

Critical Appraisal Course for Emergency Medicine Trainees

Module 6

Systematic Reviews

Systematic Reviews

- What is a systematic review?
- The literature search
- Publication bias
- Selection of studies
- Assessment of study quality
- Heterogeneity
- Meta-analysis

What is a systematic review?

- Scientific study using IMRAD
- Addresses specific question
- Uses existing data
- Secondary research, not primary
- Unbiased synthesis of available data

What is a narrative review?

- Not a systematic review
- Not a scientific study
- Broad overview of an issue
- May incorporate author's opinion
- Selected data are presented
- Entertaining, interesting or provocative, but not necessarily objective

Stages of a systematic review

1. Literature searching and retrieval
 2. Selection of appropriate papers
 3. Quality assessment of selected papers
- Ideally undertaken by two blinded, independent reviewers
 - Kappa score for selection decisions
 - Numbers of articles excluded at each stage

Literature search: published

- Electronic databases: Medline, Embase, Cinahl, Cochrane database
- Bibliographies of retrieved articles
- Hand search of key journals

Literature search: unpublished

- Grey literature: reports (government or academic), conference proceedings, internet, libraries, professional societies, Kings Fund, Nuffield
- Research registers: National Research Register, ClinicalTrials.gov
- Contact with researchers or “experts”
- Manufacturers or pharmaceutical industry

Publication bias

Relevant studies may be missed because:

- They are not written up
- They are not submitted for publication
- They are not accepted for publication
- They are published in obscure or non-English language publications

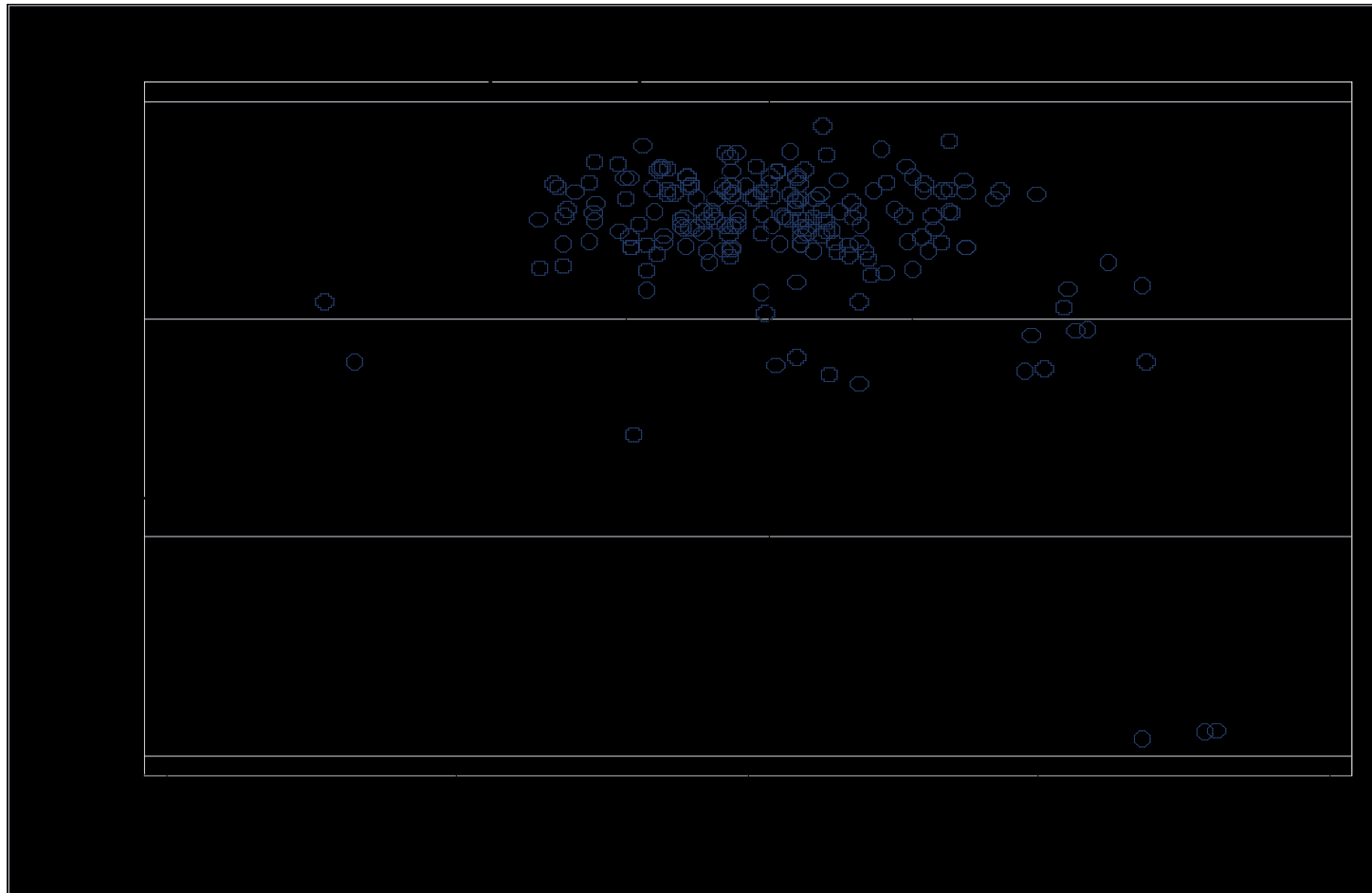
Publication bias

- Clinical trials are more likely to be written-up, submitted, published and achieve a high profile if they are positive
- Diagnostic cohort studies are (probably) more likely to be written-up, submitted, published and achieve a high profile if they report high sensitivity and specificity

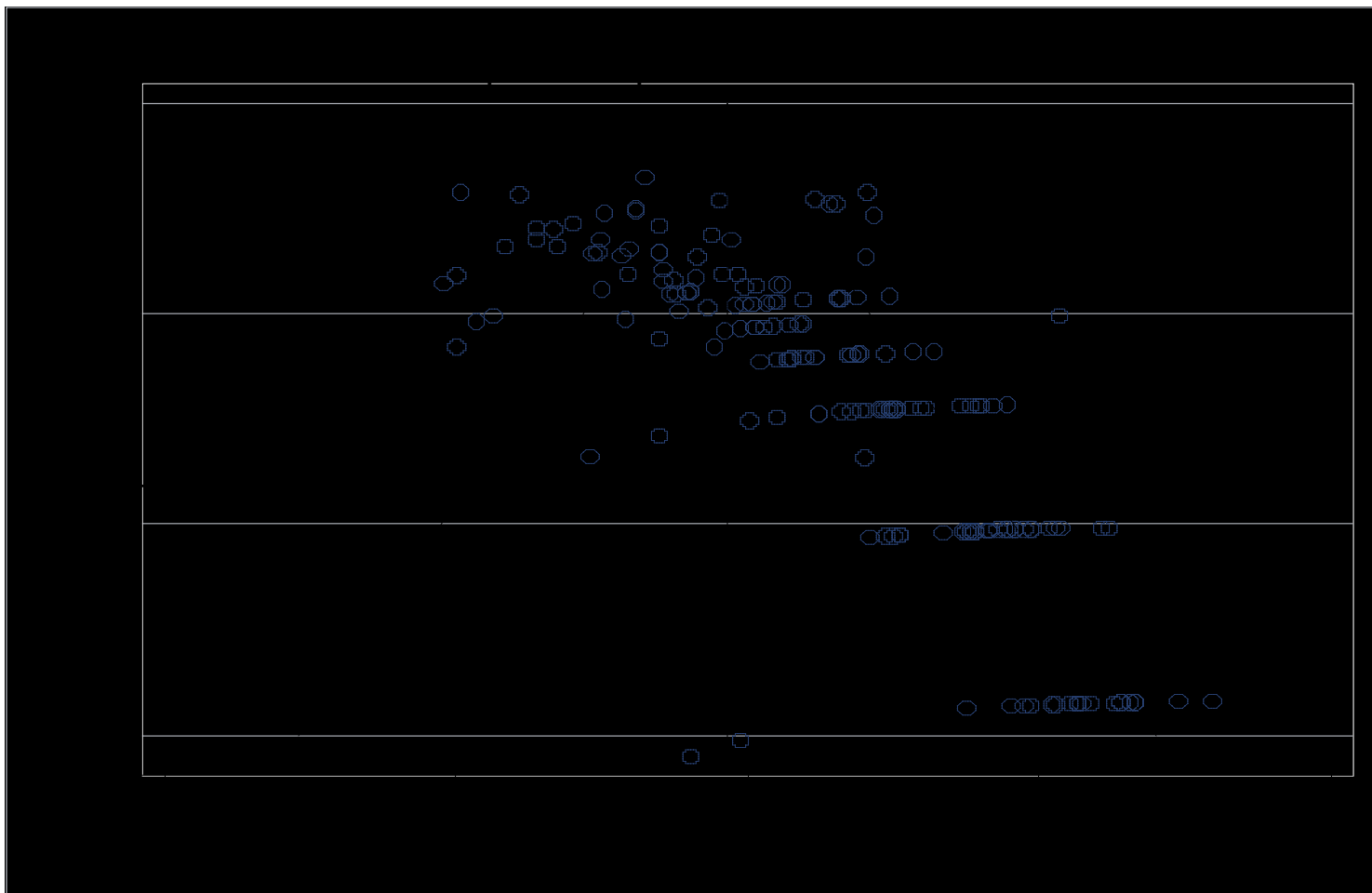
Funnel plot

- Used to seek evidence of publication bias
- Plot of a measure of study precision (e.g. sample size) against effect size (e.g. relative risk reduction)
- Should be shape of an inverted funnel
- Asymmetry suggests bias
- Insensitive and subjective

Symmetrical funnel plot



Asymmetrical funnel plot



Selection of articles

Two-stage process:

- Scanning abstracts / titles
- Review of full articles

Study objective should determine
selection criteria

Selection criteria

- Study population
- The intervention (and control)
- Outcome
- Study design

Other criteria

- Sample size
- Language of publication
- Mainstream journals only
- Insufficient data presented
- Year of publication

Assessment of study quality

- Objective criteria known to influence study quality
- Two blinded, independent reviewers
- Clinical trials: allocation concealment, blinding, follow-up (Jadad score)
- Diagnostic studies: independent reference standard, blinding, case-control v cohort

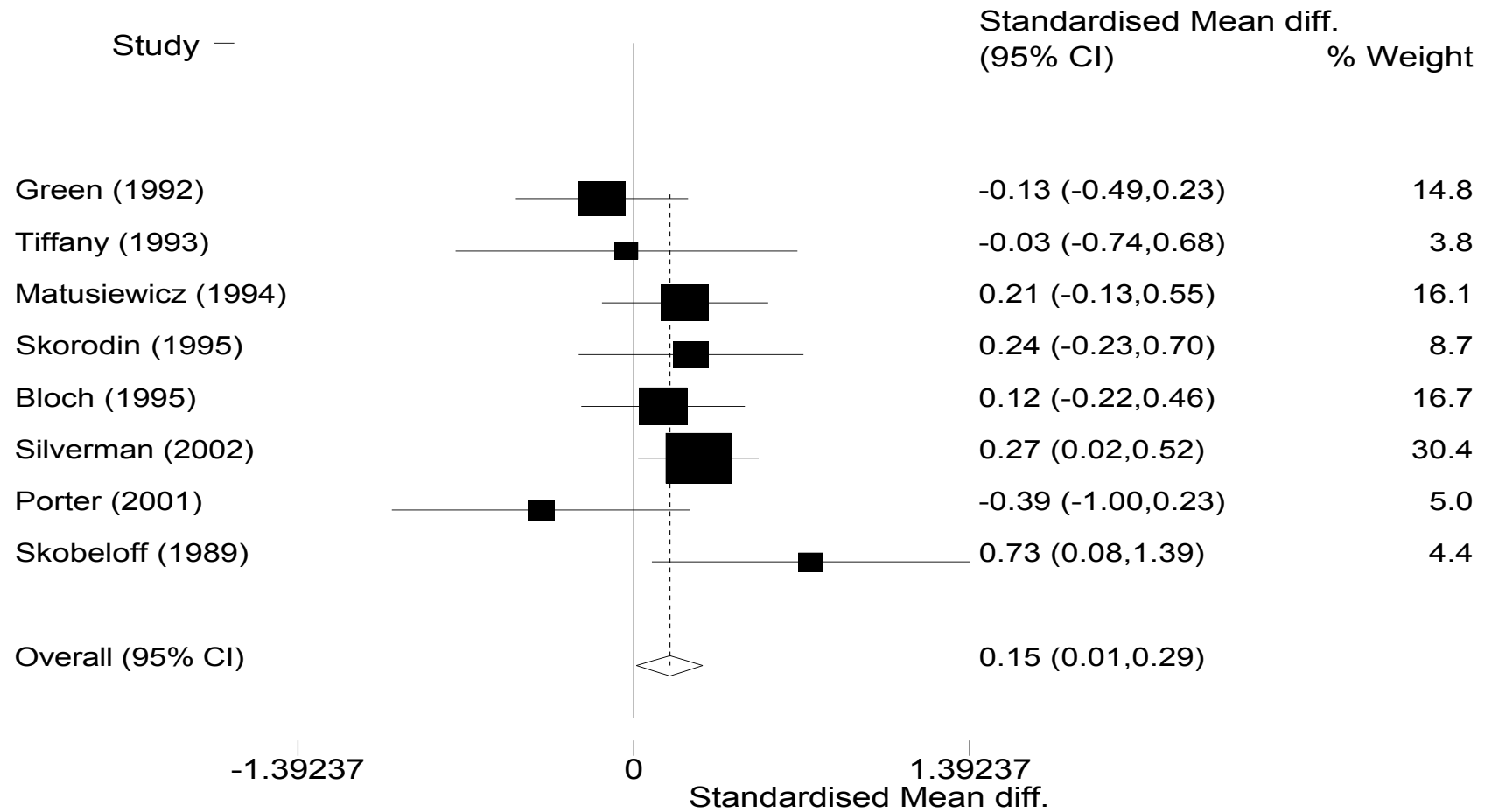
Heterogeneity of effect

- Studies addressing the same question should give the same answer
- Results should only differ because of random error
- If variation in results is more than expected due to random error, then heterogeneity is present
- May be due to differences between study populations, interventions, outcome measurement or study design

Looking for heterogeneity

- The Forest plot: Do confidence intervals overlap?
- Statistical tests of heterogeneity: Significant test provides evidence of heterogeneity (non-significant does not rule out)
- Look at study population characteristics, interventions, controls, outcomes and design (quality criteria)

Forest Plot



Meta-analysis

- Synthesis of data from separate studies to give overall estimate of effect
- Increases precision of estimates to overcome type II (false negative errors)
- Does not overcome bias: combining biased data will produce a precise, inaccurate result
- Combining heterogeneous studies is controversial

Appraising meta-analysis

- Does it make sense to combine these studies?
- Are the patients the same?
- Are the interventions the same?
- Are the controls the same?
- Are the outcomes comparable?
- Are the primary studies biased?

Summary

- Is this a systematic or narrative review?
- Is the literature search comprehensive?
- Have studies been objectively selected?
- Has primary study quality been assessed?
- Is there evidence of heterogeneity?
- Is meta-analysis appropriate?

Any questions or comments?