

Supplementary Information for “A rotated multivariate linear mixed model for dual large-scale genome-wide association study”

The Supplementary information contain the following contents:

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Supplementary Note 1: Deriving the distribution of TOP2 statistic.

Let $p_1, \dots, p_d$ be independent and identically distributed (i.i.d.) random variables from uniform distribution $U(0, 1)$, and denote by $p_{(1)} \leq p_{(2)} \leq \dots \leq p_{(d)}$ the corresponding order statistics. The joint probability density function (PDF) of $p_{(1)}$ and $p_{(2)}$ for $0 < x < y < 1$ is given by

$$f_{p_{(1)}, p_{(2)}}(x, y) = d(d-1)(1-y)^{d-2}.$$

We define the test statistic as

$$\text{TOP2} = -2 \ln p_{(1)} - 2 \ln p_{(2)}.$$

To find its cumulative distribution function (CDF) with $F_{\text{TOP2}}(s) = P(\text{TOP2} \leq s)$, we integrate the joint PDF of $p_{(1)}$ and $p_{(2)}$ over the region corresponding to the event $\{\text{TOP2} \leq s\}$.

Integral formulation and limits. The event $\{\text{TOP2} \leq s\}$ is equivalent to $\{p_{(1)}p_{(2)} \geq e^{-s/2}\}$. Let $b = e^{-s/2}$, the CDF is the probability $P(p_{(1)}p_{(2)} \geq b)$. This is calculated by integrating the joint PDF over the region $D = \{(x, y) \mid 0 < x < y < 1, xy \geq b\}$,

$$P(\text{TOP2} \leq s) = \iint_D d(d-1)(1-y)^{d-2} dx dy.$$

To establish the integration limits, we analyze the constraints on x and y as follows:

- (1) the constraint from the order statistics is $0 < x < y < 1$;
- (2) the constraint from the event is $xy \geq b$;
- (3) combining $x < y$ and $xy \geq b$, we have $y^2 > xy \geq b$, which implies $y > \sqrt{b}$;
- (4) for a fixed y in the range $(\sqrt{b}, 1]$, the variable x is constrained by $b/y \leq x < y$.

Thus, the iterated integral is set up as

$$P(\text{TOP2} \leq s) = \int_{\sqrt{b}}^1 \left(\int_{b/y}^y d(d-1)(1-y)^{d-2} dx \right) dy.$$

We first solve the inner integral with respect to x ,

$$\int_{b/y}^y d(d-1)(1-y)^{d-2} dx = d(d-1)(1-y)^{d-2} \left(y - \frac{b}{y} \right).$$

Let $a = \sqrt{b} = e^{-s/4}$ for notational simplicity, the integral becomes

$$\begin{aligned} P(\text{TOP2} \leq s) &= d(d-1) \int_a^1 (1-y)^{d-2} \left(y - \frac{a^2}{y} \right) dy \\ &= d(d-1) \left[\underbrace{\int_a^1 y(1-y)^{d-2} dy}_{I_1} - a^2 \underbrace{\int_a^1 \frac{(1-y)^{d-2}}{y} dy}_{I_2} \right]. \end{aligned} \quad (1)$$

Evaluation of integral I_1 . We evaluate this integral using two complementary approaches.

Analytical solution via integration by parts. Let $u = y$ and $dv = (1-y)^{d-2} dy$, then $du = dy$ and $v = -\frac{(1-y)^{d-1}}{d-1}$. We can calculate I_1 as

$$\begin{aligned} I_1 &= \left[-\frac{y(1-y)^{d-1}}{d-1} \right]_a^1 + \int_a^1 \frac{(1-y)^{d-1}}{d-1} dy \\ &= \frac{a(1-a)^{d-1}}{d-1} + \left[-\frac{(1-y)^d}{d(d-1)} \right]_a^1 \\ &= \frac{a(1-a)^{d-1}}{d-1} + \frac{(1-a)^d}{d(d-1)}. \end{aligned} \quad (2)$$

Multiplying it by $d(d-1)$ gives the first term of our CDF calculation,

$$d(d-1)I_1 = da(1-a)^{d-1} + (1-a)^d = (1-a)^{d-1} [1 + (d-1)a].$$

Probabilistic solution via binomial distribution. The term $d(d-1)I_1$ can be interpreted probabilistically. The integrand $d(d-1)y(1-y)^{d-2}$ is the PDF of Beta(2, $d-1$) distribution. This is also the distribution of the second order statistic $p_{(2)}$ from a sample of d i.i.d. $U(0, 1)$ variables. Therefore,

$$d(d-1)I_1 = P(p_{(2)} > a).$$

53 The event $\{p_{(2)} > a\}$ occurs if and only if at most one of the original p_i values is less than or
 54 equal to a . Let M be the count of $p_i \leq a$, then $M \sim \text{Binomial}(d, a)$.

$$\begin{aligned}
 55 \quad P(p_{(2)} > a) &= P(M = 0) + P(M = 1) \\
 56 \quad &= \binom{d}{0} (1-a)^d + \binom{d}{1} a^1 (1-a)^{d-1} \\
 57 \quad &= (1-a)^d + da(1-a)^{d-1} \\
 58 \quad &= (1-a)^{d-1} [1 + (d-1)a].
 \end{aligned}$$

59 **Evaluation of integral I_2 .** For $I_2 = \int_a^1 \frac{(1-y)^{d-2}}{y} dy$, we substitute $u = 1 - y$ (so $y = 1 - u$
 60 and $dy = -du$),

$$61 \quad I_2 = \int_{1-a}^0 \frac{u^{d-2}}{1-u} (-du) = \int_0^{1-a} \frac{u^{d-2}}{1-u} du.$$

62 Using the finite geometric series identity $\frac{u^n}{1-u} = \frac{1}{1-u} - \sum_{j=0}^{n-1} u^j$ with $n = d - 2$,

$$\begin{aligned}
 63 \quad I_2 &= \int_0^{1-a} \left(\frac{1}{1-u} - \sum_{j=0}^{d-3} u^j \right) du \\
 64 \quad &= [-\ln(1-u)]_0^{1-a} - \sum_{j=0}^{d-3} \left[\frac{u^{j+1}}{j+1} \right]_0^{1-a} \\
 65 \quad &= -\ln a - \sum_{j=0}^{d-3} \frac{(1-a)^{j+1}}{j+1} = -\ln a - \sum_{k=1}^{d-2} \frac{(1-a)^k}{k}. \tag{3}
 \end{aligned}$$

66 This formula holds for $d \geq 3$. When $d = 2$, $I_2 = -\ln a$.

67 **Final CDF and p -value.** Combining the results for I_1 (Equation 2) and I_2 (Equation 3)
 68 into Equation 1 yields the CDF,

$$69 \quad P(\text{TOP2} \leq s) = (1-a)^{d-1} (1 + (d-1)a) + d(d-1)a^2 \ln a + d(d-1)a^2 \sum_{k=1}^{d-2} \frac{(1-a)^k}{k}.$$

70 The p -value is $P(\text{TOP2} > s_{obs}) = 1 - P(\text{TOP2} \leq s_{obs})$, where s_{obs} is the observed value of
 71 TOP2. For the numerical stability, we can express this using the CDF of the Beta distribution.
 72 From the probabilistic interpretation, we know $d(d-1)I_1 = P(p_{(2)} > a) = 1 - F_{\text{Beta}}(a; 2, d-1)$,
 73 where $F_{\text{Beta}}(x; \alpha, \beta)$ is the Beta CDF and (α, β) are shape parameters. Then we can obtain a
 74 numerically stable closed form of p -value,

$$\begin{aligned}
 75 \quad p\text{-value} &= 1 - (d(d-1)I_1 - d(d-1)a^2 I_2) \\
 76 \quad &= 1 - ((1 - F_{\text{Beta}}(a; 2, d-1)) - d(d-1)a^2 I_2) \\
 77 \quad &= F_{\text{Beta}}(a; 2, d-1) + d(d-1)a^2 I_2 \\
 78 \quad &= F_{\text{Beta}}(a; 2, d-1) - d(d-1)a^2 \left(\ln a + \sum_{k=1}^{d-2} \frac{(1-a)^k}{k} \right),
 \end{aligned}$$

79 where $a = e^{-s_{obs}/4}$. When $d = 2$, $p\text{-value} = a^2(1 - 2 \ln a)$.

Supplementary Note 2: Derivation of the rotated covariance matrix V .

Recall the multivariate linear mixed model (mvLMM)

$$\tilde{\mathbf{Y}} = \tilde{\mathbf{X}}\tilde{\boldsymbol{\gamma}}^\top + \tilde{\mathbf{g}}\tilde{\boldsymbol{\beta}}^\top + \tilde{\mathbf{B}} + \tilde{\mathbf{E}}, \quad (4)$$

where $\tilde{\mathbf{Y}}$ be an $n \times d$ phenotypic value matrix with n and d representing the number of individuals and traits, respectively, $\tilde{\mathbf{g}}$ be an n -dimensional genotype score vector at a given SNP locus, and $\tilde{\mathbf{X}}$ be an $n \times c$ covariate observation matrix including a column of ones to model the intercept term. $\tilde{\boldsymbol{\gamma}}$ is the $d \times c$ coefficient matrix, $\tilde{\boldsymbol{\beta}}$ is the d -dimensional coefficient column vector of genetic effects, $\tilde{\mathbf{B}}$ is the $n \times d$ random polygenic effect matrix, $\tilde{\mathbf{E}}$ is an $n \times d$ random error matrix, and the superscript $\top$ indicates the transpose of a vector or a matrix. Let $\text{vec}(\cdot)$ represent the column-wise vectorization of a matrix and $\otimes$ denote the Kronecker product. The vectorized forms of $\tilde{\mathbf{B}}$ and $\tilde{\mathbf{E}}$ have the multivariate normal distributions with $\text{vec}(\tilde{\mathbf{B}}) \sim \mathcal{N}(\mathbf{0}_{nd}, \mathbf{V}_b \otimes \mathbf{K})$ and $\text{vec}(\tilde{\mathbf{E}}) \sim \mathcal{N}(\mathbf{0}_{nd}, \mathbf{V}_e \otimes \mathbf{I}_n)$, where $\mathbf{0}_{nd}$ is the nd -dimensional column vector of all zero units. $\mathbf{V}_b$ and $\mathbf{V}_e$ are $d \times d$ random polygenic and error covariance matrices, respectively, and $\mathbf{K}$ is an $n \times n$ sample relatedness matrix. The covariance matrix of $\text{vec}(\tilde{\mathbf{Y}})$ is $\text{Cov}(\text{vec}(\tilde{\mathbf{Y}})) = \mathbf{V}_b \otimes \mathbf{K} + \mathbf{V}_e \otimes \mathbf{I}_n$, where $\text{Cov}(\cdot)$ indicates the product of taking the covariance of a random vector.

In an multivariate GWAS, the correlations among multiple phenotypes can confound association signals and thus are non-negligible. We employ an orthogonal rotation-based modeling approach to decorrelate the individuals and phenotypes. The decorrelation procedure involves three sequential eigendecompositions as

$$\begin{aligned} \mathbf{K} &= \mathbf{Q}_k \boldsymbol{\Lambda}_k \mathbf{Q}_k^\top, \\ \mathbf{V}_e &= \mathbf{Q}_e \boldsymbol{\Lambda}_e \mathbf{Q}_e^\top = \mathbf{Q}_e \boldsymbol{\Lambda}_e^{1/2} (\mathbf{Q}_e \boldsymbol{\Lambda}_e^{1/2})^\top, \\ \boldsymbol{\Lambda}_e^{-\frac{1}{2}} \mathbf{Q}_e^\top \mathbf{V}_b (\boldsymbol{\Lambda}_e^{-\frac{1}{2}} \mathbf{Q}_e^\top)^\top &= \mathbf{U} \boldsymbol{\Xi} \mathbf{U}^\top, \end{aligned}$$

where $\boldsymbol{\Lambda}_k$, $\boldsymbol{\Lambda}_e$ and $\boldsymbol{\Xi}$ are the diagonal eigenvalue matrices, and $\mathbf{Q}_k$, $\mathbf{Q}_e$ and $\mathbf{U}$ are the corresponding orthogonal eigenvector matrices. Subsequently, model rotation is performed by simultaneously left-multiplying matrix $\mathbf{Q}_k^\top$ and right-multiplying matrix $\mathbf{Q}_e \boldsymbol{\Lambda}_e^{-1/2} \mathbf{U}$ on the two-sides of mvLMM (4).

Denote

$$\begin{aligned} \mathbf{Y} &= \mathbf{Q}_k^\top \tilde{\mathbf{Y}} \mathbf{Q}_e \boldsymbol{\Lambda}_e^{-1/2} \mathbf{U}, \quad \mathbf{X} = \mathbf{Q}_k^\top \tilde{\mathbf{X}}, \quad \mathbf{g} = \mathbf{Q}_k^\top \tilde{\mathbf{g}}, \\ \boldsymbol{\gamma}^\top &= \tilde{\boldsymbol{\gamma}}^\top (\mathbf{Q}_e \boldsymbol{\Lambda}_e^{-1/2} \mathbf{U}), \quad \boldsymbol{\beta}^\top = \tilde{\boldsymbol{\beta}}^\top (\mathbf{Q}_e \boldsymbol{\Lambda}_e^{-1/2} \mathbf{U}), \\ \mathbf{B} &= \mathbf{Q}_k^\top \tilde{\mathbf{B}} \mathbf{Q}_e \boldsymbol{\Lambda}_e^{-1/2} \mathbf{U}, \quad \mathbf{E} = \mathbf{Q}_k^\top \tilde{\mathbf{E}} \mathbf{Q}_e \boldsymbol{\Lambda}_e^{-1/2} \mathbf{U}. \end{aligned}$$

Model 4 is transformed into the rotated multivariate linear mixed model as

$$\mathbf{Y} = \mathbf{X}\boldsymbol{\gamma}^\top + \mathbf{g}\boldsymbol{\beta}^\top + \mathbf{B} + \mathbf{E}. \quad (5)$$

114 According to the properties of Kronecker product, the covariance matrix of $\text{vec}(\mathbf{Y})$ can be
 115 derived as

$$\begin{aligned}
 \mathbf{V} &= \text{Cov}(\text{vec}(\mathbf{Y})) = \text{Cov}(\text{vec}(\mathbf{B} + \mathbf{E})) \\
 &= \text{Cov}\left(\text{vec}\left(\mathbf{Q}_k^\top \tilde{\mathbf{Y}} \mathbf{Q}_e \Lambda_e^{-\frac{1}{2}} \mathbf{U}\right)\right) \\
 &= \text{Cov}\left(\left(\mathbf{U}^\top \Lambda_e^{-\frac{1}{2}} \mathbf{Q}_e^\top \otimes \mathbf{Q}_k^\top\right) \text{vec}(\tilde{\mathbf{Y}})\right) \\
 &= \left(\mathbf{U}^\top \Lambda_e^{-\frac{1}{2}} \mathbf{Q}_e^\top \otimes \mathbf{Q}_k^\top\right) \mathbb{V}\mathbb{A}\mathbb{R}(\text{vec}(\tilde{\mathbf{Y}})) \left(\mathbf{U}^\top \Lambda_e^{-\frac{1}{2}} \mathbf{Q}_e^\top \otimes \mathbf{Q}_k^\top\right)^\top \\
 &= \left(\mathbf{U}^\top \Lambda_e^{-\frac{1}{2}} \mathbf{Q}_e^\top \otimes \mathbf{Q}_k^\top\right) (\mathbf{V}_b \otimes \mathbf{K} + \mathbf{V}_e \otimes \mathbf{I}_n) (\mathbf{Q}_e \Lambda_e^{-\frac{1}{2}} \mathbf{U} \otimes \mathbf{Q}_k) \\
 &= \mathbf{U}^\top \Lambda_e^{-\frac{1}{2}} \mathbf{Q}_e^\top \mathbf{V}_b \mathbf{Q}_e \Lambda_e^{-\frac{1}{2}} \mathbf{U} \otimes \mathbf{Q}_k^\top \mathbf{K} \mathbf{Q}_k + \mathbf{U}^\top \Lambda_e^{-\frac{1}{2}} \mathbf{Q}_e^\top \mathbf{V}_e \mathbf{Q}_e \Lambda_e^{-\frac{1}{2}} \mathbf{U} \otimes \mathbf{Q}_k^\top \mathbf{I}_n \mathbf{Q}_k \\
 &= \mathbf{U}^\top \mathbf{U} \mathbf{\Xi} \mathbf{U}^\top \mathbf{U} \otimes \mathbf{Q}_k^\top \mathbf{Q}_k \Lambda_k \mathbf{Q}_k^\top \mathbf{Q}_k + \mathbf{U}^\top \Lambda_e^{-\frac{1}{2}} \mathbf{Q}_e^\top \mathbf{Q}_e \Lambda_e \mathbf{Q}_e^\top \mathbf{Q}_e \Lambda_e^{-\frac{1}{2}} \mathbf{U} \otimes \mathbf{I}_n \\
 &= \mathbf{\Xi} \otimes \Lambda_k + \mathbf{I}_d \otimes \mathbf{I}_n.
 \end{aligned}$$

117 Since both $\mathbf{\Xi}$ and Λ_k are diagonal matrices, the covariance matrix $\mathbf{V}$ is diagonal, the rows and
 118 columns of $\mathbf{Y}$ are thus mutually uncorrelated. Therefore, the correlations among the rotated
 119 phenotypic matrix $\mathbf{Y}$ are eliminated in the rotated model (5).

120 **Supplementary Note 3: Iterative estimation algorithm for** 121 **estimating $\mathbf{V}_b$ and $\mathbf{V}_e$**

122 The restricted maximum likelihood (REML) estimation is used to get the variance compo-
 123 nent estimation, as it provides an unbiased estimate by accounting for the degrees of freedom
 124 lost in estimating fixed effects [1]. However, its direct application in the state-of-art soft-
 125 ware GEMMA [2] is computationally challenging. Conventional second-order optimization
 126 algorithms for REML, such as Newton-Raphson's algorithm and Average Information REML
 127 algorithm, encounter prohibitive costs $\mathcal{O}(nd^6)$ or $\mathcal{O}(nd^7)$ per iteration [2]. The computational
 128 complexity stems from calculating the inverse, determinant, and Hessian matrix of the nd -
 129 dimensional covariance matrix [2]. Furthermore, as the number of phenotypes increases, the
 130 number of parameters to be optimized by the REML log-likelihood function grows quadrat-
 131 ically. This makes it more challenging to identify the global optimum and destabilizes the
 132 optimization process.

133 We propose a novel iterative algorithm that integrates the method-of-moments (MoM) es-
 134 timation and REML estimation of the rotated model (5). Specifically, given initial estimates
 135 of the $\mathbf{V}_b$ and $\mathbf{V}_e$, the mvLMM model (4) is decoupled into d independent univariate models (5)
 136 through rotation (Supplementary Note 2). $\mathbf{V}_b$ is updated by solving these d one-dimensional
 137 optimization problems and performing inverse rotations, and $\mathbf{V}_e$ is updated based on the closed-
 138 form expression for MoM estimation, until the norms of both matrices converge.

139 The advantage of this hybrid approach is twofold. First, the MoM estimation provides
 140 an efficient closed-form expression. Second, by rotating the model, the mvLMM is decou-
 141 pled into d independent, univariate heteroscedastic linear regressions (5). This critical step

replaces the complex and high-dimensional joint optimization problem with d separate and simple one-dimensional REML problems. Importantly, both the MoM closed-form estimation and the one-dimensional REML optimizations are numerically stable and efficient when compared with complex high-dimensional joint optimization, and there is no need to calculate the high-dimensional Hessian matrix. The derivation of MoM estimation and the specific steps of the iterative algorithm are as follows.

Method-of-moments estimation of V_e given V_b

Let the combined random error term be defined as

$$\widetilde{\mathbf{H}} := \widetilde{\mathbf{B}} + \widetilde{\mathbf{E}}.$$

The covariance matrix of its vectorized form after left-multiplying by $\mathbf{Q}_k^\top$ is

$$\text{Cov}(\text{vec}(\mathbf{Q}_k^\top \widetilde{\mathbf{H}})) = \mathbf{V}_b \otimes \mathbf{\Lambda}_k + \mathbf{V}_e \otimes \mathbf{I}_n.$$

Let $\widetilde{\mathbf{h}}_i$ denote the i -th row vector of $\mathbf{Q}_k^\top \widetilde{\mathbf{H}}$. The block-diagonal covariance structure implies that the rows $\widetilde{\mathbf{h}}_i$ are mutually independent. Each row follows a multivariate normal distribution

$$\widetilde{\mathbf{h}}_i \sim \mathcal{N}(0, \lambda_i \mathbf{V}_b + \mathbf{V}_e),$$

where λ_i is the i -th eigenvalue of the sample relatedness matrix $\mathbf{K}$, $i = 1, \dots, n$. The rows are thus independent but heteroscedastic. The expected outer product of the vector $\widetilde{\mathbf{h}}_i$ is

$$\mathbb{E}[\widetilde{\mathbf{h}}_i \widetilde{\mathbf{h}}_i^\top] = \lambda_i \mathbf{V}_b + \mathbf{V}_e.$$

Averaging over all individuals and rearranging for $\mathbf{V}_e$ yields

$$\mathbf{V}_e = \frac{1}{n} \sum_{i=1}^n \mathbb{E}[\widetilde{\mathbf{h}}_i \widetilde{\mathbf{h}}_i^\top] - \frac{\text{tr}(\mathbf{K})}{n} \mathbf{V}_b,$$

where we used the fact that $\text{tr}(\mathbf{K}) = \text{tr}(\mathbf{\Lambda}_k) = \sum \lambda_i$ and $\text{tr}(\cdot)$ denotes the trace of a square matrix. In practice, we compute the residual matrix $\widehat{\widetilde{\mathbf{H}}} = \widetilde{\mathbf{Y}} - \mathbf{X} \widehat{\boldsymbol{\gamma}}^\top$ using the estimates of the fixed effects under the null hypothesis. Let $\widehat{\mathbf{h}}_i$ be the i -th row of the rotated residual matrix $\mathbf{Q}_k^\top \widehat{\widetilde{\mathbf{H}}}$. Replacing the expectation with the sample average gives the MoM estimator for $\mathbf{V}_e$, we have

$$\widehat{\mathbf{V}}_e = \frac{1}{n} \sum_{i=1}^n \widehat{\mathbf{h}}_i \widehat{\mathbf{h}}_i^\top - \frac{\text{tr}(\mathbf{K})}{n} \mathbf{V}_b.$$

Iterative estimation algorithm of V_b and V_e

Since the rotated covariance matrix $\mathbf{V}$ is diagonal (Supplementary Note 2), the rows and columns of $\mathbf{Y}$ are thus mutually uncorrelated. Denote $\mathbf{Y} = (\mathbf{y}_1, \dots, \mathbf{y}_d)$, $\boldsymbol{\gamma}^\top = (\gamma_1, \dots, \gamma_d)$,

170 and $\mathbf{B} + \mathbf{E} = (\boldsymbol{\varepsilon}_1, \dots, \boldsymbol{\varepsilon}_d)$. Under the null hypothesis, the rotated model (5) is equivalent to d
 171 univariate heteroscedastic linear regression models

$$172 \quad \mathbf{y}_j = \mathbf{X}\boldsymbol{\gamma}_j^\top + \boldsymbol{\varepsilon}_j, \quad (6)$$

173 where $\text{cov}(\boldsymbol{\varepsilon}_j) = \boldsymbol{\Sigma}_j = \xi_j \boldsymbol{\Lambda}_k + \mathbf{I}_n$, and ξ_j is the j -th diagonal element of $\boldsymbol{\Xi}$.

174 Perform a one-time pre-calculation, including the eigendecomposition of $\mathbf{K} = \mathbf{Q}_k \boldsymbol{\Lambda}_k \mathbf{Q}_k^\top$,
 175 and the rotations of $\mathbf{Q}_k^\top \widetilde{\mathbf{X}}$, $\mathbf{Q}_k^\top \widetilde{\mathbf{Y}}$. Let subscript t denote the iteration index, initialized with
 176 $t = 0$ and $\mathbf{V}_e^{(0)} = \mathbf{V}_b^{(0)} = \mathbf{I}_d$. Then the iteration process is expressed as the following MoM-
 177 REML algorithm.

178 *MoM-REML Algorithm.*

179 (1) Eigendecompositions and rotations.

- 180 a) Compute the eigendecomposition of $\mathbf{V}_e^{(t)} = \mathbf{Q}_e^{(t)} \boldsymbol{\Lambda}_e^{(t)} (\mathbf{Q}_e^{(t)})^\top$.
- 181 b) Compute $\mathbf{S}^{(t)} = (\boldsymbol{\Lambda}_e^{(t)})^{-1/2} (\mathbf{Q}_e^{(t)})^\top \mathbf{V}_b^{(t)} \mathbf{Q}_e^{(t)} (\boldsymbol{\Lambda}_e^{(t)})^{-1/2}$.
- 182 c) Compute the eigendecomposition of $\mathbf{S}^{(t)} = \mathbf{U}^{(t)} \boldsymbol{\Xi}^{(t)} (\mathbf{U}^{(t)})^\top$.
- 183 d) Compute $\mathbf{y}_j^{(t)}$, where $\mathbf{y}_j^{(t)}$ denotes the j -th column of $\mathbf{Q}_k^\top \widetilde{\mathbf{Y}} (\mathbf{Q}_e^{(t)} (\boldsymbol{\Lambda}_e^{(t)})^{-1/2} \mathbf{U}^{(t)})$.

184 (2) Optimize REML on d univariate linear models.

- 185 a) Estimate $\widehat{\boldsymbol{\Xi}}^{(t+1)} = \text{diag}(\widehat{\xi}_1^{(t+1)}, \dots, \widehat{\xi}_d^{(t+1)})$ via REML with respect to ξ_j on the models
 186 $\mathbf{y}_j^{(t)} = \mathbf{Q}_k^\top \widetilde{\mathbf{X}} \boldsymbol{\gamma}_j^\top + \boldsymbol{\varepsilon}_j$, where $\boldsymbol{\varepsilon}_j \sim N(\mathbf{0}, \xi_j \boldsymbol{\Lambda}_k + \mathbf{I}_n)$, $j = 1, \dots, d$.
- 187 b) Estimate $\widehat{\boldsymbol{\gamma}}^{(t+1)} = (\widehat{\gamma}_1^{(t+1)}, \dots, \widehat{\gamma}_d^{(t+1)})^\top$ via generalized least squares (GLS).

188 (3) Update $\mathbf{V}_b$ by rotation and update $\mathbf{V}_e$ by MoM estimation.

- 189 a) Compute $\mathbf{V}_b^{(t+1)} = (\mathbf{Q}_e^{(t)} (\boldsymbol{\Lambda}_e^{(t)})^{1/2} \mathbf{U}^{(t)}) \widehat{\boldsymbol{\Xi}}^{(t+1)} (\mathbf{Q}_e^{(t)} (\boldsymbol{\Lambda}_e^{(t)})^{1/2} \mathbf{U}^{(t)})^\top$.
- 190 b) Compute $\widehat{\boldsymbol{\gamma}}^{(t+1)} = (\mathbf{Q}_e^{(t)} (\boldsymbol{\Lambda}_e^{(t)})^{1/2} \mathbf{U}^{(t)}) \widehat{\boldsymbol{\gamma}}^{(t+1)}$.
- 191 c) Compute $\widehat{\mathbf{h}}_i^{(t+1)}$, where $\widehat{\mathbf{h}}_i^{(t+1)}$ denotes the i -th row of $\mathbf{Q}_k^\top \widehat{\widetilde{\mathbf{H}}}^{(t+1)} = \mathbf{Q}_k^\top \widetilde{\mathbf{Y}} - (\mathbf{Q}_k^\top \widetilde{\mathbf{X}}) \widehat{\boldsymbol{\gamma}}^{(t+1)\top}$.
- 192 d) Compute $\mathbf{V}_e^{(t+1)} = \frac{1}{n} \sum_{i=1}^n \widehat{\mathbf{h}}_i^{(t+1)} \widehat{\mathbf{h}}_i^{(t+1)\top} - \frac{\text{tr}(\mathbf{K})}{n} \mathbf{V}_b^{(t+1)}$.

193 Repeat steps (1) to (3) until $\|\mathbf{V}_b^{(t)}\|$ and $\|\mathbf{V}_e^{(t)}\|$ converge and then output the estimates of $\mathbf{V}_b$
 194 and $\mathbf{V}_e$ as well as the estimate of $\boldsymbol{\gamma}$.

195 In addition, by concatenating the rotated covariate observation matrix $\mathbf{X}$ and the rotated
 196 genotype score vector $\mathbf{g}$ to form the design matrix under the alternative hypothesis, we can
 197 obtain the GLS estimate of the rotated genetic effect $\boldsymbol{\beta}$, and rotate it to obtain the estimate of
 198 $\widetilde{\boldsymbol{\beta}}$.

Supplementary Note 4. Computational complexity analysis of the iterative algorithm.

We provide a detailed analysis of the computational complexity of the iterative algorithm for estimating the covariance matrices $\mathbf{V}_b$ and $\mathbf{V}_e$. It also includes details of the efficient implementation of the algorithm. Let n be the number of individuals, d be the number of traits, c be the number of covariates, and t be the total number of iterations required for convergence. In typical genetic studies, we assume $n \gg d$ and $n \gg c$. The algorithm's total cost can be decomposed into two main parts: a one-time preprocessing cost and t per-iteration cost.

Preprocessing (one-time cost)

Before the iterative process begins, several calculations are performed only once.

Eigendecomposition of sample relatedness matrix. The relatedness matrix $\mathbf{K}$ is of size $n \times n$. Its spectral decomposition $\mathbf{K} = \mathbf{Q}_k \mathbf{\Lambda}_k \mathbf{Q}_k^\top$ is the most computationally intensive step of the entire analysis, requiring $\mathcal{O}(n^3)$ operations.

Data rotation. The phenotype matrix $\tilde{\mathbf{Y}}$ ($n \times d$) and covariate matrix $\tilde{\mathbf{X}}$ ($n \times c$) are left-multiplied by $\mathbf{Q}_k^\top$ ($n \times n$). These operations cost $\mathcal{O}(n^2d)$ and $\mathcal{O}(n^2c)$, respectively. The total preprocessing cost is therefore dominated by the eigendecomposition, resulting in a complexity of $\mathcal{O}(n^3 + n^2d + n^2c)$.

Per-iteration cost

Within each iteration of the algorithm, the following costs are incurred.

Eigendecompositions and rotations (Step1). First three steps (a) to (c) involve operations on $d \times d$ matrices. It includes two eigendecompositions of $\mathbf{V}_e^{(t)}$ and $\mathbf{S}^{(t)}$ and several matrix multiplications. The dominant cost for these steps is $\mathcal{O}(d^3)$. The pre-rotated phenotype data ($\mathbf{Q}_k^\top \tilde{\mathbf{Y}}$, size $n \times d$) is multiplied by a newly computed $d \times d$ transformation matrix, which has a complexity of $\mathcal{O}(nd^2)$.

Optimize REML on d univariate linear models (Step2). This step requires solving d independent univariate REML problems to estimate the parameters ξ_j , $j = 1, \dots, d$. For each trait, the REML optimization involves multiple evaluations of the likelihood function. The covariance matrix $\mathbf{\Sigma}_j = \xi_j \mathbf{\Lambda}_k + \mathbf{I}_n$ is diagonal. The REML log-likelihood evaluation requires three main components: the log-determinants $\log |\mathbf{\Sigma}_j|$, $\log |\mathbf{X}^\top \mathbf{\Sigma}_j^{-1} \mathbf{X}|$, and the quadratic form $\mathbf{y}_j^\top \mathbf{P}_j \mathbf{y}_j$. We analyze the cost of computing these components for a single function evaluation within the optimizer.

- 230 (1) **Log-determinant of Σ_j .** Since Σ_j is a diagonal matrix, calculating its log-determinant
 231 is simply the sum of the logarithms of its n diagonal elements, which has a cost $\mathcal{O}(n)$. The
 232 inverse Σ_j^{-1} is also computed in $\mathcal{O}(n)$.
- 233 (2) **Log-determinant of $\mathbf{X}^\top \Sigma_j^{-1} \mathbf{X}$.** This requires computing the $c \times c$ matrix $\mathbf{A}_j = \mathbf{X}^\top \Sigma_j^{-1} \mathbf{X} =$
 234 $\mathbf{X}^\top (\Sigma_j^{-1} \mathbf{X})$. The inner product $\Sigma_j^{-1} \mathbf{X}$ costs $\mathcal{O}(nc)$ because Σ_j^{-1} is diagonal. The subse-
 235 quent multiplication by $\mathbf{X}^\top$ costs $\mathcal{O}(nc^2)$. The determinant and inverse of the resulting
 236 small matrix $\mathbf{A}_j$ cost $\mathcal{O}(c^3)$.
- 237 (3) **Quadratic form $\mathbf{y}_j^\top \mathbf{P}_j \mathbf{y}_j$.** This term is computed efficiently without explicitly forming the
 238 $n \times n$ projection matrix $\mathbf{P}_j$. Instead, the vector $\mathbf{P}_j \mathbf{y}_j$ is calculated by leveraging the GLS
 239 estimate of the fixed effects $\boldsymbol{\gamma}_j^\top = \mathbf{A}_j^{-1} (\mathbf{X}^\top \Sigma_j^{-1} \mathbf{y}_j)$. The calculation proceeds as follows.
- 240 a) Compute $\mathbf{X}^\top \Sigma_j^{-1} \mathbf{y}_j = \mathbf{X}^\top (\Sigma_j^{-1} \mathbf{y}_j)$ in $\mathcal{O}(n + nc)$.
- 241 b) Compute $\mathbf{A}_j^{-1} (\mathbf{X}^\top \Sigma_j^{-1} \mathbf{y}_j)$. Since $\mathbf{A}_j$ and its inverse are already computed, this is a
 242 matrix-vector product costing $\mathcal{O}(c^2)$.
- 243 c) Compute $\mathbf{P}_j \mathbf{y}_j = \Sigma_j^{-1} (\mathbf{y}_j - \mathbf{X} \boldsymbol{\gamma}_j^\top) = \Sigma_j^{-1} \mathbf{y}_j - (\Sigma_j^{-1} \mathbf{X}) (\mathbf{A}_j^{-1} (\mathbf{X}^\top \Sigma_j^{-1} \mathbf{y}_j))$. Since $\Sigma_j^{-1} \mathbf{y}_j$
 244 and $\Sigma_j^{-1} \mathbf{X}$ are already computed, this step costs $\mathcal{O}(nc + n)$.
- 245 d) Compute the final dot product $\mathbf{y}_j^\top (\mathbf{P}_j \mathbf{y}_j)$ in $\mathcal{O}(n)$.

246 Combining these steps for three components, the dominant cost for a single evaluation of the
 247 REML likelihood is the multiplication of $\mathbf{X}^\top \Sigma_j^{-1} \mathbf{X}$ and the corresponding determinant and
 248 inverse. It is $\mathcal{O}(nc^2 + c^3)$. Assuming a constant number of evaluations, the total cost for
 249 estimating all ξ_j and fixed effects $\boldsymbol{\gamma}_j$ (i.e., $\boldsymbol{\Xi}$ and $\boldsymbol{\gamma}$) is $\mathcal{O}(d(nc^2 + c^3))$.

250 **Update $\mathbf{V}_e$ and $\mathbf{V}_e$ (Step3).** The update for $\mathbf{V}_b^{(t+1)}$ involves $d \times d$ matrix multiplications,
 251 which costs $\mathcal{O}(d^3)$. The rotation for $\widehat{\boldsymbol{\gamma}}^{(t+1)}$ involves the multiplication of $d \times d$ matrix and $d \times c$
 252 matrix, which costs $\mathcal{O}(cd^2)$. Leveraging the pre-computed data $\mathbf{Q}_k^\top \widetilde{\mathbf{Y}}$ and $\mathbf{Q}_k^\top \widetilde{\mathbf{X}}$, the rotated
 253 residual matrix is computed as $\mathbf{Q}_k^\top \widehat{\mathbf{H}}^{(t+1)} = \mathbf{Q}_k^\top \widetilde{\mathbf{Y}} - (\mathbf{Q}_k^\top \widetilde{\mathbf{X}}) \widehat{\boldsymbol{\gamma}}^{(t+1)\top}$. The dominant cost for
 254 this step is the matrix multiplication $(\mathbf{Q}_k^\top \widetilde{\mathbf{X}}) \widehat{\boldsymbol{\gamma}}^{(t+1)\top}$, which is $\mathcal{O}(ncd)$.

255 The update for $\mathbf{V}_e^{(t+1)}$ requires computing the outer product sum $\sum \widehat{\mathbf{h}}_i^{(t+1)} (\widehat{\mathbf{h}}_i^{(t+1)})^\top$, which
 256 is equivalent to $(\mathbf{Q}_k^\top \widehat{\mathbf{H}}^{(t+1)})^\top (\mathbf{Q}_k^\top \widehat{\mathbf{H}}^{(t+1)})$. This multiplication of a $d \times n$ matrix by an $n \times d$
 257 matrix costs $\mathcal{O}(nd^2)$.

258 Total complexity for fitting a single RmvLMM

259 The total complexity is the sum of the one-time preprocessing cost and the per-iteration cost
 260 multiplied by the number of iterations, t . That is

$$261 \quad \text{Total Cost} = \underbrace{\mathcal{O}(n^3 + n^2d + n^2c)}_{\text{Preprocessing}} + t \cdot \underbrace{\mathcal{O}(d^3 + c^3d + cd^2 + nd^2 + nc^2d)}_{\text{Per Iteration}}.$$

This can be written compactly as

$$\mathcal{O}(n^3 + n^2d + n^2c + t(c^3d + d^3 + cd^2 + nd^2 + nc^2d)).$$

Assuming that $n \gg d$ and $n \gg c$, it can be also written as

$$\mathcal{O}(n^3 + t(nd^2 + nc^2d)).$$

Supplementary Note 5: Efficient genome-wide association scan and complexity analysis.

After the one-time estimation of covariance matrices, the genome-wide association scan is performed. For each of the p SNPs, we conduct a series of tests across the d decorrelated traits efficiently leveraging the orthogonal projection strategy. The procedure can be broken down as follows.

Genotype rotation. For each SNP, its $n \times 1$ genotype vector $\tilde{\mathbf{g}}$ must be rotated into the decorrelated space using the pre-computed eigenvector matrix $\mathbf{Q}_k$ of sample relatedness matrix $\mathbf{K}$, i.e., $\mathbf{g} = \mathbf{Q}_k^\top \tilde{\mathbf{g}}$, which costs $\mathcal{O}(n^2)$ per SNP.

Per-trait F -test. Assume that covariance matrices $\mathbf{V}_b$ and $\mathbf{V}_e$ are fixed. For each decorrelated trait, the rotated model is

$$\mathbf{y}_j = \mathbf{X}\boldsymbol{\gamma}_j^\top + \mathbf{g}\beta_j + \boldsymbol{\varepsilon}_j, \quad \text{Cov}(\boldsymbol{\varepsilon}_j) = \boldsymbol{\Sigma}_j = \xi_j\boldsymbol{\Lambda}_k + \mathbf{I}_n, \quad (7)$$

where $\boldsymbol{\Lambda}_k$ contains the eigenvalues of the sample relatedness matrix $\mathbf{K}$ and ξ_j is the eigenvalues of $\boldsymbol{\Xi}$ from the rotation transformations. We leverage the orthogonal projection strategy to improve the computational efficiency of the F -tests in GWAS. The steps for efficient computation are as follows.

(1) **QR decomposition of covariates.** Perform QR decomposition of the weighted covariate matrix,

$$\boldsymbol{\Sigma}_j^{-1/2}\mathbf{X} = \mathbf{Q}_j\mathbf{R}_j, \quad \mathbf{Q}_j^\top\mathbf{Q}_j = \mathbf{I}_c.$$

Here, $\mathbf{Q}_j\mathbf{Q}_j^\top$ is the orthogonal projection operator onto the column space of $\boldsymbol{\Sigma}_j^{-1/2}\mathbf{X}$. The matrix multiplication $\boldsymbol{\Sigma}_j^{-1/2}\mathbf{X}$ costs $\mathcal{O}(nc)$ and QR decomposition for $\boldsymbol{\Sigma}_j^{-1/2}\mathbf{X}$ costs $\mathcal{O}(nc^2)$. This step only needs to be done once per trait in the entire GWAS and falls under the category of precomputation.

(2) **Residual sum of squares (RSS) under H_{0j} .** Using the projection, the RSS under $H_{0j} : \beta_j = 0$ is

$$\text{RSS}_{H_{0j}} = \|(\mathbf{I}_n - \mathbf{Q}_j\mathbf{Q}_j^\top)\boldsymbol{\Sigma}_j^{-1/2}\mathbf{y}_j\|^2,$$

which can be computed in $\mathcal{O}(nc)$ time by multiplying from right to left. This step only needs to be done once under H_{0j} per trait.

- (3) **RSS difference for all SNPs.** Define the component of the rotated SNP vectors and the rotated phenotypic values vectors orthogonal to the rotated covariates for $j = 1, \dots, d$,

$$\mathbf{g}_j^\perp = (\mathbf{I}_n - \mathbf{Q}_j \mathbf{Q}_j^\top) \boldsymbol{\Sigma}_j^{-1/2} \mathbf{g}, \quad \mathbf{y}_j^\perp = (\mathbf{I}_n - \mathbf{Q}_j \mathbf{Q}_j^\top) \boldsymbol{\Sigma}_j^{-1/2} \mathbf{y}_j.$$

By the Frisch–Waugh–Lovell theorem [3], fitting the full model is equivalent to the simple univariate regression,

$$\mathbf{y}_j^\perp = \mathbf{g}_j^\perp \beta_j + \boldsymbol{\varepsilon}_j^\perp.$$

In this univariate regression, the reduction in residual sum of squares due to adding $\mathbf{g}$ is

$$\begin{aligned} \text{RSS}_{H_{0j}} - \text{RSS}_{H_{1j}} &= \|(\mathbf{I}_n - \mathbf{Q}_j \mathbf{Q}_j^\top) \boldsymbol{\Sigma}_j^{-1/2} \mathbf{y}_j\|^2 - \|\mathbf{y}_j^\perp - \mathbf{g}_j^\perp \frac{(\mathbf{g}_j^\perp)^\top \mathbf{y}_j^\perp}{(\mathbf{g}_j^\perp)^\top \mathbf{g}_j^\perp}\|^2 \\ &= \|\mathbf{y}_j^\perp\|^2 - \|\mathbf{y}_j^\perp - \mathbf{g}_j^\perp \frac{(\mathbf{g}_j^\perp)^\top \mathbf{y}_j^\perp}{(\mathbf{g}_j^\perp)^\top \mathbf{g}_j^\perp}\|^2 \\ &= \|\mathbf{y}_j^\perp\|^2 - \|\mathbf{y}_j^\perp\|^2 + \|\mathbf{g}_j^\perp \frac{(\mathbf{g}_j^\perp)^\top \mathbf{y}_j^\perp}{(\mathbf{g}_j^\perp)^\top \mathbf{g}_j^\perp}\|^2 \\ &= \|\mathbf{g}_j^\perp \frac{(\mathbf{g}_j^\perp)^\top \mathbf{y}_j^\perp}{(\mathbf{g}_j^\perp)^\top \mathbf{g}_j^\perp}\|^2 = \frac{((\mathbf{g}_j^\perp)^\top \mathbf{y}_j^\perp)^2}{(\mathbf{g}_j^\perp)^\top \mathbf{g}_j^\perp}. \end{aligned}$$

To compute this efficiently without explicitly forming the vector $\mathbf{g}_j^\perp$ (which would be memory-intensive and computationally redundant), we exploit the algebraic properties of the projection matrix $\mathbf{P}_j^\perp = \mathbf{I}_n - \mathbf{Q}_j \mathbf{Q}_j^\top$.

For the numerator $((\mathbf{g}_j^\perp)^\top \mathbf{y}_j^\perp)^2$, utilizing the symmetry $\mathbf{P}_j^\perp = (\mathbf{P}_j^\perp)^\top$ and idempotence $\mathbf{P}_j^\perp \mathbf{P}_j^\perp = \mathbf{P}_j^\perp$ of the projection operator, the inner product simplifies to

$$(\mathbf{g}_j^\perp)^\top \mathbf{y}_j^\perp = (\mathbf{P}_j^\perp \boldsymbol{\Sigma}_j^{-1/2} \mathbf{g})^\top (\mathbf{P}_j^\perp \boldsymbol{\Sigma}_j^{-1/2} \mathbf{y}_j) = (\boldsymbol{\Sigma}_j^{-1/2} \mathbf{g})^\top \mathbf{P}_j^\perp (\boldsymbol{\Sigma}_j^{-1/2} \mathbf{y}_j) = \mathbf{g}^\top (\boldsymbol{\Sigma}_j^{-1/2} \mathbf{y}_j^\perp).$$

Since $\mathbf{y}_j^\perp$ has been computed when calculating $\text{RSS}_{H_{0j}}$, this step requires only a simple dot product between the rotated genotype vector $\mathbf{g}$ and the weighted residual vector $\boldsymbol{\Sigma}_j^{-1/2} \mathbf{y}_j^\perp$, which costs $\mathcal{O}(n)$. A significant advantage of this calculation method is that $\boldsymbol{\Sigma}_j^{-1/2} \mathbf{y}_j^\perp$ not involves SNP and we do not need to handle $\mathbf{g}$ additionally, thus reducing a huge amount of computation.

For the denominator $(\mathbf{g}_j^\perp)^\top \mathbf{g}_j^\perp$, we apply the Pythagorean theorem. Since

$$(\mathbf{I}_n - \mathbf{Q}_j \mathbf{Q}_j^\top) \boldsymbol{\Sigma}_j^{-1/2} \mathbf{g} \perp \mathbf{Q}_j \mathbf{Q}_j^\top \boldsymbol{\Sigma}_j^{-1/2} \mathbf{g},$$

we have

$$(\mathbf{g}_j^\perp)^\top \mathbf{g}_j^\perp = \|\mathbf{P}_j^\perp \boldsymbol{\Sigma}_j^{-1/2} \mathbf{g}\|^2 = \|\boldsymbol{\Sigma}_j^{-1/2} \mathbf{g}\|^2 - \|\mathbf{Q}_j \mathbf{Q}_j^\top \boldsymbol{\Sigma}_j^{-1/2} \mathbf{g}\|^2.$$

Since $\mathbf{Q}_j$ has orthonormal columns, $\mathbf{Q}_j^\top \mathbf{Q}_j = \mathbf{I}_c$,

$$\begin{aligned}\|\mathbf{Q}_j \mathbf{Q}_j^\top \Sigma_j^{-1/2} \mathbf{g}\|^2 &= (\mathbf{Q}_j \mathbf{Q}_j^\top \Sigma_j^{-1/2} \mathbf{g})^\top (\mathbf{Q}_j \mathbf{Q}_j^\top \Sigma_j^{-1/2} \mathbf{g}) \\ &= (\Sigma_j^{-1/2} \mathbf{g})^\top \mathbf{Q}_j \mathbf{Q}_j^\top \mathbf{Q}_j \mathbf{Q}_j^\top (\Sigma_j^{-1/2} \mathbf{g}) \\ &= (\mathbf{Q}_j^\top \Sigma_j^{-1/2} \mathbf{g})^\top (\mathbf{Q}_j^\top \Sigma_j^{-1/2} \mathbf{g}) \\ &= \|\mathbf{Q}_j^\top \Sigma_j^{-1/2} \mathbf{g}\|^2.\end{aligned}$$

Calculating the total weighted norm $\|\Sigma_j^{-1/2} \mathbf{g}\|^2$ costs $\mathcal{O}(n)$. The term $\mathbf{Q}_j^\top \Sigma_j^{-1/2} \mathbf{g}$ involves multiplying a $c \times n$ matrix by an $n \times 1$ vector, costing $\mathcal{O}(nc)$, followed by $\mathcal{O}(c)$ for its norm. Thus, the dominant cost for the denominator is $\mathcal{O}(nc)$. Combining these steps, the total complexity of RSS difference per SNP per trait remains $\mathcal{O}(nc)$. This step (3) needs to be done for all p SNPs. In practice, when our software processes a large number of SNPs simultaneously, it does not handle each SNP individually. Instead, it considers multiple partitioned SNP matrices and converts the aforementioned computational process into matrix computation, further enhancing computational efficiency.

Noting that

$$\hat{\beta}_j = \frac{(\mathbf{g}_j^\perp)^\top \mathbf{y}_j^\perp}{(\mathbf{g}_j^\perp)^\top \mathbf{g}_j^\perp},$$

we only need one division to obtain the coefficient estimate within step (3). Its variance is estimated by

$$\widehat{\text{Cov}}(\hat{\beta}_j) = \frac{\hat{\sigma}_j^2}{(\mathbf{g}_j^\perp)^\top \mathbf{g}_j^\perp},$$

where $\hat{\sigma}_j^2 = \text{RSS}_{H_{1j}}/(n - c - 1)$. To recover the GLS estimates for the original traits, denoted as $\tilde{\boldsymbol{\beta}}$, we apply the inverse of the known rotation transformation,

$$\begin{aligned}\mathbf{W} &= ((\mathbf{Q}_e \Lambda_e^{-1/2} \mathbf{U})^\top)^{-1} \\ \tilde{\boldsymbol{\beta}} &= \mathbf{W} \hat{\boldsymbol{\beta}},\end{aligned}$$

which costs $\mathcal{O}(d^2)$ per SNP. Since the residuals of the decorrelated traits are orthogonal, the error covariance matrix of $\hat{\boldsymbol{\beta}}$ is diagonal. This allows us to recover the standard error (SE) of the j -th original trait efficiently by a weighted sum of variances,

$$\text{SE}(\tilde{\beta}_j) = \left(\sum_{k=1}^d W_{jk}^2 \cdot \widehat{\text{Var}}(\hat{\beta}_k) \right)^{1/2}.$$

This formulation reduces the recovery complexity to $\mathcal{O}(d)$ per trait per SNP. Consequently, the time complexity to estimate the GLS genetic effects and SEs for all traits is $\mathcal{O}(d^2)$ per SNP.

Combing the step (1) to (3) in the per-trait F -test and GLS estimation of $\tilde{\boldsymbol{\beta}}$, across d traits and p SNPs, the cost of all F -tests and GLS estimation is $\mathcal{O}(dnc^2 + pdnc + pd^2)$.

p -value combination and genome-wide scan. Once per-trait F -tests are computed, the d p -values can be combined using TOP2 statistics. The cost of combining p -values is $\mathcal{O}(d)$ per SNP. Including genotype rotation, F -tests and GLS estimation of $\tilde{\beta}$, the total cost for a genome-wide scan over p SNPs is

$$\mathcal{O}(nc^2d + p(n^2 + ncd + d^2)).$$

Further considering the complexity of the $\mathbf{V}_b$ and $\mathbf{V}_e$ estimation algorithm, the final result is

$$\mathcal{O}(n^3 + n^2d + n^2c + t(c^3d + d^3 + cd^2 + nd^2 + nc^2d) + p(n^2 + ncd + d^2)).$$

Where, t is the number of iterations. Assuming that $n \gg d$, $n \gg c$, $p \gg d$ and $p \gg c$, this can be also written as

$$\mathcal{O}(n^3 + t(nd^2 + nc^2d) + p(n^2 + ncd)).$$

Supplementary Note 6. The generalized gamma approximation for the TOP2-O statistic null distribution.

The generalized gamma distribution (GGD) is a flexible continuous probability distribution supported on $(0, +\infty)$. Due to its ability to model diverse tail behaviors, it serves as an ideal candidate for approximating the null distribution of the TOP2-O statistic.

Parameter estimation of the GGD

The GGD and its flexibility. The GGD [4, 5] is a flexible distribution family. Prentice [6] gave its reparameterization. Let X be a generalized gamma random variable. The PDF of X is defined by location parameter $\mu \in \mathbb{R}$, scale parameter $\sigma > 0$, and shape parameter $Q \in \mathbb{R}$ as

$$f(x; \mu, \sigma, Q) = \left[\frac{|Q|}{\sigma \Gamma(Q^{-2})} (Q^{-2})^{Q^{-2}} \right] \frac{1}{x} \exp\left(\frac{Qw - e^{Qw}}{Q^2}\right), \quad x > 0,$$

where $w = (\ln x - \mu)/\sigma$, and $\Gamma(\cdot)$ is the Gamma function.

The GGD encompasses the Weibull ($Q = 1$), Gamma ($Q = \sigma$), and Log-normal ($Q \rightarrow 0$) distributions as special cases. This allows it to effectively model the long-tailed characteristics observed in test statistics.

Challenges in parameter estimation. Estimating the parameters of the GGD presents significant mathematical and computational challenges, rendering standard approaches often ineffective.

The MoM estimation for GGD leads to a system of transcendental equations involving ratios of Gamma functions. The k -th moment of the GGD admits a closed-form expression. Under Prentice parameterization [6], it can be written as

$$\mathbb{E}(X^k) = \exp(k\mu) \frac{\Gamma(Q^{-2} + k\sigma/Q)}{\Gamma(Q^{-2})(Q^{-2})^{k\sigma/Q}}.$$

Analytical inversion of this system is impossible, and numerical root-finding is highly unstable due to the sensitivity of the Gamma function to small parameter perturbations.

Furthermore, the derivative of the log-likelihood function involves the digamma function $\psi(\cdot)$ and exponential terms $\exp(Qw_i)$. Direct MLE optimization based on gradients faces risks of floating-point overflow, especially if the optimizer explores regions implying a lighter tail than the data suggests (e.g., tail observations with a large shape parameter). This instability prevents standard gradient-descent algorithms from converging.

Non-Gradient MLE optimization with log-moment initialization. We adopt a hybrid estimation approach combining log-moment initialization with a robust derivative-free optimization.

Log-moment initialization. We employ MoM estimation on the log-transformed data to obtain high-quality initial estimates. Let $W = (\ln X - \mu)/\sigma$ and $V = e^{QW}/Q^2$, then V follows a Gamma distribution with shape parameter $k = Q^{-2}$ and scale parameter 1 [6]. Thus $\ln X = \mu + \frac{\sigma}{Q}(\ln V - \ln k)$. The skewness of $\ln X$ is invariant under translation and scaling (up to a sign),

$$\text{skewness}(\ln X) = \text{sgn}\left(\frac{\sigma}{Q}\right) \cdot \text{skewness}(\ln V) = \text{sgn}(Q) \cdot \text{skewness}(\ln V),$$

where $\text{skewness}(\cdot)$ is the skewness operator, and $\text{sgn}(\cdot)$ is the sign function. For $V \sim \Gamma(k, 1)$, the skewness of $\ln V$ is given by polygamma functions $\psi'(\cdot)$ and $\psi''(\cdot)$ [7],

$$\text{skewness}(\ln V) = \frac{\psi''(k)}{(\psi'(k))^{3/2}}.$$

The equation below gives the log-moment estimate of Q ,

$$\text{skewness}(\ln X) = \text{sgn}(Q) \frac{\psi''(Q^{-2})}{(\psi'(Q^{-2}))^{3/2}}.$$

Note that $\psi''(k)$ is negative. Using the asymptotic expansions for large k (small Q) [8],

$$\psi'(k) \approx 1/k, \quad \psi''(k) \approx -1/k^2,$$

then we have

$$\text{skewness}(\ln X) \approx -\text{sgn}(Q) \cdot |Q| = -Q.$$

Thus, the shape parameter Q is approximately the negative skewness of the log-transformed data when Q is small. This yields the following initialization:

$$\begin{aligned} \hat{\mu}_{init} &= \frac{1}{n} \sum_{i=1}^n \ln x_i, \\ \hat{\sigma}_{init} &= \left[\frac{1}{n-1} \sum_{i=1}^n (\ln x_i - \hat{\mu}_{init})^2 \right]^{\frac{1}{2}}, \\ \hat{Q}_{init} &= -\frac{1}{n} \sum_{i=1}^n (\ln x_i - \hat{\mu}_{init})^3 / \hat{\sigma}_{init}^3. \end{aligned}$$

This method provides a robust starting point that is typically close to the MLE solution. Even if Q is not very small, the above initialization can correctly determine the sign of Q and provide a reasonable initial estimate.

Non-Gradient MLE. Starting from these values, we perform MLE using the Nelder-Mead simplex algorithm [9]. This derivative-free algorithm avoids unstable gradient calculations and converges quickly in low-dimensional optimization problems with proper initial values.

Fitting and evaluation of the TOP2-O null distribution

To validate the effectiveness of the generalized gamma approximation, we conducted a systematic evaluation using the same UKB dataset employed in our primary GWAS analysis, comprising 323,839 European-ancestry individuals and 26 blood biochemistry phenotypes. Following the divided-and-combined strategy described in the main text, the TOP2-O statistic was constructed as

$$\text{TOP2-O} = -2 \sum_{k=1}^q \ln p_{\text{TOP2},k},$$

where q is the number of disjoint groups. We set $q = 33$ to ensure that the sample size within each group remains below 10,000, thereby maintaining high computational efficiency.

We generated the empirical null distribution based on tens of thousands approximately independent SNPs. Specifically, we selected 24,574 approximately independent SNPs through distance-based pruning, and truncated top and bottom 0.5% of the calculated TOP2-O statistics as outliers, resulting in 24,328 empirical statistics. All subsequent evaluations were based on the empirical distribution formed by these statistics.

Comparative goodness-of-fit. We applied the non-gradient MLE with log-moment initialization method to fit the empirical distribution using the GGD. For comparison, we also fitted four candidate distributions using standard MLE: the Chi-square distribution, Gamma distribution, Log-normal distribution and Weibull distribution.

As illustrated in Figure S1(A), the GGD provides the most precise fit to the empirical histogram, accurately capturing the overall profile, the peak, and the tail behavior. The Weibull distribution exhibits substantial deviations across the entire range. Regarding the peak behavior, the Gamma and Log-normal distributions underestimate the maximum density, and the Chi-square distribution overestimates the peak density. Furthermore, both the Gamma and Chi-square distributions exhibit a rightward shift in their modes compared to the empirical distribution. Regarding the tail behavior, all candidate distributions except the GGD underestimate the tail probabilities, with their density curves falling consistently below the empirical histogram in the tail region.

We evaluated the fitting performance of the several candidate distributions based on commonly used metrics including the AIC (Akaike information criterion), BIC (Bayes information

442 criterion), Kullback-Leibler (KL) divergence. As shown in Figure S1(B), the GGD performed
443 best under the AIC, BIC and KL divergence.

444 **False positive rate (FPR) control.** We computed omnibus p -values using the CDFs of
445 the five candidate distributions and evaluated the observed FPR at various significance levels
446 $\alpha \in \{5 \times 10^{-2}, 1 \times 10^{-2}, 1 \times 10^{-3}, 1 \times 10^{-4}\}$. As summarized in Supplementary Table S32, the
447 GGD, Gamma and Chi-square distribution approximation maintains well-controlled FPR across
448 all tested thresholds. In contrast, the Log-normal distribution exhibits overconservatism in the
449 extreme tail regions, while the Weibull distribution severely underestimates tail probabilities
450 in the extreme upper tail regions, leading to inflation. All of these results demonstrate that
451 the GGD, estimated via our robust log-moment initialization and Nelder-Mead optimization,
452 provides a superior approximation for null distribution of the TOP2-O statistics.

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474 **Supplementary Tables**

Table S1: Statistical power comparison of RmvLMM and GEMMA in a simulated study, where the number of phenotypes was set to $d = 10$ and the sample size $n = 500$. We generated phenotype data from the full mvLMM, i.e., $\tilde{\mathbf{Y}} = \tilde{\mathbf{X}}\tilde{\boldsymbol{\gamma}}^\top + \tilde{\mathbf{g}}\tilde{\boldsymbol{\beta}}^\top + \tilde{\mathbf{B}} + \tilde{\mathbf{E}}$, where $\text{vec}(\tilde{\mathbf{B}}) \sim \mathcal{N}(\mathbf{0}_{nd}, \mathbf{V}_b \otimes \mathbf{K})$ and $\text{vec}(\tilde{\mathbf{E}}) \sim \mathcal{N}(\mathbf{0}_{nd}, \mathbf{V}_e \otimes \mathbf{I}_n)$. The settings of covariate matrix ($\tilde{\mathbf{X}}$), covariate coefficient component ($\tilde{\boldsymbol{\gamma}}$), polygenic covariance matrix ($\mathbf{V}_b$), random error covariance matrix ($\mathbf{V}_e$), and sample relatedness matrix ($\mathbf{K}$) were kept consistent with those used in the FPR simulation (Table S5). The SNP genotype vector $\tilde{\mathbf{g}} = (\tilde{\mathbf{g}}_i)_{n \times 1}$ for n -individual was generated from a binomial distribution parameterized by five different minor allele frequencies (MAFs), such that $\tilde{\mathbf{g}}_i \sim \text{Binomial}(2, \text{MAF})$ with $\text{MAF} \in \{0.1, 0.2, 0.3, 0.4, 0.5\}$. For a robust cross-method performance evaluation, these five MAFs were stratified into three groups: $\{0.1\}$, $\{0.2\}$, and $\{0.3, 0.4, 0.5\}$. Corresponding to each group, we generated the SNP effect vector $\tilde{\boldsymbol{\beta}}^\top = (\tilde{\boldsymbol{\beta}}_j)_{1 \times d}$. Under the setting of $d = 10$, we adopted a dense signal model where the SNP exerts an effect on all phenotypes. Specifically, the effect size of the SNP on the j -th phenotype β_j , was sampled from a uniform distribution, $\beta_j \sim U(-0.5, 0.5)$. Statistical power was estimated as the proportion of significant p -values across 1,000 simulation replicates, with significance levels set at $\alpha = 1 \times 10^{-3}, 1 \times 10^{-4}, 1 \times 10^{-5}, 1 \times 10^{-6}, 1 \times 10^{-7}, 1 \times 10^{-8}$.

<i>maf</i>	Method	Significance level α					
		1×10^{-3}	1×10^{-4}	1×10^{-5}	1×10^{-6}	1×10^{-7}	1×10^{-8}
0.1	RmvLMM	0.943	0.827	0.680	0.508	0.371	0.241
	GEMMA	0.933	0.791	0.605	0.400	0.247	0.132
0.2	RmvLMM	0.963	0.909	0.795	0.656	0.496	0.361
	GEMMA	0.960	0.891	0.738	0.552	0.380	0.245
0.3	RmvLMM	0.965	0.899	0.789	0.634	0.479	0.324
	GEMMA	0.959	0.868	0.723	0.522	0.343	0.206
0.4	RmvLMM	0.988	0.959	0.879	0.778	0.625	0.456
	GEMMA	0.980	0.935	0.834	0.694	0.500	0.364
0.5	RmvLMM	0.989	0.957	0.905	0.812	0.679	0.544
	GEMMA	0.986	0.949	0.867	0.738	0.588	0.414

Table S2: Statistical power comparison of RmvLMM and GEMMA in a simulated study, where the number of phenotypes was set to $d = 10$ and the sample size $n = 1,000$. All other simulation settings, the method for calculating statistical power, and the number of simulation replicates were the same as those described in Table S1.

maf	Method	Significance level α					
		1×10^{-3}	1×10^{-4}	1×10^{-5}	1×10^{-6}	1×10^{-7}	1×10^{-8}
0.1	RmvLMM	0.959	0.890	0.775	0.621	0.470	0.336
	GEMMA	0.952	0.849	0.683	0.514	0.344	0.216
0.2	RmvLMM	0.982	0.921	0.822	0.693	0.552	0.407
	GEMMA	0.973	0.884	0.765	0.597	0.425	0.284
0.3	RmvLMM	0.975	0.905	0.811	0.686	0.524	0.386
	GEMMA	0.962	0.884	0.740	0.561	0.405	0.268
0.4	RmvLMM	0.989	0.962	0.910	0.813	0.702	0.556
	GEMMA	0.983	0.952	0.870	0.731	0.579	0.417
0.5	RmvLMM	0.994	0.970	0.914	0.833	0.731	0.600
	GEMMA	0.989	0.962	0.885	0.752	0.622	0.469

Table S3: Statistical power comparison of RmvLMM and GEMMA in a simulated study, where the number of phenotypes was set to $d = 10$ and the sample size $n = 5,000$. All other simulation settings and the method for calculating statistical power were the same as those described in Table S1, except that the number of simulation replicates was set to 300.

maf	Method	Significance level α					
		1×10^{-3}	1×10^{-4}	1×10^{-5}	1×10^{-6}	1×10^{-7}	1×10^{-8}
0.1	RmvLMM	0.923	0.867	0.753	0.620	0.440	0.323
	GEMMA	0.903	0.787	0.630	0.447	0.277	0.150
0.2	RmvLMM	0.963	0.867	0.770	0.660	0.507	0.333
	GEMMA	0.917	0.800	0.660	0.460	0.323	0.207
0.3	RmvLMM	0.953	0.883	0.790	0.617	0.493	0.377
	GEMMA	0.933	0.810	0.643	0.467	0.340	0.203
0.4	RmvLMM	0.980	0.950	0.893	0.787	0.650	0.503
	GEMMA	0.970	0.907	0.797	0.610	0.453	0.317
0.5	RmvLMM	0.970	0.960	0.923	0.803	0.690	0.557
	GEMMA	0.957	0.903	0.810	0.660	0.520	0.387

Table S4: Statistical power comparison of RmvLMM and GEMMA in a simulated study, where the number of phenotypes was set to $d = 10$ and the sample size $n = 10,000$. All other simulation settings and the method for calculating statistical power were the same as those described in Table S1, except that the number of simulation replicates was set to 200.

maf	Method	Significance level α					
		1×10^{-3}	1×10^{-4}	1×10^{-5}	1×10^{-6}	1×10^{-7}	1×10^{-8}
0.1	RmvLMM	0.735	0.550	0.395	0.285	0.150	0.100
	GEMMA	0.685	0.440	0.260	0.165	0.075	0.040
0.2	RmvLMM	0.950	0.865	0.735	0.575	0.405	0.300
	GEMMA	0.895	0.740	0.570	0.400	0.255	0.145
0.3	RmvLMM	0.955	0.880	0.765	0.635	0.480	0.330
	GEMMA	0.945	0.825	0.645	0.470	0.275	0.175
0.4	RmvLMM	0.980	0.920	0.885	0.735	0.595	0.460
	GEMMA	0.970	0.890	0.610	0.610	0.415	0.300
0.5	RmvLMM	0.985	0.955	0.870	0.775	0.660	0.580
	GEMMA	0.965	0.930	0.770	0.625	0.525	0.405

Table S5: False positive rates (FPRs) comparison of RmvLMM and GEMMA in a simulated study, where the number of phenotypes was set to $d = 10$ and the sample sizes ranged from small to moderate ($n = 500, 1,000, 5,000$, and $10,000$). We generated phenotype data from the null mvLMM, i.e., $\tilde{\mathbf{Y}} = \tilde{\mathbf{X}}\tilde{\boldsymbol{\gamma}}^\top + \tilde{\mathbf{B}} + \tilde{\mathbf{E}}$, where $\text{vec}(\tilde{\mathbf{B}}) \sim \mathcal{N}(\mathbf{0}_{nd}, \mathbf{V}_b \otimes \mathbf{K})$ and $\text{vec}(\tilde{\mathbf{E}}) \sim \mathcal{N}(\mathbf{0}_{nd}, \mathbf{V}_e \otimes \mathbf{I}_n)$. For simplicity, only a single covariate was considered. The covariate matrix $\tilde{\mathbf{X}} = (\tilde{x}_{ij})_{n \times 1}$ had independent entries each following a standard normal distribution ($\tilde{x}_{ij} \sim N(0, 1)$), and the coefficient vector $\tilde{\boldsymbol{\gamma}} = (\tilde{\gamma}_j)_{d \times 1}$ had independent entries each following a uniform distribution ($\tilde{\gamma}_j \sim U(0.1, 0.5)$). The polygenic covariance matrix $\mathbf{V}_b$ was set to be a compound symmetric structure with a pairwise phenotypic correlation of 0.5, i.e., $\mathbf{V}_b = (1 - \rho)\mathbf{I}_d + \rho\mathbf{1}_d \cdot \mathbf{1}_d^\top$ ($\rho = 0.5$), and the random error covariance matrix $\mathbf{V}_e$ was configured to an autoregressive structure with a decay correlation of 0.4, i.e., $\mathbf{V}_e = (\rho^{|i-j|})_{d \times d}$ ($\rho = 0.4$). The relatedness matrix $\mathbf{K}$ is calculated by the product of the centered and scaled SNP genotypes of n individuals randomly selected from the real UKB dataset. We calculated the FPRs at significance levels of $\alpha \in \{5 \times 10^{-2}, 1 \times 10^{-2}, 5 \times 10^{-3}, 1 \times 10^{-3}, 5 \times 10^{-4}, 1 \times 10^{-4}\}$, and implemented 10^5 simulation replicates.

n	Method	Significance level α					
		5×10^{-2}	1×10^{-2}	5×10^{-3}	1×10^{-3}	5×10^{-4}	1×10^{-4}
500	RmvLMM	5.01×10^{-2}	1.00×10^{-2}	5.03×10^{-3}	9.50×10^{-4}	5.50×10^{-4}	1.00×10^{-4}
	GEMMA	4.64×10^{-2}	8.81×10^{-3}	4.37×10^{-3}	8.71×10^{-4}	3.65×10^{-4}	1.11×10^{-4}
1,000	RmvLMM	5.03×10^{-2}	9.56×10^{-3}	5.00×10^{-3}	8.80×10^{-4}	4.20×10^{-4}	7.00×10^{-5}
	GEMMA	4.91×10^{-2}	9.28×10^{-3}	4.37×10^{-3}	9.76×10^{-4}	5.33×10^{-4}	9.05×10^{-5}
5,000	RmvLMM	5.08×10^{-2}	1.09×10^{-2}	5.33×10^{-3}	1.13×10^{-3}	5.30×10^{-4}	9.00×10^{-5}
	GEMMA	4.98×10^{-2}	1.02×10^{-2}	5.20×10^{-3}	8.90×10^{-4}	4.50×10^{-4}	1.33×10^{-4}
10,000	RmvLMM	5.14×10^{-2}	1.00×10^{-2}	4.75×10^{-3}	9.70×10^{-4}	4.20×10^{-4}	7.00×10^{-5}
	GEMMA	4.99×10^{-2}	1.03×10^{-2}	5.23×10^{-3}	1.00×10^{-3}	5.42×10^{-4}	1.81×10^{-4}

Table S6: False positive rates (FPRs) of RmvLMM and GEMMA in a simulated study, where the number of phenotypes was set to $d = 10$ and the sample size $n = 1,000$. We calculated the FPRs at significance levels of $\alpha = 5 \times 10^{-2}$, 1×10^{-2} , 5×10^{-3} , 1×10^{-3} , 5×10^{-4} , 1×10^{-4} , 5×10^{-5} , 1×10^{-5} , 5×10^{-6} , 1×10^{-6} , 5×10^{-7} , 1×10^{-7} , and implemented 10^8 simulation replicates. The other simulation settings were the same as those described in Table S5.

Significance level α	RmvLMM	GEMMA
5×10^{-2}	5.00×10^{-2}	4.80×10^{-2}
1×10^{-2}	9.95×10^{-3}	9.29×10^{-3}
5×10^{-3}	4.96×10^{-3}	4.57×10^{-3}
1×10^{-3}	9.85×10^{-4}	8.73×10^{-4}
5×10^{-4}	4.90×10^{-4}	4.27×10^{-4}
1×10^{-4}	9.56×10^{-5}	8.10×10^{-5}
5×10^{-5}	4.70×10^{-5}	4.01×10^{-5}
1×10^{-5}	9.17×10^{-6}	7.74×10^{-6}
5×10^{-6}	4.73×10^{-6}	3.86×10^{-6}
1×10^{-6}	4.00×10^{-7}	6.45×10^{-7}
5×10^{-7}	5.00×10^{-7}	3.02×10^{-7}
1×10^{-7}	8.00×10^{-8}	6.04×10^{-8}

Table S7: Statistical power of RmvLMM in a simulated study, where the number of phenotypes was set to $d = 50$ and the sample size $n = 500$. We generated phenotype data from the full mvLMM, i.e., $\tilde{\mathbf{Y}} = \tilde{\mathbf{X}}\tilde{\boldsymbol{\gamma}}^\top + \tilde{\mathbf{g}}\tilde{\boldsymbol{\beta}}^\top + \tilde{\mathbf{B}} + \tilde{\mathbf{E}}$, where $\text{vec}(\tilde{\mathbf{B}}) \sim \mathcal{N}(\mathbf{0}_{nd}, \mathbf{V}_b \otimes \mathbf{K})$ and $\text{vec}(\tilde{\mathbf{E}}) \sim \mathcal{N}(\mathbf{0}_{nd}, \mathbf{V}_e \otimes \mathbf{I}_n)$. The settings of covariate matrix ($\tilde{\mathbf{X}}$), covariate coefficient component ($\tilde{\boldsymbol{\gamma}}$), polygenic covariance matrix ($\mathbf{V}_b$), random error covariance matrix ($\mathbf{V}_e$), and sample relatedness matrix ($\mathbf{K}$) were kept consistent with those used in the FPR simulation (Table S19). The SNP genotype vector $\tilde{\mathbf{g}} = (\tilde{\mathbf{g}}_i)_{n \times 1}$ for n -individual was generated from a binomial distribution parameterized by five different minor allele frequencies (MAFs), such that $\tilde{\mathbf{g}}_i \sim \text{Binomial}(2, \text{MAF})$ with $\text{MAF} \in \{0.1, 0.2, 0.3, 0.4, 0.5\}$. For a robust cross-method performance evaluation, these five MAFs were stratified into three groups: $\{0.1\}$, $\{0.2\}$, and $\{0.3, 0.4, 0.5\}$. Corresponding to each group, we generated the SNP effect vector $\tilde{\boldsymbol{\beta}}^\top = (\tilde{\boldsymbol{\beta}}_j)_{1 \times d}$. Under the setting of $d = 50$, we adopted a sparse signal model to better mimic real-world scenarios, where the SNP affects only a small fraction of phenotypes. Specifically, the SNP effect vector $\tilde{\boldsymbol{\beta}}$ was generated as $\tilde{\boldsymbol{\beta}}^\top = (\underbrace{-\tilde{\beta}_1, -\tilde{\beta}_2, \dots, -\tilde{\beta}_a}_{a = \left\lfloor \frac{d - \lfloor 0.618d \rfloor}{2} \right\rfloor}, \underbrace{0, 0, \dots, 0}_{a' = \frac{d}{2} - a}, \underbrace{\tilde{\beta}_{1'}, \tilde{\beta}_{2'}, \dots, \tilde{\beta}_{b'}}_{b' = \left\lceil \frac{d - \lfloor 0.618d \rfloor}{2} \right\rceil}, \underbrace{0, 0, \dots, 0}_{b = \frac{d}{2} - b'})$. The number of phenotypes with zero effects was $\lfloor 0.618d \rfloor$, and the nonzero elements are independently and identically distributed (i.i.d) as $\tilde{\beta}_j \stackrel{\text{i.i.d.}}{\sim} U(0, 0.5)$ for $j = 1, \dots, a$ and $j = 1', \dots, b'$. Here, $\lfloor \cdot \rfloor$ and $\lceil \cdot \rceil$ denote the floor and ceiling functions, respectively. Statistical power was estimated as the proportion of significant p -values across 1,000 simulation replicates, with significance levels set at $\alpha = 1 \times 10^{-3}, 1 \times 10^{-4}, 1 \times 10^{-5}, 1 \times 10^{-6}, 1 \times 10^{-7}, 1 \times 10^{-8}$. Notice that the GEMMA method is computationally intractable in these scenarios, so we did not include it in the comparison.

<i>maf</i>	Method	Significance level α					
		1×10^{-3}	1×10^{-4}	1×10^{-5}	1×10^{-6}	1×10^{-7}	1×10^{-8}
0.1	RmvLMM	0.903	0.809	0.711	0.585	0.460	0.350
0.2	RmvLMM	0.971	0.920	0.865	0.768	0.676	0.575
0.3	RmvLMM	0.928	0.848	0.761	0.633	0.517	0.400
0.4	RmvLMM	0.977	0.934	0.872	0.774	0.666	0.567
0.5	RmvLMM	0.981	0.949	0.907	0.829	0.748	0.629

Table S8: Statistical power of RmvLMM in a simulated study, where the number of phenotypes was set to $d = 50$ and the sample size $n = 1,000$. All other simulation settings and the method for calculating statistical power were the same as those described in Table S7, except that the number of simulation replicates was set to 300.

<i>maf</i>	Method	Significance level α					
		1×10^{-3}	1×10^{-4}	1×10^{-5}	1×10^{-6}	1×10^{-7}	1×10^{-8}
0.1	RmvLMM	0.907	0.790	0.663	0.560	0.407	0.287
0.2	RmvLMM	0.943	0.867	0.793	0.663	0.527	0.413
0.3	RmvLMM	0.957	0.893	0.813	0.693	0.523	0.397
0.4	RmvLMM	0.983	0.943	0.903	0.823	0.737	0.620
0.5	RmvLMM	0.980	0.963	0.930	0.873	0.753	0.690

Table S9: Statistical power of RmvLMM in a simulated study, where the number of phenotypes was set to $d = 50$ and the sample size $n = 5,000$. All other simulation settings and the method for calculating statistical power were the same as those described in Table S7, except that the number of simulation replicates was set to 300.

<i>maf</i>	Method	Significance level α					
		1×10^{-3}	1×10^{-4}	1×10^{-5}	1×10^{-6}	1×10^{-7}	1×10^{-8}
0.1	RmvLMM	0.927	0.830	0.737	0.573	0.473	0.320
0.2	RmvLMM	0.960	0.907	0.810	0.700	0.563	0.413
0.3	RmvLMM	0.957	0.873	0.777	0.630	0.490	0.390
0.4	RmvLMM	0.977	0.950	0.893	0.810	0.673	0.557
0.5	RmvLMM	0.987	0.947	0.900	0.837	0.737	0.600

Table S10: Statistical power of RmvLMM in a simulated study, where the number of phenotypes was set to $d = 50$ and the sample size $n = 10,000$. All other simulation settings and the method for calculating statistical power were the same as those described in Table S7, except that the number of simulation replicates was set to 200.

maf	Method	Significance level α					
		1×10^{-3}	1×10^{-4}	1×10^{-5}	1×10^{-6}	1×10^{-7}	1×10^{-8}
0.1	RmvLMM	0.930	0.840	0.765	0.640	0.510	0.375
0.2	RmvLMM	0.955	0.900	0.820	0.685	0.540	0.400
0.3	RmvLMM	0.855	0.725	0.600	0.430	0.305	0.175
0.4	RmvLMM	0.935	0.850	0.765	0.585	0.455	0.330
0.5	RmvLMM	0.935	0.855	0.785	0.635	0.465	0.340

Table S11: Statistical power of RmvLMM in a simulated study, where the number of phenotypes was set to $d = 100$ and the sample size $n = 500$. All other simulation settings, the method for calculating statistical power and the number of simulation replicates were the same as those described in Table S7.

maf	Method	Significance level α					
		1×10^{-3}	1×10^{-4}	1×10^{-5}	1×10^{-6}	1×10^{-7}	1×10^{-8}
0.1	RmvLMM	0.830	0.719	0.600	0.468	0.359	0.263
0.2	RmvLMM	0.943	0.874	0.780	0.691	0.583	0.484
0.3	RmvLMM	0.954	0.886	0.836	0.743	0.639	0.528
0.4	RmvLMM	0.984	0.961	0.926	0.868	0.795	0.708
0.5	RmvLMM	0.991	0.964	0.940	0.892	0.832	0.769

Table S12: Statistical power of RmvLMM in a simulated study, where the number of phenotypes was set to $d = 100$ and the sample size $n = 1,000$. All other simulation settings and the method for calculating statistical power were the same as those described in Table S7, except that the number of simulation replicates was set to 300.

maf	Method	Significance level α					
		1×10^{-3}	1×10^{-4}	1×10^{-5}	1×10^{-6}	1×10^{-7}	1×10^{-8}
0.1	RmvLMM	0.840	0.727	0.630	0.510	0.410	0.280
0.2	RmvLMM	0.893	0.760	0.643	0.547	0.423	0.333
0.3	RmvLMM	0.853	0.737	0.570	0.450	0.327	0.243
0.4	RmvLMM	0.937	0.850	0.750	0.620	0.480	0.380
0.5	RmvLMM	0.963	0.893	0.803	0.650	0.520	0.437

Table S13: Statistical power of RmvLMM in a simulated study, where the number of phenotypes was set to $d = 100$ and the sample size $n = 5,000$. All other simulation settings and the method for calculating statistical power were the same as those described in Table S7, except that the number of simulation replicates was set to 300.

maf	Method	Significance level α					
		1×10^{-3}	1×10^{-4}	1×10^{-5}	1×10^{-6}	1×10^{-7}	1×10^{-8}
0.1	RmvLMM	0.830	0.653	0.493	0.380	0.297	0.207
0.2	RmvLMM	0.897	0.790	0.670	0.530	0.427	0.310
0.3	RmvLMM	0.917	0.773	0.667	0.547	0.450	0.363
0.4	RmvLMM	0.960	0.903	0.827	0.680	0.583	0.473
0.5	RmvLMM	0.977	0.933	0.867	0.787	0.667	0.533

Table S14: Statistical power of RmvLMM in a simulated study, where the number of phenotypes was set to $d = 100$ and the sample size $n = 10,000$. All other simulation settings and the method for calculating statistical power were the same as those described in Table S7, except that the number of simulation replicates was set to 200.

<i>maf</i>	Method	Significance level α					
		1×10^{-3}	1×10^{-4}	1×10^{-5}	1×10^{-6}	1×10^{-7}	1×10^{-8}
0.1	RmvLMM	0.885	0.765	0.620	0.480	0.340	0.255
0.2	RmvLMM	0.970	0.910	0.840	0.730	0.600	0.490
0.3	RmvLMM	0.960	0.900	0.830	0.710	0.610	0.475
0.4	RmvLMM	0.985	0.955	0.910	0.810	0.725	0.630
0.5	RmvLMM	0.985	0.965	0.920	0.850	0.735	0.630

Table S15: Statistical power of RmvLMM in a simulated study, where the number of phenotypes was set to $d = 200$ and the sample size $n = 500$. All other simulation settings and the method for calculating statistical power were the same as those described in Table S7, except that the number of simulation replicates was set to 300.

<i>maf</i>	Method	Significance level α					
		1×10^{-3}	1×10^{-4}	1×10^{-5}	1×10^{-6}	1×10^{-7}	1×10^{-8}
0.1	RmvLMM	0.853	0.763	0.623	0.527	0.430	0.347
0.2	RmvLMM	0.937	0.807	0.740	0.637	0.523	0.413
0.3	RmvLMM	0.900	0.813	0.730	0.610	0.530	0.447
0.4	RmvLMM	0.980	0.920	0.903	0.843	0.740	0.647
0.5	RmvLMM	0.993	0.950	0.920	0.867	0.800	0.723

Table S16: Statistical power of RmvLMM in a simulated study, where the number of phenotypes was set to $d = 200$ and the sample size $n = 1,000$. All other simulation settings and the method for calculating statistical power were the same as those described in Table S7, except that the number of simulation replicates was set to 300.

<i>maf</i>	Method	Significance level α					
		1×10^{-3}	1×10^{-4}	1×10^{-5}	1×10^{-6}	1×10^{-7}	1×10^{-8}
0.1	RmvLMM	0.913	0.807	0.717	0.627	0.567	0.457
0.2	RmvLMM	0.943	0.873	0.807	0.727	0.627	0.553
0.3	RmvLMM	0.893	0.783	0.680	0.580	0.470	0.380
0.4	RmvLMM	0.973	0.903	0.833	0.733	0.640	0.567
0.5	RmvLMM	0.973	0.917	0.857	0.773	0.687	0.617

Table S17: Statistical power of RmvLMM in a simulated study, where the number of phenotypes was set to $d = 200$ and the sample size $n = 5,000$. All other simulation settings and the method for calculating statistical power were the same as those described in Table S7, except that the number of simulation replicates was set to 300.

maf	Method	Significance level α					
		1×10^{-3}	1×10^{-4}	1×10^{-5}	1×10^{-6}	1×10^{-7}	1×10^{-8}
0.1	RmvLMM	0.900	0.790	0.683	0.570	0.437	0.330
0.2	RmvLMM	0.920	0.803	0.713	0.540	0.377	0.277
0.3	RmvLMM	0.913	0.843	0.737	0.607	0.483	0.350
0.4	RmvLMM	0.963	0.917	0.850	0.743	0.653	0.540
0.5	RmvLMM	0.970	0.940	0.877	0.793	0.703	0.623

Table S18: Statistical power of RmvLMM in a simulated study, where the number of phenotypes was set to $d = 200$ and the sample size $n = 10,000$. All other simulation settings and the method for calculating statistical power were the same as those described in Table S7, except that the number of simulation replicates was set to 200.

maf	Method	Significance level α					
		1×10^{-3}	1×10^{-4}	1×10^{-5}	1×10^{-6}	1×10^{-7}	1×10^{-8}
0.1	RmvLMM	0.940	0.855	0.680	0.370	0.300	0.295
0.2	RmvLMM	0.960	0.905	0.755	0.455	0.385	0.370
0.3	RmvLMM	0.985	0.905	0.680	0.460	0.385	0.385
0.4	RmvLMM	0.995	0.890	0.685	0.455	0.435	0.430
0.5	RmvLMM	0.990	0.910	0.685	0.490	0.430	0.425

Table S19: False positive rates (FPRs) of RmvLMM in a simulated study, where the number of phenotypes was set to $d = 50$ and the sample sizes ranged from small to moderate ($n = 500, 1,000, 5,000$, and $10,000$). The generation process of the simulated phenotypes, the significance levels for calculating FPRs, and the number of simulation replicates were all the same as those described in Table S5. Notice that the GEMMA method is computationally intractable in these scenarios, so we did not include it in the comparison.

n	Method	Significance level α					
		5×10^{-2}	1×10^{-2}	5×10^{-3}	1×10^{-3}	5×10^{-4}	1×10^{-4}
500	RmvLMM	4.83×10^{-2}	9.02×10^{-3}	4.29×10^{-3}	9.20×10^{-4}	4.60×10^{-4}	1.00×10^{-4}
1,000	RmvLMM	5.00×10^{-2}	1.04×10^{-2}	5.38×10^{-3}	1.07×10^{-3}	5.30×10^{-4}	1.10×10^{-4}
5,000	RmvLMM	5.13×10^{-2}	1.00×10^{-2}	5.03×10^{-3}	1.07×10^{-3}	5.30×10^{-4}	1.20×10^{-4}
10,000	RmvLMM	5.00×10^{-2}	1.02×10^{-2}	4.99×10^{-3}	1.07×10^{-3}	4.40×10^{-4}	7.00×10^{-5}

Table S20: False positive rates (FPRs) of RmvLMM in a simulated study, where the number of phenotypes was set to $d = 100$ and the sample sizes ranged from small to moderate ($n = 500, 1,000, 5,000$, and $10,000$). The generation process of the simulated phenotypes, the significance levels for calculating FPRs, and the number of simulation replicates were all the same as those described in Table S5. Notice that the GEMMA method is computationally intractable in these scenarios, so we did not include it in the comparison.

n	Method	Significance level α					
		5×10^{-2}	1×10^{-2}	5×10^{-3}	1×10^{-3}	5×10^{-4}	1×10^{-4}
500	RmvLMM	4.76×10^{-2}	9.32×10^{-3}	4.47×10^{-3}	9.60×10^{-4}	5.20×10^{-4}	9.00×10^{-5}
1,000	RmvLMM	4.61×10^{-2}	5.99×10^{-3}	1.56×10^{-3}	1.10×10^{-4}	1.10×10^{-4}	1.10×10^{-4}
5,000	RmvLMM	5.05×10^{-2}	9.82×10^{-3}	5.22×10^{-3}	1.09×10^{-3}	5.40×10^{-4}	1.00×10^{-4}
10,000	RmvLMM	4.95×10^{-2}	1.01×10^{-2}	5.11×10^{-3}	1.03×10^{-3}	4.50×10^{-4}	7.00×10^{-5}

Table S21: False positive rates (FPRs) of RmvLMM in a simulated study, where the number of phenotypes was set to $d = 200$ and the sample sizes ranged from small to moderate ($n = 500, 1,000, 5,000$, and $10,000$). The generation process of the simulated phenotypes, the significance levels for calculating FPRs, and the number of simulation replicates were all the same as those described in Table S5. Notice that the GEMMA method is computationally intractable in these scenarios, so we did not include it in the comparison.

n	Method	Significance level α					
		5×10^{-2}	1×10^{-2}	5×10^{-3}	1×10^{-3}	5×10^{-4}	1×10^{-4}
500	RmvLMM	4.74×10^{-2}	9.24×10^{-3}	4.49×10^{-3}	8.80×10^{-4}	4.70×10^{-4}	1.00×10^{-4}
1,000	RmvLMM	4.94×10^{-2}	9.68×10^{-3}	4.74×10^{-3}	1.09×10^{-3}	4.80×10^{-4}	8.00×10^{-5}
5,000	RmvLMM	5.06×10^{-2}	1.02×10^{-2}	5.13×10^{-3}	1.04×10^{-3}	4.80×10^{-4}	8.00×10^{-5}
10,000	RmvLMM	4.95×10^{-2}	1.02×10^{-2}	5.08×10^{-3}	1.00×10^{-3}	4.30×10^{-4}	1.00×10^{-4}

Table S22: Statistical power of RmvLMM in a simulated study, where the number of phenotypes was set to $d = 10$ and the sample size $n = 50,000$. We generated phenotype data from the full mvLMM, i.e., $\tilde{\mathbf{Y}} = \tilde{\mathbf{X}}\tilde{\boldsymbol{\gamma}}^\top + \tilde{\mathbf{g}}\tilde{\boldsymbol{\beta}}^\top + \tilde{\mathbf{B}} + \tilde{\mathbf{E}}$, where $\text{vec}(\tilde{\mathbf{B}}) \sim \mathcal{N}(\mathbf{0}_{nd}, \mathbf{V}_b \otimes \mathbf{K})$ and $\text{vec}(\tilde{\mathbf{E}}) \sim \mathcal{N}(\mathbf{0}_{nd}, \mathbf{V}_e \otimes \mathbf{I}_n)$. For simplicity, only a single covariate was considered. The covariate matrix $\tilde{\mathbf{X}} = (\tilde{x}_{ij})_{n \times 1}$ had independent entries each following a standard normal distribution ($\tilde{x}_{ij} \sim N(0, 1)$), and the coefficient vector $\tilde{\boldsymbol{\gamma}} = (\tilde{\gamma}_j)_{d \times 1}$ had independent entries each following a uniform distribution ($\tilde{\gamma}_j \sim U(0.1, 0.5)$). The polygenic covariance matrix $\mathbf{V}_b$ was set to be a compound symmetric structure with a pairwise phenotypic correlation of 0.5, i.e., $\mathbf{V}_b = (1 - \rho)\mathbf{I}_d + \rho\mathbf{1}_d \cdot \mathbf{1}_d^\top$ ($\rho = 0.5$), and the random error covariance matrix $\mathbf{V}_e$ was configured to an autoregressive structure with a decay correlation of 0.4, i.e., $\mathbf{V}_e = (\rho^{|i-j|})_{d \times d}$ ($\rho = 0.4$). The SNP genotype vector $\tilde{\mathbf{g}} = (\tilde{g}_i)_{n \times 1}$ for n -individual was generated from a binomial distribution parameterized by five different minor allele frequencies (MAFs), such that $\tilde{g}_i \sim \text{Binomial}(2, \text{MAF})$ with $\text{MAF} \in \{0.1, 0.2, 0.3, 0.4, 0.5\}$. For a robust cross-method performance evaluation, these five MAFs were stratified into three classes: $\{0.1\}$, $\{0.2\}$, and $\{0.3, 0.4, 0.5\}$. Corresponding to each class, we generated the SNP effect vector $\tilde{\boldsymbol{\beta}}^\top = (\tilde{\beta}_j)_{1 \times d}$. Under the setting of $d = 10$, we adopted a dense signal model where the SNP exerts an effect on all phenotypes. Specifically, the effect size of the SNP on the j -th phenotype β_j , was sampled from a uniform distribution, $\beta_j \sim U(-0.5, 0.5)$. In the case of a large sample size ($n = 50,000$), storing sample relatedness matrix ($\mathbf{K}$) requires enormous memory. Therefore, we partitioned the individual samples into q groups, with each group containing 10,000 individuals. The sample relatedness matrix ($\mathbf{K}$) for each group was calculated by the product of the centered and scaled SNP genotypes of 10,000 individuals randomly selected from the real UKB dataset. We then computed the p -values for each of the q groups, and substituted them into the omnibus test statistic TOP2-O. Statistical power was estimated as the proportion of significant p -values across 200 simulation replicates, with significance levels set at $\alpha = 1 \times 10^{-3}, 1 \times 10^{-4}, 1 \times 10^{-5}, 1 \times 10^{-6}, 1 \times 10^{-7}, 1 \times 10^{-8}$. Notice that the GEMMA method is computationally intractable in these scenarios, so we did not include it in the comparison.

<i>maf</i>	Method	Significance level α					
		1×10^{-3}	1×10^{-4}	1×10^{-5}	1×10^{-6}	1×10^{-7}	1×10^{-8}
0.1	RmvLMM	0.920	0.800	0.615	0.425	0.270	0.185
0.2	RmvLMM	0.920	0.805	0.640	0.435	0.270	0.150
0.3	RmvLMM	0.875	0.685	0.500	0.305	0.205	0.110
0.4	RmvLMM	0.930	0.815	0.690	0.520	0.340	0.240
0.5	RmvLMM	0.955	0.885	0.760	0.600	0.465	0.310

Table S23: Statistical power of RmvLMM in a simulated study, where the number of phenotypes was set to $d = 10$ and the sample size $n = 100,000$. All other simulation settings, the method for calculating statistical power and the number of simulation replicates were the same as those described in Table S22.

maf	Method	Significance level α					
		1×10^{-3}	1×10^{-4}	1×10^{-5}	1×10^{-6}	1×10^{-7}	1×10^{-8}
0.1	RmvLMM	0.900	0.815	0.670	0.495	0.360	0.225
0.2	RmvLMM	0.945	0.860	0.715	0.515	0.350	0.240
0.3	RmvLMM	0.970	0.865	0.715	0.525	0.350	0.215
0.4	RmvLMM	0.990	0.915	0.825	0.700	0.525	0.370
0.5	RmvLMM	0.995	0.930	0.845	0.715	0.615	0.465

Table S24: Statistical power of RmvLMM in a simulated study, where the number of phenotypes was set to $d = 10$ and the sample size $n = 200,000$. All other simulation settings, the method for calculating statistical power and the number of simulation replicates were the same as those described in Table S22.

maf	Method	Significance level α					
		1×10^{-3}	1×10^{-4}	1×10^{-5}	1×10^{-6}	1×10^{-7}	1×10^{-8}
0.1	RmvLMM	0.930	0.820	0.655	0.525	0.375	0.270
0.2	RmvLMM	0.970	0.900	0.770	0.635	0.525	0.340
0.3	RmvLMM	0.930	0.860	0.770	0.625	0.460	0.300
0.4	RmvLMM	0.990	0.985	0.955	0.850	0.715	0.590
0.5	RmvLMM	0.995	0.975	0.945	0.850	0.765	0.665

Table S25: Statistical power of RmvLMM in a simulated study, where the number of phenotypes was set to $d = 10$ and the sample size $n = 300,000$. All other simulation settings, the method for calculating statistical power and the number of simulation replicates were the same as those described in Table S22.

maf	Method	Significance level α					
		1×10^{-3}	1×10^{-4}	1×10^{-5}	1×10^{-6}	1×10^{-7}	1×10^{-8}
0.1	RmvLMM	0.955	0.885	0.760	0.610	0.485	0.290
0.2	RmvLMM	0.990	0.970	0.880	0.765	0.635	0.480
0.3	RmvLMM	0.915	0.830	0.655	0.535	0.310	0.230
0.4	RmvLMM	0.965	0.920	0.810	0.725	0.580	0.425
0.5	RmvLMM	0.985	0.945	0.875	0.755	0.610	0.440

Table S26: Statistical power of RmvLMM in a simulated study, where the number of phenotypes was set to $d = 20$ and the sample size $n = 50,000$. We generated phenotype data from the full mvLMM, i.e., $\tilde{\mathbf{Y}} = \tilde{\mathbf{X}}\tilde{\boldsymbol{\gamma}}^\top + \tilde{\mathbf{g}}\tilde{\boldsymbol{\beta}}^\top + \tilde{\mathbf{B}} + \tilde{\mathbf{E}}$, where $\text{vec}(\tilde{\mathbf{B}}) \sim \mathcal{N}(\mathbf{0}_{nd}, \mathbf{V}_b \otimes \mathbf{K})$ and $\text{vec}(\tilde{\mathbf{E}}) \sim \mathcal{N}(\mathbf{0}_{nd}, \mathbf{V}_e \otimes \mathbf{I}_n)$. The data generation procedures of covariate matrix ($\tilde{\mathbf{X}}$), covariate coefficient component ($\tilde{\boldsymbol{\gamma}}$), polygenic covariance matrix ($\mathbf{V}_b$), random error covariance matrix ($\mathbf{V}_e$), and sample relatedness matrix ($\mathbf{K}$) were kept consistent with those used in the previous simulation scenario $d = 10, n = 50,000$ (Table S22). The SNP genotype vector $\tilde{\mathbf{g}} = (\tilde{\mathbf{g}}_i)_{n \times 1}$ for n -individual was generated from a binomial distribution parameterized by five different minor allele frequencies (MAFs), such that $\tilde{\mathbf{g}}_i \sim \text{Binomial}(2, \text{MAF})$ with $\text{MAF} \in \{0.1, 0.2, 0.3, 0.4, 0.5\}$. For a robust cross-method performance evaluation, these five MAFs were stratified into three classes: $\{0.1\}$, $\{0.2\}$, and $\{0.3, 0.4, 0.5\}$. Corresponding to each class, we generated the SNP effect vector $\tilde{\boldsymbol{\beta}}^\top = (\tilde{\boldsymbol{\beta}}_j)_{1 \times d}$. Under the setting of $d = 20$, we adopted a sparse signal model to mimic real-world scenarios, where the SNP affects only a small fraction of phenotypes. Specifically, the SNP effect vector $\tilde{\boldsymbol{\beta}}$ was generated as $\tilde{\boldsymbol{\beta}}^\top = (\underbrace{-\tilde{\beta}_1, -\tilde{\beta}_2, \dots, -\tilde{\beta}_a}_{a = \left\lfloor \frac{d - \lfloor 0.618d \rfloor}{2} \right\rfloor}, \underbrace{0, 0, \dots, 0}_{a' = \frac{d}{2} - a}, \underbrace{\tilde{\beta}_{1'}, \tilde{\beta}_{2'}, \dots, \tilde{\beta}_{b'}}_{b' = \left\lceil \frac{d - \lfloor 0.618d \rfloor}{2} \right\rceil}, \underbrace{0, 0, \dots, 0}_{b = \frac{d}{2} - b'})$. The number of phenotypes with zero effects was $\lfloor 0.618d \rfloor$, and the nonzero elements are independently and identically distributed (i.i.d) as $\tilde{\beta}_j \stackrel{\text{i.i.d.}}{\sim} U(0, 0.5)$ for $j = 1, \dots, a$ and $j = 1', \dots, b'$. Here, $\lfloor \cdot \rfloor$ and $\lceil \cdot \rceil$ denote the floor and ceiling functions, respectively. Statistical power was estimated as the proportion of significant p -values across 200 simulation replicates, with significance levels set at $\alpha = 1 \times 10^{-3}, 1 \times 10^{-4}, 1 \times 10^{-5}, 1 \times 10^{-6}, 1 \times 10^{-7}, 1 \times 10^{-8}$. Notice that the GEMMA method is computationally intractable in these scenarios, so we did not include it in the comparison.

<i>maf</i>	Method	Significance level α					
		1×10^{-3}	1×10^{-4}	1×10^{-5}	1×10^{-6}	1×10^{-7}	1×10^{-8}
0.1	RmvLMM	0.920	0.825	0.695	0.565	0.400	0.240
0.2	RmvLMM	0.985	0.940	0.855	0.780	0.645	0.495
0.3	RmvLMM	0.955	0.860	0.700	0.525	0.370	0.230
0.4	RmvLMM	0.975	0.940	0.875	0.745	0.630	0.465
0.5	RmvLMM	1.000	0.980	0.930	0.820	0.640	0.555

Table S27: Statistical power of RmvLMM in a simulated study, where the number of phenotypes was set to $d = 20$ and the sample size $n = 100,000$. All other simulation settings, the method for calculating statistical power and the number of simulation replicates were the same as those described in Table S26.

maf	Method	Significance level α					
		1×10^{-3}	1×10^{-4}	1×10^{-5}	1×10^{-6}	1×10^{-7}	1×10^{-8}
0.1	RmvLMM	0.960	0.885	0.740	0.565	0.370	0.275
0.2	RmvLMM	0.990	0.930	0.860	0.720	0.560	0.400
0.3	RmvLMM	0.975	0.865	0.740	0.565	0.405	0.285
0.4	RmvLMM	0.990	0.980	0.915	0.795	0.635	0.460
0.5	RmvLMM	0.995	0.970	0.910	0.830	0.705	0.565

Table S28: Statistical power of RmvLMM in a simulated study, where the number of phenotypes was set to $d = 20$ and the sample size $n = 200,000$. All other simulation settings, the method for calculating statistical power and the number of simulation replicates were the same as those described in Table S26.

maf	Method	Significance level α					
		1×10^{-3}	1×10^{-4}	1×10^{-5}	1×10^{-6}	1×10^{-7}	1×10^{-8}
0.1	RmvLMM	0.955	0.870	0.695	0.500	0.320	0.195
0.2	RmvLMM	0.990	0.930	0.860	0.745	0.590	0.450
0.3	RmvLMM	0.930	0.780	0.640	0.420	0.270	0.160
0.4	RmvLMM	0.990	0.955	0.850	0.690	0.545	0.425
0.5	RmvLMM	0.995	0.980	0.930	0.750	0.585	0.435

Table S29: Statistical power of RmvLMM in a simulated study, where the number of phenotypes was set to $d = 20$ and the sample size $n = 300,000$. All other simulation settings, the method for calculating statistical power and the number of simulation replicates were the same as those described in Table S26.

maf	Method	Significance level α					
		1×10^{-3}	1×10^{-4}	1×10^{-5}	1×10^{-6}	1×10^{-7}	1×10^{-8}
0.1	RmvLMM	0.960	0.880	0.750	0.580	0.455	0.300
0.2	RmvLMM	0.975	0.920	0.810	0.670	0.465	0.325
0.3	RmvLMM	0.970	0.900	0.790	0.630	0.490	0.310
0.4	RmvLMM	0.995	0.975	0.920	0.805	0.655	0.495
0.5	RmvLMM	1.000	0.965	0.905	0.815	0.690	0.595

Table S30: False positive rates (FPRs) of RmvLMM in a simulated study with large sample sizes, where the number of phenotypes was set to $d = 10$ and the sample sizes were set to $n = 50,000, 100,000, 200,000$, and $300,000$. We extracted 10 blood biochemical phenotypes from the real UKB dataset, and partitioned the individual samples into q groups, with each group containing 10,000 individuals. For each group, we computed the p -values for each of the q groups, and substituted them into the omnibus test statistic TOP2-O. Meanwhile, we performed 10^5 repeated simulations, from which 10,000 TOP2-O values were randomly sampled to approximate the parameters of the generalized gamma distribution (GGD), thus deriving the final p -value for each run. We calculated the FPRs at significance levels of $\alpha \in \{5 \times 10^{-2}, 1 \times 10^{-2}, 5 \times 10^{-3}, 1 \times 10^{-3}, 5 \times 10^{-4}, 1 \times 10^{-4}\}$. Notice that the GEMMA method is computationally intractable in these scenarios, so we did not include it in the comparison.

n	Method	Significance level α					
		5×10^{-2}	1×10^{-2}	5×10^{-3}	1×10^{-3}	5×10^{-4}	1×10^{-4}
50,000	RmvLMM	4.95×10^{-2}	1.05×10^{-2}	5.48×10^{-3}	1.21×10^{-3}	5.40×10^{-4}	7.00×10^{-5}
100,000	RmvLMM	4.99×10^{-2}	9.74×10^{-2}	4.70×10^{-3}	9.30×10^{-3}	4.10×10^{-4}	6.00×10^{-5}
200,000	RmvLMM	5.06×10^{-2}	1.01×10^{-2}	4.94×10^{-3}	1.01×10^{-3}	4.70×10^{-4}	1.30×10^{-4}
300,000	RmvLMM	5.00×10^{-2}	1.03×10^{-2}	5.39×10^{-3}	1.04×10^{-3}	5.50×10^{-4}	6.00×10^{-5}

Table S31: False positive rates (FPRs) of RmvLMM in a simulated study with large sample sizes, where the number of phenotypes was set to $d = 20$ and the sample sizes were set to $n = 50,000, 100,000, 200,000$, and $300,000$. We extracted 20 blood biochemical phenotypes from the real UKB dataset. The calculation method of FPR, the significance level settings, and the number of simulation replicates were all the same as those described in Table S30. Notice that the GEMMA method is computationally intractable in these scenarios, so we did not include it in the comparison.

n	Method	Significance level α					
		5×10^{-2}	1×10^{-2}	5×10^{-3}	1×10^{-3}	5×10^{-4}	1×10^{-4}
50,000	RmvLMM	4.95×10^{-2}	9.94×10^{-3}	4.82×10^{-3}	9.60×10^{-4}	4.90×10^{-4}	1.10×10^{-4}
100,000	RmvLMM	5.08×10^{-2}	1.04×10^{-2}	5.27×10^{-3}	9.50×10^{-4}	5.70×10^{-4}	1.30×10^{-4}
200,000	RmvLMM	4.90×10^{-2}	9.60×10^{-3}	4.62×10^{-3}	8.70×10^{-4}	4.20×10^{-4}	1.00×10^{-4}
300,000	RmvLMM	5.06×10^{-2}	9.91×10^{-3}	4.89×10^{-3}	8.10×10^{-4}	3.90×10^{-4}	6.00×10^{-5}

Table S32: False positive rates (FPRs) in a simulated study for evaluating the fit of five distributions to the TOP2-O null distribution.

d	n	Method	Significance level α			
			5.00×10^{-2}	1.00×10^{-2}	1.00×10^{-3}	1.00×10^{-4}
10	100,000	Generalized Gamma	4.99×10^{-2}	9.74×10^{-3}	9.30×10^{-4}	6.00×10^{-5}
		Gamma	5.00×10^{-2}	9.86×10^{-3}	9.40×10^{-4}	6.00×10^{-5}
		Log-normal	3.89×10^{-2}	4.17×10^{-3}	6.00×10^{-5}	0.00×10^0
		Chi-square	5.07×10^{-2}	1.01×10^{-2}	9.60×10^{-4}	6.00×10^{-5}
		Weibull	5.62×10^{-2}	1.90×10^{-2}	5.26×10^{-3}	1.70×10^{-3}
	300,000	Generalized Gamma	5.00×10^{-2}	1.03×10^{-2}	1.04×10^{-3}	6.00×10^{-5}
		Gamma	4.98×10^{-2}	1.02×10^{-2}	1.01×10^{-3}	6.00×10^{-5}
		Log-normal	4.36×10^{-2}	6.75×10^{-3}	3.20×10^{-4}	2.00×10^{-5}
		Chi-square	5.12×10^{-2}	1.06×10^{-2}	1.08×10^{-3}	6.00×10^{-5}
		Weibull	5.65×10^{-2}	2.04×10^{-2}	6.75×10^{-3}	2.69×10^{-3}
20	100,000	Generalized Gamma	5.08×10^{-2}	1.04×10^{-2}	9.50×10^{-4}	1.30×10^{-4}
		Gamma	5.07×10^{-2}	1.03×10^{-2}	9.40×10^{-4}	1.20×10^{-4}
		Log-normal	3.97×10^{-2}	4.52×10^{-3}	1.40×10^{-4}	0.00×10^0
		Chi-square	4.99×10^{-2}	9.85×10^{-3}	8.60×10^{-4}	1.10×10^{-4}
		Weibull	5.72×10^{-2}	1.90×10^{-2}	5.68×10^{-3}	1.73×10^{-3}
	300,000	Generalized Gamma	5.06×10^{-2}	9.91×10^{-3}	8.10×10^{-4}	6.00×10^{-5}
		Gamma	5.09×10^{-2}	1.01×10^{-2}	8.50×10^{-4}	6.00×10^{-5}
		Log-normal	4.53×10^{-2}	6.75×10^{-3}	3.20×10^{-4}	0.00×10^0
		Chi-square	5.04×10^{-2}	9.94×10^{-3}	8.30×10^{-4}	6.00×10^{-5}
		Weibull	5.64×10^{-2}	2.08×10^{-2}	6.38×10^{-3}	2.45×10^{-3}

Table S33: Advanced names of the 26 UKB blood biochemistry phenotypes. The sample size after quality control is 323,839 participants. The first column shows the abbreviation, the second column provides the UKB data field ID, the third column indicates the number of non-missing records available for analysis, and the fourth column provides the full name of each phenotype.

Abbr	UKB-field	Count	Description
ALT	30620	470,126	Alanine aminotransferase
ALB	30600	431,857	Albumin
ALP	30610	470,327	Alkaline phosphatase
ApoA	30630	429,312	Apolipoprotein A
ApoB	30640	467,984	Apolipoprotein B
AST	30650	468,579	Aspartate aminotransferase
CRP	30710	469,326	C-reactive protein
Ca	30680	431,708	Calcium
TC	30690	470,314	Total Cholesterol
Cr	30700	470,092	Creatinine
CysC	30720	470,285	Cystatin C
GGT	30730	470,072	Gamma glutamyltransferase
Glu	30740	431,364	Glucose
HbA1c	30750	467,390	Glycated haemoglobin (HbA1c)
HDL-C	30760	431,654	HDL cholesterol
IGF-1	30770	467,858	IGF-1
LDL-C	30780	469,477	LDL direct
P	30800	431,043	Phosphate
SHBG	30830	427,697	SHBG
T	30850	426,570	Testosterone
TBil	30840	468,356	Total bilirubin
TP	30860	431,390	Total protein
TG	30870	469,945	Triglycerides
UA	30880	469,765	Urate
Urea	30670	470,006	Urea
Vit D	30890	449,443	Vitamin D

Table S34: Multi-trait GWAS (RmvLMM) for 26 blood biochemistry phenotypes in 323,839 European-ancestry individuals from the UKB. Only significant SNPs (p -value $< 5 \times 10^{-8}$) are listed here.

CHR	POS	SNP	Major Allele	Minor Allele	MAF	p -value
1	16,482,976	rs6603883	G	A	0.3924	2.57×10^{-15}
1	16,505,908	rs4661718	T	C	0.3765	5.11×10^{-22}
1	16,534,255	rs221057	C	G	0.2599	1.84×10^{-12}
1	16,534,646	rs221058	C	G	0.2579	5.33×10^{-12}
1	16,582,686	rs1008529	A	G	0.2695	1.92×10^{-12}
1	16,731,510	rs525409	C	G	0.2392	1.64×10^{-10}
1	21,731,734	rs7555660	C	T	0.0865	1.69×10^{-14}
1	21,743,972	rs2316260	A	G	0.3850	1.95×10^{-12}
1	21,755,747	rs41310412	A	G	0.0732	3.15×10^{-11}
1	21,765,211	rs6680628	G	A	0.2311	3.62×10^{-33}
1	21,793,378	rs60515836	T	C	0.1522	2.31×10^{-15}
1	21,794,061	rs17420195	C	T	0.2178	6.30×10^{-33}
1	21,795,432	rs35175190	G	GA	0.1781	1.04×10^{-19}
1	21,797,204	rs72872292	G	C	0.0503	1.37×10^{-8}
1	21,800,219	rs10916996	T	C	0.2823	7.00×10^{-23}
1	21,817,365	rs75824579	A	G	0.1454	6.42×10^{-17}
1	21,820,961	rs10799699	T	C	0.4638	4.51×10^{-36}
1	21,821,757	rs1780324	G	A	0.4635	9.14×10^{-36}
1	21,826,530	rs115239632	C	T	0.0359	5.32×10^{-15}
1	21,839,690	rs975000	T	C	0.3037	1.79×10^{-11}
1	21,840,048	rs61778369	G	A	0.0709	4.01×10^{-11}
1	21,844,496	rs80320018	A	G	0.1456	8.26×10^{-23}
1	21,856,119	rs1697407	C	T	0.0402	1.13×10^{-9}
1	21,857,130	rs77936121	G	A	0.0360	5.21×10^{-12}
1	21,870,726	rs9662008	A	G	0.0621	5.88×10^{-25}
1	21,876,492	rs1256342	C	T	0.1473	1.60×10^{-25}
1	21,883,742	rs17421553	G	A	0.0498	6.58×10^{-10}
1	21,889,760	rs149344982	G	A	0.0138	3.22×10^{-46}
1	21,891,931	rs6656120	C	T	0.1092	5.42×10^{-20}
1	21,894,307	rs10917008	T	C	0.2827	5.24×10^{-10}
1	21,905,604	rs36053309	C	T	0.1964	5.56×10^{-12}
1	21,906,604	rs72659192	C	T	0.2040	2.05×10^{-34}
1	21,917,234	rs10917021	T	C	0.1204	1.43×10^{-13}
1	21,924,912	rs61775974	A	G	0.0401	2.51×10^{-8}
1	21,940,555	rs2275363	C	T	0.4500	4.65×10^{-12}
1	21,942,683	rs829416	T	C	0.1151	2.53×10^{-9}
1	21,952,884	rs1130564	G	A	0.0585	1.54×10^{-27}
1	21,953,026	rs12039278	A	C	0.1096	1.44×10^{-13}
1	21,957,666	rs116503681	C	T	0.0358	2.49×10^{-8}
1	21,959,957	rs72660339	G	A	0.1397	5.95×10^{-11}
1	21,968,741	rs78915636	C	T	0.0426	5.16×10^{-10}
1	25,293,356	rs4265380	C	T	0.4967	5.97×10^{-10}
1	25,303,576	rs10903122	G	A	0.4906	3.08×10^{-9}
1	27,001,711	rs34175245	A	G	0.0831	8.36×10^{-11}
1	27,017,325	rs35917448	C	T	0.0782	3.03×10^{-11}
1	27,019,744	rs12738345	T	C	0.0802	9.57×10^{-12}
1	27,037,154	rs12729444	T	G	0.0790	7.77×10^{-12}
1	27,079,931	rs12742115	T	C	0.0791	6.62×10^{-12}
1	27,138,393	rs12748152	C	T	0.0780	5.63×10^{-12}
1	27,239,920	rs6659176	C	G	0.0778	4.65×10^{-11}
1	27,272,600	rs145685168	A	ATCT	0.0814	2.29×10^{-10}
1	27,278,573	rs17360994	T	C	0.0778	3.25×10^{-11}
1	27,285,195	rs12742376	C	T	0.0776	4.85×10^{-11}
1	55,505,647	rs11591147	G	T	0.0170	4.65×10^{-24}
1	62,950,858	rs10889332	C	T	0.3559	4.69×10^{-30}
1	62,984,897	rs10889338	C	T	0.3522	3.11×10^{-30}

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Table S34: (Continued)

CHR	POS	SNP	Major Allele	Minor Allele	MAF	p-value
1	62,996,838	rs1168013	G	C	0.3602	5.53×10^{-31}
1	63,025,942	rs2131925	T	G	0.3617	9.07×10^{-31}
1	63,083,289	rs2031373	A	C	0.3799	3.48×10^{-15}
1	63,118,196	rs10889353	A	C	0.3494	7.36×10^{-30}
1	63,171,063	rs6682423	T	C	0.3605	2.52×10^{-29}
1	63,191,777	rs12130333	C	T	0.2117	7.25×10^{-18}
1	63,266,709	rs11208033	A	G	0.1652	7.07×10^{-9}
1	66,058,513	rs1137101	A	G	0.4447	6.08×10^{-13}
1	66,075,952	rs1805094	G	C	0.1689	8.84×10^{-11}
1	66,089,782	rs6700896	C	T	0.3819	3.90×10^{-33}
1	66,102,257	rs1805096	G	A	0.3746	1.40×10^{-33}
1	66,105,944	rs1892534	C	T	0.3788	2.59×10^{-33}
1	66,127,075	rs28788308	C	T	0.1918	2.62×10^{-14}
1	66,132,900	rs59677396	T	G	0.1914	5.55×10^{-14}
1	66,152,889	rs2375803	T	C	0.1678	1.13×10^{-10}
1	66,169,679	rs12753193	A	G	0.3729	1.61×10^{-32}
1	66,199,223	rs5010905	T	C	0.2656	1.22×10^{-14}
1	66,238,379	rs12046844	G	A	0.1864	8.51×10^{-9}
1	66,257,838	rs11208750	C	A	0.1947	1.90×10^{-8}
1	66,304,768	rs34280859	T	G	0.2365	1.93×10^{-9}
1	66,339,048	rs1316871	C	T	0.4789	9.20×10^{-9}
1	91,533,297	rs165316	A	G	0.1948	9.88×10^{-16}
1	107,546,375	rs17496332	A	G	0.3330	1.42×10^{-10}
1	107,573,565	rs2335077	A	G	0.3480	2.00×10^{-14}
1	107,599,918	rs2232016	C	T	0.2123	4.57×10^{-8}
1	109,757,295	rs4970829	G	A	0.0685	4.59×10^{-13}
1	109,789,795	rs585362	T	C	0.1595	4.85×10^{-14}
1	109,806,834	rs6698843	C	T	0.4499	3.38×10^{-16}
1	109,817,192	rs7528419	A	G	0.2226	1.65×10^{-41}
1	109,817,590	rs12740374	G	T	0.2232	4.05×10^{-42}
1	109,817,838	rs660240	C	T	0.2189	6.17×10^{-41}
1	109,818,306	rs629301	T	G	0.2261	8.94×10^{-42}
1	109,818,530	rs646776	T	C	0.2262	8.46×10^{-42}
1	109,820,884	rs11577931	A	G	0.0888	8.39×10^{-25}
1	109,839,400	rs55660224	C	T	0.0818	7.24×10^{-13}
1	110,232,983	rs140584594	G	A	0.2644	1.35×10^{-14}
1	110,470,764	rs333947	G	A	0.1507	2.07×10^{-12}
1	145,630,111	rs75246752	G	C	0.0123	2.81×10^{-16}
1	145,725,689	rs12129861	G	A	0.4638	9.91×10^{-10}
1	150,658,287	rs17599629	A	G	0.2249	2.76×10^{-8}
1	150,940,625	rs267738	T	G	0.2117	3.52×10^{-11}
1	150,951,477	rs267734	T	C	0.2093	2.35×10^{-11}
1	154,382,049	rs1386821	T	G	0.1992	6.41×10^{-9}
1	154,404,336	rs7549250	T	C	0.4241	7.74×10^{-11}
1	154,418,879	rs4537545	C	T	0.4179	4.39×10^{-23}
1	154,422,067	rs4845625	C	T	0.4236	1.74×10^{-12}
1	154,426,264	rs4129267	C	T	0.3993	3.36×10^{-24}
1	154,589,232	rs9427104	C	T	0.4724	7.26×10^{-10}
1	155,033,308	rs11589479	G	A	0.1605	8.05×10^{-10}
1	155,106,697	rs12904	G	A	0.4098	5.90×10^{-15}
1	155,132,836	rs12028043	A	G	0.4052	3.63×10^{-14}
1	155,140,648	rs11264339	C	T	0.4898	1.75×10^{-11}
1	155,151,493	rs11264341	C	T	0.4237	1.10×10^{-13}
1	155,162,067	rs4072037	T	C	0.4589	2.63×10^{-13}
1	155,178,782	rs760077	T	A	0.3956	4.91×10^{-16}
1	158,517,142	rs41273491	C	T	0.2308	2.19×10^{-16}
1	158,577,109	rs857685	A	C	0.2525	7.52×10^{-19}
1	158,612,548	rs857721	T	A	0.2624	7.30×10^{-20}
1	159,647,988	rs12093699	G	A	0.3004	1.40×10^{-33}

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Table S34: (Continued)

CHR	POS	SNP	Major Allele	Minor Allele	MAF	p-value
1	159,648,693	rs17459069	C	T	0.0382	4.21×10^{-8}
1	159,670,967	rs72698573	T	C	0.0823	5.34×10^{-11}
1	159,674,933	rs876537	C	T	0.3828	2.71×10^{-47}
1	159,678,816	rs2794520	C	T	0.3288	4.41×10^{-49}
1	159,682,233	rs1205	C	T	0.3263	7.10×10^{-49}
1	159,691,559	rs1341665	G	A	0.3367	8.43×10^{-48}
1	159,692,372	rs3116656	A	G	0.2981	9.20×10^{-38}
1	159,698,549	rs7553007	G	A	0.3278	2.68×10^{-49}
1	159,700,039	rs11265260	A	G	0.0597	7.52×10^{-33}
1	159,710,517	rs11265263	C	A	0.0674	3.07×10^{-37}
1	159,722,056	rs4131568	C	T	0.3277	1.19×10^{-26}
1	159,724,520	rs11265268	T	C	0.3880	5.63×10^{-11}
1	161,200,487	rs4073054	A	C	0.3644	3.74×10^{-9}
1	161,403,307	rs56383975	G	T	0.0998	3.04×10^{-24}
1	161,456,186	rs6698806	T	G	0.3393	1.16×10^{-14}
1	161,479,745	rs1801274	G	A	0.4711	6.45×10^{-14}
1	161,513,406	Affx-35410767	T	G	0.1002	4.38×10^{-12}
1	161,520,931	rs56199187	C	T	0.1146	1.64×10^{-33}
1	161,651,064	rs723177	C	T	0.2918	2.11×10^{-23}
1	161,653,554	rs114384494	C	T	0.0364	1.58×10^{-33}
1	161,655,516	rs12121021	C	T	0.3256	1.95×10^{-24}
1	161,671,306	rs61804211	G	T	0.1022	3.44×10^{-38}
1	161,673,859	rs61801160	C	G	0.0246	5.00×10^{-10}
1	182,168,885	rs1689800	A	G	0.3551	8.75×10^{-9}
1	220,970,028	rs2642438	G	A	0.2921	1.79×10^{-14}
1	220,973,563	rs2642442	T	C	0.3138	3.88×10^{-12}
1	221,030,589	rs10863570	T	C	0.2470	4.13×10^{-10}
1	221,053,545	rs12141189	T	C	0.2407	3.46×10^{-9}
1	221,091,157	rs1414518	T	C	0.2552	1.37×10^{-9}
1	230,279,582	rs4846905	G	A	0.1893	6.80×10^{-9}
1	234,858,597	rs514230	T	A	0.4710	3.92×10^{-8}
2	21,127,044	rs74629722	G	C	0.1172	6.62×10^{-13}
2	21,190,107	rs68093099	G	T	0.2783	3.15×10^{-9}
2	21,233,972	rs533617	T	C	0.0389	7.09×10^{-35}
2	21,233,999	rs1801699	T	C	0.0189	7.39×10^{-9}
2	21,249,716	rs12691202	C	T	0.0378	5.57×10^{-12}
2	21,276,008	rs72902579	T	C	0.0443	1.19×10^{-14}
2	21,359,828	rs312965	A	G	0.0525	3.76×10^{-8}
2	21,371,068	rs11687710	T	C	0.3226	1.64×10^{-15}
2	21,382,976	rs525172	G	T	0.1971	1.23×10^{-30}
2	21,400,661	rs12477249	G	A	0.3374	1.32×10^{-20}
2	21,402,957	rs1820914	C	T	0.1774	6.62×10^{-14}
2	21,406,568	rs484399	A	C	0.2482	6.33×10^{-28}
2	21,418,083	rs67599264	G	A	0.1943	7.53×10^{-30}
2	21,453,733	rs10166144	A	G	0.1308	2.08×10^{-15}
2	27,497,815	rs60631624	T	G	0.2112	1.25×10^{-8}
2	27,589,810	rs2280737	T	C	0.3917	3.42×10^{-19}
2	27,670,307	rs11126999	G	A	0.3887	6.37×10^{-19}
2	27,711,631	rs1260328	T	C	0.4194	7.52×10^{-16}
2	27,715,416	rs2303369	C	T	0.3885	1.72×10^{-19}
2	27,725,572	rs715325	C	A	0.3987	6.78×10^{-19}
2	27,730,940	rs1260326	C	T	0.3841	2.32×10^{-42}
2	27,741,237	rs780094	C	T	0.3754	1.31×10^{-40}
2	27,742,603	rs780093	C	T	0.3740	1.99×10^{-40}
2	27,743,154	rs780092	A	G	0.1652	7.66×10^{-22}
2	27,748,624	rs1260333	G	A	0.4291	1.87×10^{-35}
2	27,801,493	rs1919127	T	C	0.2528	8.06×10^{-29}
2	27,801,759	rs1919128	A	G	0.2513	1.78×10^{-29}
2	27,815,510	rs13022873	A	C	0.2517	1.58×10^{-28}

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Table S34: (Continued)

CHR	POS	SNP	Major Allele	Minor Allele	MAF	p-value
2	27,816,593	rs62138965	T	C	0.2115	4.75×10^{-17}
2	27,834,152	rs12987055	T	C	0.2503	1.92×10^{-29}
2	27,844,601	rs1881396	T	G	0.2157	3.78×10^{-17}
2	27,851,918	rs3749147	G	A	0.2446	2.04×10^{-28}
2	27,934,524	rs58199976	T	C	0.2642	2.00×10^{-18}
2	27,960,776	rs62139017	C	T	0.1189	2.81×10^{-12}
2	28,244,926	rs62140395	G	C	0.1110	1.18×10^{-11}
2	28,281,545	rs6547820	A	G	0.2191	2.69×10^{-11}
2	43,672,508	rs77059113	T	G	0.0703	1.31×10^{-10}
2	43,732,823	rs7578597	T	C	0.1117	1.88×10^{-8}
2	44,066,247	Affx-20090007	G	C	0.0650	1.65×10^{-8}
2	44,073,881	rs6544713	C	T	0.3138	4.39×10^{-8}
2	44,074,431	rs4245791	T	C	0.3162	9.81×10^{-9}
2	64,926,764	rs6756943	A	G	0.3022	1.49×10^{-8}
2	64,959,331	rs12994639	T	G	0.2397	2.40×10^{-8}
2	64,982,415	rs847803	G	A	0.3249	8.21×10^{-9}
2	97,396,403	rs68026712	T	C	0.3933	5.08×10^{-11}
2	97,423,626	rs968470	T	C	0.3877	1.07×10^{-10}
2	97,439,001	rs994430	A	T	0.3932	8.61×10^{-11}
2	97,454,650	rs6576983	T	G	0.3901	1.91×10^{-10}
2	113,841,030	rs6734238	A	G	0.3999	1.06×10^{-10}
2	121,306,440	rs17050272	G	A	0.4003	2.19×10^{-10}
2	165,545,615	rs75297654	C	T	0.1196	4.46×10^{-10}
2	165,555,539	rs79953491	A	G	0.1198	1.62×10^{-9}
2	169,757,354	rs1402837	C	T	0.2329	9.49×10^{-27}
2	169,779,712	rs496550	C	T	0.4628	3.57×10^{-26}
2	169,779,764	rs495714	T	C	0.4649	2.19×10^{-26}
2	169,789,016	rs497692	C	T	0.4661	1.90×10^{-26}
2	169,807,362	rs7558863	T	C	0.2176	2.32×10^{-21}
2	169,961,897	rs12328794	T	C	0.4955	1.32×10^{-10}
2	170,010,985	rs2075252	C	T	0.2397	7.60×10^{-9}
2	211,540,507	rs1047891	C	A	0.3135	4.70×10^{-27}
2	211,569,399	rs12613336	T	C	0.2061	2.59×10^{-14}
2	211,616,894	rs2216405	A	G	0.1725	3.10×10^{-13}
2	211,671,984	rs986294	G	A	0.2438	2.41×10^{-9}
2	227,093,745	rs2943641	C	T	0.3474	6.55×10^{-12}
2	227,099,180	rs2943645	T	C	0.3493	3.35×10^{-12}
2	227,116,365	rs2972143	G	A	0.3491	4.59×10^{-12}
2	227,125,254	rs2943659	A	G	0.3632	1.75×10^{-12}
2	227,179,630	rs925735	G	C	0.3562	1.81×10^{-10}
2	234,142,619	rs72974350	G	A	0.0434	8.12×10^{-15}
2	234,154,269	rs72974369	C	T	0.0447	1.59×10^{-14}
2	234,158,839	rs10210302	T	C	0.4820	5.64×10^{-14}
2	234,168,951	rs6758317	C	T	0.2036	6.99×10^{-11}
2	234,169,302	rs62192932	C	T	0.1809	1.54×10^{-33}
2	234,180,410	rs3828309	G	A	0.4816	1.48×10^{-13}
2	234,183,368	rs2241880	G	A	0.4808	4.11×10^{-14}
2	234,183,738	rs73998327	A	G	0.0724	5.16×10^{-21}
2	234,184,417	rs3792109	A	G	0.4792	1.42×10^{-13}
2	234,189,961	rs62192955	A	G	0.1122	6.14×10^{-23}
2	234,199,537	rs6431262	T	G	0.3003	2.30×10^{-9}
2	234,211,048	rs6431270	A	G	0.3128	5.77×10^{-16}
2	234,219,952	rs80271431	G	A	0.0315	1.40×10^{-11}
2	234,227,523	rs2304777	G	A	0.2657	1.10×10^{-13}
2	234,229,295	rs72976383	C	T	0.0322	3.07×10^{-25}
2	234,229,320	rs7565275	A	G	0.0518	3.02×10^{-14}
2	234,229,926	rs61062196	T	G	0.1023	2.37×10^{-10}
2	234,231,401	rs78936963	A	G	0.0260	3.88×10^{-27}
2	234,245,384	rs75560791	G	A	0.0659	5.32×10^{-16}

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Table S34: (Continued)

CHR	POS	SNP	Major Allele	Minor Allele	MAF	p-value
2	234,246,503	rs57592542	C	T	0.0515	1.75×10^{-12}
2	234,255,547	rs1046974	G	A	0.4084	4.23×10^{-25}
2	234,272,484	rs1441093	G	A	0.2426	4.02×10^{-30}
2	234,273,242	rs838705	A	G	0.3882	3.12×10^{-38}
2	234,277,638	rs74448524	G	A	0.0402	1.12×10^{-26}
2	234,287,822	rs77900844	G	A	0.0334	2.48×10^{-16}
2	234,289,895	rs838713	C	G	0.3944	6.00×10^{-19}
2	234,311,271	rs114252547	T	G	0.0353	8.90×10^{-23}
2	234,315,394	rs78447894	A	C	0.0583	3.69×10^{-20}
2	234,321,058	rs115604196	A	G	0.0199	2.06×10^{-13}
2	234,325,052	rs838737	A	G	0.4294	1.17×10^{-20}
2	234,326,071	rs72980341	T	C	0.0282	5.20×10^{-22}
2	234,329,140	rs74608404	A	G	0.0333	3.71×10^{-28}
2	234,329,549	rs2971868	C	T	0.3779	4.41×10^{-23}
2	234,356,623	rs72980357	C	T	0.0365	2.69×10^{-33}
2	234,358,286	rs2242100	T	C	0.3462	3.73×10^{-27}
2	234,359,375	rs72980361	A	G	0.0948	1.25×10^{-29}
2	234,373,701	rs116663413	C	T	0.0286	9.11×10^{-16}
2	234,375,944	rs2305540	C	T	0.3079	7.58×10^{-28}
2	234,386,134	rs2971863	A	G	0.2121	1.58×10^{-15}
2	234,394,111	rs62192762	G	A	0.0389	1.17×10^{-15}
2	234,394,569	rs2603547	A	G	0.2117	2.47×10^{-15}
2	234,406,655	rs6704644	G	T	0.0984	2.07×10^{-38}
2	234,407,420	rs114099762	G	C	0.0267	2.74×10^{-32}
2	234,417,564	rs111712352	C	T	0.0396	9.31×10^{-31}
2	234,429,739	rs141501074	T	TTTC	0.2058	1.60×10^{-15}
2	234,432,017	rs838543	A	G	0.2070	4.07×10^{-15}
2	234,449,316	rs2167884	A	G	0.2071	2.73×10^{-15}
2	234,475,415	rs62192778	G	A	0.1541	6.28×10^{-35}
2	234,482,250	rs13002399	T	C	0.2314	7.65×10^{-23}
2	234,500,290	rs17862831	G	A	0.1111	3.80×10^{-36}
2	234,526,871	Affx-36452635	C	G	0.2506	1.76×10^{-46}
2	234,536,637	rs1377460	G	A	0.1957	6.53×10^{-23}
2	234,545,294	rs11683356	G	A	0.0326	9.34×10^{-42}
2	234,545,861	rs17854828	C	T	0.1581	9.06×10^{-42}
2	234,553,314	rs2602372	A	C	0.0270	8.87×10^{-40}
2	234,563,065	rs114346341	A	G	0.0280	5.91×10^{-39}
2	234,565,283	rs11892031	A	C	0.0909	2.11×10^{-40}
2	234,567,916	rs1112310	G	T	0.2607	5.52×10^{-48}
2	234,578,693	rs6731242	T	G	0.1756	1.47×10^{-42}
2	234,584,324	rs2602381	C	T	0.4598	1.59×10^{-69}
2	234,590,527	rs7586110	T	G	0.3838	2.09×10^{-78}
2	234,593,117	rs4261716	G	T	0.4053	6.58×10^{-78}
2	234,601,669	rs6759892	T	G	0.4064	4.65×10^{-78}
2	234,601,965	rs1105880	A	G	0.3415	1.16×10^{-85}
2	234,602,191	rs2070959	A	G	0.3184	$< 1.00 \times 10^{-85}$
2	234,602,202	rs1105879	A	C	0.3403	1.54×10^{-85}
2	234,621,787	rs3755322	C	G	0.0877	3.19×10^{-11}
2	234,621,825	rs3755321	T	C	0.0874	2.08×10^{-11}
2	234,622,110	rs12475068	C	G	0.0854	4.19×10^{-11}
2	234,622,310	rs17862867	C	T	0.0872	3.46×10^{-11}
2	234,638,006	rs17868336	A	G	0.0478	1.86×10^{-43}
2	234,639,656	rs17868337	G	A	0.0222	3.80×10^{-11}
2	234,652,308	rs34622615	G	T	0.0306	3.76×10^{-48}
2	234,657,512	rs17862876	G	T	0.0171	1.93×10^{-33}
2	234,661,537	rs76026343	G	A	0.0276	1.72×10^{-41}
2	234,665,782	rs10929302	G	A	0.2886	$< 1.00 \times 10^{-85}$
2	234,668,570	rs887829	C	T	0.3195	$< 1.00 \times 10^{-85}$
2	234,672,639	rs6742078	G	T	0.3181	$< 1.00 \times 10^{-85}$

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Table S34: (Continued)

CHR	POS	SNP	Major Allele	Minor Allele	MAF	p-value
2	234,673,309	rs4148325	C	T	0.3183	$< 1.00 \times 10^{-85}$
2	234,681,416	rs10929303	C	T	0.2142	7.51×10^{-34}
2	234,681,544	rs1042640	C	G	0.1992	8.06×10^{-34}
2	234,681,645	rs8330	C	G	0.2278	1.79×10^{-34}
2	234,685,650	rs115836766	G	A	0.0414	2.87×10^{-11}
2	234,688,036	rs6431631	A	C	0.2087	1.40×10^{-36}
2	234,689,090	rs4663335	G	A	0.1544	1.15×10^{-36}
2	234,698,790	rs2361502	T	C	0.2897	3.69×10^{-73}
2	234,700,578	rs10170160	T	C	0.3743	4.25×10^{-20}
2	234,701,664	rs75235703	A	C	0.0486	2.37×10^{-18}
2	234,702,459	rs1500481	C	T	0.4508	1.02×10^{-9}
2	234,704,076	rs17864714	G	A	0.0379	1.14×10^{-19}
2	234,712,921	rs10175949	A	G	0.1239	1.56×10^{-31}
2	234,713,681	rs79208193	G	T	0.0464	2.12×10^{-16}
2	234,717,448	rs12053445	T	G	0.4608	1.62×10^{-12}
2	234,725,502	rs726016	C	T	0.1434	1.78×10^{-17}
2	234,728,078	rs1500480	C	T	0.1531	2.37×10^{-22}
2	234,730,104	rs17863818	A	G	0.0519	6.77×10^{-10}
2	234,737,125	rs17862901	G	A	0.1584	6.96×10^{-16}
2	234,740,136	rs879665	G	A	0.1344	4.24×10^{-21}
2	234,741,401	rs2270854	C	T	0.0626	1.24×10^{-19}
2	234,741,443	rs213548	G	A	0.3633	3.66×10^{-9}
2	234,749,258	rs10511	T	C	0.0942	3.20×10^{-9}
2	234,749,354	rs12582	G	A	0.0946	2.05×10^{-9}
2	234,750,831	rs3806589	C	T	0.3992	2.10×10^{-11}
2	234,751,581	rs6431641	G	T	0.3978	6.43×10^{-11}
2	234,775,346	rs13384181	G	A	0.0788	5.63×10^{-16}
2	234,854,540	rs13004520	G	C	0.0466	7.15×10^{-12}
2	234,854,552	rs17868387	A	G	0.0470	2.74×10^{-12}
2	234,871,343	rs10929321	A	G	0.3300	2.37×10^{-9}
3	12,269,266	rs13066322	C	T	0.4184	3.93×10^{-9}
3	12,301,893	rs35939242	A	C	0.3319	8.78×10^{-10}
3	58,397,102	rs62258127	G	A	0.3635	9.06×10^{-16}
3	58,410,554	rs34579268	C	T	0.3615	6.81×10^{-16}
3	121,869,044	rs73184035	A	C	0.1260	1.07×10^{-11}
3	121,904,211	rs7628990	G	T	0.1528	5.79×10^{-10}
3	121,950,136	rs4300957	C	T	0.1754	1.11×10^{-8}
3	121,963,285	rs1979869	C	T	0.3133	5.23×10^{-14}
3	122,003,757	rs1801725	G	T	0.1298	4.32×10^{-45}
3	122,011,154	rs10934581	C	T	0.3416	7.23×10^{-24}
3	122,011,351	rs13085674	G	A	0.3172	4.25×10^{-28}
3	122,051,183	rs73186059	T	C	0.1437	2.59×10^{-41}
3	122,060,404	Affx-21056635	C	T	0.1290	3.98×10^{-38}
3	122,066,887	rs112613540	A	G	0.0532	8.44×10^{-11}
3	122,125,052	rs6768280	G	A	0.4217	5.70×10^{-24}
3	122,128,394	rs1127343	A	G	0.4134	9.64×10^{-20}
3	122,145,470	rs17201246	C	A	0.1411	5.94×10^{-33}
3	122,174,804	rs12488797	T	G	0.2615	1.92×10^{-15}
3	122,177,260	rs116555124	C	T	0.0347	1.58×10^{-16}
3	122,178,602	rs12487598	T	C	0.4198	1.01×10^{-23}
3	122,230,869	rs7638174	A	G	0.2623	1.16×10^{-15}
3	122,233,647	rs28384492	C	T	0.1042	2.59×10^{-25}
3	122,259,640	rs28365795	T	C	0.1410	4.02×10^{-33}
3	122,270,446	rs77732258	G	T	0.0151	7.15×10^{-12}
3	122,277,268	rs34006803	G	A	0.1031	3.00×10^{-25}
3	123,065,778	rs11708067	A	G	0.2380	1.81×10^{-12}
3	123,094,451	rs2877716	C	T	0.2618	1.47×10^{-10}
3	123,095,312	rs6798189	G	A	0.2592	7.42×10^{-11}
3	123,131,254	Affx-21069786	C	T	0.2654	2.45×10^{-9}

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Table S34: (Continued)

CHR	POS	SNP	Major Allele	Minor Allele	MAF	p-value
3	135,926,622	rs645040	T	G	0.2281	1.55×10^{-18}
3	135,926,784	rs61789562	T	C	0.1157	7.06×10^{-10}
3	135,956,305	rs684773	C	A	0.2312	1.18×10^{-17}
3	136,069,286	rs1145101	C	T	0.1823	1.13×10^{-12}
3	136,109,696	rs61789642	C	T	0.1226	2.75×10^{-9}
3	136,272,805	rs7612160	C	A	0.3422	2.21×10^{-8}
3	136,356,464	rs9845762	T	C	0.2894	3.01×10^{-13}
3	136,489,602	rs71336078	G	A	0.1442	4.05×10^{-9}
3	136,581,611	rs71630059	G	A	0.2061	7.91×10^{-9}
3	170,631,635	rs55692140	A	G	0.0788	9.63×10^{-9}
3	170,649,749	rs6770420	G	A	0.3685	2.17×10^{-13}
3	170,724,955	rs5404	C	T	0.1011	7.58×10^{-11}
3	172,165,727	rs572169	C	T	0.3089	1.36×10^{-9}
3	187,713,718	rs10937329	T	A	0.3098	6.42×10^{-9}
3	187,717,540	rs4686914	C	T	0.3102	5.98×10^{-9}
4	3,446,091	rs3748034	G	T	0.1394	4.80×10^{-11}
4	3,447,243	rs16844383	C	T	0.1680	1.01×10^{-8}
4	3,449,652	rs16844401	G	A	0.0651	5.10×10^{-10}
4	3,473,139	rs6831256	A	G	0.4270	7.44×10^{-12}
4	9,511,324	rs11737509	G	A	0.0222	1.53×10^{-10}
4	9,635,408	rs10014826	T	C	0.1341	3.44×10^{-13}
4	9,671,025	rs73084845	C	T	0.1356	6.39×10^{-12}
4	9,693,253	rs7678732	C	T	0.0395	2.71×10^{-8}
4	9,766,888	rs1878943	C	T	0.1904	7.63×10^{-21}
4	9,809,859	rs12500086	A	G	0.1939	8.51×10^{-23}
4	9,849,528	rs2176644	C	T	0.2151	2.72×10^{-36}
4	9,895,070	rs7698858	T	C	0.2495	5.66×10^{-36}
4	9,916,133	rs75181558	A	G	0.0192	6.32×10^{-31}
4	9,917,484	rs34213329	C	G	0.0221	1.11×10^{-27}
4	9,921,931	rs6823877	C	T	0.3511	2.80×10^{-53}
4	9,922,170	rs73225891	C	G	0.0258	1.15×10^{-14}
4	9,946,163	rs16891234	T	C	0.2151	1.07×10^{-21}
4	9,956,079	rs4481233	C	T	0.1872	1.89×10^{-68}
4	9,959,267	rs79323395	A	G	0.0595	4.17×10^{-16}
4	9,966,380	rs7442295	A	G	0.2204	8.12×10^{-69}
4	9,978,142	rs62295971	A	G	0.4815	4.82×10^{-56}
4	9,992,862	rs62296002	C	T	0.0488	4.55×10^{-16}
4	9,995,182	rs3775948	C	G	0.2483	2.74×10^{-68}
4	10,050,141	rs733175	T	C	0.1814	7.90×10^{-59}
4	10,056,376	rs7671266	C	T	0.2150	1.89×10^{-64}
4	10,061,147	rs75341455	C	T	0.0291	1.57×10^{-31}
4	10,065,873	rs35150828	G	A	0.2878	1.97×10^{-38}
4	10,094,042	rs34517659	G	A	0.0579	3.12×10^{-16}
4	10,104,670	rs717615	A	G	0.4739	7.38×10^{-47}
4	10,135,421	rs10009765	T	C	0.4043	2.37×10^{-17}
4	10,145,794	rs4484300	G	A	0.4401	1.15×10^{-22}
4	10,148,122	rs74475455	C	A	0.0170	4.47×10^{-21}
4	10,149,784	rs4697717	C	G	0.1963	6.71×10^{-59}
4	10,152,302	rs4697939	G	A	0.0167	4.02×10^{-21}
4	10,173,019	rs4697952	G	A	0.3999	6.78×10^{-9}
4	10,182,836	rs115602652	A	C	0.0129	7.57×10^{-14}
4	10,204,421	rs74912465	G	T	0.0101	5.66×10^{-11}
4	10,209,873	rs76696560	C	T	0.0180	3.18×10^{-22}
4	10,235,622	rs2080072	G	C	0.4536	5.78×10^{-48}
4	10,240,806	rs74534386	G	A	0.0149	6.31×10^{-26}
4	10,291,550	rs114695316	G	A	0.0317	2.26×10^{-31}
4	10,293,246	rs11725910	G	T	0.0752	2.55×10^{-45}
4	10,296,114	rs6839820	T	C	0.3371	2.72×10^{-41}
4	10,302,359	rs73224420	G	A	0.0662	8.87×10^{-14}

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Table S34: (Continued)

CHR	POS	SNP	Major Allele	Minor Allele	MAF	p-value
4	10,304,641	rs4698022	C	A	0.1152	5.24×10^{-52}
4	10,304,726	rs4698023	A	G	0.2116	4.27×10^{-60}
4	10,316,350	rs17477692	A	G	0.0166	4.13×10^{-12}
4	10,324,160	rs9291683	G	A	0.4803	4.79×10^{-43}
4	10,328,335	rs79020759	A	G	0.0246	2.32×10^{-20}
4	10,331,294	rs4698036	T	G	0.2156	3.35×10^{-60}
4	10,331,887	rs74453475	C	G	0.0181	3.47×10^{-22}
4	10,335,496	rs75816008	C	T	0.0325	3.12×10^{-29}
4	10,350,765	rs17420450	T	C	0.1346	1.36×10^{-30}
4	10,360,091	rs76835013	G	T	0.0756	9.78×10^{-24}
4	10,370,537	rs62286747	C	T	0.0513	3.31×10^{-14}
4	10,387,559	rs10020891	C	A	0.4366	2.72×10^{-15}
4	10,407,572	rs4643800	G	T	0.2103	2.89×10^{-56}
4	10,439,114	rs80139786	C	G	0.0267	2.54×10^{-10}
4	10,446,906	rs10016022	G	A	0.2602	8.98×10^{-20}
4	10,447,168	rs66538112	C	G	0.2604	6.83×10^{-20}
4	10,452,986	rs5028371	C	G	0.4940	3.18×10^{-18}
4	10,473,180	rs114359078	T	C	0.0106	4.45×10^{-9}
4	10,493,961	rs13115661	C	T	0.0729	3.62×10^{-19}
4	10,498,830	rs6819820	G	A	0.4292	4.30×10^{-9}
4	10,499,344	rs12504795	T	C	0.2762	9.38×10^{-24}
4	10,514,681	rs16869379	T	C	0.3161	2.55×10^{-20}
4	10,524,671	rs997219	G	A	0.4494	1.60×10^{-15}
4	10,544,125	rs76356518	A	G	0.0206	3.70×10^{-15}
4	69,306,774	rs34041362	T	G	0.2635	1.67×10^{-8}
4	69,342,169	rs983745	G	C	0.4149	1.18×10^{-8}
4	69,343,287	rs976002	A	G	0.2418	9.25×10^{-11}
4	69,536,084	rs1902023	A	C	0.4764	1.81×10^{-10}
4	72,572,374	rs395371	G	A	0.3254	5.91×10^{-19}
4	72,594,801	rs13117483	C	T	0.2615	2.75×10^{-16}
4	72,608,383	rs2282679	T	G	0.2852	4.62×10^{-52}
4	72,618,323	rs4588	G	T	0.2865	1.94×10^{-52}
4	72,632,642	rs75774690	C	T	0.0480	5.59×10^{-13}
4	72,639,207	rs62302166	T	G	0.0594	4.22×10^{-21}
4	72,639,282	rs62302167	C	T	0.2831	1.51×10^{-48}
4	72,682,451	rs114360759	G	A	0.0300	5.87×10^{-9}
4	72,718,873	rs12504112	T	C	0.1926	1.09×10^{-21}
4	72,751,722	rs6814839	A	G	0.0696	2.38×10^{-12}
4	72,755,840	rs10010987	A	G	0.2549	3.86×10^{-15}
4	72,786,422	rs13108630	T	C	0.0630	3.91×10^{-10}
4	77,278,251	rs7677266	G	A	0.2568	3.66×10^{-12}
4	77,305,346	rs17001890	A	G	0.2564	2.41×10^{-12}
4	77,364,799	rs4859673	G	A	0.2517	7.40×10^{-16}
4	77,440,333	rs11097396	C	G	0.2542	6.21×10^{-10}
4	88,160,018	rs10006766	A	G	0.2319	2.28×10^{-9}
4	88,186,509	rs7694379	G	A	0.4249	3.22×10^{-11}
4	88,188,514	rs13130929	G	A	0.2798	1.28×10^{-11}
4	88,231,392	rs72613567	T	TA	0.2686	1.64×10^{-11}
4	88,591,554	rs114791459	G	A	0.0190	1.40×10^{-8}
4	89,020,934	rs4148157	G	A	0.0975	1.02×10^{-35}
4	89,039,622	rs45570646	T	C	0.0224	2.19×10^{-10}
4	89,052,323	rs2231142	G	T	0.1130	2.29×10^{-44}
4	89,064,581	rs3114018	C	A	0.4644	2.01×10^{-26}
4	89,068,455	rs17731799	G	T	0.4661	3.66×10^{-29}
4	89,078,924	rs2622604	C	T	0.2472	3.15×10^{-15}
4	89,083,666	rs3114020	T	C	0.4642	4.35×10^{-30}
4	89,126,647	rs7672194	C	T	0.4604	4.08×10^{-15}
4	89,249,061	rs4693211	T	C	0.0642	1.07×10^{-11}
4	100,045,616	rs1126673	T	C	0.2944	9.78×10^{-11}

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Table S34: (Continued)

CHR	POS	SNP	Major Allele	Minor Allele	MAF	p-value
4	100,047,812	rs1126672	G	A	0.2672	1.32×10^{-8}
4	100,048,414	rs1126671	C	T	0.2947	1.08×10^{-10}
4	100,052,733	rs1126670	A	C	0.2939	1.67×10^{-10}
4	102,926,923	rs34592089	G	A	0.0598	5.21×10^{-10}
4	103,188,709	rs13107325	C	T	0.0726	2.25×10^{-14}
4	103,283,117	rs34333163	A	G	0.0688	2.35×10^{-8}
4	144,659,515	rs5016159	G	A	0.3200	2.61×10^{-8}
4	144,682,019	rs17018200	C	A	0.3171	4.50×10^{-8}
4	144,878,907	rs6537214	A	G	0.3060	1.35×10^{-9}
4	144,879,189	rs7662736	T	C	0.3062	1.31×10^{-9}
4	144,908,114	rs1877235	A	G	0.3022	4.78×10^{-9}
4	144,913,903	rs75270861	G	A	0.3072	3.24×10^{-9}
4	145,011,740	rs35793856	G	A	0.3093	3.48×10^{-8}
4	145,024,799	rs6844670	A	G	0.3457	8.40×10^{-9}
4	146,794,621	rs4547811	T	C	0.1683	2.94×10^{-21}
4	146,797,543	rs56293839	C	T	0.1693	2.08×10^{-21}
4	146,821,410	rs4835265	C	A	0.1589	2.84×10^{-22}
5	31,020,521	rs6888304	A	G	0.2790	4.39×10^{-9}
5	40,626,753	rs11955175	T	C	0.0708	5.97×10^{-15}
5	40,681,254	rs2228058	C	T	0.0708	1.25×10^{-15}
5	40,821,816	rs75929994	T	C	0.0698	8.85×10^{-14}
5	52,193,125	rs4074793	A	G	0.0741	1.30×10^{-8}
5	55,438,580	rs6859219	C	A	0.2006	2.12×10^{-11}
5	55,444,683	rs7731626	G	A	0.3666	8.57×10^{-12}
5	55,806,751	rs459193	G	A	0.2592	7.36×10^{-9}
5	55,807,370	rs464605	T	C	0.2601	7.03×10^{-9}
5	55,861,894	rs9687846	G	A	0.1990	2.00×10^{-8}
5	74,576,285	rs7722186	G	A	0.4158	1.70×10^{-8}
5	74,615,021	rs17671591	C	T	0.3449	6.89×10^{-9}
5	74,625,487	rs7703051	C	A	0.3775	1.92×10^{-10}
5	74,648,603	rs12654264	A	T	0.3761	1.93×10^{-10}
5	74,655,726	rs3846663	C	T	0.3731	1.12×10^{-10}
5	74,656,539	rs12916	T	C	0.3989	2.78×10^{-11}
5	156,383,422	rs1363232	G	A	0.3402	1.81×10^{-14}
5	156,398,169	rs1501908	C	G	0.3680	1.22×10^{-15}
5	168,256,240	rs4282339	G	A	0.2060	2.80×10^{-8}
5	176,784,512	rs4075958	G	A	0.2593	2.11×10^{-11}
5	176,784,612	rs4075959	G	A	0.2848	5.19×10^{-10}
5	176,794,191	rs12654812	G	A	0.3425	7.13×10^{-10}
5	176,798,306	rs11746443	G	A	0.2556	1.20×10^{-10}
5	176,806,636	rs35716097	C	T	0.3021	6.69×10^{-10}
5	176,817,636	rs6420094	A	G	0.3112	2.14×10^{-11}
6	7,211,818	rs1334576	G	A	0.4245	2.92×10^{-8}
6	24,315,442	rs72830895	A	G	0.0627	4.60×10^{-8}
6	24,401,654	rs9393553	G	T	0.2765	3.04×10^{-11}
6	24,418,348	rs2793422	G	A	0.3522	4.06×10^{-8}
6	24,425,447	rs41271779	G	A	0.1527	5.33×10^{-22}
6	24,441,746	rs9467160	G	A	0.2954	4.89×10^{-28}
6	24,464,429	rs78420872	C	A	0.1033	5.67×10^{-21}
6	24,484,957	rs7765515	G	A	0.1302	4.23×10^{-21}
6	24,489,652	rs1126617	C	T	0.3463	2.06×10^{-25}
6	24,489,741	rs2076316	A	C	0.3799	2.25×10^{-20}
6	24,499,551	rs7775073	A	G	0.3460	2.19×10^{-16}
6	24,503,590	rs2760118	C	T	0.3503	7.99×10^{-15}
6	24,506,316	rs72834956	A	C	0.2916	6.05×10^{-12}
6	24,533,505	rs2744601	G	C	0.1622	7.20×10^{-10}
6	24,544,903	rs699463	G	A	0.2783	4.55×10^{-16}
6	24,551,664	rs807534	T	C	0.1464	5.53×10^{-9}
6	25,488,583	rs2274089	C	T	0.0938	1.19×10^{-9}

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Table S34: (Continued)

CHR	POS	SNP	Major Allele	Minor Allele	MAF	p-value
6	25,641,200	rs932316	T	C	0.1907	2.68×10^{-10}
6	25,818,588	rs1185567	G	A	0.4229	2.30×10^{-22}
6	25,820,428	rs6913879	T	C	0.2656	1.49×10^{-12}
6	25,821,770	rs17342717	C	T	0.0997	1.05×10^{-16}
6	25,826,119	rs6456703	C	T	0.2528	1.15×10^{-12}
6	25,831,603	rs1185569	G	A	0.4435	1.66×10^{-21}
6	25,840,485	rs6905614	A	C	0.4526	1.62×10^{-21}
6	25,840,946	rs1408273	G	A	0.4610	4.76×10^{-22}
6	25,842,605	rs9393672	G	T	0.4611	4.03×10^{-22}
6	25,842,951	rs1408272	T	G	0.0750	1.05×10^{-20}
6	25,843,746	rs3887266	C	T	0.1136	1.27×10^{-13}
6	25,850,845	rs56027330	C	T	0.1157	1.77×10^{-13}
6	25,859,554	rs1182814	T	C	0.2543	1.22×10^{-12}
6	25,862,466	rs1165165	C	T	0.2384	1.28×10^{-10}
6	25,863,605	rs1165162	C	T	0.2545	1.78×10^{-12}
6	25,863,650	rs17271121	T	C	0.1150	1.88×10^{-13}
6	25,864,362	rs1165161	C	T	0.2532	1.24×10^{-12}
6	25,864,625	rs1165159	A	G	0.2545	1.07×10^{-12}
6	25,864,898	rs1165158	C	A	0.2540	2.31×10^{-12}
6	25,870,542	rs1165205	A	T	0.4406	5.78×10^{-21}
6	25,870,745	rs556339	C	T	0.2615	3.76×10^{-12}
6	25,876,089	rs12664474	A	G	0.1658	9.16×10^{-14}
6	25,878,361	rs566530	C	T	0.4744	8.12×10^{-22}
6	25,890,834	rs9348697	C	T	0.3675	3.89×10^{-11}
6	25,914,572	rs2071300	T	C	0.4833	1.32×10^{-14}
6	25,918,225	rs80215559	T	C	0.0727	1.84×10^{-23}
6	25,919,549	rs9467636	A	C	0.3916	2.23×10^{-13}
6	25,945,211	rs2051541	G	A	0.4834	7.98×10^{-16}
6	25,969,958	rs1436310	G	C	0.4376	2.91×10^{-12}
6	26,027,135	rs3752420	G	A	0.4012	5.64×10^{-13}
6	26,091,179	rs1799945	C	G	0.1465	4.89×10^{-17}
6	26,125,342	rs129128	T	C	0.1351	2.97×10^{-14}
6	32,565,979	rs28383172	A	G	0.1441	1.56×10^{-8}
6	32,574,014	rs2647073	A	C	0.1447	1.91×10^{-8}
6	32,585,500	rs28383249	C	T	0.1430	3.94×10^{-8}
6	32,628,698	rs9273529	C	T	0.2501	3.85×10^{-11}
6	32,634,467	rs3891175	C	T	0.2486	7.46×10^{-11}
6	33,647,095	rs57642896	A	G	0.0491	4.09×10^{-16}
6	33,706,479	rs9469578	C	T	0.0723	4.15×10^{-25}
6	43,811,762	rs9472138	C	T	0.2852	3.34×10^{-9}
6	74,463,894	rs6909201	G	A	0.4808	8.69×10^{-11}
6	74,493,432	rs10455097	C	A	0.4813	3.04×10^{-11}
6	127,436,313	rs1936801	G	A	0.4745	3.76×10^{-9}
6	127,452,639	rs9491696	C	G	0.4868	9.36×10^{-10}
6	127,452,935	rs2745353	T	C	0.4793	1.02×10^{-8}
6	127,472,624	rs6932207	A	G	0.4777	2.06×10^{-9}
6	127,476,516	rs1892172	A	G	0.4535	1.98×10^{-8}
6	127,490,524	rs4620145	A	G	0.4778	1.25×10^{-9}
6	127,493,611	rs6569474	T	A	0.4536	2.43×10^{-8}
6	135,411,228	rs9376090	T	C	0.2500	4.05×10^{-11}
6	135,418,635	rs7775698	C	T	0.2565	3.46×10^{-10}
6	135,422,296	rs11759553	A	T	0.2708	2.41×10^{-8}
6	135,426,573	rs4895441	A	G	0.2637	1.85×10^{-9}
6	135,427,144	rs9376092	C	A	0.2667	2.92×10^{-9}
6	135,427,817	rs9402686	G	A	0.2633	2.19×10^{-10}
6	160,564,476	rs662138	C	G	0.1815	3.32×10^{-9}
6	160,668,389	rs2279463	A	G	0.1394	1.69×10^{-10}
6	160,670,282	rs316019	C	A	0.1036	1.38×10^{-9}
6	160,997,118	rs74617384	A	T	0.0731	3.41×10^{-12}

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Table S34: (Continued)

CHR	POS	SNP	Major Allele	Minor Allele	MAF	p-value
6	161,010,118	rs10455872	A	G	0.0751	1.52×10^{-12}
7	17,284,577	rs4410790	C	T	0.3751	1.30×10^{-8}
7	44,223,721	rs730497	G	A	0.1766	8.57×10^{-29}
7	44,229,068	rs1799884	C	T	0.1766	1.06×10^{-28}
7	44,231,216	rs3757840	T	G	0.4893	3.21×10^{-20}
7	44,231,886	rs6975024	T	C	0.1750	3.92×10^{-28}
7	44,235,668	rs4607517	G	A	0.1748	4.24×10^{-28}
7	44,247,258	rs3824065	C	T	0.4176	1.06×10^{-15}
7	46,008,110	rs11977526	G	A	0.4027	1.80×10^{-8}
7	46,719,105	rs35640690	T	C	0.2640	3.21×10^{-24}
7	46,753,553	rs700752	G	C	0.3446	1.68×10^{-31}
7	46,760,129	rs856554	T	C	0.2433	3.46×10^{-14}
7	46,785,285	rs12537178	G	A	0.1815	7.63×10^{-18}
7	50,305,863	rs4917014	T	G	0.3121	2.07×10^{-8}
7	72,854,549	rs71556711	C	T	0.0873	3.93×10^{-26}
7	72,856,269	rs2240466	G	A	0.1212	8.87×10^{-31}
7	72,856,430	rs1178979	T	C	0.1959	1.84×10^{-28}
7	72,864,869	rs714052	A	G	0.1221	1.27×10^{-30}
7	72,878,645	rs12056034	A	G	0.1221	2.07×10^{-30}
7	72,904,810	rs17145713	C	T	0.1959	1.78×10^{-28}
7	72,971,231	rs13233571	C	T	0.1212	2.22×10^{-31}
7	72,982,874	rs17145738	C	T	0.1214	2.41×10^{-31}
7	72,987,354	rs2286276	C	T	0.2809	3.19×10^{-27}
7	73,007,943	rs1051921	G	A	0.1932	2.90×10^{-29}
7	73,012,042	rs35332062	G	A	0.1261	4.45×10^{-32}
7	73,020,301	rs799157	C	T	0.0421	3.60×10^{-9}
7	73,020,337	rs3812316	C	G	0.1262	1.78×10^{-32}
7	73,026,378	rs17145750	C	T	0.1587	2.81×10^{-31}
7	73,043,101	rs34958196	G	A	0.1313	4.18×10^{-30}
7	73,048,095	rs13230514	A	G	0.2856	7.74×10^{-21}
7	73,060,006	rs799160	C	T	0.4908	2.78×10^{-10}
7	97,868,033	rs17169479	C	T	0.1629	7.20×10^{-15}
7	97,993,362	rs3779195	T	A	0.1852	1.45×10^{-18}
7	98,042,527	rs7783611	A	G	0.3273	9.08×10^{-10}
7	99,332,948	rs45446698	T	G	0.0382	3.99×10^{-9}
7	130,585,492	rs157934	T	C	0.3037	2.39×10^{-13}
7	151,397,343	rs6947064	A	G	0.3629	2.43×10^{-9}
7	151,407,801	rs7805747	G	A	0.2711	8.64×10^{-19}
8	9,177,732	rs983309	G	T	0.1201	1.66×10^{-28}
8	9,178,268	rs6984305	T	A	0.1161	8.73×10^{-29}
8	9,183,358	rs9987289	G	A	0.0932	4.66×10^{-33}
8	9,184,691	rs6601299	C	T	0.1005	3.11×10^{-31}
8	9,185,146	rs2126259	C	T	0.1029	1.84×10^{-31}
8	9,201,787	rs11782386	C	T	0.1107	1.77×10^{-24}
8	9,211,723	rs11779870	G	A	0.1130	1.05×10^{-24}
8	9,239,958	rs11786900	G	C	0.0983	3.11×10^{-15}
8	18,272,438	rs4921914	T	C	0.2222	2.60×10^{-9}
8	18,273,300	rs1495743	C	G	0.2222	2.50×10^{-9}
8	19,727,047	rs1441778	T	C	0.1574	4.99×10^{-8}
8	19,777,695	rs75218485	C	T	0.0228	1.38×10^{-11}
8	19,805,708	rs1801177	G	A	0.0175	4.20×10^{-11}
8	19,813,180	rs264	G	A	0.1417	5.06×10^{-21}
8	19,813,529	rs268	A	G	0.0173	6.40×10^{-19}
8	19,813,702	rs271	G	A	0.1443	1.04×10^{-19}
8	19,816,238	rs295	A	C	0.2372	4.23×10^{-31}
8	19,816,934	rs301	T	C	0.2325	9.98×10^{-31}
8	19,819,077	rs320	T	G	0.2703	1.60×10^{-29}
8	19,819,328	rs325	T	C	0.1006	1.69×10^{-34}
8	19,819,439	rs326	A	G	0.2968	2.23×10^{-31}

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Table S34: (Continued)

CHR	POS	SNP	Major Allele	Minor Allele	MAF	p-value
8	19,819,724	rs328	C	G	0.1005	1.69×10^{-34}
8	19,822,809	Affx-52343806	GC	G	0.1058	2.00×10^{-33}
8	19,824,492	rs13702	T	C	0.2890	1.29×10^{-32}
8	19,824,667	rs15285	C	T	0.2890	4.26×10^{-33}
8	19,826,373	rs2197089	A	G	0.4484	3.30×10^{-18}
8	19,832,646	rs17482753	G	T	0.1000	3.55×10^{-34}
8	19,844,222	rs12678919	A	G	0.0979	2.47×10^{-33}
8	19,845,376	rs7841189	C	T	0.1196	5.37×10^{-33}
8	19,847,690	rs10503669	C	A	0.0967	3.43×10^{-33}
8	19,849,757	rs17091905	G	A	0.1240	1.20×10^{-32}
8	19,855,344	rs17489373	G	A	0.2638	3.31×10^{-31}
8	19,863,803	rs186868868	C	A	0.0158	1.37×10^{-8}
8	19,865,175	rs2083637	A	G	0.2630	1.98×10^{-31}
8	19,876,746	rs7016880	G	C	0.0994	4.57×10^{-33}
8	19,890,612	rs10103634	G	A	0.3226	6.30×10^{-15}
8	19,907,912	rs11991231	T	C	0.1041	2.61×10^{-33}
8	19,941,027	rs11204087	C	T	0.4230	5.58×10^{-14}
8	19,974,789	rs74737417	C	G	0.0606	3.22×10^{-8}
8	23,751,151	rs10109414	C	T	0.4051	1.12×10^{-10}
8	41,542,093	rs34265667	G	A	0.0326	9.46×10^{-16}
8	41,543,675	rs34664882	G	A	0.0329	6.12×10^{-16}
8	59,388,565	rs2081687	C	T	0.3328	8.03×10^{-9}
8	118,184,783	rs13266634	C	T	0.3062	3.64×10^{-12}
8	118,185,025	rs3802177	G	A	0.3048	1.02×10^{-11}
8	118,185,733	rs11558471	A	G	0.3125	3.29×10^{-12}
8	126,477,978	rs2001945	C	G	0.4738	8.45×10^{-28}
8	126,479,315	rs6982636	G	A	0.4674	1.72×10^{-26}
8	126,479,362	rs6982502	T	C	0.4706	5.82×10^{-28}
8	126,481,952	rs2954020	G	A	0.3117	1.18×10^{-21}
8	126,484,526	rs2954026	G	T	0.2969	1.56×10^{-22}
8	126,486,409	rs17321515	A	G	0.4740	1.14×10^{-27}
8	126,493,746	rs2954033	G	A	0.2963	1.31×10^{-22}
8	126,507,389	rs2954038	A	C	0.2948	3.72×10^{-24}
9	15,289,578	rs471364	T	C	0.1140	1.28×10^{-9}
9	15,296,034	rs643531	A	C	0.1320	3.42×10^{-13}
9	71,434,707	rs4744712	C	A	0.3971	3.37×10^{-8}
9	107,629,336	rs13301006	C	T	0.1503	3.79×10^{-8}
9	107,647,655	rs3890182	G	A	0.1215	9.42×10^{-11}
9	107,653,426	rs12686004	G	A	0.1159	2.31×10^{-11}
9	107,657,070	rs3905000	G	A	0.1386	2.19×10^{-10}
9	107,664,301	rs1883025	C	T	0.2594	8.01×10^{-18}
9	107,665,739	rs2575876	G	A	0.2547	4.54×10^{-18}
9	107,666,414	rs2254819	T	C	0.4751	3.78×10^{-9}
9	131,465,481	rs13283282	C	G	0.1444	5.54×10^{-9}
9	131,497,832	rs3750329	C	T	0.1269	4.80×10^{-8}
9	136,042,264	rs7868232	T	C	0.2396	1.84×10^{-20}
9	136,049,780	rs6597604	A	G	0.2882	4.58×10^{-27}
9	136,081,319	rs11244035	C	T	0.1008	8.08×10^{-36}
9	136,131,347	rs8176745	G	A	0.2425	1.65×10^{-21}
9	136,131,437	rs8176742	C	T	0.2397	2.30×10^{-21}
9	136,131,472	rs8176740	A	T	0.2416	1.37×10^{-20}
9	136,132,908	rs8176719	T	TC	0.3389	2.78×10^{-54}
9	136,133,506	rs512770	G	A	0.2085	2.17×10^{-21}
9	136,134,472	rs638756	A	C	0.2469	5.83×10^{-22}
9	136,135,238	Affx-33347130	C	T	0.2451	1.59×10^{-21}
9	136,136,770	rs688976	C	A	0.2452	1.22×10^{-21}
9	136,137,065	rs687621	A	G	0.3211	1.65×10^{-55}
9	136,139,265	rs657152	C	A	0.3410	5.45×10^{-54}
9	136,142,355	rs643434	G	A	0.3424	7.29×10^{-54}

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Table S34: (Continued)

CHR	POS	SNP	Major Allele	Minor Allele	MAF	p-value
9	136,143,442	rs612169	A	G	0.3215	1.29×10^{-55}
9	136,147,702	rs581107	T	C	0.4653	3.52×10^{-40}
9	136,149,229	rs505922	T	C	0.3183	7.57×10^{-56}
9	136,149,399	rs507666	G	A	0.1786	1.05×10^{-58}
9	136,153,875	rs651007	C	T	0.2026	6.40×10^{-56}
9	136,154,168	rs579459	T	C	0.2026	7.09×10^{-56}
9	136,191,010	rs11244084	C	T	0.0696	2.85×10^{-34}
9	136,208,044	rs621907	C	T	0.0762	2.74×10^{-9}
9	136,237,672	rs56343119	C	A	0.1351	2.30×10^{-43}
9	136,268,037	Affx-52371914	ACGCTGGGC	A	0.4217	3.64×10^{-8}
9	136,270,538	rs41302673	T	G	0.0875	1.11×10^{-36}
9	136,317,767	rs117164445	C	T	0.0150	8.47×10^{-9}
9	136,323,845	rs4962050	G	C	0.3152	2.65×10^{-15}
9	136,340,200	rs2073935	G	T	0.2725	8.91×10^{-28}
9	136,350,150	Affx-33350288	C	T	0.2740	6.52×10^{-11}
9	136,359,599	rs73553519	C	T	0.0925	2.97×10^{-17}
9	136,371,224	rs9330459	G	T	0.0381	5.28×10^{-14}
9	139,327,599	rs71269007	G	GCGCCCACCCCT CCAGCCA	0.3092	3.81×10^{-8}
9	139,378,914	rs34376913	T	C	0.2575	5.06×10^{-9}
10	5,138,036	rs2518049	G	A	0.1733	6.42×10^{-9}
10	5,247,784	rs3829125	C	G	0.1502	1.06×10^{-13}
10	5,254,847	rs1832007	A	G	0.1482	8.18×10^{-14}
10	5,257,647	rs75406471	G	A	0.1505	2.34×10^{-13}
10	5,260,682	rs17134592	C	G	0.1495	2.47×10^{-13}
10	9,328,651	rs10491003	C	T	0.0912	1.42×10^{-12}
10	17,634,752	rs4748388	A	C	0.2289	7.40×10^{-15}
10	17,674,369	rs73603824	T	A	0.1066	3.28×10^{-17}
10	17,682,090	rs61842261	A	G	0.2278	9.14×10^{-10}
10	17,682,941	rs12416367	A	G	0.1202	5.75×10^{-15}
10	17,745,996	rs2688787	A	G	0.2091	1.35×10^{-11}
10	17,748,172	rs2688786	A	G	0.2424	1.07×10^{-12}
10	17,806,504	rs143235698	A	G	0.1758	3.52×10^{-30}
10	17,845,995	rs117163080	T	C	0.1365	6.56×10^{-36}
10	17,856,444	rs118160793	A	G	0.1698	5.64×10^{-26}
10	17,875,857	rs56278466	G	T	0.3378	2.02×10^{-48}
10	17,877,539	rs56096309	C	A	0.1141	9.32×10^{-11}
10	17,889,190	rs141682912	T	C	0.2309	6.11×10^{-25}
10	18,056,696	rs56278220	G	A	0.1186	6.39×10^{-13}
10	18,087,629	rs199734634	CTG	C	0.2138	3.38×10^{-32}
10	18,103,401	rs75921639	C	T	0.3542	5.99×10^{-36}
10	18,112,620	rs187269912	A	G	0.0998	1.77×10^{-10}
10	18,125,222	rs149076262	A	G	0.0940	7.87×10^{-12}
10	18,136,543	rs55942822	G	A	0.1390	5.76×10^{-40}
10	18,138,488	Affx-52324238	AC	A	0.2185	2.77×10^{-43}
10	18,227,444	rs483809	A	G	0.1981	3.01×10^{-22}
10	18,242,311	rs10764176	A	G	0.3021	1.61×10^{-16}
10	18,266,989	rs2478568	A	G	0.3581	1.69×10^{-11}
10	18,281,176	rs58377250	T	C	0.1411	6.34×10^{-17}
10	18,282,427	rs2478571	G	A	0.2977	1.67×10^{-20}
10	18,291,222	rs41277356	A	G	0.0242	1.48×10^{-11}
10	61,413,353	rs12356193	A	G	0.1619	1.73×10^{-10}
10	61,449,564	rs7094971	A	G	0.1453	7.82×10^{-9}
10	61,450,121	rs35209863	T	C	0.1452	1.01×10^{-8}
10	61,465,838	rs1171619	G	A	0.2111	7.12×10^{-13}
10	64,761,387	rs72820803	C	T	0.3155	4.35×10^{-8}
10	64,822,828	rs4746855	G	A	0.4061	5.13×10^{-16}
10	64,829,314	rs10822120	T	C	0.4012	5.30×10^{-16}
10	64,840,665	rs7904321	G	A	0.4025	6.22×10^{-16}

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Table S34: (Continued)

CHR	POS	SNP	Major Allele	Minor Allele	MAF	p-value
10	64,872,411	rs10822136	C	T	0.2265	2.22×10^{-13}
10	64,927,823	rs1935	C	G	0.4708	5.28×10^{-40}
10	65,006,456	rs6479891	C	T	0.1435	3.52×10^{-20}
10	65,027,610	rs10761731	A	T	0.4179	4.73×10^{-37}
10	65,048,306	rs7080386	C	A	0.4151	1.03×10^{-36}
10	65,058,224	rs12773283	T	C	0.1515	2.47×10^{-20}
10	65,101,207	rs10740118	G	C	0.4175	4.67×10^{-37}
10	65,106,551	rs7081275	T	G	0.1437	4.11×10^{-20}
10	65,126,832	rs6479896	T	C	0.4711	4.27×10^{-40}
10	65,133,156	rs2393967	A	C	0.3079	1.17×10^{-26}
10	65,133,822	rs7923609	A	G	0.4718	3.46×10^{-40}
10	65,172,328	rs10761756	C	T	0.4669	2.45×10^{-39}
10	65,261,184	rs2893923	C	T	0.3109	3.55×10^{-27}
10	65,274,927	rs10761779	A	G	0.4716	5.46×10^{-40}
10	65,275,214	rs117212080	T	C	0.0510	5.05×10^{-11}
10	65,315,397	rs12411988	G	C	0.1379	3.47×10^{-19}
10	65,315,433	rs10740134	T	C	0.4776	4.77×10^{-39}
10	65,323,809	rs10733793	T	G	0.4836	2.96×10^{-38}
10	65,328,326	rs113803069	C	T	0.1402	1.46×10^{-8}
10	65,337,153	rs10822184	T	C	0.4934	1.54×10^{-37}
10	65,376,395	rs7076601	G	A	0.3209	1.20×10^{-14}
10	65,392,260	rs12246748	C	T	0.3027	1.39×10^{-11}
10	71,025,852	rs7919018	A	G	0.3166	3.16×10^{-8}
10	71,062,762	rs4746839	A	G	0.0762	3.36×10^{-20}
10	71,093,392	rs16926246	C	T	0.1286	2.05×10^{-55}
10	71,099,913	rs7072268	C	T	0.4864	8.08×10^{-28}
10	71,124,228	rs7909192	G	A	0.3632	3.96×10^{-31}
10	71,138,133	rs10128330	C	T	0.0432	6.99×10^{-14}
10	79,665,173	rs55910200	T	C	0.2461	1.35×10^{-10}
10	79,682,918	rs12220902	C	T	0.2479	1.23×10^{-10}
10	94,839,642	rs2068888	G	A	0.4530	6.01×10^{-16}
10	101,190,520	rs2862614	A	G	0.0867	7.93×10^{-9}
10	101,213,280	rs2494657	T	C	0.4625	1.02×10^{-9}
10	113,913,222	rs2297991	C	T	0.2791	1.24×10^{-12}
10	113,933,886	rs2255141	G	A	0.2687	8.04×10^{-13}
10	113,940,329	rs2792751	C	T	0.2682	4.87×10^{-13}
10	114,756,041	rs4506565	A	T	0.3136	1.57×10^{-16}
10	114,758,349	rs7903146	C	T	0.2843	1.34×10^{-18}
10	114,788,815	rs12243326	T	C	0.2808	9.77×10^{-15}
10	114,808,902	rs12255372	G	T	0.2843	1.31×10^{-14}
10	126,445,630	rs4962696	G	A	0.2599	1.01×10^{-9}
11	2,149,864	rs11042751	T	C	0.2349	2.00×10^{-12}
11	2,170,143	Affx-4739950	G	A	0.3827	6.37×10^{-13}
11	2,181,073	rs3842752	G	A	0.2198	1.79×10^{-9}
11	14,282,877	rs72632971	T	C	0.0738	6.01×10^{-10}
11	14,285,900	rs4756786	C	A	0.3077	1.11×10^{-10}
11	14,303,975	rs1431374	T	C	0.3084	1.11×10^{-10}
11	14,380,998	rs11023197	G	A	0.3479	1.20×10^{-14}
11	14,616,038	rs11023265	C	T	0.3395	1.37×10^{-20}
11	14,679,247	rs1879888	A	G	0.4975	4.69×10^{-15}
11	14,747,297	rs73412653	T	C	0.0882	9.84×10^{-9}
11	14,903,636	rs11023374	T	C	0.2610	1.03×10^{-17}
11	14,912,417	rs7129781	T	C	0.0795	1.79×10^{-11}
11	14,914,878	rs10741657	G	A	0.3980	1.59×10^{-31}
11	14,915,310	rs2060793	G	A	0.4006	3.91×10^{-31}
11	14,922,950	rs1553006	G	A	0.4475	3.14×10^{-19}
11	30,754,837	rs55733296	G	A	0.0370	5.39×10^{-10}
11	47,354,787	rs1052373	C	T	0.3280	1.73×10^{-10}
11	47,623,890	rs12363232	C	T	0.3378	2.79×10^{-8}

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Table S34: (Continued)

CHR	POS	SNP	Major Allele	Minor Allele	MAF	p-value
11	61,531,443	rs10792318	A	G	0.2454	4.12×10^{-8}
11	61,599,347	rs61897793	G	A	0.1817	1.73×10^{-15}
11	61,605,215	rs2072114	A	G	0.1238	3.25×10^{-19}
11	61,609,750	rs174583	C	T	0.3499	5.01×10^{-31}
11	61,617,676	rs174591	T	A	0.2679	9.39×10^{-21}
11	61,627,811	rs174609	T	C	0.4650	4.12×10^{-17}
11	62,199,817	rs17157266	T	C	0.1785	4.33×10^{-8}
11	64,331,462	rs17300741	G	A	0.4593	4.55×10^{-20}
11	64,333,296	rs1783811	G	A	0.3025	1.25×10^{-8}
11	65,506,822	rs4014195	C	G	0.3391	3.90×10^{-10}
11	65,549,570	rs11227299	C	G	0.3390	1.87×10^{-10}
11	65,551,648	rs11604462	G	A	0.3397	5.70×10^{-11}
11	65,552,154	rs948493	C	T	0.3378	2.14×10^{-10}
11	71,122,820	rs72961181	C	T	0.2083	4.41×10^{-17}
11	71,182,901	rs11233800	G	A	0.0391	1.53×10^{-8}
11	75,451,187	rs11821808	C	T	0.0993	2.74×10^{-8}
11	75,455,021	rs499974	C	A	0.1607	1.64×10^{-9}
11	92,673,828	rs1387153	C	T	0.2931	6.65×10^{-13}
11	92,681,013	rs10830956	C	T	0.2799	3.26×10^{-11}
11	92,691,532	rs2166706	T	C	0.3924	1.14×10^{-8}
11	116,520,434	rs506222	A	C	0.0993	1.38×10^{-21}
11	116,532,314	rs1145188	G	A	0.2358	4.90×10^{-8}
11	116,607,437	rs1558861	T	C	0.0695	6.69×10^{-43}
11	116,619,073	rs28927680	C	G	0.0675	1.16×10^{-35}
11	116,626,258	rs11825181	G	A	0.0672	3.34×10^{-35}
11	116,633,862	rs11820589	G	A	0.0667	9.01×10^{-36}
11	116,643,436	Affx-4282707	G	T	0.3901	8.21×10^{-11}
11	116,648,917	rs964184	C	G	0.1350	4.41×10^{-53}
11	116,649,135	rs11823543	G	A	0.0666	1.75×10^{-35}
11	116,652,207	rs12286037	C	T	0.0659	3.72×10^{-35}
11	116,653,296	rs2075290	T	C	0.0712	8.82×10^{-44}
11	116,654,435	rs603446	C	T	0.4431	2.11×10^{-18}
11	116,655,600	rs35120633	G	A	0.0600	1.04×10^{-37}
11	116,660,686	rs2266788	A	G	0.0693	1.72×10^{-44}
11	116,662,407	rs3135506	G	C	0.0609	4.93×10^{-38}
11	116,673,315	rs12791103	G	T	0.0999	1.06×10^{-9}
11	116,673,464	rs61905132	C	T	0.0233	1.30×10^{-20}
11	116,692,293	rs12721043	C	A	0.0106	1.25×10^{-11}
11	116,693,871	rs12721041	C	T	0.0152	3.87×10^{-11}
11	116,705,719	rs12718462	T	C	0.0661	2.52×10^{-11}
11	116,728,630	rs12225230	G	C	0.1734	5.47×10^{-28}
11	116,762,829	rs75158858	G	A	0.1048	1.99×10^{-21}
11	116,780,567	rs75188049	G	A	0.0327	1.32×10^{-11}
11	116,883,777	rs61905706	G	T	0.1342	2.44×10^{-21}
11	116,963,897	rs7950381	C	A	0.1344	1.55×10^{-21}
11	116,978,627	rs116943892	A	G	0.0321	2.15×10^{-10}
11	117,030,633	Affx-52324980	T	TC	0.0576	1.74×10^{-9}
11	117,042,408	rs186808413	C	T	0.0105	3.92×10^{-12}
11	117,065,476	rs1784042	G	A	0.4056	2.45×10^{-15}
11	117,076,972	rs45574931	A	C	0.0607	2.92×10^{-8}
11	117,084,410	rs79278568	G	A	0.0324	2.45×10^{-10}
11	117,100,029	rs4938362	G	A	0.1535	5.86×10^{-11}
11	117,101,311	rs74988348	C	T	0.0328	2.21×10^{-9}
11	117,175,658	rs116987336	G	A	0.0242	2.10×10^{-16}
11	122,522,375	rs7941030	T	C	0.3827	1.27×10^{-10}
11	126,218,541	rs17135399	A	G	0.0651	3.52×10^{-9}
11	126,219,396	rs35887873	T	C	0.2251	2.11×10^{-9}
11	126,226,775	rs73632737	G	C	0.0763	1.71×10^{-11}
11	126,243,952	rs11220462	G	A	0.1311	3.15×10^{-11}

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Table S34: (Continued)

CHR	POS	SNP	Major Allele	Minor Allele	MAF	p-value
11	126,278,203	rs2298475	T	C	0.0738	4.98×10^{-8}
11	126,281,897	rs4937126	G	A	0.3155	1.28×10^{-10}
11	126,285,301	rs7949566	G	A	0.4264	3.88×10^{-14}
12	2,908,330	rs56196860	C	A	0.0296	4.04×10^{-8}
12	4,597,481	rs10849081	A	C	0.1872	4.48×10^{-11}
12	4,606,168	rs2970818	T	A	0.1011	5.21×10^{-19}
12	4,635,045	rs11063214	A	G	0.1206	6.17×10^{-19}
12	20,908,165	rs10841614	G	A	0.3397	2.11×10^{-13}
12	20,915,109	rs2090274	C	T	0.3412	1.29×10^{-13}
12	21,038,609	rs74528913	G	A	0.0239	2.96×10^{-9}
12	21,320,501	rs73062310	C	T	0.0131	7.34×10^{-16}
12	21,329,813	rs11045819	C	A	0.1546	3.51×10^{-17}
12	21,331,549	rs4149056	T	C	0.1476	5.72×10^{-37}
12	21,368,722	rs4363657	T	C	0.1635	4.99×10^{-36}
12	21,379,398	rs7966581	G	A	0.3429	5.13×10^{-12}
12	21,382,619	rs11045879	T	C	0.1621	3.20×10^{-36}
12	21,392,562	rs4149087	T	G	0.4039	8.22×10^{-10}
12	21,392,819	rs11045893	T	C	0.1797	4.69×10^{-16}
12	21,468,230	rs73069053	A	G	0.0159	7.30×10^{-16}
12	21,487,544	rs10841795	A	G	0.1271	1.21×10^{-8}
12	48,416,023	rs11168359	G	A	0.1266	1.08×10^{-11}
12	48,512,285	rs4760682	A	C	0.1819	4.58×10^{-18}
12	111,522,000	rs16941230	A	C	0.0347	1.42×10^{-8}
12	111,800,258	rs3809272	G	A	0.2975	1.96×10^{-8}
12	121,075,606	rs2859266	C	A	0.2472	6.19×10^{-13}
12	121,122,676	rs57830821	C	T	0.1471	3.05×10^{-25}
12	121,138,350	Affx-7006664	T	G	0.0263	3.55×10^{-8}
12	121,162,854	rs2948149	T	G	0.3970	4.41×10^{-8}
12	121,371,233	rs868795	C	T	0.2098	5.86×10^{-10}
12	121,374,264	rs2133638	C	T	0.3336	3.48×10^{-29}
12	121,388,962	rs2650000	C	A	0.3363	4.73×10^{-48}
12	121,402,932	rs7305618	C	T	0.2350	4.02×10^{-32}
12	121,403,724	rs7953249	A	G	0.4126	8.57×10^{-51}
12	121,416,864	rs1800574	C	T	0.0295	3.87×10^{-14}
12	121,416,988	rs2244608	A	G	0.3174	1.06×10^{-50}
12	121,420,430	rs1169282	C	T	0.0256	5.47×10^{-11}
12	121,420,807	rs1183910	G	A	0.3086	8.10×10^{-52}
12	121,423,956	rs2393791	T	C	0.3799	1.38×10^{-53}
12	121,423,998	rs2245407	C	A	0.0735	1.24×10^{-10}
12	121,424,861	rs7310409	G	A	0.3813	7.37×10^{-54}
12	121,432,114	Affx-52326773	CG	C	0.2967	6.49×10^{-30}
12	121,435,587	rs2259816	G	T	0.3505	1.49×10^{-49}
12	121,437,113	Affx-80247044	C	A	0.1851	1.90×10^{-28}
12	121,437,114	rs55834942	G	A	0.1849	2.09×10^{-28}
12	121,438,844	rs735396	T	C	0.3518	1.44×10^{-49}
12	121,439,433	rs1169310	G	A	0.3511	1.46×10^{-49}
12	121,454,257	rs2258227	A	T	0.1901	2.70×10^{-14}
12	121,454,622	rs1182933	C	T	0.2936	1.01×10^{-47}
12	121,458,400	rs12819210	C	T	0.1831	2.56×10^{-15}
12	121,460,686	rs7957197	T	A	0.1870	1.27×10^{-28}
12	121,470,256	rs10849829	G	A	0.4369	3.24×10^{-38}
12	121,476,423	rs10774580	G	A	0.3878	2.51×10^{-24}
12	121,489,377	rs10849835	C	T	0.1306	1.42×10^{-20}
12	121,579,024	rs17434647	T	G	0.1185	3.27×10^{-11}
13	95,258,944	rs6492721	C	T	0.3192	2.79×10^{-10}
13	113,358,584	rs282578	C	T	0.1241	5.25×10^{-9}
14	94,795,492	rs4905179	A	G	0.2013	2.00×10^{-8}
14	94,838,142	rs112635299	G	T	0.0192	3.23×10^{-27}
14	94,844,947	rs28929474	C	T	0.0186	1.75×10^{-28}

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Table S34: (Continued)

CHR	POS	SNP	Major Allele	Minor Allele	MAF	p-value
14	103,484,784	rs35030701	G	A	0.0340	4.54×10^{-11}
14	103,530,768	rs62006938	C	T	0.3821	5.51×10^{-13}
14	103,563,195	rs8017161	G	A	0.3998	2.84×10^{-32}
14	103,566,785	rs2297067	C	T	0.2428	2.07×10^{-36}
14	103,566,835	rs2297066	C	G	0.2414	1.01×10^{-35}
14	103,572,815	rs944002	A	G	0.2467	6.97×10^{-36}
14	103,603,570	Affx-10131553	G	T	0.1053	5.50×10^{-11}
15	42,683,787	rs2412710	G	A	0.0188	5.73×10^{-11}
15	43,622,265	rs3742970	C	A	0.0945	3.17×10^{-9}
15	43,820,717	rs55707100	C	T	0.0248	7.90×10^{-25}
15	45,702,799	rs3737267	A	G	0.0723	3.25×10^{-10}
15	45,902,779	rs12909221	T	C	0.4303	1.67×10^{-8}
15	58,674,695	rs4775041	G	C	0.2959	4.15×10^{-32}
15	58,678,512	rs10468017	C	T	0.2880	3.87×10^{-34}
15	58,680,643	rs35853021	G	T	0.3610	4.05×10^{-34}
15	58,680,954	rs2043085	C	T	0.3938	2.63×10^{-34}
15	58,683,366	rs1532085	G	A	0.3899	1.69×10^{-34}
15	58,686,338	rs16940174	G	A	0.1371	1.62×10^{-9}
15	58,689,187	rs11855284	T	C	0.1938	1.10×10^{-28}
15	58,700,311	rs17240869	T	C	0.2019	1.77×10^{-26}
15	58,712,945	rs11854656	A	C	0.3296	1.06×10^{-15}
15	58,724,706	rs11632618	G	A	0.0668	1.22×10^{-15}
15	58,725,986	rs17269250	T	G	0.0155	4.73×10^{-8}
15	58,726,744	rs261334	C	G	0.2132	5.23×10^{-34}
15	58,742,418	rs261336	A	G	0.1640	1.80×10^{-25}
15	60,878,030	rs340005	A	G	0.3769	3.72×10^{-15}
15	60,883,281	rs339969	A	C	0.3820	1.17×10^{-15}
15	60,931,471	rs1054156	C	T	0.4304	6.35×10^{-9}
15	96,693,928	rs12437483	T	C	0.1995	1.50×10^{-10}
15	96,708,291	rs8023580	T	C	0.2778	1.48×10^{-16}
15	96,712,226	rs4984514	T	G	0.1954	8.07×10^{-13}
16	20,361,087	rs111285796	T	TTCTGCCAGA	0.1795	3.78×10^{-11}
16	20,364,588	rs4293393	A	G	0.1843	1.47×10^{-11}
16	20,365,654	rs13333226	A	G	0.1872	2.02×10^{-11}
16	20,367,690	rs12917707	G	T	0.1753	2.83×10^{-11}
16	20,388,929	rs35208507	A	G	0.3060	4.33×10^{-8}
16	20,400,839	rs11864909	C	T	0.2807	6.82×10^{-9}
16	51,158,710	rs10521222	C	T	0.0468	5.80×10^{-13}
16	51,436,882	rs17616063	A	G	0.0715	1.78×10^{-24}
16	51,450,938	rs118106133	C	T	0.0220	3.82×10^{-8}
16	56,811,692	rs8062292	T	C	0.3142	3.69×10^{-12}
16	56,859,897	rs74765290	A	G	0.0520	1.14×10^{-8}
16	56,873,840	rs2304477	G	A	0.1675	2.23×10^{-16}
16	56,883,924	rs735144	A	G	0.4322	7.70×10^{-13}
16	56,899,006	rs4784733	T	C	0.3002	4.89×10^{-20}
16	56,900,931	rs13306673	C	T	0.0920	1.07×10^{-18}
16	56,908,045	rs13330096	C	T	0.2035	5.15×10^{-16}
16	56,918,125	rs35797045	C	A	0.0449	2.52×10^{-13}
16	56,920,146	rs55901950	G	A	0.0816	1.02×10^{-10}
16	56,933,519	rs11643718	G	A	0.1034	1.58×10^{-11}
16	56,969,148	rs2217332	G	A	0.1408	2.24×10^{-17}
16	56,985,139	rs9989419	G	A	0.3956	2.90×10^{-46}
16	56,985,555	rs12448528	G	A	0.2163	1.44×10^{-47}
16	56,988,044	rs173539	C	T	0.3280	1.58×10^{-60}
16	56,989,590	rs247616	C	T	0.3203	3.17×10^{-62}
16	56,990,716	rs247617	C	A	0.3183	3.90×10^{-62}
16	56,991,524	rs6499862	G	A	0.1573	3.21×10^{-23}
16	56,991,624	rs28888131	G	A	0.1898	1.92×10^{-45}
16	56,993,324	rs3764261	C	A	0.3174	2.39×10^{-61}

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Table S34: (Continued)

CHR	POS	SNP	Major Allele	Minor Allele	MAF	p-value
16	56,994,894	rs4783961	A	G	0.4939	4.25×10^{-35}
16	56,995,236	rs1800775	C	A	0.4894	1.12×10^{-58}
16	56,996,288	rs708272	G	A	0.4249	5.53×10^{-58}
16	56,997,233	rs1864163	G	A	0.2608	7.61×10^{-57}
16	57,002,732	rs9939224	G	T	0.2115	5.22×10^{-56}
16	57,005,479	rs1532624	C	A	0.4264	1.43×10^{-56}
16	57,006,590	rs7499892	C	T	0.1832	2.28×10^{-57}
16	57,007,353	rs5883	C	T	0.0529	8.65×10^{-23}
16	57,008,508	rs289715	T	A	0.1232	4.78×10^{-26}
16	57,010,232	rs56208677	C	T	0.0650	2.22×10^{-28}
16	57,015,091	rs5880	G	C	0.0543	1.37×10^{-42}
16	57,017,319	rs1800777	G	A	0.0379	2.37×10^{-40}
16	57,021,433	rs12934552	A	G	0.1328	6.89×10^{-11}
16	57,033,696	rs1875236	G	A	0.1062	4.69×10^{-9}
16	57,161,020	rs117892711	C	T	0.0179	3.18×10^{-8}
16	58,752,466	rs11076256	C	T	0.0824	7.35×10^{-15}
16	67,928,042	rs16942887	G	A	0.1176	4.65×10^{-8}
16	72,078,907	rs1424241	G	A	0.1750	7.62×10^{-9}
16	79,703,829	rs4243177	G	A	0.3725	2.47×10^{-10}
16	79,711,336	rs74037508	T	C	0.3284	7.21×10^{-14}
16	79,744,548	rs17767419	C	T	0.3079	4.26×10^{-16}
16	79,749,353	rs3813582	T	C	0.3078	5.10×10^{-16}
16	79,925,400	rs28384289	C	T	0.1487	1.44×10^{-8}
16	88,516,940	rs904800	A	G	0.4275	8.72×10^{-11}
16	88,541,140	rs7196578	C	T	0.3368	1.73×10^{-11}
16	88,853,729	Affx-13430005	T	C	0.4429	7.26×10^{-13}
17	1,618,363	rs11078597	T	C	0.1898	4.14×10^{-17}
17	1,623,675	rs1574525	A	G	0.2763	1.70×10^{-12}
17	1,640,793	rs8077638	C	T	0.2209	2.97×10^{-15}
17	1,648,502	rs2070863	C	T	0.2215	1.15×10^{-15}
17	7,080,316	rs55714927	C	T	0.1871	6.16×10^{-26}
17	7,091,650	rs314253	T	C	0.3485	1.94×10^{-16}
17	7,101,292	rs3826408	C	T	0.4528	7.36×10^{-12}
17	7,124,506	rs77680021	G	A	0.0947	4.48×10^{-14}
17	7,133,162	rs222836	A	G	0.4842	1.50×10^{-8}
17	7,273,063	rs8066451	C	T	0.4066	3.01×10^{-9}
17	7,285,723	rs34768933	T	C	0.1051	4.52×10^{-8}
17	7,303,143	rs56206519	G	A	0.3907	1.82×10^{-10}
17	7,310,006	rs35386490	T	C	0.2272	7.10×10^{-26}
17	7,319,325	Affx-14343876	C	T	0.0345	1.06×10^{-13}
17	7,322,087	rs76749877	G	A	0.0806	2.69×10^{-13}
17	7,363,088	rs9217	T	C	0.3515	9.88×10^{-10}
17	7,366,619	rs34914463	T	C	0.1253	2.90×10^{-18}
17	7,380,681	rs3867594	C	T	0.1467	2.48×10^{-21}
17	7,385,454	rs3760422	G	A	0.1461	6.15×10^{-21}
17	7,394,968	rs8069501	A	G	0.0721	9.57×10^{-16}
17	7,400,815	rs2228128	T	C	0.2934	1.32×10^{-20}
17	7,402,600	rs2228129	C	T	0.2546	1.91×10^{-11}
17	7,410,212	rs7215922	G	T	0.2485	1.48×10^{-11}
17	7,417,663	rs6761	T	C	0.3926	2.23×10^{-30}
17	7,441,756	rs34445439	C	T	0.2933	3.15×10^{-45}
17	7,446,027	rs9892297	A	G	0.3379	1.38×10^{-33}
17	7,452,977	rs9899183	T	C	0.2636	1.23×10^{-46}
17	7,455,610	rs117322070	C	T	0.0276	2.70×10^{-10}
17	7,457,352	rs4968210	G	A	0.3907	8.24×10^{-10}
17	7,457,421	rs11654281	C	T	0.0507	2.64×10^{-18}
17	7,478,402	rs78414518	C	G	0.0711	7.17×10^{-24}
17	7,478,498	rs78553499	G	A	0.1326	2.69×10^{-30}
17	7,484,812	rs9901675	G	A	0.0525	6.08×10^{-24}

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Table S34: (Continued)

CHR	POS	SNP	Major Allele	Minor Allele	MAF	p-value
17	7,491,177	rs4227	T	G	0.2766	1.66×10^{-49}
17	7,512,074	rs11653545	G	A	0.0179	4.56×10^{-17}
17	7,529,902	rs13894	G	A	0.0748	8.62×10^{-41}
17	7,536,460	rs55784804	G	T	0.1001	1.52×10^{-30}
17	7,536,527	rs6259	G	A	0.1222	7.61×10^{-21}
17	7,537,792	rs727428	C	T	0.4466	7.74×10^{-52}
17	7,543,894	rs12051767	C	T	0.0670	7.69×10^{-40}
17	7,552,123	rs72829446	C	T	0.1105	6.92×10^{-24}
17	7,557,419	rs1642763	G	A	0.2355	1.05×10^{-9}
17	7,569,542	rs74351250	G	A	0.0493	9.99×10^{-12}
17	7,569,698	rs8073498	A	C	0.3855	1.05×10^{-13}
17	7,578,115	rs1625895	C	T	0.1295	1.53×10^{-16}
17	7,588,750	rs17883687	G	T	0.0138	6.26×10^{-9}
17	7,617,378	rs62062590	G	A	0.2958	1.84×10^{-21}
17	7,767,378	rs72841430	A	G	0.0188	4.34×10^{-21}
17	7,771,462	rs76730553	C	T	0.0765	4.03×10^{-8}
17	7,847,837	rs62623385	A	T	0.0317	9.29×10^{-15}
17	16,833,139	rs3751993	C	T	0.3280	8.79×10^{-13}
17	16,860,054	rs113436029	A	G	0.0438	4.59×10^{-16}
17	16,863,638	rs4985726	C	G	0.1027	2.45×10^{-33}
17	16,874,981	rs6416870	T	C	0.4005	4.10×10^{-8}
17	37,457,480	rs9890198	A	C	0.1570	2.04×10^{-8}
17	37,543,449	rs7208487	T	G	0.1580	2.90×10^{-8}
17	37,828,496	rs2952151	C	T	0.3041	3.08×10^{-8}
17	41,776,943	rs76868109	A	C	0.0337	2.66×10^{-11}
17	41,840,849	rs77697917	C	T	0.0275	6.66×10^{-16}
17	41,926,126	rs72836561	C	T	0.0304	4.64×10^{-17}
17	45,700,384	rs80256006	CCTA	C	0.4803	4.30×10^{-8}
17	47,283,815	rs55634267	C	T	0.3020	1.24×10^{-12}
17	47,306,829	rs74584378	C	T	0.2433	2.56×10^{-8}
17	47,314,413	rs624177	A	G	0.3512	3.68×10^{-8}
17	47,331,987	rs663576	T	C	0.4500	4.85×10^{-17}
17	47,336,931	rs74659133	C	T	0.0868	2.32×10^{-17}
17	47,440,466	rs16948048	A	G	0.3610	1.51×10^{-19}
17	47,455,752	rs73324348	G	A	0.0876	6.38×10^{-16}
17	47,472,365	rs11653775	A	G	0.0732	1.79×10^{-11}
17	47,512,945	rs9900373	C	G	0.0885	2.72×10^{-8}
17	47,514,665	rs2584652	A	C	0.1346	9.23×10^{-12}
17	53,381,796	rs4793788	A	C	0.3592	2.88×10^{-9}
17	58,930,419	rs9910365	A	G	0.1439	2.28×10^{-10}
17	59,096,752	rs72844903	G	A	0.1406	1.84×10^{-9}
17	64,210,580	rs1801689	A	C	0.0294	1.96×10^{-16}
17	64,305,051	rs78357146	A	G	0.0291	5.12×10^{-15}
17	64,361,924	rs117524772	C	A	0.0255	1.65×10^{-8}
17	67,060,872	rs113408695	T	C	0.0359	6.43×10^{-10}
17	67,424,508	rs75016991	C	A	0.0249	4.05×10^{-11}
17	76,121,864	rs2748427	A	G	0.2233	5.66×10^{-23}
17	76,126,094	rs454139	T	C	0.1226	2.86×10^{-19}
17	80,680,449	rs2243523	G	T	0.3829	2.98×10^{-8}
17	80,685,533	rs1046896	C	T	0.3141	1.12×10^{-23}
17	80,690,632	rs2459703	T	C	0.4615	2.00×10^{-24}
17	80,708,024	rs2248894	T	C	0.3733	1.35×10^{-18}
17	80,708,601	rs1056534	G	C	0.3944	2.35×10^{-14}
17	80,721,000	rs2677914	A	G	0.3960	4.11×10^{-14}
17	80,734,906	rs635999	T	G	0.4281	3.11×10^{-13}
17	80,752,787	rs11655811	T	G	0.4122	6.11×10^{-12}
17	80,780,486	rs601555	G	A	0.4307	4.40×10^{-8}
17	80,893,992	rs7218129	C	G	0.4040	7.35×10^{-14}
18	47,109,955	rs77960347	A	G	0.0127	8.13×10^{-21}

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Table S34: (Continued)

CHR	POS	SNP	Major Allele	Minor Allele	MAF	p-value
18	47,159,090	rs7240405	G	A	0.1753	1.08×10^{-19}
18	47,160,953	rs7241918	T	G	0.1709	2.98×10^{-19}
18	47,166,694	rs9947684	G	A	0.3512	1.72×10^{-13}
18	47,181,668	rs2156552	T	A	0.1735	3.09×10^{-20}
18	47,196,870	rs80175721	A	G	0.0101	1.29×10^{-11}
18	56,095,378	rs4940691	G	T	0.2022	9.92×10^{-12}
18	56,109,859	rs8099014	A	C	0.2675	1.89×10^{-9}
19	8,429,323	rs116843064	G	A	0.0186	5.25×10^{-19}
19	11,188,153	rs55791371	A	C	0.1178	1.75×10^{-29}
19	11,202,306	rs6511720	G	T	0.1193	8.84×10^{-30}
19	11,231,203	rs72658867	G	A	0.0123	2.68×10^{-10}
19	11,330,942	rs17699030	A	G	0.0353	1.09×10^{-9}
19	17,252,151	rs35365035	T	C	0.3932	2.32×10^{-12}
19	17,312,226	rs116189680	G	A	0.0267	4.62×10^{-8}
19	18,244,690	rs885683	G	A	0.2510	3.21×10^{-8}
19	19,155,672	rs73008942	G	A	0.0479	1.47×10^{-10}
19	19,295,875	rs11668319	A	G	0.1430	1.80×10^{-8}
19	19,329,924	rs2228603	C	T	0.0736	5.66×10^{-22}
19	19,379,549	rs58542926	C	T	0.0749	8.12×10^{-29}
19	19,440,066	rs3764567	T	C	0.3475	8.12×10^{-10}
19	19,445,856	rs11085259	C	T	0.1794	4.09×10^{-13}
19	19,505,087	rs10415849	C	T	0.1221	1.12×10^{-19}
19	19,508,013	rs10424702	A	G	0.1278	3.62×10^{-19}
19	19,658,472	rs16996148	G	T	0.0841	1.59×10^{-24}
19	19,662,220	rs17216525	C	T	0.0810	4.32×10^{-25}
19	19,789,528	rs2304130	A	G	0.0888	8.97×10^{-18}
19	33,356,891	rs12460876	T	C	0.3938	6.00×10^{-11}
19	33,364,628	rs8101881	T	C	0.4023	1.78×10^{-11}
19	35,550,878	rs45512696	C	T	0.1675	7.39×10^{-14}
19	35,559,474	rs11671010	T	C	0.1732	3.91×10^{-14}
19	44,836,400	rs8107530	C	T	0.0357	5.83×10^{-19}
19	44,894,070	rs62116778	G	T	0.0368	2.09×10^{-22}
19	44,934,842	rs17347726	G	C	0.1095	4.06×10^{-11}
19	44,957,310	rs62116303	A	G	0.1328	7.42×10^{-10}
19	45,122,043	rs62119261	A	C	0.0456	1.36×10^{-22}
19	45,197,732	rs62120566	C	G	0.0239	1.74×10^{-36}
19	45,220,896	rs11881756	T	C	0.1151	2.33×10^{-34}
19	45,225,345	rs2965109	C	T	0.3709	2.06×10^{-21}
19	45,232,161	rs62117160	G	A	0.0437	2.56×10^{-54}
19	45,232,205	rs1004165	G	A	0.4269	3.28×10^{-14}
19	45,235,700	rs74607435	T	C	0.0491	1.67×10^{-8}
19	45,237,812	rs2965101	T	C	0.3262	4.78×10^{-27}
19	45,241,638	rs2927437	G	A	0.1878	1.35×10^{-14}
19	45,245,015	rs2965174	G	A	0.4782	1.44×10^{-8}
19	45,296,806	Affx-16018598	C	T	0.0349	1.15×10^{-38}
19	45,299,199	rs76560105	G	T	0.0337	7.55×10^{-40}
19	45,316,588	rs28399654	G	A	0.0319	3.20×10^{-41}
19	45,324,138	rs28399637	G	A	0.3064	1.98×10^{-31}
19	45,326,664	rs10405693	C	T	0.3162	4.62×10^{-32}
19	45,348,522	rs12162222	G	T	0.2807	5.78×10^{-31}
19	45,351,516	rs41289512	C	G	0.0401	3.34×10^{-27}
19	45,365,817	rs11665829	G	A	0.3673	1.46×10^{-9}
19	45,372,354	rs8104483	T	G	0.2734	3.77×10^{-14}
19	45,373,276	rs11879589	G	A	0.0961	2.35×10^{-9}
19	45,376,284	rs519113	C	G	0.2464	1.22×10^{-28}
19	45,377,098	rs11672399	C	A	0.0740	5.36×10^{-9}
19	45,377,467	rs2075642	G	A	0.1975	1.14×10^{-8}
19	45,379,309	rs3852859	T	C	0.1991	3.98×10^{-8}
19	45,382,034	rs6859	G	A	0.4176	8.15×10^{-36}

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Table S34: (Continued)

CHR	POS	SNP	Major Allele	Minor Allele	MAF	p-value
19	45,382,966	rs3852860	C	T	0.4217	5.44×10^{-19}
19	45,389,224	rs283814	G	A	0.0753	2.58×10^{-8}
19	45,389,596	rs7254892	G	A	0.0344	1.88×10^{-60}
19	45,395,619	rs2075650	A	G	0.1424	1.12×10^{-50}
19	45,395,714	rs157581	T	C	0.2187	5.42×10^{-43}
19	45,403,412	rs1160985	C	T	0.4343	3.62×10^{-20}
19	45,408,836	rs405509	G	T	0.4842	2.17×10^{-47}
19	45,410,002	rs769449	G	A	0.1196	1.09×10^{-54}
19	45,410,444	rs769450	G	A	0.3932	6.55×10^{-18}
19	45,414,451	rs439401	C	T	0.3652	7.36×10^{-38}
19	45,415,640	rs445925	G	A	0.1112	2.00×10^{-70}
19	45,422,946	rs4420638	A	G	0.1851	1.09×10^{-55}
19	45,432,557	rs7259004	G	C	0.1090	3.63×10^{-50}
19	45,447,221	rs12721109	G	A	0.0249	4.38×10^{-47}
19	45,448,465	rs5167	T	G	0.3525	5.21×10^{-13}
19	45,457,180	rs3760627	T	C	0.4581	1.31×10^{-22}
19	45,480,037	rs2075620	A	G	0.2726	3.03×10^{-10}
19	45,619,946	rs11672271	A	G	0.3194	3.99×10^{-9}
19	45,662,459	rs8109620	G	A	0.3256	2.73×10^{-8}
19	46,180,414	rs34783010	G	T	0.1909	4.40×10^{-10}
19	46,181,392	rs1800437	G	C	0.1918	2.45×10^{-10}
19	46,182,304	rs10423928	T	A	0.1872	6.54×10^{-10}
19	46,295,223	rs73045960	A	G	0.0152	2.74×10^{-9}
19	46,387,344	rs11550348	G	A	0.1259	2.97×10^{-8}
19	48,368,777	rs296390	A	C	0.1665	2.58×10^{-11}
19	48,384,749	rs10426201	A	G	0.1628	7.19×10^{-13}
19	48,401,893	rs2637125	G	A	0.1530	6.59×10^{-13}
19	48,465,312	rs2972516	C	T	0.1645	1.23×10^{-11}
19	49,158,138	rs8103121	A	G	0.3340	4.77×10^{-13}
19	49,202,859	rs16982241	G	A	0.1308	6.66×10^{-11}
19	49,214,470	rs281380	T	C	0.3598	1.49×10^{-29}
19	49,217,261	rs281385	G	A	0.1265	4.65×10^{-9}
19	49,233,406	rs281408	C	A	0.4171	1.67×10^{-26}
19	49,244,218	Affx-52359426	C	CAA	0.4262	1.34×10^{-24}
19	49,253,261	rs4021	A	G	0.2859	1.13×10^{-15}
19	49,271,583	rs62132803	C	T	0.2809	1.43×10^{-17}
19	50,000,009	rs2280401	G	A	0.1564	8.47×10^{-10}
19	50,016,479	rs111981233	T	G	0.0781	6.27×10^{-12}
19	50,042,829	rs8108243	C	T	0.0785	1.33×10^{-9}
19	50,045,878	Affx-16089855	C	T	0.0777	2.51×10^{-9}
19	54,754,103	rs11668189	C	A	0.3565	6.19×10^{-9}
19	54,759,361	rs12975366	T	C	0.3924	1.28×10^{-13}
20	23,077,649	rs17682579	C	T	0.1040	1.04×10^{-10}
20	23,235,964	rs192455477	G	A	0.0192	2.69×10^{-14}
20	23,296,209	rs6048704	C	T	0.2496	9.86×10^{-21}
20	23,377,815	rs17750862	G	A	0.0536	1.45×10^{-12}
20	23,402,735	rs761725	G	A	0.1107	2.73×10^{-16}
20	23,405,904	rs78916169	G	T	0.0538	7.41×10^{-20}
20	23,487,503	rs3004118	C	T	0.4612	4.34×10^{-22}
20	23,517,560	rs41304816	G	C	0.1018	1.83×10^{-31}
20	23,539,846	rs73610708	C	T	0.0823	2.37×10^{-34}
20	23,544,379	rs75810394	A	G	0.0228	6.54×10^{-22}
20	23,554,317	rs117671467	T	C	0.0112	1.11×10^{-17}
20	23,565,975	rs77114334	C	T	0.0965	3.13×10^{-20}
20	23,578,189	rs1158167	A	G	0.2302	6.83×10^{-69}
20	23,595,675	rs59059917	C	T	0.2156	6.42×10^{-69}
20	23,623,917	rs73102333	G	A	0.2163	4.89×10^{-13}
20	23,633,755	rs13039144	A	G	0.1748	1.81×10^{-66}
20	23,635,691	rs73102389	C	A	0.1772	1.78×10^{-33}

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Table S34: (Continued)

CHR	POS	SNP	Major Allele	Minor Allele	MAF	p-value
20	23,642,389	rs13040731	T	C	0.1203	4.43×10^{-19}
20	23,642,839	rs2983608	T	C	0.2044	6.08×10^{-54}
20	23,661,479	rs73104320	G	A	0.2648	6.32×10^{-11}
20	23,667,865	rs112308292	C	A	0.1209	5.93×10^{-53}
20	23,671,988	rs117877399	C	A	0.0189	4.53×10^{-33}
20	23,691,153	rs66590796	G	T	0.1095	2.30×10^{-38}
20	23,700,824	rs7266357	T	G	0.1626	7.91×10^{-29}
20	23,700,872	rs4629230	G	A	0.2926	7.56×10^{-9}
20	23,711,882	rs6114248	G	A	0.2912	1.88×10^{-8}
20	23,723,592	rs116548544	G	A	0.0373	6.25×10^{-12}
20	23,732,521	rs117567509	T	C	0.0403	5.27×10^{-41}
20	23,740,511	rs67418849	G	A	0.0905	3.35×10^{-31}
20	23,740,591	rs4627645	T	C	0.3021	1.04×10^{-16}
20	23,746,310	rs6114264	C	T	0.1325	5.77×10^{-45}
20	23,750,404	rs13043045	C	T	0.0854	1.21×10^{-24}
20	23,766,277	rs8126263	C	T	0.1161	1.78×10^{-10}
20	23,783,368	rs6049135	T	C	0.2601	3.07×10^{-17}
20	23,801,950	rs6106728	C	T	0.2081	1.21×10^{-26}
20	23,813,618	rs8184710	G	A	0.1817	4.52×10^{-12}
20	23,829,486	rs117720287	G	T	0.0232	7.81×10^{-25}
20	23,847,009	rs6138150	T	C	0.1817	5.25×10^{-12}
20	23,953,105	rs2984254	C	T	0.0618	1.17×10^{-9}
20	25,298,087	rs7267979	G	A	0.4400	1.26×10^{-10}
20	25,346,082	rs6083818	A	G	0.4452	3.75×10^{-11}
20	43,042,364	rs1800961	C	T	0.0306	4.44×10^{-17}
20	44,184,375	rs2250860	T	C	0.4226	7.50×10^{-9}
20	44,229,811	rs77909272	T	C	0.0555	1.83×10^{-13}
20	44,279,061	rs45546535	C	T	0.0232	1.82×10^{-9}
20	44,302,649	rs79475204	T	C	0.1148	1.09×10^{-13}
20	44,380,052	rs77727017	G	T	0.1276	7.47×10^{-25}
20	44,453,655	rs370237	C	T	0.3331	2.97×10^{-17}
20	44,456,655	rs380397	T	G	0.3343	6.06×10^{-18}
20	44,464,356	rs117191103	C	T	0.0195	2.98×10^{-11}
20	44,468,931	rs197669	C	T	0.3211	1.28×10^{-22}
20	44,475,413	rs174745	G	A	0.3801	2.23×10^{-21}
20	44,501,458	rs6130959	G	A	0.4307	9.19×10^{-19}
20	44,503,454	rs78044163	A	G	0.0404	2.75×10^{-8}
20	44,505,973	rs2903808	C	T	0.3754	3.23×10^{-17}
20	44,506,418	rs1045493	A	G	0.4201	3.83×10^{-20}
20	44,523,782	rs4608591	T	C	0.3600	6.68×10^{-18}
20	44,534,651	rs6065904	G	A	0.2178	9.20×10^{-55}
20	44,539,492	rs441346	C	G	0.4540	1.02×10^{-17}
20	44,545,773	rs73307905	A	C	0.1877	2.89×10^{-55}
20	44,563,217	rs77617917	G	A	0.0767	1.05×10^{-38}
20	44,576,502	rs7679	T	C	0.1817	2.49×10^{-55}
20	44,578,961	rs3746503	A	G	0.1150	4.60×10^{-14}
20	44,582,187	rs73128528	A	T	0.1347	2.49×10^{-18}
20	44,585,793	rs13040315	A	G	0.4368	5.68×10^{-32}
20	44,586,036	rs3746506	A	G	0.3796	5.21×10^{-38}
20	44,607,601	rs6104410	A	G	0.2702	2.76×10^{-29}
20	44,607,661	rs7270354	G	A	0.1459	1.32×10^{-18}
20	44,636,495	rs3918279	C	T	0.0102	4.26×10^{-8}
20	44,639,692	rs2274755	G	T	0.1453	6.75×10^{-34}
20	44,640,225	rs17576	A	G	0.3566	1.35×10^{-30}
20	44,643,111	Affx-16780572	G	A	0.1457	5.67×10^{-34}
20	44,650,318	rs10432735	A	T	0.1454	6.50×10^{-34}
20	44,666,595	rs3848726	G	T	0.3617	1.17×10^{-11}
20	44,755,376	rs41282788	G	C	0.0219	9.19×10^{-11}
20	44,761,377	rs12481282	G	C	0.2771	9.54×10^{-13}

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Table S34: (Continued)

CHR	POS	SNP	Major Allele	Minor Allele	MAF	p-value
20	52,742,590	rs17217119	A	G	0.1962	8.23×10^{-12}
22	18,439,958	rs1076540	C	T	0.2360	2.57×10^{-17}
22	18,457,986	rs5992137	T	C	0.2669	1.40×10^{-13}
22	18,463,608	rs8140977	C	T	0.2610	6.03×10^{-14}
22	18,465,105	rs9605480	G	A	0.2609	1.86×10^{-13}
22	18,488,883	rs9617650	G	C	0.2097	4.26×10^{-10}
22	24,252,085	rs2154593	G	A	0.3847	5.70×10^{-9}
22	24,255,296	rs4822455	T	C	0.4199	2.23×10^{-12}
22	24,267,047	rs5751777	T	C	0.4117	2.14×10^{-12}
22	24,882,925	rs1543757	G	A	0.0313	4.09×10^{-12}
22	24,904,003	rs117038722	G	A	0.0355	7.64×10^{-20}
22	24,992,266	rs5751901	T	C	0.3437	5.02×10^{-56}
22	25,000,229	rs5751904	A	T	0.3495	4.09×10^{-57}
22	25,102,070	rs6004244	T	C	0.1632	1.02×10^{-8}
22	25,151,741	rs117329800	G	A	0.0174	4.06×10^{-8}
22	25,158,445	rs56032751	G	A	0.0149	6.21×10^{-9}
22	37,462,926	rs2235321	G	A	0.3812	3.59×10^{-8}
22	37,469,590	Affx-89007920	T	C	0.4529	8.43×10^{-16}
22	37,469,591	rs4820268	A	G	0.4610	6.35×10^{-17}
22	38,925,719	rs1980455	A	C	0.3582	1.08×10^{-9}
22	39,016,182	rs4821797	T	C	0.3338	1.04×10^{-9}
22	39,094,619	rs5750671	A	C	0.3092	6.47×10^{-9}
22	44,324,727	rs738409	C	G	0.2172	2.02×10^{-28}
22	44,325,996	rs12483959	G	A	0.1595	4.16×10^{-22}
22	44,332,570	rs2281135	G	A	0.1659	1.45×10^{-21}
22	44,332,888	Affx-19716376	T	TC	0.1657	1.66×10^{-21}
22	44,368,122	rs3761472	A	G	0.1581	1.02×10^{-19}
22	44,388,817	rs3827385	T	C	0.1817	2.01×10^{-14}
22	44,391,686	rs2143571	G	A	0.1828	3.49×10^{-13}
22	44,394,402	rs2073080	C	T	0.1802	2.28×10^{-14}
22	44,395,451	rs1007863	T	C	0.3932	1.27×10^{-13}

Table S35: SNP-gene mapping for 1,325 genome-wide significant SNPs ($p < 5 \times 10^{-8}$) identified by RmvLMM from multi-trait GWAS of 26 blood biochemistry phenotypes in UKB. Mapping was performed using MAGMA with a 5-kb window upstream and downstream of gene boundaries (NCBI build 37), yielding 373 annotated genes. Previously reported gene-phenotype associations were retrieved from PubMed using the R package ‘rentrez’.

CHR	Gene Start	Gene End	Gene Name	No. of SNPs	P Value	SNP List	PMID	Reference
1	16445832	16487582	EPHA2	1	5.89×10^{-11}	rs6603883	41508276	Kang et al. (2025)
1	16519599	16544104	ARHGEF19	2	1.16×10^{-8}	rs221057, rs221058		
1	16568339	16683965	FBXO42	1	9.29×10^{-9}	rs1008529		
1	16717101	16768919	SPATA21	1	2.56×10^{-4}	rs525409		
1	21761583	21816393	NBPF3	6	5.00×10^{-10}	rs10916996, rs17420195, rs35175190, rs60515836, rs6680628, rs72872292	35346016	Katsa et al. (2022)
1	21830475	21909905	ALPL	13	5.00×10^{-10}	rs10917008, rs1256342, rs149344982, rs1697407, rs17421553, rs36053309, rs61778369, rs6656120, rs72659192, rs77936121, rs80320018, rs9662008, rs975000	38915066	Zhu et al. (2024)
1	21917708	22001010	RAP1GAP	8	3.44×10^{-15}	rs1130564, rs116503681, rs12039278, rs2275363, rs61775974, rs72660339, rs78915636, rs829416	12690117	Bruyn et al. (2003)
1	25221002	25296648	RUNX3	1	6.88×10^{-6}	rs4265380	38735649	Xiao et al. (2024)
1	27013623	27027896	LOC101928728	2	4.63×10^{-12}	rs12738345, rs35917448		
1	27017522	27113601	ARID1A	2	1.06×10^{-11}	rs12729444, rs12742115	36509613	Chawla et al. (2023)
1	27232975	27245567	NR0B2	1	4.34×10^{-7}	rs6659176	36098472	Handelman et al. (2022)
1	27243187	27278362	NUDC	1	1.35×10^{-8}	rs145685168	22768855	Pang et al. (2012)
1	27271047	27291901	KDF1	2	1.08×10^{-10}	rs12742376, rs17360994		
1	55500149	55535526	PCSK9	1	3.19×10^{-11}	rs11591147	39985079	Duan et al. (2025)
1	62915397	63159039	DOCK7	6	7.27×10^{-15}	rs10889332, rs10889338, rs10889353, rs1168013, rs2031373, rs2131925	39086896	Zhang et al. (2024)
1	63244777	63335941	ATG4C	1	6.92×10^{-5}	rs11208033	32401642	Devis-Jauregui et al. (2021)
1	65881131	66112242	LEPROT	5	7.33×10^{-15}	rs1137101, rs1805094, rs1805096, rs1892534, rs6700896	20624279	Jeon et al. (2010)
1	66253193	66845262	PDE4B	3	2.69×10^{-8}	rs11208750, rs1316871, rs34280859	40136709	Sherstnev et al. (2025)
1	107594267	107606916	PRMT6	1	4.57×10^{-8}	rs2232016	35543755	Wang et al. (2022)
1	109751515	109785804	SARS	1	3.63×10^{-8}	rs4970829	41379187	Ferreira et al. (2025)
1	109787641	109823378	CELSR2	8	5.00×10^{-10}	rs11577931, rs12740374, rs585362, rs629301, rs646776, rs660240, rs6698843, rs7528419	19951432	Ronald et al. (2009)
1	109829987	109854663	MYBPHL	1	3.63×10^{-12}	rs55660224	41258892	Alvarez-Arce et al. (2026)
1	110225418	110245828	GSTM1	1	1.35×10^{-14}	rs140584594	38548381	Elkama et al. (2024)
1	110448233	110478616	CSF1	1	1.49×10^{-6}	rs333947	39676236	Jorgensen et al. (2025)
1	145605990	145694005	RNF115	1	3.22×10^{-9}	rs75246752	34804194	Lu et al. (2021)
1	145722662	145769207	PDZK1	1	1.83×10^{-6}	rs12129861	23687307	Mineo et al. (2013)
1	150613701	150674672	GOLPH3L	1	1.27×10^{-7}	rs17599629	40043140	Sun et al. (2025)
1	150893815	150942389	SETDB1	1	1.75×10^{-9}	rs267738	37074626	Hu et al. (2023)
1	150932649	150952479	CERS2	1	1.59×10^{-8}	rs267734	25238615	Shiffman et al. (2014)
1	154372669	154446926	IL6R	5	5.00×10^{-10}	rs1386821, rs4129267, rs4537545, rs4845625, rs7549250	37798688	Baraka et al. (2023)
1	154549533	154605456	ADAR	1	1.68×10^{-8}	rs9427104	34482352	Franco et al. (2021)
1	155018748	155040252	ADAM15	1	2.29×10^{-8}	rs11589479	25333931	Chatterjee et al. (2014)
1	155095349	155112386	EFNA1	1	1.51×10^{-8}	rs12904	24293012	Hao et al. (2013)

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Table S35: (Continued)

CHR	Gene Start	Gene End	Gene Name	No. of SNPs	P Value	SNP List	PMID	Reference
1	155136884	155156331	KRTCAP2	2	6.16×10^{-14}	rs11264339, rs11264341	38831441	Yang et al. (2024)
1	155140702	155162447	TRIM46	1	1.04×10^{-10}	rs4072037	34638981	Teng et al. (2021)
1	155160379	155182772	THBS3	1	9.23×10^{-13}	rs760077	31235756	Castells et al. (2019)
1	158511918	158522895	OR6Y1	1	1.71×10^{-8}	rs41273491		
1	158571229	158582170	OR10Z1	1	2.05×10^{-12}	rs857685		
1	158575496	158661506	SPTA1	1	4.39×10^{-13}	rs857721	8613143	Walsh et al. (1996)
1	159677079	159689396	CRP	2	5.00×10^{-10}	rs1205, rs2794520	41541628	Ando et al. (2026)
1	161190729	161205536	TOMM40L	1	5.54×10^{-6}	rs4073054		
1	161470205	161494360	FCGR2A	1	4.10×10^{-9}	rs1801274	32283413	Tang et al. (2020)
1	161506549	161525413	FCGR3A	2	1.27×10^{-12}	Affx-35410767, rs56199187	35361683	Zhang et al. (2023)
1	161627905	161653444	FCGR2B	1	3.89×10^{-16}	rs723177	40490739	Wang et al. (2025)
1	161671762	161689142	FCRLA	1	1.27×10^{-9}	rs61801160	18241881	Baranov et al. (2008)
1	220955039	220992741	1-Mar	2	1.82×10^{-12}	rs2642438, rs2642442	38619429	Jones et al. (2024)
1	221047743	221063401	HLX	1	1.60×10^{-8}	rs12141189	35693796	Ricaño-Ponce et al. (2022)
1	230197956	230422875	GALNT2	1	9.82×10^{-4}	rs4846905	23303382	Hong et al. (2013)
2	21219301	21271945	APOB	3	1.78×10^{-15}	rs12691202, rs1801699, rs533617	41303592	Pabin et al. (2025)
2	27472440	27506093	SLC30A3	1	1.99×10^{-12}	rs60631624	41300833	Bai et al. (2025)
2	27582219	27598324	EIF2B4	1	5.00×10^{-10}	rs2280737	29544907	Sassi et al. (2018)
2	27660233	27674348	KRTCAP3	1	5.00×10^{-10}	rs11126999	32855654	Wang et al. (2020)
2	27662240	27717575	IFT172	2	1.55×10^{-15}	rs1260328, rs2303369	38772745	Tsao et al. (2024)
2	27714470	27751556	GCKR	6	2.58×10^{-10}	rs1260326, rs1260333, rs715325, rs780092, rs780093, rs780094	39683606	Yang et al. (2024)
2	27794389	27810589	C2orf16	2	9.60×10^{-15}	rs1919127, rs1919128	31910446	Oh et al. (2020)
2	27800836	27851082	ZNF512	4	5.44×10^{-15}	rs12987055, rs13022873, rs1881396, rs62138965	40932219	Hao et al. (2025)
2	27843408	27856898	CCDC121	1	5.00×10^{-10}	rs3749147		
2	28108482	28566768	BRE	2	2.28×10^{-15}	rs62140395, rs6547820	30067118	Ahn et al. (2018)
2	43452975	43828185	THADA	2	2.77×10^{-7}	rs7578597, rs77059113	28399403	Moraru et al. (2017)
2	44034611	44071039	ABCG5	1	7.40×10^{-5}	Affx-20090007	39401813	Jin et al. (2024)
2	44061103	44110947	ABCG8	2	3.64×10^{-9}	rs4245791, rs6544713	39401813	Jin et al. (2024)
2	64853755	64983048	SERTAD2	3	3.61×10^{-9}	rs12994639, rs6756943, rs847803		
2	97366666	97410813	LMAN2L	1	2.94×10^{-10}	rs68026712		
2	97421639	97482628	CNNM4	3	1.67×10^{-10}	rs6576983, rs968470, rs994430	35715480	Ilenwabor et al. (2022)
2	165531695	165703678	COBLL1	2	7.25×10^{-7}	rs75297654, rs79953491	35654975	Vujkovic et al. (2022)
2	169752750	169771510	G6PC2	1	5.00×10^{-10}	rs1402837	24029012	Adeva et al. (2013)
2	169774336	169892833	ABCB11	4	7.22×10^{-16}	rs495714, rs496550, rs497692, rs7558863	29886607	Peng et al. (2018)
2	169978619	170224123	LRP2	1	6.35×10^{-5}	rs2075252	41098359	Zocchio et al. (2025)
2	211337406	211548831	CPS1	1	3.45×10^{-7}	rs1047891	24924744	Weerasinghe et al. (2014)
2	234155217	234209320	ATG16L1	9	6.27×10^{-15}	rs10210302, rs2241880, rs3792109, rs3828309, rs62192932, rs62192955, rs6431262, rs6758317, rs73998327	32160108	Wu et al. (2021)
2	234211309	234260701	SAG	9	2.43×10^{-14}	rs1046974, rs2304777, rs57592542, rs61062196, rs72976383, rs75560791, rs7565275, rs78936963, rs80271431	39138757	Zong et al. (2024)
2	234258149	234385744	DGKD	17	5.00×10^{-10}	rs114252547, rs115604196, rs116663413, rs1441093, rs2242100, rs2305540, rs2971868, rs72980341, rs72980357, rs72980361, rs74448524, rs74608404, rs77900844, rs78447894, rs838705, rs838713, rs838737	40759569	Li et al. (2025)

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Table S35: (Continued)

CHR	Gene Start	Gene End	Gene Name	No. of SNPs	P Value	SNP List	PMID	Reference
2	234379165	234480433	USP40	10	5.22×10^{-15}	rs111712352, rs114099762, rs141501074, rs2167884, rs2603547, rs2971863, rs62192762, rs62192778, rs6704644, rs838543 Affx-36452635, rs1042640, rs10929302, rs10929303, rs1105879, rs1105880, rs1112310, rs114346341, rs115836766, rs11683356, rs11892031, rs12475068, rs1377460, rs17854828, rs17862867, rs17862876, rs17868336, rs17868337, rs2070959, rs2602372, rs2602381, rs34622615, rs3755321, rs3755322, rs4148325, rs4261716, rs6731242, rs6742078, rs6759892, rs7586110, rs76026343, rs8330, rs887829	34312870	Yang et al. (2021)
2	234521291	234686946	UGT1A8	33	5.00×10^{-10}	rs10170160, rs10175949, rs12053445, rs1500480, rs1500481, rs17862901, rs17863818, rs17864714, rs213548, rs2270854, rs2361502, rs4663335, rs6431631, rs726016, rs75235703, rs79208193, rs879665		
2	234679325	234747069	MROH2A	17	5.00×10^{-10}	rs10511, rs12582, rs3806589, rs6431641	40306500	Mohamed et al. (2025)
2	234821043	234933166	TRPM8	3	1.50×10^{-15}	rs10929321, rs13004520, rs17868387	35024183	Fatima et al. (2021)
3	58313617	58416815	PXK	2	4.69×10^{-11}	rs34579268, rs62258127	31260916	Sayols-Baixeras et al. (2019)
3	121897530	122010350	CASR	4	4.39×10^{-15}	rs1801725, rs1979869, rs4300957, rs7628990	41240382	Koca et al. (2025)
3	122039011	122065816	CSTA	2	5.00×10^{-10}	Affx-21056635, rs73186059	34579920	Tang et al. (2021)
3	122098023	122133961	FAM162A	2	7.77×10^{-16}	rs1127343, rs6768280	37097350	Yang et al. (2023)
3	122135748	122238786	KPNA1	6	5.55×10^{-15}	rs116555124, rs12487598, rs12488797, rs17201246, rs28384492, rs7638174	28820290	Li et al. (2017)
3	122241757	122288523	PARP9	3	1.67×10^{-15}	rs28365795, rs34006803, rs77732258	36766731	Azzarito et al. (2023)
3	122996143	123172924	ADCY5	4	7.02×10^{-9}	Affx-21069786, rs11708067, rs2877716, rs6798189	25116423	Cash et al. (2014)
3	136050077	136476245	STAG1	4	4.12×10^{-14}	rs1145101, rs61789642, rs7612160, rs9845762	38645862	Zhou et al. (2024)
3	136576050	136675446	NCK1	1	1.12×10^{-8}	rs71630059	19193766	Miura et al. (2009)
3	170709137	170749768	SLC2A2	1	1.92×10^{-10}	rs5404	38327217	Du et al. (2024)
3	172156081	172171246	GHSR	1	2.74×10^{-5}	rs572169	16323823	Cocchi et al. (2005)
4	3310874	3446640	RGS12	1	3.28×10^{-7}	rs3748034	25808930	Dunn et al. (2015)
4	3438702	3456214	HGFAC	2	1.24×10^{-12}	rs16844383, rs16844401	25998175	Larson et al. (2015)
4	3460033	3508203	DOK7	1	4.59×10^{-8}	rs6831256	41004697	Krenn et al. (2025)
4	9822848	10046872	SLC2A9	13	3.52×10^{-13}	rs16891234, rs2176644, rs34213329, rs3775948, rs4481233, rs62295971, rs62296002, rs6823877, rs73225891, rs7442295, rs75181558, rs7698858, rs79323395	35470676	Kanbay et al. (2022)
4	10070963	10123612	WDR1	2	5.00×10^{-10}	rs34517659, rs717615	26438387	Lan et al. (2016)
4	10436497	10464032	ZNF518B	4	3.89×10^{-16}	rs10016022, rs5028371, rs66538112, rs80139786	38110883	Lee et al. (2023)
4	10486838	10691386	CLNK	6	1.02×10^{-14}	rs12504795, rs13115661, rs16869379, rs6819820, rs76356518, rs997219	26438387	Lan et al. (2016)

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Table S35: (Continued)

CHR	Gene Start	Gene End	Gene Name	No. of SNPs	P Value	SNP List	PMID	Reference
4	69308167	69368322	TMPRSS11E	2	6.97×10^{-10}	rs976002, rs983745		
4	69507315	69541494	UGT2B15	1	1.81×10^{-10}	rs1902023	39142826	Lapham et al. (2024)
4	72602410	72676237	GC	5	5.00×10^{-10}	rs2282679, rs4588, rs62302166, rs62302167, rs75774690	41536652	Wang et al. (2025)
4	77229192	77338285	CCDC158	2	4.46×10^{-9}	rs17001890, rs7677266		
4	77351253	77709406	SHROOM3	2	1.56×10^{-5}	rs11097396, rs4859673	31924810	Corredor et al. (2020)
4	88076260	88166466	KLHL8	1	1.25×10^{-5}	rs10006766	39673281	Wu et al. (2024)
4	88219941	88249056	HSD17B13	1	3.08×10^{-8}	rs72613567	38674389	Elmansoury et al. (2024)
4	89006416	89157569	ABCG2	8	9.44×10^{-15}	rs17731799, rs2231142, rs2622604, rs3114018, rs3114020, rs4148157, rs45570646, rs7672194	39537151	Zhao et al. (2025)
4	100039832	100070449	ADH4	4	8.06×10^{-10}	rs1126670, rs1126671, rs1126672, rs1126673	39710484	Yan et al. (2024)
4	102706764	103000969	BANK1	1	4.80×10^{-5}	rs34592089	21208380	Fan et al. (2011)
4	103167198	103271655	SLC39A8	1	7.42×10^{-6}	rs13107325	39940809	Radhakrishna et al. (2025)
4	144912257	144945498	GYPB	1	8.40×10^{-7}	rs75270861	30033078	Ndila et al. (2018)
4	146676874	146864607	ZNF827	3	7.23×10^{-14}	rs4547811, rs4835265, rs56293839	21909109	Kim et al. (2011)
5	40675032	40701962	PTGER4	1	1.75×10^{-8}	rs2228058	18235104	Nicola et al. (2008)
5	52079136	52254485	ITGA1	1	1.05×10^{-3}	rs4074793	37447386	Kim et al. (2023)
5	55390507	55534186	ANKRD55	2	4.64×10^{-9}	rs6859219, rs7731626	34610981	Li-Gao et al. (2021)
5	55804692	55835983	C5orf67	2	4.97×10^{-6}	rs459193, rs464605	31928498	Lind et al. (2020)
5	74627159	74662926	HMGCR	3	3.94×10^{-10}	rs12654264, rs12916, rs3846663	39571916	Zhang et al. (2025)
5	156341293	156395266	TIMD4	1	1.59×10^{-8}	rs1363232	40804101	Yang et al. (2025)
5	168083738	168733133	SLIT3	1	2.95×10^{-1}	rs4282339	35649495	Tian et al. (2022)
5	176779704	176804599	RGS14	4	1.59×10^{-11}	rs11746443, rs12654812, rs4075958, rs4075959	31754202	Chen et al. (2019)
5	176806432	176830849	SLC34A1	2	8.41×10^{-10}	rs35716097, rs6420094	37984306	Yu et al. (2023)
6	7102830	7257213	RREB1	1	1.31×10^{-8}	rs1334576	41296204	Rybczyński et al. (2025)
6	24166983	24388520	DCDC2	1	8.82×10^{-8}	rs72830895	30078246	Li et al. (2018)
6	24398141	24430816	MRS2	3	4.07×10^{-13}	rs2793422, rs41271779, rs9393553	39048033	Duan et al. (2024)
6	24421060	24500433	GPLD1	6	6.72×10^{-15}	rs1126617, rs2076316, rs7765515, rs7775073, rs78420872, rs9467160	18940312	Yuan et al. (2008)
6	24490197	24542435	ALDH5A1	3	6.11×10^{-16}	rs2744601, rs2760118, rs72834956	41261566	Tan et al. (2025)
6	24539332	24651383	KIAA0319	2	3.65×10^{-12}	rs699463, rs807534	40304040	Yao et al. (2025)
6	25274656	25625758	LRRC16A	1	9.24×10^{-6}	rs2274089	19861489	van der Harst et al. (2010)
6	25778125	25837287	SLC17A1	5	1.03×10^{-14}	rs1185567, rs1185569, rs17342717, rs6456703, rs6913879	26524967	Koyama et al. (2015)
6	25840328	25879471	SLC17A3	17	6.00×10^{-15}	rs1165158, rs1165159, rs1165161, rs1165162, rs1165165, rs1165205, rs1182814, rs12664474, rs1408272, rs1408273, rs17271121, rs3887266, rs556339, rs56027330, rs566530, rs6905614, rs9393672	36077407	Lin et al. (2022)
6	25907982	25935954	SLC17A2	3	6.45×10^{-13}	rs2071300, rs80215559, rs9467636	28905132	Bien et al. (2017)
6	25957917	25992557	TRIM38	1	5.27×10^{-7}	rs1436310	40987417	Wang et al. (2026)
6	26016907	26027278	HIST1H4A	1	1.95×10^{-9}	rs3752420	31701227	Oeckl et al. (2020)
6	26082422	26101438	HFE	1	6.39×10^{-12}	rs1799945	37118679	Barton et al. (2023)
6	26108389	26129266	HIST1H2BC	1	6.82×10^{-4}	rs129128	33302647	
6	32622241	32639466	HLA-DQB1	2	4.49×10^{-5}	rs3891175, rs9273529	14999597	López-Vázquez et al. (2004)

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Table S35: (Continued)

CHR	Gene Start	Gene End	Gene Name	No. of SNPs	P Value	SNP List	PMID	Reference
6	33582951	33669351	ITPR3	1	2.81×10^{-7}	rs57642896	41239426	Zhang et al. (2025)
6	33684415	33719762	IP6K3	1	5.67×10^{-10}	rs9469578	27577108	Moritoh et al. (2016)
6	74400508	74543041	CD109	2	2.48×10^{-7}	rs10455097, rs6909201	29100095	Nguyen et al. (2017)
6	127434844	127525626	RSPO3	7	3.98×10^{-9}	rs1892172, rs1936801, rs2745353, rs4620145, rs6569474, rs6932207, rs9491696	40285372	Li et al. (2025)
6	160537821	160585147	SLC22A1	1	2.23×10^{-8}	rs662138	39245401	Bai et al. (2024)
6	160632794	160684963	SLC22A2	2	1.20×10^{-12}	rs2279463, rs316019	20139901	Li et al. (2010)
6	160947506	161102478	LPA	2	4.43×10^{-12}	rs10455872, rs74617384	39474888	Rochmawati et al. (2025)
7	44178870	44234022	GCK	4	8.05×10^{-15}	rs1799884, rs3757840, rs6975024, rs730497	31924263	Mohammadi et al. (2020)
7	44235577	44258893	YKT6	2	1.50×10^{-15}	rs3824065, rs4607517	14767486	Kluger et al. (2004)
7	72843109	72855450	FZD9	1	3.93×10^{-26}	rs71556711	22617718	Siedlinski et al. (2012)
7	72849728	72941628	BAZ1B	5	2.83×10^{-15}	rs1178979, rs12056034, rs17145713, rs2240466, rs714052	33517564	Kawaguchi et al. (2021)
7	72945683	72977065	BCL7B	1	5.00×10^{-10}	rs13233571	25768928	Ligthart et al. (2015)
7	72978274	72998013	TBL2	2	5.00×10^{-10}	rs17145738, rs2286276	40841581	Nair et al. (2025)
7	73002524	73043903	MLXIPL	6	5.00×10^{-10}	rs1051921, rs17145750, rs34958196, rs35332062, rs3812316, rs799157	38668731	Hehl et al. (2024)
7	97839755	97886563	TECPR1	1	6.62×10^{-12}	rs17169479	30909843	Sudhakar et al. (2019)
7	97915962	98035427	BAIAP2L1	1	9.62×10^{-9}	rs3779195	17568789	Galligan et al. (2007)
7	99277302	99337819	CYP3A7-CYP3A51P	1	5.73×10^{-7}	rs45446698		
7	151248200	151579316	PRKAG2	2	1.20×10^{-7}	rs6947064, rs7805747	32277301	Okuda et al. (2020)
8	19791582	19829770	LPL	14	5.00×10^{-10}	Affx-52343806, rs13702, rs15285, rs1801177, rs2197089, rs264, rs268, rs271, rs295, rs301, rs320, rs325, rs326, rs328	38498802	Zhi et al. (2024)
8	41505744	41759280	ANK1	2	1.47×10^{-7}	rs34265667, rs34664882	36737504	Melton et al. (2023)
8	117957512	118193953	SLC30A8	3	1.11×10^{-7}	rs11558471, rs13266634, rs3802177	37116407	Park et al. (2023)
9	15165842	15312358	TTC39B	2	1.40×10^{-7}	rs471364, rs643531	29103089	Vitali et al. (2017)
9	71315188	71629092	PIP5K1B	1	2.96×10^{-5}	rs4744712	24311711	Franceschini et al. (2014)
9	107538283	107695527	ABCA1	7	2.53×10^{-14}	rs12686004, rs13301006, rs1883025, rs2254819, rs2575876, rs3890182, rs3905000	40059048	Hu et al. (2025)
9	131459802	131488199	PKN3	1	1.13×10^{-6}	rs13283282	35731922	Wang et al. (2022)
9	131487065	131539220	ZER1	1	2.08×10^{-5}	rs3750329	23765955	Fang et al. (2013)
9	136023335	136044320	GBGT1	1	9.50×10^{-8}	rs7868232		
9	136075666	136089714	OBP2B	1	5.00×10^{-10}	rs11244035	37895183	Loika et al. (2023)
9	136125563	136155630	ABO	17	5.00×10^{-10}	Affx-33347130, rs505922, rs507666, rs512770, rs579459, rs581107, rs612169, rs638756, rs643434, rs651007, rs657152, rs687621, rs688976, rs8176719, rs8176740, rs8176742, rs8176745	41092411	Wang et al. (2025)
9	136192543	136208047	SURF6	1	2.67×10^{-5}	rs621907		
9	136223325	136249820	SURF4	1	3.80×10^{-13}	rs56343119	36193893	Tang et al. (2022)
9	136238284	136276220	STKLD1	2	1.55×10^{-15}	Affx-52371914, rs41302673		
9	136274459	136329525	ADAMTS13	2	5.23×10^{-9}	rs117164445, rs4962050	40032339	Chen et al. (2024)
9	136320087	136340909	CACFD1	1	8.10×10^{-15}	rs2073935		
9	139318067	139339305	INPP5E	1	2.49×10^{-5}	rs71269007	41401927	Li et al. (2026)
9	139329548	139384297	SEC16A	1	6.84×10^{-7}	rs34376913	37400387	Dong et al. (2023)
10	5085958	5154878	AKR1C3	1	6.20×10^{-6}	rs2518049	37501650	Battista et al. (2023)
10	5233798	5265910	AKR1C4	4	8.39×10^{-11}	rs17134592, rs1832007, rs3829125, rs75406471	36480560	Karkeet et al. (2022)
10	17626031	17664383	HACD1	1	1.14×10^{-10}	rs4748388		

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Table S35: (Continued)

CHR	Gene Start	Gene End	Gene Name	No. of SNPs	P Value	SNP List	PMID	Reference
10	17681124	17763823	STAM	4	7.22×10^{-16}	rs12416367, rs2688786, rs2688787, rs61842261	31638172	Fishman et al. (2019)
10	17789260	17847866	TMEM236	2	5.00×10^{-10}	rs117163080, rs143235698		
10	18093332	18205091	MRC1	5	5.00×10^{-10}	Affx-52324238, rs149076262, rs187269912, rs55942822, rs75921639	41355949	Park et al. (2026)
10	18235768	18337221	SLC39A12	5	5.55×10^{-15}	rs10764176, rs2478568, rs2478571, rs41277356, rs58377250	41380477	Welton et al. (2026)
10	61405522	61474649	SLC16A9	4	4.31×10^{-11}	rs1171619, rs12356193, rs35209863, rs7094971	19861489	van der Harst et al. (2010)
10	64921983	65230880	JMJD1C	11	5.00×10^{-10}	rs10740118, rs10761731, rs10761756, rs12773283, rs1935, rs2393967, rs6479891, rs6479896, rs7080386, rs7081275, rs7923609	18940312	Yuan et al. (2008)
10	65276113	65389883	REEP3	6	3.06×10^{-14}	rs10733793, rs10740134, rs10822184, rs113803069, rs12411988, rs7076601	18940312	Yuan et al. (2008)
10	70975059	71032315	HKDC1	1	3.66×10^{-7}	rs7919018	39636236	Shan et al. (2024)
10	71024740	71166638	HK1	5	2.94×10^{-13}	rs10128330, rs16926246, rs4746839, rs7072268, rs7909192	33307711	Liu et al. (2021)
10	79545549	79691348	DLG5	2	1.06×10^{-7}	rs12220902, rs55910200	26898345	Paul et al. (2016)
10	94828232	94842641	CYP26A1	1	5.00×10^{-10}	rs2068888	34628270	Xiao et al. (2021)
10	101151627	101195530	GOT1	1	2.78×10^{-6}	rs2862614	35209187	Peracchi et al. (2022)
10	113902971	113980153	GPAM	3	9.97×10^{-9}	rs2255141, rs2297991, rs2792751	41046275	Miyake et al. (2025)
10	114704978	114932437	TCF7L2	4	6.81×10^{-13}	rs12243326, rs12255372, rs4506565, rs7903146	31859960	Petermann-Rocha et al. (2019)
10	126429336	126485439	METTL10	1	9.27×10^{-8}	rs4962696	39774961	Bao et al. (2025)
11	2145342	2187439	INS-IGF2	3	5.00×10^{-10}	Affx-4739950, rs11042751, rs3842752	27651384	Huang et al. (2016)
11	13979184	14294679	SPON1	2	3.40×10^{-11}	rs4756786, rs72632971	41508276	Kang et al. (2025)
11	14294466	14391052	RRAS2	2	1.97×10^{-9}	rs11023197, rs1431374	40705882	Terayama et al. (2025)
11	14521422	14670180	PSMA1	1	5.71×10^{-11}	rs11023265	39988732	Tang et al. (2025)
11	14660191	14898605	PDE3B	2	2.43×10^{-14}	rs1879888, rs73412653	30580553	Wang et al. (2019)
11	14894551	14918874	CYP2R1	4	5.00×10^{-10}	rs10741657, rs11023374, rs2060793, rs7129781	33492600	Bellastella et al. (2021)
11	47285927	47356582	MADD	1	2.65×10^{-8}	rs1052373	33845096	Zavala-Barrera et al. (2021)
11	61515121	61560990	MYRF	1	6.70×10^{-11}	rs10792318	34260928	Kohnke et al. (2021)
11	61578675	61639826	FADS2	5	2.61×10^{-14}	rs174583, rs174591, rs174609, rs2072114, rs61897793	27085774	Walle et al. (2016)
11	62196014	62319332	AHNAK	1	0.00466	rs17157266	20539882	Koshiyama et al. (2010)
11	64318098	64344002	SLC22A11	2	8.88×10^{-16}	rs17300741, rs1783811	33368618	Matsubayashi et al. (2021)
11	65536369	65553062	AP5B1	3	1.43×10^{-8}	rs11227299, rs11604462, rs948493	40391008	Yin et al. (2025)
11	71159217	71217586	NADSYN1	1	1.02×10^{-6}	rs11233800	33847345	Rivera-Paredes et al. (2021)
11	116613886	116648714	BUD13	4	5.00×10^{-10}	Affx-4282707, rs11820589, rs11825181, rs28927680	23505291	Shah et al. (2013)
11	116644276	116663739	ZPR1	8	5.00×10^{-10}	rs11823543, rs12286037, rs2075290, rs2266788, rs3135506, rs35120633, rs603446, rs964184	35999016	Fanlo-Maresma et al. (2022)
11	116686418	116699011	APOA4	2	5.00×10^{-10}	rs12721041, rs12721043	38547584	Gagnon et al. (2024)
11	116695624	116708787	APOC3	1	3.80×10^{-6}	rs12718462	38547584	Gagnon et al. (2024)
11	116709118	116974131	SIK3	5	2.66×10^{-15}	rs12225230, rs61905706, rs75158858, rs75188049, rs7950381	40455993	Höppner et al. (2025)
11	117010000	117053889	PAFAH1B2	2	4.63×10^{-10}	Affx-52324980, rs186808413	39491753	Seah et al. (2025)
11	117044626	117073161	SIDT2	1	2.69×10^{-10}	rs1784042	37902450	Wang et al. (2024)

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Table S35: (Continued)

CHR	Gene Start	Gene End	Gene Name	No. of SNPs	P Value	SNP List	PMID	Reference
11	117065040	117080508	TAGLN	1	2.20×10^{-10}	rs45574931	23906925	Hosper et al. (2013)
11	117070788	117107811	PCSK7	3	9.99×10^{-16}	rs4938362, rs74988348, rs79278568	31945259	Ashraf et al. (2020)
11	117151402	117191972	BACE1	1	1.29×10^{-12}	rs116987336	38901740	Shastri et al. (2024)
11	122521398	122690187	UBASH3B	1	8.59×10^{-5}	rs7941030		
11	126168647	126220644	DCPS	2	8.73×10^{-11}	rs17135399, rs35887873	38547072	Gao et al. (2024)
11	126220540	126289536	ST3GAL4	5	3.89×10^{-16}	rs11220462, rs2298475, rs4937126, rs73632737, rs7949566	40767522	Guo et al. (2025)
12	2899108	2919589	FKBP4	1	1.38×10^{-6}	rs56196860	31540954	Bandleon et al. (2019)
12	4591899	4652674	C12orf4	3	3.33×10^{-16}	rs10849081, rs11063214, rs2970818		
12	20843289	20911320	SLCO1C1	1	1.19×10^{-9}	rs10841614	30296914	Strømme et al. (2018)
12	20958638	21075019	SLCO1B3	1	1.71×10^{-6}	rs74528913	38327217	Du et al. (2024)
12	21279128	21397730	SLCO1B1	8	6.00×10^{-15}	rs11045819, rs11045879, rs11045893, rs4149056, rs4149087, rs4363657, rs73062310, rs7966581	41175506	Bing et al. (2025)
12	21412534	21553371	SLCO1A2	2	1.44×10^{-9}	rs10841795, rs73069053	29873816	Allegra et al. (2018)
12	48494656	48545187	PFKM	1	3.82×10^{-12}	rs4760682	21270901	Luo et al. (2011)
12	111466828	111793358	CUX2	1	4.41×10^{-8}	rs16941230	41171150	Ge et al. (2025)
12	111793455	111811925	FAM109A	1	1.96×10^{-8}	rs3809272		
12	121073422	121110129	CABP1	1	5.83×10^{-15}	rs2859266	39936944	Morris et al. (2025)
12	121119949	121144667	MLEC	2	3.43×10^{-12}	Affx-7006664, rs57830821	17196403	Liu et al. (2007)
12	121143238	121166443	UNC119B	1	1.08×10^{-7}	rs2948149	22291609	Naitza et al. (2012)
12	121410861	121445315	HNF1A	13	3.29×10^{-14}	Affx-52326773, Affx-80247044, rs1169282, rs1169310, rs1183910, rs1800574, rs2244608, rs2245407, rs2259816, rs2393791, rs55834942, rs7310409, rs735396	29067470	Yu et al. (2018)
12	121435835	121459300	C12orf43	3	2.13×10^{-14}	rs1182933, rs12819210, rs2258227	38430045	Qammar et al. (2024)
12	121453095	121482045	OASL	3	3.79×10^{-11}	rs10774580, rs10849829, rs7957197	21943158	Middelberg et al. (2011)
12	121565622	121629439	P2RX7	1	2.59×10^{-6}	rs17434647	32727592	Li et al. (2020)
13	95249104	95291899	GPR180	1	1.83×10^{-6}	rs6492721	38297830	Pandey et al. (2024)
13	113339358	113546482	ATP11A	1	0.000121	rs282578	26567335	Segawa et al. (2016)
14	94838084	94862029	SERPINA1	2	6.38×10^{-12}	rs112635299, rs28929474	35654975	Vujkovic et al. (2022)
14	103393716	103528742	CDC42BPB	1	3.99×10^{-11}	rs35030701	19210549	Adachi et al. (2009)
14	103556044	103581896	EXOC3L4	4	1.38×10^{-12}	rs2297066, rs2297067, rs8017161, rs944002	30255815	Miller et al. (2018)
14	103584762	103608776	TNFAIP2	1	2.12×10^{-8}	Affx-10131553	35659195	Barutta et al. (2023)
15	42641545	42709515	CAPN3	1	9.06×10^{-6}	rs2412710	39973406	Assia Batzir et al. (2025)
15	43614974	43627820	LCMT2	1	9.06×10^{-6}	rs3742970		
15	43798165	43828818	MAP1A	1	2.33×10^{-12}	rs55707100	38785970	Kasher et al. (2024)
15	45689514	45718617	SPATA5L1	1	2.70×10^{-9}	rs3737267	19430482	Köttgen et al. (2009)
15	45874417	45906909	BLOC1S6	1	1.32×10^{-5}	rs12909221		
15	58697953	58866073	LIPC	6	8.16×10^{-15}	rs11632618, rs11854656, rs17240869, rs17269250, rs261334, rs261336	40158091	Zhang et al. (2025)
15	60775483	61526502	RORA	3	5.91×10^{-9}	rs1054156, rs339969, rs340005	25485508	Cadenas et al. (2014)
16	20339373	20369200	UMOD	4	1.17×10^{-10}	rs111285796, rs12917707, rs13333226, rs4293393	40548378	Tamargo et al. (2025)
16	20365492	20421064	PDILT	2	6.11×10^{-11}	rs11864909, rs35208507	38896256	Chen et al. (2024)
16	56759017	56887637	NUP93	4	1.69×10^{-14}	rs2304477, rs735144, rs74765290, rs8062292	40633766	Yuan et al. (2025)
16	56894119	56954762	SLC12A3	6	1.17×10^{-15}	rs11643718, rs13306673, rs13330096, rs35797045, rs4784733, rs55901950	37984306	Yu et al. (2023)
16	56960974	56982793	HERPUD1	1	2.16×10^{-9}	rs2217332	38043868	Paredes et al. (2024)

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Table S35: (Continued)

CHR	Gene Start	Gene End	Gene Name	No. of SNPs	P Value	SNP List	PMID	Reference
16	56990835	57022757	CETP	16	5.00×10^{-10}	rs12934552, rs1532624, rs1800775, rs1800777, rs1864163, rs28888131, rs289715, rs3764261, rs4783961, rs56208677, rs5880, rs5883, rs6499862, rs708272, rs7499892, rs9939224	40596422	Xiao et al. (2025)
16	57018469	57122438	NLRC5	1	9.34×10^{-13}	rs1875236	30453994	Chen et al. (2018)
16	57121455	57187281	CPNE2	1	0.00161	rs117892711		
16	58736035	58773246	GOT2	1	0.000415	rs11076256	38915066	Zhu et al. (2024)
16	67922175	67968581	PSKH1	1	8.91×10^{-7}	rs16942887	8268911	Larsen et al. (1993)
16	88515014	88606574	ZFPM1	2	1.06×10^{-10}	rs7196578, rs904800	26292806	Everson et al. (2015)
16	88776746	88856372	PIEZO1	1	0.00267	Affx-13430005	32636802	Song et al. (2020)
17	1601084	1618662	TLCD2	1	6.64×10^{-10}	rs11078597		
17	1614817	1646893	WDR81	2	2.11×10^{-15}	rs1574525, rs8077638	23022100	Franceschini et al. (2012)
17	1641015	1663562	SERPINF2	1	2.08×10^{-10}	rs2070863	27222041	Poersch et al. (2016)
17	7071750	7087883	ASGR1	1	2.10×10^{-11}	rs55714927	37400795	Yang et al. (2023)
17	7088209	7128369	DLG4	3	1.94×10^{-14}	rs314253, rs3826408, rs77680021	37204119	Li et al. (2023)
17	7115444	7133586	ACADVL	1	2.66×10^{-11}	rs222836	23185754	Yang et al. (2012)
17	7279293	7298093	TNK1	1	1.64×10^{-5}	rs34768933	32694928	Bao et al. (2020)
17	7288046	7303162	PLSCR3	1	9.94×10^{-8}	rs56206519	34808102	Wang et al. (2021)
17	7301293	7312450	TMEM256	1	2.22×10^{-16}	rs35386490		
17	7306502	7328183	NLGN2	2	2.72×10^{-15}	Affx-14343876, rs76749877	32661233	Grigg et al. (2020)
17	7343406	7365932	CHRNA1	1	8.11×10^{-7}	rs9217	32895905	Eiris-Puñal et al. (2020)
17	7357685	7392568	ZBTB4	3	5.00×10^{-10}	rs34914463, rs3760422, rs3867594	40428403	Nehring et al. (2025)
17	7382698	7422935	POLR2A	5	5.00×10^{-10}	rs2228128, rs2228129, rs6761, rs7215922, rs8069501	30116771	Delvalle et al. (2018)
17	7447375	7466207	TNFSF12	4	5.00×10^{-10}	rs11654281, rs117322070, rs4968210, rs9899183	27889570	Grabinger et al. (2017)
17	7460309	7480287	SENTP3	2	5.00×10^{-10}	rs78414518, rs78553499	21331046	Huang et al. (2011)
17	7471024	7487324	EIF4A1	1	5.00×10^{-10}	rs9901675	24294361	Xu et al. (2013)
17	7481965	7496530	MPDU1	1	1.17×10^{-11}	rs4227	11733556	Kranz et al. (2001)
17	7489548	7523215	FXR2	1	5.00×10^{-10}	rs11653545	24188901	Roberts et al. (2014)
17	7512382	7541700	SHBG	4	5.00×10^{-10}	rs13894, rs55784804, rs6259, rs727428	40298068	Feng et al. (2025)
17	7549254	7566089	ATP1B2	2	5.00×10^{-10}	rs1642763, rs72829446	40169113	Karakuş et al. (2025)
17	7566720	7595868	TP53	4	1.61×10^{-10}	rs1625895, rs17883687, rs74351250, rs8073498	40635108	Huang et al. (2025)
17	7603520	7619693	EFNB3	1	5.00×10^{-10}	rs62062590	30262919	Wu et al. (2018)
17	7755003	7793608	NAA38	2	1.11×10^{-16}	rs72841430, rs76730553		
17	7830442	7858237	CNTROB	1	3.65×10^{-11}	rs62623385		
17	16821948	16837856	TBC1D27	1	5.00×10^{-10}	rs3751993		
17	16837398	16880432	TNFRSF13B	3	6.11×10^{-16}	rs113436029, rs4985726, rs6416870	23303382	Hong et al. (2013)
17	37403897	37563530	FBXL20	2	3.97×10^{-9}	rs7208487, rs9890198	32543267	Chu et al. (2021)
17	37819234	37831728	PNMT	1	3.08×10^{-8}	rs2952151	9716702	Gandía et al. (1998)
17	41826099	41841156	SOST	1	1.19×10^{-8}	rs77697917	38714960	Cao et al. (2024)
17	41919145	41945997	CD300LG	1	4.02×10^{-11}	rs72836561	32510982	Wang et al. (2020)
17	45595316	45705642	NPEPPS	1	2.91×10^{-7}	rs80256006		
17	47278596	47292936	GNGT2	1	7.57×10^{-8}	rs55634267	38066059	Mohamed et al. (2023)
17	47295728	47314009	PHOSPHO1	1	3.97×10^{-10}	rs74584378	32332097	Dudakovic et al. (2020)
17	47361568	47444835	ZNF652	1	6.03×10^{-13}	rs16948048	25361553	
17	53337321	53407426	HLF	1	6.85×10^{-7}	rs4793788	34991659	Li et al. (2022)
17	58750172	59475199	BCAS3	2	2.33×10^{-8}	rs72844903, rs9910365	24311711	Franceschini et al. (2014)
17	64203147	64230556	APOH	1	8.35×10^{-8}	rs1801689	35654975	Vujkovic et al. (2022)
17	64293760	64811862	PRKCA	2	0.000514	rs117524772, rs78357146	40890834	Cui et al. (2025)
17	66965773	67063442	ABCA9	1	0.000186	rs113408695		
17	67405838	67543470	MAP2K6	1	0.000474	rs75016991		

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Table S35: (Continued)

CHR	Gene Start	Gene End	Gene Name	No. of SNPs	P Value	SNP List	PMID	Reference
17	76103999	76133488	TMC6	2	3.33×10^{-16}	rs2748427, rs454139		
17	80669582	80690893	FN3KRP	3	1.50×10^{-15}	rs1046896, rs2243523, rs2459703		
17	80688452	80714073	FN3K	2	1.94×10^{-15}	rs1056534, rs2248894		
17	80704938	80906062	TBCD	5	1.32×10^{-12}	rs11655811, rs2677914, rs601555, rs635999, rs7218129		
18	47082069	47124278	LIPG	1	1.17×10^{-10}	rs77960347	24458708	Mikszutowicz et al. (2014)
19	8424011	8444257	ANGPTL4	1	6.33×10^{-13}	rs116843064		
19	11195037	11249506	LDLR	2	7.22×10^{-16}	rs6511720, rs72658867	41198423	Bello-Álvarez et al. (2025)
19	11304969	11378168	DOCK6	1	0.00172	rs17699030		
19	17181591	17329104	MYO9B	2	4.83×10^{-6}	rs116189680, rs35365035		
19	18203585	18267502	MAST3	1	3.40×10^{-7}	rs885683	36165217	Liu et al. (2022)
19	19139387	19173987	ARMC6	1	8.79×10^{-7}	rs73008942		
19	19251376	19308400	MEF2BNB-MEF2B	1	8.87×10^{-7}	rs11668319		
19	19317773	19368061	NCAN	1	1.63×10^{-11}	rs2228603	27752939	Flores et al. (2016)
19	19369841	19389074	TM6SF2	1	5.00×10^{-10}	rs58542926	30589442	Whitfield et al. (2019)
19	19426496	19474563	MAU2	2	5.05×10^{-11}	rs11085259, rs3764567		
19	19491642	19624741	GATAD2A	2	1.55×10^{-15}	rs10415849, rs10424702		
19	19644057	19662468	CILP2	2	1.25×10^{-14}	rs16996148, rs17216525	24350279	Luptáková et al. (2013)
19	19773962	19796735	ZNF101	1	1.29×10^{-9}	rs2304130	33676152	Nie et al. (2021)
19	33316417	33365683	SLC7A9	2	6.88×10^{-9}	rs12460876, rs8101881	31924810	Corredor et al. (2020)
19	35526410	35562481	HPN	2	1.06×10^{-9}	rs11671010, rs45512696	40945584	Lezo et al. (2025)
19	44825706	44865856	ZNF112	1	6.16×10^{-5}	rs8107530		
19	44884808	44910777	ZNF285	1	1.46×10^{-12}	rs62116778		
19	44925423	44957766	ZNF229	2	6.20×10^{-8}	rs17347726, rs62116303		
19	45111911	45145081	IGSF23	1	1.14×10^{-13}	rs62119261		
19	45197421	45218986	CEACAM16	1	1.11×10^{-16}	rs62120566		
19	45241070	45268301	BCL3	2	1.44×10^{-9}	rs2927437, rs2965174	19913121	Talmud et al. (2009)
19	45276126	45308903	CBLC	2	5.00×10^{-10}	Affx-16018598, rs76560105	37603032	Köpfer et al. (2023)
19	45307316	45329678	BCAM	3	4.72×10^{-15}	rs10405693, rs28399637, rs28399654	37011913	Nader et al. (2023)
19	45344393	45397485	PVRL2	15	4.40×10^{-14}	rs11665829, rs11672399, rs11879589, rs12162222, rs157581, rs2075642, rs2075650, rs283814, rs3852859, rs3852860, rs41289512, rs519113, rs6859, rs7254892, rs8104483	19913121	Talmud et al. (2009)
19	45389477	45411946	TOMM40	4	5.00×10^{-10}	rs1160985, rs405509, rs769449, rs769450	33856023	Palmer et al. (2021)
19	45404039	45417650	APOE	2	3.13×10^{-10}	rs439401, rs445925	33856023	Palmer et al. (2021)
19	45412577	45427606	APOC1	1	5.00×10^{-10}	rs4420638	37386009	Shigemizu et al. (2023)
19	45440495	45453753	APOC4	2	5.00×10^{-10}	rs12721109, rs5167	32844720	Plubell et al. (2020)
19	45444239	45457822	APOC2	1	5.00×10^{-10}	rs3760627	34046842	Abbasi et al. (2022)
19	45452842	45501604	CLPTM1	1	2.88×10^{-14}	rs2075620	36011277	Yeh et al. (2022)
19	45591431	45655543	PPP1R37	1	3.63×10^{-6}	rs11672271		
19	45648008	45668408	NKPD1	1	2.70×10^{-8}	rs8109620		
19	46166490	46190717	GIPR	3	8.42×10^{-9}	rs10423928, rs1800437, rs34783010	40452229	Jamialahmadi et al. (2025)
19	46281205	46301060	DMWD	1	2.48×10^{-6}	rs73045960		
19	46381866	46394376	IRF2BP1	1	1.46×10^{-5}	rs11550348		
19	48368723	48394654	SULT2A1	2	2.25×10^{-10}	rs10426201, rs296390	24510383	Chen et al. (2014)
19	49194228	49214191	FUT2	1	5.00×10^{-10}	rs16982241	28056490	Maroni et al. (2017)
19	49210999	49227976	MAMSTR	2	5.78×10^{-13}	rs281380, rs281385	35493725	Zhou et al. (2022)
19	49218842	49249136	RASIP1	2	1.28×10^{-12}	Affx-52359426, rs281408	35493725	Zhou et al. (2022)
19	49239073	49255831	IZUMO1	1	5.00×10^{-10}	rs4021	28247051	Yeste et al. (2017)
19	49985811	50000565	RPL13A	1	4.64×10^{-8}	rs2280401	18502965	Palmqvist et al. (2008)
19	50010536	50034685	FCGRT	1	5.10×10^{-10}	rs111981233	25654695	Roopenian et al. (2015)
19	50025875	50051891	RCN3	2	6.36×10^{-8}	Affx-16089855, rs8108243	40111510	Ding et al. (2025)

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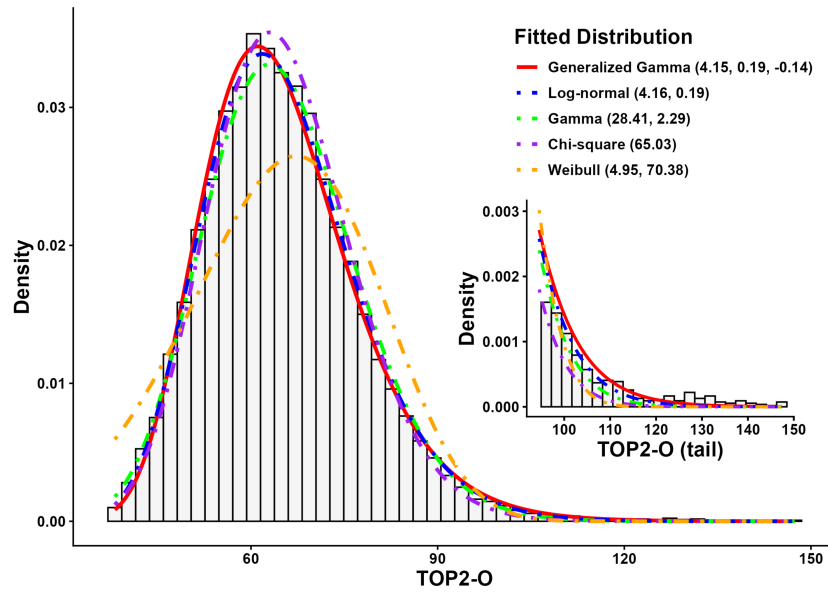
Table S35: (Continued)

CHR	Gene Start	Gene End	Gene Name	No. of SNPs	P Value	SNP List	PMID	Reference
19	54749270	54766167	LILRB5	2	1.44×10^{-12}	rs11668189, rs12975366	35543701	Murphy et al. (2022)
20	23350156	23407156	NAPB	3	2.78×10^{-16}	rs17750862, rs761725, rs78916169	31604595	Matsufuji et al. (2020)
20	23540369	23554386	CST9L	2	1.95×10^{-13}	rs117671467, rs75810394		
20	23578047	23591610	CST9	1	7.85×10^{-11}	rs1158167	35227251	Mohamed et al. (2022)
20	23661277	23674662	CST4	3	5.00×10^{-10}	rs112308292, rs117877399, rs73104320	25329717	de Sousa-Pereira et al. (2014)
20	23723190	23736574	CST1	2	9.60×10^{-15}	rs116548544, rs117567509	25329717	de Sousa-Pereira et al. (2014)
20	23799404	23812312	CST2	1	4.77×10^{-15}	rs6106728	25329717	de Sousa-Pereira et al. (2014)
20	25270379	25376618	ABHD12	2	6.22×10^{-8}	rs6083818, rs7267979	33571455	Khandelwal et al. (2021)
20	42979441	43066485	HNF4A	1	2.26×10^{-6}	rs1800961	37116407	Park et al. (2023)
20	44174791	44212989	WFDC8	1	1.95×10^{-7}	rs2250860		
20	44272202	44303878	WFDC11	2	4.57×10^{-14}	rs45546535, rs79475204		
20	44446853	44460953	TNNC2	2	5.00×10^{-10}	rs370237, rs380397	33755597	van de Loch et al. (2021)
20	44457256	44476914	SNX21	3	1.66×10^{-12}	rs117191103, rs174745, rs197669	23986476	Danson et al. (2013)
20	44481220	44512770	ZSWIM3	4	7.98×10^{-13}	rs1045493, rs2903808, rs6130959, rs78044163	39851231	Ma et al. (2025)
20	44512111	44524926	NEURL2	1	5.00×10^{-10}	rs4608591		
20	44522259	44546003	PLTP	3	5.00×10^{-10}	rs441346, rs6065904, rs73307905	24267726	Leana et al. (2013)
20	44558313	44581732	PCIF1	3	5.00×10^{-10}	rs3746503, rs7679, rs77617917	26009633	Kim et al. (2015)
20	44572292	44606560	ZNF335	3	2.67×10^{-13}	rs13040315, rs3746506, rs73128528	39061094	Theusch et al. (2024)
20	44632547	44650200	MMP9	4	5.00×10^{-10}	Affx-16780572, rs17576, rs2274755, rs3918279	41325860	Alharbi et al. (2026)
20	44645329	44693789	SLC12A5	2	1.11×10^{-16}	rs10432735, rs3848726	36645171	Tong et al. (2023)
20	44741899	44763384	CD40	2	4.91×10^{-13}	rs12481282, rs41282788	40197747	Huang et al. (2025)
22	18265415	18512325	MICAL3	5	4.16×10^{-11}	rs1076540, rs5992137, rs8140977, rs9605480, rs9617650	40397357	Zhang et al. (2025)
22	24858344	24927553	UPB1	2	5.32×10^{-13}	rs117038722, rs1543757		
22	24974629	25029972	GGT1	2	5.00×10^{-10}	rs5751901, rs5751904	28521864	Honma et al. (2017)
22	25110001	25175687	PIWIL3	2	2.35×10^{-8}	rs117329800, rs56032751		
22	37442779	37464430	KCTD17	1	2.86×10^{-7}	rs2235321	33478561	Huang et al. (2021)
22	37456476	37504693	TMPRSS6	2	5.93×10^{-11}	Affx-89007920, rs4820268	36102277	Barrows et al. (2022)
22	38909954	38971201	DMC1	1	4.45×10^{-6}	rs1980455	23182424	Sharma et al. (2013)
22	38969125	39057634	FAM227A	1	3.00×10^{-7}	rs4821797		
22	39076548	39102423	JOSD1	1	1.85×10^{-6}	rs5750671		
22	44314619	44348451	PNPLA3	4	3.89×10^{-15}	Affx-19716376, rs12483959, rs2281135, rs738409	40128159	Liu et al. (2025)
22	44346261	44397412	SAMM50	5	3.05×10^{-15}	rs1007863, rs2073080, rs2143571, rs3761472, rs3827385	34490745	Lee et al. (2022)

Table S36: Target genes, corresponding drug names, impacted blood phenotypes and treated diseases/disorders identified from DrugBank and TTD datasets.

Gene	Drug Name	Phenotype	Description
ALPL	DS-1211	ALP	a potent and selective novel small molecule tissue-nonspecific alkaline phosphatase (TNAP) inhibitor
PCSK9	Alirocumab	TC	lower the amount of cholesterol in the blood and decrease the chance of having a heart attack or stroke in selected patients
	Evolocumab	TC	help lower high cholesterol and prevent heart attacks and stroke
	Inclisiran	TC	lowers bad cholesterol levels in the blood
	Lerodalcibep	TC	combination with diet and exercise to lower cholesterol in adults
CASR	NPS-2143	Ca	Investigated for use in osteoporosis
	Calcium phosphate dihydrate	Ca	For use as an over the counter calcium and phosphate supplement, antacid, or a source of calcium and phosphate in toothpaste
	Cinacalcet	Ca	treat a gland condition that develops in kidney disease, and high calcium in the blood
	Ronacaleret	Ca	Post-menopausal women with osteoporosis
	Etelcalcetide	Ca	treat a gland condition that develops in kidney disease, and high calcium in the blood
GHSR	Ulimorelin	Glu	for both POI and diabetic gastroparesis
HMGCR	Cerivastatin	TC/LDL	Hyperlipidaemia, Multiple myeloma
	Fluvastatin	TC	Hypercholesterolaemia
	Lovastatin	TC	Hypercholesterolaemia, Cardiovascular disease
	Pravastatin	TC	Hypercholesterolaemia
	Rosuvastatin	TC	Hypercholesterolaemia
	Simvastatin	TC	Hypercholesterolaemia
	Teriflunomide	TC/LDL	Hyperlipidaemia, Multiple sclerosis, Rheumatoid arthritis, Hepatitis B virus infection
	Tocotrienol	TC/LDL	Hyperlipidaemia
ALDH5A1	Chlormerodrin	UA/Urea	diuretic
LPL	Clofibrate	TC/LDL	treat high cholesterol and high levels of fat in the blood
	Gemfibrozil	TC/LDL	lower the amount of cholesterol in the blood and decrease the chance of having a heart attack or stroke
	Omega-3-carboxylic acids	TC/LDL	lower levels of fats in the blood
	Alipogene tiparvovec	TC/LDL	the treatment of lipoprotein lipase (LPL) deficiency
	Glycyrrhizic acid	Glu	treatment of premenstrual syndrome, treatment of viral infections, anti-lipidemic and antihyperglycemic
ABCA1	Probucol	TC/LDL	lower LDL and HDL cholesterol
	Glyburide	Glu	treat diabetes in patients not taking insulin
SOST	Romosozumab	Ca	treat some types of osteoporosis, a bone disorder leading to bone weakness
GIPR	Tirzepatide	Glu	treat type II diabetes in adults

A



B

	AIC	BIC	KL	
Generalized Gamma	189800	189825	0.00409	Rank 1 (Best) 2 3 4 5 (Worst)
Log-normal	189887	189903	0.00467	
Gamma	190294	190310	0.01036	
Chi-square	190531	190539	0.01799	
Weibull	195964	195980	0.08164	

Figure S1: (A) Histogram of the TOP2-O null distribution in real data analysis, with fitted density curves from five distributions: Generalized Gamma (red), Gamma (green), Log-normal (blue), Chi-square (purple), and Weibull (orange). Inset shows a magnified view of the distribution tail. (B) Heatmap illustrating the goodness-of-fit of above-mentioned five distributions for the TOP2-O null distribution, based on five common evaluation metrics: Akaike information criterion (AIC), Bayesian information criterion (BIC), and Kullback–Leibler (KL) divergence.

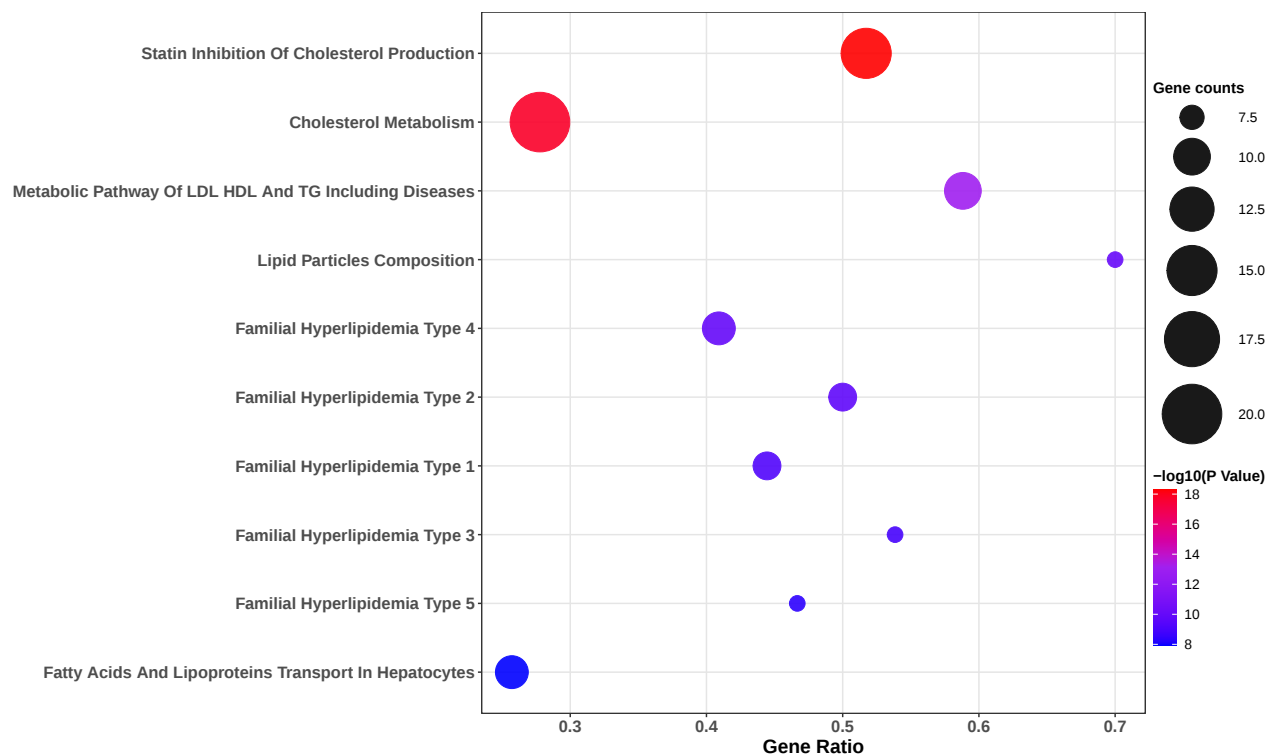


Figure S2: Bubble plot illustrating top 10 enriched biological pathways associated with the identified 373 pleiotropic genes. The x-axis represents the gene ratio (proportion of pathway genes present in the gene set), the y-axis lists enriched pathways, and bubble size corresponds to the number of genes in each pathway. Color intensity (gradient from blue to red) indicates the significance of enrichment, quantified as p -value. Pathway enrichment analysis was performed using the WikiPathways 2024 Human database via the Enrichr web server.