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Development of Alcohol and Drug Use in Youth With Manic Symptoms

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Abstract

Objective—This analysis examined alcohol and drug use over a six-year follow-up of children in the Longitudinal Assessment of Manic Symptoms (LAMS) study.

Method—LAMS screened 6- to 12.9-year-old children visiting 9 child outpatient mental health (MH) clinics, using the Parent General Behavior Inventory 10-item mania scale. All children with scores ≥12 and a matched group with scores ≤12 were invited to enroll. Children were assessed

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every 6 months. Assessments included demographics, family, MH history, child diagnoses, child stress, and alcohol and drug use. Univariate, bivariate, and interval censored survival analyses were conducted.

Results—Of those > 9 years at baseline, 34.9% used alcohol at least once with 11.9% regular users; 30.1% used drugs at least once with 16.2% regular users. Predictors of any alcohol use were parental marital status, older age at study entry, a primary diagnosis of disruptive behavior disorders at baseline, and number of impactful child life events. Predictors of regular alcohol use included parental marital status, age, and sustained high mania symptoms over the first 24 months of follow-up. Predictors of any drug use were single parent, parental substance use, and stressful child life events. Predictors of regular drug use were parental marital status, stressful child life events, and a baseline disruptive behavior disorder diagnosis. Baseline medications decreased the risk of regular drug use.

Conclusion—Longitudinal data on youth with elevated manic symptoms suggest that comorbid disruptive behavior disorder, manic symptom burden, family environment, and stress are predictors of initiation and regular use of substances.

Keywords

manic symptoms; substance use; bipolar disorders

INTRODUCTION

Substance use during adolescence is related to a host of serious health risks throughout the life span.[1] Although recent data suggest that cigarette smoking and alcohol use have declined, many US adolescents use substances, and one group of adolescents, the 13%-20% of those with mental health (MH) problems, are at greatly increased risk for co-occurring substance use and abuse.[1-3]

Longitudinal data suggest that the risk for developing substance use disorders (SUD) is greatly elevated for adults with baseline MH disorders, particularly bipolar spectrum disorders (BPSD).[4] Considerable data suggest that youth with BPSD are also at risk for SUD[5] and that those youth with comorbid SUD are more likely to be less adherent to medications[6] and have poor functional outcomes.[7] However, little is known about whether youth with symptoms characteristic of BPSD, namely mania, are at comparable risk to develop SUD. Very few studies have examined the prevalence and risk factors for SUD in youth with manic symptoms who did not meet criteria for BPSD, although severity and persistence of ADHD symptoms have been shown to be related to substance use.[8] Examining children with symptoms of mania longitudinally is important because it appears that the BPSD begins with non-specific, non-mood pathology in children and evolves to mood pathology. Given that manic symptoms may be an important risk factor for SUD, the risk for development of SUD is likely to increase with the clinical evolution of mood disorder.[9-11]

That BPSD and mania are related to SUD is not surprising given what is known about the neurobiology of addiction. It is estimated that 40%-60% of the vulnerability to addiction is

genetic, due both to variability in drug metabolism and to the reinforcing effects of a drug, specifically the increase of dopamine in the limbic brain regions.[12] However, development of SUD is multifactorial, and one pathway is a deviation in somatic and neurological maturation.[13] When such a deviation is combined with adverse environments, such as those characterized by poor parenting, abuse, and stress,[14] it produces affective and behavioral dysregulation.[15] Sloboda et al.[15] argue that dysregulation begins as teratogenic injury or difficult temperament in infancy, moves to poor impulse control/self-regulation in childhood, to substance use by early adolescence, and then to severe SUD by early adulthood. Tarter et al.[16] describe youth at high risk for SUD as impulsive, exhibiting reactive aggression, sensation seeking, and excessive risk taking. These authors postulate that these characteristics emanate from disinhibition produced by dysfunction of the prefrontal cortex, although the precise role of temperament[17] and pathology, as well as factors that modify the relationship, need to be further explored.[18]

Children with BPSD have more difficult temperaments (e.g., irritability, affective lability)[19] prior to diagnosis, considerable behavioral disinhibition, and high rates of ADHD.[20] Data suggesting that impulsiveness and high behavioral approach system sensitivity mediate the relationship between BPSD and SUD[21] argue strongly for examining the development of substance use in youth whose symptoms suggest increased risk for the development of BPSD. Therefore, this study aimed to: (1) determine rates of use and regular use of alcohol and drugs over a six-year follow-up of a cohort of children, most of whom had elevated symptoms of mania when enrolled; and (2) examine predictors of use/regular use of alcohol and drugs. Based on the findings of Wilens et al.,[22] we expected that there would be different predictors of drug and alcohol use/regular use, so they were examined separately.

METHOD

Data for these analyses came from the Longitudinal Assessment of Manic Symptoms (LAMS) study. LAMS screened 6- to 12.9-year-old children at initial visit to 9 child outpatient clinics. Participating adults of eligible children completed the Parent General Behavior Inventory–10 Item Mania Scale (PGBI-10M)[23,24] and 4 demographic questions. All children with a PGBI-10M score ≥ 12 (elevated symptoms of mania [ESM]) were invited to enroll in the longitudinal phase of the study, and a smaller matched group (on age, sex, race, insurance) of children with scores < 12 were randomly selected with replacement and invited.[25,26] A total of 707 children (n=621 with ESM; n=86 without ESM) agreed to enroll in the longitudinal cohort, and 685 were eligible after the baseline assessment.

Measures

Demographics—Age, sex, race, ethnicity, health insurance status, family structure, and a brief medical history for the child were collected.

Family History—The Modified Family History Screen (FHS)[27] collected information on 15 psychiatric disorders, including substance abuse in biological parents.

Child Diagnoses—Children and their guardians were administered the Schedule for Affective Disorders and Schizophrenia for School-Age Children–Present and Lifetime

Episode (K-SADS-PL)[28] with additional depression and manic symptom items derived from the Washington University in St. Louis Kiddie Schedule for Affective Disorders (Wash-U K-SADS).[29,30] The K-SADS also captures alcohol and drug dependence. Unmodified *DSM-IV* diagnostic criteria were used, and the criteria for BP-not otherwise specified (NOS) followed the criteria used in the Course and Outcome of Bipolar Youth Study (COBY).[31] All diagnoses were reviewed and confirmed by a licensed child psychiatrist or psychologist.

24-Month Manic Trajectories—Using growth mixture modeling of mania symptoms over the first 24 months of follow-up data, Findling et al.[32] found that 15% of the cohort belonged to 2 classes (high and rising, and unstable mania symptoms). These two classes of mania symptoms were characterized by high rates of diagnostic conversion to BPSD.

Child Stress—The Stressful Life Events Schedule (SLES)[33] asked parents to report whether 80 events occurred in their child's life during the past 12 months and the impact of each event. Events that parents rated as having a lot or somewhat of an impact on their child (vs. a little or not at all) were coded as impactful. The SLES has good test-retest reliability.[33]

Child and Adolescent Symptom Inventory (CAASI-4)—This 163-item behavioral rating scale for emotional and behavioral disorders was completed by parents of children 8-17 years of age at each visit.[34] The CAASI-4 has high internal consistency (0.74-0.94) and significant test-retest reliability (p<.001).

Youth's Inventory (YI-4)—This 128-item self-report measure, which assesses the presence and severity of behavioral, cognitive, and affective symptoms described in the *DSM-IV*, was completed by participants aged 13-17 years.[34,35] The YI-4 has good internal consistency (0.66-0.87) and test-retest reliability (r=0.54-0.92).[34]

Adult Self-Report Inventory (ASRI-4)—Participants aged 18 completed this 166-item self-report measure on the presence and severity of behavioral, cognitive, and affective symptoms described in *DSM-IV*.[36]

Outcomes: Substance Use/Regular Use—Three self-report measures developed by the Centers for Disease Control and Prevention (CDC) were used to assess whether participants had ever used alcohol or drugs and how often they had used alcohol and drugs during the past 30 days.

Students aged 10-12 years completed the middle school Youth Risk Behavior Survey (YRBS-MS), those aged 13-18 years completed the high school YRBS (YRBS-HS),[37] and participants who completed high school and were 18-22 years of age completed the YARQ.[38,39] The YRBS has good reliability (kappa ≥.60),[40,41] and three measures were used to assess the frequency of alcohol, marijuana, and other drug use during the past 6 months using a 4-point ordinal scale: never, sometimes, often, very often.

Any alcohol use was defined as having more than a few sips of alcohol on at least one occasion (ASRI-4, CAASI-4, K-SADS, YARQ, YI-4, YRBS). Regular alcohol use was defined as drinking ≥3 days during the past 30 days (YRBS), drinking ≥5 drinks in a row on

≥2 days during the past 30 days (YRBS and YARQ), or having ≥1 drink on ≥3 days in the past 30 days (YARQ). Any drug use was defined as any use of marijuana, cocaine/crack/freebase, inhalants (glue, aerosols, paints), methamphetamines, heroin, ecstasy, or hallucinogenics (ASRI-4, CAASI-4, K-SADS, YARQ, YI-4, YRBS). With the exception of the K-SADS, which assesses drug dependence, regular drug use was not measured in children before high school. For children high school age and beyond, regular drug use was defined as using drugs ≥3 times in the past 30 days (YRBS and YARQ). For each outcome, if the criteria were met on any of the relevant instruments, that outcome was coded as positive. SUD diagnoses were infrequent and, therefore, not examined.

Data Analysis

Categorical data were summarized using counts and percentages. Normally and non-normally distributed measures were described using means ± standard deviation and median (25^{th} and 75^{th} percentiles), respectively. Bivariate associations of baseline characteristics and the 24-month manic trajectories[32] with the outcomes were assessed via the chi-square test, two-sample *t*-test, and the Wilcoxon Rank-Sum test as appropriate. As the time interval during which the substance use occurred is known but the exact time it occurred is unknown, interval-censored survival analysis was used to examine adjusted associations with each outcome. Interval-censored proportional hazards models were fitted with a 2-knot spline baseline hazard. The results are summarized using adjusted hazard ratios (HR) and their 95% CIs. Analyses were performed using SAS 9.4 (SAS Institute, Inc., Cary, NC).

Participants who reported no alcohol use at baseline (n=662, 96.6%) and no drug use at baseline (n=669, 97.7%) but had some data on alcohol and drug use over the 6-year follow-up were included in the analyses of any use. The analysis of regular alcohol use included the 579 (84.5%) participants who reported their alcohol use during the past 30 days at each assessment over the 6-year follow-up. Additionally, the analyses of regular drug use included the 429 youth who reported no drug use at baseline but provided follow-up data on drug use during high school or by age 18 years, as these data were not collected prior to high school.

RESULTS

At the 6-year follow-up, children ranged from 11.1 to 19.1 years of age, 68.2% were male, and 64.6% were white. When the oldest members of the cohort are 15-18 years old, 34.9% have used alcohol and 11.9% are regular users, while 30.1% have used drugs and 16.2% are regular users (Table 1).

Adjusting for age, more impactful child life events and living in a family with a parent who is single or remarried/living with a partner are related to regular use (Tables 1 and 2). Any drug use and regular drug use were also significantly related to a greater number of impactful child life events, being African-American, having a parent with a history of substance abuse, and living in a family with a parent who is single or remarried/living with a partner, once age was controlled (Tables 1 and 2, right-hand columns).

Table 3 displays results of the interval-censored proportional hazards survival analysis of any alcohol use and regular alcohol use. Any alcohol use over the follow-up, adjusting for age, is predicted by parental marital status, having a primary diagnosis of disruptive behavior disorder (DBD) at baseline, and number of impactful child life events. Compared to children whose biological parents are married, children whose parent is single have a 94% increase in the hazard (HR=1.94), and children whose parents are remarried or living with a partner have a 74% increase in the hazard (HR=1.74). Children with a primary baseline diagnosis of DBD have a 51% increase in the hazard. Finally, each additional impactful child life event was associated with a 4% increase in the hazard. Predictors of regular alcohol use were parent marital status, baseline age, and 24-month manic trajectory. Hazards were significantly higher for children whose parents were single (HR=4.54) or remarried/living with a partner (HR=4.16) compared to children whose biological parents were married. Children of single parents also had a significantly higher hazard (HR=2.55) compared to children whose parents were separated, divorced, or widowed. The hazard was 155% higher among youth with vs. without a high and rising 24-month manic trajectory. Baseline diagnoses of anxiety, depression, or ADHD showed no incremental association with risk of alcohol use after controlling for other predictors.

Table 4 shows predictors of any and regular drug use. Any drug use in the follow-up period is predicted by living with a single parent, a parent history of substance abuse, and number of impactful child life events. A child whose parent was single had a 137% increase in the hazard relative to children whose biological parents were married, and an 83% increase in the hazard compared to children whose parents were separated, divorced, or widowed. The hazard was 70% higher for children whose biological parent(s) have a history of substance abuse. The hazard increased by 5% for each additional impactful child life event. Regular drug use was predicted by parent marital status, impactful child life events, a primary diagnosis of DBD at baseline, and the number of medications at baseline. Children whose biological parents were not married vs. married had significantly higher hazards. For each additional impactful child life event, the hazard increased by 11%. When the primary diagnosis at baseline was DBD, the hazard increased by 141%. Finally, every additional medication at baseline decreased the hazard by 33%. Again, baseline diagnoses of anxiety, depression, BPSD, or ADHD showed no significant association with risk of drug use after controlling for other predictors.

DISCUSSION

In this cohort of children enriched for ESM, children 6-8 years at baseline reported moderate rates over the follow-up period of any alcohol use (8.8%) and any drug use (9.1%) and lower rates of regular alcohol (0.8%) and drug use (2.8%). Considerably higher rates of any alcohol (34.9%), any drug (30.1%), regular alcohol (11.9%), and regular drug (16.2%) use were reported by children aged 9-12 years at baseline. Interestingly, although these children were selected for symptoms indicative of problems in self-regulation and impulsivity, hallmark predictors of substance use in the literature,[42] they and their parents report rates of substance use lower than those from a national survey.[2] There are several possible reasons for this finding. Substance use data in LAMS were developed from both interviews and self-reports for the older children, while the national data were collected from self-administered

questionnaires. Reports of risky behaviors differ across modes of administration, and more anonymous self-reports may produce more accurate rates.[43] Alternatively, these data may suggest that MH problems and seeking care for MH problems may prevent or delay the development of substance use, either because treatment improves child/family functioning or because families who seek care for their children's MH problem are more effective in preventing the development of risky behaviors associated with these problems. Treatment for MH problems has been shown to be associated with a lower risk of substance use.[44] Recent data showed that adolescents with BPSD treated with psychostimulant medication prior to their first manic episode were less likely to develop SUD,[45] an intriguing finding replicated in our data. These findings are consistent with the earlier finding of Biederman et al.,[46] who found that adolescents with ADHD medicated at baseline, compared to those untreated, were less likely to develop substance use disorders. This could be due to the successful treatment of symptoms leading to reduced risk-taking behaviors and/or the improvement in symptoms leading to better academic and social functioning, thus reducing the appeal of regular drug use, or possibly families that could access treatment and took the trouble to do so had strengths that prevented substance use in other ways.

Children who lived in families with a single parent or a parent who had remarried or was living with a partner who was not a biological parent had elevated risks of using alcohol, using alcohol regularly, using drugs, and using drugs regularly. Family composition has long been associated with the development of substance use, usually due to less parental monitoring, poor parent–child interactions, or challenges in parenting due to substance use or MH problems.[14,42]

Any alcohol or drug use, and regular drug use are predicted by the number of reported impactful child life events, suggesting that children who experience multiple, stressful life events are more likely to initiate alcohol and drug use, perhaps as a means to relieve stress.[47,48] Older age and a DBD at baseline are also associated with substance use, as has been previously documented.[42,45,49] This suggests that children with disruptive behavior who experience considerable stress and who do not live with both biological parents be targeted for substance use prevention.

Finally, children with persistently high symptoms of mania[32] were at greater risk of regularly using alcohol. This suggests that children with severe and persistent or recurrent symptoms of mania, regardless of their diagnoses, are more likely to become regular alcohol users. This finding is similar to that of Molina et al.,[8] who found that severity and persistence of ADHD symptoms predicted alcohol and drug use.

As with all data, these have limitations. Participants were recruited from mental health clinics selected for symptoms of mania, and virtually all met criteria for one or more diagnoses. Thus, these results are not generalizable to all children, comparable with many previous studies, and may not hold in other samples of treated children, even though symptoms of mania are common in children visiting outpatient mental health centers. Data were self-reported with no other verification. It is possible that rates of alcohol and drug use would have been higher in this sample if data had been collected anonymously. Finally, we did not collect data on regular drug use during middle school.

Use of substances in this cohort of children potentially at high risk for the development of substance use points to the importance of the family environment in the initiation and regular use of alcohol and illicit drugs. Although child psychopathology at baseline, specifically DBD, was a predictor of any use and regular use over a 72-month follow-up, stressful environments were more strongly related to such use. Childhood diagnoses of anxiety, depression, or ADHD were not associated with risk of later alcohol or drug use after controlling for family structure, life events, and manic symptoms. It appears from these data that stress associated with cumulating life experiences, known to have life-long health risks, begins early. These findings argue strongly for targeted attention to the family environments of dysregulated children as a means to prevent the development of future substance use.

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Table 1

Bivariate Associations of Study Design and Child Characteristics With Any or Regular Substance Use

	Alcohol				Drugs			
	Any Alcohol Use		Regular Alcohol Use		Any Drug Use		Regular Drug Use	
	No (*n*=511)	Yes (*n*=151)	No (*n*=539)	Yes (*n*=40)	No (*n*=532)	Yes (*n*=137)	No (*n*=379)	Yes (*n*=50)
Study Design Characteristics								
Site								
CWRU	121 (78.1)	34 (21.9)	128 (94.8)	7 (5.2)	135 (83.9)	26 (16.1)	87 (92.6)	7 (7.4)
Cincinnati	128 (77.6)	37 (22.4)	136 (92.5)	11 (7.5)	135 (80.8)	32 (19.2)	99 (87.6)	14 (12.4)
Ohio State University	130 (76.0)	41 (24.0)	136 (93.2)	10 (6.8)	133 (78.2)	37 (21.8)	101 (88.6)	13 (11.4)
Pittsburgh	132 (77.2)	39 (22.8)	139 (92.1)	12 (7.9)	129 (75.4)	42 (24.6)	92 (85.2)	16 (14.8)
ESM +								
No	62 (76.5)	19 (23.5)	73 (94.8)	4 (5.2)	65 (80.3)	16 (19.7)	62 (93.9)	4 (6.1)
Yes	449 (77.3)	132 (22.7)	466 (92.8)	36 (7.2)	467 (79.4)	121 (20.6)	317 (87.3)	46 (12.7)
Child Characteristics								
Baseline age group								
6-8 years	**280 (91.2)**	**27 (8.8)*****	**257 (99.2)**	**2 (0.8)*****	**279 (90.9)**	**28 (9.1)*****	**141 (97.2)**	**4 (2.8)*****
9-12 years	**231 (65.1)**	**124 (34.9)**	**282 (88.1)**	**38 (11.9)**	**253 (69.9)**	**109 (30.1)**	**238 (83.8)**	**46 (16.2)**
Sex								
Female	164 (76.6)	50 (23.4)	174 (92.1)	15 (7.9)	172 (79.3)	45 (20.7)	125 (87.4)	18 (12.6)
Male	347 (77.5)	101 (22.5)	365 (93.6)	25 (6.4)	360 (79.7)	92 (20.3)	254 (88.8)	32 (11.2)
Race								
Caucasian	337 (78.6)	92 (21.4)	338 (93.6)	23 (6.4)	**357 (82.5)**	**76 (17.5)***	**242 (91.3)**	**23 (8.7)****
African-American	124 (72.5)	47 (27.5)	143 (90.5)	15 (9.5)	**127 (73.0)**	**47 (27.0)**	**96 (80.7)**	**23 (19.3)**
Other	50 (80.7)	12 (19.3)	58 (96.7)	2 (3.3)	**48 (77.4)**	**14 (22.6)**	**41 (91.1)**	**4 (8.9)**
Hispanic Ethnicity								
No	491 (77.6)	142 (22.4)	512 (92.8)	40 (7.2)	509 (79.4)	132 (20.6)	356 (87.7)	50 (12.3)
Yes	20 (69.0)	9 (31.0)	27 (100)	0 (0)	23 (82.1)	5 (17.9)	23 (100)	0 (0)
Child Clinical Characteristics								
Primary diagnosis at baseline								

	Alcohol				Drugs			
	Any Alcohol Use		Regular Alcohol Use		Any Drug Use		Regular Drug Use	
	No (*n*=511)	Yes (*n*=151)	No (*n*=539)	Yes (*n*=40)	No (*n*=532)	Yes (*n*=137)	No (*n*=379)	Yes (*n*=50)
BD/psychosis	122 (76.7)	37 (23.3)	128 (93.4)	9 (6.6)	123 (77.9)	35 (22.1)	98 (90.7)	10 (9.3)
MDD	87 (74.4)	30 (25.6)	90 (91.8)	8 (8.2)	90 (76.3)	28 (23.7)	72 (92.3)	6 (7.7)
Anxiety disorder	31 (77.5)	9 (22.5)	37 (97.4)	1 (2.6)	33 (78.6)	9 (21.4)	25 (86.2)	4 (13.8)
DBD	156 (76.9)	47 (23.1)	161 (92.0)	14 (8.0)	169 (82.4)	36 (17.6)	93 (81.6)	21 (18.4)
ADHD	69 (78.4)	19 (21.6)	76 (93.8)	5 (6.2)	69 (77.5)	20 (22.5)	59 (92.2)	5 (7.8)
Other	46 (83.6)	9 (16.4)	47 (94.0)	3 (6.0)	48 (84.2)	9 (15.8)	32 (88.9)	4 (11.1)
Number of diagnoses at baseline								
None or One	114 (76.0)	36 (24.0)	123 (91.8)	11 (8.2)	120 (79.0)	32 (21.0)	93 (88.6)	12 (11.4)
Two	165 (74.7)	56 (25.3)	179 (92.3)	15 (7.7)	179 (80.6)	43 (19.4)	127 (88.2)	17 (11.8)
Three	126 (77.3)	37 (22.7)	129 (92.1)	11 (7.9)	126 (75.5)	41 (24.5)	80 (82.5)	17 (17.5)
Four or more	106 (82.8)	22 (17.2)	108 (97.3)	3 (2.7)	107 (83.6)	21 (16.4)	79 (95.2)	4 (4.8)
Ever diagnosed with BPSD								
No	361 (78.7)	98 (21.3)	368 (93.4)	26 (6.6)	378 (80.9)	89 (19.1)	247 (87.6)	35 (12.4)
Yes	150 (73.9)	53 (26.1)	171 (92.4)	14 (7.6)	154 (76.2)	48 (23.8)	132 (89.8)	15 (10.2)
Mania Trajectories								
High and rising	40 (72.7)	15 (27.3)	48 (85.7)	8 (14.3)	41 (74.6)	14 (25.4)	35 (81.4)	8 (18.6)
Unstable	32 (82.1)	7 (17.9)	36 (92.3)	3 (7.7)	32 (80.0)	8 (20.0)	25 (86.2)	4 (13.8)
High and falling	195 (78.3)	54 (21.7)	191 (95.5)	9 (4.5)	204 (81.3)	47 (18.7)	133 (90.5)	14 (9.5)
Low and falling	241 (76.3)	75 (23.7)	262 (92.9)	20 (7.1)	252 (78.8)	68 (21.2)	185 (88.5)	24 (11.5)

Note: N (row %) shown. Bold values are statistically significant at $p<.05$. ADHD = attention-deficit/hyperactivity disorder; BD = bipolar disorder; BPSD = bipolar spectrum disorder; CWRU = Case Western Reserve University; DBD = disruptive behavior disorder; ESM = elevated symptoms of mania; MDD = major depressive disorder.

* $p<.05$

** $p<01$

*** $p<001$

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Table 2

Bivariate Associations of Family Characteristics With Any or Regular Substance Use

	Alcohol				Drugs			
	Any Alcohol Use		Regular Alcohol Use		Any Drug Use		Regular Drug Use	
	No (*n*=511)	Yes (*n*=151)	No (*n*=539)	Yes (*n*=40)	No (*n*=532)	Yes (*n*=137)	No (*n*=379)	Yes (*n*=50)
Family Characteristics								
Medicaid insurance only								
No	241 (75.6)	78 (24.4)	266 (93.7)	18 (6.3)	262 (81.1)	61 (18.9)	196 (90.3)	21 (9.7)
Yes	270 (78.7)	73 (21.3)	273 (92.5)	22 (7.5)	270 (78.0)	76 (22.0)	183 (86.3)	29 (13.7)
Child lives with both parents								
No	334 (75.6)	108 (24.4)	351 (91.6)	32 (8.4)	**347 (77.3)**	**102 (22.7)***	**244 (85.9)**	**40 (14.1)***
Yes	176 (80.4)	43 (19.6)	187 (95.9)	8 (4.1)	**185 (84.5)**	**34 (15.5)**	**135 (93.8)**	**9 (6.2)**
Parental marital status								
Single	108 (74.5)	37 (25.5)	**116 (90.6)**	**12 (9.4)****	107 (73.3)	39 (26.7)	**73 (83.0)**	**15 (17.0)***
Married to biological parent	160 (79.6)	41 (20.4)	**174 (96.7)**	**6 (3.3)**	167 (83.1)	34 (16.9)	**130 (94.9)**	**7 (5.1)**
Remarried/living with partner	97 (75.8)	31 (24.2)	**93 (86.9)**	**14 (13.1)**	104 (80.0)	26 (20.0)	**66 (82.5)**	**14 (17.5)**
Other (e.g., separated, divorced)	146 (77.7)	42 (22.3)	**156 (95.1)**	**8 (4.9)**	154 (80.2)	38 (19.8)	**110 (88.7)**	**14 (11.3)**
Parental history of substance abuse								
No	283 (77.1)	84 (22.9)	301 (94.4)	18 (5.6)	**305 (83.1)**	**62 (16.9)****	**218 (91.6)**	**20 (8.4)***
Yes	225 (77.1)	67 (22.9)	237 (91.5)	22 (8.5)	**224 (74.9)**	**75 (25.1)**	**160 (84.2)**	**30 (15.8)**
Number of impactful stressful life events	**4 (2, 8)**	**5 (2, 9)***	4 (2, 8)	5 (2, 10)	**4 (2, 7)**	**5 (3, 9)*****	**4 (2, 7)**	**6 (4, 10)*****

Note: N (row %) shown for categorical measures; median (25^{th}, 75^{th}) percentile shown for continuous measures (stressful life events). Bold values are statistically significant at $p<.05$.

* $p<.05$

** $p<.01$

*** $p<001$

Table 3

Interval Censored Proportional Hazards Survival Analysis of Alcohol Use

	Any Alcohol Use (*n*=662)			Regular Alcohol Use (*n*=579)		
	HR	**95% CI**	**p-val**	**HR**	**95% CI**	**p-val**
Parental marital status						
Remarried/living with a partner	1.74	1.08, 2.80	.02	4.16	1.57, 10.98	.005[a]
Separated/divorced/widowed	1.35	0.87, 2.09		1.78	0.62, 5.16	
Single	1.94	1.24, 3.05		4.54	1.68, 12.27	
Baseline age ≥ 9	1.66	1.07, 2.58	.02		n/a	
Baseline age (per 1-year increase)		n/a		1.36	1.07, 1.72	.01
Primary baseline diagnosis of DBD	1.51	1.06, 2.14	.02		n/a	
Number of impactful stressful life events (per 1-event increase)	1.04	1.00, 1.07	.04		n/a	
24-month manic trajectory: high and rising vs. others		n/a		2.55	1.15, 5.68	.02

Note: Reference for parental marital status is married to biological parent. n/a indicates that variable was not statistically significant at $p<.05$ and was omitted from the model. DBD = disruptive behavior disorder; HR = hazard ratio.

[a]Regular alcohol use: single vs. separated/divorced/widowed: HR=2.55, 95% CI: 1.03, 6.31.

Table 4

Interval Censored Proportional Hazards Survival Analysis of Drug Use

	Any Drug Use (*n*=669)			Regular Drug Use (*n*=429)[a]		
	HR	**95% CI**	**p-val**	**HR**	**95% CI**	**p-val**
Parental marital status						
Remarried/living with a partner	1.58	0.94, 2.66	.003[b]	3.99	1.58, 10.09	.01
Separated/divorced/widowed	1.29	0.79, 2.10		2.86	1.14, 7.16	
Single	2.37	1.47, 3.80		4.49	1.80, 11.20	
Parental history of substance abuse	1.70	1.19, 2.43	.004		n/a	
Number of impactful stressful life events (per 1-event increase)	1.05	1.01, 1.09	.006	1.11	1.05, 1.17	<.001
Primary baseline diagnosis of DBD		n/a		2.41	1.35, 4.30	.003
Number of medications at baseline (per each additional medication)		n/a		0.67	0.50, 0.91	.01

Note: Reference for parental marital status is married to biological parent. n/a indicates that variable was not statistically significant at $p<.05$ and was omitted from the model. DBD = disruptive behavior disorder; HR = hazard ratio.

[a] Regular drug use is unknown prior to high school; thus, the sample includes those who participated in Longitudinal Assessment of Manic Symptoms Study during high school.

[b] Any drug use: single vs. separated/divorced/widowed: HR=1.83, 95% CI: 1.16, 2.89.