Supplement 1

METHOD

Additional demographics and clinical characteristics at intake, containing effect sizes, are noted in Table S1 below. In addition to the measures already described in the main body of the paper, participants were assessed for family history, socioeconomic status, pubertal development, and anxiety. Parents were interviewed at intake about the first-degree psychiatric family history and their own personal psychiatric history using a modified version of the Family History Screen (FHS) and the Structured Clinical interview for *DSM-IV* Axis I Disorder (SCID), respectively.[1] Socioeconomic status (SES) was measured using the Hollingshead 4-factor scale.[2] Pubertal status was assessed with the Petersen Pubertal Developmental Scale (PDS).[3] Anxiety symptoms were assessed using the child and parent versions of the Screen for Child Anxiety Related Emotional Disorder (SCARED).[4] As part of the intake evaluation, exposure to different psychopharmacological agents was also assessed.

Additional characterization of the percent of follow-up time spent in different mood states, containing effect sizes, is noted in Table S2 below. For longitudinal analyses, data from relevant measures of clinical symptoms and psychosocial functioning was aggregated into 2-year intervals. In all figures, the number on the x axis denotes the end of the interval (i.e., data from the start of study through month 24 encompass the 1st time-point). The Course and Outcome of Bipolar Youth (COBY) study is ongoing, and the number of participants with adequate data for the current analyses dropped off steadily after the 10th year; therefore, this was chosen as the cutoff point for analysis. Prevalence of youth with episode recurrence was calculated as the percentage of youth experiencing at least one episode characterized by a Longitudinal Interval Follow-Up Evaluation (LIFE) Psychiatric Status Rating (PSR) $\geq$5, with duration of 1 week for mania/hypomania or 2 weeks for depression.

Additional characterization of the exploratory longitudinal comparisons for Figures 1-3, and Figures S1-S2, containing estimated group effects (odds ratios [OR] and CI), is noted in Table S3 below.

Table S1: Additional Demographics and Clinical Characteristics at Intake					
Measures		BD+ASD (n=30)	BD (n=328)	Effect Size	P-value
Hollingshead Index of Social Status, mean ± SD		3.3 ± 1.1	3.4 ± 1.2	0.08 (d)	.69
Pubertal status, % at Tanner St. I/II-III/IV-V		**56/28/16**	**25/27/48**	**N/A**	**< .001**
Living with both natural parents, %		43	42	1.04 (OR)	.87
History of abuse (physical or sexual), %		7	21	0.28 (OR)	.063
SCARED	Child	23.1 ± 16.3	22.3 ± 10.7	0.07 (d)	.62
	Parent	26.3 ± 15	24.2 ± 16.1	0.13 (d)	.52
CBCL at intake, T-scores ± SD, p values controlled for age, sex					
Anxious/depressed		68.2 ± 9.3	65.1 ± 10.5	0.30 (d)	.19
Withdrawn		**69.6 ± 9.7**	**62.6 ± 9.0**	**0.77 (d)**	**<.001**
Somatic complaints		63.2 ± 8.5	62.7 ± 9.3	0.05 (d)	.85
Social problems		**70.7 ± 9.2**	**64.4 ± 10.0**	**0.63 (d)**	**.008**
Thought problems		**72.0 ± 8.3**	**65.8 ± 9.6**	**0.65 (d)**	**.005**
Attention problems		**69.0 ± 8.3**	**65.0 ± 9.7**	**0.42 (d)**	**.04**
Rule-breaking behaviors		62.7 ± 7.9	63.3 ± 8.7	0.07 (d)	.56
Aggressive behaviors		74.0 ± 9.6	71.7 ± 12.6	0.19 (d)	.96
Psychopharmacologic treatment history at intake, %					
Antidepressants		70	53	2.07 (OR)	.07
Antipsychotics		70	57	1.76 (OR)	.17
Stimulants		**83**	**53**	**4.33 (OR)**	**.001**
Other ADHD: (Strattera, α blockers)		**27**	**10**	**3.33 (OR)**	**.006**
Mood stabilizers (lithium and anticonvulsants)		50	63	0.59 (OR)	.15
1st degree family psychiatric history at intake, %					
BD		33	41	0.71 (OR)	.44
Depression or dysthymia		70	56	1.83 (OR)	.15
Anxiety disorders		43	47	0.85 (OR)	.67
ADHD		43	33	1.83 (OR)	.26
SUD		**20**	**45**	**0.31 (OR)**	**.005**

Note: ADHD = attention-deficit/hyperactivity disorder; ASD = autism spectrum disorder; BD = bipolar disorder; CBCL = Child Behavior Checklist; d = Cohen's d; OR = Odds ratio with BD as reference group; SCARED = Screen for Child Anxiety Related Emotional Disorder; SUD = substance use disorder.

Table S2: Additional Characterization of the Percent of Follow-Up Time Spent in the Following Mood States

Measures	BD+ASD (n=30)	BD (n=328)	P-value	Effect Size	P-value (age)*	P-value (age, sex)*
Asymptomatic	43 ± 27.7	49.7 ± 27	.21	0.25 (d)	.49	.43
Psychotic symptoms (delusions or hallucinations)	1.12 ± 3.2	3.6 ± 12.7	.29	0.20 (d)	.29	.35
Syndromal episode (total)	11 ± 13.2	14.5 ± 16.2	.18	0.22 (d)	.39	.52
Major depressive episode	6.5 ± 9.6	10 ± 13.1	.062	0.27 (d)	.29	.45
Manic/hypomanic episode	3.3 ± 5.0	3.5 ± 6.4	.84	0.03 (d)	.84	.83
Mixed episode	1.3 ± 2.2	1 ± 3.3	.50	0.09 (d)	.80	.87
Subsyndromal symptoms (total)	46 ± 23.7	35.8 ± 21.7	.029	0.47 (d)	.12	.13
Depressive symptoms	12.5 ± 9.0	14.1 ± 13.5	.38	0.12 (d)	.37	.41
Manic symptoms	15.1 ± 16.7	10.3 ± 12.4	.13	0.37 (d)	.11	.13
Mixed symptoms	18.4 ± 16.0	11.4 ± 14.9	.026	0.47 (d)	.10	.11

Note: ASD = autism spectrum disorder; BD = bipolar disorder; d = Cohen's d; OR = odds ratio with BD as reference group.
*P-values recalculated after controlling for subject age (left) or both age and sex (right).

Table S3: Additional Characterization (From Figures 1-3, S1, and S2) of Exploratory Longitudinal Comparisons

Exploratory Longitudinal Comparison	Follow-Up	ASD Group Effect p-value[a]	Odds Ratio (95% CI)[b]
Figure 1			
Probability of being asymptomatic at least 75% of follow-up	0-2 years	0.93	1.04 (0.38, 2.87)
	2-4 years	0.98	0.99 (0.41, 2.40)
	4-6 years	0.60	0.80 (0.35, 1.84)
	6-8 years	0.45	1.37 (0.61, 3.08)
	8-10 years	0.55	1.27 (0.57, 2.84)
Probability of being asymptomatic for less than 15% of follow-up	0-2 years	0.49	1.31 (0.60, 2.85)
	2-4 years	0.02	2.56 (1.18, 5.58)
	4-6 years	0.55	1.27 (0.58, 2.80)
	6-8 years	0.64	1.25 (0.50, 3.16)
	8-10 years	0.96	1.02 (0.39, 2.68)
Average level of difficulties with friendships	0-2 years	0.01	0.62 (0.16, 1.08)
	2-4 years	<0.0001	0.99 (0.60, 1.38)
	4-6 years	0.001	0.62 (0.26, 0.99)
	6-8 years	0.001	0.77 (0.32, 1.22)
	8-10 years	0.002	0.74 (0.27, 1.20)
Average level of difficulties with family relationships	0-2 years	0.28	-0.15 (-0.43, 0.13)
	2-4 years	0.35	-0.13 (-0.39, 0.14)
	4-6 years	0.89	0.02 (-0.27, 0.32)
	6-8 years	0.74	-0.08 (-0.53, 0.38)
	8-10 years	0.13	0.37 (-0.11, 0.84)
Average difficulty with work/school	0-2 years	0.43	-0.12 (-0.40, 0.17)
	2-4 years	0.17	0.19 (-0.08, 0.47)
	4-6 years	0.22	0.19 (-0.12, 0.50)
	6-8 years	0.13	0.23 (-0.07, 0.54)
	8-10 years	0.96	0.01 (-0.44, 0.46)
Average difficulties with life satisfaction	0-2 years	0.05	-0.23 (-0.46, 0.001)
	2-4 years	0.32	0.14 (-0.14, 0.43)
	4-6 years	0.77	-0.04 (-0.28, 0.21)
	6-8 years	0.61	0.08 (-0.23, 0.39)
	8-10 years	0.95	-0.01 (-0.40, 0.37)
Figure 2			
	MRS Items		

	Irritability	0.56	1.27 (0.57, 2.80)
	Elated mood	0.06	2.17 (0.96, 4.88)
	Mood lability	0.08	12.46 (0.72, 216.8)
	Distractibility	0.04	4.90 (1.12, 21.48)
	Increased activity	0.10	11.28 (0.65, 195.7)
	Pressured speech	0.09	2.94 (0.85, 10.21)
	Racing thoughts	0.05	2.29 (1.02, 5.17)
	Grandiosity	0.14	1.86 (0.81, 4.29)
	Hypersexuality	0.14	1.82 (0.82, 4.02)
	Psychotic symptoms	0.59	0.71 (0.20, 2.50)
	DRS Items		
	Depressed mood	0.03	2.40 (1.09, 5.28)
	Anhedonia	0.62	1.22 (0.56, 2.67)
	Mood reactivity	0.02	5.84 (1.34, 25.43)
	Diurnal variation	0.43	1.37 (0.63, 3.01)
	Social withdrawal	0.01	3.03 (1.38, 6.66)
	Sleep changes	0.62	1.23 (0.55, 2.72)
	Fatigue/aches	0.24	1.60 (0.73, 3.52)
	Negative cognitions	0.36	1.60 (0.58, 4.43)
	Self-injury	0.31	1.62 (0.64, 4.11)
	Suicidal ideation	0.85	1.11 (0.39, 3.12)
Figure 3			
Probability of depressed mood	0-2 years	0.03	2.41 (1.10, 5.30)
	2-4 years	0.75	0.88 (0.39, 1.95)
	4-6 years	0.96	1.02 (0.45, 2.30)
	6-8 years	0.67	1.19 (0.53, 2.68)
	8-10 years	0.62	0.75 (0.25, 2.29)
Probability of clinically significant social withdrawal	0-2 years	0.00	3.18 (1.46, 6.93)
	2-4 years	0.05	2.21 (1, 4.87)
	4-6 years	0.80	1.13 (0.44, 2.93)
	6-8 years	0.54	0.73 (0.27, 2)
	8-10 years	0.37	0.40 (0.05, 3.05)
Figure S1			
Probability of subsyndromal at least 50% of follow-up	0-2 years	0.11	1.85 (0.86, 3.97)
	2-4 years	0.09	1.97 (0.90, 4.27)
	4-6 years	0.76	1.13 (0.52, 2.46)
	6-8 years	0.71	1.18 (0.50, 2.82)
	8-10 years	0.53	0.73 (0.27, 1.98)
Incidence of BD episode recurrence	0-2 years	0.43	1.36 (0.64, 2.92)
	2-4 years	0.55	0.77 (0.33, 1.81)
	4-6 years	0.11	0.41 (0.14, 1.21)
	6-8 years	0.08	0.38 (0.13, 1.13)

	8-10 years	0.22	0.39 (0.09, 1.77)
Figure S2			
Prevalence of racing thoughts	0-2 years	0.05	2.24 (1.01, 4.94)
	2-4 years	0.26	1.57 (0.72, 3.42)
	4-6 years	0.89	1.07 (0.43, 2.64)
	6-8 years	0.76	0.86 (0.31, 2.35)
	8-10 years	0.52	1.52 (0.42, 5.54)
Prevalence of grandiosity	0-2 years	0.09	2 (0.89, 4.53)
	2-4 years	0.93	1.04 (0.48, 2.25)
	4-6 years	1.00	1 (0.43, 2.34)
	6-8 years	0.10	1.99 (0.89, 4.49)
	8-10 years	0.15	2.05 (0.78, 5.40)

Note: ASD = autism spectrum disorder; BD = bipolar disorder; DRS = Depression Rating Scale; MRS = Mania Rating Scale.
[a]Controlling for age and sex
[b]BD-only group is reference group
***ASD+BD mean - BD mean

Figure S1: Additional characterization of the overall symptom time course across follow-up. Note: (A) The prevalence of youths who spent more than 50% of follow-up with subsyndromal symptoms, termed "frequently subsyndromal," is elevated in bipolar disorder and autism spectrum disorder (BD+ASD) youth, especially during years 0-4 of the study. Differences in prevalence become non-significant after controlling for participant age (p=.09 for 2y and p=.068 for 4y). (B) The percent of youths with episode recurrence decreases over time for both groups, with no clinically significant between-group differences. The percentage of youth spending less than 5% of follow-up time in a mood episode followed the same trend as episode recurrence with no significant differences between groups (data not shown).

Figure S2: Additional characterization of the select symptoms across follow-up. Note: Time-course of the prevalence of select mood symptoms. (A) Racing thoughts was initially more frequent in youth with bipolar and autism spectrum disorders (BD+ASD), and decreased to levels comparable to youth with BD over time. Grandiosity (B) was more prevalent in BD+ASD youth during the initial years, with a dip in prevalence during years 2.1-6, and re-emergence of greater prevalence thereafter. * $p < .05$.

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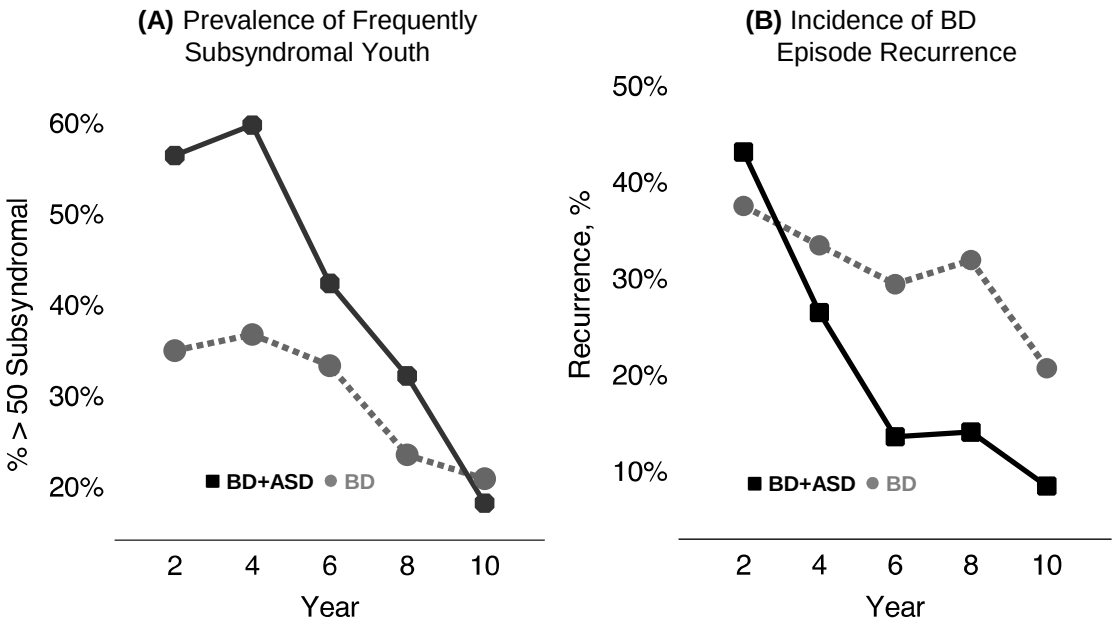
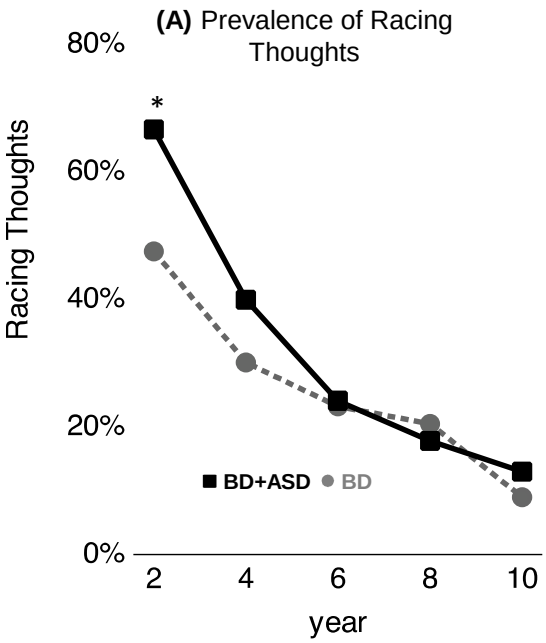
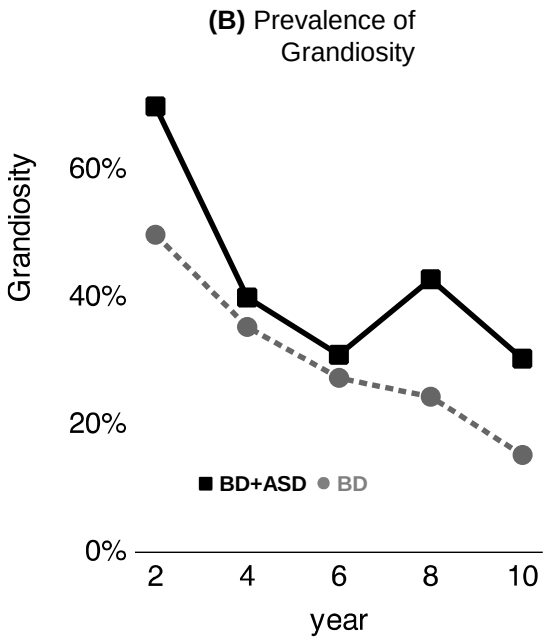


Age Conversion Legend - Mean age ± SD, n					
	2	4	6	8	10
BD+ASD	12.2 ± 2.7, 30	14.2 ± 2.7, 30	16.2 ± 2.6, 30	18.2 ± 2.7, 28	20 ± 2.7, 27
BD	14.0 ± 3.3, 338	16.0 ± 3.3, 338	18.0, ± 3.3, 338	20.0 ± 3.3, 324	21.8 ± 3.3, 266





Age Conversion Legend - Mean age ± SD, n					
	2	4	6	8	10
BD+ASD	12.2 ± 2.7, 30	14.2 ± 2.7, 30	16.2 ± 2.6, 30	18.2 ± 2.7, 28	20 ± 2.7, 27
BD	14.0 ± 3.3, 338	16.0 ± 3.3, 338	18.0, ± 3.3, 338	20.0 ± 3.3, 324	21.8 ± 3.3, 266