

The Protective Effect of Pregnancy on Risk for Drug Abuse: A Population, Co-Relative, Co-Spouse, and Within-Individual Analysis

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Objective: The authors sought to determine whether pregnancy is an intrinsic motivator for cessation of drug abuse.

Method: The authors conducted prospective cohort, co-relative, co-spouse, and within-person analyses of registration for drug abuse during pregnancy among Swedish women born between 1980 and 1990 who gave birth between ages 20 and 35 (N=149,512). Drug abuse was assessed from medical, criminal, and pharmacy registries.

Results: In the population, rates of drug abuse were lower during pregnancy (unadjusted odds ratio=0.67, 95% CI=0.60, 0.74). Compared with population results, the negative association between pregnancy and drug abuse was moderately stronger in cousins (odds ratio=0.49, 95% CI=0.39, 0.62) and substantially stronger in siblings (odds ratio=0.35, 95% CI=0.24, 0.51) discordant for pregnancy. The estimated odds ratio for drug abuse in pregnancy-discordant monozygotic twins was even stronger, at 0.17 (95% CI=0.10, 0.31). Within individuals, the odds ratio for drug abuse while pregnant compared with an equivalent prepregnancy interval was similar to that seen in pregnancy-discordant monozygotic

twins, at 0.22 (95% CI=0.19, 0.26). Compared with cohabiting fathers, mothers had a greater reduction in risk for drug abuse during pregnancy (odds ratio=0.40, 95% CI=0.34, 0.47). Pregnancy was more protective in women with low parental education and without a cohabiting, actively drug-abusing father. Compared with prepregnancy baseline, within-individual analyses indicate that risk for drug abuse is also substantially reduced in the postpartum period, for example, the odds ratio for postpartum days 0–242 was 0.13 (95% CI=0.11, 0.16).

Conclusions: Risk for drug abuse in women is substantially reduced during pregnancy. Multiple analyses suggest that this association is largely causal, suggesting that pregnancy is indeed a strong intrinsic motivator for drug abuse cessation. Similar strong protective effects may be present in the immediate postpartum period. Our results have implications for our etiologic models of drug abuse and especially for contingency management programs seeking to reduce drug abuse risk.

Am J Psychiatry 2017; 174:954–962; doi: 10.1176/appi.ajp.2017.16091006

While major advances have been made in understanding the neurobiological basis of addiction (1–3), the etiologic importance of volitional and motivational components in drug abuse has been supported by the efficacy of contingency management in drug abuse treatment (4–6). Voucher-based rewards as an extrinsic motivator for cessation are among the most effective psychosocial treatments for drug abuse (6).

In this study, we sought to expand our understanding of motivational factors in drug abuse by examining the unique natural experiment of pregnancy as a potential intrinsic motivator for reduction in drug abuse. The adverse impact of drug abuse on the developing fetus is well known (7–11), widely disseminated in modern Western cultures, and typically reinforced when pregnant women interact with health care providers

(12–14). Maternal prenatal attachment has been widely studied, and most drug-using mothers are strongly motivated to protect the health of their fetus and therefore to reduce or cease their drug use (15–17). This desire is often supported by their social network (18, 19). Thus, the degree to which rates of drug abuse decline during pregnancy can provide an estimate of the ability of motivated women to reduce their levels of substance misuse.

The causal nature of the association between pregnancy and drug abuse is likely complex. A *positive* pathway from drug abuse to pregnancy is suggested by evidence for an association between illicit substance use and teen pregnancy (20). Drug abuse and/or its risk factors likely increase the chances of unplanned and early pregnancy (21). However, longitudinal analyses have shown a reduction in use of tobacco,

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alcohol, cannabis, and cocaine during pregnancy in young adult women (22), and studies of clinical cohorts of pregnant women document a reduction in illicit substance use (23, 24), suggesting a *negative* pathway from pregnancy to drug abuse.

An optimal approach to clarifying the causal interrelationships between pregnancy and drug abuse would require a large, representative, population-based cohort that could be studied longitudinally and in which it would be possible to apply “natural” experimental methods to clarify causal pathways. We report such a study here. Using population-wide Swedish registry data, we evaluated four complementary methods to elucidate the nature of the relationship between pregnancy and drug abuse risk:

1. Population-based analyses with covariates.
2. Co-relative designs with pairs of relatives discordant for pregnancy.
3. Within-individual longitudinal designs comparing pregnancy with preceding nonpregnant periods.
4. A co-spouse design comparing changes in drug abuse risk in pregnant women and in the cohabiting fathers of their child.

We also explored whether the impact of pregnancy on risk for drug abuse varies as a function of parental education, prior deviant behaviors, school achievement, age, marital status, and drug abuse in the cohabiting father of the child. Finally, using within-individual analysis only, we examined whether the reduction in rates of drug abuse during pregnancy persisted into the immediate postpartum period.

METHOD

We utilized several different Swedish population-based registers with national coverage, linking them by each person's unique identification number. To preserve confidentiality, this identification number was replaced by a serial number. We secured ethical approval for the study from the Regional Ethical Review Board of Lund University (no. 2008/409). Drug abuse was identified in the Swedish medical registries by ICD codes (ICD-9: drug-induced mental disorders [292] and drug dependence [304], and nondependent abuse of drugs [305, excluding 305.0]; ICD-10: mental and behavioral disorders due to psychoactive substance use [F10–F19], except those due to alcohol [F10] or tobacco [F17]). Drug abuse was identified in the Suspicion Register by codes 3070, 5010, 5011, and 5012, which reflect crimes related to drug abuse, and in the Crime Register by references to laws covering narcotics (law 1968:64, paragraph 1, point 6) and drug-related driving offenses (law 1951:649, paragraph 4, subsection 2 and paragraph 4A, subsection 2). Each individual could have several registrations in the criminal (Crime and Suspicion) and medical registers. To avoid double-counting registrations, within each type of register (criminal and medical), we allowed for a 90-day period after each registration in which a new registration was not counted.

To study the association between pregnancy and drug abuse, we selected all females born in Sweden between

1980 and 1990 who had at least one child registered in the Swedish multigenerational register where the mother was likely first aware of being pregnant between the ages of 20 and 35. We assumed an average of 280 days from the end of the last menstrual period to birth, a 28-day menstrual cycle, and the strong suspicion of pregnancy arising 10 days after the missed menstrual period. Therefore, we estimated that women were aware of being pregnant 242 days before birth ($280 - [28 + 10]$).

We matched each mother to five nonrelated control women with the same year and month of birth. Furthermore, the control woman had to be alive and registered in Sweden at the time of the case woman's pregnancy and not herself registered as being a mother or having a child within 9 months after the date of birth of the case woman's child. For all control women, we studied drug abuse during the same period as the case woman (case women, $N=149,512$; control women, $N=747,560$). In the next step, we replicated the matching approach, but instead of using nonrelated random individuals as controls, we matched on female cousins and full siblings. In order to achieve a significant number of control individuals, we allowed for up to 3 years' age difference between the case woman and the relative control woman. We matched 58,640 control cousins to 50,317 case women and 19,812 control siblings to 19,115 case women. By matching on cousins and siblings, we account for a number of unmeasured genetic and environmental factors shared among cousins and siblings. Finally, we studied drug abuse using a within-individual model comparing a 242-day period before the pregnancy to the pregnancy period.

We used conditional logistic regression, with a separate stratum for each case and her control(s), in which we compared drug abuse in the case individual (i.e., drug abuse during pregnancy) with drug abuse in the controls (i.e., drug abuse during a nonpregnant period). Model 1 was only a crude model, whereas in model 2 we adjusted for midparent educational status (≤ 9 years, 10–11 years, ≥ 12 years) and the individual's school achievement (grade point average in grade 9, usually at age 16; see reference 25).

We then combined the population, full sibling, and cousin data sets and performed two co-relative analyses. The first allowed all coefficients for each sample to be independent. In the second, we modeled the genetic resemblance assuming that it equaled 0 for the population, +0.125 for cousins, and +0.5 for full siblings. We compared this model with the previous model, using the Akaike information criterion (26). If the second model fit the data well, we obtained improved estimation of the drug abuse–pregnancy association among all types of relatives. In this model, we were also able to extrapolate an odds ratio for monozygotic twins (there was only one monozygotic twin registered for drug abuse while pregnant).

In additional analyses, we investigated whether the association between pregnancy and drug abuse was moderated by the following variables: midparent educational status; school achievement of the individual; lifetime registration of drug abuse in a parent (dichotomized into yes/no); drug abuse registration in the individual prior to the pregnancy period; registration for a psychiatric diagnosis in the inpatient or

TABLE 1. Observed Association of First Pregnancy With Registration for Drug Abuse in the General Population, in Cousin and Sibling Pairs Discordant for Pregnancy, and Within Individuals

Sample	N	Frequency of Drug Abuse Registration (%)		Model 1 ^a		Model 2 ^b		Effect Size for Model 1	
		Pregnancy	Control	Odds Ratio	95% CI	Odds Ratio	95% CI	Cohen's d	95% CI
Population	149,512	0.24	0.35	0.67	0.60, 0.74	0.41	0.37, 0.46	0.22	0.17, 0.28
Cousins	50,371	0.23	0.46	0.49	0.39, 0.62	0.33	0.26, 0.42	0.39	0.26, 0.52
Siblings	19,115	0.20	0.56	0.35	0.24, 0.51			0.58	0.37, 0.79
Within individuals									
First pregnancy									
242-day period before pregnancy	150,226	0.24	0.63	0.22	0.19, 0.26			0.83	0.74, 0.92
242-day period ending 6 months before start of pregnancy	150,226	0.24	0.61	0.25	0.21, 0.29			0.76	0.68, 0.86
242-day period ending 12 months before start of pregnancy	150,226	0.24	0.61	0.26	0.22, 0.31			0.74	0.64, 0.83
Second pregnancy	75,891	0.11	0.27	0.23	0.16, 0.33			0.81	0.61, 1.01

^a Unadjusted.^b Adjusted for mean parental education and school achievement.

specialist registries; criminal registration in the individual prior to the pregnancy period (for a definition of criminal registration, see reference 27); age at pregnancy (dichotomized into ≤ 25 years and > 25 years); marital status (dichotomized into married/not married; in the analyses of married people, individuals who got married during the control or hazard period were excluded); drug abuse registration in the child's father prior to the pregnancy period; and drug abuse registration in the child's father during the pregnancy period. These moderation analyses were performed only on the within-individual sample using an interaction term between the covariate of interest and drug abuse status in the mother. In the within-individual sample, we also tested whether the decrease in drug abuse rates between control and pregnancy periods was the same for mothers and fathers. This was done by including an interaction term between a dummy variable indicating mother or father, and drug abuse status in the mother and the father.

Finally, using within-individual analyses only, we examined the rates of drug abuse in the immediate postpartum period. Our control was the 242-day period before pregnancy, and we examined three 242-day postpartum risk periods: 0–242 days, 243–484 days, and 485–726 days after childbirth. We eliminated from these analyses mothers whose child died during the risk period. We included mothers who were no longer cohabiting with their child ($N=249$, $N=871$, and $N=1,187$ for the three periods, respectively) because these mothers had substantial elevations in drug abuse rates, suggesting that in some cases the child had been removed because of problematic behavior. Excluding them would bias the postpartum drug abuse rates downward.

In all these models, the within-individual and within-family clustering was taken into consideration. In models that included information on fathers, the father had to cohabit with the mother at the end of the calendar year when

the child was born. All statistical analyses were performed in SAS, version 9.3 (28).

RESULTS

Association Between Pregnancy and Registration for Drug Abuse

In our general population sample, when examined without covariates, rates of drug abuse registration were moderately lowered during pregnancy (odds ratio=0.67, 95% CI=0.60, 0.74) (Table 1). Adding parental education and subject educational achievement to the model substantially strengthened the association (odds ratio=0.41, 95% CI=0.37, 0.46), indicating that these factors acted as negative confounders attenuating the pregnancy–drug abuse relationship.

Compared with the general population examined without covariates, the negative association between pregnancy and drug abuse was stronger in cousins discordant for pregnancy (odds ratio=0.49, 95% CI=0.39, 0.62), and especially for sisters discordant for pregnancy (odds ratio=0.35, 95% CI=0.24, 0.51). We then fitted our co-relative model to results from the general population and discordant cousin, sibling, and monozygotic twin results. Our model fit better than the raw results and estimated the odds ratio for drug abuse in pregnancy-discordant monozygotic pairs at 0.17 (95% CI=0.10, 0.31) (Table 2).

We then examined our within-person model, first comparing the rate of drug abuse during a first pregnancy with the rate observed in the comparable 242-day period immediately prior to the estimated date of impregnation. The estimated odds ratio for drug abuse using this within-person design was 0.22 (95% CI=0.19, 0.26) (Table 1). Since drug use might be reduced for some women who are planning to become pregnant, we reran these analyses with the prepregnancy period set at 6 months and 12 months earlier. The odds ratios did not appreciably change (estimated at 0.25 [95% CI=0.21, 0.29] and 0.26 [95% CI=0.22,

0.31], respectively). The negative association between pregnancy and drug abuse registration for a second pregnancy (odds ratio=0.23, 95% CI=0.16, 0.33) did not differ significantly from that observed during the first pregnancy ($p=0.12$). The results from the population-based, co-relative, and within-individual analyses are summarized in Figure 1.

Using within-person analyses, rates of drug abuse were significantly lower in the second half than in the first half of pregnancy (odds ratio=0.58, 95% CI=0.46, 0.74). To examine whether the pregnancy effect could be confounded by marital status, we reran these analyses excluding case subjects who changed marital status between the control and pregnancy periods. The odds ratio was unchanged (odds ratio=0.22, 95% CI=0.19, 0.25).

In 130,368 cases, the mother was cohabiting with the father of her child at the end of the calendar year the child was born. When examined together, the reduction in risk for drug abuse registration from the control to the pregnancy period was larger for the pregnant mother (odds ratio=0.22, 95% CI=0.18, 0.28) than for the father (odds ratio=0.62, 95% CI=0.56, 0.68). In a co-spouse design, the reduction in risk in the control compared with the pregnancy period was much greater in the mother than the father (odds ratio=0.40, 95% CI=0.34, 0.47).

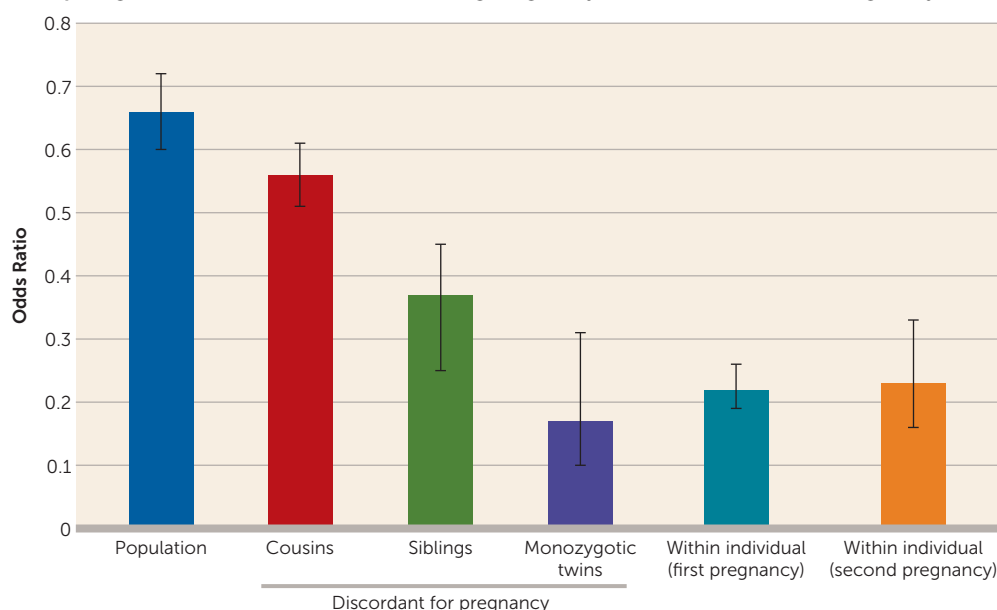
Finally, using within-individual analyses, we first examined, using a multiplicative model, a range of potential moderators of the protective effect of pregnancy on drug abuse risk (Table 3). These moderators were tested one at a time, and their p values of the interaction increased moderately if considered all together. The protective effect of pregnancy was stronger with lower compared with higher education for the mother's parents but was unrelated to drug abuse in the parents or to six other factors in the mother's background, including prior drug abuse registration. However, as illustrated in Figure 2, while we found similar risk ratios for high and low risk groups, we also saw widely varying risk differences. Pregnancy was associated with a much larger absolute reduction in drug abuse caseness in the high- versus low-risk groups, as reflected, for example, by a prior history of crime or drug abuse or single marital status. We then examined two features of drug abuse in the cohabiting spouse. The protective effect of pregnancy on drug abuse risk was

TABLE 2. Association Between Pregnancy and Drug Abuse in the General Population and in Cousins, Siblings, and Monozygotic Twins Discordant for Pregnancy, as Estimated by the Co-Relative Model^a

Sample	Estimated Odds Ratios	95% CI
Population	0.66	0.60, 0.72
Discordant cousins	0.56	0.51, 0.61
Discordant siblings	0.37	0.25, 0.45
Discordant monozygotic twins	0.17	0.10, 0.31

^a Akaike information criterion: observed=660440.34; predicted=660438.78.

FIGURE 1. Association Between Pregnancy and Risk for Drug Abuse in the General Population, in Cousins, Siblings, and Monozygotic Twins Discordant for Pregnancy, and Within Individuals (Comparing Matched Periods Before and During Pregnancy) for a First and Second Pregnancy^a



^a Odds ratios are unadjusted (that is, estimated from models without covariates). Error bars indicate 95% confidence intervals.

modestly attenuated by a prior history of drug abuse in the spouse and strongly attenuated by spousal drug abuse during pregnancy.

Risk for Registration for Drug Abuse in the Immediate Postpartum Period

To examine whether the protective effect of pregnancy on drug abuse extended into the postpartum period, we conducted within-individual analyses using as baseline the rates of drug abuse in the 242-day prepregnancy period. As shown in Table 4, rates of drug abuse registration were even lower in the immediate postpartum period (0–242 days) than during pregnancy (odds ratio=0.13, 95% CI=0.11, 0.16). The rates of drug abuse rose modestly in subsequent periods—243–484 days after childbirth (odds ratio=0.15, 95% CI=0.10, 0.18) and 485–726 days after childbirth (odds ratio=0.23, 95% CI=0.19, 0.28)—so that by 2 years postpartum, rates of drug abuse in these new mothers were similar to rates seen during their pregnancy.

TABLE 3. Potential Moderators of the Effect of Pregnancy on Risk for Drug Abuse

Measure	N	Rates of Drug Abuse (%)		Difference (%)	Interaction p	Odds Ratio	95% CI
		Pregnancy	Control				
General potential moderators							
Parental education ^a					0.026		
Low	43,458	0.32	0.84	0.52		0.19	0.15, 0.23
Mid	83,428	0.22	0.61	0.39		0.25	0.21, 0.30
High	7,967	0.20	0.36	0.16		0.34	0.23, 0.49
Drug abuse in mother's parents					0.870		
No	142,592	0.18	0.50	0.32		0.22	0.19, 0.26
Yes	7,634	1.26	2.95	1.69		0.23	0.17, 0.31
School achievement (SD units) ^b					0.286		
−2.5 to −1.5	15,853	1.07	2.79	1.72		0.21	0.18, 0.25
−1.5 to −0.5	38,047	0.30	0.81	0.51		0.23	0.20, 0.26
−0.5 to 0.5	58,622	0.09	0.28	0.19		0.25	0.20, 0.31
0.5 to 1.5	33,225	0.05	0.08	0.03		0.26	0.19, 0.37
1.5 to 2.5	4,479	0.09	0.04	−0.05		0.28	0.18, 0.45
Prior crime (in mother)					0.194		
No	139,408	0.11	0.33	0.22		0.24	0.20, 0.29
Yes	10,818	1.81	4.43	2.62		0.20	0.16, 0.25
Prior drug abuse (in mother)					0.119		
No	146,420	0.08	0.26	0.18		0.24	0.21, 0.30
Yes	3,806	6.38	14.74	8.36		0.20	0.16, 0.24
Prior psychiatric diagnosis					0.150		
No	298,494	0.23	0.62	0.39		0.23	0.20, 0.26
Yes	979	0.72	2.45	1.73		0.06	0.01, 0.38
Age at pregnancy					0.117		
−25	73,828	0.34	0.97	0.63		0.21	0.18, 0.25
25+	76,398	0.14	0.30	0.16		0.27	0.21, 0.35
Married ^c					0.652		
No	119,325	0.27	0.72	0.45		0.22	0.19, 0.26
Yes	14,870	0.14	0.37	0.23		0.19	0.10, 0.36
Features of cohabiting biological father's drug abuse as potential moderators							
Prior drug abuse in father					0.097		
No	124,408	0.03	0.13	0.10		0.16	0.11, 0.23
Yes	5,960	1.90	4.68	2.78		0.23	0.18, 0.30
Drug abuse during pregnancy in all fathers					<0.001		
No	129,700	0.05	0.19	0.14		0.17	0.13, 0.22
Yes	668	12.13	19.11	6.98		0.35	0.26, 0.46

^a Parental education was used as a continuous term in the models, hence only one interaction term. The reported odds ratios are an illustration of the odds ratios at different levels of parental education.

^b School achievement was used as a continuous term in the models, hence only one interaction term. The reported odds ratios are an illustration of the odds ratios at different levels of school achievement.

^c In the analyses of married people, individuals who got married during the control or hazard period were excluded; for these individuals, we could not separate out whether the effect was due to marriage or pregnancy.

DISCUSSION

We utilized multiple approaches to clarify the magnitude and causal nature of the association between pregnancy and drug abuse in Swedish women. We addressed five specific questions, which we review in turn here with the results.

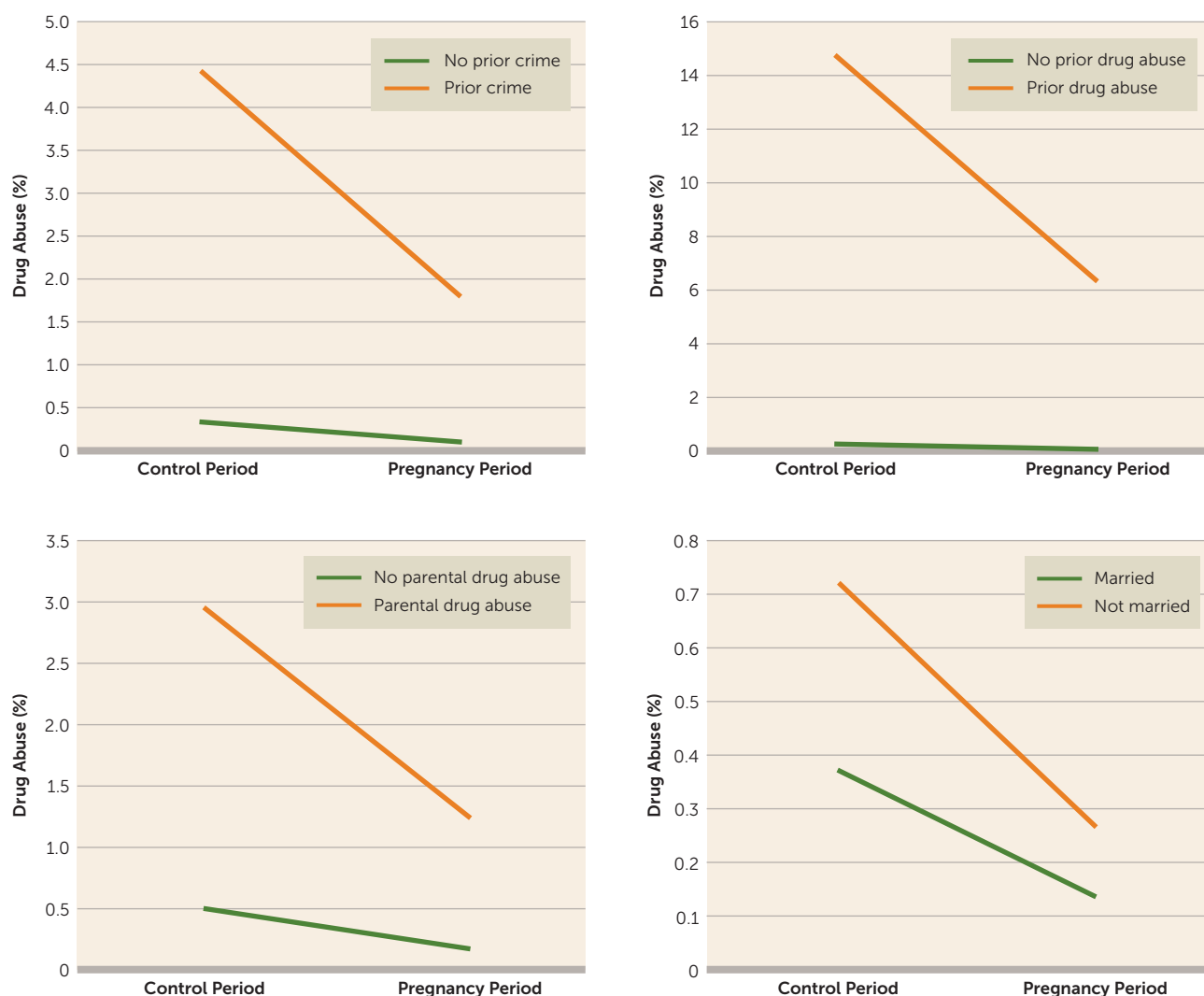
First, consistent with previous studies (20, 23, 24, 29), we showed a moderate cross-sectional inverse association between pregnancy and rates of drug abuse. When controlling for parental education and subject school achievement, this association substantially strengthened, suggesting inverse

confounding. With these covariates, rates of drug abuse were reduced by 60% during pregnancy.

Second, we applied a co-relative design examining risk for drug abuse in pairs of related women discordant for pregnancy. As expected given inverse familial confounding, the pregnancy–drug abuse association became progressively stronger the more closely related the members of the relative pair were. Using a model that fit the data well, we could predict a reduction of 83% in risk for drug abuse in a pregnant woman compared with her nonpregnant monozygotic co-twin.

Third, because pregnancy is episodic and discrete, we could conduct within-individual analyses with subjects

FIGURE 2. Estimated Risk for Drug Abuse During the Control Periods and Pregnancy as a Function of Four Potential Moderators: Prior Crime, Parental Drug Abuse, Prior Drug Abuse (in the Pregnant Mother) and Marital Status^a



^a Estimates are from logistic regression models with interaction terms (as seen in Table 3).

acting as their own control. Compared with the immediately preceding equivalent time period, rates of drug abuse declined 78% during pregnancy—nearly identical to the rate estimated in pregnancy-discordant monozygotic twins. We also showed that the protective effect of pregnancy was not affected by changing marital status, was similar in first and second pregnancies, and was stronger in the second half than in the first half of pregnancy. While conclusions from observational data are always tentative, our results from population findings with covariates, our co-relative analyses, and our within-person analyses are consistent in suggesting that the large majority of the inverse association between pregnancy and drug abuse is causal in nature.

These results can be usefully compared with results from several previous studies. In longitudinal analyses of data from the Monitoring the Future study (22), 4% of pregnant women reported using cannabis in the past 30 days, a rate one-third that of matched nonpregnant women. Multivariate analyses

found that most of this effect was independent of other predictors, including marital status. Cross-sectional analyses of recent U.S. national survey data (29) showed that the rate of recent cannabis use in the second and the third trimester of pregnancy among females 12–44 years of age was 3.6% and 1.7%, respectively, compared with 7.6% in a matched group of nonpregnant women. In a sample of 1,492 consecutive prenatal care patients from four urban U.S. clinics (23), 55.6% of mothers using illicit drugs reported cessation during pregnancy. In a sample of 1,336 mothers from the Baltimore-Washington Infant Study (24), 54.6% of mothers who reported illicit drug use quit during pregnancy. Finally, nurse-midwife reports of smoking rates in pregnant women in Sweden (30) show a decline in both heavy smoking and any smoking, from 12.3% and 21.9%, respectively, prior to pregnancy to 3.3% and 10.1%, respectively, at week 30–32. The validity of these smoking measures is supported by a much higher risk of chronic obstructive pulmonary disease in women still smoking in their third trimester (30).

TABLE 4. Within-Individual Analyses of Rates of Drug Abuse in the Prepregnancy (Control) Compared With Postpartum Periods

Risk Period	N	Prevalence of Drug Abuse (%)		Odds Ratio	95% CI
		Control Period ^a	Risk Period		
0–242 days after childbirth	126,586	0.65	0.14	0.13	0.11, 0.16
243–484 days after childbirth	110,067	0.66	0.16	0.15	0.10, 0.18
485–726 days after childbirth	93,799	0.66	0.22	0.23	0.19, 0.28

^a All control periods are the 242 days before birth.

We examined an array of variables that might moderate the impact of pregnancy on drug abuse. For most of them, including prior crime or drug abuse (which strongly predicted risk for drug abuse during pregnancy), the protective effect of pregnancy (as indexed by the odds ratio) was similar in those at low and high baseline risk. However, as shown in Figure 2, taking a risk difference approach shows that pregnancy reduces the number of drug abuse episodes far more in those at high prior risk than in those at low prior risk. Features of drug abuse in the cohabiting father of the child weakened the protective effect of pregnancy, particularly when the father was abusing drugs during the pregnancy.

Fourth, studying multiple pregnancies and patterns of drug abuse in the cohabiting child's father provides some insights into the mechanism of the drug abuse–pregnancy association. If it is driven largely by long-term changes in attitudes toward drug use, we would expect an attenuation of the protective effect over multiple pregnancies. If, by contrast, the reduction results from a time-limited desire to reduce fetal exposure, then the effect might be more similar across pregnancies. Our results that show similar protective effects for a first and second pregnancy support the latter hypothesis. The large reduction in rates of drug abuse in the pregnant woman compared with the cohabiting father allows us to isolate the impact of her direct motivation to reduce exposure to her child from more general social pressures on the couple. However, the rate of drug abuse among cohabiting fathers is reduced modestly during their partners' pregnancy, and fathers who abstain likely encourage the mothers' abstinence. Indeed, the protective effect of pregnancy on drug abuse risk in mothers weakened when the husband abused drugs during the pregnancy.

Finally, using within-individual analyses, we examined whether the large reduction in risk for drug abuse during pregnancy persisted into the immediate postpartum period. We found that it did, and indeed, during the first year postpartum, rates of drug abuse fell even lower, to 84% below their prepregnancy rates. They then climbed gradually, so that by approximately 2 years after birth, rates of drug abuse were similar to those observed during pregnancy.

Whereas postpartum drug abuse relapse is common in the United States, ranging from 27% for cocaine to 41% for marijuana (31) and up to 85% for cigarettes (32), our study showed, after birth, a further decrease in drug abuse below rates observed in pregnancy. Higher rates of breastfeeding among Swedish women (33–35) may play a role in this, as

breastfeeding appears to be protective against relapse to alcohol (36) and cigarette smoking (37). Klee (38) has reviewed the wide range of factors that might contribute to a protective effect of parenting on drug abuse. More specifically, and consistent with our findings, Bachman

et al. (39), using longitudinal data from the Monitoring the Future study, observed, among both women who remained married and those who remained single, considerable reductions in cannabis and cocaine use associated with the transition to parenthood.

Recent meta-analyses of controlled trials of contingency management in the treatment of drug abuse estimated effect sizes (Cohen's *d*) of 0.32 (5), 0.42 (4), and 0.58 (6). Using our within-person analyses, the effect size for pregnancy and early parenthood on drug abuse registration were larger ($d=0.83$, 95% CI=0.74, 0.92, and $d=1.12$, 95% CI=1.01, 1.21, respectively), suggesting strong motivation in the mother to protect her developing child and young infant from the direct and indirect effects of drug exposure.

While pregnancy intrinsically motivates many women to discontinue drug abuse, others do not quit. For them, pregnancy provides obstetrics practitioners and counselors with a “teachable moment” to kindle maternal motivation to abstain from drug use (40). Research finds that contingency management can further encourage prenatal care (41) and counseling session attendance (42, 43). Despite some evidence that extrinsic motivation interferes with intrinsic motivation to stop smoking (44), integrated therapies for drug abuse are gaining support, often pairing interventions that promote intrinsic motivation, such as motivational interviewing, with extrinsic contingency motivation (44).

These results should be interpreted in the context of five potential methodological limitations. First, our results are limited to the Swedish population and may not extrapolate to other countries. Second, drug abuse was ascertained using medical and criminal records, which are not dependent on subject cooperation or accurate recall. Compared with interviews, these methods likely generate both false positive and, particularly, false negative diagnoses. While large interview-based studies of drug abuse prevalence have not been conducted in Sweden, lifetime prevalence of drug abuse or dependence in nearby Norway is only slightly higher than the estimates we obtain using our methods in Sweden (46). Third, we cannot rule out additional factors, such as counseling from nurse midwives or threats of child removal influencing pregnant women's decisions to cease drug abuse. However, removal of children from mothers is rare in Sweden; in a recent year, it involved only 0.08% of children 0–3 years of age (47).

Fourth, because of frequent amenorrhea, drug-abusing women may have a delayed recognition of pregnancy. We therefore reran our within-person analyses assuming that

the women did not recognize their pregnancy until 32 days after what would have typically been their last menstrual period. The resulting odds ratio for drug abuse during pregnancy (odds ratio=0.23, 95% CI=0.19, 0.27) was nearly identical to that found in our main analyses.

Fifth, pregnancy could have an impact on our methods of drug abuse ascertainment. To examine this, we repeated the within-person analyses for drug abuse based on our two most common forms of ascertainment. The protective effect of pregnancy on drug abuse was clearly seen but was slightly weaker from medical (odds ratio=0.32, 95% CI=0.26, 0.40) than from criminal registration (odds ratio=0.20, 95% CI=0.16, 0.25). A similar but more striking difference was seen in the immediate postpartum period, when the protective effects were weaker from medical (odds ratio=0.19, 95% CI=0.15, 0.25) than from criminal registration for drug abuse (odds ratio=0.09, 95% CI=0.07, 0.13).

CONCLUSIONS

While definitive resolution of causal questions in observational data is impossible, multiple lines of evidence suggest that women voluntarily decrease their levels of drug abuse during pregnancy and early parenthood. Whereas we have made major advances in the understanding the biological basis of addiction (1–3), there are limitations to an exclusively brain-based view of drug abuse. Consistent with previous studies of contingency management (4–6), this study suggests that volitional and motivational components can interact with biological vulnerabilities and neurobiological changes to alter the course of drug abuse. Understanding the strong and often effective motivation demonstrated by pregnant women and young mothers to stop their drug abuse may help us improve our contingency management treatment methods.

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Supported by grants R01DA030005 and UG1DA013034 from the National Institutes of Health, grants K2012-70X-15428-08-3, 2012-2378, and 2014-10134 from the Swedish Research Council, grants 2013-1836 and 2013-0804 from the Swedish Research Council for Health, Working Life, and Welfare (Forte), and ALF (Medical Training and Research Agreement) funding from Region Skåne.

The authors report no financial relationships with commercial interests.

Received Sept. 6, 2016; revision received Feb. 20, 2017; accepted March 27, 2017; published online June 9, 2017.

REFERENCES

- Leshner AI: Addiction is a brain disease, and it matters. *Science* 1997; 278:45–47
- Koob GF, Le Moal M: *Neurobiology of Addiction*. London, Elsevier-Academic Press, 2006
- Koob GF, Volkow ND: Neurocircuitry of addiction. *Neuropsychopharmacology* 2010; 35:217–238
- Prendergast M, Podus D, Finney J, et al: Contingency management for treatment of substance use disorders: a meta-analysis. *Addiction* 2006; 101:1546–1560
- Lussier JP, Heil SH, Monge JA, et al: A meta-analysis of voucher-based reinforcement therapy for substance use disorders. *Addiction* 2006; 101:192–203
- Dutra L, Stathopoulou G, Basden SL, et al: A meta-analytic review of psychosocial interventions for substance use disorders. *Am J Psychiatry* 2008; 165:179–187
- Gunn JK, Rosales CB, Center KE, et al: Prenatal exposure to cannabis and maternal and child health outcomes: a systematic review and meta-analysis. *BMJ Open* 2016; 6:e009986
- Cain MA, Bornick P, Whiteman V: The maternal, fetal, and neonatal effects of cocaine exposure in pregnancy. *Clin Obstet Gynecol* 2013; 56:124–132
- Richardson GA, Goldschmidt L, Larkby C, et al: Effects of prenatal cocaine exposure on adolescent development. *Neurotoxicol Teratol* 2015; 49:41–48
- Kwiatkowski MA, Roos A, Stein DJ, et al: Effects of prenatal methamphetamine exposure: a review of cognitive and neuroimaging studies. *Metab Brain Dis* 2014; 29:245–254
- Baldacchino A, Arbuckle K, Petrie DJ, et al: Neurobehavioral consequences of chronic intrauterine opioid exposure in infants and preschool children: a systematic review and meta-analysis. *BMC Psychiatry* 2014; 14:104
- Smith E, Kamel I, Mastrogianis DS: Drug addiction and pregnancy, part 2: management of pregnancy complicated by substance abuse. *J Postgrad Gynecol Obs* 2014; 34:1–7
- ACOG Committee on Health Care for Underserved Women; American Society of Addiction Medicine: ACOG Committee Opinion No 524: Opioid abuse, dependence, and addiction in pregnancy. *Obstet Gynecol* 2012; 119:1070–1076
- Haug NA, Duffy M, McCaul ME: Substance abuse treatment services for pregnant women: psychosocial and behavioral approaches. *Obstet Gynecol Clin North Am* 2014; 41:267–296
- Brandon AR, Pitts S, Denton WH, et al: A history of the theory of prenatal attachment. *J Prenat Perinat Psychol Health* 2009; 23: 201–222
- Cannella BL: Maternal-fetal attachment: an integrative review. *J Adv Nurs* 2005; 50:60–68
- Yarcheski A, Mahon NE, Yarcheski TJ, et al: A meta-analytic study of predictors of maternal-fetal attachment. *Int J Nurs Stud* 2009; 46: 708–715
- Hutchins E, DiPietro J: Psychosocial risk factors associated with cocaine use during pregnancy: a case-control study. *Obstet Gynecol* 1997; 90:142–147
- Gatny H, Barber J, Kusunoki Y: Young Women and Substance Use During Pregnancy: The Role of Social Support (Report 13-788). Ann Arbor, University of Michigan, Institute for Social Research, Population Studies Center, April 2013. www.psc.isr.umich.edu/pubs/pdf/rr13-788.pdf
- Salas-Wright CP, Vaughn MG, Ugalde J, et al: Substance use and teen pregnancy in the United States: evidence from the NSDUH 2002–2012. *Addict Behav* 2015; 45:218–225
- Kirby D: Looking for Reasons Why: The Antecedents of Adolescent Sexual Risk-Taking, Pregnancy, and Child-Bearing. Washington, DC, National Campaign to Prevent Teen Pregnancy, 1999
- Bachman JG, Wadsworth KN, O'Malley PM, et al: Smoking, Drinking, and Drug Use in Young Adulthood: The Impacts of New Freedoms and New Responsibilities. Mahwah, NJ, Lawrence Erlbaum Associates, 1997
- Harrison PA, Sidebottom AC: Alcohol and drug use before and during pregnancy: an examination of use patterns and predictors of cessation. *Matern Child Health J* 2009; 13:386–394

24. Johnson SF, McCarter RJ, Ferencz C: Changes in alcohol, cigarette, and recreational drug use during pregnancy: implications for intervention. *Am J Epidemiol* 1987; 126:695–702
25. Kendler KS, Ohlsson H, Mezuk B, et al: A Swedish national prospective and co-relative study of school achievement at age 16, and risk for schizophrenia, other nonaffective psychosis, and bipolar illness. *Schizophr Bull* 2016; 42:77–86
26. Akaike H: Factor analysis and AIC. *Psychometrika* 1987; 52:317–332
27. Kendler KS, Larsson Lönn S, Morris NA, et al: A Swedish national adoption study of criminality. *Psychol Med* 2014; 44:1913–1925
28. SAS Institute: SAS/STAT User's Guide, Version 9.3. Cary, NC, SAS Institute, 2011
29. Alshaarawy O, Anthony JC: Cannabis use during pregnancy for the United States, 2005–2013 (abstract). *Drug Alcohol Depend* 2017; 171:e6–e7
30. Kendler KS, Lönn SL, Sundquist J, et al: Smoking and schizophrenia in population cohorts of Swedish women and men: a prospective co-relative control study. *Am J Psychiatry* 2015; 172:1092–1100
31. Forray A, Merry B, Lin H, et al: Perinatal substance use: a prospective evaluation of abstinence and relapse. *Drug Alcohol Depend* 2015; 150:147–155
32. Fang WL, Goldstein AO, Butzen AY, et al: Smoking cessation in pregnancy: a review of postpartum relapse prevention strategies. *J Am Board Fam Pract* 2004; 17:264–275
33. Socialstyrelsen: Statistics on Breastfeeding 2014 (Article No 2016-9-20). Stockholm, Socialstyrelsen (National Board of Health and Welfare), 2016. <http://www.socialstyrelsen.se/Lists/Artikelkatalog/Attachments/20333/2016-9-20.pdf>
34. Yngve A, Sjöström M: Breastfeeding in countries of the European Union and EFTA: current and proposed recommendations, rationale, prevalence, duration and trends. *Public Health Nutr* 2001; 4 (2B):631–645
35. Callen J, Pinelli J: Incidence and duration of breastfeeding for term infants in Canada, United States, Europe, and Australia: a literature review. *Birth* 2004; 31:285–292
36. Giglia R, Binns C: Alcohol and lactation: a systematic review. *Nutr Diet* 2006; 63:103–116
37. Forray A: Substance use during pregnancy. *F1000Res* 2016; 5:887
38. Klee H: Drugs and parenting, in *Drug Misuse and Motherhood*. Edited by Klee H, Jackson M, Lewis S. London, Routledge, 2002
39. Bachman JG, Wadsworth KN, O'Malley PM, et al: Marriage, divorce, and parenthood during the transition to young adulthood: impacts on drug use and abuse, in *Health Risks and Developmental Transitions During Adolescence*. Edited by Schulenberg J, Maggs JL. Cambridge, UK, Cambridge University Press, 1997, pp 246–281
40. McBride CM, Emmons KM, Lipkus IM: Understanding the potential of teachable moments: the case of smoking cessation. *Health Educ Res* 2003; 18:156–170
41. Elk R, Mangus L, Rhoades H, et al: Cessation of cocaine use during pregnancy: effects of contingency management interventions on maintaining abstinence and complying with prenatal care. *Addict Behav* 1998; 23:57–64
42. Svikis DS, Silverman K, Haug NA, et al: Behavioral strategies to improve treatment participation and retention by pregnant drug-dependent women. *Subst Use Misuse* 2007; 42:1527–1535
43. Jones HE, Haug N, Silverman K, et al: The effectiveness of incentives in enhancing treatment attendance and drug abstinence in methadone-maintained pregnant women. *Drug Alcohol Depend* 2001; 61:297–306
44. Curry SJ, Wagner EH, Grothaus LC: Evaluation of intrinsic and extrinsic motivation interventions with a self-help smoking cessation program. *J Consult Clin Psychol* 1991; 59:318–324
45. Budney AJ, Higgins ST, Radonovich KJ, et al: Adding voucher-based incentives to coping skills and motivational enhancement improves outcomes during treatment for marijuana dependence. *J Consult Clin Psychol* 2000; 68:1051–1061
46. Kringlen E, Torgersen S, Cramer V: A Norwegian psychiatric epidemiological study. *Am J Psychiatry* 2001; 158:1091–1098
47. Socialstyrelsen: Statistik om socialtjänstinsatser till barn och unga 2014 (Article No 2015-12-33). Stockholm, Socialstyrelsen (National Board of Health and Welfare), 2015. <http://www.socialstyrelsen.se/Lists/Artikelkatalog/Attachments/20015/2015-12-33.pdf>