Annals of Internal Medicine

Alternative Random Effects Estimators

Interactive Graphic to Accompany

'Random-effects Meta-analysis of Inconsistent Effects: A Time for Change'

Cornell et al, Ann Intern Med 2014

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Alternative Random Effects Estimators

This example is based upon simulated data.

Parameters were selected in order to generate a small group of heterogeneous studies. These are the conditions where the DL estimate has been shown to produce confidence bounds that are too narrow and p-values that are too small.

Specifically, individual study data were generated assuming a protective effect on the outcome under study (OR = 0.70), a large between study variance ($\tau^2 = 0.25$), and a small number of studies (k = 5).

Click on the links below to see how different pooling methods perform:

Example with 5 studies

Group of 5 Heterogeneous Studies: DerSimonian and Laird (DL) Estimator

Note the variability in the results from these 5 studies. Confidence bounds for studies 1 and 4 clearly don't overlap, while the CI for studies 3 and 5 barely overlap.

These 5 studies are quite heterogeneous.

Test of heterogeneity P < 0.001 $I^2 = 90.3\%$

Standard meta-analyses provide only fixed effect and the DL estimates.

Compare the DL estimator to alternatives:

Knapp-Hartung Profile Likelihood Bayesian

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Knapp-Hartung Estimator

The Knapp-Hartung approach assumes variances are estimated from small samples and makes small sample adjustments to the variance estimates.

For these 5 heterogeneous studies, the Knapp-Hartung confidence bounds are substantially wider than the DL confidence bounds.

Compare the DL estimator to other alternatives:

Profile Likelihood Bayesian

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Profile Likelihood Estimator

The profile likelihood method allows for asymmetric intervals and uncertainty in the estimation of between study variance.

For these 5 heterogeneous studies, the profile likelihood confidence bounds are substantially wider than the DL confidence bounds.

Compare the DL estimator to other alternatives:

<u>Bayesian</u> <u>Knapp-Hartung</u>

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Bayesian Estimator

The Bayesian model performs well with sparse data and few studies, though sensitivity analyses for the prior on tau are necessary.

For these 5 heterogeneous studies, the Bayesian confidence bounds are substantially wider than the DL confidence bounds.

Compare the DL estimator to other alternatives:

Knapp-Hartung Profile Likelihood All Three Alternative Estimators

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Group of 5 Heterogeneous Studies: DL and Three Alternate Estimators

The DL estimator has the narrowest confidence bounds among the 4 estimators and may underestimate the true uncertainty we have about the actual treatment effect.

The alternative estimators provide better and more reliable estimates of the between study variance when the number of studies is small and there is much heterogeneity among the trials.

Profile likelihood, Knapp-Hartung or Bayesian estimators are the better choice for summarizing the evidence in this case.

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