

**Supplementary Materials for “An Efficient and Computationally
Robust Statistical Method for Analyzing Case-Control
Mother-Offspring Pair Genetic Association Studies”** by
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**Appendix A. Derivation of the Log Profile Likelihood Function (2.5) in the
Main Text.**

We adopt the notation in the main text. The constraint on the prevalence $\text{pr}(Y = 1) = f$ can be written as $\sum_j \sum_k \sum_{i=1}^n \text{pr}(Y = 1|G^o = j, G^m = k) \text{pr}(G^o = j|G^m = k) \text{pr}(G^m = k|X_i) \pi_i = f$, or equivalently

$$\sum_{i=1}^n H_i(\Theta) \pi_i = f. \quad (\text{S1})$$

The aim is to maximize the log empirical likelihood function

$$\log L(\Theta, \boldsymbol{\pi}) = l_1(\Theta) + \sum_{i=1}^n \log \pi_i \quad (\text{S2})$$

subject to the constraints (S1) and $\sum_{i=1}^n \pi_i = 1$, where

$$l_1(\Theta) = \sum_{i=1}^n \{ \log \text{pr}(Y_i|G_i^o, G_i^m, X_i) + \log \text{pr}(G_i^o|G_i^m) + \log \text{pr}(G_i^m|X_i) \}.$$

Using the Lagrange multiplier method, this maximization problem is equivalent to maximizing

$$l_1(\Theta) + \sum_{i=1}^n \log \pi_i - \zeta \left(\sum_{i=1}^n \pi_i - 1 \right) - n\lambda \left(\sum_{i=1}^n H_i(\Theta) - f \right).$$

Set the derivative of the above function with respect to π_i to 0, we obtain

$$\frac{1}{\pi_i} = \zeta + n\lambda H_i(\Theta), \quad (\text{S3})$$

or equivalently

$$1 = \zeta \pi_i + n\lambda H_i(\Theta) \pi_i.$$

Summing the above equation over $i = 1, \dots, n$, we have that $\zeta = n(1 - \lambda f)$. Plugging this into (S3) gives

$$\pi_i = \frac{1}{n\{1 + \lambda(H_i(\Theta) - f)\}}.$$

Plugging the above expression into (S1) gives equation (2.6) in the main text, which is the constraint on the multiplier λ . The maximization problem is equivalent to maximizing (S2), or (2.5) in the main text, subject to the constraint (2.6) in the main text.

Appendix B. Derivation of Equations in (2.8) in the Main Text.

We outline the proof of the two equations in (2.8) in the main text, following that of Theorem 1 of Zhang et al. (2018). We adopt the notation in the main text. Denote $Z = (X, G^o, G^m)$, $Z_i = (X_i, G_i^o, G_i^m)$, $G = (G^o, G^m)$, $G_i = (G_i^o, G_i^m)$, $p_Z(Z; \Theta) = \text{pr}_\Theta(Y = 1|Z)$, $p_X(X; \Theta) = \text{pr}_\Theta(Y = 1|X)$. Let \mathcal{G} be the set consisting of all possible values of (G^o, G^m) . For any measurable function t , let $E\{t(Z)|Y = 1\}$ and $E\{t(Z)|Y = 0\}$ be denoted by $E_1\{t(Z)\}$ and $E_0\{t(Z)\}$, respectively. Furthermore, $E\{t(Z)\}$ denotes the expectation of $t(Z)$ in the population from which cases and controls arise.

We can show that for any measurable function t , the following results hold:

$$E_1\{t(Z)\} = E\left\{\frac{p_Z(Z; \Theta_0)}{f}t(Z)\right\} \text{ and } E_0\{t(Z)\} = E\left\{\frac{1 - p_Z(Z; \Theta_0)}{1 - f}t(Z)\right\}, \quad (\text{S4})$$

$$E\left\{\sum_{i=1}^n t(Z_i)\right\} = nE\left[\{1 + \lambda_0(p_Z(Z; \Theta_0) - f)\}t(Z)\right], \quad (\text{S5})$$

and

$$E\left\{\sum_{i=1}^n \frac{(2Y_i - 1)t(Z_i)}{1 + Y_i + (2Y_i - 1)p_Z(Z_i; \Theta)}\right\} = n\lambda_0 E\{t(Z)\}, \quad (\text{S6})$$

provided that the relevant expectations exist and are finite. Since $E\{p_Z(Z; \Theta_0)|X\} = p_X(X; \Theta_0)$ and $E\{p_X(X; \Theta_0)\} = \text{pr}_{\Theta_0}(Y = 1) = f$, applying (S5), we have that

$$E\left[\sum_{i=1}^n \frac{p_X(X_i; \Theta_0) - f}{1 + \lambda_0\{p_X(X_i; \Theta_0) - f\}}\right] = nE\left[\frac{1 + \lambda_0\{p_Z(Z; \Theta_0) - f\}}{1 + \lambda_0\{p_X(X; \Theta_0) - f\}}\{p_X(X; \Theta_0) - f\}\right] = 0. \quad (\text{S7})$$

This proves

$$E\left\{\frac{\partial}{\partial \lambda} l(\Theta_0, \lambda_0)\right\} = 0. \quad (\text{S8})$$

Next we prove that

$$E\left\{\frac{\partial}{\partial \Theta} l(\Theta_0, \lambda_0)\right\} = 0. \quad (\text{S9})$$

Note that

$$\begin{aligned} l(\Theta, \lambda_0) &= \sum_{i=1}^n \log \text{pr}_\Theta(Y_i|Z_i) + \sum_{i=1}^n \log \text{pr}_\Theta(G_i|Z_i) - \sum_{i=1}^n \log[n\{1 + \lambda_0(p_X(X_i; \Theta) - f)\}] \\ &:= \ell^{(1)}(\Theta, \lambda_0) + \ell^{(2)}(\Theta, \lambda_0) - \ell^{(3)}(\Theta, \lambda_0), \end{aligned} \quad (\text{S10})$$

We have that

$$E\left\{\frac{\partial}{\partial \Theta} \ell^{(1)}(\Theta_0, \lambda_0)\right\} = E\left\{\sum_{i=1}^n \frac{(2Y_i - 1)\partial p_Z(Z_i; \Theta_0)/\partial \Theta}{1 + Y_i + (2Y_i - 1)p_Z(Z_i; \Theta_0)}\right\} = n\lambda_0 E\left\{\frac{\partial p_Z(Z; \Theta_0)}{\partial \Theta}\right\}. \quad (\text{S11})$$

By (S4), we have that

$$\begin{aligned}
E \left\{ \frac{\partial}{\partial \Theta} \ell^{(2)}(\Theta_0, \lambda_0) \right\} &= n_1 E \left\{ \frac{p_Z(Z; \Theta_0)}{f} \frac{\partial}{\partial \Theta} \log \text{pr}_{\Theta_0}(G|X) \right\} + n_0 E \left\{ \frac{1 - p_Z(Z; \Theta_0)}{1 - f} \frac{\partial}{\partial \Theta} \log \text{pr}_{\Theta_0}(G|X) \right\} \\
&= \frac{n_0}{1 - f} E \left\{ \frac{\partial}{\partial \Theta} \log \text{pr}_{\Theta_0}(G|X) \right\} + n \lambda_0 E \left\{ p_Z(Z; \Theta_0) \frac{\partial}{\partial \Theta} \log \text{pr}_{\Theta_0}(G|X) \right\} \\
&= 0 + n \lambda_0 E \left\{ \text{pr}_{\Theta_0}(Y = 1|G) \frac{\partial}{\partial \Theta} \log \text{pr}_{\Theta_0}(G|X) \right\} \\
&= n \lambda_0 E \left\{ \sum_{g \in \mathcal{G}} \text{pr}_{\Theta_0}(Y = 1|G = g, X) \frac{\partial}{\partial \Theta} \text{pr}_{\Theta_0}(G = g|X) \right\}. \tag{S12}
\end{aligned}$$

By (S6) and (S5), we have that

$$\begin{aligned}
E \left\{ \frac{\partial}{\partial \Theta} \ell^{(3)}(\Theta_0, \lambda_0) \right\} &= \lambda_0 E \left[\sum_{i=1}^n \frac{\partial p_X(X_i; \Theta_0) / \partial \Theta}{1 + \lambda_0 \{p_X(X_i; \Theta_0) - f\}} \right] \\
&= n \lambda_0 E \left[\frac{1 + \lambda_0 \{p_Z(Z; \Theta_0) - f\}}{1 + \lambda_0 \{p_X(X; \Theta_0) - f\}} \frac{\partial p_X(X; \Theta_0)}{\partial \Theta} \right] \\
&= n \lambda_0 E \left[\frac{\partial p_X(X; \Theta_0)}{\partial \Theta} \right] \tag{S13}
\end{aligned}$$

$$\begin{aligned}
&= n \lambda_0 E \left\{ \frac{\partial}{\partial \Theta} \sum_{g \in \mathcal{G}} \text{pr}_{\Theta_0}(Y = 1|X, G = g) \text{pr}_{\Theta_0}(G = g|X) \right\} \\
&= n \lambda_0 E \left\{ \sum_{g \in \mathcal{G}} \frac{\partial}{\partial \Theta} \text{pr}_{\Theta_0}(Y = 1|X, G = g) \text{pr}_{\Theta_0}(G = g|X) \right. \\
&\quad \left. + \sum_{g \in \mathcal{G}} \text{pr}_{\Theta_0}(Y = 1|X, G = g) \frac{\partial}{\partial \Theta} \text{pr}_{\Theta_0}(G = g|X) \right\} \\
&= E \left\{ \frac{\partial}{\partial \Theta} \ell^{(1)}(\Theta_0, \lambda_0) \right\} + E \left\{ \frac{\partial}{\partial \Theta} \ell^{(2)}(\Theta_0, \lambda_0) \right\}. \tag{S14}
\end{aligned}$$

Equation (S9) follows from (S10) and (S14). The two equations in (2.8) in the main text are proved by (S8) and (S9).

Appendix C. Asymptotic Equivalence of Profile MLE and Modified Profile MLE

Here we follow the proof of Theorem 2 of Zhang et al. (2018) to show the asymptotic equivalence of the profile MLE and the modified profile MLE of Θ . It follows from equation (2.8) in the main text and the expression of the score function $\partial l_{\text{mp}}(\Theta) / \partial \Theta$ that with probability tending to 1 there exists a solution $\hat{\Theta}$ to equation (2.11), which is consistent for Θ_0 , under some regularity conditions. Likewise, with probability tending to 1 there exists a solution $(\tilde{\Theta}, \tilde{\lambda})$ to the score equations (2.7) in the main text, which is consistent for (Θ_0, λ_0) . In what follows, we outline the proof for the asymptotic equivalence of $\tilde{\Theta}$ and $\hat{\Theta}$.

If we write

$$U(\Theta) = \frac{\partial}{\partial \Theta} l_{\text{p}}(\Theta) = \frac{\partial}{\partial \Theta} l(\Theta, \lambda)|_{\lambda=\lambda(\Theta)}$$

and

$$S_0(\Theta) = \frac{\partial^2}{\partial\Theta\partial\Theta'} l(\Theta, \boldsymbol{\lambda}_0),$$

then we have that

$$n^{1/2}(\tilde{\Theta} - \Theta_0) = -\{S_0(\Theta_0)/n\}^{-1}n^{-1/2}U(\Theta_0)\{1 + o_p(1)\}. \quad (\text{S15})$$

Similarly, we have that

$$n^{1/2}(\hat{\Theta} - \Theta_0) = -\{S_0(\Theta_0)/n\}^{-1}n^{-1/2}U_0(\Theta_0)\{1 + o_p(1)\}, \quad (\text{S16})$$

where $U_0(\Theta) = \partial l(\Theta, \boldsymbol{\lambda}_0)/\partial\Theta$. Using Taylor's series expansion, we have that

$$n^{-1/2}\{U(\Theta_0) - U_0(\Theta_0)\} = \frac{1}{n} \frac{\partial^2 l(\Theta_0, \boldsymbol{\lambda}_0)}{\partial\Theta\partial\boldsymbol{\lambda}'} n^{1/2}\{\boldsymbol{\lambda}(\Theta_0) - \boldsymbol{\lambda}_0\}(1 + o_p(1)). \quad (\text{S17})$$

Futhermore, it follows from $E\{n^{-1}\partial^2 l(\Theta_0, \boldsymbol{\lambda}_0)/\partial\Theta\partial\boldsymbol{\lambda}'\} = 0$ that

$$\frac{1}{n} \frac{\partial^2 l(\Theta_0, \boldsymbol{\lambda}_0)}{\partial\Theta\partial\boldsymbol{\lambda}'} \rightarrow 0 \text{ in probability.} \quad (\text{S18})$$

It follows from (S17)-(S18) that

$$n^{-1/2}\{U(\Theta_0) - U_0(\Theta_0)\} \rightarrow 0 \text{ in probability.} \quad (\text{S19})$$

The asymptotic equivalence of $\tilde{\Theta}$ and $\hat{\Theta}$ follows from (S15), (S16), and (S19).

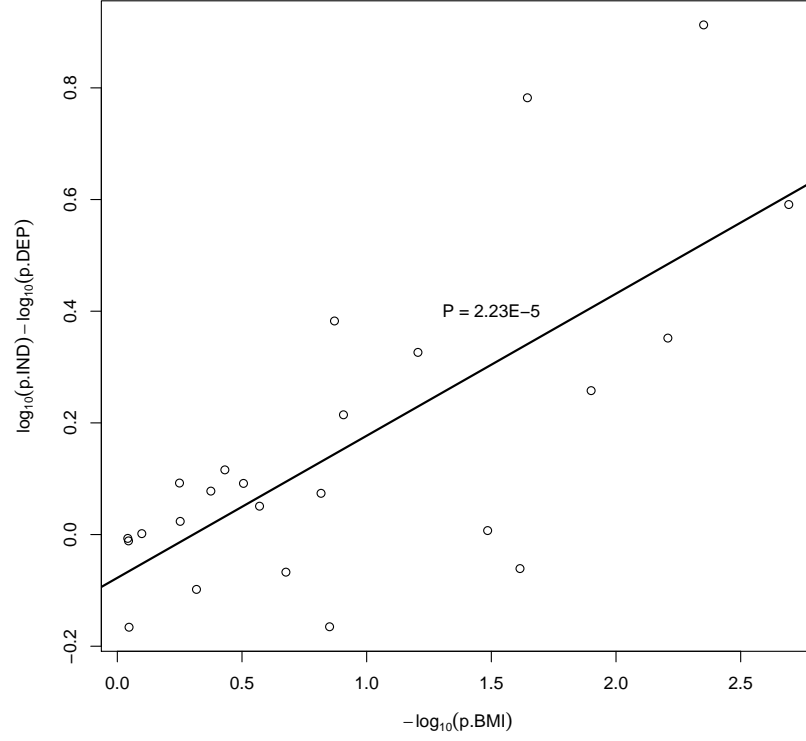


Figure S1: For the X-axis, p.BMI is the p-value for testing the association between pp-BMI and maternal genotype G^m with DEP. For the Y-axis, p.IND and p.DEP are the p-values for testing associations between offspring genotype G^o and low birth weight Y with DEP and IND, respectively. Here DEP and IND are our proposed method with and without dependence dependence assumption between X and G^m , respectively.

Table S1: Estimation and significance test results for simulation studies comparing DEP and DEP-CLH with moderate association between maternal genotype and covariate (additive mode of inheritance, $f = 0.01$, $\theta = 0.2$, $\eta = \log(1.2)$).

| $G^m \sim X^c$ | log(OR) | True ^d | DEP ^a | | | | | DEP-CLH ^b | | | | | | |
|------------------------|------------------------|------------------------|-------------------|-----------------|------------------|-----------------|--------------------|----------------------|-----------------|------------------|-----------------|--------------------|-------|-------|
| | | | Bias ^e | SE ^f | SEE ^g | CP ^h | Power ⁱ | Bias ^e | SE ^f | SEE ^g | CP ^h | Power ⁱ | | |
| The linear model (3.2) | β_{G^o} | 0.000 | -0.022 | 0.156 | 0.153 | 0.946 | 0.054 | -0.026 | 0.158 | 0.155 | 0.941 | 0.057 | | |
| | β_{G^m} | 0.000 | 0.029 | 0.148 | 0.154 | 0.948 | 0.052 | 0.033 | 0.151 | 0.155 | 0.943 | 0.055 | | |
| | $\beta_{G^o \times X}$ | 0.000 | -0.011 | 0.129 | 0.131 | 0.956 | 0.044 | -0.009 | 0.129 | 0.132 | 0.957 | 0.041 | | |
| | $\beta_{G^m \times X}$ | 0.000 | -0.011 | 0.183 | 0.171 | 0.922 | 0.078 | -0.014 | 0.192 | 0.179 | 0.915 | 0.083 | | |
| | | β_{G^o} | 0.182 | -0.016 | 0.142 | 0.149 | 0.962 | 0.182 | -0.019 | 0.147 | 0.150 | 0.960 | 0.186 | |
| | | β_{G^m} | 0.182 | 0.031 | 0.159 | 0.150 | 0.932 | 0.298 | 0.040 | 0.195 | 0.151 | 0.931 | 0.298 | |
| | | $\beta_{G^o \times X}$ | 0.000 | -0.003 | 0.129 | 0.126 | 0.926 | 0.074 | -0.004 | 0.146 | 0.127 | 0.923 | 0.077 | |
| | | $\beta_{G^m \times X}$ | 0.000 | -0.020 | 0.166 | 0.168 | 0.954 | 0.046 | -0.016 | 0.197 | 0.175 | 0.943 | 0.057 | |
| | The daLOG model (2.3) | | β_{G^o} | 0.182 | -0.025 | 0.146 | 0.146 | 0.954 | 0.204 | -0.021 | 0.157 | 0.147 | 0.937 | 0.201 |
| | | | β_{G^m} | 0.182 | 0.019 | 0.141 | 0.146 | 0.960 | 0.270 | 0.017 | 0.152 | 0.147 | 0.949 | 0.272 |
| | | $\beta_{G^o \times X}$ | -0.182 | 0.001 | 0.131 | 0.128 | 0.942 | 0.308 | 0.003 | 0.137 | 0.129 | 0.941 | 0.306 | |
| | | $\beta_{G^m \times X}$ | -0.182 | -0.003 | 0.158 | 0.168 | 0.960 | 0.184 | -0.002 | 0.174 | 0.174 | 0.949 | 0.170 | |
| | | β_{G^o} | 0.000 | 0.017 | 0.157 | 0.153 | 0.950 | 0.050 | 0.015 | 0.160 | 0.153 | 0.944 | 0.056 | |
| | | β_{G^m} | 0.000 | -0.015 | 0.157 | 0.154 | 0.936 | 0.064 | -0.010 | 0.159 | 0.155 | 0.946 | 0.054 | |
| | | $\beta_{G^o \times X}$ | 0.000 | 0.000 | 0.131 | 0.131 | 0.954 | 0.046 | 0.002 | 0.131 | 0.131 | 0.950 | 0.050 | |
| | | $\beta_{G^m \times X}$ | 0.000 | 0.008 | 0.166 | 0.171 | 0.958 | 0.042 | 0.006 | 0.173 | 0.177 | 0.944 | 0.056 | |
| | | | β_{G^o} | 0.182 | 0.025 | 0.144 | 0.149 | 0.952 | 0.290 | 0.022 | 0.146 | 0.151 | 0.953 | 0.282 |
| | | | β_{G^m} | 0.182 | -0.009 | 0.148 | 0.150 | 0.950 | 0.224 | -0.004 | 0.155 | 0.152 | 0.945 | 0.231 |
| | | $\beta_{G^o \times X}$ | 0.000 | -0.021 | 0.127 | 0.127 | 0.948 | 0.052 | -0.017 | 0.128 | 0.128 | 0.945 | 0.053 | |
| | | $\beta_{G^m \times X}$ | 0.000 | 0.010 | 0.166 | 0.168 | 0.958 | 0.042 | 0.005 | 0.180 | 0.176 | 0.945 | 0.053 | |
| | | | β_{G^o} | 0.182 | 0.010 | 0.140 | 0.145 | 0.952 | 0.248 | 0.011 | 0.169 | 0.148 | 0.940 | 0.242 |
| | | β_{G^m} | 0.182 | 0.000 | 0.145 | 0.146 | 0.952 | 0.240 | 0.012 | 0.225 | 0.148 | 0.943 | 0.259 | |
| | | $\beta_{G^o \times X}$ | -0.182 | -0.005 | 0.123 | 0.127 | 0.956 | 0.312 | -0.005 | 0.138 | 0.130 | 0.953 | 0.296 | |
| | | $\beta_{G^m \times X}$ | -0.182 | 0.006 | 0.171 | 0.169 | 0.952 | 0.186 | 0.010 | 0.212 | 0.175 | 0.947 | 0.193 | |

^aOur proposed method allowing for dependence between X and G^m ; ^bthe estimator proposed by Chen et al. (2012); ^cmodel relating G^m and X ; ^dtrue value of the log-OR parameter; ^edifference between the mean estimate and true parameter value; ^fempirical standard error; ^gmean estimated standard error; ^hempirical coverage probability of 95% CI; ⁱtype-I error/power for testing genetic effect.

Table S2: Estimation results with $\beta_X = \log(1.5)$ and $\beta_{G^o} = \beta_{G^m} = \beta_{G^o X} = \beta_{G^m X} = 0$ under the additive mode of inheritance ($f = 0.01$, $\theta = 0.2$). G^m was independent of X ($\eta = 0$ in the daLOG model).

| Model | Log-OR | DEP ^a | | | | | IND ^b | | | | | LOGIT ^c | | | |
|-------|------------------------|-------------------|-----------------|------------------|-----------------|-----------------|-------------------|-----------------|------------------|-----------------|-----------------|--------------------|-----------------|------------------|-----------------|
| | | Bias ^d | SE ^e | SEE ^f | CP ^g | RE ^h | BIAS ^d | SE ^e | SEE ^f | CP ^g | RE ^h | BIAS ^d | SE ^e | SEE ^f | CP ^g |
| M1 | β_{G^o} | 0.024 | 0.139 | 0.140 | 0.946 | 1.35 | 0.024 | 0.139 | 0.140 | 0.946 | 1.35 | 0.023 | 0.161 | 0.161 | 0.944 |
| | β_X | 0.001 | 0.047 | 0.047 | 0.948 | 1.00 | 0.001 | 0.047 | 0.047 | 0.947 | 1.00 | 0.001 | 0.047 | 0.047 | 0.948 |
| M2 | β_{G^m} | -0.022 | 0.143 | 0.144 | 0.949 | 1.28 | -0.024 | 0.139 | 0.141 | 0.951 | 1.35 | -0.026 | 0.161 | 0.162 | 0.952 |
| | β_X | 0.000 | 0.046 | 0.047 | 0.950 | 1.00 | 0.000 | 0.046 | 0.047 | 0.950 | 1.00 | 0.000 | 0.046 | 0.047 | 0.950 |
| M3 | β_{G^o} | 0.011 | 0.147 | 0.147 | 0.947 | 1.28 | 0.011 | 0.147 | 0.147 | 0.948 | 1.28 | 0.012 | 0.166 | 0.165 | 0.949 |
| | β_X | 0.000 | 0.052 | 0.052 | 0.950 | 1.21 | 0.000 | 0.052 | 0.052 | 0.949 | 1.21 | 0.001 | 0.057 | 0.057 | 0.955 |
| M4 | $\beta_{G^o \times X}$ | -0.016 | 0.120 | 0.121 | 0.948 | 1.88 | -0.018 | 0.113 | 0.114 | 0.948 | 2.10 | -0.021 | 0.164 | 0.165 | 0.952 |
| | β_{G^m} | 0.012 | 0.146 | 0.147 | 0.952 | 1.25 | 0.011 | 0.146 | 0.147 | 0.952 | 1.25 | 0.013 | 0.164 | 0.165 | 0.950 |
| | β_X | 0.005 | 0.056 | 0.057 | 0.951 | 1.04 | 0.005 | 0.052 | 0.052 | 0.948 | 1.21 | 0.004 | 0.057 | 0.057 | 0.951 |
| | $\beta_{G^m \times X}$ | -0.001 | 0.159 | 0.159 | 0.951 | 1.08 | -0.004 | 0.112 | 0.113 | 0.951 | 2.16 | 0.004 | 0.165 | 0.166 | 0.949 |
| M5 | β_{G^o} | -0.023 | 0.157 | 0.154 | 0.943 | 1.51 | -0.023 | 0.157 | 0.154 | 0.943 | 1.51 | -0.021 | 0.193 | 0.191 | 0.942 |
| | β_{G^m} | 0.021 | 0.157 | 0.153 | 0.940 | 1.56 | 0.020 | 0.157 | 0.153 | 0.940 | 1.56 | 0.023 | 0.196 | 0.191 | 0.945 |
| | β_X | 0.002 | 0.059 | 0.058 | 0.950 | 1.06 | 0.002 | 0.055 | 0.054 | 0.947 | 1.23 | 0.003 | 0.061 | 0.060 | 0.950 |
| | $\beta_{G^o \times X}$ | 0.025 | 0.132 | 0.132 | 0.951 | 2.07 | 0.025 | 0.132 | 0.132 | 0.951 | 2.07 | 0.024 | 0.190 | 0.192 | 0.957 |
| | $\beta_{G^m \times X}$ | -0.016 | 0.172 | 0.172 | 0.945 | 1.25 | -0.016 | 0.133 | 0.131 | 0.943 | 2.07 | -0.012 | 0.192 | 0.192 | 0.951 |

^aDEP, our proposed method allowing for dependence between X and G^m ; ^bIND, our proposed method with independence assumption between X and G^m ; ^cLOGIT, the conventional logistic regression method; ^ddifference between the mean estimate and true parameter value; ^eempirical standard error; ^fmean estimated standard error; ^gempirical coverage probability of the 95% confidence interval; ^hrelative efficiency defined as the asymptotic variance of LOGIT divided by that of the target method.

Table S3: Estimation results with zero genetic effects (additive mode of inheritance, $\beta_X = \log(1.5)$, $\beta_{G^o} = \beta_{G^m} = \beta_{G^o}X = 0$, $f = 0.01$, $\theta = 0.2$). G^m was correlated with X ($\eta = \log(3.0)$ in daLOG model).

| Model | Log-OR | DEP ^a | | | | | IND ^b | | | | | LOGIT ^c | | |
|-------|----------------|-------------------|-----------------|------------------|-----------------|-----------------|-------------------|-----------------|------------------|-----------------|-----------------|--------------------|-----------------|-----------------|
| | | Bias ^d | SE ^e | SEE ^f | CP ^g | RE ^h | BIAS ^d | SE ^e | SEE ^f | CP ^g | RE ^h | BIAS ^d | SE ^e | CP ^g |
| M1 | β_{G^o} | -0.008 | 0.137 | 0.137 | 0.951 | 1.35 | 0.036 | 0.133 | 0.133 | 0.941 | 1.44 | -0.008 | 0.159 | 0.953 |
| | β_X | -0.003 | 0.047 | 0.047 | 0.949 | 1.00 | -0.004 | 0.047 | 0.047 | 0.952 | 1.00 | -0.003 | 0.047 | 0.950 |
| M2 | β_{G^m} | -0.001 | 0.140 | 0.141 | 0.952 | 1.23 | 0.482 | 0.133 | 0.134 | 0.952 | 1.37 | -0.001 | 0.156 | 0.954 |
| | β_X | 0.004 | 0.048 | 0.048 | 0.954 | 1.00 | 0.001 | 0.046 | 0.046 | 0.954 | 1.08 | 0.004 | 0.048 | 0.953 |
| M3 | β_{G^o} | 0.000 | 0.151 | 0.151 | 0.951 | 1.28 | -0.215 | 0.148 | 0.148 | 0.699 | 1.32 | 0.004 | 0.170 | 0.945 |
| | β_X | -0.001 | 0.053 | 0.053 | 0.949 | 1.23 | -0.122 | 0.051 | 0.051 | 0.343 | 1.35 | 0.001 | 0.059 | 0.946 |
| M4 | $\beta_{G^o}X$ | -0.003 | 0.119 | 0.120 | 0.948 | 1.85 | 0.557 | 0.108 | 0.109 | 0.001 | 2.25 | -0.008 | 0.162 | 0.951 |
| | β_{G^m} | 0.000 | 0.153 | 0.153 | 0.951 | 1.30 | -0.076 | 0.150 | 0.151 | 0.928 | 1.35 | 0.006 | 0.174 | 0.951 |
| | β_X | 0.001 | 0.060 | 0.060 | 0.947 | 1.04 | -0.248 | 0.052 | 0.052 | 0.003 | 1.37 | 0.001 | 0.061 | 0.946 |
| | $\beta_{G^m}X$ | 0.001 | 0.150 | 0.148 | 0.949 | 1.08 | 1.066 | 0.111 | 0.109 | 0.000 | 1.99 | -0.001 | 0.156 | 0.945 |
| M5 | β_{G^o} | -0.019 | 0.156 | 0.156 | 0.949 | 1.51 | -0.102 | 0.152 | 0.153 | 0.897 | 1.59 | -0.021 | 0.192 | 0.954 |
| | β_{G^m} | 0.014 | 0.157 | 0.159 | 0.951 | 1.56 | -0.042 | 0.155 | 0.156 | 0.944 | 1.61 | 0.016 | 0.197 | 0.952 |
| | β_X | 0.001 | 0.062 | 0.061 | 0.946 | 1.10 | -0.249 | 0.054 | 0.054 | 0.004 | 1.44 | 0.001 | 0.065 | 0.948 |
| | $\beta_{G^o}X$ | -0.006 | 0.130 | 0.131 | 0.950 | 2.16 | 0.001 | 0.124 | 0.125 | 0.950 | 2.37 | -0.011 | 0.191 | 0.951 |
| | $\beta_{G^m}X$ | 0.005 | 0.164 | 0.162 | 0.951 | 1.21 | 1.070 | 0.124 | 0.125 | 0.000 | 2.13 | 0.010 | 0.181 | 0.952 |

^aDEP, our proposed method allowing for dependence between X and G^m ; ^bIND, our proposed method with independence assumption between X and G^m ; ^cLOGIT, the conventional logistic regression method; ^ddifference between the mean estimate and true parameter value; ^eempirical standard error; ^fmean estimated standard error; ^gempirical coverage probability of the 95% confidence interval; ^hrelative efficiency defined as the asymptotic variance of LOGIT divided by that of the target method.

Table S4: Estimation results with non-zero genetic effects (additive mode of inheritance, $\beta_X = \log(1.5)$, $\beta_{G^o} = \beta_{G^m} = \beta_{G^o} X = \log(1.2)$, $f = 0.01$, $\theta = 0.2$). G^m was correlated with X ($\eta = \log(3.0)$ in daLOG model).

| Model | Log-OR | DEP ^a | | | | | IND ^b | | | | | LOGIT ^c | | | | |
|-------|-----------------|-------------------|-----------------|------------------|-----------------|-----------------|-------------------|-----------------|------------------|-----------------|-----------------|--------------------|-----------------|------------------|-----------------|-----------------|
| | | BIAS ^d | SE ^e | SEE ^f | CP ^g | RE ^h | BIAS ^d | SE ^e | SEE ^f | CP ^g | RE ^h | BIAS ^d | SE ^e | SEE ^f | CP ^g | CP ^g |
| M1 | β_{G^o} | 0.010 | 0.134 | 0.135 | 0.951 | 1.35 | 0.051 | 0.130 | 0.131 | 0.932 | 1.42 | 0.000 | 0.155 | 0.158 | 0.958 | |
| | β_X | 0.007 | 0.047 | 0.047 | 0.950 | 1.00 | 0.015 | 0.047 | 0.047 | 0.937 | 1.00 | 0.008 | 0.047 | 0.047 | 0.950 | |
| M2 | β_{G^m} | 0.008 | 0.139 | 0.139 | 0.949 | 1.23 | 0.494 | 0.133 | 0.132 | 0.041 | 1.35 | 0.010 | 0.154 | 0.155 | 0.951 | |
| | β_X | -0.001 | 0.048 | 0.048 | 0.954 | 1.00 | 0.012 | 0.046 | 0.046 | 0.946 | 1.08 | -0.001 | 0.048 | 0.049 | 0.955 | |
| M3 | β_{G^o} | 0.003 | 0.150 | 0.150 | 0.951 | 1.28 | -0.239 | 0.146 | 0.147 | 0.635 | 1.35 | -0.003 | 0.169 | 0.170 | 0.949 | |
| | β_X | 0.001 | 0.055 | 0.054 | 0.946 | 1.23 | -0.120 | 0.053 | 0.052 | 0.369 | 1.32 | -0.001 | 0.061 | 0.060 | 0.945 | |
| M4 | $\beta_{G^o} X$ | -0.007 | 0.116 | 0.115 | 0.945 | 2.02 | 0.557 | 0.106 | 0.105 | 0.000 | 2.43 | 0.003 | 0.165 | 0.163 | 0.949 | |
| | β_{G^m} | 0.024 | 0.153 | 0.153 | 0.948 | 1.30 | -0.054 | 0.150 | 0.151 | 0.941 | 1.35 | 0.023 | 0.174 | 0.175 | 0.949 | |
| | $\beta_{G^o} X$ | 0.009 | 0.061 | 0.061 | 0.944 | 1.04 | -0.249 | 0.053 | 0.053 | 0.004 | 1.37 | 0.008 | 0.062 | 0.062 | 0.947 | |
| | $\beta_{G^m} X$ | -0.018 | 0.144 | 0.145 | 0.951 | 1.12 | 1.067 | 0.107 | 0.108 | 0.000 | 2.04 | -0.013 | 0.153 | 0.154 | 0.951 | |
| M5 | β_{G^o} | 0.028 | 0.161 | 0.160 | 0.943 | 1.54 | -0.062 | 0.158 | 0.156 | 0.927 | 1.59 | 0.030 | 0.199 | 0.198 | 0.942 | |
| | β_{G^m} | -0.031 | 0.163 | 0.164 | 0.947 | 1.56 | -0.091 | 0.161 | 0.161 | 0.910 | 1.59 | -0.034 | 0.203 | 0.203 | 0.945 | |
| | β_X | 0.008 | 0.063 | 0.063 | 0.950 | 1.06 | -0.259 | 0.054 | 0.055 | 0.004 | 1.44 | 0.007 | 0.065 | 0.066 | 0.949 | |
| | $\beta_{G^o} X$ | -0.036 | 0.123 | 0.124 | 0.941 | 2.46 | -0.032 | 0.118 | 0.119 | 0.943 | 2.69 | -0.024 | 0.193 | 0.194 | 0.949 | |
| | $\beta_{G^m} X$ | 0.022 | 0.159 | 0.158 | 0.945 | 1.32 | 1.112 | 0.122 | 0.123 | 0.000 | 2.25 | 0.020 | 0.183 | 0.183 | 0.955 | |

^aDEP, our proposed method allowing for dependence between X and G^m ; ^bIND, our proposed method with independence assumption between X and G^m ; ^cLOGIT, the conventional logistic regression method; ^ddifference between the mean estimate and true parameter value; ^eempirical standard error; ^fmean estimated standard error; ^gempirical coverage probability of the 95% confidence interval; ^hrelative efficiency defined as the asymptotic variance of LOGIT divided by that of the target method.

Table S5: Type-I error rates and powers for testing the genetic effects under the recessive mode of inheritance ($f = 0.01$, $\theta = 0.2$). Under the null hypothesis, $\beta_{G^o} = \beta_{G^m} = \beta_{G^m X} = \beta_{G^o X} = 0$; under the alternative hypothesis, $\beta_{G^o} = \beta_{G^m} = \beta_{G^m X} = \beta_{G^o X} = \log(1.2)$. The log-OR for X was $\beta_X = \log(1.5)$.

| η^a | Model ^b | Effect ^c | Null hypothesis | | | Alternative hypothesis | | |
|----------|--------------------|---------------------|------------------|------------------|--------------------|------------------------|------------------|--------------------|
| | | | DEP ^d | IND ^e | LOGIT ^f | DEP ^d | IND ^e | LOGIT ^f |
| 0 | M1 | Joint | 0.049 | 0.048 | 0.049 | 0.228 | 0.223 | 0.150 |
| | M2 | Joint | 0.043 | 0.042 | 0.040 | 0.193 | 0.199 | 0.152 |
| | M3 | Joint | 0.060 | 0.058 | 0.041 | 0.407 | 0.405 | 0.145 |
| | M4 | Joint | 0.049 | 0.055 | 0.036 | 0.251 | 0.459 | 0.159 |
| | M5 | Joint | 0.056 | 0.063 | 0.043 | 0.471 | 0.650 | 0.260 |
| | M5 | Offspring | 0.066 | 0.065 | 0.043 | 0.285 | 0.280 | 0.169 |
| | M5 | Maternal | 0.046 | 0.050 | 0.039 | 0.155 | 0.202 | 0.132 |
| log(3.0) | M1 | Joint | 0.052 | 0.591 | 0.051 | 0.185 | - ^e | 0.133 |
| | M2 | Joint | 0.055 | 0.994 | 0.050 | 0.192 | - | 0.160 |
| | M3 | Joint | 0.051 | 0.694 | 0.034 | 0.587 | - | 0.242 |
| | M4 | Joint | 0.053 | >0.999 | 0.047 | 0.633 | - | 0.589 |
| | M5 | Joint | 0.052 | >0.999 | 0.037 | 0.899 | - | 0.752 |
| | M5 | Offspring | 0.062 | 0.216 | 0.044 | 0.267 | - | 0.161 |
| | M5 | Maternal | 0.053 | 1.000 | 0.047 | 0.134 | - | 0.114 |

^aThe maternal genotype was either independent of ($\eta = 0$) or strongly correlated with the environmental risk factor ($\eta = \log(3.0)$), as specified in the daLOG model; ^bPenetrance models specified in (2.1) Notation,

Model and Prospective Likelihood equation.2.1); ^cGenetic effect; ^dOur proposed method allowing for dependence between X and G^m ; ^eour proposed method with independence assumption between X and G^m ;

^fthe conventional logistic regression method; ^gPower not displayed because of inflated type-I error rates.

Table S6: Type-I error rates and powers for testing the genetic effects under the dominant mode of inheritance ($f = 0.01$, $\theta = 0.2$). Under the null hypothesis, $\beta_{G^o} = \beta_{G^m} = \beta_{G^m X} = \beta_{G^o X} = 0$; under the alternative hypothesis, $\beta_{G^o} = \beta_{G^m} = \beta_{G^m X} = \beta_{G^o X} = \log(1.2)$. The log-OR for X was $\beta_X = \log(1.5)$.

| η^a | Model ^b | Effect ^c | Null hypothesis | | | Alternative hypothesis | | |
|----------|--------------------|---------------------|------------------|------------------|--------------------|------------------------|------------------|--------------------|
| | | | DEP ^d | IND ^e | LOGIT ^f | DEP ^d | IND ^e | LOGIT ^f |
| 0 | M1 | Joint | 0.051 | 0.051 | 0.052 | 0.609 | 0.610 | 0.474 |
| | M2 | Joint | 0.045 | 0.041 | 0.042 | 0.656 | 0.675 | 0.545 |
| | M3 | Joint | 0.052 | 0.054 | 0.051 | 0.959 | 0.969 | 0.753 |
| | M4 | Joint | 0.050 | 0.049 | 0.044 | 0.862 | 0.981 | 0.801 |
| | M5 | Joint | 0.052 | 0.053 | 0.051 | >0.999 | >0.999 | 0.995 |
| | M5 | Offspring | 0.053 | 0.052 | 0.042 | 0.816 | 0.817 | 0.574 |
| | M5 | Maternal | 0.050 | 0.047 | 0.048 | 0.617 | 0.748 | 0.496 |
| log(3.0) | M1 | Joint | 0.046 | 0.900 | 0.051 | 0.677 | - ^e | 0.523 |
| | M2 | Joint | 0.050 | 0.999 | 0.051 | 0.493 | - | 0.428 |
| | M3 | Joint | 0.051 | >0.999 | 0.053 | 0.982 | - | 0.782 |
| | M4 | Joint | 0.049 | >0.999 | 0.046 | 0.787 | - | 0.739 |
| | M5 | Joint | 0.046 | >0.999 | 0.047 | >0.999 | - | 0.989 |
| | M5 | Offspring | 0.048 | 0.077 | 0.046 | 0.771 | - | 0.558 |
| | M5 | Maternal | 0.041 | 1.000 | 0.048 | 0.548 | - | 0.412 |

^aThe maternal genotype was either independent of ($\eta = 0$) or strongly correlated with the environmental risk factor ($\eta = \log(3.0)$), as specified in the daLOG model; ^bPenetrance models specified in (2.1) Notation,

Model and Prospective Likelihood equation.2.1); ^cGenetic effect; ^dOur proposed method allowing for dependence between X and G^m ; ^eour proposed method with independence assumption between X and G^m ;

^fthe conventional logistic regression method; ^gPower not displayed because of inflated type-I error rates.

Table S7: Type-I error rates and powers for testing joint genetic effect with small minor allele frequency $\theta = 0.1$ (additive mode of inheritance, $f = 0.01$). Under the null hypothesis, $\beta_{G^o} = \beta_{G^m} = \beta_{G^m X} = \beta_{G^o X} = 0$; under the alternative hypothesis, $\beta_{G^o} = \beta_{G^m} = \beta_{G^m X} = \beta_{G^o X} = \log(1.2)$. The log-OR for X was $\beta_X = \log(1.5)$.

| η^d | Model | Null hypothesis | | | Alternative hypothesis | | |
|----------|-------|------------------|------------------|--------------------|------------------------|------------------|--------------------|
| | | DEP ^a | IND ^b | LOGIT ^c | DEP ^a | IND ^b | LOGIT ^c |
| 0 | M1 | 0.030 | 0.029 | 0.047 | 0.106 | 0.103 | 0.160 |
| | M2 | 0.032 | 0.032 | 0.053 | 0.088 | 0.088 | 0.140 |
| | M3 | 0.032 | 0.034 | 0.049 | 0.332 | 0.374 | 0.199 |
| | M4 | 0.042 | 0.044 | 0.052 | 0.163 | 0.306 | 0.189 |
| | M5 | 0.039 | 0.041 | 0.043 | 0.510 | 0.751 | 0.450 |
| log(3.0) | M1 | 0.030 | 0.060 | 0.044 | 0.121 | 0.290 | 0.174 |
| | M2 | 0.036 | 0.862 | 0.051 | 0.107 | - ^e | 0.152 |
| | M3 | 0.035 | 0.980 | 0.048 | 0.477 | - | 0.287 |
| | M4 | 0.039 | >0.999 | 0.045 | 0.291 | - | 0.305 |
| | M5 | 0.039 | >0.999 | 0.043 | 0.741 | - | 0.664 |

^aDEP, our proposed method allowing for dependence between X and G^m ; ^bIND, our proposed method with independence assumption between X and G^m ; ^cLOGIT, the conventional logistic regression method.

^dThe maternal genotype was either independent of ($\eta = 0$) or strongly correlated with ($\eta = \log(3.0)$) the environmental risk factor. ^ePower was not displayed because of inflated type-I error rate.

Table S8: Type-I error rates and powers for testing joint genetic effect with smaller sample size ($n_0 = n_1 = 200$, additive mode of inheritance, $\theta = 0.2$ $f = 0.01$). Under the null hypothesis, $\beta_{G^o} = \beta_{G^m} = \beta_{G^m X} = \beta_{G^o X} = 0$; under the alternative hypothesis, $\beta_{G^o} = \beta_{G^m} = \beta_{G^m X} = \beta_{G^o X} = \log(1.2)$. The log-OR for X was $\beta_X = \log(1.5)$.

| η^d | Model | Null hypothesis | | | Alternative hypothesis | | |
|----------|-------|------------------|------------------|--------------------|------------------------|------------------|--------------------|
| | | DEP ^a | IND ^b | LOGIT ^c | DEP ^a | IND ^b | LOGIT ^c |
| 0 | M1 | 0.051 | 0.049 | 0.050 | 0.098 | 0.095 | 0.086 |
| | M2 | 0.049 | 0.049 | 0.048 | 0.093 | 0.098 | 0.086 |
| | M3 | 0.054 | 0.054 | 0.049 | 0.168 | 0.180 | 0.094 |
| | M4 | 0.052 | 0.053 | 0.045 | 0.104 | 0.169 | 0.081 |
| | M5 | 0.051 | 0.051 | 0.040 | 0.187 | 0.305 | 0.132 |
| log(3.0) | M1 | 0.055 | 0.060 | 0.048 | 0.096 | 0.126 | 0.085 |
| | M2 | 0.052 | 0.350 | 0.049 | 0.090 | - ^e | 0.088 |
| | M3 | 0.053 | 0.557 | 0.049 | 0.183 | - | 0.102 |
| | M4 | 0.052 | 0.990 | 0.046 | 0.132 | - | 0.115 |
| | M5 | 0.053 | 0.984 | 0.040 | 0.242 | - | 0.178 |

^aDEP, our proposed method allowing for dependence between X and G^m ; ^bIND, our proposed method with independence assumption between X and G^m ; ^cLOGIT, the conventional logistic regression method.

^dThe maternal genotype was either independent of ($\eta = 0$) or strongly correlated with ($\eta = \log(3.0)$) the environmental risk factor. ^ePower was not displayed because of inflated type-I error rate.

Table S9: Type-I error rates and powers for the simulation study comparing DEP and EMIM (additive mode of inheritance, $f = 0.01$, $\theta = 0.2$). In all simulation scenarios, $\beta_{G^o} = \beta_{G^m} = \log(\text{OR})$ (OR = 0 or 1.2). The log-OR for X was $\beta_X = \log(1.5)$.

| Interaction ^a | e^η | OR | EMIM | | | DEP | | |
|--------------------------|----------|-----|------------------------|-----------------------|--------------------|------------------------|-----------------------|--------------------|
| | | | Offspring ^b | Maternal ^c | Joint ^d | Offspring ^b | Maternal ^c | Joint ^d |
| Zero | 1 | 1 | 0.050 | 0.054 | 0.053 | 0.048 | 0.048 | 0.054 |
| Zero | 1.2 | 1 | 0.050 | 0.085 | 0.072 | 0.050 | 0.049 | 0.055 |
| Zero | 1 | 1.2 | 0.292 | 0.271 | 0.499 | 0.264 | 0.235 | 0.380 |
| Zero | 1.2 | 1.2 | 0.315 | 0.459 | 0.674 | 0.292 | 0.220 | 0.392 |
| Non-zero | 1 | 1.2 | — ^e | — | 0.280 | — | — | 0.630 |
| Non-zero | 1.2 | 1.2 | — | — | 0.359 | — | — | 0.613 |

^a $\beta_{G^m X} = \beta_{G^o X} = 0$ (zero interaction) and $\beta_{G^m X} = \beta_{G^o X} = -\log(\text{OR})$ (non-zero interaction); ^bNull hypothesis: $\beta_{G^o} = 0$; ^cNull hypothesis: $\beta_{G^m} = 0$; ^dNull hypothesis: $\beta_{G^o} = \beta_{G^m} = 0$; ^eIt does not make sense to test main effects in the presence of interaction effects.

Table S10: Estimation and significance test results with correctly specified prevalence or mis-specified disease prevalence (additive mode of inheritance, $\theta = 0.2$, $\beta_X = \log(1.5)$).

| $(f, f^*)^a$ | $\log(\text{OR})$ | True^b | Prevalence correctly specified ($= f$) | | | | | Prevalence mis-specified ($= f^*$) | | | | |
|--------------|----------------------|-----------------|--|-----------------|------------------|-----------------|--------------------|--------------------------------------|-------|-------|-------|-------|
| | | | Bias ^c | SE ^d | SEE ^e | CP ^f | Power ^g | Bias | SE | SEE | CP | Power |
| (0.01,0.2) | β_{G^o} | 0.000 | 0.015 | 0.154 | 0.173 | 0.952 | 0.048 | 0.013 | 0.156 | 0.174 | 0.952 | 0.048 |
| | β_{G^m} | 0.000 | 0.001 | 0.159 | 0.179 | 0.948 | 0.052 | 0.002 | 0.160 | 0.179 | 0.948 | 0.051 |
| | $\beta_{G^o \times}$ | 0.000 | -0.016 | 0.129 | 0.162 | 0.951 | 0.049 | -0.015 | 0.130 | 0.164 | 0.951 | 0.048 |
| | $\beta_{G^m \times}$ | 0.000 | 0.010 | 0.161 | 0.173 | 0.950 | 0.050 | 0.009 | 0.162 | 0.173 | 0.950 | 0.051 |
| (0.2,0.01) | β_{G^o} | 0.000 | -0.007 | 0.173 | 0.153 | 0.951 | 0.049 | -0.004 | 0.171 | 0.152 | 0.951 | 0.049 |
| | β_{G^m} | 0.000 | 0.003 | 0.178 | 0.158 | 0.948 | 0.052 | 0.003 | 0.176 | 0.156 | 0.948 | 0.055 |
| | $\beta_{G^o \times}$ | 0.000 | 0.008 | 0.166 | 0.132 | 0.950 | 0.050 | 0.003 | 0.166 | 0.132 | 0.950 | 0.052 |
| | $\beta_{G^m \times}$ | 0.000 | 0.006 | 0.176 | 0.165 | 0.952 | 0.048 | 0.006 | 0.178 | 0.166 | 0.952 | 0.050 |
| (0.01,0.2) | β_{G^o} | 0.182 | 0.011 | 0.156 | 0.175 | 0.956 | 0.223 | 0.012 | 0.160 | 0.179 | 0.956 | 0.188 |
| | β_{G^m} | 0.182 | 0.003 | 0.160 | 0.180 | 0.955 | 0.204 | -0.006 | 0.163 | 0.183 | 0.955 | 0.163 |
| | $\beta_{G^o \times}$ | 0.182 | -0.016 | 0.122 | 0.164 | 0.953 | 0.261 | 0.059 | 0.124 | 0.167 | 0.953 | 0.291 |
| | $\beta_{G^m \times}$ | 0.182 | 0.007 | 0.158 | 0.172 | 0.946 | 0.222 | -0.031 | 0.158 | 0.173 | 0.946 | 0.129 |
| (0.2,0.01) | β_{G^o} | 0.182 | -0.003 | 0.173 | 0.154 | 0.952 | 0.176 | -0.007 | 0.174 | 0.154 | 0.952 | 0.212 |
| | β_{G^m} | 0.182 | 0.002 | 0.179 | 0.159 | 0.953 | 0.183 | 0.005 | 0.179 | 0.158 | 0.953 | 0.227 |
| | $\beta_{G^o \times}$ | 0.182 | 0.003 | 0.174 | 0.130 | 0.948 | 0.187 | -0.079 | 0.173 | 0.129 | 0.948 | 0.124 |
| | $\beta_{G^m \times}$ | 0.182 | 0.012 | 0.188 | 0.169 | 0.945 | 0.181 | 0.024 | 0.185 | 0.167 | 0.945 | 0.235 |

^a f : true disease prevalence, f^* : specified prevalence; ^btrue parameter value; ^cdifference between the mean estimate and true parameter value; ^dempirical standard error; ^emean estimated standard error; ^fempirical coverage probability of the 95% confidence interval; ^gpower of the significance test of genetic effect.

Table S11: Estimation and significance test results of DEP for simulations with mis-specified fixation index parameter (additive mode of inheritance, $f = 0.01$, $\theta = 0.2$, $\eta = \log(3)$).

| F^a | β | Zero genetic effect | | | | | | Non-zero genetic effect | | | | | |
|-------|----------------|---------------------|-------------------|-----------------|------------------|-----------------|--------------------|-------------------------|-------------------|-----------------|------------------|-----------------|--------------------|
| | | True ^b | Bias ^c | SE ^d | SEE ^e | CP ^f | Power ^g | True ^b | Bias ^c | SE ^d | SEE ^e | CP ^f | Power ^g |
| 0.05 | β_{G^o} | 0.000 | 0.014 | 0.153 | 0.155 | 0.951 | 0.047 | 0.182 | 0.011 | 0.145 | 0.146 | 0.950 | 0.248 |
| | β_{G^m} | 0.000 | -0.001 | 0.163 | 0.162 | 0.953 | 0.052 | 0.182 | 0.000 | 0.151 | 0.154 | 0.951 | 0.250 |
| | β_X | 0.405 | 0.003 | 0.062 | 0.062 | 0.948 | 1.000 | 0.405 | 0.004 | 0.062 | 0.062 | 0.950 | 1.000 |
| | β_{G^oX} | 0.000 | -0.016 | 0.128 | 0.129 | 0.952 | 0.050 | -0.182 | -0.010 | 0.128 | 0.128 | 0.947 | 0.315 |
| | β_{G^mX} | 0.000 | 0.011 | 0.162 | 0.163 | 0.950 | 0.050 | -0.182 | 0.006 | 0.165 | 0.164 | 0.951 | 0.209 |
| | β_{G^o} | 0.000 | 0.015 | 0.152 | 0.154 | 0.952 | 0.046 | 0.182 | 0.008 | 0.144 | 0.145 | 0.953 | 0.236 |
| 0.1 | β_{G^m} | 0.000 | -0.007 | 0.165 | 0.165 | 0.954 | 0.048 | 0.182 | -0.003 | 0.154 | 0.156 | 0.952 | 0.276 |
| | β_X | 0.405 | 0.003 | 0.062 | 0.063 | 0.952 | 1.000 | 0.405 | 0.004 | 0.062 | 0.063 | 0.951 | 1.000 |
| | β_{G^oX} | 0.000 | -0.015 | 0.127 | 0.128 | 0.952 | 0.050 | -0.182 | -0.011 | 0.124 | 0.127 | 0.954 | 0.307 |
| | β_{G^mX} | 0.000 | 0.012 | 0.164 | 0.165 | 0.950 | 0.050 | -0.182 | 0.007 | 0.163 | 0.165 | 0.956 | 0.216 |
| | β_{G^o} | 0.000 | 0.015 | 0.151 | 0.152 | 0.952 | 0.045 | 0.182 | 0.009 | 0.142 | 0.143 | 0.946 | 0.222 |
| | β_{G^m} | 0.000 | -0.008 | 0.170 | 0.170 | 0.955 | 0.048 | 0.182 | -0.004 | 0.161 | 0.160 | 0.952 | 0.321 |
| 0.2 | β_X | 0.405 | 0.003 | 0.063 | 0.064 | 0.952 | 1.000 | 0.405 | 0.004 | 0.064 | 0.065 | 0.934 | 1.000 |
| | β_{G^oX} | 0.000 | -0.013 | 0.126 | 0.126 | 0.950 | 0.050 | -0.182 | -0.008 | 0.124 | 0.126 | 0.948 | 0.296 |
| | β_{G^mX} | 0.000 | 0.011 | 0.166 | 0.167 | 0.951 | 0.050 | -0.182 | 0.008 | 0.166 | 0.168 | 0.953 | 0.248 |

^a: fixation index parameter; ^btrue parameter value; ^cdifference between the mean estimate and true parameter value; ^dempirical standard error; ^emean estimated standard error; ^fempirical coverage probability of the 95% confidence interval; ^gpower of the significance test of genetic effect.

Table S12: Type-I error rates and powers of DEP for simulations with various specified modes of inheritance ($f = 0.01$, $\theta = 0.2$, $\eta = \log(3)$).

| Effect | β | REC ^a | | | ADD ^a | | | DOM ^a | | |
|----------|---------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|
| | | REC ^b | ADD ^b | DOM ^b | REC ^b | ADD ^b | DOM ^b | REC ^b | ADD ^b | DOM ^b |
| Zero | 0 | 0.048 | 0.048 | 0.054 | 0.050 | 0.053 | 0.052 | 0.046 | 0.050 | 0.052 |
| | 0 | 0.054 | 0.048 | 0.043 | 0.051 | 0.055 | 0.054 | 0.049 | 0.048 | 0.047 |
| | 0 | 0.098 | 0.054 | 0.055 | 0.060 | 0.058 | 0.054 | 0.056 | 0.050 | 0.052 |
| | 0 | 0.054 | 0.057 | 0.053 | 0.056 | 0.057 | 0.052 | 0.054 | 0.055 | 0.055 |
| | Joint | 0.072 | 0.055 | 0.050 | 0.053 | 0.053 | 0.055 | 0.051 | 0.049 | 0.050 |
| Non-zero | 0.182 | 0.469 | 0.242 | 0.087 | 0.153 | 0.289 | 0.309 | 0.070 | 0.549 | 0.634 |
| | 0.182 | 0.042 | 0.051 | 0.078 | 0.158 | 0.244 | 0.249 | 0.074 | 0.050 | 0.052 |
| | -0.182 | 0.485 | 0.237 | 0.087 | 0.220 | 0.396 | 0.371 | 0.115 | 0.698 | 0.773 |
| | -0.182 | 0.056 | 0.051 | 0.056 | 0.120 | 0.147 | 0.165 | 0.068 | 0.053 | 0.045 |
| | Joint | 0.511 | 0.226 | 0.103 | 0.296 | 0.675 | 0.624 | 0.115 | 0.705 | 0.760 |

Table S13: Joint genetic effect, minor allele frequency, Hardy-Weinberg equilibrium, and maternal genotype and pp-BMI independence in the Tianjin Postpartum GDM Prevention Program.

| SNP | MAF ^b | HWE ^c | Genetic effects ^a | | | Independence ^g |
|------------|------------------|------------------|------------------------------|------------------|--------------------|---------------------------|
| | | | DEP ^d | IND ^e | LOGIT ^f | |
| rs3923113 | 0.144 | 0.200 | 0.173 | 0.147 | 0.231 | 0.020 (-0.488) |
| rs4402960 | 0.266 | 0.262 | 0.043 | 0.028 | 0.052 | 0.733 (0.057) |
| rs16861329 | 0.184 | 0.242 | 0.266 | 0.478 | 0.357 | 0.182 (-0.256) |
| rs7754840 | 0.465 | 0.310 | 0.273 | 0.324 | 0.311 | 0.026 (-0.316) |
| rs1799884 | 0.232 | 1.000 | 0.104 | 0.070 | 0.087 | 0.603 (0.097) |
| rs1802295 | 0.111 | 0.528 | 0.141 | 0.231 | 0.133 | 0.142 (-0.339) |
| rs4746822 | 0.268 | 0.378 | 0.205 | 0.112 | 0.180 | 0.882 (0.024) |
| rs2237895 | 0.320 | 0.285 | <0.001 | <0.001 | <0.001 | 0.587 (-0.088) |
| rs5219 | 0.433 | 0.561 | 0.244 | 0.192 | 0.144 | 0.071 (-0.249) |
| rs1387153 | 0.417 | 0.605 | 0.008 | 0.007 | 0.017 | 0.572 (-0.079) |
| rs10830963 | 0.426 | 0.949 | 0.105 | 0.096 | 0.104 | 0.546 (-0.091) |
| rs7178572 | 0.371 | 0.787 | 0.873 | 0.764 | 0.861 | 0.819 (-0.037) |
| rs2028299 | 0.189 | 0.533 | 0.978 | 0.984 | 0.977 | 0.548 (-0.099) |
| rs4812829 | 0.444 | 0.306 | 0.217 | 0.352 | 0.146 | 0.050 (0.262) |

^ep-value for testing the joint genetic effect; ^bminor allele frequency; ^dp-value for testing HWE; ^dDEP, our proposed method allowing for dependence between X and G^m ; ^eIND, our proposed method with independence assumption between X and G^m ; ^fLOGIT, the conventional logistic regression method; ^gp-value for testing the independence between the maternal genotype and pp-BMI ($H_0 : \eta = 0$), with the estimated η in the parentheses.

Table S14: Offspring SNP main effects in the Tianjin Postpartum GDM Prevention Program.

| SNP | DEP ^a | | | IND ^b | | | LOGIT ^c | | |
|------------|-----------------------|-----------------|----------------------|-----------------------|-----------------|----------------------|-----------------------|-----------------|----------------------|
| | $\hat{\beta}_{G^o}^d$ | SE ^e | P-value ^f | $\hat{\beta}_{G^o}^d$ | SE ^e | P-value ^f | $\hat{\beta}_{G^o}^d$ | SE ^e | P-value ^f |
| rs3923113 | -0.295 | 0.234 | 0.208 | -0.339 | 0.232 | 0.144 | -0.374 | 0.301 | 0.213 |
| rs4402960 | -0.038 | 0.184 | 0.835 | -0.035 | 0.183 | 0.851 | 0.057 | 0.236 | 0.809 |
| rs16861329 | 0.118 | 0.209 | 0.573 | 0.095 | 0.208 | 0.647 | 0.019 | 0.273 | 0.946 |
| rs7754840 | 0.112 | 0.163 | 0.492 | 0.091 | 0.163 | 0.575 | 0.123 | 0.209 | 0.556 |
| rs1799884 | 0.128 | 0.196 | 0.513 | 0.133 | 0.196 | 0.498 | 0.058 | 0.252 | 0.817 |
| rs1802295 | 0.178 | 0.256 | 0.487 | 0.156 | 0.255 | 0.539 | 0.364 | 0.335 | 0.277 |
| rs4746822 | 0.109 | 0.182 | 0.547 | 0.111 | 0.181 | 0.540 | 0.191 | 0.241 | 0.428 |
| rs2237895 | -0.405 | 0.185 | 0.028 | -0.412 | 0.184 | 0.025 | -0.424 | 0.228 | 0.063 |
| rs5219 | -0.044 | 0.169 | 0.794 | -0.060 | 0.169 | 0.725 | -0.033 | 0.209 | 0.876 |
| rs1387153 | -0.024 | 0.165 | 0.882 | -0.029 | 0.164 | 0.859 | 0.154 | 0.222 | 0.489 |
| rs10830963 | 0.037 | 0.169 | 0.825 | 0.030 | 0.169 | 0.859 | 0.071 | 0.216 | 0.744 |
| rs7178572 | -0.160 | 0.167 | 0.339 | -0.163 | 0.167 | 0.330 | -0.137 | 0.219 | 0.533 |
| rs2028299 | -0.027 | 0.207 | 0.897 | -0.034 | 0.207 | 0.869 | -0.107 | 0.265 | 0.685 |
| rs4812829 | -0.263 | 0.169 | 0.119 | -0.250 | 0.169 | 0.139 | -0.239 | 0.213 | 0.262 |

^aDEP, our proposed method allowing for dependence between X and G^m ; ^bIND, our proposed method with independence assumption between X and G^m ; ^cLOGIT, the conventional logistic regression method;

^destimated genetic effect; ^eestimated standard error of $\hat{\beta}_{G^o}$; ^fsignificance test p-value.

Table S15: Maternal SNP main effects in the Tianjin Postpartum GDM Prevention Program.

| SNP | DEP ^a | | | IND ^b | | | LOGIT ^c | | |
|------------|-----------------------|-----------------|----------------------|-----------------------|-----------------|----------------------|-----------------------|-----------------|----------------------|
| | $\hat{\beta}_{G^m}^d$ | SE ^e | P-value ^f | $\hat{\beta}_{G^m}^d$ | SE ^e | P-value ^f | $\hat{\beta}_{G^m}^d$ | SE ^e | P-value ^f |
| rs3923113 | -0.248 | 0.244 | 0.308 | -0.295 | 0.241 | 0.221 | -0.186 | 0.297 | 0.532 |
| rs4402960 | 0.449 | 0.181 | 0.013 | 0.450 | 0.180 | 0.013 | 0.450 | 0.238 | 0.059 |
| rs16861329 | -0.212 | 0.205 | 0.300 | -0.232 | 0.203 | 0.252 | -0.246 | 0.290 | 0.395 |
| rs7754840 | 0.240 | 0.164 | 0.143 | 0.216 | 0.163 | 0.185 | 0.253 | 0.216 | 0.240 |
| rs1799884 | 0.348 | 0.188 | 0.064 | 0.354 | 0.188 | 0.059 | 0.414 | 0.247 | 0.094 |
| rs1802295 | 0.533 | 0.257 | 0.038 | 0.507 | 0.256 | 0.048 | 0.623 | 0.327 | 0.057 |
| rs4746822 | 0.304 | 0.185 | 0.100 | 0.305 | 0.184 | 0.098 | 0.237 | 0.232 | 0.306 |
| rs2237895 | 0.768 | 0.170 | <0.001 | 0.763 | 0.170 | <0.001 | 0.830 | 0.228 | <0.001 |
| rs5219 | -0.263 | 0.172 | 0.125 | -0.280 | 0.171 | 0.102 | -0.286 | 0.209 | 0.172 |
| rs1387153 | 0.432 | 0.165 | 0.009 | 0.427 | 0.164 | 0.010 | 0.248 | 0.217 | 0.252 |
| rs10830963 | 0.335 | 0.163 | 0.040 | 0.329 | 0.163 | 0.044 | 0.313 | 0.214 | 0.144 |
| rs7178572 | 0.089 | 0.175 | 0.609 | 0.088 | 0.174 | 0.612 | 0.111 | 0.216 | 0.608 |
| rs2028299 | 0.067 | 0.211 | 0.752 | 0.061 | 0.210 | 0.771 | 0.182 | 0.267 | 0.496 |
| rs4812829 | 0.202 | 0.163 | 0.214 | 0.220 | 0.163 | 0.177 | 0.179 | 0.216 | 0.408 |

^aDEP, our proposed method allowing for dependence between X and G^m ; ^bIND, our proposed method with independence assumption between X and G^m ; ^cLOGIT, the conventional logistic regression method;

^destimated genetic effect; ^eestimated standard error of $\hat{\beta}_{G^m}$; ^fsignificance test p-value.

Table S16: Offspring SNP versus pp-BMI interaction effects in the Tianjin Postpartum GDM Prevention Program.

| SNP | DEP ^a | | | IND ^b | | | LOGIT ^c | | |
|------------|------------------------|-----------------|----------------------|------------------------|-----------------|----------------------|------------------------|-----------------|----------------------|
| | $\hat{\beta}_{G^oX}^d$ | SE ^e | P-value ^f | $\hat{\beta}_{G^oX}^d$ | SE ^e | P-value ^f | $\hat{\beta}_{G^oX}^d$ | SE ^e | P-value ^f |
| rs3923113 | 0.167 | 0.166 | 0.316 | 0.165 | 0.164 | 0.315 | -0.123 | 0.331 | 0.709 |
| rs4402960 | 0.303 | 0.149 | 0.042 | 0.303 | 0.150 | 0.043 | 0.430 | 0.249 | 0.084 |
| rs16861329 | -0.197 | 0.174 | 0.257 | -0.191 | 0.172 | 0.267 | -0.618 | 0.289 | 0.032 |
| rs7754840 | 0.138 | 0.139 | 0.319 | 0.137 | 0.138 | 0.321 | -0.115 | 0.211 | 0.585 |
| rs1799884 | -0.022 | 0.148 | 0.885 | -0.021 | 0.148 | 0.885 | -0.328 | 0.281 | 0.243 |
| rs1802295 | -0.015 | 0.218 | 0.944 | -0.016 | 0.216 | 0.943 | 0.017 | 0.351 | 0.962 |
| rs4746822 | 0.040 | 0.140 | 0.773 | 0.039 | 0.140 | 0.783 | 0.037 | 0.244 | 0.880 |
| rs2237895 | 0.144 | 0.136 | 0.291 | 0.143 | 0.136 | 0.292 | 0.275 | 0.249 | 0.269 |
| rs5219 | -0.197 | 0.138 | 0.153 | -0.195 | 0.137 | 0.155 | -0.376 | 0.225 | 0.095 |
| rs1387153 | 0.313 | 0.129 | 0.016 | 0.311 | 0.129 | 0.016 | 0.576 | 0.233 | 0.013 |
| rs10830963 | 0.182 | 0.129 | 0.160 | 0.180 | 0.129 | 0.162 | 0.339 | 0.234 | 0.147 |
| rs7178572 | 0.070 | 0.126 | 0.578 | 0.070 | 0.125 | 0.579 | 0.363 | 0.235 | 0.122 |
| rs2028299 | -0.080 | 0.174 | 0.644 | -0.083 | 0.174 | 0.634 | -0.109 | 0.284 | 0.702 |
| rs4812829 | 0.170 | 0.135 | 0.209 | 0.169 | 0.135 | 0.210 | 0.408 | 0.224 | 0.068 |

^aDEP, our proposed method allowing for dependence between X and G^m ; ^bIND, our proposed method with independence assumption between X and G^m ; ^cLOGIT, the conventional logistic regression method;

^destimated genetic effect; ^eestimated standard error of $\hat{\beta}_{G^oX}$; ^fsignificance test p-value.

Table S17: Maternal SNP versus pp-BMI interaction effects in the Tianjin Postpartum GDM Prevention Program.

| SNP | DEP ^a | | | IND ^b | | | LOGIT ^c | | |
|------------|-------------------------|-----------------|----------------------|-------------------------|-----------------|----------------------|-------------------------|-----------------|----------------------|
| | $\hat{\beta}_{G^m X}^d$ | SE ^e | P-value ^f | $\hat{\beta}_{G^m X}^d$ | SE ^e | P-value ^f | $\hat{\beta}_{G^m X}^d$ | SE ^e | P-value ^f |
| rs3923113 | 0.270 | 0.284 | 0.341 | -0.220 | 0.181 | 0.224 | 0.437 | 0.336 | 0.193 |
| rs4402960 | -0.117 | 0.226 | 0.603 | -0.059 | 0.150 | 0.695 | -0.164 | 0.240 | 0.493 |
| rs16861329 | 0.505 | 0.262 | 0.054 | 0.240 | 0.161 | 0.136 | 0.744 | 0.312 | 0.017 |
| rs7754840 | 0.112 | 0.196 | 0.568 | -0.207 | 0.133 | 0.121 | 0.242 | 0.219 | 0.268 |
| rs1799884 | -0.354 | 0.241 | 0.142 | -0.257 | 0.151 | 0.089 | -0.230 | 0.267 | 0.389 |
| rs1802295 | 0.291 | 0.323 | 0.369 | -0.052 | 0.221 | 0.812 | 0.316 | 0.346 | 0.361 |
| rs4746822 | -0.310 | 0.225 | 0.169 | -0.283 | 0.153 | 0.065 | -0.352 | 0.241 | 0.144 |
| rs2237895 | -0.201 | 0.211 | 0.340 | -0.290 | 0.136 | 0.034 | -0.286 | 0.234 | 0.222 |
| rs5219 | 0.259 | 0.198 | 0.191 | 0.008 | 0.139 | 0.956 | 0.460 | 0.227 | 0.043 |
| rs1387153 | 0.048 | 0.197 | 0.807 | -0.031 | 0.135 | 0.819 | -0.073 | 0.222 | 0.743 |
| rs10830963 | 0.126 | 0.201 | 0.530 | 0.035 | 0.130 | 0.785 | 0.071 | 0.221 | 0.749 |
| rs7178572 | -0.099 | 0.211 | 0.639 | -0.135 | 0.135 | 0.316 | -0.200 | 0.219 | 0.362 |
| rs2028299 | 0.109 | 0.248 | 0.659 | 0.010 | 0.183 | 0.956 | 0.127 | 0.281 | 0.652 |
| rs4812829 | -0.326 | 0.190 | 0.086 | -0.061 | 0.131 | 0.643 | -0.514 | 0.234 | 0.028 |

^aDEP, our proposed method allowing for dependence between X and G^m ; ^bIND, our proposed method with independence assumption between X and G^m ; ^cLOGIT, the conventional logistic regression method;

^destimated genetic effect; ^eestimated standard error of $\hat{\beta}_{G^m X}$; ^fsignificance test p-value.

Table S18: Joint genetic effect, minor allele frequency, Hardy-Weinberg equilibrium, and maternal genotype and pp-BMI independence in the Jerusalem Perinatal Study.

| SNP | MAF ^b | HWE ^c | Genetic effects ^a | | | | Independence ^h |
|------------|------------------|------------------|------------------------------|------------------|--------------------|-------------------|---------------------------|
| | | | DEP ^d | IND ^e | LOGIT ^f | EMIM ^g | |
| rs2932965 | 0.172 | 0.699 | 0.014 | 0.011 | 0.013 | 0.015 | 0.481 (-0.058) |
| rs3774921 | 0.343 | 0.076 | 0.001 | 0.005 | 0.001 | 0.001 | 0.023 (-0.149) |
| rs3755863 | 0.482 | 0.939 | 0.001 | 0.012 | 0.004 | 0.003 | 0.004 (0.166) |
| rs8192678 | 0.355 | 0.869 | 0.009 | 0.011 | 0.023 | 0.016 | 0.563 (0.037) |
| rs2970849 | 0.252 | 0.304 | 0.153 | 0.251 | 0.276 | 0.171 | 0.124 (-0.106) |
| rs1472095 | 0.169 | 0.164 | 0.030 | 0.063 | 0.054 | 0.025 | 0.062 (-0.146) |
| rs2970853 | 0.226 | 0.830 | 0.019 | 0.025 | 0.028 | 0.035 | 0.370 (-0.065) |
| rs4697046 | 0.336 | 1.000 | 0.284 | 0.339 | 0.375 | 0.436 | 0.422 (-0.050) |
| rs7665116 | 0.172 | 0.501 | 0.509 | 0.538 | 0.487 | 0.334 | 0.560 (0.044) |
| rs12374408 | 0.338 | 0.349 | 0.056 | 0.218 | 0.037 | 0.046 | 0.002 (0.185) |
| rs7437482 | 0.279 | 1.000 | 0.411 | 0.412 | 0.545 | 0.433 | 0.798 (0.017) |
| rs10002477 | 0.393 | 0.693 | 0.402 | 0.476 | 0.335 | 0.373 | 0.152 (0.087) |
| rs6850464 | 0.117 | 0.850 | 0.649 | 0.730 | 0.582 | 0.574 | 0.269 (0.089) |
| rs11724368 | 0.277 | 0.924 | 0.173 | 0.388 | 0.155 | 0.156 | 0.006 (-0.175) |
| rs4235308 | 0.480 | 1.000 | 0.349 | 0.632 | 0.238 | 0.273 | 0.013 (-0.145) |
| rs7656250 | 0.309 | 0.290 | 0.181 | 0.223 | 0.148 | 0.154 | 0.312 (0.068) |
| rs10213440 | 0.201 | 0.234 | 0.337 | 0.331 | 0.512 | 0.398 | 0.908 (0.009) |
| rs4550905 | 0.358 | 0.509 | 0.016 | 0.039 | 0.019 | 0.027 | 0.135 (-0.095) |
| rs4361373 | 0.165 | 0.271 | 0.452 | 0.440 | 0.820 | 0.393 | 0.902 (-0.010) |
| rs11734408 | 0.179 | 0.702 | 0.044 | 0.030 | 0.046 | 0.037 | 0.897 (-0.010) |
| rs3796407 | 0.299 | 0.718 | 0.712 | 0.618 | 0.879 | 0.740 | 0.024 (0.147) |
| rs12500214 | 0.256 | 0.762 | 0.777 | 0.790 | 0.746 | 0.779 | 0.033 (0.148) |
| rs2946385 | 0.483 | 0.360 | 0.217 | 0.186 | 0.274 | 0.339 | 0.211 (0.070) |
| rs2970872 | 0.445 | 0.938 | 0.057 | 0.039 | 0.069 | 0.058 | 0.141 (-0.091) |

^cp-value for testing the joint genetic effect; ^bminor allele frequency; ^dp-value for testing HWE; ^dDEP, our proposed method allowing for dependence between X and G^m ; ^eIND, our proposed method with independence assumption between X and G^m ; ^fLOGIT, the conventional logistic regression method; ^gEMIM, a method developed in Ainsworth et al. (2011a) and Howey and Cordell (2012); ^hp-value for testing the independence between the maternal genotype and pp-BMI ($H_0 : \eta = 0$), with the estimated η in the parentheses.

Table S19: Offspring SNP main effects in the Jerusalem Perinatal Study.

| SNP | DEP ^a | | | IND ^b | | | LOGIT ^c | | |
|------------|-----------------------|-----------------|----------------------|-----------------------|-----------------|----------------------|-----------------------|-----------------|----------------------|
| | $\hat{\beta}_{G^o}^d$ | SE ^e | P-value ^f | $\hat{\beta}_{G^o}^d$ | SE ^e | P-value ^f | $\hat{\beta}_{G^o}^d$ | SE ^e | P-value ^f |
| rs2932965 | 0.41 | 0.401 | 0.306 | 0.41 | 0.401 | 0.305 | 0.50 | 0.408 | 0.220 |
| rs3774921 | 0.68 | 0.323 | 0.036 | 0.68 | 0.323 | 0.035 | 0.65 | 0.343 | 0.058 |
| rs3755863 | -0.46 | 0.304 | 0.127 | -0.47 | 0.304 | 0.124 | -0.41 | 0.337 | 0.222 |
| rs8192678 | -0.74 | 0.313 | 0.018 | -0.75 | 0.313 | 0.017 | -0.66 | 0.359 | 0.065 |
| rs2970849 | 0.22 | 0.356 | 0.539 | 0.22 | 0.355 | 0.534 | 0.13 | 0.364 | 0.729 |
| rs1472095 | 0.80 | 0.386 | 0.038 | 0.80 | 0.385 | 0.039 | 0.71 | 0.414 | 0.085 |
| rs2970853 | 0.24 | 0.385 | 0.531 | 0.24 | 0.385 | 0.532 | 0.30 | 0.390 | 0.443 |
| rs4697046 | -0.25 | 0.328 | 0.443 | -0.25 | 0.328 | 0.451 | -0.29 | 0.345 | 0.406 |
| rs7665116 | -0.07 | 0.448 | 0.879 | -0.07 | 0.448 | 0.877 | -0.14 | 0.424 | 0.749 |
| rs12374408 | -0.10 | 0.353 | 0.779 | -0.10 | 0.352 | 0.781 | -0.15 | 0.350 | 0.673 |
| rs7437482 | -0.40 | 0.365 | 0.277 | -0.40 | 0.365 | 0.276 | -0.40 | 0.384 | 0.297 |
| rs10002477 | 0.11 | 0.322 | 0.737 | 0.11 | 0.322 | 0.734 | 0.19 | 0.345 | 0.586 |
| rs6850464 | -0.44 | 0.553 | 0.426 | -0.44 | 0.553 | 0.422 | -0.47 | 0.510 | 0.356 |
| rs11724368 | 0.34 | 0.353 | 0.332 | 0.35 | 0.352 | 0.326 | 0.34 | 0.366 | 0.356 |
| rs4235308 | -0.07 | 0.326 | 0.822 | -0.07 | 0.325 | 0.827 | -0.09 | 0.332 | 0.783 |
| rs7656250 | 0.31 | 0.339 | 0.366 | 0.31 | 0.339 | 0.367 | 0.33 | 0.352 | 0.347 |
| rs10213440 | -0.52 | 0.416 | 0.210 | -0.51 | 0.416 | 0.216 | -0.53 | 0.439 | 0.227 |
| rs4550905 | 0.25 | 0.344 | 0.460 | 0.25 | 0.344 | 0.461 | 0.35 | 0.337 | 0.307 |
| rs4361373 | -0.01 | 0.424 | 0.990 | 0.00 | 0.423 | 0.999 | 0.01 | 0.435 | 0.983 |
| rs11734408 | -0.13 | 0.393 | 0.742 | -0.13 | 0.393 | 0.741 | -0.09 | 0.416 | 0.820 |
| rs3796407 | -0.39 | 0.339 | 0.251 | -0.39 | 0.338 | 0.244 | -0.32 | 0.357 | 0.373 |
| rs12500214 | -0.13 | 0.327 | 0.681 | -0.14 | 0.327 | 0.659 | -0.06 | 0.390 | 0.880 |
| rs2946385 | -0.27 | 0.275 | 0.327 | -0.27 | 0.275 | 0.327 | -0.23 | 0.329 | 0.478 |
| rs2970872 | 0.31 | 0.284 | 0.268 | 0.32 | 0.284 | 0.263 | 0.20 | 0.342 | 0.556 |

^aDEP, our proposed method allowing for dependence between X and G^m ; ^bIND, our proposed method with independence assumption between X and G^m ; ^cLOGIT, the conventional logistic regression method;

^destimated genetic effect; ^eestimated standard error of $\hat{\beta}_{G^o}$; ^fsignificance test p-value.

Table S20: Maternal SNP main effects in the Jerusalem Perinatal Study.

| SNP | DEP ^a | | | IND ^b | | | LOGIT ^c | | |
|------------|-----------------------|-----------------|----------------------|-----------------------|-----------------|----------------------|-----------------------|-----------------|----------------------|
| | $\hat{\beta}_{G^m}^d$ | SE ^e | P-value ^f | $\hat{\beta}_{G^m}^d$ | SE ^e | P-value ^f | $\hat{\beta}_{G^m}^d$ | SE ^e | P-value ^f |
| rs2932965 | 0.33 | 0.412 | 0.428 | 0.32 | 0.410 | 0.436 | 0.36 | 0.421 | 0.392 |
| rs3774921 | -0.23 | 0.347 | 0.510 | -0.23 | 0.345 | 0.507 | -0.17 | 0.349 | 0.635 |
| rs3755863 | -0.05 | 0.320 | 0.884 | -0.04 | 0.320 | 0.889 | -0.21 | 0.345 | 0.539 |
| rs8192678 | 0.18 | 0.340 | 0.594 | 0.18 | 0.340 | 0.592 | 0.08 | 0.350 | 0.825 |
| rs2970849 | -0.65 | 0.362 | 0.071 | -0.65 | 0.362 | 0.070 | -0.51 | 0.383 | 0.184 |
| rs1472095 | -0.92 | 0.439 | 0.036 | -0.92 | 0.438 | 0.035 | -0.70 | 0.454 | 0.122 |
| rs2970853 | 0.53 | 0.354 | 0.131 | 0.53 | 0.353 | 0.133 | 0.65 | 0.384 | 0.093 |
| rs4697046 | 0.41 | 0.294 | 0.161 | 0.41 | 0.294 | 0.161 | 0.55 | 0.352 | 0.116 |
| rs7665116 | 0.33 | 0.420 | 0.429 | 0.33 | 0.421 | 0.434 | 0.51 | 0.413 | 0.219 |
| rs12374408 | 0.47 | 0.343 | 0.168 | 0.45 | 0.342 | 0.187 | 0.57 | 0.353 | 0.107 |
| rs7437482 | 0.20 | 0.369 | 0.596 | 0.20 | 0.370 | 0.594 | 0.22 | 0.371 | 0.556 |
| rs10002477 | 0.44 | 0.313 | 0.164 | 0.43 | 0.313 | 0.173 | 0.39 | 0.340 | 0.250 |
| rs6850464 | -0.15 | 0.517 | 0.777 | -0.16 | 0.517 | 0.760 | 0.01 | 0.508 | 0.979 |
| rs11724368 | -0.60 | 0.338 | 0.075 | -0.61 | 0.338 | 0.073 | -0.64 | 0.390 | 0.098 |
| rs4235308 | -0.26 | 0.323 | 0.417 | -0.26 | 0.323 | 0.427 | -0.25 | 0.335 | 0.447 |
| rs7656250 | 0.29 | 0.315 | 0.351 | 0.29 | 0.315 | 0.357 | 0.29 | 0.351 | 0.410 |
| rs10213440 | 0.26 | 0.388 | 0.508 | 0.25 | 0.388 | 0.516 | 0.29 | 0.403 | 0.471 |
| rs4550905 | -0.19 | 0.321 | 0.560 | -0.19 | 0.321 | 0.564 | -0.24 | 0.346 | 0.490 |
| rs4361373 | -0.22 | 0.389 | 0.564 | -0.23 | 0.39 | 0.560 | -0.14 | 0.436 | 0.752 |
| rs11734408 | 0.21 | 0.424 | 0.627 | 0.21 | 0.424 | 0.625 | 0.28 | 0.431 | 0.521 |
| rs3796407 | 0.03 | 0.326 | 0.923 | 0.02 | 0.326 | 0.939 | 0.01 | 0.362 | 0.968 |
| rs12500214 | -0.28 | 0.369 | 0.454 | -0.29 | 0.369 | 0.437 | -0.32 | 0.384 | 0.397 |
| rs2946385 | -0.40 | 0.325 | 0.219 | -0.40 | 0.326 | 0.214 | -0.48 | 0.336 | 0.156 |
| rs2970872 | 0.62 | 0.321 | 0.054 | 0.62 | 0.321 | 0.054 | 0.68 | 0.339 | 0.044 |

^aDEP, our proposed method allowing for dependence between X and G^m ; ^bIND, our proposed method with independence assumption between X and G^m ; ^cLOGIT, the conventional logistic regression method;

^destimated genetic effect; ^eestimated standard error of $\hat{\beta}_{G^m}$; ^fsignificance test p-value.

Table S21: Offspring SNP versus pp-BMI interaction effects in the Jerusalem Perinatal Study.

| SNP | DEP ^a | | | IND ^b | | | LOGIT ^c | | |
|------------|------------------------------|-----------------|----------------------|------------------------------|-----------------|----------------------|------------------------------|-----------------|----------------------|
| | $\hat{\beta}_{G^{\circ}X}^d$ | SE ^e | P-value ^f | $\hat{\beta}_{G^{\circ}X}^d$ | SE ^e | P-value ^f | $\hat{\beta}_{G^{\circ}X}^d$ | SE ^e | P-value ^f |
| rs2932965 | 0.02 | 0.410 | 0.969 | 0.01 | 0.410 | 0.974 | 0.07 | 0.392 | 0.868 |
| rs3774921 | 0.25 | 0.336 | 0.463 | 0.25 | 0.334 | 0.461 | 0.17 | 0.340 | 0.615 |
| rs3755863 | 0.34 | 0.323 | 0.295 | 0.33 | 0.320 | 0.296 | 0.27 | 0.339 | 0.426 |
| rs8192678 | 0.00 | 0.312 | 0.987 | 0.00 | 0.312 | 0.988 | -0.25 | 0.356 | 0.478 |
| rs2970849 | 0.26 | 0.369 | 0.477 | 0.26 | 0.368 | 0.477 | 0.33 | 0.364 | 0.368 |
| rs1472095 | 0.21 | 0.354 | 0.547 | 0.20 | 0.352 | 0.563 | 0.34 | 0.417 | 0.412 |
| rs2970853 | -0.56 | 0.407 | 0.172 | -0.56 | 0.407 | 0.168 | -0.48 | 0.372 | 0.199 |
| rs4697046 | -0.29 | 0.348 | 0.411 | -0.29 | 0.348 | 0.407 | -0.27 | 0.338 | 0.428 |
| rs7665116 | -0.69 | 0.473 | 0.145 | -0.69 | 0.474 | 0.145 | -0.50 | 0.401 | 0.210 |
| rs12374408 | 0.44 | 0.372 | 0.232 | 0.44 | 0.367 | 0.228 | 0.53 | 0.356 | 0.135 |
| rs7437482 | -0.61 | 0.323 | 0.060 | -0.61 | 0.324 | 0.062 | -0.58 | 0.390 | 0.138 |
| rs10002477 | 0.29 | 0.349 | 0.410 | 0.28 | 0.348 | 0.416 | 0.40 | 0.334 | 0.235 |
| rs6850464 | -0.42 | 0.584 | 0.477 | -0.41 | 0.582 | 0.485 | -0.47 | 0.502 | 0.352 |
| rs11724368 | 0.08 | 0.364 | 0.835 | 0.08 | 0.361 | 0.833 | -0.08 | 0.365 | 0.835 |
| rs4235308 | -0.25 | 0.328 | 0.445 | -0.25 | 0.325 | 0.447 | -0.34 | 0.334 | 0.305 |
| rs7656250 | 0.54 | 0.359 | 0.131 | 0.54 | 0.359 | 0.131 | 0.57 | 0.345 | 0.097 |
| rs10213440 | -0.73 | 0.367 | 0.048 | -0.73 | 0.367 | 0.047 | -0.68 | 0.439 | 0.120 |
| rs4550905 | 0.00 | 0.360 | 0.990 | 0.00 | 0.359 | 0.997 | 0.24 | 0.333 | 0.471 |
| rs4361373 | -0.62 | 0.436 | 0.156 | -0.62 | 0.436 | 0.155 | -0.32 | 0.423 | 0.456 |
| rs11734408 | 0.68 | 0.426 | 0.109 | 0.68 | 0.426 | 0.110 | 0.65 | 0.425 | 0.125 |
| rs3796407 | -0.30 | 0.321 | 0.347 | -0.31 | 0.320 | 0.336 | -0.19 | 0.348 | 0.578 |
| rs12500214 | -0.23 | 0.320 | 0.468 | -0.24 | 0.319 | 0.460 | -0.30 | 0.386 | 0.438 |
| rs2946385 | -0.31 | 0.270 | 0.257 | -0.30 | 0.270 | 0.264 | -0.34 | 0.33 | 0.303 |
| rs2970872 | 0.13 | 0.286 | 0.650 | 0.13 | 0.285 | 0.641 | 0.30 | 0.344 | 0.391 |

^aDEP, our proposed method allowing for dependence between X and G^m ; ^bIND, our proposed method with independence assumption between X and G^m ; ^cLOGIT, the conventional logistic regression method;

^destimated genetic effect; ^eestimated standard error of $\hat{\beta}_{G^{\circ}X}$; ^fsignificance test p-value.

Table S22: Maternal SNP versus pp-BMI interaction effects in the Jerusalem Perinatal Study.

| SNP | DEP ^a | | | IND ^b | | | LOGIT ^c | | |
|------------|-------------------------|-----------------|----------------------|-------------------------|-----------------|----------------------|-------------------------|-----------------|----------------------|
| | $\hat{\beta}_{G^m X}^d$ | SE ^e | P-value ^f | $\hat{\beta}_{G^m X}^d$ | SE ^e | P-value ^f | $\hat{\beta}_{G^m X}^d$ | SE ^e | P-value ^f |
| rs2932965 | 1.05 | 0.415 | 0.011 | 0.95 | 0.382 | 0.013 | 1.10 | 0.427 | 0.010 |
| rs3774921 | 1.04 | 0.338 | 0.002 | 0.79 | 0.315 | 0.012 | 1.06 | 0.355 | 0.003 |
| rs3755863 | -1.19 | 0.345 | 0.001 | -0.91 | 0.333 | 0.006 | -1.19 | 0.339 | <0.001 |
| rs8192678 | -0.89 | 0.361 | 0.014 | -0.83 | 0.354 | 0.019 | -0.71 | 0.327 | 0.029 |
| rs2970849 | 0.40 | 0.374 | 0.281 | 0.23 | 0.356 | 0.527 | 0.36 | 0.389 | 0.352 |
| rs1472095 | 0.82 | 0.424 | 0.054 | 0.57 | 0.398 | 0.152 | 0.76 | 0.466 | 0.102 |
| rs2970853 | 0.89 | 0.392 | 0.023 | 0.78 | 0.372 | 0.035 | 0.91 | 0.367 | 0.013 |
| rs4697046 | 0.52 | 0.358 | 0.146 | 0.44 | 0.345 | 0.203 | 0.56 | 0.343 | 0.103 |
| rs7665116 | 0.22 | 0.457 | 0.635 | 0.28 | 0.447 | 0.528 | 0.12 | 0.401 | 0.761 |
| rs12374408 | -0.86 | 0.373 | 0.021 | -0.53 | 0.351 | 0.128 | -0.96 | 0.368 | 0.009 |
| rs7437482 | 0.16 | 0.396 | 0.677 | 0.18 | 0.386 | 0.633 | 0.20 | 0.371 | 0.597 |
| rs10002477 | -0.29 | 0.331 | 0.375 | -0.14 | 0.313 | 0.644 | -0.34 | 0.339 | 0.321 |
| rs6850464 | -0.29 | 0.548 | 0.592 | -0.15 | 0.529 | 0.775 | -0.46 | 0.530 | 0.391 |
| rs11724368 | 0.54 | 0.371 | 0.146 | 0.24 | 0.353 | 0.496 | 0.65 | 0.398 | 0.102 |
| rs4235308 | 0.61 | 0.347 | 0.080 | 0.36 | 0.329 | 0.273 | 0.68 | 0.341 | 0.046 |
| rs7656250 | -0.53 | 0.347 | 0.126 | -0.42 | 0.328 | 0.199 | -0.50 | 0.337 | 0.138 |
| rs10213440 | 0.29 | 0.423 | 0.495 | 0.30 | 0.412 | 0.464 | 0.32 | 0.401 | 0.420 |
| rs4550905 | 0.99 | 0.330 | 0.003 | 0.83 | 0.312 | 0.008 | 0.87 | 0.341 | 0.011 |
| rs4361373 | 0.70 | 0.410 | 0.086 | 0.69 | 0.388 | 0.076 | 0.51 | 0.445 | 0.254 |
| rs11734408 | -1.18 | 0.424 | 0.005 | -1.20 | 0.411 | 0.004 | -1.14 | 0.409 | 0.005 |
| rs3796407 | 0.04 | 0.357 | 0.912 | 0.28 | 0.343 | 0.407 | 0.03 | 0.368 | 0.936 |
| rs12500214 | -0.15 | 0.383 | 0.698 | 0.09 | 0.370 | 0.803 | -0.09 | 0.397 | 0.815 |
| rs2946385 | 0.13 | 0.331 | 0.690 | 0.25 | 0.317 | 0.428 | 0.22 | 0.354 | 0.533 |
| rs2970872 | -0.15 | 0.346 | 0.669 | -0.30 | 0.33 | 0.363 | -0.24 | 0.341 | 0.477 |

^aDEP, our proposed method allowing for dependence between X and G^m ; ^bIND, our proposed method with independence assumption between X and G^m ; ^cLOGIT, the conventional logistic regression method;

^destimated genetic effect; ^eestimated standard error of $\hat{\beta}_{G^m X}$; ^fsignificance test p-value.

Table S23: The marginal distribution of the maternal and offspring genotypes under the daLOG model (2.3) in the main text. The MAF was 0.25, and the covariate X was binary with $\text{pr}(X = 1) = \text{pr}(X = 0) = 0.5$.

| | $\eta = 0$ | | | $\eta = 1$ | | | $\eta = 2$ | | |
|-------|------------|-------|-------|------------|-------|-------|------------|-------|-------|
| | 0 | 1/2 | 1 | 0 | 1/2 | 1 | 0 | 1/2 | 1 |
| G^m | 0.562 | 0.375 | 0.062 | 0.419 | 0.437 | 0.144 | 0.323 | 0.393 | 0.284 |
| G^o | 0.562 | 0.375 | 0.062 | 0.478 | 0.431 | 0.091 | 0.390 | 0.490 | 0.120 |