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## Abbreviations

Lcl = lower confidence limit

OR = odds ratio

PRS = polygenic risk score

PRS-BD = Polygenic risk score for bipolar disorder

PRS-MD = Polygenic risk score for major depression

PRS-SZ = Polygenic risk score for schizophrenia

Ucl = upper confidence limit

P = p value

Table S1. Polarity as defined by ICD-10 diagnosis

Polarity	ICD-10 Code	Code description
Depressive	F31.3	Bipolar disorder, current episode mild or moderate depression
	F31.4	Bipolar disorder, current episode severe depression without psychotic symptoms
	F31.5	Bipolar disorder, current episode severe depression with psychotic symptoms
	F32.x F33.x	Depressive episode Recurrent depressive disorder
Manic	F30.x	Manic episode
	F31.0	Bipolar disorder, current episode hypomanic
	F31.1	Bipolar disorder, current episode manic without psychotic symptoms
	F31.2	Bipolar disorder, current episode manic with psychotic symptoms
Mixed	F31.6	Bipolar disorder, current episode mixed
	F38.00	Mixed affective episode
Unspecified	F31.7	Bipolar disorder currently in remission
	F31.9	Bipolar disorder not otherwise specified
Non-psychotic depression	F31.3	Bipolar disorder, current episode mild or moderate depression
	F31.4	Bipolar disorder, current episode severe depression without psychotic symptoms
	F32 (excl. .3)	Depressive episode, excluding severe depressive episode with psychotic symptoms
	F33 (excl. .3)	Recurrent depressive disorder, excluding current episode severe with psychotic symptoms
Psychotic depression	F31.5	Bipolar disorder, current episode severe depression with psychotic symptoms
	F32.3	Severe depressive episode with psychotic symptoms
	F33.3	Recurrent depressive disorder, current episode severe with psychotic symptoms
Non-psychotic mania	F30 (exc. .2)	Manic episode, excluding severe with psychotic symptoms
	F31.0	Bipolar disorder, current episode hypomanic
	F31.1	Bipolar disorder, current episode manic without psychotic symptoms
Psychotic mania	F30.2	Manic episode, severe with psychotic symptoms
	F31.2	Bipolar disorder, current episode manic with psychotic symptoms

Note. Episodes where the diagnosis was F31.8- 'Other bipolar affective disorders' were excluded, as this category includes different polarities and could therefore not be properly placed within a polarity category.

Table S2. Individual associations between PRS and number of manic and depressive episodes

Polarity	Polygenic Risk Score								
	Bipolar Disorder			Major Depression			Schizophrenia		
	$\beta$	SE	p	$\beta$	SE	p	$\beta$	SE	p
Depressive	0.02	0.02	0.5176	0.04	0.02	0.0615	0.01	0.02	0.5525
Manic	0.24	0.04	<.0001	-0.18	0.04	<.0001	0.18	0.05	<.0001
Mixed	0.05	0.05	0.2653	0.11	0.05	0.0173	0.09	0.05	0.0711
Unspecified	0.03	0.02	0.1348	-0.00	0.02	0.8671	0.03	0.02	0.2576

Note. Associations obtained from negative binomial models with the exception of the association between PRS-MD and unspecified polarity, which was obtained from a poisson regression model. All models adjusted for gender, age at first bipolar diagnosis, the first 5 principal components and genotyping platform (iPSYCH2012 vs. iPSYCH2015).

Table S3. Pearson Correlations between PRS variables

	PRS-schizophrenia	PRS-bipolar disorder	PRS-major depression
PRS-schizophrenia	1.00	-	-
PRS-bipolar disorder	0.51915 (p < .0001)	1.00	-
PRS-major depression	0.25304 (p < .0001)	0.25246 (p < .0001)	1.00

Table S4. PRS and number of manic and depressive episodes with and without psychotic symptoms

Polarity		Polygenic Risk Score								
		Bipolar Disorder			Major Depression			Schizophrenia		
		$\beta$	SE	p	$\beta$	SE	p	$\beta$	SE	p
Any	Psychotic symptoms	0.15	0.07	0.0294	-0.32	0.06	<.0001	0.22	0.07	0.0032
Depression	No psychotic symptoms	0.01	0.03	0.8432	0.06	0.02	0.0168	-0.00	0.03	0.8561
	Psychotic symptoms	0.02	0.11	0.8410	-0.20	0.10	0.0399	0.12	0.11	0.3091
Mania	No psychotic symptoms	0.20	0.05	0.0002	-0.18	0.05	0.0001	0.08	0.05	0.1537
	Psychotic symptoms	0.27	0.09	0.0035	-0.42	0.08	<.0001	0.29	0.09	0.0023

Note. Associations obtained from negative binomial models. All models adjusted for gender, age at first bipolar diagnosis, the first 5 principal components and genotyping platform (iPSYCH2012 vs. iPSYCH2015).

Table S5. PRS and polarity and the first or any episode among 2,366 patients with bipolar disorder who had Danish-born parents

Polarity	PRS	First episode				Any episode			
		OR	lcl	ucl	p	OR	lcl	ucl	p
Depressive	PRS-BD	0.97	0.87	1.08	0.5761	0.94	0.84	1.06	0.3275
	PRS-MD	1.10	1.00	1.21	0.0487	1.14	1.02	1.26	0.0162
	PRS-SZ	0.94	0.85	1.05	0.2890	1.00	0.88	1.12	0.9390
Manic	PRS-BD	1.15	0.99	1.34	0.0607	1.27	1.12	1.44	0.0002
	PRS-MD	0.82	0.72	0.93	0.0019	0.77	0.69	0.86	<.0001
	PRS-SZ	1.14	0.99	1.33	0.0773	1.13	0.99	1.28	0.0613
Mixed	PRS-BD	0.82	0.68	0.98	0.0341	0.99	0.87	1.13	0.8419
	PRS-MD	1.26	1.07	1.48	0.0058	1.14	1.02	1.28	0.0223
	PRS-SZ	1.07	0.89	1.28	0.4905	1.03	0.90	1.18	0.6380
Unspecified	PRS-BD	1.03	0.91	1.16	0.6426	0.95	0.85	1.06	0.3349
	PRS-MD	0.93	0.84	1.03	0.1584	0.95	0.86	1.05	0.3547
	PRS-SZ	0.96	0.85	1.08	0.4609	1.00	0.90	1.12	0.9682

Note. Associations obtained from logistic regression models adjusted for gender, age at first bipolar diagnosis, the first 5 principal components and genotyping platform (iPSYCH2012 vs. iPSYCH2015).

Table S6. PRS and number of episodes of a given polarity among 2,366 patients with bipolar disorder who had Danish-born parents

Polarity	Polygenic Risk Score								
	Bipolar Disorder			Major Depression			Schizophrenia		
	$\beta$	SE	p	$\beta$	SE	p	$\beta$	SE	p
Depressive	-0.00	0.03	0.9525	0.04	0.03	0.1133	0.01	0.03	0.7601
Manic	0.24	0.05	<.0001	-0.24	0.05	<.0001	0.14	0.05	0.0097
Mixed	0.02	0.06	0.7207	0.10	0.05	0.0559	0.06	0.06	0.3262
Unspecified	0.03	0.03	0.2641	-0.02	0.02	0.4327	0.02	0.03	0.5794

Note. Associations obtained from negative binomial models with the exception of the association between PRS-MD and unspecified polarity, which was obtained from a poisson regression model. All models adjusted for gender, age at first bipolar diagnosis, the first 5 principal components and genotyping platform (iPSYCH2012 vs. iPSYCH2015).

Table S7. PRS and psychotic symptoms in the first or any manic or depressive episode among 2,366 patients with bipolar disorder who had Danish-born parents

Polarity	Psychosis (yes/no)	PRS	First episode				Any episode			
			OR	lci	ucl	p	OR	lci	ucl	p
Any	Psychotic symptoms	PRS-BD	1.09	0.87	1.35	0.4574	1.23	1.04	1.45	0.0176
		PRS-MD	0.74	0.62	0.90	0.0019	0.66	0.57	0.76	<.0001
		PRS-SZ	1.31	1.05	1.63	0.0172	1.19	1.00	1.41	0.0476
Depression	No psychotic symptoms	PRS-BD	0.98	0.88	1.09	0.7216	0.94	0.84	1.06	0.3089
		PRS-MD	1.12	1.02	1.23	0.0204	1.15	1.03	1.27	0.0100
		PRS-SZ	0.92	0.83	1.03	0.1355	0.99	0.88	1.11	0.8475
	Psychotic symptoms	PRS-BD	0.88	0.60	1.27	0.4817	1.00	0.79	1.27	0.9886
		PRS-MD	0.83	0.60	1.14	0.2542	0.79	0.64	0.97	0.0217
		PRS-SZ	1.33	0.91	1.94	0.1432	1.05	0.82	1.33	0.7013
Mania	No psychotic symptoms	PRS-BD	1.12	0.94	1.32	0.2064	1.25	1.09	1.43	0.0014
		PRS-MD	0.88	0.76	1.02	0.0974	0.82	0.73	0.92	0.0007
		PRS-SZ	1.07	0.91	1.27	0.4107	1.07	0.93	1.23	0.3241
	Psychotic symptoms	PRS-BD	1.19	0.92	1.54	0.1781	1.36	1.11	1.67	0.0030
		PRS-MD	0.72	0.57	0.90	0.0035	0.63	0.53	0.76	<.0001
		PRS-SZ	1.28	0.98	1.66	0.0649	1.29	1.05	1.59	0.0156

Note. Associations obtained from logistic regression models adjusted for gender, age at first bipolar diagnosis, the first 5 principal components and genotyping platform (iPSYCH2012 vs. iPSYCH2015).

Table S8. PRS and number of manic and depressive episodes with and without psychotic symptoms among 2,366 patients with bipolar disorder who had Danish-born parents

Polarity	Psychosis (yes/no)	Polygenic Risk Score								
		Bipolar Disorder			Major Depression			Schizophrenia		
		$\beta$	SE	p	$\beta$	SE	p	$\beta$	SE	p
Any	Psychotic symptoms	0.17	0.08	0.0237	-0.32	0.07	<.0001	0.21	0.08	0.0090
Depression	No psychotic symptoms	-0.00	0.03	0.9322	0.06	0.03	0.0229	0.00	0.03	0.9347
	Psychotic symptoms	0.01	0.12	0.9361	-0.21	0.10	0.0414	0.11	0.12	0.3769
Mania	No psychotic symptoms	0.22	0.06	0.0001	-0.17	0.05	0.0006	0.09	0.06	0.1221
	Psychotic symptoms	0.32	0.10	0.0018	-0.43	0.09	<.0001	0.29	0.10	0.0052

Note. Associations obtained from negative binomial models. All models adjusted for gender, age at first bipolar diagnosis, the first 5 principal components and genotyping platform (iPSYCH2012 vs. iPSYCH2015).

Table S9. PRS and polarity at the first or any episode during the 3-year period following initial diagnosis

Polarity	PRS	First episode				Any episode			
		OR	lcl	ucl	p	OR	lcl	ucl	p
Depressive	PRS-BD	0.99	0.88	1.11	0.8622	1.01	0.89	1.15	0.8746
	PRS-MD	1.10	1.00	1.22	0.0550	1.14	1.02	1.27	0.0244
	PRS-SZ	0.96	0.85	1.07	0.4482	0.89	0.79	1.01	0.0775
Manic	PRS-BD	1.10	0.94	1.29	0.2257	1.17	1.01	1.34	0.0328
	PRS-MD	0.76	0.67	0.88	0.0001	0.72	0.63	0.81	<.0001
	PRS-SZ	1.17	0.99	1.37	0.0648	1.23	1.06	1.42	0.0053
Mixed	PRS-BD	0.78	0.62	0.97	0.0272	0.95	0.80	1.12	0.5396
	PRS-MD	1.46	1.12	1.78	0.0002	1.24	1.07	1.43	0.0037
	PRS-SZ	1.00	0.78	1.25	0.9908	0.92	0.78	1.09	0.3359
Unspecified	PRS-BD	1.04	0.91	1.19	0.5431	1.00	0.88	1.12	0.9392
	PRS-MD	0.92	0.82	1.04	0.1873	0.94	0.85	1.05	0.2699
	PRS-SZ	0.95	0.83	1.09	0.4878	1.05	0.93	1.19	0.3975

Note. Only the subset of patients with at least 3 years in follow-up were included in these analyses (n=1926). Associations obtained from logistic regression models adjusted for gender, age at first bipolar diagnosis, the first 5 principal components and genotyping platform (iPSYCH2012 vs. iPSYCH2015).

Table S10. PRS and number of episodes of a given polarity during the 3-year period following initial diagnosis

Polarity	Polygenic Risk Score								
	Bipolar Disorder			Major Depression			Schizophrenia		
	$\beta$	SE	p	$\beta$	SE	p	$\beta$	SE	p
Depressive	0.02	0.03	0.4836	0.05	0.03	0.0515	-0.04	0.03	0.1799
Manic	0.18	0.06	0.0020	-0.25	0.05	<.0001	0.18	0.06	0.0019
Mixed	0.04	0.07	0.5766	0.16	0.06	0.0130	-0.09	0.07	0.2479
Unspecified	0.03	0.03	0.2641	-0.02	0.02	0.4327	0.02	0.03	0.5794

Note. Only the subset of patients with at least 3 years in follow-up were included in these analyses (n=1926). Associations obtained from negative binomial models except for depressive polarity, which was obtained from a poisson regression model. All models adjusted for gender, age at first bipolar diagnosis, the first 5 principal components and genotyping platform (iPSYCH2012 vs. iPSYCH2015).

Table S11. PRS and psychotic symptoms in the first or any manic or depressive episode during the 3-year period following initial diagnosis.

Polarity	Psychosis (yes/no)	PRS	First episode				Any episode			
			OR	lcl	ucl	p	OR	lcl	ucl	p
Any	Psychotic symptoms	PRS-BD	1.10	0.87	1.38	0.4370	1.19	0.99	1.44	0.0595
		PRS-MD	0.81	0.66	0.99	0.0353	0.70	0.60	0.83	<.0001
		PRS-SZ	1.27	1.00	1.61	0.0523	1.17	0.96	1.41	0.1117
Depression	No psychotic symptoms	PRS-BD	0.99	0.88	1.11	0.8961	1.02	0.90	1.15	0.8121
		PRS-MD	1.12	1.01	1.23	0.0336	1.13	1.01	1.26	0.0267
		PRS-SZ	0.94	0.84	1.06	0.2992	0.98	0.79	1.01	0.0780
	Psychotic symptoms	PRS-BD	0.98	0.65	1.48	0.9230	1.06	0.81	1.41	0.6607
		PRS-MD	0.86	0.61	1.22	0.3962	0.89	0.71	1.14	0.3749
		PRS-SZ	1.26	0.83	1.93	0.2784	0.97	0.73	1.29	0.8189
Mania	No psychotic symptoms	PRS-BD	1.07	0.89	1.29	0.4536	1.15	0.99	1.34	0.0675
		PRS-MD	0.78	0.66	0.91	0.0020	0.77	0.67	0.88	0.0001
		PRS-SZ	1.11	0.92	1.33	0.2881	1.22	1.04	1.43	0.0129
	Psychotic symptoms	PRS-BD	1.14	0.87	1.50	0.3296	1.27	1.01	1.58	0.0367
		PRS-MD	0.79	0.62	1.00	0.0471	0.66	0.54	0.80	<.0001
		PRS-SZ	1.26	0.95	1.68	0.1056	1.25	1.00	1.58	0.0522

Note. Only the subset of patients with at least 3 years in follow-up were included in these analyses (n=1926). Associations obtained from logistic regression models adjusted for gender, age at first bipolar diagnosis, the first 5 principal components and genotyping platform (iPSYCH2012 vs. iPSYCH2015).

Table S12. PRS and number of manic and depressive episodes with and without psychotic symptoms during the 3-year period following initial diagnosis

Polarity	Psychosis (yes/no)	Polygenic Risk Score								
		Bipolar Disorder			Major Depression			Schizophrenia		
		$\beta$	SE	p	$\beta$	SE	p	$\beta$	SE	p
Any	Psychotic symptoms	0.20	0.08	0.0144	-0.25	0.07	0.0003	0.18	0.08	0.0311
Depression	No psychotic symptoms	0.02	0.03	0.6146	0.06	0.03	0.0203	-0.05	0.03	0.1290
	Psychotic symptoms	0.10	0.13	0.4439	-0.11	0.12	0.3390	0.06	0.14	0.6708
Mania	No psychotic symptoms	0.13	0.06	0.0356	-0.20	0.05	0.0002	0.15	0.06	0.0220
	Psychotic symptoms	0.28	0.11	0.0073	-0.35	0.09	0.0001	0.27	0.11	0.0146

Note. Only the subset of patients with at least 3 years in follow-up were included in these analyses (n=1926). Associations obtained from negative binomial models. All models adjusted for gender, age at first bipolar diagnosis, the first 5 principal components and genotyping platform (iPSYCH2012 vs. iPSYCH2015).



Figure S1. Sample Selection Flow Chart

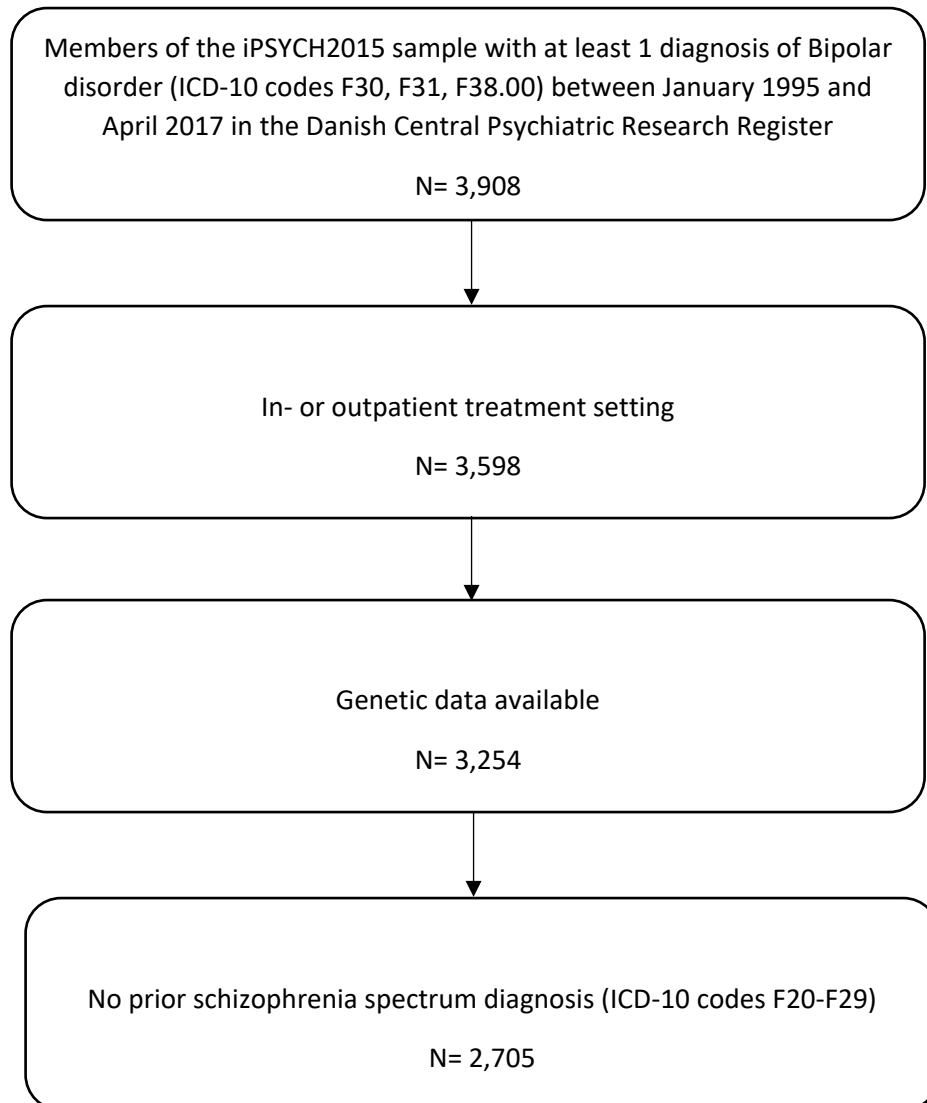
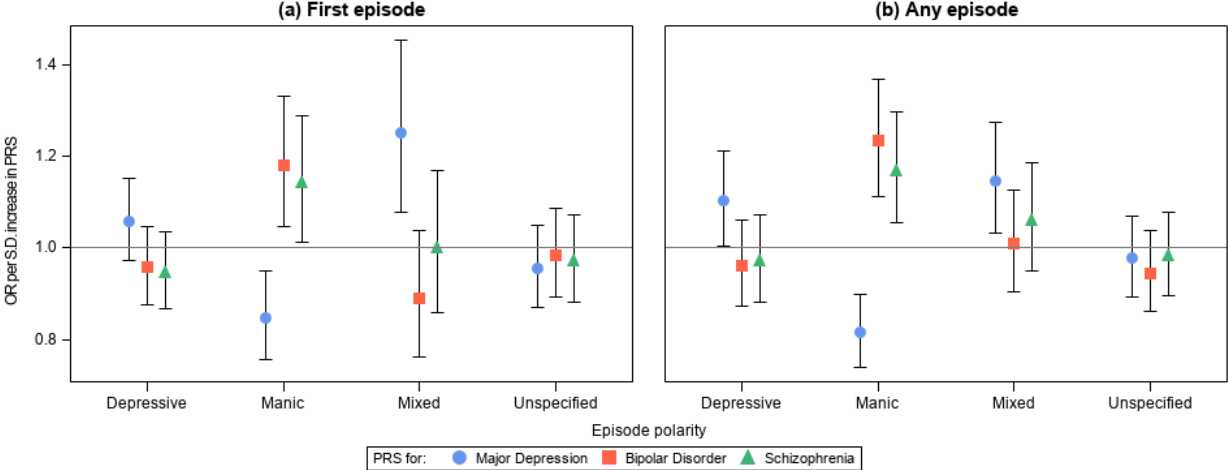
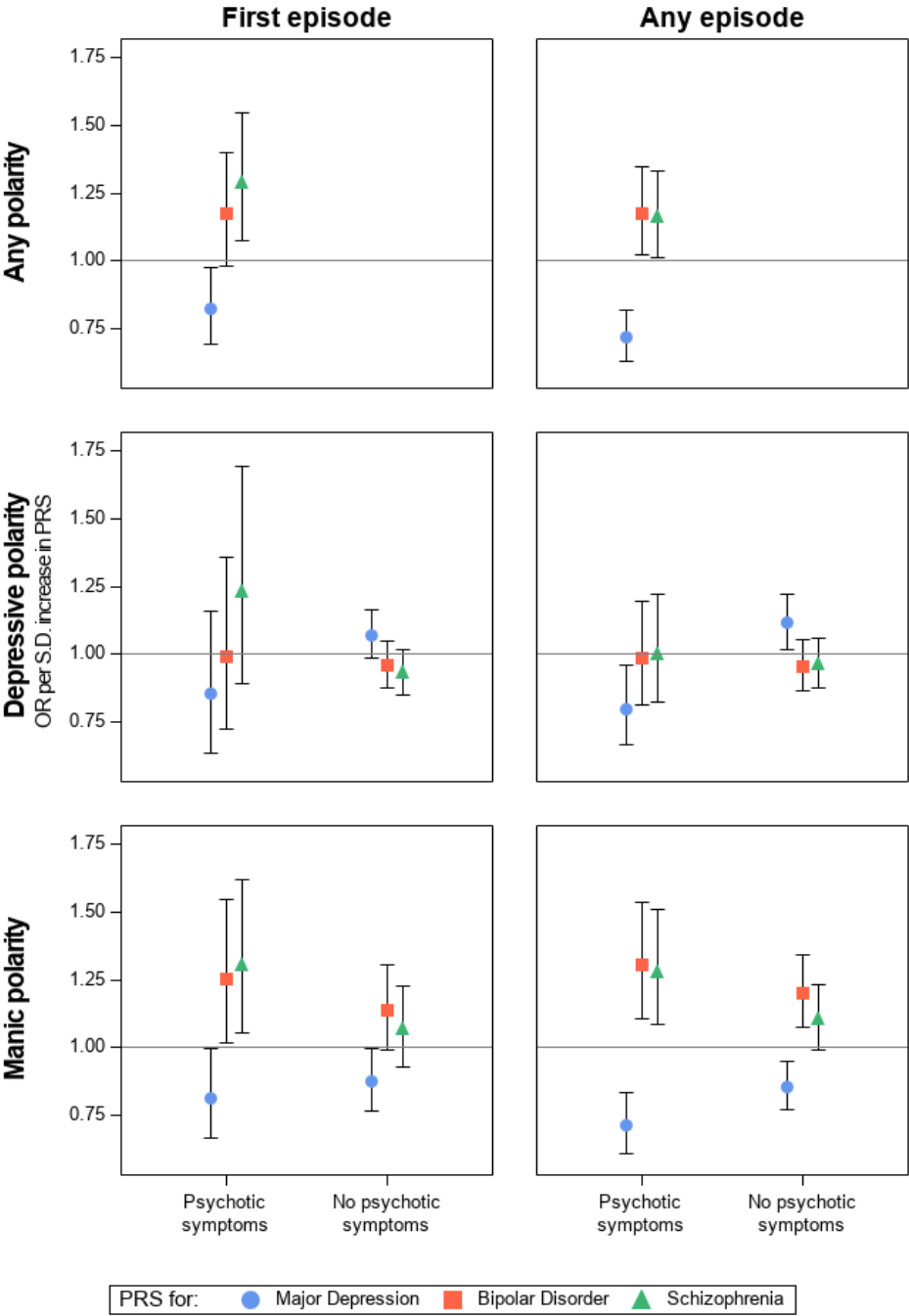


Figure S2. Individual associations between polygenic liabilities for bipolar disorder, schizophrenia and major depression and polarity and first or any episode



Note. Associations obtained from logistic regression models. All models adjusted for the first 5 principal components and genotyping platform (iPSYCH2012 vs. iPSYCH2015).

Figure S3. Individual Associations between polygenic liabilities for bipolar disorder, schizophrenia, and major depression and psychotic symptoms



Note. Associations obtained from logistic regression models. All models adjusted for the first 5 principal components and genotyping platform (iPSYCH2012 vs. iPSYCH2015).

Figure S4. Mean PRS by number of episodes of a given polarity

