THE LANCET
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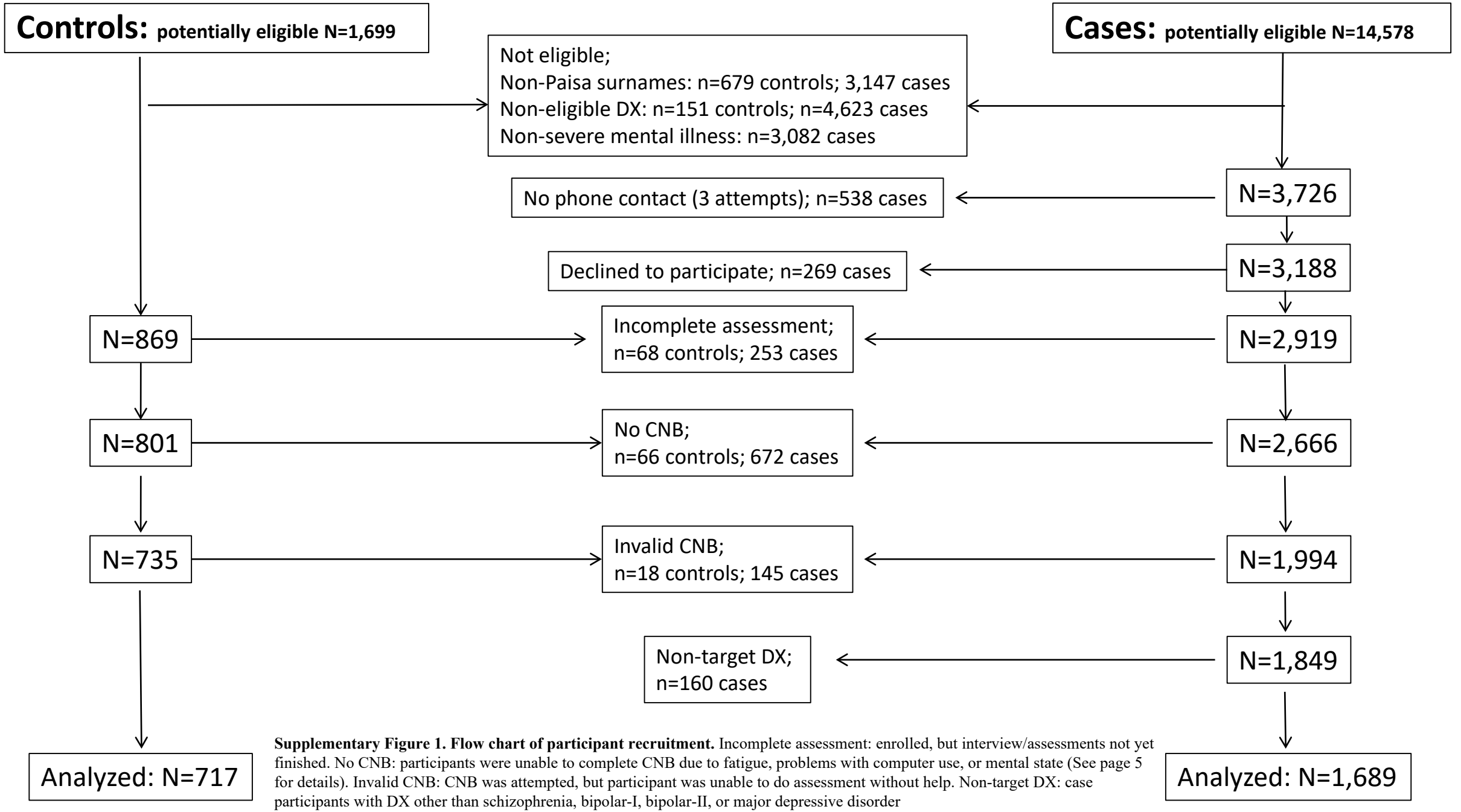
Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Service SK, Upegui CV, Ramírez MC, et al. Distinct and shared contributions of diagnosis and symptom domains to cognitive performance in severe mental illness in the Paisa population: a case-control study. *Lancet Psychiatry* 2020; **7:** 411–19.

Service et al. *Distinct and shared contributions of diagnosis and symptom domains to cognitive performance in a case-control study of severe mental illness in the Paisa population*

Appendix: Table of Contents



Supplementary Figure 1. Flow chart of participant recruitment. Incomplete assessment: enrolled, but interview/assessments not yet finished. No CNB: participants were unable to complete CNB due to fatigue, problems with computer use, or mental state (See page 5 for details). Invalid CNB: CNB was attempted, but participant was unable to do assessment without help. Non-target DX: case participants with DX other than schizophrenia, bipolar-I, bipolar-II, or major depressive disorder

Supplementary Table 1. Summary of missing data for variables analysed in 1,689 cases and 717 controls

Category	Variable	Quantitative or Categorical	Outcome or predictor	N Missing Case	N Missing Control
Penn CNB Speed; see Supplementary Table 2 for detail	SM	Quantitative	Outcome	41	8
	EDI			51	9
	EID			71	13
	WM			195	34
	FMEM			61	13
	AM			194	27
	PS			194	27
	ATT			163	17
	NVR			247	42
Penn CNB Accuracy see Supplementary Table 2 for detail	EDI	Quantitative	Outcome	51	9
	EID			71	13
	WM			194	34
	FMEM			61	13
	AM			194	27
	PS			194	27
	ATT			162	16
	NVR			218	35
Symptom	Auditory Hallucinations	Categorical	Predictor	15	NA
	Delusion of Being Controlled			30	
	Visual Hallucinations			34	
	Bizarre Delusion			27	
	Tactile Hallucinations			28	
	Delusion of Reference			32	
	Persecutory Delusion			13	
	Grossly Disorganized Behavior			16	
	Other Delusions			33	
	Disorganized Speech			14	
	Religious Delusion			23	
	Suicidal thoughts lifetime			24	
	Suicide attempt			22	
	Depressed Mood			1	
	Anhedonia			74	
	Fatigue			127	
	Hypersomnia			127	
	Flight of Ideas			214	
	Decreased Need for Sleep			207	
	Grandiosity			96	
	Avolition			2	
Factor Scores	Psychosis	Quantitative	Predictor	0	NA
	Depression			0	
	Mania			0	
pre-morbid IQ	WAT	Quantitative	Predictor	7	2
disease severity	number of hospitalizations and ER visits	Quantitative	Predictor	359	NA
current symptom severity	SA-45	Quantitative	Predictor	90	46

Supplementary Table 2. Description of tests employed in the Penn CNB

Test	Description	Abbreviation	RDoC Domain
Motor Praxis	40 total trials, including 20 test trials, to measure ability to control a computer mouse	**SM**	Sensorimotor
Measured Emotion Intensity Differentiation	36 paired faces varying in intensity to evaluate participant's ability for intensity differentiation as part of social cognition function	**EDI**	Social Communication
Penn Emotion Identification	40 faces presented with emotions that range from mild to extreme intensity that participants have to identify to evaluate social cognition function	**EID**	
Short Letter-N-Back	90 total stimuli to assess participant's working memory as part of executive functioning	**WM**	Working Memory
Penn Face Memory	20 faces to memorize one at a time to assess episodic memory function	**FMEM**	Declarative Memory
Digit Symbol	numbers paired with symbols to assess participant's speed of information processing domain (Processing Speed) as well as incidental learning (Associative Memory)	**AM**	
		PS	Attention
Short Penn Continuous Performance	180 total trials including 90 number and 90 letter trials to assess participant's Attention as part of executive function	**ATT**	
Penn Matrix Analysis	24 items with increasing difficulty to evaluate participant's complex cognition	**NVR**	Global IQ

Supplementary Table 3. Cases were asked about their current use of the following medications. They were grouped into Antidepressants, Antipsychotics, and Mood Stabilizers for analysis; a 1 in a column indicates the group to which the medication belongs. N=number of patients who report currently taking the medication

Drug	N	Antidepressant	Antipsychotic	Mood Stabilizer
Valproic Acid	487	0	0	1
Agomelatine	55	1	0	0
Amisulpride	39	0	1	0
Amitriptyline	18	1	0	0
Aripiprazole	40	0	1	0
Asenapine	1	0	1	0
Bupropion	33	1	0	0
Carbamazepine	20	0	0	1
Lithium Carbonate	175	0	0	1
Clomipramine	2	1	0	0
Clozapine	135	0	1	0
Desvenlafaxine	11	1	0	0
Duloxetine	29	1	0	0
Escitalopram	204	1	0	0
Fluoxetine	146	1	0	0
Fluvoxamine	36	1	0	0
Haloperidol	8	0	1	0
Lamotrigine	38	0	0	1
Levomepromazine	68	0	1	0
Mirtazapine	9	1	0	0
Olanzapine	85	0	1	0
Paliperidone	3	0	1	0
Paroxetine	15	1	0	0
Pipotiazine	8	0	1	0
Quetiapine	447	0	1	0
Risperidone	180	0	1	0
Sertraline	263	1	0	0
Trazodone*	184	1	0	0
Venlafaxine	39	1	0	0
Vortioxetine	2	1	0	0

*only doses in excess of 300mg were classified as antidepressants

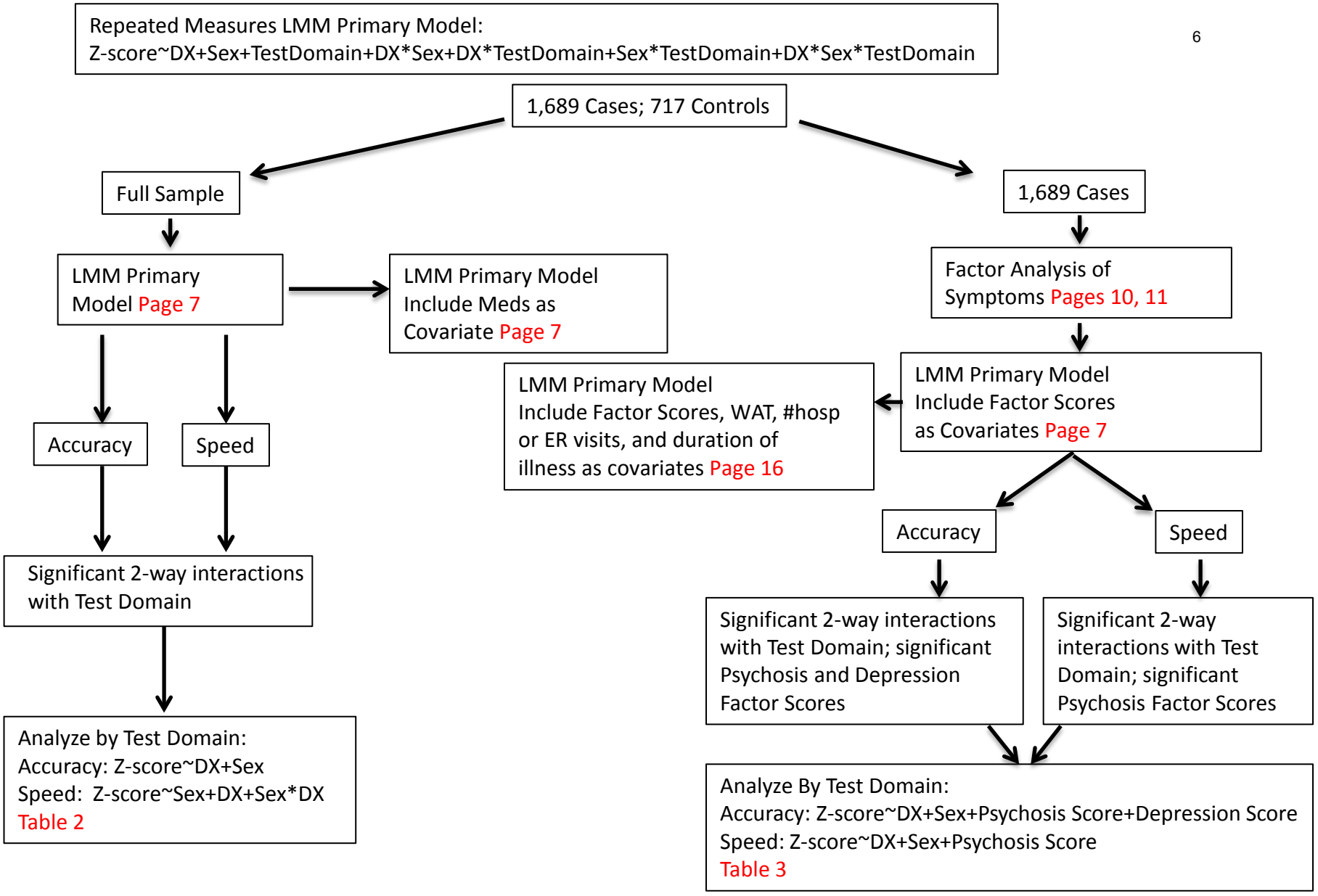
Supplementary Table 4. Breakdown of reasons for missing CNB data.

Reason	N Cases	% Cases Missing Data	N Controls	% Controls Missing Data
Invalid CNB*	145	17.75%	18	21.43%
Lack of computer skills	194	23.75%	23	27.38%
Physical limitations**	130	15.91%	11	13.10%
Symptomatic	105	12.85%	0	0.00%
Illiterate	45	5.51%	4	4.76%
Cognitive Impairment	33	4.04%	0	0.00%
Fatigue	4	0.49%	0	0.00%
Declined to participate	46	5.63%	8	9.52%
Technical or Logistical problems in test administration***	75	9.18%	16	19.05%
Unknown	40	4.90%	4	4.76%
Total	**817**	**100%**	**84**	**100%**

*Testing was initiated and halted before completion when assessors realized participants were either symptomatic, or lacked computer skills needed to complete the assessment

**Physical limitations included, but were not limited to, osteoarthritis, fibromyalgia, tremor, hand surgery, carpal tunnel, visual limitations

***Problems include internet connectivity problems and lack of time



Supplementary Figure 2. Schematic of linear mixed model analysis procedures and overview of results. Page numbers refer to pages in the Appendix

Supplementary Table 5A: Analysis of accuracy and speed as a function of diagnosis, sex, domain, and interactions among main effects. The dependent variable in analyses are z-scores on either Accuracy or Speed, the different tests administered are repeated measures in the LMM. Reference category is control-females. DX=Diagnosis. Prior to analysis, CNB data were adjusted for age and education.

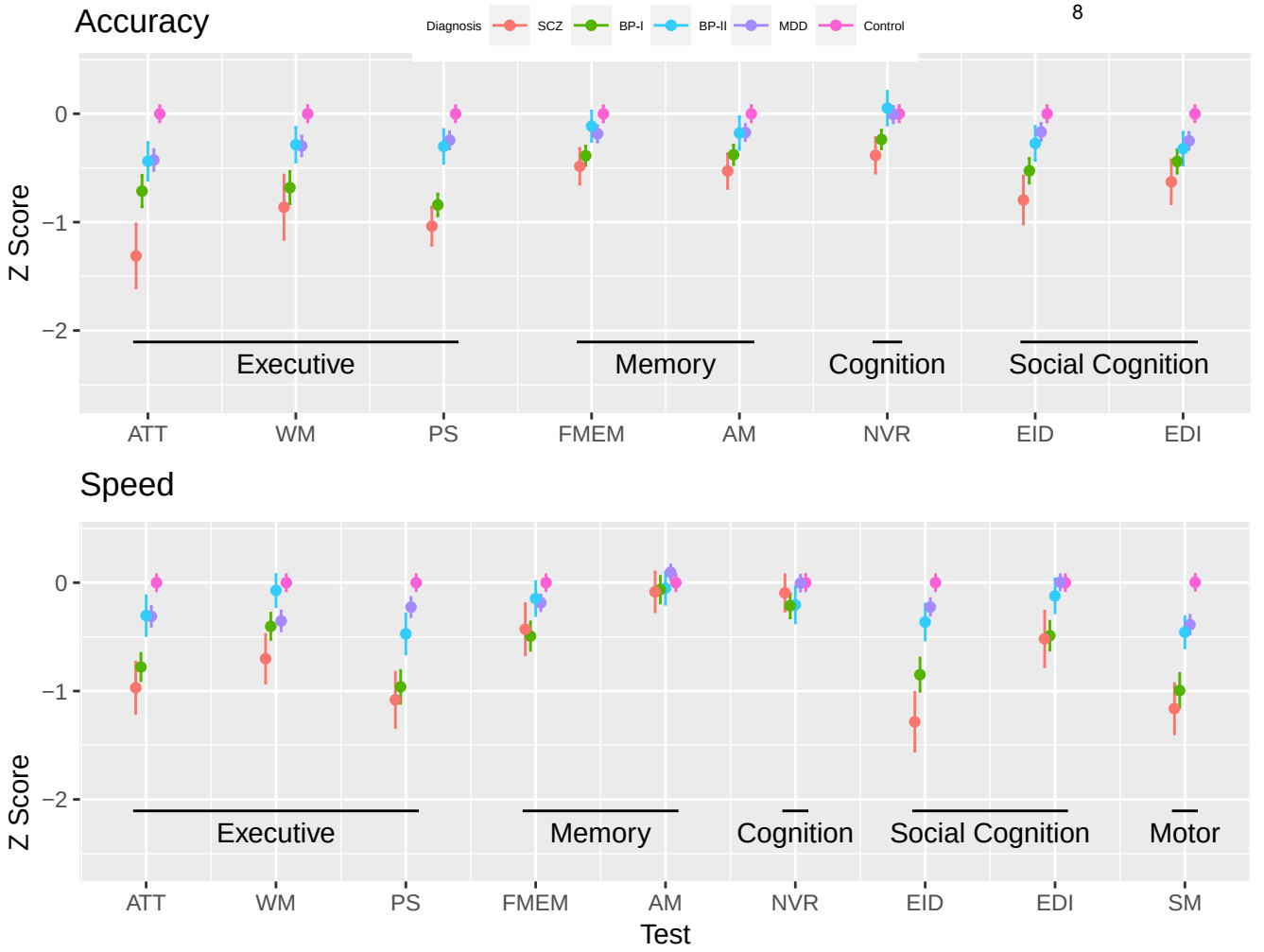
	Accuracy LMM N=2,406				Speed LMM N=2,406			
	numDF	denDF	F-value	p-value	numDF	denDF	F-value	p-value
(Intercept)	1	15453	394.5662	<.0001	1	17761	300.4544	<.0001
DX	4	2396	78.8939	<.0001	4	2396	68.28848	<.0001
Sex	1	2396	1.4032	0.2363	1	2396	4.70096	0.0302
Domain	7	15453	26.2324	<.0001	8	17761	50.46407	<.0001
DX:Sex	4	2396	2.1516	0.0721	4	2396	0.80256	0.5234
DX:Domain	28	15453	6.322	<.0001	32	17761	13.19777	<.0001
Sex:Domain	7	15453	9.937	<.0001	8	17761	13.54875	<.0001
DX:Sex:Domain	28	15453	1.1536	0.2627	32	17761	1.705	0.0078

Supplementary Table 5B: Analysis of accuracy and speed as a function of diagnosis, sex, domain, interactions among these main effects, and medication use. The dependent variable in analyses are z-scores on either Accuracy or Speed, the different tests administered are repeated measures in the LMM. Reference category is control-females. DX=Diagnosis. Prior to analysis, CNB data were adjusted for age and education.

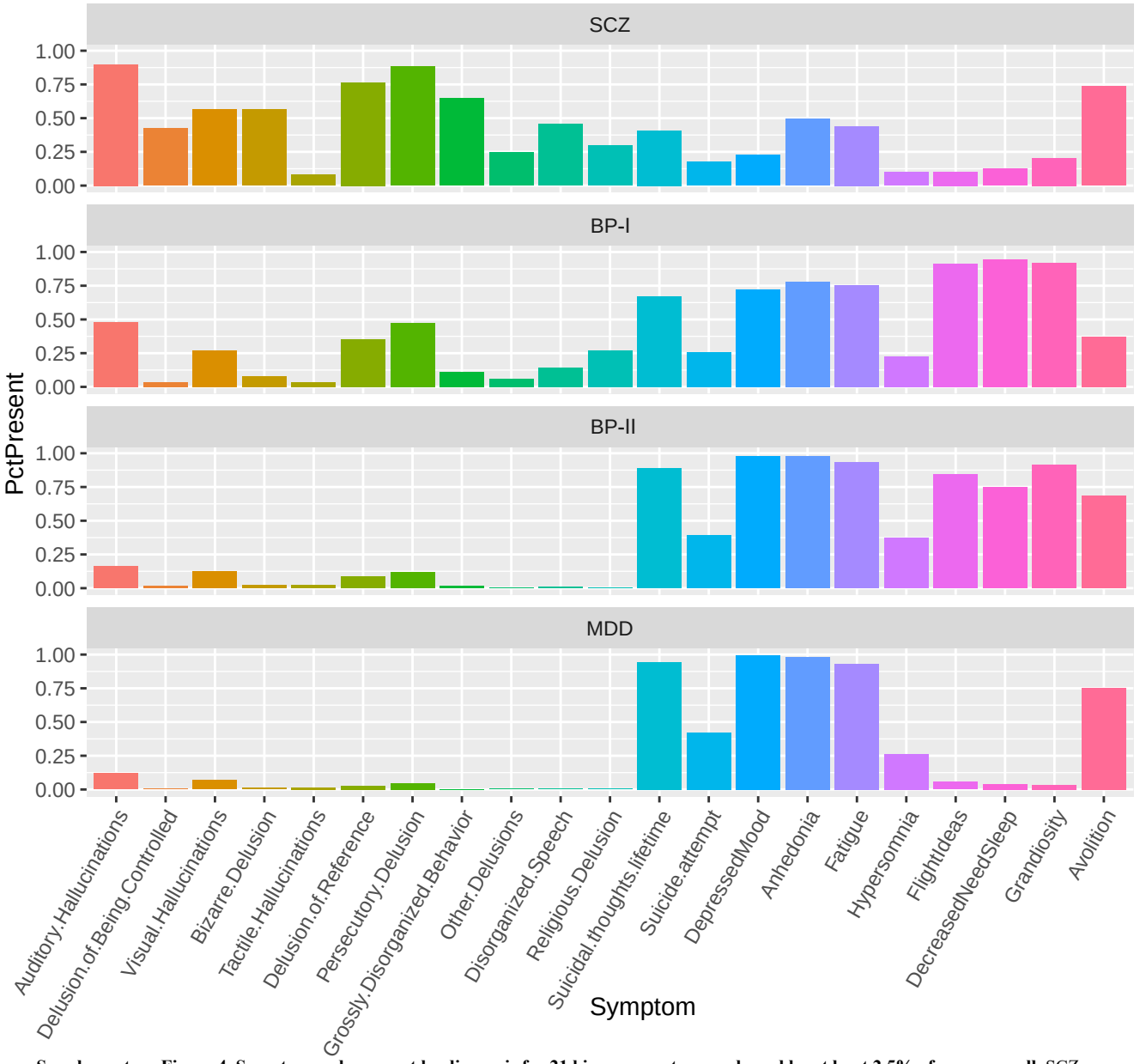
	Accuracy LMM N=2,406				Speed LMM N=2,406			
	numDF	denDF	F-value	p-value	numDF	denDF	F-value	p-value
(Intercept)	1	15453	400.12	<.0001	1	17761	302.79	<.0001
DX	4	2393	80.06	<.0001	4	2393	68.84	<.0001
Sex	1	2393	1.43	0.2326	1	2393	4.74	0.0296
Domain	7	15453	26.23	<.0001	8	17761	50.48	<.0001
On Antipsychotics	1	2393	26.41	<.0001	1	2393	6.95	0.0084
On Antidepressants	1	2393	3.96	0.0466	1	2393	9.94	0.0016
On Mood Stabilizers	1	2393	9.79	0.0018	1	2393	7.74	0.0054
DX:Sex	4	2393	1.94	0.1013	4	2393	0.83	0.5089
DX:Domain	28	15453	6.32	<.0001	32	17761	13.19	<.0001
Sex:Domain	7	15453	9.93	<.0001	8	17761	13.53	<.0001
DX:Sex:Domain	28	15453	1.14	0.2734	32	17761	1.70	0.0079

Supplementary Table 5C: Analysis of accuracy and speed as a function of diagnosis, sex, domain, interactions among these main effects, and scores on three symptom factors. The dependent variable in analyses are z-scores on either Accuracy or Speed, the different tests administered are repeated measures in the LMM. DX=Diagnosis. Prior to analysis, CNB data were adjusted for age and education.

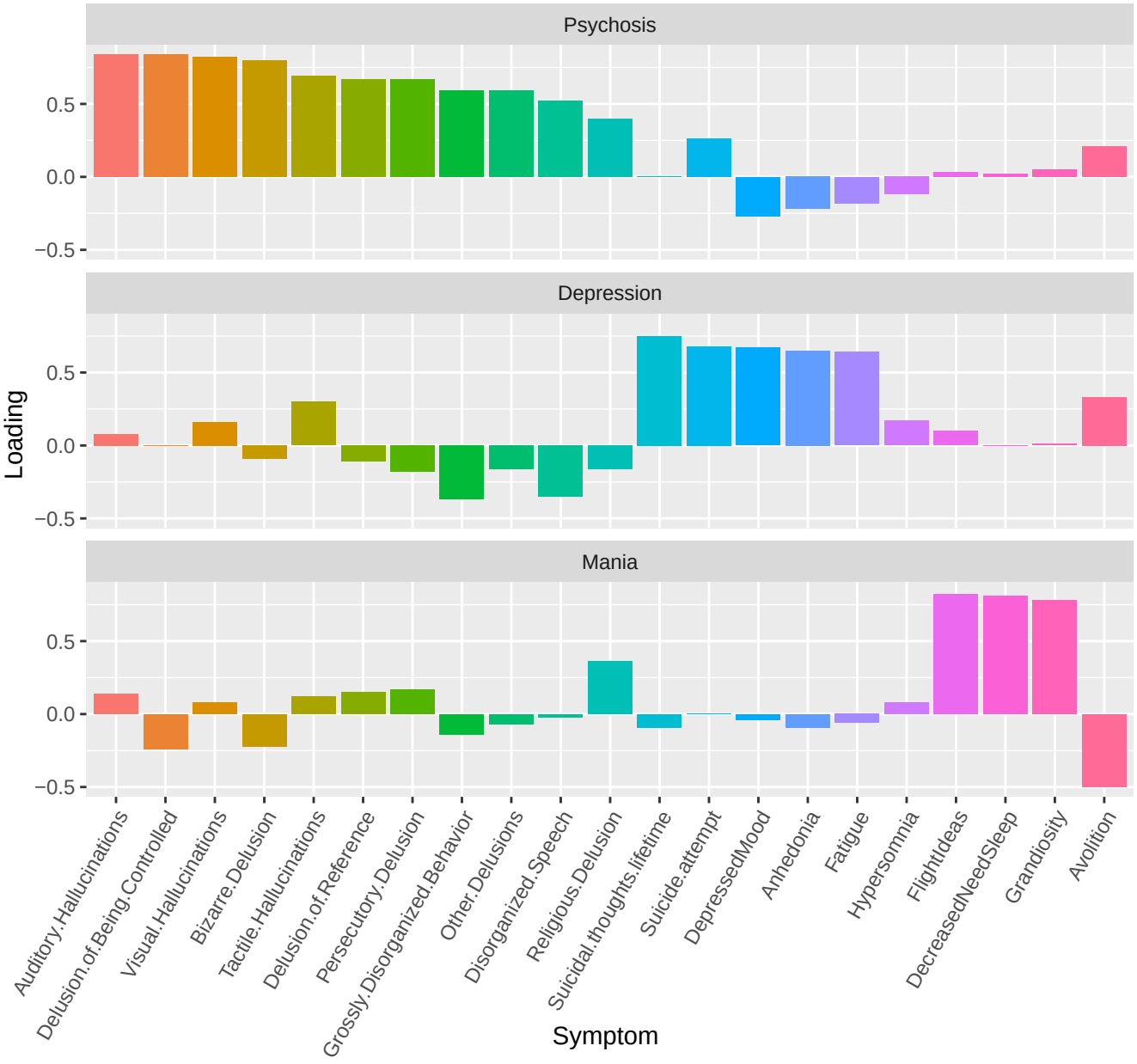
	Accuracy LMM N=1,689				Speed LMM N=1,689			
	numDF	denDF	F-value	p-value	numDF	denDF	F-value	p-value
DX	4	1678	157.90217	<.0001	4	1678	123.57637	<.0001
Sex	1	1678	0.33674	0.5618	1	1678	5.01489	0.0253
Domain	7	10623	35.47571	<.0001	8	12232	66.37686	<.0001
Psychosis	1	1678	20.90826	<.0001	1	1678	19.917	<.0001
Mania	1	1678	4.65409	0.0311	1	1678	1.31302	0.252
Depression	1	1678	10.54576	0.0012	1	1678	2.22876	0.1357
DX:Sex	3	1678	0.31288	0.8161	3	1678	0.66007	0.5766
DX:Domain	21	10623	4.16805	<.0001	24	12232	8.63453	<.0001
Sex:Domain	7	10623	7.54731	<.0001	8	12232	10.11055	<.0001
DX:Sex:Domain	21	10623	1.05686	0.3886	24	12232	1.39371	0.0953



Supplementary Figure 3. Z-scores on Accuracy (top) and Speed (bottom) profiles for tests assessing Executive Function, Memory, (Complex) Cognition, Social Cognition, and Motor Speed. Data for Speed were multiplied by -1 so that poorer performance (slower speed), would result in a lower value. Z-scores were generated relative to Controls (n=717). SCZ: schizophrenia (n=160) BP-I: bipolar disorder I (n=519), BP-II: bipolar disorder II (n=204), MDD: major depressive disorder (n=806). Test abbreviations: ATT = Continuous Performance Test; WM = Letter-N-Back test; PS = Digit Symbol Test, matching trials; FMEM = Face Memory test; AM = Digit Symbol test, recall trials; NVR = Matrix Analysis test; EID = Emotion Recognition test; EDI = Measured Emotion Differentiation test; SM = Motor Praxis test. Error bars are the 95% confidence intervals.



Supplementary Figure 4. Symptom endorsement by diagnosis for 21 binary symptoms endorsed by at least 2.5% of cases overall. SCZ: schizophrenia (n=160) BP-I: bipolar disorder I (n=519), BP-II: bipolar disorder II (n=204), MDD: major depressive disorder (n=806).



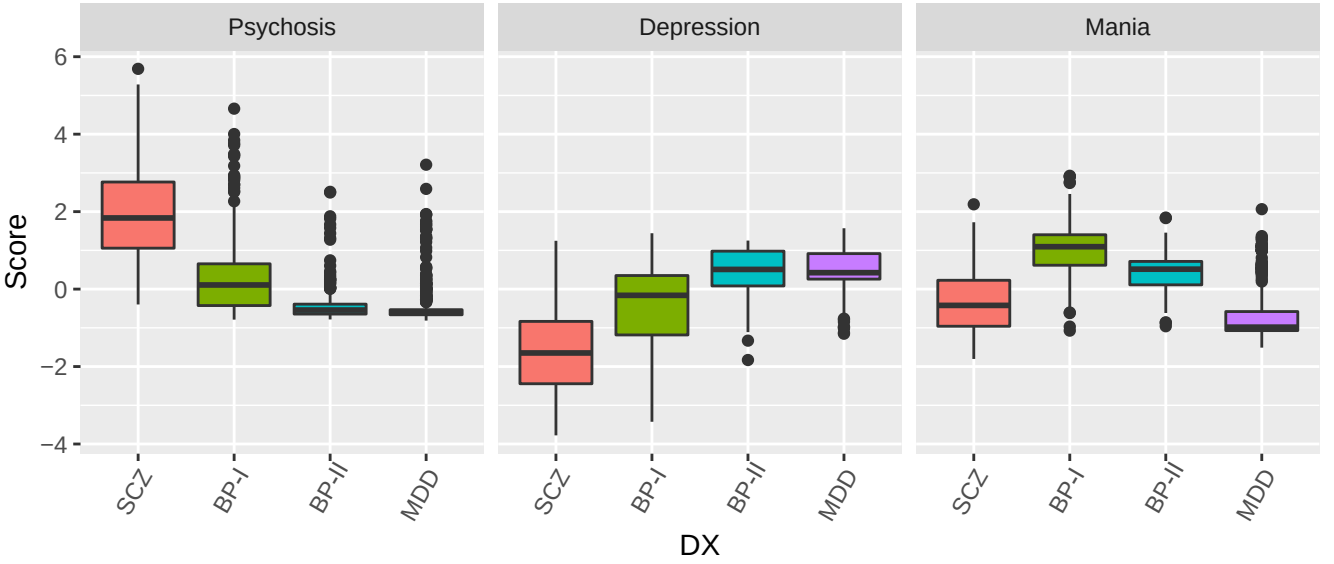
Supplementary Figure 5. Factor loadings on 21 binary symptoms in the three-factor model.

Supplementary Table 6. "Uni" is the uniqueness for each symptom from the 3-factor solution. Factor correlations are presented below the loadings

Symptom	**Uni**
Auditory Hallucinations	0.29
Delusion of Being Controlled	0.36
Visual Hallucinations	0.42
Bizarre Delusion	0.33
Tactile Hallucinations	0.66
Delusion of Reference	0.36
Persecutory Delusion	0.26
Grossly Disorganized Behavior	0.31
Other Delusions	0.54
Disorganized Speech	0.4
Religious Delusion	0.5
Suicidal thoughts lifetime	0.38
Suicide attempt	0.68
Depressed Mood	0.24
Anhedonia	0.3
Fatigue	0.38
Hypersomnia	0.94
Flight of Ideas	0.37
Decreased Need for Sleep	0.33
Grandiosity	0.37
Avolition	0.62

Correlations among factors

	Psychosis	**Depression**	**Mania**
Psychosis	1	-0.61	0.28
Depression	-0.61	1.0	-0.35
Mania	0.28	-0.35	1



Supplementary Figure 6. Distribution of scores on factors, by diagnosis. SCZ: schizophrenia (n=160) BP-I: bipolar disorder I (n=519), BP-II: bipolar disorder II (n=204), MDD: major depressive disorder (n=806).

Supplementary Table 7. Comparison of regression coefficients for Psychosis and Depression factor scores in imputed and non-imputed symptom data. Results are presented for CNB tests that are most significant in Table 3.

Measure	Test	Factor	Coefficient in imputed data	Coefficient with no imputation
Accuracy	ATT	Psychosis	-0.159	-0.033
Accuracy	PS	Psychosis	-0.158	-0.181
Accuracy	EID	Depression	0.239	0.234
Speed	ATT	Psychosis	-0.126	-0.111
Speed	PS	Psychosis	-0.154	-0.199
Speed	EDI	Psychosis	-0.176	-0.176
Speed	SM	Psychosis	-0.243	-0.201

Supplementary Table 8. Analyses by diagnosis, split by median score on Psychosis or Depression, for CNB tests that are most significant in Table 3.

				Bottom half of Factor Score			Top Half of Factor Score		
Measure	Test	Factor	DX	**mean**	**sd**	**N**	**mean**	**sd**	**N**
Accuracy	ATT	Psychosis	BP1	-0.47	1.45	97	-0.78	1.63	373
Accuracy	ATT	Psychosis	BP2	-0.20	0.87	103	-0.72	1.48	85
Accuracy	ATT	Psychosis	MDD	-0.39	1.32	597	-0.55	1.42	132
Accuracy	PS	Psychosis	BP1	-0.34	1.00	93	-0.98	1.07	353
Accuracy	PS	Psychosis	BP2	-0.20	0.97	102	-0.42	1.19	82
Accuracy	PS	Psychosis	MDD	-0.19	1.07	587	-0.46	1.12	136
Speed	ATT	Psychosis	BP1	-0.45	1.42	97	-0.85	1.37	373
Speed	ATT	Psychosis	BP2	-0.24	1.12	103	-0.41	1.45	85
Speed	ATT	Psychosis	MDD	-0.29	1.27	597	-0.50	1.21	132
Speed	PS	Psychosis	BP1	-0.37	1.43	93	-1.13	1.65	353
Speed	PS	Psychosis	BP2	-0.39	1.25	102	-0.56	1.33	82
Speed	PS	Psychosis	MDD	-0.19	1.19	587	-0.34	1.35	136
Speed	EDI	Psychosis	BP1	0.02	1.17	98	-0.63	1.55	397
Speed	EDI	Psychosis	BP2	0.04	0.94	108	-0.27	1.28	90
Speed	EDI	Psychosis	MDD	0.04	0.98	635	-0.04	1.14	157
Speed	SM	Psychosis	BP1	-0.35	1.46	99	-1.14	1.84	402
Speed	SM	Psychosis	BP2	-0.44	0.94	108	-0.50	1.16	92
Speed	SM	Psychosis	MDD	-0.32	1.08	634	-0.71	1.72	157
Accuracy	EID	Depression	SCZ	-1.04	1.43	142	0.06	0.84	11
Accuracy	EID	Depression	BP1	-0.71	1.40	339	-0.20	1.05	152
Accuracy	EID	Depression	BP2	-0.50	1.37	65	-0.12	0.99	131
Accuracy	EID	Depression	MDD	-0.18	1.21	352	-0.11	1.09	426

Supplementary Table 9. Relationship between WAT, quantile-normal transformed number of hospitalizations and ER visits, or SA45 global severity index, duration of illness (in years since first visit), and Factor Scores or DX. In models with Diagnosis, MDD is the reference.

A) factor scores	**WAT**				**number of hospitalizations and ER visits**				**Duration Illness**				**SA45 severity**			
	Estimate	**SE**	**t**	**Pr(>|t|)**	**Estimate**	**SE**	**t**	**Pr(>|t|)**	**Estimate**	**SE**	**t**	**Pr(>|t|)**	**Estimate**	**SE**	**t**	**Pr(>|t|)**
(Intercept)	30.429	0.2135	142.538	<2e-16	0.05231	0.02368	2.209	2.73E-02	6.34668	0.11629	54.575	<2e-16	43.234	1.017	42.531	<2e-16
Psychosis	-1.3073	0.2696	-4.849	1.35E-06	0.25157	0.03189	7.889	6.25E-15	0.99736	0.15647	6.374	2.52E-10	5.705	1.349	4.23	2.50E-05
Mania	0.5754	0.229	2.512	0.0121	0.30121	0.0257	11.718	<2e-16	1.37357	0.12626	10.879	<2e-16	-6.246	1.096	-5.701	1.48E-08
Depression	0.5742	0.2772	2.071	0.0385	0.05217	0.03177	1.642	0.1009	0.05494	0.15602	0.352	0.725	11.572	1.356	8.536	<2e-16
B) diagnosis + factor scores																
	Estimate	**SE**	**t**	**Pr(>|t|)**	**Estimate**	**SE**	**t**	**Pr(>|t|)**	**Estimate**	**SE**	**t**	**Pr(>|t|)**	**Estimate**	**SE**	**t**	**Pr(>|t|)**
(Intercept)	31.0897	0.4213	73.79	<2e-16	-0.210647	0.047679	-4.418	1.08E-05	5.1043	0.2374	21.499	<2e-16	49.697	2.058	24.153	<2e-16
BP-II	-0.5601	0.829	-0.676	0.49937	-0.004765	0.092057	-0.052	0.95873	0.6843	0.4582	1.494	0.135522	6.722	3.999	1.681	0.093
BP-I	-1.8966	0.831	-2.282	0.02259	0.579821	0.095522	6.07	1.66E-09	2.9819	0.4759	6.266	4.98E-10	-17.231	4.107	-4.196	2.91E-05
SCZ	-0.1169	1.1137	-0.105	0.91643	0.984789	0.127171	7.744	1.88E-14	2.5442	0.6333	4.017	6.21E-05	-22.487	5.446	-4.129	3.88E-05
Psychosis	-1.3238	0.3186	-4.155	3.41E-05	0.101732	0.03639	2.796	5.25E-03	0.6283	0.1812	3.467	5.42E-04	9.249	1.55	5.966	3.15E-09
Mania	1.2337	0.3845	3.209	0.00136	0.214045	0.045863	4.667	0.00000336	0.5841	0.2283	2.558	0.010631	-3.596	1.964	-1.831	0.0674
Depression	0.5769	0.2993	1.928	0.05406	0.141784	0.0334	4.245	2.33E-05	0.2416	0.1665	1.451	0.146941	9.047	1.443	6.269	4.98E-10
C) diagnosis																
	Estimate	**SE**	**t**	**Pr(>|t|)**	**Estimate**	**SE**	**t**	**Pr(>|t|)**	**Estimate**	**SE**	**t**	**Pr(>|t|)**	**Estimate**	**SE**	**t**	**Pr(>|t|)**
(Intercept)	31.0598	0.3111	99.823	<2e-16	-0.36988	0.03242	-11.408	<2e-16	4.4381	0.1606	27.628	<2e-16	52.478	1.446	36.279	<2e-16
BP-II	0.7932	0.6913	1.147	0.2514	0.27823	0.07254	3.835	1.31E-04	1.4979	0.359	4.173	3.21E-05	2.994	3.234	0.926	0.355
BP-I	-1.1567	0.4975	-2.325	0.0202	0.94207	0.05393	17.468	<2e-16	4.3634	0.2674	16.319	<2e-16	-24.303	2.362	-10.29	<2e-16
SCZ	-3.934	0.7653	-5.14	3.07E-07	1.00805	0.08879	11.353	0.915	3.7505	0.4394	8.536	<2e-16	-20.458	3.87	-5.287	1.47E-07

Supplementary Table 10A: Analysis of accuracy and speed as a function of diagnosis, sex, domain, interactions among these main effects, scores on three symptom factors and score on the WAT. The dependent variable in analyses are z-scores on either Accuracy or Speed, the different tests administered are repeated measures in the LMM. DX=Diagnosis. Prior to analysis, CNB data were adjusted for age.

	Accuracy LMM N=1,682				Speed LMM N=1,682			
	numDF	**denDF**	**F-value**	**p-value**	**numDF**	**denDF**	**F-value**	**p-value**
DX	4	1670	202.35	<.0001	4	1670	114.68	<.0001
Sex	1	1670	0.00	0.9938	1	1670	9.00	0.0027
Domain	7	10595	32.26	<.0001	8	12197	48.43	<.0001
wat_total	1	1670	856.92	<.0001	1	1670	334.03	<.0001
Psychosis	1	1670	13.89	0.0002	1	1670	15.33	0.0001
Mania	1	1670	0.54	0.4627	1	1670	4.66	0.031
Depression	1	1670	4.85	0.0278	1	1670	0.52	0.47
DX:Sex	3	1670	0.31	0.8195	3	1670	1.42	0.234
DX:Domain	21	10595	4.19	<.0001	24	12197	9.88	<.0001
Sex:Domain	7	10595	7.55	<.0001	8	12197	9.31	<.0001
DX:Sex:Domain	21	10595	1.03	0.4214	24	12197	1.46	0.0669

Supplementary Table 10B: Analysis of accuracy and speed as a function of diagnosis, sex, domain, interactions among these main effects, scores on three symptom factors, duration of illness, current symptom severity from the SA45, and number of hospitalizations and ER visits recorded in the electronic medical record. The dependent variable in analyses are z-scores on either Accuracy or Speed, the different tests administered are repeated measures in the LMM. DX=Diagnosis. Prior to analysis, CNB data were adjusted for age and education. Number of visits was quantile-normal transformed prior to analysis.

	Accuracy LMM N=1,330				Speed LMM N=1,330			
	numDF	**denDF**	**F-value**	**p-value**	**numDF**	**denDF**	**F-value**	**p-value**
DX	4	1259	137.63	<.0001	4	1259	92.16	<.0001
Sex	1	1259	0.11	0.7458	1	1259	4.05	0.0444
Domain	7	7830	27.68	<.0001	8	9034	51.09	<.0001
Number of visits	1	1259	0.36	0.547	1	1259	2.14	0.1438
SA45 symptom severity	1	1259	3.56	0.0594	1	1259	4.67	0.031
Duration of illness	1	1259	0.05	0.821	1	1259	3.34	0.0677
Psychosis	1	1259	13.71	0.0002	1	1259	23.49	<.0001
Mania	1	1259	0.39	0.5306	1	1259	1.46	0.2271
Depression	1	1259	7.28	0.0071	1	1259	5.74	0.0167
DX:Sex	3	1259	0.35	0.7876	3	1259	0.11	0.9558
DX:Domain	21	7830	3.77	<.0001	24	9034	6.71	<.0001
Sex:Domain	7	7830	4.87	<.0001	8	9034	8.63	<.0001
DX:Sex:Domain	21	7830	1.35	0.1335	24	9034	1.94	0.0039

Supplementary Figure 7. Z-scores on Accuracy (top) and Speed (bottom) profiles for tests assessing Executive Function, Memory, (Complex) Cognition, Social Cognition, and Motor Speed, stratified by Psychosis factor scores. Data for speed were multiplied by -1 so that poorer performance (slower speed), would result in a lower value. In order to focus on the effect of Psychosis factor score, diagnosis was regressed out of raw test data, and severe mental illness cases were categorized as being above or below the median on the Psychosis factor score. Z-scores were generated relative to the low Psychosis group. Test abbreviations are as in Supplementary Figure 3, page 8. High Psychosis=severe mental illness cases with Psychosis factor scores above the median (n=831); Low Psychosis=severe mental illness cases with Psychosis factor score below the median (n=858). Error bars are the 95% confidence intervals. The number of subjects in each Psychosis group, by diagnosis, is presented in Table 1.

Supplementary Figure 8. Z-scores on Accuracy (top) and Speed (bottom) profiles for tests assessing Executive Function, Memory, (Complex) Cognition, Social Cognition, and Motor Speed, stratified by Depression factor scores. Data for speed were multiplied by -1 so that poorer performance (slower speed), would result in a lower value. In order to focus on the effect of Depression factor score, diagnosis and sex were regressed out of raw test data, and severe mental illness cases were categorized as being above or below the median on the Depression factor score. Z-scores were generated relative to the low Depression group. Test abbreviations are as on Supplementary Figure 3, page 8. High Depression=severe mental illness cases with Depression factor scores above the median (n=752); Low Depression=severe mental illness cases with Depression factor score below the median (n=937). Error bars are the 95% confidence intervals. The number of subjects in each Depression group, by diagnosis, is presented in Table 1.