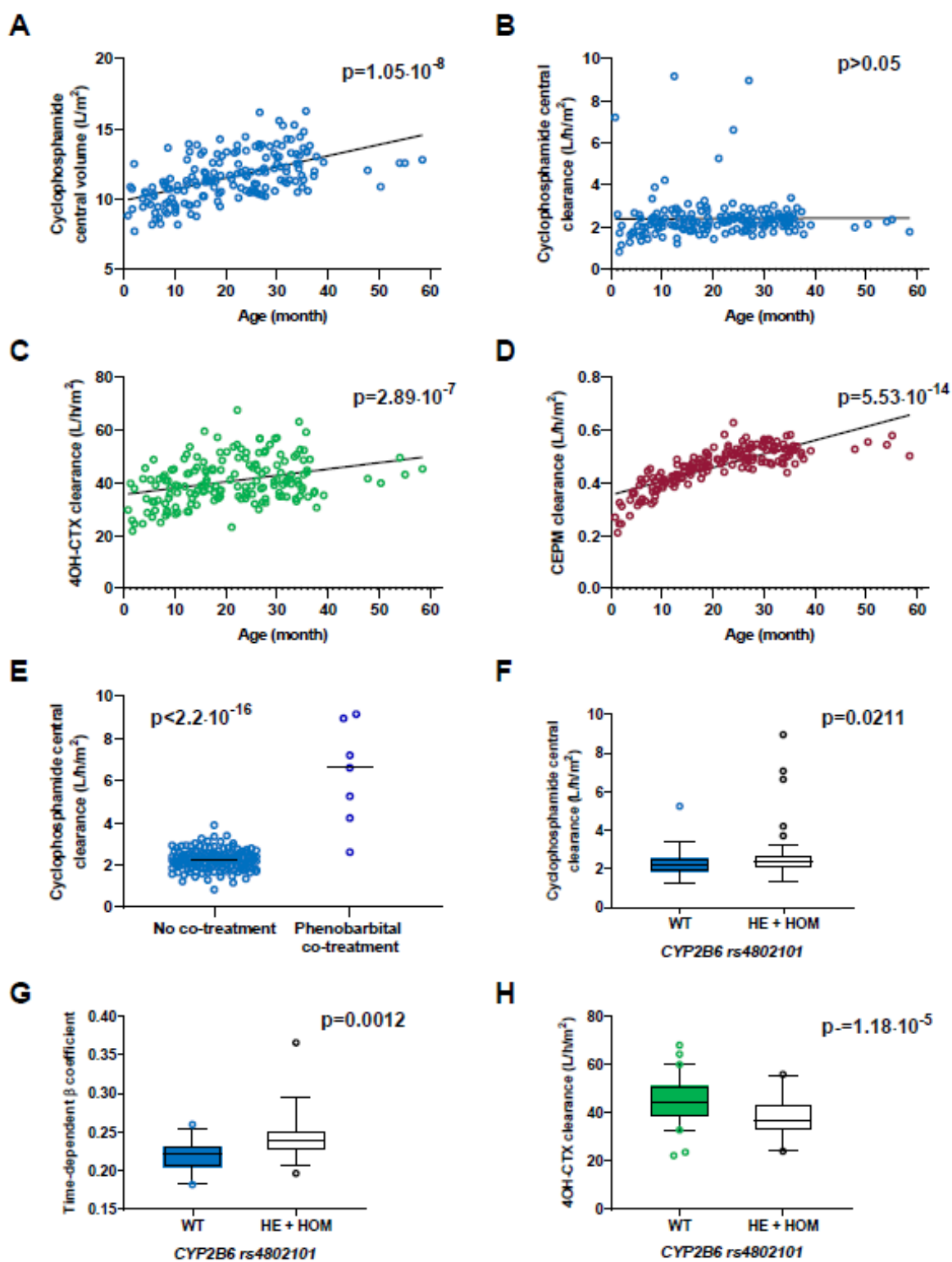


**Figure S5.** Final pharmacokinetic covariate associations with phenobarbital cotreatment, age, and *CYP2B6* genotypes.



- (A) Scatter plots of individual cyclophosphamide central volume estimates vs age.
- (B) Scatter plots of individual cyclophosphamide clearance estimates vs age.
- (C) Scatter plots of individual 4OH-CTX clearance estimates vs age.
- (D) Scatter plots of individual CEPM clearance estimates vs age.
- (E) Boxplots of individual cyclophosphamide clearance estimates vs phenobarbital cotreatment or no phenobarbital co-treatment.
- (F) Boxplots of individual cyclophosphamide clearance estimates vs *CYP2B6 rs4802101* categorized as wild-type (WT) or heterozygous + homozygous mutant (HE + HOM).
- (G) Boxplots of individual cyclophosphamide time-dependent coefficient  $\beta$  estimates vs *CYP2B6 rs4802101* categorized as WT or HE + HOM.
- (H) Boxplots of individual 4OH-CTX clearance estimates vs *CYP2B6 rs4802101* categorized as WT or HE + HOM.

*P* values correspond to Wald test examining whether the covariate coefficient on the pharmacokinetic parameter is significantly different from 0 ( $P < .05$ ). The age was not retained as a significant covariate of cyclophosphamide clearance in the final model. This graph is depicted to show that age did not affect parent drug clearance, in contrast with the metabolites.