Designing Randomized Controlled Trials to study dental implants

INTRODUCTION

- Why do I begin the study?
- What is the problem?
- What is the reason for solving the problem?
- What is my hypothesis?

Mention findings of others that I will challenge or develop

Describe how my work is developed from earlier works.

Indications
Need of e.g.,
Full arch mandibular implant reconstruction / bilateral implants in comparable posterior mandible / full-arch mandibular reconstruction edentulous mandible / Single tooth space / Edentulous / or with hopeless teeth / Completely edentulous / mandible / maxilla / Teeth for extraction, percussion-tender-free;

MATERIALS AND METHODS

- What did I do?
- To whom did I do this to? Why these?
- Which method did I use and why this one?

Describe to such details that others can evaluate your work and copy the procedures

Materials and methods – elements to consider

1. **Regional ethics institutional boards**
2. **Patient confidentiality procedures**
3. **Case report form recordings (CRFs)**
4. **Clinical research organization**
5. **Choice of clinical centers**
6. **Joint protocol development and calibration meetings.**
7. **Patient Population**
8. **Inclusion and exclusion criteria**

Considerations of inclusion criteria – common criteria that have been used

General
Age >18 years or older / 25-75y / 55-80 / >60 years old

Attitude / habits
Agree to recalls / Commitment to follow-up
Compliance of patient good
Oral hygiene adequate / excellent
Elective treatment decision / Patient consent
Willing to undergo potential risk of early implant failure
Plaque & bleeding scores low
Refuse to wear a removable denture / interim dentures

Medical
Healthy / Good general health / Health adequate to physically tolerate surgery / Physical able to tolerate surgery / Systemic health OK
Medical history revealed no contraindications to surgery

Local

Anatomy

Attached keratinized mucosa present on the alveolar crest
Bone quality Normal&good / sufficient / type I, II, III / interforaminal dense and normal (Type I,II,III bone)
Bone quantity adequate / sufficient height and width to permit ø nn x yy mm. / implants / >y mm apical to extraction socket or anticipated implant apex / 7-10 / 13-15 mm residual anterior / adequate distal to mental foramen to allow implants of at least 7 / 10 mm / Bone volume sufficient, i.e. >y mm width& >x mm height

Grafting / GBR not required for permitting implant with nn mm length.
Grafting limited to socket

Space 5.5 - 6.5 mm spaces anterior to premolars
Space for at least 2 splinted implants
Expectation of good occlusion / Opposing jaw at least 10 teeth / Inter-occlusal space at least 2 mm

Pathology, current or past

Pathology absent and none in the past
Local inflammation & mucosal diseases absent
No previous radiation therapy
Abscence of local purulent infections;

Operational
Period of edentulousness > 3 mths / > 6 mths / Healing after extraction > 6 mths
Torqued implants > 30 Ncm, >32 Ncm / Implants with good fixation

Considerations of exclusion criteria - – common criteria that have been used

General
Age / Active growth

Attitude / habits
Oral hygiene poor
Cigarettes/day > 20 / >10 / History of smoking / previous / current
Drug abuse & influence / Drug/alcohol abuse history

Medical
Bruxism signs / history /severe bruxism / clenching
General surgical contraindications
Heart disease operation within last 6 mths
Serious mental illness
Systemic diseases / Systemic diseases likely to compromise implant surgery

Local

Anatomy

Anatomical structures interference
Deep bite at upper central incisors

Maxillomandibular / Skeletal discrepancy
Type IV bone / Bone quality E
Vertical space Insufficient
Width of keratin mucosa < 2mm

Pathology, current or past
Active/ Acute Infection /inflammation / local infection / local pathology
Augmentation / grafting / Bone graft / previous unresorbed allograft / Unresorbed allograft at implant site
Bone loss extensive / Insufficient bone precluding implant of øxx and/or > nn mm.
Postextraction sites / Unhealed extraction sites
Residual roots
Radiation therapy of head&neck previously

Operational
Primary stability lacking / not achieved
Torque nm <25

OUTCOMES - – common outcomes that have been used

1. 3D-fit of suprastructure / abutment
2. 3D-position of implant
3. Adverse events: / -
    4. Altered Sensation /
    5. -Apical /
    6. -Infraposition /
    7. -Pain /
    8. -Peri-implantitis
9. Anatomy /
    10. -occlusion
    11. /-TMJ
12. Biomarker
13. Bone loss /gain
    14. Bone loss/gain on adjacent_tooth
    15. Bone-volume
16. Complications /-Biological /Technical
17. Cost
18. Detorque forces
19. Histology
20. Maintenance /
    21. -of Prosthesis
22. Microbiota
23. Operator assessed Esthetic
24. Operator assessed Function
25. Operator assessed Speech
26. Papilla
27. Patient Diet
28. Patient Esthetic Patient Esthetic-VAS
29. Patient Function Patient Function-VAS
30. Patient Function-Speech
31. Patient QOL
32. Patient Satisfaction Patient Satisfaction-VAS

33. Patient TMD
34. Perioindices
35. Softtissue Softtissue Volume
36. Stability Stability_Periotest Stability_Periotest_RFA Stability_RFA
37. Study Participation
38. Success&Survival according to specific set of criteria – 17 different
39. Surgery success
40. Time

Emerging?

Preprosthodontic procedures - considerations

Healing?

Prosthodontic procedures

Surgical procedures

Outpatient environment or a dental practice.
Prophylactic antibiotic therapy
Full-thickness mucoperiosteal flap.
Ridge alveoloplasty to obtain the necessary width of at least 7 mm
The implants used, diameters & lengths
Insertion torque
Primary implant stability -- lack of primary stability at this stage ?
Implant closure screw
Spinners?

Prosthodontic procedures

FDP?
Relined denture ?
full functional occlusion?
Cantilevers
Functional occlusion test?
Metal-ceramics vs gold-alloy FDP?

Recalls

implant mobility test?
direct finger manipulation / tapping sound /
x-ray method /
RFA

Radiographic measurements

Periapical radiographs / PAN
Rinn XCP
Bone level measurement blinded / independently by unrelated to the study.
Calibration

Statistical analyses

One vs multiple implants / statistical unit?
Non-parametric vs parametric
Distribution of the continuous responses (Kolmogorov-Smirnov test)
Sample size considerations
intent-to-treat (ITT) principle

RESULTS

- What did I find ?
- What were the answers to my question?

Separate facts from opinions.

Do not repeat what appears in tables and figures.
Present only facts limited to the theme of the study.
Include also eventual negative findings.

Results

Always start by showing the Baseline data!
Use Consort diagram (next page)

DISCUSSION

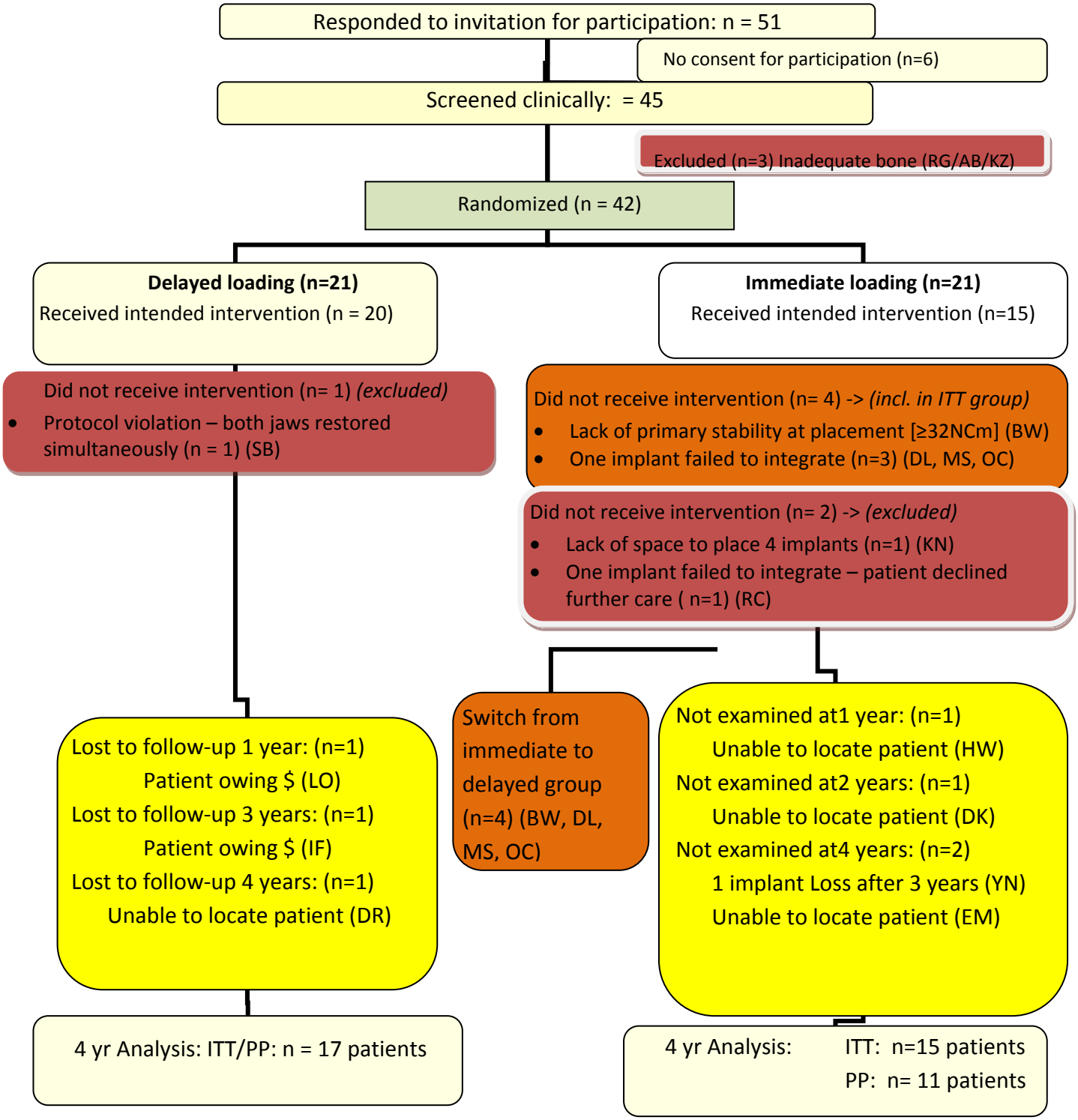
- What do the findings signify?
- Which implications do the findings have?
- Do the findings support the hypothesis?
- Does my hypothesis have validity and/or significance?
- Were the questions that led to the design and execution of the study answered?

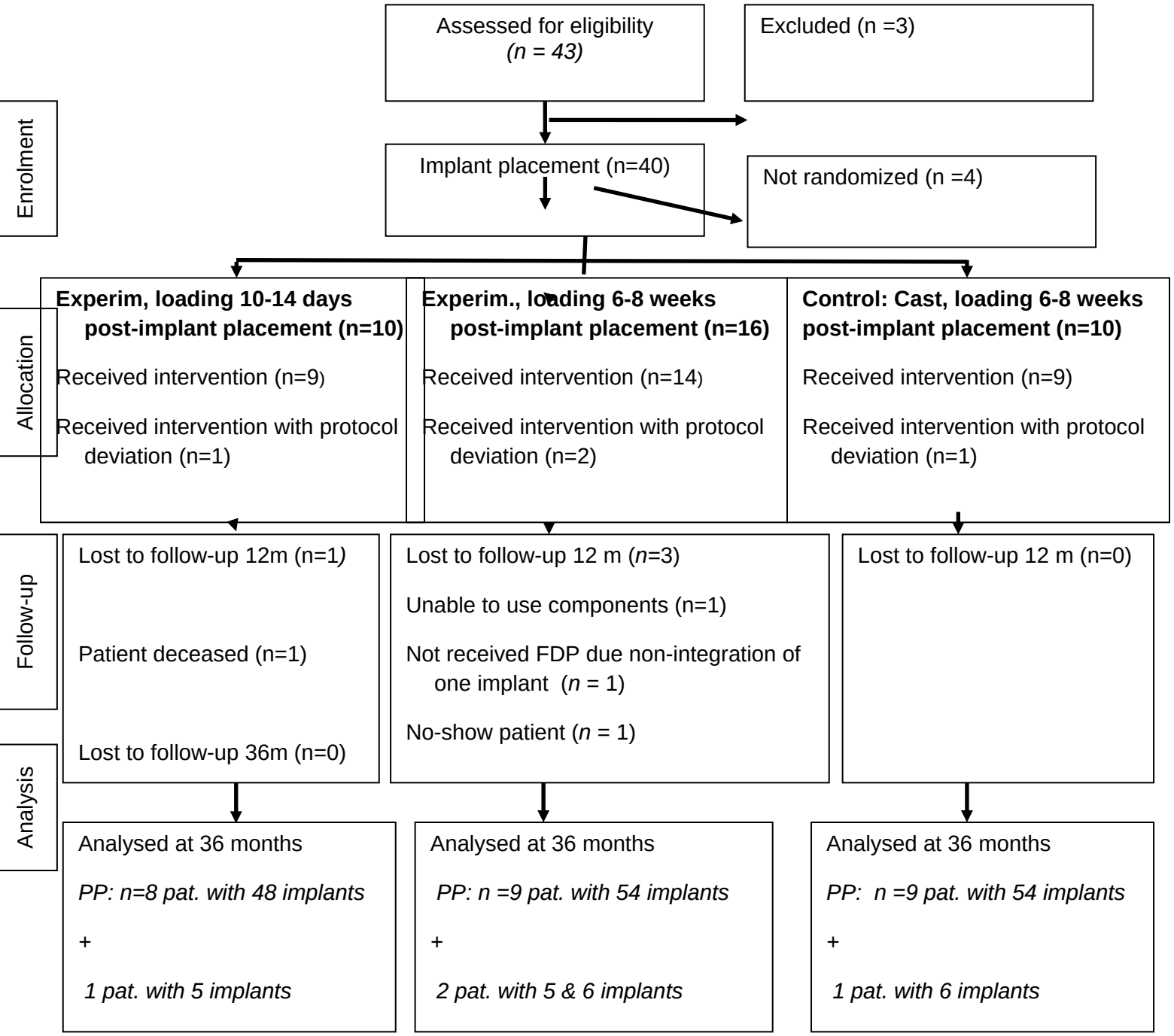
Relate to other findings or concepts

CONCLUSIONS

- I have confirmed something everyone known or
- I have confirmed what some have suspected or
- I have found something new that has never been considered
- Where do the findings lead?

EXAMPLE: Immediate Loading Study




Assessed for eligibility
(n = 43)
Excluded (n =3)
Enrolment
Implant placement (n=40)
Not randomized (n =4)
Allocation
Experim, loading 10-14 days post-implant placement (n=10)
Received intervention (n=9)
Received intervention with protocol deviation (n=1)
Experim., loading 6-8 weeks post-implant placement (n=16)
Received intervention (n=14)
Received intervention with protocol deviation (n=2)
Control: Cast, loading 6-8 weeks post-implant placement (n=10)
Received intervention (n=9)
Received intervention with protocol deviation (n=1)
Follow-up
Lost to follow-up 12m (n=1)
Patient deceased (n=1)
Lost to follow-up 36m (n=0)
Lost to follow-up 12 m (n=3)
Unable to use components (n=1)
Not received FDP due non-integration of one implant (n = 1)
No-show patient (n = 1)
Lost to follow-up 12 m (n=0)
Analysis
Analysed at 36 months
PP: n=8 pat. with 48 implants
+
1 pat. with 5 implants
Analysed at 36 months
PP: n =9 pat. with 54 implants
+
2 pat. with 5 & 6 implants
Analysed at 36 months
PP: n =9 pat. with 54 implants
+
1 pat. with 6 implants

CONSORT Statement 2001 Checklist

Items to include when reporting a randomized trial

PAPER SECTION And topic	Item	Descriptor	Reported on Page #
TITLE & ABSTRACT	1	How participants were allocated to interventions (*e.g.*, "random allocation", "randomized", or "randomly assigned").	
INTRODUCTION Background	2	Scientific background and explanation of rationale.	
METHODS Participants	3	Eligibility criteria for participants and the settings and locations where the data were collected.	
Interventions	4	Precise details of the interventions intended for each group and how and when they were actually administered.	
Objectives	5	Specific objectives and hypotheses.	
Outcomes	6	Clearly defined primary and secondary outcome measures and, when applicable, any methods used to enhance the quality of measurements (*e.g.*, multiple observations, training of assessors).	
Sample size	7	How sample size was determined and, when applicable, explanation of any interim analyses and stopping rules.	
Randomization -- Sequence generation	8	Method used to generate the random allocation sequence, including details of any restrictions (*e.g.*, blocking, stratification)	
Randomization -- Allocation concealment	9	Method used to implement the random allocation sequence (*e.g.*, numbered containers or central telephone), clarifying whether the sequence was concealed until interventions were assigned.	
Randomization -- Implementation	10	Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups.	
Blinding (masking)	11	Whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment. If done, how the success of blinding was evaluated.	
Statistical methods	12	Statistical methods used to compare groups for primary outcome(s); Methods for additional analyses, such as subgroup analyses and adjusted analyses.	
RESULTS Participant flow	13	Flow of participants through each stage (a diagram is strongly recommended). Specifically, for each group report the numbers of participants randomly assigned, receiving intended treatment, completing the study protocol, and analyzed for the primary outcome. Describe protocol deviations from study as planned, together with reasons.	
Recruitment	14	Dates defining the periods of recruitment and follow-up.	
Baseline data	15	Baseline demographic and clinical characteristics of each group.	

Numbers analyzed	16	Number of participants (denominator) in each group included in each analysis and whether the analysis was by "intention-to-treat". State the results in absolute numbers when feasible (*e.g.*, 10/20, not 50%).	
Outcomes and estimation	17	For each primary and secondary outcome, a summary of results for each group, and the estimated effect size and its precision (*e.g.*, 95% confidence interval).	
Ancillary analyses	18	Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating those pre-specified and those exploratory.	
Adverse events	19	All important adverse events or side effects in each intervention group.	
DISCUSSION Interpretation	20	Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision and the dangers associated with multiplicity of analyses and outcomes.	
Generalizability	21	Generalizability (external validity) of the trial findings.	
Overall evidence	22	General interpretation of the results in the context of current evidence.	

From Moher D, Schulz KF, Altman DG. The CONSORT statement: revised recommendations for improving the quality of reports of parallel-group randomised trials. Lancet 2001; 357(9263):1191-1194.

The CONSORT Statement 2001 checklist is intended to be accompanied with the explanatory document that facilitates its use. For more information, visit www.consort-statement.org.