SUPPLEMENTARY METHODS

DNA extraction and genotyping

The Guangzhou Biobank genetic data contains genotypes for 3,137 participants. DNA was extracted at the Guangzhou Twelfth People's Hospital from buffy coat stored at –80°C using a standard magnetic bead extraction procedure. Concentrations of DNA were examined by Nanodrop (Thermo Scientific, Waltham, MA, USA), and for those of <15 ng/μL, silica-based column method was used to re-extract DNA manually (Hipure Blood DNA Mini Kit, Magen Biotechnology, Guangzhou, China). We used the Illumina ASA (BeadChip Array Asian Screening Array-24+v1.0 HTS ASAMD-24v1-0, San Diego, CA, USA) genotyping platform (array). For ASA array (including 743,722 variants), 56.7% of the variants are common variants (with minor allele frequency [MAF] >0.05), 30.8% are low-frequency variant (with MAF between 0.01 and 0.05), and 12.5% are rare variants (MAF <0.01). ASA array includes a broad spectrum of pharmacogenomics markers (n=5,588) obtained from Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines (www.cpicpgx.org) and the Pharmacogenomics Knowledge Base (PharmGKB) database (www.pharmgkb.org). In addition, the ASA array contains about 50,000 single nucleotide polymorphisms (SNPs) selected from ClinVar database (www.ncbi.nlm.nih.gov/clinvar). More details about the ASA array can be found in the official Illumina website (https://www.illumina.com/products/by-type/microarray-kits). Genotyping assays were conducted at Guoke Biotechnology Co., LTD in Beijing, China (www.bioguoke.com).

Quality control

The quality control procedures of parameters for retaining SNPs and subjects were:

(1) SNPs with a call rate >97%;
(2) SNP missingness <0.02 (before sample removal);
(3) Samples with genotype missing rate <0.02;
(4) After checking the sex of sample, the F-value must <0.2 for women and >0.8 for men;
(5) SNPs with a MAF >0.01;
(6) SNP Hardy-Weinberg equilibrium (HWE) with $P>10^{-4}$ for samples;
(7) The participants of heterozygosity must remain ±3 standard deviation from the mean heterozygosity of all samples.

Genotype imputation

The imputation of the genotypes was performed by pre-phasing/imputation stepwise approach implemented in IMPUTE2/SHAPEIT (chunk size of 3 Mb and default parameters). The imputation reference set consisted of 2,504 samples with 5,008 phased haplotypes from the full 1000 Genomes Project dataset Phase 3 (update October 2014). Chromosome X (ChrX) imputation was conducted for subjects passing quality control for the autosomal analysis with the additional exclusions of chrX SNPs with missingness ≥0.05 or HWE $P<10^{-6}$ in females. ChrX imputation was performed separately for males and females.