Evidence Based Dentistry

Biostatistics

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1. Clinical Trials
2. Metanalysis
3. Prognosis
4. Diagnostic tests

Clinical trials

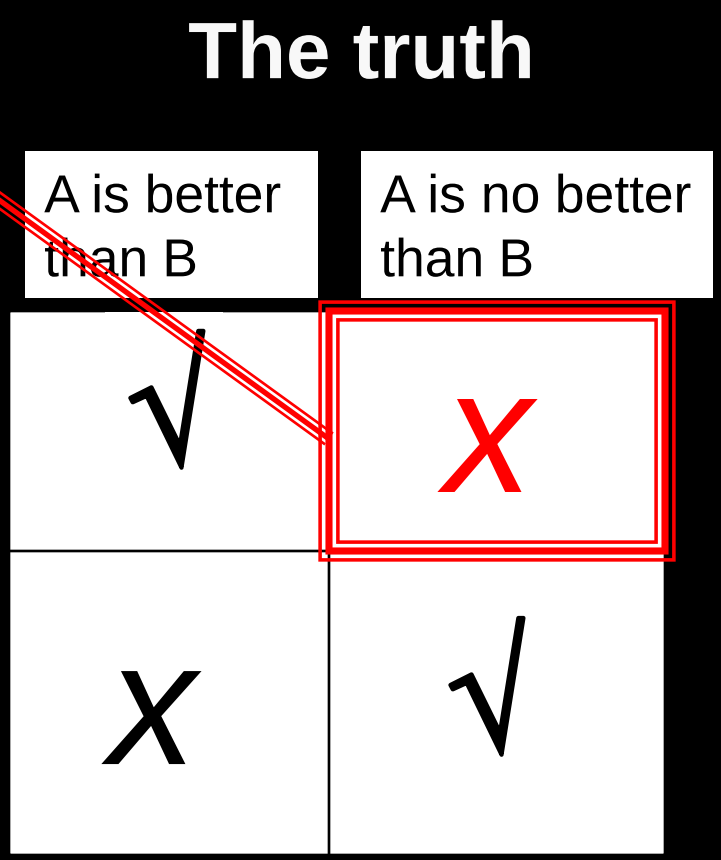
What can you show with a trial?

The truth

What the trial shows	A is better than B	A is no better than B
A is better than B	√	X
A is no better than B	X	√

What can you show with a trial?

Type 1 error
Alfa error
Optimism error

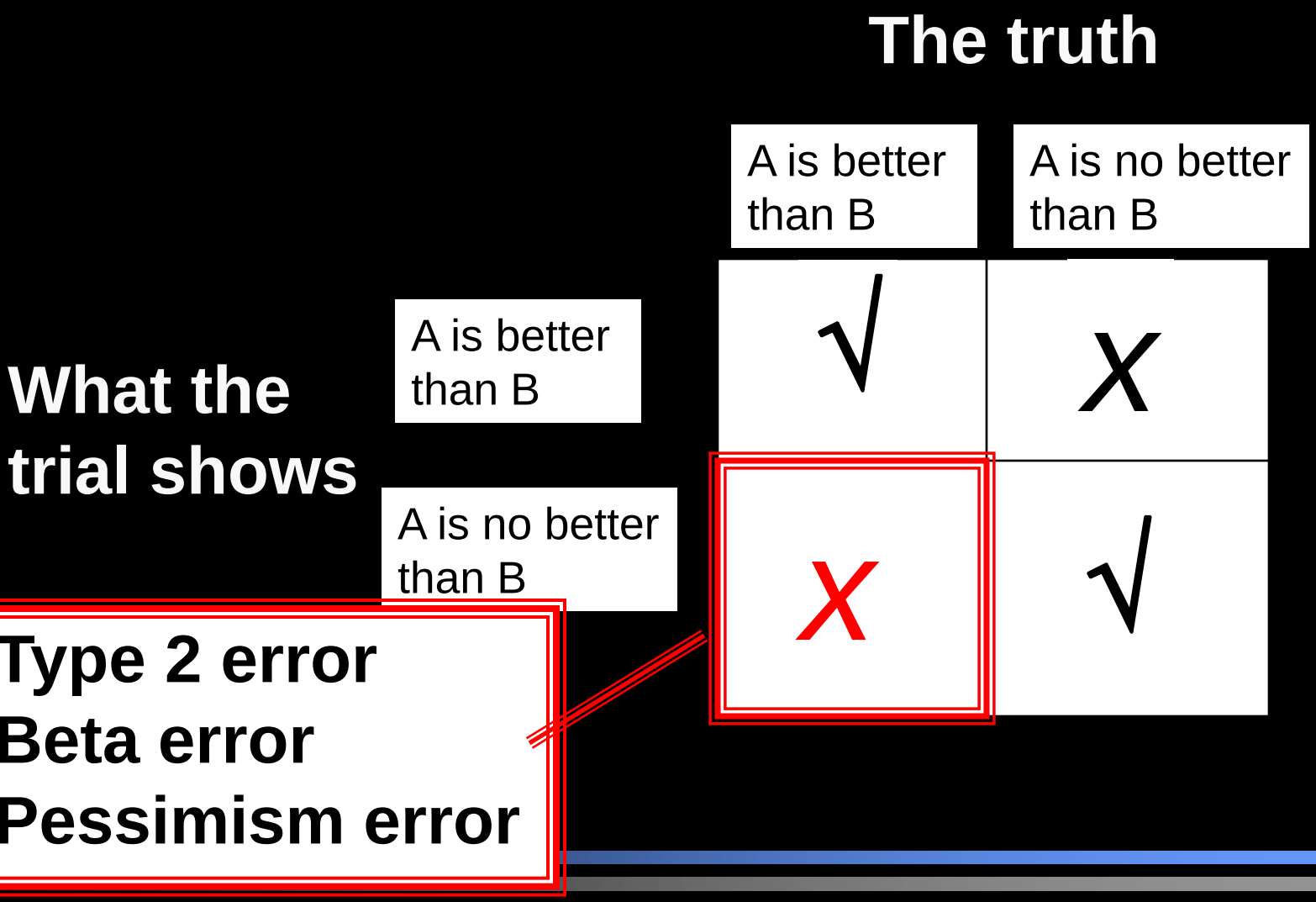


Type 1 error

Fallacies of observed clinical success

- Spontaneous remission
- Placebo response
- Multiple variables in treatment
- Radical versus conservative treatment
- Over-treatment
- Long-term failure
- Side effects and sequelae of treatment

What can you show with a trial?



Type 2 error

1. Underpowered study
2. Fallacies of observed clinical failures

- Wrong diagnosis
- Incorrect cause-effect correlations
- Multifactorial problems
- Lack of cooperation
- Improper execution of treatment
- Premature evaluation of treatment
- Limited success of treatment
- Psychological barriers to success

Meta-analysis

Meta-analysis

An overview with a specific statistical technique which summarizes the results of several studies into a single estimate

Meta-analysis/Systematic Review

- Systematic Review
  - Exhaustive exploration, critical evaluation and synthesis of all the unbiased evidence
- Meta-analysis
  - Exhaustive exploration, critical evaluation and quantitative synthesis of all the unbiased evidence
  - Combination of the results of a number of related randomised trials

		Adverse outcome	
		+	-
Treatment	+	A	B
	-	C	D

Odds ratio = (A/B)/(C/D)

Relative risk (RR) = [A/(A+B)]/[C/(C+D)]

		Adverse outcome	
		+	-
Treatment	+	A	B
	-	C	D

Odds ratio = (A/B)/(C/D)

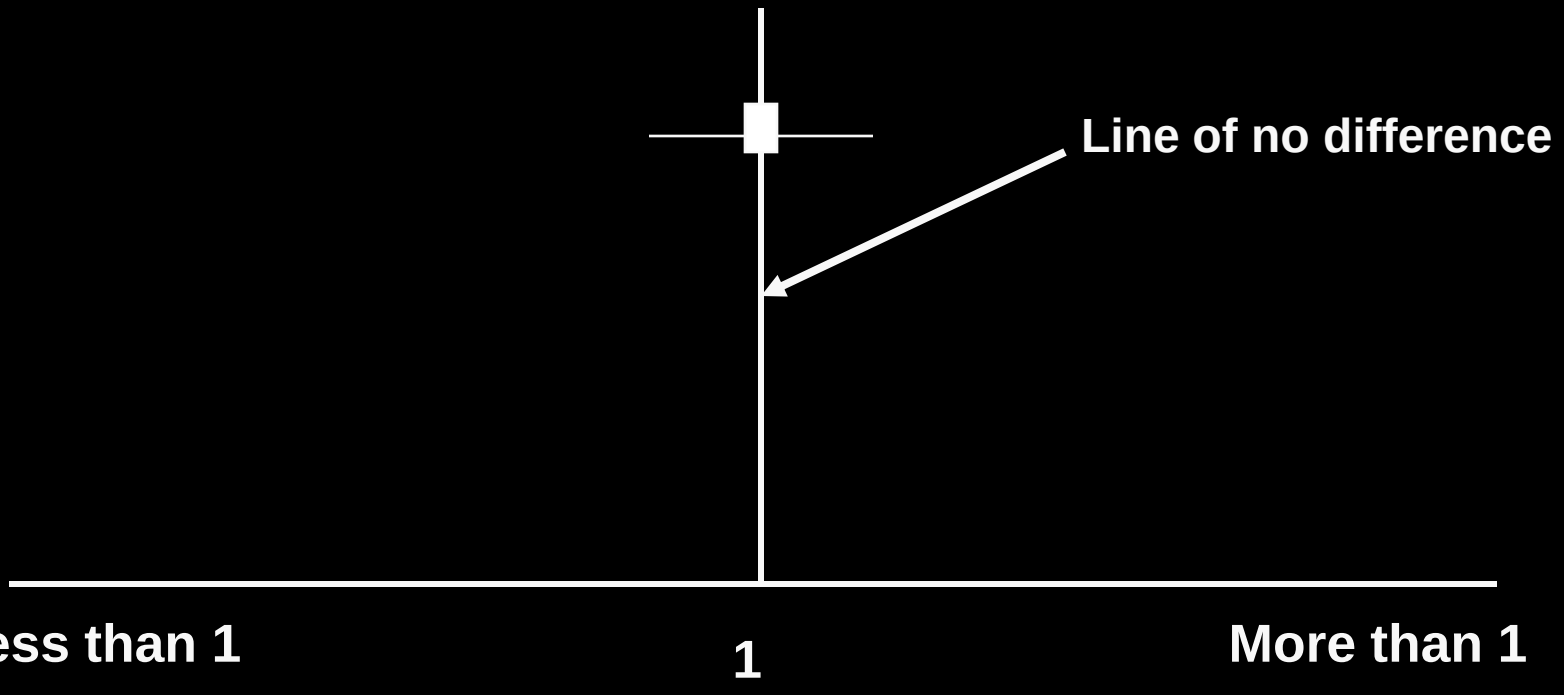
Relative risk(RR)= [A/(A+B)]/[C(C+D)]

Relative risk reduction (RRR) = 1 – RR

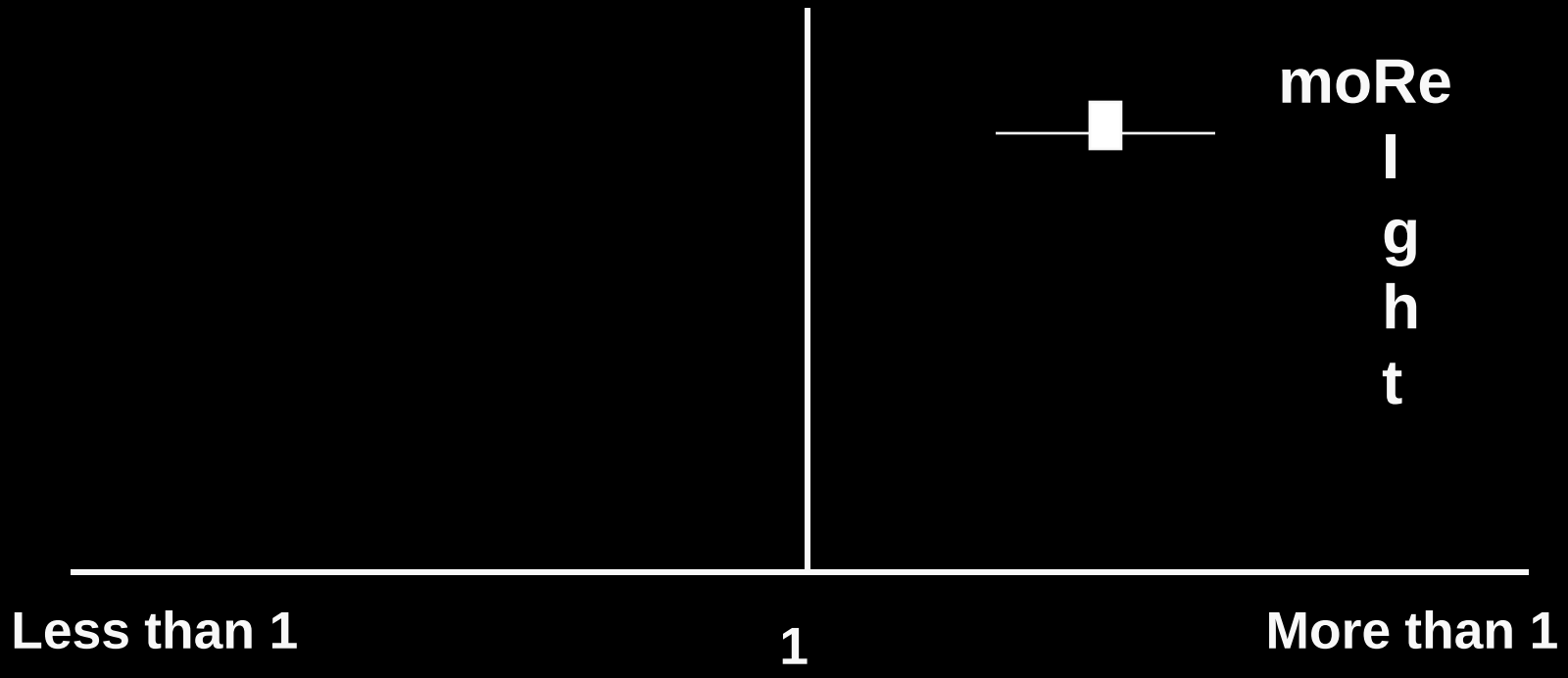
Absolute risk reduction(ARR)=A/(A+B)-C/(C+D)

Number needed to treat = 1/ARR

Odds Ratio


Line of no difference
Less than 1
1
More than 1
Favours treatment
Favours control
Therapeutic gain

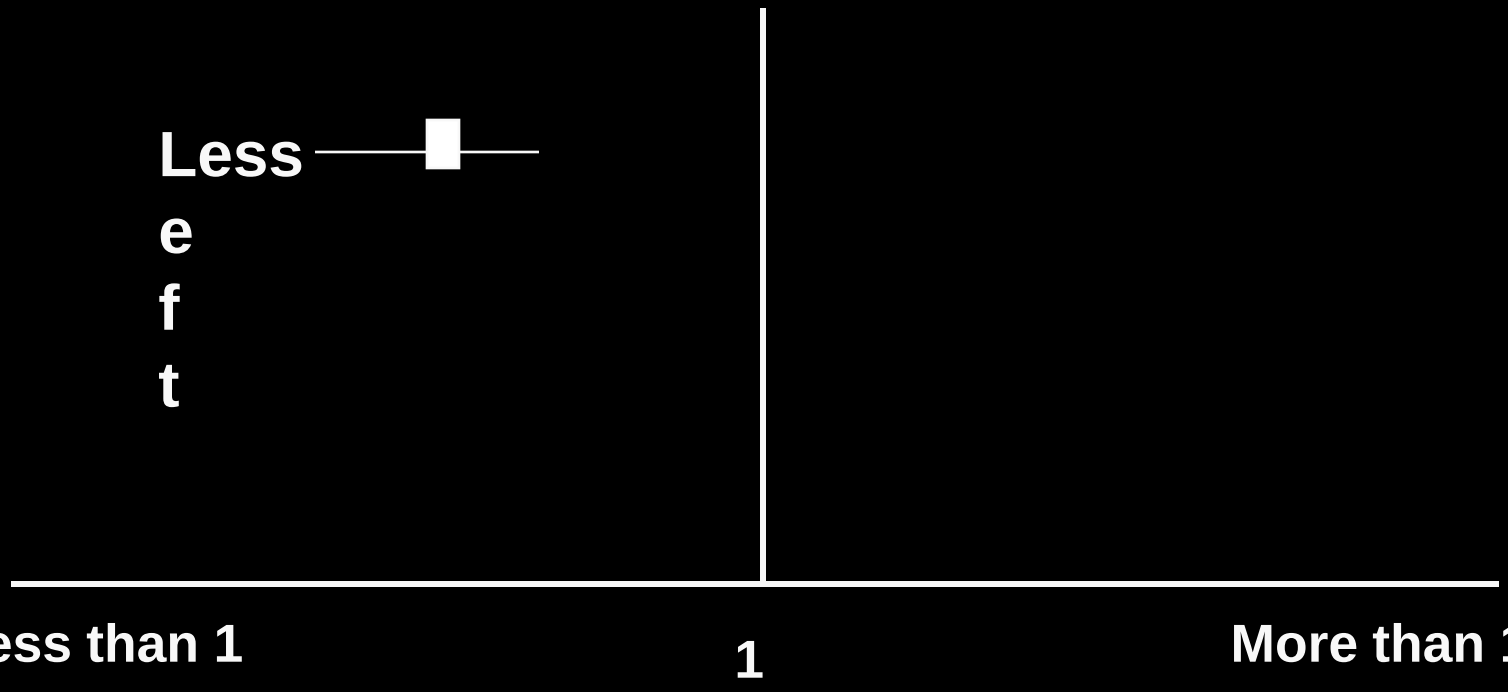
Odds Ratio



If you want more of something to happen, such as greater reduction in new cavities and the experimental intervention is successful

the results will show in the right-hand side

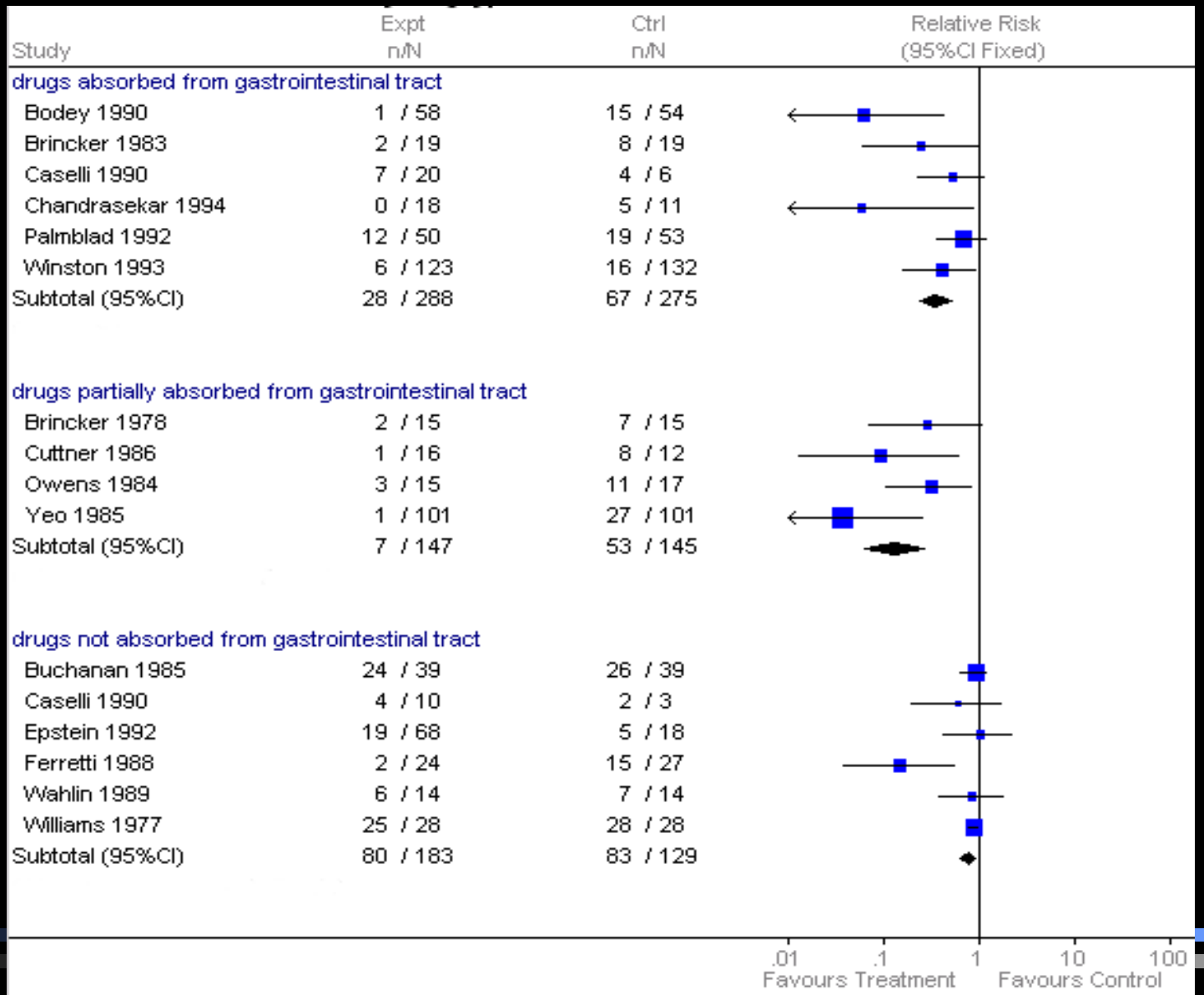
Odds Ratio



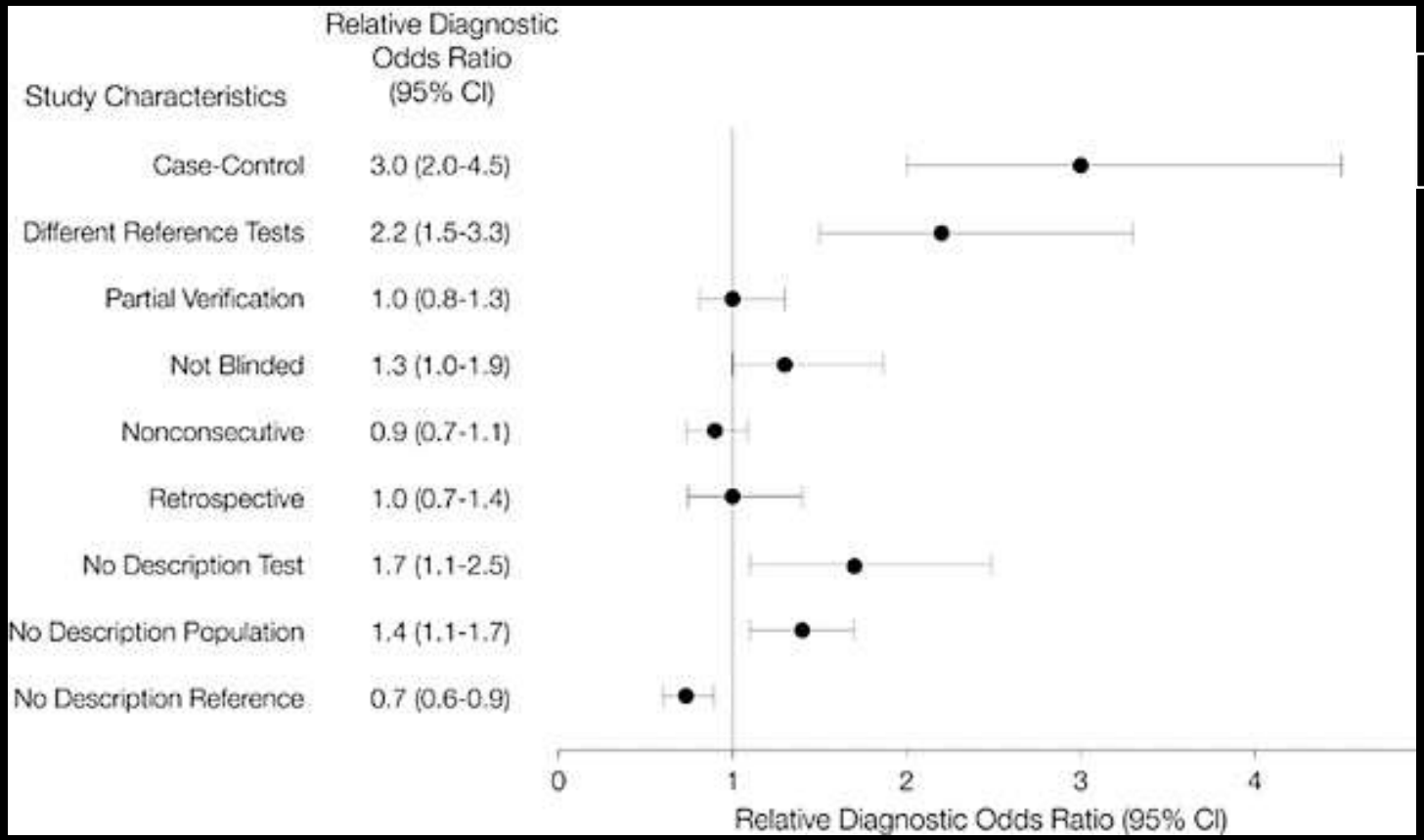
If you want less of something to happen, e.g less swelling following a minor surgical procedure if you prescribe a particular tablet and the experimental intervention is successful

the results will show in the left-hand side

Clarkson I, Worthington H. Prevention and treatment of oral mucositis and oral candidiasis for patients with cancer

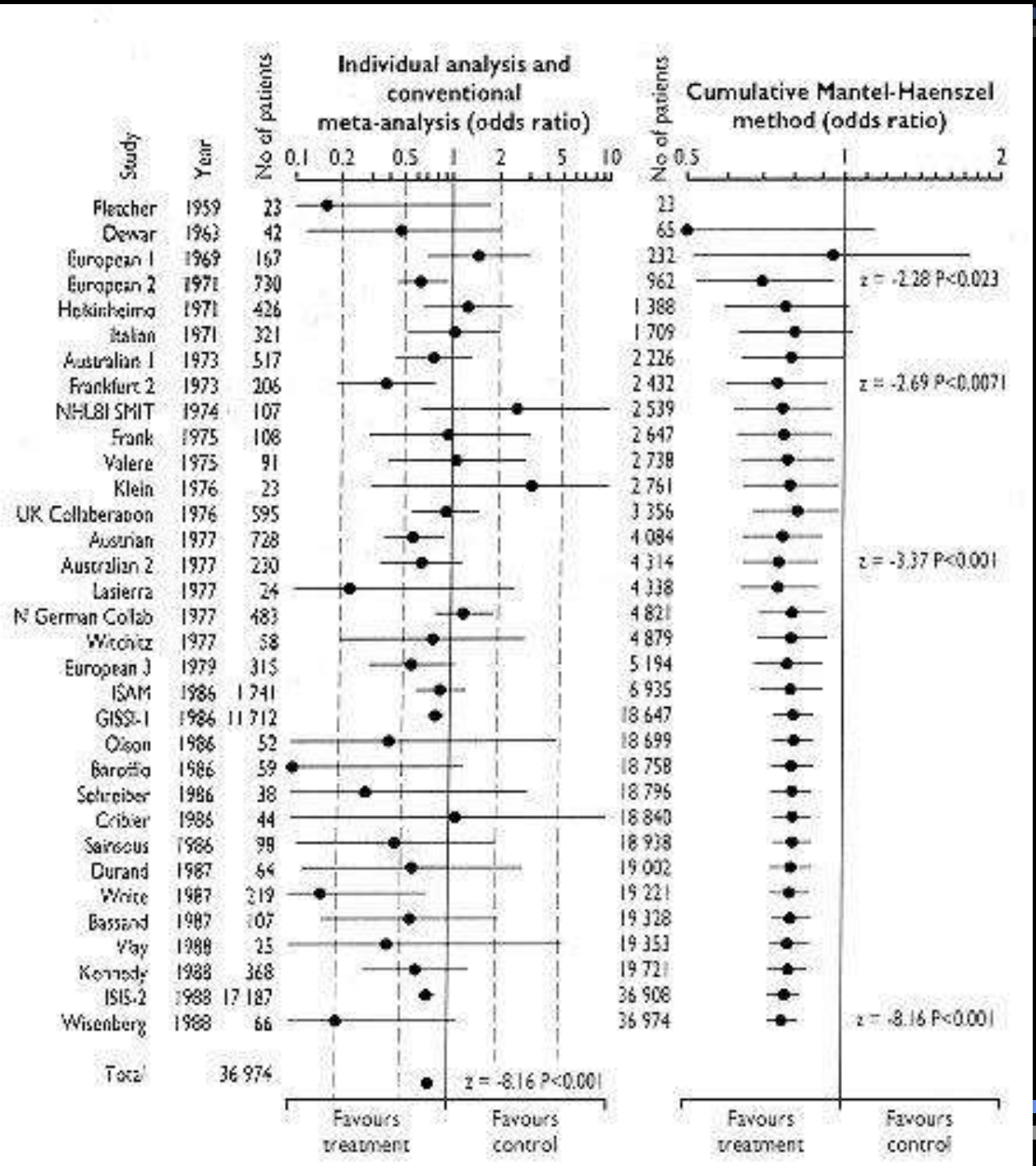


Effect of study methodology on validity

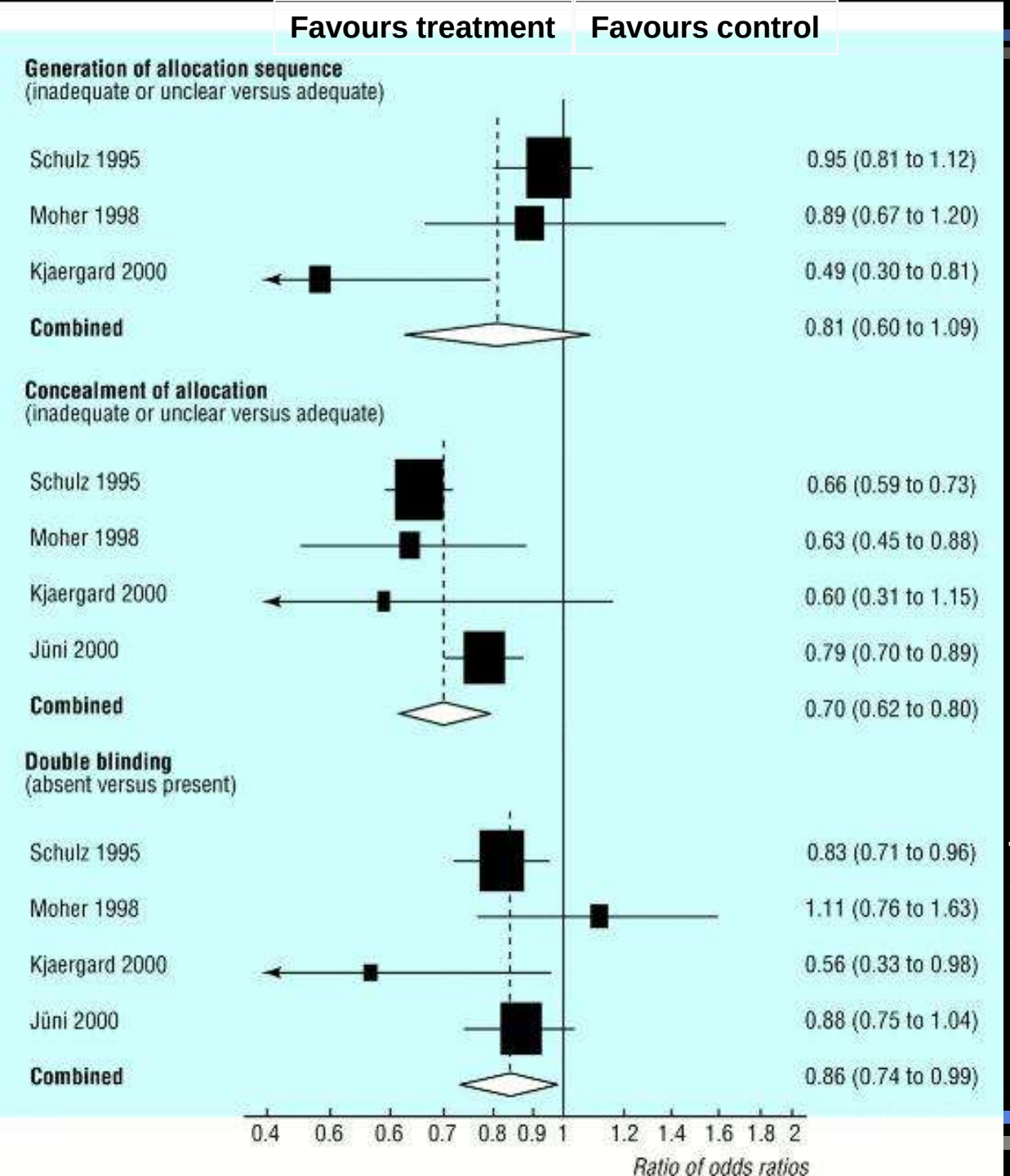


Diagnostic ”gain”

Studies of lower methodological quality, particularly those including non-representative patients or applying different reference standards, tend to overestimate the diagnostic performance of a test. Lijmer et al. JAMA, 1999; 282: 15.



Streptokinase for infarction



Effects of inadequate study design on results

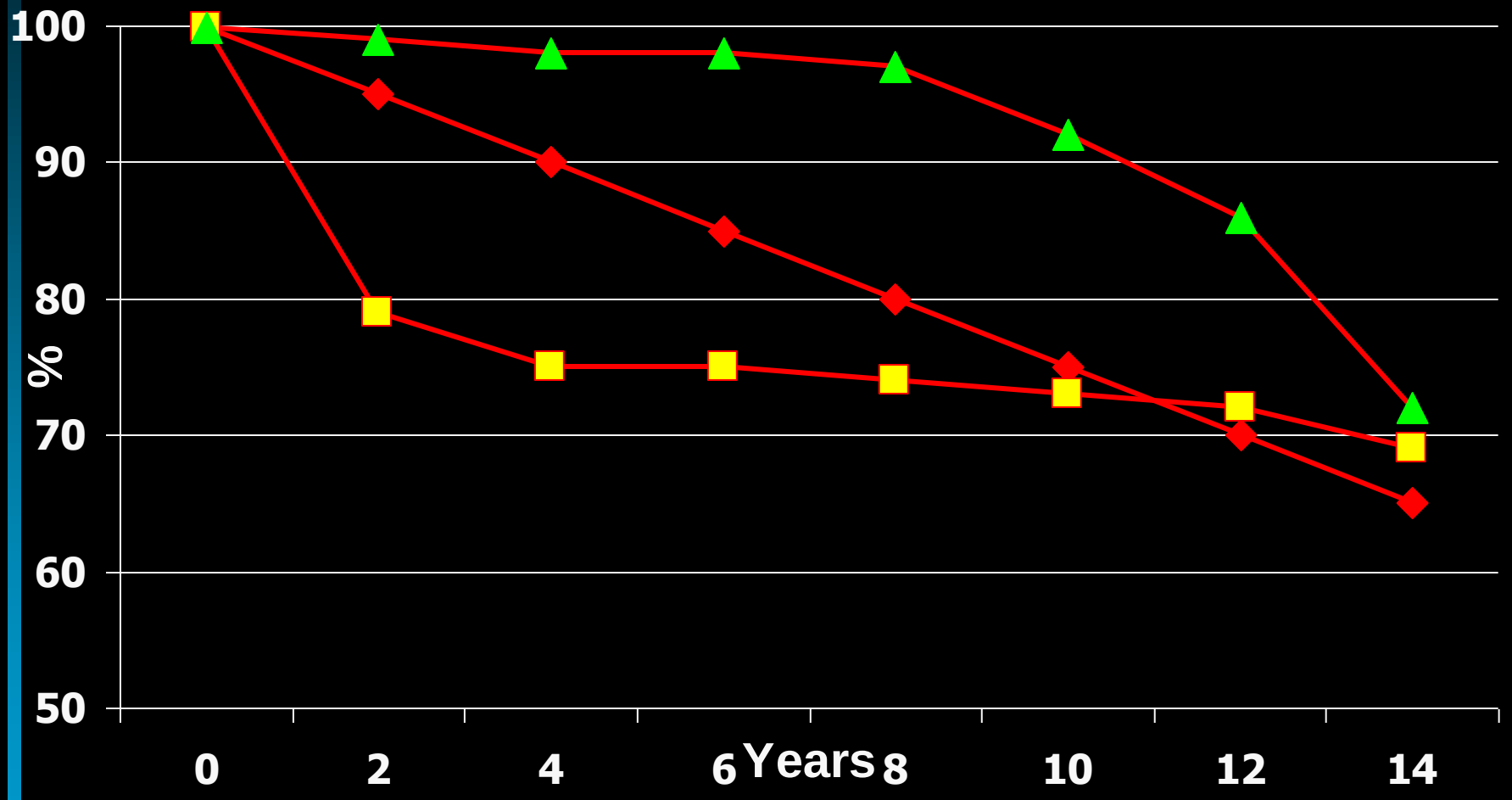
Jüni et al.Methodological quality of controlled trials and effect estimates. BMJ 2001.

Prognosis

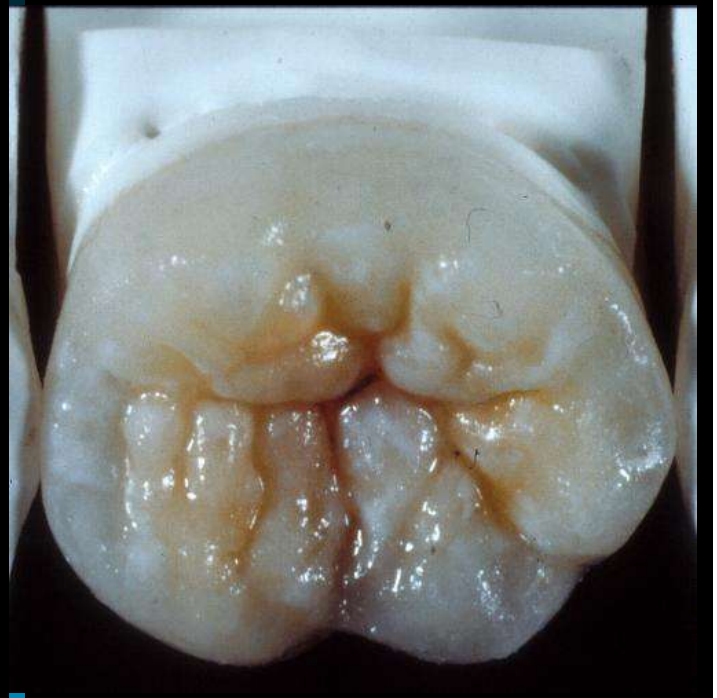
Prognosis – likelihood estimates

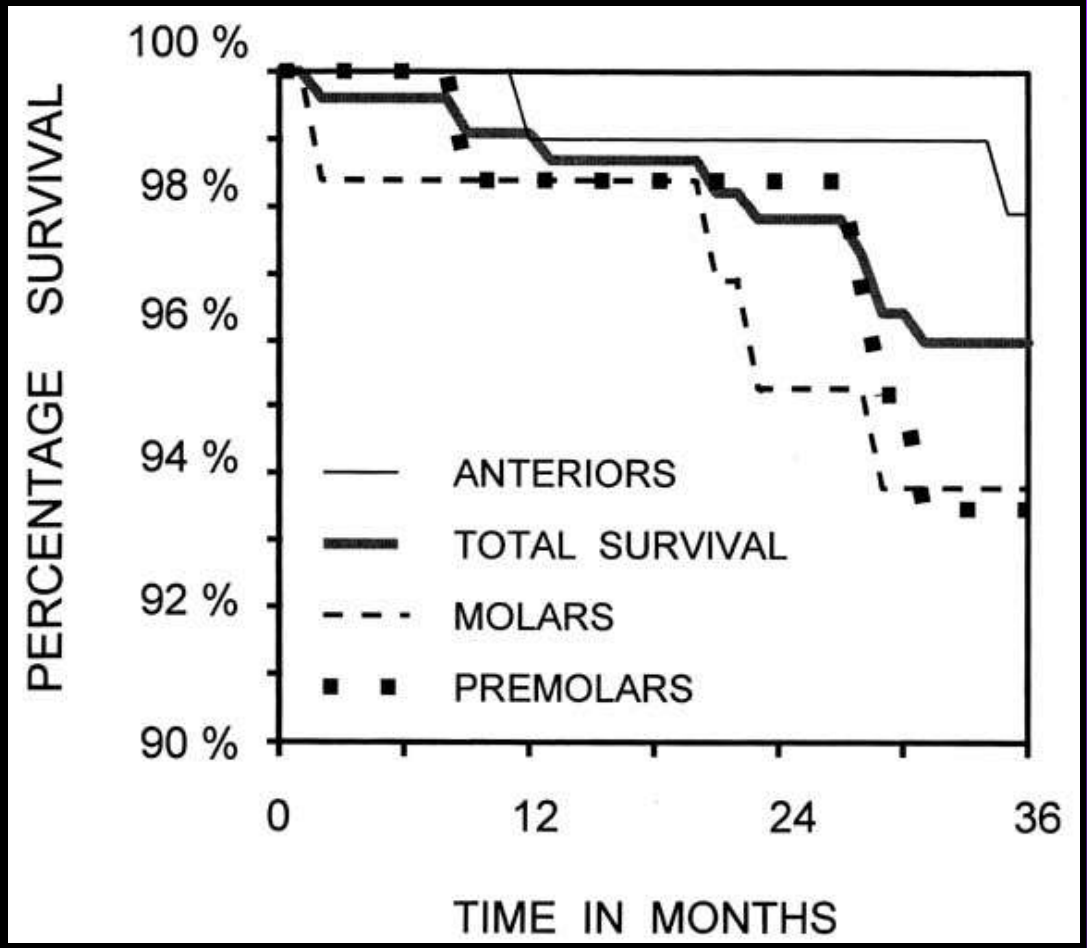
- Proportion of survival or success according to some specific criteria after a given temporal interval, e.g. after 1 or 5 years
- Median time of survival (in years), where 50% of the study unit, e.g. the patient, prosthesis, restorations or tooth, have failed, or
- Survival curves – describe for each time unit along a horizontal axis estimates of the proportion of the study unit that remain intact according to survival or success according to some specific criteria

Survival Curves

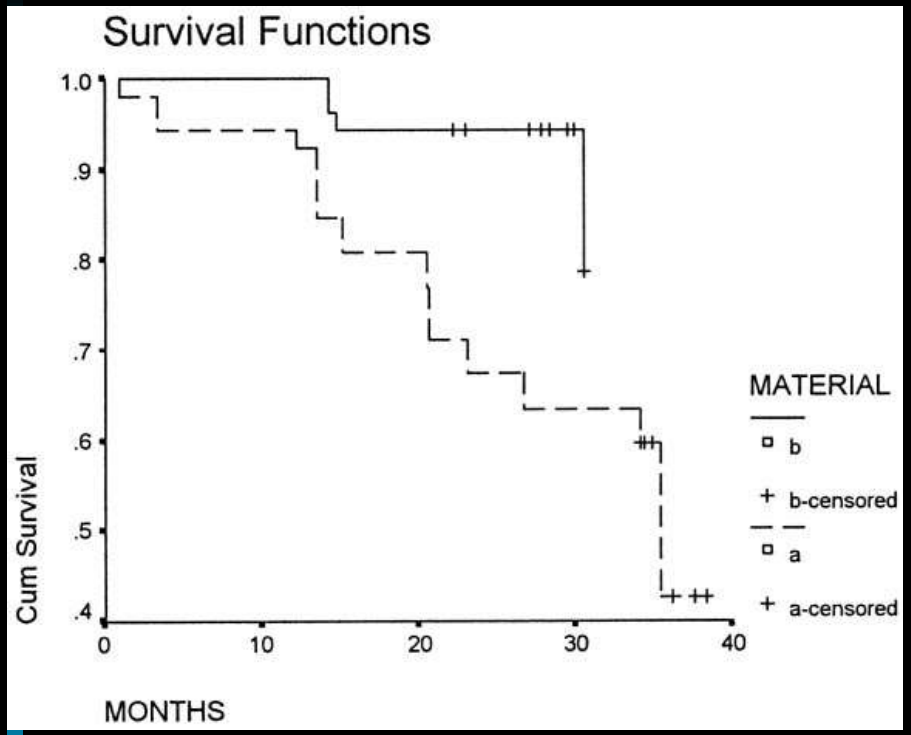


Intraoral location

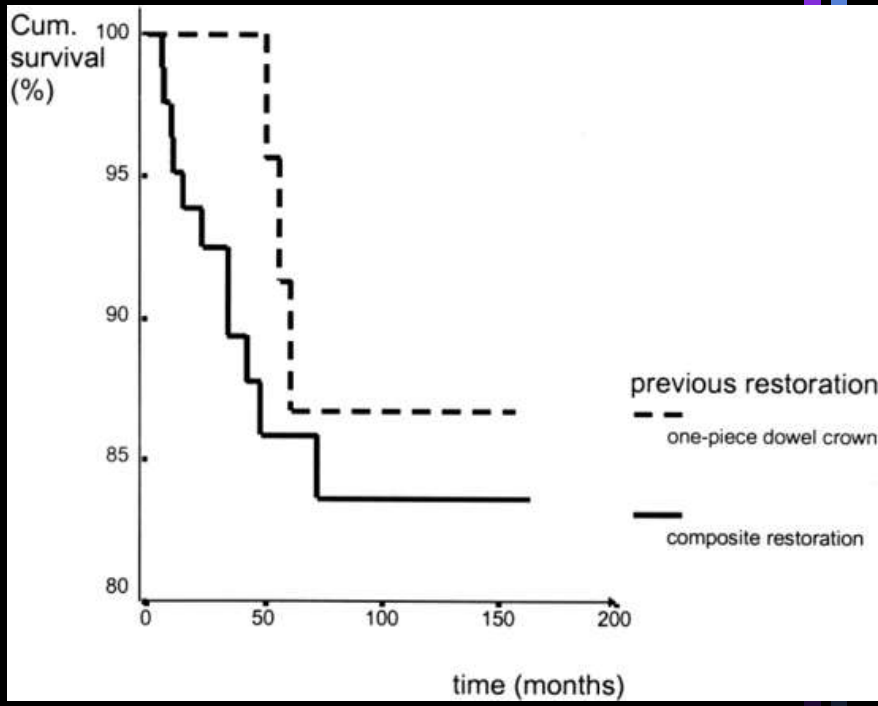




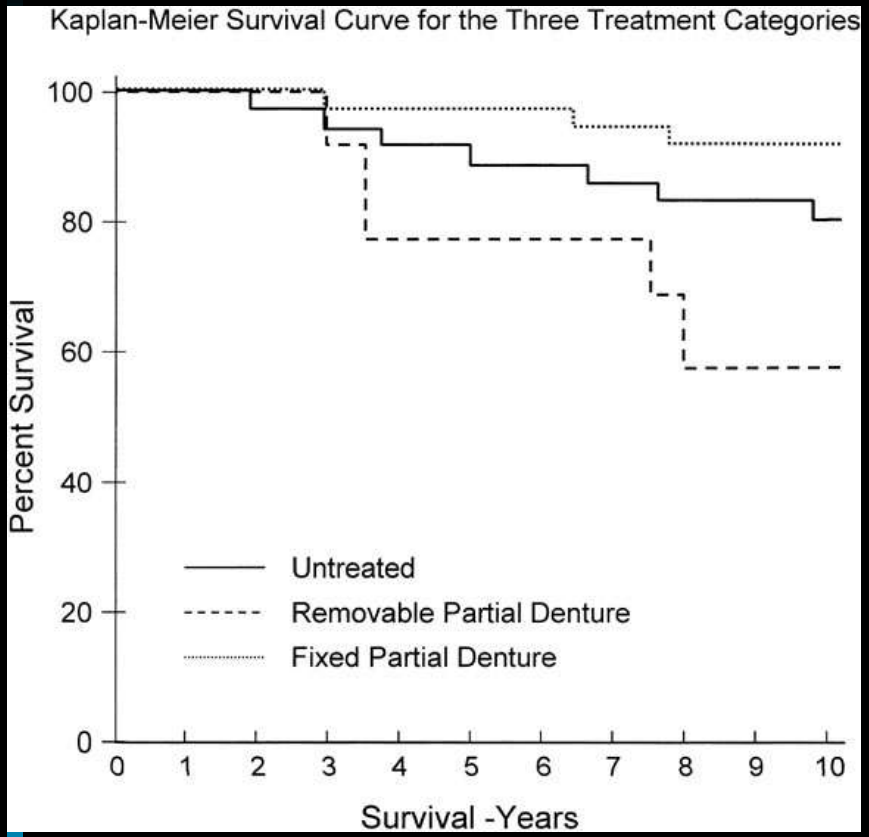
McLaren & White. J Prosthet Dent 2000



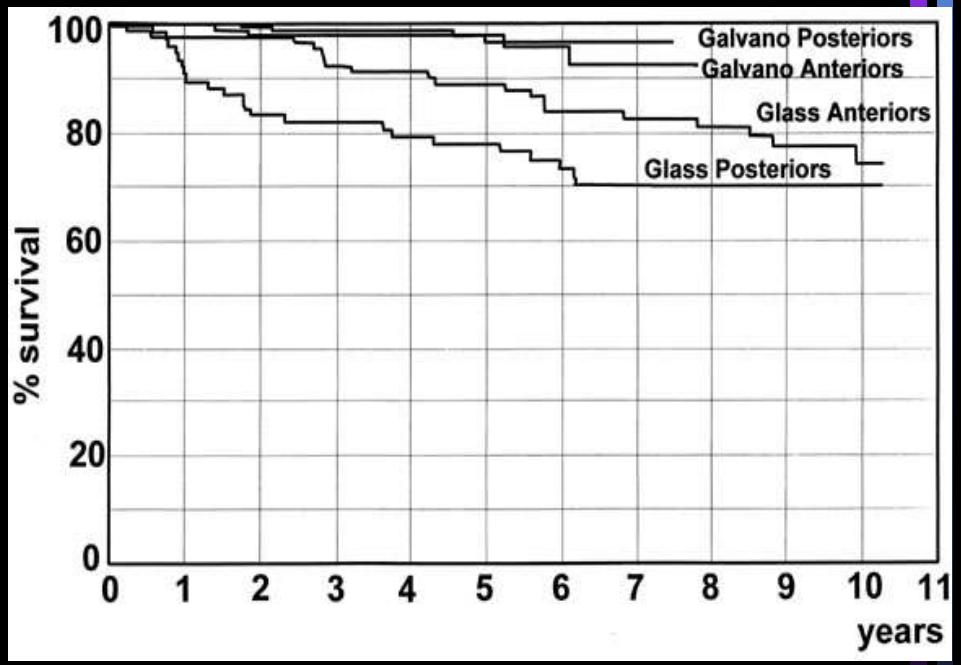
Hemmings et al. J Prosthet Dent 2000



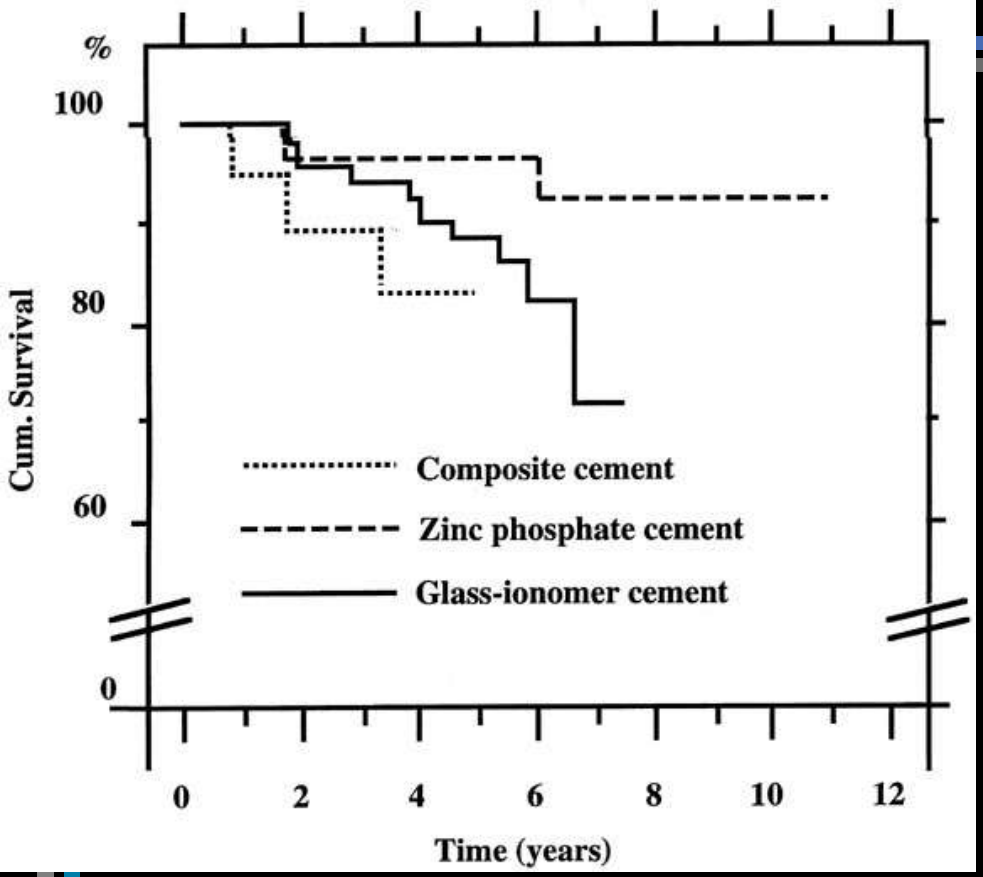
Napankangas et al. J Oral Rehabil, 2000



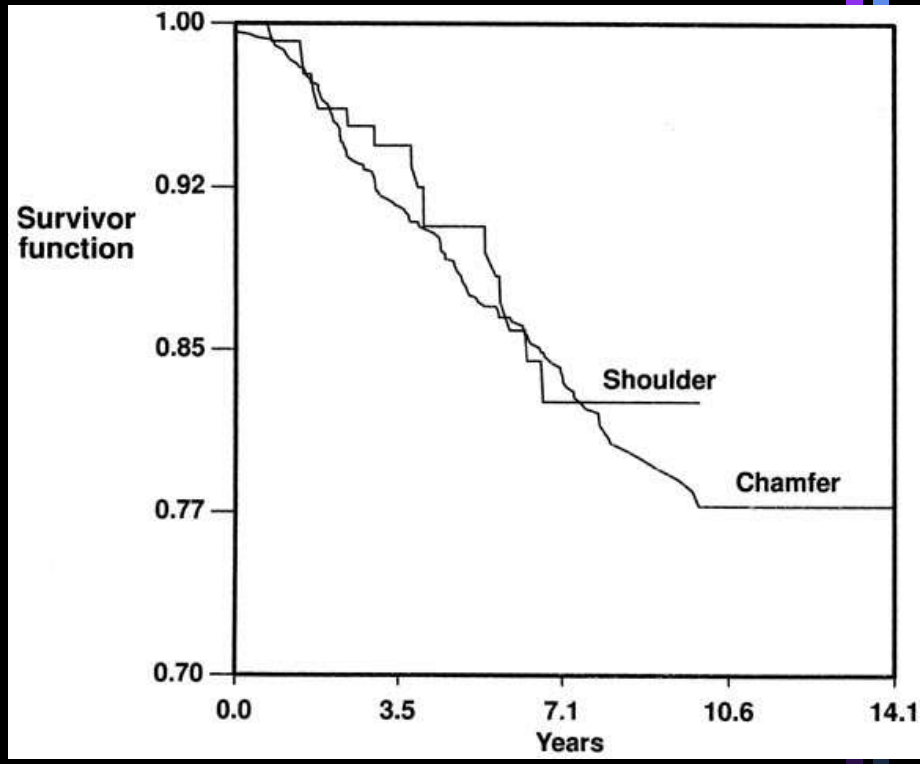
Aquilino et al. J Prosthet Dent 2001



Erpensten et al. J Prosthet Dent 2001

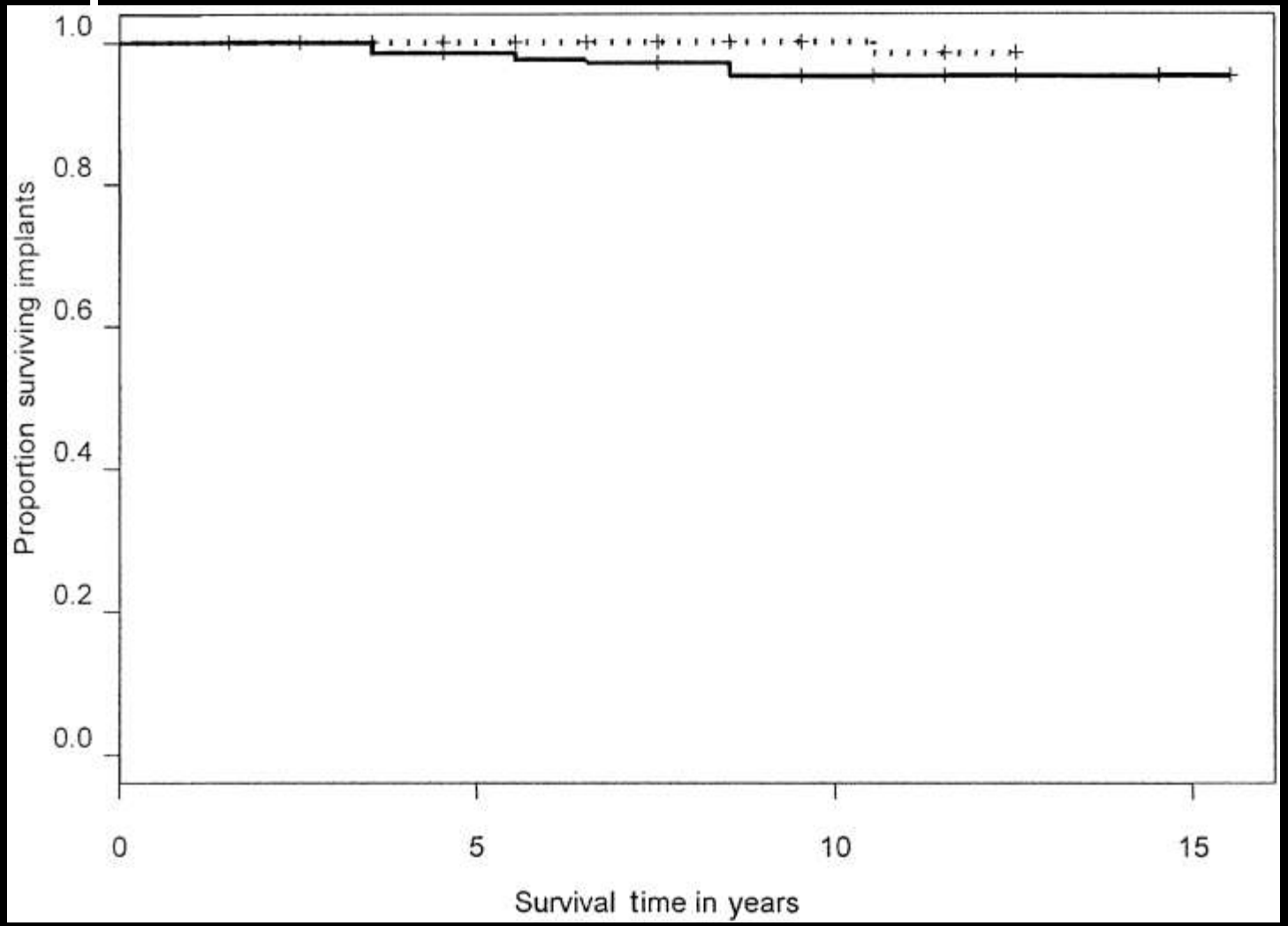


Sjögren et al. J Prosth Dent 1999



Malament et al. J Prosth Dent 1999

Implants freestand vs connected



Naert et al., Clinical Oral Implants Research, 2001

Etch bridges

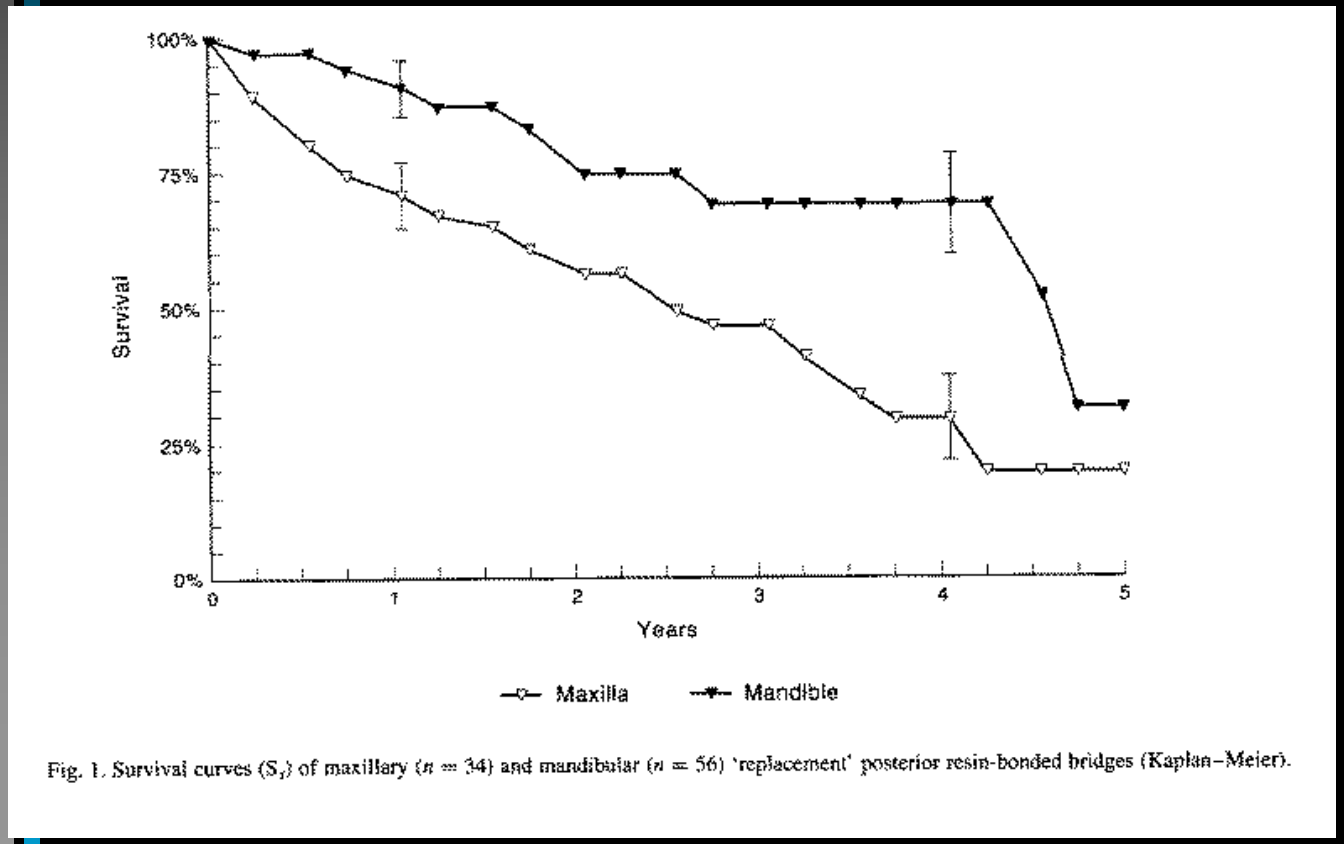


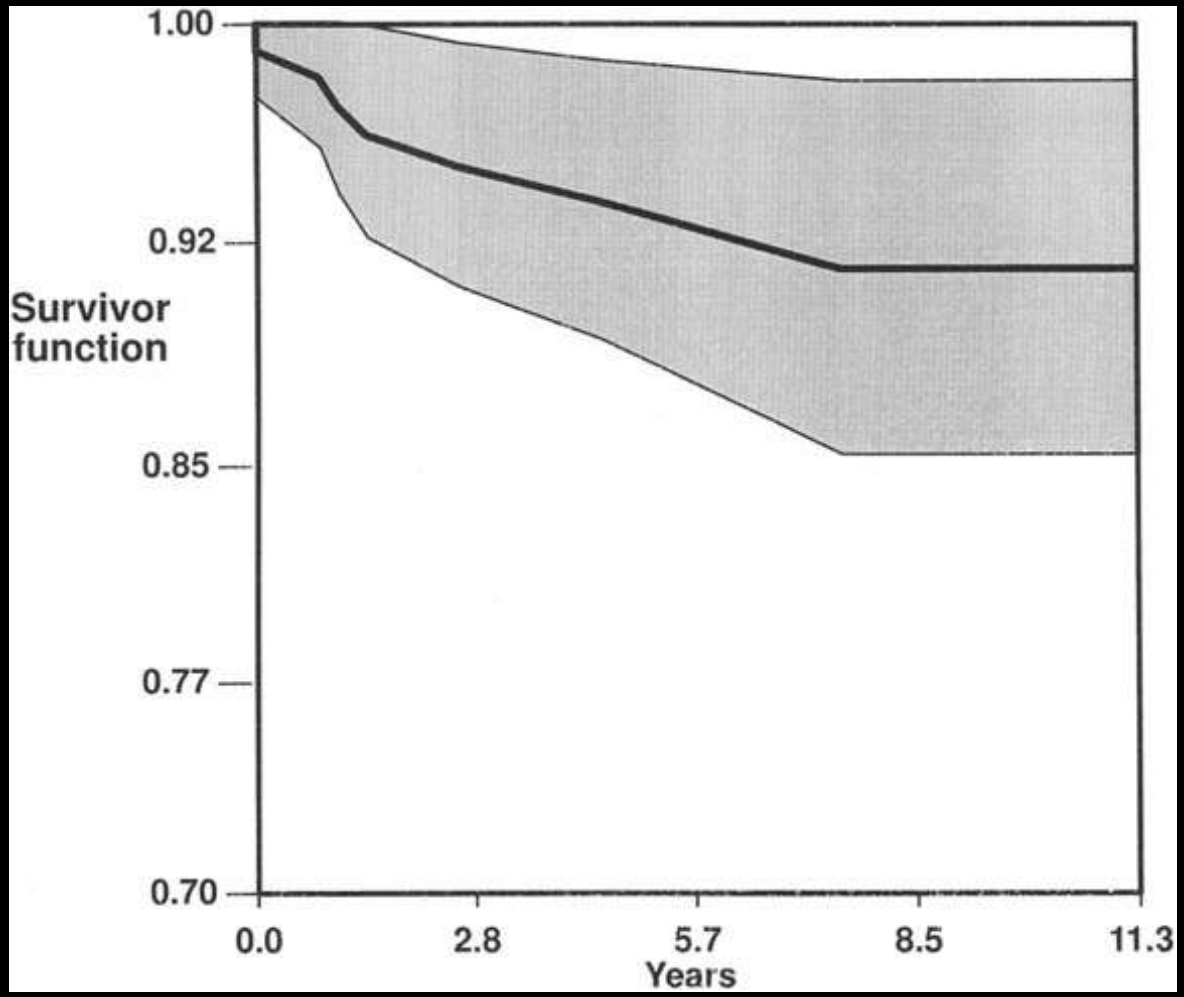
Fig. 1. Survival curves (S_y) of maxillary ($n = 34$) and mandibular ($n = 56$) 'replacement' posterior resin-bonded bridges (Kaplan–Meier).

Creugers et al. J Dent 2001

Prognosis - Precision of the likelihood estimates

- All good clinical prognosis studies include measures of confidence intervals for prognosis-estimates
- A 95% confidence interval consists of two values that indicating an interval where we can be 95% certain that the true value lies
- A narrow confidence interval is an indication of a precise estimate of the true value

Sample size and confidence interval



Malament et al. Survival of Dicor glass-ceramic dental restorations over 14 years. J Prosth Dent 1999

Diagnostic tests

Assessment of the efficacy of a diagnostic test

Parameter	Description, e.g.
Sensitivity	Ability to identify patients in a patient population
Specificity	Ability to identify non-patients in an asymptomatic population
Positive predictive value	Ability of a diagnostic test to identify a patient correctly, given that the test is positive
Negative predictive value	Ability of a diagnostic test to identify a non-patient correctly, given that the test is negative
Measurement validity	The accuracy of a measurement technique when compared with a known standard
Measurement reliability	The variability of the measurements over time and in different enviroruments
Diagnostic validity	The ability to separate those with the disease from those without the disease

Sensitivity and Specificity

- Sensitivity
  - Probability that a subject with the disease will screen positive
- Specificity
  - Probability that a subject who is disease free will screen negative

2 x 2 Tables

	Disease Present	Disease Absent	
Test Positive	a	b	a+b
Test Negative	c	d	c+d
	a+c	b+d	a+b+c+d

Sensitivity

	Disease Present	Disease Absent	
Test Positive	215	16	231
Test Negative	15	114	129
	230	130	

$$\frac{215}{230} = 93\%$$

Sensitivity = $\frac{a}{a+c}$

Specificity

	Disease Present	Disease Absent	
Test Positive	215	16	231
Test Negative	15	114	129
	230	130	

Specificity = $\frac{d}{b+d}$

$\frac{114}{130}$ = 87%

Positive and Negative Predictive Values

- Positive Predictive Value
  - probability of those testing/screening positive actually having the disease
- Negative Predictive Value
  - probability of those testing/screening negative NOT actually having the disease

<u>Relevant when you know the prevalence of the disease in the population.</u>

Positive Predictive Value

	Disease Present	Disease Absent	
Test Positive	215	16	231
Test Negative	15	114	129
	230	130	

$$\frac{215}{231} = 93\%$$

Positive predictive value = a / a+b

Negative Predictive Value

	Disease Present	Disease Absent	
Test Positive	215	16	231
Test Negative	15	114	129
	230	130	

$$\frac{114}{129} = 88\%$$

Negative predictive value = d/c+d

Likelihood Ratio

Indicates the value of the test for increasing certainty about a positive diagnosis

$$\frac{\text{Sensitivity}}{1 - \text{Specificity}}$$

$$= \frac{215/230}{1 - 114/130} = 8$$

Likelihood ratio nomogram