# Risk of Implant Failure and Marginal Bone Loss in Subjects with a History of Periodontitis: A Systematic Review and Meta-Analysis

Syarida H. Safii, DDS [Correction added after online publication 1 June 2009: Syarida H. Saffii corrected to Syarida H. Safii.];\* Richard M. Palmer, PhD, BDS, FDS RCS;<sup>†</sup> Ron F. Wilson, FIBMS, MPhil, PhD<sup>‡</sup>

### ABSTRACT

*Background:* A number of studies have suggested that implant failure and associated bone loss is greater in subjects with a history of periodontitis.

*Purpose:* To evaluate the risk for marginal bone loss around implants and implant failure in subjects with a history of periodontitis compared with periodontally healthy subjects in studies with a minimum 3-year follow-up.

*Materials and Methods:* Data sources: The MEDLINE, EMBASE, and PubMed databases and relevant journals were searched up to July 1, 2008, with restriction to English language.

*Review Methods:* Prospective and retrospective longitudinal observational clinical studies comparing periodontal/ peri-implant variables among subjects with periodontitis and subjects who were periodontally healthy were included. Screening of studies, quality assessment, and data extraction were conducted independently and in duplicate. Clarification of missing and unclear information was not sought. Outcome measures were: implant survival/failure, peri-implant parameters, changes in radiographic marginal bone level, probing pocket depth, and gingival index.

*Results:* Seventeen potential studies were identified and six studies were accepted comparing patients with periodontitis and periodontally healthy patients treated with implants. Five studies were eligible for meta-analysis of implant survival and four studies were eligible for meta-analysis of bone loss around implants. The odds ratio for implant survival was significantly in favor of periodontally healthy patients (3.02, 95% confidence intervals 1.12–8.15). A random effects model showed more marginal bone loss in periodontitis subjects compared with periodontally healthy subjects (standard mean difference 0.61, 95% confidence interval 0.14–1.09).

*Conclusions:* Within the limitations of the heterogenous studies available, a moderate level of evidence indicates that periodontitis subjects were at significantly higher risk for implant failure and greater marginal bone loss as compared with periodontally healthy subjects. Prospective observational studies with subject-based designs are recommended.

KEY WORDS: bone loss, dental implants, periodontitis, systematic review

# INTRODUCTION

Osseointegrated dental implants are used to provide a predictable restoration for missing teeth in the general

\*Postgraduate student, Periodontology, King's College London Dental Institute, Guy's Hospital Campus, London, UK, and Tutor, University of Malaya, Malaysia; <sup>†</sup>head of group, Restorative Dentistry, King's College London Dental Institute, Guy's Hospital Campus, London, UK; <sup>‡</sup>senior lecturer, Restorative Dentistry, King's College London Dental Institute, Guy's Hospital Campus, London, UK

Reprint requests: Professor Richard M. Palmer, King's College London Dental Institute, Floor 25, Tower Wing, Guy's Hospital Campus, London SE1 9RT, UK; e-mail: richard.m.palmer@kcl.ac.uk

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population. Periodontitis subjects are believed to carry an increased risk for implant failure and progressive bone loss around implants.<sup>1,2</sup> Periodontitis subjects who had been treated comprehensively have been reported with early and late dental implant failures.<sup>3–7</sup> However, several studies have shown favorable dental implant outcomes in subjects with a history of periodontitis enrolled within proper maintenance programs.<sup>8–10</sup>

Host susceptibility to periodontitis is probably the most important consideration with regard to biological complications for implants. It has been suggested that aggressive or advanced forms of periodontitis are at higher risk for dental implant failure compared with the milder forms.<sup>11–13</sup> However, a prospective study of 59

recalcitrant periodontitis patients by Nevins and Langer<sup>14</sup> reported 98% implant success rate with only seven failures out of 309 dental implants. Their findings indicated that dental implants might be an acceptable treatment option to replace missing teeth due to periodontitis.

Several narrative reviews and two systematic reviews have examined the implant and peri-implant outcomes in periodontitis subjects as compared with periodontally healthy subjects.<sup>15–20</sup> They concluded that periodontitis subjects were at higher risk for implant failure, with smoking as an important confounding factor. However, most of the studies reviewed had not taken smoking into sufficient consideration. The studies accepted in all the reviews published were prospective and retrospective in design, and were the highest available evidence in the literature so far. Neither of the systematic reviews included meta-analysis.

The aim of the present review was to evaluate evidence in the literature for the risk of marginal bone loss around implants and implant failure in subjects with a history of periodontitis compared with periodontally healthy subjects and to conduct a meta-analysis.

# MATERIALS AND METHODS

# **Inclusion Criteria**

This review included prospective and retrospective clinical studies comparing periodontal/peri-implant variables in subjects with periodontitis and subjects who were periodontally healthy. The diagnosis of any form of periodontitis was accepted. The studies to be included required a minimum of 3 years duration of follow-up after implant placement and reporting of peri-implant/ periodontal outcomes. The following outcome measures had to be reported:

- 1. Changes in bone levels measured on intra-oral radiographs and tooth/implant loss.
- 2. All subjects had to be partially dentate. There were no restrictions on age of subjects.

# Search Strategy

The literature was searched using MEDLINE, EMBASE, and PubMed databases for studies between January 1, 1990 and July 1, 2008. The search terms used were as follows:

- 1. \*Periodontitis/;
- periodontitis.mp. [mp = title, original title, abstract, name of substance word, subject heading word];
- periodontal disease\$.mp. [mp = title, original title, abstract, name of substance word, subject heading word];
- 4. Alveolar Bone Loss/;
- 5. 1 or 2 or 3 or 4;
- 6. Dental Implants/;
- peri implant\$.mp. [mp = title, original title, abstract, name of substance word, subject heading word];
- 8. 6 or 7;
- 9. 5 and 8;
- 10. limit 9 to humans.

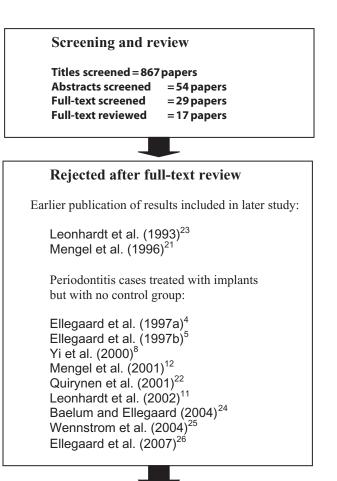
The search was restricted to English language and unpublished data were not sought. Hand searching involved the main implant and periodontal journals and included *Clinical Oral Implants Research*, *International Journal of Oral & Maxillofacial Implants*, *Clinical Implant Dentistry and Related Research*, *Journal of Clinical Periodontology*, *Journal of Periodontology*, and the bibliographies of previous reviews and all relevant papers. The original authors of the studies considered in this review were not contacted for clarification of unclear data.

# Screening Methods

The initial search yielded 865 potential studies. The titles and abstracts were independently screened by two reviewers (S.H.S. and R.M.P.). Inter-reviewer agreement was calculated with Cohen's kappa score for each screening. The disagreements between reviewers were resolved by discussion. Figure 1 outlines the process. Full-text papers were retrieved and detailed examination was carried out to assess quality of the papers and study characteristics that met the inclusion criteria. The fulltext assessment was performed independently by three reviewers (S.H.S., R.M.P., and R.F.W.). In the final review, six studies were accepted but some studies were not suitable for meta-analysis.

# **Quality Assessment**

The quality assessment of the studies undergoing screening was carried out according to the following criteria:



### Accepted after full-text review

Hardt et al.  $(2002)^{27}$ Karoussis et al.  $(2003)^9$ Mengel and Flores-de-Jacoby  $(2005)^{13}$ Ferreira et al.  $(2006)^{28}$ Mengel et al.  $(2007)^{29}$ Gatti et al  $(2008)^{30}$ 

Figure 1 Flow chart for the systematic review and meta-analysis.

- 1. the handling of data on withdrawals and dropouts
- 2. the suitability of statistical analysis used to explain data

# Data Abstraction

Standardized screening forms were filled in with data from the studies screened at different stages. This was undertaken independently and in duplicate by two reviewers (S.H.S. and R.M.P.). The information from the accepted studies was tabulated according to the study design, population characteristics, type of implant and prosthesis, and outcome measures. Data collected were based on the objectives outlined for the present systematic review.

### Data Synthesis

*Reproducibility of Reviewers.* Kappa statistics were used to assess the agreement of reviewers at every stage of screening/assessment of the articles.

Meta-analysis. Meta-analysis was performed using (http://www.medcalc.be) software. The Medcalc assumption that all the studies came from a common population was tested using a Mantel-Haenszel heterogeneity test. If the data fail this test, a random effects model would be more appropriate than a fixed effects model. A conservative approach was taken a priori, and the random effects model was used. Meta-analysis of implant survival yielded an odds ratio (OR) with 95% confidence intervals (CI) for the difference between groups. Meta-analysis of the continuous measure, bone loss, provided the "standardized mean difference" together with 95% CI. A standardized mean difference of 0.5 was accepted as indicating a moderate effect of periodontitis on bone loss around implants. A p value less than 0.05 was accepted as indicating statistical significance.

### RESULTS

The basic search provided 867 titles for consideration, and 54 were selected after screening of the abstracts. Twenty-nine studies were selected for fulltext screening, and 17 papers were selected for a full review.

The kappa score for agreement between reviewers for rejection after the full-text screening was  $\kappa = 0.87$ (95% CI: 0.54 to 1.00) and for the exclusion after fulltext review was  $\kappa = 1.00$  (95% CI 0.53 to 1.00).

### Rejected Studies after Full-Text Review

*Case Series.* A case series by Mengel and colleagues<sup>21</sup> reported various bone level outcomes after 1 year around implants placed in five patients. These patients had been treated and maintained for generalized severe periodontitis (SP) 2 to 8 years previously. Four out of thirty-six implants failed. The study was rejected as having no periodontally healthy control group, a short duration of follow-up, very small sample size, and varying prosthetic management, which included one

subject with an overdenture and another with a tooth/ implant bridge.

A 10-year retrospective study by Quirynen and colleagues<sup>22</sup> reported annual mean marginal bone loss around implants of 0.09 mm (range -0.53 to +1.05 mm, standard deviation [SD] = 0.28) and loss of 12 implants in 84 partially dentate patients. The periodontal status among the subjects was not clearly defined and no periodontally healthy control group was reported.

Prospective Studies. The 3- and 10-year prospective studies by Leonhardt and colleagues<sup>11,23</sup> evaluated subjects previously treated for periodontitis. The 10-year results showed 94.7% implant survival rate in 15 of the subjects with a history of advanced periodontitis who had been well treated and maintained before implants were placed. Higher implant survival rate was observed in the mandible (96.2%) than in the maxilla (93.5%). Although only three implants were lost out of 57 implants, they reported loss of 34 teeth. There were indications that the periodontal status among the subjects was not stabilized: 35.3% sites around the teeth bled on probing, 15.7% sites showed pocket probing depth of more than 3 mm and 3.1% sites had pocket probing depth of more than 5 mm. The study was rejected because of lack of a periodontally healthy control group.

Mengel and colleagues<sup>12</sup> reported 100% implant survival rate in subjects with a history of generalized chronic periodontitis (GCP) 3 years after prosthesis insertion, and 88.8% implant survival rate in generalized aggressive periodontitis (GAP) subjects 5 years after prosthesis insertion. All subjects had undergone comprehensive periodontal treatment and were maintained for 2 to 8 years before implants were provided. Both groups started to show deterioration after 3 years with indication of progressive pocket probing depth and attachment loss around both teeth and implants. However, the sample size from this study was very small, only three subjects in GCP group and five subjects in GAP group, and there was no periodontally healthy control group.

*Cohort Studies.* Seven cohort studies were rejected.<sup>4,5,8,10,24-26</sup> There were no periodontally healthy control subjects in any of the studies. Implant loss was reported in five of these studies. A 3-year prospective study by Yi and colleagues<sup>8</sup> reported no implant failure in 43 advanced periodontal disease subjects. The subjects were well maintained with evidence of very low plaque and bleeding on probing. Wennstrom and colleagues<sup>25</sup> reported that 15 implants experienced bone loss >2 mm in two out of 51 subjects who had been previously treated for moderate to advanced periodontitis. A similar trend of bone loss (≥3.5 mm) was observed in studies reported by Ellegaard and colleagues.4,5,24,26 Bone loss continued to progress around implants in these patients even with good plaque control and a high level of maintenance. Findings from these studies also suggested that smoking was an important confounding factor. However, smoking was not considered in the data analyses and, therefore, the magnitude of the effect cannot be estimated. However, Wennstrom and colleagues<sup>25</sup> reported more bone loss in smokers compared with nonsmoking subjects over a 5-year period. The smokers showed a bone level change of  $0.76 \pm 0.84$  mm around implants, whereas the nonsmokers showed  $0.22 \pm 0.69$  mm (p = .022). Karoussis and colleagues<sup>10</sup> showed no loss of implants in a mean 10-year prospective study of 89 subjects previously treated for periodontitis, whereas 87 teeth were lost during this period. The mean marginal bone level around implants at 10 years was 4.65 mm (range 1.42 to 10.80) mesially and 4.66 mm (range 1.21 to 10.20) distally. Although the severity of periodontitis was not adequately described, this study indicated a good level of maintenance with low plaque index (PI), gingival index, and stable periodontal health. No details on smoking were reported, although they claimed that it affected marginal bone levels.

# **Accepted Studies**

Six studies comparing patients with periodontitis and periodontally healthy patients treated with implants<sup>9,13,27–30</sup> were finally accepted for this systematic review (Table 1). The cross-sectional study by Ferreira and colleagues<sup>28</sup> found a higher prevalence of periimplantitis in periodontitis subjects (26.6%) compared with periodontally healthy subjects (6.04%) but did not provide adequate data on implant survival or radiographic bone levels. Their findings showed evidence of an association between poor periodontal status and peri-implant disease in a nonsmoking population with an OR of 3.1 (95% CI 1.1–3.5). There was a high percentage of subjects in both groups with a poor plaque score (79.72%) and bleeding on probing of more than 30% of sites (77.8%).

Authors	Study Design	Sample Characteristics	Implant/Prosthesis Characteristics	Mean Bone Loss in mm (SD)	Implant Failure Rate
Hardt et al. (2002) <sup>27</sup>	Retrospective follow-up: 5 years	CP $(n = 25)$ Age: 53.5 ± 12.5 years Healthy $(n = 25)$ Age: 57.3 ± 19.1 years Prior treatment: NR Maintenance: NR Smoking: NR	Implants $CP (n = 100)$ Healthy $(n = 92)$ System: BranemarkLocation: MaxillaProstheses: FPDs	CP: 2.2 ± 0.8 Healthy: 1.7 ± 0.8	CP: 8% Healthy: 3.3%
Karoussis et al. (2003) <sup>9</sup>	Prospective follow-up: 10 years	CP $(n = 8)$ Age: NR Healthy $(n = 45)$ Age: NR Prior treatment: Yes Maintenance: High level Smoking: smokers/ nonsmokers compared	Implants CP ( <i>n</i> = 21) Healthy ( <i>n</i> = 91) System: Straumann Location: NR Prostheses: FPDs & crowns	CP Mesial: $1.00 \pm 1.38$ Distal: $0.94 \pm 0.73$ Healthy Mesial: $0.48 \pm 1.10$ Distal: $0.50 \pm 1.08$	CP: 9.5% Healthy: 3.5% Smokers: 7.1% Nonsmokers: 3.8%
Mengel and Flores-de- Jacoby (2005) <sup>13</sup>	Prospective follow-up: 3 years	GAP $(n = 15)$ CP $(n = 12)$ Healthy $(n = 12)$ Overall age: 19–59 years Prior treatment: Yes Maintenance: High level Smoking: no smokers	Implants GAP ( <i>n</i> = 77) GCP ( <i>n</i> = 43) Healthy ( <i>n</i> = 30) System: Branemark, 3i Location: Maxilla and mandible Prostheses: Various	GAP: $1.14 \pm (NR)$ GCP: $0.86 \pm (NR)$ Healthy: $0.70 \pm (NR)$ At 1 year GAP: $0.83 \pm 0.71$ GCP: $0.68 \pm 0.54$ Healthy: $0.58 \pm 0.45$	GAP: Maxilla: 2% Mandible: 0% GCP: Maxilla: 0% Mandible: 0% Healthy: Maxilla: 0% Mandible: 0%
Ferreira et al. (2006) <sup>28</sup>	Retrospective follow up: 6m–5 years	CP $(n = 30)$ Healthy $(n = 182)$ Age: NR Prior treatment: Yes Maintenance: variable Smoking: no smokers	Implants $CP (n = NR)$ Healthy $(n = NR)$ System: variousLocation: NRProstheses: NR	NR	NR
Mengel et al. (2007) <sup>29</sup>	Prospective follow-up: 10 years	GAP $(n = 5)$ Age: 31–44 years Healthy $(n = 5)$ Age: 20–51 years Prior treatment: Yes Maintenance: High level Smoking: NR	Implants GAP ( <i>n</i> = 36) Healthy ( <i>n</i> = 7) System: Branemark Location: Maxilla and mandible Prostheses: Various	GAP: 3.37 ± (NR) Healthy: 1.24 ± (NR)	GAP: 17% Healthy: 0%
Gatti et al. (2008) <sup>30</sup>	Prospective follow-up: 5 years	SP $(n = 26)$ Age: 35–85 years MP $(n = 7)$ Age: 42–70 years Healthy $(n = 29)$ Age: 18–61 years Prior treatment: Yes Maintenance: Yes Smoking: NR	Implants SP $(n = 129)$ MP $(n = 26)$ Healthy $(n = 72)$ System: Various Location: Maxilla and mandible Prostheses: Various	SP: 2.57 ± 1.06 MP: 2.72 ± 0.44 Healthy: 1.24 ± 1.09	SP: 1.6% MP: 0% Healthy: 0%

# TABLE 1 Studies Comparing Patients with Periodontitis and Periodontally Healthy Patients Treated with Dental Implants

CP = chronic periodontitis; FPD = fixed partial denture; GAP = generalized aggressive periodontitis; MP = moderate periodontitis; NR = not recorded; SD = standard deviation; SP = severe periodontitis.

Hardt and colleagues<sup>27</sup> divided patients into two groups of 25 patients each representing the highest (periodontitis) and the lowest (periodontally healthy) quartile of bone loss around the teeth at baseline. They reported an overall implant survival rate of 94.8%, with 92.0% implant survival in periodontitis subjects and 96.7% in periodontally healthy subjects. The difference in mean bone loss after 5 years between groups was not statistically significant  $(2.2 \pm 0.8 \text{ mm in periodontitis})$ subjects,  $1.7 \pm 0.8$  mm in periodontally healthy subjects [p > .05]). However, 62% of the implants in 16 periodontitis subjects and 44% of the implants in six periodontally healthy subjects showed a mean bone loss of 2 mm or more (p < .01). Unfortunately, there were no details provided on smoking, periodontal parameters such as probing pocket depths, plaque scores, and bleeding scores, history of periodontal treatment, and frequency of maintenance.

A 10-year prospective study in 53 subjects by Karoussis and colleagues9 presented a 90.5% survival rate in periodontitis subjects and 96.5% survival rate in periodontally healthy subjects. The subjects were comprehensively treated and well maintained, with good plaque control and stable peri-implant health. Mesial bone loss around implants was  $1.00 \pm 1.38$  mm in periodontitis subjects and  $0.48 \pm 1.10$  mm in periodontally healthy subjects, while distal bone loss was 0.94  $\pm 0.73$  mm and  $0.50 \pm 1.08$ , respectively. However, the sample size was very small in the periodontitis group with only eight patients compared to 45 patients in the healthy group and no results of statistical analysis were given for a comparison of the bone levels. They reported a higher percentage of the incidence of biological complications among smokers with periodontitis than smokers without periodontitis (18.18% vs 5.8%, *p* < .017).

Mengel and Flores-de-Jacoby<sup>13</sup> reported 100% survival rate after 3 years in subjects with GCP, periodontally healthy subjects, and in the mandible of subjects with GAP. However, survival was 95.7% in the maxilla of the GAP group. There was an overall  $2 \pm 4.3\%$  implant loss observed in the GAP group after 3 years. Bone loss around implants after 3 years in GAP, GCP, and periodontally healthy group was 1.14 mm, 0.86 mm and 0.70 mm, respectively. The periodontal and periimplant conditions continued to deteriorate around some teeth/implants resulting in loss despite low PIs and gingival indices.

Another prospective study by Mengel and colleagues<sup>29</sup> focused on a group with GAP, and a longer follow-up compared with their previous study.<sup>13</sup> It was unclear whether these subjects were included in the 2005 study. There were only five subjects in each of the GAP and periodontally healthy groups. The reported implant survival rate after 10 years was 83.33% in GAP subjects and 100% in periodontally healthy subjects. Mean bone loss at the implants after 10 years was 3.37 mm in GAP subjects and 1.24 mm in periodontally healthy subjects. The findings from this study were in agreement with the other study of Mengel and colleagues.<sup>13</sup> Deterioration in periodontal and peri-implant outcomes in the GAP group continued to progress even with a high level of maintenance and good plaque control, whereas the periodontally healthy group were more stable. Smokers were excluded from the study.

A recent prospective study by Gatti and colleagues<sup>30</sup> evaluated implant-related outcomes in separate SP and moderate periodontitis (MP) groups of subjects compared with those with no periodontitis (NP). There were 26 subjects in the SP group and 29 in the NP group, but only seven in the MP group. Two subjects from each group dropped out during the study. They reported an implant survival rate of 98.4% after 5 years in SP subjects and 100% in both MP and periodontally healthy subjects. Mean bone loss at the implants after 5 years was 2.57 mm in SP subjects, 2.72 mm in MP, and 1.24 mm in periodontally healthy subjects. No details of smoking status were provided. The age of the periodontally healthy subjects was significantly less than that of the other two groups (p < .001), but the authors claimed that covariance analysis indicated no confounding (p = .62).

### Meta-Analysis

*Implant Survival.* Five studies provided data on implant failure suitable for meta-analysis.<sup>9,13,27,29,30</sup> Ferreira and colleagues<sup>28</sup> provided insufficient data for inclusion. Only those in the GAP group were entered as periodontal subjects in the case of Mengel and Flores-de-Jacoby<sup>13</sup> and those in the SP group from Gatti et al.<sup>30</sup> All five accepted studies showed more favorable survival rate in healthy patients than those with predisposing treated periodontal disease, but none showed this difference to be statistically significant. No asymmetry or heterogeneity was observed from a Mantel–Haenszel test. Despite this, a more conservative random effects model was

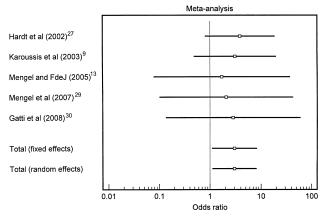


Figure 2 Forest plot and odds ratio for implant survival.

constructed. Figure 2 shows the forest plot. Metaanalysis revealed a statistically significant OR in favor of healthy patients, which was borderline (3.02, 95% CI 1.12–8.15). The "number needed to treat" was 17 implants (95% CI 10–46).

Bone Loss (millimeter). Four studies contained data suitable for meta-analysis.9,13,27,30 Ferreira and colleagues<sup>28</sup> and Mengel and colleagues<sup>29</sup> provided insufficient data for inclusion. No SD were provided for the 3-year data in Mengel and Flores-de-Jacoby<sup>13</sup> and the 1-year data was entered. Only those in the SP group were entered as periodontal subjects in the case of Gatti and colleagues<sup>30</sup> Mesial data were entered from the study by Karoussis and colleagues9 The four accepted studies showed bone loss that was greater for periodontal patients than their healthier controls, two of which were statistically significant.<sup>27,30</sup> No asymmetry or heterogeneity was observed from a Mantel-Haenszel test. Figure 3 shows the forest plot. The random effects model shows a statistically significant difference indicating marginally more bone loss in periodontal patients (standard mean difference 0.61, 95% CI 0.14-1.09).

# DISCUSSION

The literature was systematically searched and included electronic databases and hand searching of relevant journals. Six studies were accepted for the present systematic review. However, of those, only five studies were eligible for meta-analysis of implant survival and four were eligible for meta-analysis of bone loss around implants.

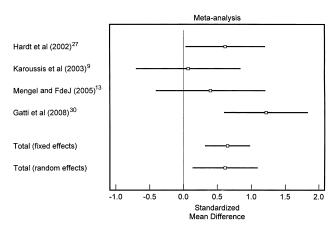


Figure 3 Forest plot and standardized mean difference for bone loss.

#### Primary Outcomes

*Implant Failure.* The studies with a duration of follow-up of 3 to 10 years that were accepted in this review suggested more implant loss in subjects with periodontitis [1.6–11.2%] than in periodontally healthy subjects [0–3.3%].<sup>9,13,27–30</sup> A paper by Quirynen and colleagues<sup>22</sup> that was not accepted in the final analysis reported 12 implant losses out of 289 implants placed in a mixed population of subjects with and without periodontitis. Their results indicated slightly higher implant loss among periodontitis subjects but did not suggest this as a contraindication for implant placement in this particular group of patients.

Bone Loss. The presentation of data on bone loss around implants from the studies in this systematic review varied. Most authors reported bone data as marginal bone loss, but others used only reported bone levels.<sup>10,28</sup> The overall findings on marginal bone loss around implants showed more loss in periodontitis subjects than in periodontally healthy subjects. Karoussis and colleagues9 found bone loss around implants of  $1.00 \pm 1.38$  mm mesially and  $0.94 \pm 0.73$  mm distally in a periodontitis group, whereas in a periodontally healthy group, mesial bone loss around implants was  $0.48 \pm 1.10$ and distal bone loss was  $0.50 \pm 1.08$  mm. Hardt and colleagues<sup>27</sup> reported  $2.2 \pm 0.8$  mm bone loss around implants in a periodontitis group and  $1.7 \pm 0.8$  mm loss in a periodontally healthy group. This suggests increased susceptibility to progressive bone loss around implants in periodontitis subjects. Their multiple regression analysis showed a significant relationship between the bone level change around implants and the age-related bone loss score (p = .029) and bone quality (p = .010) for the study duration of 5 years. However, the magnitude of bone loss was small in most studies and often not statistically significant.

### Secondary Outcomes

Most studies reported plaque accumulation on tooth and implant surfaces as PI,<sup>9,12,13,29</sup> and only Ferreira and colleagues<sup>28</sup> used plaque scores. The interpretation of the PI score is difficult, although a PI of less than 1.0 is an indication of good plaque control as reported in several of these studies. The amount of plaque reported is important in understanding the level of patient compliance, treatment success, and effectiveness of maintenance as these factors have an important bearing on the inflammatory status and loss of attachment/bone.

Some periodontitis subjects still continued to show disease progression around teeth, characterized with increased probing depth and bleeding on probing, even with good plaque control and a high level of maintenance. Most of the reported subjects had either advanced periodontitis or aggressive periodontitis that had been treated before implant therapy. This finding may suggest increased susceptibility to implant failure in more progressive forms of periodontitis but does not necessarily apply to milder forms. The findings from Leonhardt and colleagues<sup>11</sup> suggested some deterioration of support at both teeth and implants in previously treated advanced periodontitis subjects, but they provided no description of maintenance programs following implant placement. However, a series of studies from Mengel and colleagues<sup>12,21,29</sup> indicated an acceptable implant outcome in periodontitis susceptible subjects provided with comprehensive supportive care, even in aggressive cases. In addition, the findings of Karoussis and colleagues<sup>9,10</sup> also suggest favorable implant outcome in periodontitis-susceptible individuals who had very good plaque control and were under a high level of maintenance care.

Only three studies from the systematic review reported data on peri-implant mucositis/periimplantitis.<sup>9,22,28</sup> Ferreira and colleagues<sup>28</sup> found a significant association between poor plaque control and peri-implant diseases. The adjusted OR was a high 14.3 (95% CI 9.1–28.7) for prevalence of peri-implantitis and 2.9 (95% CI 2.0–4.1) for peri-implant mucositis with very poor plaque scores.

# **Confounding Factors**

Other factors associated with implant survival identified from the literature included smoking and prosthesis overloading. Smoking has been found to be an important risk factor in progressive bone loss around implants. However, most studies in this systematic review did not clearly report the smoking habits of the subjects. Several studies did not consider details of smoking at all.<sup>11,12,27,29,30</sup> Two studies did not analyze data of smokers and nonsmokers separately but considered smoking in the regression analysis,<sup>10,22</sup> while another two studies excluded smokers.<sup>13,28</sup> Karoussis and colleagues9 found a significantly higher incidence of biological complications in smokers with a history of periodontitis (4 out of 10 subjects) as compared with periodontally healthy smokers (1 out of 18 subjects) (p = .002). This study suggests that smoking may have a contributory effect in causing poorer peri-implant outcomes around osseointegrated implants but is based on a very small number of subjects. A prospective study of 51 periodontitis subjects by Wennstrom and colleagues<sup>25</sup> reported more bone loss after 5 years in smokers  $(0.76 \pm 0.84 \text{ mm})$ than in nonsmokers  $(0.22 \pm$ 0.69 mm). This study was in agreement with the findings of Baelum and Ellegaard<sup>24</sup> and the Ellegaard series of cohort studies,<sup>4,5,26</sup> reporting a higher number of smokers than nonsmokers with a reported incidence of implant loss after 2 to 10 years.

Implant overload was also implicated as one of the possible factors associated with implant failure.<sup>1</sup> No studies accepted in the present systematic review considered details on overloading of implant-supported prostheses, but some studies reported the type of prostheses provided. Unfortunately, the types of prostheses and potential loading situations varied widely.

### Meta-Analysis

Finding papers with similar protocols and data for meta-analysis proved difficult. Five papers were considered.<sup>9,13,27,29,30</sup> It was not clear from the text of the second paper from Mengel and colleagues<sup>29</sup> in 2007 whether the patients were a subset of those reported in the Mengel and Flores-de-Jacoby paper<sup>13</sup> in 2005. However, subsequent analysis using either separately did not substantially alter the results obtained from those when both were included. Some authors claimed that their study was prospective and others retrospective. Two studies included periodontitis patients who were diagnosed with

These five papers reported survival of implants, but bone loss was more problematic to extract. The Mengel and Flores-de-Jacoby<sup>13</sup> paper only reported mean bone loss as graphs without SD, while Karoussis and colleagues<sup>9</sup> reported mesial and distal bone loss separately. In addition, it was not entirely clear whether mean bone loss was calculated at the implant or patient level. In the event, mesial bone loss was included in the analysis where total bone loss was not available and the number of patients was entered into the analysis instead of the number of implants, as a more conservative approach.

Thus, the interpretation of the results from metaanalysis was considerably limited by this heterogeneity between studies. However, it was considered worthwhile to proceed in order to gain some indication as to whether the main research question might warrant further study.

Results from the meta-analysis showed less favorable implant outcome in periodontitis subjects as compared with periodontally healthy subjects. Periodontally healthy subjects were 3.02 times more likely to have better implant survival than previously treated periodontitis subjects. The model for bone loss showed a medium-sized, statistically significant difference reflecting more marginal bone loss in periodontitis subjects than periodontally healthy subjects (standardized mean difference 0.61).

# **Other Reviews**

The results of the present review are in agreement with several other reviews reporting peri-implant outcomes in subjects with a history of periodontitis.<sup>15–19</sup> The systematic review by Schou and colleagues<sup>16</sup> found a significantly increased risk of peri-implantitis in periodontitis subjects (risk ratio: 9 with CI 3.94–20.57) and increased marginal bone loss around implants after 5 years with a mean difference of 0.5 mm (95% CI 0.06–0.94), but this was based on the inclusion of only a single study.

# Quality of Studies Reviewed

The six studies accepted in the present systematic review represented 609 subjects of a mixed population with 1,801 osseointegrated implants. However, most of the studies included a small number of subjects. The available studies from the literature were limited to prospective, retrospective cross-sectional studies and case reports.

Implant survival/failure data reported from all studies were implant-based rather than subject-based. It is undoubtedly more relevant to have a subject-based analysis as there are underlying subject-based biological and behavioral factors associated with susceptibility to implant complications and failures. The characteristics of the subjects in the studies were undoubtedly heterogenous, even where outcome measures were reasonably comparable.

### Potential Biases in the Review Process

The studies reviewed were restricted to papers in the English language only. Therefore, there might be a possible publication bias. We did not seek advice from the original authors for clarification or missing data. All data presented in the systematic review were extracted from the original papers themselves and careful assumptions were made appropriately if the details were not clearly understood. The reviewers were in a good agreement at every stage of reviewing.

Thus, the main problem with interpretation of the results lies in the heterogeneity of the subjects and differences in the period of follow-up. These factors must be taken into account when considering the conclusions.

### CONCLUSION

The following conclusion was made within the limitations of the studies included in the present systematic review: A moderate level of evidence indicates that periodontitis subjects were at significantly higher risk for implant failure and marginal bone loss as compared with periodontally healthy subjects.

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