

Evidence Based Dentistry

# Principles of Clinical Studies

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### Clinical trial terminology - tower of Bable?

analytical study	ecological study	prospective cohort study
case control study (89)	etiological study	prospective follow-up study,
case serie	experimental study	observational or experimental
case study, case report	explorative study	prospective study (67)
cause-effect study	feasibility study (79)	quasi-experimental study
clinical trial (79)	follow-up study (67)	randomized clinical trial, RTC
cohort study (89)	historical cohort study	randomized controlled trial, RCT (89)
cohort study with historical controls	incidence study	retrospective cohort study
controlled clinical trial (95)	intervention study	retrospective follow-up study
cross-sectional study (89)	longitudinal study (79)	retrospective study (67)
descriptive study	N=1 trial	surveillance study
diagnostic meta-analysis	non-randomized trial with contemporaneous controls	survey, descriptive survey
diagnostic study	non-randomized trial with historical controls	therapeutic meta-analysis
double blind randomized therapeutical trial with cross-over design	observational study	trohoc study

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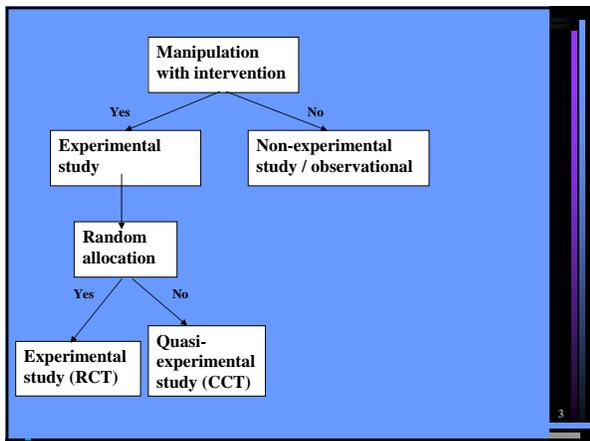
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## Experimental studies

### 1. Randomised controlled trial

Subjects are randomly allocated to groups for either the intervention/treatment being studied or control/placebo (using a random mechanism, such as coin toss, random number table, or computer-generated random numbers) and the outcomes are compared.

### 2. Pseudorandomised controlled trial

Subjects are allocated to groups for intervention/treatment or control/placebo using a nonrandom method (such as alternate allocation, allocation by days of the week, or odd-even study numbers) and the outcomes are compared. (Also called Quasiexperimental study)

### 3. Clustered randomised trial

Groups of subjects are randomised to intervention or control groups (eg community intervention trials).

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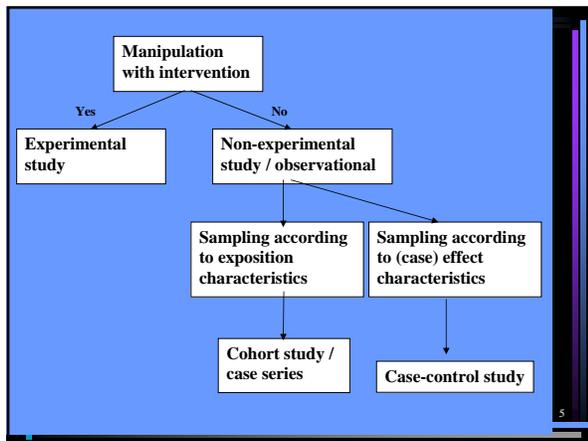
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## Comparative (nonrandomised & observational) studies

### 1. Concurrent control or cohort

Outcomes are compared for a group receiving the treatment/intervention being studied, concurrently with control subjects receiving the comparison treatment /intervention (eg usual or no care).

### 2. Case-control

Subjects with the outcome or disease and an appropriate group of controls without the outcome or disease are selected and information is obtained about the previous exposure to the treatment/intervention or other factor being studied.

### 3. Historical control

Outcomes for a prospectively collected group of subjects exposed to the new treatment/intervention are compared with either a previously published series or previously treated subjects at the same institutions.

### 4. Interrupted time series

Trends in the outcome or disease are compared over multiple time points before and after the introduction of the treatment/intervention or other factor being studied.

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Clinical study designs (MESH terms):

- Randomised Controlled Trial
- Cohort Study
- Case-Control Study
- Cross-Sectional Survey
- Case study/ case series

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EU classification: Description relative to 3 questions

1. Study objective?

- Descriptive, no comparison conducted
- Comparison as process research
- Comparison as cause-effect research

2. Procedure, intervention?

- Experimental allocation of procedure
- Survey

3. Data collection?

- Retrospective
- Cross-sectional
- Prospective / Cohort / Longitudinal

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Most publications  
in the dental  
literature are not  
Randomized  
Controlled Trials  
(RCTs)

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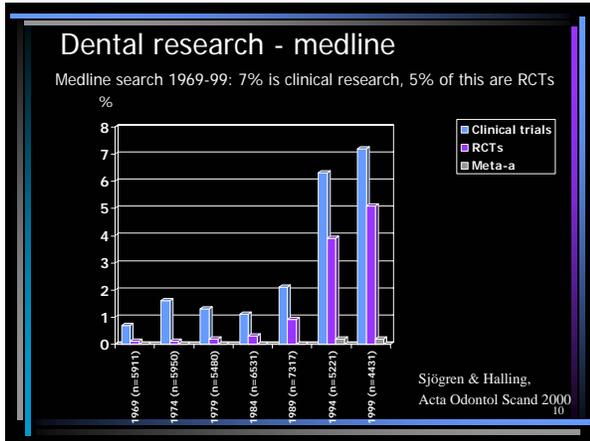
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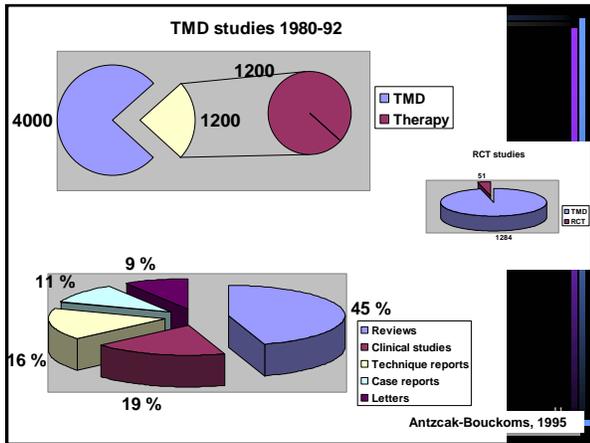
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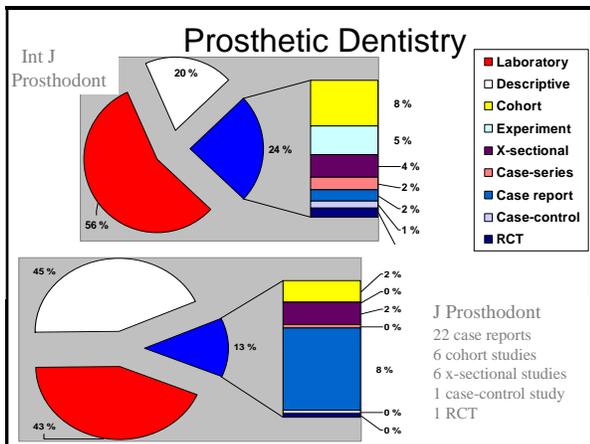
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Most publications in the dental literature are not Randomized Controlled Trials (RCTs)



# WHY not?

Because it's not always the most appropriate study design to use to address central clinical problems

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Scientific studies can be graded according to the theoretical possibility of an incorrect conclusion.

This is reflected by the design of the study in context with the clinical problem (study hypothesis)

... we will never know exact answers in science.

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# Clinical trials

what can be demonstrated?

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What can you show with a trial?

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

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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

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What can you show with a trial?

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

**Type 2 error**  
**Beta error**  
**Pessimism error**

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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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Studies: 3 general questions

1. Is the study valid?

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### Internal and external study validity

Internal validity: extent to which systematic error (bias) is minimised in a clinical trial

External validity: extent to which results of a trial provide a correct basis for generalisation to other circumstances

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### Internal validity - systematic bias

- Selection bias: biased allocation to comparison groups
- Performance bias: unequal provision of care apart from treatment under evaluation
- Detection bias: biased assessment of outcome
- Attrition bias: biased occurrence and handling of deviations from protocol and loss to follow up

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### External validity

- Patients: age, sex, severity of disease and risk factors, co-morbidity
- Treatment regimens: dosage, timing and route of administration, type of treatment within a class of treatments, concomitant treatments
- Settings: level of care (primary to tertiary) and experience and specialisation of care provider
- Modalities of outcomes: type or definition of outcomes and duration of follow up

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## 1. Is the Study Valid ?

- Is there a clear question?
- Is the most appropriate study design to answer the question used?
- Was the study conducted reliably?
- Can you follow what the authors did?

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## Studies: 3 general questions

1. Is the study valid?
2. What are the results ?

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## 2. What are the results?

- Are the results presented in a clear and simple manner ?
- Is there a clear bottom line ?
- Are they clinically important ?

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Studies: 3 general questions

1. Is the study valid?
2. What are the results ?
3. Are the results relevant to my question / problem?

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3. Are the results relevant to my question / problem ?

- Are the participants similar to my patients ?
- Is it realistic for me to apply the study methodology and results to my patients ?

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