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Supplementary Material

Article Title: Risks of Coaggregation of Major Psychiatric Disorders Among First-Degree Relatives of Patients With Bipolar I and Bipolar II Disorder: Evidence From a Nationwide Population-Based Study

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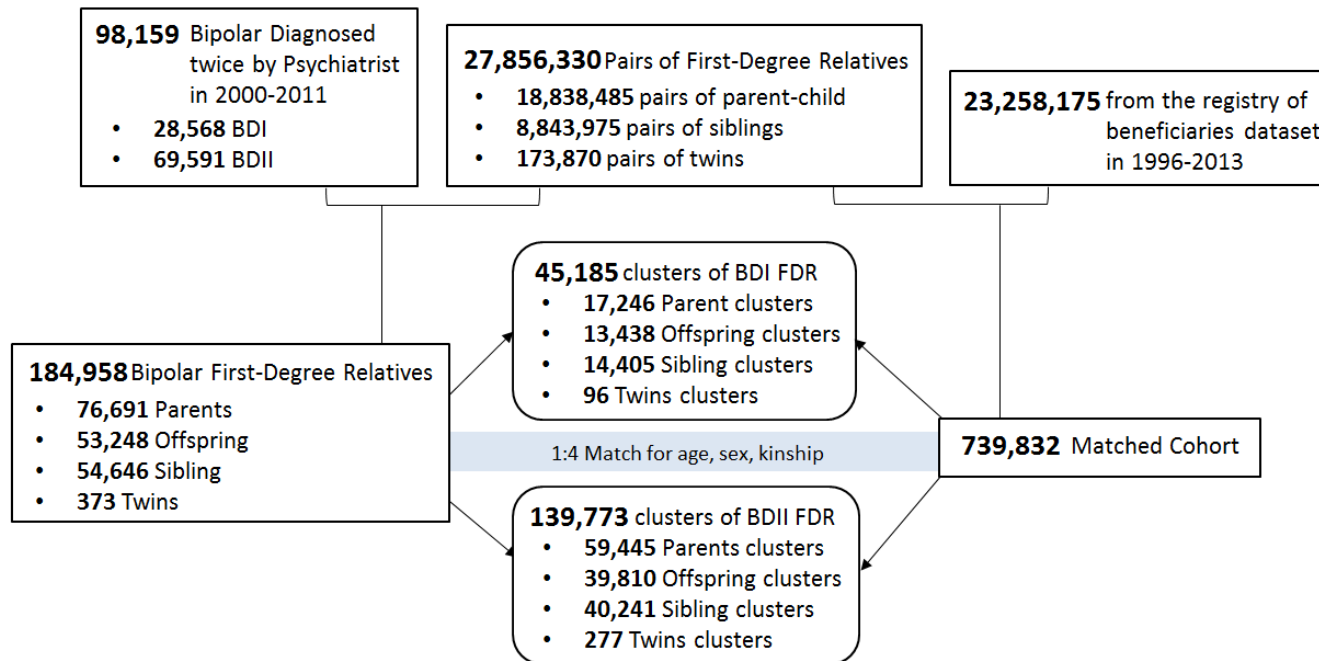
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Supplementary Figure 1. Study flow-chart



Supplementary Table 1. Adjusted relative risk of different psychiatric disorders between male FDRs with BD-I/BD-II proband and their male matched cohort

Case Number	BD-I Male Cohort			BD-II Male Cohort			p-value for comparison
	FDR of BD-I patients (n=22355)	Matched BD-I control cohort (n=89420)	Adjusted RR [‡] (95%C.I.)	FDR of BD-II patients (n=69657)	Matched BD-II control cohort (n=278628)	Adjusted RR [‡] (95%C.I.)	
SCZ	666 (2.98)	458 (0.51)	5.09 (5.24, 6.64)	1012 (1.45)	1444 (0.52)	2.84 (2.62, 3.08)	<0.001
BD	759 (3.40)	328 (0.37)	9.46 (8.31, 10.77)	1477 (2.12)	1031 (0.37)	5.81 (5.36, 6.30)	<0.001
BDI	336 (1.50)	96 (0.11)	14.03 (11.18, 17.61)	416 (0.60)	275 (0.10)	6.09 (5.23, 7.09)	<0.001
BDII	423 (1.89)	232 (0.26)	7.39 (6.29, 8.67)	1061 (1.52)	756 (0.27)	5.65 (5.14, 6.21)	0.0050
MDD	710 (3.18)	887 (0.99)	3.28 (2.97, 3.63)	1888 (2.71)	2861 (1.03)	2.68 (2.53, 2.84)	0.0008
ASD	96 (0.43)	179 (0.20)	2.18 (1.70, 2.80)	292 (0.42)	598 (0.21)	1.96 (1.71, 2.26)	0.5171
ADHD	411 (1.84)	935 (1.05)	1.87 (1.66, 2.11)	1662 (2.39)	3163 (1.14)	2.19 (2.06, 2.33)	0.0046
Anxiety	1763 (7.89)	3118 (3.49)	2.38 (2.24, 2.53)	5050 (7.25)	9487 (3.40)	2.22 (2.14, 2.30)	0.0601
OCD	117 (0.52)	180 (0.20)	2.81 (2.23, 3.55)	378 (0.54)	534 (0.19)	3.00 (2.63, 3.42)	0.5788

‡ : Adjusted for age, urbanization, income level; a: proportion(BDI)=the number of BDI/the number of BDI+BDII; b: proportion(BDII)=the number of BDII/the number of BDI+BDII.

Abbreviation: SCZ, Schizophrenia; BD, bipolar disorder; MDD, major depressive disorder; ASD, Autism spectrum disorder; ADHD, Attention Deficit Hyperactivity Disorder; OCD, obsessive-compulsive disorder; FDR, First Degree Relative; C.I. ,confidence interval; RR, relative risk.

Supplementary Table 2.

Adjusted relative risk of different psychiatric disorders between female FDRs with BD-I/BD-II proband and their female matched cohort

Case Number	BD-I Female Cohort			BD-II Female Cohort			p-value for comparison
	FDR of	Matched	Adjusted RR [‡] (95%C.I.)	FDR of	Matched	Adjusted RR [‡] (95%C.I.)	
	BD-I patients	BD-I control		BD-II patients	BD-II control		
	(n=22830)	cohort (n=91320)		(n=70116)	cohort (n=280464)		
SCZ	645 (2.83)	448 (0.49)	5.76 (5.10, 6.50)	904 (1.29)	1403 (0.50)	2.60 (2.39, 2.82)	<0.001
BD	921 (4.03)	457 (0.50)	8.28 (7.40, 9.26)	1889 (2.69)	1292 (0.46)	5.94 (5.54, 6.38)	<0.001
BDI	375 (1.64)	84 (0.09)	17.81 (14.05, 22.57)	373 (0.53)	281 (0.10)	5.30 (4.53, 6.19)	<0.001
BDII	546 (2.39)	373 (0.41)	5.94 (5.20, 6.78)	1516 (2.16)	1011 (0.36)	6.06 (5.60, 6.57)	0.7792
MDD	1166 (5.11)	1644 (1.80)	2.95 (2.73, 3.18)	3354 (4.78)	4773 (1.70)	2.92 (2.79, 3.05)	0.7928
ASD	30 (0.13)	43 (0.05)	2.75 (1.74, 4.36)	85 (0.12)	118 (0.04)	2.75 (1.74, 4.36)	0.9087
ADHD	124 (0.54)	236 (0.26)	2.12 (1.70, 2.64)	581 (0.83)	790 (0.28)	2.99 (2.68, 3.33)	0.0059
Anxiety	2455 (10.75)	4188 (4.59)	2.55 (2.42, 2.68)	7090 (10.11)	12864 (4.59)	2.37 (2.30, 2.44)	0.0235
OCD	112 (0.49)	168 (0.18)	2.94 (2.31, 3.73)	382 (0.54)	523 (0.19)	3.16 (2.77, 3.61)	0.5827

‡ : Adjusted for age, urbanization, income level; a: proportion(BDI)=the number of BDI/the number of BDI+BDII; b: proportion(BDII)=the number of BDII/the number of BDI+BDII.

Abbreviation: SCZ, Schizophrenia; BD, bipolar disorder; MDD, major depressive disorder; ASD, Autism spectrum disorder; ADHD, Attention Deficit Hyperactivity Disorder; OCD, obsessive-compulsive disorder;

FDR, First Degree Relative; C.I., confidence interval; RR, relative risk.

Supplementary Table 3. Sensitivity test for psychiatric diagnosis given by board-certified psychiatrists at least three times (model 1)

	ARR [‡] for Male (95%C.I.)			ARR [‡] for Female (95%C.I.)			ARR [‡] for All (95%C.I.)		
	BD-I Cohort	BD-II Cohort	P -value for comparison	BD-I Cohort	BD-II Cohort	P -value for comparison	BD-I Cohort	BD-II Cohort	P-value for comparison
SCZ	6.06 (5.35, 6.86)	2.85 (2.62, 3.10)	<0.001	5.68 (5.01, 6.43)	2.53 (2.32, 2.76)	<0.001	5.86 (5.37, 6.40)	2.69 (2.53, 2.86)	<0.001
BD	9.52 (8.3, 10.91)	6.02 (5.53, 6.56)	<0.001	9.02 (7.99, 10.19)	6.14 (5.69, 6.62)	<0.001	9.24 (8.43, 10.12)	6.09 (5.75, 6.44)	<0.001
BDI	13.46 (10.88, 16.65)	5.92 (5.15, 6.81)	<0.001	15.41 (12.50, 19)	5.56 (4.84, 6.39)	<0.001	14.46 (12.45, 16.78)	5.74 (5.20, 6.33)	<0.001
BDII	6.96 (5.80, 8.34)	6.01 (5.40, 6.68)	0.1726	6.13 (5.24, 7.16)	6.31 (5.77, 6.91)	0.7456	6.46 (5.74, 7.27)	6.18 (5.77, 6.62)	0.5222
MDD	3.36 (3.02, 3.74)	2.73 (2.56, 2.90)	0.0009	2.95 (2.71, 3.20)	2.95 (2.81, 3.10)	0.9894	3.09 (2.90, 3.30)	2.87 (2.76, 2.98)	0.0449
ASD	2.27 (1.75, 2.95)	2.13 (1.83, 2.48)	0.7108	3.13 (1.85, 5.28)	3.32 (2.45, 4.49)	0.8504	2.41 (1.92, 3.04)	2.32 (2.03, 2.65)	0.7955
ADHD	1.78 (1.56, 2.03)	2.32 (2.17, 2.48)	0.0004	2.43 (1.89, 3.10)	3.31 (2.92, 3.74)	0.0446	1.91 (1.70, 2.14)	2.51 (2.37, 2.66)	<0.001
Anxiety	2.44 (2.25, 2.65)	2.41 (2.30, 2.53)	0.7358	2.77 (2.58, 2.97)	2.56 (2.46, 2.67)	0.0576	2.62 (2.48, 2.76)	2.49 (2.42, 2.57)	0.0949
OCD	2.82 (2.21, 3.60)	2.99 (2.61, 3.43)	0.6769	2.69 (2.09, 3.47)	3.17 (2.76, 3.65)	0.2627	2.77 (2.32, 3.30)	3.08 (2.79, 3.40)	0.2772

‡ : Adjusted for age, sex, urbanization, income level

Abbreviation: SCZ, Schizophrenia; BD, bipolar disorder; MDD, major depressive disorder; ASD, Autism spectrum disorder; ADHD, Attention Deficit Hyperactivity Disorder; OCD, obsessive-compulsive disorder;

FDR, First Degree Relative; C.I., confidence interval; ARR, adjusted relative risk.

Supplementary Table 4. Sensitivity analysis for excluding FDRs having BD (model 2)

	ARR [‡] for Male (95%C.I.)			ARR [‡] for Female (95%C.I.)			ARR [‡] for All (95%C.I.)		
	BD-I Cohort	BD-II Cohort	P -value for comparison	BD-I Cohort	BD-II Cohort	P -value for comparison	BD-I Cohort	BD-II Cohort	P-value for comparison
SCZ	4.46 (3.88, 5.12)	2.26 (2.06, 2.49)	<0.001	4.61 (4.01, 5.3)	2.07 (1.87, 2.28)	<0.001	4.53 (4.11, 5.00)	2.17 (2.02, 2.32)	0.0001
BD	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
BDI	--	--	--	--	--	--	--	--	--
BDII	--	--	--	--	--	--	--	--	--
MDD	2.56 (2.29, 2.87)	2.29 (2.14, 2.45)	0.0987	2.47 (2.27, 2.69)	2.56 (2.43, 2.69)	0.5365	2.50 (2.33, 2.68)	2.45 (2.36, 2.55)	0.6115
ASD	1.89 (1.45, 2.46)	1.72 (1.48, 2.00)	0.5412	1.94 (1.13, 3.34)	2.30 (1.69, 3.14)	0.6351	1.90 (1.50, 2.41)	1.81 (1.58, 2.07)	0.7217
ADHD	1.82 (1.61, 2.05)	2.06 (1.94, 2.19)	0.0679	1.96 (1.56, 2.47)	2.85 (2.55, 3.18)	0.0034	1.86 (1.67, 2.07)	2.22 (2.10, 2.35)	0.0033
Anxiety	2.13 (2.00, 2.27)	2.04 (1.97, 2.12)	0.2149	2.33 (2.21, 2.47)	2.19 (2.12, 2.26)	0.0461	2.24 (2.15, 2.34)	2.12 (2.07, 2.17)	0.0205
OCD	2.04 (1.56, 2.67)	2.49 (2.15, 2.88)	0.2110	2.33 (1.77, 3.07)	2.64 (2.27, 3.06)	0.4710	2.18 (1.80, 2.64)	2.55 (2.30, 2.83)	0.1597

‡ : Adjusted for age, sex, urbanization, income level

Abbreviation: SCZ, Schizophrenia; BD, bipolar disorder; MDD, major depressive disorder; ASD, Autism spectrum disorder; ADHD, Attention Deficit Hyperactivity Disorder; OCD, obsessive-compulsive disorder;

FDR, First Degree Relative; C.I., confidence interval; ARR, adjusted relative risk.