Patient Preferences and Study Designs of Clinical Trials in Dentistry

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Prosthetic and Restorative (elective) dental care

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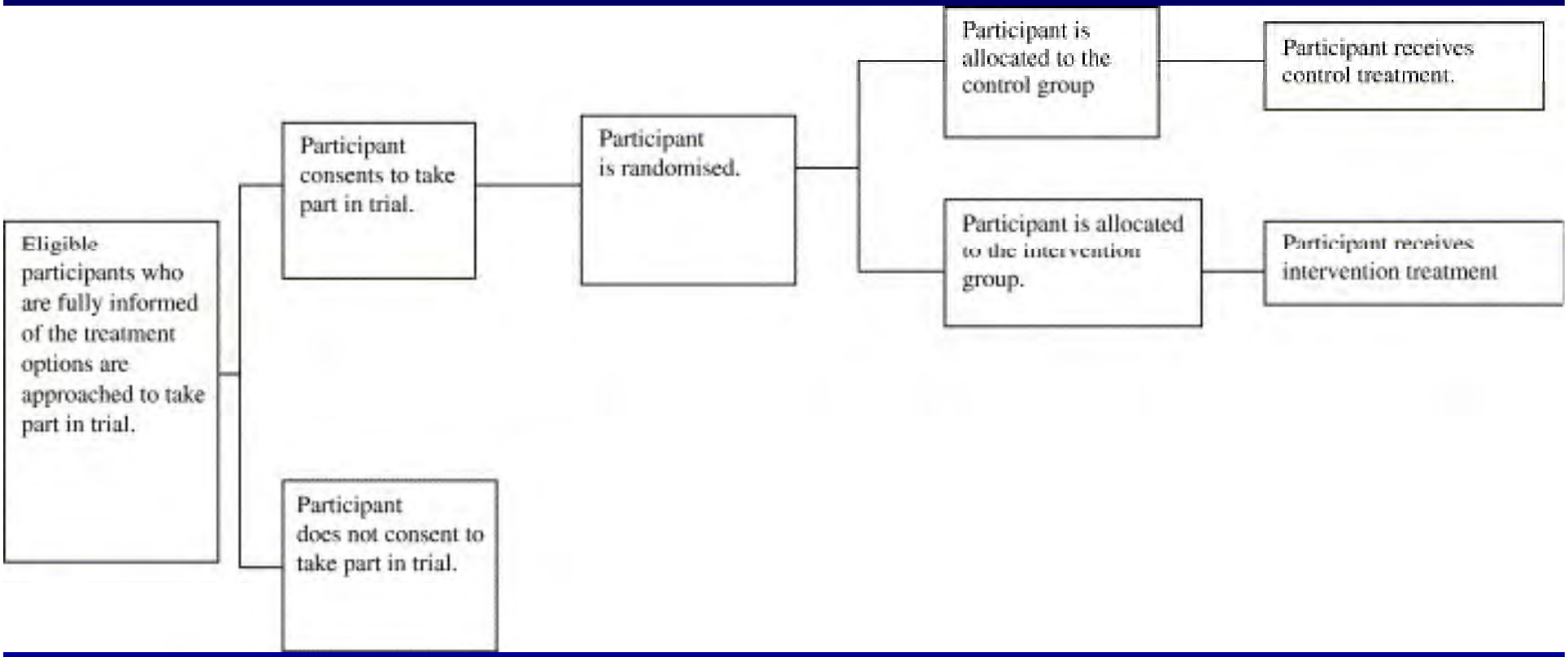
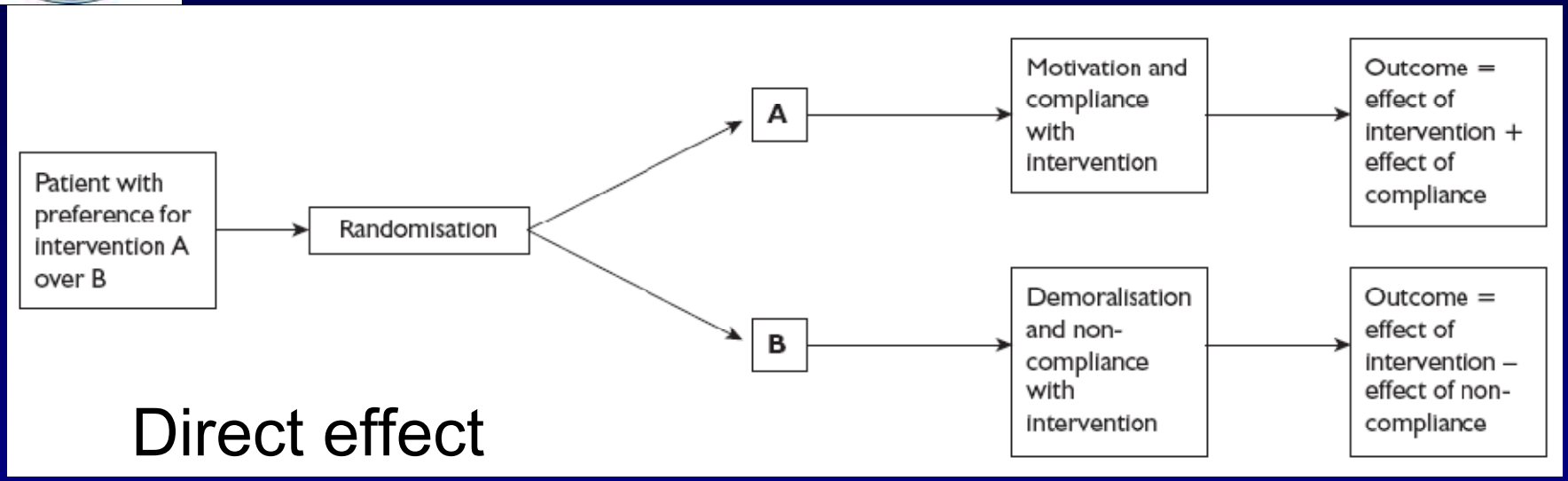


Prosthetic and Restorative (elective) dental care

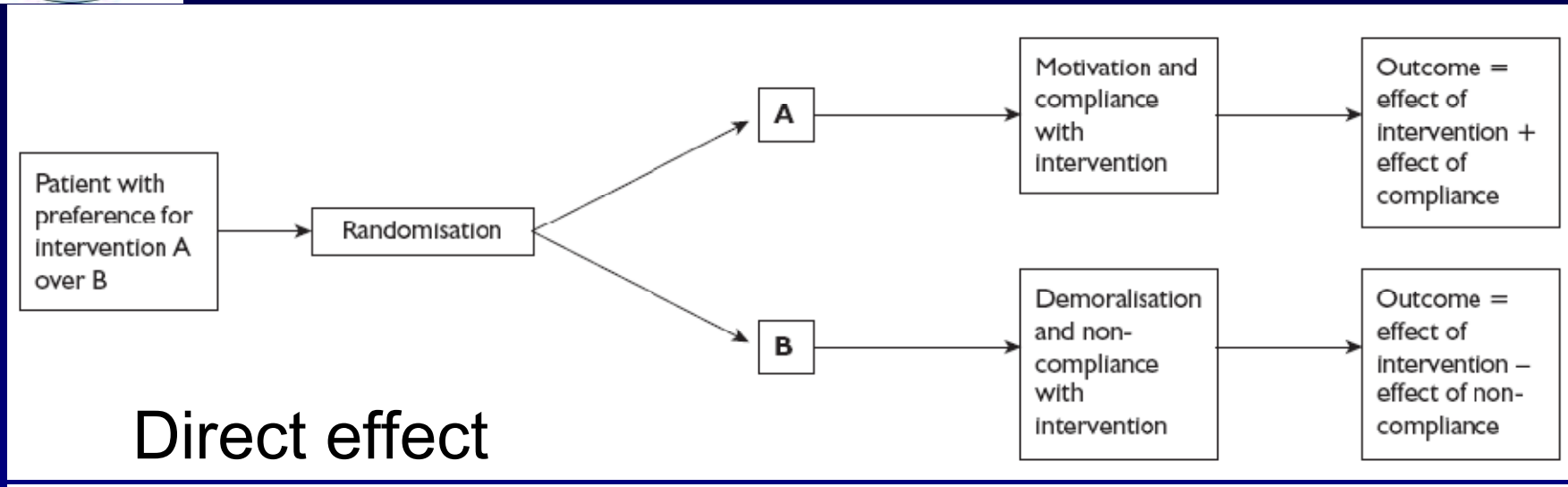
1. RCTs are the preferred study design to compare effectiveness of interventions
2. RCTs are prone to bias if strong participant and/or clinician preferences – INTERNAL VALIDITY

RCTs and possible effects of patient preferences on outcomes



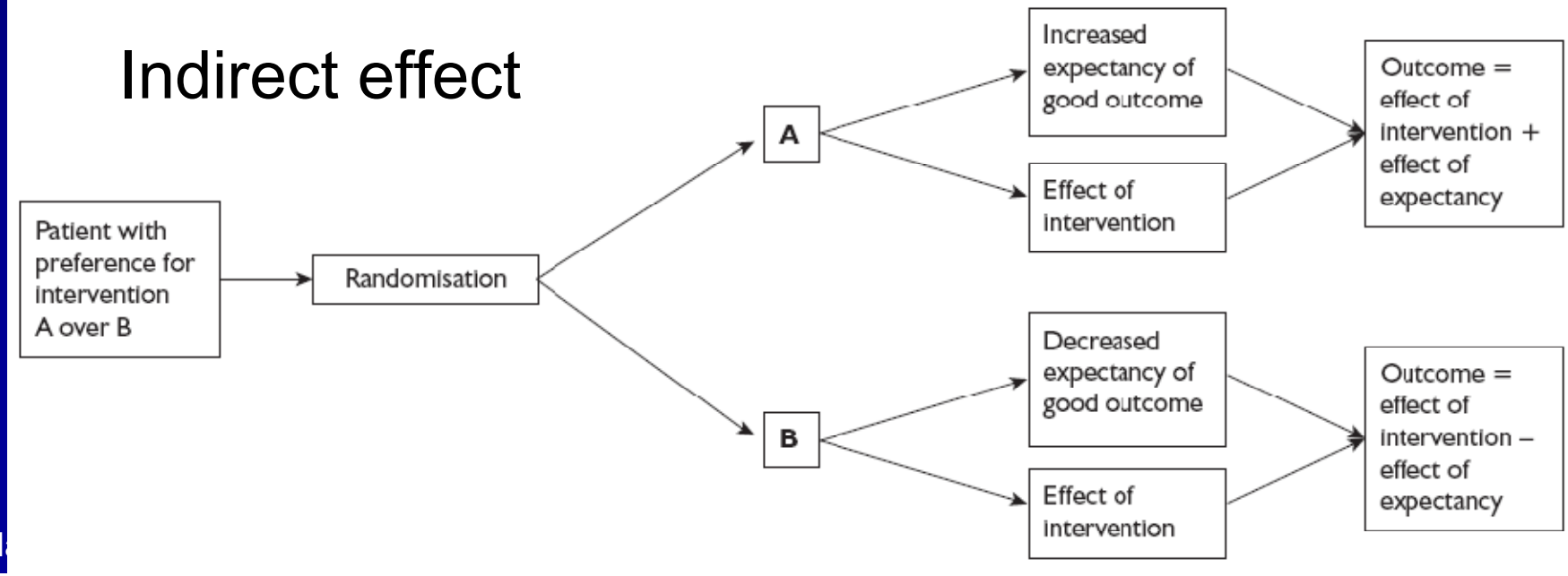
Direct effect

RCTs and possible effects of patient preferences on outcomes



Direct effect

Indirect effect



Prosthetic and Restorative (elective) dental care

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2. RCTs are prone to bias if strong participant and/or clinician preferences – INTERNAL VALIDITY
3. Participants in stringently controlled clinical studies are prone to *selection bias*
4. There are clear differences between individuals with preferences and those with no strong preferences. E.g. by levels of education, socio-economy and in the pre-treatment state – EXTERNAL VALIDITY

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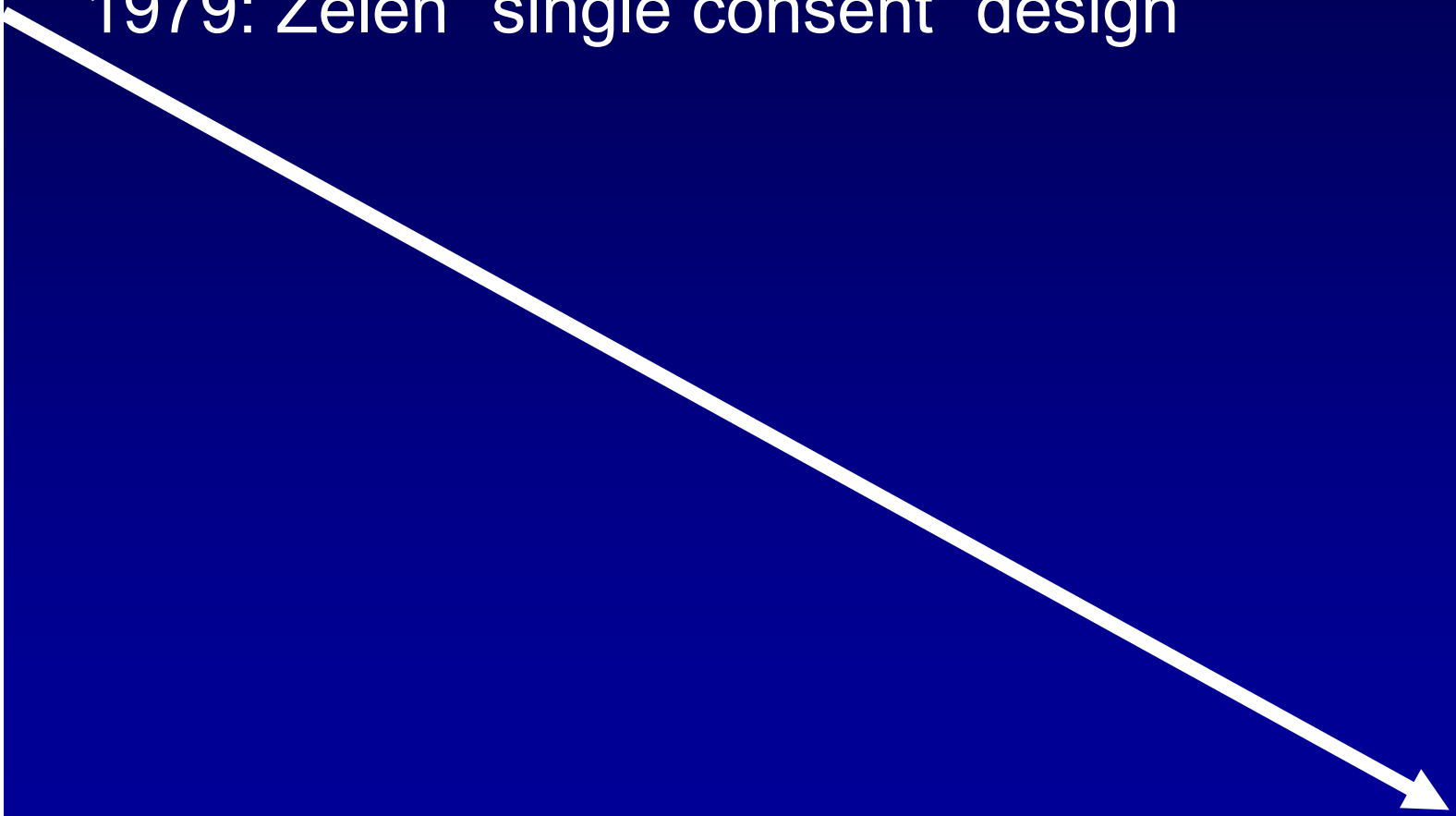
5. Trials taking patient preferences into account provide, in theory, more reliable indicators of patient-centered outcomes than ordinary RCTs

RCT study designs that take patient preferences into consideration

1979: Zelen “single consent” design



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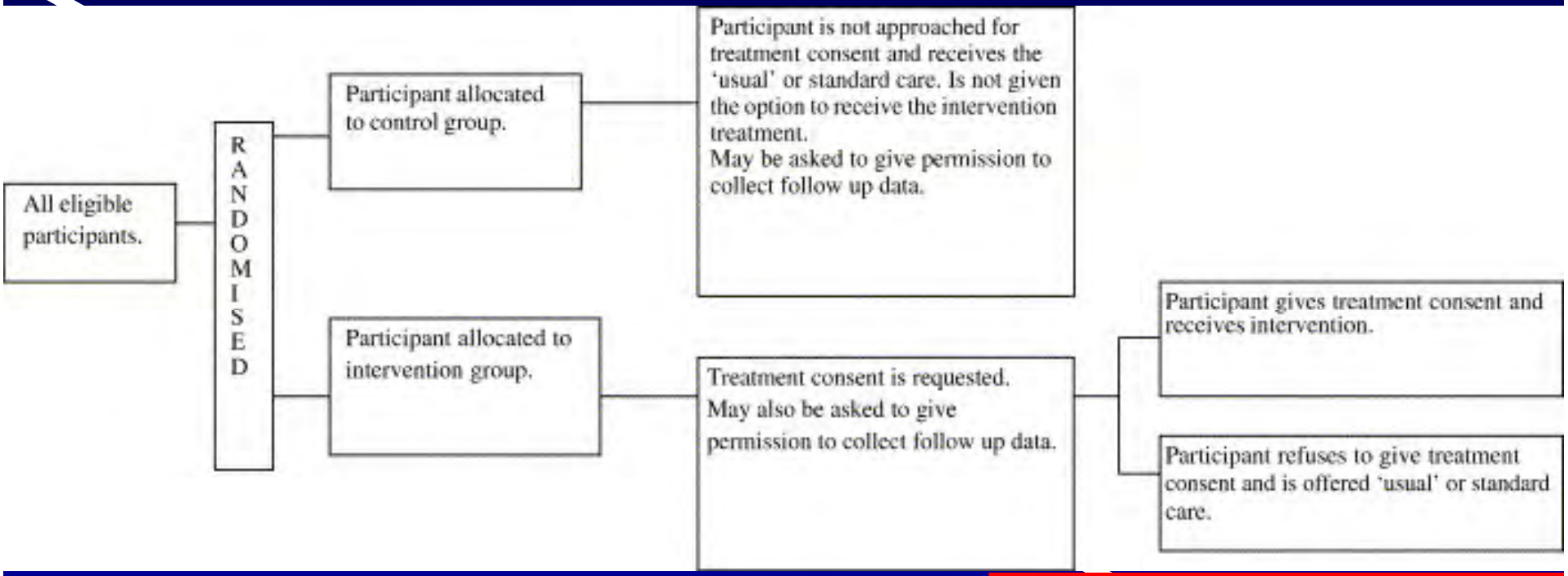

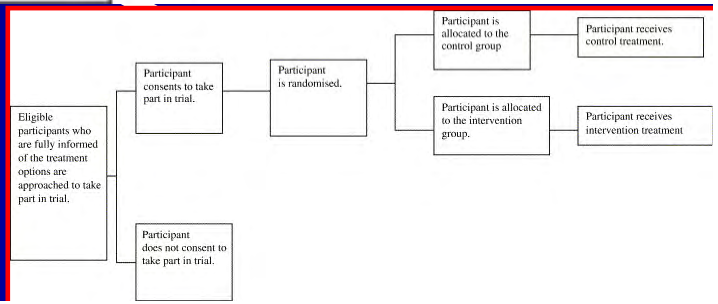

Zelen design

Zelen M. A new design for randomized controlled trials. New Engl J Med 1979; 300: 1242-45.

AKAs: (or Zelen's…)

- Zelen randomized consent design
- Zelen randomized single consent design
- (Zelen) pre-randomization design
- (Zelen) post-randomized consent design

Problems: Ethics: no consent to randomization & data collection, power, routine outcome measures

Fields: Psychiatry, neonatal medicine, addiction, experimental interventions

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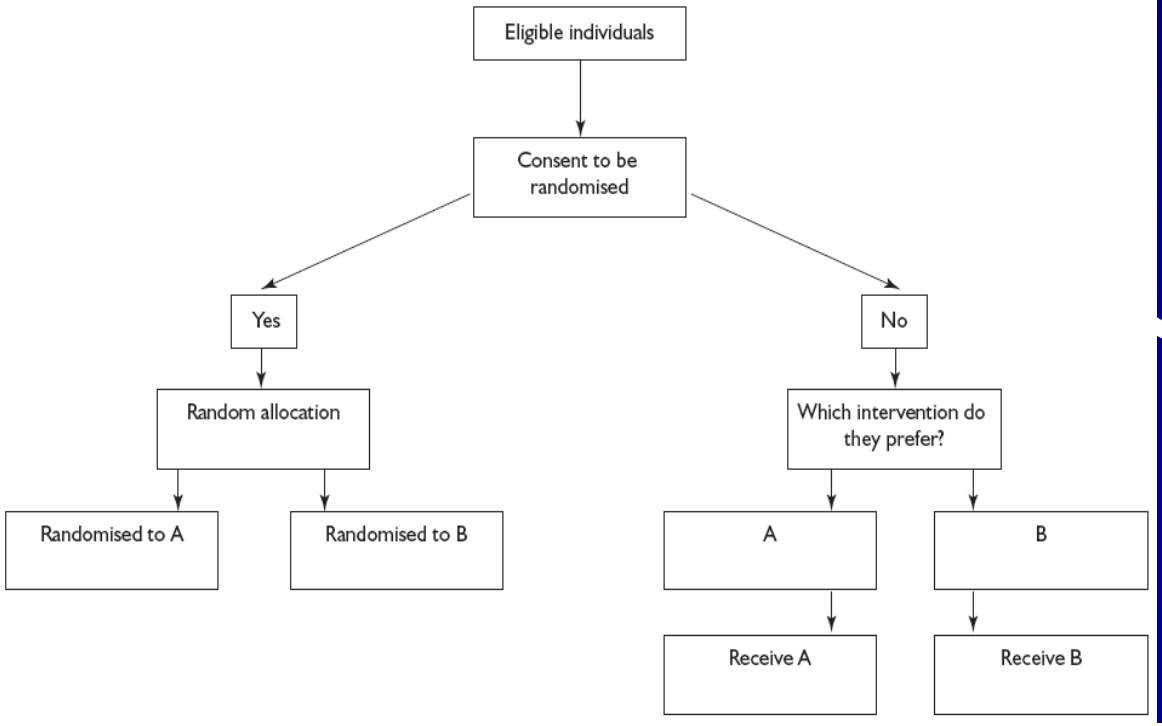

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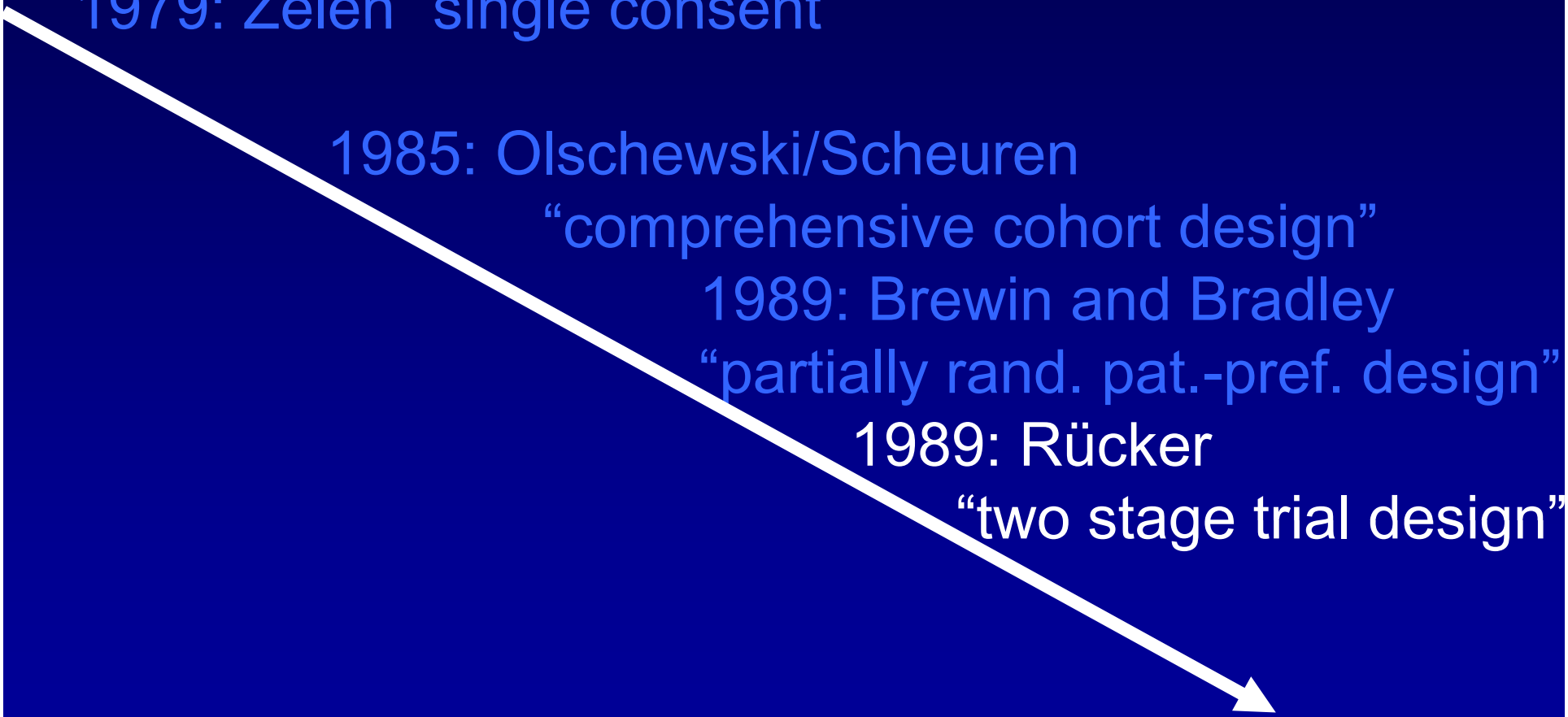

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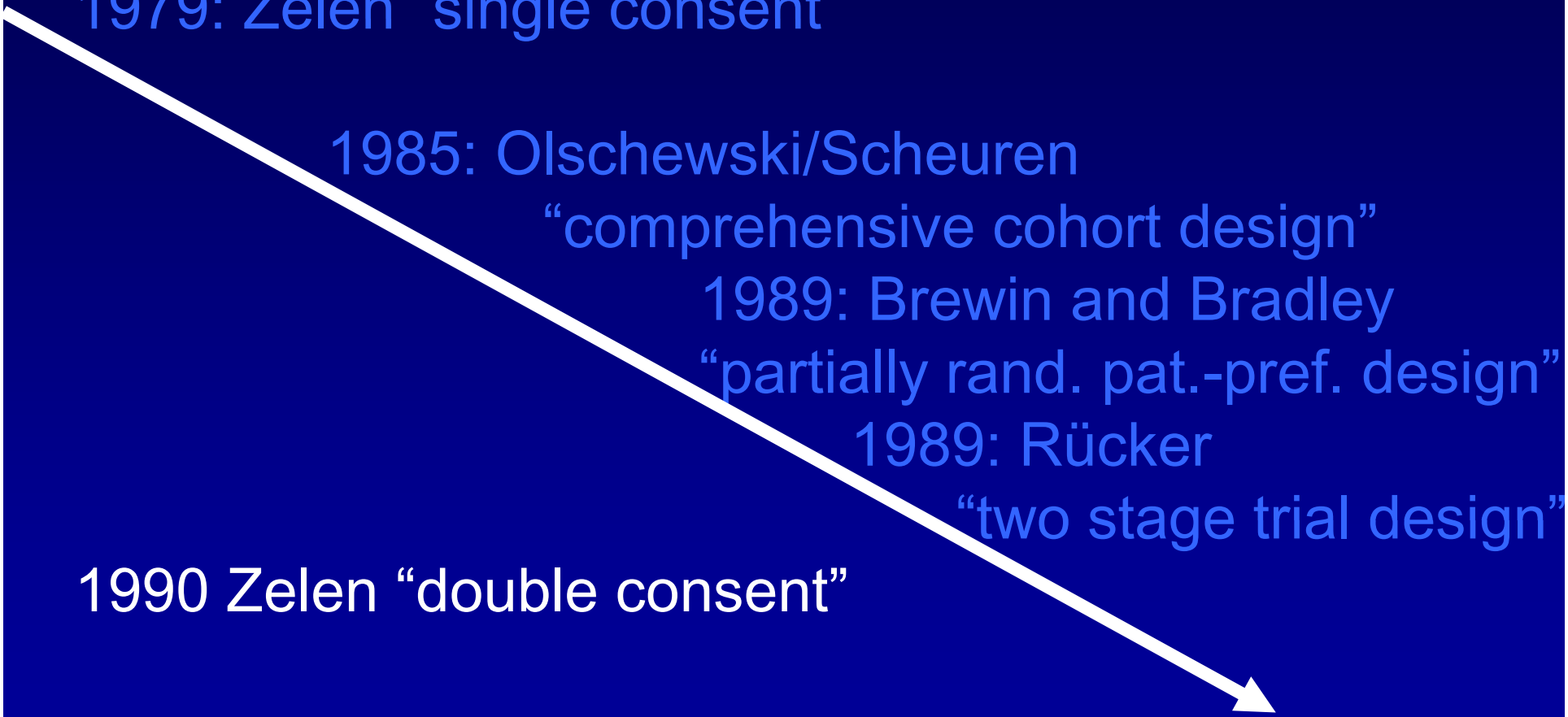

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1993: Wennberg (design)

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2005 : Millat ea. Surgical eval. design

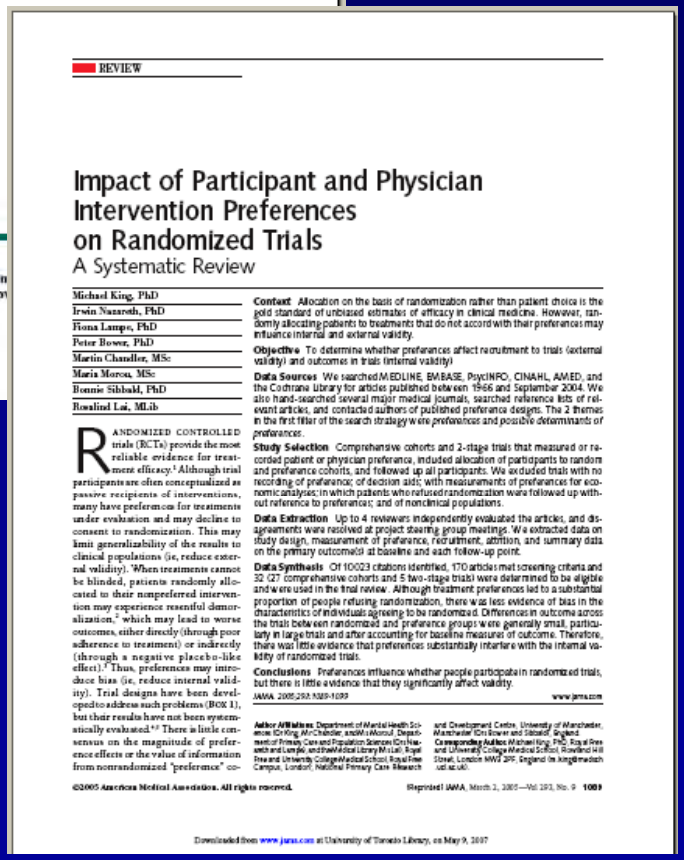
Study aim

Systematic review of the dental literature to identify the use of clinical trials that have used a study design that report taking into account the patient and/or the clinician's preferences for intervention(s).

Materials and methods

1. Search for systematic reviews in:
   - Medline
   - Embase
   - Cochrane Library
   - & hand search tables and reference lists

King et al. Health Technol Assess 2005; 9(35): 1-186.



Adamson et al. Contemp Clin Trials. 2006; 27(4): 305-19.

King et al. JAMA 2005; 293(9): 1089-99

Materials and methods

1. SRs in: Medline – Embase -Cochrane Library & hand search lists *n=3*

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2. Search for clinical trials in:

   Medline – Embase - Cochrane Library

   alt. 1: HTA Search Strategy

Ovid: Search Form - Microsoft Internet Explorer provided by Faculty of Dentistry

Edit View Favorites Tools Help

Back Search Favorites

http://gateway.ut.ovid.com/gw1/ovidweb.cgi

OVID

Ovid MEDLINE(R)
1996 to April Week 4 2007

ovid web gateway

| Change Database | Questions? Email ask.gerstein@utoronto.ca | Online Support | Help | LOGOFF
| Saved Searches/Alerts

#	Search History	Results	Display
1	zelen.tw.	28	DISPLAY
2	((single or double) adj (random$ adj consent$)).tw.	0	
3	(non adj random$ adj assign$).tw.	10	
4	(nonrandom$ adj assign$).tw.	36	
5	(comprehensive adj cohort$ adj stud$).tw.	6	
6	(partial$ adj randomi?ation).tw.	5	
7	(nonrandom$ adj (patient$ or participant$)).tw.	63	
8	(nonrandom$ adj (patient$ or participant$)).tw.	63	
9	(preference adj arm$).tw.	12	
10	or/1-9	159	
11	exp Dentistry/	72003	
12	dent$.mp.	97236	
13	exp Dentistry/	72003	
14	or/11-13	109818	
15	**10 and 14**	**3**	DISPLAY

Combine Searches | Delete Searches | Save Search/Alert

Advanced Search | Basic Search | Find Citation

More Fields | Search Tools

Materials and methods

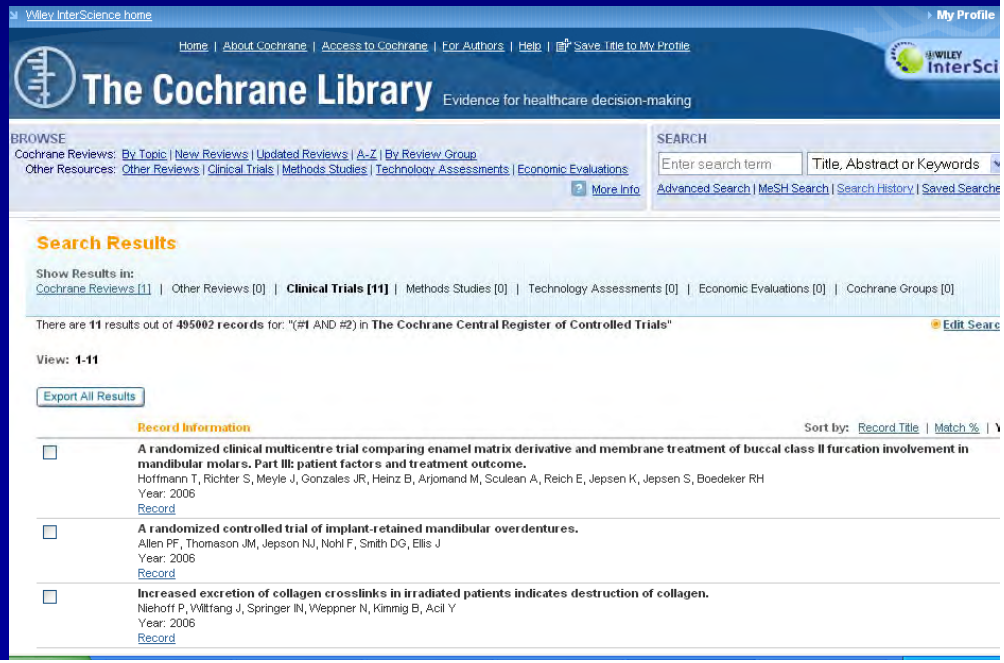
1. SRs in: Medline – Embase -Cochrane Library & hand search lists *n=3*
2. Search for clinical trials in:
   - Medline – Embase - Cochrane Library *n=3*
     - alt. 1: HTA Search Strategy
     - alt 2.: Hand-search of RCTs in the dental literature reporting intention-to-treat analyses

"Search Strategy:

intention to treat"[All Fields] AND ((("dental clinics"[TIAB] NOT Medline[SB]) OR "dental clinics"[MeSH Terms] OR dental[Text Word]) OR ("dentistry"[MeSH Terms] OR dentistry[Text Word]))

Medline: n=17

Cochrane: n= 11



Materials and methods

1. SRs in: Medline – Embase -Cochrane Library + hand search of reference lists
2. Clinical trials in: Medline – Embase - Cochrane Library + hand search of reference lists

n=3

n=12

3. *Web of Science* search for all citations to original papers:
   - Zelen (1979 New England J Medicine) *n=3*
   - Olschewski/Scheuren (1985 Inf Meth Med) *n=0*
   - Brewin&Bradley (1989 BMJ) *n=8*
   - Wennberg et al. (1993 Ann NY Acad Sciences) *n=6*

Results (n=9 (+13))

1. Review or discussion papers	2
2. Descriptive studies or surveys (with no experimental elements)	0
3. Studies with a preference cohort	2*
4. Studies with assessment and analysis of preference within a RCT	5**
5. Irrelevant (report pt preference as outcome measure)	13

** 1 trial*

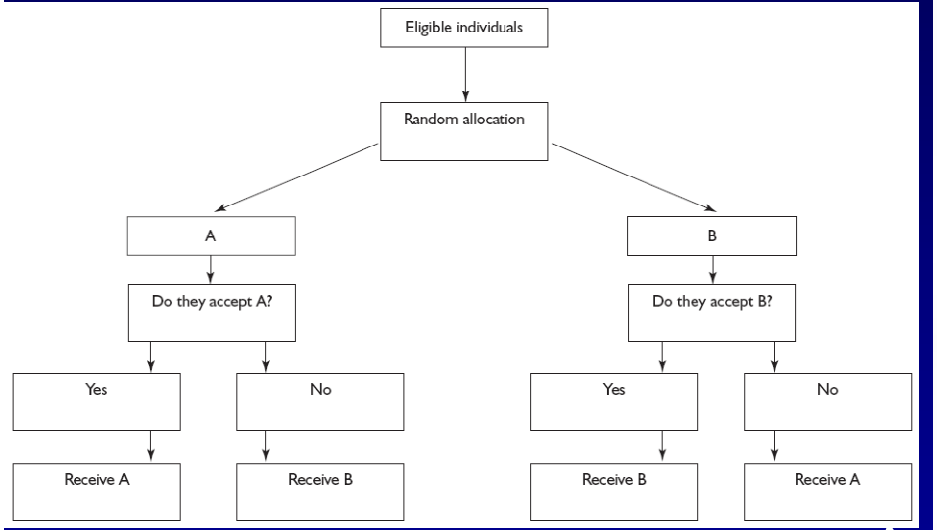
Zitzmann NU, et al. 2 papers reporting one preference cohort study

***2 trials:*

1. Feine J, Awad MA, Lund JP. 4 papers reporting one two-arm RCT.

2. Allen PF, et al. A Randomized Controlled Trial Of Implant-Retained Mandibular Overdentures. J Dent Res 2006; 85: 547-51 (Zelen design)

Allen et al. 2006



(Zelen double randomised consent design)

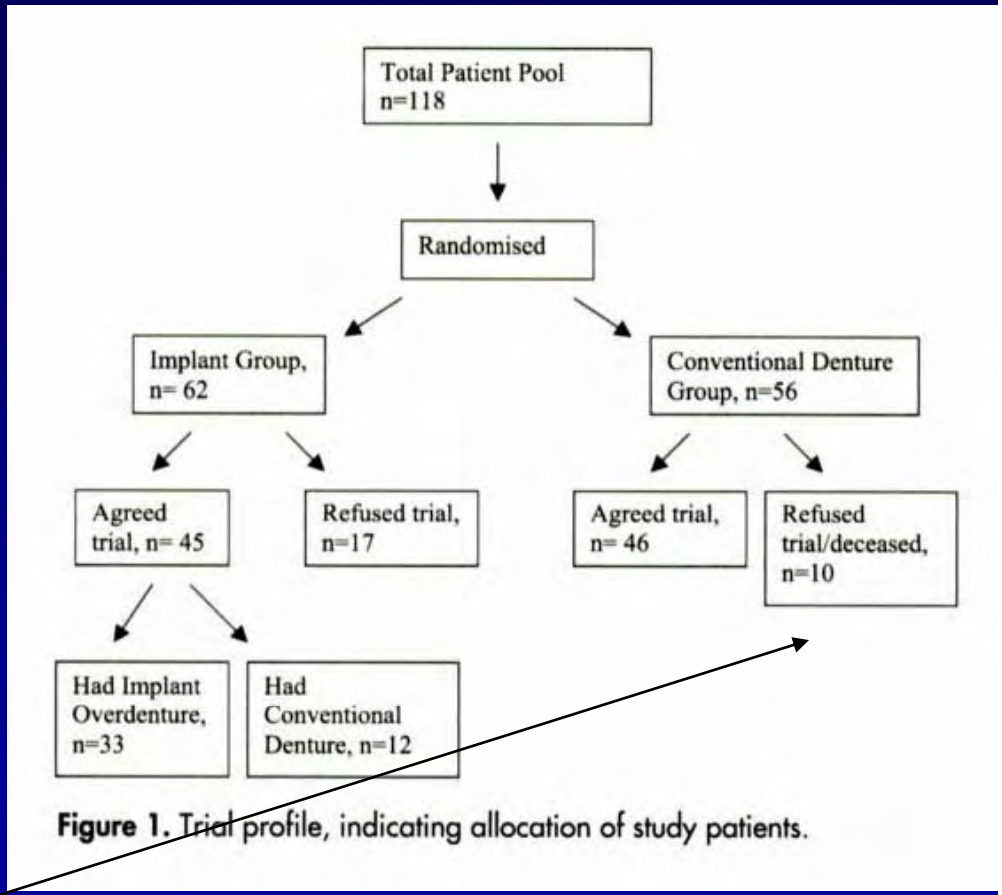


Figure 1. Trial profile, indicating allocation of study patients.

?

Discussion and conclusions

- Identifying clinical trials in bibliographic database is complex due to poor indexing
- Incorporating patient preferences in clinical trials in dentistry seems to be rare
- A few trials have been identified comparing implant-prosthetics with traditional prothodontic interventions
- There seems to exist a need for trials in dentistry taking patient-preferences into account

Appropriate Study Designs to address implementation of interventions

	Qualitative research	Survey	Case Control	Cohort	RCT	Non-exper	Systematic review
Effectiveness: Does it work?				☆	☆☆	☆	☆☆☆
Process of intervention/ delivery: How does it work?	☆☆	☆				☆	☆☆☆
Salience: Does it matter?	☆☆	☆☆					☆☆☆
Safety: Will it do more good than harm?	☆		☆	☆	☆☆	☆	☆☆☆
Acceptability: Will the patient accept the intervention?	☆☆	☆			☆	☆	☆☆☆
Cost effectiveness: Is it worth paying for the intervention?					☆☆		☆☆☆
Appropriateness: Is this the right intervention for this patient?	☆☆	☆☆					☆☆
Satisfaction with the intervention: Are users, providers and other stakeholders satisfied?	☆☆	☆☆	☆	☆			☆

"Guerir quelquefois,
soulager souvent,
consoler toujours"

"Cure occasionally,
relieve often,
console always "

Ambroise Paré
(1510 –1590)

Thank you for your kind attention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References

King M, Nazareth I, Lampe F, Bower P, Chandler M, Morou M, *et al*. Conceptual framework and systematic review of the effects of participants' and professionals' preferences in randomised controlled trials. *Health Technol Assess* 2005; 9(35).

Brewin CR, Bradley C. Patients' preferences and randomized clinical trials" BMJ 1989; 289: 313-315

Wennberg et al. (Ann N Y Acad Sci 1993;703:52-62)

Howard L, Thornicroft G. Patient preference randomised controlled trials in mental health research. Br J Psychiatry 2006; 188:303-4.

1985: Comprehensive cohort design

Olschewski et al., 1985; Brewlin & Bradley, 1989.

- All participants are followed up, regardless of randomization status.
- Outcomes of RCT and cohort groups can be compared.
- Ideal where it is likely that many patients will refuse, because patients or operators have a strong preference for one intervention.
- A disadvantage is no status of differences in baseline characteristics in the RCT and preference groups.
- Satisfaction with existing conditions very likely influence.

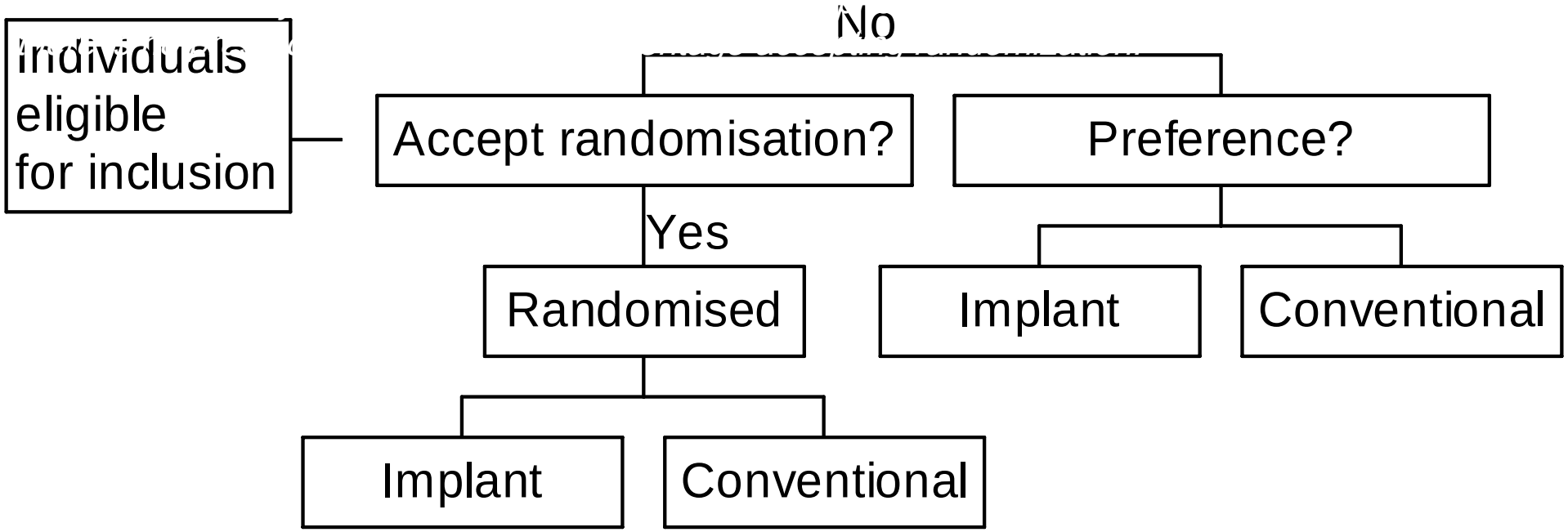
1985: Comprehensive cohort design

Design. Patients with strong preferences are offered their treatment of choice, while those without strong preferences are randomized in the conventional fashion. All patients (whether randomized or not) are followed up in the same way.

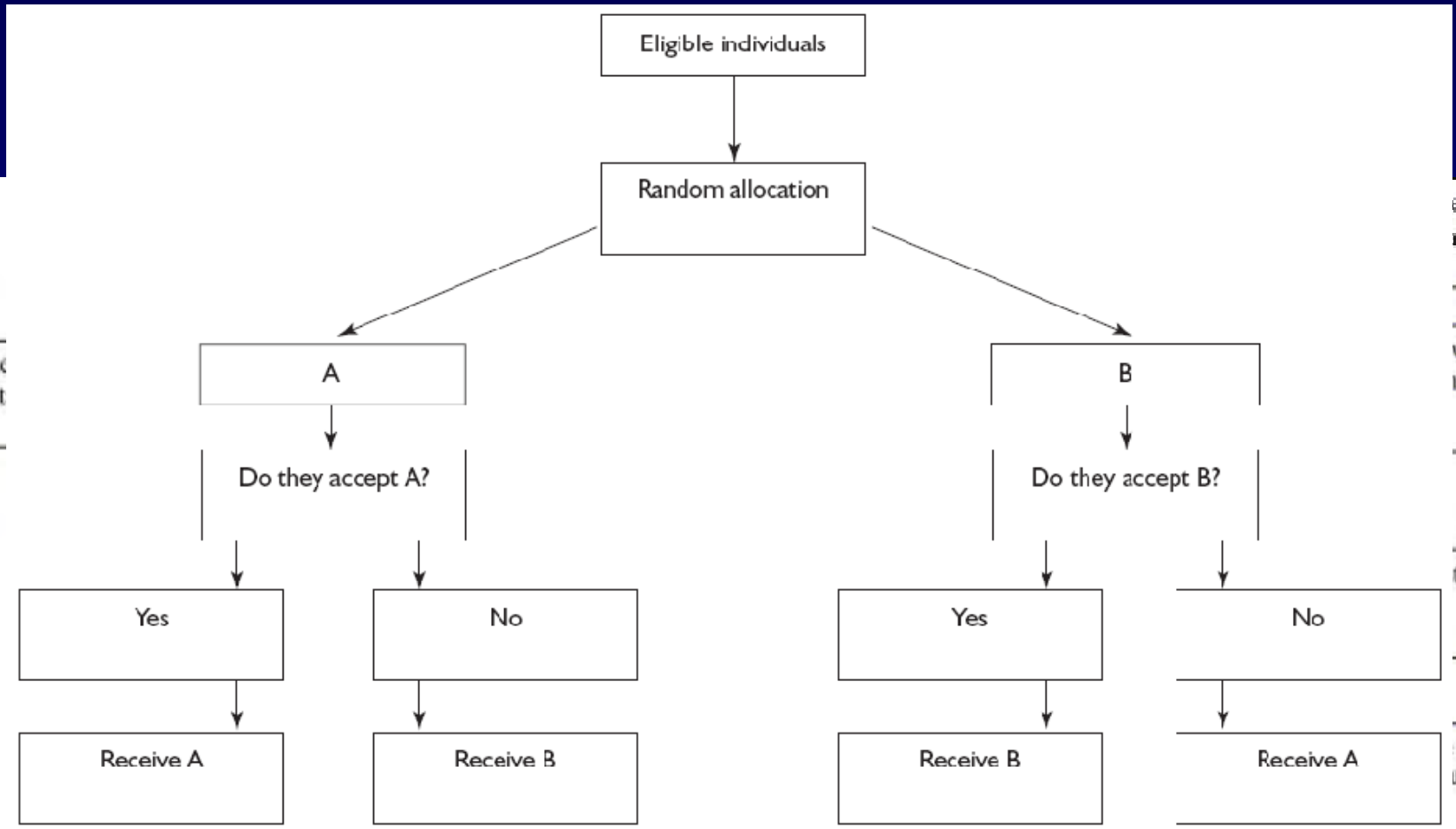
External validity. Almost all eligible patients enter the study, allowing examination of patients' characteristics with all strengths of preferences.

Internal validity. Preference effects (eg, randomization vs preference) are confounded although can be controlled.

Study administration. Potentially costly if large numbers of patients express a preference and



1990: Zelen double randomised consent design



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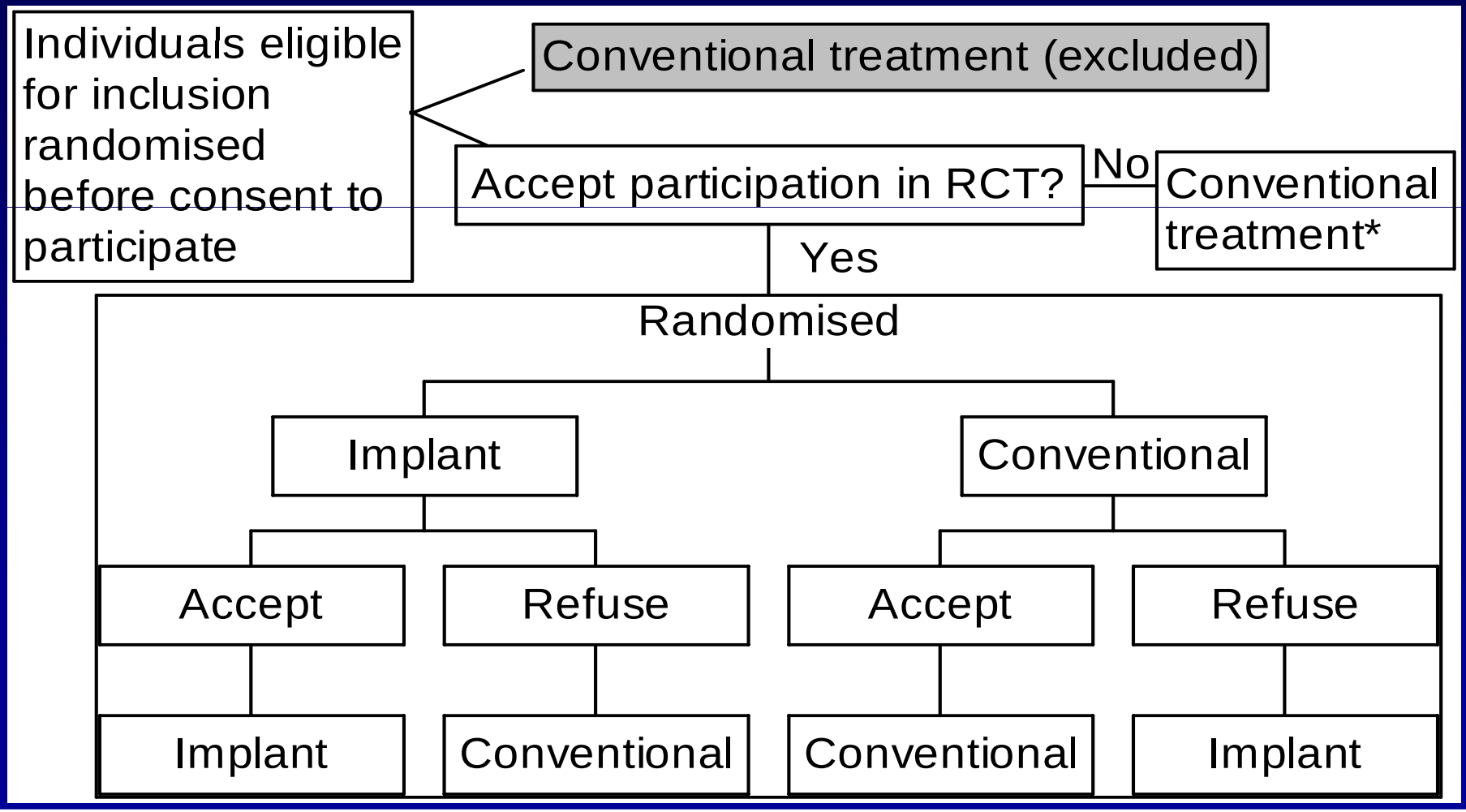
Ethical concerns overcome by offering the opportunity to switch to other group



* Given conventional treatment but analysed as if they have received exp. treatm.

Two-stage, Randomized design

Design. In the Wennberg design participants are initially randomized to 2 groups: in the first they are offered a choice of treatment while in the second they are randomized to treatment. The Rücker design is similar but participants randomized to preference in the first randomization, who do not have a strong preference for a treatment, are randomized a second time to a treatment.

External validity. Reduced because only patients accepting randomization enter the study.

Internal validity. All patients are randomized, increasing internal validity. However, randomization vs preference comparisons are still subject to confounding because patients' characteristics may determine choice of treatment.

Study administration. Individuals with strong preferences may refuse randomization.

Rücker Design

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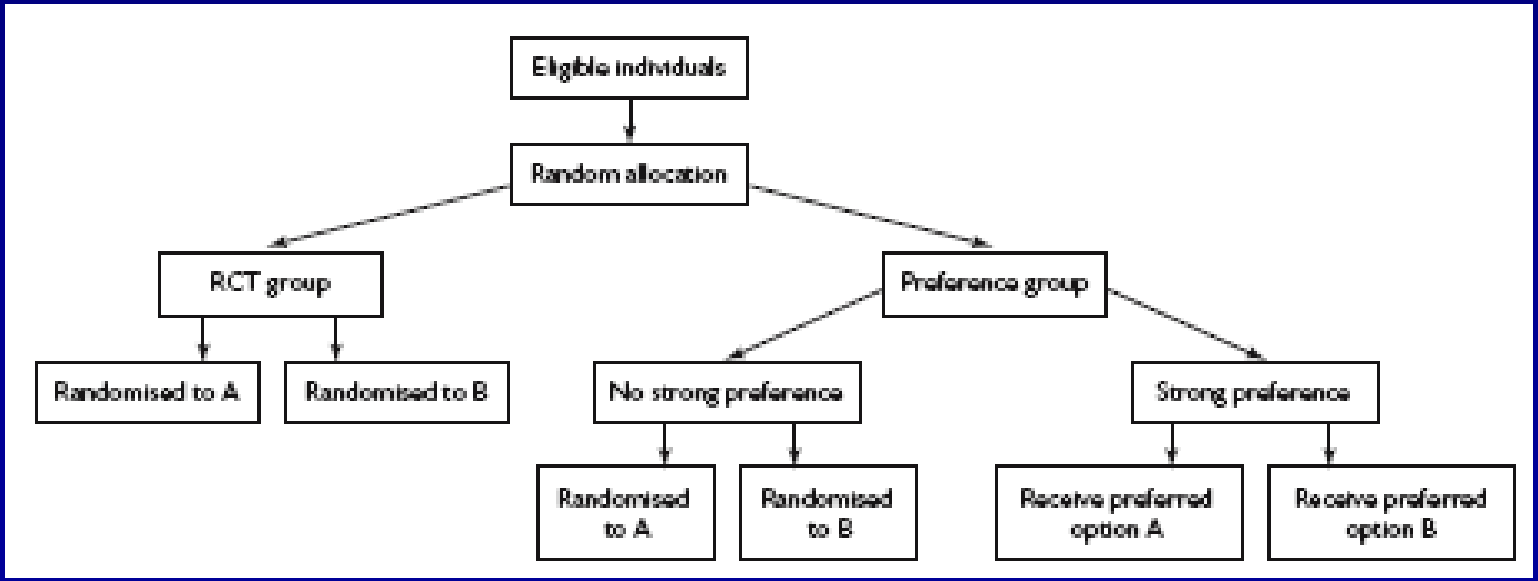

1993: Wennberg design

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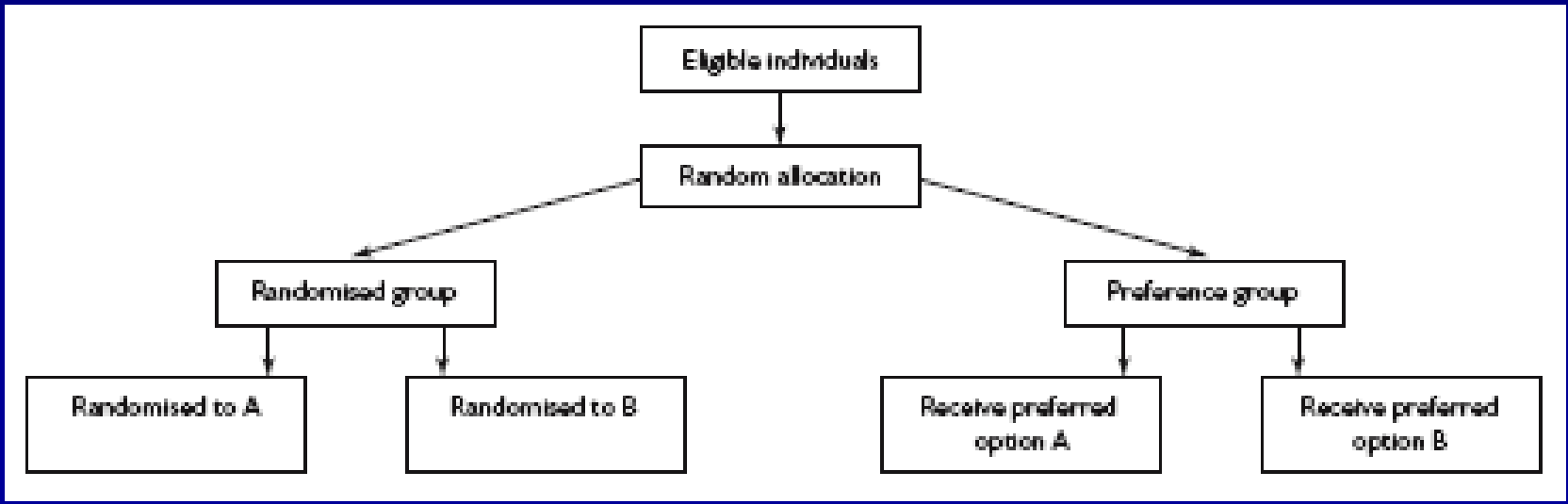
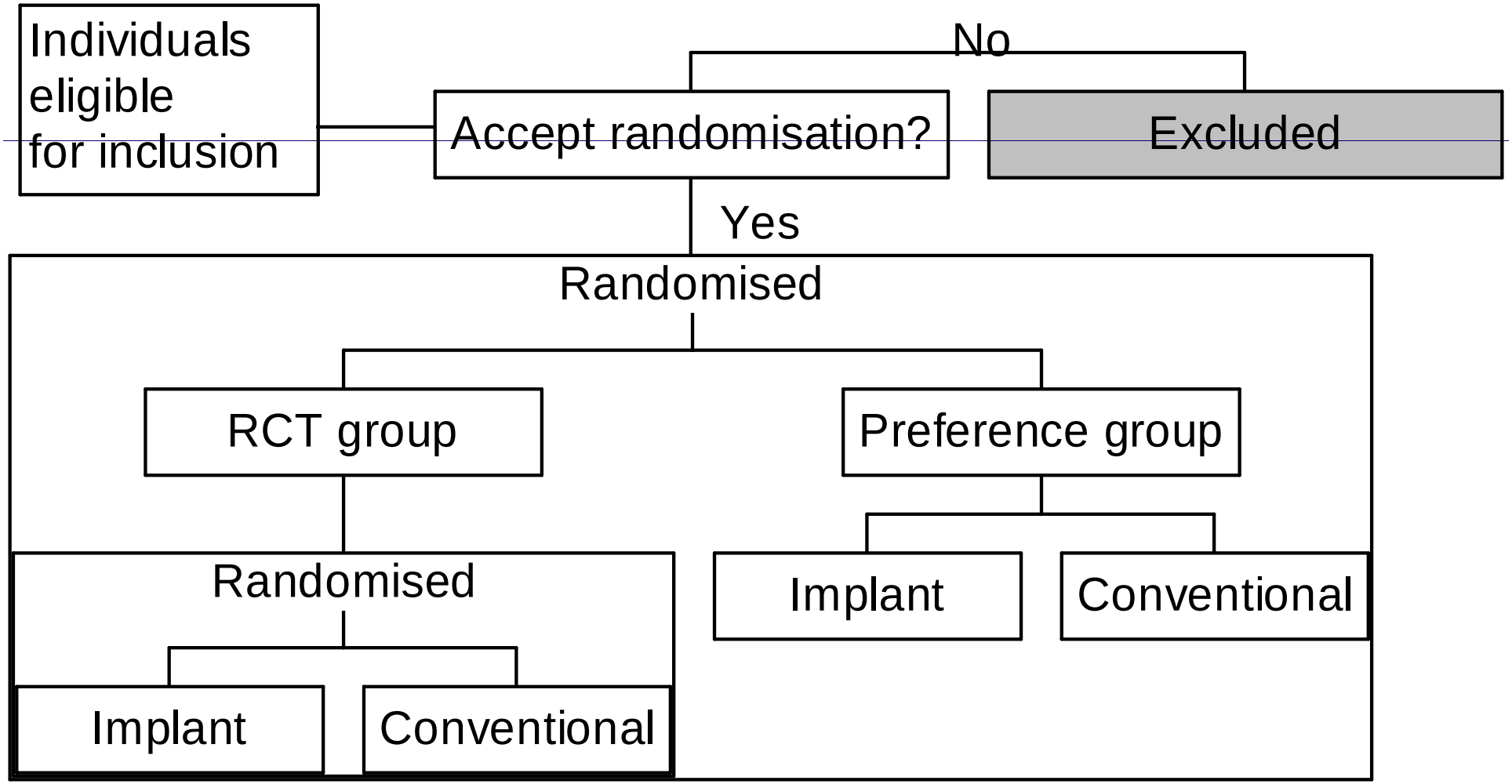


1993: Wennberg design

Include individuals who agree to be randomised



Feine & Awad

Feine J, Awad MA. Community Dent Oral Epidemiol 1998.

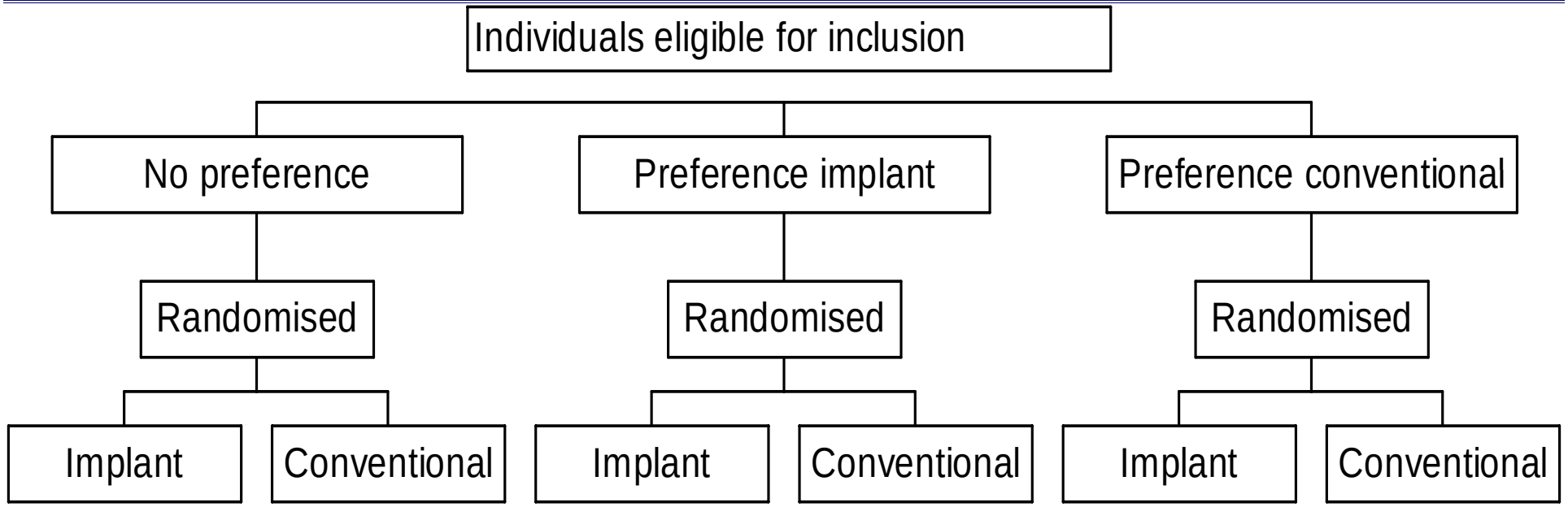


TABLE I *Advantages and disadvantages of each type of design*

Measurement of preference at baseline in a standard RCT

Internal validity – preference effects can be used as a stratification factor (to reduce the impact of preferences) or as a predictor of outcome

External validity – patents with very strong preferences may not enter the study, which may reduce or remove preference effects

Study administration – no increase in sample size, but large sample size may be required to detect preference interaction effects, valid and reliable measures of preferences required

Comprehensive cohort design

Internal validity – preference effects (e.g. R vs P) confoundec, although can be controlled

External validity – almost all eligible patients enter the study and allows examination of characteristics of patients with all strengths of preferences

Study administration – potentially costly if large numbers of patients express a preference and not feasible if very few patients have a preference. *A priori* power calculations difficult if there is no prestudy estimate of the percentage accepting randomisation

Prerandomised (Zelen) design

Internal validity – all patients randomised but, depending on consent process, ureven drop-out may occur between intervention and control arms

External validity – all eligible patients enter study but ethical objections exist over lack of fully informed consent

Study administration – potentially low cost as all eligible patients will enter study but depending on later consent process, drop-out or switching between arms may make increased recruitment necessary. Ethical concerns in designs with partial or no patient consent

Two-stage, randomised designs (Wennberg and Rücker)

Internal validity – all patients randomised, increasing internal validity. However, P vs P and R vs P comparisons still subject to confounding as patients' characteristics may determine choice of treatment

External validity – reduced because only patients accepting randomisation enter the study
Study administration – people with strong preferences may refuse randomisation

	External validity	Internal validity	Study administration
RCT			
Prerandomized			
Two-stage, random design			
Comprehensive Cohort	*Almost all eligible patients enter the study, allowing examination of patients' characteristics with all strengths of preferences.*	Preference effects (eg, randomization vs preference) are confounded although can be controlled.	Potentially costly if large numbers of patients express a preference and not feasible if very few patients have a preference. A priori power calculations are difficult if there is no prestudy estimate of the percentage accepting randomization.