Figure E1: ARDS develops by ICU day 1 in 80% of subjects who develop sepsis-associated ARDS
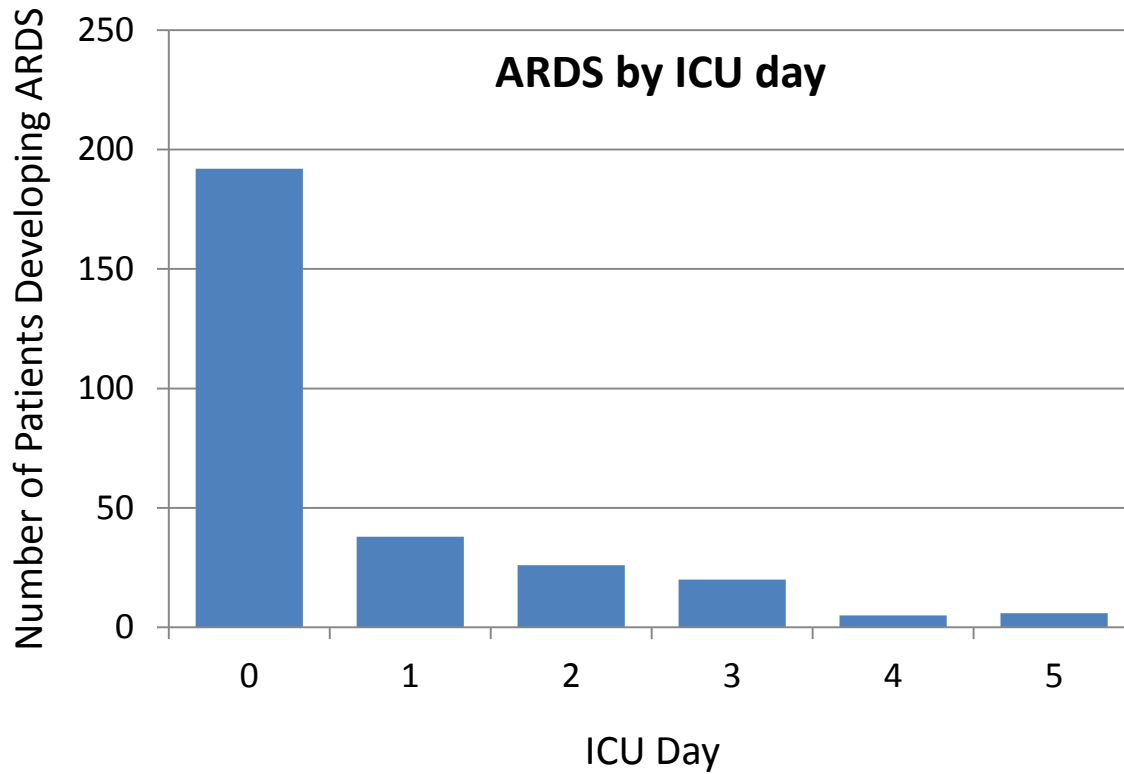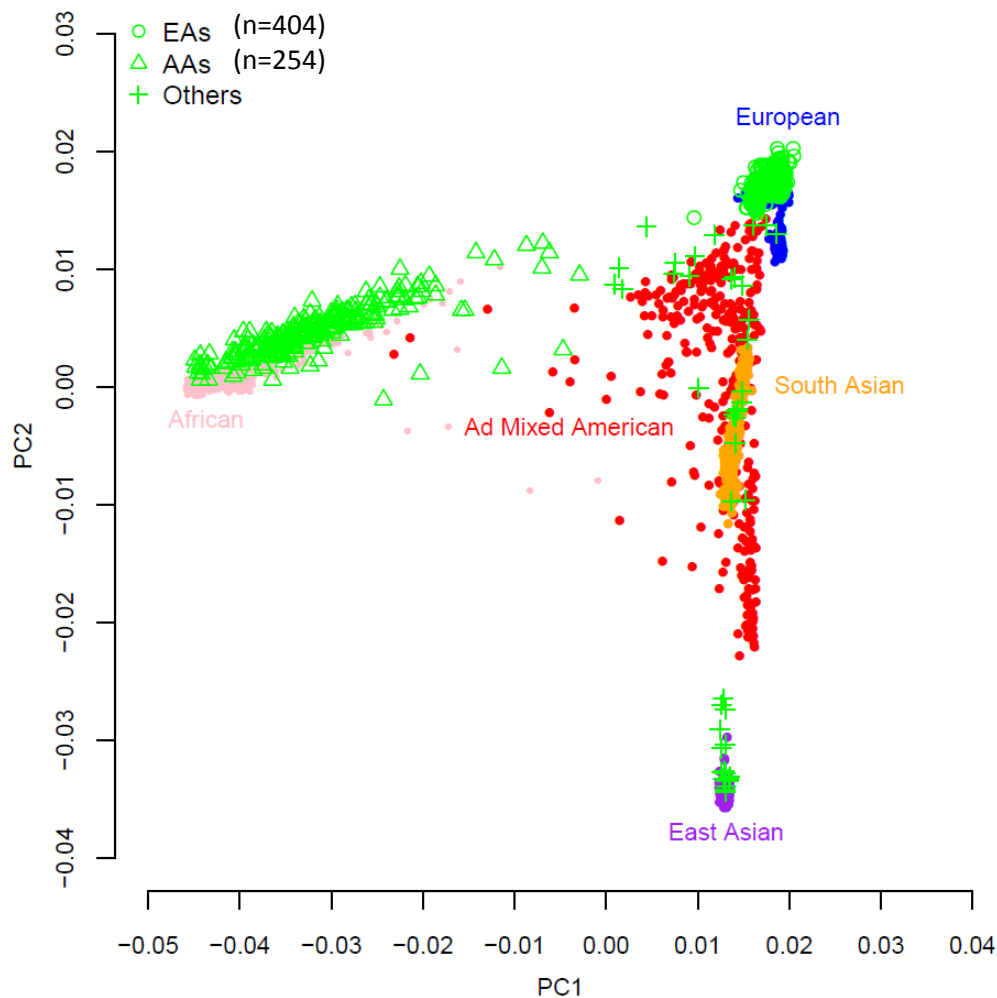
Figure E2: Genetic ancestry determination by principal components analysis (a) and linkage disequilibrium structure in *ANGPT2* (b)

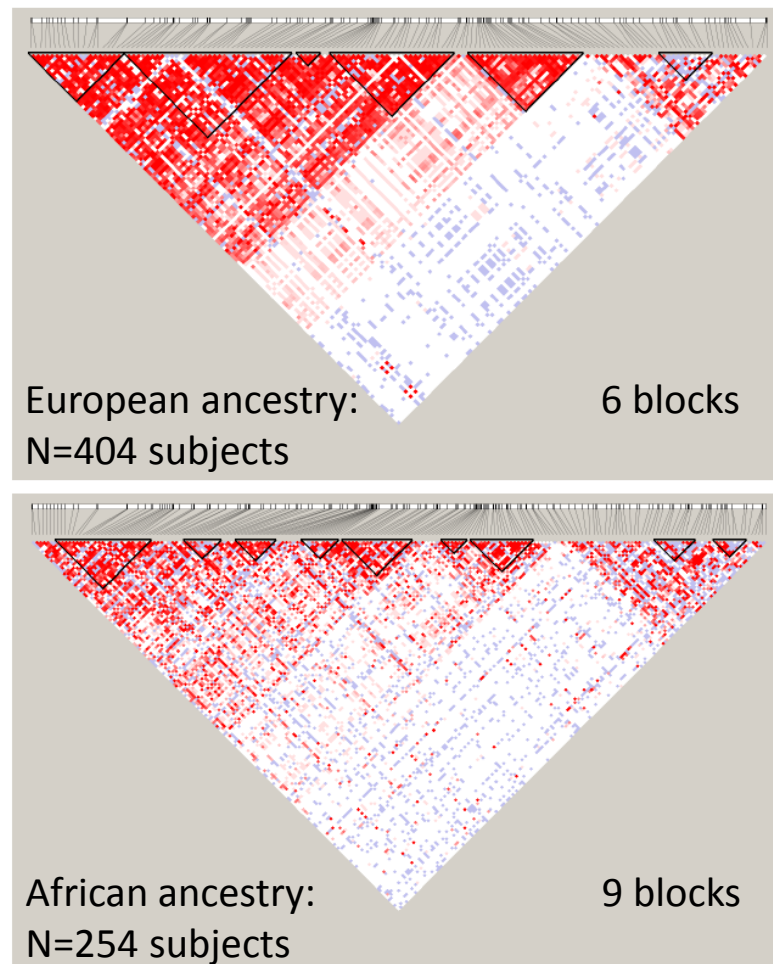## a) Genetic ancestry

b) Linkage disequilibrium blocks

European ancestry: 6 blocks
N=404 subjects

African ancestry: 9 blocks
N=254 subjects

Figure E3: MESSI study population

Screened 9265 ICU or ED subjects

→ 7102 Not septic or non-ICU

2163 Eligible

→ 355 met exclusion criteria
156 declined participation
389 no proxy or missed

1263 Enrolled

→ 379 DNA unavailable
181 Day 0 plasma unavailable

703 Analyzed - QTL

Sensitivity analysis:
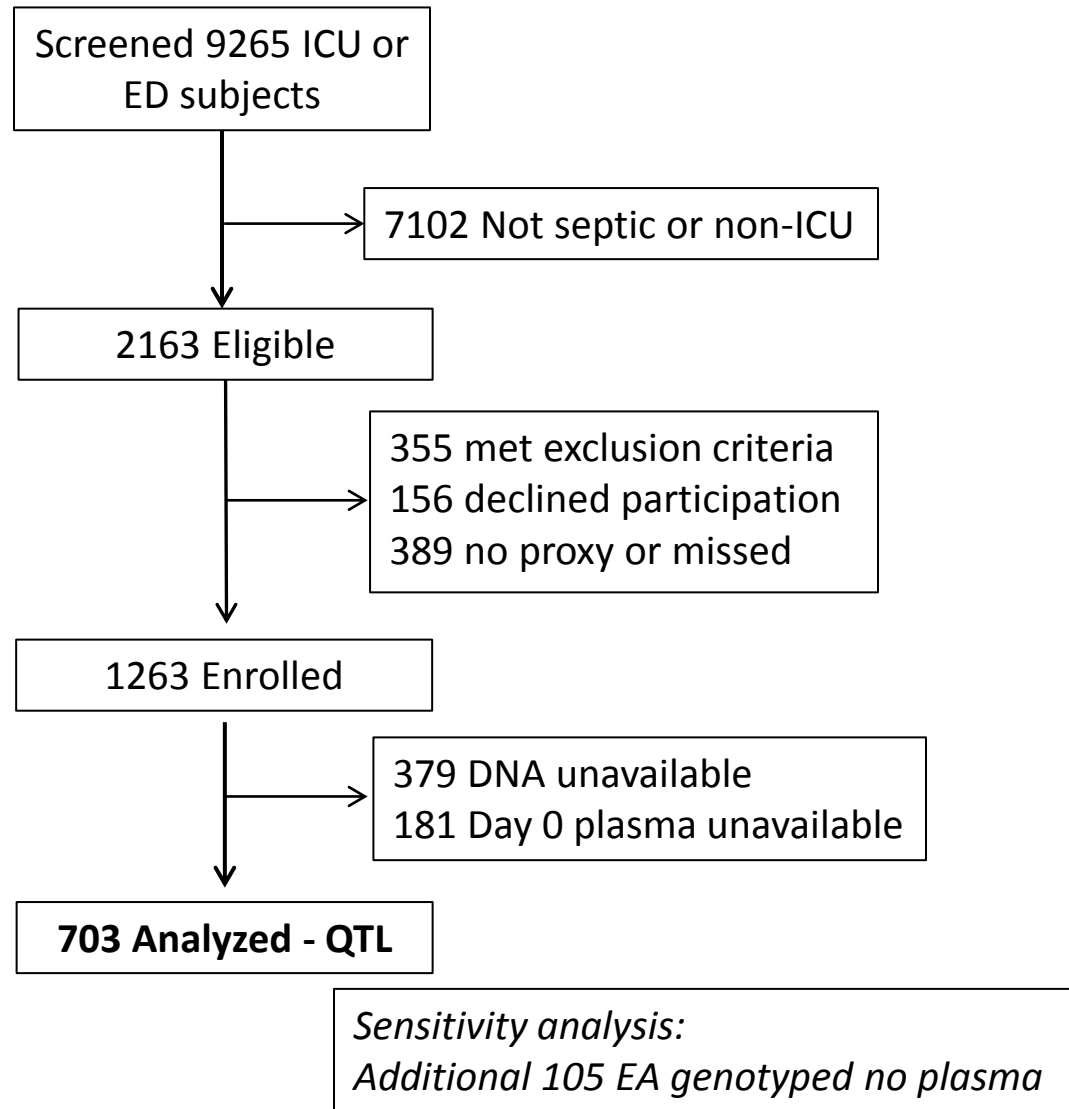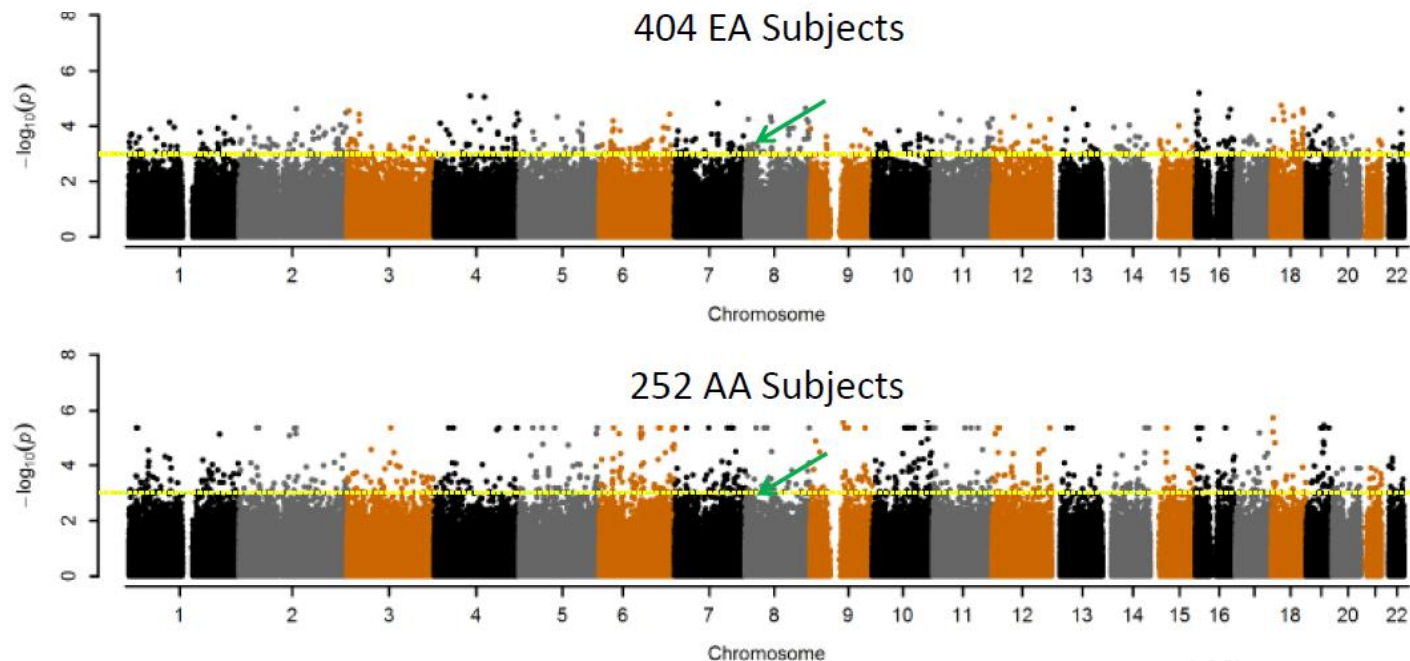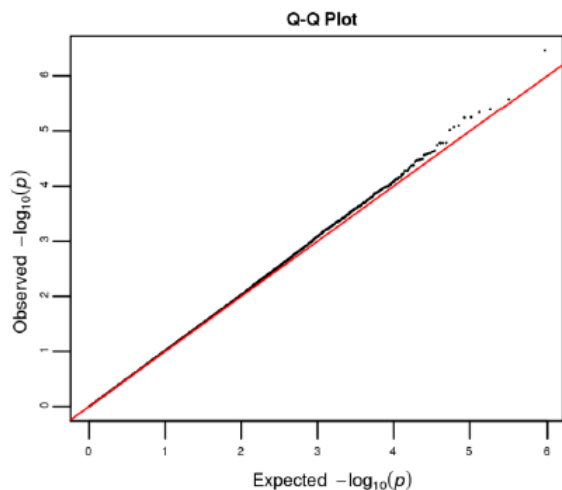*Additional 105 EA genotyped no plasma*

Figure E4: Association between *ANGPT2* locus (Chromosome 8p23.1) and plasma ANG2 varies between European and African ancestry subjects. The *ANGPT2* locus is shown the green arrows.
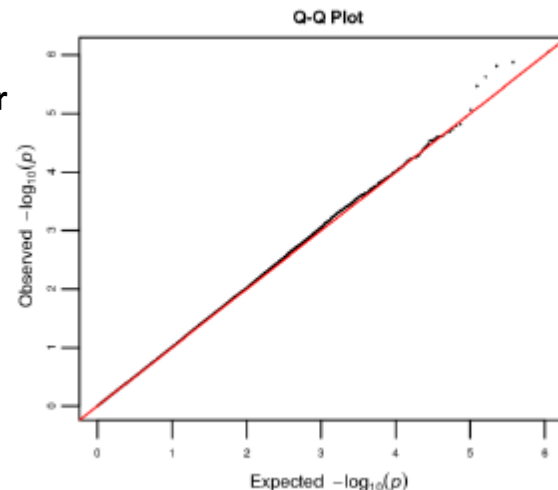
A. ANG2 QTL Analysis
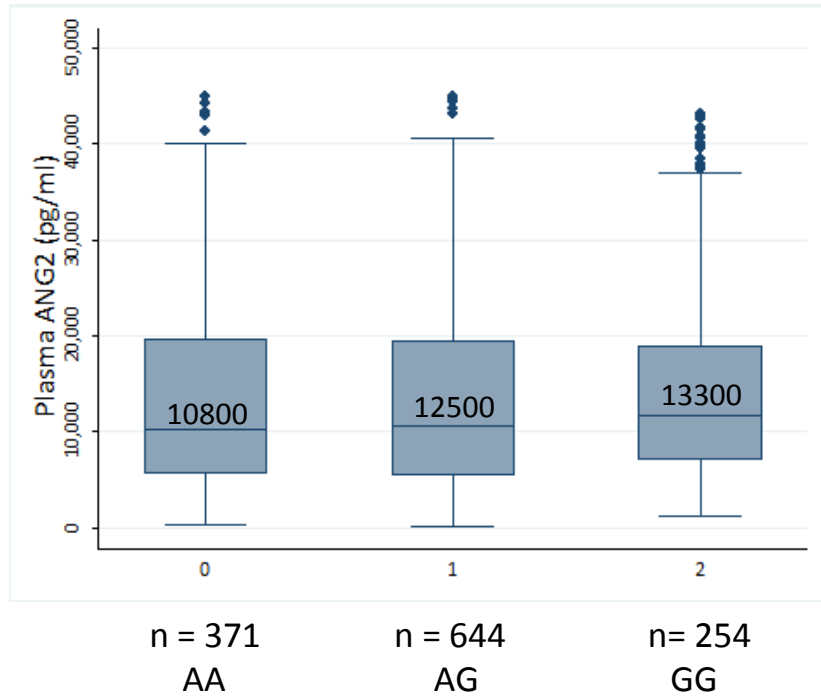

B. Genomic inflation factor (λ) in EA: 1.021

C. Genomic inflation factor (λ) in AA: 1.020

E5a

rs2442608
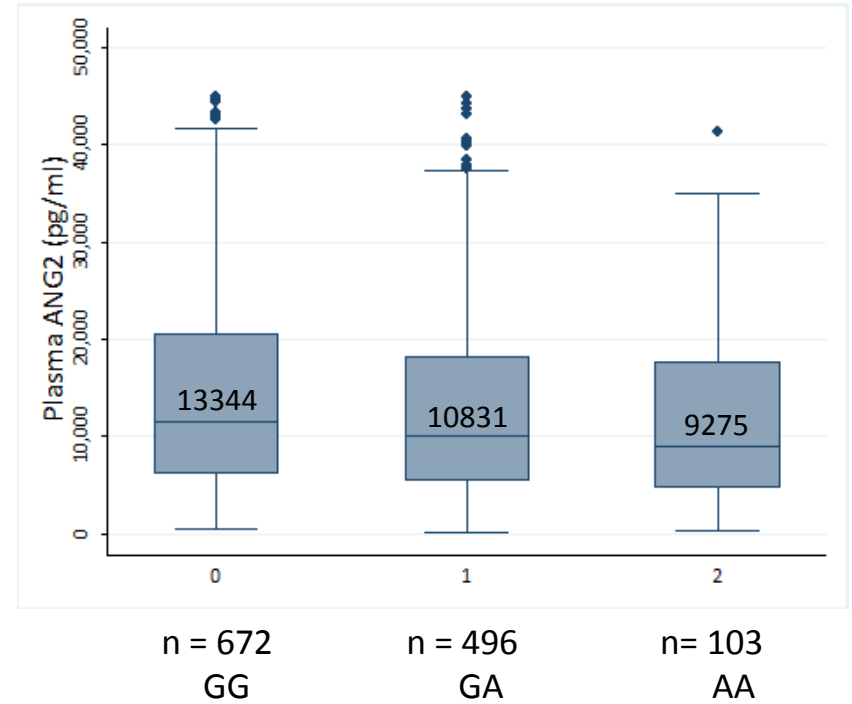p = 0.006

E5b

rs2515466
p < 0.001

Figure E5: Plasma ANG2 concentration associations with 2 *ANGPT2* SNPs, rs2442608 (a) and rs2515466 (b). Median, interquartile range, and 95% confidence intervals are shown for all subjects included in the meta-analysis. Linear regression was used to test the association of each SNP with plasma ANG2 assuming an additive model.