CEBM CENTRE FOR EVIDENCE BASED MEDICINE

Rapid Critical Appraisal of RCTs and Systematic Reviews

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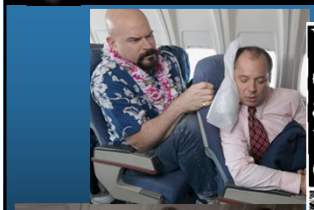
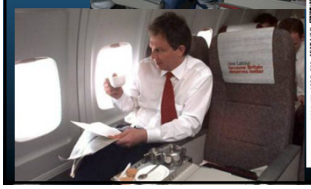


Victims of DVT are told that they can't sue

(Except if it's in Australia)



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Step 3 in EBM: appraisal

1. Formulate an answerable question
2. Track down the best evidence
3. Critically appraise the evidence for:
   - Validity
   - Impact (size of the benefit)
   - Applicability
4. Integrate with clinical expertise and patient values
5. Evaluate our effectiveness and efficiency
   - keep a record; improve the process

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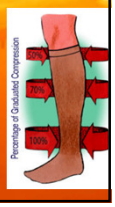
Clinical Question
In people who take long-haul flights does wearing graduated compression stockings prevent DVT?



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Google

Searching for critical appraisal checklists randomized controlled trials.

11,100 articles (0.40 seconds)

A CHECKLIST FOR APPRAISING RANDOMIZED CONTROLLED TRIALS

1. Was the objective of the trial sufficiently described?
2. Was a satisfactory statement given of the diagnostic criteria for entry to the trial?
3. Were concurrent controls used (as opposed to historical controls)?
4. Were the treatments well defined?
5. Was random allocation to treatments used?
6. Was the potential degree of blindness used?
7. Was there a satisfactory statement of criteria for outcome measures? Was a primary outcome measure identified?
8. Were the outcome measures appropriate?
9. Was a pre-study calculation of required sample size reported?
10. Was the duration of post-treatment follow-up stated?
11. Were the treatment and control groups comparable in relevant measures?
12. Were a high proportion of the subjects followed up?
13. Were the drop-outs described by treatment and control groups?
14. Were the side-effects of treatment reported?
15. How were the ethical issues dealt with?
16. Was there a statement adequately describing or referencing all statistical procedures used?
17. What tests were used to compare the outcome in test and control patients?
18. Were 95% confidence intervals given for the main results?
19. Were any additional analyses done to see whether baseline characteristics (prognostic factors) influenced the outcomes observed?
20. Were the conclusions drawn from the statistical analyses justified?

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VALIDITY

QUESTION:

Participants

Intervention Group (IG)
& Comparison Group
(CG)

Outcome

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QUESTION:

Participants

Intervention Group (IG) & Comparison Group (CG)

Outcome

	+	–
+	A	B
–	C	D

VALIDITY

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QUESTION:

Participants

Intervention Group (IG) & Comparison Group (CG)

Outcome

	+	–
+	A	B
–	C	D

VALIDITY

Recruitment

Allocation concealment? comparable groups?

Maintenance

treated equally? compliant?

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QUESTION:

Participants

Intervention Group (IG) & Comparison Group (CG)

Outcome

	+	–
+	A	B
–	C	D

VALIDITY

Recruitment

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QUESTION:

Participants

Intervention Group (IG) & Comparison Group (CG)

Outcome

	+	–
+	A	B
–	C	D

VALIDITY

Recruitment

Allocation concealment? comparable groups?

Maintenance

treated equally? compliant?

Measurements blind? OR objective?

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QUESTION:

Participants

Intervention Group (IG) & Comparison Group (CG)

Outcome

	+	–
+	A	B
–	C	D

VALIDITY

Recruitment

Allocation concealment? comparable groups?

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QUESTION: DESIGN: VALIDITY

Participants — Recruitment?

Allocation?

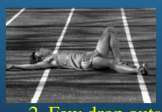
Intervention Group (IG) & Comparison Group (CG) — I G / C G

Maintenance of allocation?

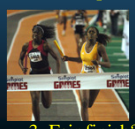
Outcome — A B C D

Measurement of outcomes?

1. Fair start?



2. Few drop outs?



3. Fair finish?

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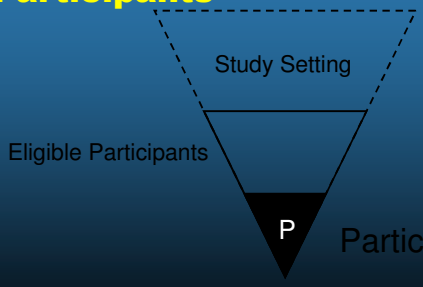
Participants



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Using the PICO to orient us

Clinical Question

In people who take long-haul flights does wearing graduated compression stockings prevent DVT?

ARTICLES

Frequency and prevention of symptomless deep-vein thrombosis in long-haul flights: a randomised trial

John H Scurr, Samuel J Machin, Sarah Bailey-King, Ian J Mackie, Sally McDonald, Philip D Coleridge Smith

Scurr et al, Lancet 2001; 357:1485-89

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Participants

Study Setting: volunteers, UK, ? 1990s

Eligible Participants: no previous DVT, > 50 yrs, planned economy air travel 2 sectors > 8 hours

P

Participants: 200, mean age 61-62 years

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Use the **RAMMbo** to check validity

Was the Study valid?

1. **Recruitment**
   - Who did the subjects represent?
2. **A**llocation
   - Was the assignment to treatments randomised?
   - Were the groups similar at the trial's start?
3. **M**aintainence
   - Were the groups treated equally?
   - Were outcomes ascertained & analysed for most patients?
4. **M**easurements blinded OR objective
   - Were patients and clinicians "**b**linded" to treatment? OR
   - Were measurements **o**bjective & standardised?

User Guide. JAMA, 1993

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Appraisal checklist - **RAMMbo**

Study biases

1. **R**ecruitment
   - Who did the subjects represent?
2. **A**llocation
   - Was the assignment to treatments randomised?
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   - Were the groups treated equally?
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   - Were patients and clinicians "blinded" to treatment? OR
   - Were measurements objective & standardised?

Study statistics (p-values & confidence intervals)

Guyatt. JAMA, 1993

ARTICLES

Frequency and prevention of symptomless deep-vein thrombosis in long-haul flights: a randomised trial

...ily McDonald, Philip D Coleridge Smith

Randomisation
Volunteers were randomised by sealed envelope to one of two groups.

...(DVT) during long-haul air travel is unknown. ...limb during long-haul economy-class air ...ockings in its prevention.

Methods We recruited 89 male and 142 female passengers over 50 years of age with no history of thromboembolic problems. Passengers were randomly allocated to one of two groups: one group wore class-I below-knee graduated elastic compression stockings, the other group did not. All the passengers made journeys lasting more than 8 h per flight (median total duration 24 h), returning to the UK within 6 weeks. Duplex ultrasonography was used to assess the deep veins before and after travel. Blood samples were analysed for two specific common gene mutations, factor V Leiden (FVL) and prothrombin G20210A (PGM), which predispose to venous thromboembolism. A sensitive D-dimer assay was used to screen for the development of recent thrombosis.

Findings 12/116 passengers (10%; 95% CI 4·8–16·0%) developed symptomless DVT in the calf (five men, seven women). None of these passengers wore elastic compression stockings, and two were heterozygous for FVL. Four further patients who wore elastic compression stockings, had varicose veins and developed superficial thrombophlebitis. One of these passengers was heterozygous for both FVL and PGM. None of the passengers who wore class-I compression stockings developed DVT (95% CI 0–3·2%).

Scurr et al, Lancet 2001; 357:1485-89

Lancet 2001; 357: 1485–89 See Commentary page 1461

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Intervention & Comparison Groups

Intervention Group
Below knee compression stockings

115 116
100 100

Comparison or Control Group (CG): no stockings

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Benefits of Randomisation (and Allocation Concealment)

- Minimises confounding - known and unknown potential confounders are evenly distributed between study groups
  - reduces bias in those selected for treatment
  - guarantees treatment assignment will not be based on patients' prognosis

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Fair Allocation – balance achieved?

Were the groups similar at the start?

- ✓ Usually Table 1 in Results section
- ✓ Do imbalances favour one treatment?

Results

Volunteers were excluded before randomisation if they did not fulfil the entry requirements or could not attend hospital for investigation both before and after travel (figure). Thus, 231 of 479 volunteers were randomised. 27 passengers were unable to attend for subsequent ultrasound investigation because of ill-health (three), change of travel plans, or inability to keep appointments (24). Two who

	No stockings	Stockings
Number	116	115
Age (years)	62 (56-68)	61 (56-66)
Number of women (%)	61 (53%)	81 (70%)
Number with varicose veins	41	45
Days of stay	17 (13-32)	16 (13-27)
Hours flying time	22 (18-36)	24 (19-35)
Haemoglobin (g/L)	142 (133-149)	140 (133-147)
WBC (×10⁹/L)	5·9 (5·0-7·3)	6·0 (5·0-6·9)
Packed cell volume	0·44 (0·42-0·47)	0·44 (0·41-0·46)
Platelets (×10⁹/L)	240 (206-272)	242 (219-290)
Number FVL positive	7	4
Number PGM positive	1	3

Median (interquartile range) shown, unless otherwise indicated. WBC=white blood cells. FVL=factor V Leiden, PGM=prothrombin gene mutation.

Table 1: **Characteristics of study groups**

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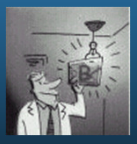
Allocation Concealment

BEST – most valid technique

- Central computer randomization



DOUBTFUL

- Envelopes, etc

NOT RANDOMISED

- Date of birth, alternate days, etc – WHY?

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Appraisal checklist - **RAMMbo**

Study biases

1. **R**ecruitment
   - Who did the subjects represent?
2. Allocation
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   - Were the groups similar at the trial's start?
3. **Maintenance**
   - **Were the groups treated equally?**
   - **Were outcomes ascertained & analysed for most patients?**
4. **Measurements**
   - Were patients and clinicians "**b**linded" to treatment? OR
   - Were measurements **o**bjective & standardised?

Study statistics (p-values & confidence intervals)

Guyatt. JAMA, 1993

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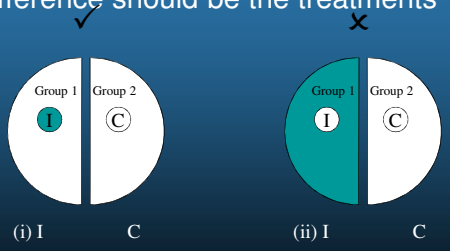
Comparable Groups: the only difference should be the treatments



(i) I C (ii) I C

Is the difference between I and C because of (i) the intervention or (ii) because the groups were not comparable in the first place?

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Equal treatment in DVT study?

	Number of Participants	
	No Stockings	Stockings
Aspirin	9	11
Hormone replacement therapy	8	16
Thyroxine	6	6
Antihypertensives, including diuretics	10	12
Antipeptic ulcer drugs	8	3

*Includes additions to usual drugs

Table 3: **All drugs taken by volunteers who attended for examination before and after air travel***

Scurr et al, Lancet 2001; 357:1485-89

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Effects of non-equal treatment

- Apart from actual intervention - groups should receive identical care!
  - Trial of Vitamin E in pre-term infants (1949)
  - Vit E "prevented" retrolental fibroplasia

Rx: Give placebo in an identical regime, and a standard protocol

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Follow-up in DVT study?

- 231 randomised (115 to stockings; 116 none)
- 200 analysed
  - 27 were unable to attend for subsequent ultrasound
  - 2 were excluded from analysis because they were upgraded to business class
  - 2 were excluded from analysis because they were taking anticoagulants

See figure on page 1486

Scurr et al, Lancet 2001; 357:1485-89

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Maintaining the Randomisation

- Principle 1 (Intention to treat)
  - Once a patient is randomised, s/he should be analysed in the group randomised to - even if they discontinue, never receive treatment, or crossover.
- Principle 2 (adequate followup)
  - "5-and-20 rule of thumb"
  - 5% probably leads to little bias
  - >20% poses serious threats to validity

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How important are the losses?

- Equally distributed?
  - Stocking group: 6 men, 9 women - 15
  - No stocking group: 7 men, 9 women - 16
- Similar characteristics?
  - No information provided

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Appraisal checklist

Study biases

1. **R**ecruitment
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Study statistics (p-values & confidence intervals)

Guyatt. JAMA, 1993

ARTICLES

Frequency and prevention of symptomless deep-vein thrombosis in long-haul flights

John H Scurr, Samuel J Machin, Sa

Evaluation
Most passengers removed their stockings on completion of their journey. The nurse removed the stockings of those passengers who had continued to wear them. A further duplex examination was then undertaken with the technician unaware of the group to which the volunteer had been randomised

Summary

Background The true freque
We sought to determine the fr
travel and the efficacy of grad

Methods We recruited 89 ma
thromboembolic problems. Pa
class-I below-knee graduated
made journeys lasting more than 8 h (median total duration 24 h), returning to the UK within 6 weeks. Duplex ultrasonography was used to assess the deep veins before and after travel. Blood samples were analysed for two specific common gene mutations, factor V Leiden (FVL) and prothrombin G20210A (PGM), which predispose to venous thromboembolism. A sensitive D-dimer assay was used to screen for the development of recent thrombosis.

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Lancet 2001; 357: 1485–89 See Commentary page 1461

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Measures in DVT study?

- Blood was taken from all participants before travel
- All participants had US once before travel (30 had US twice)
- All participants were seen within 48 hr of return flight, were interviewed and completed a questionnaire, had repeat US

Scurr et al, Lancet 2001; 357:1485-89

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Appraisal checklist

Study biases

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   - Were patients and clinicians "**b**linded" to treatment? OR
   - Were measurements **o**bjective & standardised?
5. **Placebo Effect**
6. Chance
7. Real Effect

Study statistics (p-values & confidence intervals)

Guyatt. JAMA, 1993

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Measurement Bias

- Objective
- Blinded?
  - Participants?
  - Investigators?
  - Outcome assessors?
  - Analysts?
- Papers should report WHO was blinded and HOW it was done


Figure 1: The authors: double blinded versus single blinded


Figure 2: The authors blinded and masked

Schulz and Grimes. Lancet, 2002

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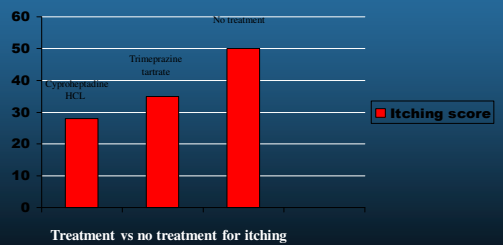
Placebo effect

Trial in patients with chronic severe itching



Treatment vs no treatment for itching

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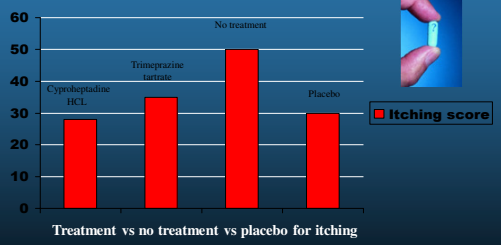
Placebo effect

Trial in patients with chronic severe itching



Treatment vs no treatment vs placebo for itching

Placebo effect - attributable to the expectation that the treatment will have an effect

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P-values (Hypothesis Testing) - in DVT study

- Incidence of DVT
  - Stocking group - 0
  - No Stocking group - 0.12

Risk difference = 0.12 - 0 = 0.12 (P=0.001)

The probability that this result would only occur by chance is

1 in 1000 → statistically significant

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Appraisal checklist

Study biases

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5. **Placebo Effect**
6. **Chance**
7. Real Effect

Study statistics (p-values & confidence intervals)

Guyatt. JAMA, 1993

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Confidence Intervals (Estimation) - in DVT study

- Incidence of DVT
  - Stocking group - 0
  - No Stocking group - 0.12

Risk difference = 0.12 - 0 = 0.12

(95% CI, 0.058 - 0.20)

The true value could be as low as 0.058 or as high as 0.20 - *but is probably closer to 0.12*

Since the CI does not include the 'no effect' value of '0' → the result is statistically significant

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Two methods of assessing the role of chance

- P-values (Hypothesis Testing)
  - use statistical test to examine the 'null' hypothesis
  - associated with "p values" - if p<0.05 then result is statistically significant
- Confidence Intervals (Estimation)
  - estimates the range of values that is likely to include the true value

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Causes of an "Effect" in a controlled trial

- Who would now consider wearing stockings on a long haul flight?

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A **Systematic Review** is a review of a ***clearly formulated question*** that uses systematic and explicit methods to ***identify, select and critically appraise*** relevant research, and to ***collect and analyse data*** from the studies that are included in the review

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What is your question?

Search for a systematic review

Does the PICO of the review fit that of your question?

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Most reviews do not pass minimum criteria

A study of 158 reviews*

- Only 2 met all 10 criteria
- Median was only 1 of 10 criteria met

* McAlister Annals of Intern Med 1999

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Using Pedometers to Increase Physical Activity and Improve Health

A Systematic Review

Dena M. Bravata, MD, MS
Crystal Smith-Spangler, MD
Vandana Sundaram, MPH
Allison L. Gienger, BA

Context Without detailed evidence of their effectiveness, pedometers have recently become popular as a tool for motivating physical activity.

Objective To evaluate the association of pedometer use with physical activity and health outcomes among outpatient adults.

- Population
- Intervention
- Comparison
- Outcome(s)

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Is the review any good? FAST appraisal

- **Q**uestion – What is the PICO?
- **F**inding
  - Did they find most studies?
- **A**ppraisal
  - Did they select good ones?
- **S**ynthesis
  - What do they all mean?
- **T**ransferability of results

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Do pedometers increase activity and improve health?

- **Find: what is your search strategy?**
  - **Databases?**
  - **Terms?**
  - **Other methods?**

Do yourself then
Get neighbour's help

METHODS

Data Sources and Search Strategies

In collaboration with a professional librarian, we developed individualized search strategies for 7 databases: MEDLINE (January 1966 to February 2007); and EMBASE, Sport Discus, PsychINFO, Cochrane Library, Thompson Scientific (formerly known as Thompson ISI), and ERIC (January 1966 to May 2006). We used search terms such as *pedometer*, *activity monitor*, and *step counter*. We also reviewed the bibliographies of retrieved articles and relevant conference proceedings and contacted experts in exercise physiology for additional studies.

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FIND: Did they find all Studies?

- Check for existing systematic review?
- Good initial search
  - Terms (text and MeSH)
  - At least 2 Databases: MEDLINE, EMBASE, CINAHL, CCTR, ...
- Plus a Secondary search
  - Check references of relevant papers & reviews and
  - Find terms (words or MeSH terms) you didn't use
  - Search again! (*snowballing*)

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Registered vs Published Studies

Ovarian Cancer chemotherapy: single v combined

	Published	Registered
No. studies	16	13
Survival ratio	1.16	1.05
95% CI	1.06-1.27	0.98-1.12
P-Value	0.02	0.25

Simes, J. Clin Oncol, 86, p1529

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Is finding all published studies enough?

- Negative studies less likely to be published than 'Positive'
- How does this happen?
- Follow-up of 737 studies at Johns Hopkins*
  - Positive SUBMITTED more than negative (2.5 times)

*Dickersin, JAMA, 1992

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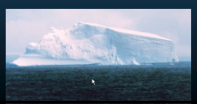
Which are biased? Which OK?

1. All positive studies
2. All studies with more than 100 patients
3. All studies published in BMJ, Lancet, JAMA or NEJM
4. All registered studies



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Registered vs Published Studies

Ovarian Cancer chemotherapy: single v combined

	Published	Registered
No. studies	16	
Survival ratio	1.16	
95% CI	1.06-1.27	
P-Value	0.02	

Simes, J. Clin Oncol, 86, p1529

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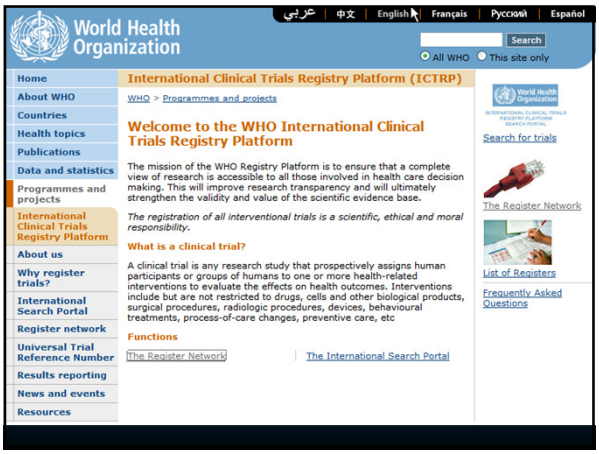
Publication Bias: Solution

- All trials registered at inception,
  - The National Clinical Trials Registry: Cancer Trials
  - National Institutes of Health Inventory of Clinical Trials and Studies
  - International Registry of Perinatal Trials
- Meta-Registry of trial Registries
  - www.controlled-trials.com


World Health Organization
عربي | 中文 | English | Français | Русский | Español
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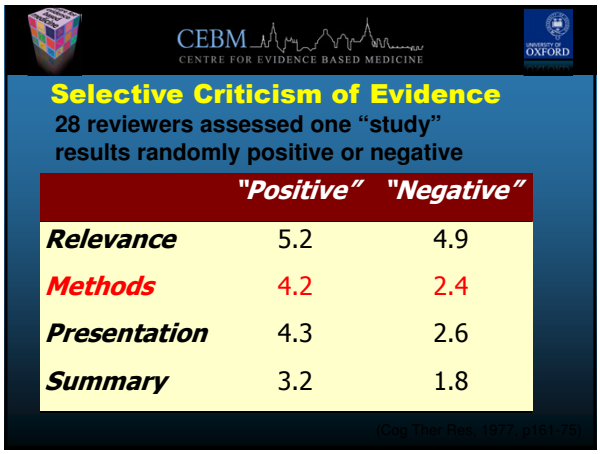
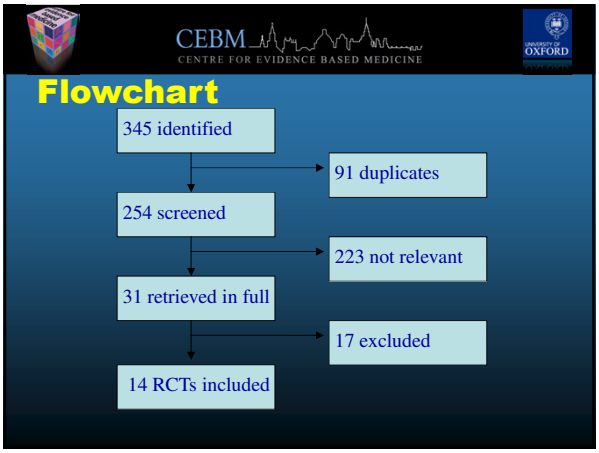
All WHO | This site only
Home
About WHO
Countries
Health topics
Publications
Data and statistics
Programmes and projects
International Clinical Trials Registry Platform
About us
Why register trials?
International Search Portal
Register network
Universal Trial Reference Number
Results reporting
News and events
Resources
International Clinical Trials Registry Platform (ICTRP)
WHO > Programmes and projects
Welcome to the WHO International Clinical Trials Registry Platform
The mission of the WHO Registry Platform is to ensure that a complete view of research is accessible to all those involved in health care decision making. This will improve research transparency and will ultimately strengthen the validity and value of the scientific evidence base.
The registration of all interventional trials is a scientific, ethical and moral responsibility.
What is a clinical trial?
A clinical trial is any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes. Interventions include but are not restricted to drugs, cells and other biological products, surgical procedures, radiologic procedures, devices, behavioural treatments, process-of-care changes, preventive care, etc
Functions
The Register Network
The International Search Portal
Search for trials
The Register Network
List of Registers
Frequently Asked Questions


CEBM
CENTRE FOR EVIDENCE BASED MEDICINE
OXFORD
Selective Criticism of Evidence
28 reviewers assessed one "study"
results randomly positive or negative
"Positive" "Negative"
Relevance 5.2 4.9
Methods 4.2 2.4
Presentation 4.3 2.6
Summary 3.2 1.8
(Cog Ther Res, 1977, p161-75)


CEBM
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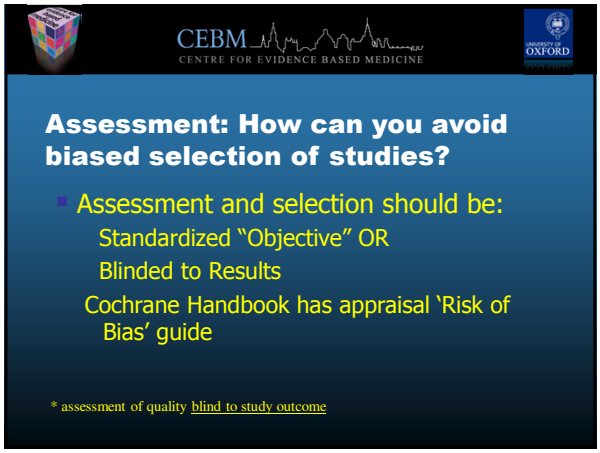
OXFORD
Flowchart
345 identified
91 duplicates
254 screened
223 not relevant
31 retrieved in full
17 excluded
14 RCTs included


CEBM
CENTRE FOR EVIDENCE BASED MEDICINE
OXFORD
Assessment: How can you avoid biased selection of studies?
Assessment and selection should be:
Standardized "Objective" OR
Blinded to Results
Cochrane Handbook has appraisal 'Risk of Bias' guide
* assessment of quality blind to study outcome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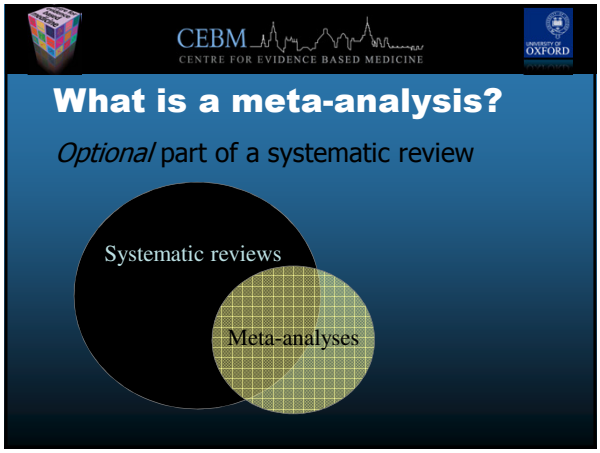
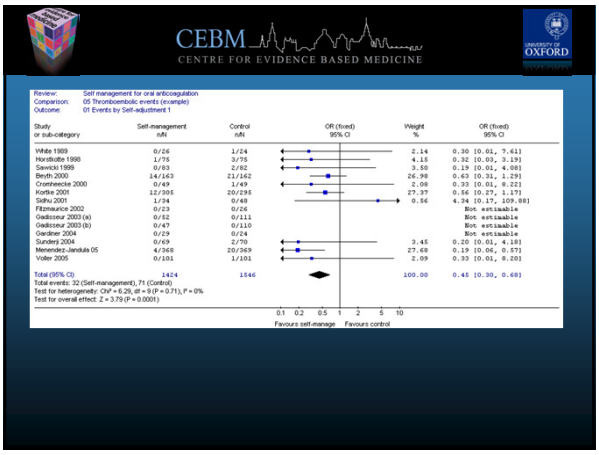
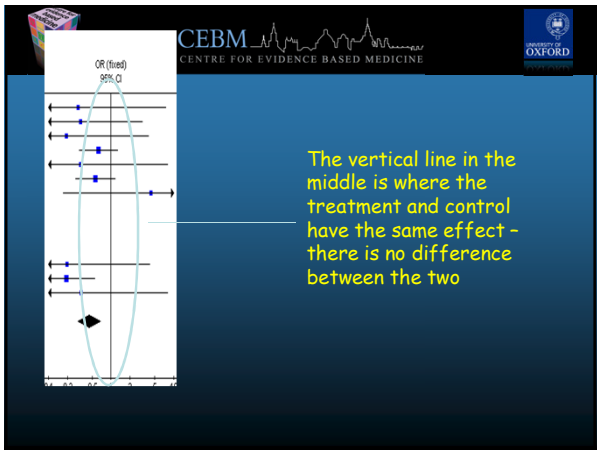
OXFORD
APPRAISE & select studies
Did they select only the good quality studies?
Bias and Confounding Trash Can


CEBM
CENTRE FOR EVIDENCE BASED MEDICINE
OXFORD
What is a meta-analysis?
Optional part of a systematic review
Systematic reviews
Meta-analyses


CEBM
CENTRE FOR EVIDENCE BASED MEDICINE
OXFORD
Review: Self management for oral anticoagulation
Comparison: 05 Thromboembolic events (example)
Outcome: 01 Events by Self-adjustment 1
Study or sub-category
Self-management n/N
Control n/N
OR (fixed) 95% CI
Weight %
OR (fixed) 95% CI
White 1989 0/26 1/24 2.14 0.30 [0.01, 7.61]
Horstkotte 1998 1/75 3/75 4.15 0.32 [0.03, 3.19]
Sawicki 1999 0/83 2/82 3.50 0.19 [0.01, 4.08]
Beyth 2000 14/163 21/162 26.98 0.63 [0.31, 1.29]
Crowtherwise 2000 0/49 1/49 2.08 0.33 [0.01, 8.22]
Kortke 2001 12/305 20/295 27.37 0.56 [0.27, 1.17]
Sidhu 2001 1/34 0/48 0.56 4.34 [0.17, 109.88]
Fitzmaurice 2002 0/23 0/26 Not estimable
Gadisseur 2003 (a) 0/52 0/111 Not estimable
Gadisseur 2003 (b) 0/47 0/110 Not estimable
Gardiner 2004 0/29 0/24 Not estimable
Sunderji 2004 0/69 2/70 3.45 0.20 [0.01, 4.18]
Menendez-Jandula 05 4/368 20/369 27.68 0.19 [0.06, 0.57]
Voller 2005 0/101 1/101 2.09 0.33 [0.01, 8.20]
Total (95% CI) 1424 1546 100.00 0.45 [0.30, 0.68]
Total events: 32 (Self-management), 71 (Control)
Test for heterogeneity: Chi² = 6.29, df = 9 (P = 0.71), I² = 0%
Test for overall effect: Z = 3.79 (P = 0.0001)
0.1 0.2 0.5 1 2 5 10
Favours self-manage
Favours control


CEBM
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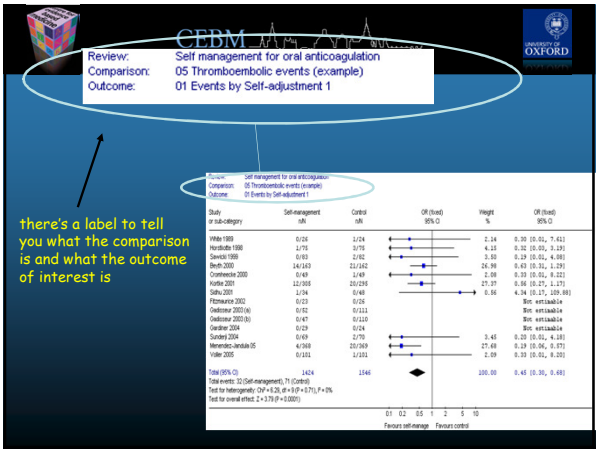
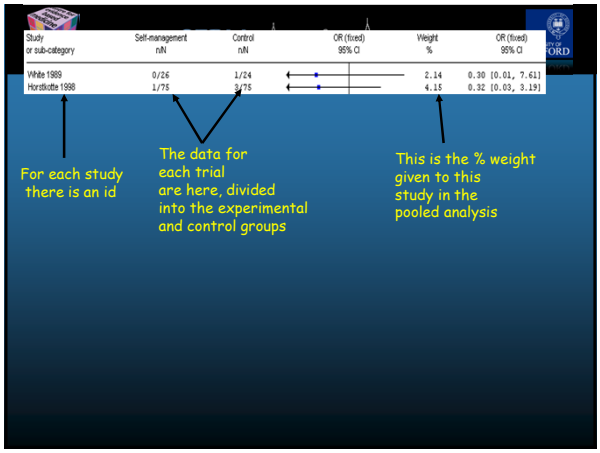
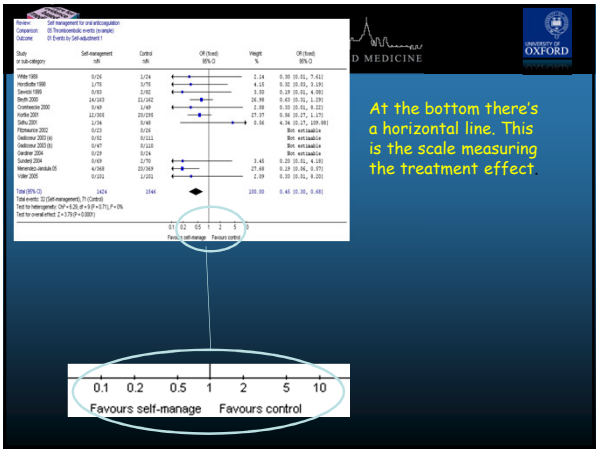
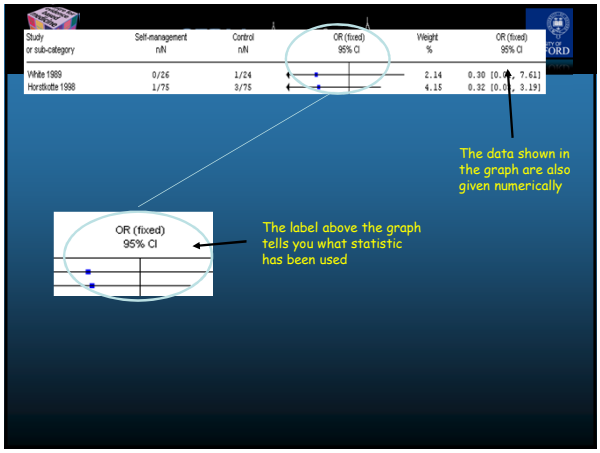
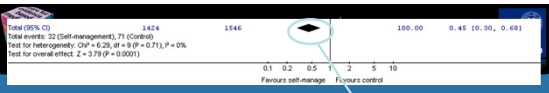
OXFORD
OR (fixed) 95% CI
The vertical line in the middle is where the treatment and control have the same effect – there is no difference between the two


CEBM
OXFORD
Review: Self management for oral anticoagulation
Comparison: 05 Thromboembolic events (example)
Outcome: 01 Events by Self-adjustment 1
there's a label to tell you what the comparison is and what the outcome of interest is


Study or sub-category
Self-management n/N
Control n/N
OR (fixed) 95% CI
Weight %
OR (fixed) 95% CI
White 1989 0/26 1/24 2.14 0.30 [0.01, 7.61]
Horstkotte 1998 1/75 3/75 4.15 0.32 [0.03, 3.19]
For each study there is an id
The data for each trial are here, divided into the experimental and control groups
This is the % weight given to this study in the pooled analysis


At the bottom there's a horizontal line. This is the scale measuring the treatment effect.
0.1 0.2 0.5 1 2 5 10
Favours self-manage
Favours control


Study or sub-category
Self-management n/N
Control n/N
OR (fixed) 95% CI
Weight %
OR (fixed) 95% CI
White 1989 0/26 1/24 2.14
Horstkotte 1998 1/75 3/75 4.15
The data shown in the graph are also given numerically
OR (fixed) 95% CI
The label above the graph tells you what statistic has been used



The pooled analysis is given a diamond shape where the widest bit in the middle is located at the calculated best guess (point estimate), and the horizontal width is the confidence interval

Note on interpretation

If the confidence interval crosses the line of no effect, this is equivalent to saying that we have found no statistically significant difference in the effects of the two interventions

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Weighting studies

- More weight to the studies which give us more information
  - More participants
  - More events
  - More precision
- Weight is proportional to the precision

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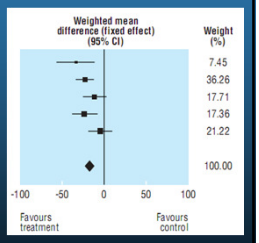
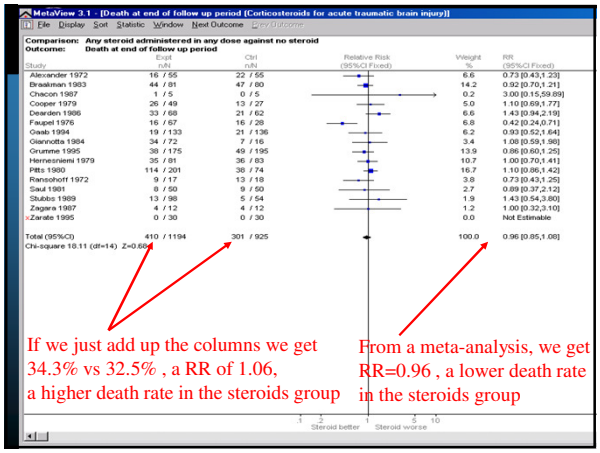
The figure on the right is from Figure 3. See if you can answer the following questions about this plot.

1. How many studies are there?
2. How many studies favour treatment?
3. How many studies are statistically significant?
4. Which is the largest study?
5. Which is the smallest study?
6. What is the combined result?





If we just add up the columns we get 34.3% vs 32.5% , a RR of 1.06, a higher death rate in the steroids group

From a meta-analysis, we get RR=0.96 , a lower death rate in the steroids group

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Meta-analysis (Forest) plot

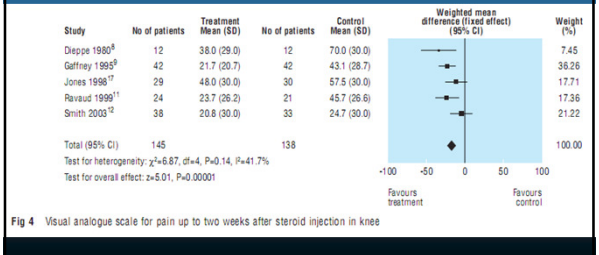

Fig 4 Visual analogue scale for pain up to two weeks after steroid injection in knee

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Transferable? Use in my patients

Is the AVERAGE effect similar across studies?

- If NO, then WHY?
  - Study methods - biases
  - PICO
- If YES, then 2 questions
  - Effect in different individuals?
  - Which version of treatment?

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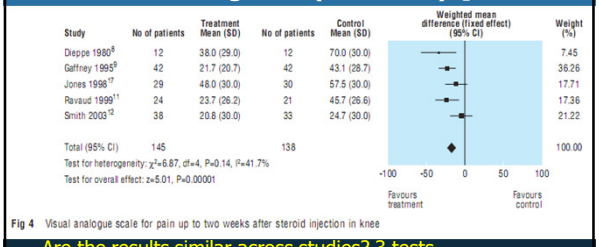
Meta-analysis (Forest) plot



Study	No of patients	Treatment Mean (SD)	No of patients	Control Mean (SD)	Weighted mean difference (fixed effect) (95% CI)	Weight (%)
Dieppe 1980[8]	12	38.0 (29.0)	12	70.0 (30.0)		7.45
Gaffney 1995[9]	42	21.7 (20.7)	42	43.1 (28.7)		36.26
Jones 1998[17]	29	48.0 (30.0)	30	57.5 (30.0)		17.71
Ravaud 1999[11]	24	23.7 (26.2)	21	45.7 (26.6)		17.36
Smith 2003[12]	38	20.8 (30.0)	33	24.7 (30.0)		21.22
Total (95% CI)	145		138			100.00

Test for heterogeneity: χ^2=6.87, df=4, P=0.14, I^2=41.7%

Test for overall effect: z=5.01, P=0.00001

-100 -50 0 50 100

Favours treatment Favours control

Fig 4 Visual analogue scale for pain up to two weeks after steroid injection in knee

Are the results similar across studies? 3 tests

- Eyeball" test – do they look they same?
- Test of "Null hypothesis" of no variation (p-value)
- Proportion of variation not due to chance (I^2)

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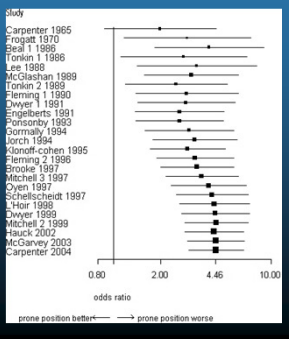

Study
Carpenter 1965
Frogatt 1970
Beal 1 1988
Tonkin 1 1988
Lee 1988
McGlashan 1989
Tonkin 2 1989
Fleming 1 1990
Dwyer 1 1991
Engelberts 1991
Ponsonby 1993
Gormally 1994
Jorch 1994
Klonoff-cohen 1995
Fleming 2 1996
Brooke 1997
Mitchell 3 1997
Oyen 1997
Schellscheidt 1997
L'Hoir 1998
Dwyer 1999
Mitchell 2 1999
Hauck 2002
McGarvey 2003
Carpenter 2004

0.80 2.00 4.46 10.00

odds ratio

prone position better ⟵ ⟶ prone position worse

Cumulative meta-analysis

When did we know that sleeping position affected mortality?

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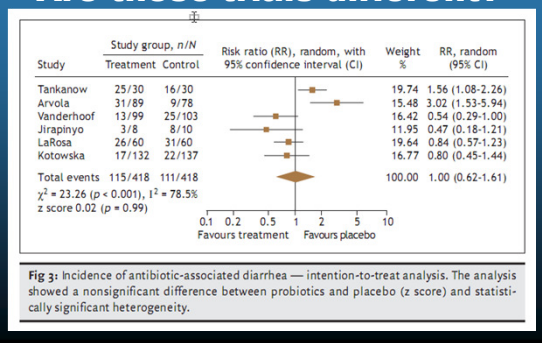
Are these trials different?



Study	Study group, n/N Treatment	Control	Risk ratio (RR), random, with 95% confidence interval (CI)	Weight %	RR, random (95% CI)
Tankanow	25/30	16/30		19.74	1.56 (1.08-2.26)
Arvola	31/89	9/78		15.48	3.02 (1.53-5.94)
Vanderhoof	13/99	25/103		16.42	0.54 (0.29-1.00)
Jirapinyo	3/8	8/10		11.95	0.47 (0.18-1.21)
LaRosa	26/60	31/60		19.64	0.84 (0.57-1.23)
Kotowska	17/132	22/137		16.77	0.80 (0.45-1.44)
Total events	115/418	111/418		100.00	1.00 (0.62-1.61)

χ^2 = 23.26 (p < 0.001), I^2 = 78.5%
z score 0.02 (p = 0.99)

0.1 0.2 0.5 1 2 5 10

Favours treatment Favours placebo

Fig 3: Incidence of antibiotic-associated diarrhea — intention-to-treat analysis. The analysis showed a nonsignificant difference between probiotics and placebo (z score) and statistically significant heterogeneity.

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Conclusion
EBM and Systematic Review

- EBM (quick & dirty)
  - Ask Question
  - Search
  - Appraise
  - Apply
- Time: 90 seconds
- < 20 articles
- This patient survives!

- Systematic Review
  - Ask Question
  - Search ++++ x 2
  - Appraise x 2
  - Synthesize
  - Apply
- Time: 6 months, team
- < 2,000 articles
- This patient is dead

Find a systematic review!! (and appraise it FAST)

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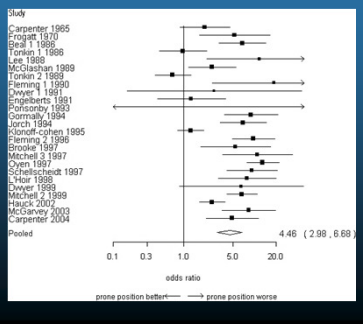
Risk of SIDS and sleeping position



Study
Carpenter 1965
Frogatt 1970
Beal 1 1988
Tonkin 1 1988
Lee 1988
McGlashan 1989
Tonkin 2 1989
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Brooke 1997
Mitchell 3 1997
Oyen 1997
Schellscheidt 1997
L'Hoir 1998
Dwyer 1999
Mitchell 2 1999
Hauck 2002
McGarvey 2003
Carpenter 2004
Pooled

4.46 (2.98 , 6.68)

0.1 0.3 1.0 5.0 20.0

odds ratio

prone position better ⟵ ⟶ prone position worse

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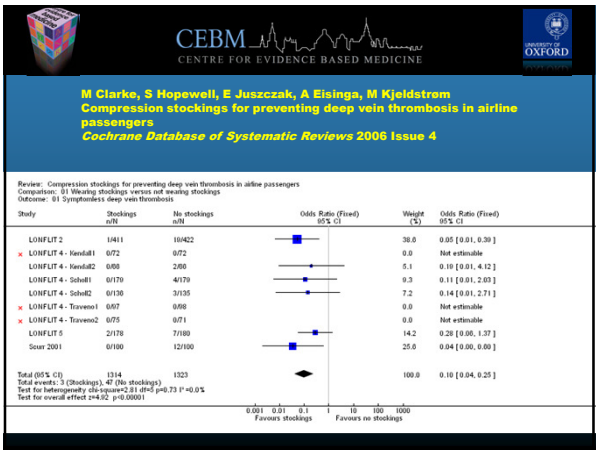
Pros and cons of systematic reviews

- Advantages
  - Larger numbers & power
  - Robustness across PICOs
- Disadvantages
  - May conclude small biases are real effects


CEBM
CENTRE FOR EVIDENCE BASED MEDICINE
UNIVERSITY OF OXFORD
M Clarke, S Hopewell, E Juszczak, A Eisinga, M Kjeldstrøm
Compression stockings for preventing deep vein thrombosis in airline passengers
Cochrane Database of Systematic Reviews 2006 Issue 4
Review: Compression stockings for preventing deep vein thrombosis in airline passengers
Comparison: 01 Wearing stockings versus not wearing stockings
Outcome: 01 Symptomless deep vein thrombosis
Study
Stockings n/N
No stockings n/N
Odds Ratio (Fixed) 95% CI
Weight (%)
Odds Ratio (Fixed) 95% CI
LONFLIT 2 1/411 10/422 38.0 0.05 [0.01, 0.39]
LONFLIT 4 - Kendall1 0/72 0/72 0.0 Not estimable
LONFLIT 4 - Kendall2 0/68 2/68 5.1 0.19 [0.01, 4.12]
LONFLIT 4 - Scholl1 0/170 4/170 9.3 0.11 [0.01, 2.03]
LONFLIT 4 - Scholl2 0/130 3/135 7.2 0.14 [0.01, 2.71]
LONFLIT 4 - Traveno1 0/67 0/68 0.0 Not estimable
LONFLIT 4 - Traveno2 0/75 0/71 0.0 Not estimable
LONFLIT 5 2/178 7/180 14.2 0.28 [0.06, 1.37]
Scurr 2001 0/100 12/100 25.6 0.04 [0.00, 0.69]
Total (95% CI) 4314 1323 100.0 0.10 [0.04, 0.25]
Total events: 3 (Stockings), 47 (No stockings)
Test for heterogeneity chi-square=2.81 df=5 p=0.73 I² =0.0%
Test for overall effect z=4.92 p<0.00001
0.001 0.01 0.1 1 10 100 1000
Favours stockings
Favours no stockings