



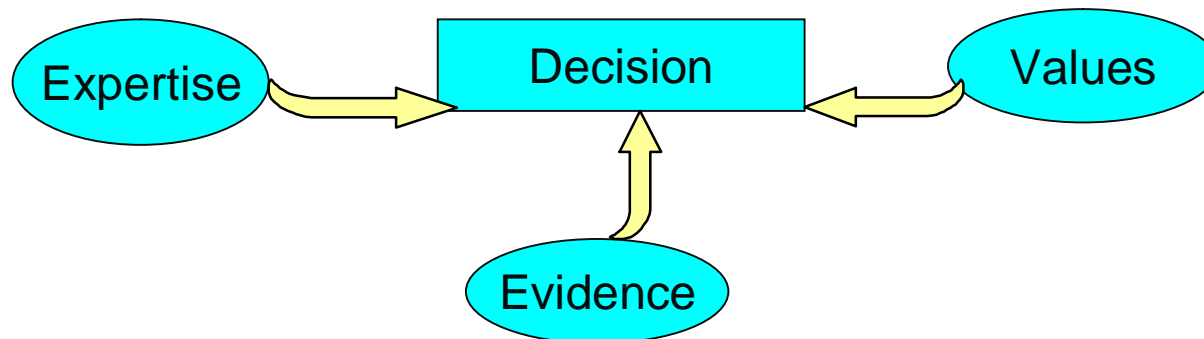
What is a systematic review?

Jos Verbeek, FIOH, Finland

Reasons for conducting a SR



- Researcher:
 - building on previous work
 - state of the art
- Practitioner / Policy-maker
 - what is the evidence that answers my question?
 - use it for decision making



Reviews: what do we want ?



- What do we want?
 - A summary of ALL the evidence for my question
 - ("but not: what has been published about this topic?")
 - Unbiased
 - Transparent
 - Up-to-date
- What problems do we encounter?
 - personal bias
 - publication bias
 - language bias
 - different study designs
 - varying study quality
 - varying study size
 - different ways of combining studies (meta-analysis)

Personal (“file drawer”) bias

- “The invited review? or, my field, from my standpoint, written by me using only my data and my ideas, and citing only my publications.”
- The author recommends a warning label for reviews:
- “The contents of this review may be dangerous to your science. This review contains statements, ideas and opinions that may be unsubstantiated. The models herein reflect the state of the author’s loose grasp of reality, and should not be confused with facts. Proceed with caution.”

Caveman. J Cell Sci 2000



Publication Bias



- J Med Ethics. 2008 Sep; 34(9):e20.
- Clinical research projects at a German medical faculty: follow-up from ethical approval to publication and citation by others.
- [Blümle A](#), [Antes G](#), [Schumacher M](#), [Just H](#), [von Elm E](#).
- 299 study protocols were included
- 109 of the 225 (48%) completed protocols corresponded to at least one full publication (total 210 articles);
- 168 of 210 identified publications (80%) were cited in articles indexed in the ISI Web of Science

Language bias

- German authors who had published different trials in both English and German language journals
- Statistically significant results more likely to be published in English (odds ratio 3.7, 95% CI: 1.2 - 11)

Egger et al. JAMA 1997; 350: 326 - 9



Study Design

Beta-carotene and cardiovascular mortality



Cohorts

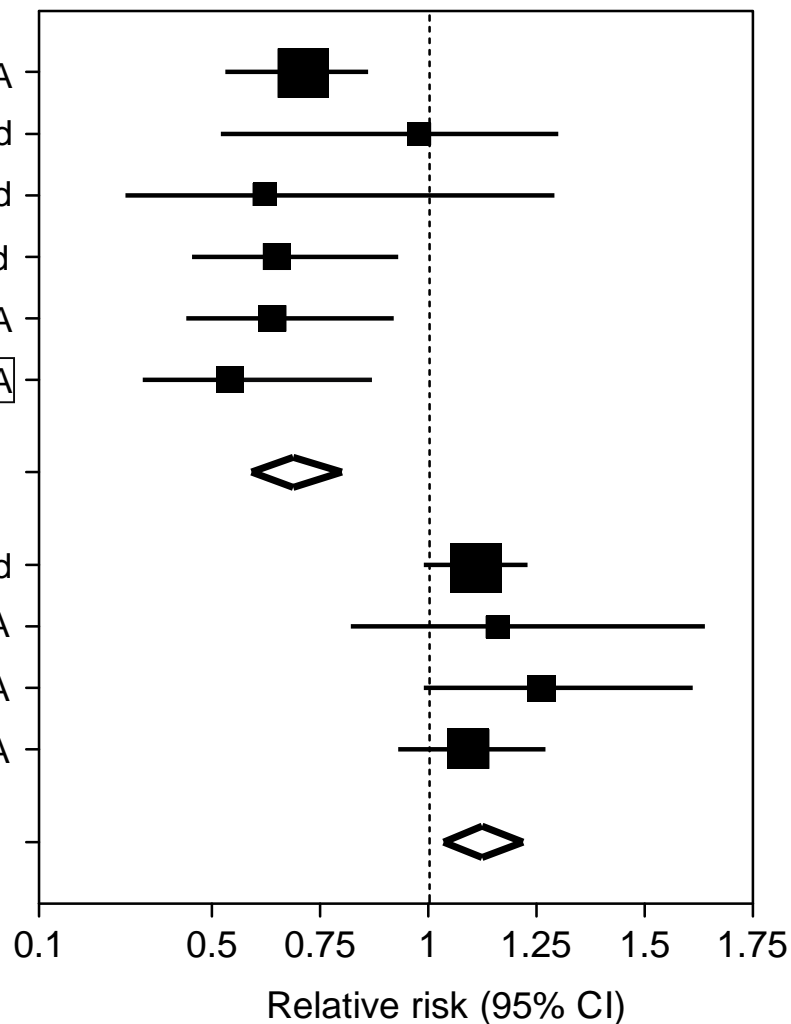
- Male health workers USA
- Social insurance, men Finland
- Social insurance, women Finland
- Male chemical workers Switzerland
- Hyperlipidaemic men USA
- Nursing home residents USA

Cohorts combined

Trials

- Male smokers Finland
- Skin cancer patients USA
- (Ex)-smokers, asbestos workers USA
- Male physicians USA

Trials combined



Study Quality

- Effect estimates were exaggerated when there was inadequate or unclear
 - allocation concealment
 - (ratio of effects 0.69 (95% CI 0.59 to 0.82))
 - lack of blinding
 - (ratio of effects 0.75 (0.61 to 0.93))
- Wood et al BMJ 2008



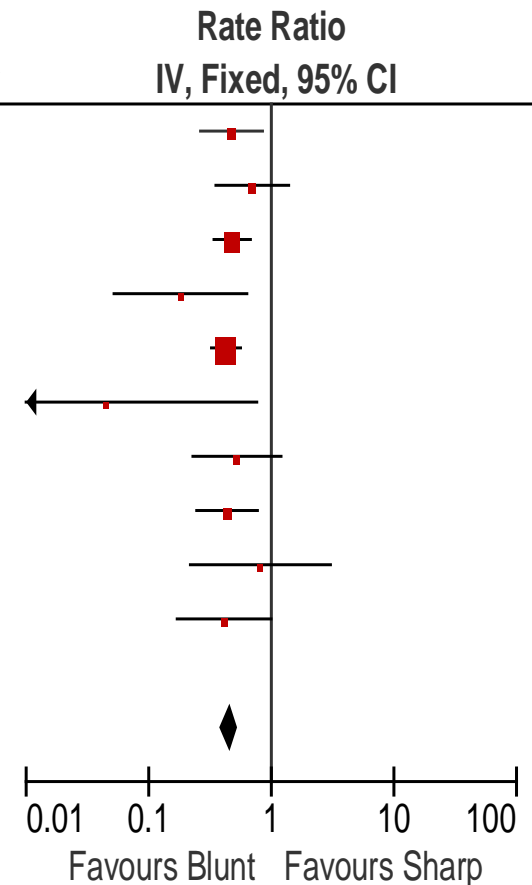
Study Size

Blunt versus Sharp Suture Needles to Prevent Needle Stick Injuries



Study or Subgroup	log[Rate Ratio]	SE	Weight	Rate Ratio		Year	Rate Ratio	
				IV, Fixed, 95% CI	Year		IV, Fixed, 95% CI	Year
Wright 1993	-0.7472144	0.296334	8.6%	0.47	[0.27, 0.85]	1993	0.47	[0.27, 0.85]
Thomas 1995	-0.35667494	0.348466	6.2%	0.70	[0.35, 1.39]	1995	0.70	[0.35, 1.39]
Mingoli 1996	-0.73315252	0.173816	25.1%	0.48	[0.34, 0.68]	1996	0.48	[0.34, 0.68]
Hartley 1996	-1.70552479	0.636209	1.9%	0.18	[0.05, 0.63]	1996	0.18	[0.05, 0.63]
Meyer 1996	-0.85131877	0.138984	39.2%	0.43	[0.33, 0.56]	1996	0.43	[0.33, 0.56]
Rice 1996	-3.11351531	1.449138	0.4%	0.04	[0.00, 0.76]	1996	0.04	[0.00, 0.76]
Ablett 1998	-0.64435702	0.421637	4.3%	0.52	[0.23, 1.20]	1998	0.52	[0.23, 1.20]
Nordkam 2005	-0.8303483	0.290628	9.0%	0.44	[0.25, 0.77]	2005	0.44	[0.25, 0.77]
Wilson 2008	-0.2048782	0.67082	1.7%	0.81	[0.22, 3.03]	2008	0.81	[0.22, 3.03]
Sullivan 2009	-0.8873032	0.449089	3.8%	0.41	[0.17, 0.99]	2009	0.41	[0.17, 0.99]
Total (95% CI)			100.0%	0.46	[0.38, 0.54]		0.46	[0.38, 0.54]

Heterogeneity: $\text{Chi}^2 = 7.45$, $\text{df} = 9$ ($P = 0.59$); $I^2 = 0\%$
 Test for overall effect: $Z = 9.03$ ($P < 0.00001$)



Meta-analysis



- A statistical procedure that integrates the results of several independent studies considered to be “combinable.”

Egger et al, BMJ 1997

- Provides a quantitative summary of the overall treatment effect (typically a pooled estimate and confidence interval)

Lau J 1999

- This increases statistical precision (minimises play of chance) and increases our certainty about true effect of treatment

Measures of treatment effect



- Dichotomous:
 - number of death / 100.000 population
 - 10 / 100.000
 - number of injuries / 100 person years
 - 5 / 100 py
 - number of workers with asthma / 100 person years
 - 0.1 / 100 py
- Continuous:
 - score on pain scale (VAS)
 - 4.5 ± 1.5 (m \pm sd)
 - score on depression scale (CESD)
 - 7.1 ± 5.2 (m \pm sd)

Measures of treatment effect



- Dichotomous:
 - RR, risk ratio
 - intervention risk / control group risk
 - OR, odds ratio
 - ratio of the odds of having adverse outcome
 - Odds Ratio = Risk Ratio only if number of events is less than 10%
- Continuous:
 - MD, mean difference
 - intervention outcome – control outcome
 - SMD, standardised mean difference (MD/SD)
 - effect size

Measures of treatment effect



- RR / OR
 - fatal injuries intervention / fatal injuries control
 - $10 / 100\text{py} / 20 / 100\text{py} = 0.5$
 - smaller than one: beneficial
 - $30 / 100\text{py} / 10 / 100\text{py} = 3.0$
 - bigger than one : harmful
 - $10 / 100\text{py} / 10 / 100\text{py} = 1.0$
 - equal to one: no effect
- NB: similar risks for different baseline rates:
 - $100\text{ per } 100\text{ py} / 200\text{ per } 100\text{ py} = 0.5$
 - $1\text{ per } 100\text{ py} / 2\text{ per } 100\text{ py} = 0.5$
- 95% confidence interval
 - 0.5 (95% CI 0.1 to 3.1)
 - 0.5 (95% CI 0.1 to 0.7)
 - 0.5 (95% CI 0.3 to 1.0)

Measures of treatment effect



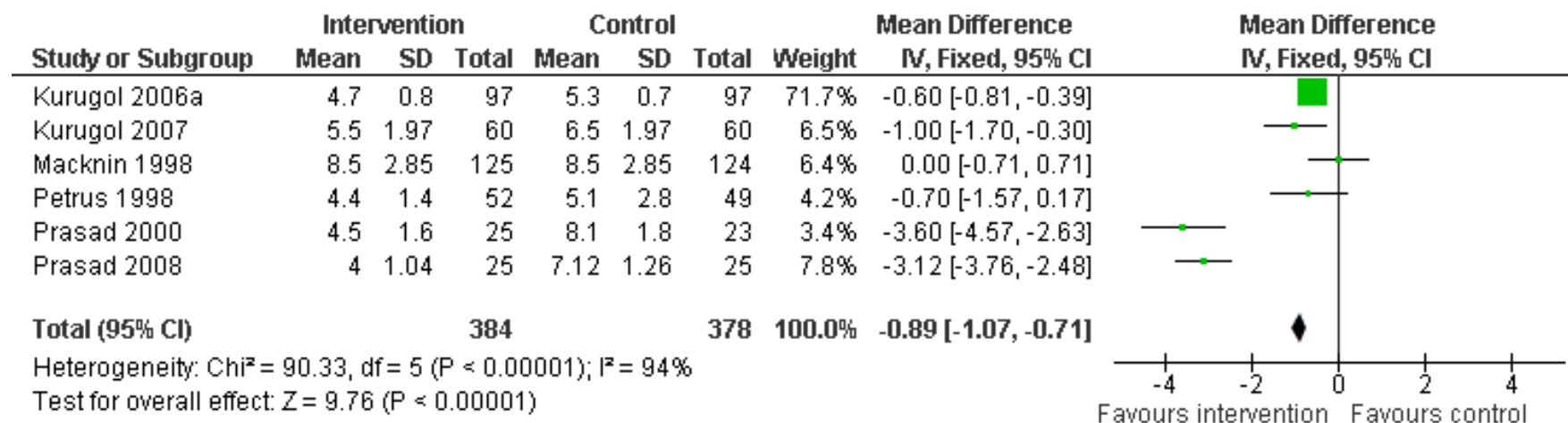
- Mean Difference
 - score on CES-D depression scale:
 - intervention score minus control score
 - $10 \text{ minus } 20 = -10$
 - smaller than 0: beneficial
 - $20 \text{ minus } 10 = 10$
 - bigger than 0 : harmful
 - $10 \text{ minus } 10 = 0$
 - equal to 1: no effect
 - 95% confidence interval
 - - 10 (95% CI -15 to - 5)
 - - 10 (95% CI -20 to 10)
 - - 10 (95% CI -16 to 0)

Heterogeneity



- If the results of studies differ greatly then it may not be appropriate to combine the results
 - (“apples and oranges” problem)
- Three approaches
 - Don’t combine
 - Combine within subgroups only
 - Use statistical test for heterogeneity and choose appropriate statistical model for combining

Zinc for Common Cold



Systematic review

“review in which bias has been reduced by the systematic identification, appraisal, synthesis, and, if relevant statistical aggregation of all relevant studies on a specific topic according to a predetermined and explicit method.”

Moher et al. Prisma Statement.
Lancet 1999; 354: 1896-900



Systematic Review

- A systematic review attempts to collate all empirical evidence that fits pre-specified eligibility criteria to answer a specific research question. It uses explicit, systematic methods that are selected with a view to minimising bias, thus providing reliable findings from which conclusions can be drawn and decisions made.
 - Prisma-statement. Liberati et al BMJ 2009



A Review

- Thoracic Outlet Syndrome: Definition, Aetiological Factors, Diagnosis, Management and Occupational Impact
- Thoracic outlet syndrome is a controversial cause of neck and shoulder pain due to complex mechanisms involving muscular dysfunction and nerve compression. Although management of thoracic outlet syndrome must be based on a multidisciplinary approach, physicians and occupational therapist should be familiar with the principles of diagnosis and treatment. The purpose of this article is to review the definitions, diagnosis and management of this syndrome. A particular emphasis was described on the links between the workplace and the individual in the pathogenesis, prevalence in the workforce and the course of this disease.



Another Review



- Occupational hazards for pregnant nurses.
- OVERVIEW:
- Depending on her working environment, specific immunities, and stage of pregnancy, a pregnant nurse may find it difficult to avoid teratogenic and fetotoxic exposures, as well as working conditions that could jeopardize her pregnancy. A clinical review of the occupational hazards faced by pregnant nurses can be useful to the concerned nurse or health care system, as can suggestions on ways to reduce risk and a list of pertinent occupational safety resources.

Another Review



- Physical conditioning programs for improving work outcomes in workers with back pain
- OBJECTIVES: To compare the effectiveness of physical conditioning programs in reducing time lost from work for workers with back pain.
- SEARCH STRATEGY: We searched the following databases...
- SELECTION CRITERIA: RCTs and cluster RCTs of workers with work disability related to back pain in physical conditioning programs.
- DATA COLLECTION AND ANALYSIS: Two review authors independently extracted data and assessed risk of bias.
- MAIN RESULTS: 23 RCTs (3676 workers) were included, 13 of which had a low risk of bias. In workers with acute back pain, there was no effect on sickness absence. For workers with subacute back pain, we found conflicting results. In workers with chronic back pain, pooled results of five studies showed a small effect on sickness absence at long-term follow-up (SMD: -0.18 (95% CI: -0.37 to 0.00)).
- AUTHORS' CONCLUSIONS....

AMSTAR checklist



- 11 items to check quality of systematic reviews
 1. a priori design
 2. duplicate study selection and data extraction
 3. comprehensive literature search
 4. inclusion regardless of publication status
 5. list of in/excluded studies
 6. characteristics of included studies
 7. methodological quality of included studies
 8. quality used in conclusions
 9. appropriate combination of studies
 10. publication bias assessed
 11. conflict of interest included

Shea J Clin Epi 2009;62:1013-20