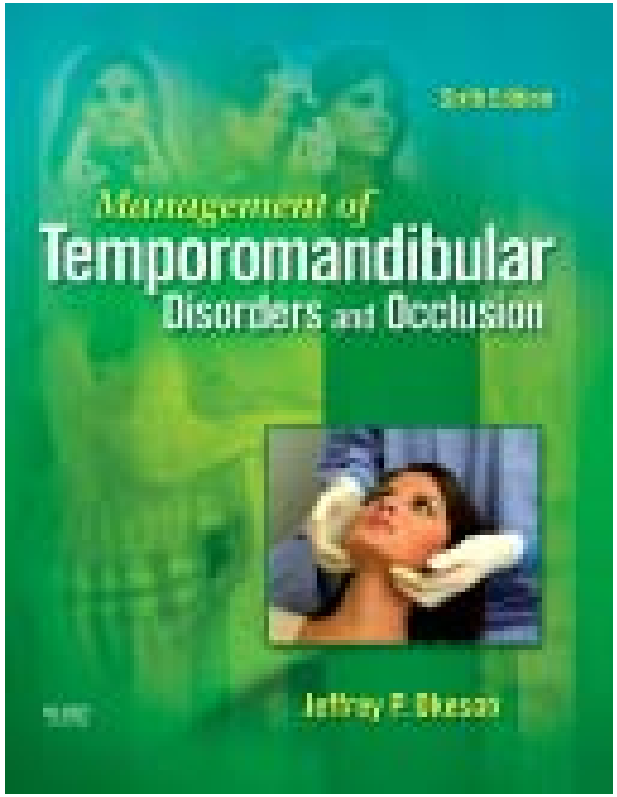
Methodological Challenges in the Study of Dental Occlusion

Asbjørn Jokstad
Professor and Head, Prosthodontics
University of Toronto, Ontario, Canada
a.jokstad@dentistry.utoronto.ca

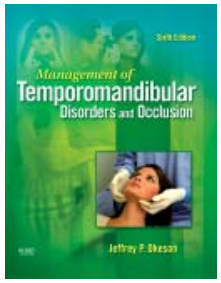
What is Dental Occlusion?

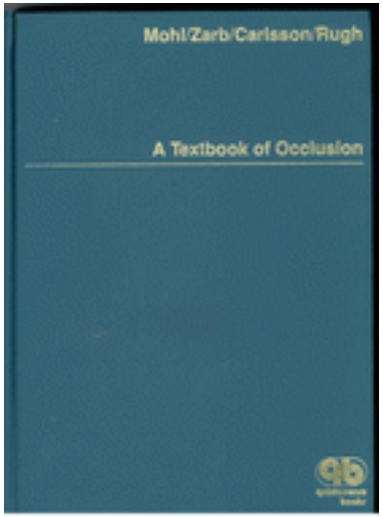
Occlusion: interpretations of the term



JP Okeson (2008) p58: "*The static relationship of the teeth*"

Occlusion: interpretations of the term



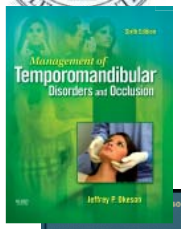


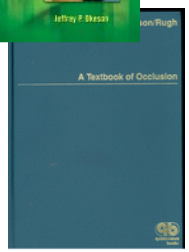
Okeson (2008) : "*The static relationship of the teeth*"

versus

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





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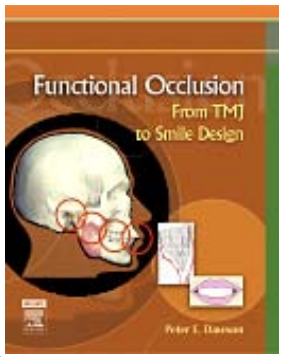
– versus

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*"



Ref. Pokorny ea JPD 2008

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)

Consequence: risk of semantic confusion

A Definition of Prosthetic Dentistry

Asbjørn Jokstad, DDS, Dr Odont[a]
Jon Ørstavik, DDS, Dr Odont[b]
Tore Ramstad, DDS[c]

Purpose: A more precise and up-to-date definition of prosthetic dentistry is warranted. The aim o the present review is to present a new core definition of the discipline on the basis of a discussio of existing definitions. **Materials and Methods:** Clinical textbooks in prosthetic dentistry and dent 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 t technologic aspects of the discipline, ie, the fabrication of prostheses; and second, definitions tha incorporated some reference to the objectives or aims of prosthetic t one or more aspects of oral function. Slightly more than half of the d related references, and this aspect tended to be most pronounced in **Conclusion:** The following definition is ventured: prosthodontics is t concerned with the consequences of congenital absence or acquire the methods for and assessment whether more good than harm is do devices made from alloplastic materials. *Int J Prosthodont 1998;11:2*

Point : Counterpoint

Harrel, Nunn & Hallmon versus Deas & Mealey.

J Am Dent Assoc 2006; 137: 1380-1385.

Is there an association between occlusion and periodontal destruction?

Yes—occlusal forces can contribute to periodontal destruction.

Stephen K. Harrel, DDS; Martha E. Nunn, DDS, PhD; William W. Hallmon, DMD, MS

Controversy over the relationship between occlusion and progression of periodontal destruction has been ongoing since the beginning of scientific studies of dental diseases. This controversy often has been heated. Some respected researchers have stated strongly that occlusal forces are a major factor in periodontal destructions and that treatment of occlusal forces is a major part of the successful treatment of periodontal disease. Other equally respected researchers have stated just as strongly that there is no relationship between occlusal forces and periodontal destruction and that there is little justification for occlusal treatment as a routine part of periodontal therapy.

There is evidence that the treatment of occlusal discrepancies should be considered an integral part of the overall treatment of periodontal disease.

This article presents a brief review of the literature concerning the relationship between periodontal disease and occlusal forces. Additionally, we will review recent research we have performed and compare it with past research findings. We also will discuss our conclusion that occlusal discrepancies are a significant risk factor for the progression of periodontal disease and our reasoning for suggesting that treatment of occlusal discrepancies should be a routine part of periodontal therapy.

HISTORICAL STUDIES

For more than a century, clinicians have postulated that a relationship existed between occlusal forces and the progression of periodontal disease. Karolyi,[1] in the early 20th century, was one of the first to publish on the relationship of occlusion to periodontal disease. He indicated that teeth undergoing excessive occlusal stress seemed to have more periodontal destruction than did teeth not experiencing occlusal stress. Also in the early 20th century, Stillman, one of the early pioneers of periodontal therapy, presented the proposition that excessive occlusal stress was the cause of periodontal disease. Stillman indicated that to treat periodontal disease successfully, the clinician must control occlusal forces.[2,3] Stillman's comments led to several studies aimed at determining whether occlusion did or did not play a causative role in periodontal disease.[4-6] These studies failed to produce conclusive results, and the controversy continued.

In the 1940s, Weinmann[7] published one of the first studies to evaluate the relationship of occlusion and periodontal disease at a cellular level. On the basis of his observations of human autopsy material, he felt that periodontal disease was related to progression of an inflammatory process that began at the gingival attachment and spread

Dr. Harrel maintains a private practice specializing in periodontics in Dallas. He also is an adjunct professor, Department of Periodontology, Baylor College of Dentistry, The Texas A&M University Health Science Center, Dallas. Address reprint requests to Dr. Harrel at 10346 Midway Rd., #101, Dallas, Texas 75229, e-mail "skh1@airmail.net".

Dr. Nunn is an associate professor, Department of Health Policy and Health Services Research, Goldman School of Dental Medicine, Boston University.

Dr. Hallmon is a professor and the chairman, Department of Periodontology, Baylor College of Dentistry, The Texas A&M University Health Science Center, Dallas.

and periodontal destruction?

Only in limited circumstances does occlusal force contribute to periodontal disease progression.

David E. Deas, DMD, MS;
Brian L. Mealey, DDS, MS

Examining the long-standing controversy about the role of occlusion in periodontal disease is a delightful look back at more than 100 years of periodontal theory and practice. The list of authors who have written on this topic in the past century reads like a "Who's Who" of some of the brightest minds in dentistry, and the debate has endured through several defined eras in the history of the specialty of periodontics. From the days when periodontics was dominated by those initially trained as pathologists, through the period when the specialty was led by master clinicians headquartered at certain universities, through an era characterized by meticulously controlled human and animal studies conducted both in the United States and abroad, up to the current period of evidence-based therapy, the debate has persisted. It is a reminder that even in this modern era, dentistry still is very much an art as well as a science.

Treatment of occlusal trauma should be directed toward the specific instances in which occlusal trauma truly exists.

Like most long-standing controversies, the debate about occlusion and periodontal disease has narrowed considerably over the years. For example, no one now believes that excessive occlusal force initiates periodontitis, nor does any credible person believe that occlusal force is incapable of causing periodontal injury. As the edges of the debate have been nibbled away over time, the crux of the remaining argument is this: Can occlusal forces exacerbate the progression of periodontitis, and is eliminating occlusal discrepancies appropriate or necessary in the treatment of the disease?

The purpose of this article is to outline the clinical and histological response of the periodontium to excessive occlusal force, to review the clinical studies that have examined the relationship between occlusion and periodontitis, and to reiterate a rational approach to managing occlusion within the context of periodontal therapy.

THE OCCLUSAL TRAUMA LESION

The term "occlusal trauma" (or "trauma resulting from occlusion") refers to the pathological or adaptive changes to the periodontium caused by the excessive occlusal force known as "traumatogenic occlusion."[8] Occlusal trauma, then, is an injury to the periodontium; traumatogenic occlusion is the etiologic factor causing the injury.

Similar in some respects to the tissue response to orthodontic forces, traumatogenic occlusion establishes distinct zones of tension and pressure within the periodontal ligament of the affected tooth. The location of these zones depends on the location and vector of the force, as well as on the

Dr. Deas is the chief of periodontics, 40th Medical Group, RAF Lakenheath, Lakenheath, England. He formerly was the director of clinical periodontics, U.S. Air Force Periodontics Residency, Wilford Hall Medical Center, Lackland Air Force Base, Texas. Address reprint requests to Dr. Deas at RAF Lakenheath, UK, PSC 41 Box 272, APO AE 09464 e-mail "David.Deas@lakenheath.af.mil".

Dr. Mealey is the graduate program director and director, Specialist Division, Department of Periodontics, University of Texas Health Science Center at San Antonio.

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

Subjective measurement?
Objective measurement?

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

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

Conceptual depiction of dental occlusion research defined within a framework of three dimensions

Forms & Positions

Subjective measurement?
Objective measurement?

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

(Oral) Functions, e.g.,

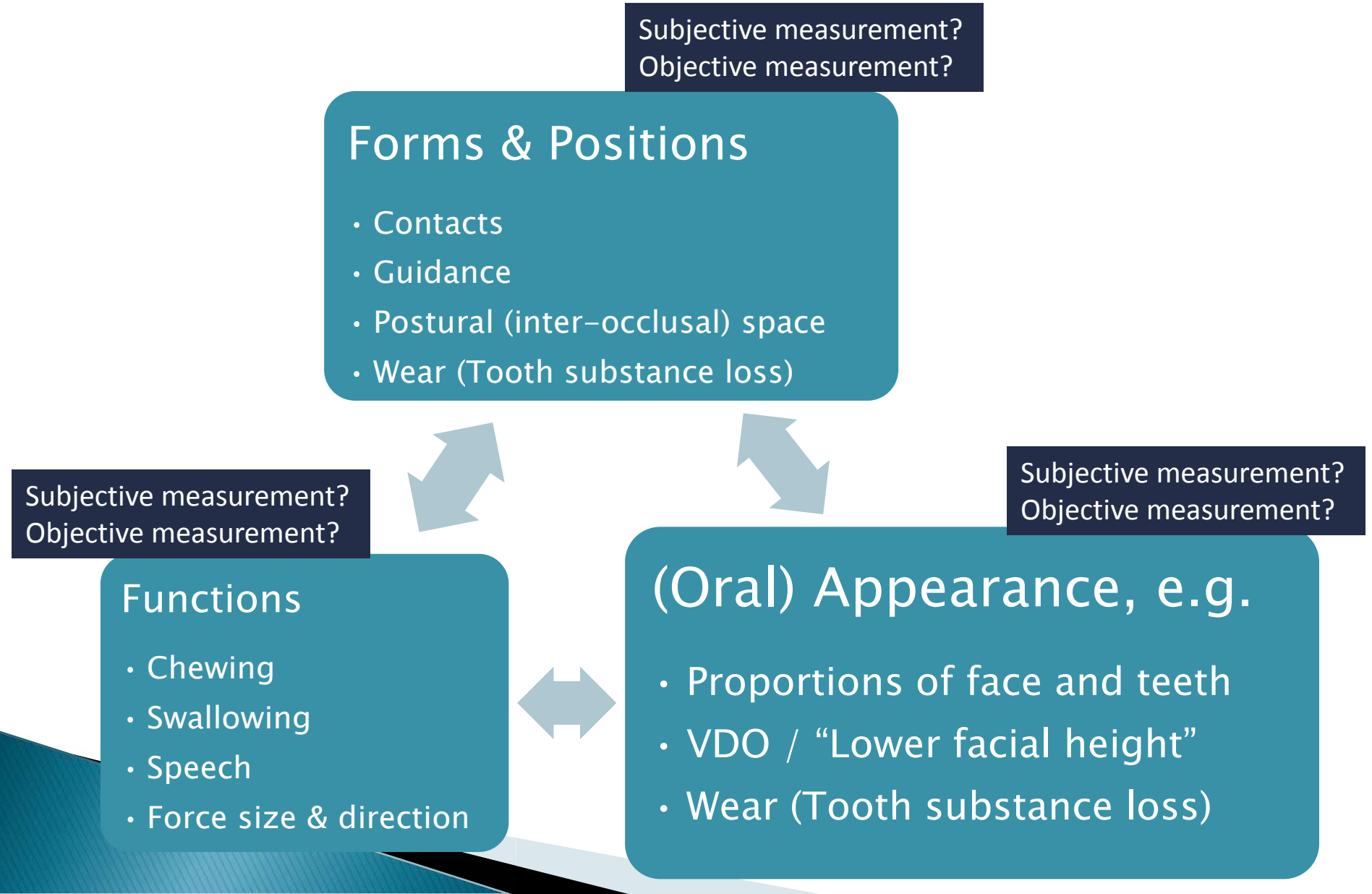
Subjective measurement?
Objective measurement?

- Chewing
- Swallowing
- Speech
- Force size & direction

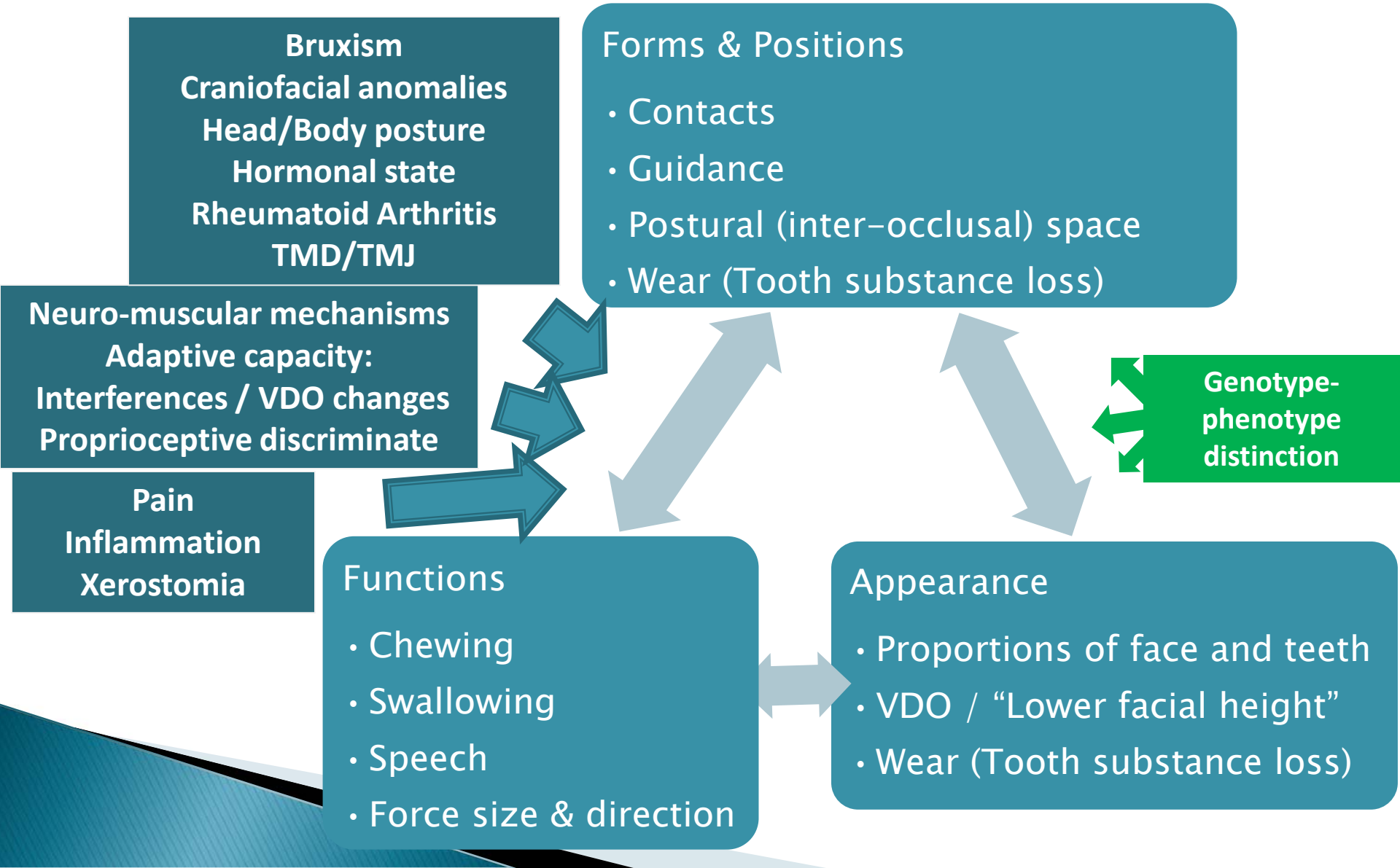
[CORE: Pullinger]

[CORE: Wang]

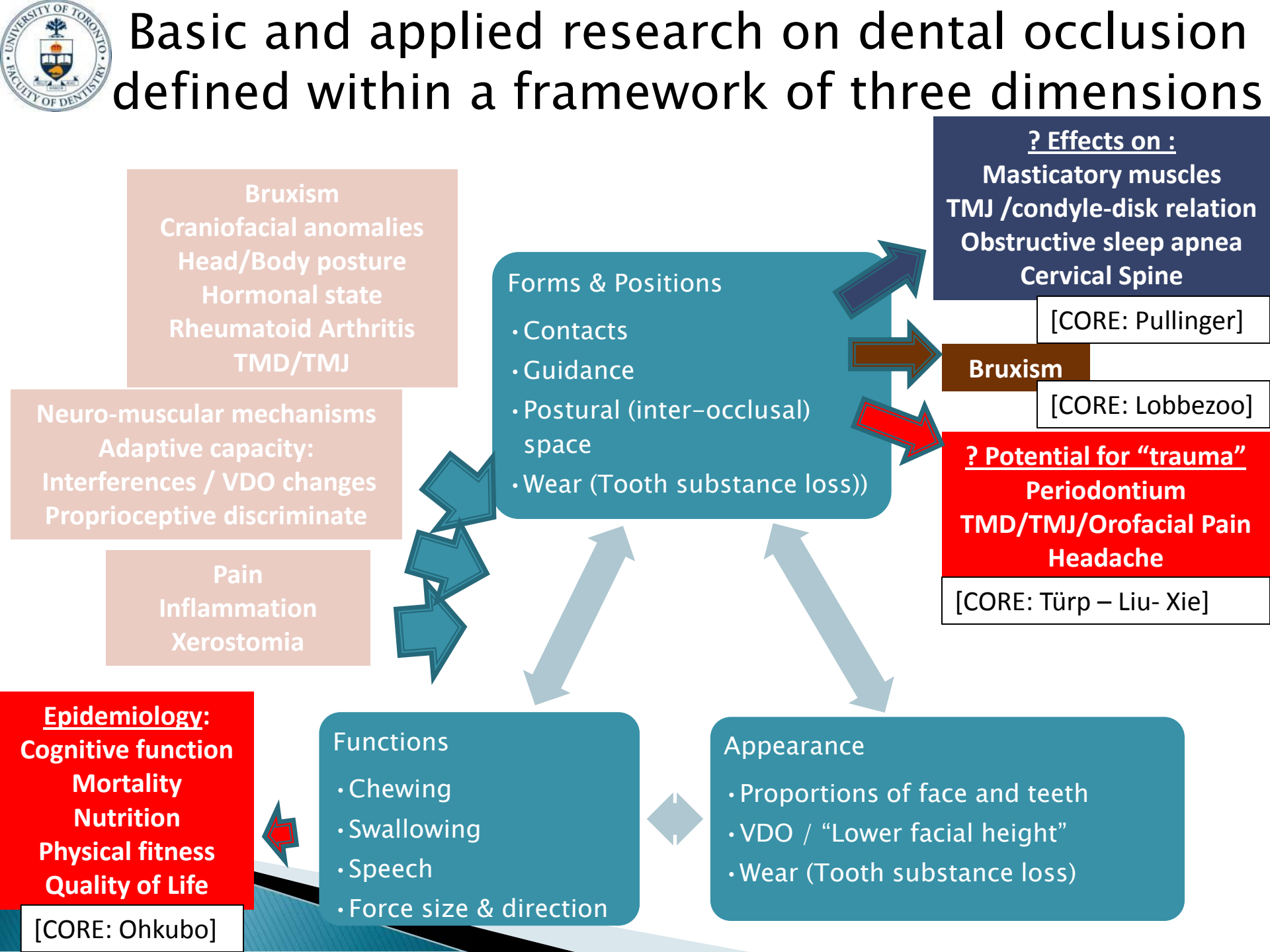
Conceptual depiction of dental occlusion research defined within a framework of three dimensions



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



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



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

Change/Restore Occlusion

- **Partnership with patient**
- **Patient expectations**
  - **Self-esteem**
  - **Psycho-social needs**
  - **Comfort**
  - **Physiological needs**
  - **Aesthetic requirements**

Subjective measurement?
Objective measurement?

Forms & Positions

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

"Phantom bite"

"Pathological wear"

"Malposition" a causal risk factor?:
- Caries
- Periodontology
- Wear
- TMD/TMJ
- Occlusal Stability

Aetiology: Friction +/- corrosion

Subjective measurement?
Objective measurement?

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

Functions

- Chewing
- Swallowing
- Speech
- Force size & direction

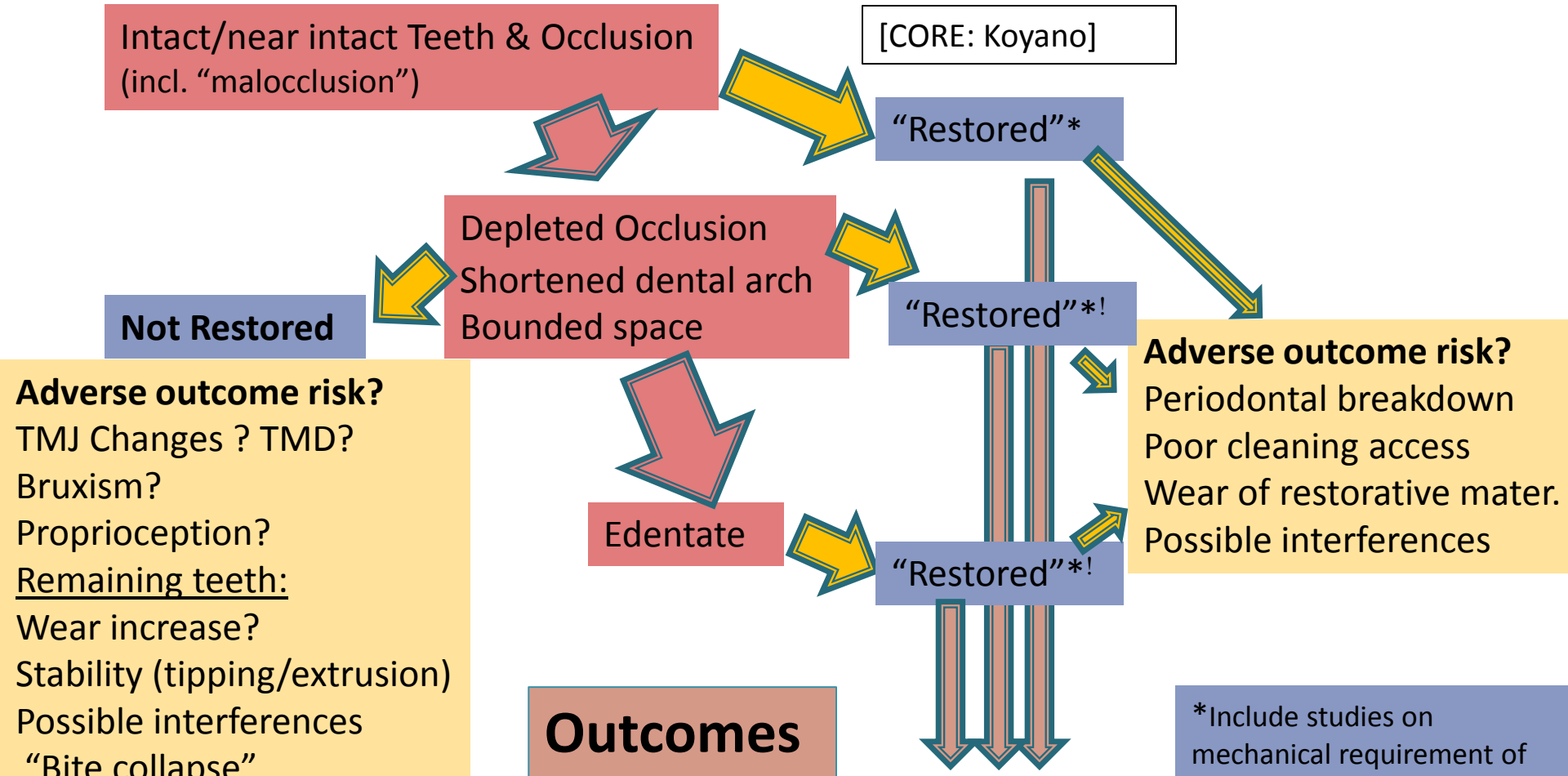
Appearance

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

Subjective measurement?
Objective measurement?

Psychosocial value
Quality of Life
Societal determinants

Research relevant to restorative management of dental occlusion



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

! Occlusion on implants introduces additional research issues

[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)

Research using scientific methods

- 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]

	Diagnosis	Prognosis	Therapy	Aetiology
Narrow search	0	16	15	15
Broad search	231	115	131	340

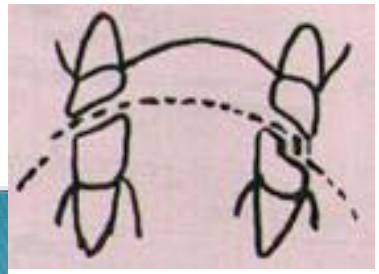
(Search August, 2011)

Why is Aetiology the most prevalent?

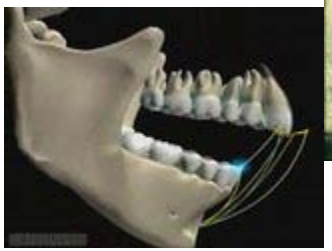
- It is more difficult to falsify a hypothesis about aetiology compared to other research issues – if using a hypothetico-deductive scientific research model
- A hypothesis must be falsifiable in order to qualify as being scientific
- The literature abounds with idea and theories that are <u>not scientific</u> and hence, refutable by proper research, however well undertaken

Excellent Textbook: Goodman & Putnam (2006) *Fact, Fiction, and Forecast*

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

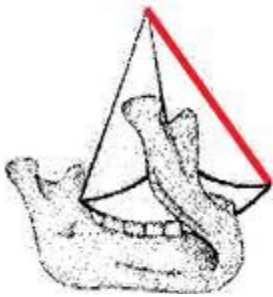


Monson curve



Posselt's path (banana)

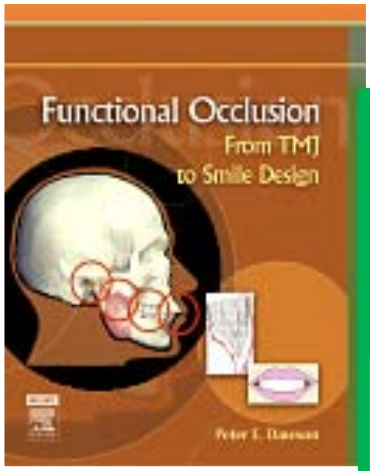
Angle's "Old Glory"

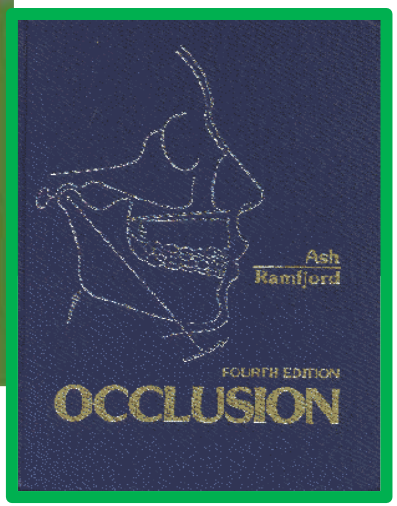


Bonwill's triangle

Dogmas in occlusion derived from deductive logic

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

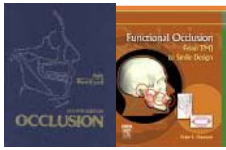




Refs: Schuyler (1935-1963), Beyron (1944-1969), Pankey (1948-1980), Ramfjord (1970-1994), Dawson (1980-2010)

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…



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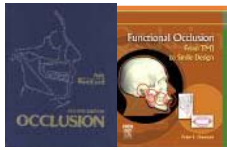

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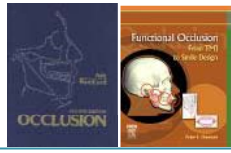
- Anterior teeth should contact and disclude the posterior teeth upon eccentrical movement…
- In the upright head position the posterior teeth should contact more prominently than the anterior tooth contacts …



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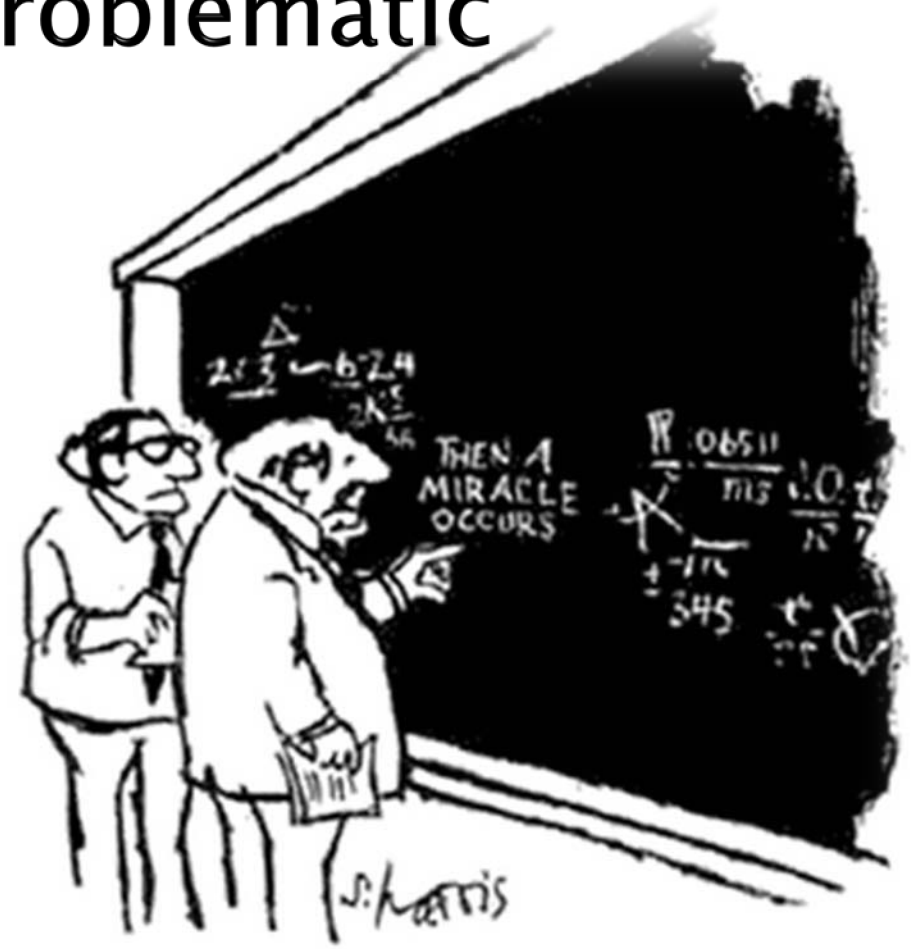
- Articular disks properly interposed between the condyles and the fossae…
- Even and simultaneous contact of posterior teeth in CR..
- Anterior teeth should contact and disclude the posterior teeth upon eccentrical movement…
- In the upright head position the posterior teeth should contact more prominently than the anterior tooth contacts
- Provide the most shallow anterior guidance patterns that disclude posterior teeth… etc. etc.

Refs: Schuyler (1935-1963), Beyron (1944-1969), Pankey (1948-1980), Ramfjord (1970-1994), Dawson (1980-2010) ++

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



Study Design Appropriateness

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

Study Design appropriateness

- 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 & Axelsson 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

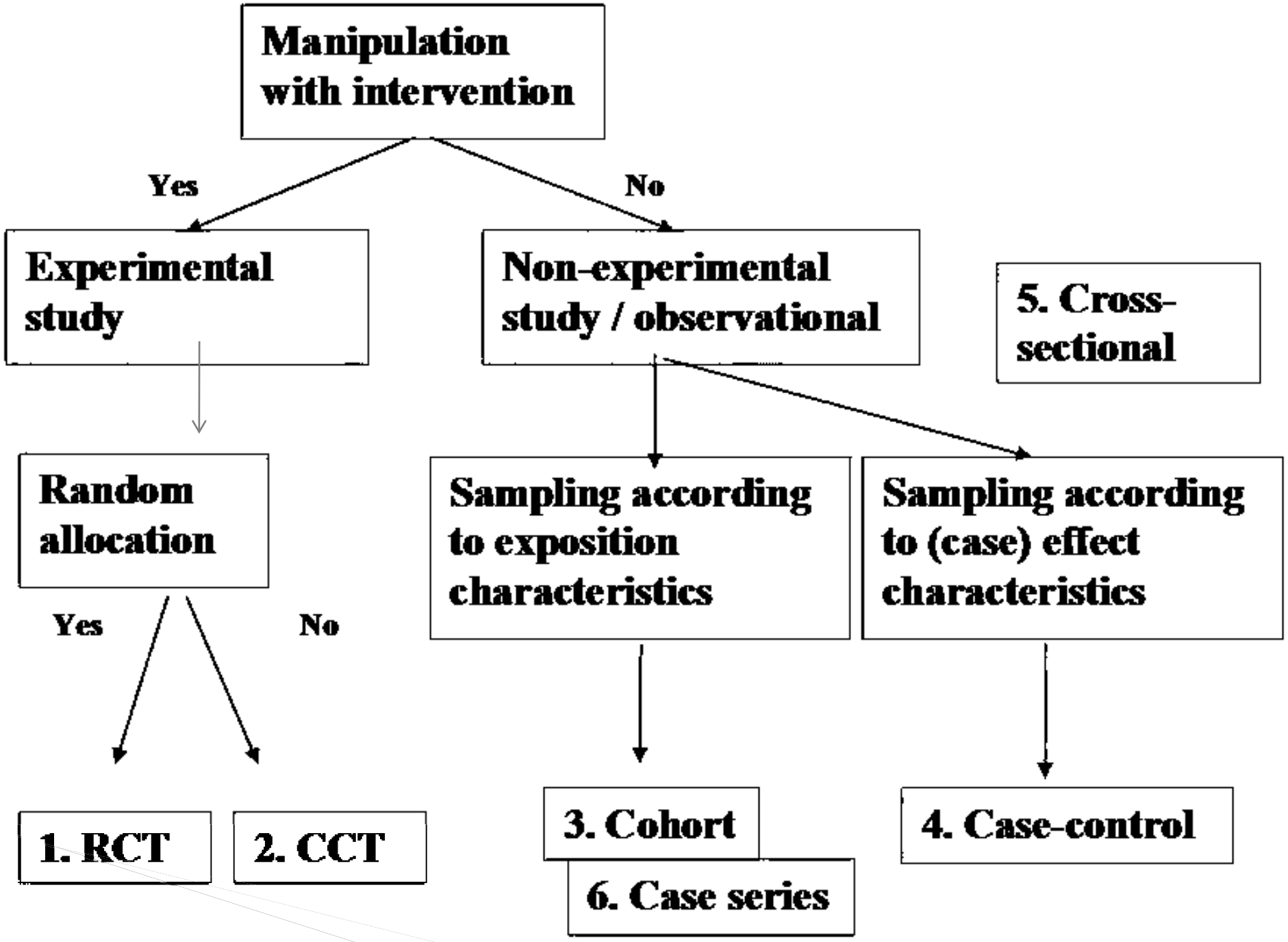
Characteristics of Biomedical Research & Clinical Research

Clinical trial terminology – perplexity → MESH terms

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

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)


Manipulation with intervention
Yes
No
Experimental study
Non-experimental study / observational
5. Cross-sectional
Random allocation
Yes
No
Sampling according to exposition characteristics
Sampling according to (case) effect characteristics
1. RCT
2. CCT
3. Cohort
6. Case series
4. Case-control

Study designs suitable for appraising:

- Diagnostic tests
- Prognosis
- Therapy
- Aetiology

Occlusion and type of research

Diagnosis	**What are the merits of using T-Scan to determine the extent and severity of occlusal interferences?**
Therapy	**Which restorative occlusion scheme / education strategy is the best on implant restorations?**
Prognosis	**What will develop due to (or following introduction of) occlusal interferences?**
Screening	**How many patients have occlusal interferences upon mediotrusion?**
Views/ Beliefs/ Perceptions	**How do occlusal interferences impact on the patient's daily life?**
Prevalence / Hypothesis generation	**How many patients have experienced occlusal interferences?**

Appropriate Study Designs

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

Diagnostic tests

Diagnostic tests, Differential diagnosis

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

  - <u>CHARACTERISTICS OF THE TEST</u>

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

<u>Relevant when you know the prevalence of the disease in the population.</u>

<u>NOT CHARACTERISTICS OF THE TEST BUT OF APPLICABILITY IN PARTICULAR POPULATIONS</u>

Prognosis

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.

Therapy

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

**Clinical, patient centred, surrogate or societal*

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

Randomised Controlled Trial – RCT

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

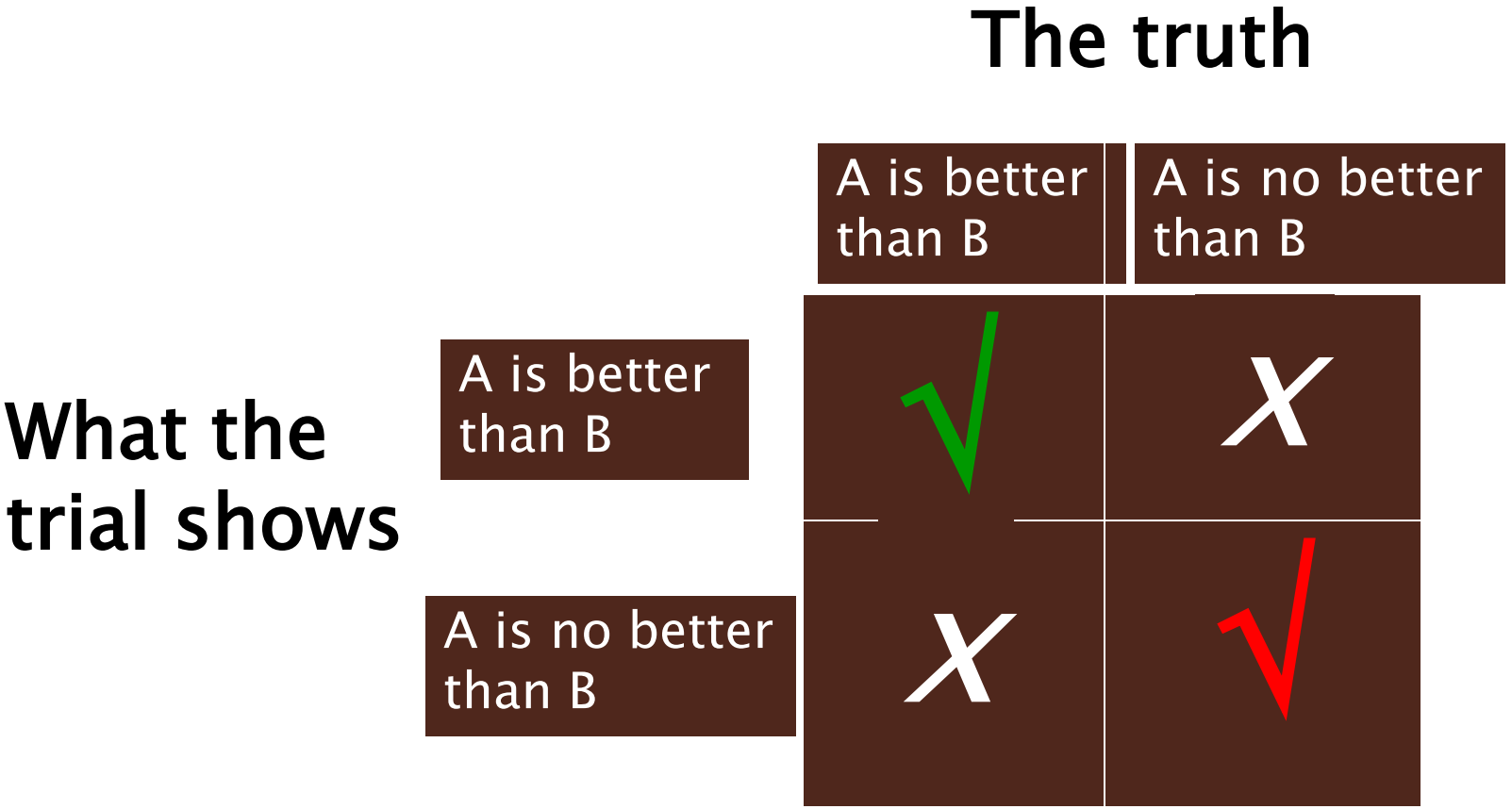
Advantages

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

Disadvantages

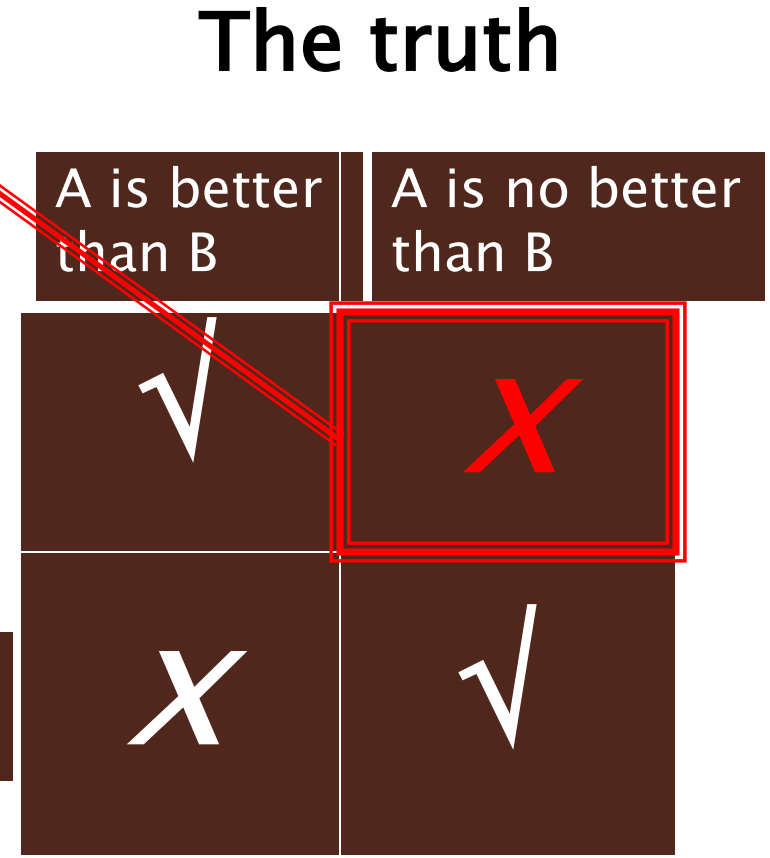
1. Size, time and money – Expensive!
2. Volunteer bias
3. Ethically problematic at times

What can you show with a trial?



What can you show with a trial?

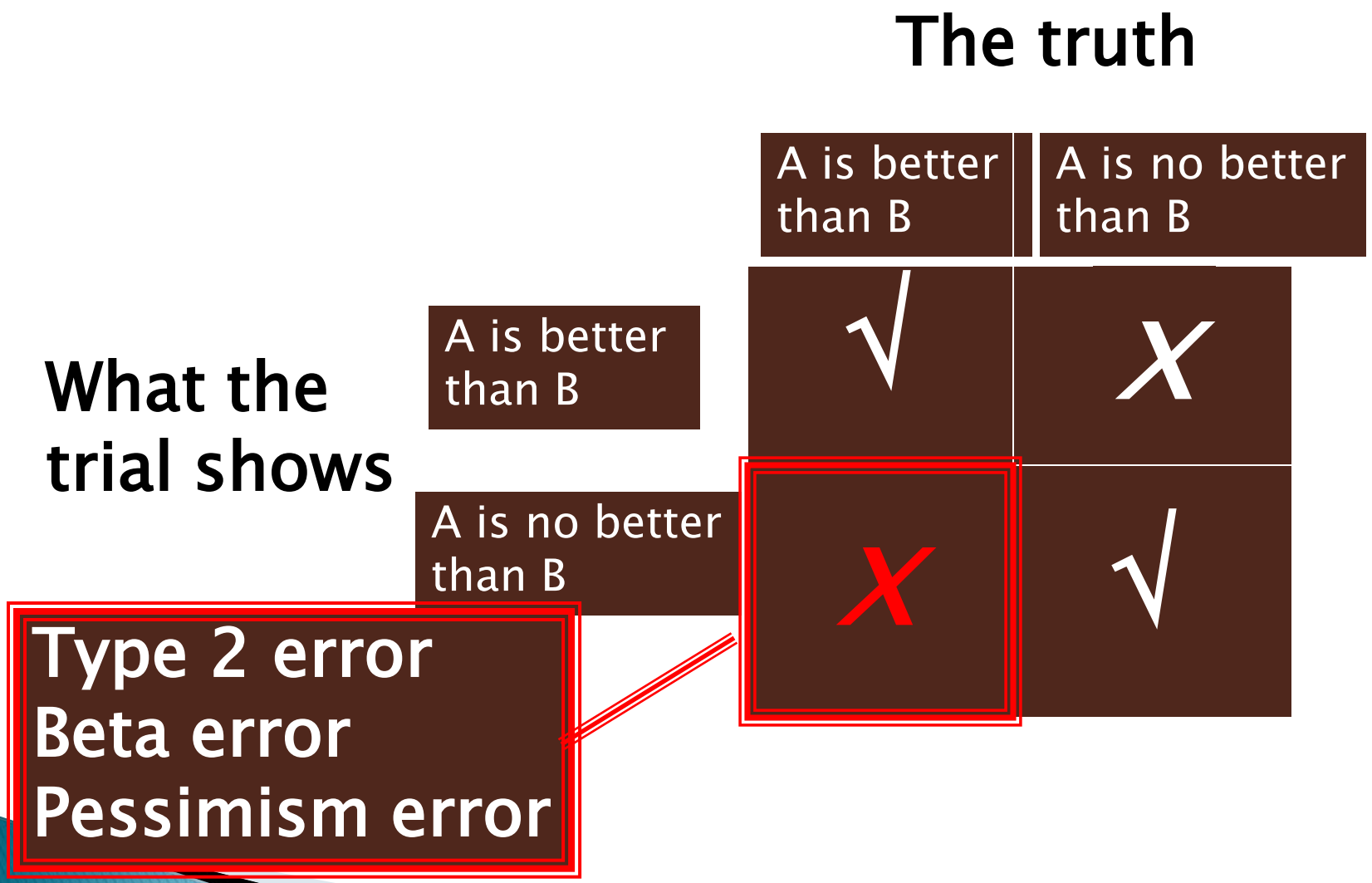
Type 1 error
Alfa error
Optimism error



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?



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

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

Advantages

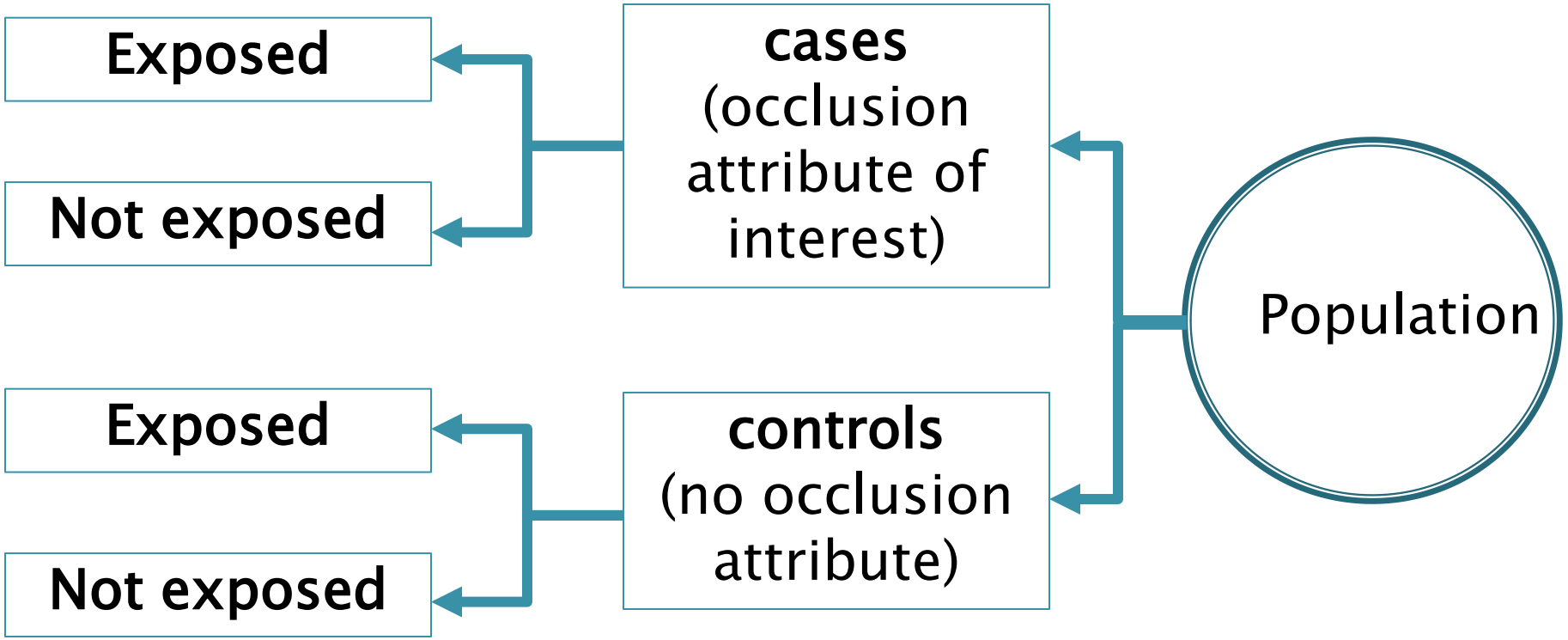
1. Cheap and simple
2. Ethically safe

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

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



Case-Control Study

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

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:

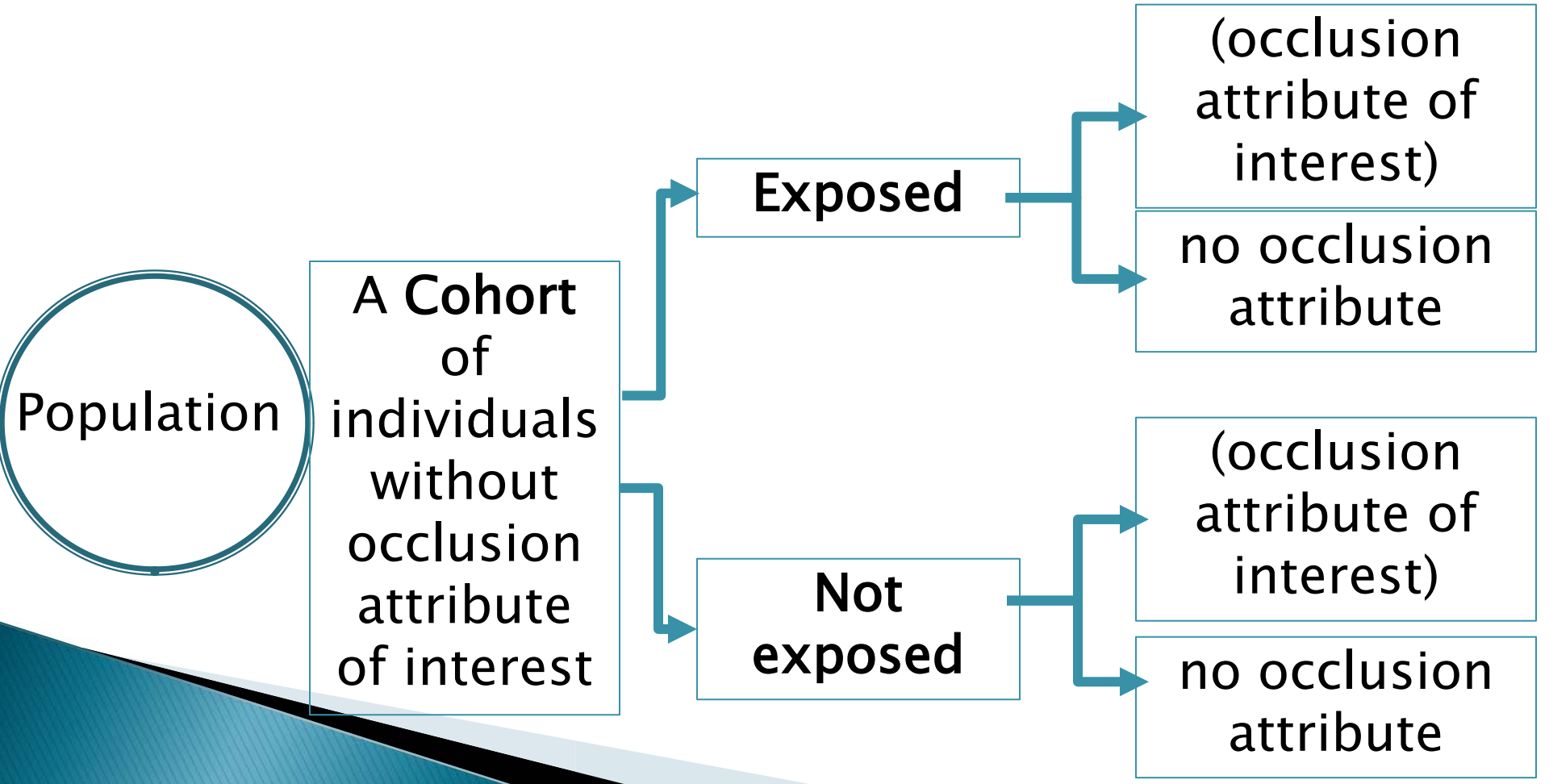
	Qualitative	Cross-Sectional	Case Control	Cohort	RCT
Diagnosis				☆	☆☆
Therapy				☆	☆☆
Prognosis				☆☆☆	
Screening			☆	☆	☆☆
Views/beliefs perceptions	☆☆☆				
Prevalence/ hypothesis generation	☆☆☆	☆☆☆			

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

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



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
- 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

Primary investigator responsibilities

- 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

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 4/6

- 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

Errors in omission –Flawed Research 5/6

- 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

a.jokstad@dentistry.utoronto.ca