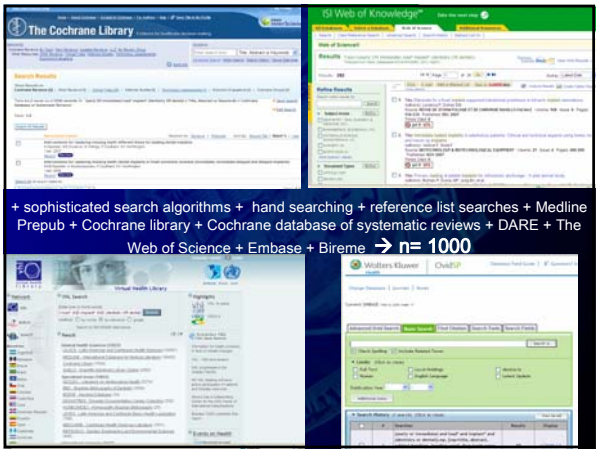
What have we learned from clinical trials about early loading of implants?

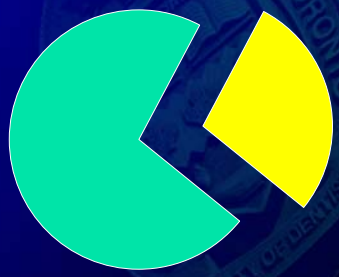
Asbjørn Jokstad, DDS, PhD
Professor and Head, Prosthodontics
Faculty of Dentistry, University of Toronto

SEARCH: (early OR immediate) load* implant* (dentistry OR dental)
→ N= 709 since 1988



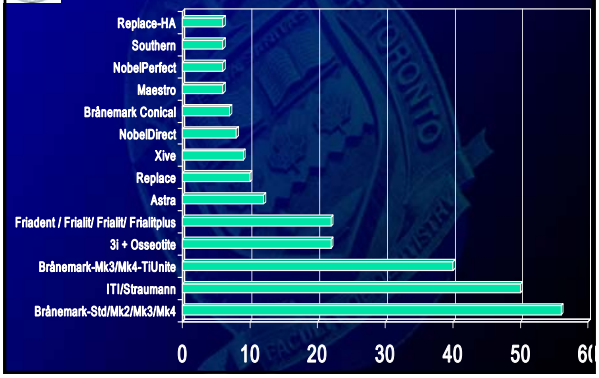
+ sophisticated search algorithms + hand searching + reference list searches + Medline Prepub + Cochrane library + Cochrane database of systematic reviews + DARE + The Web of Science + Embase + Bireme → n= 1000

Literature on shortened loading protocols (n~1000 papers)

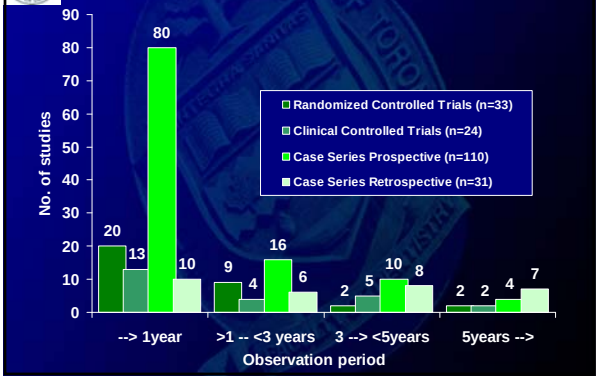


N=280 papers report data from clinical trials > n=1.

Clinical trials with focus on shortened loading protocols according to implant brand (n=280)



Shortened loading protocols in clinical trials sorted according to study design and observation period



General information

The first trials

- 1968 – 1975 (Brånemark et al. 1977: Experience from a 10-year period)
- TPS implants (Ledermann 1978); Tübinger Al_2O_3 (Schulte 1978)

The largest RCT trials

- 52 patients and 104 implants (Testori et al. 2007)
- 24 patients and 142 implants (Fischer et al. 2008)

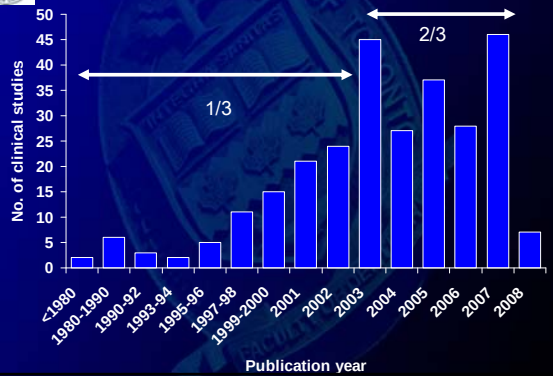
The longest follow up RCT trial

- 5 years (Roccuzzo et al., 2008 & Fischer et al. 2008)

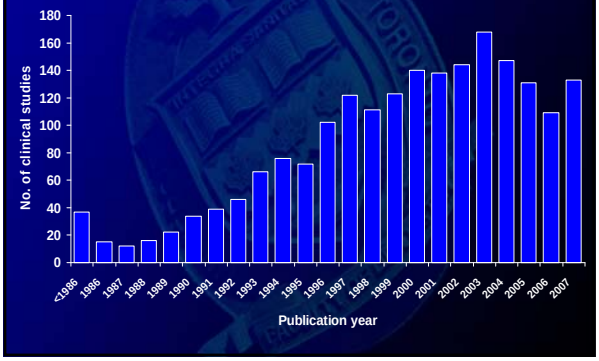
The longest observation period

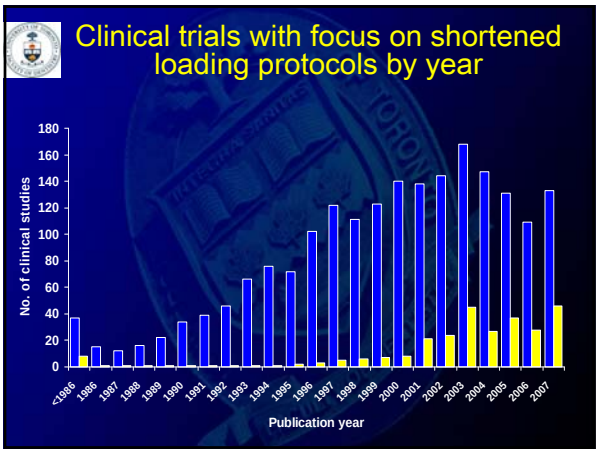
- 8-18 years, average 12, retrospective studies on ITI implants placed in the edentulous mandible (Lambrecht & Hodel 2007)

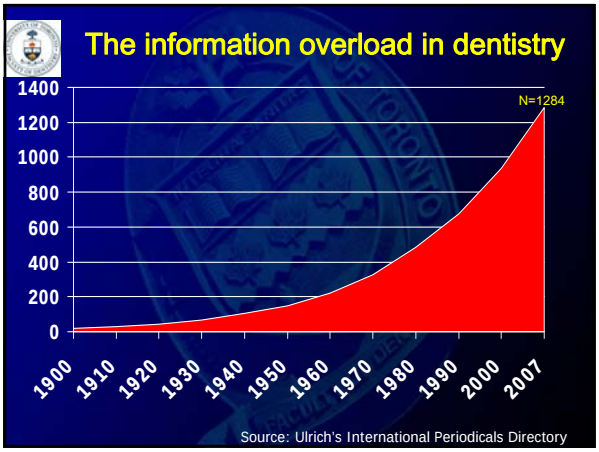
Clinical trials with focus on shortened loading protocols by year (n= 280)

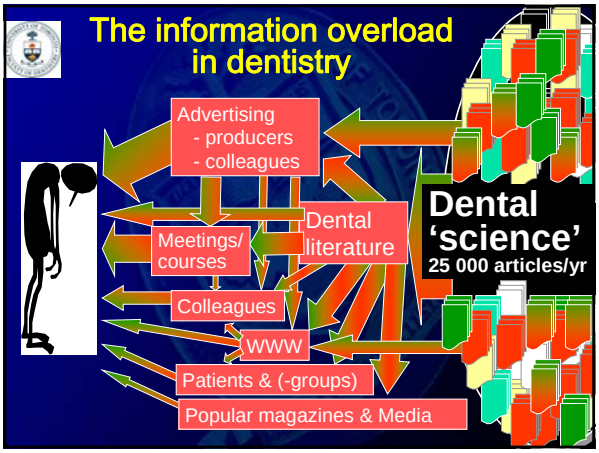


Clinical trials with focus on dental implants by year (n ~2000 trials)




Clinical trials with focus on shortened loading protocols by year
No. of clinical studies
Publication year

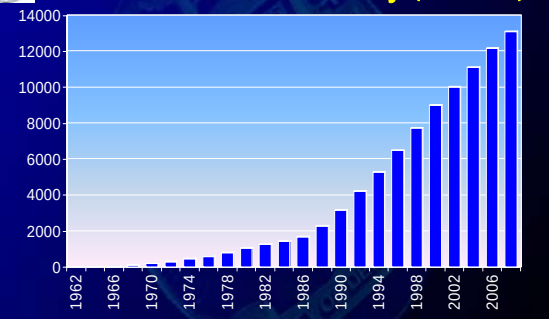

The information overload in dentistry
N=1284
Source: Ulrich's International Periodicals Directory


The information overload in dentistry
Advertising
- producers
- colleagues
Meetings/ courses
Dental literature
Colleagues
WWW
Patients & (-groups)
Popular magazines & Media
Dental 'science'
25 000 articles/yr

Solution?

Limit the reading to only Reviews?

Reviews in Dentistry (n=13.187)



(Source: Medline. OVID search strategy: review.pt + exp dentistry)

Literature on shortened loading protocols (n~1000 papers)

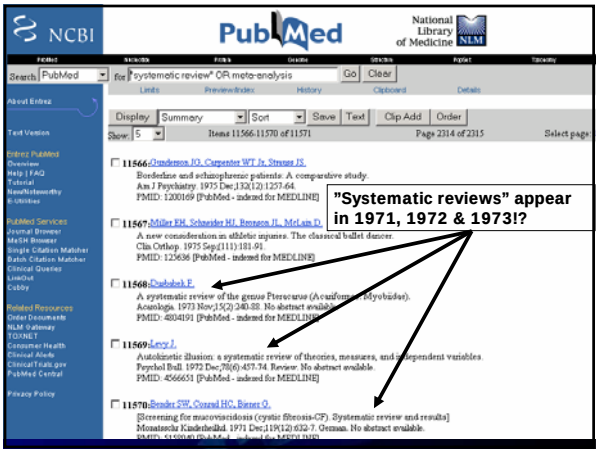
Reviews - problems

Usually:

- written by a single topic expert
- based on their understanding of the literature
- no methodology is given
- a broad based subject is addressed
- the conclusions and advises differ

Solution?

Drop the narrative style and look for the Systematic Reviews (SRs)?



"Systematic" review?

Is just a word!

Systematic Review:

5 Qualifyers are required

SR: 5 qualifyers

1. Question or hypothesis
2. All publications on the topic
3. Valid criteria to include or exclude identified studies
4. Extracted relevant data combined and compared
5. Conclusions based solely on the extracted data and the presence or absence of supporting evidence

Systematic Reviews - problems

- The selection of studies to include in SRs will reflect conclusions
- The study methodology aspects will reflect conclusions
- Need to focus on studies with good methodological designs

5 qualifyers required:

How effective is Guided Tissue Regeneration (GTR) when there is localized bone loss around teeth?

SR Conclusions: GTR attachment gain compared to open flap debridement

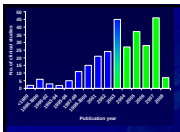
Laurell et al. *J Periodontol* 1998: 2.7 mm
- Uncontrolled and unblinded studies

Cortellini et al. *Periodontology 2000* 2000: 1.6 mm
- Unclear selection criteria for studies
- Inclusion of studies of short duration

Needleman et al. *Cochrane Review* 2001: 1.1 mm
- Randomised, controlled trials
- Trials only comparing GTR vs flap debridrement
- Trials > 12 months
- Furcation involvements excluded

In other words: Garbage in → Garbage out.

Literature on shortened loading protocols (n~1000 papers)



Best Systematic Reviews on shortened loading protocols

- Esposito et al. 2007(/2004). *Cochrane Syst Rev.*
- Jokstad & Carr. 2007. *Int J Oral Maxillofac Impl*
- Nkenke & Fenner. 2006. *Clin Oral Implants Res*
- Del Fabbro et al. 2006. *Int J Periodont Restor Dent*
- Attard & Zarb. 2005. *J Prosthet Dent*
- Cochran et al. 2004. *Int J Oral Maxillofac Impl*

Study	Esposito et al. (2007)	Jokstad & Carr (2007)	DelFabbro et al. (2006)	Nkenke & Fenner (2006)	Attard & Zarb (2005)	Cochrane et al. ITI Workshop (2004)
Dhanrajani & Al-Rafee 2005	---	Retro	---	---	---	---
Vanden Bogaerde et al. 2005	---	CCT	---	---	---	---
Ostman et al. 2005	---	excluded	---	X	---	---
Nedir et al. 2004 Bischof et al. 2004	---	CCT	---	---	---	---
Salvi et al. 2004	excluded	RCT	---	---	---	X
Fischer & Stenberg 2004	X	RCT	---	---	X	X
Testori et al. 2004	---	excluded	X	X	X	---
Cannizzaro & Leone 2003	X	CCT	X	X	X	X
Ibanez et al. 2003	---	CCT	---	---	---	---
Malo et al. 2003	---	Retro	X	---	X	---
Testori et al. 2003b	excluded	CCT	X	---	X	---
Wolfinger et al. 2003 Balshi & Wolfinger 1997	---	Submerg	X	---	X	X
Degidi & Piatelli 2003	---	excluded	X	X	X	---
Rocci et al. 2003	---	excluded	X	X	X	---
Tawse-Smith et al. 2002	X	RCT	---	---	X	X
Payne et al. 2002	X	RCT	---	---	X	X
Romeo et al. 2002	X	RCT	X	X	X	X
Gatti & Chiapasco 2002	---	excluded	X	X	X	---
Chausu et al. 2001	---	excluded	X	X	X	---
Chiapasco et al. 2001	X	RCT	X	X	X	X
De Bruyn et al. 2001	---	Submerg	---	---	X	---
Røynesdal et al. 2001	---	CCT	---	---	X	X
Ericsson et al. 2000	---	excluded	---	X	X	X
Roccuzzo et al. 2001	excluded	excluded	---	---	X	X
Jo et al. 2001	---	excluded	---	---	---	X
Randow et al. 2001	---	excluded	---	---	---	X
Schnitman et al. 1997 Schnitman et al. 1990	---	Submerg	X	---	X	X
Tarnow et al. 1997	---	Submerg	X	---	X	---

Reasons Systematic Reviews appraise different papers

- Inadequate literature search
- Selection bias
- Variable inclusion and exclusion criteria
  - CHECK: Excluded papers and reasons
- PICO question
  - Relative merit ?
  - Predictability ?

	Relative merit	*Predictability*
1.	*High quality RCT with narrow confidence Interval*	*Cohort study with ≥ 80% follow-up*
2.	*Cohort study or low quality RCT - e.g. <80% follow-up*	*Retrospective cohort study or follow-up of untreated control patients in an RCT*
3.	*Case-Control Study*	
4.	*Case-series (and poor quality cohort and case-control studies)*	*Case-series (and poor quality cohort studies)*
5.	*Expert opinion without explicit critical appraisal, or based on physiology, or bench research*	*Expert opinion without explicit critical appraisal, or based on physiology, or bench research*

Appropriate Study Designs to address implementation of interventions

	Qualitative research	Survey	Case Control	Cohort	RCT	Non-experimental	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?	☆☆	☆☆	☆	☆			☆

1882 → 187 → 22 papers

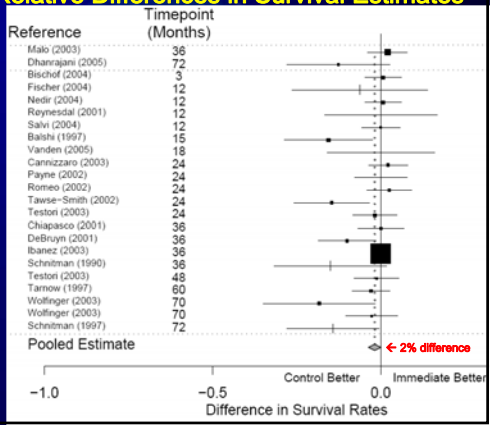
Clinical variables with potential influence on treatment outcomes

- Patient inclusion and exclusion criteria (e.g. host factors, smoking, parafunction, bone type, etc.)
- State of dentition and intra-oral implant site

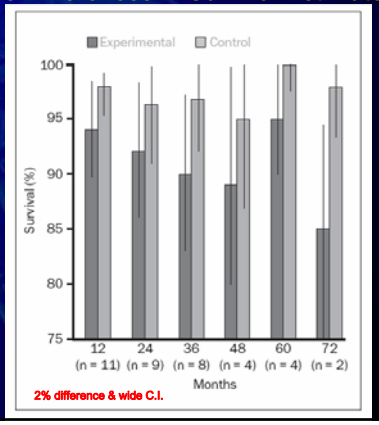
Clinical variables with potential influence on treatment outcomes

- Patient inclusion and exclusion criteria (e.g. host factors, smoking, parafunction, bone type, etc.)
- State of dentition and intra-oral implant site
- Number of implants to support a superstructure
- Nature of implant-supported superstructure
- Clinical procedures (e.g. stage of healing following extraction, site preparation, torque, etc.)
- Implant morphology (smooth, microrough, rough)
- Treatment outcome criteria
- Observation period

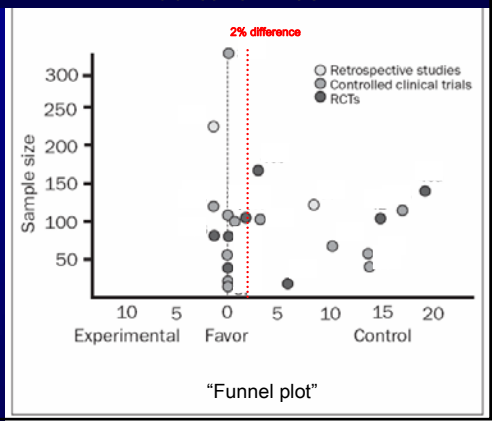
Relative Differences in Survival Estimates



Relative Differences in Survival Estimates

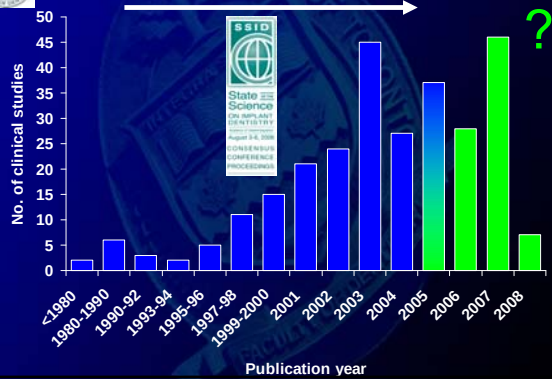


Publication Bias?

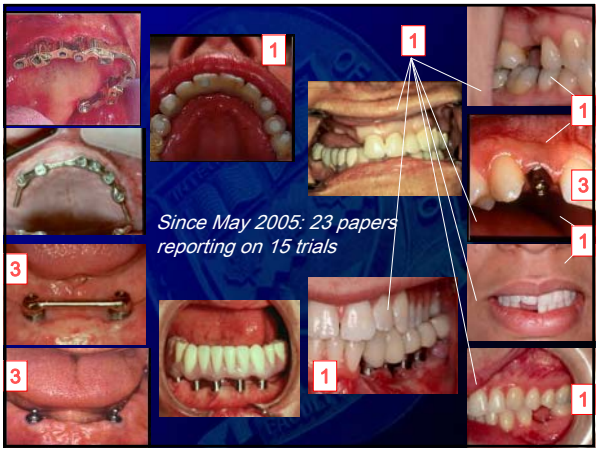


"Funnel plot"

Clinical trials with focus on shortened loading protocols by year (n= 280)



Authors	23 reports	Study	product	n-pas	n-imp	Time y.
Fischer et al.	2 reports	RCT	ITI-sla	24	142	5
Guncu et al.	2 reports	RCT	Branemark-Mk3-TiU	13	26	1-0.2
Testori et al.	1 report	RCT	Osseotite-FNT	52	104	1
De Smet et al.	1 report	CCT	Brånemark / Brånemark-Novum	30	70	2-1
Stephan et al.	1 report	CCT	Brånemark-Mk3-TiU	26	78	2
Assad et al.	1 report	RCT	Paragon	10	40	2
Romanos and Nentwig	1 report	RCT	Ankylos	12	36	2
Turkyilmaz et al.	4 reports	RCT	Branemark-Mk3-TiU	20	40	2
Turkyilmaz et al.	1 report	CCT	Branemark-Mk3-TiU	29	59	4
Oh et al.	1 report	RCT	Zimmer	24	25	0.5
Hall et al.	2 reports	RCT	Southern	28	28	1
Turkyilmaz et al.	3 reports	CCT	Brånemark-Mk3-TiU	26	52	1
Brochu et al.	1 report	CCT	Brånemark-TiU	22	41	0.3
Ottoni et al.	1 report	Other	Frialit-2	23	46	2
Tsirlis AT	1 report	CCT	Frialit-2(14) Osseotite(15) Osseotite-NT(14)	38	43	2



Summary

- In comparative trials, shortened loading protocols compared to delayed loading has in average 2% lower survival rates and more unpredictable outcomes
- Limited data suggest that shortened loading protocols in the interforaminal area can be considered as a reasonable treatment alternative to delayed loading
- It has not been demonstrated that a shortened loading protocol in itself is harmful.
- Considerations when treatment planning must be based on individual patient needs and expectations


Thank you for your
kind attention