Cochrane Colloquium 2023 Workshop

MetaInsight Worksheet

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This practical uses the latest version of the CRSU app *MetaInsight v5.1.0* which can be accessed from https://crsu.shinyapps.io/MetaInsight.

MetaInsight is a web-based app for conducting network meta-analysis (NMA) for binary and continuous outcomes using fixed- or random-effects models. It may also be used to facilitate sensitivity analysis via exclusion of studies as this practical will demonstrate.

After completing this practical, you will be able to:

- Upload data into MetaInsight
- Perform both frequentist and Bayesian NMA in MetaInsight and interpret the results
- Examine the influence on the results when studies are excluded in a sensitivity analysis

Set-up

For this practical we will use the illustrative example in the NMA chapter of the Cochrane Handbook[1] of interventions for heavy menstrual bleeding by Middleton et al[2]. Interest lies in which of the four interventions is most effective for reducing patient dissatisfaction at 12 months (primary outcome of study). Responses of 'very satisfied' or 'satisfied' were taken as a positive response, and 'very dissatisfied' or 'dissatisfied', along with 'not sure' or 'uncertain', were taken as a negative response. The data should be available from the 'materials' section of the CRSU webpage (where this worksheet is available), but is also shown below.

NMA data from Middleton et al[2] showing number of people who were 'dissatisfied' at 12 months from undergoing an intervention for heavy menstrual bleeding.						
Study	Intervention	# of Events	# of people	Intervention	# of Events	# of people
Brun	1st gen	3	16	2nd gen	2	27
Busfield	Mirena	2	37	2nd gen	9	39
Cooper_a	1st gen	5	82	2nd gen	11	154
Cooper_b	1st gen	1	101	2nd gen	3	201
Cooper_c	1st gen	33	128	2nd gen	29	121
Crosignani_a	1st gen	5	38	Hysterectomy	2	39
Crosignani_b	1st gen	2	35	Mirena	5	34
Dickersin	1st gen	13	107	Hysterectomy	7	103
Duleba	1st gen	10	72	2nd gen	16	156
Dwyer	1st gen	19	99	Hysterectomy	6	97
Hawe	1st gen	3	33	2nd gen	4	37
Meyer	1st gen	1	120	2nd gen	5	125
O'Connor	1st gen	7	106	Hysterectomy	2	50
Pellicano	1st gen	14	38	2nd gen	7	37
Perino	1st gen	5	55	2nd gen	3	56
Pinion	1st gen	13	104	Hysterectomy	4	93
Shaw	Mirena	5	25	2nd gen	5	28
Soysal_a	1st gen	19	48	2nd gen	15	45
Soysal_b	Mirena	10	32	2nd gen	9	35
Van Zon-Rabelink	1st gen	13	58	2nd gen	15	75

1st gen: 'First generation' endometrial destruction techniques; 2nd gen: 'Second generation' endometrial destruction techniques

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a) **Download** the exercise dataset from the CRSU webpage
b) Go to **MetaInsight** (https://crsu.shinyapps.io/MetaInsight)
c) Make sure to select that we're using **binary** data on the home page
d) **Load** the exercise data into MetaInsight using the 'Load Data' tab (Note: this data is in 'wide format', but MetaInsight can also take data in 'long format' – descriptions of these formats are on the 'Load Data' tab of MetaInsight) (Note: before uploading your own data, example datasets can be viewed which are inbuilt and can allow users to explore MetaInsight without having their own data).
e) Make sure that the **reference treatment** is '1st_gen'
f) Go to the 'Data Analysis' tab and make sure that the outcome is set to '**OR**', small outcomes are set to '**desirable**', and the model is set to '**random effect'**.

1. Explore the network (Data Summary Tab)

a) What is the total number of participants in the network?
b) How many pairwise comparisons are there and how many have direct data?
c) Which comparison has the greatest number of trials with direct data?
d) Which comparison (with more than one trial) had all studies favouring the same intervention?

2. Run a random-effects frequentist NMA (Frequentist analysis tab), with the outcome still in terms of odds ratios

a) Complete the table below

Intervention	Relative-effect vs 1st gen (OR)	95% CI
2nd gen		
Hysterectomy		
Mirena		

b) Compared to first-generation endometrial destruction techniques, which intervention is effective at reducing patient dissatisfaction at the 5% significance level? Interpret the respective odds ratio (If your screen is not showing the entire forest plot, you may need to download the plot).
c) What is the relative odds ratio for patient dissatisfaction (95% CI) of second-generation endometrial destruction techniques versus (with reference to) Mirena? (Tip: for the lower triangle of a matrix, values are read as column vs row).
d) Is there any evidence of inconsistency across the network?

3. Run a random-effects Bayesian NMA (Bayesian analysis tab), with the outcome in terms of risk ratios

a) What is the estimated between-study standard deviation (95% CrI) (Note: this is assumed to be the same across all comparisons)?

b) What is the relative risk ratio for patient dissatisfaction (95% CrI) of Hysterectomy versus (with reference to) Mirena? (Tip: for the lower triangle of a matrix, values are read as column vs row).

c) Which intervention is considered the 'best'? What evidence are you using to decide this?

d) Why might you take care when reporting the result of which intervention was 'best'? (Tip: consider the Radial SUCRA plot).

Optional advanced questions for Bayesian analysis. If you don't wish to tackle these, please proceed to question 4.

e) Run a node-split model. How many comparisons had both direct and indirect evidence? Interpret the results?

f) Tab '3e. Bayesian result details' contains direct R output from running the {gemtc} package with default settings of 4 chains, 5,000 simulated iterations for burn-in and 20,000 for model results. Compare the output here with the forest plot on tab '3a': which estimates are being used in the forest plot? (Tip: tab 3e displays results at Log Risk Ratio)

g) Tab '3f Deviance report' presents three diagnostic plots of the model fit in terms of the individual data points. Have a go at interpreting the plots, using the descriptions underneath each plot to help.

4. Using the same set-up for question 3, run a sensitivity analysis with studies 'Busfield', 'Crosignani_b', 'Dickersin', 'Shaw' and 'Soysal_b' removed

a) How many interventions and pairwise comparisons with direct data have been removed from the network?

b) Compare the forest plots, are there any notable differences?

c) Consider the Radial SUCRA plots, what would you say the most noticeable change is?

References

[1] Chaimani A, Caldwell DM, Li T, Higgins JPT, Salanti G. Chapter 11: Undertaking network meta-analyses. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). *Cochrane Handbook for Systematic Reviews of Interventions* version 6.4 (updated August 2023). Cochrane, 2023.

[2] Middleton LJ, Champaneria R, Daniels JP, Bhattacharya S, Cooper KG, Hilken NH, O'Donovan P, Gannon M, Gray R, Khan KS; International Heavy Menstrual Bleeding Individual Patient Data Meta-analysis Collaborative Group; Abbott J, Barrington J, Bhattacharya S, Bongers MY, Brun JL, Busfield R, Sowter M, Clark TJ, Cooper J, Cooper KG, Corson SL, Dickersin K, Dwyer N, Gannon M, Hawe J, Hurskainen R, Meyer WR, O'Connor H, Pinion S, Sambrook AM, Tam WH, van Zon-Rabelink IA, Zupi E. Hysterectomy, endometrial destruction, and levonorgestrel releasing intrauterine system (Mirena) for heavy menstrual bleeding: systematic review and meta-analysis of data from individual patients. BMJ. 2010 Aug 16;341:c3929. doi: 10.1136/bmj.c3929. PMID: 20713583; PMCID: PMC2922496.