Illicit Drug Use and Adverse Birth Outcomes: Is It Drugs or Context?

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ABSTRACT *Prenatal drug use is commonly associated with adverse birth outcomes, yet no studies have controlled for a comprehensive set of associated social, psychosocial, behavioral, and biomedical risk factors. We examined the degree to which adverse birth outcomes associated with drug use are due to the drugs versus surrounding factors. Data are from a clinical sample of low-income women who delivered at Johns Hopkins Hospital between 1995 and 1996 (n=808). Use of marijuana, cocaine, and opiates was determined by self-report, medical record, and urine toxicology screens at delivery. Information on various social, psychosocial, behavioral, and biomedical risk factors was gathered from a postpartum interview or the medical record. Multivariable regression models of birth outcomes (continuous birth weight and low birth weight [LBW] <2,500 g) were used to assess the effect of drug use independent of associated factors. In unadjusted results, all types of drug use were related to birth weight decrements and increased odds of LBW. However, only the effect of cocaine on continuous birth weight remained significant after adjusting for all associated factors (-142 g, p=0.05). No drug was significantly related to LBW in fully adjusted models. About 70% of the unadjusted effect of cocaine use on continuous birth weight was explained by surrounding psychosocial and behavioral factors, particularly smoking and stress. Most of the unadjusted effects of opiate use were explained by smoking and lack of early prenatal care. Thus, prevention efforts that aim to improve newborn health must also address the surrounding context in which drug use frequently occurs.*

KEYWORDS *Illicit drugs, Psychosocial factors, Pregnancy, Birth weight, Low birth weight*

BACKGROUND

Maternal drug use is a significant public health concern given the potential consequences for the health and well-being of both the mother and developing fetus. Recent U.S. national estimates indicate that 9.8% of all women aged 15 to 44 years and 4% of women who were pregnant reported using illicit substances in the past month.¹ Although this figure is likely to be underestimated given the reliance on self-reported data, it suggests that between 200,000 and 400,000 infants born annually in the US are prenatally exposed to drugs. Moreover, the burden of maternal drug use may not be equally distributed; prevalence estimates in low-income and/or urban populations have ranged as high as 15–30%.^{2–6} Marijuana is

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generally the most commonly used drug during pregnancy, followed by cocaine and opiates.

While illicit drug use is widely perceived to cause adverse birth outcomes, such as low birth weight, preterm birth, and growth restriction, the actual empirical evidence is less established than for the more frequently used licit substances of tobacco or alcohol.⁷⁻⁹ Cigarette smoking is strongly related to fetal growth restriction while alcohol is a known teratogen that can lead to craniofacial dysmorphology and mental retardation.

Of illicit substances, cocaine is most consistently associated with birth outcomes, particularly those that capture dimensions of fetal growth such as birth weight, low birth weight, intrauterine growth restriction, and head circumference,^{6,10-17} although not all studies have noted effects.¹⁸⁻²¹ Marijuana is weakly and unreliably related to birth weight with some studies even reporting increases in birth weight.^{6,10,11,18,20,22-25} Opiate use is also inconsistently related to birth outcomes; both large and small decrements in birth weight have been noted.^{6,10,11,20,26} Accordingly, recent analyses of a large, multisite cohort study found that use of cocaine and, to a lesser extent, opiates was related to gestational age-adjusted birth weight, and only cocaine use was related to low birth weight.^{10,11} These analyses controlled for the use of tobacco and alcohol, adequacy of prenatal care, and various medical conditions.

In addition to inadequate prenatal care utilization and the frequent concomitant use of tobacco and alcohol, illicit drug use is also associated with multiple social, psychosocial, behavioral, and biomedical risk factors including poverty, stress, depression, lack of social support, physical abuse, sexually transmitted infections, and poor nutrition.^{4,27,28} To date, no studies examining specific drug effects have accounted for the full spectrum of associated risk factors for birth outcomes, particularly psychosocial risk factors, or estimated the proportion of risk attributable to a presumed biological mechanism versus these related factors.⁹ Knowledge of the determinants underlying the differentially worse birth outcomes associated with drug use may help to direct treatment-based interventions and prioritize the factors that should be addressed to improve birth outcomes more generally. It may not be sufficient to focus on drug cessation without addressing the disadvantaged context that often surrounds, and may lead to, drug use. This study addresses this knowledge gap by evaluating the impact of drug use on birth outcomes using a biopsychosocial model that incorporates multiple related social, psychosocial, behavioral, and biomedical factors.

METHODS

Study Sample

Data for this analysis come from a hospital-based retrospective cohort study designed to examine the influence of drug use on patterns and barriers to prenatal care.²⁹ The study sample consists of low-income women (not private or transferred patients), aged 19 years or older who delivered a live birth or fetal death at the Johns Hopkins Hospital (JHH) between February 16, 1995 and May 31, 1996. Eligible women were approached in the postpartum unit by trained survey staff and, once consenting to participate, were briefly screened to determine their selection probability. All women with evidence of drug use (medical record, self-report, or toxicological screen) or no prenatal care and two out of three remaining women were selected to participate. This sampling strategy was designed to maximize

statistical power within fixed study costs. In accordance with the protocol approved by the JHH Institutional Review Board, informed consent was required for participation and confidentiality was assured with a National Institute on Drug Abuse certificate. Women were compensated \$15 for their time in completing the 1-h interview.

Of 1,201 eligible women, 1,114 (93%) consented to participate. Upon completion of the screening questionnaire, one out of three women who had received prenatal care and had no evidence of drug use were not selected as per the sampling scheme ($n=290$), resulting in 824 women with completed interviews. The analytic sample is restricted to 808 women who delivered singleton, live births.

Data Sources

Data were primarily collected from the medical record and the postpartum interview. Medical records were abstracted to determine infant birth characteristics, prenatal care utilization, drug use (from toxicology screens or report by a health care provider), and the presence of medical risk factors. The postpartum interview gathered information on social and psychosocial characteristics using standardized instruments, as well as behavioral factors, including a detailed drug use history.

Measures and Variables

Drug Use Prenatal drug use of marijuana, cocaine, and opiates was determined by positive evidence on any of three measures: a universal urine toxicological screen at admission to labor and delivery, self-report (screener questionnaire or postpartum interview), or other report in the medical record (prenatal toxicology screen or report by a health care provider). Any use of these three types of drugs (marijuana, cocaine, opiates) during pregnancy was examined with separate dichotomous indicator variables. The self-reported frequency of drug use (monthly versus weekly or daily) was also examined for the 75% of drug users who reported use in the postpartum interview. Use of any other type of drug, as determined by self-report, the medical record, or a toxicological screen for barbiturates, was controlled for in adjusted analyses.

Birth Outcomes Birth weight, as abstracted from the medical record, served as the primary outcome measure. It was analyzed both continuously as birth weight in grams and as a binary variable of low birth weight (LBW, $<2,500$ g). Growth restriction and preterm birth, the proximate determinants of low birth weight, were not examined directly out of concern for the validity of gestational age estimation in a sample overrepresented for drug use and lack of prenatal care. Therefore, observed associations can be viewed as the total effect on birth weight, irrespective of the mechanism. Reduced birth weight, particularly LBW, is related to infant morbidity and mortality,³⁰ as well as later developmental deficits.³¹

Other Independent Variables Several social, psychosocial, behavioral, and biomedical factors that have been related to both drug use and birth outcomes were evaluated as potential control variables. A biopsychosocial framework that places social and psychosocial factors as distal determinants influencing birth outcomes via proximate behavioral and biomedical factors was used to guide the analysis.³² While drug use may exacerbate social and psychosocial risk factors, it is generally accepted that adverse circumstances are fundamental causes that precipitate and promote

drug use as a self-medicating behavior.^{33,34} Thus, social, psychosocial, and other behavioral factors were treated as confounding variables rather than mediators or indirect influences. Moreover, even in the presence of reciprocal effects, other coexisting risk factors (e.g., stress, poverty) would still need to be addressed along with drug use given that they occur more broadly as fundamental causes.

Social Factors Social variables included maternal age, race, education, relationship with the father of the baby, employment during pregnancy, money for necessities, and type of housing. Money for necessities (e.g., food, housing, heating) was determined by a seven-item subscale of the Family Resources Scale (sample Cronbach's $\alpha=0.87$).³⁵

Psychosocial Factors Psychosocial variables included stress, family support, depression, pregnancy locus of control, physical abuse, and unwanted pregnancy. *Stress* was measured with a validated 11-item Hassles Scale,³⁶ which assesses chronic stress during pregnancy due to daily difficulties and circumstances (e.g., family problems, money worries, loss of a loved one, general overload). One item reflecting stress due to problems with alcohol or drugs was removed from the summed scale to prevent the adjustment of a potentially mediating factor (sample Cronbach's $\alpha=0.80$). *Family support* was measured with a three-item scale assessing the support of family members in solving problems and looking out for one another (sample Cronbach's $\alpha=0.80$). The Center for Epidemiologic Studies Depression Scale was used to measure *depressive symptoms* (sample Cronbach's $\alpha=0.88$).³⁷ *Pregnancy locus of control* was measured by five related items in the Pregnancy Belief Scale³⁸ and refers to the extent to which a woman believes that her pregnancy outcome is under internal control versus chance or fate (sample Cronbach's $\alpha=0.72$). The shortened version of the violence subscale in the Conflicts Tactic Scale (CTS)³⁹ was used to measure *physical abuse* and included the experience of any physical abuse during pregnancy by household or nonhousehold members. *Unwanted pregnancy* was defined as not wanting to have a baby at the time of learning pregnancy status.

Behavioral Factors Other behavioral factors examined were smoking, alcohol consumption, and the receipt of early prenatal care. Prenatal *smoking* and *alcohol consumption* were ordinally categorized by the average number of cigarettes smoked per day (0, 1–9, or 10+) and the frequency of drinking (never, monthly, or daily/weekly). *Early prenatal care* was defined as a first visit within the first trimester with four or more total visits.

Biomedical Factors Biomedical risk factors included *hypertensive disorders* (chronic hypertension, pregnancy-induced hypertension, preeclampsia, or eclampsia), *sexually transmitted infections* (gonorrhea, chlamydia, or syphilis), *other medical risk factors* (thromboembolic disease, vaginal bleeding, asthma requiring medication, cancer, renal disease, hepatitis, or HIV/AIDS), and *parity*. Nutritional status was examined by *prepregnancy weight* and *net weight gain* during pregnancy (subtracting infant birth weight).

Analytic Methods

Bivariate analyses were performed to examine associations between drug use and independent variables using chi-square tests. Linear (birth weight) and logistic (LBW) regression models were then used to determine the proportion of unadjusted drug use effects on birth weight (continuous, LBW) that could be explained by the

sequential control for other drug use (including tobacco and alcohol), social, psychosocial, behavioral, and biomedical block groups of factors. Variables were retained in the model if they were independently related to the birth outcome ($p < 0.10$) or if their removal altered any of the drug use coefficients by 10% or more.⁴⁰ Further efforts to isolate the contribution of specific covariates in explaining drug effects were performed by comparing effect estimates from models before and after the inclusion of single variables and through the Oaxaca decomposition technique.⁴¹

Correlation matrices were used to check for collinearity and potential interactions between the drugs and other model variables were explored. The Cronbach's α coefficient, a measure of internal consistency and reliability, exceeded 0.70 for all scale variables. Items were summed and rescaled to reflect an average response. In general, survey data were highly complete. For one scalar variable, money for necessities, missing data exceeded 5% and a dummy variable using a separate category was created to preserve the observations without making assumptions about the missing data. Otherwise, the few missing observations (<5%) for other variables were placed in the reference group.

As some biomedical variables (i.e., hypertensive disorders, nutritional status) may be the consequences of drug use rather than true confounders, the final model adjusting for biomedical factors may be viewed as estimating direct effects of drug use. Potential dose effects of drug use were also evaluated through self-reported frequency of usage as well as the examination of positive labor and delivery screens versus other sources (medical record, self-report only) as a proxy for use intensity since those with a positive screen at the end of pregnancy are likely to be heavy users.

RESULTS

Sample Description

Slightly more than one third of the women sampled used drugs during pregnancy (35%, $n=281$, not shown). Accounting for the sampling design, the estimated population prevalence was 25% (281/1,114). Cocaine was the most commonly used drug (24%), followed by opiates (19%), marijuana (15%), and other drugs (7%). Tables 1 and 2 show the distribution of social, psychosocial, behavioral, and biomedical factors for the total sample. Consistent with the population of inner city Baltimore, the majority of the sample was Black and only 12% had received education beyond high school.

Social, Psychosocial, Behavioral, and Biomedical Correlates of Drug Use

Tables 1 and 2 also show the percentage of drug use according to the selected covariates. All of the social factors were associated with at least one type of drug use during pregnancy (Table 1). Social factors associated with multiple types of drug use included older age, lower levels of education, being unemployed, and not having enough money for necessities. Psychosocial factors associated with one or more types of drug use included greater stress and depressive symptoms, less family support, and a lower internal locus of control regarding pregnancy outcomes.

Women who smoked or drank alcohol with greater intensity were significantly more likely to use marijuana, cocaine, and opiates during pregnancy (Table 2). Having an unwanted pregnancy and not receiving early prenatal care were also associated with both cocaine and opiate use. Of the biomedical risk factors

TABLE 1 Drug use (%) according to social and psychosocial factors

	Total	Drug use during pregnancy		
		Marijuana	Cocaine	Opiates
	<i>n</i> (%)	123 (15)	191 (24)	153 (19)
Social factors				
Maternal age (years)				
19–24	422 (52)	11.6**	7.4***	8.3***
25–34	318 (39)	19.8	40.6	32.7
35+	68 (9)	16.2	45.6	20.6
Race				
Black	756 (94)	14.6*	23.5	19.2
White/other	52 (6)	25.0	25.0	15.4
Relationship with baby's father				
Lives with him	228 (28)	14.0	24.6*	19.3
Contact with him	476 (59)	14.3	20.8	18.1
No relationship	104 (13)	22.1	34.6	22.1
Education				
<High school	361 (44)	18.3*	28.8***	25.5***
High school or GED	347 (44)	13.8	20.8	15.0
>High school	100 (12)	9.0	15.0	9.0
Employed during pregnancy				
Yes	328 (41)	11.0**	11.9***	7.3***
No	480 (59)	18.1	31.7	26.9
Enough money for necessities				
<Half the time	58 (7)	32.8***	62.1***	44.8***
Half the time	105 (13)	21.9	28.6	22.9
>Half the time	456 (57)	12.3	19.5	14.9
Not answered	189 (23)	13.2	19.1	18.5
Housing				
Own	146 (18)	13.0	21.9	15.8**
Rent	391 (48)	15.4	22.5	16.1
Subsidized	119 (15)	10.9	22.7	20.2
Public housing	152 (19)	20.4	29.0	28.3
Psychosocial factors				
Stress				
Little to none	307 (38)	8.1***	13.0***	11.7***
Some	389 (48)	17.7	24.9	21.1
Moderate to severe	112 (14)	25.9	48.2	31.3
Family support				
Almost always	121 (15)	12.4	12.4***	9.9***
Sometimes	538 (67)	14.7	22.1	18.4
Hardly ever	149 (18)	19.5	38.3	28.2
Depression (CESD score)				
<16	338 (42)	9.8***	14.8***	13.0***
16–19	107 (13)	18.7	19.6	15.0
20–29	198 (25)	17.2	25.3	22.2
30+	165 (20)	21.8	42.4	29.7
Pregnancy locus of control				
Little to none	246 (30)	17.5	37.0***	30.1***
Some	329 (41)	14.6	21.3	17.9
Moderate to strong	233 (29)	13.7	12.9	8.6

TABLE 1 (continued)

	Total <i>n</i> (%)	Drug use during pregnancy		
		Marijuana	Cocaine	Opiates
		123 (15)	191 (24)	153 (19)
Physical abuse				
Yes	111 (14)	20.7	28.8	16.2
No	697 (86)	14.4	22.8	19.4
History of sexual abuse				
Yes	167 (21)	25.2***	27.5	22.8
No	641 (79)	12.6	22.6	17.9

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$

examined, lower prepregnancy weight and net weight gain and higher parity were associated with more than one type of drug use. Medical risk factors were not more common among drug users. Observed associations were generally stronger for the use of cocaine and opiates than marijuana or other drugs.

Drug Use and Birth Outcomes

In unadjusted models, all types of substance use were significantly related to both continuous birth weight (Table 3) and LBW (Table 4). In multivariate models, adjusting for other types of substance use, cocaine use, opiate use, and heavy smoking were significantly related to continuous birth weight; only heavy smoking and heavy drinking were related to LBW. Marijuana use was unrelated to both birth weight and LBW after accounting for other drug use.

Cocaine After adjustment for all social, psychosocial, behavioral, and biomedical factors, cocaine use remained marginally related to continuous birth weight (-143 g, $p = 0.05$). However, about 70% of the unadjusted effect was explained by other factors, particularly cigarette smoking, stress, and the nutritional status indicators of prepregnancy weight and net weight gain. In contrast to continuous birth weight, the effect of cocaine use on LBW was not significant after adjustment for other substance use, mostly heavy smoking, and nearly all of the cocaine-related excess odds was explained by the additional control for psychosocial and behavioral characteristics.

Opiates Nearly two thirds of the unadjusted effect of opiate use on continuous birth weight was explained by overlapping cigarette smoking and cocaine use. Opiate use was not significantly related to birth weight after adjustment for lack of early prenatal care and the effect was further reduced after controlling for biomedical factors, particularly prepregnancy weight and net weight gain. Similar to continuous birth weight, opiate use was not significantly related to LBW after adjustment for smoking and lack of early prenatal care.

Licit Substances Heavy smoking remained significantly related to birth weight (-158 g, $p < 0.05$) in fully adjusted models. Neither smoking nor drinking was significantly related to LBW after adjusting for other drug use, social, and psychosocial factors.

There were no significant interactions between any type of substance use and other model variables, indicating additive rather than synergistic effects. Evaluation

TABLE 2 Drug use (%) according to behavioral and biomedical factors

	Drug use during pregnancy			
	Total	Marijuana	Cocaine	Opiates
	<i>n</i> (%)	123(15)	191(24)	153(19)
Behavioral factors				
Cigarettes per day				
0	540 (67)	5.7***	7.0***	5.7***
1–9	142 (18)	33.8	49.3	33.8
10+	126 (15)	34.9	65.9	58.7
Alcohol				
Never	662 (82)	11.2***	16.8***	14.8***
Monthly	91 (11)	26.4	47.3	31.9
Daily/weekly	55 (7)	45.5	67.3	47.3
Early prenatal care				
Yes	302 (37)	8.6***	8.6***	5.0***
No	506 (63)	19.2	32.6	27.3
Unwanted pregnancy				
Yes	178 (22)	17.4	32.0**	27.0**
No	630 (78)	14.6	21.3	16.7
Biomedical factors				
Hypertensive disorders				
Yes	85 (11)	5.9*	20.0	15.3
No	723 (89)	16.3	24.1	19.4
STI				
Yes	109 (13)	12.8	22.0	11.9*
No	699 (87)	15.6	23.9	20.0
Other medical risk factor				
Yes	158 (20)	14.6	23.4	20.3
No	650 (80)	15.4	23.7	18.6
Prepregnancy weight				
<120	186 (23)	19.4*	34.4***	28.5***
120–159	382 (47)	15.5	23.6	18.3
160–199	152 (19)	13.2	17.1	13.2
200+	88 (11)	9.1	12.5	11.4
Net weight gain				
<10	251 (31)	16.7	32.7***	29.9***
10–29	413 (51)	15.3	21.8	15.3
30–39	80 (10)	11.3	18.8	15.0
40+	64 (8)	14.1	6.3	4.7
Parity				
0	208 (26)	8.2**	6.7***	5.3***
1	225 (28)	16.4	16.0	10.7
2–3	283 (35)	18.4	36.0	30.0
4+	92 (11)	18.5	42.4	35.9

p*<0.05; *p*<0.01; ****p*<0.001

of self-reported frequency of illicit drug use generally showed dose–response trends but no effects were statistically significant (data not shown). Alternatively, examination of positive labor and delivery screens versus other sources as a proxy for use intensity did show a significant effect for cocaine on birth weight. Compared to women with no indication of cocaine use, those with a positive labor and delivery

TABLE 3 Linear regression results of birth weight and drug use

	Marijuana coefficient (95%CI)	Cocaine coefficient (95%CI)	Opiates coefficient (95%CI)	Heavy smoking 10+ cigarettes per day coefficient (95%CI)	Heavy drinking daily/weekly coefficient (95%CI)
Unadjusted	-250.0 (-384.0, -116.0)***	-475.1 (-584.6, -367.7)***	-462.3 (-582.0, -342.5)***	-543.8 (-674.3, -413.3)***	-438.3 (-629.1, -247.5)***
Adjusted for other drug use	-0.2 (-140.6, 140.2)	-219.7 (-369.4, -70.0)**	-165.1 (-324.6, -5.5)*	-307.7 (-470.1, -145.3)***	-120.5 (-319.8, 78.8)
Social factors	12.7 (-127.6, 152.9)	-225.0 (-377.4, -72.8)*	-170.2 (-330.3, -10.1)*	-278.8 (-445.1, -112.6)**	-83.7 (-284.6, 117.1)
Social and psychosocial factors	7.7 (-131.5, 146.9)	-187.2 (-339.0, -35.5)*	-162.1 (-321.0, -3.1)*	-232.2 (-398.2, -66.2)**	-68.1 (-267.7, 131.5)
Social, psychosocial, and behavioral factors	10.1 (-128.2, 148.5)	-171.3 (-322.5, -20.1)*	-129.9 (-289.2, 29.5)	-225.9 (-391.0, -60.8)**	-46.3 (-245.3, 152.6)
Social, psychosocial, behavioral, and biomedical factors	-24.6 (-155.8, 106.5)	-142.0 (-285.8, 1.8)	-85.6 (-237.7, 66.4)	-158.2 (-315.9, -0.5)*	-30.6 (-219.4, 158.2)

Social factors include maternal age, money for necessities, and housing. Psychosocial factors include stress and pregnancy locus of control. Behavioral factors include early prenatal care. Biomedical factors include hypertensive disorders, other medical risk factors, prepregnancy weight, and net weight gain.

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$

TABLE 4 Logistic regression results of LBW and drug use

	Marijuana OR (95%CI)	Cocaine OR (95%CI)	Opiates OR (95%CI)	Heavy smoking 10+ cigarettes per day OR (95%CI)	Heavy drinking daily/weekly OR (95%CI)
Unadjusted	1.94 (1.23, 3.06)**	3.09 (2.10, 4.55)***	3.31 (2.21, 4.96)***	4.53 (2.88, 7.13)***	4.13 (2.13, 7.40)***
Adjusted for other drug use	0.93 (0.55, 1.57)	1.24 (0.72, 2.14)	1.67 (0.96, 2.93)	2.49 (1.39, 4.47)**	2.13 (1.10, 4.10)*
Social factors	0.92 (0.53, 1.58)	1.30 (0.73, 2.32)	1.88 (1.04, 3.38)*	2.11 (1.12, 3.98)*	1.86 (0.92, 3.76)
Social and psychosocial factors	0.96 (0.55, 1.66)	1.17 (0.65, 2.11)	1.84 (1.02, 3.34)*	1.80 (0.95, 3.41)	1.93 (0.95, 3.94)
Social, psychosocial, and behavioral factors	0.97 (0.56, 1.67)	1.10 (0.61, 1.99)	1.60 (0.88, 2.92)	1.77 (0.93, 3.37)	1.74 (0.85, 3.57)
Social, psychosocial, behavioral, and biomedical factors	1.07 (0.60, 1.92)	1.09 (0.58, 2.05)	1.74 (0.92, 3.26)	1.52 (0.76, 3.03)	1.85 (0.86, 3.98)

Social factors include maternal age, money for necessities, and housing. Psychosocial factors include stress and pregnancy locus of control. Behavioral factors include early prenatal care. Biomedical factors include hypertensive disorders, other medical risk factors, and pre-pregnancy weight.

* $p<0.05$; ** $p<0.01$; *** $p<0.001$

screen for cocaine had significantly smaller infants (-174.2 g; 95%CI= -337.0 , -11.3 ; $p=0.04$) whereas those with another indication of use (self-report or medical record only) did not have significantly smaller infants (-80.8 g; 95%CI= -266.8 , 105.43 ; $p=0.39$).

DISCUSSION

This study provides confirmation of the multiple risks related to drug use, including inadequate material resources, stress, depression, delayed or no prenatal care, poor nutritional status, as well as concurrent use of tobacco and alcohol, and is the first to our knowledge to control for multiple social, psychosocial, behavioral, and biomedical factors when evaluating specific drug use effects on birth outcomes. In unadjusted associations, marijuana, cocaine, and opiate use were all strongly related to continuous birth weight and LBW. After controlling for overlapping substance use, these effects were attenuated but still significant for cocaine and opiates on continuous birth weight. After adjustment for all associated risk factors for reduced birth weight and LBW, however, only the use of cocaine was related to continuous birth weight. No substance was significantly more likely to result in LBW—an outcome of greater clinical significance. Altogether, these results suggest that illicit drug use is a stronger risk marker than a risk factor for adverse birth outcomes.

The observed independent effect of cocaine use on birth weight (-142 g) is similar in magnitude to that found in a large, multisite cohort study that adjusted for gestational age but no social or psychosocial factors (-151 g).¹⁰ This same study, however, also reported a sizeable LBW effect.¹¹ Of the illicit drugs examined, cocaine has the most biologically plausible effect on birth weight via vasoconstriction and reduced uteroplacental transfer.⁴² The greater birth weight decrement observed among infants of women with a positive labor and delivery urine screen is consistent with a dose-response effect and suggests that only heavier use later in pregnancy may be consequential.

Between 70% and 90% of birth weight decrements and increased odds of LBW related to the three drug types was explained by factors associated with drug use. Other substance use, psychosocial, and behavioral factors accounted for considerable proportions of cocaine-related effects on birth weight. In particular, smoking and stress individually accounted for 10% to 20% of unadjusted cocaine effects on continuous birth weight. For opiate use, smoking, early prenatal care, and the biomedical nutritional status indicators accounted for a substantial proportion of the estimated effects on both LBW and birth weight.

Thus, where birth outcomes are concerned, emphasis on illicit drug use per se may be misplaced. For example, the birth weight effects of moderate to severe stress (-243 g, $p=0.001$, not shown) and heavy smoking (-158 g, $p=0.04$) exceeded that of cocaine and accounted for a significant portion of unadjusted cocaine-related effects. Chronic stress is consistently related to birth weight and gestational age with hypothesized mechanisms via behavioral and biological pathways.^{43,44} In relation to drug use, stress may promote and reinforce substance use as a coping mechanism.⁴⁵ And in contrast to any substance, moderate to severe stress was associated with twice greater odds of LBW (OR=2.14, $p=0.03$). Similarly, living in public housing and having an external locus of control were associated with both birth weight decrements (-172 , $p=0.02$; -157 , $p=0.01$) and LBW (OR=1.6, $p=0.05$; OR=2.5, $p=0.01$). Cigarette smoking is also strongly related to fetal growth restriction and much more widely prevalent than cocaine use with general population estimates as

high as 25%.^{7,46} Alcohol too has established teratogenic effects including growth restriction;⁷ the lack of effect observed in this sample may reflect lighter consumption patterns as alcohol is less commonly used by low-income, Black women.⁴⁷

Although nutritional status may be a consequence of the anorexic effects of opiates, the use of opiates was not significantly related to either birth weight outcome before adjustment of potentially indirect biomedical factors. The absence of early prenatal care may also be a consequence of the depressive effect of opiate use.²⁹ While observed effects of prenatal care on birth outcomes may reflect unmeasured positive selection characteristics,^{48,49} the linkages to ancillary social and psychosocial services provided in prenatal care are likely to be of greatest benefit to substance users and other women with multiple psychosocial risks.⁴⁹ Thus, community outreach and other efforts to identify and enroll pregnant drug users into prenatal care are imperative.

In contrast to the findings of some studies, physical abuse and medical risk factors were not more common among drug users than nonusers and did not account for drug-related effects on birth weight. The experience of physical abuse was relatively high in this low-income sample and might reflect less severe forms of abuse that are common in some families. The report of stress because of abuse, an item in the hassles scale, was indeed twice as high among drug users (20% versus 10%; data not shown). Another study of this sample found that this single item related to abuse accounted for most of the effect of stress on birth weight as measured by the entire scale.⁵⁰ The significantly lower prevalence of sexually transmitted infections among opiate users is likely to be the result of surveillance bias due to inadequate health care utilization. As many biomedical risk factors were less common among drug users, their control introduced a form of negative confounding and generally increased estimates of drug-related effects.

In addition to the measurement and control of multiple social and psychosocial confounders, a major strength of this study was the capacity to assess independent drug effects. Unlike some previous studies that have relied on statistical control among polydrug users, there were sufficient numbers of women in our study who used only cocaine ($n=48$) and only opiates ($n=20$) to estimate independent effects. Similarly, illicit drug use and use of tobacco and alcohol were correlated but not collinear. The combination of sources for drug use ascertainment, including self-report, the medical record, and urine toxicology screens, is another major strength that reduces misclassification and increases confidence in the estimates of drug-related effects. Several sensitivity analyses were also performed. Because neighborhood disadvantage has been associated with both maternal drug use and birth outcomes,⁵¹ the residential census tract was initially included with fixed effects to control for all observed and unobserved neighborhood attributes. Drug effects were not significantly altered, however, and only individual level models were presented to preserve statistical power and the precision of effect estimates. Additional sensitivity analyses based on the propensity score, a technique that can improve covariate balance beyond that achieved by ordinary multivariable regression,⁵² essentially confirmed the results reported herein.

This study also has several limitations that deserve mention. First, the effect of amphetamine use—a drug of increasing popularity—could not be examined since only one woman reported its use and toxicological screens were not routinely performed in the mid-1990s. However, the pharmacologic effects of amphetamine use are similar to cocaine and other epidemiologic studies suggest similar effects on

birth weight.^{25,53} Second, differences in gestational age or preterm birth were not evaluated out of concern for the reliability of gestational age estimation in a sample overrepresented for drug use and lack of prenatal care. The reported date of last menstrual period is less reliable for women with social risk factors and ultrasound-based estimation is most accurate when performed in the first trimester.⁵⁴ Moreover, the existing literature is more suggestive of illicit drug effects on birth weight or fetal growth than the length of gestation.⁷ Third, relative to the number of model parameters estimated, the sample size may have been limited to assess drug effects and interactions with great precision; there were large confidence intervals in most cases (for example, the fully adjusted odds ratio for LBW associated with opiate use of 1.74 could not be distinguished from 1). Finally, the potential for recall bias and/or error exists in any retrospective study. However, there is little empirical evidence of differential reporting of exposures according to pregnancy outcome.^{55,56} Moreover, the clinic-based prospective alternative to a retrospective study would have excluded the third of drug users who did not receive prenatal care—a very high risk group. Thus, concerns of selection bias exceeded those of recall bias.

CONCLUSIONS

Although illicit drug use is often strongly related to poor birth outcomes in crude associations, it is a powerful marker for multiple social, psychosocial, behavioral, and biomedical risk factors. In this study, psychosocial and behavioral factors, including stress, smoking, and late or no prenatal care, explained most of the birth weight decrements associated with illicit drug use. These factors may, therefore, warrant special focus in drug treatment programs for women of reproductive age. Given the preeminent role of factors other than drug use, however, broader prevention efforts that aim to improve newborn health must address the surrounding context in which drug use more commonly occurs.

ACKNOWLEDGEMENTS

This analysis and the original study from which it is based were funded by grants from the National Institute on Drug Abuse, National Institutes of Health; R03-DA020632 (Schempf) and R01-DA007621 (Strobino), respectively.

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