Appendix (Supplementary material)

A.1 Statistical analysis

A.1.1 Standardized mean difference

Results of each study include the number of participants in each of the two intervention arms, their mean response and the standard deviation of their mean responses (Table A.1).

Table A.1: Continuous outcome data

Denote the pooled standard deviation across the two intervention groups

$$
s_i = \sqrt{\frac{(n_i^C - 1)(sd_i^C)^2 + (n_i^T - 1)(sd_i^T)^2}{N_i - 2}},
$$

where $N_i = n_i^C + n_i^T$.

The mean difference is given by

$$
MD_i = m_i^T - m_i^C.
$$

The standardized mean difference (SMD) is

$$
SMD_i = \frac{MD_i}{s_i} \left(1 - \frac{3}{4N_i - 9} \right),
$$

with standard error

$$
SE(SMD_i) = \sqrt{\frac{N_i}{n_i^C n_i^T} + \frac{SMD_i^2}{2(N_i - 3.94)}}
$$

.

A.1.2 Fitted hierarchical model

We describe the statistical models fitted to study data from all meta-analyses in the data set. Within each meta-analysis with outcome *j* corresponding to pair-wise comparison *k*, a random-effects model with normal within-study likelihoods was fitted to continuous outcome data y_{kj} from each study *i*, on the standardized mean difference (SMD) scale:

$$
y_{kji} \sim N(\theta_{kji}, \sigma_{kji}^2)
$$

$$
\theta_{kji} \sim N(\mu_{kj}, \tau_{kj}^2).
$$

In the defined model, θ_{kj} denotes the underlying intervention effect for the *i*-th study within outcome *j* within pair-wise comparison k , μ_{kj} is the combined intervention effect for a meta-analysis with outcome *j* corresponding to pair-wise comparison *k* and τ_{kj}^2 is the corresponding between-study heterogeneity variance.

Across meta-analyses, a hierarchical regression model was fitted to $log(\tau_{kj}^2)$, assuming a *t*-distribution with 5 degrees of freedom for the residual variation. In the model below, $x_{1kj},...,x_{8kj}$ are indicators for the type of outcome examined by meta-analysis *j* within pair-wise intervention comparison *k*. Fixed effects $\beta_1,...,\beta_7$ estimate average differences among eight outcome types, whilst the error terms $e_1,...,e_8$ allow for residual variation across meta-analyses with separate variances $\phi_1^2,...,\phi_8^2$ assumed for each outcome type. Similarly z_{1k} , z_{2k} , z_{3k} are binary indicators for the type of intervention comparison under pair-wise comparison *k*. Fixed effects γ_1 and γ_2 estimate average differences among three intervention comparison types, while the random effects u_1 , u_2 , u_3 allow for variability across pair-wise comparisons, with separate variances κ_1^2 , κ_2^2 , κ_3^2 assumed for each intervention comparison type. Covariates $a_{1kj},...,a_{10k}$ are indicators for medical areas, with fixed effects δ_1 ,..., δ_{10} estimating average differences among medical specialities.

The log-*t* model fitted to τ_{kj}^2 was:

The log-*t* model fitted to
$$
\tau_{kj}^2
$$
 was:
\n
$$
\log(\tau_{kj}^2) = \alpha_k + \beta_1 x_{1kj} + ... + \beta_7 x_{7kj} + \delta_1 a_{1kj} + ... + \delta_{10} a_{10kj} + \sum_{l=1}^8 e_{lkj} x_{lkj}
$$
\nand $\alpha_k = \alpha + \gamma_1 z_{1k} + \gamma_2 z_{2k} + \sum_{m=1}^3 u_{mk} z_{mk}$,
\nwhere $\mathbf{e}_{lkj} \sim t(0, \phi_l^2, 5)$ and $u_{mk} \sim t(0, \kappa_m^2, 5)$, for $l=1, 2, ..., 8$ and $m=1, 2, 3$.

For each setting defined by outcome type, type of intervention comparison and medical area, we obtained a predictive distribution for heterogeneity in a new meta-analysis in that setting, within the full Bayesian model:

$$
\log(\tau_{new}^2) \sim t(\alpha_{new} + \beta x_{kj} + \delta a_{kj}, \phi_i^2, 5)
$$

$$
\alpha_{new} \sim t(\alpha + \gamma z_k, \kappa_m^2, 5).
$$

We used WinBUGS to obtain a sample from the posterior distribution of $log(\tau_{new}^2)$ after convergence. To approximate the predictive distribution for heterogeneity, we used the R function *fitdistr* in the library *MASS* to fit a *t* distribution with 5 degrees of freedom to this sample of values for log (τ_{new}^2). This process provided parametric distributions approximating the predictive distributions, and these distributions were easily summarized and reported for use as priors in new meta-analyses.

A.1.3 WinBUGS code to fit a simple hierarchical model

The following code fits a simple Bayesian hierarchical model to full study-level data, estimating variation in heterogeneity without adjustment for meta-analysis characteristics as covariates.

Priors for unknown parameters

mu.all \sim dnorm(0.0.1) # vague prior for location parameter amongma.prec ~ dgamma $(0.1, 0.1)$ # Inverse-gamma prior assumed for scale parameter of t distribution amongcomp.prec \sim dgamma(0.1,0.1)

Obtain a predictive distribution for tausq expected in a new meta-analysis

```
logtausq.new ~ dt(amongma.mu.new,amongma.prec,5)
amongma.mu.new ~ dt(mu.all,amongcomp.prec,5)
tausq.new <- exp(logtausq.new)
```
}

A.2 Method-of-moments estimates for between-study variance τ²

(a) Data published on the SMD scale from 1360 meta-analyses.

(b) Data published on the mean difference scale from 5132 meta-analyses.

Figure A.2: Distribution of non-zero estimates for the between-study heterogeneity variance τ^2 , plotted on the log scale.

A.3 Predictive distributions for heterogeneity in future meta-analyses

We summarize a set of predictive *t*-distributions for $log(\tau^2)$ in future meta-analyses, across settings defined by type of outcome and type of intervention comparison, together with summary statistics for τ^2 on the untransformed scale, in meta-analyses related to respiratory diseases (Table A.3.1) and cancer (Table A.3.2). Figure A.3 illustrates the predictive *t* distributions for between-study heterogeneity in a variety of settings.

Table A.3.1: Medical area of respiratory diseases: Predictive *t* distributions for log (τ^2) in future metaanalyses, together with summary statistics for τ^2 on the untransformed scale. N denotes the number of meta-analyses of each type in the CDSR data set.

Table A.3.2: Medical area of cancer: Predictive *t* distributions for log (τ^2) in future meta-analyses, together with summary statistics for τ^2 on the untransformed scale. N denotes the number of metaanalyses of each type in the CDSR data set.

 $2(b)$

 $2(c)$

 0.01

 0.1

Between-study heterogeneity variance

 10

 0.001

 $3(b)$

Figure A.3: Examples of predictive *t* distributions for the between-study heterogeneity variance (plotted on the log scale). A vertical line highlights the probability of the variance being greater than 1.

A set of predictive inverse-gamma distributions for τ^2 in future meta-analyses, across settings defined by outcome type and type of intervention comparison, are summarized in Tables A.3.3, A.3.4 and A.3.5, together with summary statistics for τ^2 on the untransformed scale.

Table A.3.3: Medical area of respiratory disease: Predictive inverse-gamma distributions for τ^2 in future meta-analyses, together with summary statistics for τ^2 on the untransformed scale. N denotes the number of meta-analyses of each type in the CDSR data set.

Table A.3.4: Medical area of cancer: Predictive inverse-gamma distributions for τ^2 in future metaanalyses, together with summary statistics for τ^2 on the untransformed scale. N denotes the number of meta-analyses of each type in the CDSR data set.

Table A.3.5: Medical areas other than cancer and respiratory diseases: Predictive inverse-gamma distributions for τ^2 in future meta-analyses, together with summary statistics for τ^2 on the untransformed scale. N denotes the number of meta-analyses of each type in the CDSR data set.

A.4 WinBUGS code for the application to an example meta-analysis

Bayesian meta-analysis of data from studies evaluating the effectiveness of an exercise intervention for preventing depression [12], incorporating an informative prior for the between-study variance τ^2 .

Meta-analysis implementing a log-t prior for the between-study variance

```
model{ 
            for(i in 1:K){
                         MD[i]<-treat_mean[i]-ctrl_mean[i]
                         s[i]<-sqrt((((nT[i]-1)*treat_sd[i]*treat_sd[i])
                             +((nC[i]-1)*ctrl_sd[i]*ctrl_sd[i]))/(N[i]-2))
                         N[i]<-nC[i]+nT[i]
                         y[i]<-(MD[i]/s[i])*(1-(3/(4*N[i]-9)))
                         v[i]<-(N[i]/(nC[i]*nT[i]))+((y[i]*y[i])/(2*(N[i]-3.94)))
                         prec.y[i]<-1/v[i]
                         y[i]~dnorm(theta[i],prec.y[i]) # Normal distribution for observed study-level SMDs
                         theta[i]~dnorm(mu,invtausq) # Random-effects meta-analysis model
                      }
                         mu~dnorm(0,0.000001) # Vague prior for summary intervention effect (SMD scale)
                         #implement an informative prior for log(tau-squared)
                         invtausq<-1/tausq
                         tausq<-exp(log.tausq)
                         prior.prec<-1/(1.93*1.93)
                         log.tausq~dt(-3.85, prior.prec,5) 
                     # t(5df) prior with location parameter -3.85 and scale parameter 1.93
 }
```
Meta-analysis implementing an inverse-gamma prior for the between-study variance

model{

```
 for(i in 1:K){
             MD[i]<-treat_mean[i]-ctrl_mean[i]
             s[i]<-sqrt((((nT[i]-1)*treat_sd[i]*treat_sd[i])
                 +((nC[i]-1)*ctrl_sd[i]*ctrl_sd[i]))/(N[i]-2))
             N[i]<-nC[i]+nT[i]
             y[i]<-(MD[i]/s[i])*(1-(3/(4*N[i]-9)))
             v[i]<-(N[i]/(nC[i]*nT[i]))+((y[i]*y[i])/(2*(N[i]-3.94)))
             prec.y[i]<-1/v[i]
             y[i]~dnorm(theta[i],prec.y[i]) # Normal distribution for observed study-level SMDs
             theta[i]~dnorm(mu,invtausq) # Random-effects meta-analysis model
          }
             mu~dnorm(0,0.000001) # Vague prior for summary intervention effect (SMD scale)
             #implement an informative prior for tau-squared
             tausq<-1/invtausq
             invtausq~dgamma(0.46, 0.01)
                               # IG prior with shape parameter 0.46 and scale parameter 0.01
```
}

Depression data for 4 studies:

list(K=4,nT=c(11,43,11,14),nC=c(10,53,20,19),treat_mean=c(5,41.4,21.3,19.4), ctrl_mean=c(6.8,37.2,13.7,11.7),treat_sd=c(5,9.6,11.9,4),ctrl_sd=c(8.2,8.3,9.5,3.6))