Statistical considerations in indirect comparisons and network meta-analysis

Said Business School, Oxford, UK

March 18-19, 2013

Handout S1-L

Introduction

Julian Higgins

ClinicalEvidence

Hay fever in adolescents and adults

Search date April 2008

Aziz Sheikh, Sukhmeet Singh Panesar, and Sarah Salvilla

ABSTRACT

INTRODUCTION: Hay fever is found throughout the world. Epidemiological evidence suggests considerable geographical variation in its prevalence. Symptoms are caused by an IgE-mediated type 1 hypersensitivity reaction to airborne allergens such as pollen or fungal spores, and may also cause eye, sinus, respiratory, and systemic problems. METHODS AND OUTCOMES: We conducted a systematic review and aimed to answer the following clinical question: What are the effects of treatments for hay fever in adolescents and adults? We searched: Medline, Embase, The Cochrane Library, and other important databases up to April 2008 (Clinical Evidence reviews are updated periodically; please check our website for the most up-to-date version of this review). We included harms alerts from relevant organisations such as the US Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA). RESULTS: We found 211 systematic reviews, RCTs, or observational studies that met our inclusion criteria. We performed a GRADE evaluation of the quality of evidence for interventions. CONCLUSIONS: In this systematic review we present information relating to the effectiveness and safety of the following interventions: intranasal corticosteroids, oral antihistamines, intranasal antihistamines, oral leukotriene receptor antagonists, systemic corticosteroids, intranasal ipratropium bromide, oral decongestants, and combinations of these treatments.

OPTION ANTIHISTAMINES (ORAL)

Symptom relief

Compared with placebo Antihistamines (acrivastine, azatadine, brompheniramine, cetirizine, levocetirizine, ebastine, fexofenadine, loratadine, desloratadine, rupatadine, and mizolastine) are more effective at improving nasal and ocular symptoms (moderate-quality evidence).

Compared with intranasal azelastine Oral antihistamines seem equally effective at improving symptoms of rhinitis and nasal congestion (moderate-quality evidence).

Compared with montelukast We don't know how the effectiveness of loratadine and montelukast compare at reducing rhinitis symptoms (low-quality evidence).

Compared with intranasal corticosteroids (beclometasone, budesonide, fluticasone, and triamcinolone) Oral antihistamines (dexchlorpheniramine, terfenadine, astemizole, loratadine, and cetirizine) may be less effective at improving nasal symptoms, but may be equally effective at improving ocular symptoms (low-quality evidence).

Compared with antihistamines plus leukotriene antagonists Antihistamines alone may be equally effective at improving nasal symptoms (low-quality evidence).

Compared with antihistamines plus pseudoephedrine Antihistamines alone seem less effective at reducing nasal symptoms (moderate-quality evidence).

INTERVENTIONS

TREATMENT OF HAY FEVER

Beneficial

Likely to be beneficial

Unknown effectiveness

Unlikely to be beneficial

Likely to be ineffective or harmful

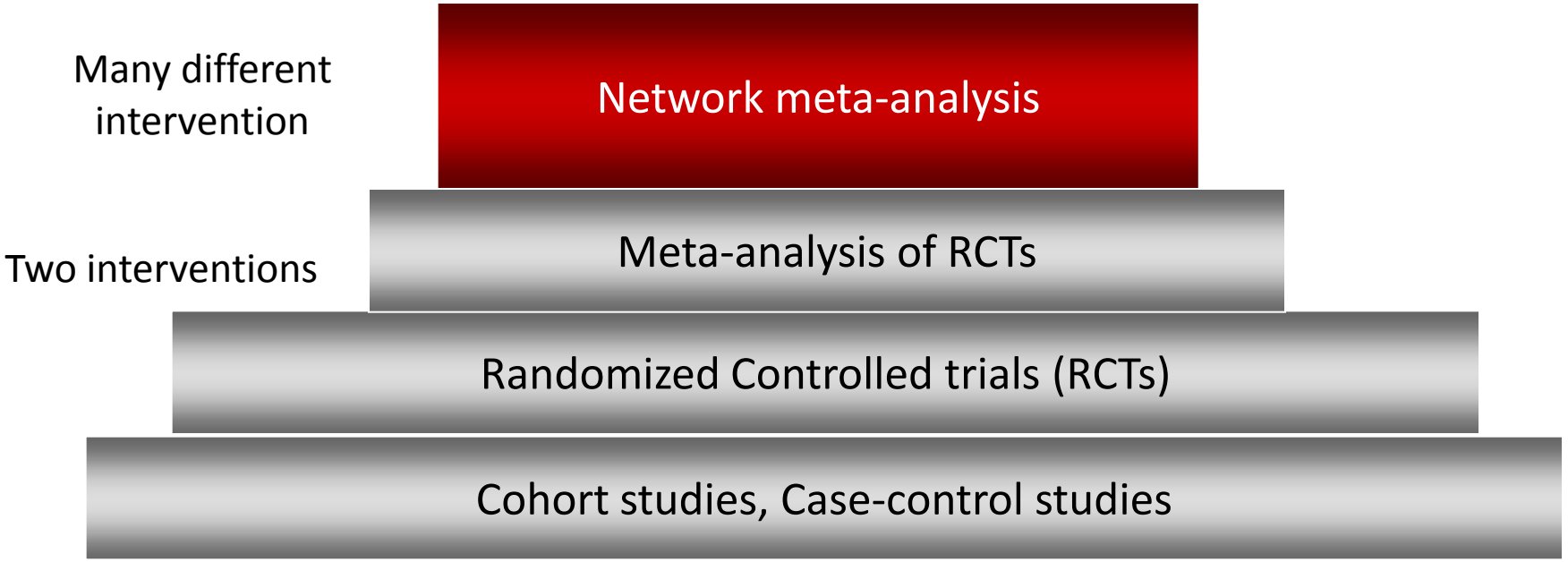
To be covered in future updates

Effects of prophylactic treatments: allergen avoidance; sodium cromoglycate; immunotherapy (intranasal, subcutaneous, and sublingual); homeopathy; and anti-immunoglobulin E.

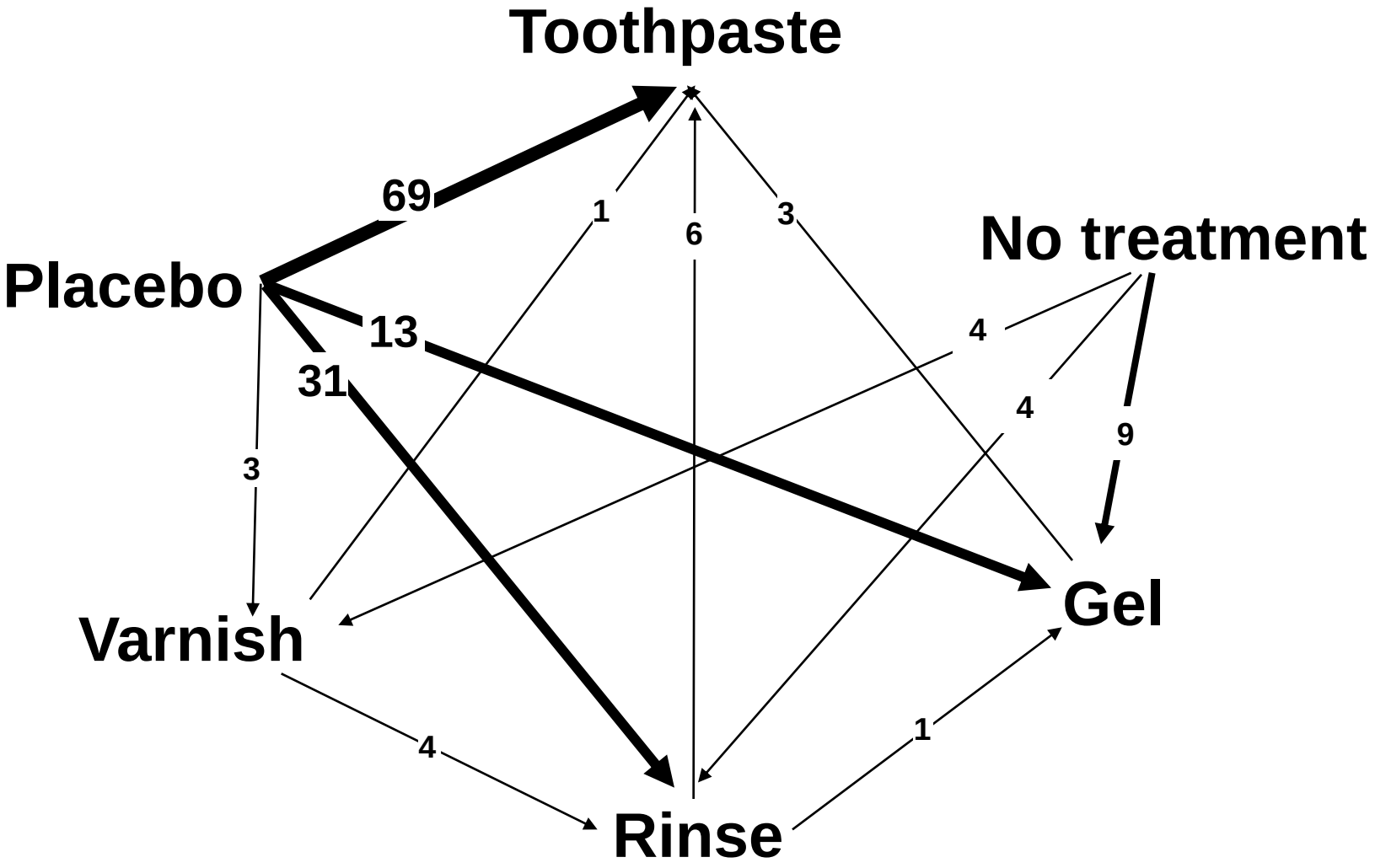
Hay fever in children

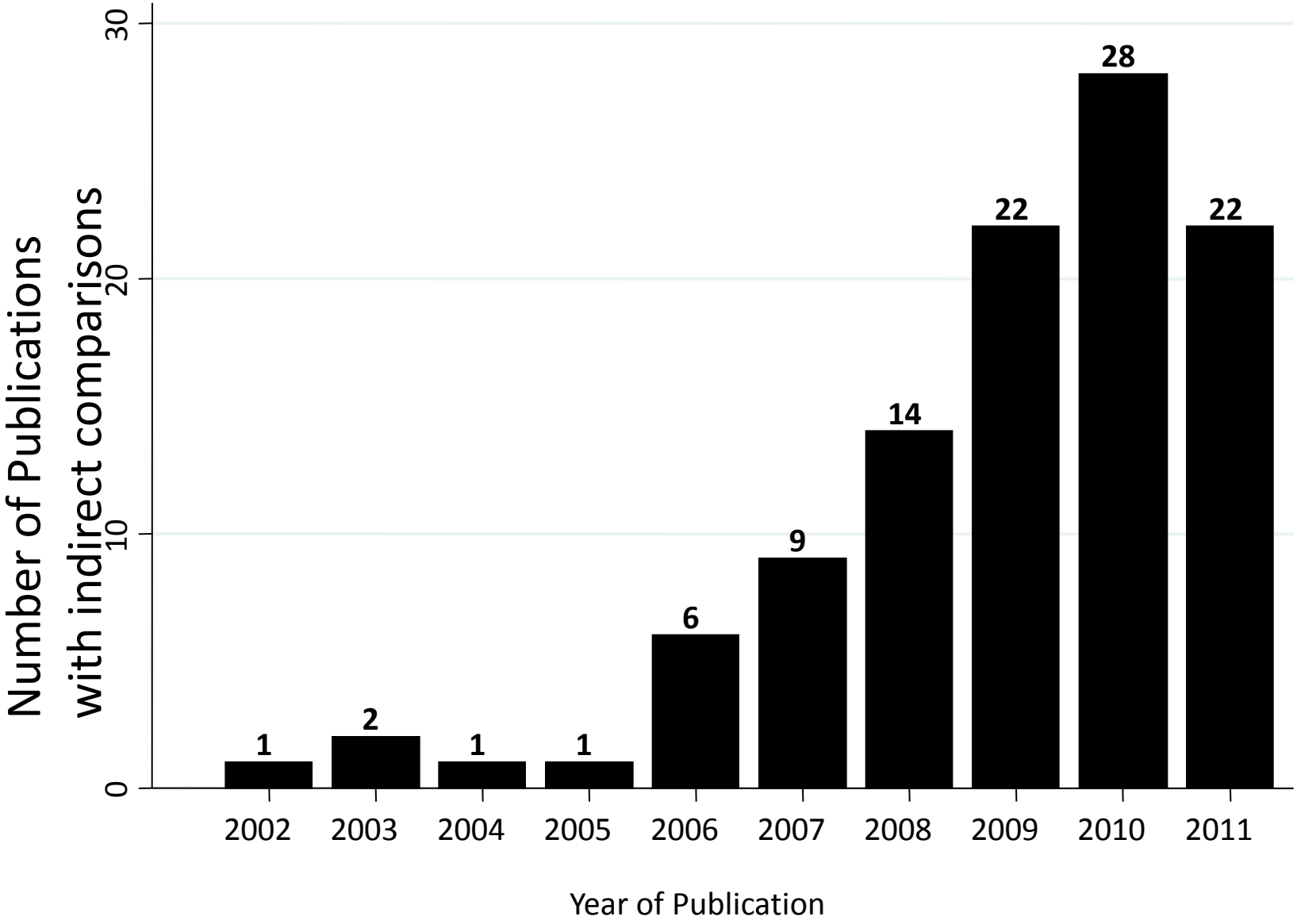
A new methodological framework

Other names:
Multiple-treatments meta-analysis,
Mixed-treatment comparison



A network of trials: topical fluoride therapy




Number of Publications with indirect comparisons
0
10
20
30
1
2
1
1
6
9
14
22
28
22
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
Year of Publication

Conditions for valid inference about 'best' treatment

	Network	Conventional
• High internal validity / low risk of bias	Yes	Yes
• Low risk of reporting bias	Yes	Yes
• Clinical diversity not relevant or low (high 'combinability')	Yes	Yes
• Good fit of statistical model	Yes	Yes

Conditions for valid inference about 'best' treatment

Considerations extend *across studies making different comparisons*

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• High internal validity / low risk of bias	Yes	Yes
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• Good fit of statistical model	Yes	Yes

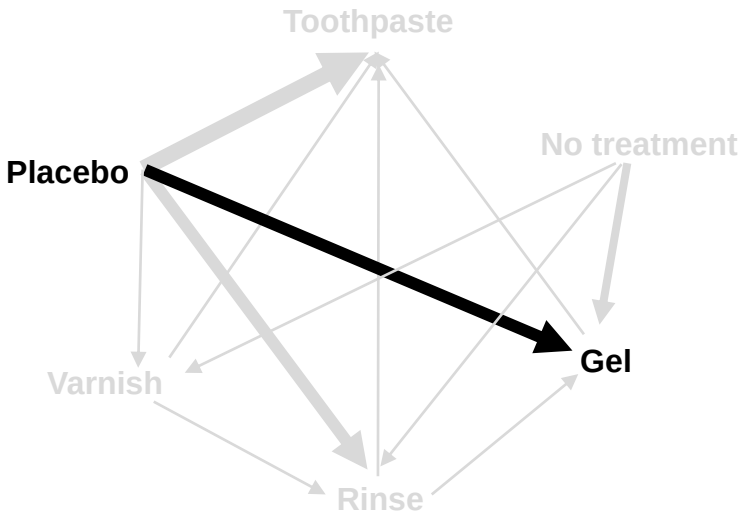
Considerations include possibility of *inconsistency* (conflict) between different types of evidence

Course objectives

- by the end of the course, participants should be able...
  - to understand the principles, steps and statistical methods involved in indirect comparisons and network meta-analyses;
  - to understand the biases that can distort indirect comparisons and network meta-analysis, including conflict among different sources of evidence, and ways to address these issues;
  - to be aware of current thinking in presenting findings from indirect comparisons and network meta-analyses, including issues related to risk of bias and quality (within Summary of Findings tables); and
  - to support Cochrane editorial bases in their support of review authors undertaking indirect comparisons and network meta-analysis.

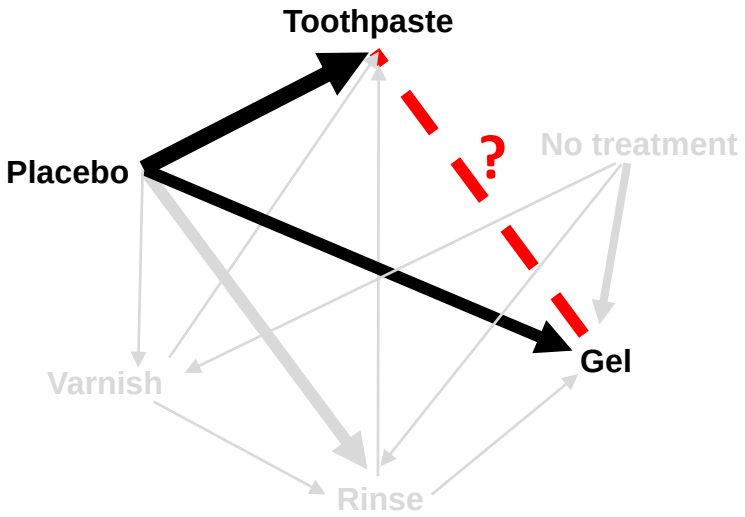
Outline of the course: Monday

- Pair-wise meta-analysis



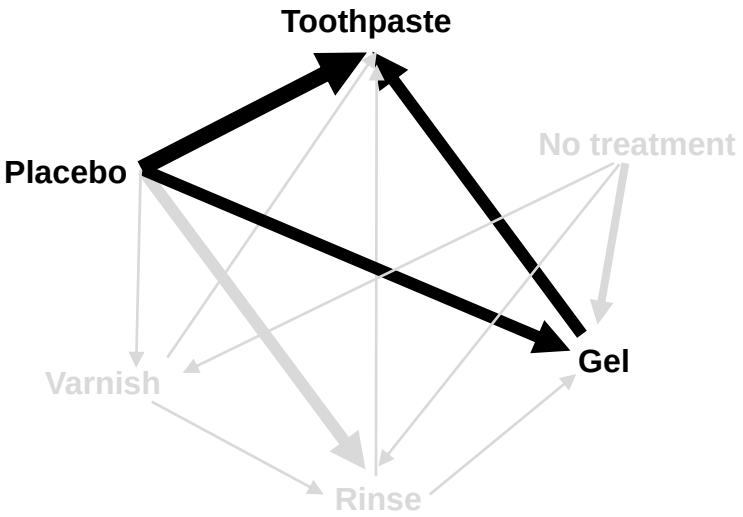
Outline of the course: Monday

- Pair-wise meta-analysis
- Indirect comparisons



Outline of the course: Monday

- Pair-wise meta-analysis
- Indirect comparisons
  - and mixed comparisons
  - ‘loops’ of evidence



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- Pair-wise meta-analysis
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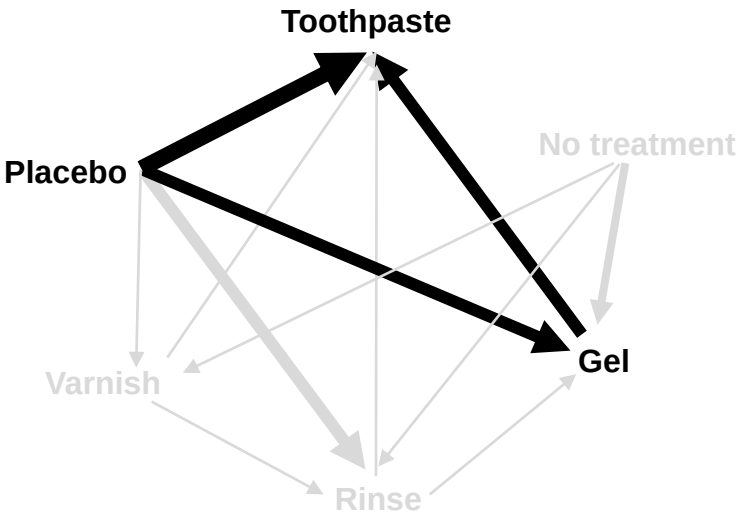
  - and mixed comparisons
  - ‘loops’ of evidence
- Meta-regression
  - for indirect comparisons



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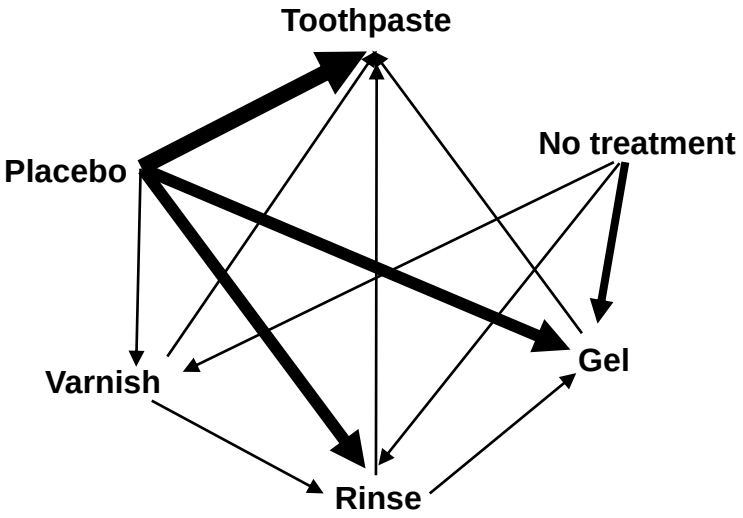
  - for network meta-analysis



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- Pair-wise meta-analysis
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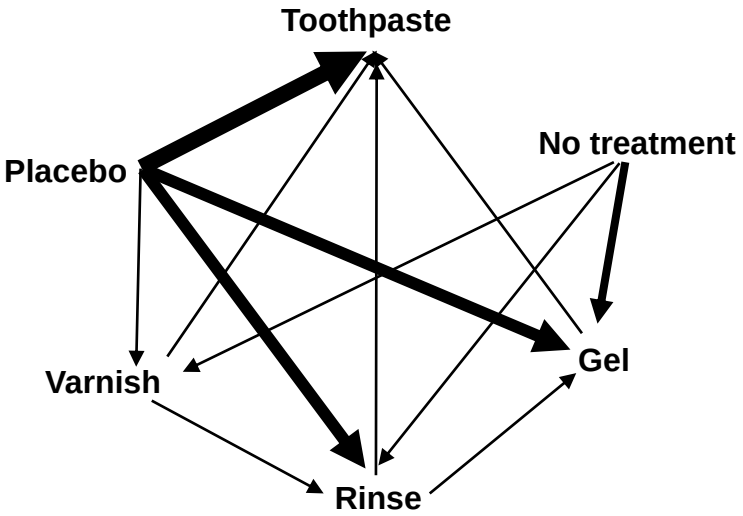
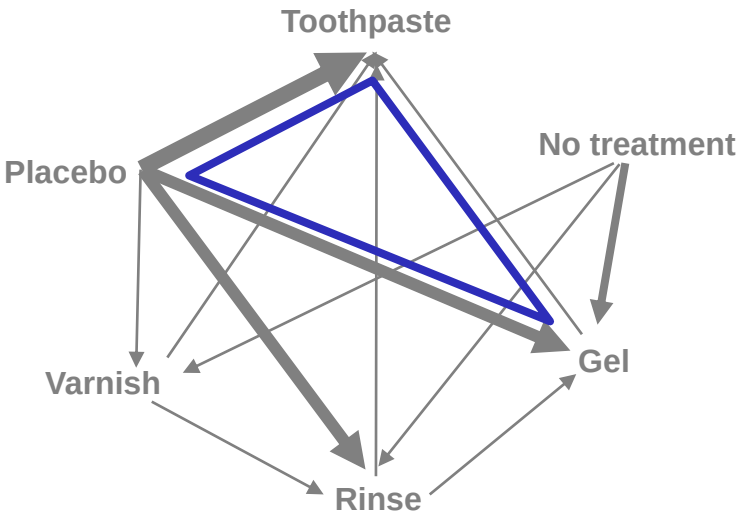
  - ‘loops’ of evidence
- Meta-regression
  - for indirect comparisons
  - for network meta-analysis

- Small group discussion
- Computer practicals



Outline of the course: Tuesday

- Problem of multi-arm studies
  - Full network meta-analysis
  - Multivariate meta-analysis



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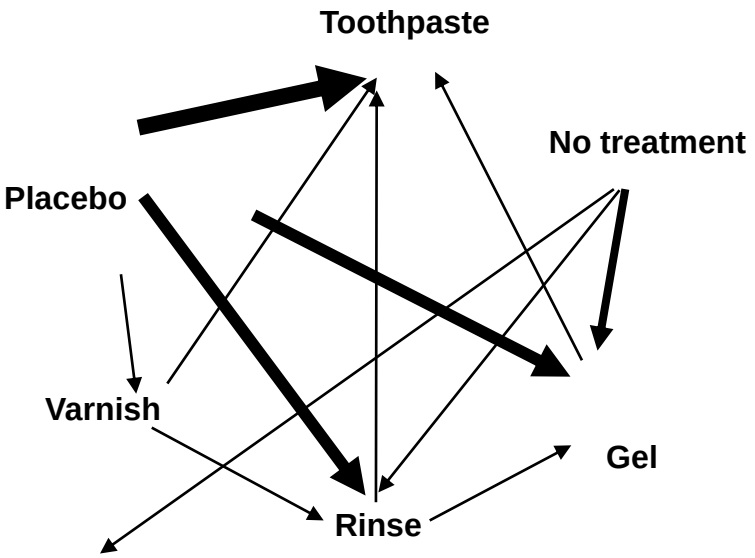
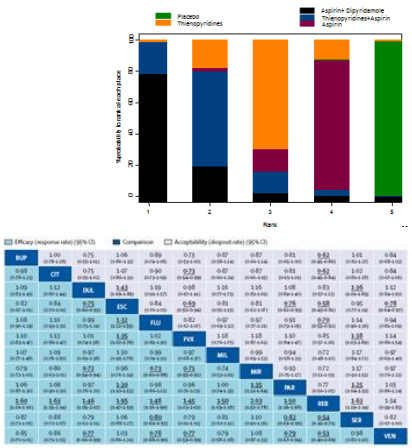
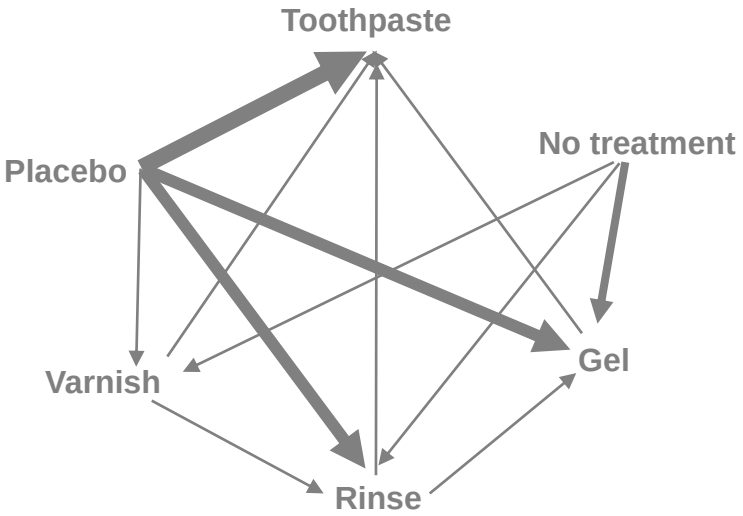
- Inconsistency (conflicting evidence)



Outline of the course: Tuesday

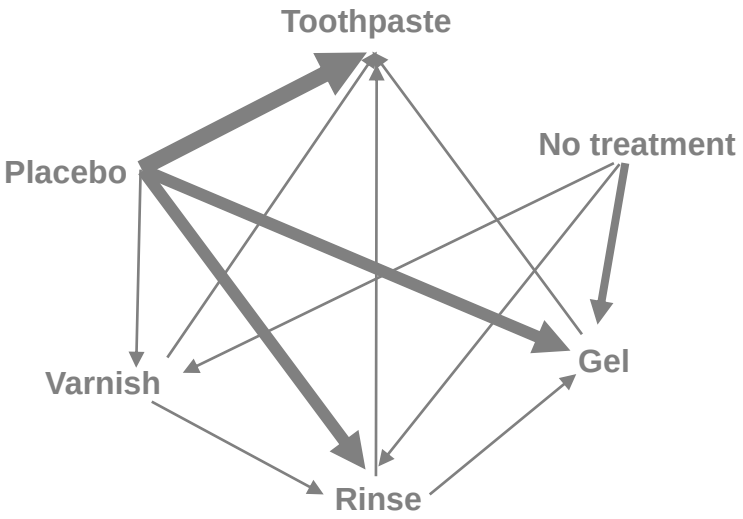
- Problem of multi-arm studies
  - Full network meta-analysis
  - Multivariate meta-analysis
- Inconsistency (conflicting evidence)
- Presentation of results





Outline of the course: Tuesday

- Problem of multi-arm studies
  - Full network meta-analysis
  - Multivariate meta-analysis
- Inconsistency (conflicting evidence)
- Presentation of results
- Presentations from small-group discussions
- Group discussion of implications for Cochrane Reviews



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