Supplementary Note

1 Regression model to estimate genetic covariance

We follow the same notations in the main text. We can approximate z_2 by

$$z_2 = \frac{Y^T \phi_2}{\sqrt{n_2}} = \frac{Y^T (Y\gamma + \delta)}{\sqrt{n_2}}.$$

Then, we have

$$\begin{aligned} E\left[X_i^T z_2 \phi_{1i}\right] &= E\left[X_i^T \frac{Y^T (Y\gamma + \delta)}{\sqrt{n_2}} \left(X_i^T \beta + \epsilon_i\right)\right] \\ &= E\left[X_i^T \left(\frac{X_S^T X_S + Y_T^T Y_T}{\sqrt{n_2}}\gamma + \frac{X_S^T \delta_S + Y_T^T \delta_T}{\sqrt{n_2}}\right) \left(X_i^T \beta + \epsilon_i\right)\right]. \end{aligned}$$

Here, Y_T is the genotype matrix of the samples exclusively included in study 2, i.e., Y_T consists of the last $n_2 - n_s$ rows of Y. We continue the derivations:

$$\begin{aligned} E\left[X_i^T z_2 \phi_{1i}\right] &= E\left[X_i^T \frac{X_S^T X_S + Y_T^T Y_T}{\sqrt{n_2}} \gamma X_i^T \beta\right] + E\left[X_i^T \frac{X_S^T \delta_S}{\sqrt{n_2}} \epsilon_i\right] \\ &= X_i^T \left[X_S^T X_S + (n_2 - n_s) R\right] X_i \frac{\rho_g}{m\sqrt{n_2}} + X_i^T X_i \mathbf{1}_{\{i \le n_s\}} \frac{\rho_e}{\sqrt{n_2}}. \end{aligned}$$

2 Regression weights

The weights in GENJI's regression are given by the reciprocal of the variance of $X_i^T z_2 \phi_{1i}$. We need to calculate $E\left[\left(X_i^T z_2 \phi_{1i}\right)^2\right]$:

$$\begin{aligned} E\left[\left(X_i^T z_2 \phi_{1i}\right)^2\right] &= E\left\{\left[X_i^T \left(\frac{X_S^T X_S + Y_T^T Y_T}{\sqrt{n_2}}\gamma + \frac{X_S^T \delta_S + Y_T^T \delta_T}{\sqrt{n_2}}\right)\right]^2 \left(X_i^T \beta + \epsilon_i\right)^2\right\} \\ &= E\left[\left(X_i^T \frac{X_S^T X_S + Y_T^T Y_T}{\sqrt{n_2}} \gamma \beta^T X_i + X_i^T \frac{X_S^T X_S + Y_T^T Y_T}{\sqrt{n_2}} \gamma \epsilon_i \right.\right. \\ &\quad \left.\left. + X_i^T \frac{X_S^T \delta_S + Y_T^T \delta_T}{\sqrt{n_2}} \beta^T X_i + X_i^T \frac{X_S^T \delta_S + Y_T^T \delta_T}{\sqrt{n_2}} \epsilon_i\right)^2\right]. \end{aligned}$$

We calculate the expectations of all the terms above and sum them up:

$$\begin{aligned} & E\left(X_i^T \frac{X_S^T X_S + Y_T^T Y_T}{\sqrt{n_2}} \gamma \beta^T X_i X_i^T \frac{X_S^T \delta_S + Y_T^T \delta_T}{\sqrt{n_2}} \epsilon_i\right) \\ =& E\left(X_i^T \frac{X_S^T X_S + Y_T^T Y_T}{\sqrt{n_2}} \gamma \epsilon_i X_i^T \beta \frac{\delta_S^T X_S + \delta_T^T Y_T}{\sqrt{n_2}} X_i\right) \\ =& \frac{\rho_g}{m n_2} E\left[X_i^T \left(X_S^T X_S + Y_T^T Y_T\right) X_i X_i^T X_S^T \delta_S \epsilon_i\right] \\ =& \frac{\rho_g \rho_e}{m n_2} X_i^T \left[X_S^T X_S + (n_2 - n_s) R\right] X_i X_i^T X_i \mathbf{1}_{\{i \le n_s\}} \end{aligned}$$

$$
\begin{aligned}
&E\left[\left(X_i^T \frac{X_S^T X_S + Y_T^T Y_T}{\sqrt{n_2}} \gamma \epsilon_i\right)^2\right] \\
=&\frac{1-h_1^2}{n_2}\frac{h_2^2}{m} E\left[X_i^T\left(X_S^T X_S + Y_T^T Y_T\right)\left(X_S^T X_S + Y_T^T Y_T\right) X_i\right] \\
=&\frac{1-h_1^2}{n_2}\frac{h_2^2}{m} X_i^T\left(X_S^T X_S + (n_2-n_s)R\right)\left(X_S^T X_S + (n_2-n_s)R\right) X_i \\
+&\frac{\left(1-h_1^2\right) h_2^2}{n_2} X_i^T\left(n_2-n_s\right) R X_i
\end{aligned}
$$

$$
\begin{aligned}
&E\left[\left(X_i^T \frac{X_S^T \delta_S + Y_T^T \delta_T}{\sqrt{n_2}} \beta^T X_i\right)^2\right] \\
=&E\left[\left(X_i^T \frac{X_S^T \delta_S + Y_T^T \delta_T}{\sqrt{n_2}}\right)^2\left(\beta^T X_i\right)^2\right] \\
=&\frac{\left(1-h_2^2\right) h_1^2}{m n_2} X_i^T X_i X_i^T\left[X_S^T X_S + \left(n_2-n_s\right) R\right] X_i
\end{aligned}
$$

$$
\begin{aligned}
&E\left[\left(X_i^T \frac{X_S^T \delta_S + Y_T^T \delta_T}{\sqrt{n_2}} \epsilon_i\right)^2\right] \\
=&\frac{\left(1-h_1^2\right)\left(1-h_2^2\right)}{n_2} X_i^T\left[X_S^T X_S + \left(n_2-n_s\right) R\right] X_i + \frac{2\rho_e^2}{n_s}\left(X_i^T X_i\right)^2
\end{aligned}
$$

$$
\begin{aligned}
&E\left[\left(X_i^T \frac{X_S^T X_S + Y_T^T Y_T}{\sqrt{n_2}} \gamma \beta^T X_i\right)^2\right] \\
=&E\left[X_i^T \frac{X_S^T X_S + Y_T^T Y_T}{\sqrt{n_2}} \gamma \beta^T X_i X_i^T \beta \gamma^T \frac{X_S^T X_S + Y_T^T Y_T}{\sqrt{n_2}} X_i\right] \\
=&E\left[X_i^T \frac{X_S^T X_S + Y_T^T Y_T}{\sqrt{n_2}}\left(2\frac{\rho_g^2}{m^2} X_i X_i^T + \frac{h_1^2 h_2^2}{m^2} X_i^T X_i \otimes I_m\right) \frac{X_S^T X_S + Y_T^T Y_T}{\sqrt{n_2}} X_i\right] \\
=&2\frac{\rho_g^2}{m^2 n_2} X_i^T X_S^T X_S X_i X_i^T X_S^T X_S X_i + 4\frac{\rho_g^2\left(n_2-n_s\right)}{m^2 n_2} X_i^T X_S X_S X_i X_i^T R X_i \\
+&2\frac{\rho_g^2\left(n_2-n_s\right)^2}{m^2 n_2}\left(X_i^T R X_i\right)^2 + 4\frac{\rho_g^2\left(n_2-n_s\right)}{m^2 n_2}\left(X_i^T R X_i\right)^2 \\
+&\frac{h_1^2 h_2^2}{m^2 n_2} X_i^T X_i X_i^T X_S^T X_S X_S^T X_S X_i + 2\frac{h_1^2 h_2^2\left(n_2-n_s\right)}{m^2 n_2} X_i^T X_i X_i^T X_S^T X_S R X_i \\
+&\frac{h_1^2 h_2^2\left(n_2-n_s\right)^2}{m^2 n_2} X_i^T X_i X_i^T R^2 X_i + \frac{h_1^2 h_2^2\left(n_2-n_s\right)}{m n_2} X_i^T X_i X_i^T R X_i
\end{aligned}
$$

Thus, after plugging these results in, we have

$$
\begin{aligned}
&Var\left(X_i^T z_2 \phi_{1i}\right) = E\left[\left(X_i^T z_2 \phi_{1i}\right)^2\right] - \left[E\left(X_i^T z_2 \phi_{1i}\right)\right]^2 \\
=&\left(X_i^T\left[X_S^T X_S + \left(n_2-n_s\right) R\right] X_i \frac{\rho_g}{m\sqrt{n_2}} + X_i^T X_i \mathbf{1}_{\{i \leq n_s\}} \frac{\rho_e}{\sqrt{n_2}}\right)^2 \\
+&\frac{1}{n_2}\left[X_i^T X_i \frac{h_1^2}{m} + \left(1-h_1^2\right)\right]\left\{X_i^T\left[X_S^T X_S + \left(n_2-n_s\right) R\right]\left[X_S^T X_S + \left(n_2-n_s\right) R\right] X_i \frac{h_2^2}{m}\right. \\
+&\left. X_i^T X_S^T X_S\left(1-h_2^2\right) + \left(n_2-n_s\right) X_i^T R X_i\right\}.
\end{aligned}
$$