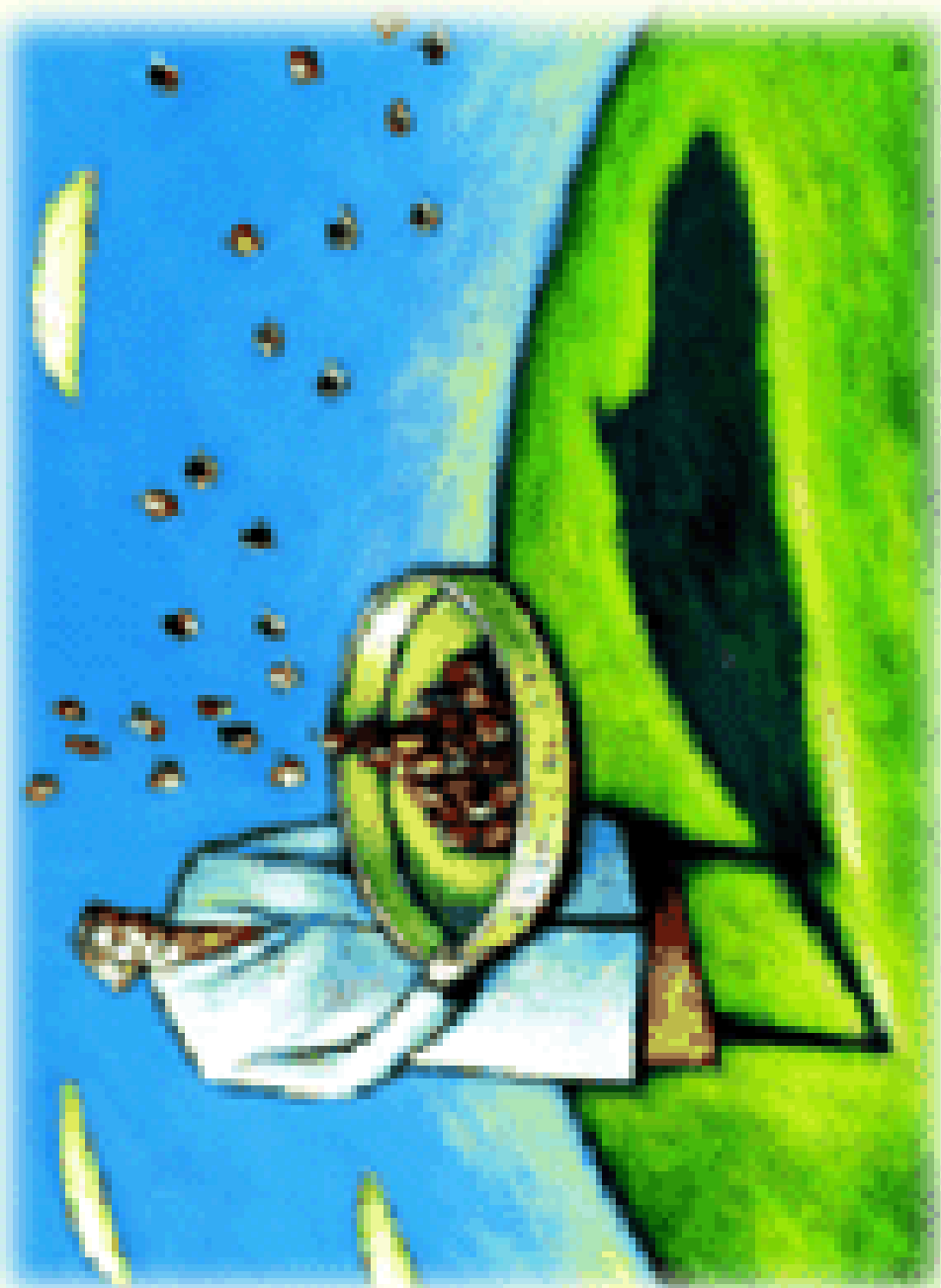


Meta-analysis in Neonatology

Can we mix apples and oranges?

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Definition

An EBM review article...

“The review article itself should be the product of scientific investigation in which the participants are original investigations (research) rather than patients”

-- R. Brian Haynes, MD, PhD

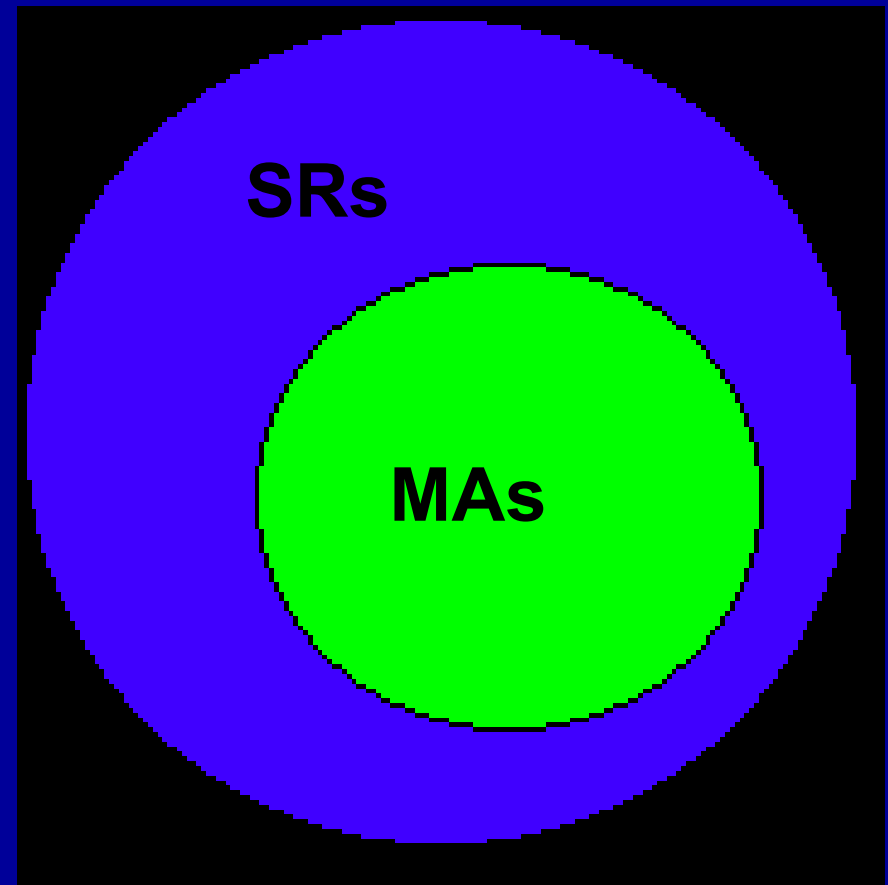
Definition

A systematic review is a summary of the medical literature that uses explicit methods to perform a thorough literature search and critical appraisal of individual studies and that uses appropriate statistical techniques to combine these valid studies

Systematic reviews Vs. Meta-analysis

Meta-analysis is part of the systematic review,


It is a collection of statistical techniques for combining studies



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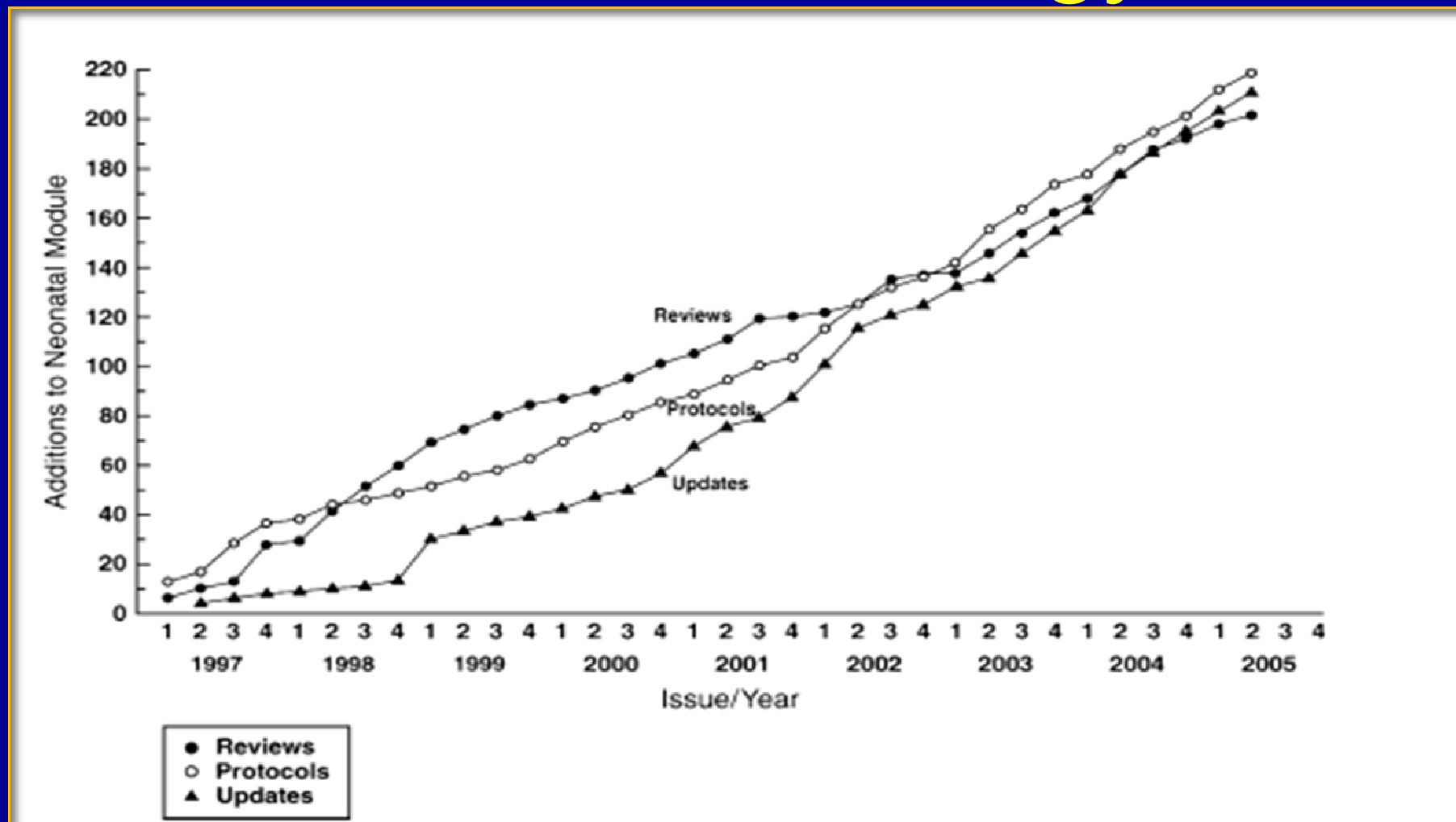
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Systematic Reviews in Neonatology



Davis, P; Cochrane reviews in neonatology: past, present and future. seminars of fetal and neonatal medicine. 2006 Apr;11(2):111-6

Types of Reviews

Feature	Narrative	Systematic
Question	Broad	Focused
Sources and Search	Not usually specified	Comprehensive
Selection	Not usually specified	Criterion based selection
Appraisal	variable	Rigorous appraisal
Synthesis	Often qualitative	Often quantitative
Inferences	Sometimes evidence based	Usually evidence based

Example of a narrative review

Treatment and prevention of necrotizing enterocolitis

Jane S. Lee, Richard A. Polin*

Columbia University, College of Physicians and Surgeons, Children's Hospital of New York-Presbyterian, CHS 115, 3959 Broadway, New York, NY 10032, USA

Received 1 June 2003; accepted 1 July 2003

Introduction

Necrotizing enterocolitis (NEC) is the most common serious, acquired gastrointestinal disease in the

Epidemiology

As a result of the many advances in neonatal intensive care, NEC has emerged as a disease of NICU survivors. The overall incidence is 1–3 cases per

Pathogenesis of necrotizing enterocolitis

Although NEC is an important cause of neonatal morbidity and mortality, its pathogenesis remains

Treatment of necrotizing enterocolitis

Following the clinical diagnosis of NEC, the mainstay of treatment remains medical stabilization. A regimen consisting of bowel rest, gastric decom-

Example of a systematic review

Prophylactic intravenous indomethacin for preventing mortality and morbidity in preterm infants (Review)

Fowlie PW, Davis PG

BACKGROUND

Premature infants with a patent ductus arteriosus are at increased risk of more prolonged and more severe respiratory distress syndrome, bronchopulmonary dysplasia and death when compared

OBJECTIVES

To determine the effectiveness of prophylactic intravenous in

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

SEARCH STRATEGY FOR IDENTIFICATION OF STUDIES

Steps in Conducting a Systematic Review

Focused clinical question

Determine the inclusion criteria

Searching the literature

Selecting studies for inclusion

Evaluating the quality of selected studies

Pooling of the data

Summary and Conclusion

Systematic Reviews

Evaluating the report

- ❑ Different tools can be used
- ❑ Users guide to medical literature
- ❑ Overview Quality Assessment Questionnaire
- ❑ QUOROM statement
- ❑ Worksheet developed by Information Mastery Working Group

Systematic Reviews - Evaluating the report

Relevance

Validity

Evaluating the Usefulness of Review Articles

Determine Relevance

Is this article worth taking the time to read? If the answer to any of these questions is No, it may be better to read other articles first.

Based on the conclusion of the abstract:

- A. Is the article proposing to answer a specific clinical question or questions? Did the authors study an outcome that patients would care about?
Yes (go on) No (stop)
- B. Is the problem studied one that is common to your practice and the intervention feasible?
Yes (go on) No (stop)
- C. Will this information, if true, require you to change your current practice?
Yes (go on) No (stop)

Determine Validity

If the answers to all three questions above are Yes, then continued assessment of the article is mandatory.

D. Finding the studies?

- Were the methods used to locate relevant studies comprehensive and clearly stated?.....Yes No (Stop)
- Did they clearly outline study inclusion criteria that generalize to my practice?.....Yes No (Stop)
- Was the study selection independently performed by at least two investigators?Yes No

E. Validity: Did the authors perform an "official" validity assessment of the studies

- using appropriate criteria?..... Yes No (Stop)
- Was the assessment independently performed by at least two investigators?.....Yes No
 - Were the included studies reasonably valid?Yes No
If not, how did the authors handle this (a priori exclusion or sub-analysis based on study quality)?
What effect might the lack of validity have on the results?

F. Analyzing the Data: Is it reasonable to combine these studies?

- Were the included studies statistically homogeneous?.....Yes No
If not, how was this addressed (reasonable explanation, random effects model)?
- Were the populations, interventions, outcomes, and outcome measurements combined in a way that makes intuitive sense?Yes No
- Could publication bias have occurred?Yes No

H. Interpreting the results: were they meaningful?

- Were the results statistically different?Yes No
 - If so, were they clinically significant?Yes No
 - If not, was the power adequate to find a difference?Yes No
- What will you do with the results?

Systematic Reviews - Evaluating the report

Determine Relevance

Is it worth reading the whole article (read the abstract conclusion):

- ✓ Did the review address an important focused question
- ✓ Did the author of the review study an outcome that it is important to the patient you are caring for!
- ✓ Is it a *common* problem in your practice
- ✓ Will the information presented require you to change your current practice

Systematic Reviews - Evaluating the report

Determine Validity Finding Studies

- ❖ Was the search strategy clearly stated and comprehensive?
 - o Appropriate terms used
 - o Reproducible
 - o Comprehensive

- ❖ Was the inclusion criteria clearly outlined?
 - o Narrow criteria..... Less generalisable

- ❖ Two investigators selected the studies independently?

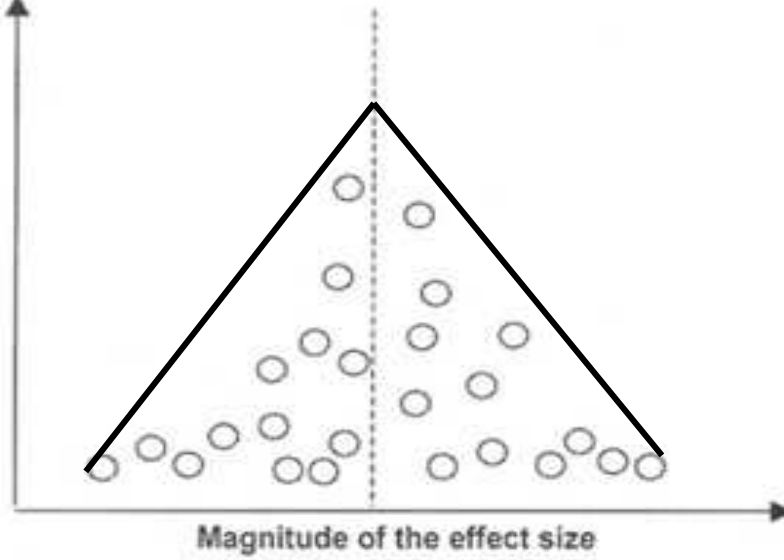
Determine Validity Finding Studies Publication Bias

Studies of significant results are more likely to be published than studies without significant results

How to assess for publication bias? **funnel plot**

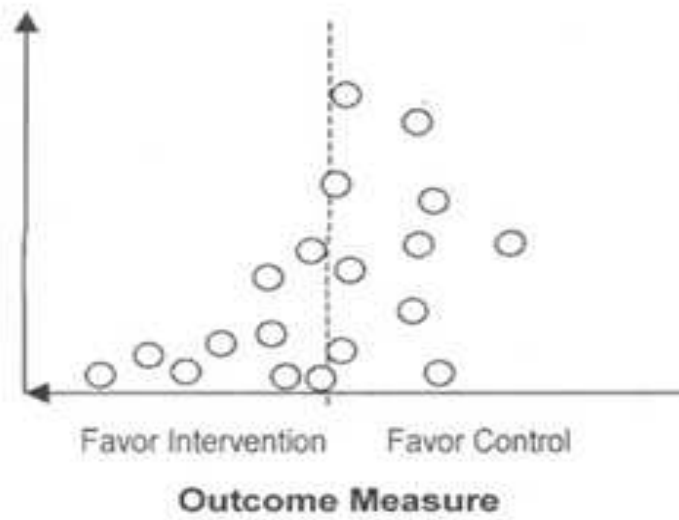
Precision of estimate of treatment effect

Sample size



Precision of estimate of treatment effect

Sample size



Systematic Reviews - Evaluating the report

Determine Validity Validity Assessment

- ❖ Was the validity of included studies assessed using appropriate criteria?
- ❖ Was it done independently?
- ❖ Were the included studies reasonably valid?

Systematic Reviews - Evaluating the report

Analyzing the Data

Homogeneity Assessment

- ✓ Did all the studies produce somewhat similar results
- ✓ Heterogeneity can be assessed by two ways:
 - ❑ graphically (forest plot)
 - ❑ statistically (test of homogeneity)

If not homogenous, how was this handled?

- o ignored
- o incorporated (using random effects)
- o explained

Homogeneity Assessment Forest Plot

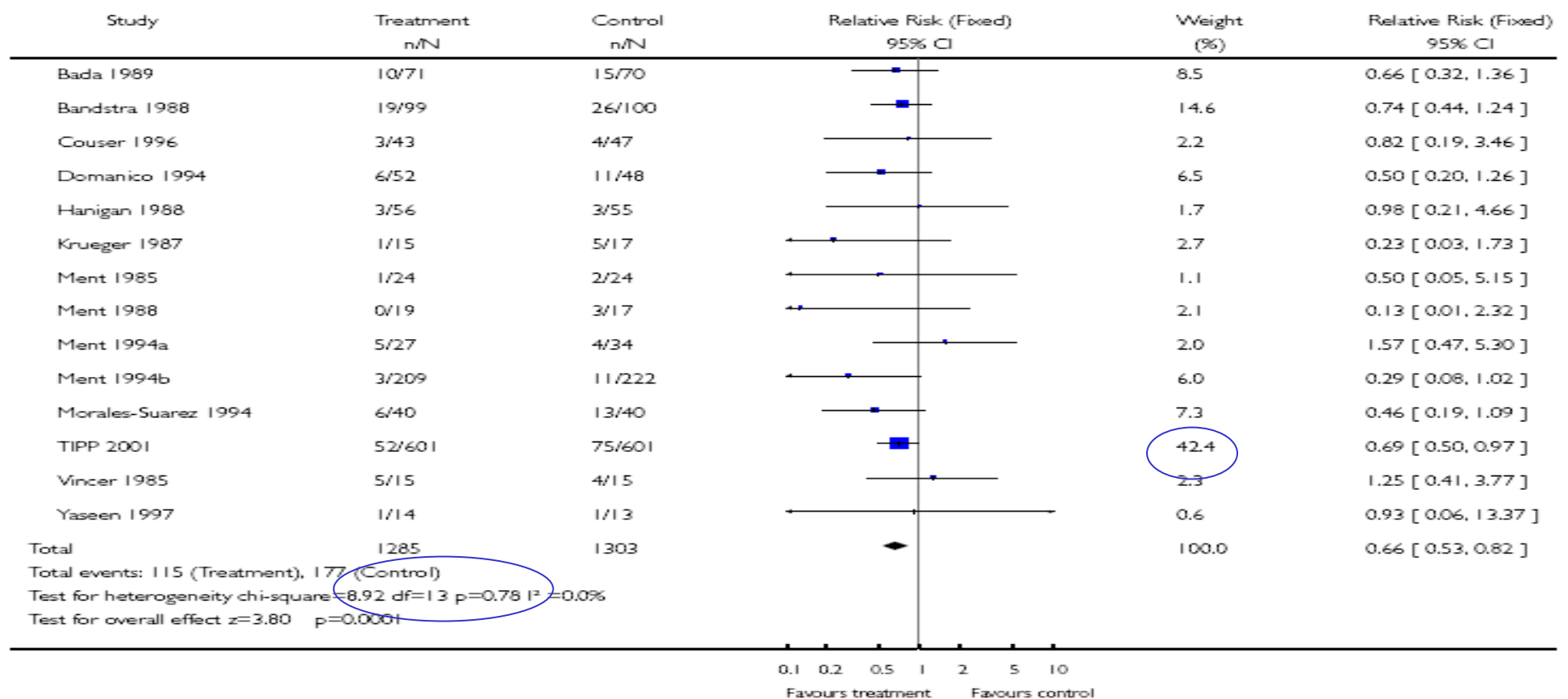
Fig. 4. Comparison 01 Prophylactic indomethacin vs. control

01.04 IVH Grade 3 and 4

Review: Prophylactic intravenous indomethacin for preventing mortality and morbidity in preterm infants

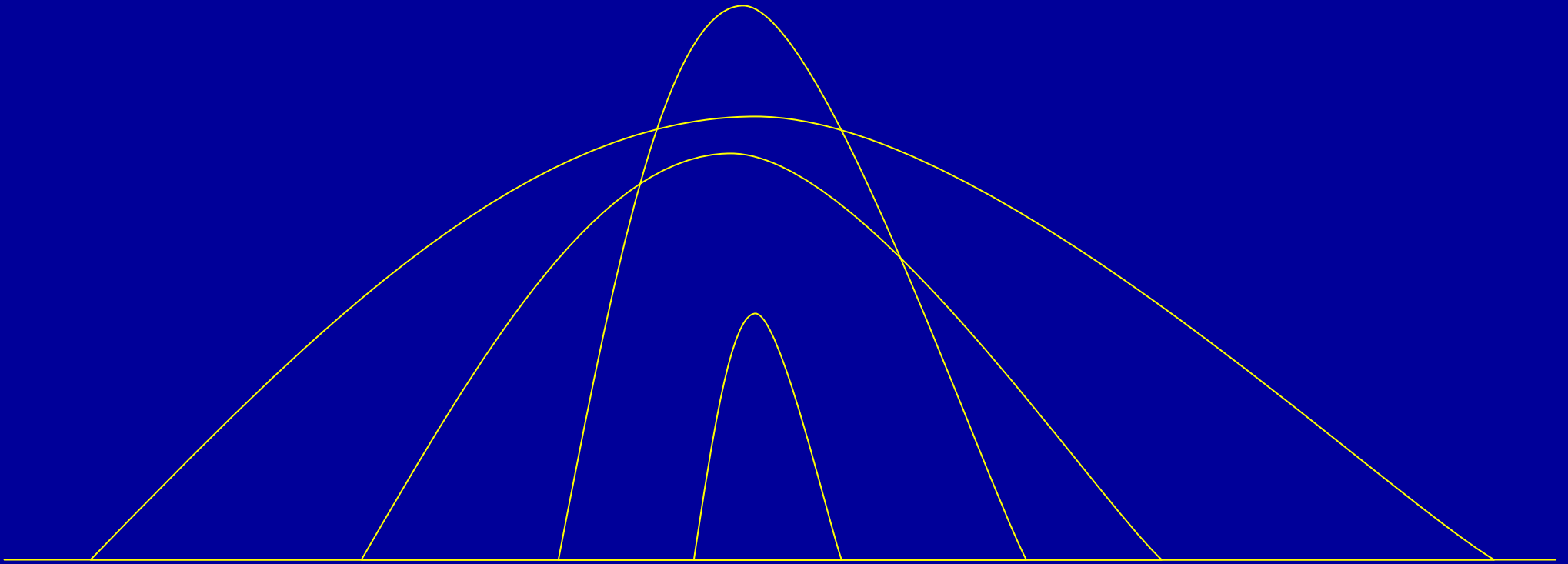
Comparison: 01 Prophylactic indomethacin vs. control

Outcome: 04 IVH Grade 3 and 4



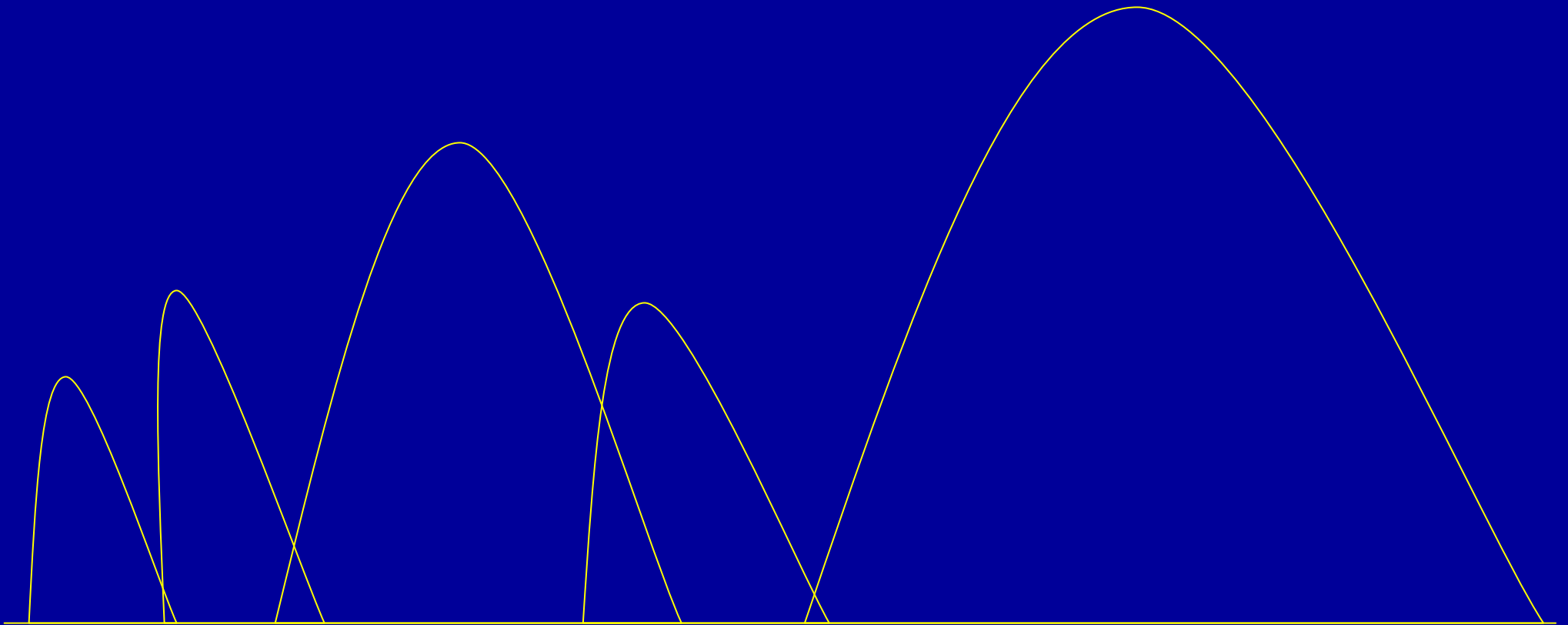
Fixed Vs. Random Effect Model

Fixed effect model



Fixed Vs. Random Effect Model

Random effect model



Systematic Reviews - Evaluating the report

Interpreting the results

Which measure to use?

<i>Outcome</i>	Binary	Continuous
<i>Effect Estimate</i>	OR, RR, RD NNT	MD and SMD

Interpreting the results Estimating the Effect

Odds ratio

- The odds of an event is the probability of it occurring compared to the probability of it not occurring
- The odds ratio, is the ratio of the odds of an event in the treatment group compared to the odds in the control group
- Odds ratio of 1 means that there is no difference

Relative risk

- The ratio of people with an event in the treatment compared to the risk in the control group
- A relative risk of 1 means that there is no difference
- Relative risk is easier to understand as compared to odds ratio
- In a rare event, OR usually equals RR
- In a common event, OR produces a larger treatment effect as compared to RR

Statistics on One Plate

$$OR = \frac{ad}{cb}$$

		Disease/ Outcome	
		+	-
Intervention/ Exposure	+	a	b
	-	c	d

$$RR = \frac{a(c+d)}{(a+b)c}$$

$$RD = \frac{a}{a+b} - \frac{c}{c+d}$$

Systematic Reviews - Evaluating the report

Interpreting the results

How Precise are the results?

Where confidence intervals around the estimate effect calculated?

❖ *if Statistically significant*

- Was it clinically significant
- Calculate the NNT and use your clinical judgment

❖ *If the results were insignificant*

- Was there enough power to find a significant difference

Systematic Reviews - Evaluating the report

What Will You Do With These results?

- Can the results be applied your patients
- Where all clinically important outcomes considered
- Are the benefits of worth the harm and cost

Thank you