Medical Statistics

AKT revision guide

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Contents

Basic Concepts

Types of studies

Case-Control • Observational and retrospective • Compares a group of people with disease to a group without • Looks for prior exposure or risk factor • Asks: “what happened?”	Measures “Odds Ratio(OR)”
Cohort study • Observational and prospective • Compares two groups, one with the other one without exposure • Looks to see if exposure increases the likelihood of disease • Asks:”What will happen?”	Measures “Relative Risk(RR)”
Cross- sectional study • Observational • Collects data from a group of people to assess frequency of disease (and related risk factors) at a particular point in time. • Asks, "What is happening?"	Asks, "What is happening?" Can show risk factor association with disease, but does not establish causality
Twin Concordance study • Compares the frequency with which both monozygotic twins or both dizygotic twins develop a disease. • Compares siblings raised by biologic vs. Adoptive •	Measures heritability
Adoption study • Compares siblings raised by biologic vs. Adoptive	Measures heritability and influence of environmental

Evaluation of diagnostic tests

Uses 2x2 table comparing test results with the actual presence of disease.

TP = true positive;

FP = false positive;

TN = true negative;

FN = false negative.

		Disease	
		+	-
Test	+	TP	FP
	-	FN	TN

Exam Tip: Important to remember "TEST" on left and "DISEASE" on top. The examiner might put the TEST on top which pivots the table.

Sensitivity (SNOUT) SeN**sitivity rules** OUT	• **Proportion of all people with disease who test positive,** • **TP / (TP + FN)** • **the ability of a test to detect a disease when it is present** • **Value approaching 1 is desirable for ruling out disease and indicates a low false-negative rate** • **Used for screening in diseases with low prevalence**
Specificity (SPIN) Sp**ecificity rules** IN	• Proportion of all people without disease who test negative, • TN / (TN + FP) • Specificity is the ability of a test to indicate non-disease when disease is not present. • Value approaching 1 is desirable for ruling in disease and indicates a low false-positive rate. • Used as a confirmatory test after a positive screening test.
Positive predictive value (PPV)	• Proportion of positive test results that are true positive. • Probability that person actually has the disease given a positive test result. • (Note: If the prevalence of a disease in a population is low, even tests with high specificity or high sensitivity will have low positive predictive values!) • TP / (TP + FP)
Negative predictive value (NPV)	• Proportion of negative test results that are true negative. Probability that person actually is disease free given a negative test result. • TN / (FN + TN)
Likelihood ratio for a positive test result	• How much the odds of the disease increase when a test is positive • sensitivity / (1 - specificity)
Likelihood ratio for a negative test	• How much the odds of the disease decrease when a test is negative • (1 - sensitivity) / specificity

result

Prevalence vs. incidence

$$Point\ prevalence = \frac{total\ cases\ in\ population\ at\ a\ given\ time}{total\ population\ at\ a\ given\ time}$$

$$Incidence = \frac{new\ cases\ in\ population\ over\ a\ given\ time\ period}{total\ population\ at\ risk\ during\ that\ time\ period2a}$$

Prevalence = incidence x disease duration

Prevalence > incidence for chronic diseases (e.g., diabetes).

Prevalence = incidence for acute disease (e.g., common cold).

Exam Tip: When calculating incidence, don't forget that people currently with the disease, or those previously positive for it, are not considered at risk.

Odds Ratio vs. Relative Risk

		Group	
		Experimental (E)	Control (C)
Event	+	EE	CE
	-	EN	CN
Total subjects		ES=EE+EN	CS=CE+CN
		EER=$\frac{EE}{ES}$	CER=$\frac{CE}{CS}$

EER= Experimental Event Rate

CER= Control Event Rate

Odds ratio (OR) **for case-control studies**	Odds of having disease in exposed group divided by odds of having disease in unexposed group Odds Ratio = $\frac{EE/EN}{CE/CN}$ **or** $\frac{EE*CN}{EN*CE}$
Relative risk (RR) **for cohort studies**	Relative probability of getting a disease in the exposed group compared to the unexposed group. Calculated as percent with disease in exposed group divided by percent with disease in unexposed group. Relative Risk = $\frac{EE/ES}{CE/CS}$ or $\frac{EER}{CER}$
Attributable risk	The difference in risk between exposed and unexposed groups, or the proportion of disease occurrences that are attributable to the exposure (e.g., smoking causes one-third of cases of pneumonia). Attributable Risk = $\frac{EE}{ES} - \frac{CE}{CS}$ or EER – CER

Absolute Risk Reduction (ARR) **And** **Absolute Risk Increase (ARI)**	The reduction or increase in risk associated with a treatment as compared to a placebo The difference between the event rate in the intervention group and that in the control group. CER – EER If < 0 then Attributable risk reduction If>0 then Attributable risk increase
Number needed to treat (NNT)	1/absolute risk reduction An NNT of 1 means that a favourable outcome occurs in every patient given the treatment and in no patient in comparison group
Number needed to harm (NNH)	1/absolute risk increase

Worked example

	Example 1: risk reduction			Example 2: risk increase	
	Experimental group (E)	**Control group (C)**	**Total**	**(E)**	**(C)**
Events (E)	EE = 15	CE = 100	115	EE = 75	CE = 100
Non-events (N)	EN = 135	CN = 150	285	EN = 75	CN = 150
Total subjects (S)	ES = EE + EN = 150	CS = CE + CN = 250	400	ES = 150	CS = 250
Event rate (ER)	EER = EE / ES = 0.1, or 10%	CER = CE / CS = 0.4, or 40%	N/A	EER = 0.5 (50%)	CER = 0.4 (40%)

Equation	Variable	Abbr.	Example 1	Example 2
CER – EER	< 0: absolute risk reduction	ARR	(–)0.3, or (–)30%	N/A
	> 0: absolute risk increase	ARI	N/A	0.1, or 10%
(CER – EER) / CER	< 0: relative risk reduction	RRR	(–)0.75, or (–)75%	N/A
	> 0: relative risk increase	RRI	N/A	0.25, or 25%
1 / (CER – EER)	< 0: number needed to treat	NNT	(–)3.33	N/A
	> 0: number needed to harm	NNH	N/A	10
EER / CER	relative risk	RR	0.25	1.25
(EE / EN) / (CE / CN)	**odds ratio**	OR	0.167	1.5
EER – CER	attributable risk	AR	(–)0.30, or (–)30%	0.1, or 10%
(RR – 1) / RR	attributable risk percent	ARP	N/A	20%
1 – RR (or 1 – OR)	preventive fraction	PF	0.75, or 75%	N/A

Results of hypthetical randomised trial

Treatment	Total number of patients treated	Number who achieved at least 50% pain relief	Number who did not achieve at least 50% pain relief
Ibuprofen 400 mg	40	22	18
Placebo	40	7	33

Calculations made from these results

Experimental event rate (EER, event rate with ibuprofen)	22/40 = 0.55 or 55%
Control event rate (CER, event rate with placebo)	7/40 = 0.18 or 18%
Experimental event odds	22/18 = 1.2
Control event odds	7/33 = 0.21
Odds ratio	1.2/0.21 = 5.7
Relative risk (EER/CER)	0.55/0.18 =3.1
Relative risk increase (100(EER-CER)/CER) as a percentage	100((0.55-0.18)/0.18) = 206%
Absolute risk increase or reduction (EER-CER)	0.55 - 0.18 = 0.37 (or 37%)
NNT (1/(EER-CER))	1/(0.55 - 0.18) = 2.7

Table 3: Outputs of meta-analysis of rizatriptan 10 mg versus placebo for acute migraine

Outcome	Number of patients with the outcome		Output					
	Treatment (2056 patients)	Placebo (1249 patients)	Odds ratio	Relative benefit	Relative risk increase (%)	Absolute risk increase (%)	NNT	Percent of patients with the outcome
Headache response at 2 hours	1460	475	3.9	1.9	87	33	3.0	71
Pain free at 2 hours	843	125	4.5	4.1	310	31	3.2	41
Headache response over 24 hours	761	225	2.5	2.1	106	19	5.3	37
Pain free over 24 hours	514	87	3.4	3.6	257	18	5.5	25
Bigger or smaller numbers better			Bigger	Bigger	Bigger	Bigger	Smaller	Bigger

Table 4: Outputs of meta-analysis of prophylaxis for NSAID-induiced gastroduodenal ulcer

Treatment	Number of patients with the outcome/total		Output						
	Treatment	Placebo	Odds ratio	Relative risk	Relative risk reduction (%)	Absolute risk reduction (%)	NNT	Percent with treatment	Percent with placebo
Standard dose H2A	48/494	75/487	0.6	0.6	33	5	17	10	15
Double dose H2A	22/151	53/147	0.3	0.4	58	21	4.7	15	36
400 ug misoprostol	21/357	49/366	0.4	0.4	54	7	13	6	13
800 ug misoprostol	8/380	45/376	0.2	0.2	83	10	10	2	12
PPI	49/443	98/331	0.2	0.3	63	19	5.4	11	30

A good resource to look at: http://www.medicine.ox.ac.uk/bandolier/Extraforbando/Outputs.pdf

And http://www.medicine.ox.ac.uk/bandolier/Extraforbando/Size.pdf be prepared to see unusual graphs in the exam and a random question about them. Most of them follow the same logic but different presentations, so make yourself familiar with different graphs and save time in the exam.

Figure 1: L'Abbé plot of DICE 1 trials

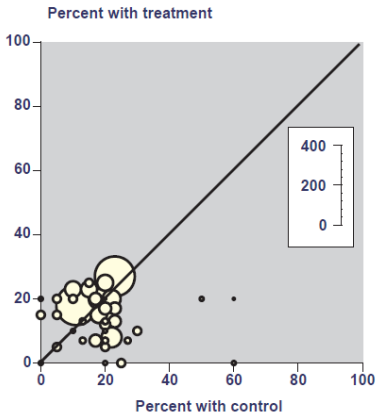


Figure 2: Odds ratios for individual DICE studies, by number in "trial". Filled bars were statistically significant

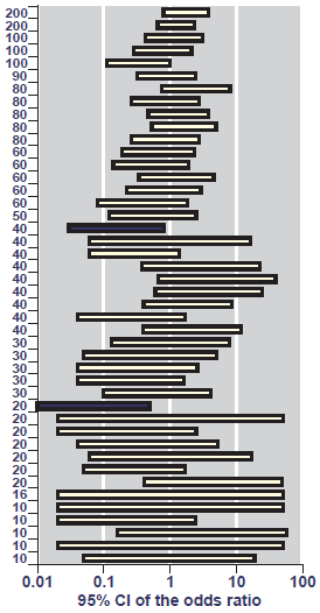


Figure 3: Percentage of events in each trial arm of DICE "trials"

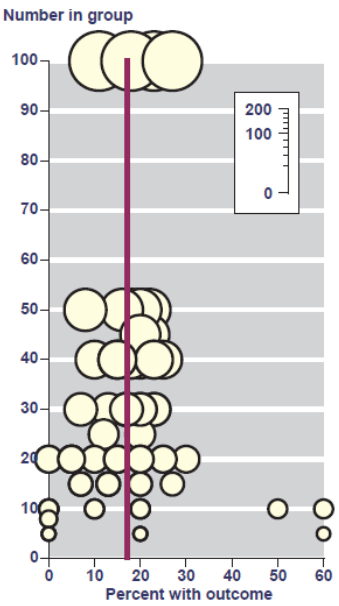


Figure 3: Trials of ibuprofen in acute pain that are randomised, double blind, and with the same outcomes over the same time in patients with the same initial pain intensity

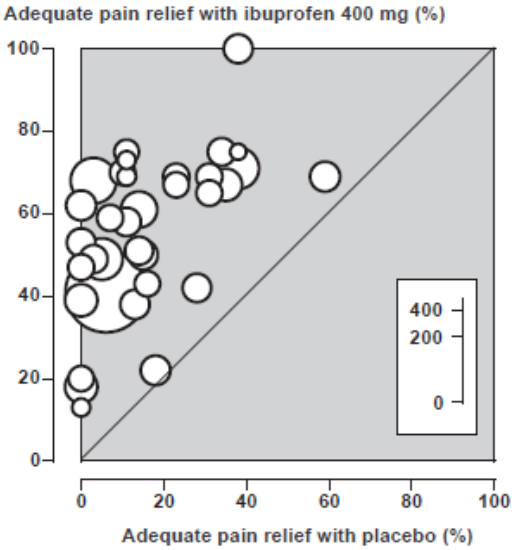
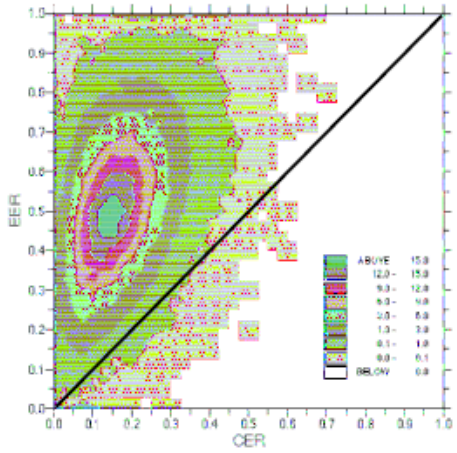


Figure 4: Computer model of trials of ibuprofen in acute pain. Intensity of colour matches probability of outcome of a single trial



In Figure 4 CER (control event rate) is equivalent to placebo and EER (experimental event rate) to ibuprofen in clinical trails

Figure 8: Difference between nicotine patch or gum and placebo patch or gum for smoking cessation after at least six months

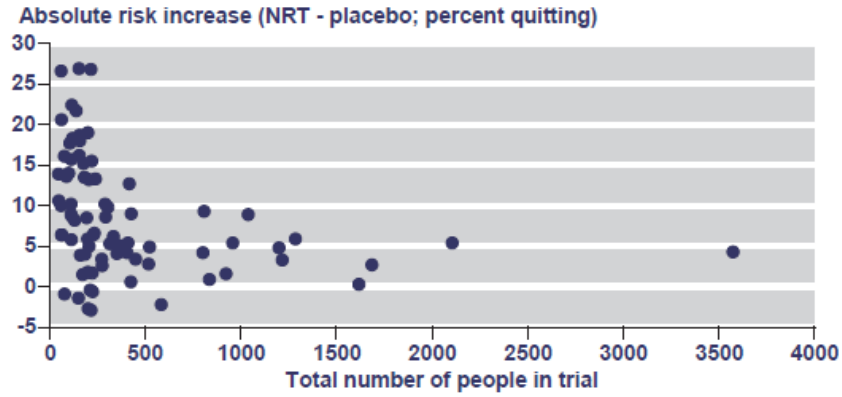


Table 8: NNTs obtained with larger or smaller trials of nicotine patch and gum

NRT type	Trial size	Number of Trials	Number of Patients	Percent quitting with NRT	Percent quitting with Placebo	NNT 95% CI
Patch	>500	9	11,170	13	8	18 (15 - 22)
	<500	22	4,508	17	9	13 (10 - 17)
Gum	>500	7	8,509	13	9	25 (18 - 38)
	<500	41	8,197	25	15	11 (9 - 13)

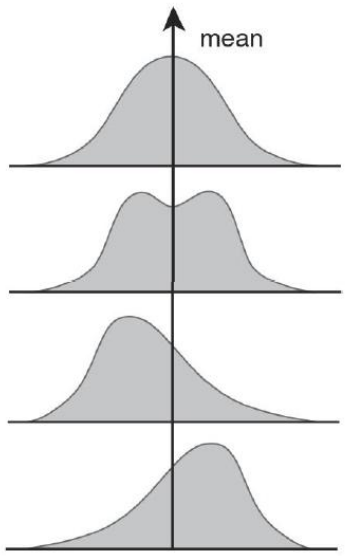
Bias

Occurs when 1 outcome is systematically favored over another.(Systematic errors)

Selection bias	Non random assignment to study group
Recall bias	knowledge of presence of disorder alters recall by subjects
Sampling bias	subjects are not representative relative to general population; therefore, results are not generalizable
Late-look bias	information gathered at an inappropriate time —e.g., using a survey to study a fatal disease (only those patients still alive will be able to answer survey)
Procedure bias	subjects in different groups are not treated the same —e.g., more attention is paid to treatment group, stimulating greater compliance
Confounding bias	occurs with 2 closely associated factors; the effect of 1 factor distorts or confuses the effect of the other
Lead-time bias	early detection confused with increased survival; seen with improved screening (natural history of disease is not changed, but early detection makes it seem as though survival has increased)
Pygmalion effect	occurs when a researcher's belief in the efficacy of a treatment changes the outcome of that treatment
Hawthorne effect	occurs when the group being studied changes its behaviour owing to the knowledge of being studied

Statistical distribution

Normal = Gaussian = bell-shaped (mean = median = mode).



Bimodal is simply 2 humps (2 modal peaks).

Positive skew—mean > median > mode. Asymmetry with tail on right.

Negative skew—mean < median < mode. Asymmetry with tail on left.

Mode is least affected by outliers in the sample

Statistical hypotheses

Null (H_0)	Hypothesis of no difference (e.g., there is no association between the disease and the risk factor in the population).
Alternative (H1)	Hypothesis that there is some difference (e.g., there is some association between the disease and the risk factor in the population).
Type I error (a)	• Stating that there is an effect or difference when none exists (to mistakenly accept the experimental hypothesis and reject the null hypothesis), • *p* = probability of making a type I error, • *p* is judged against a preset level of significance (usually < .05). • *"*False-positive error."
Type II error (β)	• Stating that there is not an effect or difference when one exists (to fail to reject the null hypothesis when in fact H_0 is false). • β is the probability of making a type II error. • "False-negative error." • Probability of accepting a hypothesis that is actually false
Power (1 - B)	• Probability of rejecting null hypothesis when it is in fact false, or the likelihood of finding a difference if one in fact exists. It depends on: 1. Total number of end points experienced by population 2. Difference in compliance between treatment groups (differences in the mean values between groups) 3. Size of expected effect

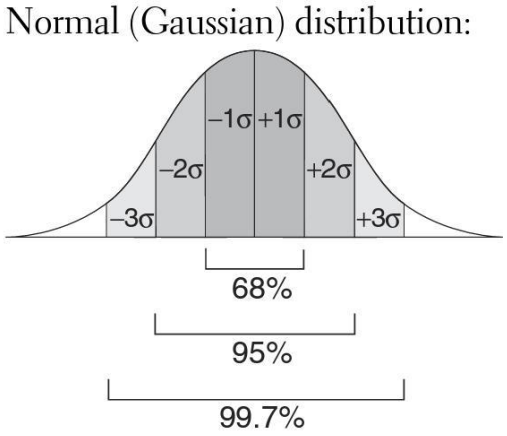
Statistical hypotheses

		Reality	
		H1	H0
Study Result	H1	Power (1-β)	α
	H0	β	

α = you "saw" a difference that did not exist—for example, convicting an innocent man.

β = you did not "see" a difference that does exist— for example, setting a guilty man free.

Standard deviation vs. standard error



n = sample size.

δ = standard deviation.

SEM = standard error of the mean.

$$SEM = \frac{\delta}{\sqrt{n}}$$

Therefore, SEM < δ and SEM decreases as "n" (Sample size) increases.

t-Test vs. ANOVA vs. x^2 vs. ANCOVA

t-Test	Checks differences between the **means** of **2** groups Mr T is MEAN
ANOVA	Checks differences between the **means** of **3 or more** groups
ANCOVA ***Analysis of covariance***	ANCOVA is an extension of analysis of variance to allow for the inclusion of continuous variables in the model.

x^2 (chi square)	x^2 test checks differences between 2 or more percentages of proportions of categorical variables (not mean values)

Variables

Categorical variable	A variable whose value represent different categorise of the same feature. Example: blood groups, different eye colour, different ethnic group
Binary variable	When variable has only two categories. Example: gender
Ordinal variable	Where there is inherent ordering Example: mild, moderate, Severe
Continuous variable	Variable can take any value within given range Example: BP reading
Discrete variable	Data can only be certain values, Example: whole numbers.

Meta-analysis

Meta analysis is a popular subject in the AKT exam. You are guaranteed to get one or two questions about meta-analysis therefore let's spend some time to understand the concept and interpretation of meta-analysis.

What is meta-analysis

- Meta-analysis is a statistical technique for combining the findings from independent studies.
- Meta-analysis is most often used to assess the clinical effectiveness of healthcare interventions; it does this by combining data from two or more randomised control trials.
- Meta-analysis of trials provides a precise estimate of treatment effect, giving due weight to the size of the different studies included.
- The validity of the meta-analysis depends on the quality of the systematic review on which it is based.
- Good meta-analyses aim for complete coverage of all relevant studies, look for the presence of heterogeneity, and explore the robustness of the main findings using sensitivity analysis.

Benefits of meta-analyses

Overcoming bias

The danger of unsystematic (or narrative) reviews, with only a portion of relevant studies included, is that they could introduce bias. Certain (perhaps favourable) reports may be more likely to be included in a review than those which show no significant differences; and informal synthesis may be tainted by the prior beliefs of the reviewer. Meta-analysis carried out on a rigorous systematic review can overcome these dangers – offering an unbiased synthesis of the empirical data.

Precision

The precision with which the size of any effect can be estimated depends to a large extent on the number of patients studied. Meta-analyses, which combine the results from many trials, have more power to detect small but clinically significant effects. Furthermore, they give more precise estimates of the size of any effects uncovered. Systematic aggregation of data from many individual studies gives a clearer picture, particularly through use of the technique of metaregression.

Transparency

Another advantages lies in the openness with which good meta-analyses reveal all the decisions that have been taken throughout the process of achieving the final aggregate effect sizes. Thus, good meta-analyses should allow readers to determine for themselves the reasonableness of the decisions taken and their likely impact on the final estimate of effect size.

Checking for publication bias

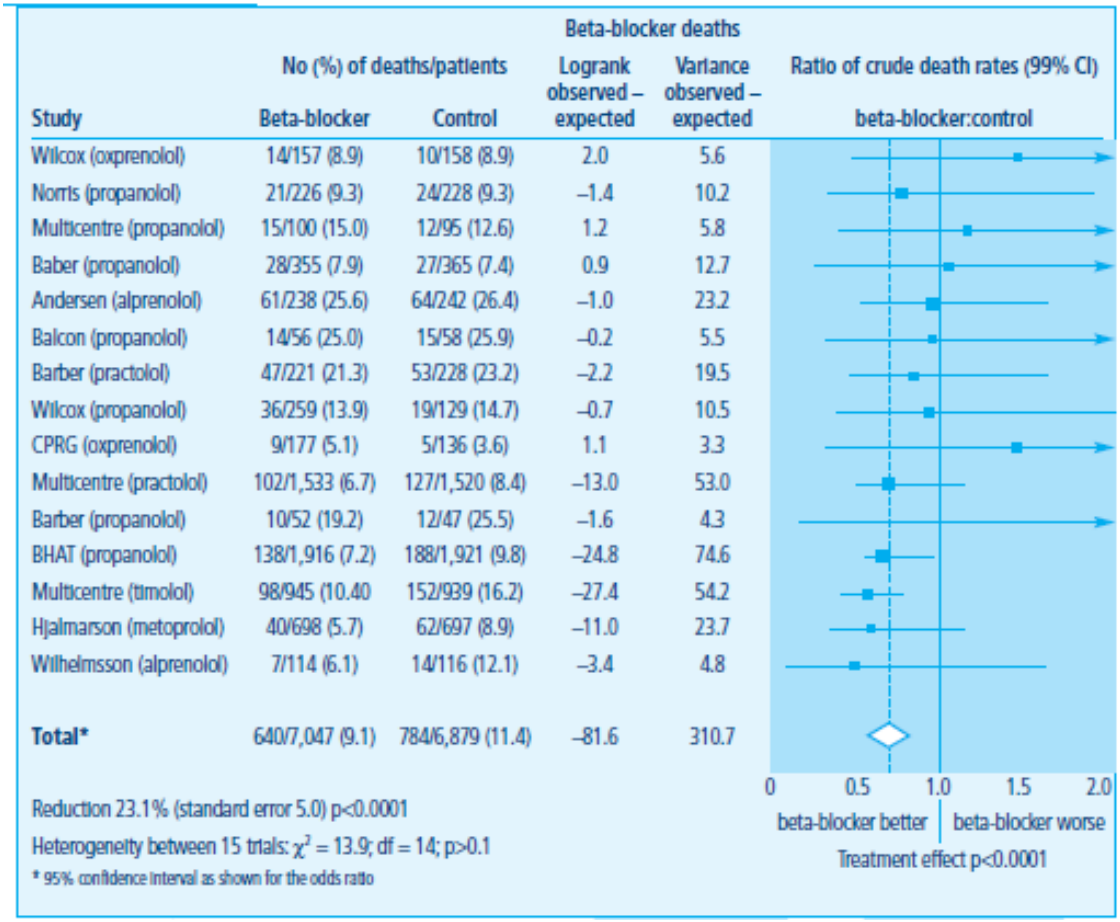
A key concern is publication bias, as clinical trials that obtain negative findings (that is, no benefit of treatment) are less likely to be published than those that conclude the treatment is effective.

One simple way of assessing the likely presence of publication bias is to examine a **funnel plot**.

Funnel plots display the studies included in the metaanalysis in a plot of effect size against sample size as smaller studies have more chance variability than larger studies, the expected picture is one of a symmetrical inverted funnel. If the plot is asymmetric, this suggests that the metaanalysis may have missed some trials – usually smaller studies showing no effect.

Sensitivity analyses

Because of the many ways in which decisions taken about selection, inclusion and aggregation of data may affect the main findings, it is usual for meta-analysts to carry out some **sensitivity analysis.** This explores the ways in which the main findings are changed by varying the approach to aggregation. A good sensitivity analysis will explore, among other things, the effect of excluding various categories of studies; for example, unpublished studies or those of poor quality. It may also examine how consistent the results are across various subgroups (perhaps defined by patient group, type of intervention or setting). In meta-analyses without sensitivity analyses, the reader has tomake guesses about the likely impact of these important factors on the key findings.



Presenting the findings

Forest plot

The usual way of displaying data from a meta-analysis is by a pictorial representation (sometimes known as a **Forest plot or blobbogram).**

Elements that you usually find in a forest plot are:

Element	Note
Blob or **Square**	• findings from each individual study as a blob or square • Squares toward the left side indicating the new treatment to be better, whereas those on the right indicate the new treatment to be less effective • The size of the blob or square is proportional to the precision of the study (roughly speaking, the sample size).
Horizontal line on each square	• Represents the 95% confidence interval • Represents the uncertainty of the estimate of the treatment effect • Wider line means less certainty about the result or wide CI • If the line passes the vertical line of no effect it means that study is not statistically significant
Diamond	• The aggregate effect size obtained by combining all the studies is usually displayed as a diamond • Width of diamond shows the 95%CI • If diamond crosses the vertical line of no effect that means overall there is no statistical significance.

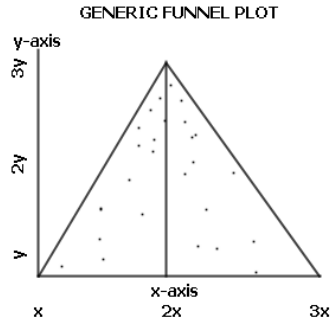
Vertical central line	• Also called line of no effect • Odd ratio of 1 • Means risk and benefit are equal • A statistical significant study does not cross this line
Horizontal line	• Has label and tells us which treatment is favoured to the left and which to the right • In above chart, treatments to the left are favoured and labelled as "Beta blocker better"
Heterogeneity	• Test for heterogeneity can be found in the lower left of the chart • If all studies is positive evidence that studies are reporting different result (heterogeneous), the P value will be significant (low low low) • Large P value, say >0.1 reassures us that the studies are likely to be all measuring the same thing.

Important notes

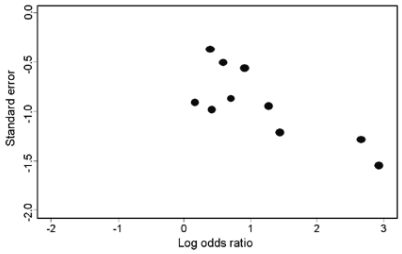
- A confidence interval calculated for **a measure of treatment effect** shows the range within which the true treatment effect is likely to lie (subject to a number of assumptions).
- A p-value is calculated to assess whether trial results are likely to have occurred simply through chance (assuming that there is no real difference between new treatment and old, and assuming, of course, that the study was well conducted).
- Confidence intervals are preferable to p-values, as they tell us the **range of possible effect sizes** compatible with the data.
- p-values simply provide a cut-off beyond which we assert that the findings are 'statistically significant' (by convention, this is p<0.05).
- A confidence interval that **embraces the value of no difference between treatments** indicates that the treatment under investigation is not significantly different from the control.
- Confidence intervals **aid interpretation of clinical trial data** by putting upper and lower bounds on the likely size of any true effect.
- **Bias must be assessed** before confidence intervals can be interpreted. Even very large samples and very narrow confidence intervals can mislead if they come from biased studies.
- **Non-significance does not mean 'no effect'.** Small studies will often report non-significance even when there are important, real effects which a large study would have detected.
- Statistical significance does not necessarily mean that the effect is real: by chance alone about **one in 20 significant findings will be spurious.**
- Statistically significant does not necessarily mean clinically important. It is the **size of the effect** that determines the importance, not the presence of statistical significance.
- **Odd ratio & Risk Ration (relative risk)** are both measure of effect size and are interpreted in the same way (although technically different)
- Ratio of 2 implies the outcome happens twice as often in the intervention group. 1 is the line of no effect so (2-1=1*%100=**increase** the risk by %100 or double the risk when compared to the line of no effect)
- Ratio of 0.5 (on the left side of plot) implies %50 **reduction** in the risk

Funnel plot

A **funnel plot** is a useful graph designed to check the existence of publication bias in systematic reviews and meta-analyses. It assumes that the largest studies will be near the average, and small studies will be spread on both sides of the average. Variation from this assumption can indicate publication bias.



If the lower left of the funnel plot has no dots then think about publication bias



The funnel plot has some limitations; for example, it can sometimes be difficult to detect asymmetry by eye.To help with this, formal statistical methods have been developed to test for heterogeneity.

Egger's regression test has been widely used to test for publication bias. It tests whether small studies tend to have larger effect sizes than would be expected (implying that small studies with small effects have not been published). Another regression test, which in some circumstances may be better than Egger's test, has been proposed. However, care is needed in the interpretation of the findings whatever test has been used. There is currently no clear direction in recent literature to indicate when to use each test.

Cox Model

What is Cox model	• The Cox model is a well-recognised statistical technique for analysing survival data. • Isolates the effects of treatment from the effects of other variables. • Using the model may improve the estimate of treatment effect by narrowing the confidence interval.
Survival times	Refers to the development of a particular symptom or to relapse after remission of a disease, as well as to the time to death.
Censored survival time	A significant feature of survival times is that the event of interest is very rarely observed in all subjects. Some patients are still alive at the end of study and we don't know when they will die therefore we don't know the survival time and is called censored survival time

	to indicate the period of observation ended before the event of interest occurred.
Kaplan–Meier method	Estimates the proportion of the population of such people who would survive a given length of time under the same circumstances from a set of observed survival times (including censored times) in a sample of individuals. (See below) The data on ten patients presented in Table 1 refer to the survival time in years following treatment for malignant melanoma of the skin.

Table 1. Calculation of Kaplan–Meier estimate of the survivor function

A Survival time (years)	B Number at risk at start of study	C Number of deaths	D Number censored	E Proportion surviving until end of interval	F Cumulative proportion surviving
0.909	10	1	0	1 – 1/10 = 0.900	0.900
1.112	9	1	0	1 – 1/9 = 0.889	0.800
1.322*	8	0	1	1 – 0/8 = 1.000	0.800
1.328	7	1	0	1 – 1/7 = 0.857	0.686
1.536	6	1	0	1 – 1/6 = 0.833	0.571
2.713	5	1	0	1 – 1/5 = 0.800	0.457
2.741*	4	0	1	1 – 0/4 = 1.000	0.457
2.743	3	1	0	1 – 1/3 = 0.667	0.305
3.524*	2	0	1	1 – 0/2 = 1.000	0.305
4.079*	1	0	1	1 – 0/1 = 1.000	0.305

* Indicates a censored survival time

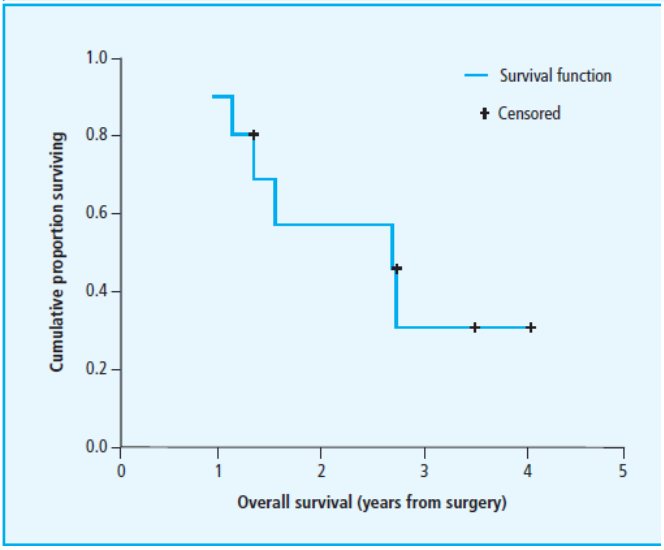


Figure: Kaplan–Meier estimate of the survival function

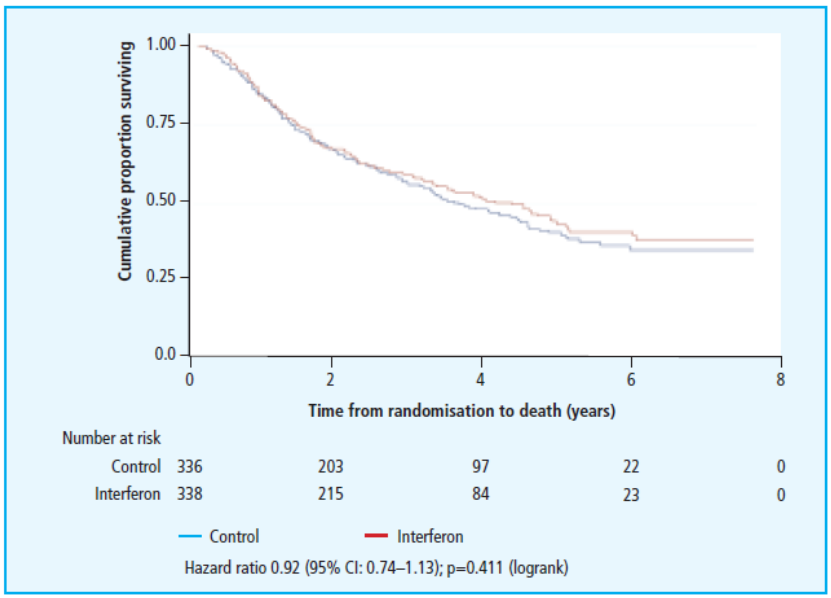
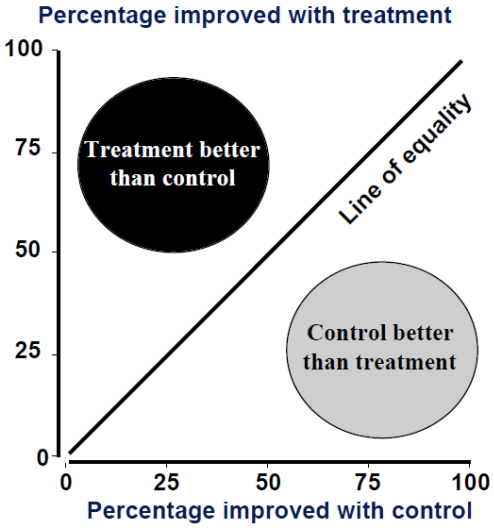


Figure: Kaplan-Meier survival curves in patients receiving treatment for malignant melanoma

regression	• If we want to describe the relationship between the values of two or more variables we can use a statistical technique called **regression**. • If we have observed the values of two variables, X (for example, age of children) and Y (for example, height of children), we can perform a regression of Y on X. • We are investigating the relationship between a **dependent variable** (the height of children) based on the **explanatory variable** (the age of children).
multiple regression	When more than one explanatory (X) variable needs to be taken into account (for example, height of the father), the method is known as **multiple regression**.

L'Abbé Plots



one of the most sensible and understandable ever written on systematic reviews. The authors suggest a simple graphical representation of the information from trials. Each point on a L'Abbé

scatter plot is one trial in the review. The proportion of patients achieving the outcome with the experimental intervention is plotted against the event rate in controls.

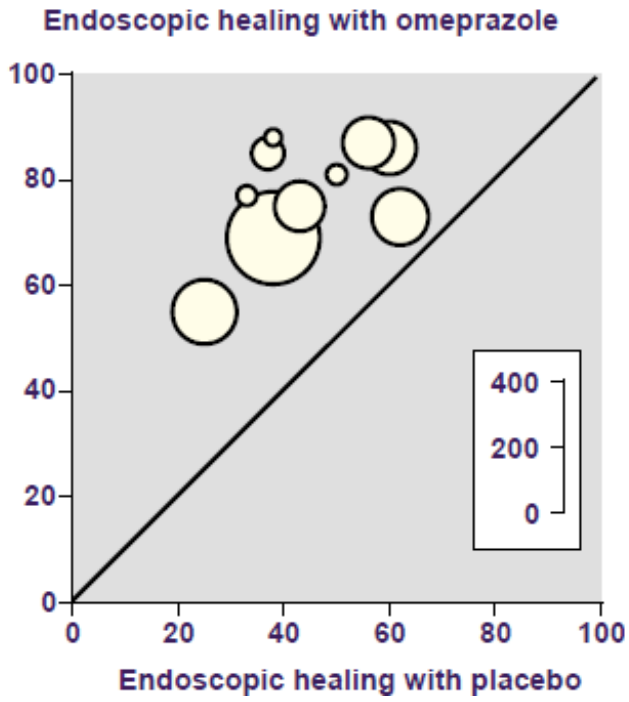


Figure above shows that all the studies are well to the upper left of the line of equality meaning that in all trials omeprazole was better than placebo.

Examples

Paracetamol in acute postoperative pain

If you were responsible for organising pain relief after day-case or minor surgery, you would want to make sure that patients had good pain relief. Your first choice of analgesic might well be Paracetamol, but then you'd ask yourself – just how good is it as an analgesic in this circumstance? Fortunately, a Cochrane review provides lots of data to help you make your decision.

In 28 randomised trials with 3,200 patients, the results were as follows.

- With paracetamol 1,000 mg, 876/1,903 (46%) patients with moderate or severe postoperative pain had the outcome of at least 50% pain relief over six hours.
- With placebo, 241/1,329 (18%) patients had the same outcome.

Can you calculate the Number Need to Treat (NNT)?

Relative risk in the first treatment group= 876/1,903= 0.46

Relative risk in the control group= 241/1,329= 0.18

So

The NNT was, therefore: 1/(876/1,903) – (241/1,329)

= 1/(0.46 – 0.18)

= 1/0.28

= 3.6

For every four patients with moderate or severe postoperative pain, one would have at least 50% pain relief who would not have that relief with placebo.

Anti-epileptics in the management of frequent migraine attacks

When people have frequent migraine attacks, a number of measures can be tried to reduce the rate. One measure is the use of antiepileptic drugs. A Cochrane review reported on randomised, mainly double-blind, trials usually lasting several months. One outcome was the number of patients having at least a 50% reduction in the number of migraine attacks over 28 days, reported in five trials for various forms of valproate. The review of these trials showed the following results.

- With valproate, 174/383 (45%) patients had the number of migraine attacks reduced by at least half.
- With placebo, 54/259 (21%) had the same outcome.

Can you calculate NNT?

0.45-0.21= 0.24

NNT = 1/0.24 = 100/24 = 4

So, for every four people with frequent migraine attacks (typically more than two attacks per month), one would have the frequency reduced by half with valproate who would not have achieved this response with placebo.

Clopidogrel plus aspirin to prevent vascular events, compared with antiplatelet monotherapy

In certain circumstances, when patients are at a high risk of adverse vascular events, the question is asked whether using two antiplatelet interventions is better than using only one. A systematic review analysed randomised trials comparing clopidogrel plus aspirin with antiplatelet monotherapy. The outcome was any major vascular event, including death, stroke or myocardial infarction. Patients included those with acute coronary syndrome, those undergoing percutaneous coronary intervention and others.

A review of eight randomised trials with over 91,000 patients showed the following results.

- With clopidogrel plus aspirin, 4,883/45,930 (11%) patients had the outcome of death, stroke, or myocardial infarction.

- With antiplaetelet monotherapy, 12,323/44,300 (%28) patients had the outcome of death, stroke, or myocardial infarction.

Calculate NNT

NNT= 1/ARR = 1/(0.28 -0.11) = 1/0.17=100/17 = 6

OddRatio

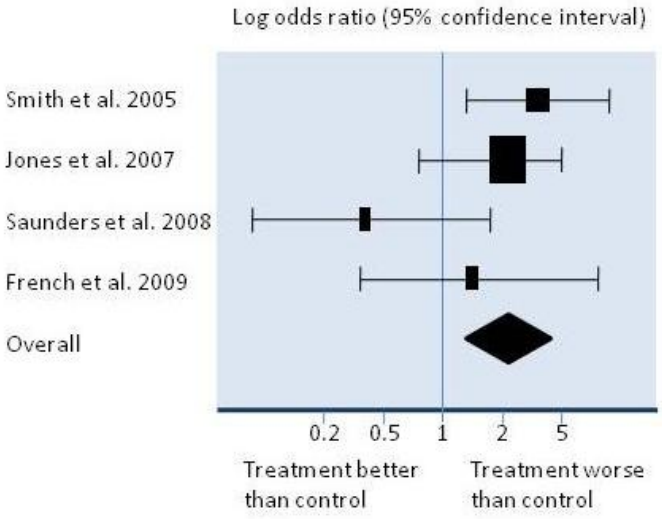
A group of 90 patients with a history of Tension type headache is matched to a group of 40 control patients with no history of headache. Thirty of the patients who've had tension type headache had stressful job compared to only 20 in the control group.

Calculate the OddRatio

Answer: 0.5

Forest Plot

A meta-analysis examine whether giving a new supplement makes symptoms of OA worse or better



Which study is clinically significant?

Which study has larger sample?

What is the overall result? Is the supplement beneficial?

For each study can you tell if the risk is more than the overall or less and what is the percentage of risk increase or reduction? (e.g Smith et al.2005 risk is %150 more than overall)

Did the Saunders study show an increased risk or reduced risk? Answer: reduced risk by %60

Finger-prick blood test

A rapid finger-prick blood test to help diagnosis deep vein thrombosis is developed. Comparing the test to current standard techniques a study is done on 1,000 patients:

	DVT present	DVT absent
New test positive	200	100
New test negative	20	680

Complete the table below:

Sensitivity	
Specificity	
Positive predictive value (PPV)	
Negative predictive value (NPV)	
Likelihood ratio for a positive test result	
Likelihood ratio for a negative test result	

Hip Protector

A study is carried out to assess the potential of hip protectors to reduce femoral neck fractures in elderly nursing home patients. The average age of the patients was 82 years. Over a two-year period 800 patients were recruited and assigned randomly either to the hip protector group or standard care group.

The results:

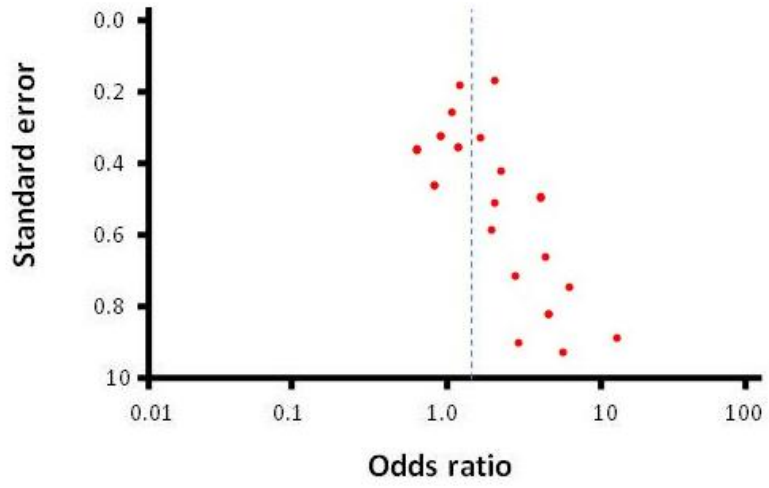
Hip protector group: 400 patients - 10 of whom had a femoral neck fracture over the two year period
Control group: 400 patients - 20 of whom had a femoral neck fracture over the two year period

Complete the following table:

Equation	Variable	Abbr.	
CER – EER	< 0: absolute risk reduction	ARR	
	> 0: absolute risk increase	ARI	
(CER – EER) / CER	< 0: relative risk reduction	RRR	
	> 0: relative risk increase	RRI	
1 / (CER – EER)	< 0: number needed to treat	NNT	
	> 0: number needed to harm	NNH	
EER / CER	relative risk	RR	
(EE / EN) / (CE / CN)	odds ratio	OR	
EER – CER	attributable risk	AR	
(RR – 1) / RR	attributable risk percent	ARP	
1 – RR (or 1 – OR)	preventive fraction	PF	

Funnel plot

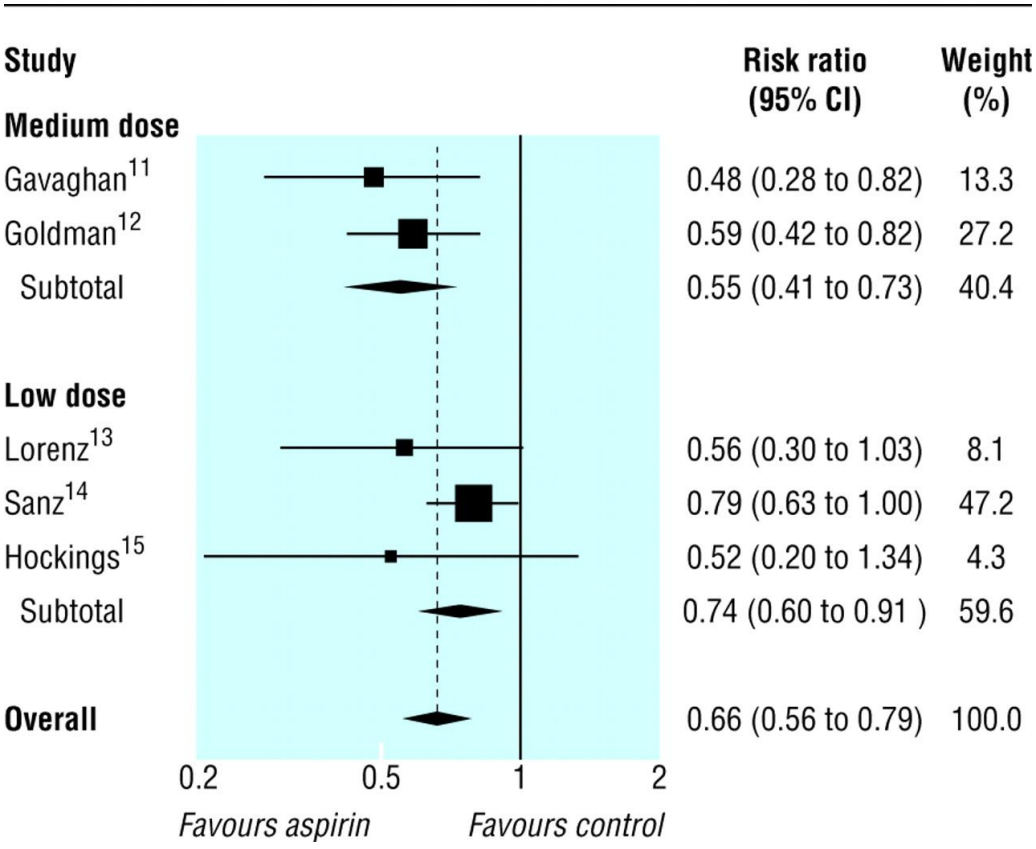
A meta-analysis looks at the benefit of Erythropoietin in patients with CKD3.The data from the 19 trials is represented in the diagram below:



Is there a publication bias here?

Aspirin after coronary surgery

Figure 2 Results of Randomised control trials of aspirin treatment after coronary surgery



Describe the Figure above