722   Additional file 3 — Extended model for assessing heterogeneity of treatment effect

723   To explore the impact of a pre-treatment covariate on the CCP effect, we developed another extension to model (3)

724   for investigating the interaction between treatment and a categorical pre-treatment covariate, which S denotes. In

725   this model, an indicator variable d_{kis} that equals 1 if the covariate S for the ith patient in the kth RCT falls in

726   stratum s, and is 0 otherwise.

The model with the interaction between treatment and a pre-specified covariate S is as follows:

$$\text{logit}\left(P\left(Y_{ki} \geq y\right)\right) = \tau_{yk} + \boldsymbol{\beta} \boldsymbol{X}_{ki} + A_{ki}\left(\delta_{k_c} + \gamma_{(ks)_c} d_{kis}\right)$$

$$\tau_{yk} \sim \text{Normal}\left(\mu = 0, \sigma = \sigma_\tau\right)$$

$$\boldsymbol{\beta} \sim \text{Normal}\left(\boldsymbol{\mu} = \boldsymbol{0}, \Sigma = \sigma_\beta^2 I_{p \times p}\right)$$

$$\delta_{k_c} \sim \text{Normal}\left(\mu = \delta_c, \sigma = \eta\right), \quad c \in (1, \dots, C)$$

$$\eta \sim \text{Cauchy}\left(\mu = 0, \sigma = \sigma_\eta\right)$$

$$\delta_c \sim \text{Normal}\left(\mu = -\Delta_{co}, \sigma = \eta_0\right)$$

$$\eta_0 \sim \text{Cauchy}\left(\mu = 0, \sigma = \sigma_{\eta_0}\right) \tag{A2}$$

$$-\Delta_{co} \sim \text{Normal}\left(\mu = 0, \sigma = \sigma_{\Delta_{co}}\right)$$

$$\gamma_{(ks)_c} \sim \text{Normal}\left(\mu = \gamma_{cs}, \sigma = \zeta\right), \quad s \in (1, \dots, S)$$

$$\zeta \sim \text{Cauchy}\left(\mu = 0, \sigma = \sigma_\zeta\right)$$

$$\gamma_{cs} \sim \text{Normal}\left(\mu = -\Gamma_s, \sigma = \zeta_0\right)$$

$$\zeta_0 \sim \text{Cauchy}\left(\mu = 0, \sigma = \sigma_{\zeta_0}\right)$$

$$-\Gamma_s \sim \text{Normal}\left(\mu = 0, \sigma = \sigma_{\Gamma_s}\right).$$

727   The extended model includes *RCT-specific* control treatment by covariate interaction parameter $\gamma_{(ks)_c}$. $\gamma_{(ks)_c}$ are

728   assumed to be centered around a control-type mean γ_{cs}. In turn, the γ_{cs}'s are centered around $-\Gamma_s$, the overall

729   "control effect" modification across RCTs.

730   The pooled effect of CCP (measured by $\log \text{OR}$) across all RCTs for all patients is still Δ_{co}, where as the pooled

731   effect for patients with covariate $S = s$ will be $\Delta_s = \Delta_{co} + \Gamma_s$.