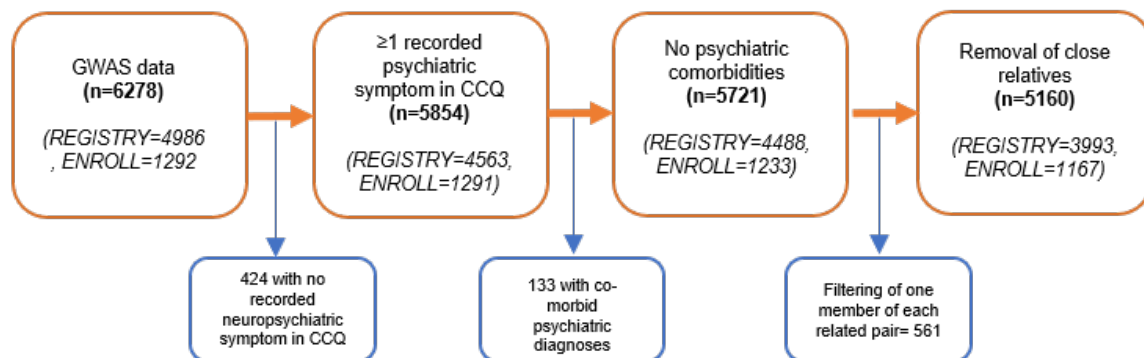


# Genetic Risk Underlying Psychiatric and Cognitive Symptoms in Huntington's Disease

## Supplementary Information

### Supplementary Figure S1:

Flow diagram showing how the sample used to test association between PRS and symptoms was derived.



**Supplementary Table S1:** Sample sizes of GWAS used as training sets for polygenic risk scores.

<b>DISORDER</b>	<b>NUMBER OF CASES</b>	<b>NUMBER OF CONTROLS</b>
Major depressive disorder (MDD)	170,756	329,443
Bipolar disorder (BPD)	20,352	31,358
Schizophrenia (SCZ)	36,989	113,075
Attention deficit hyperactivity disorder (ADHD)	20,183	35,191
Autism spectrum disorder (ASD)	18,382	27,969
Obsessive-compulsive disorder (OCD)	2,688	7,037
Alzheimer's Disease (AD)	17,008	37,154
Parkinson's Disease (PD)	26,421	442,271
Intelligence	269,867 individuals	

**Supplementary Table S2:** Correlations between symptoms.

	irb	psy	VAB	cog	apt	POB
dep	0.242	0.139	0.184	0.168	0.291	0.161
irb		0.162	0.466	0.194	0.270	0.303
psy			0.250	0.165	0.139	0.199
VAB				0.213	0.234	0.281
cog					0.300	0.210
apt						0.278

All correlations highly significant ( $p < 2.2 \times 10^{-16}$ )

dep = depression, irb = irritability, psy = psychosis, VAB = violent/aggressive behaviour. POB= perseverative/obsessive behaviour. cog=cognitive impairment, apt=apathy

**Supplementary Table S3:** Individual HD symptom-polygenic risk score associations reaching nominal significance

SYMPTOM	Risk score	PRS CUT-OFF	OR	R <sup>2</sup> (%)	AUC	P VALUE
Depression	<b>MDD</b>	<b>0.01</b>	<b>1.17</b>	<b>0.78</b>	<b>0.547</b>	<b>9.01 x 10<sup>-8</sup></b>
	<i>Schizophrenia</i>	<i>0.05</i>	<i>1.12</i>	<i>0.37</i>	<i>0.528</i>	<i>2.47 x 10<sup>-4</sup></i>
	<i>BPD</i>	<i>0.01</i>	<i>1.11</i>	<i>0.36</i>	<i>0.532</i>	<i>3.06 x 10<sup>-4</sup></i>
	Intelligence	0.001	0.93	0.18	0.519	9.51 x 10 <sup>-3</sup>
Irritability	<b>Schizophrenia</b>	<b>0.05</b>	<b>1.17</b>	<b>0.76</b>	<b>0.542</b>	<b>1.03 x 10<sup>-7</sup></b>
	<b>MDD</b>	<b>0.001</b>	<b>1.12</b>	<b>0.45</b>	<b>0.535</b>	<b>4.42 x 10<sup>-5</sup></b>
	<i>Intelligence</i>	<i>1</i>	<i>0.90</i>	<i>0.37</i>	<i>0.531</i>	<i>1.99 x 10<sup>-4</sup></i>
Psychosis	<b>Schizophrenia</b>	<b>0.001</b>	<b>1.20</b>	<b>0.64</b>	<b>0.548</b>	<b>5.98 x 10<sup>-5</sup></b>
	MDD	0.05	1.14	0.34	0.537	3.40 x 10 <sup>-3</sup>
	Alzheimer's	0.001	1.10	0.19	0.529	0.0265
	Intelligence	0.0001	0.90	0.24	0.534	0.0147
VAB	<b>Intelligence</b>	<b>0.01</b>	<b>0.89</b>	<b>0.50</b>	<b>0.537</b>	<b>2.44 x 10<sup>-5</sup></b>
	<b>Schizophrenia</b>	<b>0.05</b>	<b>1.13</b>	<b>0.46</b>	<b>0.532</b>	<b>5.46 x 10<sup>-5</sup></b>
	<b>MDD</b>	<b>0.001</b>	<b>1.13</b>	<b>0.44</b>	<b>0.536</b>	<b>8.45 x 10<sup>-5</sup></b>
	<i>BPD</i>	<i>0.001</i>	<i>1.11</i>	<i>0.34</i>	<i>0.527</i>	<i>5.35 x 10<sup>-4</sup></i>
	<i>ADHD</i>	<i>0.05</i>	<i>1.09</i>	<i>0.22</i>	<i>0.523</i>	<i>5.26 x 10<sup>-3</sup></i>
	ASD	0.01	1.06	0.11	0.517	0.0451
	POB	<i>Schizophrenia</i>	<i>0.01</i>	<i>1.12</i>	<i>0.39</i>	<i>0.531</i>
	BPD	0.5	1.08	0.18	0.521	9.25 x 10 <sup>-3</sup>
	Intelligence	0.01	0.93	0.18	0.521	0.0103
	MDD	0.5	1.07	0.15	0.519	0.0188
	<b>OCD</b>	<b>0.001</b>	<b>1.07</b>	<b>0.15</b>	<b>0.521</b>	<b>0.0190</b>
Apathy	<b>Intelligence</b>	<b>1</b>	<b>0.90</b>	<b>0.41</b>	<b>0.534</b>	<b>9.27 x 10<sup>-5</sup></b>
	<b>MDD</b>	<b>0.05</b>	<b>1.08</b>	<b>0.18</b>	<b>0.521</b>	<b>9.17 x 10<sup>-3</sup></b>
	BPD	0.001	1.07	0.14	0.519	0.0222
	<b>Schizophrenia</b>	<b>0.0001</b>	<b>1.07</b>	<b>0.13</b>	<b>0.518</b>	<b>0.0254</b>
	ASD	0.001	1.06	0.10	0.516	0.0499
Cognitive impairment	<b>Intelligence</b>	<b>0.01</b>	<b>0.89</b>	<b>0.45</b>	<b>0.535</b>	<b>3.90 x 10<sup>-5</sup></b>
	<b>Parkinson's</b>	<b>0.0001</b>	<b>1.09</b>	<b>0.26</b>	<b>0.524</b>	<b>1.67 x 10<sup>-3</sup></b>
	MDD	0.5	1.09	0.23	0.524	3.51 x 10 <sup>-3</sup>

VAB= violent/aggressive behaviour, POB=perserverative/obsessive behaviour. MDD= major depressive disorder. BPD= bipolar disorder. ASD= autism spectrum disorder. ADHD = attention deficit hyperactivity disorder. R<sup>2</sup>= Nagelkerke R<sup>2</sup>. OR= Odds ratio for presence of symptom associated with 1 s.d. increase in PRS.

Results in *italics* satisfy the Bonferroni corrected p-value cut-off 7.94 x 10<sup>-4</sup> (corrected for 63 possible PRS-phenotype comparisons), and results in **bold** satisfy the Bonferroni corrected p-value cut of 1.32 x 10<sup>-4</sup> (corrected for the 63 PRS-symptom comparisons and 6 PRS cut-offs). Primary symptom-PRS hypotheses (see text) are underlined.

**Supplementary Table S4: All PRS-symptom analyses for SCZ PRS (no MHC)**

Symptom	Statistic	PRS cutoff					
		0.0001	0.001	0.01	0.05	0.5	1
dep	OR	1.07(1.01,1.14)	1.08(1.02,1.15)	1.10(1.04,1.17)	1.12(1.05,1.18)	1.10(1.04,1.17)	1.10(1.04,1.17)
	R2	0.0015	0.0020	0.0030	0.0037	0.0029	0.0029
	p	0.0193	0.00715	0.000929	0.000247	0.00114	0.00115
irb	OR	1.09(1.03,1.16)	1.11(1.05,1.17)	1.16(1.09,1.22)	1.17(1.10,1.24)	1.15(1.09,1.22)	1.15(1.08,1.21)
	R2	0.0025	0.0035	0.0067	0.0076	0.0061	0.0060
	p	0.00213	0.000318	5.60e-7	1.03e-7	1.82e-6	2.31e-6
psy	OR	1.18(1.09,1.29)	1.20(1.10,1.31)	1.19(1.09,1.30)	1.17(1.08,1.28)	1.18(1.08,1.29)	1.17(1.08,1.28)
	R2	0.0057	0.0064	0.0060	0.0051	0.0053	0.0051
	p	0.000148	5.98e-5	0.000103	0.000342	0.000260	0.000350
apt	OR	1.07(1.01,1.13)	1.05(0.99,1.11)	1.06(1.00,1.12)	1.05(0.99,1.11)	1.03(0.98,1.09)	1.03(0.98,1.09)
	R2	0.0013	0.0008	0.0010	0.0007	0.0004	0.0004
	p	0.0254	0.0858	0.0549	0.0936	0.231	0.245
VAB	OR	1.05(0.99,1.12)	1.05(0.99,1.12)	1.11(1.05,1.18)	1.13(1.07,1.20)	1.11(1.04,1.18)	1.11(1.04,1.18)
	R2	0.0008	0.0008	0.0035	0.0046	0.0032	0.0032
	p	0.0927	0.0892	0.000432	5.46e-5	0.000807	0.000750
POB	OR	1.08(1.02,1.14)	1.11(1.05,1.18)	1.12(1.06,1.18)	1.10(1.04,1.16)	1.12(1.05,1.18)	1.12(1.05,1.18)
	R2	0.0019	0.0037	0.0039	0.0027	0.0037	0.0038
	p	0.00799	0.000246	0.000147	0.00161	0.000215	0.000208
cog	OR	1.01(0.95,1.07)	1.03(0.97,1.08)	1.05(1.00,1.11)	1.06(1.00,1.12)	1.04(0.98,1.10)	1.04(0.98,1.10)
	R2	2.87e-5	0.0002	0.0009	0.0009	0.0005	0.0005
	p	0.742	0.384	0.0678	0.0592	0.164	0.152

dep = depression, irb = irritability, psy = psychosis, apt = apathy, VAB = violent/aggressive behaviour.

POB= perseverative/obsessive behaviour. cog=cognitive impairment.

**Supplementary Table S5: All PRS-symptom analyses for MDD PRS**

Symptom	Statistic	PRS cutoff					
		0.0001	0.001	0.01	0.05	0.5	1
dep	OR	1.11(1.05,1.18)	1.13(1.06,1.19)	1.17(1.11,1.24)	1.16(1.09,1.22)	1.15(1.08,1.22)	1.15(1.09,1.22)
	R2	0.0035	0.0045	0.0078	0.0064	0.0058	0.0061
	p	0.000339	5.04e-5	9.01e-8	1.14e-6	3.97e-6	2.34e-6
irb	OR	1.12(1.06,1.18)	1.12(1.06,1.19)	1.12(1.06,1.19)	1.11(1.05,1.17)	1.10(1.04,1.16)	1.10(1.04,1.16)
	R2	0.0041	0.0045	0.0043	0.0036	0.0029	0.0030
	p	9.85e-5	4.42e-5	6.67e-5	0.000274	0.000985	0.000823
psy	OR	1.08(0.99,1.18)	1.13(1.03,1.23)	1.13(1.03,1.23)	1.14(1.04,1.24)	1.12(1.03,1.22)	1.11(1.02,1.21)
	R2	0.0012	0.0028	0.0029	0.0034	0.0026	0.0022
	p	0.0785	0.00744	0.00655	0.00340	0.0109	0.0162
apt	OR	1.02(0.96,1.07)	1.04(0.98,1.10)	1.06(1.00,1.12)	1.08(1.02,1.14)	1.07(1.01,1.13)	1.07(1.01,1.13)
	R2	7.81e-5	0.0005	0.0012	0.0018	0.0016	0.0016
	p	0.588	0.160	0.0356	0.00917	0.0157	0.0149
VAB	OR	1.09(1.03,1.16)	1.13(1.06,1.20)	1.13(1.06,1.20)	1.11(1.05,1.18)	1.12(1.06,1.19)	1.12(1.06,1.19)
	R2	0.0023	0.0044	0.0042	0.0033	0.0039	0.0040
	p	0.00379	8.45e-5	0.000116	0.000652	0.000189	0.000183
POB	OR	1.00(0.95,1.06)	1.02(0.97,1.08)	1.05(0.99,1.11)	1.06(1.00,1.12)	1.07(1.01,1.13)	1.07(1.01,1.13)
	R2	7.51e-6	0.0002	0.0007	0.0010	0.0015	0.0013
	p	0.868	0.400	0.106	0.0570	0.0188	0.0275
cog	OR	1.02(0.96,1.07)	1.07(1.01,1.13)	1.05(0.99,1.11)	1.09(1.03,1.15)	1.09(1.03,1.15)	1.08(1.02,1.14)
	R2	8.72e-5	0.0015	0.0008	0.0023	0.0023	0.0020
	p	0.566	0.0167	0.0777	0.00354	0.00351	0.00546

dep = depression, irb = irritability, psy = psychosis, apt = apathy, VAB = violent/aggressive behaviour.  
 POB= perseverative/obsessive behaviour. cog=cognitive impairment.

**Supplementary Table S6: All PRS-symptom analyses for BPD PRS**

Symptom	Statistic	PRS cutoff					
		0.0001	0.001	0.01	0.05	0.5	1
dep	OR	1.04(0.98,1.10)	1.07(1.00,1.13)	1.11(1.05,1.18)	1.11(1.05,1.18)	1.07(1.01,1.14)	1.07(1.01,1.14)
	R2	0.0005	0.0012	0.0036	0.0034	0.0016	0.0016
	p	0.198	0.0336	0.000306	0.000466	0.0161	0.0170
irb	OR	1.04(0.99,1.10)	1.04(0.98,1.10)	1.04(0.98,1.10)	1.01(0.96,1.07)	1.01(0.96,1.07)	1.01(0.96,1.07)
	R2	0.0006	0.0006	0.0005	4.20e-5	4.24e-5	4.11e-5
	p	0.138	0.150	0.161	0.692	0.691	0.695
psy	OR	1.00(0.91,1.09)	1.02(0.94,1.12)	1.05(0.97,1.15)	1.06(0.97,1.15)	1.05(0.96,1.15)	1.07(0.98,1.17)
	R2	1.72e-6	0.0001	0.0006	0.0006	0.0005	0.0009
	p	0.947	0.615	0.236	0.212	0.258	0.141
apt	OR	1.05(0.99,1.11)	1.07(1.01,1.13)	1.04(0.98,1.10)	1.00(0.94,1.05)	0.97(0.92,1.03)	0.98(0.92,1.03)
	R2	0.0006	0.0014	0.0005	3.44e-6	0.0002	0.0002
	p	0.120	0.0222	0.185	0.909	0.358	0.436
VAB	OR	1.06(1.00,1.13)	1.11(1.05,1.18)	1.08(1.01,1.14)	1.07(1.01,1.14)	1.08(1.01,1.14)	1.08(1.02,1.15)
	R2	0.0012	0.0034	0.0017	0.0014	0.0016	0.0019
	p	0.0413	0.000535	0.0152	0.0245	0.0175	0.00975
POB	OR	1.05(0.99,1.11)	1.05(0.99,1.11)	1.06(1.00,1.12)	1.07(1.01,1.13)	1.08(1.02,1.14)	1.08(1.02,1.14)
	R2	0.0008	0.0007	0.0010	0.0014	0.0018	0.0018
	p	0.0839	0.118	0.0553	0.0254	0.00925	0.0113
cog	OR	0.98(0.92,1.03)	1.00(0.95,1.06)	1.02(0.97,1.08)	1.03(0.97,1.09)	1.03(0.98,1.09)	1.03(0.97,1.09)
	R2	0.0002	3.76e-7	0.0002	0.0003	0.0003	0.0003
	p	0.421	0.970	0.451	0.305	0.275	0.323

dep = depression, irb = irritability, psy = psychosis, apt = apathy, VAB = violent/aggressive behaviour.  
 POB= perseverative/obsessive behaviour. cog=cognitive impairment.

**Supplementary Table S7: All PRS-symptom analyses for ADHD PRS**

Symptom	Statistic	PRS cutoff					
		0.0001	0.001	0.01	0.05	0.5	1
dep	OR	1.00(0.94,1.06)	1.03(0.97,1.09)	1.02(0.96,1.08)	1.02(0.96,1.08)	1.03(0.97,1.09)	1.03(0.97,1.09)
	R2	2.07e-7	0.0002	0.0001	0.0001	0.0002	0.0002
	p	0.978	0.355	0.544	0.473	0.353	0.368
irb	OR	0.99(0.94,1.05)	1.02(0.96,1.08)	1.04(0.98,1.10)	1.05(1.00,1.11)	1.05(0.99,1.11)	1.04(0.99,1.10)
	R2	2.88e-5	0.0001	0.0005	0.0009	0.0007	0.0006
	p	0.743	0.518	0.189	0.0741	0.100	0.135
psy	OR	1.00(0.91,1.09)	1.04(0.95,1.13)	0.98(0.90,1.07)	1.05(0.96,1.14)	1.07(0.98,1.16)	1.06(0.97,1.16)
	R2	1.94e-6	0.0003	9.51e-5	0.0004	0.0009	0.0007
	p	0.944	0.369	0.624	0.302	0.135	0.173
apt	OR	0.99(0.94,1.05)	1.01(0.96,1.07)	1.03(0.97,1.09)	1.03(0.98,1.09)	1.02(0.97,1.08)	1.02(0.97,1.08)
	R2	2.70e-5	4.40e-5	0.0003	0.0004	0.0002	0.0001
	p	0.750	0.684	0.324	0.239	0.432	0.477
VAB	OR	1.01(0.95,1.07)	1.02(0.96,1.08)	1.04(0.98,1.10)	1.09(1.03,1.15)	1.08(1.02,1.15)	1.07(1.01,1.14)
	R2	3.97e-5	8.54e-5	0.0004	0.0022	0.0018	0.0016
	p	0.707	0.582	0.225	0.00526	0.0108	0.0179
POB	OR	1.01(0.95,1.07)	0.98(0.93,1.04)	1.01(0.96,1.07)	1.00(0.95,1.06)	0.99(0.94,1.05)	0.98(0.93,1.04)
	R2	3.06e-5	0.0001	4.73e-5	3.64e-6	3.31e-5	0.0001
	p	0.738	0.525	0.677	0.908	0.728	0.478
cog	OR	0.97(0.92,1.03)	0.99(0.93,1.04)	1.03(0.98,1.09)	1.02(0.97,1.08)	1.05(1.00,1.11)	1.05(1.00,1.11)
	R2	0.0003	6.09e-5	0.0004	0.0002	0.0010	0.0009
	p	0.324	0.632	0.237	0.414	0.0582	0.0691

dep = depression, irb = irritability, psy = psychosis, apt = apathy, VAB = violent/aggressive behaviour.  
 POB= perseverative/obsessive behaviour. cog=cognitive impairment.

**Supplementary Table S8: All PRS-symptom analyses for ASD PRS**

Symptom	Statistic	PRS cutoff					
		0.0001	0.001	0.01	0.05	0.5	1
dep	OR	0.98(0.92,1.04)	0.98(0.93,1.04)	0.99(0.93,1.05)	0.99(0.93,1.05)	0.97(0.92,1.03)	0.97(0.92,1.03)
	R2	0.0002	8.62e-5	6.29e-5	3.78e-5	0.0003	0.0003
	p	0.446	0.574	0.631	0.710	0.304	0.291
irb	OR	1.00(0.94,1.05)	1.03(0.97,1.08)	1.01(0.95,1.07)	1.00(0.95,1.06)	1.00(0.95,1.06)	0.99(0.94,1.05)
	R2	6.72e-5	0.0002	1.72e-5	6.84e-8	8.63e-8	2.58e-5
	p	0.874	0.383	0.800	0.987	0.986	0.756
psy	OR	1.02(0.93,1.11)	1.04(0.95,1.13)	1.06(0.97,1.16)	1.04(0.95,1.13)	1.05(0.96,1.14)	1.06(0.97,1.16)
	R2	7.18e-5	0.0003	0.0008	0.0002	0.0004	0.0007
	p	0.670	0.396	0.168	0.434	0.300	0.184
apt	OR	1.03(0.97,1.09)	1.06(1.00,1.12)	1.03(0.97,1.08)	1.01(0.96,1.07)	1.00(0.94,1.05)	0.99(0.94,1.05)
	R2	0.0003	0.0010	0.0002	4.65e-5	8.93e-6	1.91e-5
	p	0.328	0.0499	0.345	0.676	0.855	0.789
VAB	OR	1.01(0.95,1.07)	1.06(1.00,1.12)	1.06(1.00,1.13)	1.03(0.98,1.10)	1.03(0.97,1.09)	1.03(0.97,1.09)
	R2	4.77e-5	0.0010	0.0011	0.0004	0.0002	0.0002
	p	0.681	0.0603	0.0451	0.255	0.379	0.366
POB	OR	0.96(0.91,1.02)	1.04(0.98,1.10)	1.02(0.97,1.08)	1.01(0.96,1.07)	1.01(0.96,1.07)	1.01(0.95,1.07)
	R2	0.0005	0.0004	0.0002	5.43e-5	5.67e-5	3.24e-5
	p	0.159	0.219	0.397	0.656	0.648	0.730
cog	OR	0.99(0.94,1.05)	1.05(1.00,1.11)	1.03(0.98,1.09)	1.03(0.98,1.09)	1.00(0.94,1.05)	1.00(0.94,1.05)
	R2	1.79e-5	0.0009	0.0003	0.0004	5.33e-6	1.40e-6
	p	0.795	0.0694	0.266	0.241	0.887	0.942

dep = depression, irb = irritability, psy = psychosis, apt = apathy, VAB = violent/aggressive behaviour.  
 POB= perseverative/obsessive behaviour. cog=cognitive impairment.



**Supplementary Table S9: All PRS-symptom analyses for OCD PRS**

Symptom	Statistic	PRS cutoff					
		0.0001	0.001	0.01	0.05	0.5	1
dep	OR	1.04(0.98,1.10)	1.00(0.95,1.06)	1.09(1.03,1.15)	1.07(1.01,1.14)	1.08(1.01,1.14)	1.08(1.02,1.14)
	R2	0.0005	6.39e-6	0.0021	0.0016	0.0016	0.0017
	p	0.170	0.878	0.00516	0.0157	0.0142	0.0129
irb	OR	1.02(0.96,1.08)	1.03(0.98,1.09)	1.02(0.96,1.08)	1.01(0.96,1.07)	1.03(0.97,1.09)	1.02(0.97,1.08)
	R2	9.30e-5	0.0004	0.0001	5.42e-5	0.0002	0.0002
	p	0.556	0.237	0.478	0.653	0.380	0.416
psy	OR	1.07(0.98,1.16)	0.98(0.90,1.07)	1.05(0.96,1.15)	0.99(0.91,1.08)	1.00(0.91,1.09)	1.00(0.91,1.09)
	R2	0.0009	7.44e-5	0.0005	2.50e-5	5.20e-6	1.09e-6
	p	0.137	0.665	0.284	0.802	0.909	0.958
apt	OR	1.01(0.96,1.07)	1.03(0.98,1.09)	0.99(0.94,1.05)	0.99(0.93,1.04)	1.00(0.95,1.06)	1.00(0.94,1.06)
	R2	7.20e-5	0.0004	1.13e-5	6.54e-5	1.60e-7	8.52e-7
	p	0.603	0.251	0.837	0.620	0.980	0.955
VAB	OR	1.02(0.96,1.08)	1.01(0.95,1.07)	1.03(0.97,1.10)	1.01(0.95,1.07)	1.01(0.95,1.07)	1.01(0.95,1.07)
	R2	0.0001	3.73e-5	0.0003	3.79e-5	2.50e-5	2.00e-5
	p	0.498	0.716	0.298	0.714	0.766	0.790
POB	OR	1.02(0.96,1.08)	1.07(1.01,1.13)	1.06(1.00,1.12)	1.05(0.99,1.11)	1.07(1.01,1.14)	1.07(1.01,1.13)
	R2	0.0001	0.0015	0.0009	0.0006	0.0015	0.0013
	p	0.515	0.0190	0.0667	0.126	0.0194	0.0281
cog	OR	1.00(0.95,1.06)	1.03(0.97,1.09)	1.01(0.96,1.07)	1.00(0.95,1.06)	1.00(0.95,1.06)	1.00(0.95,1.06)
	R2	4.78e-9	0.0003	4.94e-5	5.80e-6	7.45e-6	4.51e-6
	p	0.997	0.298	0.666	0.882	0.867	0.896

dep = depression, irb = irritability, psy = psychosis, apt = apathy, VAB = violent/aggressive behaviour.

POB= perseverative/obsessive behaviour. cog=cognitive impairment.

**Supplementary Table S10: All PRS-symptom analyses for AD PRS**

Symptom	Statistic	PRS cutoff					
		0.0001	0.001	0.01	0.05	0.5	1
dep	OR	0.97(0.92,1.03)	0.98(0.92,1.03)	0.95(0.91,1.02)	0.98(0.93,1.04)	1.01(0.96,1.07)	1.02(0.96,1.08)
	R2	0.0003	0.0002	0.0005	8.41e-5	4.77e-5	0.0001
	p	0.303	0.427	0.171	0.579	0.676	0.490
irb	OR	1.00(0.95,1.06)	1.01(0.95,1.06)	0.99(0.93,1.04)	1.00(0.94,1.05)	1.03(0.97,1.09)	1.03(0.97,1.09)
	R2	7.63e-6	1.00e-5	7.27e-5	5.57e-6	0.0003	0.0002
	p	0.866	0.847	0.602	0.885	0.316	0.346
psy	OR	1.05(0.97,1.15)	1.10(1.01,1.20)	1.08(0.99,1.18)	1.06(0.97,1.16)	1.04(0.96,1.14)	1.04(0.96,1.14)
	R2	0.0006	0.0019	0.0013	0.0007	0.0003	0.0004
	p	0.234	0.0265	0.0729	0.181	0.350	0.326
apt	OR	1.00(0.94,1.05)	0.97(0.92,1.03)	0.99(0.93,1.04)	1.01(0.95,1.07)	1.03(0.98,1.09)	1.03(0.98,1.09)
	R2	5.56e-6	0.0003	6.26e-5	2.35e-5	0.0003	0.0003
	p	0.885	0.290	0.627	0.766	0.272	0.279
VAB	OR	1.00(0.94,1.06)	1.00(0.94,1.06)	1.01(0.95,1.07)	1.03(0.97,1.09)	1.02(0.97,1.09)	1.03(0.97,1.09)
	R2	3.17e-6	7.47e-6	1.56e-5	0.0003	0.0002	0.0002
	p	0.916	0.871	0.814	0.316	0.429	0.393
POB	OR	1.00(0.95,1.06)	1.04(0.98,1.10)	1.05(0.99,1.11)	1.05(0.99,1.11)	1.05(0.99,1.11)	1.04(0.99,1.11)
	R2	1.73e-6	0.0005	0.0007	0.0007	0.0008	0.0006
	p	0.937	0.165	0.114	0.119	0.0922	0.143
cog	OR	1.00(0.95,1.06)	1.02(0.96,1.08)	0.99(0.93,1.04)	1.00(0.94,1.05)	1.00(0.95,1.06)	1.01(0.95,1.07)
	R2	1.31e-7	0.0001	5.00e-5	8.62e-6	1.68e-6	2.89e-5
	p	0.982	0.503	0.664	0.857	0.937	0.741

dep = depression, irb = irritability, psy = psychosis, apt = apathy, VAB = violent/aggressive behaviour.  
 POB= perseverative/obsessive behaviour. cog=cognitive impairment.

**Supplementary Table S11: All PRS-symptom analyses for PD PRS**

Symptom	Statistic	PRS cutoff					
		0.0001	0.001	0.01	0.05	0.5	1
dep	OR	0.99(0.94,1.05)	0.95(0.89,1.00)	0.96(0.91,1.02)	0.97(0.91,1.03)	1.00(0.94,1.06)	1.00(0.94,1.06)
	R2	1.60e-5	0.0009	0.0005	0.0003	4.90e-6	3.87e-6
	P	0.809	0.0620	0.169	0.287	0.893	0.905
irb	OR	1.02(0.97,1.08)	0.99(0.93,1.04)	0.99(0.94,1.05)	0.97(0.92,1.03)	0.98(0.93,1.04)	0.98(0.93,1.04)
	R2	0.0002	5.73e-5	2.24e-5	0.0002	0.0001	9.03e-5
	p	0.403	0.643	0.772	0.338	0.521	0.561
psy	OR	1.01(0.92,1.10)	0.94(0.87,1.03)	1.01(0.92,1.10)	1.01(0.93,1.10)	1.08(0.99,1.18)	1.08(0.99,1.18)
	R2	1.15e-5	0.0006	1.51e-5	1.78e-5	0.0011	0.0011
	p	0.865	0.203	0.845	0.832	0.0909	0.0960
apt	OR	1.01(0.96,1.07)	0.96(0.90,1.01)	0.99(0.93,1.04)	1.01(0.95,1.06)	0.99(0.93,1.04)	0.98(0.93,1.04)
	R2	2.83e-5	0.0007	6.36e-5	9.47e-6	5.47e-5	8.16e-5
	p	0.744	0.108	0.625	0.850	0.650	0.580
VAB	OR	1.05(0.99,1.12)	1.00(0.94,1.06)	0.99(0.93,1.05)	0.98(0.92,1.04)	0.98(0.93,1.04)	0.98(0.93,1.05)
	R2	0.0009	2.39e-6	5.05e-5	0.0002	8.71e-5	7.62e-5
	p	0.0798	0.927	0.672	0.419	0.578	0.603
POB	OR	1.03(0.98,1.09)	0.96(0.91,1.02)	1.00(0.95,1.06)	0.97(0.92,1.03)	0.98(0.93,1.04)	0.98(0.92,1.04)
	R2	0.0004	0.0006	7.50e-6	0.0002	0.0001	0.0002
	p	0.246	0.155	0.868	0.366	0.507	0.446
cog	OR	1.09(1.03,1.16)	1.02(0.96,1.08)	1.04(0.99,1.10)	1.01(0.96,1.07)	0.99(0.94,1.05)	0.99(0.93,1.04)
	R2	0.0026	0.0001	0.0006	5.40e-5	1.78e-5	5.59e-5
	p	0.00167	0.537	0.137	0.652	0.795	0.646

dep = depression, irb = irritability, psy = psychosis, apt = apathy, VAB = violent/aggressive behaviour.  
 POB= perseverative/obsessive behaviour. cog=cognitive impairment.

**Supplementary Table S12: All PRS-symptom analyses for intelligence PRS**

Symptom	Statistic	PRS cutoff					
		0.0001	0.001	0.01	0.05	0.5	1
dep	OR	0.95(0.90,1.01)	0.93(0.87,0.98)	0.95(0.89,1.00)	0.94(0.89,1.00)	0.93(0.88,0.99)	0.93(0.88,0.99)
	R2	0.0008	0.0018	0.0010	0.0011	0.0016	0.0016
	P	0.0799	0.00951	0.0593	0.0410	0.0152	0.0166
irb	OR	0.92(0.87,0.97)	0.93(0.88,0.99)	0.91(0.86,0.96)	0.90(0.85,0.95)	0.90(0.85,0.95)	0.90(0.85,0.95)
	R2	0.0024	0.0016	0.0032	0.0034	0.0036	0.0037
	p	0.00306	0.0139	0.000532	0.000344	0.000246	0.000199
psy	OR	0.90(0.82,0.98)	0.93(0.85,1.01)	0.94(0.86,1.02)	0.95(0.87,1.04)	0.91(0.84,1.00)	0.91(0.84,0.99)
	R2	0.0024	0.0010	0.0008	0.0004	0.0017	0.0017
	p	0.0147	0.104	0.159	0.295	0.0405	0.0371
apt	OR	0.94(0.89,1.00)	0.94(0.88,0.99)	0.93(0.88,0.98)	0.91(0.86,0.96)	0.90(0.85,0.95)	0.90(0.85,0.95)
	R2	0.0012	0.0015	0.0020	0.0030	0.0039	0.0041
	p	0.0341	0.0166	0.00650	0.000852	0.000118	9.27e-5
VAB	OR	0.91(0.86,0.97)	0.90(0.85,0.96)	0.88(0.83,0.93)	0.89(0.84,0.95)	0.88(0.83,0.93)	0.88(0.83,0.93)
	R2	0.0027	0.0031	0.0050	0.0040	0.0048	0.0048
	p	0.00198	0.00101	2.44e-5	0.000156	4.09e-5	3.94e-5
POB	OR	0.96(0.91,1.02)	0.96(0.91,1.02)	0.93(0.88,0.98)	0.93(0.88,0.99)	0.94(0.89,1.00)	0.94(0.88,0.99)
	R2	0.0006	0.0006	0.0018	0.0016	0.0013	0.0014
	p	0.150	0.152	0.0103	0.0149	0.0318	0.0247
cog	OR	0.92(0.87,0.97)	0.91(0.86,0.96)	0.89(0.84,0.94)	0.90(0.85,0.95)	0.90(0.85,0.96)	0.90(0.85,0.96)
	R2	0.0025	0.0031	0.0045	0.0040	0.0034	0.0033
	p	0.00213	0.000633	3.90e-5	0.000108	0.000378	0.000384

dep = depression, irb = irritability, psy = psychosis, apt = apathy, VAB = violent/aggressive behaviour.  
 POB= perseverative/obsessive behaviour. cog=cognitive impairment.

**Supplementary Table S13:** HD symptom – polygenic risk score associations correcting for significant clinical covariates

SYMPTOM	Risk score	PRS CUT-OFF	OR	R <sup>2</sup> (%)	AUC	P VALUE
Depression	MDD	0.01	1.17	0.73	0.600	2.17x 10 <sup>-7</sup>
	Schizophrenia	0.05	1.12	0.37	0.595	2.30 x 10 <sup>-4</sup>
	BPD	0.01	1.11	0.31	0.593	6.84 x 10 <sup>-4</sup>
	Intelligence	0.001	0.94	0.13	0.591	0.0286
Irritability	Schizophrenia	0.05	1.16	0.70	0.583	4.64 x 10 <sup>-7</sup>
	MDD	0.001	1.12	0.39	0.579	1.68 x 10 <sup>-4</sup>
	Intelligence	1	0.91	0.30	0.577	9.67 x 10 <sup>-4</sup>
Psychosis	Schizophrenia	0.001	1.18	0.55	0.604	2.40 x 10 <sup>-4</sup>
	MDD	0.05	1.13	0.30	0.602	6.80 x 10 <sup>-3</sup>
	Alzheimer's	0.001	1.11	0.24	0.598	0.0164
	Intelligence	0.0001	0.91	0.19	0.600	0.0297
VAB	Intelligence	0.01	0.88	0.45	0.608	7.17 x 10 <sup>-5</sup>
	Schizophrenia	0.05	1.14	0.48	0.608	4.22 x 10 <sup>-5</sup>
	MDD	0.001	1.11	0.33	0.607	6.74 x 10 <sup>-4</sup>
	BPD	0.001	1.11	0.32	0.605	8.61 x 10 <sup>-4</sup>
	ADHD	0.05	1.09	0.22	0.604	5.70 x 10 <sup>-3</sup>
	ASD	0.01	1.06	0.08	0.603	0.0851
POB	Schizophrenia	0.01	1.11	0.36	0.583	3.13 x 10 <sup>-4</sup>
	BPD	0.5	1.07	0.14	0.582	0.0262
	Intelligence	0.01	0.93	0.18	0.582	0.0100
	MDD	0.5	1.07	0.12	0.580	0.0329
	OCD	0.001	1.08	0.18	0.580	0.0111
Apathy	Intelligence	1	0.90	0.38	0.576	1.99 x 10 <sup>-4</sup>
	MDD	0.05	1.08	0.18	0.575	0.0103
	BPD	0.001	1.07	0.14	0.574	0.0245
	Schizophrenia	0.0001	1.07	0.16	0.575	0.0145
	ASD	0.001	1.05	0.07	0.575	0.0977
Cognitive impairment	Intelligence	0.01	0.89	0.41	0.636	7.39 x 10 <sup>-5</sup>
	Parkinson's	0.0001	1.10	0.25	0.633	2.19 x 10 <sup>-3</sup>
	MDD	0.5	1.09	0.24	0.634	2.41 x 10 <sup>-3</sup>

VAB= violent/aggressive behaviour, POB=perserverative/obsessive behaviour. MDD= major depressive disorder. BPD= bipolar disorder. ASD= autism spectrum disorder. ADHD = attention deficit hyperactivity disorder. Analyses include the covariates significantly associated with each symptom in Table 2. R<sup>2</sup>= Nagelkerke R<sup>2</sup> attributable solely to the PRS . OR= Odds ratio for presence of symptom associated with 1 s.d. increase in PRS. AUC refers to the combined prediction of covariates and PRS.

**Supplementary Table S14:** Testing for sex differences in PRS odds ratios for symptoms with both a significant sex difference and a significant PRS association

Symptom	PRS	cutoff	All		Males		Females		M vs F
			OR	p	OR	p	OR	P	P value
depression	SCZ	0.05	1.12	2.47e-4	1.16	3.79e-4	1.08	0.0894	0.207
	BPD	0.01	1.11	3.06e-4	1.17	1.96e-4	1.06	0.180	0.114
	MDD	0.01	1.17	9.01e-8	1.18	4.14e-5	1.13	3.51e-3	0.386
	INT	0.001	0.93	9.51e-3	0.92	0.0342	0.94	0.135	0.719
irritability	SCZ	0.05	1.17	1.03e-7	1.15	1.44e-3	1.18	2.74e-5	0.598
	MDD	0.001	1.12	4.42e-5	1.13	4.19e-3	1.12	6.18e-3	0.869
	INT	1	0.90	1.99e-4	0.93	0.0966	0.87	3.42e-4	0.202
VAB	SCZ	0.05	1.13	5.46e-5	1.14	3.49e-3	1.13	6.59e-3	0.904
	BPD	0.001	1.11	5.35e-4	1.07	0.0961	1.16	7.73e-4	0.203
	ADHD	0.05	1.09	5.26e-3	1.08	0.0711	1.12	0.0131	0.588
	MDD	0.001	1.13	8.45e-5	1.10	0.0243	1.15	1.41e-3	0.436
	INT	0.01	0.88	2.44e-5	0.88	2.22e-3	0.88	4.08e-3	0.999

VAB = violent/aggressive behaviour.

**Supplementary Table S15: Association of PRS with number of symptoms**

PRS	Number of symptoms								P(fac)	P(quant)
	0 (473)	1 (700)	2 (858)	3 (952)	4 (865)	5 (715)	6 (433)	7 (164)		
SCZ-0001	-0.090	-0.076	-0.024	0.002	0.051	-0.010	0.142	0.118	0.00285	4.80e-5
SCZ-001	-0.091	-0.076	-0.027	-0.002	0.039	0.024	0.162	0.109	0.00134	6.48e-6
SCZ-01	-0.114	-0.094	-0.064	0.024	0.018	0.083	0.167	0.138	5.62e-6	5.06e-9
SCZ-05	-0.128	-0.076	-0.068	0.023	0.026	0.069	0.164	0.166	5.88e-6	4.45e-9
SCZ-5	-0.108	-0.068	-0.064	0.036	0.003	0.070	0.132	0.206	4.62e-5	1.11e-7
SCZ-1	-0.112	-0.069	-0.059	0.032	0.005	0.069	0.128	0.024	6.67e-5	1.25e-7
BIP-0001	-0.039	-0.069	0.001	-0.004	0.047	-0.014	0.065	-0.021	0.327	0.067
BIP-001	-0.071	-0.066	-0.024	0.024	0.042	0.005	0.090	0.026	0.109	0.00345
BIP-01	-0.091	-0.053	-0.020	0.039	0.012	0.024	0.092	0.032	0.102	0.00268
BIP-05	-0.086	-0.035	-0.002	0.028	-0.011	0.016	0.069	0.101	0.250	0.0118
BIP-5	-0.067	-0.030	0.008	-0.005	-0.032	0.034	0.047	0.107	0.396	0.0348
BIP-1	-0.061	-0.029	0.0002	-0.011	-0.033	0.040	0.044	0.120	0.354	0.0273
MDD-0001	-0.127	-0.082	-0.003	0.032	-0.010	0.067	-0.006	0.102	0.0122	0.000897
MDD-001	-0.178	-0.069	-0.014	0.052	-0.008	0.081	0.031	0.192	4.32e-5	2.583e-6
MDD-01	-0.167	-0.074	-0.015	-0.004	0.034	0.059	0.053	0.261	2.46e-5	1.34e-7
MDD-05	-0.175	-0.082	-0.023	-0.014	0.013	0.067	0.084	0.206	3.25e-5	4.58e-8
MDD-5	-0.133	-0.117	-0.011	-0.013	0.023	0.058	0.077	0.263	1.34e-5	4.17e-8
MDD-1	-0.136	-0.116	-0.011	-0.011	0.024	0.057	0.072	0.253	2.15e-5	6.35e-8
ADHD-0001	-0.030	0.016	0.012	-0.002	0.022	-0.034	-0.022	0.020	0.945	0.800
ADHD-001	-0.024	0.000	0.005	-0.024	0.034	0.004	-0.033	0.076	0.867	0.602
ADHD-01	-0.059	-0.039	0.006	0.008	0.030	0.017	0.015	-0.046	0.762	0.203
ADHD-05	-0.061	-0.043	0.008	-0.020	0.039	0.002	0.038	0.049	0.580	0.0561
ADHD-5	-0.056	-0.032	-0.014	-0.034	0.079	0.002	0.040	0.020	0.235	0.0464
ADHD-1	-0.055	-0.029	-0.009	-0.035	0.083	-0.002	0.028	0.009	0.238	0.0821
ASD-0001	-0.026	0.089	-0.040	-0.010	-0.014	-0.001	-0.069	0.123	0.104	0.586
ASD-001	-0.004	0.040	-0.041	-0.043	-0.021	0.079	0.052	0.120	0.101	0.102
ASD-01	-0.015	0.024	-0.045	-0.022	-0.013	0.055	0.048	-0.025	0.547	0.301
ASD-05	-0.002	0.015	-0.024	-0.074	-0.004	0.045	0.025	0.004	0.426	0.470
ASD-5	0.041	0.010	-0.034	-0.076	-0.013	0.010	0.039	-0.026	0.397	0.988
ASD-1	0.044	0.008	-0.034	-0.075	-0.017	0.008	0.038	-0.025	0.409	0.958
OCD-0001	-0.066	0.020	-0.006	0.017	0.010	-0.011	0.009	0.152	0.490	0.209
OCD-001	-0.046	-0.001	0.001	0.005	0.020	-0.007	0.053	0.073	0.856	0.169
OCD-01	-0.031	-0.041	0.023	-0.010	0.050	0.009	0.071	0.005	0.523	0.0895
OCD-05	-0.035	-0.017	0.025	0.007	0.023	0.017	0.053	-0.092	0.740	0.453
OCD-5	-0.038	-0.021	0.021	0.011	-0.001	0.026	0.130	-0.101	0.159	0.137
OCD-1	-0.033	-0.025	0.022	0.006	-0.002	0.028	0.126	-0.107	0.169	0.157
INT-0001	0.114	0.101	-0.033	0.057	-0.038	-0.025	-0.038	-0.230	2.17e-4	4.15e-5
INT-001	0.100	0.112	-0.020	0.025	-0.025	-0.030	-0.086	-0.161	1.88e-3	2.81e-5
INT-01	0.121	0.118	-0.006	0.030	-0.038	-0.054	-0.113	-0.120	1.61e-4	6.25e-7
INT-05	0.123	0.116	-0.003	0.078	-0.074	-0.031	-0.136	-0.072	7.19e-6	5.26e-7
INT-5	0.093	0.113	0.014	0.059	-0.090	-0.027	-0.156	-0.103	1.24e-6	7.46e-8
INT-1	0.092	0.137	0.016	0.062	-0.089	-0.029	-0.160	-0.097	7.93e-7	5.78e-8

Number of symptoms analysed both as an 8-level factor, denoted by p(fac) and as a quantitative variable, denoted by p(quant). Numbers in columns headed by symptom count are the mean PRS among individuals with that number of symptoms.

**Supplementary Table S16:** Association of SCZ PRS with symptoms after correction for the number of other symptoms present (general severity)

PRS	psy	dep	irb	VAB	apt	POB	cog
	SCZ-0001	<b>0.00416</b>	0.234	0.138	0.914	0.458	0.187
SCZ-001	<b>0.00370</b>	0.158	0.0662	0.717	0.850	<b>0.0207</b>	0.470
SCZ-01	<b>0.0157</b>	0.104	<b>0.00293</b>	0.227	0.548	0.0589	0.929
SCZ-05	<b>0.0383</b>	0.0426	<b>0.000904</b>	0.0644	0.339	0.269	0.975
SCZ-5	<b>0.0249</b>	0.0844	<b>0.00370</b>	0.189	0.204	<b>0.0432</b>	0.694
SCZ-1	<b>0.0295</b>	0.0824	<b>0.00419</b>	0.176	0.195	<b>0.0412</b>	0.733

Nominally significant associations shown in **bold**.

dep = depression, irb = irritability, psy = psychosis, apt = apathy, VAB = violent/aggressive behaviour. POB= perseverative/obsessive behaviour. cog=cognitive impairment.

**Supplementary Table S17:** Association of MDD PRS with symptoms after correction for the number of other symptoms present (general severity)

PRS	psy	dep	irb	VAB	apt	POB	cog
	MDD-0001	0.350	<b>0.00369</b>	<b>0.00298</b>	0.0667	0.308	0.193
MDD-001	0.113	<b>0.00306</b>	<b>0.0183</b>	<b>0.0234</b>	0.468	0.243	0.318
MDD-01	0.152	<b>2.41x10<sup>-5</sup></b>	0.0589	0.0588	0.885	0.602	0.945
MDD-05	0.115	<b>3.46x10<sup>-4</sup></b>	0.196	0.258	0.759	0.749	0.202
MDD-5	0.234	<b>9.34x10<sup>-4</sup></b>	0.388	0.101	0.909	0.783	0.195
MDD-1	0.290	<b>5.44x10<sup>-4</sup></b>	0.336	0.0906	0.863	0.898	0.246

Nominally significant associations shown in **bold**.

dep = depression, irb = irritability, psy = psychosis, apt = apathy, VAB = violent/aggressive behaviour. POB= perseverative/obsessive behaviour. cog=cognitive impairment.



**Supplementary Table S18:** Association of intelligence PRS with symptoms after correction for the number of other symptoms present (general severity)

PRS	psy	dep	irb	VAB	apt	POB	cog
	INT-0001	0.179	0.862	0.277	0.110	0.544	0.842
INT-001	0.637	0.221	0.701	0.088	0.429	0.729	<b>0.022</b>
INT-01	0.988	0.848	0.167	<b>0.019</b>	0.570	0.551	<b>0.0078</b>
INT-05	0.696	0.728	0.149	0.069	0.149	0.654	<b>0.0113</b>
INT-5	0.553	0.448	0.166	<b>0.044</b>	0.069	0.939	<b>0.0444</b>
INT-1	0.535	0.487	0.149	<b>0.047</b>	0.065	0.981	<b>0.0476</b>

Nominally significant associations shown in **bold**.

dep = depression, irb = irritability, psy = psychosis, apt = apathy, VAB = violent/aggressive behaviour. POB= perseverative/obsessive behaviour. cog=cognitive impairment.

## Guidelines for the age at onset questionnaire for EHDN-HD Registry patients

This questionnaire will capture essential and detailed information on when signs and symptoms that may be related or unrelated to HD first appear. Use the suggested wording below as a guide, but ask any other questions you need to try and date the onset as accurately as possible. Ask the patient first, then the carer (explain to the carer at the beginning that you will give them a chance to state their views after you have first heard from the patient) and finally record your own judgement about onset, taking account of what has been said by both patient and carer, and also what you can find in the case notes (or any other independent sources of information). It is not uncommon to find a record by a genetic counsellor who saw the patient and noticed choreiform movements, or an interview with a relative who mentioned that the family think the patient is affected, and this information may pre-date the estimates of either the patient or the carer who is acting as your informant on this occasion. Use your own judgement about the evidence, but avoid making guesses based only on your own experience of how long the average patient would need to be affected to reach this stage in the illness.

1. **Motor symptoms:**  
When did you first notice any motor symptoms of HD, such as fidgety movements or clumsiness? Can you remember a particular occasion when this happened and you first realised you might be developing the family illness? What were you doing at the time? Where were you? Did you mention it to anyone else? (Try to identify any landmark events in the patient's life around that time, such as holidays, births, marriages & deaths in the family, etc, which might help to anchor the onset date by asking whether the onset was before or after that particular landmark)
2. **Depression:**  
Have you ever suffered from depression for a period of 4 weeks or more? Was there ever a time you felt so low that you thought about ending it all? Have you been treated with antidepressants? When was the first time this happened to you (doesn't necessarily have to have been medicated in the first or any subsequent instance)?
3. **Irritability and aggression:**  
Have there been times when you were irritable, bad tempered or 'cranky' for a period of 4 weeks or more? Have you had difficulty keeping control of your temper? When did this begin? If so, how bad was the worst ever episode? Has there been overt aggression? If so when did this first occur?
4. **Apathy:**  
Have you noticed any change in your level of motivation? For example, has there ever been a period of four weeks or more when you lost interest in things that usually matter to you, or could not be bothered with activities you usually enjoy, or needed pushing to get around to jobs that need to be done, or spent a lot of time sitting around doing nothing? Did this ever happen at a time when you were not also feeling depressed? When did you first notice this change?
5. **Perseverative or Obsessive/Compulsive behaviours:**  
Have you ever been troubled by recurrent thoughts, fears or mental images that came back over and over again, or had urges to do something over and over (e.g. double-checking, counting things, or washing your hands repeatedly)? Or perhaps found yourself unable to stop thinking about something, so that friends said you were getting it out of proportion, or getting

a 'bee in your bonnet'? If so, how bad was the worst ever episode? When was the first time this happened to you?

6. Presence of psychosis:

Has the patient ever reported symptoms resembling schizophrenia e.g. paranoid thinking, delusions and hearing voices. If so when was the first episode?

7. Cognitive symptoms:

Have you ever noticed any problems with your memory, or your ability to concentrate on things? Have you found it more difficult than it used to be to organise things, or perhaps noticed that it takes longer to get things done nowadays? Has anybody commented on this, or maybe criticised your performance at work or when doing chores at home? Can you remember the first time this happened? (probe as above and look for evidence such as job changes etc. which might suggest early cognitive difficulties)

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