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Comparing Multiple Treatments: Overviews vs. Intervention Reviews

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Essential Features

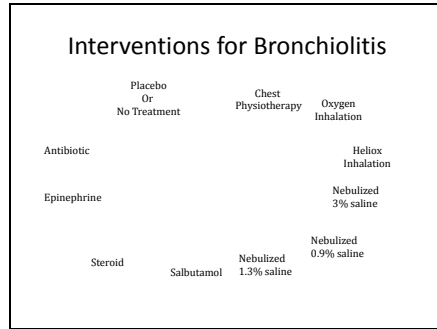
- Addresses a well-defined question
- Compares 2 or more interventions
- Search strategy uses existing reviews
- Provides a synthesis or integration across existing reviews

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A Well-Defined Question

- PICO – Population, Interventions
- “Would it be reasonable to compare these interventions in different arms of a single RCT?”
 - Important assumption for some statistical analyses
 - Useful rule of thumb for all overviews

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Compares 2 or More Interventions

- Overviews are one way of doing this
- Many Cochrane intervention reviews do this as well
- What are the differences?
- How to choose whether to use an overview or an intervention review to compare multiple interventions

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Intervention Review or Overview?

- No firm guidelines
- May depend on the question
- May depend on the available evidence
- We will explore some differences & some options for both approaches

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Differences Between Overviews and Intervention Reviews

- Search Strategy – Always differs
 - Intervention reviews search for trials
 - Overviews search for reviews
- Approach to Analysis – Sometimes differs
 - Intervention reviews use a trial level analysis
 - Overviews may be able to use a review level analysis
 - But will often use a trial level analysis instead

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Search Strategy for Overviews

- Focus on identifying relevant reviews
 - Use reviews to find relevant trials if trial level analysis is contemplated
- Extending the search
 - Some overviews use non-Cochrane reviews
 - Updating search for older reviews
 - Trial level search for interventions not included in reviews

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Synthesis or Integration

- Driven by the well-defined question
- Not driven by the individual review questions
- Outcomes part of PICO
 - Specified in overview protocol
 - Depends in part on choices made by trialists or reviewers
 - May force a trial level analysis

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Example of a trial level synthesis

12 new generation antidepressants: Which ones are the most efficacious?

paroxetine

sertraline

citalopram

escitalopram

fluoxetine

fluvoxamine

milnacipran

venlafaxine

reboxetine

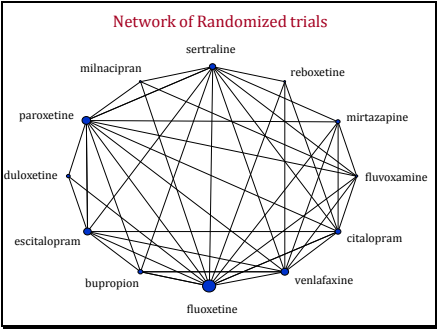
bupropion

mirtazapine

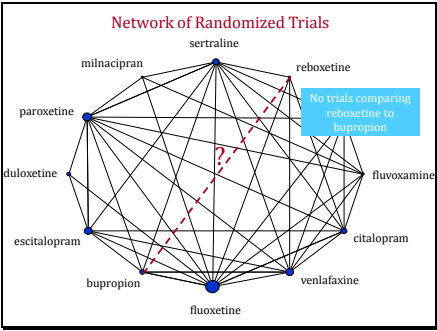
duloxetine

With thanks to Georgia Salanti

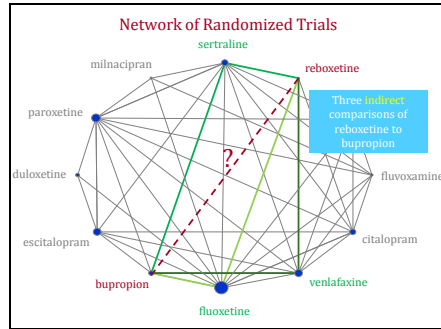
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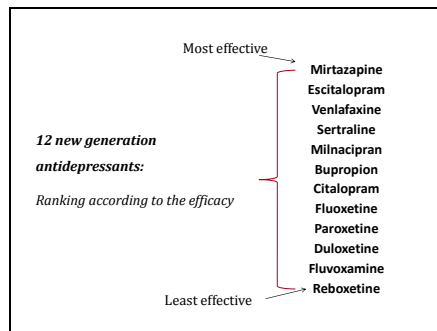
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- ## Defining treatments: are all relevant treatments included?
- Definition of relevance depends on your research question and analysis plan
 - Which is the best antidepressant?
 - Rankings may be affected by inclusion criteria.
 - Consider including placebo, TAU, older and legacy treatments
 - Do NG antidepressants improve outcome?
 - An “in principle” question.
 - Requires early collaboration with clinicians, epidemiologists etc.

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Defining treatments: lumping or splitting

'Lumping' in meta-analysis is commonplace as it only allows 2 treatments to be compared
e.g. 3 trials of 3 therapies for improving depression

- | | |
|------------------------|----------------------|
| 1. CBT vs TAU: | RR 2.00 (1.55, 2.58) |
| 2. Humanistic vs TAU: | RR 0.60 (0.26, 1.40) |
| 3. Mindfulness vs TAU: | RR 1.50 (0.77, 2.93) |
| 42 8 | |
| Psychotherapy vs TAU: | RR 1.73 (1.38, 2.17) |

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“Lumped” psychotherapy versus treatment as usual forest plot



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Meta-analysis: to lump, or to split...

Lumping treatments: Can mask heterogeneity, increased power, increase precision (spuriously?).

E.g. PTCA vs thrombolytics

- PTCA better than thrombolytics (OR 0.70 [0.58 – 0.85])

Subsequent correspondence:

- “But surely the relevant comparison is the ‘best’ thrombolytic (Acc t-PA) NOT the ‘average’ one?”
- PCTA vs Acc t-PA not “significant” (OR 0.81 [0.62 – 1.02])

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Network meta-analysis: to lump or to split...

Trials of HAART regimes for HIV

- A: 2 NRTIs
- B: 2 NRTIs + PI
- C: 2 NRTIs + NNRTI

“Indirect B vs C evidence inconsistent with direct evidence from B vs C trials”

“Indirect Comparisons unreliable for complex interventions like HAART”

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Network meta-analysis: to lump or to split...

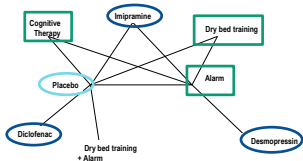
A: 2 NRTIs , B: 2 NRTIs + PI, C: 2 NRTIs + NNRTI

BUT the NRTIs in the A vs B trials were **DIFFERENT** from the NRTIs in the B vs C trials.

When the comparison was restricted to trials with the **SAME** NRTI regimes, the inconsistency no longer statistically 'significant'.

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Review Level Analysis
Interventions for Enuresis



J Clin Epidemiol. 63:875-82 PMID: 20080027

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Trial or Review summaries for NMA?

	Review level summaries		Trial level summaries	
Treatment	Prob est	RR (No treatment)	Prob est	RR (No treatment)
No treatment				
Alarm	0.08	0.40 (0.31, 0.53)	0.03	0.41 (0.30, 0.53)
DBT	0	0.82 (0.66, 1.03)	0.01	0.82 (0.66, 1.02)
Desmopressin	0	0.54 (0.35, 0.84)	0.04	0.58 (0.37, 0.88)
Imipramine	0	0.68 (0.53, 0.89)	0	0.69 (0.52, 0.89)
Psych therapy	0.01	0.65 (0.35, 1.22)	0.02	0.69 (0.35, 1.22)
DBT + alarm	0.78	0.19 (0.05, 0.76)	0.78	0.24 (0.05, 0.73)
Diclofenac	0.13	0.46 (0.16, 1.38)	0.12	0.53 (0.16, 1.38)

Work in progress: do not cite

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Example of a Synthesis

An overview of reviews evaluating the effects of financial incentives in changing healthcare professional behaviours and patient outcomes

John F. Burke¹, Kevin Wiggall², Anthony Scott³, Gerd Hoegherv⁴, Steve Parrott⁵, Peter E. Hayes⁷

DOI: 10.1002/14651858.CD008608.

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Reviews included

- 2 Cochrane reviews
- 2 non-Cochrane reviews

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Stated Aims of the Reviews

- To estimate the effectiveness and efficiency of **interventions to change outpatient referral rates** or **improve outpatient referral appropriateness**
- To review the impact of **payment systems on the behaviour of primary care physicians**.
- To assess the relationship between **explicit financial incentives and the provision of high-quality health care** by systematically reviewing empirical studies.
- To determine the effects on **drug use, healthcare utilisation, health outcomes and costs** (expenditures) of (pharmaceutical) policies, that intend to **affect prescribers by means of financial incentives**.

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A Priori Classification of Types of Incentives

- **Payment for working for a specified time period** (e.g. salary, sessional payment)
- **Payment for each service/episode/visit** (fee-for-service)
- **Payment for providing care for a patient or specific population** (e.g. capitation)
- **Payment for providing a pre-specified level or change in activity or quality of care** (e.g. includes target payments, bonuses)
- **Mixed and other** (comprising more than one of the above groups or not classifiable)

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Outcomes From The 4 Reviews

- **Consultation/Visit rates**
- **Processes of care**
- **Referrals/Admissions**
- **Compliance with guidelines**
- **Prescribing costs**

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Outcome	Consultation or Visit rates	Processes of care	Referrals or Admission	Compliance with guidelines	Prescribing costs
Intervention					
Payment for working for a specified time period					
Payment for each service episode/visit					
Payment for providing care for a patient or a specific population					
Payment for providing a pre- specified level or providing a change in activity or quality Mixed or other systems					

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Outcome	Consultation or Visit rates	Processes of care	Referrals or Admissions	Compliance with guidelines	Prescribing costs
Intervention Payment for working for a specified time period Payment for each service/visit/phone/visit Payment for providing care for a patient or a specific population Payment for providing a pre- specified level or providing a change in activity or quality Mixed or other system					

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Outcome	Consultation or Processes of Visit times	care	Referrals or Admission	Compliance with guidelines	Prescribing costs	Overall effect within intervention
Intervention						
Payment for working for a specified time period						
Payment for each service episode/visit						
Payment for providing care for a patient or a specific population						
Payment for providing a pre- specified level or providing a change in activity or quality Mixed or other systems						
Overall effect within outcomes						

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Overviews vs. Intervention Reviews

- Overviews less resource intensive
 - Easier Search
 - Possibility of review level analysis

BUT

- Depends on availability of enough good reviews
- In some cases, an intervention review may be easier

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Overview as Part of a Process

- Protocol specifies the question
- Overview as the first step
 - May adequately address the question
- Intervention review if resources allow
 - Informed by overview process and results

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Where to Learn More

- Comparing Multiple Interventions Methods Group
- Cmimg.cochrane.org
