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Parental Transmission of Risk for Cannabis Use Disorders to Offspring

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Abstract

Aims—We investigated the risk of cannabis use disorder (CUD) among probands as a function of parental psychopathology and explored parent-offspring gender concordance as a mechanism of parental CUD transmission to offspring.

Design—Four waves of data collection from a longitudinal epidemiological study of psychopathology among a regionally representative sample.

Setting—Participants were randomly selected from western Oregon, USA, and were initially assessed during mid-adolescence.

Participants—The reference sample included 719 probands and their biological mothers and fathers.

Measurements—CUD episodes among probands were assessed with semi-structured diagnostic interviews between mid-adolescence and young adulthood. Lifetime psychiatric disorders among parents of probands were assessed when probands were approximately 24 years of age.

Findings—There was an increased risk for CUD onset among probands with parental histories of CUD (hazard ratio [*HR*] = 1.93, 95% confidence interval [CI_{95}] = 1.30–2.88), hard drug use disorders (*HR* = 1.96, CI_{95} = 1.32–2.90), or antisocial personality disorder (*HR* = 1.73, CI_{95} = 1.06–2.82). A significant parent-offspring gender concordance effect indicated that females with a maternal CUD history were at higher risk for CUD onset compared with females without a maternal CUD (*HR* = 3.10, CI_{95} = 1.52–6.34). Maternal CUD was not associated with CUD onset among males (p = .570), nor was there evidence for parent-offspring gender concordance effects for paternal CUD-specific transmission (p = .114).

Conclusions—Parental histories of antisocial personality and illicit substance use disorders are associated with increased risk for CUD onset in offspring, especially among females with maternal CUD histories.

Keywords

Cannabis use disorders; marijuana; parental psychopathology; familial transmission; gender concordance

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Introduction

Cannabis abuse and dependence disorders or, collectively, cannabis use disorder (CUD), are common in industrialized societies [1–4] and pose significant public health concerns [5–8]. Risk factors for CUD include those that are family-based. Studies of parent to offspring transmission of various cannabis use phenotypes, for example, suggest familial transmission of cannabis use [9–11] as well as CUD [12–15]. In one study, twin offspring of a cannabis-dependent parent had nearly three times the odds of developing a substance use disorder, including CUD, compared to their low-risk twin counterparts [13]. Data from clinical samples also suggest significant CUD-specific familial transmission, even after controlling for other substance use disorders [14, 16].

Few studies have examined mechanisms of CUD-specific risk transmission between parent and offspring. Parent-offspring gender concordance, for example, is a central assumption of parental modeling theories of substance abuse transmission. Previous research suggests parental modeling of substance use is most likely to occur when parent-offspring relationship quality is high [17]. Others found that same-sex parent-offspring dyads experience fewer conflicts during childhood and adolescence compared to opposite sex dyads [18]. Together, these findings imply that parental modeling of behaviors, including substance use, may be more salient among same-sex parent-offspring dyads compared to opposite-sex parent-offspring dyads. Although there is some indication of parent-offspring gender concordance for cannabis use [9], other research suggests that CUD transmission is not influenced by the gender of offspring, parents, or their interaction [14].

Parental histories of other substance use disorders and antisocial personality disorder may represent non-specific risk factors for CUD among offspring. Parental histories of alcohol and hard drug use disorders, for example, have been associated with CUD in offspring [19], and adolescent cannabis users have demonstrated greater family vulnerability to externalizing psychopathology, including antisocial behavior and other substance use disorders [20, 21]. These findings are consistent with the common liability to addiction hypothesis [22], which posits an underlying liability for externalizing disorders operating within individuals and families that increases risk for substance abuse and dependence.

Internalizing disorders such as major depressive disorder and various anxiety disorders have also demonstrated significant familial aggregation with substance use disorders, inclusive of CUD, in a large cross-sectional national probability sample [23]. In a recent study that combined clinical and community samples, however, anxiety and depressive disorders aggregated independently of CUD within families [14]. Limited and equivocal findings on the risk for offspring CUD associated with parental internalizing disorders highlight the need for additional research on this possible line of transmission.

The Current Study

CUD onset among offspring (i.e., probands) was evaluated as a function of parental disorder histories. Data were drawn from the Oregon Adolescent Depression Project (OADP) [24], a prospective and multigenerational community-based study. Earlier work with OADP

indicated 19% of probands developed CUD by age 30 [4] and a significant familial aggregation of substance use disorders not further differentiated by substance type [25]. In the current study we extend these findings by addressing the following research questions:

1. What are the associations between maternal and paternal lifetime CUD histories and risk for CUD onset among probands through age 30?
2. Is the risk for CUD-specific transmission increased when both mothers and fathers have CUD histories compared to when only one parent has a history of CUD?
3. Is there evidence for a parent-proband gender concordance effect on the risk for CUD-specific transmission?
4. To what extent do other forms of maternal and paternal lifetime psychopathology, including alcohol use disorders, hard drug use disorders, antisocial personality disorder, depressive disorders, and anxiety disorders contribute to the risk for CUD onset among probands through age 30?

We hypothesized that maternal and paternal CUDs would be associated with an increased risk for CUD among probands. Limited and mixed findings related to parent-offspring gender concordance effects precluded us from making strong predictions concerning this mechanism of transmission; consequently, this aspect of our research was exploratory. Consistent with the common liability to addiction hypothesis [22], we hypothesized that parental substance use disorders and antisocial personality disorders would be associated with a greater risk for CUD onset among probands, and that statistical control of the common externalizing liability would significantly attenuate or eliminate any disorder-specific effects associated with parental CUD. Earlier equivocal findings related to the role of parental internalizing disorders precluded us from offering predictions about their role as risk factors; consequently, this aspect of our investigation is also exploratory.

Methods

Samples

Probands—The OADP was a four-panel epidemiological study (T_1 to T_4) of randomly selected high school students in western Oregon. The T_1 sample consisted of 1,709 adolescent youth (mean age = 16.6, *SD* = 1.2), the demographic characteristics of which were highly similar to corresponding census data for the region. Approximately one year following T_1, 1,507 probands (88% of the index sample) participated in a T_2 assessment (mean age = 17.7, *SD* = 1.2). Approximately 7 years following T_2, a stratified sampling procedure was implemented whereby eligible T_3 participants included all ethnic and racial minorities (to strengthen the diversity of the sample), all persons with a positive history of a psychiatric diagnosis by T_2 (*n* = 644), and a randomly selected subset of participants with no history of mental disorder by T_2 (*n* = 457 of 863 persons). Of the 1,101 probands recruited for a T_3 interview, 941 (85%) completed the evaluation (mean age = 24.6, *SD* = 0.6). Approximately 6 years after T_3 (mean age = 30.5, *SD* = 0.7), 816 of the 941 T_3 probands (87%) participated in the T_4 diagnostic evaluation. Analyses of participant attrition [4, 24, 26] revealed only minimal sample bias related to study discontinuation.

Parents—During T_3, parents of probands were also evaluated for current and lifetime psychiatric disorders. Diagnostic data were available for 730 biological mothers and 719 biological fathers of the 816 T_4 probands. The reference sample for the current study included families with diagnostic histories for both biological parents (*n* = 719 families, or 88% of the 816 T_4 probands).

Diagnostic Assessments

Probands—For the first 3 waves, psychiatric disorders among probands were assessed with the Present Episode and Epidemiologic versions of the Schedule for Affective Disorders and Schizophrenia for School-Age Children [27, 28]. At T_4, the Structured Clinical Interview for Axis I DSM-IV Disorders–Non-Patient Edition (SCID-NP) [29] was used. These interviews were supplemented with the Longitudinal Interval Follow-Up Evaluation [30] to assess disorder presence and course since the previous assessment. Symptom reports were evaluated with respect to DSM-III-R diagnostic criteria and decision rules at T_1 and T_2 and DSM-IV criteria and rules at T_3 and T_4.

Recorded interviews were randomly selected from each wave and evaluated for inter-rater reliability. The level of agreement among raters for CUD since the previous interview was good to excellent across study waves (κs: T_1 = .72, T_2 = .93, T_3 = .83, T_4 = .82). Additional information about reliability procedures used in the OADP can be found in previous reports [31, 32].

Parents—When feasible, direct (in-person or phone-based) diagnostic history interviews with the parents of probands were conducted. Direct interviews were conducted with the SCID-NP and, whenever possible, supplemented with reports from a second family member. When direct interviews were not possible, informant interviews with other first-degree relatives were conducted. These interviews usually involved at least two knowledgeable family members who were questioned individually about another family member's diagnostic history. Informant interviews were based on the Family Informant Schedule and Criteria modified for DSM-IV [33]. More mothers were directly interviewed (76%) compared to fathers (46%). All interviews were conducted blind to proband diagnoses. The best estimate method [34] was used for determining lifetime psychiatric diagnoses among parents. Inter-rater reliability was good to excellent for all parental diagnostic categories (κ > .69).

Psychopathology was categorically modeled, with a value of 0 assigned if no disorder or domain-related disorder was diagnosed and a value of 1 assigned if a given disorder or one or more domain-related disorders were diagnosed. Disorders that contributed to the externalizing domain were: CUD, alcohol use disorders (alcohol abuse or dependence), hard drug use disorders (abuse or dependence of cocaine, hallucinogens, inhalants, opioids, or sedatives), and antisocial personality disorder. Disorders that contributed to the internalizing domain were: depressive disorders (major depressive disorder, dysthymia) and anxiety disorders (simple/specific phobia, generalized anxiety, obsessive–compulsive, panic, agoraphobia without panic, post-traumatic stress, social phobia). To ensure that the temporal direction of associations between parent and proband disorders were unambiguous, an

approach similar to that used in an earlier report [35] was implemented whereby parental disorder onsets must have preceded proband disorder onset to be considered in risk transmission analyses. As such, parental disorder onsets occurring after proband onsets were coded 0 in the following analyses.

Potential Confounders

Confounder analyses included the evaluation and control of proband characteristics (i.e., gender, race [self-identified as Caucasian or of a different race], pubertal timing, history of repeating a grade before age 12), family characteristics (dual parent vs. single parent household, education levels of heads of household, age of heads of household, number of older siblings), and parent interview status (direct vs. indirect). All putative confounders, regardless of their individual significance, were included as covariates in adjusted analyses to isolate unique associations between each parental disorder category and CUD onset among probands.

Proband and family characteristics were measured at T_1 and T_2. When both T_1 and T_2 data were missing, we imputed values using the expectation maximization algorithm implemented in the SPSS Missing Value Analysis module to avoid list-wise deletion in our analyses. Data were missing for pubertal timing (< 1% missing), history of repeating a grade before age 12 (< 1% missing), education levels of head of household (4% missing), and age of heads of household (< 1% missing). All putative confounders were included as auxiliary variables in the imputation procedure.

Statistical Analyses

We described rates of CUD through age 30 for probands with and without parental disorder histories using contingency table analyses and reported the associated likelihood-ratio test statistics and *p*-values. Unadjusted and adjusted associations between parental psychopathology and age of initial CUD onset among probands were evaluated with Cox proportional hazards (PH) regression. Cox PH regression takes into account time until an outcome event, and generally have more statistical power and yield more precise effect estimates than logistic regression [36, 37]. For probands who did not develop CUD, the time to event variable was right censored at their T_4 interview age. Hazard ratios (*HR*) and their 95% confidence intervals produced from these analyses describe the relative likelihood of developing a CUD within a unit of time (months) as a function of parental psychopathology. Cox PH models were conducted using SUDAAN version 11.0.0. Because participants with no history of psychopathology were undersampled at T_3, cases were weighted as a function of the probability of selection at T_3 in all analyses.

Results

Putative Confounders and CUD Onset among Probands

We first evaluated proband characteristics, family characteristics, and parent interview status as predictors of CUD onset among the sample of probands for whom parent data were available (n = 719). Findings from these Cox PH models along with sample characteristics among probands with and without CUD onset through age 30 are presented in Table 1.

Briefly, male (vs. female) probands, those who resided in a single parent household at T_1, those with younger parents, and those without direct father interviews were significantly more likely to have CUD onset by age 30. All putative confounders were included as covariates in adjusted analyses reported below.

Parental CUD Histories and CUD Onset among Probands

Presented in Table 2 are lifetime prevalence rates of parental psychopathology and rates of CUD among probands with and without parental psychopathology. Unadjusted and adjusted associations between parental psychopathology and CUD onset among probands are also presented in Table 2. Combining maternal and paternal histories into a combined "either parent" category revealed a significantly higher risk of CUD onset among probands with a parental CUD history compared to probands without a parental CUD history (*HR* = 1.93, *p* = .001). When the presence versus absence of maternal and paternal CUDs were considered separately as predictors, both were associated with a significantly higher risk of CUD onset among probands (*HR* = 2.10, *p* = .008; and *HR* = 1.75, *p* = .012; for maternal and paternal CUDs, respectively).

We tested whether the risk of CUD-specific transmission increased when both mothers and fathers had CUD histories compared to when only one parent had a history of CUD. An unadjusted Cox PH model included maternal and paternal CUD status and the maternal CUD by paternal CUD interaction as predictors of CUD onset among probands. The maternal CUD by paternal CUD interaction was not significant (*p* = .351), implying no additional risk for CUD-specific transmission when both mothers and fathers had CUD histories. Finally, adjusted Cox PH models that controlled for the effects of all parental psychopathology and potential confounding variables listed in Table 1 revealed no significant unique associations between parental CUD and CUD onset among probands (*p*'s ≥ .136).

Given the higher rates of indirect interviews with fathers compared to mothers in the current sample, we explored the extent to which indirect interviews may have biased the above findings. Similar rates of paternal CUD were obtained across direct and indirect interviews (11% vs. 12%; likelihood ratio chi-square = 0.32, *p* = .569), and associations between paternal and maternal psychopathology and CUD onset among probands based on only direct interviews were similar in relative magnitude as those based on the complete sample. These findings suggest an absence of significant bias as a function of interview type.

Parent-Proband Gender Concordance

Proband gender was evaluated as a moderator of the associations between maternal and paternal CUD histories and CUD onset among probands. An unadjusted Cox PH model included maternal and paternal CUD status, proband gender, and the maternal and paternal CUD by proband gender interactions as predictors of CUD onset among probands. Of particular importance in the test of parent-proband gender concordance is the maternal and paternal CUD by proband gender interactions. Although there was not a significant interaction involving paternal CUD (*p* = .114), a significant maternal CUD by proband gender interaction emerged (*p* = .035), indicating that the effect of maternal CUD

significantly varied by proband gender. Decomposing the interaction revealed a greater risk for developing CUD by age 30 among female probands with a maternal CUD history compared to female probands without a maternal CUD history (*HR* [CI_{95}] = 3.10 [1.52–6.34], $p = .002$). In contrast, maternal CUD was not associated with CUD onset among male probands (*HR* [CI_{95}] = 0.71 [0.22–2.28], $p = .570$).

Because the unadjusted analysis was significant, we conducted an adjusted analysis that included all other maternal and paternal disorders and all variables in Table 1 as covariates. The maternal CUD by proband gender interaction remained significant ($p = .026$). Consistent with findings from the unadjusted analyses, there was a greater risk for CUD among female probands with a maternal CUD history compared to female probands without a maternal CUD history (*HR* [CI_{95}] = 2.66 [1.25–5.67], $p = .011$).

Other Parental Psychopathology and CUD Onset among Probands

Parental psychopathologies other than CUD were also evaluated as risk factors for CUD in probands (Table 2). Significantly higher risk of CUD onset among probands was observed when either parent had a positive versus negative history of hard drug use disorders (*HR* = 1.96, $p = .001$) or antisocial personality disorder (*HR* = 1.73, $p = .029$). When maternal and paternal disorder histories were analyzed separately, significantly higher risk of CUD onset among probands was observed for those who had fathers with histories of hard drug use disorders (*HR* = 2.03, $p = .003$) or antisocial personality disorder (*HR* = 1.71, $p = .037$). No significant unadjusted effects were noted for parental anxiety disorders, depressive disorders, or the combined internalizing domain for either parent or when mothers and fathers were considered separately. Adjusted Cox PH models that controlled for the effects of all parental psychopathology and potential confounding variables listed in Table 1 revealed no significant unique associations between parental psychopathology other than CUD and CUD onset among probands (p's $\geq .217$).

Discussion

The primary objectives of this research were to (a) estimate the associations between parental CUDs and risk for CUD among offspring; (b) evaluate parent-offspring gender concordance in parent-to-offspring CUD transmission; and (c) examine the role of other parental psychopathology in the transmission of CUD risk. Data from a multi-generational and regionally representative community sample were used in our investigation of these areas, with unadjusted and adjusted analyses reported.

Our unadjusted analyses revealed higher risks of CUD among offspring with parental histories of CUD, hard drug use disorders, and antisocial personality disorder. Further differentiating parental psychopathology into maternal and paternal disorders revealed higher risks of CUD among offspring with maternal or paternal histories of CUD, paternal histories of hard drug use disorders, or paternal histories of antisocial personality disorder. These findings are consistent with those reported by others whereby adolescent cannabis users had greater family vulnerability to externalizing disorders than non-cannabis users [19–21]. We found no significant effects for parental histories of alcohol use disorders, depressive disorders, anxiety disorders, or the superordinate internalizing disorder domain as

risk factors for CUD among offspring, suggesting that the most robust lines of familial transmission are related to illicit substances and antisocial behavior. When demographic variables and other parental psychiatric histories were controlled in adjusted analyses, however, no unique predictors emerged, suggesting that overlapping variance with CUD onsets among offspring is largely shared between parental CUDs, paternal hard drug use disorders, and paternal antisocial personality disorder.

Restricted evidence for a parent-offspring gender concordance effect on the risk for CUD-specific transmission was obtained. Female offspring with maternal CUD histories had three times the odds of experiencing CUD compared to those without maternal CUD histories. No similar pattern of gender concordance was observed for male offspring with paternal CUD histories. We found no evidence of increased risk for CUD-specific transmission when both parents had CUD histories compared to when only one parent had a history of CUD. Findings reported here suggest that parental engagement in antisocial behavior and illicit substance use might be more potent factors influencing risk than parental CUD alone, and that risk might be especially high for female offspring whose mothers' also have histories of CUD.

Implications

Adjusted analyses from this research suggest that risk of parental transmission of CUD risk is most strongly associated with parental antisocial behavior and illicit substance use disorders, inclusive of CUD, and that the combination of these characteristics is associated with the greatest risk. These findings, which warrant additional study and replication, imply an externalizing family liability for CUD restricted to illicit or rule-breaking behavior. From an applied perspective, clinicians working with youth with CUD might be sensitive to the presence of such family-based factors, particularly among mother-daughter dyads with a history of maternal CUD. Interventions for youth that target the family unit more generally compared to individual treatments may facilitate the development of family environments that decrease maladaptive behavior patterns such as problematic substance use [38, 39]. Examples include Functional Family Therapy and Multisystemic Therapy; both address familial and macroenvironmental processes and have demonstrated efficacy in reducing substance use among adolescents [40, 41].

Strengths and Limitations

The OADP has several strengths including its large-scale prospective evaluation of proband psychopathology, assessment of DSM-defined psychiatric disorders with semi-structured diagnostic interviews for both parents and probands, and the ability to control for potential confounders in adjusted analyses. Family-based studies of CUD transmission often involve clinical samples, high-risk samples, or questionnaire responses from parents about their children's behavior or vice versa. Few studies with the strengths OADP have evaluated a broad range of parental psychiatric disorder categories as risk factors for CUD among probands.

This study also has limitations, several of which are worth noting. First, participants were relatively homogenous with respect to race and geographic location. The generalizability of

our findings to more diverse groups of individuals or locations is unclear. Second, parents may or may not have met criteria for CUD while parenting, thus limiting inferences concerning cannabis-specific modeling influences in accounting for gender concordance findings. Third, data were unavailable concerning parent-offspring relationship quality, and we were consequently unable to investigate whether parent-offspring relationship quality moderated the parental transmission of CUD risk. Fourth, we did not evaluate a comprehensive list of environmental influences on CUD development among offspring. Environmental factors, for example, such as substance abuse or dependence in peers, may exert a greater influence on the risk for CUD than substance abuse or dependence in parents [42].

Conclusions

Parental histories of CUD, antisocial behavior, and rule-breaking behavior are significant risk factors for CUD among offspring. Additional research based on more diverse samples is indicated, as are well-controlled tests of behavior modeling hypotheses with relationship quality investigated as a moderator of familial transmission. A better understanding of these family-based risk factors will guide future development of relevant theory and effective intervention programs that target problematic cannabis use at a young age.

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Table 1

Sample Demographic Characteristics, Parent Interview Status, and Associations with Cannabis Use Disorder (CUD) Onset among Probands (n = 719)

Variable	Sample Demographic Characteristics				Associations with CUD Onset in Probands, *HR* [CI_{95}]
	No CUD in Proband, (*n* = 583)	CUD in Proband, (*n* = 136)	Test Statistic[a]	*p*-value	
Proband Characteristics					
Male, % (*SE*)	41.5 (2.0)	50.8 (4.3)	3.87	.049	**1.40 [1.01–1.97]**
Non-white, % (*SE*)	6.5 (1.0)	8.9 (2.4)	0.94	.333	1.38 [0.83–2.32]
Pubertal timing, % (*SE*)					
Early vs. on-time	18.3 (1.7)	22.5 (3.8)	1.06	.302	1.31 [0.85–2.01]
Late vs. on-time	14.1 (1.6)	15.9 (3.5)	0.23	.630	1.16 [0.69–1.96]
Early vs. late	57.8 (3.9)	60.6 (7.4)	0.11	.735	1.12 [0.62–2.05]
History of repeating grade before age 12, % (*SE*)	9.6 (1.2)	14.2 (3.0)	2.34	.125	1.50 [0.93–2.39]
Family Demographic Variables					
Dual versus single parent household, % (*SE*)	61.2 (2.0)	43.9 (4.3)	13.25	<.001	**0.53 [0.38–0.75]**
At least one parent completed college, % (*SE*)	45.5 (2.1)	41.4 (4.2)	0.75	.387	0.87 [0.62–1.24]
Mean parent age at T_1, *M* (*SD*)	42.4 (5.8)	41.1 (5.3)	2.36	.019	**0.96 [0.93–0.99]**
Number of older siblings, *M* (*SD*)	0.9 (1.1)	0.8 (1.1)	0.39	.698	0.97 [0.83–1.14]
Direct interview with mother, % (*SE*)	75.9 (1.7)	80.9 (3.4)	1.64	.201	1.30 [0.84–2.01]
Direct interview with father, % (*SE*)	50.2 (2.1)	39.7 (4.2)	4.87	.027	**0.69 [0.49–0.98]**

Note. *SE* = standard error; *M* = mean; *SD* = standard deviation; *HR* = hazard ratio. Statistically significant hazard ratios are bolded.

[a]Likelihood ratio chi-square and independent observation *t*-tests were conducted on categorical and continuous variables, respectively. Reference group = no proband cannabis use disorder.

Table 2

Lifetime Prevalence of Parental Psychopathology and Associations with Cannabis Use Disorder (CUD) Onset among Probands (n = 719)

Lifetime Parent Disorder	Lifetime Prevalence of Parent Disorder, *n* (%)	Rates of CUD in Probands				Associations with CUD Onset in Probands, *HR* [CI_{95}]	
		No Disorder in Parent, % [*SE*]	Disorder in Parent, % [*SE*]	LR χ^2	*p*-value	Unadjusted	Adjusted
Cannabis use disorder (either parent)	104 (14.5)	17.0 [1.5]	30.4 [4.5]	9.42	.002	**1.93 [1.30–2.88]**	1.45 [0.89–2.36]
Maternal	37 (5.1)	18.1 [1.5]	35.2 [7.9]	5.72	.016	**2.10 [1.21–3.65]**	1.29 [0.69–2.43]
Paternal	85 (11.9)	17.6 [1.5]	28.9 [4.9]	5.61	.017	**1.75 [1.13–2.72]**	1.37 [0.77–2.43]
Alcohol use disorder (either parent)	333 (46.4)	18.0 [2.0]	20.1 [2.2]	0.50	.477	1.14 [0.81–1.60]	0.84 [0.57–1.25]
Maternal	95 (13.2)	18.3 [1.6]	23.4 [4.3]	1.37	.242	1.35 [0.86–2.12]	1.01 [0.60–1.69]
Paternal	291 (40.4)	18.9 [1.9]	19.1 [2.3]	0.00	.956	1.01 [0.72–1.42]	0.80 [0.53–1.21]
Hard drug use disorder (either parent)	103 (14.4)	17.0 [1.5]	30.6 [4.5]	9.68	.001	**1.96 [1.32–2.90]**	1.36 [0.83–2.24]
Maternal	47 (6.5)	18.4 [1.5]	27.6 [6.5]	2.23	.134	1.53 [0.88–2.66]	1.10 [0.61–1.97]
Paternal	65 (9.0)	17.6 [1.5]	32.1 [5.8]	7.09	.007	**2.03 [1.27–3.24]**	1.43 [0.75–2.70]
Antisocial personality disorder (either parent)	58 (8.1)	18.0 [1.5]	29.6 [6.0]	4.21	.040	**1.73 [1.06–2.82]**	1.08 [0.61–1.89]
Maternal	2 (0.3)	18.9 [1.5]	33.3 [32.2]	NA	NA	NA	NA
Paternal	56 (7.8)	18.1 [1.5]	29.4 [6.1]	3.94	.047	**1.71 [1.03–2.82]**	0.99 [0.51–1.92]
Depressive disorder (either parent)	327 (45.5)	17.7 [1.9]	20.5 [2.2]	0.94	.331	1.18 [0.84–1.65]	1.06 [0.74–1.51]
Maternal	240 (33.4)	17.9 [1.8]	21.0 [2.6]	0.98	.322	1.19 [0.84–1.69]	1.10 [0.75–1.60]
Paternal	149 (20.8)	18.6 [1.6]	20.2 [3.3]	0.19	.659	1.10 [0.74–1.64]	1.02 [0.67–1.56]
Anxiety disorder (either parent)	147 (20.5)	18.8 [1.6]	19.6 [3.3]	0.05	.831	1.04 [0.69–1.59]	0.92 [0.58–1.45]
Maternal	116 (16.1)	19.0 [1.6]	18.7 [3.6]	0.01	.944	0.99 [0.62–1.60]	0.84 [0.50–1.40]
Paternal	48 (6.6)	18.8 [1.5]	21.1 [5.9]	0.15	.698	1.14 [0.63–2.09]	1.20 [0.60–2.39]
Any externalizing disorder (either parent)	366 (50.9)	16.2 [2.0]	21.7 [2.2]	3.54	.060	1.39 [0.98–1.96]	1.12 [0.77–1.65]
Maternal	129 (18.0)	17.7 [1.6]	24.5 [3.8]	3.00	.083	1.45 [0.98–2.14]	1.14 [0.75–1.73]
Paternal	317 (44.2)	17.4 [1.9]	20.9 [2.3]	1.35	.245	1.22 [0.87–1.71]	1.05 [0.73–1.51]
Any internalizing disorder (either parent)	364 (50.6)	17.9 [2.0]	20.0 [2.1]	0.54	.462	1.13 [0.80–1.58]	0.99 [0.69–1.41]
Maternal	280 (38.9)	18.6 [1.9]	19.6 [2.4]	0.11	.737	1.06 [0.75–1.50]	0.91 [0.63–1.32]
Paternal	177 (24.6)	18.4 [1.7]	20.7 [3.1]	0.48	.488	1.15 [0.79–1.67]	1.12 [0.76–1.65]

Note. *SE* = standard error; LR = likelihood ratio; *HR* = hazard ratio; CI95 = 95% confidence bounds; NA = not analyzed due to insufficient base rates. Statistically significant hazard ratios are bolded. Adjusted analyses included parental interview status (direct vs. indirect), variables in Table 1, and other maternal and paternal psychopathology as covariates. Reference group = no proband cannabis use disorder.