

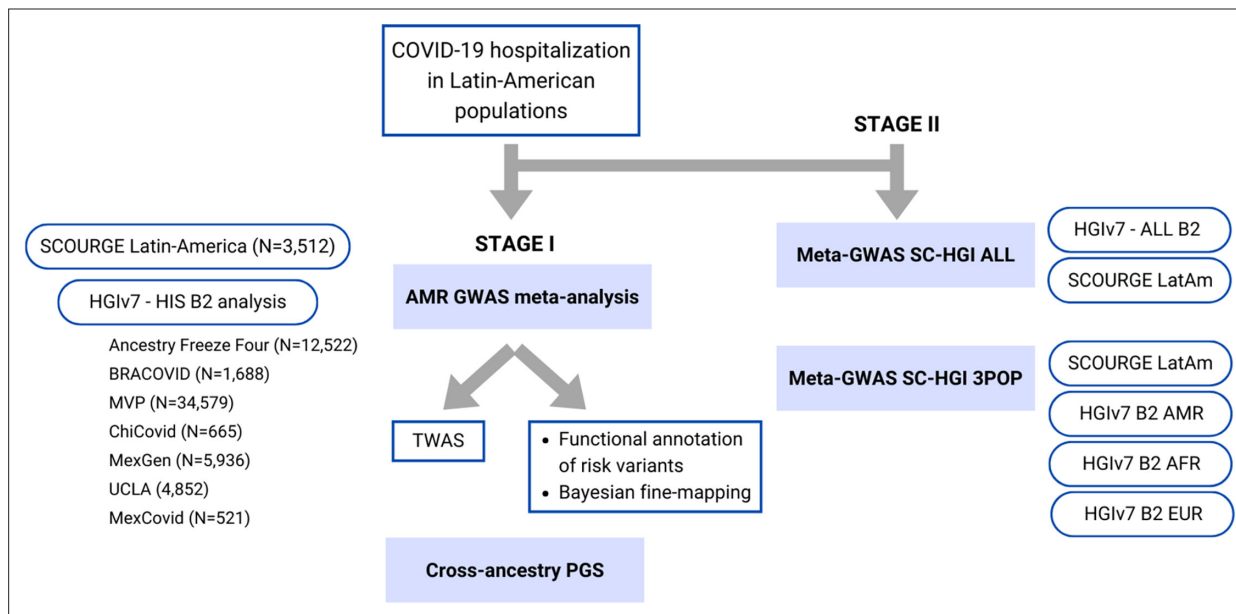


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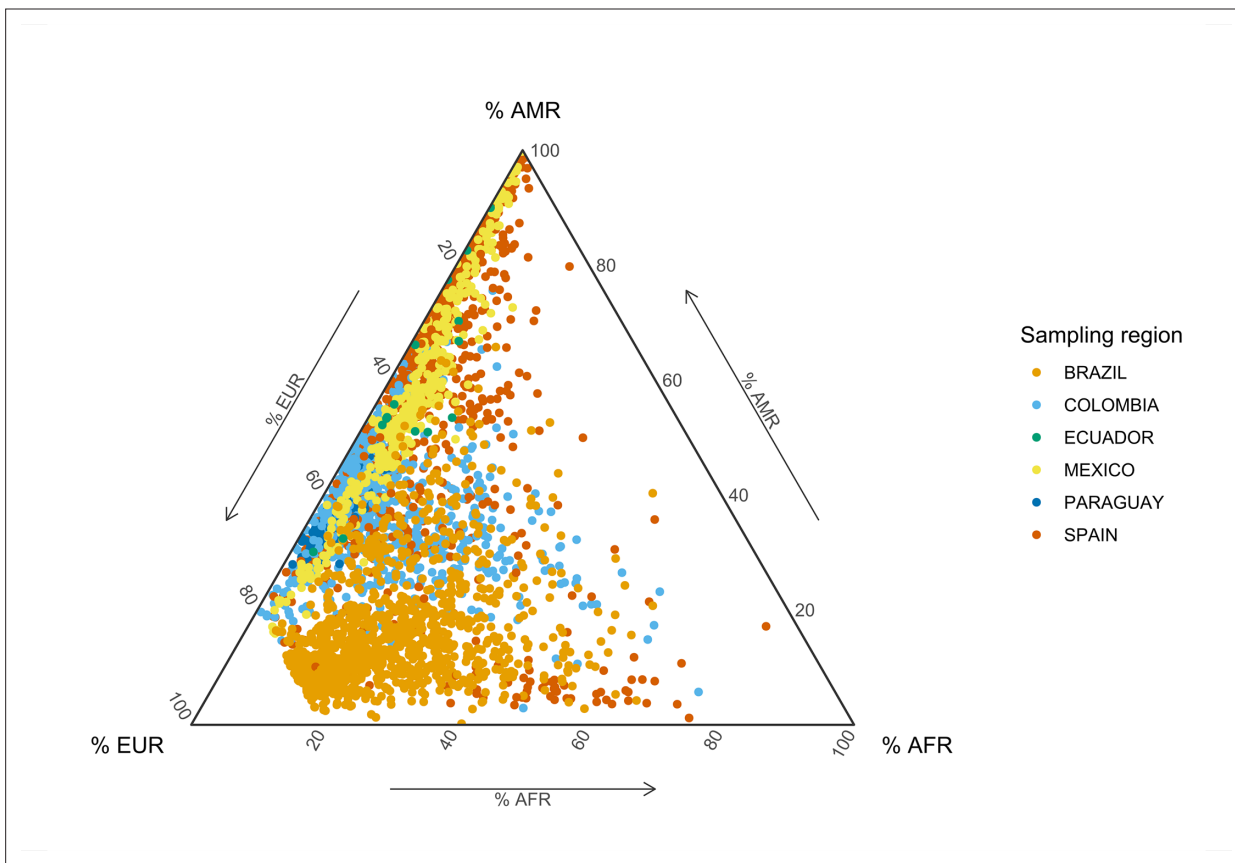
## Figures and figure supplements

Novel risk loci for COVID-19 hospitalization among admixed American populations

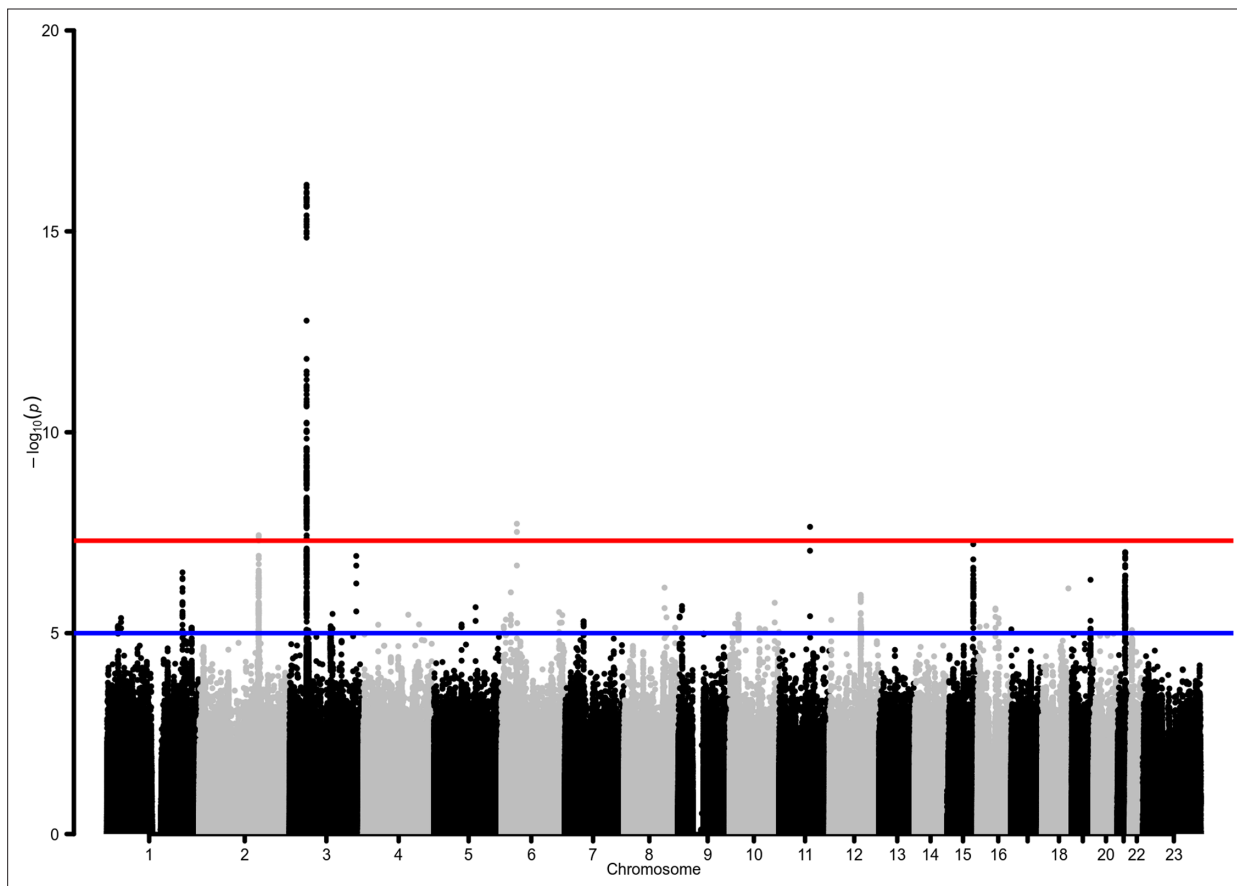
**Silvia Diz-de Almeida and Raquel Cruz *et al.***



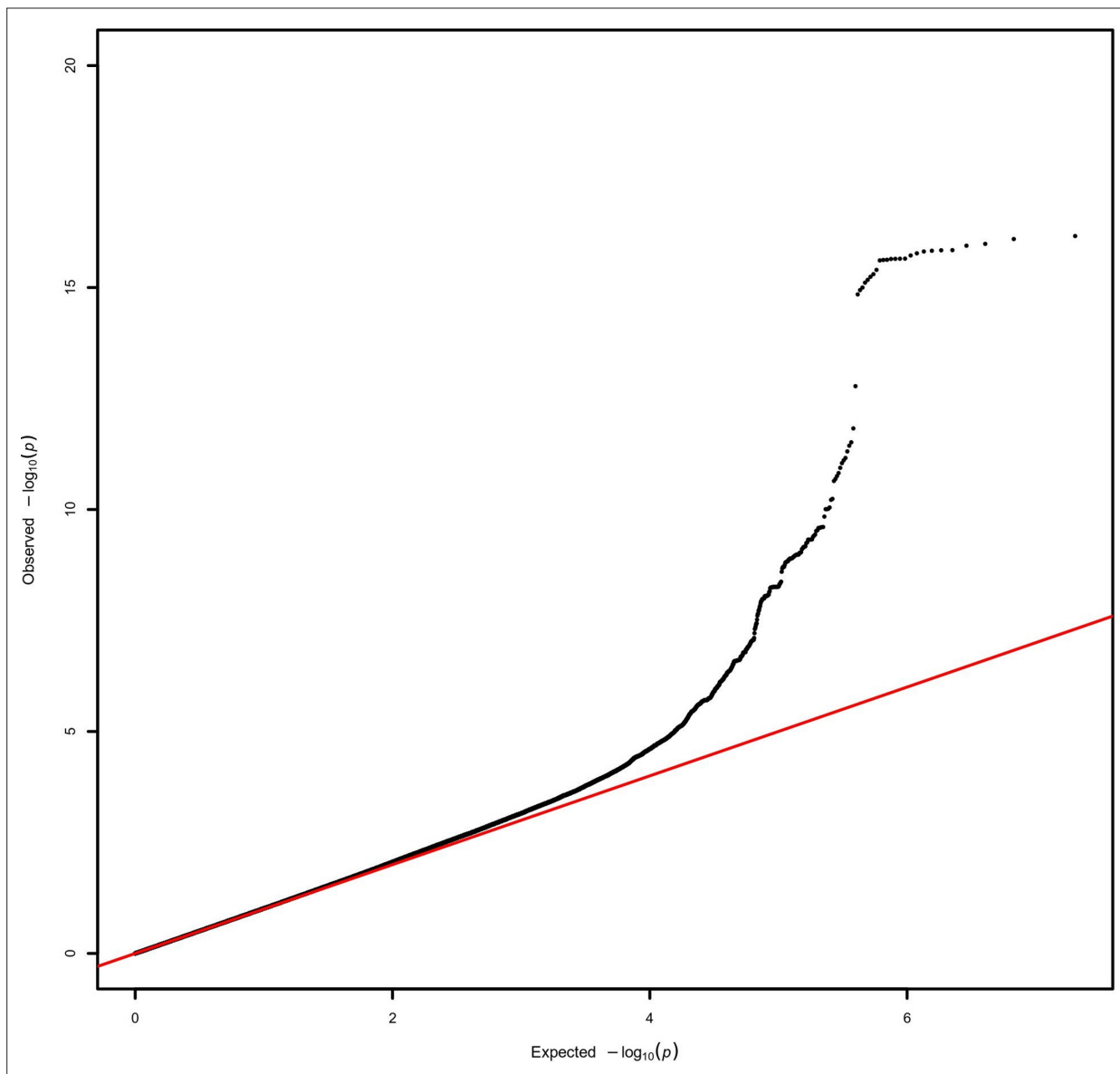
**Figure 1.** Flow chart of this study. Stage I of the study involved a meta-analysis of the Latin-American GWAS from SCOURGE and the COVID-19 Host Genetics Initiative. The resulting meta-analysis was leveraged to prioritize genes by using a Transcriptome-wide association study (TWAS), Bayesian fine-mapping and functional annotations, and to assess the generalizability of polygenic risk score (PGS) cross-population models in Latin Americans. Stage II involved two additional cross-population GWAS meta-analyses to further investigate the replicability of findings.



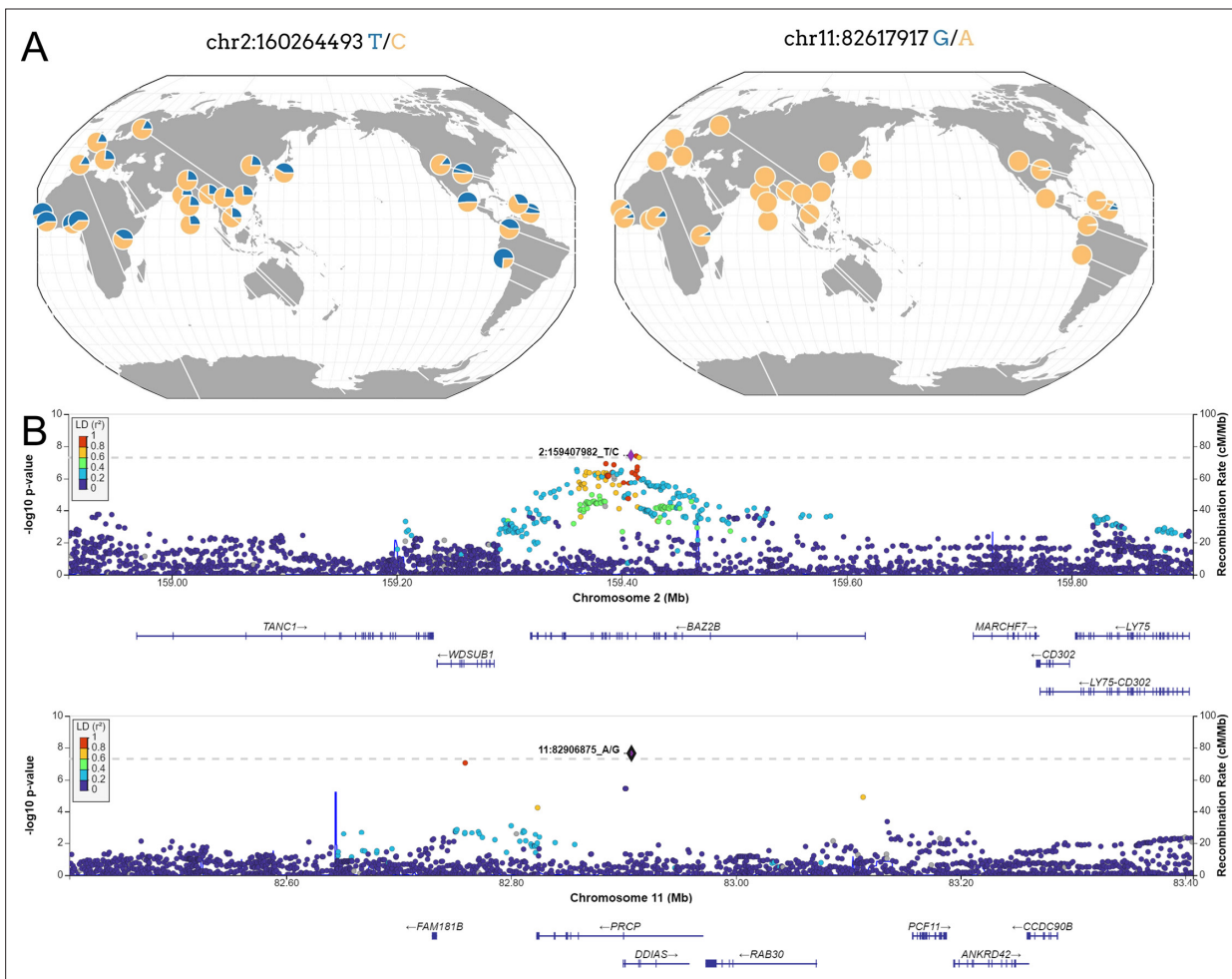
**Figure 1—figure supplement 1.** Global Genetic Inferred Ancestry (GIA) composition in the SCOURGE Latin-American cohort. European (EUR), African (AFR) and Native American (AMR) GIA was derived with ADMIXTURE from a reference panel composed of Aymaran, Mayan, Nahuatl, and Quechuan individuals of Native-American genetic ancestry and randomly selected samples from the EUR and AFR 1KGP populations. The colours represent the different geographical sampling regions from which the admixed American individuals from SCOURGE were recruited.



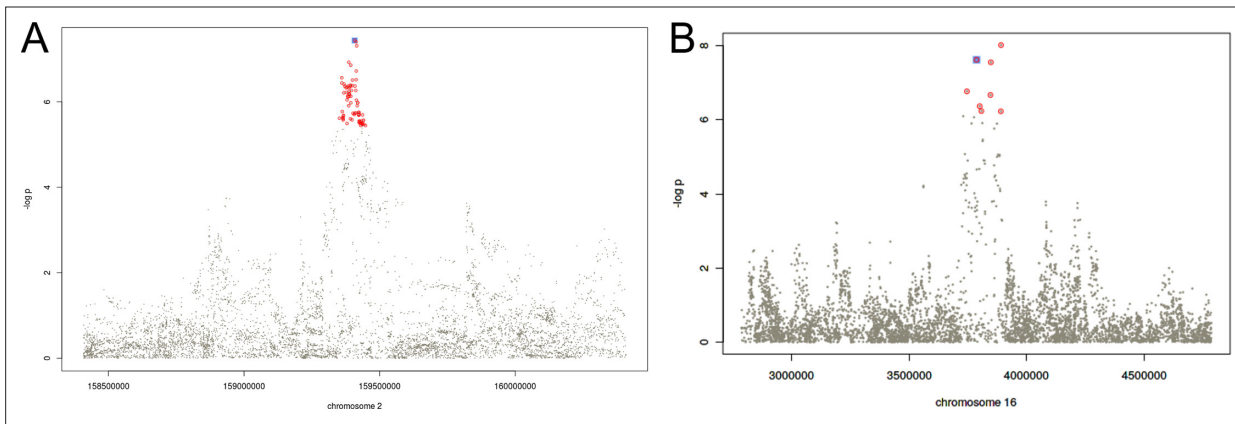
**Figure 2.** Manhattan plot for the admixed AMR GWAS meta-analysis. Probability thresholds at  $P=5 \times 10^{-8}$  and  $P=5 \times 10^{-5}$  are indicated by the horizontal lines. Genome-wide significant associations with COVID-19 hospitalizations were found on chromosome 2 (within *BAZ2B*), chromosome 3 (within *LZTFL1*), chromosome 6 (within *FOXP4*), and chromosome 11 (within *DDIAS*).



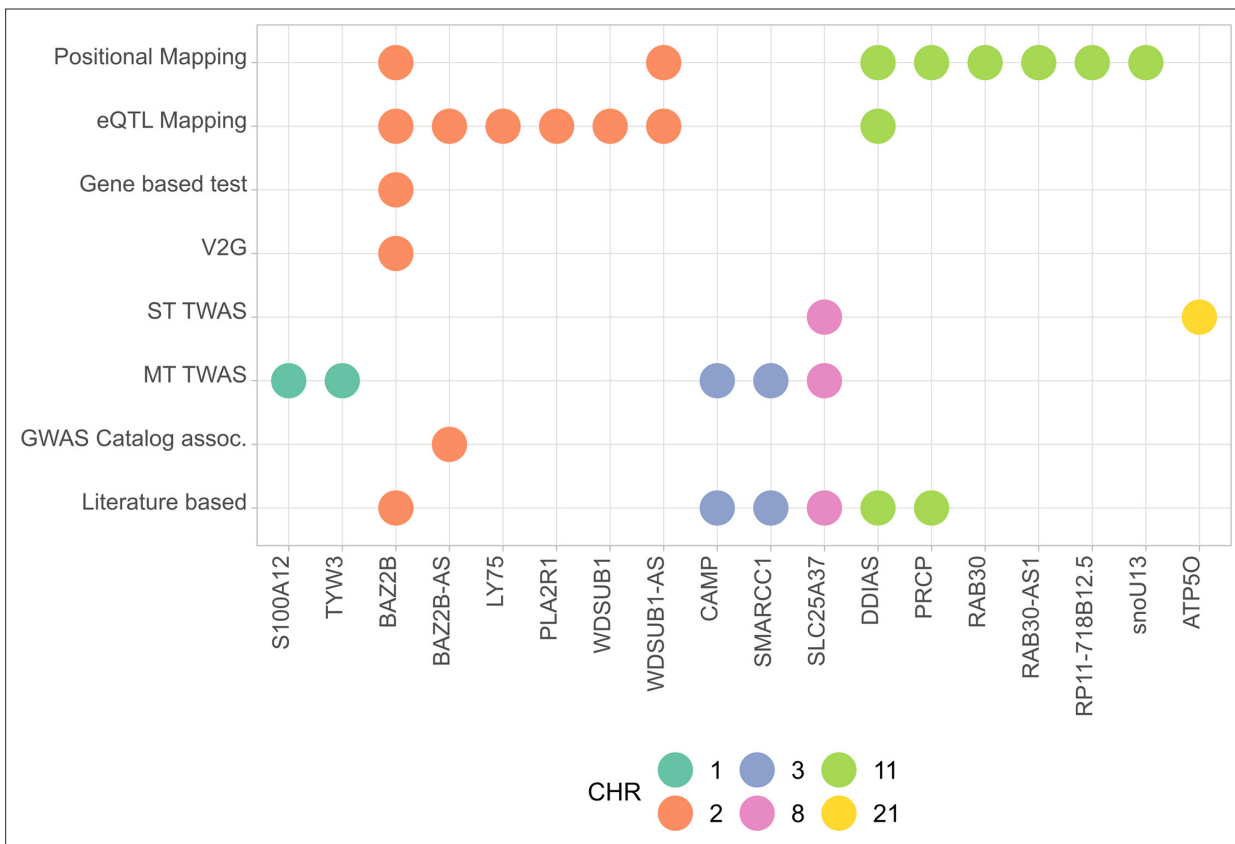
**Figure 2—figure supplement 1.** Quantile-Quantile plot for the AMR GWAS meta-analysis. A lambda inflation factor of 1.015 was obtained.



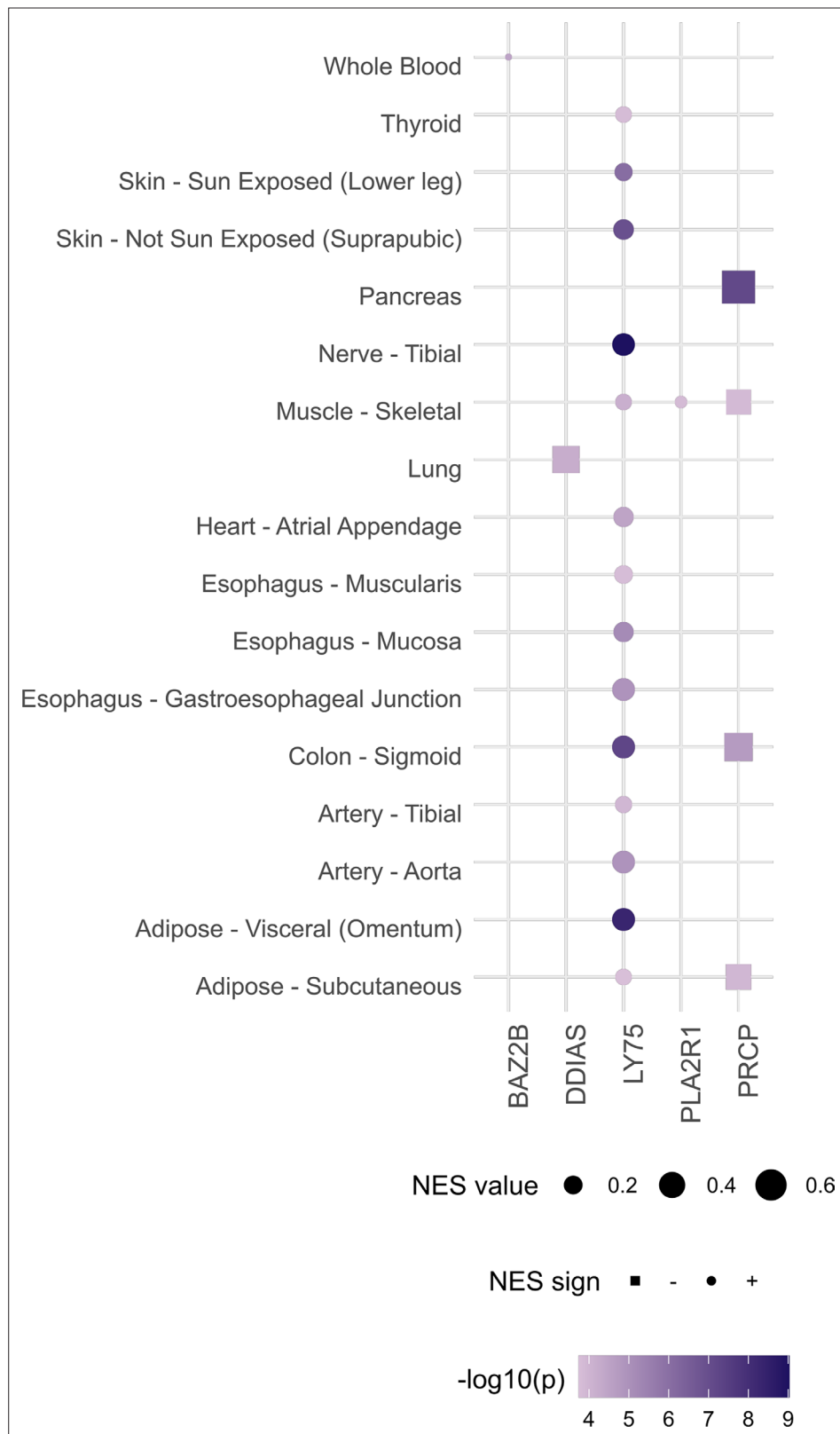
**Figure 3.** (A) Regional association plots for rs1003835 at chromosome 2 and rs7759934 at chromosome 11; (B) Allele frequency distribution across the 1000 Genomes Project populations for the lead variants rs1003835 and rs7759934. Retrieved from *The Geography of Genetic Variants Web* or GGv.



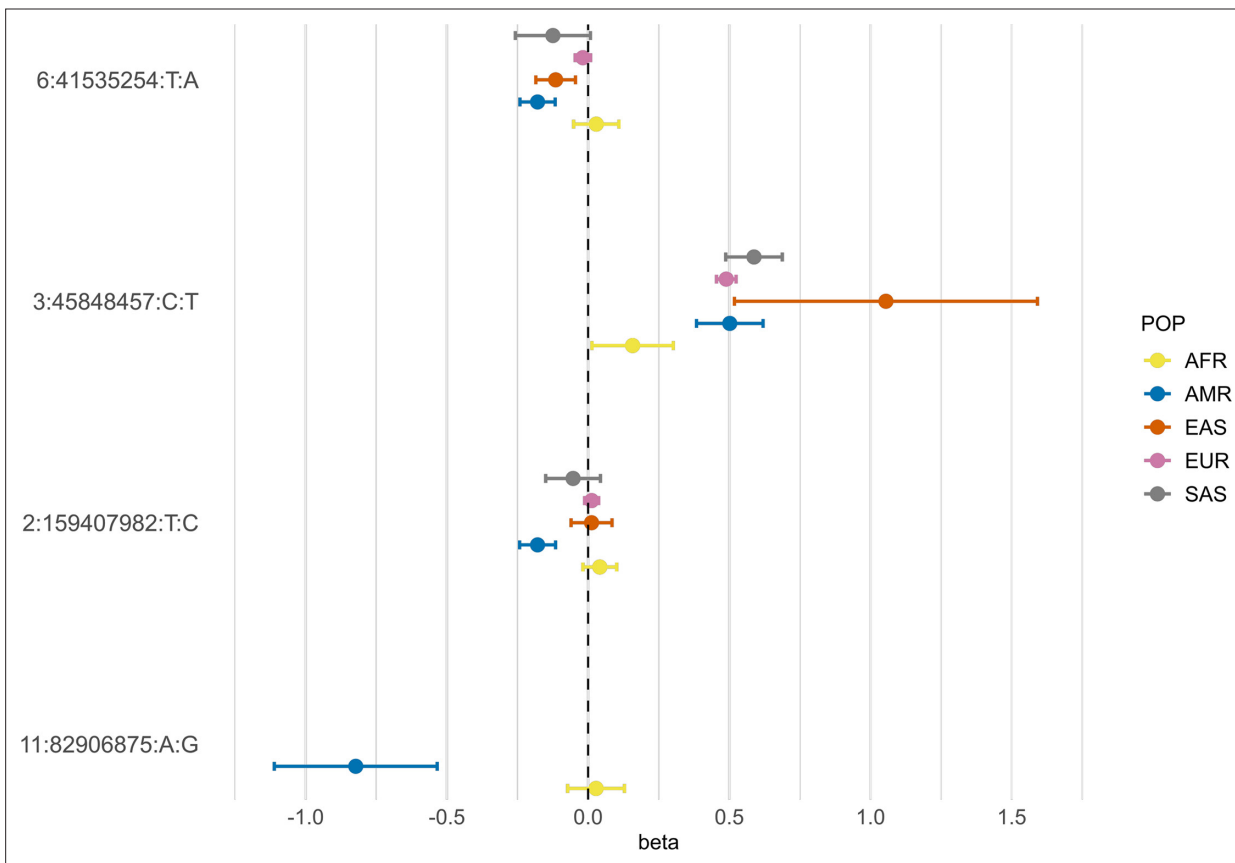
**Figure 3—figure supplement 1.** Regional association plots for the fine mapped loci in chromosomes 2 (upper panel) and 16 (lower panel). Coloured in red, the variants allocated to the credible set at the 95% confidence according to the Bayesian fine mapping. In blue, the sentinel variant.



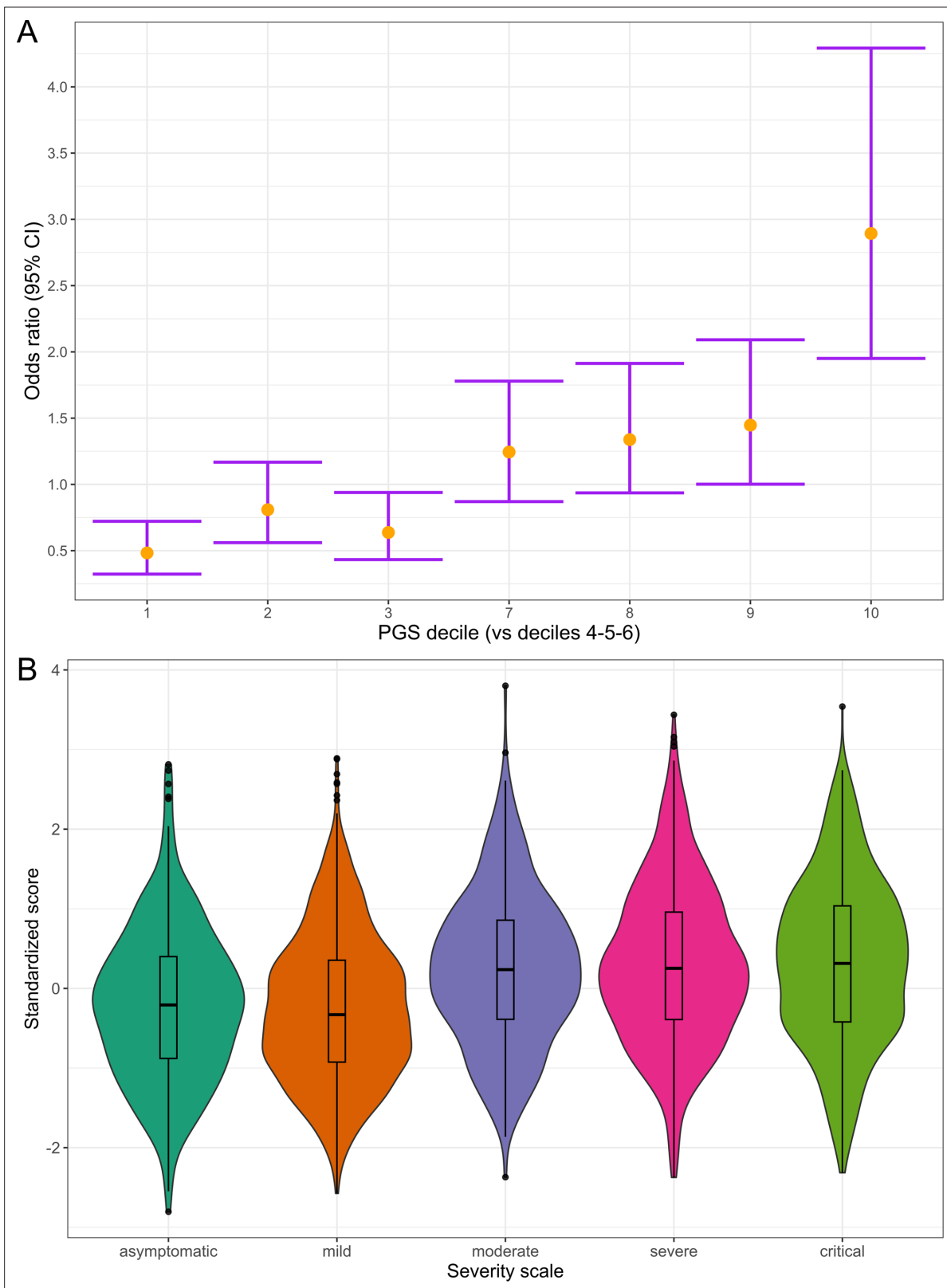
**Figure 4.** Summary of the results from gene prioritization strategies used for genetic associations in AMR populations. GWAS catalog association for *BAZ2B-AS* was with FEV/FCV ratio. Literature based evidence is further explored in discussion.



**Figure 4—figure supplement 1.** Gene-tissue pairs for which either rs1003835 or rs60606421 are significant eQTLs at FDR <0.05 (data retrieved from <https://gtexportal.org/home/snp/>). rs1003835 (chromosome 2) maps to *BAZ2B*, *LY75*, and *PLA2R1* genes. As for the lead variant of chromosome 11, rs77599934, since it was not an eQTL, we used an LD proxy variant (rs60606421). *DDIAS* and *PRCP* genes map closely to this variant. NES and p-values correspond to the normalized effect size (and direction) of eQTL-gene associations and the p-value for the tissue, respectively.



**Figure 5.** Forest plot showing effect sizes and the corresponding confidence intervals for the sentinel variants identified in the AMR meta-analysis across populations. All beta values with their corresponding CIs were retrieved from the B2 population-specific meta-analysis from the HGI v7 release, except for AMR, for which the beta value and IC from the HGI<sub>AMR</sub>-SCOURGE meta-analysis are represented.



**Figure 6.** (A) Polygenic risk stratified by PGS deciles comparing each risk group against the lowest risk group (OR-95% CI); (B) Distribution of the PGS scores in each of the severity scale classes. 0-Asymptomatic, 1-Mild disease, 2-Moderate disease, 3-Severe disease, 4-Critical disease.