Therapy – February 15, 2012
DEN1014 Clinical Epidemiology

The easy approach to evaluate treatment effects

- Compare a single group of patients given the new treatment with a group previously treated with an alternative treatment.
- Usually such studies compare two consecutive series of patients in the same settings.

The easy approach is seriously flawed:

- Multiple examples in medicine where results from RCTs negates findings from clinical trials that have used inferior study designs
- Non-RCT trials yield in general more optimistic results than RCTs.

Over-estimation of treatment effect

- Non-RCT trials 40%
- Small trials 30%
- Poor reporting quality 25%
- Duplicate information 20%
- Not double-blind 17%

Schulz KF, Chalmers I, Hayes RJ, Altman DG: Empirical evidence of bias: dimensions of methodological quality associated with estimates of treatment effects in controlled trials. JAMA 1995, 273:408-412

The easy approach is seriously flawed:

- Multiple examples in medicine where results from RCTs negates findings from clinical trials that have used inferior study designs
- Non-RCT trials yield in general more optimistic results than RCTs.
- Can never satisfactorily eliminate possible bias:) ”*an inclination to present or hold a partial perspective at the expense of (possibly equally valid) alternatives*”

Minimizing risk of Bias → Random allocation of participants

- Random allocation means that all participants have the same chance of being assigned to separate study arms
- Allows comparison of outcomes of intervention given to groups of participants who theoretically do not differ in any systematic way

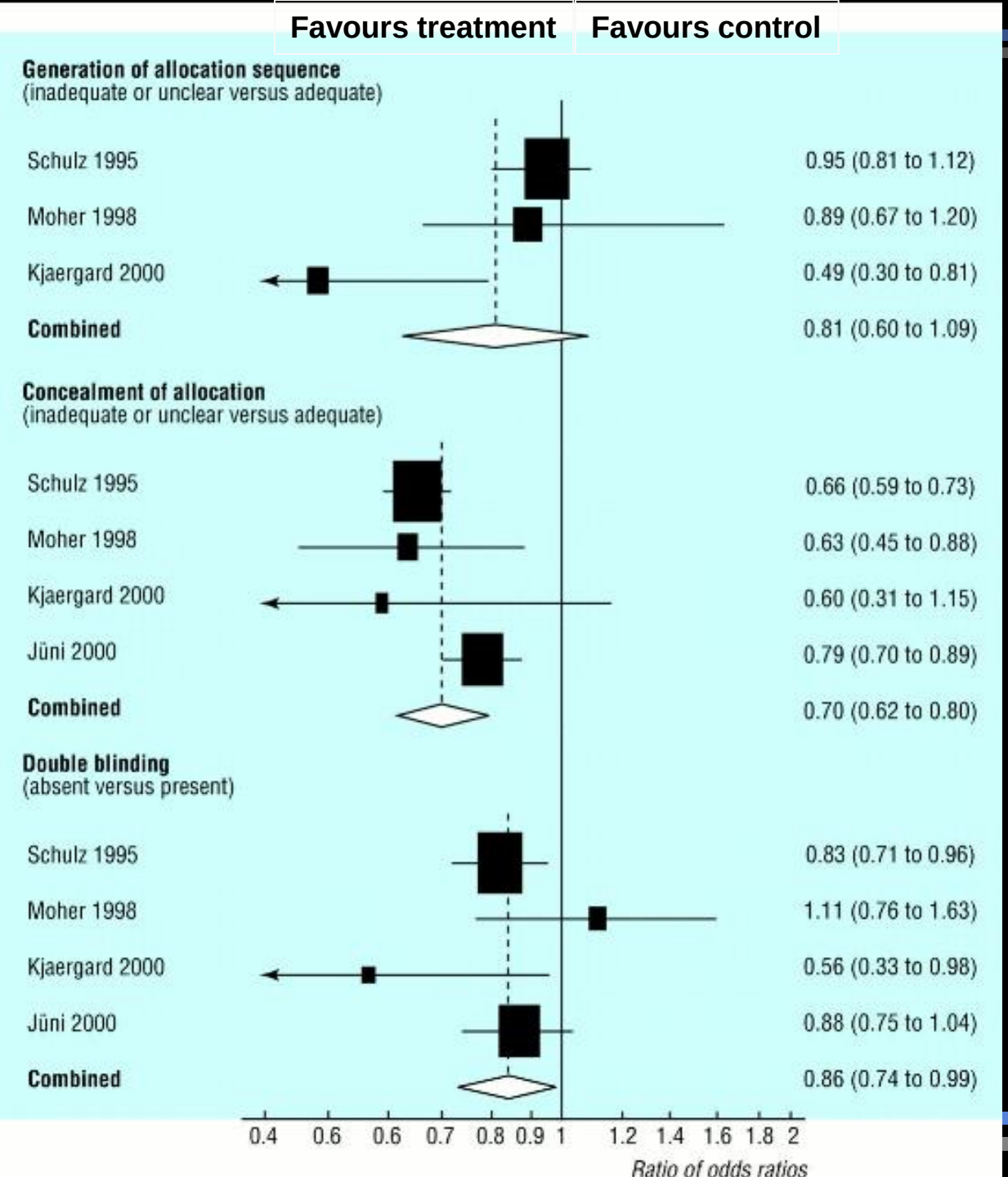
Randomisation - statistical theory

- Based on the idea of random sampling
- In a study with random allocation the differences between treatment groups behave like the differences between random samples from a single population
- We know how random samples are expected to behave and so can compare the observations with what we would expect if the treatments were equally effective

Randomisation Procedures

AIM: Allocation that can not be influenced by the investigator, the clinician, or the study participant

- ~~Alternate allocation~~
- ~~Date of birth~~
- ~~Day of study~~
- ~~Flip Coin~~
- ~~Record numbers~~
- ~~Roll of dice~~
- Computer generated random numbers
- Random number tables

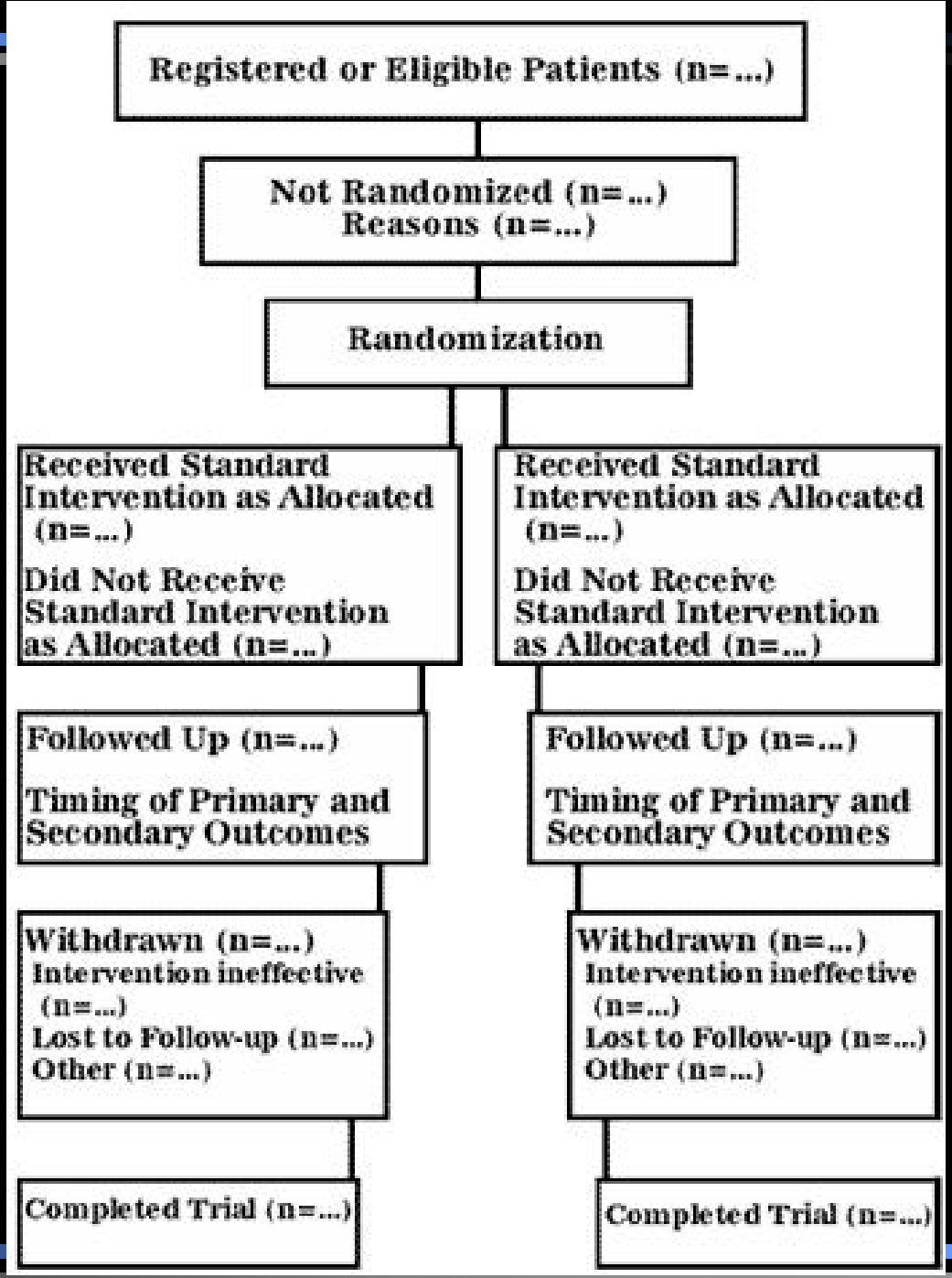


Inadequate study design and effect estimates

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

Reporting:

CONSORT



Intention to treat analysis

Analysing people, at the end of the trial, in the groups to which they were randomized, even if they did not receive the intended intervention.

What can you show with a trial?

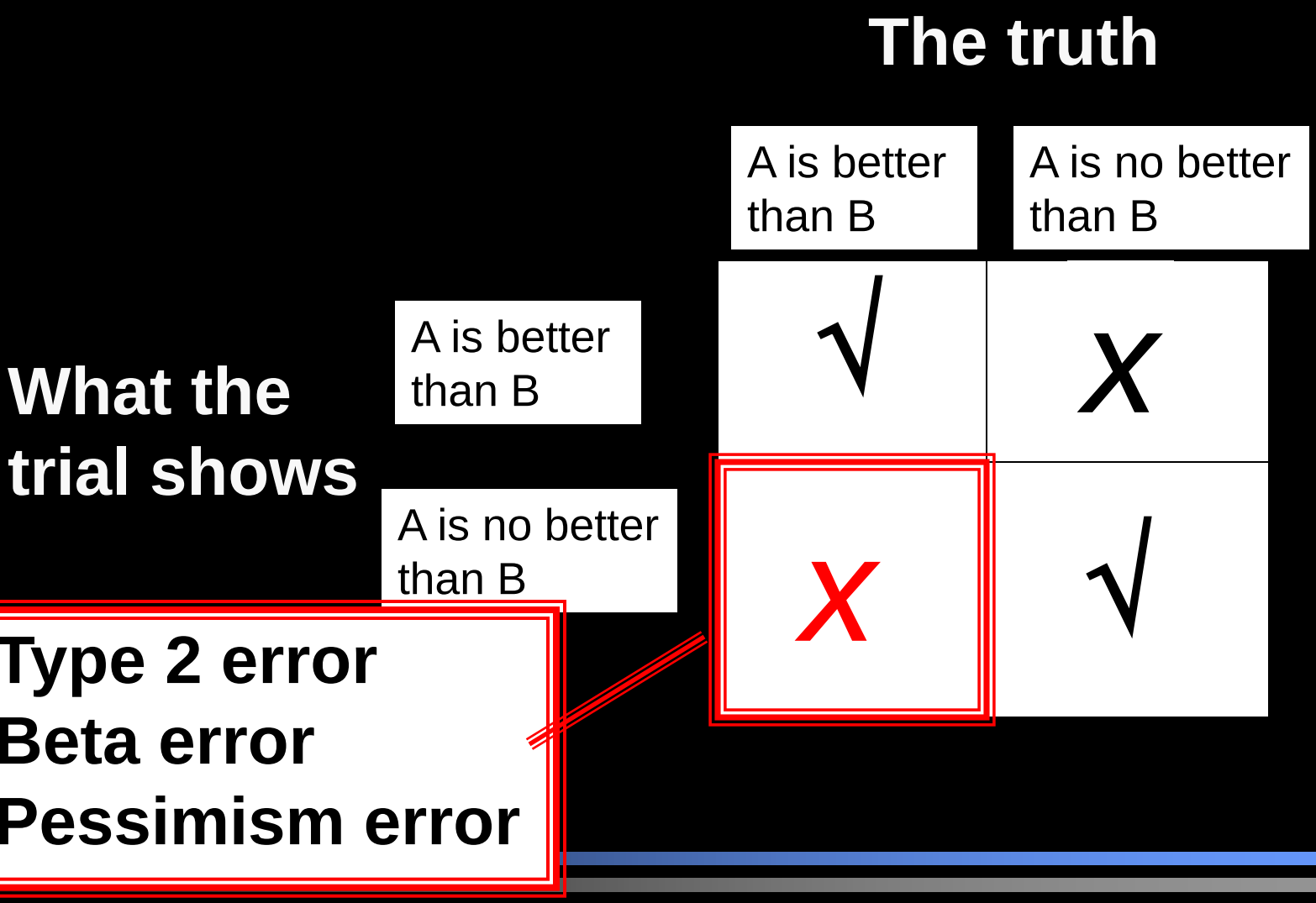
What the trial shows	The truth: A is better than B	The truth: A is no better than B
A is better than B	√	X
A is no better than B	X	√

What can you show with a trial?

Type 1 error
Alfa error
Optimism error

What the trial shows	**The truth: A is better than B**	**The truth: 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?



The history of therapeutic interventions

2000bc Here, eat this root

1000bc That root is heathen, say this prayer

1852 Praying is superstition, drink this brew

1932 That brew is snake oil, swallow this pill

1972 That pill is ineffective, take this antibiotic

2012 That antibiotic is artificial… Here, eat this root

Mason et al. A prospective, randomized, double-blind comparison of 2% lidocaine with 1:100,000 and 1:50,000 epinephrine and 3% mepivacaine for maxillary infiltrations. J Endod. 2009 Sep;35(9):1173-7

VALIDITY: Are the results of the trial valid?

A	B	C

1 Did the trial address a clearly focused issue?

A	B	C
Yes	**Can't tell**	**No**

An issue can be focused in terms

- *- the population studied*
- *- the intervention given*
- *- the outcomes considered*

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2 Was the assignment of patients to treatment randomised?			
3. Were all the patients who entered the trial properly accounted for at its conclusion • *was follow-up complete?* • *were points analysed in the groups to which they were randomised?*	**Yes**	**Can't tell**	**No**

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IMPORTANCE What are the results?

How large was the treatment effect?

- *What outcomes are measured?*

How precise was the estimate of the treatment effect ?

- *What are its confidence limits?*

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APPLICABILITY Will the results help locally?

7. Can the results he applied to the local population? **Yes** **Can't tell** **No**

- *Do you think that the patients covered by the trial are similar enough to your population?*

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9. Are the benefits worth the harms and costs?

Yes **Can't tell** **No**

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