How Do Smoking, Diabetes, and Periodontitis Affect Outcomes of Implant Treatment?

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Purpose: *Implant therapy is highly predictable and successful. However, certain risk factors can predispose individuals to lower rates of success. The purpose of this systematic review was to evaluate the available literature to assess whether smoking, diabetes, and periodontitis have an adverse affect on the outcomes of implants placed in patients with these conditions.* ***Materials and Methods:*** *The dental literature was searched using the MEDLINE, Cochrane Collaboration, and EMBASE databases. Using specific inclusion and exclusion criteria, 2 reviewers evaluated titles, abstracts, and full articles to identify articles relevant to this review. All searches were conducted for articles published through May 2005. Data from included articles for each of the risk factor groups, smoking, diabetes, and periodontitis, were abstracted and analyzed.* ***Results:*** *A detailed search of the literature and evaluation of relevant articles identified 35 articles for inclusion in this systematic review. Nineteen articles were identified for smoking, 4 articles were identified for diabetes, and 13 articles were identified for periodontitis. One article met the criteria for both smoking and periodontitis. Implant survival and success rates were reported for smokers versus nonsmokers; diabetic patients versus nondiabetic patients; and patients with a history of treated periodontitis versus patients with no history of periodontitis. The findings revealed statistically significant differences in survival and success rates for smokers (better for nonsmokers), with greater differences observed when the data were analyzed according to bone quality (less for loose trabecular bone). No difference in implant survival rate was found between patients with and without diabetes. Likewise, no difference in implant survival rates was found between patients with a history of treated periodontitis compared to patients with no history of periodontitis.* ***Conclusions:*** *The results of this systematic review of the literature demonstrated that smoking has an adverse affect on implant survival and success. The effect of smoking on implant survival appeared to be more pronounced in areas of loose trabecular bone. Type 2 diabetes may have an adverse effect on implant survival rates, but the limited number of studies included in this review do not permit a definitive conclusion. A history of treated periodontitis does not appear to adversely affect implant survival rates but it may have a negative influence on implant success rates, particularly over longer periods.* Int J Oral Maxillofac Implants 2007;22(suppl):173–202

Key words: *dental implants, dental implant survival, diabetes, periodontitis, smoking, tobacco*

The success and predictability of osseointegrated dental implants is well established. Survival and success rates in the ninetieth percentile range have been repeatedly documented and accepted for a variety of root-form, endosseous dental implant systems in various patient populations, as evidenced by 5-year survival rates of 90% to 98%[1–8] and 10-year survival rates of 89% to 95%.[3,9–11] Implant success rates tend to be lower than survival rates and vary greatly depending on the criteria used to measure success. Despite these high implant survival and success rates, there is a general appreciation that risk factors predispose individuals to more complications and implant failures and may result in lower implant survival and success rates.

Several risk factors that may lead to more implant failures, including loose trabecular bone, excessive occlusal loading, tobacco use, and some systemic diseases, have been identified. This review focuses on 3 risk factors, namely smoking, diabetes, and periodontitis. Smoking affects healing and tissue health in many ways, including impaired neutrophils, altered

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Table 1 Inclusion and Exclusion Criteria for Smoking Group

Inclusion criteria
1. Studies of patients of any age, race, or sex were included.
2. Study provided outcome data for root-form implants.
3. Study provided information about the smoking status of patients (ie, smokers, nonsmokers; cigarettes/d or packs/d).
4. Study provided implant outcome data with at least 1 year of follow-up.
5. Study was published in English.
Exclusion criteria
1. Study was an animal study.
2. Study provided outcome data for non-root-form implants (eg, blades, staples, subperiosteal, sapphire, other materials).
3. Study was an in vitro/laboratory study.
4. Study had less than 1 year of follow-up data.
5. Study was a case report or article that included data on less than 10 patients.
6. Patients had medically compromising conditions or other risk factors (eg, radiation therapy, bone metabolic disease).

Table 2 Inclusion and Exclusion Criteria for Diabetes Group

Inclusion criteria
1. Studies of patients of any age, race, or sex were included.
2. Study provided outcome data for root-form implants.
3. Study provided information about the diabetes status of patients (ie, type I, type II; controlled, poorly controlled).
4. Study provided implant outcome data with at least 1 year of follow-up.
5. Study was published in English.
Exclusion criteria
1. Study was an animal study.
2. Study provided outcome data for non-root-form implants (eg, blades, staples, subperiosteal, sapphire, other materials).
3. Study was an in vitro/laboratory study.
4. Study had less than 1 year of follow-up data.
5. Study was a case report or article that included data on less than 10 patients.
6. Patients had medically compromising conditions or other risk factors (eg, radiation therapy, bone metabolic disease).
7. Treatment included substantial bone augmentation (eg, sinus bone augmentation).

blood flow to tissues, and diminished oxygen perfusion. Diabetes is a metabolic disease that alters tissue integrity, impairs wound healing, and increases susceptibility to infections. Periodontitis is an inflammatory condition of the periodontium in response to bacterial pathogens that promotes the release of numerous cytokines and leads to periodontal attachment and bone loss. Clearly, smoking, diabetes, and periodontitis are factors that have the potential to negatively affect healing and the outcome of implant treatment.

The aim of this systematic review was to evaluate the available literature to assess whether risk factors, specifically smoking, diabetes, and periodontitis, have an adverse effect on the survival or success of implants placed in patients with these conditions. The focused question to be answered by this systematic review was: "How do smoking, diabetes and periodontitis affect outcomes of implant treatment?" Since this question, which proposes an investigation of the effect of 3 different risk factors on the outcome of implant therapy, includes 3 different populations or groups of patients with these different risk factors, it was approached as 3 separate focused questions: *(1)* "How does smoking affect outcomes of implant treatment?" *(2)* "How does diabetes affect outcomes of implant treatment?" and *(3)* "How does periodontitis affect outcomes of implant treatment?"

MATERIALS AND METHODS

The dental literature was searched using the MEDLINE, Cochrane Collaboration, and EMBASE databases. An initial low-specificity search of these databases identified more than 2,500 articles for possible inclusion in the study. The reviewers for all 8 sections participated in a review of the titles and abstracts of these 2,500+ articles. Two reviewers evaluated each title and abstract for its possible inclusion in the systematic review. Agreement between the 2 reviewers was recorded. A consensus agreement between the 2 reviewers was reached for any articles that were excluded by 1 reviewer and included by the other. If a consensus agreement could not be reached, the article continued to be included for consideration. The intention of this screening process was to be as inclusive as possible of any articles that might provide implant outcome data for at least 10 patients with at least 12 months of follow-up time. If an article could not be definitively excluded based on information from the title and abstract, it remained included. Only articles published in the English language were considered for inclusion in this systematic review. This initial low-specificity review of titles and abstracts resulted in 1,766 articles to be used as a master list of scientific articles pertaining to the clinical use of dental implants in humans.

Table 3 Inclusion and Exclusion Criteria for Periodontitis Group

Inclusion criteria
1. Studies of patients of any age, race, or sex were included.
2. Study provided outcome data for root-form implants.
3. Study provided information about the periodontitis status of patients (ie, chronic, aggressive; active, history, treated).
4. Study provided implant outcome data with at least 1 year of follow-up.
5. Study was published in English.
Exclusion criteria
1. Study was an animal study.
2. Study provided outcome data for non-root-form implants (eg, blades, staples, subperiosteal, sapphire, other materials).
3. Study was an in vitro/laboratory study.
4. Study had less than 1 year of follow-up data.
5. Study was a case report or article that included data on less than 10 patients.
6. Patients had medically compromising conditions or other risk factors (eg, radiation therapy, bone metabolic disease).
7. Treatment included substantial bone augmentation (eg, sinus bone augmentation).

An additional 48 articles were identified for possible inclusion in this systematic review from additional searching of the databases and hand searching of bibliographies from articles relevant to this review. All searches were conducted for articles published through May 2005. The reviewers (PRK and TJH) screened the titles and abstracts of the 1,814 articles independently for inclusion in this systematic review. Articles were initially screened for inclusion based on criteria intended to be more inclusive than exclusive. Articles were included if they were published in English and appeared to report any type of implant outcome data in *(1)* patients who were smokers, *(2)* patients with diabetes, or *(3)* patients with periodontitis. Articles were excluded if they did not report implant outcome data for patients with 1 of these risk factors and if they did not include at least 10 patients with a minimum of 1-year follow-up of reported outcome data. These criteria were used to eliminate articles that did not address the focused question or that were simply technique articles, case reports of less than 10 patients, or reports with outcome data of less than 1 year. If the reviewers could not determine from the title and abstract whether it met the inclusion/exclusion criteria for this review, the article remained included, and the full article was retrieved for a more detailed assessment. Articles to be included or excluded by each of the reviewers were compared for agreement. Articles that were evaluated differently were reviewed together for a consensus decision. If a consensus agreement could not be reached, the disagreement was noted, and the article remained included.

Following a detailed evaluation of the titles and abstracts, 122 articles were identified for a full-article review and final determination of inclusion or exclusion. Articles were subcategorized into 1 of 3 categories: smoking, diabetes, or periodontitis. The inclusion and exclusion criteria were defined for each of the 3 risk-factor groups (smoking, diabetes, or periodontitis) separately, and a specific abstraction form was developed for each. Tables 1, 2, and 3 list the inclusion and exclusion criteria used for smoking, diabetes, and periodontitis, respectively. (Lists of excluded articles for each section are available in the Web edition of this article.) Articles that included patients having medical conditions with the potential to adversely influence implant outcomes, such as radiation therapy, immune compromise, or bone metabolic disease, were excluded. Likewise, articles that included patients who were treated with significant bone augmentation procedures, such as sinus bone grafts, were excluded because of the potential to adversely influence implant outcomes. This latter exclusion criterion was not applied to the smoking group. Articles that reported sinus bone augmentation in smokers were included in this review.

It was anticipated that some articles might fit more than 1 of these groups because study populations are often heterogeneous, including patients with multiple risk factors and/or a mix of patients with different risk factors. When an article met the criteria for more than 1 group it was included in both groups separately (ie, the data were abstracted and analyzed for more than 1 of the 3 risk factor groups with the abstraction form specific for that subcategory). However, unless the article reported outcome data separately for the specific risk factor group being evaluated, it was excluded from this review. Articles without implant survival or implant success rates reported with specific relation to a risk factor group were excluded.

In addition to implant survival and implant success rates, the abstraction of implant outcome data included reports of bone loss, microbial assessments, peri-implantitis, and other complications. Unfortunately, most studies included in this review did not report this type of implant outcome data. Conversely, some studies reported them without reporting implant survival or success rates; such studies were excluded. As a result, several articles were excluded from this review despite the presence of potentially meaningful implant outcome data. The small number of articles included in this review that reported such additional implant outcomes precluded a statistical analysis of these data. Hence, there was no assessment of the effect of smoking, diabetes, or periodontitis on implant outcomes other than implant survival and implant success.

Table 4a Kappa Statistics for Comparison of Reviewer Agreement Following Initial Screening

	Reviewer 2		
	Accept	Reject	Total
Reviewer 1			
Accept	472	26	498
Reject	38	1278	1316
Total	510	1304	1814

Simple Kappa coefficient = 0.9121; percent agreement = 96.47%.

Table 4b Kappa Statistics for Comparison of Reviewer Agreement Following Second Screening

	Reviewer 2		
	Accept	Reject	Total
Reviewer 1			
Accept	114	5	119
Reject	3	414	417
Total	117	419	536

Simple Kappa coefficient = 0.9565; percent agreement = 98.51%.

Table 4c Kappa Statistics for Comparison of Reviewer Agreement Following Final Screening

	Reviewer 2		
	Accept	Reject	Total
Reviewer 1			
Accept	36	0	36
Reject	0	86	86
Total	36	86	122

Simple Kappa coefficient = 1.0000; percent agreement = 100%.

For purposes of this systematic review, implant survival included all implants that remained osseointegrated at the time of the last reported follow-up examination. The definition of implant success varied from article to article, as determined by authors. Some authors used well-defined success criteria such as those described by Albrektsson and associates[12] (1986) or Smith and Zarb[13] (1989), while others used slight variations of these implant success criteria. As a result, it was not possible to define a single, specific set of criteria for implant success that fit all studies included in this review. When authors described "success" or "failure" criteria that included implants with progressive or excessive bone loss (acknowledging that authors' definitions varied slightly), the outcome data were reported in this review under implant success rates. If implant success or failure criteria were not described, outcome data were considered to reflect implant survival rates and reported in this review accordingly.

Each article was abstracted for implant survival and implant success rates at all reported time intervals, but the statistical analysis was performed on data from the last follow-up visit reported in each of the respective studies. Each risk factor group (smoking, diabetes, and periodontitis) was analyzed separately. When reported, implant outcomes for patients without one of the risk factors (ie, controls) were compared to implant outcomes for patients with the specified risk factor (eg, smokers compared to nonsmokers; patients with diabetes compared to patients without diabetes; and patients with a history of treated periodontitis compared to patients with periodontal health). For the smoking group, data from articles reporting only patients with implants placed in loose trabecular bone and/or sites with significant bone grafting (eg, maxilla, maxilla with sinus bone graft) were analyzed separately as well. The results were compared to data from the remaining articles that included patients with implants placed in all anatomic locations. The latter group of studies also included implants placed in sites with loose trabecular bone, such as the posterior maxilla. However, they differed from the former group in that patients with implants placed in all sites and not just sites with loose trabecular bone were included.

A biostatistician performed the statistical analysis of data for implant survival and implant success for each of the risk factor groups. Pooled estimates of implant survival and implant success were assessed for each group. When more than 1 article included patients with and without the risk factor in the same article, the difference in implant survival (or implant success) rates was calculated and statistically analyzed. See Proskin and associates' article in this issue for a detailed description of data analysis and forest plot interpretation. In general, forest plots can be interpreted as follows: *(1)* the square represents the individual results for the study, and the size of the square is the weight given to the study in the analysis; *(2)* the horizontal line through the square represents the 95% confidence interval; *(3)* the diamond at the bottom of the plot is the pooled value of all data in the analysis; *(4)* the vertical line and the center of the diamond represent the mean value, while the horizontal points of the diamond represent the 95% confidence interval of the mean. Nonoverlapping diamonds are suggestive of statistical significance, and overlapping diamonds suggest a lack of significant differences.

Multiple articles that reported implant outcome data for the same study population at different time intervals were included in the statistical analysis. However, if multiple articles reported outcome data

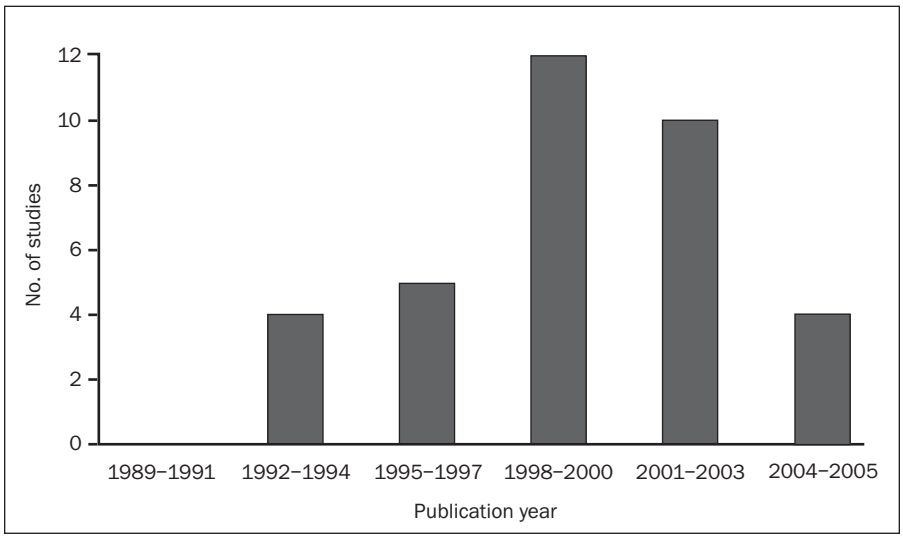

Fig 1 Articles by year of publication.

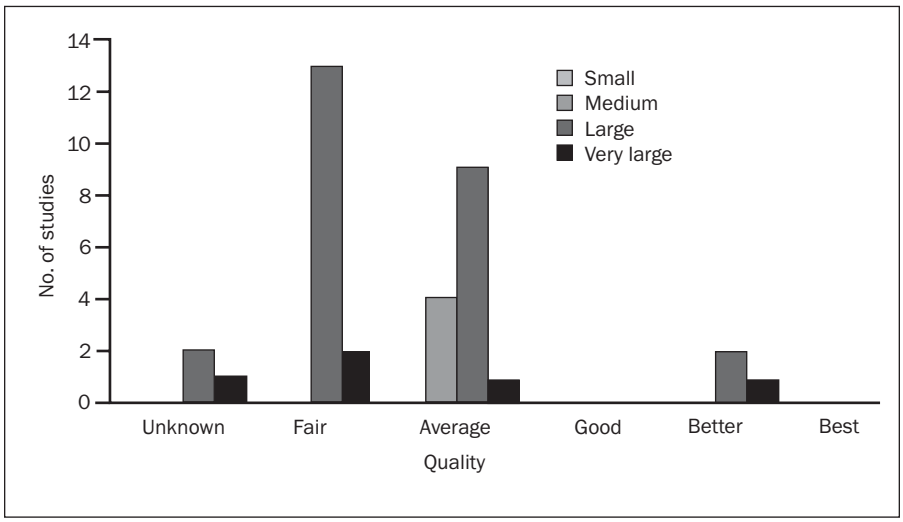

Fig 2 Articles by size and quality of study.

for the same study population at the same time interval (ie, same study results published in different journals), then 1 of the articles was excluded from the statistical analysis.

Articles included in this review were assessed for quality based on study design and ranked as best (randomized controlled trial, double blind), better (prospective clinical trial with concurrent controls), good (prospective clinical trial with historical controls), average (prospective case studies), fair (retrospective case studies), or unknown (none of the above).

RESULTS

A detailed review of 122 articles (including 47 articles for smoking, 19 articles for diabetes and 56 articles for periodontitis), identified 35 articles to be included in this systematic review. Tables 4a to 4c provide a summary and kappa statistics data regarding agreement between reviewers. Nineteen articles were identified for smoking, 4 articles were identified for diabetes, and 13 articles were identified for periodontitis. One article[14] fit the criteria to be included in both the smoking and periodontitis groups. This article was reviewed and abstracted separately with the appropriate abstraction form for each of the respective risk factor groups. Figures 1 and 2 are graphic representations of the articles by year of publication, size, and quality. The included articles were published from 1993 to 2005. The size of study populations ranged from medium (31 to 100 implants) to very large (more than 1,000 implants). The quality of articles included in this review ranged from fair (retrospective) to better (prospective with concurrent controls) studies. Studies are listed in the forest plots in rank order based on the quality of the publication (ie, study design).

Table 5 List of Included Articles for Smoking

Author(s)	Publication year	Type of study	Treatment group	No. of patients	No. of implants	% implant survival	% implant success	Last follow-up time (mo)	Implant location
Bain and Moy[15]	1993	Retrospective	Nonsmokers	540	1804		95.23	38	All (mixed)
			Current smokers	total	390		88.72	38	All (mixed)
De Bruyn and Collaert[16]	1994	Retrospective	Nonsmokers	45	166	98.19		12	Maxilla
			Smokers	16	78	91.03		12	Maxilla
Wang et al[17]	1996	Prospective	Nonsmokers	30	69	84.29	84.29	36	All sites = "poor quality bone"
			Current smokers	total	14	84.62	84.62	36	All sites = "poor quality bone"
Bain[18]	1996	Prospective	Nonsmokers		176		94.32	NA	All (mixed)
			Current smokers		13		61.54	NA	All (mixed)
Minsk et al[19]	1996	Retrospective	Nonsmokers		570	90.88		72	All (mixed)
			Current smokers		157	89.17		72	All (mixed)
Morris and Ochi[20]	1998	Prospective	Nonsmokers		1183	93.40		36	All (mixed)
			Current smokers		1005	91.10		36	All (mixed)
Watson et al[21]	1998	Prospective	Nonsmokers		75		87.00	60	All (mixed)
			Smokers		64		52.00	60	All (mixed)
Minsk and Polson[22]	1998	Retrospective	Nonsmokers	116	324	92.59		84	All (mixed)
			Current smokers	total	126	90.47		84	All (mixed)
Grunder et al[23]	1999	Prospective	Nonsmokers	55	164	98.17	98.17	30	Maxillary and mandibular posteriors
			Current smokers	19	55	100.00	100.00	30	Maxillary and mandibular posteriors
Jones et al[24]	1999	Retrospective	Nonsmokers	46	217	97.70		60	All (mixed)
			Current smokers	19	126	91.27		60	All (mixed)
Zitzmann et al[25]	1999	Retrospective	Nonsmokers (includes 2 pts on cessation)	53	76	97.37		24	All (mixed)
			Current smokers	22	36	97.22		24	All (mixed)
Keller et al[27]	1999	Retrospective	Nonsmokers		143	84.62		144	All posterior maxillary sites with bone augmentation
			Current smokers		32	78.13		144	All posterior maxillary sites with bone augmentation
Lambert et al[28]	2000	Prospective	Nonsmokers (including past smokers who quit)		1928	94.01		36	All (89% in maxilla)
			Current smokers		959	91.14		36	All (89% in maxilla)
Wallace[29]	2000	Retrospective	Nonsmokers	39	115		93.04	48	All (mixed)
			Current smokers	17	72		83.33	48	All (mixed)
Widmark et al[30]	2001	Clinical trial	Nonsmokers	12	53	88.68		36-60	Severely resorbed maxilla without bone graft
			Smokers	8	44	79.55		36-60	Severely resorbed maxilla without bone graft
Geurs et al[31]	2001	Retrospective	Nonsmokers		267	95.34		36	Posterior maxilla with sinus augmentation
			Current smokers		62	88.71		36	Posterior maxilla with sinus augmentation
Kan et al[32]	2002	Retrospective	Nonsmokers and past smokers	44	158	93.04	82.70	60	Posterior maxilla with sinus augmentation
			Current smokers	16	70	82.86	65.30	60	Posterior maxilla with sinus augmentation
Karoussis et al[14]	2003	Prospective	Nonsmokers	41	84	96.24		120	All (mixed)
			Smokers	12	28	92.86		120	All (mixed)

Smoking

The systematic review process identified 19 articles with implant outcome data for smokers. Table 5 lists the articles[14–32] that were identified for inclusion in the smoking part of this review. One of these articles (Kan and coworkers[26]) met the inclusion/exclusion criteria but was not included in the final statistical analysis because the data reported in that study were represented in another included article on the same patients (Kan and colleagues[32]). Thus, 18 articles were included in the statistical analysis.

Implant Survival in Smokers Versus Nonsmokers. Fourteen studies (14/18) included implant survival data in smokers. Figure 3 is a forest plot of the implant survival rate outcome data for smokers and nonsmokers. The number of smokers in the included studies ranged from as few as 14[17] to as many as 959.[28] The number of nonsmokers in the included studies ranged from 53[30] to 1,928.[28] The length of follow-up time, with reported implant survival data, available in these studies ranged from 12 to 144 months for both the smokers and nonsmokers. The pooled estimate for implant survival in smokers was 0.897 (95% CI: 0.87 to 0.924) or 89.7% implant survival at the last reported visit. The same 14 studies also included implant survival data for nonsmokers. The pooled estimate for implant survival in nonsmokers was 0.933 (95% CI: 0.91 to 0.956) or 93.3% implant survival at the last reported visit.

All 14 studies reported implant survival data for both smokers and nonsmokers and therefore could be analyzed for differences. The pooled estimate of the difference in implant survival between smokers and nonsmokers in these studies was 0.0268 (95% CI: 0.011 to 0.0426) or 2.68% better implant survival for nonsmokers (pairwise test; z = 3.3305). These data were represented in the forest plot in Fig 4. The difference was statistically significant ($P = .0009$).

Implant Success in Smokers Versus Nonsmokers. Seven studies (7/18) with implant success data in smokers were included. Figure 5 is a forest plot of the implant success rate outcome data for smokers and nonsmokers. The number of smokers in the included studies ranged from as few as 13[18] to as many as 390.[15] The number of nonsmokers in the included studies ranged from 69[17] to 1,804.[15] The length of follow-up time, with reported implant success data, available in these studies ranged from 30 to 48 months for both the smokers and nonsmokers. The pooled estimate for implant success in smokers was 0.77 (95% CI: 0.661 to 0.879) or 77.0% implant success at the last reported visit. The same 7 studies also included implant success data for nonsmokers. The pooled estimate for implant success in nonsmokers was 0.91 (95% CI: 0.866 to 0.954) or 91.0% implant success at the last reported visit.

All 7 studies reported implant success data for both smokers and nonsmokers and thus could be compared for differences between groups. The pooled estimate of the difference in implant success rates between smokers and nonsmokers in these studies was 0.1128 (95% CI: 0.0341 to 0.1915) or 11.28% better implant success for nonsmokers (pairwise test; z = 2.8082). These data are represented in the forest plot in Fig 6. The difference was statistically significant ($P = .005$).

Of the 14 studies that reported implant survival outcome data, 5 studies included only patients with implants placed in loose trabecular bone (referred to as "maxilla") while the other 9 studies included patients with implants placed in all anatomic locations (referred to as "mixed"). The latter papers are represented on the forest plots as "mixed," referring to the fact that a variety of implant sites were included in these studies.

Implant Survival in Smokers Versus Nonsmokers According to Bone Quality. Five (5/14) studies were included with implant survival data for smokers and nonsmokers with implants placed in loose trabecular bone. Figures 7a and 7b display forest plots of the implant survival rate outcome data for smokers and nonsmokers subdivided into maxilla and mixed categories. The number of implants in smokers in the included maxilla studies ranged from as few as 14[17] to as many as 78.[16] The number implants in nonsmokers in the included maxilla studies ranged from 53[30] to 267.[31] The length of follow-up time with reported implant survival data available in these studies ranged from 12 to 60 months for both the smokers and nonsmokers. The pooled estimate for implant survival in smokers with implants placed in loose trabecular bone sites was 0.861 (95% CI: 0.818 to 0.904) or 86.1% implant survival at the last reported visit. The pooled estimate for implant survival in nonsmokers with implants placed in loose trabecular bone sites was 0.924 (95% CI: 0.876 to 0.972) or 92.4% implant survival at the last reported visit.

All 5 studies reported implant survival data for both smokers and nonsmokers and therefore could be analyzed for differences. A pooled estimate of the difference in implant survival between smokers and nonsmokers with implants placed in loose trabecular bone was found to be 0.0743 (95% CI: 0.0316 to 0.1169) or 7.43% better implant survival for nonsmokers with implants placed in loose trabecular bone sites (pairwise test; z = 3.4139). These data are represented in the forest plot in Fig 8. The difference was statistically significant ($P = .0006$).

Nine (9/14) studies with implant survival data for smokers with implants placed in all sites (mixed) were included. See Figs 7a and 7b for the forest plot of implant survival rates for smokers and nonsmokers subdivided into maxilla and mixed groups. The number of implants in smokers in the included mixed studies ranged from as few as 28[14] to as many as 959.[28] The number of implants in nonsmokers in the included mixed studies ranged from 76[25] to as many as 1,928.[28] The length of follow-up time with reported implant survival data, available in these studies ranged from 24 to 144 months for both the

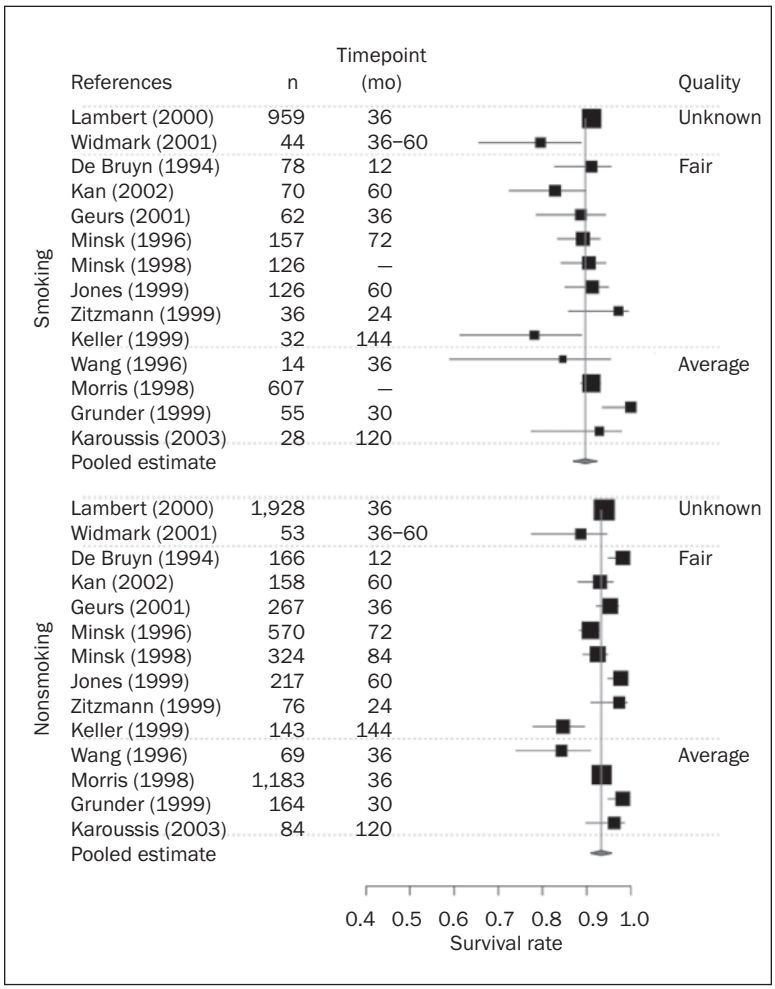

Fig 3 Last reported implant survival rate for smokers and nonsmokers. The number of implants is shown.

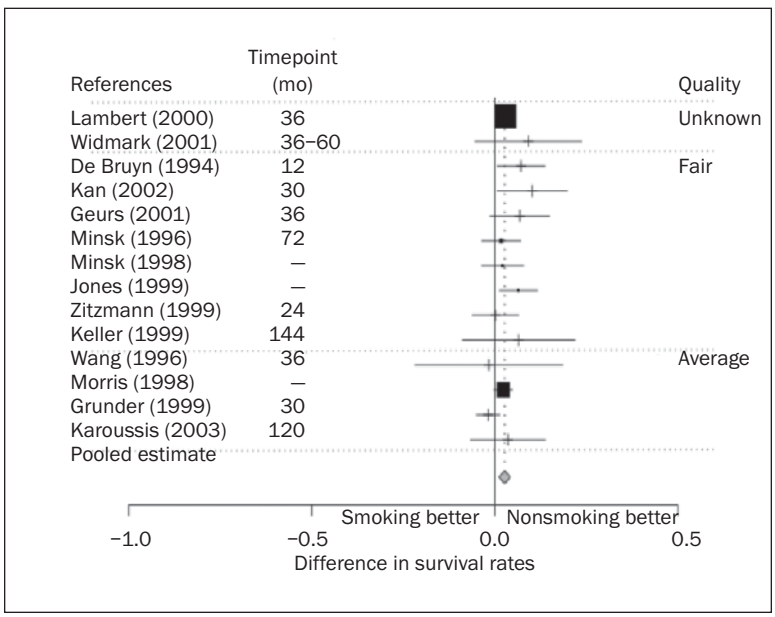

Fig 4 Difference in last reported implant survival rate for smokers and nonsmokers.

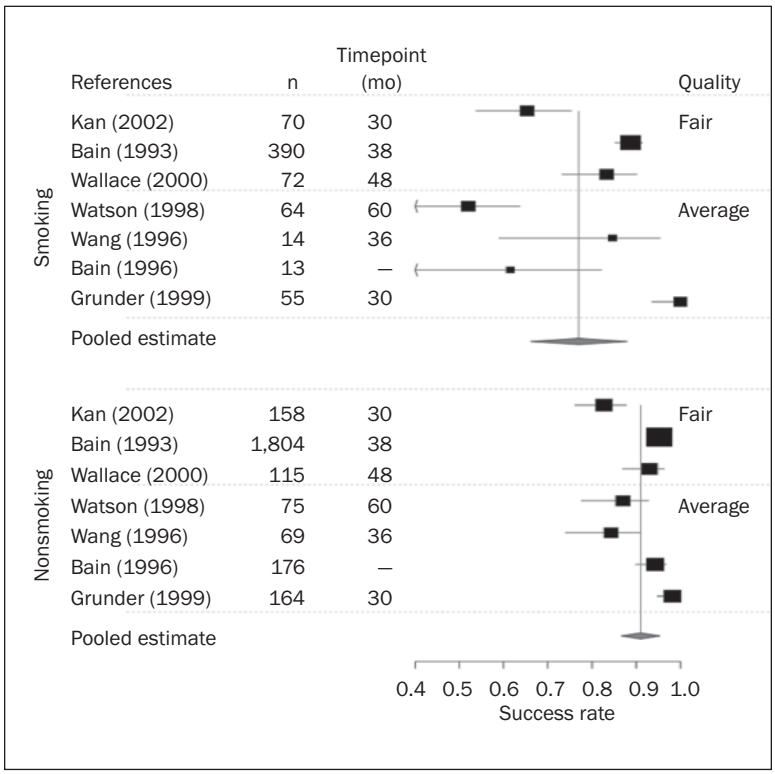

Fig 5 Last reported implant success rate for smokers and nonsmokers. The number of implants is shown.

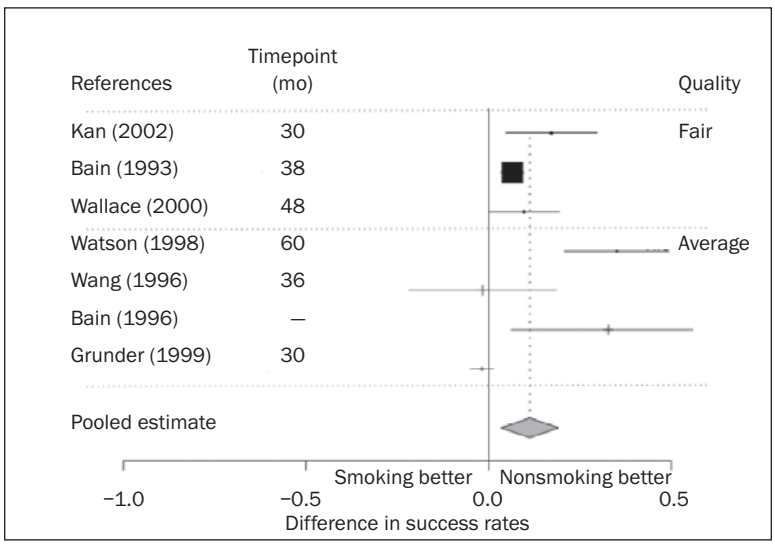

Fig 6 Difference in last reported implant success rate for smokers and nonsmokers.

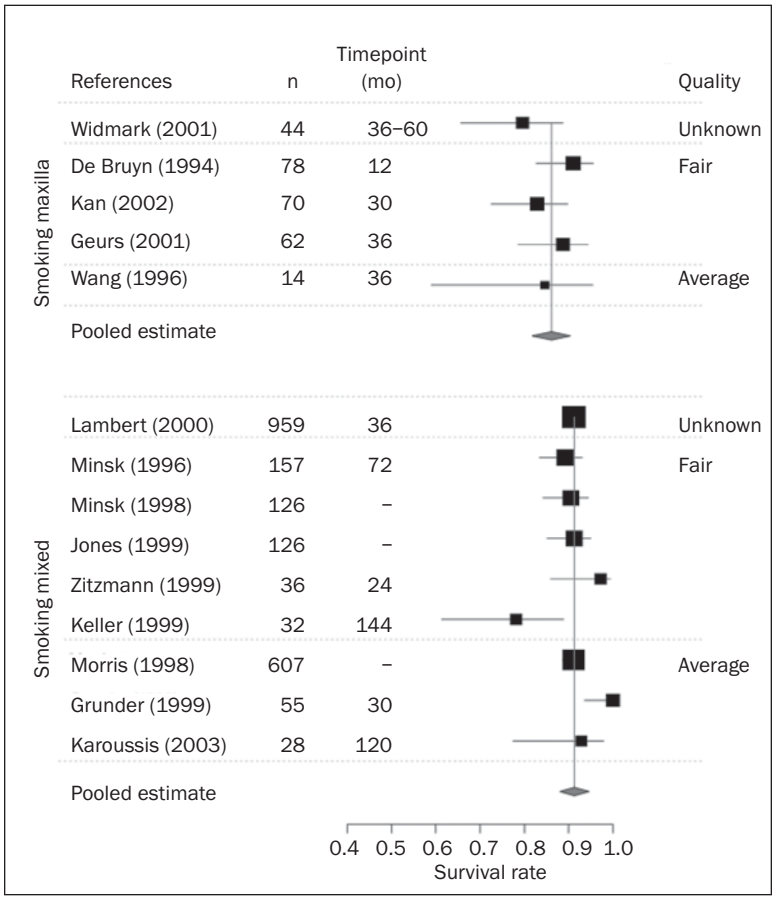

Fig 7a Last reported implant survival rate for smokers (maxilla versus mixed sites).

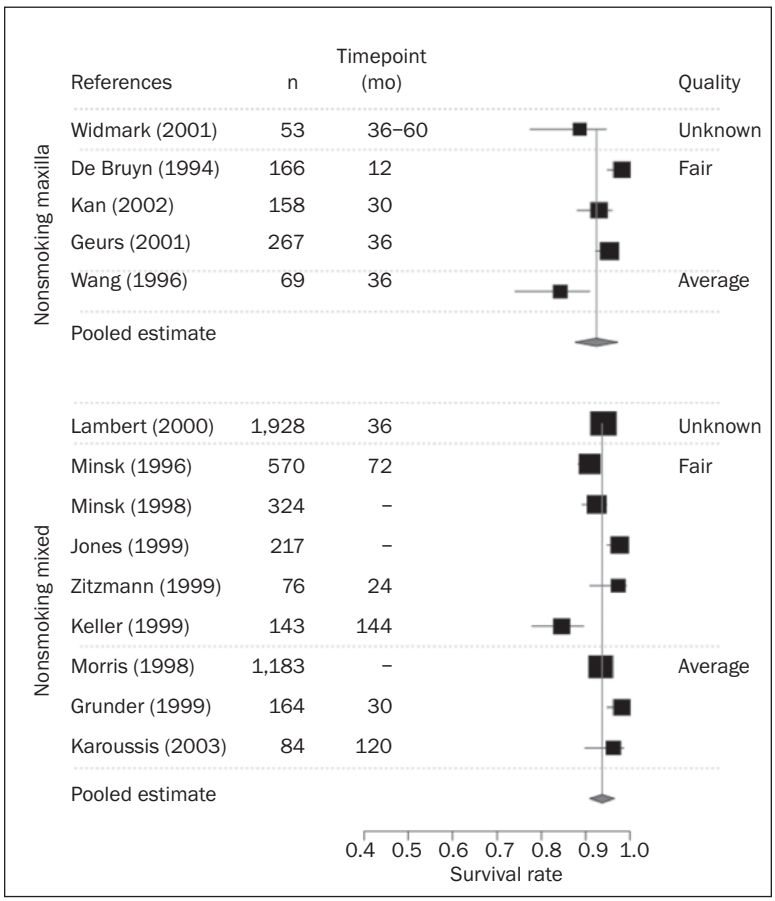

Fig 7b Last reported implant survival rate for nonsmokers (maxilla versus mixed sites).

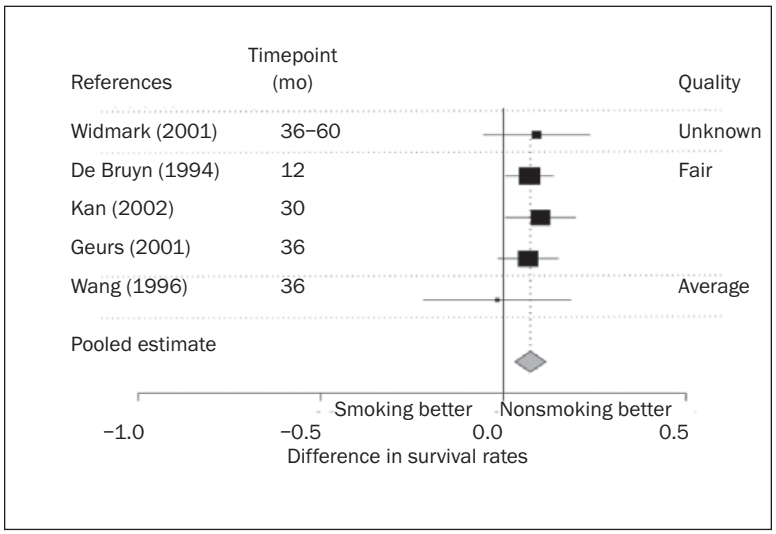

Fig 8 Difference in last reported implant survival rate for smokers versus nonsmokers in poor quality bone (maxilla).

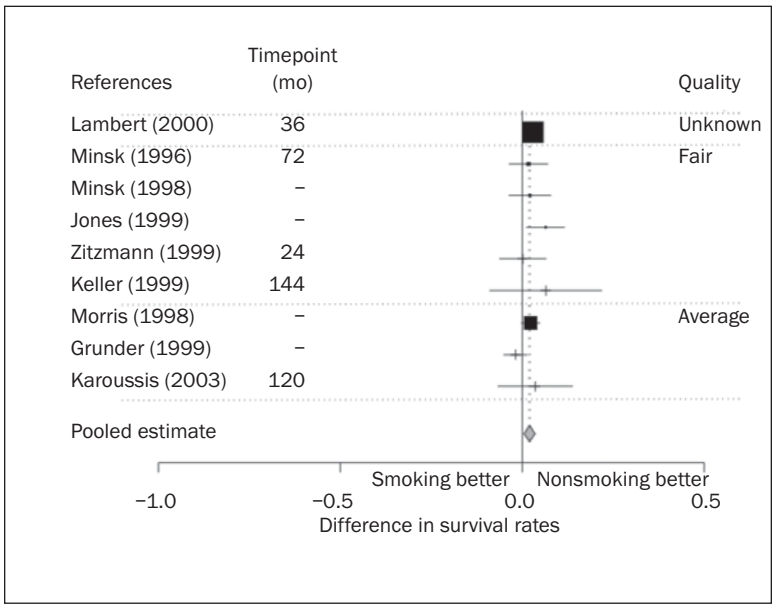

Fig 9 Difference in last reported implant survival rate for smokers versus nonsmokers in all sites (mixed).

smokers and nonsmokers. The pooled estimate for implant survival in smokers with implants placed in all anatomic sites was 0.913 (95% CI: 0.88 to 0.946) or 91.3% implant survival at the last reported visit. The pooled estimate for implant survival in nonsmokers with implants placed in all sites was 0.937 (95% CI: 0.91 to 0.964) or 93.7% implant survival at the last reported visit.

All 9 studies reported implant survival data for both smokers and nonsmokers and therefore could be analyzed for differences. The pooled estimate of the difference in implant survival between smokers and nonsmokers with implants placed in all bone sites (mixed) was 0.0201 (95% CI: 0.0049 to 0.0352) or 2.01% better implant survival for nonsmokers (pairwise test; $z = 2.5993$). These data are represented in a forest plot in Fig 9. The difference was statistically significant ($P = .0093$).

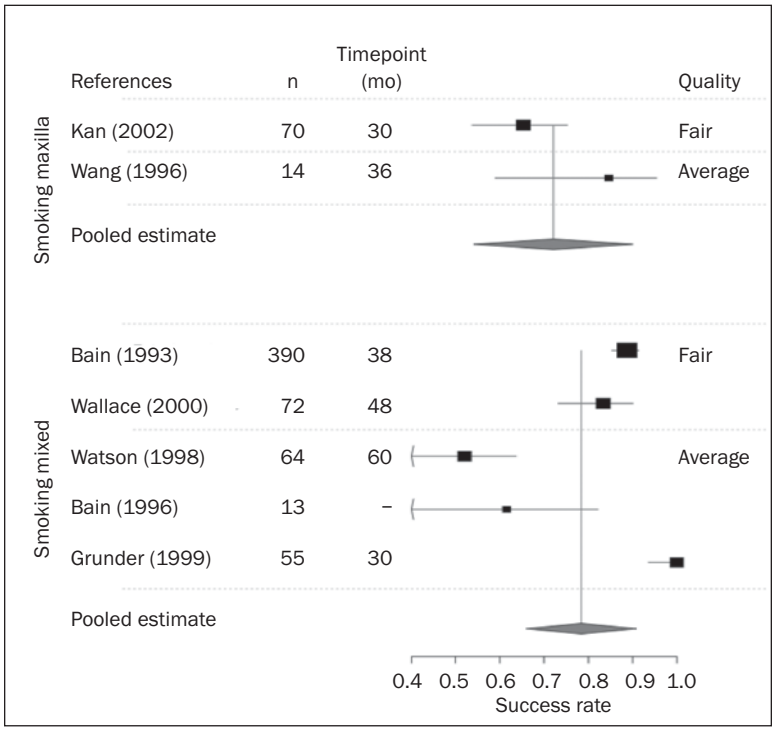

Fig 10a Last reported implant success rate for smokers (maxilla versus mixed sites).

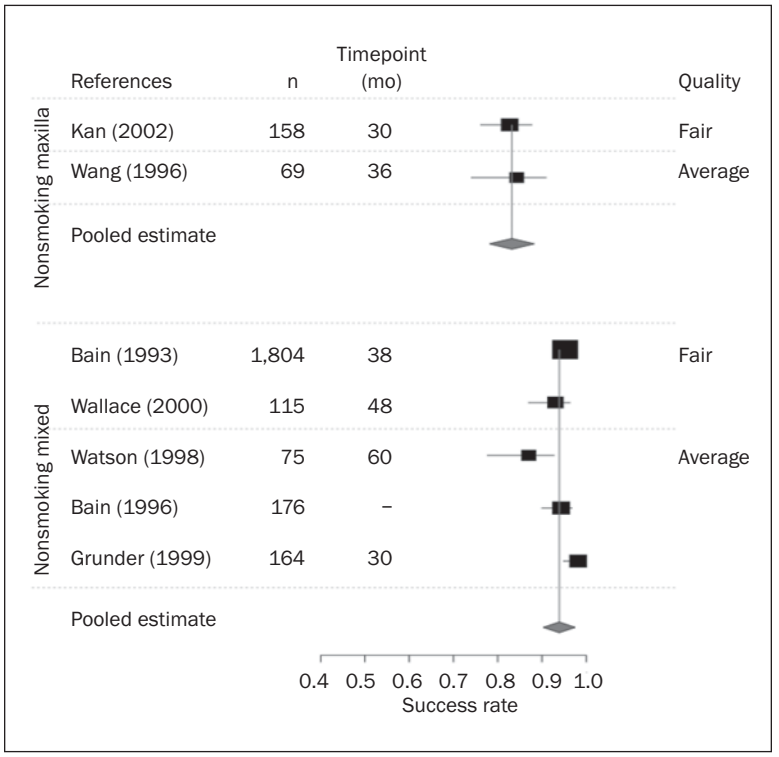

Fig 10b Last reported implant success rate for nonsmokers (maxilla versus mixed sites).

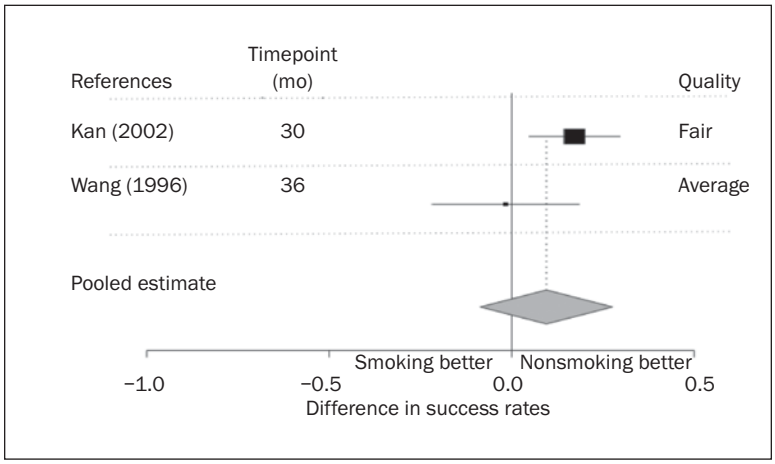

Fig 11 Difference in last reported implant success rate for smokers versus nonsmokers in poor-quality bone (maxilla).

Implant Success in Smokers Versus Nonsmokers According to Bone Quality. Of the 7 studies that reported implant success outcome data, 2 studies included only patients with loose trabecular bone (maxilla), while the other 5 studies included patients with implants placed in all anatomic locations (including sites with loose trabecular bone).

Only 2 studies with implant success data for smokers with implants placed in loose trabecular bone were included. Figures 10a and 10b show forest plots of the implant success rate outcome data for smokers and nonsmokers subdivided into maxilla and mixed groups. The number of implants in smokers placed in loose trabecular bone sites in the included maxilla studies ranged from as few as 14[17] to as many as 70.[32] The number of implants in nonsmokers placed in loose trabecular bone sites in the included maxilla studies ranged from 69 to 158.[32] The length of follow-up time, with reported implant success data, available in these studies ranged from 36 to 60 months for both the smokers and nonsmokers. The pooled estimate for implant success in smokers with implants placed in loose trabecular bone sites was 0.721 (95% CI: 0.541 to 0.901) or 72.1% implant success at the last reported visit. The pooled estimate for implant success in nonsmokers with implants placed in loose trabecular bone sites was 0.832 (95% CI: 0.782 to 0.882) or 83.2% implant success at the last reported visit.

Both studies reported implant success data for both smokers and nonsmokers and therefore could be analyzed for differences. The pooled estimate of the difference in implant success between smokers and nonsmokers with implants placed in loose trabecular bone was 0.0951 (95% CI: –0.0864 to 0.2767) or 9.51% better implant success for nonsmokers (pairwise test; z = 1.0269). These data are represented in the forest plot in Fig 11. In this case, the difference was not statistically significant ($P = 0.3045$).

Five studies (5/7) were included with implant success in smokers with implants placed in all sites (mixed). See Figs 10a and 10b for forest plots of implant success rates for smokers and nonsmokers subdivided into maxilla and mixed categories. The number of implants in smokers placed in all anatomic sites in the included mixed studies ranged from as few as 13[18] to as many as 390.[15] The number of implants in nonsmokers in the included mixed studies ranged from 75[21] to as many as 1,804.[15] The length of follow-up time, with reported implant success data, available in these studies ranged from 30 to 60 months for both the smokers and nonsmokers. The pooled estimate for implant success in smokers with implants placed in all anatomic sites was 0.784 (95% CI: 0.659 to 0.909) or 78.4% implant success at the last reported visit. The pooled estimate for implant success in nonsmokers with implants placed in all sites (mixed) was 0.939 (95% CI: 0.903 to 0.975) or 93.9% implant success at the last reported visit.

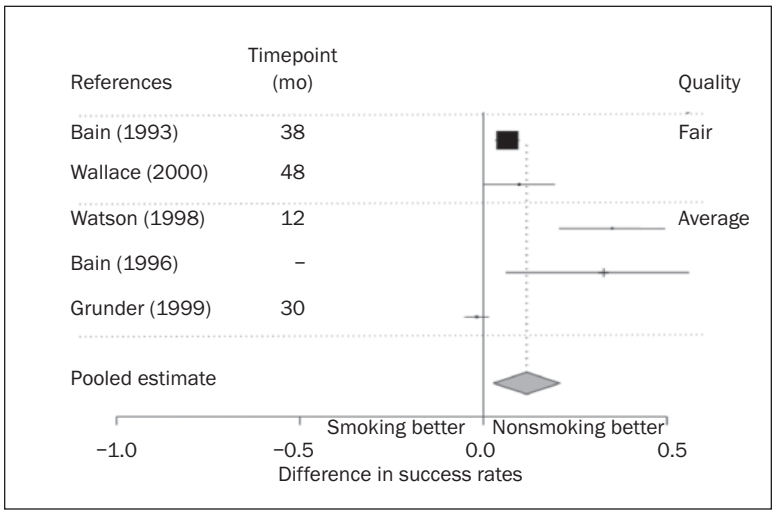

Fig 12 Difference in last reported implant success rate for smokers versus nonsmokers in all sites (mixed).

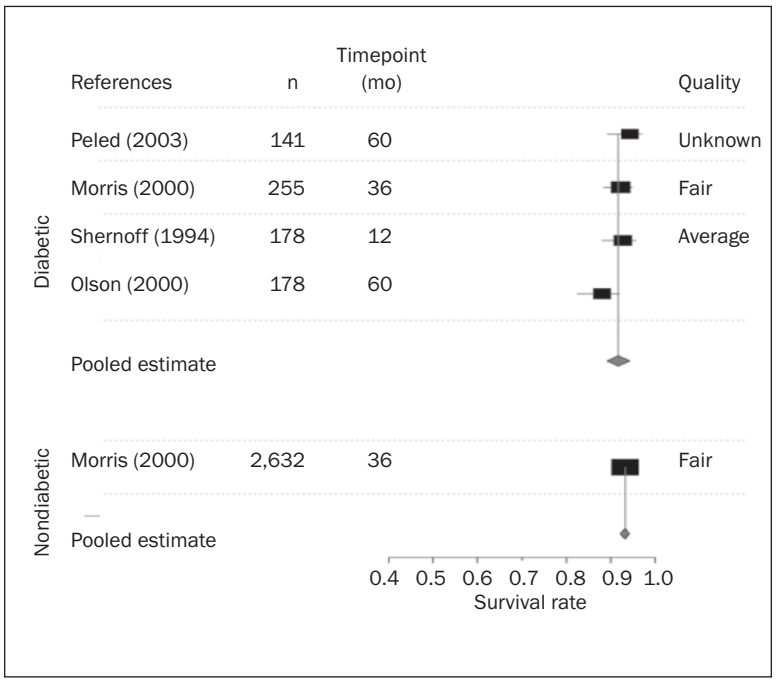

Fig 13 Last reported implant survival rate for patients with and without diabetes.

Table 6 List of Included Articles for Type 2 Diabetes

Author(s)	Publication year	Type of study	Treatment group	No. of patients	No. of implants	% implant survival	Last follow-up time (mo)	Implant location	Implant prosthesis
Shernoff et al[33]	1994	Prospective	Type 2 diabetes	89	178	92.7	12	Anterior mandible	Removable overdenture
Morris et al[34]	2000	Retrospective	Type 2 diabetes		255	92.2	36	All sites	Mixed variety
			Nondiabetic		2,632	93.2	36	All sites	Mixed variety
Olson et al[35]	2000	Prospective	Type 2 diabetes	89	178	88	60	Anterior mandible	Removable overdenture
Peled et al[36]	2003	Case study	Type 2 diabetes	41	141	94.3	60	Anterior mandible	Removable overdenture

All 5 studies reported implant success data for both smokers and nonsmokers and therefore could be analyzed for differences. The pooled estimate of the difference in implant success between smokers and nonsmokers with implants placed in all bone sites (mixed) was 0.1176 (95% CI: 0.027 to 0.2082) or 11.76% better implant success for nonsmokers (pairwise test; z = 2.5452). These data are represented in the forest plot in Fig 12. The difference was statistically significant ($P = .0109$).

Diabetes

The systematic review process identified 4 articles with implant outcome data for patients with type 2 diabetes. Table 6 lists the articles[33–36] that were included in this review with implant outcome data for these patients. Two articles, Fiorellini and colleagues[37] and Farzad and associates,[38] were identified in the process but not included in this review because they reported implant outcome data for a mixed population of patients with either type 1 or type 2 diabetes, and the outcome data were not reported separately. Similarly, an article by Kapur and associates[39] was not included in the analysis because of its mixed population sample. One additional article, Abdulwassie and Dhanrajani,[40] appeared to meet the inclusion/exclusion criteria but was not included in the final statistical analysis because survival data were reported for the 6-month examination but not for the last examination at 36 months. Consequently, only 4 articles met the inclusion/exclusion criteria and were included in the final statistical analysis for patients with type 2 diabetes.

Implant Survival in Diabetic Versus Nondiabetic Groups. All 4 studies included implant survival data for patients with type 2 diabetes. Figure 13 is a forest plot of the implant survival rate outcome data for the diabetic and nondiabetic groups. The number of implants in diabetic patients in the included studies ranged from 141[36] to 255,[34] and the number of implants in nondiabetic patients, which were only included in 1 of the studies, was 2,632.[34] The length of follow-up time with reported implant survival data, available in these studies ranged from 12 to 60 months for studies that included diabetic patients and 36 months for the study that also included nondiabetic patients. The pooled estimate for implant survival in diabetic patients was 0.917 (95% CI: 0.891 to 0.943) or 91.7% implant survival. The estimate for implant survival in nondiabetic patients was 0.932 (95% CI: 0.922 to 0.941) or 93.2% implant survival.

A pooled estimate of the difference in implant survival rates between diabetic patients and nondiabetic patients was not possible because only 1 study included both diabetic and nondiabetic patients. However, there does not appear to be a difference in implant survival between patients with type 2 diabetes and nondiabetic patients based on the statistical assessment (pooled estimates with 95% CI) of the 4 studies included in this review.

Implant Success in Diabetic Patients Versus Nondiabetic Patients. No studies in this review reported implant success outcome data in type 2 diabetic patients. Thus, estimates for implant success rates in diabetic and nondiabetic patients were not possible.

Periodontitis

The systematic review process identified 13 articles with outcome data for patients with a history of treated periodontitis. One article by Rosenberg and coworkers met the inclusion criteria but was not included in the statistical analysis because the data were not reported with defined observation periods.[41] Table 7 lists the articles[7,11,14,42–51] that were identified for inclusion in the review of outcome data for patients with a history of treated periodontitis.

Implant Survival in Patients with a History of Treated Periodontitis Versus Healthy Patients. Ten studies (10/13) were included with implant survival data in patients with a history of treated periodontitis. Figure 14 is a forest plot of the implant survival rate outcome data for patients with and without a history of treated periodontitis. The number of implants in patients with a history of treated periodontitis ranged from 12[46] to 309,[43] and the number of implants in healthy patients ranged from 30[51] to 92.[47] The length of follow-up time with reported implant survival outcome data available in these studies ranged from 36 to 120 months for both patients with and without a history of periodontitis. The pooled estimate for implant survival in patients with a history of treated periodontitis was 0.95 (95% CI: 0.918 to 0.982) or 95.0% implant survival at the last reported visit. The pooled estimate for implant survival in healthy patients was 0.971 (95% CI: 0.948 to 0.994) or 97.1% implant survival at the last reported visit.

Three studies[14,47,50] included both patients with and without a history of treated periodontitis. For these studies, the pooled estimate of the difference in implant survival rates between patients with a history of treated periodontitis and healthy patients was –0.0314 (95% CI: –0.0697 to –0.0068) or 3.14% better implant survival for patients with no history of periodontitis (pairwise test; z = –1.6096). These data are represented in the forest plot depicted in Fig 15. The difference was not statistically significant ($P = .1075$).

Table 7 List of Included Articles for Periodontitis

Author(s)	Publication year	Type of study	Treatment group	No. of patients	No. of implants	% implant survival	% implant success	Last follow-up time (mo)
Leonhardt et al[42]	1993	Clinical trial Prospective	Periodontal disease	19	63	96.83	96.83	36
Nevins and Langer[43]	1995	Retrospective	Recalcitrant periodontal disease	59	309	97.73	97.73	96
Ellegaard et al[44]	1997	Retrospective	History of periodontitis -ITI implants	56	93	95	95	60
			History of periodontitis -Astra implants	19	31	100	100	36
Brocard et al[7]	2000	Prospective	Periodontal health	297	647		88.8	84
			Periodontal disease	147	375		74.7	84
Yi et al[45]	2001	Clinical trial Prospective	History of advanced periodontitis	43	125	100	100	36
Mengel et al[46]	2001	Prospective	Generalized chronic periodontitis	5	12	100	100	36
			Generalized aggressive periodontitis	5	36	94.44	88.89	60
Leonhardt et al[11]	2002	Prospective	History of advanced periodontitis	15	57	94.7		120
Hardt et al[47]	2002	Retrospective	Periodontal health	25	92	96.74		60
			Periodontal disease	25	100	92		60
Karoussis et al[14]	2003	Prospective	Periodontal health	45	91	96.5		120
			History of chronic periodontitis	8	21	90.5		120
Evian et al[48]	2004	Retrospective	Periodontal health	72	72		91.67	12
			Chronic periodontitis	77	77		79.22	12
Baelum and Ellegaard[49]	2004	Prospective	History of periodontitis (1-stage protocol)	108	201	77.7		120
			History of periodontitis (2-stage protocol)	32	57	97.4		120
Mengel and Flores-de-Jacoby[50]	2005	Prospective	Periodontal health	12	30	100	100	36
			Chronic periodontitis	12	43	100	100	36
			Aggressive periodontitis	15	77	97.4	97.4	36
Wennstrom et al[51]	2004	Prospective	Moderate-advanced periodontal disease	51	149	97.3		60

Implant Success in Patients with a History of Treated Periodontitis Versus Healthy Patients. Eight studies (8/13) with implant success data in patients with a history of treated periodontitis were included. Figure 16 is a forest plot of the implant success rate outcome data for patients with and without a history of periodontitis. The number of implants in patients with a history of treated periodontitis in the included studies ranged from 12[46] to 375[7] and the number of implants in healthy patients ranged from 30[51] to 647.[7] The length of follow-up time with reported implant success outcome data, available in these studies ranged from 12 to 120 months for both patients with and without a history of treated periodontitis. The pooled estimate for implant success in patients with a history of treated periodontitis was 0.89 (95% CI: 0.823 to 0.957) or 89.0% implant success at the last reported visit. Four studies[7,14,48,50] were included with implant success data in patients considered to be periodontally healthy. The pooled estimate for implant success in healthy patients was 0.892 (95% CI: 0.812 to 0.972) or 89.2% implant success at the last reported visit.

The same 4 studies[7,14,48,50] included both patients with and without a history of treated periodontitis. For these studies the pooled estimate of the difference in implant success rates between patients with and without a history of treated periodontitis was –0.1105 (95% CI: –0.2006 to –0.0203) or 11.05% better implant success for patients with no history of periodontitis (pairwise test; z = –2.4016). These data are represented in the forest plot depicted in Fig 17. The difference was found to be statistically significant ($P = .0163$).

DISCUSSION

This systematic review of the literature investigated the effects of smoking, diabetes, and periodontitis on the outcome of implant treatment. The outcome data available for analysis were limited to implant survival and implant success. Most of the studies reported outcome data for implant survival, and several studies reported outcome data for implant success, but very few studies reported outcome data for prosthesis success.

It is difficult to assess the role of a single risk factor in the outcome (survival or success) of implant therapy because invariably there are many other

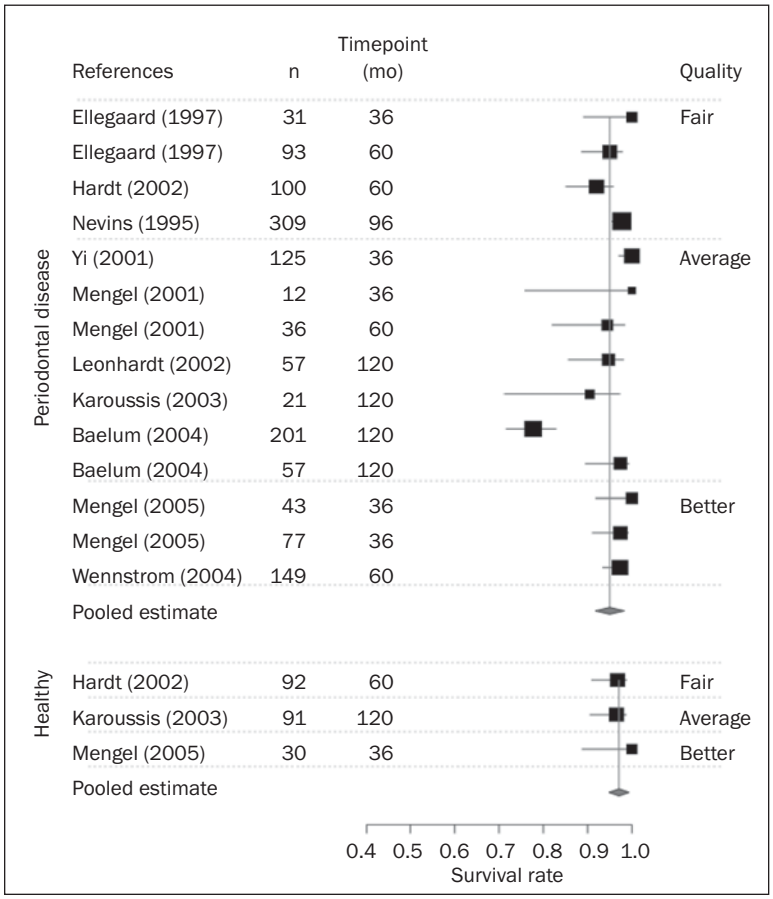

Fig 14 Last reported implant survival rate for patients with a history of treated periodontitis versus healthy patients.

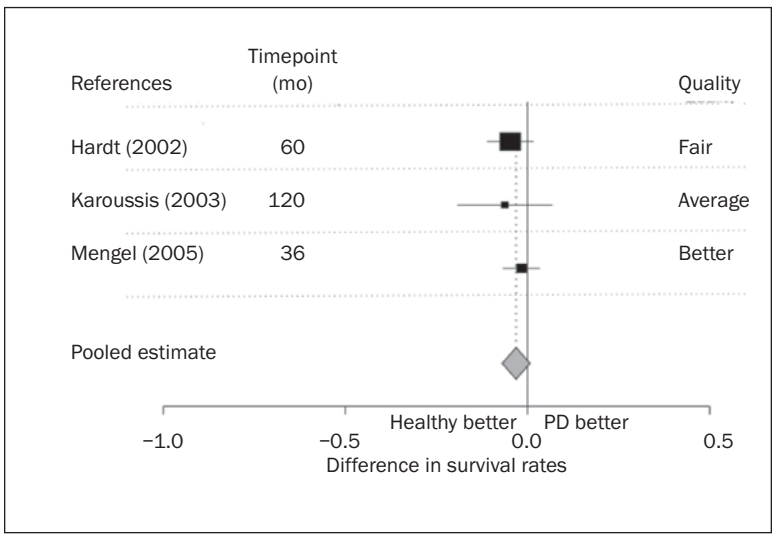

Fig 15 Difference in last reported implant survival rate for patients with a history of treated periodontitis versus periodontally healthy patients. PD = periodontal disease.

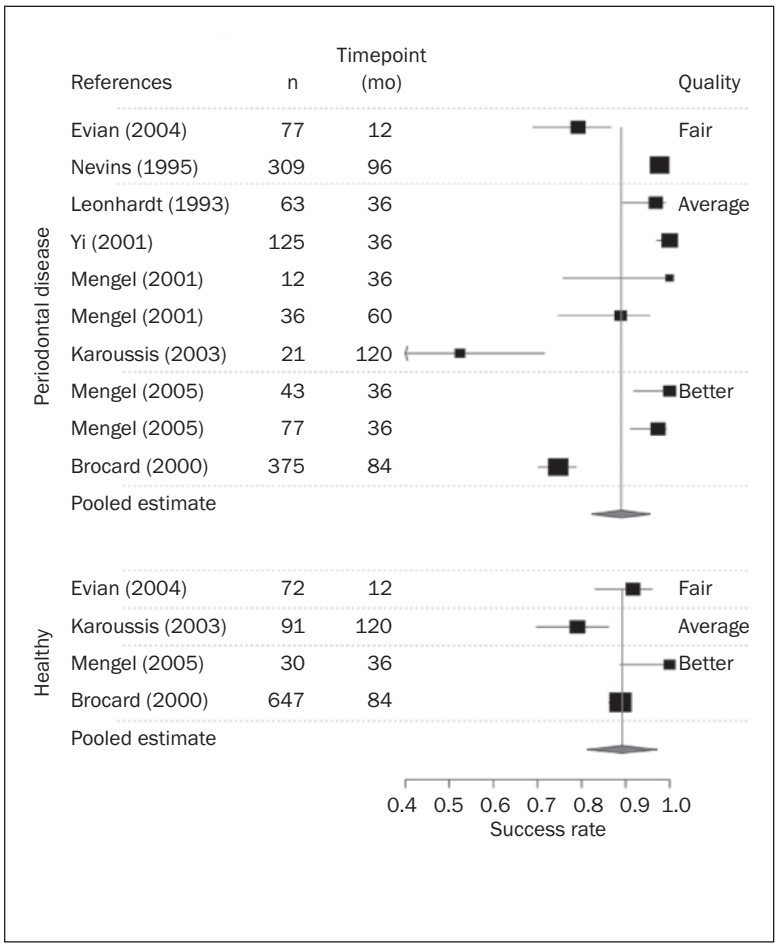

Fig 16 Last reported implant success rate for patients with a history of treated periodontitis versus periodontally healthy patients.

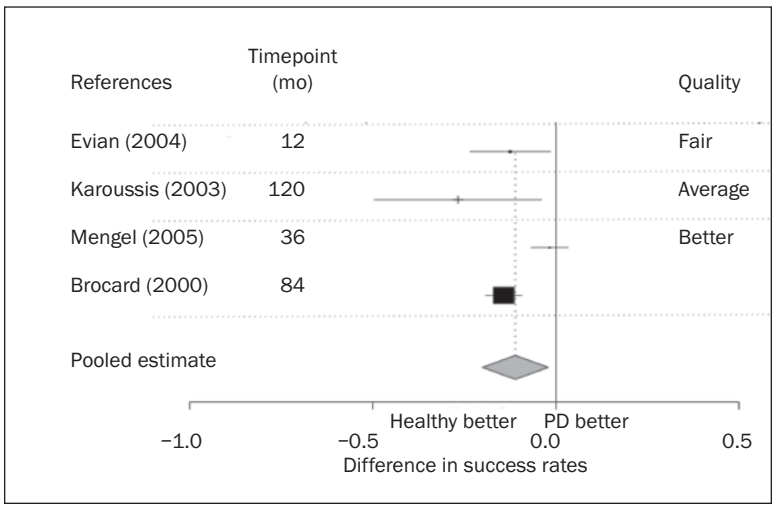

Fig 17 Difference in last reported implant success rate for patients with a history of treated periodontitis versus patients with periodontal health.

influencing factors such as bone quality, location, type of prosthesis, parafunctional habits, inadequate bone volume, grafted bone, as well as possible influencing systemic factors, including genetics, smoking, osteoporosis, and other factors influencing bone metabolism and wound healing. To precisely assess the effect of a risk factor on implant outcomes, it would be ideal to eliminate all other risk factors from the study population. The inclusion and exclusion criteria were defined to reduce the likelihood of including studies with implant outcome data for patients with multiple, possibly confounding risk factors (ie, risk factors in addition to the one being considered). However, the reality is that individual patients sometimes present with more than 1 risk factor, and groups of patients are typically heterogeneous with respect to risk factors and susceptibilities so the specific effect of an individual risk factor could be isolated neither for individual studies nor for this review. This is understandable and expected because study populations are typically representative of normal populations with various risk factors. For example, a population of patients identified as having periodontitis may include a percentage of smokers and/or patients with diabetes. Likewise, a population of patients identified as smokers will invariably include a percentage of patients with periodontitis and possibly some with diabetes as well.

Unless they are specifically excluded from a study, it is likely that most studies report on populations that include patients who smoke or have a history of smoking in addition to having other risk factors such as periodontitis or diabetes. Furthermore, since smoking is associated with periodontitis, particularly severe disease, it is highly probable that any population of patients with periodontitis will include patients who smoke, whether the authors report this information or not. Likewise, a group of patients who are smokers will most likely include patients with periodontitis. This same logic can be used to surmise that many studies evaluating smoking or periodontitis will also include some patients with diabetes. This is not to mention that there may be still other risk factors present in a population with the potential to influence implant outcomes.

Implant placement protocols, design characteristics, and prosthetic management may also influence implant outcomes. Although information about implant design, length, and surface characteristics was reported for many studies, the outcome data were usually not reported with respect to these details. Consequently, assessment of implant survival (or success) based on implant design characteristics was not possible in this review. Similarly, this review was unable to evaluate the effect of placement protocols, prosthesis designs, occlusion, or loading factors on the outcome of implant treatment. Not only does the coexistence of multiple risk factors within a study population create an inability to assess the specific effect of 1 individual risk factor, but there is a possibility that certain risk factors together may be more detrimental than the individual risk factors alone.

Smoking as a Risk Factor

All of the studies included in this systematic review for smoking as a risk factor included both patients who smoked as well as patients who did not smoke. Unfortunately, almost none of these studies reported the quantity of cigarettes smoked per day or the number of years that patients smoked. Some studies referred to individuals as "heavy" smokers but did not quantify the amount. As a result, no assessment could be made regarding the level of smoking on the outcome of implant treatment.

About half of the studies (10/19) included in this systematic review for smoking as a risk factor included patients treated with Brånemark system screw-type, machined-surface implants. Seven (7/19) studies included a combination of hydroxyapatite (HA) -coated implants, titanium plasma-spray (TPS) -coated implants, and machined implants (Steri-Oss, Spectra, Sterngold, and unstated combinations). One study used Straumann hollow screws, and 1 used Calcitek HA-coated cylinders. The data were insufficient to allow for statistical assessment of implant design characteristics.

The implant survival rates reported for these patients ranged from 78.13%[27] to 100%[23] over a period of 12 to 144 months with a pooled estimate of 89.7% for smokers compared to a pooled estimate of 93.3% for nonsmokers. The survival rate for nonsmokers is consistent with other reports for implant survival, while the rate for smokers appears slightly lower. The difference in implant survival rate (2.68% better for nonsmokers), although statistically significant, appears to be less than one might expect given the risk profile thought to be associated with smoking. This can be partially explained by considering the effect of smoking on implant survival in loose trabecular bone sites compared to other sites. To evaluate this hypothesis, the articles included in this review were stratified into 2 groups (maxilla and mixed) based on the quality of bone sites used in each study. The pooled estimate of implant survival for smokers in the maxilla group was 86.1%, and the pooled estimate of implant survival for nonsmokers in the maxilla group was 92.4%. The difference (7.43% better for nonsmokers) was statistically significant and much greater than the difference between

smokers and nonsmokers in the mixed group (2.01% better for nonsmokers). Thus, the effect of smoking on implant survival was predominantly observed in areas of loose trabecular bone.

The implant success rates reported for smokers ranged from 52.00%[21] to 100%[23] over a period of 12 to 48 months with a pooled estimate of 77.0% for smokers compared to a pooled estimate of 91.0% for nonsmokers. The success rate for nonsmokers is consistent with other reports for implant success, while the rate for smokers appears to be much lower. The difference in implant success rate (11.28% better for nonsmokers) reflects what would be anticipated for the effect of smoking on implant success.

Distinguishing differences in implant success rates in smokers and nonsmokers according to bone quality was not as revealing. In fact, although the difference in implant success rates between smokers and nonsmokers for implants placed in loose trabecular bone was considerable (9.51% better for nonsmokers), it was not statistically significant (P = .3045). The lack of statistical significance is surprising but is most likely explained by the small number of studies (only 2) reporting implant success for smokers and nonsmokers. One study,[17] which reported equal success rates for smokers and nonsmokers (84.62% and 84.29%, respectively), included only 14 smokers and used HA-coated implants. The patients were followed for only 36 months, which is a short and typically successful time interval for HA-coated implants (as compared to longer time intervals with these implants). All implants were placed in loose trabecular bone, with both smokers and nonsmokers experiencing moderate implant failures. The other study[32] reporting implant success rates for smokers and nonsmokers with implants placed in loose trabecular bone revealed a dramatically different result. The authors also used HA-coated implants placed in loose trabecular bone sites, but the follow-up period was longer (60 months). It is interesting to consider the findings of this study along with the findings of an earlier study (not included in this statistical analysis) by the same authors.[26] In the earlier study, they reported a 93.04% success for nonsmokers and an 82.82% success for smokers after a short time interval of only 12 months. In the later study, the success rate for the nonsmokers following 60 months was 82.7%, but the success rate for smokers over this period of time fell dramatically to 65.3%. Thus, if one considers the difference in success rates for smokers and nonsmokers with implants placed in loose trabecular bone sites that are followed over a longer period of time, the adverse effect of smoking may be more evident.

Smoking and Loose Trabecular Bone. The most significant differences regarding implant survival (or implant success) between smokers and nonsmokers were found in studies that identified and evaluated implants placed in the maxilla and those placed in grafted sites. It appears that smoking is a significant risk factor with an adverse affect on implant survival and success in areas of loose trabecular bone. This difference in survival between smokers and nonsmokers in studies that include all bone sites is small and may be influenced by the inclusion of loose trabecular bone sites in these studies. The effect of smoking may not be as significant for good bone sites. There is a need for studies to evaluate the effect of smoking on implants placed in different anatomic locations with variations in bone quality, including studies limited to sites with good bone quality.

Smoking and Implant Surfaces. Implant surface characteristics can influence bone-implant contact and may improve implant outcomes. It was not possible in this review to analyze the effect of implant surfaces on the outcome of implant treatment in smokers. Nonetheless, there are some interesting findings to consider regarding the influence of implant surfaces. Some authors have suggested that HA-coated implants can improve the survival or success of implants in smokers compared with nonsmokers.[20] However, 1 study included in this review[21] reported a very low implant success (ie, a high failure rate) in smokers with HA-coated implants as compared to nonsmokers with the same implants (52% versus 87%, respectively). They reported that 78% of failing/failed implants were in smokers. The significant difference reported by Watson and coworkers[21] could be attributed to the type of restoration (removable overdentures), the implant used, or a lack of residual bone for implants in the patients (who were edentulous). The nonsmokers had a moderately high implant failure rate as well. Therefore, it is possible that the high percentage of failures and failing implants was related to the design of the implants (Calcitek HA-coated cylinders) rather than to smoking alone. This was a 60-month study with no implant failures during the first 2 years. Smoking may have contributed to the increase in implant failure and complications (eg, bone loss, peri-implantitis) associated with these implants but does not explain the relatively high failure rate also experienced by the nonsmokers treated in this study.

Grunder and coworkers,[23] on the other hand, reported 100% survival of implants with an acid-etched surface placed in smokers and followed for 30 months (1 to 5 years). These implants were placed in the posterior maxilla and mandible, which are typically considered areas of loose trabecular bone. The

high implant survival rate observed in this study is in sharp contrast to studies reporting survival rates of 79.55%[30] for machined surfaced implants placed in smokers followed for a similar period of time and low implant survival rates in loose trabecular bone.

No assessments can be made about the influence of implant surfaces on the outcome of implant survival or success in smokers as a result of this review. It appears that the use of implants with an altered surface microtopography has the potential to benefit patients with risk factors such as smoking. There is a need for more studies to evaluate the outcome of implants with altered surface characteristics in smokers, and it will be important to evaluate the outcome over long periods.

Some authors have suggested that smoking cessation helps implant survival and success rates for smokers. Indeed, Bain demonstrated an improved implant success rate for smokers who quit smoking 1 week prior to implant surgery and for 8 weeks following surgery.[18] This is the only article in the present review that addresses smoking cessation. Consequently, this systematic review was not able to assess the effectiveness of smoking cessation protocols on implant survival or success rates.

Diabetes as a Risk Factor

All of the studies included in this systematic review for diabetes as a risk factor included patients with controlled type 2 diabetes. Although each of the studies reported that the patients' diabetes was under control, none of them reported the level of control. The implant survival rates reported for these patients ranged from 88.0%[35] to 94.3%[36] over a period of 12 to 60 months, with a pooled estimate of 91.7% for patients with diabetes compared to a pooled estimate of 93.2% for patients without diabetes (reported in only 1 of these studies). This implant survival rate appears to be comparable to implant survival rates reported for healthy patients when considering implants placed in all areas of the mouth and restored with various types of implant restorations (ie, fixed or removable). However, 3 of these 4 studies reported survival of implants placed in the anterior mandible used to retain mandibular overdentures, which is an anatomic area that is typically associated with very high implant survival and success rates. Two of these 3 studies, Shernoff and colleagues[33] and Olson and associates,[35] are reports of the same 89 patients followed for 12 and 60 months, respectively. If one considered that implant survival rates for the anterior mandible restored with mandibular overdentures for nondiabetic patients have been reported at 98.3% to 100%[52] and 98.8%[53] after 5 years, then the implant survival rates reported in this review would be comparatively low. The implant survival rate reported in these studies for patients with type 2 diabetes appears lower than what would be expected for implants placed in the anterior mandible for nondiabetic patients. The study with nondiabetic patients[34] included implants placed in all anatomic locations and with various prosthesis designs. Thus, the estimated survival rate for this group is comparable to expected outcomes.

It is possible that, in addition to diabetes, implant design and surface characteristics could have influenced the lower survival rate in the diabetic group. The studies included in this review reported the use of multiple implant designs, including baskets, screws, and cylinders, as well as a variety of implant surfaces such as machined, HA, and TPS coated. No single implant design was predominantly used. Therefore, an assessment of the effect of implant design characteristics was not possible.

The 5-year survival rate (94.3% at 60 months) for implants placed in type 2 diabetic patients reported by Peled and colleagues,[36] although higher than the other 3 included studies, was lower than expected survival rates for implants placed in the anterior mandible. This study reported on the use of 3 to 4 implants (MIS design) placed in the anterior mandible to retain overdentures.

The higher implant survival rate reported by Peled and colleagues[36] as compared to the other studies included in this review could be attributed to the use of antibiotics. All 41 diabetic patients in this study were treated with antibiotics starting 1 hour before and continued for 5 days following implant placement surgery. None of the other studies included in this review reported the use of antibiotics as part of the implant placement protocol. Interestingly, Morris and associates[34] reported improved implant survival for patients who were treated with antibiotics (97.1% compared to 86.6% for diabetic patients and 95.1% compared to 90.6% for nondiabetic patients). They also reported improved outcomes for patients treated with chlorhexidine. The use of antibiotics and antimicrobials may improve implant outcomes for patients with risk factors such as diabetes. More studies are indicated to assess the benefits of antibiotics and antimicrobials for implant treatment in diabetic patients.

Other risk factors, in addition to diabetes, may have influenced the observed implant survival rate. The presence (or absence) of confounding risk factors such as smoking or a history of periodontitis was not reported for patients in the included studies. Similarly, none of the included studies reported the use of or indication for bone augmentation. Thus, it was not possible to assess whether confounding risk factors affected implant survival in these studies.

This systematic review suggests the possibility that type 2 diabetes has a negative effect on implant survival. However, the small number of studies included does not allow a definitive conclusion. Considering the lower survival rates in this group, it is possible that diabetes adversely affected the outcome of implant treatment. Since the diabetic condition of patients in these studies was stated to be under control, no comment can be made about implant survival in patients with uncontrolled diabetes. Similarly, the level of survival cannot be predicted for patients with type 1 diabetes.

Implant success rates were not reported for any of the studies included in the statistical analysis and therefore cannot be assessed as part of this systematic review. It is likely that implant success would be diminished in this patient population, particularly if bone support was not maintained over time. Fiorellini and coworkers[37] reported 85.7% implant success following 78 months in a mixed population of patients with controlled type 1 or type 2 diabetes. Implants were placed in both the maxilla and the mandible and restored with fixed prostheses, including single units, multiple units, and in 2 cases, removable overdentures. The authors suggested that the failure of implants in diabetic patients may be related to altered mechanical characteristics of the bone-implant contact, which could be influenced by alterations in bone metabolism and changes caused by accumulated glycation end-products (AGEs) known to affect this patient population.

Clearly, the systematic review revealed a lack of studies reporting implant outcome data for patients with diabetes (type 1 and type 2). More studies are needed to evaluate implant survival and success in patients with both types of diabetes. These studies should include patients with implants placed in a variety of anatomic locations and used to retain or support different types of prosthetic restorations. Since implant outcomes for patients with type 1 diabetes may differ from those for patients with type 2 diabetes, it is important for studies that include both patient types to report the outcome data separately for each group. Similarly, the level of diabetic control should be reported in future studies.

Periodontitis as a Risk Factor

All of the studies included in this systematic review for periodontitis as a risk factor included patients who were treated for periodontitis and subsequently maintained at some regular and continuous recall interval. The 1 possible exception to this finding is the study by Hardt and coworkers,[47] which used radiographic bone levels to assign patients to an "assumed" periodontitis group (bottom quartile) or an "assumed" periodontal health group (top quartile). The authors did not comment on any periodontal treatment or maintenance for these patients.

The implant survival rates reported for patients with a history of treated periodontitis in this review ranged from 100%[44,45,50] at 36 months to 77.7%[49] at 10 years. This review revealed a pooled estimate of 95.0% implant survival for patients with a history of treated periodontitis compared to a pooled estimate of 97.1% implant survival for patients with periodontal health over a period of 36 to 120 months. This implant survival rate for patients with a history of treated periodontitis compares favorably to the implant survival rate observed in patients without a history of periodontitis. The difference in implant survival rate (3.14% better for periodontally healthy patients) was not statistically significant ($P = .1075$).

The implant success rates reported for patients with a history of treated periodontitis in this review ranged from 100%(45; 50) at 36 months to 52.4%(14) at 120 months. The pooled estimate for implant success of all patients with a history of treated periodontitis included in this review was 89.0% over a period of 12 to 120 months. Although this compares favorably to the 89.2% pooled estimate for implant success in patients without a history of periodontitis, the difference in implant success rates (11.05% better for periodontally healthy patients) was statistically significant ($P = .0163$). This could be explained by the limited number of studies that included success rates for patients with and without a history of treated periodontitis (4 studies). It could also be indicative of more complications experienced by patients with a history of treated periodontitis over time as compared to patients with no history of periodontitis.

Three of the 4 studies[7,14,48] that reported implant success rates for both patients with and without a history of treated periodontitis included factors (other than periodontitis) that may increase the risk of peri-implantitis or complications that can lead to increased bone loss. Brocard and associates[7] used hollow screws, hollow cylinders, and solid screws in a 1-stage protocol, and Karoussis and coworkers[14] used hollow screws in a 1-stage protocol. Evian and associates[48] used a mix of screws and cylinders that were machined, acid-etched, or HA-coated, all of which were single-tooth implants in extraction sockets (either immediate or delayed placement). The authors theorized that the numerous HA-coated implants used in their study may have adversely influenced the implant success because of the increased bone loss caused by peri-implant infections observed in the study, especially in patients with periodontitis (inferring an increased likelihood of peri-implant infections in these patients).

The study by Karoussis and associates[14] included smokers, which may have contributed to the higher failure rates observed in these patients as compared to other studies. This study found a significantly higher peri-implantitis/complication rate for patients with a history of chronic periodontitis (28.6%) compared to patients with no history of periodontitis (5.8%). They concluded that patients with a history of treated periodontitis had decreased implant survival and increased complications. It is important to point out that this study used ITI hollow screws, which also may have contributed to the increased complication rate. Interestingly, the authors also illustrated how slight changes in the criteria for success can dramatically change the implant success rate. In their study, when the success criteria was limited to probing pocket depth (PPD) ≤ 5 mm, the success rates were 71.4% and 94.5% for patients with and without a history of treated periodontitis, respectively. However, when the criteria included a threshold of PPD ≤ 6 mm, the success rates were elevated to 81.0% and 96.7%, respectively. This emphasizes the need to evaluate success criteria used by authors to report implant success rates.

The use of a 1-stage implant placement protocol may be yet another factor that contributed to the higher failure rates observed in patients with a history of treated periodontitis in these studies. In fact, the lowest implant survival and success rates[7,14,49] were reported for patients with a history of treated periodontitis and implants placed using a 1-stage protocol. All other studies, with only 1 exception,[44] reported higher survival and success rates using a 2-stage implant placement protocol for patients with a history of treated periodontitis.

A possible explanation for lower survival and success rates observed with a 1-stage protocol in patients with a history of treated periodontitis is that periodontal pathogens present in the oral cavity are transmitted from a periodontal pocket to the implant site during the critical early healing phase following implant placement. The transmission of periodontal pathogens and their presence around implants has been demonstrated.[54,55] However, the etiologic role of these bacteria in the peri-implant breakdown of bone and whether they contribute to implant failure have not been established or proven.

Another possible explanation for the lower survival and success rates observed in these studies is the longer follow-up period. Lower implant survival and success rates in longer studies may reflect differences in early versus late protocols, operator experience, treatment planning, or implant designs or may simply be influenced by longer exposure to conditions that lead to complications and failure. Rosenberg and associates[41] reported the outcome of 1,511 implants placed in 334 patients followed up to 13 years. One hundred fifty-one patients were periodontally compromised, while the other 183 patients were periodontally healthy. The implant survival rates were 90.7% and 93.7%, respectively, for patients with a history of treated periodontitis compared to patients with no history of periodontitis. Late failures caused by peri-implantitis were observed most often with HA-coated implants and occurred more frequently in the patients with a history of treated periodontitis.

Periodontitis type and severity varied widely in the included studies. Unfortunately, the disease diagnosis was not always well defined. Descriptions ranged from chronic periodontitis to aggressive periodontitis. Some authors defined the periodontitis severity of the study population as "advanced" while others simply stated that they included "patients with periodontitis." Differences in periodontitis severity and/or patient susceptibility could have an impact on implant survival and success rates, but the current authors were unable to make any assessment regarding disease severity. Nevins and Langer[43] reported implant survival and success in a population of patients with recalcitrant periodontitis. By definition, this population of patients is "refractory to treatment" and therefore considered the most challenging type of periodontitis patient to treat. They reported excellent implant survival (97.73%) in a closely monitored and maintained patient population. They also stated that patients required fewer periodontal visits, since severely compromised teeth were removed and replaced with dental implants. Patients who retain periodontally compromised teeth return to the office more frequently to manage problems associated with these teeth.

The studies included in this systematic review show that implants can be successful in patients with a history of treated periodontitis. It is important to recognize that a majority of the studies (12/13) included in this review reported that patients were treated for periodontitis with oral hygiene instructions, nonsurgical therapy, and when indicated, surgical therapy followed by enrollment in a periodontal maintenance program with regular follow-up care. One study[47] did not specifically describe treatment of periodontitis or report whether patients were maintained in a recall maintenance program. This was a study with a large population that may or may not have been closely monitored (not stated in article).

Within the limits of the studies included in this review, it appears that the patients with a history of treated periodontitis who enter into oral hygiene and preventive maintenance programs have survival

comparable to patients with no history of periodontitis. The level of implant success may be less for patients with a history of treated periodontitis. This level of implant survival and implant success cannot be predicted for individuals with untreated periodontitis.

Five of the 13 studies in the review for periodontitis used Brånemark system screw-type implants with machined surfaces, and 1 used 3i screw-type implants with an acid-etched surface. Two studies used Astra Tech implants with a blasted surface; 3 studies used ITI hollow screws, solid screws, and/or hollow cylinders; 1 study used Astra implants with a blasted surface and ITI solid-screw implants; and 1 study used Paragon/Zimmer screw-type and cylinder-type implants with machined, acid-etched, or HA-coated surfaces. Most of the studies in this review (except where described) used a 2-stage implant placement protocol. Despite the details provided in the studies about implant designs and protocols used, it was not possible to analyze or assess the effect of implant design, surface characteristics, or placement protocols on implant survival or success in patients with a history of treated periodontitis.

CONCLUSIONS

This systematic review of the literature evaluated the effect of smoking, diabetes, and periodontitis on implant outcomes. The analysis was limited to data reported for implant survival and implant success. The following conclusions can be drawn from the results of this review:

- Smoking adversely affects the outcome of implant treatment (implant survival and success). The effect of smoking on implant survival appears to be more pronounced in areas of loose trabecular bone.
- Type 2 diabetes may have a negative affect on implant outcome (survival), but the limited number of studies available for review makes this conclusion tentative.
- Based on the studies included in this review, it appears that a history of treated periodontitis does not adversely affect implant outcome (survival). However, patients with a history of treated periodontitis may experience more complications and lower success rates. This appears to be more evident in studies with longer follow-up periods.

The systematic review did not address other factors that can influence implant outcomes, such as implant design, implant surface characteristics, implant placement, loading protocols, occlusion, and prosthesis design. The review was not able to assess the influence of smoking, diabetes, or periodontitis on other important implant outcome measures such as bone loss, peri-implantitis, or other complications. More studies are needed to evaluate the effects of smoking, diabetes, and periodontitis on these implant outcome measures. This review discovered a lack of published data for implant outcomes (survival and success) in diabetic patients. More studies are needed to assess implant survival and success for patients with either type 1 or type 2 diabetes. Long-term studies are expected to be more revealing of the influence of all risk factors on implant outcomes than short-term studies. Therefore, more long-term studies are needed to evaluate the effects of risk factors on implant outcomes.

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SECTION 7
CONSENSUS REPORT

How do smoking, diabetes, periodontitis affect outcomes of implant treatment?

Members of Section 7 evaluated the systematic review on the effects of smoking, diabetes, and periodontitis on dental implants. The focused PICO question addressed by the authors, Perry R. Klokkevold and Thomas Han, of the evidence-based systematic review is: How do smoking, diabetes, and periodontitis affect outcomes of implant treatment?

1. Does the section agree that the systematic review is complete and accurate?

The section carefully analyzed the review and appreciated its completeness, thoroughness, and clarity. However, it was realized that a number of difficulties were encountered with the definition of implant outcomes. While survival rates appear to be of enough clarity (ie, representing implants still in function irrespective of the condition of the tissues around them at the last examination), the definition of success is full of ambiguity. Hence, success rates may represent various conditions in various reports, a fact which renders comparison of the articles difficult and meta-analyses almost impossible.

Two articles that contributed additional information to the discussion of the focused question with regard to the influence of smoking were reconsidered. Both articles do not explicitly state survival rates, but these can be calculated from the article. While the first article (Feloutzis A, Lang NP, Tonetti M, et al. IL-1 gene polymorphism and smoking as risk factors for peri-implant bone loss in a well-maintained population. Clin Oral Implants Res 2003;14:10–17) reports on the loss of 7 implants in 1 heavy smoker out of 182 implants in function, the second article (Gruica B, Wang H-Y, Lang NP, Buser D. Impact of IL-1 genotype and smoking status on the prognosis of osseointegrated implants. Clin Oral Implants Res 2004;15:393-400) has a survival rate of 100% in 180 patients with 292 implants. Both articles support the fact that heavy smoking, especially in IL-1 gene polymorphism–positive patients, affected the incidence of biologic complications and hence, a decreased "success rate" (complication-free implants) after 8 to 15 years in the heavy-smoking patients.

Although intentionally excluded from the review due to the lack of original data, one reconsidered additional report (Bain CA, Weng D, Meltzer A, Kohles SS, Stach RM. A meta-analysis evaluating the risk of implant failure in patients who smoke. Compend Contin Dent Educ 2002;23:695-699) presented a meta-analysis in which implants with double acid–etched surfaces were compared to those with machined surfaces. In this report of 3 prospective multicenter studies accumulating 2,614 (machined) implants and 6 prospective studies accumulating 2,274 double acid–etched implants, the 3-year cumulative survival rate was clearly higher for the double acid–etched implants than for the machined implants. However, smoking did not significantly affect these results. Therefore, it may be hypothesized that surface characteristics may mitigate the effect of smoking on long-term implant outcomes.

Initial osseointegration rates may be derived from an additional article (Kumar A, Jaffin R, Berman C. The effect of smoking on achieving osseointegration of surface-modified implants. A clinical report. Int J Oral Maxillofac Implants 2002;17:816–819) that demonstrated a 97% success rate for implants with a double acid–etched surface in smokers (n = 72 patients; 269 implants) and 98.4% in nonsmokers (n = 389 patients; 914 implants). This difference was not statistically significant.

This systematic review has not addressed the fact that implant outcomes should be divided into implant outcomes of the initial integration period, ie, rate of osseointegrated implants, and the survival rate of implants in function, ie, long term. With respect to smoking, only 1 study addressed the former, while the remainder of the studies addressed the latter without differentiation. It was felt that long-term documentation should require observation periods of at least 5 to 10 years to allow sufficient time for the development of complications potentially leading to implant loss. The section used the definition of implant survival as an implant being present in the mouth without mobility. However, implant success was defined as an implant in function without any complications (biological or technical).

With regard to the patient with diabetes, it was realized that data on type 1 diabetes is virtually nonexistent and hence, the review concentrated on type 2 diabetes. Again, no distinction had been made between initial osseointegration and long-term survival rates. Only 4 studies met the inclusion criteria and only one of them reported on control patients

without diabetes. The longest documentation for patients was 5 years.

With the addition of the articles mentioned, the section accepted the systematic review as complete and accurate.

2. Has any new information been generated or discovered since the review cutoff time?

Since May 2005, data have been published addressing the influence of smoking on survival rates in 4 articles. In the first article (Wagenberg B, Froum SJ. A retrospective study of 1,925 consecutively placed immediate implants from 1988 to 2004. Int J Oral Maxillofac Implants 2006;21:71–80), no statistically significant difference between survival rates of implants placed in immediate extraction sites in smokers (94.4%) compared to nonsmokers (96.3%) was shown after an average of 6 years in function.

A 10-year study on 2 implant systems placed in periodontally highly susceptible patients (Ellegaard B, Bælum V, Kølsen-Petersen J. Non-grafted sinus implants in periodontally compromised patients: A time-to-event analysis. Clin Oral Implants Res 2006;17:156–164) reported a hazard ratio for smokers of 2.2 (95% CI: 0.8 to 6.1) compared to nonsmokers for implants to be lost.

In the third study (Moy PK, Medina D, Shetty V, Aghaloo TL. Dental implant failure rates and associated risk factors. Int J Oral Maxillofac Implants 2006;20:569–577) the authors reported survival rates of 79.8% in smokers compared to an overall survival rate of 85.1% over a period ranging from 6 months to 21 years without a defined mean observation period. When using a regression analysis, the risk ratio for implant failure in smokers was 1.39 ($P = .03$).

As part of a study with a 9- to 14-year follow-up of 294 patients (Roos-Jansåker A-M, Renvert H, Lindahl C, Renvert S. Nine- to fourteen-year follow-up of implant treatment. Part III. Factors associated with peri-implant lesions. J Clin Periodontol 2006;33:296–301), 218 patients with 999 implants were reexamined, with 80% of the implants yielding an observation period of 10 or more years. In this cohort, smoking significantly affected the prevalence of peri-implant mucositis and peri-implantitis. However, the overall survival rate, which was 95.7%, was not affected by smoking habits (Roos-Jansåker A-M, Lindahl C, Renvert H, Renvert S. Nine- to fourteen-year follow-up of implant treatment. Part I. Implant loss and associations to various factors. J Clin Periodontol 2006;33:283–289).

Regarding the influence of diabetes on implant survival, the study by Moy et al demonstrated a risk ratio of 1.94 ($P = 0.0003$) in subjects with diabetes. It is noteworthy, however, that the survival rate in patients with diabetes was only 68.7% compared to 85.1% in the overall cohort after 6 months to 21 years.

The 9- to 14-year follow-up study of machined implants (Roos-Jansåker et al parts I and III) specifically addressed the influence of periodontitis on success criteria such as alveolar bone levels, probing depth, and presence/absence of peri-implant mucositis. Based on the alveolar bone levels of the remaining dentition, it was demonstrated that patients with treated periodontitis yielded a higher prevalence of peri-implantitis than patients without bone loss. This was irrespective of the smoking habits. With increasing numbers of complications, implant loss also increased. Consequently, patients with treated periodontitis yielded lower success rates than those without bone loss in the residual dentition. This was especially noted in the maxilla.

A follow-up examination of a periodontally compromised patient cohort (n = 68) in the Ellegaard et al study also addressed the influence of the susceptibility to periodontitis on the survival of implants. With the presence of a peri-implant pocket of 6 mm or more, the hazard ratio for losing the implant was 2.5 (95% CI: 1.3 to 4.9). If there were fewer than 20 teeth present in these patients with treated periodontitis, the hazard ratio was 3.8 (95% CI:1.4 to 10.1).

3. Does the section agree with the interpretation and conclusion of the reviewers?

The section agrees with the conclusions of the smoking and diabetes aspects. However, the recently acquired evidence on the influence of treated periodontitis on long-term outcomes suggests that in partially edentulous patients, periodontitis has to be considered a risk factor for biological complications and hence, for potentially lower long-term survival rates.

4. What further research needs to be done relative to the PICO question?

In light of the difficulties encountered with the analysis of the data reported in the present and other systematic reviews on implant outcomes, it is imperative that—in the future—reproducible parameters be reported that will be amenable to proper statistical analysis. These include the report of:

- Probing depths around implants
- Levels of attachment related to a defined reference point on the implant
- Presence or absence of peri-implant mucositis
- Presence or absence of suppuration
- Radiographic bone levels
- Preferably such parameters should be assessed at various timepoints. To analyze the influence of

various potential risk factors on such parameters, the duration of studies has to be extended to at least 5 to 10 years. For comparison, the gathering of data is proposed at 3, 5, and 10 years.

The reporting of implant success rates defined with arbitrary cutoff values may not sufficiently describe the biological complications encountered, and hence may not differentiate between a stable state and developing pathologic processes. Likewise, the monitoring of peri-implant conditions during and after interceptive therapy requires assessment of parameters hitherto known in the periodontal literature. Instead of trying to define a "success" with categorizing variables, success should be understood to be an implant in function free from complications. This may include biological, mechanical, functional, and esthetic complications.

In analyzing some of the articles for this systematic review it was noticed that the definition of structural characteristics of bone as proposed by Lekholm and Zarb (1986) is highly subjective and not readily reproducible. Furthermore, the definition of "poor bone" or "soft bone" represents nonvalidated descriptions of the structural features and has not been demonstrated to be relevant predictors of implant outcomes. Objective criteria for assessing bone characteristics should be developed and validated. Likewise, the effect of systemic conditions affecting bone characteristics should be investigated.

A distinction between failures encountered during osseointegration (early failure rate) has to be made from those occurring during the life of an implant in function (late failure rate). In this respect, data up to 1 year following implant placement should be gathered to assess the initial osseointegration rate.

Future studies on the effect of smoking should include parameters of exposure level (eg, pack years and current and ongoing consumption levels, Comprehensive Smoking Index, Dietrich et al 2005). More research on the effects of smoking cessation protocols is needed and should be a priority.

Data regarding the incorporation (osseointegration) rate of implants in the patient with diabetes are nonexistent. Hence, as a priority, studies should be initiated to address this process with special emphasis on the control of diabetes (HbA-1C). Similarly, long-term studies involving diabetic patients should include collection of ongoing data related to the level of diabetic control (HbA-1C).

It would be beneficial to assess the long-term outcomes of implant/periodontitis patients who have not received routine preventive care and periodontal maintenance.

The maintenance of implant patients should be investigated to determine optimum frequency and modalities of maintenance care visits particularly in patients with these risk factors. The continuous monitoring of clinical and radiographic parameters is imperative.

In all such studies, frequency distributions in addition to means and standard deviations should be included in statistical analysis of the parameters.

Furthermore, it is necessary to study the confounding effects of the risk factors on implant outcomes (eg, patients with diabetes who also smoke; patients with periodontitis who also smoke and/or have diabetes).

5. How can the information from the systematic review be applied for patient management?

Although survival rates for implants after 5 and 10 years have been reported to exceed the 90% level, it has to be realized that implants are removed because of ongoing complications and progressively destructive processes of the peri-implant tissues. It is evident that risk factors such as those addressed in this systematic review may affect both the survival and complication rates of implants. This review has clearly identified that smoking is associated with lower incorporation and survival rates. This may be less relevant with microroughened-surface implants. However, all patients should be informed of this potentially increased risk. Smoking cessation should be encouraged prior to implant placement (Bain 1996).

However, the section agreed that the survival rates for implant placement in smokers, and in patients with treated periodontitis, are acceptable. Therefore, based on the literature reviewed, these conditions do not represent absolute contraindications for implant placement.

Clinicians should assess risks for each individual and consider factors such as the level of smoking exposure, the level of diabetes control in patients with diabetes, and the level of infection control in patients with periodontitis.

WEB ONLY

ARTICLES EXCLUDED FOLLOWING FULL-ARTICLE REVIEW FOR SMOKING:

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