

A framework for identifying treatment-covariate  
interactions in individual participant data network  
meta-analysis: Supplementary material

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## A Additional parameterisation of within and across trial interactions

The random treatment effect model with random trial-level treatment-covariate interaction and random trial-level effect of the patient-level covariate,  $z_{ij}$ , which separates the within and across trial interactions is:

$$\begin{aligned} \ln\{H_j(t|x_{ij})\} &= s_j(\ln(t)) + \beta_{1j}\text{trt}1_{ij} + \dots + \beta_{qj}\text{trt}q_{ij} + \alpha_j(z_{ij} - \bar{z}_j) \\ &\quad + \delta_{A1j}\text{trt}1_{ij}(z_{ij} - \bar{z}_j) + \dots + \delta_{Aqj}\text{trt}q_{ij}(z_{ij} - \bar{z}_j) \\ &\quad + \delta_{B1j}\text{trt}1_{ij}\bar{z}_j + \dots + \delta_{Bqj}\text{trt}q_{ij}\bar{z}_j \\ \beta_j &\sim MVN(\mu_\beta, T_\beta) \\ \alpha_j &\sim N(\theta, \sigma^2) \\ \delta_{Aj} &\sim MVN(\mu_{\delta_A}, T_{\delta_A}) \\ \delta_{Bj} &\sim MVN(\mu_{\delta_B}, T_{\delta_B}) \end{aligned}$$

where  $z_{ij}$  is the covariate value for patient  $i$  in trial  $j$  with coefficient  $\alpha_j$  for trial  $j$  and  $\bar{z}_j$  is the mean value of  $z_{ij}$  for trial  $j$ . In this model  $\beta_{1j}, \dots, \beta_{qj}$  are random treatment effects. The within trial interaction is estimated by  $\mu_{\delta_A}$  whilst the across trial information is estimated by  $\mu_{\delta_A} + \mu_{\delta_B}$ .

The random treatment effect model with random trial-level treatment-covariate interaction and random trial-level effect of the patient-level covariate,  $z_{ij}$ , which combines the within and across trial interactions is:

$$\begin{aligned} \ln\{H_j(t|x_{ij})\} &= s_j(\ln(t)) + \beta_{1j}\text{trt}1_{ij} + \dots + \beta_{qj}\text{trt}q_{ij} + \alpha_j z_{ij} \\ &\quad + \delta_{1j}\text{trt}1_{ij}z_{ij} + \dots + \delta_{qj}\text{trt}q_{ij}z_{ij} \\ \beta_j &\sim MVN(\mu_\beta, T_\beta) \\ \delta_j &\sim MVN(\mu_\delta, T_\delta) \\ \alpha_j &\sim N(\theta, \sigma^2) \end{aligned}$$

where  $z_{ij}$  is the covariate value for patient  $i$  in trial  $j$  with coefficient  $\alpha_j$  for trial  $j$ ,  $\beta_{1j}, \dots, \beta_{qj}$  are random treatment effects and  $\delta_{1j}, \dots, \delta_{qj}$  are random treatment-covariate interaction effects.

## B Sensitivity analysis: Cervical cancer NMA with treatment-stage interactions excluding patients with missing data

Table B.1: Posterior mean and 95% credible intervals for treatment and treatment-stage interaction effects from NMA models including treatment-stage interactions with within and across trial interactions separated and combined. Patients with missing stage of disease are excluded. Reference level is stages 1A-2A. RT = radiotherapy, CT+RT = neoadjuvant chemotherapy plus radiotherapy, CT+S = neoadjuvant chemotherapy plus surgery.

	Within & across trial interactions separated	Within & across trial interactions combined
RT v CTRT	-0.460 (-1.121, 0.123)	-0.462 (-0.802, -0.128)
RT v CT+RT short cycles	-0.086 (-0.702, 0.610)	0.067 (-0.396, 0.575)
RT v CT+RT long cycles	0.043 (-0.623, 0.745)	0.181 (-0.440, 0.735)
RT v CT+S	0.303 (-0.537, 1.245)	-0.020 (-0.780, 0.671)
CTRT - stage within	0.146 (-0.087, 0.403)	
CT+RT - stage within	-0.063 (-0.317, 0.187)	
CT+S - stage within	-0.213 (-0.811, 0.374)	
CTRT - stage across	0.189 (-0.260, 0.718)	
CT+RT - stage across	0.219 (-0.281, 0.708)	
CT+S - stage across	-0.461 (-1.338, 0.372)	
CTRT - stage combined		0.178 (-0.040, 0.400)
CT+RT - stage combined		0.023 (-0.218, 0.260)
CT+S - stage combined		-0.251 (-0.723, 0.302)