

# **Supplemental Material**

**Table S1. Illness Definitions by HES and Self-Reported Data in the UKB.**

Diagnosis	ICD 9	ICD 10	Self-reported Medical History	Self-reported Operative History
Mood disorders (depression, anxiety, panic attacks, suicidality, mania, bipolar disorders)	296*, 300*, 311*	F25*, F30*, F31*, F32*, F33*, F34*, F38*, F39*, F40*, F41*	1286, 1287, 1288, 1290, 1291	
Dementia & degenerative disorders (Alzheimer's disease, vascular dementia, other degenerative neurologic conditions)	331*, 290*, 294.1	F00*, F01*, F02*, F03*, G30*, G31*	1263	
Parkinson's Disease	332*	G20*	1262	
Intellectual disability (organic brain damage, developmental delays, mental retardation)	310*, 315*, 317*, 318*, 319*	F04*, F06.7, F10.6, F70*, F71*, F72*, F73*, F78*, F79*		
Seizure disorders (epilepsy)	345*	G40*, G41*	1264	
Ischemic or Hemorrhagic Stroke	430*, 431*, 432*, 433*, 434*, 435*, 436*	I60*, I61*, I62*, I63*, G45*, I64*, G46*	1491, 1583, 1081, 1082	
Coronary Artery Disease (CAD) (history of unstable angina, myocardial infarction, chronic ischemic heart disease, prior percutaneous coronary interventions, and/or prior coronary artery bypass graft procedures)	410*, 411*, 412*, 413*, 414.0, 414.8, 414.9	I20*, I21*, I22*, I24.0, I24.8, I24.9, I25*	1074, 1075	1070, 1095, 1523

\*Inclusive of diagnostic codes with trailing digits.

ICD 9 = International Classification of Diseases, 9<sup>th</sup> revision; ICD 10 = International Classification of Diseases, 10<sup>th</sup> revision; HES = Hospital encounter statistics; UKB = UK Biobank; CAD = Coronary artery disease;

**Table S2. ACHD subgroups by lesion type (reproduced from Saha et al., Circulation 2019) Lesion types.**

	No. (%)
<b>Complex defects</b>	<b>96 (100)</b>
Single ventricle, truncus arteriosus, TOF, TGA, TAPVR, AVCD	50 (52)
Unspecified cyanotic lesion	45 (48)
<b>Non-complex defects</b>	<b>924 (100)</b>
Left-to-right shunt only (ASD, VSD, AP window, PDA, PAPVR)	448 (48)
Left sided lesion only	90 (10)
Right sided lesion only	47 (5)
Mixed shunt, left-sided, and/or right-sided lesion	50 (5)
Heart surgery prior to age 18	185 (20)
Non-specific ICD code for congenital heart disease	71 (8)
Other (coronary artery malformation, venous malformation, conduction defect)	33 (4)

ACHD = adult congenital heart disease; ASD = atrial septal defect; AP = aorto-pulmonary; AVCD = atrioventricular canal defect; ICD = International Classification of Diseases; PAPVR = partial anomalous pulmonary venous return; PDA = patent ductus arteriosus; TAPVR = total anomalous pulmonary venous return; TGA = transposition of the great arteries; TOF = tetralogy of Fallot; VSD = ventricular septal defect

**Table S3. Demographic characteristics of ACHD participants ACHD complexity in the UK Biobank.**

	Mild to moderate ACHD	Complex ACHD	p-value
<b>n</b>	924	96	
<b>Demographic Factors</b>			
Age at Enrollment (median, [IQR])	57 [49, 63]	58 [49, 64]	0.236
Male Sex (%)	428 (46.3)	54 (56.2)	0.081
Year of Birth (median [IQR])	1951 [1946, 1959]	1951 [1944, 1958]	0.243
Caucasian Ethnicity (%)	876 (94.8)	88 (91.7)	0.294
Townsend (median [IQR])	-1.92 [-3.44, 1.23]	-0.99 [-3.02, 1.86]	0.106
Smoking (%)			0.485
Never	514 (55.9)	48 (50.0)	
Current	90 (9.8)	12 (12.5)	
Previous	315 (34.3)	36 (37.5)	
Alcohol (%)			0.301
Seldom	344 (37.4)	38 (40.0)	
Daily	168 (18.2)	22 (23.2)	
Weekly	409 (44.4)	35 (36.8)	
Obese (%)	241 (26.4)	13 (13.7)	<b>0.010</b>
Systolic blood pressure (median, IQR)	134 [121, 147]	134 [118, 146]	0.302
Diastolic blood pressure (median [IQR])	79 [73, 87]	78 [71, 89]	0.470
Positive family history of cognitive disorder (%)	221 (24.6)	16 (18.0)	0.205
<b>Quality of Life Measures</b>			
Achieved college graduation (%)	278 (30.4)	30 (31.9)	0.855
Unemployed (%)	107 (11.6)	17 (17.7)	0.113
Hours worked per week (median [IQR])	37 [25, 41]	39 [28, 44]	0.317
Lives with a partner/spouse (%)	662 (88.3)	64 (90.1)	0.781
<b>Comorbid Illness</b>			
Dementia (%)	0 (0)	0 (0)	NA
Parkinsons (%)	1 (0.1)	0 (0)	1.000
Intellectual delay (%)	0 (0)	0 (0)	NA
Mood disorder (%)	71 (7.9)	6 (6.4)	0.760
Seizure disorder (%)	16 (1.7)	0 (0)	0.384
Ischemic or hemorrhagic stroke (%)	82 (9.0)	7 (7.6)	0.796
Coronary artery disease (%)	171 (19.1)	14 (14.6)	0.346

ACHD = Adult congenital heart disease; IQR = interquartile range

**Table S4. Neurocognitive performance among ACHD and non-ACHD after exclusion of complex ACHD diagnoses.**

	Least Squares Mean (95% CI)		p-value*
	Non-ACHD	ACHD	
<b>Neurocognitive testing (n)</b>	497,983	924	
Completed at Enrollment			
	492,245	914	
Reaction time, milliseconds	558 (558, 559)	562 (555, 569)	0.327
	164,041	279	
Fluid Intelligence, n correct	6.0 (6.0, 6.0)	5.8 (5.6, 6.1)	0.141
	51,324	84	
Numeric memory, n digits remembered	6.5 (6.5, 6.5)	6.1 (5.7, 6.5)	0.083
Completed at Follow-Up			
	116,903	186	
Symbol Digit Substitution, n correct	19.8 (19.7, 19.8)	19.1 (18.4, 19.8)	0.083
	103,270	174	
Numeric Trail Making (TMT-A), seconds	39.04 (38.95, 39.13)	41.63 (39.48, 43.77)	0.073
	103,268	174	
Alpha-numeric Trail Making (TMT-B), seconds	66.66 (66.50, 66.82)	72.39 (68.79, 75.99)	<b>0.015</b>
	103,268	174	
Trail Making Difference, seconds	27.62 (27.49, 27.75)	30.76 (27.79, 33.74)	0.083

ACHD = adult congenital heart disease; CI = Confidence interval; TMT-A = Numeric Trail Making; TMT-B = Alpha-numeric Trail Making