Interventions for replacing missing teeth: different times for loading dental implants (Review)

Esposito M, Grusovin MG, Achille H, Coulthard P, Worthington HV

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[Intervention Review]

Interventions for replacing missing teeth: different times for loading dental implants

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ABSTRACT

Background

To minimize the risk of implant failure, osseointegrated dental implants are conventionally kept load-free during the healing period. During healing removable prostheses are used, however many patients find these temporary prostheses rather uncomfortable and it would be beneficial if the healing period could be shortened without jeopardizing implant success. Nowadays immediately and early loaded implants are commonly used in mandibles (lower jaws) of good bone quality. It would be useful to know whether there is a difference in success rates between immediately or early loaded implants compared with conventionally loaded implants.

Objectives

To evaluate the efficacy of (1) immediate (within 1 week), early (between 1 week and 2 months), and conventional (after 2 months) loading of osseointegrated implants, and of (2) immediate occlusal versus non-occlusal loading during the bone healing phase.

Search methods

The Cochrane Oral Health Group's Trials Register, CENTRAL, MEDLINE and EMBASE were searched. Handsearching included several dental journals. Authors of all identified trials, an Internet discussion group and 55 dental implant manufacturers were contacted to find unpublished randomised controlled trials (RCTs). The last electronic search was conducted on 4 June 2008.

Selection criteria

All RCTs of root-form osseointegrated dental implants, having a follow up of 4 months to 1 year, comparing the same implant type immediately, early and conventionally loaded or occlusally and non-occlusally loaded. Outcome measures were: prosthesis and implant failures and radiographic marginal bone level changes.

Data collection and analysis

Data were independently extracted, in duplicate, by two review authors. Authors were contacted for details of randomisation and withdrawals and a quality assessment was carried out. The Cochrane Collaboration's statistical guidelines were followed.

Main results

Thirty RCTs were identified and 22 trials including 1024 participants in total were included. Twelve trials compared immediate versus conventional loading, three early versus conventional loading, six immediate versus early loading, and one occlusally versus non-occlusally loaded implants. On a patient, rather than per implant basis, there were no statistically significant differences for any of the meta-analyses.

Authors' conclusions

It is possible to successfully load dental implants immediately or early after their placement in selected patients, though not all clinicians may achieve optimal results. It is unclear whether it is beneficial to avoid occlusal contacts during the osseointegration phase. Trends suggest that immediately loaded implants fail more often than those conventionally loaded, but less commonly than those loaded early. If a clinician wishes to load the implants early, it might be wiser to load them immediately (within 1 week) rather than waiting for 1 or 2 months. A high degree of primary implant stability (high value of insertion torque) seems to be one of the prerequisites for a successful immediate/early loading procedure. More well designed RCTs are needed and should be reported according to the CONSORT guidelines (www.consort-statement.org/).

PLAIN LANGUAGE SUMMARY

Interventions for replacing missing teeth: different times for loading dental implants

Some people may be able to have artificial teeth attached to dental implants immediately instead of having to wait for months, but more research is needed to be sure.

When people have dental implants in their jaws, they wait several months for the bone around the implants to heal before artificial teeth are attached (using removable dentures in the meantime). If artificial teeth could be loaded onto the implant immediately, people might be able to start chewing comfortably the same day or within weeks. The review found some evidence from studies that immediate or early loading of artificial teeth may have a slightly poorer outcome than conventional (after waiting for several months) loading. However, it is possible to successfully load dental implants immediately or early after their placement in selected people, although not all clinicians may obtain such good results.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON *[Explanation]*

Conventional compared with immediate loading of dental implants

Patient or population: patients requiring dental implants
Settings: dental practice
Intervention: immediate loading
Comparison: conventional loading

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Conventional	Immediate				
Prosthesis failure at 1 year	Low risk population		RR 2.41 (0.76 to 7.63)	257 (6)	+000 very low	
	10 per 1000	24 per 1000 (8 to 76)				
	High risk population					
	100 per 1000	241 per 1000 (76 to 763)				

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI = confidence interval
RR = risk ratio
GRADE Working Group grades of evidence:
High quality (++++): Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality (+++0): Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality (++00): Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality (+000): We are very uncertain about the estimate.

BACKGROUND

Missing teeth and supporting oral tissues have traditionally been replaced with dentures or bridges to restore the ability of patients to eat and speak and improve appearance. However, in several instances, patients are not satisfied with the function of removable dentures and it is not always possible to place a fixed bridge if the number of remaining abutment teeth is insufficient. Since the 1970s, osseointegrated dental implants have offered an alternative (Brånemark 1977). They are surgically inserted into the jaw bones to support a dental prosthesis and are retained because of the intimacy of bone growth onto their surface (osseointegration). Dental implants have undoubtedly been one of the most significant scientific breakthroughs in dentistry over the past 30 years.

Primary implant stability and lack of micromovements are considered to be two of the main factors necessary for achieving predictable high success of osseointegrated oral implants (Albrektsson 1981). A successful osseointegrated oral implant is anchored directly to bone, however, in the presence of movement a soft tissue interface may encapsulate the implant (Brunski 1979) causing its failure. To minimize the risk of soft tissue encapsulation, it has been recommended to keep the implants load-free during the healing period (3 to 4 months in mandibles (lower jaws) and 6 to 8 months in maxillae (upper jaws)) (Brånemark 1977).

In general, during the healing period removable prostheses are used, however many patients find these temporary prostheses rather uncomfortable and it would therefore be beneficial if the healing period could be shortened without jeopardizing implant success. In 1990 the first longitudinal clinical trial was published suggesting that implants could be loaded immediately or early in the mandibles of selected patients (Schnitman 1990). Nowadays immediately and early loaded implants are commonly used particularly in mandibles of good bone quality (Brånemark 1999). Some authors also advocate that the use of some specific implant surface preparation is able to reduce the healing time (Roccuzzo 2001). To decrease the risk of immediately loaded implants failing early, various 'clinical tricks' have been suggested such as underpreparation of the implant site to achieve high primary stability (Cannizzaro 2003); the use of a non-occluding temporary prosthesis during the first 2 months of healing (Testori 2003); or the progressive loading of the prostheses. While the success of immediately loaded implants in mandibles has been documented for instance on earlier versions of the present Cochrane review (Esposito 2003; Esposito 2004; Esposito 2007b), less evidence is available regarding the efficacy of immediately loaded maxillary implants.

It would be useful to know whether there are differences in success rates between immediately or early loaded implants compared with conventionally loaded implants in different clinical indications (full and partial edentulism, mandibles and maxillae), and if there are some surface modifications able to promote a faster bone healing (for the role of the surface characteristics the reader is referred to another Cochrane review (Esposito 2007). It is likely that the effect of loading at different times would become apparent during the first 4 months to 1 year of loading and therefore it was decided to make all comparisons at 4 months to 1 year after loading, preferably at 1 year when possible. A few systematic reviews (Ioannidou 2005; Del Fabbro 2006) have been published after the previous versions of the present review, however they did not focus on the highest level of evidence (randomised controlled clinical trials), therefore their results have to be interpreted with great caution.

OBJECTIVES

(1) To test the null hypothesis of no difference in the clinical outcome between the same osseointegrated dental implants loaded immediately, early or conventionally, against the alternative hypothesis of a difference.

(2) To test the null hypothesis of no difference in the clinical outcome between the same osseointegrated dental implants occlusally or non-occlusally loaded during the osseointegration period, against the alternative hypothesis of a difference.

METHODS

Criteria for considering studies for this review

Types of studies

All randomised controlled trials of root-form osseointegrated dental implants having a follow up of 4 months to 1 year after loading (whenever possible the 1-year data were used).

Types of participants

Patients who are having osseointegrated root-form dental implants.

Types of interventions

(1) Trials comparing the same osseointegrated root-form dental implants loaded at different times. For the purpose of this review immediate loading was defined as an implant put in function within 1 week after its placement; early loading as those implants put in function between 1 week and 2 months; and conventional loading as those implants loaded after 2 months. In particular the following comparisons were planned: (1) immediately versus conventionally loaded implants; (2) early versus conventionally loaded implants; (3) immediately versus early loaded implants. Both occlusally and non-occlusally immediately loaded implants were considered as immediately loaded implants in this review.

(2) Trials comparing the same osseointegrated root-form dental implants occlusally or non-occlusally loaded during the osseointegration phase.

Types of outcome measures

- Prosthesis failure if secondary to implant failure.
- Implant failures (implant mobility and removal of stable implants dictated by progressive marginal bone loss).
- Radiographic marginal bone level changes on intraoral radiographs taken with a parallel technique.

Search methods for identification of studies

For the identification of studies included or considered for this review, we developed detailed search strategies for each database to be searched. These were based on the search strategy developed for MEDLINE (OVID) but revised appropriately for each database. The subject search (Appendix 1) used a combination of controlled vocabulary and free text terms and was run with the Cochrane Highly Sensitive Search Strategy (CHSSS) for identifying randomised controlled trials (RCTs) in MEDLINE: sensitivity maximising version (2008 revision) as referenced in Chapter 6.4.11.1 and detailed in box 6.4.c of the *Cochrane Handbook for Systematic Reviews of Interventions* 5.0.0 (updated February 2008) (Appendix 2).

Searched databases

The Cochrane Oral Health Group's Trials Register (to 4 June 2008).
The Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2008, Issue 2).
MEDLINE (1966 to 4 June 2008).
EMBASE (1980 to 4 June 2008).
The most recent electronic search was undertaken on 4 June 2008.

Language

There were no language restrictions.

Unpublished studies

We wrote to all the authors of the identified RCTs, we checked the bibliographies of all identified RCTs and relevant review articles, and we used personal contacts in an attempt to identify unpublished or ongoing RCTs. In the first version of this review we also wrote to more than 55 oral implant manufacturers and we requested information on trials through an Internet discussion group (implantology@yahoogroups.com), however we discontinued this due to poor yield.

Handsearching

Details of the journals being handsearched by the Cochrane Oral Health Group's ongoing programme are given on the website: www.ohg.cochrane.org.
The following journals have been identified as being potentially important to be handsearched for this review: *British Journal of Oral and Maxillofacial Surgery*, *Clinical Implant Dentistry and Related Research*, *Clinical Oral Implants Research*, *European Journal of Oral Implantology*, *Implant Dentistry*, *International Journal of Oral and Maxillofacial Implants*, *International Journal of Oral and Maxillofacial Surgery*, *International Journal of Periodontics and Restorative Dentistry*, *International Journal of Prosthodontics*, *Journal of Clinical Periodontology*, *Journal of Dental Research*, *Journal of Oral Implantology*, *Journal of Oral and Maxillofacial Surgery*, *Journal of Periodontology*, and *Journal of Prosthetic Dentistry*. Where these have not already been searched as part of the Cochrane Journal Handsearching Programme, the journals were handsearched by one review author up to the month in which the last electronic search was undertaken.

Data collection and analysis

The titles and abstracts (when available) of all reports identified through the electronic searches were scanned independently by two review authors. For studies appearing to meet the inclusion criteria, or for which there were insufficient data in the title and abstract to make a clear decision, the full report was obtained. The full reports obtained from all the electronic and other methods of searching were assessed independently by two review authors to establish whether the studies did meet the inclusion criteria or not. Disagreements were resolved by discussion. Where resolution was not possible, a third review author was consulted. All studies meeting the inclusion criteria then underwent validity assessment and data extraction. Studies rejected at this or subsequent stages were recorded in the Characteristics of excluded studies table, and reasons for exclusion recorded.

Data extraction

Data were extracted by two review authors independently and in duplicate using specially designed data extraction forms. The data extraction forms were piloted on several papers and modified as required before use. Any disagreement was discussed and a third review author consulted where necessary. All authors were contacted for clarification or missing information. Data were excluded until further clarification was available or if agreement could not be reached.
For each trial the following data were recorded.

- Year of publication, country of origin and source of study funding.
- Details of the participants including demographic characteristics and criteria for inclusion.

- Details of the type of intervention.
- Details of the outcomes reported, including method of assessment, and time intervals.

Quality assessment

The quality assessment of the included trials was undertaken independently and in duplicate by two review authors as part of the data extraction process.

Three main quality criteria were examined.

(1) Allocation concealment, recorded as:

(A) Adequate

(B) Unclear

(C) Inadequate.

Allocation concealment was considered adequate if it was centralised (e.g. allocation by a central office unaware of subject characteristics); pharmacy-controlled randomisation; pre-numbered or coded identical containers which were administered serially to participants; on-site computer system combined with allocation kept in a locked unreadable computer file that can be accessed only after the characteristics of an enrolled patient have been entered; sequentially numbered, sealed, opaque envelopes; and other approaches similar to those listed above, along with the reassurance that the person who generated the allocation scheme did not administer it. Some schemes may be innovative and not fit any of the approaches above, but still provide adequate concealment. Approaches to allocation concealment which were considered clearly inadequate included any procedure that was entirely transparent before allocation, such as an open list of random numbers. Ideally the surgeon should have known the group allocation just after implants were inserted. Those articles or authors stating that allocation concealment procedures were implemented but did not provide details on how this was accomplished, were coded as 'unclear'.

(2) Treatment blind to outcomes assessors, recorded as:

(A) Yes

(B) No

(C) Unclear.

(3) Completeness of follow up (is there a clear explanation for withdrawals and drop outs in each treatment group?) assessed as.

(A) No drop outs/yes. In the case that clear explanations for drop outs were given, a further subjective evaluation of the risk of bias assessing the reasons for the drop out was made.

(B) No.

After taking into account the additional information provided by the authors of the trials, studies were grouped into the following categories.

(A) Low risk of bias (plausible bias unlikely to seriously alter the results) if all criteria were met.

(B) High risk of bias (plausible bias that seriously weakens confidence in the results) if one or more criteria were not met.

Further quality assessment was carried out to assess sample size calculations, definition of exclusion/inclusion criteria, and comparability of control and test groups at entry. The quality assessment criteria were pilot tested using several articles.

Data synthesis

For dichotomous outcomes, the estimates of effect of an intervention were expressed as risk ratios (RR) together with 95% confidence intervals. For continuous outcomes, mean differences and standard deviations were used to summarize the data for each group. The statistical unit was the patient and not the implant.

Only if there were studies of similar comparisons reporting the same outcome measures was meta-analysis to be attempted. Risk ratios were combined for dichotomous data, and mean differences for continuous data, using a random-effects model. Data from split-mouth studies were combined with data from parallel group trials with the method outlined by Elbourne (Elbourne 2002), using the generic inverse variance method in Review Manager (RevMan) 5 software. The techniques described by Follmann (Follmann 1992) were to be used to estimate the standard error (SE) of the difference for split-mouth studies, where the appropriate data were not presented and could not be obtained. One study presented the mean difference (SE) for the mesial and distal radiographic scores separately (Lindeboom 2006). To calculate the total score the mean differences were averaged and a conservative standard error was calculated assuming zero correlation. For rare events odds ratios (OR) for split-mouth trials were calculated using the Becker-Balagtas methods outlined in Curtin 2002. As OR are similar to RR when the event rate is low we have simply used this value in place of RR for these studies. When using the generic inverse variance to combine studies of parallel design with studies of split-mouth design, studies with both zero events could not be imputed in the meta-analyses because RevMan 5 software does not allow it.

The significance of any discrepancies in the estimates of the treatment effects from the different trials was assessed by means of Cochran's test for heterogeneity and the I^2 statistic, which describes the percentage total variation across studies that is due to heterogeneity rather than chance. Clinical heterogeneity was to be assessed by examining the types of participants and interventions for all outcomes in each study. It was planned to undertake sensitivity analyses to examine the effect of the study quality assessment on the overall estimates of effect. In addition, the effect of including unpublished literature on the review's findings was also to be examined, but there were insufficient trials to undertake this.

The following subgroup analyses were planned, however there were insufficient studies in the meta-analysis to undertake this.

(1) Whether implants were placed in mandibles or maxillae.

(2) Whether implants were placed in partially or fully edentulous jaws.

(3) Whether implants were placed in the anterior or posterior jaw.

(4) Different number of inserted implants (for instance overdentures supported by two versus overdentures supported by four implants).

(5) Whether turned (machined) or implants with a roughened surface were used.
(6) Whether the trial was supported by implant manufacturer(s) or not.

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies; Characteristics of ongoing studies.

Characteristics of the trial settings and investigators

Of the 30 potentially eligible trials (Polson 2000; Chiapasco 2001; Roccuzzo 2001; Payne 2002; Romeo 2002; Tawse-Smith 2002; Cannizzaro 2003; Testori 2003; Fischer 2004; Salvi 2004; Ottoni 2005; Hall 2006; Lindeboom 2006; Oh 2006; Romanos 2006; Turkyilmaz 2006; Assad 2007; Göthberg 2007; Testori 2007; Turkyilmaz 2007; Cannizzaro 2008a; Cannizzaro 2008b; Cannizzaro 2008c; Cannizzaro 2008d; Crespi 2008; Donati 2008; Güncü 2008; Merli 2008; Schincaglia 2008; Zöllner 2008), eight trials had to be excluded. One trial (Polson 2000) was excluded due to insufficient data presented; four trials (Roccuzzo 2001; Testori 2003; Cannizzaro 2008c; Göthberg 2007) because of various additional confounding factors; one trial (Salvi 2004) because it tested comparisons outside the scope of the present review; and two trials because they were not randomised controlled trials (RCTs) (Ottoni 2005; Turkyilmaz 2006).
Of the 22 included trials (Chiapasco 2001; Payne 2002; Romeo 2002; Tawse-Smith 2002; Cannizzaro 2003; Fischer 2004; Hall 2006; Lindeboom 2006; Oh 2006; Romanos 2006; Assad 2007; Testori 2007; Turkyilmaz 2007; Cannizzaro 2008a; Cannizzaro 2008b; Cannizzaro 2008d; Crespi 2008; Donati 2008; Güncü 2008; Merli 2008; Schincaglia 2008; Zöllner 2008), 11 were conducted in Italy (Chiapasco 2001; Romeo 2002; Cannizzaro 2003; Testori 2007; Cannizzaro 2008a; Cannizzaro 2008b; Cannizzaro 2008d; Crespi 2008; Donati 2008; Merli 2008; Schincaglia 2008), three in New Zealand (Payne 2002; Tawse-Smith 2002; Hall 2006), two in Turkey (Turkyilmaz 2007; Güncü 2008), one in The Netherlands (Lindeboom 2006), one in Sweden (Fischer 2004), one in Germany (Romanos 2006), one in USA (Oh 2006), one in Egypt (Assad 2007), and one was run in several countries (Zöllner 2008). Nineteen trials had a parallel group study design and three a split-mouth study design (Romanos 2006; Cannizzaro 2008d; Güncü 2008). One trial (Donati 2008) of parallel group design had 10 patients treated as with a split-mouth design; these 10 patients were excluded from the calculations in the present review.
Thirteen trials were conducted at university dental clinics (Chiapasco 2001; Payne 2002; Romeo 2002; Tawse-Smith 2002; Hall 2006; Lindeboom 2006; Oh 2006; Romanos 2006; Assad 2007; Turkyilmaz 2007; Crespi 2008; Güncü 2008; Schincaglia 2008), seven (Cannizzaro 2003; Testori 2007; Cannizzaro 2008a; Cannizzaro 2008b; Cannizzaro 2008d; Donati 2008; Merli 2008) in private practices, one (Fischer 2004) in a specialist public clinic, and one in both university clinics and private practices (Zöllner 2008).
Thirteen trials received support from industry (Payne 2002; Tawse-Smith 2002; Fischer 2004; Hall 2006; Oh 2006; Lindeboom 2006; Romanos 2006; Testori 2007; Turkyilmaz 2007; Cannizzaro 2008d; Donati 2008; Merli 2008; Zöllner 2008). All studies included only adults.

Characteristics of interventions

(A) Immediate versus conventional loading

Immediate loading was compared with conventional loading in 12 trials (Chiapasco 2001; Romeo 2002; Cannizzaro 2003; Hall 2006; Oh 2006; Romanos 2006; Assad 2007; Turkyilmaz 2007; Crespi 2008; Donati 2008; Güncü 2008; Schincaglia 2008).
Chiapasco 2001; Romeo 2002; Assad 2007 and Turkyilmaz 2007 compared four implants in each edentulous mandible immediately loaded after insertion (2 to 7 days) with four implants conventionally loaded after 3 to 8 months.
Cannizzaro 2003 compared one or more implants in partially edentulous patients in both mandibles and maxillae loaded the same day with implants conventionally loaded (3.5 months for mandibles and 4.5 months for maxillae).
Hall 2006 compared one single implant loaded the same day with one single implant conventionally loaded at 6 months in the anterior maxilla (between premolars).
Oh 2006 compared one single implant loaded the same day with one single implant conventionally loaded at 4 months placed with a flapless procedure in the anterior maxilla (between premolars).
Romanos 2006 in a split-mouth design compared three mandibular implants distal to the canines loaded the same day with three implants on the contralateral side conventionally loaded at 3 months.
Crespi 2008 compared one single implant in fresh extraction sockets in the maxillary aesthetic zone immediately occlusally loaded the same day with one single implant conventionally loaded at 3 months.
Donati 2008 compared one single implant immediately loaded within 24 hours with one single implant conventionally loaded at 3 months in area 15-25 and 35-45. Immediately loaded sites were treated with two different preparation techniques (drills versus osteotomes). Ten patients were treated according to a split-mouth design and were excluded.
Güncü 2008 in a split-mouth design compared one single mandibular implant in the first molar site loaded the same day with one single contralateral implant loaded after 3 months.
Schincaglia 2008 compared one single implant loaded within 24

hours with one implant loaded after 3 months in the first or second mandibular molar site.

(B) Early versus conventional loading

Early loading was compared with conventional loading in three trials (Payne 2002; Tawse-Smith 2002; Fischer 2004).

Payne 2002 and Tawse-Smith 2002 compared two implants in fully edentulous mandibles early loaded at 6 weeks or conventionally loaded at 12 weeks.

Fischer 2004 compared five to six implants in fully edentulous maxillae early loaded (9 to 18 days) or conventionally loaded (2.5 to 5.1 months).

(C) Immediate versus early loading

Immediate loading was compared with early loading in six trials (Testori 2007; Cannizzaro 2008a; Cannizzaro 2008b; Cannizzaro 2008d; Merli 2008; Zöllner 2008).

Testori 2007 compared implants in both mandibles and maxillae of partially edentulous patients, immediately but non-occlusally loaded (when possible) within 48 hours with implants early loaded at 2 months.

Cannizzaro 2008a compared two implants in fully edentulous mandibles loaded the same day or early loaded at 6 weeks.

Cannizzaro 2008b compared five to eight implants, placed flapless, in fully edentulous maxillae loaded the same day or early loaded at 2 months.

Cannizzaro 2008d in a split-mouth design compared one single 7 mm long implant, placed flapless, occlusally loaded the same day with one implant early loaded at 6 weeks.

Merli 2008 compared implants, placed flapless, in both mandibles and maxillae of partially edentulous patients, immediately but non-occlusally loaded (when possible) within 72 hours with implants early non-occlusally loaded at 6 weeks.

Zöllner 2008 compared one to four implants in both posterior mandibles and maxillae of partially edentulous patients, immediately but non-occlusally loaded the same day with implants early non-occlusally loaded at 1 month.

(D) Occlusal versus non-occlusal loading

Occlusal loading was compared with non-occlusal loading in one trial (Lindeboom 2006).

Lindeboom 2006 compared immediately occlusally loaded single implants with immediately non-occlusally loaded implants within 1 day in the anterior and premolar region of the maxilla.

Seventeen different implant systems were used.

(1) 3i® Osseotite FNT (3i Biomet, Palm Beach, Florida, USA) titanium tapered screws (Testori 2007).

(2) 3i® Nanotite (3i Biomet, Palm Beach, Florida, USA) titanium grade 5 cylindrical screws (Cannizzaro 2008d).

(3) Ankylos® (Degussa Dental, Hanau-Wolfang, Germany) grit-roughened titanium grade 2 screws (Romanos 2006).

(4) Astra OsseoSpeed® (Astra Tech Dental, Mölndal, Sweden) titanium grade 1 screws (Donati 2008).

(5) BioComp® (BioComp Industries BV, Vught, The Netherlands) tapered titanium plasma sprayed (TPS) screws (Lindeboom 2006).

(6) Brånemark® (Nobel Biocare AB, Göteborg, Sweden) Mark II type turned titanium grade 1 screws (Chiapasco 2001).

(7) Brånemark® (Nobel Biocare AB, Göteborg, Sweden) TiUnite Mark III type titanium grade 1 screws (Turkyilmaz 2007; Güncü 2008), wide body (Schincaglia 2008).

(8) ITI® SLA (Institut Straumann AG, Waldenburg, Switzerland) solid sand-blasted large-grit acid-etched titanium grade 4 screws (Payne 2002; Romeo 2002; Fischer 2004).

(9) ITI® SLA active (Institut Straumann AG, Waldenburg, Switzerland) solid sand-blasted large-grit acid-etched titanium grade 4 screws, three standard plus implants were also used (Zöllner 2008).

(10) Outlink (Sweden & Martina, Padova, Italy) titanium plasma-sprayed cylindrical screws (Crespi 2008).

(11) Southern® (Southern Implants Irene, South Africa) sand-blasted acid-etched titanium grade 4 screws (Tawse-Smith 2002; Hall 2006).

(12) Steri-Oss® (Steri-Oss, Yorba Linda, California, USA) HL series, 3.8 mm in diameter acid-etched titanium grade 4 screws (Tawse-Smith 2002).

(13) Thommen® (SPI®Element System; Thommen Medical AG, Waldenburg, Switzerland) sand-blasted acid-etched screws. In some of the post-extraction sites SPI®Contact troncoconical screws were used (Merli 2008).

(14) Zimmer® tapered SwissPlus (Zimmer Dental, Carlsbad, California, USA) dental implants (Cannizzaro 2008a; Cannizzaro 2008b).

(15) Zimmer® Spline Twist MTX (Zimmer Dental, Carlsbad, California, USA) HA-blasted and acid-etched titanium screws (Cannizzaro 2003).

(16) Zimmer® unknown type (Zimmer Dental, Carlsbad, California, USA) dental implants (Oh 2006).

(17) Zimmer® Screw-Vent® (but described as Paragon, Core-Vent Corporation, Las Vegas, USA) titanium dental screws (Assad 2007).

Early and conventionally loaded implants were used according to a submerged (two-stage) procedure, i.e. the implants were covered by the mucosa during the healing phase, thus a second surgical intervention was necessary to connect the abutments (posts) to the implants (Chiapasco 2001; Hall 2006; Romanos 2006; Assad 2007; Crespi 2008; Donati 2008) or according to a non-submerged (one-stage) protocol, i.e. the abutments were directly connected to the implants, thus a second operation was avoided (Payne 2002; Romeo 2002; Tawse-Smith 2002; Cannizzaro 2003; Fischer 2004; Oh 2006; Testori 2007; Turkyilmaz 2007; Cannizzaro 2008a; Cannizzaro 2008b; Cannizzaro 2008d; Güncü 2008; Merli 2008; Schincaglia 2008; Zöllner 2008).

- Removable overdentures were retained by clip attachments to a bar supported by four implants (Chiapasco 2001; Romeo 2002; Assad 2007) or two implants (Cannizzaro 2008a), or were retained by two unsplinted ball attachments (Payne 2002; Tawse-Smith 2002; Turkyilmaz 2007).
- Fixed maxillary full-arch prostheses, without using provisional ones, were connected to the implant in one trial (Fischer 2004). In another trial (Cannizzaro 2008b) provisional cemented metal reinforced acrylic full-arch maxillary prostheses were replaced by metal ceramic or metal resin full-arch prostheses after 2 to 3 months.
- Temporary resin bridges/crowns were fabricated and then replaced by final restorations in 11 trials (Cannizzaro 2003; Hall 2006; Lindeboom 2006; Romanos 2006; Testori 2007; Cannizzaro 2008d; Crespi 2008; Donati 2008; Güncü 2008; Merli 2008; Zöllner 2008). In six of theses studies only single crowns were used (Hall 2006; Lindeboom 2006; Cannizzaro 2008d; Crespi 2008; Donati 2008; Güncü 2008).
- Temporary resin crowns were fabricated and then replaced by final metal-ceramic crowns in the immediately loaded group, whereas permanent metal-ceramic crowns were delivered in the conventionally loaded group in two trials (Oh 2006; Schincaglia 2008).

Occlusal or non-occlusal immediate loading

In 15 trials, the prostheses were put in full occlusion (Chiapasco 2001; Romeo 2002; Cannizzaro 2003; Lindeboom 2006; Oh 2006; Romanos 2006; Assad 2007; Turkyilmaz 2007; Cannizzaro 2008a; Cannizzaro 2008b; Cannizzaro 2008d; Crespi 2008; Donati 2008; Güncü 2008; Schincaglia 2008).
In five trials, the prostheses were not put in full occlusion for 2 (Hall 2006; Testori 2007), 5 (Zöllner 2008), or 6 months (Lindeboom 2006; Merli 2008).

Characteristics of outcome measures

- Prosthesis failures (all trials with the exception of Zöllner 2008 for which the number of prosthetic failures was assumed to be identical to the number of implant failures).
- Implant failures (all trials).
- Radiographic bone level changes were assessed in all trials with three exceptions (Oh 2006; Cannizzaro 2008a; Merli 2008). However, the peri-implant bone level measurements of seven trials were not included in the present analyses because they were performed on panoramic radiographs (Chiapasco 2001; Romeo 2002; Romanos 2006) or because data were presented in a way we could not use (Fischer 2004; Assad 2007; Donati 2008; Zöllner 2008).

Risk of bias in included studies

Allocation concealment

After considering the replies from the authors, the method of allocation concealment was considered adequate for nine trials (Cannizzaro 2003; Fischer 2004; Lindeboom 2006; Testori 2007; Cannizzaro 2008a; Cannizzaro 2008b; Cannizzaro 2008d; Güncü 2008; Merli 2008), unclear for eight trials (Payne 2002; Tawse-Smith 2002; Hall 2006; Oh 2006; Romanos 2006; Assad 2007; Crespi 2008; Donati 2008). No allocation concealment was used in five trials (Chiapasco 2001; Romeo 2002; Turkyilmaz 2007; Schincaglia 2008; Zöllner 2008).

Blinding

After considering the replies from the authors, outcome assessors were blinded in 12 trials (Chiapasco 2001; Payne 2002; Romeo 2002; Tawse-Smith 2002; Cannizzaro 2003; Hall 2006; Lindeboom 2006; Oh 2006; Cannizzaro 2008a; Cannizzaro 2008b; Cannizzaro 2008d; Güncü 2008). In four trials the outcome assessor was blinded for marginal bone level evaluation only (Testori 2007; Donati 2008; Schincaglia 2008; Zöllner 2008). In four trials the outcome assessors were not blinded (Fischer 2004; Romanos 2006; Turkyilmaz 2007; Merli 2008), though in one trial one independent assessor was used to assess implant stability (Merli 2008); in two trials it was unclear (Assad 2007; Crespi 2008).

Completeness of follow up

After considering the replies from the authors, clear explanations for drop outs were given in all trials with one exception (Zöllner 2008). For this trial it was also unclear the total number of drop outs from both study groups at 1 year.

Sample size

A priori sample size calculation was performed in seven trials (Lindeboom 2006; Testori 2007; Cannizzaro 2008a; Cannizzaro 2008b; Cannizzaro 2008d; Merli 2008; Schincaglia 2008). The sample size of one trial (Lindeboom 2006) was calculated assuming that treatment modalities were equivalent: 21 implants were needed in each group to reject the null hypothesis that the treatments were not equivalent with a power of 80% and a type I error rate of 0.05. Non-equivalence was defined as a difference in implant stability quotient (ISQ) values measured with Osstell of 10 or more. Twenty-five implants (24 patients) were included in each group. Calculations of three trials (Testori 2007; Cannizzaro 2008d; Merli 2008) were based on the outcome (implant failure) of another RCT of similar design (Ottoni 2005) and it was calculated that 26 patients per group were needed to complete the trial. Unfortunately, because of an independent decision of the clinicians in violation of the research protocol, only 25 patients were included in the immediately loaded group in one trial (Testori 2007). The other two trials (Cannizzaro 2008d; Merli 2008) achieved

the planned sample size. The sample size calculation for the other two trials (Cannizzaro 2008a; Cannizzaro 2008b) was based on a theoretical estimate of implant failures and 286 patients should have been included in each group. The sample size could not be achieved and the number of failures which actually occurred were much less than those estimated in the calculations, therefore the number of patients to be included to detect a difference should have been much greater. Another trial (Schincaglia 2008) calculated the sample size on a peri-implant marginal bone level change difference of 0.3 mm among immediately versus conventionally loaded implants based on an error of 5% and a power of 80%: 14 patients were needed in each group and 15 patients per group were enrolled.

Inclusion and exclusion criteria

The majority of trials, with seven exceptions (Testori 2007; Cannizzaro 2008a; Cannizzaro 2008b; Cannizzaro 2008d; Donati 2008; Merli 2008; Schincaglia 2008), used quite strict inclusion criteria and included mainly ideal patients. This choice is understandable since it is common sense to load implants immediately or early only in selected cases for instance when implants are placed with a high insertion torques in good quality bone of adequate volume in patients not having parafunctional habits.

Main inclusion criteria

- Completely edentulous mandible (Chiapasco 2001; Payne 2002; Romeo 2002; Tawse-Smith 2002; Assad 2007; Turkyilmaz 2007; Cannizzaro 2008a).
- Completely edentulous maxilla able to harbour at least five implants (Fischer 2004; Cannizzaro 2008b).
- Partially edentulous patients (both mandibles and maxillae) (Cannizzaro 2003; Testori 2007; Merli 2008).
- Partially edentulous patients (both mandibles and maxillae) in the posterior jaws (premolar and molar areas) allowing the placement of at least 8 mm long implants, and the bone thickness at implant sites had to be of at least 6 mm (Zöllner 2008).
- Bilaterally free-end mandibles distal to canines or premolars (Romanos 2006).
- Bilaterally missing first mandibular molars (Güncü 2008).
- Missing one first or second mandibular molar allowing the placement of one at least 8.5 mm long implant, and the bone thickness at implant site had to be of at least 7 mm (Schincaglia 2008).
- Missing one single tooth in the anterior (premolar to premolar) maxilla, with adjacent teeth present, allowing the placement of at least 10 mm long implants with a 2.5 mm diameter (Hall 2006).
- Missing one single tooth in the anterior (premolar to premolar) maxilla, allowing the placement of at least 10 mm long implants with a 3.7 mm diameter with a flapless procedure (Oh 2006).
- Missing two teeth and enough bone to allow placement of two 7 mm long implants and the bone thickness at implant sites had to be of at least 5.5 mm (Cannizzaro 2008d).
- Missing one or more single teeth in the anterior (premolar to premolar) maxilla allowing the placement of at least 8 mm long implants with a 3.4 mm diameter with no bone fenestration (Lindeboom 2006).
- Missing one or more single teeth in the anterior (premolar to premolar) jaws allowing the placement of at least 8 mm long implants with a 4 mm diameter with no bone fenestration (Donati 2008).
- Single fresh extraction socket in the aesthetic maxilla with presence of four bone walls and at least 4 mm of bone beyond the root apex (Crespi 2008).
- 13 to 15 mm of residual anterior mandibular bone or more (Chiapasco 2001; Payne 2002; Tawse-Smith 2002).
- 10 mm of residual anterior mandibular bone or more (Romeo 2002).
- 11 mm of residual posterior mandibular bone in height and 6 mm in width or more (Romanos 2006).
- Elderly patients (55 to 80 years) (Payne 2002; Tawse-Smith 2002).
- Sufficient bone to allow placement of two 15 mm long implants (Turkyilmaz 2007).
- Sufficient bone to allow placement of at least 13 mm long implants and with a diameter of 3.7 mm (Cannizzaro 2003; Assad 2007; Crespi 2008).
- Sufficient bone to allow placement of 11.5 mm long implants with a diameter of 4 mm (Güncü 2008).
- Sufficient bone to allow placement of at least 10 mm long implants and with a diameter of 3.7 mm (Cannizzaro 2008a; Cannizzaro 2008b).
- Sufficient bone to allow placement of at least 9.5 mm long implants, and the bone thickness at implant sites had to be of at least 5.5 mm (Merli 2008).
- Minimal insertion torque of 45/48 Ncm to be immediately loaded (Cannizzaro 2003; Cannizzaro 2008a; Cannizzaro 2008b).
- Minimal insertion torque of 30 Ncm for single implants (Lindeboom 2006; Testori 2007) and 20 Ncm for splinted implants (Testori 2007).
- Minimal insertion torque of 40 Ncm to be immediately loaded (Cannizzaro 2008d; Merli 2008).
- Minimal insertion torque of 25 Ncm and primary implant stability ISQ > 60 to be immediately loaded (Crespi 2008).
- Minimal primary implant stability of 20 Ncm (Donati 2008).
- Minimal primary implant stability of 20 Ncm to be immediately loaded (Schincaglia 2008).

Main exclusion criteria

- Any evidence of current or previous smoking (Payne 2002; Tawse-Smith 2002).
- Smoking (Lindeboom 2006; Güncü 2008).
- Smoking more than 10 cigarettes per day (Chiapasco 2001; Cannizzaro 2003; Fischer 2004; Crespi 2008; Zöllner 2008).
- Smoking more than 20 cigarettes per day (Romeo 2002; Hall 2006).
- Any systemic disease likely to compromise implant surgery (Chiapasco 2001; Payne 2002; Romeo 2002; Tawse-Smith 2002; Cannizzaro 2003; Fischer 2004; Lindeboom 2006; Romanos 2006; Assad 2007; Testori 2007; Turkyilmaz 2007; Cannizzaro 2008a; Cannizzaro 2008b; Cannizzaro 2008d; Crespi 2008; Donati 2008; Güncü 2008; Merli 2008; Zöllner 2008).
- Presence of severe systemic conditions (ASA III) (Schincaglia 2008).
- Previously bone grafted bone jaws (Payne 2002; Tawse-Smith 2002; Fischer 2004; Hall 2006; Turkyilmaz 2007; Cannizzaro 2008a; Cannizzaro 2008b).
- In need of tissue augmentation procedures (Güncü 2008; Schincaglia 2008).
- Previously irradiated jaws (Chiapasco 2001; Payne 2002; Romeo 2002; Tawse-Smith 2002; Cannizzaro 2003; Romanos 2006; Testori 2007; Turkyilmaz 2007) or jaws irradiated less than 1 year before (Cannizzaro 2008a; Cannizzaro 2008b; Cannizzaro 2008d; Merli 2008).
- Bone quality type IV (very soft bone) according to the classification of Lekholm 1985 detected at the time of surgery (Chiapasco 2001; Payne 2002; Romeo 2002; Tawse-Smith 2002; Cannizzaro 2003) or on radiographs (Hall 2006).
- History of bruxism (Payne 2002; Tawse-Smith 2002).
- Severe clenching or bruxism (Chiapasco 2001; Romeo 2002; Cannizzaro 2003; Hall 2006; Lindeboom 2006; Testori 2007; Cannizzaro 2008d; Crespi 2008; Güncü 2008; Merli 2008; Zöllner 2008).
- Severe maxillo-mandibular skeletal discrepancy (Chiapasco 2001; Romeo 2002; Cannizzaro 2003; Lindeboom 2006).
- Extraction sockets with a healing less than 3 (Donati 2008), 4 (Schincaglia 2008; Zöllner 2008) and 6 months (Güncü 2008).
- If primary implant stability could not be achieved (Hall 2006; Crespi 2008; Zöllner 2008).
- Previous history of failed implants (Hall 2006).
- Less than 4 mm of keratinised mucosa (Merli 2008).
- Presence of dehiscence or fenestrations of the post-extractive sites (Crespi 2008).
- Unknown exclusion criteria (Oh 2006; Assad 2007).

Comparability of control and treatment groups at entry

In general, the various groups were comparable at entry with the exception of Tawse-Smith 2002 where the early loaded implants (both Steri-Oss and Southern) seemed to be shorter than those in the conventionally loaded groups; Lindeboom 2006 in which more larger diameter implants were used in the immediately occlusally loaded group; Testori 2007 in which more early loaded implants were placed in maxillae; Cannizzaro 2008b in which more immediate post-extractive implants were placed in the early loaded group; Schincaglia 2008 where immediately loaded implants seemed longer than conventionally loaded ones; and Zöllner 2008 where immediately loaded implants were placed deeper than conventionally loaded implants. The clinical significance, if any, of these findings is difficult to interpret. For four trials the baseline patient characteristics were not sufficiently described (Assad 2007; Turkyilmaz 2007; Crespi 2008; Donati 2008).

The agreed quality of the included trials after having incorporated the information provided by the authors is summarized in 'Additional Table 1'. For each trial we assessed whether it was at low or high risk of bias. Sixteen studies were rated as at high risk of bias and six at low risk of bias (Cannizzaro 2003; Lindeboom 2006; Cannizzaro 2008a; Cannizzaro 2008b; Cannizzaro 2008d; Güncü 2008).

Effects of interventions

See: **Summary of findings for the main comparison**; **Summary of findings 2**; **Summary of findings 3**

In total 1852 implants were originally placed in 1024 patients. Of the placed implants, 846 (398 in maxillae) were immediately loaded, 593 (288 in maxillae) were early loaded, and 413 (169 in maxillae) were conventionally loaded. During the follow up considered in this review (1 year of function for all trials with the exception of Oh 2006 and Cannizzaro 2008d for which we could only use the 6 and 9 months data, respectively) 48 implants failed. Twenty-two of the failed implants were immediately loaded, 20 were early loaded and six conventionally loaded. Of the 767 planned/placed restorations (unknown number of prostheses placed in Zöllner 2008. We assumed that for each implant failure corresponded one prosthesis failure), 36 (or 34 depending on the success criteria adopted) failed: 20 in the immediately loaded group, 14 (or 12 depending on the success criteria adopted) in the early loaded group, and two in the conventionally loaded group. The majority of prosthesis failures occurred in three trials: three (25%) immediately loaded prostheses failed in one trial (Oh 2006); five (10%) immediately loaded single crowns failed in one trial (Lindeboom 2006); six prostheses failed in another study (Tawse-Smith 2002), and five (42%) of those (or three (25%) depending on the success criteria adopted) were early loaded.

The meta-analyses for prosthesis failures, implant failures and marginal bone level changes at 1 year with the exception of Oh 2006 (6 months data used), Cannizzaro 2008d (6 months data used for radiographs and 9 months data for prosthesis and implant failures), and Crespi 2008 (2 years data used for radiographs) are presented in MetaView 'Comparisons 1 to 4'.

(1) Immediate versus conventional loading after 1 year of function (Comparison 1)

Twelve trials were included (Chiapasco 2001; Romeo 2002; Cannizzaro 2003; Hall 2006; Oh 2006; Romanos 2006; Assad 2007; Turkyilmaz 2007; Crespi 2008; Donati 2008; Güncü 2008; Schincaglia 2008).

Chiapasco 2001 (parallel group design) compared four immediately loaded (2 to 3 days) Brånemark implants with four conventionally loaded (4 to 8 months) implants supporting bar-retained overdentures in totally edentulous mandibles of adequate shape and quality for 2 years. Ten patients were originally included in each group. No baseline differences were apparent for sex, age, and length of the implants used between the two groups. No withdrawals at 1 year. One implant failed in each group. There was no statistically significant difference in prosthesis or implant failures between the different loading strategies (Comparison 1, Outcome 1.2).

Romeo 2002 (parallel group design) compared four immediately loaded (2 days) ITI SLA implants with four conventionally loaded (3 to 4 months) implants supporting bar-retained overdentures in totally edentulous mandibles of adequate shape and quality for 2 years. Ten patients were originally included in each group. It was unclear whether there were baseline differences between the two groups. No withdrawals at 1 year. One implant failed for peri-implantitis in the conventionally loaded group. There was no statistically significant difference in prosthesis or implant failures between the different loading strategies (Comparison 1, Outcome 1.2).

Cannizzaro 2003 (parallel group design) compared single crowns/bridges immediately loaded (same day) Zimmer Spline twist implants with conventionally loaded implants (3.5 and 4.5 months in mandibles and maxillae respectively) in partially edentulous patients for 2 years. Fourteen patients were originally included in each group. There were no apparent baseline differences with respect to sex, age, bone quality, implant position and length between the two groups. No withdrawals at 1 year. One prosthesis/implant failed at abutment connection in the conventionally loaded group. There was no statistically significant difference in prosthesis failures, implant failures and marginal bone level changes between the different loading strategies (Comparison 1, Outcomes 1.1, 1.2 and 1.3).

Hall 2006 (parallel group design) compared single immediately non-occlusally loaded (same day) Southern tapered implants with conventionally loaded implants (6 months) in the anterior maxilla (premolar to premolar) for 1 year. Fourteen patients were originally included in each group. There were no apparent baseline differences for sex, age, bone quality, bone quantity and implant length between the two groups. One patient emigrated from the immediately loaded group (the implant was in function) versus two patients who emigrated to Australia from the conventionally loaded group at 1 year. One prosthesis/implant failed at abutment connection in the immediately loaded group. There was no statistically significant difference in prosthesis failures, implant failures and marginal bone level changes between the different loading strategies (Comparison 1, Outcomes 1.1, 1.2 and 1.3).

Oh 2006 (parallel group design) compared single immediately loaded (same day) Zimmer implants with conventionally loaded implants (4 months) in the anterior maxilla (premolar to premolar), placed with a flapless technique, for 6 months. Twelve patients were originally included in each group. There were no apparent baseline differences for sex, age, bone quality, soft tissue thickness, and implant position between the two groups. No withdrawals at 1 year. Three prostheses/implants failed in the immediately loaded group. There was no statistically significant difference in prosthesis failures and implant failures between the different loading strategies (Comparison 1, Outcomes 1.1 and 1.2).

Romanos 2006 (split-mouth design) compared three immediately loaded (same day) Ankylos implants supporting a bridge with three contralateral conventionally loaded (3 months) implants in mandibles partially edentulous distal to the canines or premolars for 2 years. Twelve patients were originally included. No baseline differences were apparent for bone quality between the contralateral sites. No withdrawals at 1 year. No implant failed. There was no statistically significant difference in prosthesis or implant failures between the different loading strategies.

Assad 2007 (parallel group design) compared four immediately loaded (within 4 days) Screw-Vent implants with four conventionally loaded (4 months) implants supporting bar-retained overdentures in totally edentulous mandibles of adequate shape for 2 years. Ten patients were originally included in each group. It was unclear whether there were baseline differences between the two groups. No withdrawals at 1 year. No implant failed. There was no statistically significant difference in prosthesis or implant failures between the different loading strategies.

Turkyilmaz 2007 (parallel group design) compared two unsplinted immediately loaded (1 week) Brånemark TiUnite implants with two unsplinted conventionally loaded (3 months) implants supporting overdentures in totally edentulous mandibles of adequate shape for 2 years. Ten patients were originally included in each group. It was unclear whether there were baseline differences between the two groups. No withdrawals at 1 year. No implant failed. There was no statistically significant difference in prosthesis failures, implant failures and marginal bone level changes between the different loading strategies (Comparison 1, Outcome 1.3).

Crespi 2008 (parallel group design) compared single Outlink Sweden & Martina 13 mm long implants placed in fresh extraction sockets immediately loaded (same day) with identical implants conventionally loaded at 3 months in maxillae (premolar to premolar area) for 2 years. Twenty patients were originally included in each group. There were no baseline differences in implant diameter and position between the two groups. No withdrawals at 1 year. No implant failed. There was no statistically significant difference in prosthesis failures, implant failures and marginal bone level changes between the different loading strategies (Compari-

son 1, Outcome 1.3).

Donati 2008 (parallel group design) compared one immediately loaded (within 1 day) Astra OsseoSpeed implant with one conventionally loaded (3 months) implant replacing a tooth in position 15-25 and 35-45 for 1 year. Three groups were formed: two groups had implants immediately loaded. The immediately loaded groups differed in the preparation of the implant site: a conventional preparation with drills (44 patients), and a preparation with osteotomes (42 patients). We considered these two groups as a single group. The control group consisted of 53 patients who had implant sites conventionally prepared and loaded. Ten patients who were treated according to a split-mouth design had to be excluded from the analyses. It was unclear whether there were baseline differences between the three groups. There were two withdrawals at 1 year from the conventionally loaded group because of poor health conditions. Three crowns/implants failed from the immediately loaded groups: one from the conventionally prepared sites and two from the osteotomes prepared sites. There was no statistically significant difference in prosthesis and implant failures between the different loading strategies (Comparison 1, Outcomes 1.1 and 1.2).

Güncü 2008 (split-mouth design) compared one immediately loaded (same day) Brånemark TiUnite implant with one contralateral conventionally loaded (3 months) implant replacing first mandibular molars for 1 year. Thirteen patients were originally included. No baseline differences were apparent between the contralateral sites. No withdrawals at 1 year. One implant/crown failed in the immediately loaded group. There was no statistically significant difference in prosthesis, implant failures and marginal bone level changes between the different loading strategies (Comparison 1, Outcomes 1.1, 1.2 and 1.3).

Schincaglia 2008 (parallel group design) compared one immediately loaded (within 1 day) Brånemark TiUnite implant with one conventionally loaded (3 to 4 months) implant replacing first or second mandibular molars for 1 year. Fifteen patients were originally included in each group. There were no apparent baseline differences in implant position and insertion torque between the two groups. However, the implants of the immediately loaded group were longer than those in the conventionally loaded group. No withdrawals at 1 year. One implant/crown failed in the immediately loaded group. There was no statistically significant difference in prosthesis and implant failures between the different loading strategies (Comparison 1, Outcomes 1.1 and 1.2), however, statistically significantly more peri-implant marginal bone loss occurred at conventionally loaded implants: mean difference (MD) random-effects -0.43 (95% confidence interval (CI) -0.78 to -0.08) (Comparison 1, Outcome 1.3).

For prosthesis failures, the meta-analysis of six trials (Cannizzaro 2003; Hall 2006; Oh 2006; Donati 2008; Güncü 2008; Schincaglia 2008) found no significant difference, risk ratio (RR) random-effects 2.41 (95% CI 0.76 to 7.63), and no evident heterogeneity, although the meta-analysis was based only on six trials because there were no failures in the other trials and the risk ratios could not be calculated.

For implant failures, the meta-analysis of eight trials (Chiapasco 2001; Romeo 2002; Cannizzaro 2003; Hall 2006; Oh 2006; Donati 2008; Güncü 2008; Schincaglia 2008) found no significant difference, RR random-effects 1.92 (95% CI 0.70 to 5.22) and no evident heterogeneity.

For marginal bone level changes, the meta-analysis of six trials (Cannizzaro 2003; Hall 2006; Turkyilmaz 2007; Crespi 2008; Güncü 2008; Schincaglia 2008) found no significant difference with MD random-effects -0.10 (95% CI -0.24 to 0.04) and no evident heterogeneity.

(2) Early versus conventional loading after 1 year of function (Comparison 2)

Three trials were included (Payne 2002; Tawse-Smith 2002; Fischer 2004).

Payne 2002 (parallel group design) compared two unsplinted early loaded (6 weeks) ITI SLA implants with two unsplinted conventionally loaded (12 weeks) implants supporting overdentures in totally edentulous mandibles of adequate shape and quality for 2 years. Twelve patients were originally included in each group. There were no apparent baseline differences in gender, bone quality and quantity between the two groups. Two withdrawals occurred from the conventionally loaded group at 1 year. No implant failed. There was no statistically significant difference in prosthesis failures, implant failures and marginal bone levels between the different loading strategies (Comparison 2, Outcome 2.3).

Tawse-Smith 2002 (parallel group design) compared two unsplinted early loaded (6 weeks) Southern or Steri-Oss implants with two unsplinted conventionally loaded (12 weeks) implants supporting overdentures in totally edentulous mandibles of adequate shape and quality for 2 years. Twelve patients were originally included in each of the four groups (Southern early loaded, Steri-Oss early loaded, Southern conventionally loaded, Steri-Oss conventionally loaded). There were no apparent baseline differences in bone quality and quantity between the two groups. However, the implants of both the Steri-Oss and Southern early loaded groups were shorter than those in the conventionally loaded groups. In the article Steri-Oss implants were described as having a turned surface, but after having analysed the surface of one implant, kindly provided by the authors, it was realized that the implant surface was chemically treated. No withdrawals at 1 year. Seven Steri-Oss implants failed in five patients of the early loaded group versus one Steri-Oss implant in the conventionally loaded group. No implants failed in the Southern groups. Most of the failed implants were placed by a surgeon who only placed some Steri-Oss implants. There was no statistically significant difference in prosthesis failures, implant failures and marginal bone levels changes between the different loading strategies (Comparison 2, Outcomes 2.1, 2.2 and 2.3).

Fischer 2004 (parallel group design) compared five to six early

loaded (9 to 18 days) ITI SLA implants with five to six conventionally loaded (2.5 to 5.1 months) ITI EstheticPlus implants supporting fixed maxillary cross-arch bridges for 5 years. Sixteen patients were originally included in the early and eight in the conventionally loaded group. There were no apparent baseline differences in implant length and cantilever length between the two groups. No withdrawals at 1 year. No prosthesis failures. One implant failed in the early loaded group versus two implants in two patients in the conventionally loaded group. There was no statistically significant difference in prosthesis and implant failures between the different loading strategies (Comparison 2, Outcome 2.2).

For prosthesis failures, the meta-analysis of one trial (Tawse-Smith 2002) found no significant difference with RR random-effects 5.00 (95% CI 0.63 to 39.67).

For implant failures, the meta-analysis of two trials (Tawse-Smith 2002; Fischer 2004) found no significant difference with RR random-effects 1.15 (95% CI 0.06 to 22.33), and no evident heterogeneity.

For marginal bone level changes, the meta-analysis of two trials (Payne 2002; Tawse-Smith 2002) found no significant difference with MD random-effects -0.04 (95% CI -0.15 to 0.07), and no evident heterogeneity.

(3) Immediate versus early loading after 1 year of function (Comparison 3)

Six trials were included (Testori 2007; Cannizzaro 2008a; Cannizzaro 2008b; Cannizzaro 2008d; Merli 2008; Zöllner 2008).

Testori 2007 (parallel group design) compared immediately non-occlusally loaded 3i FNT implants (within 48 hours) with early loaded implants (2 months) supporting single crowns/partial bridges for 1 year. Twenty-five patients were originally included in the immediately loaded group and 27 in the early loaded group. There were no baseline differences with respect to sex, age, bone quality, implant length and number between the two groups, however, more implants of the early loaded group were placed in maxillae than those of the immediately loaded group. No withdrawals at 1 year. One single implant and its related provisional crown failed after 2 months in the immediately loaded group. There was no statistically significant difference in prosthesis failures, implant failures and marginal bone levels between the different loading strategies (Comparison 3, Outcomes 3.1, 3.2 and 3.3).

Cannizzaro 2008a (parallel group design) compared two immediately loaded Zimmer SwissPlus implants (within 12 hours) with two early loaded implants (6 weeks), placed with a flapless technique, supporting mandibular bar-retained overdentures for 1 year. Thirty patients were included in each group. There were no apparent baseline differences for sex, age, smoking habits, number of maxillary dentures, number of immediate post-extractive implants, and implant length between the two groups. Two implants were immediately replaced with larger diameter ones to obtain the implant insertion torque ($\geq$ 48 Ncm) required. No withdrawals at 1 year. Two implants failed in two patients of the early loaded group which determined the failure of the overdentures, however both implants were successfully replaced. There was no statistically significant difference in prosthesis and implant failures between the different loading strategies (Comparison 3, Outcomes 3.1 and 3.2).

Cannizzaro 2008b (parallel group design) compared five to eight immediately loaded Zimmer SwissPlus implants (within 12 hours) with five to eight early loaded implants (2 months), placed with a flapless technique, supporting fixed maxillary cross-arch bridges for 1 year. Fifteen patients were included in each group. There were no apparent baseline differences for sex, age, smoking habits, number of mandibular dentures, and implant length between the two groups, though more immediate post-extractive implants were placed in the early loaded group. Four implants were immediately replaced with larger diameter ones to obtain the implant insertion torque ($\geq$ 48 Ncm) required. No withdrawals at 1 year. No prosthesis failures. One implant did not achieve a sufficient primary stability and was immediately removed and not replaced. Four implants failed: one in the immediately loaded group and three in two patients of the early loaded group. There was no statistically significant difference in prosthesis failures, implant failures and marginal bone levels between the different loading strategies (Comparison 3, Outcomes 3.2 and 3.3).

Cannizzaro 2008d (split-mouth design) compared single Biomet 3i Nanotite 7 mm long cylindrical implants, placed with a flapless technique, immediately occlusally loaded (same day) with identical implants early loaded (6 weeks) for 9 months. Thirty patients were originally included. There were no baseline differences in the number of post-extractive sites, bone quality, implant diameter and position between the two groups. Eight implants were immediately replaced with larger diameter ones to obtain the implant insertion torque ($\geq$ 40 Ncm) required. The randomisation of one implant of the immediately loaded group was subverted: the implant was early loaded according to the research protocol since a sufficient implant insertion torque ($\geq$ 40 Ncm) could not be obtained. No withdrawals at 1 year. One implant failed from each group. There was no statistically significant difference in prosthesis failures, implant failures and marginal bone level changes between the different loading strategies (Comparison 3, Outcomes 3.1, 3.2 and 3.3).

Merli 2008 (parallel group design) compared immediately non-occlusally loaded Thommen implants (within 72 hours) with early non-occlusally loaded implants (6 weeks), placed with a flapless technique, supporting single crowns/partial bridges for 1 year. Thirty patients were included in the immediately loaded group and 30 in the early loaded group. The randomisation of two patients in each group was subverted: two patients of the immediately loaded group were treated as early loaded patients according to the research protocol since a sufficient implant insertion torque ($\geq$ 40 Ncm) could not be obtained, whereas two patients of the early loaded group were immediately loaded by mistake. Five ad-

ditional patients of the early loaded group were actually conventionally loaded. There were no apparent baseline differences with respect to sex, age, bone quality, implant length and number between the two groups. No withdrawals at 1 year. No prosthesis or implant failures. There was no statistically significant difference in prosthesis and implant failures between the different loading strategies.

Zöllner 2008 (parallel group design) compared immediately non-occlusally loaded implants (the same day) with early non-occlusally loaded implants (1 month), placed in posterior jaws (premolar and molars areas) supporting single crowns/partial bridges for 1 year. 138 patients were treated in the immediately loaded group and 128 in the early loaded group. There were no apparent baseline differences in bone quality, implant length, number and position between the two groups. Unclear whether five withdrawals occurred in the immediately loaded group and one in the early loaded group prior to implant placement or during a 5-month follow-up period and it is unclear how many drop outs occurred at 1 year. Four implants failed in the immediately loaded group versus six in the early loaded group. We assumed that an equal number of prostheses were lost, since we were not able to obtain this information from the authors. There was no statistically significant difference in prosthesis and implant failures between the different loading strategies (Comparison 3, Outcomes 3.1 and 3.2).

For prosthesis failures, the meta-analysis of four trials (Testori 2007; Cannizzaro 2008a; Cannizzaro 2008d; Zöllner 2008) found no significant difference with RR random-effects 0.68 (95% CI 0.25 to 1.86), and no evident heterogeneity.

For implant failures, the meta-analysis of five trials (Testori 2007; Cannizzaro 2008a; Cannizzaro 2008b; Cannizzaro 2008d; Zöllner 2008) found no significant difference with RR random-effects 0.65 (95% CI 0.26 to 1.63), and no evident heterogeneity.

For radiographic bone levels, the meta-analysis of three trials (Testori 2007; Cannizzaro 2008b; Cannizzaro 2008d) found no significant difference with MD random-effects -0.06 (95% CI -0.16 to 0.03), and no evident heterogeneity.

(4) Occlusal versus non-occlusal loading (Comparison 4)

One trial was included (Lindeboom 2006).

Lindeboom 2006 (parallel group design) compared immediately occlusally loaded with immediately non-occlusally loaded single BioComp implants for 1 year. Twenty-four patients (25 implants) were included in each group. There were no apparent baseline differences in sex, age, previously grafted sites, and implant position between the two groups, though more larger diameter implants were used in the occlusally loaded group. No withdrawals at 1 year. Five crowns/implants failed in five patients: two in the occlusally loaded group and three in the non-occlusally loaded group. There was no statistically significant difference in prosthesis failures, implant failures and marginal bone levels changes between the different loading strategies (Comparison 4, Outcomes 4.1, 4.2 and 4.3).

For prosthesis failures, the meta-analysis of one trial (Lindeboom 2006) found no significant difference with RR random-effects 0.67 (95% CI 0.12 to 3.64).

For implant failures, the meta-analysis of one trial (Lindeboom 2006) found no significant difference with RR random-effects 0.67 (95% CI 0.12 to 3.64).

For marginal bone level changes, the meta-analysis of one trial (Lindeboom 2006) found no significant difference with MD random-effects 0.01 (95% CI -0.13 to 0.14)

Subgroup analyses

No subgroup analysis was conducted as the maximum number of trials within any meta-analysis was eight, and this was a non-significant result with no important evidence of heterogeneity.

ADDITIONAL SUMMARY OF FINDINGS *[Explanation]*

Conventional compared with early loading of dental implants

Patient or population: patients requiring dental implants
Settings: dental practice
Intervention: early loading
Comparison: conventional loading

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Conventional	Early				
Prosthesis failure at 1 year	Low risk population		RR 5.00 (0.63 to 39.67)	48 (1)	+000 very low	
	10 per 1000	50 per 1000 (6 to 397)				
	High risk population					
	100 per 1000	241 per 1000 (63 to 1000)				

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI = confidence interval
RR = risk ratio
GRADE Working Group grades of evidence:
High quality (++++): Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality (+++0): Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality (++00): Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality (+000): We are very uncertain about the estimate.

Early compared with immediate loading of dental implants

Patient or population: patients requiring dental implants
Settings: dental practice
Intervention: immediate loading
Comparison: early loading

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Early	Immediate				
Prosthesis failure at 1 year	Low risk population		RR 0.68 (0.25 to 1.86)	408 (4)	++00 low	
	50 per 1000	34 per 1000 (13 to 93)				
	High risk population					
	240 per 1000	163 per 1000 (60 to 446)				

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI = confidence interval
RR = risk ratio
GRADE Working Group grades of evidence:
High quality (++++): Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality (+++0): Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality (++00): Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality (+000): We are very uncertain about the estimate.

DISCUSSION

The question of whether implants could be immediately or early loaded after their insertion has relevant clinical implications since the treatment period could be drastically reduced for the benefit of the patients. The main outcome for this type of studies is the success of the prosthesis since implant loss may not always jeopardize prosthesis success. It was decided to consider only a relatively short follow up (4 months to 1 year) since it was felt that such follow ups would be sufficient to understand the role of loading on the establishment of osseointegration.

No statistically significant differences in prosthesis success, implant success and marginal bone levels were observed when different loading regimens were applied, however the number of included trials and patients may still be insufficient to draw definitive conclusions. Nevertheless some clear trends could be observed. Immediately loaded implants (eight trials) appear to be at higher risk of failures than conventionally loaded ones. This observation is not unexpected since the additional risks of loading implants immediately or early are known for decades (Brånemark 1977). A useful clinical observation could be that the risk of failure can be substantially minimized by a proper patient selection and well-trained operators. A more interesting observation is the noticed trend (five trials) of having more failures among the early than the immediately loaded implants. The sample size is still too small to draw solid conclusions, but it seems there are no apparent advantages to loading implants early. It could make more clinical sense to load an implant immediately if its primary stability is good and there are not other factors believed to negatively influence its prognosis. In the case of poor primary implant stability or other suspected negative prognostic variables, it might be preferable to wait for a conventional healing period to give bone more chances to properly heal around the implant. Possible reasons which may explain the trend (if any) for more implant failures among early loaded implants could be that the provisional prostheses might transfer excessive forces to the healing implants since all studies used a 1-stage technique. The prosthetic procedures may also disrupt the bone healing around the implant(s) in a period when primary implant stability might have been decreased.

While in general the overall success was high, two trials (Tawse-Smith 2002; Oh 2006) reported higher failure rates. In one trial (Tawse-Smith 2002) seven Steri-Oss implants in five patients failed out of 24 implants (12 patients). Since mandibular overdentures supported by two implants were used, the loss of a single implant could determine the failure of the entire treatment (prosthesis). However, the author of the study, acting as one of the referees for this review, argued that it is possible to have a successful overdenture supported by only one implant as observed in two of their patients. While this may be true, this may not be a common procedure and many clinicians and patients may not be fully satisfied with the result. If we consider an overdenture supported by a single implant as a failure, then the loss of five overdentures out of 12 may have some important clinical implications. On the other hand, it is likely that other confounding factors might have played a determinant role in the final outcome such as the surgical skill of one operator who placed only some of the Steri-Oss implants and who accounted for almost all the failures, or the presence of shorter implants in the early loaded group. In another study of 6 months duration (Oh 2006), three out of 12 single implants placed with a flapless procedure and immediately loaded failed, yielding a 25% failure rate versus none in the conventionally loaded group. In this trial, it may be speculated that the flapless placement of dental implants, which is technically demanding, might have contributed to the sub-optimal success rates of immediately loaded implants. We suspect that there is some publication bias on this topic which tends to underestimate failures of immediately loaded implants as suggested by a series of published abstracts (Polson 2000) and the information of a trial aborted in UK due to excessive implant failures. Unfortunately, we were not supplied with the requested information.

This review update is substantial since in less than 2 years the number of included patients has tripled. This underscores the clinical importance of this matter. Not only were there several new studies, there were also two large multicentre sponsored trials (Donati 2008; Zöllner 2008). The evaluation of these trials was not simple due to the insufficient amount of information presented in the articles. Thanks to the kindness of the main authors who provided us a lot of relevant information, we were able to include those trials. While it is recognized that running large multicentre clinical trials is not an easy task, more efforts should be made at protocol level to decrease the risk of bias, for instance by randomising patients after implant placement to have the ideal allocation concealment, to select centres able to conduct clinical research, to clearly report drop outs and exclusions and their reasons, and moreover to report results according to international standards (www.consort-statement.org). In particular, the power of one trial (Donati 2008) was sensibly decreased by having two groups testing different techniques for installing implants to be immediately loaded, and by having 10 patients treated according to a split-mouth design, despite the study being designed with parallel arms. There was no report of drop outs for the other trial (Zöllner 2008) meaning that it was even unknown how many patients completed the trial after 1 year, and it was also unclear how many prostheses were delivered. Interestingly, it was acknowledged that the lack of allocation concealment possibly resulted in patients being treated differently (implants in the immediate loaded group were placed deeper probably in the attempt to increase insertion torques). While the authors (Zöllner 2008) attributed no clinical significance to this observation, it clearly underscores the importance of having a proper allocation concealment.

Another aspect which could be debatable is whether immediate 'non-occluding' loading (i.e. a provisional restoration is placed on the implants and is not in contact with the opposite dentition, also called 'immediate provisionalisation'), as opposed to 'occlusal'

loading (the restoration is in full occlusal contact with the opposite dentition), could be considered as a real immediate loading procedure. We decided that from a patient's point of view, this difference may not be very significant since patients do prefer to have their new teeth as soon as possible (Schropp 2004), and that non-occluding restorations are actually functionally used when chewing. However, in order to have an evidence-based answer to this question, a new secondary hypothesis has been added to this review update. The only randomised controlled trial (RCT) that investigated this hypothesis (Lindeboom 2006) did not find any statistically significant difference or trend by comparing immediate occlusal versus non-occlusal loading, but the sample size is yet too small to reach any acceptable conclusion. In a few trials (Cannizzaro 2008a; Cannizzaro 2008b; Cannizzaro 2008d; Merli 2008) the number of implants which were immediately replaced in order to obtain the required insertion torque was reported. It is interesting to observe that in one study (Cannizzaro 2008d), 8 out of 60 placed implants (13%) were immediately replaced by larger diameter ones to obtain an insertion torque > 40 Ncm. While this appears to be a costly procedure, the following observations should be made: (1) all implants were only 7 mm long and were placed according to a flapless procedure even in fresh extraction sites (30%), therefore it is understandable that to achieve high insertion torques is not easy; (2) it is unknown which is the minimal insertion torque still able to allow high success rates for immediately loaded implants, it may be that lower insertion torques in the range of 30 Ncm might be sufficient; (3) this was a clinical trial and it was decided at protocol level that the operator could replace the implants with larger diameter ones in order to conduct the study in the most appropriate way, in everyday clinical practice, the loading of these implants can be delayed to allow osseointegration to take place.

It is worth having a brief overview of the excluded studies, since they do present relevant clinical information. In general success rates were very high (Roccuzzo 2001; Testori 2003; Salvi 2004; Turkyilmaz 2006; Cannizzaro 2008c) confirming the main conclusion of this review, i.e. that immediate and early loading of dental implants are viable and successful treatment options. However, there was a single but relevant exception: a study done for a master's degree thesis having the student as the main operator (Ottoni 2005), which deserves some additional comments. In this controlled clinical trial of split-mouth design which used an alternation method to allocate sites to different loading strategies, and not a randomised controlled trial as described in the original article, single non-occlusally immediately loaded implants failed significantly more than conventionally loaded dental implants. Ten out of 23 immediately loaded implants failed (44% of failures) versus only one out of 23 of the conventionally loaded group. The authors were able to demonstrate a strong correlation between implant failures and the initial insertion torque of the implants. Nine of the 10 implants inserted with a 20 Ncm torque failed, versus only one out of 10 placed with a 32 Ncm torque in the immediately loaded group. The authors confirmed to us that no technique of 'sub-preparation' of the implant sites was used to increase insertion torque (primary stability), and that their patients did not follow any post-operative diet restriction regarding chewing on hard food. Since the majority of successful RCTs used techniques to increase torque values at implant placement, though this was not always sufficiently described in the materials and method sections, it can be concluded that a high degree of primary stability at implant insertion is a key prerequisite for a successful immediate or early loading procedure.

The generalisation from the results of the included trials to ordinary clinical practice should be made with extreme caution. In the majority of the included trials, the inclusion criteria were strict and only patients known to be ideal candidates for implant treatment were recruited. In general operators were highly experienced, and it is important to observe that in those trials with less experienced operators prosthetic failures were clinically higher ranging from 25% to 42% (depending on the success criteria adopted) (Tawse-Smith 2002), and 44% (Ottoni 2005). On the other hand, it has been shown that in selected patients it is possible to load dental implants immediately with good success rates.

AUTHORS' CONCLUSIONS

Implications for practice

It is possible to successfully load dental implants immediately or early after their placement in selected patients, though not all clinicians may be able to achieve optimal results. Trends (no statistically significant differences) suggest that immediately loaded implants fail more often than those conventionally loaded, but less commonly than those early loaded. If a clinician or a patient wish to load the implants early, it might be wiser to load them immediately (within 1 week) rather than waiting for 1 or 2 months. It is unclear whether it is beneficial to avoid occlusal contacts during the osseointegration phase. A high degree of primary implant stability (high value of insertion torque) seems to be one of the prerequisites for a successful procedure.

Implications for research

More well designed randomised controlled trials (RCTs) are needed to understand how predictable the protocols for immediate and early loading are. We still need to know whether it is advantageous to avoid occlusal contacts during the bone healing phase. Such trials should be simply designed and reported according to the Consolidated Standards of Reporting Trials (CONSORT) guidelines (Moher 2001) (www.consort-statement.org). It is suggested that priority should be given to trials assessing the effectiveness of immediately versus early loaded implants to improve patient satisfaction and decrease treatment time.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Assad 2007

Methods	2-year follow up, randomised, parallel group study. Unclear whether outcome assessor was blinded. No withdrawals at 1 year
Participants	Patients with edentulous mandibles allowing the placement of 4 12 mm long and 3.7 mm wide implants. Exclusion criteria were any systemic or local disease that might contraindicate implant placement. Adults treated in the Prosthodontic Department, Al Zahraa University Hospital, Egypt. 10 enrolled (5 patients in each group) and results given for 10
Interventions	4 implants supporting a bar and an overdenture conventionally loaded (4 months) versus 4 implants immediately loaded (within 4 days from insertion). Screw-Vent (Paragon, Core-Vent Corporation, Las Vegas, NV, USA) submerged titanium screws were used
Outcomes	Prosthesis/implant failures, implant percussion, marginal bone level changes on standardised intraoral radiographs, gingival index, plaque index, probing pocket depth. 1-year data used
Notes	

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Cannizzaro 2003

Methods	2-year follow up, randomised, parallel group study. Outcome assessor was blinded. No withdrawals at 1 year
Participants	Partially edentulous patients (both mandibles and maxillae) allowing the placement of at least 13 mm long implants with a diameter of 3.7 mm. For implants to be immediately loaded, a primary implant stability of 45 Ncm had to be achieved at insertion. Exclusion criteria were patients with type IV bone quality (very soft bone) according to the Lekholm and Zarb classification detected at implant insertion, less than 3 years irradiated jaws, severe bruxism, smoking habits (more than 10 cigarettes per day), substance abusers, pregnancy, uncontrolled diabetes, and any systemic diseases likely to compromise implant surgery. Adults treated in an Italian private practice. 28 enrolled (14 in each group) and results given for 28
Interventions	1 or more adjacent implants restored first with acrylic restorations in full occlusion and then with cemented metal-ceramic prostheses, either the same day or after 3.4 months (mandibles) or 4.5 months (maxillae). Zimmer (Zimmer, Carlsbad, Ca, USA) Spline Twist MTX titanium screws were used
Outcomes	Prosthesis/implant failures, Periotest, Osstell, marginal bone level changes on standardised intraoral radiographs, plaque accumulation, probing pocket depth. 1-year data used

Cannizzaro 2003 (*Continued*)

Notes		
Risk of bias		
Item	**Authors' judgement**	**Description**
Allocation concealment?	Yes	A - Adequate

Cannizzaro 2008a

Methods	1-year follow up, randomised, parallel group study. Outcome assessor was blinded. No withdrawals at 1 year
Participants	Patients with edentulous mandibles allowing the placement of 2 implants at least 10 mm long and with a diameter of 3.7 mm. For implants to be immediately loaded, a primary implant stability of 48 Ncm had to be achieved at insertion. Exclusion criteria were less than 1 year irradiated jaws, substance abusers, pregnancy, uncontrolled diabetes, and any systemic diseases likely to compromise implant surgery, need for augmentation procedures, lack of opposite occluding dentition/prosthesis, psychiatric problems. Adults treated in an Italian private practice. 60 enrolled (30 in each group) and results given for 60
Interventions	2 implants, placed with a flapless procedure, supporting a bar and an overdenture immediately (same day) or early loaded (6 weeks). Zimmer SwissPlus (Zimmer, Carlsbad, Ca, USA) non-submerged solid titanium screws were used
Outcomes	Prosthesis/implant failures, Osstell, patient satisfaction, complications. 1-year data used
Notes	

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Cannizzaro 2008b

Methods	1-year follow up, randomised, parallel group study. Outcome assessor was blinded. No withdrawals at 1 year
Participants	Patients with edentulous maxillae allowing the placement of 5 to 8 implants at least 10 mm long and with a diameter of 3.7 mm. For implants to be immediately loaded, a primary implant stability of 48 Ncm had to be achieved at insertion. Exclusion criteria were less than 1 year irradiated jaws, substance abusers, pregnancy, uncontrolled diabetes, and any systemic diseases likely to compromise implant surgery, need for augmentation procedures, lack of opposite occluding dentition/prosthesis, psychiatric problems. Adults treated in an Italian private practice. 30 enrolled (15 in each group) and results given for 30

Cannizzaro 2008b (*Continued*)

Interventions	5-8 implants, placed with a flapless procedure, immediately (same day) or restored after 2 months with metal reinforced acrylic provisionals replaced 2 to 3 months after by full-arch metal ceramic or metal resin prostheses with short cantilevers. Zimmer SwissPlus (Zimmer, Carlsbad, Ca, USA) non-submerged solid titanium screws were used
Outcomes	Prosthesis/implant failures, Osstell, marginal bone level changes on intraoral radiographs, patient satisfaction, complications. 1-year data used
Notes	

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Cannizzaro 2008d

Methods	9-month follow up, randomised, split-mouth group study. Outcome assessor was blinded. No withdrawals at 9 months
Participants	Partially edentulous patients needing 2 7 mm long single implants in bone at least 5.5 wide. For implants to be immediately loaded, a primary implant stability of 40 Ncm had to be achieved at insertion. Exclusion criteria were less than 1 year irradiated jaws, substance abusers, pregnancy, uncontrolled diabetes, severe bruxism or clenching, and any systemic diseases likely to compromise implant surgery, need for augmentation procedures with exception of Bio-Oss in fresh extractions sockets, lack of opposite occluding dentition/prosthesis, psychiatric problems. Adults treated in an Italian private practice. 30 enrolled and results given for 30
Interventions	2 single implants, placed with a flapless procedure, immediately (same day) or early loaded after 6 weeks with acrylic crowns replaced by metal-ceramic crowns after 9 (immediate loading) or 3 (early loading) weeks. 7 mm long Biomet 3i (Palm Beach, Florida, USA) Nanotite cylindrical titanium-alloy implants non-submerged were used
Outcomes	Prosthesis/implant failures, marginal bone level changes on intraoral radiographs, patient satisfaction, complications. 9-month data used
Notes	

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Chiapasco 2001

Methods	2-year follow up, randomised, parallel group study. Outcome assessor was blinded. No withdrawals at 1 year
Participants	Patients that have been edentulous in the mandible for at least 3 months. Mandibles allowing the placement of 4 implants at least 13 mm long. Exclusion criteria were patients with type IV bone quality (very soft bone) according to the Lekholm and Zarb classification detected at implant insertion (none), previously irradiated jaws, severe bruxism, smoking habits (more than 10 cigarettes a day) and any systemic diseases likely to compromise implant surgery. Adults treated in a university dental clinic of the University of Milan, Italy. 20 enrolled (10 patients in each group) and results given for 20
Interventions	4 implants supporting a bar and an overdenture conventionally loaded (4 to 8 months) versus 4 implants immediately loaded (within 3 days from insertion). Brånemark (Nobel Biocare AB, Göteborg, Sweden) submerged turned titanium MKII screws were used
Outcomes	Prosthesis/implant failures, Periotest, marginal bone level changes on panoramic radiographs, plaque accumulation, modified bleeding index, probing pocket depth. 1-year data used
Notes	

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	No	C - Inadequate

Crespi 2008

Methods	2-year follow up, randomised, parallel group study. Unclear whether outcome assessor was blinded. No withdrawals at 1 year
Participants	Patients rehabilitated with single implants in maxillary (premolar to premolar) fresh extraction sockets with 4 bony walls and at least 4 mm of bone beyond the root apex and the presence of adjacent teeth. Exclusion criteria were presence of dehiscence or fenestration of the residual bony walls, signs of acute infection around the alveolar bone at the implant site, bruxism, patients smoking more than 10 cigarettes a day, uncontrolled diabetes, coagulation disorders, alcohol or drug abuse. Adults treated in "Vita Salute" University, San Raffaelle Hospital, Milan, Italy. 40 enrolled (20 patients in each group) and results given for 40
Interventions	13 mm long single implants loaded immediately (the same day) or conventionally at 3 months. Outlink (Sweden & Martina, Padova, Italy) titanium solid screws were used
Outcomes	Prosthesis/implant failures, marginal bone level changes on periapical radiographs. 1-year data used
Notes	

Risk of bias

Item	Authors' judgement	Description

Crespi 2008 (*Continued*)

Allocation concealment?	Unclear	B - Unclear

Donati 2008

Methods	1-year follow up, multicentre, randomised, parallel group study with 3 arms. Outcome assessor was blinded only for marginal bone levels. 2 withdrawals at 1 year from the conventionally loaded group because of poor health. 10 patients who were treated according to a split-mouth design were excluded from the calculations by us
Participants	Patients missing a single tooth in area 15-25 and 35-45 allowing the placement of 8 mm long and 4 mm large single implant. Exclusion criteria were post-extractive implants (at least 3 months healing was required), insertion torque < 20 Ncm, and any systemic diseases likely to compromise implant surgery. Adults treated in 8 Italian private practices. 139 enrolled (42 in the immediately loaded group prepared with drills; 42 in the immediately loaded group prepared with osteotomes; and 53 in the conventionally loaded group prepared with drills) and results given for 137
Interventions	Single immediate implants restored within 24 hours or after 3 months with occluding screw-retained acrylic crowns, replaced after 6 months by cemented or screw-retained metal-ceramic crowns. Immediately loaded implants were randomised to 2 different groups: in one group the implant sites were conventionally prepared with drills, whereas in the other group osteotomes were used. Astra OsseoSpeed® (Astra Tech Dental, Mölndal, Sweden) titanium grade 1 screws were used
Outcomes	Prosthesis/implant failures, marginal bone level changes on standardised intraoral radiographs, plaque accumulation, mucositis, probing pocket depth, changes in papilla height and width of the keratinised mucosa. 1-year data used
Notes	

Risk of bias

Item	**Authors' judgement**	**Description**
Allocation concealment?	Unclear	B - Unclear

Fischer 2004

Methods	5-year follow up, randomised, parallel group study. Outcome assessor was not blinded. No withdrawals at 1 year
Participants	Patients with edentulous maxillae allowing the placement of 5 to 6 implants. Exclusion criteria were smoking habits (more than 10 cigarettes a day), use of augmentation procedures at the implanted sites, and any systemic diseases likely to compromise implant surgery. Adults treated in the County Hospital, Falun, Sweden. 24 enrolled (16 in the early and 8 in the conventionally loaded group) and results given for 24
Interventions	5-6 implants restored directly with definitive full-arch titanium-resin prosthesis with cantilevers (7-11 mm long) at 9-18 days or 2.5-5.1 months. ITI SLA (Institut Straumann AG, Waldenburg, Switzerland) non-

Fischer 2004 (*Continued*)

	submerged solid titanium screws were used in the early loading group and submerged ITI EstheticPlus implants in the conventionally loaded group
Outcomes	Prosthesis/implant failures, marginal bone level changes on standardised intraoral radiographs, plaque index, sulcus bleeding index, width of the keratinised mucosa. 1-year data used
Notes	

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Güncü 2008

Methods	1-year follow up, randomised, split-mouth group study. Outcome assessor was blinded. No withdrawals at 1 year
Participants	Patients missing both mandibular first molars allowing the placement of 11.5 mm long and 4 mm large single implants with an implant to crown length ratio 1/1. Exclusion criteria were smoking, osteoporosis, severe parafunctional habits, post-extractive implants, untreated periodontal disease, poor oral hygiene, drug or alcohol abuse, need of augmentation procedures at the implanted sites, and any systemic diseases likely to compromise implant surgery. Adults treated in the Faculy of Dentistry, Hecettepe University, Ankara, Turkey. 13 enrolled and results given for 13
Interventions	Single implants restored first with acrylic crown and after 1 week with occluding cemented metal-ceramic crowns, either the same day or after 3 months. Brånemark® (Nobel Biocare AB, Göteborg, Sweden) non-submerged TiUnite Mark III type titanium screws were used
Outcomes	Prosthesis/implant failures, Osstell, marginal bone level changes on intraoral radiographs, plaque index, gingival index, probing depths, bleeding time index. 1-year data used
Notes	

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Hall 2006

Methods	1-year follow up, randomised, parallel group study. Outcome assessor was blinded. 3 withdrawals at 1 year, 1 for the immediately loaded group and 2 from the conventionally loaded group for emigration
Participants	Patients missing a single tooth in anterior maxilla (premolar to premolar) with adjacent teeth present, allowing the placement of at least 10 mm long implant with a diameter of 2.5 mm. Exclusion criteria were patients with type IV bone quality (very soft bone) according to the Lekholm and Zarb classification detected on radiograpphs, severe bruxism, smoking habits (more than 20 cigarettes per day), previous history of failed implants, and sites requiring augmentation surgery. Adults treated at the university dental clinic of the University of Otago, Dunedin, New Zealand. 28 enrolled (14 in each group) and results given for 25
Interventions	Single implants restored first with acrylic restorations (not in occlusion for the immediately loaded group) and then with screw-connected metal-ceramic crowns, either the same day or after 6 months. Southern (Southern Implants Ltd, Irene, South Africa) tapered sand-blasted acid-etched titanium screws were used
Outcomes	Prosthesis/implant failures, Periotest, marginal bone level changes on standardised intraoral radiographs, plaque accumulation, sulcus bleeding index, unspecified peri-implant soft tissues and prosthetic outcomes measures including the Papilla Index by Jemt 1997. 1-year data used
Notes	

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Lindeboom 2006

Methods	1-year follow up, randomised, parallel group study. Outcome assessor was blinded. No withdrawals at 1 year
Participants	Healthy (ASA I) patients missing single teeth in anterior maxilla (premolar to premolar), allowing the placement with no fenestration of a at least 8 mm long implant with a diameter of 3.4 mm placed with an insertion torque of at least 30 Ncm. Exclusion criteria were patients with smoking habits, parafunctional habits, drug or alcohol abuse, lack of a stable occlusion, lack of adequate proper oral hygiene and compliance and any systemic diseases likely to compromise implant surgery. Adults treated in the Oral and Maxillofacial Surgery Department of the Academic Medical Center of the University of Amsterdam, The Netherlands. 48 enrolled (24 in each group) and results given for 48
Interventions	Single implants immediately restored within 1 day with acrylic single crowns in occlusion or not in occlusion. Permanent ceramic crowns were provided after 6 months. BioComp® (BioComp Industries BV, Vught, The Netherlands) tapered TPS screws were used
Outcomes	Prosthesis/implant failures, Osstell, marginal bone level changes on intraoral radiographs, Papilla Index by Jemt 1997 and midbuccal gingival levels. 1-year data used
Notes	

Lindeboom 2006 (*Continued*)

Risk of bias		
Item	**Authors' judgement**	**Description**
Allocation concealment?	Yes	A - Adequate

Merli 2008

Methods	1-year follow up, randomised, parallel group study. Outcome assessor was independent but not blinded. No withdrawals at 1 year
Participants	Partially edentulous patients (both mandibles and maxillae) allowing the placement of at least 9.5 mm long implants and the bone thickness at implant sites had to be of at least 5.5 mm. For implants to be immediately loaded, a primary implant stability of 40 Ncm had to be achieved at implant insertion. Exclusion criteria were patients irradiated in the head and neck area for less than 1 year, severe bruxism, substance abusers, pregnancy, uncontrolled diabetes, and any systemic diseases likely to compromise implant surgery, lack of opposing occluding dentition, a need for bone-augmentation procedures with exception of Bio-Oss granules in post-extractive sites, presence of less than 4 mm of keratinised mucosa. Adults treated in Italian private practice. 60 enrolled (30 in the immediately and 30 in the early loaded group) and results given for 60
Interventions	1 or more implants placed with a flapless technique and restored with non-occluding acrylic restorations, either within 72 hours or after 6 weeks, and after 6 months with occluding cemented metal-ceramic crowns. SPI®Element System (Thommen Medical AG, Waldenburg, Switzerland) sand-blasted acid-etched screws, and in some of the post-extraction sites SPI®Contact troncoconical screws were used
Outcomes	Prosthesis/implant failures and complications. 1-year data used
Notes	

Risk of bias		
Item	**Authors' judgement**	**Description**
Allocation concealment?	Yes	A - Adequate

Oh 2006

Methods	6-month follow up, randomised, parallel group study. Outcome assessor was blinded. No withdrawals at 6 months
Participants	2 single teeth missing in the anterior maxilla (premolar to premolar) allowing the placement of at least 10 mm long implants with a diameter of 3.8 mm. No exclusion criteria specified. Adults treated at the university dental clinic of the University of Michigan, Ann Arbor, USA. 24 enrolled (12 in each group) and results given for 24

Oh 2006 (*Continued*)

Interventions	Single implants placed with a flapless technique and restored first with acrylic restorations (immediately group only) and then with cemented metal-ceramic crowns, either the same day or after 4 months. Zimmer (Zimmer, Carlsbad, Ca, USA) non-submerged implants were used
Outcomes	Prosthesis/implant failures, probing pocket depths, plaque index, sulcus bleeding index, marginal level of soft tissues, soft tissue thickness, width of the keratinised mucosa, Papilla Index by Jemt 1997. 6-month data used
Notes	

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Payne 2002

Methods	2-year follow up, randomised, parallel group study. Outcome assessor was blinded. 2 withdrawals at 1 year from the conventionally loaded group for emigration
Participants	Patients with edentulous mandibles having 13 to 15 mm of residual anterior bone height. Exclusion criteria were patients with type IV bone quality (very soft bone) according to the Lekholm and Zarb classification detected at implant insertion (none), previously bone-grafted or irradiated jaws, history of bruxism, any evidence of current or previous smoking and any systemic diseases likely to compromise implant surgery. Adults treated at the university dental clinic of the University of Otago, Dunedin, New Zealand. 24 enrolled (12 in each group) and results given for 22
Interventions	2 unsplinted implants with ball attachments supporting an overdenture conventionally loaded at 12 weeks versus 2 unsplinted implants with ball attachments early loaded at 6 weeks. ITI (Institut Straumann AG, Waldenburg, Switzerland) SLA non-submerged solid titanium screws were used
Outcomes	Prosthesis/implant failures, Periotest, Osstell, marginal bone level changes on standardised intraoral radiographs, plaque accumulation, modified sulcus bleeding index, probing pocket depth, width of the keratinised mucosa. 1-year data used
Notes	

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Romanos 2006

Methods	2-year follow up, randomised, split-mouth group study. Outcome assessor was not blinded. No withdrawals at 1 year
Participants	Patients with bilateral free-end lower jaws distal to the canines or premolars having residual bone of 11 mm in height and 6 mm in width. Patients have to show high levels of compliance and to be in good general health. Exclusion criteria were alcohol abuse, drug or medication dependent patients, pregnancy, patients after radio- or chemotherapy. Adults treated at the university dental clinic of the Dental School of Frankfurt, Frankfurt, Germany. 12 enrolled and results given for 12
Interventions	3 implants supporting a partial fixed bridge conventionally loaded (3 months) versus 3 contralateral implants immediately loaded (same day of placement). Ankylos (Degussa Dental, Hanau-Wolfang, Germany) grit-roughened titanium screws were used
Outcomes	Prosthesis/implant failures, Periotest, marginal bone level changes on panoramic radiographs, plaque accumulation, sulcus bleeding index, probing pocket depth, width of the keratinised mucosa. 1-year data used
Notes	

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Romeo 2002

Methods	2-year follow up, randomised, parallel group study. Outcome assessor was blinded. No withdrawals at 1 year
Participants	Patients that have been edentulous in the mandible for at least 3 months. Mandibles allowing the placement of 4 implants of at least 10 mm length. Exclusion criteria were patients with type IV bone quality (very soft bone) according to the Lekholm and Zarb classification detected at implant insertion (none), previously irradiated jaws, severe bruxism, smoking habits (more than 20 cigarettes a day) and any systemic diseases likely to compromise implant surgery. Adults treated at a university dental clinic of the University of Milan, Italy. 20 enrolled (10 patients in each group) and results given for 20
Interventions	4 implants supporting a bar and an overdenture conventionally loaded (3 to 4 months) versus 4 implants immediately loaded (within 2 days from insertion). ITI (Institut Straumann AG, Waldenburg, Switzerland) SLA non-submerged solid titanium screws were used
Outcomes	Prosthesis/implant failures, Periotest, marginal bone level changes on panoramic radiographs, plaque accumulation, modified bleeding index, probing pocket depth. 1-year data used
Notes	

Risk of bias

Romeo 2002 (*Continued*)

Item	Authors' judgement	Description
Allocation concealment?	No	C - Inadequate

Schincaglia 2008

Methods	1-year follow up, randomised, parallel group study. Outcome assessors were blinded only for marginal bone levels. No withdrawals at 1 year
Participants	Patients missing 1 mandibular first or second molars allowing the placement of a single implant at least 8.5 mm long and 5 mm large with a minimal insertion torque of 20 Ncm. Exclusion criteria were severe systemic conditions (ASA III), in need of bone augmentation, and if the tooth was extracted less than 4 months before. Adults treated at the School of Dentistry, University of Bologna, Italy. 30 enrolled (15 patients in each group) and results given for 30
Interventions	Single immediate implants restored the same day with occluding screw-retained acrylic crowns, replaced after 3 to 4 months by cemented or screw-retained metal-ceramic crowns. Conventionally loaded implants were directly restored with cemented or screw-retained metal-ceramic crowns. Brånemark® (Nobel Biocare AB, Göteborg, Sweden) non-submerged TiUnite Mark III Wide-Platform type titanium screws were used
Outcomes	Prosthesis/implant failures, marginal bone level changes on intraoral radiographs, buccal peri-implant marginal soft tissue levels. 1-year data used
Notes	

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	No	C - Inadequate

Tawse-Smith 2002

Methods	2-year follow up, randomised, parallel group study. Outcome assessors were blinded. No withdrawals at 1 year
Participants	Patients with edentulous mandibles having 13 to 15 mm of residual anterior bone height. Exclusion criteria were patients with type IV bone quality (very soft bone) according to the Lekholm and Zarb classification detected at implant insertion (none), previously bone-grafted or irradiated jaws, history of bruxism, any evidence of current or previous smoking and any systemic diseases likely to compromise implant surgery. Adults treated at the university dental clinic of the University of Otago, Dunedin, New Zealand. 48 enrolled (12 patients in each of the 4 groups) and results given for 48
Interventions	2 unsplinted implants with ball attachments supporting an overdenture conventionally loaded at 12 weeks versus 2 unsplinted implants with ball attachments early loaded at 6 weeks. The comparison was done using 2 different implant systems: Steri-Oss® (Steri-Oss, Yorba Linda, California, USA) non-submerged acid-etched titanium screws HL series, 3.8 mm in diameter and Southern (Southern Implants Ltd, Irene,

Tawse-Smith 2002 (*Continued*)

	South Africa) non-submerged sand-blasted acid-etched titanium screws
Outcomes	Prosthesis/implant failures, Periotest, marginal bone level changes on standardised intraoral radiographs, plaque accumulation, modified sulcus bleeding index, probing pocket depth, width of the keratinised mucosa. 1-year data used
Notes	Most of the failed implants were placed by a surgeon who placed only Steri-Oss implants

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Testori 2007

Methods	1-year follow up, randomised, parallel group study. Outcome assessors were blinded only for marginal bone levels. No withdrawals at 1 year
Participants	Partially edentulous patients (both mandibles and maxillae) allowing the placement of at least 8.5 mm long implants with a diameter of 4 mm. For implants to be immediately loaded, a primary implant stability of 20 or 30 Ncm had to be achieved at insertion for implants which were going to be splinted and single implants, respectively. Exclusion criteria were patients irradiated in the head and neck area, severe bruxism, substance abusers, pregnancy, uncontrolled diabetes, and any systemic diseases likely to compromise implant surgery, lack of opposing occluding dentition, need for augmentation procedures. Adults treated in 5 Italian private practices. 52 enrolled (25 in the immediate and 27 in the early loaded group) and results given for 52
Interventions	1 or more implants restored first with acrylic restorations (not in occlusion for the immediately loaded group) and then with cemented metal-ceramic crowns, either within 48 hours or after 2 months. 3i (3i Biomet , Palm Beach, FL, USA) Osseotite FNT tapered titanium screws were used; 1 of the centres used some similar prototypes in both groups
Outcomes	Prosthesis/implant failures, marginal bone level changes on intraoral radiographs, buccal peri-implant marginal soft tissue levels. 1-year data used
Notes	

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Turkyilmaz 2007

Methods	2-year follow up, randomised, parallel group study. Outcome assessors were not blinded. No withdrawals at 1 year
Participants	Patients with edentulous mandibles allowing the placement of 2 15 mm long implants. Exclusion criteria were patients with previously bone-grafted or irradiated jaws, and any systemic diseases likely to compromise implant surgery. Adults treated in the Faculy of Dentistry, Hecettepe University, Ankara, Turkey. 20 enrolled (20 patients in each group) and results given for 20
Interventions	2 unsplinted implants with ball attachments supporting an overdenture immediatally loaded at 1 week versus 2 unsplinted implants with ball attachments conventionally loaded at 3 months. Brånemark® (Nobel Biocare AB, Göteborg, Sweden) non-submerged TiUnite Mark III type titanium screws were used
Outcomes	Prosthesis/implant failures, Osstell, marginal bone level changes on standardised intraoral radiographs, complications. 1-year data used
Notes	

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	No	C - Inadequate

Zöllner 2008

Methods	1-year follow up, randomised, parallel group study. Outcome assessors were blinded only for marginal bone levels. Possibly 5 withdrawals from the immediately loaded group (3 subjects withdrew consent and 2 could not be located) and 1 from the early loaded group (withdrew consent) at 5 months (it is unclear whether patients were lost prior to or after implant placement) and unknown number of withdrawals at 1 year
Participants	Patients missing teeth in premolar and molar areas allowing the placement of 8 mm long and 4.1 mm large single implant. Exclusion criteria were post-extractive implants (at least 4 months healing was required) , lack of primary implant stability, opposing fixed dentition, smoking > 10 cigarettes per day, severe bruxism/clenching, and any systemic diseases likely to compromise implant surgery. Adults treated in 20 universities or private practices all over the world. 266 patients treated (138 in the immediately loaded group and 128 in the early loaded group) and results given for an unknown number
Interventions	1 or 4 implants restored with non-occluding acrylic restorations, either the same day or after 1 month, and after 5 months with occluding cemented or screw-retained restorations made of porcelain, acrylic resin or gold. ITI® SLA active (Institut Straumann AG, Waldenburg, Switzerland) solid sand-blasted large-grit acid-etched titanium grade 4 screws, 3 standard plus implants were also used
Outcomes	Prosthesis/implant failures, marginal bone level changes on standardised intraoral radiographs. 1-year data used
Notes	

Zöllner 2008 (*Continued*)

Risk of bias		
Item	**Authors' judgement**	**Description**
Allocation concealment?	No	C - Inadequate

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Cannizzaro 2008c	Trial comparing flapless surgery + modified implant installation technique + immediate loading versus conventional surgery and loading
Göthberg 2007	Ongoing trial comparing immediate versus early loading in partially edentulous patients. Patients are subsequentially randomised again to 3 different abutment solutions (no abutment, abutment with a rough surface and abutment with a machined surface)
Ottoni 2005	The author informed us that the study was not a randomised clinical trial
Polson 2000	Insufficient data presented. No reply to letter.
Roccuzzo 2001	Trial comparing early versus conventional loading of different implant types
Salvi 2004	Trial comparing 2 early loading procedures (2 versus 6 weeks). Such comparison does not fit within our hypothesis
Testori 2003	Trial comparing immediate non-occluding loading versus conventional loading but at the same time patients were also randomised to 2 different implant types
Turkyilmaz 2006	The author informed us that the study was not a randomised clinical trial

Characteristics of ongoing studies *[ordered by study ID]*

den Hartog 2007

Trial name or title	Single tooth replacement with dental implants in the aesthetic zone. A randomised clinical trial of different implant designs and different times of restorations
Methods	
Participants	120 patients missing a maxillary single tooth from first to first premolars
Interventions	Immediate versus conventional loading with NobelReplace Groovy (NobelBiocare). The same trial is also comparing 3 different implant types conventionally loaded

den Hartog 2007 (*Continued*)

Outcomes	Implant survival, marginal bone levels, recession, various aesthetic indexes, patient satisfaction
Starting date	1 September 2004.
Contact information	Dr den Hartog L, University Medical Center Groningen (UMCG), The Netherlands
Notes	

DATA AND ANALYSES

Comparison 1. Immediate versus conventional loading

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Patients with prosthesis failures	6	270	risk ratio (Random, 95% CI)	2.41 [0.76, 7.63]
2 Patients with implant failures	8		risk ratio (Random, 95% CI)	1.92 [0.70, 5.22]
3 Marginal bone level changes	6	162	Mean Difference (Random, 95% CI)	-0.10 [-0.24, 0.04]

Comparison 2. Early versus conventional loading

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Patients with prosthesis failures	1	48	Risk Ratio (M-H, Random, 95% CI)	5.0 [0.63, 39.67]
2 Patients with implant failures	2	72	Risk Ratio (M-H, Random, 95% CI)	1.15 [0.06, 22.33]
3 Marginal bone level changes	2	70	Mean Difference (IV, Random, 95% CI)	-0.04 [-0.15, 0.07]

Comparison 3. Immediate versus early loading

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Patients with prosthesis failures	4	438	Risk Ratio (Random, 95% CI)	0.68 [0.25, 1.86]
2 Patients with implant failures	5	468	Risk Ratio (Random, 95% CI)	0.65 [0.26, 1.63]
3 Marginal bone level changes	3	136	Mean Difference (Random, 95% CI)	-0.06 [-0.16, 0.03]

Comparison 4. Occlusal versus non-occlusal loading

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Patients with prosthesis failures	1	48	Risk Ratio (M-H, Random, 95% CI)	0.67 [0.12, 3.64]
2 Patients with implant failures	1	48	Risk Ratio (M-H, Random, 95% CI)	0.67 [0.12, 3.64]
3 Marginal bone level changes	1	43	Mean Difference (IV, Random, 95% CI)	0.01 [-0.13, 0.14]

Analysis 1.1. Comparison 1 Immediate versus conventional loading, Outcome 1 Patients with prosthesis failures.

Review: Interventions for replacing missing teeth: different times for loading dental implants

Comparison: 1 Immediate versus conventional loading

Outcome: 1 Patients with prosthesis failures

Study or subgroup	Immediate loading N	Conventional loading N	log [risk ratio] (SE)	risk ratio IV,Random,95% CI	Weight	risk ratio IV,Random,95% CI
Cannizzaro 2003	14	14	-1.1 (1.6)		13.5 %	0.33 [0.01, 7.66]
Donati 2008	84	53	1.43 (1.5)		15.4 %	4.18 [0.22, 79.04]
Gnc 2008	13	13	0.7673 (1.093)		29.0 %	2.15 [0.25, 18.35]
Hall 2006	13	12	0.995 (1.645)		12.8 %	2.70 [0.11, 67.98]
Oh 2006	12	12	1.955 (1.48)		15.8 %	7.06 [0.39, 128.48]
Schincaglia 2008	15	15	1.099 (1.6)		13.5 %	3.00 [0.13, 69.06]
Total (95% CI)					**100.0 %**	**2.41 [0.76, 7.63]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 2.23$, df = 5 (P = 0.82); $I^2 = 0.0\%$

Test for overall effect: Z = 1.49 (P = 0.14)

Analysis 1.2. Comparison 1 Immediate versus conventional loading, Outcome 2 Patients with implant failures.

Review: Interventions for replacing missing teeth: different times for loading dental implants

Comparison: 1 Immediate versus conventional loading

Outcome: 2 Patients with implant failures

Study or subgroup	log [risk ratio] (SE)	risk ratio IV,Random,95% CI	Weight	risk ratio IV,Random,95% CI
Cannizzaro 2003	-1.1 (1.6)		10.2 %	0.33 [0.01, 7.66]
Chiapasco 2001	0 (1.342)		14.5 %	1.00 [0.07, 13.88]
Donati 2008	1.43 (1.5)		11.6 %	4.18 [0.22, 79.04]
Gnc 2008	0.7673 (1.093)		21.8 %	2.15 [0.25, 18.35]
Hall 2006	0.995 (1.645)		9.6 %	2.70 [0.11, 67.98]
Oh 2006	1.955 (1.48)		11.9 %	7.06 [0.39, 128.48]
Romeo 2002	-0.1086 (1.6)		10.2 %	0.90 [0.04, 20.64]
Schincaglia 2008	1.099 (1.6)		10.2 %	3.00 [0.13, 69.06]
Total (95% CI)			**100.0 %**	**1.92 [0.70, 5.22]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 2.84$, df = 7 (P = 0.90); $I^2 = 0.0\%$

Test for overall effect: Z = 1.27 (P = 0.20)

Analysis 1.3. Comparison 1 Immediate versus conventional loading, Outcome 3 Marginal bone level changes.

Review: Interventions for replacing missing teeth: different times for loading dental implants

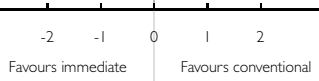
Comparison: 1 Immediate versus conventional loading

Outcome: 3 Marginal bone level changes

Study or subgroup	Immediate loading N	Conventional loading N	Mean Difference (SE)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Cannizzaro 2003	14	13	0.02 (0.047)		37.4 %	0.02 [-0.07, 0.11]
Crespi 2008	20	20	-0.14 (0.164)		13.3 %	-0.14 [-0.46, 0.18]
Gnc 2008	11	11	-0.23 (0.1484)		15.2 %	-0.23 [-0.52, 0.06]
Hall 2006	12	12	-0.14 (0.568)		1.5 %	-0.14 [-1.25, 0.97]
Schincaglia 2008	14	15	-0.43 (0.1777)		11.8 %	-0.43 [-0.78, -0.08]
Turkyilmaz 2007	10	10	0 (0.114)		20.8 %	0.0 [-0.22, 0.22]
Total (95% CI)					**100.0 %**	**-0.10 [-0.24, 0.04]**

Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 8.57$, df = 5 (P = 0.13); $I^2 = 42\%$

Test for overall effect: Z = 1.39 (P = 0.16)



Analysis 2.1. Comparison 2 Early versus conventional loading, Outcome 1 Patients with prosthesis failures.

Review: Interventions for replacing missing teeth: different times for loading dental implants

Comparison: 2 Early versus conventional loading

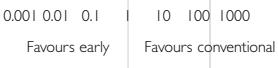
Outcome: 1 Patients with prosthesis failures

Study or subgroup	Early loading n/N	Conventional loading n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Tawse-Smith 2002	5/24	1/24		100.0 %	5.00 [0.63, 39.67]
Total (95% CI)	**24**	**24**		**100.0 %**	**5.00 [0.63, 39.67]**

Total events: 5 (Early loading), 1 (Conventional loading)

Heterogeneity: not applicable

Test for overall effect: Z = 1.52 (P = 0.13)



Analysis 2.2. Comparison 2 Early versus conventional loading, Outcome 2 Patients with implant failures.

Review: Interventions for replacing missing teeth: different times for loading dental implants

Comparison: 2 Early versus conventional loading

Outcome: 2 Patients with implant failures

Study or subgroup	Early loading n/N	Conventional loading n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Fischer 2004	1/16	2/8		48.9 %	0.25 [0.03, 2.36]
Tawse-Smith 2002	5/24	1/24		51.1 %	5.00 [0.63, 39.67]
Total (95% CI)	**40**	**32**		**100.0 %**	**1.15 [0.06, 22.33]**

Total events: 6 (Early loading), 3 (Conventional loading)

Heterogeneity: $Tau^2 = 3.36$; $Chi^2 = 3.76$, df = 1 (P = 0.05); $I^2 = 73\%$

Test for overall effect: Z = 0.10 (P = 0.92)

Analysis 2.3. Comparison 2 Early versus conventional loading, Outcome 3 Marginal bone level changes.

Review: Interventions for replacing missing teeth: different times for loading dental implants

Comparison: 2 Early versus conventional loading

Outcome: 3 Marginal bone level changes

Study or subgroup	Early loading N	Mean(SD)	Conventional loading N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Payne 2002	12	0.27 (0.18)	10	0.35 (0.22)		39.9 %	-0.08 [-0.25, 0.09]
Tawse-Smith 2002	24	0.12 (0.19)	24	0.13 (0.29)		60.1 %	-0.01 [-0.15, 0.13]
Total (95% CI)	**36**		**34**			**100.0 %**	**-0.04 [-0.15, 0.07]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.39$, df = 1 (P = 0.53); $I^2 = 0.0\%$

Test for overall effect: Z = 0.69 (P = 0.49)

Analysis 3.1. Comparison 3 Immediate versus early loading, Outcome 1 Patients with prosthesis failures.

Review: Interventions for replacing missing teeth: different times for loading dental implants

Comparison: 3 Immediate versus early loading

Outcome: 1 Patients with prosthesis failures

Study or subgroup	Immediate N	Early N	log [Risk Ratio] (SE)	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
Cannizzaro 2008a	30	30	-1.609 (1.5)		11.6 %	0.20 [0.01, 3.78]
Cannizzaro 2008d	30	30	0 (1.45)		12.4 %	1.00 [0.06, 17.15]
Testori 2007	25	27	1.172 (1.61)		10.1 %	3.23 [0.14, 75.76]
Zllner 2008	138	128	-0.478 (0.63)		65.9 %	0.62 [0.18, 2.13]
Total (95% CI)					**100.0 %**	**0.68 [0.25, 1.86]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 1.69$, df = 3 (P = 0.64); $I^2 = 0.0\%$

Test for overall effect: Z = 0.75 (P = 0.45)

Test for subgroup differences: Not applicable

Analysis 3.2. Comparison 3 Immediate versus early loading, Outcome 2 Patients with implant failures.

Review: Interventions for replacing missing teeth: different times for loading dental implants

Comparison: 3 Immediate versus early loading

Outcome: 2 Patients with implant failures

Study or subgroup	Immediate N	Early N	log [Risk Ratio] (SE)	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
Cannizzaro 2008a	30	30	-1.609 (1.5)		9.8 %	0.20 [0.01, 3.78]
Cannizzaro 2008b	15	15	-0.693 (1.2)		15.4 %	0.50 [0.05, 5.25]
Cannizzaro 2008d	30	30	0 (1.45)		10.5 %	1.00 [0.06, 17.15]
Testori 2007	25	27	1.172 (1.61)		8.5 %	3.23 [0.14, 75.76]
Zllner 2008	138	128	-0.478 (0.63)		55.7 %	0.62 [0.18, 2.13]
Total (95% CI)					**100.0 %**	**0.65 [0.26, 1.63]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 1.75$, df = 4 (P = 0.78); $I^2 = 0.0\%$

Test for overall effect: Z = 0.92 (P = 0.36)

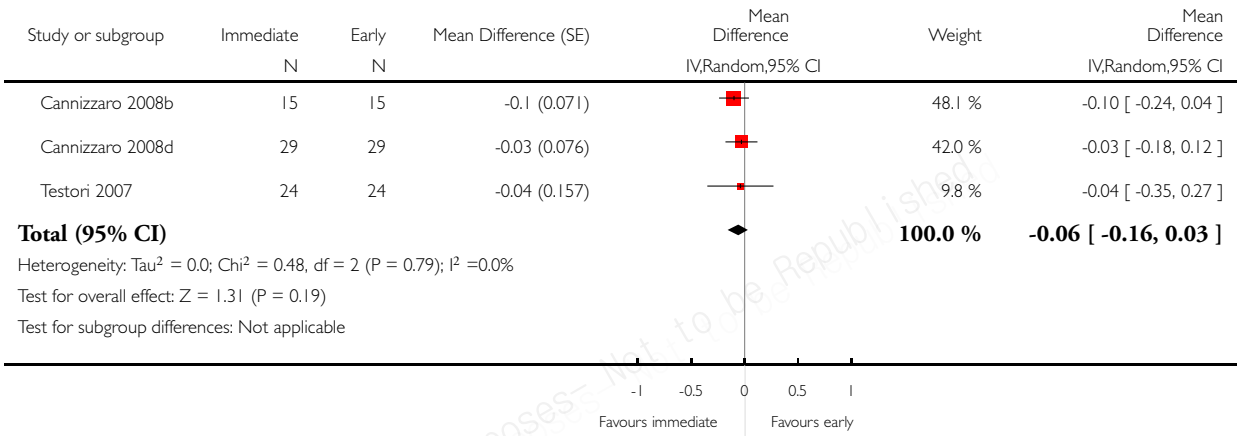
Test for subgroup differences: Not applicable

Analysis 3.3. Comparison 3 Immediate versus early loading, Outcome 3 Marginal bone level changes.

Review: Interventions for replacing missing teeth: different times for loading dental implants

Comparison: 3 Immediate versus early loading

Outcome: 3 Marginal bone level changes

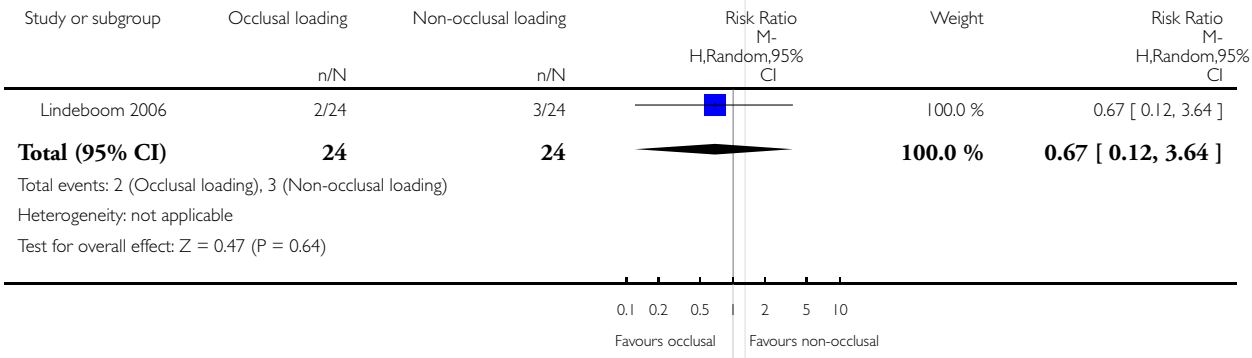


Analysis 4.1. Comparison 4 Occlusal versus non-occlusal loading, Outcome 1 Patients with prosthesis failures.

Review: Interventions for replacing missing teeth: different times for loading dental implants

Comparison: 4 Occlusal versus non-occlusal loading

Outcome: 1 Patients with prosthesis failures



Analysis 4.2. Comparison 4 Occlusal versus non-occlusal loading, Outcome 2 Patients with implant failures.

Review: Interventions for replacing missing teeth: different times for loading dental implants

Comparison: 4 Occlusal versus non-occlusal loading

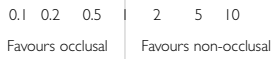
Outcome: 2 Patients with implant failures

Study or subgroup	Occlusal loading n/N	Non-occlusal loading n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Lindeboom 2006	2/24	3/24		100.0 %	0.67 [0.12, 3.64]
Total (95% CI)	**24**	**24**		**100.0 %**	**0.67 [0.12, 3.64]**

Total events: 2 (Occlusal loading), 3 (Non-occlusal loading)

Heterogeneity: not applicable

Test for overall effect: Z = 0.47 (P = 0.64)



Analysis 4.3. Comparison 4 Occlusal versus non-occlusal loading, Outcome 3 Marginal bone level changes.

Review: Interventions for replacing missing teeth: different times for loading dental implants

Comparison: 4 Occlusal versus non-occlusal loading

Outcome: 3 Marginal bone level changes

Study or subgroup	Occlusal loading N	Mean(SD)	Non-occlusal loading N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Lindeboom 2006	22	0.15 (0.21)	21	0.15 (0.24)		100.0 %	0.01 [-0.13, 0.14]
Total (95% CI)	**22**		**21**			**100.0 %**	**0.01 [-0.13, 0.14]**

Heterogeneity: not applicable

Test for overall effect: Z = 0.07 (P = 0.94)

Test for subgroup differences: Not applicable

ADDITIONAL TABLES

Table 1. Results of quality assessment after correspondence with authors

Study	Allocation concealment	Blinding of assessor	Withdrawals	Risk of bias
Assad 2007	Unclear	Unclear	None	High
Cannizzaro 2003	Yes	Yes	None	Low
Cannizzaro 2008a	Yes	Yes	None	Low
Cannizzaro 2008b	Yes	Yes	None	Low
Cannizzaro 2008d	Yes	Yes	None	Low
Chiapasco 2001	No	Yes	None	High
Crespi 2008	Unclear	Unclear	None	High
Donati 2008	Unclear	Partly (radiographs)	Yes, reasons	High
Fischer 2004	Yes	No	None	High
Güncü 2008	Yes	Yes	None	Low
Hall 2006	Unclear	Yes	Yes, reasons	High
Lindeboom 2006	Yes	Yes	None	Low
Merli 2008	Yes	No	None	High
Oh 2006	Unclear	Yes	None	High
Payne 2002	Unclear	Yes	Yes, reasons	High
Romanos 2006	Unclear	No	None	High
Romeo 2002	No	Yes	None	High
Schincaglia 2008	No	Partly (radiographs)	None	High
Tawse-Smith 2002	Unclear	Yes	None	High
Testori 2007	Yes	Partly (radiographs)	None	High
Turkyilmaz 2007	No	No	None	High
Zöllner 2008	No	Partly (radiographs)	Yes, unclear	High

APPENDICES

Appendix 1. MEDLINE (OVID) search strategy

1. exp Dental Implants/
2. exp Dental Implantation/ or dental implantation
3. exp Dental Prosthesis, Implant-Supported/
4. ((osseointegrated adj implant$) and (dental or oral))
5. dental implant$
6. (implant$ adj5 dent$)
7. (((overdenture$ or crown$ or bridge$ or prosthesis or restoration$) adj5 (Dental or oral)) and implant$)
8. "implant supported dental prosthesis"
9. ("blade implant$" and (dental or oral))
10. ((endosseous adj5 implant$) and (dental or oral))
11. ((dental or oral) adj5 implant$)
12. OR/1-11

Appendix 2. Cochrane RCT search filter for MEDLINE (OVID)

1. randomized controlled trial.pt.
2. controlled clinical trial.pt.
3. randomized.ab.
4. placebo.ab.
5. drug therapy.fs.
6. randomly.ab.
7. trial.ab.
8. groups.ab.
9. or/1-8
10. humans.sh.
11. 9 and 10

WHAT'S NEW

Last assessed as up-to-date: 30 October 2008.

Date	Event	Description
6 July 2009	Amended	Minor corrections.

HISTORY

Protocol first published: Issue 4, 2002

Review first published: Issue 1, 2003

Date	Event	Description
31 October 2008	New citation required and conclusions have changed	Change of authorship. We have added a secondary hypothesis, previously described in the subgroup analyses. We have updated the review adding 11 new included studies (Lindeboom 2006 (previously excluded); Assad 2007; Turkyilmaz 2007; Cannizzaro 2008a; Cannizzaro 2008b; Cannizzaro 2008d; Crespi 2008; Donati 2008; Güncü 2008; Schincaglia 2008; Zöllner 2008) and additional data from two previously included studies (Merli 2007; Testori 2007). Conclusions slightly changed.
31 October 2008	New search has been performed	The searches were updated in June 2008.
10 June 2008	Amended	Converted to new review format.
15 February 2007	New search has been performed	The searches were updated in February 2007.
15 February 2007	New citation required and conclusions have changed	Change of authorship. We have updated the review adding seven new included studies (Cannizzaro 2003 (previously excluded); Fischer 2004; Hall 2006; Oh 2006; Romanos 2006; Merli 2007; Testori 2007), and excluding eight new trials. We also included studies with a minimum follow up of 6 months in function. Conclusions slightly changed
15 March 2004	New search has been performed	The searches were updated in March 2004.
15 March 2004	New citation required and conclusions have changed	Change of authorship. We have updated the review and added three new included studies (Payne 2002; Romeo 2002; Romanos in press). We have added to the methods of the review section the following possible subgroup analyses to be conducted in the future if appropriate data become available: (1) Whether implants were placed in mandibles or maxillae (2) Whether implants were placed in partially or fully edentulous jaws (3) Whether implants were placed in the anterior or posterior jaw (4) Different number of inserted implants (for instance overdentures supported by two versus overdentures sup-

(*Continued*)

		ported by four implants) (5) Whether turned (machined) or implants with a roughened surface were used (6) Whether the trial was supported by implant manufacturer(s) or not

CONTRIBUTIONS OF AUTHORS

Conceiving, designing and co-ordinating the review (Marco Esposito (ME)).

Developing search strategy and undertaking searches (ME, Paul Coulthard (PC)).

Screening search results and retrieved papers against inclusion criteria (ME, PC, Maria Gabriella Grusovin (GG), Hubert Achille (HA)).

Appraising quality and extracting data from papers (ME, GG, HA, Helen Worthington (HW)).

Writing to authors for additional information (ME, HW).

Data management for the review and entering data into RevMan (HW, ME).

Analysis and interpretation of data (ME, HW).

Writing the review (ME).

Providing general advice on the review (HW, GG, PC).

Performing previous work that was the foundation of current study (ME, HW, PC).

DECLARATIONS OF INTEREST

Marco Esposito is among the authors of five of the included, and two of the excluded studies, however, he was not involved in the quality assessment of these trials. Marco Esposito is working as independent methodological consultant for various implant related projects for some of the companies whose implants were used both in the included and excluded trials, however, in this review, implant brands were not under evaluation.

SOURCES OF SUPPORT

Internal sources

- School of Dentistry, The University of Manchester, UK.

External sources

- No sources of support supplied

INDEX TERMS

Medical Subject Headings (MeSH)

*Dental Implantation, Endosseous; Bone Density; Dental Implants; Mandible [physiology]; Materials Testing; Randomized Controlled Trials as Topic; Time Factors; Tooth Loss [*surgery]

MeSH check words

Humans