A 5-Year Follow-up Comparative Analysis of the Efficacy of Various Osseointegrated Dental Implant Systems: A Systematic Review of Randomized Controlled Clinical Trials

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Purpose: *To test the null hypothesis that there is no difference in failure rates between various root-formed osseointegrated dental implant systems after 5 years of loading.* ***Materials and Methods:*** *A search was conducted for all randomized controlled clinical trials (RCTs) comparing different implant systems with a follow-up of 5 years. The Cochrane Oral Health Group's Trials Register, CENTRAL, MEDLINE, and EMBASE were searched. Several dental journals were also searched by hand. Written contacts were established with authors of the identified RCTs and with more than 55 oral implant manufacturers and personal contacts to identify unpublished RCTs. No language restriction was applied. The last electronic search was conducted on February 1, 2005. Screening of eligible studies, quality assessment, and data extraction were conducted in duplicate. Results were expressed as random effect models using weighted mean differences for continuous outcomes and relative risk for dichotomous outcomes with 95% confidence intervals.* ***Results:*** *Ten RCTs were identified. Four of these RCTs, reporting results from a total of 204 patients, were considered suitable for inclusion. Six different implant types were compared. On a per-patient rather than a per-implant basis, there were no statistically significant differences, with the exception of more marginal bone loss around early loaded Southern implants when compared to early loaded Steri-Oss implants (mean difference −0.35 mm; 95% CI −0.70 to −0.01). However, the difference disappeared in the meta-analysis.* ***Discussion and Conclusions:*** *There were no clinical differences among implant systems. However, these findings are based on only 4 RCTs with few participants. More RCTs should be conducted with larger patient samples.* INT J ORAL MAXILLOFAC IMPLANTS 2005;20:557–568

Key words: *follow-up studies, meta-analysis, oral implants, randomized controlled clinical trials*

Many different dental implant systems are currently available on the market. It has been estimated more than 2,000 types of implants varying in form, material, dimension, surface properties, and interface geometry are available.[1] In particular, the area of implant surface modifications has been subjected to aggressive marketing aimed at establishing the superiority of a given surface over the others. Numerous methods of modifying the surface of the implant, including machining, blasting, acid-etching, oxidation, plasma-spraying, coating with hydroxyapatite, have been developed and are currently used alone or in combination with the aim of enhancing clinical performances. It would be useful to know whether certain implant systems provide improved clinical results. Since it is difficult to determine the effectiveness and potential harms of various implant systems, it is important to condense the most reliable

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information in a systematic way, limiting bias.[2,3] In addition, dental implants are supposed to be a long-term therapy; therefore, their efficacy has to be evaluated over a long-term period.

The aim of this systematic review was to assess whether there is a difference in failure rates among various root-form osseointegrated dental implant systems after 5 years of loading. In addition, the review was designed to investigate whether there could be differences in the incidence of early failures and peri-implantitis between implant systems using turned (machined) surfaces compared to implants with roughened surfaces.

MATERIALS AND METHODS

Inclusion Criteria and Outcome Measures

The entire protocol for this review was conceived a priori, internally and externally refereed, and published electronically on the Cochrane database a priori, where it was open to public criticism. No post-hoc analyses were performed. To minimize bias[2,3] only randomized clinical trials (RCTs) of adequate quality comparing different implant systems or implant types with a follow-up of 5 years in function were included. The broadest inclusion criteria were adopted to make the findings of this systematic review more likely to be generalizable. Any RCT including any partially or totally edentulous patient treated with any type of root-form osseointegrated implant, commercially available or not, for dental replacement with any type of surgical technique or procedure was included if it reported data regarding the outcome measures described in this section.

Primary outcome measure was implant failure defined as:

- Implant mobility.
- Removal of stable implants, dictated by progressive marginal bone loss or infection (biological failures). Biological failures were presented as early failures (failure to establish osseointegration) and late failures (failure to maintain the established osseointegration). Failures that occurred before prosthesis delivery or, in the case of immediate or early loaded implants, soon afterward (ie, with a few months), were considered early failures. Implant mobility could be assessed manually or with instruments such as Periotest (Siemens, Bensheim, Germany) or resonance frequency (Osstell; Integration Diagnostics, Göteborg, Sweden).
- Implant fracture and other mechanical complications not allowing use of the implants (mechanical failures).

Secondary outcome measures were:

- Radiographic marginal bone level changes expressed in millimeters on intraoral radiographs taken with a paralleling technique.
- Occurrence of peri-implantitis, defined by the authors of the original trials as implants affected by progressive marginal bone loss with signs of infection.

Search Strategy for Identification of Studies

For the identification of studies to be included or considered for this review, detailed search strategies for each database to be searched were developed. A search strategy was first developed for MEDLINE (OVID) and then revised appropriately for each database. The search strategy used a combination of controlled vocabulary and free text terms as presented in Table 1. The following databases were searched:

- The Cochrane Oral Health Group's Trials Register (February 1, 2005)
- The Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library, Issue 1, 2005)
- MEDLINE (1966 to February 1, 2005)
- EMBASE (1980 to February 1, 2005)

The most recent electronic search was undertaken on February 1, 2005. The bibliographies of all identified RCTs and relevant review articles for studies located using these databases were checked. There were no language restrictions. All the authors of the identified RCTs and more than 55 oral implant manufacturers were contacted. Personal contacts were used and an internet discussion group (implantology@yahoogroups.com) was contacted in an attempt to identify unpublished or ongoing RCTs.

The following journals were handsearched for this review: *British Journal of Oral and Maxillofacial Surgery, Clinical Implant Dentistry and Related Research, Clinical Oral Implants Research, Implant Dentistry, International Journal of Oral & Maxillofacial Implants, International Journal of Oral and Maxillofacial Surgery, International Journal of Periodontics and Restorative Dentistry, International Journal of Prosthodontics, Journal of the American Dental Association, Journal of Biomedical Materials Research, 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 journals had not already been searched as part of the Cochrane Journal Handsearching Programme, they were handsearched by 1 reviewer. Details of the journals being handsearched by the Oral Health Group's ongoing

program are given on the web site www. cochrane-oral.man.ac.uk.

Methods of Review

The titles and abstracts (when available) of all reports identified through the electronic searches were scanned independently by 2 reviewers. If a study appeared to meet the inclusion criteria, or if there were insufficient data in the title and abstract to determine whether the study met the inclusion criteria, the full report was obtained. The full reports were assessed independently by 2 reviewers to establish whether the studies met the inclusion criteria. Disagreements were resolved by discussion. Where resolution was not possible, a third reviewer 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 table of excluded studies, and the reasons for exclusion were recorded.

QUALITY ASSESSMENT

The quality assessment of the included trials was undertaken independently and in duplicate by 2 reviewers as part of the data extraction process. Three main quality criteria were examined:

- Allocation concealment. Allocation concealment was recorded as adequate, unclear, or inadequate, as described in the *Cochrane Reviewers' Handbook*.[3]
- Blindness of outcome assessors to treatment. This was recorded as yes, no, unclear, or not possible.
- Completeness of follow-up. The question "Is there a clear explanation for withdrawals and dropouts in each treatment group?" had to be answered either yes or no.

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

- Low risk of bias—Plausible bias was considered unlikely to seriously alter the results if all of the quality criteria were met.
- Moderate risk of bias—Plausible bias could raise some doubt about the results if 1 or more of the criteria were only partly met (eg, the authors had made some attempts to conceal the allocation of the patients, blind the assessor, or explain withdrawals, but these attempts were not judged to be ideal).

Table 1 Search Strategy Developed for MEDLINE (OVID) and Revised Appropriately for Each Searched Database

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

The above search was run with phases 1 & 2 of the Cochrane Sensitive Search Strategy for RCTs as published in Appendix 5b2 of the Cochrane Handbook.
http://www.cochrane.org/resources/handbook/hbook.htm #4548]

http://www.cochrane.org/resources/handbook/hbook.htm #4548] and amended by the Cochrane Oral Health Group as follows:

1.	RANDOMIZED CONTROLLED TRIAL.pt.
2.	CONTROLLED CLINICAL TRIAL.pt.
3.	RANDOMIZED CONTROLLED TRIALS.sh.
4.	RANDOM ALLOCATION.sh.
5.	DOUBLE BLIND METHOD.sh.
6.	SINGLE BLIND METHOD.sh.
7.	CROSS-OVER STUDIES.sh.
8.	MULTICENTER STUDIES.sh.
9.	("multicentre stud$" or "multicentre trial$" or "multicenter stud$" or "multicenter trial$" or "multi-centre stud$" or "multi-centre trial$" or "multi-center stud$" or "multi-center trial$" or "multi-site trial$" or "multi-site stud$").ti,ab.
10.	MULTICENTER STUDY.pt.
11.	latin square.ti,ab.
12.	(crossover or cross-over).ti,ab.
13.	(split adj (mouth or plot)).ti,ab.
14.	or/1-13
15.	(ANIMALS not HUMAN).sh.
16.	14 not 15
17.	CLINICAL TRIAL.pt.
18.	exp CLINICAL TRIALS/
19.	(clin$ adj25 trial$).ti,ab.
20.	((singl$ or doubl$ or trebl$ or tripl$) adj25 (blind$ or mask$)).ti,ab.
21.	PLACEBOS.sh.
22.	placebo$.ti,ab.
23.	random$.ti,ab.
24.	RESEARCH DESIGN.sh.
25.	or/17-24
26.	25 not 15
27.	26 not 9
28.	16 or 27

Table 2 Eligible RCTs

Primary reference	Other follow-up publications
Geertman et al[5]	Geertman et al,[15] Meijer et al[16]
Boerrigter et al[6]	Meijer et al[17–19]
Jones et al[7]	Jones et al[20]
Batenburg et al[8]	Meijer et al[21]
Karlsson et al[9]	Gotfredsen and Karlsson[22]
Åstrand et al[10]	Engquist et al,[23] Åstrand et al[24]
Tawse-Smith et al[11]	
Geurs et al[12]	Jeffcoat et al[25]
Mau et al[13]	
Tawse-Smith et al[14]*	

In the text of the review only the "primary" reference, ie, the first published report of the RCT has been referred to. Follow-up publications are listed here after the primary publication. Unpublished information kindly provided by the authors of the RCTs was used extensively.
*A follow-up publication of Tawse-Smith et al.[11]

Table 3 Reasons for Exclusion

Geertman et al[5]	Data of 2 different RCTs were combined. Asked for separate data. No reply to letter.
Boerrigter et al[6]	Number of enrolled patients unclear. No reply to letter.
Jones et al[7]	Study not classified as a RCT. No reply to l etter.
Karlsson et al[9]	Not all patients were participating in a split-mouth study. Author reply failed to clarify the issue.
Geurs et al[12]	Unclear which implant type(s) failed. Number of dropouts also unclear. Author reply failed to clarify the issue.
Mau et al[13]	Unusually high dropout rate (only data of 189 of the 313 patients admitted in the trial were presented). Dropouts often classified as such for questionable reasons. Early failures counted as dropouts. Unclear success criteria. Not all patients followed for 5 years. No reply to letter.

- High risk of bias—Plausible bias was considered likely to seriously weaken confidence in the results if one ore more criteria were not met as described in the *Cochrane Reviewers' Handbook*.[3]

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 Extraction and Synthesis

Two reviewers extracted data independently 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 reviewer was consulted where necessary. All authors were contacted for clarification or to obtain missing information. Data were excluded until further clarification became available if agreement could not be reached.

For each trial the following data were recorded: year of publication; country of origin; source of study funding; details regarding the participants, including demographic characteristics and criteria for inclusion; details regarding the type of intervention; and details regarding the outcomes reported, including method of assessment and follow-up intervals.

For dichotomous outcomes, the estimates of effect of an intervention were expressed as relative risks (RRs) together with 95% confidence intervals (CIs). 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 implants.

Clinical heterogeneity was to be assessed by examining the types of participants, interventions, and outcomes in each study. Meta-analyses were done only if there were studies of similar comparisons reporting the same outcome measures. RRs were combined for dichotomous data, and weighted mean differences for continuous data, using a random effects model. Data from split-mouth studies were to be combined with data from parallel group trials with the method outlined by Elbourne and associates.[4]

RESULTS

Description of Studies

The first published article (ie, the "primary" reference) and the follow-up publications of the eligible RCTs are summarized in Table 2. Of the 10 eligible trials having a 5-year follow-up,[5–14] 6 were excluded[5–7,9,12,13] for various reasons (Table 3). Of the 4 included trials,[8,10,11,14] 2 were conducted in New Zealand,[11,14] 1 in the Netherlands,[8] and 1 in Sweden.[10] All trials had a parallel group study design, received support from industry, were conducted at university dental clinics or hospitals, and included only adults.

Characteristics of the Interventions and Outcome Measures

Six implant types with different modified surfaces were compared:

Table 4 Results of Quality Assessment After Correspondence with the Authors

Study ID	Allocation concealment	Blinding of assessor	Clear explanation of withdrawals	Risk of bias
Batenburg et al[8]	Inadequate	Not possible*	Yes	High
Åstrand et al[10]	Inadequate	Not possible†	Yes	High
Tawse-Smith et al[11]	Unclear	Not possible	Yes	High
Tawse-Smith et al[14]	Unclear	Not possible	Yes	High

*Radiographs were not read in sequence and not per patient to minimize bias.
†An independent assessor evaluated all radiographs.

Table 5 Main Inclusion and Exclusion Criteria for the Included RCTs

Main inclusion criteria
- Edentulous mandibles with at least 13 mm of bone height[11,14]
- Severely resorbed edentulous mandibles[8]
- Edentulous mandibles and maxillae not needing bone augmentation procedures[10]

Main exclusion criteria
- Radiotherapy in the head and neck region[8,11,14]
- Any history of bruxism[11,14]
- Any evidence of previous and current smoking[11,14]
- Very soft bone (type 4 according to the criteria of Lekholm and Zarb)[11,14,15]

1. Astra TiOblast titanium grade 3 screws (Astra Tech, Mölndal, Sweden)
2. Brånemark Standard and MKII turned titanium grade 1 screws (Nobel Biocare, Göteborg, Sweden)
3. IMZ titanium plasma-sprayed (TPS) titanium grade 2 cylinders (Friedrichsfeld, Mannheim, Germany)
4. ITI TPS hollow titanium grade 4 screws (Institut Straumann, Waldenburg, Switzerland)
5. Southern sand-blasted acid-etched titanium grade 4 screws (Southern Implants, Irene, South Africa)
6. Steri-Oss HL series, 3.8 mm in diameter acid-etched titanium grade 4 screws (Steri-Oss, Yorba Linda, CA)

In principle, 3 types of modified surfaces were analyzed:

1. Surfaces with a clear orientation of the irregularities due to the cutting procedure during turning (Brånemark turned implants)
2. Surfaces without a domination direction (orientation) treated with techniques that remove material during manufacturing (Astra, Steri-Oss, and Southern implants)
3. Surface without a dominating direction treated with processes (eg, plasma-spraying) that add material to the surface (IMZ and ITI implants)

Implants could be grouped according to their shape in 3 main categories: screws (Brånemark, Steri-Oss, Astra, and Southern implants), hollow screws (ITI implants), and cylinders (IMZ implants). All oral implants placed were made of machined commercially pure titanium; however, they differed in surface preparation, shape, degree of purity of the titanium used, and placement modality (submerged and nonsubmerged).

Astra, Brånemark, and IMZ implants were used according to a submerged (2-stage) procedure, ie, the implants were covered by the mucosa during the healing phase (3 to 6 months in the mandible and 6 to 7 months in the maxilla), and a second surgical intervention was necessary to connect the abutments (posts) to the implants. ITI, Southern, and Steri-Oss implants were placed according to a nonsubmerged (1-stage) protocol, ie, the abutments were directly connected to the implants; thus, a second operation was avoided.

Implants were placed in edentulous mandibles[8,10,11,14] and maxillae.[10] In general, final prostheses were inserted 4 to 8 months after implant placement in mandibles and 7 to 10 months in maxillae. In 1 study,[14] mandibular overdentures were attached to the implants 6 weeks after implant placement. Cross-arch fixed prostheses were retained by screws on 4 to 6 implants.[10] Removable overdentures were retained on 2 implants by clip attachments to a bar[8] or by 2 ball attachments.[11,14]

The main inclusion and exclusion criteria used by the authors of the included trials are described in Table 5.

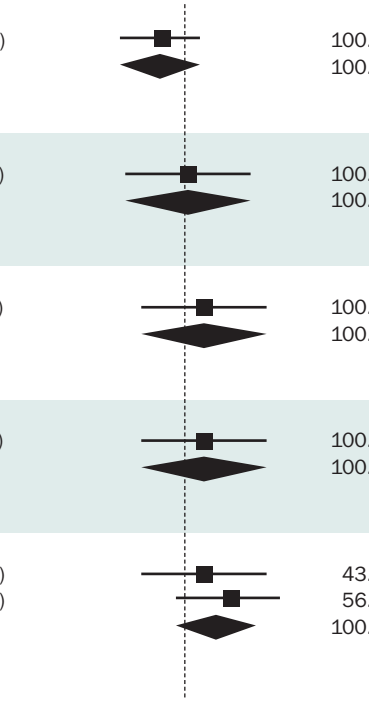
All trials reported primary and secondary outcomes, with 1 exception where no information on the occurrence of peri-implantitis was provided.[8]

Methodological Quality of Included Studies

The method of allocation concealment was considered unclear for 2 trials,[11,14] despite author clarifica-

Table 6 Data on Implant Failure in the 4 Accepted Studies

	Treatment 1 (n)	Treatment 2 (n)	Log[RR] (SE)	RR (random) (95% CI)	Weight (%)	RR (random) (95% CI)
Astra TiO_2-blasted vs Brånemark turned titanium screws						
Åstrand et al[10]	31	33	−0.8440 (0.7980)		100.0	0.43 (0.09–2.05)
Subtotal	31	33			100.0	0.43 (0.09–2.05)
Test for heterogeneity: Not applicable						
Test for overall effect: Z = 1.06 (*P* = .29)						
Brånemark turned titanium screws vs IMZ TPS titanium cylinders						
Batenburg et al[8]	27	30	0.1040 (1.3800)		100.0	1.11 (0.07–16.59)
Subtotal	27	30			100.0	1.11 (0.07–16.59)
Test for heterogeneity: Not applicable						
Test for overall effect: Z = 0.08 (*P* = .94)						
Brånemark turned titanium screws vs ITI TPS hollow titanium screws						
Batenburg et al[8]	27	27	1.0986 (1.6100)		100.0	3.00 (0.13–70.40)
Subtotal	27	27			100.0	3.00 (0.13–70.40)
Test for heterogeneity: Not applicable						
Test for overall effect: Z = 0.68 (*P* = .50)						
IMZ TPS cylinders vs ITI TPS hollow titanium screws						
Batenburg et al[8]	30	27	0.9969 (1.6100)		100.0	2.71 (0.12–63.59)
Subtotal	30	27			100.0	2.71 (0.12–63.59)
Test for heterogeneity: Not applicable						
Test for overall effect: Z = 0.62 (*P* = .54)						
Steri-Oss etched vs Southern blasted/etched titanium screws						
Tawse-Smith et al[11]	11	11	1.0986 (1.5800)		43.99	3.00 (0.14–66.38)
Tawse-Smith et al[14]	12	12	2.3980 (1.4000)		56.01	11.00 (0.71–171.05)
Subtotal	23	23			100.0	6.21 (0.80–48.43)
Test for heterogeneity: χ^2 = 0.38; df = 1; *P* = .54; I^2 = 0%						
Test for overall effect: Z = 1.74 (*P* = .08)						



tions. The method of allocation was not concealed to clinicians for the remaining 2 trials,[8,10] according to the information provided the authors.

In general, it was not possible to blind the outcome assessors to the interventions, since in all cases the different shapes of the implants and abutments were easily recognizable. However, in 1 trial[10] an independent assessor made the radiographic evaluations. In another trial[8] radiographs were read not in sequence and not per patient.

The reporting of withdrawals was adequate for all trials, with one exception[8]; however, the authors supplied the missing information.

Only 1 research team[10] undertook an a priori calculation for the sample size to detect a true difference of 0.4 mm in marginal bone levels thought to be of clinical significance.

After incorporating information provided by the authors of the studies, the quality of the included trials was assessed (Table 4). All included studies were rated as being at high risk of bias.

Comparability of Control and Test Groups at Entry

The control and test groups seemed comparable in all trials, with the exception of 1 trial[10] in which 8 patients treated with Brånemark implants were scored as having type 4 bone quality (very soft bone) according to the Lekholm and Zarb classification[26] versus 1 patient in the Astra group.

Aggregated Data on Implant Failures and Peri-implantitis

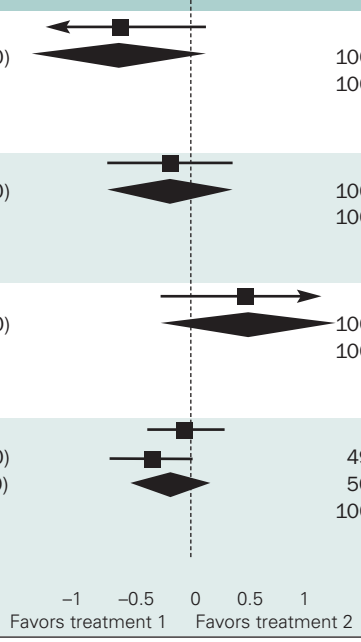
In total, 647 implants (247 turned implants and 400 implants with roughened surfaces) were originally placed in 204 patients (170 mandibles and 34 maxillae) in the 4 trials. During the 5-year follow-up period considered in this review, there were 23 implant failures (2 were implant fractures in the same patient). Eleven of the failed implants had roughened surfaces and 12 had turned surfaces. In particular, there were 16 early implant failures (10 of which were rough-surfaced implants) and 7 late failures (2 of which were rough-surfaced implants; these 2 implants fractured). Peri-implantitis (advanced marginal bone loss with signs of infection, such as suppuration, where the investigators have justified its diagnosis) affected 2 rough-surfaced implants that were successfully treated.

Primary Hypothesis

Data for implant failures and marginal bone level changes at 5 years postloading are presented in

Table 7 Forest Plot comparing Mean Marginal Bone Level Changes Measured on Intraoral Radiographs of Different Implant types at 5 Years

	Treatment 1 (n)	Treatment 2 (n)	Mean difference (SE)	Mean difference (random) (95% CI)	Weight (%)	Mean difference (random) (95% CI)
Brånemark turned titanium screws vs IMZ TPS titanium cylinders						
Batenburg et al[8]	26	30	−0.7000 (0.3820)		100.0	−0.70 (−1.45–0.05)
Subtotal	26	30			100.0	−0.70 (−1.45–0.05)
Test for heterogeneity: Not applicable						
Test for overall effect: Z = 1.83 (*P* = .07)						
Brånemark turned titanium screws vs ITI TPS hollow titanium screws						
Batenburg[8]	26	27	−0.2000 (0.2340)		100.0	−0.20 (−0.66–0.26)
Subtotal	26	27			100.0	−0.20 (−0.66–0.26)
Test for heterogeneity: Not applicable						
Test for overall effect: Z = 0.85 (*P* = .39)						
IMZ TPS cylinders vs ITI TPS hollow titanium screws						
Batenburg et al[8]	30	27	0.5000 (0.3840)		100.0	0.50 (−0.25–1.25)
Subtotal	30	27			100.0	0.50 (−0.25–1.25)
Test for heterogeneity: Not applicable						
Test for overall effect: Z = 1.30 (*P* = .19)						
Steri-Oss etched vs Southern blasted/etched titanium screws						
Tawse-Smith et al[11]	10	11	−0.0455 (0.1800)		49.61	−0.05 (−0.40–0.31)
Tawse-Smith et al[14]	7	12	−0.3532 (0.1770)		50.39	−0.35 (−0.70– −0.01)
Subtotal	17	23			100.0	−0.20 (−0.50–0.10)
Test for heterogeneity: χ^2 = 1.49; df = 1; *P* = .22; I^2 = 32.7%						
Test for overall effect: Z = 1.31 (*P* = .19)						



For each comparison, treatment 1 is the first type of implant listed; treatment 2 is the second. Radiographic data from Astrand et al[10] were not presented since the authors provided separate data for the maxilla and mandible. However, no statistically significant differences were observed.

Tables 6 and 7, respectively. The following is a comparison of the types of implants used in the 4 RCTs studied.

Astra versus Brånemark Implants. One of the RCTs[10] compared submerged Astra screw-type implants and submerged Brånemark screw-type implants using a parallel group design in totally edentulous patients. Thirty-three fully edentulous patients (17 maxillae and 16 mandibles) were originally included in each group. There were no baseline differences for sex, bone quantity, or length of the implant used between the 2 groups. However, 8 patients treated with Brånemark implants were scored as having type 4 bone quality (very soft bone) according to the Lekholm and Zarb classification,[26] versus 1 patient in the Astra group. Two withdrawals from the Astra group occurred due to death. Baseline radiographs were missing for 1 mandible in the Astra group. According to a sample size calculation, a minimum of 15 patients per group were to be included and followed in order to detect a true difference of 0.4 mm in marginal bone level changes between the tested implants with 90% power in mandibles. Ten Brånemark implants failed in 5 patients (1 patient lost 5 implants and the bridge) versus 3 Astra implant failures in 2 patients (2 of the failures were implant fractures that occurred in the same patient). Two additional Astra implants were successfully treated for peri-implantitis (suppuration combined with advanced bone loss). Considering the patient as the unit for the analysis, there was no statistically significant difference between the implant systems in regard to either failure or marginal bone level change after 5 years of function.

Brånemark versus IMZ Implants. One trial[8] with a parallel group design compared 2 submerged Brånemark implants used to support mandibular overdentures with 2 IMZ submerged implants used to support mandibular overdentures. Thirty patients were included in each group. No baseline differences in regard to sex, mean edentulous period, mandibular bone quantity, or height were noted between the 2 groups. Three patients in the Brånemark group could not attend the 5-year examination because of sickness. One Brånemark and 1 IMZ implant failed prior to the abutment connection operation. Considering the patient as the unit for the analysis, there was no statistically significant difference between the implant systems in regard to either failure or marginal bone level change.

Brånemark versus ITI Implants. One trial[8] with a parallel group design compared 2 Brånemark MKII

screw-type implants used to support mandibular overdentures with 2 ITI TPS hollow screw-type implants used to support mandibular overdentures. Thirty patients were included in each group. No baseline differences for sex, mean edentulous period, mandibular bone quantity, or height were observed between the 2 groups. Two patients of the ITI group died, and 3 patients in the Brånemark group and 1 in the ITI group could not attend the 5-year examination because of sickness. One Brånemark implant failed prior to the abutment connection operation. Considering the patient as the unit for the analysis, there was no statistically significant difference between the implant systems in regard to either failure or marginal bone level change.

IMZ versus ITI Implants. One trial[8] with a parallel group design compared 2 submerged IMZ TPS cylinders supporting mandibular overdentures with 2 nonsubmerged ITI TPS hollow screws supporting mandibular overdentures. Thirty patients were included in each group. No baseline differences for sex, mean edentulous period, mandibular bone quantity, or height were observed between the 2 groups. Two patients from the ITI group died, and 1 additional patient was sick and could not attend the 5-year examination. One IMZ implant failed prior to the abutment connection operation. Considering the patient as the unit for the analysis, there was no statistically significant difference between the implant systems in regard to either failure or marginal bone level change.

Southern versus Steri-Oss Implants. Two trials[11,14] with a parallel group design compared the use of 2 nonsubmerged, unsplinted Southern implants to support an overdenture with the use of 2 nonsubmerged, unsplinted Steri-Oss screws. The design of the 2 trials was identical, except that in 1 trial the implants were conventionally loaded at 12 weeks,[11] whereas in the other, the implants were loaded early, at 6 weeks.[14] In both articles, Steri-Oss implants were described as having a turned surface, but analysis of the surface of 1 implant, kindly provided by the authors, showed that the implant surface was chemically treated.

One trial,[11] which used a parallel group design, included 12 subjects in each of the 2 groups (conventional loading at 12 weeks). Patients having type 4 bone were to be excluded, but none were found. There were no baseline differences in regard to bone quality and quantity between the 2 groups. Two dropouts occurred, 1 in the Steri-Oss group (patient request) and 1 in the Southern group (death). One patient in the Steri-Oss group had an early implant failure. Considering the patient as the unit for the analysis, there were no statistically significant differences between the 2 groups after 5 years in function.

The other trial,[14] which also used a parallel group design, included 12 subjects in each group (early loading at 6 weeks). The 2-year data of the previous trial (conventional loading at 12 weeks) was also presented in this article. Patients having type 4 bone were to be excluded, but none was found. There were no baseline differences in regard to bone quality and quantity between the 2 groups. No dropouts occurred. Five patients in the Steri-Oss group had 7 early failures. No implants were lost in the Southern group. Most of the failed implants were placed by a surgeon with limited experience, who placed only Steri-Oss implants. Considering the patient as the unit for the analysis, the difference in failures was not statistically significant; however, the difference in marginal bone level change between the 2 implant systems was found to be statistically significant, with the Southern group having more bone loss than the Steri-Oss group (mean difference –35 mm [95 CI 0.70 to –0.01]).

Meta-analyses were done of the 2 above studies.[11,14] Considering the patient as the unit for the analysis, there were no statistically significant differences in regard to failures and marginal bone level changes between the implant systems after 5 years of function.

Secondary Hypotheses

Early Failures Between Turned and Roughened Surfaces. A meta-analysis comparing early implant failures between various implants with turned and roughened surfaces is presented in Table 8. Two trials were included.[8,10] Considering the patient as the unit for the analysis, no statistically significant differences were observed between the implants with turned surfaces and those with roughened surfaces in regard to number of early failures.

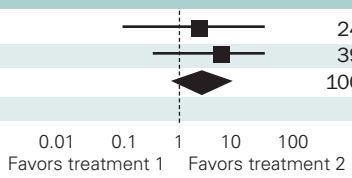
Peri-implantitis Between Turned and Roughened Surfaces at 5 Years. Only 1 trial[10] was available that compared the occurrence of peri-implantitis between various implants with turned and roughened surfaces at 5 years; data from that trial are presented in Table 9. Considering the patient as the unit for the analysis, there was no statistically significant difference in regard to occurrence of peri-implantitis between implants with turned surfaces and those with roughened surfaces. For another trial,[8] no data were presented, and the author did not supply the information requested.

DISCUSSION

It is important to know whether there are implant systems or specific implant characteristics associated

Table 8 Meta-analysis Comparing Early Implant Failures Between Implants with Turned and Rough Implant Surfaces

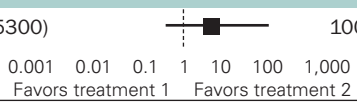
	Treatment 1 (n)	Treatment 2 (n)	Log[RR] (SE)	RR (random) (95% CI)	Weight (%)	RR (random) (95% CI)
Batenburg et al[8]	30	60	0.6930 (1.3960)		24.26	2.00 (0.13–30.85)
Åstrand et al[10]	33	33	1.3860 (1.0910)		39.72	4.00 (0.47–33.93)
Total (95% CI)	63	93			100.00	3.05 (0.79–11.73)
Test for heterogeneity: $\chi^2 = 0.15$; df = 1 ($P = .70$); $I^2 = 0\%$						
Test for overall effect: Z = 1.31 ($P = .19$)						



Treatment 1 was implants with turned surfaces; treatment 2 was implants with rough surfaces.

Table 9 Occurrences of Peri-implantitis Between Various Implants with Turned and Rough Surfaces at 5 Years

	Log[RR] (SE)	RR (random) (95% CI)	Weight (%)	RR (random) (95% CI)
Astra TiO[2]-blasted vs Brånemark turned titanium screws Åstrand et al[10]	1.7050 (1.5300)		100.00	5.50 (1.27–110.36)



with increased success rates, primarily for the patient's benefit. To properly compare the efficacy of various implant systems, well-conducted long-term RCTs are needed.

The present systematic review confirms the finding that high success rates can be achieved for all implant systems analyzed after 5 years of loading. A statistically significant mean difference of 0.35 mm for marginal bone level changes favoring Steri-Oss acid-etched implants in comparison to sand-blasted, acid-etched Southern implants was observed.[14] However, this difference disappeared when the results of this trial were combined with another similar trial[11] in the meta-analysis. The fact that a relatively small number of patients were included and that the difference in bone levels was actually caused by apparent bone gain and not bone loss may indicate that this statistically significant difference is a spurious finding.

No statistically significant differences were found when implants with turned surfaces were compared with implants with roughened surfaces for early failures or occurrence of peri-implantitis. The lack of statistically significant differences should be correctly interpreted. It does not mean that there is no difference among various implant surfaces; it is possible that, if a difference exists, it may be hidden by the low numbers of included patients and possible underreporting of the occurrence of peri-implantitis. For example the authors of a split-mouth 3-year follow-up trial displaying significant differences in the occurrence of peri-implantitis among 2 different implant systems[27] explained in correspondence that they may be discontinuing their study because 1 of the 2 implant systems under evaluation has been withdrawn from the market. This is only a single example of how the published literature can be biased toward positive results. Therefore no firm conclusions can be established yet except that additional information from well-conducted long-term RCTs is needed.

The assessment of radiographic bone level changes around implants is a secondary or surrogate outcome measure and is commonly used. A surrogate outcome can be defined as a measure of the disease process. Surrogate outcome measures cannot be recommended as primary parameters to evaluate the effectiveness of oral implants; however, they may be useful diagnostic tools for the early detection of potential problems, allowing early treatment to preserve healthy conditions.[2] Primary or true outcomes such as implant failures are often rare events,

whereas surrogate endpoints are in general sensitive predictors for the true outcomes. The problem with using mean marginal bone level assessments is that a severe marginal bone loss affecting a few implants is diluted by the averaging process. In addition, once an implant has failed, its values are removed from the calculations, suddenly improving the bone level measurements. These limitations may delay early detection of a statistically significant difference. One possible way to overcome this problem is to dichotomize the bone level measurements, establishing an arbitrary threshold level of severe bone loss (eg, 5 mm), and to count how many patients had at least 1 implant affected by such severe bone loss. Bone level values of implants that failed because of progressive bone loss should remain in the calculations.

The concealment of allocation procedure of the randomization process was not considered adequate for any trial, and this may cast doubts on the reliability of the reported results. A proper allocation procedure has been shown to minimize selection bias: RCTs in which allocation concealment procedures were inadequately conducted tended to overestimate treatment effects.[28] For this reason, all trials were judged to be at high risk of bias in the validity assessment. This aspect of trial designing and reporting needs to be improved. While it is always possible to conceal allocation to a treatment group, it is not always possible to blind patients, treatment providers, and outcome assessors. This is particularly true in the type of trials that have been assessed, where the different shapes of the implants or the prosthetic components precluded a proper blinding. However, some attempts to minimize detection bias were done: an independent outcome assessor was used in 1 trial,[10] while in another trial the radiographic reading of bone levels was not done in sequence and not per patient.[8] Investigators should always consider using independent assessors or any other possible means when proper blinding is not possible to minimize detection bias.

In another investigation, it was found that the design, analysis, and reporting of RCTs on oral implants were generally poor.[29] Indeed, a large number of trials had to be excluded from the present review because they did not meet the standards set by the present authors. Investigators should design studies carefully and choose either a parallel group design or a split-mouth design at the outset rather than combining the 2 designs in 1 study. Split-mouth studies should ideally have equal numbers of implants in each group placed per patient. The analysis of these studies should be a "paired" analysis, taking the pairing of the implants within patients into account. Another related problem is that both split-mouth and parallel group studies are analyzed at the level of the implant, which does not take the clustering of the implants within a patient into account. The design and analysis of these studies are frequently complex, and it is recommended that statisticians are involved in the initial planning stages and protocol writing.

Another interesting finding is the lack of any reliable long-term information on implants made or coated with materials other than titanium.

The generalization of the results of the included trials to ordinary clinical conditions should be considered with extreme caution. In general, treatments were delivered by experienced clinicians, and the follow-up regimens were strict. It is unlikely that dentists without comparable experience could achieve similar positive results. The observation that the inclusion of a less trained surgeon might have influenced the result of 1 trial[14] could support this suggestion.

All included trials were commercially funded. A "commercial" bias therefore may not be excluded. Conversely, these studies would probably not have taken place without commercial funding. Ideally, independent studies should be conducted.

CONCLUSIONS

Based on the available results of RCTs, there is no strong evidence supporting the superiority of some implant systems over others. These conclusions are based on a few RCTs, evaluating few implant systems in few patients; therefore, the possibility that clinical differences exist cannot be excluded. In order to understand whether there is any surface modification or material that is able to significantly improve the effectiveness of oral implants, more well-designed long-term RCTs are needed. It is recommended that

- Such trials include a sufficient number of patients to disclose a true difference, if any
- Group allocation be properly concealed
- Independent outcome assessors be used when blinding is not possible to minimize detection bias
- That such trials be of sufficient duration (5 years or more)

Such trials should be reported according to the Consolidated Standards of Reporting Trials (CONSORT) guidelines[30] (www.consort-statement.org).

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