Supplementary Table 1. TWAS applications on complex human diseases.

Disease Type	Disease	Data	Data Type	Data Source	Ancestry	Tissue	Method	Reference
Cancer	Breast Cancer	Weight of SNPs: PredictDB GWAS: discovery: "Up for a Challenge" (U4C) replication: UKBB	Individual-level GWAS	Discovery: "Up for a Challenge" (U4C) Validation: UK Biobank	Discovery: trans-ethics Validation: European	Breast, whole blood (separately)	PrediXcan	Hoffman *et al.* [49]
			Reference transcriptome data	Weight of SNPs: PredictDB				
	Breast Cancer	Reference transcriptome data: GTEx The Cancer Genome Atlas (TCGA) GWAS summary	Individual-level and summary-level GWAS	Individual-level: GTEx The Cancer Genome Atlas (TCGA) Summary-level: Breast Cancer Association Consortium (BCAC)	European	Breast	Prediction model: Elastic net method Association test: MetaXcan	Wu *et al.* [33]

		statistics: Breast Cancer Association Consortium (BCAC)	Reference transcriptome data	GTEx The Cancer Genome Atlas (TCGA)				
	Epithelia Ovarian Cancer	Reference transcriptome data: GTEx v6 GWAS summary statistics: Ovarian Cancer Association Consortium (OCAC) Consortium of Investigators of Modifiers of BRCA1/2 (CIMBA	Individual-level and summary-level GWAS	Individual-level: GTEx v6 Summary-level: Ovarian Cancer Association Consortium (OCAC) Consortium of Investigators of Modifiers of BRCA1/2 (CIMBA)	European	Ovarian-specific and cross-tissue	Prediction model: Elastic net method Association test: MetaXcan	Lu *et al.* [50]
			Reference transcriptome data	GTEx v6				

	Prostate Cancer	Reference transcriptome data: RNA-seq: GTEx v6 CommonMind Consortium Metabolic Syndrome in Men study The Cancer Genome Atlas (TCGA) Expression microarray: Netherlands Twin Registry Young Finns Study GWAS	Summary-level GWAS Reference transcriptome data	Onco Array PrCa study RNA-seq: GTEx v6 CommonMind Consortium Metabolic Syndrome in Men study The Cancer Genome Atlas (TCGA) Expression microarray: Netherlands Twin Registry Young Finns Study	European	45 tissues	Prediction model: FUSION Association test: FUSION	Mancuso *et al.* [51]

		summary statistics: Onco Array PrCa study						
	Cutaneous Squamous Cell Cacinoma	Reference transcriptome data: GTEx v6 GWAS: discovery: Kaiser Genetic Epidemiology Research in Adult Health and Aging (GERA) cohort replication: 23andMe participants	Summary-level GWAS	Discovery: Kaiser Genetic Epidemiology Research in Adult Health and Aging (GERA) cohort Validation: 23andMe dataset	European	sun-exposed lower leg skin, non-sun-exposed-suprapubic skin, whole blood and lymphocyte cell lines	Prediction model: PrediXcan Association test: Logistic regression	Ioannidis *et al.* [52]
			Reference transcriptome data	GTEx v6				

Neuropsychiatric	Schizophrenia	Reference transcriptome data: CommonMind Consortium (CMC) Netherlands Twin Registry (NTR) Young Finns Study (YFS) Metabolic Syndrome in Men study (METSIM) GWAS (summary-level): Psychiatric Genomics Consortium (PGC)	Summary-level GWAS	Psychiatric Genomics Consortium (PGC)	Multi	Dorsolateral prefrontal cortex(brain), peripheral blood, adipose	BLSMM (FUSION)	Gusev *et al.* [34]
			Reference transcriptome data	CommonMind Consortium (CMC) Netherlands Twin Registry (NTR) Young Finns Study (YFS) Metabolic Syndrome in Men study (METSIM)				

	Schizophrenia	Reference transcriptome data: CommonMind Project post-mortem human dorsolateral prefrontal cortex (DLPFC) GTEx GWAS: (summary and individual) PGC-SCZ cohort	Individual-level and summary-level GWAS	Individual-level: CommonMind Project Summary-level: PGC-SCZ cohort	European (Mostly) and Asian	Dorso-lateral prefrontal cortex and 12 other brain tissues	Prediction model: GWAS individual: best model from PrediXan, ridge regression (TWAS), BSLMM (TWAS), and linear regression GWAS summary: S-PrediXcan Association test: Logistic regression	Huckins *et al*. [53]
			Reference transcriptome data	CommonMind Project post-mortem human dorsolateral prefrontal cortex (DLPFC) GTEx				

	Parkinson's	Reference transcriptome data: CMC Fairfax et al. Cardiogenic monocyte expression data ROSMAP RNA-seq data GWAS summary statistics: discovery: International Parkinson Disease Genomics Consortium (IPDGC), PD GWAS Consortium,	Summary-level GWAS	Discovery: International Parkinson Disease Genomics Consortium (IPDGC), PD GWAS Consortium, The Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE) Consortium, PDGENE, Ashkenazi studies cohorts Validation: 23andMe (v2 and v3)	European	Primary monocytes Dorsolateral prefrontal cortex	Prediction model: FUSION Association test: FUSION	Li *et al*. [25]

		The Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE) Consortium, PDGENE, Ashkenazi studies cohorts replication: 23andMe (v2 and v3)	Reference transcriptome data	CommonMind Consortium RNA-seq data Fairfax et al. monocyte expression data Cardiogenic monocyte expression data ROSMAP RNA-seq data				
	Attention Deficit Hyperactivity Disorder	Reference transcriptome data: CMC GTEx v7 GWAS summary	Summary-level GWAS	Psychiatric Genomics Consortium (PGC-ADHD)	European	10 brain tissues	Prediction model: FUSION Association test: FUSION	Liao *et al.* [63]
			Reference transcriptome data	CommonMind Consortium GTEx v7				

		statistics: Psychiatric Genomics Consortium (PGC-ADHD)						
Other Diseases	Chronic Obstructive Pulmonary Disease	Reference transcriptome data: Lung eQTL study (Hao *et al*. [72]) replication: GTEx v6 GWAS: International COPD Genetics Consortium (ICGC)	Summary-level GWAS	International COPD Genetics Consortium (ICGC)	European	Lung	Prediction model: FUSION/S-PrediXcan Association test: FUSION/MetaXcan	Lamontagne *et al.* [54]
			Reference transcriptome data	Discovery: Lung eQTL study (Hao *et al*. [72]) Validation: GTEx v6				
	Calcific Aortic	Reference transcriptome data:	Summary-level GWAS	Discovery: QUEBEC-CAVS cohort	European	Human aortic valve	Prediction model: FUSION	Thériault *et al*. [55]

	Valve Stenosis	Valve eQTL data sets GWAS summary statistics: QUEBEC-CAVS cohort replication: UKBB		Validation: UKBB			Association test: FUSION	
			Reference transcriptome data	Valve eQTL datasets				
Other Traits	Neuroimaging	Reference transcriptome data: GTEx GWAS summary statistics: Discovery: UKBB Validation: the Human Connectome	Summary-level GWAS	Discovery: UKBB Validation: the Human Connectome Project study the Pediatric Imaging, Neurocognition, and Genetics study the Philadelphia	Multi	Cross-tissue	Prediction model: UTMOST Association test: UTMOST	Zhao *et al*. [56]

		Project study the Pediatric Imaging, Neurocognition, and Genetics study the Philadelphia Neurodevelopmental Cohort study, the Alzheimer's Disease Neuroimaging Initiative study, ENIGMA2 and ENIGMA-CHARGE collaboration		Neurodevelopmental Cohort study, the Alzheimer's Disease Neuroimaging Initiative study, ENIGMA2 and ENIGMA-CHARGE collaboration				
			Reference transcriptome data	GTEx v6				