Evidence Based Dentistry

Randomised clinical trials re-visited

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Therapy / Prevention / Education

- Random allocation of the participants to the different interventions
- Outcome measures of known or probably clinical importance for at least 80 per cent of participants who entered the investigation
- A statistical analysis consistent with the study design.

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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.

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The easy approach is seriously flawed:

Can never satisfactorily eliminate possible <u>bias</u>

Bias: a one-sided inclination of the mind

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The easy approach and risk of bias:

- If the clinician chooses which treatment to give
- If patients choose their own treatment
- If those who agree to have a treatment are compared with refusers.
- If different treatment groups are at different clinics or under different operators.
  - Probably differences in the clinical and demographic characteristics of the patients receiving the different treatments.
- Systematic differences will lead to an overestimate or underestimate of the difference between treatments.
- Bias can be avoided by using random allocation.

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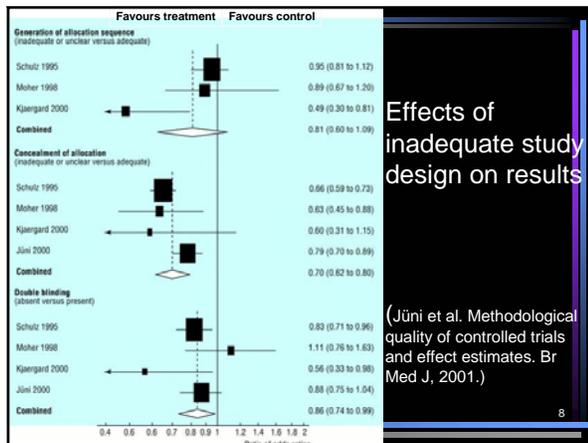
The easy approach is seriously flawed:

- Multiple examples in medicine where results from RCTs negates findings from clinical trials using inadequate study designs
- Controlled trials yield in general more optimistic results than RCTs.

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Over-estimation of treatment effect

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

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Effects of inadequate study design on results

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 0.6 0.7 0.8 0.9 1 1.2 1.4 1.6 1.8 2

(Jüni et al. Methodological quality of controlled trials and effect estimates. Br Med J, 2001.)

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Randomisation - rationale

- Main reason: prevent biases
- Random allocation means that all participants have the same chance of being assigned to each of the study groups
- Compare the outcomes of treatments given to groups of patients which do not differ in any systematic way

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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

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Randomisation Procedures

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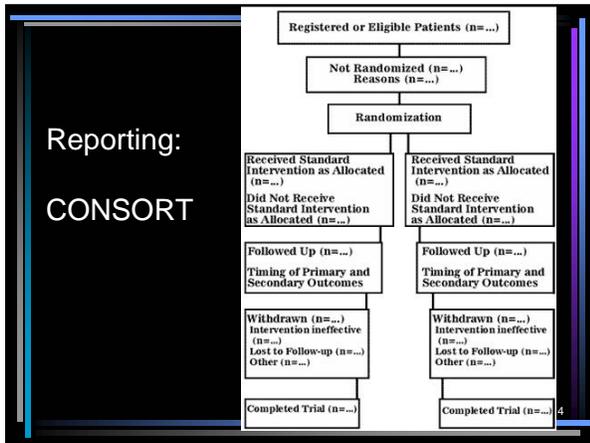- Computer generated random numbers
- Random number tables

Allocation is not determined by the investigators, the clinicians, or the study participants.

Loss to follow-up

It is important to ensure that all those that are randomized into the trial are followed up to the trials conclusion

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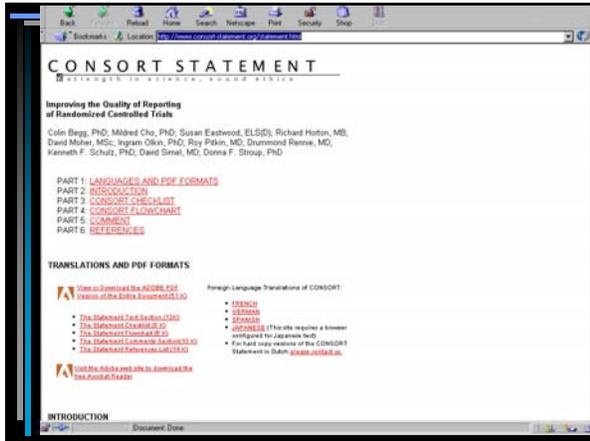
Reporting:

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.

Blinding

Blinding

• Participants don't know what healthcare intervention they are getting

Double blinding

• Those giving the healthcare don't know what the participant is receiving (i.e. doctors, healthcare professionals)

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RCTs - a checklist

• Good randomisation procedures

• Patients blind to treatment

• Clinicians blind to treatment

• All participants followed up

• All participants analysed in the groups to which they were randomised (intention to treat)

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