

Confidence in network meta-analysis (CINeMA): an example from network meta-analysis of economic evaluation study

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Outline

- Example from network meta-analysis of economic evaluation study
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 - Objective
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- Data preparation for indirectness
- Dataset and steps for running the dataset on CINeMA software online

1. An example from economic evaluation study

- Title: A network meta-analysis of cost utility analysis of oral anticoagulants for stroke prevention in atrial fibrillation patients
- Oral anticoagulants can be used for stroke prevention in atrial fibrillation patients:
 - Standard: warfarin
 - New: direct oral anticoagulants (DOACs) including dabigatran, rivaroxaban, apixaban, and edoxaban
- Objective: to determine which oral anticoagulant is being the most cost-effective for stroke prevention in atrial fibrillation patients by pooling and ranking the incremental net benefit (INBs)
- PICOS:
 - Patients (P): AF patients
 - Intervention (I): DOACs
 - Comparator (C): Warfarin
 - Outcomes (O): economic outcomes such as: cost, incremental cost, quality adjusted life years (QALYs), incremental QALYs, incremental cost-effectiveness ratio (ICER), incremental net benefit (INB)
 - Study design (S): economic evaluation
- The inputs of risk of bias/within-study bias and indirectness are required before assessing it through the online CInEMA software.

2. Data preparation for risk of bias

- Risk of bias assessment in this cost-utility study was used ECOBIAS checklist (1).
- ECOBIAS (1) checklist consists of two parts and 22 items. Each item is graded as yes, no, partly, unclear or not applicable (NA).
- To obtain data on within study bias, each item or question in ECOBIAS checklist was scored 0 for yes answer, 2 for partly or NA answer, and 3 for no answer, followed with totalling and averaging for all 22 items.
- Afterward, the level risk of bias was categorized into 1, 2, and 3 for low, moderate, and high risk of bias, respectively.
- Those steps were applied for each included study.
- The risk of bias data was then prepared in the CSV file.

2. Data preparation for risk of bias

No	Question	Harrington A, et al	sc_3	Lopez, et al	sc_4
1	Narrow perspective bias	no	2	no	2
2	Inefficient comparator bias*	yes	0	yes	0
3	Cost measurement omission bias	yes	0	yes	0
4	Intermittent data collection bias	yes	0	yes	0
5	Invalid valuation bias	yes	0	yes	0
6	Ordinal ICER bias	yes	0	yes	0
7	Double-counting bias	no	2	no	2
8	Inappropriate discounting bias	no	2	NA	2
9	Limited sensitivity analysis bias§	yes	0	yes	0
10	Sponsor bias	yes	0	yes	0
11	Reporting and dissemination bias	no	2	no	2
12	Structural assumptions bias	yes	0	yes	0
13	No treatment comparator bias*	yes	0	yes	0
14	Wrong model bias	yes	0	yes	0
15	Limited time horizon bias	yes	0	yes	0
16	Bias related to data identification	yes	0	yes	0
17	Bias related to baseline data	yes	0	yes	0
18	Bias related to treatment effects	yes	0	yes	0
19	Bias related to quality- of-life weights (utilities)	yes	0	yes	0
20	Non-transparent data incorporation bias	yes	0	yes	0
21	Limited to scope bias§	yes	0	yes	0
22	Bias related to internal consistency	no	2	no	2

NO=2

NA=2

YES=0

1. SCORING for each item

2. TOTAL for 22 items

3. AVERAGE for 22 items

4. CATEGORIZE into 3 categories

Risk of bias category:
 0.0 - ≤0.5: Low (1)
 >0.5 - 1.5: Moderate (2)
 ≥1.5: High (3)

5. PREPARE data in csv file

3. Data preparation for indirectness: Population

- Firstly, to obtain data on indirectness, population, intervention, and outcomes of each study involved were identified and scored.
- For the population, age and stroke risk of the patients modelled in the cost-utility study were identified, then scored 1 (yes) if the patient was 65 years of age and had a stroke risk usually expressed by a score of CHADS2 or CHA2DS2Vasc. Given a value of 2 (partly) if only one of the age or stroke risk was identified and given a value of 3 (no) if both age and stroke risk data were not identified.

Table identification and score for population (P)

Age (≥ 65 years)	Risk of stroke (CHADS2 or CHA2DS2VASc score)	Score population	
√	√	yes	1
√	-	partly	2
-	√	partly	2
-	-	no	3

3. Data preparation for indirectness: Intervention

- For the intervention, the anticoagulant drugs evaluated by each study involved were identified both as a comparator and as an intervention, then given a score of 1 (yes) if the comparator and the intervention used were oral anticoagulants to be analysed, either warfarin or DOACs including dabigatran , rivaroxaban, apixaban, and edoxaban.
- A score of 2 (partly) was given if only one of the anticoagulant drugs matches the anticoagulant drug that you want to analyse, and answer no with a value of 3 was given if both the comparator and the intervention were not oral anticoagulant drug.

Table identification and score for intervention (I)

Comparator (VKA or Warfarin)	Intervention (Dabigatran, Rivaroxaban, Apixaban, Edoxaban)	Score intervention	
√	√	yes	1
√	-	partly	2
-	√	partly	2
-	-	no	3

3. Data preparation for indirectness: Outcomes

- For outcomes, all economic outcomes and scenarios that were applied to each cost-utility study involved were identified. Next, a yes answer was given with a score of 1 if economic outcomes and scenarios 1 to 4 were identified from each of the studies involved.
- Graded 2 (partly) if economic outcomes and scenario 5 were identified and score of 3 (no) was applied if economic outcomes and scenarios could not be identified from each of the included studies.

Table identification and score for outcomes (O)

Economic outcomes (cost, QALYs, ICER, INB)	Scenario 1	Scenario 2	Scenario 3	Scenario 4	Scenario 5	Score outcomes	
√	√					yes	1
√		√				yes	1
√			√			yes	1
√				√		yes	1
√					√	partly	2
-	-	-	-	-	-	no	3

3. Data preparation for indirectness

- After the identification and scoring for population, interventions, and outcomes of each of the studies involved were obtained, then summed and averaged and followed by indirectness categorization, which is categorized as low (1) if it has a value of 1.5, moderate if it has a value of 1.6-2.5 and high if it has a value > 2.5 .
- The indirectness data was then prepared in the CSV file.

3. Data preparation for indirectness

ID	Author	Population (P)				Intervention (I)				Outcomes (O)			
		Age	Risks of stroke	Score population		Comparator	Intervention	Score intervention		Outcomes	Scenario	Score outcomes	
3	Harrington AR, 2013	70 yr	CHADS2 score ≥ 1	yes	1	Warfarin	Apixaban 5mg	yes	1	Costs, QALY, ICER and their SD.	3	yes	1
4	Lopez-Lopez JA, 2017	70 yr	CHADS2 score ≥ 1	yes	1	Warfarin	Apixaban 5mg	yes	1	Costs, QALY, INB and their 95% CI	2	yes	1

YES=1

YES=1

YES=1

2. TOTAL for PIO scores

3. AVERAGE for PIO scores

4. CATEGORIZE into 3 categories

5. PREPARE data in csv file

Category Indirectness:
 0.0 - <1.5 : Low (1)
 >1.6 - 2.5 : Moderate (2)
 >2.5 : High (3)

4.A. Example of dataset

Table Example of dataset in csv format to be uploaded to CINeMA software online

id	t1	t2	effect	se	ROB*	Indirectness**
1	1	2	16526.95	4830.789	1	1
2	1	2	9983.959	8542.313	1	1
3	1	2	13914.8	11629.04	1	1
4	1	2	14959.51	6238.74	1	1
5	1	2	24004.35	477174.9	1	1
6	1	2	837.6614	337430.9	1	1
7	1	2	6502.011	337467.9	1	1
8	1	2	2570.438	3378.664	2	2
etc						

Abbreviations: se, standard error; t1, comparator; t2, intervention.

*ROB category: 1=Low; 2=Moderate; 3=High risk of bias

**Indirectness category: 1=Low; 2=Moderate; 3= High indirectness

4.B. Steps for running the dataset on CINeMA software online

- Open the link to the CINeMA: <https://cinema.ispm.unibe.ch/>
- Upload the dataset in csv file to the CINeMA software online
- Set:
 - Analysis model: random effect
 - Effect measure: mean difference
 - Select intervention comparisons for evaluation:
 - Intervention: select all
 - Comparisons: containing any of the above intervention
- Proceed
- Results
 - 6 domains: within study bias, reporting bias, indirectness, imprecision, heterogeneity, and incoherence
 - Report
- Save

Thank you for your attention