Clinical studies on GTR techniques, are they science-based?

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GTR techniques- science based?

- Define the given topic
- Descriptive bibliometric data
- How to characterize “science-based”
  - Types of clinical studies
- Critical appraisal of the clinical studies
- Which GTR techniques are science based

Define the given topic

As clinicians we should train to formulate well-built clinical questions.

Well built question includes four elements:

1. Patient or problem
2. Intervention
3. Comparison intervention
4. Outcome

Well built clinical question:

1. Patient characteristic and problem?

- Bone loss
  - Adults / Adolescent
  - General / local
  - Horisontal / vertical
- Interradicular
- After 3d. molar extractions
- Implant installation
- Alveolar ridge maintenance

Well built clinical question:

1. Patient characteristic and problem?
2 & 3. Intervention & alternative intervention?

   "GTR techniques"

Guided Tissue Regeneration - MESH

Definition (1992)

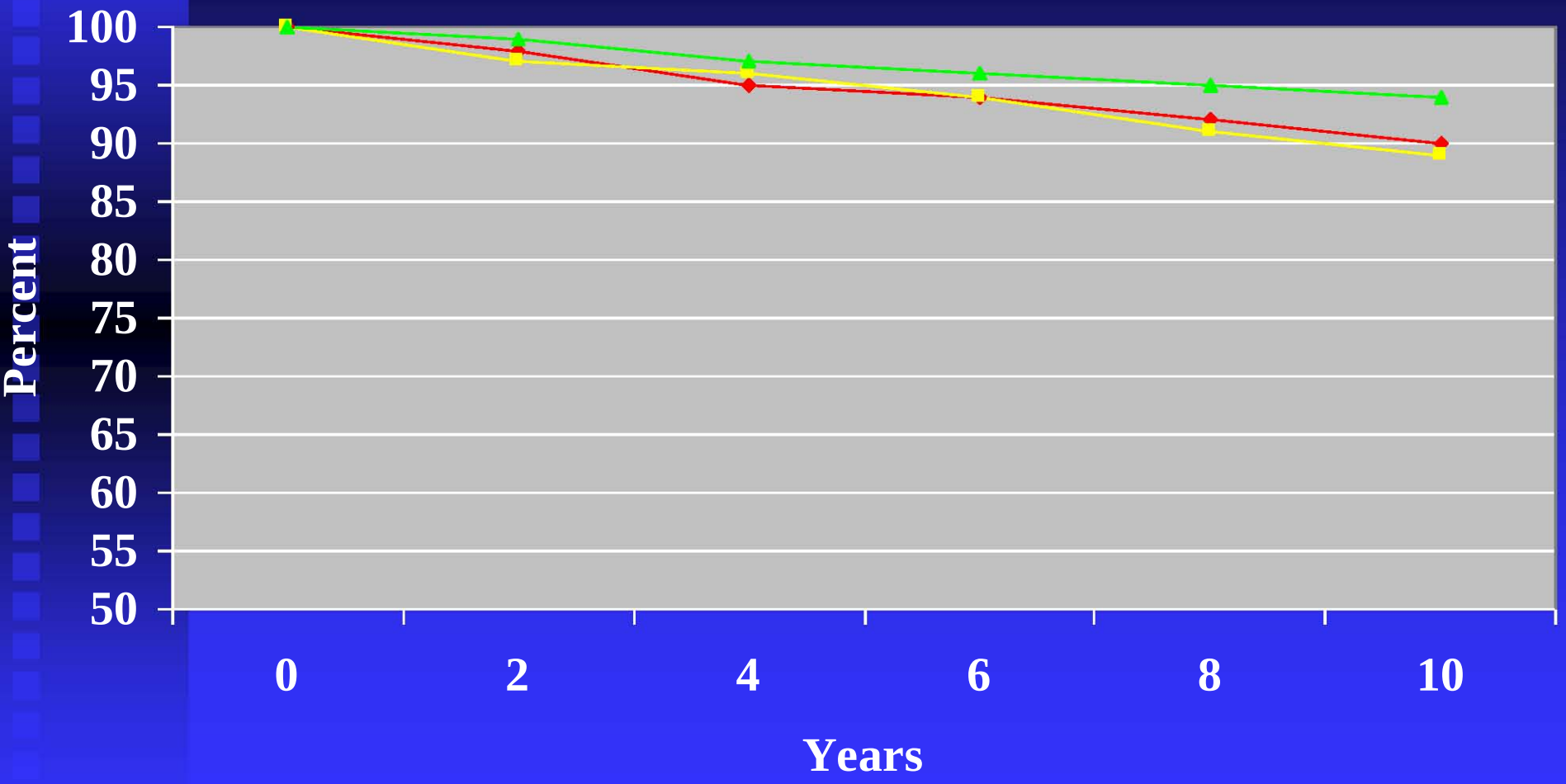
The repopulating of the periodontium, after treatment for periodontal disease. Repopulation is achieved by guiding the periodontal ligament progenitor cells to reproduce in the desired location by blocking contact of epithelial and gingival connective tissues with the root during healing. This blocking is accomplished by using synthetic membranes or collagen membranes.

Well built clinical question:

1. Patient characteristic and problem?
2 & 3. Intervention & alternative intervention?
4. Criteria for outcome

Patient or operator centered

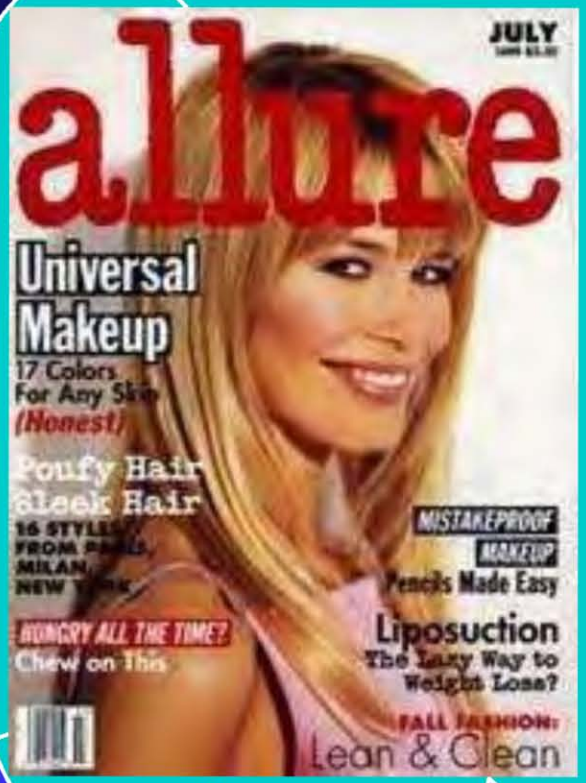
We present e.g. survival data:

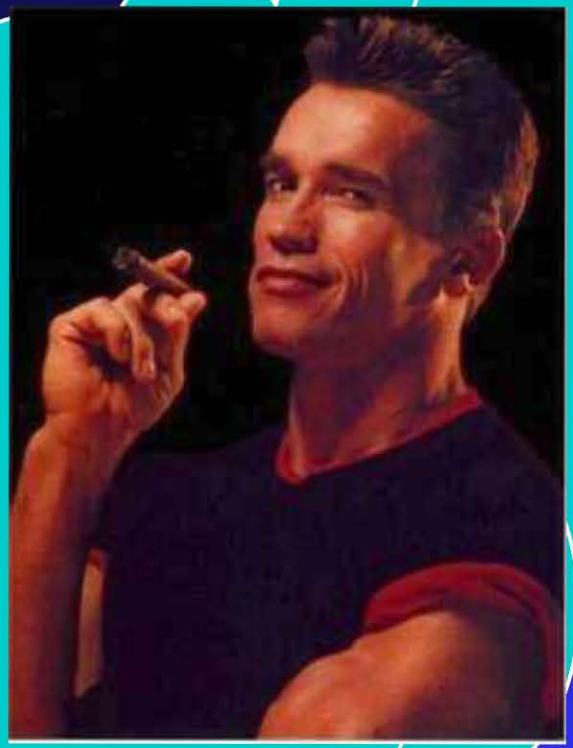


…or even odds ratios.. while patients...

Independent variables	Bi-variate odds ratios	Bivariate significance	95% Confidence intervals bivariate odds ratios	Multi-variate odds ratios	Multivariate significance	95% Confidence intervals for multivariate odds ratios
Age						
20-30	-	-	-	-	-	-
30-40	2.32	**	1.15 - 3.13	2.52	**	1.35 - 3.33
+40	2.63	***	1.43 - 3.08	2.63	***	1.83 - 3.8
Sex						
Male	-	-	-	-	-	-
Female	2.42	**	1.61 - 2.79	2.12	**	1.91 - 2.9
Material						
Gold	-	-	-	-	-	-
Metall-ceram	1.12	NS	0.13 - 1.56	1.42	NS	1.13 - 1.96
Dentists						
#1	-	-	-	-	-	-
#2	1.34	NS	0.35 - 1.61	1.04	NS	1.35 - 2.01
Location						
Mandible	-	-	-	-	-	-
Maxilla	1.55	*	1.17 - 2.04	1.15	*	1.57 - 2.14

.. really may prefer other values...





- Define the given task
- Descriptive bibliometric data

Seeking evidence

- Textbooks
- Proceedings
- Medline

Bilder av jønkøping concensus, int workshop - odont2000 , lærebok?

Ovid: Search Form - Netscape

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O V I D

Medline
1966 to December 1999 Week 1

Help

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1	exp guided tissue regeneration/ or guided tissue regeneration.mp.	1141	Display
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4	2 and 3	417	Display
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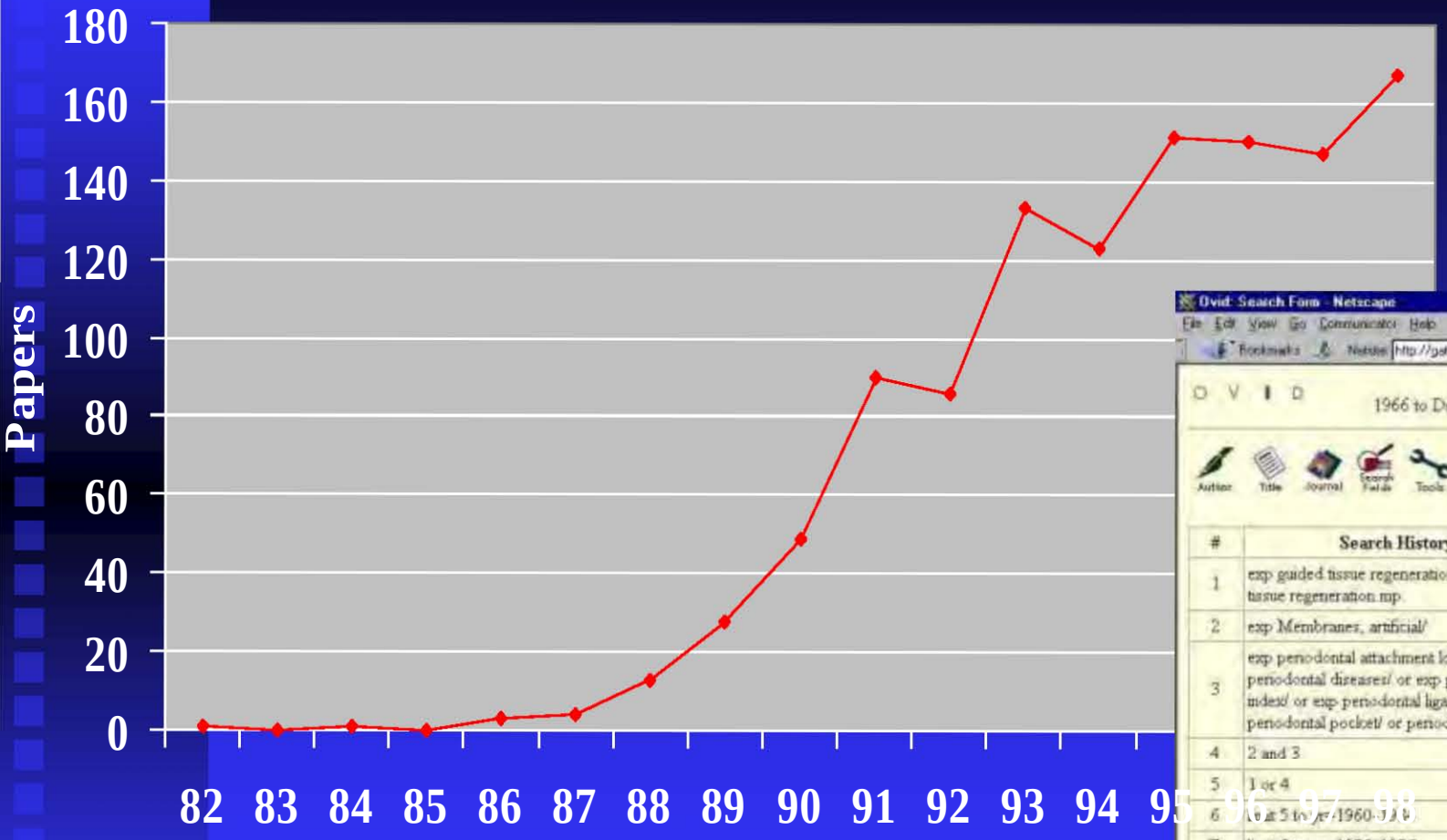
Papers focussed on GTR



Applications for use of GTR

Study design

In vivo study categories

- Define the given task
- Descriptive bibliometric data
- How to characterize “science-based”

Science:

any system of knowledge that is concerned with the physical world and its phenomena and that entails unbiased observations and systematic experimentation. In general, a science involves a pursuit of knowledge covering general truths or the operations of fundamental laws.

Scientific method:

principles and procedures for the systematic pursuit of knowledge involving the recognition and formulation of a problem, the collection of data through observation and experiment, and the formulation and testing of hypotheses

- Define the given topic
- Descriptive bibliometric data
- How to characterize “science-based”
  - Types of clinical studies

Clinical trial terminology - tower of Bable?

analytical study
case control study (89)
case serie
case study, case report
cause-effect study
clinical trial (79)
cohort study (89)
cohort study with historical controls
controlled clinical trial (95)
cross-sectional study (89)
descriptive study
diagnostic meta-analysis
diagnostic study
double blind randomized therapeutical trial with cross-over design
ecological study
etiological study
experimental study
explorative study
feasability study (79)
follow-up study (67)
historical cohort study
incidence study
intervention study
longitudinal study (79)
N=1 trial
non-randomized trial with contemporaneous controles
non-randomized trial with historical controles
observational study
prevalence 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

Describing clinical research -reduce to three questions

1. General purpose?	Descriptive, no comparison conducted
	Comparison as process research
	Comparison as cause-effect research
2. Procedure, intervention?	Experimental allocation of procedure
	Survey
3. Data collection?	Retrospective
	Cross-sectional
	Prospective / Cohort / Longitudinal

Clinical study designs (MESH terms):

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

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.Neyman bias

5.group sizes may be unequal

Case-Control Studies

Advantages:

1.quick and cheap

2.only feasible method for very rare disorders or those with long lag between exposure and outcome

3.fewer subjects needed than cross-sectional studies

Disadvantages:

1.reliance on recall or records to determine exposure status

2.confounders

3.selection of control groups is difficult

4.potential bias: recall, selection

Characteristics of a poor case-control study:

Failed to:

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

Cohort Study

Advantages:

1. ethically safe
2. subjects 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:

Failed to:

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

Randomised Controlled Trial

Advantages

1. unbiased distribution of confounders
2. blinding more likely
3. randomisation facilitates statistical analysis

Disadvantages

1. expensive: time and money
2. volunteer bias
3. ethically problematic at times

How are the different clinical study designs considered as evidence of therapeutical effectiveness?

Strength of evidence of treatment effects

US Agency of Health Care Policy & Research, 1992

Ia. Meta-analysis of randomized controlled trials

Ib. At least one randomized controlled trial

IIa. At least one well-designed controlled study without randomization

IIb. At least one other quasi-experimental study

III. Well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case-control studies.

IV. Expert committee reports or opinions and/or clinical experience of respected authorities

EBM Working Group, McMaster University 1993

Systematic reviews and meta-analyses

RCT with definite results (ie. result with CI that do not overlap the threshold clinically significant effect)

RCT with non-definite results (ie. a point estimate that suggests a clinically significant effect, but with CI overlapping the threshold for this effect)

Cohort studies

Case-control studies

Cross sectional studies

Case reports

Strength of evidence of treatment effects

Richards & Lawrence, Br Dent J 1995;175:270

- at least one published systematic review of multiple well designed randomised controlled trials

- at least one published properly designed randomised controlled trial of appropriate size and in an appropriate clinical setting
- published well-designed trials without randomisation, single group pre-post, cohort, time series or matched case controlled studies

- well-designed experimental studies from more than one centre or research group
- opinions of respected authorities based on clinical evidence, descriptive studies or reports of expert consensus committees

Sackett et al., Editorial. EBM 1995;1:4

(I-1) Based on 2 or more well designed randomised controlled trials (RCT), meta-analyses, or systematic reviews.
(I-2) Based on a RCT.

(II-1) Based on a cohort study.
(II-2) Based on a case controlled study.
(II-3) Based on a dramatic uncontrolled experiment.

(III) respected authorities, expert committees (consensus)etc.

(IV) ...someone once told me

Strength of evidence of treatment effects

CEBM,1999. (http://cebm.jr2.ox.ac.uk/docs/levels.html)

1a. Systematic review (with homogeneity of RCTs)

1b. Individual RCT (with narrow confidence interval)

1c. All or none

2a. Systematic review (with homogeneity) of cohort studies

2b. Individual cohort study (and low quality RCT; e.g.,<80% follow-up)

2c. “Outcomes” research

3a. Systematic review (with homogeneity) of case-control studies

3b. Individual case-control study

4. Case-series (and poor quality cohort and case-control studies)

5. Expert opinion without explicit critical appraisal, or based on physiology, bench research or “first principles”

- Define the given task
- Descriptive bibliometric data
- Characteristics of science
- Critical appraisal of the evidence

Critical appraisal of papers reporting treatment effects

Are the results of the trial valid?

1. Did the trial address a clearly focussed issue?

i.e. focused in terms of the population studied, the intervention, the outcomes considered

2. Was the assignment of patients to the intervention randomised?
3. Were all the patients who entered the trial properly accounted for at its conclusion?

was follow-up complete?,

were pasients analysed in the groups to which they were randomised?

Critical appraisal of papers reporting treatment effects

Are the results of the trial valid?

4. Were patients, health workers and study personnel blind to the intervention?

   patients? health workers? study personnel?

5. Were the groups similar at the start of the trial?

In terms of other factors that might effect the outcome such as age, sex and social class

6. Aside from the experimental intervention were the groups treated equally?

Critical appraisal of papers reporting treatment effects

What are the results?

7 . How large was the effect of the intervention?

What outcomes are measured?

8. How precise was the estimate of the effect of intervention?

What are its confidence limits?

Critical appraisal of papers reporting treatment effects

Will the results help my patients?

9. Can the results he applied to my patients?

   Do you think that the patients covered by the trial are similar enough to your population?

10. Were all clinically important outcomes considered?

    If not, does this affect the decision?

11. Are the benefits worth the harms and costs?

    This is unlikely to be addressed by the trial but what do you think?

- Define the given task
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- Characteristics of science
- Critical appraisal of the evidence
- Which GTR techniques are science based

Evidence of no difference =/= no evidence of difference

Evidence of no difference =/= evidence of equivalence

- May be due to low power, i.e. insignificant difference, large variance and/or small sample sizes
- May be corrected with metaanalysis- primary or secondary- but aware of methodological problems! (Garbage in garbage out).

Criteria for evaluating treatment effects

- High repeatability and accuracy
  - Histology
    - Morbidity, quantification?
  - Probing
    - Who wants to disrupt a new region?
  - Radiographic
    - Direct measurement vs. percent approach
- Concensus on appropriate criteria for reporting treatment results is critical

Presentation of trial data

	Test	Control	Total
-2 - -1 mm	10	5	15
-1 - 0 mm	3	8	11
0 - 1 mm	2	8	10
1 - 2 mm	5	11	16
2 - 3 mm	16	8	24
3 - 4 mm	4	0	4
	40	40	80

Presentation of trial data

	Test	Control	Total
-2 - -1 mm	10	5	15
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2 - 3 mm	16	8	24
3 - 4 mm	4	0	4
	40	40	80

Conclusion, presentation of means and standard deviations

	Test	Control
Mean	1,15	0,73
SD	1,8	1,3
n	40	40

P = .00894 (paired t-test, df. 39)

"XXX was significantly better than the conventional method (p < .01)"

Presentation of trial data

	Test	Control	Total
-2 - -1 mm	10	5	15
-1 - 0 mm	3	8	11
0 - 1 mm	2	8	10
1 - 2 mm	5	11	16
2 - 3 mm	16	8	24
3 - 4 mm	4	0	4
	40	40	80

Alternative 2: Choice of clinical significance was set at 2 mm

	Test	Number Control	Total
< 2 mm	20	32	52
> 2 mm	20	8	28
	40	40	80

Conclusion, focus on vertical percentages

	Test	Control	Total
< 2 mm	50%	80%	52
> 2 mm	50%	20%	28
	40	40	80

"Improvement for half the patients treated with XXX compared to only one fifth with the conventional method."

Presentation of trial data

	Test	Control	Total
-2 - -1 mm	10	5	15
-1 - 0 mm	3	8	11
0 - 1 mm	2	8	10
1 - 2 mm	5	11	16
2 - 3 mm	16	8	24
3 - 4 mm	4	0	4
	40	40	80

Alternative 2: Choice of clinical significance was set at 2 mm

	XXX	Number Control	Total
< 2 mm	20	32	52
> 2 mm	20	8	28
	40	40	80

Conclusion, focus on horisontal percentages

	Test	Control	Total
< 2 mm	32%	68%	52
> 2 mm	70%	30%	28
	40	40	80

"70% percent of all the patients with improvement had been treated with XXX while the others had been treated with the conventional method."

Presentation of trial data

Alternative 2: Choice of clinical significance was set at 2 mm

	Number		
	Test	Control	Total
< 2 mm	20	32	52
> 2 mm	20	8	28
	40	40	80

Conclusion, focus on percentage improvement:

" The treatment with XXX resulted in a x2.5 / alt. 250% improvement compared to conventional methods".

Presentation of trial data

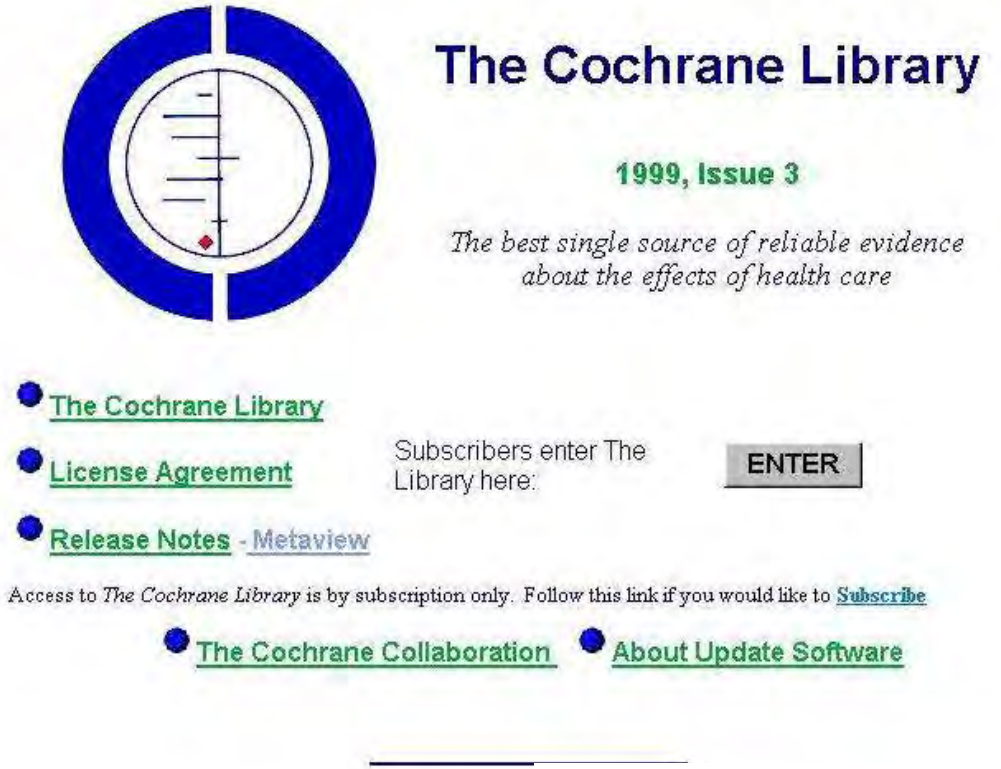
	Test	Control	Total
-2 - -1 mm	10	5	15
-1 - 0 mm	3	8	11
0 - 1 mm	2	8	10
1 - 2 mm	5	11	16
2 - 3 mm	16	8	24
3 - 4 mm	4	0	4
	40	40	80

Alternative 3:
Choice of clinical significance set at 1 mm

	Test	Control	Total
< 1 mm	15	21	36
> 1 mm	25	19	44
	40	40	80

Conclusion:

" No statistically significant results were observed".



The Cochrane Library includes:

- The Cochrane Database of Systematic Reviews - Regularly updated reviews of the effects of health care
- Database of Abstracts of Reviews of Effectiveness - Critical assessments and structured abstracts of good systematic reviews published elsewhere
- The Cochrane Controlled Trials Register - Bibliographic information on controlled trials
- Other sources of information on the science of reviewing research and evidence-based health care

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Search MeSH

Options History

Search term: (GUIDED and (TISSUE and REGENERATION)) [Re-construct]

Database	Hits [Total]
The Cochrane Database of Systematic Reviews	
Complete reviews	0 [0]
Protocols	1 [393]
Database of Abstracts of Reviews of Effectiveness	
Abstracts of quality assessed systematic reviews	0 [1,227]
Other assessed reviews: bibliographic details only	0 [836]
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The Cochrane Controlled Trials Register (CENTRAL/CCTR)	
References	131 [258795]
Medical Editors Trial Amnesty	0 [0]
About CCTR	0 [1]
The Cochrane Review Methodology Database	
References	0 [667]
About the Cochrane Collaboration	
The Cochrane Collaboration	0 [1]
Collaborative Review Groups - CRGs	2 [50]
Fields	0 [0]
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Options History

Guided tissue regeneration (GTR) for periodontal infra-bony defects [protocol]

Date of most recent substantive amendment: 20 May 1999

Date review expected: 01 September 1999

Cover sheet - Background - Methods - References

Background

Chronic Periodontitis

Chronic periodontitis (CP) is a destructive gum condition, which is estimated to affect 10 - 30% of the world-wide population (Baehni 1986; Löe 1986 and Oliver 1991). CP is caused by the bacteria within dental plaque, stimulating inflammation within the periodontal tissues. In the susceptible individual this will result in the breakdown of both the connective tissues which attach to the tooth and the supporting bone around the root. This usually results in the formation of a periodontal pocket around the root which acts as a reservoir for bacteria. The morbidity of this condition is easily underestimated and includes an uncomfortable loosening of the teeth (which may impair eating), cosmetic problems (as teeth drift or gums recede), a tendency to abscess formation within the pocket and eventual tooth loss.

Treatment of periodontitis

The objectives for treating periodontitis are mainly concerned with stabilising or arresting the condition and the crucial role of the patient's home care plaque control is well recognised (Lindhe 1975). The debridement of bacterial deposits coating the surface of the root, deep within the periodontal pocket is also essential and is achieved in the first instance, by scaling techniques. In addition, periodontal surgery is used where the depth of the deposits within the pocket, prevents adequate access for debridement.

The Infra-bony defect and its treatment

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Search term: (GUIDED and (TISSUE and REGENERATION)) [No restrictions]

The Cochrane Controlled Trials Register (CENTRAL/CCTR)

References (131 records selected)

1 1998 A clinical evaluation of an allograft combined with a bioabsorbable membrane versus an alloplast/allograft composite graft combined with a bioabsorbable membrane. 100 consecutively treated cases.

2 New 1998 A comparison of 2 root coverage techniques: guided tissue regeneration with a bioabsorbable matrix style membrane versus a connective tissue graft combined with a coronally positioned pedicle graft without vertical

3 1998 Bone regeneration after radicular cyst removal with and without guided bone regeneration.

4 1998 Clinical and microbiological evaluation of a bioabsorbable and a nonresorbable barrier membrane in the treatment of periodontal intraosseous lesions.

5 1998 Clinical comparison of bioabsorbable barriers with non-resorbable barriers in guided tissue regeneration in the treatment of human intrabony defects.

6 1998 Clinical comparison of cellulose and expanded polytetrafluoroethylene membranes in the treatment of class II furcations in mandibular molars with 6-month re-entry.

7 New 1998 Comparison of 2 regenerative procedures--guided tissue regeneration and demineralized freeze-dried bone allograft--in the treatment of intrabony defects: a clinical and radiographic study.

8 New 1998 Early bacterial accumulation on guided tissue regeneration membrane materials. An in vivo study.

9 1998 Effects of expanded polytetrafluoroethylene and polylactic acid barriers on healthy sites.

10 1998 Evaluation of periosteal membranes and coronally positioned flaps in the treatment of Class II furcation defects: a comparative clinical study in humans.

11 New 1998 Expanded polytetrafluoroethylene and dental rubber dam barrier membranes in the treatment of periodontal intrabony defects. A comparative clinical trial.

12 1998 GTR therapy of intrabony defects using 2 different bioresorbable membranes: 12-month results.

13 New 1998 Generalizability of the added benefits of guided tissue regeneration in the treatment of deep intrabony defects. Evaluation in a multi-center randomized controlled clinical trial.

14 1998 Guided tissue regeneration for the treatment of intraosseous defects using a biabsorbable membrane. A controlled clinical study.

15 1998 Guided tissue regeneration in Class II furcation involved maxillary molars: a controlled study of 8 split-mouth cases.

16 New 1998 Guided tissue regeneration in the treatment of human infrabony defects. Clinical, radiographical and microbiological results: a pilot study.

17 1998 Mucogingival versus guided tissue regeneration procedures in the treatment of deep recession type defects.

18 New 1998 Periodontal surgery of vertical bony defects with or without synthetic bioabsorbable barriers. 12-month results.

19 1998 Regenerative periodontal surgery with non-resorbable and biodegradable barriers: results after 24 months.

20 New 1998 Subpedicle connective tissue graft versus guided tissue regeneration with bioabsorbable membrane in the treatment of human gingival recession defects.

21 New 1998 The bone growing chamber: a new model to investigate spontaneous and guided bone regeneration of artificial defects in the human jawbone