

$$(a) GS, SNVs_{celiprolol} = 0.74^n(SLCO1A2 \text{ c.516A>C}) \times 0.86^n(ABCB1 \text{ c.3435T>C}) \times 0.78^n(ABCB1 \text{ c.2677T/G>A})$$

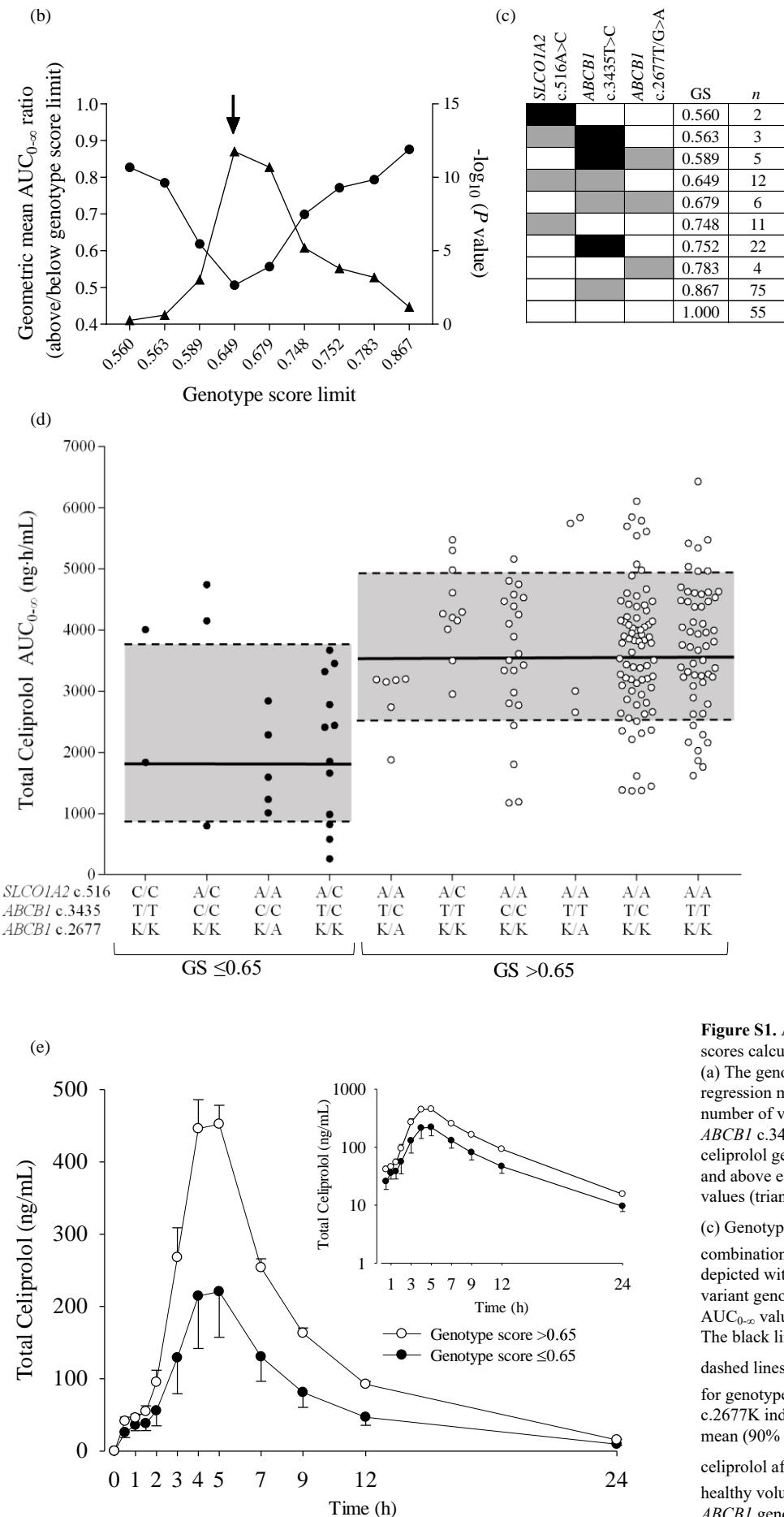


Figure S1. Associations of total celiprolol AUC_{0-∞} with genotype scores calculated with *SLCO1A2* c.516A>C and *ABCB1* SNVs.

(a) The genotype score equation of the candidate gene linear regression model employing *ABCB1* SNVs, where n is the number of variant alleles (0, 1, or 2) of *SLCO1A2* c. 516A>C, *ABCB1* c.3435T>C, or *ABCB1* c.2677T/G>A. (b) The total celiprolol geometric mean AUC_{0-∞} ratios between groups below and above each genotype score limit (circles) and respective P values (triangles). The arrow depicts the optimal cut-off value.

(c) Genotype scores (GS) for individuals with different genotype combinations. *ABCB1* and *SLCO1A2* reference genotypes are depicted with white, heterozygous with gray and homozygous variant genotypes with black rectangles. (d) The LBW-adjusted AUC_{0-∞} values of total celiprolol grouped by genotype scores. The black lines in the gray areas depict the geometric mean and dashed lines the \pm geometric standard deviation AUC_{0-∞} values for genotype score groups below and above the cut-off limit. The c.2677K indicates either the T or the G allele. (e) Geometric mean (90% CI) LBW-adjusted plasma concentrations of celiprolol after a single 200 mg oral dose of celiprolol in 195 healthy volunteers with different combinations of *SLCO1A2* and *ABCB1* genotypes. The insets depict the same data on a semilogarithmic scale. The volunteers were grouped according to the genotype score (GS) limit 0.65: GS \leq 0.65 ($n = 22$) and GS $>$ 0.65 ($n = 173$).