Evidence Based Dentistry

Clinical problems and choice of study designs

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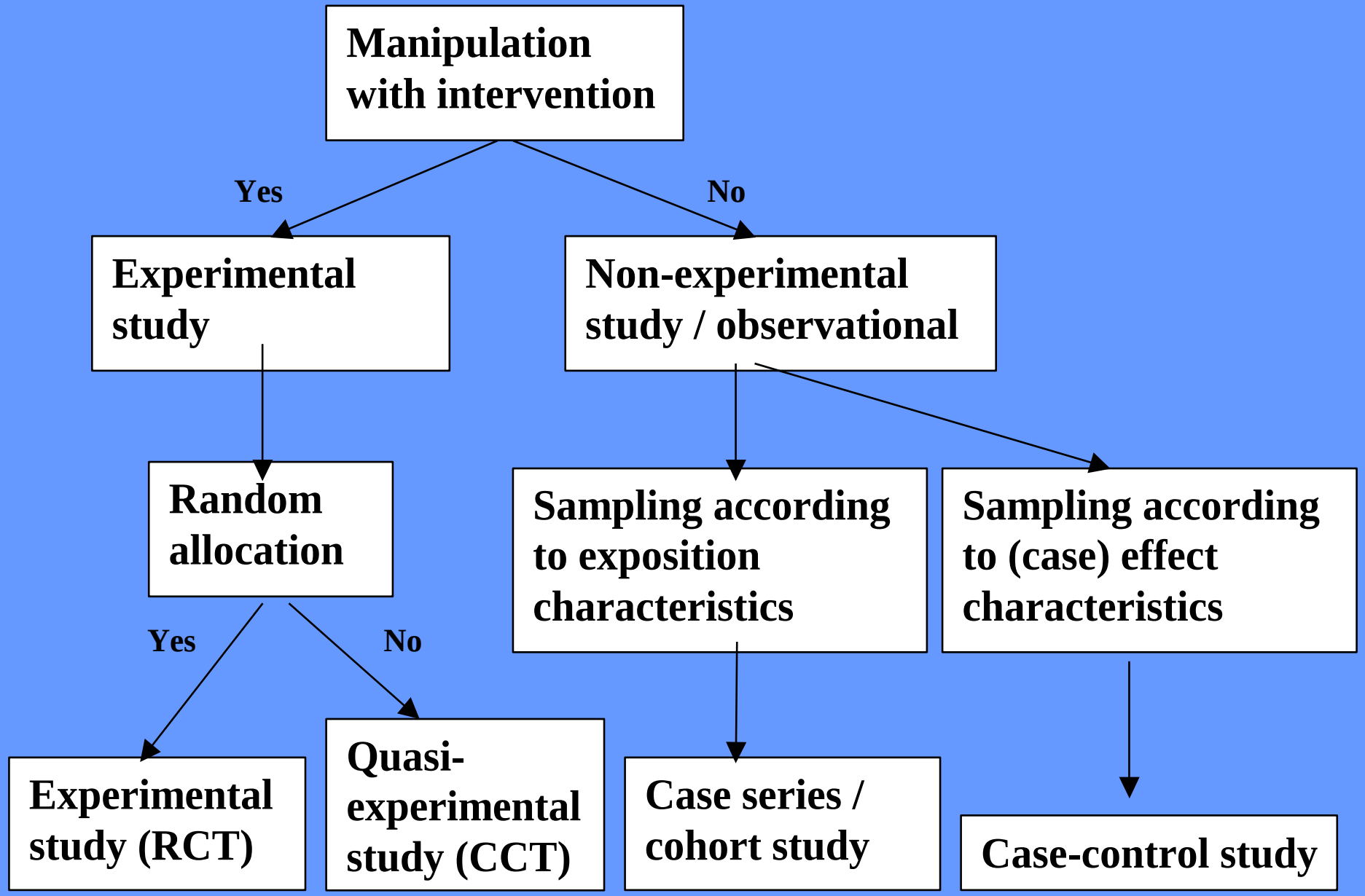

Manipulation with intervention
Yes
No
Experimental study
Non-experimental study / observational
Random allocation
Sampling according to exposition characteristics
Sampling according to (case) effect characteristics
Yes
No
Experimental study (RCT)
Quasi-experimental study (CCT)
Case series / cohort study
Case-control study

Clinical trial terminology - tower of Bable?

analytical study

case control study (89)

case serie

case study, case report

cause-effect study

clinical trial (79)

cohort study (89)

cohort study with historical controls

controlled clinical trial (95)

cross-sectional study (89)

descriptive study

diagnostic meta-analysis

diagnostic study

double blind randomized therapeutical trial with cross-over design

ecological study

etiological study

experimental study

explorative study

feasibility study (79)

follow-up study (67)

historical cohort study

incidence study

intervention study

longitudinal study (79)

N=1 trial

non-randomized trial with contemporaneous controls

non-randomized trial with historical controls

observational study

prospective cohort study

prospective follow-up study, observational or experimental

prospective study (67)

quasi-experimental study

randomized clinical trial, RTC

randomized controlled trial, RCT (89)

retrospective cohort study

retrospective follow-up study

retrospective study (67)

surveillance study

survey, descriptive survey

therapeutic meta-analysis

trohoc study

Descriptions reduced to three 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

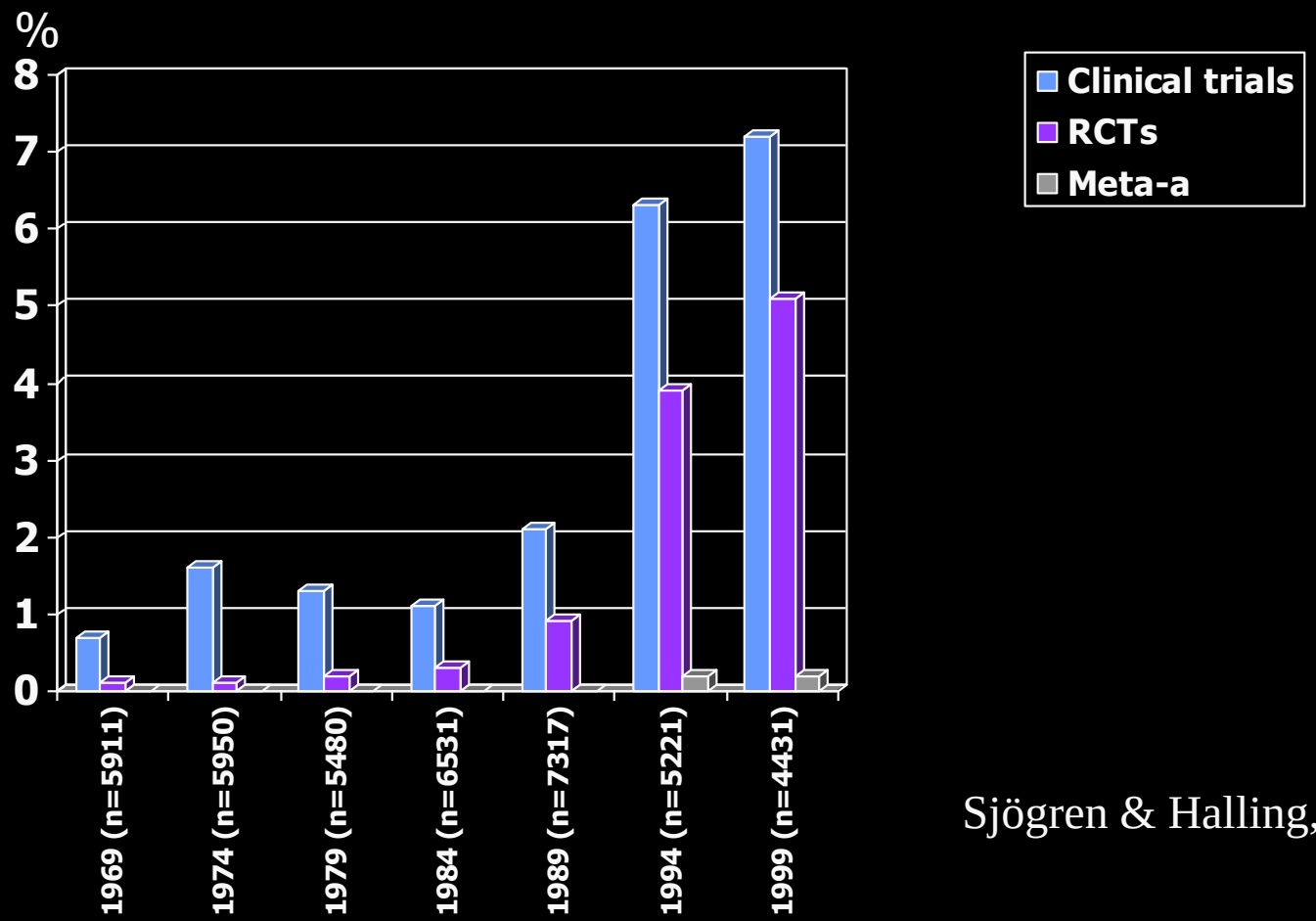
Clinical study designs (MESH terms):

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

Most publications in the dental literature are not RCTs

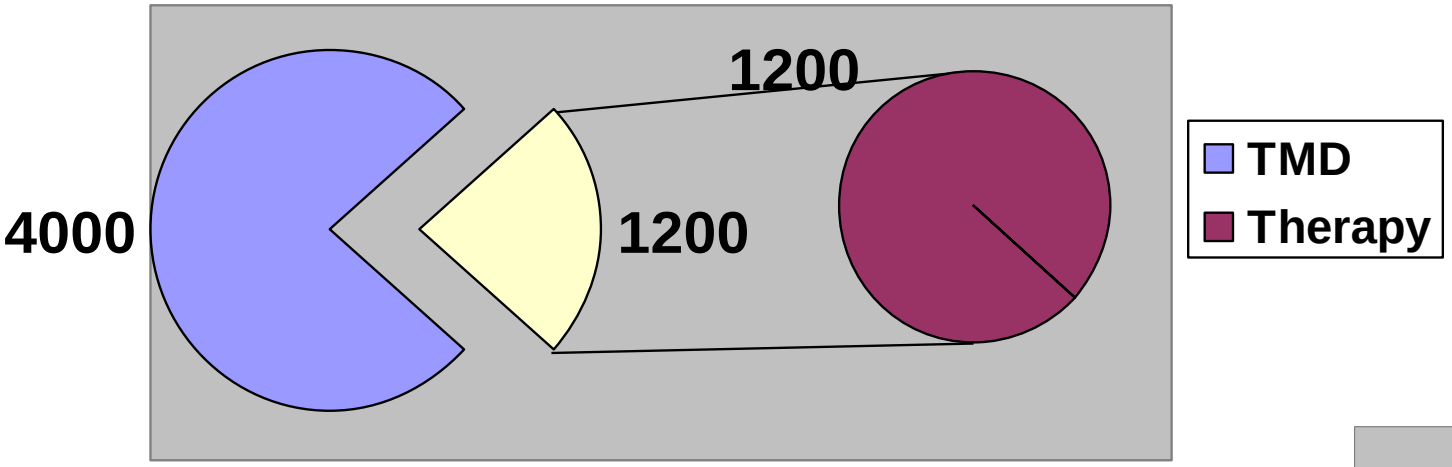
Dental research - medline

- Medline search 1969-99
  - 7% clinical research, 5% RCT

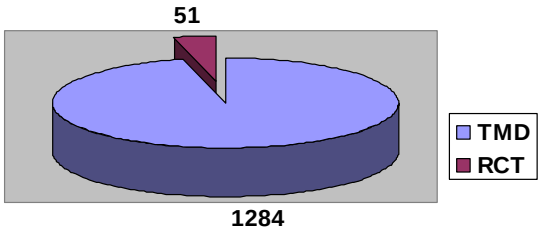


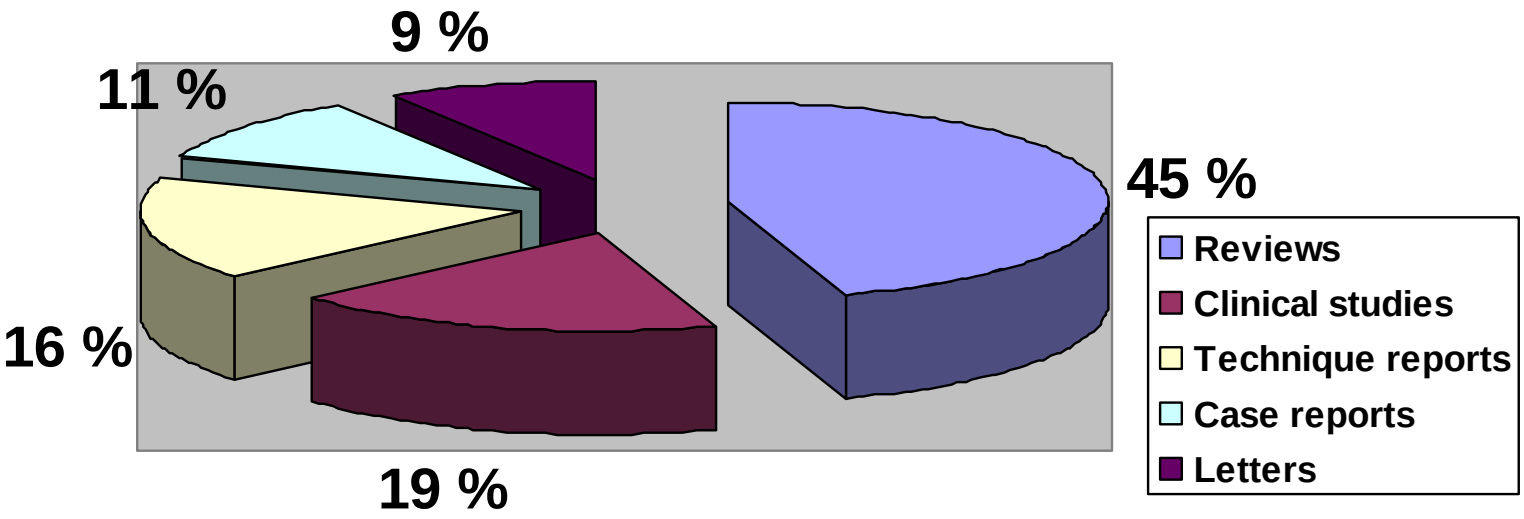
Sjögren & Halling, 2000

TMD studies 1980-92



RCT studies

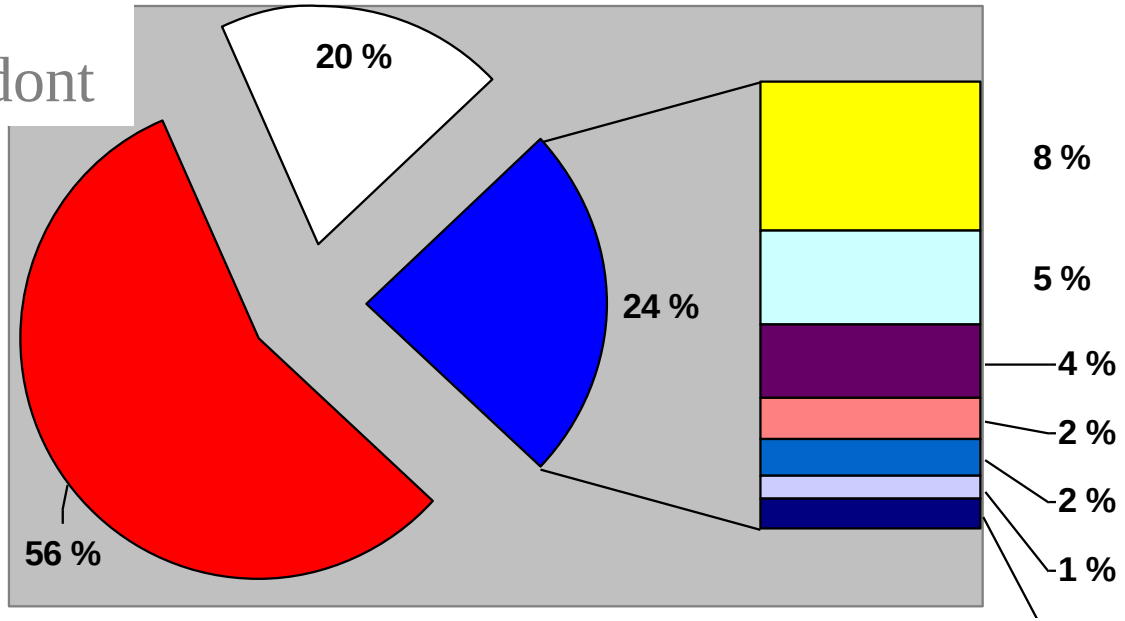




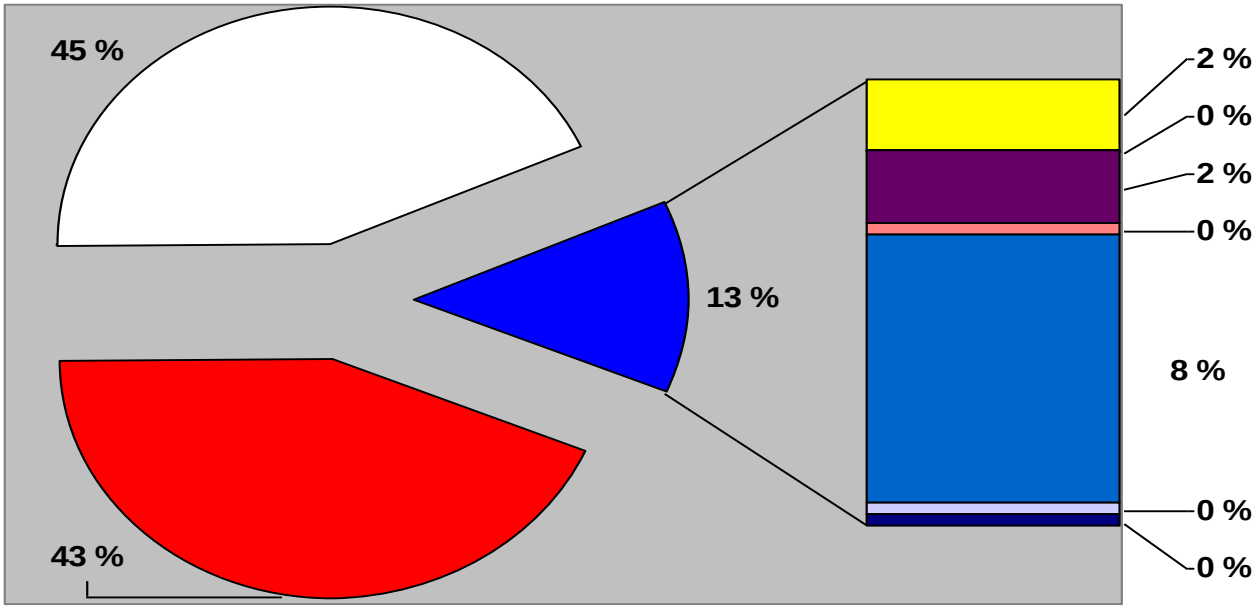
Antzcak-Bouckoms, 1995

Prosthetic Dentistry

Int J Prosthodont



- Laboratory
- Descriptive
- Cohort
- Experiment
- X-sectional
- Case-series
- Case report
- Case-control
- RCT



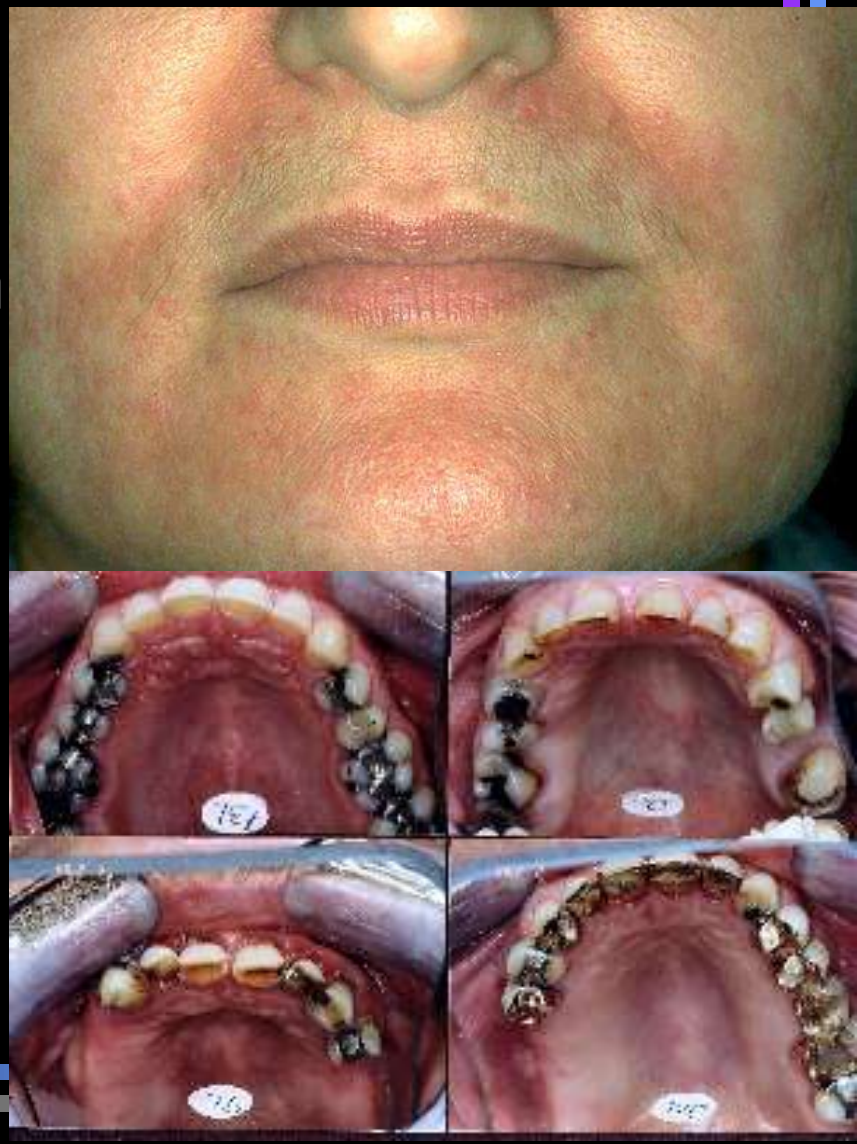
J Prosthodont

22 case reports
6 cohort studies
6 x-sectional studies
1 case-control study
1 RCT

The central tasks of clinical work

1. Clinical findings:

How to properly gather the most relevant findings from the history and physical examination, and interpret these correctly?



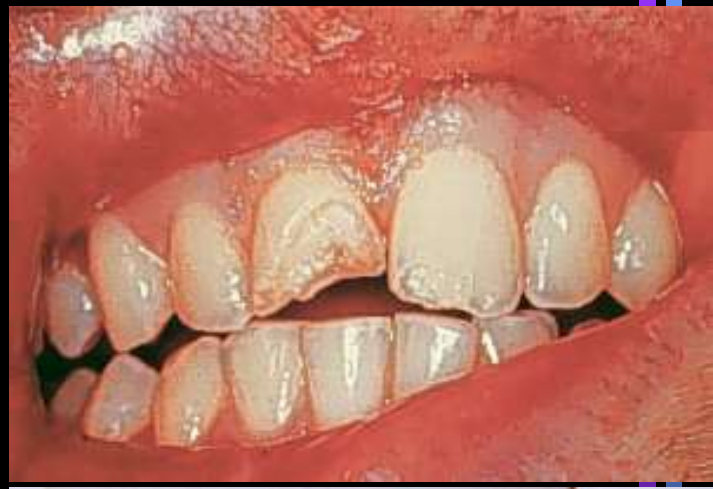
2. Etiology:

How to identify causes for disease (including its iatrogenic forms) ?

The central tasks of clinical work

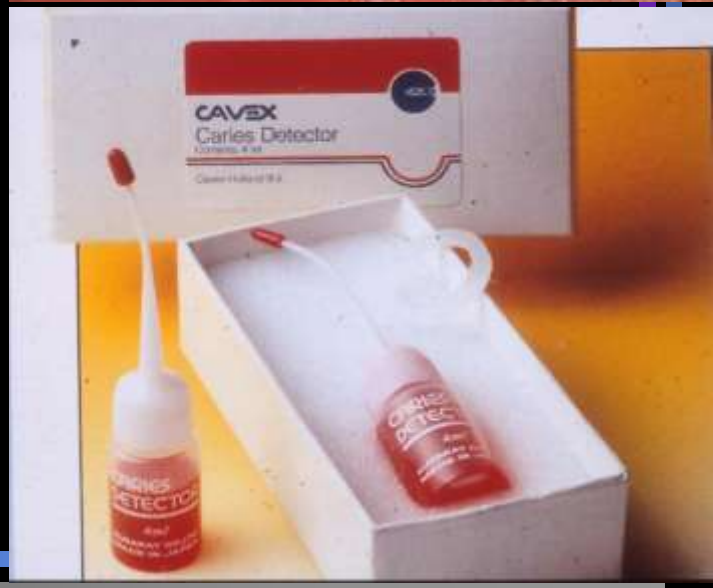
3. Differential diagnosis:

When considering the possible causes of a patient's clinical problem, how to rank them by likelihood, seriousness and treatability ?



4. Diagnostic tests

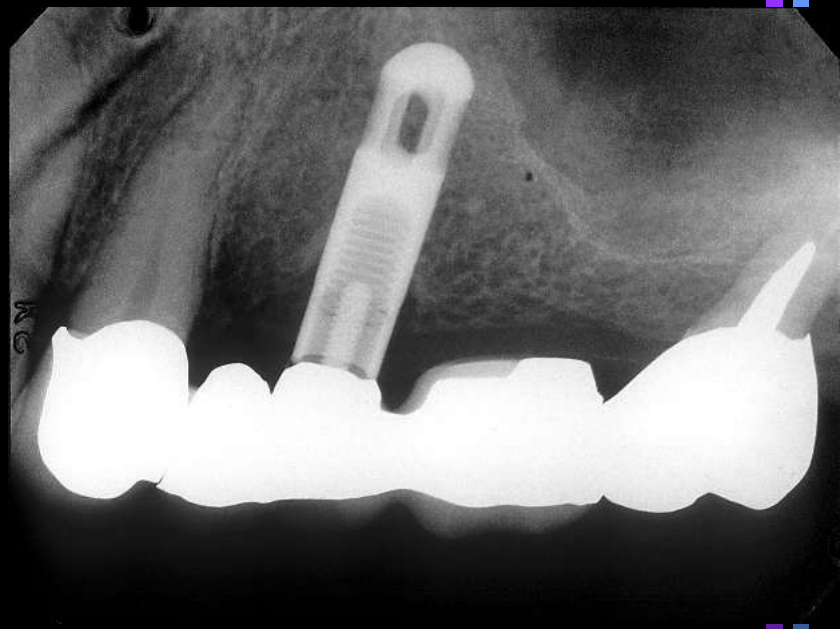
How to select and interpret diagnostic tests, in order to confirm or exclude a diagnosis, based on considering precision, accuracy, acceptability, expense, safety,



The central tasks of clinical work

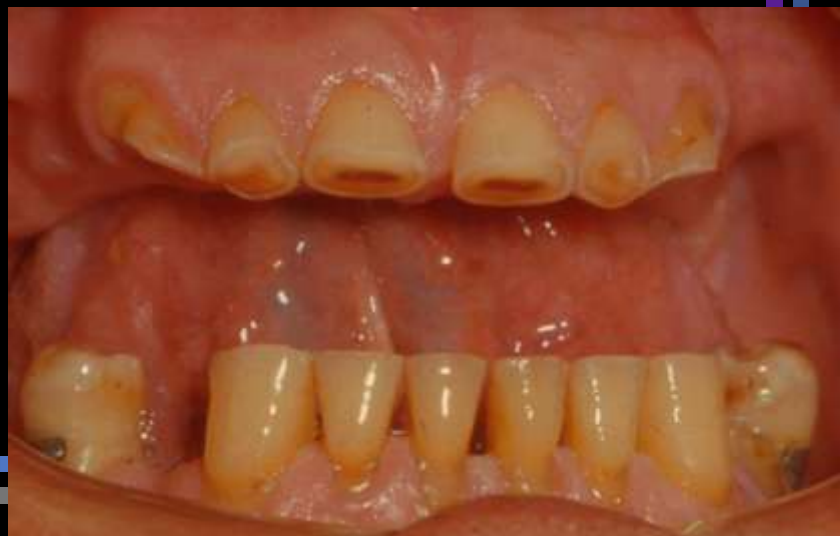
5. Prognosis:

How to estimate the patient's likely clinical course over time and anticipate likely complications?



6. Therapy:

How to select treatments to offer patients that do nore good than harm and that are worth the efforts and costs of using them?



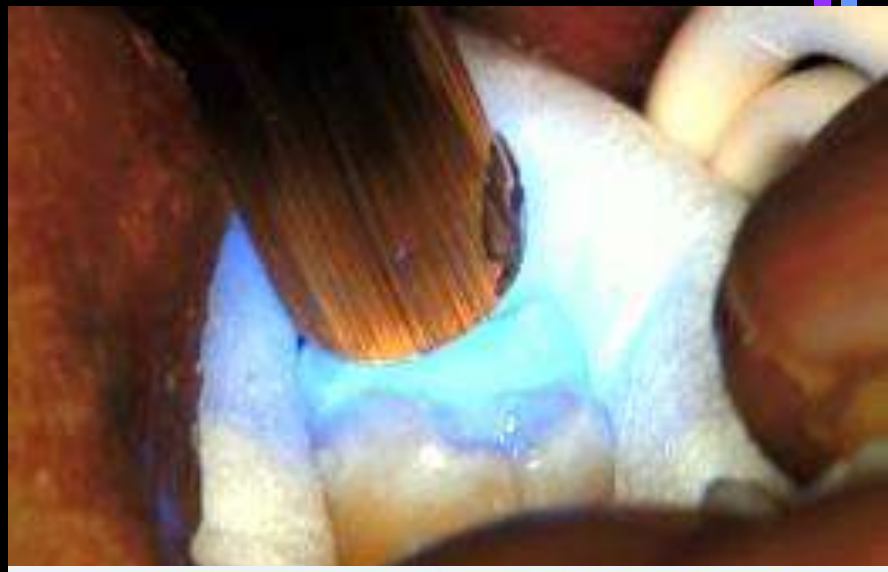
The central tasks of clinical work

7. Prevention:

How to reduce the chance of disease by identifying and modifying risk factors and how do we diagnoses disease early by screening?

8. Self-improvement:

How to keep up to date, improve our clinical skills and run a better, more efficient clinical practice?



Appropriate Study Designs

	Qualitative	Cross-Sectional	Case Control	Cohort	RCT
Diagnosis				☆	☆☆
Therapy				☆	☆☆
Prognosis				☆☆☆	
Screening			☆	☆	☆☆
Views/beliefs perceptions	☆☆☆				
Prevalence/ hypothesis generation	☆☆☆	☆☆☆			

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Qualitative research

- Aim to make sense of, or interpret, phenomena in terms of the meanings people bring to them
- May define preliminary questions which can then be addressed in quantitative studies
- Address a clinical problem through a clearly formulated question and using more than one research method (triangulation)
- Analysis of qualitative data can and should be done using explicit, systematic, and reproducible methods

Qualitative research methods -examples

- Documents - Study of documentary accounts of events
- Passive observation - Systematic watching of behaviour and talk in natural occurring settings
- Participant observation - Observation in which the researcher also occupies a role or part in the setting, in addition to observing
- In depth interviews - Face to face conversation with the purpose of exploring issues or topics in detail. Does not use preset questions, but is shaped by a defined set of topics
- Focus groups - Method of group interview which explicitly includes and uses the group interaction to generate data

	Qualitative	Cross-Sectional	Case Control	Cohort	RCT
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Cross-Sectional Survey

<u>Advantages</u>

1. Cheap and simple
2. Ethically safe

<u>Disadvantages</u>

1. Establishes association at most, not causality
2. Recall bias susceptibility
3. Confounders may be unequally distributed
4. Group sizes may be unequal

	Qualitative	Cross-Sectional	Case Control	Cohort	RCT
Diagnosis				☆	☆☆
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Case-Control Studies

Advantages:

1. Quick and cheap
2. Only feasible method for very rare disorders or those with long lag between exposure and outcome
3. Fewer individuals needed than cross-sectional studies

Disadvantages:

1. Reliance on recall or records to determine exposure status
2. Confounders
3. selection of control groups is difficult

	Qualitative	Cross-Sectional	Case Control	Cohort	RCT
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Views/beliefs perceptions	☆☆☆				
Prevalence/ hypothesis generation	☆☆☆	☆☆☆			

Characteristics of a poor case-control study:

Fail to:

- clearly define comparison groups
- and/or fail to measure exposures and outcomes in the same (preferably blinded), objective way in both cases and controls
- and/or fail to identify or appropriately control known confounders.

Cohort Study

	Qualitative	Cross-Sectional	Case Control	Cohort	RCT
Diagnosis				☆	☆☆
Therapy				☆	☆☆
Prognosis				☆☆☆	
Screening			☆	☆	☆☆
Views/beliefs perceptions	☆☆☆				
Prevalence/ hypothesis generation	☆☆☆	☆☆☆			

Advantages:

1. Ethically safe
2. individuals can be matched
3. Can establish timing and directionality of events
4. Eligibility criteria and outcome assessments can be standardised
5. Administratively easier and cheaper than RCT

Disadvantages:

1. Controls may be difficult to identify
2. Exposure may be linked to a hidden confounder
3. Blinding is difficult
4. Randomisation not present
5. For rare disease, large sample sizes or long follow-up necessary

Characteristics of a poor cohort study:

	Qualitative	Cross-Sectional	Case Control	Cohort	RCT
Diagnosis				☆	☆☆
Therapy				☆	☆☆
Prognosis				☆☆☆	
Screening			☆	☆	☆☆
Views/beliefs perceptions	☆☆☆				
Prevalence/ hypothesis generation	☆☆☆	☆☆☆			

Fail to :

- clearly define comparison groups and/or
- measure exposures and outcomes in the same (preferably blinded), objective way in both exposed and non-exposed individuals and/or
- identify or appropriately control known confounders and/or
- carry out a sufficiently long and complete follow-up of patients.

	Qualitative	Cross-Sectional	Case Control	Cohort	RCT
Diagnosis				☆	☆☆
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Randomised Controlled Trial - RCT

Advantages

1. Unbiased distribution of confounders
2. Blinding more likely
3. Randomisation facilitates statistical analysis

Disadvantages

1. Size, time and money - Expensive!
2. Volunteer bias
3. Ethically problematic at times

Cohort & RCT Crossover Design

Advantages

1. All individuals serve as own controls -> error variance is reduced -> reduced need of large sample size
2. All individuals receive treatment (at least some of the time)
3. Statistical tests assuming randomisation can be used
4. Blinding can be maintained

Disadvantages

1. All individuals receive placebo or alternative treatment at some point
2. Washout period lengthy or unknown
3. Cannot be used for treatments with permanent effects

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

This is reflected by the design of the study.

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

Internal and external validity

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

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

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

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

Diagnostic tests, Differential diagnosis

	Qualitative	Cross-Sectional	Case Control	Cohort	RCT
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Therapy				☆	☆☆
Prognosis				☆☆☆	
Screening			☆	☆	☆☆
Views/beliefs perceptions	☆☆☆				
Prevalence/ hypothesis generation	☆☆☆	☆☆☆			

- Clearly identified comparison groups, at least one of which is free of the target disorder
- Either an objective diagnostic standard/contemporary clinical diagnostic standard with reproducible criteria for any objectively interpreted component
- Interpretation of the test without knowledge of the diagnostic standard result
- Interpretation of the diagnostic standard without knowledge of the test result
- A statistical analysis consistent with study design

Therapy / Prevention / Education

	Qualitative	Cross-Sectional	Case Control	Cohort	RCT
Diagnosis				☆	☆☆
Therapy				☆	☆☆
Prognosis				☆☆☆	
Screening			☆	☆	☆☆
Views/beliefs perceptions	☆☆☆				
Prevalence/ hypothesis generation	☆☆☆	☆☆☆			

- 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.

Prognosis

	Qualitative	Cross-Sectional	Case Control	Cohort	RCT
Diagnosis				☆	☆☆
Therapy				☆	☆☆
Prognosis				☆☆☆	
Screening			☆	☆	☆☆
Views/beliefs perceptions	☆☆☆				
Prevalence/ hypothesis generation	☆☆☆	☆☆☆			

- An inception cohort of persons, all initially free of the outcome of interest
- Follow-up of at least 80 per cent of patients until the occurrence of either a major study criteria or the end of the study
- A statistical analysis consistent with the study design.

Etiology - Harm - Causation

- Clearly identified comparison group for those at risk for, or having, the outcome of interest
- Masking of observers of outcomes to exposures
- Observers of exposures masked to outcomes for case-control studies and individuals masked to exposure for all other study designs
- A statistical analysis consistent with the study design.

Critical Appraisal Criteria

Exists for studies focused on e.g. :

- therapy
- diagnosis
- screening
- harm
- prognosis
- causation of disease (etiology)
- quality of care
- economic analyses
- .....

Three general questions

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

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?

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 ?

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 ?