History of Treated Periodontitis and Smoking as Risks for Implant Therapy

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Purpose: *The aim of this review was to evaluate a history of treated periodontitis and smoking, both alone and combined, as risk factors for adverse dental implant outcomes.* ***Materials and Methods:*** *A literature search of MEDLINE (Ovid) and EMBASE from January 1, 1966, to June 30, 2008, was performed, and the outcome variables* implant survival, implant success, occurrence of peri-implantitis *and* marginal bone loss *were evaluated.* ***Results:*** *Considerable heterogeneity in study design was found, and few studies accounted for confounding variables. For patients with a history of treated periodontitis, the majority of studies reported implant survival rates > 90%. Three cohort studies showed a higher risk of peri-implantitis in patients with a history of treated periodontitis compared with those without a history of periodontitis (reported odds ratios from 3.1 to 4.7). In three of four systematic reviews, smoking was found to be a significant risk for adverse implant outcome. While the majority of studies reported implant survival rates ranging from 80% to 96% in smokers, most studies found statistically significantly lower survival rates than for nonsmokers.* ***Conclusions:*** *There is an increased risk of peri-implantitis in smokers compared with nonsmokers (reported odds ratios from 3.6 to 4.6). The combination of a history of treated periodontitis and smoking increases the risk of implant failure and peri-implant bone loss.* Int J Oral Maxillofac Implants 2009;24(suppl):39–68

Key words: *implant success, implant survival, peri-implantitis, periodontitis, smoking, tobacco*

As an increasing number of patients receive implants to replace missing teeth lost due to periodontitis, the question arises as to whether a history of periodontitis affects implant outcomes. In addition, the effect of cigarette smoking must be considered with respect to implant loss, increased risk of peri-implant disease, and peri-implant marginal bone loss.

The aim of this review paper was to evaluate the association of cigarette smoking and a history of treated periodontitis with implant outcomes. The paper addresses the available evidence for these two factors, both alone and combined, as potential risk factors for adverse implant outcome.

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MATERIALS AND METHODS

Search Strategy

A literature search was performed of two databases—MEDLINE (Ovid) and EMBASE—from January 1, 1966, to June 30, 2008. The search strategy included the following terms ([*dental implants* or *oral implants* or *endosseous implants* or *implant-supported prosthesis*] AND [*smoking* or *tobacco*]) OR ([*dental implants* or *oral implants* or *endosseous implants* or *implant-supported prosthesis*] AND [*periodontitis* or *periodontal diseases* or *periimplant$*]). Articles in the English, French, and German languages were considered, and the search resulted in 1,491 articles. Titles and abstracts were screened, and the full texts of publications reporting implant outcomes in smokers, or in patients with a history of periodontitis, were obtained. The articles were then evaluated for adherence to one of the following inclusion criteria:

- Systematic reviews addressing smoking and/or history of treated periodontitis as a risk factor for adverse implant outcome
- Longitudinal or cross-sectional cohort studies reporting implant outcomes where the periodontal history/status of the subjects was clearly defined, ie, with a subgroup of patients with and without a history of treated periodontitis

- Longitudinal or cross-sectional studies reporting implant outcomes in patients with a history of treated periodontitis
- Longitudinal or cross-sectional cohort studies of implant outcomes where the smoking status/history of the subjects was clearly defined, ie, with subgroups of smokers and nonsmokers
- Longitudinal or cross-sectional studies reporting implant outcomes in smokers

Case series articles of fewer than 10 patients were excluded. In addition, the bibliographies of systematic review papers were hand searched.

Implant Outcomes

The following four outcomes were evaluated:

- *Implant survival.* This refers to the presence of an implant with or without complications. If reported, the time of implant loss was described as early (prior to loading) or late (after loading) loss. Where authors included additional criteria for implant survival, these descriptions were recorded. Implant survival was expressed as cumulative survival rates following life table analysis, or survival rates.
- *Implant success.* This refers to the presence of an implant in the absence of complications of either a biologic or technical nature. Various authors have proposed a range of success criteria. In this review all descriptions of success criteria were included. Implant success was expressed as cumulative success rates following life table analysis, or success rates.
- *Occurrence of peri-implantitis.*
- *Radiographic peri-implant marginal bone loss.*

RESULTS: HISTORY OF TREATED PERIODONTITIS

A total of 47 publications were included in this section of the review. Table 1 describes the characteristics of retrospective and prospective cohort studies (19 publications, 17 studies) including subgroups of patients with and without a history of treated periodontitis. Table 2 describes the characteristics of retrospective and prospective studies (20 publications, 18 studies) reporting on implant outcomes in patients with a history of treated periodontitis.

There have been eight recent systematic reviews addressing implant outcomes in patients with a history of treated periodontitis versus nonperiodontitis patients.[1–8] The systematic reviews vary in methodology and inclusion criteria. Two papers carried out meta-analyses,[3,6] while six reported that meta-analysis was not possible due to heterogeneity of study characteristics. Some systematic reviews assessed the quality and risk of bias in the included studies.[2,3,6,8] A high to medium level of bias was indicated. The studies included in the individual systematic reviews are identified in Tables 1 and 2.

Summary of Study Characteristics

The studies identified in this section of the review (Tables 1 and 2) vary considerably in study design, making comparisons of outcomes difficult. Variables found to be inconsistent among studies included patient population with respect to periodontal status, length of follow-up, survival data, success data, marginal bone loss, occurrence of peri-implantitis, confounding factors, maintenance care, implant characteristics, and surgical procedure for implant placement. Details follow below.

Patient Population with Respect to Periodontal Status. The definitions of periodontitis and nonperiodontitis patients differed among studies. For example, Hardt et al described an age-related bone score (history of radiographic bone loss) as a measure of susceptibility to periodontitis.[9] Other authors compared patients who had lost teeth due to periodontitis with patients who had lost teeth due to nonperiodontal reasons.[10,11] Three studies included immediate implants placed in patients with periodontitis and nonperiodontitis-related tooth extraction.[12–14]

Where a description of the type of periodontitis was given, the type of periodontal disease was usually described as chronic periodontitis. In other studies it was described as either chronic or aggressive periodontitis according to the current classification (International Workshop for Classification of Periodontal Diseases and Conditions 1999).[15] One study used the term *recalcitrant periodontitis*.[16] A number of studies did not report the type of periodontitis.

All studies indicated that patients in the periodontitis group received periodontal treatment prior to implant placement. However, the details of the treatment provided (surgical versus nonsurgical) and the periodontal status of the remaining teeth were infrequently reported.

Length of Follow-up. The length of follow-up varied from 6 months to 14 years. The majority of studies had medium-term follow-up of between 1 and 5 years. In nine studies patients were followed for 10 years or more.

Survival Data. Most studies reported implant survival as presence of retained implants over the observation period. A number of studies reported cumulative survival rates following life table analysis. Some studies reported implant survival from the time of implant placement, while others reported from the

Table 1 Cohort Studies, Including a Subgroup of Nonperiodontitis Patients (NP) and a Subgroup with a History of Treated Periodontitis (P), Evaluating a History of Treated Periodontitis as a Risk Indicator for Reduced Implant Survival and Success

Study (first author and year of publication)	Design	Patients studied	No. of patients	No. of implants	Implant survival	Implant success	Follow-up	Comments
Watson (1999)[26]	Prosp	P: CP NP	7 19	33 implants total	CSR 100% CSR 100%	CSR 100% CSR 58%	4 y	HA surface Success criteria: bone loss ≤ 4 mm, or bone loss < 1/3 of implant length Heavy smokers excluded (> 20 cigarettes per day) SPT: NR
Brocard (2000)[31] bcdef	Prosp	P NP	147 297	375 647	NR NR	CSR 74.7%* CSR 88.8%	7 y	TPS surface Success criteria: absence of pain, absence of infection, absence of mobility, absence of bone loss 132 smokers (light smokers 5 cigarettes per day) Regular SPT
Hardt (2000)[9] cdefh	Retrosp	P NP	25 25	100 92	92% 96.7%	NR NR	5 y	Turned surface Posterior maxilla History of periodontitis defined by age-related bone score Bone loss > 2 mm from time of abutment connection: P: 64%, NP: 24%, *P < .001 2 mm bone loss from abutment connection to 5 years: P: 62%, NP: 42%, P < .055 Smoking: NR SPT: NR
Karoussis (2003)[11] bcdefh	Prosp	P NP	8 45	21 91	CSR 90.5% CSR 96.5%	CSR 71.4%* CSR 94.5%	10 y	TPS surface (hollow screw) Incidence of peri-implantitis; NP: 5.8%, P: 28.6% * Clinical success (PD ≤ 5 mm, BOP negative) Regular SPT P: 47.6% of implants in smokers NP: 19.78% of implants in smokers No statistically significant difference in outcome between smokers and nonsmokers
Evian (2004)[19] def	Retrosp	P: CP NP	77 72	77 72	79.2%* 91.7%	NR NR	10 y	HA surface Immediate/delayed implant placement Implant failure defined as advanced bone loss, infection, or pain Implant failure was statistically significantly associated with a history of periodontitis Regular SPT Smoking: NR
Rosenberg (2004)[25] bdf	Retrosp	P NP	151 183	923 588	90.6% 93.7%	90.6% 93.7%	Up to 13 y	HA-coated, SLA, TPS, AE, turned surface Peri-implantitis reported as failure occurring after 1 y of loading A higher percentage of late failure (25.6%) occurred in P group compared to NP group (5.4%). This was more evident in the HA-coated implants SPT: 3 monthly Smoking: NR

Table 1 continued Cohort Studies, Including a Subgroup of Nonperiodontitis Patients (NP) and a Subgroup with a History of Treated Periodontitis (P), Evaluating a History of Treated Periodontitis as a Risk Indicator for Reduced Implant Survival and Success

Study (first author and year of publication)	Design	Patients studied	No. of patients	No. of implants	Implant survival	Implant success	Follow-up	Comments
Hanggi (2005)[30] g	Retrosp	P: AP P: CP NP	16 33 19	201 total	NR	NR	3 y	TPS, SLA surface Regular SPT 15 smokers Tendency for more bone loss in AP patients (P = .058) NS Smoking had no effect on bone loss Poor oral hygiene had a significant effect on bone loss
Mengel (2005)[32] bdefgh	Prosp	P: AP P: CP NP	15 12 12	77 43 30	95.7% 100% 100%	95.7% 100% 100%	3 y	Turned, AE surface Nonsmokers At baseline all treated periodontal patients had PPD ≤ 3 mm, no BOP Regular SPT More bone loss in AP group
Mengel (2005)[33] bgh	Prosp	P: AP NP	10 10	15 11	100% 100%	NR	3 y	Turned surface Nonsmokers Implants in AP group were placed in regenerated bone
Mengel (2007)[41]	Prosp	P: AP NP	5 5	36 7	91.67% 100%	83.3% 100%	10 y	Turned surface Regular SPT Smoking: NR Statistically significant greater bone loss in AP group
Ferreira (2006)[18] c	Retrosp	P NP	30 182	578 total	NR	NR	Mean 42 mo	Partially dentate patients Nonsmokers Patient level: 26.4% peri-implant health; 64.6% peri-implant mucositis; 8.9% peri-implantitis Implant level: 62.6% peri-implant mucositis; 7.44% peri-implantitis Multivariate analysis: increased risk for peri-implant disease History of periodontitis OR 3.1 (95% CI: 1.1 to 3.5) Gender (male) OR 2.7 (95% CI: 2.1 to 6.3) Plaque score OR 14.3 (95% CI: 9.1 to 28.7) Periodontal BOP ≥ 30% sites affected OR 3.3 (95% CI: 2.1 to 5.6) Uncontrolled diabetes OR 1.9 (95% CI: 1 to 2.2)
Roos-Jansåker (2006) [17]	Retrosp	P NP	94 62	NR	16 events* 2 events	NR	9–14 y	Statistically significant relationship between implant loss and periodontal bone loss at remaining teeth
Roos-Jansåker (2006) [29] cf								History of periodontitis significantly related to peri-implantitis OR 4.7 (95% CI: 1 to 22) No organized SPT 52 smokers
Wagenberg (2006)[14] c	Retrosp	P NP	891 total	122 1803	91.8%* 96.3%	NR	1–16 y	Turned, rough surface Immediate implant placement Immediate implants placed following extraction due to periodontitis were 2.3 times more likely to fail than following non-periodontitis extraction P = .02 No statistically significant difference between smokers and nonsmokers

Table 1 continued Cohort Studies, Including a Subgroup of Nonperiodontitis Patients (NP) and a Subgroup with a History of Treated Periodontitis (P), Evaluating a History of Treated Periodontitis as a Risk Indicator for Reduced Implant Survival and Success

Study (first author and year of publication)	Design	Patients studied	No. of patients	No. of implants	Implant survival	Implant success	Follow-up	Comments
Rosenquist (1996)[13] c	Retrosp	P NP	51 total	62 49	NR	92% 95.8%	1–67 mo (mean 30.5 mo)	Turned surface Immediate implant placement Success criteria: Albrektsson et al (1986) Incidence of infection occurred in 5 patients; in 4 patients the reason for tooth extraction was periodontitis
Cune (1996)[10]	Retrosp	P NP	102 233	375 total	NR	CSR 58% CSR 78%	Up to 3 y	Turned surface Definition of survival (interpreted as success) included absence of severe inflammation, progressive bone loss, chronic pain related to implant, injury of the mental nerve, implant mobility, damage of the implant beyond repair, implant loss; gingival index of 3 at any of the four assessed sites around the implant
Polizzi (2000)[12] ch Same cohort as Grunder (1999)[86] 3-year data	Prosp	P NP	143 total	62 49	NR	NR	5 y	Turned surface Regular SPT Smoking: NR Immediate implants (82%) or after a short healing period of 3 to 5 weeks (18%) Correlation between implant failure and periodontitis as a reason for tooth extraction 14 of 17 patients with failure had periodontitis-related extraction (not statistically significant) 3-year results show 10.2% of implants placed following tooth loss due to periodontitis failed
Cordaro (2005)[100] h	Retrosp	P NP	9 10	37 53	100% 98.2%	NR	24–94 mo	TPS, turned surface Implant-tooth-supported prostheses (rigid, nonrigid connection) Smoking reported Periodontal group < ⅔ of periodontal support remaining

CP = chronic periodontitis; AP = aggressive periodontitis; NR = not reported; SPT = supportive periodontal therapy; OR = odds ratio; BOP = bleeding on probing; TPS = titanium plasma sprayed; SLA = sandblasted large grit acid etched; HA = hydroxyapatite; AE = acid etched; Prosp = prospective; Retrosp = retrospective; CSR = cumulative survival/success rate.
*Statistically significant difference as reported by the author.
a Study included in systematic review by Van der Weijden et al.[8]
b Study included in systematic review by Karoussis et al.[11]
c Study included in systematic review by Schou et al.[6]
d Study included in systematic review by Quirynen et al.[4]
e Study included in systematic review by Klokkevold and Han.[3]
f Study included in systematic review by Ong et al.[2]
g Study included in systematic review by Al-Zahrani.[1]
h Study included in systematic review by Schou.[7]

Table 2 Studies Including Patients with a History of Treated Periodontitis Evaluating a History of Treated Periodontitis as a Risk Indicator for Reduced Implant Survival and Success

Study (first author and year of publication)	Design	No. of patients	No. of implants	Implant survival	Implant success	Follow-up	Comments
Nevins (1995)[16] de	Retrosp	59	132 Mandible 177 Maxilla	97% Mandible 98% Maxilla	NR	1–8 y	Recalcitrant periodontitis Turned surface Regular SPT
Ericsson (1986)[101] bh	Prosp	10	41	100%	NR	6–30 mo	Treated for advanced periodontitis Combined implant-tooth connection Turned surface Regular SPT Smoking: NR
Ellegaard (1997)[102] bdeh	Prosp	19 56	31 Tioblast 93 TPS	100% 97.8%	76.3% 57%	36 mo 60 mo	Treated periodontal patients with tooth loss due to periodontal disease Smokers 64% Regular SPT Success criteria: no bone loss ≥ 1.5 mm
Schwartz-Arad (1998)[103] h	Prosp	22	213	98.5% CSR	NR	5 y	Immediate implants/implant placement in healed sites Regular SPT
Daelemans (1997)[104] h	Retrosp	33	121	93%	NR	3–80 mo (mean 40 mo)	Tooth loss due to periodontitis Turned surface Implants in posterior maxilla + sinus lift and graft Smoking: NR Supra-structure 98% survival
Sbordone (1999)[105] bh	Prosp	25	42	100%	NR	3 y	Patients treated for moderate to advanced periodontitis AE surface Regular SPT Smoking: NR
Buchmann (1999)[106] h	Prosp	50	167	100%	NR	Up to 5 y	Sinus augmentation + simultaneous implant placement Turned surface Smoking: NR Regular SPT
Yi (2001)[107] deh	Prosp	39	125	100%	100%	3 y	Patients treated for severe periodontitis Turned surface Regular SPT Smoking: NR Success criteria PPD < 6 mm
Mengel (2001)[34] bdegh	Prosp	CP 5 AP 5	12 36	100% 94.4%	100% 88.8%	3 y 5 y	Regular SPT Smoking: NR Bone loss up to 3 y was significantly higher in AP patients
Leonhardt (2002)[35] Same cohort as Leonhardt (1993)[108] beh	Prosp	15	57	94.7%	NR	10 y	Partially dentate patients treated for advanced periodontitis Turned surface Regular SPT Smoking: NR 61% implant sites BOP Mean bone loss 1.7 ± 1.2 mm

Table 2 continued Studies Including Patients with a History of Treated Periodontitis Evaluating a History of Treated Periodontitis as a Risk Indicator for Reduced Implant Survival and Success

Study (first author and year of publication)	Design	No. of patients	No. of implants	Implant survival	Implant success	Follow-up	Comments
Feloutzis (2003)[75] h	Retrosp	90	182	96.15%	NR	2–12 y (mean 5.6 y after loading)	Chronic periodontitis TPS surface Regular SPT Smoking history reported (39 nonsmokers, 23 former smokers, 14 heavy smokers) IL-1 genotype recorded
Baelum (2004)[20] bdeh	Prosp	108 32	201 1-stage/TPS 57 2-stage/Tioblast	78% 97%	60% 69%	Up to 10 y	All patients had undergone periodontal surgery Regular SPT Smoking was associated with increased implant failure, HR = 2.6 Success criteria: bone loss < 1.5 mm Number of teeth remaining and % bone remaining at implant insertion influenced bone loss ≥ 3.5 mm
Wennström (2004)[109] bdeh	Prosp RCT	51	149	97.3%	NR	5 y	Partially dentate patients treated for moderate to advanced CP Turned surface/Tioblast Smokers 17 Regular SPT (individualized) Mean bone loss at 5 y: 0.41 mm No difference between implant surfaces
Jansson (2005)[74] h	Retrosp	766	1091 Maxilla 705 Mandible	97% 92%	NR	Up to 10 y	Turned surface Smoking reported Regular SPT Analysis of patients with implant failure and relationship to smoking and interleukin 1 (IL-1) genotype
Ellegaard (2006)[42] Same cohort as Ellegaard (1997)[102] bdh	Prosp	68	262	59% TPS 97% Tioblast	53% TPS 82.5% Tioblast	Up to 10 y	Tioblast TPS Non-grafted sinus implants/conventional implants Regular SPT 57% smokers Success criteria: bone loss < 1.5 mm Implant survival significantly influenced by: smoking, patient having ≥ 20 teeth
Malo (2007)[81]	Retrosp Prosp	81 103	165 268	91% CSR 96% CSR	NR NR	5 y 3 y	Turned, oxidized surface Immediate implant placement and function Smokers included Standardized surgical and maintenance protocol

Table 2 continued Studies Including Patients with a History of Treated Periodontitis Evaluating a History of Treated Periodontitis as a Risk Indicator for Reduced Implant Survival and Success

Study (first author and year of publication)	Design	No. of patients	No. of implants	Implant survival	Implant success	Follow-up	Comments
Machtei (2007)[80]	Prosp	20	49	90%	NR	1 y	Patients treated for CP; AE surface Immediate implant placement and immediate restoration/loading Regular SPT; Smokers included (4 patients)
Machtei (2008)[79]	Retrosp	56	79	83.5%	83.5%	7–78 mo	Previously failed implant sites All patients had a history of periodontitis Regular SPT; AE, turned surface; 3 of 15 implants (20%) in smokers failed 10 of 64 implants (15.6%) in nonsmokers failed. No statistically significant difference between implant survival in smokers and nonsmokers

CP = chronic periodontitis; AP = aggressive periodontitis; NR = not reported; SPT = supportive periodontal therapy; BOP = bleeding on probing; TPS = titanium plasma sprayed; SLA = sandblasted large grit acid etched; HA = hydroxyapatite; AE = acid etched; Prosp = prospective; Retrosp = retrospective; CSR = cumulative survival/success rate; PPD = pocket probing depth, HR = hazard ratio.
*Statistically significant difference as reported by the author.
a Study included in systematic review by Van der Weijden et al.[8] b Study included in systematic review by Karoussis et al.[11] c Study included in systematic review by Schou et al.[6] d Study included in systematic review by Quirynen et al.[4] e Study included in systematic review by Klokkevold and Han.[3] f Study included in systematic review by Ong et al.[2] g Study included in systematic review by Al-Zahrani.[1] h Study included in systematic review by Schou.[7]

time of loading. Some studies distinguished between early and late implant loss, while others reported on overall implant loss. The statistical unit of analysis was implant-based in the majority of studies, while others presented a patient-based analysis.[17–19]

Success Data. The definition of success varied among studies. Some studies defined their own success criteria using different thresholds for probing depths, bleeding on probing, and bone loss.[11,20,21] Other studies used published success criteria, based on clinical and radiographic parameters, as defined by various authors.[22–24] The baseline reference time point for success varied from the time of implant placement[25] to the time of loading[26] to 1 year of function.[11] Success was based on the implant as the unit of analysis for all studies.

Marginal Bone Loss. Marginal bone loss was recorded in most studies from the time of insertion of the prosthesis; however, Karoussis et al[27] measured from 1 year after loading. There were also variations in radiographic reference points due to the differences in implant designs. Few studies reported the use of standardized radiographs.

Occurrence of Peri-implantitis. Few studies reported on the occurrence of peri-implantitis, and definitions of peri-implantitis were inconsistent. Karoussis et al[11] reported on the incidence of peri-implantitis, whereas the other studies reported on the prevalence of implants or patients with peri-implantitis.[18,28]

Confounding Factors. There was inconsistency in reporting of, and adjustment for, confounding factors such as diabetes and smoking. Multivariate analyses accounting for confounding factors were performed in three studies.[17,18,29] Other studies performed univariate or bivariate analyses on smokers within the population.[11,30,31] Several studies eliminated smoking as a confounding factor by including only nonsmokers in the study population.[18,30,32,33]

Maintenance Care. The frequency of supportive periodontal therapy varied among studies and was not always reported. Furthermore, the maintenance regimen was infrequently described.

Implant Characteristics. The type of implant surface (turned, acid etched, hydroxyapatite coated, sandblasted acid etched, titanium plasma sprayed) and configuration (threaded implant, hollow screw, hollow cylinder) varied between studies.

Surgical Procedure for Implant Placement. There was variation between and within studies in the implant placement procedures with respect to the anatomical position of the implant, submerged or nonsubmerged placement, placement in regenerated bone, use of simultaneous bone-augmentation procedures, implant placement in conjunction with sinus

elevation, immediate implant placement, and immediate implant loading.

Main Findings of the Systematic Reviews

Ong et al (2008). This systematic review evaluated whether implant outcomes (survival, success, bone-level change, peri-implantitis) of partially dentate patients who had been treated for periodontitis were different from those of periodontally healthy patients.[2] Nine studies were included, but no meta-analysis was performed due to the heterogeneity of the chief study characteristics. Of the five studies presenting implant survival data, four reported higher implant survival for nonperiodontitis patients.[9,11,17,19] Two of these studies found a statistically significant difference in survival associated with the patient's periodontal status.[17,19]

Of the five studies presenting data on implant success, four reported more favorable results for patients without a history of periodontitis than for those with treated periodontitis.[11,25,31,32] Only one study, Karoussis et al,[11] showed statistical significance.

Occurrence of peri-implantitis was reported in three studies.[11,25,28] Roos-Jansåker et al[29] and Karoussis[11] reported a statistically significantly greater frequency of peri-implantitis in treated periodontitis patients than in nonperiodontitis patients.

Longitudinal radiographic bone loss around implants was associated with a history of treated periodontitis in all five studies reporting bone levels, but was statistically greater in only one study.[9]

The conclusions of this systematic review were that there is some evidence that patients treated for periodontitis may experience more implant loss and implant complications than nonperiodontitis patients. The authors concluded that the evidence was stronger for the effect on implant survival than for the effect on implant success.

Klokkevold and Han (2007). This study compared implant outcomes in patients with a history of treated periodontitis versus nonperiodontal patients.[3]

Implant Survival. A meta-analysis was performed combining results from three cohort studies[9,11,32] and reporting survival data for patients both with and without a history of periodontitis. No statistical difference in implant survival between the two patient groups was found. In a further meta-analysis, data from 10 studies including patients with a history of treated periodontitis were combined. The pooled estimate of implant survival was 0.95 (95% CI: 0.918 to 0.982), or 95%. When survival data from the three studies in nonperiodontitis patients were combined, the pooled estimate was 0.971 (95% CI: 0.948 to 0.994), or 97% survival at the last reported visit.

Implant Success. In a further meta-analysis including four cohort studies,[11,19,31,32] a statistically significant difference in success rates of implants placed in patients with and without a history of treated periodontitis was found ($P = .013$). The pooled estimate of the difference in implant success rates was 0.1105 (95% CI: –0.2006 to –0.0203). In other words, there was an 11.05% better implant success for patients without a history of periodontitis. Eight studies with implant success data in patients with a history of treated periodontitis were combined in a meta-analysis to give a pooled estimate of 0.89 (95% CI: 0.823 to 0.957), or 89% success. Four studies with success data in healthy patients were combined in a meta-analysis resulting in a pooled estimate of 0.892 (95% CI: 0.812 to 0.972), or 89% implant success. The authors concluded that a history of treated periodontitis does not seem to adversely affect implant survival, but that these patients may experience more complications and a lower success rate, particularly over longer periods.

Karoussis et al (2007). This review identified seven short-term (< 5 years) and eight long-term (≥ 5 years) prospective studies addressing the prognosis of osseointegrated implants in partially dentate patients with a history of treated periodontitis.[5] No meta-analysis was performed. Four of the 15 studies were cohort studies including both periodontitis and nonperiodontitis patients.[11,25,31,32] The authors concluded that there were no statistically significant differences in either short-term or long-term implant survival between patients with a history of treated periodontitis and nonperiodontitis patients. When evaluating success criteria, the authors concluded that patients with a history of treated chronic periodontitis exhibited significantly greater long-term probing pocket depth and marginal bone loss and a higher incidence of peri-implantitis compared with periodontally healthy subjects.

Quirynen et al (2007). This systematic review investigated the relationship between susceptibility to periodontitis and peri-implantitis.[4] Seventeen studies were included in the review; however, no meta-analysis was possible due to heterogeneity of study designs. Four of the five cohort studies comparing patients with and without a history of treated periodontitis reported a higher incidence of late implant loss and/or marginal bone loss in patients with a history of treated periodontitis. When implants with a very rough surface were used[11,19,25] or when supportive periodontal therapy was not provided,[9] the number of implant losses was almost three times higher for patients with a history of treated periodontitis. The authors concluded that in patients with a history of treated periodontitis who had implants with minimally/moderately rough surfaces and

received supportive periodontal therapy, the implant failure rates and marginal bone loss remained low. The authors also discussed that due to the lack of assessment of confounding factors (such as smoking, oral hygiene, and diabetes), definitive conclusions could not be drawn.

Schou et al (2006). This systematic review[6] included two controlled studies with at least 5 years of follow-up assessing the outcome of implant therapy in patients with previous tooth loss due to periodontitis.[9,11] Data from a total of 33 patients with tooth loss due to periodontitis and 70 patients with nonperiodontitis-associated tooth loss were combined in meta-analyses. There was no significant difference in the survival of implants after 5 and 10 years. However, there were significantly more patients with peri-implantitis in the group with periodontitis-associated tooth loss during the 10-year follow-up period, with a risk ratio of 9 (95% CI: 3.94 to 20.57). There was also significantly more marginal bone loss observed in patients with periodontitis-associated tooth loss after 5 years, with a mean difference of 0.5 mm (95% CI: 0.0 to 0.94). The authors concluded that the results of the analyses should be interpreted with caution due to the small sample size and the fact that quality assessment of both studies revealed a high risk of bias.

Schou (2008). This subsequent systematic review by Schou[7] included prospective and retrospective studies assessing implant treatment in partially and totally edentulous patients with a history of periodontitis-associated tooth loss and at least 1 year of follow–up. Studies evaluated implant outcomes, suprastructure outcomes, and the health status of periodontal tissues. The authors concluded that while implant survival is high in individuals with periodontitis-associated tooth loss, the high incidence of peri-implantitis might jeopardize the long-term outcome of implant treatment in periodontitis-susceptible patients.

Van der Weijden et al (2005). This systematic review evaluated the long-term (≥ 5 years) outcomes of implants placed in partially edentulous patients with a history of treated periodontitis.[8] Of the four selected papers, two were cohort studies,[9,11] and two were observational studies evaluating only patients with a history of treated periodontitis.[34,35] Meta-analysis was not performed. The authors concluded that implant survival and success might be different in patients with and without a history of treated periodontitis.

Al-Zahrani (2008). This systematic review addressed the survival and success of implants placed in patients treated for aggressive periodontitis.[1] Nine studies were included, four of which were case reports including fewer than 10 patients.[36–39] The remaining five studies included one short-term observational report[40] and four comparative studies.

Of the four comparative studies, Mengel et al[34] reported on survival of 36 implants in five patients treated for generalized aggressive periodontitis (followed for 5 years) and 12 implants placed in five patients treated for advanced chronic periodontitis (followed for 3 years). The implant survival was 100% for the chronic periodontitis patients and 89% for the aggressive periodontitis patients. There was significantly more bone loss around implants in the aggressive periodontitis patients.[34]

Mengel and Flores-de-Jacoby[32] compared survival of implants placed in 12 periodontally healthy patients, 12 patients treated for chronic periodontitis, and 15 patients treated for aggressive periodontitis. The 3-year survival rate was 100% for implants placed in healthy and chronic periodontitis patients and 97.4% in aggressive periodontitis patients.[32]

In another publication, Mengel and Flores-de-Jacoby[33] compared 10 patients with treated aggressive periodontitis who had implants placed in regenerated bone, and 10 periodontally healthy patients who had implants placed in nonregenerated bone. The authors reported 100% survival after 3 years, with more bone loss around implants in the treated aggressive periodontitis patients.[33]

Hanggi et al found a trend for more marginal bone loss at implants placed in patients treated for aggressive periodontitis than at implants placed in patients treated for chronic periodontitis or nonperiodontal patients.[30]

In summary, two of the four comparative studies reported lower implant survival rates, and three of four studies reported more bone loss, for implants in patients with a history of treated aggressive periodontitis. The authors concluded that implant outcomes in patients with a history of treated aggressive periodontitis are less favorable than those in nonperiodontal patients.

Main Findings of Cohort Studies in Patients With and Without a History of Treated Periodontitis (Table 1)

Of the 11 studies presenting implant survival data, nine reported higher survival in patients without a history of periodontitis. Three cohort studies found statistically significantly lower implant survival rates in patients with a history of treated periodontitis than in patients with no history of periodontitis.[14,17,19]

Implant survival in patients with a history of treated periodontitis ranged from 79.2% to 100%. The majority of studies reported survival rates > 90% in patients with a history of treated periodontitis.

Of the eight studies presenting implant success data, seven reported higher implant success for patients without a history of treated periodontitis. Only one study found a statistically significant difference in implant success between patients with and without a history of treated periodontitis.[11]

Implant success in patients with a history of treated periodontitis ranged from 58% to 100%.

Of the four studies that reported on peri-implantitis,[11,18,25,29] three found a statistically significantly greater risk of peri-implantitis in patients with a history of treated periodontitis.[11,18,29] Reported odds ratios ranged from 3.1 to 4.7.

Longitudinal radiographic bone loss around implants was associated with a history of treated periodontitis in all seven studies reporting bone levels, and was statistically significantly greater compared to patients without a history of treated periodontitis in two studies.[9,41]

Four studies including a total of 46 patients with a history of treated aggressive periodontitis reported greater marginal bone loss compared to patients without a history of treated periodontitis.[30,32,33,41]

Main Findings of Prospective and Retrospective Studies in Patients with a History of Treated Periodontitis (Table 2)

Implant survival in patients with a history of treated periodontitis ranged from 59% to 100%.

The majority of studies (17 of 18) reported high implant survival rates ≥ 90% for implants with turned or moderately rough surfaces.

All studies reported regular supportive periodontal therapy.

In the two studies where both very rough surface and moderately rough surface implants were used, lower survival rates (59% to 78%) were observed for the implants with very rough surfaces.[20,42] Only six studies reported implant success data, ranging from 53% to 100%. Success criteria differed between studies.

RESULTS: SMOKING

A total of 88 publications were included in the review of the evidence available for smoking as a risk factor for adverse implant outcomes. Table 3 describes the characteristics of the 59 cohort studies evaluating implant outcomes in a subgroup of smokers and nonsmokers. Study design, sample sizes, and implant outcomes expressed as survival and success rates are described. Risk of failure in smokers, expressed as odds ratios for implant-related data and patient-related data, both with and without augmentation procedures, are presented. Where odds ratios are presented, they were obtained from the original paper or from the systematic reviews if indicated.

Table 4 includes seven studies evaluating smoking as a risk for peri-implantitis and soft tissue complications. Table 5 includes 22 prospective or retrospective studies evaluating smoking as a risk for peri-implant bone loss.

Four recent systematic reviews, all including meta-analyses, have evaluated cigarette smoking as a risk factor for adverse implant outcome. Three of the four reviews found smoking to be a significant risk factor.[3,43,44] The studies included in the individual systematic reviews are identified in Table 3.

Summary of Study Characteristics

Variation in study design, inclusion criteria, and data analyses makes it difficult to compare the studies presented in Tables 3, 4, and 5. The following study characteristics contributed to the heterogeneity among studies: study design, the patient population with respect to smoking status, length of follow-up, survival data, success data, peri-implant marginal bone loss, occurrence of peri-implant disease, confounding factors, maintenance care, implant characteristics, and procedures for implant placement. Details follow below.

Study Design. The majority of studies were retrospective in design, while 14 were prospective. Retrospective studies have less validity than prospective clinical trials due to issues of selection bias and confounding factors. Furthermore, retrospective studies rely on the completeness of data entered in the patient's chart.

Patient Population with Respect to Smoking Status. The studies used a range of definitions for smokers, nonsmokers, and former smokers. In some studies smokers were defined as smoking one or more cigarettes per day, while other studies used a threshold of 10 cigarettes per day. Other studies had categories of smoking including light, moderate, and heavy, depending on the number of cigarettes smoked per day. One study classified nonsmokers as subjects who had never smoked or who had stopped smoking at least 1 year before implant treatment.[45]

Length of Follow-up. The length of follow-up varied from before implant loading up to 20 years. The majority of studies had a follow-up time of between three and six years.

Survival Data. Most studies reported implant survival as presence of retained implants over the observation period. However, Bain and Moy, in one of the first studies to report a significant difference in implant survival between smokers and nonsmokers, defined implant failure as implant loss or bone loss greater than 50% of the implant length.[46] A number of studies

Table 3 Cohort Studies, Including a Subgroup of Smokers (S) and Nonsmokers (NS), Evaluating Smoking as a Risk Indicator for Reduced Implant Survival and Success

Study (first author and year of publication)	Design	Patients studied	No. of patients	No. of implants	Implant survival	Implant success	Follow-up	Comments
Bain (1993)[46] abc	Retrosp	S NS	540 total	390 1,804	89%* 95%	NR	Up to 6 y	Turned surface Failure defined as implant loss or bone loss > 50% implant length Implant data without taking into consideration augmentation (b) OR 2.54 (95% CI: 1.74 to 3.72) *P* = .0001
De Bruyn (1994)[49] abc	Retrosp	S NS S NS	16 45	78 166	91.83% 98.8% 86.06% 97.58%	NR	Prior to loading 1 y	Maxilla Turned surface Implant data without taking into consideration augmentation (b) OR 5.46 (95% CI: 1.57 to 19.02) *P* = .014 Patient-related data without augmentation (b) OR 6.89 (95% CI: 1.54 to 31.57) *P* = .013
Gorman (1994)[50] ab	Retrosp	S NS	82 228	646 1,420	93.5%* 96.7%	NR	Prior to loading	Surface: NR Implant data without taking into consideration augmentation (b) OR 2.03 (95% CI: 1.32 to 3.11) *P* = .001 Patient-related data without augmentation (b) OR 2.92 (95% CI: 1.46 to 5.86) *P* = .057
Wang (1996)[84] ac	Retrosp	S NS	30 total	14 69	84.62% 84.29%	84.62% 84.29%	3 y	HA/turned surface No statistically significant difference in survival between S and NS OR 0.98 (95% CI: 0.19 to 5.02) *P* = 15.66
Bain (1996)[78] ac	Prosp	S SQ NS	78 total	13 34 176	61.54% 88.24% 94.32%	NR	< 1 y	Turned surface SQ: Smoking cessation protocol Implant data without taking into consideration augmentation (b) OR 3.93 (95% CI: 1.50 to 10.34) *P* = .007
Minsk (1996)[111] ac	Retrosp	S NS	380 total	157 570	89.17% 90.88%	NR	6 y	Turned surface, TPS, AE 80 different operators OR 1.21 (95% CI: 0.68 to 2.16) *P* = .49
Watson (1998)[112] c	Prosp	S NS	43 total	64 75	NR	52% CSR 87% CSR	3–6 y	HA surface, cylindrical implants Overdentures Success criteria: ≤ 4 mm bone loss
Minsk (1998)[113] bd	Retrosp	S NS	116 total	126 324	90.47% 92.59%	NR	7 y	Postmenopausal women Implant data without taking into consideration augmentation (b) OR 1.46 (95% CI: 0.9 to 2.36) *P* = .079
Grunder (1999)[86] bc	Prosp	S NS	19 55	55 164	100% 98.2%	NR	5 y	AE surface No statistically significant difference between S and NS All failures prior to loading Implant data without taking into consideration augmentation (b) OR 0.42 (95% CI: 0.05 to 3.41) *P* = .357
Keller (1999)[60] abc	Retrosp	S NS/FS	8 20	32 73	60.7% 94.5%	NR	12 y	Turned surface Sinus graft and implant placement OR 2.03 (95% CI: 0.59 to 7.03) *P* =.210 (b)

Table 3 continued Cohort Studies, Including a Subgroup of Smokers (S) and Nonsmokers (NS), Evaluating Smoking as a Risk Indicator for Reduced Implant Survival and Success

Study (first author and year of publication)	Design	Patients studied	No. of patients	No. of implants	Implant survival	Implant success	Follow-up	Comments
De Bruyn (1999)[85] ab	Prosp	S NS	10 13	30 32	80% 71.9%	NR	7 y	Turned surface Maxilla No statistically significant difference between S and NS Implant data without taking into consideration augmentation (b) OR 0.64 (95% CI: 0.19 to 2.08) *P* = .327 Patient-related data without augmentation (b) OR 0.29 (95% CI: 0.04 to 1.94) *P* = .195
Jones (1999)[114] abc	Retrosp	S NS	19 44	126 217	91.27%* 97.7%	NR	5 y	HA-coated/TPS surface Implant data without taking into consideration augmentation (b) OR 4.06 (95% CI: 1.38 to 11.96) *P* = .007 Patient-related data without augmentation (b) OR 12.2 (95% CI: 2.24 to 66.88) *P* = .012
Wilson (1999)[115]	Retrosp	S NS	27 35	NR	NR	NR	Up to 10 y	Turned, TPS surface 27 patients with implant loss compared to 38 patients with no loss Implant failure defined as implant loss or 50% bone loss Smoking was statistically significantly related to implant failure with a RR of 2.5 (95% CI: 1.12 to 5.56) *P* = .025
Watson (1999)[26]	Prosp	S NS	26 total	10 23	100% 100%	70% 91.3%	3–4 y	HA surface, cylindrical implants Single-implant restorations Success criteria: ≤ 4 mm bone loss
Berge (2000)[47] b	Prosp	S NS	NR	61 55	65.5%* 87.2%	NR	Mean 11.4 y	Ceramic implants Implant data without taking into consideration augmentation (b) OR 3.60 (95% CI: 1.39 to 9.33) *P* = .005
Schwartz-Arad (2000)[116] b	Retrosp	S NS	43 total	6 50	83% CSR 90% CSR	NR NR	Up to 5 y (mean 15 mo)	Immediate implants in molar sites 15 teeth extracted due to periodontitis HA/turned surface No statistics performed between NS and S Implant data without taking into consideration augmentation (b) OR 1.80 (95% CI: 0.17 to 18.64) *P* = .511
Wallace (2000)[56] ab	Retrosp	S NS	17 39	72 115	83.33% 93.04%	NR	4 y	Turned surface Implant data without taking into consideration augmentation (b) OR 2.68 (95% CI: 1.04 to 6.91) *P* = .037 Shorter implants (≤ 10 mm) more susceptible to failure in smokers
Lambert (2000)[55] abc	Prosp	S NS/FS	NR	959 1,928	91.14%* 94.01%	NR	3 y	HA-coated/noncoated Early implant failure: implants in smokers 2.6 times more likely to fail from time of uncovering to before insertion of prosthesis Implant data without taking into consideration augmentation (b) OR 1.53 (95% CI: 1.14 to 2.05) *P* = .004
Olson (2000)[64] b	Retrosp	S FS NS	29 total	51 30 35	94.1% 96.6% 100%	NR	5–71 mo	HA, turned surface Sinus grafts and simultaneous or staged implant placement Failures associated with smoking history (b) OR 9.45 (95% CI: 1.14 to 78.11) *P* = .014

Table 3 continued Cohort Studies, Including a Subgroup of Smokers (S) and Nonsmokers (NS), Evaluating Smoking as a Risk Indicator for Reduced Implant Survival and Success

Study (first author and year of publication)	Design	Patients studied	No. of patients	No. of implants	Implant survival	Implant success	Follow-up	Comments
Geurs (2001)[61] abc	Retrosp	S NS/FS	NR	62 267	88.71%* 95.34%	NR	3 y	Sinus graft and implant placement (b) OR 2.6 (95% CI: 0.99 to 6.83) *P* = .051
Widmark (2001)[62] abc	Prosp	S NS Sinus graft: S NS	8 12 3 13	44 53 23 78	79.55% 88.68% 26.09% 89.75%	NR	3–5 y	Turned surface Severely resorbed maxilla Maxilla/± sinus graft Implant data without taking into consideration augmentation (b) OR 5.30 (95% CI: 2.53 to 11.12) *P* = .0001 Nongrafted sites Maxilla (b) OR 2.01 (95% CI: 0.65 to 6.18) *P* = .169 Grafted sites (b) OR 20.0 (95% CI: 6.33 to 63.2) *P* = .0001
Kronström (2001)[59] b	Retrosp	S NS	12 68	NR	NR	NR	Up to second-stage surgery	Turned surface Smokers (10 to 20 cigarettes/day) Early implant failure 40 patients with early implant failure and 40 patients with no failure. No significant difference between smokers and nonsmokers in implant failure. 9 of the 12 smokers had implant failure (75%) 31 of the 68 nonsmokers had implant failure (45.5%) Patient-related data without augmentation (b) OR 3.58 (95% CI: 0.89 to 14.39) P = .057
Mayfield (2001)[63] b	Retrosp	S NS	3 12	13 42	43% 100%	43% 100%	4–6.5 y	Turned, TPS surface Implants placed in augmented and non-augmented bone All failed implants were in augmented bone in 2 smokers (b) Patient-related data OR 41.7 (95% CI: 3.56 to 486.9) *P* = .001
Eckert (2001)[117]	Retrosp	S NS	55 total	7 68	NR	NR	Mean 10 mo	Turned surface Multivariate Cox analysis Implant failure Current smoker: HR 2.4 History of smoking: HR 0.8
Kan (2002)[45] abc	Retrosp	S NS/FS	16 44	70 158	82.86% 93.04%	65.30% 82.70%	Up to 5 y	HA/turned surface Grafted sinus and implant placement (simultaneous and staged approach) (b) OR 2.76 (95% CI: 1.16 to 6.62) *P* = .02
Schwartz-Arad (2002)[66] ab	Retrosp	S NS	89 172	380 402	96% 98%	44% 69%	Up to 3 y	Surface: NR Immediate and delayed implant placement Success: Number of complications including cover screw exposure Implant data without taking into consideration augmentation (b) OR 2.66 (95% CI: 2.66 to 3.48) *P* = .0001
Kumar (2002)[57] b	Prosp	S NS	72 389	269 914	97% 98.4%	97% 98.4%	Prior to loading	Smokers: ≥ 10 cigarettes/day SLA surface Early implant failure: Implant data without taking into consideration augmentation (b) OR 1.84 (95% CI: 0.77 to 4.38) *P* = .164

Table 3 continued Cohort Studies, Including a Subgroup of Smokers (S) and Nonsmokers (NS), Evaluating Smoking as a Risk Indicator for Reduced Implant Survival and Success

Study (first author and year of publication)	Design	Patients studied	No. of patients	No. of implants	Implant survival	Implant success	Follow-up	Comments
van Steenberghe (2002)[51] b	Prosp	S NS	NR	156 1,107	94.87% 98.28%	NR	Up to abutment connection	Turned surface Early implant failure: One-third of early implant failures occurred in smokers Implant data without taking into consideration augmentation (b) OR 3.0 (95% CI: 1.33 to 7.20) $P = .013$
Ortorp (2002)[118] b	Prosp	S NS	43 83	729 total	NR	NR	3 y	Turned surface 10 of 15 patients with failures were smokers Smokers experienced significantly more failures than nonsmokers ($P < .006$) Patient-related data without augmentation (b) OR 4.73 (95% CI: 1.50 to 14.9) $P = .007$
Penarrocha (2002)[87] b	Retrosp	S NS	34 80	441 total	NR	NR	3 y	TPS surface 7 of the 34 smokers had implant failures 10 of the 80 nonsmokers had implant failures Patient-related data without augmentation (b) OR 1.82 (95% CI: 0.63 to 5.25) $P = .203$
Chuang (2002)[125]	Retrosp	S NS	57 497	2,349 total	NR	NR	Up to 8 y	HA, TPS surface Patients with a history of periodontitis Univariate analysis: Implant failure HR 2.7 Multivariate Cox regression analysis Implant failure HR 3.1
Beschnidt (2003)[88] b	Prosp	S NS	76 total	51 163	92.15% 93.25%	NR	3 y	Turned surface No significant difference between smokers and nonsmokers Implant data without taking into consideration augmentation (b) OR 1.18 (95% CI: 0.36 to 3.87) $P = .789$
Karoussis (2003)[11] abc	Prosp	S NS	12 41	28 84	92.86% 96.24%	64.28% 77.38%	10 y	TPS surface hollow screw No significant difference between S and NS for survival, success or incidence of biologic complications Patients with and without history of periodontitis were included Implant data without taking into consideration augmentation (b) OR 2.08 (95% CI: 0.33 to 13.12) $P = .367$
Baelum (2004)[20]	Retrosp	140	258	NR	NR	NR	10 y	TPS surface Regular SPT Cox proportional hazard model Implant failure HR smoking 2.6 (95% CI: 0.9 to 7.6)
Ortorp (2004)[120] Same cohort as Ortorp (2002)[118]	Prosp	S NS	43 83	729 total	97.67%* 99.04%	NR	5 y	Edentulous patients Turned surface Statistically significantly more implants failed in smokers than nonsmokers on the patient level ($P < .01$) as well as on the implant level ($P < .05$)

Table 3 continued Cohort Studies, Including a Subgroup of Smokers (S) and Nonsmokers (NS), Evaluating Smoking as a Risk Indicator for Reduced Implant Survival and Success

Study (first author and year of publication)	Design	Patients studied	No. of patients	No. of implants	Implant survival	Implant success	Follow-up	Comments
Kourtis (2004)[121]	Retrosp	S NS	405 total	853 839	NR	NR	Up to 12 y (mean 4.6 y)	TPS surface Regular recall 10% immediate implants Significantly greater implant loss in smokers $P < .001$
van Steenberghe (2004)[67] b	Prosp	S NS	13 32	150 total	NR	NR	1 y	Immediate implant loading Turned surface 2 of 13 smokers (15.3%) had implant failures 4 of 32 nonsmokers (12.5%) had implant failures Patient-related data without augmentation (b) OR 1.27 (95% CI: 0.2 to 7.97) $P = .567$
Moheng (2005)[122] b	Prosp	S NS	15 78	266 total	NR	NR	1 y	TPS 4 of 15 smokers had failures 3 of 78 nonsmokers had failures $P < .01$ Multivariate analysis: Implants were more likely to fail in smokers RR 14.4 Patient-related data without augmentation (b) OR 9.09 (95% CI: 1.79 to 46.18) $P = .012$
Moy (2005)[123]	Retrosp	S NS	173 967	4,680 total	NR	NR	6 mo–21 y	Turned surface Univariate analysis: Implant failure RR 1.56 ($P = .03$) Stepwise logistic regression: Implant failure RR 1.39 ($P = .03$)
Jansson (2005)[74]	Retrosp	S NS	10 12	40 66	65% 72.73%	NR	10 y	Smoking did not significantly affect implant survival Authors reported a trend toward higher implant loss in smokers: 14 of 40 implants were lost in smokers 18 of 66 implants were lost in nonsmokers Synergistic effect of smoking and IL-1 genotype
Lemmerman (2005)[89]	Retrosp	S NS	30 346	1,003 total	NR	NR	Up to 15 y	Turned, AE surface, TPS ± bone augmentation, sinus elevation No statistical correlation between smoking and implant failure Authors reported a trend toward more failures in heavy smokers (data not shown)
Wagenberg (2006)[14]	Retrosp	S NS	891 total	323 1,602	94.4% 96.3%	NR	6 y (mean 71 mo)	Immediate implant placement ± graft ± immediate loading Turned/rough surface No significant difference between S and NS ($P = .342$) No difference in implant survival between rough and turned surface implants in smokers

Table 3 continued Cohort Studies, Including a Subgroup of Smokers (S) and Nonsmokers (NS), Evaluating Smoking as a Risk Indicator for Reduced Implant Survival and Success

Study (first author and year of publication)	Design	Patients studied	No. of patients	No. of implants	Implant survival	Implant success	Follow-up	Comments
Ellegaard (2006)[42]	Retrosp	S NS	68 total	262 total	NR	NR	Up to 10 y	Nongrafted sinus implants TPS, Tioblast surface Patients with a history of periodontitis Regular SPT Implant failure: HR smoking = 2.2
DeLuca (2006)[69]	Retrosp	S NS/FS S NS/FS	104 285 104 285	494 1,045	94.74%* 96.94% 96.1% 98.02%	NR	Prior to loading 20 y	Turned surface Multivariate survival analysis: Smoking at time of surgery was a significant factor Early failure RR 1.69 Late failures: A positive smoking history (> 25 pack years) was a significant factor for late implant failures OR 2.01 Multivariate survival analysis: Smoking history was a statistically significant factor RR 1.91 Patients who were smokers at the time of surgery had a statistically significantly higher overall failure rate (23.08%) than nonsmokers (13.33%)
Roos-Jansåker (2006)[17] Roos-Jansåker (2006)[29]	Retrosp	S FS NS	57 81 80	999 total	NR	NR	9–14 y	Smoking was associated with: Peri-implant mucositis (OR 2.8) Bone loss (OR 10) Peri-implantitis (OR 4.6) Smoking was not statistically significantly associated with implant failure
Noguerol (2006)[52]	Retrosp	S > 20 S 10–20 S < 10 NS	316 total	239 166 184 521	89% 98.2% 96.2% 95.8%	NR	10 y	Turned surface Early implant failure Bivariate model: Smoking had a statistically significant effect on early implant failure Multivariate model: Early implant failure: smoking > 20 cigarettes per day OR 2.5 (95% CI: 1.3 to 4.79) Perio and nonperio patients included: Analysis showed a tendency for more early failures in patients treated for periodontitis
Peleg (2006)[65]	Retrosp	S NS	226 505	627 1,505	97.4% 98.1%	NR	9 y	HA, rough surface Sinus augmentation and simultaneous implant placement No statistically significant difference in implant failure between smokers and nonsmokers
Mundt (2006)[72]	Retrosp	S FS NS	159 total	215 247 294	85% 90.4% 96.4%	NR	120 mo	Statistically significant difference between NS and FS ($P = .036$) NS and S ($P < .001$) FS and S ($P = .003$) Multifactorial Cox regression model for 1 implant per patient: Significant association between duration of smoking and increased risk of implant failures ($P = .036$) Cox regression analysis considering correlation of implant observations within the same patient: Smoking duration was significant ($P = .004$) Clustering of failures within smokers

Table 3 continued Cohort Studies, Including a Subgroup of Smokers (S) and Nonsmokers (NS), Evaluating Smoking as a Risk Indicator for Reduced Implant Survival and Success

Study (first author and year of publication)	Design	Patients studied	No. of patients	No. of implants	Implant survival	Implant success	Follow-up	Comments
Doyle (2007)[124]	Retrosp	S NS	10 186	10 186	72.9%* 95%	48.5*% 74.8%	1 y	Single implants Included immediate implant placement Smokers had significantly fewer successes and more failures
Aykent (2007)[125]	Retrosp	S NS	34 total	38 68	89.48% 100%	CSR 75.8% CSR 97.7%	Up to 12 y	HA, TPS surface (hollow screw/hollow cylinder/solid screw) Overdentures and fixed prostheses Smokers recorded as smoking > 10 cigarettes per day Success criteria—no biologic complication Deeper probing depths and higher sulcus bleeding index in smokers ($P < .05$)
Alsaadi (2007)[53]	Retrosp	S < 10 S 10–20 S > 20 NS	2,004 total	227 320 369 6,030 6,946 total	95.15% 94.69% 92.95% 96.72%	NR	Up to abutment connection 6 mo	Turned surface Early implant failure A significant difference between heavy smoking (> 20 cigarettes/day) and no smoking groups OR 2.72 (95% CI: 1.63 to 4.54) $P < .001$
Sanna (2007)[68]	Prosp	S NS	13 17	212 total	81.2% CSR 98.9% CSR	NR	5 y	Flapless placement /immediate loading Oxidized surface Smoking defined as > 10 cigarettes per day
Machtei (2007)[80]	Prosp	S FS NS	4 3 13	13 6 30	90% overall	NR	1 y	Patients with a history of periodontitis AE surface Smoking did not significantly affect implant outcome
Streitzel (2007)[110]	Prosp	S NS	15 118	59 short implants total	80%* 100%	NR	Up to 55 mo	Short implants (11 mm, 9 mm) ± augmentation AE surface Significant influence of smoking on implant survival for short implants
Sanchez-Perez (2007)[70]	Retrosp	S LS MS HS NS	40 23 11 6 26	95 44 25 26 70	84.2% 90.9% 88% 69.23% 98.57%	NR	5 y	AE surface Regular follow-up Statistically significant difference in implant failure among groups except between HS and MS S/NS OR 13.1 LS/NS OR 7.0 MS/NS OR 9.5 HS/NS OR 31.1
Alsaadi (2008)[53]	Prosp	S NS	283 total	95 623	94.44% 98.88%	94.44% 98.88%	Up to abutment connection 6 mo	Oxidized surface Early implant failure Authors reported smokers had a tendency for more early implant failures than nonsmokers No statistically significant difference.
Alsaadi (2008)[54]	Retrosp	S < 10 S 10–20 S > 20 NS	19 20 22 351	1,514 total	89.86% 85.45% 93.94% 93.8%	NR	2 y	Turned/oxidized surface Smoking habits were not statistically significant in relation to implant loss $P = .28$

Table 3 continued Cohort Studies, Including a Subgroup of Smokers (S) and Nonsmokers (NS), Evaluating Smoking as a Risk Indicator for Reduced Implant Survival and Success

Study (first author and year of publication)	Design	Patients studied	No. of patients	No. of implants	Implant survival	Implant success	Follow-up	Comments
Sverzut (2008)[58]	Retrosp	S NS	76 5,741	197 1,431	97.19% S 96.62% NS	NR	Before loading	Univariate and bivariate analysis showed no statistical significance for early implant failure in conjunction with smoking
Machtei (2008)[79]	Retrosp	S NS FS	15 35 6	79 total	80% 84.4%	NR	7–78 mo (mean 29.9 ± 2 mo)	Previously failed implant sites AE, turned surface History of periodontitis Regular SPT 3 of 15 implants (20%) in smokers failed 10 of 4 implants (15.6%) in nonsmokers failed No significant difference between implant survival in smokers and nonsmokers ($P = .48$)
Anitua (2008)[126]	Retrosp	S NS	221 839	1,299 4,488	98.9%* 99.3%	NR	2–59 mo (median 54 mo)	Moderately rough surface Implants placed with and without augmentation Smoking was statistically significantly correlated with lower implant survival rate $P < .013$ 69.6% of patients with failures had a history of periodontitis

FS = former smokers; HS = heavy smoker; LS = light smoker; MS = moderate smoker; TPS = titanium plasma sprayed; AE = acid etched; HA = hydroxyapatite; OR = odds ratio; RR = relative risk; HR = hazard ratio; CI = confidence interval; NR = not reported; SQ = smoking cessation protocol; mo = months; y = years.
*Statistically significant difference between smokers and nonsmokers as reported by authors.
When the authors did not report success and/or survival rates, they were calculated from the data available in the original papers.
Odds ratios, where presented, were obtained from the original paper or from the systematic review by Strietzel et al[110] if indicated (b).
a Study included in systematic review by Hinode et al.[43]
b Study included in systematic review by Strietzel et al.[110]
c Study included in systematic review by Klokkevold and Han.[3]

reported cumulative survival rates following life table analysis. Some studies reported implant survival from the time of implant placement, whereas others reported from the time of loading. Therefore, some studies distinguished between early and late implant loss, while others reported on overall implant loss.

Success Data. The majority of studies did not report success rate as an outcome variable. In those studies reporting implant success, success criteria varied, and included absence of exposure of cover screw during the healing phase, absence of a biologic complication, and probing depth and/or marginal bone loss thresholds.

Peri-implant Marginal Bone Loss. Marginal bone loss was recorded in most studies from the time of insertion of the prosthesis. However, Karoussis et al measured from 1 year after loading.[27] There were also variations in radiographic reference points due to the differences in implant designs. Few studies reported the use of standardized radiographs.

Occurrence of Peri-implant Disease. Only seven studies reported on the occurrence of peri-implantitis and/or peri-implant mucositis, and definitions were inconsistent among studies.

Confounding Factors. Relatively few studies documented or accounted for confounding factors in their analysis of the effect of smoking. Factors including diabetes and a history of periodontitis were infrequently reported. Patient-related analyses accounting for patient dependence and thereby excluding cumulative effects of individual risk factors were performed only in some studies.

Maintenance Care. The frequency of supportive periodontal therapy and the maintenance regimen was infrequently reported among studies.

Implant Characteristics. The type of implant surface and configuration used was not always reported. The majority of studies included implants with turned or moderately rough surfaces. Some studies included hydroxyapatite-coated implants and implants with a very rough surface. One study used a ceramic implant.[47]

Procedures for Implant Placement. In the studies reviewed there was a wide variation between and within studies in implant placement procedures with respect to the anatomical position of the implant, submerged or nonsubmerged placement, placement in regenerated bone, use of simultaneous bone augmentation procedures, implant placement in conjunction with sinus elevation, immediate implant placement, flapless implant placement, and immediate implant loading. This makes direct comparisons between the studies difficult, as the placement protocols may represent significant confounding factors.

Main Findings of Systematic Reviews

Strietzel et al (2007). In this systematic review, any patient who smoked was classified as a smoker.[44] Meta-analyses combining results of 29 studies were performed. The meta-analyses showed a significantly increased risk of implant failure among smokers both for implant-related (odds ratio 2.25, 95% CI: 1.96 to 2.59) and patient-related (odds ratio 2.64, 95% CI: 1.70 to 4.09) data compared to nonsmokers. Smokers receiving implants with accompanying bone augmentation procedures also had an increased risk of implant failure (odds ratio 3.61, 95% CI: 2.26 to 5.77) compared to nonsmokers. The systematic review showed a significantly increased risk of biologic complications (peri-implantitis) in smokers. The authors concluded that smoking is a significant risk factor for adverse implant outcomes.

Klokkevold and Han (2007). This systematic review identified 19 articles with implant outcome data, and concluded that smoking adversely affects implant survival and success.[3]

Implant Survival. Fourteen studies included implant survival data. A meta-analysis found the pooled estimate for implant survival in smokers was 0.897 (95% CI: 0.87 to 0.924), or 89.7%, at the last reported visit. The pooled estimate for implant survival in nonsmokers was 0.9333 (95% CI: 0.91 to 0.956), or 93.3%, at the last reported visit. The pooled estimate of the difference in implant survival between smokers and nonsmokers was 0.0268 (95% CI: 0.011 to 0.0426), or 2.68% better survival for nonsmokers. This difference was statistically significant.

Implant Success. Seven studies with implant success data were included. The pooled estimate for implant success in smokers was 0.77 (95% CI: 0.661 to 0.879), or 77.0%, at the last reported visit. The pooled estimate for implant success in nonsmokers was 0.91 (95% CI: 0.866 to 0.954), or 91%, at the last reported visit. The pooled estimate of the difference in implant success rates between smokers and nonsmokers was 0.1128 (95% CI: 0.0341 to 0.1915), or 11.28% better success for nonsmokers ($P = .005$).

Bone Quality. In this systematic review, further analyses were performed to investigate the effect of bone quality on the survival and success of implants in smokers compared to nonsmokers. The review found 7.43% better implant survival for nonsmokers than for smokers with implants placed in soft bone (described as loose trabecular bone by the authors). Nine studies reported on implant survival data in all bone types. Analyses showed 2.01% better implant survival for nonsmokers compared to smokers ($P = .0093$). The authors concluded that the effect of smoking on implant survival seems more pronounced in soft bone. Five studies reported implant

Table 4 Clinical Studies Evaluating Smoking as a Risk Indicator for Peri-implantitis and Soft Tissue Complications

Study (first author and year of publication)	Design	No. of subjects/ No. implants	Implant surface	Follow-up	Findings
Haas (1996)[92]	Retrosp	Smokers 107 (366 implants) Nonsmokers 314 (1,000 implants)	TPS Turned	Mean 22 mo	In the maxilla smokers had statistically significantly greater BOP, probing depths, peri-implant mucosal inflammation, bone loss $P < .01$ No statistically significant difference between smokers and nonsmokers in the mandible
McDermott (2006)[127]	Retrosp Cohort	677 subjects (results based on 677 implants) 10.3% of patients were smokers	TPS HA-coated Uncoated	Up to 8 y (median 13.1 mo)	Multivariate analysis for inflammatory complications (including peri-implantitis) showed smoking was statistically significant Hazard ratio: 3.26 (95% CI: 1.7 to 6.10) 69 of 677 implants had inflammatory complications
Karoussis (2003)[11]	Prosp	Smokers 28 Nonsmokers 84	TPS	10 y	No statistically significant difference between smokers and nonsmokers in biologic complications S: 17.86% NS: 6.02%
Gruica (2004)[76]	Retrosp	Smokers 53 Nonsmokers 127	TPS	≥ 8 y	Statistically significantly greater risk for smokers to develop peri-implantitis, draining sinus, suppuration, and bone loss
Roos-Jansåker (2006)[29]	Retrosp	218 total 57 smokers 81 former smokers 80 never smokers N implants = 999	Turned	9–14 y	Smoking was statistically significantly associated with: Peri-implant mucositis OR 2.8 (95% CI: 1.2 to 6.2) Bone level OR 10 (95% CI: 4.1 to 26) Peri-implantitis OR 4.6 (95% CI: 1.1 to 19)
Laine (2006)[73]	Retrosp	Smokers 78 Nonsmokers 42 N implants = 365	Turned	≥ 2 y	Former smokers and current smokers were considered smokers Majority of patients had lost teeth due to periodontitis Peri-implantitis defined as bone loss ≥ 3 threads, BOP/pus Smoking represented a statistically significant risk factor for peri-implantitis OR 3.6 (95% CI: 1.5 to 8.8) $P = .004$
Weyant (1994)[128]	Retrosp	598 patients Partially dentate 42% Number of smokers not reported 2,098 implants (15 different types of cylinder implants)	HA-coated and Uncoated	4 y	Statistically significantly more soft tissue complications in smokers Soft tissue complications: 11.9% of smokers 6.8% of nonsmokers Bivariate analysis OR 1.8 for smoking

TPS = titanium plasma sprayed; HA = hydroxyapatite; Retrosp = retrospective; Prosp = prospective; mo = months; y = years; OR = odds ratio; CI = confidence interval.

Table 5 Clinical Studies Evaluating Smoking as a Risk Indicator for Peri-implant Bone Loss

Study (first author and year of publication)	Design	No. of subjects/ No. implants	Implant surface	Follow-up	Findings
Haas (1996)[92]	Retrosp	107 smokers (1,366 implants) 314 nonsmokers (1,000 implants)	TPS, Turned	22 mo	Statistically significantly more bone loss in smokers (maxilla) compared with nonsmokers $P < .01$ Bone loss mean ± SD— S: mesial 4 ± 2.45 mm NS: mesial 1.52 ± 1.35 mm S: distal 3.9 ± 2.43 mm NS: distal 1.76 ± 1.46 mm
Lindquist (1996)[129]	Prosp	47 patients (273 implants)	Turned	15 y	Statistically significantly greater bone loss in smokers
Lindquist (1997)[71]	Prosp	21 smokers 24 nonsmokers 266 implants	Turned	10 y	At 10 years 3 implants failed – survival 99% Statistically significantly greater bone loss in smokers Dose effect relationship between cigarette exposure and bone loss
Carlsson (2000)[130]	Prosp	21 smokers 23 nonsmokers	Turned	15 y	Edentulous patients Smokers lost statistically significantly more peri-implant bone in the mandible
Feloutzis (2003)[75]	Retrosp	14 heavy smokers (20 cigarettes/day) 14 moderate smokers (5–19 cigarettes/day) 23 former smokers (> 5 years) 39 nonsmokers	TPS	5.6 y	Statistically significantly more bone loss in heavy smokers compared to nonsmokers $P < .02$ Median bone loss NS: 0.18 mm Median bone loss HS: 1.98 mm
Ortorp (2004)[120] Same cohort as Ortorp (2002)[118]	Prosp	43 smokers 83 nonsmokers	Turned	5 y	No statistically significant differences in bone levels between smokers and nonsmokers $P > .05$
Karoussis (2004)[27]	Prosp	89 patients (179 implants)	TPS	10 y	Smokers (most smoked more than 10 cigarettes per day) Multiple linear regression analysis: Statistically significantly greater bone loss in smokers $P < .0001$
Penarrocha (2004)[131]	Retrosp	16 smokers (47 implants) 26 nonsmokers (61 implants)	SLA	1 y	Statistically significantly more bone loss in smokers than nonsmokers $P < .05$
Wennström (2004)[82]	Prosp	13 smokers 32 nonsmokers	Tioblast	5 y	Multiple regression analysis: Statistically significantly more bone loss in smokers $P < .05$
Galindo-Moreno (2005)[132]	Prosp	63 smokers 122 nonsmokers	Turned, HA, TPS	3 y	Bivariate analysis: Statistically significantly more bone loss in smokers $P = .0165$ Mean bone loss S: 1.36 ± 0.04 mm Mean bone loss NS: 1.25 ± 0.02 mm
Nitzan (2005)[133]	Retrosp	59 smokers (271 implants) 102 nonsmokers (375 implants)	NR	1–7 y (mean 3.8 y)	A higher incidence of marginal bone loss in smokers that was more pronounced in the maxilla Nonsmokers had a higher radiographic success rate than smokers: 97.8% versus 97.1%; $P < .001$ In the maxilla, heavy smokers had the greatest bone loss (0.1897 ± 0.1825 mm), followed by moderate smokers (0.1223 ± 0.156 mm), and nonsmokers (0.046 ± 0.070 mm); $P < .001$
Schwartz-Arad (2005)[134]	Retrosp	8 smokers (50 implants) 53 nonsmokers (277 implants)	NR	37.9 mo	Statistically significantly more bone loss in smokers; $P < .0001$ Bone loss was increased in 56% of smokers compared to 23.8% of nonsmokers

Table 5 continued Clinical Studies Evaluating Smoking as a Risk Indicator for Peri-implant Bone Loss

Study (first author and year of publication)	Design	No. of subjects/ No. implants	Implant surface	Follow-up	Findings
Aalam (2005)[135]	Retrosp	16 smokers 58 nonsmokers	AE, Turned, Oxidized	2 y	Smokers (smoked more than 10 cigarettes per day) No statistically significant difference in bone loss between smokers and nonsmokers
DeLuca (2006)[136] Same cohort as DeLuca (2006)[69]	Retrosp	146 nonsmokers 54 smokers 96 positive smoking history 108 never smoked	Turned	20 y	No statistically significant difference between smokers and nonsmokers in the first year of loading. A positive smoking history was a significant factor for bone loss in subsequent years; $P < .048$ Positive smoking history: 0.073 ± 0.263 mm bone loss Nonsmokers: 0.041 ± 0.124 mm bone loss
Roos-Jansåker (2006)[29]	Retrosp	57 smokers 81 former smokers 80 never smokers 999 implants	Turned	9–14 y	Smoking was statistically significantly associated with bone loss OR 10 (95% CI: 4.1 to 26) $P < .001$
Herzberg (2006)[137]	Retrosp	21 smokers 39 nonsmokers 212 implants	Turned	6–56.5 mo (mean 21.7 mo)	Sinus graft and simultaneous or delayed implant placement Smoking had a statistically significant effect on bone loss; $P < .01$ S: 0.24 mm/year NS: 0.09 mm/year
Norton (2006)[138]	Retrosp	7 smokers 47 nonsmokers 173 implants	Tioblast	21–91 mo (mean 3 y)	Sinus grafts included No statistically significant difference in mean marginal bone loss between smokers (0.84 mm) and nonsmokers (0.5 mm)
Watzak (2006)[139]	Retrosp	9 smokers 22 nonsmokers 124 implants	Turned Anodized	Mean 33 mo	Turned, anodized surface Smoker defined as smoking > 10 cigarettes per day Statistically significantly more bone loss in smokers Smokers: 1.46 ± 0.16 mm Nonsmokers: 1.14 ± 0.09 mm $P = .01$
Chung (2007)[140]	Retrosp	7 smokers 62 nonsmokers 339 implants	Turned, AE, TPS	3–24 y (mean 8.1 y)	Statistically significantly more bone loss in smokers, $P < 0.05$ Smokers: 0.32 mm Nonsmokers: 0.12 mm Annual bone loss was 2.7 times greater in smokers
Tandlich (2007)[141]	Retrosp	17 smokers 65 nonsmokers/former smokers 265 implants	Rough (not specified)	≥ 30 mo	Logistic regression analysis Smoking was a statistically significant predictor of bone loss OR 1.95 (95% CI: 0.05 to 1.29) $P = .04$
Sanna (2007)[68]	Prosp	13 smokers 17 nonsmokers	Oxidized	Up to 5 y (mean 2.2 y)	Flapless placement/immediately loaded Smokers defined as smoking > 10 cigarettes per day Mean marginal bone loss— Smokers: 2.6 ± 1.6 mm Nonsmokers: 1.2 ± 0.8 mm No statistical analysis
Fransson (2008)[142]	Retrosp	40 smokers 42 nonsmokers 482 implants	Turned	9–14 y	Patients with progressive bone loss at one or more implants Progressive bone loss Logistic regression analysis: OR smoking 2.2 (95%CI: 1.5 to 3.3) $P = .0002$

Odds ratios, where presented, were obtained from the original paper.
AE = acid etched; TPS = titanium plasma sprayed; Retrosp = retrospective; Prosp = prospective; OR = odds ratio; CI = confidence interval; y = years; mo = months.

success data for both smokers and nonsmokers when implants were placed in all bone types. Analyses showed 11.76% better implant success for nonsmokers ($P = .019$).

Hinode et al (2006). In this systematic review, 19 studies were combined in a meta-analysis, and the strength of the relationship between smoking and implant failure was assessed by odds ratios.[43] Implant failure was defined as loss of the implant or progressive bone loss exceeding 50% of the implant length. Meta-analysis showed an increased risk (odds ratio 2.17, 95% CI: 1.67 to 2.83) for implant failure in smokers compared to nonsmokers. In this review, studies were separated according to the length of follow-up, with mean observation periods of less than 1 year (10 studies), more than 1 year but less than 5 years (16 studies), and greater than 5 years (3 studies).

Bain et al 2002. This meta-analysis examined the effect of smoking on implant outcomes.[48] Clinical studies that monitored the performance of two implant surfaces—a turned surface and an acid-etched surface—were included. Nine prospective studies were included, with a total of 2,614 implants with a turned surface and 2,274 implants with an acid-etched surface. For the turned-surface implants, the 3-year cumulative success rate (CSR) for the 2,117 implants in the nonsmoking group was 92.8%. The corresponding CSR for the 492 implants in the smoking group was 93.5%. The 3-year CSR for the 1,877 acid-etched surface implants in the nonsmoking group was 98.4%. For the 397 implants in the smoking group, the CSR was 98.7%. No statistically significant difference was observed between smoking and nonsmoking patients.

Influence of Smoking on Early Implant Survival

Early failure rates, prior to loading, were evaluated by De Bruyn and Collaert, who reported early implant failure of 9% in smokers versus 1% in nonsmokers.[49] Analyzing the data on a patient basis, 31% of smokers experienced implant loss in this early healing period, compared to 4% of nonsmokers. The difference was statistically significant. Similarly, Gorman et al reported a higher early implant failure rate of 6.5% for smokers versus 3.31% for nonsmokers.[50] Twenty-two percent of smokers had implant failures, compared to 9% of nonsmokers. Van Steenberghe et al also reported significantly more early failures in smokers compared to nonsmokers.[51] Noguerol et al reported that early implant failure (before loading) was significantly associated with smoking habits.[52] Multivariate analysis found a significant effect of smoking > 20 cigarettes per day (odds ratio 2.5, 95% CI: 1.3 to 4.79).

In a retrospective study of 6,946 turned surface implants placed in 2004 patients, a significant difference in early implant failure between heavy smokers (> 20 cigarettes per day) and nonsmokers was found.[53] In a cross-sectional analysis, Alsaadi et al investigated potential factors associated with early implant failure.[54] Implants with an oxidized surface were placed in 283 patients and followed up to abutment connection. The overall failure rate was low (1.9%). The authors reported that due to the low failure rate, statistical analysis of risk factors was difficult. However, a tendency for more failures to occur in smokers than nonsmokers was reported. Data from a large prospective study showed no influence of smoking on early implant failure (placement to uncovering), but found more failures in smokers in the time between uncovering of the implant and before insertion of the prosthesis.[55]

In contrast, Wallace et al found no statistically significant effect of smoking in the early healing phases following implant placement.[56] Similarly, Kumar et al[57] and Sverzut et al[58] found no statistically significant difference in early failure rates between smokers and nonsmokers. Kronström et al evaluated variables associated with early implant failure.[59] Forty patients with early implant failure and 40 patients matched for age and gender with successful osseointegrated titanium implants were studied. The authors found that antibody avidity to *Tanerella forsythia* and antibody titre to *Staphylococcus aureus* were associated with early implant loss, while smoking was not a significant factor.

Effect of Smoking on Implants Placed Following Sinus Floor Elevation and Augmentation

Seven studies reported on implant outcomes in smokers and nonsmokers following sinus floor elevation and grafting.[45,60–65] Six of these studies reported a higher failure rate for implants in smokers. In contrast, one study reported no statistically significant difference in failure rate between smokers and nonsmokers for implants placed simultaneously with sinus grafts.[65] Overall, implant survival in smokers ranged from 26.09% to 94.1% in the studies reviewed.

Effect of Smoking on Outcomes Following Immediate Implant Placement

Schwartz-Arad et al evaluated the effect of smoking in patients who received immediate (288 implants) and delayed (671 implants) implant placement.[66] More complications were reported in smokers than nonsmokers, regardless of the time of implant placement. A higher incidence of complications was found among smokers who received immediate implants ($P < .05$) compared with smokers who received delayed implants.

Wagenberg and Froum (2006) evaluated the effect of smoking following immediate implant placement.[14] Survival rates were 94.4% for smokers and 96.3% for nonsmokers following 6 years of function. There was no statistically significant difference in implant survival between smokers and nonsmokers.

Effect of Smoking on Outcomes Following Immediate Implant Loading

Implant outcomes in 45 patients who were rehabilitated following an immediate loading protocol in the mandible were evaluated following 1 year of loading.[67] Implant failures occurred in 2 of 13 smokers and 4 of 32 nonsmokers. There was no statistically significant difference in implant survival between smokers and nonsmokers.

In a study evaluating flapless implant placement and immediate loading, lower implant survival and more marginal bone loss were reported in smokers (defined as > 10 cigarettes per day) compared to nonsmokers.[68]

Dose Effect of Cigarette Smoking

While there was inconsistency in the definition of a smoker between studies, a number of authors attempted to evaluate the dose effect of cigarette smoking. Schwartz-Arad et al divided the smoking patients into two subgroups according to the number of cigarettes smoked per day (mild smoker ≤ 10/day; heavy smoker > 10/day) and the duration of smoking (mild smoker ≤ 10 years; heavy smoker > 10 years).[66] Both groups of smokers were found to have significantly more complications than nonsmokers. The number of complications increased as the number of smoking years increased. In this study all complications, including exposure of a cover screw during early healing, were recorded.

DeLuca et al found a relationship between the number of cigarettes smoked and early implant failure. Failure rates of 3.51%, 4.82%, and 5.56% were found for individuals who smoked ≤ 5 cigarettes per day, 6 to 14 cigarettes per day, and ≥ 15 cigarettes per day, respectively.[69] A positive smoking history (individuals who had > 25 pack years smoking history) was a significant factor for late implant failure (odds ratio 2.01, $P = .035$). Similarly, Alsaadi et al reported a greater incidence (7.05%) of early implant failures in heavy smokers (> 20 cigarettes per day) compared to patients who smoked 10 to 20 cigarettes per day (5.31%) and those who smoked < 10 cigarettes per day (4.85%).[53]

Sanchez-Perez et al also stratified smokers according to the number of cigarettes smoked per day (never smoked or had quit at least 10 years prior, light smoker < 10 cigarettes per day, moderate smoker 10 to 20 cigarettes per day, heavy smoker > 20 cigarettes per day).[70] Cigarette smoking involved a 15.8% risk of implant failure, with an odds ratio of 13.1. Light smokers or moderate smokers had a 10.1% relative risk of implant loss, whereas heavy smokers increased this risk to 30.8%.[70] Lindquist et al reported a dose-effect relationship between tobacco use and peri-implant marginal bone loss over a 10-year period.[71]

Mundt et al considered the duration of smoking in the analysis of long-term implant survival.[72] Current smokers had a 15% implant failure rate, compared to 9.6% for former smokers and 3.6% for nonsmokers. The number of years of smoking was statistically significantly associated with an increased risk of implant failures. Long-term smoking significantly increased the hazard ratio of implant failure from 1.5 for patients who had smoked for < 10 years to 5.36 for patients who had smoked for > 40 years.[72]

Influence of Interaction Between Smoking and Genetic Factors on Implant Outcome

A number of studies have investigated the effect of smoking on implant outcome in patients with specific interleukin (IL-1) polymorphisms.[73–76] A retrospective study investigated the relationship between IL-1 gene polymorphisms and peri-implant bone loss and peri-implant mucosal inflammation in both smokers and nonsmokers.[75] Of the 90 Caucasian patients, 31.1% were IL-1 genotype positive. Patients were stratified according to smoking history. There were 14 heavy smokers (20 cigarettes per day), 14 moderate smokers (5 to 19 cigarettes per day), 23 former smokers (smoking cessation > 5 years), and 39 nonsmokers. Significant differences in marginal bone loss between heavy smokers and nonsmokers were found for the IL-1 genotype-positive group but not for the IL-1 genotype-negative group. The authors suggested that there is a synergistic effect of smoking and the carriage of the IL-1 gene polymorphism resulting in an increased risk for peri-implant bone loss.

Gruica et al also investigated the impact of the IL-1 genotype and smoking status on peri-implant tissues in a retrospective study of 292 implants which had been in function for at least 8 years. Late biologic complications were observed around 51 implants in 34 patients, while 241 implants had survived without any biologic complications. An association between heavy smokers with a positive IL-1 genotype and peri-implantitis was observed.[76] Jansson et al also found a statistically significant synergistic effect of IL-1 genotype and smoking, and reported an increased risk of early implant failure.[74]

In a study examining the influence of the IL-1 receptor antagonist genotype, Laine et al found a statistically significant association of this genotype with peri-

implantitis.[73] In the multivariate analysis, this study also reported a statistically significant association between smoking and peri-implantitis (odds ratio 3.6, 95% CI: 1.5 to 8.8; $P = .004$), where smokers were classified as individuals who were current or former smokers.

Effect of Smoking on the Outcomes of Peri-implantitis Treatment

In a 5-year follow-up study of patients treated for advanced peri-implantitis, cigarette smoking was found to have a negative effect on treatment outcome. Six of the seven implants that failed due to persistent peri-implantitis were in smokers.[77]

Effect of a Smoking Cessation Protocol on Implant Outcomes

There is one study evaluating the effect of a smoking cessation protocol on implant outcomes.[78] Bain reported that smokers had 1.69 times higher incidence of early implant failures compared to patients who had never smoked or who had stopped smoking at least 1 week prior to and 8 weeks following implant surgery.[78]

RESULTS: SMOKING COMBINED WITH A HISTORY OF TREATED PERIODONTITIS

A number of studies have evaluated the effect of smoking in patients who have a history of treated periodontitis.[20,42,74,75,79–83] Hazard ratios for implant failure of 3.1,[83] 2.6,[20] and 2.2[42] have been reported in smokers with a history of treated periodontitis. In patients with a history of treated periodontitis, Jansson et al reported that smoking resulted in statistically significantly higher early implant failure rates in smokers compared to nonsmokers.[74]

Feloutzis et al reported statistically significantly greater bone loss in patients with a history of treated chronic periodontitis who smoked more than 20 cigarettes per day compared to those who didn't smoke or who were former smokers.[75] Similarly, Wennström et al found that patients with a history of treated periodontitis who were smokers had more bone loss than similar nonsmokers.[82] Malo et al reported a 1-year mean bone loss of 1.0 ± 1.0 mm at implants placed in immediate function in 81 patients with a history of treated periodontitis.[81] In the same study, 45 patients with a history of treated periodontitis who smoked had a mean bone loss of 1.2 ± 0.9 mm.

Machtei et al[80] found no statistically significant difference in implant failure between smokers and nonsmokers who received dental implants for immediate fixed restorations and had a history of treated periodontitis. Machtei et al[79] evaluated implants placed in previously failed sites in patients with a history of treated periodontitis and found no statistically significant difference between smokers and nonsmokers.

Main Findings of Cohort Studies with Subgroups of Smokers and Nonsmokers (Table 3)

1. Of the 59 studies reporting on implant survival, the majority reported a statistically significantly higher survival rate for implants placed in nonsmokers compared with smokers. Only 17 studies reported no significant difference between smokers and nonsmokers.[11,14,17,54,58,59,65,74,79,80,84–90]
2. The majority of studies showed implant survival rates in smokers of 80% to 96%.
3. Implant survival rates in smokers ranged from 61.54% to 100% in nonaugmented bone without sinus elevation.
4. Odds ratios for implant failure in smokers ranged from 2.03 to 6.89.
5. Six of seven studies showed that cigarette smoking is detrimental to the success and survival of implants placed in grafted maxillary sinuses.
6. In smokers, the implant success rates ranged from 43% to 98.3%.
7. Six cohort studies reported a dose effect of cigarette smoking.
8. There are limited data on the survival and success rates of implants in former smokers.
9. There is conflicting evidence that smoking adversely affects initial osseointegration as measured by early implant failures.

Main Findings of Cohort Studies Evaluating Risk of Peri-implantitis (Table 4)

1. Of the six studies reporting on the occurrence of peri-implantitis, five reported a statistically significantly higher risk for smokers compared to nonsmokers.[29,73,76,91,92] Reported odds ratios ranged from 3.6 to 4.6.
2. Studies reporting on the occurrence of peri-implantitis had a follow-up ranging from 1 to 14 years.

Main Findings of Cohort Studies Evaluating Risk of Marginal Bone Loss (Table 5)

1. Of the 22 studies reporting on marginal supporting bone loss, 18 reported a statistically significantly greater risk of bone loss over time in patients who smoked.
2. Odds ratios for progressive bone loss ranged from 1.95 to 10 in smokers.
3. Studies reporting on marginal bone loss had a follow-up time ranging from 1 to 24 years.

DISCUSSION AND CONCLUSIONS

Our current understanding from the literature is that there are similarities between the etiology and pathogenesis of periodontitis and peri-implantitis (Heitz-Mayfield and Lang 2009, in preparation). Therefore, it is perhaps not surprising that many of the studies identified in this review report lower implant survival and/or success rates in individuals with a history of treated periodontitis compared to individuals without a history of periodontitis. While implant placement in patients with a history of treated periodontitis is not contraindicated, with the majority of studies reporting implant survival > 90% over a period of 3 to 16 years, there is an increased risk of peri-implantitis (reported odds ratios 3.1 to 4.7).

The same putative pathogens associated with periodontitis have been identified in high numbers and proportions in peri-implantitis sites.[93–95] Microbial colonization following implant placement has been shown to occur within a short period of time, and the composition of the microbiota within the peri-implant sulcus is similar to that found at neighboring teeth in partially dentate patients.[40,96,97] This underlines the importance of successful treatment of periodontitis prior to implant placement and individualized maintenance care following implant treatment. The definition of successful periodontal treatment and the influence of the periodontal status of the dentition at the time of implant placement need to be addressed in future research.

Smoking is a risk factor for general health and oral health. Smoking has a long-term chronic effect on many aspects of the inflammatory and immune systems. The deleterious effects of smoking include impaired wound healing, reduced collagen production, impaired fibroblast function, reduced peripheral circulation, and compromised function of neutrophils and macrophages.[98] The biologic processes involved in osseointegration and maintenance of peri-implant bone levels are likely affected by tobacco smoking, providing an explanation for the lower implant survival and success in smokers.

While cigarette smoking is not an absolute contraindication for implant placement, with the majority of studies reporting implant survival in the range of 80% to 96%, smokers should be informed that there is an increased risk of implant loss and peri-implantitis (reported odds ratios for peri-implantitis 3.6 to 4.6). Future studies are required to assess the effect of dose and duration of cigarette smoking on implant outcomes.

The link between smoking and periodontitis is well established. Smokers have a greater risk for progression of periodontitis.[99] As patients who have a history of periodontitis may also be smokers, multivariate analyses are required to appropriately assess these risk factors. Further research is required to determine the risk of cigarette smoking and a history of periodontitis combined.

REFERENCES

1. Al-Zahrani MS. Implant therapy in aggressive periodontitis patients: A systematic review and clinical implications. Quintessence Int 2008;39:211–215.
2. Ong CT, Ivanovski S, Needleman IG, et al. Systematic review of implant outcomes in treated periodontitis subjects. J Clin Periodontol 2008;35:438–462.
3. Klokkevold PR, Han TJ. How do smoking, diabetes, and periodontitis affect outcomes of implant treatment? Int J Oral Maxillofac Implants 2007;22(suppl):173–202.
4. Quirynen M, Abarca M, Van Assche N, Nevins M, van Steenberghe D. Impact of supportive periodontal therapy and implant surface roughness on implant outcome in patients with a history of periodontitis. J Clin Periodontol 2007;34:805–815.
5. Karoussis IK, Kotsovilis S, Fourmousis I. A comprehensive and critical review of dental implant prognosis in periodontally compromised partially edentulous patients. Clin Oral Implants Res 2007;6:669–679.
6. Schou S, Holmstrup P, Worthington HV, Esposito M. Outcome of implant therapy in patients with previous tooth loss due to periodontitis. Clin Oral Implants Res 2006;17(suppl 2):104–123.
7. Schou S. Implant treatment in periodontitis-susceptible patients: A systematic review. J Oral Rehabil 2008;35(suppl 1): 9–22.
8. Van der Weijden GA, van Bemmel KM, Renvert S. Implant therapy in partially edentulous, periodontally compromised patients: A review. J Clin Periodontol 2005;32:506–511.
9. Hardt CR, Gröndahl K, Lekholm U, Wennström JL. Outcome of implant therapy in relation to experienced loss of periodontal bone support: A retrospective 5-year study. Clin Oral Implants Res 2002;13:488–494.
10. Cune MS, de Putter C. A single dimension statistical evaluation of predictors in implant-overdenture treatment. J Clin Periodontol 1996;23:425–431.
11. Karoussis IK, Salvi GE, Heitz-Mayfield LJ, Brägger U, Hammerle CH, Lang NP. Long-term implant prognosis in patients with and without a history of chronic periodontitis: A 10-year prospective cohort study of the ITI Dental Implant System. Clin Oral Implants Res 2003;14:329–339.
12. Polizzi G, Grunder U, Goene R, et al. Immediate and delayed implant placement into extraction sockets: A 5-year report. Clin Implant Dent Relat Res 2000;2:93–99.
13. Rosenquist B, Grenthe B. Immediate placement of implants into extraction sockets: Implant survival. Int J Oral Maxillofac Implants 1996;11:205–209.
14. Wagenberg B, Froum SJ. A retrospective study of 1925 consecutively placed immediate implants from 1988 to 2004. Int J Oral Maxillofac Implants 2006;21:71–80.
15. Armitage GC. Development of a classification system for periodontal diseases and conditions. Northwest Dent 2000;79:31–35.
16. Nevins M, Langer B. The successful use of osseointegrated implants for the treatment of the recalcitrant periodontal patient. J Periodontol 1995;66:150–157.
17. Roos-Jansåker AM, 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.
18. Ferreira SD, Silva GLM, Cortelli JR, Costa JE, Costa FO. Prevalence and risk variables for peri-implant disease in Brazilian subjects. J Clin Periodontol 2006;33:929–935.
19. Evian CI, Emling R, Rosenberg ES, et al. Retrospective analysis of implant survival and the influence of periodontal disease and immediate placement on long-term results. Int J Oral Maxillofac Implants 2004;19:393–398.

20. Baelum V, Ellegaard B. Implant survival in periodontally compromised patients. J Periodontol 2004;75:1404–1412.
21. Ellegaard B, Baelum V, Karring T. Implant therapy in periodontally compromised patients. Clin Oral Implants Res 1997;8:180–188.
22. Albrektsson T, Zarb G, Worthington P, Eriksson AR. The long-term efficacy of currently used dental implants: A review and proposed criteria of success. Int J Oral Maxillofac Implants 1986;1:11–25.
23. Buser D, Weber HP, Lang NP. Tissue integration of non-submerged implants. 1 year results of a prospective study with 100 ITI hollow-cylinder and hollow-screw implants. Clin Oral Implants Res 1990;1:33–40.
24. Spiekermann H, Jansen VK, Richter EJ. A 10-year follow-up study of IMZ and TPS implants in the edentulous mandible using bar-retained overdentures. Int J Oral Maxillofac Implants 1995;10:231–243.
25. Rosenberg ES, Cho SC, Elian N, Jalbout ZN, Froum S, Evian CI. A comparison of characteristics of implant failure and survival in periodontally compromised and periodontally healthy patients: A clinical report. Int J Oral Maxillofac Implants 2004;19:873–879.
26. Watson CJ, Tinsley D, Ogden AR, Russell JL, Mulay S, Davison EM. A 3 to 4 year study of single tooth hydroxylapatite coated endosseous dental implants. Br Dent J 1999;187:90–94.
27. Karoussis IK, Müller S, Salvi GE, Heitz-Mayfield LJ, Brägger U, Lang NP. Association between periodontal and peri-implant conditions: A 10-year prospective study. Clin Oral Implants Res 2004;15:1–7.
28. Roos-Jansaker A-M, Lindahl C, Renvert H, Renvert S. Nine- to fourteen-year follow-up of implant treatment. Part II: Presence of peri-implant lesions. J Clin Periodontol 2006;33:290–295.
29. Roos-Jansaker 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.
30. Hanggi MP, Hanggi DC, Schoolfield JD, Meyer J, Cochran DL, Hermann JS. Crestal bone changes around titanium implants. Part I: A retrospective radiographic evaluation in humans comparing two non-submerged implant designs with different machined collar lengths. J Periodontol 2005;76:791–802.
31. Brocard D, Barthet P, Baysse E, et al. A multicenter report on 1,022 consecutively placed ITI implants: A 7-year longitudinal study. Int J Oral Maxillofac Implants 2000;15:691–700.
32. Mengel R, Flores-de-Jacoby L. Implants in patients treated for generalized aggressive and chronic periodontitis: A 3-year prospective longitudinal study. J Periodontol 2005;76:534–543.
33. Mengel R, Flores-de-Jacoby L. Implants in regenerated bone in patients treated for generalized aggressive periodontitis: A prospective longitudinal study. Int J Periodontics Rest Dent 2005;25:331–341.
34. Mengel R, Schroder T, Flores-de-Jacoby L. Osseointegrated implants in patients treated for generalized chronic periodontitis and generalized aggressive periodontitis: 3- and 5-year results of a prospective long-term study. J Periodontol 2001;72:977–989.
35. Leonhardt A, Gröndahl K, Bergström C, Lekholm U. Long-term follow-up of osseointegrated titanium implants using clinical, radiographic and microbiological parameters. Clin Oral Implants Res 2002;13:127–132.
36. Malmstrom HS, Fritz ME, Timmins DP, van Dyke TE. Osseointegrated implant treatment of a patient with rapidly progressive periodontitis: A case report. J Periodontol 1990;61:300–304.
37. Yalcin S, Yalcin F, Gunay Y, Bellaz B, Onal S, Firatli E. Treatment of aggressive periodontitis by osseointegrated dental implants. A case report. J Periodontol 2001;72:411–416.
38. Hofer D, Hammerle CH, Lang NP. Comprehensive treatment concept in a young adult patient with severe periodontal disease: A case report. Quintessence Int 2002;33:567–578.
39. Wu AY-J, Chee W. Implant-supported reconstruction in a patient with generalized aggressive periodontitis. J Periodontol 2007;78:777–782.
40. De Boever AL, De Boever JA. Early colonization of non-submerged dental implants in patients with a history of advanced aggressive periodontitis. Clin Oral Impl Res 2006;17:8–17.
41. Mengel R, Kreuzer G, Lehmann KM, Flores-de-Jacoby L. A telescopic crown concept for the restoration of partially edentulous patients with aggressive generalized periodontitis: A 3-year prospective longitudinal study. Int J Periodontics Restorative Dent 2007;27:231–239.
42. Ellegaard B, Baelum V, Kolsen-Petersen J. Non-grafted sinus implants in periodontally compromised patients: A time-to-event analysis. Clin Oral Implants Res 2006;17:156–164.
43. Hinode D, Tanabe S, Yokoyama M, Fujisawa K, Yamauchi E, Miyamoto Y. Influence of smoking on osseointegrated implant failure: A meta-analysis. Clin Oral Implants Res 2006;17:473–478.
44. Strietzel FP, Reichart PA, Kale A, Kulkarni M, Wegner B, Kuchler I. Smoking interferes with the prognosis of dental implant treatment: A systematic review and meta-analysis. J Clin Periodontol 2007;34:523–544.
45. Kan JY, Rungcharassaeng K, Kim J, Lozada JL, Goodacre CJ. Factors affecting the survival of implants placed in grafted maxillary sinuses: A clinical report. J Prosthet Dent 2002;87:485–489.
46. Bain CA, Moy PK. The association between the failure of dental implants and cigarette smoking. Int J Oral Maxillofac Implants 1993;8:609–615.
47. Berge TI, Gronningsaeter AG. Survival of single crystal sapphire implants supporting mandibular overdentures. Clin Oral Implants Res 2000;11:154–162.
48. Bain CA, Weng D, Meltzer A, Kohles SS, Stach RM. A meta-analysis evaluating the risk for implant failure in patients who smoke. Compend Contin Educ Dent 2002;23:695–699. 702, 704 passim; quiz 708.
49. De Bruyn H, Collaert B. The effect of smoking on early implant failure. Clin Oral Implants Res 1994;5:260–264.
50. Gorman LM, Lambert PM, Morris HF, Ochi S, Winkler S. The effect of smoking on implant survival at second-stage surgery: DICRG Interim Report No. 5. Dental Implant Clinical Research Group. Implant Dent 1994;3:165–168.
51. van Steenberghe D, Jacobs R, Desnyder M, Maffei G, Quirynen M. The relative impact of local and endogenous patient-related factors on implant failure up to the abutment stage. Clin Oral Implants Res 2002;13:617–622.
52. Noguerol B, Munoz R, Mesa F, de Dios Luna J, O'Valle F. Early implant failure. Prognostic capacity of Periotest: Retrospective study of a large sample. Clin Oral Implants Res 2006;17:459–464.
53. Alsaadi G, Quirynen M, Komarek A, van Steenberghe D. Impact of local and systemic factors on the incidence of oral implant failures, up to abutment connection. J Clin Periodontol 2007;34:610–617.
54. Alsaadi G, Quirynen M, Michiles K, Teughels W, Komarek A, van Steenberghe D. Impact of local and systemic factors on the incidence of failures up to abutment connection with modified surface oral implants. J Clin Periodontol 2008;35:51–57.
55. Lambert PM, Morris HF, Ochi S. The influence of smoking on 3-year clinical success of osseointegrated dental implants. Ann Periodontol 2000;5:79–89.
56. Wallace RH. The relationship between cigarette smoking and dental implant failure. Eur J Prosthodont Restor Dent 2000;8:103–106.
57. Kumar A, Jaffin RA, 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.
58. Sverzut AT, Stabile GA, de Moraes M, Mazzonetto R, Moreira RW. The influence of tobacco on early dental implant failure. J Oral Maxillofac Surg 2008;66:1004–1009.
59. Kronström M, Svenson B, Hellman M, Persson GR. Early implant failures in patients treated with Brånemark System titanium dental implants: A retrospective study. Int J Oral Maxillofac Implants 2001;16:201–207.
60. Keller EE, Tolman DE, Eckert S. Surgical-prosthodontic reconstruction of advanced maxillary bone compromise with autogenous onlay block bone grafts and osseointegrated endosseous implants: A 12-year study of 32 consecutive patients. Int J Oral Maxillofac Implants 1999;14:197–209.
61. Geurs NC, Wang IC, Shulman LB, Jeffcoat MK. Retrospective radiographic analysis of sinus graft and implant placement procedures from the Academy of Osseointegration Consensus Conference on Sinus Grafts. Int J Periodontics Restorative Dent 2001;21:517–523.
62. Widmark G, Andersson B, Carlsson GE, Lindvall AM, Ivanoff CJ. Rehabilitation of patients with severely resorbed maxillae by means of implants with or without bone grafts: A 3- to 5-year follow-up clinical report. Int J Oral Maxillofac Implants 2001;16:73–79.

63. Mayfield LJ, Skoglund A, Hising P, Lang NP, Attström R. Evaluation following functional loading of titanium fixtures placed in ridges augmented by deproteinized bone mineral. A human case study. Clin Oral Implants Res 2001;12:508–514.
64. Olson JW, Shernoff AF, Tarlow JL, Colwell JA, Scheetz JP, Bingham SF. Dental endosseous implant assessments in a type 2 diabetic population: A prospective study. Int J Oral Maxillofac Implants 2000;15:811–818.
65. Peleg M, Garg AK, Mazor Z. Healing in smokers versus nonsmokers: Survival rates for sinus floor augmentation with simultaneous implant placement. Int J Oral Maxillofac Implants 2006;21:551–559.
66. Schwartz-Arad D, Samet N, Mamlider A. Smoking and complications of endosseous dental implants. J Periodontol 2002;73:153–157.
67. van Steenberghe D, Molly L, Jacobs R, Vandekerckhove B, Quirynen M, Naert I. The immediate rehabilitation by means of a ready-made final fixed prosthesis in the edentulous mandible: A 1-year follow-up study on 50 consecutive patients. Clin Oral Implants Res 2004;15:360–365.
68. Sanna AM, Molly L, van Steenberghe D. Immediately loaded CAD-CAM manufactured fixed complete dentures using flapless implant placement procedures: A cohort study of consecutive patients. J Prosthet Dent 2007;97:331–339.
69. DeLuca S, Habsha E, Zarb GA. The effect of smoking on osseointegrated dental implants. Part I: implant survival. Int J Prosthodont 2006;19:491–498.
70. Sanchez-Perez A, Moya-Villaescusa MJ, Caffesse RG. Tobacco as a risk factor for survival of dental implants. J Periodontol 2007;78:351–359.
71. Lindquist LW, Carlsson GE, Jemt T. Association between marginal bone loss around osseointegrated mandibular implants and smoking habits: A 10-year follow-up study. J Dent Res 1997;76:1667–1674.
72. Mundt T, Mack F, Schwahn C, Biffar R. Private practice results of screw-type tapered implants: Survival and evaluation of risk factors. Int J Oral Maxillofac Implants 2006;21:607–614.
73. Laine ML, Leonhardt A, Roos-Jansåker A-M, et al. IL-1RN gene polymorphism is associated with peri-implantitis. Clin Oral Implants Res 2006;17:380–385.
74. Jansson H, Hamberg K, De Bruyn H, Bratthall G. Clinical consequences of IL-1 genotype on early implant failures in patients under periodontal maintenance. Clin Implant Dent Relat Res 2005;7:51–59.
75. Feloutzis A, Lang NP, Tonetti MS, 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.
76. Gruica B, Wang HY, 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.
77. Leonhardt A, Dahlen G, Renvert S. Five-year clinical, microbiological, and radiological outcome following treatment of peri-implantitis in man. J Periodontol 2003;74:1415–1422.
78. Bain CA. Smoking and implant failure—benefits of a smoking cessation protocol. Int J Oral Maxillofac Implants 1996;11:756–759.
79. Machtei EE, Mahler D, Oettinger-Barak O, Zuabi O, Horwitz J. Dental implants placed in previously failed sites: Survival rate and factors affecting the outcome. Clin Oral Implants Res 2008;19:259–264.
80. Machtei EE, Frankenthal S, Blumenfeld I, Gutmacher Z, Horwitz J. Dental implants for immediate fixed restoration of partially edentulous patients: A 1-year prospective pilot clinical trial in periodontally susceptible patients. J Periodontol 2007;78:1188–1194.
81. Malo P, de Araujo Nobre M, Rangert B. Implants placed in immediate function in periodontally compromised sites: A five-year retrospective and one-year prospective study. J Prosthet Dent 2007;97:S86–S95.
82. Wennström J, Zurdo J, Karlsson S, Ekestubbe A, Gröndahl K, Lindhe J. Bone level change at implant-supported fixed partial dentures with and without cantilever extension after 5 years in function. J Clin Periodontol 2004;31:1077–1083.
83. Chuang SK, Wei LJ, Douglass CW, Dodson TB. Risk factors for dental implant failure: A strategy for the analysis of clustered failure-time observations. J Dent Res 2002;81:572–577.
84. Wang IC, Reddy MS, Geurs NC, Jeffcoat MK. Risk factors in dental implant failure. J Long Term Eff Med Implants 1996;6:103–117.
85. De Bruyn H, Collaert B, Linden U, Johansson C, Albrektsson T. Clinical outcome of Screw Vent implants. A 7-year prospective follow-up study. Clin Oral Implants Res 1999;10:139–148.
86. Grunder U, Gaberthuel T, Boitel N, et al. Evaluating the clinical performance of the Osseotite implant: Defining prosthetic predictability. Compend Contin Educ Dent 1999;20:628–633, 636, 638–640.
87. Penarrocha M, Guarinos J, Sanchis JM, Balaguer J. A retrospective study (1994–1999) of 441 ITI(r) implants in 114 patients followed-up during an average of 2.3 years. Med Oral 2002;7:144–155.
88. Beschnidt SM, Muche R, Krausse A, Strub JR. Implant survival and success rates in partially edentulous patients—Part I 9 [in German]. Schweiz Monatsschr Zahnmed 2003;113:396–403.
89. Lemmerman KJ, Lemmerman NE. Osseointegrated dental implants in private practice: A long-term case series study. J Periodontol 2005;76:310–319.
90. Alsaadi G, Quirynen M, Komarek A, van Steenberghe D. Impact of local and systemic factors on the incidence of late oral implant loss. Clin Oral Implants Res 2008;19:670–676.
91. McDermott NE, Chuang SK, Woo VV, Dodson TB. Complications of dental implants: Identification, frequency, and associated risk factors. Int J Oral Maxillofac Implants 2003;18:848–855.
92. Haas R, Haimbock W, Mailath G, Watzek G. The relationship of smoking on peri-implant tissue: A retrospective study. J Prosthet Dent 1996;76:592–596.
93. Mombelli A, Van Oosten MAC, Schürch E, Lang NP. The microbiota associated with successful or failing osseointegrated titanium implants. Oral Microbiol Immunol 1987;2:145–151.
94. Leonhardt A, Renvert S, Dahlen G. Microbial findings at failing implants. Clin Oral Implants Res 1999;10:339–345.
95. Persson GR, Salvi GE, Heitz-Mayfield LJA, Lang NP. Antimicrobial therapy using a local drug delivery system (Arestin) in the treatment of peri-implantitis. I: Microbiological outcomes. Clin Oral Implants Res 2006;17:386–393.
96. Furst MM, Salvi GE, Lang NP, Persson GR. Bacterial colonization immediately after installation on oral titanium implants. Clin Oral Implants Res 2007;18:501–508.
97. Quirynen M, Vogels R, Pauwels M, et al. Initial subgingival colonization of 'pristine' pockets. J Dent Res 2005;84:340–344.
98. Palmer RM, Wilson RF, Hasan AS, Scott DA. Mechanisms of action of environmental factors–tobacco smoking. J Clin Periodontol 2005;32(suppl 6):180–195.
99. Heitz-Mayfield LJ. Disease progression: Identification of high-risk groups and individuals for periodontitis. J Clin Periodontol 2005;32(suppl 6):196–209.
100. Cordaro L, Ercoli C, Rossini C, Torsello F, Feng C. Retrospective evaluation of complete-arch fixed partial dentures connecting teeth and implant abutments in patients with normal and reduced periodontal support. J Prosthet Dent 2005;94:313–320.
101. Ericsson I, Lekholm U, Brånemark PI, Lindhe J, Glantz PO, Nyman S. A clinical evaluation of fixed-bridge restorations supported by the combination of teeth and osseointegrated titanium implants. J Clin Periodontol 1986;13:307–312.
102. Ellegaard B, Kolsen-Petersen J, Baelum V. Implant therapy involving maxillary sinus lift in periodontally compromised patients. Clin Oral Implants Res 1997;8:305–315.
103. Schwartz-Arad D, Chaushu G. Immediate implant placement: A procedure without incisions. J Periodontol 1998;69:743–750.
104. Daelemans P, Hermans M, Godet F, Malevez C. Autologous bone graft to augment the maxillary sinus in conjunction with immediate endosseous implants: A retrospective study up to 5 years. Int J Periodontics Restorative Dent 1997;17:27–39.
105. Sbordone L, Barone A, Ciaglia RN, Ramaglia L, Iacono VJ. Longitudinal study of dental implants in a periodontally compromised population. J Periodontol 1999;70:1322–1329.
106. Buchmann R, Khoury F, Faust C, Lange DE. Peri-implant conditions in periodontally compromised patients following maxillary sinus augmentation. A long-term post-therapy trial. Clin Oral Implants Res 1999;10:103–110.

107. Yi SW, Ericsson I, Kim CK, Carlsson GE, Nilner K. Implant-supported fixed prostheses for the rehabilitation of periodontally compromised dentitions: A 3-year prospective clinical study. Clin Implant Dent Relat Res 2001;3:125–134.
108. Leonhardt A, Adolfsson B, Lekholm U, Wikstrom M, Dahlen G. A longitudinal microbiological study on osseointegrated titanium implants in partially edentulous patients. Clin Oral Implants Res 1993;4:113–120.
109. Wennström JL, Ekestubbe A, Gröndahl K, Karlsson S, Lindhe J. Oral rehabilitation with implant-supported fixed partial dentures in periodontitis-susceptible subjects. A 5-year prospective study. J Clin Periodontol 2004;31:713–724.
110. Strietzel FP, Reichart PA. Oral rehabilitation using Camlog screw-cylinder implants with a particle-blasted and acid-etched microstructured surface. Results from a prospective study with special consideration of short implants. Clin Oral Implants Res 2007;18:591–600.
111. Minsk L, Polson AM, Weisgold A, et al. Outcome failures of endosseous implants from a clinical training center. Compend Contin Educ Dent 1996;17:848–850, 852–854, 856 passim.
112. Watson CJ, Ogden AR, Tinsley D, Russell JL, Davison EM. A 3- to 6-year study of overdentures supported by hydroxyapatite-coated endosseous dental implants. Int J Prosthodont 1998;11:610–619.
113. Minsk L, Polson AM. Dental implant outcomes in postmenopausal women undergoing hormone replacement. Compend Contin Educ Dent 1998;19:859–862, 864; quiz 866.
114. Jones JD, Lupori J, Van Sickels JE, Gardner W. A 5-year comparison of hydroxyapatite-coated titanium plasma-sprayed and titanium plasma-sprayed cylinder dental implants. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1999;87:649–652.
115. Wilson TG Jr, Nunn M. The relationship between the interleukin-1 periodontal genotype and implant loss. Initial data. J Periodontol 1999;70:724–729.
116. Schwartz-Arad D, Grossman Y, Chaushu G. The clinical effectiveness of implants placed immediately into fresh extraction sites of molar teeth. J Periodontol 2000;71:839–844.
117. Eckert SE, Meraw SJ, Weaver AL, Lohse CM. Early experience with wide-platform Mk II implants. Part I: Implant survival. Part II: Evaluation of risk factors involving implant survival. Int J Oral Maxillofac Implants 2001;16:208–216.
118. Ortorp A, Jemt T. Clinical experience of CNC-milled titanium frameworks supported by implants in the edentulous jaw: A 3-year interim report. Clin Implant Dent Relat Res 2002;4:104–109.
119. Chuang SK, Tian L, Wei LJ, Dodson TB. Predicting dental implant survival by use of the marginal approach of the semi-parametric survival methods for clustered observations. J Dent Res 2002;81:851–855.
120. Ortorp A, Jemt T. Clinical experiences of computer numeric control-milled titanium frameworks supported by implants in the edentulous jaw: A 5-year prospective study. Clin Implant Dent Relat Res 2004;6:199–209.
121. Kourtis SG, Sotiriadou S, Voliotis S, Challas A. Private practice results of dental implants. Part I: Survival and evaluation of risk factors—Part II: Surgical and prosthetic complications. Implant Dent 2004;13:373–385.
122. Moheng P, Feryn J-M. Clinical and biologic factors related to oral implant failure: A 2-year follow-up study. Implant Dent 2005;14: 281–288.
123. Moy PK, Medina D, Shetty V, Aghaloo TL. Dental implant failure rates and associated risk factors. Int J Oral Maxillofac Implants 2005;20: 569–577.
124. Doyle SL, Hodges JS, Pesun IJ, Baisden MK, Bowles WR. Factors affecting outcomes for single-tooth implants and endodontic restorations. J Endod 2007;33:399–402.
125. Aykent F, Inan O, Ozyesil AG, Alptekin NO. A 1- to 12-year clinical evaluation of 106 endosseous implants supporting fixed and removable prostheses. Int J Periodontics Restorative Dent 2007;27:358–367.
126. Anitua E, Orive G, Aguirre JJ, Ardanza B, Andia I. 5-year clinical experience with BTI dental implants: Risk factors for implant failure. J Clin Periodontol 2008;8:724–732.
127. McDermott NE, Chuang S-K, Woo VV, Dodson TB. Maxillary sinus augmentation as a risk factor for implant failure. Int J Oral Maxillofac Implants 2006;21:366–374.
128. Weyant RJ. Characteristics associated with the loss and peri-implant tissue health of endosseous dental implants. Int J Oral Maxillofac Implants 1994;9:95–102.
129. Lindquist LW, Carlsson GE, Jemt T. A prospective 15-year follow-up study of mandibular fixed prostheses supported by osseointegrated implants. Clinical results and marginal bone loss. Clin Oral Implants Res 1996;7:329–336.
130. Carlsson GE, Lindquist LW, Jemt T. Long-term marginal periimplant bone loss in edentulous patients. Int J Prosthodont 2000;13:295–302.
131. Penarrocha M, Palomar M, Sanchis JM, Guarinos J, Balaguer J. Radiologic study of marginal bone loss around 108 dental implants and its relationship to smoking, implant location, and morphology. Int J Oral Maxillofac Implants 2004;19:861–867.
132. Galindo-Moreno P, Fauri M, Avila-Ortiz G, Fernandez-Barbero JE, Cabrera-Leon A, Sanchez-Fernandez E. Influence of alcohol and tobacco habits on peri-implant marginal bone loss: A prospective study. Clin Oral Implants Res 2005;16:579–586.
133. Nitzan D, Mamlider A, Levin L, Schwartz-Arad D. Impact of smoking on marginal bone loss. Int J Oral Maxillofac Implants 2005;20:605–609.
134. Schwartz-Arad D, Mardinger O, Levin L, Kozlovsky A, Hirshberg A. Marginal bone loss pattern around hydroxyapatite-coated versus commercially pure titanium implants after up to 12 years of follow-up. Int J Oral Maxillofac Implants 2005;20:238–244.
135. Aalam AA, Nowzari H. Clinical evaluation of dental implants with surfaces roughened by anodic oxidation, dual acid-etched implants, and machined implants. Int J Oral Maxillofac Implants 2005;20:793–798.
136. DeLuca S, Zarb G. The effect of smoking on osseointegrated dental implants. Part II: Peri-implant bone loss. Int J Prosthodont 2006;19:560–566.
137. Herzberg R, Dolev E, Schwartz-Arad D. Implant marginal bone loss in maxillary sinus grafts. Int J Oral Maxillofac Implants 2006;21:103–110.
138. Norton MR. Multiple single-tooth implant restorations in the posterior jaws: Maintenance of marginal bone levels with reference to the implant-abutment microgap. Int J Oral Maxillofac Implants 2006;21:777–784.
139. Watzak G, Zechner W, Busenlechner D, Arnhart C, Gruber R, Watzek G. Radiological and clinical follow-up of machined- and anodized-surface implants after mean functional loading for 33 months. Clin Oral Implants Res 2006;17:651–657.
140. Chung DM, Oh T-J, Lee J, Misch CE, Wang H-L. Factors affecting late implant bone loss: A retrospective analysis. Int J Oral Maxillofac Implants 2007;22:117–126.
141. Tandlich M, Ekstein J, Reisman P, Shapira L. Removable prostheses may enhance marginal bone loss around dental implants: A long-term retrospective analysis. J Periodontol 2007;78:2253–2259.
142. Fransson C, Wennstrom J, Berglundh T. Clinical characteristics at implants with a history of progressive bone loss. Clin Oral Implants Res 2008;19:142–147.