Methodological Challenges in the Study of Dental Occlusion

Asbjørn Jokstad
Professor and Head, Prosthodontics
University of Toronto, Ontario, Canada
a.jokstad@dentistry.utoronto.ca
What is Dental Occlusion?
Occlusion: interpretations of the term

Occlusion: interpretations of the term


Mohl et al. (1988) p15: ”Occlusion encompasses all factors that serve to bring about, affect, influence, or result from mandibular position, function, parafunction, and dysfunction. It implies much more than the occlusal contact relationships of the dentition and includes reference to a dynamic biomechanical musculoskeletal system: the masticatory system”
Occlusion: interpretations of the term

Okeson (2008): “The static relationship of the teeth” – versus Mohl et al. (1988) “…occlusion encompasses all factors that serve to bring about, affect, influence, or result from mandibular position, function, parafunction, and dysfunction. It implies much more than the occlusal contact relationships …… – versus

International Gnathological Society (1926): ”the biologics of the masticating mechanisms; that is, the anatomy, morphology, histology, physiology, pathology and the therapeutics of the oral organ, especially the jaws and teeth and the vital relations of the organ to the rest of the body”
Occlusion: interpretations of the term

- The *Glossary of Prosthodontic Terms* (GPT version 8, 2005)

- *The static relationship between the incising or masticating surfaces of the maxillary or mandibular teeth or tooth analogues”*

- GPT–8 include 152 terms containing the terms “occlusion” or “occlusal” (!)
Example of terminology confusion

MAXIMAL INTERCUSPAL POSITION – synonyms:

- Acquired (centric) *occlusal position*
- Acquired *occlusion*
- Adaptive *occlusion*
- Habitual *occlusion*
- Intercuspal *occlusion*
- Interdigitated *occlusion*

(Source: GPT-8)
Purpose: A more precise and up-to-date definition of prosthetic dentistry is warranted. The aim of the present review is to present a new core definition of the discipline on the basis of a discussion of existing definitions. Materials and Methods: Clinical textbooks in prosthetic dentistry and dental implantology, as well as medical and dental glossaries were reviewed. Results: Two main categories of definitions of prosthetic dentistry were identified: first, definitions that emphasized the technologic aspects of the discipline, i.e., the fabrication of prostheses; and second, definitions that incorporated some reference to the objectives or aims of prosthetic dentistry, whether one or more aspects of oral function. Slightly more than half of the definitions reviewed appeared to be related references, and this aspect tended to be most pronounced in the definitions of prosthetic implants. Conclusion: The following definition is ventured: prosthetics is the treatment concerned with the consequences of congenital absence or acquired defect of teeth and the replacement by methods for and assessment whether more good than harm is done by devices made from alloplastic materials. Int J Prosthodont 1998;11:262-265.

Is there an association between occlusion and periodontal destruction?

Yes—occlusal forces can contribute to periodontal destruction.

**Stephen K. Harrell, DDS; Marvin E. Nunn, DDS, BDS; William W. Hallmon, DDS, MS**

**Harrel, Nunn & Hallmon versus Deas & Mealey.**

**Conclusion:** The following definition is ventured: prosthetics is the treatment concerned with the consequences of congenital absence or acquired defect of teeth and the replacement by methods for and assessment whether more good than harm is done by devices made from alloplastic materials. Int J Prosthodont 1998;11:262-265.

**Point : Counterpoint**

**Harrel, Nunn & Hallmon versus Deas & Mealey.**

**J Am Dent Assoc 2006; 137: 1380–1385.**
A Conceptual Framework for Understanding Dental Occlusion

For categorizing contemporary study objectives and their methodological challenges
Conceptual depiction of dental occlusion research defined within a framework of three dimensions

(Teeth–mandible–maxilla–)
Forms and Positions, e.g.,

- Contacts
- Guidance
- Postural (inter–occlusal) space
- Wear (AKA: Tooth substance loss (TSL) (friction +/- corrosion)

Subjective measurement?  
Objective measurement?
Conceptual depiction of dental occlusion research defined within a framework of three dimensions

**Forms & Positions**
- Contacts
- Guidance
- Postural (inter-occlusal) space
- Wear (Tooth substance loss)

**Subjective measurement?**
**Objective measurement?**

**(Oral) Functions, e.g.,**
- Chewing
- Swallowing
- Speech
- Force size & direction

**Subjective measurement?**
**Objective measurement?**

- [CORE: Wang]
- [CORE: Pullinger]
Conceptual depiction of dental occlusion research defined within a framework of three dimensions

**Forms & Positions**
- Contacts
- Guidance
- Postural (inter-occlusal) space
- Wear (Tooth substance loss)

**Functions**
- Chewing
- Swallowing
- Speech
- Force size & direction

**(Oral) Appearance, e.g.**
- Proportions of face and teeth
- VDO / “Lower facial height”
- Wear (Tooth substance loss)
Basic and applied research on dental occlusion defined within a framework of three dimensions:

- **Forms & Positions**
  - Contacts
  - Guidance
  - Postural (inter-occlusal) space
  - Wear (Tooth substance loss)

- **Functions**
  - Chewing
  - Swallowing
  - Speech
  - Force size & direction

- **Appearance**
  - Proportions of face and teeth
  - VDO / “Lower facial height”
  - Wear (Tooth substance loss)

**Neuro-muscular mechanisms**
- Adaptive capacity:
  - Interferences / VDO changes
  - Proprioceptive discriminate

**Bruxism**
- Craniofacial anomalies
- Head/Body posture
- Hormonal state
- Rheumatoid Arthritis
- TMD/TMJ

**Pain**
- Inflammation
- Xerostomia

**Genotype-phenotype distinction**
Basic and applied research on dental occlusion defined within a framework of three dimensions

**Forms & Positions**
- Contacts
- Guidance
- Postural (inter-occlusal) space
- Wear (Tooth substance loss)

**Functions**
- Chewing
- Swallowing
- Speech
- Force size & direction

**Appearance**
- Proportions of face and teeth
- VDO / “Lower facial height”
- Wear (Tooth substance loss)

**Neuro-muscular mechanisms**
- Adaptive capacity: Interferences / VDO changes
- Proprioceptive discriminate

**Adaptive capacity:**
- Interferences / VDO changes
- Proprioceptive discriminate

**Epidemiology:**
- Cognitive function
- Mortality
- Nutrition
- Physical fitness
- Quality of Life

**Potential for “trauma”**
- Masticatory muscles
- TMJ / condyle-disk relation
- Obstructive sleep apnea
- Cervical Spine

**Effects on:**
- Bruxism
- Craniofacial anomalies
- Head/Body posture
- Hormonal state
- Rheumatoid Arthritis
- TMD/TMJ

**Bruxism**
- Pain
- Inflammation
- Xerostomia

**Periodontium**
- TMD/TMJ/Orofacial Pain
- Headache

**Basic and applied research on dental occlusion defined within a framework of three dimensions**

[CORE: Türp – Liu- Xie]

[CORE: Ohkubo]

[CORE: Pullinger]

[CORE: Lobbezoo]
Research relevant to management of dental occlusion defined within a framework of three dimensions

Change/Restore Occlusion
- Partnership with patient
  - Self-esteem
  - Psycho-social needs
  - Comfort
  - Physiological needs
  - Aesthetic requirements

Forms & Positions
- Contacts
- Guidance
- Postural (inter-occlusal) space
- Wear (Tooth substance loss)

Functions
- Chewing
- Swallowing
- Speech
- Force size & direction

Appearance
- Proportions of face and teeth
- VDO / “Lower facial height”
- Wear (Tooth substance loss)

Subjective measurement? Objective measurement?
- “Phantom bite”
- “Pathological wear”
- “Malposition” a causal risk factor?:
  - Caries
  - Periodontology
  - Wear
  - TMD/TMJ
  - Occlusal Stability

Subjective measurement? Objective measurement?
- Aetiology: Friction
  +/- corrosion

“Dys-Function”
Dyskinesia
Day bruxism
REM behavior (night bruxism)
TMD
Pain

Psychosocial value
Quality of Life
Societal determinants

Subjective measurement? Objective measurement?

Research relevant to management of dental occlusion defined within a framework of three dimensions

Aetiology:
- Friction
  +/- corrosion
Research relevant to restorative management of dental occlusion

Intact/near intact Teeth & Occlusion (incl. "malocclusion")

Depleted Occlusion
Shortened dental arch
Bounded space

Edentate

"Restored"*

Adverse outcome risk?
Periodontal breakdown
Poor cleaning access
Wear of restorative mater.
Possible interferences

"Restored"*

Adverse outcome risk?
TMJ Changes ? TMD?
Bruxism?
Proprioception?
Remaining teeth:
Wear increase?
Stability (tipping/extrusion)
Possible interferences
“Bite collapse”

Outcomes

Aesthetics + Social function + Oral Functions:
Chewing: effectiveness, efficiency, trajectory
Speech: clarity, trajectory
Swallowing - Bite force

Not Restored

“Restored”*

*Include studies on mechanical requirement of materials/restoration(s)

! Occlusion on implants introduces additional research issues

[CORE: Koyano]

[CORE: Klineberg]
Characteristics of Existing Clinical Studies on Dental Occlusion
Research using scientific methods

- Aspire to find and determine facts, solve new or existing problems, prove new ideas, or develop new theories
  - The most common scientific method used today is termed the hypothetico-deductive model
  - Stepwise: formulate, test, and modify hypotheses through systematic observations, measurements, and experiments
  - Probabilistic considerations determine whether hypotheses remain or are discarded, often using “p-values” as virtual thresholds

Excellent Textbooks: Rosenberg(2000), Thompson(2011)
Aspire to find and determine facts, solve new or existing problems, prove new ideas, or develop new theories

- Basic Research
- Applied research
  - Clinical research
    - (i) animal studies
    - (ii) epidemiology
    - (iii) clinical studies on human subjects
Clinical research objectives

At the core of any doctor and patient interaction is the need of the doctor:

- to learn or know thoroughly (Greek: *Gnosis*) the patient’s condition’s:
- probable cause (Greek: *Aitio*)
- signs and symptoms apart (Greek: *Dia*)
- likely outcome in advance (Greek: *Pro*)
  - without or with a cure (Greek: *Therapeia*)

Today, clinical studies are categorized along these old Greek terms within the four domains: *Aetio–gnosis, Dia–gnosis, Pro–gnosis, Therapy*
Clinical Studies – Characteristics

Clinical query Pubmed searches yield using the search terms: "occlusion"[TI] AND "dentistry"[MeSHTerms]

<table>
<thead>
<tr>
<th></th>
<th>Diagnosis</th>
<th>Prognosis</th>
<th>Therapy</th>
<th>Aetiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Narrow search</td>
<td>0</td>
<td>16</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>Broad search</td>
<td>231</td>
<td>115</td>
<td>131</td>
<td>340</td>
</tr>
</tbody>
</table>

(Search August, 2011)
It is more difficult to falsify a hypothesis about aetiology compared to other research issues – if using a hypothetico-deductive scientific research model.

A hypothesis must be falsifiable in order to qualify as being scientific.

The literature abounds with ideas and theories that are not scientific and hence, refutable by proper research, however well undertaken.

Our heritage: Many dogmas about occlusion that reflect views derived from deductive reasoning and not by hypothetico-deductive scientific models.
Dogmas in occlusion derived from deductive logic

- Condyles resting in their most supero-anterior position against the posterior slopes of the articular eminence...

Dogmas in occlusion derived from deductive logic

- Condyles resting in their most supero-anterior position against the posterior slopes of the articular eminence...
- Articular disks properly interposed between the condyles and the fossae...
- Even and simultaneous contact of posterior teeth in CR...

Dogmas in occlusion derived from deductive logic

- Condyles resting in their most supero–anterior position against the posterior slopes of the articular eminence
- Articular disks properly interposed between the condyles and the fossae...
- Even and simultaneous contact of posterior teeth in CR..
- Anterior teeth should contact and disclude the posterior teeth upon eccentrical movement...

Dogmas in occlusion derived from deductive logic

- Condyles resting in their most superoanterior position against the posterior slopes of the articular eminence
- Articular disks properly interposed between the condyles and the fossae...
- Even and simultaneous contact of posterior teeth in CR..
- Anterior teeth should contact and disclude the posterior teeth upon eccentric movement...

- In the upright head position the posterior teeth should contact more prominently than the anterior tooth contacts ...

Dogmas in occlusion derived from deductive logic

- Condyles resting in their most superoanterior position against the posterior slopes of the articular eminence
- Articular disks properly interposed between the condyles and the fossae...
- Even and simultaneous contact of posterior teeth in CR..
- Anterior teeth should contact and disclude the posterior teeth upon eccentric movement...
- In the upright head position the posterior teeth should contact more prominently than the anterior tooth contacts

- Provide the most shallow anterior guidance patterns that disclude posterior teeth... etc. etc.

Deductive logic from basic research findings as a basis for clinical practice is problematic.

“I think you should be more explicit here in step two.”
Study Design Appropriateness
An inferior study design opens for investigator bias, which usually results in over-optimistic results. Situation is compounded by publication bias, which is the propensity of editors’ favouritism of positive findings, regardless of study methodology quality, compared to negative results.

Refs.: Polychronopoulou et al. 2010, Crawford et al. 2010
Depending on research question, some study designs are associated with less theoretical possibility of risk of bias and thus considered better scientific evidence than other study designs.

Remark the very essential detail that it is the theoretical possibility of bias.

Not equivalent to stating that all studies of a particular study design are irrefutably biased.
Study Validity

- To what extent the investigator has made every attempt to minimize bias in the planning and execution of a study is coined as the study’s "internal validity", also known as “systematic bias”
- To which extent the results of a clinical study can provide a correct basis for generalization to other circumstances is coined “external validity”
Internal Validity – typical threats

- **Selection bias**: predisposed allocation to comparison groups
- **Performance bias**: unequal provision of care apart from treatment under evaluation
- **Detection bias**: prejudiced assessment of outcome
- **Attrition bias**: disparate occurrence and handling of deviations from protocol and loss to follow up
External Validity – typical threats

- **Patients**: age, gender, severity of disease /situation, risk factors, co-morbidity
- **Treatment regimens**: type of treatment within a class of possible treatments; concomitant treatments
- **Setting**: level of care (primary, secondary or tertiary), experience and specialisation of care provider
- **Modalities of outcomes**: appropriateness of outcomes (& duration of follow up)
Choice of appropriate outcomes in clinical studies on dental occlusion
Outcomes following interventions directed towards dental occlusion

The great majority of clinical studies report outcomes in the following order:  
a) Surrogate  
b) Clinical  
c) Patient relevant

S.Rs: Türp et al. 2004; List & Axellsson 2010; Fricton et al. 2010a, 2010b
a. Surrogate outcome criteria

A laboratory measurement or a physical sign used as a substitute for a clinically meaningful endpoint that measures directly how a patient feels, functions or survives.

(Temple 1995)
a. Surrogate outcome criteria

“Objective” measurements of:
- Chewing
- Bite force
- Jaw movement tracking
- Electro-myo-graphy
- Occlusal stability
- Speech
- Vertical dimensions of occlusion

Are these outcomes really predictive of patient-relevant outcomes?
b. Clinical outcomes / criteria

Mobility range
Sounds
Complications and treatment failures
  ▸ Re-treatment (re-operation and/or remake)
  ▸ Biological or Technical Complications
  ▸ Time to re-treatment
  ▸ ...

c. Patient relevant outcomes/criteria

- Pain reduction
- Symptom relief
- Patient preference
- Satisfaction with function (e.g. chewing, dietary changes, speech)
- Satisfaction with aesthetics
- Reported changes of social activity
- Perceived change of quality of life or other health measures
Characteristics of Biomedical Research & Clinical Research
### Clinical trial terminology – perplexity → MESH terms

<table>
<thead>
<tr>
<th>Analytical Study</th>
<th>Ecological Study</th>
<th>Prospective Cohort Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case control study (89)</td>
<td>Case control study</td>
<td>Case control study</td>
</tr>
<tr>
<td>Case serie</td>
<td>Case serie</td>
<td>Case serie</td>
</tr>
<tr>
<td>Case study, case report</td>
<td>Case study, case report</td>
<td>Case study, case report</td>
</tr>
<tr>
<td>Cause-effect study</td>
<td>Cause-effect study</td>
<td>Cause-effect study</td>
</tr>
<tr>
<td>Clinical trial (79)</td>
<td>Clinical trial</td>
<td>Clinical trial</td>
</tr>
<tr>
<td>Cohort study (89)</td>
<td>Cohort study</td>
<td>Cohort study</td>
</tr>
<tr>
<td>Cohort study with historical controls</td>
<td>Cohort study with historical controls</td>
<td>Cohort study with historical controls</td>
</tr>
<tr>
<td>Controlled clinical trial (95)</td>
<td>Controlled clinical trial</td>
<td>Controlled clinical trial</td>
</tr>
<tr>
<td>Cross-sectional study (89)</td>
<td>Cross-sectional study</td>
<td>Cross-sectional study</td>
</tr>
<tr>
<td>Descriptive study</td>
<td>Descriptive study</td>
<td>Descriptive study</td>
</tr>
<tr>
<td>Diagnostic meta-analysis</td>
<td>Diagnostic meta-analysis</td>
<td>Diagnostic meta-analysis</td>
</tr>
<tr>
<td>Diagnostic study</td>
<td>Diagnostic study</td>
<td>Diagnostic study</td>
</tr>
<tr>
<td>Double blind randomized therapeutical trial with cross-over design</td>
<td>Double blind randomized therapeutical trial with cross-over design</td>
<td>Double blind randomized therapeutical trial with cross-over design</td>
</tr>
<tr>
<td>Feasibility study (79)</td>
<td>Feasibility study</td>
<td>Feasibility study</td>
</tr>
<tr>
<td>Follow-up study (67)</td>
<td>Follow-up study</td>
<td>Follow-up study</td>
</tr>
<tr>
<td>Intervention study</td>
<td>Intervention study</td>
<td>Intervention study</td>
</tr>
<tr>
<td>Longitudinal study (79)</td>
<td>Longitudinal study</td>
<td>Longitudinal study</td>
</tr>
<tr>
<td>N=1 trial</td>
<td>N=1 trial</td>
<td>N=1 trial</td>
</tr>
<tr>
<td>Non-randomized trial with contemporaneous controls</td>
<td>Non-randomized trial with contemporaneous controls</td>
<td>Non-randomized trial with contemporaneous controls</td>
</tr>
<tr>
<td>Non-randomized trial with historical controls</td>
<td>Non-randomized trial with historical controls</td>
<td>Non-randomized trial with historical controls</td>
</tr>
<tr>
<td>Observational study</td>
<td>Observational study</td>
<td>Observational study</td>
</tr>
<tr>
<td>Prospective follow-up study</td>
<td>Prospective follow-up study</td>
<td>Prospective follow-up study</td>
</tr>
<tr>
<td>Quasi-experimental study</td>
<td>Quasi-experimental study</td>
<td>Quasi-experimental study</td>
</tr>
<tr>
<td>Randomized clinical trial, RTC (89)</td>
<td>Randomized clinical trial, RTC</td>
<td>Randomized clinical trial, RTC</td>
</tr>
<tr>
<td>Randomized controlled trial, RCT (89)</td>
<td>Randomized controlled trial, RCT</td>
<td>Randomized controlled trial, RCT</td>
</tr>
<tr>
<td>Retrospective cohort study</td>
<td>Retrospective cohort study</td>
<td>Retrospective cohort study</td>
</tr>
<tr>
<td>Retrospective follow-up study</td>
<td>Retrospective follow-up study</td>
<td>Retrospective follow-up study</td>
</tr>
<tr>
<td>Retrospective study (67)</td>
<td>Retrospective study</td>
<td>Retrospective study</td>
</tr>
<tr>
<td>Surveillance study</td>
<td>Surveillance study</td>
<td>Surveillance study</td>
</tr>
<tr>
<td>Survey, descriptive survey</td>
<td>Survey, descriptive survey</td>
<td>Survey, descriptive survey</td>
</tr>
<tr>
<td>Therapeutic meta-analysis</td>
<td>Therapeutic meta-analysis</td>
<td>Therapeutic meta-analysis</td>
</tr>
<tr>
<td>Trohoc study</td>
<td>Trohoc study</td>
<td>Trohoc study</td>
</tr>
</tbody>
</table>
Current MESH terms to describe clinical study designs:

1. Case–Control Study
2. Case study/ Case series
3. Cohort Study
4. Controlled Clinical Trial (CCT)
5. Cross–Sectional Survey
6. Randomized Controlled Trial (RCT)
Study designs suitable for appraising:
Diagnostic tests
Prognosis
Therapy
Aetiology
<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>What are the merits of using T-Scan to determine the extent and severity of occlusal interferences?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy</td>
<td>Which restorative occlusion scheme / education strategy is the best on implant restorations?</td>
</tr>
<tr>
<td>Prognosis</td>
<td>What will develop due to (or following introduction of) occlusal interferences?</td>
</tr>
<tr>
<td>Screening</td>
<td>How many patients have occlusal interferences upon mediotrusion?</td>
</tr>
<tr>
<td>Views / Beliefs / Perceptions</td>
<td>How do occlusal interferences impact on the patient’s daily life?</td>
</tr>
<tr>
<td>Prevalence / Hypothesis generation</td>
<td>How many patients have experienced occlusal interferences?</td>
</tr>
</tbody>
</table>
## Appropriate Study Designs

<table>
<thead>
<tr>
<th></th>
<th>Qualitative</th>
<th>Cross-Sectional</th>
<th>Case Control</th>
<th>Cohort</th>
<th>RCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis</td>
<td></td>
<td></td>
<td>⋆</td>
<td>⋆</td>
<td>⋆⋆</td>
</tr>
<tr>
<td>Therapy</td>
<td></td>
<td></td>
<td>⋆</td>
<td>⋆</td>
<td>⋆⋆⋆</td>
</tr>
<tr>
<td>Prognosis</td>
<td></td>
<td></td>
<td>⋆⋆⋆</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Screening</td>
<td></td>
<td></td>
<td>⋆</td>
<td>⋆</td>
<td>⋆⋆</td>
</tr>
<tr>
<td>Views/beliefs</td>
<td>⋆⋆⋆</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prevalence/hypothesis generation</td>
<td>⋆⋆⋆</td>
<td></td>
<td>⋆⋆⋆</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Diagnostic tests
Clearly identified comparison groups, at least one of which is free of the target disorder
Either an objective diagnostic/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
Efficacy of a diagnostic tests – 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

- **CHARACTERISTICS OF THE TEST**
Efficacy of a diagnostic tests: Positive–Negative predictive value

- **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.

NOT CHARACTERISTICS OF THE TEST BUT OF APPLICABILITY IN PARTICULAR POPULATIONS
Prognosis
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.
Therapy

- Which product/procedure/technique/maintenance regime/education strategy provides the *best outcome*?

*Clinical, patient centred, surrogate or societal*
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
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
What can you show with a trial?

<table>
<thead>
<tr>
<th></th>
<th>A is better than B</th>
<th>A is no better than B</th>
</tr>
</thead>
<tbody>
<tr>
<td>A is better than B</td>
<td>✓</td>
<td>✗</td>
</tr>
<tr>
<td>A is no better than B</td>
<td>✗</td>
<td>✓</td>
</tr>
</tbody>
</table>

The truth
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
X

What the trial shows

A is better than B

A is no better than B

X
Type 1 ("alfa") error

• Inadequate study design methodology
• Fallacy of observed clinical success
  • Spontaneous remission
  • Placebo response
  • Multiple variables in intervention
  • Radical vs. conservative intervention
  • Long-term failure
  • Side effects and intervention sequelae
What can you show with a trial?  

<table>
<thead>
<tr>
<th>The truth</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A is better than B</strong></td>
<td><strong>A is no better than B</strong></td>
</tr>
</tbody>
</table>

What the trial shows:

- **A is better than B**
- **A is no better than B**

Type 2 error

Beta error

Pessimism error
Type 2 ("beta") error

1. Inadequate study power
2. Fallacy of observed clinical failure
   - Wrong diagnosis
   - Incorrect cause–effect correlations
   - Multifactorial problems
   - Lack of cooperation
   - Improper execution of intervention
   - Premature evaluation of intervention
   - Limited success of intervention
Therapy: No evidence of effect is not equivalent to evidence of no effect.
Etiology – Harm – Causation
Etiology – Harm – Causation

- Evidence levels: Randomised clinical trial > cohort/ clinical trial > case–control > cross-sectional > single case
- Clearly identified comparison group for those at risk for, or having, the outcome of interest
  - Observers of outcomes masked to exposures
  - Observers of exposures masked to outcomes for case–control studies and observers masked to exposure for all other study designs
  - A statistical analysis consistent with the study design.
Cross-Sectional Survey

Advantages
1. Cheap and simple
2. Ethically safe

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

<table>
<thead>
<tr>
<th>Qualitative</th>
<th>Cross-Sectional</th>
<th>Case Control</th>
<th>Cohort</th>
<th>RCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis</td>
<td></td>
<td></td>
<td>#</td>
<td>#</td>
</tr>
<tr>
<td>Therapy</td>
<td></td>
<td></td>
<td>#</td>
<td>#</td>
</tr>
<tr>
<td>Prognosis</td>
<td></td>
<td></td>
<td>#</td>
<td>#</td>
</tr>
<tr>
<td>Screening</td>
<td></td>
<td></td>
<td>#</td>
<td>#</td>
</tr>
<tr>
<td>Views/beliefs perceptions</td>
<td>#</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prevalence/hypothesis generation</td>
<td>#</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Exposed

Not exposed

Exposed

Not exposed

cases (occlusion attribute of interest)

controls (no occlusion attribute)

Population
# Case-Control Study

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

## Disadvantages:
1. Rely on recall or records to determine exposure status
2. Confounders
3. Selection of control groups is difficult
4. Potential bias: recall–, selection–
Characteristics of a poor case–control study:

Fail to:

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

Population

A Cohort of individuals without occlusion attribute of interest

Exposed

(occlusion attribute of interest)

no occlusion attribute

Not exposed

(occlusion attribute of interest)

no occlusion attribute

<table>
<thead>
<tr>
<th>Qualitative</th>
<th>Cross-Sectional</th>
<th>Case Control</th>
<th>Cohort</th>
<th>RCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis</td>
<td></td>
<td></td>
<td>⭐⭐⭐</td>
<td></td>
</tr>
<tr>
<td>Therapy</td>
<td></td>
<td></td>
<td>⭐⭐⭐</td>
<td></td>
</tr>
<tr>
<td>Prognosis</td>
<td></td>
<td></td>
<td>⭐⭐⭐</td>
<td></td>
</tr>
<tr>
<td>Screening</td>
<td></td>
<td></td>
<td>⭐⭐⭐</td>
<td></td>
</tr>
<tr>
<td>Views/beliefs perceptions</td>
<td>⭐⭐⭐</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prevalence/hypothesis generation</td>
<td>⭐⭐⭐</td>
<td>⭐⭐⭐</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Cohort Study

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:

Fail to:

- clearly define comparison groups
- measure exposures and outcomes in the same (preferably blinded), objective way in both exposed and non-exposed individuals
- identify or appropriately control known confounders
- carry out a sufficiently long and complete follow-up of patients
Preparing for a Clinical Study of Dental Occlusion
Why initiate a clinical study?

- (i) previous clinical studies have had conflicting results, been undersized or have demonstrated a difference, which needs clarification.
- (ii) findings in basic or applied research have been consistent and promising and the potential risks of adverse events in humans is considered low.
- (iii) clinical findings from studies having employed a methodologically weaker design, e.g., a case report or a case series, have been promising.
Why initiate a clinical study?

- Whether the focus is on aetiology, diagnosis, prognosis or therapy some study designs are preferable from a study methodological perspective.
- Will need to be considered in light of:
  - the local culture for clinical research
  - available resources and competencies
  - patient accrual availability
  - time and money
Primary investigator responsibilities
½ – consider:

- External clinical research organization (CRO). Protocol design, monitoring body or for other involvements
- How many and which clinical center(s) should become involved. Patient accrual number and/or time
- Face-to-face protocol development and/or calibration meetings
Target patient population with specific inclusion and exclusion criteria

Identify possible threats to patient confidentiality, establish procedures to maintain confidentiality and protocols to follow to adhere to these procedures

Design proper case report forms (CRFs), which in some parts of the world are mandatory and considered as legal documents e.g., Europe
Threats to the Proper Conduct of a Clinical Study
Correct Study Design and Reporting

... is also a question of ethics...
Incorrectly designed studies...

- Misuse patients by exposing them to unjustified risk and inconvenience
- Misuse resources, including the researchers time, which could be better employed on more valuable activities
- Leads to publishing misleading results
- If the results go unchallenged the researchers may use the same inferior study approach in future research, and others may copy them
A science of uncertainty...

How many ways can clinical research be flawed?
Flawed Research

1. Errors in study design
2. Errors in study execution
3. Errors in data analysis
4. Errors in data interpretation
5. Errors in data omission
6. Errors in data presentation
Errors in study design—Flawed Research
1/6

- inferior design
  - opens for investigator bias
  - usually over-optimistic results
  - compounded by publication bias
- pre-existing data is presented as “experimental” (and/or new data)
- choice of study sample – it **must** be representative
- bias of provider/observer
- inadequate sample size
Errors in study execution—Flawed Research 2/6

- Lack of adherence to protocol
- Data missing
- Adherence to Randomization / Allocation
Errors in data analysis – Flawed Research
3/6

- analysis methods if assumptions not met
- analysing paired data ignoring pairing
- failing to take into account ordered categories
- multiple observations on one subject
- multiple paired comparisons
- c.i. include impossible values
- correlation instead of comparison
- correlation of time-related observations
- diagnostic test sensitivity/specificity only
- presenting only subsets of participants
Errors in interpretation — Flawed Research

- P levels are **not** absolute yes/no limits
- P is **not** the probability that the observed effect is due to chance, but the probability of obtaining the observed effect when the null hypothesis test is true. (i.e. when there is **no such differences** in the population)
- P = .001 is **not** a “stronger” effect than P = .01
- Association and causation is **not** synonymous
If important information is lacking in your report the readers will assume that invalid procedures have been used.

Always use a checklist when writing your report!
Errors in presentation — Flawed Research

6/6

- Presenting means without variability
- Solely P value of statistical analyses
- Spurious precision versus no precision
- S.E. or C.I. used for descriptive data
- Graphical presentation tricks, e.g., use of
  - zero on axis -- change of scale in axis --- 3D
  - coincidence in scatterplots – regression without scatter
  - superimposing different scales
Thank you for your kind attention.