ORIGINAL ARTICLE

Familial Confounding of the Association Between Maternal Smoking During Pregnancy and Offspring Criminality

A Population-Based Study in Sweden

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Context: The association between maternal smoking during pregnancy (SDP) and offspring disruptive behaviors has been well documented, but it is unclear whether exposure to SDP or the effects of factors correlated with SDP account for the increased risk.

Objective: To test whether the association between SDP and offspring criminal convictions was consistent with a causal connection or due to familial background factors by controlling for measured covariates and using a quasi-experimental approach.

Design: We used a population-based study of children born in Sweden from 1983 to 1989 (N = 609 372) to examine the association between SDP and offspring criminal convictions while controlling for measured traits of both parents. We also compared siblings differentially exposed to SDP (n = 50 339) to account for unmeasured familial factors that could account for the association.

Setting: Population-based study of all children born in Sweden from 1983 to 1989 with information on maternal SDP and offspring criminal convictions based on national registries collected by the Swedish government.

Patients or Other Participants: Children born in Sweden from 1983 to 1989 (N = 609 372) and siblings differentially exposed to SDP (n = 50 339).

Main Outcome Measures: Violent and nonviolent convictions, based on the Swedish National Crime Register, a register with detailed information on all convictions in the country.

Results: Moderate (hazard rate [HR], 2.47; 95% confidence interval [CI], 2.34-2.60) and high (HR, 3.43; 95% CI, 3.25-3.63) levels of maternal SDP were associated with an increased risk for offspring violent convictions, even when controlling for maternal and paternal traits. There was no association between SDP and violent convictions, however, when comparing differentially exposed siblings ($HR_{moderate}$, 1.02; 95% CI, 0.79-1.30; HR_{high}, 1.03; 95% CI, 0.78-1.37). Smoking during pregnancy also was associated with nonviolent convictions in the entire population ($HR_{moderate}$, 1.62; 95% CI, 1.58-1.66; HR_{high}, 1.87; 95% CI, 1.82-1.92) and when controlling for covariates. But, there was no association when comparing siblings who were differentially exposed ($HR_{moderate}$, 0.89; 95% CI, 0.78-1.01; HR_{high}, 0.89; 95% CI, 0.78-1.02).

Conclusion: The results suggest that familial background factors account for the association between maternal SDP and criminal convictions, not the specific exposure to SDP.

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MATERNAL SMOKING during pregnancy (SDP) has consistently been linked with disruptive behaviors in offspring,[1-4] including parent-reported conduct problems,[5,6] diagnoses of oppositional defiant[7] and conduct disorders,[8-10] and arrest history from national crime registries.[11,12] Reviews have noted that the associations are consistent with a causal connection because they are specific to disruptive behaviors (and related constructs), have been found across diverse samples and using different measures, demonstrate a dose-response relationship, and are commensurate with findings from basic research, including animal studies.[1,2,13]

Many researchers, however, have noted that causal interpretations are impossible to prove because the association between SDP and offspring behavior may be due to risk factors associated with SDP rather than the influence of prenatal nicotine exposure.[1,14,15] Smoking during pregnancy is correlated with many parental and family environmental factors that also predict criminal and psychiatric problems in children, such as low socioeconomic sta-

tus,[16,17] young age of childbearing,[2,17] history of maternal[14] and paternal antisocial behavior,[18] and poor family functioning.[19] Genetic factors could also explain the relation between SDP and offspring disruptive behaviors.[13,14,20-23] Smoking during pregnancy has been shown to be influenced by genetic factors.[20,24] Mothers who smoke during pregnancy, therefore, could pass down genetic risk for disruptive behaviors to their offspring.[25]

A number of studies have used numerous quasi-experimental designs, approaches that use natural experiments, to explore the mechanisms through which SDP is associated with offspring development.[4] Recent sibling comparison,[5,6,23,26,27] children of twins,[28] and prenatal in vitro fertilization (IVF) cross-fostering[29,30] studies suggest the associations between SDP and offspring conduct problems, academic achievement, intellectual abilities, and attention-deficit/hyperactivity disorder are better explained by background familial factors. The use of quasi-experimental approaches, therefore, suggests that later neurocognitive and behavioral problems that are associated with SDP may actually be due to background familial factors rather than the teratogenic effects of SDP.

The quasi-experimental studies of the association between SDP and offspring disruptive behaviors are limited, however. The extant sibling comparison studies[5,6] are based on behaviors in young children. Using IVF to study SDP is a novel approach for disentangling genetic confounds from prenatal risks,[29,30] but the findings for SDP need to be replicated, as the results were based on parent report of behavior problems during childhood from a small study of children conceived through IVF. And, many studies are confounded by the fact that mothers reported on both SDP and offspring behaviors.[31] Certainly, causal inferences can only be drawn based on converging evidence from multiple studies using various designs, each with their own strengths and weaknesses.[32]

The current article explores the association between maternal SDP and offspring criminal behavior using a population study of all individuals born in Sweden during a span of 7 years. The study statistically controlled for measured covariates from both mothers and fathers, a limitation of many existent studies of SDP,[18] and compared siblings differentially exposed to SDP. The comparison of siblings is a powerful approach for testing causal inferences because the design rules out most genetic factors that can confound the association between SDP and offspring criminality, as well as all environmental factors that make siblings similar.[31,33,34] The assessments of criminal behavior were based on government records of convictions, which assess serious violations during late adolescence and early adulthood that are not based on parental report. The study also included assessment of the offspring that were highly associated with criminal convictions, including an independent evaluation of all men in the country as part of the mandatory armed forces evaluation at age 18 years and school grades at age 15 years, which gave the opportunity to provide converging evidence. As such, the current study provides a rigorous test of the underlying etiological factors that increase the risk for serious criminal behavior associated with maternal SDP.

METHODS

SAMPLE

The sample was based on merging Swedish population registries that are maintained by government agencies in Sweden. The current study is based on a subset of offspring with information on criminal convictions from a larger sample with reports of maternal SDP.[23]

The Swedish Medical Birth Registry, which is maintained by the Swedish Centre for Epidemiology at the National Board of Health and Welfare, includes information on more than 99% of all births in Sweden since 1973.[35] The information is gathered during pregnancy and delivery using standardized assessments and records. Beginning in 1983, the register included assessment of maternal SDP at the first antenatal visit. The Medical Birth Registry also includes assessments of demographics, family structure, maternal age, birth order, physical attributes of the children, and complications.

The National Crime Register is a register maintained by the Swedish National Council for Crime Prevention that includes all registered convictions in Sweden (from 1973-2004). The register includes information about every conviction, including the type of offense and sentence type. Merging the data set in the study provided criminal background information starting at age 15 years (the age of criminal responsibility in Sweden) for the offspring, as well as the criminal records for their mothers and fathers.

The Conscript Registry includes all 18-year-old men in Sweden since 1970 (tested for compulsory military service) with systematic data on cognitive, psychological, and physical performance.[35] The Education Register is maintained by Statistics Sweden and includes information about the highest obtained level of education and type of degree for each individual. We used the highest level of education in 2004 for the mothers and fathers of the target children in the study. The Education Register also includes assessments of achievement, including summary grades for all students at the end of grade 9.[23,26] The 1990 Swedish Population and Housing Census was an assessment of individuals in each household in Sweden, which included measures of employment, occupation, and income. The Cause of Death Register contains data on the date and cause of deaths, and the Migration Register includes the dates of migration in and out of Sweden.

The Multi-Generation Register is a large database maintained by Statistics Sweden that contains each individual's unique identifier, as well as information on the identity of the parents of each child born in Sweden since 1932 or who immigrated and became Swedish citizens before age 18 years.[36] The information allowed us to link all children to their biological fathers (based on maternal reports) and identify all siblings. Because of the focus on maternal SDP, all siblings in the current study share the same mother (ie, they are either full siblings or maternal half siblings).[23]

Between 1983 and 1989, 709 125 children were included in the Medical Birth Registry. Children who had serious malformations at birth (n=12 220), were from multiple births (eg, twins and triplets) (n=14 375), died (n=6262), or emigrated from the country (n=24 482) were not eligible for inclusion in the analyses, leaving 654 954 offspring. Offspring who were missing the identification number of their mother (n=745) or who were missing data on SDP (n=50 660) were then excluded from the sample, resulting in a sample of 609 372 offspring (93% of the targeted population and 86% of all births).

MEASURES

Offspring Outcomes

Violent crime is defined according to the Swedish Penal Code as attempted or completed murder, manslaughter, and filicide (offense codes 3:1-3:3), aggravated assault (3:5-3:6), gross violation of a person's integrity (4a), kidnapping and illegal restraint (4:1-4:2), illegal coercion and threats (4:4-4:5), harassment (4:7), aggravated robbery (8:5-8:6), aggravated arson (13:1-13:2), and/or threats or violence against an officer (17:1). Any sexual offense was also included (rape, sexual coercion, child molestation, and sexual harassment, including indecent exposure [6:1-6:10, 6:12]). This corresponds to a wider definition of violent offending that was used in earlier scientific reports on this sample.[37,38] Analyses are only based on first conviction for repeat offenders. Kaplan-Meier estimates of conviction for a violent crime in the sample indicate that 2.3% of individuals were convicted by 21.9 years of age.

Nonviolent crime is defined as all other convictions, including crimes according to the Narcotic Drugs Act and Traffic Offenses Act. Kaplan-Meier estimates from the current sample indicate a higher prevalence of nonviolent crime (10.1%) by age 21.9 years.

The sample included 93 675 men with information from the Conscript Registry. The registry includes an evaluation of military officer suitability, which is an independent evaluation of the ability of each man to hold positions of greater responsibility in the military based on 2 days of interviews and standardized assessments, including a psychiatric evaluation.[39] Previous research has shown that the scale is the most powerful predictor of later functioning in the military when compared with the other assessments included in the registry.[39] The measure of low military officer suitability, which was based on the lowest 2 stanines (6.24%), was highly associated with convictions for later violent (hazard rate [HR], 3.98; $b_{logit}=1.38$; SE=0.09; $P<.001$) and nonviolent (HR, 1.78; $b_{logit}=0.57$; SE=0.04; $P<.001$) crimes in the current sample.

The study also included assessment of performance in grade 9 for 605 294 offspring; 15.1% were identified as having low academic performance, commensurate with failing.[26] Low academic performance was highly associated with later violent (odds ratio [OR], 11.35; 95% confidence interval [CI], 10.81-11.93) and nonviolent (OR, 3.69; 95% CI, 3.61-3.78) crimes, in addition to low military officer suitability (OR, 3.99; 95% CI, 3.69-4.31).

Risk Factors

Smoking during pregnancy was assessed at the first antenatal visit using 3 responses: no smoking, 1 to 9 cigarettes per day (moderate smoking), and 10 or more cigarettes per day (high). Analyses based on collapsing the moderate and high levels were commensurate with those presented herein (results available on request). Previous studies found that only 6% of self-reported nonsmokers in Sweden had serum cotinine levels indicating active smoking.[40] Studies in the United States[41] and Sweden[42] also suggest the validity of self-reported smoking has not changed over time. In the current sample, 28.8% of the offspring were exposed to SDP; documentation of decline in SDP during this span is available elsewhere.[2]

The Medical Birth Registry also included maternal age at birth, birth order, and gestational age of each child. Family structure at the time of birth was also assessed. Women reported either cohabiting or not cohabiting with the father of the child at childbirth.

A standard measure of socioeconomic status of both the mothers and fathers, as assessed by the census, was also included in the analyses.[43] The groupings include (1) unskilled blue collar worker, (2) skilled blue collar worker, (3) low-level white collar worker, (4) intermediate-level white collar worker, (5) high-level white collar worker, (6) self-employed, (7) employed but uncategorized, and (8) not working/missing. The final category included individuals too young to be assessed (younger than 15 years) and individuals who were not working at the time of the census (because they were students or unemployed). Because previous research has shown that the groupings cannot be ordered,[44] dummy codes were created to compare each occupational group with the unskilled blue collar worker category.

Maternal and paternal highest level of education was based on 7 categories: (1) less than 9 years of primary and lower secondary education, (2) 9 years of primary and lower secondary education, (3) 1 to 2 years of upper secondary education, (4) 3 years of upper secondary education, (5) less than 3 years of postsecondary education, (6) 3 or more years of postsecondary education, and (7) postgraduate education. Dummy codes were used to compare higher levels of education with having completed less than 9 years of primary education. Maternal and paternal history of criminal behavior for mothers and fathers was based on the presence or absence of a conviction for any criminal offense in the National Crime Register through 2004.

Demographic characteristics are presented in **Table 1**. Previous analyses using the current sample have found that maternal SDP is associated with all of the covariates.[23,27] Smoking during pregnancy is associated with earlier age at childbearing for mothers and fathers, earlier gestational age, greater likelihood the mother is not cohabiting with the biological father, lower maternal and paternal occupation status, lower maternal and paternal socioeconomic status, and greater risk of maternal and paternal history of criminal convictions.

STATISTICAL ANALYSES

Estimates of Risks Comparing Unrelated Individuals and Differentially Exposed Siblings

For descriptive purposes, estimates of risk for violent and nonviolent convictions based on Kaplan-Meier estimates were calculated separately for unexposed and exposed individuals (collapsing the moderate and high SDP categories) in 2 samples. The first sample was based on all offspring and, thus, reflected the increased risk of criminal convictions associated with SDP in the total population. The second sample was based solely on differentially exposed siblings (n=29 842). The comparison of risk for convictions in differentially exposed siblings provides an estimate of the risk associated with SDP while controlling for background familial factors. If SDP caused convictions, siblings exposed to SDP would have greater risk for criminality than their siblings who were not exposed.[31,33,34]

Survival Analyses Models

Formal statistical analyses of the association between the levels of SDP and criminality were conducted using survival analyses because the measures of convictions were right censured (ie, each offspring had not lived through risk period). The models used a sandwich estimator to take into account clustering of individuals in extended families. Both moderate and high levels of SDP were compared with no SDP in each model by using dummy codes. The first model regressed each outcome on maternal SDP using the entire sample, controlling for offspring sex and birth order.

The second model explored the association between SDP and criminality while controlling for measured covariates. The

Table 1. Demographic Characteristics

Variable	Sample Size	%
Maternal age at childbirth, y, mean (SD)	609 372	29.9 (5.1)
Paternal age at childbirth, y, mean (SD)	606 951	31.4 (5.9)
Gestational age, wk, mean (SD)	608 895	39.8 (1.7)
Offspring sex (female)	609 372	48.6
Birth order	609 372	
First born		41.6
Second born		35.5
Third born		16.4
≥Fourth born		6.4
Parents not cohabiting at childbirth	599 110	2.7
Maternal education	601 271	
<9 y Primary and lower secondary education		2.4
9 y Primary and lower secondary education		11.2
1-2 y Upper secondary education		38.5
3 y Upper secondary education		13.3
<3 y Postsecondary education		16.8
≥3 y Postsecondary education		17.4
Postgraduate education		0.5
Maternal occupation	608 551	
Unskilled blue collar		28.6
Skilled blue collar		11.2
Low-level white collar		13.9
Intermediate-level white collar		16.9
High-level white collar		6.0
Self-employed		2.6
Employed, uncategorized		6.2
Not working/missing		14.6
Maternal history of criminal conviction	609 372	11.9
Paternal education	583 771	
<9 y Primary and lower secondary education		5.6
9 y Primary and lower secondary education		16.3
1-2 y Upper secondary education		37.5
3 y Upper secondary education		12.3
<3 y Postsecondary education		12.8
≥3 y Postsecondary education		14.0
Postgraduate education		1.4
Paternal occupation	603 283	
Unskilled blue collar		21.1
Skilled blue collar		22.1
Low-level white collar		8.3
Intermediate-level white collar		15.6
High-level white collar		13.3
Self-employed		7.5
Employed, uncategorized		4.8
Not working/missing		7.3
Paternal history of criminal conviction		40.7

model included offspring-specific covariates, maternal traits, and paternal traits. The models were based on subsets of the sample with complete data (pairwise deletion); the models were fit with 566 183 individuals (93% of the total sample).

The third model examined the association between SDP and each outcome comparing siblings who were differentially exposed when considering moderate and high levels of SDP (n=50 339). We used standard fixed-effects models[45] for survival analyses that fit separate hazard functions for each nuclear family.[46] The analyses controlled for all factors shared by siblings, which estimated the association between SDP and convictions using within-mother variation in SDP. The models, therefore, compare siblings who were differentially exposed.[47] The analyses also controlled for offspring sex and birth order, which is important when conducting sibling comparison models.[34]

Sensitivity Analyses

Because of the size of the data and complexity of the analyses, more advanced approaches of handling missing values[48] in model 2 were difficult to fit. The first set of sensitivity analyses, however, tested how robust the results were to the use of pairwise deletion. Two additional models were run for each measure of criminality, a worst-case and a best-case scenario. The worst-case scenario replaced each missing value with the value conferring the greater risk for the outcome (eg, parents were assigned a positive history of criminal convictions), whereas the best-case scenario assigned values associated with a decreased risk of each outcome (eg, parents were assigned a negative history of criminal convictions). Comparing the size of the SDP parameter in these 2 conditions with the value from model 2 provided an estimate of the possible bias in the parameter values due to pairwise deletion.

Additional models testing the association between SDP and low military officer suitability were also conducted to see whether the results replicated the findings for criminality. Comparisons of unrelated individuals and differentially exposed siblings were conducted using logistic regressions. Previous studies have already reported on sibling comparison analyses of low academic achievement at the end of grade 9, suggesting familial confounding of the association between SDP and grades.[23,26]

Finally, we tested the assumption inherent in the sibling comparison design that the results from women who varied their smoking across pregnancies would be different from women who did not. One way to test the assumption is to assess whether the association between SDP and each outcome among unrelated individuals is comparable in 2 groups: (1) a sample of women who varied their smoking across pregnancies and (2) a sample of women with more than 1 child who did not vary their smoking across pregnancies (the women never smoked or smoked the same in each pregnancy).[4] Survival models assessed the between-family association between SDP and each outcome in the subset of offspring from the first group (n=50 339) and second group (n=337 168) separately. We then used interaction effects to test whether the magnitude of the associations between the 2 groups was statistically significant in a subset of the data that included all offspring of women with more than 1 child (combining the 2 groups described earlier). The analyses controlled for offspring sex, birth order, and number of children in each family.

RESULTS

ESTIMATES OF RISKS COMPARING UNRELATED INDIVIDUALS AND DIFFERENTIALLY EXPOSED SIBLINGS

Kaplan-Meier estimates of risk for violent criminal convictions are presented graphically in **Figure 1**. Figure 1A graphs the increasing risk of being convicted of a violent offense across the ages of 15 to 21 years for the entire sample, depending on exposure to maternal SDP. As the graph illustrates, maternal SDP was associated with roughly a 3-fold increased risk in criminal convictions of a violent nature. Figure 1B presents the risk for violent offenses in the sample of differentially exposed siblings. Exposed and unexposed siblings had similar rates of convictions of violent crime.

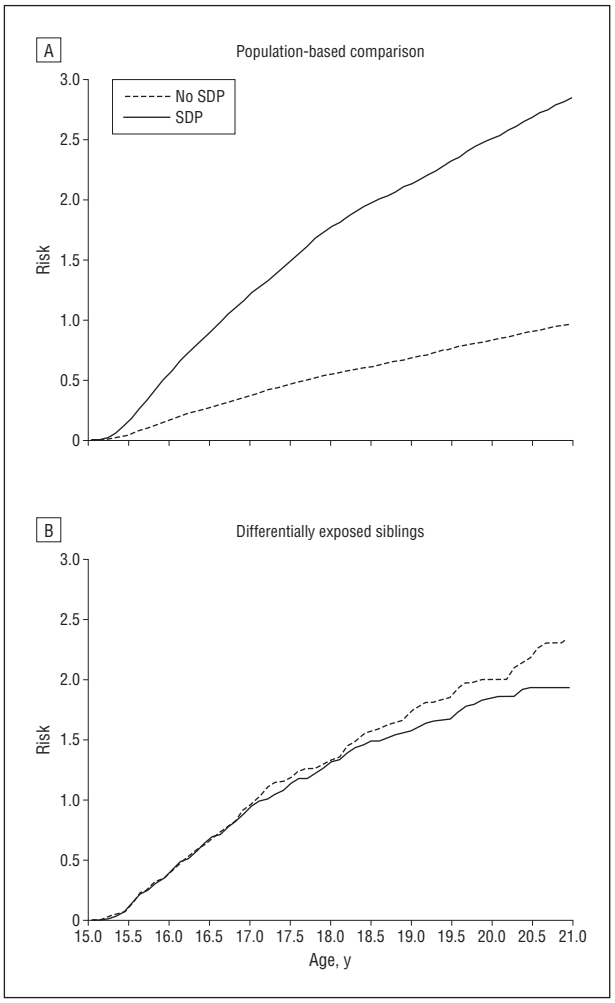

Figure 1. Association between maternal smoking during pregnancy (SDP) and offspring convictions for violent offenses. A, Population-based comparison. B, Differentially exposed siblings.

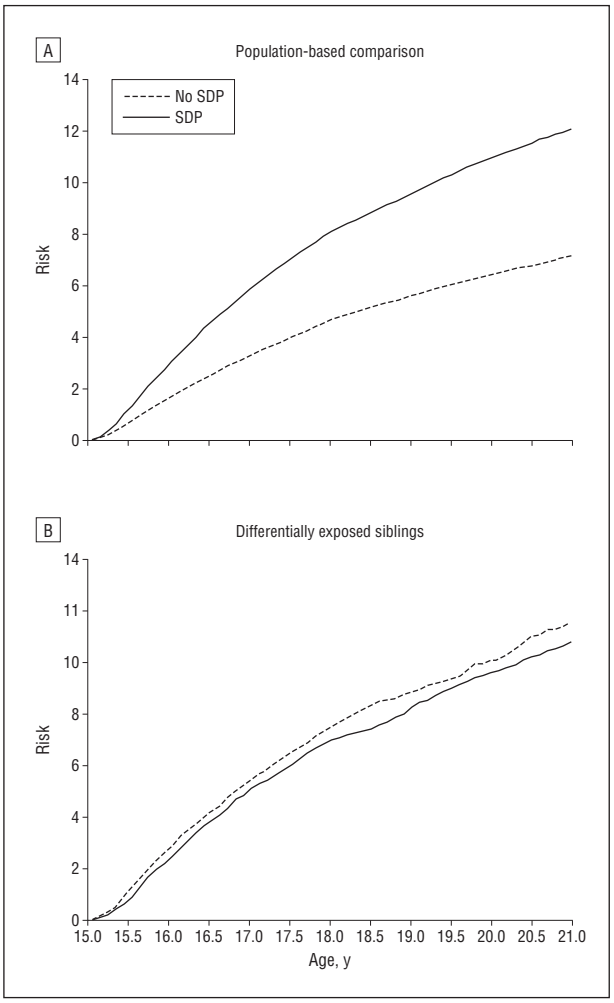

Figure 2. Association between maternal smoking during pregnancy (SDP) and offspring convictions for nonviolent offenses. A, Population-based comparison. B, Differentially exposed siblings.

Figure 2 presents the Kaplan-Meier estimates for convictions for nonviolent offenses. Figure 2A, based on the entire sample, suggests offspring exposed to SDP were at increased risk for being convicted of a nonviolent offense. Figure 2B, based on the subset of differentially exposed siblings, however, indicates that exposed and unexposed siblings had equivalent rates of nonviolent convictions. The Figures suggest that the association between SDP and criminal convictions was due to background familial risks.[32,33]

SURVIVAL ANALYSES

The results of the survival analyses predicting violent offenses are presented in **Table 2**. Model 1, which estimates the raw association with SDP, found that offspring exposed to moderate (HR, 2.47; 95% CI, 2.34-2.60) and high (HR, 3.43; 95% CI, 3.25-3.63) levels of SDP were more likely to be convicted of a violent offense. The inclusion of the measured covariates in model 2 reduced the associations, but SDP still uniquely predicted violent convictions ($HR_{moderate}$, 1.57; 95% CI, 1.48-1.67; HR_{high}, 1.87; 95% CI, 1.42-1.99). Model 3 compared differentially exposed siblings using fixed-effects models. The results indicate that SDP was not associated with violent offenses when comparing differentially exposed siblings ($HR_{moderate}$, 1.02; 95% CI, 0.79-1.30; HR_{high}, 1.03; 95% CI, 0.78-1.37), signifying that SDP was not associated with violent offenses when controlling for background familial factors.

The parameter estimates of the survival models predicting offspring nonviolent offenses are presented in **Table 3**. Model 1 indicated that SDP is associated with an increased risk of nonviolent offenses ($HR_{moderate}$, 1.62; 95% CI, 1.58-1.66; HR_{high}, 1.87; 95% CI, 1.82-1.92) in the entire population. Model 2 indicated that SDP still robustly predicted nonviolent offenses when statistically controlling for the measured covariates ($HR_{moderate}$, 1.31; 95% CI, 1.27-1.34; HR_{high}, 1.38; 95% CI, 1.34-1.42). Model 3 revealed no associations between levels of SDP and nonviolent convictions ($HR_{moderate}$, 0.89; 95% CI, 0.78-1.01; HR_{high}, 0.89; 95% CI, 0.78-1.02) when comparing differentially exposed siblings, findings consistent with the results from the models predicting violent convictions. Survival analyses on subsets of the database on year of birth (1983-1986 and 1987-1989) were consistent with those presented in the text (results available on request).

Table 2. Survival Models Predicting Violent Crimes[a]

Risk Factor	b (SE)		
	Model 1[b]	Model 2[c]	Model 3[d]
No SDP	1 [Reference]	1 [Reference]	1 [Reference]
Moderate SDP (1-9 cigarettes/d)	0.90 (0.03)[e]	0.45 (0.03)[e]	0.02 (0.12)
High SDP (≥10 cigarettes/d)	1.23 (0.03)[e]	0.62 (0.03)[e]	0.03 (0.14)
Offspring sex (female)	–1.54 (0.03)[e]	–1.57 (0.03)[e]	–1.40 (0.07)[e]
Birth order	0.10 (0.01)[e]	0.22 (0.01)[e]	0.01 (0.03)
Maternal age at childbirth		–0.06 (0.00)[e]	
Paternal age at childbirth		–0.01 (0.00)[e]	
Gestational age		0.01 (0.00)[e]	
Parents not cohabiting at childbirth		0.46 (0.05)[e]	
Maternal education <9 y		1 [Reference]	
9 y Of education		–0.13 (0.06)[e]	
1-2 y Upper secondary education		–0.25 (0.06)[e]	
3 y Upper secondary education		–0.46 (0.08)[e]	
<3 y Postsecondary education		–0.45 (0.08)[e]	
≥3 y Postsecondary education		–0.59 (0.08)[e]	
Postgraduate education		–1.23 (0.51)[e]	
Maternal occupation unskilled blue collar		1 [Reference]	
Skilled blue collar		–0.09 (0.04)[e]	
Low-level white collar		–0.12 (0.04)[e]	
Intermediate-level white collar		–0.14 (0.06)[e]	
High-level white collar		–0.24 (0.10)[e]	
Self-employed		–0.18 (0.09)[e]	
Employed, uncategorized		0.10 (0.05)[e]	
Not working/missing		0.10 (0.03)[e]	
Maternal history of criminal conviction		0.57 (0.03)[e]	
Paternal education <9 y		1 [Reference]	
9 y Of education		–0.11 (0.05)[e]	
1-2 y Upper secondary education		–0.12 (0.04)[e]	
3 y Upper secondary education		–0.22 (0.06)[e]	
<3 y Postsecondary education		–0.40 (0.07)[e]	
≥3 y Postsecondary education		–0.50 (0.08)[e]	
Postgraduate education		–0.57 (0.23)[e]	
Paternal occupation unskilled blue collar		1 [Reference]	
Skilled blue collar		–0.12 (0.03)[e]	
Low-level white collar		–0.19 (0.06)[e]	
Intermediate-level white collar		–0.30 (0.05)[e]	
High-level white collar		–0.33 (0.07)[e]	
Self-employed		–0.26 (0.05)[e]	
Employed, uncategorized		0.20 (0.05)[e]	
Not working/missing		0.29 (0.04)[e]	
Paternal history of criminal conviction		0.73 (0.03)[e]	

Abbreviation: SDP, smoking during pregnancy.
[a] Parameters are distributed as logits.
[b] Based on the total sample (N = 609 372).
[c] Based on data with no missing data (n = 566 183).
[d] Based on fixed-effects model that examined differentially exposed siblings (SDP, n = 50 339).
[e] $P < .05$.

SENSITIVITY ANALYSES

Two additional models, a worst-case and best-case scenario, were run to test whether the results from model 2 were robust to the assumptions of generalizability given pairwise deletion. For each measure of criminality, the first 2 decimal places for each unstandardized parameter estimate (logits) did not change (full results available on request). The sensitivity analyses, therefore, indicated that the results of the models that controlled for measured covariates were quite robust.

Smoking during pregnancy was associated with increased risk for low military officer suitability in the entire population ($OR_{moderate}$, 1.34; 95% CI, 1.25-1.44; OR_{high}, 1.65; 95% CI, 1.52-1.46), even when controlling for the measured covariates ($OR_{moderate}$, 1.16; 95% CI, 1.08-1.25; OR_{high}, 1.33; 95% CI, 1.21-1.46). But, the comparison of differentially exposed siblings using fixed-effects models ($OR_{moderate}$, 0.83; 95% CI, 0.61-1.13; OR_{high}, 0.93; 95% CI, 0.73-1.19) suggests no association, which parallels the findings for criminal convictions.

We tested whether the association between SDP and convictions using unrelated individuals differed for mothers who did and did not vary their smoking across multiple pregnancies. The association between SDP and violent criminal offenses in unrelated individuals in the subset of women with variation in SDP across pregnancies ($HR_{moderate}$, 2.29; 95% CI, 1.62-3.24; HR_{high}, 3.63; 95% CI,

Table 3. Survival Models Predicting Nonviolent Crimes[a]

Risk Factor	b (SE)		
	Model 1[b]	Model 2[c]	Model 3[d]
No SDP	1 [Reference]	1 [Reference]	1 [Reference]
Moderate SDP (1-9 cigarettes/d)	0.48 (0.01)[e]	0.27 (0.01)[e]	–0.12 (0.07)
High SDP (≥10 cigarettes/d)	0.63 (0.01)[e]	0.32 (0.02)[e]	–0.12 (0.07)
Offspring sex	–0.71 (0.01)[e]	–0.72 (0.01)[e]	–0.68 (0.011)[e]
Birth order	0.02 (0.00)[e]	0.07 (0.01)[e]	0.08 (0.02)[e]
Maternal age at childbirth		–0.02 (0.00)[e]	
Paternal age at childbirth		0.00 (0.00)	
Gestational age		0.02 (0.00)[e]	
Parents not cohabiting at childbirth		0.25 (0.03)[e]	
Maternal education <9 y		1 [Reference]	
9 y Of education		–0.01 (0.04)	
1-2 y Upper secondary education		–0.03 (0.03)	
3 y Upper secondary education		–0.09 (0.04)[e]	
<3 y Postsecondary education		–0.15 (0.04)[e]	
≥3 y Postsecondary education		–0.10 (0.04)[e]	
Postgraduate education		0.00 (0.10)	
Maternal occupation unskilled blue collar		1 [Reference]	
Skilled blue collar		–0.03 (0.02)	
Low-level white collar		–0.07 (0.02)[e]	
Intermediate-level white collar		–0.07 (0.02)[e]	
High-level white collar		–0.08 (0.03)[e]	
Self-employed		0.01 (0.04)	
Employed, uncategorized		0.12 (0.02)[e]	
Not working/missing		0.04 (0.02)[e]	
Maternal history of criminal conviction		0.37 (0.01)[e]	
Paternal education <9 y		1 [Reference]	
9 y Of education		0.03 (0.03)	
1-2 y Upper secondary education		0.01 (0.02)	
3 y Upper secondary education		–0.04 (0.03)	
<3 y Postsecondary education		–0.10 (0.03)[e]	
≥3 y Postsecondary education		–0.08 (0.03)[e]	
Postgraduate education		–0.02 (0.06)	
Paternal occupation unskilled blue collar		1 [Reference]	
Skilled blue collar		–0.01 (0.02)	
Low-level white collar		–0.06 (0.03)[e]	
Intermediate-level white collar		–0.10 (0.02)[e]	
High-level white collar		–0.08 (0.03)[e]	
Self-employed		–0.02 (0.02)	
Employed, uncategorized		0.18 (0.03)[e]	
Not working/missing		0.22 (0.03)[e]	
Paternal history of criminal conviction		0.43 (0.01)[e]	

Abbreviation: SDP, smoking during pregnancy.
[a] Parameters are distributed as logits.
[b] Based on the total sample (N = 609 372).
[c] Based on data with no missing data (n = 566 183).
[d] Based on fixed-effects model that examined differentially exposed siblings (SDP, n = 50 339).
[e] $P < .05$.

2.82-4.66) was somewhat smaller than in women who did not vary their smoking ($HR_{moderate}$, 2.77; 95% CI, 2.55-3.01; HR_{high}, 4.10; 95% CI, 3.77-4.46), but the differences were small and not statistically significant ($b_{logits\text{-}moderate} = -0.18$; SE = 0.18; $P = .31$; $b_{logits\text{-}high} = -0.13$; SE = 0.13; $P = .33$). The findings for nonviolent convictions were similar. The associations in women without variation in SDP ($HR_{moderate}$, 1.44; 95% CI, 1.21-1.73; HR_{high}, 1.77; 95% CI, 1.55-2.01) were generally consistent with the association in women who did not vary their smoking ($HR_{moderate}$, 1.65; 95% CI, 1.58-1.71; HR_{high}, 2.04; 95% CI, 1.95-2.13), and the differences were not statistically significant ($b_{logits\text{-}moderate} = -0.13$; SE = 0.09; $P = .16$; $b_{logits\text{-}high} = -0.13$; SE = 0.07; $P = .08$). The sensitivity analyses, thus, indicate the findings from the fixed-effects models are not due to the differences between women with and without variation in their SDP across their pregnancies.

COMMENT

The current study, which was based on a population-based study of offspring born in Sweden over 7 years, explored the risk associated with SDP for violent and nonviolent convictions, acts associated with enormous societal and personal costs. Although the association between SDP and criminality showed a dose-dependent response and

was robust when controlling for measured traits of both mothers and fathers, differentially exposed siblings had the same risk for being convicted. The results suggest that the increased risk of convictions associated with SDP is due to familial background factors, not the putative biological effects of SDP.

The results for criminality support and extend the findings of recent sibling comparison[5,6] and IVF[29] studies of SDP that were based on smaller samples and assessed conduct problems during childhood.[30] The findings are also commensurate with quasi-experimental studies of traits associated with delinquency, such as poor academic achievement,[23,26] low intellectual abilities,[27] and attention-deficit/hyperactivity disorder.[28,30] The findings for convictions were replicated using highly correlated assessments based on independent evaluations (military officer suitability), school grades,[23,26] and standardized measures of achievement[23] in the same sample. The use of quasi-experimental studies of SDP as a whole,[4] therefore, seriously calls into question causal inferences concerning the teratogenic effects of SDP for certain later neurocognitive and behavioral problems in offspring.

Most research on SDP has typically found robust statistical associations between SDP and disruptive behaviors while controlling for correlated risks,[2,13] as was the case in the current study. The results of the sibling comparison analyses, therefore, imply that familial factors that are not frequently measured (or measured well) in research protocols are actually responsible for the increased risk in offspring whose mothers smoke during pregnancy. Future research will need to include better assessment of possible environmental confounds (eg, maternal report of conduct disorder as a teenager[21] and antisocial behavior of both parents[18]) and use designs that can examine whether shared genetic liability accounts for the statistical associations.[23,29] Designs that can further elucidate the underlying causal mechanisms include randomized controlled interventions targeting SDP,[49] studies exploring variation in SDP within pregnancies,[50] different patterns of SDP across pregnancies (comparing women who stop smoking vs those who begin smoking over time),[51] adoptions studies,[52] and the children of twins/siblings,[5,20,23,53] to name a few possibilities.[4,32]

The study also has some limitations. Using criminal convictions as a measure of delinquency can limit the interpretation of the results. Children younger than 15 years cannot be convicted, and certain crimes (eg, homicide) have a higher probability of leading to a verdict. The use of convictions inevitably covers less than the true prevalence of criminal behavior, but this will not necessarily affect the magnitude of the association with SDP because findings for criminality based on self-report and official records are often similar across different exposures.[54] The assessment of convictions also was only available until the offspring reached 21.9 years of age, which does not cover the entire risk period for convictions. Future research will need to study the association between SDP and criminality throughout adulthood and specifically study whether SDP is independently associated with other outcomes, such as drug and alcohol problems.[55] The findings for convictions, however, were consistent with those for low military officer suitability, a measure available on all men in Sweden at the age of 18 years, and other traits in the entire Swedish sample (eg, academic achievement[23,26] and intellectual abilities[27]) that are highly associated with criminality. The assessment of SDP was based on maternal report, which is not as accurate as using biological assays to measure extent of smoking, and the measure only differentiated between moderate and high levels of SDP. Smoking during pregnancy was only assessed during the first trimester of pregnancy, so we were also unable to examine possible differences in the timing or pattern of use. Such assessments were included in the Medical Birth Registry in later years, which will allow researchers to examine such questions once those offspring reach late adolescence.

The sibling comparison design also has a number of inherent assumptions.[4,33] We examined whether women who varied their smoking across multiple pregnancies were comparable with women who did not. The results suggest that the association between SDP and criminality was slightly less in women who altered their smoking, but the differences were small and not statistically significant. The design can only account for environmental factors that influence siblings similarly and also assumes that traits of the offspring do not influence maternal SDP.[23]

Furthermore, we did not explore moderators of the association between SDP and offspring criminality (eg, pregnancy complications[11] or genetic risk measured by candidate genes[4]). The current findings, however, have implications for such research. Smoking during pregnancy may only influence offspring who are particularly at risk, or the identified moderators could be interacting with background familial factors.

Given the limitations of the current study and of previous quasi-experimental research, definitive conclusions concerning SDP can only be drawn from considering all research on the topic.[4,32] The challenge for the research field is to incorporate the recent quasi-experimental findings, which implicate the importance of familial confounding, with the results from the existent traditional family studies that support the causal hypothesis. More translational research is also needed to understand how these findings fit with animal studies, which some researchers suggest are not conclusive about the association between SDP and aggressive behavior.[30,56] Certainly, more interdisciplinary research is needed to truly understand mechanisms underlying the association between SDP and offspring disruptive problems. The current study, as well as other recent reports, suggests that quasi-experimental studies will play an important role in the endeavor.[4]

The results of the current study, however, do not indicate that SDP is benign. Recent quasi-experimental studies suggest that SDP causes pregnancy-related problems. Children of twins,[20] sibling comparison[5,6] (including the current sample[23]), prenatal IVF cross-fostering,[29] and intervention studies[49] indicate that the association between SDP and offspring birth weight is consistent with a causal effect. A recent study from Sweden that compared consecutive births also found that SDP is independently associated with infant mortality.[57] Reducing SDP, therefore, remains an important public health issue.

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