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Review

Dental implants inserted in fresh extraction sockets versus healed sites: A systematic review and meta-analysis

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ABSTRACT

Objectives: To test the null hypothesis of no difference in the implant failure rates, postoperative infection and marginal bone loss for the insertion of dental implants in fresh extraction sockets compared to the insertion in healed sites, against the alternative hypothesis of a difference.
Data: Main search terms used in combination: dental implant, oral implant, resh extraction socket, immediate placement, immediate insertion, immediate implant.
Sources: An electronic search was undertaken in July/2014, in PubMed, Web of Science, Cochrane Oral Health Group Trials Register plus hand-searching.
Study selection: Eligibility criteria included clinical human studies, either randomized or not.
Conclusions: The search strategy resulted in 73 publications, with 8,241 implants inserted in sockets (330 failures, 4.00%), and 19,410 in healed sites (599 failures, 3.09%). It is suggested that the insertion of implants in fresh extraction sockets affects the failure rates (RR 1.58, 95% CI 1.27–1.95, $P < 0.0001$). The difference was not statistically significant when studies evaluating implants inserted in maxillae or in mandibles were pooled, or when the studies using implants to rehabilitate patients with full-arch prostheses were pooled; however, it was significant for the studies that rehabilitated patients with implant-supported single crowns and for the controlled studies. There was no apparent significant effect on the occurrence of postoperative infection or on the magnitude of marginal bone loss. The results should be interpreted with caution due to the potential for biases and to the presence of uncontrolled confounding factors in the included studies, most of them not randomized.
Clinical significance: The question whether immediate implants are more at risk for failure than implants placed in mature bone has received increasing attention in the last years. As the philosophies of treatment alter over time, a periodic review of the different concepts is necessary to refine techniques and eliminate unnecessary procedures. This would form a basis for optimum treatment.

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1. Introduction

The insertion of dental implants immediately after teeth extractions has become a routine clinical procedure in implant dentistry. Tooth extraction results in a reduction of the bone quantity, which may prevent placement of an implant because of the decreased bone volume. Therefore, some authors advocate immediate placement. Several studies have reported that successful osseointegration is possible when implants are inserted immediately after tooth extraction, with similar survival rates when compared to implants inserted in healed sites, with or without the help of guided bone regeneration procedures. Placing an implant immediately after tooth extraction offers several advantages, including a decrease in rehabilitation treatment time, fewer surgical sessions, the ability to place the fixture in an ideal axial position, positive psychological impact on the patient, and enhanced hard and soft tissue maintenance.[1,2] However, some other studies have shown that implants placed in fresh extraction sockets shows higher failure rates than when inserted in mature bone.[3–9] Therefore, it seems that conflicting clinical data on the outcome still exists, even though a considerable number of studies comparing the techniques were already published.

The ability to anticipate outcomes is an essential part of risk management in an implant practice. Recognizing conditions that place the patient at a higher risk of failure will allow the surgeon to make informed decisions and refine the treatment plan to optimize the outcomes.[10] The use of implant therapy in special populations requires consideration of potential benefits to be gained from the therapy. To better appreciate this potential, we conducted a systematic review and meta-analysis to compare the survival rate of dental implants, postoperative infection, and marginal bone loss of dental implants inserted in fresh extraction sockets and in healed sites.

2. Materials and methods

This study followed the PRISMA Statement guidelines.[11] A review protocol does not exist.

2.1. Objective

The purpose of the present review was to test the null hypothesis of no difference in the implant failure rates, postoperative infection and marginal bone loss for the insertion of dental implants in fresh extraction sockets compared to the insertion in healed sites, against the alternative hypothesis of a difference.

2.2. Search strategies

An electronic search without time restrictions was undertaken in July 2014 in the following databases: PubMed, Web of Science, and the Cochrane Oral Health Group Trials Register. The following terms were used in the search strategy on PubMed:

{Subject AND Adjective}
{*Subject*: (dental implant OR oral implant [text words])
AND
Adjective: (fresh extraction socket OR immediate placement OR immediate insertion OR immediate implant [text words])}

The following terms were used in the search strategy on Web of Science, selecting the option 'Dentistry Oral Surgery Medicine' with the filter 'Research Areas', and 'Clinical Trial' with the filter 'Document Types':

{Subject AND Adjective}
{*Subject*: (dental implant OR oral implant [title])
AND
Adjective: (fresh extraction socket OR immediate placement OR immediate insertion OR immediate implant [title])}

The following terms were used in the search strategy on the Cochrane Oral Health Group Trials Register:

(dental implant OR oral implant AND (fresh extraction socket OR immediate placement OR immediate insertion OR immediate implant))

A manual search of dental implants-related journals, including *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 Dentistry*, *Journal of Oral Implantology*, *Journal of Craniofacial Surgery*, *Journal of Cranio-Maxillofacial Surgery*, *Journal of Maxillofacial and Oral Surgery*, *Journal of Oral and Maxillofacial Surgery*, *Journal of Periodontology*, and *Oral Surgery Oral Medicine Oral Pathology Oral Radiology and Endodontology*, was also performed.

The reference list of the identified studies and the relevant reviews on the subject were also scanned for possible additional studies. Moreover, online databases providing information about clinical trials in progress were checked (clinicaltrials.gov; www.centerwatch.com/clinicaltrials; www.clinicalconnection.com).

2.3. Inclusion and exclusion criteria

Eligibility criteria included clinical human studies, either randomized or not, comparing implant failure rates in any group of patients receiving dental implants being inserted in fresh extraction sockets compared to the insertion in healed sites. For this review, implant failure represents the complete loss of the implant. Exclusion criteria were case reports, technical reports, animal studies, *in vitro* studies, and reviews papers.

2.4. Study selection

The titles and abstracts of all reports identified through the electronic searches were read independently by the three 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. Disagreements were resolved by discussion between the authors.

2.5. Quality assessment

Quality assessment of the studies was executed according to the Newcastle–Ottawa scale (NOS).[12] The Newcastle–Ottawa scale was developed to assess the quality of nonrandomized studies with its design, content and ease of use directed to the task of incorporating the quality assessments in the interpretation of meta-analytic results. The NOS calculates the study quality on the basis of 3 major components: selection, comparability, and outcome for cohort studies. It assigns a maximum of 4 stars for selection, a maximum of 2 stars for comparability, and a maximum of 3 stars for outcome. According to that quality scale, a maximum of 9 stars/points can be given to a study, and this score represents the highest quality, where six or more points were considered high quality.

2.6. Data extraction and meta-analysis

From the studies included in the final analysis, the following data was extracted (when available): year of publication, study design, unicenter or multicenter study, number of patients, patients' age, follow-up, days of antibiotic prophylaxis, mouth rinse, implant healing period/loading, period between extraction and implant insertion in the healed site group, failed and placed implants, postoperative infection, marginal bone loss, implant surface modification, jaws receiving implants (maxilla and/or mandible), type of prosthetic rehabilitation, opposing dentition, grafting procedures, and the presence of smokers among the patients. Contact with authors for possible missing data was performed.

Implant failure and postoperative infection were the dichotomous outcomes measures evaluated. Weighted mean differences were used to construct forest plots of marginal bone loss, a continuous outcome. The statistical unit for all outcomes was the implant. Whenever outcomes of interest were not clearly stated, the data were not used for analysis. The I^2 statistic was used to express the percentage of the total variation across studies due to heterogeneity, with 25% corresponding to low heterogeneity, 50% to moderate and 75% to high. The inverse variance method was used for random-effects or fixed-effects model. Where statistically significant ($P < 0.10$) heterogeneity is detected, a random-effects model was used to assess the significance of treatment effects. Where no statistically significant heterogeneity is found, analysis was performed using a fixed-effects model.[13] The most important reason for choosing the inverse variance method was due to the fact that the weight given to each study is chosen to be the inverse of the variance of the effect estimate. Thus, larger studies, which have smaller standard errors, are given more weight than smaller studies, which have larger standard errors. This choice of weight minimizes the imprecision (uncertainty) of the pooled effect estimate. The Mantel–Haenszel method is suggested to have better statistical properties when there are rare events. However, it is not defined below which percentage of events should be considered as 'rare events' for this issue in particular (fresh extraction sockets).

The estimates of relative effect for dichotomous outcomes were expressed in risk ratio (RR) and in mean difference (MD) in millimetres for continuous outcomes, both with a 95% confidence interval (CI). Only if there were studies with similar comparisons reporting the same outcome measures was meta-analysis to be attempted. In the case where no events are observed in both groups the study provides no information about relative probability of the event and is automatically omitted from the meta-analysis.

A funnel plot (plot of effect size versus standard error) will be drawn. Asymmetry of the funnel plot may indicate publication bias and other biases related to sample size, although the asymmetry may also represent a true relationship between trial size and effect size.

The data were analyzed using the statistical software Review Manager (version 5.3.3, The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark, 2014).

3. Results

3.1. Literature search

The study selection process is summarized in Fig. 1. The search strategy resulted in 971 papers. 187 articles were cited in more than one search strategy (duplicates). The three reviewers independently screened the abstracts for those articles related to the focus question. Of the resulted 784 studies, 490 were excluded for not being related to the topic, resulting in 294 entries. Additional hand-searching of the reference lists of selected studies yielded 11 additional papers. The full-text reports of the 305 articles led to the exclusion of 232 because they did not meet the inclusion criteria (115 publications evaluated only implants inserted in fresh extraction sockets, 39 animal studies, 27 case reports, 21 studies with no implant failures, 14 reviews papers, 9 studies did not evaluate implant failures, 2 studies did not inform of the number of failed/inserted implants per group, 2 technical notes, 1 histological study, 1 human cadaver study, 1 paper was same study published in another journal). Thus, a total of 73 publications were included in the review.

3.2. Description of the studies

Detailed data of the seventy-three included studies are listed in Tables 1 and 2. Five RCTs,[2,14–17] twenty-six CCTs,[4,7,8,18–40] and forty-two retrospective analyses[3,5,6,9,41–78] were included in the meta-analysis. Sixteen studies[5,14,18,19,23,27,33,34,39,45,54,57,59,60,63,77] were multicenter.

Seventeen studies[2,7,8,14–16,19,27,31,32,36,37,39,40,58,65,71] had a maximum follow-up of up to 1 year. Two studies[45,47] did not provide information about the follow-up. From the studies with available data of patients' age, nine[3,6,22,44,45,48,53–55] included non-adults patients. Ten studies[23,25,27,37,41,42,47,51,66,76] did not inform of the patients' age. Some patients in forty-four studies[3–6,8,9,14–17,19–22,24,25,28,30,33,36,39,40,45,52,53,55–58,61,62,64–72,74,76–78] were smokers, while five studies[5,6,9,25,40]

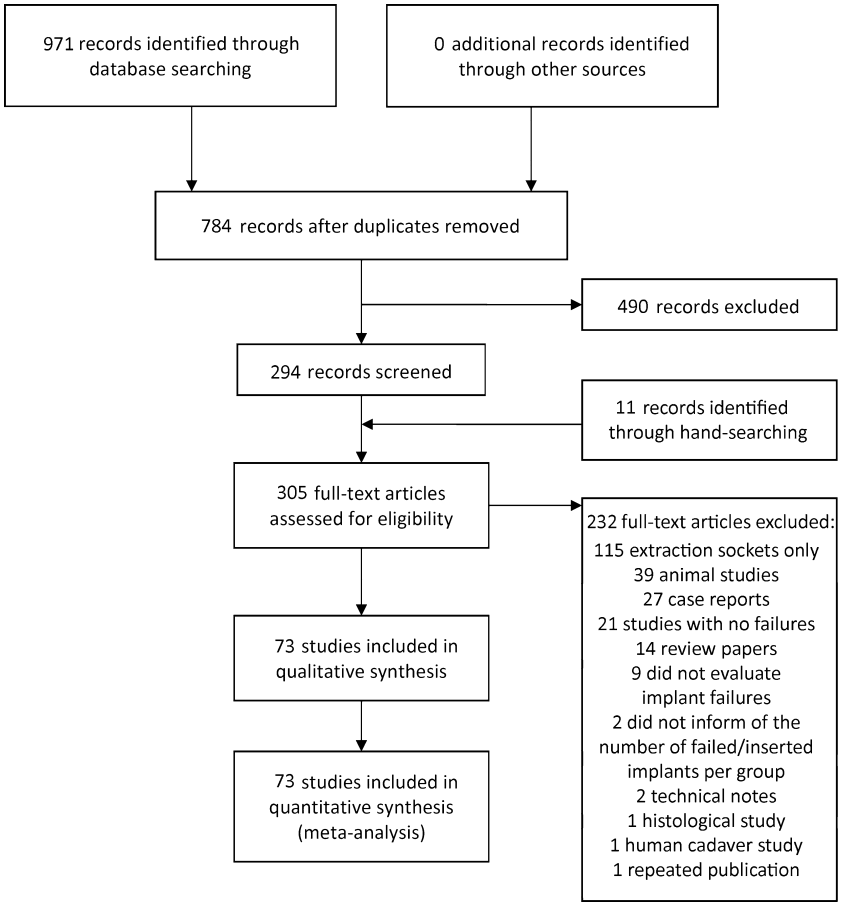

Fig. 1 – Study screening process.

reported the presence of diabetic patients. Nine studies[7,8,25,28,30,36,51,57,72] reported the inclusion of periodontally compromised patients in their studies. Periodontitis was an inclusion criterion for all patients in three studies.[7,8,25] Twenty-two studies[2,6,14,16,17,20,27,29,31–34,37–39,46,51,53,55,56,59,62] included only patients who received implants rehabilitated with single crowns, while sixteen studies[4,8,9,24,25,35,42,47,49,50,52,61,65,67,69,71] evaluated patients only receiving full-arch implant-supported prostheses. Patients were submitted to grafting procedures at the implant site in thirty-five studies.[2,9,14–16,18,20,21,23,26,29,33,36,37,39,41,42,44,45,53,57,60–64,67–69,72–74,76–78] Implants were inserted exclusively in maxillae in seventeen studies[2,16,20,27,31,33–35,37,38,52,53,59,66,71,72,74] and in mandibles in six studies.[4,32,49,50,65,75] Six studies[16,27,31,33,34,38] only evaluated implants inserted in the anterior maxillary region. Twelve studies[8,9,24,25,27,31,35,38,49,58,66,74] provided information about the dentition opposed to the implants being evaluated. All implants were immediately loaded in thirty-one studies.[3,8,9,14,19,20,22,24,27,29,31,32,34,37–39,46,47,49,52,53,55,56,59,61,62,65,66,69,71,75] In seventeen studies[5,16,17,21,23,25,30,33,35,36,40,50,57,60,68,72,77] the implants were immediately or delayed loaded, and three studies[48,70,76] did not provide information about the healing/loading time. In one study[15] the implants were not submitted to loading. In the other studies, the healing time before implant loading ranged from 'within 7 days' to 8 months. Two studies[47,74] did not inform what kind of implants was used. Twelve studies[8,14,32,34,35,38,65,66,69,71,73,77] informed whether there was a statistically significant difference or not in the implant failure rates between the procedures. Forty-four studies[2,3,6–8,14,16,17,20,22,24,26,27,29,32–36,39,40,44,46,49,52,53,55–57,59,61–66,69–71,73–76,78] provided information about the use of prophylactic antibiotics, and thirty studies[2–4,6–8,14,16,17,20,24,26,27,29,32–36,39,46,52,53,57,59,62,66,73–75] about the use of chlorhexidine mouth rinse by the patients.

From the seventy-three studies comparing the procedures, a total of 8241 dental implants were inserted in fresh extraction sockets, with 330 failures (4.00%), and 19,410 implants were inserted in healed sites, with 599 failures (3.09%). From the thirty-one controlled studies (RCTs and CCTs), a total of 2021 implants were inserted in fresh extraction sockets, with 96 failures (4.75%), and 2759 implants were inserted in healed sites, with 49 failures (1.78%). Of the seventeen studies evaluating the procedures in implants inserted only in maxillae, a total of 1254 dental implants were inserted in fresh extraction sockets (45 failures, 3.59%), and 1348 implants in healed sites (29 failures, 2.15%). The numbers for the mandible (six studies) were 377 (24 failures, 6.37%) and 709 (16 failures, 2.26%), respectively. For the twenty-two studies assessing implants being rehabilitated with single crowns only, a total of 911 dental implants (65 failures, 7.14%) were inserted in fresh extraction sockets, and 1128 implants (37 failures, 3.28%) were inserted in healed sites. The numbers

Table 1 – Detailed data of the included studies–Part 1.

Authors	Published	Study design	Patients (*n*) (number per group)	Patients' age range (average) (years)	Follow-up	Antibiotics/ mouth rinse (days)	Healing period/loading	Period between extraction and implant insertion in G2	Failed/ placed implants (*n*)	Implant failure rate (%)	P value (for failure rate)	Postoperative infection
Mensdorff-Pouilly et al.[41]	1994	RA (unicenter)	31[a]	NM	Mean 12.4 months	NM	3 months (mandible) 6 months (maxilla)	6–8 weeks	7/93 (G1) 5/97 (G2)	7.53 (G1) 5.15 (G2)	NM	NM
Watzek et al.[42]	1995	RA (unicenter)	20[a]	NM	Mean 27.1 months (range 4–83)	NM	3 months (mandible) 6 months (maxilla)	6–8 weeks	1/97 (G1) 2/37 (G2)	1.03 (G1) 5.41 (G2)	NM	NM
Haas et al.[43]	1996	RA (unicenter)	607[a]	21–86 (51.5)	Mean 26.8 months	NM	3 months (mandible) 6 months (maxilla)	NM	7/96 (G1) 72/1725 (G2)[b]	7.29 (G1) 4.17 (G2)	NM	NM
Gomez-Roman et al.[44]	1997	RA (unicenter)	376[a]	15–88 (38.8)	5 years	In some patients/NM	3–8 months	NM	1/86 (G1) 17/446 (G2)	1.16 (G1) 3.81 (G2)	NM	In 16 implants
Callan et al.[45]	2000	RA (multicenter)	663[a]	16–90 (55.3)	NM	NM	3 months (mandible) 6 months (maxilla)	NM	8/331 (G1) 7/769 (G2)	2.42 (G1) 0.91 (G2)	NM	NM
Maló et al.[3]	2000	RA (unicenter)	49[a]	16–64 (42)	6 months–4 years	14/15	Immediate	NM	4/27 (G1) 0/67 (G2)	14.81 (G1) 0 (G2)	NM	2 (G1) 0 (G2)
Polizzi et al.[18]	2000	CCT (multicenter)	143[a]	NM (47, females) NM (40, males)	1, 3, and 5 years	NM	6 months (maxilla) 3–4 months (mandible)	3–5 weeks	14/217 (G1) 3/47 (G2)	6.45 (G1) 6.38 (G2)	NM	NM
Chaushu et al.[46]	2001	RA (unicenter)	26 (17, G1; 9, G2)	18–70 (44)	6–24 months	5–7/5–7	Immediate	NM	3/17 (G1) 0/9 (G2)	17.65 (G1) 0 (G2)	NM	NM
Aires and Berger[47]	2002	RA (unicenter)	7[a]	NM	NM	NM	Immediate	NM	1/29 (G1) 1/46 (G2)	3.45 (G1) 2.17 (G2)	NM	NM
Arlin[48]	2002	RA (unicenter)	961[a]	15–70 (51)	13 years	NM	NM	NM	22/491 (G1) 117/2283 (G2)	4.48 (G1) 5.12 (G2)	NM	NM
De Bruyn and Collaert[4]	2002	CCT (unicenter)	36 (6, G1; 30, G2)	63–81 (NM)	3 years	NM/postop.	Within 8 days	>2 months	12/31 (G1) 1/153 (G2)	38.71 (G1) 0.65 (G2)	NM	NM
Maló et al.[49]	2003	RA (unicenter)	44[a]	30–79 (59)	2 years	10/NM	Immediate	NM	2/45 (G1) 3/131 (G2)	4.44 (G1) 2.29 (G2)	NM	NM
Maló et al.[19]	2003	CCT (multicenter)	76 (14, G1; 62, G2)	18–81 (41)	1 year	NM	Immediate	>1 year	0/22 (G1) 5/94 (G2)	0 (G1) 5.32 (G2)	NM	NM
Wolfinger et al.[50]	2003	RA (unicenter)	10[a]	45–70 (55)	>5 years	NM	Immediate or 3 months	NM	2/82 (G1) 3/62 (G2)	2.44 (G1) 4.84 (G2)	NM	NM
Evian et al.[51]	2004	RA (unicenter)	149 (100, G1; 49, G2)	NM	18–4030 days	NM	4–6 months	NM	15/100 (G1) 7/49 (G2)	15 (G1) 14.29 (G2)	NM	NM
Jaffin et al.[52]	2004	RA (unicenter)	34[a]	43–82 (60)	5 years	1/1	Immediate	NM	7/121 (G1) 9/115 (G2)	5.79 (G1) 7.83 (G2)	NM	NM
Kourtis et al.[5]	2004	RA (multicenter)	405[a]	18–83 (54.3)	12 years	NM	Immediate (99%) or delayed (1%)	NM	17/182 (G1) 62/1692 (G2)	9.34 (G1) 3.66 (G2)	NM	8 occurences of infection
Locante[53]	2004	RA (unicenter)	86 (46, G1; 40, G2)	12–81 (NM)	3 years	3/3	Immediate	NM	1/46 (G1) 0/40 (G2)	2.17 (G1) 0 (G2)	NM	NM
Norton[20]	2004	CCT (unicenter)	25 (16, G1; 12, G2)[c]	27–72 (48.2)	Mean 20.3 (range 13–30)	5/7	Immediate	NM	0/16 (G1) 1/12 (G2)	0 (G1) 8.33 (G2)	NM	NM
Perry and Lenchewski[54]	2004	RA (multicenter)	442[a]	17–92 (55)	Mean 24 months (range 5.8–67.4)	NM	3 months (mandible) 5 months (maxilla)	8–12 weeks	32/322 (G1) 71/777 (G2)	9.94 (G1) 9.14 (G2)	NM	NM
Davarpanah et al.[21]	2005	CCT (unicenter)	92[a]	NM (59.8)	18 months	NM	3–4 months (mandible) 5–6 months (maxilla)	NM	3/68 (G1) 1/80 (G2)[d]	4.41 (G1) 1.25 (G2)	NM	1 (G1) 0 (G2)
Dhanrajani and Al-Rafee[6]	2005	RA (unicenter)	101[a]	17–69 (NM)	6 years	5/5	Immediate or delayed	NM	2/8 (G1) 7/139 (G2)	25 (G1) 5.04 (G2)	NM	NM
Degidi et al.[55]	2006	RA (unicenter)	111 (67, G1; 44, G2)	15–83 (40)	5 years	5/NM	Immediate	NM	5/67 (G1) 0/44 (G2)	7.46 (G1) 0 (G2)	NM	NM
Lindeboom et al.[2]	2006	RCT (unicenter)	50 (25, G1; 25, G2)	19–69 (39.7)	1 year	1/7	6 months	3 months	2/25 (G1) 0/25 (G2)	8 (G1) 0 (G2)	NM	NM

Degidi et al.[56]	2007	RA (unicenter)	133 (36, G1; 97, G2)	41–80 (56)	Mean 45 months (range 15–105)	5/NM	Immediate	NM	2/36 (G1) 1/97 (G2)	5.56 (G1) 1.03 (G2)	NM	NM
Degidi et al.[22]	2007	CCT (unicenter)	NM	15–83 (55)	Mean 3 years	5/NM	Immediate	NM	4/416 (G1) 4/658 (G2)	0.96 (G1) 0.61 (G2)	NM	NM
Horwitz et al.[7]	2007	CCT (unicenter)	19 (NM)	34–79 (NM)	1 year	7/7	6 months	NM	10/42 (G1) 2/32 (G2)	23.81 (G1) 6.25 (G2)	NM	NM
Ormianer and Palti[57]	2008	RA (multicenter)	60[a]	18–78 (53)	Mean 7.5 years (range 6–8.25)	5/13	Immediate or delayed	NM	3/91 (G1) 1/174 (G2)	3.30 (G1) 0.57 (G2)	NM	0 (G1) 1 (G2)
Peñarrocha-Diago et al.[58]	2008	RA (unicenter)	100[a]	20–76 (47.5)	1 year	NM	6 weeks (mandible) 8 weeks (maxilla)	>6 months	0/32 (G1) 4/130 (G2)	0 (G1) 3.08 (G2)	NM	NM
Ribeiro et al.[59]	2008	RA (multicenter)	64[a]	23–71 (45.4)	2 years	7/1	Immediate	NM	3/46 (G1) 0/36 (G2)	6.52 (G1) 0 (G2)	NM	NM
Sennerby et al.[60]	2008	RA (multicenter)	43[a]	NM (50)	1–18 months (mean 10.2)	NM	Immediate/early (n = 95), from 6 weeks to 6 months (n = 22)	NM	1/18 (G1) 5/99 (G2)	5.56 (G1) 5.05 (G2)	NM	1 (G1) 5 (G2)
Irinakis and Wiebe[23]	2009	CCT (multicenter)	67[a]	NM	Mean 9.25 months (range 5–13)	NM	Immediate or delayed	NM	0/37 (G1) 2/70 (G2)	0 (G1) 2.86 (G2)	NM	NM
Pieri et al.[24]	2009	CCT (unicenter)	23[a]	51–72 (61.9)	Mean 19 months (range 12–31)	6/9	Immediate	NM	1/59 (G1) 1/85 (G2)	1.69 (G1) 1.18 (G2)	NM	NM
Alves et al.[25]	2010	CCT (unicenter)	23[a]	NM	3 years	NM	Immediate (n = 159), delayed (n = 9)	NM	0/108 (G1) 2/60 (G2)	0 (G1) 3.33 (G2)	NM	NM
Artzi et al.[61]	2010	RA (unicenter)	54[a]	34–81 (57.5)	36 months	7/NM	Immediate	NM	13/367 (G1) 8/309 (G2)	3.54 (G1) 2.59 (G2)	NM	NM
Bogaerde et al.[26]	2010	CCT (unicenter)	21[a]	32–79 (60)	18 months	6/10	Within 7 days	NM	1/16 (G1) 0/53 (G2)	6.25 (G1) 0 (G2)	NM	1 (G1) 0 (G2)
Cannizzaro et al.[14]	2010	RCT[e] (multicenter)	40 (10, G1; 30, G2)	18–55 (39)	1 year	Only before surgery (and 6 days for the grafted)/14	Immediate	NM	4/10 (G1) 1/30 (G2)	40 (G1) 3.33 (G2)	0.01	0 (G1) 0 (G2)
Cooper et al.[27]	2010	CCT (multicenter)	113 (55, G1; 58, G2)	NM	1 year	"Prescribed"	Immediate	NM	3/58 (G1) 1/65 (G2)	5.17 (G1) 1.54 (G2)	NM	NM
Deng et al.[8]	2010	CCT (unicenter)	12 (NM)	40–75 (62)	1 year	7/14	Immediate	NM	4/32 (G1) 0/52 (G2)	12.5 (G1) 0 (G2)	0.039	NM
Siebers et al.[28]	2010	CCT (unicenter)	76[a]	22–85 (52)	Mean of 40.3 months (range 18–87)	NM	4–6 months	NM	4/58 (G1) 1/164 (G2)	6.90 (G1) 0.61 (G2)	NM	NM
van Kesteren et al.[15]	2010	RCT (unicenter)	24 (11, G1; 13, G2)	28–76 (NM)	6 months	NM	The implants did not receive a prosthesis	3 months	1/13 (G1) 0/13 (G2)	7.69 (G1) 0 (G2)	NM	NM
Zafiropoulos et al.[62]	2010	RA (unicenter)	252 (153, G1; 99, G2)	43–70 (49)	5 years	6/35	Immediate	NM	9/153 (G1) 2/99 (G2)	5.88 (G1) 2.02 (G2)	NM	NM
Aguirre-Zorzano et al.[29]	2011	CCT (unicenter)	57[a]	26–78 (48.5)	Mean 92 weeks	7/42	Immediate	NM	1/56 (G1) 0/22 (G2)	1.79 (G1) 0 (G2)	NM	1 (G1) 0 (G2)
Bae et al.[63]	2011	RA (multicenter)	92[a]	21–71 (42)	Mean 38 months (range 22–59)	1/NM	3–4 months (mandible) 5–7 months (maxilla)	NM	0/26 (G1) 1/54 (G2)	0 (G1) 1.85 (G2)	NM	NM
Cavallaro[64]	2011	RA (unicenter)	75[a]	28–84 (61.8)	3 years	7/NM	6–8 weeks	NM	1/28 (G1) 1/176 (G2)	3.57 (G1) 0.57 (G2)	NM	NM
Felice et al.[16]	2011	RCT (multicenter)	106 (54, G1; 52, G2)	28–72 (49)	4 months after loading	6/14	Immediate or 4 months	4 months	2/54 (G1) 0/52 (G2)	3.70 (G1) 0 (G2)	NM	NM
Gillot et al.[65]	2011	RA (unicenter)	105[a]	NM (58.7)	4 months	6/NM	Immediate	NM	4/182 (G1) 4/266 (G2)	2.20 (G1) 1.50 (G2)	0.499	0 (G1) 0 (G2)
Malchiodi et al.[66]	2011	RA (unicenter)	81 (55, G1; 26, G2)	NM	Mean 6.7 years (range 6–7.3)	5/14	Immediate	NM	6/138 (G1) 2/101 (G2)	4.35 (G1) 1.98 (G2)	0.47	NM

Table 1 (*Continued*)

Authors	Published	Study design	Patients (*n*) (number per group)	Patients' age range (average) (years)	Follow-up	Antibiotics/ mouth rinse (days)	Healing period/loading	Period between extraction and implant insertion in G2	Failed/ placed implants (*n*)	Implant failure rate (%)	P value (for failure rate)	Postoperative infection
Mertens and Steveling[30]	2011	CCT (unicenter)	17[a]	40–83 (61)	5 years	NM	Immediate (*n* = 14), mean 9.5 weeks (*n* = 35)	NM	0/7 (G1) 1/42 (G2)	0 (G1) 2.38 (G2)	NM	NM
Peñarrocha-Diago et al.[67]	2011	RA (unicenter)	30[a]	36–68 (53.2)	4 years	NM	8–10 weeks (maxilla) 6–8 weeks (mandible)	NM	4/173 (G1) 4/119 (G2)	2.31 (G1) 3.36 (G2)	NM	0 (G1) 0 (G2)
Cannizzaro et al.[17]	2012	RCT[f] (unicenter)	30 (split-mouth)	18–57 (35)	4 years	1/16	Immediate (*n* = 29) or 6 weeks (*n* = 31)	NM	0/18 (G1) 2/42 (G2)	0 (G1) 4.76 (G2)	NM	0 (G1) 0 (G2)
Cosyn et al.[68]	2012	RA (unicenter)	461 (NM)	18–90 (51)	Mean 30 months (range 12–48)	NM	Immediate (25%), within 12 weeks (3%), delayed (72%)	NM	1/77 (G1) 38/1021 (G2)[g]	1.30 (G1) 3.72 (G2)	NM	NM
Covani et al.[69]	2012	RA (unicenter)	19[a]	39–72 (60)	4 years	5/NM	Immediate	NM	0/119 (G1) 8/45 (G2)	0 (G1) 17.78 (G2)	0.000	NM
Degidi et al.[70]	2012	RA (unicenter)	1045[a]	18–93 (NM)	7 years	5/NM	NM	NM	6/1184 (G1) 22/2951 (G2)	0.51 (G1) 0.75 (G2)	NM	NM
Gillot et al.[71]	2012	RA (unicenter)	113[a]	37–93 (60.4)	6 months	6/NM	Immediate	NM	5/352 (G1) 1/323 (G2)	1.42 (G1) 0.31 (G2)	0.1621	0 (G1) 0 (G2)
Ji et al.[9]	2012	RA (unicenter)	45[a]	25–88 (61.5)	Mean 42 months (range 1–125)	NM	Immediate	NM	7/31 (G1) 14/180 (G2)	22.58 (G1) 7.78 (G2)	NM	NM
Ormianer et al.[72]	2012	RA (unicenter)	46[a]	NM (50)	Mean 120 months (range 102–127)	NM	Immediate or delayed	NM	0/65 (G1) 1/108 (G2)	0 (G1) 0.93 (G2)	NM	0 (G1) 1 (G2)
Peñarrocha-Diago et al.[73]	2012	RA (unicenter)	150[a]	25–80 (55.4)	Mean 28.3 months (range 12–60)	7/7	3 months (maxilla), 2 months (mandible)	>3 months	22/480 (G1) 21/542 (G2)	4.58 (G1) 3.87 (G2)	0.502	NM
Peñarrocha-Oltra et al.[74]	2012	RA (unicenter)	70[a]	34–75 (54)	Mean 28.7 months (range 12–67)	7/7	8–10 weeks	NM	2/35 (G1) 6/88 (G2)	5.71 (G1) 6.82 (G2)	NM	1 (G1) 1 (G2)
Raes et al.[31]	2012	CCT (unicenter)	96 (46, G1; 50, G2)	18–72 (43)	1 year	NM	Immediate	Up to 1 year	1/48 (G1) 1/54 (G2)	2.08 (G1) 1.85 (G2)	NM	NM
Romanos et al.[75]	2012	RA (unicenter)	55[a]	NM (63)	Mean 61 months (range 24–125)	7/7	Immediate	NM	0/25 (G1) 3/85 (G2)	0 (G1) 3.53 (G2)	NM	NM
Urdaneta et al.[76]	2012	RA (unicenter)	291[a]	NM	2 years	1/NM	NM	NM	5/159 (G1) 4/250 (G2)	3.14 (G1) 1.6 (G2)	NM	NM
Vandeweghe et al.[77]	2012	RA (multicenter)	75[a]	25–82 (58)	Mean 14 months (range 6–34)	NM	Immediate (*n* = 29), 3 months (*n* = 64)	6 months	3/69 (G1) 1/24 (G2)	4.35 (G1) 4.17 (G2)	>0.05	NM
Atieh et al.[32]	2013	CCT (unicenter)	24 (12, G1; 12, G2)	NM (52)	1 year	1/1	Immediate	>4 months	4/12 (G1) 2/12 (G2)	33.33 (G1) 16.67 (G2)	0.35	NM
Cosyn et al.[33]	2013	CCT (multicenter)	104 (28, G1; 76, G2)	22–80 (51)	17–42 months	1/postop.	Immediate (*n* = 30), 3 months (*n* = 68), 6 months (*n* = 14)	6 weeks	2/30 (G1) 5/82 (G2)	6.67 (G1) 6.10 (G2)	NM	1 (G1) 1 (G2)
De Bruyn et al.[34]	2013	CCT (multicenter)	113 (55, G1; 58, G2)	NM (42–45)	3 years	5/7	Immediate	NM	3/55 (G1) 1/58 (G2)	5.45 (G1) 1.72 (G2)	>0.05	NM
Peñarrocha-Oltra et al.[35]	2013	CCT (unicenter)	29[a]	28–77 (55.4)	Mean 20 months (range 12–36)	6/17	Immediate or delayed (2 months)	NM	4/94 (G1) 0/99 (G2)	4.26 (G1) 0 (G2)	0.199	NM
Piek et al.[36]	2013	CCT (unicenter)	141[a]	NM (57.6)	1 year	5/13	Immediate (*n* = 137), delayed (*n* = 323)	NM	5/123 (G1) 7/337 (G2)	4.07 (G1) 2.08 (G2)	NM	NM
Raes et al.[37]	2013	CCT (unicenter)	48 (16, G1; 32, G2)	NM	1 year	NM	Immediate	4–5 months	1/16 (G1) 0/32 (G2)	6.25 (G1) 0 (G2)	NM	NM
Cakarer et al.[78]	2014	RA (unicenter)	274[a]	19–84 (50)	2–8 years	5/NM	3 months (maxilla) 2 months (mandible)	NM	0/94 (G1) 15/846 (G2)	0 (G1) 1.77 (G2)	NM	NM
Cooper et al.[38]	2014	CCT (unicenter)	113 (55, G1; 58, G2)	NM (42–45)	5 years	NM	Immediate	NM	3/55 (G1) 1/58 (G2)	5.45 (G1) 1.72 (G2)	>0.05	NM

Luongo et al.[39]	2014	CCT (multicenter)	46[a]	18–73 (44.5)	1 year	6/14	Immediate	NM	0/10 (G1) 1/47 (G2)	0 (G1) 2.13 (G2)	NM	0 (G1) 0 (G2)
Meizi et al.[40]	2014	CCT (unicenter)	155[a]	NM (47.5)	3–9 months	5/NM	Immediate, 3–6 months	>3 months	7/215 (G1) 3/129 (G2)	3.26 (G1) 2.33 (G2)	NM	NM

NM – not mentioned; CCT – controlled clinical trial; RCT – randomized controlled trial; RA – retrospective analysis; G1 – group fresh extraction sockets; G2 – group healed sites.

[a] Implants were inserted in fresh extraction sockets and in healed sites in some or all patients of the study.

[b] 99 implants (7 failures) were inserted at an early/late protocol (6–8 weeks after extraction), and were not considered.

[c] Three patients had implants inserted in fresh extraction sockets and in healed sites.

[d] Implants placed 2 months after the extraction ($n = 34$) were not considered.

[e] Randomized for immediate occlusal versus non-occlusal loading.

[f] Randomized for immediate versus early loading.

[g] Implants inserted through the so-called 'early placement' (6 weeks following tooth removal) were not considered.

for the studies assessing implants being rehabilitated only with full-arch prosthesis (sixteen studies) were 1922 (67 failures, 3.49%) and 2082 (61 failures, 2.93%), respectively.

Seventeen studies reported the incidence of postoperative infection, of which fifteen studies[3,14,17,21,26,29,33,39,57,60,65,67,71,72,74] reported the events separated by group. Thirty-five studies provided information about marginal bone loss, but only fifteen studies[2,8,24,27,32–35,37–39,41,61,63,67,74] reported the mean and standard deviation values separated by group, necessary for the performance of the meta-analysis of a continuous outcome.

3.3. *Quality assessment*

All studies except three[15,31,34] were of high quality. The scores are summarized in Table 3.

3.4. *Meta-analysis*

In this study, a random-effects model was used to evaluate the implant failure in the comparison between the procedures, since statistically significant heterogeneity was found ($P = 0.02$; $I^2 = 26\%$). The insertion of dental implants in fresh extraction sockets affected the implant failure rates ($P < 0.0001$; Fig. 2), with a RR of 1.58 (95% CI 1.27–1.95) when compared to placement in healed sites. Thus, the relative risk reduction (RRR) is −58%. In other words, being the RRR negative, the insertion of implants in fresh extraction sockets increases the risk of implant failure by 58% (95% CI 27–95%).

Sensitivity analyses were also performed for the outcome 'implant failure'. The RR was examined for the groups of studies evaluating the implants inserted in different jaws, when the implants were used for the rehabilitation of single crown or full-arch prosthesis only, and when only the controlled studies (RCTs and CCTs) were considered. When studies evaluating implants inserted only in the maxilla were pooled, a RR of 1.58 resulted (95% CI 0.97–2.59; $P = 0.07$; heterogeneity: fixed-effects model, $I^2 = 0\%$, $P = 0.79$; Fig. 3), whereas when the studies evaluating implants inserted only in the mandible were pooled, a RR of 2.15 was observed (95% CI 0.62–7.47; $P = 0.23$; heterogeneity: random-effects model, $I^2 = 65\%$, $P = 0.01$; Fig. 4). When studies using implants to rehabilitate patients only with single crowns were pooled, a RR of 2.05 resulted (95% CI 1.36–3.11; $P = 0.0007$; heterogeneity: fixed-effects model, $I^2 = 0\%$, $P = 0.84$; Fig. 5), whereas when the studies using implants to rehabilitate patients only with full-arch prosthesis were pooled, a RR of 1.22 was observed (95% CI 0.71–2.83; $P = 0.32$; heterogeneity: random-effects model, $I^2 = 62\%$, $P = 0.0005$; Fig. 6). When only the controlled studies (RCTs and CCTs) were considered, a RR of 2.27 resulted (95% CI 1.57–3.29; $P < 0.0001$; heterogeneity: fixed-effects model, $I^2 = 11\%$, $P = 0.30$; Fig. 7).

There was no apparent significant effect of implants inserted in fresh extraction sockets on the occurrence of postoperative infection (RR 2.11, 95% CI 0.81–5.46; $P = 0.13$; heterogeneity: fixed-effects model, $I^2 = 0\%$; $P = 0.85$, Fig. 8). There was no apparent significant effect of implants inserted in fresh extraction sockets on the magnitude of marginal bone loss (MD −0.08, 95% CI −0.18 to 0.01; $P = 0.09$; heterogeneity:

Table 2 – Detailed data of the included studies – Part 2.

Authors	Marginal bone loss (mean ± SD) (mm)	Implant surface modification (brand)	Region/prosthetic rehabilitation/ opposing dentition	Observations
Mensdorff-Pouilly et al.[41]	0.45 ± 1.02 (G1, *n* = 85) 0.3 ± 0.8 (G2, *n* = 88)	TPS (IMZ, Friatec, Mannheim, Germany, *n* = 121), Turned (Brånemark, Nobelpharma AB, Göteborg, Sweden, *n* = 69)	Maxilla, mandible/NM/NM	GBR performed in 76 implant sites
Watzek et al.[42]	NM	Turned (Brånemark, Nobel Biocare AB, Göteborg, Sweden; *n* = 50), titanium-plasma sprayed (TPS, Friedrichsfeld AG, Mannheim, Germany; *n* = 84)	Maxilla, mandible/FAP/NM	GBR performed in 20 implant sites
Haas et al.[43]	NM	TPS (IMZ, Friatec, Friedrichseld, Germany)	Maxilla, mandible/SC, FPP, FAP/NM	–
Gomez-Roman et al.[44]	NM	HA-coated (Frialit-2, Dentsply Friadent, Mannheim, Germany)	Maxilla, mandible/SC, FPP, FAP/NM	GBR performed for 1% of the implants
Callan et al.[45]	NM	HA-coated (NM; *n* = 992), TPS (NM; *n* = 108)	Maxilla, mandible/NM/NM	175 smokers, grafting in 466 implant sites
Maló et al.[3]	1.5 (G1, *n* = 20) 0.7 (G2, *n* = 21)	Turned (Brånemark MkII, Nobel Biocare AB, Göteborg, Sweden)	Maxilla, mandible/SC (*n* = 31), FPP (*n* = 23)/ NM	Only in anterior regions (until first premolar), patients who smoke less than 10 cigarettes/day were also included, but the exact number was not informed
Polizzi et al.[18]	1.17 ± 1.37 (maxilla, mesial, *n* = 67) 1.19 ± 1.49 (maxilla, distal, *n* = 67) 0.71 ± 1.27 (mandible, mesial, *n* = 52) 0.64 ± 0.43 (mandible, distal, *n* = 52) (5 years)	Turned (Brånemark, Nobel Biocare AB, Göteborg, Sweden)	Maxilla, mandible/SC (*n* = 76), FPP (*n* = 40), FAP (*n* = 23)/NM	Membranes used in 64 implants, 8 grafts
Chaushu et al.[46]	NM	Acid-etched and HA-coated (Steri-Oss, Steri-Oss Company, Yorba Linda, USA, *n* = 21), HA-coated (Alpha Bio, Petah-Tikva, Israel, *n* = 7)	Maxilla, mandible/SC/NM	No smokers
Aires and Berger[47]	NM	NM	Maxilla, mandible/FAP/NM	–
Arlin[48]	NM	Turned, HA-coated, titanium-plasma sprayed, sandblasted and acid-etched, acid-etched (Sulzer Dental, Nobel Biocare, Implant Innovations, Lifecore Biomedical, Straumann)	Maxilla, mandible/FPP, FAP, removable prostheses/NM	–
De Bruyn and Collaert[4]	1.4 ± 0.5 (*n* = 32) (3 years)	Turned (Brånemark, Nobel Biocare AB, Göteborg, Sweden)	Mandible/FAP/NM	Smokers were also included, but the exact number was not informed
Maló et al.[49]	1.2 ± 1.2	? (Brånemark MkII and MkIII, Nobel Biocare AB, Göteborg, Sweden)	Mandible/FAP/removable prostheses, implant-supported fixed prostheses (*n* = 14), natural teeth (*n* = 7), fixed prostheses on teeth (*n* = 5)	–
Maló et al.[19]	1.20 ± 0.94 (*n* = 85) (1 year)	Turned (Brånemark, Nobel Biocare AB, Göteborg, Sweden)	Maxilla, mandible/SC (*n* = 63), FPP (*n* = 24)/ NM	Molar regions not included, 24 smokers
Wolfinger et al.[50]	0.46 (immediately loaded) 0.53 (2-stage implants) (5 years)	Turned (Brånemark, Nobel Biocare AB, Göteborg, Sweden)	Mandible/FAP/NM	Only in edentulous mandibles
Evian et al.[51]	NM	? (Paragon, Zimmer Dental, Carlsbad, USA)	Maxilla, mandible/SC/NM	77 patients with periodontitis history

Jaffin et al.[52]	NM	Sandblasted and acid-etched (SLA, Straumann, Waldenburg, Switzerland)	Maxilla/FAP/NM	Only in edentulous maxillae, smokers were also included, but the exact number was not informed
Kourtis et al.[5]	NM	Several (IMZ, $n = 1038$; Frialit-2, $n = 597$; Free-Hex, $n = 44$; Frialoc, $n = 13$; Friadent Co., Mannheim, Germany)	Maxilla, mandible/SC, FPP, overdenture/NM	853 implants in smokers, 56 in diabetic patients
Locante[53]	NM	? (Stabledent, Crystal Medical Technology, Pelham, USA)	Maxilla/SC/NM	9 smokers, grafting in some implant sites
Norton[20]	0.4	TiO-Sandblasted (AstraTech ST, Mölndal, Sweden)	Maxilla/SC/NM	Smokers were included, as well as grafting limited to circumferential socket defects, but the exact number was not informed
Perry and Lenchewski[54]	NM	Sandblasted and acid-etched (Frialit-2, Dentsply Friadent, Mannheim, Germany)	Maxilla, mandible/NM/NM	No grafts
Davarpanah et al.[21]	NM	Acid-etched (Osseotite NT, Biomet 3i, Palm Beach Gardens, USA)	Maxilla, mandible/SC, FPP/NM	Patients who smoke less than 15 cigarettes/day were also included, but the exact number was not informed. Grafting in some sites
Dhanrajani and Al-Rafee[6]	NM	Turned (Brånemark, Nobel Biocare AB, Göteborg, Sweden, $n = 115$), acid-etched (Osseotite NT, Biomet 3i, Palm Beach Gardens, USA, $n = 19$), HA-coated (Omniloc, Calcitek Sulzer, Carlsbad, USA, $n = 8$), oxidized (Steri-Oss, Replace, Nobel Biocare AB, Göteborg, Sweden, $n = 5$)	Maxilla, mandible/SC/NM	24 smokers, 15 diabetic patients
Degidi et al.[55]	0.6 ± 0.2 (1 year) 0.9 ± 0.2 (5 years)	Several	Maxilla, mandible/SC/NM	19 smokers
Lindeboom et al.[2]	0.49 ± 0.11 (G1, mesial, $n = 23$) 0.53 ± 0.12 (G1, distal, $n = 23$) 0.52 ± 0.16 (G2, mesial, $n = 25$) 0.52 ± 0.14 (G2, distal, $n = 25$) (1 year)	Sandblasted and acid-etched (Frialit-2 Synchro, Dentsply Friadent, Mannheim, Germany)	Maxilla/SC/NM	Implants in periapical infected sites, no smokers, buccal bone grafting in all cases
Degidi et al.[56]	NM	Several	Maxilla, mandible/SC/NM	Patients who smoke less than 20 cigarettes/day were also included, but the exact number was not informed
Degidi et al.[22]	NM	Several	Maxilla, mandible/NM/NM	Patients who smoke less than 20 cigarettes/day were also included, but the exact number was not informed
Horwitz et al.[7]	NM	Sandblasted and acid-etched (MIS Implant Technologies, Shlomi, Israel)	Maxilla, mandible/SC ($n = 5$), FPP ($n = 12$), FAP ($n = 5$)/NM	Only in patients diagnosed with moderate to severe generalized chronic periodontitis
Ormianer and Palti[57]	Information provided, but not in mean $\pm$ SD	Sandblasted and acid-etched (Tapered Screw-Vent MTX; Zimmer Dental, Inc, Carlsbad, USA)	Maxilla, mandible/SC ($n = 18$), FPP ($n = 238$), removable dentures ($n = 7$)/NM	Grafting in some implant sites, 2 smokers, 32 patients with periodontitis history

Table 2 (*Continued*)

Authors	Marginal bone loss (mean ± SD) (mm)	Implant surface modification (brand)	Region/prosthetic rehabilitation/ opposing dentition	Observations
Peñarrocha-Diago et al.[58]	0.83 (G1) 0.85 (G2)	TSA surface (Defcon Avantblast, Impladent, Sentmenat, Barcelona, Spain)	Maxilla, mandible/SC (n = 55), FPP (n = 66), FAP (n = 5), overdenture (n = 2)/edentulous arch (n = 1), natural teeth (n = 91), fixed prostheses (n = 5), removable dentures (n = 2), implant-supported restoration (n = 17), combination (n = 12)	Only in the molar area, smokers (40.5%)
Ribeiro et al.[59]	NM	Sandblasted (Conexão, São Paulo, Brazil)	Maxilla/SC/NM	–
Sennerby et al.[60]	−2.6 ± 1.5 (immediate loading, n = 87) −1.6 ± 1.1 (delayed loading, n = 22)	Oxidized (TiUnite, NobelDirect, Nobel Biocare, Göteborg, Sweden)	Maxilla, mandible/SC (n = 18), FPP (n = 99)/ NM	Use of a slide-over guide sleeve to evaluate and determine the position of the implants inserted by a flapless technique (n = 76), minor bone grafting (n = 8)
Irinakis and Wiebe[23]	NM	Oxidized (NobelActive; Nobel Biocare, Göteborg, Sweden)	Maxilla, mandible/NM/NM	Some implants placed in grafted site, but the exact number was not informed
Pieri et al.[24]	0.57 ± 0.27 (G1, n = 58) 0.47 ± 0.18 (G2, n = 84) (1 year)	Bioabsorbable blast media (Keystone Dental, Burlington, USA)	Maxilla, mandible/FAP/natural dentition (n = 3), implant prosthesis (n = 6), complete denture (n = 6), FPP (n = 6), removable partial prosthesis (n = 2)	Patients who smoke less than 10 cigarettes/day were also included, but the exact number was not informed
Alves et al.[25]	NM	Several (146 Straumann, 10 Nobel Biocare, 8 Biomet 3i, and 4 Lifecore)	Maxilla, mandible/FAP/natural teeth or fixed prosthesis (n = 22), removable denture (n = 4)	In periodontally compromised patients only, 4 smokers, 4 diabetic patients
Artzi et al.[61]	0.79 ± 1.07 (G1, n = 354) 1.1 ± 1.26 (G2, n = 301) (3 years)	Sandblasted and acid-etched (DFI, ITO, and SPI, Alpha-Bio Tec, Petach Tikva, Israel)	Maxilla, mandible/FAP/NM	GBR performed in 111 implant sites, 15 sinus lifting, 21 smokers
Bogaerde et al.[26]	0.7 ± 0.7 (18 months)	Sandblasted (Bimodal, Neoss Ltd., Harrogate, UK)	Maxilla, mandible/SC, FPP/NM	Bone grafts in 7 implant sites
Cannizzaro et al.[14]	0.18 ± 0.18 (1 year)	Sandblasted zirconia (Z-Look3 zirconia, Z-Systems, Oensingen, Switzerland)	Maxilla, mandible/SC/NM	Use of zirconia implants, 10 patients grafted, 14 smokers
Cooper et al.[27]	−1.30 ± 2.52 (G1, n = 55) 0.40 ± 1.43 (G2, n = 64) (1 year)	TiO_2-blasted fluoride-modified (Osseospeed, AstraTech AB, Mölndal, Sweden)	Maxilla/SC/natural teeth	Involving teeth 15–25 only, no smokers
Deng et al.[8]	1.01 ± 0.29 (G1, n = 28) 1.24 ± 0.23 (G2, n = 52) (1 year)	Oxidized (TiUnite, Brånemark System Mk III, NobelSpeedy; Nobel Biocare, Göteborg, Sweden)	Maxilla, mandible/FAP/complete denture	All patients periodontally compromised and all received previous periodontal treatment, 9 smokers
Siebers et al.[28]	NM	Sandblasted and acid-etched (Camlog Rootline and Screw Line, Camlog Biotechnologies, Basel, Switzerland), acid-etched (Osseotite, Biomet 3i, Palm Beach Gardens, USA), blasted with HA and calcium phosphate (Restore RBM, Lifecore Biomedical, Chaska, USA)	Maxilla, mandible/SC, FPP, FAP/NM	No grafted patients, almost 20% of the patients were smokers, almost 30% were bruxers, and almost 60% were treated for periodontal disease
van Kesteren et al.[15]	NM	Sandblasted and acid-etched (SLA, Straumann, Waldenburg, Switzerland)	NM/the implants did not receive a prosthesis/NM	Patients who smoke less than 10 cigarettes/day were also included, but the exact number was not informed, freeze-dried bone allograft and collagen membrane in G2

Zafiropoulos et al.[62]	NM	Sandblasted and acid-etched (Camlog root line, Altatec, Wimsheim, Germany), sandblasted and acid-etched (SLA, Straumann, Waldenburg, Switzerland)	Maxilla, mandible/SC/NM	86 smokers, GBR performed in some cases
Aguirre-Zorzano et al.[29]	0.19 ± 0.41 (mesial, *n* = 71) 0.20 ± 0.42 (distal, *n* = 71)	TiO_2-blasted fluoride-modified (Osseospeed, Astra Tech Dental, Möndal, Sweden)	Maxilla, mandible/SC/NM	GBR performed in 5 cases
Bae et al.[63]	0.32 ± 1.3 (G1, *n* = 26) 0.29 ± 0.9 (G2, *n* = 53) (1 year)	Sandblasted and acid-etched (Seven, MIS Implants Technologies Ltd., Tel Aviv, Israel)	Maxilla, mandible/SC, FPP, overdenture/NM	GBR performed in some cases
Cavallaro[64]	0.60 (G1, mesial) 0.52 (G1, distal)	Soluble Blast Media (Implant Direct LLC, Calabasas, USA)	Maxilla, mandible/SC (*n* = 42), FPP (*n* = 49), overdenture (*n* = 9), tooth-implant-supported partial prosthesis (*n* = 9)/NM	18 smokers, GBR in some cases
Felice et al.[16]	NM	Resorbable blast media treated (EZ Plus (MegaGen, Gyeongbuk, South Korea)	Maxilla/SC/NM	Involving teeth 15–25 only, sockets filled with inorganic bovine bone and covered by a collagen barrier in G2, 22 smokers
Gillot et al.[65]	NM	Oxidized (TiUnite, Nobel Biocare, Göteborg, Sweden)	Mandible/FAP/NM	Patients who smoke less than 15 cigarettes/day were also included, but the exact number was not informed
Malchiodi et al.[66]	NM	Acid-etched (Osseotite Certain, Biomet 3i, Palm Beach Gardens, USA; *n* = 75), calcium phosphate–coated titanium plasma-sprayed (FBR Pitt-Easy, Oraltronics, Bremen, Germany; *n* = 164)	Maxilla/SC (18.8%), FPP (44.4%), FAP (36.8%)/ natural teeth (48.9%), ceramic (29.7%) or acrylic resin (21.4%) prostheses	Patients who smoke less than 20 cigarettes/day were also included, but the exact number was not informed
Mertens and Steveling[30]	0.1 ± 0.4 (5 years)	TiO_2-blasted fluoride-modified (Osseospeed, AstraTech AB, Mölndal, Sweden)	Maxilla, mandible/SC (*n* = 31), FPP (14 implants), FAP (4 implants)/NM	2 smokers, 11 patients with periodontal history
Peñarrocha-Diago et al.[67]	0.63 ± 0.18 (G1, *n* = 173) 0.58 ± 0.26 (G2, *n* = 119) (1 year)	Xx (Defcon Avantblast TSA, Impladent, Senmenat, Barcelona, Spain)	Maxilla, mandible/FAP/NM	Grafting procedures in sites of 62 implants, patients who smoke less than 10 cigarettes/day were also included, but the exact number was not informed
Cannizzaro et al.[17]	−0.37 ± 0.35 (immediate load, *n* = 28) −0.31 ± 0.36 (early load, *n* = 28) (4 years)	Acid-etched (NanoTite, Biomet 3i, Palm Beach, USA)	Maxilla, mandible/CS/NM	Flapless surgery, 12 smokers
Cosyn et al.[68]	NM	Several (Nobel Biocare, *n* = 442; Straumann, *n* = 266; Dentsply Friadent, *n* = 182; Astra Tech, *n* = 174; Biomet 3i, *n* = 125)	Maxilla, mandible/SC (14%), FPP or FAP (70%), removable partial or complete denture (16%)/NM	18% of the implants were installed in augmented bone, smokers were also included, but the exact number was not informed
Covani et al.[69]	NM	Sandblasted and acid-etched (Ossean, Intra-Lock International, Inc., Boca Raton, USA)	Maxilla, mandible/FAP/NM	Patients who smoke less than 10 cigarettes/day were also included, but the exact number was not informed, GBR in some cases
Degidi et al.[70]	NM	Sandblasted and acid-etched (Xive, Dentsply Friadent, Mannheim, Germany)	Maxilla, mandible/NM/NM	Patients who smoke less than 20 cigarettes/day were also included, but the exact number was not informed
Gillot et al.[71]	NM	Oxidized (TiUnite, MkIII, MkIV, Speedy, NobelActive, Nobel Biocare, Göteborg, Sweden)	Maxilla/FAP/NM	Patients who smoke less than 15 cigarettes/day were also included, but the exact number was not informed

Table 2 (*Continued*)

Authors	Marginal bone loss (mean ± SD) (mm)	Implant surface modification (brand)	Region/prosthetic rehabilitation/ opposing dentition	Observations
Ji et al.[9]	NM	Oxidized (TiUnite, Nobel Biocare, Göteborg, Sweden, *n* = 233), HA-coated (Zimmer Dental, Carlsbad, USA, *n* = 54), sandblasted and acid-etched (Xive, Dentsply Friadent, Mannheim, Germany, *n* = 10)	Maxilla, mandible/FAP/natural teeth (133 implants), overdenture (13), implant-supported full-arch prosthesis (*n* = 116), complete denture (19), natural teeth with removable partial denture (16)	8 smokers, 1 diabetic patient, grafting procedures in 86 implant sites
Ormianer et al.[72]	Information provided, but not in mean ± SD	Sandblasted and acid-etched (Tapered Screw-Vent MTX; Zimmer Dental, Inc, Carlsbad, USA)	Maxilla/SC (*n* = 16), FPP (*n* = 156)/NM	Grafting in 108 implant sites, 1 smoker, 29 patients with periodontitis history
Peñarrocha-Diago et al.[73]	NM	? (Defcon implants, Impladent SL, Barcelona, Spain)	Maxilla, mandible/SC (*n* = 53), FPP (*n* = 516), FAP (*n* = 297), overdentures (*n* = 116)/NM	Grafting procedures were performed in some sites, but the exact number was not informed
Peñarrocha-Oltra et al.[74]	0.56 ± 0.22 (G1, *n* = 34) 0.67 ± 0.17 (G2, *n* = 84)	NM	Maxilla/SC (*n* = 3), FPP (*n* = 74), FAP (*n* = 39), overdenture (*n* = 7)/natural teeth (*n* = 77), total denture (*n* = 1), teeth-supported fixed prosthesis (*n* = 14), implant-supported fixed prosthesis (*n* = 25), overdenture (*n* = 6)	Only in the molar region, 27 smokers, grafting at the implant site performed in some cases
Raes et al.[31]	NM	TiO_2-blasted fluoride-modified (Osseospeed, AstraTech AB, Mölndal, Sweden)	Maxilla/SC/natural dentition	Involving teeth 15–25 only, no smokers
Romanos et al.[75]	NM	Sandblasted and acid-etched (Ankylos, Friadent, Mannheim, Germany)	Mandible/tooth-implant–supported telescopic prostheses/NM	–
Urdaneta et al.[76]	NM	HA-coated (Integra-CP, Bicon, Boston, USA)	Maxilla, mandible/SC (*n* = 322), FPP (*n* = 4), overdenture (*n* = 19)/NM	Grafting procedures in 142 implant sites, smokers were included, but the exact number was not informed
Vandeweghe et al.[77]	0.46 ± 1.08 (mean 14 months)	Sandblasted (Max Southern Implants, Irene, South Africa)	Maxilla, mandible/SC (*n* = 27), FPP (*n* = 35), FAP (*n* = 24), overdenture (*n* = 1)/NM	Only in posterior regions, 10 smokers, grafting around 17 implants
Atieh et al.[32]	−0.41 ± 0.57 (G1, *n* = 8) 0.04 ± 0.46 (G2, *n* = 10) (1 year)	Sandblasted (Max Southern Implants, Irene, South Africa)	Mandible/SC/NM	Only in molar regions, no smokers
Cosyn et al.[33]	1.30 ± 0.64 (G1, *n* = 30) 1.12 ± 0.60 (G2, *n* = 49)	Oxidized (TiUnite, NobelReplace, Nobel Biocare, Göteborg, Sweden)	Maxilla/SC/NM	Involving teeth 15–25 only, 18 smokers, grafting procedures in 33 implant sites
De Bruyn et al.[34]	−1.6 ± 2.4 (G1, *n* = 52) 0.4 ± 1.5 (G2, *n* = 57) (3 years)	TiO_2-blasted fluoride-modified (Osseospeed, Astra Tech AB, Mölndal, Sweden)	Maxilla/SC/NM	Involving teeth 15–25 only, no smokers
Peñarrocha-Oltra et al.[35]	0.74 ± 0.31 (G1, immediate load, *n* = 49) 0.54 ± 0.23 (G2, immediate load, *n* = 45) 0.61 ± 0.28 (G1, delayed load, *n* = 56) 0.51 ± 0.25 (G2, delayed load, *n* = 43)	Zirconium sandblasted/acid-etched (Kohno SP, Sweden & Martina, Due Carrare, Italy)	Maxilla/FAP/natural or fixed teeth-supported (*n* = 13), fixed implant-supported (*n* = 13), overdenture (*n* = 3)	No smokers
Piek et al.[36]	NM	Sandblasted and acid-etched (Paltop Advanced Dental Solutions Ltd., Caesarea, Israel)	Maxilla, mandible/NM/NM	Smokers (11.3%), history of periodontitis (29%), grafting performed in some implant sites

Raes et al.[37]	1.05 ± 1.78 (G1, n = 16) −0.18 ± 1.26 (G2, n = 23) (1 year)	TiO_2-blasted fluoride-modified (Osseospeed, AstraTech AB, Mölndal, Sweden)	Maxilla/SC/NM	Only in the anterior region, grafting in 9 sites, no smokers
Cakarer et al.[78]	NM	Several (Astra Tech, n = 126, Straumann, n = 158; SwissPlus, n = 656)	Maxilla, mandible/SC (158 implants), FPP (n = 712), overdenture (70)/NM	246 implants in smokers, grafting in 6% of the implants
Cooper et al.[38]	−2.06 ± 2.38 (G1, n = 45) −0.1 ± 1.29 (G2, n = 49) (5 years)	TiO_2-blasted fluoride-modified (Osseospeed, AstraTech AB, Mölndal, Sweden)	Maxilla/SC/natural teeth	Involving teeth 15–25 only, flapless surgery in 68 implants
Luongo et al.[39]	0.22 ± 0.20 (G1, n = 10) 0.35 ± 0.22 (G2, n = 33) (1 year)	Nanostructured calcium-incorporated surface (AnyRidge, MegaGen, Gyeongbuk, South Korea)	Maxilla, mandible/SC/NM	17 smokers, grafting procedures at 15 implant sites
Meizi et al.[40]	NM	Sandblasted and acid-etched (Saturn, Cortex Dental, Shlomi, Israel)	Maxilla, mandible/SC, FPP/NM	7% of the patients were diabetics, and 8% were smokers, 237 flapless surgery, 107 open flap surgery

NM – not mentioned; GBR – guided bone regeneration; HA-coated – hydroxyapatite-coated; SC – single crown; FAP – full-arch prosthesis; FPP – fixed partial prosthesis.

random-effects model, $I^2 = 88\%$; $P < 0.00001$, Fig. 9) in comparison with implants placed in healed sites.

3.5. *Publication bias*

The funnel plot did not show asymmetry when the studies reporting the outcome 'implant failure' were analyzed (Fig. 10), indicating possible absence of publication bias.

4. Discussion

Potential biases are likely to be greater for non-randomized studies compared with RCTs, so results should always be interpreted with caution when they are included in reviews and meta-analyses.[79] However, narrowing the inclusion criteria increases homogeneity but also excludes the results of more trials and thus risks the exclusion of significant data.[80] This was the reason to include non-randomized studies in the present meta-analysis. However, a sensitivity analysis pooling only the controlled studies (RCTs and CCTs) was also performed. The issue is important because meta-analyses are frequently conducted on a limited number of RCTs. In meta-analyses such as these, adding more information from observational studies may aid in clinical reasoning and establish a more solid foundation for causal inferences.[80]

Several authors[18,22,24,31,33,40,48,50–52,54,60,61,65–67,70,73,74,77] have observed that implants inserted in fresh extraction sockets experience similar survival rates when compared to implants inserted in healed sites. Surprisingly, a statistically significant difference in implant failures was found in the present review, both when all studies and when controlled studies only (RCTs and CCTs) were analyzed, stressing the importance of meta-analyses to increase sample size of individual trials to reach more precise estimates of the effects of interventions. A suggested explanation for this is the fact that implant placement in fresh extraction sockets is technique-sensitive because primary implant stability is critical; these implants are usually not in direct contact with the alveolar bone because the extraction socket is broader than is the implant. The anatomic characteristics of the socket after tooth extraction are different from the socket environment after 1 year of healing. Implants placed immediately into fresh extraction sites engage precisely prepared bony walls only in their apex, whereas the coronal space is filled by the end of the healing phase.[18] It has been stated that the procedure should be limited to alveoli with sufficient bone for primary stability, which is generally achieved by exceeding the apex by 3–5 mm or by using implants that are wider than the alveolus.[81] To achieve these conditions, a minimum of 4–5 mm of alveolar crest width and a residual bone length no less than 10 mm are recommended.[82] Simultaneous bone regeneration may be required.[68] It is not known whether these suggested recommendations were followed in all included studies or whether a primary stability was effectively achieved, which might have affected the results.

It is also suggested that periodontitis-affected tissues may have a negative local influence on the failure rates due to the presence of infrabony defects, which could increase the gap between bone and implant,[83] or jeopardize the achievement of

Table 3 – Quality assessment of the studies by the Newcastle–Ottawa scale.

Study	Published	Selection				Comparability		Outcome			Total (9/9)
		Representativeness of the exposed cohort	Selection of external control	Ascertainment of exposure	Outcome of interest not present at start	Comparability of cohorts		Assessment of outcome	Follow-up long enough[a]	Adequacy of follow-up	
						Main factor	Additional factor				
Mensdorff-Pouilly et al.[41]	1994	★	★	★	★	★	★	★	0	★	8/9
Watzek et al.[42]	1995	★	★	★	★	★	★	★	0	★	8/9
Haas et al.[43]	1996	★	★	★	★	★	★	★	0	0	7/9
Gomez-Roman et al.[44]	1997	0	★	★	★	★	0	★	★	0	6/9
Callan et al.[45]	2000	★	★	★	★	★	★	★	0	0	7/9
Maló et al.[3]	2000	0	★	★	★	★	★	★	0	0	6/9
Polizzi et al.[18]	2000	★	★	★	★	★	★	★	★	0	8/9
Chaushu et al.[46]	2001	0	★	★	★	★	★	★	0	0	6/9
Aires and Berger[47]	2002	★	★	★	★	★	★	★	0	0	7/9
Arlin[48]	2002	★	★	★	★	★	★	★	★	0	8/9
De Bruyn and Collaert[4]	2002	0	★	★	★	★	★	★	0	0	6/9
Maló et al.[49]	2003	0	★	★	★	★	★	★	0	0	6/9
Maló et al.[19]	2003	0	★	★	★	★	★	★	0	★	7/9
Wolfinger et al.[50]	2003	0	★	★	★	★	★	★	★	0	7/9
Evian et al.[51]	2004	★	★	★	★	★	★	★	★	0	8/9
Jaffin et al.[52]	2004	0	★	★	★	★	★	★	★	0	7/9
Kourtis et al.[5]	2004	★	★	★	★	★	★	★	★	0	8/9
Locante[53]	2004	0	★	★	★	★	★	★	0	0	6/9
Norton[20]	2004	0	★	★	★	★	0	★	0	★	6/9
Perry and Lenchewski[54]	2004	★	★	★	★	★	★	★	0	0	7/9
Davarpanah et al.[21]	2005	★	★	★	★	★	★	★	0	★	8/9
Dhanrajani and Al-Rafee[6]	2005	0	★	★	★	★	★	★	★	0	7/9
Degidi et al.[55]	2006	★	★	★	★	★	★	★	★	★	9/9
Lindeboom et al.[2]	2006	0	★	★	★	★	★	★	0	0	6/9
Degidi et al.[56]	2007	0	★	★	★	★	★	★	0	0	6/9
Degidi et al.[22]	2007	★	★	★	★	★	★	★	0	0	7/9
Horwitz et al.[7]	2007	0	★	★	★	★	★	★	0	0	6/9
Ormianer and Palti[57]	2008	★	★	★	★	★	★	★	★	0	8/9
Peñarrocha-Diago et al.[58]	2008	0	★	★	★	★	★	★	0	★	7/9
Ribeiro et al.[59]	2008	0	★	★	★	★	★	★	0	★	7/9
Sennerby et al.[60]	2008	★	★	★	★	★	★	★	0	★	8/9
Irinakis and Wiebe[23]	2009	★	★	★	★	★	0	★	0	0	6/9
Pieri et al.[24]	2009	0	★	★	★	★	★	★	0	★	7/9
Alves et al.[25]	2010	0	★	★	★	★	★	★	0	0	6/9
Artzi et al.[61]	2010	0	★	★	★	★	★	★	0	★	7/9
Bogaerde et al.[26]	2010	★	★	★	★	★	★	★	0	★	8/9
Cannizzaro et al.[14]	2010	0	★	★	★	★	★	★	0	★	7/9
Cooper et al.[27]	2010	0	★	★	★	★	0	★	0	★	6/9
Deng et al.[8]	2010	0	★	★	★	★	★	★	0	★	7/9
Siebers et al.[28]	2010	★	★	★	★	★	★	★	0	0	7/9

van Kesteren et al.[15]	2010	0	★	★	★	★	0	★	0	0	5/9
Zafiropoulos et al.[62]	2010	0	★	★	★	★	★	★	★	0	7/9
Aguirre-Zorzano et al.[29]	2011	0	★	★	★	★	★	★	0	★	7/9
Bae et al.[63]	2011	★	★	★	★	★	★	★	0	★	8/9
Cavallaro[64]	2011	★	★	★	★	★	★	★	0	0	7/9
Felice et al.[16]	2011	0	★	★	★	★	★	★	0	★	7/9
Gillot et al.[65]	2011	0	★	★	★	★	0	★	0	★	6/9
Malchiodi et al.[66]	2011	0	★	★	★	★	★	★	★	★	8/9
Mertens and Steveling[30]	2011	★	★	★	★	★	★	★	★	★	9/9
Peñarrocha-Diago et al.[67]	2011	0	★	★	★	★	★	★	0	0	6/9
Cannizzaro et al.[17]	2012	0	★	★	★	★	★	★	0	★	7/9
Cosyn et al.[68]	2012	★	★	★	★	★	★	★	0	0	7/9
Covani et al.[69]	2012	0	★	★	★	★	★	★	0	0	6/9
Degidi et al.[70]	2012	★	★	★	★	★	★	★	★	0	8/9
Gillot et al.[71]	2012	0	★	★	★	★	★	★	0	★	7/9
Ji et al.[9]	2012	0	★	★	★	★	★	★	0	0	6/9
Ormianer et al.[72]	2012	0	★	★	★	★	★	★	★	0	7/9
Peñarrocha-Diago et al.[73]	2012	★	★	★	★	★	★	★	0	0	7/9
Peñarrocha-Oltra et al.[74]	2012	0	★	★	★	★	★	★	0	★	7/9
Raes et al.[31]	2012	0	★	★	★	★	0	★	0	0	5/9
Romanos et al.[75]	2012	0	★	★	★	★	★	★	★	0	7/9
Urdaneta et al.[76]	2012	★	★	★	★	★	★	★	0	0	7/9
Vandeweghe et al.[77]	2012	0	★	★	★	★	★	★	0	0	6/9
Atieh et al.[32]	2013	0	★	★	★	★	★	★	0	★	7/9
Cosyn et al.[33]	2013	0	★	★	★	★	★	★	0	★	7/9
De Bruyn et al.[34]	2013	0	★	★	★	★	0	★	0	0	5/9
Peñarrocha-Oltra et al.[35]	2013	0	★	★	★	★	★	★	0	★	7/9
Piek et al.[36]	2013	★	★	★	★	★	★	★	0	0	7/9
Raes et al.[37]	2013	0	★	★	★	★	★	★	0	★	7/9
Cakarer et al.[78]	2014	★	★	★	★	★	★	★	★	0	8/9
Cooper et al.[38]	2014	0	★	★	★	★	★	★	★	★	8/9
Luongo et al.[39]	2014	0	★	★	★	★	★	★	0	★	7/9
Meizi et al.[40]	2014	0	★	★	★	★	★	★	0	★	7/9

[a] 5 years of follow-up was chosen to be enough for the outcome 'implant failure' to occur.

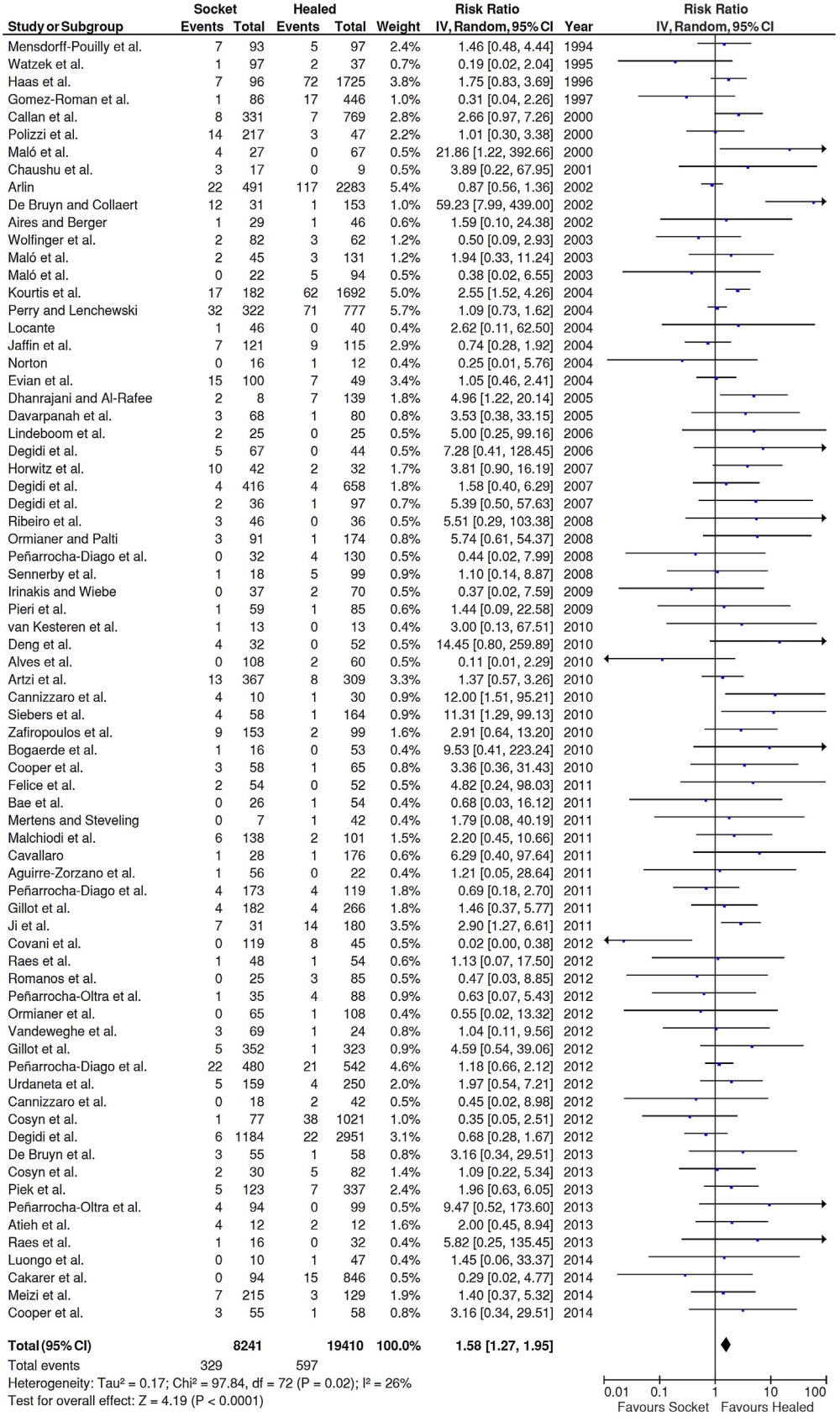

Fig. 2 – Forest plot for the event 'implant failure'.

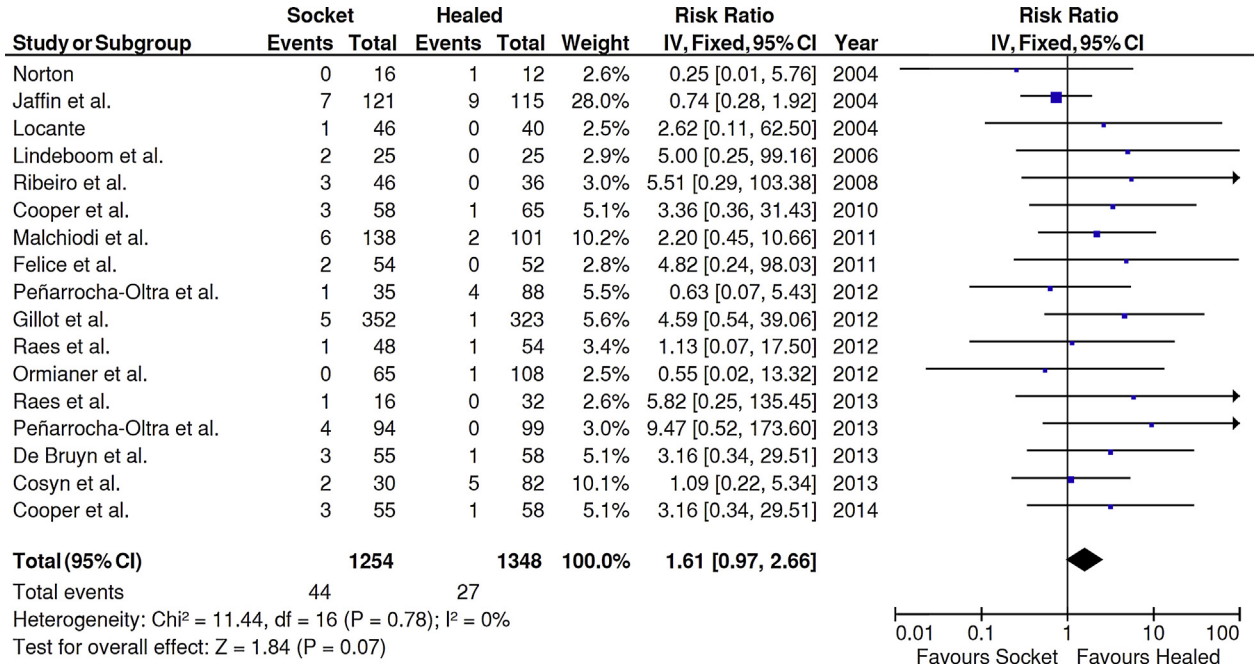

Fig. 3 – Forest plot for the event 'implant failure', when only the studies evaluating implants inserted in the maxilla only were pooled.

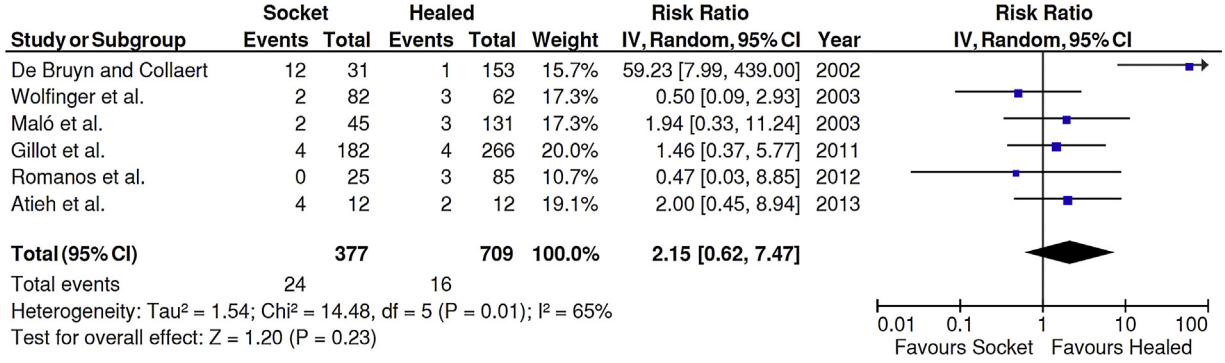

Fig. 4 – Forest plot for the event 'implant failure', when only the studies evaluating implants inserted in the mandible only were pooled.

primary stability[84] at immediate implant placement. Only few studies[7,8,25,28,30,36,51,57,72] reported the inclusion of periodontally compromised patients in their studies. Due to lack of information distinguishing implant failure between periodontally compromised and non-compromised patients on most of these nine studies, it is not known to what extent periodontitis may have contributed to the difference in failure rates between immediate and non-immediate implants. From the three studies evaluating the two procedures in periodontally compromised patients only, two[7,8] of them observed more failures in the group of immediate implants, and one study[25] in implants placed in healed sites.

The higher failure rate of immediate implants in relation to non-immediate implants in the maxilla in comparison to the mandible may be attributed to the low density of medullary bone and thin cortical plates,[5] which may have resulted in significant reduction in insertion torque for implants in the maxilla and less implants with primary stability, and further resulted in a lack of resistance to mechanical stresses.[7]

Concerning the influence of the prosthetic rehabilitation on the failure rates, a statistically significant difference between the procedures was found when studies only evaluating patients with implant-supported single crowns were pooled, the same not happening when full-arch prostheses were the only prosthetic rehabilitation performed. From a biomechanical point of view, single implants may be at higher risk of overloading,[71] because of the lack of splinting. The splinting of the implants in full-arch prostheses allows a more even distribution of the occlusal forces, thereby reducing stresses at the bone–implant interface[85] as well as micromotion.[86]

Moreover, it is suggested that the healing/loading period may also influence the implant failure rates and immediate loading may appear to be at a higher risk of failure than conventionally loaded ones. It was believed that too-early

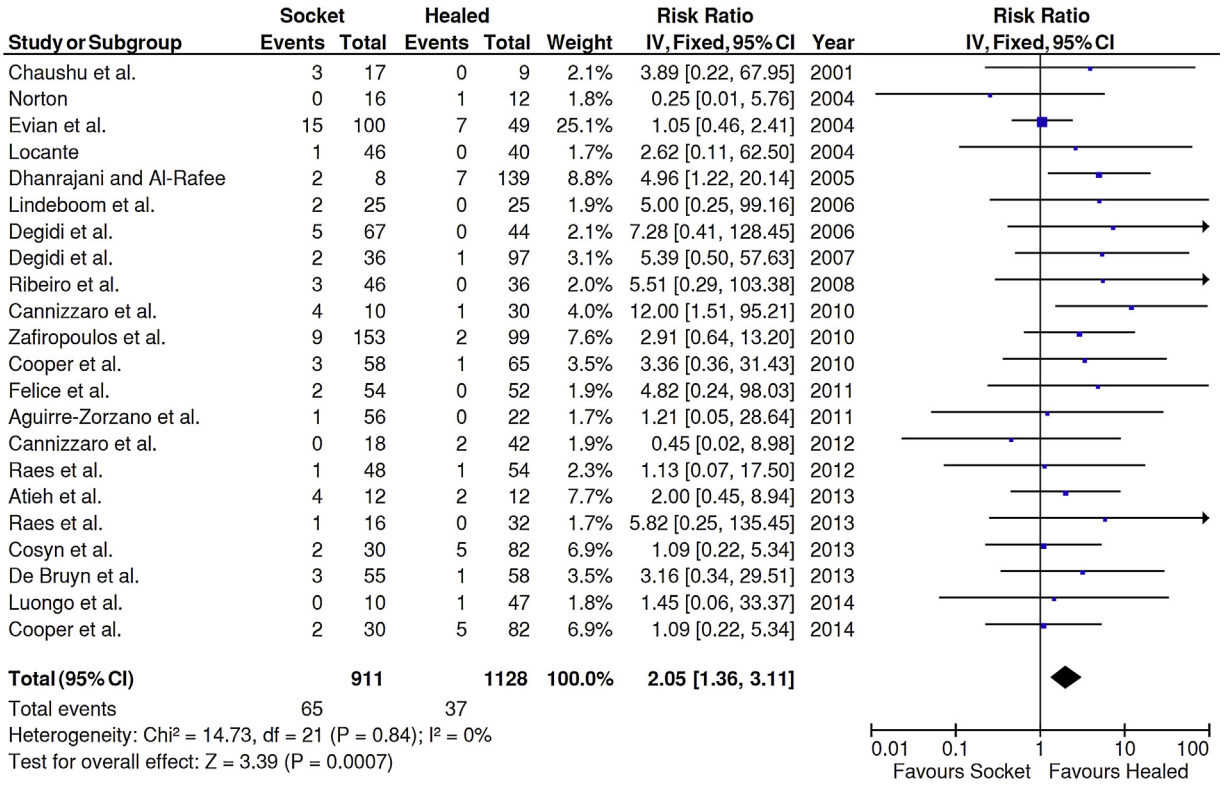

Fig. 5 – Forest plot for the event 'implant failure', when only the studies using the implants to rehabilitate patients with single crowns were pooled.

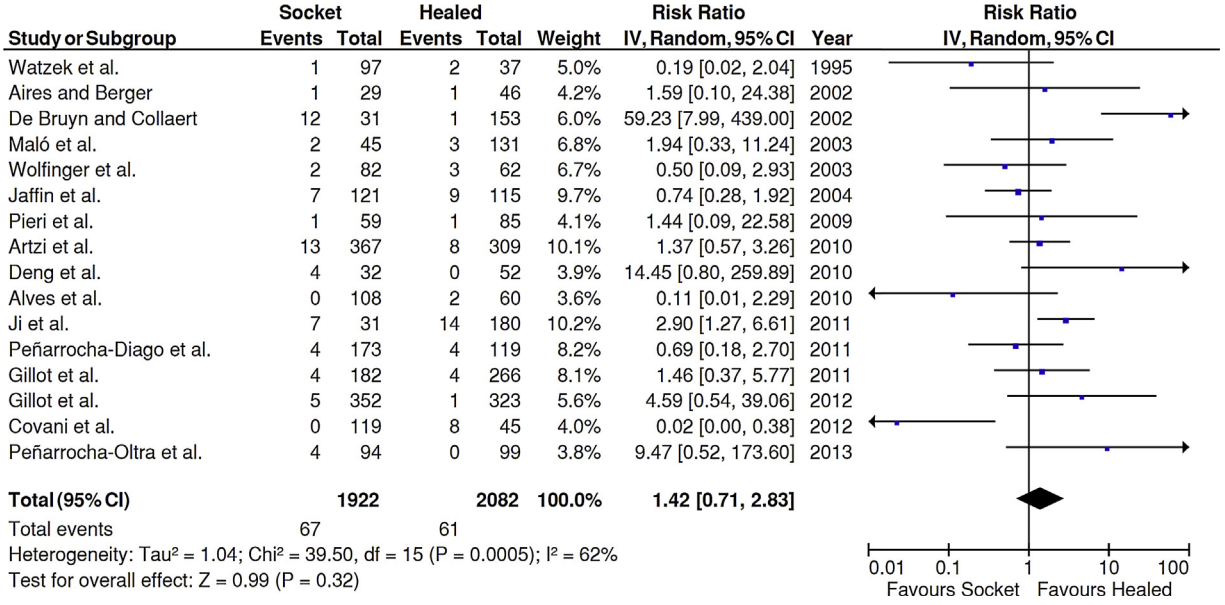

Fig. 6 – Forest plot for the event 'implant failure', when only the studies using implants to rehabilitate patients with full-arch prosthesis were pooled.

loading of an implant leads to an interfacial formation of fibrous tissue instead of bone.[87] Presently, it appears that premature loading *per se* does not lead to fibrous tissue encapsulation. Rather, it is due to an excessive amount of micromotion at the bone–implant interface, during the healing phase.[88] Most of the included studies exclusively evaluating implants being rehabilitated with single crowns or with full-arch prostheses applied immediate loading to the implants. The splinting of the implants in the full-arch prostheses might have influenced the results.

The present study found no apparent significant effect of implants inserted in fresh extraction sockets on the magnitude of marginal bone loss in comparison with implants placed in mature bone. Some studies specifically addressed

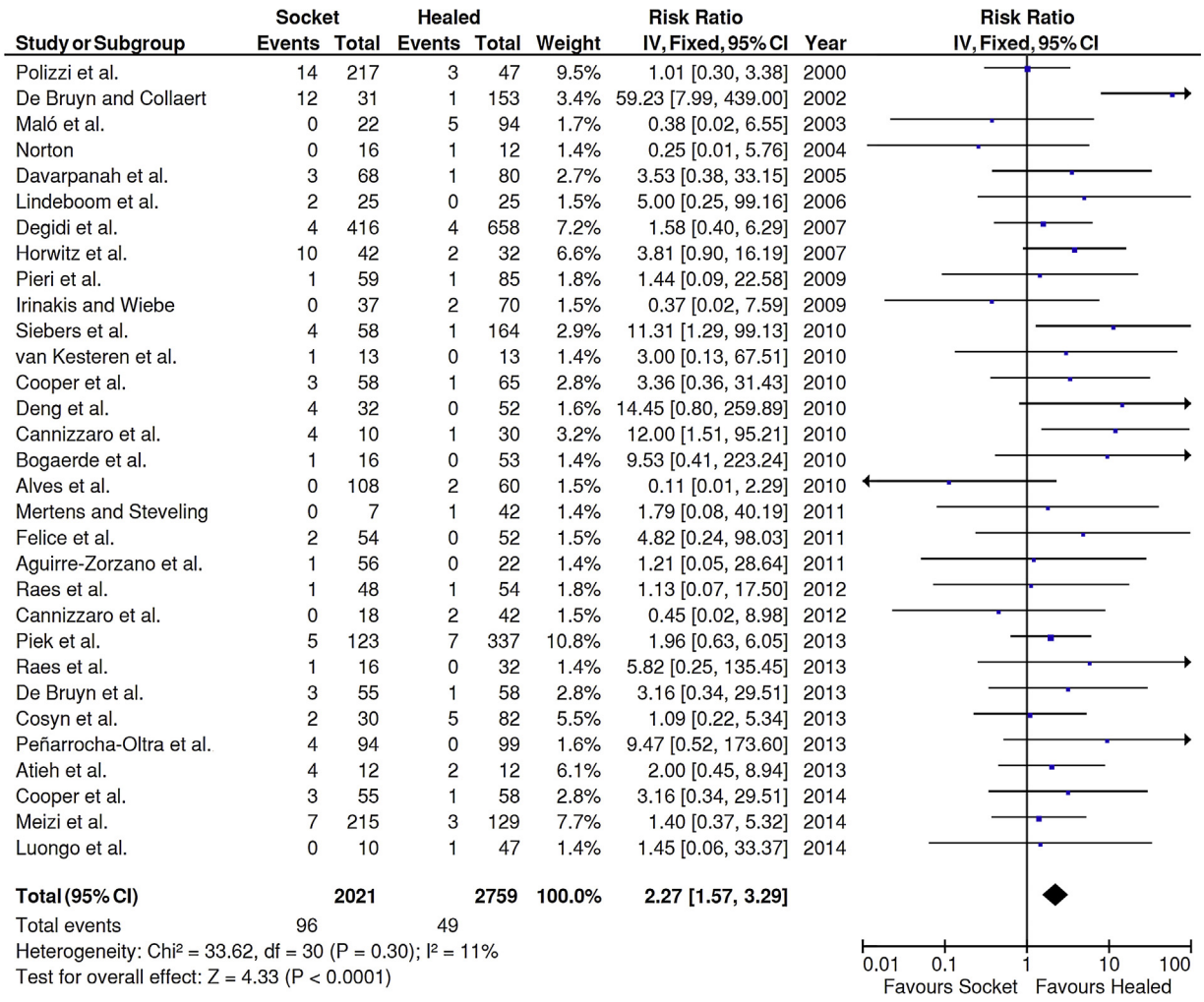

Fig. 7 – Forest plot for the event 'implant failure', when only the controlled studies (RCTs and CCTs) were pooled.

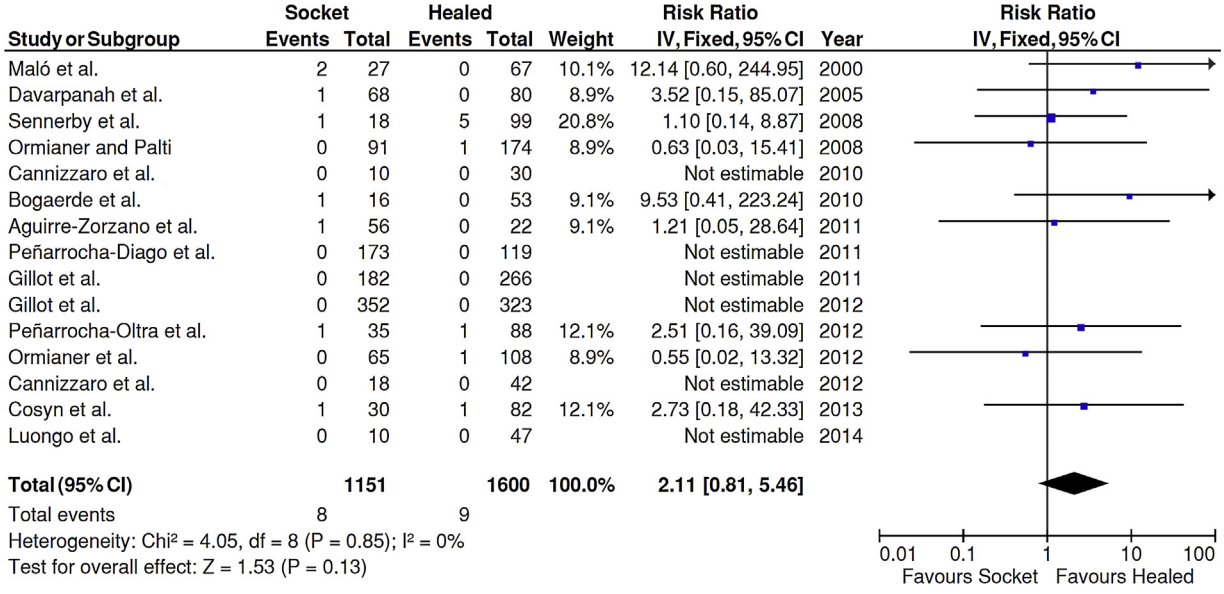

Fig. 8 – Forest plot for the event 'postoperative infection'.

Study or Subgroup	Socket Mean	SD	Total	Healed Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Year
Mensdorff-Pouilly et al.	0.45	1.02	85	0.3	0.8	88	5.2%	0.15 [-0.12, 0.42]	1994
Lindeboom et al. (mesial)	0.49	0.11	23	0.52	0.16	25	8.4%	-0.03 [-0.11, 0.05]	2006
Lindeboom et al. (distal)	0.53	0.12	23	0.52	0.14	25	8.4%	0.01 [-0.06, 0.08]	2006
Pieri et al.	0.57	0.27	58	0.47	0.18	84	8.3%	0.10 [0.02, 0.18]	2009
Cooper et al.	-1.3	2.52	55	0.4	1.43	64	1.4%	-1.70 [-2.45, -0.95]	2010
Artzi et al.	0.79	1.07	354	1.1	1.26	301	6.8%	-0.31 [-0.49, -0.13]	2010
Deng et al.	1.01	0.29	28	1.24	0.23	52	7.7%	-0.23 [-0.35, -0.11]	2010
Peñarrocha-Diago et al.	0.63	0.18	173	0.58	0.26	119	8.6%	0.05 [-0.00, 0.10]	2011
Bae et al.	0.32	1.3	26	0.29	0.9	53	2.3%	0.03 [-0.53, 0.59]	2011
Peñarrocha-Oltra et al.	0.56	0.22	34	0.67	0.17	84	8.3%	-0.11 [-0.19, -0.03]	2012
Raes et al.	1.05	1.78	16	-0.18	1.26	23	0.8%	1.23 [0.22, 2.24]	2013
Atieh et al.	-0.41	0.57	8	0.04	0.46	10	2.7%	-0.45 [-0.94, 0.04]	2013
Cosyn et al.	1.3	0.64	30	1.12	0.6	49	5.0%	0.18 [-0.10, 0.46]	2013
P.-Oltra et al. (immediate)	0.74	0.31	49	0.54	0.23	45	7.9%	0.20 [0.09, 0.31]	2013
De Bruyn et al.	-1.6	2.4	52	0.4	1.5	57	1.4%	-2.00 [-2.76, -1.24]	2013
P.-Oltra et al. (delayed)	0.61	0.28	56	0.51	0.25	43	8.0%	0.10 [-0.00, 0.20]	2013
Cooper et al.	-2.06	2.38	45	-0.1	1.29	49	1.3%	-1.96 [-2.74, -1.18]	2014
Luongo et al.	0.22	0.2	10	0.35	0.22	33	7.4%	-0.13 [-0.27, 0.01]	2014
Total (95% CI)			**1125**			**1204**	**100.0%**	**-0.08 [-0.18, 0.01]**	

Heterogeneity: Tau² = 0.03; Chi² = 142.58, df = 17 (P < 0.00001); I² = 88%
Test for overall effect: Z = 1.70 (P = 0.09)

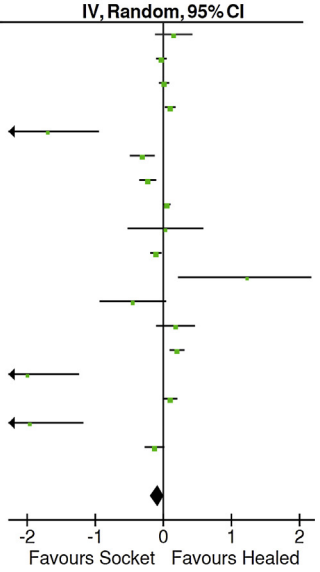

Fig. 9 – Forest plot for the event 'marginal bone loss'.

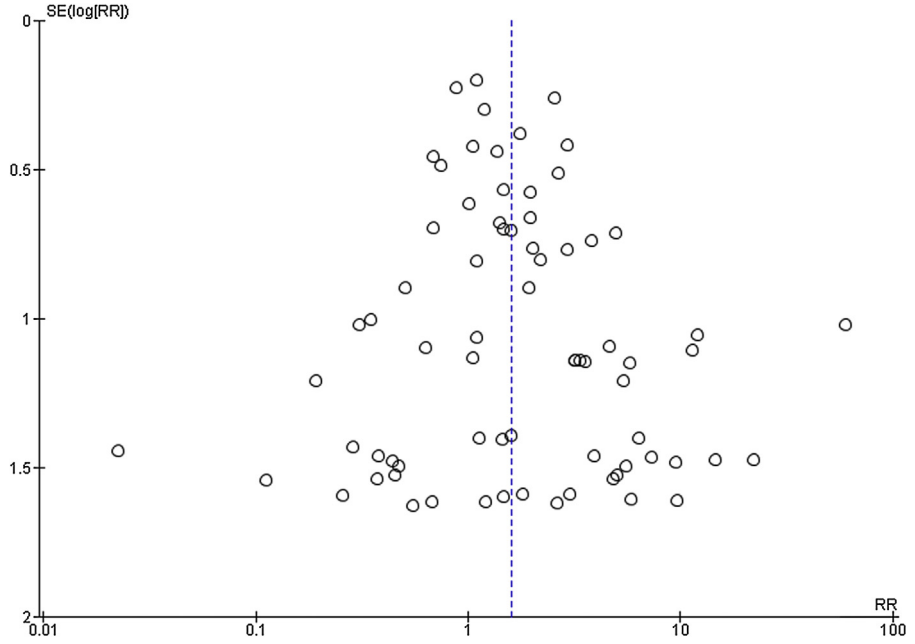

Fig. 10 – Funnel plot for the studies reporting the outcome event 'implant failure'.

this issue. In a prospective clinical study, Schropp et al.[89] observed that both delayed and immediate approach resulted in statistically significant reduction in bony defects. Other study observed less bone resorption around immediate implants compared to delayed implants.[90] Raes et al.[37] observed that a trend towards bone gain was found following insertion in fresh extraction sockets, which may be explained by the fact that the gap between the original bone and implant diminishes during healing, and the bone-to-implant contact increases in coronal direction during the healing phase. These findings can be related to a coronal bone remodelling around immediate implants and a healing pattern with new bone apposition around the neck of the implants.[91] These studies did not lead to a clear conclusion about the subject, and the possible influence of several factors[92] makes it difficult to estimate the real effect of the insertion of implants in fresh extraction sockets on the marginal bone level.

One important factor to consider is the implant position in relation to the extraction socket crestal bone level. A recent study[93] observed that there are reasons to suggest that either crestal bone loss or its preservation may be partly due to the crestal or subcrestal implant position. The study also showed that there is a marked hard tissue alteration during the 8-week healing period following tooth extraction and immediate implant placement, which affected both buccal and lingual bone plates. The experiment of Caneva et al.[94] installed

immediate implants into extraction sockets in the mandibles of six dogs and concluded that implants should be positioned approximately 1 mm below the alveolar crest and in a lingual position in relation to the centre of the alveolus to reduce or eliminate the exposure above the alveolar crest of the endosseous rough portion of the implant. In a clinical trial using a multivariate model to analyze factors that may affect bone alterations during healing after immediate implant placement, Tomasi et al.[95] observed that the position of the implant opposite the alveolar crest of the buccal ridge and its bucco-lingual implant position influenced the amount of buccal crest resorption. Furthermore, the thickness of the buccal bony wall in the extraction site and the vertical as well as the horizontal positioning of the implant in the socket must be considered because these factors will influence hard tissue changes during healing.

Another factor that may determinate the amount of bone loss that will occur at crestal bone level is the implant-abutment design.[96] The influence of different microgap configurations can cause different amount of bone loss, even before prosthetic loading. Subcrestal placement of a butt-joint microgap design may lead to more pronounced bone loss.[97,98]

It is suggested that grafting procedures may also exert some influence on the marginal bone levels. The marginal gap that may exist following implant placement in an extraction socket may be resolved by hard tissue filling during healing, which can possibly change the results, but the literature shows conflicting results. A preclinical study[99] on beagle dogs demonstrated that socket grafting modified the process of hard tissue healing, provided additional amounts of hard tissue at the entrance of the previous socket and improved the level of marginal bone-to-implant contact. In contrast, an animal study[100] on mongrel dogs demonstrated that such procedure resulted in significant buccal bone loss with low osseointegration. For last not least, the use of different radiological techniques to assess changes in crestal bone level also is an influencing factor on the results.

The studies included here have a considerable number of confounding factors, and most of the studies, if not all, did not inform how many implant were inserted and survived/lost in several different conditions. The use of grafting in some studies is a confounding risk factor, as well as the insertion of implants in different locations, different healing/loading periods, different prosthetic configurations, type of opposing dentition, splinting of the implants, and the presence of smokers, diabetics or periodontally compromised patients. Moreover, the studies included in the review made use of implants with different brands and surface treatments. It is known that the surface properties of dental implants such as topography and chemistry are relevant for the osseointegration process influencing ionic interaction, protein adsorption and cellular activity at the surface.[101] Titanium with different surface modifications shows a wide range of chemical, physical properties, and surface topographies or morphologies, depending on how they are prepared and handled,[102–104] and it is not clear whether, in general, one surface modification is better than another.[101]

It is important to stress that some publications on post-extraction implants have a short-term follow-up period, of up to 1 year. This may be one of the reasons why in some studies the failure rates were low and some groups did not even experience any failures. A longer follow-up period can lead to an increase in the failure rate, especially if it extended beyond functional loading, because other prosthetic factors can influence implant failure from that point onward. This might have led to an underestimation of actual failures in some studies. However, it is hard to define what it would be considered a short follow-up period to evaluate implant failures when comparing these techniques.

The results of the present study have to be interpreted with caution due to its limitations. First of all, all confounding factors may have affected the long-term outcomes and not just the fact that implants were placed in fresh extraction sockets patients or in healed sites, and the impact of these variables on the implant survival rate, postoperative infection and marginal bone loss[105–111] is difficult to estimate if these factors are not identified separately between the two different procedures in order to perform a meta-regression analysis. The lack of control of the confounding factors limited the potential to draw robust conclusions. Second, most of the included studies had a retrospective design, and the nature of a retrospective study inherently results in flaws. These problems were manifested by the gaps in information and incomplete records. Furthermore, all data rely on the accuracy of the original examination and documentation. Items may have been excluded in the initial examination or not recorded in the medical chart.[112–114] Third, much of the research in the field is limited by small cohort size and short follow-up periods. Fourth, some included studies are characterized by a low level of specificity, where the assessment of the insertion in fresh extraction sockets as a complicating factor for dental implants was seldom the main focus of the investigation.

5. Conclusion

The results of the present review should be interpreted with caution due to the presence of uncontrolled confounding factors in the included studies, most of them not randomized trials. Within the limitations of the existing investigations, the present study suggests that the insertion of dental implants in fresh extraction sockets affects the implant failure rates. However, it does not affect the marginal bone loss or the occurrence of postoperative infection. A statistically significant difference was not found for implant failures when studies evaluating implants inserted in maxillae or in mandibles were pooled, or when the studies using implants to rehabilitate patients with full-arch prostheses were pooled. The difference was statistically significant between the procedures for the studies that rehabilitated patients with implant-supported single crowns.

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