

# Effectiveness of Implant Therapy Analyzed in a Swedish Population: Prevalence of Peri-implantitis

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## Abstract

Peri-implantitis is an inflammatory disease affecting soft and hard tissues surrounding dental implants. As the global number of individuals that undergo restorative therapy through dental implants increases, peri-implantitis is considered as a major and growing problem in dentistry. A randomly selected sample of 588 patients who all had received implant-supported therapy 9 y earlier was clinically and radiographically examined. Prevalence of peri-implantitis was assessed and risk indicators were identified by multilevel regression analysis. Forty-five percent of all patients presented with peri-implantitis (bleeding on probing/suppuration and bone loss >0.5 mm). Moderate/severe peri-implantitis (bleeding on probing/suppuration and bone loss >2 mm) was diagnosed in 14.5%. Patients with periodontitis and with  $\geq 4$  implants, as well as implants of certain brands and prosthetic therapy delivered by general practitioners, exhibited higher odds ratios for moderate/severe peri-implantitis. Similarly, higher odds ratios were identified for implants installed in the mandible and with crown restoration margins positioned  $\leq 1.5$  mm from the crestal bone at baseline. It is suggested that peri-implantitis is a common condition and that several patient- and implant-related factors influence the risk for moderate/severe peri-implantitis (ClinicalTrials.gov NCT01825772).

**Keywords:** endosseous dental implantation, implant-supported dental prosthesis, adverse effects, multivariate analysis, biological complication, treatment outcome

## Introduction

Peri-implantitis is a pathologic condition occurring in patients with dental implants and is characterized by inflammation in peri-implant tissues and loss of supporting bone (Lindhe and Meyle 2008; Lang and Berglundh 2011). Untreated disease leads to loss of implants. Peri-implantitis lesions are considerably larger and present with more aggressive features than lesions in periodontitis around teeth (Carcuac and Berglundh 2014). Treatment of the condition can be inconvenient and uncomfortable for the patient and is demanding in terms of resources and economy. Thus, as the global number of individuals that undergo restorative therapy through dental implants increases, peri-implantitis is considered to be a major and growing problem in dentistry.

Previous reports on the prevalence of peri-implantitis are associated with several inadequacies. Tomasi and Derks (2012) reported in a review that many studies provided only implant-based data without considering the number of affected patients. In addition, analyses were performed on so-called convenience samples of limited size, and such patient groups may not be representative of the target population (Sanz and Chapple 2012). Reviews in the field have recognized 7 case definitions for peri-implantitis based on the amount of bone loss occurring over time (Mombelli et al. 2012; Tomasi and Derks 2012; Derks and Tomasi 2015). The inconsistencies in case definitions in the literature also reflected the large variation in disease

prevalence. Derks and Tomasi (2015) reported in a systematic review a weighted mean prevalence of peri-implantitis of 22% (95% confidence interval, 14% to 30%) with a positive relationship between prevalence and time in function of the implants.

Recommendations for research on the occurrence of peri-implantitis have underlined the importance of randomly selected patient samples of sufficient size and adequate assessments of crestal bone changes in radiographs (Sanz and Chapple 2012; Jepsen et al. 2015). As the adult population in Sweden is provided with federal financial support for dental care that includes implant-supported restorative therapy, the register administered by the Swedish Social Insurance Agency (Försäkringskassan) provides access to data on patients representing effectiveness in implant dentistry (Derks, Håkansson, Wennström, Tomasi, et al. 2015). Hence, in this study, we

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A supplemental appendix to this article is published electronically only at <http://jdr.sagepub.com/supplemental>.

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**Table 1.** Patient-related Information: Tested for Association with Moderate/Severe Peri-implantitis.

	Patients <sup>a</sup> (n = 588), %
Sex	
Female	55.1
Male	44.9
Smoker (2003) <sup>b</sup>	
Yes	20.6
No	79.4
Diabetes diagnosis (2003)	
Yes	2.4
No	43.2
Missing data	54.4
Myocardial infarction diagnosis (2003)	
Yes	0.9
No	43.7
Missing data	55.4
Stroke diagnosis (2003)	
Yes	0.7
No	43.9
Missing data	55.4
Periodontitis diagnosis (2003)	
Yes	10.2
No	36.2
Missing data	53.6
Periodontitis status (9-y examination)	
Healthy	59.9
Periodontitis	24.0
Edentulous	16.1
Surgical therapy	
General practitioner	21.1
Specialist	78.9
Prosthetic therapy	
General practitioner	74.0
Specialist	26.0
Maintenance therapy	
General practitioner	78.9
Specialist	16.3
Missing data	4.8
Frequency of recall visits	
Regular (annual)	80.6
Irregular	17.2
Missing data	2.2
Baseline radiograph present	
Yes	72.6 (n = 427)
No	27.4 (n = 161)

<sup>a</sup>Mean  $\pm$  SD: age (2003), 62.3  $\pm$  9.3 y; implants per patient, 4.0  $\pm$  2.8.

<sup>b</sup>Confirmed at the 9-y examination.

report on the prevalence, extent, and severity of peri-implantitis in a large and randomly selected patient sample identified from the data register of the Swedish Social Insurance Agency.

## Materials and Methods

The research protocol was approved by the regional Ethical Committee, Gothenburg, Sweden (Dnr 290-10) and registered at ClinicalTrials.gov (NCT01825772). STROBE guidelines were followed (von Elm et al. 2008). The study consisted of a combination of a retrospective analysis of patient files and a cross-sectional clinical and radiologic examination of patients about 9 y after the completion of implant-supported restorative therapy.

## Patient Sample

The patient sample was previously described (Derks, Håkansson, Wennström, Klinge, et al. 2015; Derks, Håkansson, Wennström, Tomasi, et al. 2015). Briefly, 4,716 subjects in 2 age groups (45 to 54 y and 65 to 74 y in 2003) who all had received implant-supported restorations in 2003 were randomly selected from the national data register of the Swedish Social Insurance Agency. Subjects were identified by name and a unique social security number. All were asked for consent to access their dental records, including available radiographs. About 9 y after therapy, 900 of 2,765 consenting subjects were randomly selected and invited to a free-of-cost examination at a conveniently located dental clinic in Sweden. A total of 596 subjects attended the 9-y examination (mean, 8.9  $\pm$  0.8 y). Reasons for nonattendance are outlined in the Appendix (Appendix Table 1). Attending patients and nonattending patients did not differ significantly in terms of age, sex, systemic disease, and therapy-related parameters. In total, the 596 patients were initially provided with 2,367 implants. Seventy-two implants were lost, and an additional 18 were excluded for various reasons (Appendix Table 2). The analysis included 588 subjects and 2,277 implants (Tables 1 and 2).

## Analysis of Patient Files

Information regarding patients, including treatment and treatment outcomes, was extracted from the records and entered into a database (Derks, Håkansson, Wennström, Tomasi, et al. 2015). Clinicians involved in the surgical, restorative, and maintenance therapy were categorized with regard to private or public dental clinical setting and general practitioner or specialist. Implants were grouped regarding length, diameter, and installation protocols. Bone augmentation procedures, including ridge and sinus augmentation, were recorded. Implants were also grouped according to jaw and position. Furthermore, implants were categorized according to brand (i.e., by provider and implant system). Three implant brands—Astra Tech (AT; Dentsply IH AB, Mölndal, Sweden), Nobel Biocare (NB; Zurich, Switzerland), and Straumann (S; Basel, Switzerland)—represented 91% of the 2,277 implants. Among AT implants, 96.6% had a TiOblast surface; 98.3% of the NB implants had a TiUnite surface; and all S implants had an SLA surface. Predominant brands among the remaining implants were Biomet 3i (2.5% of all implants), Lifecore (2.2%), CrescoTi (1.7%), and XiVE (1.3%). In addition, categorization included type of prosthetic retention and design of suprastructure. The frequency of recall visits following the completion of the restorative therapy was assessed.

## Clinical Examination at 9 y

Examinations were carried out by specialists in periodontics, predominantly by 2 investigators (J.D. and J.H.). All subjects were categorized as periodontally healthy, as periodontitis patients, or as edentulous. Periodontitis assessments were based on the presence of  $\geq 2$  teeth exhibiting bleeding on probing (BoP)/suppuration and attachment loss  $\geq 2$  mm as well as

pocket probing depth (PPD)  $\geq 6$  mm. The following variables were recorded at the mesial, buccal, distal, and lingual aspects of each implant:

*PPD (mm)*: measured with a manual periodontal probe (PCP15; Hu-Friedy, Chicago, IL, USA)

*BoP*: within 15 s following pocket probing

*Suppuration*: within 15 s following pocket probing

*Accessibility for self-performed oral hygiene measures*: assessed for every implant as yes/no

### Radiologic Examination at 9 y and Assessment of Bone Loss

Radiographs of implants were obtained. A total of 1,778 (78.1%) implants were examined by intraoral radiographs and 499 (21.9%) by panoramic. Radiographs stored in the patient files were analyzed together with the radiographs sampled at the 9-y examination. Analogue images were digitized with a digital camera (Coolpix 5700; Nikon, Chiyoda, Japan). The position of the marginal bone was assessed by the use of a software program (ImageJ 1.48a; Wayne Rasband, National Institutes of Health, Bethesda, MD, USA). The interthread pitch distance reported by the manufacturer or the length of the implant was used for the calibration of the “apical-coronal” measurements in each radiograph. Landmarks were chosen for the different implant systems, and the distance to the crestal bone was measured at the mesial and distal aspects of the implant. The largest value was recorded.

Bone loss was calculated by comparing measurements made in the 9-y and baseline radiographs. Radiographs obtained up to 12 mo after prosthesis connection were used as baseline. In the absence of 12-mo radiographs, documentation up to 24 mo after prosthesis connection was used. In addition, the distance from the prosthetic margin to the crestal bone was measured in the baseline radiograph (Appendix Table 3).

In cases with no available baseline radiographs, marginal bone levels located  $>2$  mm apical of a reference landmark were registered at the 9-y examination (Appendix).

Assessments in radiographs were performed by 2 of the investigators (J.D. and D.S.). Six months after the initial evaluation, radiographs of 50 patients were remeasured. The double measurements of marginal bone levels revealed for the interexaminer comparison a mean measurement error of  $0.40 \pm 0.36$  mm. For the intraexaminer agreement, the corresponding value was  $0.34 \pm 0.37$  mm. Radiographs of implants presenting with bone loss in the range from 1.0 to 2.5 mm ( $n = 251$ ) were also remeasured (mean error:  $0.25 \pm 0.33$  mm). Averages of the 2 readings were used for further analysis.

### Case Definitions for Peri-implant Mucositis and Peri-implantitis

The following conditions were identified:

*Healthy peri-implant tissues*: absence of BoP/suppuration

**Table 2.** Implant-related Information: Tested for Association with Moderate/Severe Peri-implantitis.

	Implants ( $n = 2,277$ ), %
Jaw of treatment	
Maxilla	60.1
Mandible	39.9
Position	
Anterior (canine-canine)	44.6
Posterior	55.4
Installation procedure	
1 stage	49.0
2 stage	49.6
Missing data	1.4
Bone augmentation procedure	
Yes	6.3
No	79.7
Missing data	14.0
Retention of supraconstruction	
Screw retained	77.3
Cemented	17.7
Removable	0.3
Missing data	4.7
Design of supraconstruction	
Single unit	11.4
Multiunit	88.6
Implant length, mm	
$<10$	7.4
$\geq 10$	83.3
Missing data	9.3
Implant diameter, mm	
$<4$	51.5
$\geq 4$	40.8
Missing data	7.7
Implant brand	
S <sup>a</sup>	32.6
NB <sup>b</sup>	39.4
AT <sup>c</sup>	18.4
R <sup>d</sup>	9.4
Baseline radiograph present	
Yes	69.3 ( $n = 1,578$ )
No	30.7 ( $n = 699$ )

<sup>a</sup>Straumann Dental Implant System.

<sup>b</sup>Brånemark System, Replace Select.

<sup>c</sup>Astra Tech Implant System.

<sup>d</sup>Remaining implants.

*Peri-implant mucositis*: BoP/suppuration but no detectable bone loss

*Peri-implantitis*: BoP/suppuration and detectable bone loss ( $>0.5$  mm; exceeding the measurement error)

Implant sites presenting with BoP/suppuration and bone loss  $>2$  mm were considered as moderate/severe peri-implantitis.

### Extent and Severity of Peri-implantitis

Extent of moderate/severe peri-implantitis (i.e., proportion of affected implants in patients with the condition) was assessed in subjects with  $>1$  implants. Severity was expressed as the proportion of implants presenting with varying degrees of bone loss with BoP/suppuration.

**Table 3.** Prevalence of Peri-implant Health and Diseases at the 9-y Examination: Subjects/Implants with Baseline Radiographs.

	Patient Level (n = 427)		Implant Level (n = 1,578)	
	% (n)	PPD ≥6 mm, %	% (n)	PPD ≥6 mm, %
Healthy <sup>a</sup>	23.0 (98)	9.4	39.3 (620)	3.3
Peri-implant mucositis <sup>b</sup>	32.0 (137)	26.3	35.1 (554)	16.3
Peri-implantitis: bone loss, mm <sup>c</sup>				
>0.5	45.0 (192)	43.2	24.9 (393)	34.4
>1	26.9 (115)	53.0	14.7 (232)	42.4
>2	14.5 (62)	71.0	8.0 (126)	58.7
>3	10.1 (43)	81.4	4.3 (68)	69.1
>4	5.9 (25)	92.0	2.3 (36)	80.6
Not accessible for probing	0 (0)		0.7 (11)	

PPD, probing pocket depth.

<sup>a</sup>No bleeding on probing/suppuration.

<sup>b</sup>Bleeding on probing/suppuration but no bone loss >0.5 mm.

<sup>c</sup>Bleeding on probing/suppuration and bone loss.

## Data Analysis

Continuous variables were recorded as mean ± standard deviation. Prevalence of peri-implant health, peri-implant mucositis, and peri-implantitis was assessed on the patient and implant levels. To evaluate variables affecting the probability for a patient to be diagnosed with moderate/severe peri-implantitis, a logistic regression analysis was performed with the subject as the unit of analysis. Similarly, the probability of moderate/severe peri-implantitis and associated factors at the implant level were analyzed. For these analyses, only implants/patients with baseline radiographs were considered. A multilevel logistic model was used to compensate for data clustering (Stata Statistical Software: Release 13; StataCorp LP, College Station, TX, USA). The hierarchical analysis included the patient at the higher level and the implant at the lower. Independent factors entered into the models were retrieved from the patient file database and the clinical examination and are outlined in Tables 1 and 2. For the factor “implant brand,” 4 groups were formed: AT implants, NB implants, S implants, and remaining implants. Brands representing <5% of all implants were collapsed into the remaining implants category to facilitate analysis. Continuous parameters were categorized prior to analyses. Mean or biologically/clinically relevant values were chosen as cutoff points.

The models were constructed to contain only significant factors ( $P < 0.05$ ), and possible interaction was explored. Odds ratios (ORs) and predicted probabilities, including 95% confidence intervals, were calculated. Parameters were estimated by Gauss-Hermite quadrature. For validation purposes, analyses were repeated with MLwiN 2.28 (Center of Multilevel Modelling, University of Bristol, Bristol, UK).

## Results

### Clinical Examination at 9 y

Due to bulky supraconstructions, the condition of the mucosa could not be assessed at 14 of the 2,277 implants. BoP/suppuration was found in 77.7% of subjects and at 60.9% of implants, while PPD ≥6 mm was noted in 31.2% of subjects and at 16.9%

of implants. Seventy-eight percent of all implants were regarded as accessible for self-performed oral hygiene measures.

### Radiologic Examination

Readable baseline radiographs were available for 427 patients and 1,578 (69.3%) implants. The mean bone loss from baseline to the 9-y examination was  $0.63 \pm 0.74$  mm on the patient level and  $0.72 \pm 1.15$  mm on the implant level. A total of 322 (20.4%) implants presented with bone loss >1 mm and 157 (9.9%) with bone loss >2 mm (Appendix Table 4).

### Prevalence of Peri-implant Mucositis and Peri-implantitis

In 98 (23.0%) of the 427 patients with baseline radiographs, no signs of peri-implant disease were detected (Table 3). In addition, 137 (32.0%) patients exhibited only peri-implant mucositis, while 192 (45.0%) presented with peri-implantitis. Moderate/severe peri-implantitis was observed in 62 (14.5%) patients.

### Extent of Peri-implantitis

Moderate/severe peri-implantitis was detected in 61 of 329 patients with >1 implants. The mean number of implants in this category of patients was  $5.9 \pm 2.6$  and the mean number of implants with moderate/severe peri-implantitis was  $2.1 \pm 1.1$ . The overall extent of implants with moderate/severe peri-implantitis was 40.1%.

### Severity of Peri-implantitis

The mean bone loss in the 393 implants presenting with peri-implantitis was  $1.84 \pm 1.52$  mm. The corresponding value for the 126 implants with moderate/severe peri-implantitis was  $3.57 \pm 1.58$  mm. The amount of bone loss at implants with moderate/severe peri-implantitis corresponded to 29.4% of the intraosseous portion of the implant (Appendix Table 5).

**Table 4.** Factors Associated with Moderate/Severe Peri-implantitis<sup>a</sup> at the 9-y Examination: Patient-level Regression Analysis (*n* = 427).

	Odds Ratio	95% Confidence Interval	P Value
Periodontal status (at 9-y examination)			
Healthy	1		
Periodontitis	4.08	1.88 to 8.86	<0.001
Edentulous	1.64	0.75 to 3.59	0.219
No. of implants placed			
<4	1		
≥4	15.09	6.17 to 36.88	<0.001
Prosthetic therapy			
Specialist	1		
General practitioner	4.27	1.76 to 10.41	0.001
Implant brand <sup>b</sup>			
S	1		
NB	3.77	1.60 to 8.87	0.002
AT	3.55	1.29 to 9.77	0.014
R	5.56	1.70 to 18.24	0.005

Outcome variable: patient with moderate/severe peri-implantitis (yes/no).

<sup>a</sup>Bleeding on probing/suppuration and bone loss >2 mm.

<sup>b</sup>Nine patients were provided with implants from >1 implant groups and thus not considered for analysis.

### Risk Indicators for Peri-implantitis

Significantly higher ORs for moderate/severe peri-implantitis were found for patients presenting with periodontitis (OR, 4.1), patients with ≥4 implants (OR, 15.1), for general practitioners as provider of prosthetic therapy (OR, 4.3), and for patients provided with certain implant brands (Table 4). Patients treated with NB (OR, 3.8), AT (OR, 3.6), as well as the remaining implants (OR, 5.6) showed significantly higher ORs for moderate/severe peri-implantitis when compared with patients treated with S implants. The predicted probability for a patient to be diagnosed with moderate/severe peri-implantitis is presented in Table 5.

The multilevel analysis confirmed the 4 patient-level variables and identified 2 additional, site-specific factors associated with moderate/severe peri-implantitis (Appendix Table 6). Higher ORs were observed for implants in the mandible (OR, 2.0) and for a distance from the prosthetic margin to crestal bone at baseline ≤1.5 mm (OR, 2.3). For the factor implant brand, a shift in magnitude of association was observed. The predicted probability for moderate/severe peri-implantitis for implants is presented in Appendix Table 7. No significant interaction between factors was observed.

### Analysis of Implants without Baseline Radiographs

The proportion of peri-implantitis among the 699 implants lacking baseline radiographs was 10.9% as based on bone levels >2 mm apical of a reference landmark together with BoP/suppuration (Appendix Table 8).

## Discussion

In the present study, the prevalence of peri-implantitis was assessed in a large and randomly selected patient sample. After 9 y, 45% of patients presented with peri-implantitis, and 14.5%

had moderate/severe forms of the condition. The average amount of bone loss that occurred at implants with moderate/severe peri-implantitis corresponded to about 30% of the initial bone support of the implant. Patients with periodontitis and with ≥4 implants, as well as implants of certain brands and prosthetic therapy performed by general practitioners, exhibited higher ORs for moderate/severe peri-implantitis. Similarly, higher ORs were identified for implants installed in the mandible and with crown restoration margins positioned ≤1.5 mm from the crestal bone at baseline. It is suggested that peri-implantitis is a common condition and that several patient- and implant-related factors influence the risk for moderate/severe peri-implantitis.

Case definition for peri-implantitis was a central target in the present investigation. The assessment of the occurrence of peri-implantitis required the detection of bone loss between baseline and the 9-y examination that exceeded the measurement error; hence, 45% of the patients exhibited ≥1 implants with bone loss >0.5 mm. As the recommendations for research on the occurrence of peri-implantitis in a consensus report (Sanz and Chapple 2012) considered a threshold of bone loss of 1.0 to 1.5 mm, the present study also addressed moderate/severe peri-implantitis using the case definition of >2 mm of bone loss in addition to the clinical finding of BoP. Moreover, as baseline assessments of bone levels in radiographs of the present study encompassed varying examination time points up to 24 mo after prosthetic therapy, the identification of cases with moderate/severe peri-implantitis was further justified.

Considering the great variation of case definitions used in previous studies on prevalence of peri-implantitis, the results obtained in the present study need to be evaluated in regard to corresponding definitions. Thus, Fransson et al. (2005) analyzed radiographs from 662 patients and reported that 27.8% of patients had ≥1 implants with bone levels at ≥3 threads of the implant (i.e., about 1.8 mm apical of the implant neck) and detectable bone loss (1 thread: 0.6 mm) between examinations

**Table 5.** Percentage Predicted Probability (95% Confidence Interval) for an Average Patient to Be Diagnosed with Moderate/Severe Peri-implantitis at the 9-y Examination (Patient Data,  $n = 427$ ).

	Implant Brand			
	S	NB	AT	R
Prosthetic therapy: Specialist				
Periodontally healthy				
<4 implants placed	0 (0 to 1)	1 (0 to 2)	1 (0 to 2)	1 (0 to 4)
≥4 implants placed	3 (1 to 7)	10 (4 to 21)	9 (3 to 21)	14 (4 to 32)
Periodontitis				
<4 implants placed	1 (0 to 3)	3 (1 to 8)	3 (1 to 8)	5 (1 to 14)
≥4 implants placed	11 (3 to 25)	30 (13 to 53)	29 (11 to 53)	38 (13 to 69)
Prosthetic therapy: General practitioner				
Periodontally healthy				
<4 implants placed	1 (0 to 2)	3 (1 to 7)	3 (1 to 7)	5 (1 to 12)
≥4 implants placed	10 (5 to 20)	30 (18 to 44)	29 (15 to 47)	39 (18 to 63)
Periodontitis				
<4 implants placed	3 (1 to 8)	11 (5 to 22)	11 (4 to 23)	16 (5 to 37)
≥4 implants placed	32 (16 to 53)	63 (45 to 78)	61 (39 to 80)	70 (43 to 90)

made at 1 y and 5 to 20 y of follow-up. Roos-Jansåker, Lindahl, et al. (2006) conducted a study on 216 patients with 9 to 14 y of follow-up, using a case definition for peri-implantitis that included bone loss  $\geq 1.8$  mm following the examination made at year 1, and they reported that 16% of patients had peri-implantitis at  $\geq 1$  implants. In a study on the prevalence of peri-implantitis in 109 patients, Koldslund et al. (2010) used case definitions with different thresholds of bone loss; thus, a low threshold of 0.4 mm bone loss resulted in a prevalence of 47%, while the use of 3 mm bone loss lead to the detection of 11%. It is evident that the 45% prevalence of peri-implantitis in the present study—based on the overall case definition for peri-implantitis with BoP and bone loss  $>0.5$  mm—is in agreement with the results presented in the studies referred to above, when corresponding case definitions are applied. The results from the appraisal of moderate/severe peri-implantitis in the present study—14.5% of patients—are also concurring data from previous studies. Koldslund et al. (2010, 2011) presented a figure of 20% using the term “overt” peri-implantitis for cases demonstrating implants with bone loss  $\geq 2$  mm, while Roos-Jansåker, Lindahl, et al. (2006) reported 16% to show occurrence of conditions corresponding to moderate/severe peri-implantitis. It should be realized, however, that follow-up periods varied among the studies referred to and the current investigation.

The percentage of affected patients decreased with an increasing amount of bone loss applied to the case definition of peri-implantitis. In addition, the average bone loss at implants with moderate/severe peri-implantitis in the present material amounted to about 30% of the initial bone support, thus underpinning the clinical significance of the condition.

The extent of moderate/severe peri-implantitis in the present study was 40.1%. Few studies have presented data on the extent of peri-implantitis. Fransson et al. (2009) and Mir-Mari et al. (2012) reported that, respectively, 41.8% and 37.2% of implants in an affected subject had peri-implantitis. Although both studies applied different case definitions than those of the

present report, their findings corroborate data presented in the current investigation.

The finding that patients with periodontitis and those provided with  $\geq 4$  implants had higher ORs for moderate/severe peri-implantitis is in agreement with previous reports (Roos-Jansåker, Renvert, et al. 2006; Koldslund et al. 2011; Rocuzzo et al. 2012; Renvert et al. 2014) and suggests that susceptibility to periodontitis confers higher risk for peri-implantitis. Smokers have commonly been associated with peri-implantitis in previous studies. While the initial bivariate analysis in the present investigation identified this group of subjects as a significant factor, the final regression model did not include smokers. Another factor with a higher OR for moderate/severe peri-implantitis involved cases where the prosthetic therapy was performed by general practitioners as opposed to specialists. The data from the present analysis, however, do not provide information on reasons for such differences regarding clinician categories. Similarly, although differences among certain implant brands regarding frequencies and ORs for moderate/severe peri-implantitis were evident, available data do not unravel brand-specific characteristics that may promote or prevent peri-implantitis. In this context, it should also be noted that there was a difference in the magnitude of associations between the results from the patient-based regression analysis and the multilevel evaluation. This discrepancy may be explained by variations in the extent of peri-implantitis among brand-specific patients. It should also be pointed out that implant brands were unevenly distributed in the present patient cohort.

In addition to the patient-associated factors, the multilevel analysis identified 2 implant-specific factors to be associated with peri-implantitis. While it is unclear why implants in the mandible presented with a higher OR than those in the maxilla, the short distance between the crown margin and the crestal bone at baseline, however, indicates that the crown restoration initially interfered with the mucosal seal around the transmucosal part of the implant and thereby promoted the onset of the disease.

## Author Contributions

J. Derks, contributed to data acquisition, analysis, and interpretation, drafted the manuscript; D. Schaller, contributed to data acquisition, critically revised the manuscript; J. Håkansson, contributed to data acquisition and interpretation, critically revised the manuscript; J.L. Wennström, contributed to conception, design, data analysis, and interpretation, critically revised the manuscript; C. Tomasi, contributed to data analysis and interpretation, critically revised the manuscript; T. Berglundh, contributed to conception, design, data analysis, and interpretation, drafted the manuscript. All authors gave final approval and agree to be accountable for all aspects of the work.

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