28 January 2025

Cochrane Methods

Demonstration of New Random-Effects Methods in RevMan (webinar 2)

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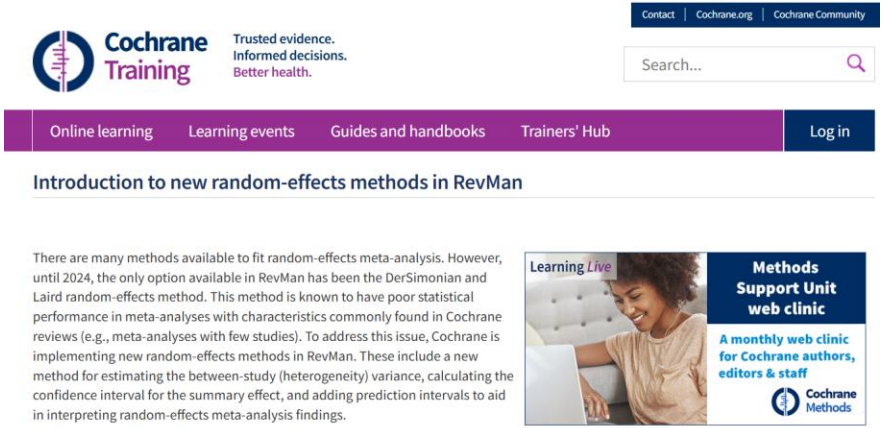
KNOWLEDGE TRANSLATION PROGRAM

UNITY HEALTH TORONTO

Webinar 1 (October 2024)



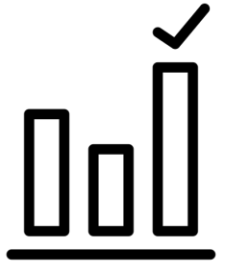
- Process used to develop the recommendations for the random-effects meta-analysis methods to be implemented in RevMan
- Outlined the new methods, along with the reasons for why the methods had been selected

Webinar 2: Objective

To demonstrate the new random-effects meta-analysis methods in RevMan

Outline

- Brief overview of the random-effects methods that are available in RevMan
  (as of the 23rd January 2025)
- Demonstration of the methods using RevMan (including what method to use in which scenario):
  - Confidence interval methods for the summary mean effect
  - Heterogeneity estimators (and confidence interval method)
  - Prediction interval
- Considerations for what to write in the protocol and review report
- Questions



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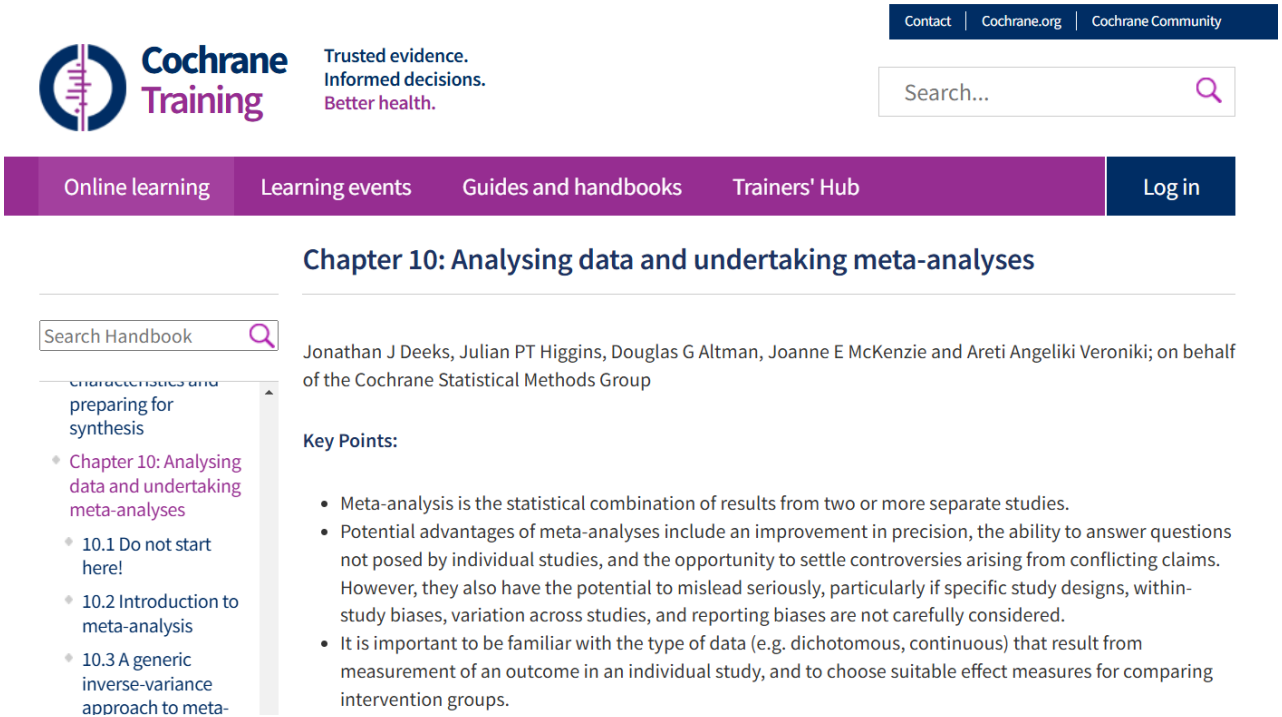
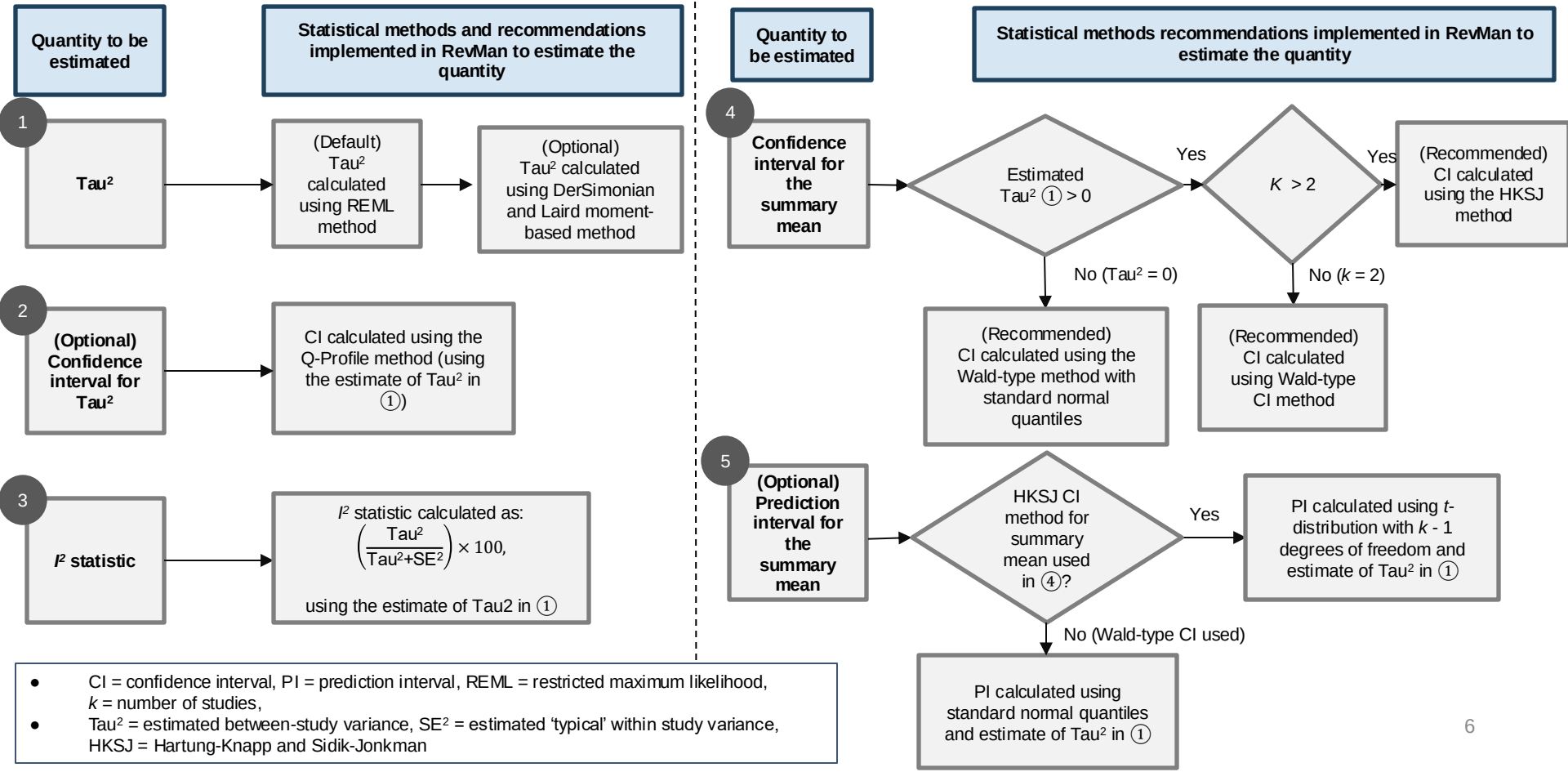
Cochrane Handbook: Chapter 10



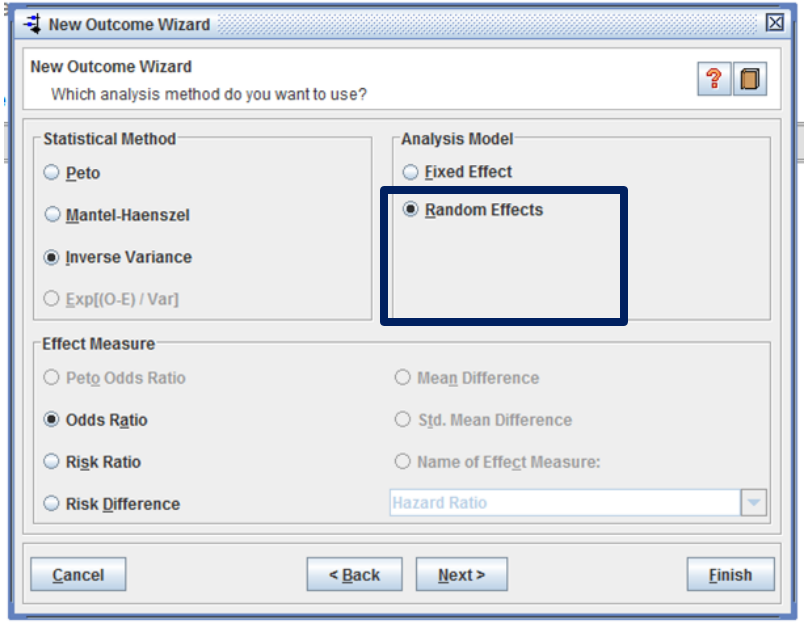
Random-effects methods implemented in RevMan



- CI = confidence interval, PI = prediction interval, REML = restricted maximum likelihood, *k* = number of studies,
- Tau² = estimated between-study variance, SE² = estimated 'typical' within study variance, HKSJ = Hartung-Knapp and Sidik-Jonkman

RevMan

Updating RevMan



Statistical method	Inverse variance
Effect measure	Odds ratio
Analysis model	Random effects
Heterogeneity estimator	○ DerSimonian and Laird (DL) ● Restricted Maximum Likelihood (REML)
	☐ Show confidence interval for heterogeneity estimator on forest plot
Totals	Totals and subtotals
	☑ Test for subgroup differences
	☐ Swap event and non-event
	☑ Show prediction interval for total on forest plot
Confidence / prediction intervals	95%
Summary effect CI method	● Wald-type (normal distribution) ○ Hartung and Knapp, Sidik and Jonkman (HKSJ) distribution

Dataset for Meta-Analysis

(Acupuncture for dysmenorrhoea – menstrual symptom score)

Study	mean.t	sd.t	n.t	mean.c	sd.c	n.c
Han 2012	1.7	1.15	80	3.03	1.71	40
Peng 2012	1.77	0.9	30	2.83	0.7	30
Qiao 2013	8.14	4.16	60	9.7	5.55	20
Ruan 2011	3.55	1.21	30	5.99	2.27	30
Wang 2014a	5.53	2.8	30	7.12	2.7	30
Zhang 2013a	2.29	1.33	30	8.21	3.87	30

Smith et al CDSR 2016: https://doi.org/10.1002/14651858.CD006930.pub3

Fitting a random-effects meta-analysis in RevMan

Inference on heterogeneity (τ^2):

- We will show the option to fit a DerSimonian-Laird (DL) (*standard option*)
- Indicate and highlight the use of the Restricted Maximum Likelihood (REML) method (*recommended*)

Inference on summary mean effect (μ):

- We will show the option to fit a Wald Type (WT) confidence interval (CI) or μ (*standard option*)
- Indicate and highlight the use of the Hartung-Knapp-Sidik-Jonkman (HKSJ) CI (*recommended when $\tau^2 > 0$ and # of studies >2*)

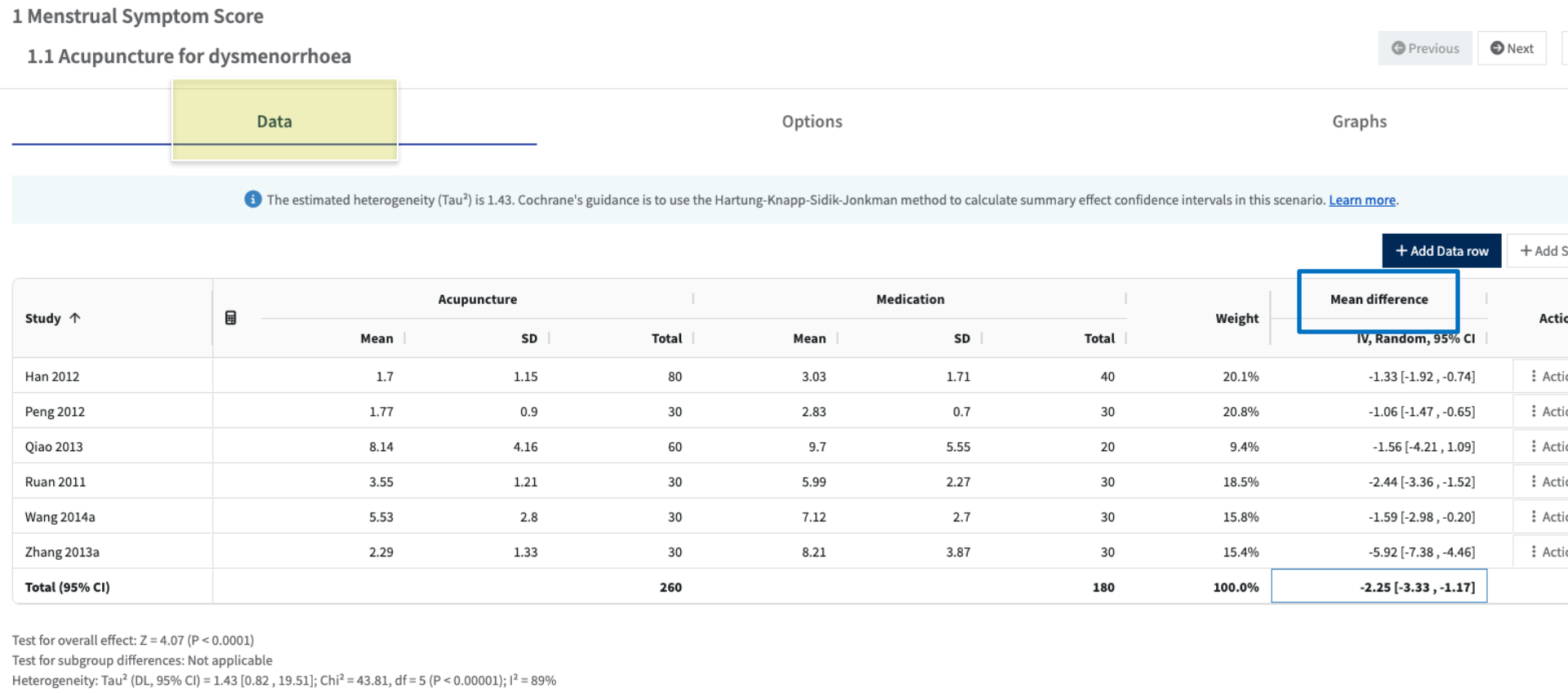
What was in RevMan up to now:

- DL and Wald Type (WT) methods

New methods:

- REML and HKSJ methods

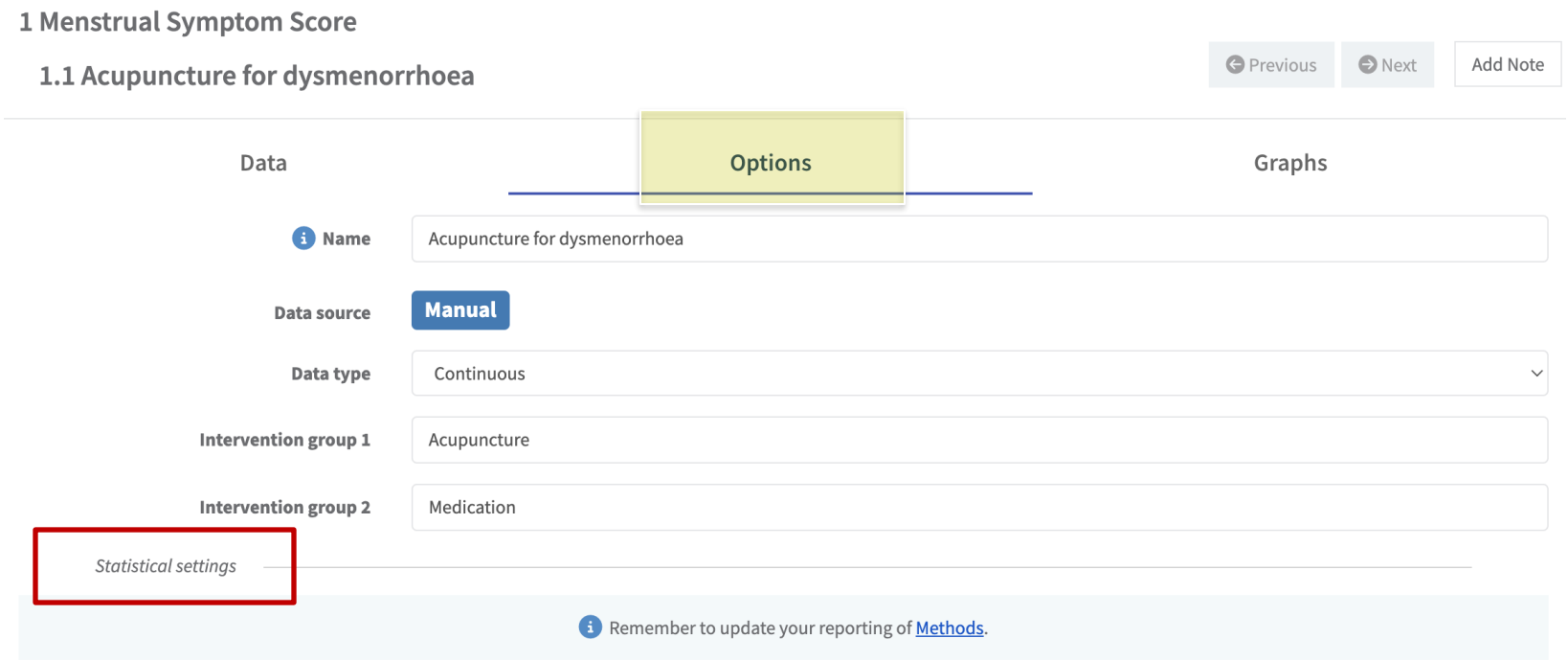
Enter Dataset in RevMan



Study	Acupuncture			Medication			Weight	Mean difference	Actio
	Mean	SD	Total	Mean	SD	Total		IV, Random, 95% CI	
Han 2012	1.7	1.15	80	3.03	1.71	40	20.1%	-1.33 [-1.92 , -0.74]	Actio
Peng 2012	1.77	0.9	30	2.83	0.7	30	20.8%	-1.06 [-1.47 , -0.65]	Actio
Qiao 2013	8.14	4.16	60	9.7	5.55	20	9.4%	-1.56 [-4.21 , 1.09]	Actio
Ruan 2011	3.55	1.21	30	5.99	2.27	30	18.5%	-2.44 [-3.36 , -1.52]	Actio
Wang 2014a	5.53	2.8	30	7.12	2.7	30	15.8%	-1.59 [-2.98 , -0.20]	Actio
Zhang 2013a	2.29	1.33	30	8.21	3.87	30	15.4%	-5.92 [-7.38 , -4.46]	Actio
Total (95% CI)			**260**			**180**	**100.0%**	**-2.25 [-3.33 , -1.17]**	

Test for overall effect: Z = 4.07 (P < 0.0001)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² (DL, 95% CI) = 1.43 [0.82 , 19.51]; Chi² = 43.81, df = 5 (P < 0.00001); I² = 89%

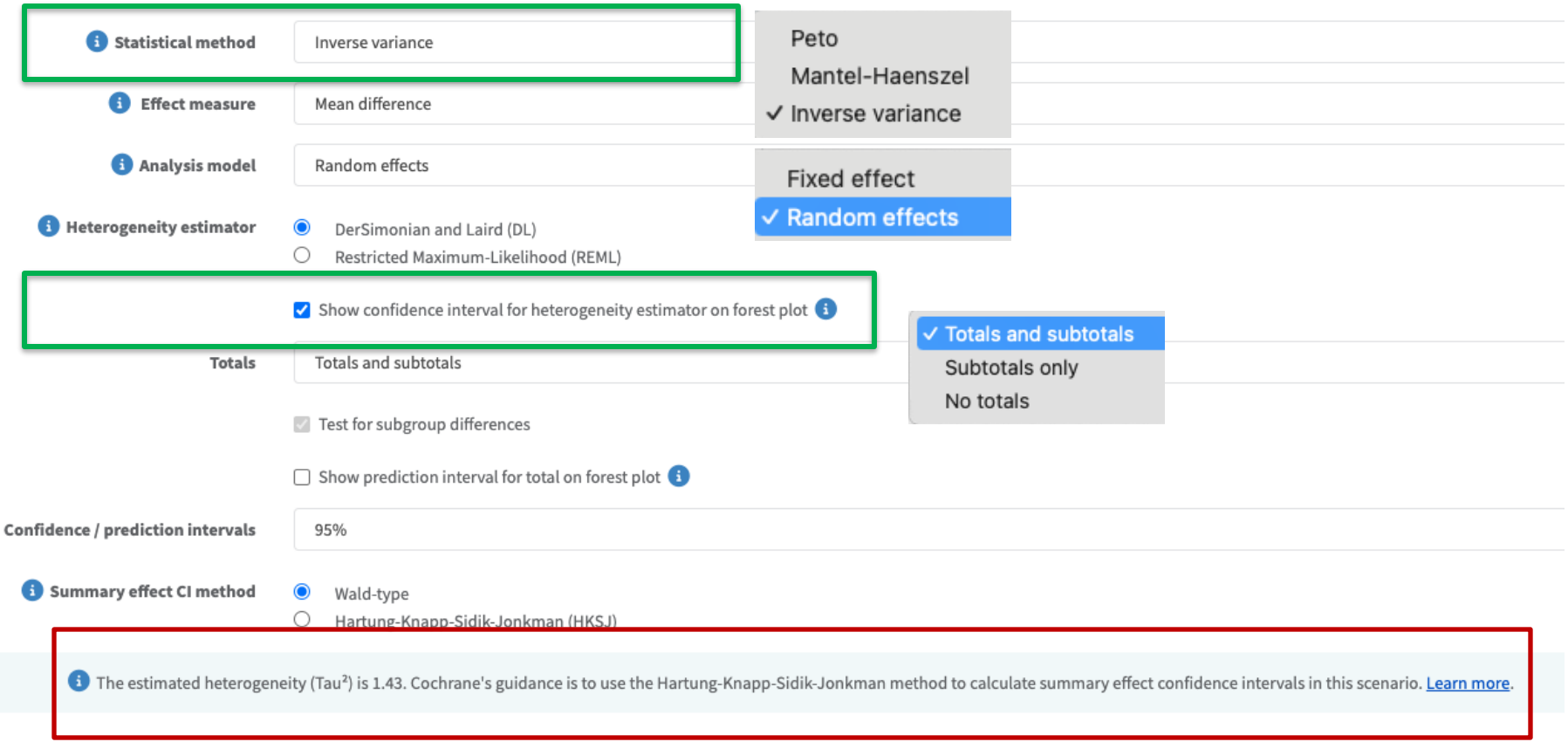
Choose Methods for a Random-Effects Analysis



Smith et al CDSR 2016: https://doi.org/10.1002/14651858.CD006930.pub3

Choose Methods for a Random-Effects Analysis

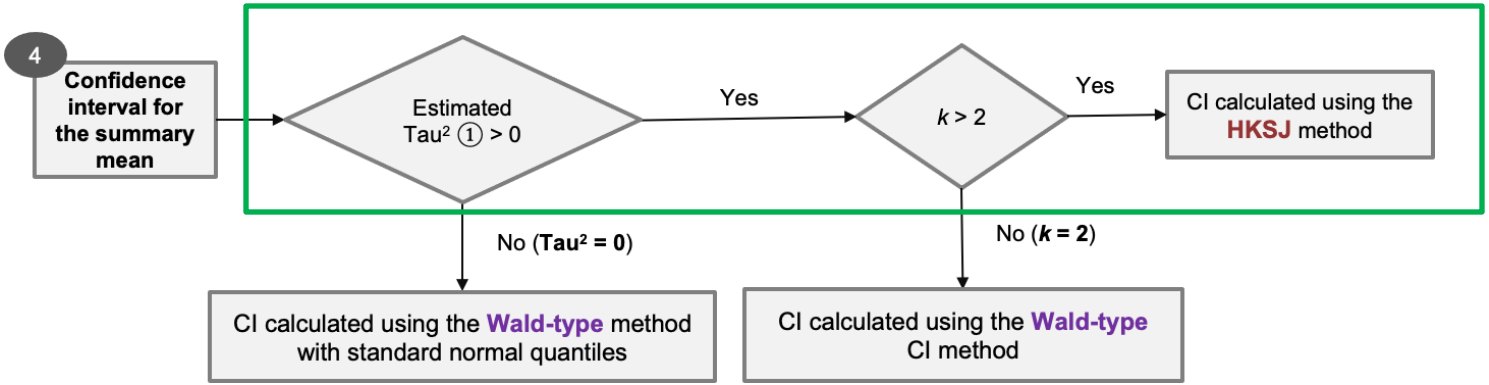
(DerSimonian and Laird [DL] and Wald-Type [WT])



Choose Methods for a Random-Effects Analysis

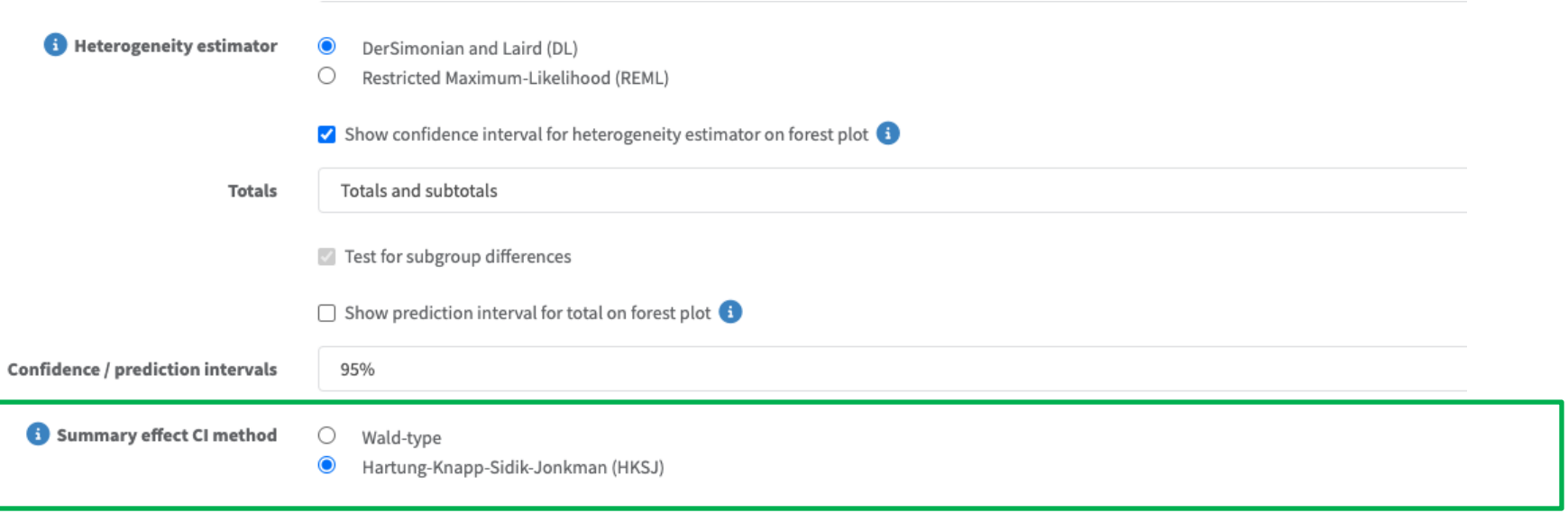
The estimated heterogeneity (Tau²) is 1.43. Cochrane's guidance is to use the Hartung-Knapp-Sidik-Jonkman method to calculate summary effect confidence intervals in this scenario. Learn more.

Quantity to be estimated	Statistical methods and decision rules implemented in RevMan to estimate the quantity



Choose Methods for a Random-Effects Analysis

Changing the option from Wald-Type to HKSJ – the pop-up disappears



Forest Plot – DL and HKSJ methods

1 Menstrual Symptom Score

1.1 Acupuncture for dysmenorrhoea

Previous | Next | Add Note

Data | Options | Graphs

Study or Subgroup	Acupuncture Mean	SD	Total	Medication Mean	SD	Total	Weight	Mean difference IV, Random, 95% CI
Han 2012	1.7	1.15	80	3.03	1.71	40	20.1%	-1.33 [-1.92 , -0.74]
Peng 2012	1.77	0.9	30	2.83	0.7	30	20.8%	-1.06 [-1.47 , -0.65]
Qiao 2013	8.14	4.16	60	9.7	5.55	20	9.4%	-1.56 [-4.21 , 1.09]
Ruan 2011	3.55	1.21	30	5.99	2.27	30	18.5%	-2.44 [-3.36 , -1.52]
Wang 2014a	5.53	2.8	30	7.12	2.7	30	15.8%	-1.59 [-2.98 , -0.20]
Zhang 2013a	2.29	1.33	30	8.21	3.87	30	15.4%	-5.92 [-7.38 , -4.46]
Total (HKSJ[a])			**260**			**180**	**100.0%**	**-2.25 [-4.12 , -0.37]**

Mean difference IV, Random, 95% CI

-10 -5 0 5 10

Favours [experimental] Favours [control]

Test for overall effect: Z = 4.07 (P < 0.0001)

Test for subgroup differences: Not applicable

Heterogeneity: Tau² (DL[b], 95% CI) = 1.43 [0.82 , 19.51]; Chi² = 43.81, df = 5 (P < 0.00001); I² = 89%

Footnotes

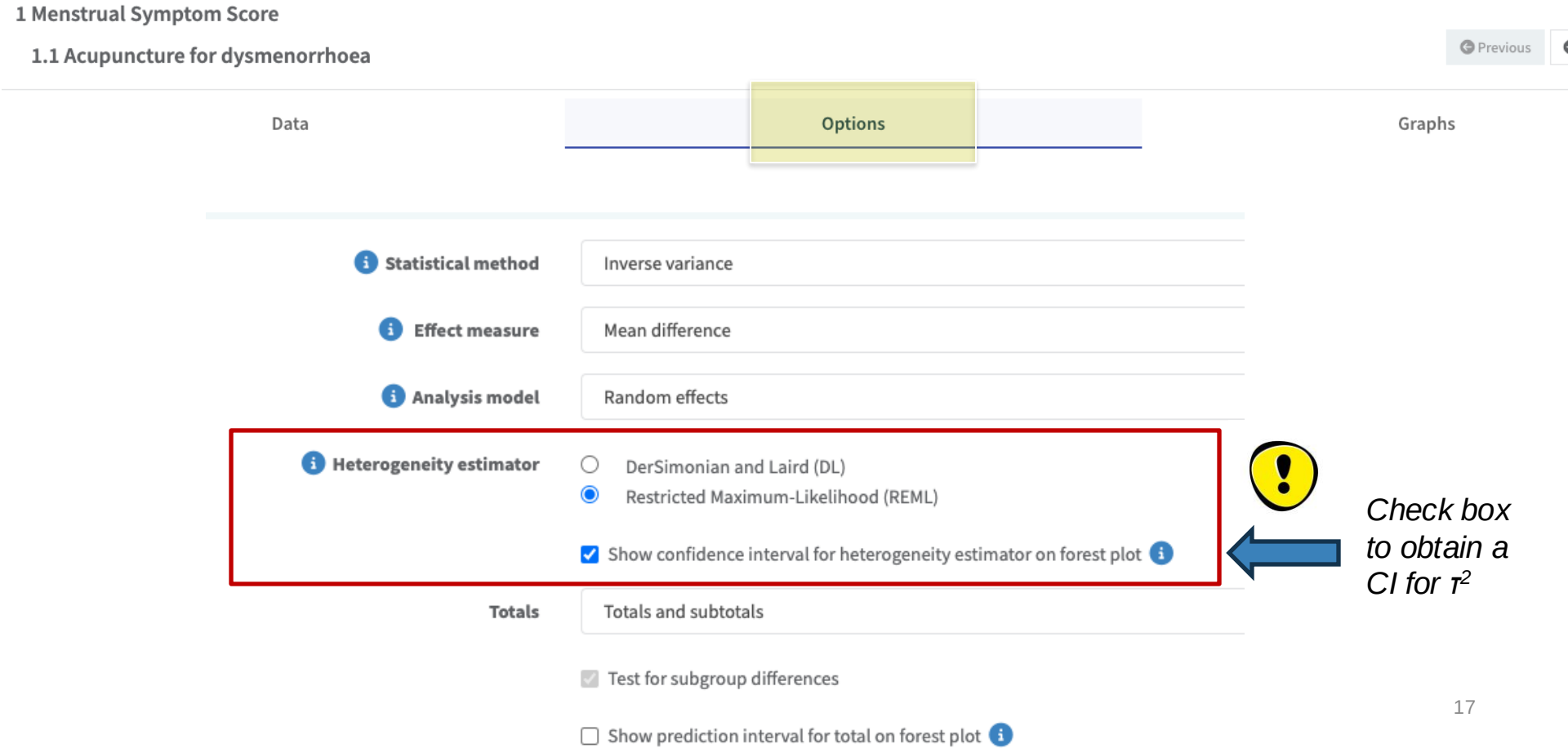
[a]CI calculated by Hartung-Knapp-Sidik-Jonkman method.

[b]Tau² calculated by DerSimonian and Laird method.

Recommended method for τ^2: REML!

Quantity to be estimated	Statistical methods and decision rules implemented in RevMan to estimate the quantity	
1 Tau²	(Default) Tau² calculated using REML method	(Optional) Tau² calculated using DerSimonian and Laird moment-based method
2 Confidence interval for Tau²	(Optional) CI calculated using the Q-Profile method (using the estimate of Tau² in ①)	
3 I^2 statistic	I^2 statistic calculated as: $\left(\frac{\text{Tau}^2}{\text{Tau}^2+\text{SE}^2}\right)\times 100,$ using the estimate of Tau2 in ①	

Choose method for τ^2



Check box to obtain a CI for τ^2

Forest Plot – REML and HKSJ methods

1 Menstrual Symptom Score

1.1 Acupuncture for dysmenorrhoea

Previous | Next | Add Note

Data | Options | Graphs

Study or Subgroup	Acupuncture Mean	SD	Total	Medication Mean	SD	Total	Weight	Mean difference IV, Random, 95% CI
Han 2012	1.7	1.15	80	3.03	1.71	40	18.7%	-1.33 [-1.92 , -0.74]
Peng 2012	1.77	0.9	30	2.83	0.7	30	19.0%	-1.06 [-1.47 , -0.65]
Qiao 2013	8.14	4.16	60	9.7	5.55	20	11.7%	-1.56 [-4.21 , 1.09]
Ruan 2011	3.55	1.21	30	5.99	2.27	30	17.9%	-2.44 [-3.36 , -1.52]
Wang 2014a	5.53	2.8	30	7.12	2.7	30	16.4%	-1.59 [-2.98 , -0.20]
Zhang 2013a	2.29	1.33	30	8.21	3.87	30	16.1%	-5.92 [-7.38 , -4.46]
Total (HKSJ[a])			**260**			**180**	**100.0%**	**-2.29 [-4.19 , -0.39]**

Mean difference IV, Random, 95% CI

-10 -5 0 5 10

Favours [experimental] Favours [control]

Test for overall effect: Z = 3.10 (P = 0.002)

Test for subgroup differences: Not applicable

Heterogeneity: Tau² (REML[b], 95% CI) = 2.82 [0.82 , 19.51]; Chi² = 43.81, df = 5 (P < 0.00001); I² = 94%

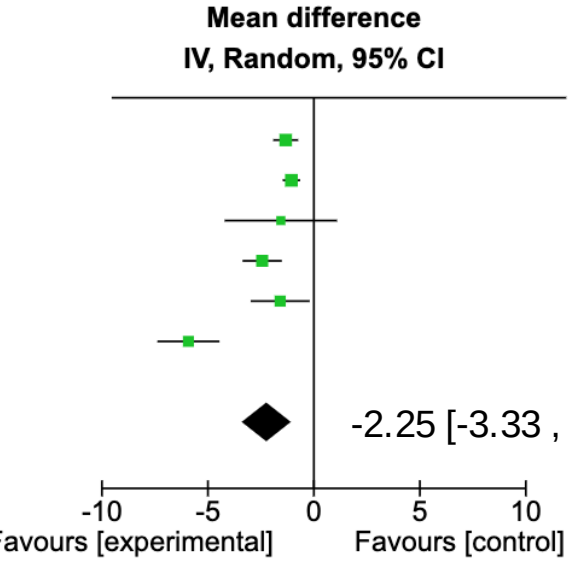
Footnotes

[a]CI calculated by Hartung-Knapp-Sidik-Jonkman method.

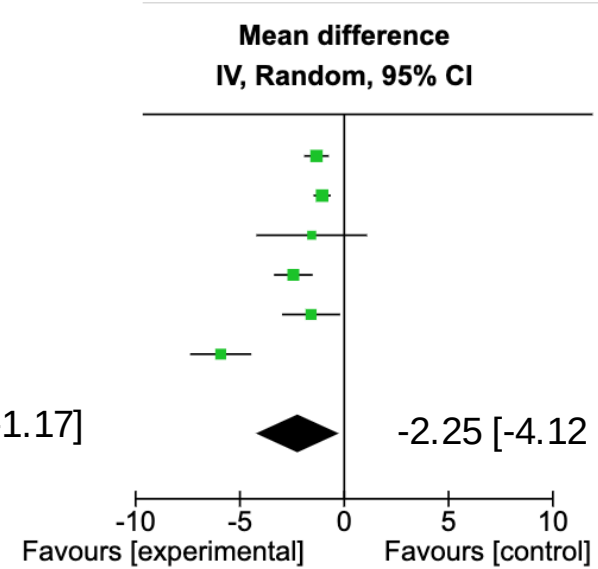
[b]Tau² calculated by Restricted Maximum-Likelihood method.

Forest plots across different choices of methods

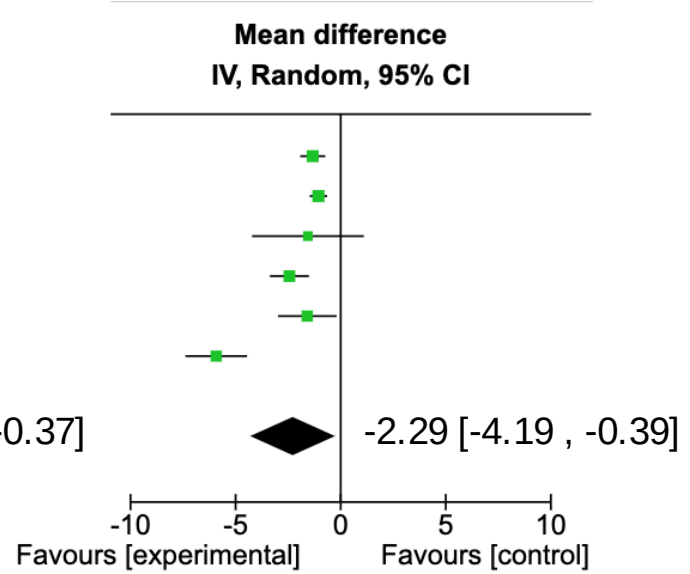
DL + WT



DL + HKSJ



REML + HKSJ



DL: $\hat{\tau}^2$= 1.43 ; I^2= 89%

REML: $\hat{\tau}^2$= 2.82 ; I^2= 94%

Confidence interval for Tau²

95% CI for $\hat{\tau}^2$: [0.82 19.51]

DL frequently under-estimates τ^2

(DerSimonian and Laird [DL] and Harung-Knapp-Sidik-Jonkman [HKSJ])

Data | Options | Graphs

The estimated heterogeneity (Tau^2) is 0.00. Cochrane's guidance is to use the Wald-type method to calculate summary effect confidence intervals in this scenario. Learn more.

+ Add Data row | + Add Subgroup

Study	Experimental		Control		Weight	Odds ratio	Action
	Events	Total	Events	Total		IV, Random, 95% CI	
Study A	9	345	40	342	29.7%	0.20 [0.10 , 0.42]	Action
Study B	3	58	5	59	7.4%	0.59 [0.13 , 2.59]	Action
Study C	7	286	24	290	22.0%	0.28 [0.12 , 0.66]	Action
Study D	4	200	13	200	12.5%	0.29 [0.09 , 0.92]	Action
Study E	12	116	22	116	28.4%	0.49 [0.23 , 1.05]	Action
Total (95% CI)	**35**	**1005**	**104**	**1007**	**100.0%**	**0.32 [0.19 , 0.54]**	

Test for overall effect: Z = 5.59 (P < 0.00001)
Test for subgroup differences: Not applicable
Heterogeneity: Tau^2 (DL, 95% CI) = 0.00 [0.00 , 1.30]; Chi^2 = 3.51, df = 4 (P = 0.48); I^2 = 0%

Data | Options | Graphs

The estimated heterogeneity (Tau^2) is 0.00. Cochrane's guidance is to use the Wald-type method to calculate summary effect confidence intervals in this scenario. Learn more.

Effect measure: Odds ratio

Analysis model: Random effects

Heterogeneity estimator:
- (•) DerSimonian and Laird (DL)
- ( ) Restricted Maximum-Likelihood (REML)

[x] Show confidence interval for heterogeneity estimator on forest plot

Totals: Totals and subtotals

[x] Test for subgroup differences

[ ] Swap event and non-event

[ ] Show prediction interval for total on forest plot

Confidence / prediction intervals: 95%

Summary effect CI method:
- ( ) Wald-type
- (•) Hartung-Knapp-Sidik-Jonkman (HKSJ)

The estimated heterogeneity (Tau^2) is 0.00. Cochrane's guidance is to use the Wald-type method to calculate summary effect confidence intervals in this scenario. Learn more.

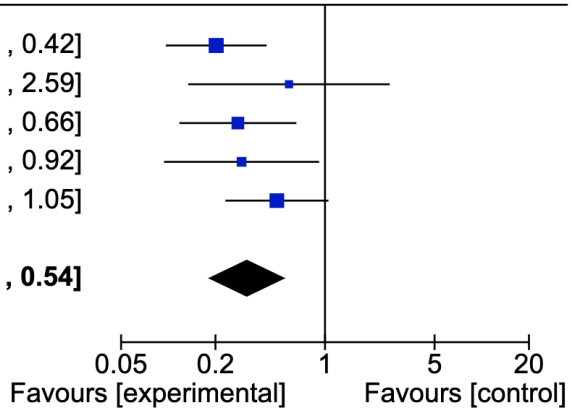
DL frequently under-estimates τ^2

Data | Options | Graphs

The estimated heterogeneity (Tau²) is 0.00. Cochrane's guidance is to use the Wald-type method to calculate summary effect confidence intervals in this scenario. Learn more.

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds ratio IV, Random, 95% CI
Study A	9	345	40	342	29.7%	0.20 [0.10 , 0.42]
Study B	3	58	5	59	7.4%	0.59 [0.13 , 2.59]
Study C	7	286	24	290	22.0%	0.28 [0.12 , 0.66]
Study D	4	200	13	200	12.5%	0.29 [0.09 , 0.92]
Study E	12	116	22	116	28.4%	0.49 [0.23 , 1.05]
Total (HKSJ[a])		**1005**		**1007**	**100.0%**	**0.32 [0.19 , 0.54]**
Total events:	35		104			

Odds ratio IV, Random, 95% CI



Test for overall effect: Z = 5.59 (P < 0.00001)

Test for subgroup differences: Not applicable

Heterogeneity: Tau² (DL[b], 95% CI) = 0.00 [0.00 , 1.30]; Chi² = 3.51, df = 4 (P = 0.48); I² = 0%

Footnotes

[a]CI calculated by Hartung-Knapp-Sidik-Jonkman method.

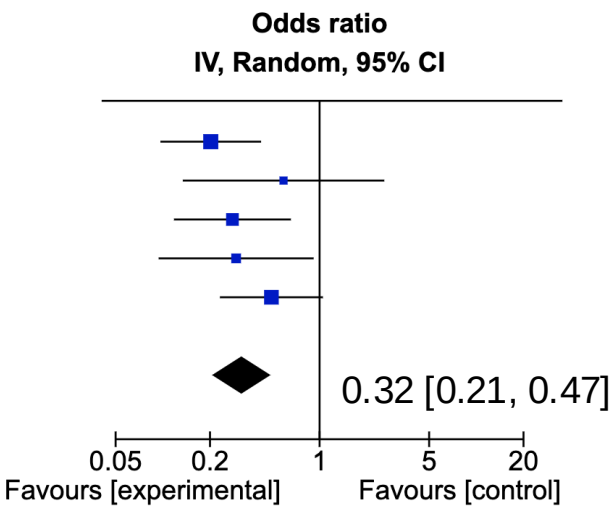
[b]Tau² calculated by DerSimonian and Laird method.

When $\tau^2=0$, use the Wald-type CI

Statistical method	Inverse variance
Effect measure	Odds ratio
Analysis model	Random effects
Heterogeneity estimator	(•) DerSimonian and Laird (DL) ( ) Restricted Maximum-Likelihood (REML)
	[x] Show confidence interval for heterogeneity estimator on forest plot
Totals	Totals and subtotals
	[x] Test for subgroup differences
	[ ] Swap event and non-event
	[ ] Show prediction interval for total on forest plot
Confidence / prediction intervals	95%
Summary effect CI method	(•) Wald-type ( ) Hartung-Knapp-Sidik-Jonkman (HKSJ)

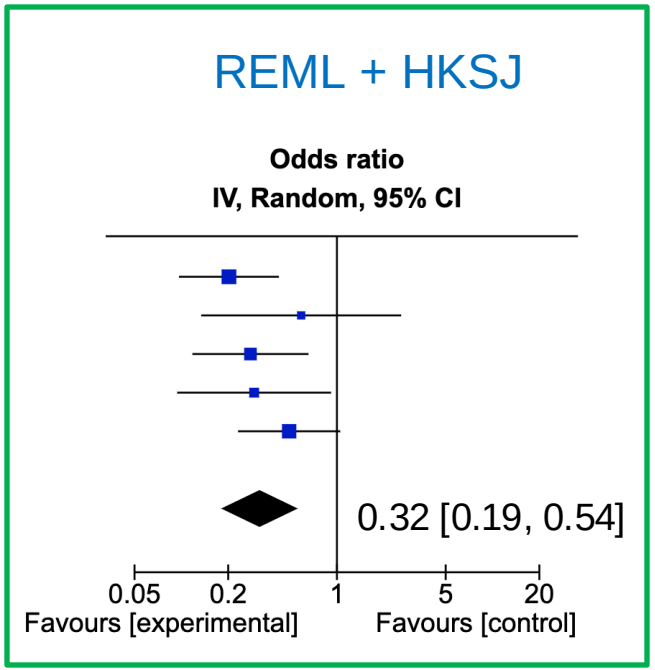
Remember: REML is recommended!

DL + WT



DL: $\hat{\tau}^2$= 0.000 ; I^2= 0%

REML + HKSJ



REML: $\hat{\tau}^2$= 0.02 ; I^2= 7%

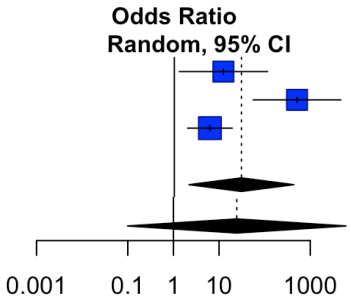
Confidence interval for Tau²

95% CI for $\hat{\tau}^2$: [0.00 1.30]

Choosing a method when the number of studies is k=3

Study	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Odds Ratio Random, 95% CI
Rabe 1985	53	54	46	55	31.2%	10.37 [1.27; 84.97]
Christensen 1984	63	64	10	65	31.3%	346.50 [42.98; 2793.60]
Ho 1983	48	53	37	58	37.4%	5.45 [1.88; 15.81]
Random effects model (Wald Type)		**171**		**178**	**100.0%**	**24.49 [2.02; 297.47]**
Random effects model (HKSJ)						**24.49 [0.10; 6035.38]**

Heterogeneity: $Tau^2 = 4.0438$; $Chi^2 = 12.10$, df = 2 ($P < 0.01$)



$\hat{\tau}^2 = 4.044$

Kapp et al CDSR 2010: https://pubmed.ncbi.nlm.nih.gov/20166091/

Data | Options | Graphs

The estimated heterogeneity (Tau^2) is 4.04. Cochrane's guidance is to use the Hartung-Knapp-Sidik-Jonkman method to calculate summary effect confidence intervals in this scenario. Learn more.

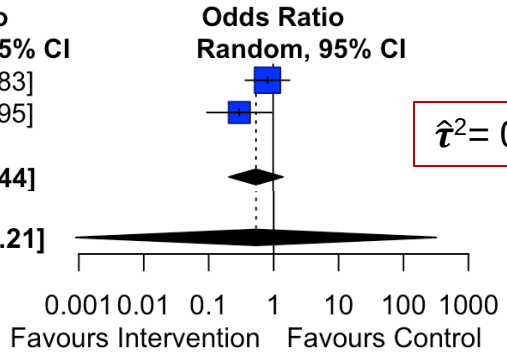
+ Add Data row | + Add Subgrou

Study	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds ratio IV, Random, 95% CI	Action
Christensen 1984	63	64	10	65	31.3%	346.50 [42.98 , 2793.60]	Action
Ho 1983	48	53	37	58	37.4%	5.45 [1.88 , 15.81]	Action
Rabe 1985	53	54	46	55	31.2%	10.37 [1.27 , 84.97]	Action
Total (95% CI)	**164**	**171**	**93**	**178**	**100.0%**	**24.49 [2.02 , 297.47]**	

Choosing a method when the number of studies is k=2

Study	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Odds Ratio Random, 95% CI
Caramez 1998	23	46	27	49	59.1%	0.81 [0.36; 1.83]
Silverman 2005	4	117	11	102	40.9%	0.29 [0.09; 0.95]
Random effects model (Wald Type)		**163**		**151**	**100.0%**	**0.54 [0.20; 1.44]**
Random effects model (HKSJ)						**0.54 [0.00; 320.21]**

Heterogeneity: $Tau^2 = 0.2585$; $Chi^2 = 1.98$, df = 1 (P = 0.16); $I^2 = 49\%$

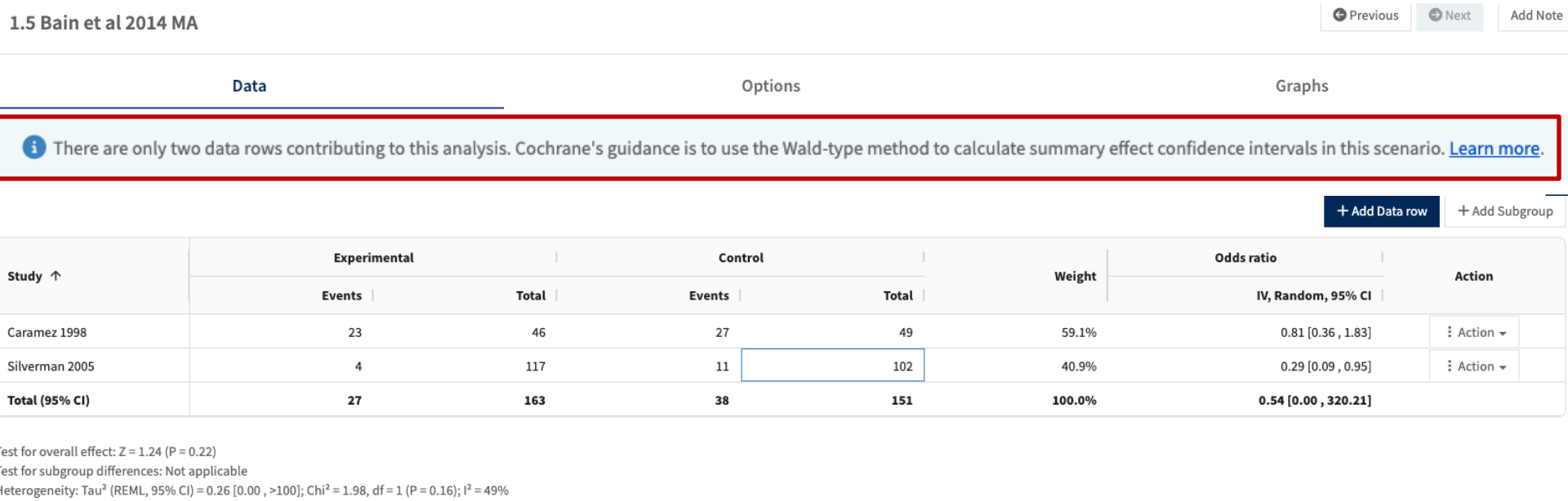


$\hat{\tau}^2 = 0.259$

Bain et al CDSR 2014: https://pubmed.ncbi.nlm.nih.gov/25331331/

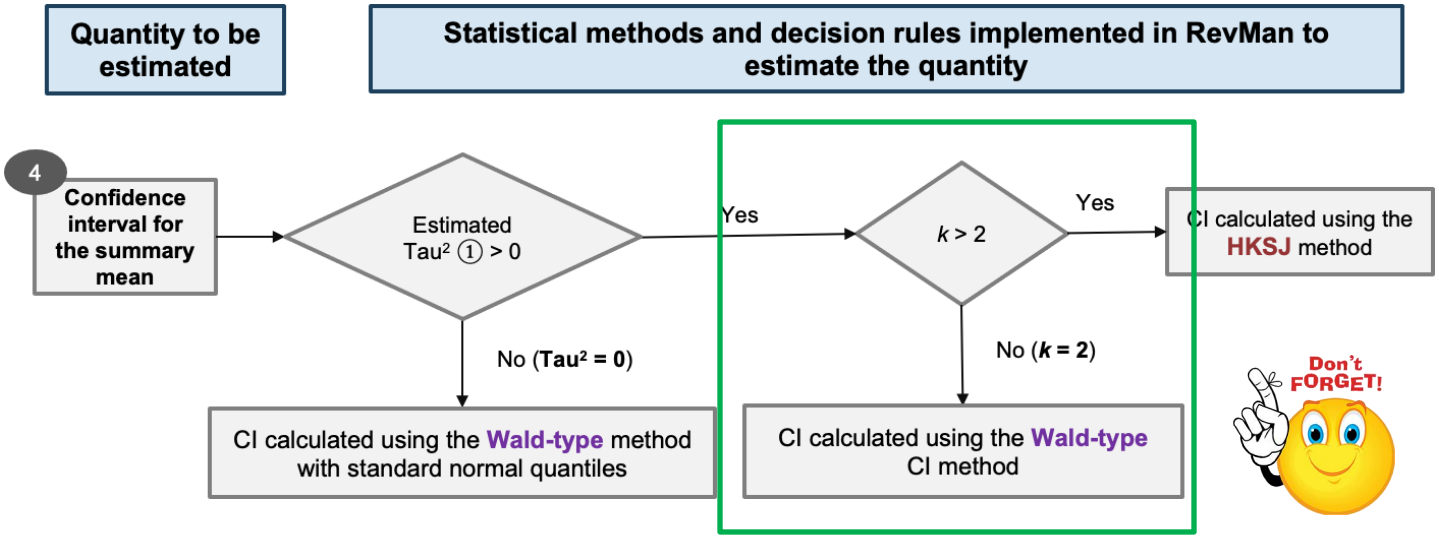
Remember: In the case of 2 studies, the HKSJ can lead to overly conservative results!

Choosing a method when the number of studies is k=2



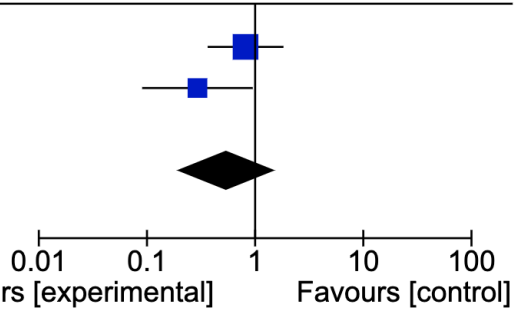
Choosing a method when the number of studies is k=2

There are only two data rows contributing to this analysis. Cochrane's guidance is to use the Wald-type method to calculate summary effect confidence intervals in this scenario. Learn more.



Choose WT when the number of studies is k=2

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds ratio IV, Random, 95% CI
Caramez 1998	23	46	27	49	59.1%	0.81 [0.36 , 1.83]
Silverman 2005	4	117	11	102	40.9%	0.29 [0.09 , 0.95]
Total (Wald[a])		**163**		**151**	**100.0%**	**0.54 [0.20 , 1.44]**
Total events:	27		38			



Test for overall effect: Z = 1.24 (P = 0.22)

Test for subgroup differences: Not applicable

Heterogeneity: Tau² (REML[b], 95% CI) = 0.26 [0.00 , >100]; Chi² = 1.98, df = 1 (P = 0.16); I² = 49%

Footnotes

[a]CI calculated by Wald-type method.

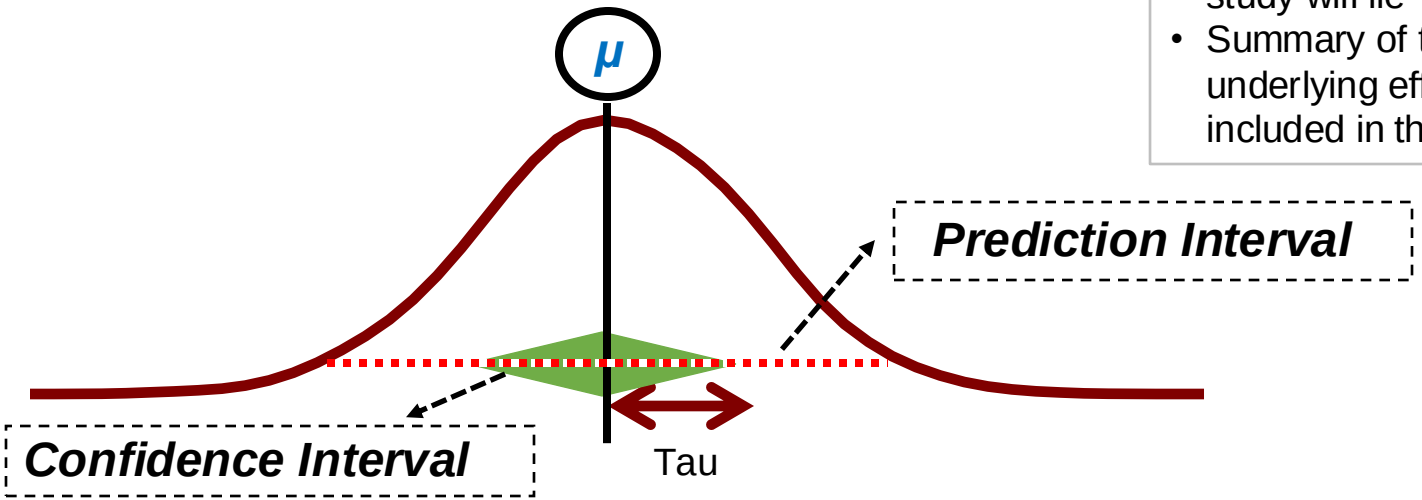
[b]Tau² calculated by Restricted Maximum-Likelihood method.

Prediction Intervals for random-effects meta-analysis

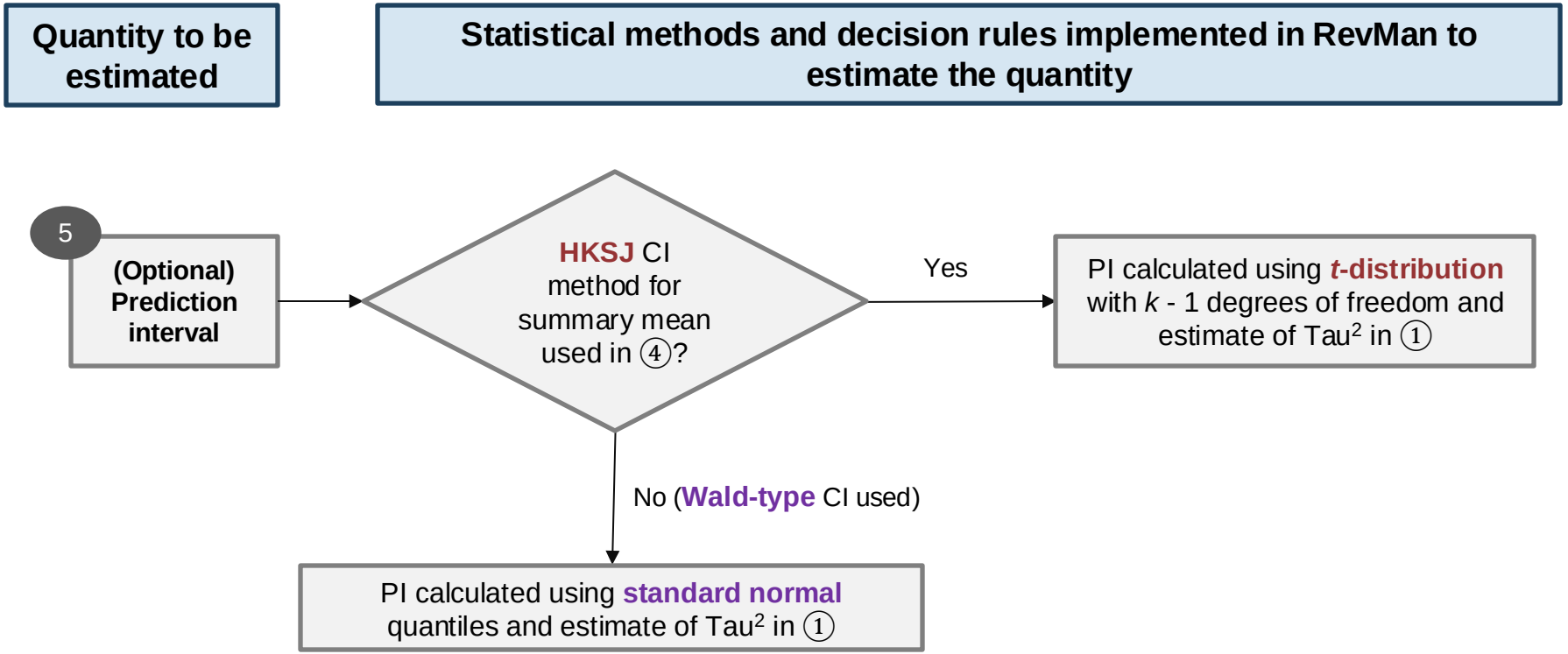
A 95% prediction interval where approximately 95% of the true treatment effects are predicted to fall is:

$$\hat{\mu} \pm 1.96 \times Tau$$

- The interval within which we expect that the effect of a future study will lie
- Summary of the spread of underlying effects in the studies included in the meta-analysis

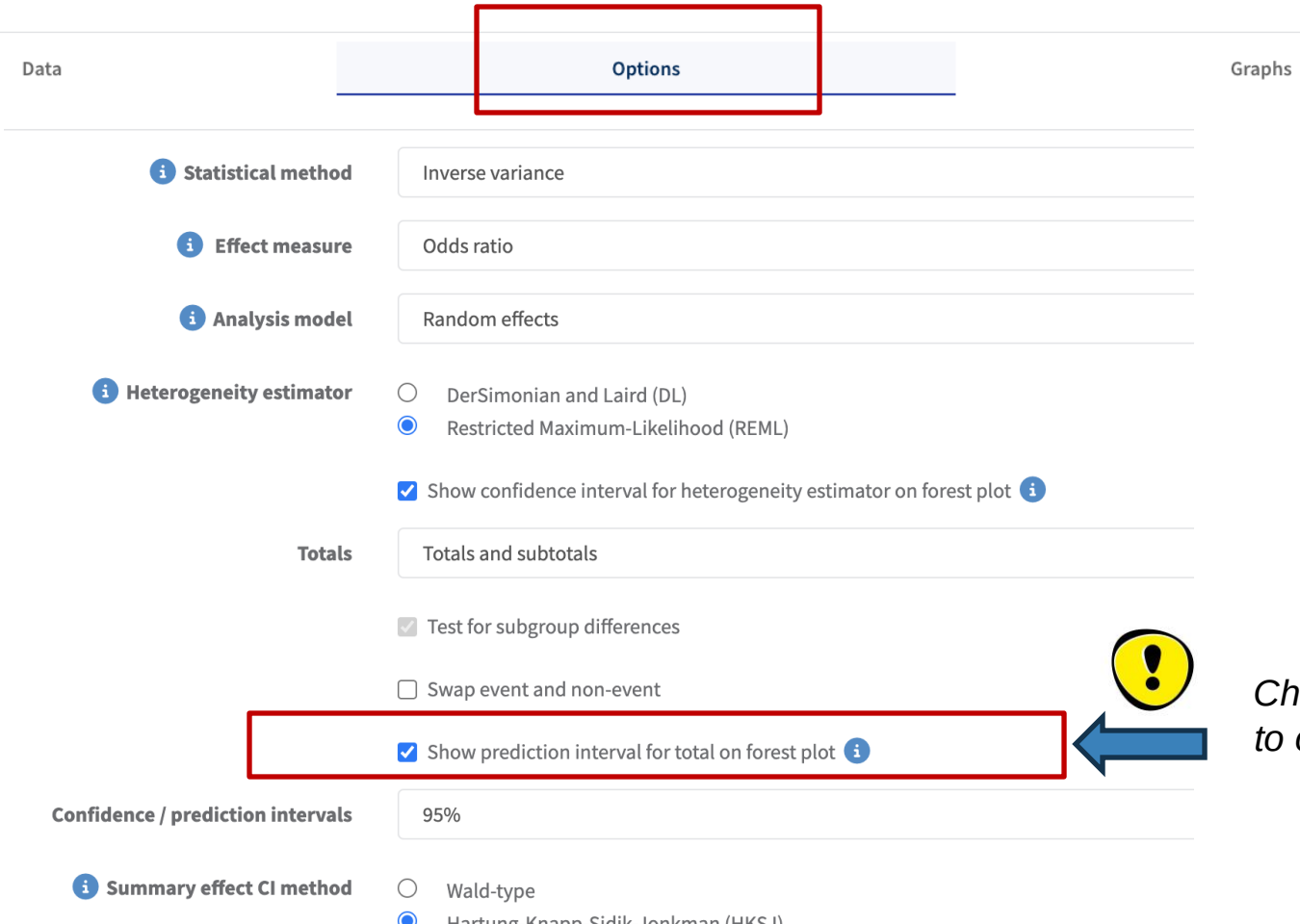


Prediction intervals for random-effects meta-analysis



- CI = confidence interval, PI = prediction interval, REML = restricted maximum likelihood, *k* = number of studies,
- Tau^2 = estimated between-study variance, SE^2 = estimated 'typical' within study variance, HKSJ = Hartung-Knapp and Sidik-Jonkman

Prediction Interval

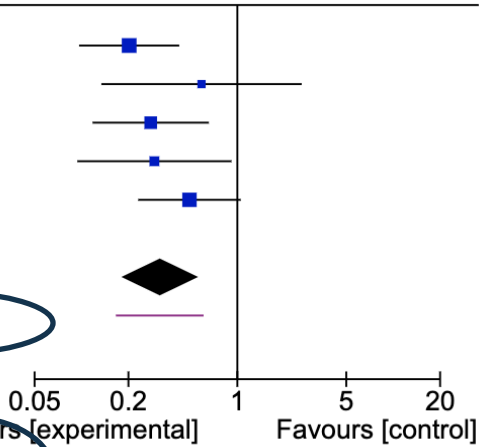


Check box to obtain a PI

Prediction Interval

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds ratio IV, Random, 95% CI
Study A	9	345	40	342	29.0%	0.20 [0.10 , 0.42]
Study B	3	58	5	59	7.9%	0.59 [0.13 , 2.59]
Study C	7	286	24	290	22.2%	0.28 [0.12 , 0.66]
Study D	4	200	13	200	13.1%	0.29 [0.09 , 0.92]
Study E	12	116	22	116	27.9%	0.49 [0.23 , 1.05]
Total (HKSJ[a])		**1005**		**1007**	**100.0%**	**0.32 [0.19 , 0.54]**
95% prediction interval						[0.17 , 0.61]
Total events:	35		104			

Odds ratio
IV, Random, 95% CI



Test for overall effect: Z = 5.32 (P < 0.00001)

Test for subgroup differences: Not applicable

Heterogeneity: Tau² (REML[b], 95% CI) = 0.02 [0.00 , 1.30]; Chi² = 3.51, df = 4 (P = 0.48); I² = 7%

Footnotes

[a]CI calculated by Hartung-Knapp-Sidik-Jonkman method.

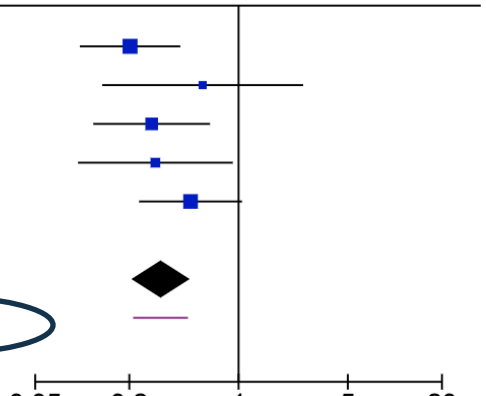
[b]Tau² calculated by Restricted Maximum-Likelihood method.

PI is equal to CI when $\tau^2=0$

PI is different between WT and HKSJ, as it is based on the standard normal and t-distribution, respectively

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds ratio IV, Random, 95% CI
Study A	9	345	40	342	29.7%	0.20 [0.10 , 0.42]
Study B	3	58	5	59	7.4%	0.59 [0.13 , 2.59]
Study C	7	286	24	290	22.0%	0.28 [0.12 , 0.66]
Study D	4	200	13	200	12.5%	0.29 [0.09 , 0.92]
Study E	12	116	22	116	28.4%	0.49 [0.23 , 1.05]
Total (Wald[a])		**1005**		**1007**	**100.0%**	**0.32 [0.21 , 0.47]**
95% prediction interval						[0.21 , 0.47]
Total events:	35		104			

Odds ratio IV, Random, 95% CI



Test for overall effect: Z = 5.59 (P < 0.00001)

Test for subgroup differences: Not applicable

Heterogeneity: Tau² (DL[b], 95% CI) = 0.00 [0.00 , 1.30]; Chi² = 3.51, df = 4 (P = 0.48); I² = 0%

Footnotes

[a]CI calculated by Wald-type method.

[b]Tau² calculated by DerSimonian and Laird method.

Considerations for what to write in the protocol and review report

- Be aware of the random-effects methods and the recommendations for what method to use in which scenario when planning the statistical methods in your review → see Chapter 10 of the Cochrane Handbook
- PRISMA 2020 helpful for guiding what to report

PRISMA 2020 – item 13d

Describe any methods used to synthesise results and provide a rationale for the choice(s). If meta-analysis was performed, **describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used**

Essential elements (some):

If meta-analysis was done, specify:

- the meta-analysis model (fixed-effect, fixed effects, or random-effects) and provide rationale for the selected model
- the method used (such as Mantel-Haenszel, inverse-variance)
- any methods used to identify or quantify statistical heterogeneity (such as visual inspection of results, a formal statistical test for heterogeneity, heterogeneity variance (τ^2), inconsistency (such as I^2), and prediction intervals

PRISMA 2020 – item 13d (continued)

Describe any methods used to synthesise results and provide a rationale for the choice(s). If meta-analysis was performed, **describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used**

Essential elements (some):

If a random-effects meta-analysis model was used, specify:

- the between-study (heterogeneity) variance estimator used (such as DerSimonian and Laird, restricted maximum likelihood (REML))
- the method used to calculate the confidence interval for the summary effect (such as Wald-type confidence interval, Hartung-Knapp-Sidik-Jonkman)

An example (protocol)

“We will combine estimates of treatment effect using inverse variance weighting, using a random-effects model. We will use a random-effects model since we expect there will be clinical diversity in … The Restricted Maximum Likelihood (REML) method will used to estimate between-trial variance, and a confidence interval will for the heterogeneity estimate will be calculated. The Hartung-Knapp-Sidik-Jonkman method will be used to calculate a confidence interval for the meta-analysis effect estimate when there are at least 3 studies and the estimate of heterogeneity is greater than zero. In other scenarios (i.e. 2 studies, or where the estimate of heterogeneity is equal to zero) we will use the Wald-type method. We will calculate prediction intervals to provide a predicted range for the true treatment effect in an individual study.”

An example (protocol)

"We will combine estimates of treatment effect using inverse variance weighting, using a random-effects model. We will use a random-effects model since we expect there will be clinical diversity in … The **Restricted Maximum Likelihood (REML) method will used to estimate between-trial variance**, and a confidence interval will for the heterogeneity estimate will be calculated. The Hartung-Knapp-Sidik-Jonkman method will be used to calculate a confidence interval for the meta-analysis effect estimate when there are at least 3 studies and the estimate of heterogeneity is greater than zero. In other scenarios (i.e. 2 studies, or where the estimate of heterogeneity is equal to zero) we will use the Wald-type method. We will calculate prediction intervals to provide a predicted range for the true treatment effect in an individual study when there are at least 10 studies."

Method used to calculate the between-study (heterogeneity) variance (Tau2)

An example (protocol)

"We will combine estimates of treatment effect using inverse variance weighting, using a random-effects model. We will use a random-effects model since we expect there will be clinical diversity in … The Restricted Maximum Likelihood (REML) method will used to estimate between-trial variance, and **a confidence interval will for the heterogeneity estimate will be calculated**. The Hartung-Knapp-Sidik-Jonkman method will be used to calculate a confidence interval for the meta-analysis effect estimate when there are at least 3 studies and the estimate of heterogeneity is greater than zero. In other scenarios (i.e. 2 studies, or where the estimate of heterogeneity is equal to zero) we will use the Wald-type method. We will calculate prediction intervals to provide a predicted range for the true treatment effect in an individual study when there are at least 10 studies."

A confidence interval for Tau2 will be calculated (note that the specific method has not been described)

An example (protocol)

"We will combine estimates of treatment effect using inverse variance weighting, using a random-effects model. We will use a random-effects model since we expect there will be clinical diversity in … The Restricted Maximum Likelihood (REML) estimator will used to estimate between-trial variance, and a confidence interval will for the heterogeneity estimate will be calculated. **The Hartung-Knapp-Sidik-Jonkman method will be used to calculate a confidence interval for the meta-analysis effect estimate when there are at least 3 studies and the estimate of heterogeneity is greater than zero. In other scenarios (i.e. 2 studies, or where the estimate of heterogeneity is equal to zero) we will use the Wald-type method.** We will calculate prediction intervals to provide a predicted range for the true treatment effect in an individual study when there are at least 10 studies."

Decision rules to determine what confidence interval method for the summary mean will be used in which scenario

An example (protocol)

"We will combine estimates of treatment effect using inverse variance weighting, using a random-effects model. We will use a random-effects model since we expect there will be clinical diversity in … The Restricted Maximum Likelihood (REML) estimator will used to estimate between-trial variance, and a confidence interval will for the heterogeneity estimate will be calculated. The Hartung-Knapp-Sidik-Jonkman method will be used to calculate a confidence interval for the meta-analysis effect estimate when there are at least 3 studies and the estimate of heterogeneity is greater than zero. In other scenarios (i.e. 2 studies, or where the estimate of heterogeneity is equal to zero) we will use the Wald-type method. **We will calculate prediction intervals to provide a predicted range for the true treatment effect in an individual study when there are at least 10 studies**."

A prediction interval will be calculated, along with the scenario when it will be calculated

Be sure to avoid …

- Fitting multiple meta-analysis methods and reporting the results that are most favourable

THANK YOU

Cochrane Methods
Statistics

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