Evidence Based Dentistry

Biostatistics

Asbjorn Jokstad
Institute of Clinical Dentistry,
University of Oslo, Norway

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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	√

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What can you show with a trial?

Type 1 error
Alfa error
Optimism error

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	√

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?

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	√

**Type 2 error
Beta error
Pessimism error**

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

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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	
		+	-
Treat ment	+	A	B
	-	C	D

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

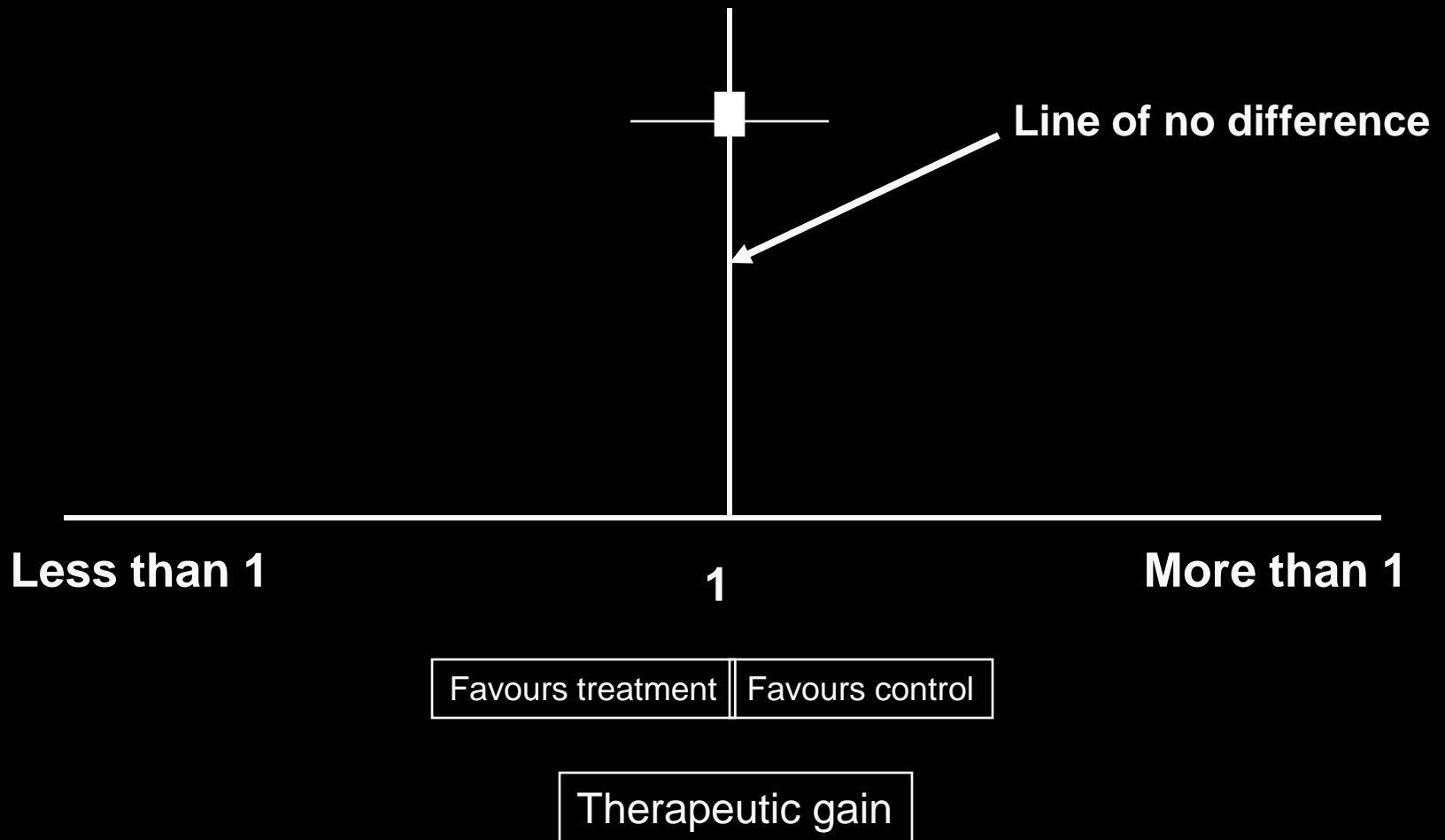|		Adverse outcome	
		+	-
Treat ment	+	A	B
	-	C	D

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

moRe I g h t

Less than 1   **1**   **More than 1**
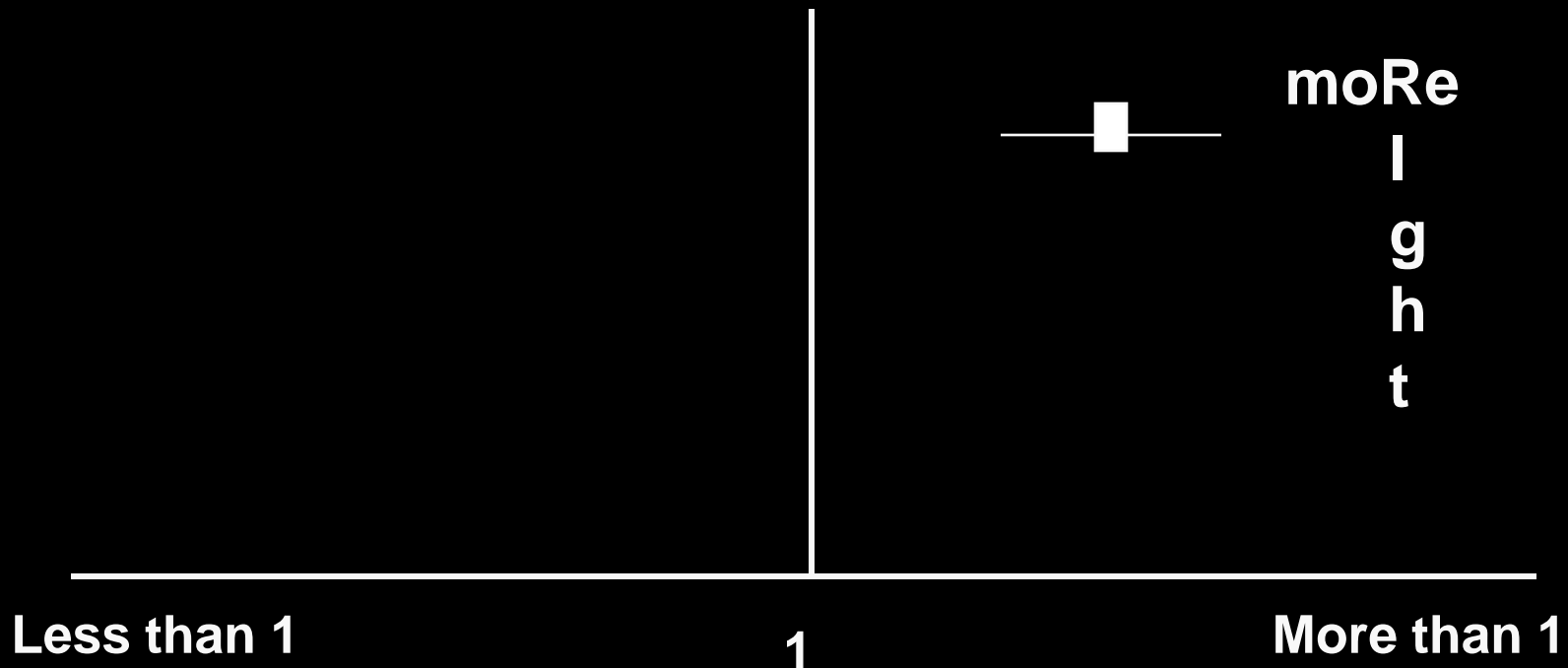
If you want more of something to happen, such as greater reduction in new cavities and the experimental intervention is successful

the results will show in the right-hand side

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Odds Ratio

Less
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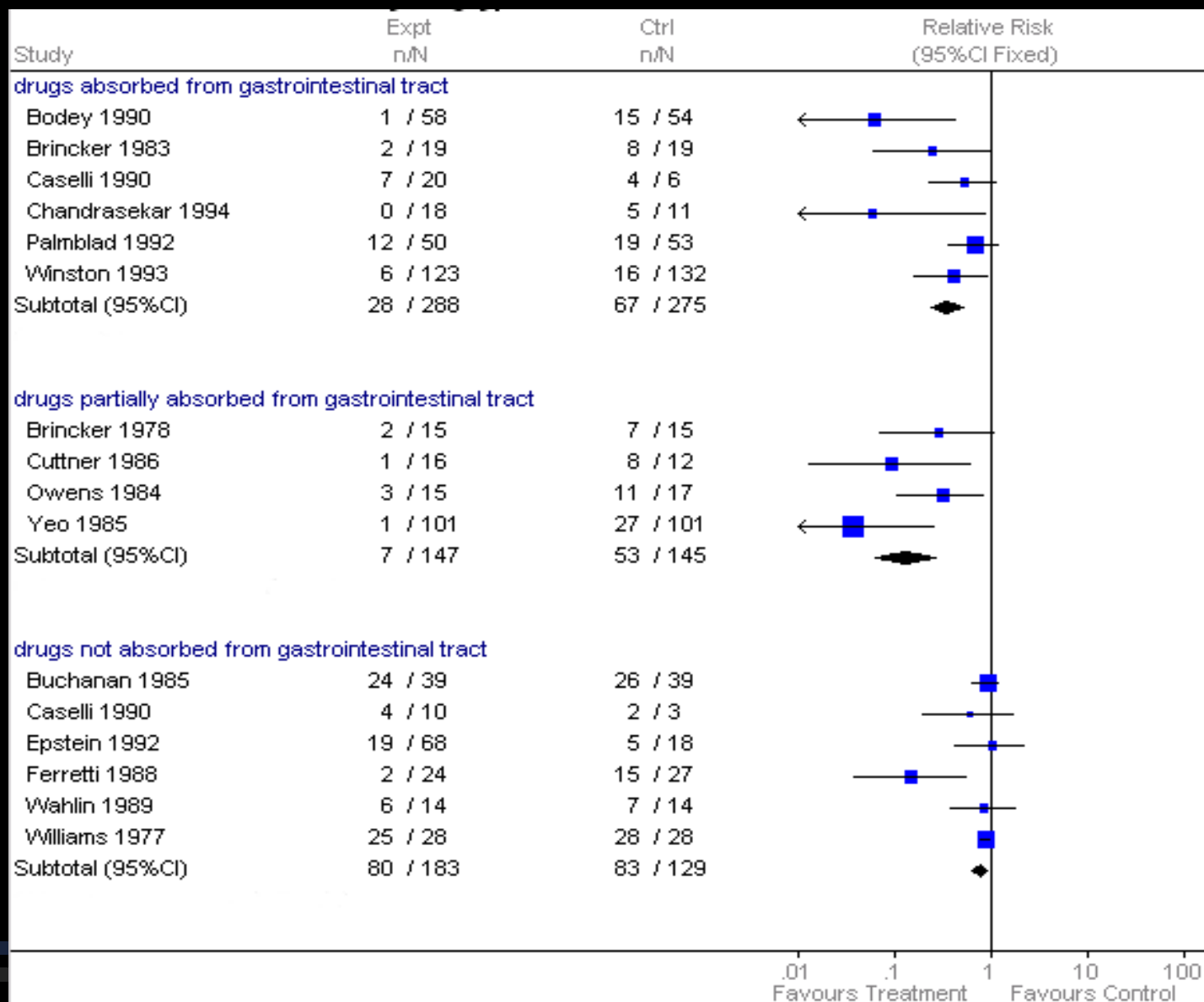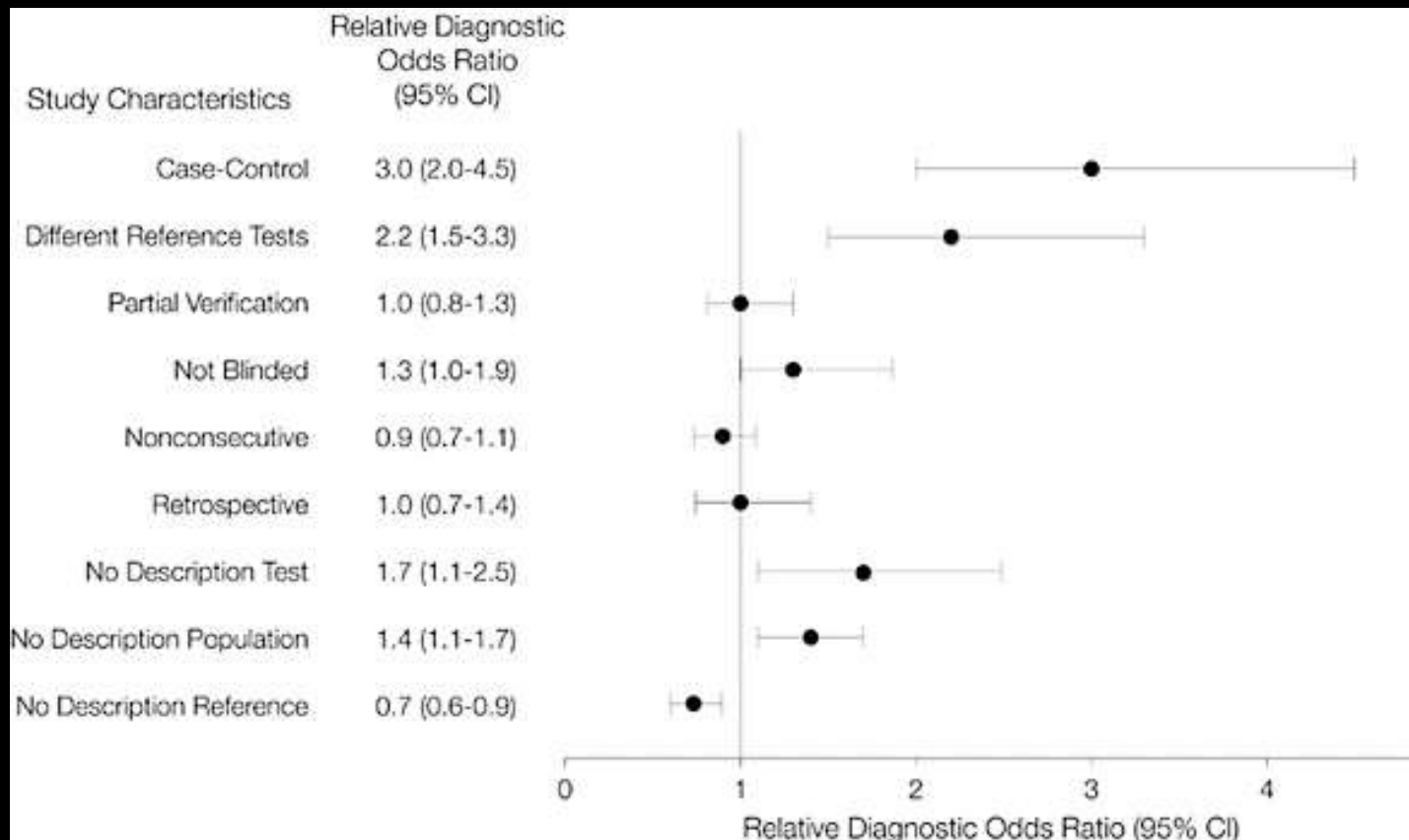**Less than 1**   **1**   **More than 1**

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

Study	Expt n/N	Ctrl n/N	Relative Risk (95%CI Fixed)
drugs absorbed from gastrointestinal tract			
Bodey 1990	1 / 58	15 / 54	
Brincker 1983	2 / 19	8 / 19	
Caselli 1990	7 / 20	4 / 6	
Chandrasekar 1994	0 / 18	5 / 11	
Palmblad 1992	12 / 50	19 / 53	
Winston 1993	6 / 123	16 / 132	
Subtotal (95%CI)	28 / 288	67 / 275	
drugs partially absorbed from gastrointestinal tract			
Brincker 1978	2 / 15	7 / 15	
Cuttner 1986	1 / 16	8 / 12	
Owens 1984	3 / 15	11 / 17	
Yeo 1985	1 / 101	27 / 101	
Subtotal (95%CI)	7 / 147	53 / 145	
drugs not absorbed from gastrointestinal tract			
Buchanan 1985	24 / 39	26 / 39	
Caselli 1990	4 / 10	2 / 3	
Epstein 1992	19 / 68	5 / 18	
Ferretti 1988	2 / 24	15 / 27	
Wahlin 1989	6 / 14	7 / 14	
Williams 1977	25 / 28	28 / 28	
Subtotal (95%CI)	80 / 183	83 / 129	

.01   .1   1   10   100
Favours Treatment   Favours Control

Effect of study methodology on validity

Study Characteristics	Relative Diagnostic Odds Ratio (95% CI)
Case-Control	3.0 (2.0-4.5)
Different Reference Tests	2.2 (1.5-3.3)
Partial Verification	1.0 (0.8-1.3)
Not Blinded	1.3 (1.0-1.9)
Nonconsecutive	0.9 (0.7-1.1)
Retrospective	1.0 (0.7-1.4)
No Description Test	1.7 (1.1-2.5)
No Description Population	1.4 (1.1-1.7)
No Description Reference	0.7 (0.6-0.9)

Relative Diagnostic Odds Ratio (95% CI)

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.

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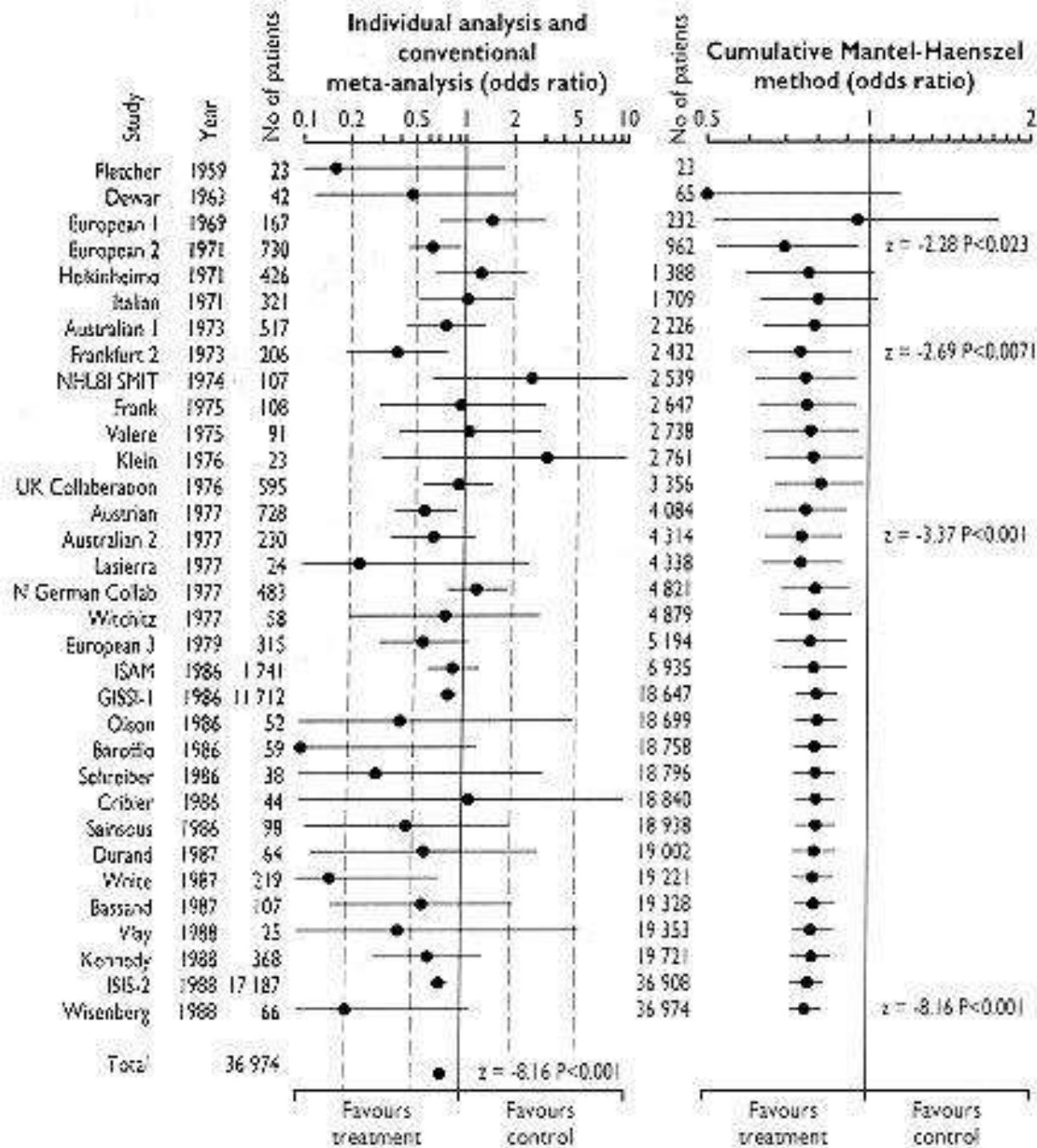
Streptokinase for infarction

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Favours treatment **Favours control**

Generation of allocation sequence
(inadequate or unclear versus adequate)

Schulz 1995 — 0.95 (0.81 to 1.12)

Moher 1998 — 0.89 (0.67 to 1.20)

Kjaergard 2000 — 0.49 (0.30 to 0.81)

Combined — 0.81 (0.60 to 1.09)
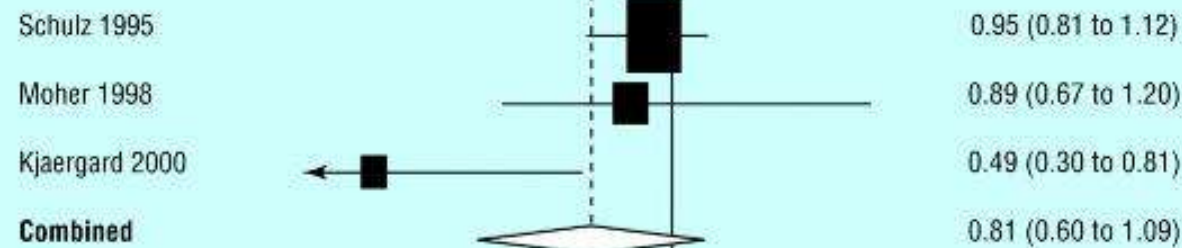
Concealment of allocation
(inadequate or unclear versus adequate)

Schulz 1995 — 0.66 (0.59 to 0.73)

Moher 1998 — 0.63 (0.45 to 0.88)

Kjaergard 2000 — 0.60 (0.31 to 1.15)

Jüni 2000 — 0.79 (0.70 to 0.89)

Combined — 0.70 (0.62 to 0.80)
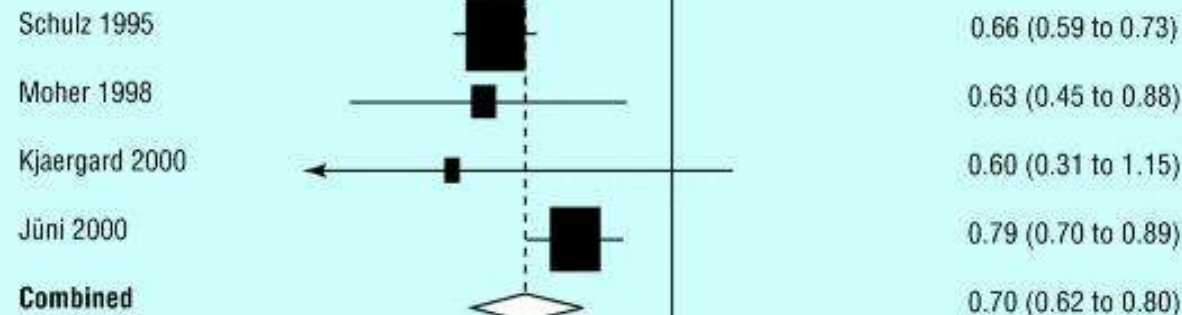
Double blinding
(absent versus present)

Schulz 1995 — 0.83 (0.71 to 0.96)

Moher 1998 — 1.11 (0.76 to 1.63)

Kjaergard 2000 — 0.56 (0.33 to 0.98)

Jüni 2000 — 0.88 (0.75 to 1.04)

Combined — 0.86 (0.74 to 0.99)
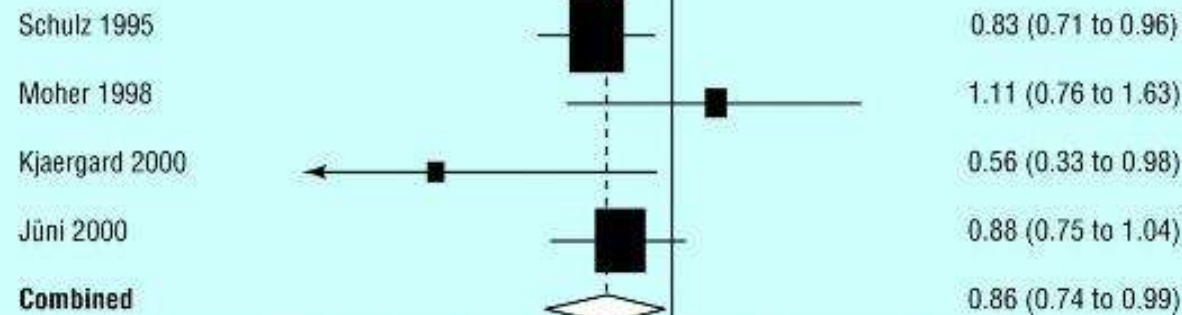
0.4 0.6 0.7 0.8 0.9 1 1.2 1.4 1.6 1.8 2

Ratio of odds ratios

Effects of inadequate study design on results

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

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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
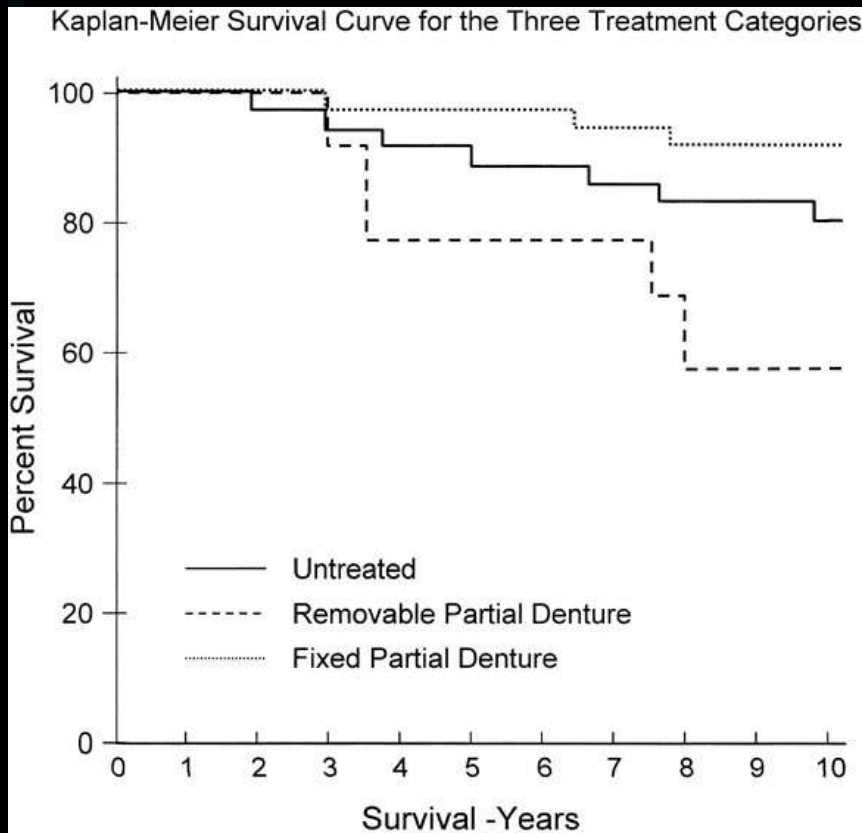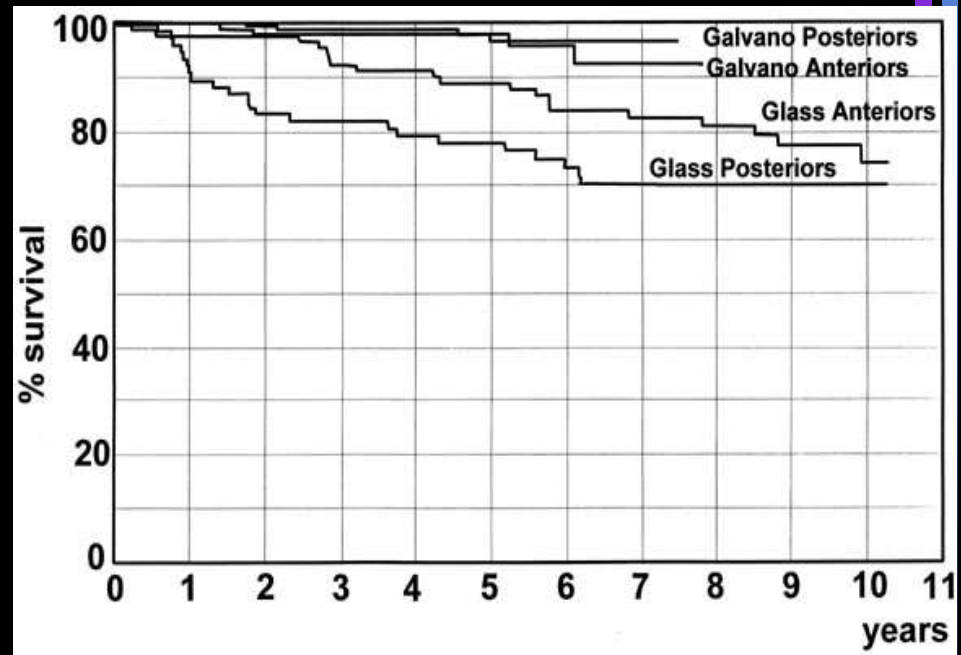
Survival Curves

Intraoral location

McLaren & White. J Prosthet Dent 2000

Survival Functions
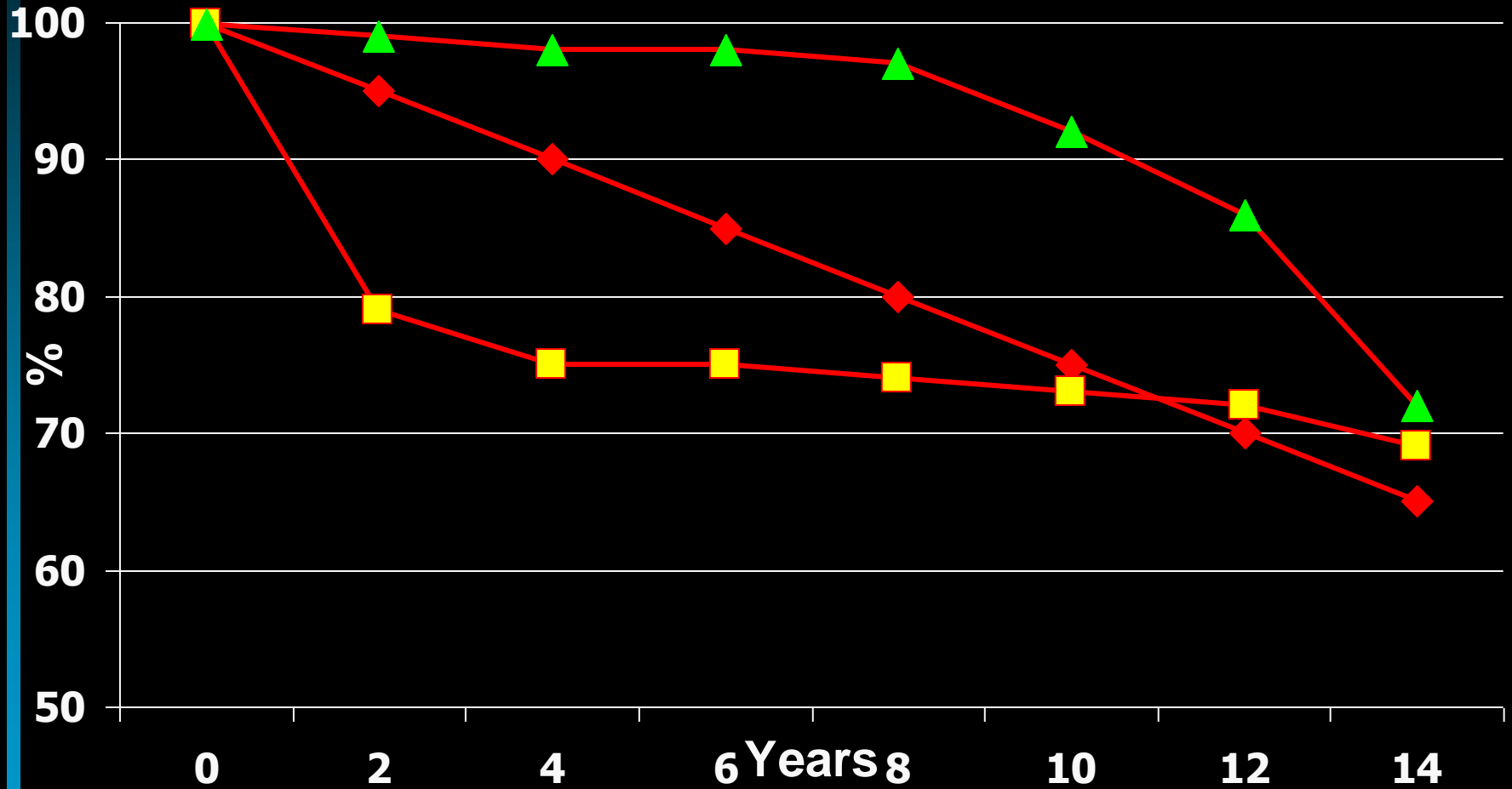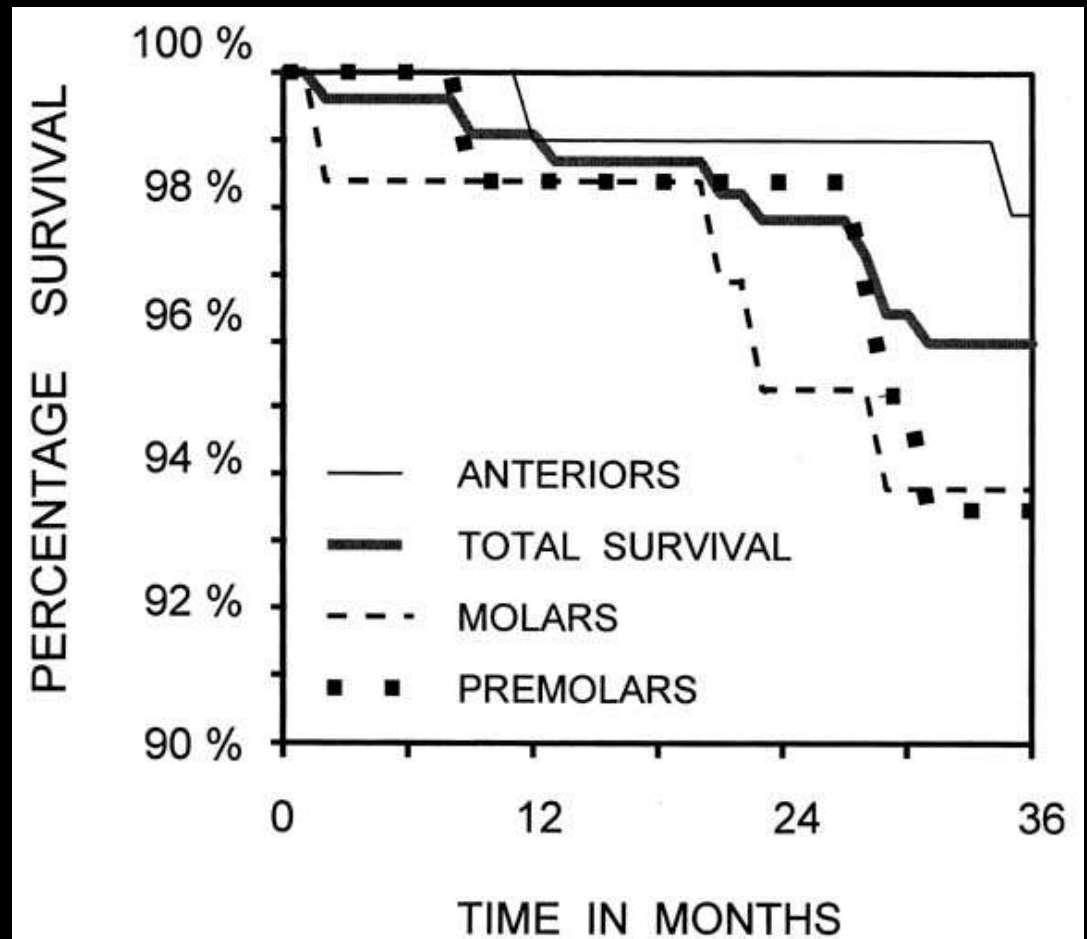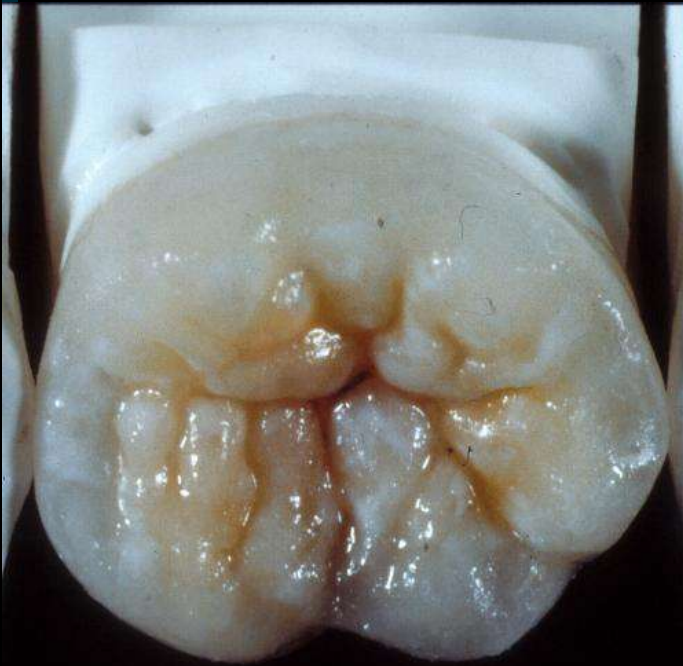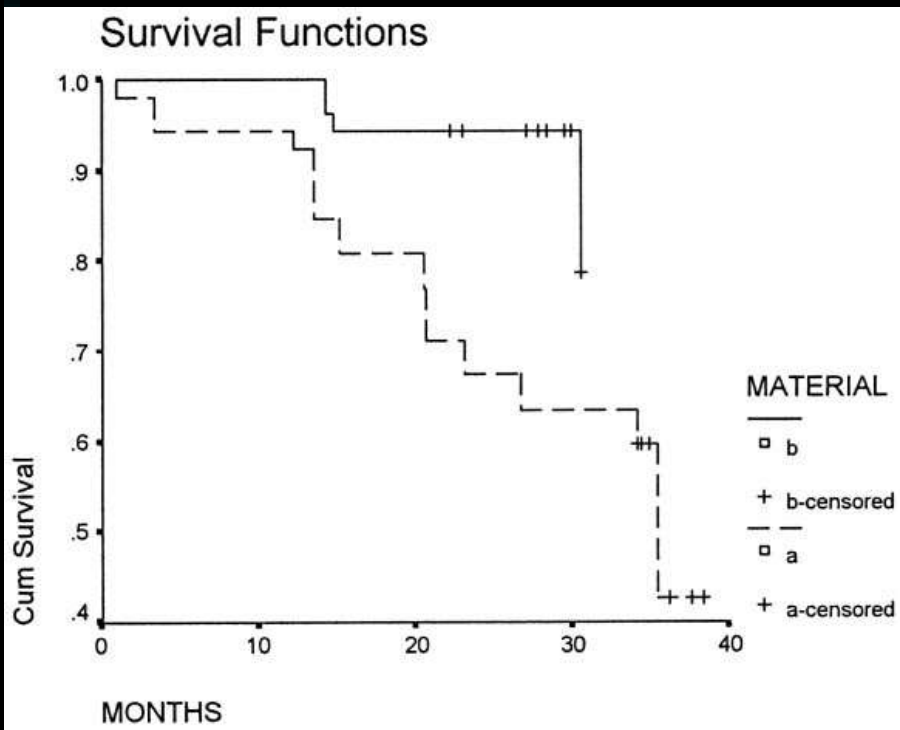
Hemmings et al. J Prosthet Dent 2000
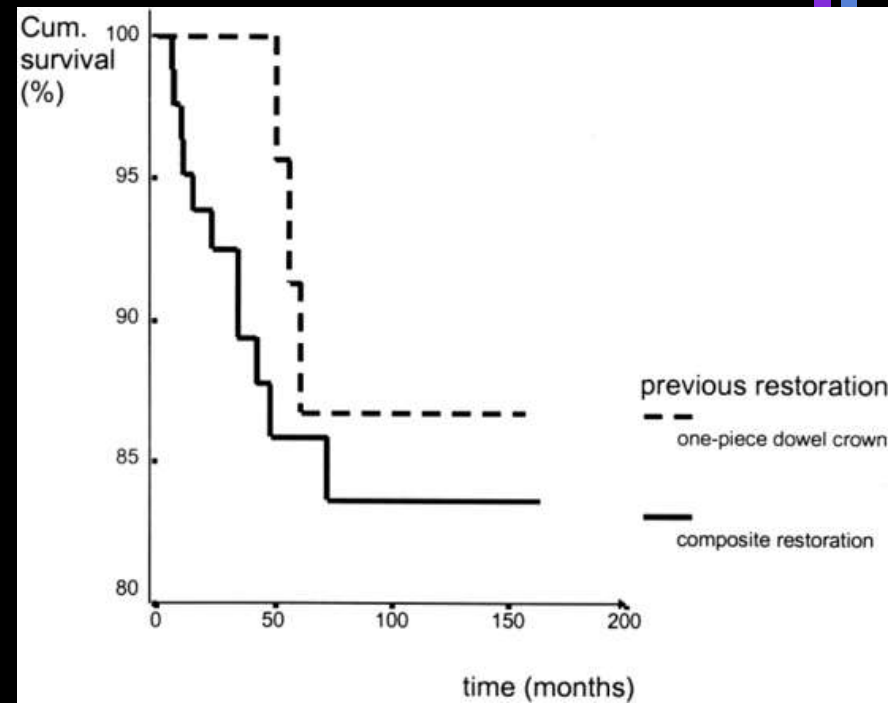
Napankangas et al. J Oral Rehabil, 2000

Kaplan-Meier Survival Curve for the Three Treatment Categories
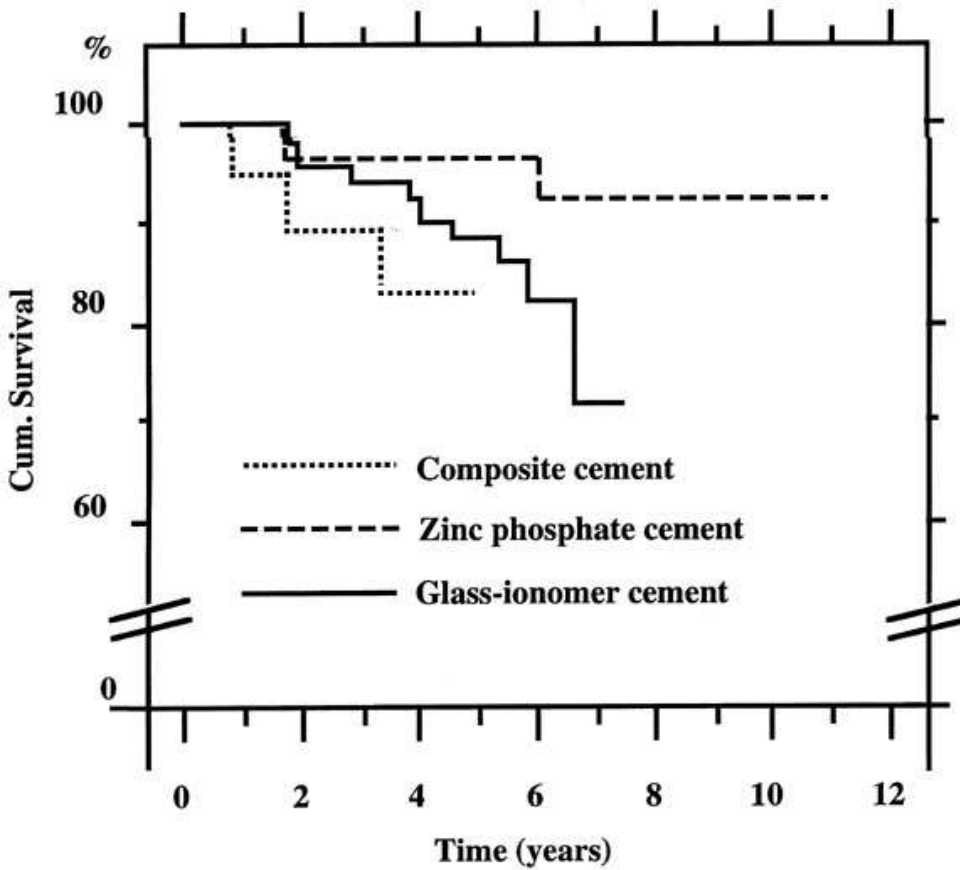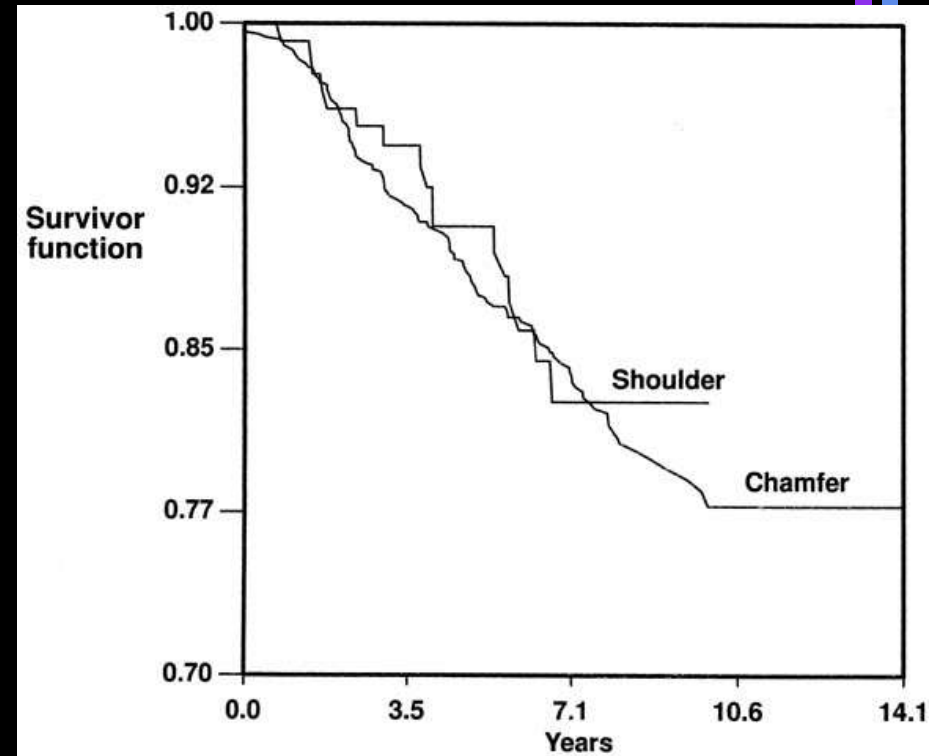
Aquilino et al. J Prosthet Dent 2001

Erpensten et al. J Prosthet Dent 2001

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Sjögren et al. J Prosth Dent 1999

Malament et al. J Prosth Dent 1999

Implants freestand vs connected

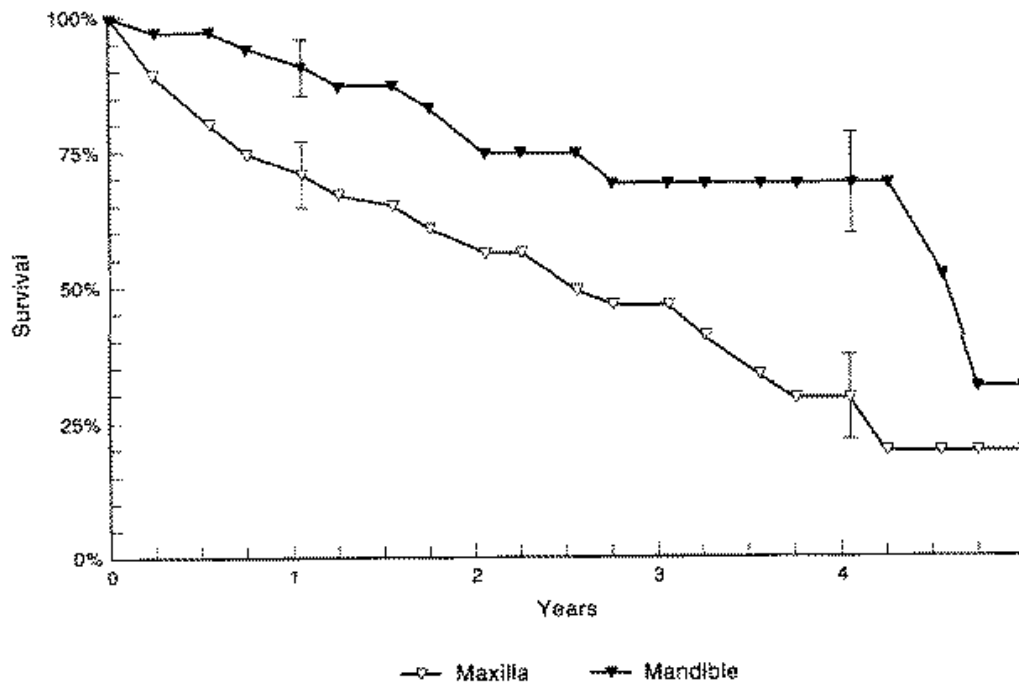Naert et al., Clinical Oral Implants Research, 2001
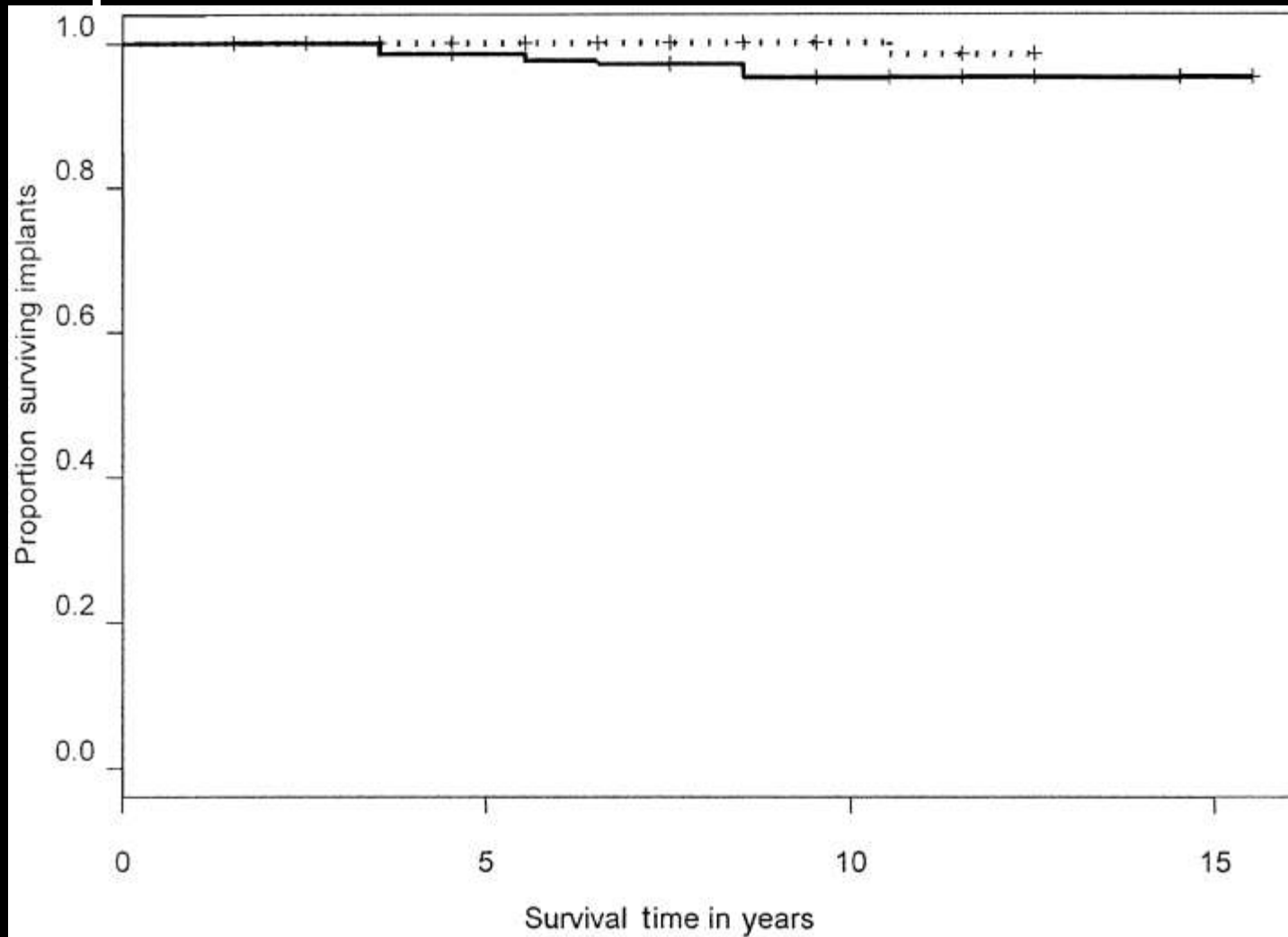
Etch bridges

Fig. 1. Survival curves (S$_x$) 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
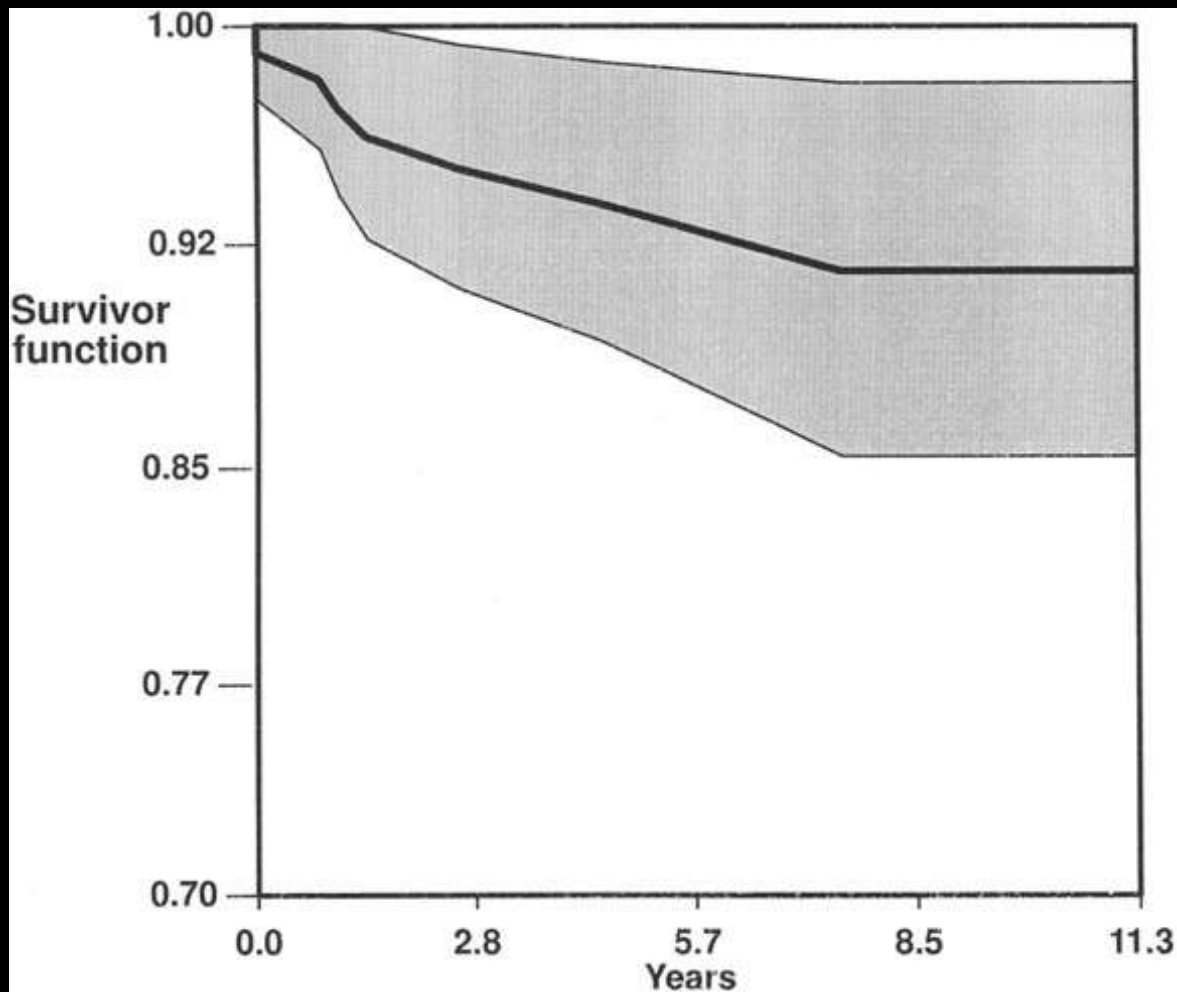
Malament et al. Survival of Dicor glass-ceramic dental restorations over 14 years. J Prosth Dent 1999

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 environurents
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	

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

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

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Specificity

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

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

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

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

Relevant when you know the prevalence of the disease in the population.

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

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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