Table S1 Posterior mean residual deviance D_{res}, effective number of parameters p_D and deviance information criterion (DIC) for the hierarchical models fitted to the ROBES data.

Model	**Design characteristic/s**	**Interaction/s between design characteristics**	**Covariates in model for τ^2**	**D_{res}**	**p_D**	**DIC**
A1	Sequence generation	N/A	-	2982	1909	4891
	Sequence generation	N/A	Outcome type	3000	1889	4889
A2	Allocation concealment	N/A	-	2972	1914	4886
	Allocation concealment	N/A	Outcome type	3003	1899	4902
A3	Blinding	N/A	-	2968	1915	4883
	Blinding	N/A	Outcome type	3003	1891	4894
B1	Sequence generation and allocation concealment	Yes	-	3001	1900	4901
	Sequence generation and allocation concealment	No	-	2988	1906	4894
B2	Sequence generation and blinding	Yes	-	2978	1908	4886
	Sequence generation and blinding	No	-	2988	1904	4892
B3	Allocation concealment and blinding	Yes	-	2996	1902	4898
	Allocation concealment and blinding	No	-	2981	1908	4889
B4	Sequence generation, allocation concealment and blinding	All possible	-	2985	1905	4890
	Sequence generation, allocation concealment and blinding	Interaction between sequence generation and blinding alone	-	2998	1899	4897
	Sequence generation, allocation concealment and blinding	No	-	2978	1913	4891
	Sequence generation, allocation concealment and blinding	No	Outcome type	2991	1895	4886

Supplementary materials

S1 Estimating total heterogeneity variance from the label-invariant model

We used label-invariant hierarchical models to analyse trial data from 117 meta-analyses in *ROBES* simultaneously. The models have been proposed in an earlier paper [9], but we describe the models briefly here to show how to derive the formulae for heterogeneity variance $\tau^2_{total,m}$ among all trials in a meta-analysis *m*.

S1.1 Univariable model for the influence of accounting for a single trial design characteristic

In a given meta-analysis *m*, trials are categorised as low risk of bias (L-trials) or high/unclear risk of bias (H-trials) for a specific design characteristic.

The L-trials provide an estimate of the underlying intervention effect θ^L_{im}, assumed to have a normal random-effects distribution with mean d_m and variance τ^2_m, specific to meta-analysis *m*. The H-trials are assumed to estimate an underlying intervention effect θ^H_{im}, assumed to be normally distributed with mean $d_m + b_m$ and variance $\lambda\tau^2_m$:

$$\theta^L_{im} \sim N(d_m, \tau^2_m)$$
$$\theta^H_{im} \sim N(d_m + b_m, \lambda\tau^2_m).$$

The average bias b_m in intervention effect in meta-analysis *m* is assumed to be exchangeable across meta-analyses, with overall mean b_0 and between-meta-analysis variance in mean bias φ^2:

$$b_m \sim N(b_0, \varphi^2)$$
$$b_0 \sim N(B_0, V_0)$$

We set an indicator X_{im} to be 1 for H trials and 0 for L trials such that

$$X_{im} = \begin{cases} 1 & \\ & \text{with probability} \\ 0 & \end{cases} \quad \begin{matrix} \pi_m \\ \\ 1-\pi_m. \end{matrix}$$

Each trial is assumed to provide an underlying estimate of intervention effect:

$$\theta_{im} = (1 - X_{im})\theta^L_{im} + X_{im}\theta^H_{im}.$$

The first term of the sum will return θ_{im}^{L} if trial *i* is at low risk of bias. The second term will return θ_{im}^{H} if the trial *i* is at high/unclear risk of bias.

The total heterogeneity variance among trials in meta-analysis *m* is given by:

$$
\begin{aligned}
\tau_{total,m}^2 &= \mathrm{var}(\theta_{im}) \\
&= \mathrm{var}((1-X_{im})\theta_{im}^{L} + X_{im}\theta_{im}^{H}) \\
&= \mathrm{var}((1-X_{im})\theta_{im}^{L}) + \mathrm{var}(X_{im}\theta_{im}^{H}) + 2\,\mathrm{cov}((1-X_{im})\theta_{im}^{L}, X_{im}\theta_{im}^{H})
\end{aligned}
$$

$$
\begin{aligned}
&= E(1-X_{im})^2\,\mathrm{var}(\theta_{im}^{L}) + E(\theta_{im}^{L})^2\,\mathrm{var}(1-X_{im}) + \mathrm{var}(1-X_{im})\,\mathrm{var}(\theta_{im}^{L}) \\
&+ E(X_{im})^2\,\mathrm{var}(\theta_{im}^{H}) + E(\theta_{im}^{H})^2\,\mathrm{var}(X_{im}) + \mathrm{var}(X_{im})\,\mathrm{var}(\theta_{im}^{H}) \\
&+ 2[E((1-X_{im})\theta_{im}^{L}X_{im}\theta_{im}^{H}) - E((1-X_{im})\theta_{im}^{L})E(X_{im}\theta_{im}^{H})]
\end{aligned}
$$

$$
\begin{aligned}
&= E(1-X_{im})^2\,\mathrm{var}(\theta_{im}^{L}) + E(\theta_{im}^{L})^2\,\mathrm{var}(1-X_{im}) + \mathrm{var}(1-X_{im})\,\mathrm{var}(\theta_{im}^{L}) \\
&+ E(X_{im})^2\,\mathrm{var}(\theta_{im}^{H}) + E(\theta_{im}^{H})^2\,\mathrm{var}(X_{im}) + \mathrm{var}(X_{im})\,\mathrm{var}(\theta_{im}^{H}) \\
&+ 2[E((1-X_{im})X_{im})E(\theta_{im}^{L}\theta_{im}^{H}) - E((1-X_{im})\theta_{im}^{L})E(X_{im}\theta_{im}^{H})]
\end{aligned}
$$

$$
\begin{aligned}
&= (1-\pi_m)^2\tau_m^2 + d_m^2(1-\pi_m)\pi_m + (1-\pi_m)\pi_m\tau_m^2 \\
&+ \pi_m^2\lambda\tau_m^2 + (d_m+b_m)^2\pi_m(1-\pi_m) + \pi_m(1-\pi_m)\lambda\tau_m^2 \\
&- 2(1-\pi_m)d_m\pi_m(d_m+b_m)
\end{aligned}
$$

$$
\begin{aligned}
&= (1-\pi_m)\tau_m^2 + d_m^2(1-\pi_m)\pi_m \\
&+ \pi_m\lambda\tau_m^2 + (d_m+b_m)^2\pi_m(1-\pi_m) \\
&- 2(1-\pi_m)d_m\pi_m(d_m+b_m)
\end{aligned}
$$

$$
= (1-\pi_m)\tau_m^2 + \pi_m\lambda\tau_m^2 + \pi_m(1-\pi_m)b_m^2
$$

S1.2 Multivariable model for the influence of accounting for **multiple trial design characteristics**

Suppose trials in a meta-analysis *m* are categorised as low risk of bias (L-trials) or high/unclear risk of bias (H-trials) for each of 2 reported design characteristics. We set the indicator X_{ijm} to be 1 for trials at high/unclear risk of bias for the *j*-th reported characteristic (*j*=1,2), and 0 for trials at low risk of bias for that characteristic such that

$$X_{ijm} = \begin{cases} 1 & \\ & \text{with probability} \\ 0 & \end{cases} \quad \begin{matrix} \pi_{jm} \\ \\ 1-\pi_{jm} \end{matrix}$$

Each trial is assumed to provide an estimate of underlying intervention effect:

$$\theta_{im} = (1 - X_{1im})(1 - X_{2im})\theta_{im}^{L} + X_{1im}(1 - X_{2im})\theta_{1im}^{H} + X_{2im}(1 - X_{1im})\theta_{2im}^{H} + X_{1im}X_{2im}\theta_{3im}^{H}$$

where

$$\begin{aligned} &\theta_{im}^{L} \sim N(d_m, \tau_m^2) \\ &\theta_{1im}^{H} \sim N(d_m + b_{1m}, \lambda_1\tau_m^2) \\ &\theta_{2im}^{H} \sim N(d_m + b_{2m}, \lambda_2\tau_m^2) \\ &\theta_{3im}^{H} \sim N(d_m + b_{1m} + b_{2m} + b_{3m}, \lambda_1\lambda_2\lambda_3\tau_m^2). \end{aligned}$$

Trials at low risk of bias for both characteristics 1 and 2 provide an estimate of intervention effect θ_{im}^{L}, as in Section S1.1. The intervention effect θ_{1im}^{H} in a trial *i* at high/unclear risk of bias for characteristic 1 but low risk of bias for characteristic 2 has a normal distribution with mean $d_m + b_{1m}$ and variance $\tau_m^2\lambda_1$. The intervention effect θ_{2im}^{H} in a trial *i* at high/unclear risk of bias for characteristic 2 but low risk of bias for characteristic 1 has a normal distribution with mean $d_m + b_{2m}$ and variance $\tau_m^2\lambda_2$. The intervention effect θ_{3im}^{H} in a trial *i* at high/unclear risk of bias for both characteristics 1 and 2 has a normal distribution with mean $d_m + b_{1m} + b_{2m} + b_{3m}$ and variance $\tau_m^2\lambda_1\lambda_2\lambda_3$.

An estimate of total heterogeneity variance among trials in meta-analysis *m* is given by:

$$
\begin{aligned}
&\tau^2_{total,m} = \mathrm{var}(\theta_{im}) \\
&= \mathrm{var}((1-X_{1im})(1-X_{2im})\theta^L_{im} + X_{1im}(1-X_{2im})\theta^H_{1im} + X_{2im}(1-X_{1im})\theta^H_{2im} + X_{1im}X_{2im}\theta^H_{3im}) \\
&= \mathrm{var}((1-X_{1im})(1-X_{2im})\theta^L_{im}) + \mathrm{var}(X_{1im}(1-X_{2im})\theta^H_{1im}) + \mathrm{var}(X_{2im}(1-X_{1im})\theta^H_{2im}) + \mathrm{var}(X_{1im}X_{2im}\theta^H_{3im}) \\
&+2\,\mathrm{cov}((1-X_{1im})(1-X_{2im})\theta^L_{im}, X_{1im}(1-X_{2im})\theta^H_{1im}) + 2\,\mathrm{cov}((1-X_{1im})(1-X_{2im})\theta^L_{im}, X_{2im}(1-X_{1im})\theta^H_{2im}) \\
&+2\,\mathrm{cov}((1-X_{1im})(1-X_{2im})\theta^L_{im}, X_{1im}X_{2im}\theta^H_{3im}) + 2\,\mathrm{cov}(X_{1im}(1-X_{2im})\theta^H_{1im}, X_{2im}(1-X_{1im})\theta^H_{2im}) \\
&+2\,\mathrm{cov}(X_{1im}(1-X_{2im})\theta^H_{1im}, X_{1im}X_{2im}\theta^H_{3im}) + 2\,\mathrm{cov}(X_{2im}(1-X_{1im})\theta^H_{2im}, X_{1im}X_{2im}\theta^H_{3im})
\end{aligned}
$$

$$
\begin{aligned}
&= (1-\pi_{1m})(1-\pi_{2m})\tau^2_m + ((1-\pi_{1m})(1-\pi_{2m}) - (1-\pi_{1m})^2(1-\pi_{2m})^2)d^2_m \\
&+\pi_{1m}(1-\pi_{2m})\lambda_1\tau^2_m + (\pi_{1m}(1-\pi_{2m}) - \pi_{1m}{}^2(1-\pi_{2m})^2)(d_m + b_{1m})^2 \\
&+\pi_{2m}(1-\pi_{1m})\lambda_2\tau^2_m + (\pi_{2m}(1-\pi_{1m}) - \pi_{2m}{}^2(1-\pi_{1m})^2)(d_m + b_{2m})^2 \\
&+\pi_{1m}\pi_{2m}\lambda_1\lambda_2\lambda_3\tau^2_m + (\pi_{1m}\pi_{2m} - \pi_{1m}{}^2\pi_{2m}{}^2)(d_m + b_{1m} + b_{2m} + b_{3m})^2 \\
&-2\pi_{1m}(1-\pi_{1m})(1-\pi_{2m})^2 d_m(d_m + b_{1m}) \\
&-2\pi_{2m}(1-\pi_{2m})(1-\pi_{1m})^2 d_m(d_m + b_{2m}) \\
&-2\pi_{1m}\pi_{2m}(1-\pi_{1m})(1-\pi_{2m})d_m(d_m + b_{1m} + b_{2m} + b_{3m}) \\
&-2\pi_{1m}(1-\pi_{2m})\pi_{2m}(1-\pi_{1m})(d_m + b_{1m})(d_m + b_{2m}) \\
&-2\pi^2_{1m}(1-\pi_{2m})\pi_{2m}(d_m + b_{1m})(d_m + b_{1m} + b_{2m} + b_{3m}) \\
&-2\pi^2_{2m}(1-\pi_{1m})\pi_{1m}(d_m + b_{2m})(d_m + b_{1m} + b_{2m} + b_{3m}).
\end{aligned}
$$

In a similar way, we derive estimates of total heterogeneity in a meta-analysis from the multivariable label-invariant models for the influence of accounting for three design characteristics.

S2 Model comparison

Bayesian hierarchical models were fitted to trial data from all 117 meta-analyses. The various models fitted to the data differed according to the indicators of design characteristics and interactions included as covariates in the model, and according to the inclusion of indicators of outcome type in the regression model for heterogeneity variance τ_m^2 among trials at low risk of bias. Results to compare model fit are given in Table S1.