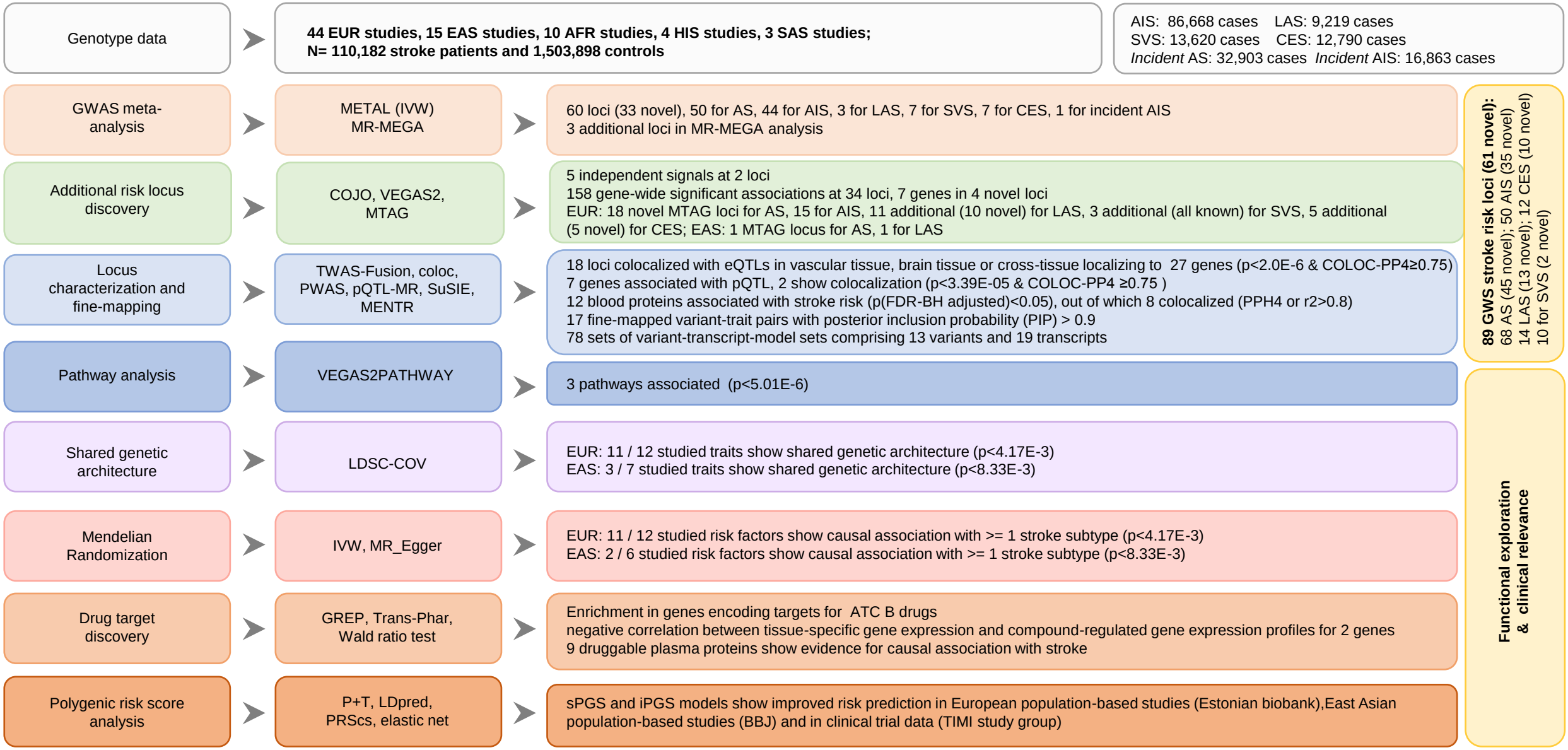
Genotype data
44 EUR studies, 15 EAS studies, 10 AFR studies, 4 HIS studies, 3 SAS studies;
N= 110,182 stroke patients and 1,503,898 controls
AIS: 86,668 cases LAS: 9,219 cases
SVS: 13,620 cases CES: 12,790 cases
Incident AS: 32,903 cases Incident AIS: 16,863 cases
GWAS meta-analysis
METAL (IVW)
MR-MEGA
60 loci (33 novel), 50 for AS, 44 for AIS, 3 for LAS, 7 for SVS, 7 for CES, 1 for incident AIS
3 additional loci in MR-MEGA analysis
Additional risk locus discovery
COJO, VEGAS2, MTAG
5 independent signals at 2 loci
158 gene-wide significant associations at 34 loci, 7 genes in 4 novel loci
EUR: 18 novel MTAG loci for AS, 15 for AIS, 11 additional (10 novel) for LAS, 3 additional (all known) for SVS, 5 additional (5 novel) for CES; EAS: 1 MTAG locus for AS, 1 for LAS
Locus characterization and fine-mapping
TWAS-Fusion, coloc, PWAS, pQTL-MR, SuSIE, MENTR
18 loci colocalized with eQTLs in vascular tissue, brain tissue or cross-tissue localizing to 27 genes (p<2.0E-6 & COLOC-PP4≥0.75)
7 genes associated with pQTL, 2 show colocalization (p<3.39E-05 & COLOC-PP4 ≥0.75)
12 blood proteins associated with stroke risk (p(FDR-BH adjusted)<0.05), out of which 8 colocalized (PPH4 or r2>0.8)
17 fine-mapped variant-trait pairs with posterior inclusion probability (PIP) > 0.9
78 sets of variant-transcript-model sets comprising 13 variants and 19 transcripts
89 GWS stroke risk loci (61 novel):
68 AS (45 novel); 50 AIS (35 novel)
14 LAS (13 novel); 12 CES (10 novel)
10 for SVS (2 novel)
Pathway analysis
VEGAS2PATHWAY
3 pathways associated (p<5.01E-6)
Shared genetic architecture
LDSC-COV
EUR: 11 / 12 studied traits show shared genetic architecture (p<4.17E-3)
EAS: 3 / 7 studied traits show shared genetic architecture (p<8.33E-3)
Mendelian Randomization
IVW, MR_Egger
EUR: 11 / 12 studied risk factors show causal association with >= 1 stroke subtype (p<4.17E-3)
EAS: 2 / 6 studied risk factors show causal association with >= 1 stroke subtype (p<8.33E-3)
Drug target discovery
GREP, Trans-Phar, Wald ratio test
Enrichment in genes encoding targets for ATC B drugs
negative correlation between tissue-specific gene expression and compound-regulated gene expression profiles for 2 genes
9 druggable plasma proteins show evidence for causal association with stroke
Polygenic risk score analysis
P+T, LDpred, PRScs, elastic net
sPGS and iPGS models show improved risk prediction in European population-based studies (Estonian biobank),East Asian population-based studies (BBJ) and in clinical trial data (TIMI study group)
Functional exploration & clinical relevance