

Supplemental Tables S1–S5

TABLE S1. Comparison of Intake Factors for Offspring With and Without Follow-Up Assessments^a

	Offspring Without Follow-Up (N=58)	Offspring With Follow-Up (N=581)	F	p
<i>Demographics (at Intake)</i>				
Age	11.5±3.8	11.9±3.6	0.24	0.6
Sex (% Female)	50.0%	51.0%	0.02	0.9
Race (% White)	62.1%	80.0%	3.96	0.05
Living status (% with both biological parents)	27.6%	51.8%	7.02	0.008
Socioeconomic status	29.2±9.4	35.7±13.9		
Mother's age at offspring's birth	24.3±5.0	27.6±5.8	9.60	0.002
Father's age at offspring's birth	25.7±6.2	30.2±7.4	9.54	0.002
<i>Diagnoses (Lifetime at Intake)</i>				
Bipolar-I disorder	0.0%	2.8%	—	—
Bipolar-spectrum disorder	8.6%	12.9%	0.79	0.4
Major depressive episode	13.8%	26.5%	3.72	0.05
Attention-deficit hyperactivity disorder	27.6%	25.7%	0.09	0.8
Oppositional defiant disorder	19.0%	20.7%	0.11	0.7
Conduct disorder	6.9%	8.1%	0.10	0.8
Any anxiety disorder	20.7%	34.1%	3.88	0.05
Substance use disorder	3.5%	17.4%	5.69	0.02
<i>Lifetime History (at Intake)</i>				
Physical abuse	6.9%	5.3%	0.24	0.6
Sexual abuse	6.9%	7.1%	0.00	1.0

^a Model adjusted for within-family correlation

TABLE S2. Parent Proband Factors

	Parents With Bipolar Disorder (N=236)	Community Control Parents (N=141)	Statistic	p
Demographics (at Intake)				
Sex (% Female)	80.5%	77.3%	$\chi^2=0.55$	0.5
Race (% White)	88.1%	75.9%	$\chi^2=9.64$	0.002
Marital status (% married)	48.3%	66.0%	$\chi^2=11.11$	0.0009
Socioeconomic status	34.3±14.4	37.2±12.9	$\chi^2=4.07$	0.04
Age	39.3±7.6	41.1±7.3	t=2.20	0.03
Number of offspring in study	1.95±1.0	2.08±0.9	t=1.14	0.26
Diagnoses (Lifetime at last assessment)				
Bipolar-I disorder	72.0%	—	—	—
Bipolar-II disorder	28.0%	—	—	—
Major depressive episode	93.2%	34.8%	$\chi^2=147.62$	<0.0001
Any nonbipolar Axis I disorder	98.7%	61.0%	$\chi^2=96.55$	<0.0001
Any nonmood Axis I Disorder	90.3%	50.4%	$\chi^2=75.62$	<0.0001
Any anxiety disorder	76.7%	28.4%	$\chi^2=84.98$	<0.0001
Panic disorder	46.2%	9.2%	$\chi^2=55.11$	<0.0001
Generalized anxiety disorder	41.1%	5.7%	$\chi^2=55.13$	<0.0001
Attention-deficit hyperactivity disorder	26.3%	3.6%	$\chi^2=31.2$	<0.0001
Oppositional defiant disorder/conduct disorder	36.9%	7.1%	$\chi^2=40.94$	<0.0001
Substance use disorder	65.7%	29.1%	$\chi^2=47.37$	<0.0001

TABLE S3. Biological Coparent Factors

	Coparents of Probands With Bipolar Disorder (N=298)	Community Control Coparents (N=186)	Stat	p
Demographics				
Sex (% Female)	20.1%	21.0%	$\chi^2=0.05$	0.8
Race (% White)	67.1%	66.7%	$\chi^2=0.01$	0.9
Age	40.7±8.1	40.3±7.1	t=0.55	0.58
SCID Assessment (%)	29.2%	33.9%	$\chi^2=1.17$	0.3
	Coparents of Probands With Bipolar Disorder (N=274) ^a	Community Control Coparents (N=165) ^b	Stat	p
Diagnoses (Lifetime at last assessment)				
Any axis I disorder	48.5%	31.5%	$\chi^2=12.24$	0.0005
Any psychotic disorder	1.8%	0.6%	$\chi^2=1.1$	0.29
Any depressive disorder	23.0%	14.5%	$\chi^2=4.63$	0.03
Bipolar-spectrum disorders	4.0%	—	—	—
Any anxiety disorder	11.7%	13.9%	$\chi^2=0.48$	0.49
Attention-deficit hyperactivity disorder	2.6%	2.4%	$\chi^2=0.01$	0.93
Oppositional defiant or conduct disorders	5.5%	2.4%	$\chi^2=2.31$	0.13
Substance use disorder	31.0%	17.6%	$\chi^2=9.69$	0.002

^a 24 coparents of probands with bipolar disorder did not have any available diagnostic information

^b 21 community control coparents did not have any available diagnostic information

TABLE S4. Association of Potential Confounding Variables With Hazard to Develop Subsequent Manic/Hypomanic Episodes in High-Risk Offspring^a

	New Onset Manic/Hypomanic Episode (N=36)	No Manic/ Hypomanic Episode (N=355)	Hazard Ratio	95% CI	χ^2	p
Offspring Age at intake (years)	12.6±2.8	11.9±3.7	0.95	0.86, 1.05	1.1	0.29
Offspring Age at last assessment (years)	19.5±3.6	18.0±4.9	0.95	0.87, 1.05	1.0	0.32
Date of Intake (year)	2003.94±1.6	2003.91±1.5	1.08	0.87, 1.35	0.5	0.47
Number of assessments	3.9±1.2	3.7±1.3	0.95	0.72, 1.26	0.1	0.73
Duration of follow-up (years)	7.3±1.7	6.7±2.3	1.00	0.87, 1.14	0.0	0.6
1st follow-up within 2 years of intake (% Yes)	77.8%	78.6%	0.76	0.34, 1.66	0.5	0.48
2nd follow-up within 3 years of intake (% Yes)	69.4%	62.8%	1.06	0.52, 2.16	0.0	0.86
Offspring sex (% Female)	52.8%	48.4%	1.18	0.61, 2.26	0.2	0.63
Socioeconomic status	34.8±14.7	33.7±14.0	1.00	0.98, 1.02	0.0	0.99
Offspring race (% White)	86.1%	80.6%	1.29	0.50, 3.32	0.3	0.60
Lives with both biological parents (% Yes)	30.6%	42.8%	0.55	0.27, 1.13	2.7	0.10
Proband parent sex (% Female)	97.2%	81.7%	8.69	1.19, 63.5	4.5	0.03
Proband parent age at onset of proband's bipolar disorder (years)	17.6±8.7	19.6±8.7	0.96	0.92, 1.00	3.4	0.06
Proband parent bipolar type (% Bipolar I disorder)	66.7%	70.4%	0.88	0.44, 1.77	0.1	0.73
Proband age at intake assessment (years)	37.5±6.8	38.9±7.2	0.93	0.88, 0.98	7.8	0.005

^a Cox regression models

TABLE S5. Association Comparing Single Versus Comorbid Prior Mood Episodes and/or Diagnoses in Hazard to Develop Subsequent Manic/Hypomanic Episodes in Offspring of Parents With Bipolar Disorder^a

Diagnoses	Hazard Ratio	p
Subthreshold hypo/manic episode	3.76	0.0001
Subthreshold hypo/manic episode and disruptive behavior disorder	4.93	0.0002
Subthreshold hypo/manic episode and any depressive episode	3.05	0.003
Subthreshold hypo/manic episode and major depressive episode	3.66	0.001
Subthreshold hypo/manic episode and attention-deficit hyperactivity disorder	3.25	0.009
Subthreshold hypo/manic episode and anxiety disorder	3.47	0.001
Any depressive episode	2.50	0.01
Any depressive episode and disruptive behavior disorder	1.76	0.13
Any depressive episode and attention-deficit hyperactivity disorder	1.98	0.07
Any depressive episode and anxiety disorder	2.06	0.03
Major depressive episode	2.58	0.005
Major depressive episode and anxiety disorder	2.59	0.005
Major depressive episode and attention-deficit hyperactivity disorder	2.48	0.02
Major depressive episode and disruptive behavior disorder	2.51	0.02
Disruptive behavior disorder	2.85	0.002
Disruptive behavior disorder and attention-deficit hyperactivity disorder	2.77	0.007
Disruptive behavior disorder and anxiety disorder	2.43	0.02
Attention-deficit hyperactivity disorder	2.04	0.03
Attention-deficit hyperactivity disorder and anxiety disorder	2.23	0.04
Anxiety disorder	1.86	0.06

^a Cox regression models