were matched to cocaine dependent subjects based on date of birth (within 1 year), ethnicity, gender, and zip code. Eighty percent of screened and eligible individuals participated. The reasons for refusal were not systematically recorded. As with the cocaine dependent subjects, the community-based individuals were required to have a full sibling within five years of their age who was willing to participate. Substance dependence and other psychiatric disorders were not exclusionary criteria for community subjects. Siblings of community probands were recruited in the same manner as siblings of cocaine dependent subjects.

Community-based subjects were matched for 96.5% of cocaine dependent cases and at least one sibling was interviewed for 97.7% of the enrolled probands. The current analyses included only paired cocaine dependent cases and community subjects with their siblings. The total sample included 1836 subjects: 459 cocaine dependent subjects (cases), 459 community-based comparison subjects, 459 siblings of cocaine dependent cases (case siblings) and 459 siblings of community-based subjects (community siblings).

## 2.2 Assessment

All participants completed an interview modeled after the Semi-Structured Assessment for the Genetics of Alcoholism (SSAGA), an evaluation designed to query alcohol and other substance dependence (Bucholz et al., 1994). Additional questions were added to comprehensively assess cocaine dependence. The SSAGA has shown good reliability in evaluating substance abuse and dependence and other psychiatric disorders (Bucholz et al., 1994; Hesselbrock et al., 1999). Interview data were checked for consistency by a senior editor and entered into a computerized data file. The lifetime diagnosis for cocaine dependence was made using a computer algorithm following the DSM-IV criteria (American Psychiatric Association, 2000). Lifetime history of substance dependence was measured for ten additional categories of drugs: nicotine, alcohol, cocaine, marijuana, stimulants, opiates, sedatives, hallucinogens, PCP, and other drugs ("other" includes solvents, combinations, and any other miscellaneous drugs).

## 2.3 Analysis

The purpose of these analyses was to compare the prevalence of substance use and dependence in cocaine dependent cases versus community-based subjects and in case siblings versus community siblings. Subjects were categorized into mutually exclusive categories for marital status, employment, and income. For education, we assessed the proportion of subjects who received a GED, high school diploma, and college degree. Thus, it is possible that a subject is accounted for in both the high school and college categories. All prevalence analyses were conducted separately for males and females because of the known gender differences in rates of alcohol and other drug dependence (Compton et al., 2005; Grant, 1997). Because of the

evidence for specific factors that contribute to nicotine, alcohol, and other drug dependence (Bierut et al., 1998), substance specific analyses were performed for the most commonly used substances: cocaine, nicotine, alcohol, marijuana, and opiates. All other queried drugs (stimulants, sedatives, hallucinogens, PCP, and “other” substances) were collapsed into a single category. Analyses were performed using SPSS version 14.0 (SPSS, 2005). The prevalence rate ratio (PRR) was calculated to compare the lifetime prevalence between the two proband groups and the two sibling groups (Rothman KJ, 1998; Zocchetti et al., 1995).

In addition, conditional rates of dependence were examined to investigate the role of drug initiation on the development of dependence in cocaine dependent families and community-based comparison families. Conditional rates are defined as the lifetime history of dependence amongst those who used the specific substance. The thresholds for use were a lifetime history of “ever used” for all substances, including nicotine.

There was no correction in the results for multiple testing.

### 3. Results

#### 3.1 Demographics

The demographic characteristics of the study groups are shown in Table 1. Though cocaine dependent and community-based subjects were matched on age, gender and community defined by zip code, cocaine dependent subjects were significantly more likely to be separated/divorced or never married, have fewer years of education, be unemployed, be disabled, and have a lower income than community-based subjects. Because matching was based on year of birth, the community-based group was approximately 1 year older than the cocaine dependent subjects due to the lag time needed to recruit the community-based individuals.

The case sibling group and community sibling group were similar in gender distribution, ethnic composition, age, and marital status with the exception of case siblings having a higher divorce/separation rate than community siblings. Differences emerged between case siblings and community-based siblings with respect to educational level, employment, and income. Case siblings had an overall lower level of educational attainment with a lower level of high school graduation and college degrees than community siblings did. In addition, case siblings reported higher rates of unemployment and lower income than community siblings did.

#### 3.2 Substance use and dependence in cocaine dependent cases and community-based subjects

Lifetime prevalence of substance use is shown in Table 2. Cocaine dependent subjects had significantly higher rates of use across all substances compared to community-based individuals with the exception of alcohol use in men. Nearly all of the cocaine dependent subjects had used nicotine, alcohol, and marijuana (> 95%). In addition, cocaine dependent males were two to three times more likely than community-based males to have used other illicit substances and four times more likely to have used intravenous (IV) drugs. Cocaine dependent women used more nicotine, alcohol and illicit drugs than did the women recruited from the community. This prevalence rate ratio was consistently higher in females with cocaine dependent subjects two to nearly eight times more likely to use other illicit substances and eleven times more likely to have used IV drugs than community subjects. It is important to note that the community-based subjects reported high rates of nicotine, alcohol, illicit drug, and IV drug use. Of the community individuals, 73.4% had used illicit drugs previously, which highlights the elevated prevalence of drug use in the communities where cocaine dependent subjects live.

The lifetime prevalence of substance dependence is shown in the bottom of Table 2. Amongst the cocaine dependent subjects recruited from treatment, polysubstance dependence was the norm. Seventy-three percent of men and 56% of women reported a lifetime dependence on alcohol. Similarly, 67% of men and 58% of women were dependent on at least one of the other illicit drugs studied. Dependence on cocaine alone was uncommon, with only 9.6% of cocaine dependent subjects reporting no other substance dependence diagnosis. Cocaine dependent subjects had significantly higher rates of dependence across all substances when compared to community-based individuals, even though the community-based comparison subjects had strikingly elevated lifetime rates of dependence when compared to other population-based studies such as the National Epidemiologic Survey on Alcohol and Related Conditions (Hasin et al., 2005).

### 3.3 Substance use and dependence in case siblings and community siblings

Siblings of the cocaine dependent cases had significantly increased prevalence of drug use compared to the siblings of the community-based comparison group for almost all substances assessed (See top of Table 3). Brothers of case probands reported a higher prevalence of use of cocaine, marijuana, opiates, other drugs, and IV drugs than did brothers of community based comparison subjects. Similarly, in women, case siblings had higher rates than community siblings for cocaine, nicotine, marijuana, opiate, other drugs, and IV drug use. These findings demonstrate that brothers and sisters of cocaine dependent subjects experimented with a wide variety of drugs with significantly more drug use than siblings of community-based comparison subjects.

When examining the lifetime prevalence of substance dependence, case siblings had higher prevalence of drug dependence than did community siblings (See bottom of Table 3). Brothers of cocaine dependent cases had a higher prevalence of dependence for all the substances studied except nicotine. Sisters of cocaine dependent probands reported a higher prevalence of cocaine, nicotine, and other drug dependence than did sisters of community-based participants. These results are consistent with a general familial clustering of substance dependence.

### 3.4 Conditional dependence

Conditional dependence is the lifetime history of dependence among individuals who have ever used a specific substance. These rates indicate the addictive nature of each substance along with an individual's predisposition to develop dependence, and provide a clearer picture of the relationship between use and dependence. Conditional dependence rates are presented in Table 4. The rates of conditional dependence were significantly higher in the cocaine dependent cases compared to the community-based group for almost all substances (cocaine, nicotine, alcohol, marijuana, and other drugs) in both men and women. Thus, the increased level of nicotine, alcohol, and other drug dependence in the cocaine dependent cases cannot be explained by the higher prevalence of use within the cocaine dependent group. Instead, this result is consistent with a general addictive vulnerability after substance use. In the community-based sample, conditional dependence rates were highest for cocaine (51.5% men, 43.6% women). In men, nicotine had the next highest rate of conditional dependence (43.5%), but in women, opiates were the next highest (33.3%) followed by nicotine (27.2%). It should be noted that there were very few users of opiates, and the conditional prevalence should be interpreted with caution.

Many of the significant differences between the case siblings and community siblings previously seen in the lifetime prevalence of dependence disappeared after conditioning upon use. Although there continued to be higher rates of dependence in case siblings for most substances, the comparisons were not statistically significant with the reduced sample size. The exception was that case brothers had significantly higher rates of conditional alcohol and marijuana dependence than did community brothers. In both male sibling groups, conditional

dependence rates were highest for cocaine (57.0% case siblings, 55.9% community siblings) followed by nicotine (44.0% case siblings, 34.1% community siblings). The female sibling groups showed a similar pattern with conditional dependence rates for cocaine being the highest (50.4% case siblings, 41.6% community siblings) followed closely by nicotine (44.7% case siblings, 37.1% community siblings).

#### 4. Discussion

This study is the first to examine the family clustering of substance use and dependence in cocaine dependent cases and their siblings. Importantly, the comparison with a community-based population helps to disentangle risks associated with family and community characteristics.

This project demonstrates that amongst cocaine dependent subjects, there were greatly elevated rates of nicotine, alcohol, and illicit drug use compared to a matched community-based comparison population. Almost all (>97%) cocaine dependent individuals used marijuana and 81% used other illicit drugs demonstrating that polysubstance use was the norm. In addition to the high rates of nicotine, alcohol, and drug use, there were elevated rates of dependence across all substances in the cocaine dependent cases compared to community-based subjects. This finding demonstrates a general vulnerability to substance dependence which is consistent with other studies of cocaine dependence (Petry, 2003; Staines et al., 2001). Thus, the treatment for cocaine dependent individuals must focus on polysubstance use and dependence, which is likely to be more difficult to treat.

Many studies have demonstrated a familial clustering with alcohol, opiate, and poly-drug dependence (Bierut et al., 1998; Merikangas et al., 1998; Nurnberger et al., 2004; Rhee et al., 2003; Rounsaville et al., 1991). The present report extends this work to the familial aggregation of specific substance use and dependence associated with cocaine dependent subjects. By starting with cocaine dependent cases recruited in chemical dependency treatment and then ascertaining community-based comparison participants, this study offers a unique opportunity to examine the influence of cocaine dependence on relatives.

Siblings of cocaine dependent cases had significantly more substance use than did siblings of the community-based comparison subjects. Brothers of cocaine dependent probands reported significantly more use of cocaine, marijuana, opiates, and other drugs compared to brothers of community-based participants. Sisters of cocaine dependent probands had used even more drugs compared to sisters of community-based participants, with significantly more use of cocaine, nicotine, marijuana, opiates, and other drugs. Thus, a sibling of a cocaine dependent case was at risk for experimentation with many different drugs, which may be a product of the increased availability of many drugs through their cocaine dependent siblings. Further, the siblings of cocaine dependent index cases demonstrated the familial aggregation of substance dependence that was seen with other family studies of alcohol and drug dependence (Bierut et al., 1998; Merikangas et al., 1998). The lifetime prevalence of dependence on many substances in siblings of cocaine dependent individuals was consistently higher than in siblings of community-based subjects, and reached statistical significance for several substances. Both the brothers and sisters of cocaine dependent cases reported higher prevalence of cocaine dependence than siblings of community-based subjects.

Were these elevated rates of dependence in the case families simply a function of the higher rate of experimentation and use of alcohol, nicotine, and other drugs? The answer is different for probands and siblings. The cocaine dependent case population remained at a significantly elevated risk of dependence compared to the community-based group even after use was taken into account. This suggests a general vulnerability for the progression of polysubstance use to

dependence among cocaine dependent individuals. In the sibling groups, the lifetime prevalence of dependence continued to be higher in case siblings than in community siblings, but the differences between the sibling groups were diminished when only those who used the substance were included in the analysis. This implies that the step of initiation of substance use was a key component in the elevated levels of dependence among siblings of cocaine dependent individuals. Thus, the availability and experimentation with a substance plays an important role in the increased family clustering of substance dependence. This has a public health implication that targeting drug initiation can be a point of intervention in reducing substance dependence in families.

Another important factor to be considered in treating cocaine dependent individuals is the neighborhoods in which they live. We found that the rates of drug use were elevated in our community-based comparison group compared to reports in other population samples. For example, Warner et al. reported a 51% prevalence of lifetime illicit drug use whereas in this study 73% of the community based subjects had used illicit drugs (Warner et al., 1995). Kendler et al. reported a 16%–18% prevalence of lifetime cocaine use whereas 34% of our community based subjects reported cocaine use (Kendler et al., 2003; Kendler and Prescott, 1998). There were also greatly increased rates of dependence in the community sample compared to other population based studies (Vega et al., 2002; Warner et al., 1995). Because our community-based subjects were matched by zip code, this suggests that socioeconomic or “neighborhood” factors contributed to these elevated rates of drug use and dependence. After discharge from the chemical dependency treatment programs, cocaine dependent individuals return to communities with high levels of use and dependence, which is likely a risk factor for relapse.

This study offers unique insights into cocaine use and the progression to dependence. Rates of cocaine use and dependence for community-based subjects were higher than accepted values for the general population (Warner et al., 1995). In addition, cocaine was the most “addictive” drug of all the substances used by the community-based comparison population, meaning that among those who have used any substance, the percentage of that group who progress to dependence was the highest. Conditional dependence for cocaine in this population was over 50% which is higher than generally recognized population rates (Vega et al., 2002; Warner et al., 1995). Similarly, in the sibling groups, cocaine was the most addictive for men and women. The conditional prevalence for nicotine dependence was the next highest. This finding is in contrast to work in nationally representative samples such as Kandel et al. where nicotine was the most likely drug to lead to dependence after use and cocaine was the second most likely drug to lead to dependence (Kandel et al., 1997). Perhaps an even greater disparity is present because Kandel et al. reported dependence conditional on use in the last 12 months. This criterion would select for a higher rate of conditional dependence because use in the last 12 months is most likely to occur in the setting of pre-existing dependence. These differences in findings may also be explained by the initial recruitment of cocaine dependent cases and the enrichment of cocaine dependence in relatives and community members.

This study has important implications for the genetic studies of substance dependence, including twin studies and adoption studies. The modeling of dependence as a multi-step process, which includes use prior to the development of dependence, focuses on genetic and environmental factors that are more specific to each step in this transition. Only a few twin studies have used this method (Agrawal et al., 2005; Heath et al., 2002; Kendler et al., 2000) though the potential pitfalls of not doing so include errors in estimation of heritability. There are likely to be minimal errors in estimates of heritability for alcohol and nicotine dependence because of the widespread availability and use of these substances. However, the estimates of heritability for drug dependence may be much less precise.



As with all studies, there are limitations to this work. Though this is not a nationally representative sample, this study allows an examination of substance use and dependence in cocaine dependent individuals in treatment for their dependence and subjects who live in their community. This study highlights the high prevalence of substance use and dependence by individuals in the community where cocaine dependent subjects live. Substance use and dependence is not distributed evenly over our nation; instead, there are clusters and communities with elevated rates of drug use (Crum et al., 1996; Hawkins et al., 2002; Schroeder et al., 2001). The finding highlights the importance of recruiting comparison subjects from the neighborhood where dependent subjects live. All subjects were recruited from St. Louis area treatment centers, and this population may differ from other cocaine dependent populations. For example, local drug prices and availability vary geographically which may result in different rates of use and dependence (National Narcotics Intelligence Consumers Committee, 1996; U.S. Department of Justice, 2005). Thus, this work is not generalizable to the general population, but more likely is representative of communities that are afflicted with cocaine dependence. In addition, many subjects used “crack” cocaine, the smokeable freebase form. This method of cocaine use is widely recognized as the most addictive form (Chen and Anthony, 2004; Hatsukami and Fischman, 1996) and different findings may be seen with other forms of cocaine.

In summary, cocaine dependent subjects have high lifetime prevalence of other drug use and dependence, which is higher than community matched comparison group. Additionally, the community-based population had greatly elevated rates of drug use and dependence compared to other population studies, which is consistent with a clustering of drug use and dependence in neighborhoods. As our cocaine dependent patients are discharged from treatment, they are returning to neighborhoods with high levels of drug use and dependence and these high rates of drug use and dependence in communities are likely to increase the risk for relapse. In addition, drug use and dependence aggregate within families. The analysis of conditional dependence is noteworthy because it demonstrated that much of the family clustering of dependence is related to the higher levels of drug use in relatives. This evidence implies that to reduce the family clustering of dependence, prevention efforts can target the initial step of experimentation.

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**Table 1**

## Demographics

	Cocaine Dependent Cases (N= 459)	Community-Based Comparisons (N=459)	Case Siblings (N=459)	Community Siblings (N=459)
<b>Sex, %</b>				
Male	47.1	47.1	35.3	33.1
Female	52.9	52.9	64.7	66.9
<b>Race, %</b>				
Black	50.3	50.3	50.3	50.3
White	49.7	49.7	49.7	49.7
Age, mean (SD), y	35.9 (8.7)	36.9 (8.9)	36.2 (9.0)	36.7 (9.3)
<b>Birth cohort, %</b>				
Before 1961	30.7	30.1	30.1	28.3
1961–1968	34.9	34.9	34.2	35.1
After 1968	34.4	35.1	35.7	36.6
<b>Marital status, % * +</b>				
Married/Widowed	13.5	39.7	32.7	38.8
Separated/Divorced	34.0	20.0	23.7	17.4
Never married	52.5	40.3	43.6	43.8
<b>Education, % * +</b>				
< High School	26.6	8.1	21.1	8.9
GED/High School	54.7	47.5	50.8	48.2
Some College	14.2	16.3	16.9	18.0
College or Higher	4.5	28.1	11.2	24.9
# years completed, mean (SD) * +	11.7 (2.0)	13.6 (2.2)	12.5 (2.2)	13.6 (4.6)
<b>Employment, % * +</b>				
Full-time	25.8	59.3	55.2	57.3
Part-time	11.6	13.1	12.1	15.9
Disabled	10.7	6.5	7.3	5.9
Unemployed	44.3	11.3	17.6	10.0
Other**	7.6	9.8	7.9	10.9
<b>Income, % * +</b>				
< \$10,000	40.5	12.2	19.6	12.0
\$10,000–\$29,999	25.9	20.0	27.2	24.0
\$30,00–\$49,999	11.5	24.0	17.6	19.8
≥ \$50,000	13.3	40.7	31.2	38.8
Unknown or refused	8.7	3.1	4.4	5.4

\* Significant difference between cases and community comparisons,  $p < .05$

+ Significant difference between case and community siblings,  $p < .05$

\*\* Includes homemaker, student, and retired

Table 2

Cocaine dependent cases compared to community-based individuals

Lifetime Prevalence of Substance Use						
Men	Substance	Case (n=216)	Community (n=216)	X <sup>2</sup> Value	P Value	PRR (95% CI)
	Cocaine	100.0	47.7	153.03	<0.001	2.10 (1.82–2.41)
	Nicotine	95.4	77.8	28.76	<0.001	1.23 (1.14–1.32)
	Alcohol	99.5	97.7	2.70	0.100	1.02 (1.00–1.04)
	Marijuana	98.6	78.2	43.80	<0.001	1.26 (1.17–1.36)
	Opiates	59.7	21.8	64.47	<0.001	2.75 (2.08–3.62)
	Other Drugs	84.7	39.4	94.40	<0.001	2.15 (1.81–2.57)
	IV Drug Use	36.1	8.3	48.21	<0.001	4.33 (2.69–6.98)
Women	Substance	Case (n=243)	Community (n=243)	X <sup>2</sup> Value	P Value	PRR (95% CI)
	Cocaine	100.0	22.6	306.60	<0.001	4.42 (3.50–5.57)
	Nicotine	96.7	74.1	49.90	<0.001	1.31 (1.21–1.41)
	Alcohol	98.8	94.7	6.46	0.011	1.04 (1.01–1.08)
	Marijuana	96.7	63.0	85.94	<0.001	1.54 (1.39–1.70)
	Opiates	46.5	6.2	101.86	<0.001	7.53 (4.53–12.53)
	Other Drugs	70.8	27.6	90.77	<0.001	2.57 (2.06–3.20)
	IV Drug Use	31.7	2.9	70.52	<0.001	11.00 (5.18–23.36)
Lifetime Prevalence of Substance Dependence						
Men	Substance	Case (n=216)	Community (n=216)	X <sup>2</sup> Value	P Value	PRR (95% CI)
	Cocaine	100.0	24.5	261.77	<0.001	4.08 (3.23–5.15)
	Nicotine	63.4	33.8	37.96	<0.001	1.88 (1.52–2.32)
	Alcohol	73.1	33.8	67.22	<0.001	2.16 (1.77–2.65)
	Marijuana	53.7	25.5	36.02	<0.001	2.11 (1.63–2.73)
	Opiates	24.5	5.6	30.44	<0.001	4.42 (2.43–8.03)
	Other Drugs	39.8	11.6	45.11	<0.001	3.44 (2.30–5.15)
Women	Substance	Case (n=243)	Community (n=243)	X <sup>2</sup> Value	P Value	PRR (95% CI)
	Cocaine	100.0	9.9	398.63	<0.001	10.13 (6.93–14.80)
	Nicotine	62.8	20.2	94.92	<0.001	3.16 (2.42–4.13)
	Alcohol	56.0	14.8	89.99	<0.001	3.78 (2.74–5.21)
	Marijuana	35.8	7.8	55.79	<0.001	4.58 (2.88–7.28)
	Opiates	22.2	2.1	46.32	<0.001	10.80 (4.40–26.53)
	Other Drugs	34.6	4.5	69.72	<0.001	7.64 (4.18–13.95)

**Table 3**  
Siblings of cocaine dependent cases compared to siblings of community-based subjects

Men	Lifetime Prevalence of Substance Use					
	Substance	Case Sibling (n=163)	Community Sibling (n=154)	X <sup>2</sup> Value	PRR (95% CI)	
	Cocaine	66.0	38.8	23.34	1.70 (1.36-2.14)	
	Nicotine	82.7	80.9	0.17	1.02 (0.92-1.14)	
	Alcohol	96.9	96.1	0.17	1.01 (0.97-1.05)	
	Marijuana	90.1	75.7	11.70	1.19 (1.07-1.32)	
	Opiates	37.0	19.1	12.45	1.94 (1.32-2.85)	
	Other Drugs	58.0	37.5	13.23	1.55 (1.21-1.97)	
	IV Drug Use	13.0	6.6	3.59	1.97 (0.96-4.05)	
Women	Substance	Case Sibling (n=299)	Community Sibling (n=308)	X <sup>2</sup> Value	PRR (95% CI)	
	Cocaine	47.5	25.1	32.82	1.89 (1.51-2.38)	
	Nicotine	85.2	75.6	8.82	1.13 (1.04-1.22)	
	Alcohol	96.3	96.7	0.09	1.00 (0.97-1.03)	
	Marijuana	78.5	65.8	11.99	1.19 (1.08-1.32)	
	Opiates	15.8	7.2	11.19	2.21 (1.37-3.57)	
	Other Drugs	44.1	26.7	20.02	1.65 (1.32-2.07)	
	IV Drug Use	5.7	1.3	8.79	4.39 (1.50-12.90)	
Men	Lifetime Prevalence of Substance Dependence					
Substance	Case Sibling (n=163)	Community Sibling (n=154)	X <sup>2</sup> Value	P Value	PRR (95% CI)	
Cocaine	37.7	21.7	9.50	0.002	1.73 (1.21-2.49)	
Nicotine	36.4	27.6	2.78	0.096	1.32 (0.95-1.83)	
Alcohol	42.0	28.3	6.43	0.011	1.48 (1.09-2.03)	
Marijuana	34.6	19.1	9.53	0.002	1.81 (1.23-2.68)	
Opiates	9.9	3.3	5.45	0.020	3.00 (1.13-8.00)	
Other Drugs	15.4	7.2	5.19	0.023	2.13 (1.09-4.18)	
Women	Substance	Case Sibling (n=299)	Community Sibling (n=308)	X <sup>2</sup> Value	P Value	PRR (95% CI)
Cocaine	23.9	10.4	19.40	<0.001	2.29 (1.56-3.73)	
Nicotine	38.0	28.0	6.88	0.009	1.36 (1.08-1.71)	
Alcohol	25.3	19.5	2.84	0.092	1.29 (0.96-1.74)	
Marijuana	13.1	10.4	1.07	0.302	1.26 (0.81-1.96)	
Opiates	2.4	1.3	0.94	0.333	1.81 (0.54-6.12)	
Other Drugs	9.8	3.9	8.18	0.004	2.50 (1.30-4.89)	

Table 4

Lifetime Prevalence of Conditional Substance Dependence

Cocaine dependent cases compared to community-based individuals						
Men	Substance	Case	Community	X <sup>2</sup> Value	P Value	PRR (95% CI)
	Cocaine	100 (n=216)	51.5 (n=103)	124.34	<0.001	1.94 (1.61–2.34)
	Nicotine	66.5 (n=206)	43.5 (n=168)	19.97	<0.001	1.53 (1.26–1.87)
	Alcohol	73.5 (n=215)	34.6 (n=211)	64.89	<0.001	2.12 (1.74–2.60)
	Marijuana	54.5 (n=213)	32.5 (n=169)	18.31	<0.001	1.67 (1.30–2.15)
	Opiates	41.1 (n=129)	23.4 (n=47)	4.65	0.031	1.76 (1.01–3.06)
	Other Drugs	47.0 (n=183)	29.4 (n=85)	7.40	0.007	1.60 (1.11–2.30)
Women	Substance	Case	Community	X <sup>2</sup> Value	P Value	PRR (95% CI)
	Cocaine	100 (n=243)	43.6 (n=55)	152.87	<0.001	2.29 (1.70–3.10)
	Nicotine	66.0 (n=235)	27.2 (n=180)	61.19	<0.001	2.42 (1.88–3.13)
	Alcohol	56.7 (n=240)	15.7 (n=230)	85.15	<0.001	3.62 (2.63–4.99)
	Marijuana	37.0 (n=235)	12.4 (n=153)	28.25	<0.001	2.98 (1.90–4.69)
	Opiates	47.8 (n=113)	33.3 (n=15)	1.11	0.291	1.43 (0.68–3.01)
	Other Drugs	48.3 (n=172)	16.4 (n=67)	20.48	<0.001	2.94 (1.68–5.16)
Siblings of cocaine dependent cases compared to siblings of community-based subjects						
Men	Substance	Case Sibling	Community Sibling	X <sup>2</sup> Value	P Value	PRR (95% CI)
	Cocaine	57.0 (n=107)	55.9 (n=59)	0.02	0.893	1.02 (0.77–1.35)
	Nicotine	44.0 (n=134)	34.1 (n=123)	2.63	0.105	1.29 (0.95–1.76)
	Alcohol	43.3 (n=157)	29.5 (n=146)	6.26	0.012	1.47 (1.08–2.00)
	Marijuana	38.4 (n=146)	25.2 (n=115)	5.06	0.025	1.52 (1.04–2.22)
	Opiates	26.7 (n=60)	17.2 (n=29)	0.96	0.326	1.55 (0.63–3.81)
	Other Drugs	26.6 (n=94)	19.3 (n=57)	1.04	0.308	1.38 (0.74–2.58)
Women	Substance	Case Sibling	Community Sibling	X <sup>2</sup> Value	P Value	PRR (95% CI)
	Cocaine	50.4 (n=141)	41.6 (n=77)	1.55	0.214	1.21 (0.89–1.65)
	Nicotine	44.7 (n=253)	37.1 (n=232)	2.89	0.089	1.21 (0.97–1.50)
	Alcohol	26.2 (n=286)	20.2 (n=297)	2.97	0.085	1.30 (0.96–1.75)
	Marijuana	16.7 (n=233)	15.8 (n=202)	0.060	0.801	1.06 (0.69–1.62)
	Opiates	14.9 (n=47)	18.2 (n=22)	0.12	0.728	0.82 (0.27–2.51)
	Other Drugs	22.1 (n=131)	14.6 (n=82)	1.83	0.177	1.51 (0.82–2.79)