

Evidence of effectiveness

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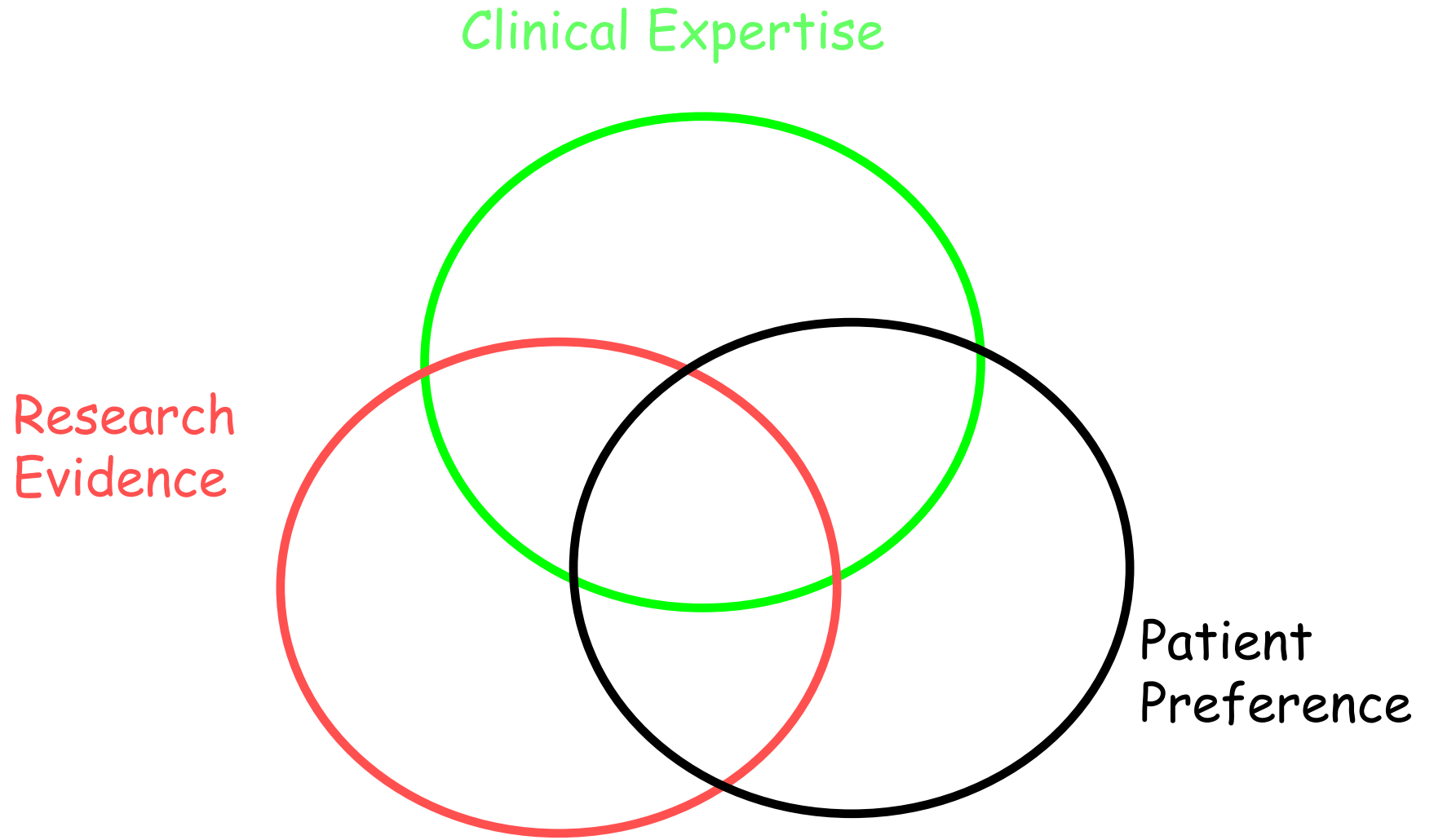
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Evidence-based medicine is:

"conscientious, explicit and judicious use of current best evidence in making decisions about individual patients"

(Sackett DL et al. BMJ 1996; 312:71-2)

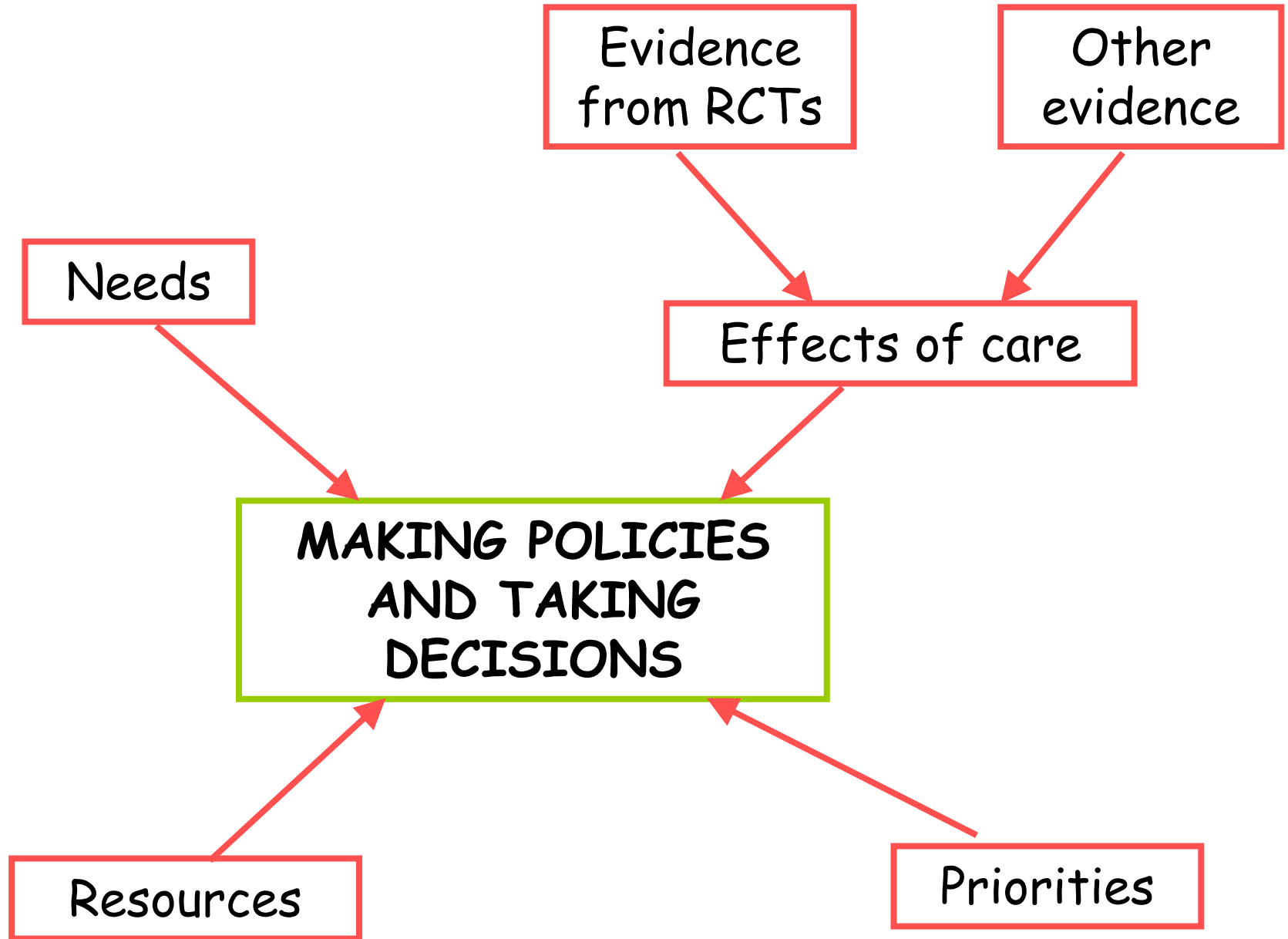


A model for evidence-based clinical decisions
(from Haynes et al, 1996)

Evidence-based health care:

Takes account of evidence at a population level as well as encompassing interventions concerned with the organisation and delivery of health care.

Evidence Based Practice in Primary Care. Silagy C & Haines A (Eds). London: BMJ Books, 1998.



What evidence?

- 3000 new medical articles per day
 - ⇒ 1000 on Medline
 - ⇒ 46 RCTs
- In 1976 Medline contained 3810 articles on hypertension. In 1996 there were 7591.

The Key to EBP

Making good quality research evidence readily available

Hence promoting EBP entails:

- location of evidence
- critical appraisal
- synthesis of findings and
- dissemination

Synthesising research evidence

- Systematic review: the application of scientific strategies that limit bias to the systematic assembly, critical appraisal, and synthesis of all relevant studies on a specific topic
- Meta-analysis: a systematic review that employs statistical methods to combine and summarise the results

Strengths of systematic reviews

- Use scientific strategies to limit bias
- Summarise accumulated state of knowledge
- Highlight important unresolved issues
- Gain power from combining multiple studies
- Address questions in a timeframe not achievable through single studies
- Quantify outcomes

Aspects of critical appraisal

→ Quality of evidence

⇒ methods used to minimise bias - about reliability of data

→ Relevance of evidence

⇒ relevance of outcome measures and applicability of results to other treatments, settings and patients

→ Strength of evidence

⇒ magnitude, precision and reproducibility of effect

External validity

- Information about typical treatment population
- Question of clinical significance
- Practicality
- Client acceptance

Systematic review quality

- Is it a review of randomised trials of the treatment you're interested in?
- Does it include a methods section that describes how all the relevant trials were found?
- Did the authors assess the trials' individual validity?
- Were the results consistent from study to study?

Meta-analysis validity

Meta-analysis is only valid where

- the primary literature is of good quality (ie. low risk of bias)
- heterogeneity in the response to treatment of the tested population is small and well-understood
- interest centres on estimation of a specific, critical parameter of outcome

Evidence rating system

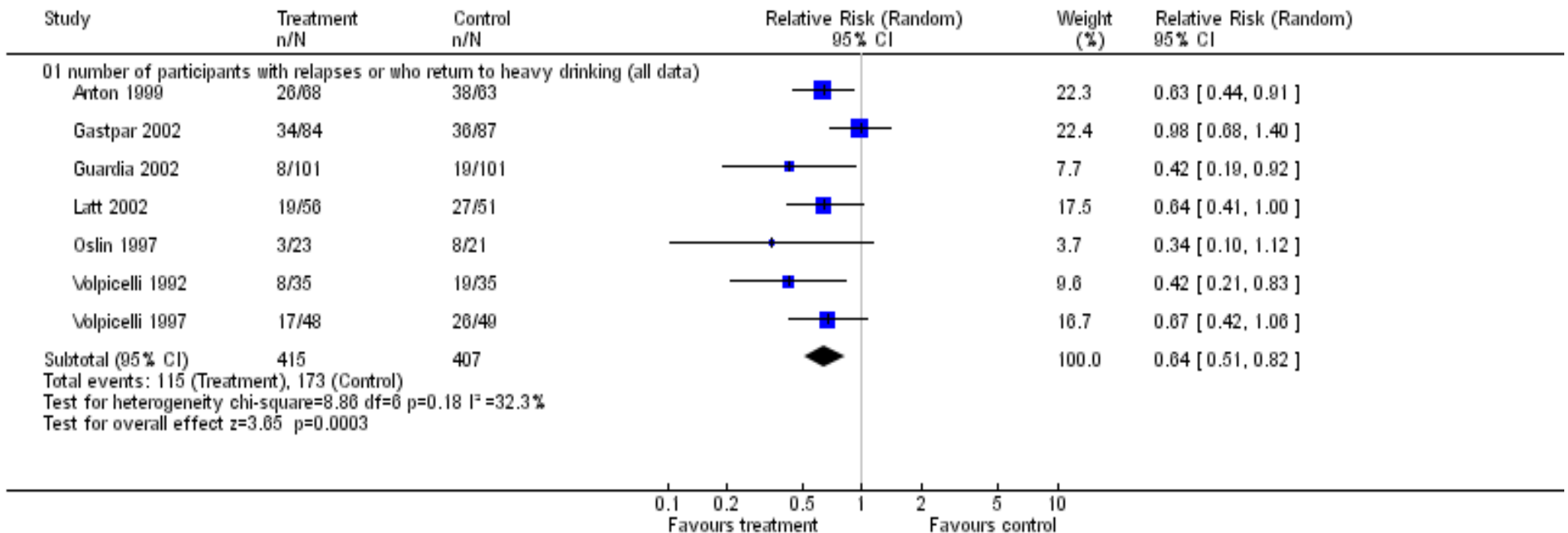
- **** Strong (≥ 3 RCTs, low risk of bias, consistent)
 - *** Good (≥ 3 RCTs, low risk of bias, variability of findings)
 - ** Moderate (2 RCTs low risk, or ≥ 3 RCTs with risk but consistent findings)
 - * Some (≥ 2 RCTs risk of bias and variability, or 1 RCT low risk of bias)
- No rating given if no RCT evidence

Opioid antagonists

- Do not increase the probability of total abstinence ***
- Decrease the risk of relapse to heavy drinking,
NNT=7****
- Decrease alcohol consumption – 1 drink/drinking day,
3.4 drinks/week, ***
- Prolong interval between drinking and relapse by 17
days ****

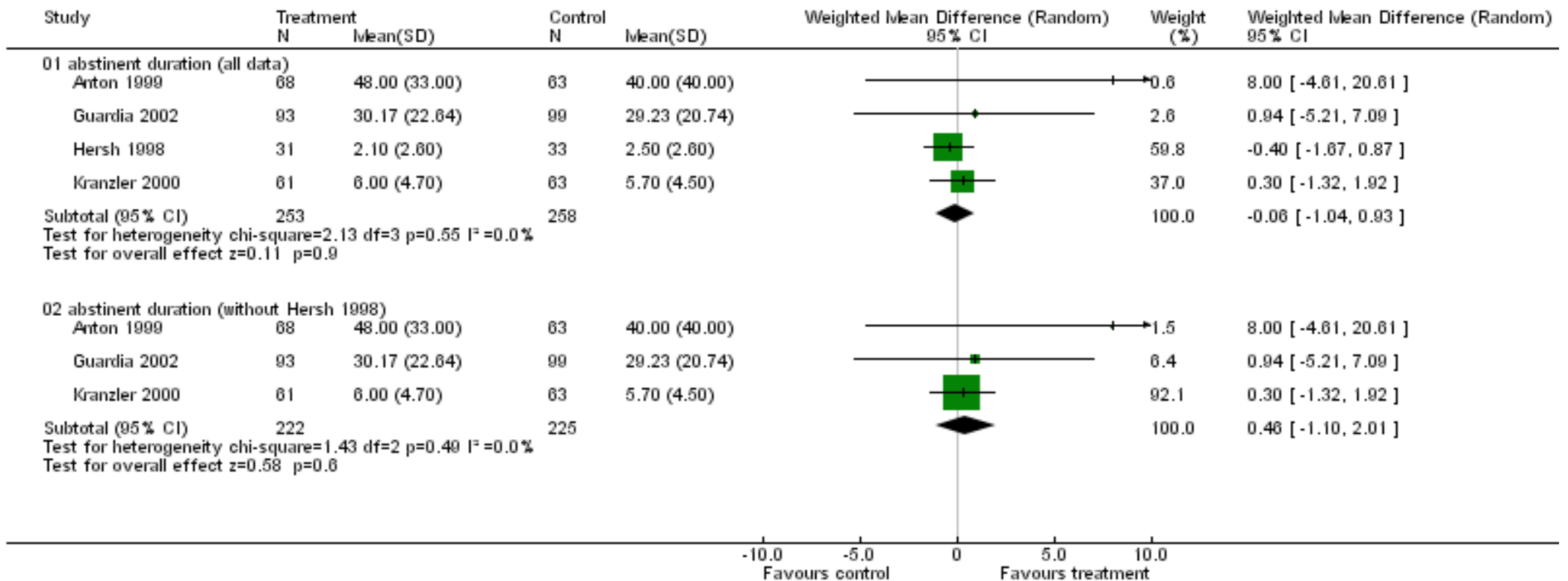
Meta-analysis example 1

Review: Opioid antagonists for alcohol dependence
 Comparison: 01 NTX vs Placebo (short-term outcomes)
 Outcome: 01 number of participants with relapses or who return to heavy drinking



Meta-analysis example 2

Review: Opioid antagonists for alcohol dependence
 Comparison: 01 NTX vs Placebo (short-term outcomes)
 Outcome: 03 time to first drink



Opioid antagonists: adverse effects

- Increase risk of abdominal pain or gastrointestinal symptoms (NNT=7) and nausea or vomiting (NNT=8) ****
- Increase risk of premature withdrawal due to adverse effects ****

Acamprosate

- Increased probability of continuous abstinence during treatment (NNT=8)****
- Decreased probability of relapse to heavy drinking (NNT=17) ****
- Increased cumulative abstinence duration – around 13% more days ****
- Effect on drinks/drinking day unclear

Acamprosate: adverse effects

- Increased risk of diarrhoea or gastrointestinal effect (NNT=14) ****
- No significant increase in headache**, overall adverse effects**, or need for dose reductions**

Naltrexone + acamprosate

- COMBINE Study raise some doubt about the value of combining naltrexone and acamprosate because of:
 - the increase risk of adverse effects
 - significantly more require dose reduction
 - apparent lack of additional benefit
 - Need more evidence

Clinical implications: acamprosate and naltrexone

- Acamprosate and naltrexone are both effective for relapse prevention
- Naltrexone is more effective in preventing lapses becoming relapses
- Acamprosate is more effective in promoting abstinence

Disulfiram

- No significant increase in number achieving and maintaining abstinence*
- May increase number of treatment days without drinking*
- Adverse drug reaction rate 1/200-2000 patients per year: fatal hepatitis 1 in 30,000 patients treated per year
- Effective in combination?

Buspirone

- Significantly increases retention of people with anxiety disorder****
- May reduce days with drinking but not likelihood of total abstinence*
- Increased risk of adverse effects (NNT=6) ***

Clinical implications: other

- Antidepressants are not effective for relapse prevention but have value for depression associated with alcohol dependence
- Buspirone has promise for comorbid anxiety disorders and alcohol dependence
- Limited evidence for other approaches

The Future

- Particular areas of research needed:
 - significance of different types and intensities of psychosocial support as adjuncts to medication
 - type and severity of alcohol dependence as factors that might influence the effectiveness of treatment