APPENDIX

A.1. Estimation

When there are p exposure variables, the model becomes, for $j = 1, 2, 3$,

$$y_j = \alpha_j + \sum_{i=1}^{p} \beta_{ij} T_i + \varepsilon_j .$$

Because of measurement error, instead of the true covariates $\boldsymbol{T}$, we observe their respective surrogates $\boldsymbol{R}$. $\boldsymbol{R}$ is related to $\boldsymbol{T}$ by an additive error model as

$$R_i = T_i + \varepsilon_{R_i}, \qquad \mathrm{E}(\varepsilon_{R_i}) = 0,\ \mathrm{Var}(\varepsilon_{R_i}) = \sigma^2_{R_i}$$

for $i = 1, \ldots, p$. The true latent variable T_i is assumed to have mean μ_i and variance $\sigma^2_{T_i}$. We designate the correlation between different exposures T_i and T_j as ρ_{T_i,T_j} , and between the random errors ε_{R_i} and ε_{R_j} as ρ_{R_i,R_j}.

When there are p exposure variables,

$$\mathrm{E}\left(\hat{\alpha}_1, \hat{\alpha}_2, \hat{\alpha}_3, \hat{\beta}_{11}, \hat{\beta}_{12}, \hat{\beta}_{13}, \ldots, \hat{\beta}_{p1}, \hat{\beta}_{p2}, \hat{\beta}_{p3}\right)' = \boldsymbol{A}^{-1}\boldsymbol{B}\left(\alpha_1, \alpha_2, \alpha_3, \beta_{11}, \beta_{12}, \beta_{13}, \ldots, \beta_{p1}, \beta_{p2}, \beta_{p3}\right)$$

where

$$\boldsymbol{A} = \begin{pmatrix} 1 & \boldsymbol{\mu}' \\ \boldsymbol{\mu} & \mathrm{Var}(\boldsymbol{R}) + \boldsymbol{\mu}\boldsymbol{\mu}' \end{pmatrix} \otimes \boldsymbol{\Delta},$$

$$\boldsymbol{B} = \begin{pmatrix} 1 & \boldsymbol{\mu}' \\ \boldsymbol{\mu} & \mathrm{Cov}(\boldsymbol{R}, \boldsymbol{T}) + \boldsymbol{\mu}\boldsymbol{\mu}' \end{pmatrix} \otimes \boldsymbol{\Delta}_{\boldsymbol{e}},$$

$$\boldsymbol{\Delta} = \begin{pmatrix} p_1' & 0 & 0 \\ 0 & p_2' & 0 \\ 0 & 0 & p_3' \end{pmatrix}$$

and

$$\boldsymbol{\Delta}_e = \begin{pmatrix} p_1(1-P_a)^2 & p_2(1-P_a)P_A & p_3P_A^2 \\ 2p_1(1-P_a)P_a & p_2((1-P_a)(1-P_A)+P_aP_A) & 2p_3P_A(1-P_A) \\ p_1P_a^2 & p_2P_a(1-P_A) & p_3(1-P_A)^2 \end{pmatrix}.$$

$\boldsymbol{\mu} = (\mu_1, \ldots, \mu_p)'$ is the mean vector of $\boldsymbol{R} = (R_1, \ldots, R_p)'$; $\mathrm{Var}(\boldsymbol{R}) = (v_{ij})$ is the variance and covariance matrix $\boldsymbol{R} = (R_1, \ldots, R_p)'$ with $v_{ii} = \sigma^2_{T_i} + \sigma^2_{R_i}$ and $v_{ij} = \rho_{T_i,T_j}\sigma_{T_i}\sigma_{T_j} + \rho_{R_i,R_j}\sigma_{R_i}\sigma_{R_j}$ for $i \neq j$; $\mathrm{Cov}(\boldsymbol{R}, \boldsymbol{T}) = (c_{ij})$ is the covariance matrix of $\boldsymbol{R} = (R_1, \ldots, R_p)'$ and $\boldsymbol{T} = (T_1, \ldots, T_p)'$ with $c_{ii} = \sigma^2_{T_i}$ and $c_{ij} = \rho_{T_i,T_j}\sigma_{T_i}\sigma_{T_j}$ for $i \neq j$; $\boldsymbol{U} \otimes \boldsymbol{V} = (u_{ij}\boldsymbol{V})$ for $\boldsymbol{U}_{m\times n} = (u_{ij})$ and $\boldsymbol{V}_{p\times q} = (v_{ij})$, the Kronecker product, is an $mp \times nq$ matrix expressible as a partitional matrix with $u_{ij}\boldsymbol{V}$ as the (i, j)th partition, $i = 1, \ldots, m$ and $j = 1, \ldots, n$.

In order to obtain unbiased estimates of the association between $\boldsymbol{T}$ and y, the crude biased estimates need correction. Asymptotically unbiased estimates for α_1, α_2, α_3, β_{11}, β_{12}, β_{13}, $\ldots$, β_{p1}, β_{p2} and β_{p3} can be obtained by multiplying the crude estimates by $\boldsymbol{B}^{-1}\boldsymbol{A}$, which equals to

$$\begin{pmatrix} 1 & -\boldsymbol{\mu}'(\mathrm{Cov}(\boldsymbol{R}, \boldsymbol{T})^{-1}\mathrm{Var}(\boldsymbol{R}) - \boldsymbol{I}) \\ \mathbf{0} & \mathrm{Cov}(\boldsymbol{R}, \boldsymbol{T})^{-1}\mathrm{Var}(\boldsymbol{R}) \end{pmatrix} \otimes \boldsymbol{\Delta}_e^{-1}\boldsymbol{\Delta}$$

with $\mathbf{0}$ being a $p \times 1$ column vector with all elements equal to zero. Simplifying the expression, we obtain the adjusted estimates $\tilde{\alpha}_1$, $\tilde{\alpha}_2$, $\tilde{\alpha}_3$, $\tilde{\beta}_{11}$, $\tilde{\beta}_{12}$, $\tilde{\beta}_{13}$, $\ldots$, $\tilde{\beta}_{p1}$, $\tilde{\beta}_{p2}$ and $\tilde{\beta}_{p3}$ for α_1, α_2, α_3, β_{11}, β_{12}, β_{13}, $\ldots$, β_{p1}, β_{p2} and β_{p3} where

$$\begin{aligned}(\tilde{\alpha}_1, \tilde{\alpha}_2, \tilde{\alpha}_3)' &= \boldsymbol{\Delta}_e^{-1}\boldsymbol{\Delta}(\hat{\alpha}_1, \hat{\alpha}_2, \hat{\alpha}_3)' - \\ &\quad \boldsymbol{\mu}'(\mathrm{Cov}(\boldsymbol{R}, \boldsymbol{T})^{-1}\mathrm{Var}(\boldsymbol{R}) - \boldsymbol{I}) \otimes \boldsymbol{\Delta}_e^{-1}\boldsymbol{\Delta}\,(\hat{\beta}_{11}, \hat{\beta}_{12}, \hat{\beta}_{13}, \ldots, \hat{\beta}_{p1}, \hat{\beta}_{p2}, \hat{\beta}_{p3})'\end{aligned}$$

$$\begin{aligned}(\tilde{\beta}_{11}, \tilde{\beta}_{12}, \tilde{\beta}_{13}, \ldots, \tilde{\beta}_{p1}, \tilde{\beta}_{p2}, \tilde{\beta}_{p3})' &= \\ &\quad \mathrm{Cov}(\boldsymbol{R}, \boldsymbol{T})^{-1}\mathrm{Var}(\boldsymbol{R}) \otimes \boldsymbol{\Delta}_e^{-1}\boldsymbol{\Delta}\,(\hat{\beta}_{11}, \hat{\beta}_{12}, \hat{\beta}_{13}, \ldots, \hat{\beta}_{p1}, \hat{\beta}_{p2}, \hat{\beta}_{p3})'.\end{aligned}$$

A.2. Precision

A.2.1. Variance-covariance matrix of the maximum likelihood estimates for p, P_a and P_A

Since the likelihood function is proportional to

$$L \propto P_{aa}^{n_{aa}}\, P_{AA}^{n_{AA}}\, (1-P_{aa}-P_{AA})^{n_{Aa}}\, \{P_{aa}P_{AA} + \frac{1}{4}(1-P_{aa}-P_{AA})^2\}^{n_{22}}\,,$$

the numerical values of P_{aa} and P_{AA} can be obtained by solving $\partial \log L/\partial P_{aa} = 0$ and $\partial \log L/\partial P_{AA} = 0$, that is

$$\frac{n_{aa}}{P_{aa}} - \frac{n_{Aa}}{1-P_{aa}-P_{AA}} + \frac{n_{22}\{P_{AA}-\frac{1}{2}(1-P_{aa}-P_{AA})\}}{P_{aa}P_{AA}+\frac{1}{4}(1-P_{aa}-P_{AA})^2} \;=\; 0$$

and

$$\frac{n_{AA}}{P_{AA}} - \frac{n_{Aa}}{1-P_{aa}-P_{AA}} + \frac{n_{22}\{P_{aa}-\frac{1}{2}(1-P_{aa}-P_{AA})\}}{P_{aa}P_{AA}+\frac{1}{4}(1-P_{aa}-P_{AA})^2} \;=\; 0$$

Substituting P_{aa} and P_{AA} by $pP_A^2+(1-p)(1-P_a)^2$ and $p(1-P_A)^2+(1-p)P_a^2$ respectively, we have two equations in terms of three quantities of p, P_a and P_A. We need one extra assumption. We assume that $P_a = P_A = P_m$ in this paper. On some occasions, p is known externally and P_a and P_A can be estimated separately.

if P_a and P_A are assumed to be equal to P_m;

$$\mathbf{\Psi} = \begin{pmatrix} 2pP_A & -2(1-p)(1-P_a) \\ -2p(1-P_A) & 2(1-p)P_a \end{pmatrix}$$

if p is known and P_a and P_A can be estimated separately.

The variance-covariance matrix of the maximum likelihood estimates are estimated by inverting the observed information matrix, in which each element is the negative of the second derivative of the log likelihood function. The observed information matrix is, thus, equal to

$$-\mathbf{\Psi}' \begin{pmatrix} \dfrac{\partial^2 \log L}{\partial P_{aa}^2} & \dfrac{\partial^2 \log L}{\partial P_{aa}\partial P_{AA}} \\ \\ \dfrac{\partial^2 \log L}{\partial P_{aa}\partial P_{AA}} & \dfrac{\partial^2 \log L}{\partial P_{AA}^2} \end{pmatrix} \mathbf{\Psi}$$

where

$$\mathbf{\Psi} = \begin{pmatrix} -(1-2P_m) & -2(1-p-P_m) \\ 1-2P_m & -2(p-P_m) \end{pmatrix},$$

$$\frac{\partial^2 \log L}{\partial P_{aa}^2} = -\frac{n_{aa}}{P_{aa}^2} - \frac{n_{Aa}}{(1-P_{aa}-P_{AA})^2} + \frac{n_{22}}{2\{P_{aa}P_{AA}+\frac{1}{4}(1-P_{aa}-P_{AA})^2\}} - \frac{n_{22}\{P_{AA}-\frac{1}{2}(1-P_{aa}-P_{AA})\}^2}{\{P_{aa}P_{AA}+\frac{1}{4}(1-P_{aa}-P_{AA})^2\}^2},$$

$$\frac{\partial^2 \log L}{\partial P_{aa}\partial P_{AA}} = -\frac{n_{Aa}}{(1-P_{aa}-P_{AA})^2} + \frac{3n_{22}}{2\{P_{aa}P_{AA}+\frac{1}{4}(1-P_{aa}-P_{AA})^2\}} - \frac{n_{22}\{P_{AA}-\frac{1}{2}(1-P_{aa}-P_{AA})\}\{P_{aa}-\frac{1}{2}(1-P_{aa}-P_{AA})\}}{\{P_{aa}P_{AA}+\frac{1}{4}(1-P_{aa}-P_{AA})^2\}^2},$$

$$\frac{\partial^2 \log L}{\partial P_{AA}^2} = -\frac{n_{AA}}{P_{AA}^2} - \frac{n_{Aa}}{(1-P_{aa}-P_{AA})^2} + \frac{n_{22}}{2\{P_{aa}P_{AA}+\frac{1}{4}(1-P_{aa}-P_{AA})^2\}} - \frac{n_{22}\{P_{aa}-\frac{1}{2}(1-P_{aa}-P_{AA})\}^2}{\{P_{aa}P_{AA}+\frac{1}{4}(1-P_{aa}-P_{AA})^2\}^2},$$

$P_{aa} = pP_m^2 + (1-p)(1-P_m)^2$ and $P_{AA} = p(1-P_m)^2 + (1-p)P_m^2$. The unknown parameters in the observed information matrix are replaced by their maximum likelihood estimates.

A.2.2. Variance-covariance matrix of the adjusted estimates

We denote $\boldsymbol{\alpha} = (\alpha_1, \alpha_2, \alpha_3)'$ and $\boldsymbol{\beta}_j = (\beta_{j1}, \beta_{j2}, \beta_{j3})'$ for $j = 1, \ldots, p$. Then, for $i, j = 1, ..., p$ and $s, t = 1, 2, 3$,

$$\begin{aligned}\mathrm{Cov}(\tilde{\alpha}_s, \tilde{\alpha}_t) &= \boldsymbol{\alpha}'\boldsymbol{D}_{st}\boldsymbol{\alpha} + (\boldsymbol{\beta}_1', \ldots, \boldsymbol{\beta}_p')\,(\boldsymbol{F}\boldsymbol{F}' \otimes \boldsymbol{D}_{st} + \mathrm{Var}(\boldsymbol{F}) \otimes \boldsymbol{r}_s\boldsymbol{r}_t')\,(\boldsymbol{\beta}_1', \ldots, \boldsymbol{\beta}_p')' \\ &\quad - \boldsymbol{\alpha}'\,(\boldsymbol{F}' \otimes \boldsymbol{D}_{st})\,(\boldsymbol{\beta}_1', \ldots, \boldsymbol{\beta}_p')' - (\boldsymbol{\beta}_1', \ldots, \boldsymbol{\beta}_p')\,(\boldsymbol{F}' \otimes \boldsymbol{D}_{st})\,\boldsymbol{\alpha}\end{aligned}$$

$$\mathrm{Cov}(\tilde{\beta}_{is}, \tilde{\beta}_{jt}) = (\boldsymbol{\beta}_1', \ldots, \boldsymbol{\beta}_p')\left(\boldsymbol{E}_{ij} \otimes \boldsymbol{r}_s\boldsymbol{r}_t' + \boldsymbol{s}_i\boldsymbol{s}_j' \otimes \boldsymbol{D}_{st}\right)(\boldsymbol{\beta}_1', \ldots, \boldsymbol{\beta}_p')'$$

$$\begin{aligned}\mathrm{Cov}(\tilde{\alpha}_s, \tilde{\beta}_{it}) &= \boldsymbol{\alpha}' \left(\boldsymbol{s}_i' \otimes \boldsymbol{D}_{st}\right) (\boldsymbol{\beta}_1', \ldots, \boldsymbol{\beta}_p')' - (\boldsymbol{\beta}_1', \ldots, \boldsymbol{\beta}_p') \left(\boldsymbol{G}_i \otimes \boldsymbol{r}_s \boldsymbol{r}_t' + \right. \\ & \left. \boldsymbol{s}_i \boldsymbol{F}' \otimes \boldsymbol{D}_{st}\right) (\boldsymbol{\beta}_1', \ldots, \boldsymbol{\beta}_p')'\end{aligned}$$

where $\boldsymbol{r}_i'$ and $\boldsymbol{s}_i'$ are the ith row of $\hat{\boldsymbol{\Delta}}_e^{-1} \hat{\boldsymbol{\Delta}}$ and $\widehat{\mathrm{Cov}}(\boldsymbol{R}, \boldsymbol{T})^{-1} \widehat{\mathrm{Var}}(\boldsymbol{R})$, respectively; $\boldsymbol{D}_{ij}$, a 3×3 matrix, is the variance and covariance matrix of $\boldsymbol{r}_i$ and $\boldsymbol{r}_j$; $\boldsymbol{E}_{ij}$, a $p \times p$ matrix, is the variance and covariance matrix of $\boldsymbol{s}_i$ and $\boldsymbol{s}_j$; $\boldsymbol{F}$ is a p dimensional column vector with the ith element as $\hat{\boldsymbol{\mu}}' \boldsymbol{s}_i - \hat{\mu}_i$; $\boldsymbol{G}_i$ is a $p \times p$ matrix with the (g, h)th element as $\sum_{j=1}^{p} \hat{\mu}_j \mathrm{Cov}(k_{jg}, k_{hi})$ with k_{uv} the (u, v)th element in $\widehat{\mathrm{Cov}}(\boldsymbol{R}, \boldsymbol{T})^{-1} \widehat{\mathrm{Var}}(\boldsymbol{R})$; and $\mathrm{Var}(\boldsymbol{F})$ is a $p \times p$ matrix with (i, j)th element as $\sum_{s=1}^{p} \sum_{t=1}^{p} \hat{\mu}_s \hat{\mu}_t \mathrm{Cov}(k_{si}, k_{tj}) + \sum_{s=1}^{p} \sum_{t=1}^{p} k_{si} k_{tj} \mathrm{Cov}(\hat{\mu}_s, \hat{\mu}_t) + \mathrm{Cov}(\hat{\mu}_i, \hat{\mu}_j) - \sum_{s=1}^{p} k_{si} \mathrm{Cov}(\hat{\mu}_s, \hat{\mu}_j) - \sum_{t=1}^{p} k_{tj} \mathrm{Cov}(\hat{\mu}_i, \hat{\mu}_t)$.