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**IMPORTANCE** Peer deviance (PD) strongly predicts externalizing psychopathologic conditions but has not been previously assessable in population cohorts. We sought to develop such an index of PD and to clarify its effects on risk of drug abuse (DA).

**OBJECTIVES** To examine how strongly PD increases the risk of DA and whether this community-level liability indicator interacts with key DA risk factors at the individual and family levels.

**DESIGN, SETTING, AND PARTICIPANTS** Studies of future DA registration in 1,401,698 Swedish probands born from January 1, 1970, through December 31, 1985, and their adolescent peers in approximately 9,200 small community areas. Peer deviance was defined as the proportion of individuals born within 5 years of the proband living in the same small community when the proband was 15 years old who eventually were registered for DA.

**MAIN OUTCOMES AND MEASURES** Drug abuse recorded in medical, legal, or pharmacy registry records.

**RESULTS** Peer deviance was associated with future DA in the proband, with rates of DA in older and male peers more strongly predictive than in younger or female peers. The predictive power of PD was only slightly attenuated by adding measures of community deprivation, collective efficacy, or family socioeconomic status. Probands whose parents were divorced were more sensitive to the pathogenic effects of high PD environments. A robust positive interaction was also seen between genetic risk of DA (indexed by rates of DA in first-, second-, and third-degree relatives) and PD exposure.

**CONCLUSIONS AND RELEVANCE** With sufficient data, PD can be measured in populations and strongly predicts DA. In a nationwide sample, risk factors at the level of the individual (genetic vulnerability), family (parental loss), and community (PD) contribute substantially to risk of DA. Individuals at elevated DA risk because of parental divorce or high genetic liability are more sensitive to the pathogenic effects of PD. Although the effect of our PD measure on DA liability cannot be explained by standard measures of community or family risk, we cannot, with available data, discriminate definitively between the effect of true peer effects and other unmeasured risk factors.
Exposure to high peer deviance (PD) in childhood and adolescence is among the strongest known risk factors for drug use, drug abuse (DA), and other externalizing behaviors\(^1-4\) and figures prominently in developmental models of externalizing disorders.\(^5-8\) Obtaining a direct measure of PD is difficult and has been assessed in only small samples.\(^9,10\) Self-reported PD is easier to measure but subject to reporting bias.\(^11\)

We present a novel, objective, and nationwide method of assessing PD. For individuals still living with their parents (proband), we identify all individuals of similar age residing in the same small geographic area. We then follow up these peers into adulthood and determine the proportion registered for the deviant outcome(s) of interest. Although typical conceptualizations of PD measure current deviance, this approach assesses future deviant behavior. To avoid confounding PD and genetic risk, we eliminate as peers all close biological relatives of the proband.

We address 4 questions about DA, defined using medical, criminal, and pharmacy records, for all individuals in Sweden born from January 1, 1970, through December 31, 1985, and their peers. First, how strongly does PD predict risk of DA in the proband and does this relationship vary by the age window for peers, the age at which PD is assessed, or sex of the peer group or proband? Second, how much of the predictive relationship between PD and DA is accounted for by traditional measures of psychosocial risk? Third, do we add to our predictive ability by widening the definition of PD to include future peer alcohol use disorder (AUD) or violent criminal behavior (VCB)? Fourth, in the Swedish population, could we demonstrate that those at high genetic risk of DA were more sensitive to the effect of high PD?

We examine cross-level interactions in pathways to DA. In Swedish adoptees,\(^12\) adverse family environments increased the effect of genetic factors on risk of DA. Prior twin studies have found that exposure to high levels of PD increase the heritability of externalizing disorders,\(^13\) delinquent involvement,\(^14\) conduct problems,\(^15\) and substance use.\(^16\)

High-quality parenting can counteract the pathogenic effects of PD.\(^5,17-19\) Adoptive parental divorce, which typically reflects family discord, predicted DA in adoptees.\(^2\) We therefore examined whether individuals in the general population who experienced parental divorce were more sensitive to the pathogenic effects of high PD.

**Methods**

We linked data from multiple Swedish nationwide registries and health care data\(^2,20\) via the unique, individual, 10-digit personal identification number assigned at birth or immigration to all Swedish residents. Our database used the following registers: Total Population Register, containing annual data on family and geographic status; Multi-Generation Register, providing information on family relations; Swedish Hospital Discharge Register, containing all hospitalizations for Swedish inhabitants from 1964 to 2009; Swedish Prescribed Drug Register, containing all prescriptions in Sweden from 2005 to 2009; Outpatient Care Register, containing information from all outpatient clinics from 2001 to 2009; Primary Health Care Register, containing outpatient primary care data on diagnoses and time for diagnoses in 2001 to 2007 for 1 million patients from Stockholm and middle Sweden; Swedish Crime Register, which included national complete data on all convictions from 1973 to 2011; Swedish Suspicion Register, which included national complete data on all individuals strongly suspected of crime from 1998 to 2011; the Swedish Mortality Register, containing causes of death; and the Longitudinal Integration Database for Health Insurance and Labour Market Studies, containing annual information on socioeconomic factors on all individuals from 16 years of age. We secured ethical approval for this study from the Regional Ethical Review Board of Lund University. Our methods for identifying DA are given in eAppendix 1 in the Supplement.

The PD database included all individuals in the Swedish population who were born from January 1, 1970, through December 31, 1985, and registered in a geographic area at their year of birth at the ages of 5, 10, and 15 years; had their mother and father registered in the Multi-Generation Register; were living in the same household as their mother, father, or one or more grandparent at the age of 15 years; and were not registered for DA by 15 years of age. This database included 1 391 425 individuals.

Peer deviance was calculated using geographic areas—Small Areas for Market Statistics (SAMSS)—defined by Statistics Sweden. There are approximately 9200 SAMSS throughout Sweden. Their boundaries are defined by homogeneous building types, they have a mean of approximately 1000 inhabitants, and they approximate the concept of neighborhoods.\(^21\) Drug abuse was defined during the entire follow-up period. Our main PD measure was calculated at the proband age of 15 years and based on the proportion of future DA in the SAMSSs of individuals in an 11-year interval around the age of the proband. The median and mean number of individuals used in the calculation of the SAMs PD measure were 217 and 285, respectively. The correlation across SAMSSs between this number and the calculated level of PD was modest (correlation = +.08; P < .001). This procedure was repeated using 3-, 5-, and 7-year intervals and examining DA in only male or female peers in an 11-year interval. We calculated a younger and older PD measure based on the share of DA among individuals 1 to 5 years younger (older) than the proband. We also calculated a PD measure for the area where the proband resided at birth and at 5 and 10 years of age and a PD measure adding future registrations for AUDs and VCB in the same way as described above (eAppendix 2 in the Supplement).

In all PD calculations, the proband and close biological relatives (twins, full and half siblings, and first cousins) and SAMSSs with fewer than 30 peers were excluded. For each SAMs, we created a neighborhood social deprivation index based on register data on all residents aged 25 to 64 years using proportion of residents with low educational levels (≤9 years), proportion of residents with low household income (below half the median income), proportion of unemployed residents, and proportion of individuals receiving social assistance.\(^22\) The SAMS
voter participation rates in municipal elections were used as a validated measure of collective efficacy.\textsuperscript{23,24}

Parental educational level was included as a proxy for family socioeconomic status and defined as the highest educational level achieved by the mother or father categorized into 3 levels: low educational level (<9 years), middle educational level (10-11 years), and high educational level (≥12 years). We also examined parental loss due to divorce when the proband was 15 years of age or younger.

We calculated a genetic risk score for DA. We estimated the morbid risk for DA for the population 15 to 49 years old. To estimate the total “lifetimes at risk,” we divided the population into 3 groups: (1) individuals in the first quartile of the distribution of age at first DA registration (15-23 years old) were weighted 0, (2) individuals in the second and third quartiles (24-42 years old) were weighted 0.5, and (3) individuals in the last quartile (43-49 years old) were weighted 1.0. Thereafter, we performed a logistic regression analysis based on information from the Swedish population born in 1965 to 1969 and 1986 to 1990 (n = 1,384,450) and their relatives (monozygotic twins, dizygotic twins, full siblings, half siblings, mother, father, and cousins). The model outcome variable was DA, and the predictor variable was the morbid risk of DA among different relative types. The resulting β weights for the genetic risk score, which followed quantitative genetic expectations, are listed in Table 1. This model produced a predicted probability for DA ranging from 2.9% to 95.2%, which we called the genetic risk score.

We examined the association between PD and subsequent DA in individuals. Because of different exposure periods based on birth year, we used Cox proportional hazards regression with first DA registration as the outcome. The key predictor variable was PD. Because siblings from the same family could be included in the analysis, we adjusted for nonindependence with a robust sandwich estimator.\textsuperscript{25} In all models, we investigated the proportional-hazards assumption. If not fulfilled, we included an interaction term between the variable of interest and the logarithm of time. For most analyses, we used raw PD so that the hazard ratios (HRs) reflected the effect of a 1% increase in DA in peers. To compare PD across sexes, in which a 1% increase in males and females would differ in meaning, we z-transformed PD.

To examine interactions between PD and parental loss and the genetic risk score on an additive scale,\textsuperscript{26} we used the Aalen linear hazards model.\textsuperscript{27} The results from this model are presented as the excess number of cases per 10,000 person-years. Statistical analyses were performed using SAS statistical software, version 9.3,\textsuperscript{28} and the R-package, version 2.14.1.\textsuperscript{29}

### Results

#### Peer Deviance

Peer deviance, which reflects the rate of future DA in peers, was assessed at 15 years of age (unless otherwise specified) using 1,357,577 individuals who had complete data, were living with their parents or grandparents, and had no prior DA registration. Biological relatives of the proband through first cousins residing in the same SAMS were censored. The mean rate of PD across SAMSSs was 3.83% with a zero-inflated and right-skewed distribution (Figure 1). Peer deviance was moderately stable, correlating at +0.75, +0.61, and +0.51 at 15 years of age with PD assessed at 10 and 5 years of age and at birth, respectively. Peer deviance was substantially correlated with rates in the same peers for VCB (correlation = +0.60) and AUD (correlation = +0.44) and more modestly correlated with SAMSS-level social deprivation (correlation = +0.36). Peer deviance measured during an 11-year window (used for all analyses below) was correlated with parallel measures in 7-, 5-, and 3-year windows (correlation = +0.94, +0.89, and +0.81, respectively). The reliability of our PD measure, assessed from taking random halves of each SAMS, was +0.59.

#### Prediction of DA

A Cox proportional hazards regression model with a simple linear effect revealed that PD robustly predicted proband risk of DA ($\chi^2 = 6717.8; P < .001$). For every percent increase in peer DA, the HR for proband DA increased 1.32-fold (95% CI, 1.31-1.32). These estimates were corrected for clustering within siblings and were unchanged when clustering within SAMSSs was added to the model. The Cox proportionality assumption failed.

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**Table 1. Weights for Calculation of Genetic Risk Score for Drug Abuse**

<table>
<thead>
<tr>
<th>Variable*</th>
<th>Estimate (SE)</th>
<th>z Value</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>3.528 (0.006)</td>
<td>623.67</td>
<td>1</td>
</tr>
<tr>
<td>Monozygotic twin</td>
<td>2.514 (0.152)</td>
<td>16.50</td>
<td>12.35</td>
</tr>
<tr>
<td>Sibling</td>
<td>1.562 (0.017)</td>
<td>92.43</td>
<td>4.77</td>
</tr>
<tr>
<td>Mother</td>
<td>1.038 (0.024)</td>
<td>42.53</td>
<td>2.82</td>
</tr>
<tr>
<td>Father</td>
<td>1.157 (0.021)</td>
<td>56.53</td>
<td>3.18</td>
</tr>
<tr>
<td>Half sibling</td>
<td>1.000 (0.020)</td>
<td>49.80</td>
<td>2.72</td>
</tr>
<tr>
<td>Cousin</td>
<td>0.503 (0.017)</td>
<td>29.83</td>
<td>1.65</td>
</tr>
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</table>

* P < .001 for all.

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**Figure 1. Distribution of Rates of Drug Abuse in Peers**

Rates were assessed at the proband age of 15 years across 7738 Small Areas for Market Statistics in Sweden.

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The effect of PD significantly decreased with time, so a correction factor (PD × log [time]) was included in all models (HR, 0.95; 95% CI, 0.95-0.95; in the simple linear model). A quadratic term was also significant, predicting linear and quadratic HRs of 1.61 (95% CI, 1.59-1.63; χ² = 4252.2; P < .001) and 0.99 (95% CI, 0.99-0.99; χ² = 1034.4; P < .001), respectively. Figure 2 depicts the strong and increasing relationship between PD and proband risk of DA.

We then added to our model, one at a time, the effect of VCB and AUD in peers and social deprivation. Focusing on linear effects for ease of interpretation, peer AUD and VCB significantly but modestly further predicted DA (HR, 1.03; 95% CI, 1.02-1.05; χ² = 26.3; P < .001; and HR, 1.05; 95% CI, 1.04-1.06; χ² = 74.6; P < .001, respectively). Social deprivation had an even smaller effect (HR, 1.02; 95% CI, 1.01-1.02; χ² = 23.6; P < .001). Inclusion of these variables produced minimal change on the linear HR for PD, altering it from 1.61 to 1.60, 1.58, and 1.61 for all 3 variables in the model, respectively. Adding voter participation rates as a measure of collective efficacy also produced a minimal change on the linear HR for PD (from 1.61 to 1.59).

With a focus again on linear effects, peer DA in individuals 1 to 5 years older than the proband had a stronger effect on DA risk than peer DA in individuals 1 to 5 years younger (HR, 1.51; 95% CI, 1.49-1.53; χ² = 3710.4; P < .001; and HR, 1.33; 95% CI, 1.32-1.35; χ² = 2699.6; P < .001, respectively).

With PD standardized across sexes, DA in male peers was more predictive of proband DA risk than DA in female peers (HR, 2.93; 95% CI, 2.84-3.02; χ² = 5049.5; P < .001; and HR, 2.12; 95% CI, 2.06-2.18; χ² = 2460.9; P < .001, respectively). No sex specificity was seen because rates of DA in males and females were both more strongly predicted by rates of DA in male than female peers.

Joint Effects of Familial Environmental and Genetic Risk and PD

Controlling for parental educational level and parental divorce robustly predicted the risk of DA (HR, 1.83; 95% CI, 1.70-1.87; χ² = 3913.5; P < .001). Little of this effect was due to genetic confounding because the HR decreased to only 1.79 (95% CI, 1.76-1.82; χ² = 3576.4; P < .001) if the proband genetic risk score for DA was added. We then examined a linear hazard model with the main effects of divorce, PD, and their interaction, controlling for genetic risk (Table 2). The interaction term was highly significant (Figure 3). For probands whose parents were not divorced, the number of new cases of DA per 10 000 person-years living in a low vs high PD area (0% or 15% peer DA) was 35.7. The parallel figure for an individual living in a high PD area was 51.2, a 43% increase.

Table 3 presents the results of our empirical weighting to assess genetic risk of DA for probands from the morbid risk of DA in parents, siblings, co-twins, half siblings, and cousins. The odds ratios are consistent with genetic theory, although among first-degree relatives, the effects are stronger within (full siblings) than across generations (parents). Table 3 also presents the predicted rates of DA from several patterns of DA in relatives. Examined in our hazard model, genetic risk was a robust predictor of risk for DA (HR, 1.07; 95% CI, 1.07-1.07; χ² = 5488.4; P < .001). We examined a linear hazard model that contained the main effects of genetic risk, PD, and their interaction (Table 4). The interaction term was highly significant and substantial in magnitude (Figure 4). For individuals with low genetic risk, residing in a SAMS with low vs high PD (peer DA of 0% vs 15%) would be associated with an increase in 28.1...
Outcomes.8,17-19 Although we had no direct measures of genetic risk were especially sensitive to the adverse effects of PD.30-33 Finally, we eliminate genetic confounders by censoring peers genetically related to the proband.

Reviewing our specific questions, we found that PD was a strong predictor of DA risk that did not vary widely by age window or age at which PD was examined. In male and older peers, DA was more predictive of future DA risk than DA in female or younger peers. A trivial proportion of the predictive power of PD was due to traditional measures of community social deprivation or collective efficacy. Widening the definition of deviance to include AUD and VCB only slightly augmented the ability of PD to predict DA.

Our adoption study of DA demonstrated a positive interaction between adoptive family characteristics and genetic risk; adoptees at high risk were more sensitive to the pathogenic effects of a bad environment. Prior twin studies demonstrated gene × environment interaction with measures of PD for a range of externalizing traits, although not for DA. Confirming and extending these previous results, we found robust interaction effects between genetic risk and PD. Congruent with our adoption results, but now far more generalizable because they were demonstrated in the entire population, individuals at high genetic risk were especially sensitive to the adverse effects of PD.

High parental monitoring and care can substantially reduce the adverse effects of high levels of PD on externalizing outcomes.8,37-39 Although we had no direct measures of parenting quality, we assessed parental divorce, which has been associated with an increased risk of a range of externalizing outcomes through several processes, including exposure to conflict, reduction of parental involvement, and a decrease in parental monitoring.37-39 Our results supported previous studies by showing that, in probands experiencing parental divorce, PD had a greater effect on future risk for DA. Genetic factors that might be correlated with DA risk can influence parental divorce.40 However, we ruled out genetic confounding by demonstrating that the interaction between parental loss and PD was unchanged when controlling for genetic risk.

There has been a long debate between research traditions about the proper level of analysis for pathological human behavior.41 Two prominent positions have been reductionism and multilevel pluralism.42-43 One argument against reductive models has been the potential importance of cross-level interactions. For example, Wikström and Sampson argued for the critical role of externalizing disorders of interactions between individual vulnerabilities and social/community context for externalizing disorders. This article examined this question for DA in Sweden. We found robust cross-level interactions between individual-level factors (ie, genetic risk for DA) and family factors (ie, parental divorce and social or community effects) indexed by our PD measure. Such results argue strongly in favor of multilevel pluralistic etiologic
models for DA. Although genetic effects expressed at the level of molecular neurobiology are surely critical in the abnormalities of DA, our results suggest that the importance of these processes can be substantially modified by social or community processes.

Our results should be interpreted in the context of 4 potentially important methodologic limitations. First, our measures of PD and DA are based on medical, legal, and pharmacy records and are certain to contain false-negative and false-positive diagnoses. We are, however, not grossly overestimating or underestimating DA prevalence because an epidemiologic study of DA conducted in neighboring Norway, with comparable rates of DA, found lifetime prevalence rates of DA diagnosed according to the DSM-III-R similar to those found using our registry-based methods. Furthermore, the odds ratios for detection by our various methods are high, suggesting cross-validation. Of concern, however, is that ascertainment of DA through criminal conviction may be biased from police practices differing across SAMSs. Therefore, we repeated all of our main analyses eliminating criminal sources of registration for DA. None of our findings changed substantially.

Second, our assessment of PD differs substantially from prior measures. Although traditional approaches examine current and past deviant behaviors, our approach measures future behaviors. Thus, we have assessed in peers a latent liability to deviant behavior that will manifest later in life. We have no way to determine, among the defined peer group for a particular proband within a SAMS, those individuals with whom he or she socialized most frequently. Measures of PD could predict externalizing behaviors because social interactions among peers encourage deviance or because the frequency of deviancy in a population reflects a broad array of social risk factors. In the former case, the peer interactions may themselves cause deviant outcomes. In the latter situation, PD acts as an index of broader social-cultural processes that themselves predict deviance. We have limited power to discriminate between these 2 hypotheses in our data. Our inability to find much stronger effects of PD on risk of DA with narrower age windows for defining peers argues more for indirect effects of our PD measure. However, the stronger effect of PD on risk of proband DA in older vs younger peers suggests that at least part of the PD-DA association may be causal and due to social transmission of behaviors related to drug use and misuse. Furthermore, the validity of our measure of PD is indirectly supported by evidence that little of its predictive effect on DA could be explained by traditional measures of social deprivation or low collective efficacy.

Third, our genetic risk score might have incorporated familial environmental factors. To examine this possibility, we calculated a modified genetic risk score excluding individuals who resided with the proband for a total of more than 3 years up to the age of 15 years. This risk score correlation was +0.92 compared with our original estimate. We repeated our key analyses with this modified risk score. Its main effect was modestly reduced, but the interaction with PD was increased. Our genetic risk × PD interaction was not biased upward by familial environmental effects.

Fourth, we could not rule out that family-level selection effects could explain part of the PD-DA relationship. However, we could control for genetic risk of DA in parents, which would likely explain at least part of any family-level selection. Including the genetic risk in parents altered the linear HR for PD trivially, from 1.61 to 1.60.

Conclusions

The results of our findings may help to further understand the social determinants of externalizing behaviors and disorders. Our definition of PD powerfully predicts risk of DA in males and females, and little of this predictive ability is captured by the traditional measures of social adversity or by indexes of genetic risk. Our measure of PD shows surprising specificity, with modest gains in predictive power by its broadening to include peer AUD or criminality. Parental divorce predicts an increased sensitivity to the adverse effects of PD. Most interestingly, consistent with our prior adoption evidence, there is robust evidence of gene environment interaction. Those at high genetic risk for DA are considerably more sensitive to the pathogenic effects of PD. A full understanding of the origin of DA will require an integration of research perspectives that include the genetic or biological, family processes, and social-cultural influences. Our findings may influence public policy strategies to promote resiliency in subgroups of high-risk children.


