Network Meta-Analysis for Comparative Effectiveness Research

Joseph C. Cappelleri, Ph.D., M.P.H.

Pfizer Inc

Groton, CT

e-mail:joseph.c.cappelleri@pfizer.com

Oral presentation at the 19th Annual Biopharmaceutical Applied Statistics Symposium, Savannah, Georgia, November 5-9, 2012


THE LATEST RESEARCH SHOWS THAT WE REALLY SHOULD DO SOMETHING WITH ALL THIS RESEARCH

Outline

- Introduce comparative effectiveness research (CER)
- Explain the concepts in network meta-analysis
- Describe the assumptions of network meta-analysis
- Illustrate its application

Comparative Effectiveness Research and the 2009 Stimulus Bill

- 2009 American Recovery and Reinvestment Act, or "Stimulus Bill," provided $1.1 billion to support comparative effectiveness research:
  - $300 million to Agency for Healthcare Research and Quality
  - $300 million to the National Institutes of Health
  - $400 million to the Office of the Secretary of Health and Human Services (HHS)

- To evaluate the relative effectiveness of different health care services and treatment options

- To encourage the development and use of clinical registries, clinical data networks, and other forms of electronic data to generate outcomes data

- $1.5 million to support an Institute of Medicine study – to make recommendations to HHS Secretary to establish national priorities on comparative effectiveness research

What is Comparative Effectiveness Research?

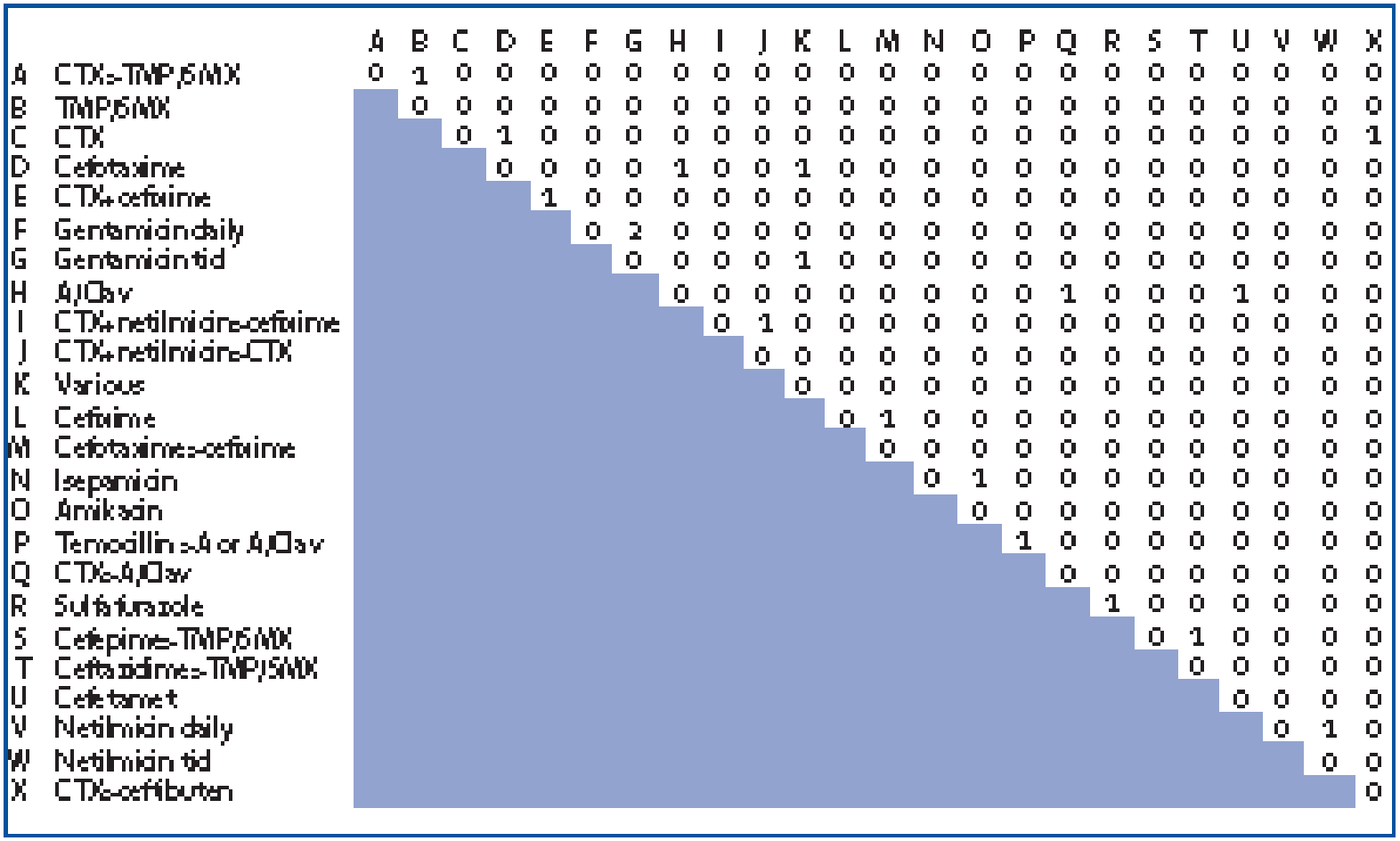
- A type of systematic review
  - Synthesizes available scientific evidence on a specific topic
- Expands the scope of a typical systematic review
  - Goes beyond the effectiveness of a single intervention
  - Compares the relative benefits and harms among a range of available treatments or interventions for a given condition
- Parallels decisions facing clinicians, patients, and policy makers who must choose among a variety of alternatives in making diagnostic, treatment, and health-care delivery decisions
  - Three key elements: relevance, timeliness, transparency

Motivation for Comparative Effectiveness Research

- Decision makers are often faced with more than one viable treatment option

- Consider a 55-year-old woman whose bone scan shows greatly decreased bone density
  - Should she take drugs, increase vitamin D and calcium intake, focus on weight-bearing exercises, or watchfully wait?
  - Drugs are effective but limited information on their long-term effects
  - Some women will develop kidney stones after calcium intake
  - No precise formulation on effective exercise prescription

Regimes for the Treatment of Children with Acute Pyelonephritis



Despite mounting evidence from 18 trials spanning and evaluating 24 regimens, evidence is available only on a few direct comparisons.

Source: Ioannidis 2006

Four Principal Steps in Comparative Effectiveness Reviews

- Step 1: Formulate the problem
- Step 2: Define the studies and search strategies
- Step 3: Evaluate applicability of studies
- Step 4: Assess benefits and harms of treatments

Examples of Comparative Effectiveness Research

- Oral Medications for Type 2 Diabetes Mellitus
  - Annals of Internal Medicine 2007; 147:386-399
  - Includes indirect treatment comparisons
- Diagnosis and Treatment of Erectile Dysfunction
  - Tsertsvadze et al. AHRQ Publication No. 08(09)-E016, Rockville, MD: Agency for Healthcare Research and Quality. May 2009
- Treatment of Overactive Bladder in Women
  - Hartmann et al. Evidence Report/Technology Assessment No. 187, AHRQ Publication No. 09-E017. Rockville, MD: Agency for Healthcare Research and Quality. August 2009.

Quantitative Synthesis: Meta-Analysis

- Integral part of comparative effectiveness research and reviews
- Should be performed to address pre-specified questions, following PRISMA guidelines (Liberati et al. 2009)
- Clinical and methodological diversity, as well as statistical heterogeneity, should be considered before pooling studies to calculate summary effect

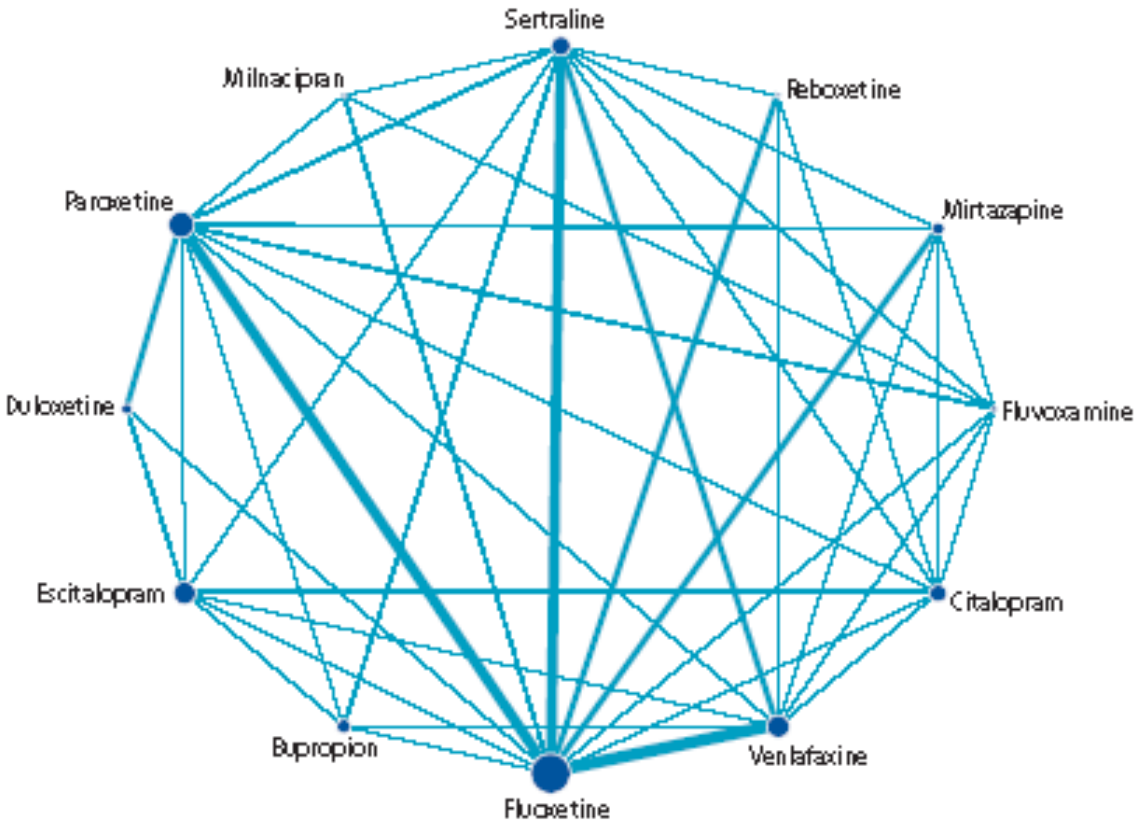
How Does CER Meta-Analysis Differ from Traditional Meta-Analysis?

- CER meta-analysis is more expansive
  - Standard meta-analysis is subsumed within CER meta-analysis
- CER meta-analysis involves all relevant treatments (even if not directly compared), not just one particular treatment or class of treatments
- CER meta-analysis considers wider net of evidence, not just from a particular type of study design and not just efficacy
- CER meta-analysis places even greater emphasis on heterogeneity, Bayesian methods, and updating results

Network Meta-Analysis

- Network meta-analysis is a key part of CER
  - Needed when there's little or no evidence from head-to-head (direct) comparisons
  - Interventions of interest with a common comparator
- Network meta-analysis enables us to combine trials involving different sets of treatments, using a network of evidence, within a single analysis
- This integrated and unified analysis incorporates all direct and indirect comparative evidence about treatments

Network of 12 Antidepressants



19 meta-analyses published in the last two years

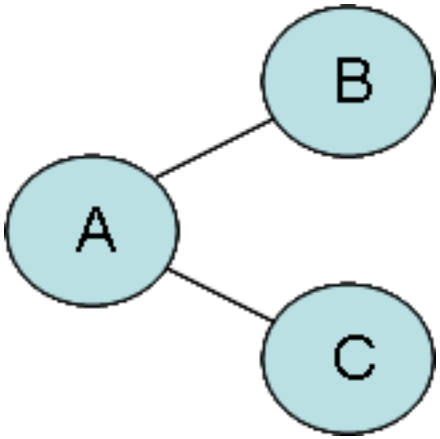
The main drawback is that meta-analysis focuses on comparing only two alternatives at a time, leading to a plethora of analyses to interpret with no quantitatively rigorous methods for integrating them

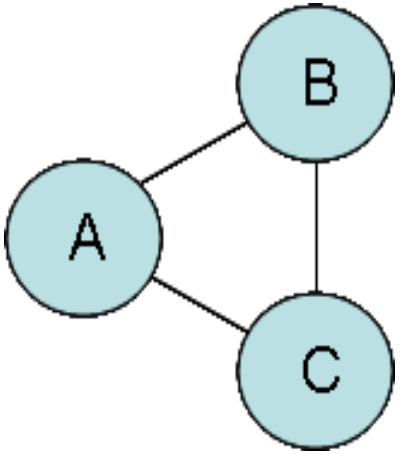
Source: Cipriani et al. 2009; Schmid 2010

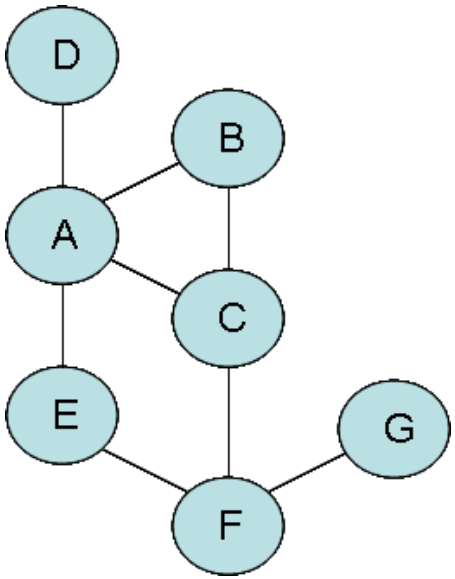
Two Specific Types of Network Meta-Analysis

- Indirect comparison – when only two (or one pair of) treatments are being compared indirectly
- Mixed treatment comparisons – a generalization of indirect comparisons with more than two (or multiple pairs of) treatments being compared indirectly
  - At least one pair of treatments is compared both directly and indirectly
- Extensions of standard pairwise meta-analysis of randomized control trials
  - Fixed-effect and random-effect network meta-analysis
- Relies on statistical methods that maintain benefits of randomization within each trial

Examples of Evidence Networks







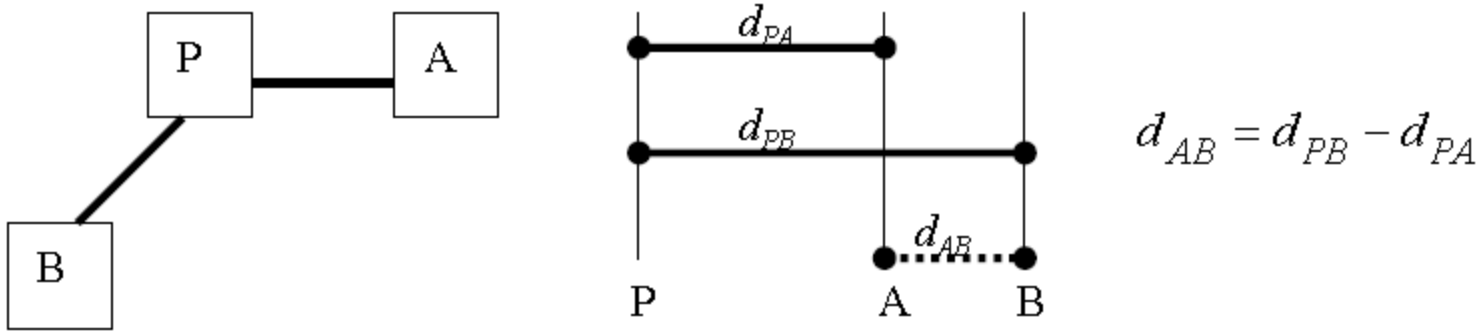
Closed loops in network: combination of direct and indirect evidence

Indirect Treatment Comparison

Mixed Treatment Comparisons

NETWORK META-ANALYSIS

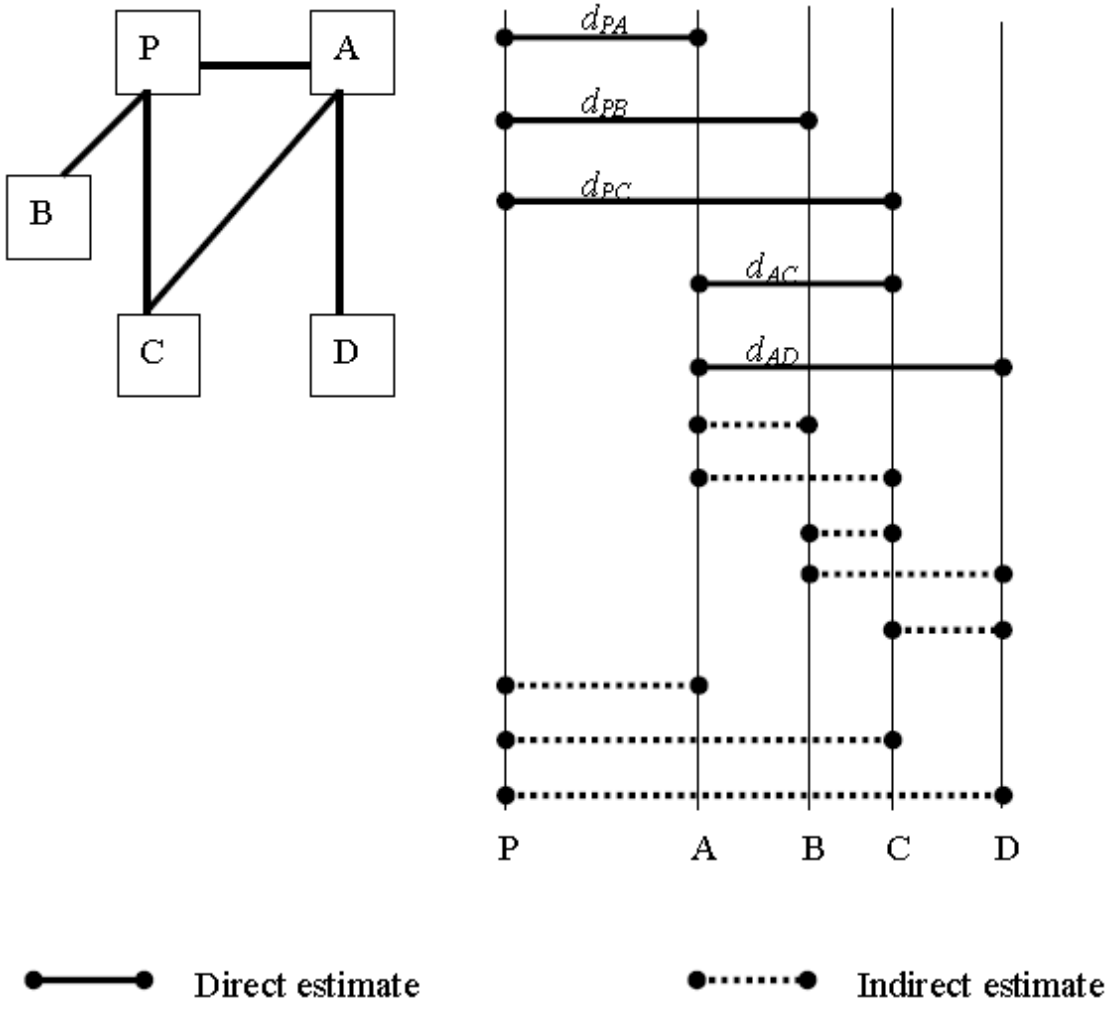
Indirect Comparison



Solid Line: Direct Comparison
Dashed Line: Indirect Comparison

Source: Adapted from Jansen et al. 2008

Mixed Treatment Comparisons



Source: Adapted from Jansen et al. 2008

Indirect Comparisons of Multiple Treatments

Trial			
1	A	B	
2	A	B	
3		B	C
4		B	C
5	A		C
6	A		C
7	A	B	C

- Want to compare A vs. B
- Direct evidence from trials 1, 2 and 7
- Indirect evidence from trials 3, 4, 5, 6 and 7
- Combining all “A” arms and comparing with all “B” arms destroys randomization
- Use indirect evidence of A vs. C and B vs. C comparisons as additional evidence to preserve randomization and within-study comparison

Source: Schmid 2010

How is an Indirect Comparison Made? Frequentist Approach

Calculate effect of A vs. C and B vs. C separately

$$T_{AB} = T_{AC} - T_{BC}$$

with its standard error being the square root of sum of variances [square root of $Var(T_{AC}) + Var(T_{BC})$]

(Bucher et al. 1997)

Basic and Functional Parameters

Four treatments (A, B, C, D) with treatment A as reference

Relative treatment effects (e.g., log odds ratios) of B, C, D relative to A are the **basic** parameters

$$d_{AB}, d_{AC}, d_{AD}$$

Remaining contrasts are **functional** parameters

$$d_{BC} = d_{AC} - d_{AB}$$
$$d_{BD} = d_{AD} - d_{AB}$$
$$d_{CD} = d_{AD} - d_{AC}$$

Basic parameters determine functional parameters

Functional parameters inform indirectly from basic parameters

Multiple Treatments Model

Again, same four treatments with treatment A as reference

Consider a binary outcome for treatment k in study i

Model: Each trial compares treatments b and k indirectly through A

Treatment effect = $\delta_{i(b,k)}$ if $k \neq b$

$\delta_{i(b,k)} \sim N(d_{bk} = d_{Ak} - d_{Ab}, \sigma^2)$

(random-effects model)

Fixed effects if $\sigma^2 = 0$

Note how functional and basic parameters inform each other

Note: Add priors on d_{Ak} and σ^2 for Bayesian analysis

Source: Lu and Ades 2004

What are the Basic Assumptions of Network Meta-Analysis?

- Homogeneity assumption for standard meta-analysis
- Similarity assumption for indirect comparison
- Consistency assumption for the combination of direct and indirect evidence

What Can Go Wrong If Assumptions Are Not Met?

Meta-analysis of Risperidone versus Haloperidol for Schizophrenia: Outcome is No Clinical Improvement (Frequentist Approach with Random-Effects Model)

Adjusted indirect comparison:

$lnOR'_{RH} = lnOR_{RP} - lnOR_{HP}$

$lnOR'_{RH}$ = -0.909 – (-1.707)
$lnOR'_{RH}$ = 0.798

Standard error $SE(lnOR'_{RH})$ = square root of $\{[SE(lnOR_{RP})]^2 + [SE(lnOR_{HP})]^2\}$

$SE(lnOR'_{RH})$ = square root of $[(0.218)^2 + (0.318)^2] = 0.386$

Results suggest that risperidone was less efficacious than haloperidol: Odds Ratio = exp(0.798) = 2.22; 95% CI = exp(0.798 ± 1.96*0.386) = 1.04 to 4.72

Comparison	Number of trials	Log odds ratio (SE)	Odds ratio (95% CI)	I² %
Placebo controlled trials				
Risperidone vs placebo	3	–0.909 (0.218)	0.40 (0.26, 0.62)	37%
Haloperidol vs placebo	9	–1.707 (0.318)	0.18 (0.10, 0.34)	11%
Risperidone vs haloperidol				
Direct comparison	10	–0.262 (0.142)	0.77 (0.58, 1.02)	14%
Adjusted indirect comparison	3/9	0.798 (0.386)	2.22 (1.04, 4.72)	
Combination of direct and indirect estimates	10+(3/9)	0.207 (0.527)	1.23 (0.44, 3.45)	85%

NB: Random-effects model was used in meta-analyses of trials and for the combination of the direct and indirect estimates. Odds ratio = EXP(log odds ratio).

CI: confidence interval; SE: standard error

Source: Song 2009

But in the 10 head-to-head comparisons, risperidone tended to be more efficacious than haloperidol: Odds ratio = 0.77, 95% CI = 0.58 to 1.02.This example of inconsistent evidence between indirect and direct estimates calls into question combining them.

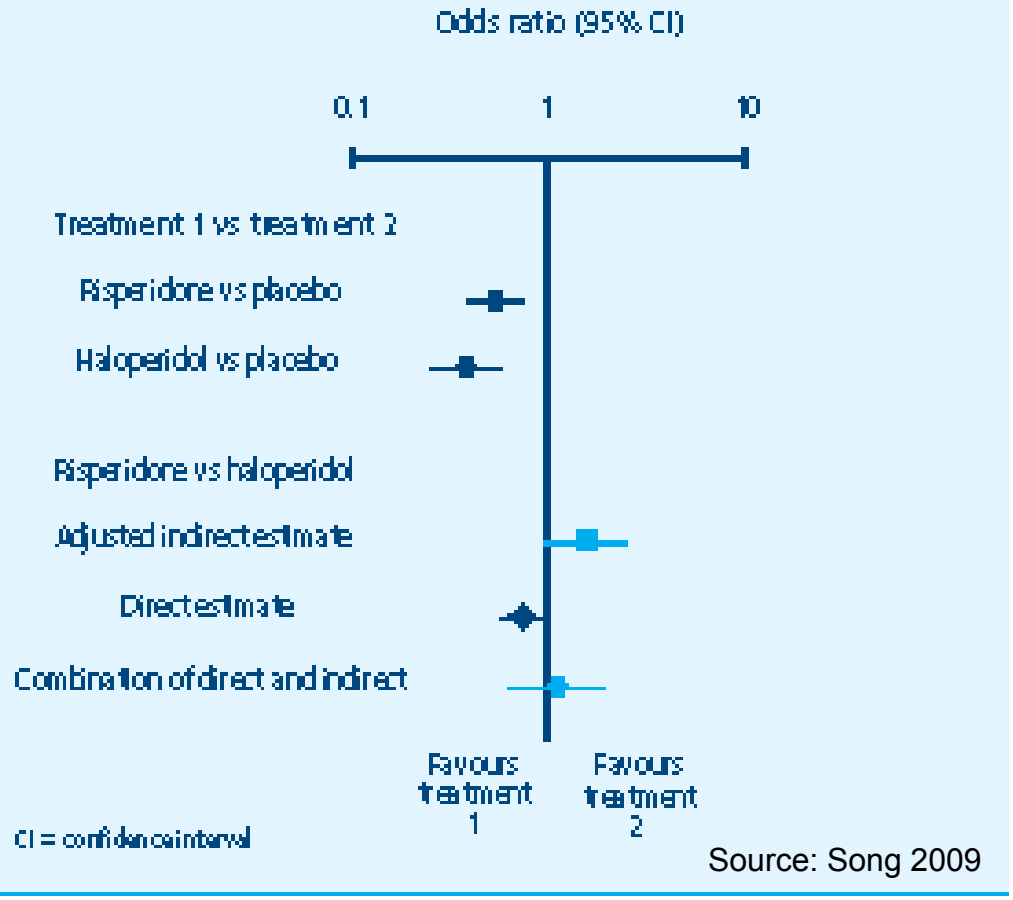
Results of Different Methods of Comparing Risperidone and Haloperidol for Schizophrenia (Outcome: Not Clinically Improved)

Informal indirect comparison: Odds ratio of haloperidol vs. placebo suggested a greater treatment effect than the odds ratio of risperidone vs. placebo, despite the overlapping confidence intervals

Formal indirect comparison: Favors haloperidol over risperidone

Direct comparison: Favors risperidone over haloperidol

Combination of direct and indirect: Validity doubtful given their inconsistent evidence



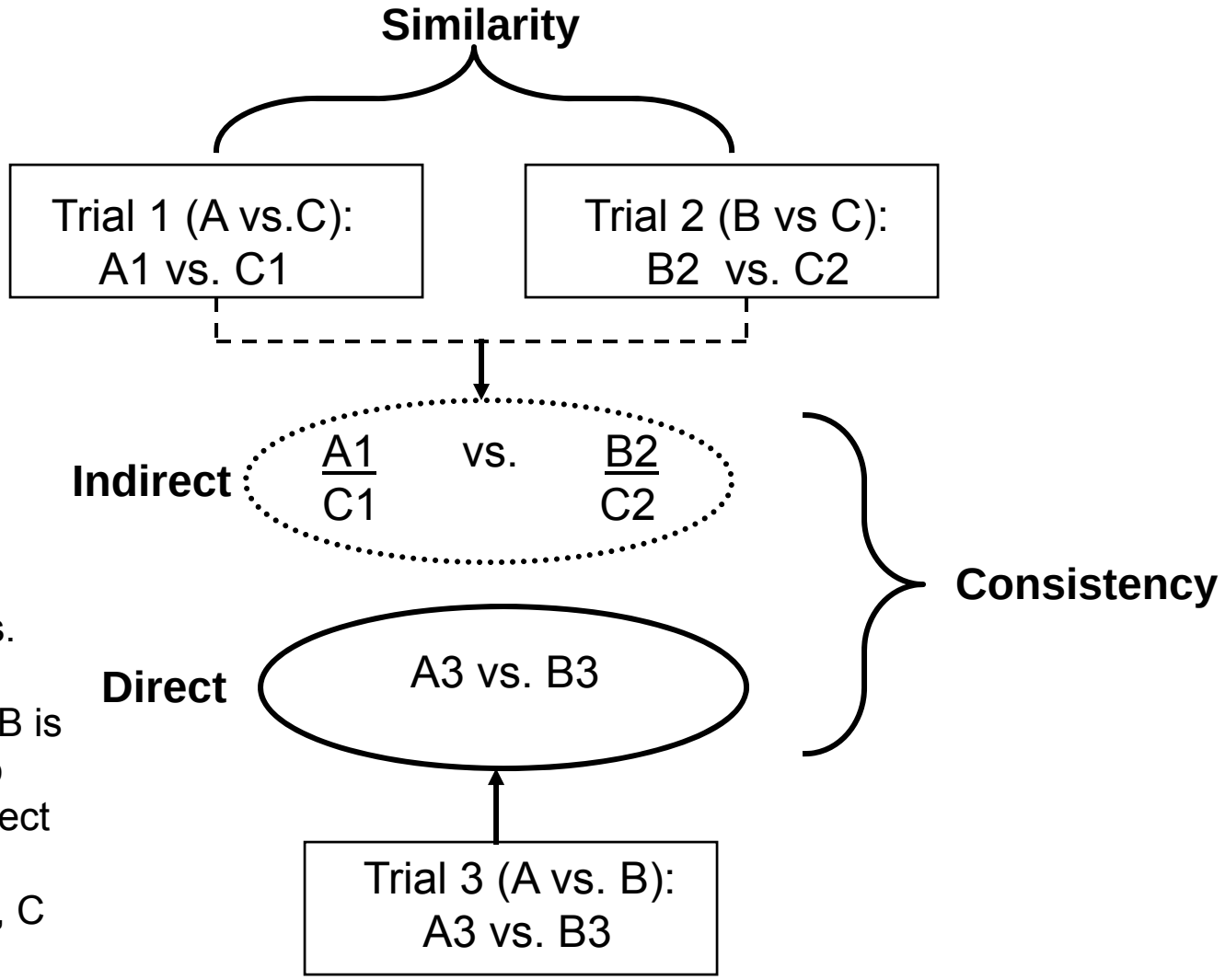
Source: Song 2009

Homogeneity Assumption for Standard Meta-Analysis

- Results from multiple trials can be pooled in meta-analyses before an indirect comparison is conducted

- In standard meta-analysis, it is assumed that different trials estimate the same single effect (fixed-effects model) or different effects are distributed around a typical value (random-effects model)
  - The underlying assumption is the trials are sufficiently homogeneous to be quantitatively combined
  - Heterogeneity can be tested using chi-square test and I-square (the proportion of total variation in results that is due to heterogeneity rather than chance)

Indirect Comparison Between Treatments A and B: Example from Three Trials



Note: In contrast to direct within-trial comparison, indirect comparison means a between-study comparison of different interventions. Here the indirect comparison of A and B is adjusted according to the results of their direct comparison with a common intervention, C

Similarity Assumption for Indirect Comparison

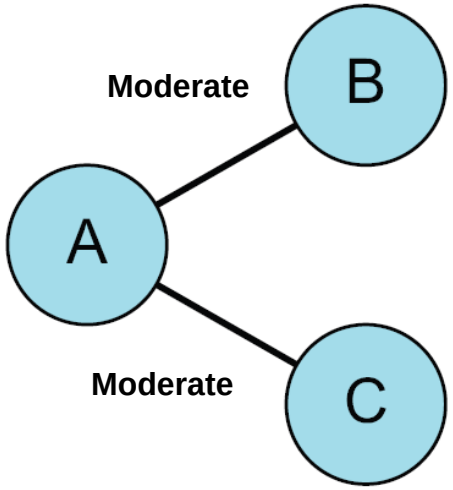
- This assumption requires that the patients included should be sufficiently similar in the sets of randomized-controlled studies
  - If so, the relative effect estimated by trials of A vs. C is generalizable to patients in trials of B vs. C (and vice versa)

- In addition to clinical similarity, methodological similarity (e.g., quality, definition of outcomes) is required for valid estimates
  - If there is imbalance in the distribution of effect modifiers (treatment-by-covariate interactions) between trials, then estimates become biased

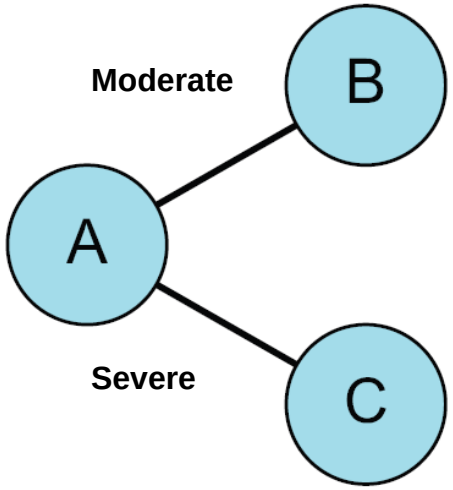
- Indirect assessment of risperidone versus haloperidol for schizophrenia
  - Patient characteristics, dose of drug, and treatment duration were similar between the two sets of placebo-controlled trials
  - But clinical improvement was defined differently
    - Placebo-controlled trials of risperidone: 20% or more greater reduction in total score on the Positive and Negative Syndrome Scale or Brief Psychiatric Rating Scale
    - Placebo-controlled trials of haloperidol: rated by clinicians using the Clinical Global Impression or other scales

Indirect Treatment Comparison

Unbiased



Biased



Severity of disease is an effect-modifier of the AB and AC effect

Similarity (transitivity) assumption holds:

$$d_{BC}^{indirect} = d_{AC}^{direct} - d_{AB}^{direct}$$

AB and AC have a different distribution of effect-modifiers

The transitivity assumption does not hold

The BC estimate is affected by confounding bias due to differences in effect-modifiers across comparisons

Source: Jansen et al. 2012

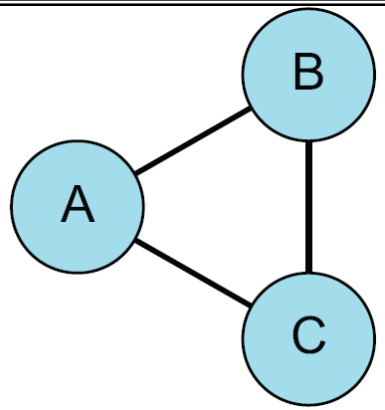
Consistency Assumption for Combining Direct and Indirect Estimates

- When both direct and indirect evidence are available, an assumption of consistency is required to combine the direct and indirect estimates
- Inconsistent results between them (say, as measured by I-square) may give invalid and misleading results
  - Example: risperidone versus haloperidol for schizophrenia (large *I*-square = 85%)
- When results are inconsistent, it is important to investigate possible causes of discrepancy
  - Chance, invalid indirect comparison, invalid head-to-head comparison, clinically meaningfully heterogeneity across trials
- Methods have been proposed to evaluate consistency (Salanti et al. 2008; Dias et al. 2010)

Analysis of Inconsistency

- Bucher method
- Inconsistency models
- Node splitting

Bucher Method for Inconsistency



$$\hat{d}_{BC}^{indirect} = \hat{d}_{AC}^{direct} - \hat{d}_{AB}^{direct}$$

Estimate of inconsistency:

$$\hat{\omega}_{BC} = \hat{d}_{BC}^{direct} - \hat{d}_{BC}^{indirect}$$

$$\mathrm{var}\left(\hat{\omega}_{BC}\right) = \mathrm{var}\left(\hat{d}_{BC}^{direct}\right) + \mathrm{var}\left(\hat{d}_{BC}^{indirect}\right)$$

An approximate test of the null hypothesis that there is no inconsistency can be obtained by

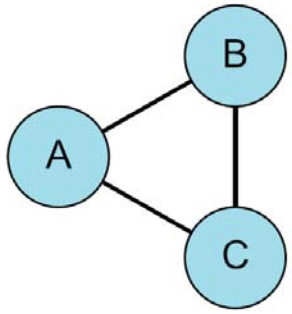
$$z_{BC} = \frac{\hat{\omega}_{BC}}{\sqrt{\mathrm{var}\left(\hat{\omega}_{BC}\right)}}$$ according to the normal distribution.

The method can only be applied to 3 independent sources of data.
Three-arm trials cannot be included.

Source: Bucher et al. 1997

Inconsistency Models

- Network meta-analysis (consistency) model with *k*-1 basic parameters (e.g., d_{AB} d_{AC}) in trial *j*



$$\delta_{jkb} \sim Normal\left(d_{bk}, \sigma^2\right) = Normal\left(d_{Ak} - d_{Ab}, \sigma^2\right)$$

$$d_{AA} = 0$$

- "Inconsistency" model with *N* basic parameters for every contrast where there is direct evidence: d_{AB}, $d_{AC,}$ $d_{BC,}$

$$\delta_{jxy} \sim Normal\left(d_{xy}, \sigma^2\right)$$

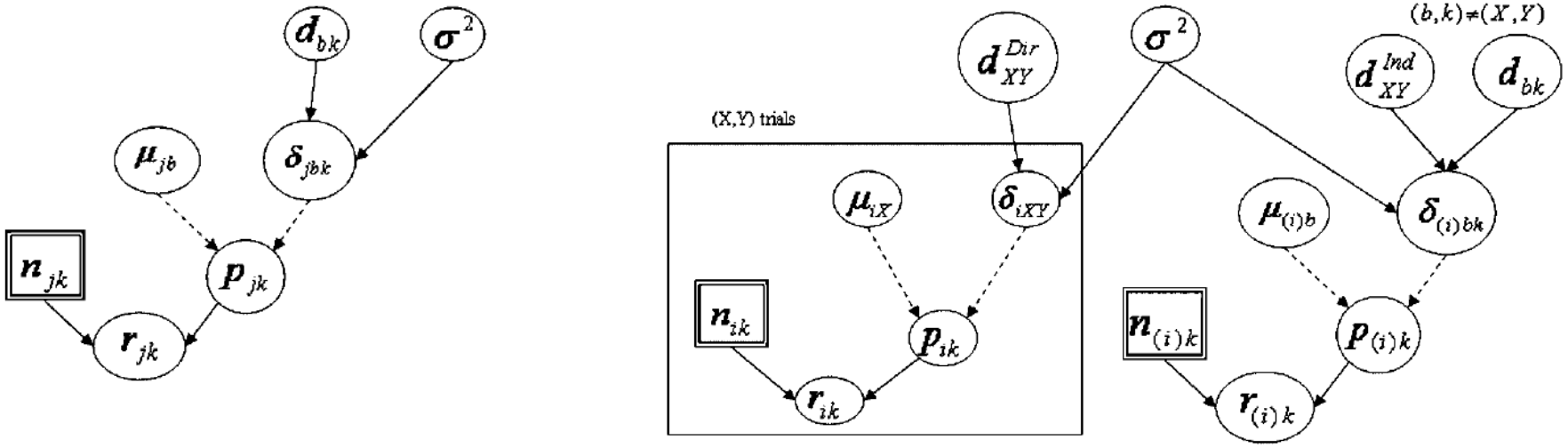
- Compare network meta-analysis model with inconsistency model regarding results of contrast, deviance, and model fit.

Source: Dias et al. 2011

Node Splitting

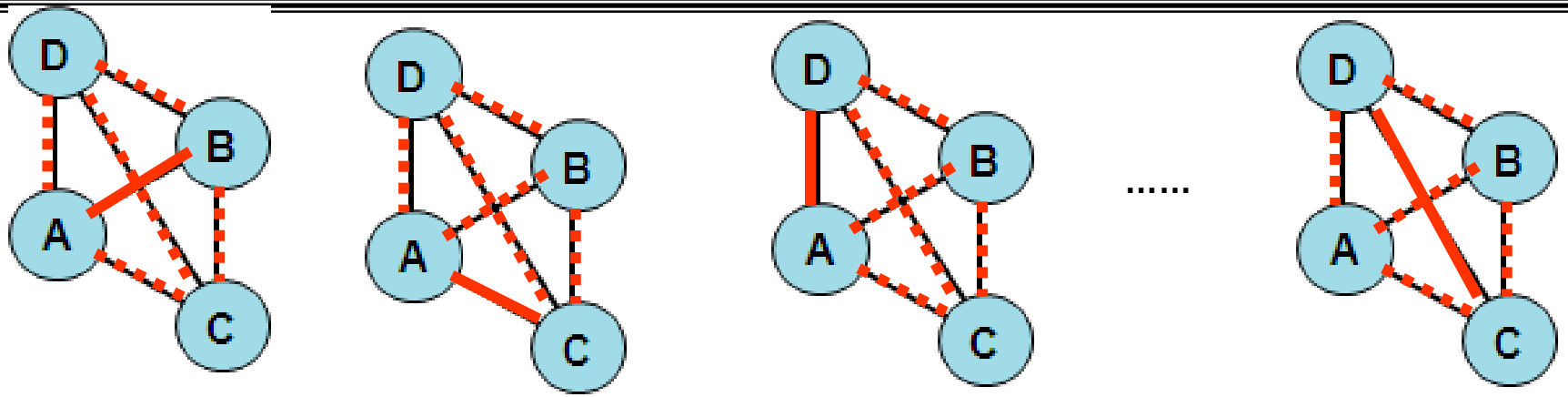
- Assess the discrepancies in the direct and indirect evidence for each mean treatment effect by splitting the information in the model into direct and indirect information on each node d_{bk}.

- Two posterior distributions are obtained for the mean treatment effect d_{XY}
  - one based on studies comparing treatments *X* and *Y* directly: d_{XY}^{direct}
  - and another from a network meta-analysis of all the *remaining* studies, i.e. using only indirect evidence $d_{XY}^{indirect}$.



Source: Dias et al. 2010

Node splitting



Treatments		MTC		Direct		Indirect		Inconsistency estimate	
X	*Y*	Mean	se	Mean	se	Mean	se	Mean	se
A	B	0.493	0.406	0.342	0.55	0.706	0.635	−0.365	0.840
A	C	0.844	0.240	0.845	0.254	0.673	0.679	0.171	0.716
A	D	1.106	0.442	1.360	0.829	1.108	0.539	0.253	0.983
B	C	0.352	0.416	−0.052	0.702	0.519	0.503	−0.571	0.853
B	D	0.613	0.488	0.676	0.698	0.511	0.684	0.165	0.966
C	D	0.261	0.419	−0.085	0.479	1.708	0.893	−1.793	1.009

$$\delta_{jxy} \sim Normal\left(d_{xy}^{Direct}, \sigma^2\right)$$

$$\delta_{jkb} \sim Normal\left(d_{bk}, \sigma^2\right) = Normal\left(d_{Ak} - d_{Ab}, \sigma^2\right)$$

$$d_{AA} = 0$$

$$(b,k) \neq (X,Y)$$

$$\omega_{XY} = d_{XY}^{direct} - d_{XY}^{indirect}$$

Source: Dias et al. 2010

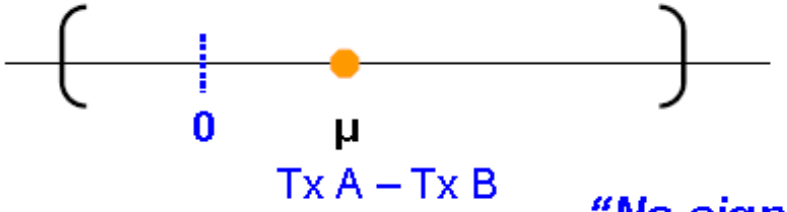
Bayesian Network Meta-Analysis

- Bayesian methods have been developed to conduct network meta-analysis of multiple treatments and to combine direct and indirect evidence
  - Well-suited for mixed treatment comparisons
- Allows probability statements that one drug is better (e.g., more efficacious, safer) than another
- Provides probability calculation that a particular drug is best, second best, third best, and so on
  - Rank-order the interventions for each outcome
- Lu and Ades 2004; Jansen et al. 2008; Sutton et al. 2008; Cipriani et al. 2009

Bayesian Approach

- Posterior distribution is a weighted average of currently observed data and prior information
- Output is a probability distribution
- As more data become available, the influence of the prior gets reduced
- Inferences are intuitive and relevant to decision making

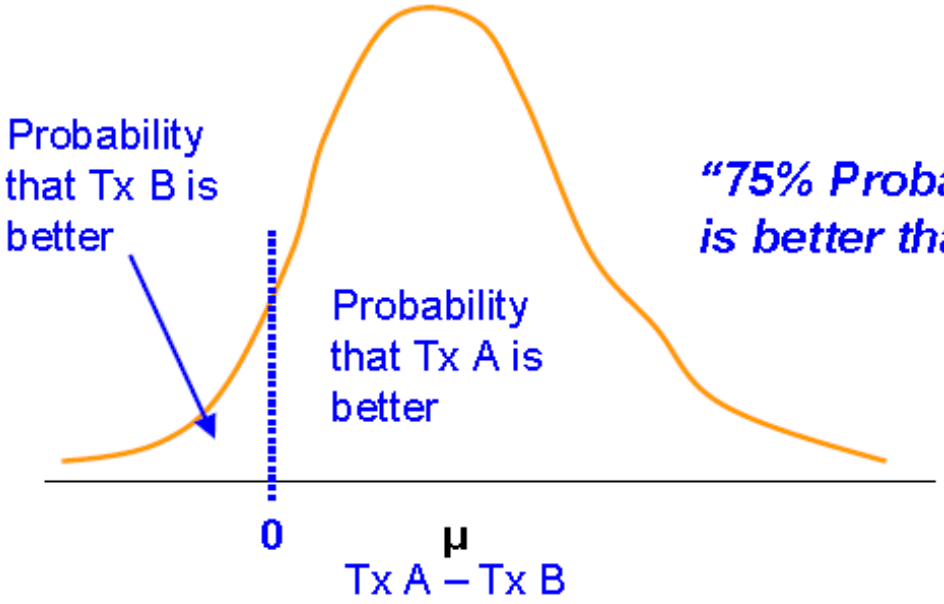
Frequentist vs. Bayesian Output



Frequentist output:

Point estimate (with 95%CI)

"No significant difference between Tx A and Tx B"



"75% Probability that Tx A is better than Tx B"

Bayesian output:

Probability distribution

Health Assessment Questionnaire (HAQ) in Rheumatoid Arthritis

- Results of Bayesian MTC (with a random-effects model) showed that, based on reduced HAQ scores, the probability that
  - Placebo is best = 1%
  - Methotrexate is best = 1%
  - Anti-TNFα is best = 8%
  - Anti-TNFα + methotrexate = 90%

- There was a 95% chance that anti-TNFα + methotrexate resulted in more favorable (reduced) HAQ scores than placebo
  - The probability is 95% that this reduction in HAQ scores is between 0.10 and 1.06 points
  - Range on HAQ: 0 to 3 points

Source: Jansen et al. 2008

Multiple Treatments for Acute Myocardial Infarction

Evidence structure for comparison of multiple treatments used in two meta-analyses: number of randomised controlled trials directly comparing seven treatments for acute myocardial infarction. Ps denote the treatments compared

No of trials	Streptokinase	Alteplase-	Accelerated alteplase	Streptokinase +alteplase	Reteplase	Tenecteplase	PCTA
Boland et al							
8	P	P					
1	P		P	P			
1	P			P			
1	P				P		
2			P		P		
1			P			P	
Keeley et al							
8	P						P
3		P					P
11			P				P

PCTA = primary percutaneous transluminal coronary angioplasty.

Source: Caldwell et al. 2005.

One overview covered 14 randomized controlled trials with two or three-way comparisons of six thrombolytic treatments.

The other overview featured 22 randomized controlled trials in which primary percutaneous transluminal coronary angioplasty (PTCA) was compared with thrombolytic treatment (streptokinase, alteplase, or accelerated alteplase). Because this meta-analysis collapsed the three thrombolytic treatments as a single comparator, the approach was criticized as the relevant comparator should have been the best thrombolytic drug, not the average one.

Multiple Treatments for Acute Myocardial Infarction

- The two sets of overviews with 36 randomized controlled trials were integrated across the seven treatments
- Estimates for all the 21 possible pair-wise comparisons (10 based on direct data and 11 based on indirect data) rendered empirical evidence of which treatment is most likely to have the lowest mortality (the winner was PTCA, with at least a 95% probability of being best) (Caldwell et al. 2005)
- Mixed treatment comparison integrated and connected all available data so that relevant treatments can be compared, including those that would not have been otherwise, and direct evidence can be made more precise (by combining direct comparisons for which data were available with their corresponding indirect estimates)
- For example, although the direct evidence showed PTCA not to be statistically better than alteplase [fixed effects odds ratio = 0.81, 95% confidence interval (CI) = 0.64 to 1.02], the mixed treatment comparison clearly did (odd ratio = 0.89, 95% CI = 0.61 to 0.89) as it capitalized on information from the indirect comparisons as well as the available direct comparison

Thrombolytic Treatments for Acute Myocardial Infarction

Probability that each treatment is best for acute myocardial infarction example (reproduced from Caldwell et al.)

Treatment	Fixed effect (%)	
	35-day mortality	probability treatment the best
SK	6.5	0
t-PA	6.4	0
Acc t-PA	5.6	40
SK+t-PA	6.2	1
r-PA	5.8	15
TNK	5.6	43

Acc t-PA = accelerated alteplase; r-PA = reteplase; SK = streptokinase; SK+t-PA = streptokinase + alteplase; TNK = tenecteplase; t-PA = alteplase.

Source: Sutton et al. 2008

Reconsider the overview of 14 randomized controlled trials with two or three-way comparisons of six thrombolytic treatments.

In terms of reducing 35-day mortality, a Bayesian analysis revealed that the probability that tenecteplase is best is 43%; accelerated alteplase, 40%; reteplase, 15%; streptokinase plus alteplase, 1%; streptokinase, 0%; and alteplase, 0%

International Society for Pharmacoeconomics and Outcomes Research (ISPOR)

- ISPOR Task Force on Indirect Treatment Comparisons Good Research Practices
- ISPOR conference presentations on network meta-analysis
- Two articles published in Value in Health 2011
  - Part 1: Guidance on interpretation for decision-makers (Jansen et al.)
  - Part 2: Guidance on conducting (Hoaglin et al.)

NICE (2011) Decision Support Unit: Technical Support Documents(TSD)

http://www.nicedsu.org.uk/Evidence-Synthesis-TSDseries%282391675%29.htm

- **TSD 1: Introduction to evidence synthesis for decision making**
- **TSD 2: A general linear modelling framework for pairwise and network meta-analysis fo randomized controlled trials, with WinBUGS files**
- **TSD 3: Heterogeneity: subgroups, meta-regression, bias, and bias-adjustment, with WinBUGS files**
- **TSD 4: Inconsistency in networks of evidence based on randomized controlled trials, with WinBUGS files**
- **TSD 5: Evidence synthesis in the baseline natural history model, with WinBUGS files**
- **TSD 6: Embedding evidence synthesis in probabilistic cost-effectiveness analysis – software choices.**
- **TSD 7: Evidence synthesis of treatment efficacy in decision making: a reviewer's checklist.**

Network Meta-Analysis Requires Utmost Care

In the same spirit as the

Lesson Learned from Choosing the Right Study Design

An Early Clinical Trial (n = 2)

J Int Med. October 1991:289 - introduction to editorial from Nordic School of Public Health, Goteborg, Sweden

Reprinted in Ann Intern Med 1992;117:30

Coffee Example

In the late 18th century, King Gustav III of Sweden decided that coffee was poison and ordered a clinical trial.

1. Study:
    1) The king condemned a convicted murderer to drink coffee every day
    2) Control: another murderer was condemned to drink tea daily
    3) Outcome - death
    4) Two physicians were appointed to determine the outcome

2. Results:
    1) The two doctors died first
    2) The king was murdered
    3) Both convicts enjoyed long life until the tea drinker died at age 83. (No age was given for the coffee drinker)

Coffee Example

3. Discussion:
   – One should not rely on such a small sample size
   – Perhaps the end point was too hard
   – The outcome of the trial had no effect on the decision makers
   – Coffee was forbidden in Sweden in 1794 and again in 1822

4. Conclusion:
   – None possible
   – External events and other biases may have confounded the result
     (Kings should not mess with clinical trials)

References

- Bucher et al. 1997. Journal of Clinical Epidemiology. 50:683-691
- Caldwell et al. 2005. BMJ. 331:897-900
- Cipriani et al. 2009. Lancet. 373:746-758
- Dias et al. 2010. Statistics in Medicine. 29:932-944
- Dias et al. 2011. NICE DSU Technical Support Document 4. http://www.nicedsu.org.uk/Evidence-Synthesis-TSD-series%282391675%29.htm
- Hoaglin et al. 2011. Value in Health. 14:429-437
- Ioannidis. 2006. Lancet. 368:1470-1472
- Jansen et al. 2008. Value in Health. 11:956-964
- Jansen et al. 2011. Value in Health. 14:417-428
- Jansen et al. 2012. Journal of Clinical Epidemiology. 65:798-807
- Liberati et al. 2009. Annals of Internal Medicine. 151:W-65-W-94
- Lu and Ades. 2004. Statistics in Medicine. 23:3105-3124
- NICE 2011. http://www.nicedsu.org.uk/Evidence-Synthesis-TSD-series%282391675%29.htm
- Salanti et al. 2008. Statistical Methods in Medical Research.17:279-301
- Schmid. 2010. Presentation at Pfizer Inc, New York, NY.
- Song. 2009 (February). What is indirect comparison. Part of the “What is…?” series
- Sutton et al. 2008. Pharmacoeconomics. 26:753-767

Summary

- Placed network meta-analysis in context of CER
- Highlighted concepts on network analysis
- Described and analyzed its basic assumptions
- Provided examples with frequentist indirect comparisons and Bayesian mixed treatment comparisons